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## The Molecular and Crystal Structure of *N*-( $\beta$ -D-Ribofuranosyl)imidazole

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*N*-( $\beta$ -D-Ribofuranosyl)imidazole crystallizes from an ethanol-ether solution with two molecules per unit cell and space group  $P2_1$ . The unit-cell dimensions are  $a = 5.190$  (1),  $b = 7.775$  (1),  $c = 11.198$  (2) Å and  $\beta = 92.49$  (2)°. Diffractometer data with Mo  $K\alpha$  radiation ( $2\theta \leq 60^\circ$ ) at room temperature were collected, the structure solved and refined to weighted and unweighted  $R$  values of 0.04 and 0.03 respectively. The ribose ring may be described as C(3')-*endo*-C(2')-*endo* with C(3') and C(2') 0.604 and 0.055 Å from the plane defined by C(1'), O(1') and C(4'). The glycosidic torsion angle defined by O(1')-C(1')-N(1)-C(2) is  $-97.8^\circ$  and thus in the *syn* conformation. The torsion angle for the C(5')-C(4') bond is described as *gauche-trans* with  $\varphi_{OO} = +64.3$  and  $\varphi_{OC} = +180.4^\circ$ . The crystal structure is fixed by a system of three hydrogen bonds which link each molecule to six neighbouring molecules. The final difference electron-density map has significant features in the expected locations for  $\sigma$ -bonding electrons between carbon atoms and lone-pair electrons in the vicinity of the imidazole nitrogen N(3) and ribose oxygen atom O(5').

### Introduction

The anomeric effect is a well established phenomenon in carbohydrate chemistry (for a recent review see: Zefirov & Shekhtman, 1971). Comparison of crystal-structure studies of several pyranose-ring-containing carbohydrates has provided evidence for carbon-oxygen bond shortening in the region of the anomeric carbon atom C(1) (Berman, Chu & Jeffrey, 1967). When an electronegative atom is substituted at the anomeric carbon atom of a pyranose ring there is considerable stabilization of the axial anomer over that of the equatorial (Lemieux & Chü, 1958; Angyal, 1969). The reason for this stabilization is uncertain, but dipole-dipole attraction or repulsion forces may contribute to this effect. However if a positively charged group is substituted on the anomeric carbon atom, the equatorial anomer becomes the more stable conformation and this observation has been termed the reverse anomeric effect (Lemieux & Morgan, 1965). These authors report a  $1C$  chair conformation for *N*-(tetra-*O*-acetyl- $\alpha$ -D-glucopyranosyl)-4-methylpyridinium bromide rather than the more common  $C1$  chair. An X-ray crystallographic study of this compound (James, 1969) has shown that the conformation of this molecule in the crystals is the  $2.5B$  with the acetyl groups on C(2) and C(3) in a quasi-

axial orientation and the 4-methylpyridinium moiety in a quasi-equatorial position.

It is certain that this reverse anomeric effect plays an

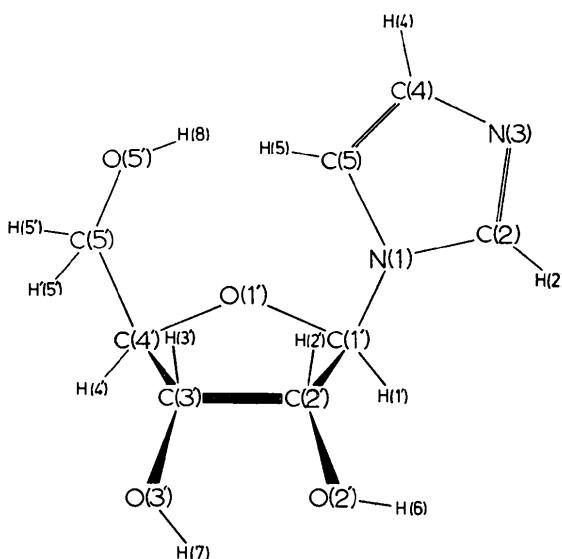


Fig. 1. Atomic numbering scheme for *N*-( $\beta$ -D-ribofuranosyl)imidazole used in this structure analysis.

important role in determining the conformation of the  $\beta$ -D-ribose moieties in the pyridine dinucleotides NAD<sup>+</sup> and NADP<sup>+</sup>. In the enzymatic reactions for which these species act as co-enzymes the electronic state of the nicotinamide aglycone changes from the positively charged species in the oxidized form to the neutral species in the reduced form. A similar situation has been observed in the several crystal-structure determinations of protonated and unprotonated cytidine derivatives (Sundaralingam & Jensen, 1965; Furberg, Petersen & Rømming, 1965; Bugg & Marsh, 1967; Subramanian & Hunt, 1970). The ribose conformation in cytidine (Furberg, Petersen & Rømming, 1965) may be described as C(3')-endo whereas in the two structures of cytidylic acid *b* (Sundaralingam & Jensen, 1965; Bugg & Marsh, 1967) in which the pyrimidine moieties are protonated at N(3) the ribose conformation is C(2')-endo. The protonated deoxycytidine cation (Subramanian & Hunt, 1970) has an intermediate conformation C(3')-endo-C(2')-exo and this may be attributed to the lack of a 2' OH group.

In order to pursue these results further we have carried out the crystal and molecular structure of *N*-( $\beta$ -D-ribofuranosyl)imidazole (hereinafter referred to as IMR) which has an imidazole ring as the aglycone. The chemical formula and the atomic numbering scheme of IMR as used in this study are shown in Fig. 1. As described in the *Experimental* and *Results* sections the data were of sufficiently good quality to depict important features in the final difference electron density map.

### Experimental

The purified compound was kindly supplied by Dr R. U. Lemieux of the Chemistry Department, University of Alberta. It was subsequently recrystallized by slow vapour diffusion of diethyl ether into an ethanolic solution. Crystals of an approximately equidimensional habit resulted from this recrystallization.

Preliminary oscillation, Weissenberg and precession diffraction photographs taken with Cu K $\alpha$  radiation showed that the crystals were monoclinic with the only

systematic absences being  $0k0=2n+1$ . An experimental density was not obtained because of a paucity of crystals. The unit-cell dimensions were determined from the  $2\theta$  values of twelve reflexions in the range  $35 < 2\theta < 46^\circ$  ( $\lambda=0.70926$  Å) using the least-squares procedure described by Busing & Levy (1967). These values and other crystal data are included in Table 1.

Table 1. *Crystal data for N-( $\beta$ -D-ribofuranosyl)-imidazole*

Molecular formula	C <sub>8</sub> H <sub>12</sub> N <sub>2</sub> O <sub>4</sub>
M.W.	200.2 Dalton
System	Monoclinic
<i>a</i>	5.190 (1) Å
<i>b</i>	7.775 (1)
<i>c</i>	11.198 (2)
$\beta$	92.49 (2) <sup>o</sup>
<i>V</i>	451.4 Å <sup>3</sup>
<i>d</i> <sub>calc</sub>	1.473 g cm <sup>-3</sup>
Crystal size	0.28 × 0.27 × 0.21 mm
$\mu$ (Mo K $\alpha$ )	1.28 cm <sup>-1</sup>
Systematic absences	0 <i>k</i> 0, <i>k</i> odd
Space group	<i>P</i> 2 <sub>1</sub>
Number of reflexions scanned	1414
Number of observed reflexions	1280 (90.7% of total)
$2\theta$ range explored	3 < $2\theta$ < 60 <sup>o</sup>
Temperature during data collection	20–24 <sup>o</sup> C

The intensity data were collected at room temperature from a single crystal of dimensions 0.28 × 0.27 × 0.21 mm using graphite monochromated Mo K $\alpha$  radiation and a Picker FACS-1 diffractometer. The reflexions were scanned in the  $\theta$ - $2\theta$  mode with a scan speed of 1<sup>o</sup> per minute and a basic peak width of 1.5<sup>o</sup>. Background counts were taken for 10 sec at either end of the  $2\theta$  scan for each reflexion. Crystal decomposition and instrument instability were monitored by measuring three reflexions, 007, 039 and 023, after every 30 reflexions of the data run. At the start and finish of the complete data collection the intensities of these monitor reflexions agreed to within 2%, indicating only minor experimental instability. The total number of independent reflexions in the range  $3 < 2\theta < 60^\circ$  was 1414, slightly more than available in

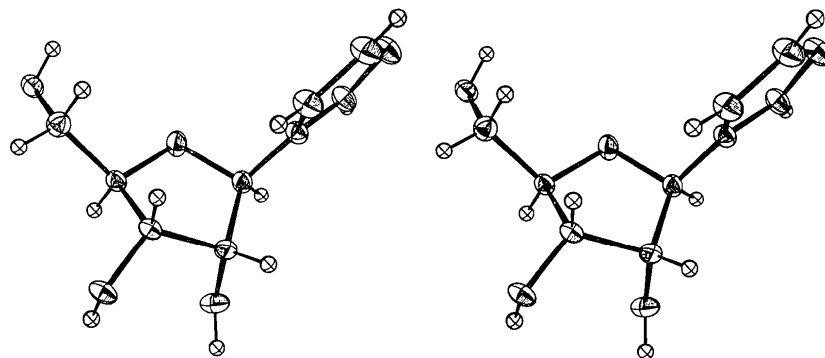


Fig. 2. Stereoscopic diagram of the molecule of IMR as determined here. The thermal ellipsoids include 30% probability and the hydrogen atoms were drawn with artificial temperature factors of 1.0 Å<sup>2</sup>. This drawing and that in Fig. 6 were done with the program ORTEP (Johnson, 1965).



bility of some positions was initially in doubt. The other non-hydrogen atom positions were obtained in two ways: (i) from a symmetry-minimum function map (Simpson, Dobrott & Lipscomb, 1965) and (ii) from a difference-Fourier map based on a partial molecular structure of eight atoms. The initial  $R$  value ( $R = \sum(|F_o| - |F_c|) / \sum |F_o|$ ) for the first 14 atom structure was 0.34. The  $y$  coordinate of atom N(1) was fixed at 0.0 in all subsequent least-squares computations. A difference Fourier map computed following two initial block-diagonal least-squares cycles on the complete molecular structure, contained reasonable peaks for 10 of the 12 hydrogen atoms; the two which did not appear on this map were hydroxyl hydrogen atoms. Six cycles of block-diagonal least squares with unit weights for all reflexions refined the non-hydrogen atomic parameters. A second difference-Fourier map clearly showed the other two hydrogen atoms and resolved the N(3) position of the imidazole ring on the basis of bond lengths C(2)-N(3) 1.34 Å compared with the C(4)-C(5) distance of 1.37 Å. Four further least-squares cycles using observational weights ( $\sqrt{w} = 2F_o/[T + (0.04 I)^2 + I^2 B]^{1/2}$ ) and refinement of all atomic positional parameters, anisotropic thermal parameters for nonhydrogen atoms and isotropic  $B$  values for the hydrogen atoms reduced the residual to 0.034.

A close examination of the data at this stage showed five reflections that were probably suffering from secondary extinction or counter paralysis. These reflections, 020, 011, 003, 110 and 102, were excluded from the data set and further least-squares cycles. Three final cycles of refinement of the 175 atomic parameters were computed using the full-matrix least-squares program *ORFLS* (Busing, Martin & Levy, 1962). These cycles were based on minimizing the quantity  $\sum w(|F_o| - k|F_c|)$  using an artificial weighting scheme  $\sqrt{w} = a/[a^2 + (F_o - b)^2]^{1/2}$ , with  $a = 2.3$  e and  $b = 3.7$  e. The following refinement parameters resulted from these computations;  $R = 0.030$ ,  $R_w\{\sum w(|F_o| - k|F_c|)^2 / \sum w|F_o|^2\}^{1/2} = 0.040$  and the goodness of fit,  $\{\sum w(|F_o|$

$-k|F_c|)^2/(m-n)\}^{1/2} = 1.11$ . From the final cycle of full-matrix least squares, all parameter shifts for the non-hydrogen atoms were less than  $\frac{1}{3}$  of the corresponding e.s.d. and those for the hydrogen atoms were all less than  $\frac{1}{2}$  of the corresponding e.s.d.

In the above calculations the form factors of Cromer & Mann (1968) were used for C, N and O; the hydrogen scattering curve was that of Stewart, Davidson & Simpson (1965). The C, N and O curves were corrected for the real part of anomalous scattering  $\Delta f'$  (Cromer & Liberman, 1969). In addition to the program *ORFLS* the block-diagonal refinement was carried out with the NRC set of programs (Ahmed, Hall, Pippy & Huber, 1966) on the IBM 360/67 computer.

The structure amplitudes ( $|F_o|$  and  $|F_c|$ )  $10 \times$  absolute scale) are given in Table 2. The final positional and thermal parameters for all the atoms are listed in Table 3. The absolute configuration of the IMR molecule has not been determined in the present study, but the atomic coordinates do conform to the configuration accepted for  $\beta$ -D-ribose.

## Results and discussion

The molecular conformation of IMR is shown in Fig. 2. The molecular geometry is given in Fig. 3 (*a*) and (*b*) which contain the bond lengths with the estimated standard deviations in parentheses and the bond angles in degrees. The average standard deviation for bond angles between non-hydrogen atoms is  $0.2^\circ$  whereas that for angles involving hydrogen atoms is  $2.0^\circ$ . All e.s.d.'s in atomic positions were determined from the diagonal elements of the inverse matrix in the last least-squares calculation.

### (i) Imidazole ring

The bond lengths and angles in the imidazole moiety agree well with the corresponding parameters from the structure determination of imidazole at  $-150^\circ\text{C}$  (Martinez-Carrera, 1966). In this latter structure the imid-

Table 3. Final atomic positional parameters and anisotropic thermal parameters with their standard deviations (in parenthesis)

The coordinates of the nonhydrogen atoms have been multiplied by  $10^5$ ; the  $U_{ij}$  by  $10^4$ . The anisotropic temperature factor is in the form  $\exp[-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^* + 2U_{23}klb^*c^* + 2U_{13}hla^*c^*)]$ .

	$x/a$	$y/b$	$z/c$	$U_{11}$	$U_{22}$	$U_{33}$	$U_{12}$	$U_{23}$	$U_{13}$
N(1)	26441 (27)	0 (0)	41179 (12)	600 (12)	597 (13)	447 (11)	25 (10)	35 (10)	-60 (9)
C(2)	37308 (34)	-5148 (33)	51769 (14)	724 (16)	885 (20)	464 (13)	122 (15)	85 (13)	-108 (11)
N(3)	24487 (36)	524 (34)	60860 (14)	968 (17)	1078 (21)	497 (13)	146 (16)	12 (13)	-64 (12)
C(4)	4206 (42)	9817 (38)	55796 (16)	969 (19)	925 (20)	648 (15)	213 (18)	-105 (16)	14 (14)
C(5)	5139 (37)	9682 (36)	43679 (15)	790 (16)	804 (18)	633 (14)	256 (16)	14 (15)	-77 (13)
C(1')	37124 (29)	-3219 (29)	29596 (13)	526 (12)	581 (15)	468 (12)	-34 (11)	81 (11)	-57 (10)
C(2')	16913 (29)	-7169 (28)	19457 (13)	529 (13)	538 (14)	483 (12)	-45 (11)	-15 (11)	-69 (10)
C(3')	14395 (27)	10229 (28)	13011 (11)	469 (11)	553 (13)	386 (10)	36 (11)	-32 (10)	-38 (9)
C(4')	41726 (28)	17396 (28)	14475 (12)	485 (13)	528 (13)	397 (11)	-1 (10)	21 (10)	-48 (10)
C(5')	42973 (32)	36732 (29)	14002 (16)	619 (16)	563 (14)	642 (14)	-22 (12)	30 (12)	-30 (12)
O(1')	50785 (24)	11733 (27)	26173 (11)	689 (11)	881 (16)	577 (11)	-313 (11)	258 (10)	-271 (8)
O(2')	28260 (27)	-19654 (26)	12231 (12)	815 (14)	582 (12)	783 (13)	74 (10)	-192 (10)	-181 (11)
O(3')	4617 (22)	9238 (27)	1102 (9)	611 (11)	758 (12)	429 (9)	148 (10)	-59 (9)	-137 (8)
O(5')	68776 (25)	42838 (26)	15329 (10)	786 (12)	779 (14)	454 (10)	-249 (11)	-6 (9)	30 (8)

Table 3 (cont.)

The hydrogen atom fractional coordinates are  $\times 10^4$ ; the  $U_{iso}$  for hydrogen atoms are  $\times 10^3$ .

	$x/a$	$y/b$	$z/c$	$U_{iso}$
H(2)	5294 (52)	-1204 (41)	5258 (23)	44 (7)
H(4)	-1015 (69)	1513 (64)	6052 (30)	81 (11)
H(5)	-552 (54)	1489 (44)	3720 (24)	46 (7)
H(1')	4883 (41)	-1272 (32)	3102 (18)	25 (5)
H(2')	79 (43)	-1141 (37)	2224 (20)	32 (6)
H(3')	325 (46)	1789 (36)	1696 (20)	32 (6)
H(4')	5289 (41)	1286 (31)	881 (18)	23 (5)
H(5')	3661 (56)	4072 (47)	685 (26)	51 (8)
H'(5')	3229 (49)	4157 (39)	2003 (23)	41 (6)
H(6)	1771 (69)	-2445 (57)	797 (32)	60 (9)
H(7)	1515 (49)	388 (40)	-342 (24)	36 (6)
H(8)	7098 (54)	4505 (45)	2229 (27)	47 (7)

azole molecules were linked together into ribbons by an intermolecular hydrogen bond  $>N(1)-H \cdots N(3) \leq$ . A similar situation is observed in the present structure with the formation of an intermolecular hydrogen bond  $[-O(5')-H \cdots N(3) \leq]$  having the nitrogen atom accepting a proton from the 5' hydroxyl of a  $2_1$  screw axis related molecule. Within the ring all of the distances correspond to bonds of intermediate order and there is more than a significant difference between bonds which one would expect to exhibit similar lengths. This fact coupled with the elongated appearance of the bonding electron-density peaks on the final difference map indicates the considerable aromatic nature of imidazole.

Least-squares planes for the atoms of the imidazole

Table 4. Least squares planes for *N*-( $\beta$ -D-ribofuranosyl)imidazole

(a) Equations of the least-squares planes.

Plane	Equation†				$\chi^2$
	$p$	$q$	$r$	$d$	
A	-0.5631x	-0.8256y	-0.0360z	+0.8265=0	1.84
B	-0.5544x	-0.8304y	-0.0555z	+0.9363=0	1919.7
C	0.6852x	-0.5887y	-0.4289z	+0.0622=0	124.3
D	0.7036x	-0.5762y	-0.4160z	-0.0212=0	—

†  $x, y, z$  refer to the  $a, b$  and  $c^*$  axes respectively,  $p, q$  and  $r$  are the direction cosines,  $d$  is in Å.

ring are included in Table 4. This structural feature is exceptionally planar with all atoms less than one standard deviation from the plane. (The  $\chi^2$  value is 1.84 and the maximum displacement is 0.002 Å). Atom C(1') is, however, 0.090 Å from the plane of the imidazole ring and on the same side of the ring as is atom O(1'). Atom N(1) is therefore definitely not trigonal but it has considerable tetrahedral character. The resulting partial lone-pair electrons on N(1) apparently reside on the opposite side of the imidazole plane as are O(1') and C(1').

### (ii) Ribose ring

The dimensions of the ribose ring are similar to those found in other nucleosides and nucleotides [for reviews, see Arnott (1970); Sundaralingam (1969)]. As found in these other structures there is a large discrepancy between C(1')-O(1'), 1.423(3) Å and C(4')-O(1'), 1.441(2) Å. This distinction between the two ring C-O bond lengths most likely has its source in the anomeric effect (Berman, Chu & Jeffrey, 1967).

The carbon-oxygen hydroxyl bond lengths are C(2')-O(2'), 1.409(3) Å; C(3')-O(3'), 1.408(2) Å and C(5')-O(5'), 1.423(3) Å. Although the first two are considerably shorter than the last it appears that these former are normal lengths in ribose-containing nucleosides (Lai & Marsh, 1972; Viswamitra, Swaminatha Reddy, James & Williams, 1972; Thewalt, Bugg & Marsh, 1970; Rao & Sundaralingam, 1970). The C(4')-C(5') length of 1.506(3) Å which at first sight appears short for a C( $sp^3$ )-C( $sp^3$ ) bond is not unusual but lies within the range found for other nucleosides (Sundaralingam & Jensen, 1965; Saenger & Scheit, 1970; Thewalt, Bugg & Marsh, 1970; Rao & Sundaralingam, 1970; Lai & Marsh, 1972; Viswamitra *et al.*, 1972).

The conformation of the ribose ring as determined here is C(3')-endo-C(2')-endo (Fig. 4). The displacements of these two atoms are almost identical with the displacements of the corresponding atoms in the structure of adenosine (Lai & Marsh, 1972) and adenosine-3'-phosphate dihydrate (Sundaralingam, 1966). In considering the detail of the ribose conformation as expressed by the torsion angles around the ring (Fig. 5),

Table 4 (cont.)

(b) Distances (Å) of atoms from least-squares planes. Plane C represents the best four-atom plane for the ribose ring.

	Plane A	Plane B	Plane C	Plane D
N(1)	0.001 (1)*	0.032 (1)*	C(1')	0.011 (2)*
C(2)	0.000 (2)*	0.014 (2)*	C(2')	-0.007 (2)*
N(3)	-0.001 (2)*	-0.015 (2)*	C(3')	-0.562 (2)
C(4)	0.002 (3)*	-0.014 (3)*	C(4')	0.007 (2)*
C(5)	-0.001 (3)*	0.011 (3)*	O(1')	-0.012 (2)*
C(1')	-0.090 (2)	-0.028 (3)*	C(5')	-0.809 (2)
C(2')	0.767 (2)	—		
O(1')	-1.444 (2)	—		
H(2)	-0.01 (3)	—		
H(4)	0.07 (5)	—		
H(5)	-0.02 (3)	—		
r.m.s. $\Delta$	0.0011 Å	0.020 Å	0.0094 Å	—

\* These atomic positions were used to define the least-squares plane.

that conformation which the present study most closely resembles is adenosine-3'-phosphate.

In light of the fact that the aglycone is imidazole and not a pyrimidine or purine base, the definition of glycosidic torsion angle,  $\chi$ , and arguments restricting its possible values are not enforced. The imidazole ring resembles the five-membered ring of the purines and comparison of the bond lengths and angles of this portion of the adenine ring (Lai & Marsh, 1972, and references quoted therein) with those in the present structure shows that this resemblance is indeed close. The glycosidic torsion angle  $\chi$  (Sundaralingam, 1969) is when referred to the angle C(2)-N(1)-C(1')-O(1') -97.8° (262.2°) and thus falls in the *syn* range. The conformation of nucleosides exhibiting *syn* glycosidic torsional angles has been discussed (Rao & Sundaralingam, 1970; Saenger & Scheit, 1970).

In an appendix to their paper Saenger & Scheit (1970) point out the multitudinous definitions of the glycosidic torsion angle and the possible confusions that can arise in assigning *syn* or *anti* to the conformations. In an attempt to overcome the confusion these authors add another definition  $\tau_{CN}$  for this angle and refer it to the dihedral angles C(2')-C(1')-N(9)-C(8) in purine nucleosides or C(2')-C(1')-N(1)-C(6) in pyrimidine nucleosides. They point out the rather arbitrary choice of O(1') as reference atom in the earlier definitions. Arnott (1970) also uses the sugar atom C(2') as the reference point for his definition of this torsion angle ( $\chi$ ). For completeness sake the  $\tau_{CN}$  value for the present structure is 142.6° (*syn*) and the  $\chi$  value in Arnott's notation is 217.4° (*syn*). Perhaps the only complete

way of presenting data of this sort is in the form of a Newman projection (Fig. 5), and this is the preference given herein.

The torsion angles about the bond C(4')-C(5') are also shown in Fig. 5. The conformation is *gauche-trans* referred to O(1') and C(3') respectively with the torsion angles O(5')-C(5')-C(4')-O(1'), +64.3° and O(5')-C(5')-C(4')-C(3'), +180.4°. This latter value is very close to the 177.0° found by Lai & Marsh for adenosine. This is not the most commonly observed conformation of the C(4')-C(5') bond, but Wilson & Rahman (1971) have shown that for the 3'-*endo* ribose conformation, the variation in non-bonded interaction energy was not sufficiently large to exhibit a preference of one conformation over another of the three allowed, *gauche-gauche*, *gauche-trans* or *trans-gauche*. In the present crystal structure the O(5') *gauche-trans* conformation is adopted apparently because of the advantageous hydrogen bonding attainable for O(5').

The average bond length for the carbon-hydrogen bonds is 0.97(3) Å and that for the oxygen-hydrogen bonds is 0.82(3) Å. Both of these values are approximately 0.10-0.15 Å shorter than expected for the inter-nuclear separation but this has been a common observation in other X-ray diffraction analyses.

The bond angles in the ribose moiety are also close to those found in other nucleosides and nucleotides (Arnott, 1970). There are some differences in the exocyclic angles however, the most notable those angles at C(2'). Whereas the angles C(2')-C(3')-O(3'), 114.6(2)° and C(4')-C(3')-O(3'), 114.6(2)° agree with the values observed for the corresponding angles in adenosine

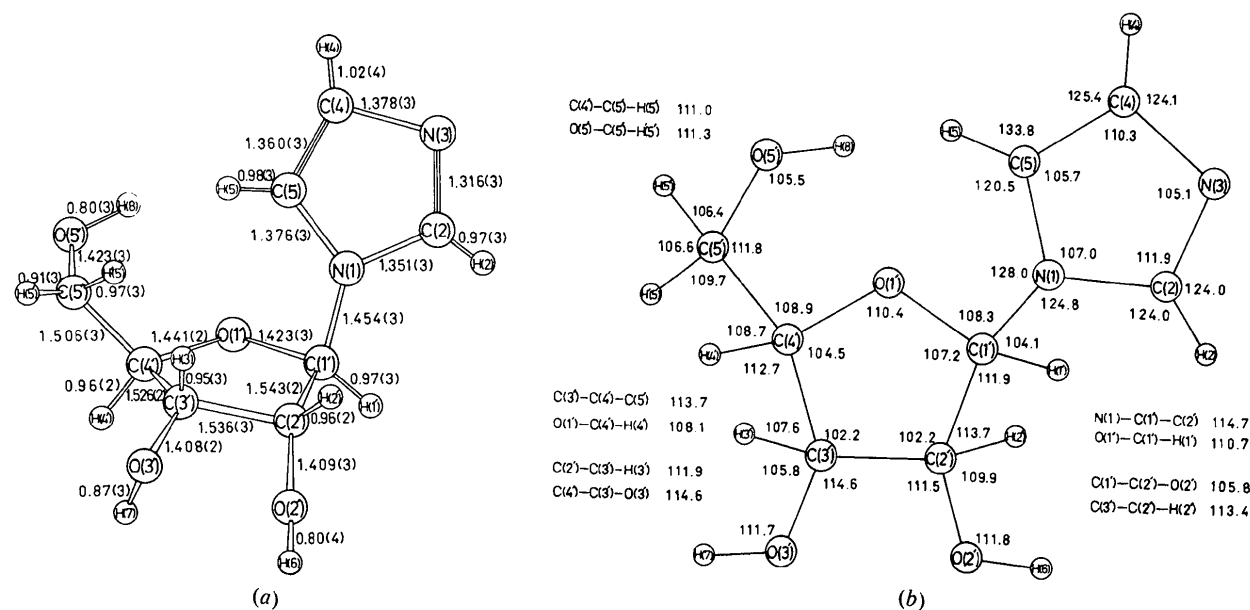


Fig. 3. (a) Schematic diagram showing interatomic bond lengths (Å) with the estimated standard deviations in parentheses. There are no corrections for thermal vibrations. (b) Schematic diagram showing the interbond angles in degrees. The average standard deviation for bond angles between non-hydrogen atoms is 0.2° whereas that for angles involving hydrogen atoms is 2.0°.

(Lai & Marsh, 1972), the angles  $C(1')-C(2')-O(2')$ ,  $105.8(2)^\circ$  and  $C(3')-C(2')-O(2')$ ,  $111.5(2)^\circ$  differ by almost  $4^\circ$  from the corresponding angles,  $109.5(2)^\circ$  and  $107.9(2)^\circ$  observed in adenosine.

### (iii) Solution conformational studies

The n.m.r. spectrum of the present compound in  $D_2O$  has been described by Lemieux & Saluja, (1971). The solution conformation was interpreted from the proton-coupling constants of the ring hydrogens and led to the conclusion that there was a *C(2')-endo*, *C(3')-endo* equilibrium population with the *C(3')-endo* conformation contributing only 28%. In the crystal structure the conformation is definitely *C(3')-endo-C(2')-endo* (Fig. 4) with the atomic displacements  $0.604$  and  $0.055 \text{ \AA}$  respectively. This ring pucker and the glycosidic torsion angle of  $-97.8^\circ$  cause relatively short contacts between  $H(5)$  and  $H(3')$  of  $2.34(4) \text{ \AA}$  and between  $H(3')$  and  $H(2')$  of  $2.36(4) \text{ \AA}$ .

The dihedral angles  $H(1')-H(2')$ ,  $H(2')-H(3')$  and  $H(3')-H(4')$  are  $95.5$ ,  $41.6$  and  $-160.7^\circ$  respectively and would predict coupling constants  $J_{1',2'}$   $0.0$ ,  $J_{2',3'}$   $3-4$  and  $J_{3',4'}$   $8-10$  Hz respectively. The observed values are  $5.8$ ,  $5.2$  and  $3.6$  Hz. One suspects that there could be relatively large forces in the crystal packing to retain a preferred conformation. It might be reasoned that the hydrogen bonding present in this structure would provide ample energy to fix this conformation. However, the crystal and molecular structure of tri-*O*-acetyl- $\beta$ -D-ribofuranosylimidazole (James & Matsu-shima, unpublished results) indicates that this is not true, for the ribose ring has the *C(3')-endo-C(2')-exo* conformation in this crystal structure which has no hydrogen bonding present or possible.

### (iv) Molecular packing

Fig. 6 shows a stereoscopic view of the packing of IMR in the crystal as viewed almost parallel to the *a* axis of the crystal. The molecular packing is clearly dominated by the formation of hydrogen bonds. Each nucleoside is hydrogen bonded to six neighboring molecules; all nitrogen and oxygen atoms except  $N(1)$  and  $O(1)$  are involved in this bonding scheme. The distances between the oxygen atoms and the hydrogen bond acceptors and the angles  $O-H \cdots X$  are listed in Table 5. All three of these are normal hydrogen bonds (*cf.* Donohue, 1968).

From Fig. 6 it may be seen that there is a hydrophilic surface parallel to the *ab* plane. The imidazole rings are stacked by the  $2_1$  screw axis through  $\frac{1}{2}, y, \frac{1}{2}$  but there is no base stacking *per se* as occurs with other nucleosides (Bugg, Thomas, Rao & Sundaralingam, 1971) because

the imidazole rings are not coplanar in this structure. The angle between adjacent imidazole planes is  $68.7^\circ$ . Oxygen atoms  $O(3')$  and  $O(5')$  act both as hydrogen-bond acceptors and donors whereas  $O(2')$  acts only in a donor role, donating its proton  $H(6)$  to oxygen  $O(3')$  at  $\bar{x}, y - \frac{1}{2}, \bar{z}$ . Oxygen  $O(3')$  donates its proton  $H(7)$  to oxygen  $O(5')$  at  $1-x, y - \frac{1}{2}, -z$  and oxygen  $O(5')$  donates its proton to nitrogen atom  $N(3)$  in the imidazole ring of the molecule at  $1-x, \frac{1}{2}+y, 1-z$ .

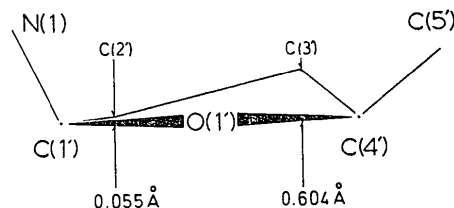


Fig. 4. Schematic drawing showing the displacements of atoms  $C(2')$  and  $C(3')$  from the plane defined by atoms  $C(1')$ ,  $O(1')$  and  $C(4')$  with the equation given in Table 5 for plane *D*.

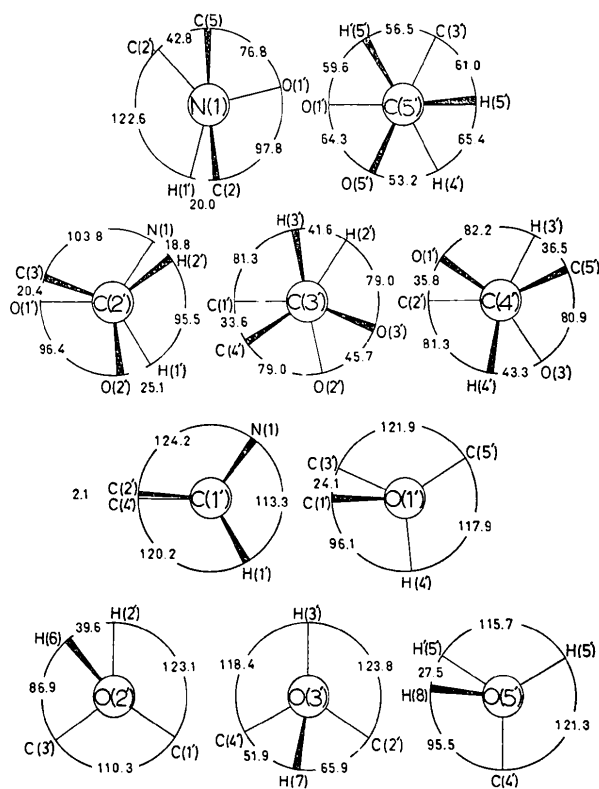


Fig. 5. Conformation angles for the ribose ring in the form of Newman projections.

Table 5. Hydrogen bond distances ( $\text{\AA}$ ) and angles ( $^\circ$ )

O-H $\cdots$ X		O $\cdots$ X	H $\cdots$ X	$\angle$ O-H $\cdots$ X
$O(2')-H(6)\cdots O(3')$	$(-x, y - \frac{1}{2}, -z)$	2.759	1.970	167.7
$O(3')-H(7)\cdots O(5')$	$(1-x, y - \frac{1}{2}, -z)$	2.672	1.818	167.3
$O(5')-H(8)\cdots N(3)$	$(1-x, y + \frac{1}{2}, 1-z)$	2.740	1.938	178.8

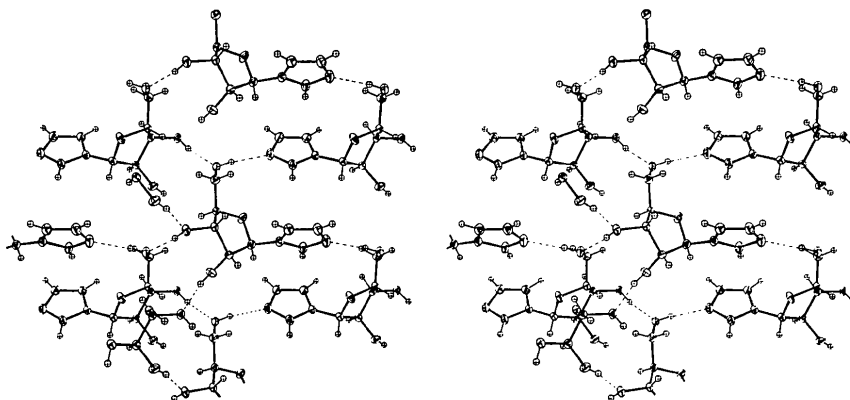


Fig. 6. Stereoscopic drawing of the unit cell contents projected along the  $a$  axis. The intermolecular hydrogen bonds are identified by broken lines.

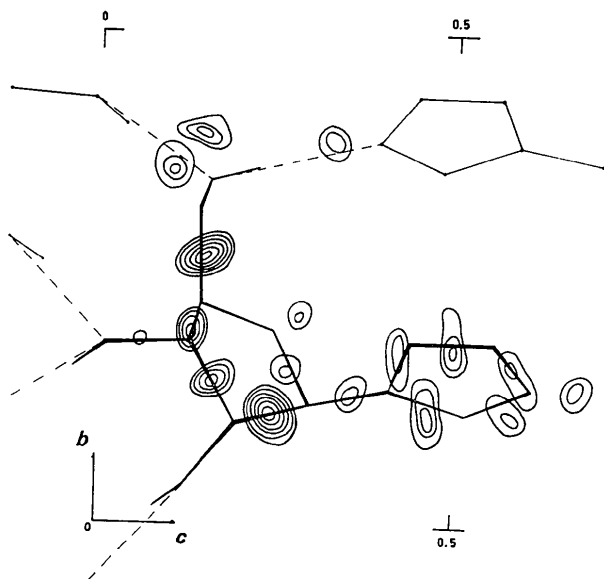


Fig. 7. Composite drawing of the final difference electron-density map showing those features greater than twice the estimated standard deviation of the electron density ( $0.037 e \text{ \AA}^{-3}$ ). The first contour is at  $0.075 e \text{ \AA}^{-3}$  and the contour interval is  $0.025 e \text{ \AA}^{-3}$ . The negative contours have been omitted from this drawing.

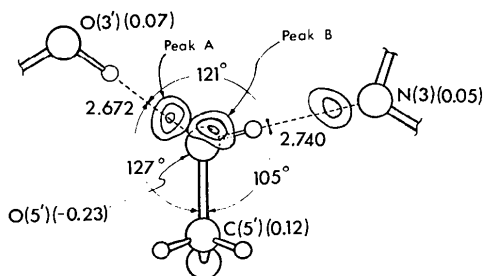


Fig. 8. Diagrammatic sketch of the region around the atom  $O(5')$  showing the hydrogen-bond distances and coordination angles. The numbers in parentheses after the atom symbols refer to the distances those atoms are from the plane with equation  $-0.5555x + 0.8310y - 0.0297z - 1.0107 = 0$ . Peak  $A$  is  $-0.20 \text{ \AA}$  from this plane, peak  $B$  is  $+0.56 \text{ \AA}$  from this plane.

#### (v) Final difference electron density

A residual electron-density map shown in Fig. 7 was computed from the final  $\Delta F$  values. The overall standard deviation in electron density computed from the formula given by Cruickshank (1967) is  $\pm 0.04 e \text{ \AA}^{-3}$ . largest peak,  $+0.21 e \text{ \AA}^{-3}$ , on this map occurs along the bond mid-way between atoms  $C(1')-C(2')$ . The other large peaks shown on Fig. 7 occur between  $\sigma$ -bonded carbon atoms in the ribose moiety and all have peak heights greater than  $+0.15 e \text{ \AA}^{-3}$ . The peaks of the residual density around the imidazole ring were extended perpendicular to the plane of the ring whereas the bonding density in the ribose was more spherical. It is of interest to note that there was little if any bonding electron density in the  $C-O$  bonds. The fact that the bonding electron density was less along  $C-O$  bonds than along the  $C-C$  bonds was also noted in a comparison of the X-ray and neutron structural studies of sucrose by Hanson, Sieker & Jensen (1972).

There is an interesting region occurring around oxygen atom  $O(5')$  which indicates that hydrogen bond formation may be causing a distortion in the electron density. The density in the bond  $C(5')-O(5')$  is less than  $0.075 e \text{ \AA}^{-3}$  but there are two peaks of  $+0.13 e \text{ \AA}^{-3}$  in the region where one might expect lone-pair electron-cloud density for  $O(5')$ . There is also a peak of  $+0.10 e \text{ \AA}^{-3}$  in the region neighboring atom  $N(3)$  of the imidazole ring along the line joining  $O(5')-H \cdots N(3)$ . One of the peaks (peak  $A$  in Fig. 8) near  $O(5')$  is along the line  $O(3')-H(7) \cdots O(5')$ . The geometry of the atomic grouping is such that atoms  $C(5')$ ,  $O(5')$ ,  $N(3)$  and  $O(3')$  lie approximately in a single plane (maximum displacement  $0.23 \text{ \AA}$ ). The distance of the second residual density peak (peak  $B$  in Fig. 8) from this plane is  $0.55 \text{ \AA}$  and it lies almost directly above the oxygen atom  $O(5')$ . The situation is shown diagrammatically in Fig. 8. The approximate trigonal coordination of  $O(5')$  has thus shifted the lone-pair electrons on this atom away from the expected  $sp^3$  tetrahedral position.

Clearly further experimental work will have to be carried out before the significance of this apparent



distortion can be assessed. From the work on sucrose it is obviously very important to use more than one crystal, more than one temperature, extinction and absorption corrections and a comparison of X-ray and neutron diffraction data if details of bonding density are to be evaluated. The present compound would be ideal for such a study as large crystals are easily grown by the vapour-diffusion technique.

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