and asymmetry parameters (Duax, Weeks & Rohrer, 1976) are listed in Table 3. Ring *A* has a $1\alpha,10\beta$ half-chair conformation, ring *B* exhibits a transition form between 9α envelope (sofa) and $9\alpha,10\beta$ half-chair, while rings *C* and *F* adopt a chair conformation. The five-membered *D* ring has a $13\beta,14\alpha$ half-chair conformation, while ring *E* is in an envelope form with the N atom at the flap. The β-axial C(18) methyl group is almost eclipsed with the C(19) methyl moiety as shown by the non-bonded torsion angle C(19)—C(10)···C(13)—C(18) = −3·3 (4)°. The position of the C(27) methyl group is equatorial, while C(21) assumes an α-pseudo-equatorial position.

The packing arrangement along **c** is presented in Fig. 2. The interactions between molecules, which lie almost parallel to the diagonals of the *ab* plane, occur only through van der Waals contacts.

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Structure and Conformation of a Novel *N*-Glycosylimidazole Nucleoside: Ethyl 5-Amino-1-(2,3-*O*-isopropylidene-β-ribofuranosyl)imidazole-4-carboxylate

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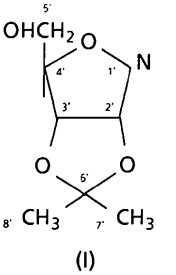
Abstract. $C_{14}H_{21}N_3O_6$, $M_r = 327{\cdot}7$, tetragonal, $P4_3$, $a = 9{\cdot}154\ (2)$, $c = 19{\cdot}066\ (5)$ Å, $V = 1597{\cdot}7\ (7)$ Å^3, $Z = 4$, $D_m = 1{\cdot}35\ (1)$, $D_x = 1{\cdot}361$ g cm^{-3}, $\lambda = 0{\cdot}71069$ Å, μ(Mo $K\alpha$) = 0·68 cm^{-1}, $F(000) = 696$, $T = 298$ K, final $R = 0{\cdot}030$ for 1062 observed reflections. In the crystal structure the imidazole base planes are mutually perpendicular rather than parallel and the only intermolecular hydrogen-bonding distance is 2·90 (2) Å from the ribofuranosyl O(5′) to N(3) in the imidazole ring. Close intramolecular approaches are 2·84 (2) Å from the imidazole amino N(5) to ethoxy O(7) [rather than to carboxy O(6)] and 3·14 (2) Å from N(5) to the sugar O(5′). The bicyclic furanodioxalane group has a flattened '*W*' shape with both rings in an envelope form (sugar pucker $^0T_1$) and the conformation of the glycosidic linkage C(2)—N(1)—C(1′)—O(1′) is within the *syn* range.

Introduction. For the synthesis of aminoimidazole nucleosides, related to active intermediates in *de novo* purine nucleotide biosynthesis and to natural nucleosides with anti-tumour activity, the use of 2,3-*O*-isopropylidene-D-ribofuranosylamine (I) has been developed by G. Shaw and co-workers (*e.g.* Mackenzie, Shaw & Thomas, 1976). Thus, its toluene-*p*-sulfonate in ethanolic NaOH can react with the imidate formed from refluxing ethyl α-amino-α-cyanoacetate and triorthoformate in acetonitrile to give a gum from which the title β-nucleoside, EARIC, was eventually recrystallized from ethanol (Cusak, Hildick, Robinson, Rugg & Shaw, 1973). 220 MHz ^{1}H NMR spectroscopy (Jones, Mokoena, Robinson & Shaw, 1981) shows that in DMSO solution EARIC assumes a dynamic conformational equilibrium between *N*- and *S*-type furanose ring-puckering modes; the preferred glycosidic rotational conformation is *anti* and the preferred exocyclic CH_2OH is *gg*. A single-crystal X-ray analysis performed on EARIC now indicates an *S*-type conformation in the solid state.



(I)

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Experimental. Slow evaporation of an ethanolic solution of EARIC (G. Shaw) gave colourless tetragonal prisms with *c*-axis elongation. D_m by KI flotation. Systematic absences $00l$ when $l = 2n + 1, 2, 3$, together with photographs taken about the *a* and *b* axes, indicated the tetragonal space group $P4_1$ (or its enantiomorph $P4_3$). Photographically determined cell dimensions confirmed by diffractometer (15 reflections $35 < 2\theta < 40°$). X-ray intensity data collected from $0{\cdot}45 \times 0{\cdot}20 \times 0{\cdot}20$ mm crystal on a Syntex $P2_1$ diffractometer (Chemistry Department, Leeds University) with graphite-monochromatized Mo $K\alpha$ radiation within 2θ range 3–45°. Collection details: $\omega/2\theta$ scan, scan rates 1·5–29·3° mm^{-1}, index ranges *h* 0 to 9, *k* −9 to 9, *l* 0 to 20, intensity of standard reflection 004, monitored every 50 reflections, constant within 3%. 2230 measured reflections (1086 unique) yielded 1062 observed reflections with $|\Delta F| > 2\sigma(F)$ ($R_{int} = 0{\cdot}020$).

Structure solution by non-centrosymmetric direct-methods routine *TANG* in *SHELX76* (Sheldrick, 1976) from 200 *E* values > 1·2. The only two non-H atoms not found in the *E* map with highest CFOM were located by difference Fourier synthesis. Following full-matrix least-squares isotropic refinement to $R = 0{\cdot}064$, further ΔF maps revealed plausible positions for, successively, 14 and then 20 H atoms; location of the remaining H(5′), evidently participating in an O(5′)—H(5′)···N(5) bond, was less clear. For final stages of least-squares refinement on *F*, anisotropic for C, N, O, separate U_{iso} for each group of H, 270 parameters, $w = [\sigma^2(F) + 3{\cdot}66 \times 10^{-3}|\Delta F|^2]^{-1}$, maximum shift/e.s.d. = 1·0, $R = 0{\cdot}030$ ($wR = 0{\cdot}030$) over 1069 reflections. Scattering factors from Stewart, Davidson & Simpson (1965) for H and Cromer & Mann (1968) for C, N, O. Maximum peak/troughs $\pm 0{\cdot}25$ e $Å^{-3}$ in final difference map did not reveal H(5′) on O(5). No correction for absorption or extinction.

Table 1. *Fractional atomic coordinates and equivalent isotropic temperature factors, e.s.d.'s in parentheses*

$U_{eq} = (U_{11} + U_{22} + U_{33})/3.$

	x	*y*	*z*	U_{eq} (Å²)
N(1)	0·4421 (2)	0·0403 (3)	0·4523 (2)	0·035 (2)
C(2)	0·5897 (3)	0·0468 (4)	0·4651 (2)	0·041 (2)
N(3)	0·6635 (3)	−0·0419 (3)	0·4255 (2)	0·042 (2)
C(4)	0·5597 (3)	−0·1130 (3)	0·3846 (2)	0·037 (2)
C(5)	0·4215 (3)	−0·0629 (3)	0·4012 (2)	0·032 (2)
N(5)	0·2872 (3)	−0·0926 (3)	0·3744 (2)	0·042 (2)
C(6)	0·6013 (4)	−0·2170 (4)	0·3319 (2)	0·043 (2)
O(6)	0·7250 (3)	−0·2579 (3)	0·3203 (2)	0·057 (2)
O(7)	0·4847 (3)	−0·2673 (3)	0·2960 (2)	0·058 (2)
C(8)	0·5106 (6)	−0·3745 (5)	0·2420 (3)	0·070 (3)
C(9)	0·5638 (8)	−0·3074 (7)	0·1751 (3)	0·092 (3)
C(1′)	0·3322 (3)	0·1327 (4)	0·4835 (2)	0·035 (2)
C(2′)	0·2516 (4)	0·2321 (3)	0·4327 (2)	0·036 (2)
C(3′)	0·0937 (4)	0·2298 (4)	0·4582 (2)	0·040 (2)
C(4′)	0·0880 (3)	0·1182 (3)	0·5167 (2)	0·038 (2)
O(1′)	0·2271 (2)	0·0418 (2)	0·5145	0·040 (2)
O(2′)	0·2980 (2)	0·3784 (2)	0·4396 (2)	0·055 (2)
O(3′)	0·0728 (3)	0·3738 (3)	0·4848 (2)	0·059 (2)
C(6′)	0·1716 (4)	0·4680 (3)	0·4497 (2)	0·044 (2)
C(7′)	0·1144 (7)	0·5193 (5)	0·3803 (3)	0·072 (3)
C(8′)	0·2118 (7)	0·5904 (5)	0·4976 (3)	0·077 (3)
C(5′)	−0·0285 (4)	0·0033 (4)	0·5105 (2)	0·044 (2)
O(5′)	−0·0232 (3)	−0·0639 (3)	0·4437 (2)	0·052 (2)

Table 2. *Bond lengths* (Å), *e.s.d.'s in parentheses*

N(1)—C(2)	1·374 (4)	C(1′)—O(1′)	1·402 (4)
N(1)—C(5)	1·370 (4)	C(2′)—C(3′)	1·525 (5)
N(1)—C(1′)	1·443 (4)	C(2′)—O(2′)	1·411 (4)
C(2)—N(3)	1·298 (5)	C(3′)—C(4′)	1·515 (4)
N(3)—N(4)	1·390 (4)	C(3′)—O(3′)	1·426 (4)
C(4)—C(5)	1·382 (4)	C(4′)—C(5′)	1·502 (5)
C(4)—C(6)	1·435 (5)	C(4′)—O(1′)	1·453 (4)
C(5)—N(5)	1·359 (4)	O(2′)—C(6′)	1·431 (4)
C(6)—O(6)	1·213 (4)	O(3′)—C(6′)	1·418 (4)
C(6)—O(7)	1·349 (4)	C(6′)—C(7′)	1·498 (6)
O(7)—C(8)	1·442 (5)	C(6′)—C(8′)	1·492 (6)
C(8)—C(9)	1·497 (8)	C(5′)—O(5′)	1·415 (5)
C(1′)—C(2′)	1·521 (5)		

Discussion. The final fractional coordinates for non-H atoms are given in Table 1 (as for β-D-ribofuranosyl in $P4_3$ since preparation of EARIC was *via* D-ribose) and the bond lengths in Table 2.* Fig. 1 shows the atomic numbering and molecular conformation while the crystal packing diagram (Fig. 2) shows that the highly planar imidazole bases are orthogonal (mutual inclination 92°) rather than stacked parallel as is common among nucleosides. Only one oxygen, O(5′) (which is also an intramolecular hydrogen-bond acceptor), appears to participate in intermolecular hydrogen bonding. Although the O(5′) H atom was not directly located, distances and angles are consistent with donation to N(3) on the imidazole ring at $1 - x, y, z$ [O(5′)···N(3) 2·90 Å]. An analogous O(5′)···N(3) hydrogen bond [labelled O(5′)—H(O5′)···N(13)] occurs in 4-(*p*-methylbenzyl)-5-guanidino-1-β-ribofuranosylimidazole (MEBGRIFI) (Carrell, Zacharias, Glusker, Moschel, Hudgins & Dipple, 1982), which crystallizes in the same space group as EARIC. Methyl C atoms C(7′), C(8′) and C(9) in EARIC all have U_{11} about twice those of adjacent non-H atoms and there is a steady increase in U_{eq}'s along the chain C(4), C(6), O(7), C(8), C(9).

Bond angles in the imidazole ring of EARIC are similar to those in imidazole (McMullen, Epstein,

* Lists of structure factors, anisotropic thermal parameters, bond lengths and angles involving H atoms, and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53047 (10 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Ruble & Craven, 1979) and in the few structures of imidazole-based nucleosides that have been reported; in all, angle N(1)—C(2)—N(3) tends to be about 1° smaller and angle C(2)—N(3)—C(4) about 1° larger than in neutral guanine and adenine (Taylor & Kennard, 1982*a*,*b*). However, bond lengths N(1)—C(2) and N(3)—C(4) are about 0·02 Å longer when the ring is substituted as in EARIC and in 5-amino-1-β-D-ribofuranosylimidazole-4-carboxamide (AICAR) (Adamiak & Saenger, 1979), 5-amino-1-(2,3:5,6)-di-*O*-isopropylidene-α-D-mannofuranosyl)-imidazole-4-carboxamide (ADIMIC) (Briant & Jones, 1988) and MEBGRIFI, than in imidazole itself and in *N*-(β-D-ribofuranosyl)imidazole (RIBFIM) (James & Matsushima, 1973). Instead of utilizing its carboxyl O(6) to accept a hydrogen bond from the imidazole 5-amino H, as happens in AICAR, EARIC makes a 2·84 (2) Å intramolecular hydrogen [H(51)] bond from N(5) to O(7) to form an almost planar ring C(4), C(5), N(5), H(51)···O(7), C(6). The other amino hydrogen, H(52), deviates by −0·4 (1) Å from the imidazole-ring plane and is suitably oriented for a long 3·14 (2) Å intramolecular hydrogen bond N(5)—H(52)···O(5′) to the primary-alcohol hydroxyl oxygen [−0·93 (1) Å out of the imidazole-ring plane] of the sugar.

The ribose sugar ring adopts the unusual envelope form, ${}^{O}T_{1}$, with O(1′)-*endo* and slight C(1′)-*exo* ring puckering, $P = 102{\cdot}3°$ and $\tau_m = 28{\cdot}6$, type *S*; the dioxolane ring is also in the envelope form with C(6′)-*endo* and slight O(3′)-*exo*, and pseudorotation parameters $P = 100{\cdot}9$ and $\tau_m = 35{\cdot}4°$. Overall, the bicyclic furanodioxolane group has a shallow '*W*' shape in which the outer wings O(1′)—C(1′)—C(4′) and O(2′)—O(3′)—C(6′) have a mutual inclination of only 8·2 (2)°. Differences within the bond-length pairs C(1′)—O(1′) and C(4′)—O(4′), C(2′)—O(2′) and C(3′)—O(3′), and O(2′)—C(6′) and O(3′)—C(6′) are slightly greater than normal. Finally, the dihedral torsion angle (Sprang, Rohrer & Sundaralingam, 1978) C(2)—N(1)—C(1′)—O(1′), $\tau = 125{\cdot}5\ (3)°$ [*cf.* 61·3 (6)° in MEBGRIFI] defines the glycosidic linkage between base and sugar as *syn* rather than *anti* as appears to predominate in solution (Jones, Mokoena, Robinson & Shaw, 1981); conformation about the exocyclic C(4′)—C(5′) bond is *gg*, as in solution.

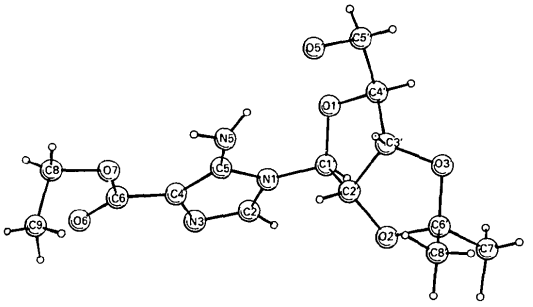

Fig. 1. Numbering of atoms and conformation.

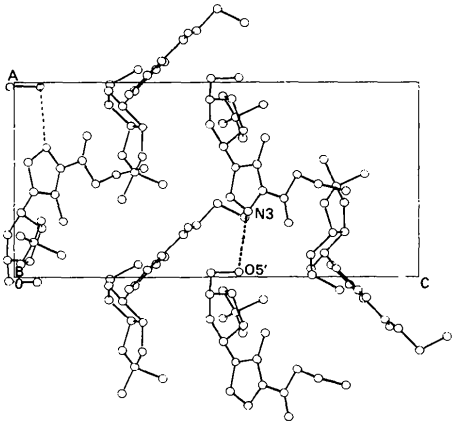

Fig. 2. View down the *b* axis of crystal packing, showing the close O(5′)···N(3) intermolecular approach.

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