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Nebularine, 9-β-D-Ribofuranosylpurine

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Abstract. $C_{10}H_{12}N_4O_4$, a nucleoside antibiotic isolated from the mushroom *Agarius* (*clitocybe*) *nebularis* Batsch [Ehrenberg, Hedstom, Lofgren & Takman, (1946). *Svensk Kem. Tidsskr.* **58**, 269–270]. Crystals were obtained from an acetone solution. $P2_1$, $a=4{\cdot}943$ (3), $b=11{\cdot}601$ (3), $c=9{\cdot}620$ (3) Å $\beta=99{\cdot}54$ (3)°, $Z=2$, $D_m=1{\cdot}54$, $D_x=1{\cdot}54$ g cm^{-3}. The relative orientation of the purine and ribose groups is *anti*, $\chi_{\rm CN}=+13{\cdot}5°$. The sugar puckering is C(3′)-*endo*–C(2′)-*exo* ($^3T_2$), and the conformation about C(4′)–C(5′) is *gauche–gauche*.

Experimental and structure determination. Using Zr-filtered Mo $K\alpha$ radiation ($\lambda=0{\cdot}7107$ Å), the intensity of each reflexion ($7{\cdot}5° < 2\theta < 60°$) was measured three times consecutively on a Hilger–Watts linear diffractometer. Out of 1528 independent reflexions, 'unobserved' reflexions [$I < 2\sigma(I)$] and also $h00$ and $00l$ were excluded since the latter were greatly affected by white radiation. The remaining 1218 reflexions were used for the structure determination. No absorption corrections were made. By the symbolic addition method (Karle & Karle, 1966) using the equation $\varphi_{\mathbf{h}}=\varphi_{\mathbf{h}-\mathbf{k}}+\varphi_{\mathbf{k}}$, phases of 123 reflexions ($|E_o|\geqq 1{\cdot}5$) were derived from three origin-defining and three symbol phases. Four sets with different symbol values were refined by the tangent formula. An E map using 367 reflexions ($|E_o|\geqq 1{\cdot}2$) in the set with the lowest R value showed part of the structure. Starting from reliable phases of 92 reflexions ($|E_o|\geqq 1{\cdot}5$) calculated on the basis of the partial structure (Karle, 1968), the tangent-formula refinement was used to give the phases of 362 reflexions ($|E_o|\geqq 1{\cdot}2$). The resulting E map gave all the non-hydrogen atoms. Structural parameters including anisotropic temperature factors were refined by the block-diagonal least-squares method. All the hydrogen atoms were found on a difference map. Thermal parameters of the hydrogen atoms were taken as being equal to the reduced isotropic thermal parameters of the atoms directly bonded to them, and were not refined. The three strongest reflexions were excluded in the later stages of refinement, because they suffered from secondary extinction. The final R was 0·073. The weighting scheme was $w=27{\cdot}3/|F_o|$ if $|F_o|>27{\cdot}3$, $w=1$ if $0{\cdot}6\leqq|F_o|\leqq 27{\cdot}3$, $w=0{\cdot}2$ if $|F_o|<0{\cdot}6$. Atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1962). Atomic coordinates and thermal parameters are given in Table 1.*

Table 1. *Fractional atomic coordinates and thermal parameters*

The coordinates and thermal parameters of the non-hydrogen atoms have been multiplied by 10^4. Coordinates of the hydrogen atoms are $\times 10^3$. The form of the anisotropic temperature factor is $\exp(-\beta_{11}h^2-\beta_{22}k^2-\beta_{33}l^2-\beta_{12}kh-\beta_{13}hl-\beta_{23}kl)$. Estimated standard deviations are in parentheses.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
N(1)	−1380 (12)	3890 (6)	5706 (6)	359 (25)	82 (5)	76 (6)	8 (19)	117 (19)	−29 (9)
C(2)	31 (14)	2908 (7)	5912 (6)	420 (32)	69 (5)	71 (6)	10 (23)	113 (23)	9 (10)
N(3)	1808 (11)	2477 (5)	5111 (5)	335 (22)	67 (4)	70 (6)	−5 (18)	59 (18)	−18 (8)
C(4)	1984 (11)	3165 (6)	4010 (5)	263 (23)	58 (5)	45 (5)	4 (17)	49 (17)	−14 (8)
C(5)	628 (12)	4209 (6)	3696 (6)	280 (25)	53 (4)	67 (6)	−40 (17)	27 (19)	−40 (9)
C(6)	−1114 (13)	4555 (7)	4607 (7)	303 (27)	77 (6)	91 (8)	92 (21)	41 (22)	−34 (11)
N(7)	1334 (12)	4685 (5)	2480 (6)	453 (28)	65 (5)	86 (7)	68 (20)	97 (22)	26 (10)
C(8)	3016 (14)	3909 (6)	2087 (7)	402 (31)	67 (6)	73 (7)	37 (22)	76 (23)	2 (10)
N(9)	3481 (9)	2982 (5)	2954 (4)	257 (19)	54 (4)	48 (4)	18 (15)	100 (14)	−23 (7)
C(1′)	5206 (10)	1956 (5)	2807 (6)	207 (20)	51 (4)	47 (5)	0 (15)	69 (16)	−10 (7)
O(1′)	6838 (8)	2210 (4)	1773 (4)	219 (15)	73 (4)	63 (4)	−52 (13)	83 (13)	−17 (7)
C(2′)	3455 (10)	885 (6)	2291 (6)	174 (19)	56 (4)	73 (6)	5 (16)	118 (17)	−1 (9)
O(2′)	4929 (8)	−112 (4)	2729 (4)	323 (18)	59 (4)	78 (5)	73 (14)	183 (16)	37 (7)
C(3′)	3153 (10)	1058 (6)	671 (5)	194 (20)	49 (4)	60 (6)	21 (15)	28 (16)	6 (8)
O(3′)	2570 (9)	−3 (5)	−27 (5)	362 (20)	68 (4)	94 (6)	−55 (16)	−5 (17)	−34 (8)
C(4′)	5954 (11)	1526 (5)	510 (5)	187 (20)	58 (4)	48 (5)	16 (15)	63 (16)	−2 (8)
C(5′)	6016 (12)	2244 (7)	−784 (6)	293 (25)	89 (6)	63 (6)	−31 (21)	157 (20)	−16 (11)
O(5′)	3755 (9)	3000 (5)	−998 (4)	365 (20)	75 (4)	64 (4)	−3 (16)	76 (15)	33 (7)

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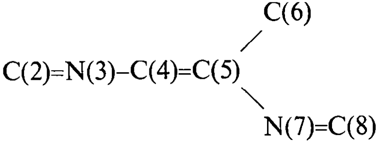
* A table of observed and calculated structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30290 (9 pp.). Copies can be obtained from The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 1 (*cont.*)

	x	y	z	B(Å^2)
H(2)	17 (16)	244 (8)	686 (8)	2·7
H(6)	−232 (16)	525 (7)	429 (8)	2·7
H(8)	336 (17)	365 (8)	129 (9)	2·6
H(1′)	641 (14)	172 (7)	378 (8)	1·7
H(2′)	159 (14)	104 (8)	255 (7)	1·8
H(O2′)	401 (15)	−50 (7)	309 (8)	2·3
H(3′)	183 (14)	162 (7)	43 (8)	1·7
H(O3′)	130 (16)	14 (8)	−66 (8)	2·9
H(4′)	719 (14)	96 (8)	54 (7)	1·8
H(15′)	773 (16)	267 (7)	−60 (8)	2·5
H(25′)	570 (15)	171 (7)	−147 (8)	2·5
H(5′)	413 (17)	365 (7)	−139 (9)	2·5

Results and discussion. In the crystal structure, shown in Fig. 1, a three-dimensional network is formed by hydrogen bonds whose lengths and angles are given in Table 2. The features of the present hydrogen-bond scheme, in contrast with the other closely related purine nucleosides, are the bond O(2′)···O(5′) between the sugar moieties and the absence of a hydrogen bond involving N(3). Any other distances between non-bonded atoms are not abnormally shorter than the usual van der Waals contacts.

The bond lengths and angles are shown in Fig. 2 and those involving hydrogen atoms are given in Table 3. In many of purine nucleosides, the bond alternation



$$C(2){=}N(3){-}C(4){=}C(5)\begin{array}{l} \diagup C(6) \\ \diagdown N(7){=}C(8) \end{array}$$

is observed, which is probably due to the double-bond character between C(6) and the substitutional atom. In nebularine, however, such a tendency is not seen, suggesting more π-delocalization.

Table 3. *Bond lengths involving hydrogen atoms*

Estimated standard deviations are 0·08–0·09 Å.

C(2)–H(2)	1·06 Å	C(4′)–H(4′)	0·90 Å
C(6)–H(6)	1·02	C(5′)–H(15′)	0·97
C(8)–H(8)	0·87	C(5′)–H(25′)	0·90
C(1′)–H(1′)	1·06	O(2′)–H(O2′)	0·76
C(2′)–H(2′)	1·01	O(3′)–H(O3′)	0·82
C(3′)–H(3′)	0·92	O(5′)–H(O5′)	0·87

Table 2. *Hydrogen-bond lengths and angles*

Donor atom	Acceptor atom	Position of acceptor atom	Distance $D\cdots A$	$H\cdots A$		
O(2′)	N(1)	$-x,\quad y-\frac{1}{2},\ -z+1$	2·750 Å	2·01 Å	O(2′)–H(O2′)–N(1)	164°
O(3′)	N(7)	$-x,\quad y-\frac{1}{2},\ -z$	2·813	2·07	O(3′)–H(O3′)–N(7)	152
O(5′)	O(2′)	$-x+1,\ y+\frac{1}{2},\ -z$	2·890	2·04	O(5′)–H(O5′)–O(2′)	165

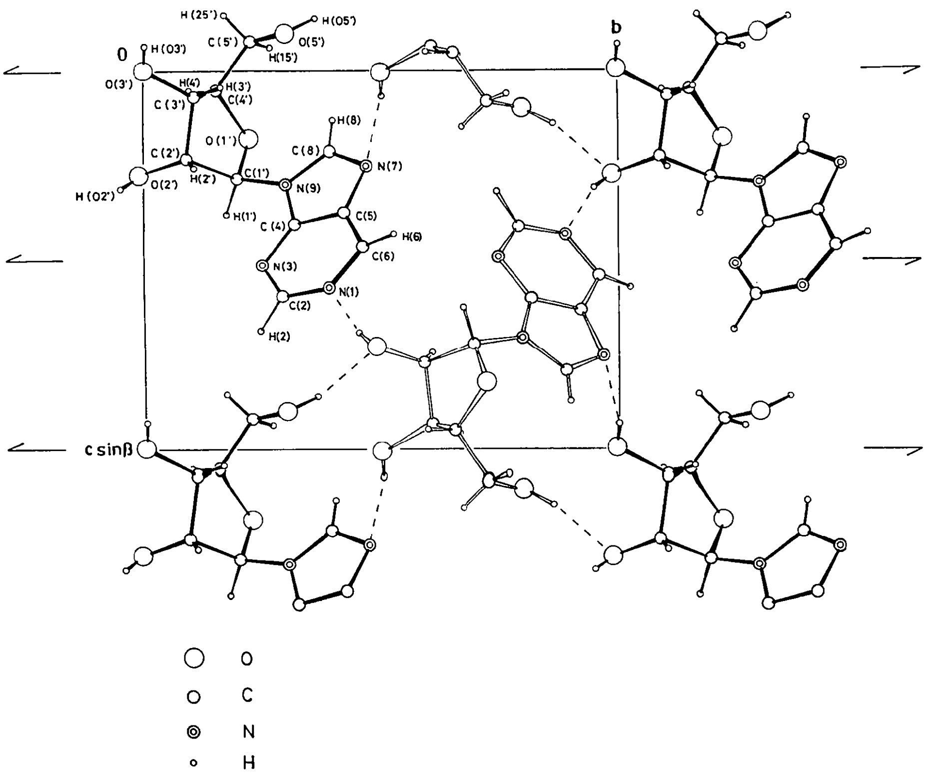


Fig. 1. The crystal packing viewed along the *a* axis (the *a* axis downward). The hydrogen bonds are represented by broken lines.

The purine ring is planar within 0·02 Å, as shown in Table 4. But a closer examination shows that the purine base has a tendency to bend, as seen in adenosine (Lai & Marsh, 1972). The dihedral angle between the five- and six-membered rings is 1·7°. In the sugar ring, there is a significantly large difference (0·045 Å) between the C(4′)–O(1′) and C(1′)–O(1′) lengths. The ring C–C bond distances range between 1·519 and 1·554 Å, the average, 1·540 Å, being slightly larger than the usual value (Sundaralingam, 1965). The C(4′)–C(5′) length is not different from those in other nucleosides. All the C–O bonds, especially C(2′)–O(2′), are shorter than the normal C–O bond (Venkateswarlu & Gordy, 1955). The sugar puckering is C(3′)-*endo* referring to the least-squares plane of the four atoms, C(1′), O(1′), C(2′) and C(4′), or C(3′)-*endo*-C(2′)-*exo* (${}^3T_2$) referring to the plane of the three atoms, C(1′), O(1′) and C(4′). The dihedral angle between the mean plane of the purine base and the four-atom plane of the sugar is 69·4°. The glycosidic torsional angle χ_{CN}[C(8)–N(9)–C(1′)–O(1′)] (Sundaralingam, 1969) is +13·5° and the conformation is *anti*. As shown in Table 5, all the sugar puckerings of the closely related compounds are C(3′)-*endo* conformations, and the glycosidic torsional angles lie in a very narrow range from +9·9 to +13·5°. The torsional angles φ_{CO}[C(3′)–C(4′)–C(5′)–O(5′)] and φ_{OO} [O(1′)–C(4′)–C(5′)–O(5′)] are 42·9 and −75·9°, respectively. The conformation about the exocyclic C(4′)–C(5′) bond is *gauche–gauche* (Shefter & Trueblood, 1965).

Table 4. *Deviations of the atoms from the least-squares planes*

Coordinates X,Y,Z are in Å referred to the orthogonal axes a, b and c^*.

I: Purine plane: $-0·6817X-0·4840Y-0·5487Z+4·0846=0$
II: Ribose plane: $-0·6765X+0·6391Y-0·3658Z+1·0157=0$
III: Ribose plane: $-0·5869X+0·7233Y-0·3640Z+0·5756=0$

	Plane I		Plane II	Plane III
N(1)	0·015† Å	C(1′)	0·054† Å	0·000† Å
C(2)	0·006†	O(1′)	−0·056†	0·000†
N(3)	−0·020†	C(2′)	−0·031†	−0·261
C(4)	−0·012†	C(3′)	0·585	0·380
C(5)	−0·013†	C(4′)	0·034†	0·000†
C(6)	0·005†	C(5′)	0·855	0·910
N(7)	−0·017†			
C(8)	0·014†			
N(9)	0·021†			
C(1′)	0·076			
C(4′)	1·012			

† Atoms included in the calculation of the least-squares plane.

Table 5. *The conformations of closely related compounds*

	χ_{CN}	Dihedral angle between base and sugar	Sugar puckering	φ_{CO}–φ_{OO}
Nebularine	+13·5°	69·4° (${}^3E$)	C(3′)-*endo*	*gauche-gauche*
Adenosine[a]	+9·9	67	C(3′)-*endo*	*trans-gauche*
Adenosine in the complex[b]	+12·4	70	C(3′)-*endo*	*gauche-gauche*
Inosine[c]	+12·5	71	C(3′)-*endo*	*trans-gauche*

References: (*a*) Lai & Marsh (1972); (*b*) Haschemeyer & Sobell (1965); (*c*) Munns & Tollin (1970).

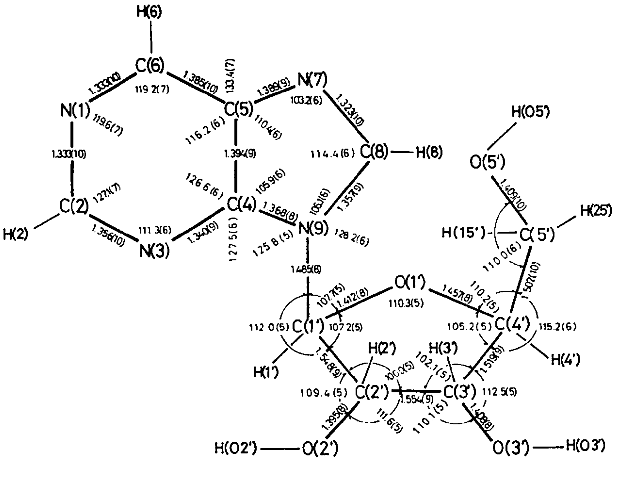


Fig. 2. Bond lengths (Å) and bond angles (°). Estimated standard deviations are in parentheses.

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