Table 3. *Some intramolecular non-bonded short distances* (Å)

C(10)–C(13^{i})	3·286 (2)	C(11)–C(12^{i})	3·246 (2)
C(11)–C(13^{i})	3·316 (2)	C(10)–H(13^{i}*B*)	2·74 (1)
C(11)–H(12^{i}*A*)	2·43 (1)	C(11)–H(13^{i}*B*)	2·65 (1)
C(12)–H(11^{i}*A*)	2·64 (1)	C(13)–H(10^{i}*B*)	2·53 (2)
C(13)–H(11^{i}*A*)	2·59 (1)	H(10*B*)–H(13^{i}*A*)	2·35 (2)
H(10*B*)–H(13^{i}*B*)	1·97 (2)	H(11*A*)–H(12^{i}*A*)	1·94 (2)
H(11*A*)–H(13^{i}*B*)	1·89 (2)	H(11*B*)–H(12^{i}*A*)	2·22 (2)

Symmetry code: (i) $1-x, -y, -z$.

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The Structure of 1-Methylisoguanine Dihydrate, $C_6H_7N_5O.2H_2O$

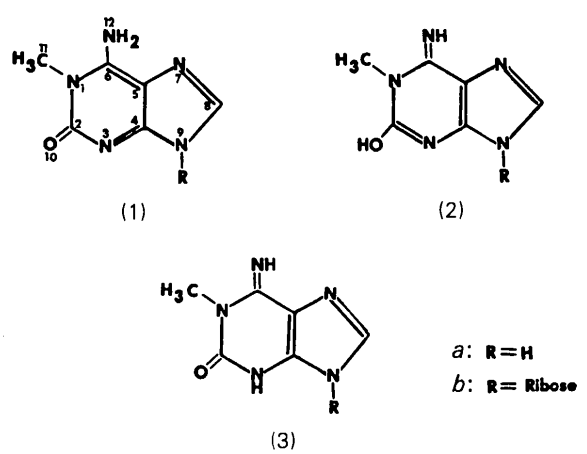
BY ROSALIND Y. WONG AND RONALD J. NACHMAN

Western Regional Research Center, Agricultural Research Service, US Department of Agriculture, Berkeley, CA 94710, *USA*

(*Received* 9 *December* 1983; *accepted* 6 *April* 1984)

Abstract. $M_r = 201·2$, triclinic, $P\bar{1}$, $a = 4·110$ (2), $b = 9·454$ (5), $c = 12·303$ (7) Å, $\alpha = 74·09$ (5), $\beta = 84·52$ (5), $\gamma = 79·96$ (4)°, $V = 452·1$ (4) Å^3, $Z = 2$, $D_x = 1·48$ g cm^{-3}, Cu $K\alpha$, $\lambda = 1·5418$ Å, $\mu = 9·8$ cm^{-1}, $F(000) = 212$, $T = 295$ K, $R(R_w) = 0·045$ (0·046) for 1043 unique observed reflections. 1-Methylisoguanine crystallizes from aqueous solution as the dihydrate. In the crystal structure, the 1-methylisoguanine molecules are linked together in an infinite chain by N–H···N hydrogen bonds. Each of these molecules is hydrogen bonded further to two different water molecules through its carbonyl and amino substituents on the pyrimidine ring. The pair of water molecules enhances the formation of a more complete system of hydrogen bonds. The 1-methylisoguanine molecule occurs in the N(12) amino rather than imino tautomeric form.

Introduction. 1-Methylisoguanine (1*a*) (Pratt & Kraus, 1981) is the base component of the nucleoside dorisdosine (1-methylisoguanosine) (1*b*), a potent cardioactive natural product (Kim, Nachman, Pavelka, Mosher, Fuhrman & Fuhrman, 1981; Fuhrman, Fuhrman, Kim, Pavelka & Mosher, 1980; Cook, Bartlett, Gregson & Quinn, 1980). Like doridosine, 1-methylisoguanine can potentially exist as one of three tautomers represented by structures (1*a*), (2*a*), and (3*a*). This is complicated further by an additional possible tautomeric equilibrium between N(7) and N(9) in (1*a*). Therefore, we chose to determine the tautomeric preference of the base (1*a*) in the hydrated crystal by means of X-ray crystallography. While the results of the X-ray analysis cannot be directly extrapolated to describe aqueous solution behavior, it nevertheless determines absolutely the most stable tautomer of this base in the *hydrated* crystalline form. Such information may be of interest to those investigating the mode of action of the parent nucleoside, doridosine. Evidence compiled by Davies, Quinn and co-workers (Davies, Taylor, Gregson & Quinn, 1980; Norton, Gregson & Quinn, 1980) from analysis of ^{13}C NMR spin-lattice



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relaxation times of the quaternary carbons and comparison of the cardiovascular/muscle relaxant and adenylate cyclase stimulation activities of doridosine and analogs suggests that the predominant tautomer in solution is (1*b*). Interestingly, Davies and co-workers have further postulated that those purine nucleosides with the N(12) amino form are capable of cardiovascular/muscle relaxant activity whereas those nucleosides with an N(12) imino form are not.

Experimental. Colorless square prismatic crystals obtained from aqueous solution by slow evaporation; D_m not determined. Crystal dimensions 0·3 × 0·2 × 0·2 mm. Nicolet *R*3* diffractomer, monochromatic Cu $K\alpha$ radiation. θ–2θ scan, variable scan speed 4 to 30° min^{-1}. Unit-cell dimensions determined by least-squares fit to setting angles of 20 independent reflections measured on diffractometer. 1226 independent reflections measured within range $3 < 2\theta < 114°$, 1043 of which considered observed with $|F_o| \geq 2\sigma|F_o|$. During data collection 2 check reflections, monitored periodically for crystal and instrument stabilities, showed only statistical fluctuations. Intensity data corrected for background, Lorentz and polarization effects, not for absorption. Structure solved by direct-methods program *SHELXTL* (Sheldrick, 1979). Atomic coordinates, thermal parameters and scale factors refined by 'cascade matrix' least-squares method with *SHELXTL*. Function minimized $\sum w(|F_o| - |F_c|)^2$, where $w = [\sigma^2(F_o) + 0{\cdot}0001|F_o|^2]^{-1}$. Scattering factors from *International Tables for X-ray Crystallography* (1974); those of O and N corrected for anomalous dispersion. Positions of all H atoms located on difference Fourier maps and included in structure factor calculation. A formal secondary extinction correction (0·019) (Larson, 1967) included in final cycles of refinement to minimize discrepancy between observed and calculated structure factors of the most intense reflections. Least-squares refinement of parameters of the 14 non-H atoms with anisotropic temperature factors and 11 H atoms with isotropic temperature factors with no restriction on their positional parameters converged at $R = 0{\cdot}045$ and $R_w = 0{\cdot}046$. Standard deviation of unit weight is 3·01; average parameter shift in final refinement cycle $0{\cdot}04\sigma$; final difference Fourier synthesis excursions within $\pm 0{\cdot}2$ e Å^{-3}. All calculations were carried out on a Nova-3 computer.

* Reference to a company and/or product named by the Department is only for purposes of information and does not imply approval or recommendation of the product to the exclusion of others which may also be suitable.

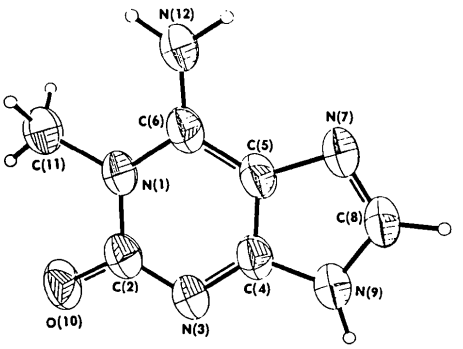

Fig. 1. Perspective view of 1-methylisoguanine with the atom numbering system. Thermal ellipsoids at the 50% probability level and H atoms with 0·1 Å radii.

Discussion. The molecular conformation of 1-methylisoguanine with atom numbering scheme and thermal ellipsoids is illustrated in Fig. 1. The final atomic coordinates, equivalent isotropic thermal parameters and their e.s.d.'s are listed in Table 1.*

The purine ring system is relatively planar; the maximum deviation is 0·017 (5) Å for C(2) and the r.m.s. deviation is 0·009 (7) Å. The substituent atoms, O(10), C(11) and N(12), are displaced from the mean plane by +0·054 (6), −0·011 (8) and −0·005 (6) Å, respectively. The bond lengths and bond angles excluding hydrogen atoms are listed in Table 2.

As in the other related purine structures, the endocyclic C—N bonds display appreciable amounts of double-bond character. The eight C—N bonds, varying from 1·301 to 1·430 Å, in the purine ring have an average of 1·36 Å which is in agreement with 1·36 Å in isoguanine sulfate monohydrate (Subramanian & Marsh, 1971), and 1·37 Å in caffeine (Sutor, 1958) and 9-methylisoguanine hydrochloride dihydrate (Banerjee, Saenger, Lesyng, Kazimierczuk & Shugar, 1978). The relatively longer C—N bond length of 1·430 Å between N(1) and C(2) is probably due to the effect of methyl substitution at N(1); similar bond lengthening is also reported for caffeine and theophylline (Sutor, 1958). The two C—C bonds of the purine ring are compatible with analogous bonds found in other purine compounds. There is a significant difference between the two exocyclic C—N bonds outside the pyrimidine ring. The one involving an sp^3 C atom [N(1)—C(11) = 1·462 Å] corresponds well with the normal C—N single bond of 1·472 (5) Å (Sutton, 1965). The other C—N bond involving a trigonally hybridized C atom [C(6)—N(12)] is considerably shorter. Shortening of this C—NH_2 bond is often observed in purine or pyrimidine compounds; the observed value of 1·317 Å compares well with those values for the analogous bond

* Lists of structure factors, anisotropic thermal parameters and H-atom coordinates have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39371 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Atom coordinates* ($\times 10^4$) *and temperature parameters* ($Å^2 \times 10^3$) *with e.s.d.'s in parentheses*

	x	y	z	U_{eq}*
N(1)	6192 (6)	8499 (3)	2439 (2)	51 (1)
C(2)	3725 (8)	9700 (3)	2605 (3)	54 (1)
N(3)	2358 (7)	9697 (3)	3635 (2)	55 (1)
C(4)	3575 (8)	8525 (3)	4474 (2)	50 (1)
C(5)	6002 (8)	7359 (3)	4378 (2)	51 (1)
C(6)	7381 (8)	7325 (3)	3305 (2)	51 (1)
N(7)	6604 (7)	6360 (3)	5429 (2)	57 (1)
C(8)	4564 (9)	6951 (4)	6117 (3)	62 (1)
N(9)	2648 (7)	8263 (3)	5594 (2)	57 (1)
O(10)	2925 (5)	10729 (2)	1744 (2)	66 (1)
C(11)	7542 (10)	8555 (4)	1287 (3)	66 (1)
N(12)	9706 (7)	6259 (3)	3115 (2)	61 (1)
Ow(1)†	7229 (7)	12764 (3)	1111 (2)	81 (1)
Ow(2)	3286 (9)	15617 (3)	1155 (2)	116 (2)

* Equivalent isotropic U defined as one third of the trace of the orthogonalized U_{ij} tensor.

† Ow water oxygen.

Table 2. *Bond lengths* (Å) *and bond angles* (°) *with e.s.d.'s in parentheses*

N(1)–C(2)	1·430 (5)	N(1)–C(6)	1·367 (4)
N(1)–C(11)	1·462 (5)	C(2)–N(3)	1·335 (5)
C(2)–O(10)	1·252 (4)	N(3)–C(4)	1·350 (4)
C(4)–C(5)	1·375 (5)	C(4)–N(9)	1·360 (5)
C(5)–C(6)	1·391 (5)	C(5)–N(7)	1·391 (4)
C(6)–N(12)	1·317 (5)	N(7)–C(8)	1·301 (5)
C(8)–N(9)	1·376 (5)		

C(2)–N(1)–C(6)	123·1 (3)	C(2)–N(1)–C(11)	118·0 (3)
C(6)–N(1)–C(11)	118·8 (3)	N(1)–C(2)–N(3)	120·7 (3)
N(1)–C(2)–O(10)	116·7 (3)	N(3)–C(2)–O(10)	122·5 (3)
C(2)–N(3)–C(4)	114·8 (3)	N(3)–C(4)–C(5)	127·4 (3)
N(3)–C(4)–N(9)	126·7 (3)	C(5)–C(4)–N(9)	105·9 (3)
C(4)–C(5)–C(6)	118·4 (3)	C(4)–C(5)–N(7)	110·9 (3)
C(6)–C(5)–N(7)	130·7 (3)	N(1)–C(6)–C(5)	115·5 (3)
N(1)–C(6)–N(12)	121·0 (3)	C(5)–C(6)–N(12)	123·5 (3)
C(5)–N(7)–C(8)	103·4 (3)	N(7)–C(8)–N(9)	114·0 (3)
C(4)–N(9)–C(8)	105·8 (3)		

in a number of other purine compounds tabulated by Watson, Sutor & Tollin (1965). The carbonyl double-bond length [C(2)–O(10)] of 1·252 Å is slightly longer than a normal C=O bond of 1·215 (5) Å (Sutton, 1965). The large difference between the internal C–N–C angles at N(1) (123·1°) and N(3) (114·8°) is noteworthy. The angle at N(1) is enlarged, presumably to compensate for the smaller endocyclic angle at the neighboring C atom C(6), which results from the double-bond character in the C(6)–N(12) bond; this is a common feature among purine structures. The average value for the internal C–N–C angles in the imidazole ring is 104·6°, which is compatible with those observed in other purine derivatives.

As reported in other related pyrimidine and purine compounds, the present structure also manifests the characteristic feature of forming a network of intermolecular hydrogen bonds in the crystal. Molecules of methylisoguanine related by the center of symmetry are bound together by two pairs of hydrogen bonds, N(9)–H···N(3) = 2·846 and N(12)–H···N(7) = 2·902 Å. The two water molecules, $W(1)$ and $W(2)$, are associated in pairs with a hydrogen bond of 2·906 Å between them. The first water molecule, $W(1)$, forms two H-bonds by sharing its two H atoms with the carbonyl groups of two different adjacent methylisoguanine molecules at 2·746 and 2·783 Å. The second water molecule, $W(2)$, forms a hydrogen bond by sharing a hydrogen atom from the amino group of the adjacent methylisoguanine molecule at 2·856 Å. The pair of water molecules also form additional hydrogen bonds with the nearby pair of water molecules in the adjacent unit cell at $W(2)$–H··· $W'(1)$ = 2·796 Å, which forms an approximately trigonal arrangement of hydrogen bonds about $W(2)$ while $W(1)$ assumes the usual distorted tetrahedral water coordination. A single hydrogen-bonded layer in the crystal structure is illustrated in Fig. 2. 1-Methylisoguanine dihydrate is highly stable at room temperature and no dehydration reaction was observed during data collection. The stability of the hydrated methylisoguanine crystals is presumably due to the presence of the number of relatively strong hydrogen bonds from solvent to the host molecule and the compactness in structural arrangement. Apart from these hydrogen bonds, all intermolecular distances are longer than the sum of the van der Waals radii.

In order to determine the tautomeric form of 1-methylisoguanine dihydrate in the solid state, it is necessary to know the positions of three H atoms among the five available positions in such a way that the valencies of all atoms are satisfied. The evidence for the distribution of these H atoms can be deduced from the observed values of the intramolecular bond lengths and the disposition of the intermolecular hydrogen bonds. The short bond length of 1·301 Å observed

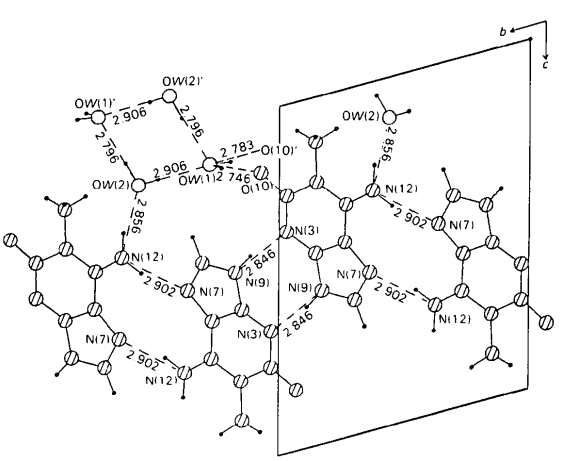

Fig. 2. 1-Methylisoguanine dihydrate crystal structure viewed along **a**, showing a single hydrogen-bonded layer. Broken lines indicate intermolecular hydrogen bonds and distances in Å; mean e.s.d. is 0·043 Å. Open circles represent hydrate molecules.

between N(7) and C(8) suggests predominantly double-bond character. O(10) is assigned as a carbonyl oxygen based on its bond length of 1·252 Å with C(2) and being capable of forming relatively strong intermolecular hydrogen bonds with one of the pair of water molecules. As shown in Fig. 2, the two water molecules are linked to each other and also to the neighboring pair of water molecules in the adjacent unit cell. Such a hydrogen-bond arrangement is only possible when $W(2)$ shares its H atoms with $W(1)$, since the latter shares its H atoms with the two symmetry-related carbonyl oxygen atoms. N(12) is presumably covalently bonded to two H atoms in order for it to be hydrogen bonded to N(7) and $W(2)$ simultaneously. A double bond is designated between C(5) and C(6) owing to its bond length of 1·391 Å, which is almost equivalent to a benzene bond [1·395 (3) Å] (Sutton, 1965). The observed distance of 2·846 Å between N(3) and N(9) suggests that they are linked by a rather strong H-bond. As a result, (2*a*) and (3*a*) can be eliminated as possible tautomers. The structure (1*a*) appears to be the stable tautomer for 1-methylisoguanine dihydrate in the solid state.

We wish to thank the WRRC Internal Competitive Grants Committee for financial support.

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Structure and Conformation of L-Tyrosyl-L-tyrosine Dihydrate, $C_{18}H_{20}N_2O_5.2H_2O$

BY M. COTRAIT AND J. P. BIDEAU

Laboratoire de Cristallographie et de Physique Cristalline associé au CNRS, LA 144, *Université de Bordeaux* I, 351 *cours de la Libération*, 33405 *Talence, France*

AND GEZINA BEURSKENS, W. P. BOSMAN AND PAUL T. BEURSKENS

Laboratorium voor Kristallografie, Universiteit Nijmegen, Toernooiveld, 6525 *ED Nijmegen, The Netherlands*

(*Received* 17 *October* 1983; *accepted* 19 *March* 1984)

Abstract. $M_r = 380{\cdot}40$, orthorhombic, $C222_1$, $a = 12{\cdot}118$ (2), $b = 12{\cdot}800$ (2), $c = 24{\cdot}523$ (3) Å, $V = 3803{\cdot}8$ Å^3, $Z = 8$, $D_m = 1{\cdot}34$, $D_x = 1{\cdot}329$ g cm^{-3}, $\bar{\lambda}$(Cu $K\alpha$) = 1·5418 Å, $\mu = 12{\cdot}7$ cm^{-1}, $F(000) = 1616$, $T = 298$ K. Final $R = 0{\cdot}037$ for 1568 independent observed reflections. The structure was solved using successively *MULTAN* and *DIRDIF* programs applied first to $C2$ space group, then extended to $C222_1$. The dipeptide exists in the crystal as a zwitterion and adopts a fully extended $\beta\beta$ conformation; χ_1 angles are close to −60 and 180° and χ_{2_1} to 60 and 120°, respectively, for the two residues. The crystallographic work was completed by a conformational analysis of the dipeptide using empirical calculations. Several stable conformations are found, the extended $\beta\beta$ being the most stable.

Introduction. The L-tyrosyl-L-tyrosine (L-Tyr-L-Tyr) dipeptide structure determination was undertaken in a general study of dipeptide structures with aromatic side chains. Unfortunately, we could not completely solve the structure, either by direct methods (*MULTAN*78, Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978), or through Patterson-function studies. We decided then to use our recent experience with *DIRDIF* (direct methods applied to difference structure factors,

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