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Nucleic-Acid Constituents.
IX.* The Crystal and Molecular Structure of 2-*N*-Methylguanosine Monohydrate

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Crystals of 2-*N*-methylguanosine monohydrate, $C_{11}H_{15}N_5O_5.H_2O$ are triclinic with space group $P1$ and Z = 1. The lattice constants at 20°C are a = 5·012 (2), b = 7·434 (6), c = 10·076 (7) Å, α = 96·18 (6), β = 101·08 (6) and γ = 113·60 (6)°. Using Mo $K\alpha$ radiation 1387 significant reflexions were measured at room temperature with a three-circle diffractometer. The structure was solved by Patterson methods and refined by least squares (R_w = 3·06%). The guanine base is *syn*-oriented ($\chi = -114{\cdot}9°$) with respect to the sugar. The ribose ring has an *S*-type [C(2′)-*endo*] conformation with pseudorotation angle P = 168·0° and $\varphi_{\max}$ = 36·4°. The exocyclic C(5′)H$_2$–O(5′)H moiety has a *trans–gauche* (g^-) orientation with respect to O(1′) and C(3′). The molecules are stacked along [100] and the packing is determined by hydrogen bonds.

Introduction

This report is a continuation of a series of earlier publications on synthesis, NMR research and crystal structure determination of nucleosides and oligonucleotides. 2-*N*-Methylguanosine is a modified nucleoside occurring in non-helical regions of tRNA, namely tRNA$^{\mathrm{Phe}}$. In contrast with inosine and 2-*N*-dimethylguanosine (Brennan, Weeks, Shefter, Rao & Sundaralingam, 1972) a Watson–Crick type hydrogen bonding between base pairs is still possible; however, the presence of an extra methyl group at N(2) in 2-*N*-methylguanosine (hereafter NMG) introduces a steric hindrance which might preclude this conformation. NMG was synthesized according to a method outlined by Gerster & Robins (1966). The numbering of atoms is indicated in Fig. 1(*a*).

Experimental

NMG was crystallized by slow evaporation of an aqueous ethanol solution. The crystals are colourless, triclinic needles elongated along [100]. The lattice constants at 20°C were determined with a three-circle diffractometer using Mo $K\alpha$ radiation (λ = 0·71069 Å): a = 5·012 (2), b = 7·434 (6), c = 10·076 (7) Å, α = 96·18 (6), β = 101·08 (6) and γ = 113·60 (6)°. Assuming the presence of one molecule per unit cell a calculated density d_{calc} = 1·493 g cm^{-3} was obtained. Afterwards the unit cell was found to contain an additional water molecule resulting in d_{calc} = 1·584 g cm^{-3}.

A needle fragment with dimensions 0·4 × 0·2 × 0·2 mm was used for collection of reflexion intensity data at 20°C. The measurements were carried out on an

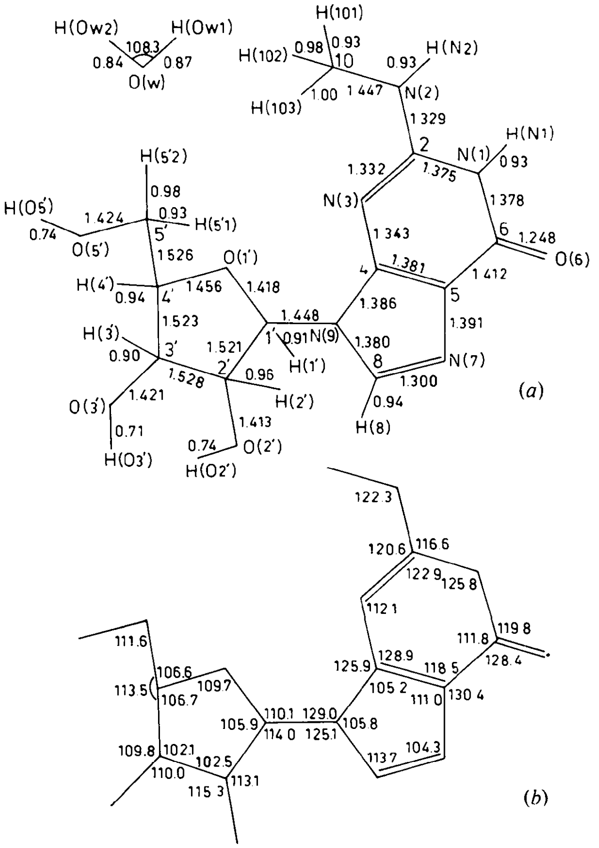

Fig. 1. The numbering of atoms in 2-*N*-methylguanosine monohydrate. (*a*) Bond distances (Å), (*b*) valence angles (°).

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* Part VIII: Hoogendorp & Romers (1978).

automatic three-circle diffractometer using graphite-monochromatized Mo $K\alpha$ radiation. A total of 1520 symmetry-independent reflexions were measured with the $\theta/2\theta$ scan in the range between $\theta_{\min} = 4$ and $\theta_{\max} = 27{\cdot}5°$. The intensities of 72 reflexions were smaller than twice the background scattering and 61 reflexions were considered not observed. The remaining 1387 reflexions were reduced to structure factors in the usual way, but no absorption correction was applied ($\mu = 1{\cdot}44$ cm^{-1}).

Refinement

The orientation of the planar guanine base was decided from a Patterson function using squared normalized structure factors as Fourier coefficients. The correct solution also gave an indication for the position of the sugar ring atoms O(1′), C(1′) and C(2′). The heavy atoms remaining as well as an extra water molecule were located in a Fourier map. The positions of all H atoms were derived from difference Fourier maps calculated after isotropic least-squares refinement of the heavy atoms. Finally the heavy atoms were refined anisotropically (9 × 9 blocks) and the H atoms isotropically (4 × 4 blocks). The scattering factors of the heavy atoms were taken from *International Tables for X-ray Crystallography* (1974) and those of H from Stewart, Davidson & Simpson (1965). The anisotropic temperature factors are defined as $\exp[-2\pi^2 \sum_{ij} a_i^* a_j^* h_i h_j U_{ij}]$, $i, j = 1, 2, 3$. The final unweighted ($R = \sum \| F_o| - |F_c\| / \sum |F_o|$) and weighted $\{R_w = [\sum w(|F_o| - |F_c|)^2 / \sum wF_o^2]^{1/2}\}$ discrepancy values are 3·39 and 3·06%.† The positional parameters of the heavy atoms are given in Table 1.

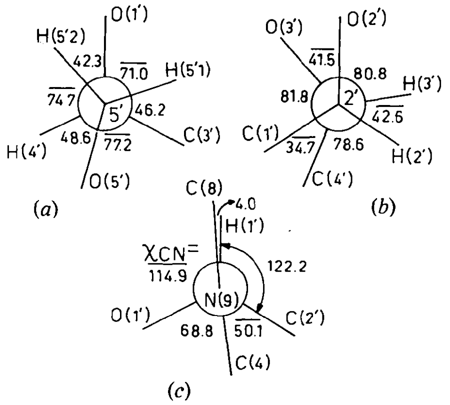

Fig. 2. Newman projections of NMG along the bonds (*a*) C(5′)–C(4′), (*b*) C(2′)–C(3′) and (*c*) N(9)–C(1′).

Table 1. *Fractional coordinates* (×10⁴) *of the heavy atoms with e.s.d.'s in parentheses*

	x	*y*	*z*
C(1′)	−3191 (5)	−1579 (3)	3665 (2)
C(2′)	−205 (5)	−1711 (3)	4087 (2)
C(3′)	1389 (5)	−156 (3)	5439 (2)
C(4′)	314 (5)	1450 (3)	5169 (2)
C(5′)	2421 (5)	3103 (3)	4583 (2)
O(1′)	−2550 (4)	458 (2)	4122 (2)
O(2′)	−555 (4)	−3674 (2)	4175 (2)
O(3′)	354 (4)	−1000 (2)	6547 (2)
O(5′)	5019 (4)	4484 (3)	5627 (2)
C(2)	11 (5)	8 (3)	2 (2)
C(4)	−3348 (5)	−1613 (3)	1111 (2)
C(5)	−5590 (5)	−2753 (3)	−72 (2)
C(6)	−4996 (5)	−2464 (4)	−1365 (2)
C(8)	−7503 (5)	−3633 (3)	1593 (2)
C(10)	5081 (6)	2567 (4)	1124 (3)
N(1)	−2100 (5)	−1049 (3)	−1225 (2)
N(3)	−541 (4)	−227 (3)	1228 (2)
N(2)	2686 (5)	1312 (3)	−85 (2)
N(7)	−8195 (4)	−4009 (3)	251 (2)
N(9)	−4594 (4)	−2202 (3)	2195 (2)
O(6)	−6728 (4)	−3295 (3)	−2540 (2)
O(*W*)	−3237 (5)	−7080 (4)	8114 (2)

Discussion of the structure

The mean positional estimated standard deviations (e.s.d.'s) are 0·0019, 0·0023, 0·0025, 0·0026 and 0·034 Å for O, N, C, O(water) and H atoms respectively. Taking into account a 40% underestimation due to the block-diagonal refinement we arrive at e.s.d.'s of 0·004, 0·0045 and 0·005 Å for the lengths of C—O, C—N and C—C bonds and at e.s.d.'s of 0·04 Å for bond lengths involving H atoms. The e.s.d.'s of valency and torsion angles are about 0·2 and 0·3°. The geometry of the molecule is depicted in Fig. 1. A number of torsion angles are listed in Table 2.

The resulting pattern of bond lengths and valency angles hardly needs comment. In agreement with earlier observations the ribose ring shows the well known anomeric effect (*cf.* de Graaff, Admiraal, Koen & Romers, 1977, and literature cited therein): the length of

Table 2. *Selected torsion angles* (°) *of NMG*

Notation	Designation	Angle	Conformation
τ_0	C(4′)–O(1′)–C(1′)–C(2′)	−18·6	
τ_1	O(1′)–C(1′)–C(2′)–C(3′)	33·6	*S*-type
τ_2	C(1′)–C(2′)–C(3′)–C(4′)	−34·7	C(2′)-*endo*
τ_3	C(2′)–C(3′)–C(4′)–O(1′)	24·7	$P = 168{\cdot}0°$
τ_4	C(3′)–C(4′)–O(1′)–C(1′)	−4·2	$\varphi_{\max} = 36{\cdot}4°$
ψ'	O(3′)–C(3′)–C(4′)–C(5′)	150·9	
ψ	C(3′)–C(4′)–C(5′)–O(5′)	282·8	g^- (*trans–gauche*)
	O(1′)–C(4′)–C(5′)–O(5′)	165·6	
χ	O(1′)–C(1′)–N(9)–C(8)	−114·9	*syn*-orientation
	O(2′)–C(2′)–C(3′)–O(3′)	−41·5	

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† Lists of structure factors, thermal parameters and positional parameters for H atoms have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33636 (7 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 3. *The geometry of the 2-N-methylguanine moiety*

Angles α are in degrees, distances l in Å. σ = estimated standard deviation; $S = [n^{-1}(n-1)^{-1}\,\Sigma_i(q_i - q_{\rm AV})^2]^{1/2}$. S is given in numbers of the last digit, within parentheses. The average values $\langle\alpha\rangle$ and $\langle l\rangle$ are computed from guanosine HBr [two independent N(7)-protonated molecules: Tougard & Chantot, 1974], disodium deoxyguanosine-5′-phosphate (Young, Tollin & Wilson, 1974), guanosine-5′-phosphate (Murayana, Nagashima & Shimizu, 1969), guanosine dihydrate and inosine dihydrate (both compounds, two independent molecules: Thewalt, Bugg & Marsh, 1970), 2-*N*-dimethylguanosine (Brennan, Weeks, Shefter, Rao & Sundaralingam, 1972), sodium guanosine cyclic-3′,5′-monophosphate sodium tetrahydrate (Chwang & Sundaralingam, 1974) and this work.

	α	$\langle\alpha\rangle S$
N(7)—C(8)—N(9)	113·7	112·3 (6)
C(6)—N(1)—C(2)	125·8	125·0 (2)
N(1)—C(2)—N(2)	116·5	116·4 (2)
N(1)—C(2)—N(3)	122·8	124·0 (4)
N(2)—C(2)—N(3)	120·6	120·0 (2)
C(2)—N(3)—C(4)	112·1	112·1 (3)
N(3)—C(4)—C(5)	128·8	128·2 (2)
N(3)—C(4)—N(9)	125·9	125·9 (3)
N(9)—C(4)—C(5)	105·2	105·8 (2)
C(4)—C(5)—C(6)	118·5	119·4 (2)
C(4)—C(5)—N(7)	111·0	109·9 (6)
N(7)—C(5)—C(6)	130·4	130·7 (4)
C(5)—C(6)—O(6)	128·4	128·6 (3)
C(5)—C(6)—N(1)	111·8	111·1 (1)
N(1)—C(6)—O(6)	119·8	120·2 (2)
C(5)—N(7)—C(8)	104·3	105·3 (6)
C(8)—N(9)—C(1)	125·1	126·2 (4)
C(8)—N(9)—C(4)	105·8	106·6 (4)
C(1′)—N(9)—C(4)	129·0	126·9 (6)

	l	$\langle l\rangle S$
N(1)—C(2)	1·375	1·372 (4)
C(2)—N(2)	1·329	1·337 (2)
C(2)—N(3)	1·331	1·329 (8)
C(4)—N(3)	1·342	1·350 (3)
C(4)—C(5)	1·381	1·383 (3)
C(5)—C(6)	1·411	1·421 (4)
C(6)—O(6)	1·248	1·232 (2)
C(6)—N(1)	1·378	1·403 (4)
C(5)—N(7)	1·391	1·388 (5)
N(7)—C(8)	1·300	1·308 (5)
C(8)—N(9)	1·380	1·367 (6)
N(9)—C(4)	1·386	1·375 (4)
N(9)—C(1′)	1·448	1·466 (5)

$\sigma(\alpha) = 0{\cdot}2$

$\sigma(l) = 0{\cdot}004_5$

bond C(4′)—O(1′) (1·456 Å) is significantly greater than the length of bond O(1′)—C(1′) (1·418 Å). A comparison of the 2-*N*-guanine ring system with guanine, hypoxanthine and 2-*N*-dimethylguanine moieties observed in known structures (Table 3) shows only a few important deviations, namely the carbonyl bond C(6)=O(6) (1·248 Å), the glycoside bond N(9)—C(1′) (1·448 Å) and the angle C(1′)—N(9)—C(4) (129·0°) which deviate significantly from the mean values on a level better than 99·5%. Acceptance of two hydrogen bonds by O(6) may result in reduced double-bond character of C(6)=O(6) and an increase of its length. Lo, Shefter & Cochran (1975) have analysed the N-glycosyl bond lengths occurring in 36 purine and pyrimidine analogs of nucleosides and nucleotides. They observed a variation of the bond length between 1·436 and 1·519 Å and postulated a linear relationship between the torsion angle φ[N—C(1′)—O(1′)—C(4′)] and bond length l[N—C(1′)]. However, using the values of this dihedral angle of NMG and their equation (1) we calculate the value 1·466 Å for bond length N(9)—C(1′).

With the exception of O(6) the 2-*N*-methylguanine base is quite planar within experimental error (see Table 4). The methylamino group C(10)—N(2)—H(N2) is only slightly displaced from this plane, the largest deviation being −0·030 Å for C(10). In the case of 2-*N*-dimethylguanosine (DMG: Brennan, Weeks, Shefter, Rao & Sundaralingam, 1972) the corresponding deviations (Table 4) for C(10) and C(11) in the group C(10)—N(2)—C(11) from the least-squares plane are −0·031 and −0·094 Å, respectively. In both compounds O(6) and the ribose atom C(1′) deviate significantly from the least-squares planes.

Table 4. *Distances* (Å) *from least-squares planes through atoms of NMG* (*2-N-methylguanosine*) *and DMG* (*2-N-dimethylguanosine*)

The asterisks indicate the atoms used for the calculation of the planes.

	NMG	NMG	DMG
N(1)	0·006*	−0·001*	0·009*
C(2)	0·001*	0·003*	0·004*
N(2)	0·003*	0·007	−0·041
N(3)	−0·011*	−0·004*	−0·014*
C(4)	−0·002*	0·001*	−0·003*
C(5)	0·016*	0·011*	0 *
C(6)	0·005*	−0·007*	−0·003*
O(6)	−0·018*	−0·037	−0·035
N(7)	0·008*	0·001*	−0·004*
C(8)	−0·005*	−0·005*	−0·002*
N(9)	−0·005*	0·001*	−0·014*
H(8)	0·02	0·02	
H(N1)	0·03	0·02	
H(N2) or C(11)	−0·02	−0·02	−0·094
C(10)	−0·043	−0·030	−0·031
C(1′)	−0·054	−0·059	−0·053

Table 5. *Intermolecular distances d*(Å) *in NMG*

The first atom refers to the reference molecule I at *x*,*y*,*z*. H-accepting and other atoms are located in translated molecules. The distances *d*′(Å) refer to bonds between H and H-accepting atoms.

Molecule	Operation			Bond	*d*	*d*′
I	*x*,	*y*,	*z*	O(*W*)–H···O(5′)	3·000	2·16
II	*x*,	*y*,	−1 + *z*	N(2)–H···O(*W*)	2·792	2·29
II	*x*,	*y*,	−1 + *z*	N(1)–H···O(3′)	2·757	1·87
III	1 + *x*,	*y*,	1 + *z*	O(3′)–H···O(6)	2·778	2·08
IV	1 + *x*,	1 + *y*,	1 + *z*	O(5′)–H···O(6)	2·833	2·10
V	−1 + *x*,	−1 + *y*,	*z*	O(2′)–H···O(5′)	2·861	2·12
Other contacts						
III	1 + *x*,	*y*,	1 + *z*	O(*W*)···N(1)	3·331	
VI	1 + *x*,	*y*,	*z*	H(2′)···H(8)	2·53	
VI	1 + *x*,	*y*,	*z*	H(2′)···H(1′)	2·73	
VII	*x*,	1 + *y*,	*z*	H(5′2)···H(O2′)	2·59	
VII	*x*,	1 + *y*,	*z*	H(5′2)···O(2′)	2·42	
VIII	*x*,	*y*,	1 + *z*	O(*W*)···C(10)	3·310	

The conformation about the bonds C(5′)–C(4′), C(2′)–C(3′) and N(9)–C(1′) is depicted in Fig. 2. The overall shape of the molecule can be viewed in Fig. 3. The ribose ring has an *S*-type conformation with C(2′) *endo* with respect to the C(5′)–O(5′) side group. It is characterized by a phase angle of pseudorotation $P = 168{\cdot}0°$ and a maximum puckering angle $\varphi_{\max} = 36{\cdot}4°$ (Altona & Sundaralingam, 1973). According to Fig. 2 and the data in Table 2 the orientation of the side group C(5′)–O(5′)H is *trans–gauche* (g^-). The usual conformation of this group is, however, *gauche–gauche* (g^+) for *S*-type ribose rings. Interestingly the conformation of the side group is *gauche–trans* (*t*) in the *S*-type nucleoside DMG.

Packing

Fig. 3 is one layer of molecules in a projection along [100]. The dashed lines with arrows indicate hydrogen bridges from donating towards accepting atoms. Since all translational operations (see Table 5) are involved in the formation of these bonds, the molecules are closely packed. The water molecule donates a weak hydrogen bond to O(5′) and accepts a weak bond from N(2). Furthermore it has contacts with C(10) and N(1). Its role seems to be confined to filling the gaps between layers of molecules parallel to (010). Since N(2) is able to donate a weak hydrogen bond to O(*W*) we cannot exclude the possibility of a Watson–Crick type base-pairing between cytosine and 2-*N*-methylguanine. In principle NMG might even occur in helical regions of RNA.

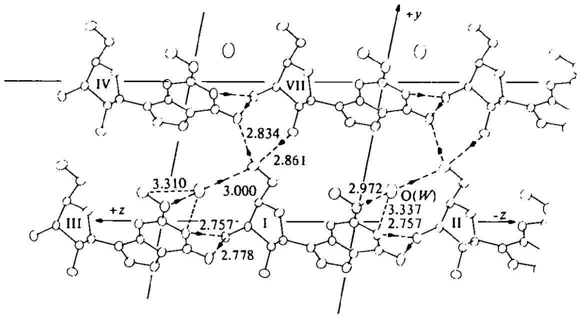

Fig. 3. Projection of one layer of NMG molecules along *a**.

The bond C(1′)–N(9) runs roughly parallel to [100]. Rotation of the ribose ring by ~165° (clockwise) about this bond, necessary to obtain the *anti*-configuration with $\chi_{\mathrm{CN}} \sim 50°$, disrupts the hydrogen bridges between O(5′) and the atoms O(6) and O(2′) in the next layer parallel to (010). A similar disruption of the packing would occur if we were to rotate the bond C(5′)–O(5′) by ~120° (anticlockwise) about C(5′)–C(4′) in order to obtain the normal g^+ orientation.

The twelvefold coordination of the molecules is completed by hydrophobic contacts between H atoms in the direction [100] and between H and O(2′) and H(O2′) in the direction [010].

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