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The Structure of Deuterated Cytosine Monohydrate at 82 K by Neutron Diffraction

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Abstract

At 82 K, deuterated cytosine monohydrate ($C_4H_2D_3$-$N_3O.D_2O$) is monoclinic, space group $P2_1/c$, with four molecules per unit cell and lattice parameters $a = 7.713$ (1), $b = 9.830$ (4), $c = 7.505$ (4) Å and $\beta = 100.52$ (2)°. A structure refinement to $R_w(F^2) = 0.049$ has been carried out using neutron intensities for 1993 reflections measured at wavelength $\lambda = 0.9094$ (1) Å and 270 at $\lambda = 1.0441$ (1) Å. At the shorter wavelength there appeared to be double Bragg reflection of 2λ neutrons from the Be monochromator. All atoms, particularly H(D), are more accurately located than in previous X-ray determinations at 298 K, to give

bond lengths with e.s.d. 0·001 Å (0·002 Å for N—D, C—H and O—D). The thermal expansion of the crystal lattice from 82–292 K has been related to the molecular packing and hydrogen-bonding arrangement.

greater detail and to locate the positions of all nuclei with greater accuracy in connection with an electronic charge density study of the structure at low temperature.

Introduction

The structure of cytosine monohydrate (Fig. 1) at room temperature was first determined from photographic X-ray intensity data by Jeffrey & Kinoshita (1963). McClure & Craven (1973), hereafter MC, redetermined the structure with greater accuracy using diffractometer data in order to resolve a seeming discrepancy in the bond length of the carbonyl group in anhydrous (Barker & Marsh, 1964) and hydrated cytosine. Also, Neidle, Achari & Rabinovich (1976) have used cytosine monohydrate as a test in their check on the accuracy of structural parameters obtained from intensity data recorded photographically and integrated with a scanning densitometer.

The present investigation by neutron diffraction was carried out to describe the hydrogen-bonding scheme in
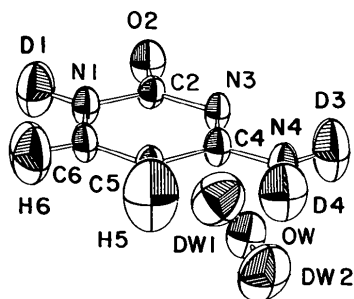

Fig. 1. Atomic nomenclature in deuterated cytosine monohydrate, and thermal ellipsoids with envelopes at the 99% probability level (Johnson, 1976).

Experimental

Crystals were obtained by thee cycles of evaporation from a solution of cytosine in D_2O. They grew as platelets tabular on (100) and elongated along the b axis. Most crystals large enough for neutron diffraction were found to be twinned on the (100) plane. The small crystal [1·4 (1) mm³] finally chosen was shown to be untwinned by means of X-ray Laue photographs, and by extensive ω and $\theta/2\theta$ scans with the neutron diffractometer. The crystal was mounted approximately along its b direction on a hollow Al pin, inserted under helium atmosphere into an Al can and the whole assembly was fastened to the cold finger of a closed-cycle helium cryostat.* Temperatures were corrected (2·6 K) by a calibration based on the observed magnetic transition of FeF_2 (78·4 K; Hutchings, Shulhof & Guggenheim, 1972). The cryostat was mounted on the χ circle of the neutron diffractometer at port H6M of the Brookhaven High Flux Beam Reactor. Cooling to 90 K took place over a period of three hours.

The neutron cell parameters at each temperature (Table 1) were determined by a least-squares fit to $\sin^2 \theta$ values for 30 (19 at 295 K) reflections (43° < 2θ < 60°). The X-ray cell parameters at the temperature of the X-ray data collection (Weber & Craven, 1979) are also in Table 1. The neutron intensity data were collected at 82 K because this gave the minimum value

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* Air Products and Chemicals, Inc., DISPLEX® Model CS-202.

Table 1. *Crystal data for deuterated cytosine monohydrate*

Monoclinic, $P2_1/c$; $Z = 4(C_4H_2D_3N_3O.D_2O)$ per unit cell

T (K)	D^*	a (Å)	b (Å)	c (Å)	β (°)	V (Å³)	λ (Å)
Neutron diffraction measurements							
72	8	7·711 (2)	9·834 (4)	7·505 (3)	100·54 (2)	560 (2)	0·9094 (1)
77	3	7·715 (2)	9·829 (4)	7·505 (3)	100·56 (2)	560 (2)	0·9094 (1)
81	10	7·711 (1)	9·834 (4)	7·508 (2)	100·52 (2)	560 (2)	0·9094 (1)
82	2	7·713 (4)	9·830 (4)	7·505 (4)	100·52 (2)	560 (2)	0·9094 (1)
87	10	7·718 (1)	9·828 (3)	7·510 (2)	100·52 (2)	560 (2)	0·9094 (1)
92	18	7·718 (2)	9·834 (5)	7·511 (3)	100·45 (2)	561 (2)	0·9094 (1)
182	–	7·745 (1)	9·846 (4)	7·563 (3)	100·10 (2)	568 (2)	1·0441 (2)
295	–	7·813 (5)	9·842 (8)	7·645 (6)	99·68 (4)	580 (4)	1·0441 (2)
X-ray diffraction measurement (Weber & Craven, 1979)							
		7·714 (1)	9·825 (1)	7·506 (2)	100·52 (1)	559 (1)	Mo $K\alpha_1$

* $D = \sum_{i=1}^{4} [a(N)_i - a(X)_i]^2/[\sigma^2(N)_i + \sigma^2(X)_i]$ where a_i and σ_i are the lattice parameters and their e.s.d.'s as determined by the present neutron (N) measurements and the X-ray (X) measurements of Weber & Craven (1979).

for the discriminating function D as defined in Table 1.*

Integrated intensities were measured for reflections in two octants of reciprocal space ($\pm h,k,l$). To confirm the diffraction symmetry ($2/m$), selected reflections in other octants were measured as well. Averaging the equivalent reflections yielded an agreement factor $\sum_H w(\langle F_o^2\rangle - F_o^2)/(\sum_H wF_o^2) = 0.007$. There were no significant variations in the intensities of selected reference reflections throughout the data collection.

In previous related structure determinations with this neutron facility, such as parabanic acid (Craven & McMullan, 1979), a neutron beam of wavelength ~ 1.05 Å was obtained by reflection from the (002) planes of a beryllium crystal. In the present work, the beryllium crystal was tuned to reflect neutrons with $\lambda = 0.9094$ (1) Å, as determined by least-squares fit to $\sin^2\theta$ data for a standard KBr crystal ($a_0 = 6.600$ Å). The shorter neutron wavelength permitted intensity data collection with $(\sin\theta/\lambda)_{max} = 0.90$ Å^{-1}, extending closer to the limiting value (1.0 Å^{-1}) obtained in the X-ray data collection (Mo $K\alpha$ radiation).

However, in the least-squares refinement of the structure parameters based on the neutron data, there were about 40 reflections with even indices ($2h,2k,2l$) for which the F_{obs}^2 value was much greater than F_{calc}^2 (up to 60σ). It was noted that the discrepancies were greater when the F_{obs}^2 value was large for the corresponding hkl reflection. Such differences also occurred in a refinement of 9-methyladenine based on neutron data collected under similar experimental conditions (McMullan, Benci & Craven, 1980). It appeared that the neutron beam reflected from the Be crystal contained both λ and 2λ components. The implied reflection of 2λ neutrons from the space-group-absent (001) of Be could arise from a double

* The temperature of the crystal during X-ray data collection could not be accurately measured in a direct way. From the match of X-ray and neutron cell parameters (Table 1), it is estimated that the X-ray intensity data were collected at 82 ± 5 K.

Bragg reflection, as proposed by Hay (1959). Further data which support this explanation are described by McMullan, Benci & Craven (1980). All 354 $2h,2k,2l$ reflections were rejected from the structure refinement and 243 of these were remeasured together with 27 other reflections at a longer wavelength, $\lambda = 1.0446$ (2) Å. Table 2 summarizes the experimental conditions for both data sets.

When the intensity profile of each reflection was examined, several low-angle reflections were found to display broad shoulders or skewed features, which were attributed to scattering from the aluminum parts of the diffractometer or the cryostat. These reflections were omitted from the refinement. The range of integration was a variable determined from the plots of the scans. The integrated intensities were corrected for absorption by an analytical method (de Meulenaer & Tompa, 1965; Templeton & Templeton, 1973). The mass-absorption coefficient for H was assumed to have the value (23.9×10^{-4} m^2 g^{-1}) determined experimentally for barbital II (McMullan, Fox & Craven, 1978).

The atomic parameters of MC were taken as the initial values in the refinement of the structure. A full-matrix least-squares procedure was used to minimize $\sum w(F_{obs}^2 - k^2 F_{calc}^2)^2$ using a modified version of the computer program by Busing, Martin & Levy (1962). The weights were assumed to be $w = 1/\sigma^2(F_{obs}^2) = [\sigma^2 + (0.01F_{obs}^2)^2 + 0.27]^{-1}$ where σ^2 is the variance in F^2 due to counting statistics. This was found to give a constant value of $\Delta F^2/\sigma(F_{obs}^2)$ over the whole range of $\sin\theta/\lambda$. Reflections with $F_{obs}^2 < 0$ were included in the refinement to avoid a shifted bias in the results (Hirshfeld & Rabinovich, 1973). All positional

Table 3. *Nuclear parameters for deuterated cytosine monohydrate*

Values of neutron scattering lengths (b) without e.s.d.'s are taken from Koester (1977). The positional parameters are $\times 10^5$. E.s.d.'s given in parentheses refer to the least significant digit in the parameter value.

	b(fm)	x	y	z
N(1)	9.30 (5)	8590 (5)	412 (7)	21869 (10)
C(2)	6.648	226 (12)	12456 (11)	23993 (13)
O(2)	5.803	−14816 (14)	11988 (13)	28342 (16)
N(3)	9.27 (5)	7904 (9)	24405 (8)	21080 (11)
C(4)	6.648	23622 (13)	24300 (11)	15689 (14)
N(4)	9.33 (6)	31121 (9)	36152 (7)	13098 (11)
C(5)	6.648	32256 (13)	11843 (11)	12585 (14)
C(6)	6.648	24276 (13)	138 (10)	16102 (14)
D(1)	6.18 (5)	2545 (18)	−8613 (13)	24390 (20)
D(3)	6.25 (6)	25285 (19)	44991 (14)	15881 (21)
D(4)	6.22 (5)	42900 (17)	36103 (15)	8911 (21)
H(5)	−3.72 (5)	44610 (33)	11967 (29)	7743 (39)
H(6)	−3.64 (5)	29780 (34)	−9838 (24)	14278 (38)
O(W)	5.803	−35348 (15)	29108 (13)	2610 (17)
D(W1)	6.17 (6)	−28248 (17)	23746 (16)	12053 (19)
D(W2)	6.12 (5)	−27173 (19)	32368 (15)	−4733 (21)

Table 2. *Experimental data*

Monochromator	Be(002) in reflection geometry	
Scan mode	θ–2θ steps	
Average scan rate	4.6 min/reflection	
Scan range	3.60° for $2\theta \le 45°$,	
	(7.90 tan θ − 0.3)° for $2\theta > 45°$	
Reference reflections	102, 44$\bar{6}$, 7$\bar{4}$2	
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.829	
Number of reflections used in refinement	2263	
Wavelength (Å)	0.9094 (1)	1.0441 (1)
Number of reflections measured	2785	346
Number of independent reflections	2024	270
Mass-absorption coefficient (mm^{-1})	0.0514	0.0610
Transmission factor	0.949–0.975	0.946–0.969

and anisotropic thermal parameters were varied in the full-matrix least-squares refinement, together with two scale factors, one for each wavelength in the data collection. In the last two cycles an isotropic extinction parameter (Zachariasen, 1968) and the coherent scattering lengths for N and H atoms were varied as well. The refinement converged (shifts $<0.2\sigma$) with an agreement factor $R_w(F^2) = (\sum w|F_{obs}^2 - F_{calc}^2|^2/\sum w^2 \times F_{obs}^4)^{1/2} = 0.049$ (unweighted: 0.043), and a goodness of fit $S = [\sum w| F_{obs}^2 - F_{calc}^2|^2/(n_{obs} - n_{param})]^{1/2} = 0.919$. The extinction was moderate, giving $g = 327(40)$ rad^{-1}. The reflection most affected was 102 for which the correction was $0.89 F_{calc}^2$. A refinement of the first data set with the extinction formalism proposed by Becker & Coppens (1974) led to no significant changes in the nuclear parameters. Nuclear positional parameters and scattering lengths are in Table 3.* The initial values of the neutron scattering lengths were $b = -3.74$ fm† for H and 6.67 fm for D nuclei (Koester, 1977). At the five exchangeable hydrogen sites, there are no differences in b values after refinement. The average value of 6.19 (8) fm has been used to calculate the D/H exchange ratio from $6.67r - 3.74(1 - r) = 6.19$, giving $r = 0.954$ (8). Within the error estimates, no exchange occurs at H(5) and H(6). The r.m.s. value for b_N after refinement is 9.30 (2) fm. This and other values obtained from related structure determinations, 9.237 (5) fm in barbital II (McMullan, Fox & Craven, 1978) and 9.240 (6) fm in perdeuterated parabanic acid–urea (Weber, Ruble, Craven & McMullan, 1980), are smaller than the scattering length for N of 9.36 (2) fm given by Koester (1977).

Discussion

Bond lengths and angles (Fig. 2) are uncorrected for thermal motion since this effect is believed to be small. On the assumption that the cytosine molecule without H and D atoms is a rigid body (Schomaker & Trueblood, 1968), the librational corrections* were less than 0.001 Å in bond lengths and 0.01° in angles. There is good agreement with the room-temperature librationally corrected X-ray bond lengths and angles, except for the C(5)—C(6) bond length. The MC value of 1.333 (2) Å, which becomes 1.338 Å after librational correction, remained unchanged in a new refinement based on the MC data, in which we included an

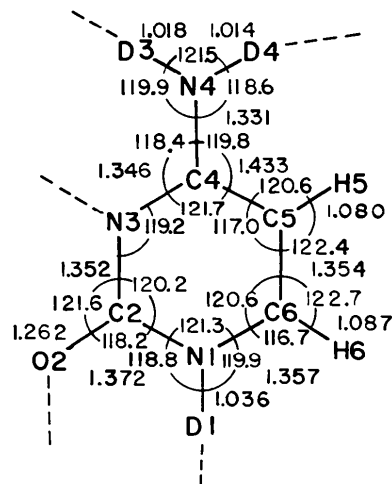Fig. 2. Deuterated cytosine bond lengths (Å) and angles (°), uncorrected for thermal motion. The e.s.d.'s in bond lengths are 0.001 Å, or 0.002 Å for C—H, N—D. E.s.d.'s in bond angles are 0.1° or less.

isotropic extinction parameter (Becker & Coppens, 1974). Using X-ray data with $\sin\theta/\lambda \geq 0.65$ Å^{-1} collected at 82 K (Weber & Craven, 1979), the C(5)—C(6) bond length refined to the value 1.348 (5) Å, intermediate between the neutron value of 1.354 (1) Å and the corrected MC value, 1.338 Å. We cannot explain the apparent discrepancy, although we doubt that it is real.

Conformational details involving slight puckering of the molecular framework* are in close agreement with the room-temperature X-ray results. The amino group is slightly twisted from the ring plane to give a torsion angle D(3)—N(4)—C(4)—N(3) of 3.4 (5)°.

The water O—D bond lengths [0.969 (2), 0.965 (2) Å] are equal within experimental error, while the D—O—D angle, 105.0 (2)°, is close to the value 104.5° obtained from the infrared spectrum for free D_2O in its vibrational ground state (Kuchitsu & Bartell, 1962). The water O atom is 0.18 Å from the plane of the three atoms to which it is hydrogen bonded (Table 4). The hydrogen bonds in which water is donor make an angle $O(2)\cdots O(W)\cdots O(2)'$ of 108.8 (1)°, only

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* See deposition footnote.

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† The femtometre (1 fm = 10^{-15} m) is not to be confused with the Fermi unit.

Table 4. Hydrogen bonds

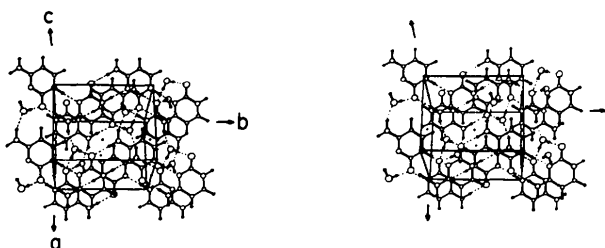| X—D$\cdots Y$	X–D (Å)	D$\cdots Y$ (Å)	$X\cdots Y$ (Å)	$\angle X$–D$\cdots Y$ (°)
N(1)—D(1)$\cdots$N(3)	1.036 (1)	1.912 (2)	2.947 (2)	178.1 (2)
N(4)—D(3)$\cdots$O(2)	1.018 (1)	1.940 (2)	2.957 (2)	178.3 (2)
N(4)—D(4)$\cdots$O(W)	1.014 (1)	1.950 (2)	2.920 (2)	159.4 (2)
O(W)—D(W1)$\cdots$O(2)'	0.969 (2)	1.856 (2)	2.821 (2)	173.9 (2)
O(W)—D(W2)$\cdots$O(2)"	0.965 (2)	1.809 (2)	2.765 (2)	170.4 (2)

Fig. 3. Stereoview of the crystal structure of deuterated cytosine monohydrate normal to the plane of the cytosine molecules, which is (103). Circles in order of decreasing size represent O, N, C and H(D) atoms. Dashed lines represent the hydrogen bonds, and dots mark the crystallographic inversion centers.
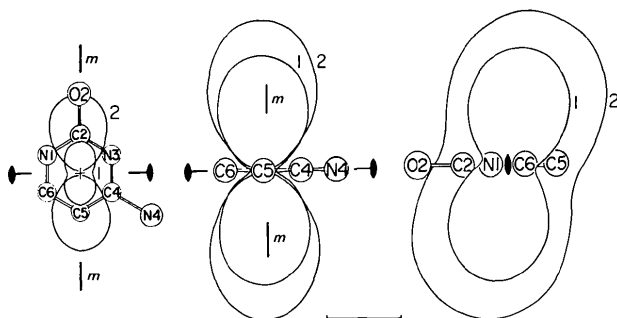

Fig. 4. Polar graphs of the mean thermal-expansion coefficient with respect to the orientation of a cytosine molecule. The orientation of the other three molecules can be derived from the crystallographic point-group symmetry $2/m$. Curve 1: 82–182 K; curve 2: 182–295 K. The scale represents 7×10^{-5} deg^{-1}.

3·8° larger than the D—O—D bond angle. Except for N···N which is unchanged, the N···O and O···O hydrogen-bond distances are from 0·02 to 0·03 Å shorter than the X-ray room-temperature values.*

The stereoview of the crystal structure (Fig. 3) complements the projections along a and b shown by Jeffrey & Kinoshita (1963). The mean thermal-expansion tensor for the crystal lattice† has been obtained from the cell constants in Table 1. The corresponding elongation per unit length per degree is shown with respect to the crystal point symmetry in Fig. 4. As expected, the largest thermal expansion is close to the normals of the cytosine ring planes, and this is also close to the preferred directions for the individual atomic thermal vibrations (Fig. 1). The smallest

* The $W(m)$···O(2) hydrogen-bond distance of 2·99 Å in MC (Fig. 1) should be 2·85 Å.

† See deposition footnote.

expansion is along **b**, presumably due to the restraining effect of the hydrogen bonding which links cytosine molecules in ribbons along this direction.

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