

Table 2. Bond distances (Å) and angles (°)

C(1)—C(2)	1.510 (4)	N(6)—C(14)	1.472 (3)
C(1)—O(8)	1.224 (3)	C(11)—C(12)	1.478 (5)
C(1)—N(7)	1.341 (3)	C(12)—C(13)	1.405 (6)
C(2)—C(3)	1.539 (3)	C(13)—C(14)	1.506 (6)
C(3)—C(4)	1.426 (3)	N(7)—C(15)	1.471 (3)
C(3)—O(9)	1.231 (3)	N(7)—C(18)	1.452 (3)
C(4)—C(5)	1.387 (3)	C(15)—C(16)	1.508 (5)
C(5)—N(6)	1.333 (3)	C(16)—C(17)	1.498 (5)
C(5)—C(10)	1.495 (3)	C(17)—C(18)	1.527 (5)
N(6)—C(11)	1.472 (3)		
C(2)—C(1)—N(7)	117.1 (2)	C(11)—N(6)—C(14)	110.7 (2)
C(2)—C(1)—O(8)	120.9 (2)	N(6)—C(11)—C(12)	103.9 (2)
N(7)—C(1)—O(8)	122.0 (2)	C(11)—C(12)—C(13)	109.8 (3)
C(1)—C(2)—C(3)	113.1 (2)	C(12)—C(13)—C(14)	108.2 (3)
C(2)—C(3)—C(4)	113.7 (2)	C(13)—C(14)—N(6)	104.0 (2)
C(2)—C(3)—O(9)	118.4 (2)	C(1)—N(7)—C(15)	126.4 (2)
C(4)—C(3)—O(9)	127.9 (2)	C(1)—N(7)—C(18)	121.5 (2)
C(3)—C(4)—C(5)	127.1 (2)	C(15)—N(7)—C(18)	112.0 (2)
C(4)—C(5)—N(6)	120.8 (2)	N(7)—C(15)—C(16)	103.6 (3)
C(4)—C(5)—C(10)	123.1 (2)	C(15)—C(16)—C(17)	104.4 (3)
N(6)—C(5)—C(10)	116.1 (2)	C(16)—C(17)—C(18)	104.2 (3)
C(5)—N(6)—C(11)	123.7 (2)	C(17)—C(18)—N(7)	103.2 (3)
C(5)—N(6)—C(14)	125.6 (2)		

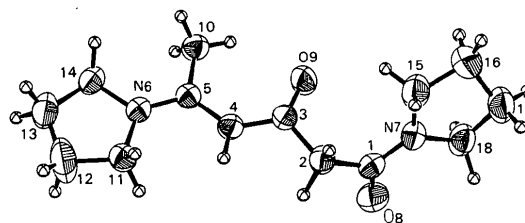


Fig. 1. View of the molecule, (3), showing the numbering scheme and the vibrational ellipsoids (50% probability level).

C(5) is in configuration *Z* (or *cis*) with respect to the carbonyl group at C(3), and the structure is stabilized by two intramolecular hydrogen bonds between the N(6) and N(7) H atoms and the carbonyl O atom at C(3). The molecule will then undergo cyclization by attack of N(6) on C(1) to produce the 2-pyridone. In (3) the pyrrolidine group at C(5) is in configuration *E* (or *trans*) with respect to the carbonyl bond at C(3). A *Z* arrangement is excluded on steric grounds.

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## Structure of 5-Methylcytosine Hydrochloride

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**Abstract.**  $C_5H_8N_3O^+ \cdot Cl^-$ ,  $M_r = 161.6$ , monoclinic,  $P2_1/c$ ,  $a = 6.431(1)$ ,  $b = 16.132(2)$ ,  $c = 7.030(1)$  Å,  $\beta = 97.33(1)^\circ$ ,  $V = 723.29$  Å<sup>3</sup>,  $Z = 4$ ,  $D_x = 1.48$ ,  $D_m = 1.49$  Mg m<sup>-3</sup>,  $\lambda(Cu K\alpha) = 1.5418$  Å,  $\mu = 0.423$  mm<sup>-1</sup>,  $F(000) = 336$ ,  $T = 295$  K,  $R = 0.042$  for 1146 observed reflections with  $I > 3\sigma(I)$ . The cytosine base is protonated at N(3). The crystal structure is stabilized by hydrogen bonds of the type N(3)—H...Cl

and direct electrostatic interactions between Cl and atoms of the base. Molecules related by the *c*-glide are nearly parallel (angular deviation  $\approx 17^\circ$ ) and are separated by approximately 3.5 Å. A comparison of the stacking interactions observed in the present structure and in related molecules suggests that 5-methylation of the cytosine base generally results in reduced ring overlap.

**Introduction.** 5-Methylation of cytosine bases in eukaryotic DNA has been proposed to function in many ways such as control of transcription, establishment of preferred sites of mutation and increasing the stability of DNA against enzymatic degradation (Ehrlich & Wang, 1981). We report here the structure of 5-methylcytosine hydrochloride. Crystal structures of such compounds are useful in studying structural features such as the stacking of bases, which has relevance to the photodimerization reactions of these bases (Smith, 1977) induced by UV light.

**Experimental.** Crystals were grown from an aqueous solution of the compound (Sigma Chemicals) by direct evaporation. They were unstable under atmospheric conditions and were sealed in a thin-walled capillary tube. The density was measured by flotation in  $\text{CCl}_4/\text{acetone}$ . Space group and cell parameters determined by rotation and Weissenberg methods; cell dimensions refined by least squares using 25 reflections,  $10 \leq \theta \leq 29^\circ$ , on a CAD-4 Enraf-Nonius diffractometer. Intensity data, from a crystal of dimensions  $0.3 \times 0.3 \times 0.1$  mm, was collected up to  $(\sin \theta)/\lambda \leq 0.626 \text{ \AA}^{-1}$  with  $\omega$ - $2\theta$  scans using Ni-filtered  $\text{Cu K}\alpha$  radiation. Three standard reflections (310, 410, 530) monitored at regular intervals, crystal stable to X-rays. Analytical absorption correction (North, Phillips & Mathews, 1968) was applied, transmission factor varied from 0.649 to 0.997. Index range for unique data  $-8 \leq h \leq 8$ ,  $0 \leq k \leq 20$ ,  $0 \leq l \leq 8$ . A total of 2589 reflections from the octants  $hkl$ ,  $\bar{h}kl$ ,  $h\bar{k}l$  and  $\bar{h}\bar{k}l$  collected, symmetry-related reflections averaged with a merging  $R$  factor on  $F_o$  of 0.025. Of the 1547 unique reflections, 1146 were considered to be observed [ $I > 3\sigma(I)$ ]. Structure solved by direct methods using *MULTAN80* (Germain, Main & Woolfson, 1971). All H atoms located from difference electron density map. Full-matrix least squares on  $F_o^2$  using *SHELX76* (Sheldrick, 1976), with non-hydrogen atoms refined anisotropically and hydrogen atoms isotropically, converged at  $R = 0.042$ . Individual weights  $w \propto 1/[\sigma^2(F) + 0.001(F)^2]$ ,  $wR = 0.045$ , maximum  $\Delta/\sigma = 0.02$ ;  $\Delta\rho$  in final difference map within  $+0.28$  and  $-0.65 \text{ e \AA}^{-3}$ . The atomic scattering factors were as supplied in *SHELX76*. Calculations were performed using the Enraf-Nonius (1979) *SDP* on a PDP11/44 computer.

**Discussion.** Final positional and thermal parameters for the atoms are given in Table 1.\* Bond lengths and bond angles are shown in Fig. 1 along with the atomic

\* Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and bond lengths, torsion angles and least-squares-plane data for the cytosine ring have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44173 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Final fractional coordinates and temperature factors of the non-hydrogen atoms, with e.s.d.'s in parentheses

$$U_{eq} = \frac{1}{3} \sum_i \sum_j U_{ij} a_i^* a_j^* a_i a_j$$

	x	y	z	$U_{eq}(\text{\AA}^2)$
Cl	0.8521 (1)	0.1205 (0)	0.3356 (1)	0.0398 (2)
N(1)	0.2971 (3)	0.3557 (1)	0.0757 (3)	0.0399 (7)
C(2)	0.3774 (4)	0.2776 (2)	0.0927 (3)	0.0364 (7)
O(2)	0.2876 (3)	0.2163 (1)	0.0263 (3)	0.0522 (7)
N(3)	0.5767 (3)	0.2741 (1)	0.1923 (3)	0.0351 (6)
C(4)	0.6839 (4)	0.3395 (1)	0.2740 (3)	0.0328 (6)
N(4)	0.8721 (4)	0.3253 (2)	0.3651 (3)	0.0463 (8)
C(5)	0.5915 (4)	0.4195 (1)	0.2571 (3)	0.0348 (7)
C(6)	0.3976 (4)	0.4236 (2)	0.1559 (4)	0.0384 (7)
C(7)	0.7067 (5)	0.4937 (2)	0.3422 (5)	0.0494 (9)

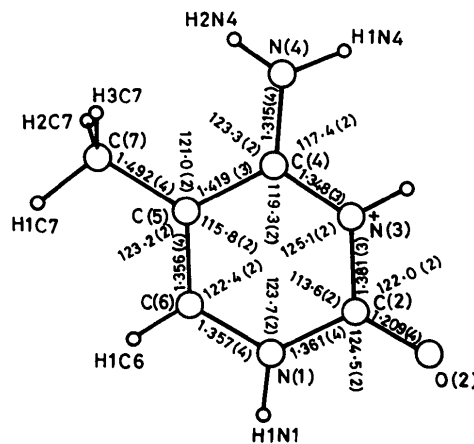


Fig. 1. Atomic numbering scheme for the 5-methylcytosine molecule along with the bond lengths (Å) and bond angles ( $^\circ$ ).

numbering scheme for the 5-methylcytosine hydrochloride molecule.

The cytosine ring is planar and the base is protonated at N(3) with angles C(2)—N(3)—C(4), N(1)—C(2)—N(3) and N(3)—C(4)—C(5) of 125.1 (2), 113.6 (2) and 119.3 (2) $^\circ$  respectively. These values are in good agreement with corresponding data for similar protonated structures, e.g. cytosine hydrochloride: 124.3 (2), 115.6 (2), 118.0 (2) $^\circ$  (Mandel, 1977); deoxycytidine 5'-phosphate monohydrate: 124.6 (5), 115.8 (6), 117.0 (6) $^\circ$  (Viswamitra, Swaminatha Reddy, Hung-Yin Lin & Sundaralingam, 1971); 1-methylcytosine hydrochloride: 126.1 (3), 114.8 (3), 116.8 (3) $^\circ$  (Trus & Marsh, 1972). In unprotonated species C(2)—N(3)—C(4) decreases by 5–6 $^\circ$  and N(1)—C(2)—N(3) and N(3)—C(4)—C(5) increase by 3–5 $^\circ$  (Taylor & Kennard, 1982); thus in unprotonated cytosine (Barker & Marsh, 1964) the corresponding angles are 119.8 (2), 118.1 (2), 122.0 (2) $^\circ$ . The C(2)—O(2) bond length is known to vary depending on the different hydrogen-bonding configurations available in the crystal (Mandel, 1977). Here, O(2) is not involved in hydrogen-bond formation and this is reflected in the

short C(2)–O(2) bond length [1.209 (3) Å], characteristic of a double bond.

**Crystal packing.** The crystal structure is stabilized by hydrogen bonds, N(3)–H...Cl = 3.136 Å [N(3)–H...Cl angle 159°] as well as direct electrostatic interactions between Cl and atoms of the base. Fig. 2 shows the crystal packing.

The molecules related by the *c*-glide are nearly parallel (angular deviation  $\approx 17^\circ$ ) and *ca* 3.5 Å apart,

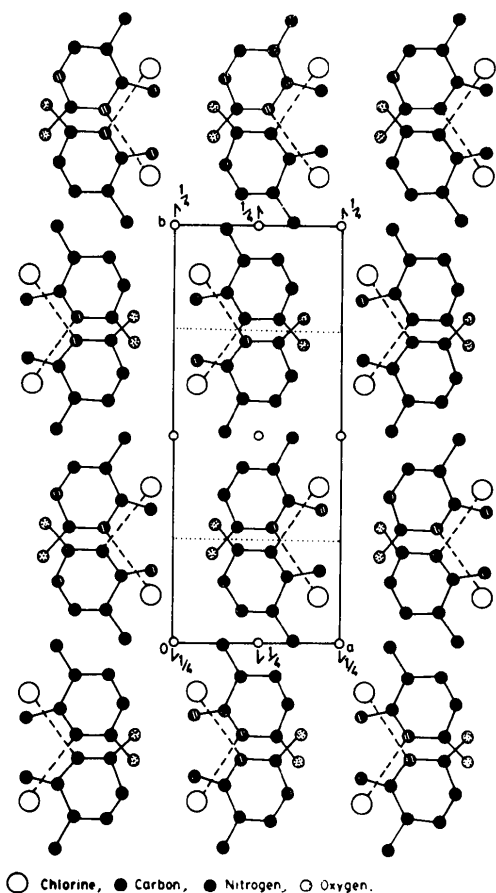


Fig. 2. The crystal packing viewed down the *c* axis.

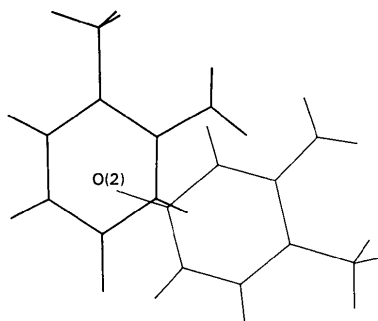


Fig. 3. A view perpendicular to the cytosine plane, indicating base stacking.

indicating stabilization through stacking interactions. Stacking of cytosine bases in crystal structures is common, but generally the stacked molecules are related by either lattice translation or crystallographic inversion centres (Bugg, Thomas, Sundaralingam & Rao, 1971). Fig. 3 shows the type of base stacking observed in the present structure where the bases are *c*-glide-related. Unmethylated structures, cytosine, cytosine hydrochloride and deoxycytidine 5'-phosphate monohydrate, show base stacking with ring–ring overlap. The methylated structures, 1-methylcytosine hydrochloride and the present structure, show no such overlap of the rings, although the exocyclic atoms may be found involved in the base-stacking interactions. In the present structure, O(2) of the cytosine base is involved in base stacking. No such interactions were found in the crystal structure of 1-methylcytosine hydrochloride.

The lack of base stacking in protonated pyrimidine structures compared with the extensive base stacking found in unprotonated pyrimidine structures is well documented (Bugg *et al.*, 1971). Protonation of the cytosine base may be expected to contribute to a decrease in base overlap because of the electrostatic interactions between the like charges. However, in the crystal structure of cytosine hydrochloride, where the cytosine bases are protonated, base overlap has been observed. This is attributed to the presence of a very strong hydrogen bond N(3)–H...Cl [N(3)–H...Cl = 3.02 Å, and N(3)–H...Cl 169°], which helps delocalize the positive charge on N(3), allowing the bases to stack (Mandel, 1977). In the present structure a somewhat similar hydrogen bond, N(3)–H...Cl [N(3)–H...Cl = 3.136 Å, N(3)–H...Cl 159°] exists, but without any ring overlap, possibly as a result of methylation of the base. It is of interest here that in 5-methyldeoxycytidine 5'-monophosphate dihydrate (Lalitha, Ramakumar & Viswamitra, 1987), no overlap of cytosine rings is observed, although the bases are not protonated.

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## The Structure of Hexamethylene Diperoxide Diamine

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**Abstract.** 3,4,8,9-Tetraoxa-1,6-diazabicyclo[4.4.2]do-decane(HMDD),  $C_6H_{12}N_2O_4$ ,  $M_r = 176.17$ , monoclinic,  $C2/c$ ,  $a = 11.937(1)$ ,  $b = 5.864(1)$ ,  $c = 11.890(1)$  Å,  $\beta = 110.00(1)^\circ$ ,  $V = 782.1(3)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_m = 1.44(2)$ ,  $D_x = 1.50$  g cm<sup>-3</sup>,  $\lambda(\text{Mo } K\alpha) = 0.71073$  Å,  $\mu = 1.35$  cm<sup>-1</sup>,  $F(000) = 376$ ,  $T = 294$  K,  $R = 0.0305$  for 681 independent reflections. The bridge-head N atoms adopt a nearly planar configuration [each is only 0.13(1) Å out of the plane of the C atoms to which it is bonded], as expected from similar compounds. N–C bonds to the peroxide bridges [average length 1.416(2) Å] are shorter than those to the all-carbon bridge [1.449(2) Å], again as expected from similar compounds.

**Introduction.** Schaefer, Fourkas & Tiemann (1985), Fourkas & Schaefer (1986), and Fourkas, Schaefer & Marsh (1987) have reported structures of three medium-ring bicyclic compounds with peroxide bridges: hexamethylene triperoxide diamine (HMTD, 3,4,8,9,12,13-hexaoxa-1,6-diazabicyclo[4.4.4]tetradecane), benzene tetramethylene diperoxide diamine (BTDD, 10,11,14,15-tetraoxa-1,8-diazatricyclo[6.4.4.0<sup>2,7</sup>]hexadeca-2(7),3,5-triene) and cyclohexane tetramethylene diperoxide diamine (CTDD, 10,11,14,15-tetraoxa-1,8-diazatricyclo[6.4.4.0<sup>2,7</sup>]hexadecane), which have planar or nearly planar bridge-head N atoms. We have now synthesized an additional analogous compound, HMDD, in order to study further this unusual geometry.

**Experimental.** 45 g H<sub>2</sub>O<sub>2</sub> (30% aqueous solution) and 60 ml formaldehyde solution (37%) were mixed and

cooled to 273 K; 2 ml ethylene diamine added, stirred for one hour; crystals collected, washed with ethanol; recrystallization from *n*-pentyl acetate; elemental analysis satisfactory for C, N, H; irregular crystal, 0.48 × 0.37 × 0.33 mm;  $D_m$  by flotation in an aqueous ZnBr<sub>2</sub> solution; Nonius CAD-4 diffractometer; monoclinic; intensity measurements with graphite-monochromated Mo  $K\alpha$  radiation,  $\theta$ - $2\theta$  scans, 2° min<sup>-1</sup> in  $2\theta$ , backgrounds measured for each reflection at each end of scan, average background as a function of  $2\theta$  calculated and used to correct measured scan counts; unit cell: 25 reflections,  $15 < 2\theta < 25^\circ$ , least-squares refinement; max.  $(\sin\theta)/\lambda$  0.59 Å<sup>-1</sup>; 2767 reflections collected over entire sphere with  $h$  –14 to 14,  $k$  –6 to 6, and  $l$  –14 to 14,  $4 < 2\theta < 50^\circ$ ; three check reflections monitored every 10 000 s, intensities corrected for linear decay of 7.5% in  $F$  magnitudes; no absorption correction applied,  $\mu r_{\text{max}} = 0.093$ ; individual reflections assigned a variance  $1/w$  based on counting statistics plus a term  $(0.014I)^2$  to account for errors proportional to intensity (0.014 chosen by considering duplicate measurements); systematic absences  $hkl$ ,  $h+k$  odd and  $h0l$ ,  $l$  odd suggested  $C2/c$ ; 681 independent forms used in structure solution and refinement, no reflections deleted;  $S_{\text{int}} = 1.03$ ,

$$S_{\text{int}} = \left[ \sum_{i=1}^N \left\{ \sum_{j=1}^M w_j (I_j - \bar{I})^2 / (M-1) \right\} / N \right]^{1/2},$$

where the outer sum is over the 681 independent forms and the inner sum is over all the equivalent reflections (usually 4) contributing to a form; variances of merged reflections obtained by standard propagation of error plus an additional term,  $(0.014\bar{I})^2$ , to account for other errors; structure solved with *MULTAN78* (Main, Hull,

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