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Structure of 3-(1-Cytosinyl)propionamide, $C_7H_{10}N_4O_2$

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Abstract. $M_r = 182{\cdot}18$, triclinic, $P\bar{1}$, $a = 8{\cdot}491$ (1), $b = 8{\cdot}906$ (1), $c = 7{\cdot}065$ (1) Å, $\alpha = 110{\cdot}26$ (1), $\beta = 95{\cdot}33$ (1), $\gamma = 118{\cdot}15$ (1)°, $V = 420{\cdot}3$ (1) Å^3, $Z = 2$, $D_m = 1{\cdot}45$, $D_x = 1{\cdot}439$ g cm^{-3}, Mo $K\alpha$, $\lambda = 0{\cdot}71073$ Å, $\mu = 1{\cdot}18$ cm^{-1}, $F(000) = 192$, room temperature, $R = 0{\cdot}059$ for 1495 reflections. Bond distances and angles agree with those of other cytosine derivatives and carbamoyl groups. The pyrimidine ring is planar. The cytosine moieties form a pair through N(4)—H···N(3) hydrogen bonds around an inversion center. The carbamoyl group of the adjacent molecule is hydrogen-bonded with O(2) of the paired cytosine.

Introduction. In a serial study on model crystals for protein–nucleic acid interactions, we have reported hydrogen bonding of the carbamoyl group with adenine (Takimoto, Takenaka & Sasada, 1981, 1982, 1983) and with uracil (Fujita, Takenaka & Sasada, 1984). To reveal the preference of the four bases, the title compound involving cytosine and the carbamoyl group has been prepared and examined by X-ray analysis.

Experimental. Synthesis by reaction of cytosine with β-propiolactone in the presence of *N,N*-dimethyl-4-pyridylamine in dimethyl sulfoxide at 383 K, esterification with HCl-saturated MeOH and then ammonolysis with NH_3-saturated MeOH. Thin plate-like crystals from MeOH solution; D_m by flotation in mixture of hexane and tetrachloromethane; unit-cell dimensions determined with 79 high-angle reflections. Crystal 0·4 × 0·4 × 0·1 mm; Rigaku four-circle diffractometer; graphite-monochromated Mo $K\alpha$ radiation; scan range $2 < 2\theta < 55°$; scan speed 4° (in ω) min^{-1}; $\omega/2\theta$ scan, scan width 1·3° (in ω) plus α_1–α_2 divergence; five reference reflections monitored showed no significant intensity deterioration; correction for Lorentz and polarization factors, not for absorption; of 1927 independent reflections, 394 weak reflections below background were considered zero reflections; standard deviations estimated by $\sigma^2(F_o) = \sigma_p^2(F_o) + qF_o^2$, where $\sigma_p(F_o)$ was evaluated by counting statistics and q estimated to be $2{\cdot}16 \times 10^{-3}$ from measurement of monitored reflections (McCandlish & Stout, 1975). Structure solved by direct methods and refined by full-matrix least-squares method; all H atoms found on difference map; $\sum w(|F_o| - |F_c|)^2$ minimized, where $w = 1/\sigma^2(F_o)$; zero reflections with $|F_c| \geq F_{\lim}$ ($F_{\lim} = 1{\cdot}047$) included in the refinement by assuming $F_o = F_{\lim}$ with $w = w(F_{\lim})$; all atom positions refined, non-H atoms anisotropic, H atoms isotropic; final R 0·059 for 1495 reflections with $F_o > 3\sigma$ ($R_w = 0{\cdot}076$, $S = 1{\cdot}09$); max. $\Delta = 0{\cdot}7\sigma$; $\Delta\rho$ peak 0·23 e Å^{-3}; atomic scattering factors from *International Tables for X-ray Crystallography* (1974); all calculations with *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978), *LSAP*80 (Takenaka & Sasada, 1980), *DCMS*82 (Takenaka & Sasada, 1982) and *LISTUP* (Takenaka & Sasada, 1983). Final atomic parameters are given in Table 1.†

† Lists of structure factors, H-atom parameters, anisotropic thermal parameters of non-H atoms, bond distances and angles involving H atoms, least-squares planes for the pyrimidine ring and the carbamoyl group, and hydrogen-bond geometry have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39451 (15 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Fractional coordinates and equivalent isotropic temperature factors*

B values are calculated from the anisotropic thermal parameters using the equation $B = 8\pi^2(U_1 + U_2 + U_3)/3$, where U_1, U_2 and U_3 are principal components of the mean-square displacement matrix U. Values in ⟨⟩ are anisotropicity defined by $|\sum(B - 8\pi^2 U_i)^2/3|^{1/2}$ and those in ( ) are e.s.d.'s; they refer to last decimal places.

	x	y	z	B(Å^2)
N(1)	0·2721 (3)	0·3152 (3)	0·3014 (3)	2·41 ⟨84⟩
C(2)	0·3346 (3)	0·1960 (3)	0·3045 (4)	2·27 ⟨40⟩
O(2)	0·3423 (3)	0·1647 (3)	0·4624 (3)	3·31 ⟨154⟩
N(3)	0·3859 (3)	0·1211 (3)	0·1402 (3)	2·39 ⟨65⟩
C(4)	0·3754 (3)	0·1596 (3)	−0·0264 (3)	2·29 ⟨52⟩
N(4)	0·4334 (3)	0·0886 (3)	−0·1818 (3)	2·93 ⟨124⟩
C(5)	0·3029 (4)	0·2723 (4)	−0·0380 (4)	3·39 ⟨174⟩
C(6)	0·2554 (4)	0·3484 (4)	0·1284 (4)	3·29 ⟨143⟩
C(7)	0·2293 (4)	0·4080 (4)	0·4885 (4)	2·59 ⟨59⟩
C(8)	0·0340 (4)	0·2782 (4)	0·4909 (4)	2·78 ⟨72⟩
C(9)	0·0064 (4)	0·3708 (4)	0·6979 (4)	2·74 ⟨73⟩
N(9)	−0·1338 (4)	0·2591 (4)	0·7499 (4)	3·36 ⟨112⟩
O(9)	0·1088 (3)	0·5438 (3)	0·8098 (3)	4·65 ⟨291⟩

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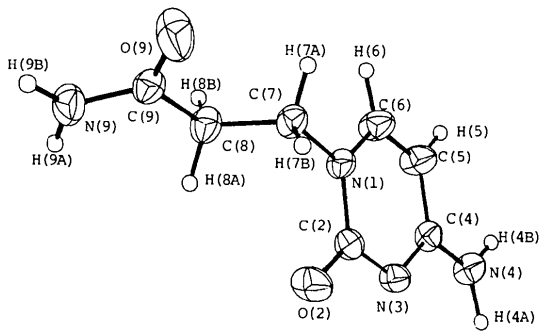

Fig. 1. Molecular structure of 3-(1-cytosinyl)propionamide with 50% probability ellipsoids for non-hydrogen atoms, showing the atomic numbering.

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

Standard deviations are given in parentheses.

N(1)–C(2)	1·397 (3)	N(1)–C(6)	1·363 (4)
N(1)–C(7)	1·476 (3)	C(2)–O(2)	1·244 (3)
C(2)–N(3)	1·347 (3)	N(3)–C(4)	1·342 (3)
C(4)–N(4)	1·328 (3)	C(4)–C(5)	1·422 (4)
C(5)–C(6)	1·341 (4)	C(7)–C(8)	1·515 (4)
C(8)–C(9)	1·512 (4)	C(9)–N(9)	1·326 (4)
C(9)–O(9)	1·233 (3)		

C(2)–N(1)–C(6)	120·0 (2)	C(2)–N(1)–C(7)	119·5 (2)
C(6)–N(1)–C(7)	120·6 (2)	N(1)–C(2)–O(2)	118·0 (2)
N(1)–C(2)–N(3)	119·8 (2)	O(2)–C(2)–N(3)	122·3 (2)
C(2)–N(3)–C(4)	120·0 (2)	N(3)–C(4)–N(4)	118·2 (2)
N(3)–C(4)–C(5)	121·2 (2)	N(4)–C(4)–C(5)	120·5 (2)
C(4)–C(5)–C(6)	117·9 (3)	N(1)–C(6)–C(5)	121·0 (3)
N(1)–C(7)–C(8)	112·2 (2)	C(7)–C(8)–C(9)	110·0 (2)
C(8)–C(9)–N(9)	117·3 (2)	C(8)–C(9)–O(9)	120·5 (2)
N(9)–C(9)–O(9)	122·2 (2)		

Discussion. Fig. 1 shows the molecular structure of 3-(1-cytosinyl)propionamide. Bond distances and angles are given in Table 2. The bond distances and angles of the cytosine moiety are in good agreement with those of 1-methylcytosine (Rossi & Kistenmacher, 1977) and cytidine (Furberg, Petersen & Rømming, 1965). The pyrimidine ring is planar within ±0·019 (3) Å. The dimensions of the carbamoyl group are in good agreement with those of asparagine (Ramanadham, Sikka & Chidambaram, 1972) and of glutamine (Koetzle, Frey, Lehmann & Hamilton, 1973). The torsion angles around the methylene chain are 184·4 (2) for N(3)–C(2)–N(1)–C(7), 277·4 (3) for C(2)–N(1)–C(7)–C(8), 173·0 (2) for N(1)–C(7)–C(8)–C(9), and 197·7 (2)° for C(7)–C(8)–C(9)–N(9). The conformation of the carbamoyl ethyl group is similar to those of the side chains of asparagine and glutamine.

The crystal structure is shown in Fig. 2 with N···N and N···O distances indicated. The cytosine moieties form a pair around the inversion center at ($\frac{1}{2}$,0,0) through the N(4)–H···N(3) hydrogen bonds, the N–H···N angle being 179 (4)°. The amino group is

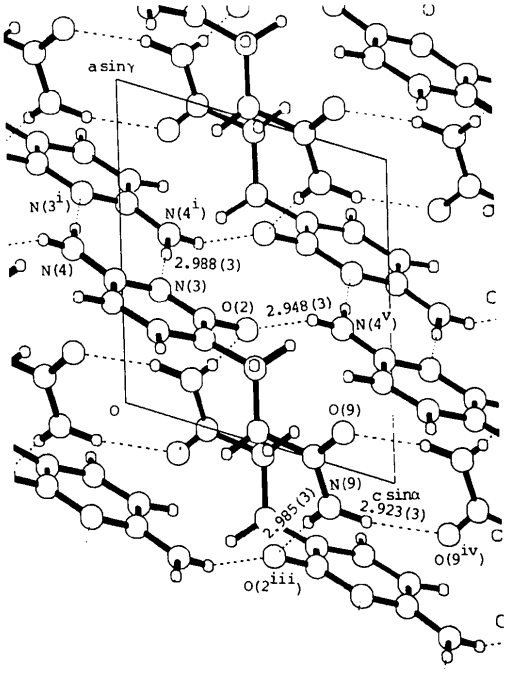

Fig. 2. The crystal structure of 3-(1-cytosinyl)propionamide projected along the *b* axis; distances are in Å. Symmetry code: (i) $1-x, -y, -z$; (iii) $-x, -y, 1-z$; (iv) $-x, 1-y, 2-z$; (v) $x, y, 1+z$.

further hydrogen-bonded with O(2) of the lateral base pair at (x, y, $-1+z$); angle N(4)–H···O(2) 161 (3)°. On the other hand, the carbamoyl group at ($-x$, $-y$, $1-z$) interacts with O(2) of the paired cytosine through the N–H···O hydrogen bond; N–H···O angle is 170 (4)°. In addition, the carbamoyl groups form a dimer around the inversion center at (0,$\frac{1}{2}$,1) through N(9)–H···O(9) hydrogen bonds with N–H···O angle 168 (4)°.

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Drimenol, (1*S*,2*R*,6*S*)-1,3,7,7-Tetramethylbicyclo[4.4.0]dec-3-ene-2-methanol, $C_{15}H_{26}O$*

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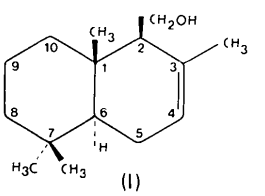
Abstract. $M_r = 222{\cdot}37$, monoclinic, $P2_1$, $a = 12{\cdot}384$ (1), $b = 22{\cdot}615$ (2), $c = 7{\cdot}462$ (1) Å, $\beta = 93{\cdot}23$ (1)°, $V = 2086{\cdot}5$ (2) Å^3, $Z = 6$, $D_m = 1{\cdot}07$ (1), $D_x = 1{\cdot}062$ (1) Mg m^{-3}, λ(Mo $K\alpha_1$) = 0·7093 Å, μ(Mo $K\alpha$) = 0·069 mm^{-1}, $F(000) = 744$, $T = 294$ K, final $R = 0{\cdot}063$ for 3177 unique observed reflexions. The absolute stereochemistry stated in the title was proposed in a chemical study of this natural product, where some doubt remained as to the orientation of the hydroxymethyl group; this doubt has now been dissipated. The three symmetry-independent molecules have the same conformation. The cyclohexane ring (chair) and the cyclohexene ring (half-chair) are *trans*-fused. There is a steric repulsion between the two axial methyl groups on the cyclohexane ring. The molecules, with the hydroxyl group as the connecting link, form hydrogen-bonded infinite chains parallel to the *c* axis. The differences in the corresponding dimensions and angles of the three molecules are not statistically significant, except for those in angles involving the hydroxyl groups which may be explained by packing effects.

Introduction. Drimenol was isolated from the bark of the Chilean canelo tree (*Drymis winteri* Forst) together with several other interesting products (Appel & Dohr, 1958) and has been shown to possess some biological activity in plant-growth regulation (Appel, Quilhot, Vidal & Araneda, 1980). The present work, starting with new samples of pure and well crystallized drimenol, has confirmed the absolute stereochemistry (I) proposed by Appel, Brooks & Overton (1959) and established that the cell parameters and space group published by Garaycochea & Wittke (1961) do not correspond to drimenol, but to another isolated product, a lactone named canelin, $C_{15}H_{22}O_2$, $D_m = 1{\cdot}10$ Mg m^{-3}.



(I)

Experimental. Colourless prismatic crystals, m.p. 369–370 K, D_m measured with pycnometer and water; a block of 0·15 × 0·15 × 0·10 mm cut from single crystal, Philips PW1100 diffractometer, graphite-monochromatized Mo $K\alpha$, $\omega/2\theta$ scan; cell parameters by least squares from 28 strong reflexions with $5 < 2\theta < 36°$; two standard reflexions every 50 measurements, variation in intensity less than ± 2% of its mean value; 4076 hkl and $\bar{h}kl$ ($|h| \le 14$, $k \le 26$, $l \le 8$) up to $\sin\theta/\lambda = 0{\cdot}6$ Å^{-1}, 3774 independent, 597 unobserved with $I \le \sigma(I)$, $R_{int} = 0{\cdot}006$ from merging 302 equivalent $hk0$ pairs, systematic absences $0k0$, k odd; Lp correction, absorption ignored. Structure solved with *MULTAN*76 (Main, Lessinger, Woolfson, Germain & Declercq, 1976) only when the stereochemistry (I) was used for molecular scattering factors and the K curve for scaling; four C atoms of methyl groups located by a difference map; after isotropic refinement (y parameter for one atom kept invariant for fixing the origin), calculated H-atom positions (bond distance 1 Å) matched well with difference-map peaks with exception of methyl H atoms which were not resolved; these were

* A preliminary version of this paper was presented to the XII Congress of the International Union of Crystallography in Ottawa, Canada, August 1981 (Escobar & Wittke, 1981).

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