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1,2,4,5-Tetrahydro-7-methoxy-3*H*-benz[*g*]indazol-3-one Monohydrate

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Abstract. $C_{12}H_{12}N_2O_2.H_2O$, triclinic, $P\bar{1}$, a = 3·9194 (6), b = 18·371 (5), c = 7·873 (1) Å, α = 90·26 (1), β = 100·81 (1), γ = 100·59 (2)°, V = 546·9 Å^3, D_c = 1·423 Mg m^{-3} at 113 K; a = 3·967 (4), b = 18·42 (2), c = 7·93 (1) Å, α = 90·5 (1), β = 101·1 (1), γ = 99·9 (1)°, V = 560·1 Å^3, D_c = 1·389 Mg m^{-3}, D_m = 1·388 Mg m^{-3} (aqueous KI) at 299 K, Z = 2. The compound was synthesized for potential use in cancer chemotherapy [Hashem, Berlin, Chestnut & Durham (1976). *J. Med. Chem.* **19**, 229–239]. The O atom of the pyrazolone ring acts as an acceptor in three strong hydrogen bonds. Of the possible tautomers which may exist for the heterocyclic five-membered ring the 1,2-dihydro-3-pyrazolone is found in the solid state.

Introduction. A suitable single crystal in the shape of a rectangular plate (0·64 × 0·28 × 0·07 mm) was obtained by recrystallization from 90% aqueous ethanol. A preliminary examination of the data crystal indicated a triclinic lattice. The space group was determined to be $P\bar{1}$ by structure solution and refinement. Integrated intensity data were measured at 113 K on a Nonius CAD-4 automatic diffractometer equipped with an Enraf–Nonius cold-stream cooling device. The intensities of 2232 reflections comprising all unique data with $2\theta < 150°$ were measured using θ–2θ scan techniques and Ni-filtered Cu $K\alpha$ radiation (λ = 1·5418 Å). The maximum time spent on each measurement was 60 s. The intensity of a monitor reflection, measured after every 20 reflections, showed a variation of 3% during the data collection. The orientation matrix was checked after every 100 measurements. 99 intensities were considered indistinguishable from the background on the basis that the intensity [I = Pk − 2(LB + RB)] was less than $2\sigma(I)$ where Pk = peak count, LB = left background count and RB = right background count. These reflections were assigned intensities of $1{\cdot}4(T^{1/2})$ (T = total count) for further data analysis. Lorentz and polarization corrections were applied and individual structure factor amplitudes derived but no absorption correction was made (μ = 0·87 mm^{-1}). An experimental weight (w_F) based on counting statistics was assigned to each structure factor (Ealick, van der Helm & Weinheimer, 1975).

The structure was solved using *MULTAN* (Germain, Main & Woolfson, 1971) which yielded the positions of all C, N and O atoms. The 14 H atoms were located from a difference Fourier map and refined with isotropic thermal parameters. The structure was refined using block-diagonal least squares in which the quantity $\sum w_F(|kF_o| - |F_c|)^2$ was minimized. The R value $(= \sum ||kF_o| - |F_c||/\sum |kF_o|)$ based on the final parameters (Tables 1 and 2)* was 0·043 for all data and 0·037 for the 2081 reflections used in least-squares refinement. The goodness-of-fit was 2·55 e. The atomic scattering factors for C, N and O atoms were taken from *International Tables for X-ray Crystallography*

Table 1. *Positional parameters for* C, N *and* O *atoms* ($x \times 10^4, y, z \times 10^5$)

The standard deviations for the last digit are in parentheses.

	x	y	z
N(1)	2289 (3)	87793 (5)	22803 (12)
N(2)	1390 (3)	92915 (5)	11052 (12)
C(3)	1160 (3)	90185 (6)	−5283 (13)
C(4)	2444 (3)	77464 (6)	−16613 (13)
C(5)	1682 (3)	69691 (6)	−9533 (14)
C(6)	4487 (3)	62623 (6)	15148 (14)
C(7)	5848 (3)	61989 (6)	32668 (14)
C(8)	6103 (3)	67861 (6)	44405 (14)
C(9)	5096 (3)	74388 (6)	38704 (14)
C(9a)	3766 (3)	75130 (6)	21089 (14)
C(1a)	2722 (3)	81869 (6)	13930 (13)
C(3a)	2036 (3)	83061 (6)	−3617 (13)
C(5a)	3424 (3)	69193 (6)	9276 (14)
O(10)	263 (2)	93884 (4)	−18809 (10)
O(11)	6998 (3)	55878 (4)	39687 (11)
C(12)	6843 (3)	49711 (6)	28355 (16)
O(13)	4011 (2)	90871 (5)	57083 (10)

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* Lists of structure factors and thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34630 (12 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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(1974) while those for H atoms were from Stewart, Davidson & Simpson (1965). A final difference Fourier map was calculated in which all residual electron density was between −0·3 and 0·3 e Å^{-3}. A structure factor analysis showed no significant variation of $\overline{w_F \Delta F^2}$ with $|F_o|$ or $\sin^2\theta/\lambda$ thus validating the weighting scheme used. Interatomic distances and angles involving C, N and O atoms are given in Figs. 1 and 2, respectively. Bond distances involving H atoms range from 0·93 to 1·02 Å with an average value of 0·98 (2) Å. An examination of observed and final calculated structure factor magnitudes indicated the presence of secondary extinction effects for which no correction was made.*

Discussion. The primary reasons for studying this molecule were to determine which pyrazoline tautomer exists in the solid state and to ascertain if any structural features could be correlated to its known antineoplastic activity. In addition, it was not possible to exclude the existence of those isomers in which atom C(1) or C(2) was sp^3 hybridized based on the data available prior to undertaking a single-crystal X-ray study. Based on the following observations, we conclude that the 1,2-dihydro-3-pyrazolone tautomer exists in the solid state. (1) The sum of the bond angles at atoms C(1a) and C(3a) are 360·1 (2) and 360·0 (2)°, respectively [*i.e.* atoms C(1a) and C(3a) are sp^2 hybridized], (2) H atoms bonded to both N(1) and N(2) were located from a difference Fourier map and behaved normally under least-squares refinement, and (3) a final difference Fourier map showed no peaks around atom O(10) which could be interpreted as an H atom.

It is also concluded from inspection of the bond distances that the two resonance forms with a negative charge on O(10) and a positive charge on either N(1) or N(2) are significant contributors to the electronic structure. The resulting negative charge on O(10) makes it an unusually strong hydrogen-bond acceptor. Similar conclusions were made for the structures of antipyrin (Singh & Vijayan, 1973) and urea (Vaughan & Donohue, 1952).

One of the most interesting features is the crystal packing which is illustrated in Fig. 3. All active H atoms [H(1), H(2), H(13*A*) and H(13*B*)] are involved in strong hydrogen bonds with H···O distances between 1·73 and 1·82 Å. The water molecule, O(13), is acceptor for one hydrogen bond and donor for two

Table 2. *Positional parameters* (×10^3) *for hydrogen atoms*

Standard deviations for the last digit are in parentheses. Thermal parameters vary between 1·5 (H4*A*) and 4·1 (H13*A*) Å^2.

	x	*y*	*z*
H(1)	277 (5)	892 (1)	349 (3)
H(2)	69 (5)	975 (1)	145 (3)
H(4*A*)	490 (4)	783 (1)	−185 (2)
H(4*B*)	85 (4)	777 (1)	−278 (2)
H(5*A*)	−93 (4)	684 (1)	−98 (2)
H(5*B*)	242 (4)	659 (1)	−170 (2)
H(6)	437 (4)	588 (1)	68 (2)
H(8)	707 (4)	673 (1)	561 (2)
H(9)	526 (5)	787 (1)	467 (2)
H(12*A*)	441 (4)	475 (1)	230 (2)
H(12*B*)	782 (5)	459 (1)	357 (2)
H(12*C*)	813 (4)	512 (1)	188 (2)
H(13*A*)	265 (5)	922 (1)	646 (3)
H(13*B*)	627 (5)	916 (1)	646 (2)

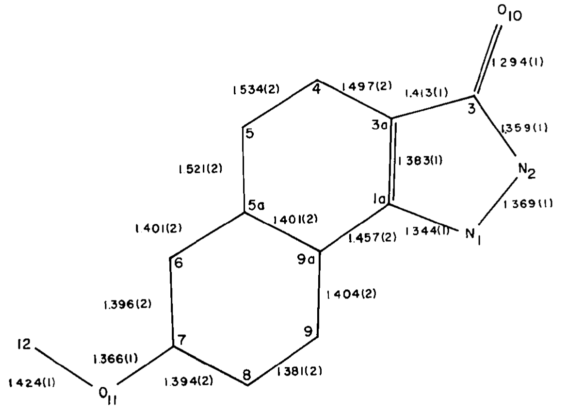

Fig. 1. Bond distances (Å).

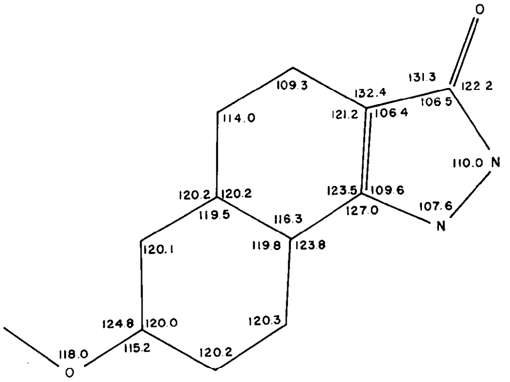

Fig. 2. Bond angles (°). Standard deviations are 0·1°.

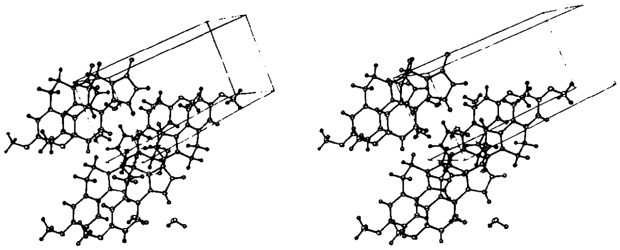

Fig. 3. *ORTEP* packing drawing (Johnson, 1965) and intermolecular hydrogen bonding (shown as dotted lines).

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* See previous footnote.

Table 3. *Hydrogen bonding*

D–H$\cdots A$	D–H	$D\cdots A$	H$\cdots A$	$\angle D$–H$\cdots A$
N(1)–H(1)$\cdots$O(13)	0·96 Å	2·687 Å	1·73 Å	173°
O(13)–H(13*A*)$\cdots$O(10)$^{\text{I}}$	0·93	2·721	1·80	172
O(13)–H(13*B*)$\cdots$O(10)$^{\text{II}}$	0·96	2·768	1·82	171
N(2)–H(2)$\cdots$O(10)$^{\text{III}}$	0·99	2·718	1·73	173

Symmetry code: (I) $x, y, z+1$; (II) $x+1, y, z+1$; (III) $-x, 2-y, -z$.

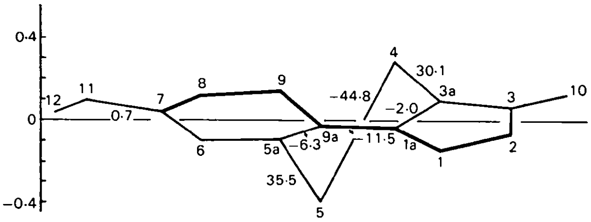

Fig. 4. Conformational angles around the cyclohexadiene ring and the methoxy group. The view is with respect to the least-squares plane through the molecule.

others. O(10) acts as an acceptor for three strong hydrogen bonds. The three H atoms plus atom C(3) form an approximate tetrahedron about the acceptor O(10). The two strongest hydrogen bonds in the structure are those in which atoms N(1) and N(2) are the donors. All of these observations are consistent with the distribution of charge inferred from the derived geometrical parameters. The details of the geometry of the hydrogen bonds are given in Table 3.

The cyclohexadiene ring exists in the half-chair conformation as can be seen from the torsion angles given in Fig. 4. The distances from the best plane through the molecule are also shown in Fig. 4 illustrating the relative flatness of the molecule. The dihedral angle between the planes defined by the atom coordinates of the five-membered and those of the benzene ring is 20°. This molecular flatness and the ability of the system to form strong hydrogen bonds may be responsible for its antineoplastic activity.

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Structure of Diacetylmorphine (Heroin)

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Abstract. $C_{21}H_{23}NO_5$ [7,8-didehydro-4,5α-epoxy-17-methylmorphinan-3,6α-diol diacetate (ester)], orthorhombic, $P2_12_12_1$, $a = 8{\cdot}003\ (5)$, $b = 14{\cdot}373\ (6)$, $c = 16{\cdot}392\ (7)$ Å at 296 K, $D_{\text{calc}} = 1{\cdot}32$ Mg m^{-3}, $Z = 4$, $F(000) = 784$, $\mu(\text{Mo}\ K\alpha) = 0{\cdot}101$ mm^{-1}. Direct methods were used to determine the structure from four-circle diffractometer intensity measurements. Least-squares refinement converged with $wR = 0{\cdot}057$. The skeleton of the molecular structure exhibits the T configuration already observed with other morphine derivatives.

Introduction. The present structural analysis of diacetylmorphine (Fig. 1) was carried out in the course of a continuing research project, aimed at identifying

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