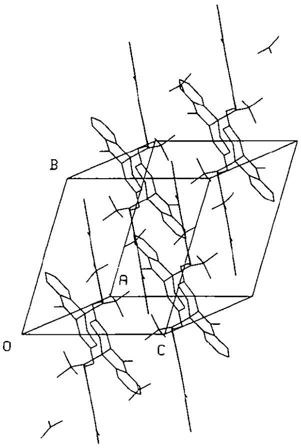

Fig. 2. Packing diagram of the unit cell: the planar three-ring fragment of each molecule appears as a straight line.

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Covalently Linked Purine–Pyrimidine Analogs. The Structure of 7-(5-Hydroxy-3-oxo-2,3-dihydro-4-pyrazolyl)theophylline Monohydrate,* $C_{10}H_{10}N_6O_4.H_2O$

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Abstract. $M_r = 296\cdot24$, orthorhombic, $Pca2_1$, $a = 19\cdot049\,(14)$, $b = 8\cdot307\,(5)$, $c = 7\cdot869\,(5)$ Å, $V = 1245\,(2)$ Å^3, $Z = 4$, D_m(flotation) $= 1\cdot58$, $D_x = 1\cdot58$ Mg m^{-3}, Mo $K\alpha$, $\lambda = 0\cdot71069$ Å, $\mu = 0\cdot14$ mm^{-1}, $F(000) = 616$, room temperature, $R = 0\cdot058$ and $R_w = 0\cdot082$ for 1431 independent reflections with $I > 2\cdot0\sigma(I)$. The monocyclic nucleus is in the enolic form and the lengthening of its carbonyl bond may be favoured by its participation in a strong intermolecular hydrogen bond with the enolic group. The packing is governed by a network of hydrogen bonds in which, apart from the water molecule, all the acceptor and donor sites of the pyrazoline ring take part and by a short contact between methyl and carbonyl groups belonging to different molecules translated along the **b** direction.

Introduction. In a previous paper (Gavuzzo, Mazza, Tamburrini, Casini & Carotti, 1984) we reported the crystallographic investigation of 7-(4,6-dioxo-5-pyrimidinyl)theophylline dihydrate. As a continuation of our studies we here report the structural study of the title compound in which the theophylline is linked, through an N—C single bond, to a 5-hydroxy-3-oxo-2,3-dihydropyrazolic nucleus. Besides the possibility of its interfering with biological functions of cell components (Balis, 1968) this compound might have anti-inflammatory properties because of the presence of a second pharmacophoric group, the 3,5-dioxo-4*H*-pyrazoline ring (Shen, 1981), which is the dicarbonilic tautomeric form of the monocyclic moiety present in our compound.

Experimental. Compound first synthesized by Roushdi, Ibrahim El-Sebai, Rida & Ashour (1973), more easily prepared according to Carotti, De Laurentis, Ferappi &

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* Theophylline is 3,7-dihydro-1,3-dimethyl-1*H*-purine-2,6-dione.

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Ottolino (1977); single crystals suitable for X-ray analysis from aqueous solution by slow evaporation; approximate unit-cell dimensions and space group determined from oscillation and Weissenberg photographs; crystal $0{\cdot}3 \times 0{\cdot}2 \times 0{\cdot}2$ mm, automatic Syntex $P2_1$ diffractometer, graphite monochromator, Mo $K\alpha$ radiation; unit-cell parameters obtained by least-squares fit of angular settings of 15 reflections in the range $5 < \theta < 20°$; max. 2θ 58·0°, ω-scan technique; 3 reflections, 202, 312 and 121, measured after every 97, showed only small deviations from means; 2305 independent reflections, h 0–27, k 0–12, l 0–11, 1431 with $I > 2{\cdot}0\sigma(I)$ considered observed and used for calculations, Lorentz and polarization corrections applied, no correction for extinction and absorption; structure solved by *MULTAN* (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978), 300 reflections and 4815 $\sum_2$ relationships used in phase-determining procedure; E map computed with phases of the set with highest figures of merit revealed all non-H positions, refined isotropically then anisotropically by block-diagonal least squares; $\sum w(|F_o| - |F_c|)^2$ minimized, $w = (a + |F_o| + c|F_o|^2)^{-1}$, a and c are $2F_o$(min) and $2/F_o$(max), respectively; all H-atom positions detected from final difference Fourier synthesis. Around the C atom of both methyl groups six peaks were found in good agreement with two different conformations each *trans* to every N—C ring bond; therefore, six hydrogen atoms with an occupancy factor of 0·5 were assumed for each methyl group in the calculations. These and all other H positional parameters and isotropic thermal values of the order of those of the carrier atoms before anisotropic refinement were included and kept fixed in refinement; max. Δ/σ in the final refinement cycle 0·10, final R and R_w are 0·058 and 0·082; scattering factors taken from *International Tables for X-ray Crystallography* (1974); all the calculations carried out on the HP 21MX minicomputer (Cerrini & Spagna, 1977) of the CNR Research Area.

Discussion. The final atomic parameters of the non-H atoms are reported in Table 1,* while Fig. 1 shows the numbering scheme adopted together with the relative bond lengths and angles involving non-H atoms.

The geometry of the theophylline ring is in agreement with those of some recent structural determinations (Gavuzzo, Mazza, Tamburrini, Casini & Carotti, 1984, and references quoted therein). The largest atomic deviation from the least-squares plane of the nine atoms of the theophylline ring is 0·021 (5) Å for the C(5) atom.

Table 1. *Final fractional coordinates and B_{eq} values of the non-*H *atoms with e.s.d.'s in parentheses*

$$B_{\rm eq} = \tfrac{4}{3}\textstyle\sum_i\sum_j b_{ij}\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	$B_{\rm eq}$(Å^2)
N(1)	0·3106 (2)	−0·1238 (5)	0·3021 (6)	2·1 (1)
C(1)	0·2589 (3)	−0·0359 (7)	0·1977 (9)	3·3 (2)
C(2)	0·2999 (3)	−0·2859 (6)	0·3224 (8)	2·5 (2)
O(2)	0·2506 (3)	−0·3549 (5)	0·2586 (7)	3·8 (2)
N(3)	0·3493 (2)	−0·3699 (4)	0·4154 (6)	2·3 (2)
C(3)	0·3425 (3)	−0·5445 (6)	0·4326 (13)	4·4 (3)
C(4)	0·4046 (2)	−0·2881 (5)	0·4867 (6)	1·8 (1)
C(5)	0·4127 (2)	−0·1249 (5)	0·4669 (6)	1·7 (1)
C(6)	0·3663 (2)	−0·0300 (5)	0·3683 (6)	1·8 (1)
O(6)	0·3706 (2)	0·1142 (4)	0·3386 (6)	2·8 (1)
N(7)	0·4741 (2)	−0·0874 (4)	0·5540 (6)	1·9 (1)
C(8)	0·4983 (2)	−0·2273 (5)	0·6175 (7)	2·2 (2)
N(9)	0·4582 (2)	−0·3528 (4)	0·5791 (6)	2·3 (2)
N(11)	0·5597 (2)	0·2967 (5)	0·5323 (6)	2·4 (2)
N(12)	0·5054 (2)	0·3298 (4)	0·6447 (6)	2·3 (1)
C(13)	0·4673 (2)	0·1929 (5)	0·6684 (7)	1·0 (2)
O(13)	0·4125 (2)	0·1879 (4)	0·7623 (5)	2·6 (1)
C(14)	0·5009 (2)	0·0700 (5)	0·5757 (7)	1·9 (2)
C(15)	0·5576 (2)	0·1390 (5)	0·4913 (6)	1·9 (2)
O(15)	0·6063 (2)	0·0797 (4)	0·3936 (6)	2·8 (1)
O(1)	0·6433 (2)	0·5385 (5)	0·4281*	4·2 (2)

* Held fixed to define the origin.

Table 2. *Hydrogen bonds*

Standard deviations are estimated to be 0·005–0·007 Å for $D\cdots A$ distances, *ca* 0·06 Å for D—H and H$\cdots A$, *ca* 5° for D—H$\cdots A$ angles.

D	A	D—H (Å)	$D\cdots A$ (Å)	H$\cdots A$ (Å)	D—H$\cdots A$ (°)
O(1$^{\rm i}$)	O(2)	0·97	2·878	1·98	152
N(12$^{\rm ii}$)	N(9)	0·88	2·832	1·98	161
N(11)	O(1)	0·93	2·691	1·78	165
O(1$^{\rm iii}$)	O(13)	0·87	2·828	2·09	143
O(15$^{\rm iv}$)	O(13)	0·87	2·477	1·62	169

Symmetry code: (i) $-\frac{1}{2} + x, -y, z$; (ii) $x, y - 1, z$; (iii) $1 - x, 1 - y, \frac{1}{2} + z$; (iv) $1 - x, -y, \frac{1}{2} + z$.

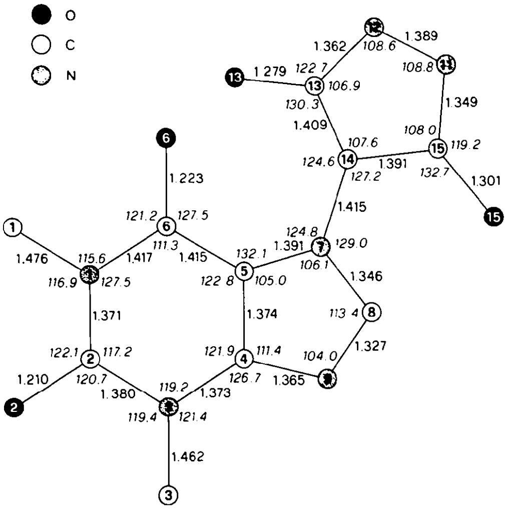

Fig. 1. The numbering scheme adopted together with bond lengths (Å) and angles (°). E.s.d.'s are in the ranges 0·005–0·008 Å and 0·4–0·6°, respectively, for bond lengths and angles.

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* Lists of structure factors, anisotropic thermal parameters of the non-H atoms, coordinates of the H atoms and least-squares-planes' data have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39249 (13 pp.). Copies may be obtained through the Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

The C(14) malonic atom is deprotonated and sp^2 hybridized [the sum of the bond angles is 359·4 (5)°], whereas only one of the two oxygens of the monocyclic nucleus, the O(15) atom, is protonated, as found in the final difference Fourier synthesis. Therefore, the monocyclic nucleus, for which keto–enolic tautomerism is possible, is in the enolic form. Moreover, since the two C—C bond lengths are of aromatic type and the two C—N lengths are of amidic type and the N—N bond length is signficantly shorter than that of a single bond (1·44 Å, *International Tables for X-ray Crystallography*, 1968) there must be an appreciable degree of delocalization over the whole of this heterocyclic system. This is supported by the planarity of the ring, the largest deviation from the least-squares plane of its five atoms being 0·016 (5) Å for the N(12) atom.

The C(13)—O(13) carbonyl bond length of 1·279 (6) Å is considerably longer than the normal value [compare, for example, with the C(2)—O(2) and C(6)—O(6) lengths, respectively of 1·210 (7) and 1·223 (5) Å]. The lengthening of this bond could be due to, apart from the possible delocalization of the π electrons over the five-membered ring, the two hydrogen bonds in which the O(13) atom is engaged, with the water molecule and with the hydroxyl group H—O(15) of screw-related molecules. Of these two interactions, the second one particularly, with an O···O distance of 2·477 (5) Å, indicates a very strong hydrogen bond. Lengthening of the C—O carbonylic groups participating in strong intramolecular hydrogen bonds with enolic groups have been found in crystals of 1,3-diphenyl-1,3-propanedione (Williams, 1966) with C—O and O···H—O values, respectively, of 1·292 (5) and 2·468 (5) Å, as well as in crystals of nitromalonamide (Simonsen & Thorup, 1979) with C—O and O···H—O values, respectively, of 1·281 (4) and 2·384 (4) Å.

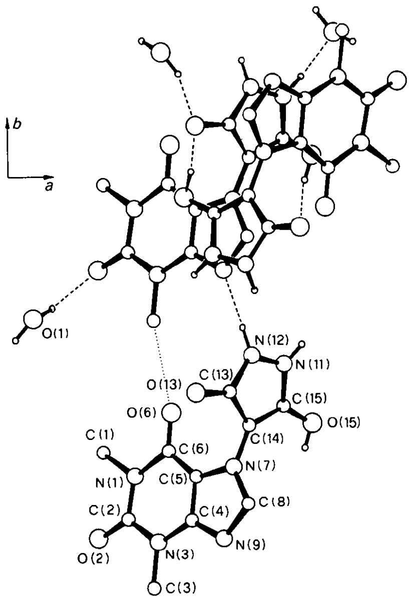

Fig. 2. A view along **c** of the molecular conformation of the compound showing the main interactions present in the crystal. Dashed lines represent hydrogen bonds and the dotted line represents the methyl–carbonyl short contact. The oxygen of the water molecule is indicated as O(1).

The dihedral angle between the least-squares planes of the two five-membered rings is 71·8 (2)°.

The packing is governed by hydrogen bonding. Screw-related molecules interact, as already mentioned, with a very strong hydrogen bond, 2·477 (5) Å long, occurring between the carbonylic O(13) and the enolic O(15) atoms of the dihydropyrazole ring. Another hydrogen bond between the imidazolic N(9) atom and the dihydropyrazole N(12)—H group allows further interaction between molecules translated along **b**. The water molecule takes part in three hydrogen bonds, being donor in two of them, with the carbonylic O(2) and O(13) atoms, and acceptor in the third with the N(11)—H dihydropyrazole group. The atoms participating in hydrogen bonding together with some relevant geometrical values are summarized in Table 2, while the scheme of their interactions is shown in Fig. 2.

The methyl C(3) and carbonyl O(6) atoms of different molecules translated along **b** make a contact of 2·979 (6) Å, significantly shorter than the sum of their van der Waals radii (3·4 Å). Similar short contacts and their nature have already been discussed (Sutor, 1963).

Drawings were prepared by Mr M. Viola.

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