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Structure of *N*6-Benzoyladenine* (6BA)†

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Abstract

$C_{12}H_9N_5O$ is monoclinic, space group $P2_1/c$, with a = 7·098 (2), b = 10·612 (4), c = 14·465 (5) Å, β = 102·58 (1)°, Z = 4, M_r = 239·2, D_o = 1·494, D_c = 1·487 Mg m^{-3}, λ(Cu $K\alpha$) = 1·5418 Å. Final R = 0·062 for 1682 reflections. The adenine moiety is in the N(7)–H tautomeric form. An intramolecular hydrogen bond N–H···O is observed and the molecules are stacked along **a**. The stacked planes are approximately parallel to the *bc* plane and are separated by 3·5 Å.

Introduction

Besides the five major bases that are present in nucleic acids, several modified bases have received considerable attention with regard to structure elucidation in the solid state and biochemical function. Some of these bases occur in several nucleic acids, specifically tRNA, while others have been synthesized by suitable alterations of the parent base, such as simple methylation, replacement of O by S, saturation of a double bond or more extensive modifications. The commonest purine analogues bear substitutions at the 2 or 6 positions or both. Some of the resulting substances like 6-mercaptopurine and thioguanine have pronounced antitumor activity while others like 6-histaminopurine and 6-benzyladenine, which are closely related to the plant hormone kinetin, have morphological effects on cells in tissue culture. Nevertheless all purine and pyrimidine derivatives and their analogues exhibit a common feature in that stacking forms an important type of interaction both in aqueous solution and in the solid state (Bugg, 1972). Also each of a large number of N(6) monosubstituted adenine derivatives exhibits a distal conformation of the substituent with respect to the imidazole ring. It is in the light of these observations that an analysis of 6BA has been undertaken. The chemical significance of this compound is that, as a plant hormone, 6BA induces growth of root and stem (Thimann, 1969).

* 6-(Benzoylamino)purine.

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Experimental

6BA was crystallized as yellow needles from methanol. Weissenberg photographs showed that the crystals are monoclinic, space group $P2_1/c$.

A crystal 0·4 × 0·2 × 0·2 mm was mounted with b parallel to the φ axis of a Picker four-circle diffractometer. Intensities for 1788 reflections with $2\theta \leq 130°$ were collected with Ni-filtered Cu $K\alpha$ radiation by the $\theta/2\theta$ scan technique with a 2° min^{-1} scan speed. The background was measured for 10 s at each end of the scan. 106 reflections with net negative or zero counts were considered unobserved. The cell parameters were determined by least squares (Main & Woolfson, 1963) from 2θ values of 39 reflections. The data were corrected for Lorentz and polarization effects but not for absorption.

Structure determination and refinement

The structure was solved with *MULTAN* (Germain, Main & Woolfson, 1971). 210 reflections ($|E| \geq 1·54$) and 2000 triple phase relationships were considered. Three reflections to define the origin, three from Σ_1 relations with probability $\geq 0·98$ and three more with variable (symbolic) phases constituted the starting set. This was developed by tangent refinement to give eight phase sets, one of which with the highest combined figure of merit (2·48) and lowest residual (20·24) yielded an electron-density map which revealed the complete molecule.

A structure-factor calculation with all the 18 non-H atoms gave R = 0·39. After least-squares refinement (Shiono, 1968) with isotropic temperature factors R dropped to 0·15. A difference map computed at this stage revealed all nine H atoms. R fell to 0·09 when the H atoms were included in the structure-factor calculation during anisotropic refinement of the non-H atoms. Final refinement was carried out by full-matrix least squares (Gantzel, Sparks & Trueblood, 1961) with isotropic temperature factors for H, anisotropic for the non-H atoms and unit weights for all the observed reflections and led to convergence at 0·062.

Table 1. *Fractional positional parameters* ($\times 10^4$) *and equivalent isotropic temperature factors of the non-H atoms, with e.s.d.'s in parentheses*

For monoclinic cells $B_{eq} = \frac{4}{3}[a^2b_{11} + b^2b_{22} + c^2b_{33} + 2ac \times (\cos\beta)b_{13}]$, $\sigma(B_{eq}) = \frac{4}{3}[a^2\{\sigma(b_{11})\} + b^2\{\sigma(b_{22})\} + c^2\{\sigma(b_{33})\} + 2ac\cos\beta\{\sigma(b_{13})\}]$.

	x	y	z	B (Å^2)
O(1)	2143 (3)	−590 (2)	5701 (1)	4·16 (8)
N(1)	2972 (4)	3089 (2)	4964 (1)	4·46 (8)
C(2)	3158 (7)	4117 (3)	5508 (2)	5·47 (11)
N(3)	3423 (4)	4209 (2)	6439 (1)	4·84 (8)
C(4)	3503 (4)	3086 (3)	6850 (2)	3·71 (9)
C(5)	3338 (4)	1939 (2)	6369 (1)	3·17 (7)
C(6)	3050 (4)	1968 (2)	5383 (1)	3·28 (7)
N(6)	2875 (3)	957 (2)	4758 (1)	3·28 (7)
N(7)	3585 (3)	1042 (2)	7061 (1)	3·82 (8)
C(8)	3847 (5)	1659 (3)	7895 (2)	4·37 (11)
N(9)	3800 (3)	2892 (2)	7819 (1)	4·13 (8)
C(10)	2357 (4)	−251 (2)	4922 (1)	3·33 (8)
C(11)	2015 (4)	−1145 (2)	4107 (1)	3·17 (6)
C(12)	1854 (5)	−777 (3)	3174 (2)	3·65 (9)
C(13)	1478 (5)	−1664 (3)	2449 (2)	4·75 (11)
C(14)	1276 (5)	−2910 (3)	2648 (2)	4·72 (13)
C(15)	1431 (5)	−3295 (3)	3580 (2)	5·08 (12)
C(16)	1801 (5)	−2413 (3)	4304 (2)	4·39 (12)

The final shifts in the atomic parameters of the non-H atoms were $<0{\cdot}25\sigma$.

Scattering factors were taken from *International Tables for X-ray Crystallography* (1962). The final positional parameters of the non-H atoms are given in Table 1.*

Description and discussion of the structure

Fig. 1 presents the bond lengths and angles. Structural studies on numerous adeninium compounds indicate that the adenine residue is first protonated at N(1). The present study discloses that N(1) is unprotonated and concurs with the results of Reddy & Viswamitra (1975) and Kistenmacher & Rossi (1977) for neutral adenine. The bond lengths and angles of the adenine group compare well with those of neutral adenine (Shieh & Voet, 1975).

The bond lengths and angles in the imidazole ring compare well with those of caffeine (Sutor, 1958; Shefter, 1968) and theobromine (Shefter, Brennan & Sackman, 1971). Both these molecules are similar to 6BA in possessing N(9) free from substituents. The adenine moiety assumes an N(7)—H rather than the N(9)—H tautomeric form. A similar N(7)—H tautomeric form was reported for 2-mercapto-6-methylpurine monohydrate (Donohue, 1969) and 6-histaminopurine dihydrate (Thewalt & Bugg, 1972). H(N7) appeared in the difference map at a height of 0·8 e Å^{-3}. The observation that C(8)—N(7)—C(5) is 3·5° larger than C(8)—N(9)—C(4) and N(7)—C(8) is 0·037 Å longer than C(8)—N(9) is in accordance with the N(7)—H tautomeric form (Voet & Rich, 1970). The presence of the N(7)—H tautomeric form is further substantiated by the hydrogen-bonding scheme.

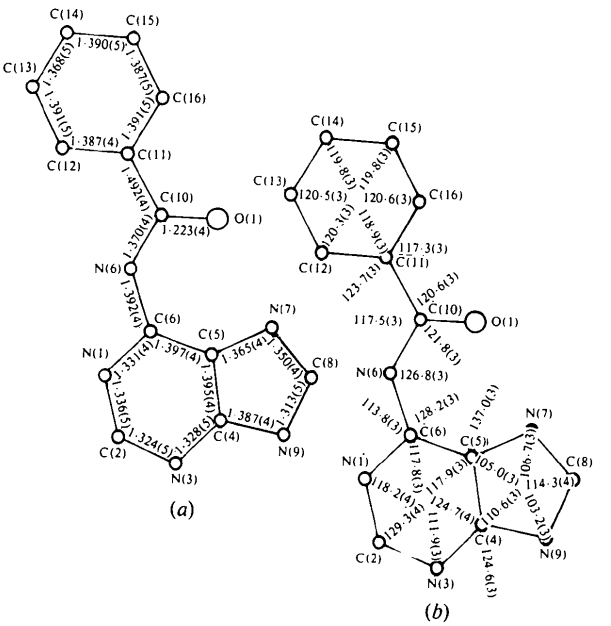

Fig. 1. (*a*) Bond lengths (Å) and (*b*) bond angles (°) with e.s.d.'s in parentheses.

The average bond length in the benzene ring of the benzoyl group is 1·404 (4) Å. C(10)—C(11) is 1·492 (4) Å, an observation consistent with that in benzoic acid (Sim, Robertson & Goodwin, 1955) and *p*-chlorobenzoic acid (Toussaint, 1951). The C(10)=O(1) length [1·223 (4) Å] in the benzoyl group is close to those reported for some γ-lactones [1·198, Jeffrey, Rosenstein & Vlasse (1967); 1·215 Å, High & Kraut (1966)]. The C(6)—N(6)—C(10) angle [126·8 (3)°] is widened as a result of steric interaction between the benzoyl and adenine groups. A similar enlargement (127·6°) occurs in acetanilide (Brown, 1966). For the same reason, N(6)—C(6) is stretched [1·392 (4) Å].

The adenine ring, the benzene ring and the amide group linking these rings define three planes. The equations of the planes through these regions of the molecule are listed in Table 2. The whole molecule is approximately planar. The interplanar angle between the adenine group and the benzene ring is 7·4°. The amide plane makes angles of 18·5 and 12·4° with the adenine and benzene groups respectively. C(10)=O(1) is *trans* to C(12) and *cis* to C(6), the torsion angles being 166·7 (3) and −6·2 (4)° respectively.

* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36061 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Equations of the least-squares planes and deviations* (Å) *of atoms from them*

(I) Plane through the adenine group

$$0{\cdot}9975X - 0{\cdot}0094Y + 0{\cdot}0693Z = 1{\cdot}0042$$

N(1)	−0·009 (3)	C(4)	0·016 (3)
C(2)	−0·014 (4)	C(5)	0·019 (2)
N(3)	−0·003 (3)	C(6)	0·013 (2)
*N(6)	−0·006 (3)	N(7)	−0·016 (2)
N(9)	0·011 (2)	C(8)	−0·017 (3)

(II) Plane through the amide group

$$-0{\cdot}9299X - 0{\cdot}2580Y + 0{\cdot}2617Z = 2{\cdot}0221$$

N(6)	0·009 (2)	C(10)	0·006 (3)
O(1)	−0·006 (2)	H(N6)	−0·008 (26)
*C(6)	0·010 (3)	*C(11)	0·151 (3)

(III) Plane through the benzene ring

$$0{\cdot}9863X - 0{\cdot}1374Y + 0{\cdot}0908Z = 0{\cdot}8401$$

C(11)	0·000 (2)	C(14)	−0·002 (3)
C(12)	−0·001 (3)	C(15)	0·001 (3)
C(13)	0·002 (3)	C(16)	0·000 (3)
*C(10)	0·037 (3)		

* Not included in the least-squares plane calculation.

The molecular configuration in the present structure is sterically favored and is stabilized by intramolecular hydrogen bonding between N(7) and O(1). The N(7)···O(1) distance is 2·65 Å and the N(7)–H(N7)···O(1) angle 117·4°. Similar intramolecular hydrogen bonds have been reported for anthramycin methyl ether monohydrate [Arora, 1979; N···O = 2·57 (1) Å, N–H···O = 113·3 (8)°], 9-ethyladenine–parabanic acid–oxaluric acid monohydrate (Shieh & Voet, 1975; N···O = 2·66 Å, N–H···O = 129°), and 4-amino-1-[4-amino-2-oxo-1(2*H*)-pyrimidinyl]-1,4-dideoxy-β-D-glucopyranuronic acid (*C*-substance) monohydrate (Swaminathan, McAlister & Sundaralingam, 1980; N···O = 2·85 Å, N–H···O = 129°). The cyclic polypeptide valinomycin has also been reported to be stabilized by intramolecular hydrogen bonds of lengths ranging from 2·88 to 2·98 Å and N–H···O angles between 128 and 138° (Duax & Hauptman, 1972).

The N(7)···O(1) hydrogen bond (2·65 Å), which would ordinarily imply a strong hydrogen bond, is weak in the present study due to the strain imposed by the N(7)–H(N7)···O(1) angle (117·4°). The IR spectrum of 6BA in a KBr pellet shows that the absorption bands of C=O and N–H occur at 1675 and 3350 cm^{-1} respectively; the stretching frequencies are shifted by 15 and 50 cm^{-1}, which though inconclusive, is nevertheless indicative of a weak hydrogen bond.

The packing viewed down **a** is illustrated in Fig. 2. The molecules are not involved in any intermolecular hydrogen bonding and antiparallel stacking is a major stabilizing force in this case. The molecules are parallel

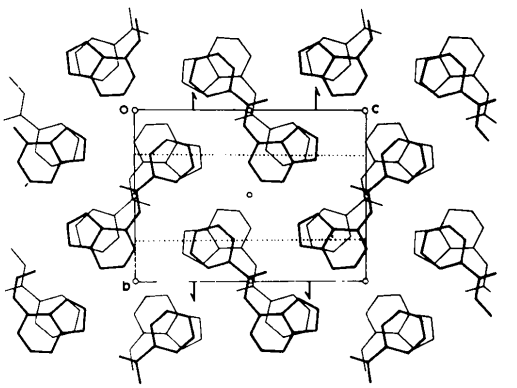

Fig. 2. The crystal structure viewed down [100].

to **a** and the normal to the base plane is only 6·2° away from **a**. The molecules are stacked forming continuous columns which run parallel to **a**. The adenine base and the benzene ring are stacked in an alternating pattern, the adenine base interacting with the benzene ring of a parallel molecule. The stacking distance between the molecules is 3·5 Å and is comparable to the list of stacking distances reported by Reddy & Viswamitra (1975).

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The Structure of the β Modification of Chloramphenicol Palmitate – a Redetermination

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Abstract

$C_{27}H_{42}Cl_2N_2O_6$, M_r = 560·6, is orthorhombic, $P2_12_12_1$, with a = 7·805 (3), b = 52·503 (15), c = 7·414 (2) Å, U = 3038·15 Å^3, Z = 4, D_x = 1·226 Mg m^{-3}. Final R = 0·064 for 2378 reflections. All the H atoms were located. Thus, exact statements on the molecular geometry and especially on the hydrogen bonds are possible. There exists only one intermolecular O–H···O hydrogen bond. The location of the H atoms shows that the intramolecular N–H···O hydrogen bond [Eguchi & Iitaka (1974). *Acta Cryst.* B**30**, 2781–2783] does not exist. This result is in agreement with IR spectroscopic measurements.

Introduction

Several investigations on chloramphenicol palmitate (CAP) have been carried out to relate physicochemical properties with the therapeutic efficacy of this antibiotic (Tamura & Kuwano, 1961; Aguiar, Krc, Kinkel & Samyn, 1967; Aguiar & Zelmer, 1969; Miyamoto, Kiyotaki, Kisoh, Mitsunaga & Maeda, 1973; Andersgaard, Finholt, Gjermundsen & Hoyland, 1974; Burger, 1977; Szulzewsky, Kulpe, Schulz, Fichtner & Schinkowski, 1981). This contribution is concerned with a single-crystal X-ray analysis and IR spectroscopic measurements on the β modification of CAP. Crystallization proceeded in the following way: methods described by Burger (1977), Aguiar *et al.* (1967) and Tamura & Kuwano (1961) were used and crystals suitable for single-crystal diffractometry of the β modification and a crystalline powder of the α modification were obtained. Crystals of the γ modification suitable for single-crystal diffractometry were obtained by heating a CAP–ethanol solution to ~350 K and then cooling to room temperature. Weissenberg and Guinier photographs of the γ modification indicated the space group $P2_1$ and lattice constants a = 35·528 (20), b = 16·449 (10), c = 5·185 (6) Å, β = 90·15 (4)° (Szulzewsky *et al.*, 1981). An attempt to reconcile the crystal structure of the β modification of CAP obtained by Eguchi & Iitaka (1974) with IR spectroscopic results failed. Neither the wavenumbers nor the shapes of all bands explain completely the proposed structure, especially the strong intramolecular hydrogen bond involving O(3) and N(1)–H. This prompted us to redetermine the structure of the β modification.

The intensities of the X-ray reflections were collected on a Hilger & Watts four-circle diffractometer operating in an ω-scan with Mo $K\alpha$ radiation (λ = 0·7107 Å) monochromatized by a graphite crystal. 2395 reflections up to θ = 23° were measured. Intensities were corrected for Lorentz and polarization effects. The dimensions of the approximately cube-shaped crystal were 0·35 × 0·25 × 0·40 mm. For the structure determination the non-hydrogen parameters given by Eguchi & Iitaka (1974) were used to start with, and were refined by full-matrix least squares. The function minimized was $\sum w(|F_o| - |F_c|)^2$ with w = 1. Scattering factors for neutral Cl, O, N, C and H together with anomalous-dispersion terms for Cl were taken from *International Tables for X-ray Crystallography* (1974). The H atoms of tertiary CH groups, secondary CH_2 groups and aromatic CH groups were placed in their calculated positions with the CH_3, OH

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