

Crystal Structure of 3-Ethyladenine

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The crystal structure of 3-ethyladenine has been derived from 1760 reflections measured by counter methods. The value of R is 0.062 and the estimated standard deviations in distances between non-hydrogen atoms are 0.002–0.003 Å. The molecular structure is compared with that of 9-substituted purines. The bonds N1–C6–C5–N7, as well as C5–C4, are left relatively unaltered by the tautomerization, whereas those in the fragment N1–C2–N3–C4–N9 are changed by 0.02–0.03 Å. Hydrogen bonds N6–H...N7 link the molecules together in dimers.

In the purines the proton may be attached to N1, N3, N7, or N9, corresponding to four fundamental tautomeric forms. Derivatives of all forms are known, and the structure has been established by X-ray analysis for a number

of N7- and N9-tautomers.^{1,2} For the other forms the geometries have had to be assumed.³ In the present paper the structure of an N3-derivative, 3-ethyladenine, is reported. The compound is of considerable biological interest, as an appreciable proportion of alkyl groups is attached to adenine N3 by alkylation of DNA.¹⁰ Different molecular mechanisms have been discussed for such alkyl-induced mutations.^{11,12}

EXPERIMENTAL. STRUCTURE ANALYSIS

A sample of 3-ethyladenine ($C_7N_5H_8$, M. W. = 163.1) was kindly supplied by Dr. Peter Brookes of the Chester Beatty Research Institute. Unit cell dimensions are $a = 9.007(4)$ Å, $b = 7.139(3)$ Å, $c = 13.806(5)$ Å, and $\beta = 118.58(2)^\circ$. The

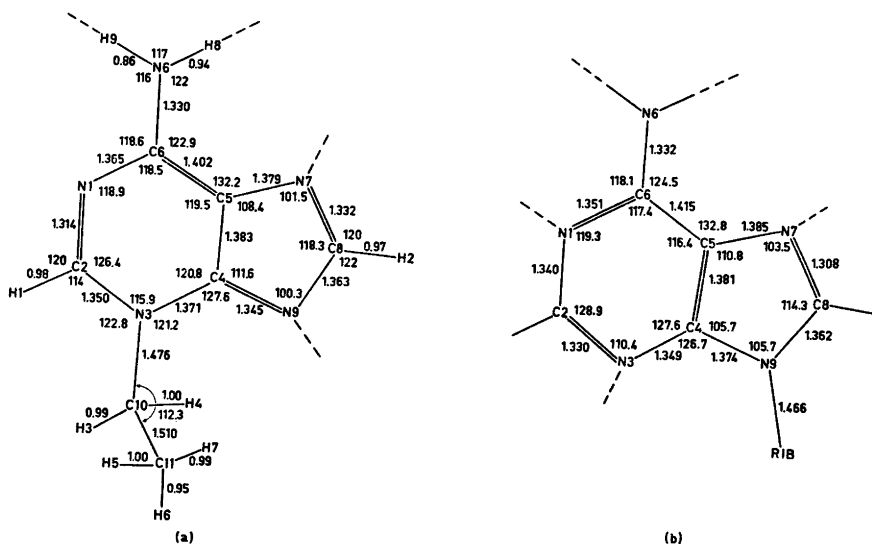


Fig. 1. Bond lengths and bond angles in 3-ethyl-adenine (a) and adenosine (b). E.s.d.'s in both compounds are about 0.003 Å and 0.2°.

Table 1. Positional and thermal parameters for non-hydrogen atoms ($\times 10^5$) with estimated standard deviations. The anisotropic temperature factor is $\exp \{- (B_{11}h^2 + B_{22}k^2 + B_{33}l^2 + B_{12}hk + B_{13}hl + B_{23}kl)\}$.

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> ₁₁	<i>B</i> ₂₂	<i>B</i> ₃₃	<i>B</i> ₁₂	<i>B</i> ₁₃	<i>B</i> ₂₃
C2	15270	55899	33804	1263	1722	451	578	646	456
	25	28	16	38	44	14	66	38	43
C4	31226	46146	51824	942	1322	401	-75	647	69
	22	25	14	31	37	13	56	33	36
C5	34856	29773	48022	886	1342	375	94	615	19
	21	25	14	30	36	12	55	31	35
C6	28035	26921	36636	933	1569	400	-67	665	-13
	22	26	15	31	40	12	58	33	38
C8	46675	29590	65321	1549	2039	382	1009	627	116
	27	30	17	40	50	14	76	38	45
C10	18663	77953	48622	1538	1268	648	75	1030	115
	27	27	17	40	40	16	64	43	42
C11	7242	76162	53770	2408	1830	1054	1124	2288	342
	34	36	22	57	54	25	91	65	62
N1	17884	40493	29629	1334	1843	421	552	643	169
	20	23	13	33	39	12	55	32	35
N3	21466	59826	44618	1074	1312	470	128	733	131
	19	21	12	29	32	11	48	30	32
N6	30726	11425	32357	1636	1919	385	696	819	-81
	22	23	12	35	38	11	59	33	35
N7	45132	18862	56998	1359	1758	405	771	698	178
	20	23	12	30	36	11	55	30	34
N9	38555	46423	62904	1511	1797	420	646	726	-89
	21	23	13	33	38	12	59	32	35

Table 2. Hydrogen atom coordinates ($\times 10^3$) and temperature factors.

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> (\AA^2)
H1	83	659	289	2.4
H2	532	252	729	3.8
H3	140	868	423	3.7
H4	298	838	538	4.7
H5	-46	736	480	7.7
H6	70	878	570	5.1
H7	111	662	594	5.0
H8	386	24	367	3.3
H9	282	120	255	3.3

space group is $P2_1/c$. Flotation gave a density of 1.38 g/cm³, corresponding to four (calc. 3.97) molecules in the unit cell.

Intensity measurements were carried out on a crystal of dimensions 0.4 × 0.2 × 0.12 mm using a Picker automatic diffractometer and MoK α radiation ($\lambda = 0.71069$ Å, graphite monochromator). The $\omega/2\theta$ scan technique (rate 2°/min) was employed and 1760 reflections with $2\theta < 65^\circ$ were recorded with measurable intensities, using a cut-off limit of 2σ . The in-

tensities of two standard reflections showed no systematic variation during the data collection. Absorption and extinction corrections were not applied.

The structure was solved by direct methods and refined by full matrix least squares calculations to $R = 0.062$ ($R_w = 0.059$). The weighting scheme was based on standard deviations from counter statistics and an assumed 2% fluctuation in diffractometer stability. Anisotropic temperature factors were applied to the non-hydrogen atoms, isotropic ones to the hydrogen atoms. Positional and thermal parameters are given in Tables 1 and 2 and the corresponding bond lengths and angles in Fig. 1. Estimated standard deviations lie in the range 0.0022–0.0031 Å for bond lengths and 0.15–0.18° for bond angles involving non-hydrogen atoms and are about ten times as large for those involving hydrogen atoms.

The programs used are described in Ref. 4. The atomic scattering factors were those of Hanson *et al.*⁵ for non-hydrogen atoms and of Stewart *et al.*⁶ for hydrogen atoms. A table of observed and calculated structure factors will be supplied by the authors on request.

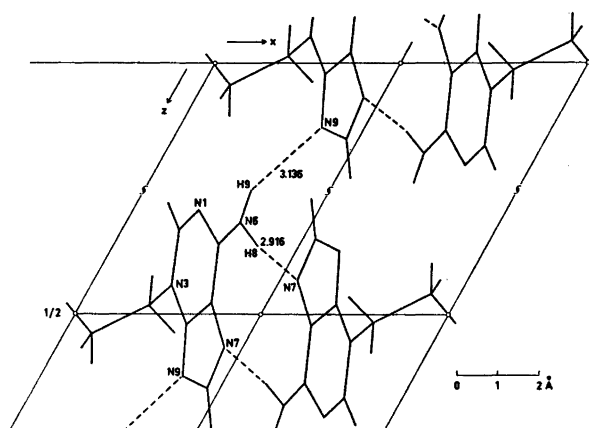


Fig. 2. The crystal structure viewed along *b*.

Table 3. Distances (Å) from the purine plane.

C2	0.002	N3	0.021
C4	-0.003	N7	0.011
C5	0.008	N9	-0.018
C6	0.003	C10	0.119
C8	-0.003	C11	-1.153
N1	-0.019	N6	-0.009

DISCUSSION

In Table 3 distances from the least squares plane through the nine ring atoms are given. It is seen that the purine ring is essentially, but not exactly, planar. The deviations cannot be described in terms of the bending about C4-C5 characteristic for most purines.⁷ The terminal methyl group points away from the plane.

The molecule is in its amino form as shown by the positional and thermal parameters of atoms H8 and H9. This is in agreement with spectroscopic measurements.⁹

For comparison the geometry of a representative N9-tautomer, adenosine,³ is also shown in Fig. 1. The main difference between the N3- and the N9-tautomer occurs in the internal ring angles at atoms N3 and N9. This is consistent with earlier evidence that bonding of an extra-annular atom to a ring nitrogen atom causes the ring angle to increase.^{1,8} In the present structure the ring angle at N3 is 5.5° greater and that at N9 5.4° smaller than in the N9-tautomer. Adjacent ring angles are corre-

spondingly adjusted.

A surprising feature of the structure is that the bonds N1-C6, C6-C5, and C5-C4 differ very little from the corresponding ones in the N9-tautomer, in spite of the fact that the principal valence bond structure is entirely different, as indicated in Fig. 1. The bond N1-C6 is thus considerably shorter (1.365 Å) than C6-C5 (1.402 Å) also in the N3-tautomer. Evidently the principal canonical structure does not "contribute" decisively to the electronic structure. A general comparison of the bond lengths in the two tautomers shows that the bonds N1-C6-C5-N7, as well as C5-C4, are not much altered by the tautomerization, whereas those in the fragment N1-C2-N3-C4-N9 all are considerably changed (by 0.020-0.029 Å). The same holds in a general way for the bond angles.

The geometry found in the present structure analysis differs considerably from that assumed in theoretical calculations on the N3-tautomer of purine.³

In the crystal (Fig. 2) the molecules are linked together in pairs across centres of symmetry by N6-H8...N7 hydrogen bonds of length 2.916 Å. The adenine moieties of a pair are approximately coplanar. The pairs are connected by weak N6-H9...N9 hydrogen bonds of length 3.136 Å. The methyl groups pack in columns along (0,*y*,0) and (0,*y*,1/2), the distances between neighbouring methyl carbon atoms in the columns being 3.61 and 3.93 Å.

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