Elementary Patterns in Protein-Nucleic Acid Interactions. III.† Crystal Structure of Adenine:Phthalic Acid (3:1) Complex Hexahydrate

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Crystal of adenine:phthalic acid (3:1) complex hexahydrate were obtained from an aqueous solution containing equimolar amounts of adenine and *N,N*-phthaloyl-DL-glutamic acid. The space group is $P\bar{1}$ with unit-cell dimensions of $a=14.232(2)$, $b=16.730(2)$, $c=7.336(1)$ Å, $\alpha=78.97(1)$, $\beta=96.14(1)$, and $\gamma=68.99(1)°$. The structure was solved by the direct method and its parameters were refined by a block-diagonal least-squares technique. The two carboxyl groups of the phthalic acid are dissociated and they are hydrogen-bonded to the amino group and the protonated N(1) of the two adeninium monocations. The geometrical characteristics in adeninium monocations are explained with the electronic structures perturbed by the surroundings. A typical feature of the C–H···N hydrogen bond is observed between the adeninium cations. The third adenine molecule is neutral and disordered. A comparison of the dissociation constants of the related compounds suggests that the protonation of adenine occurs when the hydrogen bonds are formed between the carboxyl group of acidic amino acid residue in protein and the unpaired adenine base in nucleic acid.

We have been engaged in the structural studies on elementary patterns in protein-nucleic acid interactions, using crystals in which nucleotide base and amino acid coexist.[1–6] In case of the systems containing cytosine and carboxyl group, for instance, the α-carboxyl group is dissociated and hydrogen-bonded to the amino group and the protonated N(3) atom in cytosine,[1,2] whereas the γ-carboxyl group of glutamic acids interacts with the amino group of base-paired cytosine.[3] In the present paper, we deal with the system containing adenine and carboxyl group.

Experimental

Single crystals of adenine: phthalic acid (3:1) complex hexahydrate were obtained by slow evaporation of an aqueous solution containing equimolar amounts (0.2 mmol) of adenine and *N,N*-phthaloyl-DL-glutamic acid, both of which were purchased from Tokyo Kasei Kogyo Co. An elementary analysis. Found: C, 40.7; H, 4.5; N, 30.5%. Calcd. for $3C_5H_5N_5\cdot C_8H_6O_4\cdot 6H_2O$: C, 40.6; H, 4.9; N, 30.9%. It means that *N,N*-phthaloyl-DL-glutamic acid is hydrolyzed by heating the solution in presence of adenine. A crystal, $0.2\times0.3\times0.6$ mm³ in size, was used for X-ray data collection on a Rigaku four-circle diffractometer with graphite-monochromated Mo $K\alpha$ radiation ($\lambda=0.71073$ Å). The unit-cell dimensions were calculated with 65 high-angle reflexions. The crystal data are given in Table 1.

Diffraction intensities were measured in the $\omega/2\theta$ scan mode with a scan width of 1.3° (in ω) plus α_1-α_2 divergence and a scan speed of 4° (in 2θ) min^{-1}. Five reference reflexions showed no significant intensity deterioration throughout the data collection. The intensities were corrected for Lorentz and polarization factors but not for absorption effects. Of 7193 independent reflexions in the range $2<2\theta<55°$, 3117 weak reflexions with F_o less than $3\sigma_p(F_o)$ were considered to be unobserved, where $\sigma_p(F_o)$ is evaluated by counting statistics. The standard deviations were estimated by the equation of $\sigma^2(F_o)=\sigma_p^2(F_o)+qF_o^2$, where q (7.77×10^{-5}) was derived from the variations of the monitored reflexions.[7]

Table 1. Crystal data

Adenine:Phthalic (3:1) complex hexahydrate	
$3C_5H_5N_5:C_8H_6O_4\cdot6H_2O$	*F.W.* 679.6
Space group: $P\bar{1}$	
$a=14.232(2)$ Å	$\alpha=78.97(1)°$
$b=16.730(2)$ Å	$\beta=96.14(1)°$
$c=7.336(1)$ Å	$\gamma=68.99(1)°$
$U=1570.7(4)$ Å³	$Z=2$
$D_x=1.437$ g·cm^{-3}	$D_m=1.43_7$ g·cm^{-3}

Structure Determination

The space group was assumed to be $P\bar{1}$ from normalized structure factor statistics. The phases were derived by using the MULTAN programme[8] with 436 E's ($E>1.9$); two reflexions with the largest E's (>5.0) were omitted in the calculation. Molecular skeletons of phthalic acid and three adenines were found on the E map derived from the phase set with the smallest R_{Karle} value.[9] Subsequent electron density calculations gave the positions of the six water molecules and then revealed that one of the three adenines was disordered in the two modes of orientations and that one of the six waters occupied the two sites. Positional and thermal parameters of the non-hydrogen atoms were refined by block-diagonal least-squares techniques, half occupancies being assumed for the disordered atoms. Hydrogen atoms except for the water and disordered adenine molecules were found on a difference map, which were included in later refinements. The quantity minimized was $\Sigma w(|F_o|-|F_c|)^2$ with $w=1/\sigma^2(F_o)$. The final R was 0.085 for the observed 4076 reflexions; the maximum shift of parameters in the last cycle was 0.2σ for C, N, and O atoms and 0.7σ for H atoms.

Atomic scattering factors used were taken from "International Tables for X-Ray Crystallography."[10] Atomic parameters are listed in Table 2.[11]

† Part II of this series is Ref. 6.

TABLE 2. FRACTIONAL COORDINATES AND ISOTROPIC TEMPERATURE FACTORS

The B values accompanied with ⟨ ⟩ are the equivalent isotropic temperature factors calculated from 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 $(\sum(B-8\pi^2U_i)^2/3)^{1/2}$. The e.s.d.'s in ( ) refer to last decimal places.

Atom	x	y	z	B/Å^2	Atom	x	y	z	B/Å^2
N (1A)	0.0199 (2)	0.2197 (2)	0.1283 (5)	3.0⟨9⟩	C (3P)	0.4949 (3)	0.3872 (3)	0.1998 (7)	3.9⟨12⟩
C (2A)	0.1092 (3)	0.2272 (3)	0.1932 (7)	3.4⟨9⟩	C (4P)	0.4598 (3)	0.4414 (3)	0.3196 (7)	3.7⟨7⟩
N (3A)	0.2008 (3)	0.1639 (2)	0.2245 (5)	3.5⟨8⟩	C (5P)	0.3757 (3)	0.5209 (3)	0.2498 (6)	3.2⟨5⟩
C (4A)	0.1978 (3)	0.0884 (3)	0.1839 (6)	3.1⟨5⟩	C (6P)	0.3259 (3)	0.5465 (3)	0.0610 (6)	2.5⟨6⟩
C (5A)	0.1113 (3)	0.0745 (3)	0.1229 (6)	2.7⟨5⟩	C (7P)	0.3123 (3)	0.5189 (3)	−0.2643 (6)	2.8⟨5⟩
C (6A)	0.0147 (3)	0.1440 (3)	0.0914 (6)	3.0⟨7⟩	C (8P)	0.2326 (3)	0.6309 (3)	0.0006 (6)	2.9⟨6⟩
N (6A)	−0.0747 (3)	0.1430 (2)	0.0330 (6)	3.9⟨22⟩	O (71P)	0.3170 (2)	0.4569 (2)	−0.3473 (4)	3.5⟨11⟩
N (7A)	0.1377 (3)	−0.0107 (2)	0.0987 (5)	3.3⟨11⟩	O (72P)	0.2662 (2)	0.5989 (2)	−0.3451 (4)	3.5⟨10⟩
C (8A)	0.2386 (3)	−0.0443 (3)	0.1438 (7)	3.8⟨13⟩	O (81P)	0.1465 (2)	0.6269 (2)	−0.0446 (4)	3.5⟨15⟩
N (9A)	0.2788 (3)	0.0123 (2)	0.1973 (6)	3.8⟨17⟩	O (82P)	0.2441 (2)	0.7015 (2)	0.0071 (5)	4.5⟨26⟩
N (1B)	0.1512 (3)	0.4993 (2)	0.4067 (5)	2.9⟨7⟩	O (1W)	0.4408 (4)	0.1706 (3)	0.0006 (7)	10.6⟨24⟩
C (2B)	0.1457 (3)	0.4244 (3)	0.3687 (6)	3.4⟨7⟩	O (2W)	0.2468 (3)	0.7768 (2)	0.5438 (5)	6.1⟨16⟩
N (3B)	0.0653 (3)	0.4176 (2)	0.2798 (5)	3.3⟨8⟩	O (3W)	0.4284 (3)	0.2809 (2)	0.6613 (6)	6.3⟨16⟩
C (4B)	−0.0160 (3)	0.4969 (3)	0.2272 (6)	2.7⟨5⟩	O (4W)	0.3641 (3)	0.7429 (2)	0.2687 (5)	5.8⟨27⟩
C (5B)	−0.0193 (3)	0.5765 (3)	0.2563 (6)	2.6⟨4⟩	O (5W)	0.3726 (4)	0.2186 (4)	0.3308 (8)	12.2⟨69⟩
C (6B)	0.0702 (3)	0.5784 (3)	0.3546 (6)	2.7⟨3⟩	O (6W)	0.4880 (5)	−0.0459 (6)	0.346 (1)	8.0⟨49⟩
N (6B)	0.0799 (3)	0.6483 (2)	0.3993 (5)	3.4⟨13⟩	O (7W)	0.4796 (6)	−0.0149 (7)	0.176 (2)	11.3⟨77⟩
N (7B)	−0.1164 (3)	0.6415 (2)	0.1834 (5)	3.0⟨4⟩	H (61A)	−0.132 (3)	0.193 (3)	0.013 (6)	2.4 (11)
C (8B)	−0.1677 (3)	0.5990 (3)	0.1108 (6)	3.2⟨7⟩	H (62A)	−0.079 (3)	0.093 (3)	0.007 (6)	2.8 (11)
N (9B)	−0.1112 (3)	0.5111 (2)	0.1340 (5)	3.0⟨7⟩	H (1A)	−0.047 (3)	0.271 (3)	0.104 (6)	2.5 (11)
N (1C)	−0.3346 (3)	0.9882 (4)	0.2741 (7)	7.1⟨37⟩	H (2A)	0.101 (3)	0.291 (3)	0.211 (6)	3.2 (12)
C (2C)	−0.3306 (5)	1.0633 (5)	0.3076 (9)	8.8⟨54⟩	H (9A)	0.352 (4)	−0.004 (3)	0.244 (7)	5.4 (14)
N (3C)	−0.2356 (3)	1.0646 (3)	0.3613 (6)	6.2⟨24⟩	H (8A)	0.281 (4)	−0.111 (3)	0.143 (7)	5.6 (15)
C (4C)	−0.1612 (4)	0.9845 (4)	0.3684 (7)	5.1 (32)	H (61B)	0.143 (3)	0.643 (3)	0.474 (6)	2.3 (11)
C (5C)	−0.1489 (7)	0.8953 (6)	0.333 (1)	3.8⟨14⟩	H (62B)	0.019 (3)	0.714 (3)	0.370 (6)	3.5 (12)
C (6C)	−0.2476 (7)	0.8942 (7)	0.283 (1)	4.9⟨21⟩	H (1B)	0.213 (3)	0.492 (3)	0.490 (6)	1.8 (10)
C (5'C)	−0.2353 (7)	0.9508 (6)	0.309 (1)	3.5⟨11⟩	H (2B)	0.212 (3)	0.369 (3)	0.415 (6)	1.8 (10)
C (6'C)	−0.1847 (7)	0.8662 (6)	0.301 (1)	3.2⟨6⟩	H (9B)	−0.131 (3)	0.467 (3)	0.098 (6)	3.6 (12)
N (6C)	−0.2460 (4)	0.8169 (3)	0.2470 (6)	5.8⟨29⟩	H (8B)	−0.237 (3)	0.625 (2)	0.048 (5)	0.7 (9)
N (7C)	−0.0654 (3)	0.8300 (2)	0.3520 (6)	4.5⟨16⟩	H (2P)	0.476 (3)	0.375 (3)	−0.087 (6)	2.2 (10)
C (8C)	−0.0069 (5)	0.8731 (3)	0.4043 (7)	6.1⟨44⟩	H (3P)	0.560 (3)	0.325 (3)	0.256 (6)	3.6 (12)
N (9C)	−0.0573 (3)	0.9586 (3)	0.4172 (6)	4.7⟨19⟩	H (4P)	0.494 (3)	0.426 (3)	0.466 (6)	2.2 (10)
C (1P)	0.3613 (3)	0.4920 (3)	−0.0592 (6)	2.3⟨3⟩	H (5P)	0.347 (3)	0.562 (3)	0.340 (6)	1.9 (10)
C (2P)	0.4456 (3)	0.4124 (3)	0.0106 (6)	3.2⟨8⟩					

Results and Discussion

Molecular Structure. Both the two carboxyl groups of phthalic acid, I and II, are dissociated and the two adenine molecules, A and B, are monoprotonated at N(1), as confirmed by a difference synthesis. The third adenine, C, is neutral and disordered in the two modes of orientations. Bond distances and angles are shown in Fig. 1.

The two C–O distances in the carboxyl group I differ significantly from each other, while those in the carboxyl group II are almost the same. The longer C(7P)–O(71P) bond suggests that the negative charges are localized mainly on O(71P). The benzene ring of the phthalic acid is planar within 0.002 Å, from which the carboxyl carbon atoms, C(7P) and C(8P), are deviated by −0.050 Å and 0.070 Å, respectively, perhaps owing to repulsions between them. The mean planes of the carboxyl groups make angles of 27.6(2)° for I and 64.6(2)° for II with that of the benzene ring. These values do not seem to be inherent though they resemble those of bivalent phthalic acid salt;[12] the relative orientation of the carboxyl groups varies easily by packing effects of crystal.[13]

It is known that adenine molecule exists in acidic circumstances as mono- or di-cation, whose bond lengths and angles are dependent on protonation.[14,15] The dimensions of the present adeninium cations, A and B, correspond to typical ones of the monocationic species.[14] Figure 2 shows the environments of molecules surrounded by hydrogen bonds. The protonated N(1) and the amino nitrogen N(6) atoms in adeninium B are hydrogen bonded to the carboxylate oxygens, O(71P) and O(72P) of the group I, respectively, while those in A form a similar double-

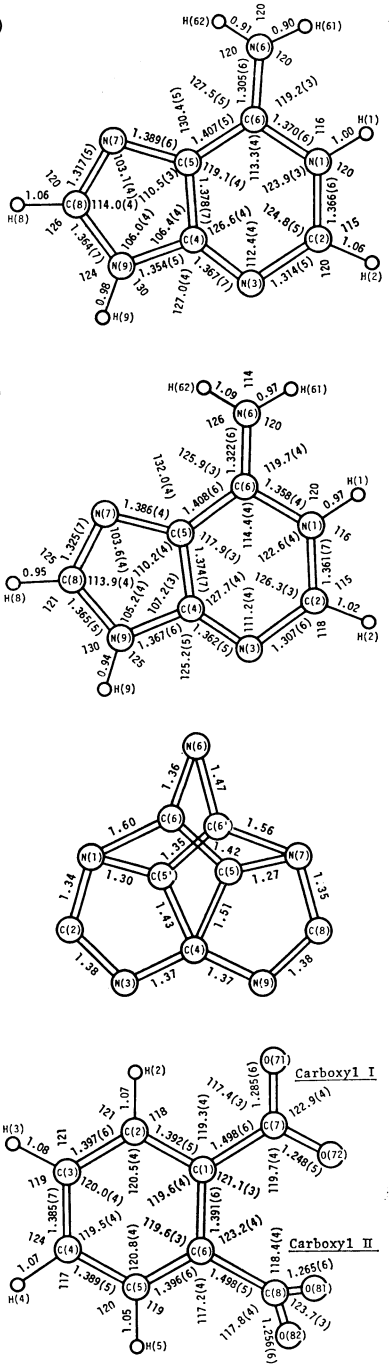
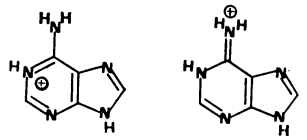


Fig. 1. Bond lengths (l/Å) and angles (ϕ/°) of adenine: phthalic acid (3:1) complex hexahydrate.
(a) Adenine A, (b) adenine B, (c) adenine C, and (d) phthalic acid. E.s.d.'s are 0.05 Å and 4° for H atoms.

hydrogen bond with the carboxyl group II. Here it is noted that the N(1)···O(71P) hydrogen bond (2.594(5) Å) is significantly shorter than the others, and the negative charges are predominant at O(71P), as mentioned above. In such situation, the adeninium B is perturbed, so that the contribution of canonical formula **1** increases, as compared with the adeninium A in which the canonical formula **2** is predominant. The shorter C(6)–N(6) bond of adeninium A, accompanied by the slightly longer C(6)–N(1) bond



1 **2**

than that of B, is consistent with this anticipation. Table 3 shows the atomic net charges calculated by CNDO approximation[16] for these two adeninium cations. In adeninium A, the positive charges on the amino group increase and those on N(1)–H(1) group decrease, as compared with those in B. These charges, though small, seem to be consistent with the above interpretation.

The adeninium monocations so far analysed show the marked differences in C(6)–N(6) and C(6)–N(1) bond distances, which suggest the change in relative contributions from the two canonical formulae, **1** and **2**. The difference between adenosine hydrochloride[14f] and adenine hydrochloride hemihydrate[14d] can be correlated to the hydrogen bond distances, just as mentioned above. It may be concluded that the adenine cation can be adapted to the various surroundings by changing its electronic structure to some extent.

Crystal Structure. The crystal structure viewed down the c axis is shown in Fig. 3. Hydrogen bond distances and angles are given in Fig. 2 and Table 4.

The adenine C is disordered with a local approximate mirror symmetry; the mirror plane is perpendicular to the adenine plane passing through N(6) and C(4). As seen from Fig. 3, only the C(5) and C(6) atoms give the resolved peaks on the electron density map. The disordered adenine molecules around the inversion centre at 0,0,1/2 may be hydrogen bonded with the scheme shown in Fig. 4. According to this scheme, the water oxygen, O(6W) and O(7W), are also disordered by the hydrogen bonds with the adenine C.

Table 3. Net charge distribution

	Adenine A	Sum for the group	Adenine B	Sum for the group
N (1)	−0.112	0.057	−0.109	0.064
H (1)	0.169		0.173	
C (2)	0.241	0.288	0.237	0.280
H (2)	0.047		0.043	
N (3)	−0.165		−0.161	
C (4)	0.243		0.236	
C (5)	−0.045		−0.041	
C (6)	0.335		0.338	
N (7)	−0.164		−0.165	
C (8)	0.190	0.233	0.196	0.240
H (8)	0.043		0.044	
N (9)	−0.105		−0.114	
H (9)	0.168		0.169	
N (6)	−0.203	0.156	−0.200	0.153
H (61)	0.171		0.160	
H (62)	0.181		0.193	

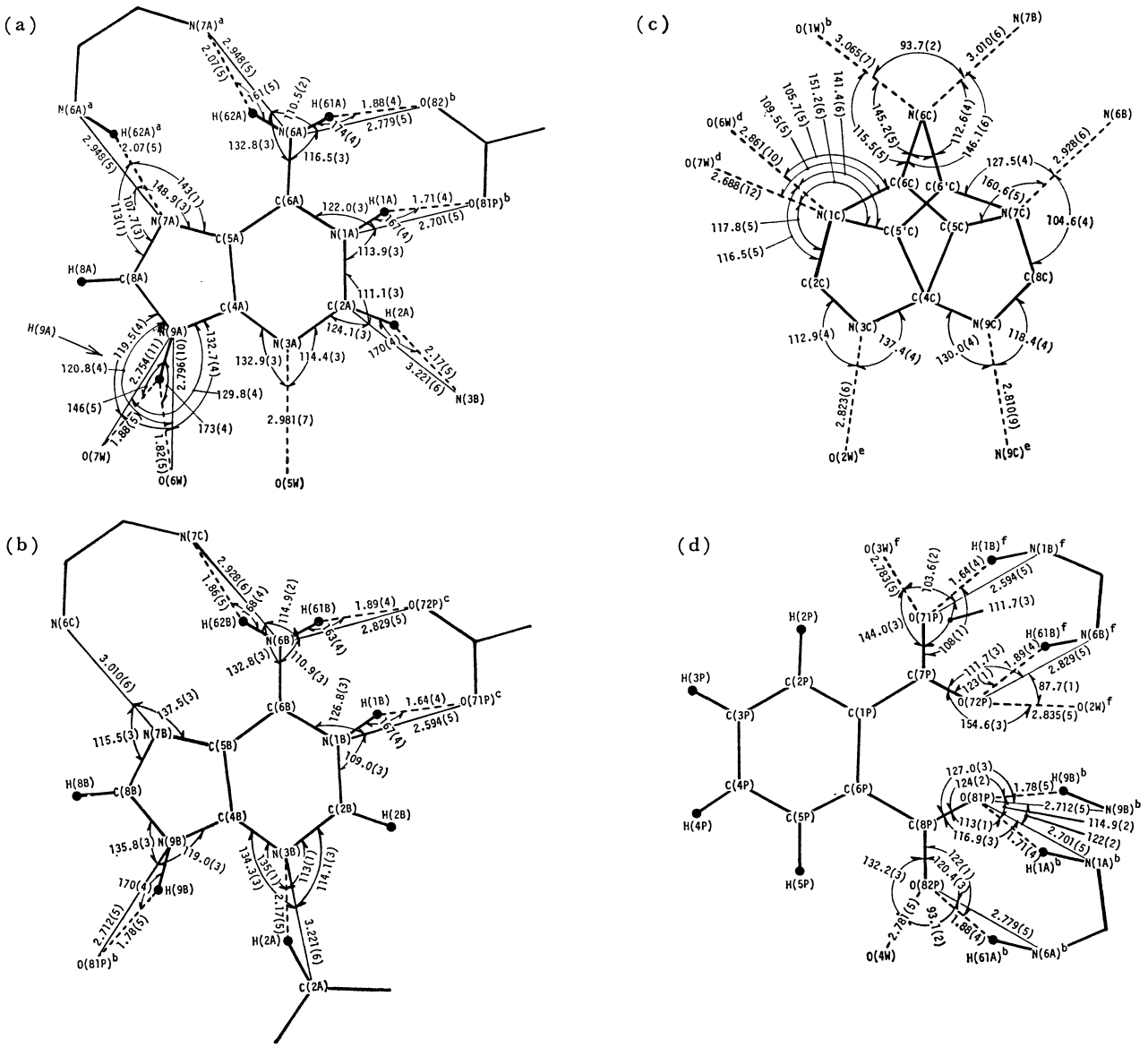


Fig. 2. Hydrogen bond distances (l/Å) and angles (ϕ/°) for (a) adenine A, (b) adenine B, (c) adenine C, and (d) phthalic acid.
The symmetry codes, a—f, are the same as those in Table 4.

The two adeninium A's form a dimer around the inversion centre at 0,0,0 through the N(6)–H···N(7) hydrogen bond. The adeninum B forms a dimer with the adenine C through the N(7B)···H–N(6C) and N(6B)–H···N(7C) [or disordered N(1C)] hydrogen bonds.

Intermolecular stackings are made with different kinds of adenine. The adeninium A and the adenine C at $-x,1-y,-z$ are stacked alternatively along the c axis with the dihedral angle of 2.4(1)° and with the spacings of 3.26 and 3.56 Å. The adeninium B is stacked parallel to that related by the inversions at 0,1/2,0 or 0,1/2,1/2 along the c axis with the spacings of 3.23 and 3.33 Å, respectively. By this way, all kinds of adenines form a layer parallel to the bc plane.

The phthalic acid is linked to the three adeninium cations by the hydrogen bonds between the carboxyl I and the adeninium B [N(6) and the protonated N(1)] and between the carboxyl II and the adeninium A [the same atoms as B] at $-x,1-y,-z$, O(81P) of the latter carboxyl group II being at the same time an acceptor of hydrogen bond from N(9) of adeninium B at $-x,1-y,-z$. The benzene ring of this acid is stacked parallel to that related by the inversion at 1/2,1/2,1/2 with the spacing of 3.45 Å. The water molecules lie between the adenine layers, forming hydrogen bonds with adenine, phthalic acid, and other water molecules.

A short C–H···N contact is observed between the adeninium A and B, as shown in Fig. 2. The C(2)–H(2) bond points to a lone pair lobe of N(3). Since N(3) is significantly negative and the C(2)–H(2) group is positive (Table 3), this contact is favourable to assume the C–H···N hydrogen bond, which has been proposed in hydrogen cyanide,[17] α-1-[(*p*-bromophenyl)-

TABLE 4. HYDROGEN BOND DISTANCES AND ANGLES OF WATER MOLECULES

Some short contacts are also shown. Standard deviations are given in parentheses.

Distances(l/Å)		Angles(ϕ/°)	
O (1W) ··· N (6C) [b]	3.065 (5)	N (6C) [b] ··· O (1W) ··· O (3W) [f]	76.0 (2)
O (1W) ··· O (3W) [f]	2.747 (7)	N (6C) [b] ··· O (1W) ··· O (5W)	103.7 (2)
O (1W) ··· O (5W)	2.853 (8)	N (6C) [b] ··· O (1W) ··· O (7W)	88.6 (3)
O (1W) ··· O (7W)	2.948 (12)	O (3W) [f] ··· O (1W) ··· O (5W)	127.9 (3)
O (1W) ··· O (7W) [j]	3.040 (12)	O (3W) [f] ··· O (1W) ··· O (7W)	141.8 (3)
		O (5W) ··· O (1W) ··· O (7W)	89.4 (3)
O (2W) ··· N (3C) [e]	2.823 (6)	N (3C) [e] ··· O (2W) ··· O (72P) [c]	150.0 (2)
O (2W) ··· O (72P) [c]	2.835 (5)	N (3C) [e] ··· O (2W) ··· O (4W)	111.1 (2)
O (2W) ··· O (4W)	2.768 (5)	O (72P) [c] ··· O (2W) ··· O (4W)	92.6 (2)
O (3W) ··· O (71P) [d]	2.783 (5)	O (71P) [c] ··· O (3W) ··· O (1W) [c]	111.4 (2)
O (3W) ··· O (1W) [c]	2.747 (7)	O (71P) [c] ··· O (3W) ··· O (4W) [g]	105.9 (2)
O (3W) ··· O (4W) [g]	2.810 (5)	O (71P) [c] ··· O (3W) ··· O (5W)	116.5 (2)
O (3W) ··· O (5W)	2.957 (7)	O (1W) [c] ··· O (3W) ··· O (4W) [g]	94.6 (2)
		O (1W) [c] ··· O (3W) ··· O (5W)	113.0 (2)
		O (4W) [g] ··· O (3W) ··· O (5W)	113.2 (2)
O (4W) ··· O (82P)	2.781 (5)	O (82P) ··· O (4W) ··· O (2W)	103.5 (2)
O (4W) ··· O (2W)	2.768 (5)	O (82P) ··· O (4W) ··· O (3W) [g]	134.4 (2)
O (4W) ··· O (3W) [g]	2.810 (5)	O (2W) ··· O (4W) ··· O (3W) [g]	120.3 (2)
O (5W) ··· N (3A)	2.981 (7)	N (3A) ··· O (5W) ··· O (1W)	85.8 (2)
O (5W) ··· O (1W)	2.853 (8)	N (3A) ··· O (5W) ··· O (3W)	131.5 (2)
O (5W) ··· O (3W)	2.957 (7)	O (1W) ··· O (5W) ··· O (3W)	142.6 (3)
O (6W) ··· N (9A)	2.796 (10)	N (9A) ··· O (6W) ··· N (1C) [h]	140.9 (4)
O (6W) ··· N (1C) [h]	2.861 (10)	N (9A) ··· O (6W) ··· O (6W) [i]	108.2 (3)
O (6W) ··· O (6W) [i]	3.026 (17)	N (1C) [h] ··· O (6W) ··· O (6W) [i]	79.9 (3)
O (7W) ··· N (9A)	2.754 (11)	N (9A) ··· O (7W) ··· N (1C) [h]	156.9 (5)
O (7W) ··· N (1C) [h]	2.688 (12)	N (9A) ··· O (7W) ··· O (1W)	96.2 (4)
O (7W) ··· O (1W)	2.948 (12)	N (9A) ··· O (7W) ··· O (7W) [j]	115.9 (5)
O (7W) ··· O (7W) [j]	2.705 (22)	N (1C) [h] ··· O (7W) ··· O (1W)	78.8 (3)
O (7W) ··· O (1W) [j]	3.040 (12)	N (1C) [h] ··· O (7W) ··· O (7W) [j]	82.7 (4)
		O (1W) ··· O (7W) ··· O (7W) [j]	64.9 (3)

Symmetry codes (a) $-x, -y, -z$, (b) $-x, 1-y, -z$, (c) $x, y, 1+z$, (d) $-1+x, 1+y, z$, (e) $-x, 2-y, 1-z$, (f) $x, y, -1+z$, (g) $1-x, 1-y, 1-z$, (h) $1+x, -1+y, z$, (i) $1-x, -y, 1-z$, (j) $1-x, -y, -z$.

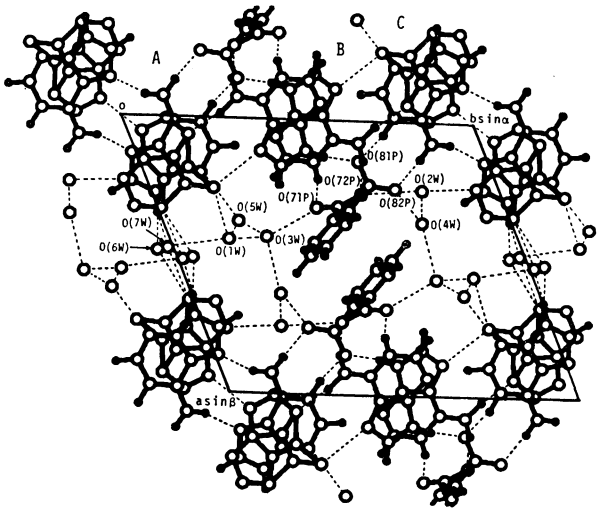


Fig. 3. Crystal structure of adenine:phthalic acid (3:1) complex hexahydrate, projected along the c axis. Adenine, A, B, C, and atomic numbering of water molecules are shown. The broken lines indicate the hydrogen bonds.

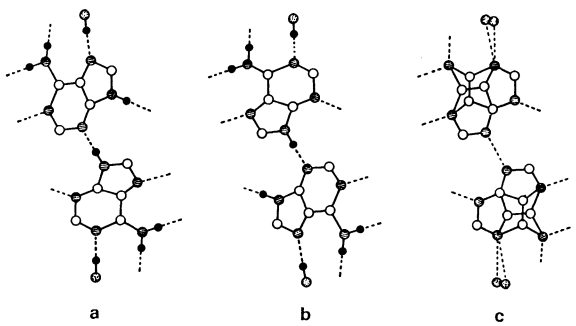


Fig. 4. Hydrogen-bonding scheme of disordered adenine C; (a) and (b) for alternative arrangements. Superposition of (a) and (b) can well explain the electron density map (c).

phenylmethylene]-3-oxo-1,2-diazetidinium inner salt,[18] and (5-methyl-2-pyridinecarbaldehyde 2-pyridylhydrazone)tetracarbonylmolybdenum(0).[19]

Hydrogen Bonding between Adenine and Carboxyl Group. As mentioned above, the two dissociated carboxyl groups of phthalic acid interact respectively with the two protonated adenines by the double hydrogen bond, as shown in Fig. 5. This pattern resembles that found in adenine:*m*-bromobenzoic acid (2:4) complex.[20a] In the latter complex, however, the proton-transfer between the two components is ambiguous due to the disordered structure.[20b]†† The dihedral angle between the base and the carboxyl group is 12.9(2)° for adeninium A and 45.6(2)° for adeninium B; the binding geometry is given in Table 5. Such non-planarity occurs because the phthalic acid is bridged between the two adeninium A and B which are stacked in the different columns, ACAC.. and BB.., respectively. The hydrogen bond scheme with the smaller dihedral angle may be more favourable one.

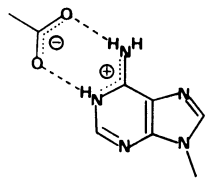


Fig. 5. Interaction pattern between adenine and carboxyl group.

Table 5. Geometrical data to define the interaction between adenine and carboxyl group

The symmetry codes, b and c, are the same as those in Table 4. Hydrogen bond distances and angles are shown in Fig. 2.

i	*j*	*k*	*l*	Torsion angle (ϕ_{ijkl}/°)
C(6P)	C(8P)	O(81P)	N(1A)[b]	175.8
C(6P)	C(8P)	O(82P)	N(6A)[b]	191.9
C(8P)	O(81P)	N(1A)[b]	C(6A)[b]	348.5
C(8P)	O(81P)	N(1A)[b]	C(2A)[b]	174.0
C(8P)	O(82P)	N(6A)[b]	C(6A)[b]	348.2
O(81P)	N(1A)[b]	C(6A)[b]	N(6A)[b]	7.4
O(81P)	N(1A)[b]	C(2A)[b]	N(3A)[b]	172.7
O(82P)	N(6A)[b]	C(6A)[b]	N(1A)[b]	0.2
O(82P)	N(6A)[b]	C(6A)[b]	C(5A)[b]	180.0
C(1P)[c]	C(7P)[c]	O(71P)[c]	N(1B)	143.8
C(1P)[c]	C(7P)[c]	O(72P)[c]	N(6B)	220.7
C(7P)[c]	O(71P)[c]	N(1B)	C(6B)	5.0
C(7P)[c]	O(71P)[c]	N(1B)	C(2B)	199.3
C(7P)[c]	O(72P)[c]	N(6B)	C(6B)	345.1
O(71P)[c]	N(1B)	C(6B)	N(6B)	14.7
O(71P)[c]	N(1B)	C(2B)	N(3B)	166.6
O(72P)[c]	N(6B)	C(6B)	N(1B)	349.9
O(72P)[c]	N(6B)	C(6B)	C(5B)	169.1

†† Lancelot has reported the three types of hydrogen bonds for adenine with butyric acid in chloroform solution from NMR study.[21] Although one of them is similar to the present pattern, the proton transfer is not assumed between the two components.

We have attempted an interpretation in terms of dissociation constant, which was successful for the binding mode in cytosine:glutamic acid system.[2a] Since the pK_a^I value of phthalic acid (2.95) is lower than that of adenine (4.25), the latter molecule is easily protonated by the first dissociation of phthalic acid in solution, but it could scarcely take a proton from the second dissociation because of higher pK_a^{II} (5.41) than that of adenine. In the present crystal, however, even the latter dissociation takes place. It is suggested that when the carboxyl group approaches adenine within a distance sufficient to form hydrogen bonds, their mutual perturbation favours to induce the ionizations.

The pK_a value of acidic side group of proteins is near pK_a of *N*-acetylglutamic acid α-methylamide (4.34),[22] whose value is comparable to that of the second carboxyl group of phthalic acid. On the other hand, adenine bases in nucleic acid would have a pK_a close to that of adenosine-5′-monophosphate (3.74) or its deoxy form (4.4), which is approximate to the adenine's value. Therefore, the pattern of hydrogen bonding, as shown in Fig. 5, would be found in the interaction between the side group of an acidic amino acid residue in protein and an unpaired adenine base in nucleic acid; the proton transfer must occur and their hydrogen bonds would be strengthened by an ionic effect induced.

Figure 3 was drawn by TSD:XTAL[23] for a NOVA 3 computer. The present work was supported in part by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture, and by the Kawakami Foundation, to which the authors' thanks are due.

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