bond distance of 1.665 Å.[11] The intermediate C–C distance is shortened to 1.36 Å from an expected 1.46 Å[10] for an sp^2–sp^2 single bond.

The phosphorus–ylide carbon bond length (1.713 Å) in 2,2,3,3,4,4-hexafluoro(triphenylphosphoranylidene)-cyclobutane is closer to a phosphorus–carbon double bond length (1.665 Å) than a phosphorus–carbon single bond length (1.828 Å in triphenylphosphine),[12] indicative of a considerable amount of double bond character formed by the overlap of the phosphorus d orbitals with the ylide carbon p orbitals.

The cyclobutane ring distances show a marked similarity in the C(1)–C(2) and C(1)–C(4) bond lengths. These bond lengths, 1.436 (4) and 1.438 (4) Å, agree within one standard deviation with the average (1.440 Å) of the standard carbon single (sp^3–sp^3) bond length (1.543 Å) and the carbon double (sp^2–sp^2) bond length (1.337 Å).[10] The carbon–fluorine bond lengths on the α-ring positions (C(2) and C(4)) appear to be slightly elongated, since the average carbon–fluorine bond length in perfluorocyclobutane is 1.333 Å.[13]

The phosphorus and the carbon skeleton of the cyclobutane ring lie in a plane, the deviations being P, −0.001 Å; C(1), 0.015 Å; C(2), −0.013 Å; C(3), 0.012 Å; C(4), −0.013 Å. The fluorine atoms form parallel planes above and below the phosphorus–cyclobutane ring plane. The lack of puckering in the four-membered ring also lends some support to the partial double bond character in the C(1)–C(2) and C(1)–C(4) bonds. Thus, the shortened C(1)–C(2) and C(1)–C(4) bond distance average (1.437 Å) compared with the C(2)–C(3) and C(4)–C(3) bond distance average (1.515 Å), the lengthened fluorine bonds to C(2) and C(4), and the shortened P–C bond length support a delocalized version of the ylide structure.

A conclusive statement cannot be made about bond distances in the phenyl rings since none of the atom positions were corrected for thermal motion. The average aromatic carbon–carbon bond length is 1.379 Å, and the average carbon–hydrogen bond length is 0.98 Å.

The bond angles associated with the cyclobutane ring (Table II) are similar to those found in perfluorocyclobutane,[13] while the bond angles about phosphorus are essentially tetrahedral as in the other triphenylphosphonium ylides listed in Table III. The F(2)–C(2)–F(2′) and F(4)–C(4)–F(4′) bond angles are significantly smaller than the F(3)–C(3)–F(3′) bond angle, again indicating the occurrence of delocalized bonding.

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Structures of Analogs of Nicotinamide–Adenine Dinucleotide. I. Crystal Structure of *N*-(3-(Aden-9-yl)propyl)-3-carbamoylpyridinium Bromide Trihydrate, (Ade-C_3-Nic^+)$Br^-\cdot 3H_2O$[1]

Paul L. Johnson, Carol A. Maier, and Iain C. Paul*[2]

Contribution from the W. A. Noyes Chemical Laboratory,
School of Chemical Sciences, University of Illinois, Urbana, Illinois 61801.
Received December 29, 1972

Abstract: The crystal structure of *N*-(3-(aden-9-yl)propyl)-3-carbamoylpyridinium bromide trihydrate, (Ade-C_3-Nic^+)Br^-, a molecule containing the bases of NAD^+ with a trimethylene bridge linking the adenine and pyridinium moieties, has been determined. The crystals of $(C_{14}H_{16}N_7O)^+Br^-\cdot 3H_2O$ are triclinic with a = 10.258 (2), b = 16.423 (2), and c = 5.664 (1) Å; α = 88.48 (2), β = 91.63 (2), and γ = 103.98 (2)°, and there are two molecules in the unit cell; the space group is $P\bar{1}$. The structure has been refined to an R factor of 0.058 on the 2932 nonzero reflections collected on an automatic diffractometer (Cu Kα radiation). The trimethylene chain is extended as the N–C–C–C torsion angles in the chain are completely staggered. The amide group is twisted out of the plane of the pyridinium ring by 38°48′. The adenine ring is linked to another centrosymmetrically related adenine ring by two N(6)–H···N(7) hydrogen bonds and is overlapped by another centrosymmetrically related and hence parallel adenine ring (related to the first by a translation in c) at a distance of 3.35 Å. The >C(6)–NH_2 group of one adenine ring overlaps the five-membered portion of the other ring. There is extensive hydrogen bonding in the crystal involving the pyridinium and adenine rings, the bromide anion, and the three water molecules. Rather surprisingly, the amide oxygen atom is not involved in hydrogen bonding.

The nicotinamide–adenine dinucleotide coenzymes NAD^+ (I) and NADH (II) have been detected in many living systems and play an important role in enzymatic oxidation–reduction reactions.[3] While the constitution and stereochemistry are well established,[4]

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[1] This work was supported by USPH Grants GM 12470 and GM 19336 and Training Grant GM 722.

[2] Alfred P. Sloan Research Fellow, 1968–1970.

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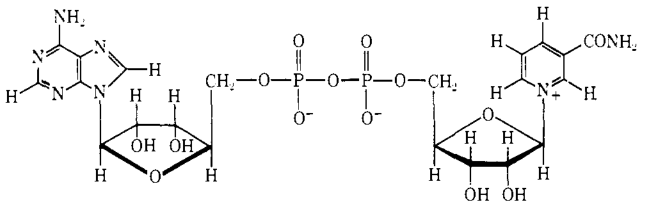

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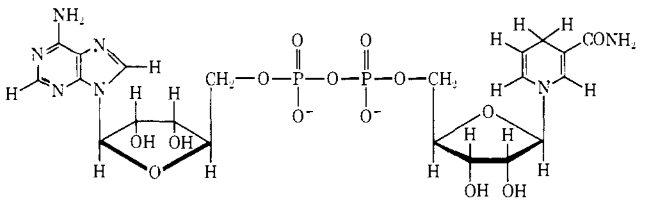
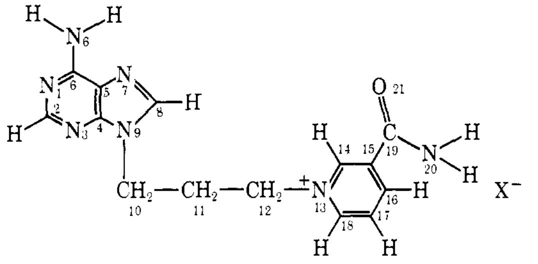


II

the three-dimensional conformations of NAD+ and NADH have not been determined unequivocally. Unfortunately, neither state of the coenzyme has as yet formed crystals suitable for X-ray analysis. Spectroscopic studies on NAD+ in solution have provided evidence for intramolecular interaction between the adenine and pyridinium rings,[5] and such studies on the model compound, the *N*-(3-(aden-9-yl)propyl)-3-carbamoylpyridinium cation, Ade-C_3-Nic+ (III), provided similar information.[6] Interposition of three methylene groups between the aromatic rings provides enough torsional flexibility that the two rings in a single molecule could be planar and overlapped or "stacked," yet they are not constrained in such a conformation. The availability of model compound III provided the opportunity to study a molecule that incorporates both the aromatic and electrostatic features of NAD+.[6] Leonard and coworkers[6] observed hypochromism for III in the same range as was observed for NAD+,[5] suggesting intramolecular stacking of the aromatic rings in solution. A crystal structure analysis was carried out on a hydrated bromide salt of Ade-C_3-Nic+ (III). While X-ray studies on other models for NAD+ have been reported,[7-10] none of these models has incorporated the possibility of intramolecular stacking. An X-ray analysis has also been completed on the hydrated dibromide salt of (AdeH+-C_3-Nic+).[11] The utility of the trimethylene bridge as a means of studying the structural basis for interactions between linked nucleic acid bases has been recently demonstrated for the case of 1,1′-trimethylenebisthymine.[12]



III

Experimental Section

Transparent, prismatic crystals of the bromide salt of Ade–C_3–Nic+ (III), although stable for several months when maintained in contact with water, rapidly powdered upon removal from mother liquor and exposure to the atmosphere. Analytical data[13] on a freshly filtered sample indicated the presence of at least one water molecule of crystallization. In view of the limited number of crystals at our disposal and their propensity to lose water, we did not attempt to measure the density. The results of the X-ray analysis indicated the presence of three molecules of water of crystallization per molecule of III.

Preliminary X-ray photographs indicated that the crystals belonged to the triclinic system. All X-ray work was carried out upon crystals sealed along with some mother liquor in thin-walled glass capillaries.

Crystal data: $(C_{14}H_{16}N_7O)Br \cdot 3H_2O$, $M = 432.3$, triclinic, $a = 10.258$ (2), $b = 16.423$ (2), and $c = 5.664$ (1) Å; $\alpha = 88.48$ (2)°, $\beta = 91.63$ (2)°, and $\gamma = 103.98$ (2)°, $V = 925{,}3$ Å^3, $Z = 2$, $\rho_{calcd} = 1.55$ g cm^{-3}; $F(000) = 444$, $\mu = 36.6$ cm^{-1}. No systematic absences, space group $P1$ or $P\bar{1}$.

The cell parameters were determined by a least-squares fit to the settings for the four angles of 12 reflections on a Picker FACS-1 diffractometer (Cu Kα, $\lambda = 1.54178$ Å). The crystal was mounted along the *c* axis. The dimensions of the crystal along the *a*, *b*, and *c* axes were 0.32 mm × 0.44 mm × 0.64 mm, respectively. The maximum and minimum transmission factors were estimated as 0.31 and 0.14.

Data were collected using a Picker FACS-1 system employing nickel-filtered Cu Kα radiation and a θ–2θ scan technique. Attenuators were inserted when the count rate exceeded 10,000 counts/sec. A scintillation counter equipped with a pulse height analyzer was used to determine the diffracted intensity. The scan rate was 2°/min with 10-sec backgrounds measured at the two extremes of the scan. The scan range had a base width of 2.0°, with a dispersion factor being applied at higher 2θ values. The octants of data hkl, $\bar{h}kl$, $h\bar{k}l$, and $hk\bar{l}$ were measured to give a total of 3362 reflections. Of these, 2932 were considered to be significantly above background using the criteria that the net count must be greater than 10% of the total background count, or in the situation where 10% of the background count is less than 10 counts, be greater than 10 counts.[14] A standard reflection was monitored after every 50 measurements; there was no evidence for crystal decomposition during the period of data collection. Lorentz and polarization corrections were made to the data, but no correction was made for absorption.

Solution and Refinement of the Structure. The structure was solved by the heavy atom method based on bromine and refined smoothly in the centrosymmetric space group $P\bar{1}$. Four cycles of least-squares refinement on positional and isotropic temperature factors for the nonhydrogen atoms reduced R to 0.13. Unit weights were used for all the nonzero reflections, while the quantity minimized was $\Sigma w||F_o| - |F_c||^2$. With the introduction of anisotropic temperature factors for all the atoms, refinement had to be carried out in two partial cycles due to computer storage limitations. One partial cycle consisted of refinement of the N(1), C(2), N(3), C(4), C(5), C(6), N(6), N(7), C(8), N(9) atoms, while the other consisted of atoms C(12), N(13), C(14), C(15), C(16), C(17), C(18), C(19), N(20), and O(21); the atoms Br, C(10), C(11), W(22), W(23), and W(24) were common to both cycles. Four cycles of such refinement reduced R to 0.075.

The positions of all the hydrogen atoms in the cation were clearly evident from a three-dimensional difference map, although the hydrogen atoms attached to the water molecules could not be rec-

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[13] Found: C, 42.86; H, 4.62; Br, 20.37. Calcd for $C_{14}H_{16}BrN_7O$: C, 44.4; H, 4.2; Br, 21.2. Calcd for $C_{14}H_{16}BrN_7O \cdot H_2O$: C, 42.4; H, 4.5; Br, 20.2. Calcd for $C_{14}H_{16}BrN_7O \cdot 2H_2O$: C, 40.6; H, 4.8; Br, 19.3.

[14] Using NRC-2A, written by F. R. Ahmed, S. R. Hall, M. E. Pippy, and C. P. Saunderson, "NRC Crystallographic Programs for the IBM 360 System," National Research Council, Ottawa, Canada, 1967.

Table I. Final Atomic Coordinates in Fractions of the Unit Cell Edge[a]

	x	y	z
Br	1.02842 (6)	0.14771 (5)	0.1564 (1)
N(1)	0.7438 (5)	0.4529 (3)	0.5519 (9)
C(2)	0.6996 (6)	0.3919 (4)	0.7102 (12)
N(3)	0.5806 (4)	0.3388 (3)	0.7233 (8)
C(4)	0.4976 (5)	0.3523 (3)	0.5437 (9)
C(5)	0.5302 (5)	0.4137 (3)	0.3660 (10)
C(6)	0.6613 (5)	0.4659 (3)	0.3760 (10)
N(6)	0.7036 (6)	0.5269 (3)	0.2153 (11)
N(7)	0.4232 (5)	0.4093 (3)	0.2133 (8)
C(8)	0.3280 (6)	0.3482 (3)	0.3005 (11)
N(9)	0.3675 (4)	0.3111 (3)	0.5011 (8)
C(10)	0.2890 (6)	0.2403 (3)	0.6345 (11)
C(11)	0.3203 (5)	0.1586 (3)	0.5574 (10)
C(12)	0.2245 (5)	0.0842 (3)	0.6681 (11)
N(13)	0.2530 (4)	0.0046 (2)	0.5852 (7)
C(14)	0.3298 (5)	−0.0338 (3)	0.7241 (9)
C(15)	0.3510 (5)	−0.1099 (3)	0.6584 (9)
C(16)	0.2986 (5)	−0.1438 (3)	0.4450 (9)
C(17)	0.2225 (6)	−0.1018 (3)	0.3039 (10)
C(18)	0.1990 (6)	−0.0276 (3)	0.3808 (10)
C(19)	0.4295 (5)	−0.1515 (3)	0.8331 (9)
N(20)	0.3846 (6)	−0.2343 (3)	0.8505 (10)
O(21)	0.5247 (4)	−0.1097 (2)	0.9445 (7)
W(22)	1.0138 (7)	0.4583 (4)	1.2223 (15)
W(23)	1.0353 (8)	0.3306 (5)	0.8071 (16)
W(24)	0.8883 (6)	0.2989 (4)	0.3544 (13)
H(2)[b]	0.761 (6)	0.380 (4)	0.82 (1)
H(6a)	0.663 (6)	0.532 (4)	0.12 (1)
H(6b)	0.790 (5)	0.558 (3)	0.23 (1)
H(8)	0.223 (5)	0.326 (3)	0.24 (1)
H(10a)	0.191 (6)	0.238 (3)	0.59 (1)
H(10b)	0.321 (5)	0.248 (3)	0.81 (1)
H(11a)	0.319 (6)	0.152 (3)	0.38 (1)
H(11b)	0.416 (5)	0.161 (3)	0.62 (1)
H(12a)	0.131 (5)	0.087 (3)	0.63 (1)
H(12b)	0.236 (7)	0.090 (4)	0.84 (1)
H(14)	0.366 (4)	−0.007 (3)	0.86 (1)
H(16)	0.302 (6)	−0.203 (4)	0.40 (1)
H(17)	0.189 (7)	−0.126 (4)	0.17 (1)
H(18)	0.131 (5)	−0.004 (3)	0.30 (1)
H(20a)	0.299 (7)	−0.259 (4)	0.80 (1)
H(20b)	0.416 (5)	−0.254 (3)	0.91 (1)
H(23a)	0.976 (14)	0.319 (8)	0.72 (2)
H(23b)	1.030 (11)	0.401 (7)	0.90 (2)
H(24a)	0.916 (8)	0.274 (5)	0.24 (1)
H(24b)	0.975 (10)	0.346 (6)	0.34 (2)

[a] Standard deviations in parentheses. [b] Hydrogen atoms are given the number of the atom to which they are attached.

Table II. Bond Lengths (Å)[a] and Bond Angles (deg)[b]

Bond Lengths			
N(1)–C(2)	1.331 (8)	C(11)–C(12)	1.505 (8)
N(1)–C(6)	1.335 (7)	C(12)–N(13)	1.496 (7)
C(2)–N(3)	1.320 (8)	N(13)–C(14)	1.348 (6)
N(3)–C(4)	1.356 (7)	N(13)–C(18)	1.335 (7)
C(4)–C(5)	1.394 (7)	C(14)–C(15)	1.381 (7)
C(4)–N(9)	1.360 (7)	C(15)–C(16)	1.384 (7)
C(5)–C(6)	1.410 (8)	C(16)–C(17)	1.386 (8)
C(5)–N(7)	1.367 (7)	C(17)–C(18)	1.380 (8)
C(6)–N(6)	1.335 (8)	C(15)–C(19)	1.509 (7)
N(7)–C(8)	1.316 (7)	C(19)–N(20)	1.329 (8)
C(8)–N(9)	1.373 (7)	C(19)–O(21)	1.219 (7)
N(9)–C(10)	1.451 (7)		
C(10)–C(11)	1.531 (8)		
Bond Angles			
C(2)–N(1)–C(6)	119.1 (4)	N(9)–C(10)–C(11)	110.3 (5)
N(1)–C(2)–N(3)	129.3 (6)	C(10)–C(11)–C(12)	110.3 (5)
C(2)–N(3)–C(4)	111.2 (5)	C(11)–C(12)–N(13)	109.9 (5)
N(3)–C(4)–C(5)	125.8 (3)	C(12)–N(13)–C(14)	118.6 (3)
N(3)–C(4)–N(9)	128.0 (5)	C(12)–N(13)–C(18)	119.6 (3)
C(5)–C(4)–N(9)	106.2 (3)	C(14)–N(13)–C(18)	121.8 (5)
C(4)–C(5)–C(6)	116.5 (5)	N(13)–C(14)–C(15)	119.7 (3)
C(4)–C(5)–N(7)	110.2 (5)	C(14)–C(15)–C(16)	119.6 (3)
C(6)–C(5)–N(7)	133.3 (4)	C(14)–C(15)–C(19)	116.1 (5)
N(1)–C(6)–C(5)	118.2 (4)	C(16)–C(15)–C(19)	124.3 (4)
N(1)–C(6)–N(6)	120.1 (4)	C(15)–C(16)–C(17)	119.2 (3)
C(5)–C(6)–N(6)	121.7 (5)	C(16)–C(17)–C(18)	119.3 (3)
C(5)–N(7)–C(8)	104.4 (5)	N(13)–C(18)–C(17)	120.3 (4)
N(7)–C(8)–N(9)	113.4 (3)	C(15)–C(19)–N(20)	114.1 (4)
C(4)–N(9)–C(8)	105.6 (4)	C(15)–C(19)–O(21)	120.5 (4)
C(4)–N(9)–C(10)	127.1 (4)	N(20)–C(19)–O(21)	125.4 (3)
C(8)–N(9)–C(10)	127.2 (4)		

[a] The C–H lengths range from 0.90 to 1.10 Å with esd in range 0.05–0.07 Å; two of the N–H lengths (N(20)–H(20b) and N(6)–H(6a)) are rather short, 0.62 (5) and 0.69 (6) Å, respectively, while the other two are normal, 0.91 (6) and 0.92 (7). [b] The C–C–H angles external to the pyridinium ring range from 117 to 124° with esd of 3–6°.

ognized from this map. Inclusion of 16 hydrogen atoms in the appropriate partial cycle of refinement (*i.e.*, that which contained the atom to which they were bonded) reduced R to 0.066, and R_2, defined as $\{\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2\}^{1/2}$, to 0.078. Both positional and isotropic thermal parameters for the hydrogen atoms were refined and the resulting B_θ values ranged from −0.1 to 4.9 Å^2. The lowest B_θ value corresponded to one of the hydrogen atoms, H(20b), attached to the nitrogen atom of the amide group, while the resulting N–H bond was rather short, 0.6 Å. Another difference map was calculated omitting this atom from the structural model. The highest positive peak on this map corresponded to the position for H(20b), with a height of 0.8 electron/Å^3. There were two other peaks in the range 0.7–0.8 electron/Å^3 within 1 Å of the bromide anion. The next highest peak on the map was one of 0.4 electron/Å^3 near W(24) (assigned to a hydrogen atom). Careful inspection of this map provided evidence for geometrically reasonable positions for two hydrogen atoms on each of W(23) and W(24), but no definite location of hydrogen atoms bonded to W(22) could be made. As W(22) is within hydrogen bonding distance to another W(22) molecule across a center of symmetry, there is probably disorder in the arrangement of the hydrogen atoms bonded to this atom, and it is therefore not surprising that these hydrogen atoms could not be located. Least-squares refinement of the structure, including the hydrogen atoms attached to W(23) and W(24), led to final values for R and R_2 of 0.058 and 0.067 on the nonzero reflections. The final shifts were less than the estimated standard deviations for all the refined parameters. The temperature factors for the hydrogen atoms of the water molecules are quite large (6–18 Å^2) when compared to those for the hydrogen atoms in the cation (1.6–5.2 Å^2), and this fact would indicate substantial disorder of these hydrogen atoms or very high librational motion of the water molecules.

The scattering curves for Br$^-$, C, N, O were taken from the compilation in "International Tables for X-ray Crystallography,"[15] that for Br$^-$ being corrected for anomalous dispersion.[16] The scattering curve for hydrogen was that calculated by Stewart, *et al.*[17]

The final atomic coordinates are listed in Table I. The final values for the thermal parameters and of h, k, l, $|F_o|$, and F_c will appear in the microfilm edition of the journal.[18]

Results and Discussion

Figures 1 and 2 are stereoscopic views of the contents of the unit cell. A view of a single molecule is shown in the following paper.[11] Bond lengths and angles are listed in Table II.

Molecular Dimensions in the Cation. The only dimensions in the adenine moiety that differ by more than

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(15) "International Tables for X-Ray Crystallography," Vol. III, Kynoch Press, Birmingham, England, 1962, pp 201-209.

(16) Reference 15, pp 213-216.

(17) R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, 42, 3175 (1965).

(18) The final values for the thermal parameters, the list of h, k, l, $|F_o|$, and F_c, and some details of best plane calculations, will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N.W., Washington, D. C. 20036. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche, referring to code number JACS-73-5370.

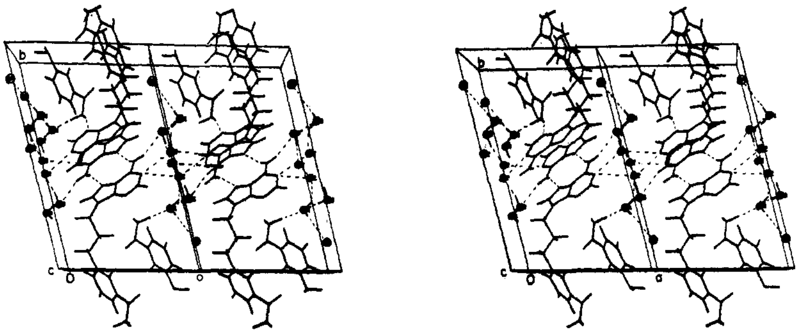

Figure 1. Stereoscopic view of the molecular packing looking along the *c* axis. Hydrogen bonding is shown by discontinuous lines.

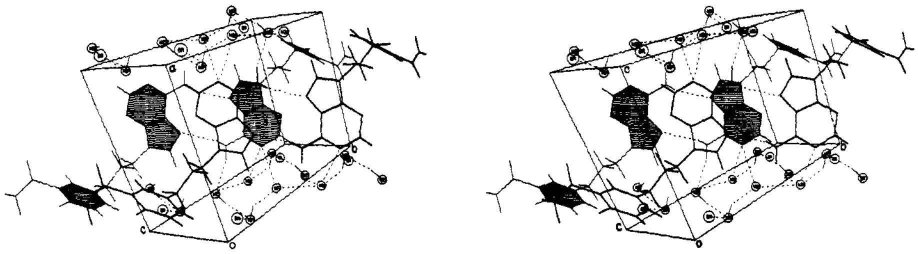

Figure 2. Stereoscopic drawing of the structure viewed almost normal to the planes of the adenine rings. The hydrogen bonding is shown by discontinuous lines.

the quoted root mean square deviations from the values given in a survey of neutral adenine derivatives[19] are the C(4)–C(5) bond lengths (1.394 (7) Å as compared to the value of 1.370 ± 0.014 Å given by Donohue) and the external angles at C(6) and C(9). A similar conclusion can be drawn by comparison with an average set of dimensions for neutral adenine derivatives published by Voet and Rich.[20] A C(4)–C(5) length of 1.392 (10) Å was, however, found in the structure of deoxyadenosine monohydrate.[21] On the basis of best plane calculations, the nine atoms of the adenine group are not strictly coplanar; deviations range from −0.009 (N(9)) to 0.011 Å (N(7)). Full details of these calculations are in the microfilm edition.[18] This is among the more planar adenine rings studied by X-ray methods.[20] The six-membered ring [N(1)–C(6)] is definitely planar, while the planarity of the five-membered ring [(C(4), C(5), N(7), C(8), N(9)] is marginal, and there is a dihedral angle of 0°43′ between the best planes through these two rings. The two heavy atom substituents, N(6) and C(10), lie −0.014 and 0.025 Å, respectively, from the best plane through the adenine moiety.

The C–C lengths (1.380–1.386 Å) in the pyridinium ring agree well with the accepted values for C–C lengths in phenyl rings.[22] The pyridinium ring is slightly, but quite significantly nonplanar[18] with deviations ranging from −0.015 (C(15)) to 0.017 Å (C(14)). The deviations from planarity in the pyridine rings in AdeH$^+$-C$_3$-Nic$^+$[11] and in the 1,1′-trimethylenebisnicotinamide cation (Nic$^+$-C$_3$-Nic$^+$)[23] are not significant. However, the results of a χ^2 test on the deviations of the atoms in the pyridinium ring in *N*-phenyl-2,4,6-trimethylpyridinium perchlorate[24] suggest a slight, but significant nonplanarity in that ring also. The endocyclic C–N$^+$–C angle in the pyridine ring is 121.8 (5)°; in AdeH$^+$-C$_3$-Nic$^+$ this angle was 120.5 (5)°,[11] while in Nic$^+$-C$_3$-Nic$^+$, the angles were 119.8 (2) and 120.3 (3)°.[23] The corresponding angles in the pyridine rings in *N*-phenyl-2,4,6-trimethylpyridinium perchlorate[24] and in pyridoxine hydrochloride[25] are 122.1 (4) and 124.5 (3)°, respectively. In the case of the neutral pyridine molecule in the gas phase, microwave measurements give a C–N–C angle of 116.7°,[26] while crystallographic data on picolinamide[27] give an angle of 117.3 (4)°. These data would suggest a significant change in the geometry at nitrogen upon substitution and formation of a cation.

The two carbon substituents C(12) and C(19) lie 0.056 and 0.096 Å out of the best plane through the six atoms of the pyridine ring. In addition to the "bending" out of the ring plane by the amide group, there is a twist of 38°48′ between the plane of the pyridinium ring and the exact plane through C(15), C(19), N(20), and O(21). Virtual coplanarity of the amide group with the planar portion of the heterocyclic ring was found in the hydrated salt of AdeH$^+$-C$_3$-Nic$^+$,[11] in Nic$^+$-C$_3$-Nic$^+$,[23] in *N*-(2,6-dichlorobenzyl)-6-hydroxy-1,4,5,6-tetrahydronicotinamide (IV),[10] and in *N*-benzyl-1,4-dihydronicotinamide,[8] and also in the less detailed analysis of *N*-(2,6-dichlorobenzyl)nicotinamide iodide monohydrate,[9] although there is a large angle of rotation (41°) in nicotinamide itself.[7] With the sole exception of nicotinamide, the oxygen atom of the

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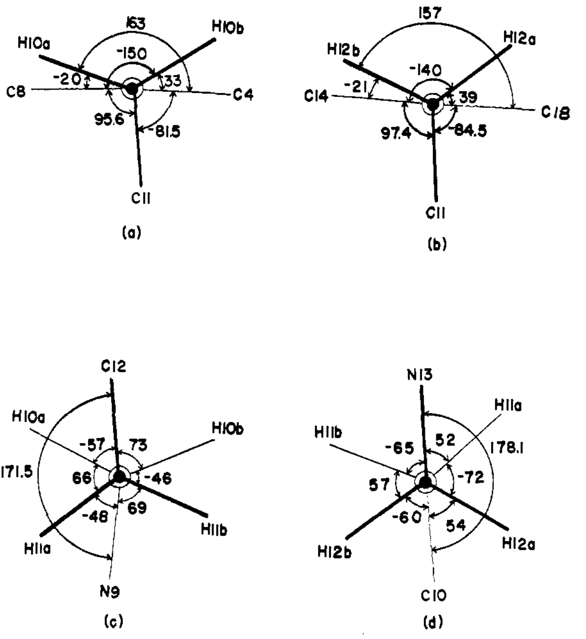
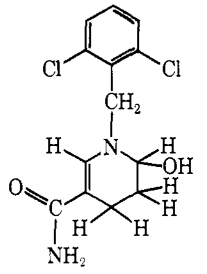
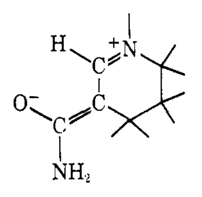


Figure 3. Torsion angles about (a) the C(10)–N(9) bond, (b) the C(12)–N(13) bond, (c) the C(11)–C(10) bond, and (d) the C(12)–C(11) bond. Angles (ABCD) are considered positive if when looking along the BC bond, atom A has to be rotated clockwise to eclipse atom D.

amide group is located on the side of the ring containing the nitrogen atom in all the above structures. The dimensions of the amide group agree well with those compiled by Bracher and Small[28] and make an interesting comparison with those for IV, where a substantial contribution from the dipolar structure V was proposed.[10] The exocyclic C–C, C–O, and C–N lengths in IV were 1.449 (4), 1.262 (4), and 1.348 (4) Å, and the C–C–O, C–C–N, and N–C–O angles were 122.6 (3), 118.5 (3), and 118.9 (3)° respectively, whereas the corresponding values in III are 1.509 (7), 1.219 (7), and 1.329 (8) Å, and 120.5 (4), 114.1 (4), and 125.4 (3)°. These differences are consistent with the contributions from V to the overall structure of IV and the lack of conjugation of the amide group with the aromatic ring in III.



IV



V

Conformation of the Cation. The cation is extended so that there is no intramolecular overlapping of the adenine and nicotinamide groups. The C–C bonds in the methylene chain have the fully staggered arrangements; the torsion angles N(9)–C(10)–C(11)–C(12) and C(10)–C(11)–C(12)–N(13) are −171.5 and 178.1°, respectively (Figure 3). Indeed, the maximum deviation of an atom, C(11), from the best plane through the five atoms N(9), C(10), C(11), C(12), and N(13) is only 0.096 Å.[18] The staggered conformation of the methylene chain results in the adenine and pyridine rings being inclined at 108°11′ to each other. The centers of mass of the adenine and pyridine ring systems are 7.31 Å apart.

Haschemeyer and Rich[29] have discussed the torsion angles about the glycosidic (C–N) bond in nucleosides and nucleotides and rationalized the values obtained in terms of intramolecular nonbonded contacts between the atoms in the sugar residue and N(3), C(8), and H(8) (in the case of adenine nucleosides and nucleotides). A view of the torsion angles about the C(10)–N(9) bond in III is shown in Figure 3a. The H(8)· · ·H(10a) distance is 2.41 (8) Å, which does not imply significant interference between these atoms even if one accepts the rather large value (1.2 Å) given by Pauling[30] for the van der Waals radius of hydrogen. The rotational conformation around the C(12)–N(13) bond (Figure 3b) is very similar to that around the C(10)–N(9) bond. The methylene chain is oriented almost (but not quite) perpendicularly with respect to the heterocyclic ring in each case. The H(12b)· · ·H(14) and H(12a)· · ·H(18) distances are 2.31 (8) and 2.44 (7) Å, respectively. The nitrogen atom of the pyridine ring and its three substituent carbon atoms can be considered planar only at the 0.005 significance level; the carbon of the methylene chain, C(12), lies 0.045 Å out of the plane defined by C(14), N(13), and C(18).

Hydrogen Bonding. Two centrosymmetrically related adenine groups are paired by two N(6)–H· · ·$N(7^{I})$ hydrogen bonds; the N(6)· · ·$N(7^{I})$ distance is 3.005 (8) Å (Table III). Somewhat similar types of hydrogen bonding have been encountered previously in adenine hydrochloride,[31] in the complex 9-ethyl-8-bromoadenine-1-methyl-5-bromouracil,[32] between two crystallographically independent sets of 9-ethyl-8-bromoadenine molecules in a 1:2 phenobarbital-9-ethyl-8-bromoadenine complex,[33] in uridylyl(3′,5′)adenosine phosphate hemihydrate,[34] and in polyadenylic acid.[35] The hydrogen bonding in the structure of $AdeH^+$-C_3-Nic^+ also involves centrosymmetrically related N(6)–H· · ·N(7) interactions.[11] A more detailed description of the various hydrogen bonding schemes among adenine molecules has been given by Voet and Rich.[20] In polyadenylic acid[35] the hydrogen-bonded adenine

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Table III. Molecular Dimensions Relevant to the Hydrogen Bonding Scheme[a]

Bond	Å	Angle	Deg
		Hydrogen Atoms from Ade-C$_3$-Nic$^+$	
N(6)···N(7$^{\mathrm{I}}$)	3.005 (8)	C(6)–N(6)···N(7$^{\mathrm{I}}$)	134.3 (4)
N(6)···W(23$^{\mathrm{II}}$)	3.11 (1)	C(6)–N(6)···W(23$^{\mathrm{II}}$)	131.4 (4)
H(6a)···N(7$^{\mathrm{I}}$)	2.34 (6)	N(6)–H(6a)···N(7$^{\mathrm{I}}$)	162 (5)
H(6b)···W(23$^{\mathrm{II}}$)	2.24 (6)	N(6)–H(6b)···W(23$^{\mathrm{II}}$)	159 (3)
N(20)···N(3$^{\mathrm{III}}$)	2.987 (7)	C(19)–N(20)···N(3$^{\mathrm{III}}$)	124.9 (3)
N(20)···W(24$^{\mathrm{IV}}$)	2.959 (9)	C(19)–N(20)···W(24$^{\mathrm{IV}}$)	114.2 (3)
H(20b)···N(3$^{\mathrm{III}}$)	2.45 (5)	N(20)–H(20b)···N(3$^{\mathrm{III}}$)	148 (6)
H(20a)···W(24$^{\mathrm{IV}}$)	2.05 (7)	N(20)–H(20a)···W(24$^{\mathrm{IV}}$)	172 (5)
		Environment of W(24)	
W(24)···Br$^-$	3.384 (6)	Br$^-$···W(24)···W(22$^{\mathrm{V}}$)	115.1 (3)
W(24)···W(22$^{\mathrm{V}}$)	2.72 (1)	Br$^-$···W(24)···W(23)	98.7 (3)
W(24)···N(20$^{\mathrm{IV}}$)	2.959 (9)	Br$^-$···W(24)···N(20$^{\mathrm{IV}}$)	97.7 (3)
W(24)···W(23)	2.93 (1)	W(22$^{\mathrm{V}}$)···W(24)···N(20$^{\mathrm{IV}}$)	115.7 (3)
H(24a)···Br$^-$	2.67 (8)	W(23)···W(24)···N(20$^{\mathrm{IV}}$)	142.1 (3)
H(24b)···W(22$^{\mathrm{V}}$)	1.9 (1)	W(22$^{\mathrm{V}}$)···W(24)···W(23)	87.3 (3)
W(24)–H(24a)	0.85 (8)	H(24a)–W(24)–H(24b)	88 (8)
W(24)–H(24b)	1.03 (12)	W(24)–H(24a)···Br$^-$	143 (7)
		W(24)–H(24b)···W(22$^{\mathrm{V}}$)	134 (9)
		Environment of W(23)	
W(23)···W(24)	2.93 (1)	W(24)···W(23)···W(22)	130.3 (3)
W(23)···W(22)	3.24 (1)	W(24)···W(23)···N(6$^{\mathrm{II}}$)	114.0 (2)
W(23)···N(6$^{\mathrm{II}}$)	3.11 (1)	W(22)···W(23)···N(6$^{\mathrm{II}}$)	74.1 (3)
H(23a)···W(24)	2.2 (1)	H(23a)–W(23)–H(23b)	107 (11)
H(23b)···W(22)	2.1 (1)	W(23)–H(23a)···W(24)	154 (14)
W(23)–H(23a)	0.78 (15)	W(23)–H(23b)···W(22)	143 (5)
W(23)–H(23b)	1.29 (12)		
		Environment of W(22)	
W(22)···W(22$^{\mathrm{VI}}$)	2.87 (1)	W(22$^{\mathrm{VI}}$)···W(22)···W(23)	72.4 (4)
W(22)···W(23)	3.24 (1)	W(22$^{\mathrm{VI}}$)···W(22)···W(24$^{\mathrm{VII}}$)	127.4 (3)
W(22)···W(24$^{\mathrm{VII}}$)	2.72 (1)	W(22$^{\mathrm{VI}}$)···W(22)···N(1$^{\mathrm{VII}}$)	109.5 (3)
W(22)···N(1$^{\mathrm{VII}}$)	3.37 (1)	W(22$^{\mathrm{VI}}$)···W(22)···N(1$^{\mathrm{VI}}$)	107.9 (2)
W(22)···N(1$^{\mathrm{VI}}$)	2.848 (9)	W(23)···W(22)···W(24$^{\mathrm{VII}}$)	70.3 (3)
		W(23)···W(22)···N(1$^{\mathrm{VII}}$)	126.7 (2)
		W(23)···W(22)···N(1$^{\mathrm{VI}}$)	118.0 (3)
		W(24$^{\mathrm{VII}}$)···W(22)···N(1$^{\mathrm{VII}}$)	68.1 (2)
		W(24$^{\mathrm{VII}}$)···W(22)···N(1$^{\mathrm{VI}}$)	122.0 (3)
		N(1$^{\mathrm{VII}}$)···W(22)···N(1$^{\mathrm{VI}}$)	111.8 (2)

[a] I refers to $1 - x, 1 - y, -z$; II, $2 - x, 1 - y, 1 - z$; III, $1 - x, -y, 2 - z$; IV, $1 - x, -y, 1 - z$; V, $x, y, -1 + z$; VI, $2 - x, 1 - y, 2 - z$; VII, $x, y, 1 + z$.

residues are related by a twofold rotation axis and in uridylyl(3′,5′)adenosine phosphate hemihydrate[34] by a near twofold axis; thus the molecular planes are not required to be parallel by symmetry. In Ade-C$_3$-Nic$^+$, the other hydrogen atom on N(6) forms a hydrogen bond to W(23). It is almost certain that N(1) acts as acceptor for hydrogen bonds from two different W(22) water molecules, while N(3) acts as an acceptor for a hydrogen atom, H(20b), from a nicotinamide group in another molecule. It is not surprising that N(1) can act as an acceptor for two hydrogen bonds as this is the most basic nitrogen atom in adenine and is the first site of protonation. The other hydrogen atom on N(20) (the amide nitrogen atom) forms a hydrogen bond to W(24). The oxygen atom of the amide group is not involved in hydrogen bonding unless it be a C–H···O hydrogen bond (see below). Leiserowitz and Schmidt[36] have recently described the crystal packing of amides in a large number of structures and find that only in a few cases does this group fail to form a centrosymmetrically related hydrogen bonded pair. The present structure where the oxygen atom is not involved in N–H···O or O–H···O hydrogen bonding, is therefore quite unusual.

Table IV. Intermolecular Contacts (<3.6 Å) Other Than Those Involved in Hydrogen Bonding[a]

N(1)···N(7$^{\mathrm{VIII}}$)	3.46	C(4)···N(20$^{\mathrm{IV}}$)	3.42
C(4)···N(6$^{\mathrm{VIII}}$)	3.51	C(5)···N(20$^{\mathrm{IV}}$)	3.53
C(5)···C(5$^{\mathrm{VIII}}$)	3.44	C(11)···C(19$^{\mathrm{IV}}$)	3.46
C(5)···C(6$^{\mathrm{VIII}}$)	3.48	C(11)···O(21$^{\mathrm{IV}}$)	3.50
C(6)···N(7$^{\mathrm{VIII}}$)	3.40	C(15)···W(24$^{\mathrm{IV}}$)	3.46
C(6)···C(8$^{\mathrm{VIII}}$)	3.58	C(16)···W(24$^{\mathrm{IV}}$)	3.01
N(6)···C(8$^{\mathrm{VIII}}$)	3.54	C(11)···O(21$^{\mathrm{III}}$)	3.37
N(6)···N(9$^{\mathrm{VIII}}$)	3.38	C(12)···O(21$^{\mathrm{III}}$)	3.29
C(10)···W(23$^{\mathrm{IX}}$)	3.46	C(14)···O(21$^{\mathrm{III}}$)	3.11
Br···C(17$^{\mathrm{X}}$)	3.57	C(14)···C(17$^{\mathrm{VII}}$)	3.56

[a] Roman numerals indicate the transformations listed in Table III and in this table, VIII refers to $1 - x, 1 - y, 1 - z$; IX refers to $-1 + x, y, z$; X refers to $1 - x, -y, -z$.

The hydrogen bonding pattern involving the three crystallographically independent water molecules is rather difficult to establish unambiguously in view of the uncertainty in the location of some of the hydrogen atoms. The most reasonable arrangement is shown in Figures 4 and 5, and the dimensions are presented in Table III. As W(22) forms a hydrogen bond (2.87 (1) Å) across a center of symmetry to another W(22) molecule, there must be disorder in the hydrogen atoms in this water molecule, a fact which undoubtedly con-

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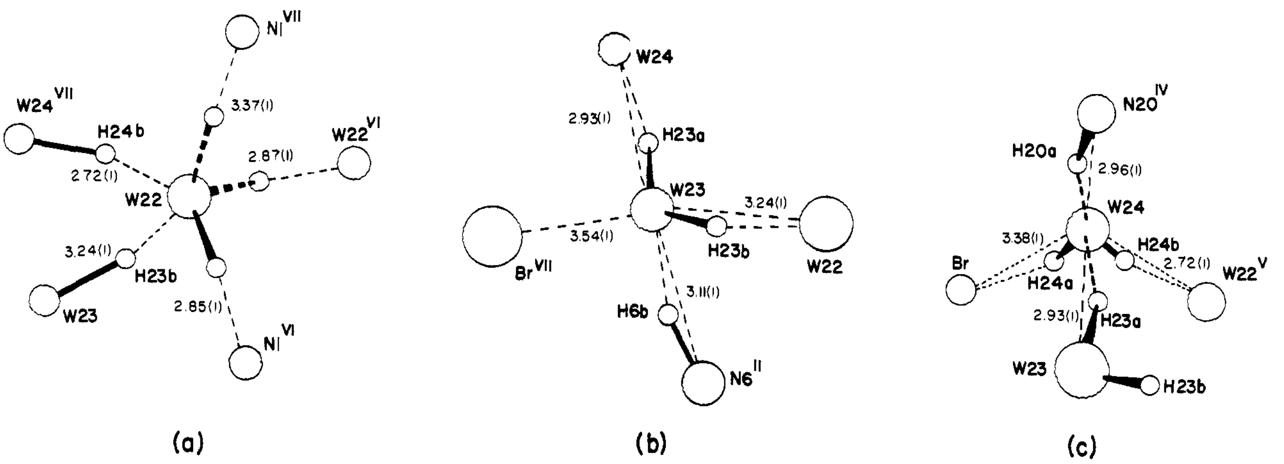

Figure 4. Schematic representation of the hydrogen bonding for (a) W(22), (b) W(23), and (c) W(24). The Roman numerals refer to the equivalent positions listed in Table III. The heavy dashed lines in a represent the probable disorder in the positions of one of the hydrogen atoms attached to W(22).

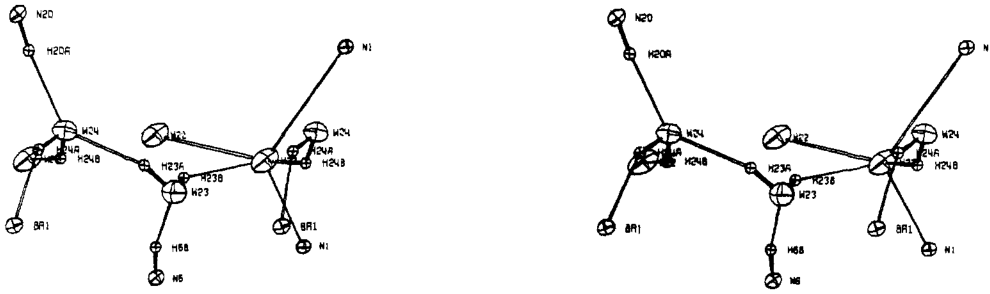

Figure 5. Stereoscopic pair showing the hydrogen bonding scheme involving the water molecules.

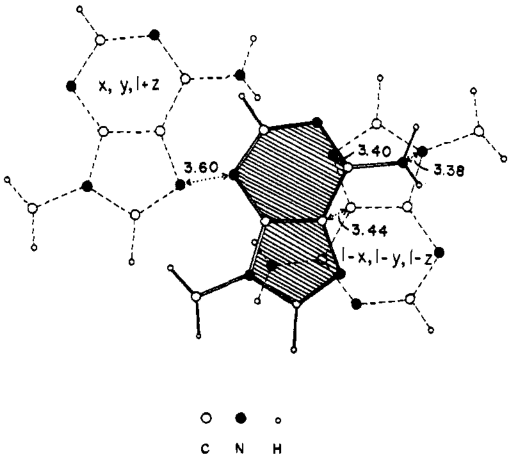

Figure 6. The projection of the adenine groups at $1 - x$, $1 - y$, $1 - z$ and x, y, $1 + z$ onto the plane defined by the nine atoms of the basic adenine group.

tributes to the failure to locate these atoms on the difference maps.

Intermolecular contacts other than those clearly involved in hydrogen bonding are listed in Table IV. Neither H(2) nor H(8) is sufficiently close to water molecules for there to be any possibility of C–H···O hydrogen bonding as has been found in other adenine structures.[37,38] Of particular interest is the C(14)···O(21^{III}) contact of 3.112 (7) Å. The H(14)···O(21^{III}) distance is 2.28 (5) Å and the C(14)–H(14)···O(21^{III}) angle is 152 (3)°. This situation would appear to be quite favorable for a C–H···O hydrogen bond.[39] The shortest contact in Table IV is between C(16) and W(24^{IV}), 3.011 (8) Å; the direction of the C–H bond is, however, inconsistent with a C–H···O hydrogen bond in this case. The only $Br^- \cdots N(13)^+$ contact less than 4 Å is one of 3.646 (4) Å to N(13) in the molecule related to that in Table I by $1 - x$, $-y$, $1 - z$.

Overlap of Bases. Two adenine bases related by the center of symmetry at $^1/_2$, $^1/_2$, $^1/_2$ overlap to the extent shown in Figure 6. In this figure, the atoms of one adenine group are projected onto the plane of the other group. The $>C-NH_2$ of one molecule lies over the five-membered ring of the second molecule. Somewhat similar patterns of overlap of adenine groups (although in molecules related by translation rather than by inversion) occur in the crystal structures of deoxyadenosine monohydrate,[21] adenosine 5′-phosphate,[40] and the adenosine-5-bromouridine complex,[41] as recently classified by Sundaralingam and coworkers.[42] In all three of these examples, the amino nitrogen atom, but not C(6), lies over the imidazole ring.

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(37) M. Sundaralingam, *Acta Crystallogr.*, **21**, 495 (1966).

(38) M. Sundaralingam and J. Abola, *J. Amer. Chem. Soc.*, **94**, 5070 (1972).

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Two adenine rings, related by a center of symmetry, overlap considerably in the crystal of the 9-ethyladenine-1-methyl-5-fluorouracil complex.[43] In that case, however, the C(6)–NH_2 group lies outside the plane of the other ring, and the main overlap was between the respective five- and six-membered rings. In the structure of α-D-2′-amino-2′-deoxyadenosine monohydrate,[44] there was overlap of the C(6)–NH_2 group with the pyrimidine ring of a molecule related by a screw axis. In the structure of adenosine triphosphate,[45] there was interleaving of adenine rings with extensive overlap of the two six-membered rings. In Ade–C_3–Nic^+, the interplanar spacing between the adenine rings is 3.35 Å, while the shortest interatomic contact between the parallel adenine groups is 3.38 Å between N(6) and N(9) (Table IV). The plane of the adenine moiety at x, y, $1 + z$ is also 3.35 Å on the same side of plane of the basic adenine residue as the ring at $1 - x$, $1 - y$, $1 - z$ (Figure 6). The shortest interatomic contact (excluding hydrogen) is 3.60 Å between N(3) and N(7) in the cation at x, y, $1 + z$. The other side of the adenine ring is not overlapped by any parallel planar group (Figure 1). The closest approaches are 2.88 Å between N(3) and H(16) in the molecule at $1 - x$, $-y$, $1 - z$ and 3.34 Å between C(4) and H(20b) in the same molecule.

There is also a slight overlap of pyridinium rings related by the center of symmetry at $^1/_2$, 0, $^1/_2$. The projections of atoms C(14) and C(15) in the symmetry-related ring onto the plane defined by the six ring atoms in the initial molecule lie within the ring. The interplanar distance, however, is 4.14 Å. The N(13)$\cdots$O(21) distance between these two molecules is 3.92 Å.

A comparison of the conformation in Ade-C_3-Nic^+ with those found in $AdeH^+$-C_3-Nic^+ and in solution will be given in the following paper.[11]

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Structures of Analogs of Nicotinamide–Adenine Dinucleotide. II. Crystal Structure of *N*-(3-(Aden-9-yl) propyl)-3-carbamoylpyridinium Bromide Hydrobromide Dihydrate, $(AdeH^+\text{-}C_3\text{-}Nic^+)2Br^- \cdot 2H_2O$[1]

Paul L. Johnson, JoAnn K. Frank, and Iain C. Paul*[2]

Contribution from the W. A. Noyes Chemical Laboratory,
School of Chemical Sciences, University of Illinois, Urbana, Illinois 61801.
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Abstract: The crystal structure of *N*-(3-(aden-9-yl)propyl)-3-carbamoylpyridinium bromide hydrobromide dihydrate, $(AdeH^+\text{-}C_3\text{-}Nic^+)2Br^- \cdot 2H_2O$, a dicationic species containing the bases found in NAD^+ linked by a trimethylene bridge, has been determined. The crystals are monoclinic with $a = 9.468$ (1), $b = 19.318$ (2), $c = 13.845$ (2) Å, and $\beta = 131°32'$ (2′), and there are four molecules of $(C_{14}H_{17}N_7O)^{2+}2Br^- \cdot 2H_2O$ in the unit cell; the space group is $P2_1/c$. The structure has been refined to an R factor of 0.059 on 3062 nonzero reflections collected on an automatic diffractometer (Cu Kα radiation). The anion sites are occupied by chloride ions 33% of the time. The orientation of the trimethylene chain is such that the adenine and nicotinamide rings are close to being parallel (dihedral angle 4°58′) and the distances of atoms in the nicotinamide moiety from the best plane of the adenine ring range from 2.77 to 3.22 Å. While there is no intramolecular overlap of nonhydrogen atoms between the two rings, there is a close approach of C(2) and N(3) in the adenine ring to C(14) and O(21) in the nicotinamide moiety. The shortest interatomic contact is between N(3)$\cdots$C(14) at 3.06 (1) Å. The amide group is rotated by 3°54′ out of the plane of the pyridine ring. The adenine ring is linked to another centrosymmetrically related adenine ring by two N(6)–H$\cdots$N(7) hydrogen bonds. There is possible C–H$\cdots$O hydrogen bonding between two pairs of centrosymmetrically related C(14) and O(21) atoms. The water molecules are involved in hydrogen bonding to the halide anions. In addition to the close intramolecular approach of an adenine ring to the nicotinamide group, there are some close approaches between the adenine ring and nicotinamide groups from other molecules. The dramatic differences in the conformations found for Ade-C_3-Nic^+ and $AdeH^+$-C_3-Nic^+ in the solid and in solution are discussed.

In the course of the preparation of the *N*-(3-(aden-9-yl)propyl)-3-carbamoylpyridinium bromide, (Ade-C_3-Nic^+)$Br^- \cdot 3H_2O$ (I), samples,[3] crystals that were initially considered to be a different crystalline modification of I were obtained. These crystals are monoclinic

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(3) P. L. Johnson, C. A. Maier, and I. C. Paul, *J. Amer. Chem. Soc.*, **95**, 5370 (1973).

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