

# Crystal Structure of *N*(6),*N*(6)-Dimethyladeninium Hemisulfate Hydrate. The Tautomerism of *N*(6)-Substituted Adeninium Ions Elucidated by Molecular-Packing Analysis

Tor Dahl

Institute of Mathematical and Physical Sciences, University of Tromsø, N-9000 Tromsø, Norway

Dahl, T., 1993. Crystal Structure of *N*(6),*N*(6)-Dimethyladeninium Hemisulfate Hydrate. The Tautomerism of *N*(6)-Substituted Adeninium Ions Elucidated by Molecular-Packing Analysis. – Acta Chem. Scand. 47: 38–42.

The title compound crystallizes in the monoclinic space group *Ia* with cell dimensions  $a = 7.003(3)$ ,  $b = 41.213(11)$ ,  $c = 7.062(2)$  Å,  $\beta = 101.47^\circ$ . The structure was refined to  $R = 0.054$  for 1933 observed reflections. The two crystallographically independent *N*(6),*N*(6)-dimethyladeninium ions are both protonated at N(1) and N(9) and are stacked in two separate, nearly identical columns with interplanar distances of 3.341(2) and 3.360(2) Å. One of these ions is hydrogen-bonded to a water molecule at N(1)–H(1) and to a sulfate ion at N(9)–H(9). The other is also hydrogen-bonded to a water molecule and a sulfate ion, but at N(9)–H(9) and N(1)–H(1), respectively.

The finding that a sulfate ion is hydrogen-bonded to an N(1)-H(1) group is contrary to an earlier suggestion that the tautomerism observed for *N*(6)-substituted adeninium ions is a result of steric hindrance of hydrogen bond formation from N(1)–H(1) to bulky anions. An alternative explanation is therefore suggested. According to this, the protonation depends on whether the adeninium ion is linked by hydrogen bonds to two anions, or by one such bond to an anion and one to a neighbouring adeninium ion. Results of molecular-packing analysis based on atom-to-atom potentials seem to confirm this explanation.

The protonation of the ring N atoms in *N*(6)-mono-substituted and *N*(6),*N*(6)-disubstituted adeninium ions is different in different compounds and depends on the anion present. In some compounds the protonation is at N(1) and N(9),<sup>1,2</sup> as also observed in all compounds of the unsubstituted adeninium ion.<sup>3</sup> In several other compounds the protonation is at N(3) and N(7),<sup>4-7</sup> and in one case it has been found to be at N(3) and N(9).<sup>8</sup> <sup>15</sup>N NMR spectra show that protonation of *N*(6),*N*(6)-dimethyladenine by trifluoroacetic acid in dimethyl sulfoxide solution results in an equilibrium between different tautomers.<sup>9</sup>

It has been suggested that a major reason for this tautomerism is steric hindrance of hydrogen-bond formation to a bulky anion from an H-atom at N(1).<sup>7</sup> In *N*(6),*N*(6)-dimethyladeninium (DMA) hemisulfate hydrate, hydrogen bonds may be formed from the DMA ion both to the large sulfate ion and to the smaller water molecule. A crystal structure of this compound was therefore considered well suited for testing this hypothesis.

As the tautomerism is obviously in some way caused by interactions between the adeninium ion and its environment, molecular packing analysis may be of help in order to find an explanation of the phenomenon. Such analysis based on atom-to-atom potential-energy calculations was therefore performed.

## Experimental

Colourless crystals of the title compound were obtained by slow evaporation of the solvent from a solution of *N*(6),*N*(6)-dimethyladenine and sulfuric acid in the molar ratio 2 : 1. Plate-shaped, monoclinic crystals were obtained when a mixture of ethanol and methanol was used as solvent. When pure methanol was used, twinned, triclinic crystals with cell dimensions very close to those of the monoclinic crystals were obtained. The crystal used for data collection was a monoclinic one with the approximate dimensions 0.2 × 0.1 × 0.2 mm along the *a*, *b*- and *c*-axes, respectively.

The cell parameters and X-ray intensities were measured on an Enraf-Nonius CAD4 diffractometer using CuK $\alpha$  radiation ( $\lambda = 1.5418$  Å). The cell parameters were obtained from the setting angles of 25 reflections. The intensities were collected for reflections with  $\Theta < 75^\circ$  by an  $\omega/2\Theta$  scan at a rate in  $\omega$  of 0.5–2.0° min<sup>-1</sup>. For the structure determination 1933 reflections with  $I > 2\sigma(I)$  were used. Corrections were made for a continuous reduction down to 91% of the original intensities of the standard reflections, for Lorentz and polarization effects and for absorption, using an empirical method<sup>10</sup> (min/max transmission factor = 0.852).

*Crystal data.* *N*(6),*N*(6)-dimethyladeninium hemisulfate

hydrate,  $C_7H_{10}N_5^+ \cdot \frac{1}{2}SO_4^{2-} \cdot H_2O$ ,  $M_r = 230.24$ : space group  $Ia$  (No. 9),  $a = 7.003(3)$ ,  $b = 41.213(11)$ ,  $c = 7.062(2)$  Å,  $\beta = 101.47(3)^\circ$ ,  $V = 1997.5(1.1)$  Å<sup>3</sup>,  $Z = 8$ ,  $D_x = 1.531$ ,  $D_m = 1.57$  g cm<sup>-3</sup> (floatation),  $\mu(CuK\alpha) = 19.27$  cm<sup>-1</sup>.

### Structure determination and refinement

The position of the S atom was found from a Patterson map. Using this as a starting point for successive Fourier syntheses it was possible to localize all non-H atoms. Two space-groups,  $Ia$  and  $I2/a$ , were possible from the Laue symmetry and the systematic absences. The Fourier syntheses clearly showed that the former, non-centrosymmetrical space group, is the correct one. All H atoms were found from difference maps, except three methyl-H atoms. Approximate positions of these H atoms could be calculated. In the last part of the least-squares refinement positional parameters for all atoms and thermal parameters, anisotropic for non-H atoms and isotropic for H atoms, were refined. The weighting scheme used was  $w = [226.8t_1(x) + 307.3t_2(x) + 82.3t_3(x)]^{-1}$ , where  $t_n(x)$  is the Chebyshev polynomial and  $x = |F_o|/|F_o(\max)|$ .<sup>11</sup> The final  $R = 0.054$  and  $R_w = [\sum w(F_o - F_c)^2/wF^2]^{1/2} = 0.069$ . The maximum electron density in the final dif-

ference map is  $0.68$  e Å<sup>-3</sup>. The final positional parameters and  $U_{eq}$  values for non-H atoms are given in Table 1.

Rigid-body-motion analysis showed that all non-H atoms of the two independent DMA ions and all atoms of the sulfate ion rotate approximately as rigid groups.<sup>12</sup> For the DMA ions the corrections of bond distances for librational motion are smaller than the standard deviations. For the sulfate ion the corrected S–O distances are  $0.021$ – $0.023$  Å longer than the uncorrected ones. Uncorrected bond distances and angles not involving H atoms and the geometries of the hydrogen bonds between the DMA ions and their environments are shown in Fig. 1. The packing of ions and molecules is shown in Fig. 2. Scattering factors were taken from Ref. 13. All computer programs used are included in Ref. 14.

Lists of observed and calculated structure factors, anisotropic temperature factors, positions and  $U_{iso}$ -values for H atoms, and bond distances involving H atoms may be obtained from the author on request.

### Results of structure analysis

The two crystallographically independent DMA ions are both protonated at N(1) and N(9). No corresponding bond distances or angles in these ions deviate significantly

Table 1. Positional parameters and equivalent temperature factors (in Å<sup>2</sup>) for non-H atoms.<sup>a</sup>

Atom	x	y	z	$U_{eq}^b$
S(1)	0.25	0.129 41(2)	0.0	0.0241
O(1)	0.1257(6)	0.113 02(11)	0.1165(7)	0.0435
O(2)	0.4538(5)	0.124 35(10)	0.0886(7)	0.0335
O(3)	0.2032(8)	0.116 24(11)	-0.1975(6)	0.0479
O(4)	0.2082(6)	0.164 52(9)	-0.0081(7)	0.0409
O(5)	0.2598(7)	-0.087 15(9)	0.0234(7)	0.0395
O(6)	0.0096(8)	0.362 24(13)	-0.0648(7)	0.0509
N(1)	0.1702(6)	-0.035 15(11)	-0.1988(6)	0.0278
C(2)	0.2384(7)	-0.011 59(13)	-0.0660(7)	0.0332
N(3)	0.2239(7)	0.019 32(10)	-0.0943(6)	0.0334
C(4)	0.1304(7)	0.026 68(11)	-0.2756(7)	0.0292
C(5)	0.0547(6)	0.005 43(11)	-0.4260(7)	0.0263
C(6)	0.0778(6)	-0.028 45(12)	-0.3859(6)	0.0253
N(7)	-0.0305(7)	0.022 62(11)	-0.5887(6)	0.0331
C(8)	-0.0040(8)	0.052 64(14)	-0.5361(8)	0.0345
N(9)	0.0911(6)	0.056 88(11)	-0.3488(7)	0.0321
N(6)	0.0209(6)	-0.052 94(10)	-0.5054(6)	0.0309
C(10)	0.0500(11)	-0.086 94(14)	-0.4463(10)	0.0444
C(11)	-0.0696(9)	-0.046 54(14)	-0.7087(8)	0.0387
N(1)'	-0.0248(5)	0.214 42(9)	-0.0985(6)	0.0246
C(2)'	0.1054(7)	0.237 77(13)	-0.0328(7)	0.0303
N(3)'	0.0753(6)	0.268 98(10)	-0.0450(7)	0.0323
C(4)'	-0.1088(7)	0.275 80(11)	-0.1402(7)	0.0266
C(5)'	-0.2556(6)	0.254 19(10)	-0.2150(6)	0.0242
C(6)'	-0.2126(6)	0.220 51(11)	-0.1923(6)	0.0243
N(7)'	-0.4219(6)	0.270 99(10)	-0.3014(6)	0.0290
C(8)'	-0.3714(8)	0.301 50(14)	-0.2750(8)	0.0344
N(9)'	-0.1856(7)	0.305 93(11)	-0.1793(7)	0.0333
N(6)'	-0.3322(6)	0.195 61(10)	-0.2464(7)	0.0292
C(10)'	-0.2690(8)	0.161 88(12)	-0.2096(11)	0.0404
C(11)'	-0.5360(8)	0.200 43(15)	-0.3378(9)	0.0354

<sup>a</sup> Standard deviations in parentheses. <sup>b</sup>  $U_{eq} = (U_1 U_2 U_3)^{1/3}$ ;  $U_1, U_2, U_3$  are principal axes of the thermal ellipsoid.

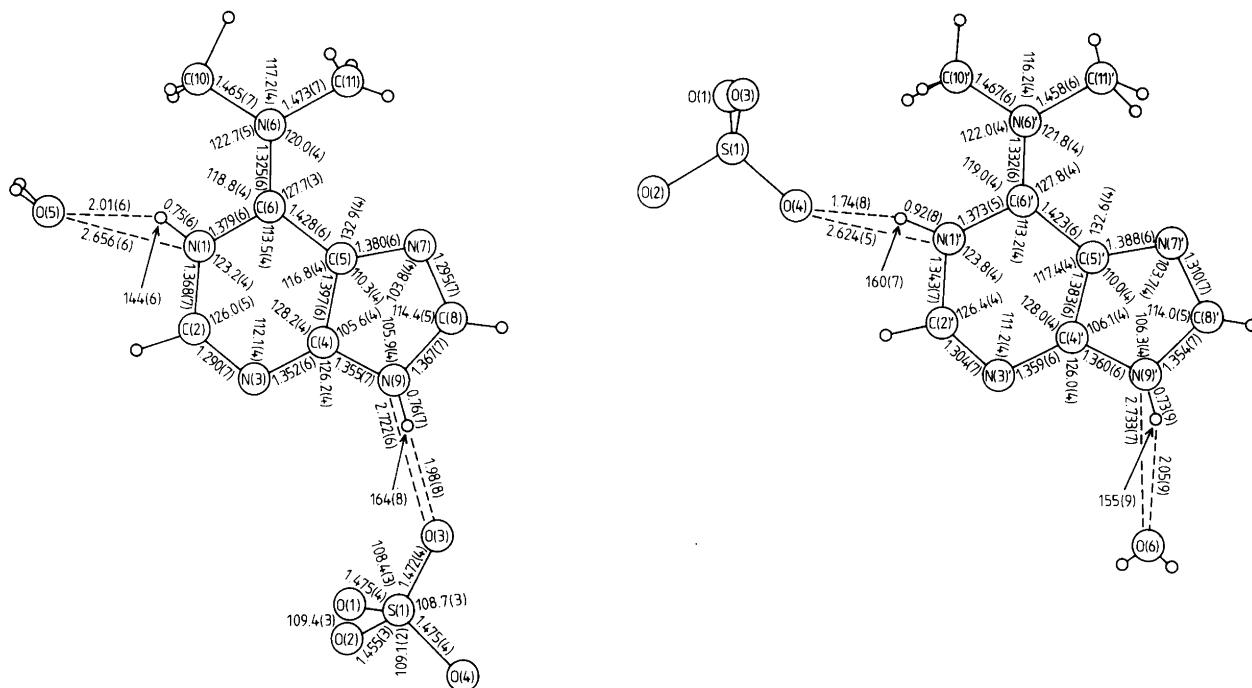


Fig. 1. Bond distances (in Å) and angles (in °), not corrected for librational motion. The angles O(1)–S(1)–O(4) and O(2)–S(1)–O(3), which are not shown in the figure, are 109.6(3) and 111.7(3)°, respectively.

from each other or from those found for DMA ions with the same protonation in other compounds. The atoms belonging to the ring systems of the DMA ions are all coplanar. The distances from these planes for N(6), C(10), C(11), N(6)', C(10)' and C(11)' (Fig. 1) are

0.033(4), 0.016(7), 0.123(6), 0.058(5), 0.089(7) and 0.144(7) Å, respectively.

It appears from Fig. 2 that the two independent DMA ions are stacked in two separate, almost identical, infinite columns. The stacks are running along the *a*- and *b*-axis

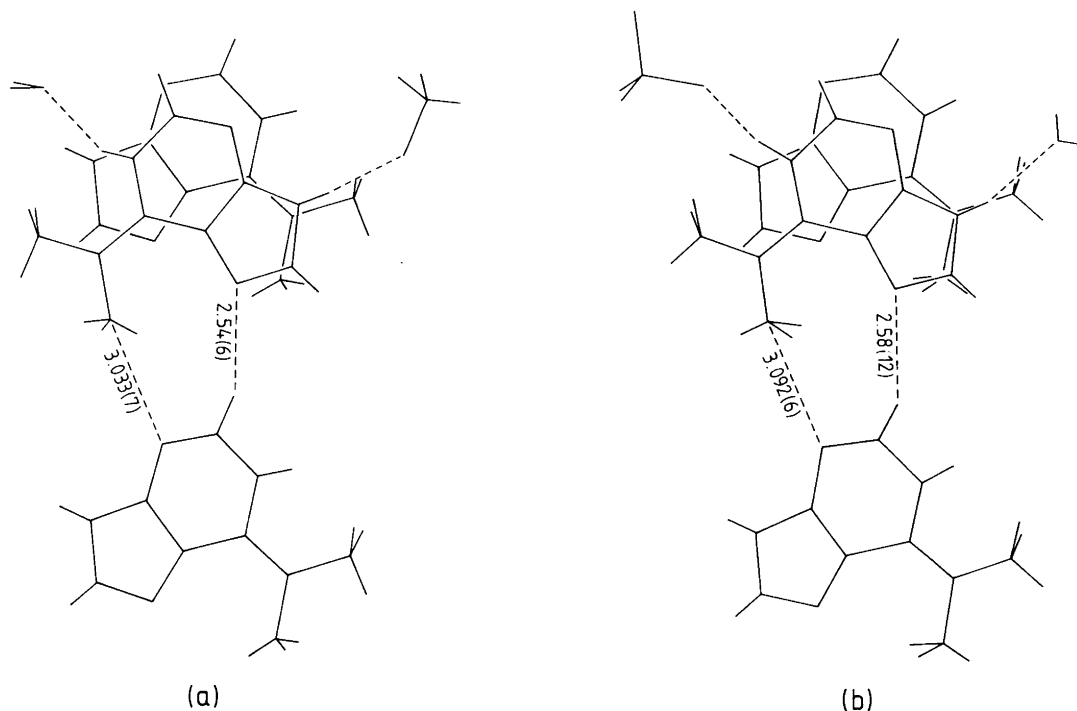


Fig. 2. The packing of the ions and molecules, viewed perpendicular to the planes of the DMA ions stacked along [100] (a) and along [001] (b). Some short contacts (in Å) are indicated.

with the planes of the DMA ions approximately parallel to (20 $\bar{1}$ ) and (10 $\bar{2}$ ) and with remarkably short interplanar distances of 3.341(2) and 3.360(2) Å, respectively. Fig. 2 shows that also the packing of neighbouring DMA stacks is almost equal, with some relatively short contacts.

It appears from the figures that one DMA ion is hydrogen-bonded to a water molecule at N(1)–H(1) and to a sulfate ion at N(9)–H(9). The other DMA ion is also hydrogen-bonded to a water molecule and a sulfate ion, but at N(9)–H(9) and N(1)–H(1), respectively. The finding that the DMA ions have the same protonation, in spite of different binding to neighbouring ions and molecules, indicates that the different protonation in other compounds has no relationship with the size of these ions or molecules. If a hydrogen bond from an N(1)–H(1) group to a sulfate ion is possible in this compound, it is unlikely that steric hindrance of a corresponding bond to a nitrate ion should be the reason why the DMA ion in DMA nitrate<sup>7</sup> is N(3),N(7) protonated.

In addition to the hydrogen bonds shown in the figures there are hydrogen bonds from all H atoms of the water molecules to the sulfate ion with O–H...O distances from 2.732 to 2.820 Å. Each of the DMA ions is thus linked to two sulfate ions, directly or through a water molecule.

#### Molecular-packing analysis of DMA compounds

For the molecular packing analysis the computer program PCK83<sup>15</sup> was used. With this program the lattice energy may be calculated from eqn. (1) and minimized by varying the cell parameters and moving the

$$E = \sum_j \sum_k -A_{jk} r_{jk}^{-6} + B_{jk} \exp(-C_{jk} r_{jk}) + q_j q_k r_{jk}^{-1} \quad (1)$$

molecules or ions in the cell. The non-bonding parameters  $A_{jk}$ ,  $B_{jk}$  and  $C_{jk}$  were taken from Refs. 16 (C,H,N), 17 (O), 18 (C) and 19 (S), intermolecular contacts  $r_{jk}$  up to 9 Å were included in the sum, and the net atomic charges  $q$  were calculated by the AM1-method,<sup>20</sup> using the computer program GASSIAN 86.<sup>21</sup> The geometries of ions and molecules were those of the experimental structures, except for C–H, N–H and O–H distances, which were adjusted to be 1.00, 0.93 and 0.89 Å, respectively.

In the ordinary energy expression hydrogen-bond energy is not included. Various methods have been used to include such bonds in lattice-energy calculations. A fairly common method, originally suggested by Hagler *et al.*,<sup>22</sup> is to set  $A_{jk}$  and  $B_{jk}$  to zero for H atoms involved in hydrogen bonding. When used on DMA compounds, this method gave unreasonably short hydrogen bond distances in the minimum energy structures between ions of opposite charge. When  $A_{jk}$  for H atoms in such bonds were set to zero and  $B_{jk}$  to 20% of the value used for ordinary H atoms, reasonable distances for these bonds were obtained.

Using these parameters minimum-energy crystal structures relatively close to the experimental structures were

obtained for DMA nitrate,<sup>7</sup> DMA chloride hydrate<sup>2</sup> and DMA hemisulfate hydrate. For the last compound the mean interplanar distances in the stacks were, however, larger in the minimum-energy structure than in the experimental structure. When the calculated energy for this compound was minimized by varying only crystallographic axes, thus keeping the molecular overlap as in the experimental structure, the interplanar distances increased by 0.062 and 0.045 Å, respectively, for the stacks along [100] and [001]. This result indicates that there are contributions to the stacking interactions in addition to those included in the analytical energy expression.

In principle the hypothesis that the tautomerism of the N(6)-substituted adeninium ions is caused by steric factors can be tested by lattice-energy calculations and minimizations, using as starting points experimental and constructed crystal structures of the same compounds with different protonations. Reasonable crystal structures are, however, difficult to construct. The interaction energy calculations were therefore performed on isolated units consisting of one DMA ion and one anion. The calculations were performed for DMA chloride and DMA nitrate with DMA protonated at N(1) and N(9), as observed in the structure of the former compound,<sup>2</sup> and at N(3) and N(7), as observed in the structure of the latter compound.<sup>7</sup> The anions were hydrogen-bonded at N(1)–H(1) and N(7)–H(7), respectively. The results are shown in Table 2. All four calculations gave minimum-energy structures with reasonable geometries of the hydrogen bonds. The interaction energies are lower for the N(1),N(9) tautomer for both compounds. This indicates that there is no strong steric hindrance of hydrogen bond formation from N(1)–H(1) to the nitrate ion, and that the different protonation is not a result of the different size of the anions. The results of these calculations, as well as those of the crystal structure analysis of DMA hemisulfate hydrate, thus show that another explanation of the tautomerism is needed.

A starting point for an alternative explanation may be the observation that in all N(3),N(7) protonated compounds there are N(3)–H(3)...N(9) hydrogen bonds between neighboring adeninium ions, resulting in dimers<sup>4-6</sup> or chains.<sup>7</sup> A similar N(9)–H(9)...N(3) bond has not been observed between any N(1),N(9)-protonated N(6)-substituted adeninium ions. In a few unsubstituted N(1),N(9) protonated adeninium com-

Table 2. Calculated minimum interionic interaction energies,  $E$ , (in kJ mol<sup>-1</sup>) and hydrogen bond distances (in Å) for different tautomers of DMA with chloride and nitrate ions and for DMA dimers.

	N(1),N(9)		N(3),N(7)	
	$E$	Distance	$E$	Distance
DMA chloride	-418.9	3.07	-411.3	3.12
DMA nitrate	-396.1	2.84	-392.0	2.85
DMA dimer	-70.5	2.86	-80.7	2.76

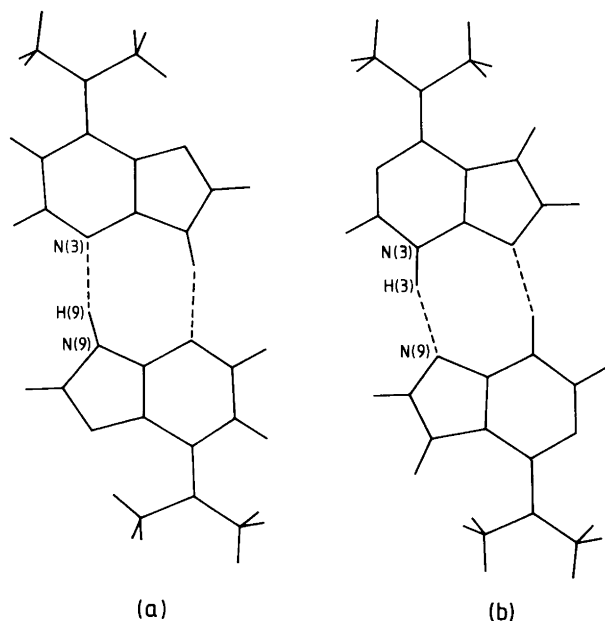


Fig. 3. Dimers of N(1),N(9)-protonated (a) and N(3),N(7)-protonated (b) DMA ions.

pounds such a bond is present,<sup>3,23,24</sup> but with a longer N–H...N distance (mean value 2.95 Å) than those of N(3)–H(3)...N(9) bonds (mean value 2.85 Å).

These indications of stronger N–H...N bonds between N(3),N(7)-protonated ions than between N(1),N(9)-protonated ions are in agreement with interaction energy calculations for DMA dimers, shown in Fig. 3. The N–H...N distance in the minimum-energy structures (Table 2), which were obtained with zero values for both  $A_{jk}$  and  $B_{jk}$ , is 0.10 Å shorter for N(3),N(7)-protonated ions, and the interaction energy is 10.2 kJ mol<sup>-1</sup> lower. As the charges of the H and N atoms directly involved in the hydrogen bonds are approximately the same in both cases, these differences must be due to differences in geometry and charge distribution of a larger part of the ion.

The protonation of *N*(6)-substituted adeninium ions seems to depend the nature of the ion to which the two N–H groups are hydrogen-bonded. When both these groups are linked to anions, directly or through a water molecule, N(1),N(9)-protonation is preferred. When one group is bonded to an anion, the other to a neighbouring adeninium ion, N(3),N(7)-protonation is preferred. The reason seems to be that in the latter case, the higher stability of the hydrogen bond to the neighbouring adeninium ion obtained with this protonation more than compensates for the lower stability of the bond from N(7)–H(7) to the anion compared to a bond from N(1)–H(1).

The reason why the *N*(6)-substituted adeninium ions are linked to different kinds of ions in different compounds may be the variation in strength of the hydrogen bonds to the anion. In the N(1),N(9)-protonated compounds the H-accepting atoms of the anion (chloride,

sulfate) have greater negative charges than those in the N(3),N(7)-substituted compounds (nitrate, picrate, tricyanoethenolate), thus forming stronger hydrogen bonds.

The N(3),N(7) protonation in DMA picrate,<sup>8</sup> where both N–H groups are hydrogen-bonded to the same anion, is probably a special case. This is the only protonation which allows the characteristic hydrogen-bond system involving two H atoms of DMA and three O-atoms of the picrate ion, similar to those formed by N(6)–H(6) and N(7)–H(7) in the picrates of the *N*(6)-furfuryladeninium ion<sup>5</sup> and the *N*(6)-methyladeninium ion.<sup>6</sup>

## References

1. Sternglanz, H. and Bugg, C. E. *Cryst. Mol. Struct.* 8 (1978) 263.
2. Dahl, T. *Acta Chem. Scand., Ser. A* 38 (1984) 485.
3. Hingerty, B. E., Einstein, J. R. and Wei, C. H. *Acta Crystallogr., Sect. B* 37 (1981) 140.
4. Dahl, T. *Acta Chem. Scand., Ser. A* 37 (1983) 353.
5. Soriano-Garcia, M., Toscano, R. A. and Espinosa, G. *J. Crystallogr. Spectrosc. Res.* 15 (1985) 651.
6. Dahl, T. and Riise, B. *Acta Chem. Scand.* 43 (1989) 493.
7. Dahl, T. and Riise, B. *Acta Chem. Scand.* 43 (1989) 882.
8. Dahl, T. *Acta Chem. Scand., Ser. B* 40 (1986) 226.
9. Gonella, N. C., Nakanishi, H., Holtwick, J. B., Horowitz, D. S., Kanamori, K., Nelson, J. L. and Roberts, J. D. *J. Am. Chem. Soc.* 105 (1983) 2050.
10. North, A. C. T., Phillips, D. C. and Mathews, F. S. *Acta Crystallogr., Sect. A* 24 (1968) 351.
11. Carruthers, J. R. and Watkin, D. J. *Acta Crystallogr., Sect. A* 35 (1979) 698.
12. Schomaker, V. and Trueblood, K. N. *Acta Crystallogr., Sect. B* 24 (1968) 63.
13. *International Tables for X-Ray Crystallography*, Kynoch Press, Birmingham 1974, Vol. 4, p. 99.
14. Watkin, D. J., and Carruthers, J. R. *CRYSTALS: User Manual*, Chemical Crystallography Laboratory, University of Oxford, Oxford, UK, 1983.
15. Williams, D. E. *PCK83: A Crystal Molecular Packing Analysis Program*, University of Louisville 1983; Quantum Chemistry Program Exchange, Program No. 481, Department of Chemistry, Indiana University, IN.
16. Williams, D. E. and Cox, S. R. *Acta Crystallogr., Sect. B* 40 (1984) 404.
17. Cox, S. R., Hsu, L. Y. and Williams, D. E. *Acta Crystallogr., Sect. A* 37 (1981) 293.
18. Hsu, L. Y. and Williams, D. E. *Acta Crystallogr., Sect. A* 36 (1980) 277.
19. Burgos, E. and Righini, R. *Chem. Phys. Lett.* 96 (1983) 584.
20. Dewar, M. J. S., Zoebish, E. G., Healy, E. F. and Stewart, J. J. P. *J. Am. Chem. Soc.* 107 (1985) 3902.
21. Frisch, M. J., Brinkley, J. S., Schlegel, H. B., Raghaavachari, K., Melius, C. F., Martin, L., Stewart, J. J. P., Bobrowicz, F. W., Rohlfing, C. M., Kahn, L. R., de Frees, D. J., Seeger, R. A., Whiteside, R. A., Fox, D. J., Fleuder, E. M. and Pople, J. A. *GAUSSIAN 86*, Carnegie-Mellon Quantum Chemistry Publishing Unit, Pittsburg, PA 1984.
22. Hagler, A. T., Huler, E. and Lifson, S. *J. Am. Chem. Soc.* 96 (1974) 5319.
23. Langer, V. and Huml, K. *Acta Crystallogr., Sect. B* 34 (1978) 2229.
24. Langer, V., Huml, K. and Zachova, J. *Acta Crystallogr., Sect. B* 35 (1979) 1148.

Received June 26, 1992.