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Crystal Structures of *N*(6),*N*(6)-Dimethyladeninium Bisulfate and *N*(6)-Methyladeninium Hemisulfate Dihydrate

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N(6),*N*(6)-Dimethyladeninium bisulfate crystallizes in the monoclinic space group C2/*c* with cell dimensions $a = 22.649(4)$, $b = 6.5910(7)$, $c = 14.471(2)$ Å, $\beta = 106.661(13)°$. The structure was refined to $R = 0.039$ for 1874 observed reflections. *N*(6)-Methyladeninium hemisulfate dihydrate crystallizes in the orthorombic space group *Cmcm* with cell dimensions $a = 22.201(3)$, $b = 14.937(2)$, $c = 6.490(3)$ Å. The structure was refined to $R = 0.060$ for 1000 observed reflections.

In both compounds the methylated adeninium ion is protonated at N(1) and N(9). There are several strong hydrogen bonds from the adeninium ions to the anions and to water molecules, but no hydrogen bonds between the methylated adeninium ions. This is in agreement with observations for other *N*(6)-methylated adeninium ions with *N*(1),*N*(9) protonation, and different from observations for those with *N*(3),*N*(7) protonation. The results seem to confirm an explanation put forward earlier that the tautomerism in this kind of compound is due to differences in strength of possible hydrogen bonds between the adeninium ions and the anions.

The protonation of the ring N atoms in *N*(6)-monosubstituted 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),[1–3] as also observed in all compounds of the unsubstituted adeninium ion.[4] In several other compounds the protonation is at N(3) and N(7),[5–8] and in two cases it has been found to be at N(3) and N(9).[9,10] ^{15}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.[11]

In all *N*(3),*N*(7)-protonated compounds there are hydrogen bonds from N(3)–H(3) to N(9) in the neighbouring adeninium ion. In all *N*(6)-methylated compounds with *N*(1),*N*(9) protonation investigated so far there are hydrogen bonds both from N(1)–H(1) and N(9)–H(9) to the anion, directly or through water molecules, not to the neighbouring adeninium ion. The hydrogen-accepting atoms of the anion have larger negative charges in the *N*(1),*N*(9)-protonated than in the *N*(3),*N*(7)-protonated compounds. An explanation has therefore been put forward that the tautomerism of the *N*(6)-substituted adeninium ion is a result of different strengths of the possible hydrogen bonds between the adeninium ion and the anion.[3] When these hydrogen bonds are so weak that one N–H group prefers to be hydrogen-bonded to the neighbouring adeninium ion, the ion is *N*(3),*N*(7)-protonated. A comparison of the N(3)–H(3)···N(9) distances with N(9)–H(9)···N(3) distances observed in some unsubstituted adeninium compounds[4,12,13] and results of atom-to-atom molecular packing analysis[3] indicate that protonation at N(3) gives the strongest hydrogen bonds between adeninium ions.

According to this explanation of the tautomerism the adeninium ion should be *N*(1),*N*(9)-protonated both in *N*(6),*N*(6)-dimethyladeninium (DMA) bisulfate and in *N*(6)-methyladeninium (MA) hemisulfate dihydrate. The structure investigations were carried out to see whether other factors, such as steric factors or differences in molecular packing, may be of importance for the protonation. If steric factors were important, N(7) might be expected to be protonated in MA hemisulfate dihydrate, as a single substituent on N(6) in adenine derivatives usually are directed away from the imidazole ring, leaving more space for hydrogen bonding to a bulky anion from N(7)–H(7) than from N(1)–H(1).

Experimental

By slow evaporation of the solvent from solutions of *N*(6),*N*(6)-dimethyladenine and sulfuric acid in the molar ratio 1:1 and *N*(6)-methyladenine and sulfuric acid in the

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Table 1. Crystal data and experimental conditions.

Compound	*N*(6),*N*(6)-Dimethyl-adeninium bisulfate	*N*(6)-Methyladeninium hemisulfate dihydrate
Formula	$C_7N_5H_{10}^+ \cdot HSO_4^-$	$C_6N_5H_8^+ \cdot 1/2\ SO_4^{2-} \cdot 2H_2O$
M_r	261.26	234.22
Crystal system	Monoclinic	Orthorombic
Space group	*C*2/*c*	*Cmcm*
a/Å	22.649(4)	22.201(3)
b/Å	6.5910(7)	14.937(2)
c/Å	14.471(2)	6.490(3)
β/°	106.661(13)	
V/Å^3	2069.5(8)	2152.1(1.1)
Z	8	8
D_x/g cm^{-3}	1.677	1.446
D_m/g cm^{-3} (flotation)	1.69	1.49
μ(Cu *K*α)/cm^{-1}	29.1	18.7
Absorption corr. (max/min)	1.533/0.698	2.053/0.747
Crystal dimensions/mm	0.12×0.30×0.25	0.11×0.08×0.34
Scan mode	ω/2Θ	ω/2Θ
Scan speed of ω/° min^{-1}	0.5–2.4	0.5–2.4
Θ range/°	0–75	0–75
Criterion for significance	$I > 2.5\sigma(I)$	$I > 3\sigma(I)$
No. of independent reflections measured	2058	1251
No. of reflections used in final refinement	1874	1000
$A=w=1$ for $\|F_o\| < A$, $(A/F_o)^2$ for $\|F_o\| > A$,	25	40
$R=\Sigma \|\|F_o\| - \|F_c\|\|/\Sigma\|F\|$	0.039	0.060
$R_w=[\Sigma w(F_o-F_c)^2/\Sigma wF^2]^{1/2}$	0.058	0.069
Max. Δρ/e Å^{-3}	0.40	0.42

molar ratio 2:1, needle-shaped, colourless crystals of DMA bisulfate and MA hemisulfate dihydrate, respectively, were obtained. For the former compound methanol was used as solvent and for the latter a mixture of methanol and ethanol. The cell parameters and X-ray intensities were measured on an Enraf-Nonius CAD4 diffractometer using Cu *K*α radiation (λ = 1.5418 Å). The cell parameters were obtained from the setting angles of 25 reflections. Crystal data and experimental conditions are given in Table 1. Corrections were made for small, continous reductions of the intensities of the standard reflections and for Lorentz and polarization effects. The crystals of both compounds had very irregular shapes, and the dimensions were difficult to measure. Corrections for absorption were performed by the empirical method of Walker and Stuart[14] during the structure refinement, before merging of equivalent reflections, and before anisotropic temperature factors were introduced.

All computer programs used in the structure determination and refinement are included in Ref. 15. Scattering factors were taken from Ref. 16. For both structures all non-H atoms were found by direct methods using MULTAN80.[17] All H atoms were found from difference maps, except two methyl-H atoms in DMA bisulfate. Approximate positions of these atoms could be calculated. For DMA bisulfate positional parameters for all atoms and thermal parameters, anisotropic for non-H atoms and isotropic for H atoms, were refined in the final least-squares refinement.

For MA hemisulfate dihydrate two space-groups, *Cmcm* and *Cmc*2$_1$, were possible from the Laue symmetry and the systematic absences. Refinement based on both space groups were therefore performed. During the refinement it became obvious that there were systematic errors in the intensities for some low-angle *hk*0 reflections and for 113, probably due to diffuse scattering. 41 reflections were therefore omitted in the final refinements.

Refinements based on the non-centrosymmetrical space group *Cmc*2$_1$ gave unreasonable results, and could not bring the *R*-value much below 0.10. With *Cmcm* the structure could be refined satisfactory when orientational disorder of the sulfate ion was introduced. This disorder is shown in Fig. 1. In the final least-squares refinement the positional parameters and the anisotropic thermal parameters of the disordered O atoms were refined separately in alternate cycles. For all other atoms positional parameters and thermal parameters, anisotropic for

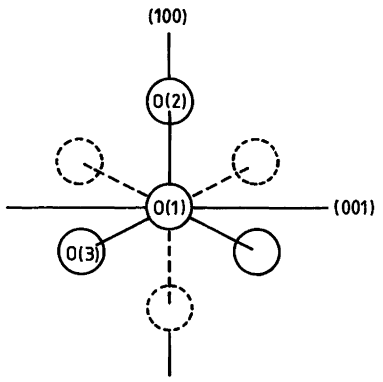

Fig. 1. The disorder of the sulfate ion in *N*(6)-methyladeninium hemisulfate dihydrate.

Table 2. Positional parameters and equivalent temperature factors (in Å^2) for non-H atoms.[a]

Atom	*x*	*y*	*z*	U_{eq}[b]
N(6),*N*(6)-Dimethyladeninium bisulfate				
N(1)	0.417 00(7)	0.2830(3)	−0.1050(1)	0.0317(4)
C(2)	0.454 58(9)	0.2891(3)	−0.1641(1)	0.0350(5)
N(3)	0.513 84(7)	0.2762(3)	−0.1360(1)	0.0356(5)
C(4)	0.535 86(8)	0.2543(3)	−0.0390(1)	0.0291(5)
C(5)	0.502 79(8)	0.2448(3)	0.0282(1)	0.0277(5)
C(6)	0.437 60(8)	0.2598(3)	−0.0066(1)	0.0276(5)
N(7)	0.542 45(7)	0.2199(3)	0.1199(1)	0.0341(4)
C(8)	0.597 11(8)	0.2158(3)	0.1064(1)	0.0363(5)
N(9)	0.596 27(7)	0.2364(3)	0.0123(1)	0.0334(5)
N(6)	0.397 54(7)	0.2540(3)	0.0441(1)	0.0321(4)
C(10)	0.331 55(9)	0.2640(4)	−0.0021(2)	0.0448(6)
C(11)	0.417 17(9)	0.2346(4)	0.1496(1)	0.0419(5)
S(1)	0.710 70(2)	0.25021(8)	−0.16890(3)	0.0335(2)
O(1)	0.771 06(7)	0.2939(3)	−0.1083(1)	0.0545(5)
O(2)	0.660 57(6)	0.2789(3)	−0.1281(1)	0.0469(5)
O(3)	0.707 55(6)	0.0181(1)	−0.1918(1)	0.0564(5)
O(4)	0.698 82(6)	0.3528(1)	−0.2626(1)	0.0517(5)
N(6)-Methyladeninium hemisulfate dihydrate				
N(1)	0.1832(2)	0.1832(2)	0.250	0.027(1)
C(2)	0.2311(2)	0.2394(3)	0.250	0.027(1)
N(3)	0.2875(2)	0.2159(2)	0.250	0.028(1)
C(4)	0.2942(2)	0.1249(3)	0.250	0.023(1)
C(5)	0.2493(2)	0.0620(3)	0.250	0.023(1)
C(6)	0.1888(2)	0.0917(3)	0.250	0.024(1)
N(7)	0.2728(2)	−0.0236(2)	0.250	0.028(1)
C(8)	0.3316(2)	−0.0100(3)	0.250	0.030(1)
N(9)	0.3471(2)	0.0792(2)	0.250	0.029(1)
N(6)	0.1416(2)	0.0395(3)	0.250	0.034(1)
C(10)	0.0790(2)	0.0699(4)	0.250	0.047(1)
S	0.50	0.2142(1)	0.250	0.0293(4)
O(1)	0.50	0.3125(4)	0.250	0.069(2)
O(2)[c]	0.50	0.1820(3)	0.4756(5)	0.054(2)
O(3)[c]	0.4471(2)	0.1798(3)	0.1587(4)	0.047(1)
O(4)	0.0906(1)	0.2968(2)	0.250	0.041(1)
O(5)	0.3737(2)	0.3593(2)	0.250	0.062(1)

[a] Standard deviations in parentheses. [b] $U_{eq} = 1/3\Sigma\Sigma U_{ij} a_i^* a_j^* a_i a_j \cos \alpha_{ij}$. [c] Occupancy factor 0.5.

non-H atoms and isotropic for H atoms, were refined simultanously.

The final positional parameters and U_{eq}-values for non-H atoms are given in Table 2. Bond distances and angles not involving H atoms and the geometry of the hydrogen bonds are shown in Fig. 2. Lists of observed and calculated structure factors, anisotropic temperature factors, positions and U_{iso}-values for H atoms and bond distances and angles involving H atoms may be obtained from one of the authors (T. D.) on request.

Results

In both compounds the adeninium ion is protonated at N(1) and N(9). No bond distances or angles deviate significantly from those observed in other DMA and MA ions with the same protonation. In the DMA ion no non-H atoms deviate significantly from planarity, except C(10) and C(11), which are 0.054(2) and −0.029(2) Å, respectively, out of the molecular plane. The non-H part of the MA ion is restricted to be planar by the space group symmetry. Bond distances and angles in the bisulfate ion agree relatively well with those observed for this ion in other compounds.[18,19] The large differences in the S–O distances in the sulfate ion may indicate that the model used for the disorder of this ion is too simple.

In DMA bisulfate there is a bifurcated hydrogen bond from the DMA ion to two bisulfate ions. A short C–H···O contact, indicated in Fig. 2, also seems to be important for the packing of this compound. In addition to those shown on the figure there are hydrogen bonds between the bisulfate ions in DMA bisulfate and from one of the water molecules to the sulfate ion in MA hemisulfate dihydrate. In DMA bisulfate there are hydrogen bonds directly to the anion both from N(1)–H(1) and N(9)–H(9). In MA bisulfate there are also hydrogen bonds to the anion, directly from N(9)–H(9), and through

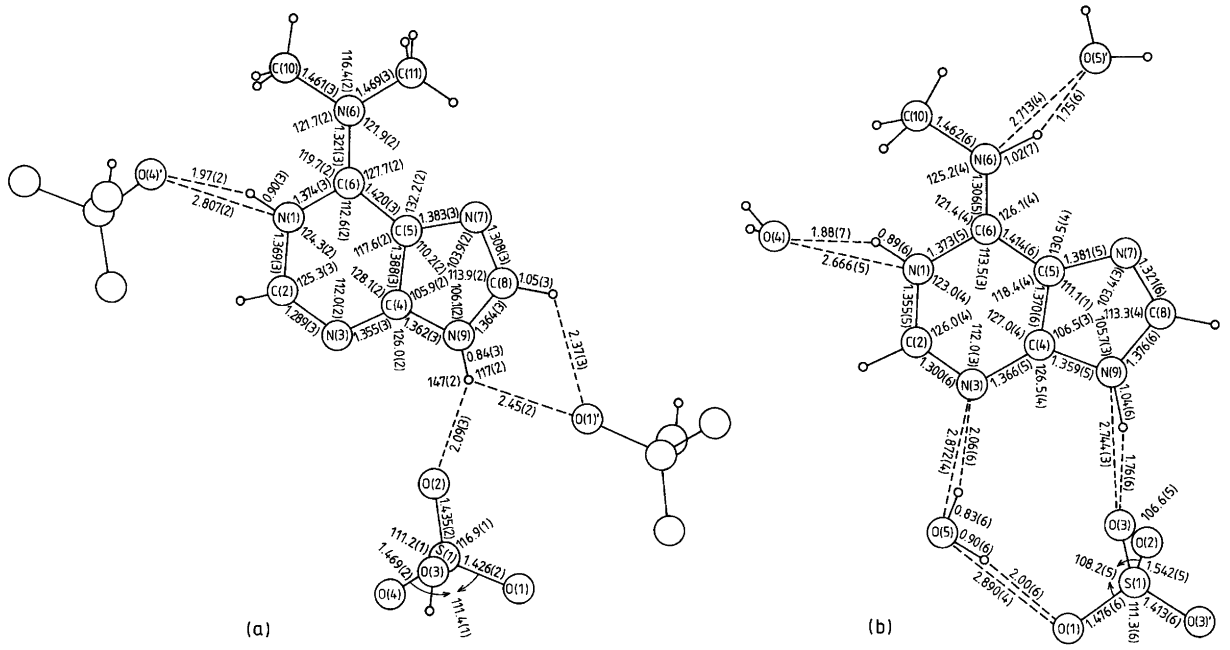

Fig. 2. Bond distances (in Å) and angles (in °) in *N*(6),*N*(6)-dimethyladeninium bisulfate (a) and *N*(6)-methyladeninium hemisulfate dihydrate (b). The angles O(1)–S(1)–O(3), O(2)–S(1)–O(3) and O(3)–S(1)–O(4) in *N*(6),*N*(6)-dimethyladeninium bisulfate, which are not shown in the figure, are 107.8(1), 102.9(1) and 105.6(1)°, respectively. The distance S(1)–O(3) is 1.562(2) Å.

a water molecule from N(1)–H(1). For both compounds the protonation and the hydrogen-bond pattern is thus as predicted in the introduction.

In both compounds the adeninium ions are stacked in infinite columns. In DMA bisulfate the interplanar distance is 3.271(1) Å, and there is a considerable overlap of neighbouring ions in the stack. In MA hemisulfate dihydrate the interplanar distance is 3.245(3) Å. Apart from two overlapping C(8) atoms with an intermolecular distance of 3.259(4) Å, there is little overlap between neighbouring ions in the stack. The molecular packing was analyzed by atom-to-atom lattice-energy calculations, using the computer program PCK83.[20] The parameters A_{jk}, B_{jk} and C_{jk} in the energy expression

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

are those by Williams *et al.*,[21,22] and the net atomic charges q were calculated by the AM1 method,[23] using the computer program GAUSSIAN 86.[24] For hydrogen-bonding H-atoms $A_{jk} = 0$, and B_{jk} was reduced to 0–25% of the value used for other H atoms. For both structures the interplanar distance in the minimum-energy structure turned out to depend strongly on the value of this modified B_{jk} parameter. Using values which gave approximately the experimental distances for the hydrogen bonds along the stack, minimum-energy interplanar distances close to the experimental distances were obtained. The experimental interplanar distances thus indicate no unexpected stacking interactions in the structures.

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. Dahl, T. *Acta Chem. Scand. 47* (1993) 38.
4. Hingerty, B. E., Einstein, J. R. and Wei, C. H. *Acta Crystallogr., Sect. B 37* (1981) 140.
5. Dahl, T. *Acta Chem. Scand., Ser. A 37* (1983) 353.
6. Soriano-Garcia, M., Toscano, R. A. and Espinosa, G. *J. Crystallogr. Spectrosc. Res. 15* (1985) 651.
7. Dahl, T. and Riise, B. *Acta Chem. Scand. 43* (1989) 493.
8. Dahl, T. and Riise, B. *Acta Chem. Scand. 43* (1989) 882.
9. Dahl, T. *Acta Chem. Scand., Ser. B 40* (1986) 226.
10. Dahl, T. and Rasmussen, I. *Acta Chem. Scand. To be published.*
11. 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.
12. Langer, V. and Huml, K. *Acta Crystallogr., Sect. B 34* (1978) 2229.
13. Langer, V., Huml, K. and Zachova, J. *Acta Crystallogr., Sect. B 35* (1979) 1148.
14. Walker, N. and Stuart, D. *Acta Crystallogr., Sect. A 39* (1983) 158.
15. *MolEN, An Interactive Structure Solution Procedure*, Enraf-Nonius, Delft 1990.
16. *International Tables for X-Ray Crystallography*, Kynoch Press, Birmingham 1974, Vol. 4, p. 99.
17. Main, P., Fiske, S. J., Hull, S. E., Lessinger, L., Germain, G., DeClerq, J. P. and Wolfson, M. M. *MULTAN80, A System of Computer Programs for the Automatic Solution of Crystal Structures from X-Ray Diffraction Data*, University of York, York 1980.
18. Cruickshank, D. W. J. *Acta Crystallogr. 17* (1964) 682.
19. Dupont, L., Dideberg, O., Toussaint, J. and Delarge, J. *Acta Crystallogr., Sect. B 36* (1980) 2170.

20. Williams, D. E. *PCK83: A Crystal Molecular Packing Analysis Program*, University of Louisville, Louisville, KT 1983; Quantum Chemistry Program Exchange, Program No. 481, Department of Chemistry, Indiana University, IN 1983.
21. Williams, D. E. and Cox, S. R. *Acta Crystallogr., Sect. B 40* (1984) 404.
22. Cox, S. R., Hsu, L. Y. and Williams, D. E. *Acta Crystallogr., Sect. A 37* (1981) 293.
23. Dewar, M. J. S., Zoebish, E. G., Healy, E. F. and Stewart, J. J. P. *J. Am. Chem. Soc. 107* (1985) 3902.
24. 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.

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