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, $\beta = 106.661(13)^\circ$. The structure was refined to $R = 0.039$ for 1874 observed reflections. $N(6)$-Methyladeninium hemisulfate dihydrate crystallizes in the orthorhombic 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 13N 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. 5 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 6,12,13 and results of atom-to-atom molecular packing analysis 2 indicate that protonation at $N(3)$ gives the strongest hydrogen bonds between adeninium ions.

According to this explanation of the tautomersim the adeninium ion should be $N(3),$ $N(9)$-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
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 Kα 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, continuous 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 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 Cmc21, 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 hk0 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 Cmc21 gave unreasonable results, and could not bring the R-value much below 0.10. With Cmcm the structure could be refined satisfactorily 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 M(6)-methyladeninium hemisulfate dihydrate.](image-url)
non-H atoms and isotropic for H atoms, were refined simultaneously.

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 $U_{eq}$-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. 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.

### Table 2. Positional parameters and equivalent temperature factors (in Å²) for non-H atoms

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<tr>
<th>Atom</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>$U_{eq}$</th>
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### M(6)-Methyladeninium hemisulfate dihydrate

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* Standard deviations in parentheses. $U_{eq} = 1/3 \Sigma U_{ij} a_i^* a_j^* \cos \alpha_{ij}$. Occupancy factor 0.5.
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. 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., and the net atomic charges $q$ were calculated by the AM1 method, using the computer program GAUSSIAN 86. 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


Received 19 May 1995.