Symmetry and Hydrogen Bonding in the Crystal Structure of 9-Aminoacridine Hemihydrate

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Symmetrical packing and hydrogen bonding arrangements characterise the crystal structure of 9-aminoacridine hemihydrate in which the molecules of the free base retain their twofold symmetry and the acridine nitrogen atoms accept pairs of symmetrical hydrogen bonds.

The crystal structures of two salts[1] and a number of complexes with dinucleotides[2] of 9-aminoacridine, the classical DNA intercalating agent,[3] have been reported. In all these structures the molecule (Figure 1) exists as a cation with protonation at the acridine nitrogen.[1] The *X*-ray structure analysis of the unprotonated free base has revealed some interesting features of crystal packing and hydrogen bonding which are reported here.

Crystals of the hemihydrate were grown from a solution of the free base in a water–acetone mixture and diffractometric data were collected based on the face-centred orthorhombic lattice (space group *Fddd*) reported earlier.[4] Repeated failures at solving the structure by direct methods[5] led to a scrutiny of the intensity distribution in the data and a reassignment to the true space group $F4_1/ddc$ or the more conventional body-centred alternative $I4_1/acd$. The indices were transformed accordingly and the equivalent reflections were merged ($R_S = \Sigma|I - I_i|/\Sigma I_i = 0.039$, where I is the mean intensity of equivalent reflections).

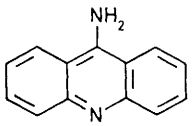

Figure 1. The free base of 9-aminoacridine. The molecular twofold axis is along the line joining the nitrogen atoms.

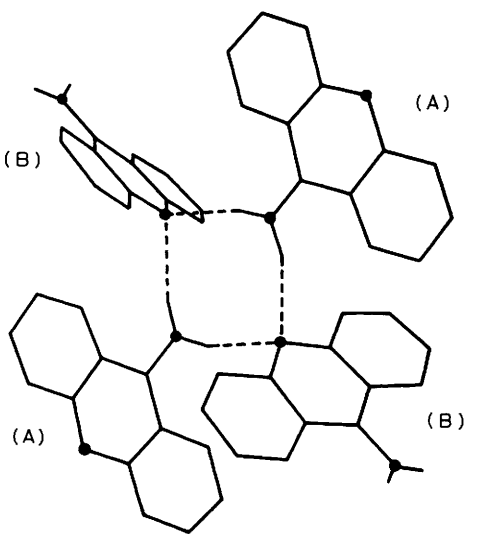

Figure 2. A perspective view of a hydrogen bonded tetramer of 9-aminoacridine.

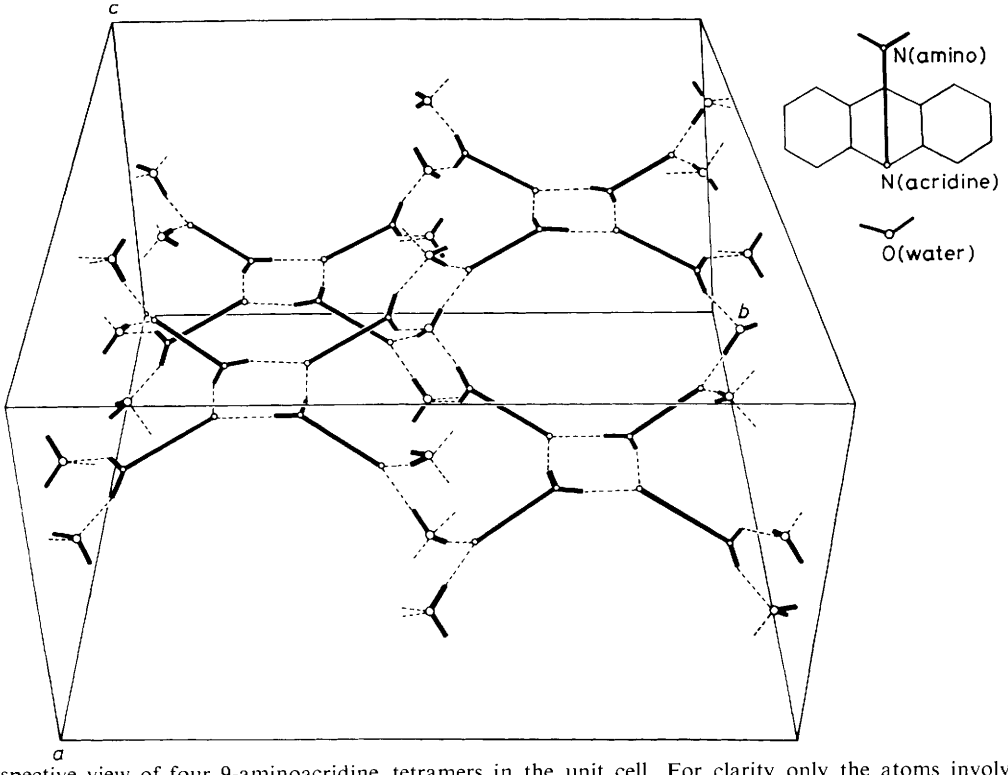

Figure 3. A perspective view of four 9-aminoacridine tetramers in the unit cell. For clarity only the atoms involved in hydrogen bonding are shown. Broken lines represent hydrogen bonds.

Crystal data: $C_{13}H_{10}N_2 \cdot \frac{1}{2}H_2O$, M = 203.25, tetragonal, $I4_1/acd$, $a = b$ = 24.477(3), c = 14.161(2) Å, U = 8484(3) Å^3, D_m = 1.277 g cm^{-3} (ref. 4), D_c = 1.272 g cm^{-3}, Z = 32, Cu-K_α radiation, λ = 1.5418 Å, μ = 6.42 cm^{-1}, 1805 unique reflections with only 803 'observed' [$I \geqslant 3\sigma(I)$].

The structure, which was solved by trial and error methods using the *hk*0 and *h*0*l* weighted reciprocal lattice sections,[6] contained two crystallographically independent types of 9-aminoacridine molecule. Molecules of type (A) were oriented parallel to the *ab* face while those of type (B) were tilted. Full-matrix least-squares refinement converged to R 0.049 and R_w 0.051 for the 'observed' reflections with all hydrogens included in the refinement.

In the crystal structure, the twofold axes of symmetry of the 9-aminoacridine and the water molecules both coincide with crystallographic twofold axes. The asymmetric unit is rather unusual for an organic structure in having two half molecules of the base and half a molecule of water.[7] This not unexpected[8] partial retention of molecular symmetry is interesting in view of the suggestion that symmetry is possibly used in the binding of small symmetrical or pseudo-symmetrical ligands to DNA.[9]

The molecules of the free base tetramerise through hydrogen bonding. Each of a pair of type (A) amino nitrogen atoms donate two symmetrical hydrogen bonds to two type (B) acridine nitrogen atoms (Figure 2). The tetramers are linked together through water-bridged hydrogen bonds. Each water oxygen atom is the donor in two symmetrical hydrogen bonds to two type (A) acridine nitrogen atoms and is the acceptor in two symmetrical hydrogen bonds from two type (B) acridine nitrogen atoms (Figure 3). Each acridine nitrogen atom, then, accepts a pair of symmetrical hydrogen bonds, the presence of which are rare in such systems.† Participation in these multiple hydrogen bonds by the ring nitrogen atoms may be significant in intermolecular recognition in biology.[10]

The crystal structure lacks the characteristic stacking observed in similar structures.[1] Symmetry and hydrogen bonding are the dominant features in the aggregation of the molecules.

The author thanks Drs. P. Roy Chowdhury and S. K. Mazumdar and several other colleagues for very useful discussions.

Received, 21st July 1983; Com. 983

† An example is found in the crystal structure of 9-(3-indol-3-yl-propyl)adenine where a ring nitrogen atom accepts two (unequal) hydrogen bonds (G. Bunick and D. Voet, *Acta Crystallogr., Sect. B*, 1982, **38**, 575).

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