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THE CRYSTAL AND MOLECULAR STRUCTURE OF 1-METHYL-3-CARBAMOYL-PYRIDINIUM:INDOLE-3-ACETIC ACID (1:1) MONOHYDRATE COMPLEX. A MODEL FOR THE INTERMOLECULAR STACKING INTERACTION BETWEEN THE INDOLE RING AND NAD$^+$

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SUMMARY

The crystal and molecular structure of the title complex has been determined by X-ray diffraction methods. The crystals contain one water molecule per asymmetric unit, which plays a important role in the molecular packing by forming hydrogen bonds with two carboxyl oxygen atoms of indole-3-acetic acid and a carbamoyl nitrogen atom of the 1-methyl-3-carbamoylpyridinium cation. Prominent stacking between the indole ring and the pyridinium ring, caused by the π_D-π_A interaction, is observed. This overlap with substantial result may provide a model for the stacking interaction between NAD$^+$ and the tryptophanyl residues in the proteins.

INTRODUCTION

The π_D-π_A charge transfer complex formation between the indole ring of tryptophan and the pyridinium ring of NAD$^+$ has been well known for a long time(1), and this unusual character has been used for the structural investigation on the environment of the tryptophanyl residues in the proteins(2-4). However, the X-ray crystallographic evidence, indicating the π_D-π_A charge transfer interaction, is meager(5,6).

To investigate the extent a protonation of the nitrogen atom

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of the pyridine ring is actually important for the interaction of an indole ring and NAD$^+$, we have determined the crystal structures of two complexes; indole-3-acetic acid(IAA)** as a donor molecule in both complexes and nicotinamide(NA)** or the 1-methyl-3-carbamoylpyridinium cation(1-MNA)** as an acceptor molecule, respectively. In the former complex,IAA:NA, which was reported previously(7), the π_D-π_A interaction between the indole ring and pyridine ring was not observed , although the many short contacts were formed between the carboxyl group in IAA molecule and the pyridine ring in NA molecule. On the other hand, the prominent overlap between the indole ring and the pyridinium ring was formed in the latter complex,IAA:1-MNA, and we wish to describe here the crystal and molecular structure of the IAA:1-MNA complex, briefly.

MATERIALS AND METHODS

1-MNA iodide in aqueous solution was converted to the (1-MNA)$^+$ form by using a column of Amberlite IRA-401 anion-exchange resin in the alkali form, and then an equimolar portion of IAA dissolved in ethyl alcohol was added to the solution. The mixture show the light-green color, corresponding to the charge transfer band, as well as the IAA:1-MNA chloride complex (8), whereas the solutions of the components are colorless. The crystals were prepared by slightly modified procedure from that reported by Ash.*et al.*(6). Light-breen needle crystals were obtained; they are monoclinic, the space group is $P2_1/c$ with four units of the chemical formula, $(C_7H_9N_2O)^+\cdot(C_{10}H_8NO_2)^-\cdot H_2O$, in the unit cell: a=12.663(2) Å, b=9.605(1) Å, c=13.501(2) Å and β=101.66(1)°. The intensity data for 2831 independent reflections were collected by a computer-controlled four-circle diffractometer(Rigaku Denki Co.) with Mo-Kα radiation using the ω-2θ scan technique, and 1788 reflections with $I>3\sigma$ were used for the structure determination and refinement. The structure was determined by the direct method with the "MULTAN" program(9), using 498 reflections with $|E|\geq 1.2$, and refined by a block-diagonal least-squares method to an R-value of 0.073.

RESULT AND DISCUSSION

The b-axis projection of the complex is presented in Fig.1,

** Abbreviations: IAA, indole-3-acetic acid; NA, nicotinamide;
1-MNA, 1-methyl-3-carbamoylpyridinium cation;

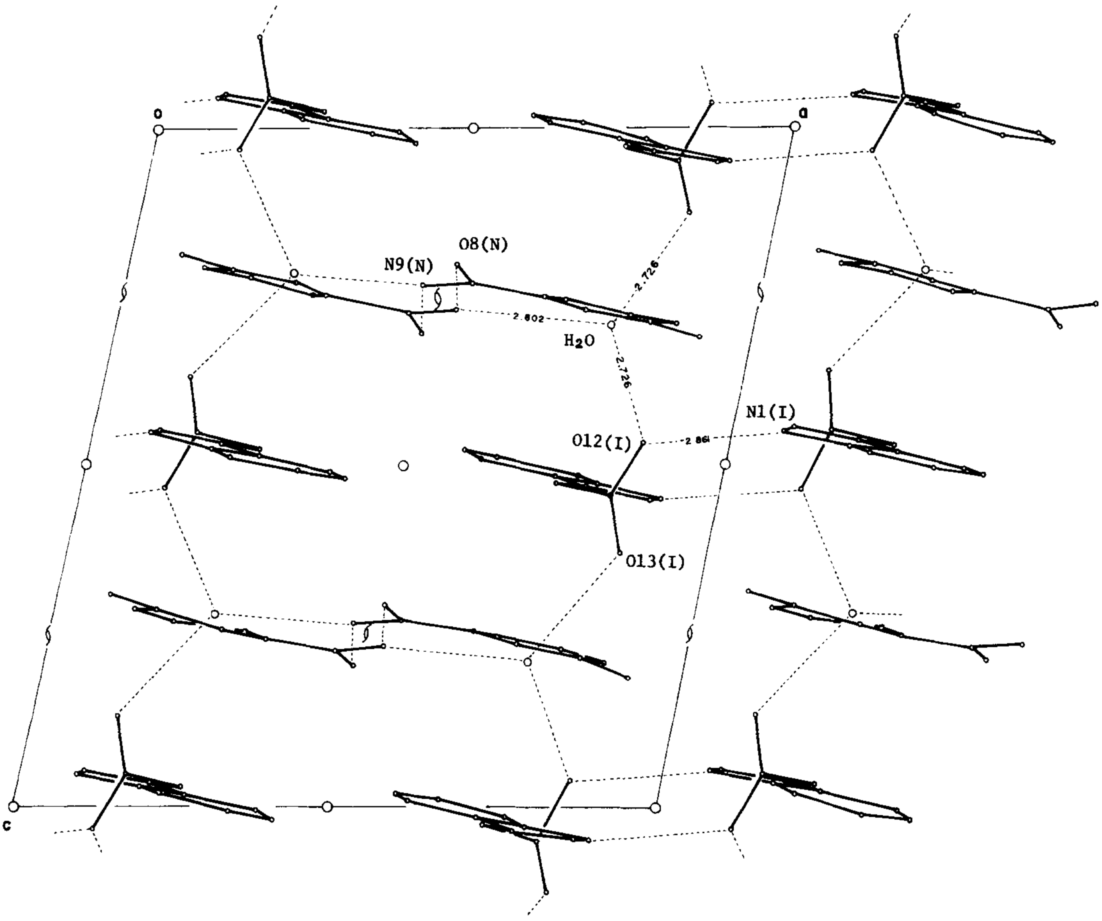

Fig.1. The crystal structure of the complex projected along *b*-axis. The dotted lines represent the possible hydrogen bonds.

where the dotted lines represent the possible hydrogen bonds. A water molecule lies almost on the *c*-glide plane, playing an important role in the molecular packing of the molecular complex by forming hydrogen bonds to the O12(I) and O13(I) atoms of the neighboring IAA translated by the *c*-glide plane and N9(N) atom of 1-MNA translated by a two-fold screw axis. No direct hydrogen-bond formation was observed between rings, as well as side chains, of the IAA and 1-MNA molecules.

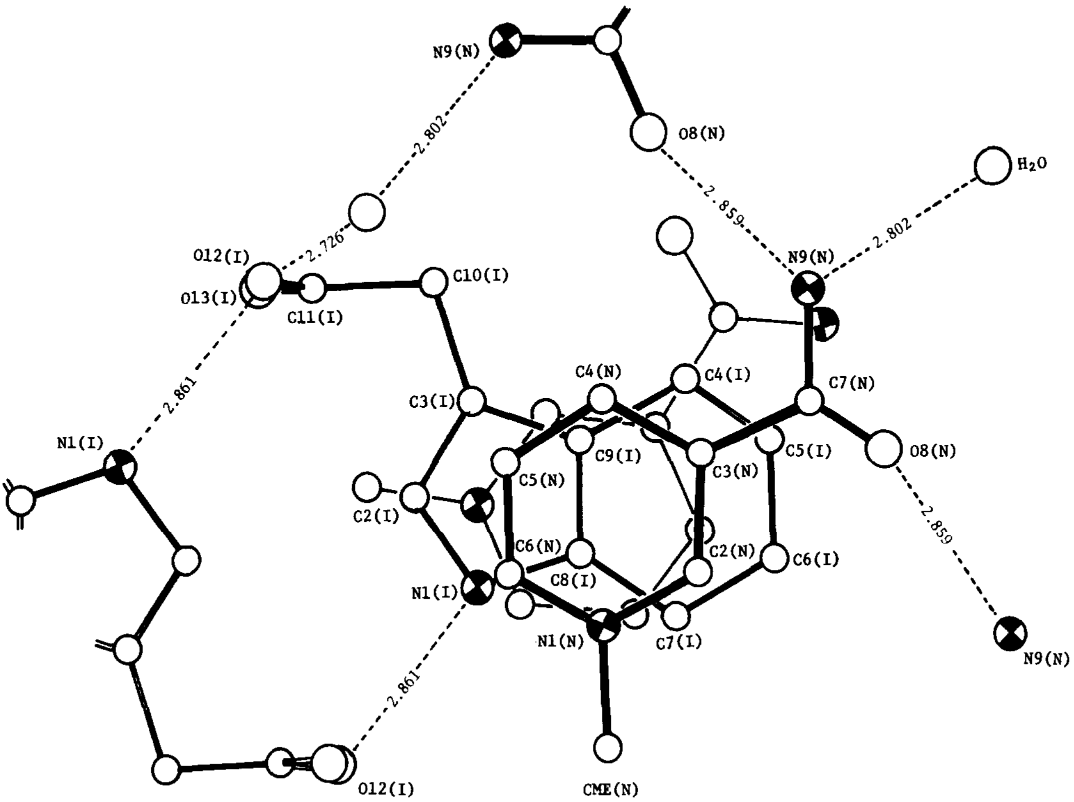

Fig.2. The stacking between the indole ring and its two nearest pyridinium rings, projected on the indole ring. The letters, N and I, in parentheses indicate 1-MNA and IAA molecule, respectively.

As a whole, the crystal structure consists of the alternate layers of IAA and 1-MNA dimers, which are piled up in the *c*-direction by the strong π_D-π_A interaction; the molecular packing is additionally stabilized by the water molecule participating in hydrogen bond formation in the *a*- and *b*-directions.

Figure 2 illustrates the stacking of the nearest neighbor donor-acceptor molecules viewed perpendicular to the indole ring. Both pyridinium rings of the upper and the lower of 1-MNA molecules are quite well stacked on the indole ring of the central IAA molecule, and their dihedral angles are 3.1° for the upper-IAA-1-MNA pair, 1.8° for the lower pair respectively.

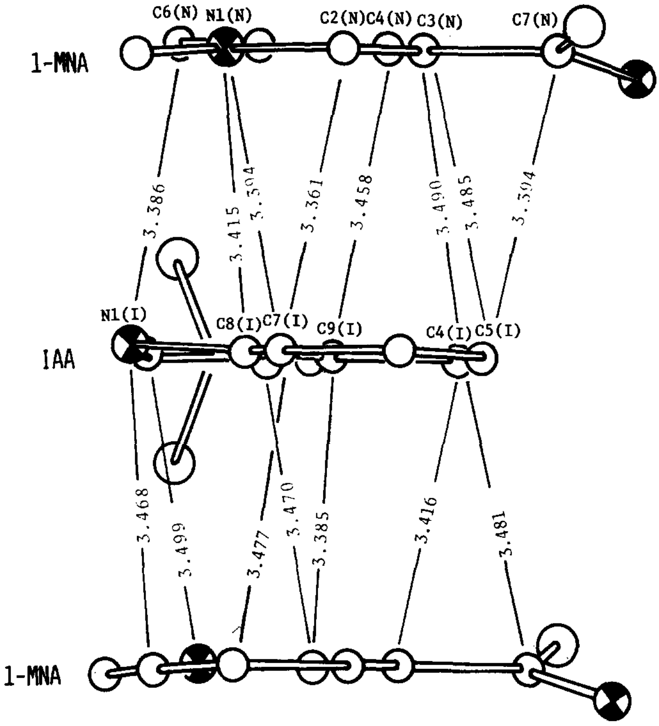

Fig.3. The interatomic distances between a IAA molecule and its stacked 1-MNA molecules.

These facts imply the existence of the strong π_D-π_A interaction between 1-MNA and IAA molecules in crystal as well as in solution (8). These stacking schemes differ significantly from that of 1-MNA:N-acetyl-*l*-tryptophanate complex(6), but are rather similar to that of the skatole:trinitrobenzene or indole:trinitrobenzene complex(10). The interatomic distances between an IAA molecule and its two nearest stacked 1-MNA molecules are presented in Fig.3. The distances between N1(I) and C6(N), C7(I) and C2(N), and C9(I) and C2(N) are somewhat shorter than the others. The averaged interplanar spacing in the overlapping area is 3.36 Å for the upper pair and 3.39 Å for the lower pair. It is of interest that the mutual orientation of the indole and pyridinium rings in this complex is different from that of 1-[2-(3-indolyl) ethyl]-3-carbamoyl pyridinium chloride(5) and also that of 1-MNA: N-acetyl-*l*-tryptophanate complex(6), suggesting the diversity of the interaction geometry. Theoretical considerations on this point are now in progress.

From the comparison of this result with that of the NA:IAA complex(7), it is obvious that the protonation of the nitrogen atom of the pyridine ring is important for the stacking between the indole ring and the pyridine ring due to π_D-π_A interaction.

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