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AN X-RAY EVIDENCE FOR THE CHARGE-TRANSFER INTERACTION BETWEEN ADENINE AND INDOLE RINGS: CRYSTAL STRUCTURE OF 1,9-DIMETHYL-ADENINE–INDOLE-3-ACETIC ACID TRIHYDRATE COMPLEX

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SUMMARY

The crystal structure of the 1:1 molecular complex of 1,9-dimethyladenine and indole-3-acetic acid trihydrate has been determined by X-ray diffraction method. Both the molecules are stacked in a pair by what is clearly a charge-transfer interaction. X-ray results suggest that the charge-transfer interaction between adenine and tryptophan may be important in nucleic acid–protein mutual recognition.

INTRODUCTION

The specific recognition of nucleic acids by proteins requires direct interaction between the chemical groups constituting each of the two macromolecules. Amino acids having the basic or acidic group could bind to nucleic acids (phosphates, riboses or bases) by hydrogen bonding or electrostatic interactions, which provide a specificity in the selective recognition of nucleic base sequences by proteins(1-3). On the other hand, such aromatic amino acids as tryptophan and tyrosine may play a special role in the recognition, due to their abilities to form stacked complexes with nucleic acid bases(4-6).

In studies of adenine–tryptophan interactions, diverse spectroscopic methods(7-9) have suggested intermolecular

*Abbreviations: DMA, 1,9-dimethyladenine
IAA, indole-3-acetic acid

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stacking or charge-transfer interactions between both aromatic rings, but such interactions have not so far been observed in the crystal structures of these complexes(10,11). In order to elucidate the mode of stacking between nucleic acid bases and indole rings at the molecular level, we are performing a series of the X-ray crystallographic studies(12-14).

We now report the crystal structure of 1,9-dimethyadenine (DMA)*: indole-3-acetic acid(IAA)* trihydrate complex, which is the first example providing direct evidence for the existence of charge-transfer interactions between adenine and indole rings in the crystalline state.

MATERIALS AND METHODS

The complex was prepared from DMA hydroxide(15,16) and IAA, dissolved in 50% aqueous dioxane. Transparent platelet crystals were formed from the solution(2×10^{-4}M) standing at room temperature(after about 3 weeks). Crystals used for X-ray study were sealed in glass capillaries with some mother liquid. Crystals are monoclinic, the space group is $P2_1/c$ with four units of the chemical formula, $(C_7H_{10}N_5)\cdot(C_{10}H_8NO_2)\cdot3H_2O$, in the unit cell: a=7.217(1), b=21.004(4), c=12.704(2) Å, β=91.14(1)°. Intensity data were collected on a Rigaku automatic diffractometer with Cu Kα radiation within $\sin\theta/\lambda\leq0.590$ Å^{-1}. The structure was solved by a direct method(program MULTAN(17)) and refined to the present discrepancy index R of 0.10 for 3288 independent reflections($I\geq3\sigma(I)$).

UV spectra in the range 220–320nm at 25°C were recorded on a Hitachi 624 spectrophotometer using 10-mm cells. The spectra were measured three times, and were averaged, using 0.10×10^{-4}M solution of DMA chloride, 1-methyladenosine-5'-phosphate sodium and IAA in 20% aqueous ethanol.

RESULTS AND DISCUSSION

In this complex, the layers consisting of alternate DMA and IAA molecules are stacked in the a-direction, and are stabilized by three water molecules participating in hydrogen bonding in the b- and c-directions.

The stacking mode between the adenine and indole rings with two up-and-down stacked pairs is illustrated in Fig.1.

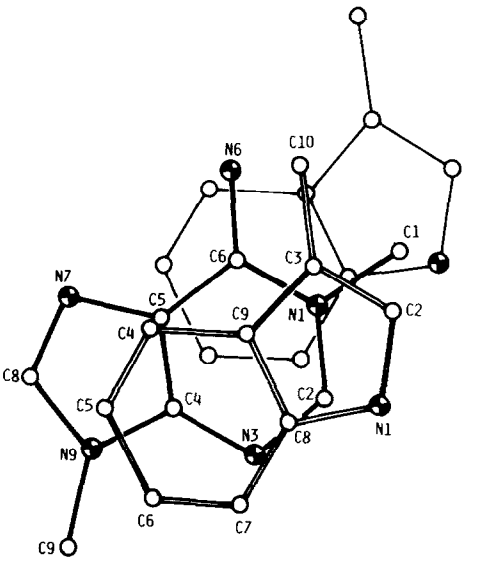

Fig.1 Stacking between the adenine and its two nearest indole rings, projected perpendicular to the central adenine ring.

Both the upper and lower indole rings are well stacked on the central adenine ring. The dihedral angles are 2.7(2)° for both pairs, and the average interplanar spacing in the overlapping area is 3.497(7) Å for the upper pair and 3.351(7) Å for the lower pair(see Fig.2). In the lower pair, such a parallel stacking arrangement with an interplanar spacing less than the normal van der Waals separation(3.4 Å) and with no direct hydrogen bond formation between the rings suggests that both rings are linked by charge-transfer from the indole ring to the lowest unoccupied orbital of the adenine ring in the ground state. The charge-transfer interaction was also observed in 20% aqueous solution. Figure 3 shows the absorption spectra of IAA, IAA plus DMA vs. DMA and IAA plus 1-methyl-adenosine-5'-phosphate vs. 1-methyladenosine-5'-phosphate, respectively. The decrease of the absorption of IAA at 237–283 nm region is caused by the hypochromic effect, indicating

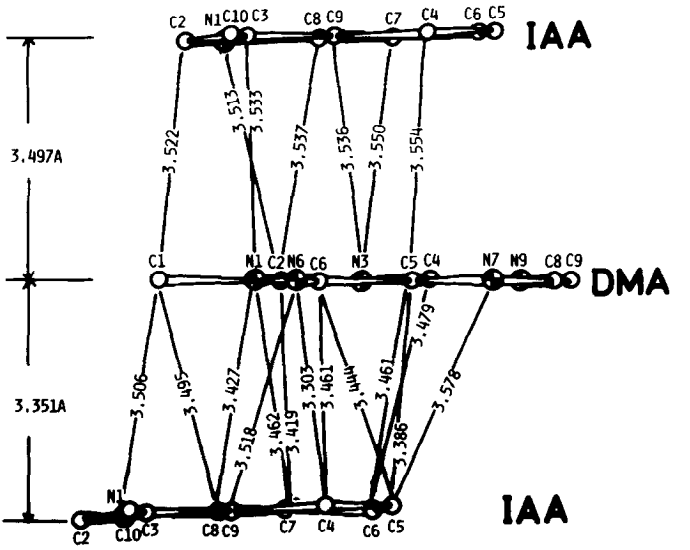

Fig.2 View of an adenine ring and its two nearest neighboring indole rings indicating selected interatomic distances between the two pairs. The estimated standard deviations of these distances are 0.006 - 0.008 Å.

the stacking interaction between indole and adenine rings. Furthermore, the positive broad band at above 283 nm tailing into 320 nm could be assigned to the charge-transfer band

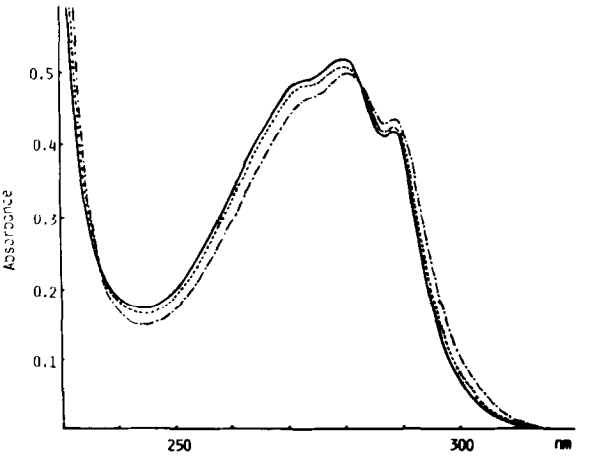

Fig.3 Absorption spectra of IAA(—), IAA plus DMA chloride vs. DMA chloride(····) and IAA plus 1-methyladenosine -5'-phosphate sodium vs. 1-methyladenosine-5'-phosphate sodium(—·—·—) in 20% aqueous ethanol solution(0.1×10^{-4}M).

resulting from electron transfer from the indole ring to the adenine ring. Thus, the charge-transfer force may play an imortant role in the interaction between adenine, especially protonated adenine, and tryptophan in nucleic acid–protein mutual recognition.

It is worthwhile noting that the indole ring may stack preferentially with the pyrimidine portion rather than with the imidazole portion of adenine. Proton magnetic resonance studies of serotonin–polyadenylic acid interactions at 296°K(18) showed the H8 resonance of the adenine ring undergoes a downfield shift due to the decrease of the adenine–adenine stacking interaction, while the H2 resonance is shifted upfield due to the ring-current effects of the indole ring in the indole–adenine stacked complexes. The stacking mode observed in the present complex (Fig.1) may account well for the above-mentioned proton behaviour of polyadenylic acid.

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