03.2–2 COMPLEXES OF THE CH_3Hg^+ ION WITH CYTOSINE AND 1-METHYLCYTOSINE. By A.L. Beauchamp and M. Simard, Département de chimie, Université de Montréal, Montréal, Canada.

The general problem of heavy-metal interactions with DNA bases has been investigated in this laboratory for several years. The methylmercury cation, a mutagenic agent, has been used to identify the potential sites of reaction for heavy metals. Results with 1-methylcytosine (mCyt) and unblocked cytosine (Cyt) are described in the present paper. Neutral and cationic complexes with metal:ligand ratios ranging from 1:1 to 3:1 have been prepared for these two ligands.

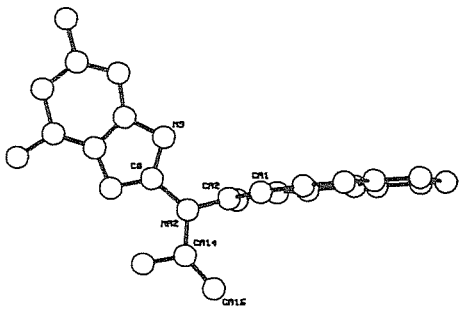
Extensive use has been made of X-ray diffraction techniques to caracterize 12 cristalline solids. The participation of the heterocyclic N3 site has been observed in all the cationic complexes. Substitution of the amino group is found to occur in an unexpected way, the hydrogen atom closer to N3 being preferentially replaced in four complexes of the type $[(CH_3Hg)_2(mCyt\text{-}H)]X$, where $X = ClO_4$, HCO_3 and two NO_3 forms. Two neutral complexes, $[CH_3Hg(mCyt\text{-}H)]$ and $[(CH_3Hg)_2(Cyt\text{-}2H)]$, show the same geometry, but N3 is not used for complexation in these cases. Both amino protons can be replaced, as evidenced from the structure of $[(CH_3Hg)_3(mCyt\text{-}2H)]NO_3$. For cytosine, N1 appears to be the first site to participate in the reactivity pattern for the neutral complexes, but this order is not always observed in the cationic series, for instance, in the non-stoichiometric $[(CH_3Hg)_2(Cyt\text{-}H)]ClO_4$ compound.

03.2–3 CONFORMATION OF THE C8 SUBSTITUTED GUANINE ADDUCT OF THE CARCINOGEN ACETYLAMINOFLUORENE: MODEL FOR A POSSIBLE Z-DNA MODIFIED STRUCTURE. By R. Kuroda, S. Neidle, F.E. Evans, S. Broyde and B.E. Hingerty, Department of Biophysics, King's College, London WC2B 5RL, England, National Center for Toxicological Research, Jefferson, Arkansas 72079, Biology Department, New York University, New York 10002, and Health and Safety Research Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee 37830.

Conformational changes imposed on double stranded DNA following covalent modification by 2-(acetylamino)-fluorene (AAF) are thought to be relevant to the carcinogenic activity of the compound. Binding of AAF at C8 of guanine in DNA causes base displacement or 'insertion-denaturation', while the adduct with poly (dG-dC).poly (dG-dC) stabilizes a Z-DNA structure. The present work describes an examination of the C8-bound guanine adduct of AAF, by a combination of X-ray crystal structural work and semi-empirical potential energy minimization calculations. This is the first report of X-ray structural information on the interaction between AAF and a nucleic acid constituent.

The crystals are monoclinic, space group C 2/c with a=26.179(3), b=9.453(2), c=14.253(1)Å, β=105.23(1)° and Z=8. The structure was solved by direct methods using the program MULTAN 82. The final R value was 0.118. The compound adopts a trans conformation about the amide bond (γ, C8-NA2-CA14-CA15=178(4)°). Other relevant acetyl torsion angles, α (N9-C8-NA2-CA2) and β (C8-NA2-CA2-CA1) are -28(3) and 108(3)°, respectively. Both the fluorene and guanine moieties are planar within experimental error, and the dihedral angle between the two planes is 95°. A near perpendicular orientation between the fluorene and guanine has been previously predicted for the d(CpG)-AAF adduct. The conformation of the acetylamino group in G-AAF is at variance with that observed in the crystal structure of hydroxylated AAF's. In these compounds, torsion angles equivalent to β are in the range 172-220°, and those equivalent to γ lie between -5° and 17°. G-AAF does not exhibit coplanarity of the acetyl and fluorene groups seen in hydroxylated AAF compounds. Therefore, it seems likely that the conformation observed in these structures is not directly relevant to the conformation of AAF when bound to nucleobase.

Semi-empirical energy minimization of G-AAF shows four discrete low-energy domains, I-IV, depending on α and β values. Our X-ray structural work shows that the conformation of G-AAF lies in region IV. Comparison with similar energy calculations for d(CpG)-AAF indicates that conformations in this region can be adopted only by Z-like structures, where the AAF is situated in a flexible position at the exterior of the DNA helix.



03.2–4 PATTERNS OF PEPTIDE AGGREGATION AND THE CRYSTAL STRUCTURE OF A 1:1 COMPLEX BETWEEN L-HISTIDYL-L-SERINE AND GLYCYL-L-GLUTAMIC ACID. By C.G.Suresh and M.Vijayan, Molecular Biophysics Unit, Indian Institute of Science, Bangalore-560 012, India.

We have shown earlier that peptide-like head-to tail sequences, which are of probable relevance to prebiotic polymerisation, are an intrinsic feature of amino acid aggregation in crystals (FEBS lett.1980,112,135; Int.J.Peptide Protein Res.1983,22,129 & 617). A careful study reveals that head-to-tail sequences remain the main feature of the crystal structures of un-end-protected peptides also. These sequences and the periodic arrangements generated by hydrogen bonds involving the peptide nitrogen, give rise to characteristic patterns of peptide aggregation. These patterns can be easily explained in terms of simple geometrical and hydrogen-bonding considerations.

The crystal structure of a highly hydrated complex between L-histidyl-L-serine and glycyl-L-glutamic acid (P1, a=4.706, b=8.578, c=16.521 Å, α=85.9, β=89.7, γ=77.4°, Z=1, R=0.046 for 2150 observed reflections), the first of its kind to be prepared and X-ray analysed, indicates that the basic patterns of peptide aggregation are retained in complexes as well. The structure consists of alternating layers of unlike molecules. Each layer is made up of head-to-tail sequences of peptide molecules, interconnected by hydrogen bonds involving the peptide group. The adjacent layers are held together by interactions between side-chain imidazole and carboxylate groups, and water bridges.