

**03.2-06** COMPLEXES OF THE  $\text{Ag}^+$  AND  $\text{CH}_3\text{Hg}^+$  IONS WITH METHYL DERIVATIVES OF CYTOSINE, THYMINE AND HYPOXANTHINE. By A.L. Beauchamp, F. Bélanger-Gariépy, J.-P. Charland, F. Guay and M. Simard, Département de Chimie, Université de Montréal, Montréal, Canada.

The present work is part of a systematic study of the structures of  $\text{Ag}^+$  and  $\text{CH}_3\text{Hg}^+$  complexes with the purines and pyrimidines found in nucleic acids. We intend to clarify the role played by these metal ions when added to solutions of polynucleotides or nucleic acids and to provide basic chemical informations which could be extrapolated to the interactions of Pt anti-cancer drugs with DNA.

Chelate formation between N7 and the carbonyl oxygen O6 of guanine is one of the model mechanisms used to explain the attack of Pt complexes on DNA. In order to assess the reactivity of O6 toward soft metal ions, silver complexes with 9-methylhypoxanthine (HMPx), a guanine-like ligand, were prepared. With  $\text{AgClO}_4$ , a complex of the formula  $[(\text{HMPx})_2\text{Ag}]\text{ClO}_4 \cdot \text{H}_2\text{O}$  was obtained, in which  $\text{Ag}^+$  is linearly bonded to N7 atoms of two ligands, whereas O6 is involved only in H-bonding. The nitrate has the stoichiometry  $[(\text{HMPx})\text{Ag}]\text{NO}_3 \cdot \text{H}_2\text{O}$ . The solid consists of infinite chains in which the ligand bridges two  $\text{Ag}^+$  ions along the chain via N7 and the uncommon endocyclic N3 atom. The carbonyl group is free. The preference for the strained N3 position over the unhindered O6 group is an indication of the poor basicity of the latter site in the non-deprotonated form of the ligand.

$\text{CH}_3\text{HgNO}_3$  forms with 1-methylcytosine (MCy) a compound  $[\text{CH}_3\text{Hg}(\text{MCy})]\text{NO}_3$  in which the Hg atom is bonded to the usual N3 site. By reacting an excess of  $\text{CH}_3\text{HgNO}_3$  in basic or slightly acidic solutions, one amino proton is displaced by mercury, while the second  $\text{CH}_3\text{Hg}^+$  ion is found on N3. The most peculiar feature of this structure is the *syn* configuration of the  $\text{CH}_3\text{Hg}$  groups bonded to N3 and N4, respectively, instead of the presumably less constrained *anti* arrangement.

With 1-methylthymine (HMT), the substitution of H3 by  $\text{CH}_3\text{Hg}^+$  yields the neutral 1:1 compound  $[\text{CH}_3\text{Hg}(\text{MT})] \cdot \frac{1}{2}\text{H}_2\text{O}$ . The carbonyl groups O2 and O4 interact only weakly with the Hg atom of adjacent molecules and with the water molecule. This neutral complex forms "addition compounds" with a number of simple salts of alkaline or alkaline-earth cations. The structure of  $[\text{CH}_3\text{Hg}(\text{MT})] \cdot \frac{1}{2}\text{NaNO}_3$  was determined. The  $[\text{CH}_3\text{Hg}(\text{MT})]$  unit has the same structure as in the hemihydrate, but the residual basicity of O2 and O4 is now fulfilled by interactions with the  $\text{Na}^+$  ions, which assume an octahedral environment of carbonyl and nitrate oxygen atoms.

**03.2-07** RESTRICTION OF PEPTIDE CONFORMATION BY  $\alpha$ -METHYL SUBSTITUTION. Patrick Van Roey, G. David Smith and William L. Duax, Medical Fdn. of Buffalo, Inc., 73 High St., Buffalo, NY 14203 and T. M. Balasubramanian and G. R. Marshall, Dept. of Physiology and Biophysics, Washington University, St. Louis, MO 63110.

The conformational space accessible to a peptide can be severely limited by  $\alpha$ -methyl substitution on one or more of the constituent amino acids. All except one of the 22 crystallographic observations of  $\alpha$ -aminoisobutyrate ( $\alpha$ -methylalanine) in linear peptides fall within a region which is midway between the conformations of an  $\alpha$ - and a  $3_10$ -helix and with an average value of  $\phi = 56.5^\circ$  and  $\psi = 39.8^\circ$ . The single exception is that of the conformation of the second Aib residue in the peptide BOC-Aib-OBzl, for which the  $\phi$  and  $\psi$  torsion angles are observed to be  $51.4^\circ$  and  $-138.5^\circ$ , respectively. This latter value is about  $180^\circ$  removed from the expected value and therefore maintains the spatial relationship between the side chain methyl groups and the carboxyl oxygen atoms observed for the other Aib residues. The observed conformation of BOC-Phe( $\alpha$ Me)-Val-OBzl shows that  $\alpha$ -methyl substitution of amino acids other than alanine restricted the backbone conformation in a similar fashion. The observed values of the  $\phi$  and  $\psi$  torsion angles of  $59.0^\circ$  and  $33.3^\circ$  for the  $\alpha$ -methylphenylalanine residue nearly coincide with the average values for Aib residues. Furthermore, the restriction of the backbone conformation is accomplished without altering the conformation of the side chain or the remainder of the peptide. Research supported in part by Grant No. GM-19684 from the National Institute of General Medical Sciences, DHEW (PVR, GDS AND WLD).

**03.2-08** INFLUENCE DE L'HYDRATATION SUR LE REPLIEMENT  $\beta$ . Par A. Aubry et J. Protas, Laboratoire de Minéralogie et Cristallographie, Case Officielle n°140, 54037 Nancy Cedex, France et G. Boussard, B. Vitoux et M. Marraud, Laboratoire de Chimie Physique Macromoléculaire, E.N.S. I.C., 1 Rue Grandville, 54000 Nancy, France.

Les structures cristallines des deux formes anhydre et hydratée de la N-pivaloyl-L-prolyl-N,N'-diméthyl-D-alaninamide ont été résolues par diffraction des rayons X. Le dérivé anhydre présente un repliement de type  $\beta$ II avec les angles conformationnels  $\phi_1 = -58^\circ$ ,  $\psi_1 = 136^\circ$ ,  $\phi_2 = 97^\circ$  et  $\psi_2 = -19^\circ$  stabilisé par la liaison hydrogène  $\text{O}^{\text{---}}\text{---}\text{N}^{\text{---}}$  de longueur 2,97 Å. Dans le composé hydraté, la molécule d'eau vient se placer en pont entre les atomes  $\text{O}^{\text{---}}$  et  $\text{N}^{\text{---}}$  réalisant un système complexe de liaisons hydrogène  $\text{---}\text{C}^{\text{---}}\text{O}^{\text{---}}\text{---}\text{H}\text{---}\text{N}^{\text{---}}\text{---}\text{H}\text{---}\text{N}^{\text{---}}$  ( $\text{W}\text{---}\text{O}^{\text{---}} = 2,75 \text{ \AA}$ ,  $\text{N}^{\text{---}}\text{---}\text{W} = 2,82 \text{ \AA}$ ,  $\text{N}^{\text{---}}\text{---}\text{W}\text{---}\text{O}^{\text{---}} = 128^\circ$ ,  $\text{O}^{\text{---}}\text{---}\text{N}^{\text{---}} = 5,00 \text{ \AA}$ ). Les angles conformationnels sont alors :  $\phi_1 = -69^\circ$ ,  $\psi_1 = 164^\circ$ ,  $\phi_2 = 139^\circ$ ,  $\psi_2 = -35^\circ$ . Bien que les angles dièdres  $\psi_1$  et  $\phi_2$  subissent respectivement une rotation d'environ  $30^\circ$  et  $40^\circ$ , la forme générale de la molécule est conservée. L'hydratation provoque donc une ouverture du repliement  $\beta$  à 10 atomes pour permettre l'insertion d'une molécule d'eau, le cycle passant ainsi à douze atomes. C'est la première fois qu'une molécule peptidique est étudiée à la fois sous forme anhydre et hydratée à l'état solide et c'est la première fois qu'une molécule d'eau a été mise en évidence dans une telle disposition. Ce phénomène devra être pris en considération dans l'étude conformationnelle des polypeptides linéaires en solution aqueuse.