03.2-06 COMPLEXES OF THE Ag^+ AND CH_3Hg^+ 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 Ag^+ and CH_3Hg^+ 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 anticancer 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 $AgClO_4$, a complex of the formula $[(HMPx)_2Ag]ClO_4.H_2O$ was obtained, in which Ag^+ is linearly bonded to N7 atoms of two ligands, whereas O6 is involved only in H-bonding. The nitrate has the stoichiometry $[(HMPx)Ag]NO_3.H_2O$. The solid consists of infinite chains in which the ligand bridges two 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 O6group is an indication of the poor basicity of the latter site in the non-deprotonated form of the ligand.

CH_3HgNO_3 forms with 1-methylcytosine (MCy) a compound $[CH_3Hg(MCy)]NO_3$ in which the Hg atom is bonded to the usual N3 site. By reacting an excess of CH_3HgNO_3 in basic or slightly acidic solutions, one amino proton is displaced by mercury, while the second CH_3Hg^+ ion is found on N3. The most peculiar feature of this structure is the syn configuration of the CH_3Hg groups bonded to N3 and N4, respectively, instead of the presumably less constrained anti arrangement.

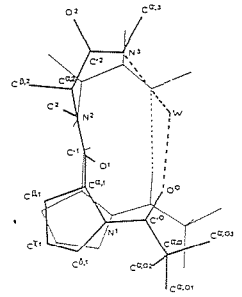
With 1-methylthymine (HMT), the substitution of H3 by CH_3Hg^+ yields the neutral 1:1 compound $[CH_3Hg(MT)].\frac{1}{2}H_2O$. The carbonyl groups O2 and O4 interact only weakly the Hg atom of adjacent molecules and with the water molecule. This neutral complex forms "addition compounds" with a number of simple salts of alkaline or alkaline-earth cations. The structure of $[CH_3Hg(MT)].\frac{1}{2}NaNO_3$ was determined. The $[CH_3Hg(MT)]$ unit has the same structure as in the hemihydrate, but the residual basicity of O2 and O4 is now fulfilled by interactions with the Na^+ ions, which assume an octahedral environment of carbonyl and nitrate oxygen atoms.

03.2-07 RESTRICTION OF PEPTIDE CONFORMATION BY α-METHYL SUBSTITUTION. Patrick Van Roey, G. David Smith and William L. Duax, Medical Fndn. 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.

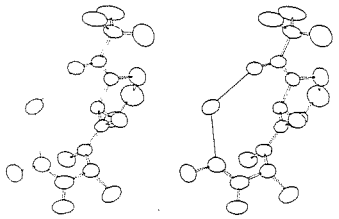
The conformational space accessible to a peptide can be severely limited by α-methyl substitution on one or more of the constituent amino acids. All except one of the 22 crystallographic observations of α-aminoisobutyrate (α-methylalanine) in linear peptides fall within a region which is midway between the conformations of an α- and a 3_{10}-helix and with an average value of ϕ=56.5° and ψ =39.8°. The single exception is that of the conformation of the second Aib residue in the peptide BOC-Aib-Aib-OBzl, for which the ϕ and ψ torsion angles are observed to be 51.4° and -138.5°, respectively. This latter value is about 180° 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(αMe)-Val-OBzl shows that α-methyl substitution of amino acids other than alanine restricted the backbone conformation in a similar fashion. The observed values of the ϕ and ψ torsion angles of 59.0° and 33.3° for the α-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 β. 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.

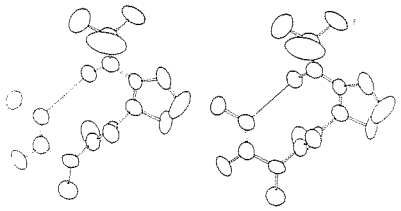
Les structures cristallines des deux formes anhydre et hydratée de la N-pivaloyl-L-prolyl-N,N'-dimethyl-D-alaninamide ont été résolues par diffraction des rayons X. Le dérivé anhydre présente un repliement de type βII avec les angles conformationnels ϕ_1=-58°, ψ_1=136°, ϕ_2=97° et ψ_2=-19° stabilisé par la liaison hydrogène $O^\circ\cdots N^3$ de longueur 2,97 Å. Dans le composé hydraté, la molécule d'eau vient se placer en pont entre les atomes O° et N^3 réalisant un système complexe de liaisons hydrogène $>C'^{O}=O^\circ\cdots H-W\cdots H-N^3<$ ($W\cdots O^\circ$=2,75 Å, $N^3\cdots W$=2,82 Å, N^3-W-O°=128°, O°-N^3=5,00 Å). Les angles conformationnels sont alors : ϕ_1=-69°, ψ_1=164°, ϕ_2=139°, ψ_2=-35°. Bien que les angles dièdres ψ_1 et ϕ_2 subissent respectivement une rotation d'environ 30° et 40°, la forme générale de la molécule est conservée. L'hydratation provoque donc une ouverture du repliement β 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.



Projection des deux molécules sur les squelettes peptidiques



Vues stéréoscopiques des molécules



03.2-09 X-RAY STUDIES OF AMINO ACID - VITAMIN INTERACTIONS. THE CRYSTAL STRUCTURE OF LYSINE PANTOTHENATE. By D.M. Salunke and M. Vijayan, Molecular Biophysics Unit, Indian Institute of Science, Bangalore 560012, India.

Non-covalent interactions play a crucial role in the structure, binding and action of proteins. As part of an attempt to study, at the atomic resolution, the possible geometrical features of such interactions through the x-ray analysis of crystalline complexes of amino acids and short peptides among themselves as well as with other biomolecules (Acta Cryst. (1980) B36, 125-128, and the references therein), the crystal structure of a 1:1 complex between lysine and pantothenic acid has been determined. The complex crystallizes in the monoclinic space group $P2_1$ with two formula units in a cell of dimensions a = 5.883, b = 16.218, c = 10.024 Å and β = 106.6°. The structure, solved by the direct method, has been refined to a current R value of 0.059 for 1868 observed reflections. The zwitterionic positively charged lysine molecules in the structure exist in the fully extended conformation whereas the pantothenate anions have a somewhat folded structure. The unlike molecules aggregate into separate alternating layers in the crystal structure as in several other crystalline complexes involving amino acids. Among the interactions which hold the adjacent layers together, those involving the side chain amino group of lysine and the carboxylate group in the pantothenate anion are of particular interest.

03.2-10 CRYSTAL STRUCTURES OF 4-NITRO-L-HISTIDINE AND $N^{(\alpha)}$-ACETYL-4-NITRO-L-HISTIDINE. By X. Solans, and M. Font-Altaba. Dept. Crystallography and Mineralogy, University of Barcelona, Gran Via 585, Barcelona-7. Spain.

4-Nitro-L-histidine, monohydrate (I): $C_6H_8N_4O_4 \cdot H_2O$, orthorhombic, $P2_12_12_1$, Z = 4, a = 12.519 (4), b = 10.757(3), c = 6.590(1) Å, V = 887.5 (7) $Å^3$, Dc = 1.63 Mg m^{-3}. 1127 observed reflections.

$N^{(\alpha)}$-acetyl-4-nitro-L-histidine (II): $C_8H_{10}N_4O_5$ orthorhombic, $P2_12_12_1$, Z = 4, a = 15.425(3), b = 9.756(2), c = 6.822(1) Å, V = 1026.6(7) $Å^3$, Dc = 1.57 Mg m^{-3}. 1534 observed reflections

Intensity data were recorded on a Philips PW-1100 four-circle diffractometer, and both structures were solved using MULTAN80 system of computer programs and refined by full-matrix least-squares method using SHELX76 program. The final R values are 0.045 for (I) and 0.063 for (II).

The nitro substituent modifies the bond distances in the imidazolyl ring with respect to those obtained in the L-histidine. The torsion angles are similar to those obtained in the L-histidine, with the exception of -C-COOH bond in the $N^{(\alpha)}$-acetyl-4-nitro-L-histidine, which is twisted -98.5?

The packing of the molecules is due in the two compounds to hydrogen bonds, which are different in each structure.