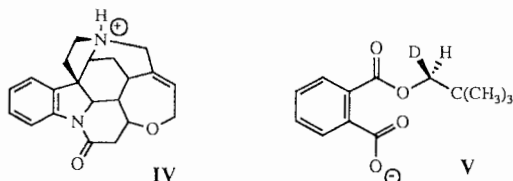


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Neutron diffraction analysis of the strychnine salt (IV) of (+)neopentyl-phthalate-1-*d* (V) then showed that the absolute configuration of the CHD group of V is *S*.<sup>3</sup>



This pair of neutron diffraction analyses shows that (+)-ethanol-1-*d* (II) and (+)-neopentanol-1-*d* (III), prepared by complementary methods (Schemes 1 and 2, respectively), have opposite absolute configurations (*R* and *S*, respectively), as predicted,<sup>4</sup> despite the fact that their ORD rotations are of the same sign (+), in both cases.<sup>5</sup> This work shows unequivocally that alcohol dehydrogenase delivers hydrogen atoms to the *re* face of an aldehyde, and also confirms suspicions<sup>4</sup> that the optical rotatory properties of ethanol-1-*d* is different than those of its higher homologs.

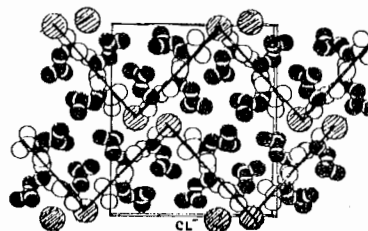
(+)(*R*)-Ethyl-1-*d* (-)(1*S*)-camphanate (I) crystallizes in the orthorhombic space group  $P2_12_12_1$ , with  $a = 6.422(1)$ ,  $b = 21.004(4)$ ,  $c = 9.275(2)$  Å. Neutron data were collected at room temperature on a sample with dimensions  $2.2 \times 3.7 \times 2.4$  mm<sup>3</sup> at the Brookhaven High Flux Beam Reactor. The structure was refined to final agreement factors of  $R(F^2) = 0.083$  and  $R(wF^2) = 0.075$  for 1093 reflections with  $F_o^2 > 1\sigma(F_o^2)$ .

- (1) (a) H. Guenther, F. Biller, M. Kellner and H. Simon, *Angew. Chem. Internat. Edit.*, 12, 146-147 (1973)
- (b) H. S. Mosher and C. W. Mosher, *Ind. J. Chem.*, 31, 900 (1992)
- (2) W. Klyne and J. Buckingham, *Atlas of Stereochemistry*, 2nd. ed., Oxford University Press, London, Vol. 1, page 85 (1978).
- (3) (a) Hanna S. H. Yuan, Ph. D. Dissertation, Univ. of Southern Calif. (1989)
- (b) H.S.H. Yuan, R.C. Stevens, R. Bau and H.S. Mosher, manuscript in prep.
- (4) C. Fisher, E. Morse, B. Romer, T. P. You, C. W. Mosher and H. S. Mosher, *Tetrahedron*, 48, 2993-3000 (1992)
- (5) A. Gedanken, C. W. Mosher and H. S. Mosher, *Chem. Commun.*, 430 (1992)

**OPS-04.01.10 PEPTIDE MODELS FOR UNDERSTANDING PACKING INTERACTIONS IN THE INTERIOR OF GLOBULAR PROTEINS: CRYSTAL STRUCTURE OF LEUCYL-LEUCYL-LEUCINE HCL.** By E. Subramanian, S.S.Rajan and V.Jayashree, Department of Crystallography and Biophysics, University of Madras, Madras 600 025, INDIA.

The interior of globular proteins is characterized by tightly packed sidechains of hydrophobic residues. Prediction of protein folding requires an understanding of the patterns of packing of these sidechains. As a starting model for prediction, one can use the geometry of packing interactions as observed in the crystal structures of small peptides containing hydrophobic residues. A study of the pairwise interactions of the 20 different residues, as observed in the interior of several proteins whose crystal structures are known, reveals that leu...leu interactions are the most frequent. To understand the pattern of leu...leu interactions, the peptide leucyl-leucyl-leucine HCl has been crystallised. The crystals are orthorhombic, space group  $P2_12_12_1$ , with  $a=5.174(2)$ ,  $b=19.371(3)$ ,  $c=22.976(3)$  Å and  $Z=4$ .  $CuK\alpha$  diffractometer data ( $\theta \leq 60^\circ$ ) were used to solve the structure by direct methods, and to refine it to an *R*-index of 0.08. The  $C^\delta$  atoms in all the sidechains display high thermal motion. The peptide units are *trans*. The peptide backbone assumes an extended parallel beta sheet conformation, with  $\Psi_1=128$ ,  $\omega_1=171$ ,  $(\phi_2, \Psi_2)=(-119,133)$ ,  $\omega_2=179$ ,  $(\phi_3, \Psi_3)=(-85, 170)$ . The three leucyl sidechains adopt the commonly observed and energetically favourable conformations (*t*<sub>g</sub><sup>+</sup>), (*g*<sup>+</sup>, *t*) and (*g*<sup>+</sup>, *t*) respectively.

Crystal packing involves successive peptide molecules, related by the *a*-translation of the lattice, forming an infinitely extended ribbon of parallel beta pleated sheet structure, with one inter-chain hydrogen bond of length 3.05 Å between backbone amide and carbonyl groups. The leucyl sidechains stick out on both sides of the sheet. Symmetry-related molecules also lie in similar ribbons, and all such sheets are linked by 'hinges' formed of hydrogen bonds between  $Cl^-$  ions on the one hand and  $NH_3^+$  and  $-COOH$  terminals of the peptide molecules on the other. The net result is to produce a zig-zag 'head-to-tail' link up of the peptide molecules, effectively creating a super-pleated-sheet arrangement. The packing of such super-pleated sheets introduces a novel way of segregating the hydrophobic groups. The layers of polar groups are arranged in a zig-zag pleated fashion, reminiscent of 'corrugated' sheet structures. The polar 'ridges' in the 'corrugated' sheets face the polar 'grooves' of neighbouring sheets and vice versa. All the hydrophobic leucyl sidechains are effectively confined to the gaps between the corrugated sheets. Details of sidechain interactions will be presented.



**PS-04.01.11 THE EFFECTS OF METAL-BINDING ON A NUCLEOBASE: A COMPARISON OF CHARGE DENSITY IN ADENINE HYDROCHLORIDE AND ITS ZINC COMPLEX.** By L.M. Cunane and M.R. Taylor\*, School of Physical Sciences, The Flinders University of South Australia, GPO Box 2100, Adelaide, S.A., 5001, Australia.

This study of charge density and electrostatic properties in adeninium hydrochloride hemi-hydrate and  $1H^+$ -adeniniumtrichlorozinc(II) is part of a broader investigation into the effects of substituents, protonation and bound metal ions on electron density distributions in some nucleobase derivatives.

High-resolution X-ray data sets to  $\sin\theta/\lambda = 1.32 \text{ \AA}^{-1}$  were subjected to conventional and multipole refinement. These show that there are significant differences between the dimensions of the nucleobases in the two structures. The charge density was determined from refined pseudoatom models at the octapole level. Final difference maps had minima and maxima of  $-0.16$  and  $+0.20 \text{ e \AA}^{-3}$  for the hydrochloride and  $-0.29$  and  $+0.38 \text{ e \AA}^{-3}$  for the zinc complex.

Deformation density maps have been calculated, and details of the electron density distributions in the bonds have been deduced. Net atomic charges from the multipole refinements have reasonable values with N1, C4, C5 and C8 being more positive in the zinc complex than in the hydrochloride indicating the net withdrawal of electron density from the complexed nucleobase. In both compounds, C8 has a significant negative charge and the C8-H8 bond is the most polar of the C-H bonds in line with the acidic nature of this proton.

The electrostatic potential of the molecules, isolated from the crystal structure, have also been mapped. The lines of positive equipotential are much more compact in the hydrochloride, compared with its zinc complex, where the positive potential extends well out from the molecule. As a consequence the protons of the complexed nucleobase are shown to be more acidic than those of the uncomplexed one. The increased positive electrostatic potential for the nucleobase bound to zinc will enhance base-base hydrogen bonding.