03.3-23 THE STRUCTURAL ASPECTS OF RESOLUTION WITH TARTARIC ACID. By K. Simon, E. Ecssery and J. Rohonczy, Chinoin Research Center P.O. Box 110, H-1325 Budapest, Hungary, and E. Fogassy, M. Ecsery and J. Rohonczy, Chinoin Research Center P.O. 43-24 CRYSTAL Organic Chemical Technology, Technical University, H-1521 Budapest, Hungary.

In the course of the synthesis of the anti-parkinsonic agent (-)-Selegiline.HCl (JUNEX®), (-)-methamphetamine is resolved with (+)-tartaric acid from aqueous HCl. After recrystallization from water the structures of the less soluble salt, (-)-methamphetamine(+)-bitartrate.2H2O, (-), a =10.15(1), b =7.047(2), c=12.312(2) Å, b =110.42(2), p2, z=2, R=0.027 and of the more soluble salt, (+)-methamphetamine(-)-bitartrate, (+), a=14.377(2), b=6.854(1), c=7.826(1) Å, s=93.90(2), p2, z=2, R=0.037 were determined by X-ray analysis. The conformation of the ions in the two salts is identical with N-C=C-C-C (cation) and C=C-C-C-C (anion) in anti-periplanar position.

The hydrogen bonding system is, however, different with 11 hydrogen bonds in (-) and only 6 in (+). In the former case O-hydroxy...H,N type hydrogen bonds and closed hydroxogen bond rings, while no such bonds were observed in the latter case.

In all cases in the crystal structures of bitartrate salts (12 structures, Cambridge Crystallographic Data Base, Jan., 1984), the dimension of one well defined direction is determined by the bitartrate...bitartrate periodicity (7.05-7.83 Å) held together by the strongest hydrogen bond (O...H 2.49-2.63 Å). The structures can be grouped in two classes: A one screw axis is parallel, while in B no screw axis is parallel with the bitartrate chain.


The synthesis of 2,4-disubstituted 2-furazanols via the ring opening of glycidic esters by benzamidin (Marsura et al., 8th I.C.H.C., 1981), surprisingly afforded a complex of 4-oxymethylene carbonyl, 2,4-disopropyl, 5,5-dimethyl, 1,3-dioxan with one molecule of benzamidin.

The structure of this complex was partially elucidated by 1H, 13C N.M.R. 1.A. and Mass spectra. The complete assignment was achieved by X-ray data: the tittle compound is monoclinic, space group P21/a, a =11.253(3), b =9.880(2) c =19.183(4) and S =100.62(2) at 120 K with S =4; its crystal structure was determined by application of Multiple programs (Germain et al., 1971) and refined to R =2.8 % for 2889 reflections.

The molecule has a chair conformation and shows that the methylene carbonyl and isopropyl groups are in equatorial positions (ClS, configurations). The acid function was likely in interaction with the amidin group by hydrogens bonds.

03.3-25 CRYSTAL AND MOLECULAR STRUCTURE OF 2,4-DICHLOROBENZOSUBERENONE. By J. Huis and C. Miravitlles, Ins. Med. Bio, Univ. de Barcelona, Spain.

The investigation of the crystal structure of 2,4-dichlorobenzosuberone was taken as a part of a study of dibenzo-(a,d)-cicloheptane compounds with potentially antifungal activity and for providing basic structural data to better understand the influence of the stereochemistry on their biological activity.

This compound (C1501C12H8) crystallizes in the triclinic space group P1 with a =8.184(2), b =9.570(2), c =8.872(2) a =102.08(2), B =100.46(2), y =97.83(2), y =99.65(2), Z =2. The crystal structure was solved using direct methods (MOLTAN 11/82) and was refined by least-squares to an R value of 5.7% for 808 unique observed reflections.

The seven-membered ring shows a boat conformation with the origin at the prow. The normals to the planes of the two benzene rings make an angle of 35.7(6)° with each other. No intermolecular hydrogen bonds could be detected.

03.4-1 X-RAY CRYSTALLOGRAPHIC STUDIES ON THE BINDING OF TWO DI-PHENYLETHANEDIOXYL DERIVATIVES TO DEOXY-HAEMOGLOBIN. By A.J. Geddles, F.K.R. Rah and A.C.T. North, Astbury Dept. of Biophysics, University of Leeds, Leeds LS2 9JT, Great Britain.

Several diphenylethanedialdehyde (DIPEDAL) derivatives have been designed by the Wellcome Laboratories to bind specifically to the DPG binding site in deoxy-haemoglobin and their potency has been demonstrated (Beddell, Br. J.Pharmac. (1976) 57, 201). A difference Fourier analysis at 5.5 Å resolution has now been completed to establish the exact mode of binding for a bisulphite derivative (I) and an oxycetic acid derivative (II) of DIPEDAL.

Crystals of the protein/diuretic complexes were obtained by co-crystallisation from PEG 6000 in the presence of a 10-fold excess of compound 1 or II. All crystals were isomorphous with those described by Ward et al. (J.Nat. Biol. (1975) 96, 161). Difference maps were calculated by using observed structure factor moduli from diffractometer data and calculated phases from a high resolution structure (Brzozowski, Nature (1984) 307, 74).

The two highest features in the difference map for compound I are situated near the B-termini at the entrance to the central cavity indicating that the drug crosses the B-chains as predicted. The B-terminal microns and the sidechains of His 2 and Lys 82 can be coordinated to the peaks although the participation of His 143 is doubtful.

The binding of compound II could be demonstrated less clearly, although the DPG binding site is filled with positive electron density. Two modes of binding can be proposed, one as predicted crosslinking the B-terminus, the second one covalently linking of one B-chain to the sidechain of Lys 82 of the other subunit.