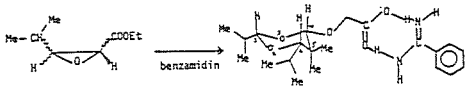
**03. 3–23** THE STRUCTURAL ASPECTS OF RESOLUTION WITH TARTARIC ACID. By K. Simon, Z. Ecsery and J. Rohonczy, Chinoin Research Center P.O. Box 110, H-1325 Budapest, Hungary, and E. Fogassy, M. Acs and F. Faigl, Department of Organic Chemical Technology, Technical University, H-1521 Budapest, Hungary.

In the course of the synthesis of the anti-parkinsonic agent (-)-Selegiline.HCl (JUMEX$^{R}$), (±)-methamphetamine is resolved with (+)-tartaric acid from aqueous HCl. After recrystallization from water the structures of the less soluble salt, (-)-methamphetamine-(+)-bitartrate.2H$_2$O, (-+), (a=10.351(1), b=7.047(2), c=12.352(1) Å, β=110.45(2)°, P2$_1$, 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, β=93.90(2)°, P2$_1$, 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 (cation) and 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(hydroxyl)...N$^{+}$ type hydrogen bonds and closed hydrogen 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 cell 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.

**03. 3–24** CRYSTAL AND MOLECULAR STRUCTURE OF A NEW COMPLEX : 4-OXYMETHYLENE-CARBONYLYL-2,6-DIISOPROPYL-5, 5-DIMETHYL-1,3-DIOXAN/BENZAMIDINE. By Y. Le Page and D. Tran Qui, Laboratoire de Cristallographie, C.N.R.S., associé à l'U.S.M.G., 166 X, 38042 Grenoble Cedex, France. A. Marsura, C. Luu-Duc, G. Gellon, U.E.R. de Pharmacie de Grenoble, Groupe Pharmacochimie (Equipe de Recherche B ), 38700 La Tronche, France. C. Gey, C.E.R.M.A.V., C.N.R.S., 38041 Saint Martin d'Hères, France.

The synthesis of 2,4-disubstituted 2-imidazolin-5ones 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 carboxylyl, 2,6-diisopropyl, 5,5-dimethyl, 1,3-dioxan with one molecule of benzamidin.




The structure of this complex was partially elucidated by $^{13}C$, $^{1}H$ N.M.R. I.R. and Mass spectra. The complete assignement was achieved by X-ray data ; the title compound is monoclinic, space group P2$_1$/a, a = 11.251(3), b = 9.880(2) c = 19.153(4) and β = 100.62(2) at 120 K with Z = 4 ; its crystal structure was determined by application of Multan programme (Germain et al., 1971) and refined to Rw = 2,8 % for 2889 reflections.

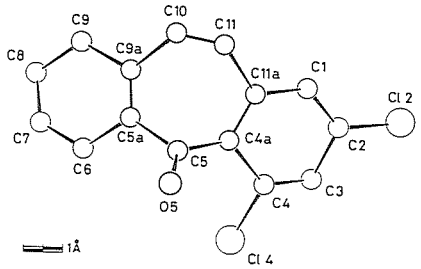
The molecule has a chair conformation and shows that the methylene carboxylyl and isopropyl groups are in equatorial positions (Cis, configurations). The acid function was likely in interaction with the amidin group by hydrogens bonds.

**03. 3–25** CRYSTAL AND MOLECULAR STRUCTURE OF 2,4-DICHLOROBENZOSUBERENONE. By J. Rius and C. Miravitlles, Inst. Nac. Seg. e Higiene en el Trabajo and Inst. "Jaime Almera" C.S.I.C. c/. Alcarria, s/n. Aptdo. Correos 30102, Barcelona, Spain.

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

This compound ($C_{15}O_1Cl_2H_8$) cristallizes in the triclinic space group P$\bar{1}$ with a= 8.194(2), b= 8.570(2),c= 8.972(2) α= 102.08(2), β= 100.45(2), γ= 97.52(3)°, V= 596.5Å$^3$, Z=2. The crystal structure was solved using direct methods (MULTAN 11|82) and was refined by least-squares to an R value of 5,7% for 898 unique observed reflections.

The seven-membered ring shows a boat conformation with the origen 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 DIPHENYLETHANEDIALDEHYDE DERIVATIVES TO DEOXY-HAEMOGLOBIN. By A.J.Geddes, F.Körber 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 5.5Å resolution has now been completed to establish the exact mode of binding for a bisulfite derivative (I) and an oxyacetic acid derivative (II) of DIPEDAL.

Crystals of the protein/drug complexes were obtained by co-crystallisation from PEG 6000 in the presence of a 5-fold excess of compound I or II. All crystals were isomorphous with those described by Ward et al. (J.Mol. Biol. (1975) 98, 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 β-N-termini at the entrance to the central cavity indicating that the drug crosslinks the β-chains as predicted. The N-terminal nitrogens 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 β-N-termini, the second one covalently linking the N-terminus of one β-chain to the sidechain of Lys 82 of the other subunit.