03.3.23 THE STRUCTURAL ASPECTS OF RESOLUTION WITH TARTARIC ACID. By E. Simon, S. Ecsery and J. Rohonczy, Chinoin Research Center, P.O. Box 110, H-1325 Budapest, Hungary, and E. Pogasy, M. Acz and F. Falgi, Department of Organic Technology, Technical University, H-1521 Budapest, Hungary.

In the course of the synthesis of the anti-

glykinic agent (-)-Selegline HCl (JUSEM X ,)

(+)-methamphetamine is resolved with (+)-tar-

taric acid from aqueous HCl. After recrys-

tallization from water the structures of the less

soluble salt, (-)-methamphetamine (+)-bitar-

trate, Zn.HO, (-), a=10.15[1](1), b=9.071(2),
c=12.352(1) A, Z=2, R=0.027, and of the more soluble salt, (+)-methamphetamine (+)-bitartrate, (+), a=14.377(2), b=9.765(1) A, Z=93.90(2), P21, Z=2, R=0.037 were determined by X-ray analy-

sis. The conformations 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, dif-

ferent with 11 hydrogen bonds in (-+) and only 6 in (+-). In the former case O(hydrox-

yl)....H type hydrogen bonds and closed hydro-

gen bond rings, while no such bonds were ob-

served in the latter case. In all cases in the crystal structures of bitartrate salts (12 structures, Cambridge Crystallographic Data Base, Jan., 1984), the seven-membered ring is parallel with the bitartrate chain. The axis is parallel, while in B no screw

axis is parallel.

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.

The molecule has a chair conformation and shows that the seven-membered ring can be proposed, one as predicted crosslinking the beta-termini at the entrance to the central cavity indicating that the drug crosslinks the beta-chains as predicted. The beta-terminal microgends 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 beta-termini, the second one covalently linking the terminus of one beta-chain to the sidechain of Lys 82 of the other subunit.


The investigation of the crystal structure of 2,4-Dichloro-

benzosuberone was taken as a part of a study of diben-

zo(a,d)-cycloheptane compounds with potentially antifun-

gicide 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= 8.194(2), b= 9.570(2), c= 9.872(2) A, a= 103.08(2), b= 100.04(2), + = 97.96(3)°, V= 656.5A³, Z=2. The crystal structure was solved using direct metho-

ds (MOLean 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.

The synthesis of 2,4-disubstituted 2,3-diaminol-zones via the ring opening of glycidic esters by benzanilid (Masera et al., 8th I.C.N.C, 1981) surprisingly afforded a com-

plex of 4-oxymethylene carboxyl, 2,6-diisopropyl, 5,5-

dimethyl, 1,3-dioxan with one molecule of benzanilid.

The structure of this complex was partially elucidated by 1H, 13C H.M.R. I.A. and Mass spectra. The complete assi-

gnment was achieved by X-ray data; the ticle compound is noncrinic, space group P21/a, a= 11.251(3), b= 9.880(2) c= 19.139(4) and V= 200.82(2) A at 120 K with Tr, a= 4; its conformation was determined by a program of Mullan

programmes (Garman et al., 1971) and refined to Rw = 2.8 ± 2889 reflections.

The molecule has a chair conformation and shows that the

methylene carboxyl and isopropyl groups are in equato-

rial positions (C1s, configurations). The acid function was likely in interaction with the amion group by hydro-

gens bonds.

03.4-1 X-RAY CRYSTALLOGRAPHIC STUDIES ON THE BIND-

ING OF THE DIPHENYLMETHANEDIALDEHYDE DERIVATIVES TO

Several diphenylethanedialdehyde (DIPEDAL) derivatives have been designed by the Welcombe Laboratories to bind specifically to the DPG binding site in deoxy-haemoglobin and their poteney has been demonstrated (Beddell, Br J Pharmac (1976) 57, 201). A difference Fourier analysis at 5.5A resolution has now been completed to establish the exact mode of binding for a bisulfite derivative (I) and an oxoacetic 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) 95, 161). Difference maps were calculated by using observed structure factor moduli from diffractometer data and calculated phases from a high resolution structure (Brazovszki, Nature (1984) 307, 74). The two highest features in the difference map for compound I are situated near the 8-N-termini at the other subunit.