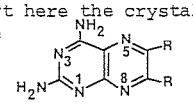
03.3-05 CRYSTAL STRUCTURES OF TWO PTERIDINES WITH DIURETIC AND ANTIFOLATE ACTIVITY. By C.H. Schwalbe and G.J.B. Williams, Department of Pharmacy, University of Aston, Birmingham B4 7ET, England, and Department of Chemistry, Brookhaven National Laboratory, Upton, N.Y. 11973, U.S.A.

Clinically valuable diuretics such as triamterene and antifolates such as amethopterin both contain the 2,4-diaminopteridine moiety. We report here the crystal structures of 2,4-diaminopteridine monohydrate (I) and a protonated derivative, 2,4-diamino-6,7-dimethylpteridine hydrochloride monohydrate (II), which themselves are effective diuretics with some antifolate activity.



R=H,CH_3

	a	b	c(Å)	α	β	γ(°)	Z	S.G.
I	6,750	7,304	8,536	98,75	98,82	109,70	2	PĪ
II	9,455	10,835	11,840	71,36	76,48	76,01	4	PĪ

Date were collected on an Enraf-Nonius CAD4 system and refined to R=0.060 for 1308 observed reflections with I and R=0.059 for 3300 observed data with II. Corresponding bond distances and angles in the two independent molecules of II are identical within 0.006Å and 0.6°. Relative to I, the effect of protonation at N(1) of II is chiefly to lengthen the ring bonds to N(1), shorten the bridge bond and the exocyclic C-N bonds, expand the ring angle at N(1) and contract the adjacent endocyclic angles. A hydrogen-bonded water molecule acts as a proton donor near N(3) of I but as a proton acceptor near N(1) of II. Both species form hydrogen-bonded pairs about a center or pseudo-center of symmetry but use different parts of the molecule.

03.3-06 THE CRYSTAL STRUCTURES OF (S) AND (R) BACLOFEN AND CARBAMAZEPINE By Chong-Hwan Chang, Daniel S.C.Yang, Chung Soo Yoo, Bi-chen Wang, James Pletcher and Martin Sax, Department of Crystallography, University of Pittsburgh, PA 15260 and Biocrystallography Lab., VA Medical Center, Pittsburgh, PA 15240

The crystal structures of the three title compound have been determined. All of the three are used as a muscle relaxant for the relief of spasticity with varying degrees of activity. The relationship between the drug activity and three-dimensional structure among these three compounds has been investigated.

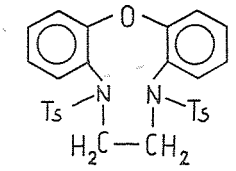
The baclofen crystals are orthorhombic, space group $P2_12_12_1$, a = 6.378(1), b = 7.319(1), c = 25.689(4) and Z = 4. The structures were determined by a combination of direct methods and Fourier techniques yielding final R factor of 2.9% for the S form and 4.0% for the R form. The absolute configurations were determined using anomalous scattering techniques. The side chain assumes a gauche conformation with respect to the C3 - C4 bond.

The carbamazepine crystal is triclinic, space group PĪ, a = 9.001(3), b = 7.441(2), c = 13.755(3), α = 119.48(2), β = 78.96(2), γ = 101.61(2) and Z = 2. The structure was solved by MULTAN and the R factor is 5.4% at this stage. The angle between the benzene rings is 126°. There is good three-dimensional overlap between the carbamazepine and baclofen(R,S).

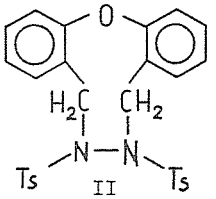
03.3-07 CRYSTAL STUDIES OF DIBENZOOXADIAZANINE DERIVATIVES. A. Stępień, E. Wajsman, Dept. of Crystallography, Institute of Chemistry, University of Łódź, Nowotki 18, 91-416 Łódź, Poland, and R. Glinka, Institute of Chemistry and Technology of Drugs, School of Medicine, 90-145 Łódź, Poland.

Pharmacological investigations of the family of compounds given in the title have shown their action on the central nervous system and especially their neuroleptic action. The strongest pharmacological action is shown by N,N'-ditosyl and N,N'-ditrimethoxybenzoyl derivatives.

Two compounds have been investigated:



I



II

Space groups are: Pbcn (Z=4) for (I), PĪ for (II). Molecules of (I) occupy 2-fold axes.

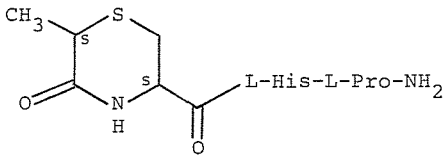
The nine-membered rings of both compounds have the twist-crown conformation.

Tosyl groups in (I) are axial while in (II) one of them is axial, the other equatorial.

The phenyl rings of the tosyl groups in (I) are nearly coplanar to the phenyl rings of dibenzo-oxadiazanine. This causes an intramolecular charge-transfer interaction.

03.3-08 THE CRYSTAL AND MOLECULAR STRUCTURE OF (3S, 6S)-6-METHYL-5-OXO-THIOMORPHOLIN-3-CARBONYL-L-HIS-L-PRO-NH_2. By Emil Eckle and John J. Stezowski, Institut für Organische Chemie, Biochemie und Isotopenforschung der Universität Stuttgart, Pfaffenwaldring 55, D-7000 Stuttgart 80, Federal Republic of Germany.

The crystal structure determination of the title compound, I, presents a continuation of our study of the conformational properties of TRH analogs. In addition



I

to its thyrotropin releasing activity, TRH is also a central nervous system (CNS) stimulant. I displays much greater CNS activity than TRH but only about 20% of that of its 6-epimer, II for which we reported a crystal structure earlier (Stezowski, J. J. and Eckle, E. (1980) Abstracts, 6th European Crystallography Meeting, 275).

I crystallizes as a tetrahydrate with space group symmetry $P2_12_12_1$: a = 8.510(1)A, b = 11.507(1) and c = 23.739(3) (at ~120K); Z = 4. A total of 4656 data contributed to the refinement of 417 variables to give R = 0.043, R_w = 0.049 and sigma = 1.12.

A quantitative comparison of the conformation of I and II will be presented.