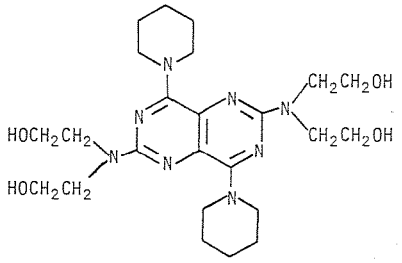
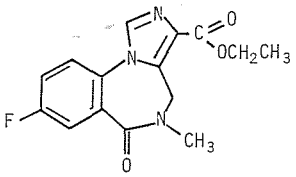
the side chains; the torsion angles vary by 5-10° in the hydroxyethyl groups. The molecular inversion center is approximately conserved.



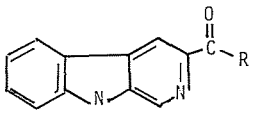
This work was supported by the Alberta Heritage Foundation for Medical Research and the Medical Research Council of Canada (grant MA-8087 to PWC).

of the orientations of the side chains.

A potential antagonist binding site that is consistent with binding data from rat cerebral cortex has been identified by superpositions of RO15-1788, MeBCC, and NCBC. This model superimposes the six membered aromatic rings, the ester and amide side chains and an aromatic nitrogen atom. This binding site model may be interpreted either as evidence of multiple receptor sites or of a dynamic receptor. RO15-1788: $P4_2/n$, a = b = 19.395(5)Å, c = 7.172(3)Å, Z = 8
MeBCC: $P2_1/c$, a = 11.4866(9), b = 5.8091(3), c = 32.147(3)Å, β = 97.111(3)°, Z = 8
NCBC: C2/c, a = 16.220(4), b = 7.728(2), c = 19.623(6)Å, β = 104.16(1)°, Z = 8



RO15-1788



MeBCC R = OCH_3
NCBC R = $NHCH_2CH_3$

This work was supported by the Alberta Heritage Foundation for Medical Research and the Medical Research Council of Canada (grant MA-8087 to PWC).

03.1–5 STRUCTURAL STUDIES OF BENZODIAZEPINE ANTAGONISTS. Alastair K.S. Muir and Penelope W. Codding, Departments of Chemistry and of Pharmacology and Therapeutics, University of Calgary, Calgary, Alberta, T2N 1N4, Canada.

A natural receptor for benzodiazepine anti-anxiety drugs like diazepam has been identified in the brain. The endogenous ligand for this receptor and its pharmacological function are being sought. Several derivatives of β-carboline have been found to have the highest affinity of the endogenous compounds; however, the actual formulation of the natural β-carboline has not been found. Some of the high affinity β-carbolines are antagonists of the action of benzodiazepines and are thus anxiety-producing compounds. These findings suggest that the natural function of the benzodiazepine receptor may be to mediate alertness and related attributes. Several compounds that are antagonists at this receptor have been studied to develop a model for the binding of antagonists to the benzodiazepine receptor.

The structures of one benzodiazepine, ethyl-8-fluoro-5,6-dihydro-5-methyl-6-oxo-4H-imidazo[1,5a][1,4]benzodiazepine-3-carboxylate (RO15-1788), and two β-carboline, methyl β-carboline-3-carboxylate (MeBCC) and N-ethyl-3-carbamyl-β-carboline (NCBC), antagonists were determined. A comparison of the antagonist benzodiazepine to an agonist, oxazepam (Gilli, Bertolasi, Sacerdoti, and Borea, Acta Crystallogr. (1978), B34, 2826), indicates that the 1,2 annelation induces only small changes in the conformation of the azepine ring. Thus the difference in activity must be due to the relative numbers of bonding groups and their electronic character.

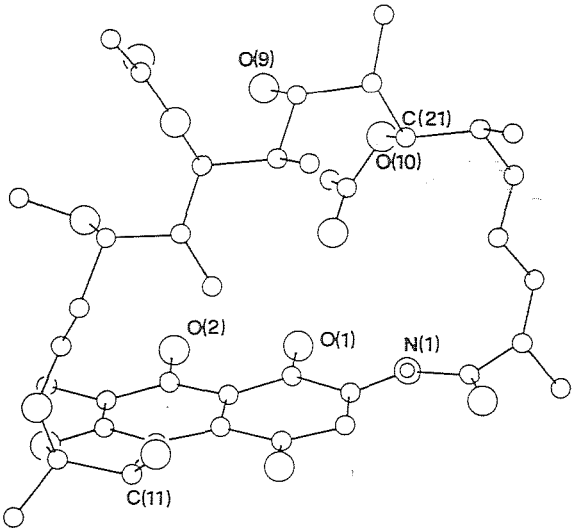
In each of the three antagonists the ester or amide side chain is coplanar with the ring of attachment. The formation of hydrogen bonds is an important determinant

03.1–6 THE CRYSTAL AND MOLECULAR STRUCTURE OF 21-ACETOXY-11-(*R*)-RIFAMYCINOL S.

By M.Brufani, L.Cellai, S.Cerrini, D.Lamba and A.Segre. Istituto di Strutturistica Chimica "G. Giacomello" – C.N.R. Rome, ITALY.

Rifamycins are a class of natural and semisynthetic antibiotics belonging to the family of naphthalenic ansamycins. They specifically inhibit bacterial DNA-dependent RNA polymerase (M.Brufani, The Ansamycins. Topics in Antibiotic Chemistry. Ed. P.G.Sammes, Ellis Horwood Ltd., Chichester (1977) 1, 91). The basic requirement for the biological activity of these molecules (M.Brufani, S.Cerrini, W.Fedeli and A.Vaciago, J.Mol. Biol. (1974) 87, 409) is a proper spatial relationship of the four oxygen atoms O(1), O(2), O(9), O(10). They act as acceptors and/or donors of hydrogen bond in the complex with the enzyme.
Recently a comparative study of the conformation of rifamycins in solution and in the solid state has been accomplished (L.Cellai, S.Cerrini, A.Segre, M.Brufani, W.Fedeli and A.Vaciago, J.Org.Chem. (1982) 47, 2652). It is there pointed out that, in the two states, the conformation of the molecule experiences only minor changes, which do not affect the structural features responsible for the biological activity. The crystal structure of the 21-acetoxy-11-(*R*)rifamycinol S has been determined in order to investigate the factors affecting and stabilyzing the conformation of the aliphatic ansa-chain of these molecules.

Crystal Data: S.G. P 2_1, a=11.860, b=9.139, c=20.423 Å, β=90.72° ,$C_{39}H_{49}NO_{13}.CH_3OH.H_2O$, F.W.=789.85, Dc=1.20 g.cm^{-3} for Z=2; Mo-K_α radiation.



In spite of the chemical substitution on position 21 of the ansa-chain and the reduction on position 11 of the chromophore rings, the conformation of the molecule is comparable with that of the other rifamycins. Further conformational and structural features will be discussed.

03.1–7 CAN THE CLATHRATES OF BINAPHTYL-DICARBOXYLIC ACID SERVE AS STRUCTURAL MODELS FOR THE RELATIONS IN THE ACTIVE SITE OF NATIVE SERINE PROTEASES?

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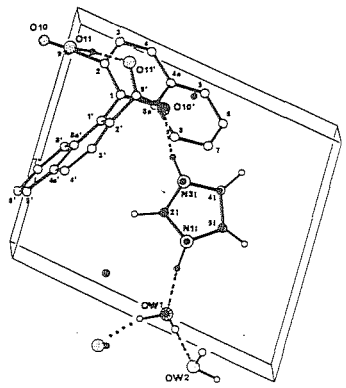
E. Weber, *Institut für Organische Chemie und Biochemie der Universität Bonn, Gerhard-Domagk-Str. 1., D – 5300 BONN 1, BRD*

THE USE OF INCLUSION COMPOUNDS AS MODEL ENZYMES IS A RECOGNIZED APPROACH IN BIOORGANIC CHEMISTRY (Dugas,H., Penney,C. *Bioorganic Chemistry*, Springer, 1981). 1,1'-BINAPHTYL-2,2'-DICARBOXYLIC ACID (*BNDA*) HAS BEEN SHOWN TO ACT AS A VERSATILE COORDINATO-CLATHRATE HOST (Weber, *press*). THEREFORE WE ATTEMPTED TO GET COMPLEXES OF *BNDA* WITH *imidazole* BOTH IN AQUEOUS AND WATER-FREE MEDIA. THE STRUCTURE OF THE CRYSTALS OBTAINED FROM AN AQUEOUS SOLUTION (*Figure*) SHOWED SIMILARITY BOTH IN FORMAL STOICHIOMETRY (*BNDA:imidazole:2H$_2$O*) AND SPATIAL ARRANGEMENT (Δ-0.3 Å FOR SEVEN FITTED ATOMS) OF THE FUNCTIONS CORRESPONDING TO *Asp102, His57 and 2 internal water* FOUND IN THE NATIVE CRYSTALS OF *SGPA* (James,M.N.G., Sielecki,A., 1983, *Private communication*). A FURTHER POINT OF THIS STUDY IS ALSO ILLUSTRATED IN THE *Figure*, WHICH SHOWS THAT A PROTON IS TRANSFERRED FROM THE *-COOH* MIMICKING THE ROLE OF *Asp102* TO THE IMIDAZOLE RING IMITATING *His57* IN THE PROTEIN. THE WHOLE PROCESS SEEMS TO BE ATTENUATED BY THE PRESENCE OF THE WATER MOLECULES WHICH FORM CHAINS OF HYDROGEN BONDS TO DIFFERENTLY CHARGED MOIETIES THUS RENDERING FURTHER (ELECTROSTATIC) RESEMBLANCE TO THE SITUATION FOUND IN MANY SERINE PROTEASES (Kossiakoff,A.A., Spencer,S.A., 1981, *Biochemistry*, 20, 6462-6474.



Csöregh, Stensland, Czugler, *J.Amer.Chem.Soc., in the*

Crystal data: Form (I) $C_{22}H_{13}O_4^-.C_3H_5N_2^+.2H_2O$, triclinic $P\bar{1}$, Z = 2, R = 0.028 for 1975 obs. data

Form (II) $C_{22}H_{14}O_4.C_3H_4N_2$, monoclinic $P2_1/c$, Z = 4, R = 0.096 for 924 obs. data.

03.1–8 THE CRYSTAL STRUCTURES OF DI- AND TRIMETHOXYLATED 1,4-PHENANTHRENE QUINONES WITH DIFFERENT ALLERGENIC POTENCY.

By H.W. Schmalle and O.H. Jarchow, Mineralogisch-Petrographisches Institut der Universität, Grindelallee 48, 2000 Hamburg 13, FRG; B.M. Hausen, R. Werdin and K.H. Schulz, Abt. Allergologie der Universitäts-Hautklinik UKE, Martinistraße 52, 2000 Hamburg 20, FRG; and K. Krohn and U. Look, Institut für Organische Chemie der Technischen Universität, Schleinitzstraße, 3300 Braunschweig, FRG.

The first naturally occurring 1,4-phenanthrene quinone (PQ) with sensitizing potency, separated from the orchid Cypripedium calceolus L., has been identified by X-ray analysis and named cypripedin (2,8-Dimethoxy-7-hydroxy-1,4-PQ). Its two independent molecules showed slightly different conformations in the crystalline state (Schmalle & Hausen, Nat. Wiss. (1979) 66, 527). In order to study their sensitizing properties and cross-reactivities, a series of 12 cypripedin related PQs have been synthesized and used for sensitizing experiments in guinea pigs. As it was not possible to identify the position of one methoxy group in the quinonoid ring system by spectroscopic methods, X-ray structure determination has been performed for three PQs:

3,7,8-Trimethoxy-1,4-PQ (I)
3,5,8- " " (II)
3,8-Dimethoxy- " (III).
5,8- " -10-hydroxy-1,4-PQ (IV) was identified as a by-product of the quinone synthesis. All synthetic PQs are strong sensitizers if not being substituted in the C(2) and C(3) position of the quinonoid ring.The