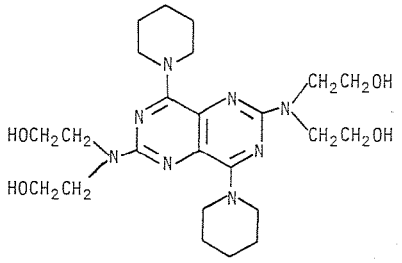
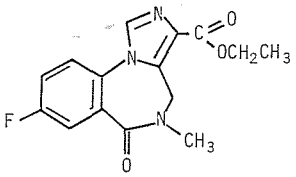
the side chains; the torsion angles vary by 5-10° in the hydroxyethyl groups. The molecular inversion center is approximately conserved.



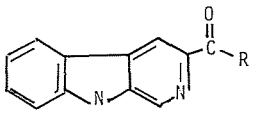
This work was supported by the Alberta Heritage Foundation for Medical Research and the Medical Research Council of Canada (grant MA-8087 to PWC).

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.