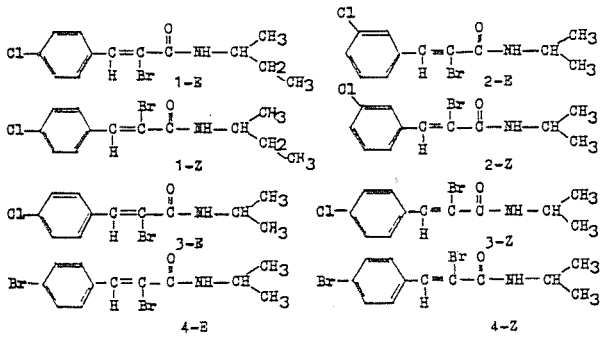
03.1-3 STUDY ON STRUCTURE-ACTIVITY RELATIONSHIP FOR SOME ISOMERS OF CINNAMAMIDES. By Xu Xiaojie, Guan Yue, Tang Youqi, Department of Chemistry, Peking University, and Wang Shuyu College of Pharmacology, Beijing Medical University, Beijing, China.

Since it was found from a folk recipe medicine by Beijing Medical University that Cinnamamides have antiepileptic activity, nearly 200 of them have been synthesized. The differences in anticonvulsant activities of isomers evoked by the differences in their configurations have been especially noticed. Dozens of isomeric compounds of cinnamamides have been synthesized recently. Four pairs of isomers were subjected to structural determination. Six crystal structures were determined by X-ray analysis and the other two derived indirectly from the known structures of their respective isomers.



Chemical structures of the four isomeric pairs

The selected structural parameters are listed in the following table:

No	Crystal Data a(Å)	b(Å)	c(Å)	β(°)	Space Group	Phenyl -O (Å)	Phenyl -N (Å)
1-E	9.675(5)	11.887(8)	13.132(9)	110.3	$P2_1/a$	4.85	4.10
2-E	9.847(4)	5.627(3)	23.715(13)	100.90	$P2_1/a$	6.24	5.77
2-Z	8.975(1)	9.527(2)	31.778(5)	90.0	Pbca	4.85	4.12
3-E	10.263(4)	15.942(9)	17.092(13)	90.0	$P2_12_12_1$	5.61	6.32
3-Z	15.898(9)	5.022(2)	18.055(10)	99.6	$P2_1/a$	4.98	4.27
4-Z	9.685(9)	12.047(11)	13.245(10)	110.76	$P2_1$	4.87	4.06

Using DPCILO and OPEC programs we performed conformational analysis for 8 compounds to determine the stable conformer in the isolated state, the so-called dominant conformer. CNDO/2+EP program was used to calculate their electronic structures and molecular electrostatic fields for dominant conformers of the 8 isolated molecules. XFIT program was used to fit the 8 molecules with a reference compound and the two isomeric molecules for each pair. The common overlap steric volumes were calculated by means of the method described by Hopfinger (A.J. Hopfinger, J. Am. Chem. Soc., 1980, 102, 7196). Molar volume and free surface for each atom were calculated by OPEC program. MSA-QSAR was performed by Hansch approach. The result shows that the distances between benzene ring and N, O atoms have a bearing on the pharmacological effect and the molecular shape significantly influences the pharmacological activity. From the above results, we conclude that the benzene ring and N and O atoms may be the three important sites of the drug molecule. The distances between the three sites and the configuration involved should have certain steric compatibility with the receptor.

03.1-4 MAPPING THE β-CARBOLINE BINDING SITE ON THE BENZODIAZEPINE RECEPTOR OLIGOMER. By Penelope W. Codding and Maria B. Szkaradzinska, Departments of Chemistry and of Pharmacology and Therapeutics, University of Calgary, Calgary, Alberta, Canada and James M. Cook and Timothy J. Hagen, University of Wisconsin-Milwaukee, Milwaukee, Wisconsin, USA.

The search for an endogenous ligand for the anxiety-mediating benzodiazepine receptor identified several high affinity β-carboline alkyl esters that have either antagonist or convulsant effects. Pharmacological studies have been inconclusive regarding the recognition site for the β-carbolines; thus, it is not clear whether they bind to the same site as the anxiety-relieving benzodiazepines or to a site that allosterically affects the binding of the agonist compounds. Additionally, a full structure function profile on the β-carboline series has not been completed. In this work, we report the structures of three novel β-carbolines that bind to the receptor. The structures of these new compounds will be compared to five known structures to characterize the binding site for the β-carbolines and to compare this site to the structures of other benzodiazepine receptor ligands.

Crystal data: 3-*t*-butoxycarbonyl-β-carboline, $C_{16}H_{16}N_2O_2$, monoclinic, $P2_1/c$, a = 11.756(1), b = 11.2324(8), c = 11.964(2)Å, β = 105.99(1)°, Z = 4, R = 0.049, R_w = 0.063.

6-benzylamino-3-methoxycarbonyl-β-carboline ethylacetate solvate, $C_{20}H_{17}N_3O \cdot 0.5\ C_4H_8O_2$, triclinic, $P\bar{1}$, a = 11.052(1), b = 11.500(2), c = 16.400(2)Å, α = 69.622(9), β = 81.838(9), γ = 82.23(1)°, Z = 4, dx = 1.295 gcm^{-3}, dm = 1.29 gcm^{-3}, R = 0.063, R_w = 0.079.

6-benzylamino-β-carboline methanol hydrate, $C_{18}H_{15}N_3 \cdot 1.5\ C_2H_4O_2 \cdot 0.5\ H_2O$, triclinic, $P\bar{1}$, a = 6.1108(7), b = 18.753(2), c = 19.802(2)Å, α = 61.297(9), β = 79.30(1), γ = 83.002(9)°, Z = 4, dx = 1.265 gcm^{-3}, dm = 1.25 gcm^{-3}, R = 0.075, R_w = 0.096.