[Chem. Pharm. Bull. 27(9)2227—2228(1979)]

UDC 547.587.42.02.03 : 547.586.2.02.03

A Molecular Orbital Study on the Side Chain Structures of Tyrosine and Phenylalanine

HIDEAKI UMEYAMA and SETSUKO NAKAGAWA

School of Pharmaceutical Sciences, Kitasato University[1]

(Received March 2, 1979)

The structure of the side chains of tyrosine and phenylalanine was analyzed by *ab initio* LCAO-MO calculations. The conformation of the tyrosine side chain of glycyltyrosine, the conformations of the side chains of many tyrosine and phenylalanine residues in proteins, and the conformation of tyrosine could be explained on the basis of calculations for ethylbenzene. It is shown that the dihedral angle (C_α–C_β–C_γ–C_{δ_1}) of these molecules is determined by the exchange repulsion between the aromatic ring and the C_α–C_β bond.

Keywords——MO; molecular orbital; molecular structure; *ab initio*; protein; tyrosine; phenylalanine; conformation; rotational isomer; glycyltyrosine

Koshio *et al.* studied the conformation of the tyrosine side chain of glycyltyrosine.[2] The number of rotational isomers and their ratios were reported; three isomers (G^+, T and G^-) are shown in Fig. 1 and the dihedral angles χ_1 (N–C_α–C_β–C_γ) and χ_2 (C_α–C_β–C_γ–$C_{\delta 1}$) are given in Table I.[2] Koshio *et al.* also studied the conformations of the side chains of tyrosine and phenylalanine residues in proteins.[3] The ratios of G^+, T and G^- for 397 tyrosine and 397 phenylalanine side chains are given in Table II; the values of χ_2 are largely between 60° and 120°.[3] From an X-ray analysis of tyrosine, χ_2 for the G^- conformation is 86°.[4] The proportion of the G^- conformation may be the largest, since the aromatic

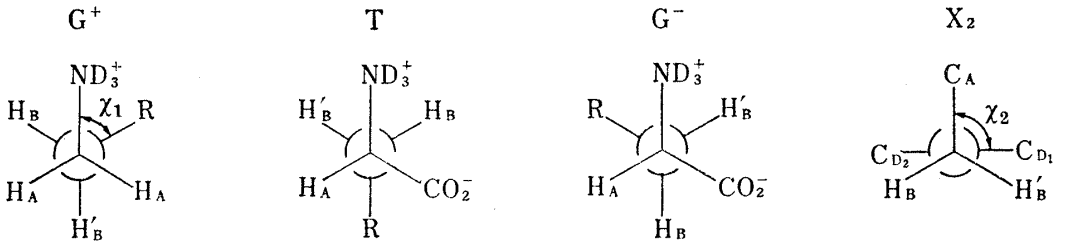

Fig. 1. Rotation Isomers of the Tyrosine Side Chain of Glycyltyrosine

TABLE I. Values of the Dihedral Angles χ_1 (N–C_α–C_β–C_γ) and χ_2 (C_α–C_β–C_γC–C_δ) in Fig. 1[2]

	χ_1 (degrees)	χ_2 (degrees)	Ratio (%)
G^+	57±34.6	96±29.2	8± 2.3
T	184±14.2	63± 9.2	24± 7
G^-	295± 5.6	90±24.4	68±18

1) Location *9-1, Shirokane 5-chome, Minato-ku, Tokyo 108, Japan.*
2) O. Koshio, F. Inagaki, M. Tasumi, and T. Miyazawa, presented in part at the 4th Annual Meeting of the Japanese Biomolecular Structure Society, Oct, 1977.
3) O. Koshio, M. Tasumi, and T. Miyazawa, presented in part at the 3th Annual Meeting of the Japanese Biomolecular Structure Society, Oct, 1976.
4) P.M. Cotrait and J.P. Bideau, *Acta Cryst.*, **B30**, 1024 (1974).

Table II. Ratios of G^+, T and G^- for Tyrosine and Phenylalanine Residues in Proteins[3]

	Tyrosine (%)	Phenylalanine (%)
G^+	11.8	12.6
T	30.5	35.0
G^-	57.7	52.4

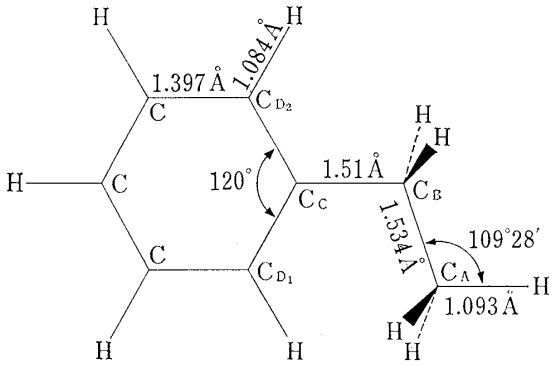

Fig. 2. Ethylbenzene Structure in which the Dihedral Angle χ_2 is Zero

Table III. Total Energies for Rotation of the Phenyl Ring in Ethylbenzene Using the STO-3G Basis Set

χ_2	Total energy (a.u.)	Difference (kcal/mol)
0°	−305.04551	4.9
30°	.04680	4.1
60°	.05197	0.9
90°	.05338	0
120°	.05197	0.9
160°	.04680	4.1
180°	.04551	4.9

group of the side chain is far from the –COO^- or –CO– group in the G^- conformation. If χ_2 is almost 90° in the G^- conformation because of the exchange repulsion between the aromatic ring and the C_α–C_β bond, χ_2 in the structure of ethylbenzene should be 90°.

Based on these considerations, *ab initio* LCAO–MO calculations using the STO-3G basis set[5] with the Gaussian 70 program[6] were carried out for the four conformations of ethylbenzene. The structure in which χ_2 is 0° is shown in Fig. 2. The results are given in Table III. The structure is most stable when χ_2 is 90°. However, when the value of χ_2 increases or decreases from 90° by 30°, the change of the total energy is only 0.9 kcal/mol, so the side chain will rotate easily by about 30°. The result for χ_2 of ethylbenzene is in good agreement with χ_2 of the G^- conformation of glycyltyrosine.[2] The finding that the structure of ethylbenzene changes freely within $60° \leqq \chi_2 \leqq 120°$ also agrees with findings for the G^- conformation of tyrosine and phenylalanine residues in many proteins.[3] Accordingly, the dihedral angle (χ_2) of the G^- conformation of tyrosine or phenylalanine in proteins or peptides is determined by the exchange repulsion between the aromatic ring and the C_α–C_β bond.

5) W.J. Hehre, R.F. Stewart, and J.A. Pople, *J. Chem. Phys.*, **54**, 724 (1971).
6) W.J. Hehre, W.A. Lathan, R. Ditchfield, M.D. Newton, and J.A. Pople, Gaussian 70 Program 236, Quantum Chemistry Program Exchange, Indiana University, 1974.