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Kinetics and mechanism of acyl transfer reactions. Part 20. Quantum-chemical study of mechanisms of dipeptides acylation reactions in the gas phase

**Ludmila B. Kochetova, Tatyana P. Kustova,*⁺ Uliana V. Troitskaya,
Ekaterina V. Vasilieva, and Marina V. Moiseeva**

Department of Fundamental and Applied Chemistry, Ivanovo State University.

Ermak St., 39, Ivanovo, 153025, Russia. Phone: +7 (84932) 37-37-03.

E-mail: kustova_t@mail.ru

*Supervising author; ⁺Corresponding author

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Abstract

Quantum-chemical simulation of the mechanisms of the reactions of dipeptides acylation by carbonyl and sulfonylating agents has been carried out. The RHF//6-31G(d) method was used to calculate the three-dimensional potential energy surfaces of the reactions of glycylglycine with chlorides of benzoic and benzenesulfonic acids, α -alanyl- α -alanine with 3-nitrobenzenesulfonyl chloride, and tyrosylproline with 4-nitrophenyl ester of benzoic acid in the gas phase. It was found that in the reactions of glycylglycine and α -alanyl- α -alanine a single route containing a single saddle point can be realized. In reactions with the participation of sulfonyl chlorides, a route is realized that begins with an axial attack of the nucleophile with a subsequent decrease in the angle of attack as the reagent molecules approach each other, and in the reaction with the participation of benzoyl chloride, the dipeptide molecule attacks the π^* -orbital of the carbonyl group. The processes proceed according to the bimolecular concerted mechanism of nucleophilic substitution S_N2 , which implies the formation of a single transition state along the path of the reaction. It was found that in the tyrosylproline reaction the axial and rear directions of attack assumed on the basis of the literature data are not realized. It was found that in the reaction of glycylglycine with benzoyl chloride, a tetrahedral "tight" transition state is formed, in which the C-N bond formation is somewhat ahead of the cleavage of the C-Cl bond. In the transition states of the reactions of glycylglycine with benzenesulfonyl chloride and α -alanyl- α -alanine with 3-nitrobenzenesulfonyl chloride, the reaction centers have a structure intermediate between trigonal-bipyramidal and tetragonal-pyramidal. The transition state of α -alanyl-

α -alanine reaction with 3-nitrobenzenesulfonyl chloride is "synchronous", as evidenced by the equal values of the orders of the breaking S-Cl bond and the forming S-N bond. The activation energies of the reactions are calculated; they were 121 kJ·mol⁻¹ in the reaction of glycylglycine with benzoyl chloride, 199 kJ·mol⁻¹ in the reaction of glycylglycine with benzenesulfonyl chloride, and 70 kJ·mol⁻¹ – in the reaction of α -alanyl- α -alanine with 3-nitro-benzenesulfonylchloride. It is shown that the obtained ratio of the activation energies for the processes in the gas phase is consistent with the reactivity of the acylation participants when carrying out the reactions in solution, and with the concept of the effect of substituents in the reagents structure on the rate of the processes under study.

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