

Electron and energy transfer processes in linked systems with chiral drugs. Spin chemistry and photochemistry investigation

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Photoinduced elementary processes in chiral linked systems, consisting of drugs and tryptophan (Trp) residues, attract considerable attention due to several aspects. First, these models allow one to trace the full and partial charge transfer underlying the binding of drugs to enzymes and receptors. On the other hand, Trp fluorescence is widely used to establish the structure and conformational mobility of proteins due to its high sensitivity to the microenvironment. Therefore, the study of mechanisms of Trp fluorescence quenching in various systems has both fundamental and practical interest. In order to study the elementary processes, in this work model systems are studied, including (S)- and (R)-ketoprofen (KP) bound to the amino acid Trp using fluorescence spectroscopy and CIDNP techniques. According to the literature data, two mechanisms of Trp fluorescence quenching in biomolecules are possible: electron transfer (ET) and singlet-singlet energy transfer (SSET). An analysis of the CIDNP effects of KP-Trp diastereomers indicates intramolecular ET between the Trp donor in the singlet excited state and the KP acceptor in the ground state. In this work, an attempt was made to estimate the contributions of the processes of ET and SSET in dyad diastereomers using the CIDNP effects and fluorescence quenching. Assuming that the fraction of the ET channel in diastereomers is proportional to the ratio of CIDNP enhancement coefficient, and using the radical pair theory, modified by prof. Doktorov, we estimated the concentration ratio of biradical-zwitterions BZ(SS)/BZ(RS) to be 7.5. Analysis of the fluorescence spectra of diastereomers indicates stereoselective quenching of Trp in the dyad, and the ratio of fluorescence quenching constants (S,S)/(R,S) is 2. This suggested that the (R,S)-diastereomer is predominantly quenched by the SSET mechanism, while the ET contribution is more significant for the (S,S)-diastereomer. Quantum-chemical calculations of distances between chromophores in diastereomers, as well as experimental 1D NOE data, showed that shorter distances are typical for the (R,S)-diastereomer. Thus, it was shown that the stereoselectivity of ET and SSET can be due to both differences in the distances between partners and the orientation of the transition dipole moments of KP and Trp in the diastereomers of the dyad.

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