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Synthesis and characterization of new molecular switches with azobenzene motif

Summary

Among various known photoswitches, azobenzenes are characterized by the unique advantage related to change of the molecular geometry (and dipole moment) as a result of the light-induced interconversion between the planar *trans* isomer and the non-planar *cis* isomer. The introduction of these molecular switches into a biopolymer matrix leads to creation of a smart hybrid system which can find a variety of applications from nanotechnology to biotechnology. Particularly interesting in such systems is not only that they are characterized by changed optical and biological properties, but above all, the possibility of use of light as a non-invasive stimuli to control their properties.

Therefore, the goals of the present dissertation included the synthesis of chiral and achiral azobenzene derivatives, determination of the correlation between the structure and properties of azobenzene derivatives, and the construction and characterization of new hybrid systems based on azobenzene derivatives and biomolecules.

The first part of the dissertation contains the description of the synthesis of 10 new derivatives of azobenzene substituted at *para*, *meta* position (*ortho* positions were rejected due to steric hindrance) with EWG, EDG or EDG/EWG simultaneously. The properties of the obtained azobenzene derivatives were then examined. The ^1H NMR technique was used to determine the composition of the isomers at PSS_Z and PSS_E. The thermal stability of the *cis* form was determined by measuring the changes of the absorbance as a function of time at a given temperature. The stability of the -N = N- bond in the presence of glutathione - reducing agent naturally occurring in the cells, was followed by observation of changes at the UV-Vis spectrum. The conducted research allowed to determine the correlation between the structure and properties of azobenzene derivatives.

The second part of the doctoral thesis concerned obtaining chiral azobenzene derivatives substituted at 4, 4 by L-tyrosine, D-tyrosine as well as L-lysine, D-lysine, L-threonine,

D-threonine, due to the fact that chiral compounds should exhibit selectivity of binding toward naturally chiral DNA/protein matrices. Azobenzene derivatives with tyrosine have

been incorporated into the HSA structure, while azobenzene derivatives with lysine or threonine have been introduced into the B-DNA and right- and left-handed G-quadruplex matrix. The studies of the interactions ligand-biopolymer were carried out using different spectroscopic approaches like absorption, fluorescence and CD measurements. The chiral DNA/HSA structure imposes a specific geometric orientation of the switch, which causes induction and enhancement the optical response. As the isomerization process can be regulated by light, the obtained hybrid chiroptical system can be modulated with spatiotemporal precision.

Hybridization and melting phenomena of oligonucleotides are important steps in biotechnological processes, at the same time in addition they form the basis of the developing field of DNA nanotechnology, which makes that the external photocontrol of these processes an attractive strategy. Therefore, in the last part of the doctoral thesis, it was decided to check the possibility of controlling the melting temperature of DNA using light. For this purpose, *ortho*-fluorine derivatives of azobenzene were obtained, for which the isomerization process can be induced by visible light. Photosensitive ligands were introduced into a B-DNA matrix of various lengths and into the G4 structures. The analysis of ligand-biopolymer interactions was carried out using the same experimental techniques as in the second part of this work. The obtained results suggest that the isomerization process controlled by the blue (*cis-trans*) and green (*trans-cis*) light allows to photocontrol the melting temperature of DNA (short and long duplexes). At the same time, the examined compounds do not affect the melting point of G-quadruplexes.

The implementation of the doctoral project objectives has allowed not only to obtain a number of new molecular switches based on the azobenzene motif and to determine their properties, but above all enabled to find new hybrid systems that may potentially be useful for future biological and/or photonic applications.