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A New Class of Ultrafast Photoswitchable Chromopeptides

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Abstract. The photochemical properties of a new ultrafast photoswitch based on hemithioindigo derivatives are investigated by transient absorption spectroscopy. The applicability as a trigger molecule for fast structural changes in small peptides is tested on a biologically relevant structure.

1. Introduction

Folding is one of the most important still unresolved phenomenon of living nature. The transformation of an amino acid chain from the random coil to the functional protein with a defined 3-dimensional structure is a complex process with only very little understanding of the basic principles. A deeper insight into folding processes is expected via the investigation of small systems, where the incorporation of an optical trigger molecule in a peptide allows to induce fast structural changes with a welldefined starting time. Recently different types of azobenzene compounds (APB, AMPB, AMPP) have been introduced as trigger molecules and used to study a great variety of peptides [1-3]. These experiments have shown that peptide dynamics may be very fast occurring on the 20 ps time scale. Since the chemical stability of the azobenzene switch strongly depends its surroundings, it is important to introduce new types of photo-switchable molecules with sufficient switching speed and large structural changes exerting strong forces on the attached peptides. The chemical properties of these switches should be different to those of azobenzene. In this paper we present time resolved data on a new photoswitchable molecule based on hemithioindigo-derivates (HTI, see left part of Fig. 1.).

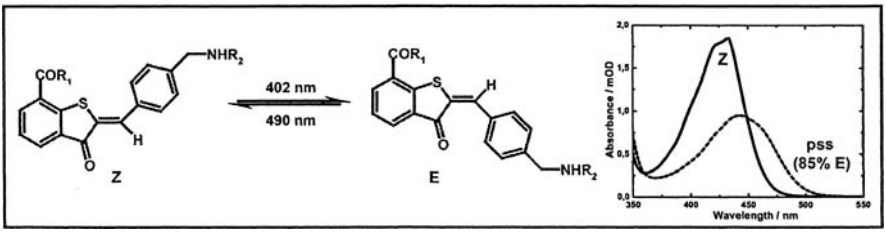

Fig.1. Chemical structures and absorption spectra of both HTI-isomers. The residues are R_1 = OH and R_2 = H (pure switch), R_1 = Lys and R_2 = Lys-Leu-Phe-Val-Asn-Val-Pro (linear peptide) and $R_{1,2}$ = cyc(Lys-Leu-Phe-Val-Asn-Val-Pro-Lys) for the cyclic peptide. The absorption spectra (right) shows the absorption of the pure switch.

The ultrafast response to visible excitation of the isolated switch as well as linear and cyclic peptides containing this new switch are shown. Detailed information concerning the experimental methods are given in [1,4]. More details about the used peptide motif in the chromopeptides derived from receptor tyrosine kinases is found in [6].

2. Results and Discussion

The HTI-switch discussed in this paper consits of a hemithioindigo part connected to a hemistilbene [5]. Upon illumination these molecules can isomerize around the double bond connecting the two molecular parts. The two corresponding conformations Z and E and their absorption spectra are shown in Fig.1. Illumination of the Z-form (solid line) with cw light at 418/430 nm allows to form a photo stationary state which contains approximately 85 % of the molecules in the E-form (broken). Due to the negligible absorption of the Z-form at long wavelength, illumination at $\lambda > 490$ nm leads to the complete reformation of the Z-form. This has important consequences for time resolved measurements: The absorption properties of the two isomers allow to excite the E-isomer exclusively. At room temperature the Z-form is stable while the E-form reconverts on a timescale of several hours [5]. Fig. 2. shows transient absorption data of both switching directions:

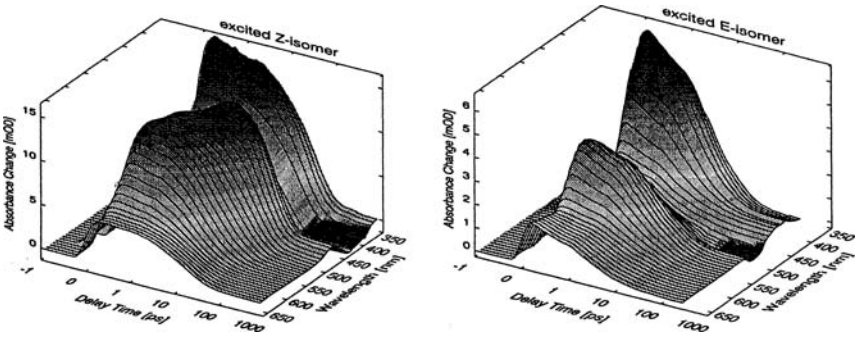

Fig.2. Transient 3D-Spectra for the Z→E process (left) and the E→Z process (right).

Excitation of the Z-form (left) with light at 402 nm leads to the rapid formation of an absorption increase extending throughout the complete visible and UV range (excited state absorption). We find bleaching of the ground state around 430 nm and stimulated emission (around 480 nm). In the 10 ps time range different transients related to motions on the excited state potential surface are observed. At first the molecule departs from the Franck-Condon range. This reaction are connected with a reduction of the stimulated emission (red-shift of the fluorescence) and a modified excited state absorption. Finally the isomerization is completed with the transition to the electronic ground state, which occurs on the time scale of 30 ps. At late delay times we find the absorption change expected

from the formation of the E-form: absorption increase around 470 nm and a bleach of the Z-absorption band around 430 nm. On the right part of Fig.2. the experimental results for inverse reaction (E → Z) are shown. Again there is a rapid formation of the excited state absorption with a strongly modulated spectrum showing excited state bands around 400 and 550 nm with bleach and stimulated emission in between (ca. 450 nm). There is a weak S_1 transient with 2 ps followed by the transition to the ground state with a time constant of 8 ps. During this process the formation of the Z-isomer can be observed at 430 nm and 470 nm. The experimental data on the molecular switch shows that the isomerization occurs on the picosecond time scale for both directions of the isomerization.
The applicability of the HTI-switch as a trigger molecule for peptides is demonstrated in Fig.3. for a spectral range giving information on the decay of the excited state. We find a nearly identical time behavior for the HTI-switch and the linear peptide-construct for both switching directions. The most prominent difference between peptides and switch occours for the E→Z reaction. The S_1-state of the cyclic peptide decays slower (10 ps instead of 8 ps) and an additional long lasting non-monoexponential decay is observed (100 ps - 1000 ps). For the cyclic chromopeptide, the steric hinderance modifies the excited state energy surface and may delay the formation of the planar Z-form.

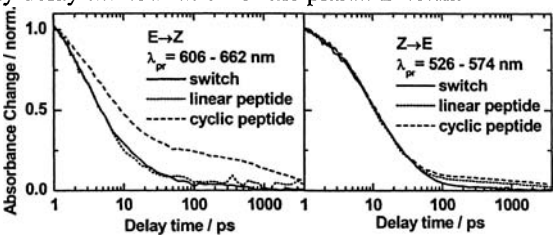

Fig. 3. Transient S_1-absorption of the HTI-chromopeptides for both switching directions.

In conclusion, we have shown that hemithioindigo derivatives can be used as fast switching molecules inducing rapid structural changes in peptides and proteins. The differences in the structural and chemical properties of the new HTI-switch and the formerly used azobenzene switch greatly extend the range of applications of backbone switches for protein research.

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