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Multistate Photoswitches: Macrocyclic Dihydroazulene/Azobenzene Conjugates

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Abstract: Molecules comprised of three covalently linked bi-stable switches can exist in states described by a combination of binary numbers, one for each individual switch: <000>, <001>, etc. Here we have linked three photo-/thermoswitches together in a rigid macrocyclic structure, one azobenzene (bit no 1) and two dihydroazulenes (DHAs; bits no 2 and 3) and demonstrate how electronic interactions and unfavorable strain in some states can be used to control the speed by which a certain state is reached. More specifically, upon irradiation of state <000>, the AZB isomerizes from trans to cis and the two DHAs to vinylheptafulvenes (VHFs), generating <111>. The thermal VHF-to-DHA back-reactions from this state also occur stepwise and can be accelerated by photoinduced AZB cis-to-trans conversion, proceeding via <011> to ultimately furnish <000>. Overall, the accessibility to a specific state of one bit was found to depend on the states of its neighboring bits.

Multimode photoswitches that can exist in several states have found interest in areas ranging from molecular electronics, optical data storage, and fluorescence emission modulation to molecular machines, sensors, and storage of solar energy.^[1] When individual units are combined into a single molecular system, the state of one unit (bit) may be used to control the state of a neighboring one. The accessibility to a specific state of one bistable molecular bit can thereby depend on the state of its neighbors. Access to <111> might be allowed from <110> but not from <011>, or allowed at different rates.

The dihydroazulene/vinylheptafulvene (DHA/VHF) system is a photo-/thermoswitch as first reported by Daub and coworkers,^[2] and we have found that macrocyclic dimers can exist in three states (DHA-DHA, DHA-VHF, VHF-VHF).^[3] Conversion from DHA-DHA to VHF-VHF via DHA-VHF is stimulated by light, while return of the VHF-VHF to DHA-DHA is thermally stimulated. Alternatively, azobenzene (AZB) undergoes cis/trans photoisomerization and has been integrated in various macrocyclic structures.^[4] By cyclizing two DHA units and one AZB unit at least six distinct isomers may result (Figure 1). The trans/cis-AZB-DHA-DHA states can each exist as pairs of diastereoisomers (one meso and a pair of enantiomers), and the trans/cis-AZB-DHA-VHF states can exist as pairs of

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enantiomers. Figure 1 lists the Gibbs free energies of the lowestenergy conformers, calculated using the CAM-B3LYP/6-311G(d,p) method in Gaussian09.^[5] trans-AZB-DHA-DHA (RR/SS) is most stable, while cis-AZB-VHF-VHF is least.



b (RS; meso): 54.5 kJ mol⁻¹

trans-AZB-DHA-DHA a (RR / SS): 0 kJ mol⁻¹ b (RS; meso): 0.4 kJ mol⁻¹

Figure 1. Relative Gibbs free energies of formation (CAM-B3LYP/6-311G(d,p)) of isomeric macrocycles.

Herein we show that three out of six states can be reached by appropriate application of light and heat stimuli. We shall label the lowest- and highest-energy states by <000> and <111>, respectively, where the first number refers to AZB (trans/cis) and the second and third to DHA/VHF. The <001> and <010> states are degenerate (as stereoisomers are ignored) as are <101> and <110>.

Synthesis of trans-AZB-DHA-DHA (<000>) was accomplished in a cyclization between acid chloride 1^[6] and diol $2^{[3a]}$ in the presence of N,N-dimethylaminopyridine (DMAP) (Scheme 1). The reaction provides a mixture of diastereoisomers a and b in yields of 11 and 9%, which exhibit similar UV-Vis absorption spectra. The structure of the meso form (b) was confirmed by X-ray crystallography (Figure 2), revealing a dimeric packing arrangement in which the DHA-DHA moieties of two cycles occupy each other's cavities.



Scheme 1. Synthesis of trans-AZB-DHA-DHA (a/b diastereoisomers).



Figure 2. Left: Molecular structure of *trans*-AZB-DHA-DHA (b isomer) with thermal ellipsoids shown at 50% probability level; H atoms were omitted for clarity. Right: Crystal packing of two macrocycles. CCDC 1588810.

Photoisomerization of trans-AZB-DHA-DHA a was conducted by irradiation with 365 nm light until a photostationary state was reached. A large absorption decrease was observed in the range of 300-400 nm (trans-AZB and DHA), and a simultaneous increase in the range of 420-620 nm (VHF) (Figure 3, top). By considering the characteristic absorptions of the monomeric parent trans-AZB (λ_{max} = 317 nm) and DHA (λ_{max} = 354 nm) (Figures S1 and S2), the changes above are accounted for by a simultaneous isomerization of trans- to cis-AZB as well as both DHAs to VHFs, leading to a state predominated by cis-AZB-VHF-VHF (<111>) (possibly also some trans-AZB-VHF-VHF is present). The spectrum of the resulting cis-AZB-VHF-VHF presents a lower than expected molar absorptivity in the region of λ_{max} = 492 nm. Previous studies suggest that this can be the result of structural (out-of-plane) distortion of VHF.[3b],[7] This is supported by computational geometry optimizations conducted for cis-AZB-VHF-VHF (Figures S21-S22), showing a symmetrical distortion in both VHFs and hence an equal absorbance contribution from both, yet with individually lower molar absorptivities than expected for two structurally undistorted VHFs. Although we cannot exclude the presence of residual DHA-VHF, ¹H-NMR studies do reveal isomerization of the second DHA. Based on rate constants from UV-Vis studies we estimate a photostationary state with ca. 86% VHF-VHF under our experimental conditions. Photoisomerization of trans-AZB-DHA-DHA was monitored by following formation of VHF at 494 nm over time (Figure 3, middle). Similar to previously studied macrocycles,^[2] the increase in absorbance as a function of irradiation time could be modeled by a sum of two exponential functions, $A(t) = c_1 \exp(-t/\tau_1) + c_2 \exp(-t/\tau_2) + A_{\infty}$ (with $\tau_2/\tau_1 = 11$); the DHA-to-VHF conversions hence seem approximately independent of the AZB state.



Figure 3. Top: UV-Vis absorption spectra showing conversion of *trans*-AZB-DHA-DHA a (<000>) to *cis*-AZB-VHF-VHF (<111>) in MeCN by irradiation at 365 nm. Middle: Absorbance at 494 nm plotted as a function of irradiation time and fitted by: $A(t) = c_1 \exp(-tt\tau_1) + c_2 \exp(-tt\tau_2) + A_m$. Bottom: Spectra showing conversion of *cis*-AZB-VHF-VHF (<111>) to *trans*-AZB-VHF-VHF (<011>) in MeCN by irradiation at 410 nm.

cis-AZB-VHF-VHF only has one photochromic subunit, namely *cis*-AZB, and two solely thermochromic VHFs. By irradiation at 410 nm and stimulation of the *cis*-AZB $n \rightarrow \pi^*$ transition, a photostationary state consisting of *trans*-AZB-VHF-VHF (<011>) (and possibly also some *cis*-AZB isomer) was observed (Figure 3, bottom). Not only are we stimulating the *cis*-AZB to *trans*-AZB conversion by choosing a wavelength where *cis*-AZB has a stronger absorption, but *trans*-AZB-VHF-VHF is also calculated to be more stable than *cis*-AZB-VHF-VHF (by 40.7 kJ mol⁻¹). The conversion of *cis*- to *trans*-AZB-VHF-VHF was accompanied by the emergence of the *trans*-AZB $\pi \rightarrow \pi^*$

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absorption (318 nm) along with no significant decrease observed for the VHF absorption (492 nm). Minor changes in the area around 462 nm can be assigned to changes in VHF absorption as a result of *cis/trans*-AZB isomerization. Excited state calculations (CAM-B3LYP/6-311+G(d,p)//CAM-B3LYP/6-311G(d,p)) also show only a minor difference in optical properties of the VHF-VHF in the two macrocycles (SI, Table S1).

Thermal isomerization of VHF-VHF to DHA-DHA can be initiated from two starting points, either *trans*-AZB-VHF-VHF or *cis*-AZB-VHF-VHF. These two processes were monitored at 30, 40, 50, 60, and 70 °C in MeCN and in each case observed to occur stepwise via an intermediate DHA-VHF. The decay in VHF absorbance was modelled by the sum of two exponential decay functions. Neither *cis*- nor *trans*-AZB exhibits a significant absorbance in the 494-nm region nor does their isomerization significantly effect the absorbance of the VHFs. The effect of AZB isomerization is thus only reflected in the rate of the VHF-to-DHA reactions.

Relaxation of cis-AZB-VHF-VHF to trans-AZB-DHA-DHA was observed to initially proceed via a fast decay ($t_{\frac{1}{2}}$ = 36 min at 30 °C) followed by a much slower process ($t_{1/2}$ = 1900 min at 30 °C). The isomerizations were monitored at the VHF λ_{max} of 494 nm as well at the combined AZB and DHA λ_{max} of 332 nm. By comparing the changes at these two wavelengths, it is observable that the first event exhibits a decrease in the VHF absorption but no significant increase in the trans-AZB absorption at 318 nm. In fact, conversion of half of the VHF species to DHA (one moiety per macrocycle) is observed before any significant switching of cis- to trans-AZB (Figure 4). This first event can thus be assigned to relaxation of cis-AZB-VHF-VHF (<111>) to cis-AZB-DHA-VHF (<101>) (Scheme 2). The cis-AZB-VHF-VHF absorption at 492 nm is assigned to two individual but structurally similar VHFs, which sequentially switch to DHA.



Figure 4. UV-Vis absorption spectra showing the thermal isomerization of *cis*-AZB-VHF-VHF (<111>) to *cis*-AZB-DHA-VHF (<101>) and then to *trans*-AZB-DHA-DHA (<000>).

The relaxation of *trans*-AZB-VHF-VHF (<011>) to *trans*-AZB-DHA-DHA (<000>) also proceeded via a fast and a slow thermal decay, accounting for two VHF \rightarrow DHA isomerizations with half-lives of 31 and 620 min at 30 °C. By comparing the two

pathways from *cis*-AZB-VHF-VHF to *trans*-AZB-DHA-DHA, one fully thermally activated and the other first light-activated and then thermally (Scheme 2), it is notable that the first VHF \rightarrow DHA, <**x11**> \rightarrow <**x01**>, is unaffected by the state of AZB; **x** = **1** (*cis*) or **0** (*trans*). The major effect of *cis*-*ltrans*-AZB is on the second VHF ring closure, <**x01**> \rightarrow <**x00**>, lowering $\Delta G_{slow}^{\dagger}$ from 105 to 101 kJ mol⁻¹ (30 °C) when changing **x** from **1** to **0** (3-fold faster reaction) (Figure 5). Based on studies in solvents of different polarity, we hypothesize that DHA-VHF to DHA-DHA proceeds as <**101**> \rightarrow <**001**> \rightarrow <**000**> with the former being the rate-determining step (*cis*-AZB to *trans*-AZB). The rate of VHF ring closure is usually slower in an apolar solvent.^[117] This, was indeed observed for conversion of VHF-VHF to DHA-VHF in cyclohexane/CHCl₃ 1:1, while the subsequent conversion into DHA-DHA was not significantly influenced.



Scheme 2. Two pathways of isomerization from *cis*-AZB-VHF-VHF to *trans*-AZB-DHA-DHA: thermally via *cis*-AZB-DHA-VHF (dark green arrows) and photo/thermally via *trans*-AZB-VHF-VHF (maroon arrows).



Figure 5. Absorbance decay at 494 nm corresponding to the conversions of *trans*-AZB-VHF-VHF (maroon; <011>) and *cis*-AZB-VHF-VHF (dark green; <111>) to *trans*-AZB-DHA-DHA (<000>).

In conclusion, if we assign the *trans*-AZB-DHA-DHA state as <000>, *cis*-AZB-VHF-VHF as <111> and *trans*-AZB-VHF-VHF as <011>, photoisomerization of <000> leads to <111>. Regeneration of <000> can be achieved thermally from <111> in a slow process or in a fast by first photoisomerizing <111> to <011>. The macrocyclic structure thus presents a convenient way of controlling accessibility to specific states; however, a data density of 3 bits per molecule is only hypothetical as data is stored in an ensemble of molecules.

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Keywords: Azo compounds • Electrocyclic reactions • Isomerization • Macrocycles • Photochromism

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Switching switching: Three photochromic units (two

dihydroazulenes/vinylheptafulvenes, *blue/red*, and one azobenzene, *green/orange*) influence each other's photo/thermal switching behavior when incorporated in a macrocyclic structure, meaning that accessibility to one specific state described by a combination of three binary numbers depends on the pathway to this state.

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