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Photochromic Switches

Photon-Quantitative Reaction of a Dithiazolylarylene in Solution**

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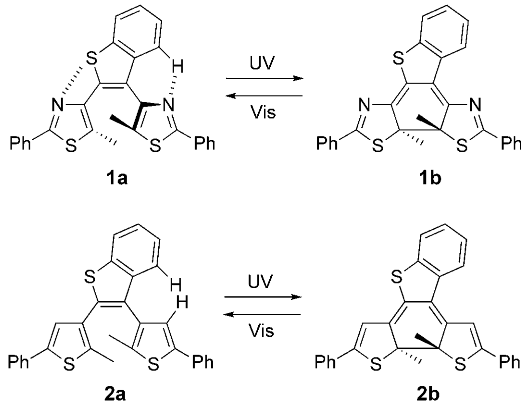
In the cascade of mammalian vision, the *cis*-to-*trans* photoisomerization reaction of the retinal chromophore bound to the opsin apoprotein acts as the first trigger for the conversion of light signals into electrical pulses, which are finally transmitted to the brain. One of the specific chemical characteristics of retinal chromophore is its high quantum yield of *cis*-to-*trans* photoisomerization, $\Phi_{cis-trans} = 65\,\%$, which affords the high sensitivity of the rod rhodopsin, an opsin–retinal complex required for night vision.[1] Interestingly, the $\Phi_{cis-trans}$ value of retinal decreased to less than 30 % in solution without the protein. This observation suggests that the environmental conditions of the binding pocket in rhodopsin may be responsible for the high photochemical reactivity of retinal. The hydrophobic pocket in rhodopsin is thought to favor appropriate noncovalent bonding to regulate the geometry of the guest molecule in preparation for the photoisomerization reaction.[2] With the aim of developing highly efficient and sensitive photochromic molecules on the basis of the opsin–retinal system, we designed an organic photochromic molecule with a terarylene structure and demonstrated its photon-quantitative reaction.

Photochromic terarylenes are composed of three aromatic rings connected to form a hexatriene backbone,[3] which is converted into a cyclohexadiene structure upon UV irradiation, as similarly observed for the photochromism of diarylethenes.[4] Recent studies on terarylenes have highlighted their high photocyclization quantum yields, which exceed 60 %[3b,d,5] and are apparently higher than those of conventional diarylethenes.[4] Since the photoelectrocyclic reactions typically occur in less than 200 fs, the photocyclization quantum yield is generally determined by the electronic structure in the excited state, which is directly interpreted as the molecular conformation in the ground state. Diarylethenes are known to possess two conformations in solution, with the two rings in mirror symmetry (parallel conformation) or C_2 symmetry (antiparallel conformation). As the photocyclization reaction proceeds only from the C_2-symmetrical conformation, the quantum yield is about 50 % at most.[4a] In contrast, some diarylethenes undergo a quantitative photocyclization reaction in the crystalline state, when their conformation is fixed in the antiparallel conformation and the distance between reactive carbon atoms is sufficiently short: typically less than 0.4 nm.[6] These observations indicate that the ground-state conformation plays a crucial role in the photoinduced pericyclization reaction. Therefore, various attempts have been made to regulate the ground-state geometry of diarylethenes so that they have C_2 symmetry.[7] We herein propose a concept for the design of highly reactive photochromic hexatriene molecules that is inspired by the design of foldamers;[8] thus, multiple intramolecular interactions were used to stabilize the photoreactive conformation of a terarylene.

The 2,3-dithiazolylbenzothiophene **1a** was designed as a representative photochromic molecule whose conformation is expected to be stabilized in the photoreactive conformation through intramolecular interactions, as depicted by dotted lines in Scheme 1. The rotation of one side-chain thiazolyl ring would be suppressed by an S–N heteroatom-contact interaction.[9] Such interactions are considered to be responsible for the planarity of conjugated polymers composed of, for example, co-thiophene-benzo[*c*]1,2,5-thiadiazole structures.[9a] S–N close contacts shorter than the sum of the van der Waals radii were also observed for crystal structures of π-conjugated oligomers consisting of alternate N- and S-heteroaromatic rings with a coplanar conformation.[9b,c] Weak CH–N hydrogen bonding[3b,10] would tether the other thiazolyl ring. In combination with these interactions, which favor the coplanarity of the three heteroaromatic rings, steric hindrance between the methyl groups at the reactive carbon centers causes the side-chain thiazolyl rings to tilt slightly and direct the adoption of the photoreactive conformation in



Scheme 1. Photochromism of dithiazolylbenzothiophene **1a** and the reference compound **2a** (dithienylbenzothiophene).

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which the hexatriene moiety has C_2 symmetry. The 2,3-dithienylbenzothiophene **2a** was also designed as a reference compound.

The 2,3-diarylbenzothiophenes **1a** and **2a** were synthesized by conventional cross-coupling reactions of the corresponding arylene units. Their chemical structures were confirmed by high-resolution mass spectroscopy, ^{1}H and ^{13}C NMR spectroscopy, and elementary analysis. Both **1a** and **2a** could be recrystallized from solutions in hexane, and their crystal structures were determined by X-ray crystallographic analysis.[11] The single crystal of **1a** turned blue upon irradiation with UV light, whereas **2a** showed no photochromism in the crystal. The crystal structure of **1a** showed the photoreactive conformation with C_2 symmetry of the hexatriene moiety (Figure 1a). In particular, the distance between H1 and N2 was estimated to be 0.269 nm, which is shorter than the sum of the van der Waals radii of the H (0.12 nm) and N atoms (0.155 nm). The distance between the N1 and S1 atoms, 0.295 nm, was also shorter than the sum of the van der Waals radii of the S (0.185 nm) and N atoms (0.155 nm). These atomic contacts clearly indicate noncovalent interactions of the sort mentioned above, which are considered to stabilize the reactive quasi-C_2-symmetrical conformation of **1a** in the crystalline phase. Furthermore, CH–π interactions were also suggested by the short distances between the hydrogen atoms on reactive methyl carbon atoms and the molecular planes of the thiazolyl rings (0.31 and 0.32 nm). On the other hand, the geometry of **2a** in the crystal is apparently unsuitable for a photocyclization reaction (Figure 1b).

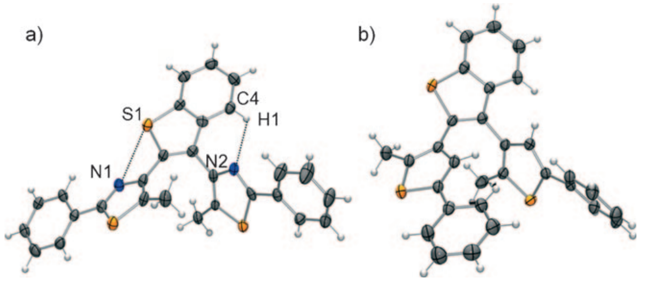

Figure 1. ORTEP drawings (showing 50% probability displacement ellipsoids) of the open-ring isomer in a) crystal **1a** and b) crystal **2a**.

To evaluate intramolecular interactions in solution, we performed temperature-dependent ^{1}H NMR spectroscopy on compound **1a** in the nonpolar solvent [D$_8$]toluene. The signal of H1 (in Figure 1), which is expected to participate in CH–N hydrogen bonding, appeared at $\delta = 8.12$ ppm at 293 K, as indicated by the arrow in Figure 2. This chemical shift is well downfield of those for other arylene hydrogen atoms in **1a**, whereas it was observed below $\delta = 8.0$ ppm and overlapped with those of other arylene hydrogen atoms in CD$_3$OD (see the Supporting Information). A chemical shift at such a low field was also reported for intramolecular weak CH–N hydrogen bonding in 4-arylthiazolyl derivatives.[12] Meanwhile, the hydrogen atoms at the reactive methyl carbon atoms gave a single peak at $\delta = 1.79$ ppm, and thus at a very high field for methyl-substituted thiazole derivatives. The upfield shift of methyl hydrogen atoms would originate from the ring-current effect of the neighboring thiazole ring and indicates CH–π interactions between the methyl groups and side-chain thiazole units. Upon heating, the H1 signal showed a continuous upfield shift from $\delta = 8.12$ ppm at 293 K to $\delta = 7.99$ ppm at 353 K, as indicated by arrows in Figure 2. This observation suggests that the CH–N interaction became weak as the temperature was raised. The signals of other arylene hydrogen atoms between $\delta = 7.9$ and 8.0 ppm showed a slight upfield shift by 0.05 ppm at most; thus, these signals were not shifted to such a significant degree as the signal of H1. Moreover, the signal for methyl hydrogen atoms underwent a progressive downfield shift and splitting upon heating (Figure 2). This behavior indicates the weakening of CH–π interactions and a consequent decrease in the structural symmetry around the hexatriene moiety. In contrast, the signal of H1 exhibited no marked temperature dependence in CD$_3$OD. These experimental ^{1}H NMR spectroscopic data strongly suggest that CH–N hydrogen bonding and CH–π interactions stabilize the photoreactive conformation of **1a** at room temperature in nonpolar solvents; such an effect is not expected in protic solvents.

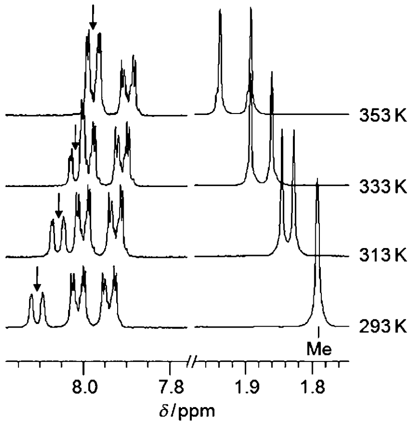

Figure 2. Temperature-dependent ^{1}H NMR spectra of **1a** in [D$_8$]toluene. The arrow indicates the signal of hydrogen atom H1 (Figure 1).

The results of a density functional theory (DFT)[13] study at B3LYP/6-31G* to optimize the structure of **1a** were in good agreement with the results of X-ray crystallography and ^{1}H NMR spectroscopy. A photoreactive conformation of **1a** was obtained as the optimized structure, which was almost identical to the crystal structure shown in Figure 1a. The atomic contacts between H1 and N2 and between S1 and N1 (estimated distance: H1–N2, 0.26 nm; S1–N1, 0.32 nm) are consistent with CH–N and S–N intramolecular interactions. The distances between hydrogen atoms on reacting methyl carbon atoms and the molecular planes of side-chain thiazole units were evaluated to be about 0.31 and 0.35 nm, which are also short enough for CH–π interactions.

Finally, we investigated the photochromic performance of **1a** in solution. Irradiation of a solution of **1a** in hexane with light of wavelength 313 nm resulted in the immediate changes in the UV/Vis absorption spectrum that are typical for

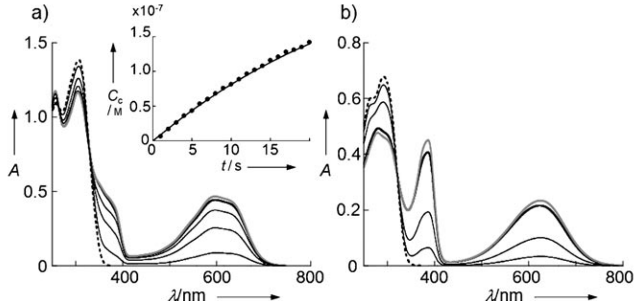

Figure 3. Absorption spectral changes of a) **1** (4.7×10^{-5} M) and b) **2** (1.9×10^{-5} M) in hexane. Spectra for the photostationary state under irradiation with light of wavelength 313 nm and for the closed form (**1 b** or **2 b**) are depicted by bold black and gray lines, respectively. Inset: Progression of the generation of ring-closed isomer **1 b** by UV irradiation. The plot was fitted by a kinetic equation in which $\Phi_{o\text{–}c}$ and $\Phi_{c\text{–}o}$ were assumed to be 0.98 and 0.008, respectively.

diarylethenes and terarylenes. The absorption band of **1a** at 307 nm observed in the original state decreased, and a new absorption band appeared at around 600 nm (Figure 3), which corresponds to the formation of **1b**. The chemical structure of **1b** was confirmed by ^{1}H NMR spectroscopy. The change in the absorption spectrum upon photoirradiation was accompanied by an isosbestic point at 330 nm, which clearly indicated the two-component photochromic reaction between the open form **1a** and the closed form **1b**. Irradiation of the colored solution with visible light led to the recovery of an absorption spectrum identical to that of the initial solution of **1a**. Similar photochromic behavior was also observed for **2**. The conversion ratios between the colorless and colored photostationary states upon irradiation with UV light ($\lambda = 313$ nm) were estimated to be more than 96 % for **1** and 90 % for **2**. The photochromic properties of **1** and **2**, including the reaction quantum yields, are summarized in Table 1. The quantum yields of the photochromic reaction were evaluated by the standard procedure by using 1,2-bis(2-methylbenzo[*b*]-thiophen-3-yl)perfluorocyclopentene[14] and 1,2-bis(2,3-dimethyl-5-phenyl-3-thienyl)perfluorocyclopentene[15] as references for the photocyclization and cycloreversion reactions, respectively. The detailed procedure for determining the quantum yield is described in the Supporting Information.

Table 1: Absorption maxima and coefficients of the open- and closed-ring isomers of **1** and **2**, together with the quantum yields in solution.

Isomer	λ_{max} [nm][a] (ε [10^4 M^{-1} cm^{-1}][a])	$\Phi_{o\text{–}c}$	$\Phi_{c\text{–}o}$
1a	307 (2.9)	0.98,[a] 0.54[b]	–
1b	597 (0.95)	–	0.008[a]
2a	292 (3.5)	0.49,[a] 0.38[b]	–
2b	653 (1.2)	–	0.029[a]

[a] In hexane. [b] In methanol.

The photocyclization quantum yield, $\Phi_{o\text{–}c}$, of **1a** in hexane was 98 ± 2 %, which is among the largest values for known synthetic photochromic molecules.[7d] This $\Phi_{o\text{–}c}$ value indicates that the absorbed photons quantitatively induce the photoisomerization of **1a** to **1b**. We also measured the progression curve of the concentration of ring-closed isomer **1b** (C_c) on the basis of the absorbance at 600 nm as a function of UV irradiation time to verify these quantum-yield values (Figure 3, inset). It was numerically reproduced by using an equation assuming the ideal photochemical reaction scheme with cyclization and cycloreversion quantum yields of 0.98 and 0.008, respectively. In contrast, **1a** showed a marked decrease in cyclization quantum yield, $\Phi_{o\text{–}c} = 0.54$, in methanol. The decrease in $\Phi_{o\text{–}c}$ in a protic solvent also supports the hypothesis that the weak CH–N hydrogen bonding is predominantly responsible for the stabilization of the photoreactive conformation, in agreement with the results of the ^{1}H NMR spectroscopic study described above. In contrast, the photocyclization quantum yields of **2a** were substantially lower and showed less-prominent solvent dependence than that observed for **1a**.

In summary, we designed and synthesized a triangle terarylene with high photochromic-coloration performance. The photocyclization quantum yield of compound **1a** in hexane was almost 100 %, whereas that in methanol was considerably lower. Multiple intramolecular noncovalent interactions that tether the geometry of **1a** in the photoreactive conformation, including weak CH–N hydrogen bonds as well as S–N and CH–π interactions, were demonstrated by X-ray crystallography, ^{1}H NMR spectroscopy, and DFT calculations. The molecular design based on supramolecular interactions provided an artificial photochromic system with greater sensitivity than that of a natural biological system, such as an opsin–retinal complex, as a result of precise control of the ground-state conformation.

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[11] Crystallographic data for **1a**: $C_{56}H_{40}N_4S_6$, $a = 11.8337(7)$, $b = 12.7853(7)$, $c = 15.7682(8)$ Å, $\alpha = 95.9830(16)$, $\beta = 102.3609(17)$, $\gamma = 92.221(2)°$, triclinic, space group $P\bar{1}$, $Z = 2$, $V = 2313.1(2)$ Å^3, $\rho_{calcd} = 1.355$ g cm^{-3}; of 19341 reflections up to $2\theta = 50.7°$, 8444 were independent ($R_{int} = 0.058$), and 5831 were with $I > 2\sigma(I)$; the structure was solved by direct methods and refined with a full matrix against all F^2 data; hydrogen atoms were calculated in riding positions; $wR = 0.1592$, $R = 0.0514$. For **2a**: $C_{30}H_{22}S_3$, $a = 10.1529(10)$, $b = 11.1215(11)$, $c = 11.4418(10)$ Å, $\alpha = 80.729(2)$, $\beta = 68.156(2)$, $\gamma = 79.614(2)°$, triclinic, space group $P\bar{1}$, $Z = 2$, $V = 1173.27(19)$ Å^3, $\rho_{calcd} = 1.355$ g cm^{-3}; of 9720 reflections up to $2\theta = 50.7$, 4295 were independent ($R_{int} = 0.032$), and 3392 were with $I > 2\sigma(I)$; the structure was solved by direct methods and refined with a full matrix against all F^2 data; hydrogen atoms were calculated in riding positions; $wR = 0.1166$, $R = 0.0460$. CCDC 796946 (for **1a**) and 796949 (for **2a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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