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Dynamic Control of Racemization Rate through *E*−*Z* Photoisomerization of Azobenzene and Subsequent Partial Photoresolution under Circular Polarized Light

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Reversible enantio-differentiating photoisomerization is known for some compounds, where photoresolution and photoracemization occur with circular polarized and normal light, respectively.[1−3] This process has attracted much attention because the application of such compounds to rewritable optical recording media makes it possible to read-out memories—without their destruction—by monitoring the difference in the optical rotation of the two states at a wavelength at which the absorbance is weak. Another important reason for studying such photoreactions is that they provide one possible mechanism for the origin of homochirality in bioorganic compounds; this theory proposes that a state displaying a partial enantiomeric excess can be obtained under the influence of circular polarized electromagnetic radiation, and then it can undergo a chiral amplification reaction.[4−8] To examine the probability of such a mechanism occurring, we investigated a new example of the photoresolution reaction using circular polarized light (CPL). To date, the only compounds known to display reversible enantio-differentiating photoisomerization directly between two enantiomers are some chromium complexes and ethylene derivatives.[1,2,9]

Azobenzene is a well-known photochromic compound that displays reversible photoisomerization between its *E* and *Z* isomers, which have different physical properties, e.g., different shapes, absorption spectra, and dipole moments. This photochromic reaction has been utilized as an optical switch in the functioning of a range of materials, including host molecules for metal ions, liquid crystals, organic conductors, organogels, photonic crystals, and polymers.[10]

In this study, we designed the bicyclic azobenzene dimers **1** and **2**, expecting that their racemization would be affected by photo-induced isomerization of their azobenzene units. As indicated in Figure 1, if the "flip-flop" process of the 2,2-diphenylpropane unit is sufficiently slow, a pair of enantiomers is associated with a molecule that possesses one element of planar chirality. Furthermore, the *E* and *Z* forms of each azobenzene unit introduce another set of isomers, resulting in the existence of a total of six isomers, including three pairs of enantiomers. The *E*,*E* isomer containing straight *E*-azobenzene units has a rigid ring structure with a deep pocket that may hinder racemization through the "flip-flop" mechanism, while the *Z*,*Z* isomer containing bent *Z*-azobenzene units has a flexible and shallow pocket that may accelerate the racemization. In this paper, we report the synthesis, photoisomerization, X-ray crystallographic analysis, photoinduced racemization, and partial resolution of **2**.

We synthesized racemic **1** and **2** through reduction of the corresponding tetranitro compounds under dilute conditions. The reaction yields were low because undesired azo compounds with less ring strain were formed in high yield through coupling between terminal nitro groups.

Compound **2** undergoes efficient photochromic reactions. Upon irradiation of an acetonitrile solution of racemic *E*,*E*-**2** at 366 nm,

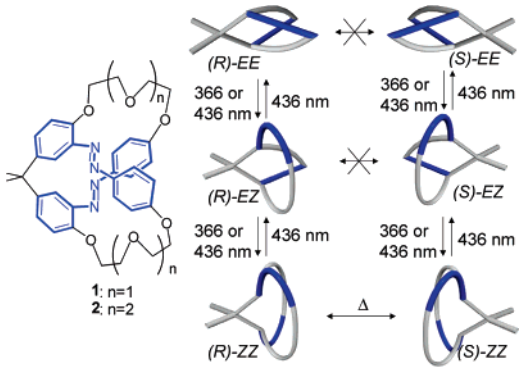

Figure 1. Structures of the bicyclic azobenzene dimers (left) and the scheme of the racemization and *E*−*Z* isomerization of the compounds (right). Blue bars in the right scheme represent azobenzene units.

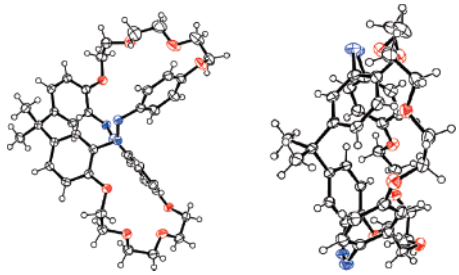

Figure 2. X-ray crystal structures of *E*,*E*- (left) and *Z*,*Z*-**2** (right).

its absorption band centered at 349 nm decreased in intensity, and new bands formed that were centered at ca. 300 and 430 nm. Subsequent irradiation of the solution at 436 nm induced a reversal in the absorption spectrum to another photostationary state (PSS) exhibiting almost half the absorbance at 349 nm relative to that of the initial state. The photochromic reactions of **2** proceed with isosbestic points seeming to shift during the isomerization (between 292 and 297 nm for one and between 254 and 258 nm for the other), which indicates an interconversion between more than two states. HPLC indicated that the solution after photoirradiation contained two new compounds in addition to the initial *E*,*E* isomer. From absorption spectra and X-ray crystal structure analyses, we assign these two photoproducts to the *E*,*Z* and *Z*,*Z* isomers of **2**. The relative concentrations of the *E*,*E*, *E*,*Z*, and *Z*,*Z* isomers in the PSSs were 0, 7, and 93%, respectively, at 366 nm and 26, 48, and 26%, respectively, at 436 nm. The quantum yield of the photoisomerization from *E*,*E* to *E*,*Z* isomer was 0.37 at 366 nm. Figure 2 displays the solid-state structures of the *E*,*E* and *Z*,*Z* isomers; we isolated the latter from an irradiated solution of the *E*,*E* isomer. As expected, the pocket of the *Z*,*Z* isomer is shallower than that of the *E*,*E* isomer, suggesting the lower activation energy in the racemization reaction by the "flip-flop" mechanism. The depth of

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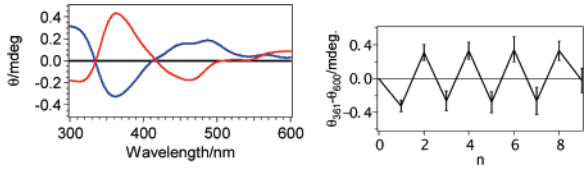

Figure 3. CD spectrum of **2** in acetonitrile upon irradiation with *r* (blue line)- and *l* (red line)-CPL (left). The difference in CD absorption at 361 and 600 nm ($\Delta\epsilon_{361} - \Delta\epsilon_{600}$) for a solution of **2** upon alternating irradiation with *l*- (n = even) and *r*- (n = odd) CPL and nonpolarized light (n = 0, 9). Error bars represent a standard error of mean values for five independent experiments (right).

the pocket in the *Z*,*Z* isomer of compound **1** is relatively shallow,[11] but because of its shorter ethylene glycol linkages the flexibility of the two rings during the "flip-flop" process of *Z*,*Z*-**1** is lower than that of *Z*,*Z*-**2**.

We resolved racemic *E*,*E*-**2** through preparative HPLC using a chiral column. The enantiomer that eluted first, which we assigned as (*S*)-*E*,*E*-**2**,[11] exhibited CD bands at 317, 361, and 455 nm with values of $\Delta\epsilon$ of −34.8, +47.0, and −22.8 M^{-1} cm^{-1}, respectively. The enantiomers are quite thermally stable: we did not observe any racemization (monitoring with chiral HPLC) in a 2-propanol/hexane solution of **2** that we maintained at room temperature in the dark for over 3 months.

HPLC analysis (chiral column) of the mixture of *E*,*E*-, *E*,*Z*-, and *Z*,*Z*-**2** obtained by irradiation of racemic *E*,*E*-**2** at 366 or 436 nm displayed a pair of peaks for each isomer. Furthermore, the resolution of the two peaks for the enantiomers of the *Z*,*Z* isomer did not approach the baseline, but instead formed a plateau, obviously caused by molecules that had inverted their enantiomeric configuration during resolution and then traveled at the speed of the antipode. We further confirmed the racemization of the *Z*,*Z* isomer through the observation that sequential irradiation of enantiomeric pure (*S*)-*E*,*E*-**2** at 366 nm followed by at 436 nm led to the formation of the completely racemized mixture of *E*,*E* enantiomers. This result clearly indicates that thermally stable (*S*)-*E*,*E*-**2** racemizes through a four-step photochemical reaction, i.e., via *E*,*Z*-**2** and *Z*,*Z*-**2**, the latter of which has a sufficiently low activation energy for racemization at room temperature. The chiral HPLC chromatogram of the photoreaction mixture of enantiomeric pure (*S*)-*E*,*E* at the early stage revealed that the peak areas for the *Z*,*Z* enantiomers were the same, while the peak area of one of the *E*,*Z* enantiomers was larger than that of the other; this result suggests that racemization of the *E*,*Z* isomer is much slower than that of the *Z*,*Z* isomer or thermally prohibited and occurred through sequential two-step photochemical reaction via *Z*,*Z* isomer. In contrast, **1**, which possesses shorter ethylene glycol chains, does not racemize via its *Z*,*Z* isomer; rather, the pure enantiomer *E*,*E*-**1** formed only its corresponding *E*,*Z* and *Z*,*Z* enantiomers, as we verified through HPLC experiments.

Next, we examined the possibility of enriching one enantiomer through the photoisomerization of racemic **2** under the influence of *l*- or *r*-CPL, using CD spectroscopy as the detection technique. We used CPL at 436 nm to obtain a PSS having a relatively higher *E*,*E* isomer ratio. Irradiation of racemic *E*,*E*-**2** with *r*- or *l*-CPL at 436 nm resulted in an active CD spectrum (Figure 3, left). Because the peak position and the sign of the CD spectrum for the solution irradiated with CPL matched that of one of the pure enantiomers of *E*,*E*-**2**, that enantiomer was partially enriched upon photoirradiation with CPL. Alternating irradiation using *r*- and *l*-CPLs induced an alternation in the sign of the peaks in the CD spectra. Further irradiation with nonpolarized light returned the solution to the inactive CD state, i.e., the compound returned to a racemic state (Figure 3, right).

From the value of $\Delta\epsilon_{361}$ and the induced CD value of 0.3 mdeg at 361 nm for the 6.3×10^{-5} M solution of **2** in its PSS at 436 nm, which contained the *E*,*E* isomer as 26% of the total isomers, we calculated the photoinduced ee of the *E*,*E* isomer to be 1.1%.

The enrichment of one of the enantiomers of *E*,*E*-**2** is possible through one of two enantiodifferentiating photoisomerization paths, i.e., either from *E*,*E* to *E*,*Z* or from *E*,*Z* to *E*,*E*. The induced CD can be estimated from half of the anisotropy factor *g*, which is calculated using the following equation:[4,12]

$$g = \frac{(\epsilon_l - \epsilon_r)}{\epsilon} = \frac{\Delta\epsilon}{\epsilon}$$

By using values of 3700 and 21 M^{-1} cm^{-1} for ϵ_{436} and $\Delta\epsilon_{436}$, respectively, for *E*,*E*-**2** at 436 nm, we calculated a value of *g*/2 of 0.28% for the photoisomerization path from *E*,*E* to *E*,*Z*. The remaining contribution to the ee (0.82%) can be attributed to the reaction from *E*,*Z* to *E*,*E*. In fact, the photochemically generated (*S*)-*E*,*Z*-**2** exhibited the sign opposite to that of the corresponding *E*,*E* enantiomer in its value of $\Delta\epsilon_{436}$.[11] Unfortunately, it is difficult to isolate pure (*S*)-*E*,*Z*-**2** to estimate the actual values of $\Delta\epsilon_{436}$ and *g*/2 for the photoisomerization path from *E*,*Z* to *E*,*E*.

In summary, we have synthesized bicyclic azobenzene dimers that possess enantiomers whose racemization rates could be controlled reversibly through *E*−*Z* photoisomerization of the azobenzene units. Upon alternating the exposure to *r*- and *l*-CPL, we were able to repeatedly perform partial enrichment of (*S*)- and (*R*)-enantiomers, respectively. We believe that such an enantiodifferentiating photoisomerization of new bicyclic azobenzene dimers can be applied to a type of rewritable recording medium that can record with CPL and read through changes in the optical rotation at wavelengths beyond the absorption range.

Supporting Information Available: Preparation of *rac*-**1** and **2**; CIF data of X-ray crystal structure of *rac*-**1** and **2**; change of absorption spectra of *rac*-**2**; separation, absorption, and CD spectra of the enantiomers of **2**; HPLC traces of the racemates and enantiomers of **2** before and after photoirradiation. This material is available free of charge via the Internet at http://pubs.acs.org.

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