DOI: 10.1002/chem.200902123

A Light-Controlled Molecular Brake with Complete ON–OFF Rotation

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Abstract: A light-controlled molecular machine based on cyclic azobenzenophanes consisting of a dioxynaphthalene rotating unit and a photoisomerizable dioxyazobenzene unit bridged by methylene spacers is reported. In compounds **1** and **2**, 1,5- and 2,6-dioxynaphthalene moieties, respectively, are linked to *p*-dioxyazobenzene by different methylene spacers ($n=2$ in **1a** and **2**; $n=3$ in **1b**), whereas a 1,5-dioxynaphthalene moiety is bonded to *m*-dioxyazobenzene by bismethylene spacers in **3**. In **1b** and **2**, the naphthalene ring can rotate freely in both the *trans* and *cis* states at room temperature. The rotation speed can be controlled either by photoinduced reversible *trans–cis* (*E–Z*) isomerization of the azobenzene or by keeping the system at low temperature, as is evident from its NMR spectra. Furthermore, for the first time, we demonstrate a light-controlled molecular brake, wherein the rotation of the naphthalene moiety through the cyclophane is completely OFF in the *trans* isomer of compound **3** due to its smaller cavity size. Such restricted rotation imparts planar chirality to the molecule, and the corresponding enantiomers could be resolved by chiral HPLC. However, the rotation of the naphthalene moiety is rendered ON in the *cis* isomer due to its increased cavity size, and it is manifested experimentally by the racemization of the separated enantiomers by photoinduced *E–Z* isomerization.

Keywords: azo compounds · molecular brake · molecular machines · photochemistry · photoisomerization

Introduction

The ability to control motion at a molecular level is one of the prerequisites for the design of molecular machines.[1] Many efforts have been directed towards the design of chemically- or light-controlled linear and rotary motions.[1,2] Among the most elegant examples have been the "molecular brakes" designed by Kelly and co-workers,[3] which consisted of a rigid triptycene wheel with a bipyridyl molecular recognition unit as a brake. This chemically-controlled brake was operated by coordination of a metal ion at a recognition site, which induced a conformational change that reversibly halted the rotation of the rigid triptycene wheel. However, light-controlled molecular systems have many advantages compared to chemically-controlled systems, because the formation of waste products during a chemical process will compromise the operation of the machine unless they are removed from the system as in the case of natural systems.[2b,4] One of the first attempts to design such a light-controlled system was described by Feringa and co-workers, wherein control of the rate of rotation of a xylyl rotor by *cis–trans* isomerization of a thioxanthene-based sterically overcrowded alkene was demonstrated.[5] The presence of *o*-methyl groups on the rotor was expected to cause restricted rotation about the arene–arene single bond due to steric interactions with the naphthalene moiety in the upper part of the molecule. Consequently, the rate of rotation was presumed to be different in the *cis* and *trans* isomers. J.-S. Yang and co-workers recently reported a pentiptycene-derived light-controlled molecular brake that could function at room temperature.[6] In their design, the rigid pentiptycene group served as a four-bladed wheel, and an *E–Z* photoisomerizable dinitrostyryl group functioned as a photoresponsive brake unit. In the resulting molecular brake, the pentiptycene rotor showed distinct rates of rotation in the *trans* and *cis* states, which differed by about nine orders of magnitude. In this context, it is noteworthy that a

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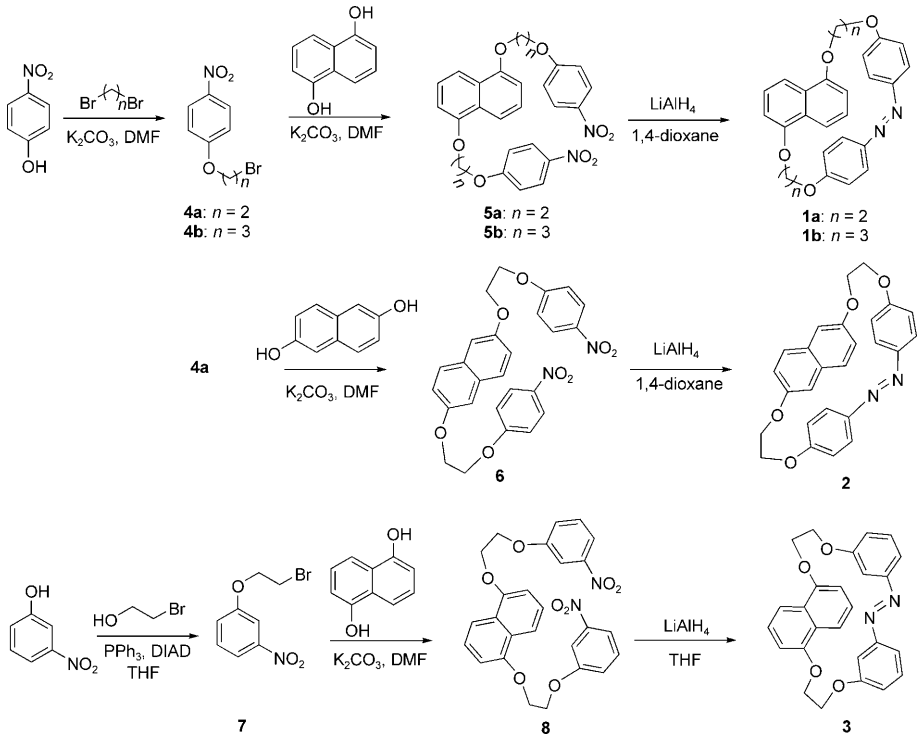
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.200902123.

molecular system with complete ON–OFF rotation has not yet been achieved.

Recently, azobenzene-containing systems have attracted much attention for the construction of light-controlled molecular-level machines due to their *E–Z* photoisomerization properties, which induce drastic changes in molecular length and occupied volume.[7] In our previous reports, we described the synthesis of some cyclic azobenzene dimers and it was observed that the isomerization of the azobenzene unit in the frame of these cycles had an enormous effect on the structure or motion of other parts of the molecules.[8] More recently, we have reported the synthesis of a cyclic azobenzenophane consisting of a 1,5-dioxynaphthalene moiety bonded at the *meta* positions of azobenzene by bismethylene spacers. This system showed conformational restriction on the free rotation of the naphthalene moiety, thereby imparting the molecule with planar chirality, and the corresponding enantiomers could be resolved and preparatively separated by chiral HPLC.[9] Photoinduced *E–Z* isomerization of this compound and its separated enantiomers proceeds without racemization, indicating that the size of the cyclophane cavity is not large enough in either the *trans* or *cis* state to allow free rotation of the naphthalene ring through it. This compound was successfully employed as a chiroptical switch in commercially available nematic liquid crystals, allowing the attainment of phototunable reflection colors. In the work described herein, a variety of cyclic azobenzenophanes with 1,5- or 2,6-dioxynaphthalene rotating units bonded at the *meta* or *para* positions of photoisomerizable dioxyazobenzene by different methylene spacers have been investigated. Furthermore, we demonstrate for the first time a "molecular brake" exhibiting a complete ON–OFF rotation, wherein rotation of the naphthalene moiety is completely OFF (brake on) in the *trans* isomer of the cyclic azobenzenophane, but is ON (brake off) in the *cis* isomer as a result of photoinduced *E–Z* isomerization of the azobenzene moiety.

Results and Discussion

Synthesis and structural characterization: A variety of cyclic azobenzenophanes (**1**–**3**) consisting of a naphthalene rotating unit linked to photoisomerizable dioxyazobenzene by methylene spacers were synthesized. In compounds **1** and **2**, 1,5- and 2,6-dioxynaphthalene units, respectively, are connected to *p*-dioxyazobenzene by different methylene spacers ($n=2$ in **1a** and **2**; $n=3$ in **1b**), while in **3** a 1,5-dioxynaphthalene unit is bonded to *m*-dioxyazobenzene by bismethylene spacers. An overview of the synthetic strategy used to obtain the target compounds is presented in Scheme 1.



Scheme 1. Synthetic route to the target compounds.

Compounds **1**–**3** were successfully synthesized by reduction of their corresponding dinitro compounds. The crude products obtained were purified by column chromatography on silica gel followed by recrystallization from CH_2Cl_2/hexane by the vapor diffusion method to obtain the required compounds in their pure *trans* forms. The structures of these compounds were determined by ^{1}H NMR, ^{13}C NMR, and mass spectrometry (ESI or MALDI-TOF). Moreover, single-crystal X-ray analyses corroborated the suggested structures of the respective compounds.

In order to obtain a preliminary insight into the rotation behavior of the naphthalene units in these azobenzenophanes, their ^{1}H NMR spectra were carefully examined. It was found that at room temperature *trans*-**1b** (600 MHz, CD_2Cl_2) displays three resonances at $\delta=2.20$, 3.86, and 4.62 ppm due to the methylene protons ($-OCH^a_2CH^b_2CH^c_2O-$), two resonances at $\delta=7.13$ and 7.18 ppm due to the azobenzene protons, and three resonances at $\delta=6.34$, 7.06, and 7.27 ppm due to the naphthalene protons (Figure 1). Correspondingly, three resonances due

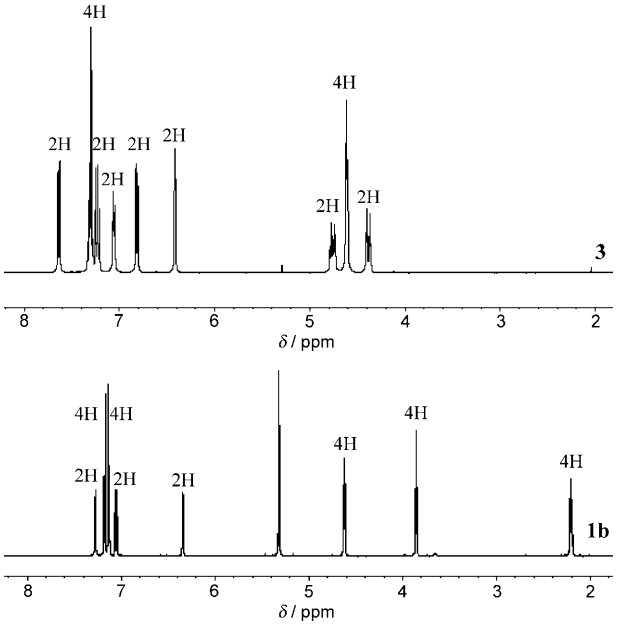


Figure 1. ^{1}H NMR spectra of **1b** and **3** in CD_2Cl_2 and $CDCl_3$, respectively, at room temperature.

to the methylene protons at $\delta = 2.26$, 3.99, and 4.45 ppm, two resonances due to the azobenzene protons at $\delta = 6.51$ and 6.58 ppm, and three resonances due to the naphthalene protons at $\delta = 6.88$, 7.18, and 7.75 ppm were obtained for *cis*-**1b**. Similar observations were made in the case of compound **2**.[10] These results suggest that rotation of the naphthalene moiety occurs rapidly on the NMR time scale. In contrast, four resonances at $\delta = 3.90$, 4.38, 4.43, and 4.69 ppm due to the methylene protons (-OCH^{a}H^{b}CH^{c}H^{d}O-), three resonances at $\delta = 6.91$, 7.20, and 7.25 ppm due to the azobenzene protons, and three resonances at $\delta = 6.23$, 6.92, and 7.11 ppm due to the naphthalene protons were observed in the case of *trans*-**1a** in $C_2D_2Cl_4$ at room temperature.[10] The room temperature ^{1}H NMR spectrum of *trans*-**3** features three resonances at $\delta = 4.38$, 4.61, and 4.76 ppm due to the methylene protons (-OCH^{a}H^{b}CH$_2^c$O-), four resonances at $\delta = 6.42$, 6.82, 7.06, and 7.64 ppm due to the azobenzene protons, and three resonances at $\delta = 7.23$, 7.29, and 7.33 ppm due to the naphthalene protons (Figure 1). In these spectra, the splitting of the aliphatic (-OCH^{a}H^b-) proton signals is due to the diastereotopic nature of the molecule when the exchange of the enantiomers is rendered slow on the NMR time scale. This feature of splitting of the aliphatic proton signals is unchanged up to 373 K in [D_6]DMSO (Figure S10 in the Supporting Information). Thus, these results suggest that restricted rotation of the naphthalene unit through the cyclophane cavity on the NMR time scale imparts planar chirality to the molecule.[9,11]

Single-crystal X-ray analysis and computational prediction of the molecular structures: Recrystallization from CH_2Cl_2/hexane by the vapor diffusion method yielded orange crystals of **1**–**3** suitable for X-ray crystal analysis. A crystal of *cis*-**1** was obtained by first dissolving *trans*-**1** in CH_2Cl_2, irradiating the solution with UV light, and then separating the corresponding *cis* product by column chromatography on silica gel. The product was subsequently recrystallized from chloroform/hexane. However, suitable crystals of *cis*-**2/3** could not be obtained in this way. The crystal structures of *trans*-**1**, *cis*-**1**, *trans*-**2**, and *trans*-**3** are shown in Figure 2. The

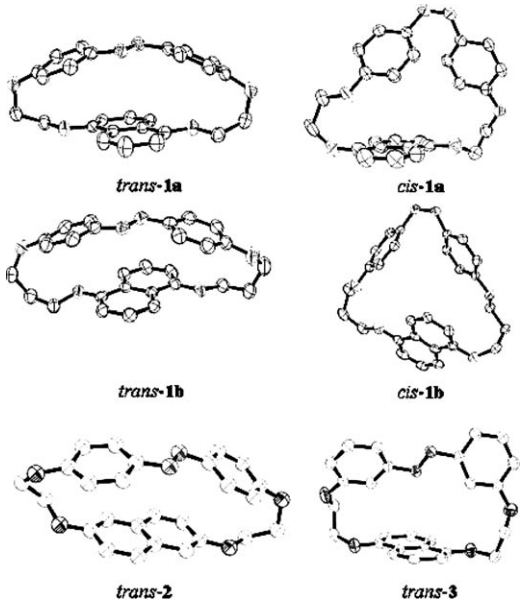


Figure 2. X-ray crystal structures of *trans*-**1**–**3** and *cis*-**1**.

most stable structure of *cis*-**3** was predicted by DFT calculation.[10] The presence of ring strain in both *trans*-**1a** and *trans*-**1b** was verified by the 12–14° deviations in the torsion angles of their C–N=N–C bonds from that (180°) of unsubstituted azobenzene.[12] Moreover, analysis of the structures obtained from single-crystal X-ray diffraction data indicated that the long axes of the azobenzene and naphthalene rotating units were close and positioned parallel to each other in the *trans* isomers of compounds **1**, **2**, and **3**. However, in the *cis* isomers of **1a**, **1b**, and **3**, the azobenzene was found to be positioned away from the naphthalene rotating unit, leaving a large cavity size that may permit fast rotation of the naphthalene unit through it.

Absorption spectra and photochemical isomerization: Figure 3 shows the changes in the absorption spectrum of **3** that occurred upon irradiation with light of wavelengths 366 and 436 nm in tetrahydrofuran (THF) at room temperature. Initially, compound **3** exhibited absorption maxima at 227 nm (ε/M^{-1}cm^{-1} 31366) and in the region 260–400 nm ($\lambda_{max} = 297$ nm, ε/M^{-1}cm^{-1} 10573). The former band is due to the ^1B_b transition of the naphthalene chromophore, while the latter is due to the ^1L_a and ^1L_b transitions of the naphthyl group and the π–π* transition of the azobenzene chromophore. Moreover, a very weak absorption band due to the n–π* transition of azobenzene at 440 nm can also be

seen. Upon irradiation with light of wavelength 366 nm to its photostationary state (PSS), due to *E–Z* isomerization, the intensity of the π–π* band decreased with no concomitant increase in the intensity of the n–π* band. The reverse spectral changes were obtained upon irradiation with light of wavelength 436 nm. We confirmed that the photochemical *E–Z* and *Z–E* isomerization processes could be repeated by alternating between irradiation at 366 and at 436 nm for more than ten cycles without any fatigue (inset in Figure 3).

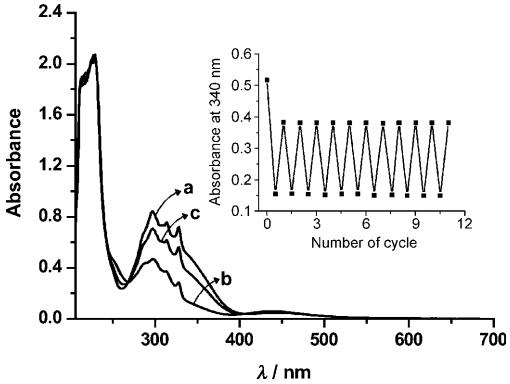


Figure 3. Evolution of the absorption spectrum of **3** in THF upon irradiation at room temperature: a) initial state before irradiation, b) PSS after irradiation at 366 nm, and c) PSS after irradiation at 436 nm (reverse reaction). The inset shows the absorption spectral changes observed at 340 nm after alternating irradiations at 366 and 436 nm over ten complete cycles.

The PSS composition of *trans*-**3** upon UV/Vis irradiation, as determined by HPLC, is discussed in the following section. Compound **1b** exists as a stable *trans* isomer in solution at room temperature when maintained in the dark, whereas compound **1a** is transformed from the *trans* to the *cis* isomer in the dark to reach an equilibrium state with an isomer ratio of 42:58. Similar phenomena have been observed for cyclic azobenzenes connected through their 4- and 4′-positions.[8g,13] In acetonitrile at room temperature, the molar extinction coefficients ($\varepsilon/M^{-1}cm^{-1}$) of *trans*-**1a** at 298, 355, and 442 nm were found to be 29855, 21600, and 1680, respectively, while those for *trans*-**1b** at 298, 358, and 452 nm were measured as 34232, 20200, and 2720, respectively. Photoirradiation of *trans*-**1/2** with UV light ($\lambda_{max}=$ 366 nm) caused the absorption spectra to change,[10] with the presence of isosbestic points indicating *E–Z* isomerization of azobenzene. Irradiation of the resulting solutions with visible light ($\lambda_{max}=436$ nm) brought about the reverse spectral changes, with the same isosbestic points as those observed for the *E–Z* reactions. By NMR analysis, the isomer compositions at the photostationary states were estimated to be 6:94 and 44:56 for **1a**, 6:94 and 50:50 for **1b**, and 12:88 and 64:36 for **2** after irradiation at 366 and 436 nm, respectively.

Variable-temperature NMR studies (VT-NMR): VT-NMR studies of compounds **1b** and **2** were conducted to determine the rates of rotation of the naphthalene unit through the cyclophane cavity. NMR spectra of *trans*/*cis*-**1b** at room temperature indicate that the naphthalene moiety rotates rapidly on the NMR time scale, showing three signals due to the aliphatic protons. However, upon decreasing the temperature from 203 to 183 K the dynamic processes are slowed, resulting in broadening of the line width and eventually leading to separation of the signals due to the methylene protons of *trans*-**1b** into six resonances at $\delta=2.16$, 2.32, 3.85, 3.90, 4.55, and 4.87 ppm, which we assign to the $CH^aH^{a'}CH^bH^{b'}CH^cH^{c'}$ protons (Figure 4). The signals of the aromatic protons of the azobenzene unit are also broadened, eventually separating into three resonances at $\delta=$ 6.85, 7.22, and 7.37 ppm (two of the four expected resonances are coincident). In contrast, the signals of the naphthalene protons remain essentially unchanged, even at 183 K, as they are unaffected by the rotation process. Similar phenomena occur in other 1,5-naphthalenophane systems.[14] It is also noteworthy that the number of signals in the NMR spectrum of *cis*-**1b** remained the same, even at 183 K (Figure S8 in the Supporting Information), which indicates that the naphthalene unit rotates more rapidly in the *cis* form than in the *trans* form due to the larger cavity of the cyclophane. NMR spectral analysis of the *trans* and *cis* isomers of compound **2** indicated that the rotation of the naphthalene unit is rapid at room temperature compared to that at lower temperatures (Figures S3 and S9 in the Supporting Information).

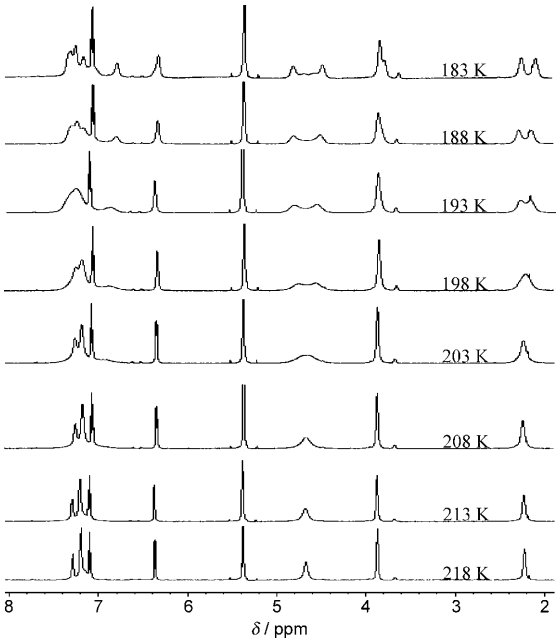


Figure 4. ^{1}H NMR spectra of *trans*-**1b** at various temperatures.

The rate of rotation of the naphthalene ring through the cyclophane cavity was determined by simulating the resonance signal of the methylene protons nearest to the naphthalene ring.[15] Simulated spectra of *trans*-**1b** with the corre-

sponding rate constants, along with matching experimental spectra at different temperatures, are shown in Figure 5. The activation parameters for its rotation obtained from the Arrhenius plot were found to be $\Delta H^{\neq} = 24.4\ kJ\,mol^{-1}$, $\Delta S^{\neq} = -67.6\ J\,mol^{-1}\,K^{-1}$, and $\Delta G^{\neq} = 37.5\ kJ\,mol^{-1}$ at 193 K. The experimental spectra of *cis*-**1b** and the well-fitted simulated spectra are shown in the Supporting Information. The various activation parameters calculated for the rotation of the naphthalene moiety in *cis*-**1b** were found to be $\Delta H^{\neq} = 27.9\ kJ\,mol^{-1}$, $\Delta S^{\neq} = -14.1\ J\,mol^{-1}\,K^{-1}$, and $\Delta G^{\neq} = 30.7\ kJ\,mol^{-1}$ at 193 K.[10] The different values of the rate constant k obtained for *trans*-**1b** ($210\ s^{-1}$) and *cis*-**1b** ($7000\ s^{-1}$) after simulation at 188 K supported the photoinduced switching of the rotational speed of the naphthalene unit through the change in size of the cyclophane cavity upon isomerization of the azobenzene unit.

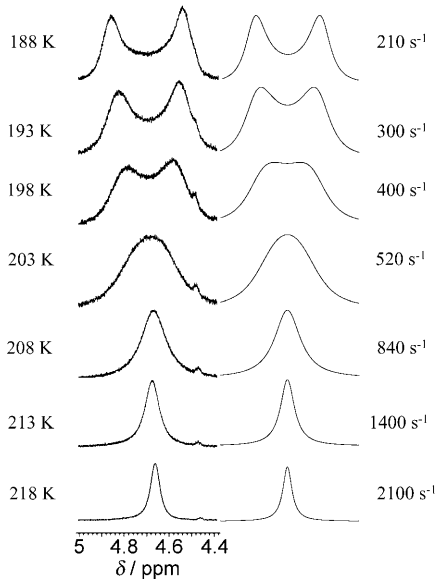


Figure 5. Temperature-dependent NMR signals of the methylene protons adjacent to the naphthalene ring (600 MHz in CH_2Cl_2) of compound *trans*-**1b** (left) and the corresponding simulated spectra with the rate constants (right).

Molecular brake with ON–OFF rotation: In cyclophanes **1b** and **2**, rotation of the naphthalene unit occurs in both the *trans* and *cis* isomers, and the speed of rotation can be controlled either by photoinduced reversible *E–Z* isomerization of the azobenzene moiety or by keeping the system at low temperature, as is evident from the NMR spectra. Nevertheless, photochemically-controlled switching on and off of the rotation is more interesting and challenging, with potential in the realm of molecular machines. The ^1H NMR spectra of compounds **1a** and **3** at room temperature provide information on the restricted rotation of the naphthalene ring through the cyclophane cavity, which can impart planar chirality to the molecule. However, optical resolution of compound **1a** was not possible by any of the chiral columns available in our laboratory. Moreover, the thermal equilibrium seen between the *trans* and *cis* isomers of this compound at room temperature may preclude optical resolution into one of the isomers. On the other hand, chiral HPLC of *trans*-**3** could be performed and the respective resolved enantiomers were separated at retention times of 28.4 min (*trans*-$\mathbf{3_A}$) and 35.1 min (*trans*-$\mathbf{3_B}$) using THF/hexane (3:7) as eluent at a flow rate of $1\ mL\,min^{-1}$ on a Chiralpak IB column (Figure 6a). Furthermore, the resolved enantiomers were isolated in pure form, as shown in Figure 6b. The photoinduced isomerization properties, as well as the isomer compositions at the photostationary states after irradiation with light of wavelengths 366 and 436 nm, were also investigated. On exposure of *trans*-**3** to light of wavelength 366 nm, *E–Z* photoisomerization was induced and a peak due to *cis*-**3** at a retention time of 44.7 min was obtained. Irradiation of the resulting solution with light of wavelength 436 nm induced the reverse reaction and hence the intensity of the *cis*-**3** peak decreased with the formation of *trans*-**3** (Figure 6a). More interestingly, photoisomerization of the first-eluted enantiomer, *trans*-$\mathbf{3_A}$, resulted in peaks consistent with completely racemized *trans*-**3** and *cis*-**3** in the photostationary states after irradiations at 366 and 436 nm, as shown in Figure 6b. Thus, the photoinduced *E–Z* isomerization of the separated enantiomers proceeded with racemization, revealing that the cavity of the cyclophane is sufficiently large in the *cis* isomer to permit rotation of the naphthalene ring through it. Thus, we succeeded in demonstrating a "molecular brake" with ON–OFF rotation function in a simple system, wherein rotation of the naphthalene unit was completely OFF (brake on) in the *trans* isomer of the cyclic azo-

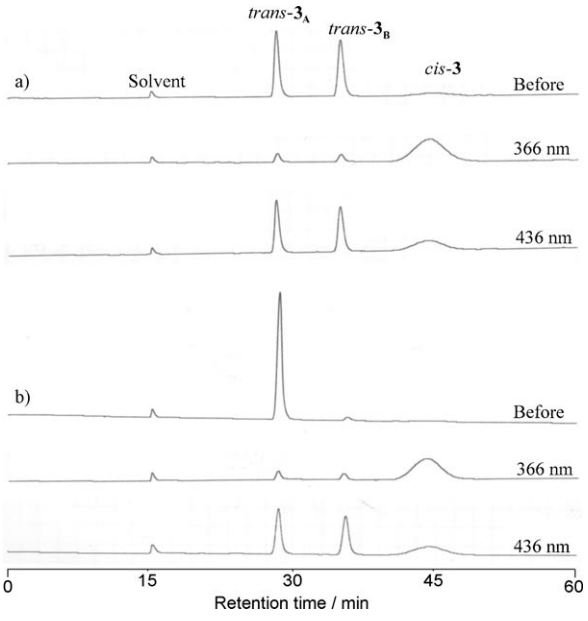
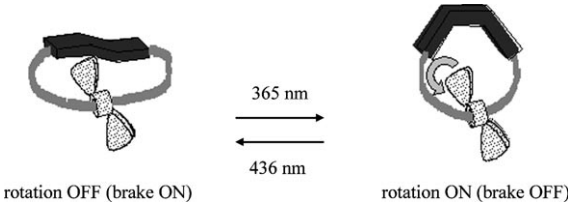


Figure 6. Chromatograms of a) a racemic mixture of *trans*-**3** before irradiation, the PSS after irradiation at 366 nm, and the PSS after irradiation at 436 nm, and b) *trans*-$\mathbf{3_A}$ before irradiation, the PSS after irradiation at 366 nm, and the PSS after irradiation at 436 nm, as obtained by chiral HPLC (Chiralpak IB column; eluent: THF/hexane, 30:70, v/v; flow rate: $1\ mL\,min^{-1}$).

benzenophane but ON (brake off) in the *cis* isomer as a result of photoinduced *E–Z* isomerization of the azobenzene moiety (Scheme 2). By chiral HPLC analysis, the PSS ratios for **3** were calculated as 16:84 (*trans*/*cis*) and 67:33 (*cis*/*trans*) after irradiation at 366 and 436 nm, respectively.



Scheme 2. Schematic illustration of the photochemically controlled molecular brake system.

To further probe the chiral properties of compound **3**, CD spectra of the pure separated enantiomers obtained after chiral HPLC were measured in THF, and the results are shown in Figure 7. It can be seen that *trans*-$\mathbf{3_A}$ shows weak negative CD bands at 294 and 444 nm, a positive CD band at 327 nm, and a strong positive exciton couplet centered at 218 nm. As expected, the second-eluted enantiomer *trans*-$\mathbf{3_B}$ showed the complete mirror image spectrum to that of *trans*-$\mathbf{3_A}$. Exposure of *trans*-$\mathbf{3_A}$ to light of wavelength 366 nm caused *E–Z* isomerization and led to a gradual decrease in the CD signal and finally a silent CD signal was obtained at the PSS. Irradiation of the resulting solution with light of wavelength 436 nm reversed the isomerization, with no signature of any CD signal.[10] Similar observations were made in the case of *trans*-$\mathbf{3_B}$.[10] Thus, CD studies were also indicative of photoinduced racemization of the pure enantiomers due to *E–Z* isomerization upon irradiation with light of wavelengths 366 or 436 nm. At temperatures below 273 K, it was possible to measure the racemization rate in the *cis* form by monitoring the change in intensity of the characteristic transient CD band at around 426 nm, with a band of opposite sign due to the *trans* isomer emerging after irradiation at 366 nm (Figure S16 in the Supporting Information).

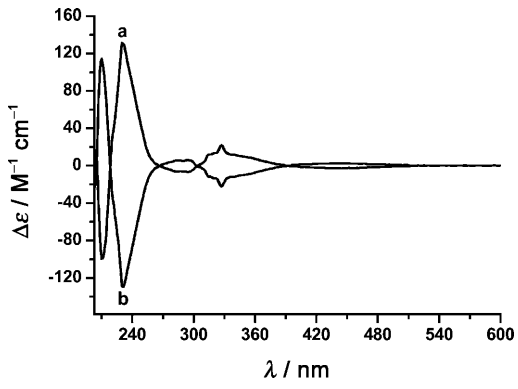


Figure 7. CD spectra of the separated enantiomers in THF at room temperature: a) *trans*-$\mathbf{3_A}$ (first-eluted enantiomer) and b) *trans*-$\mathbf{3_B}$ (second-eluted enantiomer).

The thermodynamic parameters obtained for racemization in the *cis* form were $\Delta H^{\neq} = 32.5\ \mathrm{kJ\,mol^{-1}}$, $\Delta S^{\neq} = -180\ \mathrm{J\,mol^{-1}\,K^{-1}}$, and $\Delta G^{\neq} = 81.2\ \mathrm{kJ\,mol^{-1}}$ at 193 K.[10] Hence, based on ^{1}H NMR, chiral HPLC, and CD spectral studies, we have unambiguously demonstrated the unique behavior of **3** as a molecular brake.

Conclusion

We have described the design and synthesis of a light-controlled molecular machine based on an azobenzenophane consisting of a dioxynaphthalene rotating unit and a dioxyazobenzene photoisomerizable moiety connected by methylene spacers of different lengths. In the course of our studies, three kinds of azobenzenophanes have been assembled and their molecular-mechanical properties have been investigated. Our previous study showed that a cyclophane in which a 1,5-dioxynaphthalene moiety was bonded at the *meta* positions of azobenzene by bismethylene spacers had sufficiently large conformational restriction on free rotation of the naphthalene in both the *trans* and *cis* isomers to form resolvable planar-chiral enantiomers.[9] In the current design, 1,5-dioxynaphthalene and 2,6-dioxynaphthalene units bonded at the *para* positions of dioxyazobenzene by trimethylene (**1b**) and bismethylene (**2**) spacers, respectively, have been found to function as molecular rotors with controllable rates of rotation of the naphthalene moiety through the cyclophane cavity. More interestingly, a cyclophane having a 1,5-dioxynaphthalene moiety attached to the *meta* positions of dioxyazobenzene by bismethylene spacers (**3**) has been demonstrated to function as a light-controlled molecular brake, wherein free rotation of the naphthalene unit is completely stopped in the *trans* isomer (brake on) but is switched on (brake off) in the *cis* isomer after photoinduced *E–Z* isomerization of the azobenzene. Thus, our design strategy has illustrated that control of the rotation of the naphthalene moiety can be achieved by selection of an appropriate spacer length between the rotating and isomerizing units as well as by the choice of position for attachment of the spacer. We anticipate that such control over molecular motion may be exploited in the future development of artificial molecular machines to achieve molecular-level transportation.

Experimental Section

General: All solvents and chemicals were obtained from commercial sources and used without further purification, unless otherwise stated. ^{1}H NMR (300, 400, or 600 MHz) and ^{13}C NMR (75 or 400 MHz) spectra were recorded on Varian Gemini 300, JEOL ECX 400, and Varian Gemini 600 NMR spectrometers using tetramethylsilane as an internal standard. Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) was performed on an Applied Biosystems Voyager-DE pro instrument. X-ray crystallographic data were acquired using a Bruker Smart Apex diffractometer. Absorption spectra were recorded on a JASCO J-830 spectrophotometer. CD spectra were

recorded on a JASCO J-720 spectropolarimeter. Photoisomerization studies were conducted using radiation from a super-high-pressure mercury lamp (500 W, USHIO Inc.) after passage through appropriate filters (366 or 436 nm). High-performance liquid chromatography (HPLC) was conducted on a Hitachi Elite La Chrome HPLC system using a CHIRALPAK IB column (DAICEL Chemical Industries Ltd.). Photostationary-state compositions were determined by NMR analysis in the case of compounds **1** and **2** and by HPLC analysis in the case of compound **3**. All line-shape simulations were performed using the program gNMR V4.1.0, provided by Cherwell Scientific, Oxford, Great Britain.

General procedure for the synthesis of compounds 1 and 2: A mixture of an appropriate amount of 1,5- or 2,6-dihydroxynaphthalene (20 mmol) and potassium carbonate (K_2CO_3) (20 mmol) in dry DMF (100 mL) was stirred at room temperature for 1 h. A solution of **4** (46 mmol) in DMF (50 mL) was then added, and the mixture was heated at 80 °C for 48 h. After cooling to room temperature, the solvent was distilled off under reduced pressure. The insoluble residue obtained was washed with dichloromethane (CH_2Cl_2) and aqueous K_2CO_3 solution, and dried under vacuum overnight. The highly insoluble powders containing compound **5** or **6** were used for the next step reaction without further purification. Thus, this compound (20 mmol) was added to a suspension of $LiAlH_4$ (200 mmol) in dry 1,4-dioxane (300 mL), and the mixture was heated under reflux for 48 h under a nitrogen atmosphere. After cooling the reaction mixture in an ice bath, water (20 mL) was carefully added. The precipitate formed was filtered off, and the solvent was removed from the filtrate by evaporation under vacuum. The residual orange solid was then redissolved in CH_2Cl_2, and the solution was washed with water, dried, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel followed by recrystallization from CH_2Cl_2/hexane to afford the desired product. *trans*-**1a**: Orange solid, 1.2%. ^{1}H NMR (600 MHz, $C_2D_2Cl_4$, 25 °C, TMS): δ = 7.25 (dd, J_1 = 15.6, J_2 = 7.8 Hz, 4H), 7.20 (d, J = 7.8 Hz, 2H), 7.11 (d, J = 8.4 Hz, 2H), 6.92 (t, J = 8.4 Hz, 2H), 6.91 (d, J = 7.8 Hz, 2H), 6.23 (d, J = 8.4 Hz, 2H), 4.69 (dd, J_1 = 12.6 Hz, J_2 = 7.8 Hz, 2H), 4.43 (dd, J_1 = 12.6, J_2 = 4.2 Hz, 2H), 4.38 (dd, J_1 = 12.6, J_2 = 7.8 Hz, 2H), 3.90 ppm (dd, J_1 = 12.6, J_2 = 4.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 159.3, 152.1, 149.9, 123.0, 121.7, 121.2, 115.3, 113.8, 103.2, 72.8, 66.6 ppm; MS (ESI): m/z: calcd for $C_{26}H_{23}N_2O_4$ $[M+H]^+$: 427.16; found 427.20. *trans*-**1b**: Orange solid, 2.5%. ^{1}H NMR (600 MHz, CD_2Cl_2, 25 °C, TMS): δ = 7.27 (d, J = 8.4 Hz, 2H), 7.18 (d, J = 8.9 Hz, 4H), 7.13 (d, J = 9.1 Hz, 4H), 7.06 (t, J = 7.7 Hz, 2H), 6.34 (d, J = 7.7 Hz, 2H), 4.62 (t, J = 5.4 Hz, 4H), 3.86 (t, J = 5.6 Hz, 4H), 2.20 ppm (q, J = 5.5 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 162.2, 153.5, 147.7, 125.7, 124.5, 123.8, 119.1, 114.1, 104.1, 69.2, 63.4, 31.5 ppm; MS (ESI): m/z: calcd for $C_{28}H_{27}N_2O_4$ $[M+H]^+$: 455.19; found 455.24. *trans*-**2**: Orange solid, 1.0%. ^{1}H NMR (600 MHz, CD_2Cl_2, 25 °C, TMS): δ = 7.35 (d, J = 9.0 Hz, 4H), 7.12 (d, J = 8.7 Hz, 2H), 7.08 (d, J = 9.0 Hz, 4H), 6.63 (dd, J_1 = 8.7 Hz, J_2 = 2.7 Hz, 4H), 6.37 (d, J = 2.7 Hz, 2H), 4.62 (t, J = 3.6 Hz, 4H), 4.25 ppm (t, J = 3.6 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 158.1, 153.5, 148.3, 128.7, 126.9, 123.8, 121.4, 116.5, 107.1, 71.1, 65.8 ppm; MS (ESI): m/z: calcd for $C_{26}H_{23}N_2O_4$ $[M+H]^+$: 427.19; found 427.21.

Compound 7: Diisopropyl azodicarboxylate (40% in toluene) (4.36 g, 21.57 mmol) was added dropwise to a mixture of 3-nitrophenol (2 g, 14.38 mmol), 2-bromoethanol (2.2 g, 17.27 mmol), and PPh_3 (5.66 g, 21.57 mmol) in THF (10 mL) at 0 °C under an argon atmosphere. After completion of the addition, the reaction mixture was allowed to slowly warm to room temperature and stirred overnight. Thereafter, the solvent was evaporated, the residue was extracted with CH_2Cl_2, and the combined extracts were dried over anhydrous $MgSO_4$. The product was subsequently purified by column chromatography on silica gel to obtain **7** (2.5 g, 71%) as a pale-yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.24–7.87 (m, 4H), 4.38 (t, J = 6.0 Hz, 2H), 3.68 ppm (t, J = 6.0 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 158.7, 149.2, 130.3, 121.8, 116.4, 109.2, 68.5, 28.8 ppm; MS (MALDI-TOF): m/z: calcd for $C_8H_9BrNO_3$ $[M+H]^+$: 245.97; found: 245.28.

Compound 8: A stirred mixture of compound **7** (1.8 g, 7.32 mmol), 1,5-dihydroxynaphthalene (509 mg, 3.18 mmol), and K_2CO_3 (965 mg, 6.99 mmol) in dry DMF (10 mL) was heated at 60 °C for 12 h under an argon atmosphere. The reaction mixture was then poured into excess water (100 mL) and the precipitate formed was collected by filtration and washed with ethyl acetate to obtain the pure compound **8** (1.1 g, 71%) as a brown solid. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 6.89–7.88 (m, 14H), 4.51–4.56 ppm (m, 8H); MS (MALDI-TOF): m/z: calcd for $C_{26}H_{23}N_2O_8$ $[M+H]^+$: 491.14; found: 491.24.

***trans*-3**: A solution of compound **8** (1.0 g, 2.04 mmol) in dry THF (300 mL) was added dropwise over 4 h to a solution of $LiAlH_4$ (776 mg, 20.4 mmol) in dry THF (100 mL) under an argon atmosphere. The reaction mixture was refluxed during the addition of the dinitro compound and was then left to stir at room temperature for 12 h. After cooling the mixture in an ice bath, the reaction was carefully quenched by the addition of water. The precipitate formed was filtered off and the solvent was evaporated under reduced pressure. The residual orange solid obtained was redissolved in ethyl acetate, and this solution was washed with water and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the product was purified by column chromatography on silica gel to afford **1** (70 mg, 8%) as an orange solid. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.64 (d, J = 8.6 Hz, 2H), 7.33 (d, J = 7.7 Hz, 2H), 7.29 (d, J = 6.0 Hz, 2H), 7.23 (t, J = 8.04 Hz, 2H), 7.06 (tt, J = 2.3 Hz, 2.4 Hz, 2H), 6.82 (d, J = 7.68 Hz, 2H), 6.42 (s, 2H), 4.76 (dt, J = 5.3, 4.76 Hz, 2H), 4.61 (t, J = 3.28 Hz, 4H), 4.38 ppm (tt, J = 3.4 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 147.4, 142.8, 142.3, 123.6, 122.1, 120.1, 116.7, 114.3, 112.2, 106.7, 105.2, 73.9, 73.5 ppm; MS (MALDI-TOF): m/z: calcd for $C_{26}H_{23}N_2O_4$ $[M+H]^+$: 427.16.

Acknowledgements

This work was supported by a grant-in-aid for science research in a priority area "New Frontiers in Photochromism (No. 471)" from the Ministry of Education, Culture, Sports, Science, and Technology (MEXT), Japan. We thank Dr. Midori Goto and Ms. Hiroko Kobashi from AIST Tsukuba for helping with the X-ray crystallographic and variable-temperature ^{1}H NMR spectroscopic analyses, respectively.

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[10] See the Supporting Information.

[11] It is well known that the azo moiety N=N is rotating very rapidly, even in the macrocyclic structure.[8] Hence, a 3,3-disubstituted azobenzene has reflection symmetry with the plane passing through the center of the azo moiety and perpendicular to the azobenzene plane. This means that the azobenzene plane cannot be the plane for an element of planar chirality, and that the rotation of the azobenzene has no effect on whether or not the molecule has an element of planar chirality.

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[15] All line-shape simulations were performed using the gNMR V4.1.0 program, provided by Cherwell Scientific, Oxford (UK).

Received: July 30, 2009
Revised: December 3, 2009
Published online: February 5, 2010

