Chirality Switch

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# A Bridged Azobenzene Derivative as a Reversible, Light-Induced Chirality Switch**

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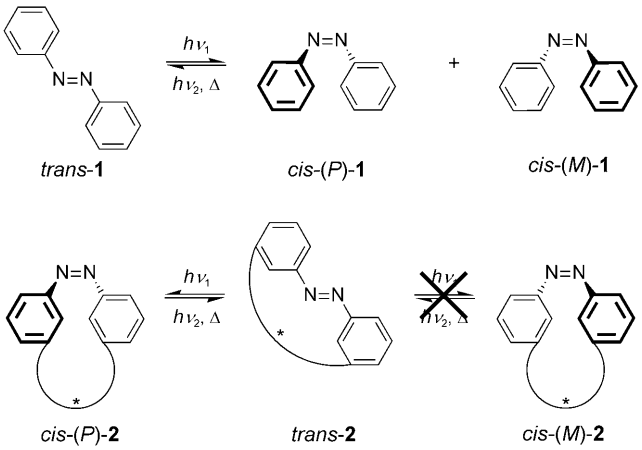
*Dedicated to Professor Rolf Gleiter*

Photochromic molecules, which can be switched reversibly between two isomeric forms having different structures and properties, are of great interest for the development of optical memory devices,[1] and molecular motors[2] and machines.[3] A prominent example of a light-induced switching process is the *trans*→*cis* isomerization of azobenzene and its derivatives.[4–6] The high-amplitude change between the stretched *trans* form and the compact *cis* isomer, the relatively high reversibility, and the photostability which allows a multitude of switching cycles, make azobenzene derivatives among the most frequently used switching devices.[2–6] A closer look at the switching process of azobenzene shows that the transition of the *trans* to the *cis* isomer implies not only a structural change but also the generation of helical chirality; that is, two enantiomeric *cis* isomers are formed (Scheme 1). The development of a unidirectional switching process that takes place exclusively between the achiral, planar *trans* isomer and only one of the chiral *cis* isomers would extend the range of applications of azobenzenes tremendously. Such a process would provide a switch with which, in addition to the amplitude change, a useful helical chirality element can be switched on and off.




***Scheme 1.*** Light-induced switching of azobenzene (**1**; bidirectional) and of the chiral azobenzene derivative **2** (unidirectional).

Azobenzene derivatives have been used for several switching processes in which chirality is critical, for example in molecular scissors,[7] switchable peptides,[8] and chiral nematic phases,[9] and for the stabilization of helical structures.[10,11] However, the unidirectional switching of the azobenzene unit and thus a targeted use of the helical chirality element has not been possible so far.[11] The use of circularly polarized light leads to a partially unidirectional switching of the azobenzene unit;[12] however, in solution this is followed by fast racemization of the *cis* isomers. Only in the case of tetrasubstituted alkenes with sterically demanding substituents could unidirectional light-induced switching be achieved without subsequent racemization.[13,14]

By implementation of a chiral clamp this could be, in principle, also achieved with azobenzenes (**2** in Scheme 1). The clamp should be flexible enough to allow a strong amplitude change upon *trans*→*cis* isomerization, but should simultaneously destabilize one of the *cis* conformations (here the *cis*-(*M*) isomer) to such an extent that only one isomer (here the *cis*-(*P*)-isomer) is present in solution under standard conditions.

As we had already succeeded in accomplishing a unidirectional switching of bipyridine derivatives by means of chiral cyclic imidazole peptides,[15] we decided to use the chiral clamp **3**[16] also for the synthesis of the unidirectionally switchable azobenzene **2** (Scheme 2). Simple alkylation of **3** with dibromide **4** using $Cs_2CO_3$ as the base in acetonitrile provided the desired azo compound **2** in 22 % yield. To clarify whether the azo compound **2** combines both desired properties—high amplitude change along with the energetic discrimination of one of the *cis* isomers—the structures of *trans*-**1**, *trans*-**2**, *cis*-(*P*)-**1**, *cis*-(*P*)-**2**, and *cis*-(*M*)-**2** were determined by geometry optimization using B3LYP and the 6-31G* basis set.[17] We found that the difference in energy between *trans*-**1** and *cis*-(*P*)-**1**, which amounts to 63.4 kJ mol$^{-1}$, is similar to that between *trans*-**2** and *cis*-(*P*)-**2** (57.7 kJ mol$^{-1}$) (Table 1). Hence, also for azobenzene **2**, a *trans*→*cis* isomerization should be possible under standard conditions. The high amplitude change found in azobenzene **1**, which is reflected, for example, in the change of the C2–C2′ and C5–C5′ distances, is also present in the switching process from *trans*-**2** to *cis*-(*P*)-**2**. For both azobenzenes (**1** and **2**), the *trans*→*cis* isomerzation results in a reduction of the C5–C5′ distance by

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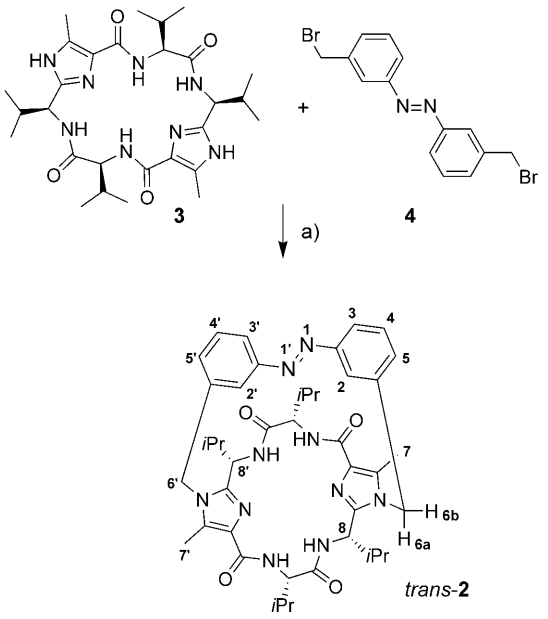



***Scheme 2.*** Synthesis of the chiral azo compound *trans*-**2**. Reaction conditions: a) $Cs_2CO_3$, $CH_3CN$, Δ, 22%.

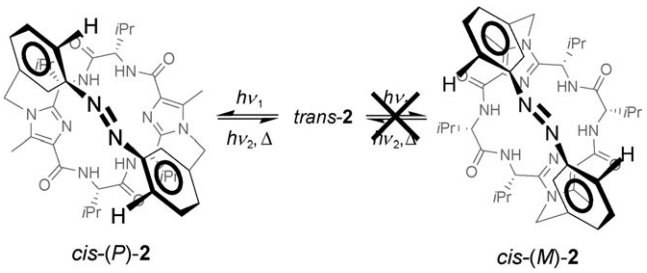
***Table 1:*** Selected experimental data and values obtained by DFT calculations (energy differences and absorption maxima in the CD spectra) of the azobenzene compounds *trans*-**1**, *trans*-**2**, *cis*-(*P*)-**1**, *cis*-(*P*)-**2**, and *cis*-(*M*)-**2**.

| | *trans*-**1** | *cis*-(*P*)-**1** | *trans*-**2** | *cis*-(*P*)-**2** | *cis*-(*M*)-**2** |
|---|---|---|---|---|---|
| $\Delta E$ [kJ mol$^{-1}$][a] | 0.0 | 63.4 | 0.0 | 57.7 | 148.2 |
| n→π* transitions: | | | | | |
| $\lambda_{max,exp.}$ [nm][b] | 449[18] | 440[18] | 442 | 406 | |
| $\lambda_{max,calcd}$ [nm][c] | 478 | 468 | 476 | 437 | 557 |
| algebraic sign of $\Delta\varepsilon$[b] | | | minus | minus | |
| algebraic sign of $\Delta\varepsilon$[c] | | minus | minus | minus | plus |

[a] Energy differences of the respective stereoisomers calculated using DFT/6-31G*. [b] [**2**] = $2.0\times10^{-4}$ M in acetonitrile. [c] Calculated using TD-DFT-PBE1PBE/6-31G* in $CH_3CN$ as solvent.

more than 2.5 Å. Comparing the energy values of the *cis* isomers (*P*)-**2** and (*M*)-**2** shows that the peptide clamp also fulfills the second requirement, namely the energetic discrimination of one *cis* isomer: the *M* isomer is destabilized by 90 kJ mol$^{-1}$ relative to the *P* isomer. This high value implies that only the *P* isomer is present in solution under standard conditions. The high destabilization of the *M* conformation results from the strong repulsive interaction between the aromatic ring of the azobenzene unit and the methyl group of the imidazole rings. Accordingly, the unidirectional switching of **2** should be possible (Scheme 3).

The photoisomerization between *trans*-**2** and *cis*-**2** was studied in dilute solution in chloroform for the NMR experiments and in acetonitrile for the UV/CD analyses. The *trans*→*cis* isomerization was induced by UV irradiation using a laser (Spectra Physics Quanta Ray) with a wavelength of 355 nm. The reverse isomerization process was achieved by irradiation with visible light or by slight warming. The recorded $^1$H NMR spectra show that after synthesis the azo




***Scheme 3.*** Unidirectional switching of the cyclic azo compound **2**.

compound **2** is present in a *trans*/*cis* ratio of 95:5. At the photostationary state at 355 nm a *trans*/*cis* ratio of 15:85 is achieved. The reverse isomerization leads back to the starting mixture without the formation of any by-products. Even after the switching cycle was repeated ten times we could not observe any sign of photochemical degradation of **2** in the NMR spectra. The lifetime of the *cis* isomer is about 5 days at 298 K in the dark. In the 2D NOESY spectra of both isomers only the *cis* isomer gives a coupling between the protons H2 and H3. This effect is due to the structural change that occurs during the isomerization process. The NOESY experiments do not afford exact distances, but the spectra show that the present *cis* isomer must be the *cis*-(*P*) conformer: There are cross-coupling signals between H5 and H8, but none between H5 and H6b, and this can be explained only by the presence of exclusively *cis*-(*P*)-**2**.

The *trans*→*cis* isomerization can also be observed in the UV spectrum by the decrease of the absorption band at 325 nm (Figure 1). This change in the π→π* band of the *trans* form is typical for isomerization of azobenzene derivatives. The n→π* band is shifted from 446 nm to 413 nm as a result of the *trans*-to-*cis* isomerization. A corresponding hypsochromic shift of the negative Cotton effect of the n→π* band is also observed in the CD spectrum (Table 1). Simultaneously, a positive Cotton effect at 242 nm is observed for the *cis* isomer. The reverse isomerization leads back to the original spectrum.

For a better assignment and interpretation of the absorption spectra, the UV and CD spectra of *trans*-**1**, *trans*-**2**, *cis*-(*P*)-**1**, *cis*-(*P*)-**2**, and *cis*-(*M*)-**2** in acetonitrile as solvent were simulated on the basis of time-dependent density functional theory (TD-DFT) with the PBE1PBE functional and by employing the 6-31G* basis set.[17] As the intensities of the calculated curves are always higher, they were normalized to the experimentally determined intensities. Both the UV and the CD spectra for *trans*-**2** are in good agreement with the experimental spectra (Figures 1 and 2). In both CD spectra there is a strong positive Cotton effect at roughly 200 nm, a negative Cotton effect at about 250 nm, and in particular a negative Cotton effect of the n→π* transition at values above 400 nm (Table 1).

The experimentally determined spectrum of the *cis* isomer is in agreement only with the spectrum of *cis*-(*P*)-**2**, but not with that of the *cis*-(*M*)-**2**. Accordingly, only the *cis*-(*P*) isomer is present in solution, as already proved by the calculated energy differences and the NMR data. Especially noticeable are the absorption bands around 200 nm and the

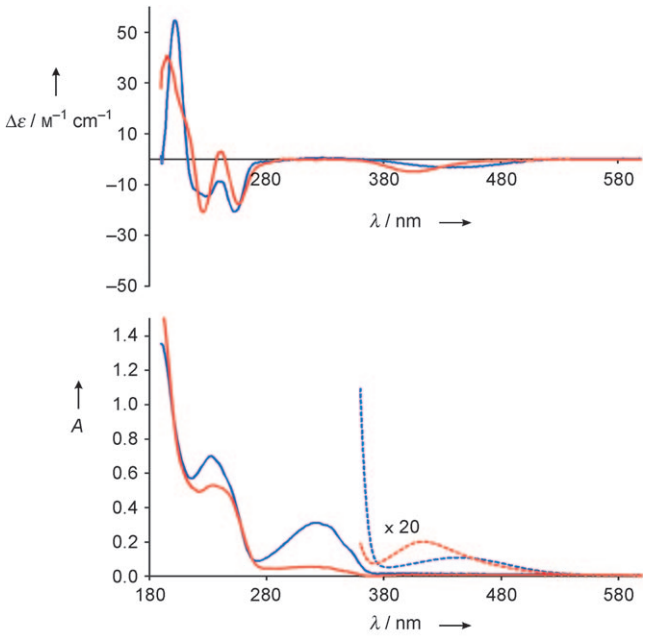



***Figure 1.*** CD spectra (top) and UV spectra (bottom) of the chiral azo switch **2** before (blue) and after (red) UV irradiation ($\lambda = 355$ nm) ($c = 2.0 \times 10^{-4}$ M in acetonitrile). The dashed lines at wavelengths exceeding 380 nm represent the 20fold enlargement of the spectra.

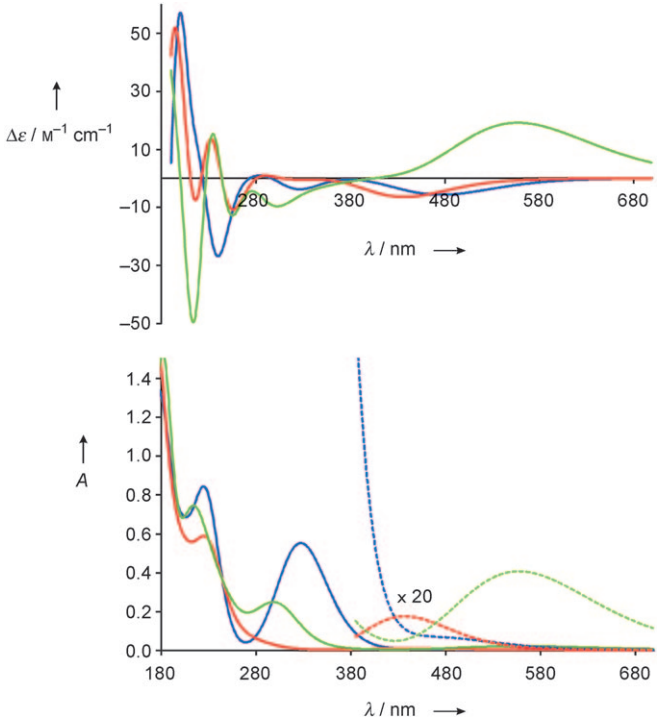



***Figure 2.*** CD (above) and UV spectra (below) of *trans*-**2** (blue), *cis*-(*P*)-**2** (red), and *cis*-(*M*)-**2** (green) calculated using TD-DFT-PBE1PBE/6-31G*. The dashed lines at wavelengths exceeding 380 nm represent the 20-fold enlargement of the spectra.

n→π* bands: In the experimentally determined spectrum of the *cis* isomer as well as in the calculated spectrum of *cis*-(*P*)-**2**, the band at 200 nm is strongly positive, while the n→π* band is negative and hypsochromically shifted relative to the analogous band of the *trans* isomer. Since the n→π* bands of the simple azobenzene *cis*-(*P*)-**1** also show negative values (Table 1), this is definite evidence for the existence of the azo unit in the *P* conformation. In the calculated spectrum of *cis*-(*M*)-**2** the opposite effect is evident: The Cotton effect at 214 nm is strongly negative and the n→π* band is positive and bathochromically shifted relative to the analogous band of the *trans* isomer. The calculated spectra thus prove unambiguously that the azo compound *trans*-**2** is switched unidirectionally to the *cis*-(*P*) isomer.

In summary we could show that by the use of a chiral clamp it is possible to switch the azobenzene unit unidirectionally by irradiation with light. Thus the range of applications of azobenzene derivatives has been extended by an important effect: Beside the amplitude change, the switchable chirality element can also be used in a deliberate way. Because of the simple synthesis of the azobenzene derivative **2** and possibilities for further substitution (at C3, C4, and C5), **2** may be used for prospective novel switching processes, in which chirality of the switched states plays an important role.

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