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Enantiopure Sulfinyl Azobenzenes as Chiroptical Switches

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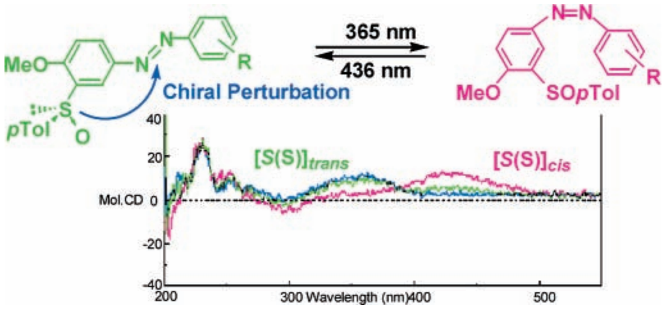
ABSTRACT



Photoswitchable enantiopure sulfinyl azo compounds have been synthesized. A remarkable perturbation of the azo system by the stereogenic sulfinyl moiety has been observed by CD in both the *trans* and the *cis* azobenzenes resulting by photoisomerization. After five irradiation cycles, the configurational integrity of these chiral switches remains unchanged.

The light-driven reversible isomerization between *trans* and *cis* forms of azobenzenes makes them excellent candidates for new molecular devices.[1,2] Current research of this *E/Z* isomerization has allowed design of new devices such as photoresponsive crown ethers,[3] molecular shuttles,[4] or smart nanotubes.[5] Moreover, the introduction of azobenzene dyes and liquid crystalline azobenzene materials into liquid crystal hosts has led to holographic recording and photooptic properties in patterned optical matrixes.[6,7]

Photomodulation of chiroptical properties has been studied on systems bearing azo groups included on chiral macrostructures for biological recognition,[8] photoregulation functions,[9] or photoresponsive polymers.[10] Chiral stereogenic carbons are in these cases responsible for the changes observed with chiroptical techniques, such as circular dichroism (CD), measurements of the pitch of cholesteric liquid

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(1) (a) Nanotech: The Science of Small Gets Down to Business. Special issue. *Sci. Am.* **2001**, September. (b) Astumian, R. D. *Sci. Am.* **2001**, *285*, 56−64.

(2) (a) *Photochromism; Molecules and Systems*; Dürr, H., Bouas-Laurent, H., Eds.; Elsevier Science: New York, 1900. (b) *Chem. Rev.* **2000**, *100*, 1685−1890 (monographic issue). (c) Crano, J. C.; Flood, T.; Knowles, D.; Kumar, A.; VanGemert, B. *Pure Appl. Chem.* **1996**, *68*, 1395−1398. (d) Feringa, L.; van Delden, R. A.; Ter Wiel, M. K. J. In *Molecular Switchers*; Feringa, B. L., Ed.; Wiley-VCH: Weinheim, 2001; Chapter 5.

(3) Shinkai, S.; Nakaji, T.; Nishida, Y.; Ogawa, T.; Manabe, O. *J. Am. Chem. Soc.* **1980**, *102*, 5860−5865.

(4) Murakami, H.; Kawabuchi, A.; Kotoo, K.; Kutinake, M.; Nakashima, N. *J. Am. Chem. Soc.* **1997**, *119*, 7605−7606.

(5) Banerjee, I. A.; Yu, L.; Matsui, H. *J. Am. Chem. Soc.* **2003**, *125*, 6542−6543.

(6) Kelker, H.; Hatz, R. *Handbook of Liquid Crystals*; Verlag Chemie: Weinheim, 1980.

(7) (a) Kubo, S.; Gu, Z.-Z.; Takahashi, K.; Ohko, Y.; Sato, O.; Fujishima, A. *J. Am. Chem. Soc.* **2002**, *124*, 10950−10951. (b) Kubo, S.; Gu, Z.-Z.; Takahashi, K.; Fujishima, A.; Segawa, H.; Sato, O. *J. Am. Chem. Soc.* **2004**, *126*, 8314−8319. (c) Urbas, A.; Tondiglia, V.; Natarajan, L.; Sutherland, R.; Yu, H.; Li, J.-H.; Bunning T. *J. Am. Chem. Soc.* **2004**, *126*, 13580−13581.

(8) (a) Srinivas, O.; Surolia, A.; Jayaraman, N. *J. Am. Chem. Soc.* **2002**, *124*, 2124−2125. (b) Caamaño, A. M.; Vázquez, M. E.; Martínez-Costas, J.; Castedo, L.; Mascareñas, J. L. *Angew. Chem., Int. Ed.* **2000**, *39*, 3104−3107. (c) Yashima, E.; Noguchi, J. Okamoto, Y. *Macromolecules* **1995**, *28*, 8368−8374.

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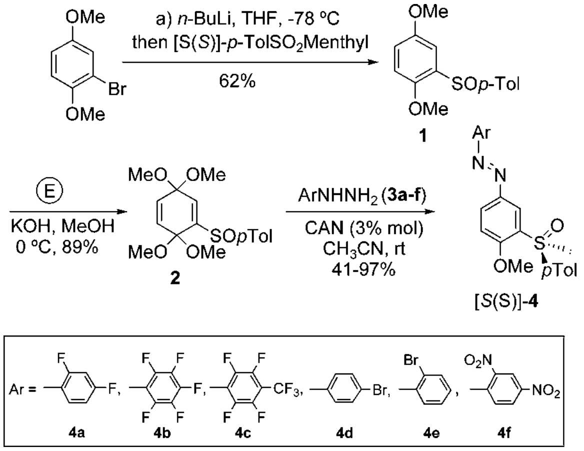
crystals, or optical rotation. Photoinduced chirality was observed by irradiating an achiral azobenzene containing polymer with circularly polarized light.[11] Axially chiral azobenzenes, derived from binaphthyls, were reported to behave as chiroptical switches,[12] but simple analogues with central chirality have been barely explored.[10,12b]

Despite the extensive use of sulfoxides in asymmetric synthesis,[13] there are no examples of their incorporation into chiral molecular switches. Recently, we have reported a new synthesis of azobenzenes bearing a variety of substituents on the aromatic fragments from quinone bisacetals and aryl hydrazines.[14] We now report on the synthesis and chiroptical properties of enantiopure sulfoxides with an azobenzene core. The preliminary studies reported herein illustrate a chiral perturbation in both the *trans* and the *cis* isomers from the sulfoxide to the azobenzene moiety, as a consequence of the extended conjugation. The influence of different substitution of the aromatic rings on the photoisomerization process is evidenced.

The starting enantiopure [S(*S*)]-2-*p*-tolylsulfinyl-1,1,4,4-tetramethoxy-2,5-cyclohexadiene **2**,[15] was readily available from 2-bromo-1,4-dimethoxybenzene, following the sequence metalation-sulfinylation[16] and anodic oxidation of the resulting 2-*p*-tolylsulfinyl-1,4-dimethoxybenzene [S(*S*)]-**1**. Reaction of arylhydrazines **3a**−**f** with the quinone bisacetal **2** in the presence of a catalytic amount of $(NH_4)_2[Ce(NO_3)_6]$ (CAN) regioselectively yielded [S(*S*)]-3′-*p*-tolylsulfinylazobenzenes *trans*-**4a**−**f** in good to excellent yields (Scheme 1).

Scheme 1. Synthesis of 3′-[S(*S*)]-*p*-Tolylsulfinyl Azobenzenes **4**



The photoisomerization of azobenzenes **4a**−**f** was monitored by UV−vis and circular dichroism (CD). The UV−vis spectra of **4** show absorptions in the region of $\lambda < 250$ nm due to the sulfoxide and a band at 350−380 nm ($\pi \rightarrow \pi^*$ transition) related to the aromatic azo chromophore.[12c,17] When compounds **4a**−**e** were irradiated with a 150-W Xe lamp, filtered to transmit light of 365 nm, the absorptions at $\lambda < 250$ nm were not altered, whereas the intensity of the band centered at 350 nm clearly decreased: the photostationary states (PSSs) were reached in 5 min (see Figure 1 for the representative compound **4a**). This latter spectral change is a common feature of the *trans*-to-*cis* isomerization of azobenzenes.[18] The absorption spectrum of the dinitro derivative **4f** remained unchanged upon irradiation in different solvents (hexane, MeCN, EtOH, or $CHCl_3$), indicating that it undergoes a reduced photoreactivity.[19]

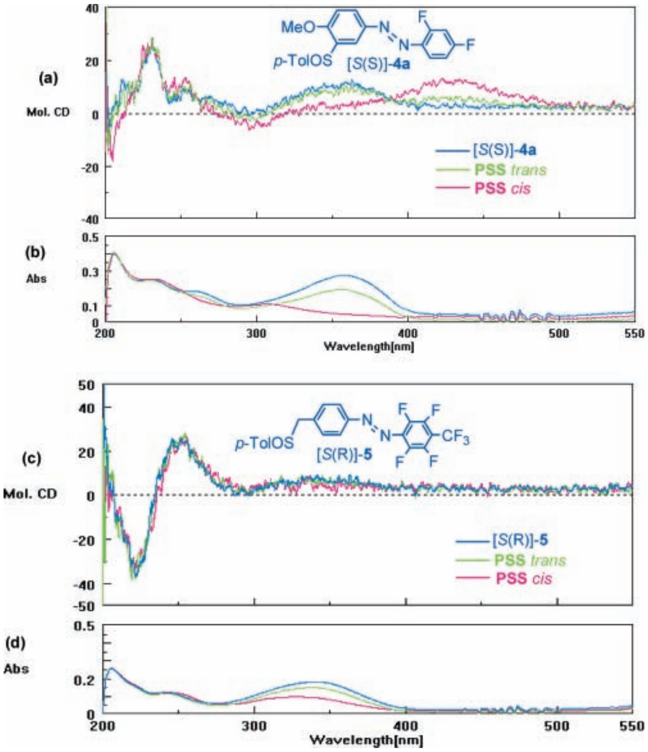


Figure 1. (a) Representative CD spectra of **4a** and (b) UV−vis spectra of **4a** (1.16 mM THF): blue line is the original spectrum of *trans*-**4a**, pink line is PSS at 365 nm (excess *cis*), green line is PSS at 436 nm (excess *trans*). (c) CD spectra of **5** and (d) UV−vis spectra of **5**: blue line is the original spectrum of *trans*-**5**, pink line is PSS at 365 nm (excess *cis*), green line is PSS at 436 nm (excess *trans*).

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(9) (a) Ulysse, L.; Cubillos, J.; Chmielewski, J. *J. Am. Chem. Soc.* **1995**, *117*, 8466−8467. (b) Matsunaga, D.; Asanuma, H.; Komiyama, M. J. *Am. Chem. Soc.* **2004**, *126*, 11452−11453 and references therein.

(10) (a) Kurihara, S.; Nomiyama, S.; Nonaka, T. *Chem. Mater.* **2000**, *12*, 9−12. (b) Kurihara, S.; Nomiyama, S. Nonaka, T. *Chem Mater.* **2001**, *13*, 1992−1997. (c) Iftime, G.; Natanshon, A.; Rochon, P. *Macromolecules* **2002**, *35*, 365−369. (d) Leclair, S.; Mathew, L.; Giguère, M.; Motabelli, S.; Zhao, Y. *Macromolecules* **2003**, *36*, 9024−9032. (e) Müller, M.; Zentel, R. *Macromolecules* **1996**, *29*, 1609−1617. (f) Mayer, S.; Maxein, G.; Zentel, R. *Macromolecules* **1998**, *31*, 8522−8525.

(11) (a) Kim, M.-J. Shin, B.-G.; Kim, J.-J.; Kim, D.-Y. *J. Am. Chem. Soc.* **2002**, *124*, 3504−3505. (b) Wu, Y.; Natanshon, A.; Rochon, P. *Macromolecules* **2004**, *37*, 6801−6805.

(12) (a) Pieraccini, S.; Masiero S.; Spada, G. P.; Gottarelli, G. *Chem. Commun.* **2003**, 598−599. (b) Pieraccini, S.; Gottarelli, G.; Labruto, R.; Masiero, S.; Pandoli, O.; Spada, G. P. *Chem. Eur. J.* **2004**, *10*, 5632−5639. (c) Van Delden, R. A.; Mecca, T. Rosini, C. Feringa, B. L. *Chem. Eur. J.* **2004**, *10*, 61−70. (d) Jaycox, G. D. *J. Polym. Sci., Part A*: *Polym. Chem.* **2004**, *42*, 566−577. (e) Lustig, S. R.; Everlof, G. J.; Jaycox, G. D. *Macromolecules* **2001**, *34*, 2364−2372.

(13) (a) Solladié, G. *Synthesis* **1981**, 185−196. (b) Carreño, M. C. *Chem. Rev.* **1995**, *95*, 1717−1760. (c) Fernández, I.; Khiar, N. *Chem. Rev.* **2003**, *103*, 3651−3705.

Also in the CD spectra of **4a**−**e** the bands corresponding to the sulfoxide at $\lambda < 250$ nm remained unaltered upon irradiation at 365 nm, showing a high configurational stability of the sulfur stereogenic center. Significant changes were instead observed in the region 360−430 nm: while the positive Cotton effect observed at 360 nm for the *trans*-isomers reduces in intensity upon irradiation, a new positive CD band at ca. 430 nm appears (see Figure 1a for **4a**). These spectral changes suggested that the *E/Z* isomerization of the azo moiety has a notable influence on the overall geometry and chirality of **4a**−**e**.[20] Upon irradiation at 436 nm, reverse CD and UV−vis spectral changes occurred: the PSSs were obtained in 5 min. The sequential irradiation was repeated five times without alteration of the CD and UV−vis spectra for the PSSs, confirming the configurational integrity of the stereogenic center.

The photoisomerization of a related enantiopure azo compound with the sulfoxide separated by a CH_2 from the azo aromatic core [S(*R*)]-**5**[21] (see Figure 1) presents a similar UV−vis spectrum, with the expected decreasing absorption band at 350 nm after irradiation, but in contrast no changes was observed in the CD spectra after irradiation at 365 and 436 nm, indicating that the photoisomerization was not influencing the chiroptical properties of this azo compound, probably as a consequence of the increased distance between the azo core and the stereogenic unit (Figure 1c and d).

The isomeric compositions (*cis*/*trans* ratio) of the photostationary states were analyzed by HPLC for compound **4a** (Table 1).[20] Irradiation of *trans*-**4a** (10^{-4} mM in ^{i}PrOH) at 365 nm provided a 97:3 mixture of *cis*/*trans* **4a**. Subsequent irradiation at $\lambda = 436$ nm resulted in a photostationary state in which 65% of azo compound reisomerized to *trans*-**4a**. Additionally, thermal back *cis*-to-*trans* isomerization of **4a** had a half-life of ca. 1 week at room temperature.

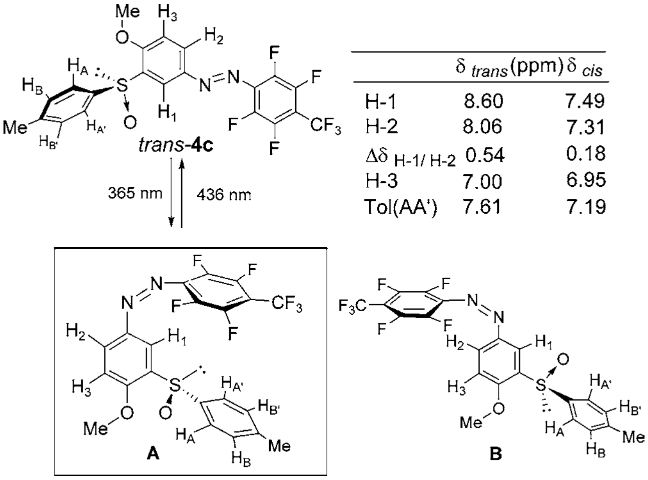
Table 1. Ratios of *trans*/*cis* Isomers of **4a** in Photostationary States in ^{i}PrOH[a]

trans:*cis*	
$\lambda = 436$	$\lambda = 365$
3:97	65:35

[a] Determined by HPLC analysis using commercially available Chiralpack OD column with hexanes/isopropyl alcohol (80/20) as eluent at 0.6 mL min^{-1}, with an isosbestic point of 210 nm. The elution order is *trans*-**4a** (15.05 min), *cis*-**4a** (21.26 min).

Trans-to-*cis* isomerization was also observed by ^{1}H NMR spectroscopy (Scheme 2). Analysis of the ^{1}H NMR of *trans*-**4c** reveals a notable deshielding for H-1 (δ 8.60 ppm). This observation suggested a fixed 1,3-parallel disposition of the sulfinylic oxygen with respect to the vicinal H-1,[22] which was confirmed by X-ray diffraction.[20] This conformation, with the *p*-tolyl group far from both the OMe and H-1, must be the most stable one.[23]

Scheme 2. ^{1}H NMR Analysis of the Photoisomerization of **4c**



	δ_{trans} (ppm)	δ_{cis}
H-1	8.60	7.49
H-2	8.06	7.31
$\Delta\delta_{\text{H-1/H-2}}$	0.54	0.18
H-3	7.00	6.95
Tol(AA')	7.61	7.19

Upon irradiation (400-W Hg lamp) at 365 nm of *trans*-**4c** (0.01 M in $CDCl_3$), a 80:20 mixture of *cis*/*trans* isomers was formed. The characteristic upfield shift of the aromatic protons in the *cis*-azobenzene unit[24] was observed after isomerization;[9a,18] this is a consequence of the nonplanar structure of *cis*-azobenzenes due to the close proximity of the aromatic rings. The δ values of some selected aromatic hydrogens, before (δ_{trans}) and after (δ_{cis}) irradiation, are shown in Scheme 2. In *cis*-**4c**, H-1 is still the most deshielded hydrogen (δ 7.49 ppm), but the small $\Delta\delta = 0.18$ ppm between H-1 *cis*/H-2 *cis* compared to the related $\Delta\delta = 0.54$ ppm in the *trans* isomer suggested the existence of a different conformation of the sulfoxide in the *cis* azo compound. Moreover, the AA′ system of the tolyl group, which appeared at δ 7.61 in *trans*-**4c**, was shielded to δ 7.19 ppm in *cis*-**4c**. These δ values suggested a disposition of the aromatic *p*-tolylsulfinyl group in the edge-face of the perfluorotolyl substituent (conformation **A**). In conformer **B**, situating the sulfoxide outside this region, the most stable disposition around the C−S bond would place the sulfinylic oxygen 1,3-parallel with H-1, and therefore the great shielding of H-1 and the AA′ tolyl group of *cis*-**4c** would not match with this arrangement. According to these observations, the sulfoxide is defining a rigid structure in both *trans*- and *cis*-**4c**, which

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(14) Carreño, M. C.; Fernández Mudarra, G.; Merino, E.; Ribagorda, M. *J. Org. Chem.* **2004**, *69*, 3413−3416.

(15) Carreño, M. C.; García Ruano, J. L.; Mata, J. M.; Urbano, A. *Tetrahedron* **1991**, *47*, 605−614.

(16) Solladié, G.; Hutt, J.; Girardin, A. *Synthesis* **1987**, 173.

(17) Suzuki, H. *Electronic Absorption Spectra and Geometry of Organic Molecules*; Academic Press: New York, 1967; p 503.

(18) See for instance: Muraoka, T.; Kinbara, K.; Kobayashi, Y.; Aida, T. *J. Am. Chem. Soc.* **2003**, *125*, 5612−5613.

(19) For a discussion on the effect of *meta*/*para* substitution on the photoreactivity of an azobenzene, see: Cisnetti, F.; Ballardini, R.; Credi, A.; Gandolfi, M. T.; Masiero, S.; Negri, F.; Pieraccini, S.; Spada, G. P. *Chem. Eur. J.* **2004**, *10*, 2011−2021.

(20) For details see Supporting Information.

(21) For synthesis of compound **5,** see ref 14.

(22) (a) Foster, A. B.; Inch, T. D.; Qadir, M. H.; Weber, J. M. *J. Chem. Soc., Chem. Commun.* **1968**, 1086−1087. (b) Cook, M. J. *Kem. Kemie* **1976**, *3*, 16.

(23) Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 7399−7400.

(24) Chambers, S. M.; Hawthorn, I. S. *J. Chem. Soc., Chem. Commun.* **1994**, 1631−1632.

could be essential for future applications. Finally, irradiation of the *cis*-rich PSS of **4c** at 436 nm led to a PSS with a 28:72 *cis/trans* composition.

In summary, we have succeeded in the design of new optically active azobenzenes whose reversible *E/Z* photoisomerization occurs quickly. The presence of the tolylsulfinyl group determines significant changes in the chiroptical properties during isomerization, as a consequence of the extended conjugation. In fact, CD variations with photoisomerization have not been observed when the sulfinyl group is not directly linked to the azobenzene. CD intensities of both *trans* and *cis* isomers remain unchanged after five irradiation cycles, indicating the configurational integrity of the stereocenter. According to these features, sulfinylazobenzenes fulfill the criteria of optical switches. The use of these chiral azobenzenes as dopants of nematics for the preparation of liquid crystal chiral switches is under investigation.

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Supporting Information Available: Experimental procedures, compound characterization data, CD and UV−vis spectra of **4b**−**f**, and HPLC and X-ray crystallography file of **4a** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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