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Photoinduced Conformational Switch of Enantiopure Azobenzenes Controlled by a Sulfoxide

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Abstract: Two series of enantiopure azobenzenes with a *p*-tolylsulfoxide at the ortho or meta position with respect to the azo group, have been regioselectively synthesized. Both can act as enantiopure molecular switches showing different structural features owing to the presence of the stereogenic sulfur. The photoisomerization process, studied by UV−vis, circular dichroism (CD), NMR, and chiral HPLC evidenced a double role of the sulfoxide. A transfer of chirality from the sulfoxide to the azo system was observed by CD in both cis and trans-isomers of the meta sulfinyl derivatives **3**, whereas this perturbation was evident for the ortho sulfinyl series **7** only in the cis isomer. The NMR study evidenced that the *s*-cis rigid conformation of the bisaromatic sulfoxide was fixing a different orientation of the overall system in each series both in the trans and cis isomers, by forcing a final U-shaped structure in *cis*-**3** and an S-shaped structure in *cis*-**7**. Very different values of specific optical rotations were measured in both trans and cis isomers, also reflecting the existence of distinct chiral entities in the photostationary states. The easy and reversible changes occurring between different conformational states could find applications in the photocontrol of several molecular switches.

Introduction

Among the strategies developed to control molecular motion, photoinduced transformations are of increasing importance because of the reversibility and selectivity that can be achieved by using light of a defined wavelength.[1] Photochemical *E/Z* isomerization of azobenzenes has been shown to be an efficient tool to modulate the relative movement of different moieties integrated into a molecule. Numerous photoswitchable devices based on the N=N photoisomerization, such as crown ethers,[2] molecular shuttles,[3] and nanotubes[4] have been reported. When included in biological systems such as polypeptides[1e,5] or enzymes[6] the photoresponse may modify the activity. The photoisomerization of an azo group can produce a change in folding and/or conformational preference of a polymer[7,8] or a dendrimer[9] evidencing that local fluctuation can be correlated with macrostructural movements. A recent study has shown that, upon irradiation, the motion of a molecule containing an azobenzene is able to regulate the movement of a complementary substrate.[10] The interconnectivity between conformation and reactivity is motivating the design of new devices both from biological and chemical systems where the local conformation

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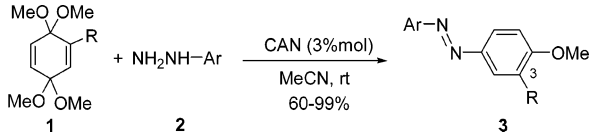
of a chromophore can be modified by irradiation thus opening the way to new applications of azobenzenes.[11]

Trans azobenzenes usually display a nearly planar structure, which after isomerization adopts a bent geometry as a consequence of the more stable edge to face orientation of both aryl groups present in the cis azo isomer.[5g,12−14] Unsubstituted or symmetrically substituted azobenzenes exist as single conformers for each *E* and *Z* isomers. The presence of ortho or meta substituents in the benzene rings introduces a structural distortion where different conformations can coexist. These features are particularly relevant in the photochromic properties of azobenzenes. When the azobenzene is included on chiral macrostructures, photomodulation of chiroptical properties has been exploited for biological recognition,[15] photoregulation functions[16] or photoresponsive polymers.[17d] Chiral stereogenic carbons are in these cases responsible for the changes observed with chiroptical techniques, such as circular dichroism (CD) or optical rotation. The few studies reported on simple analogues with central chirality as dopants for liquid crystals (LC), had shown that the helical twisting power (β),[18] a parameter measuring the influence of a dopant to torque a nematic phase in its lower concentration limit, is generally medium-to-low.[21b,19] Photoinduced chirality was observed by irradiating an achiral azobenzene containing polymer with circularly polarized light.[20] Axially chiral azocompounds, derived from binaphthyls, have been reported to induce remarkable variation in optical switching of LC.[21]

In spite of the extensive use of sulfoxides in asymmetric synthesis,[22] they have been scarcely incorporated into chiral molecular switches. To the best of our knowledge, this motif had only been involved in the nematic doping technique to determine the absolute configuration of some alkyl aryl sulfoxides.[23]

Scheme 1. Synthesis of 4-Methoxy-3-substituted Aryl Azobenzenes **3** from Subtituted *p*-Benzoquinone Bisketals **1** and Arylhydrazines **2**



1 2 3

In 2004, we reported a new synthesis of azobenzenes,[24] based on the reaction of *p*-benzoquinone bisketals **1** with arylhydrazines **2** (Scheme 1). The method was shown to be general to other *p*-benzoquinone ketals. Moreover, the soft conditions required, allowed us to introduce an enantiopure sulfoxide on the aromatic moiety without loss of configurational integrity.

Taking into account the easy incorporation of the enantiopure sulfoxide into the azobenzene, we decided to study the behavior of the resulting systems in the photoisomerization process. A preliminary investigation of the chiroptical properties of [S(*S*)]-3-*p*-tolylsulfinyl azobenzenes **3**[25] (Scheme 1, R = SO*p*-Tol), revealed that the pendant sulfoxide had a significant influence on the overall geometry and chirality of the azo moiety. With the aim of validating the role of the sulfoxide to induce a chiral perturbation on the azocompound, we embarked on the study of a series of enantiopure azobenzenes where the sulfoxide was situated at different positions. In this paper we report the regiocontrolled synthesis of a novel family of enantiopure azobenzenes where the ortho or meta position of the sulfoxide with respect to the N=N group, is able to produce a chiral perturbation on the *E* or *Z* isomers. A study of the photoisomerization by UV, CD, and NMR has revealed that, upon irradiation, the fixed conformation of the *E*-isomers undergoes a conformational change which is fully controlled by the sulfoxide. The sulfinyl azobenzenes have been tested as chiral dopants for liquid crystals by measuring the β values induced by the photoisomerization in a crystalline environment. Our previous work on the synthesis and preliminary study of the photochromic properties of 3-sulfinyl substituted azobenzenes[25] is also discussed in full detail, including results not described in our earlier communication.

Results and Discussion

Both 2- and 3-(*p*-tolylsulfinyl) azobenzenes **3** and **7** were prepared from a common enantiopure starting material, [S(*S*)]-1,4-dimethoxy-2-(*p*-tolylsulfinyl)benzene **4**,[26] readily available from 2-bromo-1,4-dimethoxy benzene after bromo-lithium exchange followed by reaction with menthyl [S(*S*)]-*p*-toluene sulfinate[27,28] (Scheme 2). The anodic oxidation of **4** (single cell, Pt/Cu, 1 A, 2 V, MeOH, KOH, 0 °C)[29] led to 2-(*p*-tolylsulfinyl)-

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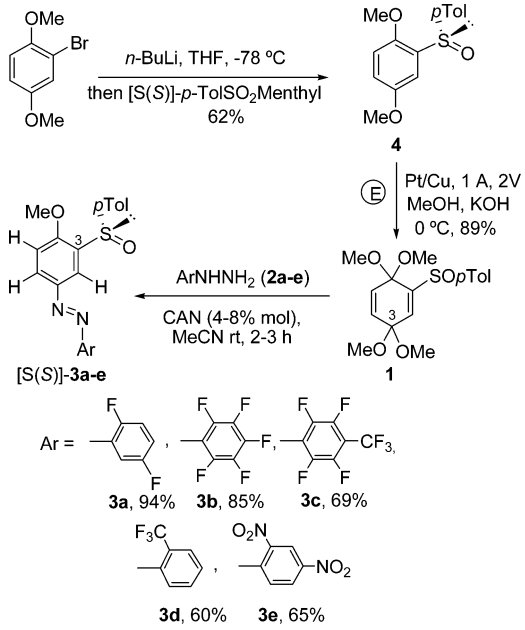
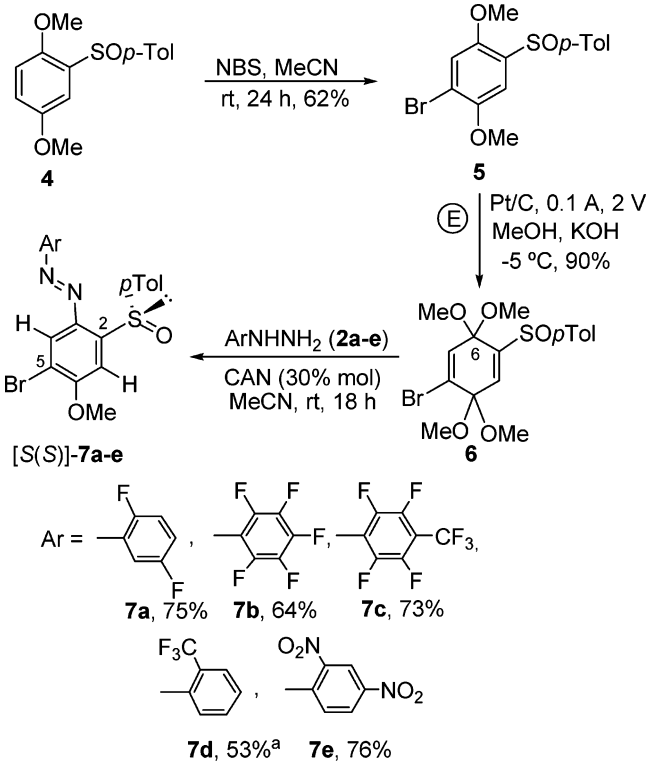
Scheme 2. Synthesis of [S(*S*)]-4-Methoxy-3-*p*-tolylsulfinyl-azobenzenes **3a**−**e**



Scheme 3. Synthesis of [S(*S*)]-5-Bromo-4-methoxy-2-*p*-tolylsulfinyl Azobenzenes **7a**−**e**[a]



[a] Reaction of **6** with *o*-$CF_3C_6H_4NHNH_2$ was performed in refluxing MeCN without CAN.

p-benzoquinone tetramethylbisketal **1** in 89% yield. Reaction of **1** with differently substituted arylhydrazines **2a**−**e**, in the presence of a catalytic amount (4−8% mol) of $Ce(NH_4)_2(NO_3)_6$ (CAN), yielded azobenzenes **3a**−**e**. This reaction led to the exclusive formation of the regioisomers situating the sulfoxide at the meta position (C-3) of the aromatic ring with respect to the azo group, in good to excellent yields (60−94%). The regioselectivity is due to the preferred attack of the arylhydrazines **2** to the less hindered dimethyl ketal group of **1**, placed far from the sulfoxide.

On the basis of this methodology, we planned the access to regioisomeric azobenzenes **7**, bearing the sulfoxide closer to the azo moiety. Taking into account the steric control of these reactions, we reasoned to direct the attack of the hydrazine to the ketal group situated close to the sulfoxide by hindering the reaction at the ketal situated far from it. With this aim, we introduced an extra bulky substituent at C-4 of the 1-*p*-tolylsulfinyl-3,3,6,6-tetramethoxy-1,4-cyclohexadiene **1**, which could direct the hydrazine attack to C-6. Considering these steric requirements, we thought of a C-4 bromo derivative. The bromine could be introduced in the precursor **4** by reaction with NBS in MeCN.[30] To our delight, aryl bromination of **4** occurred in a highly regioselective manner giving exclusively the 5-bromo-2-*p*-tolylsulfinyl derivative **5**, which precipitated from the reaction mixture and was isolated pure in 62% yield (Scheme 3). Anodic oxidation of **5** (1 A, 2 V, MeOH, KOH, 0 °C) led to a 60:40 mixture of the desired [S(*S*)]-4-bromo-1-*p*-tolylsulfinyl-3,3,6,6-tetramethoxy-1,4-cyclohexadiene **6** and the debrominated product **1**, respectively. Although it is known that in the anodic oxidation of bromo aromatic compounds a reductive debromination can occur by cathodic cleavage,[31] Swenton et al. had reported that the C−Br bond rupture can be minimized by lowering the reaction temperature to −3 °C[32] or performing the anodic oxidation in a divided cell.[33] In our case, the decrease of the temperature was not effective enough and it was necessary to optimize the electrochemical conditions. Fortunately, the anodic oxidation of **5** could be successfully conducted in a single cell apparatus using a cylindrical 5 cm diameter × 5 cm 45 mesh Pt anode and a carbon electrode situated inside as a cathode, in a methanol solution with KOH as electrolyte and lowering the current efficiency to 0.1 A and the reaction temperature to −5 °C. Under these conditions a 96:4 mixture of **6** and **1** resulted, from which compound **6** could be separated as pure by chromatography in a 90% yield (Scheme 3).

Next, we treated bisketal **6** with arylhydrazines **2a**−**e**. In all cases but one, the formation of azobenzenes was successfully achieved by treating a MeCN solution of **6** and **2** with CAN (30 mol %) at room temperature. The reaction of **6** with *ortho*-CF_3 substituted phenylhydrazine **2d** gave better yields in refluxing MeCN and in the absence of CAN. The 5-bromo-4-methoxy-2-*p*-tolylsulfinyl azobenzene derivatives **7** were obtained as single regioisomers in good yields. A detailed comparison of the behavior of both quinone bisketals **1** and **6** revealed that the formation of azobenzenes **7** required higher amounts of CAN and longer reaction times than the 3-sulfinyl substituted analogues **3**. The structure of the azocompounds **3** and **7** was inferred from their NMR parameters, including NOESY experiments (discussed later) to establish the substitution at the sulfoxide-bearing ring. Moreover, the structures of **3c** and **7b** were unequivocally assigned by X-ray crystal structure analysis (Figure 1).[34]

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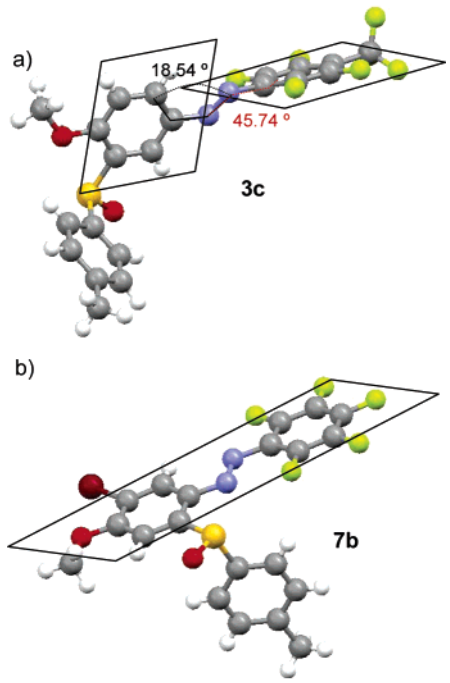


Figure 1. Molecular diagrams derived from X-ray crystal structures of (a) *trans*-**3c** and (b) *trans*-**7b**.

A comparative analysis of the X-ray crystal structures of *trans*-**3c** and *trans*-**7b** revealed that, while *trans*-**7b** adopted the general coplanar rodlike disposition of azobenzenes (Figure 1b), *trans*-**3c** displayed an uncommon torsion angle of 45.74° (red angle) for the perfluorotolyl N═N moiety and 18.54° (black angle) for the sulfinylaryl N═N fragment (Figure 1a). Such a deviation of planarity would have been more predictable for the ortho-substituted sulfinyl azobenzene, since a similar aryl rotation in ortho,ortho-disubstituted azobenzenes has been reported,[35] which is enhanced by increasing the volume of the ortho substituent. In our case, this exceptional twisted disposition must be forced by the remote aromatic ring of the sulfoxide situated at the meta position in **3c**, which is strongly influencing the overall geometry. Moreover, the conformer around the C−S bond of the sulfoxide in both **3b** and **7b** is the one situating the sulfinyl oxygen in a 1,3-parallel disposition with respect to the vicinal hydrogen (*s*-cis conformation). Although this could be influenced by the packing in the solid state, this is unlikely since the *s*-cis rotamer has been found to be the most stable in both aromatic and vinyl sulfoxides.[36]

Photoisomerization UV and CD Studies. To evaluate the changes associated with the photoisomerization of **3a**−**e** and **7a**−**e** containing the enantiopure sulfoxide, we irradiated the azobenzenes and monitored the process by UV−vis and CD in THF (**3a**−**e**) and $CHCl_3$ (**7a**−**e**).[37] The initial UV−vis spectra of both regioisomers were very similar. Two main absorption bands appeared in the trans isomer, one in the region of $\lambda <$ 250 nm where the sulfoxide group absorbs, and a band at 350−400 nm ($\pi \rightarrow \pi^*$ transition) owing to the aromatic azochromophore.[21c,38] The UV−vis spectra of **3a**−**d** and **7a**−**d** are shown in Figures 2 and 3 (b, d, f, and h), respectively. Upon irradiation with a 150 W Xe-lamp, the absorptions of the sulfoxide were not altered.

The changes observed in the absorption bands corresponding to the azo group evidenced the $E \rightarrow Z$ isomerization. A decrease of the intensity of this band was observed in all cases. These spectral changes are a common feature of the trans to cis isomerization of azobenzenes.[12] The *Z* photostationary states, PSScis, were reached in 5 min for azocompounds **3** and in 19−40 min for **7**. The different rate of photoisomerization, which is very similar in different solvents within a series, is noteworthy. A slower photoisomerization of ortho-ortho′ disubstituted azobenzenes bearing bulky substituents had been previously reported.[35] On this basis, we assume that the slower process observed in **7** must be due to the ortho sulfoxide. Thermal relaxation was much slower than the photoinduced isomerization. For example, the initial states of *trans*-**3a** and *trans*-**7d** were regained after keeping the samples in the dark for 7 and 9 days at 22−25 °C, respectively.

The absorption spectra of the dinitro-substituted derivatives **3e** and **7e** remained unchanged upon irradiation at different wavelengths and in different solvents (hexane, MeCN, EtOH, or $CHCl_3$). A very fast switching between trans and cis isomers at room temperature can be disregarded since it was already known the reduced photoreactivity of nitro-substituted azobenzenes that they cannot be used as photochemical switches.[39]

The CD spectra of the *trans*-**3a**−**d** showed two main bands: one at $\lambda <$ 250 nm,[40] corresponding to the [S(*S*)]-sulfoxide, and a second positive Cotton effect at ca. 350 nm, which was assigned to the azo group, reflecting some transfer of chirality from the sulfoxide to the azo system.[41] Upon irradiation of a THF solution of **3a**−**d** ($\lambda = 365$ nm), the CD band at 250 nm remained unaltered confirming the configurational photostability of the enantiopure sulfoxide. This configurational integrity was also verified by HPLC analysis of **3c** before and after irradiation, where no racemization was observed.

The $\pi \rightarrow \pi^*$ transition bands at 350 nm, reduced their intensity upon irradiation, while a new positive CD signal at ca. 430 nm (n $\rightarrow \pi^*$ transition) appeared (Figure 2a, c, e, and g, pink line). These spectral changes suggested that the *E*/*Z* isomerization of the azo moiety has a notable influence on the overall geometry and chirality of **3a**−**d**. The appearance of the new band at 430 nm in the cis isomers suggests that the sulfoxide is inducing a different chiral perturbation in the *E* and *Z* isomers. Reverse CD spectral changes occurred after irradiation of **3a**−**d** at $\lambda = 436$ nm for 5 min (Figure 2a, c, e, and g, green line). The sequential irradiation was repeated five times without alteration of the CD and UV−vis spectra for the PSSs, confirming the configurational integrity of these systems.

Enantiopure trans azobenzenes **7a**−**d** showed the positive CD signal at $\lambda <$ 250 nm of the sulfur stereogenic center (Figure 3a, c, e, and g, blue line). To our surprise, the dichroic signal around 350 nm for the azo group did not appear, suggesting

(34) (a) For details see Supporting Information. (b) Space group for *trans*-**3c** is *P*2(1)2(1)2(1) and for *trans*-**7b** is *P*1.
(35) Rau, H.; Yu-Quan, S.; *J. Photochem. Photobiol., A: Chem.* **1988**, 42 1631−1632.
(36) Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 7399−7400.
(37) The solvent was chosen according to the major changes observed in the CD spectra before and after irradiation.
(38) Suzuki, H. *Electronic Absorption Spectra and Geometry of Organic Molecules*, Academic Press: New York, 1967; p 503.
(39) For a discussion on the effect on 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.
(40) The lower Cotton effect observed for the sulfoxide band in **3b** is not easy to explain.
(41) The Cotton effect of such an intrinsically achiral electronic transition may be due to its coupling with the electronic transition of the chiral sulfoxide.

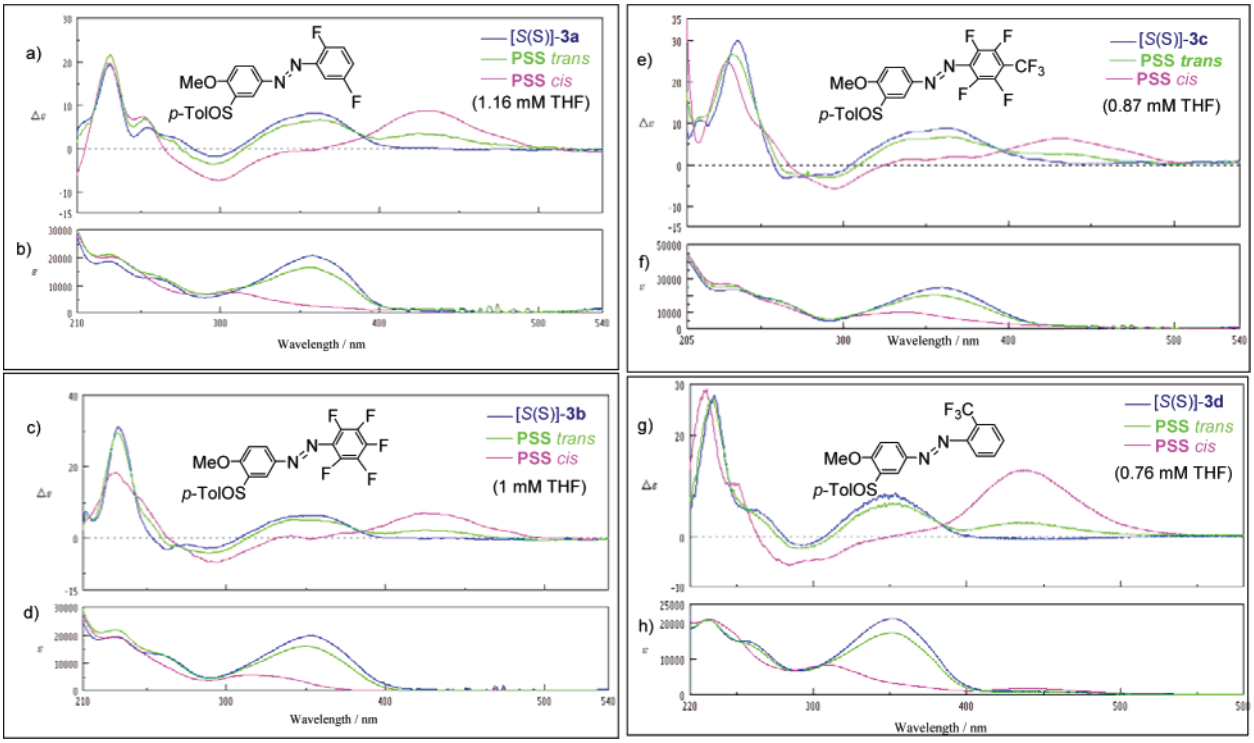


Figure 2. CD (a, c, e, and g) and UV−vis spectra (b, d, f, and h) of **3a**−**d** in THF: blue line, original spectra of trans-isomer; pink line, PSS at 365 nm (excess cis); green line, PSS at 436 nm (excess trans).

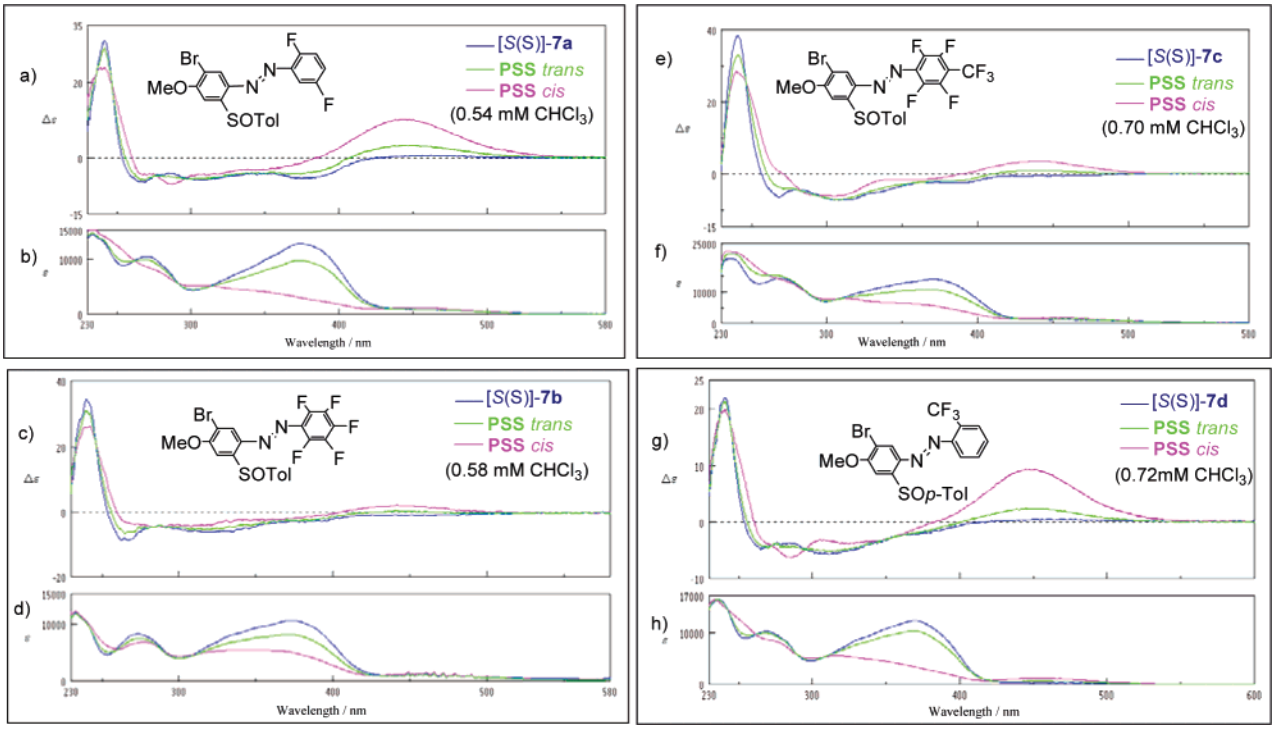
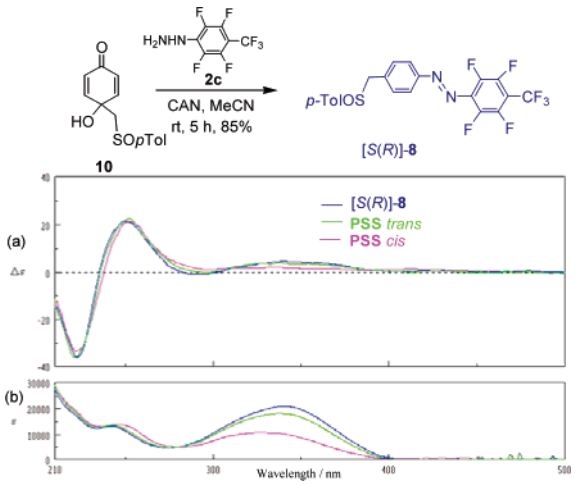


Figure 3. (a) CD (a, c, e, and g) and UV−vis spectra (b, d, f, and h) of **7a**−**d** in $CHCl_3$: blue line, original spectra of trans-isomer; pink line, PSS at 365 nm (excess cis), green line, PSS at 436 nm (excess trans).

that the ortho sulfoxide was not able to transfer the chirality so efficiently. Upon irradiation of **7a**−**d** at $\lambda = 365$ nm, the sulfoxide band remained unaltered, whereas a positive Cotton effect appeared at 450 nm when the PSScis was reached. This was especially remarkable in the cases of **7a** and **7d** (Figure 3a and g, pink line). Again, reverse CD spectral changes occurred after irradiation at 436 nm for 20−45 min.

To demonstrate that the sulfoxide directly linked to the aromatic ring was responsible for the chiral perturbation observed in the azo group, we evaluated the behavior of [S(*R*)]-2′,4′,5′,6′-tetrafluoro-4′-trifluoromethyl-4-(*p*-tolylsulfinyl)methyl azobenzene **8**, a related enantiopure azocompound with the sulfoxide separated by a CH_2 from the azo aromatic core. Compound **8** was obtained, as previously reported,[24] from [S(*R*)]-4-[(*p*-

Scheme 4. Synthesis of [S(*R*)]-2′,4′,5′,6′-Tetrafluoro-4′-trifluoromethyl-4-[(*p*-tolylsulfinyl)methyl] Azobenzene **8** and CD (a) and UV−Visible Spectra (b) in 0.75 mM THF[a]



[a] Blue line, original spectra of trans-isomer; pink line, PSS at 365 nm (excess cis); green line, PSS at 436 nm (excess trans).

tolylsulfinyl)methyl]-4-hydroxy-2,5-cyclohexadienone **10**,[42] by reaction with perfluorotolyl hydrazine **2c** (Scheme 4). The UV−vis spectrum of **8** displayed similar bands than **3** and **7**. Upon irradiation at 365 and 436 nm, UV−vis spectra showed the typical variation of the trans to cis photoisomerization. In comparison with the sulfinyl azocompounds **3** and **7**, no changes were evident in the CD spectra after irradiation at 365 and 436 nm (Scheme 4a) which suggested that, although photoisomerization occurred, the lack of conjugation between the stereogenic sulfur and the aromatic azo core was interrupting the chiral perturbation of the N═N in both trans and cis isomers of **8**.

The trans/cis ratio of the photostationary states of representative **3a**,**b**,**d** and **7a**,**b**,**d** were analyzed by HPLC.[43] Specific optical rotation ($[\alpha]^{20}_D$) values were also measured simultaneously with the chiral HPLC analysis, before and after irradiation, ensuring a correct interconnection between the trans/cis ratio and the $[\alpha]^{20}_D$ observed. The initial values of $[\alpha]^{20}_D$ given in Table 1, correspond to the specific optical rotation of the azocompound **3** or **7** using ^{i}PrOH as solvent and a concentration of $c = 0.018$. The samples were carefully prepared in the dark to avoid trans to cis isomerizations. However, in the case of azo derivatives **3**, the HPLC analysis revealed that in the initial stage, the ^{i}PrOH solution already had a considerable proportion of the *cis* isomer, especially remarkable in the case of azo **3b**, where an initial 35:65 trans/cis ratio was evident (Table 1, entry 2). The PSScis $[\alpha]^{20}_D$ represent the specific optical rotation values of the azocompound after irradiation (400 W Hg lamp) at 365 nm for the time indicated in each case.[44]

The first HPLC analysis of the 2′,5′-difluoro and 2′-CF_3-3-(*p*-tolylsulfinyl) azobenzenes **3a** and **3d** showed a 66% and a 65% of the trans isomer with an initial $[\alpha]^{20}_D$ value of +411 (**3a**) and +228 (**3d**). Upon irradiation a 16:84 (**3a**) and 13:87 (**3d**) mixture of trans/cis, with higher specific optical rotations

Table 1. Values of $[\alpha]^{20}_D$ (^{i}PrOH) and HPLC Analysis of [S(*S*)]-**3a**,**b**,**d** and [S(*S*)]-**7a**,**b**,**d**

entry	azo	initial[a] $[\alpha]^{20}_D$	initial[a] trans/cis[b]	PSScis (irradiation at λ 365) trans/cis/ (time (h))	PSScis $[\alpha]^{20}_D$[b]	$\Delta[\alpha]^{20}_D$	PSStrans (irradiation at λ 436) trans:cis/ (time (h))
1	**3a**	+411	66:34[c]	16:84/(2)	+671	260	65:35/(1)
2	**3b**	+355	35:65[c]	0:>99/(4)	+611	246	40:60/(3)
3	**3d**	+228	65:35[c]	13:87/(2)	+556	328	68:32/(3)
4	**7a**	−17	100:0[d]	33:67/(2)	+187	204	73:27/(2.5)
5	**7b**	−211	100:0[e]	67:33/(1)	+83	294	75:25/(1.5)
6	**7d**	+16	90:10[d]	25:75/(2)	+551	535	67:33/(2)

[a] Optical rotation and HPLC were recorded immediately after preparation of the corresponding solution of **3** or **7**; solvent ^{i}PrOH, $c = 0.018$. [b] Same solvent and *c* than the initial $[\alpha]^{20}_D$. [c] Chiralpack OD column, hexane/^{i}PrOH (80/20) as eluent, 0.6 mL min^{-1}. [d] Chiralpack OD column, hexane/^{i}PrOH (95/5), 0.6 mL min^{-1}. [e] Chiralpack +AD column, hexane/ ^{i}PrOH (90/10), 0.5 mL min^{-1}.

resulted (Table 1, entries 1 and 3). Similar initial trans/cis ratios were regained by irradiation at $\lambda = 436$ nm. Perfluorophenyl azo derivative **3b**, having the initially higher ratio of cis isomer (35:65 trans/cis), evolved into a PSScis with a > 99% of cis isomer and a specific optical rotation of $[\alpha]^{20}_D = +611$ and reisomerized upon irradiation at 436 nm into a 40:60 trans/cis mixture (Table 1, entry 2). The 2′,5′-difluoro derivative **7a** (initial $[\alpha]^{20}_D = -17$) and 2′-CF_3 derivative **7d** (initial $[\alpha]^{20}_D = +16$) reached a PSScis having a 33:67 (**7a**) and 25:75 (**7d**) mixture of trans/cis isomers. Again the specific optical rotation becomes higher while increasing the percentage of the cis isomer (Table 1, entries 4 and 6). This effect was outstanding in the case of **7d** whose PSScis showed an $[\alpha]^{20}_D = +551$ (Table 1, entry 6). Reisomerization afforded new photostationary states similar to the initial. Contrary to the regioisomer **3b** (Table 1, entry 2), the perfluorophenyl 2-*p*-tolylsulfinyl azo derivative **7b** was somewhat difficult to isomerize, resulting in a 67:33 mixture of trans/cis isomers after 1 h irradiation (Table 1, entry 5).[44] Despite this low cis conversion, the variation of the specific optical rotation was of similar order than the other azo derivatives studied, varying from a negative $[\alpha]^{20}_D = -211$ value to a positive $[\alpha]^{20}_D = +83$ ($\Delta[\alpha]^{20}_D = 294$). Finally, irradiation at 436 nm gave a 75:25 mixture of *trans/cis*-**7b**. From these HPLC analyses we can establish that the photoisomerization occurs on both regioisomeric sulfinyl azocompounds **3a**, **b**, and **d** and **7a**, **b**, and **d**. In comparison, higher ratios of cis isomers were reached from the 3-sulfinyl azo derivatives **3**. Variations of $[\alpha]^{20}_D$ values were similar for both systems upon reaching the PSScis states, with a significant increase around 250. Among the cases considered, the *o*-CF_3 substituted azobenzenes **3d** and **7d** displayed the higher $[\alpha]^{20}_D$ changes from PSStrans to PSScis ($\Delta[\alpha]^{20}_D$ 328 and 535, respectively). Although the photoisomerization process occurred always, the CD spectra evidenced different chiroptical responses in both regioisomers. The origin of this difference could be in the twisted molecular shape of *trans*-**3c** (X-ray crystal structure, Figure 1a), where the transfer of chirality to the N═N group observed in the CD spectra (transition $\pi \rightarrow \pi^*$ at ca. 360 nm, see Figure 2e) could be reinforced somewhat by the helicity. The planar structure of *trans*-**7b** (Figure 1b) could explain the lack of a significant positive Cotton effect in the region of the azo absorption. The positive band of the n $\rightarrow \pi^*$ transition observed at $\lambda = 430$ nm in the CD spectra of both enantiopure *cis*-**3** and *cis*-**7** must be associated to a bent structure of the cis

(42) (a) Carreño, M. C.; Pérez-González, M.; Ribagorda, M.; Houk, K. N. *J. Org. Chem.* **1998**, *63*, 3687−3693. (b) Carreño, M. C.; Pérez González, M.; Fischer, J. *Tetrahedron Lett.* **1995**, *36*, 4893−4896.
(43) The elution order is *trans*-**3a** (14.92 min), *cis*-**3a** (21.70 min), *trans*-**3b** (13.12 min), *cis*-**3b** (16.51 min), *trans*-**3d** (13.51 min), *cis*-**3d** (22.15 min), *trans*-**7a** (27.22 min), *cis*-**7a** (32.69 min), *trans*-**7b** (20.66 min), *cis*-**7b** (41.98 min), and *trans*-**7d** (29.39 min), *cis*-**7d** (34.91 min).
(44) Longer irradiation times gave same trans/cis ratio.

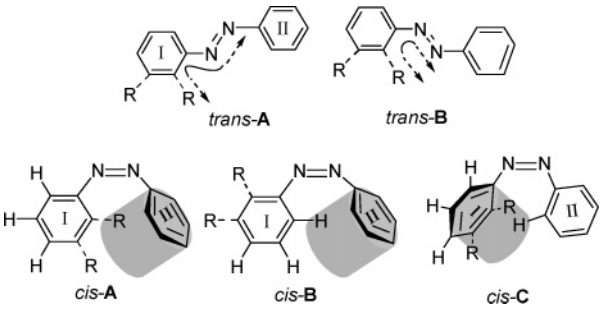


Figure 4. Possible conformations of trans and cis isomers of 2- or 3-substituted azobenzenes.

azobenzene. Taking into account the invariable CD spectrum of sulfinylmethyl azo-**8**, before and after photoisomerization (Scheme 4), it seems important as well to have the sulfoxide directly bonded to the aryl azo structure. Regarding the CD spectra of the PSScis of **7**, it is noteworthy to mention that the lower cis ratio observed in the photoisomerization process of **7b** (67:33 trans/cis) could also explain the modest variation observed in the PSScis CD spectrum (Figure 3c) compared with **7a** and **7d** (Figure 3a and g). From all these results, we can conclude that the position of the chiral sulfoxide on these systems has a notable influence on the overall chirality and the *E/Z* isomerization of the azo moiety, more significant in both *E* and *Z* isomers of the meta-substituted systems **3**. For the ortho-sulfinyl substituted analogues **7**, the chiroptical properties of the azo moiety stand out only in the *Z* isomers. Additionally, photoisomerization of regioisomers **3** is more efficient than that of **7**, reaching always better cis conversions. The associated bent structure of the *Z* isomer of azobenzenes always displayed higher values of optical rotation in both azo sulfoxides.

Photoisomerization NMR Studies. To gain a deeper insight into the geometry adopted by the trans and cis isomers we next examined the photoisomerization of **3** and **7** by ^{1}H NMR spectroscopy in $CDCl_3$. It is empirically known that cis azobenzenes present a nonplanar structure, owing to the close proximity of the aromatic rings.[5g,12−14] Caused by this bent structure, ^{1}H NMR of the trans → cis isomerization exhibits a characteristic upfield shift of the aromatic protons.[45] Before discussing the effects found in the NMR study of **3** and **7**, it is important to analyze all the conformations that can be found in the differently substituted achiral azobenzenes. Unsubstituted or symmetrically substituted azobenzenes such as para-disubstituted aromatic derivatives present a unique conformer for the trans and cis isomers. It has been reported that symmetrically 2,3-disubstituted azobenzenes can present up to three different conformations for the trans and cis isomers.[46] However, a detailed conformational analysis of an azobenzene bearing different substitution pattern in both aryl groups at ortho or meta positions has not been reported. Such azobenzenes can display up to three conformations for each isomer. In Figure 4 we have represented all the possible conformations of a general situation for a 2- or 3-substituted azobenzene. The conformer labeled *trans*-**A**, which displays the ortho R (or meta R) substituent in the opposite direction of the azo group, is more rodlike shaped. The *trans*-**B** conformer with the ortho or meta R substituent in

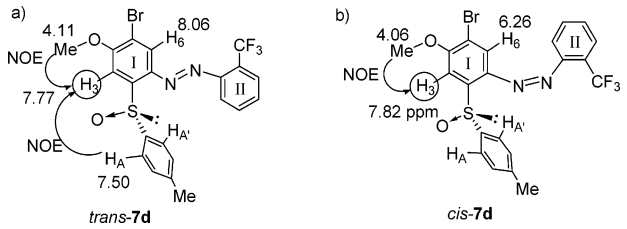


Figure 5. NOESY NMR analysis of the 5-bromo-2-*p*-tolylsulfinyl azobenzene **7d**.

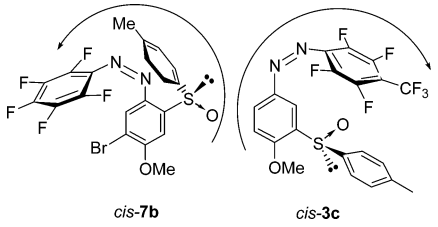


Figure 6. S-shaped and U-shaped geometry of cis *p*-tolylsulfinyl azobenzenes **7b** and **3c**.

the 1,3-parallel orientation with the N═N double bond is showing a steric interaction between R and the azo group, and should be less stable. Regarding the possible conformations for the cis isomer and assuming the favored bent structure, where one aryl ring is in the edge-face of the other, we should consider three different rotamers. The conformation labeled *cis*-**A**, which disposes the R substituent under the aromatic ring-II situated out of the plane, must be sterically congested. In such a disposition, in the NMR spectra, the chemical shift of the R substituent should be suffering the anisotropic influence of ring-II. Conformer *cis*-**B** is alleviating this steric congestion by placing the R substituent far from the influence of ring-II and the azo group. In this case, the hydrogens of ring-I must be under the influence of the orthogonal ring-II. Finally, a third conformer *cis*-**C** with the aromatic ring-I out of the plane, must be considered. In this case, the anisotropic effect should be observed in the chemical shift of the hydrogens of ring-II (Figure 4).

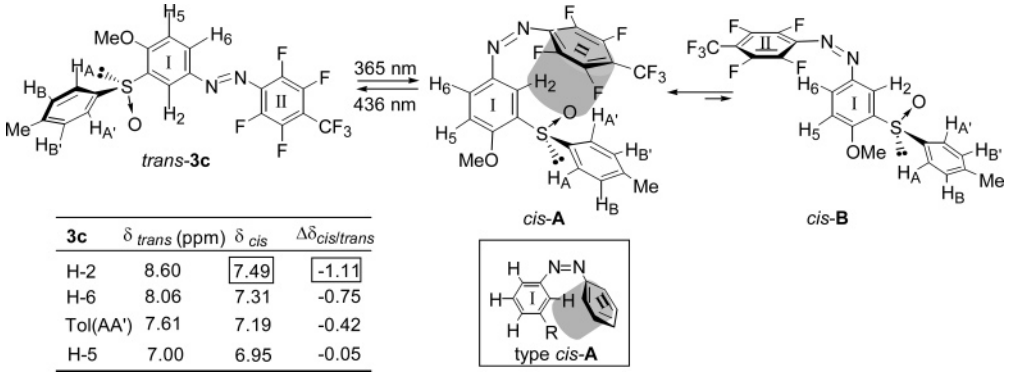
For the shake of clarity, the discussion of the possible conformations of the sulfinyl azoderivatives, will be referred to the trans and cis type conformations depicted in Figure 4, considering that the R susbtituent is the SO*p*-Tol.

The X-ray crystal structure of *trans*-**7b** (Figure 1) revealed that, in the solid state, the *trans*-**A** disposition and the *s*-cis conformation around the C−S bond are preferred. To monitor the photoisomerization of **3** and **7** by ^{1}H NMR, spectra of 0.01 M solutions in $CDCl_3$ were recorded before and after irradiation with a 400 W Hg lamp at 365 nm.[47] In all cases, but one, the mixture resulting after irradiation ranged between 70:30 and 55:45 trans/cis. The chemical shifts of the more significant protons for the conformational study of the trans and cis-isomers of **3c** are summarized in Scheme 5.

The spectrum of *trans*-**3c** discloses a noteworthy deshielding for H-2 (δ = 8.60 ppm), which is in accordance with the 1,3-parallel disposition of the sulfinylic oxygen with respect to the vicinal H-2,[48] observed by X-ray diffraction (Figure 1). After

(45) Chambers, S. M.; Hawthorn, I. S. *J. Chem. Soc., Chem. Commun.* **1994**, 1631−1632.
(46) For a similar trans-cis conformational analysis with symmetrically 2,3-disubstituted azobenzene see: Ruslim, C.; Ichimura, K. *J. Mater. Chem.* **1999**, *9*, 673−681.
(47) For spectra details of the photoisomerized azocompounds see Supporting Information.
(48) (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.

Scheme 5. ^{1}H NMR Analysis of the Photoisomerization of **3c**



3c	δ_{trans} (ppm)	δ_{cis}	$\Delta\delta_{cis/trans}$
H-2	8.60	7.49	-1.11
H-6	8.06	7.31	-0.75
Tol(AA')	7.61	7.19	-0.42
H-5	7.00	6.95	-0.05

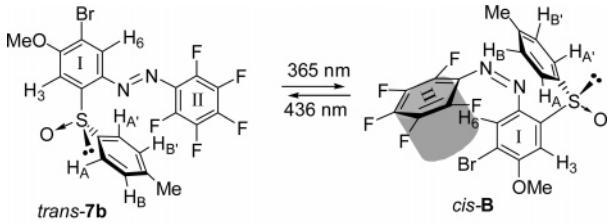
irradiation, an exceptionally high ratio of cis isomer (trans/cis of 20/80) was formed. All the signals suffer the expected shielding in the *cis*-**3c** isomer. It should be pointed out that H-2 exhibits the highest upfield shift (H-2 $\delta_{trans} = 8.60$ moves to $\delta_{cis} = 7.49$ ppm, $\Delta\delta_{cis/trans} = -1.11$ ppm) (Scheme 5). Surprisingly, despite the apparent distance between the *p*-tolyl group of the sulfoxide and the other aromatic rings, the AA′ hydrogens of the AA′BB′ system of *cis*-**3c**, suffered a significant upfield shift and appeared at $\delta_{cis} = 7.19$ ppm ($\Delta\delta_{cis/trans} = -0.42$ ppm). These observations suggested a preferred conformation situating the perfluorotolyl ring-II in the edge-face of the *p*-tolylsulfinyl group. This is a *cis*-**A** type conformation (Figure 4, R = SO*p*-Tol and Scheme 5) which from the steric point of view was not expected to be stable. Although the conformer *cis*-**B**, situating the sulfoxide outside the influence of the perfluorotolyl ring, was expected to be more favorable from the steric point of view, the NMR parameters observed did not match with the distance existing between the *p*-tolyl ring of the sulfoxide and the perfluorotolyl ring-I in such a conformation. According with these observations, the sulfoxide is defining a particular rigid conformer in both the *trans*-**3c** and *cis*-**3c**, the latter adopting a U shape, which could be essential for further applications.

The ^{1}H NMR spectrum of 2-*p*-tolylsulfinyl azocompound *trans*-**7d** showed two singlets at δ 7.77 ppm and δ 8.06 corresponding to H-3 and H-6 of the sulfoxide bearing ring-(I). The unequivocal assignment of H-3 was based on the NOE effect observed between the proton appearing at $\delta = 7.77$ ppm and the signal of the MeO group at $\delta = 4.14$ ppm,[46] and the AA′ part of the AA′BB′ *p*-tolyl system appearing at 7.50 ppm (Figure 5a). After photoisomerization of **7d**, two new singlets appeared at $\delta = 7.82$ and 6.26 ppm corresponding to H-3 and H-6, respectively. These signals were similarly assigned from NOESY NMR experiments (Figure 5b).[49]

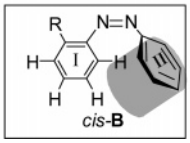
The most significant ^{1}H NMR data of both *trans*- and *cis*-**7b** are included in Scheme 6. Only H-6 suffered the expected upfield shift of the aromatic hydrogens in the isomer *cis*-**7b** ($\delta_{trans} = 8.05$ to $\delta_{cis} = 6.60$ ppm : $\Delta\delta_{cis/trans} = -1.45$ ppm), whereas an unusual small deshielding effect resulted for H-3 ($\Delta\delta_{cis/trans} = 0.02$ ppm) and the AA′BB′ system of the *p*-tolyl group (AA′: $\Delta\delta_{cis/trans} = 0.15$ ppm). These observations are consistent with the *cis*-**7b** isomer having a conformation of type *cis*-**B** represented in Scheme 6, where the perfluorophenyl aromatic ring-II is out of the plane of the azo group, in the opposite side of the *p*-tolylsulfinyl substituent. In such a

(49) Similar NOE effects were observed for **7b** and **7e** (see Supporting Information).

Scheme 6. ^{1}H NMR Analysis of the Photoisomerization of **7b**



7b	δ_{trans} (ppm)	δ_{cis}	$\Delta\delta_{cis/trans}$
H-3	7.83	7.85	0.02
H-6	8.05	6.60	-1.45
Tol(AA')	7.50	7.65	0.15



conformation, only H-6 of the 2-*p*-tolylsulfinyl aryl-substituted ring-I suffers the anisotropic effect of the ring-II.

Comparing the structures of the cis sulfinyl derivatives **3c** and **7b**, a very different disposition of the sulfoxide aromatic ring with respect to the perfluoro aryl substituent in the cis-bent structure is evident. Thus, while the conformation of azobenzene *cis*-**3c** approaches the *p*-tolyl group to the perfluorinated moiety adopting U-shaped geometry, the conformation of *cis*-**7b** is an S shape, situating the *p*-tolyl group far from the perfluorinated ring (Figure 6).

The study of azo compounds **3a** and **7a**, or **3d** and **7d**, with an dissymmetrically substituted 2′,5′-difluorophenyl or 2′-CF_3 moiety in the azobenzene, provided information about how the asymmetric substitution pattern in the aryl ring-II affected the conformation of trans and cis isomers. Here again, we have to consider that the presence of a second ortho or meta substituent in the ring-II increases the number of possible conformations. Therefore, following the same criteria, differently 2,2′- or 3,2′-disubstituted or 2,2′,5′- or 3,2′,5′-substituted azobenzenes could display up to four conformers for each trans and cis isomers. Conformers *trans*-**E**, *trans*-**F**, and *trans*-**G** depicted in Figure 7 show at least one destabilizing interaction R/N═N, whereas in conformer *trans*-**D** such interaction is not present. Conformers existent in the cis isomers could situate ring-II (Figure 7, *cis*-**D** and *cis*-**E**) or ring-I (Figure 7, *cis*-**F** and *cis*-**G**) out of the plane containing the azo group. The effects of the orthogonal rings on the chemical shifts of the aromatic substituents under their influence must be noticed on the R substituents of ring-I in *cis*-**D** and on the R′ substituent of ring-II in conformer *cis*-**F**. The hydrogens of the rings I and II in conformers *cis*-**E** and *cis*-**G**, respectively, must also suffer the anisotropic effect of the orthogonal aromatic ring-II. For later discussion, we

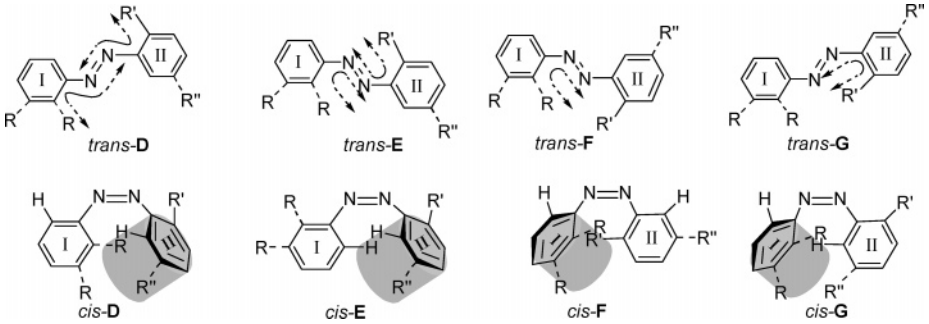
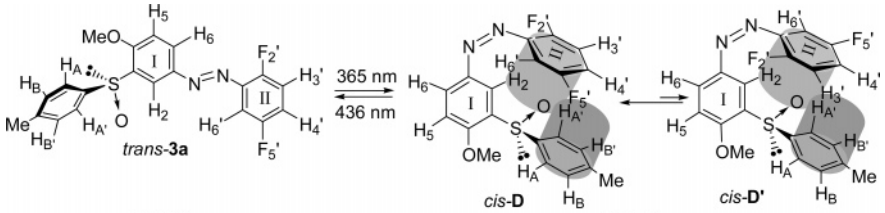


Figure 7. Conformers of trans and cis isomers of 2,2′- or 3,2′-disubstituted or 2,2′,5′- or 3,2′,5′-substituted azobenzenes.

Scheme 7. ^{1}H NMR Analysis of the Photoisomerization of **3a**



Ring-I

3a	δ_{trans} (ppm)	δ_{cis}	$\Delta\delta_{cis/trans}$
H-2	8.60	7.38	-1.22
H-6	8.03	7.31	-0.72
Tol(AA')	7.64	7.31	-0.33
H-5	6.97	6.83	-0.14

Ring-II

3a	δ_{trans} (ppm)	δ_{cis}	$\Delta\delta_{cis/trans}$
H-6'	7.48 (ddd) (J = 9.0, 5.1, and 3.1 Hz)	6.74 (ddd) (J = 7.7, 5.4, and 2.6 Hz)	-0.73
H-4'	7.15-7.11	6.90-6.86	-0.34
H-3'	7.25-7.20		-0.25

labeled ring-I to the *p*-tolylsulfinyl-substituted aryl group (R = SO*p*-Tol) and ring-II to the fluorine-bearing aryl moiety (R′ = R″ = F for **3a** and **7a** and R′ = CF_3 and R″ = H for **3d** and **7d**).

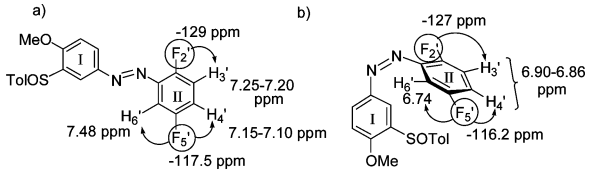
We started the NMR analysis with azo derivatives **3a** and **3d**. The ^{1}H NMR parameters of *trans*-2′,5′-difluoro-substituted azocompound **3a** were similar to those observed for **3c**. Thus, the chemical shifts of the hydrogens of ring-I appeared at δ_{H-2} = 8.60, δ_{H-6} = 8.03 and δ_{H-5} = 6.97, (table of ring-I in Scheme 7). The assignment of the aromatic hydrogens of the 2′,5′-difluoro aryl-substituted ring-II ($\delta_{H-6'}$ = 7.48, $\delta_{H-4'}$ = 7.25−7.20, $\delta_{H-3'}$ = 7.15−7.11) was based on the ^{19}F,^{1}H heteronuclear overhauser spectroscopy (HOESY) and double resonance (H,H) NMR experiments.[47] The ^{19}F,^{1}H HOESY spectrum of *trans*-**3a** exhibited two cross-peaks between the fluorine atom at −117.5 ppm and the signals appearing at δ = 7.48 and δ = 7.15−7.10 ppm, that should correspond to the interaction between F-5′ with H-6′ and H-4′ (Figure 8a). ^{19}F signal at −129 ppm showed only one NOE interaction with the ^{1}H-signal at 7.25−7.20 ppm, which consequently were assigned to F-2′ and H-3′, respectively. Additionally, the hydrogen signal at δ = 7.48 ppm (ddd, J = 9.0, 5.1, and 3.1 Hz) displayed the typical coupling constants values of a ^1J ortho (H,F) (8.9 Hz), ^2J meta (H,F) (5.7 Hz), ^2J meta (H,H) (1−3 Hz),[50], and therefore it was assigned to H-6′.

The NMR data for *cis*-**3a** are also depicted in Scheme 7. All the protons appeared more shielded than in *trans*-**3a**, but the hydrogen *cis*-H-2 is suffering the highest shielding effect ($\Delta\delta_{cis/trans}$ = −1.22 ppm). The signals corresponding to the protons of ring-II were also assigned on the base of ^{19}F,^{1}H HOESY (Figure 8b) and double resonance experiments.[47]

A considerable upfield shift was observed for proton H-6′ after photoisomerization (δ_{cis} = 6.74 ppm, $\Delta\delta_{cis/trans}$ = −0.73 ppm), while H-3′ and H-4′ appeared together as a multiplet at δ_{cis} = 6.90−6.86 ppm, with a moderate shielding effect of $\Delta\delta_{cis/trans}$ = −0.34 and −0.25 ppm, respectively (table ring-II in Scheme 7). The high shielding effect observed for H-2 of ring-I in *cis*-**3a** could match with a *cis*-**D**-type conformation placing the 2′,5′-difluorophenyl ring-II in the edge-face of the *p*-tolylsulfinyl group, where H-2 is under the influence of the anisotropic effect of ring-II. The shielding effect observed in H-6′ (aryl group-II) which appeared at δ_{cis} = 6.74 ppm, could suggest another cis conformer that situates the sulfinyl substituted ring-I out of the plane containing the azo group (*cis*-**G** (**3**) in Figure 9).

In such disposition, the hydrogens of ring-II would suffer the anisotropic effect of the orthogonal aromatic moiety (I), but it would not justify the high shielding observed for H-2 ($\Delta\delta$ = −1.22 ppm). This key observation led us to consider that the *p*-tolyl group of the sulfoxide was again playing an important role in the conformation of the *cis* -**3a** isomer, fixing the sulfinyl oxygen and H-2 in a 1,3-parallel disposition, providing an additional rigidity to the azo system, and leaving the *p*-tolyl group outside of the plane. In such a U-shaped disposition, one of the edge-faces of the substituted aryl ring-II can suffer the anisotropic π-cloud effect of this *p*-tolyl group. When this aryl ring-II is differently substituted, like in the case of **3a**, two possible conformations (*cis*-**D** and *cis*-**D′)** can be considered (Scheme 7). Thus, the *cis*-**D**-type conformation, situating the F at C-2′ (R′) substituent far from the *p*-tolyl influence, will shield the H-6′ and H-5′ ring-II protons, whereas in the *cis*-**D′** conformation this effect will turn over H-3′ and the F at C-2′ (R′) substituents. The upfield shift observed for H-6′ in the difluorophenyl substituted ring-II of *cis*-**3a** suggested the major participation of conformer *cis*-**D** where the *p*-tolyl group is oriented to exert its anisotropic effect directly on the edge face containing H-6′.

(50) Prestsch, E.; Bühlmann, P.; Affolter, C.; Herrera, A.; Martínez, R. In *Structure Determination of Organic Compounds*; Springer-Verlag: Berlin, Heidelberg, New York, 2004.



trans-**3a**	^{19}F-NMR	*cis*-**3a**
δ -129 and -117.5 ppm		-127 and -116.2 ppm

Figure 8. HOESY ^{19}F-^{1}H NMR analysis of the 3-*p*-tolylsulfinyl azobenzene **3a**.

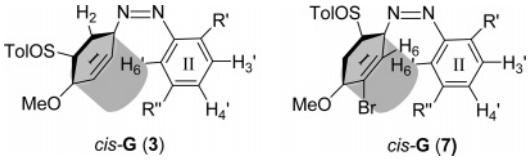
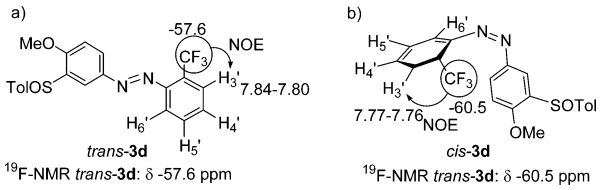


Figure 9. The *cis*-**G** conformation of 2′,5′-substituted sulfinyl azobenzenes **3** and **7**.



^{19}F-NMR *trans*-**3d**: δ -57.6 ppm

^{19}F-NMR *trans*-**3d**: δ -60.5 ppm

Figure 10. HOESY ^{19}F-^{1}H NMR analysis of the 3-*p*-tolylsulfinyl azobenzene **3d**.

Concerning the 2′-CF_3-3-*p*-tolylsulfinyl azobenzene-**3d**, the most significant changes observed in the chemical shifts of the ring-I protons in the photoisomerization process, are shown in Scheme 8 (Table Ring-I). Unfortunately, the assignment of all the protons of the trifluoromethylphenyl ring-II was difficult to pursue, because of their proximal δ values. Nevertheless, as shown in Figure 10a, the ^{1}H,^{19}F HOESY spectrum of *trans*-**3d** revealed a cross-peak between the ^{19}F signal at −57.6 ppm and the ^{1}H signal at $\delta = 7.84-7.80$ ppm which corresponded to two hydrogens belonging to ring-II.[47] This (H, F) NOE effect allowed us to assign H-3′ of *trans*-**3d** to one of the hydrogens appearing at $\delta_{trans} = 7.84-7.80$ ppm. Besides the expected chemical shift changes of the ring-I in *cis*-**3d** (Table Ring-I, δ_{cis} in Scheme 8), the most significant feature was again the presence of an upfielded signal at $\delta = 6.29-6.27$ ppm and two additional cis-signals at $\delta = 7.77-7.76$ and $7.32-7.30$ ppm. The ^{19}F,^{1}H HOESY spectrum of *cis*-**3d** revealed a ^{19}F signal at −60.5 ppm displaying a NOE interaction with the ^{1}H signal at $\delta = 7.77-7.76$ ppm, integrating for 1H, which was then assigned to *cis*-H-3′ (Figure 10b). Therefore, the new shielded signal appearing at $\delta = 6.29-6.27$ ppm should match with H-4′, H-5′, or H-6′ protons. By analogy with the upfield shift observed for H-6′ in *cis*-**3a**, we assigned the signal at $6.29-6.27$ ppm to H-5′ or H-6′. On the basis of these data, we also assumed that azocompound *cis*-**3d** adopted the *cis*-**D** type conformation shown in Scheme 8, where the *ortho*-CF_3 ring-II substituent is placed far from the anisotropic influence of the *p*-tolyl group of the sulfoxide, and therefore its effect will lay into the H-6′-H-5′ edge face of ring-II.

A similar NMR study of **7a** and **7d** evidenced the variations of chemical shifts depicted in Schemes 9 and 10, respectively, for the most significant protons of cis and trans isomers. All the ^{1}H NMR signals of sulfinyl substituted ring-I and protons of the AA′ tolyl system suffered trans to cis changes similar to those observed for the perfluorophenyl derivative **7b** (Scheme 6). The conformation *cis*-**E** represented in Scheme 9 for *cis*-**7a** and in Scheme 10 for *cis*-**7d** justifies the high shield observed for H-6 ($\Delta\delta_{cis/trans} = -1.64$ and -1.75, respectively) owing to the effect of the π-cloud of the fluorinated aryl ring-II situated out of the plane. The assignment of the hydrogens of ring-II both in *trans*-**7a** and *cis*-**7a** was based on double resonance (H,H) experiments and the values of the coupling constants (J(H,F) and J(H,H)) measured in the ^{1}H NMR spectra.[46] In the case of *cis*-**7a**, it is noteworthy that proton H-6′ also suffered a considerable shielding effect ($\Delta\delta_{cis/trans} = -1.79$ ppm), while H-3′ and H-4′ present a more moderate effect of $\Delta\delta_{cis/trans} = -0.28$ and -0.34 ppm, respectively [Table Ring-II in Scheme 9]. All these data matched with the fixed conformation *cis*-**E** for **7a**, where the *p*-tolyl group of the sulfoxide was again playing an important shielding role over H-6′. We also considered the conformer placing the ring-I outside the plane, (Figure 9 *cis*-**G** (**7**), R′ = CF_3 and R″ = H) but, as mentioned before, this conformation would not justify the upfield shift observed for H-6. As shown in Scheme 9, a second conformer like *cis*-**E**′ with a different orientation of ring-(II′) could be considered for *cis*-**7a**, but in such a disposition the high shielding observed for H-6′ could not be justified (Scheme 9).

In the case of **7d** (Scheme 10) the unequivocal assignment of all the hydrogens of ring-II (H-3′, H-4′, H-5′, and H-6′) was more difficult. The ^{19}F,^{1}H HOESY spectrum of *trans*-**7d** revealed two cross-peaks between the ^{19}F signal at −57.5 ppm and the ^{1}H signals at 7.89 ppm (d, $J = 7.7$ Hz, 1H), assigned to H-3′, and 8.01 ppm (s, 1H), assigned to H-6 of ring-I (Figure 11a). Upon photoisomerization the ^{19}F signal of *cis*-**7d** at −60.5 ppm displayed a NOE interaction with the ^{1}H signal at 7.73 ppm (d, $J = 8$ Hz, 1H), thus attributed to *cis*-H-3′. In this case, the more shielded signal of ring-II appeared at 4.92 ppm (brd, $J = 8$ Hz, Scheme 10, Table Ring-II). Another significant feature of *cis*-**7d** corresponded to the aryl ring-II hydrogen observed at 7.05 ppm (brt, $J = 7.7$ Hz) which matched H-6′ with the doublet appearing at 4.92 ppm, that should have an ortho coupling constant J(H,H) with the vicinal H-5′. In turn, H-5′ was assigned to the triplet at 7.05 ppm, showing two ortho-J(H,H) coupling constants. With all these data, we can conclude that the shielding

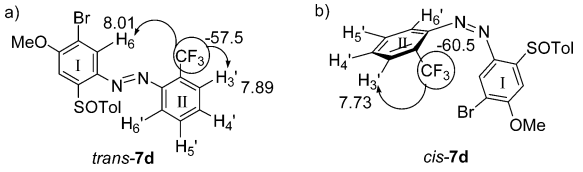
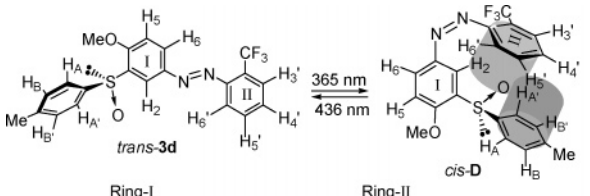


Figure 11. HOESY ^{19}F-^{1}H NMR analysis of the 2-*p*-tolylsulfinyl azobenzene **7d**.

Scheme 8. ^{1}H NMR Analysis of the Photoisomerization of **3d**



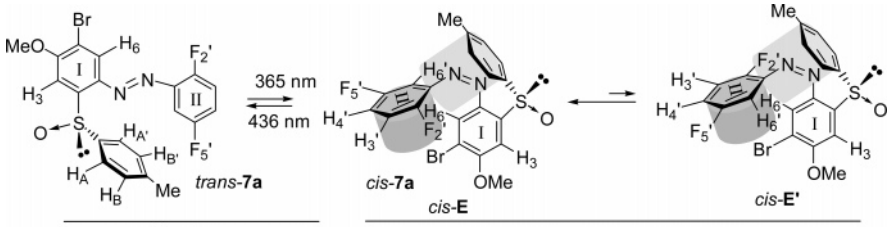
Ring-I

3d	δ *trans* (ppm)	δ *cis*	Δδ *cis/trans*
H-2	8.61	7.48	-1.13
H-6	8.00	7.19-7.16	-0.83
Tol(AA')	7.65	7.34	-0.31
H-5	6.99	6.76	-0.23

Ring-II

3d	δ *trans*	(ppm) δ *cis*	Δδ *cis/trans*
H-3'+H-?	7.84-7.80	(H-3')7.77-7.76	-0.05
H-4',5',6'	7.68-7.64	6.29-6.27	
	7.56-7.53	7.32-7.30	

Scheme 9. ^{1}H NMR Analysis of the Photoisomerization of **7a**



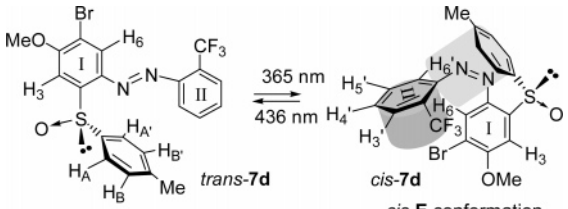
Ring-I

7a	δ_{trans} (ppm)	δ_{cis}	$\Delta\delta_{cis/trans}$
H-6	8.11	6.47	-1.64
H-3	7.83	7.82	-0.01
Tol(AA')	7.49	7.62	+0.13

Ring-II

7a	δ_{trans} (ppm)	δ_{cis}	$\Delta\delta_{cis/trans}$
H-6'	7.29 (ddd) (J = 9.3, 6.1, and 3.2 Hz)	5.50 (ddd) (J = 8.2, 5.5, and 3.0 Hz)	-1.79
H-4'	7.25 (td) (J = 9.7 and 4.7 Hz)	6.97 (td) (J = 9.0 and 4.4 Hz)	-0.28
H-3'	7.22-7.17 (m)	6.87-6.84 (m)	-0.34

Scheme 10. ^{1}H NMR Analysis of the Photoisomerization of **7d**



Ring-I

7d	δ_{trans} (ppm)	δ_{cis}	$\Delta\delta_{cis/trans}$
H-6	8.01	6.26	-1.75
H-3	7.79	7.82	+0.03
Tol(AA')	7.51	7.66	+0.15

Ring-II

7d	δ_{trans} (ppm)	δ_{cis}	$\Delta\delta_{cis/trans}$
H-3'	7.89 (d, J = 7.7 Hz)	7.73 (d, J = 8 Hz)	-0.16
H-4',5',6'	7.70-7.64 (m, 2H)	4.92 (d, J = 8 Hz)	-2.75
	7.60 (t, J = 7.5 Hz)	7.05 (t, J = 7.7 Hz)	-0.55

effect observed for H-6 (ring-I) in *cis*-**7d** is due to the π-cloud of the fluorinated aryl ring-II, while the upfield shift of H-6′ (ring-II) is a consequence of the anisotropic effect of the *p*-tolyl ring, in the conformer *cis*-**E** represented in Scheme 10.

All the information deduced from the NMR data indicated that once the photoisomerization process had occurred, the orientation of the *cis*-azobenzene in both regioisomers **3** and **7** is controlled by the *p*-tolylsulfinyl group situated at C-2 or C-3. When the sulfoxide is placed at C-3 of ring-I (azocompounds **3**), the trans to cis photoisomerization of the N═N double bond leaves the ring-II preferentially toward the edge-face of the 3-*p*-tolylsulfinyl substituent leading to a U-shaped disposition of the three aromatic rings. The preferred orientation after N═N photoisomerization of 2-sulfinylazobenzenes **7** is situating the *p*-tolyl group toward the edge-face of the ring-II. The favored fixed 1,3-parallel disposition of the sulfinyl oxygen with respect to the vicinal H-2 or H-3 hydrogens (in **3** or **7**, respectively) is the origin of the final stable ordered geometries observed for the trans and cis isomers. In both **3** and **7**, when an ortho substituent is present in the aryl ring-II, this substituent is projected far from the anisotropic effect of the *p*-tolyl group of the sulfoxide.

Photomodulation of Cholesteric Liquid-Crystalline Mesophases. As the helical sense and pitch of an induced cholesteric phase are dependent on the (isomeric) state of the dopant, the incorporation of a photoswitchable molecule in nematic LC solvents offers the possibility to control the supramolecular chirality of a cholesteric phase, and this property can be applied in all optical devices.[51] The azobenzene moiety is the most frequently applied photoactive bistable group in liquid crystal research.[19c,21a,b,52] In fact, because of the large differences in structure, the helical twisting power of trans and cis isomers are usually quite different which allows efficient modulation of the cholesteric pitch. The behavior of our chiral switches as dopants for liquid crystals was studied with enantiopure 2′-CF_3 aryl azocompounds **3d** and **7d**, which had displayed the higher changes in the CD spectra upon photoisomerization. Commercially available nematic solvent E7 was used. Concentrations of **3d** and **7d** are indicated in Table 2, together with the β values obtained for the trans-azo derivatives and the two photostationary states produced upon irradiation. In comparison with other centrally chiral azo derivatives, enantiopure sulfinyl compounds **3d** and **7d** exhibited a significant twisting power of −39.5 and −16.4 μm^{-1}, respectively. Irradiation at 365 nm decreased the relative β value [β (**3d**) = −26.4 μm^{-1} and β (**7d**) = −15.9 μm^{-1}], while subsequent irradiation at 436 nm reverted to −34.7 and −15.9 μm^{-1}, respectively. Both enantiopure azobenzenes showed a negative screw sense of the cholesteric packing induced by the [S(*S*)]-*p*-tolylsulfinyl stereogenic center. The relationship between the negative β values of some alkyl aryl sulfoxides (measured in E7 nematic phase) and the [S(*S*)]-configuration of the stereogenic sulfur atom has been reported,[23] however no studies have been made with bisaryl sulfoxides. Our previous results indicate that this correlation between the negative β value and the [S(*S*)]-configuration endure as well in the cases of the bisaryl sulfoxides **3d** and **7d**. It is worthy to

Table 2. Helical Twisting Power (β) of Enantiopure Dopants **3d** and **7d** in E7 for the Trans Configuration and the Photostationary Composition after Irradiation at 365 and 436 nm

		β (μm^{-1})[a]	
dopant	pure *E*	PSS (λ 365 nm)	PSS (λ 436 nm)
3d	−39.5	−26.4	−34.7
7d	−16.4	−7.9	−15.9

[a] $\beta = (pcee)^{-1}$, where p is the pitch of the cholesteric, c is the molar fraction of the dopant and ee its enantiomeric excess; see ref 18.

(51) (a) Ichimura, K. *Chem. Rev.* **2000**, *100*, 1847−1874. (b) Ikeda, T.; Kanazawa, A. In *Molecular Switches*; Feringa, B. L., Ed.; Wiley-VCH: Weinheim, Germany, 2001; pp 363−397. (c) Eelkem, R.; Feringa, B. L. *Org. Biomol. Chem.* **2006**, *4*, 3729−3745.
(52) Yoshioka, T.; Alam, M. D. Z.; Ogata, T.; Nonaka, T.; Kurihara, S. *Liq. Cryst.* **2004**, *31*, 1285−1291.

mention that the presence of the sulfoxide at the azobenzene produced a significant increase of the helical twisting power compared with the β values reported for simple alkyl aryl sulfoxides (around -10 to -1.1 in E7 nematic phase). Once again, considering the different position of the sulfoxide at C-2 or C-3 of the aryl moiety of the azocompound, better results were obtained from the 3-sulfinyl azo derivative **3d** which displayed a bigger β value than **7d**.

Conclusion

In summary, we have succeeded in the regioselective synthesis of new optically pure 2- or 3-*p*-tolylsulfinyl azobenzenes, from commercially available arylhydrazines and *p*-tolylsulfinyl functionalized *p*-quinone bisketals. Reaction always occurs by preferential attack of the arylhydrazine to the less-hindered ketal group. The presence of a 4-bromo substituent in the 1-*p*-tolylsulfinyl-*p*-quinone dimethyl bisketal allowed the regiocontrolled preferential attack at the ketal group close to the sulfoxide giving rise to 2-*p*-tolylsulfinyl azobenzenes **7**. The study of their photoresponsive behavior by CD, evidenced that the position of the sulfoxide group in the azobenzene causes two different chiral responses. Thus, the presence of the *p*-tolylsulfinyl group at C-3 induced a transfer of chirality from the stereogenic sulfur to the N═N group in both the trans and cis isomers, while when the sulfoxide is at C-2, this transfer of chirality only occurred in the cis-isomers. This different chiroptical response is a consequence of a conformation fixed by the sulfoxide, as deduced by NMR studies. Cis-isomers of both sulfinyl azocompounds **3** and **7**, show a complementary disposition of the substituents around the N═N moiety. Thus, choosing the appropriate location of the sulfoxide in the azobenzene (ortho or meta to the N═N), a conformational change could be induced in a controlled manner by irradiation. The presence of such a chiral *p*-tolylsulfinyl group in the azobenzene is acting as a stem in a sunflower, where upon light exposure phototropy is induced. The overall disposition of the systems can be controlled by the C-2 or C-3 sulfinyl substitution during the trans to cis N═N double bond isomerization. As a result, a photomodulable molecular switch with a particular rigid and compact conformation and chiral response has been described. The easy and reversible change observed between the different conformational states could find applications in the photocontrol of several molecular processes. Finally, two sulfinyl azobenzenes were tested as chiral dopants in nematic LC systems, showing interesting β values for such centrally chiral azocompounds and a notably photoisomerization process in a liquid crystalline cholesteric phase.

Acknowledgment. This work is dedicated to Prof. Miguel A. Yus on the occasion of his 60th birthday. We thank Dirección General de Investigación Científica y Técnica (Grant CTQ2005-02095/BQU), Acción Integrada Hispano-Italiana 2004-0027, Comunidad de Madrid (GR/MAT/0152/2004), and Ministero dell'Università e della Ricerca, Italy, (PRIN 2005) for financial support. M.R. thanks Ministerio de Educación y Ciencia for a Ramón y Cajal contract and I.N. and E.M. for a fellowship.

Supporting Information Available: Detailed experimental procedures and full characterization of all compounds. Copies of selected ^{1}H, ^{13}C, 2D (H,H) (H,F) NMR spectra, HPLC, and X-ray crystallography.

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