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ARTICLE TYPE

Chirality Transfer from Chiral Solvents and its Memory in Azobenzene Derivative Exhibiting Photo-switchable Racemization

Reji Thomas[a] and Nobuyuki Tamaoki[a]*

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The transfer and dynamic fixation of chirality in cyclic azobenzenes using *R*-(+)-1-phenylethylalcohol (*R*-PEA) and *S*-(-)-1-phenylethylalcohol (*S*-PEA) as solvents or additives are investigated. The cyclic azobenzenes used in this study carry 1,5-dioxynaphthalene moiety as rotating unit, connected to the photoisomerizing (*E*-*Z*) azobenzene unit with spacers of varying lengths. With the suitable lengths of the spacers the molecules exhibit stable enantiomers originated from the element of planar chirality in the *E* form due to the stopped rotation of the rotor, while in the *Z* form the allowed rotation results in racemization. The CD spectra of racemic compounds in *E* form in chiral solvents were inert or almost negligible before irradiation, while 366 nm irradiation causing *E*-*Z* photoisomerization resulted in induction of clear CD bands. The thermal or photochemical reverse *Z*-*E* isomerization causes a change in the CD spectra to the new ones which are reasonably matching with the spectra of the pure enantiomers recorded in non-chiral solvents. The obtained new CD spectra are maintained even in a racemic solvent system attained by the dilution with equal amount of chiral solvent of opposite stereo structure. These results indicate that the chirality is transferred from the chiral solvents or additives to the racemizing *Z* form of cyclic azobenzene and it is fixed in the non-racemizing *E* form. The molecule without racemization in both *E* and *Z* forms did not show any significant induced CD bands irrespective of *E*-*Z* isomerizations. The molecule showing racemization in *E* and *Z* form just show the non fixed induced CD. The property of the photo-switchable racemization is necessary for the effective transfer and temporal fixation of the chirality in this type of chirality sensors.

Introduction

The induction, transfer, amplification and memory of chirality are extensively discussed topics in the various fields of science such as chemistry, biology, pharmacology and material science.[1] The research in this area ranges from the basic research to explore the origin of homochiral structures in nature[2] to the practical aspects of chirality transfer which focuses on the enantio selective synthesis,[3] sensing[4] and molecular device applications.[5] Concerning the molecular sensors for chirality, in particular the dynamic induction and memory of chirality in molecular structures or alignment are important. There are many works on induced CD of organic molecules such as benzophenone[6] or *Z*-azobenzene[7] in chiral solvents. In these systems the chiral information is dynamically transferred from solvents to the molecules, but on removal of the chiral solvents the chiral information is disappeared. Yashima et al. demonstrated a new system where the helicity is induced on a stereo regular cis-transoidal poly((4-carboxyphenyl)acetylene) by an optically active chiral amine.[4a] This macromolecular system also showed a non-volatile memory effect of the induced helicity on removal of the chiral amine. However, the induced helical structure should be in an equilibrated state, since the secondary structure of the polymer, which is the origin of the chirality in this study, is stabilized just by weak intramolecular interactions. Hence the chiral memory based on secondary structure of the polymer is incomplete. In this perspective, small molecules with well defined enantiomeric structures and switchable racemization property are preferable for chiral sensors.

Azobenzene-based compounds received greater attention in the field of photo-switchable molecular systems attributed to the large structural change upon *E*-*Z* isomerization.[8,9] Recently, we have demonstrated the dynamic racemization property in a newly synthesized cyclic azobenzene by photo switching of the on-off rotation of a naphthalene rotor.[10] The stopped rotation of the 1,5-substituted naphthalene in the macro cyclic structure is the origin of the planar chiral nature of this molecule. The rotation of the naphthalene rotor *viz.* racemization is dynamically switched by changing the cavity size of the macrocycle achieved by the photoinduced *E*-*Z* isomerization of the azobenzene unit.

In this study we apply aforesaid dynamically racemizing molecular system as a chirality sensor with the memory effect. The temporal chirality is transferred from the solvents or additives to the cyclic azobenzene in the *Z* form and it is memorized in the *E* form by *Z*-*E* isomerization.

Experimental

All the starting materials for the synthesis of the cyclic azobenzenes were obtained from commercial suppliers (TCI and Wako pure chemicals) and were used as obtained without further purifications. The chiral solvents *R*-(+)-1-phenylethylalcohol (*R*-PEA) and *S*-(-)-1-phenylethylalcohol (*S*-PEA) of 98% enantiomeric purity were purchased from Wako pure chemicals Ltd.

Synthesis of cyclic azobenzenes (1 - 3)

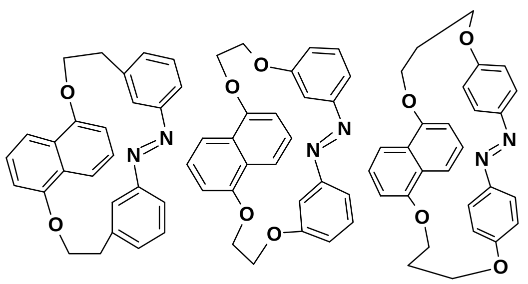
All the cyclic azobenzenes, presented in this study were synthesized using the previously reported procedures from our group.[10] The cyclic azobenzenes (compound **1**, **2** and **3**) were synthesized by the reduction of corresponding dinitro compounds. The structure and purity of the compounds were assessed using NMR spectroscopy (JEOL ECX 400 NMR spectrometer) and matrix assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI TOF MS).

UV-Vis and Circular Dichroism Spectroscopic Experiments

The samples for the CD spectroscopic studies were prepared by dissolving the weighed quantity of the *E* cyclic azobenzenes (racemic) in known volume of chiral solvents *R*-PEA or *S*-PEA. The absorption spectra of the solutions were measured on a single beam UV-Vis spectrometer illuminated with a diode array laser and the CD spectra were recorded on JASCO J-720U spectropolarimeter. Photoisomerization studies were conducted on a super high-pressure mercury lamp (500W, USHIO Inc.) using appropriate filters (366 or 436 nm). The measurements of absorption and CD spectra and the photoisomerization studies were conducted in a cuvette with a 1-mm light path.

Results and discussions

Scheme 1 shows chemical structure of the cyclic azobenzene used in this study. Compound **1** has stable enantiomers due to the stopped rotation of the naphthalene moiety both in *E* and *Z* forms. Compound **3** shows the free rotation of the naphthalene rotor irrespective of structure of azobenzene. In contrast to this, compound **2** shows switchable rotation of the rotor moiety. The



1 2 3

Scheme 1: Molecules presented in this study

rotation is completely hindered in *E* form while it is allowed in *Z* form, affording the photo-switchable racemization in this molecule. These observations can be explained by the difference in the cavity size of the macrocycles tuned by the spacer length and the *E*-*Z* isomerization of the azobenzene part. UV-visible spectrum for the dilute solution of racemic *E*-**1** in chiral solvent *R*-PEA showed similar characteristics of *E* azobenzenes with absorption maxima at 302 nm corresponding to the π-π* transitions and at 450 nm due to the n-π* transitions of the azobenzene in addition to the structured features assignable to naphthyl group around 300 nm (see supporting information Fig. S1a), which are similar to those in non chiral solvents.[5a]

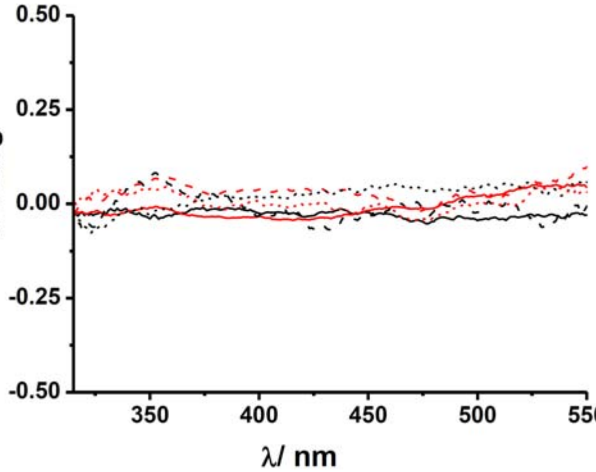


Fig. 1 CD Spectra of the racemic mixture of compound **1** in chiral solvents *R*-PEA (black) and *S*-PEA (red) (a) before irradiation (solid), (b) after irradiation with 366 nm (dashed) and (c) irradiated with 436 nm (short dash). Solution concentration: $4.6x10^{-4}$ M.

The CD spectra of the racemic *E*-**1** in chiral solvent *R*- and *S*-PEA are shown in Fig. 1. The spectra do not exhibit any significant bands in both the solvents. Even after irradiation with 366 nm (PSS_{366}) and subsequent irradiation with 436 nm light featureless CD spectra were retained. A dilute solution of **3** in both the chiral solvents *R*- and *S*-PEA exhibited UV-Vis absorption bands with maxima at 300, 360 and 450 nm (supporting information Fig. S1c). The CD spectra for a solution

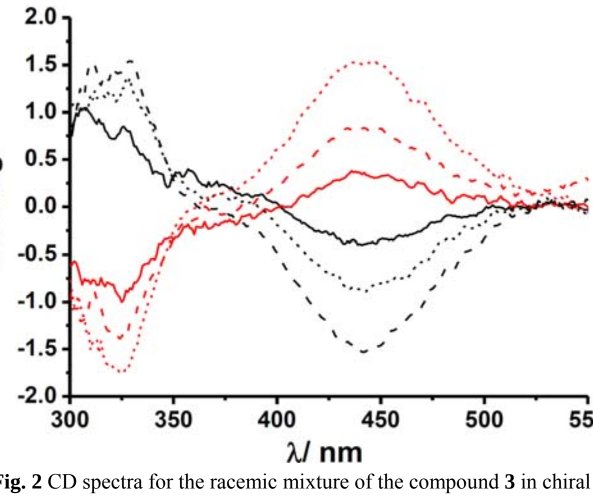


Fig. 2 CD spectra for the racemic mixture of the compound **3** in chiral solvent *R*-PEA (black) and *S*-PEA (red) (a) as prepared (solid), (b) after 366 nm light irradiation, (dashed) and (c) after 436 nm irradiation (short dash). Solution concentration: $7.73x10^{-4}$ M.

in *R*-PEA showed relatively intense bands with positive (330 nm and 370 nm) and negative (442 nm) signs (Fig. 2). After irradiation with 366 nm a significant increase in the intensity of the band at 442 nm was observed. It is noteworthy that the positive band observed at 370 nm is completely disappeared on irradiation of 366 nm light, while the band at 330 nm showed a small increase in intensity. The CD spectrum recorded after 436 nm irradiation was the intermediate of those before and after 366 nm irradiation. The complete thermal *Z-E* isomerisation brought the CD spectra to the initial one.

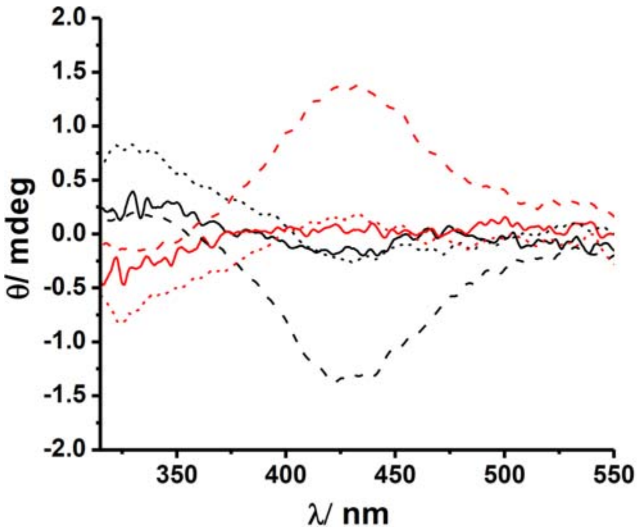


Fig. 3 CD spectra for the racemic mixture of the compound **2** in chiral solvent *R*-PEA (black) and *S*-PEA (red) (a) as prepared (solid), (b) after 366 nm light irradiation, (dashed) (c) after *Z-E* isomerization by keeping in dark at 25° C for 72 hours (short dash). Solution concentration 9.1x10^{-4} M.

A similar experiment with compound **2** in chiral solvents *R*-PEA and *S*-PEA were carried out. The absorption spectra of the dilute solutions of **2** in chiral solvents *R*-PEA and *S*-PEA showed absorption bands with λ_{max} at 297 nm and 440 nm (see Fig. S1b) comparable to the band structure in non-chiral solvents.[10] The CD spectrum of **2** in *R*-PEA showed a weak positive band centered around 327 nm along with a weak negative band at 428 nm (see Fig. 3). A mirror image spectrum was obtained for *E*-**2** (racemic) in *S*-PEA. The exposure of **2** in *R*-PEA to 366 nm light resulted in the *E-Z* isomerisation. The UV-vis absorption spectrum showed a decrease in the intensity of the π-π^* transition band (297 nm) of azobenzene chromophore along with a small increment in the intensity of the band at 440 nm (n-π^* transition) (see Fig. S1b). The corresponding CD spectrum showed a significant change with the formation of a strong negative band at 428 nm accompanied by a weaker positive band at 327 nm. In contrast to compound **3** a complete thermal *Z-E* isomerization of **2** in chiral solvent did not bring the CD spectra of the solution to the initial one, but to the new spectrum with an intense band at 327 nm and a weak band at 428 nm (See Fig. 3). A mirror image spectrum was obtained with the solution of **2** in *S*-PEA. The features of the CD spectra obtained after thermal isomerization completely matches with those of the pure enantiomers of *E*-**2** in non-chiral solvents.[10] The origin of a peak at 327 nm along with a small band at 428 nm may be due to the enrichment of one of the stable chiral structure (enantiomer) in the *E*- state.

To prove the role of chiral solvent in chiral induction of cyclic azobenzenes we have performed an experiment where the chiral solvents used as additive in dichloromethane solutions of **2** (see Fig. 5). The CD spectra recorded for dichloromethane solutions before and after irradiation (366 nm) were silent in nature (see

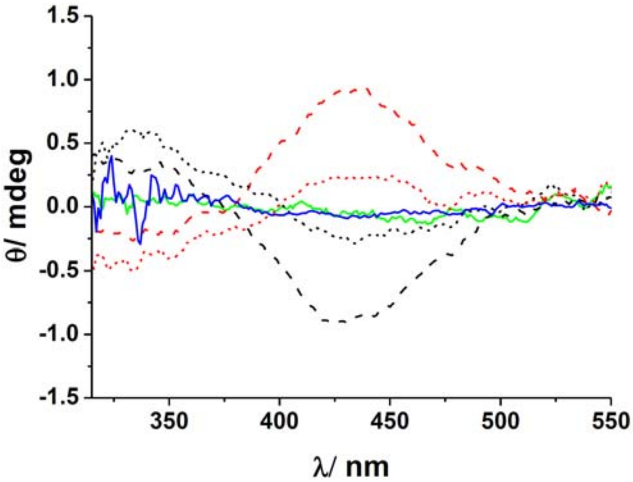


Fig. 4 Chiral solvents as additives to a dichloromethane solution of **2**: CD spectra of (a) **2** in dichloromethane (blue), (b) after 366 irradiation (green) (c) on addition of chiral solvent to the 366 irradiated solution (dashed curves) (d) after reverse (Z-E) isomerization by 436 nm irradiation (short dash). Solution concentration: 1.7x10^{-3} M.

blue and green curves) whereas, that recorded after the addition of an equal volume of chiral solvent to the 366 nm irradiated solution of **2** in dichloromethane (dashed curves) showed significant bands. The band at 428 nm of the spectra clearly indicates the influence of the chiral solvent on *Z*- **2** in modifying the naphthalene rotor to a favored orientation which in turn results in a chiral structure. The photo controlled chirality transfer and the memory of chiral structure were confirmed by the irradiation of the solution under 436 nm light which gives an *E* and *Z* isomer ratio of 67:33. The CD spectra recorded for the solution after the irradiation with 436 nm light showed a change in the intensity ratio of the spectra with a decrease in intensity at 428 nm with a concomitant increase in intensity at 327 nm. The changes in the spectral features once again confirm that the chiral solvent induces preferred orientation the structure in *Z* states of

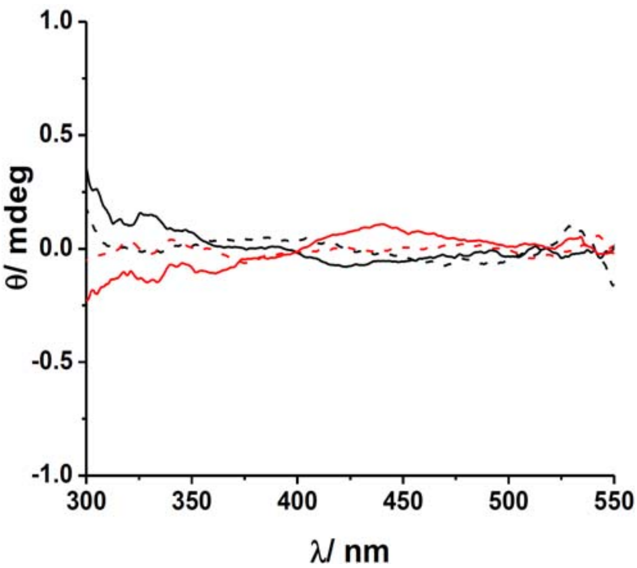


Fig. 5 CD spectra for the racemic mixture of the compound **2** in chiral solvent *R*-PEA (black) and *S*-PEA (red) (a) as prepared (solid) (b) after addition of the equal amount of chiral solvent with opposite sterio structure (dashed). Solution concentration: 9.45×10^{-4} M.

the **2** and *Z*-*E* isomerisation fixes the chiral structure in *E* state.

In order to confirm the origin of CD band at 428 nm and 327 nm observed on thermal *Z*-*E* reverse isomerization, we have performed an experiment by mixing chiral solvents, where the chiral solvent *S*-PEA is added to a solution of **2** in *R*-PEA or vice versa. Fig. 5 shows the CD spectra recorded for a solvent mixing experiment conducted for **2** before irradiation. The spectra of **2** in *R*-PEA showed small induced CD signal at 327 nm and 428 nm, while the addition of equal amount of *S*-PEA to this solution resulted in a featureless CD spectra. A similar observation can be made in an experiment, where an equal amount of *R*-PEA is added to a solution of **2** in *S*-PEA.

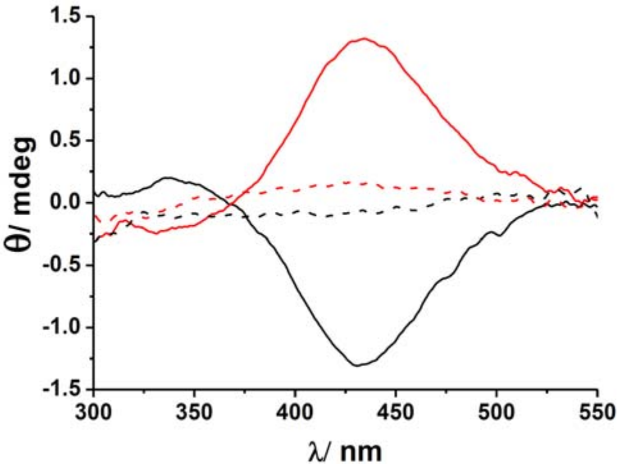


Fig. 6 CD spectra for the racemic mixture of the compound **2** in chiral solvent *R*-PEA (black) and *S*-PEA (red) (a) after 366 nm irradiation (solid) (b) after addition of the equal amount of chiral solvent with opposite sterio structure (dashed). Solution concentration: 9.45×10^{-4} M.

Consequently, a solvent mixing experiment with solutions of **2** in chiral solvents after 366 nm irradiation showed a diminished intensity at 327 nm and 428 nm indicating these bands are clearly due to induced CD signal of *Z*-**2** in chiral solvents (Fig. 6). In a similar experiment, we added the solvent of opposite chiral structure to the solutions of *E*-**2** formed by reverse isomerization

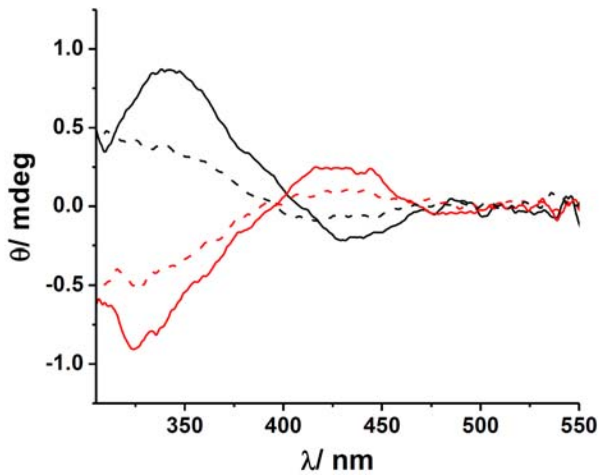
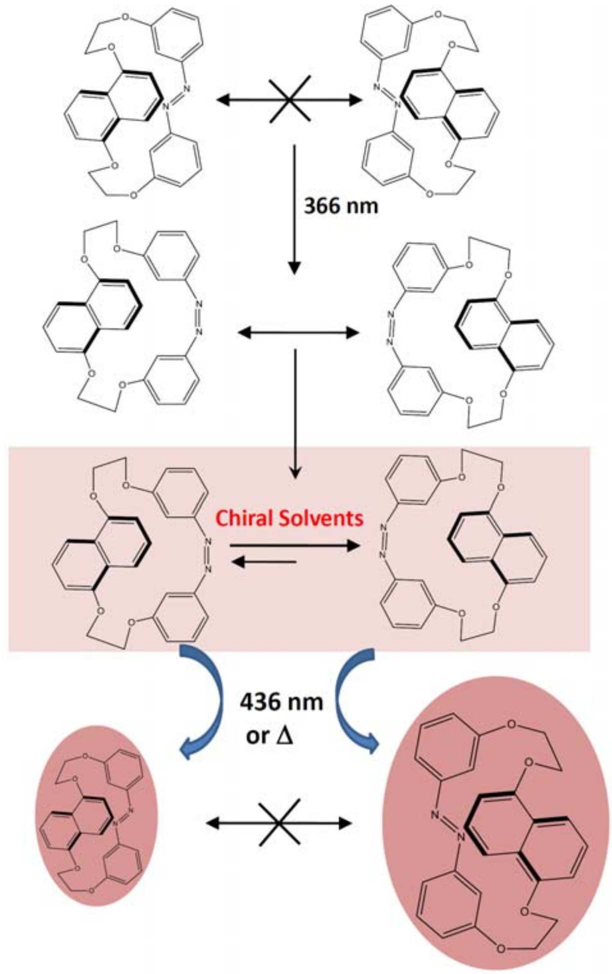


Fig. 7 CD spectra for the racemic mixture of the compound **2** in chiral solvent *R*-PEA (black curves) and *S*-PEA (red curves) (a) after thermal *Z*-*E* isomerization (solid) (b) after addition of the equal amount of chiral solvent of opposite chirality (dashed). Solution concentration: 9.45×10^{-4} M.



Scheme 2. Photochemical and thermal processes involved in chiral sensing of molecule **2**, in *R*-PEA and *S*-PEA.

from the photochemically formed *Z* state. In contrast to the previous solvent mixing experiments the CD spectra recorded for this solution retained the signal at 327 nm and 428 nm but with reduction in intensity into half due to the dilution (Fig. 7). This result suggests that the observed CD signal obtained after thermal reverse isomerization from the photochemically formed *Z* state is due to the formation of stable enantiomeric excess.

We have estimated the extent of fixation of the transferred chirality (memory) from chiral solvents to the cyclic azobenzene **2** by a quantitative analysis of CD spectra. The comparison of the CD band intensities at 327 nm for compound **2** with that of its pure enantiomers in same racemic mixture of chiral solvents showed a chiral enrichment of 1.5 % respectively (CD spectra of authentic pure enantiomers are shown in Fig. S2). The chiral HPLC analysis of the pure enantiomers in chiral solvents showed that these enantiomers are stable over a week (see Fig. S3). Thus, we could achieve the photo fixation of the transferred chirality in cyclic azobenzene with rendered (*E*) and allowed rotations (*Z*).

Scheme 2 depicts the plausible mechanism of chiral sensing of the cyclic azobenzene **2** in chiral solvents *R*-PEA and *S*-PEA. The chiral solvent favors one of the enantiomeric structures of **2** in *Z* state by the orientation of naphthalene rotor which in turn results in a shift of the enantiomeric equilibrium. The CD signal observed from the solution of Z-**2** in chiral solvents is clearly an induced signal as evident from the solvent mixing experiment. The sustained CD signal observed for *E*-**2** after thermal *Z-E* isomerization even in the presence chiral solvent of opposite chiral structure substantiate the formation of fix chiral structure of **2**. A similar but permenant formation of chiral structure has been studied previously in the case of electrochemical pinacolization[11] and photochemical reactions with helicenes in chiral solvents[12] While, the present study demonstrate a dynamic fixation of transferred chirality sensor which is controlled by simple *E-Z* photoisomerizations.

Conclusion

In summary, we demonstrated the transfer and dynamic fixation of the chirality in a cyclic azobenzene with napthalene rotor in chiral solvents. In contrast to the previously reported polymeric systems where the chirality is fixed as an indefinite secondary structure, here in molecule **2**, the transferred chirality is memorized as a well defined planar chirality of the single small molecule.

Notes and references

[a] *Research Institute for electronic Science, Hokkaido University, Kita-Ku, N-20, W-10, Sapporo, 001-0020, Japan. Fax: +81 11 706 9357; Tel: +81 11 706 9356;*
E-mail: tamaoki@es.hokudai.ac.jp

† Electronic Supplementary Information (ESI) available: Uv-vis spectra of compounds **1**, **2** and **3** in chiral solvents, CD spectra of enatiomers of **2** in chiral solvents and enantiomeric stability of **2** in chiral solvents monitored by chiral HPLC. See DOI: 10.1039/b000000x/

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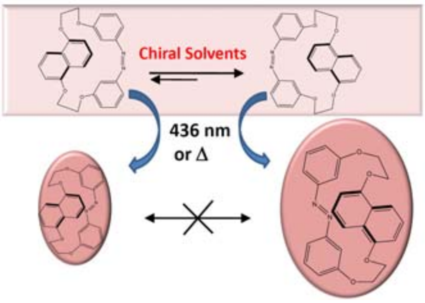

The chirality is trasferred form a chiral solvent and memorized as a well defined planar chirality of the single small molecule.