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Novel chiral Schiff base macrocycles containing azobenzene chromophore: gelation and guest inclusion

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ABSTRACT

A novel chiral Schiff base macrocycle **1** was synthesized by [3+3] condensation of enantiomerically pure *trans*-1,2-diaminocyclohexane with azobenzene-4,4′-dicarbaldehyde. Subsequent reduction of **1** afforded macrocyclic hexamine **2** having three azobenzene units. The former could be converted into a benzene gel, while the latter could include several aromatic guest molecules.

Recently, chiral Schiff base macrocycles having cavities of various sizes have been synthesized, and their applications have been investigated.[1] Gawronski et al. developed a new strategy for the synthesis of chiral macrocycles via the [3+3] cyclocondensation of *trans*-(1*R*,2*R*)-diaminocyclohexane with terephthalaldehyde and isophthalaldehyde.[2] Later, several research groups synthesized chiral macrocyclic Schiff bases having central cavities of different sizes[3] and studied their applications in molecular recognition, optical resolution, fluorescence sensing, and asymmetric catalysis.[4] Recently, we investigated the molecular recognition ability of the aforementioned types of host compounds and reported that they can be used as chiral NMR shift reagents[5], chiral catalysts for asymmetric Henry reaction[6], and photochromic crystals.[7] Herein, we report the synthesis, crystal structure, photochromic properties, and inclusion and gelation properties of a novel chiral Schiff base macrocycle having an azobenzene chromophore **1** and the reduced form of this macrocycle **2**.

The chiral Schiff base macrocycle (*R*,*R*,*R*,*R*,*R*,*R*)-**1** was synthesized by the [3+3] cyclocondensation of enantiomerically pure (*R*,*R*)-1,2-diaminocyclohexane with azobenzene-4,4′-dicarbaldehyde[8] in CH_2Cl_2, as shown in Scheme 1. The product was confirmed by NMR and mass spectrometry.[9] Subsequent sodium borohydride reduction of (*R*,*R*,*R*,*R*,*R*,*R*)-**1** gave the corresponding macrocyclic hexamine (*R*,*R*,*R*,*R*,*R*,*R*)-**2** in good yield.[10] Similarly, (*S*,*S*,*S*,*S*,*S*,*S*)-**1** and (*S*,*S*,*S*,*S*,*S*,*S*)-**2** were synthesized by the condensation of azobenzene-4,4′-dicarbaldehyde with (*S*,*S*)-1,2-diaminocyclohexane. The chiral nature of macrocycles **1** and **2** was determined from their circular dichroism (CD) spectra. (Figs. 1 and 2) These spectra showed mirror images; further, because the degree of extended conjugation in the macrocyclic imine **1** was greater than that in the macrocyclic amine **2**, Cotton effects were observed at a longer wavelength in the case of the former.

Upon irradiation of a $CHCl_3$ solution of (*R*,*R*,*R*,*R*,*R*,*R*)-**1** by 365 nm light for 30 min, the intensity of the absorption peak at 348 nm decreased, while that of the bands at 273 nm and 450 nm increased. The original spectrum was recovered when the irradiated solution was allowed to stand at room temperature for 48 h (Fig. 3).

Figure 4 shows similar changes in the absorption spectrum of (*R*,*R*,*R*,*R*,*R*,*R*)-**2** after irradiation of a $CHCl_3$ solution of **2** by 365 nm light for 30 min. The absorption peak at 329 nm decreased, while the bands at 247 nm and 436 nm increased. The original spectrum could be recovered by allowing the irradiated solution to stand at room temperature for 48 h.

Unexpectedly, a gel was obtained when **1** (2 mg) was dissolved in benzene (1 mL) and the solution was cooled to room temperature, as shown in Figure 5 (left). The gel was translucent and orange colored because of the azobenzene chromophore. To obtain visual insights into the molecular aggregate, we dried the abovementioned gel and analyzed it by scanning electron microscopy (SEM). The SEM photograph in Figure 5 (right) shows the presence of elongated fibers with diameters of around 1 μm in the dried gel. Photoirradiation of the gel by UV light (300–400 nm) for several hours led to gel–sol transformation; the original gel was recovered upon heating the sol.

Compound **2** can accommodate various aromatic organic guest molecules in its cavity to form inclusion complexes with different host:guest stoichiometric ratios, as shown in Table 1. The host:guest stoichiometric ratio is 1:1 when using benzene and toluene as the guest molecules and 2:1 when using *o*-, *m*-, and *p*-xylenes as the guests. This indicates that xylene molecules are too large to be accomodated in the host cavity of 2 as a 1:1 host–guest ratio. Figure 6 shows the thermogravimetric (TG) trace of the 1:1 inclusion crystals obtained by the inclusion of toluene in **2**.

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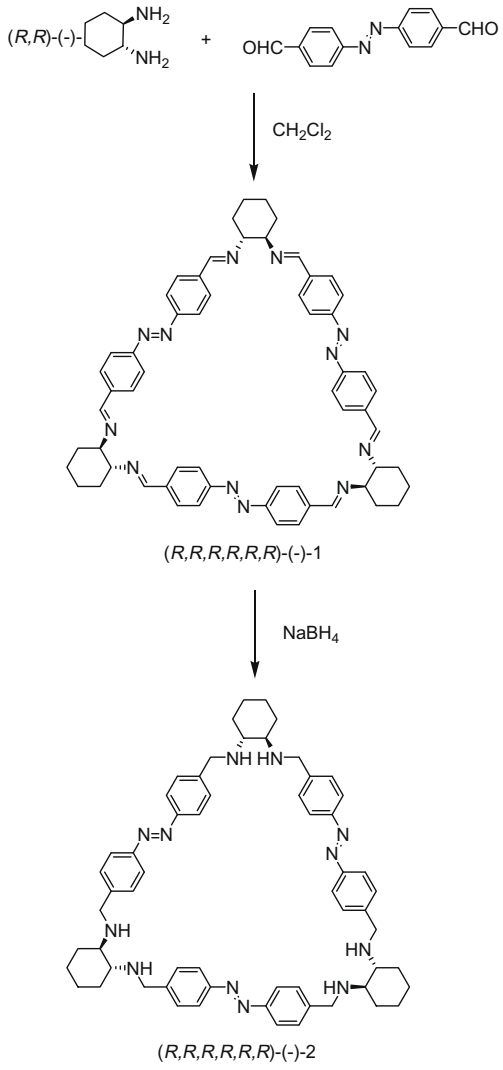

Scheme 1. Synthesis of (*R,R,R,R,R,R*)-**1** and **2**.

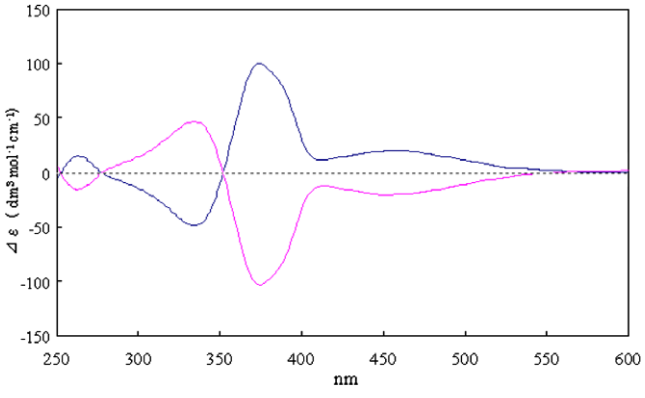

Figure 1. CD spectra of (*R,R,R,R,R,R*)-**1** (red) and (*S,S,S,S,S,S*)-**1** (blue) in $CHCl_3$.

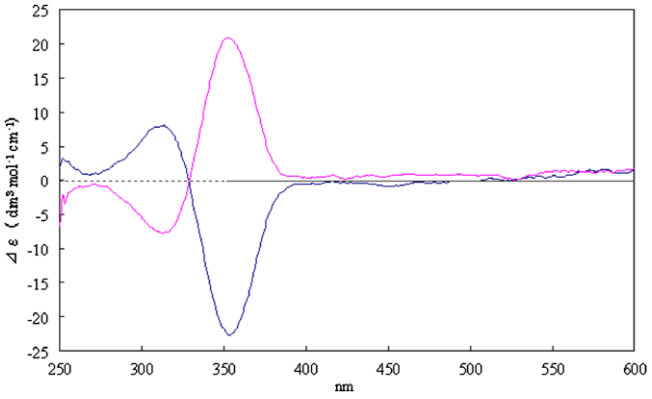

Figure 2. CD spectra of (*R,R,R,R,R,R*)-**2** (red) and (*S,S,S,S,S,S*)-**2** (blue) in $CHCl_3$.

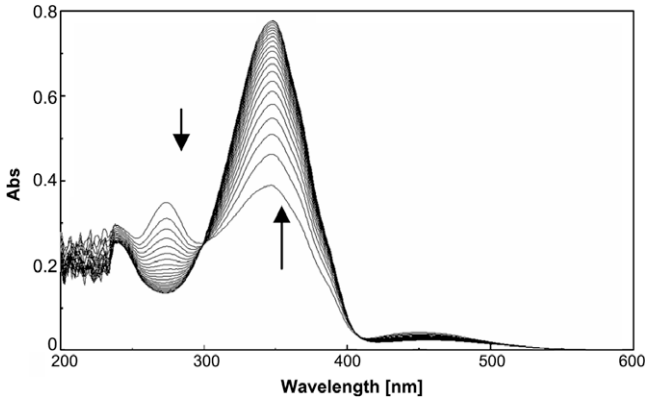

Figure 3. Change in absorption spectrum of **1** in $CHCl_3$. From bottom (photostationary state upon irradiation with 365-nm light) to top (after maintaining at the solution room temperature for 48 h).

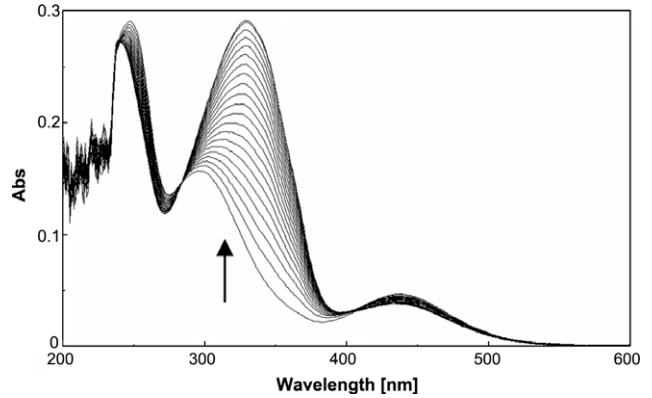

Figure 4. Change in absorption spectrum of **2** in $CHCl_3$. From bottom (photostationary state upon irradiation with 365-nm light) to the top (after maintaining the solution at room temperature for 48 h).

The X-ray structure of the 1:1 inclusion crystals obtained from **2** and toluene was determined.[11] The host resembles a regular triangle in shape. The intercentroid distances, that is, A···B, B···C, and C···A, were 19.003 Å, 19.221 Å, and 19.212 Å, respectively. Angles BAC, ABC, and ACB were 60.39°, 60.36°, and 59.26°, respectively. The methyl group of toluene was disordered between two positions that have equal probabilities of being occupied as shown in Figure 7. NH–π interactions were observed between N(12)–H(82) and the centroid of phenyl ring *C2* [2.835 Å, (x, y, x) to ($1/2 + x$, $1.5 - y$, $1 - z$)]; The toluene molecules are trapped inside the

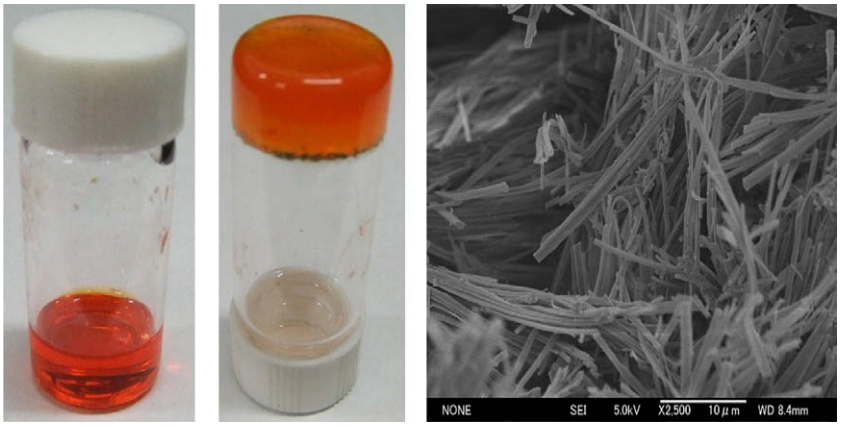

Figure 5. Photographs of typical benzene gels (left) and SEM image of dried gels (right).

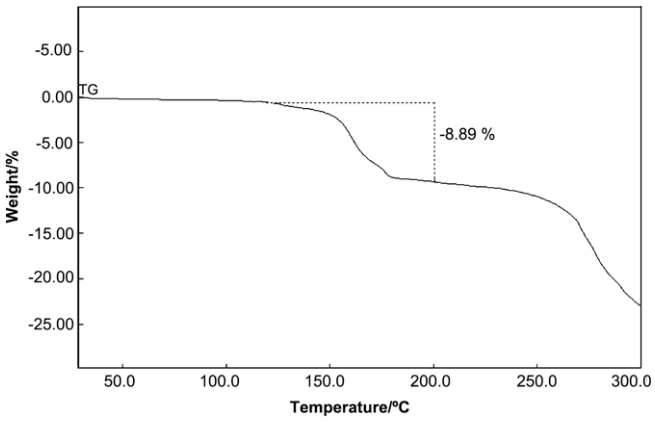

Figure 6. TG trace of 1:1 inclusion crystals obtained from **2** and toluene.

Table 1
Inclusion and gelation properties of chiral Shiff base macrocycles **1** and **2**

Guest	1	2
Benzene	Gel	1:1[a]
Toluene	—	1:1
o-Xylene	—	2:1
m-Xylene	—	2:1
p-Xylene	—	2:1

[a] Host–guest ratios were determined by thermogravimetry (TG) and ^{1}H NMR.

cavity of macrocycle. CH–π interactions were observed between C(60)–H(66) and the centroid of C2 [2.799 Å; (x, y, z) to ($-1/2 + x$, $1.5 - y$, $1 - z$)].

In conclusion, we report the synthesis of new chiral Shiff base macrocycles having three azobenzene chromophores and the inclusion, gelation, and photochromic properties of the macrocy-

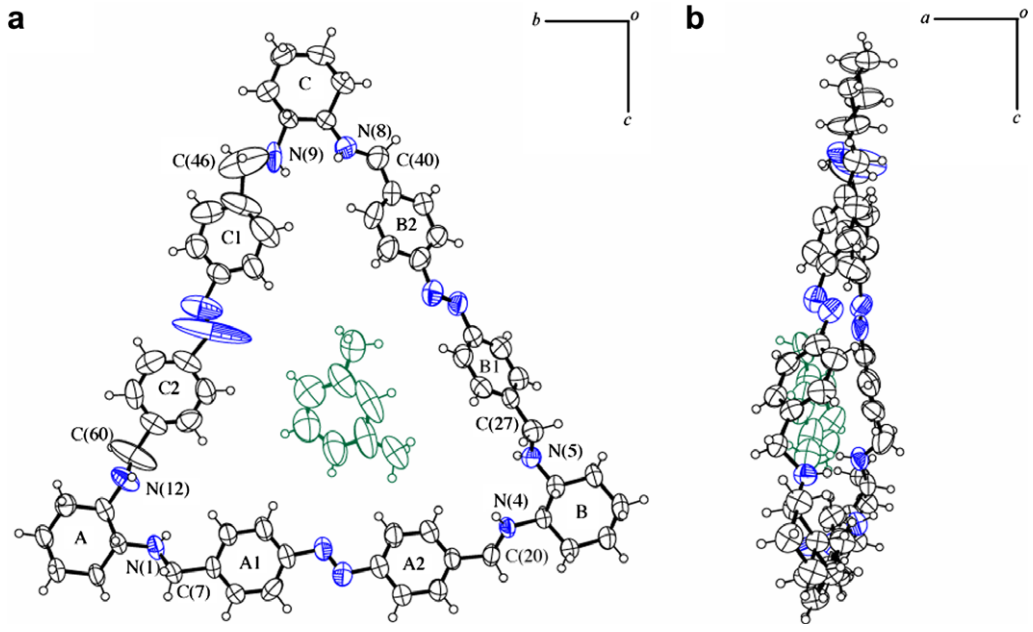

Figure 7. ORTEP diagram of 1:1 toluene complex of **2** with rings and selected atoms labeled. A, B, and C indicate cyclohexane; A*n*, B*n*, and C*n* (n = 1, 2) indicate phenyl rings. The guest toluene molecules are represented in green color.

cles. Research on further applications of these types of compounds is currently in progress.

Acknowledgment

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9. Synthesis of (*R,R,R,R,R,R*)-**1**: A mixture of azobenzene-4,4′-dicarbaldehyde (0.35 g, 1.47 mmol) and (1*R*,2*R*)-*trans*-1,2-diaminocyclohexane (0.17 g, 1.47 mmol) in $CHCl_3$ (40 mL) was stirred at rt for 24 h. The solvent was evaporated, and the residue was crystallized from a chloroform–ethyl acetate mixture to obtain orange needles of (*R,R,R,R,R,R*)-**1** in 91% yield (0.42 g). Mp >300 °C $[\alpha]_D$ −2439 (*c* 0.58, $CHCl_3$). IR 1639 cm^{-1} (C=N). ^1H NMR (400 MHz, $CDCl_3$): 8.62 (s, 6H, CH=N); 7.80 (d, 12H, *J* = 8.0 Hz, Ar); 7.70 (d, 12H, *J* = 8.0 Hz, Ar); 3.46 (m, 6H, CH); 1.86–1.52 (m, 24CH_2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 160.1; 153.5; 138.4; 128.7; 123.1; 74.5; 32.79; 24.5. ESI-MS: *m/z* 949.58 $[M+H]^+$. (*S,S,S,S,S,S*)-**1**: Prepared by the method described above. Yield: 84%. $[\alpha]_D$ +2465 (*c* 0.58, $CHCl_3$). Spectra were identical to those of (*R,R,R,R,R,R*)-**1**.
10. Synthesis of (*R,R,R,R,R,R*)-**2**: To a solution of (*R,R,R,R,R,R*)-**1** (0.093 g, 0.098 mmol) in $CHCl_3$ (10 mL) a solution of sodium borohydride (0.072 g, 1.9 mmol) in MeOH (10 mL) was added. The mixture was stirred at room temperature for 24 h. The solvents were evaporated and the product was extracted into chloroform. The combined chloroform extracts were dried over $MgSO_4$, and then the solvent was evaporated. The crude product was purified by recrystallization from chloroform–ethyl acetate mixture giving orange needles of (*R,R,R,R,R,R*)-**2** in 67% yield (0.063 g). Mp >300 °C $[\alpha]_D$ +274 (*c* 0.58, $CHCl_3$). IR 3285 cm^{-1} (NH). ^1H NMR (400 MHz, $CDCl_3$): 7.91 (d, 12H, *J* = 8.4 Hz, Ar); 7.47 (d, 12H, *J* = 8.4 Hz, Ar); 4.00 (d, 6H, *J* = 13.2 Hz, CH_2); 3.71 (d, 6H, *J* = 13.2 Hz, CH_2); 2.35–2.21 (m, 12H, CH_2); 1.95 (br s, 1H, NH); 1.78 (m, 6H, CH); 1.29–1.09 (m, 12H, CH_2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 151.7; 144.1; 128.6; 122.9; 60.7; 50.4; 31.4; 25.0. (*S,S,S,S,S,S*)-**2**: Prepared by the method described above. Yield: 64%. $[\alpha]_D$ −281 (*c* 0.58, $CHCl_3$). Spectra were identical with those of (*R,R,R,R,R,R*)-**2**.
11. Crystal data for 1:1 complex of **2** with toluene: $C_{67}H_{80}N_{12}$, *M* = 1053.45, orthorhombic, *a* = 8.0527(12) Å, *b* = 24.347(4) Å, *c* = 30.443(4) Å, *V* = 5968.6(15) $Å^3$, *T* = 173.1 K, space group $P2_12_12_1$, *Z* = 4, μ(Mo Kα) = 0.071 mm^{-1}, 52338 reflections measured, 13,353 independent reflections (R_{int} = 0.115). The final R_1 and *wR*(F^2) values were 0.1087 ($I > 2\sigma(I)$) and 0.3400 (all data), respectively. The goodness of fit on F^2 was 1.012. CCDC 763695 contains the supplementary crystallographic data for this Letter. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.