Chirality-Transfer Control Using a Heterotopic Zinc(II) Porphyrin Dimer

Yuji Kubo,*[,†] Takamoto Ohno,[†] Jun-ichi Yamanaka,[†] Sumio Tokita,[†] Takeaki Iida,[§] and Yoshihiro Ishimaru[§]

Department of Applied Chemistry
Faculty of Engineering, Saitama University
255 Shimo-ohkubo, Saitama 338-8570, Japan
Department of Functional Materials Science
Faculty of Engineering, Saitama University
255 Shimo-ohkubo, Saitama 338-8570, Japan

Received June 1, 2001

There is much growing interest in the control of chirality at the molecular level, which would be immediately applicable for the field of asymmetric catalysts,[1] sensors,[2] actuators,[2] and so on. Although considerable effort has been focused on the related manipulations involving chiral (helicity) induction[3] and the memory system of chirality,[4] there still remains the exploration of a cogent strategy toward this end. The key dynamic process is a conformational regulation associated with host−guest interaction. To tailor the molecular system for the approach, we have taken advantage of an anti-cooperative binding event (e.g., negative allostery[5]) as a potent methodology: *in a system, one effector entity can lead the system to commit an induced chirality to memory, whereas, under an alternative condition, the same effector can also suppress to induce the chirality to the system (Figure 1)*. Here, we report that a heterotopic zinc(II) porphyrin dimer **1**[6] does, in fact, serve as such a desired system.

System **1** contained paired porphyrin chromophores that allow us to monitor an induced chirality easily.[3b] Another remarkable feature is to employ a crown-strapped 1,1′-biphenyl unit as a spacer between the porphyrins, where two chiral atropisomers due to axial chirality exist. These isomers rapidly interconvert to one another in a solution at ambient conditions because of the low chiral barrier ($\Delta G^{\ddagger}_{340} = \sim 15$ kcalmol^{-1})[7] between them, corresponding to no circular dichroism (CD) in **1**. However, the binding of a chiral inducer which can ditopically interact with the concave porphyrins accompanying a preferential orientation would efficiently transfer the chirality to **1** through the complexation. To test this hypothesis, we employed Tröger's base analogue **2**[8] as a putative one, possessing a chiral "V"-shaped geometry as well as the amine N−N distance of 12 Å. We thus expected that **2** would bidentately bind to **1** in the concave cavity of the bis(porphyrin) with an induced-fit fashion since the optimized porphyrin center-to-center distance of **1** is ca. 21 Å.[6] Worthy of particular note is that this geometrical feature could lead a Ba^{2+}-assisted negative allostery for binding a α,ω-diamine with diamine N−N distance of 12 Å.[6]

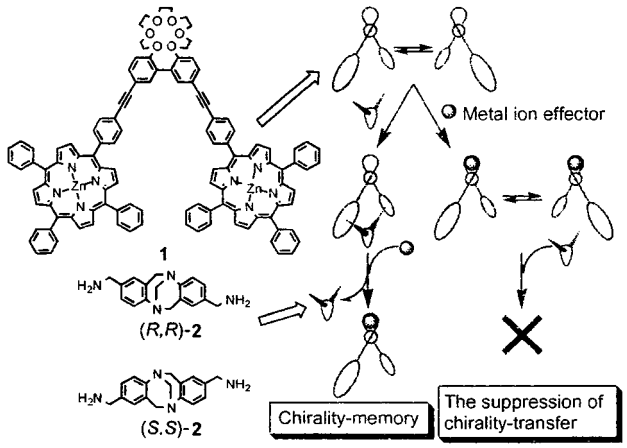

Figure 1. Design of chirality-transfer control using an anti-cooperative binding motif.

After the successful optical resolution of **2** (see Supporting Information), the significant interaction between **1** and (*R*,*R*)-**2** was observed using a UV/vis titration in CH_2Cl_2−MeCN (9:1 v/v); the Soret band of **1** bathochromically shifted from 423 to 429 nm after the addition of incremental amounts of **2**, the stoichiometric assessment by a Job plot[9] suggesting a 1:1 complex formation. The binding constant (log K_a) was estimated to be 5.91 ± 2% using a nonlinear curve-fitting plot. The following CD measurement was carried out to give rise to a positive exciton-coupled CD spectra as a result of a chiral twist of the built-in porphyrins, reflecting that the *S*-enantiomer of **1** was induced by (*R*,*R*)-**2** through the complexation motif as shown in Figure 1. When (*S*,*S*)-**2** was also added to the solution, an anticlockwise twist was induced in **1**, which could be read in the form of negative CD exciton coupling. The chelation was supported by ^{1}H NMR spectra in $CDCl_3$−CD_3CN (9:1 v/v) at room temperature where the proton resonances of (*R*,*R*)-**2** entirely upfield-shifted upon complexation with **1**. Particularly, the resonances arising from the 2,8-bis(aminomethyl) protons clearly appeared as a broad signal at −4.28 ppm and as one pair of doublets at −1.80 ppm (J = 13.2 Hz) and −1.60 ppm (J = 15.2 Hz). The spectrum further showed no signals assignable to a thermodynamically unfavorable diastereoisomer, indicating that the almost 100% diastereoisomeric excess was obtained. Further, the control experiment using zinc(II) tetraphenylporphyrin and (*R*,*R*)-**2** did not show any induced CD spectra.

[†] Department of Applied Chemistry.
[§] Department of Functional Materials Science.

(1) Feringa, B. L.; van Delden, R. A. *Angew. Chem., Int. Ed.* **1999**, *38*, 3418−3438.
(2) Robertson, A.; Shinkai, S. *Coord. Chem. Rev.* **2000**, *205*, 157−199.
(3) For chiral induction, see: (a) Knof, U.; von Zelewsky, A. *Angew. Chem., Int. Ed.* **1999**, *38*, 302−322. (b) Borovkov, V. V.; Lintuluoto, J. M.; Inoue, Y. *J. Am. Chem. Soc.* **2001**, *123*, 2979−2989 and references therein. (c) For helical induction, see: Mizutani, T.; Sakai, N.; Yagi, S.; Takagishi, T.; Kitagawa, S.; Ogoshi, H. *J. Am. Chem. Soc.* **2000**, *122*, 748−749; Yamamoto, M.; Takeuchi, M.; Shinkai, S.; Tani, F.; Naruta, Y. *J. Chem. Soc., Perkin Trans. 2* **2000**, 9−16; Jung, O.-S.; Kim, Y. J.; Lee, Y.-A.; Park, J. K.; Chae, H. K. *J. Am. Chem. Soc.* **2000**, *122*, 9921−9925; Ky Hirschberg, J. H. K.; Brunsveld, L.; Ramzl, A.; Vekemans, J. A. J. M.; Sijbesma, R. P.; Meijer, E. W. *Nature* **2000**, *407*, 167−170; Lahiri, S.; Thompson, J. L.; Moore, J. S. *J. Am. Chem. Soc.* **2000**, *122*, 11315−11319; Allen, W. E.; Fowler, C. J.; Lynch, V. M.; Sessler, J. L. *Chem. Eur. J.* **2001**, *7*, 721−729; Ikeda, A.; Udzu, H.; Zhong, Z.; Shinkai, S.; Sakamoto, S.; Yamaguchi, K. *J. Am. Chem. Soc.* **2001**, *123*, 3872−3877; Nakashima, H.; Koe, J. R.; Torimitsu, K.; Fujiki, M. *J. Am. Chem. Soc.* **2001**, *123*, 4847−4848.
(4) Frusho, Y.; Kimura, T.; Mizuno, Y.; Aida, T. *J. Am. Chem. Soc.* **1997**, *119*, 5267−5268; Mizuno, T.; Takeuchi, M.; Hamachi, I.; Nakashima, K.; Shinkai, S. *Chem. Commun.* **1997**, 1793−1794; Yashima, E.; Maeda, K.; Okamoto, Y. *Nature* **1999**, *399*, 449−451; Sugisaki, A.; Ikeda, M.; Takeuchi, M.; Robertson, A.; Shinkai, S. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3259−3264; Yashima, E.; Maeda, K.; Yamanaka, T. *J. Am. Chem. Soc.* **2000**, *122*, 7813−7814; Jung, J. H.; Ono, Y.; Shinkai, S. *Chem. Eur. J.* **2000**, *6*, 4552−4557; Prins, L. J.; De Jong, F.; Timmerman, P.; Reinhoudt, D. N. *Nature* **2000**, *408*, 181−184.
(5) For a review of allostery, see: Nabeshima, T. *Coord. Chem. Rev.* **1996**, *148*, 151−169.
(6) Kubo, Y.; Murai, Y.; Yamanaka, J.; Tokita, S.; Ishimaru, Y. *Tetrahedron Lett.* **1999**, *40*, 6019−6023.
(7) In VT NMR experiment using 5,5′-diethynyl-2,2′-biphenyl-20-crown-6, the methylene resonances of the crown segment did not show any broadening of the spectra even at −49 °C in $CDCl_3$−CD_3CN (9:1 v/v), indicating that the strapped crown does not affect the rotational barrier of the biaryl unit. As a result, the $\Delta G^{\ddagger}_{340}$ could be taken as the similar value of 2,2′-dimethoxy-1,1′-biphenyl, see: Bott, G.; Field, L. D.; Sternhell, S. *J. Am. Chem. Soc.* **1980**, *102*, 5618−5626.
(8) For the synthesis of the racemic mixtures, see: Wilcox, C. S. *Tetrahedron Lett.* **1985**, *26*, 5749−5752.
(9) Job, P. *Ann. Chim. Ser.* **1928**, *9*, 113−134.

10.1021/ja0113448 CCC: $20.00
Published on Web 11/17/2001

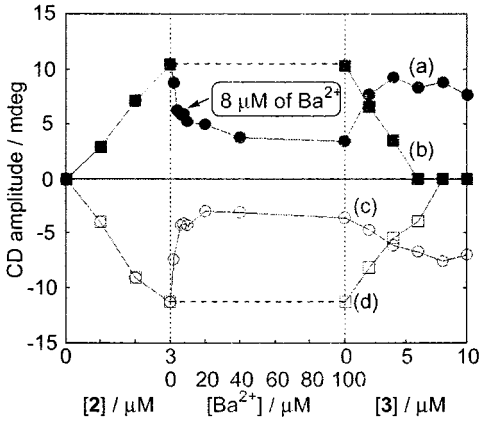

Figure 2. (a) Changes in CD amplitude induced by (*R*,*R*)-**2** addition and subsequent Ba^{2+} and **3** addition. (b) Changes in CD amplitude induced by (*R*,*R*)-**2** addition and subsequent **3** addition. (c) Changes in CD amplitude induced by (*S*,*S*)-**2** addition and subsequent Ba^{2+} and **3** addition. (d) Changes in CD amplitude induced by (*S*,*S*)-**2** addition and subsequent **3** addition: the CD amplitude represents the total amplitude of CD couplets ($\Delta\theta = \theta_{\text{first Cotton}} - \theta_{\text{second Cotton}}$). These data were collected in CH_2Cl_2−MeCN (9:1 v/v) at 25 °C when the concentration of **1** is 2.0 μM.

At the next stage, we investigated to see if a metal ion effector could regulate the binding event with **2** and guide to fix the induced chirality. The addition of Ba^{2+} as a ClO_4^- salt caused a significant decrease in the absorption intensity at 429 nm due to the **1**·(*R*,*R*)-**2** complex, suggesting that the complex dissociated.[10] This is attributable to the fact that the Ba^{2+} accommodated in the strapped crown has made the porphyrin units to be apart from each other and then to disrupt the necessary binding geometry for (*R*,*R*)-**2**. Looking the CD spectra (Figure 2), the CD amplitude of **1** induced by 1.5 equiv of (*R*,*R*)-**2**, where the ratio of complexation between **1** and (*R*,*R*)-**2** is ca. 70%, progressively decreased up to 4 equiv of Ba^{2+} addition (8 μM), but there still remained CD active with $[\theta] = 3.45°$ ever in the presence of an excess Ba^{2+} (100 μM). The reduced CD intensity might be due to the conformational flexibility by the competitive binding event between **1**·(*R*,*R*)-**2** and **1**·Ba^{2+}. Thus, to remove (*R*,*R*)-**2** from the complexation event completely as well as to fix the conformation of **1**, we added achiral 1,10-diaminodecane **3.**[11] Consequently, the CD amplitude was found to increase again, clearly indicating that the added **3** fixed the chirality induced by (*R*,*R*)-**2**. This result is the most striking finding because the addition of **3** to a Ba^{2+}-free solution of **1** and (*R*,*R*)-**2** resulted in a silent CD.[12] The assessment was also taken by ^{1}H NMR spectra; in the presence or absence of Ba^{2+}, the proton resonances due to the dissociated (*R*,*R*)-**2** were almost completely detected after treating with **3**. On the other hand, when (*S*,*S*)-**2** was employed, the CD spectra showed mirror-image behaviors (Figure 2). The simple metal ion, Ba^{2+}, playing an important role for dynamically regulating the host−guest interaction involving the chiral inducer **2** as well as the motion of the rotatable biphenyl unit, showed a high chirality-memory efficiency. The memory on **1** was comparatively stable: the CD intensity showed little decrease after 1 day.

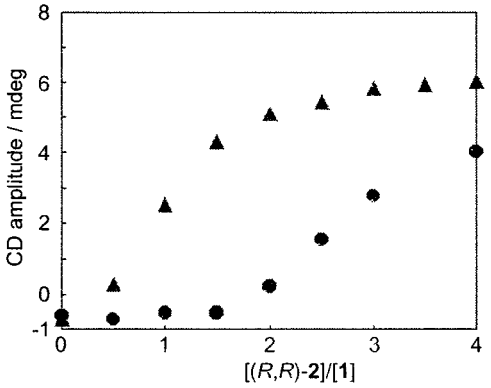

Figure 3. Changes in CD amplitude ($\Delta\theta$) of **1** (2 μM) induced by (*R*,*R*)-**2** addition in the presence of Ba^{2+} (100 μM) (●) or the absence of Ba^{2+} (▲). These data were collected in CH_2Cl_2-MeCN (9:1 v/v) at 25 °C.

An alternative issue of interest is to see if the functional metal ion could suppress the chiral induction by **2**. When adding 50 equiv of Ba^{2+} to a solution of **1** prior to complexation with **2**, the appearance of CD band with incremental amounts of (*R*,*R*)-**2** was significantly suppressed (Figure 3). Of particular interest is that the chiral induction by adding 1.5 equiv of (*R*,*R*)-**2**, the amount being equal with that in the condition of the chiral fixation (vide supra), has been completely prevented by the Ba^{2+}.

Although a more detailed estimation as well as the use of other effective ions is in progress, the preliminary results described here lead us to suggest a new approach to the generation of chirality-transfer control. Further, by meeting with porphyrin chemistry,[13] we feel that such systems would be most welcome in the field of porphyrin-based molecular architectures of nanoscale technology. Most notably, the chiral inducer could be automatically removed from the bis(porphyrin)-containing cavity by the effector (Ba^{2+}). It means that the porphyrin-based chiral microenvironment could be created as one pleases.

Acknowledgment. Y.K. acknowledges PRESTO (Precursory Research for Embryonic Science and Technology) of Japan Science and Technology Corporation (JST) for the financial support. Also, this work has been partly supported by The Nishida Research Fund For Fundamental Organic Chemistry and Mitsubishi Chemical Corporation Fund.

Supporting Information Available: The assignment data of **1** and **2**, the experimental data of optical resolvement of **2**, the monitoring of chirality transfer control by means of UV/vis and CD spectra (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA0113448

(10) The Ba^{2+}-assisted dissociation of (*R*,*R*)-**2** form **1** was checked by using ^{1}H NMR analysis; the upfield-shifted amino (−4.28 ppm) and methylene (−1.80 and −1.60 ppm) resonances almost disappeared after solid[Ba-$(ClO_4)_2$]−liquid[2.0 mM of **1** and 1.0 mM of (*R*,*R*)-**2** in $CDCl_3$−CD_3CN (9:1 v/v)] two-phase solvent extraction. The low solubility of $Ba(ClO_4)_2$ in the employed solvent system could not allow us to assess the K_a value between **1** and Ba^{2+} by means of a NMR study. However, we currently found that the fluorescence of 5,5′-diethynyl-2,2′-biphenyl-20-crown-6 as the spacer unit of **1** ($\lambda_{ex} = 240$ nm, $\lambda_{em} = 350$ nm) in CH_2Cl_2−MeCN (9:1 v/v) was efficiently quenched by adding Ba^{2+}. Thus, by making use of fluorescent titrations based on this phenomenon, the binding constant (log K_a) for the complexation between the spacer unit of **1** and Ba^{2+} could be estimated to be 6.09 ± 4%, being larger than that of **1** and **2**.

(11) The affinity of guest diamine with **1** would depend on its N−N length; a better complementarity of **1** and **3** allowed to form a strong complex (log $K_a = 6.24 \pm 2\%$) between them.

(12) The racemization is so fast that the CD spectrum change cannot be followed by the conventional spectroscopic method even at −10 °C.

(13) *The Porphyrin Handbook*; Kadish, K., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, 2000.