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Effective cation-assisted chirality induction using a dibenzo-diaza-30-crown-10 with bis(zinc(II) porphyrin) units†

Yuji Kubo,* Yusuke Ishii, Toshiharu Yoshizawa and Sumio Tokita

Department of Applied Chemistry, Faculty of Engineering, Saitama University, 255 Shimo-ohkubo, Sakura-ku, Saitama 338-8570, Japan. E-mail: yuji@apc.saitama-u.ac.jp; Fax: +81-48-858-3514; Tel: +81-48-858-3514

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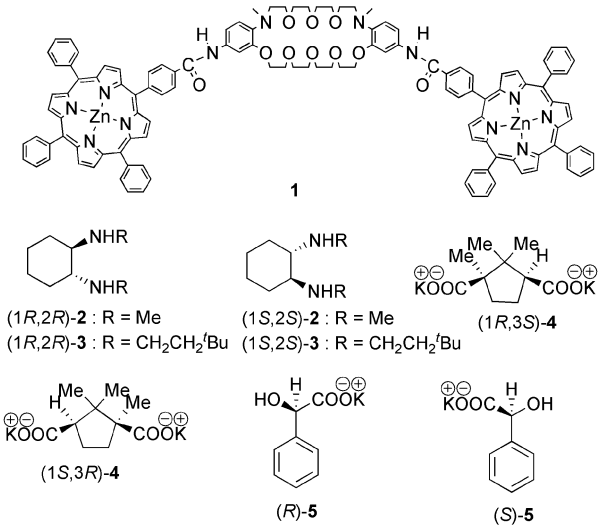
The first rationalized crown ether–bis(porphyrin) conjugate with a large ring-based conformation flexiblity 1 has been synthesized; the achiral-to-chiral transformation upon complexation with chiral diamines is assisted by K^+ accommodated in the crowned moiety, and it is possible to determine the chirality of carboxylates as potassium salts.

Exploration of how to manipulate chirality at the molecular level is a burgeoning research field with wide application including chiral sensors,[1] asymmetric catalysts,[2] chirality memory systems,[3] and actuators such as molecular motors.[4] Chirality induction (chirogenesis),[5] in which a chiral-orientated conformation is created by the transfer of chiral information from an external species by means of noncovalent interaction has great potential toward this approach. On the other hand, there is interest in "shape" regulation of molecular systems that respond to external stimuli, so-called "allostery", in the basic design of function-switchable molecular systems.[6] Therefore, chirality induction associated with allosteric control is now an intriguing topic.[7] Bis(porphyrin)s are good units of chirality induction[5] because they serve as ditopic chiral guest binding sites, and also as reporters of chirality induction by means of circular dichroism (CD) spectroscopy. However, the derivative capable of controlling chirality induction is still in its infancy,[8] even though it is already possible to generate chirality memory event at the supramolecular level.[9] Our approach toward this subject is thus to use a highly flexible dibenzo-30-crown-10 scaffold,[10] in which K^+ is wrapped significantly to induce the topological change into tweezer-like structure,[10a] and which generates a chiral screw conformation.[10b] These characteristics allow the synthesis of the first rationalized crown ether–bis(porphyrin) conjugate **1** (see, ESI†), showing an effective cation-assisted chirality induction. The intriguing aspects are reported in this contribution.

Upon complexation with a suitable bidentate ligand, the conformational flexibility of the crowned spacer in **1** allows for switching of the porphyrin orientation into the tweezer. As expected, significant interaction between **1** and chiral *N*,*N*′-dimethylcyclohexane-1,2-diamine (1*R*,2*R*)-**2** was observed in a UV/Vis titration in CH_2Cl_2–MeCN (8 : 2 v/v). However, the Soret band at 423 nm did not show a clear spectral change with increasing amount of (1*R*,2*R*)-**2**, possibly because the Soret band was affected by an intramolecular exciton interaction of the porphyrin-chromophores accompanying the conformation switch (*vide infra*). Complexation was therefore assessed from the shift of Q(1,0)-band, from 555 nm to 562 nm; use of a Job plot[11] suggests a 1 : 1 complex formation, and the binding constant (log K_a) was estimated to be 6.04 ± 2% using a nonlinear curve fitting method. The following CD measurement was carried out to give rise to a positive exciton coupled CD spectra (Fig. 1a), and leading to a clockwise twist between the porphyrins [$\Delta\varepsilon$ + 416 $M^{-1}cm^{-1}$ (433 nm)/−354 $M^{-1}cm^{-1}$ (422 nm)] when 6 equiv. of (1*R*,2*R*)-**2** was added to the solution. This follows from the generation of a chiral screw structure of **1** *via* a steric repulsion mechanism between the coordinated diamine **2** and the neighbouring porphyrin rings, as shown in Fig. 1b. The complexation was verified by ^1H NMR spectra in which the proton resonances due to (1*R*,2*R*)-**2** were entirely up-field shifted: in particular, the methyl resonances of **2** was found to shift from 2.38 ppm to −3.71 ppm by adding **1**. In contrast, the addition of (1*S*,2*S*)-**2** into a solution of **1** gave a negative exciton coupled CD spectrum (Fig. 1a), indicating that the chirality induced in **1** reflects the geometry of the chiral diamine.



A further feature of **1** is that a suitable metal ion accommodated in the crown segment can induce a tweezer-like structure: the UV/Vis titration monitoring the Soret band of **1** upon adding $KClO_4$ in CH_2Cl_2–MeCN (8 : 2 v/v) showed a hypsochromic shift by 2 nm, along with significantly decreasing absorption intensity (Fig. 2a). The spectral change is almost saturated upon adding a stoichiometric amount of K^+, indicating that cofacialization of the porphyrin units takes place effectively in these conditions. This result led us to study how the encapsulated metal ion could assist in chirality induction. Fig. 2b shows CD amplitude changes as a function of the incremental amounts of chiral **2** in the absence or presence of 5 equiv. of K^+: the presence of K^+ gave a steep

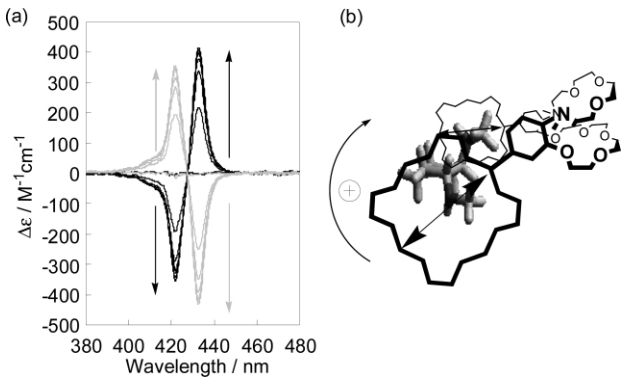


Fig. 1 (a) CD spectral changes of **1** upon adding of (1*R*,2*R*)-**2** (black line) or (1*S*,2*S*)-**2** (gray line) in CH_2Cl_2–MeCN (8 : 2 v/v) at 25 °C, [**1**] = 2.0 μM; [**2**] = 0, 2.0, 4.0, 6.0, 8.0, 10, 12 μM: (b) A plausible binding motif of **1**-(1*R*,2*R*)-**2** complex.

† Electronic supplementary information (ESI) available: synthesis of **1**. See http://www.rsc.org/suppdata/cc/b4/b403684k/

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ascending behaviour in the CD amplitude compared to K^+-free conditions. It virtually reached a plateau at a [(1*R*,2*R*)-**2**] : [**1**] ratio of 2 : 1 where 45% enhanced amplitude of CD spectra was observed. This result is supported by the fact that the apparent association constant of **1**-(1*R*,2*R*)-**2** complex under K^+-coordinated conditions is twice as great as without K^+, meaning that allosteric effect in which the K^+-binding tunes the conformation to bind (1*R*,2*R*)-**2** can assist chirality induction in **1**. A similar enhancement was also obtained in the case of (1*S*,2*S*)-**2**.‡ K^+-assisted chirality induction was found to be critical in the case of (1*R*,2*R*)-**3** with bulky substituents at the amino groups. The hindered alkyl group prevented ditopic interactions involving the terminal amino nitrogens and the Zn(II) porphyrins, the CD being silent even *ca*. 26 h later after addition of **3** (Fig. 3a). However, the presence of K^+ led to a small but significant CD signal being detected (Fig. 3b). Upon adding 60 equiv. of (1*R*,2*R*)-**3**, a negative exciton-coupled CD spectrum ($\Delta\varepsilon$ -38 $M^{-1}cm^{-1}$ (438 nm)/$+33$ $M^{-1}cm^{-1}$ (422 nm)) was observed, although its sign is opposite to that in the case of (1*R*,2*R*)-**2**. A different binding orientation from that for **2** may result in inversion of the twist direction.

Note that **1** is not limited in its utility to the chiral diamines; using **1** it is possible to read out the chirality of potassium salts of carboxylates such as camphorates and mandelates through solid/liquid two-phase extraction. The procedure is as follows: excess chiral carboxylates as K^+ salts (**4** and **5**) were respectively added to a 2.0 μM of CH_2Cl_2–MeCN (2 : 8 v/v) solution of **1**. The mixtures were sonicated for 2 min and stirred at room temperature, the excess salt of each mixture was then filtered out and the filtrate was examined by CD spectroscopy. Exciton coupled CD spectra were clearly observed, corresponding to chirality of the guest carboxylates (Table 1). These results imply that making use of the extractability of potassium salts due to the crown segment as well as the K^+-assisted tweezer-like conformation would be a potent way for chirality sensing of organic salts which are scarcely soluble in nonpolar solvent.

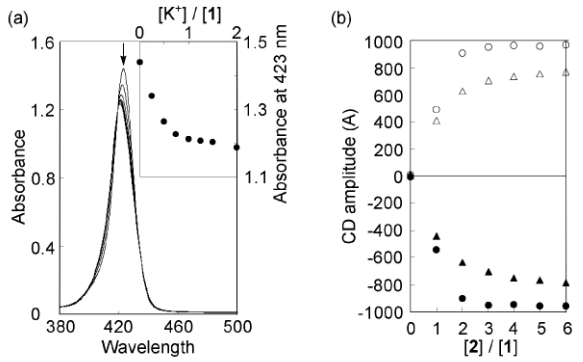

Fig. 2 (a) UV/Vis spectral changes of **1** upon adding of K^+ in CH_2Cl_2–MeCN (8 : 2 v/v) at 25 °C, [**1**] = 2.0 μM; [K^+] = 0, 0.5, 1.0, 1.5, 2.0, 3.0, 4.0 μM. (b) Changes in CD amplitude [A (= $\Delta\varepsilon_1 - \Delta\varepsilon_2$)] of **1** (2 μM) upon complexation with chiral **2** in the presence or absence of K^+ (5 equiv.) in CH_2Cl_2–MeCN (8 : 2 v/v) at 25 °C: (○) (1*R*,2*R*)-**2** with K^+; (△) (1*R*,2*R*)-**2** without K^+; (●) (1*S*,2*S*)-**2** with K^+; (▲) (1*S*,2*S*)-**2** without K^+.

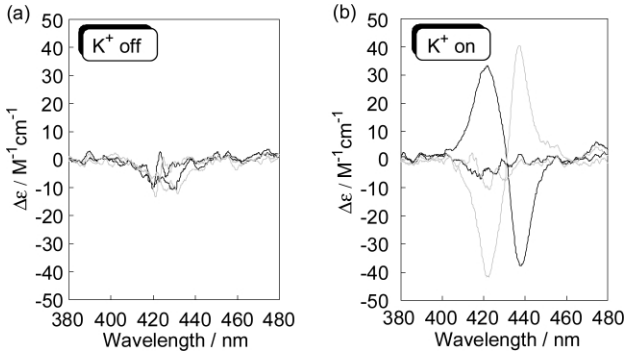

Fig. 3 Changes in CD amplitude of **1** (2 μM) upon complexation with chiral **3** in the absence (a) or presence of 5 equiv. of K^+ (b) in CH_2Cl_2–MeC (8 : 2 v/v) at 25 °C: [**1**] = 2.0 μM; [(1*R*,2*R*)-**3**] = 0, 120 μM (black line); [(1*S*,2*S*)-**3**] = 0, 120 μM (gray line).§

Table 1 CD spectral data after solid [**4** or **5**]/liquid [**1**] in CH_2Cl_2–MeCN (2 : 8 v/v) two-phase extraction at 25 °C[a]

Guest	CD sign and peak position/nm		Total amplitude
	1st Cotton effect	2nd Cotton effect	A (= $\Delta\varepsilon_1 - \Delta\varepsilon_2$)/$M^{-1}$ cm^{-1}
(1*R*,3*S*)-**4**	+430	−421	+56
(1*S*,3*R*)-**4**	−430	+421	−38
(*R*)-**5**	+435	−419	+43
(*S*)-**5**	−435	+419	−37

[a] [**1**] = 2.0 μM.

In conclusion, the results described in this paper clearly show a new potential of synthetic receptors possessing crown ether units. The large ring-sized macrocycle is easily modified by inserting porphyrin units to tailor it for application as a new type of chiral probe capable of determining the absolute configurations of various kinds of substrates. The exploration of chirality-memory systems using **1** is also one of our subjects.

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Notes and references

‡ The CD amplitude is influenced by the polarity of the employed solvent. The CD amplitude of **1** in CH_2Cl_2 upon addition of (1*S*,2*S*)-**2** increased by 9% compared to the case in CH_2Cl_2–MeCN (8 : 2 v/v)).

§ These spectra were measured when *ca*. 26 h passed after the mixing of **1** and **3** because the chiral induction is kinetically slow. The details involving the time-dependency are under investigation.

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