Chirality induction in a cation-driven assembly using a crowned metalloporphyrin†

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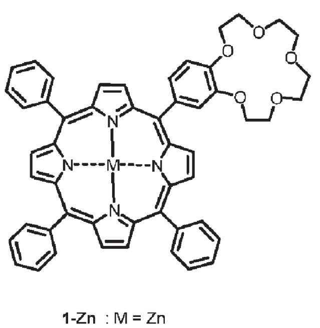
15-Crown-5-appended metalloporphyrin causes a K$^+$-driven self-organization to bind a bifunctional guest ditopically, thereby allowing the circular dichroism (CD) detection of chirality induced in the ensemble when chiral amines are employed as the guest; the chiroptical properties are discussed.

The investigation of the interdisciplinary area between supramolecular and chiral chemistry has currently attracted considerable attention because the information obtained contributes to chirotechnology.[1] In particular, the efficient generation and control of chirality lead to the development of advanced functional materials such as sensors,[2] asymmetric catalysis,[3] liquid crystals,[4] nonlinear optics[5] and other elaborated systems.[6] In this regard, porphyrins are useful molecular tools because of their synthetic versatility and associations involving host–guest interaction. Therefore, the related systems developed so far serve as artificial receptors for chiral recognition[7] as well as chiral catalysts.[8] Further, the chromophoric properties, characterized by an intense Soret band, enable us to monitor chiral interactions by circular dichroism (CD) spectroscopy, thereby allowing us to develop CD reporters.[9] In this context, bis(metalloporphyrin) systems with suitable spacers have been widely used to determine the absolute configuration of chiral species; the guest binding and host–guest steric interaction induce a unidirectional screw conformation of the porphyrins, displaying the CD spectrum to read out the chirality.[10] On the other hand, one of the intriguing topics in supramolecular chirality is the control of chirality in porphyrin-based self-assembling architectures, wherein the induced chiral aggregation is easily monitored by the CD technique.[11] Thus, we realize that the synthesis of porphyrin derivatives capable of producing a discrete self-assembly with tweezers geometry could lead to the development of noncovalently organized chiroptical tools. We expect that clockwise or anticlockwise-twisted geometry in the porphyrin ensemble would be generated by coordination with an asymmetric guest. With this background, we focus on crowned porphyrins[12] in which crown ether could serve as a noncovalent linker in the presence of a suitable metal ion to produce the required organization.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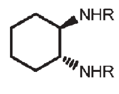
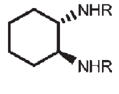
1-Mg : M = Mg


(1*R*,2*R*)-**2** : R = Me
(1*R*,2*R*)-**3** : R = H
(1*R*,2*R*)-**4** : R = $CH_2CH_2{}^tBu$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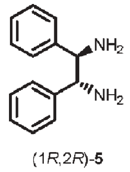
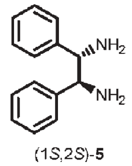
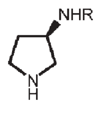

(1*R*,2*R*)-**5**


(1*S*,2*S*)-**5**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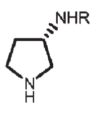
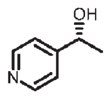
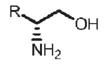
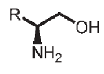
(3*R*)-**7** : R = H


(3*S*)-**6** : R = Me
(3*S*)-**7** : R = H


(*R*)-**8**


(*R*)-**9** : R = Bn
(*R*)-**10** : R = Ph


(*S*)-**9** : R = Bn
(*S*)-**10** : R = Ph

In this contribution, we report discrete self-assembled systems using 15-crown-5-appended metalloporphyrins (**1**–Zn and **1**–Mg); K$^+$ is used as a key element for the generation. K$^+$ is sandwiched between 15-crown-5 entities that append to each porphyrin, resulting in a noncovalent tweezers-type bis(porphyrin). Although the details are described below, we present for the first time metal ion-driven self-organized chiroptical tools for various chiral amines. First, the porphyrin unit, **1**–Zn,[13] was synthesized using a known procedure (see ESI†). To ensure that the desired self-assembly would occur in solution, we performed UV-vis titrations of **1**–Zn with bifunctional 1,4-diazabicyclo[2.2.2]octane (DABCO) (see Fig. S1 in the ESI†). The addition of incremental amounts of DABCO to a CH_2Cl_2–MeCN (9 : 1 v/v) solution of **1**–Zn at 25 °C caused the absorption of the Soret band to shift bathochromically by 8 nm, and the obtained titration curve reproduced a 1 : 1 binding model to give the association constant of 4.31×10^5 M^{-1} ($R^2 = 0.999$).‡ This value is consistent with that reported by Sanders *et al.*[14] However, in the presence of K$^+$ (0.5 equiv.), the spectral behaviour for increasing amounts of DABCO was different from that in K$^+$-free conditions; the lower absorption intensity at 428 nm than that in the K$^+$-free conditions indicated excitonic coupling in the Soret bond. This implied that the porphyrins were close to each other in the presence of K$^+$. Moreover, the titration curvature with DABCO fitted a stoichiometric 2 : 1 (**1**–Zn : DABCO) binding model to give an apparent association constant of (6.46×10^{10}) M^{-2} ($R^2 = 0.982$).‡ The

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† Electronic supplementary information (ESI) available: Synthesis of **1**–Zn and **1**–Mg and spectroscopic data. See DOI: 10.1039/b703670a

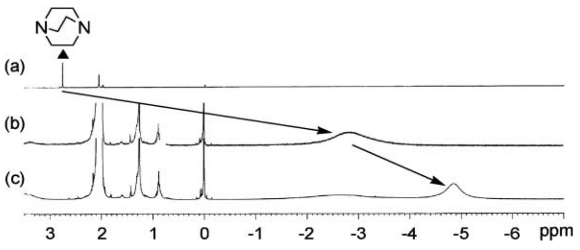

Fig. 1 ^{1}H NMR spectra of (a) DABCO, (b) DABCO with **1**–Zn and (c) DABCO with **1**–Zn in the presence of K$^+$ in CDCl$_3$–CD$_3$CN (4 : 1 v/v) at 23 °C. [DABCO] = 4 mM, [**1**–Zn] = 8 mM.

K$^+$-controllable interaction between **1**–Zn and DABCO was examined by ^{1}H NMR measurements (Fig. 1); a CDCl$_3$–CD$_3$CN (4 : 1 v/v) solution of DABCO (4 mM) was titrated with **1**–Zn (8 mM) in the absence or presence of K$^+$. The top spectrum in Fig. 1(a) shows protons due to the guest amine, where methylene resonance was detected at 2.77 ppm. When 2 equiv. of **1**–Zn (Fig. 1(b)) was added, the signal was shifted to a high field by 5.59 ppm with signal broadening. The observed broad signals can be attributed to the exchange of free and DABCO-coordinated species, which occurs at a rate observable within the NMR time scale. However, the solid [KClO$_4$]–liquid [**1**–Zn (8 mM) and DABCO (4 mM) in CDCl$_3$–CD$_3$CN (4 : 1 v/v) solution] two-phase solvent extraction led to a further upfield shift ($\Delta\delta$ = 2.04 ppm) that sharpened the signals to a certain extent (Fig. 1(c)). This can be explained on the basis of the summation of the ring current effects, which supports the fact that K$^+$-assisted dimerization facilitates the ditopic association of DABCO. Direct evidence for the formation of the supramolecular ensemble was obtained by using a cold-spray ionization mass spectrometer (CSI-MS).[15] A CH$_2$Cl$_2$–MeCN solution (9 : 1 v/v) comprising **1**–Zn (0.4 mM) and DABCO (0.2 mM) in the presence of KClO$_4$ (0.2 mM) was prepared, and the sample was injected into the mass spectrometer at a spray temperature of −30 °C. KClO$_4$ produced significant peaks in the spectrum, wherein ensemble peaks of [2(**1**–Zn) + K]$^+$ and [2(**1**–Zn) + K + DABCO]$^+$ were clearly observed at *m*/*z* 1771.63 (calcd. 1771.45) and *m*/*z* 1883.71 (calcd. 1883.55), respectively (Fig. 2). Overall, these results indicate that the porphyrin assembly creates a microenvironment to bind DABCO ditopically. Evidently, a very complicated CSI-MS spectrum was obtained in the absence of K$^+$ (see Fig. S5(a) in the ESI†).

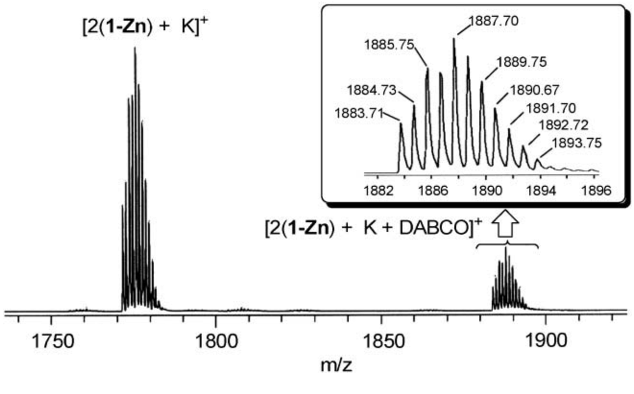

Fig. 2 CSI-MS spectra of **1**–Zn in the presence of K$^+$ upon addition of DABCO in CH$_2$Cl$_2$–MeCN (9 : 1 v/v). [**1**–Zn] = 0.4 mM, [DABCO] = 0.2 mM, [KClO$_4$] = 0.2 mM.

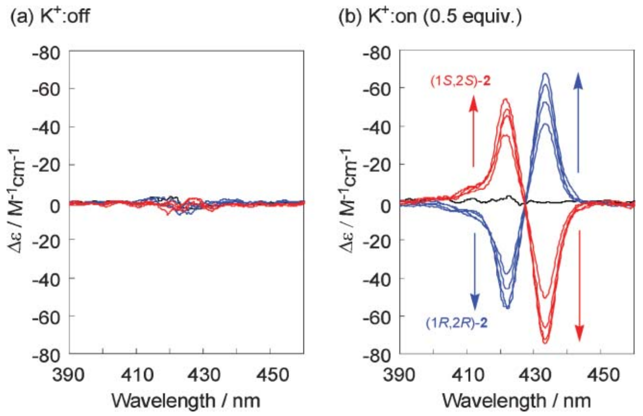

Fig. 3 CD spectral changes of **1**–Zn upon adding of (1*R*,2*R*)-**2** (blue line) or (1*S*,2*S*)-**2** (red line) in the absence (a) or presence (b) of K$^+$ in CH$_2$Cl$_2$–MeCN (9 : 1 v/v) at 25 °C. [**1**–Zn] = 4.0 μM, [KClO$_4$] = 2.0 μM, [(1*R*,2*R*)-**2**] = [(1*S*,2*S*)-**2**] = 0, 4, 8, 12, 16 μM.

It is interesting to examine if asymmetric diamines as bifunctional guests could induce chirality in the K$^+$-assisted dimerization of **1**–Zn. Fig. 3 shows that the CD amplitude changes as a function of the incremental amounts of optically active *N*,*N*′-dimethylcyclohexane-1,2-diamine **2** in the presence and absence of 0.5 equiv. of K$^+$. CD was not observed when chiral **2** was added to the solution under K$^+$-free conditions, whereas 0.5 equiv. of K$^+$ allowed us to detect exciton-coupled bisignate CD spectra with each chiral **2** [$\Delta\varepsilon$ + 67.1 M^{-1} cm^{-1} (433 nm)/ −55.8 M^{-1} cm^{-1} (422 nm) for 4 equiv. of (1*R*,2*R*)-**2**; [$\Delta\varepsilon$ −74.1 M^{-1} cm^{-1} (433 nm)/+53.2 M^{-1} cm^{-1} (422 nm) for 4 equiv. of (1*S*,2*S*)-**2**].§ The bisignate CD curves serve as evidence for the chiral twist conformation between two **1**–Zn units in the ensemble, wherein coordinated (1*R*,2*R*)-**2** and (1*S*,2*S*)-**2** induce clockwise and anticlockwise screw structures of the ensemble, respectively. The results indicate the potential use as a self-organized chiroptical tool capable of monitoring the chirality of the analytes on the basis of the CD exciton chirality method.[16] Thus, we measured the CD spectra of the system with several amines, as summarized in Table 1. The use of asymmetric 1,2-diaminocyclohexanes **3** induced significant CD spectra in the presence of K$^+$; the values of the CD amplitude *A* upon addition of 8 μM of (1*R*,2*R*)-**3** and (1*S*,2*S*)-**3** to the solution are −60.1 M^{-1} cm^{-1} and +65.0 M^{-1} cm^{-1}, respectively, at 0 °C. It should be noted that the chirality signs induced by **3** were opposite to those for the corresponding **2**. The CD sign depends on the stereospecific orientation of the interacting electric transitions[17] in the ensemble, wherein a unidirectional twist of the porphyrins occurs in a direction govened by the guest's stereochemistry. Here, we should consider the reason why opposite CD signs were observed between the **1**–Zn·**2**·K$^+$ and **1**–Zn·**3**·K$^+$ systems. *trans*-Cyclohexane-1,2-diamines have two types of conformational isomers in the chair form; both amino groups are positioned at equatorial (1,2-ee) and at axial (1,2-aa). The observed CD signs may reflect the stabilized conformation of the diamines. Borovkov *et al.* have reported an X-ray structure of the complex of the ethane-bridged bis(zinc porphyrin) with (1*R*,2*R*)-**3** in which the cyclohexane ring has a chair conformation in a direction parallel to the porphyrin rings. It

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Table 1 CD spectral data of **1**–Zn or **1**–Mg with various chiral guests in the presence of K^+ in CH_2Cl_2–MeCN (9 : 1 v/v) in a 1 cm optical cell

Entry	Guest	CD sign and peak position/nm		Total amplitude/ M^{-1} cm^{-1}
		1st Cotton effect	2nd Cotton effect	A (=$\Delta\varepsilon_1 - \Delta\varepsilon_2$)
1[a]	(1*R*,2*R*)-**3**[c,d]	−(436)	+(421)	−60.1
2[a]	(1*S*,2*S*)-**3**[c]	+(436)	−(421)	+65.0
3[a]	(1*R*,2*R*)-**4**[e]	nd[f]	nd[f]	nd[f]
4[a]	(1*S*,2*S*)-**4**[e]	nd[f]	nd[f]	nd[f]
5[a]	(1*R*,2*R*)-**5**[c]	+(433)	−(421)	+24.8
6[a]	(1*S*,2*S*)-**5**[c]	−(433)	+(421)	−23.2
7[a]	(3*R*)-**6**[e]	−(433)	+(423)	−91.4
8[a]	(3*S*)-**6**[e]	+(433)	−(423)	+86.8
9[a]	(3*R*)-**7**[e]	−(434)	+(422)	−31.9
10[a]	(3*S*)-**7**[e]	+(434)	−(422)	+34.3
11[b]	(*R*)-**8**[c]	+(429)	−(421)	+43.8
12[b]	(*R*)-**9**[c]	+(432)	−(420)	+70.7
13[b]	(*S*)-**9**[c]	−(432)	+(420)	−71.4
14[b]	(*R*)-**10**[c]	+(432)	−(420)	+68.5
15[b]	(*S*)-**10**[c]	−(432)	+(420)	−67.6

[a] [**1**–Zn] = 4.0 μM. [Guest] = 8.0 μM. [$KClO_4$] = 2.0 μM. [b] [**1**–Mg] = 4.0 μM. [Guest] = 4.0 mM. [$KClO_4$] = 2.0 μM. [c] 0 °C. [d] Time dependence on the CD spectra was examined so that the CD sign was maintained with a somewhat diminished intensity after 24 h. [e] 25 °C. [f] not detected.

shows that the two N atoms of the ligand are connected to Zn in the equatorial position.[17] Our speculation using the CPK molecular model is that equatorial (1,2-ee) type of (1*R*,2*R*)-**3** in the complex should produce an anticlockwise twist of the porphyrins, corresponding to the negative CD sign, whereas (1*R*,2*R*)-**2**, the bis(methylamino) analogue, may adopt (1,2-aa) conformation to be less sterically accommodated in two porphyrin planes because of the bulkiness of the Me group. Subsequently, the coordination produces a clockwise twist of the organized porphyrin, following the positive CD sign. This phenomenon appears to be a unique chirality inversion that reflects on the conformation change in the chiral guest.[18] Moreover, we performed CD titrations with chiral **4** with more bulky substituents at the amino groups and obtained no CD sign. This implies that the hindered alkyl groups prevent the ditopic interactions of the amino nitrogens of **4** with zinc porphyrins in the ensemble. Other plausible asymmetric 1,2-diphenylethylenediamines **5** were employed; clear exciton-coupled bisignate CD spectra were observed at 0 °C, corresponding to the chirality of each stereoisomer (Table 1, Entries 5 and 6). Further, it is noteworthy that the **1**–Zn assembly can read out the absolute configurations of five-membered aminopyrrolidines (**6** and **7**) (Table 1, Entries 7–10) because the derivative is a homo chiral building block utilized in the preparation of numerous drug candidates.[19]

The utility of our system is not limited to the diamines.¶ The replacement of coordinated zinc(II) with magnesium(II) in the porphyrin ring allows us to investigate whether our system is useful for sensing the chirality of asymmetric guests other than diamines. Thus, we have newly synthesized **1**–Mg by treating its free base **1** with $MgBr_2 \cdot OEt_2$ (see ESI†) and then found that the addition of chiral aminoalcohols such as α-methyl-4-pyridinemethnol **8**, α-phenylalaninol **9** and α-phenylglycinol **10** into the solution of **1**–Mg gave bisignate CD signals at the Soret region (Table 1, entries 11–15). The ease of incorporation of metal into the porphyrin unit may allow us to develop versatile related systems capable of monitoring the chirality of a wide range of chiral analytes.

In conclusion, we have shown that a crowned metalloporphyrin produces a self-assembly by the cation accommodated in the crown and then serves as a self-organized chiroptical tool for bifunctional chiral guests. This insight may provide a new way to design chiral sensors that can be produced easily since a versatile organization would be achieved based on various synthetic modifications of the porphyrin unit. Research in this regard is in progress. We thank Dr. Y. Furusho, Dr. H. Goto and Prof. E. Yashima of Yashima Super-structured Helix Project, ERATO, for the measurement of CSI-MS spectroscopy.

Notes and references

‡ The value was estimated based on the intensity change in the absorbance at 603 nm (Q-band) because the Soret band is affected by the exciton interaction between the porphyrins (see ESI†).

§ Replacing **1**–Zn with the corresponding free-base porphyrin **1** in the titration led to no CD sign.

¶ Our preliminary results indicate that by using **1**–Zn, it is possible to read out the chirality of several potassium salts of amino acids at 0 °C through solid [the potassium salt]/liquid [**1**–Zn in CH_2Cl_2–MeCN (1 : 4 v/v)] two-phase extraction.

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