Dibenzodiaza-30-crown-10-appended bis(zinc porphyrin) tweezers: synthesis and crown-assisted chiroptical behaviour†

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In our program for developing chirality manipulation systems, we synthesized bis(zinc porphyrin) **1**, with a dibenzodiaza-30-crown-10 as a linker unit. Two structural features were examined. The aza-crown segment exhibited an intermolecular interaction with the zinc(II) of the porphyrin, capable of causing aggregation to form spherical nanostructures, as inferred by concentration-dependency of ^{1}H NMR as well as scanning electron microscopy (SEM) observation. We also consider the crown-based conformation flexibility, in which accommodated K^+ tunes the porphyrin orientation into the tweezers conformation, assisting chirality induction upon complexation with chiral diamine **2**. The circular dichroism (CD) intensity change essentially reached a plateau at a [(1*R*,2*R*)-**2**] : [**1**] ratio of 2 : 1 for which a 45% enhancement in the amplitude of CD spectra was observed compared to the K^+-free conditions. Use of the crown linker of **1** is not limited to promoting chirality induction with diamines in the presence of K^+; chiroptical probing of unprotected amino acids (Lys, His, Trp, and Phe) using **1** was attained through liquid (**1** in CH_2Cl_2)–liquid (the amino acids in 1 N KOH) two-phase extraction. The amphiphilic properties of the crown segment, as well as the K^+-assisted tweezers conformation, make it possible to explore a potent way to develop chirality sensors for amino acids in water.

Introduction

The design of systems which can manipulate chirality information has become important in the interdisciplinary area between supramolecular chemistry and chiral chemistry. As motivation, the chiroptical outcome is predictable and immediately applicable in chirotechnology.[1] Applications include sensors,[2] asymmetric catalysis,[3] actuators such as molecular motors,[4] photochromic materials,[5] nonlinear optical materials,[6] liquid crystalline systems,[7] and other valuable products.[8] A common methodology of chirality induction (chirogenesis)[9] at the molecular level would be of use in the approach in which a chiral-orientated conformation is created by the transfer of chiral information from an external species by noncovalent interaction. Bisporphyrins are known to be chiral receptors and circular dichroism (CD) reporters.[10] If a porphyrin bischromophore in the system, with known electric transitions, can be arranged in a clockwise or anticlockwise sense upon complexation with chiral guests, its behaviour will allow us to determine the absolute configuration by means of CD spectroscopy.[9,11] In such molecular architectures, synthetic exploration of systems capable of controlling chirality induction is still in its infancy. Use of allostery[12] in inducing chirality is an interesting approach in which shape control of a system that responds to an external stimulus may affect its function controllably. In 2000, Mizutani *et al.* reported allosteric chirality amplification using a zinc bilinone dimer.[13] The zinc bilinone is a helical molecule which undergoes racemization between right-handed (*P*) and left-handed (*M*) conformers in solution. Since coordination of a chiral guest (*e.g.*, L-Asp(OMe)–OMe) to the zinc can induce helical chirality due to the shift in *P*–*M* equilibrium, chirality is amplified allosterically in the system. Recently, by taking advantage of homotropic allostery based on a cerium double decker porphyrin, highly enantioselective recognition has successfully taken place.[14] Our approach is to employ dynamic action based on heterotropic allostery which should be easier to handle than homotropic allostery in molecular manipulation.[15] It is well known that crown ethers are powerful tools for constructing target systems because of their structural topology and superior synthetic susceptibility.[16] Conformational flexibility increases with ring size,[17] such that the crown ligands (*e.g.*, 30-crown-10) tend to wrap cations of small size. Accordingly, we have focused on a highly flexible dibenzo-30-crown-10 scaffold, in which K^+ is significantly wrapped to induce topological change into a tweezers-like structure,[18] and which generates a chiral screw conformation.[19] The insight that chirality can be induced in the highly flexible crown ether congener led us to synthesize a bisporphyrin system possessing this unit as the linker.

Another intriguing issue is whether the crowned bisporphyrin can be applied to chirality sensing of unprotected amino acids.[20] Lipophilic zinc porphyrins are not capable of binding with free amino acids. Thus, to attain significant interactions with amino acids, it is crucial to insert water soluble groups into the porphyrin scaffold to provide an electrostatic interaction.[21] CD probing using the porphyrin systems has been therefore applicable mainly to protected amino acids.[22] However, Tamiaki *et al.* proposed lanthanide porphyrin systems serving as excellent CD probes of amino acids, which successfully extracted the amino acids from neutral water.[23] The key factor is the strong binding property of the lanthanide porphyrin with the COO^- site of the guest. As an

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alternative approach, the crown-assisted chiroptical properties of **1** should allow it to act as a CD probe of free amino acids in water.

Here we describe the synthesis of title compound **1**, as well as its spectroscopic properties.[24] In the latter section we begin by addressing self-association of **1** through intermolecular Zn–N interaction. Allosteric behaviour for chirality induction in **1** is then discussed, in which the CD amplitude upon complexation with chiral diamine **2** is enhanced by K^+ accommodated in the crowned cavity. Further, taking advantage of the crown segment, the chirality of several unprotected amino acids could be read out by **1** when we employed liquid–liquid two-phase extraction using 1 N KOH solution. CD activity was not observed when crown ether-free bisporphyrin tweezers were used, in place of **1**.

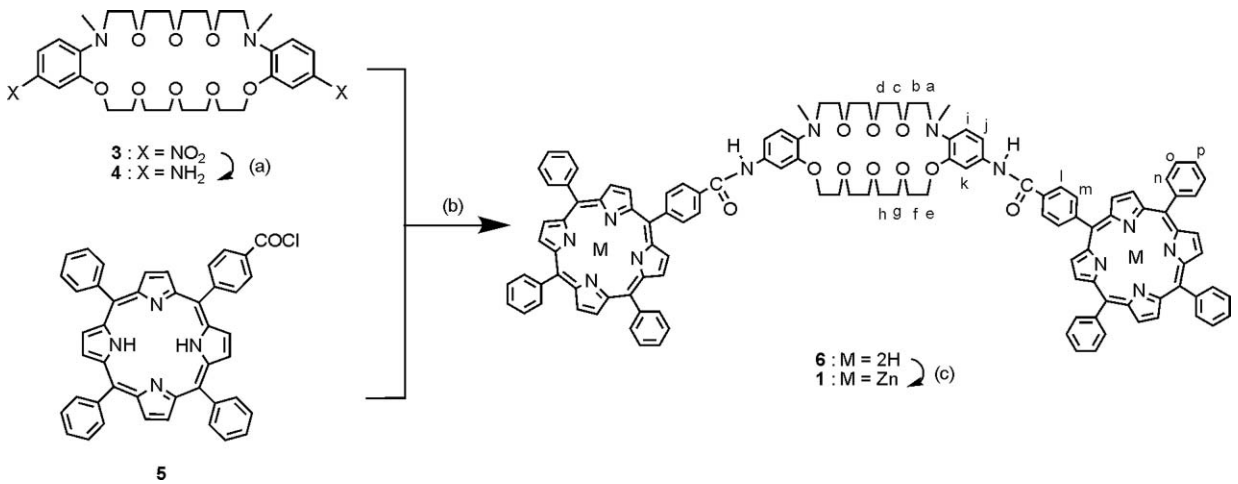
Results and discussion

Synthesis

The synthesis is shown in Scheme 1. The key step in reaching the target is to regioselectively insert porphyrin segments on the terminal benzene rings of the dibenzo-30-crown-10 skeleton. Regioselective modification is usually not easy.[25] However, by targeting a diaza-congener it is possible to regioselectively synthesize dinitro-substituted **3** from a commercially available material, 5-nitroguaiacol, in only three steps.[18] Compound **3** was reduced to the corresponding diamino derivative **4** with H_2, and condensing with tetraphenylporphyrin (TPP) acid chloride derivative **5**[26] with a small amount of NEt_3 in dry CH_2Cl_2 then gave **6** in 48% yield. Metallation using $Zn(OAc)_2{\cdot}2H_2O$ then gave the target **1** in 98% yield.

Self-association

The structure of **1** was assigned according to various spectroscopic data; Fig. 1 shows the ^1H NMR data at room temperature using CD_2Cl_2. The chemical shifts of the crown segment broadened more than those due to the porphyrins even in low concentration (0.1 mM) as a result of restricted mobility of the large-ring crown, which increases the relaxation time in NMR. The spectra



Scheme 1 Synthesis of **1**. *Reaction conditions*: (a) 10% Pd/C, H_2 (2.5 atm), EtOH, r.t.; (b) dry CH_2Cl_2 with a few drops dry Et_3N, 0 °C, under Ar, 48%; (c) sat. $Zn(OAc)_2{\cdot}2H_2O$ in MeOH, CH_2Cl_2, r.t., 98%.

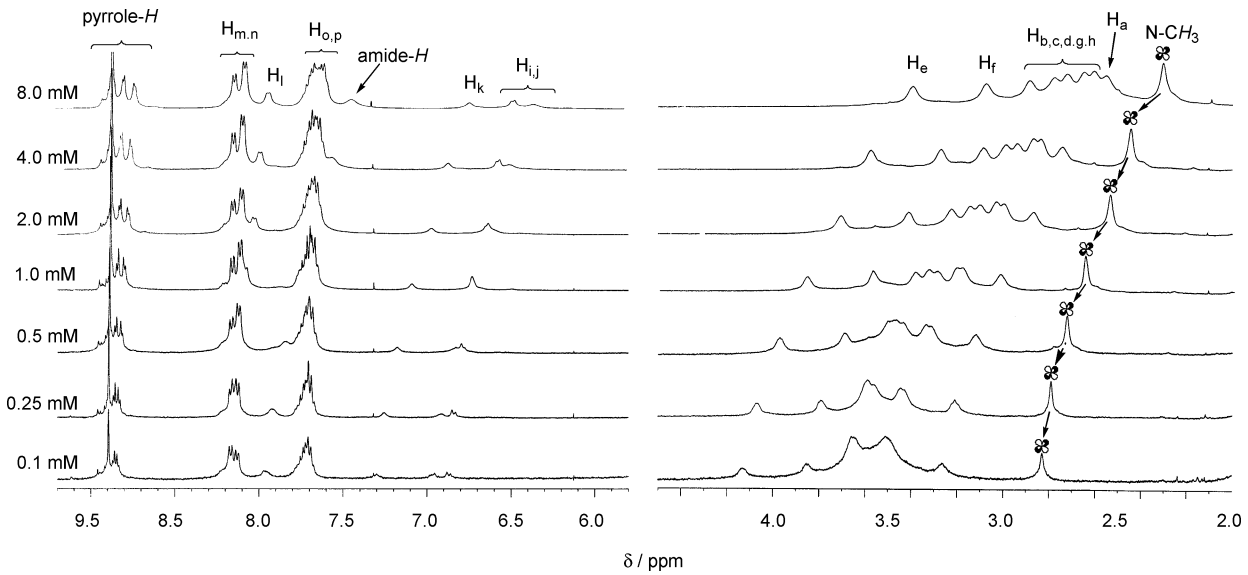


Fig. 1 ^1H NMR spectra of **1** at various concentrations in CD_2Cl_2 at 23 °C.

also show changes in the shift of protons in **1** with varying concentration from 8 mM to 0.1 mM; a significant down-field shift, due to protons of the dibenzodiaza-30-crown-10 as well as the amido-linked benzene units, was observed in which a large shift difference of 0.526 ppm for N–CH_3 was clearly detected. Self-association of **1** through intermolecular Zn–N coordination between the porphyrins and the dibenzodiaza-30-crown-10 most likely accounts for the observation at relatively high concentration at room temperature. The change in chemical shift of protons near to aza-segments of the crown ring can be therefore ascribed to a ring current effect of porphyrin. Although this behaviour is partly consistent with the observation in the case of dimerization of diaza-18-crown-6-bridged zinc-free base bisporphyrin,[27] the N–CH_3 resonances simply shifted, meaning that both nitrogens interact with the central zinc (II) in the porphyrins to form extended aggregates (*vide infra*). The ^{1}H NMR dilution experiments in CD_2Cl_2 on **1** enable us to estimate an association constant (K_a), by monitoring the shift of the sensitive singlet (N–CH_3) upon changing the concentration ($K_a = 440 \pm 32$ M^{-1}).[28] This parameter indicates that **1** exists mainly as a monomer (98%) at 0.1 mM, so that at a UV–vis or CD detectable concentration **1** does not undergo self-association.

To obtain insight into the morphology of the association, a field emission-scanning electron microscopy (FE-SEM) experiment was carried out; spherical structures of **1** were formed after direct casting of the toluene solution on an aluminium plate (Fig. 2). This formation process was found to involve aggregation of **1**, followed by stacking of the aggregates to minimize the interfacial free energy between the particles and solvent. No such nanostructure was obtained in the case of zinc tetraphenylporphyrin (ZnTPP) as a control. Intermolecular Zn–N coordination plays a key role in the extended aggregation.

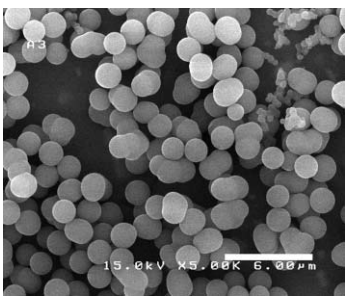
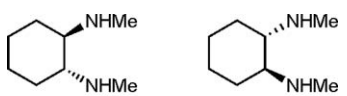


Fig. 2 FE-SEM images of **1** (1.2 mM). The scale bar corresponds to 6 μm.

Cation-assisted chirality induction



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

The conformational flexibility of the crowned spacer in **1** permits switching of the porphyrin orientation into the tweezers-like conformation upon complexation with a bidentate ligand. We selected optically active *N*,*N*′-dimethylcyclohexane-1,2-diamines **2** as target guests, because these are simple C_2 symmetric molecules suitable for investigation of crown-assisted chirality induction using **1**. Moreover, 1,2-diaminocyclohexane derivatives are useful in both asymmetric synthesis[29] and as a building block of chiral receptors.[30] A UV–vis titration of **1** upon adding incremental amounts of (1*R*,2*R*)-**2** in CH_2Cl_2–MeCN (4 : 1 v/v) at 25 °C was first carried out, the result is shown in Fig. 3. The Soret band at 423 nm did not show a clear spectral change with increasing amounts of (1*R*,2*R*)-**2**, possibly due to an intramolecular exciton coupling interaction[31] of the porphyrin-chromophores accompanying the conformation switch which affects the Soret band (*vide infra*). Thus, the complexation phenomenon can be quantified based on the shift of the Q(1,0)-band, from 555 nm to 562 nm; use of a Job plot[32] suggests a 1 : 1 complex formation (Fig. S1), and the association constant (log K_a) was estimated to be 6.04 ± 0.09 using a nonlinear curve fitting method. We thus investigated CD properties of the system upon adding incremental amounts of (1*R*,2*R*)-**2** under similar conditions. While **1** is inherently CD inactive, addition of the chiral guest gave bisignated Cotton effects at 433 and 422 nm (Fig. 4). The λ_{CD} value is in good agreement with the λ value of the Soret band of the porphyrin, leading to a clockwise twist between the chromophores. The presence of 6 equiv. of (1*R*,2*R*)-**2** allows us to detect positive exciton coupled CD spectra [$\Delta\varepsilon$ +416 M^{-1} cm^{-1} (433 nm), −354 M^{-1} cm^{-1} (422 nm)], the total

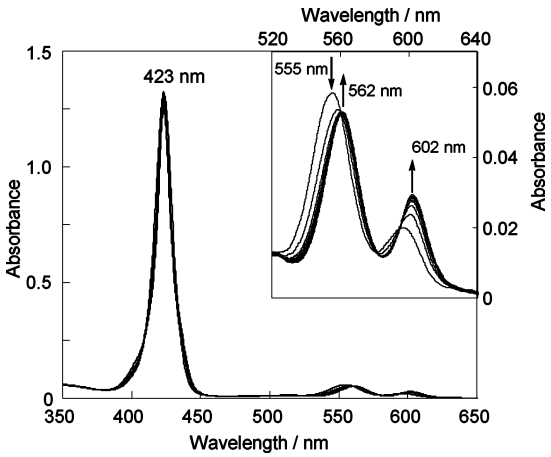


Fig. 3 UV–vis spectra of **1** upon adding (1*R*,2*R*)-**2** in CH_2Cl_2–MeCN (4 : 1 v/v) at 25 °C, [**1**] = 2.0 μM, [(1*R*,2*R*)-**2**] = 0, 2.0, 4.0, 6.0, 8.0, 10, 12, 16, 20, 30 μM.

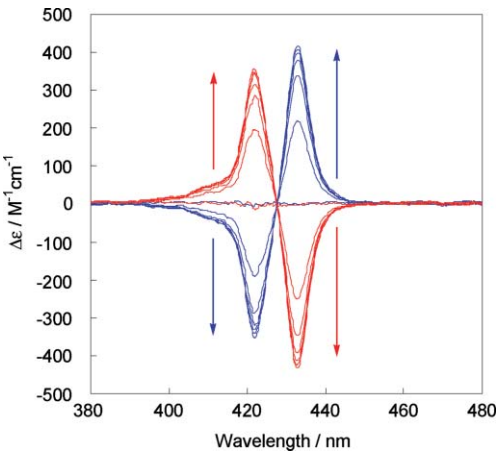


Fig. 4 CD spectral changes of **1** upon addition of (1*R*,2*R*)-**2** (blue line) or (1*S*,2*S*)-**2** (red line) in CH_2Cl_2–MeCN (4 : 1 v/v) at 25 °C, [**1**] = 2.0 μM; [**2**] = 0, 2.0, 4.0, 6.0, 8.0, 10, 12 μM.

amplitude being 770 M^{-1} cm^{-1}. This finding can be explained on the basis of a steric repulsion mechanism between the coordinated diamine **2** and the neighboring porphyrin rings, which generates a chiral screw structure of **1**.[33] The complexation was verified by ^{1}H NMR spectra in which the proton resonances due to (1*R*,2*R*)-**2** were entirely upfield shifted; the methyl resonances of **2** shifted from 2.38 ppm to −3.71 ppm upon adding **1** (*vide infra*). On the other hand, addition of (1*S*,2*S*)-**2** into a solution of **1** gave a negative exciton coupled CD spectrum (Fig. 4), indicating that the chirality induced in **1** reflects the geometry of the chiral diamine.

Dynamic conformational change of the dibenzodiaza-30-crown-10 skeleton by cation complexation leads us to investigate heterotropic allostery in the chirality induction, it is expected that K^+ can be wrapped by the crown segment to induce a tweezers-like conformation. Indeed, UV–vis titration, monitoring the Soret band of **1** upon adding $KClO_4$ in CH_2Cl_2–MeCN (4 : 1 v/v), showed a hypsochromic shift by 2 nm along with significantly decreasing absorption intensity (Fig. 5a). The change in absorption intensity at 423 nm is almost saturated upon adding a stoichiometric amount of K^+, indicating that cofacialization of the porphyrin units takes place. This is supported by ^{1}H NMR experiments obtained after solid[$KClO_4$]–liquid[1.0 mM of **1** in CD_2Cl_2–CD_3CN (4 : 1 v/v)] two-phase extraction, in view of the low solubility of $KClO_4$ in NMR detectable conditions. K^+ coordination in the crown ring was inferred from the upfield-shifted N–CH_3 and N–CH_2 resonances, as well as the downfield-shifted CH_2–O resonances (Fig. S2). The upfield-shift of protons adjacent to the aza-segments could be explained on the basis of hyperconjugation which was diminished by K^+–N interactions. Fig. 5b shows how porphyrin aromatic protons reflect the K^+-induced conformation change: upon interaction with K^+, the spectrum changed from broad signals to split patterns. The amide protons shifted downfield by 0.75 ppm, whereas the changes of pyrrole-resonances were greater and upfield. A 2D COSY experiment (Fig. S3) led us to assign the signals as three pairs of doublets in a 3 : 3 : 2 integral intensity ratio: 8.76 (J = 4.4 Hz) and 8.58 (J = 4.8 Hz), 8.67 (J = 4.4 Hz) and 8.32 (J = 4.8 Hz) as well as 8.53 (J = 7.6 Hz) and 8.34 (J = 8.0 Hz).[34] These observations support the hypothesis that the dynamic conformational change of **1** is restricted by encapsulated K^+ to the tweezers conformation, where the terminal porphyrin units are close to each other. It is interesting to see how the encapsulated K^+ could assist in chirality induction. Fig. 6 shows CD amplitude changes as a function of the incremental amounts of chiral **2** in the absence or presence of 5 equiv. of metal ion (K^+ or Li^+); presence of K^+ gave a steeper ascending behaviour in the CD amplitude compared to metal ion free conditions. It essentially reached a plateau at a [(1*R*,2*R*)-**2**] : [**1**] ratio of 2 : 1, where a 45% enhancement in the amplitude of CD spectra was observed. Similar enhancement was also obtained in the case of (1*S*,2*S*)-**2**; the CD amplitude increased by 43% upon adding 2 equiv. of the diamine. These results suggest that the allosteric effect in which the K^+-binding tunes the conformation to bind chiral **2**, can assist chirality induction in **1**. As a control experiment, when we measured CD spectra under similar conditions using Li^+ instead of K^+, there was no enhancement in the CD spectra. Also use of Cs^+ induced some CD enhancement but to a lesser degree than K^+. We postulate that the enhanced CD intensity in the presence of K^+ is due to a cooperative association of K^+ and the chiral diamine toward **1**. To verify this, we estimated the apparent association constants with **2** in the presence or absence of K^+ (5 equiv.) by monitoring

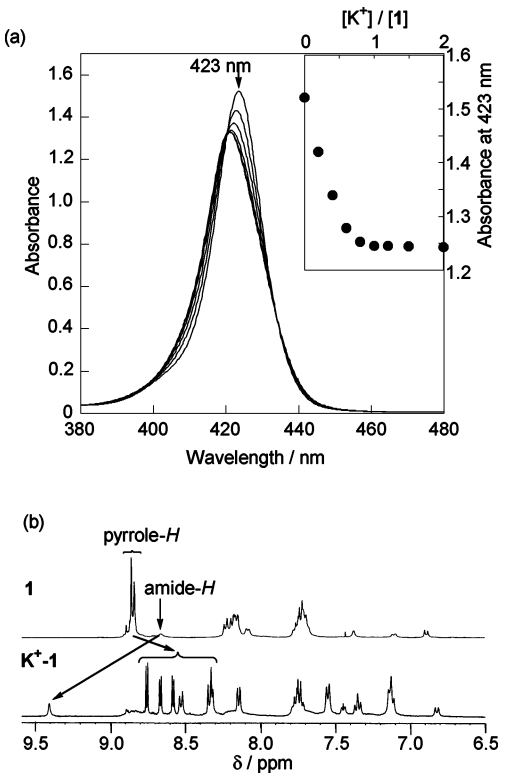


Fig. 5 (a) UV–vis spectral change of **1** upon adding $KClO_4$ in CH_2Cl_2–MeCN (4 : 1 v/v) at 25 °C. [**1**] = 2.0 μM; [K^+] = 0, 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 4.0 μM. (b) ^{1}H NMR spectra of **1** and K^+–**1** complex in CH_2Cl_2–CD_3CN (4 : 1 v/v) at 23 °C. [**1**] = 1.0 mM.

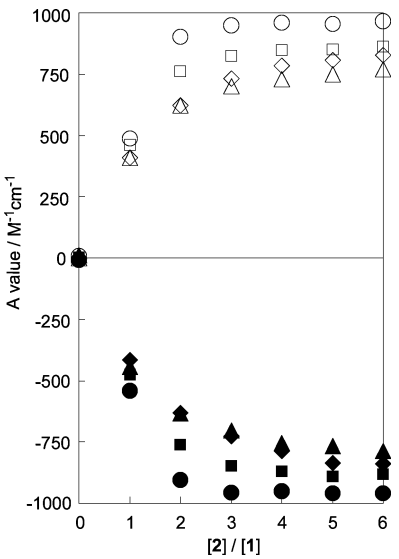


Fig. 6 Changes in CD amplitude [A (= $\Delta\varepsilon_1 - \Delta\varepsilon_2$)] of **1** (2 μM) upon complexation with chiral **2** in the presence or absence of K^+, Li^+ or Cs^+(5 equiv.) in CH_2Cl_2–MeCN (4 : 1 v/v) at 25 °C: (○) (1*R*,2*R*)-**2** with K^+; (◇) (1*R*,2*R*)-**2** with Li^+; (□) (1*R*,2*R*)-**2** with Cs^+; (△) (1*R*,2*R*)-**2**; (●) (1*S*,2*S*)-**2** with K^+; (◆) (1*S*,2*S*)-**2** with Li^+; (■) (1*R*,2*R*)-**2** with Cs^+; (▲) (1*S*,2*S*)-**2**.

the absorption intensity at 602 nm due to the perturbation of the Q-band in the porphyrin-chromophore. As shown in Fig. 7, a nonlinear curve-fitting procedure, assuming (K^+–**1**–(1*R*,2*R*)-**2**) complex formation, reproduces the experimental titration data with a residual square sum of 2.81×10^{-7}, in which the estimated association constant (log K_a) is 6.27, being twice the value as without K^+ (log $K_a = 5.98$).

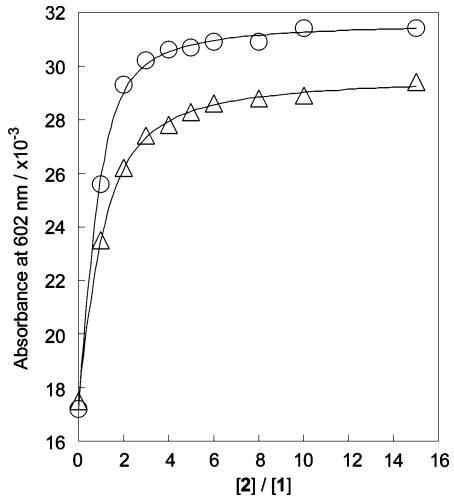


Fig. 7 The change in absorption intensity at 602 nm as a function of incremental amounts of (1*R*,2*R*)-**2** in the presence (○) and absence (△) of 5 equiv. of K^+ in CH_2Cl_2–MeCN (4 : 1 v/v) at 25 °C.

Direct evidence for the K^+-assisted interaction between **1** and **2** was found by ^{1}H NMR measurements; a $CDCl_3$–CD_3CN (4 : 1 v/v) solution of (1*R*,2*R*)-**2** (5 mM) was titrated with **1** in the absence or the presence of K^+ (Fig. 8). The methylamino group of **2** should become a useful probe for monitoring the complexation motif. The spectrum in Fig. 8a shows protons due to the guest diamine, where the singlets for NHC*H*$_3$ and N*H*Me were detectable at 2.38 and 3.37 ppm, respectively. When adding 2 equiv. of **1** (Fig. 8b), the proton resonances due to **2** were observed wholly in higher magnetic field than 0 ppm with signal broadening, indicating that the guest was located in the concave cavity between porphyrin units. The observed broad signals can be ascribed to the exchange between free and complexed species, which occurs

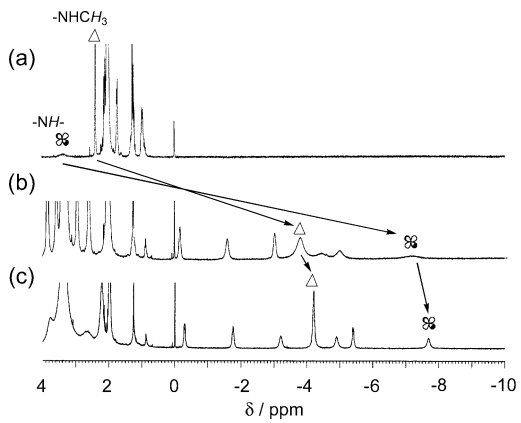


Fig. 8 ^{1}H NMR spectra of: (a) (1*R*,2*R*)-**2**; (b) (1*R*,2*R*)-**2** with 2 equiv. of **1**; (c) (1*R*,2*R*)-**2** with 2 equiv. of **1** in the presence of K^+, in $CDCl_3$–CD_3CN (4 : 1 v/v) at 23 °C. [**1**] = 10 mM, [(1*R*,2*R*)-**2**] = 5 mM.

at a rate observable within the NMR time scale. However, solid [$KClO_4$]–liquid [**1** (10 mM) and (1*R*,2*R*)-**2** (5 mM) in $CDCl_3$–CD_3CN (4 : 1 v/v) solution] two-phase solvent extraction led to a further upfield shift, sharpening the signals (Fig. 8c). In particular, the resonances for NHC*H*$_3$ and N*H*Me shifted further upfield, by 0.40 and 0.49 ppm, respectively, than under K^+-free conditions.[35] This means that equilibrium was more shifted to the complex, supporting the CD enhancement in the presence of K^+.

Chirality sensing of unprotected amino acids

We have found that the crown-assisted chirality induction described here is applicable to chirality sensing of unprotected amino acids. This result is highlighted by the fact that hydrophobic bis(zinc porphyrin) tweezers cannot sense the chirality of free amino acids using CD spectroscopy.[9] Insertion of the amphiphilic crown segment in **1** allowed us to investigate an assay of several enantiomer pairs of common amino acids by liquid–liquid two-phase extraction and subsequent CD measurements. We first selected basic L-Lys as a putative guest, based on our supposition that ditopic binding with bis(zinc porphyrin) tweezers takes place. There are no CD responses from the extraction of the amino acid from neutral aqueous solution to a CH_2Cl_2 solution of **1** (39 μM), but use of 1 N KOH solution as an aqueous phase induced an exciton-coupled bisignate CD curve [first Cotton, 434 nm ($\Delta\varepsilon$ −101 M^{-1} cm^{-1}; second Cotton, 426 nm ($\Delta\varepsilon$ +123 M^{-1} cm^{-1})], Fig. 9, line (b). The negative exciton coupling CD spectrum suggests an anticlockwise screw sense of the porphyrin units, consistent with that in the case of **1** with L-Lys–OMe in CH_2Cl_2 (Fig. 9, line (e)). Of particular interest is that upon replacement of KOH with LiOH or NaOH, the CD spectra remained silent (Fig. 9, lines (c) and (d)), consistent with Fig. 6 in which the K^+-induced CD enhancement is more efficient than in the presence of Li^+. This strongly suggests that the K^+-coordinated dibenzodiaza-30-crown-10 linker assists the extractability from the aqueous solution to CH_2Cl_2, accompanying K^+-induced conformational rearrangement in **1**. Indeed, no CD sign was detected in a similar

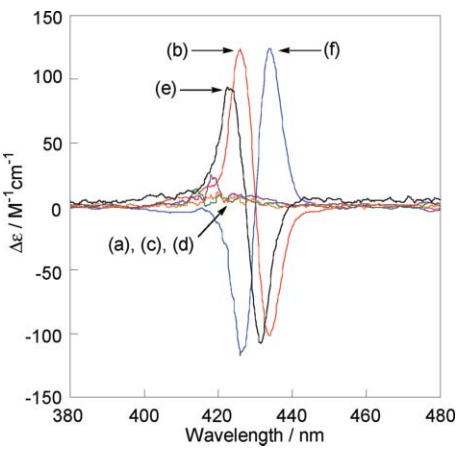


Fig. 9 CD spectra of **1** in CH_2Cl_2 after shaking (30 min) with an aqueous solution of L-Lys (a), with a 1 N KOH solution of L-Lys (b), with a 1 N LiOH solution of L-Lys (c), with a 1 N NaOH solution of L-Lys (d). CD spectrum of **1** with L-Lys–OMe in CH_2Cl_2 (e). CD spectrum of **1** in CH_2Cl_2 after shaking (30 min) with a 0.1 N KOH solution of D-Lys (f). Conditions: [**1**] = 13 μM, [L-Lys] = [D-Lys] = 0.1 M, [L-Lys–OMe] = 260 μM at 25 °C and optical length of employed cell is 0.2 cm.

liquid–liquid two phase extraction using crown-free bis(zinc porphyrin) tweezers, such as ethane-bridged bis(zinc porphyrin).[36] We tried to determine the amount of L-Lys extracted by **1** from the 1 N KOH phase using ninhydrin colorimetry.[37] Defining the extraction (%) as the ratio of extracted amino acid concentration *versus* the concentration of **1**, the value is 61%.[38] Also investigated was a similar liquid–liquid two-phase extraction with the D-Lys enantiomer to give a mirror image in the CD spectrum [$\Delta\varepsilon$ +124 M^{-1} cm^{-1} (434 nm), −117 M^{-1} cm^{-1} (426 nm)], see line (f) in Fig. 9.

His, possessing a basic imidazole sidechain, was also checked in a similar extraction study, giving significant bisignate CD curves [$\Delta\varepsilon$ +178 M^{-1} cm^{-1} (435 nm), −114 M^{-1} cm^{-1} (424 nm) for L-His; $\Delta\varepsilon$ −160 M^{-1} cm^{-1} (435 nm), +119 M^{-1} cm^{-1} (424 nm) for D-His] in which the CD intensity is somewhat larger than with Lys (Fig. 10). The chirality signs induced by His are opposite to those for Lys. The sign of the induced CD depends on the steric bulkiness of the substituents at the chiral center, which play the major role in the stereospecific orientation of the interacting electric transitions in the complex. This forces the complex motif to adopt the least sterically hindered conformations.[22c] We suggest that the Lys sidechain does not affect the porphyrin arrangement in the complex, whereas the more rigid imidazole residue in His mainly determines the chirality screw sense of the porphyrins.

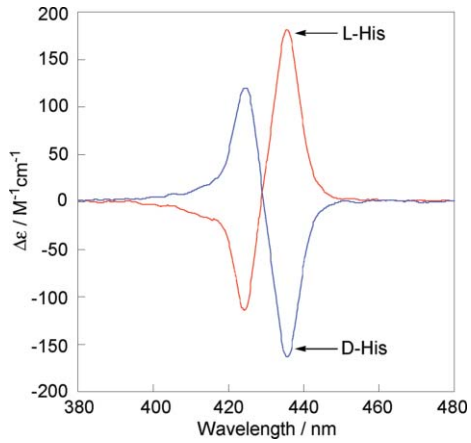


Fig. 10 CD spectra of **1** (13 μM) in CH_2Cl_2 after shaking (30 min) with a 1 N KOH solution of His (0.1 M) at 25 °C. Optical length of employed cell is 0.2 cm.

The assay of various common amino acids was further investigated; it is interesting to note that chirality sensing for Trp and Phe was implemented through an extraction study using 1 N KOH solution, as shown in Fig. 11. The bisignate CD curves are evidence for dipole–dipole electric interaction between the two porphyrins. Despite ^{13}C NMR and IR measurements to gain insight into the interaction between coordinated Zn(II)–COO^-, we have not obtained any evidence as to whether two-point complexation between **1** and the aminocarboxylate takes place through the extraction process. However, we postulate that K^+ in the crown moiety guides the carboxylate into the concave cavity in **1**; significant hydrophobic interactions are believed to occur between the hydrophobic side chains of Trp and Phe[39] and the bisporphyrin tweezers. This effect is not expected for amino acids with no hydrophobic side chain, such as L-Asp. As a control experiment, we measured CD spectra of **1** (13 μM) in CH_2Cl_2 upon

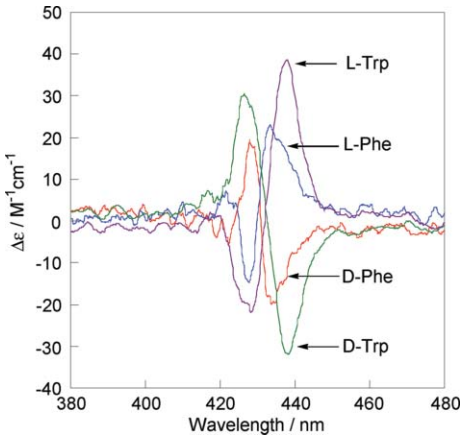


Fig. 11 CD spectra of **1** (13 μM) in CH_2Cl_2 after shaking (30 min) with a 1 N KOH solution of Trp and Phe (0.1 M) at 25 °C. Optical length of employed cell is 0.2 cm.

addition of incremental amounts of L-Trp–OMe (0 → 20 equiv.); there were no bisignate spectra based on the exciton coupling of porphyrins (Fig. S5). Overall, the extractability of the amino acids (Trp and Phe) as aminocarboxylate potassium salts is ascribed to both the amphiphilic properties of the crown segment and the K^+-guided hydrophobic interactions between the guest and the concave cavity of **1**, allowing chirality sensing of the amino acids in water.

Conclusion

The present results show a novel capability potential of bisporphyrin systems possessing a large ring-sized crown ether as the spacer. Their highly flexible conformation property led us to explore their utility as a chiral probe because of the ease of the achiral-to-chiral transformation, along with complexation of chiral diamines in the terminal porphyrin segments. In particular, the combination of the crown and porphyrin units in the system provides cooperative chiroptical properties in the presence of K^+, where K^+ accommodated in the crown ring acts as an allosteric factor to tune the conformation to bind the diamines, resulting in a CD enhancement. We further found that **1** provides an extraction and chirality probing of unprotected amino acids (aminocarboxylates) in 1 N KOH as a result of the amphiphilic property of the crowned spacers, where encapsulated K^+ can guide carboxylate into the tweezers. We believe that the success of chirality sensing for amino acids using **1** would provide a new way to develop porphyrin-based CD probes. Our results further explore how to manipulate chirality at the molecular level, which remains an intriguing challenge in supramolecular chemistry.

Experimental

General

NMR spectra were taken on Bruker DPX 400 or DRX 400 (400 MHz) spectrometers. Chemical shifts (δ) are reported downfield from the initial standard Me_4Si. Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectroscopy was performed with a $CHCl_3$ solution of dithranol (20 mg mL^{-1}) as a matrix on a Shimadzu AXIMA-CFRTM. Electronic absorption

spectra were recorded on a Shimadzu UV-3100 spectrophotometer. Circular dichroism (CD) spectra were recorded on a JASCO J-720 spectropolarimeter. Elemental analyses were obtained using an EISON EA1108.

Materials

The starting materials were of available commercial grade and were used without further purification. Dry solvents were prepared according to standard procedures. Optically active *N*,*N*′-dimethylcyclohexane-1,2-diamines as well as amino acids were purchased from Tokyo Chemical Industry Co., Ltd, of which L-Trp–OMe was purchased as a hydrochloride salt and treated with NaOH to convert the salt to the corresponding free amine. The CH_2Cl_2 and MeCN for UV–vis and CD measurements were purchased as analytical grade and used as received.

17,37-Bis[4-(10,15,20-triphenyl-21*H*,23*H*-porphine-5-yl)phenylcarbonylamino]-21,33-dimethyl-2,5,8,11,14,24,27,30-octaoxa-21,33-diazatricyclo[32.4.0.0^{15,20}]octatriaconta-1(38),15(20),16,18,34,36-hexene (6). Regioselectively dinitro-inserted dibenzodiaza-30-crown-10 **3** (103.5 mg, 0.16 mmol) and 10% Pd/C (52.6 mg) were dispersed in EtOH (80 mL). The mixture was stirred for *ca.* 6 hrs at room temperature under a H_2 atmosphere (2.5 atm). After filtration using Celite, evaporation to dryness gave the corresponding diamino derivative **4**. Subsequently, **4** and a tetraphenylporphyrin (TPP) acid chloride derivative **5** (183.1 mg, 0.27 mmol) were dissolved in dry CH_2Cl_2 (15 mL). After adding NEt_3 (0.3 mL) the mixture was stirred for 2.5 hrs at 0 °C. The resulting solution was treated with water (50 mL) and extracted with CH_2Cl_2 (50 mL × 3). The organic phase was evaporated, chromatographed on silica gel (Wakogel C-300) using CH_2Cl_2–AcOEt–MeOH (10 : 2 : 1 v/v) as eluent, and further purified by GPC using $CHCl_3$ as eluent. In this way, 122 mg of **6** were obtained (48% yield). ^{1}H NMR (400 MHz, DMSO-d_6, 10 mM, 23 °C) δ 10.44 (s, 2H), 8.82 (s, 8H), 8.81 (s, 8H), 8.34 (d, J = 8.0 Hz, 4H), 8.29 (d, J = 8.0 Hz, 4H), 8.18 (d, J = 6.4 Hz, 12H), 7.83–7.76 (m, 18H), 7.58 (s, 2H), 7.47 (d, J = 8.0 Hz, 2H), 6.91 (d, J = 8.0 Hz, 2H), 4.14 (br s, 4H), 3.83 (br s, 4H), 3.66–3.60 (m, 12H), 3.52 (s, 8H), 3.23–3.20 (m, 4H), 2.79 (s, 6H), −2.91 (s, 4H); ^{13}C NMR (100.7 MHz, DMSO-d_6, 23 °C) δ 164.91, 150.41, 144.13, 141.12, 138.02, 134.61, 134.17, 133.21, 131.55, 131.34, 131.16, 128.07, 126.96, 126.13, 120.24, 120.12, 118.92, 117.64, 112.75, 106.05, 69.98, 69.89, 69.76, 69.17, 69.07, 67.33, 54.24; MALDI-TOF, m/z 1872 (M^+), 1873 ([M + H]$^+$); elemental analysis, anal. calcd for $C_{120}H_{104}N_{12}O_{10}\cdot 2H_2O$: C, 75.45, H, 5.70, N, 8.80; found: C, 75.54, H, 5.47, N, 8.70%.

17,37-Bis{4-[(10,15,20-triphenylporphinato)zinc(II)-5-yl]phenylcarbonylamino}-21,33-dimethyl-2,5,8,11,14,24,27,30-octaoxa-21,33-diazatricyclo[32.4.0.0^{15,20}]octatriaconta-1(38),15(20),16,18,34,36-hexene (1). Compound **6** (71.2 mg, 0.038 mmol) was dissolved in CH_2Cl_2 (5 mL). A $Zn(OAc)_2$-saturated MeOH solution (0.5 mL) was added to the solution, and the mixture was stirred for 12 hrs at room temperature. The resulting solution was treated with water (30 mL) and extracted with CH_2Cl_2 (300 mL × 3). The organic phase was evaporated *in vacuo*, and then washed with MeOH. In this way, 74.4 mg of **1** were obtained in 98% yield. ^{1}H NMR (400 MHz, DMSO-d_6, 10 mM, 23 °C) δ 10.44 (s, 2H), 8.80 (s, 8H), 8.78 (s, 8H), 8.37–8.31 (m, 8H), 8.19–8.17 (m, 12H), 7.79–7.77 (m, 18H), 7.59 (d, J = 1.2 Hz, 2H), 7.47 (dd, J = 8.5 and 1.2 Hz, 2H), 6.92 (d, J = 8.7 Hz, 2H), 4.15 (br s, 4H), 3.84 (br s, 4H), 3.67–3.63 (m, 12H), 3.54 (s, 8H), 3.23 (t, J = 5.8 Hz, 4H), 2.80 (s, 6H); ^{13}C NMR (100.7 MHz, DMSO-d_6, 23 °C) δ 165.11, 150.44, 149.39, 149.32, 148.97, 145.83, 142.68, 138.02, 134.14, 133.29, 131.83, 131.66, 131.39, 127.50, 126.60, 125.81, 120.60, 120.47, 119.23, 117.69, 112.76, 106.08, 70.00, 69.93, 69.91, 69.79, 69.20, 69.11, 67.36, 54.27; MALDI-TOF, m/z 1996 (M^+), 1997 ([M + H]$^+$); elemental analysis, anal. calcd for $C_{120}H_{100}N_{12}O_{10}Zn_2\cdot 2H_2O$: C, 70.76, H, 5.15, N, 8.25; found: C, 70.67, H, 4.94, N, 8.16%.

FE-SEM measurements

The sample (10 mg) was dissolved in hot toluene (4 mL) and dried at room temperature on an aluminum plate. It was shielded by Pt–Pd and examined with a HITACHI S-4100 field emission-scanning electron microscope.

Liquid–liquid two-phase extraction

The chirality sensing of amino acids by **1** was carried out by adding a CH_2Cl_2 solution of **1** (3.9×10^{-5} M, 0.8 mL) to an aqueous solution of amino acids (0.1 M, 0.8 mL) in the absence or presence of 1 N MOH (M = Li, Na, and K). After the mixture was stirred for 30 min, the extracted organic phase (200 μL) was diluted with 400 μL of CH_2Cl_2, and then measured by CD spectroscopy where a 0.2 cm length cell was used. On another front, the concentration of L-Lys in the organic phase was determined by ninhydrin colorimetery;[37] the organic phase (20 mL) obtained by stirring a mixture of a CH_2Cl_2 solution of **1** (3.9×10^{-5} M) and a 1 N KOH solution of L-Lys (0.1 M) for 30 min was extracted by water (10 mL × 3). The extracted water phases were collected and evaporated *in vacuo*. The residue was dissolved in a pH 5 buffer solution (AcOH and AcONa in 5 mL) containing ninhydrin (1.0×10^{-2} M) under an Ar atmosphere, and was then heated to 110 °C for 20 min. The resulting solution was cooled to 25 °C and measured by UV–vis spectroscopy.

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