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Absolute Stereochemical Determination of Chiral Carboxylates Using an Achiral Molecular Tweezer

Hongsik Yoon, Chi-Hwa Lee, and Woo-Dong Jang*[a]

Abstract: A new type of molecular tweezer (**1**) has been synthesized for the direct determination of the absolute configuration of chiral carboxylates without analyte derivatization. Upon the addition of diamine and anionic guests, **1** exhibited shifts in its absorption spectrum with clear isosbestic points. The continuous variation method indicated that both the diamine and anionic guests form 1:1 host–guest complexes with **1** with very high binding affinity. When Boc-L-Ala (BLA) as a form of tetrabutylammonium salt was added to **1**, a weak negative CD signal was observed. This weak CD signal was dramatically changed to a strong positive CD couplet upon addition of achiral 1,12-diaminododecane. Such a positive CD couplet was observed for all of the tested L-amino acid derivatives, while the D-amino acid derivatives gave the opposite signals. As a result of these unique characteristics of **1**, it can be utilized as a highly sensitive probe for the absolute stereochemical determination of chiral carboxylates.

Keywords: chirality · circular dichroism · host–guest systems · molecular tweezer · porphyrinoids

Introduction

Determination of absolute configuration remains a very important topic in chemistry because many bioactive molecules are only effective if they have a specific stereo-configuration.[1] To date, various techniques have been developed for the determination of absolute configuration in chiral compounds, including optical rotation, circular dichroism (CD), nuclear magnetic resonance, chiral chromatography, and X-ray crystallography.[2] Among the various methods, one of the most powerful tools for determining absolute configuration is CD spectroscopy, in which enantiomers give spectroscopic data with differential absorption of either left- or right-circularly polarized light.[3] To obtain reliable CD signals, molecules should have an appropriate chromophore with a strong absorption. Recently, several porphyrin tweezer systems as probes for absolute stereochemical determination have been developed based on exciton-coupled circular dichroism (ECCD).[4] The binding of a chiral guest to the porphyrin tweezer induces a chiral twist of the two porphyrin units to minimize steric repulsion. The ECCD method has been successfully applied to a wide variety of compounds, including chiral alcohols, amines, amino alcohols, amino acid derivatives, and bifunctional amide conjugates. However, this potentially powerful approach suffers from a severe limitation that precludes its current use in high-throughput screening or other real-time analyses. Specifically, derivatization is required in the case of substrates bearing only a single ligation site.[5] Herein, we present a solution to this problem that is based on the combination of a porphyrin tweezer system with remote guest-binding receptor modules. In general, the chirality of the guest molecule is directly transferred to the achiral porphyrin tweezer in the form of a twisted conformation through bidentate metal coordination. Owing to the significantly large extinction coefficient of porphyrin units in the visible range, the conformational twist of the porphyrin tweezer system results in large signal amplification.[6] However, tedious derivatizations of monoamines or monocarboxylic acids tend to decrease their applicability in chiral sensing. Furthermore, a large excess of these guest molecules is often needed to elicit a reliable CD signal due to their weak binding affinities. Because most naturally occurring chiral compounds can only be isolated in very small quantities, stereochemical determination without derivatization as well as probes with high binding affinity would be highly desirable. To this end, we have introduced two urea groups in a porphyrin tweezer system as remote guest-binding modules, which provided significantly high binding affinity for chiral carboxylates without derivatization. Although the ECCD signal of the tweezer system manifested upon chiral carboxylate binding was relatively weak, great signal amplification was achieved upon additional binding of an achiral diamine guest to the porphyrin units.

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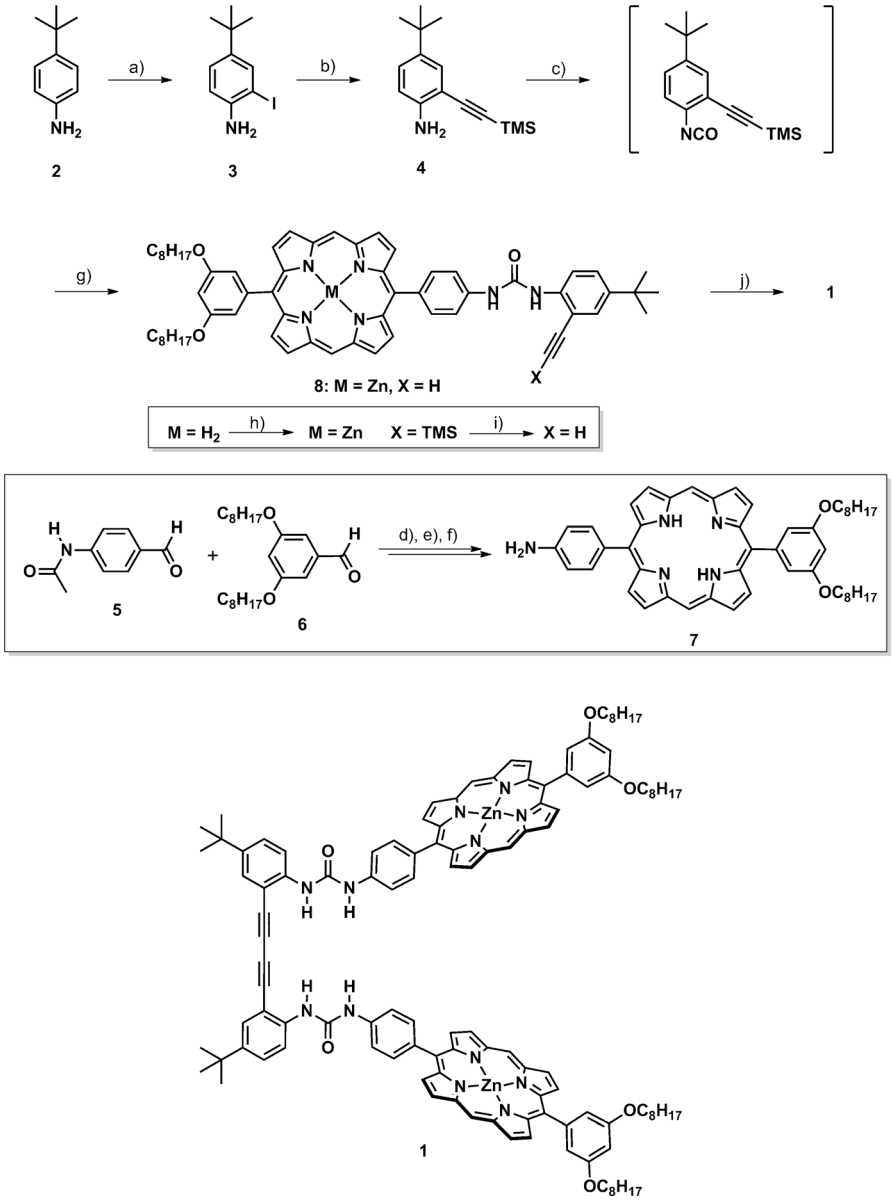
Results and Discussion

The synthesis of the molecular tweezer (**1**) is outlined in Scheme 1. Briefly, iodination of *tert*-butyl aniline (**2**) afforded **3**, which was reacted with trimethylsilylacetylene to give **4**. The amine group in **4** was converted into an isocyanate group using triphosgene in CH_2Cl_2, and then the isocyanate was further reacted with the amino-porphyrin (**7**) to generate the urea-bearing porphyrin derivative (**8**). The amino-porphyrin was synthesized from **5**, **6**, and dipyrrolomethane by an acid-catalyzed cross-condensation reaction and subsequent deprotection of the acetyl group. Metallation of the porphyrin was accomplished with $Zn(OAc)_2$, and subsequent removal of the trimethylsilyl group gave **8**. Finally, dimerization of **8** yielded **1**, which was unambiguously characterized by ^1H and ^{13}C NMR and MALDI-TOF-MS analyses.

Compound **1** exhibited Soret absorption at 419 nm with a remarkably strong shoulder at 409 nm (Figure 1), at which the extinction coefficient in CH_2Cl_2 for the Soret band was determined to be $5.42\times10^5\,M^{-1}cm^{-1}$. The absorption spectrum of the monomeric porphyrin (**8**) was also measured and featured a single sharp Soret absorption at 409 nm that was coincident with the position of the shoulder. Since the monomeric porphyrin absorbs at the same position as the shoulder of **1**, the major absorption of **1** at 419 nm is probably caused by exciton coupling of the two porphyrin units.[7]

Because an amine group can bind to the Lewis acidic zinc porphyrin as an axial ligand,[8] we expected that **1** could accommodate diamine guests. As shown in Figure 2a, the addition of 1,12-diaminododecane (DAD) to **1** resulted in a hypsochromic shift of the absorption maximum from 419 to 418.5 nm with clear isosbestic points at 379, 414, 511, 545, and 575 nm. The bandwidth of the Soret absorption band was also reduced along with disappearance of the shoulder after formation of the host–guest complex. The continuous variation method indicated that **1** and DAD formed a 1:1 host–guest complex with a very high binding affinity, the association constant for which was determined to be $1.2\times10^7\,M^{-1}$ through a nonlinear curve-fitting method using hypspec software. Because axial ligation by the amine increases the electron density of the zinc porphyrin, the absorption bands should exhibit a bathochromic shift. However, after complexation of DAD, **1** exhibited a hypsochromic shift of the absorption maximum but a bathochromic shift in the position of the shoulder. This spectroscopic change indicated that the two porphyrin units in **1** partially engage in the formation of a slipped-cofacial structure through π–π interaction, which was diminished upon insertion of DAD between them.[8]



Scheme 1. Synthesis of **1**. Reagents and conditions: a) I_2, Ag_2SO_4, EtOH, 25 °C, 2 h; b) trimethylsilylacetylene, CuI, $[Pd(PPh_3)_2Cl_2]$, Et_3N, 25 °C, 12 h; c) triphosgene, Et_3N, CH_2Cl_2, 0 °C, 2 h; d) dipyrromethane, TFA, CH_2Cl_2/MeOH, 25 °C, 12 h; e) *p*-chloranil, 25 °C, 4 h; f) HCl, EtOH, reflux, 2 h; g) **7**, reflux, 12 h; h) $Zn(OAc)_2$, CH_2Cl_2/MeOH, 25 °C, 12 h; i) TBAF, THF, 25 °C, 30 min; j) $Cu(OAc)_2\cdot H_2O$, pyridine, 25 °C, 12 h.

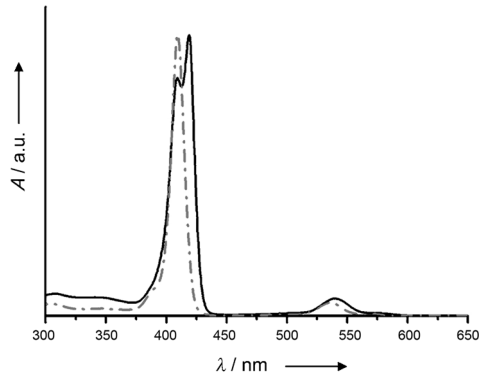


Figure 1. UV/Vis absorption spectra of a) **1** (solid line) and b) **8** (broken line) in CD_2Cl_2 at 25 °C.

Meanwhile, the two urea moieties in **1** provide strong hydrogen-bond donor groups for binding anionic guest molecules.[9] In fact, upon the addition of several different anionic guests, **1** exhibited a remarkably strong spectral shift with peak broadening, indicating a strong interaction between its two porphyrin units after anion binding (Figure 2b). The existence of clear isosbestic points and the result of the continuous variation method (Figure 2; Job's plot) indicated the formation of a very stable host–guest complex with a 1:1 binding stoichiometry, with the association constant for BLA exceeding $10^8\,M^{-1}$.

As mentioned above, the UV/Vis absorption spectrum of **1** is indicative of an interaction between the two porphyrin units of the tweezer. Variable-temperature (VT)-NMR and temperature-dependent UV/Vis absorption studies of **1** in $C_2D_2Cl_4$ were carried out to obtain further information on the initial conformation (Figure S1 in the Supporting Information). In the VT-NMR study, all peaks became sharp upon increasing the temperature, indicating rapid conformational interchange at high temperature. In contrast, all peaks disappeared on lowering the temperature due to poor solubility, with **1** precipitating from $C_2D_2Cl_4$ solution at low temperature. Although the VT-NMR experiments indicated slight downfield shifts of all peaks, the information provided was insufficient to confirm the initial conformation of **1**. Therefore, the ^{1}H NMR spectrum of **8** was compared with that of **1** (Figure 3). The signals of the pyrrolic and meso protons of **1** were seen to be located further upfield than those of **8**, indicating a partial overlapping of the porphyrin rings such that they were mutually affected by their respective ring currents. A UV/Vis absorption study in $C_2D_2Cl_4$ also indicated partial overlapping of the porphyrin rings (Figure S2 in the Supporting Information). The absorption spectrum of **1** in $C_2D_2Cl_4$ showed similar spectral shape to that in CH_2Cl_2, with the Soret absorption at 421 nm and a remarkably strong shoulder at 411 nm. The absorption intensity at 421 nm was gradually decreased on increasing the temperature, indicating a higher proportion of the *trans*-conformation at high temperature.

On the other hand, ^{1}H NMR study clearly showed spectral changes upon the addition of anionic guests. Upon addition of Boc-L-alanine (BLA) as the tetrabutylammonium salt, the urea NH signals exhibited a significant downfield shift, indicating the formation of strong hydrogen bonds between the carboxylate anion and the NH protons (Figure 3). At the same time, the signals of the pyrrole β and meso protons of the porphyrin were remarkably upfield shifted upon the addition of BLA. This strong upfield shift can be explained in terms of π–π interaction between the two porphyrin units. Due to the partial overlapping of the porphyrin

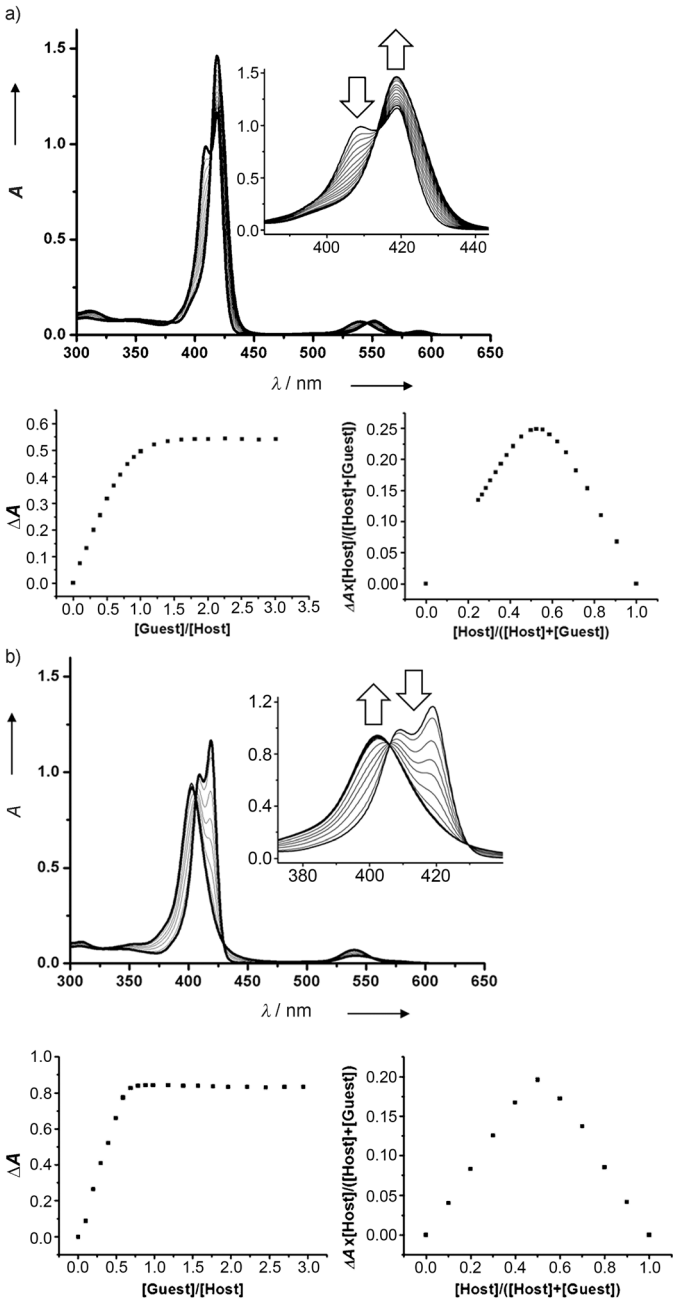


Figure 2. UV/Vis spectroscopic titration of **1** with DAD and BLA in CH_2Cl_2 at 25 °C. Lower left and right graphs are binding isotherm and Job's plot, respectively. a) [DAD]/[**1**] = 0–3.0, [**1**] = 2.15×10^{-6} M, ΔAbs was monitored at 408 nm, b) [BLA]/[**1**] = 0–3.0, [**1**] = 2.15×10^{-6} M, ΔAbs was monitored at 420 nm.

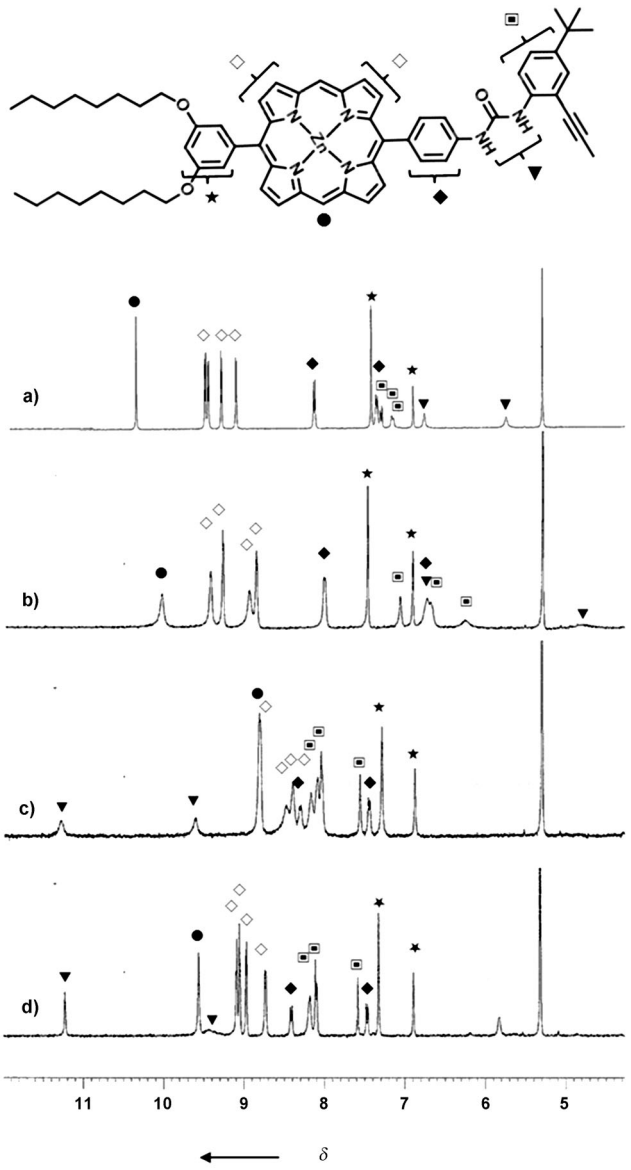


Figure 3. Partial ^{1}H NMR spectra of a) **8**, b) **1**, c) **1**⊃BLA, and d) **1**⊃BLA·DAD in CD_2Cl_2 at 25 °C.

units by π–π interaction, the pyrrole β and meso protons were greatly influenced by the porphyrin ring-current effect. When both BLA and DAD were added to **1**, the degree of upfield shift of the pyrrole β and meso proton signals was greatly decreased. The distance between the two porphyrin units was increased by the insertion of DAD, and hence the influence of their ring-current effects was greatly decreased. In sharp contrast to the proton signals corresponding to the porphyrin units, the chemical shift of the urea NH protons was not changed by the addition of DAD, indicating that the urea groups maintained their hydrogen bonds.

In the presence of one equivalent of BLA, **1** was again titrated with DAD. In this experiment, the absorption spectrum exhibited a bathochromic shift with clear isosbestic points at 441, 444, 516, and 540 nm (Figure 4a). The bandwidth of the Soret absorption also narrowed. When **1** was titrated with BLA in the presence of one equivalent of DAD, the Soret absorption was slightly broadened with clear isosbestic points at 412, 429, and 559 nm, indicating simultaneous accommodation of the anion and diamine guests within **1** (Figure 4b). The results of the continuous variation method indicated the formation of 1:1 host–guest complexes for both the diamine and anionic guests.

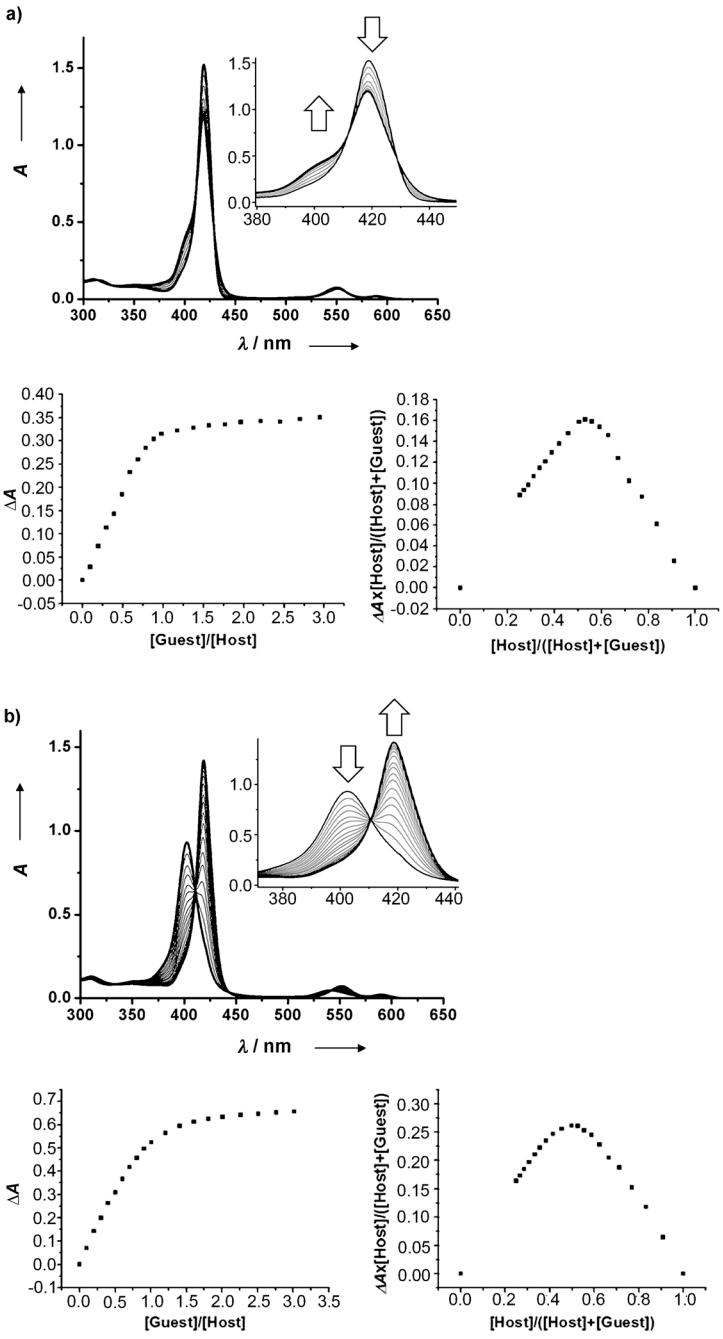


Figure 4. UV/Vis spectroscopic titration of **1** with DAD and BLA in CH_2Cl_2 at 25 °C in the presence of 1 equivalent BLA and DAD, respectively. Lower left and right graphs are binding isotherm and Job's plot, respectively. a) [BLA]/[**1**⊃DAD] = 0–3.0, [**1**⊃DAD] = 2.13×10^{-6} M, ΔAbs was monitored at 420 nm, b) [DAD]/[**1**⊃BLA] = 0–3.0, [**1**⊃BLA] = 2.13×10^{-6} M, ΔAbs was monitored at 402 nm.

Because **1** exhibited strong binding affinities towards both the diamine and anionic guests, the binding of chiral guests induced a conformational change of the host compound, which in turn generated ECCD signals. Therefore, CD spectra of **1** were measured at 20 °C upon the addition of several chiral amino acid derivatives. While **1** showed essentially no observable CD signals, a very weak negative CD signal appeared around the Soret region after the addition of three equivalents of BLA (Figure 5). Conversely, **1** exhibited a

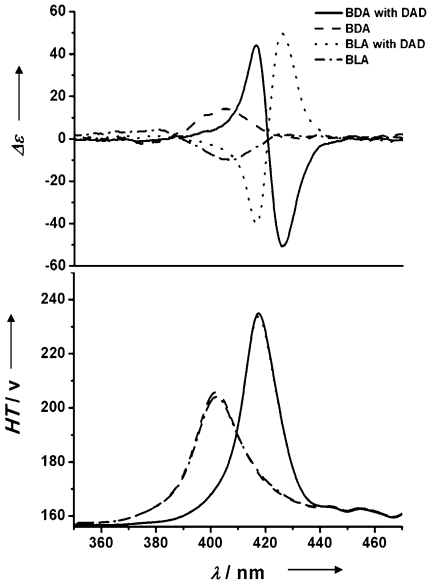


Figure 5. CD spectra of **1** in CH_2Cl_2 in the presence of three equivalents of BLA or BDA, with or without DAD (scan number 8, scan speed 200 nm min^{-1}, 293 K, bandwidth = 1 nm, [**1**] = 1.69×10^{-6} M).

weak positive CD signal upon the addition of Boc-D-alanine (BDA) as the tetrabutylammonium salt. For many other amino acid derivatives, very weak induced CD signals appeared. Although induced CD signals appeared after the addition of chiral amino acid derivatives, the intensity of these signals was very weak and their signs were not perfectly correlated with the chirality of guest molecules. The low intensity of the induced CD signal upon carboxylate binding to **1** might be explained in terms of the formation of a slipped-cofacial structure due to the strong π–π interaction between the two porphyrin units. In addition, the binding of anionic guests at the remote site away from the porphyrin units will not cause strong ECCD signals at the Soret band.

Because the strong interaction between the two porphyrin units in **1** was diminished by the insertion of DAD, we speculated that a conformational change of the porphyrin units might be enhanced by the addition of this diamine. Therefore, CD spectra were again measured after the addition of three equivalents of DAD. Very interestingly, the weak induced CD signals observed with BLA were converted into a strong positive couplet after the addition of DAD (Figure 5). Based on this information, we re-evaluated the CD signal amplification of **1** upon the addition of several other amino acid derivatives. All of the tested L-amino acid derivatives gave rise to a positive CD couplet, while D-amino acid derivatives gave the opposite signals. Furthermore, the intensities of the CD couplet were sufficiently strong to identify the absolute stereo-configurations (Table 1). Because **1** exhibited a significant and useful

Table 1. CD amplitudes of **1** induced by the binding of carboxylates in the presence of 3 equiv DAD at 20 °C in a 1 cm optical cell.[a]

Guests	Asymmetry	1st/nm [Δε]	2nd/nm [Δε]	A_{CD}[b]
BDA	*R*	427.2 [−32.5]	419.2 [+25.7]	−58.2
BLA	*S*	428.2 [+28.0]	418.4 [−33.4]	+61.4
Boc-D-Leu	*R*	426.9 [−56.0]	418.9 [+42.5]	−98.5
Boc-L-Leu	*S*	426.7 [+49.2]	418.5 [−53.1]	+102.3
Boc-D-Phe	*R*	427.6 [−67.9]	418.4 [+67.3]	−135.2
Boc-L-Phe	*S*	427.4 [+65.2]	418.5 [−70.9]	+136.1
Boc-L-Pro	*S*	428.3 [+70.4]	418.5 [−67.9]	+138.2
Boc-L-Ser	*S*	429.1 [+6.8]	415.5 [−7.9]	+14.7
Boc-L-Thr	*S*	426.3 [+32.5]	418.7 [−29.3]	+61.8
Boc-L-Val	*S*	427.7 [+48.5]	418.6 [−51.2]	+99.7
Mandelate	*S*	427.4 [+32.1]	417.6 [−40.2]	+72.3

[a] Solvent: CH_2Cl_2, scan speed: 200 nm min^{-1}, scan number: 8, [**1**] = 1.69×10^{-6} M, [carboxylates] = 5.07×10^{-6} M, [b] L mol^{-1} cm^{-1}.

CD signal response upon the addition of amino acid derivatives together with achiral DAD, computer-aided molecular modeling studies were carried out using the MM3 force-field to study the possible underlying conformational changes.[10] Depending on the initial conformation, the energy-minimized structure of **1** exhibited both *cis*- and *trans*-conformers (Figure 6a and Scheme 2). A slipped-cofacial structure of the two porphyrin units could be observed

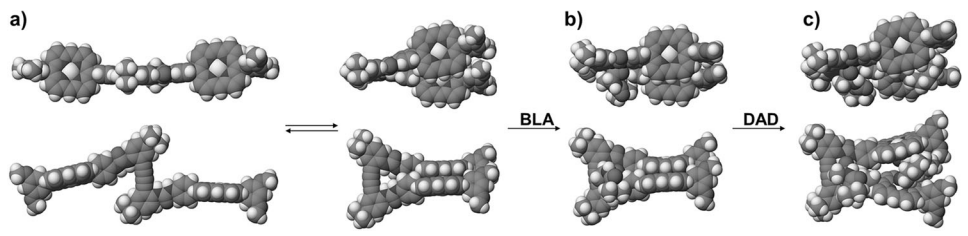
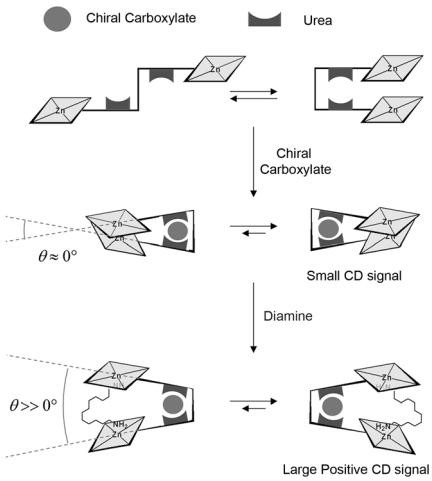


Figure 6. Energy-minimized structures of a) **1**, b) **1**⊃BLA, and c) **1**⊃BLA·DAD with omission of alkyl chains.



Scheme 2. Proposed mechanism of CD enhancement of **1** by the binding of guests.

in the *cis*-conformation, which is consistent with the observations based on the electronic absorption spectra. Accordingly, upon formation of the BLA adduct with **1** (**1**⊃BLA), **1** adopted the *cis*-conformation through the formation of multiple hydrogen bonds (Figure 6b). In this state, the two porphyrin units are spatially very close to each other due to their π–π interaction. More importantly, the directions of the transition dipole moments for the two porphyrin rings, which run from the 5- to the 15-position of the porphyrin units, become almost parallel in the **1**⊃BLA complex. This could be the reason for the generation of weak ECCD signals upon the addition of BLA to **1**. Considering the addition of DAD to **1**⊃BLA, the angle between the transition dipole moments of the two porphyrin units becomes much greater following insertion of the diamine. Therefore, the molecular chirality of the carboxylate may strongly induce either a right-handed or left-handed twist to the structure of **1**. In fact, the angle between the transition dipole moments of the two porphyrin units in the energy-minimized structure of **1**⊃BLA·DAD was much wider than that in **1**⊃BLA, which presumably gave rise to the strong ECCD signals (Figure 6c). The process of chiral recognition can be summarized as shown in Scheme 2. The porphyrin tweezer adopts a *cis*-conformation by carboxylate inclusion due to the formation of multiple hydrogen bonds. In this process, the two urea groups are twisted in different directions depending on the chirality of the amino acid derivatives in order to minimize steric repulsion (Figure 7). Because of the chiral twist of the urea groups, **1** should exhibit ECCD signals. However, the electronic absorption of the urea groups lies in the invisible UV range. Moreover, the two porphyrin units in **1** form a slipped-cofacial structure due to the strong π–π interaction. Therefore, **1** exhibits only weak CD signals due to the parallel orientation of transition dipoles. On the other hand, the chiral distortion of the urea groups is transferred to the two porphyrin units by the insertion of DAD, because the strong π–π interaction is diminished. Therefore,

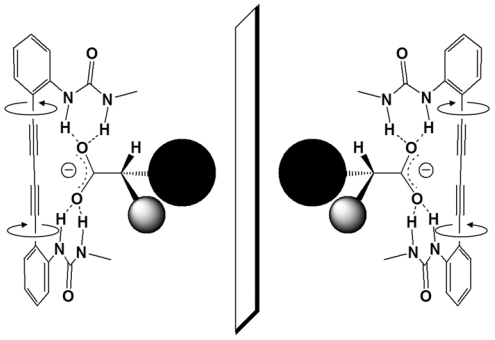


Figure 7. Twist of urea groups by the formation of multiple hydrogen bonding with carboxylate.

strong ECCD signals become observable upon the addition of DAD to a chiral carboxylate complex of **1**. In this process, the size and rigidity of the side groups of chiral amino acids greatly influence the intensity of the CD signals, with the order of signal intensity being as follows: Pro ≈ Phe > Leu ≈ Val > Thr ≈ Ala > Ser. The ECCD is induced by a structural twist of the two porphyrin units to minimize steric interaction, and bulky and rigid side groups will induce more twisted structures than smaller ones. The relative intensities of ECCD upon additions of Phe, Leu, Val, and Ala clearly reflect the influences of the side groups.

Conclusion

We have synthesized a new type of porphyrin-based molecular tweezer with two urea groups, which exhibits strong ECCD signals upon the simultaneous complexation of chiral carboxylate and achiral diamine guests. Because the two urea groups and porphyrin units exhibit significantly strong binding affinities towards chiral carboxylate and diamine guests, respectively, the molecular tweezer can be successfully utilized as a highly sensitive probe for the absolute stereochemical determination of chiral carboxylates. Unlike other porphyrin-based molecular tweezers, monodentate carboxylates can be directly utilized without derivatization to determine their molecular chirality. Therefore, the concept demonstrated herein provides a new strategy for the design of efficient chiral probes.

Experimental Section

Measurements: Electronic absorption spectra were recorded on a JASCO model V-660 spectrometer. CD spectra were recorded on a JASCO model J-815 spectrometer at 20 °C in CH_2Cl_2 (scan speed: 200 nm min^{-1}, scan number: 8, bandwidth: 5 nm). ^{1}H and ^{13}C NMR spectra were recorded on Bruker Advance DPX250 and DPX400 spectrometers at 25 °C in CD_2Cl_2 or $CDCl_3$. MALDI-TOF-MS was performed on an Applied Biosystems 4700 proteomics analyzer with α-cyano-4-hydroxycinnamic acid as the matrix.

Synthesis of 3:[11] I_2 (3.57 g, 14.07 mmol) and Ag_2SO_4 (4.39 g, 14.07 mmol) were added to a solution of 4-*tert*-butylaniline (2.00 g, 13.4 mmol) in

EtOH (50 mL) and the mixture was stirred for 2 h at 25 °C and then filtered through Celite. The filtrate was concentrated and the residue was purified by column chromatography on silica eluting with CH_2Cl_2/hexane (1:3) to give **3** (1.1 g, 30 %). ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): $\delta = 7.62$ (s, 1H), 7.19–7.16 (d, $J = 8$ Hz, 1H), 6.72–6.69 (d, $J = 8$ Hz, 1H), 3.96 (s, 2H), 1.26 ppm (s, 9H).

Synthesis of 4:[11] **3** (1.05 g, 3.81 mmol), CuI (36 mg, 0.19 mmol), and [Pd(PPh_3)$_2Cl_2$] (133 mg, 0.19 mmol) were placed in a Schlenk flask. The flask was degassed under high vacuum and back-filled with N_2; this process was repeated three times. Dried THF (15 mL), Et_3N (3 mL), and trimethylsilylacetylene (0.94 mL, 15.24 mmol) were added. The reaction mixture was stirred for 16 h at 50 °C and then filtered through Celite. The filtrate was concentrated and then purified by column chromatography on silica eluting with CH_2Cl_2/hexane (1:5) to give **4** (0.80 g, 86 %). ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): $\delta = 7.30$ (s, 1H), 7.18–7.15 (d, $J = 8$ Hz, 1H), 6.66–6.63 (d, $J = 8$ Hz, 1H), 4.11 (s, 2H), 1.26 (s, 9H), 0.27 ppm (s, 9H).

Synthesis of 7:[6b] TFA (2 mL, 26.12 mmol) was added to a solution of **5** (1.23 g, 7.51 mmol), **6** (2.72 g, 7.51 mmol), and dipyrromethane (2.20 g, 15.03 mmol) in CH_2Cl_2 (830 mL) and MeOH (170 mL), and the mixture was stirred for 12 h at 25 °C. Thereafter, *p*-chloranil (8.49 g, 34.2 mmol) was added and the reaction mixture was stirred for a further 4 h. It was then concentrated to a volume of 200 mL and chromatographed on silica gel eluting with 20 % EtOAc/CH_2Cl_2. Without further purification, the product was dissolved in a mixture of EtOH (40 mL) and aqueous HCl (60 mL) and the solution was refluxed for 12 h. The reaction mixture was purified by column chromatography on silica, eluting with CH_2Cl_2, and the eluate was concentrated to dryness. The residue was recrystallized from CH_2Cl_2/hexane to give **7** as a reddish-purple powder (0.44 g, 8 %). ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): $\delta = 10.29$ (s, 2H), 9.40–9.37 (m, 4H), 9.20–9.16 (m, 4H), 8.08–8.05 (d, $J = 8$ Hz, 2H), 7.43 (s, 2H), 7.14–7.11 (d, $J = 8$ Hz, 2H), 6.92 (s, 1H), 4.18–4.13 (t, $J = 6.5$ Hz, 4H), 4.06 (s, 2H), 1.92–1.86 (m, 4H), 1.53–1.28 (m, 10H), 0.90–0.85 (t, $J = 6$ Hz, 6H), −3.08 ppm (br s, 2H); MALDI-TOF-MS: m/z: calcd for $C_{48}H_{55}N_5O_2$: 733.98 [M^+]; found: 736.61.

Synthesis of 8:[12] Triphosgene (0.14 g, 0.40 mmol) in CH_2Cl_2/Et_3N (3 mL:0.2 mL) was added to a solution of **4** (0.11 g, 0.40 mmol) in CH_2Cl_2 (7 mL) and the mixture was stirred for 2 h at 0 °C. Thereafter, a solution of **7** (0.2 g, 0.27 mmol) in CH_2Cl_2 (10 mL) was added, the reaction mixture was refluxed for 12 h, and then the solvents were evaporated. The residue was filtered through silica gel with EtOAc. Without further purification, the product was dissolved in 10 % MeOH/CH_2Cl_2 (20 mL) containing $Zn(OAc)_2$ (0.434 g, 1.98 mmol) and the solution was stirred for 12 h at 25 °C. The reaction mixture was purified by column chromatography on silica, eluting with 20 % EtOAc/hexane to give a reddish-purple solid. The residue was redissolved in THF containing TBAF (78 μL, 0.27 mmol) and the solution was stirred for 30 min at 25 °C. The reaction mixture was purified by column chromatography on silica eluting with EtOAc/hexane (1:4) to give **8** (0.1 g, 37 %). ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): $\delta = 10.26$ (s, 2H), 9.42–9.36 (m, 4H), 9.28–9.26 (d, $J = 4.5$ Hz, 2H), 9.06–9.04 (d, $J = 4.5$ Hz, 2H), 8.16–8.13 (d, $J = 8$ Hz, 2H), 7.45–7.40 (m, 4H), 7.33–7.26 (m, 2H), 7.03 (s, 1H), 6.92 (s, 1H), 5.73 (s, 2H), 4.17–4.10 (m, 4H), 3.36 (s, 1H), 1.92–1.81 (m, 4H), 1.48–1.23 (m, 10H), 0.88–0.82 ppm (m, 6H); MALDI-TOF-MS: m/z: calcd for $C_{61}H_{66}N_6O_3Zn$: 996.63 [M^+]; found: 994.13.

Synthesis of 1:[13] **8** (0.1 g, 0.10 mmol) and $Cu(OAc)_2 \cdot H_2O$ (40 mg, 0.20 mmol) were placed in a Schlenk flask. The flask was degassed under high vacuum and back-filled with N_2; this process was repeated three times. Dry pyridine (10 mL) was added. The reaction mixture was stirred for 12 h at 25 °C, and then the solvent was evaporated. The residue was purified by column chromatography on silica eluting with EtOAc/hexane (1:3) to give **1** (80 mg, 40 %). ^{1}H NMR (400 MHz, CD_2Cl_2, 25 °C): $\delta =$ 10.08 (s, 4H), 9.46 (br s, 4H), 9.30 (br s, 4H), 8.98 (br s, 4H), 8.89 (br s, 4H), 8.04 (br d, $J = 5.6$ Hz, 4H), 7.50 (s, 4H), 7.08 (s, 2H), 6.94 (s, 2H), 6.75 (br s, 6H), 6.70 (br s, 2H), 6.28 (br s, 2H), 4.78 (br s, 2H), 4.19–4.15 (t, $J = 6.4$ Hz, 8H), 1.59–1.05 (m, 20H), 0.84 ppm (s, 12H); ^{13}C NMR (100 MHz, CD_2Cl_2, 25 °C): $\delta = 158.59$, 150.41, 149.93, 149.89, 149.46, 145.04, 136.11, 133.88, 132.01, 131.94, 130.15, 128.09, 120.73, 120.29, 118.47, 115.02, 106.55, 101.17, 79.58, 79.07, 72.44, 68.85, 61.94, 34.36, 32.18, 31.28, 30.08, 29.82, 29.78, 29.61, 26.50, 23.00, 14.21 ppm; MALDI-TOF-MS: m/z: calcd for $C_{132}H_{96}N_{12}O_8Zn_2$: 1991.23 [$M^+$]; found: 1990.16.

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