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COMMUNICATION

Chiral porphyrin dimer with a macrocyclic cavity for intercalation of aromatic guests†‡

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Chiral diporphyrin receptor 1, which has a macrocyclic cavity to sandwich aromatic guest molecules *via* double π–π stacking interactions, enabled the naked-eye detection of an aromatic explosive as well as chiral discrimination in NMR.

The π–π stacking interaction plays an important role in biomolecules such as DNA and proteins, crystal structures of organic compounds, and host–guest complexes.[1–3] When this weak interaction is used in a host–guest system, other interactions such as hydrogen bonds are often combined to strengthen the association.[4] Although chiral recognition/discrimination has been extensively studied because of its importance,[5–8] there are few examples that employ the π–π stacking interaction as a sole driving force. Recent elegant works on the chiral recognition of fullerenes and carbon nanotubes have demonstrated the effectiveness of the π–π stacking interaction.[9,10]

We envisioned that both binding capacity and chiral discrimination power could be enhanced by adopting the following strategy: (i) two porphyrins, which have rigidity, a large π-surface, and a great ring-current effect, are disposed in parallel at a distance of *ca.* 7 Å to create a macrocyclic cavity suitable for the inclusion of aromatic guests; (ii) chiral spacers are used to link the two porphyrins, forming a chiral cavity. We selected BINOL as a chiral spacer because BINOL has moderate rigidity and flexibility in addition to the ring-current effect. Fig. 1 shows a new chiral receptor **1** designed by MM calculations according to the above strategy. The two porphyrins are arranged in an offset face-to-face geometry with an interplanar distance of 5.8–7.2 Å, which is suitable for sandwiching aromatic molecules. We also expected that the macrocyclic framework would be useful for the restriction of freedom of the bound guest, which would have an advantageous effect on chiral discrimination, and for the suppression of aggregation of the receptor. Here we report the synthesis, binding, and chiral discrimination of **1**. During this study, we found that **1** can act as a naked-eye sensor for an aromatic explosive.

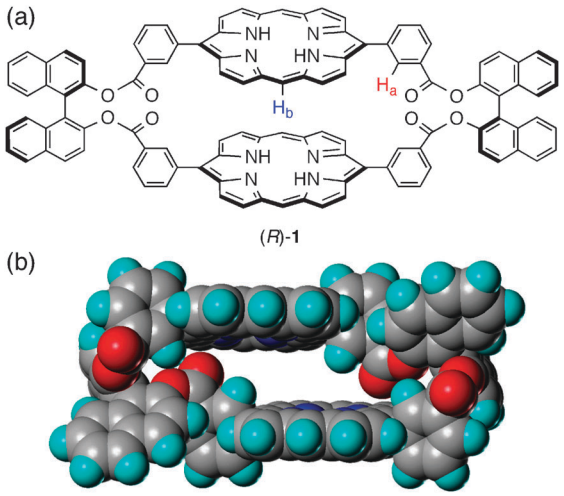

Fig. 1 (a) Chemical and (b) optimized structures of (*R*)-**1**. NMR complexation-induced shifts (Δδ) for the H_a and H_b atoms are shown in Fig. 3. The geometry was optimized by MM3 calculations with CAChe WorkSystem Pro ver. 5.02 (Fujitsu).

The synthetic scheme for **1** is shown in Scheme 1. Porphyrin **3**, prepared in 67% yield by the acid-catalyzed condensation of dipyrromethane **2**[11] and methyl 3-formylbenzoate followed by oxidation with DDQ according to the literature method,[12] was hydrolyzed to give diacid **4**[13] in 93% yield. Esterification of **4** with BINOL afforded diol **5** in 61% yield. Finally, the esterification of **5** with **4** was achieved under high dilution conditions to give macrocycle **1** in 28% yield. The IR spectrum of **1** exhibited an absorption band at 1737 cm^{-1} (C=O stretching vibration), which was much higher than that for **5** (1715 cm^{-1}). The ^1H NMR spectrum of **1** showed the *meso*-H signal at 8.83 ppm and the NH signal at −6.91 ppm, which appeared at a higher magnetic field than those for **5** (10.32 ppm for *meso*-H and −3.17 ppm for NH). UV–Vis spectra indicated that the Soret band of **1** was blue-shifted by 16 nm relative to that of **5**, and the CD spectrum of **1** was much more intense than that of **5** (ESI‡). All of these spectra strongly support the formation of the target macrocycle **1** with two porphyrin chromophores disposed in a face-to-face but chiral manner.

Complexation of **1** with **G1–G7** and **G9–G10** (Fig. 2) in $CDCl_3$ was monitored at 25 °C by ^1H NMR. Upon addition of

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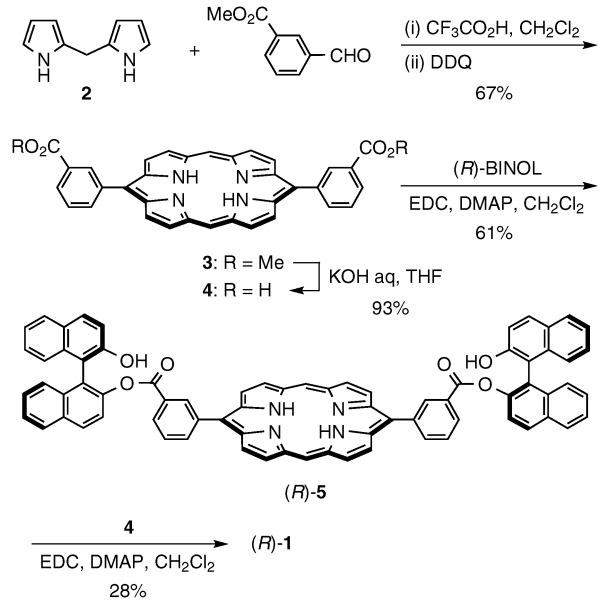
‡ Electronic supplementary information (ESI) available: Synthesis, UV–Vis and CD spectra of **1** and **5**, Job plots, determination of binding constants, copies of ^1H and ^{13}C NMR spectra of **1–5** and guest compounds, and MM calculations. See DOI: 10.1039/c1cc11572c



Scheme 1

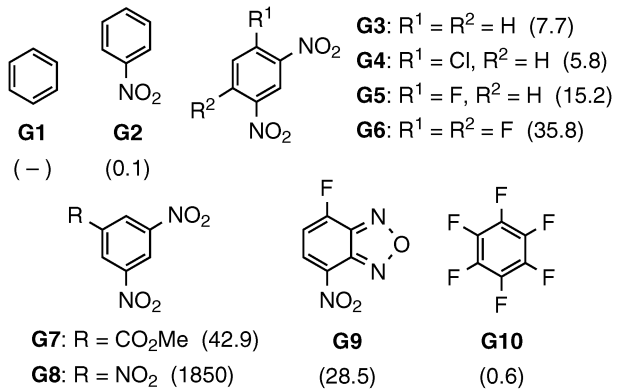


Fig. 2 Guest compounds. Binding constants (K_a) of (*R*)-**1** in chloroform at 25 °C are shown in parentheses, where the bar indicates that the K_a value was too small to determine.

any guest except **G1**, the H_a signal underwent an upfield shift, while the H_b signal experienced a downfield shift, as represented in Fig. 3 (H_a and H_b atoms are designated in Fig. 1). The fact that the H_b signal for **1** (8.83 ppm) appeared at a higher magnetic field than that for **5** (10.32 ppm) suggests that **1** takes a conformation where the edge of one porphyrin ring, such as the H_b atom, is in proximity to the other porphyrin ring. We suppose that the two porphyrin rings become parallel

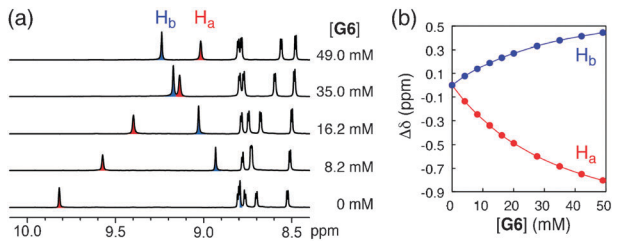


Fig. 3 (a) Complexation-induced shifts ($\Delta\delta$) for the aromatic protons of (*R*)-**1** (10 mM) as a function of [**G6**] in $CDCl_3$ at 25 °C. (b) Plots of the $\Delta\delta$ values for the H_a and H_b protons of (*R*)-**1** as a function of [**G6**]. The H_a and H_b atoms are designated in Fig. 1.

upon inclusion of a guest molecule and that the chemical shifts of the H_a and H_b atoms in **1** become closer to those of the corresponding atoms in **5**.

Job plots indicated 1 : 1 complexation (ESI‡). The binding constants (K_a) were determined by NMR titrations; the nonlinear least-squares method was applied to the H_a signal that was upfield shifted upon addition of the guest.[14] As for **G8**, the K_a value was determined by UV–Vis titration. The data are summarized in Fig. 2. The K_a value increases in the following order: **G1** < **G2** < **G3** < **G5** < **G6** < **G8**. This trend indicates the greater affinity of **1** for a more electron-deficient aromatic guest, suggesting that the electrostatic contribution is a predominant factor in complexation between the electron-rich (π-basic) porphyrin and the electron-deficient (π-acidic) aromatic compound. The complexation between **1** and **G8** (K_a = 1850 M^{-1}) was much stronger than that between porphyrin monomer **3** and **G8** (K_a = 50 M^{-1}). This result clearly indicates that **G8** was intercalated into the cavity of **1** *via* the cooperative double π–π stacking. The van't Hoff plots confirmed that the complexation between **1** and **G8** (ΔH° = −8.4 kcal mol^{-1}, $T\Delta S^\circ$ = −4.0 kcal mol^{-1} at 25 °C) was more enthalpy-driven than that between **3** and **G8** (ΔH° = −5.7 kcal mol^{-1}, $T\Delta S^\circ$ = −3.4 kcal mol^{-1} at 25 °C). The K_a values of **1** for the electron-deficient guests **G7** and **G9** were reasonably high, whereas that for **G10**, which is electron-deficient enough, was much lower than expected. The latter result may be due to the specific nature of the cavity in **1**, such as size exclusion and electrostatic repulsion against the six fluorine atoms.

During the NMR titrations, we noticed that precipitates were formed only when **G8** was added to a solution of **1** in $CDCl_3$. Because **G8** is an explosive that is more powerful than 2,4,6-trinitrotoluene (TNT), and because the development of chemosensors for aromatic explosives has been a challenging subject,[15] we decided to investigate the utility of **1** as a sensor for **G8**. As shown in Fig. 4a and b, a dark-red solution of **1** in $CHCl_3$ turned into a colloidal suspension upon addition of **G8**, and the light illuminated from the front side was scattered. This suspension was stable for more than a week. On the other hand, fluorescence was also useful for the selective detection of **G8** with the naked eye. Upon addition of **G8** to a dilute solution of **1**, no precipitates appeared, and fluorescence was quenched as shown in Fig. 4c and d. These phenomena were specific to **G8**, and **1** acted as a unique naked-eye explosive sensor.

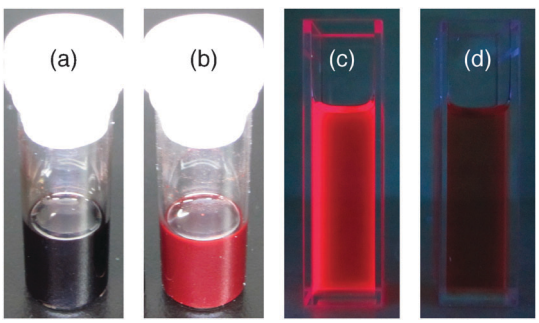
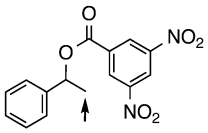
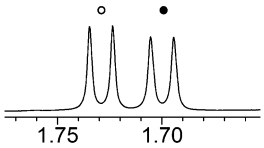
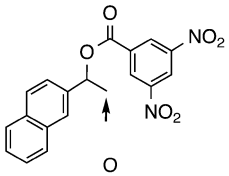
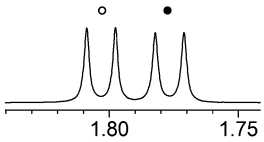
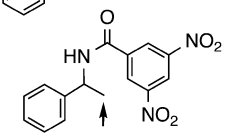
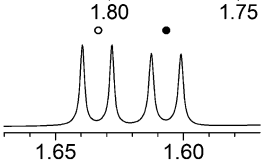
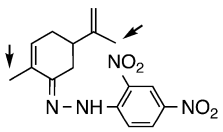
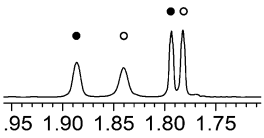


Fig. 4 The naked-eye detection of explosive **G8**. A solution of (*R*)-**1** (10 mM) in $CHCl_3$ (a) before and (b) after addition of **G8** (1 equiv.). Fluorescence of a solution of (*R*)-**1** (50 μM) in $CHCl_3$ (c) before and (d) after addition of **G8** (5.3 mM). λ_{ex} = 365 nm.

Table 1 Selected regions of NMR spectra of racemic guests **G11–G14** in the presence of (*R*)-**1**[a]

Guest	Spectrum
G11 	
G12 	
G13 	
G14 	

[a] 600 MHz ^{1}H NMR of **G11–G14** in the presence of (*R*)-**1** (10 mM, 1 equiv.) in $CDCl_3$ at 22 °C. The resonances for the protons indicated by the arrows are shown in the right column, where (*R*)- and (*S*)-enantiomers are represented by filled and open circles, respectively.

We next evaluated the chiral discrimination ability of **1**. In view of the moderate affinity of **1** for dinitrobenzene derivatives (Fig. 2), alcohol, amine, and ketone were converted into 3,5-dinitrobenzoyl ester, 3,5-dinitrobenzoyl amide, and 2,4-dinitrophenylhydrazone, respectively. We measured NMR spectra for the 1 : 1 mixtures of (*R*)-**1** and **G11–G14** (10 mM) in $CDCl_3$ (Table 1). To our delight, the signals for esters **G11** and **G12** and amide **G13** were resolved completely, where the signals for the methyl group of the (*R*)-enantiomers appeared at a higher magnetic field. The signals for the two methyl groups of **G14** were also split. We observed that the signals of **G11** split even in d_6-DMSO (not shown). Thus, excellent chiral discrimination has been achieved despite the use of only π–π stacking as a driving force of complexation. When **5** was used as a chiral host for **G11**, no chiral discrimination was attained, which indicates that the specific cavity in **1** is essential for binding and chiral discrimination of the guest.

In summary, this is the first example of arraying two porphyrins in a parallel but chiral manner at a distance suitable for the intercalation of aromatics *via* double π–π stacking interactions. The synthesis was achieved only in five steps from pyrrole. **1** functioned as a naked-eye sensor for an explosive, 1,3,5-trinitrobenzene (**G8**), and also discriminated the enantiomers by NMR.

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