Triptycene-based tetralactam macrocycles: synthesis, structure and complexation with squaraine†

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Two novel triptycene-based tetralactam macrocycles as a pair of diastereomers were synthesized, and showed highly efficient complexation with squaraine, which could subsequently protect the squaraine dye from polar solvents.

In host–guest chemistry, a permanent and challenging topic is to design and synthesize novel macrocyclic hosts with the capability to strongly and selectively bind specific substrate species.[1] Tetralactam macrocycles, with their ability to include anions and organic molecules, have drawn much attention in different fields such as templated synthesis,[2] and supramolecular chemistry[3] during the past decade. In particular, they have been widely applied to construct a variety of interlocked supramolecular assemblies,[4] develop new molecular motors and machines,[5] and improve the properties of organic dyes by molecular encapsulation.[6]

Squaraines are a family of fluorescent near-IR dyes with specific photophysical properties for wide potential applications such as imaging, nonlinear optics, photovoltaics, and ion sensing.[7] However, their inherent reactivity with nucleophiles and the tendency to form non-fluorescent aggregates in water limit the use of these dyes.[8] To improve the chemical stability and the photophysical properties of the dyes, some squaraine-derived rotaxanes have been developed in recent years, which could provide an effective approach to protect the dyes.[9,10] Recently, we[11] were interested in the development of new supramolecular systems based on triptycene with a unique 3D rigid structure. As part of our continuing work, we herein report the synthesis and structures of a pair of novel triptycene-based tetralactam macrocycles **1** and **2** (Fig. 1), which show highly efficient complexation abilities toward squaraine **3**, and subsequently protect the dye from polar solvents.

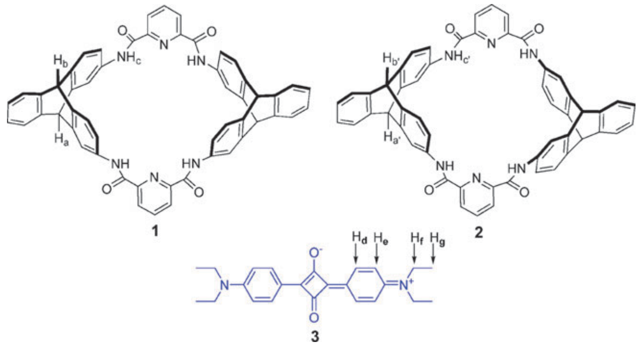

Fig. 1 Structures and proton designations of hosts **1** and **2**, and guest **3**.

The synthesis of the macrocyclic hosts **1** and **2** is depicted in the ESI (see Scheme S1).† By the reaction of pyridine-2,6-dicarbonyl dichloride and 2,7-diaminotriptycene in dry THF in the presence of Et_3N, the 2 + 2 cyclization products **1** and **2** were readily obtained in 26% and 20% yield, respectively. Macrocycles **1** and **2** are a pair of diastereomers. Their ^{1}H NMR spectra are greatly different from each other,† but show only one signal for the NH protons and two single signals for the bridgehead protons of the triptycene moieties, which indicates that both **1** and **2** have highly symmetric structures.

We obtained single crystals[12] of **1** and **2** suitable for X-ray analysis from slow evaporation of CH_3OH or cyclohexane into a $CHCl_3$ solution, respectively. As shown in Fig. 2, the crystal structures showed that compound **1** was a *cis* isomer and compound **2** was a *trans* isomer. Similar to that observed for calix[4]arene,[13] **1** adopted a cone conformation, in which the dihedral angle between the two pyridine rings was 133.59°, while a dihedral angle of 81° between the face-to-face benzene rings in triptycene existed. Due to the intramolecular hydrogen bonds (average $d_{N\cdots H}$ = 2.32 Å, $\theta_{N-H\cdots N}$ = 107.10°) between the amide protons and the adjacent pyridyl nitrogen, the conic cavity surrounded by four residues in **1** showed a wider rim of 11.97 × 16.04 Å and a narrower rim of 7.34 × 10.95 Å.† Moreover, it was found that the four carbonyl groups attached to the wider rim and the four amide NH protons defined the narrower rim. For the *trans* isomer **2**, the pyridine rings were parallel to each other and inclined by 6.59° to the plane formed by four carbonyl oxygen atoms. Meanwhile, the two triptycene moieties were *trans*-connected by the pyridyl amide subunits with the distances between the parallel planes of the face-to-face benzene rings in triptycene of 6.42 Å and 6.66 Å, respectively, which resulted in an almost prism cavity with a chair conformation. Moreover, the two pyridyl nitrogen atoms pointed inward with a distance of 11.27 Å, while four carbonyl groups pointed outward. Similar to **1**, the intramolecular hydrogen bonds (average $d_{N\cdots H}$ = 2.24 Å, $\theta_{N-H\cdots N}$ = 111.70°) in **2** also played an important role in the formation of its specific conformation.

With the novel macrocyclic hosts **1** and **2** in hand, we then tested their complexation with squaraine **3**. The complex studies were first carried out by a ^{1}H NMR spectral method. As shown in Fig. 3, the ^{1}H NMR spectra of the hosts and guest

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† Electronic supplementary information (ESI) available: Synthesis and characterization data of new compounds; crystal structures and/or packing of **1**, **2**, and **2·3**; determination of the association constants (K_a) for pseudorotaxanes **1·3** and **2·3**, and the quantum yields (Φ). CCDC 697888–697890. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b813804d

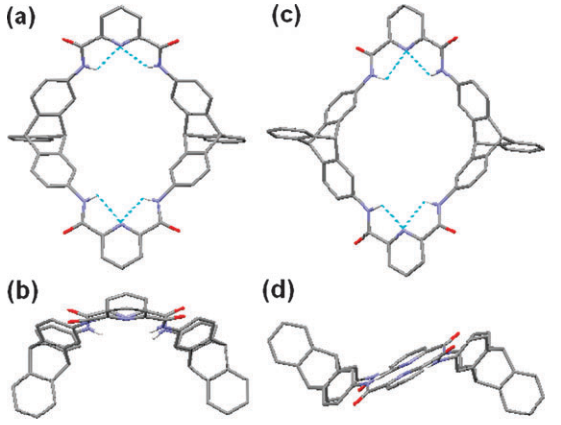

Fig. 2 Crystal structures. (a) Top view and (b) side view of **1**; (c) top view and (d) side view of **2**. Blue dashed lines denote the intramolecular N–H···N hydrogen bonds. Solvent molecules and hydrogen atoms not involved in the hydrogen bonding are omitted for clarity.

3 (3.0 mM each) mixed in $CDCl_3$ displayed only one set of well-defined resonances and a great difference from those for the free hosts and the free guest. Particularly, striking downfield shifts ($\Delta\delta = 1.64$ ppm for **1** and 1.95 ppm for **2**) for NH signals were observed, which might be attributed to the intermolecular hydrogen bonding and the strong deshielding effect of the squaraine. Moreover, the signals of the bridgehead protons (H_a, H_b, $H_{a'}$, $H_{b'}$) of the triptycene shifted upfield ($\Delta\delta = -1.10$ ppm, -0.36 ppm for **1**, and -0.46 ppm, -0.40 ppm for **2**), which might be due to the strong shielding effect of the aromatic rings in the squaraine. These observations suggested that the stable complexes **1**·**3** and **2**·**3** formed. Interestingly, it was further found that the guest protons in complex **1**·**3** all displayed two sets of signals (Fig. 3b), which indicated that half of the guest molecule was positioned at the wide rim of the macrocycle, while the other half was at the narrow rim of the macrocycle. Consequently, the guest displayed an environment-induced-asymmetry upon complexation with the host **1** with the cone conformation. Comparatively, because host **2** has a C_2 symmetrical axis, the complexation-induced-asymmetry of the guest in complex **2**·**3** was not observed. It is also noteworthy that different kinetic rates of association of squaraine **3** with macrocycles **1** and **2** were observed. For host **1** and guest **3**, the complexation completed within about 12 h,† whereas, for host **2** and guest **3**, the process immediately completed upon mixing, which can be explained by the difference between the cavities of the macrocycles **1** and **2** shown in Fig. 2.

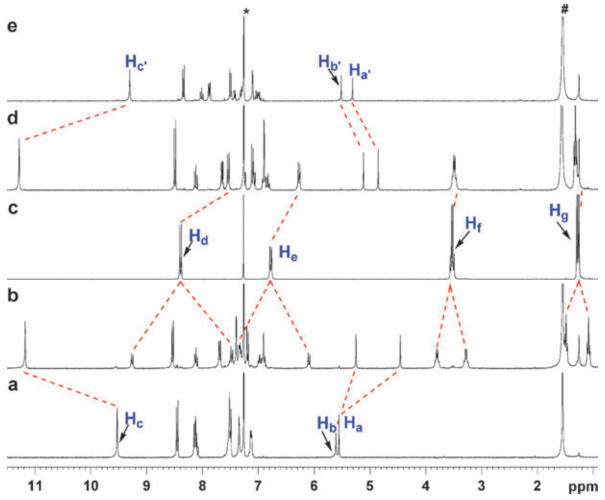

Fig. 3 ^1H NMR spectra (300 MHz, $CDCl_3$, 298 K) of (a) free host **1**, (b) **1** and 1.0 equiv. of **3**, (c) free guest **3**, (d) **2** and 1.0 equiv. of **3**, (e) free host **2**. [**1**] = [**2**] = 3.0 mM. Peak * denotes the signal of the solvent, peak # denotes the signal of water.

Fortunately, we also obtained the crystal structure of complex **2**·**3**,[12] which provided further evidence for the formation of the complex. As shown in Fig. 4a and Fig. 4b, the squaraine penetrated through the host **2** to form a [2]pseudorotaxane-type complex in the solid state, in which the cyclobutene core of **3** was positioned in the centre of **2**. As expected, hydrogen bonding interactions existed ($d_{\mathrm{H\cdots O}}$ = 2.33 Å for a, and 2.28 Å for b) between the amide protons of **2** and the carbonyl oxygen atoms of **3**. Moreover, two pairs of C–H···π interactions ($d_{\mathrm{H\cdots\pi}}$ = 2.75 Å for c, and 2.87 Å for e) between the aromatic protons of the guest and the benzene rings of the triptycene subunit, and a pair of π–π interactions between the aromatic rings of **3** and the benzene rings of triptycene with a distance of 3.23 Å (d) were also observed. These multiple noncovalent interactions played an important role in the formation of the stable complex, which is consistent with the results in solution. Interestingly, we found that the macrocyclic molecules in complex **2**·**3** can further self-assemble into tubular superstructures with the aromatic rings as the inner face[14] (Fig. 4c), and the guest molecules position in the channels (Fig. 4d).

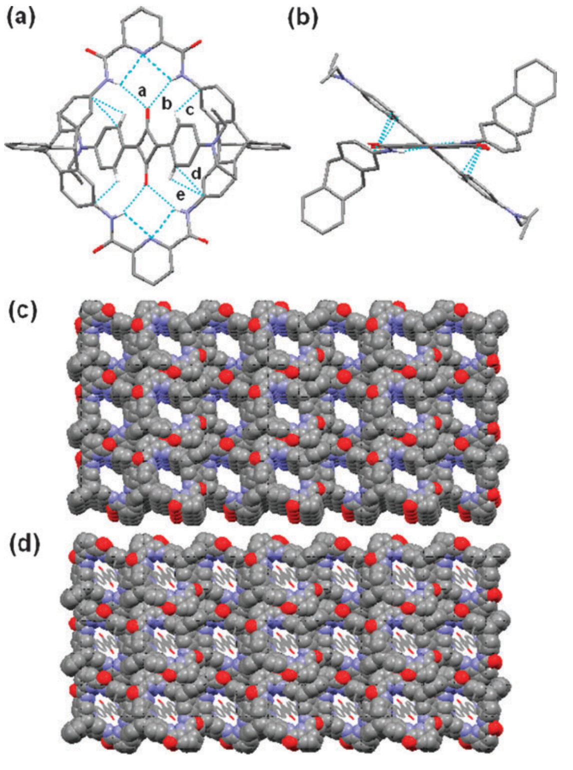

Fig. 4 (a) Top view and (b) side view of the crystal structure of complex **2**·**3**. Blue dashed lines denote the noncovalent interactions. Views of the tubular assemblies of the complex (c) in the absence and (d) in the presence of guest **3**. Solvent molecules and hydrogen atoms not involved in the hydrogen bonding interactions are omitted for clarity.

Table 1 Absorption and emission of **3**, **1·3**, and **2·3** in $CHCl_3$[a]

Compound	λ_{abs}/nm	Log ε	λ_{em}/nm	Φ_f[b]
3	633	5.52	658	0.72
1·3	637	5.44	666	0.22
2·3	642	5.43	667	0.49

[a] Solutions were excited at 580 nm and emission monitored in the region 600–750 nm for estimating Φ_f. [b] Fluorescence quantum yields were determined using 4,4-[bis-(*N*,*N*-dimethylamino)phenyl] squaraine dye as the standard ($\Phi_f = 0.7$ in $CHCl_3$), error limit ±5%.

Furthermore, we investigated the photophysical properties of the squaraine dye in the presence of the macrocycles **1** and **2**, and the results are summarized in Table 1. It was found that both the absorption and fluorescence emission† showed red shifts, which are similar to the cases of the squaraine-derived rotaxanes.[9] Compared with free guest **3**, the fluorescence quantum yields for the complexes were all decreased, but complex **2·3** showed a bigger quantum yield than that for complex **1·3**, which implied that **2** has a stronger complexation with **3** than that of **1**. Moreover, the association constants between the hosts and the guest in chloroform were determined by the change in absorption maxima[9c] to be $(6.8 \pm 0.3) \times 10^5\ M^{-1}$ for complex **1·3** and $(1.3 \pm 0.3) \times 10^6\ M^{-1}$ for complex **2·3**, respectively, which indicated that the macrocycles **1** and **2** were excellent hosts for the squaraine dye in weakly polar solvent.

The complexation processes between the hosts and the guest in polar solvent were also examined. The results showed that when guest **3** and the complexes **1·3** and **2·3** were separately dissolved in a 4 : 1 THF–water solution, they displayed a similar blue color. But after 4 days guest **3** underwent hydrolytic decomposition to turn colorless, whereas the solutions containing complexes **1·3** and **2·3** retained the blue color until three weeks and two weeks, respectively. These observations suggested that the macrocyclic hosts **1** and **2** could protect the squaraine dye from decomposition by polar solvents.

In summary, we have synthesized a pair of novel triptycene-based tetralactam macrocycles **1** and **2** with well-defined conformations, and also proved that they are highly efficient hosts for complexation with squaraine to form a new kind of stable pseudorotaxane-type complex in solution and in the solid state, which could subsequently show protection for the squaraine dye from polar solvents. Moreover, complexation-induced-asymmetry of the guest in complex **1·3** was also observed, owing to the cone conformation of host **1**. We believe that the results presented here can provide many opportunities for developing new supramolecular assemblies, such as constitutionally isomeric oriented rotaxanes[15] and supramolecular polymers, which are now in progress in our laboratory.

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12 Crystal data for **1**: $C_{58}H_{40}Cl_{12}N_6O_5$, $M_w = 1326.36$, crystal size $0.12 \times 0.10 \times 0.08\ mm^3$, orthorhombic, space group $P2_12_12_1$, $a = 12.9178(12)$, $b = 21.121(2)$, $c = 21.125(2)$ Å, $U = 5763.6(10)$ Å^3, $Z = 4$, $D_c = 1.529\ Mg\ m^{-3}$, $T = 113(2)$ K, $\mu = 0.632\ mm^{-1}$, 51 613 reflections measured, 12 695 unique ($R_{int} = 0.1249$), final R indices [$I > 2\sigma(I)$]: $R_1 = 0.0672$, w$R_2 = 0.1574$, R indices (all data): $R_1 = 0.0948$, w$R_2 = 0.1742$. Crystal data for **2**: $C_{54}H_{34}N_6O_4$, $M_w = 830.87$, crystal size $0.14 \times 0.12 \times 0.08\ mm^3$, monoclinic, space group $C2/c$, $a = 28.750(6)$, $b = 11.657(2)$, $c = 14.303(3)$ Å, $\beta = 99.60(3)°$, $U = 4726.5(16)$ Å^3, $Z = 4$, $D_c = 1.168\ Mg\ m^{-3}$, $T = 113(2)$ K, $\mu = 0.075\ mm^{-1}$, 16 512 reflections measured, 5437 unique ($R_{int} = 0.0596$), final R indices [$I > 2\sigma(I)$]: $R_1 = 0.0699$, w$R_2 = 0.1853$, R indices (all data): $R_1 = 0.0950$, w$R_2 = 0.2036$. Crystal data for **2·3**: $C_{80}H_{64}Cl_6N_8O_6$, $M_w = 1446.09$, crystal size $0.20 \times 0.08 \times 0.04\ mm^3$, triclinic, space group $P\bar{1}$, $a = 10.589(3)$, $b = 13.760(4)$, $c = 24.086(8)$ Å, $\alpha = 89.709(9)$, $\beta = 88.570(10)$, $\gamma = 78.582(8)°$, $U = 3438.9(19)$ Å^3, $Z = 2$, $D_c = 1.397\ Mg\ m^{-3}$, $T = 113(2)$ K, $\mu = 0.313\ mm^{-1}$, 35 589 reflections measured, 12 114 unique ($R_{int} = 0.0631$), final R indices [$I > 2\sigma(I)$]: $R_1 = 0.0768$, w$R_2 = 0.1994$, R indices (all data): $R_1 = 0.1160$, w$R_2 = 0.2346$. CCDC 697888 (**1**), 697889 (**2·3**), and 697890 (**2**)†.

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