Guest-dependent directional complexation based on triptycene derived oxacalixarene: formation of oriented rotaxanes†

Han-Xiao Wang,ac Zheng Meng,ac Jun-Feng Xiang,a Yu-Xiang Xia,a Yihua Sun,b Shu-Zhen Hu,a Hui Chen,b Jiannian Yaoa and Chuan-Feng Chen*a

The manipulation of supramolecular devices to carry out sophisticated and programmed tasks is bound up with the spatial allocation of their components, especially the threading direction of the guest, which controls the host–guest orientation in the device. However, insights are needed to probe more possibilities for steering the threading direction. We have developed a new system consisting of a three-dimensional nonsymmetric oxacalixarene (H) with a fixed conformation and (bipyridinium salts [G1–G3], in which we found that based on the intrinsic discrepancies between the two semi-cavities of H, the electron densities of the axles greatly affect the threading direction. This was unequivocally demonstrated by NMR spectra and single crystal structures. With elaborate design, unidirectional threading was achieved, resulting in an oriented rotaxane. Therefore, we describe a new approach in which the threading direction and final orientation may be finely controlled by adjustment of the structure of the guest.

Introduction

During the last two decades, great progress has been made in the synthesis of mechanically interlocked molecules (MIMs) such as rotaxanes and catenanes, with interest arising not only from their aesthetic appeal but also their perceived potential to act as sophisticated molecular machines, switches and sensors. The general approach to constructing (pseudo)-rotaxanes requires a macrocycle and a linear guest as the wheel and the axle, respectively; if neither of them is in the D_{nh} point group, two isomers will be obtained via the threading process, resulting in different orientations of components in the final MIMs. Owing to differences in the spatial arrangement, a pair of orientational isomers may generate quite different properties. However, the separation of isomers poses a big problem, so unidirectional threading that leads to an oriented rotaxane is highly appealing. Using cyclodextrin as the wheel, unidirectional threading has been realized due to either kinetic or thermodynamic stability, resulting in various oriented rotaxanes. Calixarenes with three-dimensional nonsymmetric structures have provided another candidate to form oriented rotaxanes, based on the formation of endo-cavity complexes with organic cations. Using triphenylureido-calix[6]arene as the host and dialkylviologen salt as the guest, Arduini and coworkers succeeded in synthesizing an oriented pseudorotaxane through a kinetically controlled process. On that basis, they prepared a pair of isomeric oriented rotaxanes for the first time by reversing the sequence in which two different stopper groups were introduced onto the axle. In contrast to the kinetically controlled unidirectional threading strategy, Neri and coworkers developed an “endo-alkyl” rule controlling the threading directionality of alkylbenzylammonium axles with calix[6]arenes. Applying the rule, they constructed stereoisomeric (pseudo)[3]rotaxanes and an oriented handcuff rotaxane. Although some important results have been obtained, the formation of oriented rotaxanes based on controllable threading directionality is still emerging as a challenge to be overcome.

Heterocalixarenes are a kind of calixarenes obtained by replacing conventional methylene bridges with heteroatoms. Introducing bridging heteroatoms makes it possible to finely tune the size, conformation and binding properties of the macrocycle, since heteroatoms can not only adopt different electronic configurations but also form various degrees of conjugation with the neighboring aromatic rings. Due to the difficulty of forming “through-the-annulus” complexes with linear guests, the utilization of heterocalixarenes as hosts to realize directional threading and construction of oriented...
rotaxanes is still a rather unexplored field. Previously, we reported that a triptycene-derived oxaclixarene \( H^{16a} \) (Fig. 1a), with an upper semi-cavity encircled by two naphthyrindine moieties and a lower semi-cavity encircled by two triptycene moieties, could incorporate various 4,4'-bipyridinium salts to form pseudo-rotaxanes.\(^{16a}\) We applied this property to the synthesis of rotaxanes based on \( H \) and symmetric 4,4'-bipyridinium salts. Theoretically, if we mixed \( H \) with a nonsymmetric axle, a pair of isomeric pseudorotaxanes might be obtained. The crystal structure of \( H^{16a} \) disclosed that the portal of the lower semi-cavity was more crowded than that of the upper one (Fig. 1a, 8.53 Å versus 13.57 Å). Moreover, triptycene is known to be more electron-rich than the naphthyrindine moiety (the N atoms excluded). Hence, we hypothesized that the discrepancies in size and electron density between the two semi-cavities of \( H \) might exert different induction effects upon the threading of guests. Herein, we report a system employing \( H \) as the wheel, in which we can control the dominant threading direction by partially changing the structures of the axles, thus tuning their interaction with \( H \) in the threading process.

### Results and discussion

#### Directional complexation between macrocycle \( H \) and bipyridinium salts \( G1 \) and \( G2 \) with alkyl chains of different lengths

We initially designed a linear nonsymmetric bipyridinium salt \( G1 \) (Fig. 1b), stoppering one of its ends with a bulky terminal group in order to easily clarify its threading direction into the macrocycle. By comparison of the \(^1H\) NMR spectra of \( H, G1 \), and a 1 : 1 mixture of the two in CDCl\(_3/\)CD\(_3\)CN solution at room temperature, complexation between the two components was observed (Fig. S31, ESI†). The \(^1H\) NMR spectrum of the complex always exhibited only one set of signals, regardless of whether the host or the guest was in excess (Fig. S34, ESI†), indicating a fast equilibrium on the NMR timescale. To acquire information on the relative orientation of the two components, we stoppered the pseudorotaxanes to synthesize the corresponding rotaxanes (Scheme 1).

As we demonstrated in our previous work that macrocycle \( H \) adopted a fixed 1,3-alternate conformation and would not undergo conformational inversion mainly due to the bulky triptycene moieties,\(^{16c}\) the orientation of the obtained rotaxanes could represent the original threading direction of the axe into the wheel on a statistical basis.\(^{16b}\) The stoppered products were isolated as a mixture of two orientational isomers, as revealed by both \(^1H\) NMR spectra and ESI-HRMS. The integrals in the \(^1H\) NMR spectrum (see Fig. S27†) showed that the relative ratio of the two sets of signals (and thus the amounts of the two isomers, \( R1a \) and \( R1b \)) was approximately 4 : 1. The ratio

---

### Scheme 1

Synthesis of isomeric [2]rotaxanes \( R1a/b \) and \( R2a/b \).

Conditions: (a) 3,5-di-tert-butylbenzoic anhydride, \((n\text{-}Bu)_3P\), CHCl\(_3/\)CH\(_3\)CN (2 : 1, v/v), r.t.

---

### Fig. 1

(a) Structure and representation of \( H \) and its crystal structure,\(^{16a}\) denoting sizes of the portals on both sides. (b) Structure and representation of guests \( G1-G2 \) and their directional threading into \( H \). (c) Structure and representation of guest \( G3 \) and its directional threading into \( H \).

---

### Fig. 2

(a) Side and (b) top view of the crystal structure of \( H@G1 \). (c) Side and (d) top view of the crystal structure of [2]rotaxane \( R1a \). Hydrogen atoms and PF\(_6^-\) counterions are omitted for clarity.
calculated from the NMR spectrum revealed that the threading was highly directionally selective, but we could not ascertain the relative orientation of the wheel and axle in the two isomers.

Fortunately, single crystals of both the pseudorotaxane cultivated from the CHCl$_3$/CH$_3$CN solution of the complex (Fig. 2a and b) and rotaxane R1a cultivated from its CHCl$_3$ solution (Fig. 2c and d) were obtained. Both crystal structures showed that the axle had threaded into the wheel from the triptycene rim (the lower rim, Fig. 1b).§ Weak correlations in the 2D ROESY spectrum of R1a (Fig. S22, ESI†) between H$_2$ and H$_c$, H$_2$ and H$_d$, and H$_8$ and H$_c$ were also detected, which indicated the same orientation of the host and guest in R1a as was deduced from the crystal structure.

In order to determine which part of the axle might have exerted a crucial impact on the threading direction, we first altered the length of the alkyl chain by replacing the hydroxypropyl group with a hydroxyhexyl group (G2, Fig. 1b). We synthesized the corresponding isomeric rotaxanes R2a and R2b (the ratio was also found to be about 4 : 1, Fig. S28, ESI†) (Scheme 1) and compared the $^1$H NMR spectrum of the major product R2a with that of R1a. After unambiguous assignment of all signals in the $^1$H NMR spectrum of R2a on the basis of 2D NMR experiments (Fig. S23 and S24, ESI†), it was found that all the corresponding hydrogens of the two rotaxanes had almost the same chemical shifts (Fig. S9 and S13, ESI†), indicating identical orientation of the wheel and axle in R1a and R2a. Thus it could be summarized that the length of the terminal alkyl chain had a negligible influence on the threading direction, at least when the chain was not very long.

### Table 1

<table>
<thead>
<tr>
<th>Entry</th>
<th>Temperature (K)</th>
<th>Ratio of R1a and R1b$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>298</td>
<td>4 : 1</td>
</tr>
<tr>
<td>2</td>
<td>313</td>
<td>1.7 : 1</td>
</tr>
<tr>
<td>3</td>
<td>333</td>
<td>1.2 : 1</td>
</tr>
</tbody>
</table>

$^a$ Determined by $^1$H NMR.

Unidirectional complexation between macrocycle H and pyridinium salt G3

In the dominant threading direction of G1, the process was electrostatically favorable but sterically unfavorable. Therefore, to disclose whether electrostatic effects might have played an important part in the directional selectivity, we replaced the terminal pyridyl ring in G1 with a more electron-rich phenyl ring substituted by an electron-donating alkoxy group (Fig. 1c). Pyridinium salt G3 was encapsulated by H as expected (Fig. S33, ESI†), and similarly, the complex was in fast exchange on the NMR timescale (Fig. S40, ESI†). As the relevant data of the pseudorotaxane provided barely any information about the threading direction, the host–guest complex was stoppered to give the corresponding rotaxane (Scheme 2). To our surprise, the product showed only one set of signals in the $^1$H NMR spectrum (Fig. S19, ESI†), which meant that only one (R3b) of the isomeric rotaxanes was actually formed and thus the threading had occurred unidirectionally. To clarify the

---

---

---

---
threading direction of G3, we cultivated a single crystal that was suitable for X-ray crystal analysis by slow evaporation of diethyl ether into an acetone solution of R3b (Fig. 3). The crystal structure showed that G3 had threaded into H from the naphthyridine rim (Fig. 1c), the direction of which was completely reversed compared with the dominant threading direction of G1 and G2. This agrees well with the 2D ROESY experiment (Fig. S26, ESI†) in which correlations were observed between H3 and H/Hδ, H2 and Hδ/Hδ, Hδ and Hδ, and Hδ and Hβ.

**Study on the directionally selective mechanism**

These results were exciting but not beyond expectation, and could be tentatively explained as follows. In the threading process of G1 (the bipyridinium salt), the electrostatic effect dominated the threading direction while the steric effect posed an opposite influence. As a result, a pair of orientationally isomeric rotaxanes in a ratio of 4 : 1 was obtained, and in the major product the pre-stopped end was in proximity to the lower rim of H. However, when axle G3 (the pyridinium salt) threaded into the macrocycle, the electrostatic effect and the steric effect acted in a cooperative way, generating a single compound in which the pre-stopped end was in proximity to the upper rim of H. Moreover, to manifest the high selectivity in the threading direction of G3 into H in an *in situ* manner, a variable-temperature 1H NMR experiment on the CDCl3/CD3CN solution of the pseudorotaxane based on G3 and H (G3 : H = 1.5 : 1) was conducted (Fig. S43–45, ESI†). From the spectra, we observed that when the temperature was brought down to approximately 233 K, the peaks of the free guest started to appear, indicating that the threading and dethreading had become a slow exchange process on the NMR timescale. Meanwhile, it was found that the pseudorotaxane still appeared as a single set of signals, which meant that at and below this temperature, the 1H NMR spectra clearly showed that the threading of G3 into H occurred unidirectionally.

DFT theoretical modeling was carried out in order to establish whether, for each axle, the orientational outcome is dictated by kinetic factors or by the different thermodynamic stability of the two isomers.† We calculated the relative Gibbs free energies of the two orientational isomers of pseudorotaxane H@G1 (PR1a and PR1b), and found that the free energy of PR1a (corresponding to the orientation of R1a) was lower than that of its isomer PR1b by only 0.9 kcal mol⁻¹. However, for the pseudorotaxanes based on G3 and H (PR3a and PR3b), the calculations indicated that the relative Gibbs free energy of PR3b (corresponding to the orientation of rotaxane R3b) was lower than that of PR3a by a sizable 3.6 kcal mol⁻¹. Thus, the DFT calculations verified the relative stabilities of the two pairs of isomers: both dominant isomers (PR1a and PR3b) were the relatively more stable ones, though PR1a only had a small advantage over PR1b energetically.

The ESPs of H in the absence of guest molecules were also calculated, as depicted in Fig. 4a and b. Two features were notable; one was the electron-rich character of the phenyl rings of the triptycene semi-cavity, and the other was the polarity of the naphthyridine moieties, characterized by the electron-rich N atoms and the electron-poor remaining part. The difference in the electron densities of guests G1 and G3 was visualized by comparing their ESPs (Fig. 4c and d). G3 had a clearly higher electron density than G1, especially with respect to the unstoppered end (the phenyl ring). Therefore, the structures revealed the electrostatic repulsion of the electron-poor pyridinyl ring (the one further from the pre-stopper) in G1 and the attraction of the electron-rich phenyl ring in G3 exerted by the upper semi-cavity, and also the repulsion of the phenyl ring in G3 by the lower semi-cavity, in the threading processes of the two guests.

From the above calculations, we concluded that the two isomers of H@G1 had similar stability, but in forming PR1b from the less crowded upper rim, the barrier posed by the electrostatic effect might be higher than that in forming PR1a, while the subordinate factor, the steric effect, acted oppositely; as a result, two isomers in a ratio of 4 : 1 were obtained. However, with regard to H@G3, on the one hand PR3b was more stable than its isomer by 3.6 kcal mol⁻¹, and on the other hand, threading from the upper rim was favorable in terms of both electrostatic and steric effects; thus, unidirectional threading was attained.

As we hypothesized that the directional selectivity in the H@G1 system resulted mainly from the difference in energy barriers in the threading processes in each direction, increasing the temperature ought to narrow the gap between them. To verify this consideration, rotaxanes based on G1 and H were synthesized at raised temperatures (313 K and 333 K), and the ratios of the isomers were determined *via* 1H NMR analysis (Fig. S29–30, ESI†). In agreement with our prediction, the directional selectivity in the threading process of G1 decreased with the increase in temperature (Table 1). However, in the same experiments on G3 and H, the orientational isomer of R3b could not even be traced. The results further demonstrated that at ambient temperature the threading of G1 was kinetically controlled.

**Conclusions**

In this work, we successfully demonstrated that the threading direction of (bipyridinium salts (G1–G3)) into a triptycene-derived oxacalixarene (H) could be effectively controlled by tuning the electron densities of the guests, and the single crystal structures of (pseudo)rotaxanes exclusively manifested the orientation of the host and the guests. As the directional selectivity could be varied by tuning the roles played by steric and electrostatic effects, this work potentially provides a new approach towards the construction of oriented and well-aligned hierarchical assemblies. This is the first report on selective or unidirectional threading based on oxacalixarenes, and high directional selectivity was attained without either the use of special counteranions⁵,¹¹ for the guest or further functionalization of the calixarene.⁵ The design of new guests and modification of the macrocycle by replacing the naphthyridine moieties with other electron-deficient moieties to obtain more precise control of directional selectivity from both sides, and the construction of high-order mechanically interlocked...
structures capable of performing unidirectional motion, are currently under investigation in our laboratory.

Experimental

General remarks

The synthesis of precursors of the rotaxanes is described in the ESI.† All the other reagents and solvents were bought from commercial suppliers and used as received.

Synthesis of R1a and R1b

A mixture of H (62 mg, 0.075 mmol) and G1 (53 mg, 0.075 mmol) in chloroform (10 mL) and acetonitrile (5 mL) was stirred at ambient temperature for 12 h. 3,5-Di-tert-butylbenzoic anhydride (135 mg, 0.3 mmol) and (n-Bu)3P (3 mg, 0.015 mmol) were then added to the mixture. The reaction mixture was stirred under argon for 24 h at ambient temperature. The solvent was removed under vacuum, and the residue was purified by column chromatography (CH2Cl2/acetonite, 100 : 1 v/v) to give R1a and R1b as a mixture (73 mg) in 56% total yield. The macrocycle in the unreacted pseudorotaxanes could be recycled nearly quantitatively. The mixture was further separated carefully by preparative thin-layer chromatography to give pure R1a and R1b, both as yellow powders, for characterization.

**R1a.** Mp: 229–232 °C. 1H NMR (300 MHz, CDCl3): δ 9.03 (d, J = 6.3 Hz, 2H), 8.45 (d, J = 6.4 Hz, 2H), 8.33 (d, J = 6.3 Hz, 2H), 8.00 (d, J = 8.6 Hz, 4H), 7.97 (s, 2H), 7.71 (s, 1H), 7.57 (s, 2H), 7.51 (m, 3H), 7.20 (d, J = 6.7 Hz, 2H), 7.13 (d, J = 6.7 Hz, 2H), 7.04–7.05 (m, 4H), 6.92 (d, J = 8.6 Hz, 4H), 6.72–6.83 (m, 8H), 6.40 (d, J = 7.9 Hz, 4H), 5.79 (s, 2H), 5.24 (s, 4H), 4.25 (t, J = 6.8 Hz, 2H), 3.94 (t, J = 5.8 Hz, 2H), 1.93–2.02 (m, 2H), 1.36 (s, 18H), 1.29 (s, 18H).13C NMR (75 MHz, CDCl3): δ 166.8, 164.1, 153.6, 153.3, 151.3, 151.2, 150.7, 149.1, 147.8, 146.7, 145.3, 145.1, 144.8, 144.3, 141.4, 140.3, 131.2, 128.5, 127.9, 127.4, 126.1, 125.3, 124.9, 124.4, 124.2, 123.7, 123.5, 117.2, 116.4, 116.0, 112.6, 60.4, 58.0, 57.0, 53.2, 53.1, 53.4, 34.9, 31.7, 31.3, 29.7. ESI-HRMS caled for C99H90N6O6 [M – PF6]3+ 729.8472; found 729.8485.

**R1b.** Mp: 223–225 °C. 1H NMR (300 MHz, CDCl3): δ 8.58 (d, J = 6.3 Hz, 2H), 8.20–8.22 (m, 6H), 8.06 (s, 2H), 7.82 (d, J = 6.3 Hz, 2H), 7.76 (s, 1H), 7.67 (d, J = 6.3 Hz, 2H), 7.55 (s, 1H), 7.21–7.30 (m, 4H), 7.14–7.16 (m, 4H), 7.12 (s, 2H), 7.02–7.05 (m, 8H), 6.88–6.91 (m, 4H), 6.67 (d, J = 7.9 Hz, 4H), 5.53 (s, 2H), 5.37 (s, 2H), 5.32 (s, 2H), 4.28 (t, J = 6.2 Hz, 2H), 4.03 (t, J = 6.3 Hz, 2H), 1.99–2.02 (m, 2H), 1.38 (s, 18H), 1.29 (s, 18H).13C NMR (125 MHz, CDCl3): δ 167.4, 164.0, 153.1, 151.7, 151.2, 148.7, 148.3, 147.2, 145.0, 144.8, 144.6, 144.3, 141.6, 141.2, 130.1, 129.7, 129.5, 129.0, 128.1, 125.4, 125.3, 125.0, 124.5, 124.1, 124.0, 123.7, 123.4, 117.8, 116.6, 115.9, 113.4, 60.6, 58.6, 54.8, 52.9, 52.2, 35.1, 35.0, 31.4, 31.3, 29.7. ESI-HRMS caled for C99H90N6O6 [M – 2PF6]3+ 729.8472; found 729.8454.

Acknowledgements

The authors thank the National Natural Science Foundation of China (21332008, 21202172, and 21290194), the National Basic Research Program (2011CB932501), and the Strategic Priority

This is an Open Access article distributed under the Creative Commons Attribution 3.0 License.
In this paper, isomers of pseudorotaxanes and rotaxanes are denoted such that a indicates that the corresponding guest is threaded from the triptycene rim, while b indicates that the corresponding guest is threaded from the naphthylamine rim. The absence of the pseudorotaxane in which the macrocycle and axle are oriented the other way (PR1b) in the crystal might be caused by the difference in the amounts of the two isomeric pseudorotaxanes and the selective crystallization of the dominant one.

Notes and references


8 For selected examples in biological systems and materials science in which a difference in spatial arrangement caused a change in properties, see: (a) E. Tajkhoshid, P. Nollert, M. O. Jensen, L. J. W. Miercke, J. O’Connell, R. M. Stroud and K. Schulten, Science, 2002, 296, 525–530; (b) Y. Sagara and T. Kato, Nat. Chem., 2009, 1, 605–610.


