Unidirectional Threading of Triphenylureidocalix[6]arene-Based Wheels: Oriented Pseudorotaxane Synthesis

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Abstract: Triphenylureidocalix[6]arenes **5a**,**b** are heteroditopic receptors having a pinched cone structure able to interact with both the cation and the anion of ion pairs. They are able to act as wheels and form complexes of the pseudorotaxane type with axles derived from dialkylviologen salts. An investigation into the possibility of exploiting the different structural and chemical information present on the two distinct rims of the calixarene wheel as control elements to pivot the direction of the axle threading processes and give access to oriented pseudorotaxanes is reported. It was verified that, in C_6D_6, an asymmetric dicationic axle derived from 4,4′-bipyridil bearing two alkyl chains, one of which has a stopper, and triphenylureidocalix[6]arenes **5a** or **5b** form 1:1 supramolecular complexes belonging to the class of pseudorotaxanes. The structure of these complexes has been inferred through ^{1}H NMR techniques. The data show that the axle accesses the calixarene cavity only through the wider rim. To further verify this issue, the new rotaxane **8**, obtained by stoppering the pseudorotaxane derived from **5b** and the symmetrical axle **7** with diphenylacetyl chloride, was synthesised. In the ^{1}H NMR spectrum of **8**, the aliphatic protons of the axle portion that resides at the wide rim of the wheel show chemical shifts that are almost identical to those observed in pseudorotaxanes **6**. On the other hand, those that stick out of the narrow rim of **8** experience chemical shifts that could not be found in the oriented pseudorotaxanes **6**.

Keywords: calixarenes · host–guest systems · oriented pseudorotaxanes · rotaxanes · unidirectional threading

Introduction

Pseudorotaxanes and rotaxanes[1] are very interesting and promising tools for the construction of working devices and molecular machines.[2] In simple instances a pseudorotaxane can derive from the assembly of two distinct components: a sufficiently large macrocycle, which acts as a wheel, and an acyclic component, which, by threading the wheel, acts as an axle. The insertion of two bulky stoppers at the ends of the axle inserted into the wheel yields a rotaxane. By exploiting the principles of supramolecular chemistry, and in particular of "organic template synthesis",[3] several classes of wheels and axles that have complementary sizes have been employed so far for the construction of such complex systems.[4] Particularly attractive, and consequently widely studied as wheels, are the cyclodextrins, characterised by a shallow truncated cone structure.[5]

In this context, although no systematic studies have been reported so far, an aspect that is gaining increasing attention is the threading processes of these wheels with asymmetrical axles. Almost a decade ago, Kaifer and Isnin[6] succeeded in the synthesis of two isomeric [2]rotaxanes that differ by the orientation of the α-cyclodextrin wheel with respect to the two different stoppers, while Matsuo and co-workers have shown that cyclodextrines can form "stable" oriented pseudorotaxanes with appropriate asymmetrical axles.[7] More recently, the problem of the direction of guest insertion and orientation was studied by using axles in which the included portion of the asymmetric axle pivots the direction of its insertion into the toroidal wheels.[8] In contrast, the preparation of polyrotaxanes composed of cyclodextrins and various polymers that do not control the access to the cavity, afford a head-to-tail orientation of these wheels along the polymer chain.[9,10]

Calix[*n*]arenes are phenolic macrocycles widely used in host–guest chemistry as versatile platforms for the synthesis of versatile and efficient receptors.[11] They are frequently compared to cyclodextrins because of their truncated cone structure and their ability to form *endo*-cavity inclusion complexes with suitable guests. In solution, however, the

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Supporting information for this article is available on the WWW under http://www.chemeuj.org or from the author: full spectral characterisation of new compounds **3b** and **8**, 2D NMR spectra of pseudorotaxane **6b**.

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cavities of these two types of hosts possess complementary binding properties. In fact, while cyclodextrins experience high affinity towards neutral organic species, typically in aqueous media, calixarenes better host quaternary ammonium cations in apolar media.[12]

The binding properties of the latter macrocycles have recently been applied by us to the synthesis of the first example of a rotaxane having a calix[6]arene derivative as a wheel.[13] We have also shown that, in apolar media, the triphenylureidocalix[6]arene derivative **5a** can be threaded by dioctylviologen diiodide and yields a pseudorotaxane (**I**). In the solid state, pseudorotaxane **I** (see Figure 1) is stabilised by

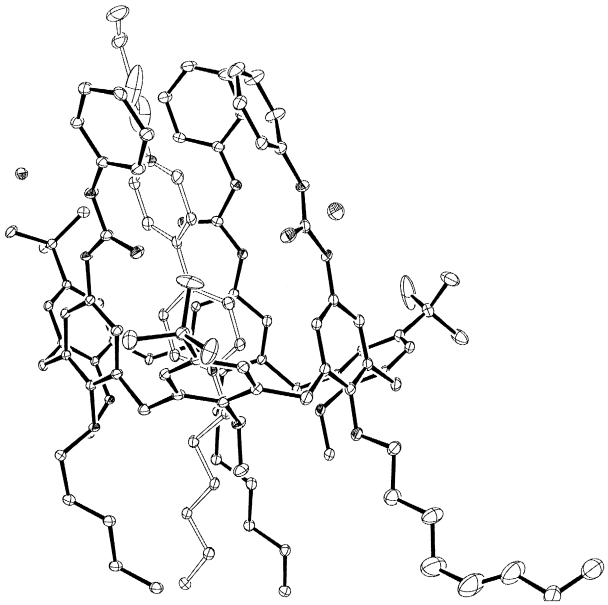


Figure 1. X-ray crystal structure of pseudorotaxane **I** derived from **5a** and dioctylviologen diiodide.[13]

a combination of several supramolecular interactions that involve all parts of the wheel. In fact, the phenyl groups of the phenylurea moieties—the aromatic walls of the calixarene and the oxygen atoms present at the narrow rim—are involved in stabilising this supramolecular complex. In addition, the two counteranions are hydrogen bonded to the six ureido NH groups present at the wide rim of the wheel.

The observation that the cationic portion of the axle is located at the π-donor calix[6]arene walls reflects the host–guest properties of calixarenes and is opposite and complementary to that for cyclodextrins, in which the same cationic portion along analogous axles can be employed as stopper.[14]

We envisaged that because of the large number of possibilities for inserting functional groups and binding sites onto both rims of the calixarene skeleton,[11,15] the synthesis of rotaxanes or pseudorotaxanes having a calixarene as wheel could contribute to the development of new molecular devices that have properties governed by a wider range of control elements.

In this paper we wish to describe a synthetic and structural study to verify whether the different chemical and structural information attached to the two distinct rims of triphenylureidocalix[6]arene derivatives **5** could be exploited as control

Figure 2. Schematic representation of the two possible pseudorotaxane isomers derived from a calix[6]arene wheel and an asymmetrical axle carrying only one stopper.

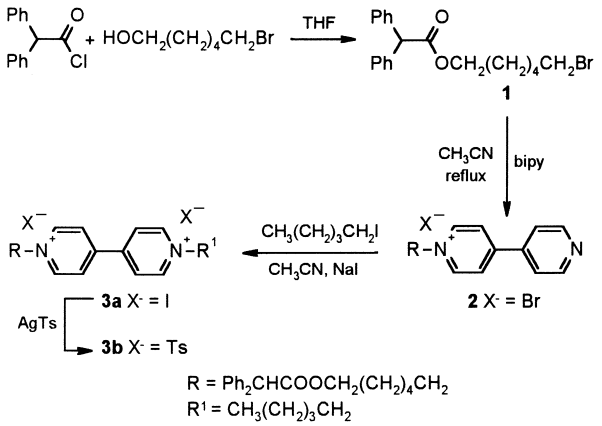
elements to guide the threading process of dicationic axles derived from 4,4′-bipyridyl (Figure 2).

The starting considerations for the present study arise from the observation that the calix[6]arene skeleton, because of its ring size, possesses an annulus that is large enough to allow a guest having the size of the bipyridyl to cross the two rims. Therefore in the absence of control elements the threading process could take place both from the wider or narrower rim of the macrocycle. In the triphenylureido calix[6]arene **5**, however, the wide rim is rather hydrophilic, because of the three ureido moieties, while the narrow rim, which bears alkyl groups, is hydrophobic. This difference could be exploited as a control element to guide axle-insertion processes.

To address this issue, we synthesised an asymmetric axle derived from 4,4′-bipyridyl functionalised with two alkyl chains, one of which bears a stopper, and studied the structure of the complexes formed with triphenylureidocalix[6]arene derivatives.

Results and Discussion

Axles **3a**,**b** were obtained through the stepwise synthesis reported in Scheme 1 by treating diphenylacetyl chloride with ω-bromohexanol to give **1**, which was treated with 4,4′-bipyridine in refluxing CH_3CN to give **2**. Alkylation of the



Scheme 1.

second nitrogen atom of **2** with iodopentane in CH_3CN afforded **3a** as a red solid in 33% overall yield. Then, an anion-exchange reaction with silver tosylate gave axle **3b** in 85% yield as pale yellow solid.

Axles **3a**,**b** are not sufficiently soluble in chloroform or benzene for an accurate NMR analysis.[16] The main common

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features of their ^{1}H NMR spectra taken in CD_3CN are that protons 6, 9 and 7, 8 of the bipyridyl system resonate as doublets at about $\delta = 9.0$ and 8.5 ppm, respectively, while protons 5 and 10 resonate at $\delta = 4.65$ and 4.60 ppm, respectively (see Scheme 2 for numbering). Unambiguous assignment of all other signals was achieved through ^{1}H–^{1}H TOCSY spectra (see Supporting Information).

Initially the ability of **3a** to act as axle was evaluated by using the ready available wheel **5a**,[17] through ^{1}H NMR analysis of the solution obtained by equilibrating a solution of **5a** in C_6D_6 with a slight excess of solid **3a**. The NMR spectrum of the deep red solution obtained after filtration of the undissolved axle appears as a single set of signals consistent with a 1:1 host–guest complex that is in slow exchange on the NMR timescale.[18]

In the ^{1}H NMR spectrum of the complex **6a**, the protons of the methoxy groups (e), which are expelled from the calixarene cavity as consequence of threading,[19] are downfield shifted of about 1 ppm. The six NH protons i and l suffer a downfield shift of about 2 ppm because of their involvement in hydrogen bonding with the two halide counteranions. The eight protons of the bipyridyl group 6, 7, and 8 and 9 are substantially upfield shifted by about 2.3, 2.0, 1.5 and 0.7 ppm, respectively, because of their proximity to the calixarene cavity and the phenyl rings of the phenylureido groups. However the extensive peaks overlapping in the spectral region between 2 and 0.5 ppm, where most of the signals of the calixarene octyl chains resonate, precluded the unequivocal assignment of several protons of the axle. Therefore the new calix[6]arene **5b**, in which the basic skeleton of the wheel remains almost intact and bears the 2-ethoxyethyl groups in the place of the octyl chains of **5a**, was synthesised by treating **4b**[17] with phenylisocyanate to give 80% yield (Scheme 2).

Contrary to that of **5a**, the ^{1}H NMR of **5b** is rather broad, also at different temperatures, and shows the same features in all deuterated solvents used, probably because of its conformational flexibility. In C_6D_6 at 300 K, for example, the protons of the three methoxy groups resonate as a very broad signal at about $\delta = 2.9$ ppm, while those of the pseudo-axial and pseudo-equatorial bridging methylene resonate as broad signals at $\delta = 4.5$ and 3.5 ppm, respectively (see Figure 3c).

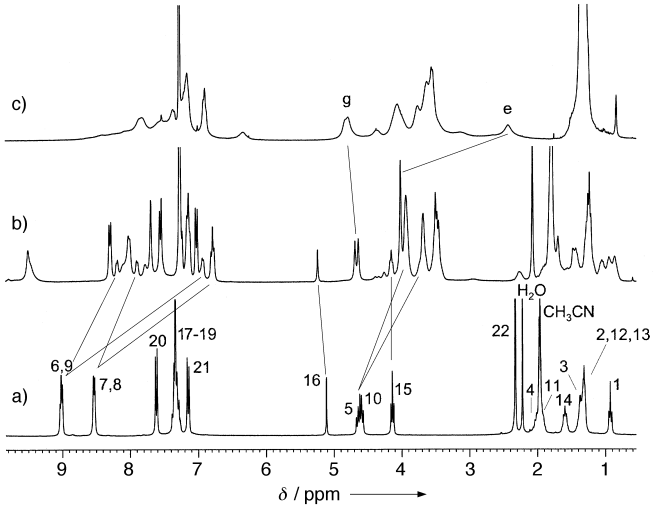
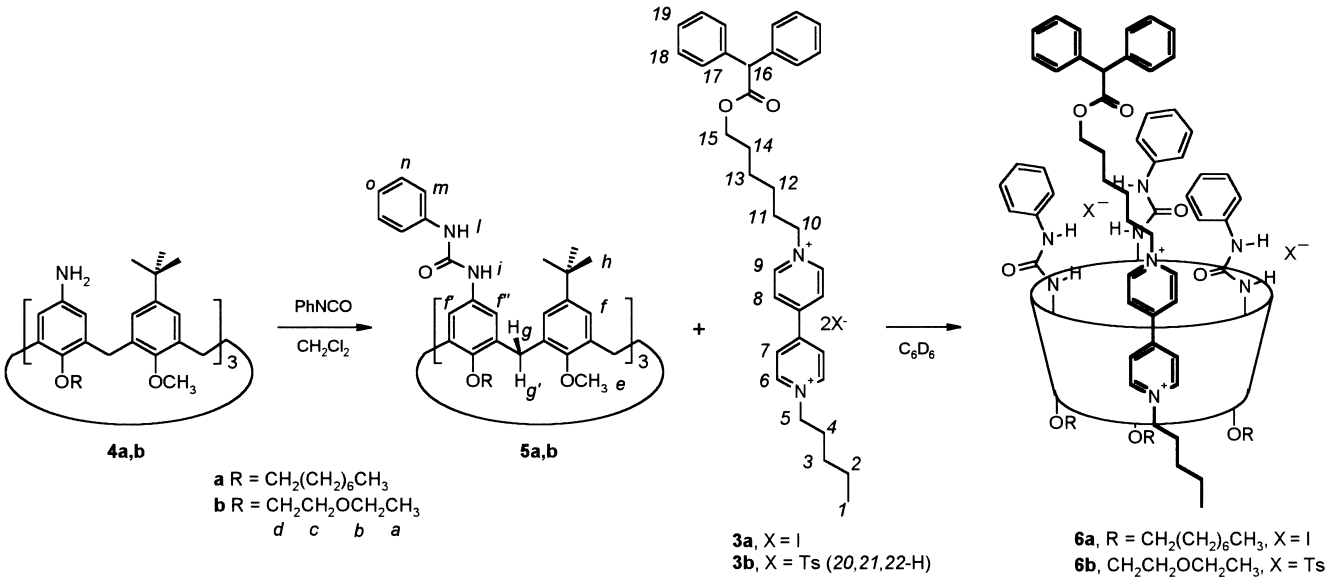


Figure 3. ^{1}H NMR spectra (300 MHz, 300 K) of a) **3b** in CD_3CN;[16] b) pseudorotaxane **6b** in C_6D_6; c) triphenylureidocalix[6]arene **5b** in C_6D_6.

To study the possible effects of the two halides of **3a** on the pseudorotaxane structure, the ditosylate **3b** was submitted to complex formation with calix[6]arene **5b**. In the ^{1}H NMR spectrum of the deep red solution obtained by adding an equimolecular amount of solid **3b** to a 0.01 M solution of **5b** in C_6D_6, the signals of calixarene **5b** have a sharper peak pattern consistent with a *cone* structure (Figure 3b).

The chemical shift variation (see Figure 4) experienced by the protons of the axle observed in the spectrum of this complex parallels those observed in the complex **6a** (derived from **5a** and **3a**), and the counteranions seem to have only a negligible effect on the complex structure.



Scheme 2.

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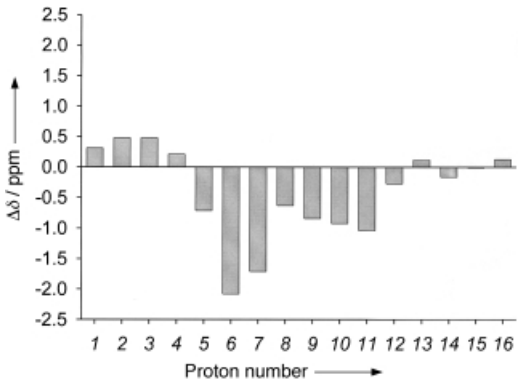

Figure 4. Protons downfield (+) and upfield (−) shifts (Δδ, ppm) of selected signals of pseudorotaxane **6b** (for proton assignment and numbering see Scheme 2).

All signals of the NMR spectrum of **6b** were identified and assigned by ^{1}H–^{1}H DQF-COSY spectra (see Supporting Information). Particularly informative is the observation that the chemical shift of protons 1, 2, and 3, belonging to the pentyl chain of the axle, are downfield shifted upon complex formation by 0.3, 0.4 and 0.5 ppm, while protons 4 and 5 experience an upfield shift of 0.21 and 0.71 ppm, respectively. On the other hand, protons 10 are upfield shifted by about 0.9 ppm, and these upfield shifts propagate, with the exception of protons 13, through the hexyl chain to protons 14; here this shift had decreased to 0.16 ppm. Protons 15 and 16 remain almost unaffected by complex formation. These data suggest that the portion of the axle between protons 5 and 14 is subjected to the anisotropy shielding effect of the aromatic domains of the calixarene host, while all the others are downfield shifted.

Unequivocal information on the relative orientation of the two components of **6b** was deduced from ROESY experiments that, together with the expected intramolecular cross peaks of both pseudorotaxane components, showed axle–wheel intermolecular cross peaks between protons 8 and 9 with h, 10 and 11 with m and 11 and 12 with n (see Figure 5). In addition, protons 2, 3 and 4 of the pentyl chain show cross peaks with protons d and e of the wheel. These ROESY data, together with the chemical-shift variation experienced by the protons of both pseudorotaxane components, are consistent with the hypothesis of a structure in which the axle points its pentyl chain towards the groups present at the narrow rim of the calix[6]arene, while the stopper is located in the region of the phenylureido moieties.

However, the lack of the parent isomeric pseudorotaxane derived from the access of the axle to the narrow of rim of the wheel and having the stopper in proximity to the calix[6]arene alkyl chains, prompted us to synthesise rotaxane **8** (see Scheme 3) to establish whether the protons of its identical stoppered arms, because of their different orientation inside the wheel, resonate as distinguishable set of signals in the ^{1}H NMR spectrum.

In fact in this rotaxane, because of its orientation towards the phenylureido groups of the calixarene, the portion of the axle between protons 6 and 1 should manifest chemical-shift variations comparable with those observed in **6b**. On the other hand, the protons of the axle portion between protons 6′ and 1′, because of their proximity to the narrow rim of the wheel, could represent a model for the pseudorotaxane derived from the insertion of axle **3b** from the narrow rim of the calixarene wheel.

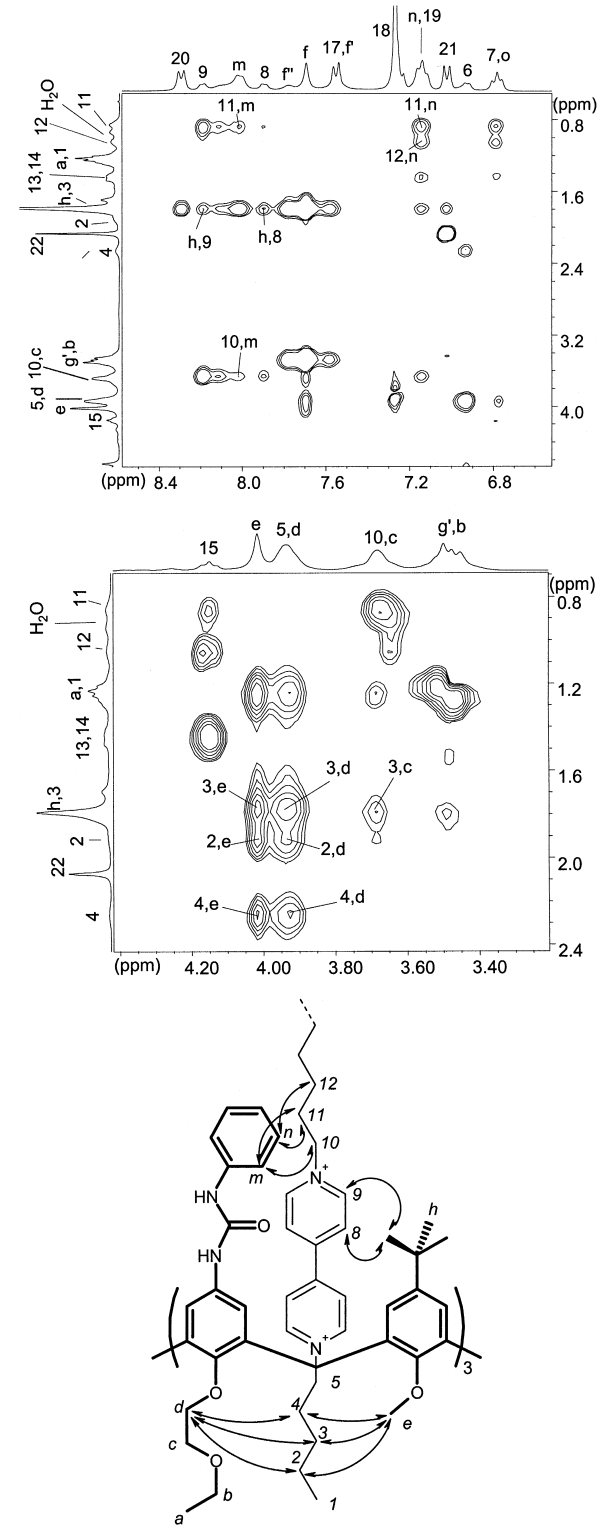

Figure 5. Selected expanded portions of ^{1}H 2D-ROESY NMR (300 MHz, spin-lock 200 ms) spectrum of pseudorotaxane **6b** in C_6D_6, showing the more representative axle–wheel intermolecular cross-peaks (for full 2D spectrum attribution see Supporting Information).

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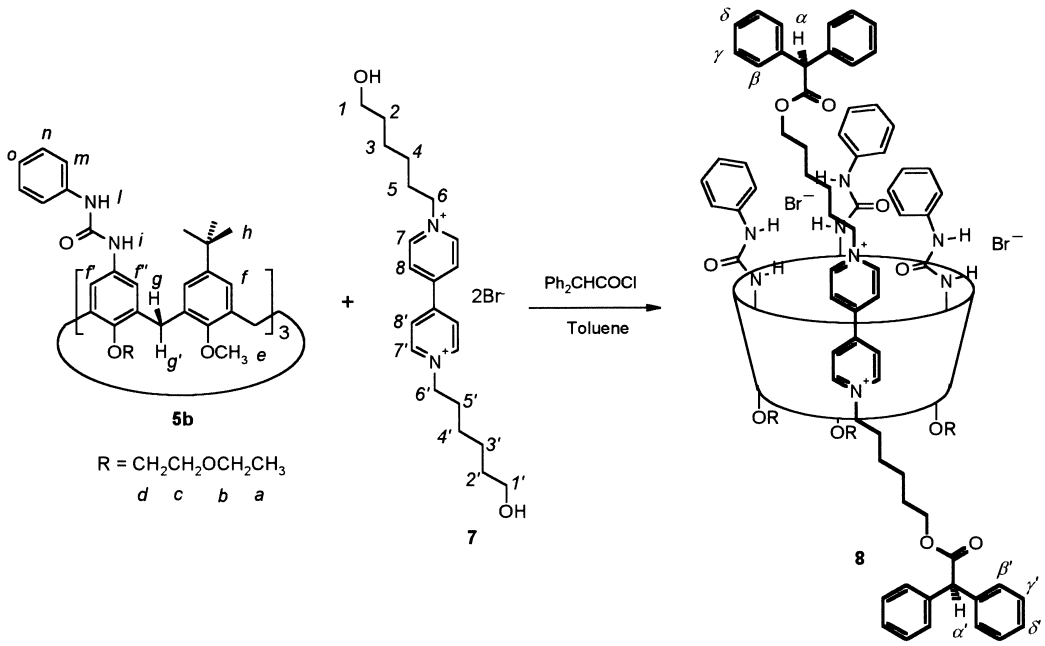

Scheme 3.

Rotaxane **8** was synthesised in 20% yield by adding a slight excess of diphenylacetyl chloride to the homogeneous solution obtained by heating equimolecular amounts of wheel **5b** and the diol **7** in dry toluene under reflux for 24 hrs. Although the complete assignment of all signals of the axle was not possible because of extensive overlapping and broadening of some signals in the region 0.5–2 ppm, the ^{1}H NMR spectrum of **8** in C_6D_6 (see Figure 6) shows that protons α and 1, which resonate at $\delta = 5.23$ and 4.17 ppm, experience chemical shifts that are almost identical to those of protons 16 ($\delta = 5.24$) and 15 ($\delta = 4.15$) of pseudorotaxane **6b** (see Scheme 3 for numbering).

In addition, from the ^{1}H–^{1}H COSY spectrum it emerges that protons 2, 5 and 6, which resonate at about $\delta = 1.5$, 0.8 and 3.5 ppm, respectively, experience chemical shifts that are very similar to those of protons 14 ($\delta = 1.44$), 11 ($\delta = 0.87$) and 10 ($\delta = 3.68$) of **6b**. On the other hand, protons α′ and 1′ resonate at $\delta = 5.28$ and 4.44 ppm because of their proximity to the narrow rim of the wheel and could not be detected in the spectra of **6b**. These data further support the hypothesis that the formation of complexes derived from the access of the axle to the narrow rim of the calix[6]arene wheel does not takes place.

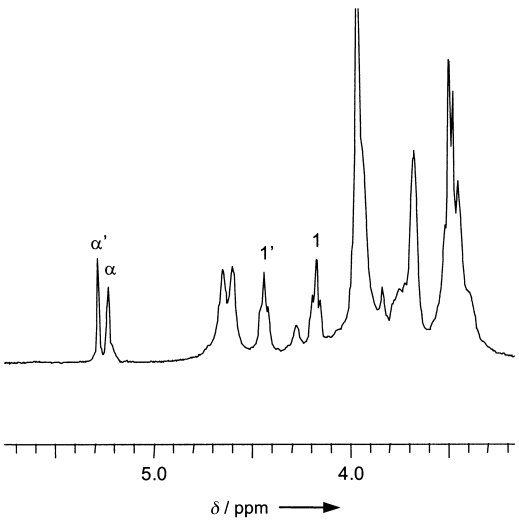

Figure 6. Partial ^{1}H NMR spectra (300 MHz, 300 K) of rotaxane **8** in C_6D_6.

A tentative explanation of this findings could derive from a combination of the following factors: a) in C_6D_6, the three methoxy groups present at the narrow rim of the calix[6]arene are oriented inwards towards the cavity, occupying it and thus disfavouring, by repulsive intermolecular interactions, the access of the axle to the narrow rim. b) The size and binding ability of the wheel inner volume are suitable only for the inclusion of the cationic portion of the axle. c) In the apolar C_6D_6, axles **3a**,**b** are present as tight ion pairs. It is therefore reasonable to assume that a process that implies, at least, the partial separation of the dication from its counteranions should take place before cation insertion into the wheel.[20] d) The hydrophilic ureido groups present at the wider rim of the calix are potent hydrogen-bond-donor groups and participate in the overall complexation process by ligating the two anions of the axle. In this way, the formation of a ligand-separated ion pair is favoured.

On these bases, it could be that hydrogen bonding interactions between the two anions and the phenylureido NH groups pivot the direction of the cationic axle insertion from the wider rim of the calixarene wheel.

Conclusion

In summary a new strategy to control the direction of the threading of heteroditopic calix[6]arene based wheel has been disclosed. The exploitation of this property for the synthesis of new molecular machines is under investigation in our laboratory and will be published in due course.

Experimental Section

All reactions were carried out under nitrogen; all solvents were freshly distilled under nitrogen and stored over molecular sieves for at least 3 h prior to use. All other reagents were of reagent-grade quality as obtained from commercial suppliers and were used without further purification. Column chromatography was performed on silica gel 63–200 mesh. NMR spectra were recorded in $CDCl_3$ unless otherwise indicated. Mass spectra were determined in the CI (CH_4) or ESI mode as appropriate.[21] Melting points are uncorrected. Elemental analyses[22] were carried out at the laboratory of microanalysis of the Instituto di Chimica Farmaceutica e Tossicologica of the University of Parma. Compounds **5a** and **4b** were synthesised according to literature procedures.[17] Attribution and numbering of the NMR signals for new compounds **1**, **3a**,**b** and **5b** follows that reported throughout the manuscript (see Schemes 2 and 3 and Supporting Information).

Synthesis of 6-bromohexyl diphenylacetate (1): 6-Bromohexan-1-ol (0.66 g, 3.6 mmol) and diphenylacetyl chloride (1.0 g, 4.3 mmol) were dissolved in dry THF (100 mL), and the solution was stirred overnight at room temperature. The solvent was evaporated under reduce pressure, and the oily residue was purified by column chromatography (hexane/ethyl acetate 9:1) to give 0.99 g (73%) of **1** as a colourless liquid. ^{1}H NMR (400 MHz, 298 K) $\delta = 7.27-7.36$ (m, 10H; 17,18,19-H), 5.05 (s, 1H; 16-H), 4.17 (t, $J =$ 6.6 Hz, 2H; 15-H), 3.36 (t, $J = 6.6$ Hz, 2H; 10-H), 1.81 (m, 2H; 11-H), 1.65 (m, 2H; 14-H), 1.40 (m, 2H; 12-H), 1.31 (m, 2H; 13-H); ^{13}C NMR (75 MHz, 298 K) $\delta = 172.4$, 138.7, 128.6, 128.5, 127.2, 64.9, 57.2, 33.5, 32.5, 28.3, 27.6, 24.9; MS, CI(+) m/z: 376 [M^+].

Synthesis of 1-[6-(Diphenylacetoxyhexyl)]-4-pyridin-4-yl-pyridinum bromide (2): Bromoester **1** (0.96 g 2.5 mmol) and 4,4′-bipyridyl (0.8 g, 5.1 mmol) were dissolved in dry CH_3CN (100 mL), and the solution was heated under reflux for 24 h to give an heterogeneous mixture. The white solid was filtered off, and the solvent was completely evaporated under reduced pressure to give a yellow solid, which was crystallised from CH_2Cl_2/hexane and gave 0.67 g (49%) of **2**. M.p. 108–110 °C; ^{1}H NMR (300 MHz, CD_3CN, 298 K) $\delta = 9.15$ (d, $J =$ 5.2Hz, 2H; 9-H), 8.81 (d, $J = 4.1$ Hz, 2H; 6-H), 8.39 (d, $J = 5.2$ Hz, 2H; 8-H), 7.82 (d, $J = 4.1$ Hz, 2H; 7-H), 7.2–7.4 (m, 10H; 17,18,19-H), 5.10 (s, 1H; 16-H), 4.71 (t, $J = 7.5$ Hz, 2H; 10-H), 4.09 (t, $J = 6.4$ Hz, 2H; 15-H), 1.93 (m, 2H; 11-H), 1.57–1.52 (m, 2H; 14-H), 1.33–1.25 (m, 4H; 12,13-H); ^{13}C NMR (75 MHz, [D$_6$]DMSO) $\delta = 173.2$, 153.1, 151.8, 146.2, 141.7, 139.8, 129.3, 129.2, 127.9, 126.2, 122.8, 65.3, 61.1, 56.7, 31.4, 28.5, 25.7, 25.5; MS (ESI, CH_3OH) m/z: 451.0 [M^+].

Synthesis of 3a: Compound **2** (0.26 g, 0.5 mmol) and an excess of iodopentane (0.26 mL, 2.0 mmol) were heated under reflux in dry CH_3CN (50 mL) for 10 days to give a deep purple homogeneous solution, which was evaporate to dryness. The residue was dissolved in the minimum quantity of CH_3OH (ca. 2 mL), then NaI (0.75 g, 5.0 mmol) was added. The resulting heterogeneous solution was stirred. After 1 h, the solid suspension was filtered off, and ethyl acetate was added until complete precipitation of **3a**, which was collected by filtration and washed with ethyl acetate. The purity of **3a** was checked by TLC (CH_3OH/33% NH_4OH 99:1). After drying, 0.34 g (94%) of pure **3a** were obtained. M.p. 225–227 °C; ^{1}H NMR (400 MHz, CD_3CN, 298 K): $\delta = 9.05$ and 9.03 (2d, $J = 6.1$ Hz, 4H; 6,9-H), 8.50 (d, 4H; 7,8-H), 7.3–7.2 (m, 10H; 17,18,19-H), 5.09 (s, 1H; 16-H), 4.67 (t, $J = 7.5$ Hz, 2H; 5-H), 4.62 (t, $J = 7.5$ Hz, 2H; 10-H), 4.13 (t, $J = 6.6$ Hz, 2H; 15-H), 2.04 (brt, 2H; 4-H), 1.97 (brt, 2H; 11-H), 1.60 (brt, 2H; 14-H), 1.4–1.3 (m, 8H; 3,2,12,13-H), 0.93 (t, $J = 7.2$ Hz, 3H; 1-H); ^{13}C NMR (75 MHz, CD_3CN), $\delta = 171.7$, 150.6, 146.2, 139.9, 129.2, 127.9, 127.8, 65.3, 62.9, 57.3, 31.4, 31.3, 28.5, 28.2, 25.6, 25.4, 22.3, 22.3; UV/Vis (CH_3CN): λ_{max}(Ge) = 447 nm (990.5 mol^{-1} dm^{-3} cm^{-1}); MS (ESI, CH_3OH) m/z: 521.1 [$M^{2+} - H^+$]$^+$; elemental analysis calcd (%) for $C_{35}H_{42}I_2N_2O_2$ (776.54): C 54.14, H 5.45, N 3.61; found: C 53.79, H 5.38, N 3.64.

Synthesis of 3b: A solution of silver tosylate (0.28 g, 1.0 mmol) in water (10 mL) was added to a solution of **3a** (0.20 g, 0.3 mmol) dissolved in H_2O/methanol (1:1). The resulting heterogeneous mixture was concentrated at reduced pressure and diluted with CH_3CN, and the precipitate was removed by filtration. The filtrate was completely evaporated to dryness affording 0.22 g (85%) of **3b**. M.p. 240 °C (dec.); ^{1}H NMR (300 MHz, CD_3CN, 298 K): $\delta = 9.00-9.02$ (m, 4H; 6,9-H), 8.54 (d, $J = 6.1$ Hz, 4H; 7,8-H), 7.62 (d, $J = 7.8$ Hz, 4H; 20-H), 7.4–7.2 (m, 10H; 17,18,19-H), 7.15 (d, $J =$ 7.8 Hz, 4H; 21-H), 5.11 (s, 1H; 16-H), 4.64 (t, 2H; $J = 7.5$ Hz, 5-H), 4.60 (t, $J = 7.5$ Hz, 2H; 10-H), 4.14 (t, $J = 6.6$ Hz, 2H; 15-H), 2.33 (s, 6H; 22-H), 2.05–1.85 (m, 4H; *4,11-H*), 1.60 (brt, 2H; 14-H), 1.4–1.3 (m, 8H; 3,2,12,13-H), 0.93 (t, $J = 7.2$ Hz, 3H; 1-H); ^{13}C NMR (75 MHz, CD_3CN), $\delta = 172.9$, 149.5, 146.4, 146.3, 139.9, 139.1, 129.2, 128.9, 127.8, 126.3, 65.3, 62.5, 62.4, 57.3, 31.4, 31.3, 28.5, 28.3, 25.6, 25.4, 22.4, 20.9, 13.7; MS (ESI, CH_3CN/H_2O) m/z: 521.1 [M^{2+}+H$^+$]; elemental analysis calcd (%) for $C_{49}H_{56}N_2O_8S_2 \cdot 2H_2O$ (901.18): C 65.31, H 6.71, N 3.11, S 7.12; found: C 65.33, H 6.65, N 3.07, S 7.05.

Synthesis of wheel 5b: Phenyl isocyanate (0.14 g, 1.0 mmol) and **4b** (0.16 g, 0.14 mmol) were mixed in CH_2Cl_2 (100 mL) and stirred at *RT* overnight. The solvent was evaporated, and the residue purified by column chromatography (hexane/ethyl acetate 3:2) to give 0.16 g (80%) of **5b**. M.p. 174–176 °C; ^{1}H NMR (300 MHz, C_6D_6, 300 K) $\delta = 7.3$, 7.25, 6.9, 6.7 (4brs, 33H; m,n,o,f,f′,f″-H and i,l-H), 4.5 (brd, 6H; g′-H), 3.9, 3.8, 3.6, 3.4 (4brs, 36H; d,c,b,g-H), 2.9 (brs, 9H; e-H), 1.3 (s, 27H; h-H), 1.1 (brs, 9H; a-H); ^{1}H NMR (300 MHz, $CDCl_3$, 300 K) $\delta = 7.1$ (brs, 21H; m,n,o,l,f′,f″-H), 6.9 (brs, 3H; i-H), 6.3 (brs, 6H; f-H), 4.3 (brs, 6H; g′-H), 4.1, (brs, 6H; d-H), 3.8 (brs, 6H; c-H), 3.7-3.6 (m, 12H; b,g′-H), 2.9 (brs, 9H; e-H), 1.2 (s, 27H; h-H), 0.85 (t, $J = 6.5$ Hz, 9H; *a-H*); ^{13}C NMR (75 MHz, $CDCl_3$) $\delta =$ 154.7, 152.0, 146.7, 138.2, 135.7, 132.9, 132.4, 128.9, 127.5, 123.3, 123.0, 120.3, 72.3, 70.0, 69.8, 66.8, 60.2, 34.1, 31.4, 30.9, 15.23; MS (ESI, CH_3OH) m/z: 1488.7 [M^++Na$^+$]; elemental analysis calcd (%) for $C_{90}H_{108}N_6O_{12} \cdot$ ½CH_2Cl_2 (1508.4): C 72.07, H 7.28, N 5.57; found: C 72.33, H 7.19, N 5.61.

Synthesis of axle 7: 4,4′-bipyridyl (0.5 g, 3.2 mmol) and 6-bromohexan-1-ol (1.74 g, 9.6 mmol) were heated under reflux in CH_3CN (100 mL) for 48 h. The yellow heterogeneous mixture was filtered, and the solid was collected and washed with CH_3CN (2×20 mL) to give 0.57 g (34%) of **7** as yellow solid. M.p. 247 °C (dec.); ^{1}H NMR (300 MHz, [D$_6$]DMSO) $\delta = 9.41$ (d, $J =$ 6.9 Hz, 4H; 7,7′-H), 8.80 (d, 4H; 8,8′-H), 4.71 (t, $J = 7.5$ Hz, 4H; 6,6′-H), 3.37 (t, $J = 4.5$ Hz, 4H; 1,1′-H), 1.98 (m, 4H; 5,5′-H), 1.4–1.3 (m, 12H; 2,3,4,2′,3′,4′-H); ^{13}C NMR (75 MHz, [D$_6$]DMSO) $\delta = 149.4$, 146.6, 127.5, 61.8, 61.4, 33.0, 31.7, 26.2, 25.8; MS (ESI, CH_3OH) m/z: 357.9 [$M^{2+} - H^+$]$^+$.

Synthesis of rotaxane 8: Wheel **5b** (0.04 g, 0.03 mmol) and axle **7** (0.014 g, 0.03 mmol) were heated under reflux in toluene (50 mL) for 24 h, then diphenylacetyl chloride (0.018 g, 0.08 mmol) was added. The mixture was heated under reflux for a further 48 h, then the solvent was completely removed under reduced pressure. Purification of the resulting red residue by chromatography (hexane/ethyl acetate/*n*PrOH 7:2:1) afforded 0.015 g (20%) of **8** as red solid. M.p. 95–99 °C; ^{1}H NMR (300 MHz, C_6D_6) $\delta = 9.8$ and 9.6 (2brs, 6H; i,l-H), 7.9 (brd, 2H; 7-H), 7.8 (brd, 6H; m-H), 7.66 (s, 6H; f-H), 7.6–7.5 (m, 18H; *β,β′,γ,γ′*,8-H), 7.3–7.2 (m, 10H; f′,f″,*δ,δ′*-H), 7.1 (brt, 6H; n-H), 6.9 (brd, 2H; 7′-H), 6.8–6.7 (m, 5H; o,8′-H); 5.28 (s, 1H; *α′*-H), 5.23 (s, 1H; *α*-H), 4.61 (brd, 6H; g′-H), 4.44 (t, $J = 6.6$ Hz, 2H; 1′-H), 4.17 (t, 2H; $J = 6.6$ Hz, 1-H), 4.0 (brs, 15H; d,e-H), 3.8 (brs, 2H; 6′-H), 3.7 (brs, 6H; c-H), 3.5-3.3 (m, 14H; 6,b,g-H), 2.1 (brs, 2H; 5′-H), 1.87 (s, 27H; h-H), 1.5–1.4 (brs, 6H; 2,3′,4′-H), 1.23 (t, $J = 6.5$ Hz, 9H; a-H), 1.1–1.0 (m, 4H; 3,4-H), 0.8–0.6 (m, 2H; 5-H); ^{13}C NMR (75 MHz, C_6D_6) $\delta = 174.9$, 171.0, 162.4, 153.9, 153.3, 148.7, 144.2, 143.3, 141.2, 139.6, 137.3, 132.6, 129.7, 129.3, 129.1, 129.0, 128.4, 128.1, 127.8, 127.4, 125.2, 124.7, 121.4, 117.8, 116.8, 91.8, 72.9, 70.3, 66.7, 65.3, 64.9, 61.4, 60.7, 57.8, 57.7, 35.1, 32.0, 30.2, 29.7, 28.8, 28.0, 26.3, 25.8, 25.4, 15.6, 11.4; MS (ESI, CH_3OH) m/z: 1106.0 [M^{2+}].[23]

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