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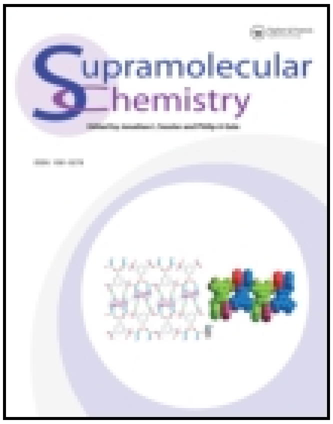

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Threading of a double-calix[6]arene system with dialkylammonium axles

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Threading of a double-calix[6]arene system with dialkylammonium axles

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The threading of a double-calix[6]arene system (**4**) with dialkylammonium axles (**2** and **3**) has been investigated in the presence of the 'superweak' tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (TFPB) anion. NMR and ESI(+)-mass spectrometry analyses showed that singly and doubly threaded pseudorotaxanes can be stepwise formed under appropriate conditions. The directional threading of an alkylbenzylammonium axle with double-calix[6]arene **4** occurs with an *endo*-alkyl preference in accordance with the '*endo*-alkyl rule'. DFT calculations confirmed this preference and evidenced that the pseudo[3]rotaxane complexes are characterised by an *anti*-conformation around the $O^{calix}—CH_2^{bridge}$ bonds, which led to a spatial divergence of the two calix-cavities.

Keywords: double-calixarene; directional threading; TFPB superweak anion; pseudorotaxane

1. Introduction

Rotaxanes and catenanes (*1*) have gained a prominent position in the field of nanotechnology wherein they have been used as molecular machines (*2*) or molecular electronics (*3*). In addition, novel and fascinating functions have been shown in the last couple of years for these interpenetrated architectures. For example, a prototypical, rotaxane-based, artificial ribosome has been reported by Leigh and coworkers, which is able to perform a sequence-specific synthesis of a peptide (*4*).

Rotaxane and catenane architectures can be efficiently obtained through a template-directed synthesis (*5*) by exploiting the threading of a linear axle through a macrocycle to form a pseudorotaxane complex, which can be considered the most common precursor to both rotaxanes and catenanes. One of the early applications of this strategy provides the use of dialkylammonium ions as axles and macrocycles such as crown ethers (*6*), cyclodextrins (*7*) and cucurbiturils (*8*).

In the last few years, we have shown (*9*) that the *through-the-annulus* threading of simple calix[6]arene hosts (e.g. **1**, Chart 1) (*10*) with dialkylammonium axles (e.g. $\mathbf{2}^+$ and $\mathbf{3}^+$) can be obtained through the inducing effect of the superweak tetrakis[3,5-bis(trifluoromethyl)Phenyl] borate (TFPB) anion (*11*) that gives free 'naked' dialkylammonium cations (*12*). Thus, through this 'superweak anion approach', we have obtained interesting examples of stereoprogrammed (*13*) and self-sorting (*14*) calixarene-based pseudorotaxane architectures and the corresponding interlocked counterparts such as [2 and 3] rotaxane (*15*) and [2]catenane (*16*) systems. Recently, we have also shown that the larger 32-membered calix[8]arene macrocycle gives *through-the-annulus* threading with dialkylammonium axles only upon partial pre-organisation of the native macroring by 1,5-intrabridging to generate two smaller subcavities (*17*). Our study showed that such 1,5-bridged calix[8]arene hosts gave pseudo[2]rotaxanes in which only one dialkylammonium axle was threaded into one of the two subcavities, leaving the other unoccupied.

Concerning the hosts with multiple cavities or rings, spectacular interpenetrated architectures have been obtained by double-threading through systems in which two macrocycles are covalently linked to one another in a handcuff-like fashion (*18*) (e.g. double-crown ethers or amide-based double macrocycle). In particular, non-trivial 'handcuff' catenane (*19*) architectures have been reported where two covalently linked macrocycles have a single larger macrocycle passing through both rings.

Regarding double-calixarene systems (e.g. **4**) (*20*), their threading with dialkylammonium ions was unexplored until very recently (*21*) when our group obtained the first examples of 'handcuff' architectures $\mathbf{6}^{2+}$ by double-threading double-calix[6]arene **4** with bis(ammonium) axle $\mathbf{5}^{2+}$ (*22*). As a complement to that preliminary report, we have extended our study to the threading features of **4** with dialkylammonium axles $\mathbf{2}^+$ and $\mathbf{3}^+$ and we report the obtained results here.

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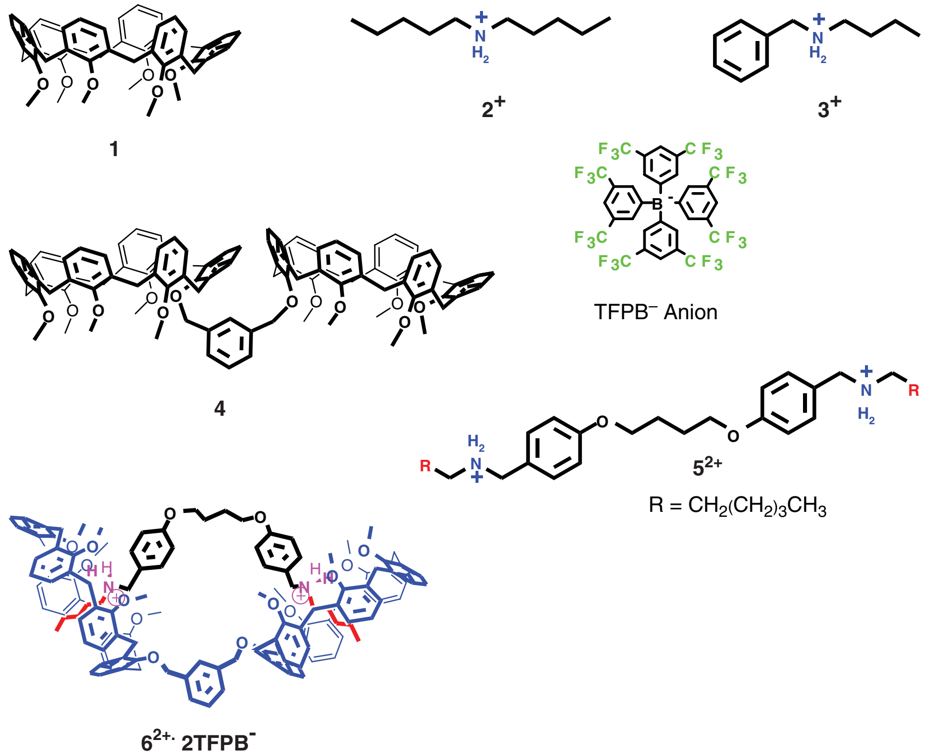


Chart 1. (Colour online) Structures of calix[6]arene hosts **1** and **4**, alkylammonium axles **2**$^+$, **3**$^+$ and **52**$^+$, TFPB anion, and pseudo[2]rotaxane **62**$^+$.

2. Results and discussion

Double-calix[6]arene **4** was synthesised exploiting the reaction sequence shown in Scheme 1 (*23*). In particular, *p*-H-calix[6]arene **7** (*24*) was monobenzylated with benzylbromide and K_2CO_3 to give **8** in 40% yield (*25*), which was exhaustively methylated with MeI in the presence of Cs_2CO_3 as the base to give **9** in 90% yield. This derivative was then subjected to hydrogenolysis with Pd/C to give pentamethoxycalix[6]arene-mono-ol **10** in 45% yield, which was reacted with 1,3-bis(bromomethyl) benzene in the presence of NaH to give double-calix[6] arene **4** in 33% yield.

The ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **4** at 298 K (Figure 1, bottom) shows sharp signals indicating a fast conformational interconversion. This is due to the small dimension of both the methoxy groups at the lower rim and the *p*-H 'substituents' at the upper rim, which allow the *through-the-annulus* passage of both rims (*26*). Therefore, at room temperature, double-calix[6]arene **4** is conformationally mobile.

2.1. *Threading of double-calix[6]arene 4 with di-n-pentylammonium axle 2$^+$*

Interestingly, the addition of di-*n*-pentylammonium salt **2**$^+$·TFPB$^-$ to a $CDCl_3$ solution of double-calix[6]arene **4** caused dramatic changes in its ^{1}H NMR spectrum (Figure 1). In fact, upon addition of 1 equiv. of **2**$^+$·TFPB$^-$ salt, a new set of signals emerged (Figure 1 (c)) due to the formation of the singly threaded pseudo[2] rotaxane ion **2**$^+$⊂**4** (Scheme 2). Under these conditions (1 equiv. of axle **2**$^+$), the formation of a singly threaded pseudo[2]rotaxane ion **2**$^+$⊂**4** (Scheme 2) was ascertained

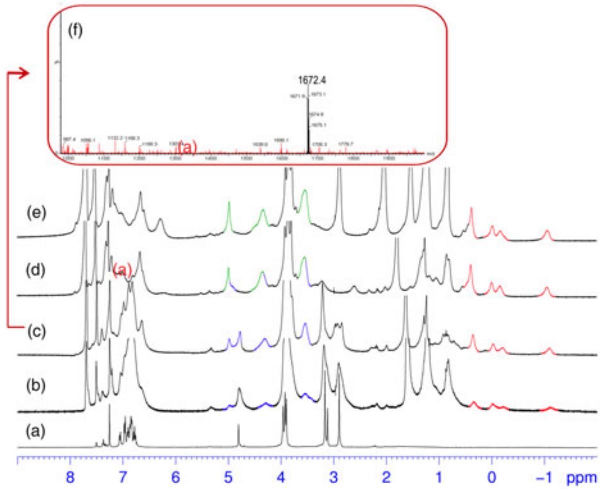


Figure 1. (Colour online) ^{1}H NMR spectra (400 MHz, 298 K, $CDCl_3$) of: (a) **4** (2.6×10^{-3} M); (b) **4** and 0.5 equiv. of **2**$^+$; (c) **4** and 1 equiv. of **2**$^+$; (d) **4** and 2 equiv. of **2**$^+$; (e) **4** and 3 equiv. of **2**$^+$; (f) significant portion of the ESI(+)-MS of a mixture of **4** and 1 equiv. of **2**$^+$.

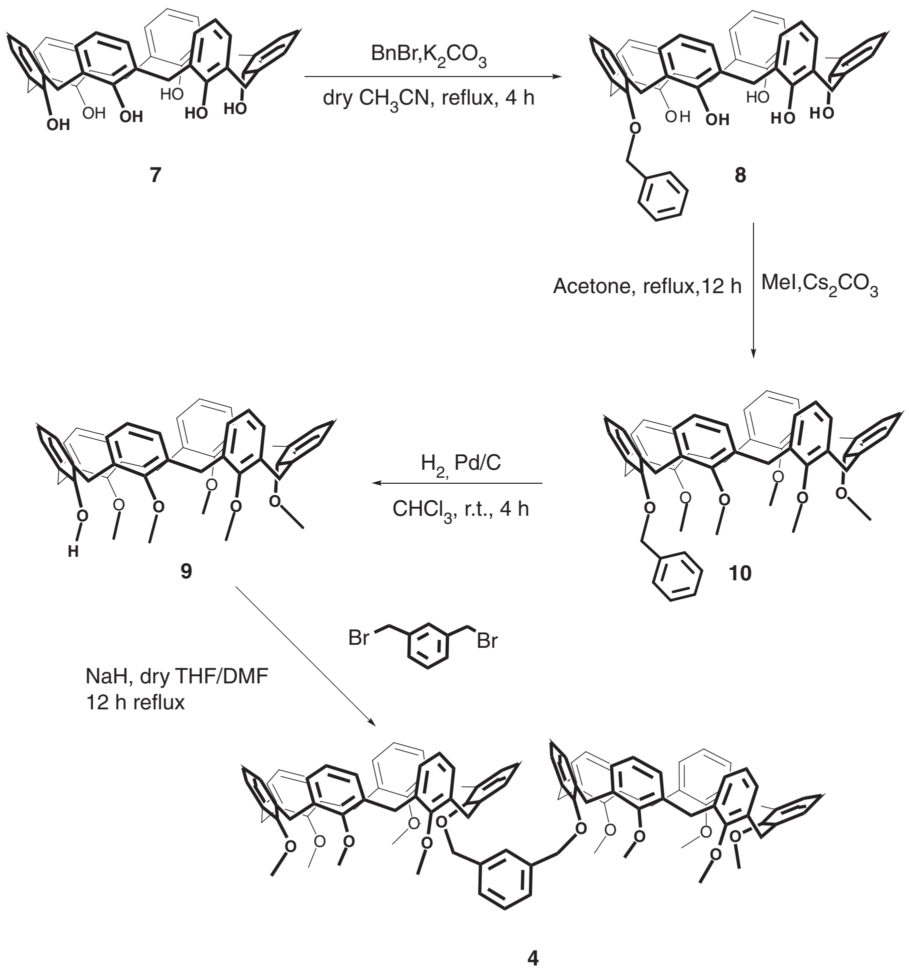
by the ESI(+)-mass spectrum (MS) that gave a value of 1672.4 *m/z* as the base peak (Figure 1(f)), corresponding to a 1:1 host/guest stoichiometry, in which only one dialkylammonium axle was threaded into one of the two macrocycles of **4**.

In addition, the appearance of *n*-alkyl resonances in the upfield negative region of the ^{1}H NMR spectrum of the 1:1 mixture of $\mathbf{2}^+$ and **4** in $CDCl_3$ and the formation of AX systems for $ArCH_2Ar$ groups corroborate the formation of the pseudo[2]rotaxane (*9*). The 1:1 stoichiometry was confirmed by spectral integration. A COSY-45 spectrum ($CDCl_3$, 400 MHz, 298 K) of the 1:1 mixture of thread $\mathbf{2}^{2+}$ and double-calix[6]arene **4** allowed a complete confident assignment of all shielded alkyl resonances. Thus, α protons at −0.02 ppm show a coupling with β methylene group at −1.07 ppm, which presents a cross-peak with γ protons at −0.17 ppm, finally coupled with δ protons at 0.37 ppm (accidentally isochronous with ε methyl) (Figure 2).

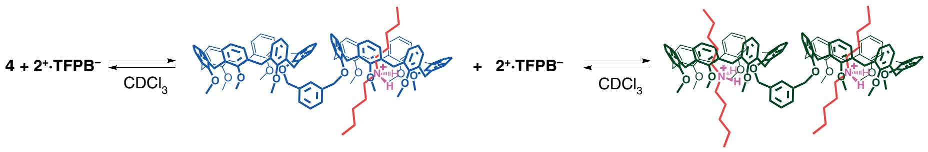
Interestingly, a 2D HSQC spectrum (Figure 3) revealed the presence of two cross-peaks between two singlets at 4.99 and 4.78 ppm and two pertinent carbon resonances at 75.4 and 74.5 ppm, which can be assigned to OCH_2 groups of the *m*-xylylene bridge. Naturally, these ^1J direct correlations were consistent with a singly threaded pseudo[2]rotaxane structure.

Further addition of 1 equiv. of di-*n*-pentylammonium axle $\mathbf{2}^+$ led to a simplification of the ^{1}H NMR spectrum of the mixture of $\mathbf{2}^+\cdot$TFPB$^-$ and **4** (Figure 1(c),(d)). In particular, the appearance of a new singlet at 4.98 ppm (integrating for 4H) relative to OCH_2 groups of the *m*-xylylene bridge, and the presence of three singlets relative to OMe groups were indicative of the formation of a new, higher-symmetry, doubly threaded pseudo[3]rotaxane $(\mathbf{2}^+)_2\subset\mathbf{4}$ in which two axles $\mathbf{2}^+$ were threaded into the two macrocycles of **4**. This was confirmed by ^{1}H NMR signal integration and by an ESI(+)-MS of a 2:1 mixture of $\mathbf{2}^+\cdot$TFPB$^-$ and **4**, which gave a value of 915.5 *m/z* as the base peak, corresponding to a 1:2 host/guest stoichiometry.

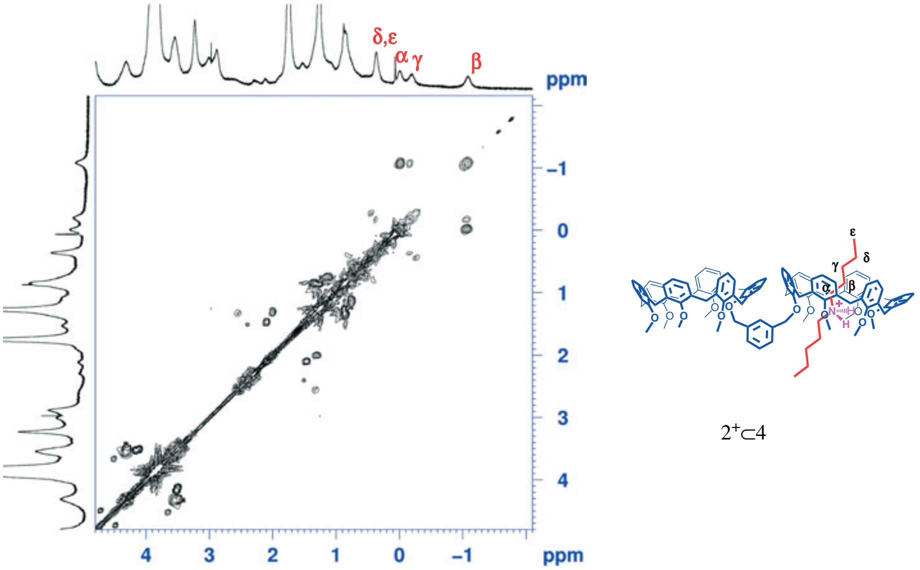
DFT calculations at the B3LYP/6-31G* level of theory (*27*) evidenced strongly stabilising N—H···O hydrogen bonds (Figure 4(a)) between the ammonium threads and the calix-wheels. Interestingly, the optimised



Scheme 1. Synthesis of double-calix[6]arene **4**.



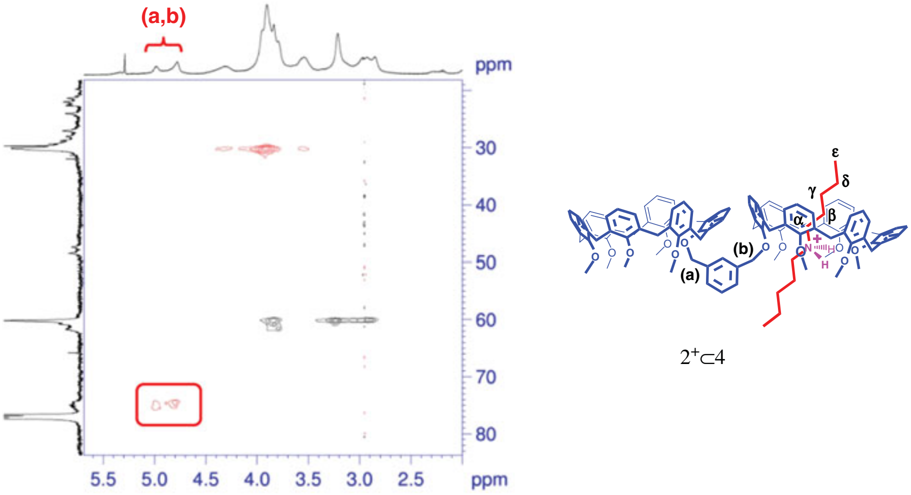
Scheme 2. (Colour online) Threading equilibria of double-calix[6]arene **4** with di-N-pentylammonium axle $\mathbf{2}^{+}$.



$\mathbf{2}^{+}\subset\mathbf{4}$

Figure 2. (Colour online) Significant portion of the 2D COSY spectrum (400 MHz, 298 K, $CDCl_3$) of the 1:1 mixture of **4** and $\mathbf{2}^{+}$·TFPB^{-}.

structure of the $(\mathbf{2}^{+})_2\subset\mathbf{4}$ complex (Figure 4(a)) revealed an approximate C_2 symmetry axis bisecting the *m*-xylyl bridge and an *anti* conformation around the $O^{\text{calix}}—CH_2^{\text{xylyl}}$ bonds with dihedral angles of 168.2° and 167.2° (Figure 4(b)). Consequently, the two calix cavities are diverging with their main axes almost perpendicular. In particular, the two mean planes of the calixarene oxygens form an angle of 60.0°. The preference for the *anti*-conformation around the $O^{\text{calix}}—CH_2^{\text{xylyl}}$ bonds was confirmed by molecular dynamics (MD) simulation at 500 K which clearly evidenced that about 48% of the coconformers sampled during the entire MD simulation (20,000 ps)



$\mathbf{2}^{+}\subset\mathbf{4}$

Figure 3. (Colour online) Expansion of the HSQC spectrum (400 MHz, 298 K, $CDCl_3$) spectrum of an equimolar solution of $\mathbf{2}^{+}$ and **4**.

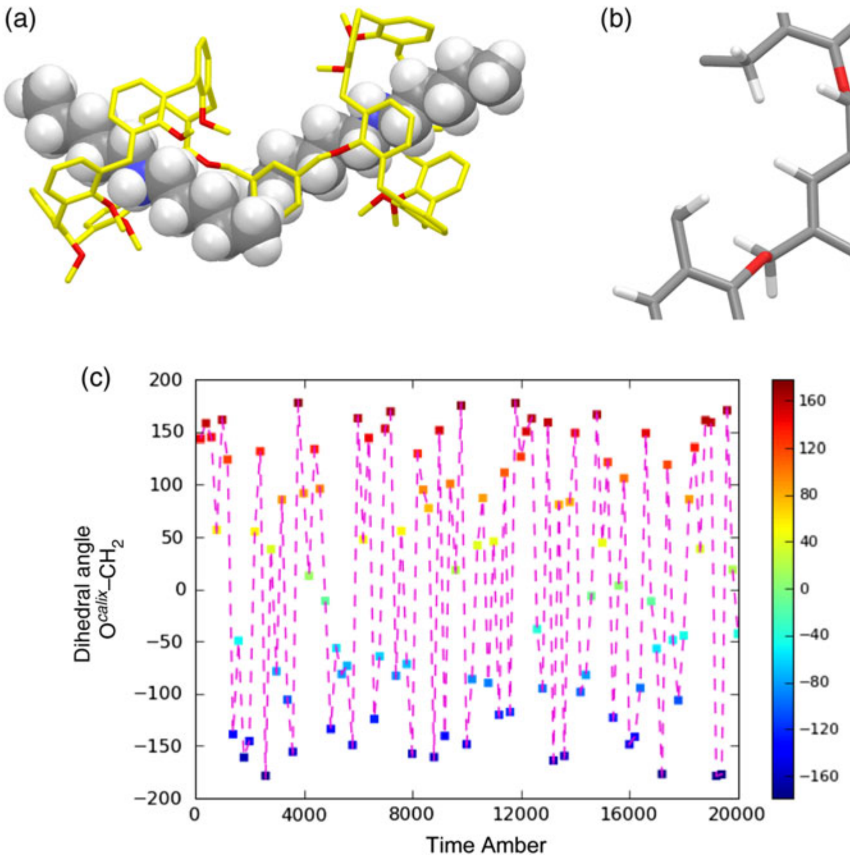


Figure 4. (Colour online) (a) Energy-minimised structure of the $(\mathbf{2}^+)_2\subset\mathbf{4}$ complex (B3LYP DFT calculations using the 6-31G* basis set). (b) Detailed view of the predicted *anti* conformations around O^{calix}—CH_2 bonds of the *m*-xylyl bridge. (c) Variation in the dihedral angle between O^{calix}—CH_2 observed during the MD simulation at 500 K (time given in ps).

showed a dihedral angle in the 150–170° range around the O^{calix}—CH_2^{xylyl} bonds (Figure 4(c)).

The total binding constant (K_{tot}) for $(\mathbf{2}^+)_2\subset\mathbf{4}$ complex, determined by quantitative ^{1}H NMR analysis of its 2:1 titration mixture in $CDCl_3$ and using tetrachloroethane (TCHE) as internal standard (*28a*), gave a value $>10^7\,M^{-2}$, which was beyond the limit of reliability of the NMR technique. Therefore, in order to have more accurate measurements (*28b*) we decided to evaluate K_{tot} in the presence of a polar competing solvent such as CD_3CN (*9*). Thus, in a mixture of $CDCl_3/CD_3CN$ (99/1, v/v), we were able to measure a value of $K_{tot} = 4.4 \pm 0.3 \times 10^4\,M^{-2}$ for the $(\mathbf{2}^+)_2\subset\mathbf{4}$ complex by quantitative ^{1}H NMR analysis and using TCHE as internal standard.

2.2. *Directional threading of double-calix[6]arene 4 with non-symmetrical n-butylbenzylammonium axle 3^+*

Recently, we have shown that the threading of a non-symmetrical directional alkylbenzylammonium cation (e.g. $\mathbf{3}^+$, Chart 1) by a calix[6]arene (e.g. **1**) leads to a marked preference for the *endo*-alkyl stereoisomer $\mathbf{11}^+$ over the *endo*-benzyl one (Figure 5) (*9*). Successively, we showed that encoding the appropriate alkylbenzyl sequence along bis-ammonium axles, it was possible to obtain a specific stereosequence (*H*,*H* or *H*,*T* in Figure 5) of the two calix-wheels in (*H*,*H*)-$\mathbf{12}^{2+}$ and (*H*,*T*)-$\mathbf{13}^{2+}$ pseudo[3]rotaxane architectures (*13*). Analogously, the stereoprogrammed synthesis of a catenane orientational isomer $\mathbf{14}^+$ (an oriented calix[2]catenane) has been obtained after macrocyclisation, by using a directional alkylbenzylammonium axle (*16*).

From these studies, we have deduced a sort of ‘molecular code’ which has been used to develop an integrative self-sorting (*14*). This molecular code includes the following stereochemical ‘*endo*-alkyl rule’ (Figure 5): ‘threading of a directional alkylbenzylammonium axle (e.g. $\mathbf{3}^+$) through a *p*-H-hexaalkoxycalix[6] arene (e.g. **1**) occurs with an *endo*-alkyl preference’ (*14*).

On the basis of these results, we decided to verify the validity of the *endo*-alkyl rule on double-calix[6]-arene host **4**. In fact, the threading of **4** with the *n*-butylbenzylammonium axle $\mathbf{3}^+$ could give rise to three directional double-threaded pseudo[3]rotaxane diastereoisomers with *endo*-alkyl/*endo*-alkyl, *endo*-benzyl/*endo*-

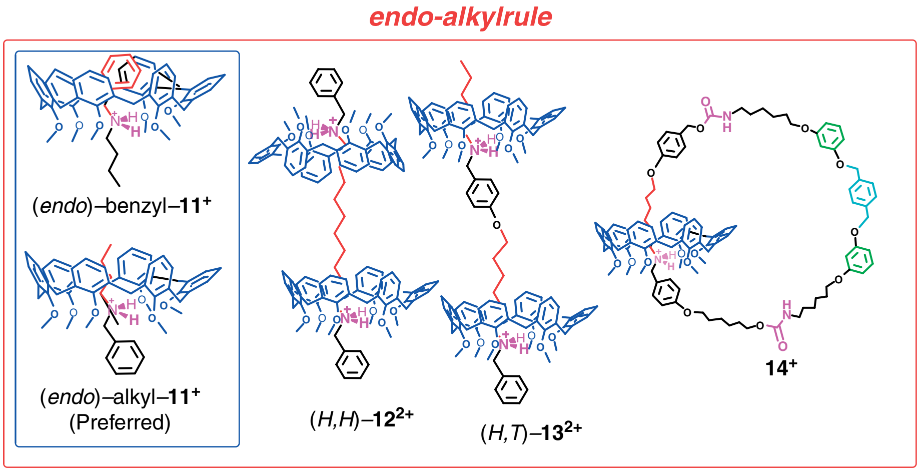


Figure 5. (Colour online) The ‘*endo*-alkyl rule’ and related examples of oriented interpenetrated architectures.

alkyl or *endo*-benzyl/*endo*-benzyl relative orientations (Figure 6).

Of course, on the basis of the above-discussed *endo*-alkyl rule (Figure 5), we expected that the *endo*-alkyl/*endo*-alkyl stereoisomer should be favoured. As in the previous instance, the addition of butylbenzylammonium $\mathbf{3}^+$ to a solution of **4** in $CDCl_3$ caused significant changes in its ^1H NMR spectrum. In particular, 1 equiv. of butylbenzylammonium $\mathbf{3}^+$ led to a new species corresponding to the singly threaded complex $\mathbf{3}^+\subset\mathbf{4}$, in slow exchange with the free host **4**. The 1:1 host/guest stoichiometry was confirmed by means of ESI(+)-MS and integration of ^1H NMR signals. In fact, the ESI(+)-MS of a 1:1 mixture of $\mathbf{3}^+\cdot TFPB^-$ and **4** gave a value of 1680.3 *m*/*z* as the base peak (Figure 7(g)), corresponding to a singly threaded pseudo[2]rotaxane ion $\mathbf{3}^+\subset\mathbf{4}$ (Scheme 3).

In analogy to the above-discussed $\mathbf{2}^+\subset\mathbf{4}$ pseudorotaxane, also in this case, two singlets at 4.96 ppm and 4.77 ppm relative to the OCH_2 protons of the *m*-xylylene bridge corresponding to the singly threaded pseudo[2] rotaxane were observed in the ^1H NMR spectrum of the 0.75:1 mixture of $\mathbf{3}^+$ and **4** (Figure 7(d)). The progressive addition of $\mathbf{3}^+$ led to the disappearance of these two singlets while a new singlet emerged at 4.96 ppm corresponding to the doubly threaded pseudo[3]rotaxane $(\mathbf{3}^+)_2\subset\mathbf{4}$, as confirmed by ESI(+)-MS and ^1H NMR signal integration.

As concerns the stereochemistry of the threading, the ^1H NMR spectra of the 1:1 and 1:2 mixtures of **4** and $\mathbf{3}^+$ showed typical signatures at highfield negative values (from 1.0 to -1.0 ppm) characteristic of an *endo*-alkyl complexation (*9*, *13*). This result and the absence of shielded benzylic resonances in the 4–6 ppm region, typical of an *endo*-benzyl complexation, were clear-cut proofs that in both singly and doubly threaded pseudorotaxanes an *endo*-alkyl orientation of butylbenzylammonium threads was present (*10*). This result demonstrated the validity of the *endo*-alkyl rule also for double-calixarenes and confirmed the possibility to control the directionality of the double-threading in these systems.

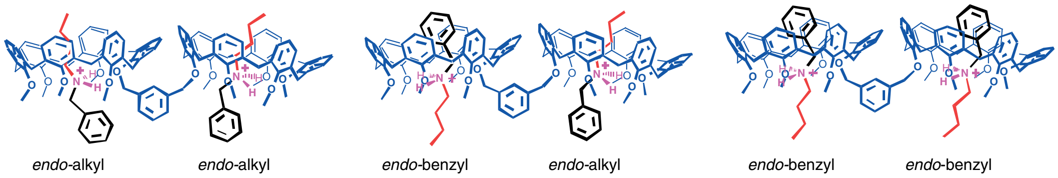
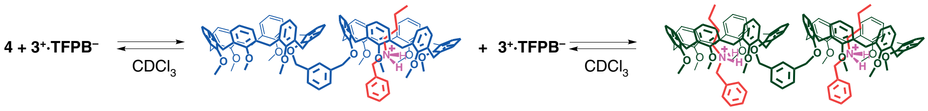


Figure 6. (Colour online) Possible double-threaded pseudo[3]rotaxane stereoisomers by directional threading of **4** with the *n*-butylbenzylammonium axle $\mathbf{3}^+$.



Scheme 3. (Colour online) Threading equilibria of double-calix[6]arene **4** with n-butylbenzylammonium axle $\mathbf{3}^+$.

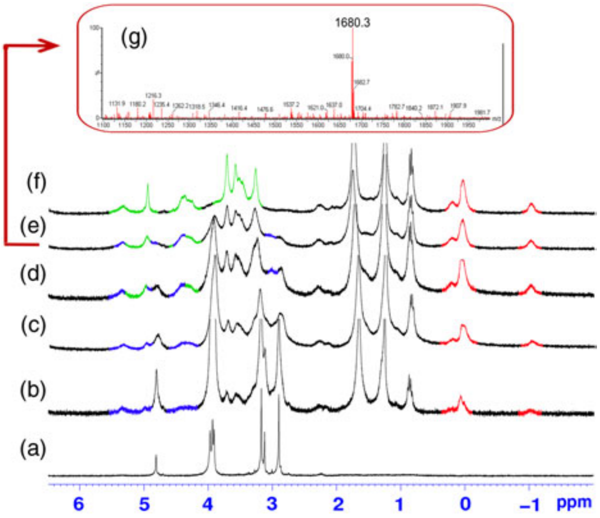


Figure 7. (Colour online) ^{1}H NMR spectra (400 MHz, 298 K, $CDCl_3$) of: (a) **4** (2.6×10^{-3} M); (b) **4** and 0.25 equiv. of $\mathbf{3}^{+}$; (c) **4** and 0.5 equiv. of $\mathbf{3}^{+}$; (d) **4** and 0.75 equiv. of $\mathbf{3}^{+}$; (e) **4** and 1.0 equiv. of $\mathbf{3}^{+}$; (f) **4** and 2.0 equiv. of $\mathbf{3}^{+}$; (g) significant portion of the ESI(+)-MS of a mixture of **4** and 1 equiv. of $\mathbf{3}^{+}$.

In analogy to the $(\mathbf{2}^{+})_2\subset\mathbf{4}$ complex above described, DFT calculations at the B3LYP/6-31G* level of theory (*27*) also in this case confirmed the presence of stabilising N—H···O hydrogen bonds (Figure 8(a)) between the ammonium cations and the calixarene oxygens. The optimised structure of the $(\mathbf{3}^{+})_2\subset\mathbf{4}$ complex (Figure 8(a)) was very similar to that of $(\mathbf{2}^{+})_2\subset\mathbf{4}$, showing again an *anti*-conformation around $O^{calix}—CH_2^{xylyl}$ bonds with dihedral angles of 162.7° and 166.1°. This conformational preference was confirmed by MD simulation at 500 K, which clearly evidenced that about 46% of the sampled coconformers showed a dihedral angle in the 150–170° range around the $O^{calix}—CH_2^{xylyl}$ bonds (Figure 8(b)).

The extension of DFT calculations to the other *endo*-benzyl/*endo*-alkyl and *endo*-benzyl/*endo*-benzyl orientational isomers of $(\mathbf{3}^{+})_2\subset\mathbf{4}$ (Figure 9) confirmed the higher stability of *endo*-alkyl/*endo*-alkyl orientation experimentally evidenced by ^{1}H NMR. In fact, this latter orientation was 3.9 kcal/mol more stable than the *endo*-benzyl/*endo*-alkyl orientation, which in turn was 4.3 kcal/mol more stable than the *endo*-benzyl/*endo*-benzyl orientational isomer.

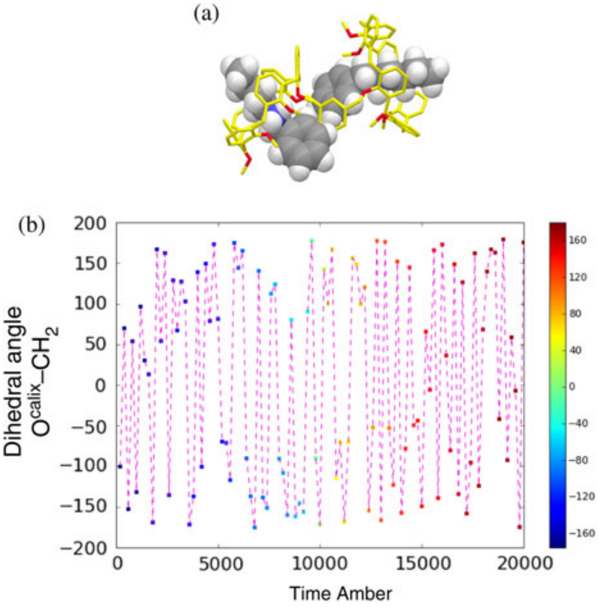


Figure 8. (Colour online) (a) Energy-minimised structure of the $(\mathbf{3}^{+})_2\subset\mathbf{4}$ complex (B3LYP DFT calculations using the 6-31G* basis set). (b) Variation in the dihedral angle between $O^{calix}—CH_2$ observed during the MD simulation at 500 K (time given in ps).

As discussed above, also in this case, the total binding constant (K_{tot}) of the $(\mathbf{3}^{+})_2\subset\mathbf{4}$ complex was determined by quantitative ^{1}H NMR analysis of its 2:1 titration mixture in $CDCl_3/CD_3CN$ (99/1, v/v), to give a value of $8.8 \pm 0.2 \times 10^{4}\,M^{-2}$. This value is only slightly higher than that found ($4.4 \pm 0.3 \times 10^{4}\,M^{-2}$) for dipentylammonium complex $(\mathbf{2}^{+})_2\subset\mathbf{4}$.

3. Conclusion

In summary, we have reported on the threading abilities of a double-calix[6]arene host with dialkylammonium axles in the presence of TFPB superweak anion. ^{1}H NMR and ESI(+)-MS spectra evidenced the stepwise formation of singly and doubly threaded pseudorotaxane architectures by changing the host/guest stoichiometry from 1:1 to 1:2. The directional threading of non-symmetrical *n*-butylbenzylammonium axle $\mathbf{3}^{+}$ with double-calix[6]arene host **4** occurs with an *endo*-alkyl preference in accordance with

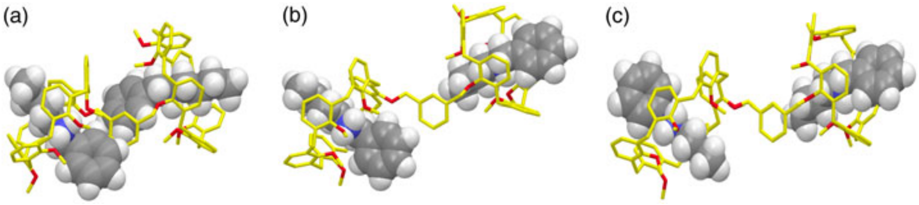


Figure 9. (Colour online) Energy-minimised structures of *endo*-alkyl/*endo*-alkyl (a), *endo*-benzyl/*endo*-alkyl (b) and *endo*-benzyl/*endo*-benzyl (c) orientational isomers of pseudo[3]rotaxane $(\mathbf{3}^{+})_2\subset\mathbf{4}$ (B3LYP DFT calculations using the 6-31G* basis set).

the known '*endo*-alkyl rule'. DFT calculations indicated that the lowest-energy structures of the pseudo[3]rotaxane complexes are characterised by an *anti*-conformation around the $O^{calix}—CH_2^{xylyl}$ bonds which led to a spatial divergence of the two calix-cavities.

4. Experimental section

4.1. General comments

ESI(+)-MS measurements were performed on a Micromass Bio-Q triple quadrupole mass spectrometer (Micromass/Waters, Milford, MA, USA) equipped with electrospray ion source, using $CHCl_3$ as solvent. All chemicals were reagent grade and were used without further purification. When necessary, compounds were dried *in vacuo* over $CaCl_2$. Reaction temperatures were measured externally. Derivative $\mathbf{2}^+\cdot TFPB^-$ (*9*), $\mathbf{3}^+\cdot TFPB^-$ (*9*) and **4** (*22*) were synthesised according to literature procedures. NMR spectra were recorded on a Bruker Avance-400 spectrometer (Bruker BioSpin GmbH, Karlsruhe, DE) [400 (^{1}H) and 100 MHz (^{13}C)]; chemical shifts are reported relative to the residual solvent peak ($CHCl_3$: δ 7.26, $CDCl_3$: δ 77.23). COSY-45 spectra were taken using a relaxation delay of 2 s with 30 scans and 170 increments of 2048 points each. HSQC spectra were performed with gradient selection, sensitivity enhancement and phase-sensitive mode using an Echo/Antiecho-TPPI procedure. A typical experiment comprised 20 scans with 113 increments of 2048 points each. Monte Carlo conformational searches (10,000 steps) were performed with the MacroModel-9.0/Maestro-4.1 program using $CHCl_3$ as solvent (GB/SA model). MD simulations were performed at $T = 500$ K, for 20,000 ps, using a time step of 1.0 fs.

4.2. Synthesis and characterisation of double-calixarene 4 (23)

NaH (1.30 g, 54.2 mmol) was added at 0 °C, under stirring, to a solution of derivative **9** (1.47 g, 2.07 mmol) in dry THF/DMF (75 ml, 7/3 v/v). The mixture was kept at 25 °C under stirring, and after 1 h, 1,3-bis(bromomethyl)benzene (0.26 g, 0.98 mmol) was added. The reaction was stirred at reflux for 12 h under a nitrogen atmosphere, then the solvent was removed under reduced pressure and the mixture was partitioned between CH_2Cl_2 and H_2O. The organic layer was washed with 1 N HCl (50 ml), brine (50 ml) and dried over Na_2SO_4. The crude product was purified by column chromatography (SiO_2; Et_2O/CH_2Cl_2 3/97) to give derivative **4** as a white solid (1.04 g, 0.69 mmol, 33%). ESI(+)-MS: $m/z = 1516$ (MH^+); ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ 7.06–6.78 (overlapped ArH, 40H), 4.80 (s, OCH_2Ar, 4H), 3.96 (s, $ArCH_2Ar$, 8H), 3.92 (s, $ArCH_2Ar$, 8H), 3.90 (s, $ArCH_2Ar$, 8H), 3.16 (s, OCH_3, 12H), 3.11 (s, OMe, 6H), 2.89 (s, OCH_3, 12H); ^{13}C NMR (75 MHz, $CDCl_3$, 298 K): δ 156.7, 156.6, 156.3, 154.5, 137.9, 134.9, 134.8, 134.7, 134.6, 134.5, 130.0, 129.7, 129.3, 128.9, 128.8, 128.7, 128.2, 127.5, 127.4, 123.6, 74.9, 60.4, 60.2, 30.7, 30.4. Anal. Calcd for $C_{102}H_{98}O_{12}$: C, 80.82; H, 6.52. Found: C, 81.80; H, 6.43.

4.3. Preparation of singly-threaded pseudo[2]-rotaxanes

Double-calixarene derivative **4** (2.0×10^{-3} g, 1.3×10^{-3} mmol) and the dialkylammonium derivative $\mathbf{2}^+$ or $\mathbf{3}^+$ (1.3×10^{-3} mmol) were dissolved in 0.5 ml of $CDCl_3$, and the mixture was stirred for 5 min at 25 °C. Then, the solution was transferred into an NMR tube for 1D and 2D NMR spectra acquisition.

Selected spectral data for singly threaded pseudo[2] rotaxane ion $\mathbf{2}^+\subset\mathbf{4}$. ESI(+)-MS: $m/z = 1672.4$ $[\mathbf{2}\subset\mathbf{4}]^+$. ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K): δ −1.07 [broad, $(CH_2)_\beta$, 2H], −0.17 [broad, $(CH_2)_\gamma$, 2H], −0.02 [broad, $(CH_2)_\alpha$, 2H], 0.37 [broad, $(CH_2)_\delta + (CH_3)_\varepsilon$, 5H], 3.53 and 4.29 (broad overlapped, $ArCH_2Ar$, 24H), 2.87, 2.99, 3.23 (br s, OCH_3, 6H, 3H, 6H), 3.78, 3.84, 3.90 (br s, OCH_3, 3H, 6H, 6H), 4.79 (br s, OCH_2, 2H), 4.98 (br s, OCH_2, 2H), 6.63–6.99 (overlapped, ArH, 40H).

Selected spectral data for singly threaded pseudo[2] rotaxane ion $\mathbf{3}^+\subset\mathbf{4}$. ESI(+)-MS: $m/z = 1680.3$ $[\mathbf{3}\subset\mathbf{4}]^+$. ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K): δ −1.02 [broad, $(CH_2)_\beta$, 2H], 0.04 [broad, $(CH_2)_\gamma + (CH_3)_\delta$, 5H], 0.22 [broad, $(CH_2)_\alpha$, 2H], 2.30 [broad, $(H_2N^+CH_2^\alpha Ph)$, 2H], 2.87–3.93 (broad overlapped OCH_3 + $ArCH_2Ar$, 42H), 4.31–4.41 (broad overlapped, $ArCH_2Ar$, 12H), 4.78 (br s, OCH_2, 2H), 4.98 (br s, OCH_2, 2H), 5.37 (br s, $^+NH_2$, 2H), 6.76–7.40 (overlapped, ArH, 45H).

4.4. Preparation of pseudo[3]rotaxanes

Double-calixarene derivative **4** (2.0×10^{-3} g, 1.3×10^{-3} mmol) and the dialkylammonium derivative $\mathbf{2}^+$ or $\mathbf{3}^+$(2.6×10^{-3} mmol) were dissolved in 0.5 ml of $CDCl_3$, and the mixture was stirred for 5 min at 25 °C. Then, the solution was transferred into an NMR tube for 1D and 2D NMR spectra acquisition.

Selected spectral data for doubly threaded pseudo[3] rotaxane ion $(\mathbf{2}^+)_2\subset\mathbf{4}$. ESI(+)-MS: $m/z = 915.5$ $[(\mathbf{2})_2\subset\mathbf{4}]^{2+}$. ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K): δ −1.07 [broad, $(CH_2)_\beta$, 4H], −0.18 [broad, $(CH_2)_\gamma$, 4H], −0.01 [broad, $(CH_2)_\alpha$, 4H], 0.39 [broad, $(CH_2)_\delta + (CH_3)_\varepsilon$, 10H], 3.52 and 4.33 (broad, $ArCH_2Ar$, 24H), 3.79, 3.84, 3.91 (br s, OCH_3, 6H, 12H, 12H), 4.98 (br s, OCH_2, 4H), 6.66–7.61 (overlapped, ArH, 40H).

Selected spectral data for doubly threaded pseudo [3]rotaxane ion $(\mathbf{3}^+)_2\subset\mathbf{4}$. ESI(+)-MS: $m/z = 921.5$ $[(\mathbf{3})_2\subset\mathbf{4}]^{2+}$. ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K):

δ − 1.01 [broad, $(CH_2)_\beta$, 4H], 0.03 [broad, $(CH_2)_\gamma$ + $(CH_3)_\delta$, 10H], 0.23 [broad, $(CH_2)_\alpha$, 4H], 2.27 [broad, $(H_2NCH_2^\alpha Ph)$, 4H], 3.28, 3.59, 3.70 (s, OCH_3, 6H, 12H, 12H), 3.50 and 4.44 (broad, $ArCH_2Ar$, 8H), 3.52 and 4.32 (broad, $ArCH_2Ar$, 8H), 3.58 and 4.43 (broad, $ArCH_2Ar$, 8H), 4.97 (br s, OCH_2, 4H), 5.35 (br s, $^+NH_2$, 4H), 6.64–7.59 (overlapped, ArH, 50H).

4.5. *Determination of* K$_{ass}$ *values of* $(2^+)_2\subset 4$ *and* $(3^+)_2\subset 4$ *complexes by quantitative* ^1H *NMR analysis* (28a)

The samples were prepared by dissolving **4** (1.24 $\times 0^{-3}$ mmol) and the appropriate alkylammonium guest $\mathbf{2}^+$ or $\mathbf{3}^+$(2.48×10^{-3} mmol) in $CDCl_3$ (0.4 ml) containing 1 μl of 1,1,2,2-TCHE ($d = 1.59$ g/ml) as internal standard. The complex concentration [complex] was evaluated by integration of the ^1H NMR signal of $CHCl_2CHCl_2$ versus the shielded signals at negative values of the guest molecule. The following equation (*28a*) was used to obtain the moles of the complex:

$$\frac{G_a}{G_b} = \frac{F_a}{F_b} \times \frac{N_b}{N_a} \times \frac{M_a}{M_b},$$

where G_a are the grams of 1,1,2,2-TCHE; G_b are the grams of complex; F_a and F_b are the areas of the signals of 1,1,2,2-TCHE and the shielded signal of the guest, respectively; N_a and N_b are the numbers of nuclei which cause the signals (N_a for 1,1,2,2-TCHE; N_b for guest); and M_a and M_b are the molecular masses of 1,1,2,2-TCHE (a) and complex (b), respectively.

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