

Threading of Conformationally Stable Calix[6]arene Wheels Substituted at the Methylene Bridges

Marina Tranfić Bakić,^{†,||} Veronica Iuliano,^{‡,||} Carmen Talotta,^{*,‡,||} Silvano Geremia,[§] Neal Hickey,[§] Aldo Spinella,[‡] Margherita De Rosa,^{‡,||} Annunziata Soriente,^{‡,||} Carmine Gaeta,^{‡,||} and Placido Neri^{*,‡,||}

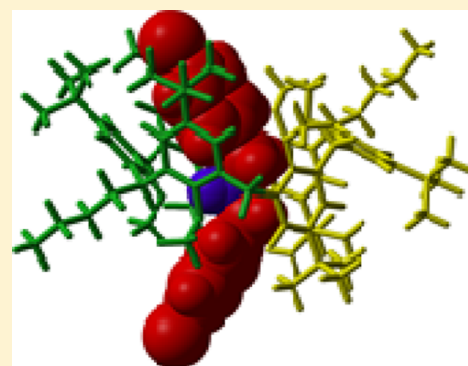
[†]Department of Chemistry and Biochemistry, Faculty of Food Technology and Biotechnology, University of Zagreb, Pierottijeva 6, 10000 Zagreb, Croatia

[‡]Laboratory of Supramolecular Chemistry, Department of Chemistry and Biology "A. Zambelli", University of Salerno, Via Giovanni Paolo II 132, I-84084 Fisciano, Salerno, Italy

[§]Centro di Eccellenza in Biocristallografia Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Trieste, via L. Giorgieri 1, I-34127 Trieste, Italy

Supporting Information

ABSTRACT: Calix[6]arenes disubstituted at the methylene bridges, which are stable in the cone or 1,2,3-alternate conformation, form pseudorotaxanes with dialkylammonium axles. The cone wheel-based pseudorotaxanes are 10–100 times more stable than those obtained with the native conformationally mobile calix[6]arene wheel, as a consequence of their higher degree of preorganization. The threading of conformationally stable 1,2,3-alternate calix[6]arenes is unprecedented in the literature. Therefore, very peculiar NMR features are here evidenced for this threading process involving the less symmetrical 1,2,3-alternate calix[6]arene conformation, which implies a peculiar rototranslation motion of the axle.



■ INTRODUCTION

Calixarene¹ macrocycles have a bowl-shaped architecture with an internal cavity of adjustable shape and dimension depending on the conformation of their skeleton.¹ Thanks to their synthetic and conformational versatility, calixarenes are considered as one of the most widespread macrocyclic platforms for the design of host molecules.¹ In particular, calixarene threading has been investigated by us² and by Arduini and coworkers,³ with the aim to obtain mechanically interlocked molecules. In 2010,^{4a} we demonstrated that scarcely preorganized calix[6]arene derivatives (e.g., **1a,b**) can be threaded by dialkylammonium axles only when they are associated with the weakly coordinating superweak anion tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (TFPB⁻) (Figure 1). In addition, we observed that the efficiency of the threading was closely associated with the conformational mobility of the calix wheel.^{4a} Thus, calix[6]-wheel **1b^{cone}**, bearing longer hexyl chains at the lower rim, was threaded by dialkylammonium axles **2a⁺**–**4⁺**, more efficiently than hexamethoxy-**1a^{cone}** as a result of its higher degree of preorganization.^{4a} Recently, we have focused our attention on the threading of calix[6]-wheels whose conformation is different from that of the cone one.

Previously reported data⁵ showed clearly that the most stable conformations for calix[6]arene hexaethers (e.g., **1a,b**) are the cone (**1a,b^{cone}**) and the 1,2,3-alternate (**1a,b^{1,2,3-alt}**)

ones. In particular, we have shown that **1b^{1,2,3-alt}** is threaded faster than **1b^{cone}** in the presence of the bis(4-biphenylmethyl)-ammonium cation as the TFPB⁻ salt.^{5a} The pseudorotaxane initially formed (the kinetic product) shows the calix wheel in the 1,2,3-alternate conformation^{5a} and is conformationally less stable; therefore, it interconverts to a new one (the thermodynamic product) in which the calix wheel adopts a cone conformation.^{5a} Very recently,⁶ it was found that the introduction of alkyl groups at the methylene bridges⁷ of the calix[6]arene macrocycle leads to new derivatives (e.g., **5a** and **6a**), which show a high degree of conformational stability. Thus, derivatives fixed in the 1,2,3-alternate conformation (e.g., **6a**) have been isolated and characterized both in solution, by one-dimensional (1D) and two-dimensional (2D) nuclear magnetic resonance (NMR) studies, and in the solid state, by X-ray diffractometry.⁶ On this basis, now the question arises as to whether the calix[6]arene bearing alkyl groups at the methylene bridges are also capable of threading with dialkylammonium axles **2⁺**–**3⁺**.

In addition, we wonder whether the conformational stability of the 1,2,3-alternate calix[6]-wheels could lead to thermodynamically stable pseudorotaxane architectures well observable via NMR.

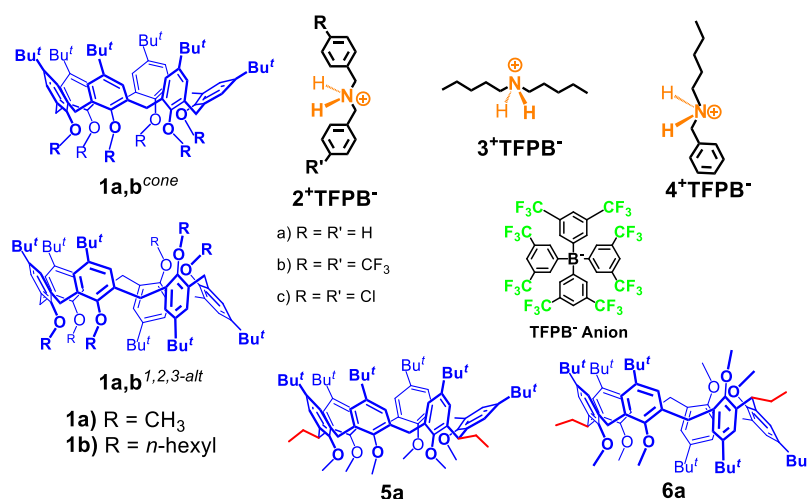
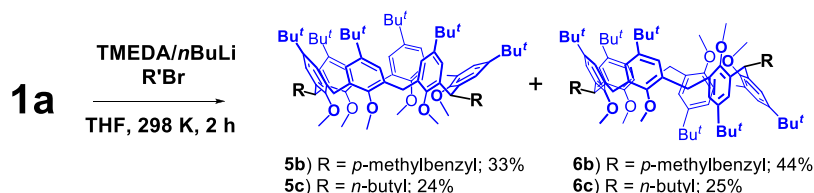


Figure 1. Structures of calix[6]arene wheels **1a,b**, ammonium cations **2⁺–3⁺**, and TFPB⁻ anion.

Scheme 1. Synthesis of Derivatives **5b/5c** and **6b/6c**



Prompted by these considerations, we have investigated the threading ability of methylene-functionalized calix[6]arene macrocycles with dialkylammonium axles, and we report here the result of this study.

RESULTS AND DISCUSSION

Initially, derivatives **5b/6b** and **5c/6c** were synthesized following the procedure reported by Singh and coworkers.^{6,7} In detail, *p*-*tert*-butylcalix[6]arene hexamethyl ether **1a** was first treated with *n*-BuLi/TMEDA, and the anion was then reacted with the corresponding alkyl halide electrophile, leading to derivatives **5** and **6** fixed in the cone or 1,2,3-alternate conformation, respectively (Scheme 1). Successively, derivatives **5b/6b** and **5c/6c** were characterized by 1D and 2D NMR in accordance with the considerations reported in the literature.^{6,7a} The cone and 1,2,3-alternate structural assignment was confirmed by solid-state X-ray structures of derivatives **6c** and **5c** (Figure 2).

The ¹H NMR spectrum of **5c** in CDCl₃ at 298 K showed the presence of an AX system at 3.46 and 4.51 ppm and of a broad triplet at 4.78 ppm, attributable, respectively, to the methylene

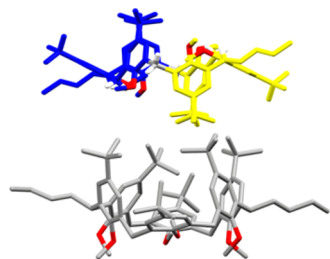


Figure 2. X-ray structures of **6c** (up) and **5c** (down). H atoms have been omitted for clarity.

and methine bridges. In addition, two singlets were present at 3.28 and 2.83 attributable to the OMe groups. By lowering the temperature, a broadening for the OMe singlets was detected at 183 K and analogously for the aromatic protons of **5c**. In a similar way, the derivative **5b** showed a broadening of the OMe singlets at the same temperature, which can be attributed to the slowing of the OMe-through-the-annulus passage.⁸

The threading study was started by exploring the complexation ability of cone **5b** with dibenzylammonium axle **2a⁺**·TFPB⁻. When this salt was added to a CDCl₃ solution of **5b** (1:1 ratio), significant changes appeared in the ¹H NMR spectrum of **5b** (Figure S11), indicative of the formation of pseudorotaxane **2a⁺** ⊂ **5b**. The cone conformation of the calix-wheel **5b** in **2a⁺** ⊂ **5b** pseudorotaxane was ascertained by 1D and 2D NMR studies (Figures S11 and S12). Regarding the signals of the dibenzylammonium axle in **2a⁺** ⊂ **5b** pseudorotaxane, the presence of resonances of two different benzylic units was clearly evident: one accommodated inside the cavity and shielded at 4.48, 5.27, and 5.95 ppm (*ortho*-, *meta*-, and *para*-BnH, respectively) and the other outside the calix cavity, resonating at typical chemical shift values (7.44, 7.58, and 7.44 ppm, *ortho*-, *meta*-, and *para*-BnH, respectively).

The formation of **2a⁺** ⊂ **5b** was confirmed by the HR ESI(+) mass spectrum which gave as the base peak a value of 1327.036 *m/z* corresponding to the pseudorotaxane system. The threading of **2a⁺** inside **5b** reached the equilibrium immediately after mixing. The determination of the apparent association constant of pseudorotaxane **2a⁺** ⊂ **5b** was carried out by means of a competition experiment^{4a} (Figure S56) with the native hexamethoxycalix[6]arene **1a**. In particular, 1 equiv of **2a⁺**·TFPB⁻ was mixed with a 1:1 mixture of **5b** and **1a** (in CDCl₃) and equilibrated for 15 min at 298 K. The NMR spectrum indicated that pseudorotaxane **2a⁺** ⊂ **5b** was favored over **2a⁺** ⊂ **1a** in a 10:1 ratio (Figure S47). From these data, an

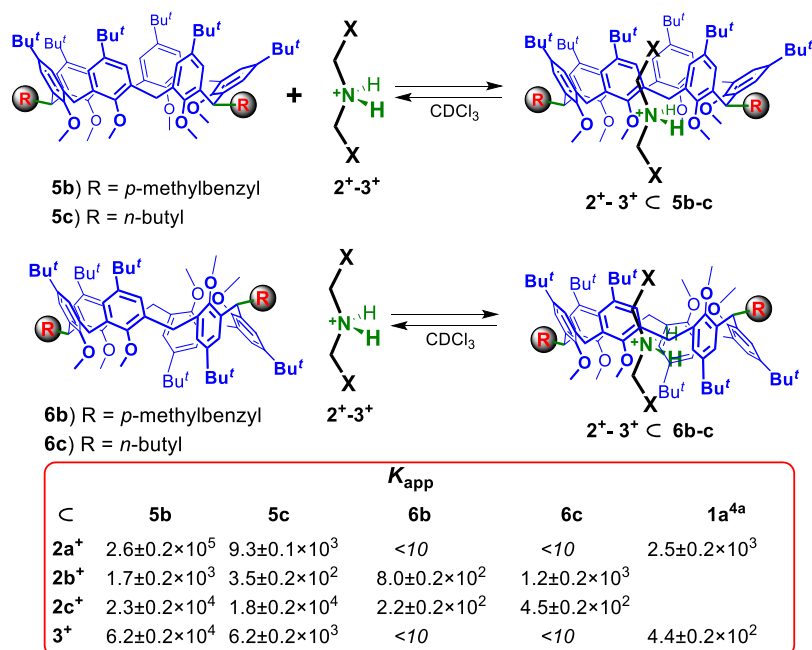


Figure 3. Threading of calix[6] wheels substituted at the methylene bridges and K_{app} values measured for the formation of the corresponding pseudorotaxanes.

apparent association constant value of $2.6 \pm 0.2 \times 10^5 \text{ M}^{-1}$ was calculated for $2a^+ \subset 5b$, which is significantly higher than that observed for $2a^+ \subset 1a$ ($2.5 \times 10^3 \text{ M}^{-1}$).^{4a} In summary, these initial results indicate that the higher conformational stability of cone **5b** leads to a dibenzylammonium-based pseudorotaxane with a higher thermodynamic stability with respect to the native conformationally mobile calix[6]arene-wheel **1a**. A close inspection of the K_{app} values⁹ reported in **Figure 3** clearly indicates a general trend within the methylene-functionalized calix[6]arene complexes: the calix wheels **5b** and **5c**, fixed in the cone conformation, give pseudorotaxane complexes with ammonium axles $2a^+$ and 3^+ more stable than the analogue obtained by threading the mobile calix[6]arene-wheel **1a**, as a consequence of their higher degree of preorganization. In line with this conclusion, the cone wheel with the bigger *p*-methylbenzyl substituent **5b** gives pseudorotaxane adducts 10–100 times more stable than **5c**, bearing the smaller *n*-butyl group (**Figure 2**). At this point, our attention was turned to the threading of conformationally stable 1,2,3-alternate calix[6]arene derivatives **6b,c**. While the threading of calix[6]wheels in the cone conformation is well documented in the literature,^{4,5} the threading of a stable 1,2,3-alternate calix[6]arene has never been described.¹⁰ Consequently, a very limited NMR information has been reported for the characterization of pseudorotaxanes in which the calix wheel adopts a 1,2,3-alternate structure.⁹ The ¹H NMR spectrum of the free calix wheel **6c** (CDCl₃, 298 K, 600 MHz) in the 1,2,3-alternate conformation showed the presence of an AB system at 4.06 and 3.65 ppm (8 H) attributable to the unsubstituted ArCH₂Ar groups. As previously described by Biali,^{7a} the presence of only one AB system for these two different ArCH₂Ar groups is justified on the basis of a rapid topomerization equilibrium in which the two aromatic rings A and B in **Figure 4** undergo a flipping process.

Interestingly, the $\Delta\delta$ value of 0.41 ppm between the two doublets is small and can also be rationalized by this rapid topomerization (**Figure 4**).^{7a} Thus, the diastereotopic protons

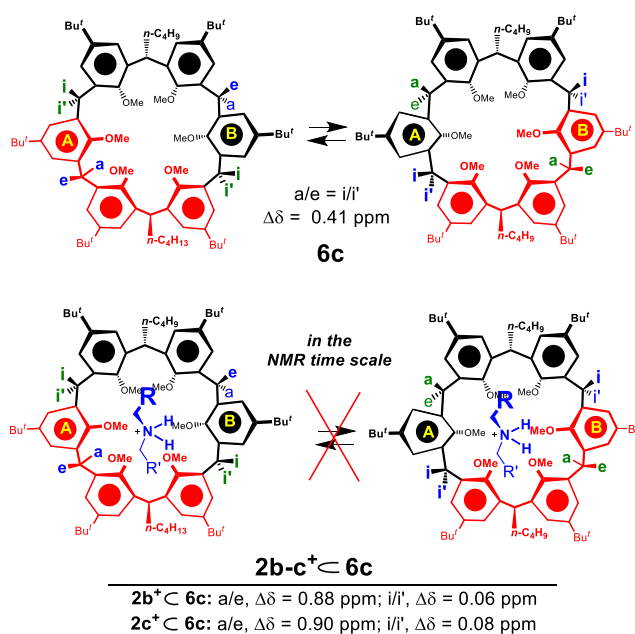


Figure 4. Topomerization equilibrium^{7a} in 1,2,3-alternate **6c** (top). The presence of the axle inside the cavity of **6c** obstructs the flipping of the aromatic rings A and B in the corresponding pseudorotaxane (bottom).

a and *e*, which are expected at very different chemical shifts (AX system), exchange with the isoclinal protons *i* and *i'*, which are expected to display similar chemical shifts (AB system).^{7a} In conclusion, in a fast exchange situation, two averaged doublets result with a smaller difference of chemical shift with respect to the values expected for *a* and *e*.^{7a} A ¹H VT NMR study was performed in order to highlight the conformational mobility of the derivative **6b,c**. By lowering the temperature, the ¹H NMR spectrum of **6c** in CD₂Cl₂

showed a broadening of the AB system at 4.06 and 3.65 ppm at 193 K.¹¹

Analogously, the derivative **6b** shows a similar behavior with a broadening at 193 K.¹¹ Interestingly, after addition of **2b**⁺·TFPB⁻ to the CDCl₃ solution of **6c**, an AX system was detected at 4.38 and 3.50 ppm (blue in Figure 5b) with a $\Delta\delta$

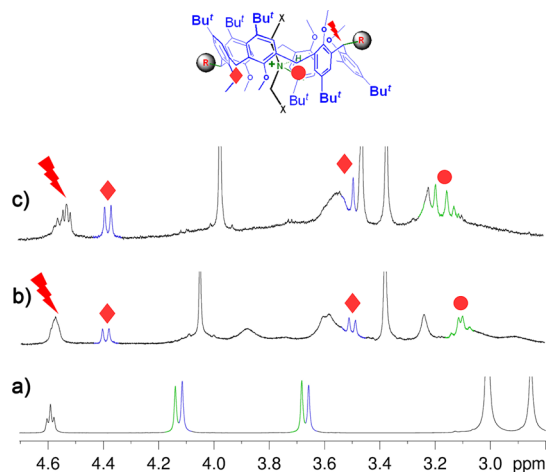


Figure 5. Methylene region of ¹H NMR spectra (CDCl₃, 600 MHz, 298 K) of (a) **6c**; (b) **2b**⁺ **6c**; and (c) **2c**⁺ **6c**.

value of 0.88 ppm significantly higher than that observed in the ¹H NMR spectrum of the free host **6c** ($\Delta\delta = 0.41$ ppm). This AX system showed a correlation in the heteronuclear single quantum coherence (HSQC) spectrum with a carbon resonance at 28.9 ppm, indicative of an ArCH₂Ar group between syn-oriented Ar rings.¹² Therefore, we confidentially assigned these resonances at the *a* and *e* hydrogen atoms in Figure 4 (bottom). In addition, an AB system was observed at 3.12/3.06 ppm (4H, green in Figure 5b), which correlates in the HSQC spectrum with a carbon resonance at 34.8 ppm, indicative of an ArCH₂Ar system between anti-oriented Ar rings and attributable to isoclinal *i* and *i'* protons (Figure 4, bottom).

These results clearly indicate that after threading of the axle **2b**⁺ through the annulus of **6c**, the flipping of the two Ar rings A and B in Figure 4 is blocked with respect to the NMR time scale (600 MHz). In this way, no exchange can be observed between *a/e* and *i/i'* protons. Consequently, the AB systems in the ¹H NMR spectrum of free **6c** (8H, $\Delta\delta = 0.41$ ppm) for the unsubstituted ArCH₂Ar groups are split, upon threading with **2b**⁺, in one AX system (4H) with $\Delta\delta = 0.88$ ppm (*a* and *e* ArCH₂Ar groups in Figure 4) and one AB system (4H) with

$\Delta\delta = 0.06$ ppm (*i* and *i'*, ArCH₂Ar groups in Figure 4). In a similar way, when the *p*-chloro-substituted axle **2c**⁺ was added to the CDCl₃ solution of **6c**, again the threading of the 1,2,3-alternate wheel was evidenced by the appearance of one AX system at 3.50/4.40 ppm ($\Delta\delta = 0.90$ ppm, blue in Figure 5c) and an AB system at 3.23/3.15 ppm ($\Delta\delta = 0.08$ ppm, green in Figure 5c).

The above trend is confirmed with the 1,2,3-alternate calix[6]arene **6b**, bearing two *p*-Me-benzyl groups at the methylene bridges, which shows an AB system at 4.94/3.63 ppm, with a $\Delta\delta = 0.41$ ppm, for the unsubstituted ArCH₂Ar groups. Upon addition of **2b**⁺·TFPB⁻ salt, the formation of **2b**⁺ **6b** pseudorotaxane is outlined by the appearance of an AX system at 3.45/4.29 ppm with a $\Delta\delta = 0.84$ ppm and an AB system at 3.06/3.12 ppm with a $\Delta\delta = 0.06$ ppm.

Another interesting feature concerns the signals of the axle. In fact, the ¹H NMR spectrum of dibenzylammonium-based pseudorotaxanes^{4a} in which the calix wheel adopts a cone conformation usually evidences the presence of two sets of shielded and unshielded benzyl resonances (see above for **2a**⁺ **5b**),^{4a} corresponding to their endo- or exo-cavity disposition.^{4a} Surprisingly, the ¹H NMR spectrum of the **2b**⁺ **6c** pseudorotaxane evidences the presence of only one set of benzylic resonances of **2b**⁺ shielded inside the aromatic cavity of the calix-wheel **6c**. In details, the aromatic H-atoms of **2b**⁺ form an AB system at 6.75/5.96 ppm ($\Delta\delta = \delta_{\text{free}} - \delta_{\text{complex}} = 0.78$ and 1.42 ppm, respectively), while the CH₂ groups in α to the ⁺NH₂ group form an AB system at 2.56/2.61 ppm ($\Delta\delta = 1.59$ and 1.54 ppm, respectively). In addition, the 2D COSY spectrum of **2b**⁺ **6c** shows three meta-coupled aromatic signals for **6c** at 7.64/7.36, 7.41/6.98, and 7.14/6.95 ppm. This observation clearly indicates that in the **2b**⁺ **6c** pseudorotaxane, the two 3/4-cone subcavities (red and blue in Figure 6) are equivalent. This result is unexpected because the C-shape of the axle **2b**⁺ and its H-bonding in pseudorotaxane **2b**⁺ **6c** (see the DFT-optimized structure in Figure 7) should make nonequivalent the two 3/4-cones of **6c** (see the blue and red colors in Figure 6). Thus, the NMR spectra of **2b**⁺ **6c** can be justified on the basis of the equilibrium highlighted in Figure 6, in which the rototranslation motion of the axle **2b**⁺ between the anti-oriented O atoms (red and blue in Figure 6) makes equivalent the two subcavities of **6c**.

Of course, the equilibrium highlighted in Figure 6 is fast with respect to the NMR time scale (600 MHz) at room temperature. By lowering the temperature at 223 K, it can be slowed down, thus allowing the detection of the asymmetric enantiomeric pair of Figure 6. Thus, 4 AX systems attributable to the ArCH₂Ar groups emerged at 4.60/3.54, 4.51/3.48, 4.37/

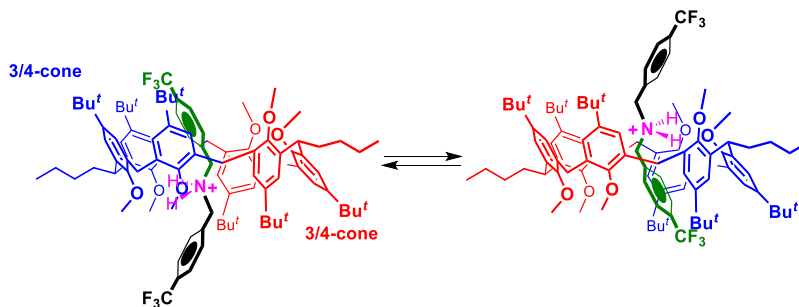


Figure 6. Rototranslation motion of the dibenzylammonium axles **2b**⁺ inside the cavity of the calix[6]-wheel **6c** in the 1,2,3-alternate conformation.

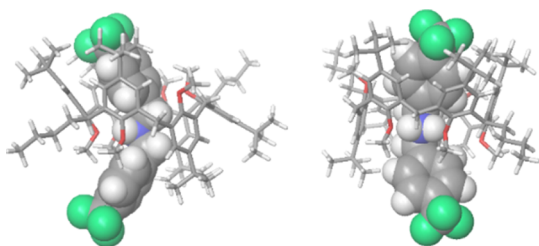


Figure 7. Different views of the DFT-optimized structure of the $2b^+$ C $6c$ pseudorotaxane at the B3LYP/6-31G(d,p) IOP(3/124 = 3) level of theory. Two H-bonding interactions are present between the ammonium group of the axle and the oxygen atoms of a 3/4-cone subcavity, with an average $N^+ \cdots O$ distance of 2.94 Å and a $N-H \cdots O$ angle of 163.5°.

3.52, and 4.24/3.42 ppm. In addition, two sets of aromatic *p*-CF₃-benzylammonium signals for the axle $2b^+$ (green and black in Figure 6) emerged in the 1D and 2D NMR spectra at 223 K. Furthermore, 6 AB systems were detected at 7.18/6.50 (6 H), 7.43/6.64 (2H), 7.32/6.80 (2H), 7.30/6.78 (2H), 6.90/6.82 (2H), and 6.72/6.61 (2H) ppm for the six nonequivalent Ar rings of $6c$. By these data and considering the temperature of coalescence at 233 K, (Supporting Information) an energy barrier of 10.2 kcal/mol¹³ was calculated for the rototranslation motion of the dibenzylammonium axle $2b^+$ inside the cavity of the calix[6]-wheel $6c$.

CONCLUSIONS

In conclusion, we have here reported the first examples of pseudorotaxanes obtained by the threading of ammonium axles through calix[6]arene macrocycles substituted at the methylene bridges. Thanks to their conformational stability, the cone structures $5b$ and $5c$ form pseudorotaxane complexes more stable than those obtained by the native conformationally mobile calix[6]arene-wheel $1a$. The NMR features of the threading process between ammonium axles and calix wheels in the stable 1,2,3-alternate conformation have been described in detail, evidencing a rototranslation motion of the axle inside the 1,2,3-alternate wheel, which could be blocked at low temperatures. These results can be considered useful reference points for future studies.

EXPERIMENTAL SECTION

General Information. Reactions under anhydrous conditions were conducted under an inert atmosphere (nitrogen) using dry solvents. The commercial reagents were purchased by Aldrich and Fluka and were used without further purification. The reactions were controlled by thin-layer chromatography with Macherey-Nagel plates coated with silica gel (0.25 mm) with a fluorescence indicator UV254 and visualized using UV light and nebulization with an indicator solution of H₂SO₄-Ce(SO₄)₂. The reaction temperatures were measured externally using electronic thermometers. The reaction products were purified by Macherey-Nagel silica gel chromatography (60, 70–230 mesh). NMR spectra were recorded on a Bruker AVANCE-600 spectrometer [600 (¹H) and 150 MHz (¹³C)] and a Bruker AVANCE-400 spectrometer [400 (¹H) and 100 MHz (¹³C)]. Chemical shifts are reported relative to the residual solvent peak (CHCl₃; δ 7.26, CDCl₃; δ 77.16). Standard pulse programs, provided by the manufacturer, were used for 2D NMR experiments. High-resolution (HR) mass spectra were acquired with a Bruker Solarix spectrometer equipped with a Tesla magnet. Matrix-assisted laser desorption/ionization was used for sample ionization. 2,5-Dihydroxybenzoic acid was used as the matrix. Samples were prepared in CHCl₃ (1 mg/mL).

Synthesis of Derivatives $5b$ and $6b$. In a dry round flask, under N₂, hexamethoxycalix[6]arene 1 (0.502 g, 0.45 mmol) was dissolved in freshly distilled tetrahydrofuran (THF) (50 mL). Subsequently, tetramethylethylenediamine (TMEDA, 0.57 mL, 3.59 mmol) and *n*-BuLi (1.50 mL of a solution 2.5 M in hexane, 3.59 mmol) were added at room temperature. A persistent blood red colored anion was generated. Afterward, a solution of *p*-methylbenzyl bromide (0.724 g, 3.59 mmol) in THF (dry, 20 mL) was added dropwise to the reaction mixture. Gradually, the color of the mixture first changed to green and then to pale yellow. Stirring was continued for an hour at room temperature. After the reaction was stopped by addition of 1 N HCl, the solution was extracted with ethyl acetate. The organic phase was dried over anhydrous Na₂SO₄ and filtered, and the solvent was evaporated. The raw product was purified by column chromatography on silica gel, and using a solvent mixture of 74% hexane/21% chloroform/5% ethyl acetate as the eluent, cone $5b$ was isolated with a 25% yield and 1,2,3-alternate $6b$ conformer with a 22% yield. Derivative $5b$: ¹H NMR (600 MHz, CDCl₃, 298 K): δ 7.16 (s, 4H, ArH), 7.04 (d, *J* = 7.6 Hz, 4H, ArH), 7.02 (s, 4H, ArH), 6.96 (d, *J* = 7.6 Hz, 4H, ArH), 6.86 (s, 4H, ArH), 5.13 (bt, 2H, ArCH(*p*-MeBn)Ar), 4.41 and 3.45 (AX system, *J* = 15.3 Hz, 8H, ArCH₂Ar), 3.23–3.19 (overlapped, -CH₂Ph, 16H, -OCH₃), 2.70 (s, 6H, -OCH₃), 2.23 (s, 6H, -BnCH₃), 1.16 (s, 18H, -C(CH₃)₃), 1.07 (s, 36H, -C(CH₃)₃). ¹³C NMR (150 MHz, CDCl₃, 298 K): δ 154.0, 153.6, 145.7, 145.2, 137.9, 136.5, 135.0, 133.1, 133.1, 128.9, 128.7, 126.3, 125.3, 123.9, 60.2, 60.0, 41.9, 34.2, 34.1, 31.4, 31.4, 29.9, 20.9. HRMS (*m/z*): calcd for C₈₈H₁₁₂NaO₆, 1287.8351; found, 1287.8378. Derivative $6b$: ¹H NMR (600 MHz, CDCl₃, 298 K): δ 7.12 (s, 4H, ArH), 7.02–7.02 (overlapped, 8H, ArH), 6.96–6.94 (overlapped, 8H, ArH), 4.89 (bt, 2H, ArCH(*p*-MeBn)Ar), 4.05 and 3.64 (AX system, *J* = 14.8 Hz, 8H, ArCH₂Ar), 3.25 (d, *J* = 7.3 Hz, 4H, -CH₂Ph), 2.96 (s, 12H, -OCH₃), 2.80 (s, 6H, -OCH₃), 2.22 (s, 6H, -BnCH₃), 1.17 (s, 18H, -C(CH₃)₃), 1.15 (s, 36H, -C(CH₃)₃). ¹³C NMR (150 MHz, CDCl₃, 298 K): δ 154.2, 154.1, 145.7, 145.3, 137.9, 136.7, 135.0, 133.5, 133.1, 128.9, 128.7, 126.3, 125.8, 124.4, 69.0, 60.1, 59.6, 40.9, 34.2, 34.1, 31.4, 20.9. Elemental Analysis: Calcd for C₈₈H₁₁₂O₆: C, 83.50; H, 8.92; O, 7.58. Found: C, 83.48; H, 8.93; O, 7.59.

Synthesis of Derivatives $5c$ and $6c$. In a dry round flask, under N₂, hexamethoxycalix[6]arene 1 (1.575 g, 0.94 mmol) was dissolved in freshly distilled THF (150 mL). Subsequently, TMEDA (1.73 mL, 7.52 mmol) and *n*-BuLi (4.50 mL of a solution 2.5 M in hexane, 7.52 mmol) were added at room temperature. A persistent blood red colored anion was generated. Afterward, a solution of 1-bromobutane (1.23 mL, 7.60 mmol) in THF (dry, 60 mL) was added dropwise to the reaction mixture. Gradually, the color of the mixture first changed to green and then to pale yellow. Stirring was continued for an hour at room temperature. After the reaction was stopped by addition of 1 N HCl, the solution was extracted with ethyl acetate. The organic phase was dried over anhydrous Na₂SO₄ and filtered, and the solvent was evaporated. The raw product was purified by column chromatography on silica gel, and using a solvent mixture of 74% hexane/21% chloroform/5% ethyl acetate as eluents, cone $5c$ was isolated with a 27% yield and 1,2,3-alternate $6c$ conformer with a 10% yield. Derivative $5c$: ¹H NMR (600 MHz, CDCl₃, 298 K): δ 7.06 (s, 4H, ArH), 7.01 (s, 4H, ArH), 6.92 (s, 4H, ArH), 4.78 (t, *J*_{ab} = 7.6 Hz, 2H, ArCH(*n*Bu)Ar), 4.51 and 3.46 (AX system, *J* = 15.3 Hz, 8H, ArCH₂Ar), 3.28 (s, 12H, OCH₃), 2.83 (s, 6H, OCH₃), 1.92 (q, *J*_{ba} = 7.6 Hz, *J*_{bc} = 14.7, 4H, -CH₂CH₂CH₂CH₃), 1.34–1.28 (m, 8H, -CH₂CH₂CH₂CH₃), 1.13 (s, 18H, -C(CH₃)₃), 1.06 (s, 36H, -C(CH₃)₃), 0.86 (t, -CH₂CH₂CH₂CH₃, *J* = 7.1 Hz, 6H). ¹³C NMR (150 MHz, CDCl₃, 298 K): δ 153.8, 153.5, 145.7, 145.4, 137.4, 133.2, 133.1, 126.1, 125.2, 123.4, 69.0, 60.3, 60.1, 36.9, 36.4, 34.2, 34.1, 31.4, 30.5, 29.8, 22.7, 14.0. HRMS (*m/z*) calcd for C₈₀H₁₁₂O₆Na, 1191.8351; found, 1191.8399. Derivative $6c$: ¹H NMR (600 MHz, CDCl₃, 298 K): δ 7.08–7.02 (overlapped, 12H, ArH), 4.58 (t, *J*_{ab} = 7.6 Hz, 2H, ArCH(*n*Bu)Ar), 4.11 and 3.66 (AX system, *J* = 15.0 Hz, 8H, ArCH₂Ar), 3.00 (s, 12H, OCH₃), 2.84 (s, 6H, OCH₃), 1.93 (q, *J*_{ba} = 7.6 Hz, *J*_{bc} = 14.9, 4H, -CH₂CH₂CH₂CH₃), 1.34–1.28 (m, 8H, -CH₂CH₂CH₂CH₃), 1.19 (s, 54H, -C(CH₃)₃), 0.86 (t, *J* = 7.1 Hz, 6H, -CH₂CH₂CH₂CH₃).

¹³C NMR (150 MHz, CDCl₃, 298 K): δ 154.5, 154.3, 145.8, 145.6, 137.5, 133.7, 133.4, 126.6, 126.0, 124.0, 60.3, 59.8, 38.0, 35.7, 34.4, 34.3, 32.2, 31.6, 30.7, 22.9, 14.2. Elemental Analysis: Calcd for C₈₀H₁₁₂O₆: C, 82.14; H, 9.65; O, 8.21. Found: C, 82.13; H, 9.67; O, 8.20.

AUTHOR INFORMATION

Corresponding Authors

*E-mail: ctalotta@unisa.it (C.T.).

*E-mail: neri@unisa.it (P.N.).

ORCID

Marina Tranfić Bakić: 0000-0002-0315-5900

Carmen Talotta: 0000-0002-2142-6305

Margherita De Rosa: 0000-0001-7451-5523

Annunziata Soriente: 0000-0001-6937-8405

Carmine Gaeta: 0000-0002-2160-8977

Placido Neri: 0000-0003-4319-1727

Author Contributions

^{||}M.T.B. and V.I. contributed equally to this work.

Notes

The authors declare no competing financial interest.

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(8) It was not possible to lower the temperature below 183 K, and consequently, we were not able to study the ¹H NMR spectrum of **5b,c** under slow exchange kinetic (with respect to the NMR time scale). Because of this, it is not possible to calculate the energy barrier using the known equations (see ref 13).

(9) Regarding the complexes **2b**⁺ < **6b**, **3**⁺ < **5b**, **2a**⁺ < **5c**, **2c**⁺ < **5c**, and **3**⁺ < **5c**, the calculation of the apparent association constants has been performed by integration of the ¹H NMR signals of the complexes and free hosts ([Supporting Information](#)). For the complexes **2b**⁺ < **5b**, **2c**⁺ < **5b**, **2c**⁺ < **6b**, **2b**⁺ < **5c**, **2b**⁺ < **6c**, and **2c**⁺ < **6c**, the *K*_{app} values have been calculated by qNMR.

(10) The formation of pseudorotaxanes in which the calix wheel adopts a 1,2,3-alternate structure has been described in ref.^{5a,b} In these cases, the 1,2,3-alternate pseudorotaxanes were the kinetic species, which evolved toward the more stable cone conformation.

(11) Probably, the broadening of the ArCH₂Ar signals is attributable to the slowing of the flipping motion represented in [Figure 4](#) (top). Because of the instrumental limitations, it was not possible to lower the temperature below 183 K, and consequently, we were not able to detect the freezing of the flipping motion.

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