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Synthesis, Structures, and Conformational Characteristics of Triptycene-Derived Calix[5]arenes

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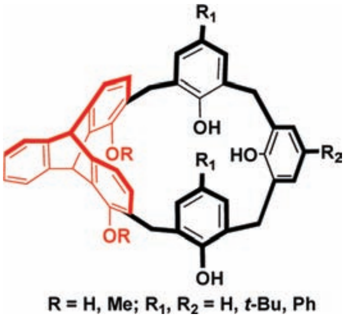
ABSTRACT



A series of novel calix[5]arenes 5 containing one 1,8-dimethoxytriptycene moiety were synthesized through an efficient fragment coupling strategy. The subsequent demethylation of 5 with BBr_3 in dry dichloromethane gave the calix[5]arenes 6. Debutylation of both 5a∼b and 6a∼b with $AlCl_3$ resulted in the same products 7a∼7b. The structural studies revealed that all of the macrocyclic compounds have well-defined structures with fixed cone conformations in both solution and solid state. Moreover, it was also found that the triptycene-derived calix[5]arenes could encapsulate small neutral molecules in the solid state.

Design and synthesis of a new class of hollow host compounds with the interior cavities large enough to encapsulate organic guests is always an interesting and exciting research topic in supramolecular chemistry. Among various types of known macrocyclic molecules, calixarenes[1,2] as a class of well-defined phenol-derived cyclic oligomers bridged by methylene groups have been the focus of considerable attention in the last two decades. However, compared with other hollow hosts such as cyclodextrins, cyclotriveratrylenes, or resorcinarenes, the calixarenes exhibit a higher degree of conformational mobility. Although in the family of calixarenes the calix[4]arenes have been most extensively studied owing to their readily available and easy chemical modification on either smaller (lower) or larger (upper) rims,[1,3] they have cavities too small to complex with ordinary organic guests. Comparatively, the calix[5]arenes are more sizable and appropriate for the inclusion of organic

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(1) (a) *Calixarenes 2001*; Asfari, Z., Böhmer, V., Harrowfield, J., Vicens, J., Eds.; Kluwer, Academic Publishers: Dordrecht, Holland, 2001; (b) Gutsche, C. D. *Calixarenes Revisited Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; Royal Society of Chemistry: Cambridge, 1998.

(2) Some recent examples, see: (a) Sameni, S.; Jeunesse, C.; Matta, D.; Harrowfield, J. *Chem. Soc. Rev.* **2009**, *38*, 2117. (b) Li, G.-K.; Xu, Z.-X.; Chen, C.-F.; Huang, Z.-T. *Chem. Commun.* **2008**, 1774. (c) Xu, Z.-X.; Zhang, C.; Yang, Y.; Chen, C.-F.; Huang, Z.-T. *Org. Lett.* **2008**, *10*, 477. (d) Kogan, K.; Biali, S. E. *J. Org. Chem.* **2009**, *74*, 7172. (e) Zorzi, R.; Guidolin, N.; Randaccio, L.; Purrello, R.; Geremia, S. *J. Am. Chem. Soc.* **2009**, *131*, 2487. (f) Mendoza-Espinosa, D.; Hanna, T. A. *Inorg. Chem.* **2009**, *48*, 10312. (g) Mendoza-Espinosa, D.; Hanna, T. A. *Inorg. Chem.* **2009**, *48*, 7452.

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guests.[4] However, the development of calix[5]arenes has lagged behind due to the synthetic elusiveness and increasing mobility in comparison with their tetramer analogues.[5]

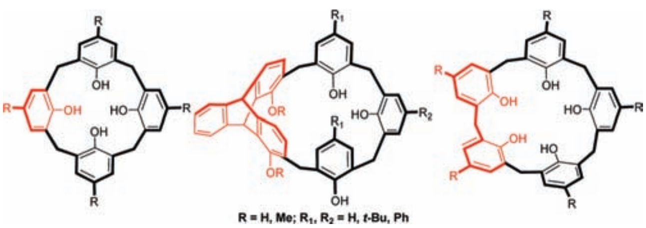
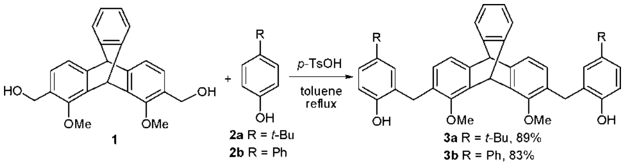


Figure 1. Structures of calix[4]arenes (left), triptycene-derived calix[5]arenes (middle), and calix[5]arenes (right).

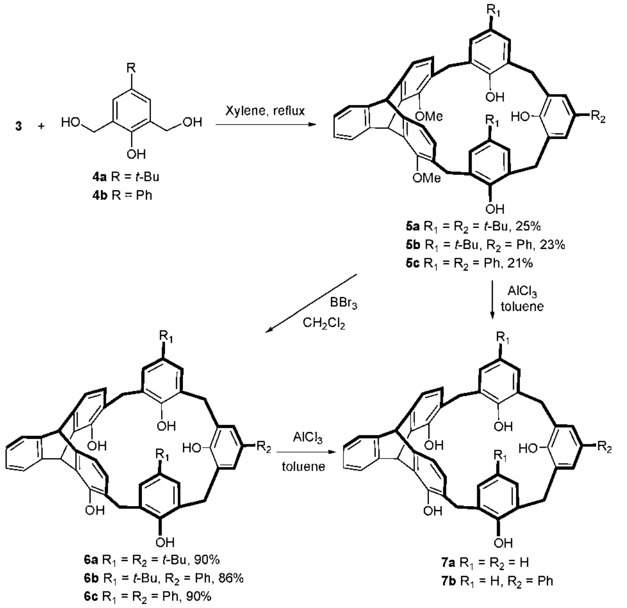
Recently, we[6] have proven that the triptycenes with unique 3D rigid structure could be used as useful building blocks for the synthesis of different kinds of novel macrocyclic hosts with specific structures and properties. Thus, we envisioned that if a suitable triptycene moiety with the 3D rigid structure took the place of one or more phenol group(s) in the calix[4]arenes a new class of calixarenes with large cavities and fixed conformations could thus be obtained. As a result, we[7] recently reported a couple of novel triptycene-derived calix[6]arenes with fixed conformations. Herein, we report the synthesis of a series of novel calix[5]arenes **5a**−**c** containing one 1,8-dimethoxytriptycene moiety and their demethylated and debutylated derivatives (Figure 1). The structural studies show that owing to the 3D rigid structure of the triptycene moiety the triptycene-derived calix[5]arenes all exhibit the fixed cone conformations in both solution and solid state. Moreover, it is found that the calix[5]arenes can also encapsulate the small neutral molecules inside their cavities in the solid state.

1,8-Dimethoxy-2,7-dihydroxymethyltriptycene **1** was prepared according to our previously reported method.[7] When we treated compound **1** with excess *p*-*tert*-butylphenol **2** in refluxed toluene in the presence of a catalytic amount of *p*-toluenesulfonic acid, the 1 + 2 product **3a** was obtained in 89% yield. Similarly, the trimer **3b** was also synthesized by the reaction of **1** with the *p*-phenylphenol in 83% yield (Scheme 1). With the trimers **3** in hand, we first tested the synthesis of the triptycene-derived calix[5]arenes **5** by the heat-induced fragement coupling reactions. Consequently, when the trimer **3a** reacted with the 2,6-dihydroxymethyl-4-*tert*-butylphenol in refluxed xylene for two days, calix[5]arene **5a** could be produced in 25% yield. Under the same conditions, the triptycene-derived calix[5]arenes **5b** and **5c** were obtained in 23% and 21% yield, respectively (Scheme 2). Furthermore, it was found that when **5a**−**c** were treated with BBr_3 in dry CH_2Cl_2 the demethylated compounds **6a**−**c** could be obtained in high yields. Treatment of **6a** and **6b** with $AlCl_3$ in toluene at room temperature resulted in the debutylated products **7a** and **7b** in 82% and 75% yield, respectively. Under the same conditions, we also found that the macrocycles **5a** and **5b** could be not only debutylated but also demethylated to yield **7a** and **7b** in high yields, respectively (Scheme 2).

Scheme 1. Synthesis of the Trimers **3a**,**b**



Scheme 2. Synthesis of the Triptycene-Derived Calix[5]arenes



We first investigated the structures of the triptycene-derived calix[5]arenes **5a**−**c** in solution by ^1H NMR spectroscopy. As shown in Figure 2a, the ^1H NMR spectrum of

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(3) (a) Ikeda, A.; Shinkai, S. *Chem. Rev.* **1997**, *97*, 1713. (b) Shimizu, S.; Moriyama, A.; Kito, K.; Sasaki, Y. *J. Org. Chem.* **2003**, *68*, 2187. (c) Lhoták, P.; Bílá, A.; Budka, J.; Pojarováb, M.; Stibor, I. *Chem. Commun.* **2008**, 1662.

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(6) (a) Zhu, X.-Z.; Chen, C.-F. *J. Am. Chem. Soc.* **2005**, *127*, 13158. (b) Zong, Q.-S.; Chen, C.-F. *Org. Lett.* **2006**, *8*, 211. (c) Han, T.; Chen, C.-F. *Org. Lett.* **2006**, *8*, 1069. (d) Peng, X.-X.; Lu, H.-Y.; Han, T.; Chen, C.-F. *Org. Lett.* **2007**, *9*, 895. (e) Xue, M.; Chen, C.-F. *Chem. Commun.* **2008**, 6128. (f) Xue, M.; Chen, C.-F. *Org. Lett.* **2009**, *11*, 5294.

(7) Tian, X.-H.; Hao, X.; Liang, T.-L.; Chen, C.-F. *Chem. Commun.* **2009**, 6771.

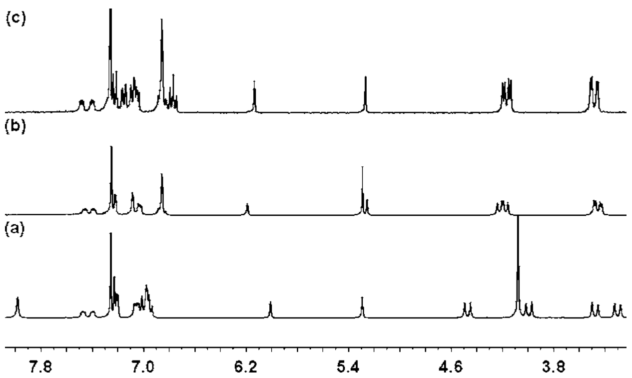

Figure 2. Partial ^{1}H NMR spectra (300 MHz, $CDCl_3$) of (a) **5a**, (b) **6a**, and (c) **7a**.

5a in $CDCl_3$ showed two singlets (2:1 ratio) at 1.18 and 1.29 ppm, respectively, for the *p*-*tert*-butyl groups, one singlet at 3.97 ppm for the methoxyl groups, and two singlets at 5.29 and 6.01 ppm for the bridgehead protons of the triptycene moiety. Especially, two pairs of doublets at 3.30, 3.48, 3.99, and 4.47 ppm for the bridged methylene protons in **5a** were observed, which are quite similar to those of the *p*-*tert*-butylcalix[4]arene with a cone conformation.[1b] Moreover, it was found that the ^{13}C NMR spectrum of **5a** showed only two signals for the *p*-*tert*-butyl carbons, one signal for the methoxyl carbons, two signals for the methylene carbons, and two signals for the bridgehead carbons in the triptycene moiety. The NOE contacts between the bridged methylene protons and the aromatic and hydroxyl protons in **5a** were also observed.[8] In addition, we further found that the IR spectrum of **5a** showed low stretching frequency of the OH bonds (ca. 3303 cm^{-1})[8] similar to that of the *p*-*tert*-butylcalix[4]arene with cone conformation,[5b] indicating that there existed the strong intramolecular hydrogen bonding in **5a**. In the case of the macrocycles **5b**,**c**, they also showed the spectral features similar to those of **5a**.[8] These indicated that the triptycene-derived calix[5]arenes **5a**−**c** containing two dimethoxy groups not only have C_s symmetric structures but also adopt a fixed cone conformation in solution. These results are obviously different from their *p*-*tert*-butylcalix[5]arene analogue with two adjacent methoxyl groups, which showed a highly flexible conformation with the coalescence temperature of −31 °C corresponding to an inversion barrier of 11.1 kcal mol^{-1}.[5c]

Similarly, the ^{1}H NMR spectra of the demethylated compounds **6a** (Figure 2b) and **6b** in $CDCl_3$ also showed two pairs of doublets for the bridged methylene protons. Meanwhile, two signals for the methylene carbons were found in their ^{13}C NMR spectra. These indicated that **6a** and **6b** have the same fixed cone conformation as their precursors **5**. Because **6c** is insoluble in $CDCl_3$, its ^{1}H NMR and ^{13}C NMR spectra were carried out in acetone-d_6,[8] and the results were also consistent with its fixed cone conformation. These triptycene-derived calix[5]arenes are obviously different from their *p*-*tert*-butylcalix[5]arene analogue, in which the signal of the bridged methylene protons showed a broad singlet at room temperature and a pair of doublets at lower temperature.[5a,c] For the debutylated macrocycles **7a** (Figure 2c) and **7b**, their ^{1}H NMR and ^{13}C NMR spectral features for the bridged methylene protons are quite similar to those of their precursors **5** and **6**, indicating that **7a** and **7b** have likewise fixed cone conformations. These cases are also in contrast to their debutylated calix[5]arene analogue, which showed an even more flexible conformation arising from lack of steric hindrance.[9]

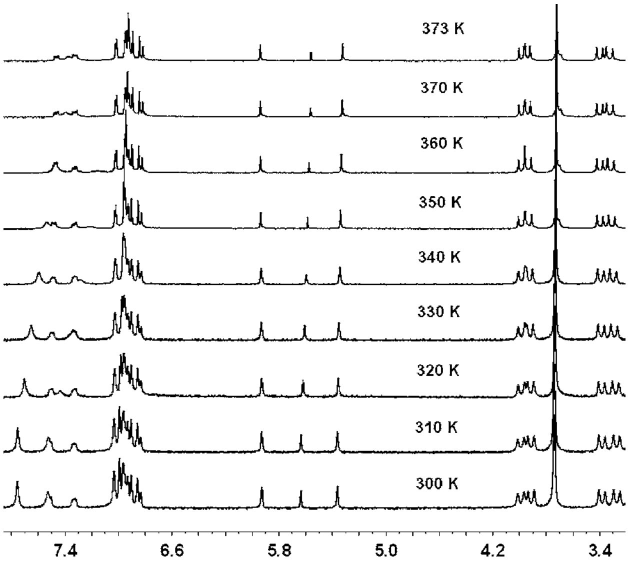

Figure 3. Variable-temperature ^{1}H NMR spectra of **5a** in DMSO-d_6 at 300 MHz.

To further investigate the conformational mobility, the variable-temperature ^{1}H NMR experiments of **5a** in DMSO-d_6 were also carried out. As shown in Figure 3, it was found that no obvious changes of the methylene proton signals in **5a** were observed with the increase of the temperature, which not only is in accord with its fixed conformation but also indicates that the conformational inversion barrier of **5a** is considerably high. Moreover, it was also found that the variable-temperature ^{1}H NMR experiments of **6a** and **7a** showed the results similar to those of **5a**. Therefore, it could be concluded that the significant contributor in determining the conformational mobility of the triptycene-derived calix[5]arenes is not due to the intramolecular hydrogen bonds and the bulky *tert*-butyl groups in the para position of phenol groups but mainly attributed to the introduction of the triptycene moiety with the 3D rigid structure.

We further obtained the single crystals of **5a**[10] and **6a**[11] suitable for X-ray crystallography from a CH_2Cl_2/CH_3OH

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(8) See Supporting Information for details.

(9) Harada, T.; Shinkai, S. *J. Chem. Soc., Perkin Trans. 2* **1995**, 2231.

(10) Crystal data for **5a**·1.5CH_2Cl_2: $C_{57.50}H_{63}Cl_{2.5}O_5$, M = 922.70, triclinic, space group P-1, a = 11.632 (2) Å, b = 11.974 (2) Å, c = 20.206 (4) Å, α = 86.16 (3)°, β = 87.59 (3)°, γ = 64.59 (3)°, V = 2536.3 (9) Å^3, Z = 2, T = 113(2) K, 17 139 reflections measured, 8841 independent, 5617 used. R_1 = 0.0760, wR_2 = 0.2129 ($I > 2\sigma(I)$); R_1 = 0.1117, wR_2 = 0.2410 for all data.

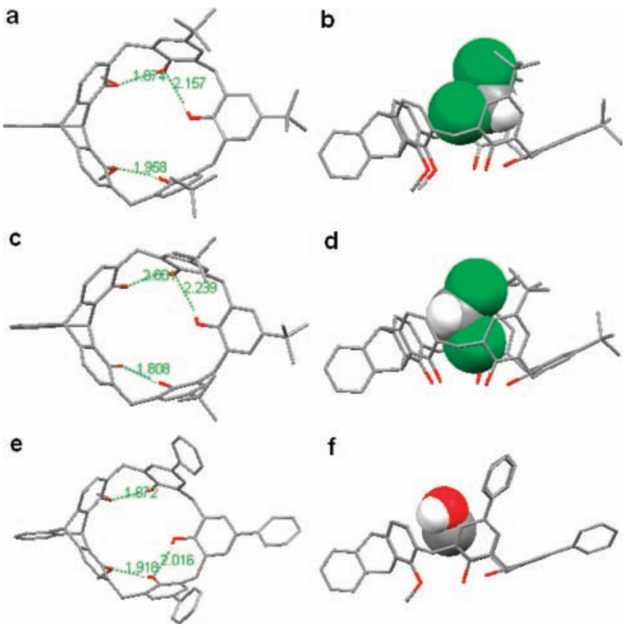

Figure 4. Crystal structures. (a) Top view of **5a** and (b) side view of **5a@**CH_2Cl_2; (c) top view of **6a** and (d) side view of **6a@**CH_2Cl_2; (e) top view of **5c** and (f) side view of **5c@**CH_3OH. Other solvent molecules and hydrogen atoms not involved in the hydrogen bonding interactions are omitted for clarity.

solution and the single crystals of **5c**[12] from a $CHCl_3$ and CH_3OH mixture solution. As shown in Figure 4, the crystal structures of **5a**, **6a**, and **5c** showed that they all adopted cone conformations, which are consistent with the results in solution. For **5a**, the four bridged methylene carbons are coplanar, and the dihedral angle between the coplanar and the phenol ring opposite to the triptycene moiety is 36.7°. The dihedral angle between the two face-to-face phenol rings is 50.75°. The cavity cross-section ranges from 7.94 × 10.88 Å (upper rim) to 6.71 × 7.09 Å (low rim). Moreover, there existed the O−H···O hydrogen bondings between the ether oxygen atoms and their adjacent phenol hydroxyl protons with the distances of 1.96 and 1.87 Å, respectively, and between two adjacent phenol hydroxyl groups with the distance of 2.16 Å. These structural features made **5a** able to easily encapsulate guests inside its cavity. Consequently, it was found that **5a** could encapsulate a CH_2Cl_2 molecule through a pair of C−H···π interactions ($d_{C-H\cdots\pi}$ = 2.898 and 2.895 Å) between the protons of CH_2Cl_2 and the phenol rings (Figure 4b). For the macrocycles **6a** and **5c**, it was found that they showed similar structural features to those of **5a**. The dihedral angles between the coplanar of the four bridged methylene carbons and the phenol ring opposite to the triptycene moiety are 43.4° and 32.6°, respectively. The cavity cross sections of 7.35 × 10.96 Å (upper rim) and 6.64 × 7.18 Å (low rim) for **6a** and 8.12 × 11.08 Å (upper rim) and 6.57 × 7.23 Å (low rim) for **5c** were shown. Moreover, there existed intramolecular hydrogen bondings between the adjacent phenol hydroxyl groups or between the ether oxygen atoms and their adjacent phenol hydroxyl protons, which might play an important role in the formation of their fixed cone conformations. Furthermore, it was also found that a dichloromethane molecule was encapsulated inside the cavity of **6a** (Figure 4d), while in **5c** a methanol molecule was encapsulated inside its cavity (Figure 4f).

In conclusion, we have synthesized a series of novel calix[5]arenes containing one 1,8-dimethoxytriptycene moiety through an efficient fragment coupling strategy and also conveniently obtained their demethylated and debutylated calix[5]arene derivatives in high yields. The structural studies showed that owing to the introduction of the 3D rigid structure of triptycene, the triptycene-derived calix[5]arenes all adopted fixed cone conformations in solution and solid state, which are in contrast to their classical calix[5]arene analogues. Moreover, it was also found that the triptycene-derived calix[5]arenes with fixed cone conformations and large enough cavities could encapsulate dichloromethane and methanol molecules inside their cavities in the solid state. We believe that the results presented here could have wide potential applications in molecular recognitions and assemblies, which are now underway in our laboratory.

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Supporting Information Available: Experimental procedures and characterization data for new compounds. Variable-temperature ^1H NMR spectra of **6a** and **7a**. The X-ray crystallographic files (CIF) for compounds **5a**, **6a**, and **5c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) Crystal data for **6a**·CH_2Cl_2·$2CH_3OH$: $C_{57}H_{66}Cl_2O_7$, M = 934.00, triclinic, space group P-1, a = 11.303 (2) Å, b = 12.251 (3) Å, c = 21.395 (4) Å, α = 75.70 (3)°, β = 79.57 (3)°, γ = 62.73 (3)°, V = 2543.8 (9) Å^3, Z = 2, T = 113(2) K, 18 944 reflections measured, 8932 independent, 6408 used. R_1 = 0.0780, wR_2 = 0.2334 ($I > 2\sigma(I)$); R_1 = 0.1040, wR_2 = 0.2564 for all data.

(12) Crystal data for **5c**·$2CHCl_3$·CH_3OH: $C_{65}H_{54}Cl_6O_6$, M = 1143.78, monoclinic, space group $P2(1)/c$, a = 13.746 (3) Å, b = 16.676 (3) Å, c = 24.705 (5) Å, β = 90.44 (3)°, V = 5662.7 (19) Å^3, Z = 4, T = 173(2) K, 33 309 reflections measured, 9786 independent, 8768 used. R_1 = 0.1220, wR_2 = 0.2673 ($I > 2\sigma(I)$); R_1 = 0.1337, wR_2 = 0.2768 for all data.