ORGANIC LETTERS

2009
Vol. 11, No. 4
923−926

One-Pot Formation and Characterization of Macrocyclic Aromatic Tetrasulfonates

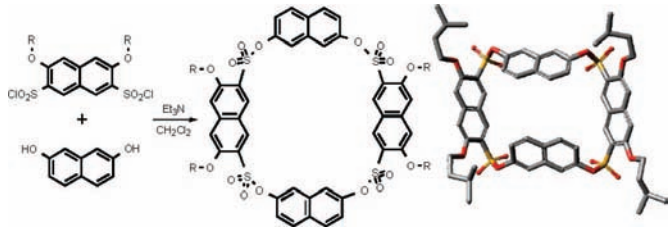
Mingwei Geng,[†] Dechun Zhang,[†] Xiangxiang Wu,[†] Lan He,*[,†] and Bing Gong*[,†,‡]

Colleges of Chemistry and Resources Science and Technology, State Key Laboratory of Earth Surface Processes and Resource Ecology, Beijing Normal University, Beijing 100875, China, and Department of Chemistry, University at Buffalo, The State University of New York, Buffalo, New York 14260

bgong@chem.buffalo.edu; helan1961@yahoo.com.cn

Received December 15, 2008

ABSTRACT



Aromatic tetrasulfonate macrocycles were prepared in one pot by treating arenedisulfonyl chlorides with dihydroxyarenes. X-ray structures revealed that these cyclic molecules have noncollapsible cavities and well-defined conformations resembling the cone and partial cone conformations of calix[4]arenes. Incorporating aromatic residues of different sizes leads to macrocycles with different cavity sizes.

Many cavity-containing macrocyclic compounds have been designed and extensively studied over the last several decades, among which cyclophanes, calixarenes, resorcinarenes, and cyclodextrins have attracted wide attention in developing receptors for various organic molecules.[1−5] Macrocycles with rigid, noncollapsible cavities are particularly interesting because these molecules possess unique properties such as acting as hosts that bind guest molecules with enhanced specificity and strength[6] and providing scaffolds for the presentation of chemical functionality, which lead to efficient catalysts and precise control of intermolecular association.[7] Many strategies have been tested to create molecules with noncollapsible cavities of different sizes and properties. For example, covalent modification of

[†] Beijing Normal University.
[‡] The State University of New York.

(1) (a) Bohmer, V. *Angew. Chem., Int. Ed.* **1995**, *34*, 713. (b) Sanchez-Garcia, D.; Sessler, J. L. *Chem. Soc. Rev.* **2008**, *37*, 215.

(2) (a) Arduini, A.; Pochini, A.; Secchi, A.; Ugozzoli, F. *Calixarenes 2001*; Asfari, Z., Böhmer, V., Harrowfield, J., Vicens, J., Eds.; Kluwer Academic Publishers: Dordrecht, The Netherlands, 2001; Chapter 25. (b) Thondorf, I. *Calixarenes 2001*; Asfari, Z., Böhmer, V., Harrowfield, J., Vicens, J., Eds.; Kluwer Academic Publishers: Dordrecht, The Netherlands, 2001; Chapter 15.

(3) Dalla Cort, A.; Mandolini, L. *Calixarenes in Action*; Mandolini, L., Ungaro, R., Eds.; Imperial College Press: London, 2000; Chapter 5.

(4) Rebek, J. *Chem. Commun.* **2000**, 637–643.

(5) Some examples of other macrocycles and assemblies: (a) Gallant, A. J.; MacLachlan, M. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 5307. (b) Jiang, H.; Leger, J.-M.; Guionneau, P.; Huc, I. *Org. Lett.* **2004**, *6*, 2985. (c) Höger, S. *Chem.−Eur. J.* **2004**, *10*, 1320. (d) Yuan, L. H.; Feng, W.; Yamato, K.; Sanford, A. R.; Xu, D. G.; Guo, H.; Gong, B. *J. Am. Chem. Soc.* **2004**, *126*, 11120. (e) Xing, L. Y.; Ziener, U.; Sutherland, T. C.; Cuccia, L. A. *Chem. Commun.* **2005**, 5751. (f) Zhang, W.; Moore, J. S. *J. Am. Chem. Soc.* **2005**, *127*, 11863. (g) Rotger, C.; Pina, M. N.; Vega, M.; Ballester, P.; Deya, P. M.; Costa, A. *Angew. Chem., Int. Ed.* **2006**, *45*, 6844. (h) Sakamoto, J.; Schluter, A. D. *Eur. J. Org. Chem.* **2007**, 2700. (i) Campbell, F.; Plante, J.; Carruthers, C.; Hardie, M. J.; Prior, T. J.; Wilson, A. J. *Chem. Commun.* **2007**, 2240. (j) Shin, S. B. Y.; Yoo, B.; Todaro, L. J.; Kirshenbaum, K. *J. Am. Chem. Soc.* **2007**, *129*, 3218. (k) Zhu, Y. Y.; Li, C.; Li, G. Y.; Jiang, X. K.; Li, Z. T. *J. Org. Chem.* **2008**, *73*, 1745. (l) Alfonso, I.; Bolte, M.; Bru, M.; Burguete, M. I.; Luis, S. V.; Rubio, J. *J. Am. Chem. Soc.* **2008**, *130*, 6137.

(6) (a) Arduini, A.; McGregor, W. M.; Pochini, A.; Secchi, A.; Ugozzoli, F.; Ungaro, R. *J. Org. Chem.* **1996**, *61*, 6881. (b) Arduini, A.; Van Hoorn, W. P.; Morshuis, M. G.; van Veggel, F. C. J. M.; Reinhoudt, D. N. *J. Phys. Chem. A* **1998**, *102*, 1130. (c) Kusano, T.; Tabatabai, M.; Okamoto, Y.; Böhmer, V. *J. Am. Chem. Soc.* **1999**, *121*, 378. (d) Vysotsky, M. O.; Mogck, O.; Rudzevich, Y.; Shivanyuk, A.; Böhmer, V.; Brody, M. S.; Cho, Y. L.; Rudkevich, D. M.; Rebek, J. *J. Org. Chem.* **2004**, *69*, 6115.

(7) Rudzevich, Y.; Vysotsky, M. O.; Böhmer, V.; Brody, M. S.; Rebek, J.; Broda, F.; Thondorf, I. *Org. Biomol. Chem.* **2004**, *2*, 3080.

10.1021/ol8028884 CCC: $40.75
Published on Web 01/16/2009

resorcinarenes has led to rigid, deep cavitands that completely encapsulate sizable molecules.[8] Numerous self-assembling structures have been developed based on cyclodextrins.[9] Herein we would like to report the preparation, characterization, and solid-state structures of a new class of macrocyclic molecules with aromatic oligosulfonate backbones containing noncollapsible cavities surrounded by four aromatic residues of adjustable sizes.

The current work stemmed from a class of aromatic oligosulfonamide macrocycles that were discovered by us in recent years.[10] The oligosulfonamide macrocycles, as exemplified by **1** (Figure 1a), consisting of four aromatic

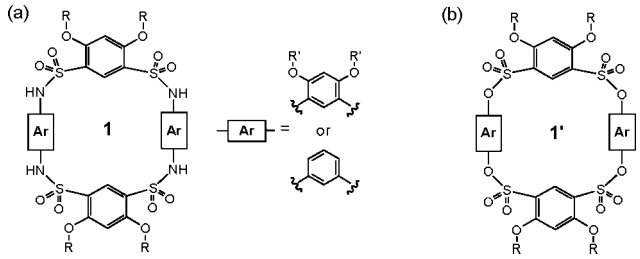
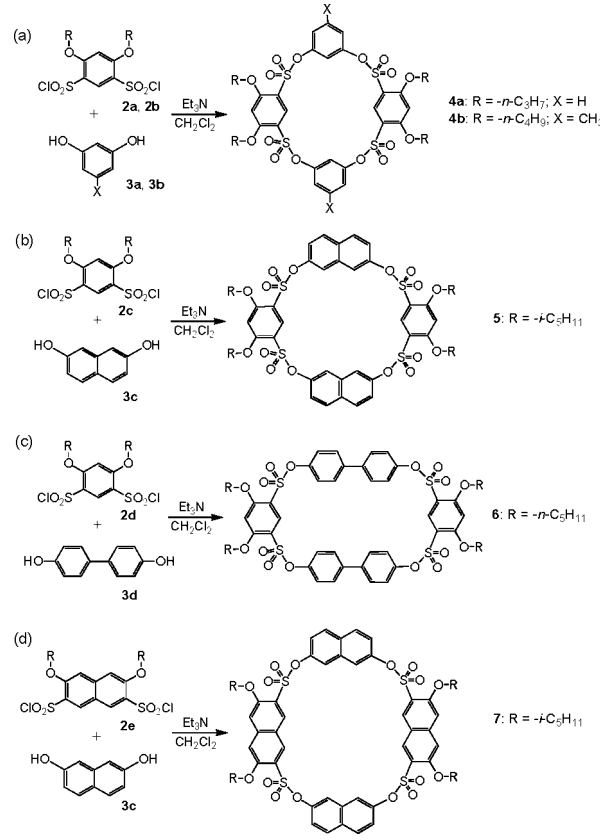


Figure 1. (a) NH groups of macrocyclic sulfonamides **1** are not involved in any intra- or intermolecular H-bonding interaction,[10] which implies that replacing the NH groups with O atoms might lead to (b) the macrocyclic oligosulfonate shown by the general structure **1′**.

(benzene or naphthalene) residues connected by sulfonamide linkages, were found to adopt stable, conelike conformations. The crystal structures of these cyclic tetrasulfonamides revealed that the NH groups of the sulfonamide moieties pointed away from the center of the cavity and were not involved in any intramolecular or intermolecular hydrogen bonding interactions. This observation seemed to suggest that the sulfonamide H atoms of **1**, in contrast to the original expectation of participating in intramolecular H-bonding, might not play any role in shaping the overall conformations of these macrocycles. This hypothesis in turn suggests that replacing the NH groups of a cyclic tetrasulfonamide like **1** with atoms of a similar size, such as oxygen, could lead to a new series of aromatic sulfonate macrocycles **1′**. Thus, similarly to the synthesis of macrocyclic sulfonamides such as **1**, a one-step reaction between an arenedisulfonyl chloride and a dihydroxyarene might lead to the formation of an aromatic oligosulfonate macrocycle.

This possibility was first probed by treating the readily available resorcinol **3a** with 4,6-dipropyloxy-1,3-benzenedisulfonyl chloride **2a**[10] in CH_2Cl_2 in the presence of triethylamine (Scheme 1a).[11] Thus, resorcinol (2 mM) and

Scheme 1. One-Step Formation of Aromatic Tetrasulfonate Macrocycles



2a (2 mM) were dissolved in CH_2Cl_2 (30 mL), followed by the addition of triethylamine (4 mM) at room temperature. The reaction mixture was then heated under reflux overnight (12−24 h). After removing solvent, the crude product was purified by using column chromatography on silica gel (petroleum: EtOAc = 1.5:1, R_f = 0.11 by TLC on silica gel) leading to the purified product as a white solid (22%). The purified product **4a** was then analyzed by using techniques including MALDI and ^1H and ^{13}C NMR experiments,[11] which fully established the cyclic nature of **4a**.

The successful preparation of macrocycle **4a** prompted us to explore the generality of such a one-step synthesis. Reactions between the commercially available dihydroxyarenes **3b**−**d** with benzenedisulfonyl chlorides **2b** and **2c** or with naphalenedisulfonyl chloride **2d**, which was prepared from the commercially available 3,6-dihydroxynaphthalene-2,7-disulfonic acid disodium salt, were carried out under the same conditions for preparing **4a** (Scheme 1).[11] Products **4b**, **5**, **6**, and **7** were isolated and purified using column chromatography on silica gel, with yields ranging from 16% to 35%.[11] These compounds were characterized based on

(8) Hooley, R. J.; Rebek, J. *J. Am. Chem. Soc.* **2005**, *127*, 11904.

(9) (a) Wenz, G. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 803–822. (b) Harada, A. *Acc. Chem. Res.* **2001**, *34*, 456–464.

(10) (a) He, L.; An, Y.; Yuan, L. H.; Yamato, K.; Feng, W.; Gerlitz, O.; Zheng, C.; Gong, B. *Chem. Commun.* **2005**, 3788. (b) He, L.; An, Y.; Yuan, L. H.; Feng, W.; Li, M. F.; Zhang, D. C.; Yamato, K.; Zheng, C.; Zeng, X. C.; Gong, B. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 10850.

(11) See Supporting Information.

MALDI and ^{1}H and ^{13}C NMR experiments, data from which provided conclusive evidence confirming their cyclic structures.[11] It needs to be pointed out that these compounds were prepared and purified for the purpose of confirming their formation from the one-step reactions. No special efforts have thus far been attempted to optimize their yields. Nevertheless, strategies such as performing the reactions under high dilution conditions or in the presence of potential templates should greatly improve the yields of these macrocycles, allowing their preparation on large scales.

Thus, similar to the one-step preparation of macrocyclic aromatic tetrasulfonamides we reported before, aromatic tetrasulfonate macrocycles can also be obtained from the one-step reactions involving arenedisulfonyl chloride and dihydroxyarenes. The fact that different arenesulfonyl chlorides and dihydroarenes all led to the formation of the macrocyclic tetrasulfonates demonstrates that this is a general approach that allows the convenient preparation of a new series of macrocycles containing cavities surrounded by four aromatic rings. The cavity size can be easily tuned by incorporating aromatic residues of different sizes.

During the isolation and purification of these new macrocycles, it was noticed that many of these molecules were prone to crystallization, giving high-quality single crystals suitable for analysis by X-ray crystallography. Therefore, before performing detailed but time-consuming structural analysis in solution, we decided to first determine the crystal structures of these macrocycles, which led to a direct examination and comparison of the conformations and cavity sizes of these new porous molecules in atomic details.

Single crystals of **4a** suitable for study by X-ray crystallography were obtained by slow evaporation of solvent (acetone/petroleum ether = 10/1). The X-ray structure is shown in Figure 2a. In the solid state, the structure of **4a** (Figure 2a, left) is reminiscent of the cone conformation of calix[4]arene. A difference between the cone conformation of calix[4]arene and that of **4a** is that, in the crystal structure of **4a**, the two aromatic residues derived from resorcinol incline toward the center of the cavity by approaching each other from their unsubstituted sides that are not attached to the sulfonate groups (Figure 2, right), leading to the "capping" of the internal cavity.

The single crystals of compounds **4b**, **5**, **6**, and **7** were also obtained, based on which the corresponding crystal structures were determined.[11] Because of their different aromatic residues, these macrocycles have cavities of different dimensions that are indicated by their widths and lengths (Table 1).

Table 1. Cavity Dimensions[a] of Macrocycles **4**−**7** Based on Crystal Structures

	4a	**4b**	**5**	**6**	**7**
width (Å)	5.55	5.78	5.26	6.64	6.76
length (Å)	7.90	6.72	10.64	11.55	11.09

[a] Measured as the centroid distances between nonadjacent aromatic rings of each macrocycle.

As expected, the cavity size of a macrocycle can be tuned by incorporating aromatic residues of different dimensions (Figure 2, top views). Thus, the cavities of macrocycles **4a**

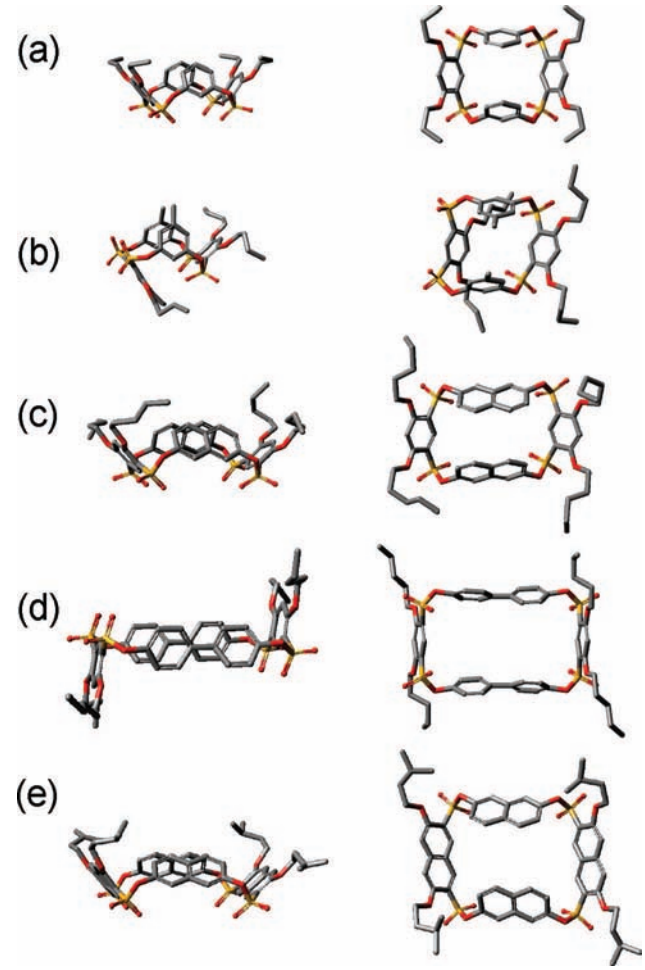


Figure 2. Side (left) and top (right) views of the crystal structures of (a) **4a**, (b) **4b**, (c) **5**, (d) **6**, and (e) **7**. Hydrogen atoms are deleted for clarity.

and **4b**, which are surrounded by benzene residues, are the smallest among the five macrocycles. Incorporating naphthalene or biphenyl residues leads to the rectangular cavitites of **5** and **6**. Surprisingly, macrocycle **7**, with all four residues derived from naphthalene, has a cavity with dimension similar to that of **6**.

A closer examination of the conformation of **7** revealed that the unexpected small width of its cavity was due to the inward inclination of its two residues derived from 2,7-dihydroxynaphthalene, which reduce the centroid distance between these two naphthalene rings (Figure 2e, top view). The same inward inclination of naphthalene rings was also observed for **6**, which defines the width of its cavity. In fact, macrocycles **4a**, **5**, and **7** share the similar "cone" conformations in which two nonadjacent residues derived from dihydroxyarenes tilt inwardly, leading to the capping and reduction of their cavities. This phenomenon is probably

associated with the need of these molecules to partially fill the "vaccum" created by the cavity formed by the rigid macrocyclic backbones. In spite of the absence of sufficiently large guest molecules, none of these cavities collapses in the solid state, demonstrating the robustness of these macrocyclic structures. By growing cocrystals in the presence of appropriate guest species, it will be interesting to probe how much these molecules will be able to accommodate different guest molecules by adjusting their conformations.

In contrast to the cone conformation shared by **4a**, **5**, and **7**, compound **6** adopts a conformation in which the two benzenedisulfonyl residues lie above and below the plane as defined by the four sulfur atoms (Figure 2d, right). Even more interesting is the conformation of **4b**. In spite of its close similarity to **4a** that adopts a cone conformation, macrocycle **4b** adopts a conformation reminiscent of the partial cone conformation of calix[4]arenes, in which one of the benzenedisulfonyl residues flips downward (Figure 2b, side view). These results indicate that it may be possible to control the conformations of these aromatic tetrasulfonate macrocycles based on subtle structural modification. Elucidating the rules governing such conformational change would be invaluable in designing molecules with conformations suitable for various applications.

The packing of the five molecules in their solid state structures reveals an interesting trend. Except for compound **4b**, the other four compounds all align along either exactly or roughly the same direction, leading to the formation of channels in the extended structures. The packing of **4b** is different, with no obvious columns or channels observed in its solid state strcture. Details of the crystal packing, the solution conformation, and other properties of these molecules are currently being investigated.

In summary, this paper reports the one-step preparation and characterization of macrocyclic aromatic tetrasulfonates, a new series of porous molecules containing robust cavities. These molecules were conveniently prepared from the one-step reaction between arenedisulfonyl chlorides and dihydroxyarenes. Given the ready availability of various arenedisulfonic acids and dihydroxyarenes, the described method allows the preparation of macrocyclic tetrasulfonates with a wide range of cavity sizes. Examining the crystal structures of these macrocycles revealed that they all contain well-defined cavities in the absence of complexed guest molecules. The conformations of these molecules in the solid state are similar to the cone or partial cone conformations of calix[4]arenes. Molecules such as **4a** and **4b**, with very small difference in their structures, adopt different conformations. Efforts are being made to elucidate the factors influencing the conformation in each case, which could lead to the rational design of novel cavity-containing molecules of defined shapes.

Acknowledgment. This work was supported by the Changjiang Scholar Program and the Cultivation Fund of the Key Scientific and Technical Innovation Project, Ministry of Education of China Grant 706009 (to BG), the NSFC Grant 20672015 and 20772012, RFDP Grant 20070027038 and Beijing NSFC Grant 2073024 (to L.H.), and National Science Foundation Grant CHE-0314577 (to B.G.). The Beijing Municipal Commission of Education and the Beijing New Medical Discipline Based Group (XK100270569).

Supporting Information Available: Experimental procedures, analytical data, copies of MALDI and ^{1}H and ^{13}C NMR spectra, and X-ray data of **4a**, **4b**, **5**, **6**, and **7** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

OL8028884