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Benzo-21-Crown-7/Secondary Dialkylammonium Salt [2]Pseudorotaxane- and [2]Rotaxane-Type Threaded Structures

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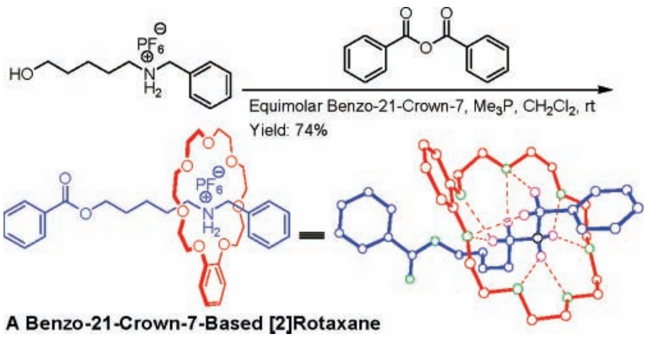
ABSTRACT



A Benzo-21-Crown-7-Based [2]Rotaxane

We demonstrate that secondary dialkylammonium salts can thread through the cavity of benzo-21-crown-7 to form [2]pseudorotaxanes with binding constants (527–1062 M^{-1} in acetone) higher than the corresponding values (135–261 M^{-1} in acetone) of the analogous complexes with their traditionally used host, dibenzo-24-crown-8. Based on this new benzo-21-crown-7/secondary dialkylammonium salt recognition motif, a [2]rotaxane was successfully prepared. The formation of these threaded structures was confirmed by proton NMR spectroscopy, electrospray ionization mass spectrometry, and X-ray single crystal analysis.

Threaded structures have been attractive to scientists not only because of their topological importance but also due to their many potential applications.[1] Crown ethers and their derivatives have been widely used in preparing threaded structures as hosts for organic salts, such as paraquat derivatives[2] and secondary dialkylammonium salts.[3] The threading of secondary dialkylammonium salts through the cavity of crown ethers was the genesis of a diverse range of interlocked molecules including molecular machines.[4] How big a mac-

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(1) Raymo, F. M.; Stoddart, J. F. *Chem. Rev.* **1999**, *99*, 1643−1663. (b) Huang, F.; Fronczek, F. R.; Gibson, H. W. *J. Am. Chem. Soc.* **2003**, *125*, 9272−9273. (c) Huang, F.; Gibson, H. W.; Bryant, W. S.; Nagvekar, D. S.; Fronczek, F. R. *J. Am. Chem. Soc.* **2003**, *125*, 9367−9371. (d) Wang, L.; Vysotsky, M. O.; Bogdan, A.; Bolte, M.; Boehmer, V. *Science* **2004**, *304*, 1312−1314. (e) Qu, D.-H.; Wang, Q.-C.; Tian, H. *Angew. Chem., Int. Ed.* **2005**, *44*, 2−5. (f) Huang, F.; Gibson, H. W. *Prog. Polym. Sci.* **2005**, *30*, 982−1018. (g) Sindelar, V.; Silvi, S.; Kaifer, A. E. *Chem. Commun.* **2006**, 2185−2187. (h) Liu, Y.; Li, X.-Y.; Zhang, H.-Y.; Li, C.-J.; Ding, F. *J. Org. Chem.* **2007**, *72*, 3640−3645. (i) Loeb, S. J. *Chem. Soc. Rev.* **2007**, *36*, 226−235. (j) Serreli, V.; Lee, C. F.; Kay, E. R.; Leigh, D. A. *Nature* **2007**, *445*, 523−527. (k) Kay, E. R.; Leigh, D. A.; Zerbetto, F. *Angew. Chem., Int. Ed.* **2007**, *46*, 72−191. (l) Han, T.; Zong, Q.-S.; Chen, C.-F. *J. Org. Chem.* **2007**, *72*, 3108−3111. (m) Hidalgo Ramos, P.; Coumans, R. G. E.; Deutman, A. B. C.; Smits, J. M. M.; de Gelder, R.; Elemans, J. A. A. W.; Nolte, R. J. M.; Rowan, A. E. *J. Am. Chem. Soc.* **2007**, *129*, 5699−5702. (n) Nygaard, S.; Hansen, S. W.; Huffman, J. C.; Jensen, F.; Flood, A. H.; Jeppesen, J. O. *J. Am. Chem. Soc.* **2007**, *129*, 7354−7363.

(2) Huang, F.; Jones, J. W.; Slebodnick, C.; Gibson, H. W. *J. Am. Chem. Soc.* **2003**, *125*, 14458−14464. Long, B.; Nikitin, K.; Fitzmaurice, D. *J. Am. Chem. Soc.* **2003**, *125*, 15490−15498. Huang, F.; Zakharov, L. N.; Rheingold, A. L.; Ashraf-Khorassani, M.; Gibson, H. W. *J. Org. Chem.* **2005**, *70*, 809−813. Badjic, J. D.; Ronconi, C. M.; Stoddart, J. F.; Balzani, V.; Silvi, S.; Credi, A. *J. Am. Chem. Soc.* **2006**, *128*, 1489−1499. Roithova, J.; Milko, P.; Ricketts, C. L.; Schroeder, D.; Besson, T.; Dekoj, V.; Belohradsky, M. *J. Am. Chem. Soc.* **2007**, *129*, 10141−10148.

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rocycle should be for threading to occur is a basic and important question in threaded structure chemistry.[3a] For a long time, it has been widely accepted that a macrocycle needs at least 24 C, N, O, or S atoms for the threading of an alkyl group into its cavity,[1a,3a,4a,5] although Schill et al.[6a,b] reported very low yields of rotaxanes by statistical threading of 21-membered and 23-membered macrocycles more than two decades ago, and more recent results suggest that 20-membered macrocycles can be threaded[6c] and demonstrate that some dibenzo-22- and 23-membered[6d] crown ethers interact only weakly with secondary ammonium ions (but without proof of threading). Dibenzo-24-crown-8 (**DB24C8**) derivatives are the most widely used hosts for secondary dialkylammonium salts.[3,4] Crown ethers with less than 24 atoms in their macrorings have been observed to form face-to-face complexes with secondary dialkylammonium salts.[7] However, herein, we have found that secondary dialkylammonium salts can thread through the cavity of benzo-21-crown-7 (**B21C7**) to form [2]pseudorotoaxane- and [2]-rotaxane-type threaded structures.

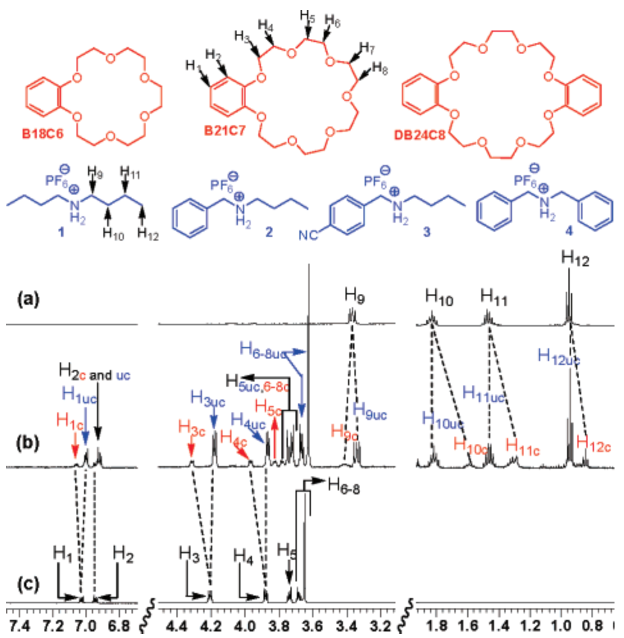

Figure 1. Partial ^{1}H NMR spectra (500 MHz, acetone-d_6, 22 °C) of 1.00 mM secondary dialkylammonium salt **1** (a), 1.00 mM **B21C7** and **1** (b), and 1.00 mM **B21C7** (c). Complexed and uncomplexed species are denoted by “c” and “uc”, respectively.

The ^{1}H NMR spectrum (Figure 1) of an equimolar solution of **B21C7** and dibutylammonium salt **1 in** acetone-d_6 shows three sets of resonances for uncomplexed **B21C7**, uncomplexed **1**, and the complex between **B21C7** and **1**, indicating slow-exchange complexation on the ^{1}H NMR time scale.[3a] This implied the threading of **1** through the cavity of **B21C7** to form a pseudorotaxane. In the same way, complexations of **B21C7** with secondary ammonium salts **2** and **3** were also found to be slow-exchange systems. From integrations of all peaks, the stoichiometries of all three complexation systems were determined to be 1:1. The association constants (K_a) of 1:1 complexes,[8] **B21C7·1**, **B21C7·2**, and **B21C7·3** in acetone-d_6 are 527 (±4) M^{-1}, 615 (±36) M^{-1}, and 1062 (±102) M^{-1}, respectively. These values are higher than the corresponding K_a values of 135 (±6) M^{-1},[9] 155 (±8) M^{-1}, and 261 (±13) M^{-1} for **DB24C8**-based complexes[8] **DB24C8·1**, **DB24C8·2**, and **DB24C8·3** and the previously reported K_a value, 360 M^{-1},[3a] for **DB24C8·4** in acetone-d_6, indicating that secondary dialkylammonium salts fit the cavity of **B21C7** better than the cavity of **DB24C8** so more efficient hydrogen bonding interactions can form. The K_a increase from **B21C7·1** to **B21C7·2** to **B21C7·3** is a result of the acidity increase of *N*-methylene and ammonium hydrogens due to the increasing electron-withdrawing ability from propyl to phenyl to *p*-cyanophenyl substituents.

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(3) (a) Ashton, P. R.; Chrystal, E. J. T.; Glink, P.; Menzer, T. S.; Schiavo, C.; Spencer, N.; Stoddart, J. F.; Tasker, P. A. White, A. J. P.; Williams, D. J. *Chem. Eur. J.* **1996**, *2*, 709−728. (b) Ashton, P. R.; Fyfe, M. C. T.; Schiavo, C.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Tetrahedron Lett.* **1998**, *39*, 5455−5458. (c) Cantrill, S. J.; Fyfe, M. C. T.; Heiss, A. M.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Org. Lett.* **2000**, *2*, 61−64. (d) Tachibana, Y.; Kawasaki, H.; Kihara, N.; Takata, T. *J. Org. Chem.* **2006**, *71*, 5093−5104.

(4) (a) Amabilino, D. B.; Stoddart, J. F. *Chem. Rev.* **1995**, *95*, 2725−2828. (b) Glink, P. T.; Oliva, A. I.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 1870−1875. (c) Tachibana, Y.; Kihara, N.; Furusho, Y.; Takata, T. *Org. Lett.* **2004**, *6*, 4507−4509. (d) Badjic, J. D.; Ronconi, C. M.; Stoddart, J. F.; Balzani, V.; Silvi, S.; Credi, A. *J. Am. Chem. Soc.* **2006**, *128*, 1489−1499. (e) Chiu, C.-W.; Lai, C.-C.; Chiu, S.-H. *J. Am. Chem. Soc.* **2007**, *129*, 3500−3501.

(5) *Molecular Catenanes, Rotaxanes and Knots*; Sauvage, J.-P., Dietrich-Buchecker, C. O., Eds.; Wiley-VCH: Weinheim, Germany, 1999. Cantrill, S. J.; Pease, A. R.; Stoddart, J. F. *J. Chem. Soc., Dalton Trans.* **2000**, 3715−3734. Hubin, T. J.; Busch, D. H. *Coord. Chem. Rev.* **2000**, *200−202*, 5−52. Takata, T.; Kihara, N. *Rev. Heteroatom Chem.* **2000**, *22*, 197−218. Mahan, E.; Gibson, H. W. In *Cyclic Polymers*, 2nd ed.; Semlyen, J. A., Ed.; Kluwer Publishers: Dordrecht, The Netherlands, 2000; pp 415−560. Panova, I. G.; Topchieva, I. N. *Russ. Chem. Rev.* **2001**, *70*, 23−44.

(6) (a) Schill, G.; Beckmann, W.; Vetter, W. *Chem. Ber.* **1980**, *113*, 941−54. (b) Schill, G.; Beckmann, W.; Schweickert, N.; Fritz, H. *Chem. Ber.* **1986**, *119*, 2647−2655. (c) Gibson, H. W.; Nagvekar, D. S.; Yamaguchi, N.; Bhattarcharjee, S.; Wang, H.; Vergne, M.; Hercules, D. M. *Macromolecules* **2004**, *37*, 7514−7529. (d) Tokunaga, Y.; Yoshioka, M.; Nakamura, T.; Goda, T.; Nakata, R.; Kakuchi, S.; Shimomura, Y. *Bull. Chem. Soc. Jpn.* **2007**, *80*, 1377−1382.

(7) Metcalfe, J. C.; Stoddart, J. F.; Jones, G. *J. Am. Chem. Soc.* **1977**, *99*, 8317−8319. Metcalfe, J. C.; Stoddart, J. F.; Jones, G.; Atkinson, A.; Kerr, I. S.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1980**, 540−543. Abed-Ali, S. S.; Brisdon, B. J.; England, R. *J. Chem. Soc., Chem. Commun.* **1987**, 1565−1566. Cantrill, S. J.; Pease, A. R.; Stoddart, J. F. *J. Chem. Soc., Dalton Trans.* **2000**, 3715−3734.

(8) The K_a values of **B21C7**-based complexes, slow-exchange complexation systems, were calculated from integrations of complexed and uncomplexed peaks. The K_a values of **DB24C8**-based complexes, fast-exchange complexation systems, were calculated from chemical shift changes. All of these K_a values are at 1.00 mM host and guest in acetone. Though **DB24C8·1**, **DB24C8·2**, and **DB24C8·3** are fast-exchange complexation systems, **DB24C8·4** is a slow exchange complexation system. These were also observed by Stoddart et al.[3a] From these, we can know whether a complexation system is fast-exchange or slow-exchange is mainly dependent on the relative sizes of the end groups of the guest.

(9) The K_a values reported in ref 3a for **DB24C8·1** is 50 M^{-1} by proton NMR titration and 70 M^{-1} by proton NMR dilution in acetonitrile.

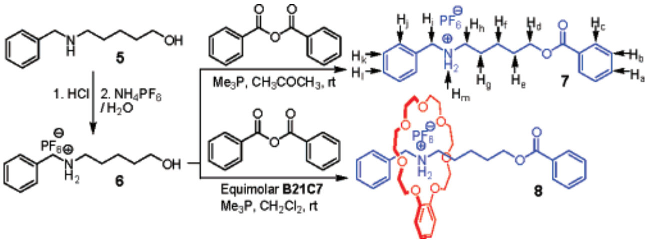
(10) From Figure 3, it is obvious that the benzene ring of **B21C7** is not a required part for the threading of secondary ammonium salts through the caviety of **B21C7**. Therefore, 21-crown-7, the corresponding crown ether without a benzene ring, should also be able to form threaded structures with secondary ammonium salts. Previously, Loeb et al. found that both of **DB24C8** and 24-crown-8 can complex *N*-benzylanilinium salts (Loeb, S. J.; Tiburcio, J.; Vella. S. J. *Org. Lett.* **2005**, *7*, 4923−4926).

Electrospray ionization (ESI) mass spectra of equimolar acetone solutions of **B21C7** and each of **1**, **2**, and **3** confirmed the 1:1 stoichiometries. A common mass fragment of [**M** − PF_6]$^+$ was found: *m*/*z* 486.1 (37%) for **B21C7·1**, 520.1 (100%) for **B21C7·2**, and 545.0 (55%) for **B21C7·3**. For both **B21C7·1** and **B21C7·3** the base peak is at *m*/*z* 379.0, corresponding to [**B21C7** + Na]$^+$.

Furthermore, we found that secondary dialkylammonium salts cannot thread through the cavity of benzo-18-crown-6 (**B18C6**) based on proton NMR characterizations; neither chemical shift changes nor signal doubling occurred upon mixing **B18C6** and **1** in acetone-d_6. Therefore, **B21C7** is the smallest benzocrown ether which is capable of forming threaded structures with secondary dialkylammonium salts.[10] In the same way, we found dibenzylammonium salt **4** cannot thread through the cavity of **B21C7**; thus, the phenyl group is big enough to work as a stopper for **B21C7**.

We then prepared rotaxane **8** using two phenyl groups as the stoppers (Scheme 1). While **6** is only slightly soluble in dichloromethane, it becomes soluble in this solvent after the addition of 1 molar equiv of **B21C7**, indicating the formation of a stable complex **B21C7·6**. An equimolar dichloromethane solution of **B21C7** and **6** was treated with benzoic anhydride in the presence of trimethylphosphine as the catalyst[3d] to afford rotaxane **8** in 74% yield. Partial proton NMR spectra of the dumbbell-shaped component **7**, rotaxane **8** and **B21C7** in DMSO-d_6 are shown in Figure 2. The aromatic protons H_1 and H_2 and ethyleneoxy protons H_3 and H_4 of **B21C7** and methylene protons H_d, H_h, and H_i on **7** moved downfield after the formation of rotaxane **8**. These chemical shift changes, which persisted even after the ammonium site was neutralized by triethylamine, in DMSO proved that **8** is a rotaxane, since no complexation is expected in this highly polar solvent.[3a] The ESI mass spectrum of rotaxane **8** has a single peak at *m*/*z* 654.4 (100%) corresponding to [**8** − PF_6]$^+$.

Scheme 1. Synthesis of Dumbbell-Shaped Component **7** and Rotaxane **8**



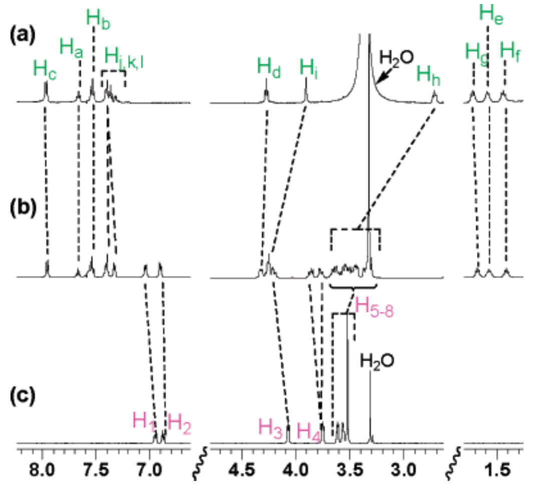


Figure 2. Partial ^1H NMR spectra (500 MHz, DMSO-d_6, 22 °C) of dumbbell-shaped component **7** (a), rotaxane **8** (b), and **B21C7** (c).

The formation of [2]rotaxane **8** was further confirmed by X-ray crystallographic analysis (Figure 3) of a colorless single-crystal grown by vapor diffusion of petroleum ether into an ethyl acetate solution of **8**. All four *N*-methylene hydrogens and two *N*-H hydrogens of dumbbell-shaped component **7** are involved in nine hydrogen bonds (Figure 3) with the oxygen atoms of **B21C7**, indicating the good size fit between the host and guest.

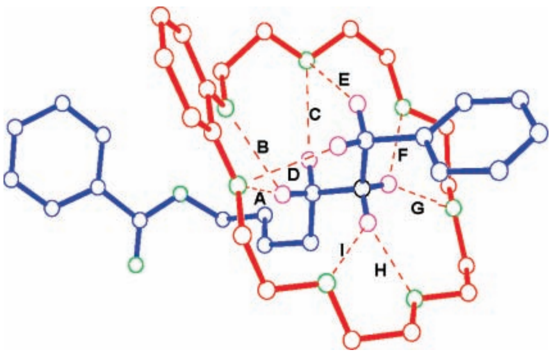


Figure 3. Crystal structure of the [2]rotaxane **8**. A PF_6 counterion and hydrogens except the ones involved in hydrogen bonding have been omitted for clarity. **B21C7** is red, **7** is blue, hydrogens are magenta, oxygens are green, and nitrogen is black. Hydrogen-bond parameters: H···O distances (Å), C(N)−H···O angles (deg) **A**, 2.48, 152; **B**, 2.48, 122; **C**, 2.43, 150; **D**, 2.56, 144; **E**, 2.72, 144; **F**, 2.50, 129; **G**, 2.04, 154; **H**, 2.11, 140; **I**, 2.33, 139.

In summary, our successful preparation of **B21C7**-based [2]pseudorotaxane- and [2]rotaxane-type threaded structures proves that macrocycles consisting of less than 24 atoms can be threaded by alkyl groups. Furthermore, we found that **B21C7** can bind secondary dialkylammonium salts more strongly than the traditional crown ether host **DB24C8**. Because **B21C7** is smaller than **DB24C8**, it is easier to find stoppers for preparation of rotaxanes based on **B21C7** instead of **DB24C8**. Considering the easy availability of benzo-21-crown-7 derivatives and secondary dialkylammonium salts and the efficient binding between them, we believe that the work presented here will stimulate further studies on threaded structures based on the benzo-21-crown-7/secondary dialkylammonium salt recognition motif.

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Supporting Information Available: Synthetic procedures, characterizations, and crystal data for rotaxane **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

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