## ORGANIC LETTERS 2007 Vol. 9, No. 26

5553-5556

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

Chuanju Zhang, Shijun Li, Jinqiang Zhang, Kelong Zhu, Ning Li, and Feihe Huang\*

Department of Chemistry, Zhejiang University, Hangzhou 310027, P. R. China

fhuang@zju.edu.cn

Received October 14, 2007

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.<sup>1</sup> Crown ethers and their derivatives have been widely used in preparing threaded structures as hosts for organic salts, such as paraquat derivatives<sup>2</sup> and secondary dialkylammonium salts.<sup>3</sup> 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.<sup>4</sup> How big a mac-

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.; Bronczek, F. R. J. Am. Chem. Soc. 2003, 125, 9367–9371. (d)
 Vang, 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.; 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)
 Loep, S. J. Chem. 2007, 445, 523–527. (k)
 Kay, E. R.; Leigh, D. A.; Zerbetto, F. Angew. Chem., Int. Ed. 2007, 72, 3108–3111. (m)
 Hiadgo 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.

<sup>(2)</sup> 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.

rocycle should be for threading to occur is a basic and important question in threaded structure chemistry.<sup>3a</sup> 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 20membered macrocycles can be threaded<sup>6c</sup> and demonstrate that some dibenzo-22- and 23-membered<sup>6d</sup> 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.<sup>3,4</sup> Crown ethers with less than 24 atoms in their macrorings have been observed to form faceto-face complexes with secondary dialkylammonium salts.<sup>7</sup> However, herein, we have found that secondary dialkylammonium salts can thread through the cavity of benzo-21crown-7 (B21C7) to form [2]pseudorotoaxane- and [2]rotaxane-type threaded structures.

The <sup>1</sup>H NMR spectrum (Figure 1) of an equimolar solution



Figure 1. Partial <sup>1</sup>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.

of **B21C7** and dibutylammonium salt **1** in acetone- $d_6$  shows three sets of resonances for uncomplexed **B21C7**, uncom-

plexed 1, and the complex between B21C7 and 1, indicating slow-exchange complexation on the <sup>1</sup>H NMR time scale.<sup>3a</sup> 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<sub>a</sub>) of 1:1 complexes,<sup>8</sup> B21C7·1, B21C7·2, and B21C7·3 in acetone- $d_6$  are 527 (±4) M<sup>-1</sup>, 615 (±36) M<sup>-1</sup>, and 1062  $(\pm 102)$  M<sup>-1</sup>, respectively. These values are higher than the corresponding  $K_a$  values of 135 (±6) M<sup>-1</sup>,<sup>9</sup> 155 (±8)  $M^{-1}$ , and 261 (±13)  $M^{-1}$  for **DB24C8**-based complexes<sup>8</sup> DB24C8·1, DB24C8·2, and DB24C8·3 and the previously reported  $K_a$  value, 360 M<sup>-1</sup>,<sup>3a</sup> 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 electronwithdrawing ability from propyl to phenyl to *p*-cyanophenyl substituents.

(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.

(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, fastexchange 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 fastexchange complexation systems, **DB24C8**-4 is a slow exchange complexation system. These were also observed by Stoddart et al.<sup>3a</sup> From these, we can know whether a complexation system is fast-exchange or slowexchange 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<sup>-1</sup> by proton NMR titration and 70 M<sup>-1</sup> 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).

<sup>(3) (</sup>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.

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  $[\mathbf{M} - \mathrm{PF}_6]^+$  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  $[\mathbf{B21C7} + \mathrm{Na}]^+$ .

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.<sup>10</sup> 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



**Figure 2.** Partial <sup>1</sup>H NMR spectra (500 MHz, DMSO-*d*<sub>6</sub>, 22 °C) of dumbbell-shaped component **7** (a), rotaxane **8** (b), and **B21C7** (c).

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<sup>3d</sup> 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<sub>1</sub> and H<sub>2</sub> and ethyleneoxy protons H<sub>3</sub> and H<sub>4</sub> of **B21C7** and methylene protons H<sub>d</sub>, H<sub>h</sub>, and H<sub>i</sub> 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.<sup>3a</sup> The ESI mass spectrum of rotaxane **8** has a single peak at m/z 654.4 (100%) corresponding to [**8** – PF<sub>6</sub>]<sup>+</sup>.

The formation of [2]rotaxane **8** was further confirmed by X-ray crystallographic analysis (Figure 3) of a colorless



Figure 3. Crystal structure of the [2]rotaxane 8. A PF<sub>6</sub> 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.

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.

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 dialky-lammonium salt recognition motif.

**Acknowledgment.** This work was supported by the National Natural Science Foundation of China (20604020) and Zhejiang Province of China (2006R10003)

**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.

OL702510C