ORGANIC LETTERS

2013
Vol. 15, No. 14
3538–3541

Benzo-21-Crown-7/Secondary Ammonium Salt [2]Rotaxanes with Fluoro/Chlorocarbon Blocking Groups

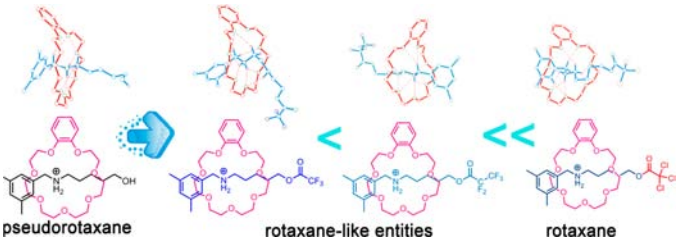
Bo Zheng, Mingming Zhang, Shengyi Dong, Xuzhou Yan, and Min Xue*

Department of Chemistry, Zhejiang University, Hangzhou 310027, China

xuemin@zju.edu.cn

Received May 3, 2013

ABSTRACT



Three threaded structures capped by fluoro/chlorocarbon blocking groups with different sizes were constructed by template synthesis based on the benzo-21-crown-7/secondary ammonium salt recognition motif, as confirmed by ^{1}H NMR, electrospray mass spectrometry and single crystal X-ray analysis. The transformation from a rotaxane-like entity into a rotaxane was achieved by replacing the end group from the trifluoroacetic ester group to its trichloroacetic ester analogue.

In the past two decades, rotaxanes, which contain macrocyclic molecules threaded by dumbbell shaped axles with bulky stoppers, have attracted increasing attention due to their specific structural features and wide applications in molecular machines and devices.[1] When the terminal groups of the axles are small enough to allow threading and dethreading processes, supramolecular complexes, called pseudorotaxanes, are generated.[2] Therefore, the end groups of the linear components play a crucial role in distinguishing pseudorotaxanes and rotaxanes, which show very different functions in the construction of molecular machines and supramolecular polymeric materials.[3,4] Sometimes, even very small changes in terminal units of the axles can lead to different results.[5] Investigation of such changes is important for a new host–guest recognition motif to fabricate threaded structures.

The recognition with crown ethers and their derivatives as hosts and organic cationic salts as guests has been widely used in the construction of pseudorotaxane-, rotaxane-type threaded structures.[1,6] In 2007, the benzo-21-crown-7

(1) (a) Ashton, P. R.; Belohradsky, M.; Philp, D.; Stoddart, J. F. *J. Chem. Soc., Chem. Commun.* **1993**, 1269–1274. (b) Huang, F.; Gibson, H. W. *Prog. Polym. Sci.* **2005**, *30*, 982–1018. (c) Klivansky, L. M.; Koshkakaryan, G.; Liu, Y. *Angew. Chem., Int. Ed.* **2009**, *48*, 4185–4189. (d) Jiang, Y.; Guo, J.-B.; Chen, C.-F. *Chem. Commun.* **2010**, *46*, 5536–5538. (e) Zhu, K.; Vukotic, V. N.; Loeb, S. J. *Angew. Chem., Int. Ed.* **2012**, *51*, 2168–2172. (f) Zhu, K.; Vukotic, V. N.; Noujeim, N.; Loeb, S. J. *Chem. Sci.* **2012**, *3*, 3265–3271. (g) Pun, A.; Hanifi, D. A.; Kiel, G.; O'Brien, E.; Liu, Y. *Angew. Chem., Int. Ed.* **2012**, *51*, 13119–13122.

(2) (a) Shen, Y. X.; Engen, P. T.; Berg, M. A. G.; Merola, J. S.; Gibson, H. W. *Macromolecules* **1992**, *25*, 2786–2788. (b) Huang, F.; Fronczek, F. R.; Gibson, H. W. *J. Am. Chem. Soc.* **2003**, *125*, 9272–9273. (c) Li, S.-L.; Xiao, T.; Hu, B.; Zhang, Y.; Zhao, F.; Ji, Y.; Yu, Y.; Lin, C.; Wang, L. *Chem. Commun.* **2011**, *47*, 10755–10757. (d) Li, C.; Han, K.; Li, J.; Zhang, H.; Ma, J.; Shu, X.; Chen, Z.; Weng, L.; Jia, X. *Org. Lett.* **2012**, *14*, 42–45. (e) Li, C.; Shu, X.; Li, J.; Fan, J.; Chen, Z.; Weng, L.; Jia, X. *Org. Lett.* **2012**, *14*, 4126–4129. (f) Yu, G.; Han, C.; Zhang, Z.; Chen, J.; Yan, X.; Zheng, B.; Liu, S.; Huang, F. *J. Am. Chem. Soc.* **2012**, *134*, 8711–8717. (g) Yu, G.; Xue, M.; Zhang, Z.; Li, J.; Han, C.; Huang, F. *J. Am. Chem. Soc.* **2012**, *134*, 13248–13251. (h) Yu, G.; Zhou, X.; Zhang, Z.; Han, C.; Mao, Z.; Gao, C.; Huang, F. *J. Am. Chem. Soc.* **2012**, *134*, 19489–19497. (i) Gao, L.; Han, C.; Zheng, B.; Dong, S.; Huang, F. *Chem. Commun.* **2013**, *49*, 472–474.

(3) (a) Saha, S.; Leung, K. C.-F.; Nguyen, T. D.; Stoddart, J. F.; Zink, J. I. *Adv. Funct. Mater.* **2007**, *17*, 685–693. (b) Nguyen, T. D.; Tseng, H.-R.; Celestre, P. C.; Flood, A. H.; Liu, Y.; Stoddart, J. F.; Zink, J. I. *Proc. Acad. Natl. Sci. U. S. A.* **2005**, *102*, 10029–10034.

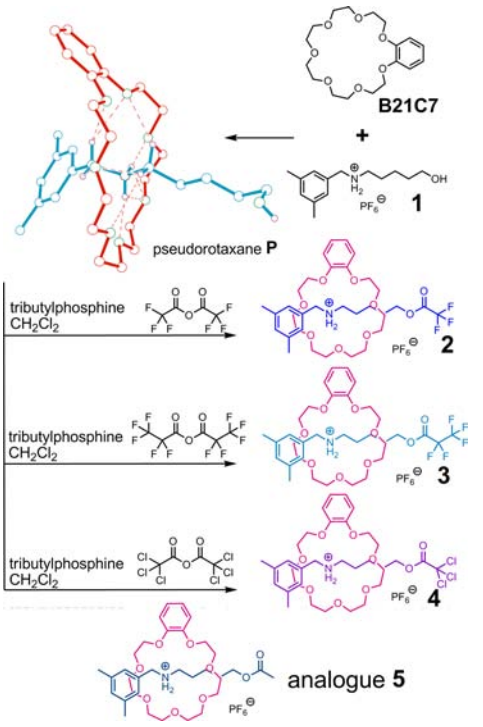
(4) (a) Wang, F.; Han, C.; He, C.; Zhou, Q.; Zhang, J.; Wang, C.; Li, N.; Huang, F. *J. Am. Chem. Soc.* **2008**, *130*, 11254–11255. (b) Zhang, Z.; Luo, Y.; Chen, J.; Dong, S.; Yu, Y.; Ma, Z.; Huang, F. *Angew. Chem., Int. Ed.* **2011**, *50*, 1397–1401. (c) Zheng, B.; Wang, F.; Dong, S.; Huang, F. *Chem. Soc. Rev.* **2012**, *41*, 1621–1636. (d) Zhang, M.; Xu, D.; Yan, X.; Chen, J.; Dong, S.; Zheng, B.; Huang, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 7011–7015. (e) Yan, X.; Wang, F.; Zheng, B.; Huang, F. *Chem. Soc. Rev.* **2012**, *41*, 6042–6065. (f) Hu, X.-Y.; Wu, X.; Duan, Q.; Xiao, T.; Lin, C.; Wang, L. *Org. Lett.* **2012**, *14*, 4826–4829.

(5) (a) Felder, T.; Schalley, C. A. *Angew. Chem., Int. Ed.* **2003**, *42*, 2258–2260. (b) Ashton, P. R.; Baxter, I.; Fyfe, M. C. T.; Raymo, F. M.; Spencer, N.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc.* **1998**, *120*, 2297–2307.

10.1021/ol401241w
Published on Web 07/09/2013

(B21C7)/secondary ammonium salt recognition motif was reported by Huang and co-workers, and subsequently widely used in different ways.[7,8] Many groups have artfully exploited the similarities and differences between dibenzo-24-crown-8 (DB24C8) and B21C7 to construct advanced systems. Because of the small cavity of B21C7, benzene rings are big enough to defend the loss of the wheels, leading to the formation of B21C7-based rotaxanes.[7] In order to find the smallest group to prevent the dethreading process, a series of ester units used as end groups of the axle component in B21C7-based threaded structures was introduced.[9] They showed surprising gradual changes for the stability of these rotaxane-like entities. The carbonyl group could slow down the dissociation process of the threaded structures, and the alkyl tails endowed these structures with further stability. However, relatively stable threaded structures could not be obtained by simply elongating the *n*-alkyl tails. As shown in the crystal structures of those B21C7-based threaded complexes, the small cavity of B21C7 is almost filled by the alkyl axles, which means that even a slight size increase of the end groups may change the pseudorotaxanes into rotaxanes. Probably one of the smallest steric changes that can be made in a molecule is the replacement of hydrogen atoms by halogen atoms, which has been still rarely introduced into the structures of rotaxanes, either in the wheels or in the axles.[10] It is well-known that fluorine is the most electronegative element, and fluorine atoms are high in electron density. Specifically, the van der Waals volume (cm^3/mol) of a methyl group is 13.7, while that of perfluoro-substituted methyl increases to 21.3, with an increase of the radius by ca. 15%.[11] Besides, the van der Waals radius of chlorine is 175 pm, which is even larger than that of fluorine, 147 pm.[11] That makes the chlorocarbon analogue an even more bulky end group. Herein, we choose two fluorocarbon groups and a chlorocarbon group to replace the alkyl groups on the ester units, and expect to find a new type of end group for the construction of rotaxanes and enrich the variety of B21C7-based host–guest systems.

Scheme 1. Syntheses of **2**, **3**, and **4**



We employed the threading-followed-by-stoppering approach to construct rotaxanes. The axle-like molecule **1** was first mixed with B21C7 in dichloromethane to form the expected pseudorotaxane **P**. Although **1** is not soluble in dichloromethane, it could be gradually dissolved after the addition of equimolar B21C7, indicating the formation of a pseudorotaxane structure, which was also confirmed by single crystal X-ray analysis (Scheme 1 and Figure S12, Supporting Information). Then, the hydroxyl group at the axle terminus of the pseudorotaxane was acylated by different acid anhydrides in the presence of tributylphosphine as the catalyst[12] to afford the corresponding fluoro-containing threaded structures **2** and **3** (Scheme 1). The reaction mixtures were concentrated, and finally the products were purified by recrystallization from ethyl acetate or ethyl acetate/diisopropyl ether.

After the crystals of **2** were obtained, electrospray ionization mass spectrometry (ESI-MS) was employed

(6) (a) Gong, C.; Gibson, H. W. *Angew. Chem., Int. Ed.* **1998**, *37*, 310–314. (b) Huang, F.; Gibson, H. W.; Bryant, W. S.; Nagvekar, D. S.; Fronczek, F. R. *J. Am. Chem. Soc.* **2003**, *125*, 9367–9371. (c) Huang, F.; Gibson, H. W. *J. Am. Chem. Soc.* **2004**, *126*, 14738–14739. (d) Huang, F.; Nagvekar, D. S.; Slebodnick, C.; Gibson, H. W. *J. Am. Chem. Soc.* **2005**, *127*, 484–485. (e) Li, S.; Liu, M.; Zhang, J.; Zheng, B.; Zhang, C.; Wen, X.; Li, N.; Huang, F. *Org. Biomol. Chem.* **2008**, *6*, 2103–2107. (f) Han, T.; Chen, C.-F. *J. Org. Chem.* **2008**, *73*, 7735–7742. (g) Wang, F.; Zhang, J.; Ding, X.; Dong, S.; Liu, M.; Zheng, B.; Li, S.; Zhu, K.; Wu, L.; Yu, Y.; Gibson, H. W.; Huang, F. *Angew. Chem., Int. Ed.* **2010**, *49*, 1090–1094. (h) Dong, S.; Luo, Y.; Yan, X.; Zheng, B.; Ding, X.; Yu, Y.; Ma, Z.; Zhao, Q.; Huang, F. *Angew. Chem., Int. Ed.* **2011**, *50*, 1905–1909. (i) Lee, M.; Moore, R. B.; Gibson, H. W. *Macromolecules* **2011**, *44*, 5987–5993. (j) Dong, S.; Zheng, B.; Xu, D.; Yan, X.; Zhang, M.; Huang, F. *Adv. Mater.* **2012**, *24*, 3191–3195. (k) Ji, X.; Yao, Y.; Li, J.; Yan, X.; Huang, F. *J. Am. Chem. Soc.* **2013**, *135*, 74–77.

(7) (a) Zhang, C.; Li, S.; Zhang, J.; Zhu, K.; Li, N.; Huang, F. *Org. Lett.* **2007**, *9*, 5553–5556. (b) Yan, X.; Zhou, M.; Chen, J.; Chi, X.; Dong, S.; Zhang, M.; Ding, X.; Yu, Y.; Shao, S.; Huang, F. *Chem. Commun.* **2011**, *47*, 7086–7088. (c) Zheng, B.; Zhang, M.; Dong, S.; Liu, J.; Huang, F. *Org. Lett.* **2012**, *14*, 306–309. (d) Yan, X.; Xu, D.; Chi, X.; Chen, J.; Dong, S.; Ding, X.; Yu, Y.; Huang, F. *Adv. Mater.* **2012**, *24*, 362–369.

(8) (a) Jiang, W.; Winkler, H. D. F.; Schalley, C. A. *J. Am. Chem. Soc.* **2008**, *130*, 13852–13853. (b) Hsu, C.-C.; Chen, N.-C.; Lai, C.-C.; Liu, Y.-H.; Peng, S.-M.; Chiu, S.-H. *Angew. Chem., Int. Ed.* **2008**, *47*, 7475–7478. (c) Zhang, Z.-J.; Zhang, H.-Y.; Wang, H.; Liu, Y. *Angew. Chem., Int. Ed.* **2011**, *50*, 10834–10838. (d) Chen, L.; Tian, Y.-K.; Ding, Y.; Tian, Y.-J.; Wang, F. *Macromolecules* **2012**, *45*, 8412–8419. (e) Qi, Z.; de Molina, P. M.; Jiang, W.; Wang, Q.; Nowosinski, K.; Schulz, A.; Gradzielski, M.; Schalley, C. A. *Chem. Sci.* **2012**, *3*, 2073–2082.

(9) Zheng, B.; Zhang, M.; Yan, X.; Huang, F. *Org. Biomol. Chem.* **2013**, *11*, 3880–3885.

(10) (a) Berna, J.; Leigh, D. A.; Lubomska, M.; Mendoza, S. M.; Perez, E. M.; Rudolf, P.; Teobaldi, G.; Zerbetto, F. *Nat. Mater.* **2005**, *4*, 704–710. (b) Mahan, E. J.; Dennis, J. A. *Org. Lett.* **2006**, *8*, 5085–5088. (c) Dasgupta, S.; Huang, K.-W.; Wu, J. *Chem. Commun.* **2012**, *48*, 4821–4823.

(11) Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441–451. See also DFT calculated structural data of model compounds in the Supporting Information, Figure S23.

(12) Tachibana, Y.; Kawasaki, H.; Kihara, N.; Takata, T. *J. Org. Chem.* **2006**, *71*, 5093–5104.

(Figure S4, Supporting Information). The resultant spectrum of **2** reveals that there is only one kind of species in the gaseous phase: m/z 674.3 (100%), corresponding to $[\mathbf{2} - PF_6]^+$, indicating that **2** was capped by the perfluorinated acetyl group. ^{1}H NMR studies provide important insights into the internal structure of **2** in solution. The crystals of **2** were dissolved in acetone-d_6 and the resultant ^{1}H NMR spectrum of **2** is very complicated (Figure 1, spectrum b), indicating the existence of threaded structures in solution. By comparison to the ^{1}H NMR spectra of secondary ammonium salt **1** and B21C7 (Figure 1, spectra a and c), the signals of **2** were accurately assigned. The protons of catechol ring in B21C7 were downfield-shifted, while the protons of the benzene ring of **1** were upfield-shifted, merging into a single peak. The aminobenzylic and phenylmethyl protons of **1** shifted upfield, and there was only one set of proton NMR peaks. As such complexes show slow-exchange complexation on the ^{1}H NMR time scale,[9] it is indicated that only interlocked species existed in solution. Even after the acetone-d_6 solution of **2** was heated at 333 K over a week (Figure S13, Supporting Information), all the spectra were identical with the freshly prepared one. The acetyl group capped analogue **5**[9] started to dissociate after being heated for 3 h (Figure S14, Supporting Information), meaning that the stability of the threaded structure increases dramatically by replacing the acetyl group with the perfluorinated one. In order to test the stability of **2** under more extreme conditions, the crystals of **2** were dissolved in DMSO-d_6. As the time progressed, **2** gradually dissociated into discrete units (Figure S15, Supporting Information), and finally after 10 days, the ^{1}H NMR spectra of **2** (Figure S15e and f, Supporting Information) recorded in DMSO-d_6 showed relatively clear peaks, corresponding to the uncomplexed components. Since the ammonium centers are preferentially solvated by the highly polar solvent molecules, the hydrogen bonds between B21C7

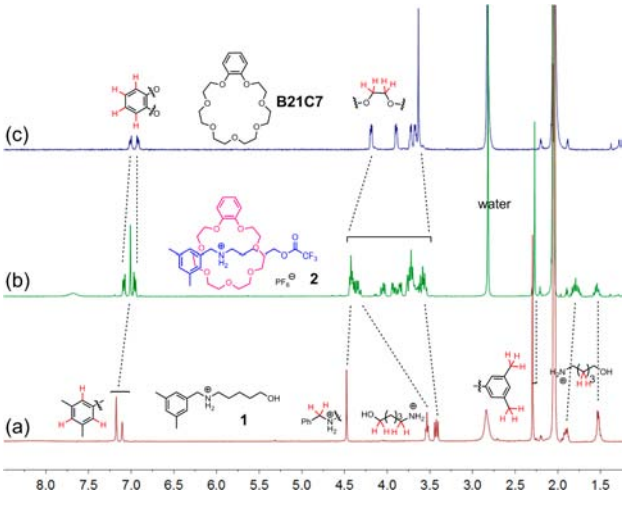


Figure 1. Partial ^{1}H NMR spectra (400 MHz, acetone-d_6, 295 K) of (a) 5.00 mM secondary ammonium salt **1**, (b) 5.00 mM **2**, and (c) 5.00 mM B21C7.

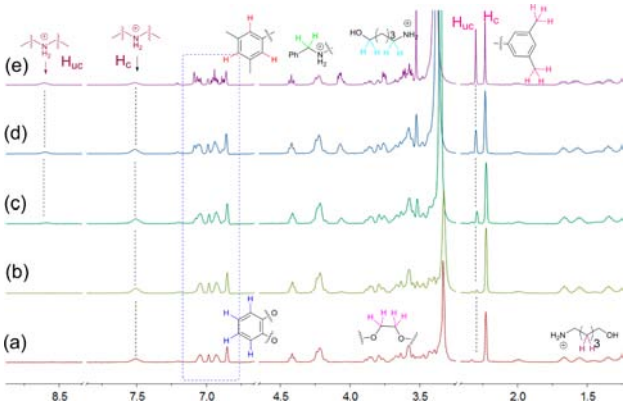


Figure 2. Partial ^{1}H NMR spectra (400 MHz, DMSO-d_6, recorded at 295 K) of 5.00 mM of **3**: (a) freshly prepared; maintained at rt for (b) 6 days, (c) 15 days, (d) 21 days, and (e) 34 days. "c" and "uc" denote complexed and uncomplexed species, respectively.

and the ammonium center were destroyed, and the macrocycle slipped off. From that, we found that this perfluorinated acetyl group is not big enough to prevent dethreading.

In order to increase the stability of the threaded structure, we chose a longer perfluorinated tail, pentafluoropropionic ester (Scheme 1). After maintaining the pure products at low temperature for 2 days, we also obtained crystals of **3**. ^{1}H NMR and mass spectrometry reveal that the threaded complex was capped by the pentafluoropropionic ester group (Figures S5 and S8, Supporting Information). ^{19}F NMR provides additional information to confirm that the crystals are the expected products. We found that there was one sharp peak in Figure S3 (Supporting Information) and two peaks in Figure S7 (Supporting Information), besides the two peaks corresponding to the fluorine atoms of the hexafluorophosphate counterion. The acetone-d_6 solution of **3** was maintained at 283 K for over 18 days and all the spectra were identical with the freshly prepared one (Figure S16, Supporting Information). After the addition of excess triethylamine (TEA) to the acetone-d_6 solution of **3** in order to deprotonate the ammonium protons to destroy the interpenetrated structures (Figure S17, Supporting Information), it was found that the ^{1}H NMR spectra of the mixture did not show obvious changes within 2 days, and the dethreaded and threaded portions were almost the same after 6 days (Figure S17 inset, Supporting Information), suggesting that the deslippage of the threaded structure **3** became slower influenced by the end group with longer fluorous tail. The spectrum became much simpler, and the threaded portion could not be found after 20 days, indicating the completion of dissociation. Furthermore, the crystals of **3** were dissolved in DMSO-d_6. After maintaining the DMSO-d_6 solution for a week, threaded structure **3** just started to dissociate. We found that it did not completely dissociate even after a month (Figure 2). Compared with the results for **2**, the stability of the threaded structure **3** is

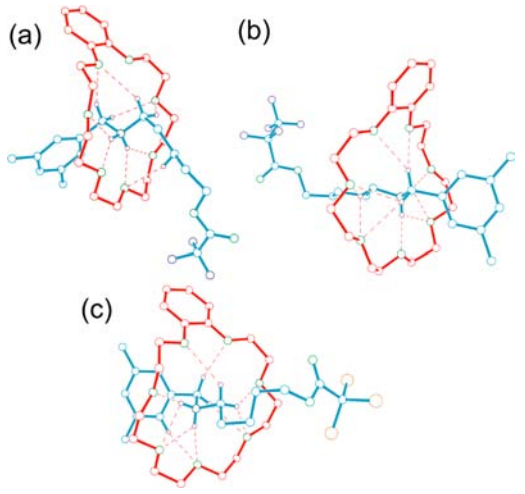


Figure 3. Ball-stick views of the crystal structures of **2** (a), **3** (b), and **4** (c). PF_6 anions and hydrogens, except the ones involved in hydrogen bonding were omitted for clarity. B21C7 parts are red, secondary ammonium salt parts are light blue, hydrogens are purple, oxygens are green, fluorines are dark blue, chlorines are yellow, and nitrogens are black.

greatly increased. By heating the DMSO-d_6 solution of **3** to accelerate the dissociation process, we found that the dethreaded portion was larger than the threaded portion after 22 h at 353 K, by integrations of complexed (H_c) and uncomplexed peaks (H_{uc}) of the phenylmethyl protons of **3** (Figure S19, Supporting Information).

Although we found that the stability of the threaded structure can be enhanced by elongation the fluorous tail, obtaining a kinetically stable [2]rotaxane at room temperature or in low polar solvents, we still could not obtain a real mechanically interlocked [2]rotaxane by simply utilizing longer fluorous tails according to the above results. Therefore, we intended to further increase the volume of the end group. Trichloroacetic ester was chosen to cap the pseudorotaxane **P** (Scheme 1). Threaded structure **4** was synthesized (Figures S9−S11, Supporting Information). The crystals of **4** were directly dissolved in DMSO-d_6, and the resultant solution was heated to 353 K and maintained for 36 h (Figure S20, Supporting Information). Besides, addition of excess TEA into the acetone-d_6 solution of **4** was carried out and the solution was maintained for 18 h at 333 K (Figure S21, Supporting Information). All the ^{1}H NMR spectra of **4** under the above conditions provide direct and strong evidence for the formation of a rotaxane structure and the sufficient stability of the [2]rotaxane against dethreading of the wheel.

X-ray crystallographic analyses reveal that the tethers penetrate into the B21C7 cavities, and **2**, **3**, and **4** are threaded structures in the solid state (Figure 3). Each of these structures is fixed by multiple hydrogen bonds, comprising four [N^+—H···O] hydrogen bonds and five or six [C—H···O] hydrogen bonds (Figures 3 and S22, Supporting Information). Similar to previously reported crystal structures of B21C7-based threaded complexes,[7] all the oxygen atoms of the polyether macrocycles of **3** and **4** participate in these hydrogen bonds with the ammonium or the closest methylene hydrogens. The crystal structure of **2** is a little bit different, and an oxygen atom of B21C7 does not participate in the formation of these hydrogen bonds (Figure 3a), indicating that the crown ethers containing less than 21 atoms may encircle around the ammonium center more tightly. For **2**, the hydrogen bonding pulls the tether from the catechol ring and fixes it more tightly at the "bottom" of the polyether macrocycle. The ring plane/ring plane inclinations of these structures are 84.48° (Figure 3a), 62.71° (Figure 3b), and 67.32° (Figure 3c). Therefore, there is no face-to-face π-stacking interaction involved, preferring the existence of hydrogen bonds.

In summary, we constructed three threaded structures based on the B21C7/secondary ammonium salt recognition motif by employing three similar end-capped groups with different sizes: perfluoroacetic ester, perfluoropropionic ester, and perchloroacetic ester. The tiny differences among the ester groups have a remarkable influence on the stability of these threaded structures. Compared with the *n*-alkyl capped threaded structures,[9] the stability was enhanced by the fluorous tails. They both keep their threaded structures in acetone at room temperature but dissociate slowly when the temperature increases or after adding base to deprotonate the ammonium center. In DMSO, the tethers do slip off, but the dissociation process for the perfluoropropionic ester is much slower than that for the perfluoroacetic ester, indicating that the longer the fluorous tail is, the higher the stability is. For the chloro-capped one, whether heating its acetone solution for a long time or dissolving it in hot DMSO, it is still quite stable and does not suffer any change under these conditions, providing the formation of an interlocked rotaxane. In the future, these different stoppers can be utilized to meet different requirements. The slowly dissociated ones can be used to construct controlled-release systems, while the interlocked one can be used to enhance the mechanical strength.

Acknowledgment. This work was supported by the National Natural Science Foundation of China (31002701).

Supporting Information Available. Synthetic procedures, characterizations, and other materials. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.