ChemPubSoc Europe

DOI: 10.1002/chem.201400323

CHEMISTRY
A European Journal
Communication

Macrocycles

Rotaxanes Synthesized Through Sodium-Ion-Templated Clipping of Macrocycles Around Nonconjugated Amide and Urea Functionalities

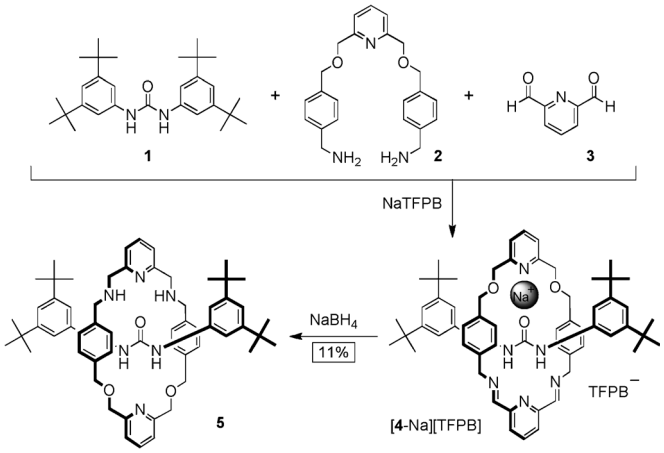
Tsung-Hsien Ho,[a] Chien-Chen Lai,[b] Yi-Hung Liu,[a] Shie-Ming Peng,[a] and Sheng-Hsien Chiu*[a]

Abstract: A single urea or amide functionality in a dumbbell-shaped guest can be "clipped" by a macrocycle generated from a diamine and a dialdehyde through the templating effect of a Na^+ ion (see scheme). The resulting imine-containing rotaxanes can then be reduced to allow isolation of stable amine-based rotaxanes.

Because rotaxanes have potential applications in many research fields (e.g., molecular electronics;[1] gelation;[2] molecular preservation and transportation[3]), several synthetic approaches have been developed to facilitate their syntheses using different molecular designs and employing various synthetic conditions.[4] Among them, the "clipping" approach provides high synthetic flexibility: the interlocked macrocycle is generated in situ and, therefore, the reaction conditions, the selection of suitable stoppering groups, and the assembly of the dumbbell-shaped component are less restricted than in other approaches (Figure 1). Many elegant interlocked molecules have been synthesized using this approach, through both kinetic (irreversible) and thermodynamic (reversible) reactions.[5] Previously, we reported a new recognition system in which sodium ions template the threading of linear molecules, featuring non-conjugated urea and amide functionalities, through the cavity of bis-*p*-xylyl[26]crown-6 (BPX26C6) to form pseudorotaxanes and indicated its potential for application in the formation of (pseudo)rotaxane structures from peptide and nylon units.[6] For this present study, we wished to develop a "clipping" version of this recognition system to extend the capability and flexibility of introducing interlocked structures into important artificial and biological (macro)molecules. Herein, we report that a macrocycle generated from a diamine and a dialdehyde can be "clipped" around a single urea or amide functionality in a dumbbell-shaped guest through the templating effect of a Na^+ ion, with subsequent reduction of the imine-containing rotaxane allowing isolation of a stable amine-based rotaxane.

Figure 1. Cartoon representation of the "clipping" approach in rotaxane synthesis.

To realize the concept, we synthesized the dumbbell-shaped urea **1**, diamine **2**, and dialdehyde **3** (Scheme 1) and mixed them with sodium tetrakis(3,5-trifluoromethylphenyl)borate (NaTFPB)[7] as an equimolar (10 mM) solution in $CDCl_3$. The rapid appearance and disappearance of the signals for the imine and aldehyde groups, respectively, in the region δ 8.0–10.0 in the ^1H NMR spectra suggested that imine bond formation between the diamine **2** and the dialdehyde **3** was favored under these conditions (Figure 2b). To accelerate the reaction toward equilibrium, we heated the solution at 323 K, resulting in a gradual increase in the set of signals for the corresponding



Scheme 1. "Clipping" synthesis of the [2]rotaxane **5** from a conjugated urea-containing dumbbell-shaped component.

[a] *T.-H. Ho, Y.-H. Liu, Prof. S.-M. Peng, Prof. S.-H. Chiu*
Department of Chemistry and Center for Emerging Material and Advanced Devices
National Taiwan University
No. 1, Sec. 4, Roosevelt Road, Taipei, Taiwan, 10617, (R.O.C.)
Fax: (+886) 2-33661677
E-mail: shchiu@ntu.edu.tw

[b] *Prof. C.-C. Lai*
Institute of Molecular Biology, National Chung Hsing University and Department of Medical Genetics, China Medical University Hospital, Taichung, Taiwan (R.O.C.)

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201400323.

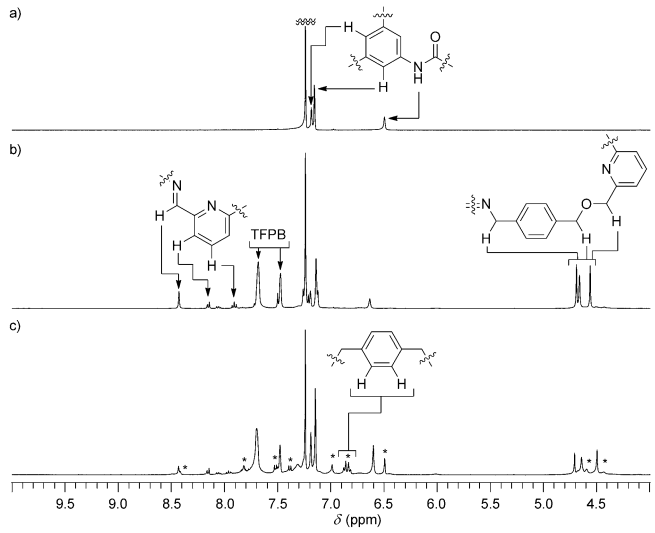


Figure 2. Partial ^{1}H NMR spectra (400 MHz, $CDCl_3$, 298 K) of a) the dumbbell-shaped urea **1** and b, c) an equimolar mixture of **1**, the diamine **2**, the dialdehyde **3**, and NaTFPB (10 mM) after heating at 323 K for b) 0 and c) 33 h.

imine-containing [2]rotaxane [**4**·Na][TFPB].[8] We estimated the yield of [**4**·Na][TFPB] generated at equilibrium under these conditions after 33 h to be 24%, based on integration of the signal at δ 6.80–6.90, which we assign to the shielded aromatic protons of the xylyl unit in the imine-containing [2]rotaxane. Subsequent $NaBH_4$-mediated reduction of the imino bonds of [**4**·Na][TFPB] provided the [2]rotaxane **5** in 11% yield (in two steps) after column chromatography.[9]

We obtained single crystals suitable for X-ray crystallography after vapor diffusion of hexanes into a CH_2Cl_2 solution of the [2]rotaxane **5**. The solid state structure reveals[10,11] the expected [2]rotaxane geometry (Figure 3), in which the urea unit is encircled by the aza-macrocycle, with the urea C=O and NH units hydrogen bonded to the secondary amino groups and one of the oxygen atoms of the macrocycle, respectively.

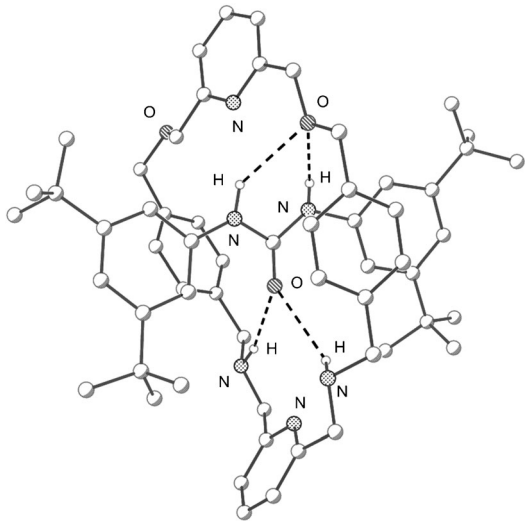
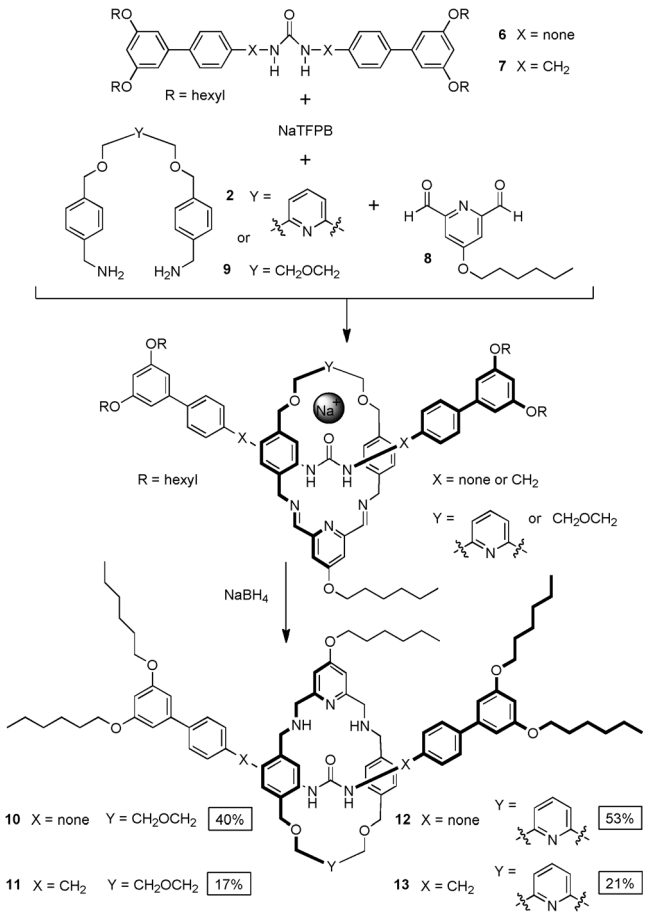


Figure 3. Ball-and-stick representation of the solid state structure of the [2]rotaxane **5**.

Although we had successfully isolated the [2]rotaxane **5** after using Na^+ ions to template the synthesis of a macrocycle around a single conjugated urea functionality, the low efficiency of this reaction, most likely related to the originally low complexation ratio in the formation of the imine-containing [2]rotaxane [**4**·Na][TFPB], certainly required improvement. We suspected that the proximity of the bulky 3,5-di-*tert*-butyl group to the urea functionality in the dumbbell-shaped molecule **1** might have disturbed the formation of the imine-containing macrocycle and/or the π-stacking of its aromatic rings with those of **1**, thereby decreasing the efficiency of the formation of the imine-containing [2]rotaxane. Moreover, because imine-containing oligomers and/or polymers would presumably be generated in solution prior to the formation of such [2]rotaxanes, we wished to increase their solubility in less-polar solvents to avoid the formation of precipitates or gels. Thus, we synthesized the dumbbell-shaped threadlike molecules **6** and **7** (which have their urea functionalities conjugated and non-conjugated to aromatic rings, respectively) and dialdehyde **8**, all presenting hexyl groups (Scheme 2).

Because BPX26C6 can encircle a single urea functionality through the templating effect of a Na^+ ion,[6a] we suspected that diamine **9**, which mimics part of the structure of BPX26C6 (one diethylene glycol chain linked to two xylyl groups), would be a possible clipping component. As revealed in Figure 4, an



Scheme 2. "Clipping" syntheses of [2]rotaxanes from two dumbbell-shaped molecules, each containing a single urea functionality.

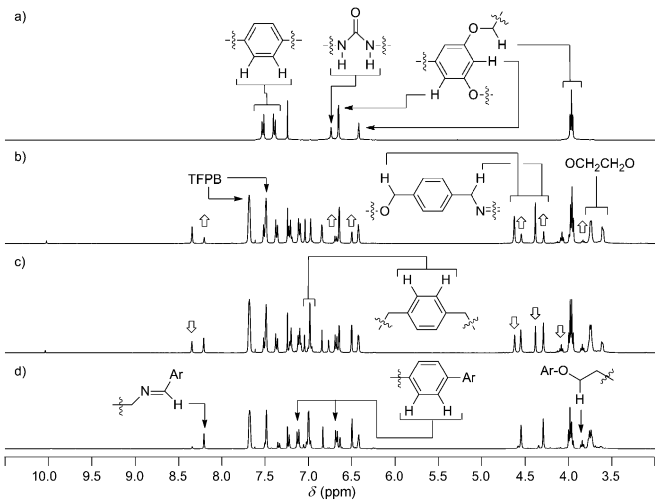


Figure 4. Partial ^{1}H NMR spectra (400 MHz, $CDCl_3$, 298 K) of a) the dumbbell-shaped urea **6** and b–d) an equimolar mixture of **6**, the dialdehyde **8**, the diamine **9**, and NaTFPB (10 mM) heated at 323 K for b) 0, c) 1, and d) 8 h.

equimolar (10 mM) mixture of the dumbbell-shaped urea derivative **6**, dialdehyde **8**, diamine **9**, and NaTFPB in $CDCl_3$ reached equilibrium after heating at 323 K for 8 h. The gradual growth of two sets of signals for the benzylic and *para*-disubstituted phenyl protons—at $\delta = 4.35/4.55$ and 6.70/7.20, respectively, representing the complexed imine-containing macrocyclic and the dumbbell-shaped components, respectively—in the ^{1}H NMR spectra suggested that the desired imine-containing [2]rotaxane was generated over time. Based on integration of the signals in the ^{1}H NMR spectra, the yield of the imine-containing [2]rotaxane generated under these conditions reached 82% at equilibrium.[12] The significantly higher yield of the imine-containing [2]rotaxane generated in solution when using **6** as the dumbbell-shaped urea derivative instead of **1** supported our hypothesis that the proximity of the bulky 3,5-di-*tert*-butyl groups to the urea station in **1** was a factor affecting the efficiency of the clipping process. The reaction of an equimolar (10 mM) mixture of the dumbbell-shaped urea **7** (containing a non-conjugated and less-acidic NH urea unit), the dialdehyde **8**, the diamine **9**, and NaTFPB in $CDCl_3$ at 323 K also produced a corresponding imine-containing [2]rotaxane, but with relatively low efficiency (27%) and a longer time (22 h) required to reach equilibrium. The relatively low yield at equilibrium for the formation of the imine-containing [2]rotaxane incorporating the dumbbell-shaped urea **7**, relative to that incorporating **6**, was likely due to the urea functionality in the former not being conjugated to aromatic rings; that is, its less-acidic NH units formed weaker hydrogen bonds to the oxygen and/or nitrogen atoms of the encircling imine-containing macrocycle. Reduction of these two imine-containing [2]rotaxanes gave the amine-containing [2]rotaxanes **10** (40% yield) and **11** (17% yield), in which the dumbbell-shaped components featured conjugated and non-conjugated urea functionalities, respectively. Table 1 lists the yields of the various imine-containing [2]rotaxanes prepared in this study as well as those of their corresponding amine-containing [2]rotaxanes.

Equimolar (10 mM) mixtures of the dumbbell-shaped urea derivative **6** or **7**, the dialdehyde **8**, the diamine **2**, and NaTFPB in $CDCl_3$ reached equilibrium after being heated at 323 K for 8 and 24 h, respectively; we estimated the yields of the corresponding imine-containing [2]rotaxanes to be 69 and 28%, respectively, based on integration of various signals in the ^{1}H NMR spectra (see Supporting Information). Using $NaBH_4$ to reduce the imino bonds, we isolated the [2]rotaxanes **12** (53% yield) and **13** (21% yield) in which the aza-macrocyclic components encircled the conjugated and non-conjugated urea stations, respectively. This result suggested that the 2,6-dihydroxymethylpyridine and the diethylene glycol motifs present in the diamines **2** and **9**, respectively, were structurally similar components when constructing urea-based rotaxanes through such a "clipping" approach.

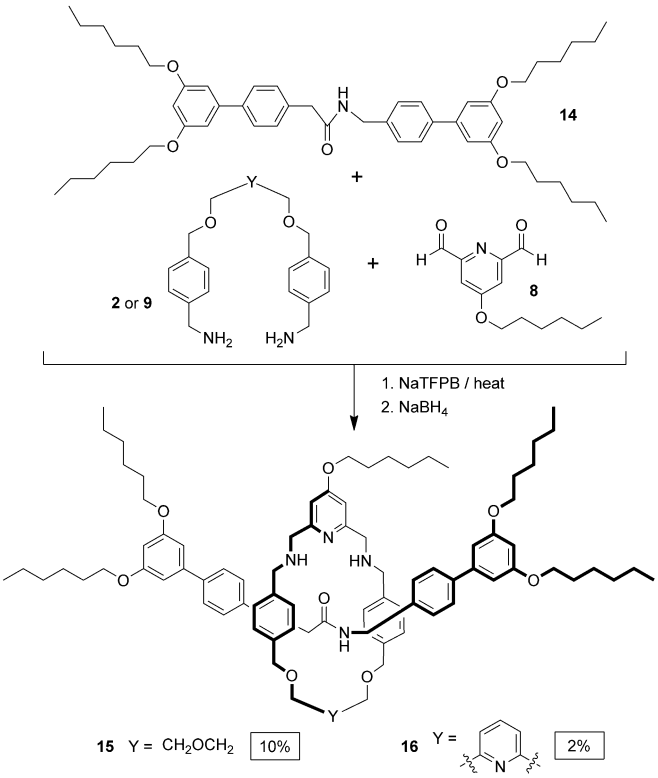
Having proven that "clipping" could be applied to both conjugated and non-conjugated *urea* derivatives, we wished to demonstrate that such an approach could also be used to form a macrocycle around a dumbbell-shaped component featuring a single non-conjugated *amide* unit. Therefore, we heated an equimolar (10 mM) mixture of the dumbbell-shaped amide **14**, the dialdehyde **8**, the diamine **9** (**2**), and NaTFPB in $CDCl_3$ at 323 K for 28 (36) h and then performed $NaBH_4$-mediated reduction to afford the [2]rotaxane **15** (**16**) in 10% (2%) yield after column chromatography (Scheme 3). Because the corresponding intermediate imine-containing [2]rotaxanes were generated in approximately 23 and 9% yields at equilibrium (see the Supporting Information), we suspect that the low efficiencies of the syntheses of the amine-containing [2]rotaxanes **15** and **16** arose from relatively weak interactions between the templating Na^+ ion, the imine-containing macrocycle, and the dumbbell-shaped amides.

Although the use of Na^+ ions to template the clipping of imine-containing macrocycles around a dumbbell-shaped com-

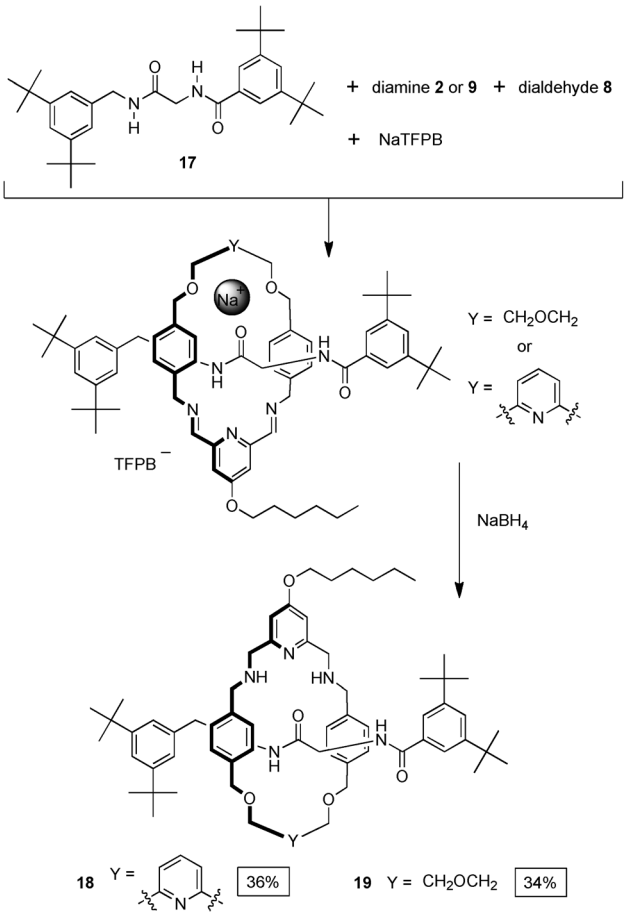
Table 1. Efficiencies of the "clipping" syntheses of imine-containing [2]rotaxanes and yields of corresponding amine-containing [2]rotaxanes.[a]

[2]Rotaxane	Diamine	Dumbbell	Imine[2]rotaxane [%][b]	Amine[2]rotaxane [%][c]	*t* [h][d]
10	**9**	**6**	82	40	8
11	**9**	**7**	27	17	22
12	**2**	**6**	69	53	8
13	**2**	**7**	28	21	24
15	**9**	**14**	23	10	28
16	**2**	**14**	9	2	36
18	**9**	**17**	65	36	24
19	**2**	**17**	58	34	28

[a] Experiments performed using an equimolar mixture of the dialdehyde **8**, NaTFPB, a diamine, and a dumbbell-shaped guest (10 mM) at 323 K. [b] Determined from integration of signals in the ^{1}H NMR spectra. [c] Isolated yield from the $NaBH_4$-mediated reduction of the imine precursor. [d] Time required for the reaction to reach equilibrium.



Scheme 3. "Clipping" syntheses of [2]rotaxanes from a dumbbell-shaped component containing a single non-conjugated amide functionality.



Scheme 4. "Clipping" syntheses of two [2]rotaxanes from a dumbbell-shaped component containing two peptide-like amido groups.

ponent featuring a single non-conjugated amide unit appeared to be less efficient than those reactions involving urea-containing counterparts, presumably because of weaker noncovalent interactions, we suspected that the situation could be improved significantly if the dumbbell-shaped component presented two proximal amide units. Therefore, we synthesized the dumbbell-shaped molecule **17** (Scheme 4), which contains a glycine residue amidated at both its N- and C-termini to mimic the linking of amino acids in common peptides, and mixed it with the diamine **2** (**9**), the dialdehyde **8**, and NaTFPB (each 10 mM) in $CDCl_3$. The ^{1}H NMR spectra of the solutions containing the diamines **2** (Figure 5 b and c) and **9** (Figure 5 d and e) both displayed the growth of new sets of signals after mixing. The intensities of these sets of signals reached their maxima (i.e., equilibria were established) after heating at 323 K for 28 and 24 h, respectively; we estimated the yields for the corresponding rotaxanes to be 58 and 65%, respectively, based on integration of pertinent signals in the ^{1}H NMR spectra.[13] Using $NaBH_4$ to reduce the imine-containing macrocyclic components, we isolated, after column chromatography, the [2]rotaxanes **18** (36% yield) and **19** (34% yield), incorporating 2,6-dihydroxypyridine and diethylene glycol units, respectively, in their interlocked macrocyclic components. The significantly higher yields of the [2]rotaxanes **18** and **19** (and of their imine-containing precursors) relative to that of the [2]rotaxanes **15** and **16** indicated that, although such a "clipping" approach might not be particularly efficient for the recognition of a single non-conjugated amide functionality, its application to

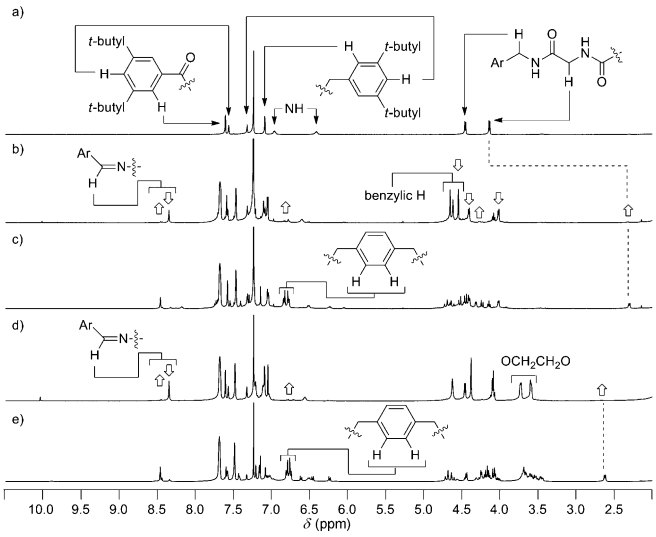


Figure 5. Partial ^{1}H NMR spectra (400 MHz, $CDCl_3$, 298 K) of a) the dumbbell-shaped diamide **17**; b, c) an equimolar (10 mM) mixture of **17**, the dialdehyde **8**, the diamine **2**, and NaTFPB after heating at 323 K for b) 0 and c) 28 h; and d, e) an equimolar (10 mM) mixture of **17**, the dialdehyde **8**, the diamine **9**, and NaTFPB after heating at 323 K for d) 0 and e) 24 h.

the syntheses of interlocked structures from dumbbell-shaped molecules presenting multiple amide bonds (e.g., peptides) has the potential to be reasonably efficient. These results suggest that such a clipping approach has potential for application in the construction of interlocked molecules from peptides containing multiple C- and N-terminal amidated amino acid residues, especially glycine residues.[14]

We have demonstrated that Na^+ ions are capable of templating the formation of imine-containing macrocycles around single non-conjugated urea or amide functionalities in dumbbell-shaped guests (yields of up to 82%), with subsequent $NaBH_4$-mediated reductions affording corresponding thermodynamically stable amine-containing [2]rotaxanes (yields of up to 53%). We have also demonstrated that such a "clipping" approach has high potential for application in the construction of rotaxanes from guests having peptide-like structures. We believe that the requirement of only a single common urea or amide functionality in the dumbbell-shaped component and the ease of formation of the macrocyclic components from linear species will make this synthetic approach and recognition system practically useful for introducing interlocked structures into artificial or biological (macro)molecules, a direction that we are current investigating.

Acknowledgements

We thank the National Science Council (Taiwan) (NSC-102-2119 M-002-007) and National Taiwan University (NTU-102-R890913) for financial support.

Keywords: amide · clipping · molecular recognition · rotaxane · template · urea

[1] a) *Molecular Electronics: Science and Technology* (Eds.: A. Aviram, M. Ratner), New York Academy of Sciences, New York, **1998**; b) J. E. Green, J. W. Choi, A. Boukai, Y. Bunimovich, E. Johnston-Halperin, E. Delonno, Y. Luo, B. A. Sheriff, K. Xu, Y. S. Shin, H.-R. Tseng, J. F. Stoddart, J. R. Heath, *Nature* **2007**, *445*, 414 – 417.

[2] a) Y.-L. Zhao, I. Aprahamian, A. Trabolsi, N. Erina, J. F. Stoddart, *J. Am. Chem. Soc.* **2008**, *130*, 6348 – 6350; b) S.-Y. Hsueh, C.-T. Kuo, T.-W. Lu, C.-C. Lai, Y.-H. Liu, H.-F. Hsu, S.-M. Peng, C.-h. Chen, S.-H. Chiu, *Angew. Chem.* **2010**, *122*, 9356 – 9359; *Angew. Chem. Int. Ed.* **2010**, *49*, 9170 – 9173; c) Y. Kohsaka, K. Nakazono, Y. Koyama, S. Asai, T. Takata, *Angew. Chem.* **2011**, *123*, 4974 – 4977; *Angew. Chem. Int. Ed.* **2011**, *50*, 4872 – 4875.

[3] a) A. Fernandes, A. Viterisi, F. Coutrot, S. Potok, D. A. Leigh, V. Aucagne, S. Papot, *Angew. Chem.* **2009**, *121*, 6565 – 6569; *Angew. Chem. Int. Ed.* **2009**, *48*, 6443 – 6447; b) M. W. Ambrogio, T. A. Pecorelli, K. Patel, N. M. Khashab, A. Trabolsi, H. A. Khatib, Y. Y. Botros, J. I. Zink, J. F. Stoddart, *Org. Lett.* **2010**, *12*, 3304 – 3307; c) J. M. Baumes, J. J. Gassensmith, J. Giblin, J.-J. Lee, A. G. White, W. J. Culligan, W. M. Leevy, M. Kuno, B. D. Smith, *Nat. Chem.* **2010**, *2*, 1025 – 1030.

[4] For recent examples, see: a) S.-Y. Hsueh, J.-L. Ko, C.-C. Lai, Y.-H. Liu, S.-M. Peng, S.-H. Chiu, *Angew. Chem.* **2011**, *123*, 6773 – 6776; *Angew. Chem. Int. Ed.* **2011**, *50*, 6643 – 6646; b) R. Ahmed, A. Altieri, D. M. D'Souza, D. A. Leigh, K. M. Mullen, M. Papmeyer, A. M. Z. Slawin, J. K. Y. Wong, J. D. Woollins, *J. Am. Chem. Soc.* **2011**, *133*, 12304 – 12310; c) Z. Niu, F. Huang, H. W. Gibson, *J. Am. Chem. Soc.* **2011**, *133*, 2836 – 2839; d) K. Zhu, V. N. Vukotic, N. Noujeim, S. J. Loeb, *Chem. Sci.* **2012**, *3*, 3265 – 3271; e) B. M. Rambo, H.-Y. Gong, M. Oh, J. L. Sessler, *Acc. Chem. Res.* **2012**, *45*, 1390 – 1401; f) M. Xue, Y. Yang, X. Chi, Z. Zhang, F. Huang, *Acc. Chem. Res.* **2012**, *45*, 1294 – 1308; g) H. Li, Z. Zhu, A. C. Fahrenbach, B. M. Savoie, C. Ke, J. C. Barnes, J. Lei, Y.-L. Zhao, L. M. Lilley, T. J. Marks, M. A. Ratner, J. F. Stoddart, *J. Am. Chem. Soc.* **2013**, *135*, 456 – 467.

[5] For recent examples, see: a) J. B. Wittenberg, M. G. Costales, P. Y. Zavalij, L. Isaacs, *Chem. Commun.* **2011**, *47*, 9420 – 9422; b) A. Carlone, S. M. Goldup, N. Lebrasseur, D. A. Leigh, A. Wilson, *J. Am. Chem. Soc.* **2012**, *134*, 8321 – 8323; c) C. Wang, S. M. Dyar, D. Cao, A. C. Fahrenbach, N. Horwitz, M. T. Colvin, R. Carmieli, C. L. Stern, S. K. Dey, M. R. Wasielewski, J. F. Stoddart, *J. Am. Chem. Soc.* **2012**, *134*, 19136 – 19145; d) H. W. Gibson, H. Wang, Z. Niu, C. Slebodnick, L. N. Zhakharov, A. L. Rheingold, *Macromolecules* **2012**, *45*, 1270 – 1280; e) N. G. White, P. D. Beer, *Org. Biomol. Chem.* **2013**, *11*, 1326 – 1333; f) J.-C. Chambron, J.-P. Sauvage, *New J. Chem.* **2013**, *37*, 49 – 57.

[6] a) Y.-H. Lin, C.-C. Lai, Y.-H. Liu, S.-M. Peng, S.-H. Chiu, *Angew. Chem.* **2013**, *125*, 10421 – 10426; *Angew. Chem. Int. Ed.* **2013**, *52*, 10231 – 10236; for pseudorotaxanes or rotaxanes formed from diamide-based macrocycles and urea- or amide-containing threadlike species, see: b) G. A. Breault, C. A. Hunter, P. C. Mayers, *Tetrahedron* **1999**, *55*, 5265 – 5293; c) C. Reuter, W. Wienand, G. M. Hubner, C. Seel, F. Vögtle, *Chem. Eur. J.* **1999**, *5*, 2692 – 2697; d) M. R. Sambrook, P. D. Beer, J. A. Wisner, R. L. Paul, A. R. Cowley, *J. Am. Chem. Soc.* **2004**, *126*, 15364 – 15365; e) J. Berná, G. Bottari, D. A. Leigh, E. M. Perez, *Pure Appl. Chem.* **2007**, *79*, 39 – 54; f) Y.-L. Huang, W.-C. Hung, C.-C. Lai, Y.-H. Liu, S.-M. Peng, S.-H. Chiu, *Angew. Chem.* **2007**, *119*, 6749 – 6753; *Angew. Chem. Int. Ed.* **2007**, *46*, 6629 – 6633; g) A. Vidonne, D. Philp, *Tetrahedron* **2008**, *64*, 8464 – 8475.

[7] a) S. H. Strauss, *Chem. Rev.* **1993**, *93*, 927 – 942; b) C. Gaeta, F. Troisi, P. Neri, *Org. Lett.* **2010**, *12*, 2092 – 2095; c) N.-C. Chen, C.-J. Chuang, L.-Y. Wang, C.-C. Lai, S.-H. Chiu, *Chem. Eur. J.* **2012**, *18*, 1896 – 1900; d) L.-Y. Wang, J.-L. Ko, C.-C. Lai, Y.-H. Liu, S.-M. Peng, S.-H. Chiu, *Chem. Eur. J.* **2013**, *19*, 8850 – 8860.

[8] Imine formation has been applied to construct rotaxanes by "clipping" macrocycles onto dibenzylammonium or pyridinium ion-containing dumbbell-shaped guests, see: a) C. D. Meyer, C. S. Joiner, J. F. Stoddart, *Chem. Soc. Rev.* **2007**, *36*, 1705 – 1723; b) J. Yin, S. Dasgupta, J. Wu, *Org. Lett.* **2010**, *12*, 1712 – 1715; c) Y. Liu, Z.-T. Li, *Aust. J. Chem.* **2013**, *66*, 9 – 22; for an example of using imine formation to synthesize a [2]catenane from two Na^+ ion-templated diethylene glycol units, see: S.-T. Tung, C.-C. Lai, Y.-H. Liu, S.-M. Peng, S.-H. Chiu, *Angew. Chem.* **2013**, *125*, 13511 – 13514; *Angew. Chem. Int. Ed.* **2013**, *52*, 13269 – 13272.

[9] Using selenophenol (PhSeH) as the reductant in the same reaction, we obtained only 3% of the desired [2]rotaxane **5** after column chromatography.

[10] CCDC-960810 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data request/cif.

[11] Crystal data for **5**: $[C_{59}H_{76}O_3N_6]$; $M_r = 917.26$; orthorhombic; space group P2(1)2(1)2(1); $a = 10.4439(2)$; $b = 13.3308(4)$; $c = 39.3404(9)$ Å.; $V = 5477.2(2)$ Å^3; $\rho_{calcd} = 1.112$ g cm^{-3}; $\mu(Cu_{K\alpha}) = 0.533$ mm^{-1}; $T = 200(2)$ K.; colorless plate; 9955 independent measured reflections; F^2 refinement; $R_1 = 0.0768$; $wR_2 = 0.2108$.

[12] When we replaced NaTFPB with LiTFPB or KTFPB and performed the synthesis of the [2]rotaxane **10** under similar conditions, the yields of the imine-containing [2]rotaxane generated in solution, based on integration of signals in ^{1}H NMR spectra (72 and 35%, respectively), were relatively lower, suggesting that the Na^+ ion is a better template in this "clipping" reaction.

[13] Possibly because of stronger solvation of the templating Na^+ ion in more-polar solvents, a similar "clipping" reaction performed in CD_3CN provided no observable signals belonging to the corresponding [2]rotaxane in the ^{1}H NMR spectra of the reactants.

[14] For more examples of systems related to peptide rotaxanes, see: a) G. Bottari, D. A. Leigh, E. M. Perez, *J. Am. Chem. Soc.* **2003**, *125*, 13360 – 13361; b) D. A. Leigh, A. R. Thomson, *Org. Lett.* **2006**, *8*, 5377 – 5379; c) A. Fernandes, A. Viterisi, V. Aucagne, D. A. Leigh, S. Papot, *Chem. Commun.* **2012**, *48*, 2083 – 2085.

Received: January 26, 2014
Published online on March 13, 2014