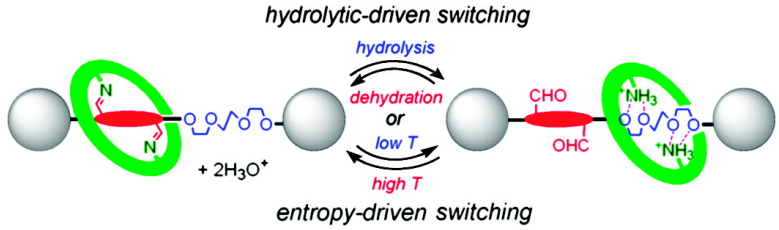
Article

Entropy- and Hydrolytic-Driven Positional Switching of Macrocycle between Imine- and Hydrogen-Bonding Stations in Rotaxane-Based Molecular Shuttles

Takeshi Umehara, Hidetoshi Kawai, Kenshu Fujiwara, and Takanori Suzuki

J. Am. Chem. Soc., **2008**, 130 (42), 13981-13988 • DOI: 10.1021/ja804888b • Publication Date (Web): 26 September 2008



More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

View the Full Text HTML

J|A|C|S
ARTICLES

Published on Web 09/26/2008

Entropy- and Hydrolytic-Driven Positional Switching of Macrocycle between Imine- and Hydrogen-Bonding Stations in Rotaxane-Based Molecular Shuttles

Takeshi Umehara,[†] Hidetoshi Kawai,*[,†,‡] Kenshu Fujiwara,[†] and Takanori Suzuki[†]

Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo 060-0810, Japan, and PRESTO, Japan Science and Technology Agency (JST), 4-1-8 Honcho, Kawaguchi, Saitama 332-0012, Japan

Received June 26, 2008; E-mail: kawai@sci.hokudai.ac.jp

Abstract: The construction and switching properties of a novel class of molecular shuttles **1** with imine-bonding stations for macrocyclic diamine parts are reported. Studies on dithioacetalized [2]rotaxane **4** with two hydrogen-bonding stations and a masked imine-bonding station showed that protonation of a macrocycle increases the shuttling barrier due to hydrogen-bond formation between NH_3^+ groups and the TEG-stations. Hydrolysis of the imine-bonds of the imine-bridged molecular shuttles **1b**,**c** with TEG-stations could exclusively give the [2]rotaxane **2b**,**c**·$2H^{2+}$, with the macrocycle hydrogen-bonded with the TEG-station. In contrast, **1a** without TEG-stations gave an equilibrated mixture of **1a**, monoimine **3a**·H^+, and **2a**·$2H^{2+}$ under similar acidic hydrolytic conditions. The equilibrium between **1b**,**c** and **2b**,**c**·$2H^{2+}$ to control the position of the macrocycle could be successfully switched to either side by applying acidic hydrolytic or dehydrating conditions. Furthermore, the equilibrium was largely biased to [2]rotaxane **2b**,**c**·$2H^{2+}$ under acidic hydrolytic conditions and could be reversed in favor of bis-imine **1b**,**c** just by heating. This is a successful example of a molecular shuttle exhibiting entropy-driven translational isomerism with remarkable positional discrimination. An examination of thermodynamic parameters showed that imine-bond hydrolyses and the formation of hydrogen bonds between the macrocycle and the station are thermodynamically matched processes, because both processes are enthalpically favored and accompanied by a loss of entropy. The combination of imine-bonding and hydrogen-bonding station in a rotaxane system is the key to realizing the clear entropy-driven positional switching of the macrocycle observed.

Introduction

The incorporation of multiple recognition motifs into molecular structures is a prerequisite for controlling component and substrate motion in future generations of molecular-level machines.[1] Stimuli-responsive molecular shuttles[2−11] are promising candidates, where translocation of the macrocycle between different sites ("stations") on an axle of rotaxanes is controlled by an external trigger, such as a redox process,[3] pH change,[4] ion exchange,[5] polarity,[6] light,[7] temperature,[8] or covalent bond-formation,[9,10] as well as the kind of macrocycle motion that is regulated.[11]

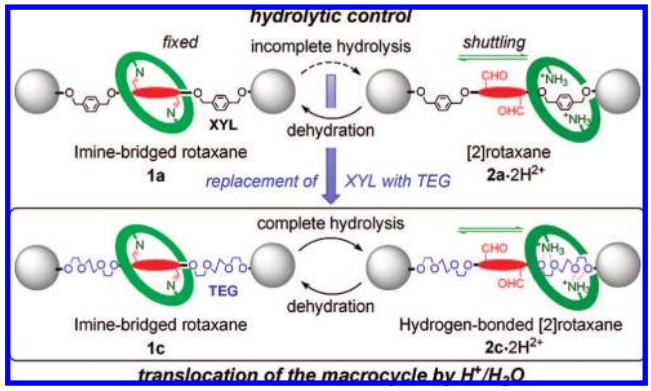
Imine bonds[12] can be equilibrated with an amine−aldehyde pair under hydrolytic conditions. The use of this dynamic covalent bond[13] to link components seems to be promising as a mean to control the on/off switching of subunit mobility or to change the position of the macrocycle on the axle in rotaxanes. We recently reported in a preliminary communication the successful preparation of a novel type of rotaxane **1a** by threading an axle molecule bearing two formyl groups into a macrocyclic diamine, cross-linking to form imine bonds,[14] and attaching bulky end-groups.[10] In that report, [2]rotaxane **2a** was successfully generated in equilibrium with **1a** in an acidic medium (Scheme 1), from which **1a** could be completely regenerated under dehydrating conditions. Thus, we demonstrated the translocation of a macrocycle by the application of H_2O/H^+. In addition, the independent mobility of the axle and macrocycle components in the rotaxane can be regulated on the basis of the controllable reversibility of the dynamic covalent bond.

However, the low equilibrium ratio of **2a** under acidic hydrolytic conditions (∼23% at 233 K in 0.08% TFA/$CDCl_3$) accompanied by a considerable amount of intermediary monoimine **3a** (∼40%) was inappropriate for achieving efficient switching, with which a stimuli-responsive molecular shuttle can be converted to another form. Therefore, we sought to

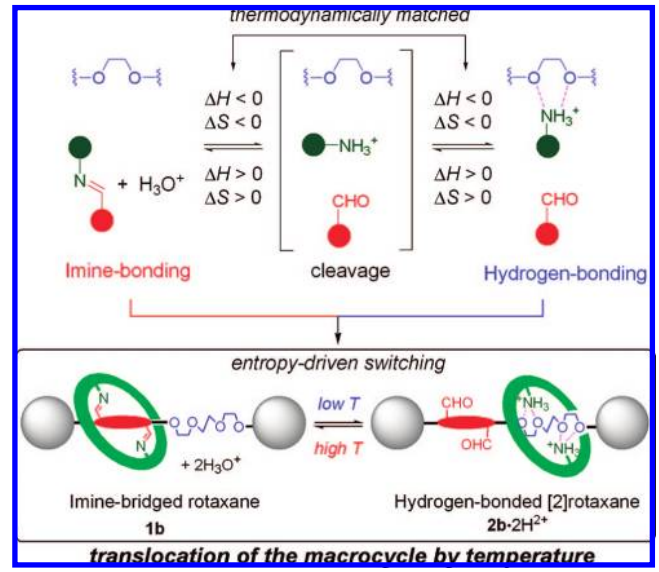
[†] Hokkaido University.
[‡] PRESTO.

(1) (a) *Molecular Devices and Machines- A Journey into the Nano World*; Balzani, V.; Credi, A.; Venturi, M., Eds.; Wiley−VCH: Weinheim, 2003. (b) Balzani, V.; Credi, A.; Raymo, F. M.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2000**, *39*, 3348–3391. (c) Flood, A. H.; Ramirez, R. J. A.; Deng, W.-Q.; Muller, R. P.; Goddard, W. A.; Stoddart, J. F. *Aust. Chem.* **2004**, *57*, 301–322. (d) Kinbara, K.; Aida, T. *Chem. Rev.* **2005**, *105*, 1377–1400. (e) Browne, W. L.; Feringa, B. L. *Nat. Nanotechnol.* **2006**, *1*, 25–35. (f) Tian, H.; Wang, Q. C. *Chem. Soc. Rev.* **2006**, *35*, 361–374. (g) Chatterjee, M. N.; Kay, E. R.; Leigh, D. A. *J. Am. Chem. Soc.* **2006**, *128*, 4058–4073. (h) Balzani, V.; Credi, A.; Silvi, S.; Venturi, M. *Chem. Soc. Rev.* **2006**, *35*, 1135–1149. (i) Bonnet, S.; Collin, J.-P.; Koizumi, M.; Mobian, P.; Sauvage, J.-P. *Adv. Mater.* **2006**, *18*, 1239–1250. (j) Kay, E. R.; Leigh, D. A.; Zerbetto, F. *Angew. Chem., Int. Ed.* **2007**, *46*, 72–191.
(2) (a) Anelli, P.-L.; Spencer, N.; Stoddart, J. F. *J. Am. Chem. Soc.* **1991**, *113*, 5131–5133. (b) Bissell, R. A.; Córdova, E.; Kaifer, A. E.; Stoddart, J. F. *Nature* **1994**, *369*, 133–137.

Scheme 1. Hydrolytic Control of Positional Switching of Macrocycle in Rotaxane-Based Molecular Shuttles with/without Hydrogen-Bonding Stations



Scheme 2. Thermodynamic Interplay of Imine- and Hydrogen-Bonding in a Rotaxane-Based Molecular Shuttle Exhibiting Entropy-Driven Translational Isomerism



design novel imine-bridged molecular shuttles that can be completely transformed to [2]rotaxane under hydrolytic conditions. Although the dynamic covalent properties of imine bonds (formation/cleavage) are generally compatible with various types of noncovalent interactions such as hydrogen-bonding, $\pi-\pi$ interaction, and metal-coordination, as proven by the successful construction of many supramolecular architectures,[15−17] we envisaged that imine-bond cleavage under dynamic acidic hydrolytic conditions would be assisted by the formation of hydrogen-bonds by the resulting primary ammoniums (NH_3^+) with suitable newly attached hydrogen-bonding acceptors.[18] Therefore, we designed novel imine-bridged molecular shuttles **1b**,**c** attached to triethylene glycol (TEG)-stations, which could be completely transformed to hydrolyzed [2]rotaxane under hydrolytic conditions due to hydrogen-bond formation between the macrocycle and the TEG-station.

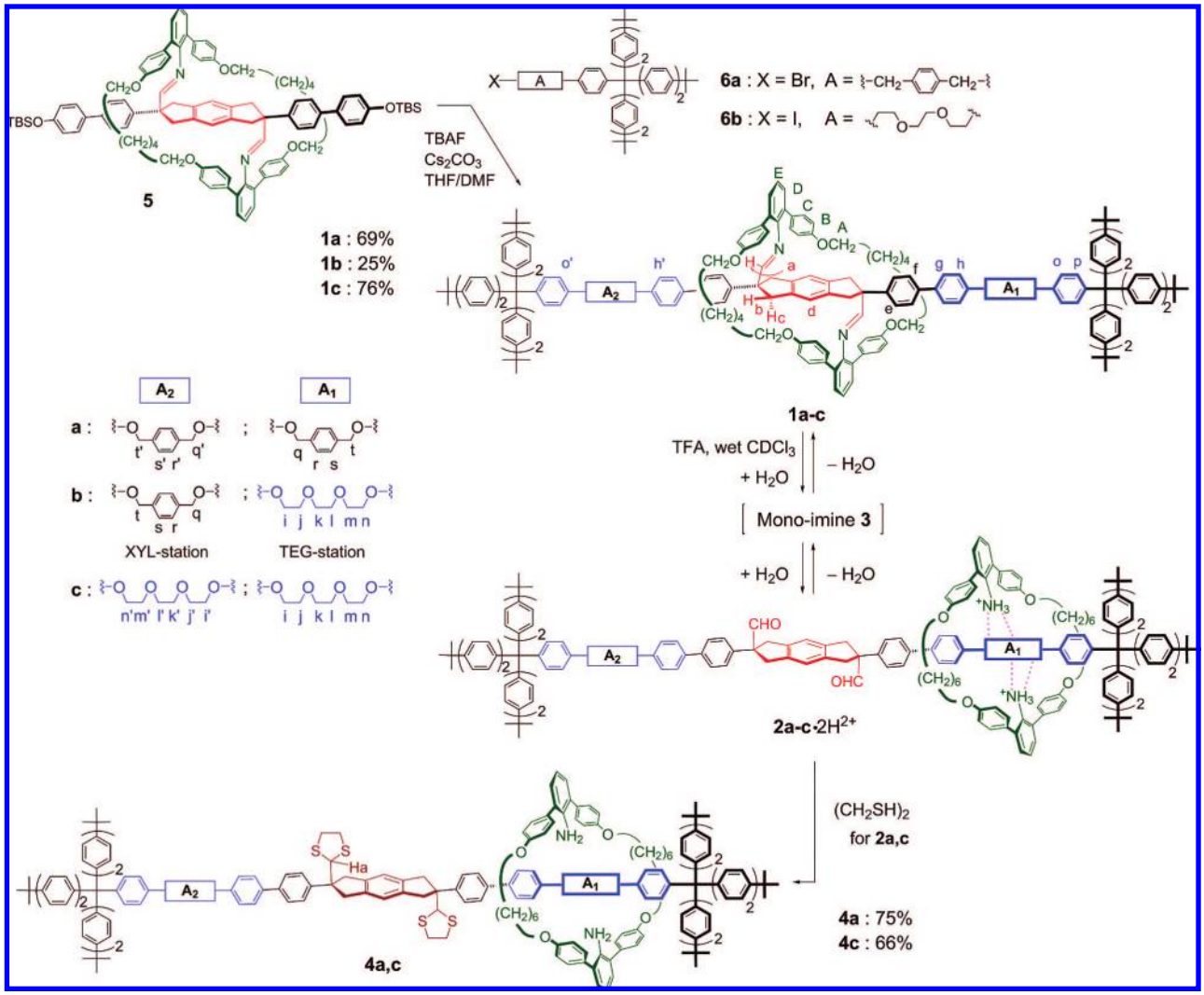
Furthermore, from the viewpoint of thermodynamic contributions, the combination of imine-bonding and hydrogen-bonding has to work synergistically for entropy-driven positional switching of the macrocycle in a rotaxane structure (Scheme 2): hydrogen-bond formation is an enthalpically favored interaction that is accompanied by a loss of entropy, whereas imine-bond formation is an entropically favored process in a rotaxane structure, since we reported[10] that **1a** was generated as an entropically preferred species under acidic hydrolytic conditions in the equilibrated mixture containing **2a** and **3a** (see below). Giuseppone and Lehn have also reported the equilibrium ratio of imine form in dynamic combinatorial libraries (DCLs) under low acidic conditions was increased with increasing temperature.[12e] Thus, imine-bond cleavage and hydrogen-bond formation are thermodynamically matched processes (enthalpically favored and entropically disfavored processes). The reverse processes, that is, hydrogen-bond cleavage and imine-bonding, have also to be matched processes (enthalpically disfavored and entropically favored processes). Accordingly, it is expected that the incorporation of both imine-bridging and hydrogen-bonding stations into a rotaxane axle would give a novel rotaxane-based molecular shuttle that exhibits the entropy-driven translational isomerism.[8a]

We report here the construction of a novel class of molecular shuttles **1b**,**c** with imine-bridging and hydrogen-bonding stations. Their shuttling properties were compared to those of derivatives with or without a hydrogen-bonding station (**1a**−**c**) or an imine-

(3) Recent examples of molecular shuttles controlled by redox: (a) Choi, J. W.; Flood, A. H.; Steuerman, D. W.; Nygaard, S.; Braunschweig, A. B.; Moonen, N. N. P.; Laursen, B. W.; Luo, Y.; DeIonno, E.; Peters, A. J.; Jeppesen, J. O.; Xu, K.; Stoddart, J. F.; Heath, J. R. *Chem.-Eur. J.* **2006**, *12*, 261–279. (b) Ikeda, T.; Saha, S.; Aprahamian, I.; Leung, K. C.-F.; Williams, A.; Deng, W.-Q.; Flood, A. H.; Goddard, W. A.; Stoddart, J. F. *Chem. Asian J.* **2007**, *2*, 76–93. (c) Green, J. E.; Choi, J. W.; Boukai, A.; Bunimovich, Y.; Johnston-Halperin, E.; DeIonno, E.; Luo, Y.; Sheriff, B. A.; Xu, K.; Shin, Y. S.; Tseng, H.-R.; Stoddart, J. F.; Heath, J. R. *Nature* **2007**, *445*, 414–417. (d) Nguyen, T. D.; Liu, Y.; Saha, S.; Leung, K. C.-F.; Stoddart, J. F.; Zink, J. I. *J. Am. Chem. Soc.* **2007**, *129*, 626–634. (e) Nygaard, S.; Leung, K. C.-F.; Aprahamian, I.; Ikeda, T.; Saha, S.; Laursen, B. W.; Kim, S.-Y.; Hansen, S. W.; Stein, P. C.; Flood, A. H.; Stoddart, J. F.; Jeppesen, J. O. *J. Am. Chem. Soc.* **2007**, *129*, 960–970. (f) Sindelar, V.; Silvi, S.; Parker, S. E.; Sobransingh, D.; Kaifer, A. E. *Adv. Funct. Mater.* **2007**, *17*, 694–701. (g) Aprahamian, I.; Dichtel, D. R.; Ikeda, T.; Heath, J. R.; Stoddart, J. F. *Org. Lett.* **2007**, *9*, 1287–1290. (h) Mateo-Alonso, A.; Fioravanti, G.; Marcaccio, M.; Paolucci, F.; Rahman, G. M. A.; Ehli, C.; Guldi, D. M.; Prato, M. *Chem. Commun.* **2007**, 1945–1947. (i) Durola, F.; Sauvage, J.-P. *Angew. Chem., Int. Ed.* **2007**, *46*, 3537–3540. (j) Saha, S.; Flood, A. H.; Stoddart, J. F.; Impellizzeri, S.; Silvi, S.; Venturi, M.; Credi, A. *J. Am. Chem. Soc.* **2007**, *129*, 12159–12171. (k) Altobello, S.; Nikitin, K.; Stolarczyk, J. K.; Lestini, E.; Fitzmaurice, D. *Chem.-Eur. J.* **2008**, *14*, 1107–1116. (l) Nikitin, K.; Lestini, E.; Stolarczyk, J. K.; Müller-Bunz, H.; Fitzmaurice, D. *Chem.-Eur. J.* **2008**, *14*, 1117–1128. (m) Jagesar, D. C.; Hartl, F.; Buma, W. J.; Brouwer, A. M. *Chem.-Eur. J.* **2008**, *14*, 1935–1946. (n) Fioravanti, G.; Haraszkiewicz, N.; Kay, E. R.; Mendoza, S. M.; Bruno, C.; Marcaccio, M.; Wiering, P. G.; Paolucci, F.; Rudolf, P.; Brouwer, A. M.; Leigh, D. A. *J. Am. Chem. Soc.* **2008**, *130*, 2593–2601. (o) Zhao, Y.-L.; Aprahamian, I.; Trabolsi, A.; Erina, N.; Stoddart, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 6348–6350.

(4) Recent examples of molecular shuttles controlled by pH change: (a) Schmidt-Schäffer, S.; Grubert, L.; Grummt, U. W.; Buck, K.; Abraham, W. *Eur. J. Org. Chem.* **2006**, 378–398. (b) Badjić, J. D.; Ronconi, C. M.; Stoddart, J. F.; Balzani, V.; Silvi, S.; Credi, A. *J. Am. Chem. Soc.* **2006**, *128*, 1489–1499. (c) Cheng, K. W.; Lai, C. C.; Chiang, P. T.; Chiu, S. H. *Chem. Commun.* **2006**, 2854–2856. (d) Choi, H. S.; Hirasawa, A.; Ooya, T.; Kajihara, D.; Hohsaka, T.; Yui, N. *ChemPhysChem* **2006**, *7*, 1671–1673. (e) Ooya, T.; Inoue, D.; Choi, H. S.; Kobayashi, Y.; Loethen, S.; Thompson, D. H.; Ko, Y. H.; Kim, K.; Yui, N. *Org. Lett.* **2006**, *8*, 3159–3162. (f) Leigh, D. A.; Thomson, A. R. *Org. Lett.* **2006**, *8*, 5377–5379. (g) Tuncel, T.; Ozsar, Ö.; Tiftika, H. B.; Salih, B. *Chem. Commun.* **2007**, 1369–1372. (h) Vella, S. J.; Tiburcio, J.; Loeb, S. J. *Chem. Commun.* **2007**, 4752–4754. (i) Crowley, J. D.; Leigh, D. A.; Lusby, P. J.; McBurney, R. T.; Perret-Aebi, L.-E.; Petzold, C.; Slawin, A. M. Z.; Symes, M. D. *J. Am. Chem. Soc.* **2007**, *129*, 15085–15090. (j) Berná, J.; Goldup, S. M.; Lee, A.-L.; Leigh, D. A.; Symes, M. D.; Teobaldi, G.; Zerbetto, F. *Angew. Chem., Int. Ed.* **2008**, *47*, 4392–4396. (k) Coutrot, F.; Busseron, E. *Chem.-Eur. J.* **2008**, *14*, 4784–4787.

Scheme 3. Synthesis of Imine-Bridged Rotaxanes **1a**−**c**, Hydrogen-Bonded [2]Rotaxanes **2a**−**c**·$2H^{2+}$, and Dithioacetalized [2]Rotaxanes **4a**,**c**



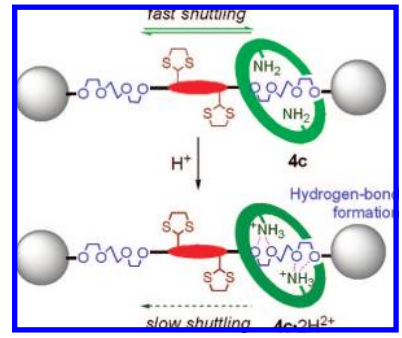
bonding station (**4a**,**c**). The equilibrium between **1b**,**c** and **2b**,**c** gives position-control for the macrocycle, which could be sufficiently biased toward either side by applying acidic hydrolytic or dehydrating conditions. Furthermore, the equilibrium that was biased toward the side of [2]rotaxane **2b**,**c** under acidic hydrolytic conditions could be reversed in favor of bis-imine **1b**,**c** simply by heating. This is a successful example of molecular shuttles exhibiting an entropy-driven translational isomerism[8] with remarkable positional discrimination.[19]

Results and Discussion

Synthesis. Imine-bridged molecular shuttles **1a**−**c** with xylylene (XYL) units as a non-hydrogen-bonding station or triethylene glycol ether (TEG) units as a hydrogen-bonding station were prepared by introducing end-groups **6a**,**b** with a XYL- or TEG-unit into imine-bridged pseudorotaxane **5**,[10] which was prepared from a hydrindacene axle and a macrocyclic diamine through the threading method directed by imine-bond formation (Scheme 3). Neutral dithioacetalized [2]rotaxanes **4a**,**c** were obtained by treating the solution of **1a**,**c** under acidic hydrolytic conditions with ethanedithiol.

Shuttling Control of Dithioacetalized [2]Rotaxane 4 by Protonation of the Macrocycle. First, the shuttling properties of dithioacetalized [2]rotaxanes **4a**,**c** with a protected imine-bridging station were investigated along with their protonated species to evaluate the effectiveness of the TEG-station as a hydrogen-bonding station toward ammoniums (Scheme 4). In the ^{1}H NMR spectra of neutral [2]rotaxanes **4a**,**c** in $CDCl_3$ (Figure 1), the two XYL- ($H^{q,t}$) or TEG-stations (H^{i-n}) and their linking phenylene groups (H^o and H^h) resonated at a higher field than did those of the axle molecules **7a**,**c**. The two stations appeared as one set of signals and did not exhibit any peak-splitting, even at low temperatures (188−298 K in CD_2Cl_2 for **4a** and 223−298 K in $CDCl_3$ for **4c**, respectively). The central

Scheme 4. Shuttling Control of Dithioacetalized [2]Rotaxane **4c** by Protonation



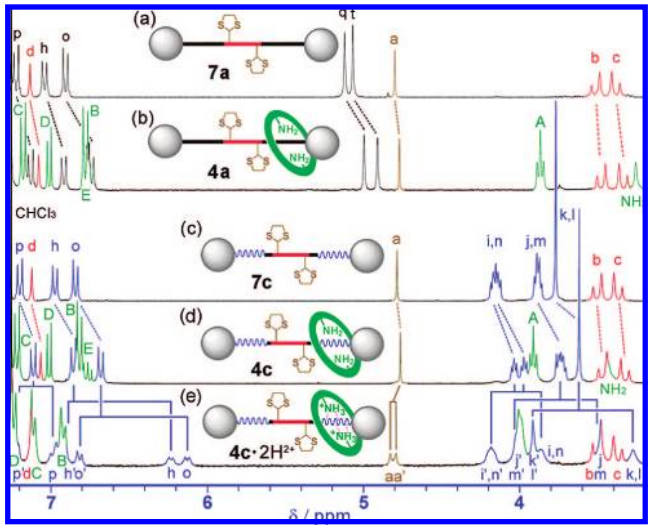


Figure 1. ^{1}H NMR spectra (300 MHz, $CDCl_3$, at 298 K) of (a) axle **7a**, (b) neutral [2]rotaxane **4a**, (c) axle **7c**, (d) neutral [2]rotaxane **4c**, and (e) protonated [2]rotaxane **4c**·$2H^{2+}$ generated upon the addition of TFA to a solution of **4c**. The lettering corresponds to the assignments shown in Scheme 3.

hydrindacene part ($\delta = 3.3-3.5$ for $H^{b,c}$ and 7.0−7.1 ppm for H^d) and dithioacetal moieties ($\delta = 4.8$ ppm for H^a) were slightly magnetically shielded as compared to those of the axles **7a**,**c**. These results indicate that the macrocycle in neutral [2]rotaxane **4a**,**c** rapidly shuttles between the two XYL- or TEG-stations.

Upon the addition of trifluoroacetic acid (TFA) to the solution of **4c** in $CDCl_3$, the signals around TEG-stations (H^{h-o}) and the dithioacetal moieties (H^a) of **4c**·$2H^{2+}$ split into two sets of signals at 298 K (Figure 1e), where one set appeared at a high field and another set appeared at a low field similar to the signals in bis-imine **1c** (Figure 2c). These split signals clearly show that the shuttling is slower than the NMR-time scale, although they coalesced upon heating above 328 K (Figure S1). In contrast, the addition of TFA to the solution of **4a** did not cause any peak-splitting. These observations indicate that the protonated [2]rotaxane **4c**·$2H^{2+}$ has an increased shuttling-barrier for the macrocycle as compared to neutral **4c** and protonated **4a**·$2H^{2+}$, due to the thermodynamic stabilization of **4c**·$2H^{2+}$ by hydrogen-bond formation between the ammonium groups of the macrocycle and $-OCH_2CH_2O-$ groups of the TEG-station. Accordingly, the results demonstrated that the TEG-station is an effective hydrogen-bonding station for ammonium groups, whereas stabilization by the XYL-station is negligible in the present molecular-shuttle system. The dithioacetalized [2]rotaxane **4c** is yet another example of a pH-responsive molecular shuttle.[4]

Generation of [2]Rotaxanes 2a−c by Hydrolysis of Imine-Bonds in Imine-Bridged Rotaxanes 1a−c. We next investigated the dynamic equilibrium under acidic hydrolytic conditions between **1b**,**c** and **2b**,**c**·$2H^{2+}$ with TEG-stations to examine whether the preferred position of a macrocycle could switch from the imine-bridging hydrindacene-station to the TEG-station on the rotaxane axle (Scheme 5).

As reported in the preliminary communication, hydrolytic control with the use of **1a** is incomplete due to the lack of hydrogen-bonding stations. Upon the addition of TFA to a solution of **1a** in wet $CDCl_3$, two sets of resonances of hydrolyzed [2]rotaxane **2a**·$2H^{2+}$ and monoimine **3a**·H^+ appeared as a dynamic equilibrated mixture with **1a** (Figure 2a,b).[20] These signals were fully assigned to the structures of **1a**, **3a**·H^+, and **2a**·$2H^{2+}$ based on ROESY, respectively (Figure S2). Although both sets of signals of **2a**·$2H^{2+}$ and **3a**·H^+ enhanced in intensity at the expense of those from **1a** as the recording temperature was lowered, bis-imine **1a** was still the major species in the equilibrated mixture. The equilibrium ratio of **1a**:**3a**·H^+:**2a**·H^{2+} was 42:35:23 at 233 K and 81:9:1 at 313 K (see below). The signals of the two XYL-stations in **2a**·$2H^{2+}$ in the equilibrated mixture appeared as a single set at a higher field than those of **1a** and **3a**·H^+, indicating that the macrocycle of **2a**·$2H^{2+}$ rapidly shuttles between the two XYL-stations.

In contrast to the case of **1a**, where three species coexist under acidic conditions, upon the addition of TFA to a solution of **1b** with a TEG- and an XYL-station in wet $CDCl_3$, the ^{1}H NMR spectrum showed the disappearance of signals derived from the bis-imine **1b** and the appearance of a new set of signals assignable to a single species including C*H*O signals ($H^{a,a'}$) at

(5) Recent examples of molecular shuttles controlled by ion exchange: (a) Marlin, D. S.; Cabrera, D. G.; Leigh, D. A.; Slawin, A. M. Z. *Angew. Chem., Int. Ed.* **2006**, *45*, 77–83. (b) Marlin, D. S.; Cabrera, D. G.; Leigh, D. A.; Slawin, A. M. Z. *Angew. Chem., Int. Ed.* **2006**, *45*, 1385–1390. (c) Tokunaga, Y.; Nakamura, T.; Yoshioka, M.; Shimomura, Y. *Tetrahedron Lett.* **2006**, *47*, 5901–5904. (d) Lin, C.-F.; Lai, C.-C.; Liu, Y.-H.; Peng, S.-M.; Chiu, S.-H. *Chem.-Eur. J.* **2007**, *13*, 4350–4355. (e) Huang, Y.-L.; Hung, W.-C.; Lai, C.-C.; Liu, Y.-H.; Peng, S.-M.; Chiu, S.-H. *Angew. Chem., Int. Ed.* **2007**, *46*, 6629–6633. (f) Zhou, W.; Li, J.; He, X.; Li, C.; Lv, J.; Li, Y.; Wang, S.; Liu, H.; Zhu, D. *Chem.-Eur. J.* **2008**, *14*, 754–763. (g) Chen, N.-C.; Lai, C.-C.; Liu, Y.-H.; Peng, S.-M.; Chiu, S.-H. *Chem.-Eur. J.* **2008**, *14*, 2904–2908.

(6) Recent examples of molecular shuttles controlled by polarity: (a) Mateo-Alonso, A.; Fioravanti, G.; Marcaccio, M.; Paolucci, F.; Jagesar, D. C.; Brouwer, A. M.; Prato, M. *Org. Lett.* **2006**, *8*, 5173–5176. (b) Tsukagoshi, S.; Miyawaki, A.; Takashima, Y.; Yamaguchi, H.; Harada, A. *Org. Lett.* **2007**, *9*, 1053–1055. (c) Mateo-Alonso, A.; Ehli, C.; Rahman, G. M. A.; Guldi, D. M.; Fioravanti, G.; Marcaccio, M.; Paolucci, F.; Prato, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 3521–3525. (d) Mateo-Alonso, A.; Iliopoulos, K.; Couris, S.; Prato, M. *J. Am. Chem. Soc.* **2008**, *130*, 1534–1535.

(7) Recent examples of molecular shuttlescontrolled by light: (a) Balzani, V.; Clemente-León, M.; Credi, A.; Semeraro, M.; Venturi, M.; Tseng, H.-R.; Wenger, S.; Saha, S.; Stoddart, J. F. *Aust. J. Chem.* **2006**, *59*, 193–206. (b) Balzani, V.; Clemente-León, M.; Credi, A.; Ferrer, B.; Venturi, M.; Flood, A. H.; Stoddart, J. F. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 1178–1183. (c) Cheetham, A. G.; Hutchings, M. G.; Claridge, T. D. W.; Anderson, H. L. *Angew. Chem., Int. Ed.* **2006**, *45*, 1596–1599. (d) Tsuda, S.; Aso, Y.; Kaneda, T. *Chem. Commun.* **2006**, 3072–3074. (e) Qu, D.-H.; Ji, F.-Y.; Wang, Q.-C.; Tian, H. *Adv. Mater.* **2006**, *18*, 2035–2038. (f) Serreli1, V.; Lee1, C.-F.; Kay, E. R.; Leigh, D. A. *Nature* **2007**, *445*, 523–527. (g) Abraham, W.; Buck, K.; Orda-Zgadzaj, M.; Schmidt-Schäffer, S.; Grummt, U.-W. *Chem. Commun.* **2007**, 3094–3096. (h) Zhou, W.; Chen, D.; Li, J.; Xu, J.; Lv, J.; Liu, H.; Li, Y. *Org. Lett.* **2007**, *9*, 3929–3932. (i) Li, Y.; Li, H.; Li, Y.; Liu, H.; Wang, S.; He, X.; Wang, N.; Zhu, D. *Org. Lett.* **2007**, *9*, 4835–4838. (j) Raiteri, P.; Bussi, G.; Cucinotta, C. S.; Credi, A.; Stoddart, J. F.; Parrinello, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 3536–3539.

(8) Examples of molecular shuttles controlled by temperature: (a) Bottari, G.; Dehez, F.; Leigh, D. A.; Nash, P. J.; Pérez, E. M.; Wong, J. K. Y.; Zerbetto, F. *Angew. Chem., Int. Ed.* **2003**, *42*, 5886–5889. (b) Choi, H. S.; Yamamoto, K.; Ooya, T.; Yui, N. *ChemPhysChem* **2005**, *6*, 1081–1086. (c) Kidowaki, M.; Zhao, C.; Kataoka, T.; Ito, K. *Chem. Commun.* **2006**, 4102–4103. (d) Kataoka, T.; Kidowaki, M.; Zhao, C.; Minamikawa, H.; Shimizu, T.; Ito, K. *J. Phys. Chem. B* **2006**, *110*, 24377–24383.

(9) Examples of molecular shuttles controlled by covalent bonding: (a) Cao, J.; Fyfe, M. C. T.; Stoddart, J. F.; Cousins, G. R. L.; Glink, P. T. *J. Org. Chem.* **2000**, *65*, 1937–1946. (b) Hannam, J. S.; Lacy, S. M.; Leigh, D. A.; Saiz, C. G.; Slawin, A. M. Z.; Stitchell, S. G. *Angew. Chem., Int. Ed.* **2004**, *43*, 3260–3264. (c) Leigh, D. A.; Pérez, E. M. *Chem. Commun.* **2004**, 2262–2263. (d) Tachibana, Y.; Kawasaki, H.; Kihara, N.; Takata, T. *J. Org. Chem.* **2006**, *71*, 5093–5104.

(10) Kawai, H.; Umehara, T.; Fujiwara, K.; Tsuji, T.; Suzuki, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 4281–4286.

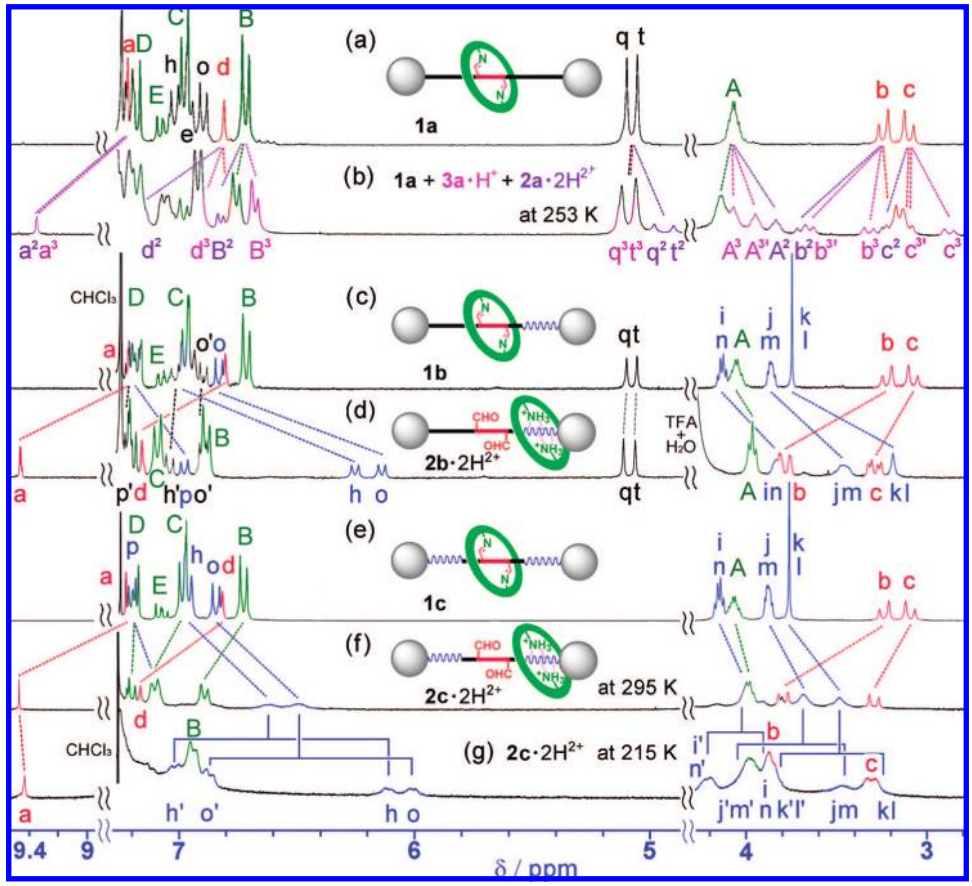
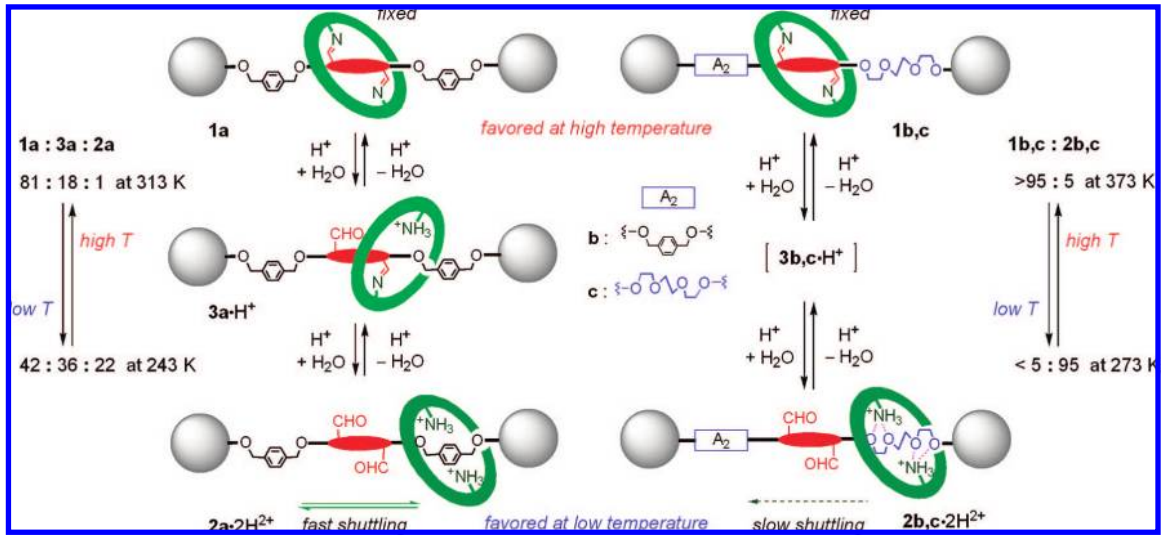


Figure 2. ^{1}H NMR spectra (300 MHz, wet $CDCl_3$) of (a) imine-bridged rotaxane **1a**, (b) the equilibrated mixture of **1a**, monoimine **3a**·H^+, and protonated [2]rotaxane **2a**·$2H^{2+}$ generated upon the addition of TFA to a solution of **1a** at 253 K, (c) imine-bridged rotaxane **1b**, (d) protonated [2]rotaxane **2b**·$2H^{2+}$ generated upon the addition of TFA to a solution of **1b** at 298 K, (e) imine-bridged rotaxane **1c**, (f) protonated [2]rotaxane **2c**·$2H^{2+}$ generated upon the addition of TFA to a solution of **1c** at 295 K, and (g) the same sample as in (f) at 215 K. The lettering corresponds to the assignments shown in Scheme 3 and in the Supporting Information. The superscript in the letterings in (b) corresponds to the compound number.

Scheme 5. Transformation between Imine-Bridged Rotaxanes **1a**−**c** and [2]Rotaxanes **2a**−**c** under Acidic Hydrolysis/Dehydration Conditions



$\delta = 9.4$ ppm even at 298 K (Figure 2c,d). The signals around the TEG-station (H^{i-n}, H^o, and H^h) of the newly generated species appeared at a higher field than those of the bis-imine **1b**, whereas those around the XYL-station ($H^{h',o'}$ and $H^{q,t}$) remained unchanged. Thus, the newly generated species was assigned as a [2]rotaxane **2b**·$2H^{2+}$ in which the macrocycle was located at the TEG-station on the axle due to hydrogen-bond formation. The ROESY spectra of **2b**·$2H^{2+}$ also provided evidence for the localization of the macrocycle at the TEG-station (Figure S3). Only trace amounts of the bis-imine **1b** and the monoimine **3b**·H^+ were observed at 298 K.

Similarly, the exclusive generation of [2]rotaxane **2c**·$2H^{2+}$ from **1c** was observed under acidic hydrolytic conditions at 295 K (Figure 2e,f). In the ^{1}H NMR spectrum, the two TEG-stations

of $\mathbf{2c}\cdot 2H^{2+}$ appeared as a single set of broader signals at 295 K, which indicated that shuttling of the macrocycles between two TEG-stations was slower than in the case of $\mathbf{2a}\cdot 2H^{2+}$ between XYL-stations. With a decrease in temperature, these signals split into two sets of distinct broad signals (Figure 2g), where one set appeared at a high field similar to the signals of the TEG-station of $\mathbf{2b}\cdot 2H^{2+}$ and another set appeared at a low field similar to the signals of the TEG-stations of bis-imine **1c**.[21] These observations indicate that the macrocycle of $\mathbf{2c}\cdot 2H^{2+}$ shuttled between two TEG-stations on the axle at a speed comparable to the NMR-time scale. The rate and the energy barrier for the shuttling of the macrocycle of $\mathbf{2c}\cdot 2H^{2+}$ were determined by the coalescence method on the variable-temperature (VT) NMR spectra: $k_{273} = 574\ s^{-1}$ and $\Delta G^{\ddagger} = 12.5 \pm 0.2$ kcal mol^{-1} at 273 K (T_c). The larger shuttling-barrier in $\mathbf{2c}\cdot 2H^{2+}$ than in $\mathbf{2a}\cdot 2H^{2+}$ must be due to hydrogen-bond formation between the macrocycle and the TEG-station.

When these acidic solutions containing $\mathbf{2b,c}\cdot 2H^{2+}$ were subjected to dehydrating conditions, bis-imines **1b,c** could be quantitatively regenerated as in the case of **1a**.[22] Thus, we demonstrated that the incorporation of hydrogen-bonding TEG-stations into imine-bridged rotaxanes could realize novel molecular shuttles where a macrocycle can be translocated reversibly between the imine-bridging station and the TEG-station by hydrolytic control with a complete positional discrimination.[19]

Entropy-Driven Translational Isomerism between Imine-Bridged Rotaxane and Hydrogen-Bonded [2]Rotaxane. In addition to the successful switching to bis-imines **1** and [2]rotaxanes $\mathbf{2}\cdot 2H^{2+}$ by hydrolytic control, we found that switching between **1** and $\mathbf{2}\cdot 2H^{2+}$ could also be realized by simply changing the temperature under acidic hydrolytic conditions. In particular, $\mathbf{1b,c/2b,c}\cdot 2H^{2+}$ with TEG-stations could be completely switched from one station to another as a function of temperature, which demonstrates the entropy-driven positional switching of the macrocycle in a molecular shuttle.[8]

When a solution of [2]rotaxane $\mathbf{2b}\cdot 2H^{2+}$ in C_6D_5Br under acidic hydrolytic conditions was heated above 298 K, new sets of signals assignable to the bis-imine **1b** were enhanced in intensity at the expense of those from $\mathbf{2b}\cdot 2H^{2+}$ (Figure 3g to b and Figure 5a). Bis-imine **1b** finally became an exclusive species above 343 K, consistent with the fact that the bis-imine **1b** was an entropically favored species. When the solution was cooled to 273 K, $\mathbf{2b}\cdot 2H^{2+}$ was completely regenerated. The monoimine $\mathbf{3b}\cdot H^{+}$ was not observed in either heating or cooling. Also, in the case of $\mathbf{2c}\cdot 2H^{2+}$, reversible switching was observed between **1c** and $\mathbf{2c}\cdot 2H^{2+}$ with a change in the temperature (Figure S4). The release of water molecules accompanied by intramolecular imine-bond formation from $\mathbf{2b,c}\cdot 2H^{2+}$ to **1b,c** seems to contribute to the gain in entropy under heating (see below). Thus, the equilibrium ratio of **1b,c/2b,c**, which determines the preferred position of the macrocycle between the imine-bridging and hydrogen-bonding stations, could be completely reversed as a function of temperature (the ratios of $\mathbf{1b,c/2b,c}\cdot H^{2+} = <5/95$ at 273 K; >95/5 at 373 K, respectively). There are very few examples of entropy-driven translational isomerism,[8] and thus the complete positional discrimination in our molecular shuttle system is noteworthy.

(11) (a) Jiang, L.; Okano, J.; Orita, A.; Otera, J. *Angew. Chem., Int. Ed.* **2004**, *43*, 2121–2124. (b) Wang, Q.-C.; Qu, D.-H.; Ren, J.; Chen, K.; Tian, H. *Angew. Chem., Int. Ed.* **2004**, *43*, 2661–2665. (c) Ghosh, P.; Federwisch, G.; Kogej, M.; Schalley, C. A.; Haase, D.; Saak, W.; Lützen, A.; Gschwind, R. M. *Org. Biomol. Chem.* **2005**, *3*, 2691–2700. (d) Létinois-Halbes, U.; Hanss, D.; Beierle, J. M.; Collin, J.-P.; Sauvage, J.-P. *Org. Lett.* **2005**, *9*, 5753–5756. (e) Hirose, K.; Ishibashi, K.; Shiba, Y.; Doi, Y.; Tobe, Y. *Chem. Lett.* **2007**, *36*, 810–811. (f) Horie, M.; Sassa, T.; Hazhizume, D.; Suzaki, Y.; Osakada, K.; Wada, T. *Angew. Chem., Int. Ed.* **2007**, *46*, 4983–4986. (g) Hirose, K.; Shiba, Y.; Ishibashi, K.; Doi, Y.; Tobe, Y. *Chem.-Eur. J.* **2008**, *14*, 981–986. (h) Hirose, K.; Shiba, Y.; Ishibashi, K.; Doi, Y.; Tobe, Y. *Chem.-Eur. J.* **2008**, *14*, 3427–3433. (i) Hirose, K.; Ishibashi, K.; Shiba, Y.; Doi, Y.; Tobe, Y. *Chem.-Eur. J.* **2008**, *14*, 5803–5811.

(12) (a) Schiff, H. *Ann.* **1864**, *131*, 118. (b) Layer, R. W. *Chem. Rev.* **1963**, *63*, 489–510. (c) *The Chemistry of the Amino Group*; Patai, S., Ed.; John Wiley & Sons: London, 1968; Chapter 7. (d) Giuseppone, N.; Schmitt, J.-L.; Schwartz, E.; Lehn, J.-M. *J. Am. Chem. Soc.* **2005**, *127*, 5528–5539. (e) Giuseppone, N.; Lehn, J.-M. *Chem.-Eur. J.* **2006**, *12*, 1715–1722.

(13) (a) Lehn, J.-M. *Chem.-Eur. J.* **1999**, *5*, 2455–2463. (b) Rowan, S. J.; Cantrill, S. J.; Cousins, G. R. L.; Sanders, J. K. M.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2002**, *41*, 899–952. (c) Corbett, P. T.; Leclaire, J.; Vial, L.; West, K. R.; Wietor, J.-L.; Sanders, J. K. M.; Otto, S. *Chem. Rev.* **2006**, *106*, 3652–3711. (d) Lehn, J.-L. *Chem. Soc. Rev.* **2007**, *36*, 151–160.

(14) Other rotaxane syntheses based on covalent bond methods: (a) Hiratani, K.; Suga, J.; Nagawa, Y.; Houjou, H.; Tokuhisa, H.; Numata, M.; Watanabe, K. *Tetrahedron Lett.* **2002**, *43*, 5747–5750. (b) Kameta, N.; Hiratani, K.; Nagawa, Y. *Chem. Commun.* **2004**, 466–467. (c) Hirose, K.; Nishihara, K.; Harada, N.; Nakamura, Y.; Masuda, D.; Araki, M.; Tobe, Y. *Org. Lett.* **2007**, *9*, 2969–2972.

(15) (a) Meyer, C. D.; Joiner, C. S.; Stoddart, J. F. *Chem. Soc. Rev.* **2007**, *36*, 1705–1723. (b) Borisova, N. E.; Reshetova, M. D.; Ustynyuk, Y. A. *Chem. Rev.* **2007**, *107*, 46–79.

(16) Recent examples of interlocked molecules assembled by combination of imine bonds with noncovalent interactions: (a) Northrop, B. H.; Aricó, F.; Tangchiavang, N.; Badjić, J. D.; Stoddart, J. F. *Org. Lett.* **2006**, *8*, 3899–3902. (b) Williams, A. R.; Northrop, B. H.; Chang, T.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 6665–6669. (c) Pentecost, C. D.; Chichak, K. S.; Peters, A. J.; Cave, G. W. V.; Cantrill, S. J.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2007**, *46*, 218–222. (d) Nitschke, J. R. *Acc. Chem. Res.* **2007**, *40*, 103–112. (e) Yates, C. R.; Benítez, D.; Khan, S. I.; Stoddart, J. F. *Org. Lett.* **2007**, *9*, 2433–2436. (f) Leung, K. C.-F.; Aricó, F.; Cantrill, S. J.; Stoddart, J. F. *Macromolecules* **2007**, *40*, 3951–3959. (g) Haussmann, P. C.; Khan, S. I.; Stoddart, J. F. *J. Org. Chem.* **2007**, *72*, 6708–6713. (h) Wu, J.; Leung, K. C.-F.; Stoddart, J. F. *Proc. Natl. Acad. Sci. U.S.A.* **2007**, *104*, 17266–17271.

(17) Recent examples of giant structures assembled by imine bonds: (a) Hui, J. K.-H.; MacLachlan, M. J. *Chem. Commun.* **2006**, 2480–2482. (b) Liu, X.; Warmuth, R. *J. Am. Chem. Soc.* **2006**, *128*, 14120–14127. (c) Giuseppone, N.; Schmitt, J.-L.; Lehn, J.-M. *J. Am. Chem. Soc.* **2006**, *128*, 16748–16763. (d) Hartley, C. S.; Elliot, E. L.; Moore, J. S. *J. Am. Chem. Soc.* **2007**, *129*, 4512–4513. (e) Chow, C.-F.; Fujii, S.; Lehn, J.-M. *Angew. Chem., Int. Ed.* **2007**, *46*, 5007–5010. (f) Liu, Y.; Liu, X.; Warmuth, R. *Chem.-Eur. J.* **2007**, *13*, 8953–8959. (g) Xu, S.; Giuseppone, N. *J. Am. Chem. Soc.* **2008**, *130*, 1826–1827. (h) Giuseppone, N.; Schmitt, J. L.; Allouche, L.; Lehn, J.-M. *Angew. Chem., Int. Ed.* **2008**, *47*, 2235–2239. (i) Ulrich, S.; Lehn, J.-M. *Angew. Chem., Int. Ed.* **2008**, *47*, 2240–2243. (j) Xu, D.; Warmuth, R. *J. Am. Chem. Soc.* **2008**, *130*, 7520–7521.

(18) Chiu, S.-H.; Stoddart, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 4174–4175.

(19) A Boltzmann distribution at 298 K requires a $\Delta\Delta E$ (or $\Delta\Delta G$) value between translational co-conformers of about 2 kcal mol^{-1} for 95% occupancy of one station in a positionally bistable shuttle: Altieri, A.; Bottari, G.; Dehez, F.; Leigh, D. A.; Wong, J. K. Y.; Zerbetto, F. *Angew. Chem., Int. Ed* **2003**, *42*, 2296–2300.

(20) When a small amount of TFA (0.08% v/v) was added to the solution of **1a** in wet $CDCl_3$, the dynamic equilibrium in Figure 2b was observed. However, when a large excess of TFA (>1% v/v) was added, hydrolysis of the imine bonds was not observed. This observation resembles the results observed in DCLs by Giuseppone and Lehn.[12e]

(21) As the exclusive generation of $\mathbf{2c}\cdot 2H^{2+}$ at low temperature region (215−295 K) was also evidenced from the integrated intensity of the formyl proton (H^a), the observed split of the signals is due to the slow shuttling of the macrocycle of $\mathbf{2c}\cdot 2H^{2+}$ but not due to the chemical exchange between **1c** and $\mathbf{2c}\cdot 2H^{2+}$.

(22) Thanks to the increased equilibrium ratios of the [2]rotaxane $\mathbf{2b,c}\cdot 2H^{2+}$ under the acidic hydrolysis conditions, neutral [2]rotaxane **2b,c** was obtained with a small amount of bis-imine **1b,c** by treating the acidic solution of $\mathbf{2b,c}\cdot 2H^{2+}$ with aqueous $NaHCO_3$ or by passing the solution through a short column of aluminum oxide. On the other hand, the similar treatment of $\mathbf{1a/2a}\cdot 2H^{2+}$ quantitatively gave bis-imine **1a**.

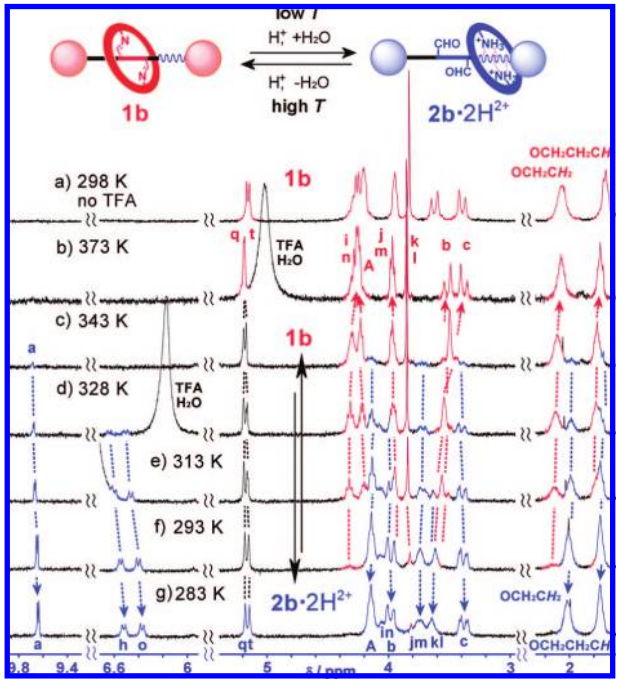


Figure 3. ^{1}H NMR spectra (300 MHz, wet C_6D_5Br) of (a) imine-bridged rotaxane **1b**, and (b)−(g) a hydrolyzed mixture containing **1b** and **2b**·2H^{2+}: (b) measured at 373 K, (c) 343 K, (d) 328 K, (e) 313 K, (f) 293 K, and (g) 283 K. The lettering corresponds to the assignments shown in Scheme 3.

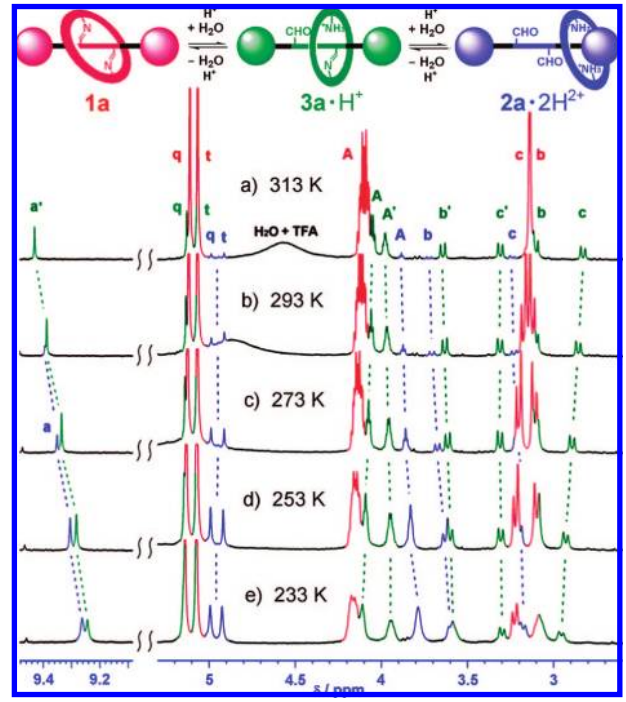


Figure 4. ^{1}H NMR spectra (600 MHz, wet $CDCl_3$) of (a)−(e) a hydrolyzed mixture containing **1a**, **3a**·H$^+$, and **2a**·2H^{2+}: (a) measured at 313 K, (b) 293 K, (c) 273 K, (d) 253 K, and (e) 233 K. The lettering corresponds to the assignments shown in Scheme 3 and Figure S1.

In contrast, in the case of **1a/3a/2a** with two XYL-stations,[10] ^{1}H NMR spectra in $CDCl_3$ or C_6D_5Br under acidic hydrolytic conditions showed the coexistence of bis-imine **1a**, monoimine **3a**, and [2]rotaxane **2a** as an equilibrated mixture over the range of 243−378 K, although the equilibrium ratio shows moderate temperature dependence (**1a**:**3a**:**2a** = 42:36:22 at 243 K to 81:18:∼1 at 313 K in $CDCl_3$, Figures 4, 5b, and S5).

If we compare the temperature dependence of the equilibrium ratio of **1b/2b** with that of **1a/3a/2a** in C_6D_5Br (Figure 5a,b), we see that incorporation of a TEG-station brings about two interesting thermodynamic effects on the equilibrium between **1** and **2**: (1) a TEG-station biases the equilibrium in favor of [2]rotaxane due to hydrogen-bond formation with the macrocycle under acidic hydrolytic conditions; and (2) the equilibrium ratio in the molecular shuttle **1b**,**c**/**2b**,**c**·2H^{2+} with TEG-stations changes within a narrower temperature range than in the case of **1a/2a**·2H^{2+} without TEG-station. These effects can be explained in terms of thermodynamic parameters for the hydrolysis of **1** to **2**·2H^{2+}, which was estimated from a van't Hoff plot of the temperature-dependent equilibrium ratios (Figure 5c and Table 1).

The enthalpy and entropy differences between **1a** and **2a**·2H^{2+} are both negative ($\Delta H = -6.0 \pm 0.4$ kcal mol^{-1} and $\Delta S = -26.0 \pm 1.4$ cal mol^{-1} K^{-1}), indicating that the hydrolysis of imine-bonds is an enthalpically favored and entropically disfavored process (Table 1, Scheme 2). The negative entropy change for imine hydrolysis indicates that the entropy loss by addition of two water molecules more than offset the entropy gain by mobilization of the macrocycle in the rotaxane structure. For further consideration, the thermodynamic parameters of imine-hydrolysis were determined by considering the intermediary monoimine **3a**·H$^+$. The van't Hoff plots of each step in the imine-hydrolysis of **1a** revealed that differences in both enthalpy and entropy from **1a** to **3a**·H$^+$ ($\Delta H = -2.9 \pm 0.2$ kcal mol^{-1} and $\Delta S = -12.3 \pm 0.6$ cal mol^{-1} K^{-1}) and from **3a**·H$^+$ to **2a**·2H^{2+} ($\Delta H = -3.1 \pm 0.3$ kcal mol^{-1} and $\Delta S = -13.8 \pm 1.2$ cal mol^{-1} K^{-1}) have similar values and the steps are noncooperative (see Supporting Information). Thus, without the extra stabilization of **2** by hydrogen-bonding, a considerable amount of intermediary **3a**·H$^+$ coexists during the interconversion of **1a** and **2a**·2H^{2+}.

On the other hand, the changes in both enthalpy and entropy from **1b** to **2b**·2H^{2+} ($\Delta H = -16.7 \pm 0.7$ kcal mol^{-1} and $\Delta S = -52.2 \pm 2.1$ cal mol^{-1} K^{-1}) were larger than those in the change from **1a** to **2a**·2H^{2+}, as shown by the steeper regression line for the plot of **1b/2b**·2H^{2+} (Figure 5c). This drastic difference in the enthalpy and entropy changes originates from the incorporation of a TEG-station in place of a XYL-station: that is, the additional enthalpic stabilization and loss of entropy due to hydrogen-bonding of the macrocycle with the TEG-station in **2b**·2H^{2+} ($\Delta\Delta H_{b-a} = -10.7$ kcal mol^{-1} and $\Delta\Delta S_{b-a} = -26.2$ cal mol^{-1} K^{-1} for hydrogen-bond formation with a TEG-station). The conformational restriction of TEG-moiety accompanied by hydrogen-bonding might contribute to the additional negative ΔS term.[23] Consequently, the incorporation of a TEG-station with hydrogen-bonding ability into imine-bridged rotaxanes not only biased the equilibrium between **1** and **2b**·2H^{2+} under acidic hydrolytic conditions in favor of hydrolyzed [2]rotaxane, but also enables entropy-driven positional switching[8] of the macrocycle by supplying additional enthalpic and entropic changes. Furthermore, these thermodynamic parameters show that both imine-bond hydrolysis and hydrogen-bond formation between the macrocycle and the station in the rotaxane system are thermodynamically matched processes, that is, enthalpically favored processes accompanied by a loss of entropy, whereas both hydrogen-bond cleavage and

(23) Meot-Ner, M. *J. Am. Chem. Soc.* **1983**, *105*, 4912–4915.

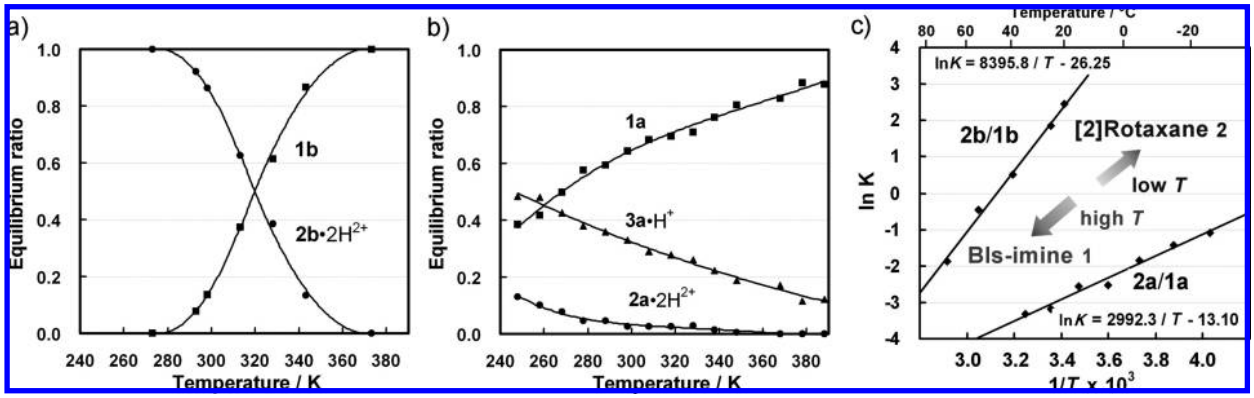


Figure 5. (a) Temperature dependence of the equilibrium ratio of **1b** and **2b**·$2H^{2+}$ in the hydrolyzed mixture in C_6D_5Br, and (b) temperature dependence of the equilibrium ratio of **1a**, **3a**·H^+, and **2a**·$2H^{2+}$ in the hydrolyzed mixture in C_6D_5Br. (c) van't Hoff plots for the hydrolysis of **1b** to **2b**·$2H^{2+}$ and **1a** to **2a**·$2H^{2+}$.

Table 1. Thermodynamic Parameters for the Conversions of Bis-imine **1** to Monoimine **3**·H^+ and [2]Rotaxane **2**·$2H^{2+}$ in C_6D_5Br

compounds	ΔH (kcal mol^{-1})	ΔS (cal mol^{-1} K^{-1})	ΔG_{273}, ΔG_{373} (kcal mol^{-1})
1a to **2a**·$2H^{2+}$	-6.0 ± 0.4	-26.0 ± 1.4	$+1.1$, $+3.7$
[**1a** to **3a**·H^+]	-2.9 ± 0.2	-12.3 ± 0.6	$+0.5$, $+1.7$
[**3a**·H^+ to **2a**·$2H^{2+}$]	-3.1 ± 0.3	-13.7 ± 1.2	$+0.6$, $+2.0$
1b to **2b**·$2H^{2+}$	-16.7 ± 0.7	-52.2 ± 2.1	-2.4, $+2.8$

imine-bond formation are entropically favored processes (Scheme 1). Consequently, the competitive combination of imine-bonding and hydrogen-bonding stations in a rotaxane system enables the entropy-driven positional switching of the macrocycle to give novel molecular shuttles with a sharp transition by synergistic effects of entropy terms, as demonstrated here.

Conclusion

We have shown that the incorporation of a hydrogen-bonding TEG-station into imine-bridged rotaxane can lead to novel molecular shuttles, in which the position of the macrocycle can be switched between imine- and hydrogen-bonding stations with complete positional discrimination by dehydration/hydrolysis or simply by changes in temperature under hydrolytic conditions. The capability of the primary amine/ammonium group for both dynamic imine- and hydrogen-bond formation is the key feature for realizing entropy-driven translational isomerism in the novel molecular shuttle. This interplay could play an important role in the design of entropy-driven molecular machines that exhibits a sharp transition in response to small temperature changes. The further application of this interplay to molecular shuttles and switches is a subject of current interest.

Acknowledgment. H.K. acknowledges support by JSPS KAKENHI (No. 18750024), the Global COE Program (Project No. B01: Catalysis as the Basis for Innovation in Materials Science) from MEXT, and JST PRESTO project. T.U. gratefully acknowledges a JSPS Research Fellowship for Young Scientist. We are grateful to K. Watanabe of the GC−MS and NMR Laboratory (Hokkaido University) for the mass spectrometric analyses and to Dr. Y. Kumaki of the High-Resolution NMR Laboratory (Hokkaido University) for the ROESY measurements.

Supporting Information Available: Experimental details and additional spectroscopic data for the rotaxanes. This material is available free of charge via the Internet at http://pubs.acs.org.

JA804888B