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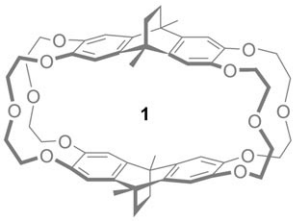
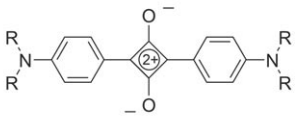
Squaraine-Based [2]Rotaxanes that Function as Visibly Active Molecular Switches

Sheng-Yao Hsueh,[a] Chien-Chen Lai,[b] and Sheng-Hsien Chiu*[a]

Molecular switches undergo reversible (co)conformational shifts or molecular transformations, under the influence of pH,[1] photons,[2] cations,[3] anions,[4] heat,[5] and/or electrons,[6] between two or more different stable states. Although many external stimuli (inputs) are available to operate molecular switches, the most important outputs are generally mechanical forces and optical signals: the former allows the construction of artificial molecular machines[7] and the latter provides the possibility for molecular sensing.[8] Thanks to burgeoning growth in the synthesis of interlocked molecules, several rotaxane- and catenane-based molecular switches have been developed in which detectable optical signals accompany the migration of interlocked macrocycles between different recognition sites; such materials are potentially useful for constructing complicated molecular logic[9] and optical devices.[10] Light-active molecular switches providing fluorescence outputs at long wavelengths, approaching the near-infrared (NIR) region, have potential practical importance in biomedicine and photodynamic therapy for sensing and signaling in living tissues and cells.[11] Squaraine-based fluorescence dyes generally exhibit low quantum yields in polar solvents; in their host-encapsulated forms, however, they can experience less-polar local environments and, therefore, exhibit significantly increased quantum yields, even in polar solvents.[12] This behavior suggests a straightforward approach toward the design of squaraine-based optical switches: if the solvent-exposed and encapsulated forms of a squaraine unit can be generated as two distinguishable stable states of a switchable rotaxane in a polar solvent, variations in the optical signals in the long-wavelength-fluorescence region should be produced within each switching cycle. Herein, we report the synthesis and operation of squaraine-based optical molecular switches, which display striking changes in their fluorescence signals that are visible to the naked eye.

Previously, we reported that the molecular cage **1** forms complexes with the squaraine derivatives **2** under the assistance of Na^+ ions as templates.[13] Thus, we anticipated that the [2]rotaxane[**4**-long·Na_2][$4\,ClO_4$] (Scheme 1) would function as a molecular switch in CD_3CN if we could remove the templating Na^+ ions and, thereby, move the molecular cage from the squaraine station to the bipyridinium one; this process should have the effect of decreasing the intensity of the long-wavelength-fluorescence emission of the [2]rotaxane.





2: R = C_3H_7
3: R = C_4H_9

We synthesized the molecular switches [**4**-long·Na_2]-[$4\,ClO_4$] and [**4**-short·Na_2][$4\,ClO_4$], each featuring one squaraine and one bipyridinium station, but differing in the length of the alkyl spacer (C_{16} and C_8 units, respectively) between them, through the reactions of the squaraine-containing pyridine derivatives **6**-long·Br and **6**-short·Br, respectively, with the benzyl bromide **7** in the presence of the molecular cage **1** and $NaClO_4$ (42:42:63:105 mM) in CH_3CN. Our reasons for choosing to install bipyridinium moieties as competing recognition units in these [2]rotaxanes were twofold: 1) their potentially strong binding to the crown ether like (C–H···O hydrogen bonds) and catechol (π stacking) motifs of the molecular cage moiety would allow the macrocycle to reside at these stations after removing the Na^+ template

[a] S.-Y. Hsueh, Prof. S.-H. Chiu
Department of Chemistry, National Taiwan University
No. 1, Sec. 4, Roosevelt Road, Taipei, Taiwan (ROC)
Fax: (+886) 2-3366-1677
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 (ROC)

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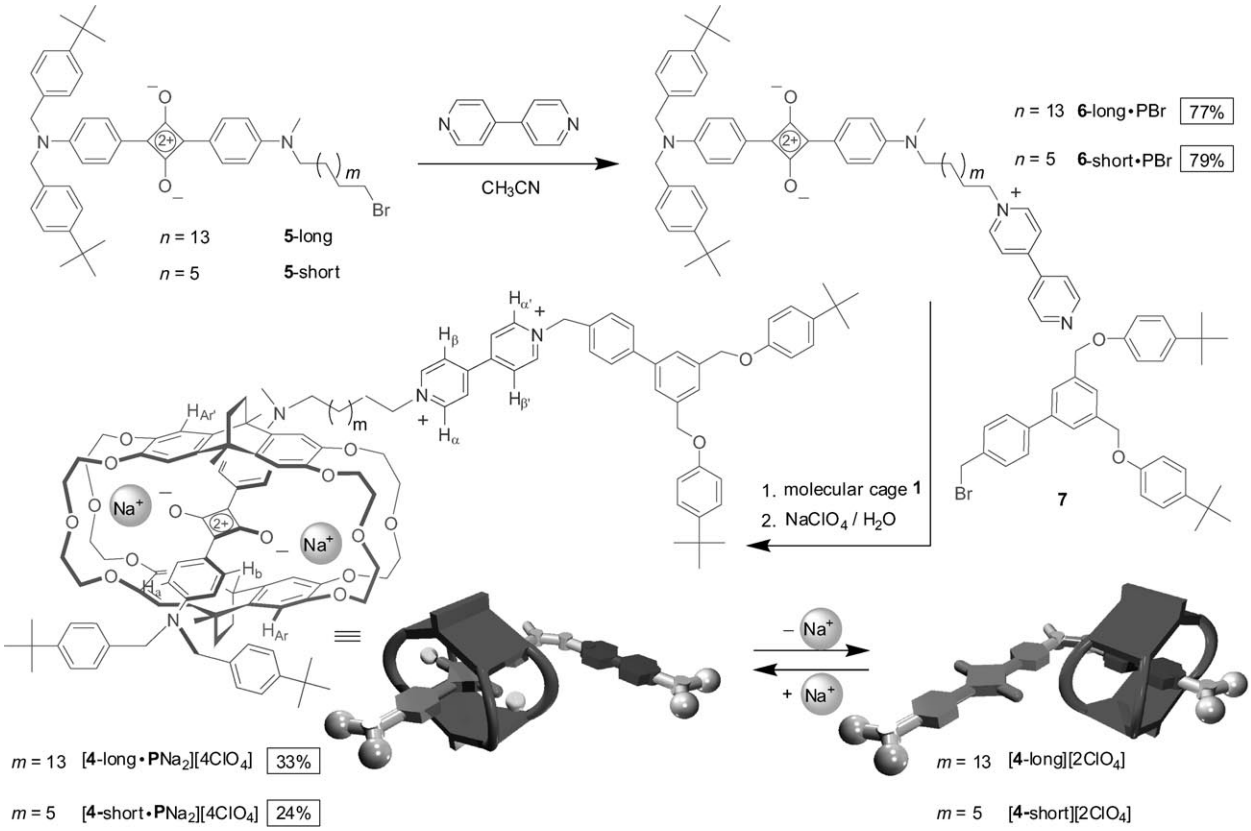


Scheme 1.

ions and 2) their fluorescence quenching ability would allow the tuning of the fluorescence intensity of the squaraine units by controlling the distance between the two guest stations.[14]

2D COSY and NOSY experiments allowed us to identify most of the signals in the ^{1}H NMR spectrum of the [2]rotaxane [**4**-long•Na_2][4 ClO_4] in CD_3CN at 298 K (Figure 1 a); we confirmed that, under these conditions, the molecular cage resided around the squaraine station (see the Supporting Information). The addition of [2.2.2]cryptand to a solution of the [2]rotaxane[**4**-long•Na_2][4 ClO_4] in CD_3CN, thereby sequestering the Na^+ ions, resulted in significant shifts to several of the signals in the ^{1}H NMR spectrum (Figure 1 b), suggesting the migration of the molecular cage moiety from the squaraine unit to the bipyridinium station. The 2D NOSY spectrum of this mixture displayed (see the Supporting Information) cross peaks between the signals of the aromatic protons (H_{Ar}) of the molecular cage moiety and the bipyridinium protons (H_α and H_β), confirming the encircling of the macrocyclic component around the bipyridinium station under these conditions. Subsequent addition of $NaClO_4$ (2 equiv) returned the macrocycle back to its original position around the squaraine station (Figure 1 c), thereby demonstrating the reversible translocation of the molecular cage unit within the [2]rotaxane [**4**-long•Na_2][4 ClO_4].

We determined the quantum yields of the [2]rotaxanes [**4**-long]$^{2+}$ and [**4**-long•Na_2]$^{4+}$ in CH_3CN to be 0.11 and 0.22, respectively (Table 1); the former value is higher and the latter lower than that of the free squaraine dye **3** ($\Phi = 0.15$) under the same conditions, suggesting that the fluorescence enhancement caused by encapsulating the squaraine dye within **1** and the fluorescence quenching caused by installing

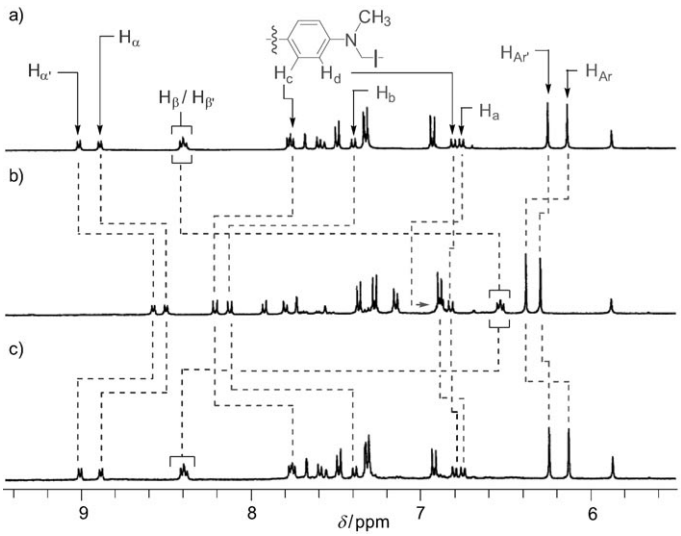


Figure 1. Partial ^{1}H NMR spectra (400 MHz, CD_3CN, 298 K) of a) the [2]rotaxane [**4**-long•Na_2][4 ClO_4] (3 mM), b) the mixture obtained after adding [2.2.2]cryptand (2 equiv) to the solution in a), and c) the mixture obtained after adding $NaClO_4$ (2 equiv) to the solution in b).

Table 1. Absorption and emission properties of [2]rotaxane-based molecular switches in CH_3CN.

Compound	λ_{abs} [nm]	$\log \varepsilon$	λ_{em}[a] [nm]	Φ_f[b]
[**4**-long·Na_2][4 ClO_4]	629	5.33	641	0.22
[**4**-long][2 ClO_4]	634	5.32	645	0.11
[**4**-short·Na_2][4 ClO_4]	630	5.39	643	0.09
[**4**-short][2 ClO_4]	634	5.38	653	0.05
[**9**·Na_2][3 ClO_4]	630	5.12	635	0.22
[**9**][ClO_4]	635	5.10	648	0.18

[a] Solutions of [**4**-long·Na_2][4ClO_4], [**4**-long][2 ClO_4], [**4**-short·Na_2]-[4 ClO_4], [**4**-short][2ClO_4], [**9**·Na_2] [3 ClO_4], and [**9**][ClO_4] were excited at 639, 649, 637, 644, 639, and 645 nm, respectively. [b] Fluorescence quantum yields were determined by using the squaraine dye **3** as the standard ($\Phi_f = 0.15$ in CH_3CN; see ref. [12b]); error: ±10%.

the bipyridinium station were well balanced in this molecular switch. Figure 2 reveals that, when irradiated with 365 nm UV light, the fluorescence intensity of [**4**-long·Na_2][4 ClO_4] slowed the rate of shuttling of the molecular cage unit between the two competing binding sites in the ground state,[15] thereby providing more-effective macrocycle encapsulation of the squaraine station and, consequently, enhanced fluorescence.

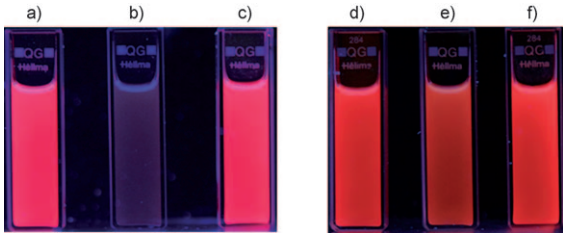


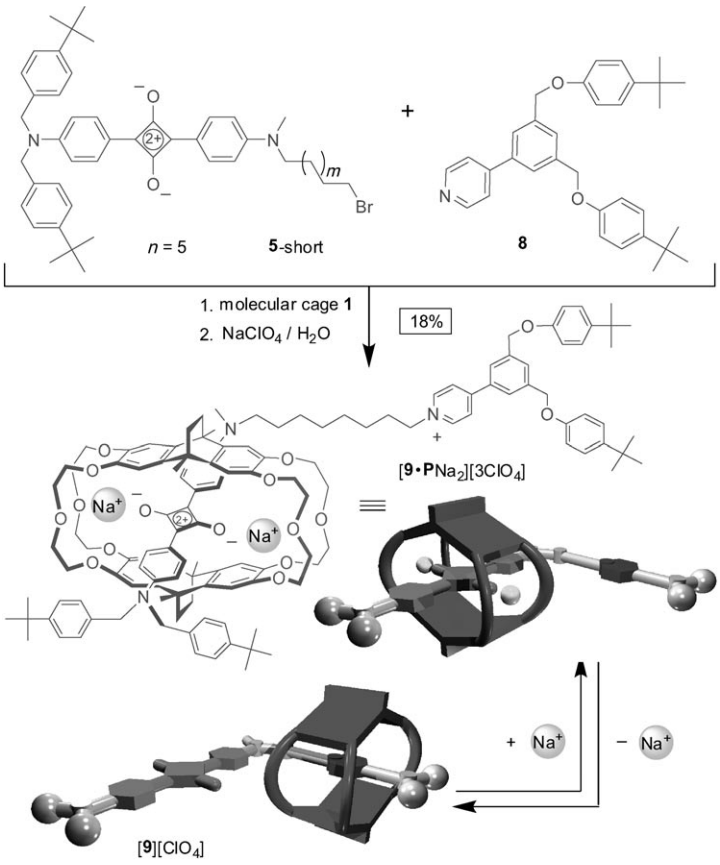
Figure 2. Photographic images of solutions of molecular switches (2 mM) in CH_3CN in the presence and absence of Na^+ ions (excited at 365 nm): a) [**4**-long·Na_2][4 ClO_4]; b) [2.2.2]cryptand (2 equiv) added to the solution in a); c) $NaClO_4$ (2 equiv) added to the solution in b); d) [**9**·Na_2][3ClO_4]; e) [2.2.2]cryptand (2 equiv) added to the solution in d); f) $NaClO_4$ (2 equiv) added to the solution in e).

The [2]rotaxane [**4**-short·Na_2][4 ClO_4], which contains a relatively short linker between the stations, exhibited switching of the interlocked molecular cage unit between its squaraine and bipyridinium moieties, mediated by the removal and addition of Na^+ ions, that was similar to that of the [2]rotaxane [**4**-long·Na_2][4 ClO_4], as confirmed by using ^{1}H NMR spectroscopy. The quantum yields of the [**4**-short]$^{2+}$ and [**4**-short·Na_2]$^{4+}$ species ($\Phi = 0.05$ and 0.09, respectively) were, however, both significantly lower than those of [**4**-long]$^{2+}$ and [**4**-long·Na_2]$^{4+}$.

Thus, the length of the spacer unit influenced the fluorescence quenching effect of the bipyridinium unit dramatically, consistent with previous findings.[14] In addition, we suspect that the longer spacer between the stations in the [2]rotaxane [**4**-long·Na_2][4 ClO_4] slowed the rate of shuttling of the molecular cage unit between the two competing binding sites in the ground state,[15] thereby providing more-effective macrocycle encapsulation of the squaraine station and, consequently, enhanced fluorescence.

We also prepared the [2]rotaxane [**9**·Na_2][3 ClO_4] (Scheme 2) to examine the effect of replacing the strongly fluorescence-quenching bipyridinium ion in [**4**-short·Na_2]-[4 ClO_4] with a (mono)pyridinium unit (i.e., a much weaker fluorescence quencher and a much more weakly interacting station for the molecular cage unit). Although ^{1}H NMR spectroscopy revealed the successful reversible migration of the molecular cage moiety between the squaraine and pyridinium stations in this [2]rotaxane when adding and removing Na^+ ions, disappointingly the quantum yields of the [2]rotaxanes [**9**·Na_2]$^{3+}$ and [**9**]$^+$ did not decrease significantly (0.22 and 0.18, respectively). Figure 2 reveals that no striking fluorescence changes occurred after adding-[2.2.2]cryptand (2 equiv) to a solution of the [2]rotaxane [**9**·Na_2][3 ClO_4] (2 mM) in CH_3CN irradiated with UV light (365 nm). Compared with the behavior of [**4**-short·Na_2]$^{4+}$ ($\Phi = 0.09$), the absence of a strong fluorescence quencher in [**9**·Na_2]$^{3+}$ ($\Phi = 0.22$) appears to be the key factor affecting its higher quantum yield.

The molecular cage moiety has, however, a relatively weak binding affinity for the (mono)pyridinium station in



Scheme 2.

$[\mathbf{9}]^+$ ($\Phi = 0.18$), resulting in its rapid shuttling along the rod-like unit of the dumbbell-shaped component and, therefore, shielding the squaraine unit to some extent; this behavior leads to a slightly higher quantum yield than that of the nonencapsulated squaraine dye **3** ($\Phi = 0.15$).

In conclusion, we have developed a visibly active molecular switch, [2]rotaxane [**4**-long·Na_2][$4\,ClO_4$], that provides outputs in the long-wavelength-fluorescence region that can be discriminated by the naked eye. This molecular switch functions through the selective encapsulation and exposure of the squaraine station of a two-station [2]rotaxane upon the addition and removal of Na^+ ions, respectively. The lengthy spacer unit between the squaraine and bipyridinium moieties allows the bipyridinium unit to function as a fluorescence quencher. We are currently investigating the possibility of extending this system into molecular switches capable of producing multiple optical outputs.

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Keywords: bipyridinium ions · molecular cages · molecular switches · rotaxanes · squaraines

[1] a) A. M. Elizarov, S.-H. Chiu, J. F. Stoddart, *J. Org. Chem.* **2002**, *67*, 9175–9181; b) J. D. Badjić, V. Balzani, A. Credi, S. Silvi, J. F. Stoddart, *Science* **2004**, *303*, 1845–1849; c) F. Huang, K. A. Switek, H. W. Gibson, *Chem. Commun.* **2005**, 3655–3657; d) M.-L. Yen, W.-S. Li, C.-C. Lai, I. Chao, S.-H. Chiu, *Org. Lett.* **2006**, *8*, 3223–3226.

[2] a) R. Ballardini, V. Balzani, M. Clemente-Leon, A. Credi, M. T. Gandolfi, E. Ishow, J. Perkins, J. F. Stoddart, H.-R. Tseng, S. Wenger, *J. Am. Chem. Soc.* **2002**, *124*, 12786–12795; b) J. Berná, D. A. Leigh, M. Lubomska, S. M. Mendoza, E. M. Perez, P. Rudolf, G. Teobaldi, F. Zerbetto, *Nat. Mater.* **2005**, *4*, 704–710; c) S. Saha, J. F. Stoddart, *Chem. Soc. Rev.* **2007**, *36*, 77–92; d) D. Pijper, M. G. M. Jongejan, A. Meetsma, B. L. Feringa, *J. Am. Chem. Soc.* **2008**, *130*, 4541–4552.

[3] a) J.-P. Collin, C. Dietrich-Buchecker, P. Gavina, M. C. Jimenez-Molero, J.-P. Sauvage, *Acc. Chem. Res.* **2001**, *34*, 477–487; b) G. Kaiser, T. Jarrosson, S. Otto, Y.-F. Ng, A. D. Bond, J. K. M. Sanders, *Angew. Chem.* **2004**, *116*, 1993–1996; *Angew. Chem. Int. Ed.* **2004**, *43*, 1959–1962; c) T. Iijima, S. A. Vignon, H.-R. Tseng, T. Jarrosson, J. K. M. Sanders, F. Marchioni, M. Venturi, E. Apostoli, V. Balzani, J. F. Stoddart, *Chem. Eur. J.* **2004**, *10*, 6375–6392.

[4] a) C. M. Keaveney, D. A. Leigh, *Angew. Chem.* **2004**, *116*, 1242–1244; *Angew. Chem. Int. Ed.* **2004**, *43*, 1222–1224; b) B. W. Laursen, S. Nygaard, J. O. Jeppesen, J. F. Stoddart, *Org. Lett.* **2004**, *6*, 4167–4170; c) C.-F. Lin, C.-C. Lai, Y.-H. Liu, S.-M. Peng, S.-H. Chiu, *Chem. Eur. J.* **2007**, *13*, 4350–4355; d) 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; e) T.-C. Lin, C.-C. Lai, S.-H. Chiu, *Org. Lett.* **2009**, *11*, 613–616.

[5] a) A. Altieri, G. Bottari, F. Dehez, D. A. Leigh, J. K. Y. Wong, F. Zerbetto, *Angew. Chem.* **2003**, *115*, 2398–2402; *Angew. Chem. Int. Ed.* **2003**, *42*, 2296–2300; b) K.-S. Jeong, K.-J. Chang, Y.-J. An, *Chem. Commun.* **2003**, 1450–1451; c) Y. Liu, A. H. Flood, J. F. Stoddart, *J. Am. Chem. Soc.* **2004**, *126*, 9150–9151; d) P.-T. Chiang, P.-N. Cheng, C.-F. Lin, Y.-H. Liu, C.-C. Lai, S.-M. Peng, S.-H. Chiu, *Chem. Eur. J.* **2006**, *12*, 865–876.

[6] a) N. Armaroli, V. Balzani, J.-P. Collin, P. Gaviña, J.-P. Sauvage, B. Ventura, *J. Am. Chem. Soc.* **1999**, *121*, 4397–4408; b) A. Altieri, F. G. Gatti, E. R. Kay, D. A. Leigh, D. Martel, F. Paolucci, A. M. Z. Slawin, J. K. Y. Wong, *J. Am. Chem. Soc.* **2003**, *125*, 8644–8654; c) W. S. Jeon, A. Y. Ziganshina, J. W. Lee, Y. H. Ko, J.-K. Kang, C. Lee, K. Kim, *Angew. Chem.* **2003**, *115*, 4231–4234; *Angew. Chem. Int. Ed.* **2003**, *42*, 4097–4100; d) H.-R. Tseng, S. A. Vignon, P. C. Celestre, J. Perkins, J. O. Jeppesen, A. Di Fabio, R. Ballardini, M. T. Gandolfi, M. Venturi, V. Balzani, J. F. Stoddart, *Chem. Eur. J.* **2004**, *10*, 155–172.

[7] For reviews, see: a) V. Balzani, A. Credi, F. M. Raymo, J. F. Stoddart, *Angew. Chem.* **2000**, *112*, 3484–3530; *Angew. Chem. Int. Ed.* **2000**, *39*, 3348–3391; b) T.-A. V. Khuong, J. E. Nunez, C. E. Godinez, M. A. Garcia-Garibay, *Acc. Chem. Res.* **2006**, *39*, 413–422; c) B. Champin, P. Mobian, J.-P. Sauvage, *Chem. Soc. Rev.* **2007**, *36*, 358–366; d) S. Bonnet, J.-P. Collin, *Chem. Soc. Rev.* **2008**, *37*, 1207–1217.

[8] a) A. Ajayaghosh, *Acc. Chem. Res.* **2005**, *38*, 449–459; b) N.-C. Chen, P.-Y. Huang, C.-C. Lai, Y.-H. Liu, S.-M. Peng, S.-H. Chiu, *Chem. Commun.* **2007**, 4122–4124; c) S. J. Vella, J. Tiburcio, S. J. Loeb, *Chem. Commun.* **2007**, 4752–4754; d) T. Ogoshi, A. Harada, *Sensors* **2008**, *8*, 4961–4982; e) A. P. de Silva, T. P. Vance, M. E. S. West, G. D. Wright, *Org. Biomol. Chem.* **2008**, *6*, 2468–2480; f) M. J. Chmielewski, J. J. Davis, P. D. Beer, *Org. Biomol. Chem.* **2009**, *7*, 415–424.

[9] a) P.-N. Cheng, P.-T. Chiang, S.-H. Chiu, *Chem. Commun.* **2005**, 1285–1287; b) A. P. de Silva, S. Uchiyama, *Nat. Nanotechnol.* **2007**, *2*, 399–410; c) D. C. Magri, T. P. Vance, A. P. de Silva, *Inorg. Chim. Acta* **2007**, *360*, 751–764; d) D. Zhang, J. Su, X. Ma, H. Tian, *Tetrahedron* **2008**, *64*, 8515–8521.

[10] a) W.-Q. Deng, A. H. Flood, J. F. Stoddart, W. A. Goddard III, *J. Am. Chem. Soc.* **2005**, *127*, 15994–15995; b) T. Ikeda, S. Saha, I. Aprahamian, K. C.-F. Leung, A. Williams, W.-Q. Deng, A. H. Flood, W. A. Goddard III, J. F. Stoddart, *Chem. Asian J.* **2007**, *2*, 76–93.

[11] a) E. Arunkumar, N. Fu, B. D. Smith, *Chem. Eur. J.* **2006**, *12*, 4684–4690; b) E. Arunkumar, P. K. Sudeep, P. V. Kamat, B. C. Noll, B. D. Smith, *New J. Chem.* **2007**, *31*, 677–683; c) J. Stokes, A. Ingram, J. Gallagher, D. R. Armstrong, W. E. Smith, D. Graham, *Chem. Commun.* **2008**, 567–569; d) S. Sreejith, K. P. Divya, A. Ajayaghosh, *Angew. Chem.* **2008**, *120*, 8001–8005; *Angew. Chem. Int. Ed.* **2008**, *47*, 7883–7887.

[12] a) R. W. Bigelow, H. J. Freund, *Chem. Phys.* **1986**, *107*, 159–174; b) K. Y. Law, *J. Photochem. Photobiol. A* **1994**, 84, 123–132; c) E. Arunkumar, C. C. Forbes, B. C. Noll, B. D. Smith, *J. Am. Chem. Soc.* **2005**, *127*, 3288–3289; d) S. Sreejith, P. Carol, P. Chithra, A. Ajayaghosh, *J. Mater. Chem.* **2008**, *18*, 264–274.

[13] S.-Y. Hsueh, C.-C. Lai, Y.-H. Liu, S.-M. Peng, S.-H. Chiu, *Angew. Chem.* **2007**, *119*, 2059–2063; *Angew. Chem. Int. Ed.* **2007**, *46*, 2013–2017.

[14] a) V. Balzani, H. Bandmann, P. Ceroni, C. Giansante, U. Hahn, F.-G. Klaerner, U. Mueller, W. M. Mueller, C. Verhaelen, V. Vicinelli, F. Voegtle, *J. Am. Chem. Soc.* **2006**, *128*, 637–648; b) J. N. Wilson, Y. N. Teo, E. T. Kool, *J. Am. Chem. Soc.* **2007**, *129*, 15426–15427; c) A. Arduini, R. Bussolati, A. Credi, A. Pochini, A. Secchi, S. Silvi, M. Venturi, *Tetrahedron* **2008**, *64*, 8279–8286.

[15] Although Scheme 1 depicts the molecular cage unit in [**4**-long·Na_2]-[$4\,ClO_4$] as surrounding the squaraine station, in actuality this macrocyclic unit shuttles between the two stations, but with a preference for the squaraine moiety because of stronger noncovalent interactions. A longer alkyl spacer provides a greater energy barrier to shuttling, thereby reducing the rate of translocation.

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