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LETTERS

Rotaxane-based molecular switch with fluorescence signaling

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Abstract

A pseudorotaxane containing cucurbituril (as a molecular 'bead') threaded on fluorenyltriamine (as a 'string') behaves as a fluorescent, reversible molecular switch. The switching of the molecular bead from one site to the other site on the 'string' induced by pH change is easily detected by change in color and fluorescence.

Keywords: supramolecular chemistry; rotaxane; molecular switch; fluorescence.

We have been studying self-assembly of interlocked structures such as rotaxanes, polyrotaxanes and molecular necklaces using cucurbituril (CB) as a molecular 'bead'.[1] In an effort to develop interlocked structures with functions we became interested in rotaxane-based molecular switches. Molecular switches that are controllable, reversible and readable at molecular level are an essential component of molecular electronics.[2] Several rotaxane-based molecular switches that involve mechanical movement of a 'ring' component between two sites on a 'string' induced by external stimuli such as changes in pH or electrical potentials, and light have been reported.[3,4] Although fluorescence has been widely used as one of the most sensitive detection means in sensors,[2,5] no rotaxane-based molecular switch capable of fluorescence signaling has been reported. Here we report a rotaxane-based molecular switch, that can be turned on and off chemically with changes in fluorescence as well as color.

Mock reported a rotaxane-based molecular switch which consists of a CB 'bead' and a triamine 'string' $PhNH(CH_2)_6NH(CH_2)_4NH_2$.[4a] When all the nitrogen atoms of the 'string' are protonated at low pH, the 'bead' resides at the protonated diaminohexane site, because CB forms a more stable complex with diprotonated diaminohexane than with diprotonated diaminobutane. Upon deprotonation of the aniline nitrogen (pKa=6.7), the 'bead' migrates to the diprotonated diaminobutane site because binding with the monoprotonated diaminohexane is weaker. Based on this elegant work, we designed a fluorescent molecular switch **1** (Fig. 1) which can signal the change in the 'bead' position by color and fluorescence changes.

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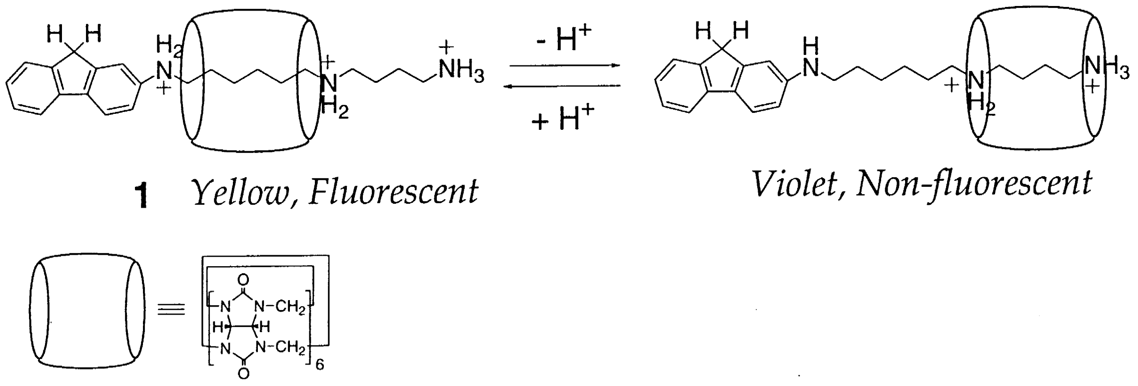
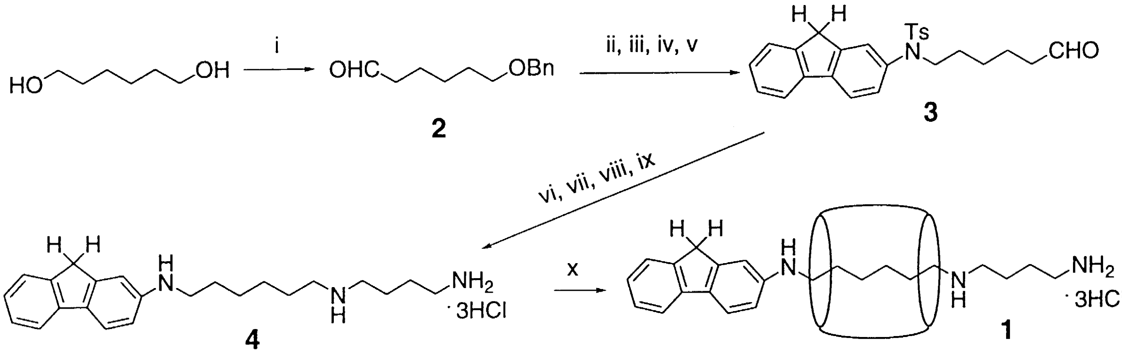


Fig. 1. Fluorescent, reversible rotaxane-based molecular switch **1**

The synthesis of **1** is outlined in Scheme 1. Mono-protection of 1,6-hexanediol by benzyl bromide, followed by oxidation affords **2**. Reductive alkylation of 2-aminofluorene with **2** produces a secondary amine. Protection of the amine group with TsCl, followed by deprotection of the benzyl group and oxidation of alcohol affords **3**. Coupling of **3** with mono-cbz-protected 1,4-diaminobutane followed by deprotection gives the fluorenyltriamine ligand **4**. The complex formation of **4** with cucurbituril in water produces (pseudo)rotaxane **1**.[6] All the compounds have been characterized by $^1H/^{13}C$ NMR spectroscopy, mass spectrometry and/or elemental analysis.



Scheme 1. Reagents and conditions: (i) BnBr, NaH, DMF, 6 h and then PCC, CH_2Cl_2; (ii) 2-amino-fluorene, Et_3N, CH_2Cl_2, 12 h and then $NaBH_4$, MeOH, 12 h, 62%; (iii) TsCl, Et_3N, CH_2Cl_2, 12 h, 93%; (iv) H_2, Pd/C (10%), EtOH, 12 h, 92%; (v) PCC, CH_2Cl_2, 6 h, 95%; (vi) mono-cbz-1,4-diaminobutane, Et_3N, CH_2Cl_2, 12 h and then $NaBH_4$, MeOH, 12 h, 81%; (vii) 30% HBr in AcOH, PhOH, 60°C, 74%; (viii) NaOH (aq.), CH_2Cl_2; (ix) concd HCl, MeOH, 87%; (x) cucurbituril, water, 95%

Fig. 2 compares ^1H NMR spectra of **1** at pHs, 1.0, 4.4 and 8.0. Each peak has been assigned unambiguously from 2D COSY spectra. The signals for the methylene groups located inside CB are shifted to higher field due to the shielding effect of CB. These NMR spectra are consistent with the interpretation that the CB bead resides at the (protonated) diaminohexane site at pH of 1.0, but translocates to the (protonated) diaminobutane site at pH=8.0. At intermediate pH, we observe both species, one with the bead at the diaminohexane site and one with the bead at the diaminobutane site, in equilibrium. The shuttling of CB between the two sites is slow on the NMR time scale as separate resonances are observed for each binding mode.

Most importantly, the switching of CB from one site to the other in **1** is easily detected by change in color and fluorescence with high sensitivity. Fig. 3 displays changes in UV–visible and emission spectra of **1** with the pH change.[7] The intensity of the absorption band at 265 nm decreases while that

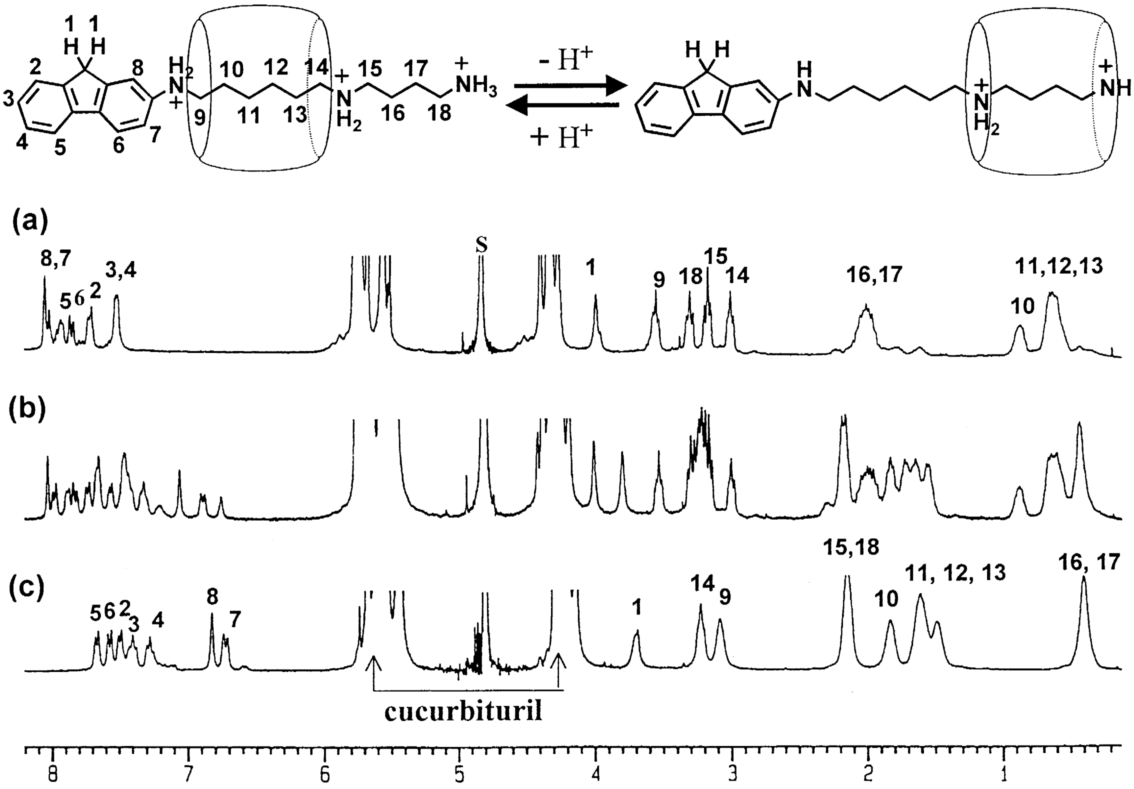


Fig. 2. ^{1}H NMR (300 MHz) spectra of **1** at pHs, (a) 1.0, (b) 4.4 and (c) 8.0.

at 300 nm increases with an isosbestic point at 275 nm as the pH of the solution increases. The color of the aqueous solution of **1** at pH 1.0 is yellow, which changes slowly with increasing pH and becomes violet at pH 7.0. The solution of **1** at pH 1.0 is highly fluorescent with an emission maximum at 308 nm.[7] The fluorescence intensity decreases with increasing pH due to the deprotonation of the aromatic nitrogen. The fluorescence is almost completely quenched at pH 7.0. Such fluorescence quenching upon deprotonation of nitrogen attached to a fluorophore is known to occur through a photo-induced electron transfer mechanism.[5] The pKa of the aromatic nitrogen in **1** estimated from these spectral changes is 5.7 which is in good agreement with the value obtained from the NMR data.[7] Taken together, this data suggests that the molecular bead resides predominantly at the (diprotonated) diaminohexane site at a pH lower than the pKa, but translocates to (diprotonated) diaminobutane site when the pH of the solution becomes higher than the pKa. Since the switching in **1** can be easily detected with a 10^{-7} M solution (by fluorescence), the readability of the present molecular switch is 10^2–10^4 times better than other rotaxane-based molecular switches.[3,4]

In summary, we have synthesized the first fluorescent, reversible molecular switch based on rotaxane. The switching of the molecular bead from one site to the other site induced by pH change is easily detected by changes in color and fluorescence with high sensitivity. We are currently investigating the applications of this fluorescent molecular switch.

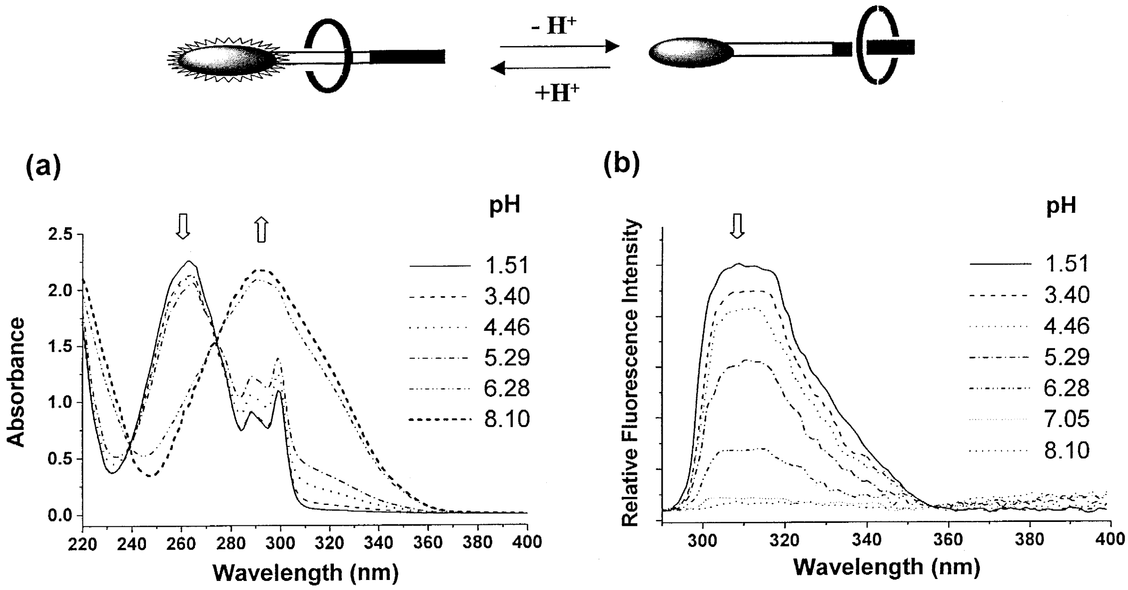


Fig. 3. (a) Absorption and (b) emission (with excitation at 260 nm) spectra of **1** in aqueous solution (concentration: 2.0×10^{-5} M in (a) and 2.0×10^{-7} M in (b) at pHs 1.0–8.0)

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6. Selected data for **1**: ^{1}H NMR (300 MHz, D_2O, 25°C): δ 8.01 (d, 1H), 7.90 (m, 1H), 7.81 (d, 2H), 7.48 (d, 2H), 6.57 (br, 1H), 5.72 (d, 6H), 5.76 (d, 12H), 5.48 (s, 12H), 4.33 (d, 6H), 4.21 (d, 6H), 4.0 (s, 2H), 3.51 (t, 2H), 3.27 (m, 2H), 3.13 (t, 2H), 2.98 (m, 2H), 1.95 (m, 4H), 0.83 (m, 2H), 0.60 (m, 6H); ^{13}C NMR (75 MHz, D_2O, 25°C): δ 157.10, 144.4, 143.9, 143.7, 141.9, 137.9, 135.6, 129.8, 128.2, 127.5, 126.5, 125.5, 120.5, 111.0, 70.8, 51.9, 50.7, 44.1, 37.3, 28.3, 26.3, 21.9; UV–vis (water): λ_{max}=265, 292, 299 nm (pH=1.0), 300 nm (pH=7.0); fluorescence (excitation at 260 nm, water): λ_{max}=308 nm; ESI-MS: *m/z*=674.90 ($[M+2H]^{2+}$ requires 674.94). Anal. calcd for $C_{59}H_{72}N_{27}O_{12}\cdot3PF_6\cdot9H_2O$: C, 36.37; H, 4.66; N, 19.41. Found: C, 36.28; H, 4.56; N, 19.62.

7. The UV–visible spectrum of the ‘string’ **4** and its pH dependence are similar to those of **1**. However, the emission spectrum of **4** is different from that of **1**. The ‘string’ **4** shows two emission bands at 312 and 388 nm with almost equal intensity at pH 1 whereas **1** shows only one emission band at 308 nm. As the pH of the solution increases, the intensities of the emission bands of **4** decrease rapidly. While the emission at 312 nm is completely quenched at pH 7 or above, the intensity of the band at 388 nm at pH 7 becomes about a half of that at pH 1 and does not change any further at higher pH. The pKa of the aromatic nitrogen in **4** estimated from the absorption and emission spectral changes is 4.4. The presence of CB ‘bead’ on the ‘string’ increases the pKa of the aromatic nitrogen to 5.7, which is consistent with the observation made by Mock.[4a]