ORGANIC LETTERS

2002
Vol. 4, No. 19
3207−3209

Modulation of Metal Recognition by a Novel Calix[4]arene Bearing Two Bipyridine Units as a Molecular Gate

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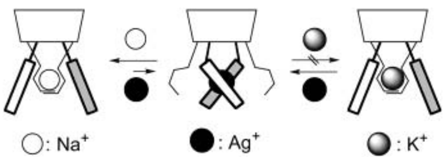
Received June 14, 2002

ABSTRACT



A novel multiregulation system of ion recognition was constructed by utilizing a molecular gate. Interaction between the host and an Ag^+ is controlled with an Na^+ ion.

The design and synthesis of artificial systems for regulation of ion recognition utilizing external information at the molecular level, i.e., metal ion, electron, organic molecule, have attracted much attention.[1] The method of controlling the molecular functions by an external effector is important for constructing intelligent and responding molecules. All-or-none regulation of guest recognition, however, seems to be very difficult even by using this strategy because guest binding via an induced-fit mechanism is only minimally inhibited. To break through this problem, we introduced a concept of a redox gate for all-or-none Ag^+ recognition by quantitative redox reactions between thiol and disulfide.[2]

An alternative useful way to construct a molecular gate would be to utilize complexation between a transition metal and ligands, because metal coordination is often reversible and proceeds quantitatively and very quickly. Thus, we have designed novel calix[4]arene[3] derivative **1** bearing two 2,2′-bipyridine moieties and two ester groups. The host **1** is expected to recognize an alkali metal ion, because ester groups on the lower rim of the calixarenes bind to alkali metal ions.[4] The binding strength and selectivity are varied significantly by changing the substituents on the lower rim. If suitable metal ions are chosen, multiple regulation of ion binding should be achieved on the basis of the concept of a molecular gate. Namely, complexation of **1** with a transition metal (M) possessing moderate affinity to **1** restricts complexation of **1** with an alkali metal (M1) possessing weak affinity to the ester moieties of **1** by closing the gate. To the contrary, recognition of M is disturbed by an alkali metal (M2) with strong affinity (Figure 1). Here we have achieved such a sophisticated regulation system for recognition of Ag^+, K^+, and Na^+ as M, M1, and M2, respectively.

Bisbipyridyl calix[4]arene **2**[5] was treated with methyl bromoacetate in the presence of NaH to give **1** in 47% yield (Scheme 1).[6]

The difference in the ^1H NMR chemical shifts ($\Delta\delta$ 1.33 ppm) between the two kinds of methylene groups in the calix[4]arene and ^{13}C NMR signal (δ 31.7 ppm) for the

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[1] For reviews, see: (a) Lehn, J.-M. *Supramolecular Chemistry, Concepts and Perspectives*; VCH: Weinheim, Germany, 1995. (b) Lehn, J.-M. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 89−112. (c) Nabeshima, T. *Coord. Chem. Rev.* **1996**, *148*, 151−169. (d) Linton, B.; Hamilton, A. D. *Chem. Rev.* **1997**, *97*, 1669−1680. (e) Nabeshima, T.; Akine, S.; Saiki, T. *Rev. Heteroatom Chem.* **2000**, *22*, 219−239.

[2] Nabeshima, T.; Furusawa, H.; Yano, Y. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1750−1751.

[3] For reviews, see: (a) Gutsche, C. D. Carixarenes. In *Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; Royal Society of Chemistry: Cambridge, 1989. (b) *Calixarenes: A Versatile Class of Macrocyclic Compounds*; Vicens, J., Böhmer, V., Eds.; Kluwer Academic Publishers: Dordrecht, 1991. (c) Gutsche, C. D. Carixarenes Revisited. In *Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; Royal Society of Chemistry: Cambridge, 1998.

[4] McKervey, M. A.; Seward, E. M.; Ferguson, G.; Ruhl, B.; Harris, S. J. *J. Chem. Soc., Chem. Commun.* **1985**, 388−390.

10.1021/ol026367l CCC: $22.00

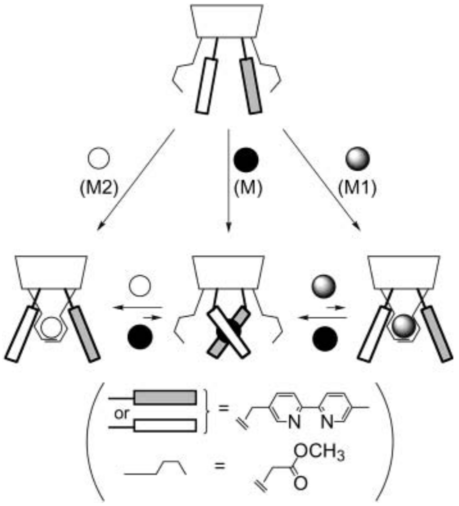


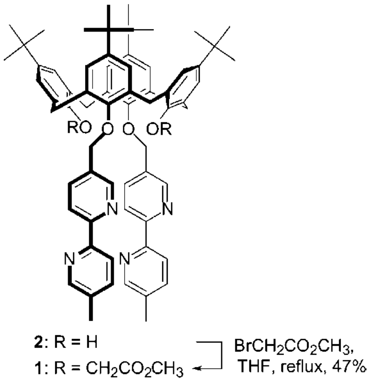
Figure 1. Regulation of ion recognition by gating.

methylene groups in the calix[4]arene skeleton clearly shows the cone conformation of **1**.[4a,7]

We chose Ag$^+$ as a transition metal effector to the gate, because Ag$^+$ would react with two bipyridines to give a tetrahedral or distorted tetrahedral complex.[8] Ag$^+$ caused a red shift of the absorption maximum of **1** from 290 to 300 nm (Figure 2). The Job plot using the absorption at 290 nm supports the quantitative formation of the 1:1 complex. In ^{1}H NMR (toluene-d_8:CD$_3$CN = 6:5), significant changes were observed in aromatic, CH$_2$-bpy, and CH$_2$CO$_2$ methylene protons up to 1 equiv of Ag$^+$. These results indicate the complexation between Ag$^+$ and the two bipyridine moieties of **1**. The accurate association constant K_a between **1** and Ag$^+$ was too large to be determined by using the spectroscopic methods.[9] Thereby, the binding site of **1** to alkali metal ions is expected to be closed effectively by the bipyridine-Ag$^+$ complexation. In **2**, complexation occurs similarly.

The binding affinity of **1** and **2** to alkali metal cations was evaluated by ^{1}H NMR. NaPF$_6$ or KPF$_6$ did not cause detectable spectral changes of **2** due to the lack of ester groups. On the other hand, 1 equiv of NaPF$_6$ resulted in new signals of **1** ascribed to formation of the Na$^+$ complex, and those of free **1** disappeared completely in the presence of 1 equiv of Na$^+$. ^{1}H NMR titration shows nearly quantitative 1:1 complexation with 1 equiv of Na$^+$. An accurate binding constant was not determined due to the high affinity to Na$^+$,[9] but in K$^+$, the nonlinear regression analysis affords K_a (200 ± 25 M^{-1}) (Figure 3). This high Na$^+$ selectivity is caused probably by the size effect of the cavity.[10]

Scheme 1. Synthesis of Host **1**.



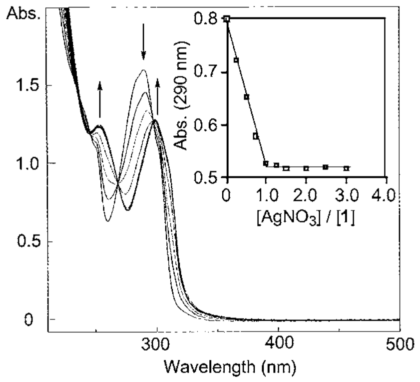


Figure 2. UV–vis spectral changes of **1** by the addition of AgNO$_3$ in CH$_3$CN:CH$_2$ClCH$_2$Cl = 1:10. [**1**] = 1.92 × 10^{-5} M.

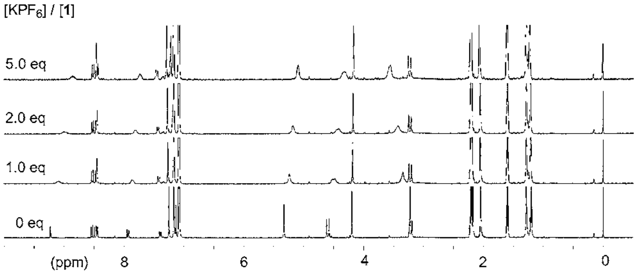


Figure 3. ^{1}H NMR spectral changes of **1** by the addition of KPF$_6$ at 300 MHz in toluene-d_8:CD$_3$CN = 6:5. [**1**] = 2.00 × 10^{-3} M.

NaPF$_6$ (1 equiv) did not affect the ^{1}H NMR spectrum (toluene-d_8:CD$_3$CN = 6:5) of **1**·Ag$^+$, although colorless

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(5) (a) Ulrich, G.; Ziessel, R. *Tetrahedron Lett.* **1994**, *35*, 6299–6302. (b) Ulrich, G.; Ziessel, R.; Manet, I.; Guardigli, M.; Sabbatini, N.; Fraternali, F.; Wipff, G. *Chem. Eur. J.* **1997**, *3*, 1815–1822.

(6) **1**: mp 205.0–207.0 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.01 (s, 18H), 1.11 (s, 18H), 2.40 (s, 6H), 3.05 (d, J = 13 Hz, 4H), 3.67 (s, 6H), 4.38 (d, J = 13 Hz, 4H), 4.45 (s, 4H), 5.25 (s, 4H), 6.69 (s, 4H), 6.80 (s, 4H), 7.62 (dd, J = 8, 2 Hz, 2H), 7.86 (dd, J = 8, 2 Hz, 2H), 8.29–8.32 (m, 4H), 8.51 (d, J = 2 Hz, 2H), 8.79 (d, J = 2 Hz, 2H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 18.3, 31.3, 31.4, 31.7, 33.7, 33.9, 51.5, 70.9, 73.8, 119.9, 120.7, 125.2, 125.3, 133.0, 133.2, 133.4, 134.0, 137.4, 138.2, 145.1, 145.2, 149.5, 150.5, 152.4, 152.6, 153.6, 155.5, 170.5; ESI MS observed m/z 1157.7 ([M + H]$^+$). Anal. Calcd. for **1**· 0.5H$_2$O: C, 76.19; H, 7.34; N, 4.80. Found: C, 76.03; H, 7.09; N, 4.80.

(7) (a) Jaime, C.; de Mendoza, J.; Prados, P.; Nieto, P. M., Sànchez, C. *J. Org. Chem.* **1991**, *56*, 3372–3376. (b) Araki, K.; Iwamoto, K.; Shinkai, S.; Matsuda, T. *Chem. Lett.* **1989**, 1747–1750. (c) Iwamoto, K.; Araki, K.; Shinkai, S. *J. Org. Chem.* **1991**, *56*, 4955–4962.

(8) Baxter, P. N. W.; Lehn, J.-M.; Fischer, J.; Youinou, M.-T. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2284–2287.

precipitates appeared.[11] However, an additional 1 equiv of $NaPF_6$ caused disappearance of the signals of $\mathbf{1}{\cdot}Ag^+$ and appearance of new signals assigned to $\mathbf{1}{\cdot}Na^+$. The value of $K_a(Na^+)/K_a(Ag^+)$ determined from the ratio of $[\mathbf{1}{\cdot}Na^+]$ and $[\mathbf{1}{\cdot}Ag^+]$ in the ^1H NMR spectra is 2.5. Hence, the complex $\mathbf{1}{\cdot}Ag^+$ releases an Ag^+ ion and captures an Na^+ ion instead because of the lower affinity of **1** to Ag^+ than to Na^+.

Interestingly, even excess KPF_6 did not cause a spectral change of $\mathbf{1}{\cdot}Ag^+$ (Figure 4). This fact shows that the recognition of K^+ with host **1** was suppressed completely (all-or-none regulation) by closing the gate via complexation between the two bipyridine moieties of **1** and Ag^+. Consequently, this system is a multiregulation system of ion recognition, i.e., Ag^+ and K^+ binding are regulated by Na^+ and Ag^+, respectively.

In conclusion, we have designed and synthesized **1** with two bipyridines that act as a gate in the guest recognition site. The recognition of K^+ is completely suppressed by addition of Ag^+. This gate system utilizing the coordination of a transition metal will provide a general and useful strategy to regulate molecular function by an external effector, and further development as a multiregulation receptor is also expected. Now we are working to incorporate a coordinating gate into artificial receptors for organic molecules.

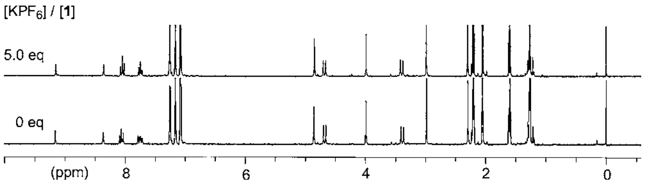

Figure 4. ^1H NMR spectral changes of $\mathbf{1}{\cdot}AgNO_3$ by the addition of KPF_6 at 300 MHz in toluene-d_8:CD_3CN = 6:5. $[\mathbf{1}{\cdot}AgNO_3] = 2.00 \times 10^{-3}$ M.

Acknowledgment. This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

Supporting Information Available: Experimental procedures and spectral characterization for compound **1**, a Job plot for complexation between **1** and $AgNO_3$, ^1H NMR spectral changes of **1** by the addition of $AgNO_3$ and $NaPF_6$, and the results of ^1H NMR titration between $\mathbf{1}{\cdot}AgNO_3$ and $NaPF_6$. This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) The K_a for Ag^+ was roughly estimated to be $>1.9 \times 10^5$ M^{-1} from the titration isotherm (toluene-d_8:CD_3CN = 6:5). The K_a for Na^+ is 2.5 times as large as that for Ag^+. The value for Na^+ was determined to be $(3.5 \pm 0.5) \times 10^4$ M^{-1} by solvent extraction by using a $CDCl_3-H_2O$ biphasic system in a manner similar to that reported by: Moore, S. S.; Tarnowski, T. L.; Newcomb, M.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 6398−6405.

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(11) $NaNO_3$ was probably precipitated in the solvent system.