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Metal-induced Conformational Change in Pyrene-appended Calix[4]crown-4 Which Is Useful for Metal Sensing and Guest Tweezing

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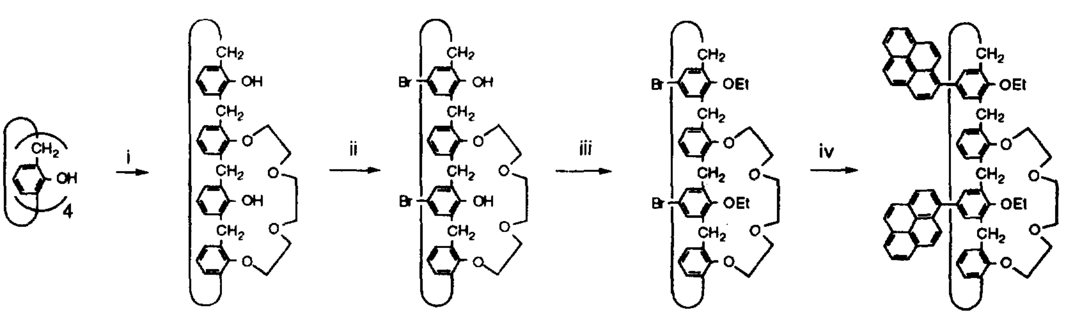
Abstract: Calix[4]crown (**1**) bearing an ionophoric cavity on the lower rim and two pyrene groups on the upper rim was synthesized. The metal-binding to the ionophoric cavity changed the distance between two pyrene moieties, which was reflected by a large change in the monomer/excimer fluorescence intensity ratio. This phenomenon was applied to (i) fluorescence sensing of alkali metal cations and (ii) metal-controlled tweezing of a guest (trinitrobenzene). It was shown that the ionophoric cavity can accept only Li^+ and Na^+ ($Na^+ > Li^+$) but not at all K^+.

The ^1H NMR spectra of calix[4]arene-25,26,27,28-tetrol derivatives feature a pair of doublets for the $ArCH_2Ar$ methylene protons, indicating that they adopt C_{4v} symmetry.[1-3] In contrast, X-ray crystallographic studies and computational studies indicate that they adopt C_{2v} symmetry with two stand-up distal phenol units and two flattened distal phenol units.[4-6] It is ambiguous, therefore, whether they enjoy rapid C_{2v}-C_{2v} interconversion or adopt regular C_{4v} symmetry in solution. Very recently, we obtained direct evidence from the ^1H NMR measurement at -85 °C that they actually employ C_{2v} symmetry and the rate of C_{2v}-C_{2v} interconversion is faster than the NMR time-scale at room temperature.[7] On the other hand, when two distal phenol units are bridged by a short strap, they are obligatorily flattened and the residual two nonbridged distal phenol units stand up.[8,9] When a metal cation is bound to the oxygenic cavity, the nonbridged phenol units are more or less flattened so as to interact with the bound metal cation. Here, it occurred to us that this metal-induced distance change between these two nonbridged phenol units would be applied to fluorescence sensing of alkali metal cations. Furthermore, the distance change in the large π-rings appended in the nonbridged phenol units would be useful for tweezing electron-deficient guest molecules. With these objects in mind we designed compound **1**: in the absence of metal cations two pyrene moieties directly connected to stand-up phenol units would be close to each other whereas in the presence of metal cations they would be separated because of metal-induced flattening. Actually, we have found that the fluorescence intensities of monomer and excimer emission are sensitively affected by added metal cations and accordingly, the guest-tweezing ability is influenced.



Scheme 1. Reagents: i, $TsO(CH_2CH_2O)_3Ts$, Na_2CO_3 in acetonitrile (Yield 60%); ii, Br_2 in $CHCl_3$ (85%); iii, C_2H_5Br, NaH in DMF (80%); iv, pyrenylboronic acid, $Pd(PPh_3)_4$, Na_2CO_3 in toluene+MeOH+H_2O (12%).

Compound **1** (decomp. > 350 °C) was synthesized from calix[4]arene-25,26,27,28-tetrol according to Scheme 1. The structure was identified by IR, Mass (SIMS *m/z* 994 (M^+)), and ^1H NMR spectral evidence and elemental analysis. In mass spectroscopic analysis the Na^+ complex (*m/z* 1017) was also observed. Our previous study established that in a calix[4]crown-4 the ethyl group is bulky enough to suppress the rotation of the nonbridged phenol units.[8] In ^1H NMR spectroscopy ($CDCl_3$, 25 °C) a pair of doublets for the $ArCH_2Ar$ methylene protons appeared at δ_H 3.40 and 4.65 ppm. The result indicates that **1** is immobilized to a cone conformation. In the absence of alkali metal cations the δ_H values for the pyrenyl protons appeared at 5.95-7.62 ppm whereas in the presence of excess $NaClO_4$ they shifted to 7.25-7.99 ppm. The change implies that two pyrene moieties on the upper rim are more separated when Na^+ is bound to the oxygenic cavity on the lower rim.

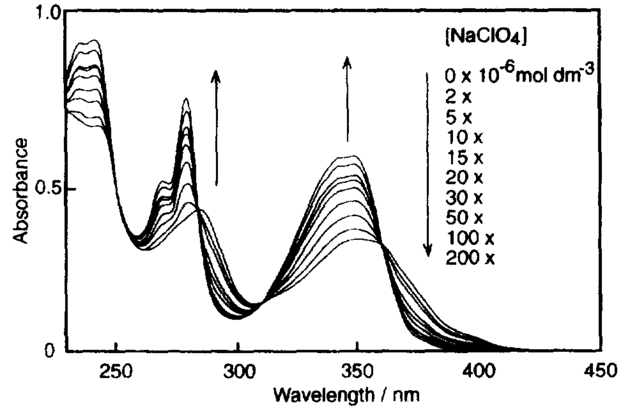


Figure 1. Absorption spectra of **1** (1.0×10^{-5} mol dm^{-3}) in MeCN:THF = 1000:1 v/v at 25 °C with successive addition of $NaClO_4$.

Figure 1 shows the absorption spectral change induced by the addition of $NaClO_4$. The similar spectral change was observed for the addition of $LiClO_4$. From plots of A_{350} *vs.* [$MClO_4$] we determined the association constants (K_{ass}): log K_{ass} = 4.65 for $LiClO_4$ and 5.16 for $NaClO_4$. In contrast, the addition of $KClO_4$ (up to [K^+] / [**1**] = 30) scarcely changed the absorption spectrum.[10] We have already reported that the ionophoric cavity in **1**, the size of which is designed just in the intermediate of Li^+ and Na^+, strongly rejects K^+ and shows recordbreaking, more than 10^5-fold Na^+ / K^+ selectivity.[8] The high Na^+ selectivity is reproduced here again in **1** bearing two chromophoric pyrene pendants.

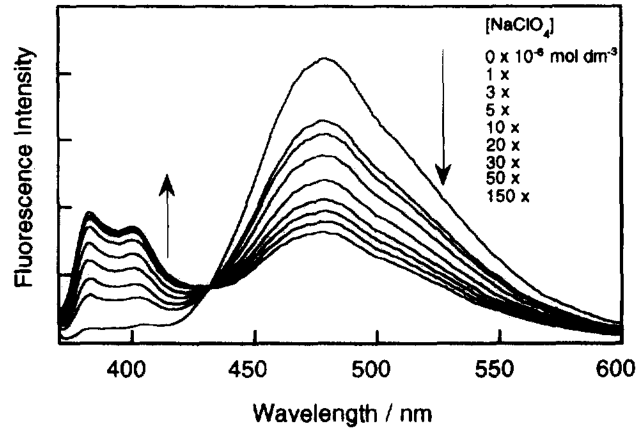


Figure 2 Fluorescence spectra of 1 (2.0×10^{-7} mol dm^{-3}) in MeCN:THF = 1000:1 v/v at 25°C with successive addition of $NaClO_4$; excitation wavelength 362 nm.

The isosbestic points in the absorption spectral change appeared at 285, 308, and 362 nm. We chose 362 nm as an excitation wavelength for the measurement of the fluorescence spectra (Figure 2). It is clearly seen from Figure 2 that with increasing $NaClO_4$ concentration monomer emission (390 nm) increases while excimer emission (480 nm) decreases. The log K_{ass} was estimated to be 5.48.[11] The similar spectral change was observed for the addition of $LiClO_4$ and the log K_{ass} was estimated to be 4.84.[11] Here again, the fluorescence spectrum was not affected by the addition of $KClO_4$ (up to $[K^+]$ / [**1**] = 250).

When trinitrobenzene (5.0×10^{-4} mol dm^{-3}: δ_H 9.40 ppm) was mixed with **1** (4.1×10^{-3} mol dm^{-3}) in $CDCl_3$ at 25°C, the δ_H moved to higher magnetic field (9.00 ppm). This indicates that two pyrene groups appended in the non-bridged stand-up phenyl units can strongly bind trinitrobenzene. When tetrakis[3,5-bis(trifluoromethyl)-phenyl]borate sodium salt (4.1×10^{-3} mol dm^{-3}) was added, the δ_H returned to lower magnetic field (9.09 ppm), indicating that the metal-binding causes the dissociation of the **1**•trinitrobenzene complex. In the absence of **1** the δ_H of trinitrobenzene was not affected by the addition of the Na salt [$(1.0 - 5.0) \times 10^{-3}$ mol dm^{-3}]. Conceivably, adjacent two pyrene groups can tweeze a trinitrobenzene guest whereas Na^+ induces the separation of two pyrene groups and the cooperative tweezing action can no longer work.[12]

The foregoing results consistently support that **1** acts as a useful neutral ligand for the sensing of alkali metal cations which shows very high Na^+ / K^+ (at least higher than 10^3) selectivity and the binding process is conveniently "read-out" by both absorption and fluorescence spectroscopic methods. Furthermore, the metal-induced conformational change is useful for the tweezing of guest molecules in an allosteric manner. As expected in introduction, large spectral changes can be induced by a subtle change in the calix[4]arene conformation. We believe that this molecular design concept is very important and very universal for facile and sensitive sensing of metal cations and neutral molecules.[13]

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11. The K_{ass} values determined with an absorption spectroscopic method are somewhat smaller than those determined with a fluorescence spectroscopic method. The discrepancy is mainly due to the concentration range for **1** (1×10^{-5} mol dm^{-3} for the former and 2×10^{-7} mol dm^{-3} for the latter), which is inevitable to set up the most appropriate measurement conditions.
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