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Alkali Metal Sensing with a Fluorescent 5,11,17,23-Tetraphenylcalix[4]arene and the Mechanism of the Fluorescence Change

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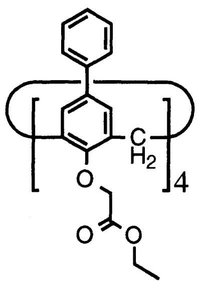
The fluorescence intensity of a tetraester derivative of the title compound increases markedly upon the Na^+-binding. Hence, this is useful as a new, convenient Na^+-sensing system. The mechanism of the fluorescence increase is discussed by comparing the fluorescence properties of several reference compounds.

It has been shown that calix[4]aryl esters and amides possess high Na^+ selectivity.1) To read out the Na^+-binding event by convenient spectroscopic methods, several chromogenic calix[4]arenes have been designed.2-6) In these precedent examples, however, chromophores are introduced around the Na^+-binding lower rim site and therefore the syntheses are fairly complicated. In some cases, furthermore, a ligand ester or amide group is sacrificed for introduction of a chromophoric substituent. In contrast, the calix[4]arene skeleton is used only as a "platform" for holding the rigid ionophoric cavity. It occurred to us that if the calix[4]arene itself acts as a chromophoric group and the spectral characteristics are affected by the Na^+-binding, the molecular design of such chromogenic calix[4]arenes will become much easier. Furthermore, one can expect novel spectral changes arising from the Na^+-induced conformational change. An expeditious candidate which satisfies this requirement is 5,11,17,23-tetraphenylcalix[4]arene-25,26,27,28-tetrol7,8) which includes four fluorescent biphenyl units within a molecule. Hence, we synthesized compound **1** as well as **2** and **3** as reference compounds. We have found that the fluorescence intensity of **1** is markedly affected by the Na^+-binding.



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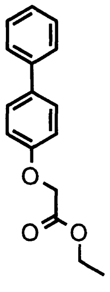

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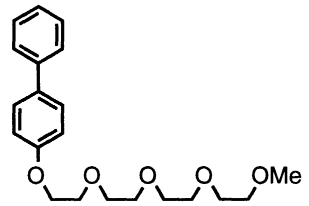

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Compound **1** was synthesized from 5,11,17,23-tetraphenylcalix[4]arene-25,26,27,28-tetrol7,8) and ethyl bromoacetate in DMF in the presence of Na_2CO_3: mp 183-185 °C, yield 31%. The product was confirmed by ^1H NMR and Mass spectral evidence (SIMS m/z 1073 (M^+)) and elemental analysis. The ^1H NMR spectroscopic study ($CDCl_3$, 25 °C) showed that the conformation is immobilized to a cone (δ_H for $ArCH_2Ar$, a pair of doublets at 3.38 and 5.02 ppm). Figure 1 shows the effect of added $NaClO_4$ on the absorption spectra of

1. The absorption maximum (258 nm) shifts to shorter wavelength with an isosbestic point at 258 nm. This implies that the electron density on the phenolic oxygens is reduced upon complexation with Na^+. The association constant (*K*) estimated from Fig. 1 is 2.19 x 10^5 dm^3 mol^{-1}. The fluorescence spectra were measured using 258 nm for excitation (Fig. 2). Very interestingly, the fluorescence intensity (*I*) at around 330 nm increased markedly with increasing $NaClO_4$ concentration. From a plot of *I* *vs*. [$NaClO_4$] (Fig. 3) the *K* was determined to be 3.47 x 10^5 dm^3 mol^{-1}. The results show that **1** acts as a new fluorogenic calix[4]arene which is conveniently usable for the Na^+-sensing.

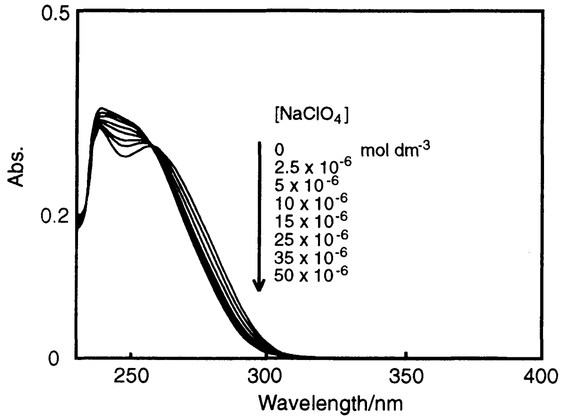


Fig. 1. Absorption spectra of **1** in $CHCl_3$:THF:MeOH = 50:50:1 v/v/v at 25 °C with successive addition of $NaClO_4$; [**1**] = 5.00 x 10^{-6} mol dm^{-3}, [$NaClO_4$] = 0 - 5.00 x 10^{-5} mol dm^{-3}.

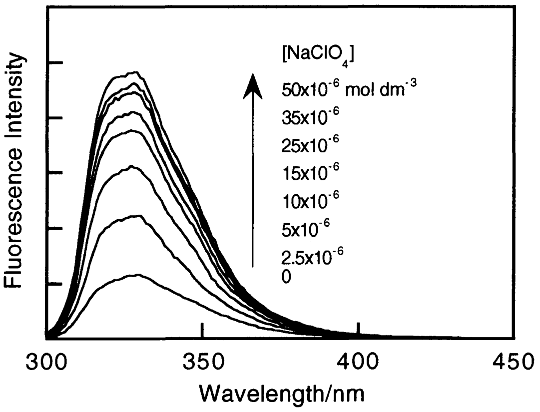
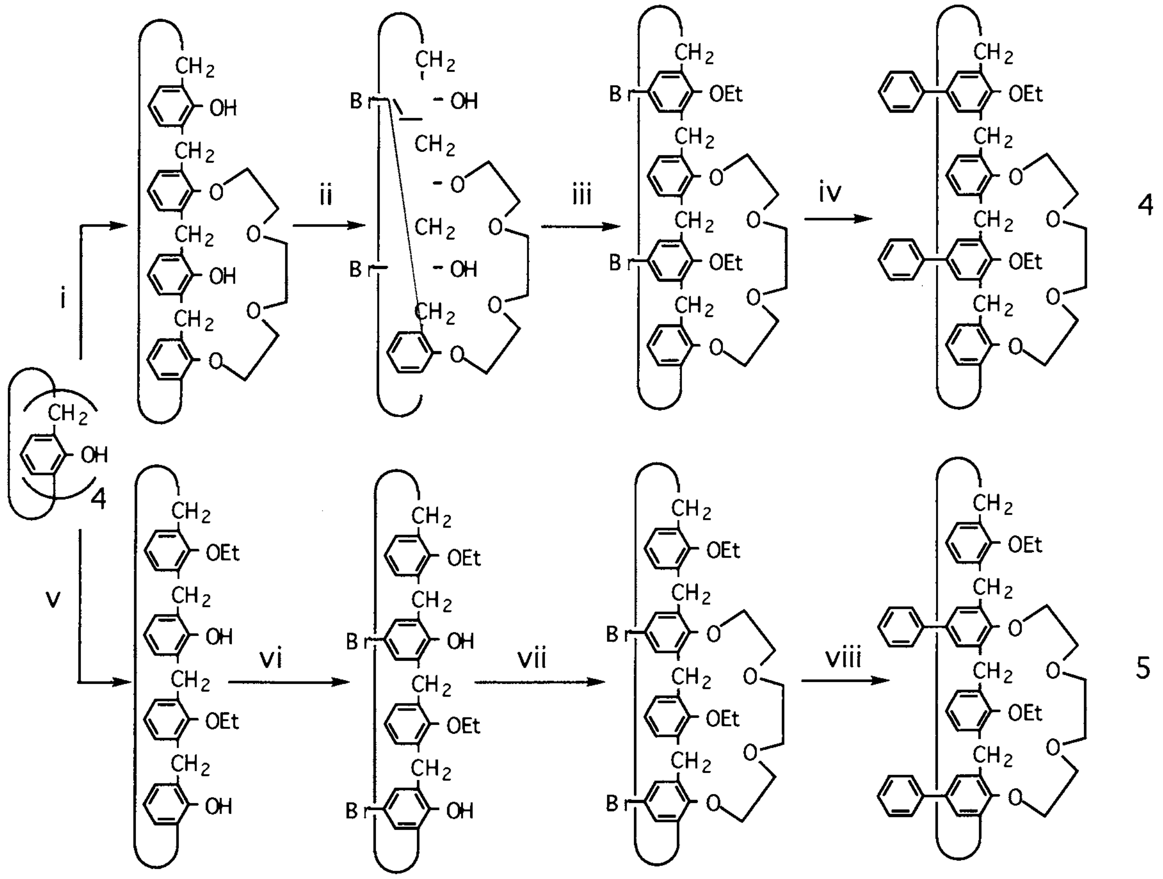


Fig. 2. Fluorescence spectra of **1** (5.00 x 10^{-6} mol dm^{-3}) in $CHCl_3$:THF:MeOH = 50:50:1 v/v/v at 25 °C with successive addition of $NaClO_4$; excitation wavelength 258 nm.

Why does the inclusion of Na^+ in **1** increase the fluorescence intensity? Two possible answers come to our minds: (i) calix[4]arenes adopt C_2 symmetry with two flattened phenyl units and two stand-up phenyl units and the distance between the latter two phenyl units is so short that the fluorescence is quenched intramolecularly whereas the Na^+-binding changes C_2 to regular C_4 symmetry and the intramolecular fluorescence quenching is suppressed, and (ii) a change from C_2 to regular C_4 symmetry suppresses the molecular motion and the quantum yield is enhanced owing to "rigidification"[9]. To clarify the mechanism we estimated the effect of added $NaClO_4$ (1.00 x 10^{-3} mol dm^{-3}) on the fluorescence intensity of **2** and **3** (2.00 x 10^{-5} mol dm^{-3}) in $CHCl_3$ at 25 °C. Although the fluorescence intensity of **2** was scarcely changed, that of **3** was increased by 12%. This suggests that mechanism (ii) is likely but mechanism (i) cannot yet be ruled out.

To find decisive evidence for the mechanism we synthesized **4** and **5** according to Scheme 1. As we have shown previously,[10] the Et group is bulky enough to suppress the oxygen-through-the-annulus rotation. The ^1H NMR spectroscopic studies showed that both **4** and **5** are immobilized to a cone. In **4** the motility of two EtO-carrying fluorescent biphenyl units are inhibited upon the Na^+-binding whereas in **5** the motility of bridged fluorescent biphenyl units are already inhibited by a short crown strap.[11] Furthermore, in **4** two phenyl units are flattened because of the short crown strap while two biphenyl units stand up whereas **5** provides the reverse combination of phenyl and biphenyl units. These structural characteristics are supported by their ^1H NMR spectra; the meta protons in the stand-up phenyl units in **5** appear at higher magnetic field (6.23 ppm) than those in the flattened phenyl units in **4** (7.19 ppm). The absorption spectra are shown in Fig. 4. The change of the absorption of **4** was smaller than that of **5**, because it was assumed that the Na^+-binding site of both complexes



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 *N,N*-dimethylformamide (DMF) (80%); iv, phenylboronic acid, $Pd(PPh_3)_4$, Na_2CO_3 in toluene+MeOH+H_2O (28%); v, C_2H_5I, K_2CO_3 in acetone (86%); vi, Br_2 in $CHCl_3$ (77%); vii, $TsO(CH_2CH_2O)_3Ts$, NaH in DMF (54%); viii, phenylboronic acid, $Pd(PPh_3)_4$, Na_2CO_3 in toluene+MeOH+H_2O (44%).

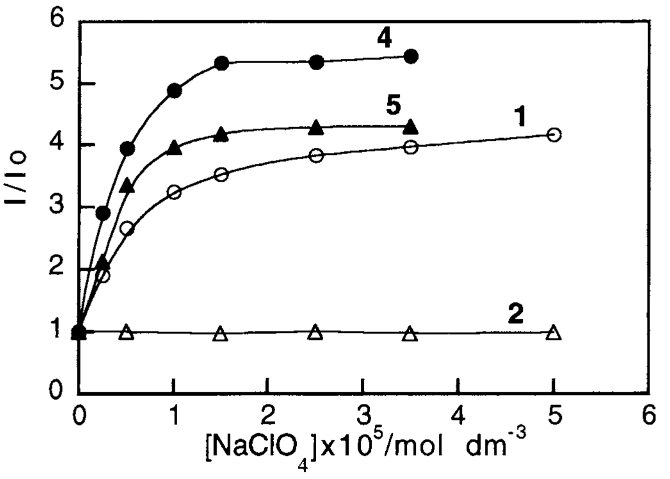


Fig. 3. Plots of increment of fluorescence intensity *vs.* [$NaClO_4$]; [**1**], [**4**], [**5**] = 5.00 x 10^{-6} mol dm^{-3}, [**2**] = 2.00 x 10^{-5} mol dm^{-3}; excited at each isosbestic point.

was mainly at the crown oxygens. The fluorescence spectra were measured using the isosbestic point wavelengths for excitation. As summarized in Fig. 3 the increase of the fluorescence intensities of **4** was larger than that of **5**; the association constants were estimated from these plots to be K= 1.10 x 10^6 dm^3 mol^{-1} for **4** and 1.10 x 10^6 dm^3 mol^{-1} for **5**. The foregoing results unambiguously prove that the fluorescence increase in **1** cannot be rationalized by mechanism (i) but is reasonably explained by mechanism (ii).

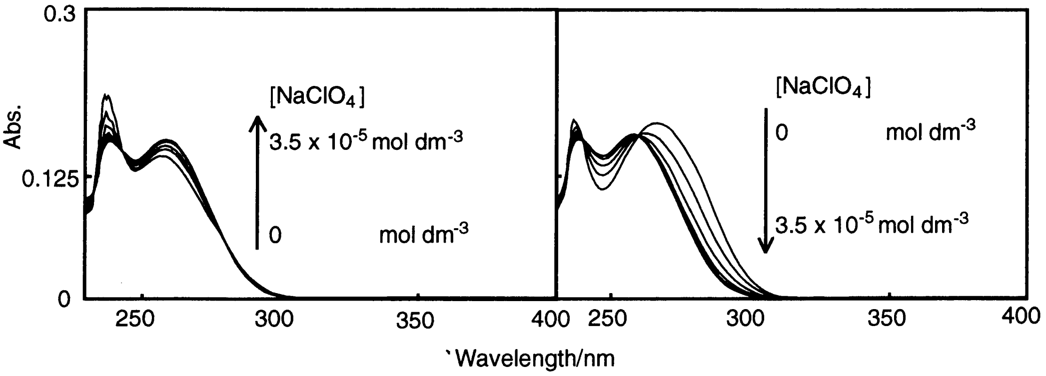


Fig. 4. Absorption spectra of **4** (left) and **5** (right) in $CHCl_3$:THF:MeOH = 50:50:1 v/v/v at 25 °C with successive addition of $NaClO_4$; [**4**], [**5**] = 5.00 x 10^{-6} mol dm^{-3}, [$NaClO_4$] = 0 - 3.50 x 10^{-5} mol dm^{-3}.

In compounds **1**, **4**, and **5** their mother calix[4]arene skeleton is fluorescent. Hence, one can conveniently design various fluorogenic metal and molecule receptors from these compounds and apply to sensings. The present study has established that the key point to induce a fluorescent change is the rigidification of calix[4]arene skeleton by the metal cation.

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11) The fluorescence intensities of **4** and **5** decreased with increasing temperature; $I_{50\,°C} / I_{15\,°C}$ = 0.35 for **4**, $I_{50\,°C} / I_{15\,°C}$ = 0.55 for **5**. These results suggest that the motility of biphenyl units of **5** is inferior to that of **4**.

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