Fluorescent Calix[4]arene which responds to Solvent Polarity and Metal Ions

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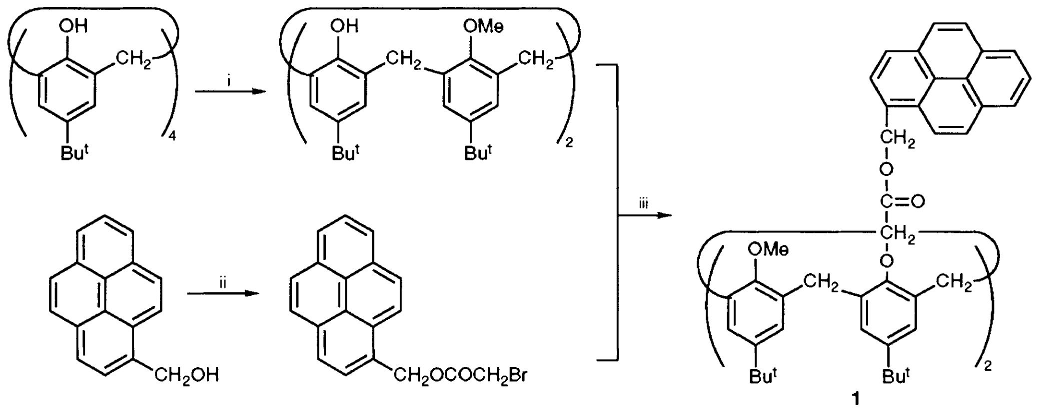
A calix[4]arene having two pyrene moieties on the lower rim has been synthesized; the ratio of the monomer *vs.* excimer emission was sensitively affected by solvent polarity and added metal ions.

Although cyclodextrins and calixarenes have a cavity-shaped architecture, there exists an essential difference: *i.e.* the conformation of cyclodextrins is mostly immobilized whereas the conformational freedom of calixarenes still remains.[1,2] The mobility of the phenyl units in calixarenes is a serious disadvantage when one uses the cavity as a recognition site for guest metals and molecules. In molecular recognition in an aqueous system, in fact, calixarenes as host show a broad guest selectivity.[3,4] We wondered if this disadvantage could be changed to an advantage. We previously found an interesting conformational isomerism in tetra-*O*-methylated calix[4]arenes: it occurs because of a facile oxygen-through-the



Scheme 1 *Reagents*: i, MeI, K_2CO_3 in acetone; ii, $BrCH_2COCl$ in tetrahydrofuran (THF); iii, NaH in THF; in compound **2**, the pyrenylmethoxycarbonylmethoxy units are replaced by methoxy

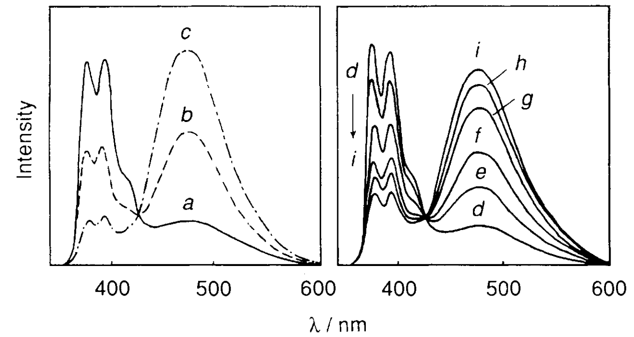


Fig. 1 Typical fluorescence spectra of **1** (2.00×10^{-6} mol dm^{-3}) at 25°C. Solvent: (*a*) methanol, (*b*) propan-2-ol, (*c*) n-hexane, (d)–(i) mixtures of dimethyl sulfoxide and dichloromethane [dimethyl sulfoxide content, (*d*) 100, (*e*) 80, (*f*) 60, (*g*) 40, (*h*) 20, (*i*) 0, volume %]. Excitation wavelength, 342 nm.

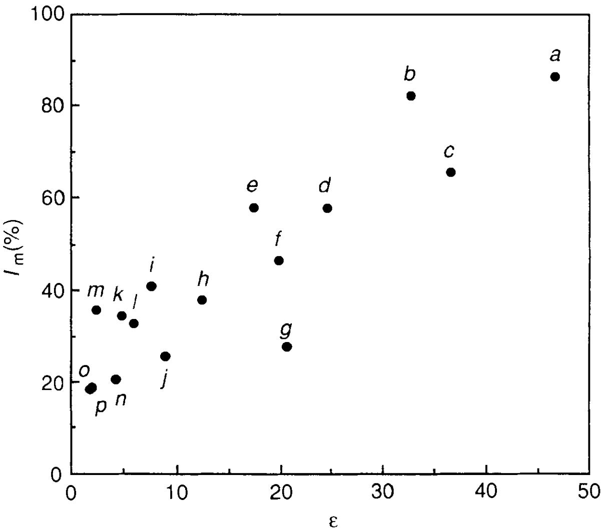


Fig. 2 Plots of I_m(%) *vs.* dielectric constant (relative permittivity). Solvent (*a*) dimethyl sulfoxide, (*b*) methanol, (*c*) *N*,*N*-dimethylformamide, (*d*) ethanol, (*e*) butan-1-ol, (*f*) propan-2-ol, (*g*) acetone, (*h*) 2-methylpropan-2-ol, (*i*) tetrahydrofuran, (*j*) dichloromethane, (*k*) chloroform, (*l*) ethyl acetate, (*m*) benzene and toluene, (*n*) diethyl ether, (*o*) cyclohexane, (*p*) n-hexane; [**1**] = 2.00×10^{-6} mol dm^{-3}, at 25°C.

annulus rotation of the benzene units and is affected by solvent polarity and metal template effects.[5] The conformer distribution can be determined, at present, only by the splitting pattern of the $ArCH_2Ar$ methylene protons in ^1H NMR spectra.[5-7] It occurred to us that if appropriate chromophoric groups were appended to calix[4]arenes, the conformational change induced by solvents and metal ions may be conveniently detected by other spectroscopic methods. Furthermore, the spectroscopic detection of solvent polarity and metal ions would lead to the development of a calixarene-based, novel sensory system. With these objectives in mind, we have synthesized compound **1** which has two fluorescent pyrene molecules on the lower rim. We have found that the ratio of the monomer *vs.* intramolecular excimer emission of **1** is sensitively affected by solvent polarity and added metal ions.

Compound **1** (m.p. 134°C) was synthesized by the method in Scheme 1 and identified by IR and ^1H NMR spectroscopy and elemental analysis. Typical fluorescence spectra of **1** are illustrated in Fig. 1. The monomer emission (*ca.* 380 nm) increases with increasing solvent polarity whereas the excimer emission (*ca.* 480 nm) decreases. We therefore measured the relative peak intensity of the monomer emission [$I_m(\%) = 100 \times I_{monomer}/(I_{monomer} + I_{excimer})$] in various solvents. As shown in Fig. 2, I_m(%) is correlated with the solvent polarity (*e.g.* dielectric constant). These findings suggest that I_m(%) may serve as a new parameter for solvent polarity.

Why does the I_m(%) value change so sensitively? We previously found that the cone : partial-cone ratio in 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetramethoxycalix-[4]arene **2** increases with increasing solvent polarity.[5] This change was explained in terms of the difference in the dipole moment of these two conformational isomers: cone-**2** (dipole moment 0.843 D) having four dipoles orientated in the same direction is more polar than partial-cone-**2** (dipole moment 0.538 D) having one inverted dipole.[5] We thus estimated the cone : partial-cone ratio of **1** by a ^1H NMR method (250 MHz). As recorded in Table 1, I_m(%) is clearly correlated with the cone : partial-cone ratio; the I_m(%) value increases with increasing cone : partial-cone ratio. This supports the view that the interaction of the two pyrene moieties occurs more easily in partial-cone-**1** rather than in cone-**1**. In **1**, the phenyl units bearing the pyrenyl group no longer rotate because of steric hindrance whereas the residual phenyl units bearing the methoxy group can still rotate. In cone-**1**, the calix[4]arene skeleton adopts a bowl-shaped cavity, the lower rim of which is sterically crowded.[8] This makes the interaction of two pyrene molecules very difficult. In partial-cone-**1**, in contrast, the inverted phenyl unit and the two adjacent phenyl units (which bear the pyrenyl group in **1**) are almost parallel.[8] This situation makes the interaction of two pyrene molecules much easier because of the space provided on the lower rim.

As shown in Fig. 3, the I_m(%) value was also affected by added alkali metal cations: I_m(%) increases with increasing metal concentration.† In other words, $I_{excimer}$ sharply de-

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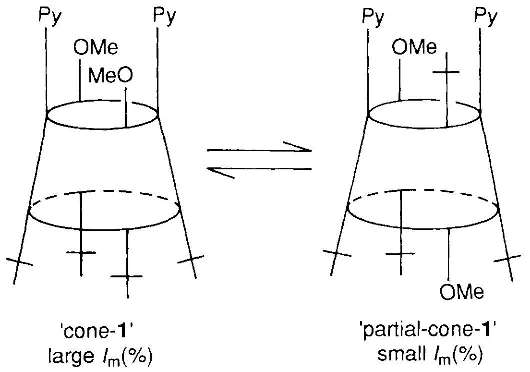
† Diethyl ether was used because I_m(%) changed sensitively in this solvent. A similar tendency, although not so sensitive as in diethyl ether, was observed in other solvents such as methanol and tetrahydrofuran.



Py: Pyren-1-ylmethoxycarbonylmethoxy

Table 1 Relative intensity of monomer emission [I_m(%)] and the cone : partial-cone ratio

Solvent[a]	I_m(%)[b]	Cone : partial-cone[c]
[$^2H_6$]DMSO-[$^2H_7$]DMF (30/70, v/v)	72.1	93 : 7
[$^2H_7$]DMF	65.4	90 : 10
$CDCl_3$	34.6	58 : 42
$CDCl_3$-[$^2H_{12}$]cyclohexane (50/50, v/v)	27.2	52 : 48
$CDCl_3$-LiSCN	92.8[d]	>95[e]

[a] *Abbreviations used*: DMSO, dimethyl sulfoxide: DMF, *N,N*-dimethylformamide. [b] Measured at 25°C, [**1**] = 2.00×10^{-6} mol dm^{-3}. [c] Determined by ^1H NMR spectroscopy at −30°C. At room temperature the ratio could not be determined because of peak broadening. [d] [LiSCN] = 2.0×10^{-3} mol dm^{-3}. [e] [**1**] = 2.0×10^{-2} mol dm^{-3}, [LiSCN] = 4.0×10^{-2} mol dm^{-3}, at room temperature.

creases in the presence of metal cations. From plots of $I_{excimer}$ against [M^+] we conclude that **1** forms 1 : 1 complexes with Li^+, Na^+ and K^+ (the spectral change was too small to estimate the complexation with Cs^+): log K_{ass}/dm^3 mol^{-1} = 4.73 for LiSCN, 5.34 for NaSCN, and 4.06 for KSCN (at 25 °C in diethyl ether). It is known that the cone : partial-cone ratio in **2** increases when Li^+ or Na^+ is added.[5] The increase in cone-**2** may be ascribed to metal–MeO interactions, like metal–crown interactions, which selectively stabilize the cone conformation. In the present study, we found that the increase in I_m(%) on the addition of alkali metal cations may also be explained by the increase in cone-**1** (Table 1). In addition, we consider that the cone-**1**–M^+ complex may have a I_m(%) value larger than that of the 'free' cone-**1** if the bound metal cation interferes with the interaction of the two pyrene moieties.

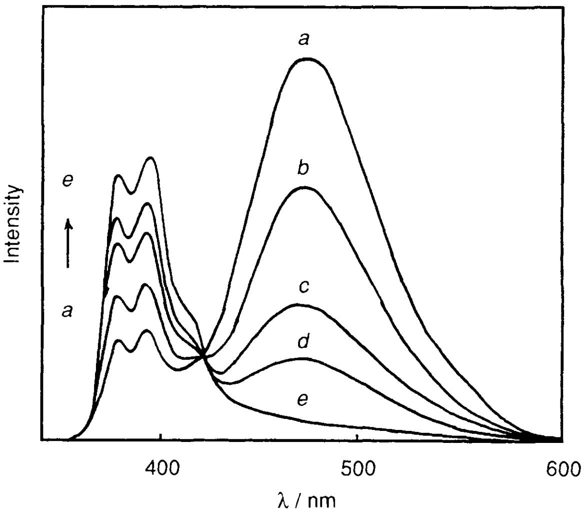


Fig. 3 Fluorescence spectra of **1** (2.00×10^{-6} mol dm^{-3}) in diethyl ether at different LiSCN concentrations: [LiSCN]/mol dm^{-3} = (*a*) 0, (*b*) 1.0×10^{-5}, (*c*) 4.0×10^{-5}, (*d*) 1.0×10^{-4}, (*e*) 2.0×10^{-3}

In conclusion, the present paper demonstrates that introduction of fluorescent groups into ionophoric calixarenes provides a new, promising host–guest sensory system.

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References

1 C. D. Gutsche, B. Dhawan, J. A. Levine, K. Hyun and L. J. Bauer, *Tetrahedron*, 1983, **39**, 409.
2 K. Araki, K. Iwamoto, S. Shinkai and T. Matsuda, *Chem. Lett.*, 1989, 1747.
3 S. Shinkai, K. Araki, M. Kubota, T. Arimura and T. Matsuda, *J. Org. Chem.*, 1991, **56**, 295.
4 T. Arimura, M. Kubota, K. Araki, S. Shinkai and T. Matsuda, *Tetrahedron Lett.*, 1989, **30**, 2563.
5 S. Shinkai, K. Iwamoto, K. Araki and T. Matsuda, *Chem. Lett.*, **1990**, 1263.
6 J-D. Loon, L. C. Groenen, S. S. Wijmenga, W. Verboon and D. N. Reinhoudt, *J. Am. Chem. Soc.*, 1991, **113**, 2378.
7 L. C. Gronene, J-D. Loon, W. Verbon, S. Harkema, A. Casrati, R. Ungaro, A. Pochini, F. Ugozzoli and D. N. Reinhoudt, *J. Am. Chem. Soc.*, 1991, **113**, 2385.
8 P. D. J. Grootenhuis, P. A. Kollman, L. C. Groenen, D. N. Reinhoudt, G. J. van Hummel, F. Vgozzoli and G. D. Andreetti, *J. Am. Chem. Soc.*, 1990, **112**, 4165.