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Metal Sensor of Water Soluble Dansyl-modified Thiacalix[4]arenes

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Abstract: The water soluble thiacalix[4]arene derivatives, which are modified with di- and tri-dansyl moieties, have been prepared to investigate their metal sensing abilities in aqueous solution. It is the first example that water soluble thiacalix[4]arene derivatives can detect metal cations directly in aqueous solution by variation of fluorescence intensity upon addition of a metal cation.

Detection of molecules by fluorescent sensors is of current interest.[1] One of mechanisms for sensing is a use of host-guest complexation phenomena of inclusion compounds, such as cyclodextrins, crown ether or calixarene derivatives.[2] Thiacalix[4]arene is composed benzene rings, linked via sulfide bridges, which itself can make host-guest complexation with metal cations because sulfide functional group has affinity for metal cations.[3] On the other hand, calixarene itself,[4] which is an analogue of thia-calixarene, hardly can make host-guest complexation with metal cations. So far, extensive studies of the host-guest complexation of calixarenes with functional groups forming the upper and lower rims of calixarenes have been done. Recently, the convenient synthetic method of thiacalixarene has been reported by Kumagai et al.[5] We have reported the dansyl-modified cyclodextrins, which exhibit variation of fluorescence intensity upon addition of a guest such as neutral compounds in aqueous solution.[6] The mechanism of the host-guest complexation is going on the induced-fit type. In this system, the dansyl moiety is moved out from the cyclodextrin cavity toward the outside, of which the environment is high polarity than that of the cyclodextrin cavity, causing the decreasing of the fluorescent intensity of the dansyl moiety. For further extension of this work, we tried the synthesis of water soluble dansyl-modified thiacalixarens (**1** and **2**), because the titled compounds could be used as molecular sensors, as shown for dansyl-modified cyclodextrins. Compounds **1** and **2** were prepared from thiacalix[4]arene by treating with dansylsufonyl chloride in the presence of NaH as shown in Fig. 1.[7] The resulting reaction mixture gives four spots on the TLC, which was developed on n-hexane:ethylacetate system. The main products are **1** and **2**, and mono and tetra substituted derivatives are obtained as a minor product. The ^{1}H-NMR spectrum of **1**

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shows two peaks at 1.25 and 0.82 ppm attributed to the signal of tert-butyl groups. It is well known that calix[4]arene can adopt four extreme geometries, which have designated as cone, partial-cone, 1,2-alternate, and 1,3-alternate conformations.[4]

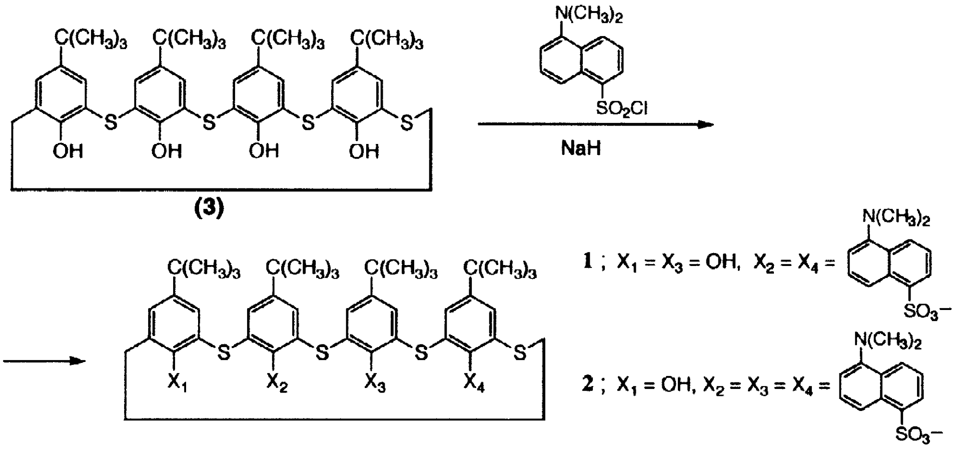

Fig. 1 Preparations of **1** and **2**.

The splitting signal of the tert-butyl group of **1** suggests that the configuration of **1** might not be cone conformation. On the other hand, the ^{1}H-NMR spectrum of native thiacalix[4]arene (**3**) shows that the signal of tert-butyl group appears at 1.22 ppm as a singlet, which shows that **3** has a cone configuration. The position of modification of dansyl moieties for **1** should be 1,3-position of the benzene ring because of its less of stereo-hindrance than that of 1,2-position. In the case of **2**, the ^{1}H-NMR spectrum shows two peaks at 0.83 ppm and 1.31 ppm attributed to tert-butyl group, indicating that the configuration of **2** should be similar to **1**. On the other hand, the signal attributed to dimethyl amino group appears at 2.79 and 2.93 ppm as singlet with integrated intensity as 1:2, respectively, in contrast with the case of **1**, of which the signal appears as singlet at 2.90 ppm. It is indicating that the configuration of **2** is much more complicated than that of **3**. The fluorescence spectra of **1** in 10 vol.-% DMF of Sörensen buffer solution (pH 7.41) in the presence and absence of Al^{3+} cation are given in Fig. 2.

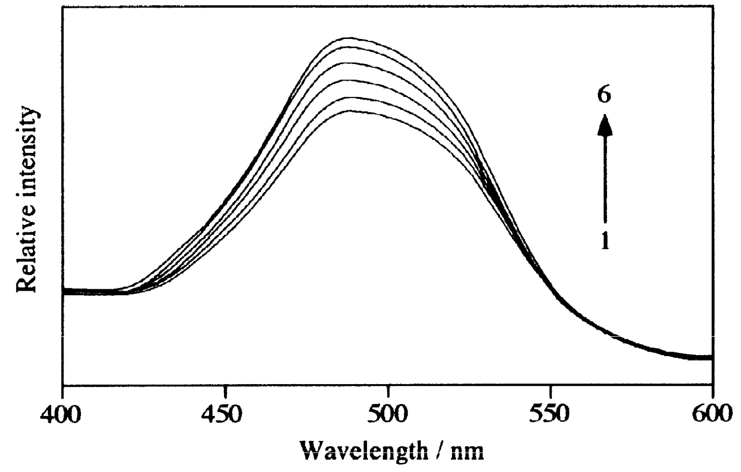

Fig. 2 Fluorescence spectra of **1** (1×10^{-6} M) in 10 vol.% DMF aqueous solution at pH 7.41 with various concentrations of Al^{3+} cations : (1) 0; (2) 6.0×10^{-5}; (3) 1.2×10^{-4}; (4) 1.8×10^{-4}; (5) 2.4×10^{-4}; (6) 3.0×10^{-4} M.

The spectrum of **1** and **2** alone exhibit a peak at 489 nm, and the intensity increases or decreases with increasing metal cation concentration. It is reported that the fluorescence of the dansyl unit is enhanced in the hydrophobic microenvironment of enzymes or micelles.[8] This is why the dansyl unit can be used as a probe to describe host-guest complexation behaviors of the host compound. The result obtained from fluorescence spectra of **1** and **2** for Al^{3+} suggests that the dansyl moieties moved from the outside bulk water environment toward the interior of the hydrophobic thiacalix[4]arene cavity while simultaneously a metal cation is included in the cavity of **1** and **2**. The binding constants of **1** and **2** for Al^{3+} were obtained by the analysis of the guest-induced fluorescence variations using Eq.1.

$$\frac{1}{I_f - I_{f0}} = \frac{1}{a[\mathrm{CAPS}]} + \frac{1}{a[\mathrm{CAPS}]K} \cdot \frac{1}{[\mathrm{Metal}]} \qquad \text{Eq. 1}$$

Here, I is the fluorescence intensity at 489 nm (I_f for complex, I_{f0} for the host alone), [CAPS] is the total host concentration, [Metal] is the total guest concentration, and a is constant. The binding constants of **1** and **2** for Al^{3+} are obtained as 3,500±600 and 1,200±170, respectively, roughly parallel with the sensitivity factors. The extent of variation of the fluorescence intensity of **1** and **2** depends on the nature of a metal cation, even at a common concentration; therefore, **1** and **2** can be used to be sensing molecules. To display the sensing ability of **1** and **2**, the $\Delta I/I^0$ value as sensitivity parameter was used. Here ΔI is $I - I^0$, where I^0 is the fluorescence intensity for the host alone, and I is the fluorescence intensity for a complex. The sensing parameters of **1** and **2** for a couple of metal cations shown in Fig. 3.

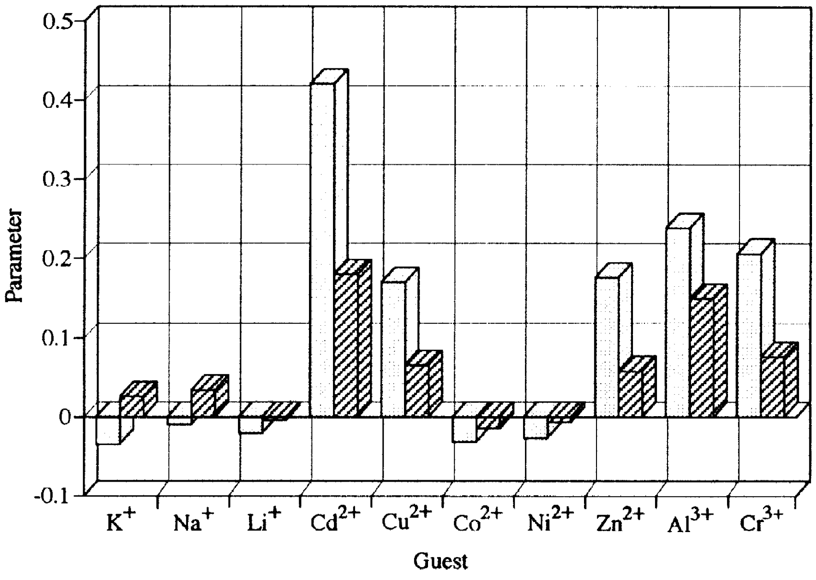

Fig. 3 Sensitivity factors of **1** (1×10^{-6} M : □) and **2** (1×10^{-6} M : ▨) for a couple of metal cations (3×10^{-4} M).

The concentrations of a host and metal cation are 1×10^{-6} M and 3×10^{-4} M, respectively. Compounds **1** and **2** detect Cd^{2+} with the most highest sensitivity. The sensitivity of **1** and **2** for metal cations decreases in the sequence: $Cd^{2+} > Al^{3}+ > Cr^{3+} > Zn^{2+} > Cu^{2+}$ for **1**: $Cd^{2+} > Al^{3}+ > Cr^{3+} > Cu^{2+} > Zn^{2+} >$ for 2. The sensing ability of **1** is higher than those of **2**. Because the dansyl moieties of **2** are much crowded in comparison with the case of **1**, three appended moieties make less effort the elevate host-guest binding ability than two appended moieties. The sensing abilities of **1** and **2** for neutral guests such as borneol, nerol, (-)-menthol, cyclohexanol, cyclooctanol, and 1-adamantanecarboxylic acid are also studied. Hosts **1** and **2** recognize nerol with the parameter values of 0.123 and 0.058, respectively, whereas other guests can be hardly detected by those hosts. It is probably that molecular size of nerol, which is the smallest among guests examined, is just fit to the cavity of the titled compounds. In conclusion, the host-guest binding mechanism as shown in the dansyl modified cyclodextrins is also happened in the water soluble dansyl modified thiacalix[4]arenes.

References and notes:

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7. Experimental data:**1**; TLC (Kiesegel 60F254; n-hexane:AcOEt 2:1 v/v) Rf 0.54; ^{1}H-NMR ($CDCl_3$) δ = 8.65 (4H, d, J=8.7 Hz, Ar-H), 8.18 (2H, d, J=8.7 Hz, Ar-H), 7.54 (8H, m, Ar-H), 7.21 (2H, d, J=8.7 Hz, Ar-H), 6.98 (4H, br.s, Ar-H), 2.90 (12H, s, $-N(CH_3)_2$), 1.25 (18H, s, $-C(CH_3)_3$), 0.82 (18H, s, $-C(CH_3)_3$). Anal. Calcd. for $C_{64}H_{70}N_2O_8S_6$, C 65.44, H 6.23, N 1.47 % ; Found, C 65.22, H 6.02, N 1.46 %. MS(FAB)[m/z], 1187 ([M+H$^+$]). **2**; TLC (Kiesegel 60F254; n-hexane:AcOEt 2:1 v/v) Rf 0.46; ^{1}H-NMR ($CDCl_3$) δ = 8.44 (1H, d, J=8.7 Hz, Ar-H), 8.28 (3H, d-d, J=8.7 Hz, Ar-H), 7.98 (2H, d, J=8.7 Hz, Ar-H), 7.92 (3H, d-d, J=8.7 Hz, Ar-H), 7.72 (2H, s, Ar-H), 7.62 (2H, s, Ar-H), 7.38-7.50(2H, m, Ar-H), 7.20 (3H, d-d, J=8.7 Hz, Ar-H), 7.11 (2H, d-d, J=8.7 Hz, Ar-H), 6.90-6.95 (6H, m, Ar-H), 2.93 and 2.79 (12H, s, $-N(CH_3)_2$), 1.31 (18H, s, $-C(CH_3)_3$), 0.83 (18H, s, $-C(CH_3)_3$). Anal. Calcd. for, $C_{76}H_{81}N_3O_{10}S_7$, C 64.72, H 5.94, N 2.36 %; Found, C 64.54, H 5.75, N 2.54 %. MS(FAB)[m/z], 1420 ([M+H$^+$]).

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