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NEW WATER-SOLUBLE HOST MOLECULES DERIVED FROM CALIX[6]ARENE

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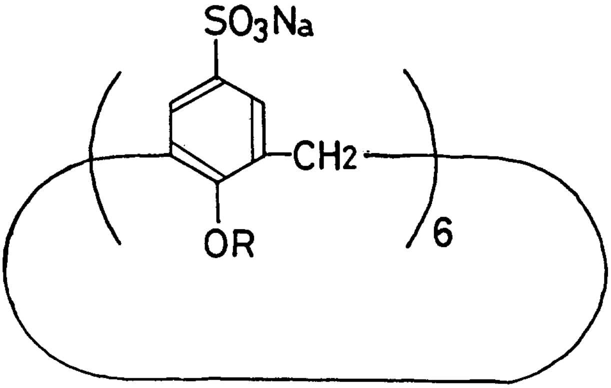
4-Sulfonate derivatives of calix[6]arene and O-n-hexylcalix[6]arene (1a and 1b, respectively) were synthesized. Measurements using fluorescence and absorption spectral probes indicated that the cavity of calix-[6]arene can accept a naphthalene molecule but not a pyrene molecule and that (1b) has a hydrophobic cavity constructed from the aggregate of the hexyl groups while (1a) provides a reaction field apparently more polar than water. This is the first example for water-soluble host molecules derived from calix[6]arene.

The chemistry of cyclodextrins and cyclophanes has occupied a central interest in host-guest chemistry in last two decades, and many functionalized host molecules which can mimic the in vivo action of enzymes by means of simple in vitro chemical systems have been exploited.1-4) Recently, Gutsche and co-workers5) have reported on a series of cyclic host molecules called "calixarenes" which may possess an architecture similar to the cyclodextrins and thus be useful to design enzyme mimics in totally synthetic systems. Although several groups have already reported on the ionophoric functions,5-8) the inclusion properties in aqueous solution are rather unknown. Calixarenes can include several small molecules in the solid state.5,9,10) We believe, however, that in order to utilize calixarenes as binding sites in enzyme mimics, one has to understand the host-guest-type interactions in aqueous systems more clearly. Here, we wish to report new water-soluble host molecules (1) derived from calix[6]arene.



(1a): R=H

(1b): R=n-C_6H_{13}

First, p-t-butylcalix[6]arene was debutylated to yield calix[6]arene.$^{5)}$ The sulfonate derivative of calix[6]arene (1a) was prepared from calix[6]arene by treatment with conc. H_2SO_4 at 100 °C. The solution was neutralized with $CaCO_3$ and then Na_2CO_3, and evaporated to dryness. The residue was reprecipitated several times from water to methanol: yield 75%. (1a) was treated with n-hexyl bromide and NaOH in dimethylsulfoxide at 90 °C. Upon cooling to room temperature after 18 h, white crystals (1b: sulfonate derivative of O-n-hexylcalix[6]arene) precipitated: yield 46%. (1a) and (1b) were identified by elemental analysis, PC, IR, NMR, and titration of the sulfonic acid groups (the sulfonate groups of (1a) and (1b) were neutralized by treating with ion-exchange resin and then titrated).

The inclusion properties of (1a) and (1b) in aqueous solution were examined by fluorescence and absorption spectroscopic methods. The fluorescence emission maxima of aminonaphthalene derivatives show strong solvent dependence. Here, we employed 2-anilinonaphthalene(AN) as a fluorescence probe. As shown in Fig. 1, the emission maximum of AN correlates linearly with the methanol concentration (vol%) in water-methanol mixed solvent. The emission maxima shifted to shorter wavelengths with increase in the concentrations of (1a) and (1b), the saturation values being 446 nm and 427 nm, respectively (Fig. 2). One may consider, therefore, that the cavities of (1a) and (1b) have the reaction field similar to 7 and 70 vol% aqueous methanol, respectively.

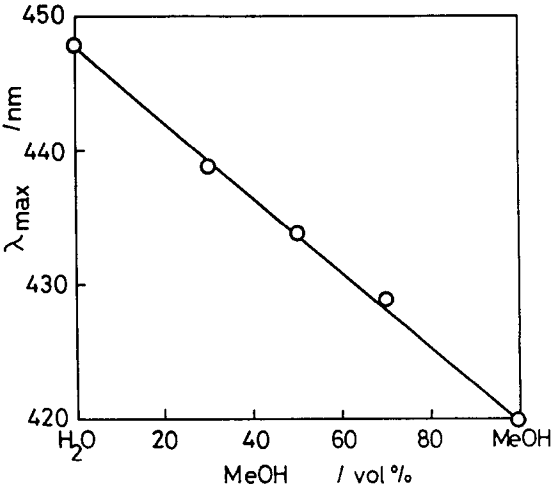


Fig. 1. Emission maximum of 2-anilinonaphthalene (6.1×10^{-6} M) in water-methanol mixed solvent at 30 °C: excitation 310 nm.

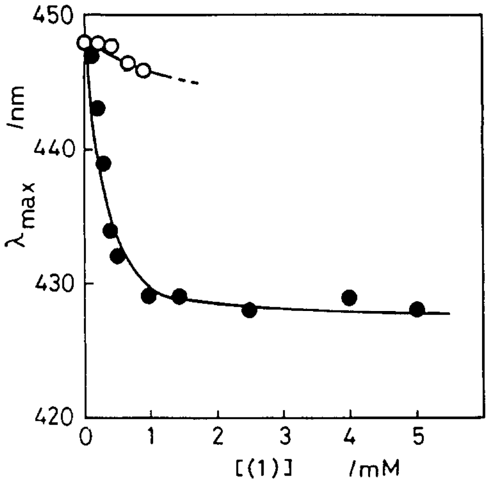


Fig. 2. Plots of emission maximum of 2-anilinonaphthalene vs. [(1)] in water at 30 °C: [2-anilinonaphthalene]=3.1×10^{-5} M for (1a) (○) and 6.1×10^{-6} M for (1b) (●). The fluorescence intensities for (1a) above 1 mM were too weak to accurately determine the λ_{max}.

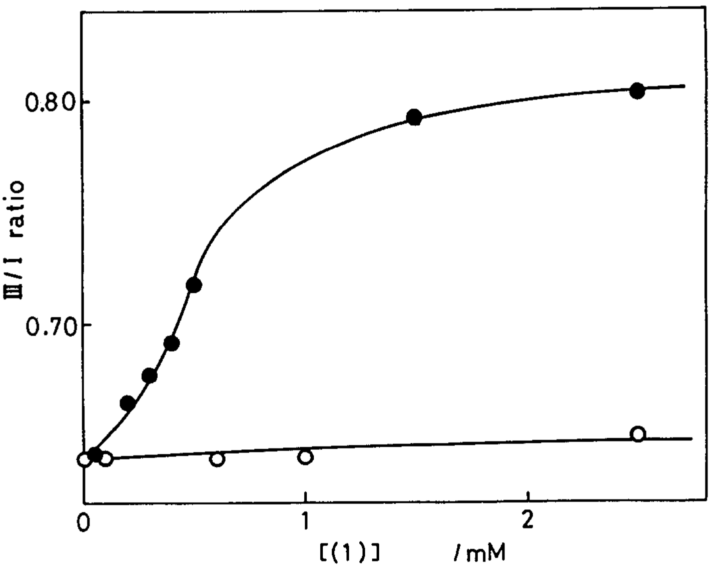
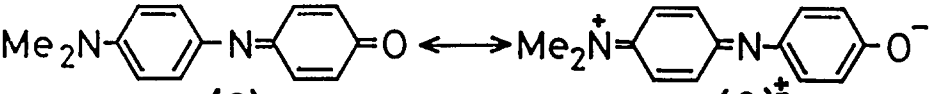


Fig. 3. Plots of III/I ratio vs. [(1)] in water at 30 °C: ○(1a), ●(1b).

Kalyanasundaram and Thomas[11)] have demonstrated that vibronic band intensities in pyrene monomer fluorescence is a convenient probe to accurately determine critical micelle concentrations(cmc): the ratio (band III/band I)=0.63-0.66 in water and below cmc and 0.90 above cmc in aqueous sodium dodecylsulfate (SDS) solution. We found that the III/I ratio of pyrene (2.0×10^{-6} M, excitation 310 nm) in aqueous solution at 30 °C increases with increasing (1b) concentration and reaches a saturation value (ca. 0.80) above 1.5×10^{-3} M (Fig. 3). The result indicates that the hydrophobicity of the cavity (1b) is almost comparable with that of the SDS micelle. On the other hand, the increase in the III/I ratio was not observed for (1a) under the same experimental conditions. This implies that probably, the cavity of calix[6]arene is large enough to bind a naphthalene molecule (vide supra) but too small to accept a pyrene molecule. One may presume, therefore, that in (1b) pyrene binds to the hydrophobic domain constructed from six hexyl chains. In other words, one may regard (1b) as a "hexapus" host molecule. According to Kalyanasundaram and Thomas,[11)] the III/I ratio of pyrene fluorescence changes noncotinuously at cmc. We found, importantly, that the plot of III/I vs. [(1b)] is a continuous saturation curve. Probably, (1b) does not form a so-called micelle-like aggregate but behaves as a "unimolecular micelle" owing to the calixarene cap tying six hexyl chains.

Brooker and Sprague[12)] suggested to use Phenol Blue (2) as a solvent property indicator: the absorption maximum (668 nm in water[12)]; 658 nm according to our measurement at 30 °C) shifts to shorter wavelengths in nonpolar solvents (e.g., 552 nm in cyclohexane).



(2) (2)±

In the presence of (1b)(5.00 mM), the λ_{max} shifted to shorter wavelength by 15 nm. Very interestingly, we unexpectedly found that the λ_{max} in the presence of (1a) (5.00 mM) shifts to longer wavelength (λ_{max} 685 nm). This red shift (by 27 nm) implies that apparently, (1a) can provide a reaction field much more polar than water! Such red shift of (2) could not be produced by the addition of sodium poly(p-styrenesulfonate) (5.00 monomeric unit mM, λ_{max} 612 nm), SDS(10.0 mM, 630 nm), and KCl(2.0 M, 657 nm). Only when 2.0 M of sodium benzenesulfonate were added, the λ_{max} shifted a little to longer wavelength (672 nm). Conceivably, the six sulfonate groups lined on the edge of the calix[6]arene are capable of stabilizing the excited-state structure $(2)^{\pm}$ through the electrostatic interaction, and it leads to the unusual red shift. This finding suggests that (1a) may serve as an excellent catalyst for the reactions involving cationic intermediates (or transition states).

In conclusion, the present study indicates that a new class of water-soluble host molecules can be derived from calix[6]arene: they provide not only the hydrophobic cavity but also the unusally strong anionic reaction field. Further studies on electric conductivity, surface tension, and introduction of different O-substituents are currently continued in this laboratory.

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