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Diazo-Coupling with a Resorcinol-Based Cyclophane. A New Water-Soluble Host with a Deep Cleft

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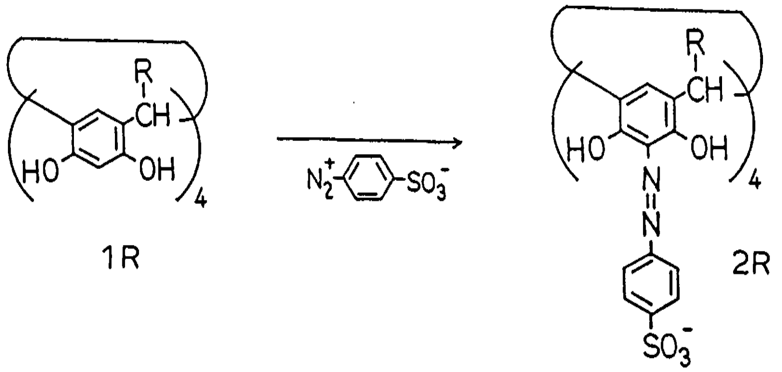
A new water-soluble host molecule was synthesized by the diazo-coupling reaction of a resorcinol-based tetrameric cyclophane and p-sulfonatobenzenediazonium. In an aqueous system the product could include large guest molecules such as adamantane, pyrene, and coronene, the association constants being $(2.0-4.6) \times 10^4$ M^{-1}.

Macrocyclic compounds that can easily be synthesized from phenol and its homologs have been of much concern in relation to molecular design of new receptors for small guest molecules.1-3) Since these compounds have a stoma composed of benzene rings, they have been expected to form host-guest-type complexes. It is still difficult, however, to find evidence for the formation of host-guest-type complexes in organic media. In aqueous media, on the other hand, the formation of host-guest-type complexes easily occurs because of hydrophobic interactions broadly operating between host and guest molecules. Taking calixarenes, for instance, it has already been established that water-soluble ones are capable of forming such complexes in water.1) In contrast to calixarenes, the application of resorcinol-based $[1_4]$cyclophane (1R) as host molecules has been an escaped attention. Recently, Aoyama et al.4,5) demonstrated that they serve as a unique extractant for sugar molecules. It occurred to us that if one can make 1R water-soluble, then they would serve as a unique host molecule in water. Thus, we introduced hydrophilic sulfonate groups into **1**Me through the diazo-coupling reaction with p-sulfonatobenzenediazonium.6) We have found that the product (**2**Me) is actually water-soluble and includes several organic guest molecules.

1Me was synthesized from resorcinol and acetaldehyde according to the

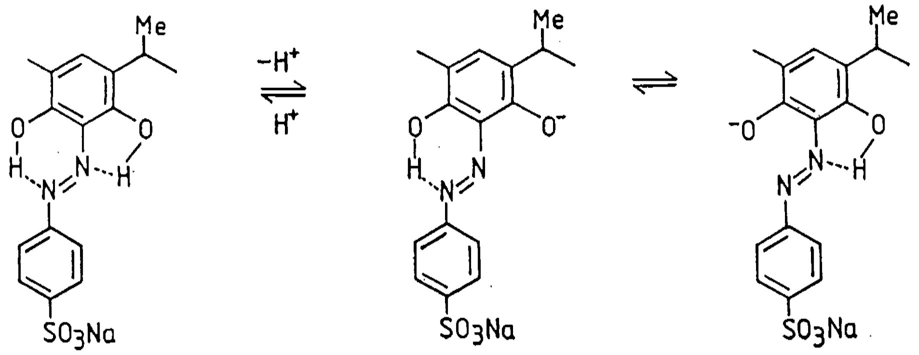


1R

2R

method of Reimer and Tobin.[7] **1**Me (0.50 g, 0.92 mmol) was treated with p-sulfonatobenzenediazonium (0.81 g, 4.4 mmol) in DMF (30 ml) in the presence of pyridine (6 ml) at 0-5 °C for 40 h. The solution was concentrated in vacuo and the product (**2**Me) was crystallized by dilution with water. This was purified by repeating a salting-out operation with sodium bromide. Finally, the product was isolated as tetrasodium salt: mp > 300 °C, yield 28.6%. This compound was identified by IR, NMR, and elemental analysis.[8]

In aqueous solution at 30 °C, **1**Me gave an absorption maximum at 415 nm (ε 86100). The spectrum scarcely changed at pH 1.0-8.5 (ionic strength 0.1 with KCl). With increasing pH above 8.5, the absorbance at 415 nm decreased with tight isosbestic points (367 and 441 nm) and a new absorption band appeared at around 520 nm. As shown in Fig. 1, the plots of OD vs. pH give pK_a = 10, which turned out to be due to the dissociation of four protons. The relatively high pK_a value reflects the strong intramolecular hydrogen-bonding interaction between OH and azo groups.



Inclusion properties of **2**Me were estimated by a turbidity method: that is, a methanol solution (0.05 ml) of guest molecules was injected into an aqueous solution (not buffered, pH 5.4 where none of the eight OH groups is dissociated) and the absorbance at 700 nm was measured. Guest molecules used here were adamantane, pyrene, and coronene. The typical result is shown in Fig. 2. In every case, the critical concentration for turbidity in the presence of **2**Me (i.e., $[G_C]$) is higher than that in the absence of **2**Me (i.e., $[G_O]$). The difference ($[G_C]-[G_O]$) corresponds to the guest concentration dissolved in water through inclusion in **2**Me. Thus, the association constant (K) for G + **2**Me $\rightleftharpoons$ G·**2**Me in water can be defined as Eq. 1.[9)]

$$K = \frac{[G_C]-[G_O]}{[G_O]([\mathbf{2}Me]-([G_C]-[G_O]))} \qquad (1)$$

We thus obtained $K = 2.0 \times 10^4\ M^{-1}$ for adamantane, $3.7 \times 10^4\ M^{-1}$ for pyrene, and $4.6 \times 10^4\ M^{-1}$ for coronene.

Gutsche et al.[8)] previously synthesized water-soluble p-(2-carboxyethyl)calix[n]arenes(3_n: n = 4—8). Among them, the cyclic tetramer 3_4 cannot include either pyrene or coronene (i.e., K=0).[10)] Thus, the present study established that the diazo-coupling reaction of p-sulfonatobenzenediazonium with **1**Me not only makes the product water-soluble but provides a large, extended cavity which can accept large guest molecules. This indicates that the method is useful for improving the binding ability (and probably the selectivity, too) in host-guest-type complexation.

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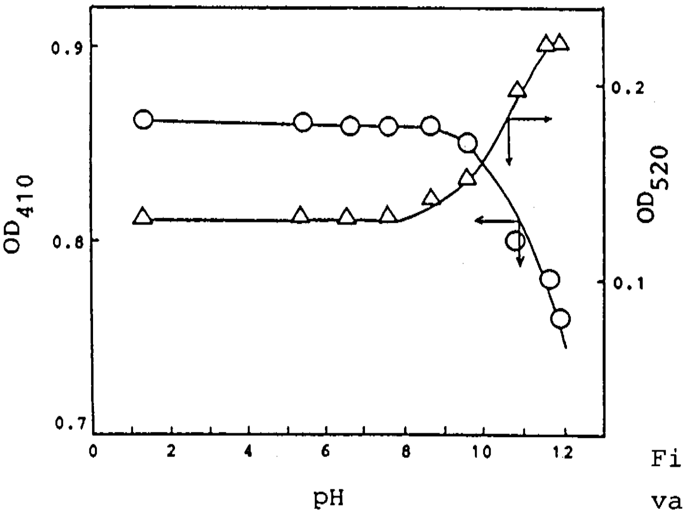

Fig. 1. Plots of absorbances (410 and 520 nm) against medium pH: [**2**Me] = 1.00×10^{-5} M, ionic strength 0.1 with KCl, 30 °C.

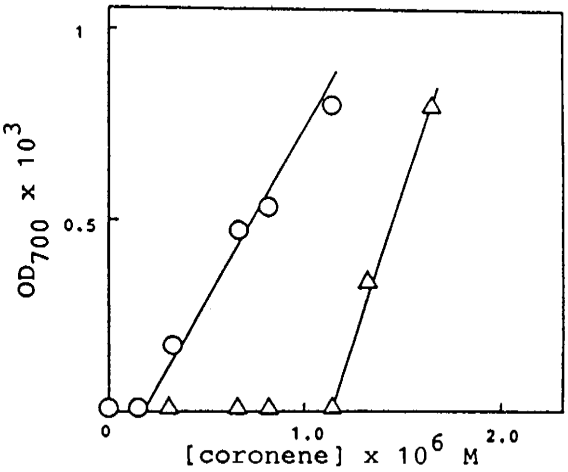

Fig. 2. Determination of the K value for coronene by a turbidity method. The turbidity was estimated at 700 nm and 30 °C.

○ : [**2**Me] = 0 M

△ : [**2**Me] = 1.00×10^{-4} M.

References

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8) Anal. Calcd for $(C_{14}H_{11}O_5N_2SNa)_4 \cdot 2HCON(CH_3)_2 \cdot 1.6NaBr$: C, 44.32; H, 3.48; N, 8.34; Br, 7.61. Found: C, 44.35; H, 3.42; N, 8.30; Br, 7.61.

9) The critical micelle concentration for 2Me was estimated to be 4.3 x 10^{-4} M (30 °C) by a conductance method. Thus, 2Me (1.00 x 10^{-4} M) does not form aggregates under the measurement conditions. Although it is not easy to specify the stoichiometry of the complexes by a turbidity method, we consider that the 1:1 complexes are predominantly formed under the measurement condition [2Me]>>[guest].

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