Association of *n*-Alcohol with *p*-Sulfonato Calixarenes in an Aqueous Medium Determined by Headspace Gas Chromatography

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The associations of *n*-alcohols (C_4 to C_9) with water-soluble *p*-sulfonato calix[4, 6, and 8]arenes have been determined in aqueous solutions at 25 °C. In contrast to the case of cyclodextrins, the alkyl chain length does not contribute to the stability of the associated complex.

In analogy with cyclodextrins (CyD's), calixarenes (CA's) are cyclic oligomers, which act as hosts, and form inclusion complexes with various guest substances. While complexations with CyD's have been studied in an aqueous medium, it was not until the appearance of water-soluble CA's that those with CA's in an aqueous solution became applicable to the practical field of chemistry. Of the many types of water-soluble CA's, *p*-sulfonato CA's (PSCA's) are widely used for capillary electrophoresis,[1] the determination of a cationic surfactant,[2] reversed-phase LC as a mobile-phase additive,[3] or as a stationary phase,[4] and so on. Very little is known, however, about how the complex formation of PSCA differs from that of CyD. The present work was concerned with clarifying this difference. We employed a homologous series of *n*-alcohol as guests for this purpose. The association constants of these guests with α-, β-, and γ-CyD have recently been determined by headspace GC.[5]

Experimental

Water-soluble *p*-sulfonato calix[*n*]arenes (PSC[*n*]A's or simply [*n*]), where *n* is 4, 6, and 8, were obtained from Sugai Kagaku Co. and used after recrystallization from a water-methanol mixture. Aqueous solutions of PSC[*n*]A in the range of 0.01 to 0.1 M were prepared and standardized by titration with a standard 0.01 M NaOH solution, as described in the literature (1 M = mol dm^{-3}).[2]

Preparations of alcohol solutions and headspace GC measurements were made in the same manner as described in our previous paper.[5] The association constants were determined at 25.0±0.1 °C.

Results and Discussion

Assuming a 1:1 (alcohol/CA) complex, the association constant (K) was determined in the same way as described in a previous paper,[5]

$$A_0/A = 1 + K[\mathrm{CA}]. \quad (1)$$

In the case of [8], which has a larger cavity than that of the other PSCA's, a 2:1 (alcohol/CA) complex may be formed, as pointed out by Shinkai et al.[6] If this is correct, it seems reasonable under the experimental conditions that $[\mathrm{Alc}]_0$ is smaller than $[\mathrm{CA}]_0$ to use the overall formation constant (β_2) rather than a stepwise formation constant,

$$\mathrm{CA} + 2\mathrm{Alc} \rightleftharpoons \mathrm{CA \cdot Alc_2}. \quad (2)$$

In this case, we can calculate β_2 using the following equations:

$$[\mathrm{Alc}]_0 = [\mathrm{Alc}] + 2\beta_2[\mathrm{CA}][\mathrm{Alc}]^2 \quad (3)$$

and

$$[\mathrm{CA}] = [\mathrm{CA}]_0 - \{[\mathrm{Alc}]_0 - [\mathrm{Alc}]\}/2, \quad (4)$$

where [Alc] can be determined experimentally by the chromatogram peak area (A). Because the thus-calculated β_2 was found to vary with $[\mathrm{CA}]_0$, we eliminated the possibility of 2:1 complex formation.

Some examples of the experimental results are given in Table 1. For the alcohol–CA combinations studied in this work, good linear relationships were observed between A_0/A and [CA], from which we eliminated the possibility of 1:2 (alcohol/CA) complex formation. If such a complex formed, A_0/A vs. [CA] plots would show an upward-curve, as demonstrated in a previous paper.[7]

The least-squares method was applied to determine K. The results are summarized in Table 2. Although *n*-alcohols are fundamental organic nonelectrolytes, very little data have been reported so far about the association with water-soluble CA's. To the best of our knowledge, only ethanol has been studied for association with three different water-soluble CA's including PSC[4]A, the K value of which was reported to be 29.5 M^{-1} based on ^{1}H NMR measurements.[8] Although a direct comparison of this value with the present data is impossible, because our method is quite different in principle from that employed in the literature, the data of PSC[4]A listed in Table 2 seem to be in a reasonable range.

In order to see the dependence of the K values on the carbon number of *n*-alcohol, the data obtained in this work are plotted

Table 1. Some Examples of Experimental Results

$[\mathrm{CA}]_0/10^{-3}$ M	A_0/A	$[\mathrm{Alc}]/10^{-3}$ M	$[\mathrm{CA}]/10^{-3}$ M
1-Butanol–calix[4]arene, $[\mathrm{Alc}]_0 = 1.01 \times 10^{-2}$ M			
4.03	1.21	8.38	2.33
8.06	1.38	7.40	5.39
12.1	1.63	6.32	8.34
16.1	1.82	5.67	11.7
20.2	2.01	5.18	15.3
1-Pentanol–calix[6]arene, $[\mathrm{Alc}]_0 = 1.02 \times 10^{-2}$ M			
4.40	1.04	9.81	4.02
8.80	1.08	9.48	8.09
13.2	1.13	9.09	12.1
22.0	1.21	8.52	20.3
35.2	1.38	7.52	32.5

Table 2. Alcohol–*p*-sulfonato Calix[4, 6, and 8]arenes Association Constant at 25 °C

Alcohol	Type of PSCA	Association constant[a)]/M^{-1}	(Correlation coefficient)
1-Butanol	[4]	63±2	(0.997)
	[6]	0.7±0.1	(0.978)
	[8]	7.6±0.2	(0.998)
1-Pentanol	[4]	62±1	(0.999)
	[6]	12±1	(0.997)
	[8]	21±1	(0.999)
1-Hexanol	[4]	49±3	(0.991)
	[6]	14±1	(0.999)
	[8]	35±1	(0.998)
1-Heptanol	[4]	42±2	(0.998)
	[6]	20±1	(0.996)
	[8]	31±2	(0.994)
1-Octanol	[4]	41±1	(0.999)
	[6]	21±2	(0.991)
	[8]	32±3	(0.991)
1-Nonanol	[4]	38±7	(0.995)
	[6]	25±1	(0.995)
	[8]	32±2	(0.994)

a) The ± sign means the standard deviation at a confidence level of 95%.

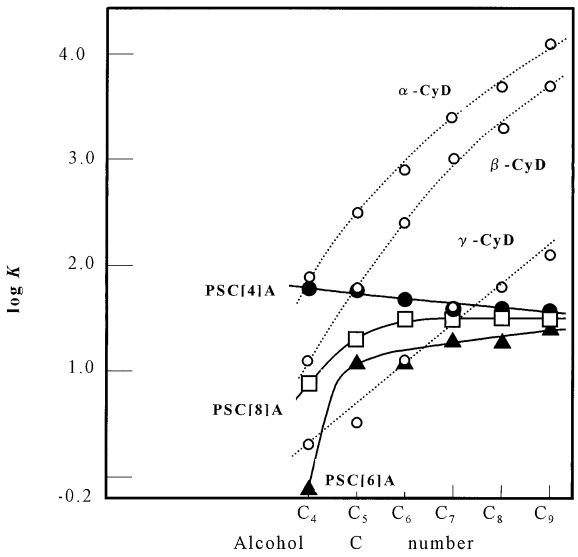

Fig. 1. Association constants as a function of alcohol carbon number for CyD (dotted) and for PSCA (solid).

in Fig. 1, where those for CyD[5] are also shown for a comparison. It can be seen from Fig. 1 that the PSCA's differ significantly from the CyD's in the *K* dependence on the guest carbon number. This is probably due to the difference in both the host-guest association mechanism and the cavity size (and shape) of the two host types.

In the case of CyD, the cavity is in a rather hydrophobic environment, and the hydrophobic interaction of a guest molecule inside the cavity plays an important role. On the other hand, it has been suggested that by using Phenol Blue as a polarity indicator, PSC[6]A provides an environment more polar than water.[9] The polar domain of this host originates from its OH groups; its SO_3^- groups not only contribute to the polarity, but also exhibit an electrostatic interaction with a positively charged part of a guest molecule.[9] The hydrophobicity of a water-soluble CA cavity is not so well established, perhaps because the cavity, itself, is not very clearly defined. The hydrophobic part of CA is a ring made up of benzene units meta linked by methylene bridges. The thickness of this ring is not very large and, hence, the depth of the cavity, itself, is small compared to the CyD cavity. Moreover, the cavity is rigid for CyD, while it is conformationally flexible for CA.

A recent NMR study indicates that ethanol is included into the PSC[4]A cavity with the alkyl residue pointing towards the cavity and the hydroxy group being exposed to the bulk of the water molecules.[8] This may also be the case for the present *n*-alcohol guests. The shallow cavity of PSC[4]A is probably responsible for the *K* value being almost independent of the alkyl chain length.

In accordance with the cavity size, *n*-alcohol with a cross-section diameter of 4.5 Å forms more stable complexes with β-CyD (cavity diameter, 6.9 Å) than γ-CyD (8.5 Å),[5] while this is not the case for PSCA's: the *K* value for [8] (cavity diameter,[10] 8.6 Å) is always larger than that for [6] (cavity diameter,[3] 7.6 Å) at the corresponding alcohol. This may arise from the CA cavity being flexible. In addition to the ring size, the ring flexibility seems to play an important role in the complex formation of CA's, as pointed out by Shinkai et al.[6] They also suggested that upon including positively charged guest molecules, the conformation of PSCA's is fixed to a "cone" through electrostatic interactions with sulfonate anions.[6] Such stabilization by electrostatic interactions cannot be expected for *n*-alcohol. The present work with nonelectrolyte guests provides an example to demonstrate the difference in the association mechanism between CyD and CA.

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