New Water-Soluble Calixarenes Bearing Sulphonate Groups on the 'Lower Rim': the Relation between Calixarene Shape and Binding Ability

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Association constants have been determined for pyrene as a guest molecule for 9 water-soluble calix[*n*]arenes (*n* = 4, 6, and 8) bearing sulphonate groups on the 'upper rim' (**1**) or on the 'lower rim' (**2**). The results have established that calixarene (**1**) has a strong but non-selective binding site whereas calixarene (**2**) has a relatively weak but selective binding site.

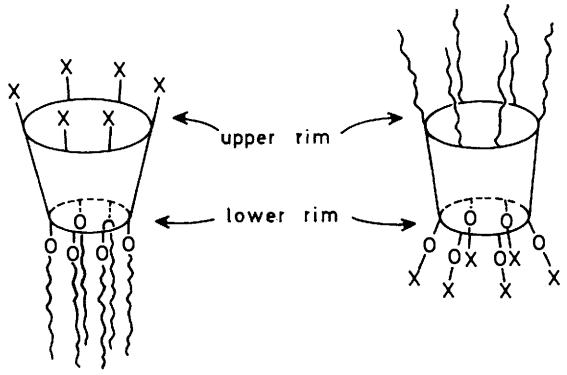
The 'calixarenes' are cyclic oligomers which are composed of benzene units (*cf.* cyclodextrins from glucose units). They would be expected, therefore, to be useful building-blocks in the design of functionalised host molecules and ultimately of synthetic enzyme mimics. Nevertheless, evidence supporting the formation of host-guest type complexes in solution was not found until a long time after the discovery of the calixarenes.[1,2] In order to find evidence for solution complexes, we previously synthesized water-soluble, *p*-sulphonated calixarenes (**1**) which have hydrophilic sulphonate groups on the 'upper rim' and hydrophobic alkyl groups on the 'lower rim' of the calixarene cavity.[3,4] We found for the first time that compound (**1**) can form host-guest type complexes with various organic guest molecules in water with the aid of a hydrophobic interaction.[3–6] However, the guest selectivity of the calixarene cavity is not well understood.[3–6] In order to investigate further this guest selectivity we synthesized compounds (**2**) which have hydrophilic sulphonate groups on the 'lower rim' and hydrophobic alkyl groups on the 'upper rim' of the calixarene cavity and we systematically estimated the potential relationships between the calixarene shape and binding ability. Compounds (**2**) were synthesized from propane-1,3-sultone and the corresponding *p*-alkylcalix[*n*]arene in tetrahydrofuran with NaH as base. The products were identified by i.r. and n.m.r. spectroscopy, and elemental analysis.

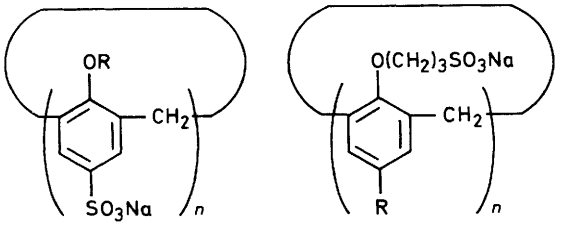
The purpose of the present study was related to molecular recognition. Thus the measurements performed must be below the c.m.c. (critical micelle concentration) of (**1**) and (**2**). The c.m.c.s determined by electric conductance[4] are summarised in Table 1. It is evident that (**1**; R = Me, *n* = 6) does not form the micellar aggregate but other water-soluble calixarenes have a c.m.c. at 0.40—2.5 mmol dm^{-3}. We thus carried out measurements in a concentration range (10^{-6}—10^{-5} mol dm^{-3}) much lower than the c.m.c. We used pyrene as a guest molecule because the fluorescence intensity of the first band (382 nm; excitation wavelength 310 nm) decreased markedly with increasing calixarene concentration, owing to the quenching effect of the calixarene π-system. The stoicheiometry estimated

Table 1. Critical micelle concentrations (c.m.c.s) of (**1**) and (**2**) at 30 °C

	C.m.c./mmol dm^{-3}		
Calixarene	n = 4	6	8
(**1**; R = Me)	—	*a*	—
(**1**; R = Bu)	2.5	1.0	0.70
(**1**; R = Hex)	—	0.67	—
(**2**; R = Bu^t)	0.55	0.58	0.40
(**2**; R = Bu)	—	0.43	—

[a] The c.m.c. was not detected up to 20 mmol dm^{-3}.





(**1**) (**2**)

by the molar ratio method suggested that both (**1**) and (**2**) formed 1:1 complexes with pyrene. This view was also supported by the absence of excimer emission (480 nm region) characteristic of dimeric pyrene. The K values were determined by a nonlinear least-squares computation of I/I_0 (relative fluorescence intensity) *vs* concentration of (**1**) or (**2**) (Table 2).

Examination of Table 2 reveals several new relationships between the calixarene shape and binding ability. (*a*) The K values in the calixarene (**1**) series increase dramatically (× 326) on moving from R = Me to R = Bu but increase no further on moving from R = Bu to R = Hex. Examination of Corey-Pauling-Koltun (C.P.K.) molecular models suggests that the cavity size of calix[6]arene exactly fits the molecular size of pyrene but is not enough to fully enclose the molecule. In order to fully enclose a pyrene molecule in the calixarene cavity, additional alkyl groups which serve as a hydrophobic lid must be incorporated into the calixarene entity. The results indicate

Table 2. Association constants (K) for aqueous solutions of pyrene at 30 °C[a]

	K (dm^3 mol^{-1} × 10^{-5})		
Calixarene	n = 4	6	8
(**1**; R = Me)	—	0.12	—
(**1**; R = Bu)	35.4	39.1	55.7
(**1**; R = Hex)	—	23.1	—
(**2**; R = Bu^t)	6.2	41.1	3.7
(**2**; R = Bu)	—	6.3	—

[a] Excitation 310 nm, emission 382 nm, [pyrene] = 1.02 × 10^{-6} mol dm^{-3}.

that the attachment of butyl groups sufficiently extends the cavity to allow the binding of pyrene. (*b*) Calixarenes (**1**) with alkyl groups on the 'lower rim' have K values which are greater than those for calixarenes (**2**) which have alkyl groups on the 'upper rim'. Since the 'lower rim' is the closed side of the calixarene cavity, incorporated alkyl groups are able to serve co-operatively as a binding site. In contrast, alkyl groups incorporated onto the 'upper rim' (opened side) are so distant that co-operative action as a binding site would be rather difficult. This difference in cavity shape should be reflected in the binding ability. Thirdly, and most importantly, (**2**; R = Bu^t, n = 6) in the (**2**; R = Bu^t) series shows a significant selectivity towards pyrene whereas the (**1**; R = Bu) series shows no such selectivity, the K values increasing with increasing ring size. This suggests that the butyl groups in (**1**; R = Bu) can serve co-operatively as a binding site, so that the K values increase simply with the number of butyl groups. In contrast, the K values for (**2**; R = Bu^t) reflect the cavity size: according to C.P.K. models pyrene is too large for (**2**; R = Bu^t, n = 4), too small for (**2**; R = Bu^t, n = 8) but exactly fits (**2**; R = Bu^t, n = 6). This implies that the selectivity rule based on ring size is effective in the extended cavity constructed by *para*-substitution.

In conclusion, the present study has established that the incorporation of alkyl groups into the 'lower rim' results in a strong but non-selective binding site, whereas incorporation of alkyl groups into the 'upper rim' results in a relatively weak but selective binding site. This conclusion contributes strongly to the molecular design of new functionalised calixarenes which could be used eventually as potential recognition sites in synthetic enzyme mimics.

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Received 18*th January* 1989; *Paper* 9/00301K