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A Reversed-phase HPLC Study of the Complexation of Benzene Derivatives Guest Molecules with 5,17-bis(*N*-Tolyliminomethyl)-25,27-dipropoxycalix[4]arene in Acetonitrile–Water Solution†

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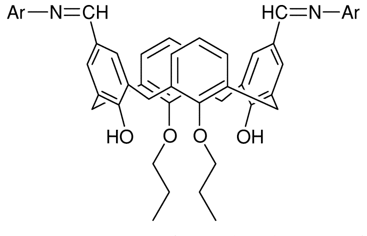
Stability constants of the host–guest complexes of 5,17-bis(*N*-tolyliminomethyl)-25,27-dipropoxycalix[4]arene with benzene derivatives were determined by reversed-phase HPLC in acetonitrile–water solution.

Calixarenes, owing to their bowl-like shape, have been widely investigated in the last decade.[1–4] The ability of calixarene derivatives to form host–guest inclusion complexes with organic molecules is one of their most striking features.[3–5] One promising application of this is the development of calixarene-based chemical sensors.[6–12] One important stage in designing such sensors consists of estimating the stability constants of the calixarene complexes with trapped molecules. The stability constants have until now mainly been determined by NMR.[13,14] Recently,[15,16] we have developed a convenient reversed-phase high-performance liquid chromatography (RP HPLC) method for determining stability constants of calixarene inclusion complexes with aromatic molecules in solution. Some phosphorus-containing calixarene and calixresorcinarene host molecules were investigated by this method.

In this work we used the RP HPLC method for determination of stability constants of 5,17-bis(*N*-tolyliminomethyl)-25,27-dipropoxycalix[4]arene (C[4]A) complexes with a number of benzene derivative pollutants.



According to NMR and molecular mechanics,[17] the C[4]A molecule exists in the stereochemically rigid cone conformation suitable for inclusion of aromatic guest molecules into the cavity formed by the four upwardly oriented aromatic rings of the macrocyclic skeleton. Benzene, alkylbenzenes and halogenated benzenes were investigated as guest molecules (Table 1).

The chromatographic method developed for stability constant determination is based on the relationship between the guest capacity factors and the concentration of the macrocyclic host in the mobile phase. Addition of C[4]A to a mobile acetonitrile–water phase decreases retention time of the aromatic solutes due to formation of host-guest inclusion complexes. The linear relationship of the solute's capacity factors k' *vs.* the C[4]A concentration confirms formation of a 1:1 stoichiometry of the host–guest complexes in the concentration range investigated. For 1:1 stoichiometry eqn. (1)[18] can be used to calculate the stability constants K_A:

$$1/k' = 1/k'_0 + [\mathrm{CA}]\, K_A\, k'_0 \qquad (1)$$

In eqn. (1) k'_0 and k' are capacity factors in the absence and presence of the C[4]A in the mobile phase, [CA] is the host concentration in the mobile phase. The chromatographic peak of the C[4]A injected after the saturation of the column (see the Experimental) possesses high symmetry (the asymmetry coefficient is 1.1) as additional experiment showed. The column plate number after saturation did not depend on the C[4]A concentration. In these conditions sorption of C[4]A on the stationary phase may be neglected and [CA] is similar to the original concentrations indicated in the Experimental and Table 1. The stability constants K_A determined from eqn. (1) are summarized in Table 1. The constants are in the range 69–728 $\mathrm{dm^3\,mol^{-1}}$ depending on the nature, quantity and position of the substituents in the benzene rings. The lowest K_A parameters are observed for the chlorinated benzenes. The introduction of one or two chlorine atoms in the benzene molecule decreases K_A from 116 to 69–78 $\mathrm{dm^3\,mol^{-1}}$. In contrast, the introduction of methyl groups, nitro groups and bromine atoms increases the host–guest interaction. The highest association constants 674 and 728 $\mathrm{dm^3\,mol^{-1}}$ are found for *ortho-* and *meta-*dibromobenzenes, respectively.

A similar increase of the association constants influenced by the insertion of a bromine atom into an aromatic guest molecule was observed for complexes of α-cyclodextrin with butyrophenone derivatives.[19] For example, spectrophotometric investigation of the complexation in water showed that the replacement of a Cl atom in the *para*-chlorobutyrophenone guest molecule ($K_A = 72\ \mathrm{dm\,mol^{-1}}$) by a Br atom leads to a tenfold increase in K_A (K_A for *para*-bromobutyrophenone is 760 $\mathrm{dm^3\,mol^{-1}}$).

The complexing ability of calixarenes is caused by weak non-covalent bonds, *i.e.* coulombic, dipole–dipole forces, CH-π, solvatophobic interactions *etc.* between host and guest molecules. The influence of these forces on the complexation process is rather complicated. The determination of the dependence of K_A on the nature of guest substituents needs additional investigation.

Experimental

All sample compounds were of the best quality available and were purchased from various suppliers. C[4]A was prepared by the method described previously.[17] The mobile phase was an acetonitrile–water (86:14 v/v) solution and the solution contained C[4]A concentrations of 3×10^{-4}, 4.5×10^{-4} and 5.8×10^{-4} M. Sample solutes were prepared so as to give a concentration of

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Table 1 Capacity factors of the guests before (k'_0) and after (k') calixarene addition in the mobile phase, and the host–guest stability constants K_A

		k'_0	k'			
		Calixarene concentration in mobile phase/M				
Entry	Guest	0	3×10^{-4}	4.5×10^{-4}	5.8×10^{-4}	K_A/dm^3 mol^{-1} (RSD, %)
1	*o*-Dichlorobenzene	1.51	1.48	1.47	1.45	69 (8.03)
2	Chlorobenzene	1.51	1.48	1.47	1.46	75 (7.85)
3	*p*-Dichlorobenzene	1.51	1.48	1.46	1.45	78 (8.23)
4	Benzene	1.0	0.97	0.95	0.93	116 (16.75)
5	*m*-Dinitrobenzene	0.90	0.85	0.83	0.81	198 (5.50)
6	2,6-Dimethylnitrobenzene	1.12	1.0	0.97	0.94	362 (9.21)
7	*p*-Xylene	1.05	0.91	0.86	0.80	519 (5.99)
8	Toluene	1.26	1.09	1.04	1.0	524 (7.27)
9	*m*-Xylene	1.74	1.50	1.41	1.35	545 (6.42)
10	*o*-Dibromobenzene	1.98	1.61	1.52	1.43	675 (6.53)
11	*m*-Dibromobenzene	2.28	1.86	1.72	1.62	728 (3.85)

1×10^{-5} M for each guest. Each sample was analysed five times. Retention times of the solutes were determined after 7 h elution in a C[4]A saturated column. The capacity factor of C[4]A was 0.89. The dead time was measured with $NaNO_2$.

For liquid chromatography a Type 333 HPLC unit (Institute of Physical Chemistry, Polish Academy of Sciences, Warsaw, Poland) equipped with a 10^{-4} ml cell was used. The column (250 × 1 mm I.D.) was packed with LiChrosorb RP 18 (Merck, Germany), with UV detection at λ 254 nm. The flow rate was 0.04 ml min^{-1}. All measurements were performed at 21 °C.

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