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Catalytic Effect of Reverse Micelles of a Cationic Surfactant on the Reaction of Calix[4]resorcinolarenes with 4-Nitrophenyl Bis(chloromethyl)phosphinate

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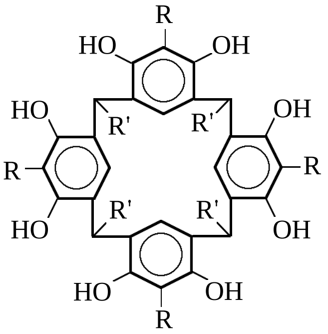
Abstract—The presence of the aminomethyl fragment in the calix[4]resorcinolarene molecule favors its phosphorylation in chloroform. Reverse micelles of (2- hydroxyethyl)dimethylpentadecylammonium bromide catalyze this reaction, the catalytic effect being dependent on the length of the hydrocarbon chain of a calixarene and detergent concentration.

Micellar systems are precursors of higher-order colloid systems, e.g., liquid crystals, playing an important role in functioning of biomembranes [1]. The use of micellar systems, particularly reverse, is one of the ways to control the route and rate of chemical reactions. Studies in the field of micellar catalysis in nonaqueous media are important for organic synthesis [2, 3] and enzymatic catalysis [4].

Reverse micellar catalysis of nucleophilic substitution in four-coordinate phosphorus acid esters was studied for reactions involving amines [5, 6], OH ions [7], water [8], *o*-(aminomethyl)phenols [9, 10], and ethanolamine [11]. Previously [12] we studied the effect of reverse micelles of alkyl(2-hydroxyethyl)dimethylammonium bromides (Alk = C_nH_{2n+1}, n = 12, 15, 18) in chloroform on phosphorylation of aminomethylated calix[4]resorcinolarene. It was demonstrated that aggregates of the surfactants used catalyze phosphorylation, the catalytic efficiency being dependent on the hydrophobicity of a detergent. Another result of the solubilization of reactants by micellar aggregates is change in the micelle-forming properties of 2-hydroxyethyl surfactants [12]. At the same time, the questions of the effect of the calixarene structure on the catalytic reaction and also of the possibility of self-association of calixarenes in nonaqueous media remain to be understood.

In this work we studied the reaction of 4-nitrophenyl bis(chloromethyl)phosphinate **I** with aminomethylated calix[4]resorcinolarenes **II**–**V** and compound **VI** in chloroform in the presence and absence of the micelle-forming cationic surfactant (2-hydroxyethyl)dimethylpentadecylammonium bromide **VII**.



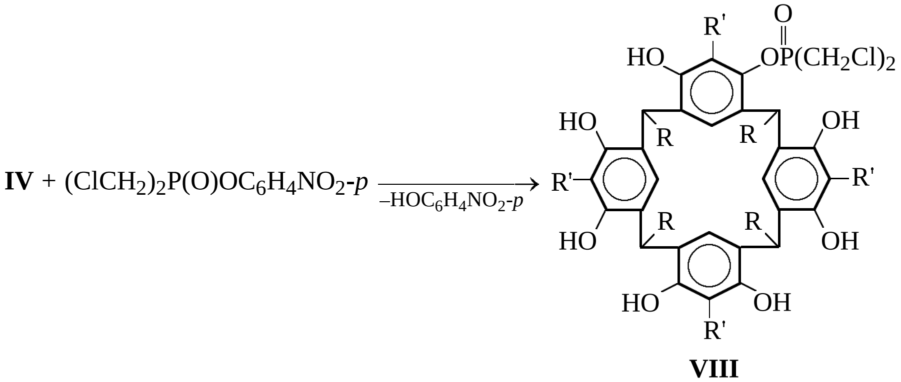
II–**VI**

R = CH_2NMe_2, R' = C_mH_{2m+1}, m = 1 (**II**), 6 (**III**), 9 (**IV**), 11 (**V**); R = H, R' = C_9H_{19} (**VI**).

The micelle-forming properties of **VII** were described in [12]. At 20°C, the critical micelle concentration (CMC) of **VII** in the presence and absence of calixarene **IV** ($c = 5\times10^{-4}$ M) was found to be 2×10^{-3}–4×10^{-3} M.

Calixarenes **III**–**V** were studied by the dielcometric titration method [12] to estimate their tendency to self-association in chloroform. Figure 1 shows the concentration dependences of the dielectric constant ε of chloroform solutions of calixarenes **III**–**V**. At a concentration of 1×10^{-4} M (compound **III**) and 1.2×10^{-4} M (compounds **IV** and **V**), we observed inflections in the ε curves, which, according to [12], can be attributed to association of calixarenes.

The appearance of the absorption band of 4-nitrophenol (322–334 nm) in the UV spectra, observed in the course of the reaction of calixarenes **II**–**V** and **VI** with phosphinate **I**, suggests formation of calix[4]resorcinolarene phosphorylated at the hydroxy groups. In particular, for calixarene **IV**, under pseudomonomolecular conditions, i.e., at a considerably lower concentration of substrate **I** (δ_P 39.5 ppm) compared to the nucleophile, the reaction produces compound **VIII** (δ_P 38.4 ppm).



VIII

R = C_9H_{19}, R' = CH_2NMe_2.

It was interesting to estimate the effect of the aminomethyl fragment on the reactivity of calixarenes. It is known that the presence of the aminomethyl group in the molecule of *o*-(aminomethyl)phenols favors phenolysis by virtue of intramolecular hydrogen bonding and enhanced nucleophilicity of the reactive center [9, 13]. The formation of an intramolecular hydrogen bond in calixarene **IV** was confirmed by the UV and IR data. In the UV spectrum of aminomethylated calixarene **IV** in chloroform, we observed the absorption band at 291.5 nm. Compound **VI** shows the adsorption at 286.5 nm. In the presence of an amine (cetylamine), capable of forming an intermolecular hydrogen bond with the OH group of **VI**, this band shifts toward lower frequencies (292 nm), i.e., it takes practically the same position as in **IV**, which may be attributed to the formation of an intramolecular hydrogen bond in **IV** between the nitrogen atoms of the aminomethyl groups and the phenolic OH groups. Furthermore, we observed partial transfer of the proton from the OH group to the nitrogen atom with formation of the zwitterionic form of the calixarene, as demonstrated by the OH absorption band at 3250 cm^{-1} and a broad diffuse band at 2500–2750 cm^{-1} typical of quaternary ammonium salts [14].

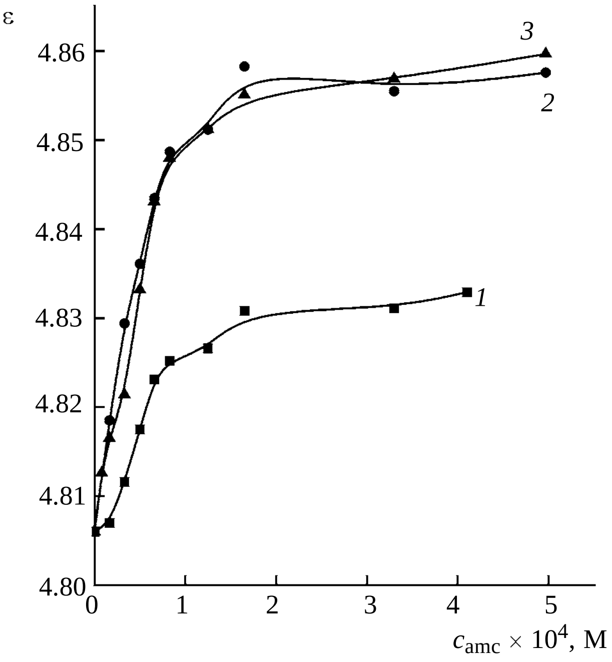


Fig. 1. Dielectric constant ε of calixarene solutions in chloroform as a function of their concentration c_{amc} at 20°C: (*1*) **III**, (*2*) **IV**, and (*3*) **V**.

Table 1 shows that the aminomethyl fragment involved in intramolecular hydrogen bonding in the molecules of **II**–**IV** favors phosphorylation. The rate constant *k* of the reaction of phosphinate **I** with calixarene **IV** is considerably higher than that of the reactions with calixarene **VI** containing no aminomethyl fragment. Formation of an intermolecular bond between the OH group of calixarene **VI** and the hydrogen atom of *N*,*N*-dimethylbenzylamine **IX** during the reaction of substrate **I** with **VI** in the presence of amine **IX** (**VI** : **IX** = 1 : 4 by moles) has a less favorable effect (Table 1).

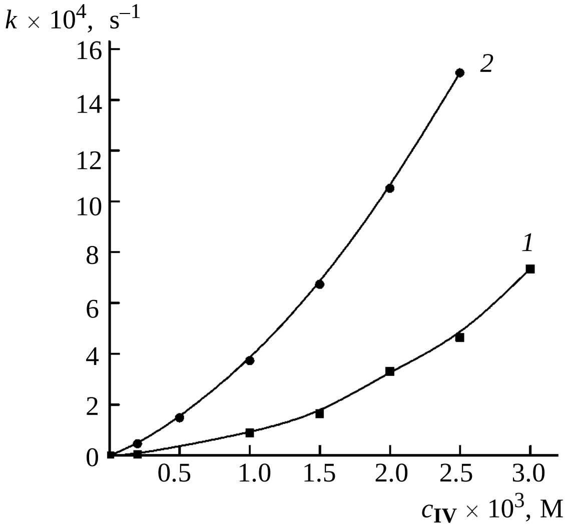


Fig. 2. Apparent rate constant *k* of the reaction of phosphinate **I** with calixarene **IV** in chloroform at 50°C (*1*) in the presence and (*2*) in the absence of surfactant **VII** (*c* 0.05 M) as a function of the calixarene concentration.

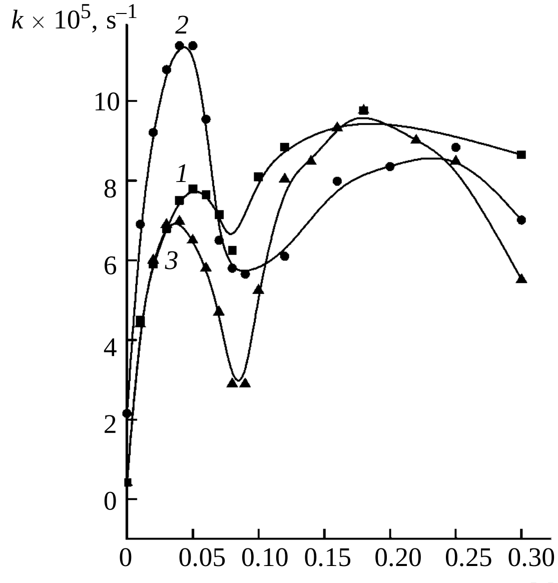


Fig. 3. Apparent rate constant *k* of the reaction of phosphinate **I** with calixarenes (*1*) **II**, (*2*) **III**, and (*3*) **IV** as a function of the (2-hydroxyethyl)dimethylpentadecylammonium bromide (**VII**) concentration in chloroform (50°C; c_{Nu} 0.0002 M).

The dependence of the apparent rate constant of phosphorylation on the concentration of the aminomethylated calixarene (Fig. 2) is described by a second-order equation.

$$k = k_{1,0}c_{Nu} + k_{2,0}c^2_{Nu}.$$

For the reaction of phosphinate **I** with calixarene **IV**, we obtained $k_{1,0}$ = 0.016 l mol^{-1} s^{-1} and $k_{2,0}$ = 73 l^2 mol^{-2} s^{-1} (50°C). Note that a second-order kinetics is typical of nucleophilic substitution in four-coordinate phosphorus acid esters in nonaqueous media [15]. This is associated with the reaction catalysis by the second molecule of a nucleophilic agent [5, 15, 16]. In this case, unlike aqueous-organic solutions [17], self-association of the calix[4]resorcinolarenes studied in chloroform has no influence on the form of the kinetic equation (Fig. 2). The reaction considerably accelerates in micellar solutions of **VII** (Figs. 2, 3), but the concentration dependence of the apparent rate constant (Fig. 2) remains to be second-order (subscript SAC denotes surfactant).

$$k_{2,SAC}c_{Nu} + k_{2,SAC}c^2_{Nu}.$$

Here, for the reaction of calixarene **IV** with 0.05 M surfactant **VII**, we obtained $k_{1,SAC}$ = 0.22 l mol^{-1} s^{-1} and $k_{2,SAC}$ = 153 l^2 mol^{-2} s^{-1} (50°C).

In the dependences of the rate constants of phosphorylation of **II**–**IV** on the concentration of surfactant **VII**, we observed two maxima (Fig. 3). The first maximum may be a result of dilution of solubilized reactants as the amount of micellar aggregates in the solution increases [18]. The second maximum is probably due to structural reorganization of the micellar aggregates. Presumably, the effect of structural transformation of the micelles on the chemical reaction dominates at high surfactant concentrations, resulting in the appearance of the second maximum.

In the range near the first maximum, the concentra-

Table 1. Apparent rate constants of the reactions of calixarenes **VI** and **IV** with phosphinate **I** (*c* 10^{-4} M) in chloroform at 0°C

Comp. no.	c_{Nu}, M	k, s^{-1}	k_{Nu}/k_{VI}
VI	0.001	1.8×10^{-6}	1
	0.002	4.8×10^{-6}	1
IV	0.001	9×10^{-5}	50
	0.002	3.2×10^{-4}	67
VI + **IX**	0.001[a]	1.6×10^{-5}	9
	0.002[b]	2.5×10^{-5}	5

[a] c_{IX} = 0.004 M. [b] c_{IX} = 0.008 M.

Table 2. Parameters of micelle-catalyzed reaction of phosphinate **I** with calixarenes **II**–**IV** in the presence of surfactant **VII** in chloroform at 50°C[a]

Comp. no.	K_S, l mol^{-1}	K_{Nu}, l mol^{-1}	k_{2m}, l mol^{-1} min^{-1}	*CMC*, M	$(k_a/k_0)_{max}$[b]	F_m	F_c	F_mF_c
II	124	5.3	1.9	0.011	19	1.5	12	18
III	286	5.3	2.5	0.012	5.3	0.4	14	5.4
IV[c]	471	4.8	1.6	0.009	17	1.3	13	17

[a] Concentration of calixarenes **II**–**IV** 0.0002 M. [b] (k_a) Maximal apparent pseudo-first-order rate constant of the reaction in micellar solutions of the surfactant and (k_0) pseudo-first-order rate constant in the absence of surfactant. [c] Data from [12].

tion dependences are described by the equation corresponding to the pseudophase model of micellar catalysis [19].

$$k = \frac{k_{2,0} + (k_{2,m}/V)K_S K_{Nu} c_{SAC}}{(1 + K_S c_{SAC})(1 + K_{Nu} c_{SAC})},$$

where $k_{2,0}$ and $k_{2,m}$ are the second-order rate constants in the solvent and micellar pseudophase, respectively; K_S and K_{Nu}, constants of association of the substrate and nucleophile with micellar aggregates; V is the molar volume of the surfactant; and c_{SAC}, its concentration less the critical micelle concentration. The results of data processing by this equation are given in Table 2. Lengthening of the hydrocarbon radical in calixarenes **II**–**IV** results in increase in the constant of association of the nucleophile and in the reaction rate constant in the micellar phase. It is known that the effect of micellar catalysis is a resultant of integral contribution of factors controlling the microenvironment around the solubilized reactants (F_m),

$$F_m = k_{2,m}/k_{2,0},$$

and the effect of concentration of the reactants in the micellar phase (F_c) [19].

$$F_c = \frac{K_S K_{Nu}}{V[(K_S)^{1/2} + (K_{Nu})^{1/2}]^2}.$$

The experimental maximal catalytic effect in micellar solutions is equal to the product of these two factors (Table 2), concentration of the reactants in micelles being the crucial factor. For calixarenes **II** and **IV**, the microenvironmental factor is slightly above unity, also favoring the process. Only in the case of calixarene **III** $F_m < 1$, and the maximal catalytic effect for this compound is lower than that for calixarenes **II** and **IV** (Table 2).

Finally, the results obtained show that phosphorylation of calix[4]resorcinolarenes in a nonaqueous weakly polar medium can be accelerated by more than an order of magnitude, if the reaction is performed in a micellar solution of a cationic surfactant. In this case, the catalytic effect depends on the hydrophobicity of a calixarene, approaching considerable values even at low surfactant concentrations.

EXPERIMENTAL

4-Nitrophenyl bis(chloromethyl)phosphinate **I** and calixarenes **II**–**VI** were synthesized according to the procedures described in [15, 20, 21]. (2-Hydroxyethyl)dimethylpentdecylammonium chloride was obtained by quaternization of 2-(dimethylamino)-ethanol with pentadecyl bromide [22]. *N*,*N*-Dimethylbenzylamine was distilled prior to use. Chloroform was purified using standard procedure [23].

The reaction kinetics (pseudo-first-order approximation) was monitored spectrophotometrically (Specord UV-Vis) by the increase in the optical density at 322–334 nm (absorption band of 4-nitrophenol).

Infrared spectra were registered on an IR-75 spectrometer. The ^{31}P NMR spectra were registered on a Bruker MSL-400 instrument (162 MHz). The chemical shifts were determined against H_3PO_4 as an external reference.

Dielcometric titration was carried out according to the procedure described in [24]. The dielectric permittivities of a series of solutions were determined using an E12-I dielectric spectrometer of the beat frequency type and a measuring cell representing a temperature-controlled capacitor [25].

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