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Supramolecular Catalytic Systems for Decomposition of Toxic Esters of Acids of Phosphorus*

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Abstract

Efficient nanocontainers based on noncovalent electrostatic complexes, such as sulfonated calix(4)resorcinol – cationic surfactants (CR–CS) with regulated solubilization and catalytic activity, were developed. Mono-, di-, and tetra-quaternized derivatives of 1,4-diazabicyclo(2.2.2)octane were used as CS. Reaction kinetics for hydrolysis of esters of acids of phosphorus, namely, 4-nitrophenyl-O-ethyl chloromethyl phosphonate, in the presence of CR–CS mixed compositions was studied by UV spectroscopy method during the variation in the number of cationic centres of CS and addition of a hydrophobic dye (Orange OT). Reaction parameters (the specific reaction rate in the micellar phase, substrate binding constant with aggregates, and the critical micelle concentration) attest to the fact that CR – mono-cationic surfactant system has the maximum catalytic activity.

Keywords: supramolecular catalysis, calix(4)resorcinol, cationic surfactant, 1,4-diazabicyclo(2.2.2)octane, esters of acids of phosphorus, critical micelle concentration

INTRODUCTION

Supramolecular systems find applications in a broad range of areas: new materials, techniques, diagnosis and treatment procedures, catalysts, drugs, cosmetic products, etc. [1–4]. Perimolecular structures containing macrocyclic receptors, such as cyclodextrins [5, 6], cucurbiturils [7, 8], and calixarenes [9, 10] are of special interest.

Macrocycles may take part in guest – host interactions [11, 12] due to the presence of a molecular cavity and preorganization of functional groups, which is extremely crucial

in terms of creating biomimetic systems. Macrocyclic platform geometry allows using them as drug delivery systems [13–15]. The production of efficient nano-reactors to decompose organophosphorus ecotoxicants becomes possible through covalent immobilization of calixarenes onto a mineral substrate [16]. Efficient polyfunctional catalytic systems to cleave carboxylic and phosphonic acid esters [17] and the Suzuki cross-coupling reaction [18] have been created *via* variation of the structure of amphiphiles and the nature of solvents and various additives.

Sulphonated calix[n]arenes have a number of advantages [19] among various macrocycles, in particular: high water solubility and biocompatibility [20], the ability to selectively bind

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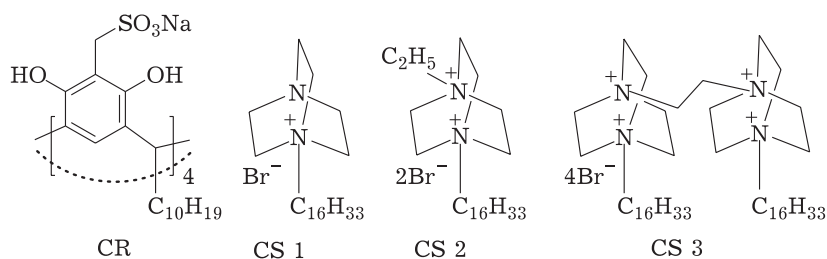


Fig. 1. Structure of sulphonated calix[4]resorcinol (CR), mono- (CS 1), di- (CS 2), and tetracationic (CS 3) surfactants.

biological [21–24] and medicinal [25–27] substances.

The goal of the present work was the development of supramolecular systems based on sulphonated calix[4]resorcinol (CR) and cationic surfactants (CS 1–3) that act as efficient nano-reactors to cleave organophosphorus substrates (Fig. 1). It is known that esters of acids of phosphorus are acetylcholinesterase inhibitors and poisoning agents [28, 29], therefore the issue of their detoxication is of relevance.

To develop nanocontainers with improved solubilization properties and catalytic activity, non-covalent CR–CS complexes were studied with the variation of the structure of CS (the number of charged ammonium fragments) were studied. The interest to the selected research objects is driven by their properties (catalytic, solubilization, and biological activity [30, 31]), that exceed those of traditional CS. Furthermore, the toxicity of CS 1 is less compared to that of a classical CS (cetyltrimethylammonium bromide) [32]. The use of CS with a varying number of cationic centres in a composition with calixarene containing four anionic fragments would contribute to the optimization of system composition and properties. Non-covalent (electrostatic) CR–CS complexes are able to form nanoassemblies with improved solubilization properties in relation to organic guests, while decomposition process of esters of acids of phosphorus may be monitored by changing external conditions and varying building blocks of amphiphilic nature.

EXPERIMENTAL

The interaction of 1,4-diazabicyclo[2.2.2]octane with hexadecyl bromide yielded CS 1 (hexadecyl mono-quaternized derivative of 1,4-diazabicyclo[2.2.2]octane). Synthesis of CS

2 (hexadecyl bis-quaternized derivative of 1,4-diazabicyclo[2.2.2]octane) was carried out by quaternization of CS 1 with ethyl bromide and 2-bromoethanol, respectively [31]. Paper [33] gives details of synthesis of CS 3 (hexadecyl tetra-quaternized derivative of 1,4-diazabicyclo[2.2.2]octane). Synthesis of O-4-nitrophenyl-O-ethyl chloromethyl phosphonate (NECP) was performed according to the procedure described in [34, 35]. The reaction kinetics was explored *via* the spectrophotometric method according to an increase in the optical density of adsorption of 4-nitrophenolate anion near 400 nm in thermostated cuvettes using a spectrophotometer. The observed reaction rate constants (k_o , s⁻¹) were determined according to a first order equation:

$$\lg(D_\infty - D_t) = -0.434k_o t + \text{const} \quad (1)$$

where D_∞ and D_t are the optical densities at reaction completion and at time t , respectively.

The concentration of NECP in the beginning of the reaction was $(5 \cdot 10^{-5}) - (1 \cdot 10^{-4})$ mol/L.

Parameters of the process catalysed by micelles were found according to the equation of the pseudo-phase model of micellar catalysis [36, 37]:

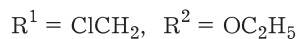
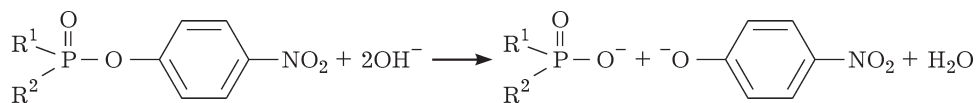
$$k_o = \frac{k_m K_s (C_{CS} - CCM) + k_0}{1 + K_s (C_{CS} - CCM)} \quad (2)$$

where k_m and k_0 are first order reaction rate constants in the micellar phase and in the solvent mass, respectively; K_s is the binding constant of the substrate to the micelles, L/mol; CCM is critical concentration of micelle formation.

To prepare the solutions under study, water treated using Direct-Q 5 UV system (Millipore S.A.S. 67120 Molsheim-France) was used.

RESULTS AND DISCUSSION

The reaction kinetics in the presence of the systems under study was explored on an



Scheme 1.

example of NECP hydrolysis. Scheme 1 gives a reaction mechanism.

Figure 2 presents the observed rate constant of NECP hydrolysis (k_o) vs the concentration of KS for mixed CR-CS systems. All of the have a linear profile, which attests to binding of NECP and a nucleophile (OH^-) by a micellar nucleus of mixed CR-CS aggregates [33] similarly to the formation of enzyme-substrate complexes in biocatalysis.

Quantitative parameters of a micellar catalysed process were determined by equation (2) within the pseudo-phase model of micellar catalysis. As demonstrated by calculations, CR-CS 1 system has the maximum catalytic effect ($k_m/k_o \sim 3$). There is the maximum binding constant ($K_S = 9500 \text{ L/mol}$) in case of CR-CS 3 system. However, the latter has the minimum effect ($k_m/k_o \sim 1.1$).

As a rule, low catalytic activity in the presence of micellar systems is driven by micro-surroundings of reagents (substrate and nucleophile). However, in this case, a decrease in catalytic activity at the transition from CR-CS 1 to CR-CS 3 is probably explained by the low binding constant of a nucleophile (OH^-). In the case of mixed CR-CS 3 composition containing four ammonium fragment and calixarene with four anion fragments due to electrostatic interactions, a stable non-covalent

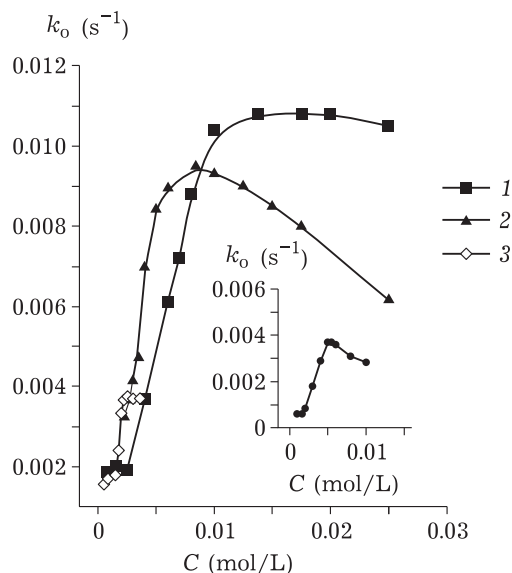


Fig. 2. Dependencies of the observed rate constant (k_o) of hydrolysis of O-4-nitrophenyl-O-ethylchloromethylphosphonate (NECP) in solutions of CR-CS 1 (1), CR-CS 2 (2), and CR-CS 3 (3) on CS concentration; inset: CR-CS 1 system in the presence of Orange OT dye; $C_{\text{CR}} = 0.0005 \text{ mol/L}$, $C_{\text{NaOH}} = 0.001 \text{ mol/L}$, 25°C .

complex is generated. Charge compensation right up to a change in its sign for CR-CS 3 system [33] occurs, which may lead to electrostatic repulsion of a nucleophile (OH^-) during the reaction and as a result, to a decrease in the catalytic activity of non-covalent CR-CS complex.

TABLE 1

Parameters of alkaline hydrolysis of NECP in the presence of mixed CR-CS systems and Orange OT dye ($C_{\text{NaOH}} = 0.001 \text{ mol/L}$, 25°C)

System	k_m, s^{-1}	$K_S, \text{L/mol}$	$\text{CCM} \cdot 10^3, \text{mol/L}$	k_m/k_o^{**}
CR-CS 1	0.01220	620	5.4	3.0
CR-CS 1*	0.00750	220	2.3	1.9
CR-CS 2	0.01020	1840	3.5	2.6
CR-CS 3	0.00415	9500	1.6	1.1

* In the presence of a dye (Orange OT).

** k_o is the observed rate constant of aqueous hydrolysis of O-4-nitrophenyl-O-ethylchloromethylphosphonate (NECP).

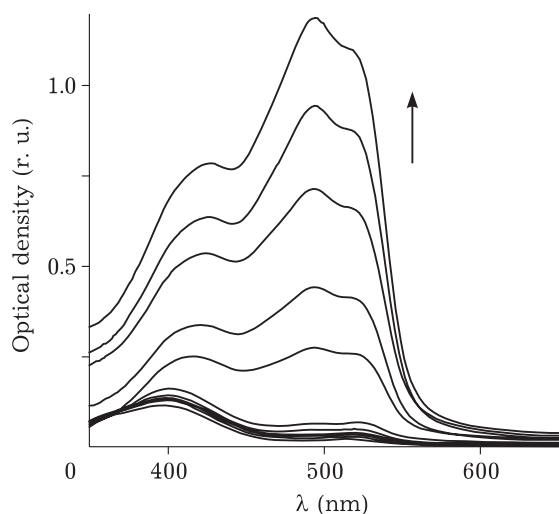


Fig. 3. Absorption spectra of Orange OT dye in CR-CS 1 solutions with increasing concentrations of CS 1 in the presence of reaction products of NECP hydrolysis (0.0001 mol/L, $C_{CR} = 0.0005$ M, $C_{NaOH} = 0.001$ mol/L, $L = 0.1$ cm, 25 °C).

An approach with the involvement of competitive guests that are able to bind with CR-CS nanoassembly and displace reagents (substrate and/or nucleophile) was tested as an alternative procedure to regulate the catalytic activity of CR-CS system. The study of NECP hydrolysis occurred in the presence of hydrophobic Orange OT dye (see Fig. 2, inset). Table 1 gives parameters of a micellar catalysed reaction. Catalytic effect and substrate binding constant with micelles for CR-CS 1 system are 1.5 and 3 time lower, respectively than in its absence, as established. Most likely, in the used approach (competitive dye and substrate binding), NECP substrate is displaced from a micelle and consequently, the studied reaction rate is reduced.

Figures 3 and 4 present the study results of the solubilization ability of CR-CS 1 system in relation to a hydrophobic Orange OT dye and the effect on it of reaction products of hydrolysis of NECP – *para*-nitrophenolate ion ($\lambda = 400$ nm) and O-ethyl chloromethylphosphonic acid. It can be seen (see Fig. 3) that the optical density of adsorption of Orange OT ($\lambda = 495$ nm) with a concentration of KS 1 above CCM increases, which attests to dye solubilization by micellar CR-CS 1 assembly. There is the absorption band shift of *para*-nitrophenolate ion in the 400 nm range.

The data regarding a change in the density

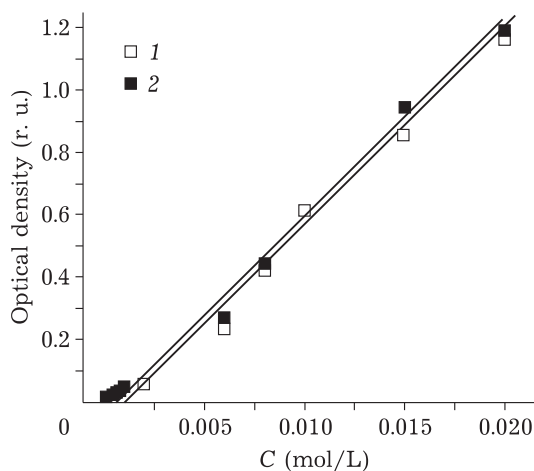


Fig. 4. Optical density of absorbing Orange OT dye in aqueous solutions of CR-CS 1 in the absence (1) and the presence (2) of reaction products of NECP hydrolysis versus the concentration of CS 1 ($C_{CR} = 0.0005$ mol/L, $\lambda = 495$ nm, $L = 0.1$ cm, 25 °C).

of adsorption of Orange OT with variation in the concentration of CR-CS 1 in the presence and absence of reaction products (see Fig. 4) attest to the fact that the presence of reaction products in a solution does not affect the solubilization ability of CR-CS 1 aggregates.

CONCLUSION

Thus, supramolecular systems based on sulphonated calix[4]resorcinol, cationic surfactants (hexadecyl mono-, di- and tetra- quaternized derivatives of 1,4-diazabicyclo(2.2.2) octane) and Orange OT dye are catalysts for O-4-nitrophenyl-O-ethyl chloromethyl phosphonate. The catalytic efficiency depends on mixed composition content and cationic surfactant structure, as established. An increase in the number of charged ammonium fragments in cationic surfactant structure and the presence of a competitive guest that is hydrophobic orange dye leads to a decrease in a catalytic effect by 3 and 1.5 times, respectively.

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