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Reactivity of Supramolecular Systems Based on Calix[4]resorcinarene Derivatives and Surfactants in Hydrolysis of Phosphorus Acid Esters

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Summary: The formation of mixed micelles of amphiphilic calix[4]resorcinarenes with aminomethyl (AMC, PAMC), tris(hydroxymethyl)amide (THAC) fragments and the cationic surfactant cetyl trimethylammonium bromide (CTAB) in water and aqueous DMF solutions (10-50 % DMF) leads to the decrease of the critical micelle concentration of the systems and the increase of the size of the mixed micelles in comparison with CTAB micelles. The catalytic activity of the mixed systems in the hydrolysis of phosphorus acid esters is higher than those of CTAB micelle and AMC, PAMC or THAC aggregates.

Keywords: amphiphilic calix[4]resorcinarene; critical micelle concentration; kinetics; micelle formation; mixed micelle; surfactant

Introduction

Micelle formation in mixtures of surfactants is of considerable interest from both fundamental and practical points of view. The behavior of such mixtures, in particular, the catalytic activity is quite different from that of the individual surfactants. Recently the approaches to the syntheses of functionalized amphiphilic compounds are intensivly developed[1,2]. Calix[4]resorcinarenes or resorcarenes (CRA) attracted much attention as cyclooligomes with a stronge inherent amphiphilicity[3,4]. Two feathers are essential for any amphiphilic compounds: the adsorption at the interface and the aggregation in solution. The amphiphilicity of resorcarenes was used for the formation of organized mono- and multi-layers at the air-water interface or on solid surface[3,4]. However, the aggregation of calix[4]resorcinarenes and their derivatives in the solutions and the effect of the nature of surfactants on the aggregate behavior, the properties and the reactivity of calix[4]resorcinarenes has been insufficiently studied until now[5,6].

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The aim of this work was to study the micellization in mixed systems based on different calix[4]resorcinarenes (CRA) **1-6** and the cationic surfactant cetyltrimethylammonium bromide (CTAB) in water and aqueous DMF solutions, as well as the study of catalytic activity of mixed micellar systems on the base of these compounds in the hydrolysis of 4-nitrophenyl bis(chloromethyl)phosphinate (NBCP) **7** (Scheme 1). The previously obtained results reveal that aggregates of amphiphilic resorcarenes strongly bind phosphorus acid esters and exhibit high hydrolytic activity at low concentrations of resorcarenes[7,8].

We investigated the aggregation behavior and the reactivity of amphiphilic derivatives of resorcarene with different polar head groups. Two types of resorcarene were included for the investigation. First are resorcarene derivatives with aminomethyl (AMC **1, 2**) or tris(hydroxymethyl)amide (THAC **5, 6**) fragments as hydrophilic groups and long alkyl chain as hydrophobic group. Second are resorcarenes with four strong polar alkylphosphonic acid (PAMC **3,4**) fragments instead of hydrophobic tails of AMC. These are compounds without a clear separation between hydrophilic and hydrophobic parts.

Experimental

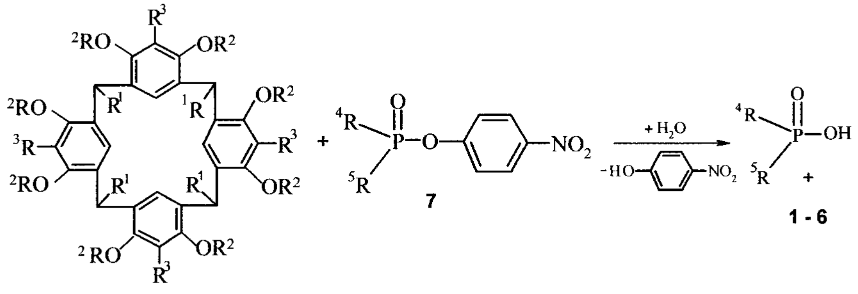
AMC, PAMC were synthesized according to literature[9,10]. THAC **5, 6** were obtained from the corresponding derivatives of resorcarene [11] and tris(hydroxymethyl)aminomethan. The structures of compounds **1-6** were proved by means of FTIR, NMR ^{1}H, ^{13}C, ^{31}P spectroscopy and MALDI TOF mass spectroscopy. The aggregation of the compounds was explored by surface tension (σ) and conductivity (χ) measurements. The size of aggregates and mixed micelles was estimated by the NMR FT-PGSE method. The conformation of resorcarenes and the intra- and intermolecular interactions were studied by ROESY NMR. The experiments were carried out in water and water/DMF solutions in presence and in absence of the cationic surfactant CTAB. The kinetics of the reactions was studied by spectrophotometry from the increase in optical density due to the formation of p-nitrophenolate (λ 400 nm) and ^{31}P NMR measurements under pseudo-first order conditions at 30 °C. The quantitative treatment of the experimental kinetic data (the observed rate constant for hydrolysis, k_{obs}) in terms of a pseudo-phase model of micellar catalysis permitted to characterize on the known equation [12] the reactivity of compounds in a micellar microenvironment (the rate constant in micellar phase, k_m), to estimate the binding efficiency of reagents with micelles (the constant of binding of substrate by the aggregates, K_b) and to evaluate the critical micelle concentration (CMC). As AMC are practically water-insoluble, these compounds were studied in aqueous DMF solutions. THAC and PAMC are very readily soluble in aqueous solutions.

Results and discussion

It was found, that AMC **1**, **2** and PAMC **3**, **4** are surfactants in a water-DMF and aqueous solutions. The CMC values of PAMC **3** and **4** are practically the same. Table 1 presents the CMC values of studied compounds. The aggregation behavior of THAC **5**, **6** surprisingly differs from those of AMC **1**, **2** and PAMC **3**, **4**. THAC **5** and **6** are not surface active at least at $1\cdot10^{-2}$ mol·l^{-1} in water and aqueous media containing 10% of DMF or 30 % of DMSO as far as surface tensions are concerned (Figure 1). Nevertheless an indication of their amphiphilic nature comes from their broadened ^{1}H NMR signals in D_2O.

Indeed combined evidence from NMR FTPGSE method and molecular simulation by HYPERCHEM indicates that THACs form small micelle-like nanoparticles in water. Molecular simulation has shown that the maximum intramolecular distance between protons of THAC **5** molecule in 1,3-alternate conformation equals 28 Å. The study of aggregate formation of THAC **5** by NMR FTPGSE method reveals that the effective hydrodynamic diameter of kinetic particles in water are 66 Å and 77 Å at the concentration of THAC $1\cdot10^{-3}$ and $5\cdot10^{-3}$ mol·l^{-1}, correspondingly. Taking into account the molecule size of THAC these values of diameters of kinetic particles mean that in warer THAC **5** forms the small aggregates, which are composed of 3-4 molecules of THAC.

Scheme 1. Hydrolysis of 4-nitropheny bis(chloromethyl)phosphinate in the presence of various resorcarenes.



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AMC -**1**: R^1= C_9H_{19}; R^2= H; R^3= $CH_2N(CH_3)_2$; **2**: R^1= $C_{11}H_{23}$; R^2= H; R^3= $CH_2N(C_2H_5)_2$
PAMC- **3**: R^1= $CH_2P(O)(OH)(OC_3H_7)$; R^2= H; R^3= $CH_2N(C_2H_5)_2$; **4**: R^1= $CH_2P(O)(OH)(OC_4H_9)$; R^2= H; R^3= $CH_2N(C_2H_5)_2$
THAC- **5**:R^1= C_8H_{17}; R^2= $CH_2C(O)NHC(CH_2OH)_3$; R^3= H ; **6**: R^1= $C_{11}H_{23}$; R^2= $CH_2C(O)NHC(CH_2OH)_3$; R^3= H
NBCP- **7**: R^4= R^5= $ClCH_2$

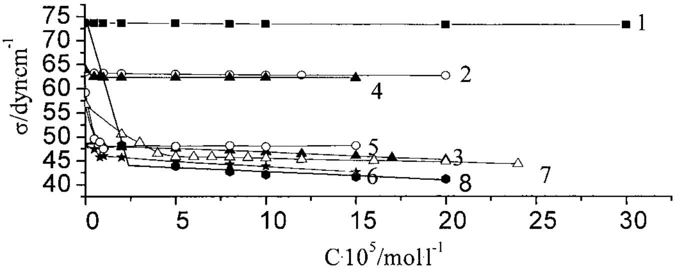

Figure 1. Surface tension of aqueous solutions of CRA as a function of their concentration; reaction conditions: *T* = 30 °C, medium: 1 = THAC **5**, **6** -water, 2 = THAC **5**-10 % DMF, 3 = THAC **5**-30% DMF, 4 = THAC **5**-30% DMSO, 5 = THAC **5** -50 % DMSO, **6** - 30% 1,4-dioxan, 7 = AMC **1**-30% DMF, 8 = PAMC **4**-water.

Recently it was shown[13,14] that analogous resorcarenes having four long alkyl chains ($R^1=C_{11}H_{23}$) and eight saccharide moieties are surface inactive in water. Nevertheless these compounds form unusual stable and essentially irreversible small micelle-like nanoparticals in the solvent. That is, perhaps, aggregates of THAC are irreversible small micelle-like nanoparticals too. THACs nanoparticles shows no surface activity even in concentration $1 \cdot 10^{-2}$ mol·l^{-1} indicating that there is no equilibrium dissociation of an aggregate into monomers in water and in aqueous media containing 10% of DMF or 30 % of DMSO.

However, THAC are the micelle forming surfactants in the solutions with the higher concentration of organic solvent, for example 30% of DMF and 1,4-dioxan or 50 % of DMSO (Figure 1).

Table 1. CMC values (mol×l^{-1}) of CTAB, AMC **1**, PAMC **3, 4** and mixtures of CRA with CTAB in water and in aqueous DMF solutions.

Content of DMF in v. %	CMC/mol×l^{-1}					
	CTAB	AMC **1**	PAMC **3,4**	AMC**1**-CTAB	PAMC **3,4**-CTAB	THAC **5**-CTAB
0	8×10^{-4}	_	2×10^{-5} 1×10^{-4}	_	$^a2\times10^{-4}$, $^b8\times10^{-4}$	$^a2\times10^{-5}$, $^b5\times10^{-5}$, $^c3\times10^{-4}$, $^d1\times10^{-3}$
30	7×10^{-3}	$5 \cdot 10^{-5}$	2×10^{-5} 1×10^{-4}	$^a1\times10^{-4}$ $^d3\times10^{-3}$	7×10^{-4}	$^a2\times10^{-5}$, $^c6\times10^{-4}$, $^d1\times10^{-3}$
50	6×10^{-3}	$7 \cdot 10^{-5}$	6×10^{-4}	3×10^{-4}	8×10^{-4}	-

^{a}CMC-1, ^{b}CMC-2, ^{c}CMC-3, ^{d}CMC-4 based on data of figure 2 for PAMC **3** and THAC **5**.

The study of aggregate formation of THAC **5** by NMR FTPGSE method in aqueous DMF (30 vol.% of DMF) allowed us to determine the effective hydrodynamic diameter of kinetic particles in the solutions, wich are 47 Å. Obviously, such organic solvents as DMF or DMSO cause the micelle transition leading to the decrease of micelle size and the appearance of equilibrium dissociation of a aggregate into monomers, that is surface activity of THAC.

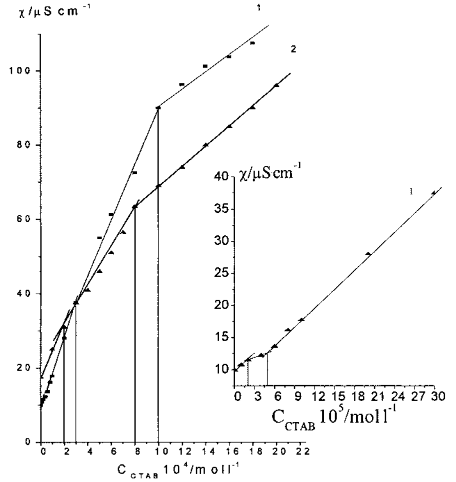

Figure 2. Specific conductance of aqueous CTAB solutions as a function of CTAB concentration in presence of THAC **5** (1) and PAMC **3** (2); reaction conditions: T = 30 °C , C_{THAC} = 2×10^{-5} ; C_{PAMC} =1×10^{-4} mol×l^{-1}. Insert: Specific conductance of aqueous CTAB solutions as a function of CTAB concentration in presence of THAC **5** (1); reaction conditions: T = 30 °C, C_{THAC} = 2×10^{-5} mol×l^{-1}.

Thus, it was determined that all studied amphiphilic resocarenes are micelle forming amphiphiles and surfactants in the water-DMF solutions. PAMC are the micelle forming amphiphiles and the surfactants in water and aqueous DMF solutions. Micellization of macrocyclic resocarene surfactants is characterized by CMC values, which are less than conventional surfactant such as CTAB (Table 1).

The study of self-organization of resorcarenes **1-6** in the presence of CTAB confirms the formation of mixed micelles based on these compounds. The mixed aggregate formation is accompanied by the change of CMC values of the individual systems (Table 1). Another confirmation of the formation of mixed aggregates is the peculiarity of the aggregation behavior of mixtures observed at different ratios of components.

Figure 2 shows the availability of several transition points corresponding to the CMC values summarized in Table 1. The interaction of resocarenes with CTAB yields mixed aggregates of variable composition depending on the molar ratio of components. The first CMC points (CMC-1) appear at the ratio resorcarene: CTAB in region from 1:1 to 1:5 depending on the nature of resorcarene, in particular, 1:1 for THAC and 1:5 for AMC. The increase of concentration of CTAB leads to the formation of larger aggregates (CMC-2).

Thus, resorcarene forms aggregates with a monomeric form or cations of CTAB (CMC-1, CMC-2), if the surfactant is in deficiency. The increase of concentration of CTAB leads to a penetration of resorcarenes into the CTAB micelles at the ratios of resorcarene: CTAB approximately from 1:10 to 1:50 (CMC-3, CMC-4). Such aggregation behavior of mixed systems indicates a gradual formation of CRA-CTAB mixed aggregates.

The kinetic study of the reaction of 4-nitrophenyl bis(chloromethyl)phosphinate (NBCP) **7** with CRA was carried out in the absence and in the presence of the surfactant CTAB (Table 2).

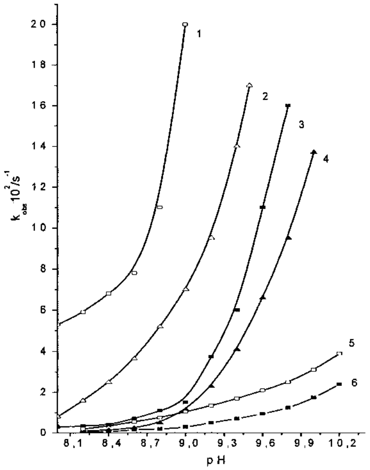

Figure 3. Observed rate constants of the reaction (k_{obs}) of 7 with THAC **5** and PAMC **4** as a function of pH in water and in aqueous DMF (30% vol. of DMF) solution in absence and in presence CTAB; reaction conditions: T = 30 °C, C_{PAMC}= 6×10^{-4} mol×l^{-1}, C_{THAC}= 4×10^{-4} mol×l^{-1}, C_{CTAB}= 5×10^{-3}, medium: 1 = PAMC-CTAB-water, 2 = THAC-CTAB-water, 3 = PAMC-water, 4 = THAC-water, 5 = THAC-CTAB-DMF-water, 6 = THAC-DMF-water.

The kinetic study in depending of pH has shown that the reactivity of water-soluble PAMC and THAC is slightly different in neutral or weak basic aqueous solutions (Figure 3). In theory the reactivity of PAMC have to be higher then THAC due to presence of strong nucleophilic phenoxyl and amino groups, but in reality is lower. Furthermore, mixed system PAMC **4**/CTAB/DMF/water differs from those based on AMC **2** by less efficiency of substrate binding and the less catalytic activity (Table 2). Apparently, the some functional groups of PAMC take part on the self-organization or a mixed aggregate formation. This leads to decreases the reactivity of PAMC aggregates and their mixed micelles. The presence of DMF decreases the reactivity of both water-soluble resorcarenes, but aggregates of THAC are more sensitive to addition of DMF (Figure 4 and Figure 5).

The unusual stable or irreversible assemblies of THAC have a higher substrate binding efficiency compared with both AMC and PAMC. The study of intermolecular interaction between THAC and p-nitrophenol by ROESY NMR revealed the very strong interaction between aromatic protons of p-nitrophenol and methylene groups of alkyl chains of THAC.

Table 2. Parameters of the reaction of substrate **7** with AMC **2**, THAC **5**, PAMC **4**, and CTAB in water and aqueous DMF solution (30% vol. of DMF).

It clearly confirms the formation of a stable substrate-micelle complex. The formation of mixed aggregates is accompanied by a sharp increase in the catalytic activity of the systems, a decrease in their critical micelle concentration in comparison with the CTAB micelles and a shift of reactivity from weak basic to neutral pH of the reaction mixture (Figure 3-5, Table 2). Mixed micelles of THAC are characterized by the low CMC value, a high substrate binding efficiency and a high reactivity in hydrolysis of PAE in weak basic media (Table 2). By analogy with resorcinarene aggregates the reactivity of mixed micelles decreases in presence of DMF. This process occurs very sharply in a case of mixed micelles of THAC (Figure 5).

Table 2.

Systems	CMC/mol$\times$l^{-1}	K_b/l$\times$mol^{-1}	k_m/s^{-1}	pH
AMC **2**-CTAB-DMF-water $C_{CTAB}=5\times10^{-3}$ mol$\times$l^{-1}	2×10^{-4}	1700	6.7×10^{-2}	8
AMC **2**-CTAB-DMF-water $C_{CTAB}=1\times10^{-2}$ mol$\times$l^{-1}	2×10^{-4}	1745	1.5×10^{-1}	8
THAC **5**-DMF-water	3.6×10^{-4}	4600	1.2×10^{-2}	9,2
THAC **5**-CTAB-DMF-water, $C_{CTAB}=5\times10^{-3}$ mol$\times$l^{-1}	2.7×10^{-4}	4000	2.4×10^{-2}	9,2
THAC **5**-water	1×10^{-4}	4500	3.4×10^{-2}	9,2
THAC **5**-CTAB-water, $C_{CTAB}=5\times10^{-3}$ mol$\times$l^{-1}	1×10^{-5}	6000	2.1×10^{-1}	9,2
PAMC **4**-water	3×10^{-4}	2500	3.2×10^{-2}	9.0
PAMC **4**-DMF-water	6×10^{-4}	1300	2.2×10^{-2}	9.0
PAMC **4**-DMF(50%)-water	5×10^{-4}	2400	4.2×10^{-3}	9.0
PAMC **4**-CTAB-water $C_{PAMC}=4\times\cdot10^{-4}$ mol$\times$l^{-1}	8×10^{-4}	420	3.6×10^{-2}	8.0
PAMC **4**-CTAB-DMF-water $C_{PAMC}=4\times10^{-4}$ mol$\times\cdot$l^{-1}	1.5×10^{-3}	90	1.3×10^{-2}	8.0
CTAB-DMF-water	6×10^{-3}	100	1×10^{-2}	8.0

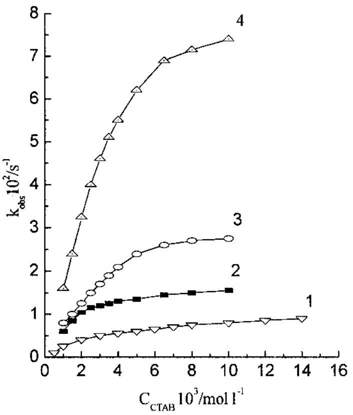

Figure 4. Observed rate constants of the reaction (k_{obs}) of 7 with PAMC **4** in water (2-4) and in aqueous DMF solution (1) (30% vol. of DMF) as a function of CTAB concentration; reaction conditions: T = 30 °C, pH = 8, 1 = C_{PAMC} = 4×10^{-4} mol$\times$l^{-1}, 2 = C_{PAMC} = 2×10^{-4} mol$\times$l^{-1}, 3 = C_{PAMC} = 4×10^{-4} mol$\times$l^{-1}, 4 = C_{PAMC} = 6×10^{-4} mol$\times$l^{-1}.

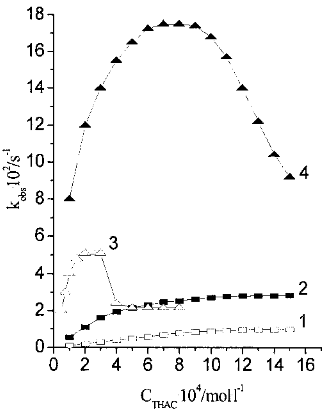

Figure 5. Observed rate constants of the reaction (k_{obs}) of 7 with THAC **5** as a function of THAC concentration in water (2-4) and aqueous DMF solution (1) (30% vol. of DMF) in absence (1, 2) and in presence of CTAB; reaction conditions: T = 30 °C, pH= 9.2, 3 = C_{CTAB} = 1×10^{-3} mol$\times$l^{-1} , 4 = C_{CTAB} = 5×10^{-3} mol$\times$l^{-1}.

Conclusion

1. Self-organization of amphiphilic derivatives of resorcarenes leads to the formation of surface inactive in water irreversible micelle-like nanoparticals, to surface-active aggregates in water and water-organic media and to the formation of mixed aggregates in water-surfactant and in water-organic-surfactant systems. Micellization of the macrocyclic calixarene surfactants is characterized by CMC values, which are less than those of amphiphilic phenols and conventional surfactants such as CTAB. The mixed aggregate formation is accompanied by a decrease of CMC values of CTAB and an increase of the micelles size.
2. The resorcarene aggregates and mixed micelles based on these compounds and CTAB are the catalytic systems, which provide a specific microenvironment for substrate binding and subsequent hydrolysis of phosphorus esters in water and water-DMF media. The formation of mixed aggregates is accompanied by a sharp increase in the catalytic activity of the systems, a decrease in their critical micelle concentration compared with the CTAB micelles.

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