The influence of the structure of ethyl aryl chloromethylphosphonates on the catalytic effect of direct and reverse micellar systems

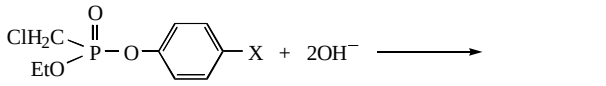
Lucia Ya. Zakharova,* Raissa A. Shagidullina, Farida G. Valeeva and Lyudmila A. Kudryavtseva

A. E. Arbuzov Institute of Organic and Physical Chemistry, Kazan Scientific Centre, Russian Academy of Sciences, 420088 Kazan, Russian Federation. Fax: +7 8432 75 2253; e-mail: vos@iopc.kcn.ru

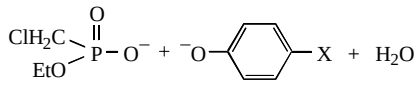
The reactivity of ethyl aryl chloromethylphosphonates in the basic hydrolysis reactions in direct micelles of cetyltrimethylammonium bromide depends on both electronic and hydrophobic properties of the substituent in the aryl group, while in the sodium dodecyl sulfate–hexanol–water micellar system it depends only on the electronic nature.

Organised media such as micelles, microemulsions and liquid crystals are considered as biomimetic systems acting *via* the host–guest mechanism.[1] One of the most important features of biocatalysts is their substrate specificity, *i.e.*, their high selectivity both in respect to the compounds of different functional classes and within homologous series.[2] It is of interest to study the influence of the substrate structure on the catalytic effect of direct and reverse micelles in order to elucidate the catalytic mechanism of confined systems in polar and nonpolar media and to evaluate the contribution of noncovalent interactions to micellar catalysis.

In this study, the kinetics of the basic hydrolysis of ethyl aryl chloromethylphosphonates **1**–**7** in direct micelles of cetyltrimethylammonium bromide (CTAB) and in the sodium dodecylsulfate (SDS)–hexanol–water reverse micellar system has been investigated (Scheme 1). Substrates **1**–**7** were prepared according to the previously reported procedure.[3] The surfactants CTAB and SDS of 'pure' grade were twice recrystallised from ethanol. Micellar solutions were prepared by mixing ingredients in appropriate proportions and shaking vigorously until a transparent solution was obtained.[4] The reaction was carried out under pseudo-first-order conditions and monitored by observing the absorption of leaving group anions using a Specord M-400 spectrophotometer equipped with temperature-controlled cell holders.



1–**7**



1 X = NO_2 **5** X = Bu
2 X = Br **6** X = *n*-octyl
3 X = H **7** X = *i*-dodecyl
4 X = Et

Scheme 1

The reaction in water with no surfactant added. In the series of substrates **1**–**3**, a marked decrease in the reactivity occurs because of weakening the electron-seeking effect of the substituent X, resulting in destabilization of the leaving group. In the series of **3**–**7**, a smoother decrease in the reactivity is observed because of an increase in the positive inductive effect with increasing alkyl chain length.[5]

The reaction in CTAB direct micelles. In the CTAB micellar solutions, the reaction rate increases by a factor of about 25 as compared with the reaction in water. This increase results from the electrostatic attraction of hydroxide ions to positively charged CTAB micelles (Figure 1). The observed rate constant (k_{obs}) decreases with decreasing electronegativity of X in the series of **1**–**3**. The tendency in the reactivity change in the series of substrates **3**–**7** is opposite to that in water, namely, the highest k_{obs} value is observed for **6** (X = *n*-octyl), and the lowest one, for **3** and **4** (X = H and Et, respectively). The substituent effect on the reactivity in CTAB micelles decreases in the following order: NO_2 > Br > *n*-octyl > *i*-dodecyl > *n*-hexyl > Bu ~ Et ~ H.

The kinetic data were treated in terms of a pseudophase model using the equation:[6]

$$k_{obs} = \frac{k_{2,w} + k_{2,m}K_S K_{OH} C/V}{(1 + K_S C)(1 + K_{OH} C)}, \quad (1)$$

where $k_{2,w}$ and $k_{2,m}$ ($dm^3\ mol^{-1}\ s^{-1}$) are the second-order rate constants in the aqueous and micellar phases, respectively; K_S and K_{OH} ($dm^3\ mol^{-1}$) are the substrate and nucleophile binding constants, respectively; V is the molar volume of the surfactant, assumed to be equal to 0.3 $dm^3\ mol^{-1}$; C is the CTAB concentration minus the critical micelle concentration (cmc).

The approach developed by Berezin makes it possible to differentiate the factors responsible for the micellar rate effects expressed as $(k_{obs}/k_w)_{max}$ using the equation

$$(k_{obs}/k_w)_{max} = \frac{k_{2,m}}{k_{2,w}} \frac{K_S K_{OH}}{V(K_S^{1/2} + K_{OH}^{1/2})^2}, \quad (2)$$

where k_w is the pseudo-first-order rate constant of the reaction in water.

The first term in the right side of equation (2) is associated with the influence of the micellar microenvironment (F_m) and the second term reflects concentrating the reagents in micelles (F_c). Table 1 demonstrates that the main reason for the acceleration of the reaction is an increase in local concentrations of the reagents in the CTAB micelles. The concentration factor (F_c) increases with alkyl chain length of X and varies in the range 150–640. This means that an acceleration by two orders of magnitude can be observed if the micellar microenvironment favours the reaction. However, a dramatic decrease in the reactivity with transferring the reaction from water to a micellar pseudophase ($F_m < 1$) results in the reduction of the micellar rate effect by a factor of 6–25.

The reaction in the SDS reverse micellar system. In accordance with the pseudophase approach, there are three pseudophases

Table 1 Kinetic data (Figure 1) treated in terms of equation (1).

Substrate	$k_{2,w}$/$dm^3\ mol^{-1}\ s^{-1}$	$(k_{obs}/k_w)_{max}$	K_S/$dm^3\ mol^{-1}$	K_{OH}/$dm^3\ mol^{-1}$	$k_{2,m}$/$dm^3\ mol^{-1}\ s^{-1}$	F_c	F_m	F_cF_m
1	4.0	7.5	1775	240	0.055	432	0.014	6
2	0.55	5.5	945	135	0.016	240	0.028	6.3
3	0.24	5	400	90	0.01	144	0.042	6
4	0.19	7	800	75	0.0098	146	0.053	7.7
5	0.16	9	1675	87	0.0082	190	0.051	9.8
6	0.12	22	2350	350	0.0043	604	0.037	22.5
7	0.08	24	1490	470	0.0031	640	0.039	24.9

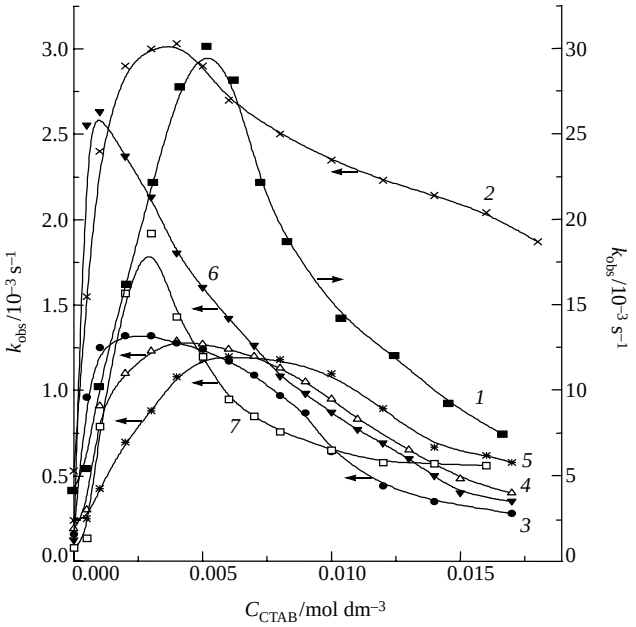


Figure 1 The observed rate constants of basic hydrolysis of **1**–**7** in CTAB micellar solutions as functions of the surfactant concentration (0.001 M NaOH, 25 °C). The curve numbers correspond to those of the substrates in Scheme 1.

in reverse micelles (water pool formed with incased water surrounded by a surfactant monolayer with polar head groups turned into the micellar interior and hydrophobic tails at the exterior in contact with oil).[7] It is believed that the reaction of a hydrophobic substrate with a hydrophilic nucleophile occurs at the interface where the hydrophilic microenvironment favours the solubilization of both reagents. The kinetics of the reaction was measured at the molar ratios $W = [H_2O]/[SDS]$ and $Z =$ = [hexanol]/[SDS] varied within the limits 9.8–37 and 5–22, respectively. The kinetic data are shown in Figures 2–4. Note that depending on the substrate structure and experimental conditions (surfactant, NaOH and water concentrations) either catalysis or inhibition of the reaction can be observed, as compared with the reaction in water. As can be seen in Figures 2 and 3, in the series of substrates **1**–**4** a marked reduction in the reactivity occurs. The highest acceleration factors for these substrates are 30, 14, 4 and 2, respectively. An increase in the alkyl-chain length in the series of **4**–**7** does not

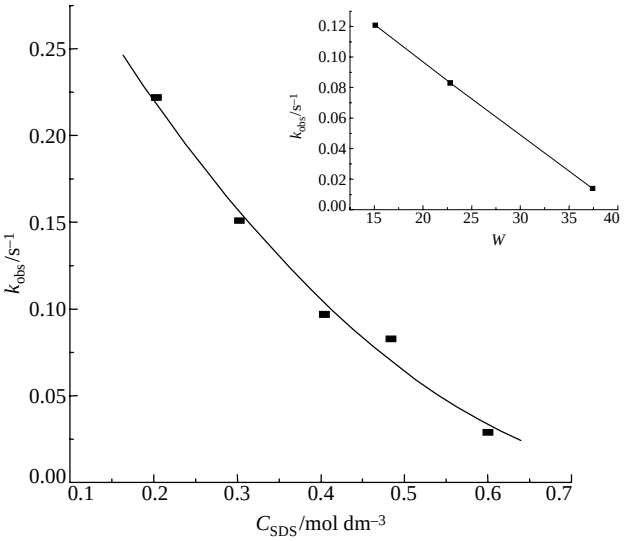


Figure 2 The observed rate constants of basic hydrolysis of **1** in the SDS reverse micellar system as function of the surfactant concentration (W = 22.8, 0.002 M NaOH, 25 °C). Insert: the dependence of the observed rate constant of basic hydrolysis of **1** in the SDS reverse micellar system on the water content.

Table 2 Kinetic data (Figure 3) treated in terms of the pseudophase model.[a]

Substrate	P_S	P_{OH}	k_i/s^{-1}	$k^b_{2,i}$/ dm^3 mol^{-1}	$k_{2,w}$/dm^3 mol^{-1}	$k_{2,i}/k_{2,w}$
2	100	7	5.40	2.00	0.55	3.6
3	80	2.2	1.90	0.70	0.24	2.9
4	80	40	0.15	0.05	0.20	0.26
5	70	9.4	0.3	0.11	0.16	0.69
6	90	90	0.14	0.05	0.12	0.42
7	60	40	0.14	0.05	0.08	0.62

[a]Kinetics of the basic hydrolysis of **1** in 0.002 M NaOH is inconsistent with equation (3) (see ref. 11). [b]In order to calculate $k_{2,i}$, the micellar molar volume V was assumed to be equal to 0.37 dm^3 mol^{-1}.[8]

affect k_{obs}. Thus, in the SDS-based reverse micellar system, a decrease in the electron-seeking effect of X results in a marked lowering of k_{obs}, while an increase in the hydrophobicity exerts no effect. In general, the reactivity in the SDS reverse micellar system decreases in the following order: NO_2 > Br > H > Et ~ ~ Bu ~ *n*-octyl ~ *i*-dodecyl. The observed rate constants decrease with surfactant concentration and, for **1**–**3**, with water content. An analogous tendency was observed in earlier studies for the reactions occurring at the interface.[8,9] It is of interest that, in the case of substrates **4**–**7**, k_{obs} was found to be independent of W (Figure 4).

The kinetic data were treated in terms of the pseudophase model by analogy with ref. 9. For a reaction occurring at the interface, in the case when one of the reactants is distributed between an aqueous pseudophase and a surface layer, and the other reactant is distributed between an oil pseudophase and the surface layer, k_{obs} is expressed as follows:[8]

$$k_{obs} = \frac{k_i P_S P_{OH}[OH]_r}{(P_S + Z)(P_{OH} + W)[SDS]}, \quad (3)$$

where k_i can be expressed in terms of the pseudo-first-order rate constant k'_i and the molar ratio between the nucleophile at the interface and the [SDS], $k'_i = k_i[OH]/[SDS]$; P_S and P_{OH} are the partition coefficients of the substrate and the nucleophile. The model was detailed earlier.[10]

Table 2 demonstrates that the partition constants P_S of the substrates are almost unaffected by the substrate hydrophobicity. Note that, for substrates **2** and **3**, $k_{2,i}/k_{2,w} > 1$, *i.e.*, the micellar microenvironment exerts a favourable influence on the reaction rate, while for substrates **4**–**7**, the above ratio is less than 1, thus indicating an unfavourable effect on the reactivity of the reaction transfer from water to the interface. Apparently, in this reaction series, high sensitivity to the microenvironment of reagents is observed so that even a slight change in the local polarity or orientation can result in the transition from catalysis to inhibition.

Thus, we found that in the direct micelles of CTAB catalysis of the test reaction was observed. The main factor contributing to the micellar rate effect is concentrating reagents in micelles, while the micellar microenvironment exerts a negative effect

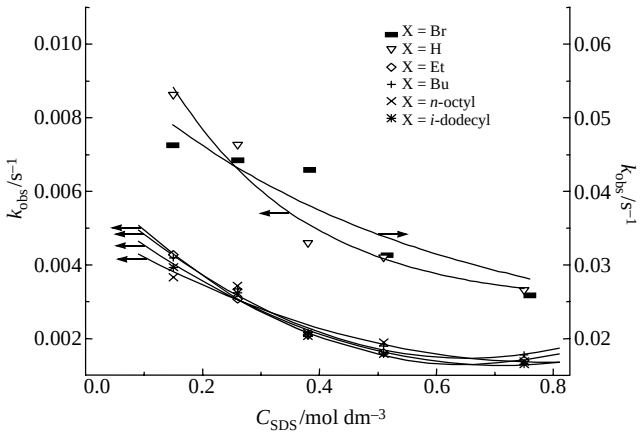


Figure 3 The observed rate constants of basic hydrolysis of **2**–**7** in the SDS reverse micellar system as functions of the surfactant concentration (W = 15.1, 0.01 M NaOH, 25 °C).

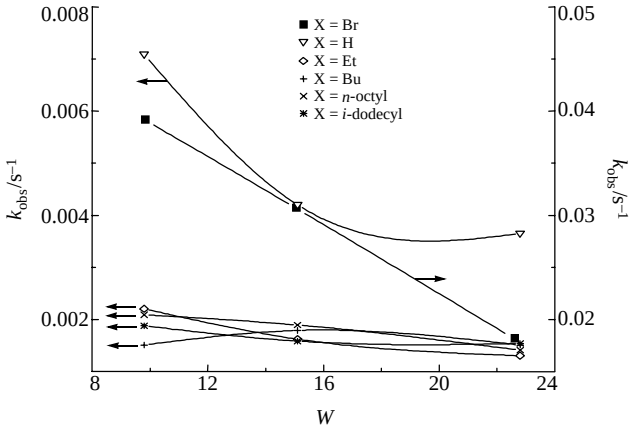


Figure 4 The observed rate constants of basic hydrolysis of **2**–**7** in the SDS reverse micellar system as functions of the water content (0.01 M NaOH, 25 °C).

on the reactivity. In the CTAB micelles, a principle of the recognition of substrates depending on their hydrophobicity is valid, *i.e*., a differentiating effect on the reactivity is observed. The electronic properties of substituents exert no influence on the micellar rate effect expressed as $(k_{obs}/k_w)_{max}$.

In the SDS reverse micellar system, both catalysis and inhibition of the reaction were observed depending on the substrate structure and experimental conditions. The micellar microenvironment mainly contributes to the micellar rate effect, while the concentration factor plays a minor role. In the reverse system, leveling in the reactivity of substrates of different hydrophobicity, as compared to water, was observed.

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