Amphiphilic quaternary pyridinium ketoximes as functional hydrolytic micellar catalysts — does the nucleophilic function position influence their reactivity?

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Abstract

Hydrolytic efficiency of isomeric amphiphilic quaternary pyridinium ketoximes comicellized with cetyltrimethylammonium bromide (CTAB) was investigated using 4-nitrophenyl diphenyl phosphate (PNPDPP) as a model substrate. Nucleophilicity of the deprotonated hydroxyimino group in these functional surfactants depends on its position relative to micellar surface. © 2001 Elsevier Science B.V. All rights reserved.

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Many different types of functional surfactants and metallosurfactants have been designed as potential hydrolytic micellar catalysts within the last 3 decades. The effort to mimic hydrolytic enzymes as well as possible applications, especially hydrolysis of neurotoxic derivatives of phosphoric and phosphonic acid have stimulated extensive research in this area [1–3]. However, until now low attention has been paid to the influence of the relative position of polar "head" group, hydrophobic alkyl chain and nucleophilic function on hydrolytic efficiency of functional surfactants [4,5]. In our previous communication [6] we described remarkable difference in hydrolytic activity of several isomeric amphiphilic quaternary pyridinium ketoximes. For example, homomicelles made of 1-methyl-4-[1-(hydroxyimino)tridecyl]pyridinium bromide (**1a**) whose nucleophilic hydroxyimino group is located below micellar surface are more efficient in the cleavage of various lipophilic 4-nitrophenyl esters than homomicelles made of isomeric 1-dodecyl-4-[1-(hydroxyimino)ethyl]pyridinium bromide (**1b**) whose hydroxyimino group is sticking out into aqueous phase as shown in an idealized chart (Fig. 1).

Higher hydrolytic activity of salt **1a** compared to salt **1b** can be a consequence of different aggregation ability of these surfactants. Indeed, critical micelle concentration of **1a** is lower than that of **1b** [6]. Nevertheless, there exists another explanation of the observed difference in the reactivity of both isomers: lipophilic esters are solubilized in micellar interior and therefore the probability of their attack by nucleophilic function should be higher in the case of salt **1a**. Moreover, lost of the solvation cover in micellar interior should increase the reactivity of the oximate anion which in fact is the nucleophile attacking the substrate. If this assumption were correct, a new generation of powerful hydrolytic micellar catalysts could

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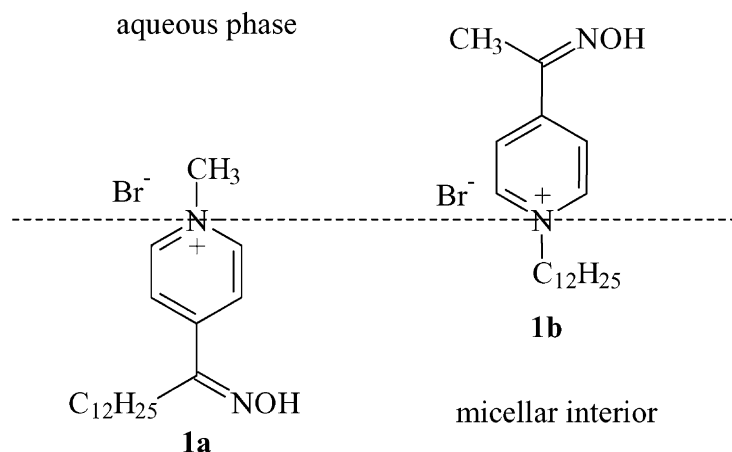*E-mail address:* frantisek.hampl@vscht.cz (F. Hampl).

Fig. 1. Orientation of surfactants **1a** and **1b** at micelle/water interface.

be prepared. This attractive hypothesis made us to perform more detailed study focused on the assumed relationship between the position of the nucleophilic function relative to micellar surface and hydrolytic activity of the functional surfactant.

We considered the previously studied [6] isomeric quaternary pyridinium ketoximes **1a** and **1b** as suitable models of functional surfactants differing in the nucleophilic function position relative to micellar surface. 4-Nitrophenyl diphenyl phosphate (PNPDPP) was employed as a lipophilic model substrate; its concentration in the reaction mixture was 2.0×10^{-5} mol l^{-1} in all cases. To ensure the existence of the same type of aggregates in all investigated micellar systems, both surfactants **1a** and **1b** were solubilized in micellar matrix of non-functional cationic surfactant cetyltrimethylammonium bromide (CTAB). All reactions were performed in 0.01 mol l^{-1} CTAB under pseudo-first-order conditions, i.e. [functional surfactant] $\gg$ [substrate] at 25°C using described procedure [6]. pH of the reaction mixture was kept at constant value of 7.2 (HEPES buffer 0.05 mol l^{-1}) during the kinetic runs. The hydrolytic systems were prepared directly in spectrophotometric cells by mixing appropriate volumes of stock solutions of CTAB, buffer and quaternary ketoxime **1a** and **1b**, respectively (total volume 1950 μl). The reactions were initiated by injection of 50 μl of the 8×10^{-4} mol l^{-1} PNPDPP solution in acetonitrile. The substrate hydrolysis was monitored by UV spectroscopy at 400 nm

(maximum of the released 4-nitrophenoxide ion absorption). The pseudo-first-order rate constants k_{obs} were obtained by non-linear regression analysis of the absorbance versus time data.

The obtained pseudo-first-order rate constant k_{obs} of the PNPDPP cleavage versus concentration c_{oxime} of the quaternary pyridinium oximes **1a** and **1b** plots are shown in Fig. 2a. On the first sight, the results seem to be disappointing since no significant difference can be observed between the reactivity of comicellar systems made of salts **1a** and **1b**. However, one must keep in his mind that it is the deprotonated hydroxyimino group which acts as the nucleophile attacking the substrate. Since the acidity of the oxime **1b** (pK_a = 9.3) is higher than that of the oxime **1a** (pK_a = 9.9) by a factor of four [1] almost the same observed reactivity can be achieved at approximately quarter concentration of the oximate anion in the case of the surfactant **1a**. Therefore, the apparent second-order rate constant $(k_2)_{app}$ values (Table 1) obtained as a slope of the pseudo-first-order rate constant k_{obs} of the PNPDPP cleavage versus oximate anions concentration $c_{oximate}$ plots (Fig. 2b) give an unambiguous evidence of higher reactivity of the anion formed from the surfactant **1a**. Concentrations

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[1] Apparent pK_a values of the amphiphilic quaternary pyridinium salts **1** in water were determined spectrophotometrically at two wavelengths (maxima of the =NOH and =NO$^-$ form, respectively) using the procedure described in [6].
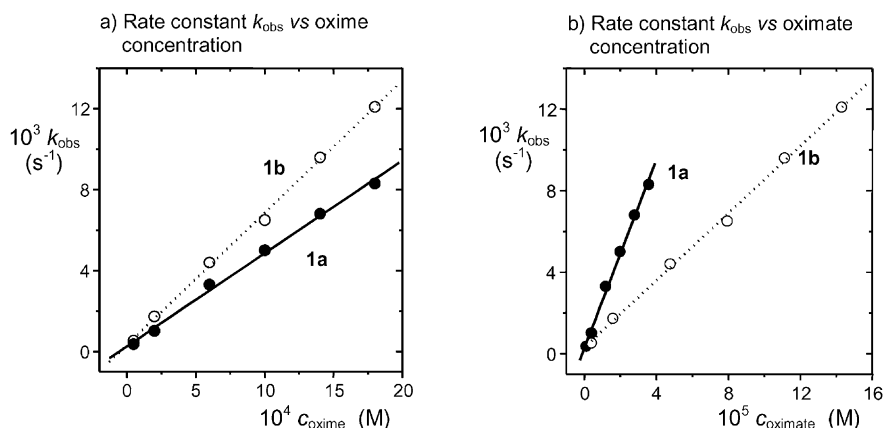
Fig. 2. PNPDPP cleavage by **1a** (full symbols, solid) and **1b** (empty symbols, dotted) in comicelles with CTAB (0.01 mol l^{-1}). Conditions: pH 7.2 (HEPES: buffer 0.05 mol l^{-1}), $t = 25°C$.

Table 1
Second-order rate constants of the PNPDPP cleavage in the presence of pyridinium ketoximes **1**

Oxime	$(k_2)_{app}(1 \, mol^{-1} \, s^{-1})$	$(k_2)_m \, (1 \, mol^{-1} \, s^{-1})$	$(k_2)_w(1 \, mol^{-1} \, s^{-1})$
1a[a]	2310 ± 76	8.6 ± 0.3	–
1b[a]	824 ± 18	3.05 ± 0.07	–
1c[b]	–	–	0.82 ± 0.03

[a] See caption to Fig. 2.
[b] [PNPDPP] = 5.0×10^{-6} mol l^{-1}, pH 8.2 (HEPES: buffer 0.05 mol l^{-1}), $t = 25°C$.

$c_{oximate}$ of the deprotonated form of salts **1** were calculated from the analytical concentrations c_{oxime} and the corresponding pK_a values using the Eq. (1)

$$c_{oximate} = c_{oxime} \frac{K_a}{K_a + [H^+]} \tag{1}$$

Recently, Scrimin [7] has published a study evaluating the influence of micelles on the reactivity of hydrolytic metallocatalysts. They concluded that the substance of the reaction rate enhancement in micellar systems (compared to reactions carried out in homogeneous solutions) consists only in changes of effective concentrations of the reactants, i.e. in bringing together the substrate with the nucleophile. They demonstrated that the second-order rate constants $(k_2)_m$ of the ester hydrolysis in metallomicellar systems containing lipophilic complexes and $(k_2)_w$ of the same reaction in homogeneous solution of homologous water soluble complexes are similar if local molarities of the reactants in metallomicelles are

taken into account. The second-order rate constants $(k_2)_m$ were calculated using the Eq. (2)

$$k_{obs} = (k_2)_m \frac{[Nu]}{V_M[Surf]} \tag{2}$$

where V_M is the molar volume of micellar pseudophase and [Nu] and [Surf] are molar concentrations of the nucleophile and surfactant, respectively, written in terms of total solution volume.

We decided to apply the above-mentioned considerations to our systems. Both investigated surfactants, i.e. salt **1a** having its nucleophilic function hidden in micellar interior and salt **1b** with its nucleophilic function oriented into aqueous phase have the same non-amphiphilic homologue: 4-(1-hydroxyiminoethyl)-1-methylpyridinium bromide **1c** (Fig. 3). Therefore, we wondered which of the second-order rate constant $(k_2)_m$ values of the PNPDPP cleavage in comicellar systems **1a**/CTAB and **1b**/CTAB would be closer to $(k_2)_w$ value
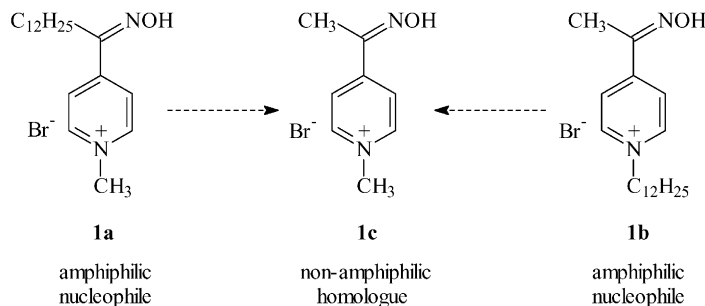
Fig. 3. Structure relationship in a series of pyridinium ketoximes **1a–1b**.

of the same reaction in homogeneous solution of **1c**.[2]

The obtained results are summarized in Table 1. The second-order rate constant $(k_2)_w$ value was obtained as a slope of the pseudo-first-order rate constant k_{obs} of the PNPDPP cleavage versus concentration $c_{oximate}$ of the deprotonated oxime **1c** plot at given conditions. The second-order rate constant $(k_2)_m$ values for both surfactants **1a** and **1b** were calculated from kinetic data shown in Fig. 2 using Eq. (2). The molar volume V_M value of $0.37 \, l \, mol^{-1}$ (the most frequently value used for trimethylammonium surfactants [8]) was used for the calculation.

From the data given in Table 1 it is evident that it is the compound **1b** whose intrinsic reactivity towards PNPDPP in CTAB micelles is closer to that of the **1c** in homogeneous solutions while the reactivity of **1a**/CTAB is markedly higher. This fact is in accord with our assumption of the influence of the nucleophilic function position on hydrolytic efficiency of functional surfactants. In the case of **1c** and **1b**/CTAB both reactions proceed in similar milieu: homogeneous aqueous solution and aqueous phase close to micellar surface, respectively. On the other hand, micellar interior increases the nucleophilicity of deprotonated hydroxyimino group in the case of **1a**/CTAB.

In conclusion, we have shown that nucleophilic reactivity of functional surfactants in micellar systems is influenced by the relative position of the polar head group and nucleophilic function in the surfactant molecule. We believe that this fact is not limited on this particular case only and can be utilized in design and synthesis of new and more powerful micellar catalysts.

Acknowledgements

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[2] Salt **1c** was prepared from 4-acetylpyridine using the procedure described in [6]. This new compound was characterized as follows: mp 211–215°C elemental analysis (calculated/found): C: 41.58/40.43, H: 4.80/5.08, N: 12.12/11.73 ^{1}H NMR (D$_2$O): 2.22 s, 3H, (C–CH$_3$) 4.23 s, 3H, ($^+$N–CH$_3$) 8.12 d, 2H, $J(3,2) = J(5,6) = 6 \, Hz$, H(3), H(5) 8.64 d, 2H, $J(2,3) = J(6,5) = 6 \, Hz$, H(2), H(6).