

# EFFECT OF HEXADECYLTRIMETHYLAMMONIUM BROMIDE MICELLES ON THE RATE OF OXIMOLYSIS OF ESTERS

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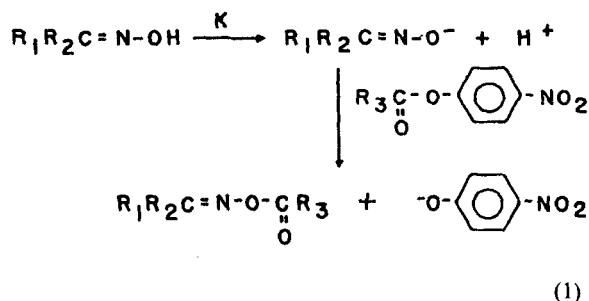
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Two amphiphilic oximes, 10-phenyl-10-hydroxyiminodecanoic acid (oxime II) and 4-(9-carboxynonyl)-1-(9-carboxy-1-hydroxyimino nonanyl)benzene (oxime III) were synthesized. The  $pK_a$  values of oximes II and III and acetophenoxime (oxime I) and the rates of oximolysis of *p*-nitrophenyl acetate (NPA) and *p*-nitrophenyl octanoate (NPO) were determined in the presence and absence of micellar hexadecyltrimethylammonium bromide (CTAB). The rates of oximolysis increased by up to  $3 \times 10^2$ -fold in the presence of CTAB. Quantitative analysis of micellar effects, using an ion-exchange pseudo-phase model, allowed the determination of the second-order rate constants for the reactions of oximes I–III with NPA and NPO in the micellar pseudo-phase. The calculated rate constants in the micellar pseudo-phase were lower than those in water, demonstrating that the rate enhancements were due to substrate concentration in the micelles. Comparison of the rate constants in micelles and water suggests that the sites of reaction of oximes I–III with NPO and NPA are similar to those in bulk aqueous solution. Micellar incorporation of the hydrophobic oximes II and III does not lead to a major change in the nucleophilicity of the oximate anion.

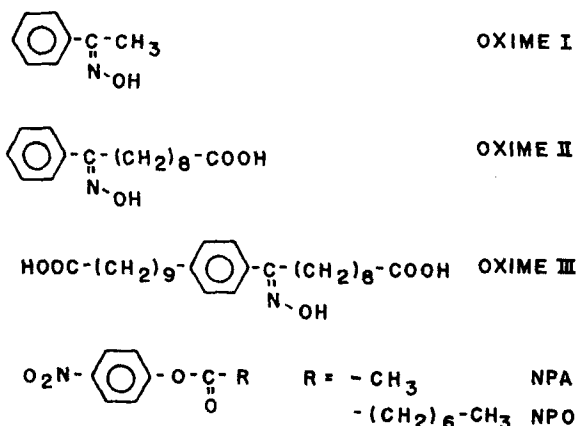
## INTRODUCTION

Quantitative analysis of micellar effects on the rates of chemical reactions has been used to show that the rate constants of bimolecular reactions in the aggregate rarely differ from those in the bulk aqueous phase by more than tenfold.<sup>1</sup> This observation also applies to reactions in other amphiphile aggregates such as microemulsions<sup>2a,b</sup> and vesicles.<sup>2c</sup> Most of the data has been obtained with ionic or water-soluble nucleophiles attacking micelle-incorporated substrates.<sup>1,2</sup> Nucleophilic reactivity in aqueous solution is limited by partial desolvation of the reactants.<sup>3</sup> Since nucleophilic reactivity in micelles and in water are similar, the (micellar) reaction sites are considered to be water-like.<sup>1</sup> It would be interesting to study reactions of nucleophiles designed, in principle, to penetrate the hydrophobic core of a micelle at different positions in order to investigate their reactivity relative to water.



In this paper we describe the effect of micelles on the rate oximolysis [reaction (1)] of *p*-nitrophenyl acetate (NPA) and octanoate (NPO) by water-soluble (oxime **I**), Scheme 1 and hydrophobic oximes (oximes **II** and **III**). We found that the calculated rate constants for the oximolysis reactions are very similar. Therefore, for these compounds, the conformational freedom of the micelle-incorporated nucleophiles and the hydration of the attacking group impose a water-like reaction site even between oxime **III** and NPO.

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Scheme 1. Oxime I, acetophenoxime; oxime II, 10-phenyl-10-hydroxyiminodecanoic acid; oxime III, 4-(9-carboxynonyl)-1-(9-carboxy-1-hydroxyiminononyl)benzene; NPA, *p*-nitrophenyl acetate; NPO, *p*-nitrophenyl octanoate

## RESULTS

Micelles produce major changes in the acid dissociation constants of (micellar-bound) acids,<sup>1</sup> hence the determination of micellar effects on the  $pK_a$  values is essential for analysing reactions in which the nucleophile is the dissociated species of a weak acid.<sup>1,4</sup> Quantitative analysis of the effect of amphiphile aggregates on the  $pK_a$  values of weak acids is facilitated by independent determination of the species incorporation constants.<sup>2c,4,5</sup> The association constant of the protonated form of oxime I to hexadecyltrimethylammonium bromide (CTAB) micelles ( $K_{HA}$ ) was measured by UV spectrophotometry (see Experimental).<sup>6</sup> Using three different conditions (water, 0.02M borate buffer and Tris-HBr buffer) the value of  $K_{HA}$  for oxime I was  $110 \pm 10 \text{ l mol}^{-1}$ . This value is within the range of water-micelle distribution constants for compounds of similar structure.<sup>6</sup> Oximes II and III were totally incorporated in CTAB micelles at any detergent concentration above the critical micelle concentration (CMC) (not shown), as expected from published data on similar systems.<sup>6</sup> Addition of salt did not change the spectra of micellar-bound II or III at either high or low pH (not shown).<sup>7</sup>

The  $pK_a$  values of oximes I, II and III in the absence of added detergent were determined from the effect of pH on the spectra of the protonated oxime (HOX) and oximate anion (OX) (see Experimental). The  $pK_a$  values were  $11.58 \pm 0.04$  (lit.<sup>8</sup> 11.48) for oxime I,  $12.05 \pm 0.05$  for oxime II and  $12.2 \pm 0.04$  for oxime III.

The apparent  $K_a$  in the presence of micelles ( $K_{ap}$ ) was defined as<sup>5a</sup>

$$K_{ap} = [H_f] \times \frac{[OX_f] + [OX_b]}{[HOX_f] + [HOX_b]} \quad (2)$$

where  $[H_f]$  is the  $H^+$  ion concentration in the intermicellar aqueous pseudo-phase calculated from the measured pH,  $[OX]$  and  $[HOX]$  are the analytical concentrations of the oximate anion and protonated oxime, respectively, and the subscripts f and b refer to species that are 'free' in the intermicellar aqueous pseudo-phase or bound to the micelle, respectively. The effect of micelles on the  $pK_{ap}$  (see Experimental) of oximes I-III is shown in Figure 1.

At the same pH, the rates of oximolysis and hydrolysis of NPA and NPO without micelles are similar. The second-order rate constants for oximolysis ( $k_{2ox}$ ) were

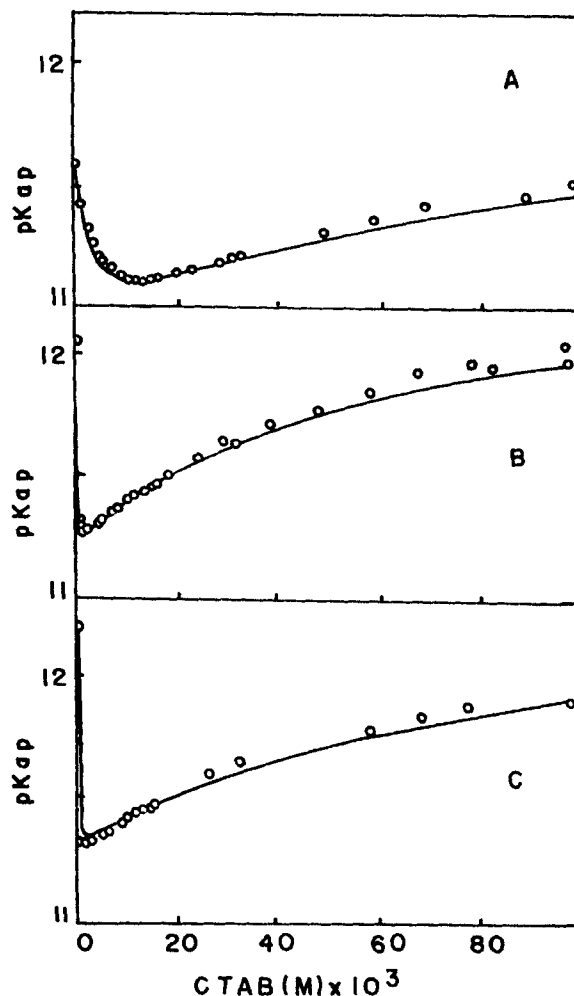


Figure 1. Effect of CTAB on the apparent  $pK_a$  ( $pK_{ap}$ ) of oximes (A) I, (B) II and (C) III.  $pK_{ap}$  was determined as described under *Methods*; curves are calculated, as described in the text. Buffer was triethylamine (0.02 M)-HBr. The following parameters were used in the curve fitting:  $\alpha$  (degree of counter-ion dissociation), 0.2;<sup>1a</sup>  $K_{OH/Br}$ , 0.08<sup>5b</sup>

calculated from

$$k_{2ox} = \frac{k_{\psi} - k_{2OH}[OH^{-}]}{[OX]} \quad (3)$$

where  $k_{\psi}$  is the observed first-order rate constant and  $k_{2OH}$  is the second-order rate constant for the attack of  $OH^{-}$  ion on the same ester. The concentration of the oximate anion  $[OX]$  was calculated from the (measured)  $pK_a$  of the oxime (see above) and pH. It was not possible to determine experimentally the value of  $k_{2ox}$  for oxime **III**. At high enough concentrations of oxime **III** to yield competitive oximolysis, the first-order plots were not linear, strongly suggesting aggregation of the oxime and a change in the charge of the aggregate as the reaction proceeded.<sup>9</sup> In the calculations we assumed that the second-order rate constant for oximolysis by oxime **III** has the same value as that obtained for oxime **II**. The second-order rate constant for ester oximolysis is not very sensitive to the chain length of the oxime.<sup>10</sup>

As expected, the products of oximolysis of NPA were *p*-nitrophenol and the corresponding acyloxime (see Experimental).

Figure 2 shows representative data for the effect of [CTAB] on the rate of NPA and NPO oximolysis. the rate acceleration produced by CTAB depends on both oxime and ester. For the more hydrophobic ester (NPO) the maximum rate enhancement [maximum observed rate constant ( $k_{\psi}^{max}$ ) divided by the calculated rate of oximolysis in the absence of micelles at the same pH ( $k_{\psi}^{ox}$ )] reaches more than  $10^4$ -fold (Table I).

For the same nucleophiles  $k_{\psi}^{max}/k_{\psi}^{ox}$  is, at best, 1000-fold when the substrate is NPA. Identification of the source of these different rate enhancements requires quantitative analysis of the micellar effect on these reactions (see Discussion).

## DISCUSSION

The model used to analyse quantitatively the data presented here is the pseudo-phase model with explicit consideration of ion exchange (PPIE).<sup>1a,5a</sup> This model assumes that the micelles are a separate pseudo-phase and that the micellar surface is saturated with respect to ions and, thus, the degree of ion dissociation from the surface can be considered constant.<sup>1,5a</sup> The PPIE model, and also every two-state model,<sup>2</sup> also assumes that two separate rate constants describe the kinetics of

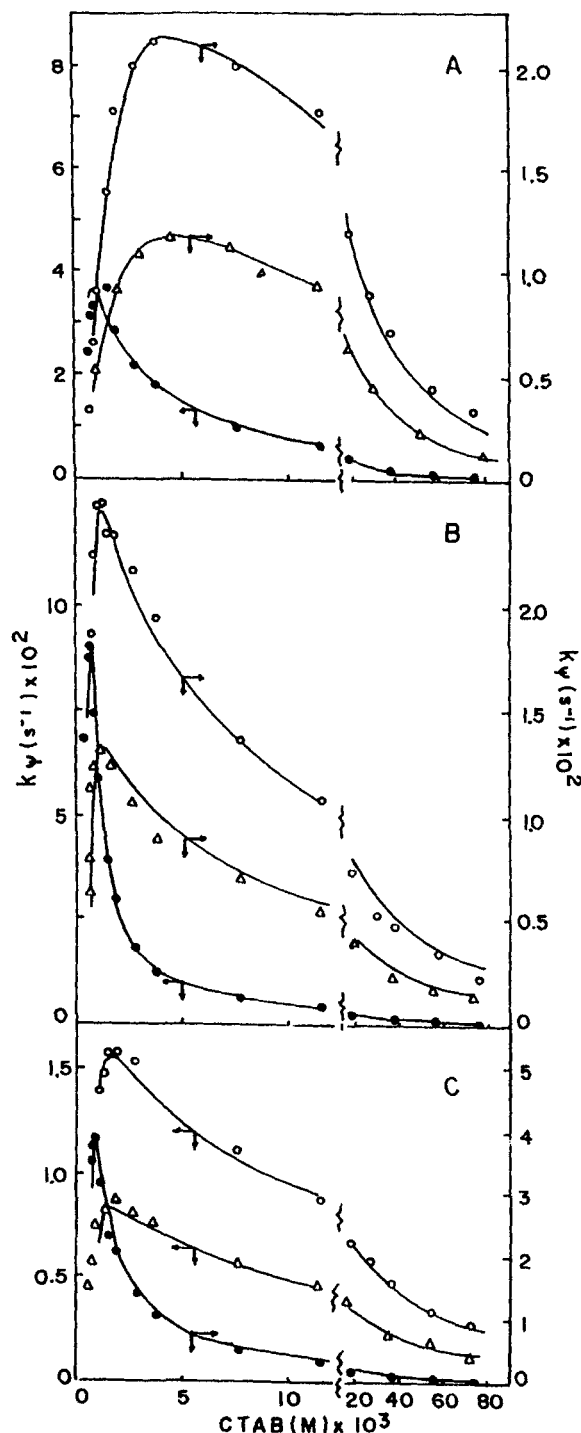


Figure 2. Effect of CTAB on the rate of oximolysis of *p*-nitrophenyl acetate (NPA) and octanoate (NPO) by oximes (A) **I**, (B) **II** and (C) **III**. Borate buffer (0.01 M) was used throughout, the total oxime concentration was  $2 \times 10^{-5}$ – $5 \times 10^{-5}$  M and the ester concentration was  $3 \times 10^{-6}$ – $4 \times 10^{-6}$  M. pH 9.2, NPO (•), NPA (Δ); pH 9.5, NPA (○). Parameters used in curve fitting were as in Fig. 1 and are described in the text.

Table 1. Maximum effects of CTAB micelles on the rate of oximolysis of *p*-nitrophenyl acetate (NPA) and *p*-nitrophenyl octanoate (NPO)

Oxime	Ester	$k_{\psi}^{\max}$ ( $s^{-1} \times 10^3$ ) <sup>d</sup>	Maximum rate acceleration ( $k_{\psi}^{\max}/k_{\psi}^{ox}$ ) <sup>d</sup>
I <sup>a</sup>	NPO	7.5	2800
II <sup>a</sup>	NPO	19.0	17900
III <sup>a</sup>	NPO	15.2	20300
I <sup>b</sup>	NPO	36.0	5400
II <sup>b</sup>	NPO	90.0	33950
III <sup>b</sup>	NPO	40.0	21300
I <sup>b</sup>	NPA	11.8	550
II <sup>b</sup>	NPA	13.2	1190
III <sup>b</sup>	NPA	7.5	960
I <sup>c</sup>	NPA	21.2	500
II <sup>c</sup>	NPA	24.8	1130
III <sup>c</sup>	NPA	15.8	1010

<sup>a</sup> pH 8.80, Tris-HCl buffer, 0.01 M.<sup>b</sup> pH 9.2, borate buffer, 0.01 M.<sup>c</sup> pH 9.5, borate buffer, 0.01 M.<sup>d</sup> The maximum observed rate constant ( $k_{\psi}^{\max}$ ) was obtained from Figure 2 taking the maximum  $k_{\psi}$ .  $k_{\psi}^{ox}$  was calculated as described in the text.

a reaction in the presence of micelles, namely a rate constant in the intermicellar aqueous phase ( $k_w$ ) and a rate constant in the micellar pseudo-phase ( $k_m$ ). This model can be applied to reactions that are, as in the present case, slow with respect to the rate of monomer-micelle equilibration.<sup>2</sup> Moreover, the PPIE model can be applied when the salt and detergent concentrations are relatively low and the predominant ions in solution are not heavily hydrated (e.g. OH<sup>-</sup> or F<sup>-</sup>).<sup>11</sup>

Details of the calculations using the PPIE model to fit the experimental data on the effect of detergent concentration in the reaction rate have been extensively described.<sup>5,7</sup> Only the equations used for data analysis are presented in each case. The best-fit values of adjustable parameters were calculated using a computer program that fits a theoretical expression (such as equations 4–7) to a set of experimental data (Figures 1 and 2) using a multiple regression expression.<sup>7</sup>

For oxime **I** the expression relating the variation of  $K_{ap}$  with [CTAB] is<sup>5</sup>

$$K_{ap} = K_a \times \frac{1 + K_{ox/Br} [Br_b/Br_f]}{1 + K_{HA} C_D} \quad (4)$$

where  $K_{ox/Br}$  is the oximate/bromide selectivity constant for ion exchange,  $K_{HA}$  the association constant of the protonated form of the oxime to the micelle and  $C_D$  the concentration of micellized detergent [ $C_D$  = total concentration of added detergent ( $C_T$ ) – CMC]. The value of  $K_{HA}$  for oxime **I** was 110 l mol<sup>-1</sup> (see Results) and the value of  $K_{ox/Br}$  was used as an adjustable parameter

to fit the data. The calculated value of  $K_{ox/Br}$  for oxime **I** was 4.8, well in the range of ion selectivities of anions of comparable hydrophobicities.<sup>7</sup>

For oximes **II** and **III** the equation describing the effect of micelles on  $K_{ap}$  is

$$K_{ap} = K_a K' \left[ \frac{Br_b}{Br_f C_D} \right] \quad (5)$$

where  $K'$  ( $K' = K_{ox/Br}/K_{HA}$ ) is an adjustable parameter. The best-fit values of  $K'$  for oximes **II** and **III** were 0.037 and 0.067, respectively. The equation used to analyse the effect of CTAB on the rate of oximolysis of esters is<sup>5</sup>

$$k_{\psi} = [OX_T] K_a k_{2ox} \times \frac{(k_{2m}/k_{2ox})(1/\bar{V}) K_s K_{ox/Br} [Br_b/Br_f] + 1}{(1 + K_{HA} C_D)(H_f^+ + K_{ap})(1 + K_s C_D)} \quad (6)$$

where  $k_{2m}$  is the second-order rate constant in the micellar pseudo-phase and  $\bar{V}$  ( $\bar{V} = 0.37$  l mol<sup>-1</sup>)<sup>12</sup> the molar volume of the micellized detergent. The values of the association constants of the esters with micellar CTAB ( $K_s$ ) were 54 l mol<sup>-1</sup> for NPA and  $1.5 \times 10^4$  l mol<sup>-1</sup> for NPO.<sup>12</sup>

For oximes **II** and **III**, it can be shown that the expression relating  $k_{\psi}$  with detergent concentration is<sup>5a,12c</sup>

$$k_{\psi} = [OX_T] k_{2ox} K_{ap} \times \frac{(k_{2m}/k_{2ox})(1/\bar{V})}{(H_f^+ + K_{ap})(1 + K_s C_D)} \quad (7)$$

Since the values of all other constants are fixed, the only adjustable parameter needed for the computer fit of equation (7) with the kinetic data was  $k_{2m}$ . In all cases the effect of CTAB on the rate of hydrolysis of the esters was corrected.<sup>7</sup> This correction becomes important at high detergent concentration. Best-fit values for  $k_{2m}$  are presented in Table 2. The  $k_{2m}$  values calculated for oximolysis of NPA at pH 9.2 were used to generate the curves fitting the results at pH 9.5 (Fig. 2). In all cases the correspondence of the calcu-

Table 2. Calculated second-order rate constants for the oximolysis of *p*-nitrophenyl acetate (NPA) and *p*-nitrophenyl octanoate (NPO)<sup>a</sup>

Oxime	Substrate			
	NPO		NPA	
	$k_{2ox}$	$k_{2m}$	$k_{2ox}$	$k_{2m}$
<b>I</b>	20.0	8.0	64.0	47.0
<b>II</b>	23.5	5.4	93.0	33.5
<b>III</b>	(23.5) <sup>b</sup>	2.8	(93.0) <sup>b</sup>	18.0

<sup>a</sup> Rate constants in l mol s<sup>-1</sup>; see text for the calculation procedures.<sup>b</sup> The value of  $k_{2ox}$  for oxime **III** was assumed to be that for oxime **II** (see text).

lated curves with the results was within experimental error.

The calculated second-order rate constant in the micellar pseudo-phase ( $k_{2m}$ ) was lower than that in the aqueous phase ( $k_{2ox}$ ) for all oxime-ester reactions (Table 2). The rate constants for oximolysis in micelles decreased with the increase in hydrophobicity of the ester (Table 2).<sup>1</sup> A decrease in the second-order rate constant observed on transferring the reaction from water to the micellar pseudo-phase has been reported for several bimolecular reactions.<sup>1</sup> The increase in hydrophobicity of the oxime nucleophile did not cause any major change in the calculated second-order rate constant in the micelle. The difference between the  $k_{2m}$  values for oximolysis of NPA and NPO by any oxime was higher than the difference in  $k_{2m}$  values for the reaction of oximes I–III with either NPA or NPO (Table 2).

The present model for a micelle (at low added salt and detergent concentrations from the CMC to up to two orders of magnitude above) depicts the aggregate as a constantly fluctuating structure, containing *ca* 100 monomers. Part of the hydrocarbon backbone is exposed to water and the interior is essentially composed of a hydrophobic core.<sup>13</sup>

Chemical reactions occurring in this aggregate can be affected to various extents when compared with the same reaction in solution.<sup>1</sup> For monomolecular reactions, several distinct features of the micellar structure have been proposed as the source of the micellar effect. Conformer selection, transition-state stabilization, local dielectric constant-related medium effects, partial desolvation of the attacking group, electrostatic effects on the energy of the initial state and specific stabilization of transition states by charged groups have been proposed as sources of micellar effects for different chemical reactions.<sup>1,2,14,15</sup> All these elements, plus the concentration of the reagents in the micelles, must apply for higher molecular reactions.

As a rule, the reactivity of oxygen nucleophiles incorporated in the micelle decreases rather than increases.<sup>1,16</sup> Exceptions for this rule are intramolecular cyclization reactions.<sup>17,18</sup> The rate acceleration caused by micelles on the cyclization of [*o*-(3-halopropoxy)phenoxide] has been ascribed to the partial desolvation of the attacking phenoxide ion.<sup>18</sup>

Micelle modification of ester oximolysis has been described and, on the basis of observations made at a single detergent concentration, CTAB micelles have been found to accelerate the reaction.<sup>10</sup> Here we show that CTAB can increase the rate by simply increasing the local reagent concentration. In the present case it is evident that the differences in oxime structure were not sufficient to cause a significant change in the reaction site. Thus, even for oxime III, where partial desolvation could be expected on incorporation of the undissociated

head group deeper into the micellar hydrophobic core, the calculated second-order rate constants were similar to those of the more hydrophilic oxime I. Careful quantitative analysis of ester reactions in mixed micelles containing functional detergents has been used to propose that desolvation of anionic nucleophiles is not a relevant source of micellar rate enhancement.<sup>19</sup> The energy for desolvation of the closely bound water molecules in the first solvation shell seems to be sufficiently large to exclude the possibility of desolvating even a relatively small portion of an otherwise hydrophobic substrate.<sup>20</sup> This is in agreement with experimental<sup>13a</sup> and theoretical<sup>13b,c</sup> data showing that all segments of the amphiphilic chain have approximately the same probability of being in contact with water, although water penetration in the micellar core is negligible.

## EXPERIMENTAL

### Materials

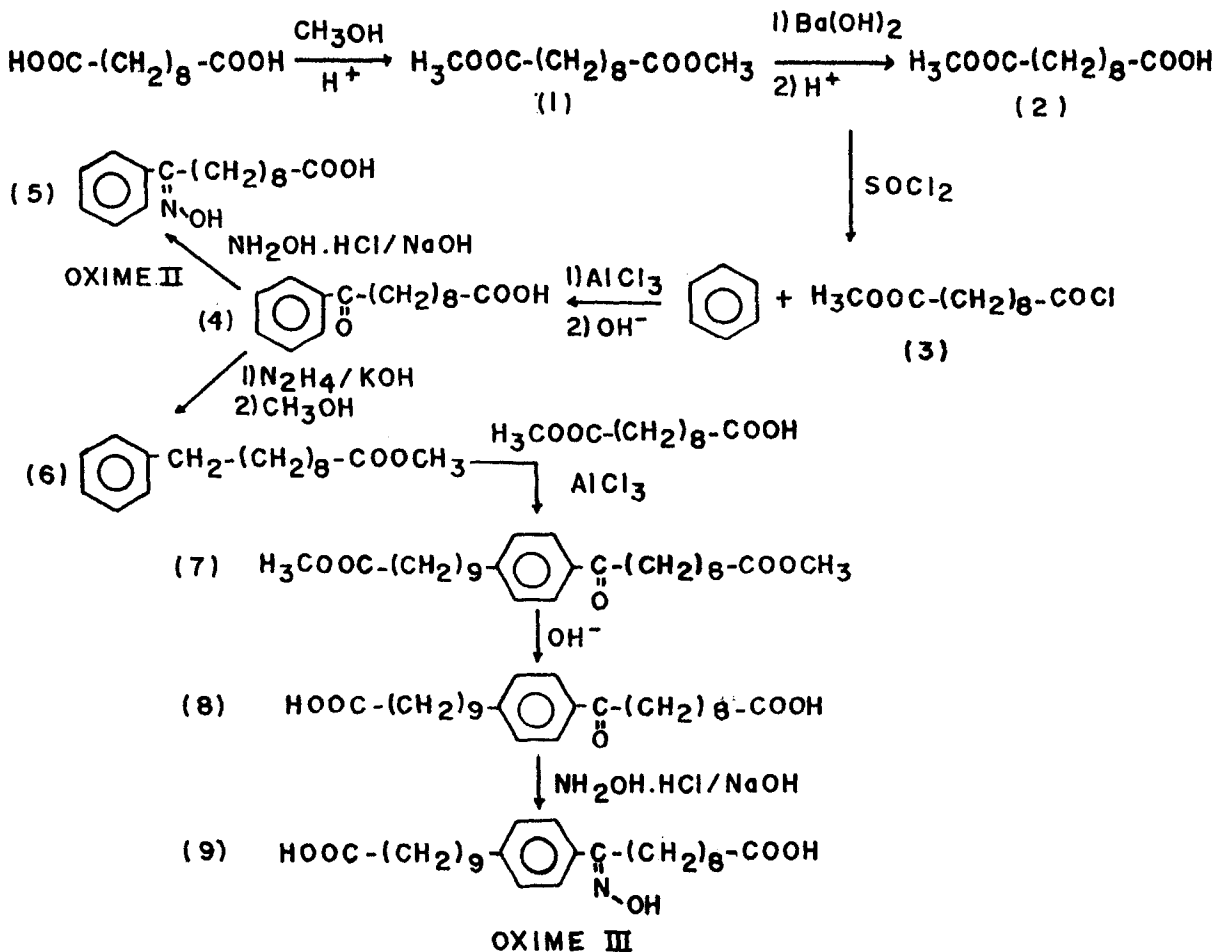
Acetophenoxime was prepared from acetophenone (Carlo Erba, Brazil) and hydroxylamine (Baker, USA).<sup>21a</sup> The recrystallized product had m.p. 59 °C (lit. 60 °C;<sup>21b</sup> 57.5–57.8 °C<sup>21c</sup>).

CTAB was obtained from Merck (Darmstadt, Germany) and recrystallized from acetone-ethanol. *p*-Nitrophenyl acetate (NPA) was obtained from Sigma (St. Louis, MO, USA). *p*-Nitrophenyl octanoate was a pure sample donated by Professor O. A. El-Seoud (Instituto de Química, Universidade de São Paulo, Brazil). Water was deionized and doubly distilled in glass. All other reagents were at least of analytical grade.

The synthetic routes leading to oximes II and III are presented in Scheme 2.

Dimethyl sebacate was prepared from sebacic acid (BDH, Poole, UK) and methyl sebacate by treatment of dimethyl sebacate with Ba(OH)<sub>2</sub>.<sup>22,23</sup> Methyl 9-benzoylnonanoate ester was prepared by acylation of benzene with monomethylsebacyl chloride (3).<sup>24</sup> The crude ester was hydrolysed in 1 M NaOH (reflux 1 h) to yield 9-benzoylnonanoic acid (4). After treatment with charcoal and recrystallization (hexane-benzene, 85 : 15, v/v) the m.p. was 82–83 °C (lit.<sup>24</sup> 78–79 °C). Elemental analysis, IR and <sup>1</sup>H NMR spectra were consistent with the structure.

*10-Phenyl-10-hydroxyiminodecanoic acid (oxime II, Schemes 1 and 2)* To 2.0 g of 4 dissolved in ethanol, 1.0 g of hydroxylamine hydrochloride and 1.83 g of powdered NaOH were added. The mixture was refluxed for 25 min, cooled and acidified with HCl. The oily phase solidified on standing. The solid was filtered and recrystallized from ethanol-water. Analysis: calculated for C<sub>16</sub>H<sub>23</sub>NO<sub>3</sub>, C 69.29, H 8.36, N 5.05; found, C 69.12, H 8.25, N 5.03%. M.p. = 58–60 °C. IR (KBr),



Scheme 2.

3100, 1700, 3280  $\text{cm}^{-1}$ . NMR (in  $\text{CDCl}_3$ )  $\delta$ (ppm) 7.2–7.6 (m, 5H), 2.82 (t, 2H), 2.34 (t, 2H), 1.2–2 (m, 12H). UV (EtOH), 244.5 nm ( $\log \epsilon_{\text{max}} = 4.02$ ).

**Methyl 10-phenyldecanoate (6).** Compound 4 was reduced with  $\text{N}_2\text{H}_4\text{--KOH}$ , esterified with MeOH ( $\text{H}_2\text{SO}_4$ ) and purified by vacuum distillation. NMR, IR and UV data were in accord with the structure.

**4-(9-Carbomethoxynonyl)-1-(1-oxo-8-carbomethoxyoctyl)benzene (7).** A 70 g amount of 6 was dissolved in 270 ml of tetrachloroethane containing 110 g of anhydrous  $\text{AlCl}_3$ , then 63 g of 3 were added slowly (1 h). The (slow) liberation of HCl continued over 2 h. The mixture was agitated at room temperature overnight. The temperature was adjusted to 45 °C and after 4 h no further gas was evolved. The reaction mixture was poured over 150 ml of concentrated HCl and

diluted (1:1) with ice. The resulting mixture was extracted with benzene and the organic phase washed with water and dried. Solvent was stripped off and the remaining solid was recrystallized from hexane. Analysis: calculated for  $\text{C}_{28}\text{H}_{44}\text{O}_5$ , C 73, H 9.63; found, C 72.8, H 9.93%. M.p. = 58–60 °C. UV (EtOH), 254 nm ( $\log \epsilon_{\text{max}} = 4.1$ ). NMR ( $\text{CDCl}_3$ ),  $\delta$ (ppm) 7.81 (d, 2H), 7.15 (d, 2H), 3.65 (s, 6H), 2.88 (t, 2H), 2.65 (t, 2H), 2.3 (t, 4H), 1.2–1.9 (m, 26 H).

**4-(9-Carboxynonyl)-1-(1-oxo-9-carboxynonyl)benzene (8).** A 2 g amount of 7 was dissolved in 100 ml of 95% (v/v) ethanol and after addition of 0.7 g of NaOH the solution was refluxed for 1.5 h. After cooling and acidification (HCl), the white precipitate was washed with water and recrystallized from 95% ethanol (yield 1.6 g). Analysis: calculated for  $\text{C}_{26}\text{H}_{40}\text{O}_5$ , C 72.19, H 9.32; found, C 71.95, H

9.30%. M.p. = 128–130 °C. UV (EtOH), 255 nm ( $\log \epsilon_{\max} = 4.2$ ). IR and NMR spectra were consistent with the structure.

*4-(9-Carboxynonan-1-yl)-1-(9-carboxy-1-hydroxyimino-nonan-1-yl)benzene (oxime III)* (Schemes 1 and 2). To 1.3 g of **8** dissolved in 70% ethanol, 0.4 g of  $\text{NH}_2\text{OH}\cdot\text{HCl}$  and 0.8 g of powdered  $\text{NaOH}$  was added. After refluxing for 30 min the solution was cooled and acidified with dilute (1:3)  $\text{HCl}$ . The resulting solid was recrystallized with ethanol–water and dried *in vacuo*. Analysis: calculated for  $\text{C}_{26}\text{H}_{41}\text{NO}_5$ , C 69.77, H 9.223, N 3.13; found, C 69.50, H 9.13, N 2.99%. M.p. = 67–69 °C. UV (EtOH), 251 nm ( $\log \epsilon_{\max} = 4.16$ ). NMR and IR spectra were consistent with the structure.

**Methods.** All kinetic,  $pK$  and distribution constant determinations were done at 30 °C. Rates of oximolysis or hydrolysis were determined following the appearance of *p*-nitrophenoxide ion at 403 nm. Reactions were started by addition of a 1- $\mu\text{l}$  aliquot of the ester to a temperature-equilibrated (1.5–3.0 ml) solution containing all other reagents. Rate constants, calculated from linear first-order plots, are the averages of at least three separate experiments with a maximum deviation of 5%.

**Determination of  $pK_a$ .** The  $pK_a$  values of oximes **I–III** were determined from the effect of pH on the spectra of the protonated and deprotonated species. The wavelength of maximum absorption (nm) ( $\log \epsilon_{\max}$ ) for the protonated oximes and oximate anions were as follows: **I**, 239, 262 (4.01, 4.06); **II**, 239, 261 (3.96, 4.01); and **III**, 246, 262 (4.06, 4.09). Typically the spectra of a  $6 \times 10^{-5}$  M solution of the oximes were recorded as a function of pH in 0.02 M buffers. The spectra of deprotonated and protonated oximes were obtained in 0.1 M  $\text{NaOH}$  and 0.02 M  $\text{Tris-HBr}$  buffer (pH 8.8), respectively. The effect of CTAB on the  $pK_{ap}$  values of the oximes was determined at a pH near the  $pK_a$  of the oxime in 0.02 M triethylamine-HBr buffer.  $pK_{ap}$  was calculated from the expression<sup>4</sup>

$$pK_{ap} = \text{pH} + \log \left( \frac{Ab_{s1} - Ab_{s\psi}}{Ab_{s\psi} - Ab_{s2}} \right) \quad (8)$$

where  $Ab_{s1}$  and  $Ab_{s2}$  are the absorbances of the totally deprotonated and protonated species in CTAB, respectively.  $Ab_{s1}$  and  $Ab_{s2}$  were obtained in 0.1 M  $\text{NaOH}$  and 0.02 M  $\text{Tris-HBr}$  buffer (pH 7.5), respectively.  $Ab_{s\psi}$  is the measured absorbance at pH 11.1, 11.3 and 11.0 for oximes **I**, **II** and **III** respectively.

**Determination of micelle–water distribution constant.** The distribution constant of oxime **I** was obtained by determining the effect of CTAB on the absorbance of a  $5 \times 10^{-5}$  M solution of the compound at 255 nm.<sup>6</sup>

The determination was carried out in water at pH 8.1 (0.02 M  $\text{Tris-HBr}$  buffer) and pH 9.1 (0.02 M borate buffer).

**Analysis of the reaction products between oxime I and *p*-nitrophenyl acetate.** A 3.0 mg amount of **I** was dissolved in 300 ml of 0.01 M borate buffer (pH 10.0) and 1.0 ml of ethanol containing 4.5 mg of NPA was added. After 3 h the reaction mixture was extracted with diethyl ether. The aqueous solution contained *p*-nitrophenol (spectra). The ethereal fraction was dried with  $\text{MgSO}_4$  and the residue was shown to contain unreacted NPA and acetoxypheinoxime (APO) by thin-layer chromatography in three different solvents [Ethyl acetate–benzene (2:20), ethyl acetate–benzene–heptane (1:17:3) and diethyl ether–heptane (4:1)]. NPA and APO were used as standards.

#### ACKNOWLEDGEMENTS

This work was partially supported by the following Brazilian agencies: CAPES, FINEP, FAPESP, CNPq. We are grateful to Dr I. M. Cuccovia for discussions and Dr M. Armelin for assistance with the manuscript.

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