Rate of Reaction of 1 and $P(p\text{-tol})_3$. The following procedure is representative. A 5-mm NMR tube was charged with **1** (16.0 mg, 0.028 mmol) and $P(p\text{-tol})_3$ (170.0 mg, 0.559 mmol) and capped with a septum. A N_2 atmosphere was established, and C_6D_6 (0.7 mL) was added. The tube was transferred to a NMR probe, and rate data were acquired as described above. The concentrations of **1** and **4** were assayed by integration of the ^{31}P NMR resonances (17.2 and 14.4 ppm, 39 °C). The data are presented in Table II.

Rate of Reaction of (*RRRR*)-2a and $P(p\text{-tol})_3$. The following procedure is representative. A 5-mm NMR tube was charged with (*RRRR*)-**2a** (16.3 mg, 0.023 mmol), $P(p\text{-tol})_3$ (72.0 mg, 0.239 mmol), and C_6D_6 (0.7 mL) in a manner analogous to the preceding experiment. The tube was transferred to a NMR probe, and rate data were acquired as described above. Concentrations of (*RRRR*)-**2a** and (*RRRR*)/(*SRRR*)-$(\eta^5\text{-}C_5H_5)Re(NO)(P(p\text{-tol})_3)(OC_{10}H_{17})$ (**5a**) were assayed by integration of the ^{31}P NMR resonances (17.2, 13.2, and 14.2 ppm, 29 °C). The data are presented in Table II.

Acknowledgment. We thank the DOE for support of this research, Dr. C. M. Garner for preliminary observations, and the Ministry of Education and Science of Spain and the Fulbright Commission for a postdoctoral fellowship (I.S.L.).

Supplementary Material Available: Details of additional experiments (2 pages). Ordering information is given on any current masthead page.

Electrostatic Micellar Effects on the Rate of Spontaneous Decomposition of *m*-Nitrophenyl 9-Fluorenecarboxylate

Valdir R. Correia,[†] Iolanda Midea Cuccovia, Magaly Stelmo, and Hernan Chaimovich[*]

Contribution from the Departamento de Bioquimica, Instituto de Quimica da Universidade de Sao Paulo, Caixa Postal 20780, Sao Paulo, SP, CEP 01498, Brazil.

Received December 17, 1990. Revised Manuscript Received October 23, 1991

Abstract: The effects of neutral, ionic, and zwitterionic micelles on the rate of the spontaneous decomposition of *m*-nitrophenyl 9-fluorenecarboxylate (I) were determined. Neutral micelles of a poly(oxyethylene) detergent produce a small increase in the decomposition rate. Negatively charged micelles of sodium dodecyl sulfate catalyze the reaction 2-fold while positively charged micelles of hexadecyltrimethylammonium bromide (CTAB) inhibit by a similar factor. Micelles of *N*-hexadecyl-*N*,*N*-dimethylammonium 3-propanesulfonate inhibit the decomposition of I to a larger extent than those of *O*-hexadecylphosphorylcholine while lysolecithin micelles do not affect the reaction rate. Thus, charge orientation of the monomer does not determine the kinetic effects of zwitterionic micelles on the rate of decomposition of I. The rate modifications produced by micelles on this reaction are consistent with electrostatic effects on the relative energies of initial and transition states.

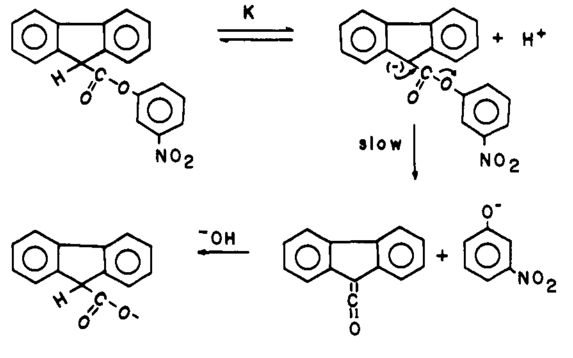
Introduction

Micellar incorporation of a substrate decomposing spontaneously can produce major effects in the reaction rate.[1] For different reactions distinct features of the micellar interface have been singled out as determining the observed effect. These include (a) conformer stabilization,[2] (b) decrease of hydration of the nucleophile,[3] (c) medium effects related to local polarity,[4] and (d) specific interactions of ionic head groups with transition states.[5]

The consideration of micelles as a separate pseudophase has greatly facilitated mechanistic descriptions and quantitative rate analysis of chemical reactions in micelles.[1] However, the micellar reaction site is not a continuous phase.[1] Reactions of hydrophilic (and relatively hydrophobic) substrates occur in the micelle–water interface.[1] At this site the effective polarity may differ significantly from that in the bulk solvent, and the local electrostatic field in both ionic and zwitterionic micelles may be considerable.[1,6,7] It has been suggested that specific effects of micellar charge in rates of unimolecular reactions can only be expected when formation of the transition state involves a ionization, as is the case for hydrolysis of *tert*-butyl chloride.[8] A study of the effect of micelles of detergents exhibiting different charge and/or dipoles on a monomolecular reaction should contribute to a better understanding of Coulombic effects on interfacial reactions.

Here we report that the E1cB decomposition of *m*-nitrophenyl 9-fluorenecarboxylate (I) (Scheme I) is catalyzed by negatively charged micelles, unaffected by neutral micelles, and inhibited by positively charged micelles. The effects of zwitterionic micelles depend on the nature of the detergent. These effects can be accommodated with current models of micellar structure and are consistent with stabilization of the initial state by ion pairing of

Scheme I



---

[*] To whom correspondence should be addressed.

[†] Present address: Departamento de Quimica, Universidade Federal de Santa Catarina, Florianopolis, SC.

(1) (a) Fendler, J. H. *Membrane Mimetic Chemistry*; Wiley-Interscience: New York, 1982. (b) Bunton, C. A.; Savelli, G. *Adv. Phys. Org. Chem.* **1986**, *22*, 231–309.

(2) (a) Oliveira, A. G.; Cuccovia, I. M.; Chaimovich, H. *J. Pharm. Sci.* **1990**, *79*, 37–42. (b) Oliveira, A. G.; Nothenberg, M. S.; Cuccovia, I. M.; Chaimovich, H. *J. Phys. Org. Chem.* **1991**, *4*, 19–24. (c) Cuccovia, I. M.; Schroter, E. H.; de Baptista, R. C.; Chaimovich, H. *J. Org. Chem.* **1977**, *42*, 3400–3403.

(3) Cerichelli, G.; Luchetti, L.; Mancini, G.; Muzzioli, M. N.; Germani, R.; Ponti, P. P.; Spreti, N.; Savelli, G.; Bunton, C. A. *J. Chem. Soc., Perkin Trans. 2* **1989**, 1081–1085.

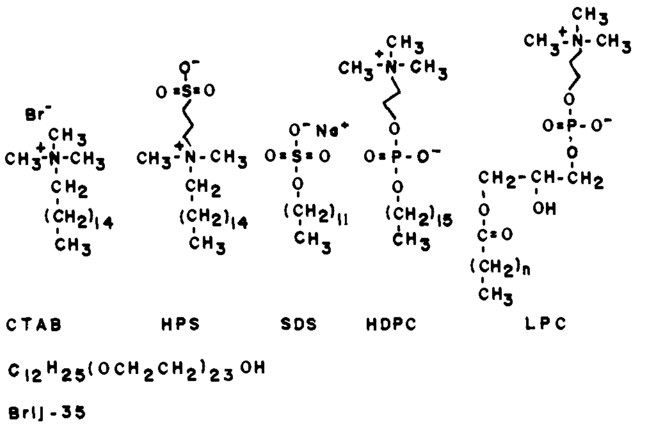
(4) Bunton, C. A.; Minch, M. J.; Sepulveda, L.; Hidalgo, J. *J. Am. Chem. Soc.* **1973**, *95*, 3262–3272.

(5) Bunton, C. A. In *Solution Chemistry of Surfactants*; Mittal, K. L., Ed.; Plenum Press: New York, 1979; Vol. 2, pp 519–540.

(6) Handa, T.; Nakagaki, M.; Miyajima, K. *J. Colloid Interface Sci.* **1990**, *137*, 253–262.

0002-7863/92/1514-2144$03.00/0 © 1992 American Chemical Society

Chart I



I with the alkylammonium group and preferential destabilization of the initial state by neighboring negatively charged groups in the micellar surface.

Experimental Section

m-Nitrophenyl 9-fluorenecarboxylate (I) was prepared from 9-fluorenecarboxylic acid (Aldrich Chemical Co.) and *m*-nitrophenol (Aldrich) as described.[9] Melting point, UV, and NMR spectral data as well as elemental analysis were in accord with those of the structure. Hexadecyltrimethylammonium bromide (CTAB) (E. Merck, Darmstadt, Germany; analytical grade) was recrystallized from acetone–ethanol. The critical micelle concentration (cmc) of CTAB measured by conductivity (9.0×10^{-4} M) corresponded to literature values.[1a] Sodium dodecyl sulfate (SDS) (BDH Chemicals, Poole, England) was Soxhlet-extracted with ether and recrystallized from methanol–water–acetone (1:1:15, v/v/v). SDS did not exhibit a minimum in the surface tension vs concentration curves[10] and exhibited a cmc of 8.0×10^{-3} M.[1a] *N*-Hexadecyl-*N*,*N*-dimethylammonium 3-propanesulfonate (HPS), obtained from Dr. Mario J. Politi from this institute, was triply recrystallized from acetone–methanol. The conductance of a 0.1 M aqueous solution of HPS was 16 μS. *O*-Hexadecylphosphorylcholine (HDPC) was prepared and purified using published procedures.[11] The conductance of a 0.1 M solution of HDCP in water was 30 μS. Egg lysolecithin (LPC) obtained from Sigma Chemical Co. (St. Louis, Mo.) was purified by silica gel chromatography. Reproducible data were obtained with LPC which did not contain free fatty acids (thin-layer chromatography) and exhibited a conductance (0.1 M aqueous solution) of 75 μS, corresponding to a maximum salt contamination of 5×10^{-4} M.[12]

The rate of decomposition of I at 30 °C was followed in a Beckman M25 spectrophotometer at 326 nm, the maximum absorption wavelength of the carbanion of I (Scheme I). First-order rate constants were calculated from ln absorbance vs time plots linear for at least 4 half-lives. Values are the average of at least four experiments with an average deviation of 5%.

Results and Discussion

The structures of the monomers are presented in Chart I, and the effects of micelles formed by these detergents on the rate of spontaneous decomposition of *m*-nitrophenyl 9-fluorenecarboxylate (I) are presented in Figure 1.

The mechanism of the decomposition of I in aqueous solution has been investigated in detail.[9] In basic solutions the hydrolysis of I is rate-limited by the decomposition of the carbanion (Scheme I).[9] The ensuing E1cB elimination is characterized by the development of considerable negative charge on the phenoxide moiety of the transition state with some solvation effects and/or nucleophilic assistance by solvent of leaving group expulsion.[9] Since the negative charge in the carbanion of I is largely delocalized, movement along the reaction coordinate results in charge localization on the phenoxide oxygen as the transition state is reached.

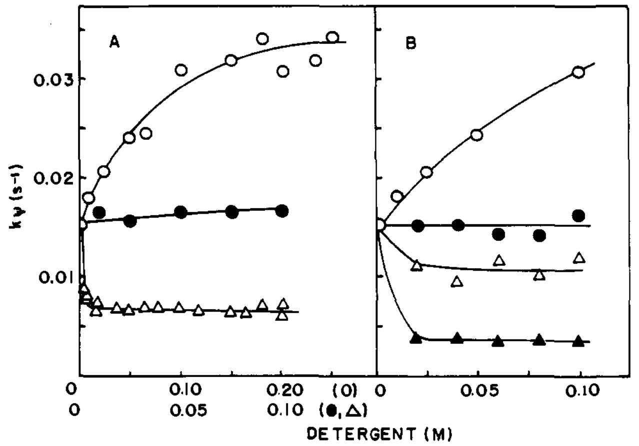


Figure 1. Micellar effects in the spontaneous decomposition of *m*-nitrophenyl 9-fluorenecarboxylate (I) (0.02 M NaOH): (A) (△) CTAB, (○) SDS, (●) Brij-35; (B) (○) SDS, (●) LPC, (△) HDPC, (▲) HPS. The value of k_ψ without detergents was 0.0154 s^{-1}, in good agreement with published data.[9]

Neutral micelles have been used as adequate systems to investigate the effect of the change in local dielectric constant occurring when the reaction site is transferred from bulk aqueous solution to a micellar interface.[13] The difference between the rate constant in water (k_w) and that in the presence of micellized Brij-35 (k_m) (Figure 1) was significant within our error (<5%), being 15% higher than that measured in water (Figure 1A). It is expected that a hydrophobic substrate such as I should incorporate efficiently in Brij-35 micelles.[14] Hence, a change in local dielectric constant, at least in Brij-35 micelles, is not sufficient to alter the rate of decomposition of I by more than a few percent.

The effect of hexadecyltrimethylammonium bromide (CTAB) on the decomposition of I (Figure 1A) is typical of a efficient micellar incorporation of a substrate decomposing spontaneously with $k_m < k_w$.[15a] In CTAB micelles, as a limit, k_w/k_w was 0.5. CTAB micelles are known to produce a decrease of the pK_a of several different acids;[1] thus, one would not expect inhibition, but rather activation, if the effect of the micelles were related to the relative amount of carbanion. CTAB activates the E1cB hydrolysis of *o*-nitrophenyl cyanoacetate (NPCA) at pHs lower than the pK_a of the substrate.[16] At higher pHs, where the addition of CTAB cannot increase the relative proportion of the carbanion, positively charged micelles inhibit the decomposition of NPCA.[16] Direct experimental proof for the lack of CTAB effect on the relative concentration of the carbanion of I was obtained showing that the initial absorbance, which measures the amount of dissociated carbanion (see the Experimental Section), does not change upon CTAB addition (not shown). Another possible source of CTAB inhibition is the reversal of phenoxide elimination (Scheme I). Although highly unlikely,[9] this latter possibility was discarded, showing that the rate of decomposition of I, in the presence or absence of 0.05 M CTAB, was unaffected by the addition of either phenol or *m*-nitrophenol in a final concentration equal to 10 times the substrate concentration (not shown). The simplest way to explain the inhibition by CTAB in this reaction is postulating a larger stabilization of the initial state, in relation to the transition

---

(7) (a) Baptista, M. S.; Politi, M. J. *J. Phys. Chem.* **1991**, *95*, 5932–5942. (b) da Silva, M. B.; Cuccovia, I.; Chaimovich, H.; Politi, M. J.; Reed, W. F. *J. Phys. Chem.*, in press.

(8) Berezin, I. V.; Martinek, K.; Yatsimirskii, A. K. *Russ. Chem. Rev.* (*Engl. Ed.*) **1973**, *42*, 787–802.

(9) (a) Alborz, M.; Douglas, K. T. *J. Chem. Soc., Chem. Commun.* **1980**, 728–730. (b) Alborz, M.; Douglas, K. T. *J. Chem. Soc., Perkin Trans. 2* **1982**, 331–339.

(10) Harrold, S. P. *J. Colloid Sci.* **1960**, *15*, 280–288.

(11) Kaatze, U.; Müller, S. C.; Eibl, H. *Chem. Phys. Lipids* **1980**, *27*, 263–280.

(12) Impure LPC catalyzed the decomposition of I, presumably because fatty acids are solubilized in LPC micelles yielding a negatively charged aggregate. Addition of fatty acids to micelles obtained from pure LPC caused progressive rate enhancement.

(13) Fernandez, M. S.; Fromhertz, P. *J. Phys. Chem.* **1977**, *81*, 1755–1761.

(14) Sepulveda, L.; Lissi, E.; Quina, F. H. *Adv. Colloid Interface Sci.* **1986**, *25*, 1–58.

(15) (a) Quina, F. H.; Chaimovich, H. *J. Phys. Chem.* **1979**, *83*, 1844–1850. (b) Miola, L.; Abakerli, R. B.; Ginani, M. F.; Berci, P.; Toscano, V. G.; Quina, F. H. *J. Phys. Chem.* **1983**, *87*, 4417–4425.

(16) Al-Lohedan, H.; Bunton, C. A. *J. Am. Chem. Soc.* **1981**, *46*, 3929–2930.

state by electrostatic interaction of I with the alkylammonium group of the detergent. Negatively charged aromatics are located at the micellar surface in CTAB,[17] and cationic head groups interact most strongly with anions exhibiting dispersed charge.[1b] Therefore, the inhibition by CTAB can be understood in terms of a small decrease in the interaction energy between I and the alkylammonium head group in the micelle in going from a charge-dispersed initial state to a charge-localized transition state.

Zwitterionic micelles of *N*-hexadecyl-*N*,*N*-dimethylammonium 3-propanesulfonate (HPS) inhibited the spontaneous decomposition of I (Figure 1B). The inhibition by HPS, where the positively charged alkylammonium group must reside very close to the hydrocarbon interface is even higher than that caused by CTAB (Figure 1). HPS micelles efficiently bind hydrophobic anions at the interface, and these anions can be displaced by addition of salt, suggesting that the binding site is near the alkylammonium moiety.[7a] Inhibition by HPS can be explained using the same arguments used for rationalizing CTAB inhibition of the decomposition of I. Zwitterionic betaine-derived micelles catalyze the unimolecular decompositions of hydrophobic anions where there is charge dispersion in the transition state.[18] In the present case HPS micelles inhibit the reaction (Figure 1B), strengthening our suggestion that the initial state for the decomposition of I is more stabilized by interaction with the alkylammonium group than the corresponding transition state.

Micelles of hexadecylphosphorylcholine (HDPC), where the monomer dipole is inverted when compared with HPS (Chart I), inhibited the decomposition of I, but to a smaller extent than HPS micelles (Figure 1B). Selective binding of hydrophobic anions to dipole-inverted zwitterionic micelles has been described, and it is not evident whether the choline group is perpendicular to the micellar interface.[7a] Thus, inhibition by HDPC can be rationalized in terms of the stabilization of the initial state by the formation of an ion pair of the substrate with the choline moiety of the detergent. Lysophosphatidylcholine (LPC) micelles did not affect the rate of decomposition of I (Figure 1B). Spontaneous decarboxylations with charge dispersal in the transition state are catalyzed efficiently by betaine micelles and very little affected by LPC micelles.[19] Therefore, in both the case of catalysis[19] or inhibition the effect of LPC micelles is smaller than other zwitterionic systems, even when compared with HDPC, an analogue where the monomer has the same relative orientation of the hydrophilic dipole. The choline group is more mobile in LPC than in HDCP micelles.[11] Thus, any rate modification caused by the interaction of the choline group with a substrate should be less effective with LPC.

Negatively charged micelles of sodium dodecyl sulfate (SDS) catalyzed the spontaneous decomposition of I (Figure 1). The inhibitory effect of HPC micelles and the small activation obtained with Brij-35 strongly suggest that the observed catalysis by SDS is not due simply to a change in the local dielectric constant. Several probes have been used to measure the local or effective dielectric constant of micelles.[1] Although the values of the local parameter vary with the probe, there are no major disputes in that, at the micellar surface, independent of the nature of the detergent, the effective polarity is lower than water, higher than a hydrocarbon solvent, and comparable to a solvent such as ethanol.[1] Therefore, the effect of SDS cannot be due to a change in the local dielectric constant.

Addition of SDS caused an increase in the observed rate constant (k_ψ), reaching a plateau at high detergent concentration (Figure 1A). The shape of this k_ψ/detergent function is typical of the effect of detergent in the rate of a unimolecular reaction where $k_m > k_w$.[1] Since the substrate is not neutral and behaves as a pseudomonomer,[15] the value of k_m can only be calculated from these data using two adjustable parameters, i.e., k_m and the substrate incorporation constant. The minimum value for the catalysis of the decomposition of I by SDS (k_m/k_w) is 2.0 (Figure 1).[15] In absolute terms, the catalytic efficiency of the SDS micelle is modest. In the case of detergents containing a alkylammonium group, postulating an ion pair as the source of the inhibition is the simplest form to explain the inhibition. In the case of SDS it is difficult to rationalize the rate enhancement in terms of specific interactions between the negatively charged initial state and the head group sulfate. The simplest way to explain the results is by proposing that catalysis by (the negatively charged micellar) SDS stems from the Coulombic destabilization of the initial state.

Unfavorable initial state Coulombic interactions are important in enzymatic catalysis.[20] It is obvious, however, that the precise orientation observed in enzyme–substrate complexes cannot be achieved in micellar solubilized substrates. We have shown that Coulombic destabilization of the initial state can be achieved with charged micelles, and even though the catalytic factors are relatively small, the nature of the effect is clear. Moreover, the inhibition by ionic and zwitterionic micelles can also be rationalized in terms of differential Coulombic interactions between the head groups and the initial and transition states for the unimolecular decomposition of I.

Acknowledgment. This work was partially supported by grants from the following Brazilian Agencies: CAPES, CNPq, FAPESP, FINEP, BID-USP. We thank Dr. M. Armelin for her help with the paper and Marcia A. da Silva, Benedita Pereira, and Neusa M. S. Ferreira for excellent technical help. We also thank the reviewers for valuable suggestions made on an earlier version of this paper.

Registry No. I, 75761-85-2.

---

[17] Bacaloglu, R.; Bunton, C. A.; Cerichelli, G.; Ortega, F. *J. Phys. Chem.* **1989**, *93*, 1490–1497.

[18] Meyer, G. *J. Org. Chem.* **1979**, *44*, 3983–3984.

[19] Bunton, C. A.; Kamego, A. A.; Minch, M. M.; Wright, J. L. *J. Org. Chem.* **1975**, *40*, 1321–1327.

[20] Jencks, W. P. In *Advances in Enzymology and Related Areas of Molecular Biology*; Meister, A., Ed.; Wiley: New York, 1975; Vol. 43, pp 219–410.