PAPER

NJC
www.rsc.org/njc

Tautomerization of 2-acetylcyclohexanone in assemblies of cationic surfactants

Emilia Iglesias

Departamento de Química Física e E. Q. I., Facultad de Ciencias, Universidad de La Coruña, 15071 La Coruña, Spain. E-mail: qfemilia@udc.es

Received (in Montpellier, France) 30th September 2004, Accepted 23rd November 2004
First published as an Advance Article on the web 27th January 2005

The kinetic study of the keto-enol interconversion of 2-acetylcyclohexanone (ACHE) has been performed in organic solvents such as dimethylsulfoxide, 1-propanol, 2-propanol, methanol, dioxane, tetrahydrofuran and acetonitrile, as well as in aqueous micellar solutions of the cationic surfactants tetradecyltrimethylammonium chloride and tetradecyltrimethylammonium bromide at 25 °C. Either the solvent-assisted or H^+-catalyzed reaction rates of tautomerization are reduced in both organic solvents and in micellar medium. In 70% v/v solvent–water or at fixed concentration of any cationic surfactant, the observed rate constant moderately increases with $[H^+]$. The nitrosation of the enol has also been studied in micellar solutions of both cationic and anionic surfactants. Under experimental conditions of first-order dependence on $[H^+]$, [nitrite], and $[X^-]$ (X = Cl or Br), the presence of cationic micelles reduces strongly the rate of nitrosation, whereas in the presence of anionic micelles, the first-order rate constant, k_o, goes through a maximum on increasing the surfactant concentration.

Introduction

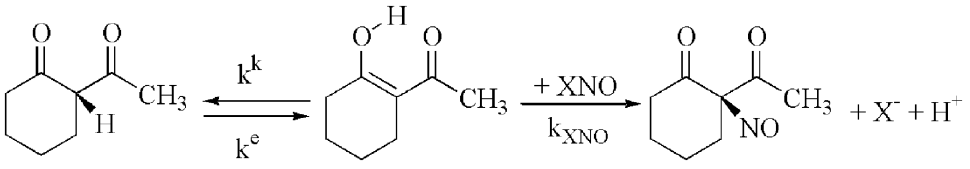
Aqueous micellar solutions are highly anisotropic solvents whose properties change gradually between those of pure water to those of hydrocarbon-like liquids on going from the bulk water phase to the interior of the micelle (the micellar core).[1–5] Because of this, the presence of micelles affects reaction rates and equilibria. The keto-enol equilibrium of 1,3-dicarbonyl compounds is largely influenced in aqueous micellar media due to its extremely sensitive dependence on the solvent nature.[6–9] The origin of this phenomenon resides in the difference of molecular interactions between the solvent and the keto or enol tautomers. Hydrogen-bonding interactions with solvent molecules stabilize the keto tautomer, which predominates in hydrogen-bond donor solvents, whereas aprotic and/or apolar solvents increase the enol content due to enol stabilization by intramolecular hydrogen bonding.

Under equilibrium conditions, more than 40% of the total 2-acetylcyclohexanone (ACHE) concentration exists in water in the enol form. This percentage increases strongly in organic solvents such as dioxane. On the other hand, since the tautomerization in the ACHE system occurs slowly, it is possible to study the approach to equilibrium by using conventional methods.

In a previous work, the characterization of the keto-enol equilibrium of ACHE in water in both acid and basic medium was presented.[10] In aqueous neutral or acid medium, a mixture of both keto and enol tautomers exists at equilibrium; the corresponding equilibrium constant has been measured to be $K_E = 0.72$. The absorption band centred at 291 nm ($\varepsilon_{EH} = 15\,300\ M^{-1}\ cm^{-1}$) due to the enol, shifts in alkaline medium to higher wavelength ($\lambda_{max} = 309$ nm, $\varepsilon_E = 32\,000\ M^{-1}\ cm^{-1}$) due to the enolate formation. The overall pK_a was determined as 9.85. The subsequent acidification of an alkaline solution of ACHE yields the enol tautomer in stoichiometric proportions, which then tautomerizes slowly to the keto form until the equilibrium proportions are reached again. The kinetic features of enol ketonization in water have been investigated. The observed rate constant, k_o, remains practically unchanged on varying the ionic strength of the aqueous medium. Nevertheless, k_o increases smoothly with $[H^+]$, resulting in $k_o = k_w + k_H[H^+]$ with $k_w = 1.4 \times 10^{-3}\ s^{-1}$ and $k_H = 5.8 \times 10^{-3}\ M^{-1}\ s^{-1}$ at 25 °C in water; these values are strongly reduced in D_2O. In contrast, the rates of enol-ketonization are highly accelerated in aqueous buffered solutions of acetic acid–acetate and its chloride derivatives. The measured rate constants increase with both the pH of the reaction medium and the total buffer concentration.

Moreover, we showed that the enol of ACHE reacts with nitrosating agents XNO (X = H_2O, Cl, Br or SCN) to give the C-nitroso compound (Scheme 1). The reaction performed in water showed a first-order dependence with respect to both [nitrite] and [ACHE]; nevertheless, contrary to other common nitrosation reactions, the observed rate constant increases with both $[H^+]$ and $[X^-]$ (X = Cl, Br or SCN) by following nonlinear relationships.

These experimental findings were interpreted on the basis of a reaction mechanism, in which the slow reaction path is the



Scheme 1

DOI: 10.1039/b415219k

O → C internal rearrangement of the NO^+ group occurring in the chelate–nitrosyl complex intermediate that is generated at steady-state concentrations in the preceding reaction step between the enol and the nitrosation agent, XNO.[11] The same reaction mechanism has been proposed in the interpretation of previous results obtained in the nitrosation of different substrates, like 2-acetylcyclopentanone[9] or aliphatic nitro compounds,[12] but the presence of the intermediate was not required in the mechanistic explanation of the results obtained in the nitrosation of many simple enols[13,14] or even in enols of other 1,3-dicarbonyl compounds.[15]

The present report details the results obtained in the kinetic study of both keto enolization and enol nitrosation of ACHE performed in organic solvents and in aqueous micellar solutions of cationic surfactants forming micelles.

Experimental

2-Acetylcyclohexanone, a Merck product of the highest available purity, was used as supplied. Surfactants, dodecyltrimethylammonium bromide (DTABr), tetradecyltrimethylammonium bromide (TTABr), cetyltrimethylammonium bromide (CTABr) and sodium dodecyl sulfate (SDS), of the highest purity were used without further purification; tetradecyltrimethylammonium chloride (TTACl) was prepared by using an ion exchange resin. Organic solvents of spectrophotometric grade were from Merck. All other reagents were also purchased from Merck and used as received. Aqueous solutions were prepared with doubly distilled water obtained from a permanganate solution. Freshly prepared solutions were used in all experiments.

A double-beam UV-visible spectrophotometer, equipped with a thermostatted cell holder, was used in monitoring reaction rates by following the changes in absorbance at λ = 291 nm due to the enol absorption. A matched pair of quartz cells with a ℓ = 1 cm light path was used. Kinetic measurements were carried out under pseudo-first-order conditions, with ACHE being the limiting reagent. In every case, the experimental data (absorbance A and time t) fit to eqn. (1):

$$A = A_\infty + (A_\infty - A_0)e^{-k_o t} \quad (1)$$

where A_0, A_∞ and A mean absorbance readings at times 0, infinity and t, respectively, and k_o represents the pseudo-first-order rate constant.

To measure rates of nitrosation, the decrease in absorbance at 291 nm was monitored as a function of time. In contrast with the tautomerization process, here the A_∞ values are in every case close to zero ($A_\infty < 0.05$) due to complete consumption of the enol, the limiting reagent, whilst the initial absorbance readings are also constant but equal to approximately 0.90. The observed rate constant of tautomerization is the sum of the rate constants corresponding to enol ketonization, k_o^k, and keto enolization: k_o^e ($k_o = k_o^k + k_o^e$).

Results and discussion

Tautomerization

General features. Addition of an aliquot of a concentrated dioxane solution of ACHE to a neutral or acidic water sample caused a loss of the intensity of the maximum absorption band centred at 291 nm. In contrast, an increase of the absorbance at 291 nm was observed when an aliquot of a solution in water of ACHE was diluted into a high volume of any organic solvent or into an aqueous micellar medium. These findings indicate that tautomerization of ACHE occurs at rates sufficient for monitoring the effects of various solvents on the reaction rate. Several organic solvents and aqueous micellar solutions of surfactants forming micelles were investigated. The reaction can occur *via* an acid-catalyzed (k_H) pathway and an uncatalyzed (k_u) pathway [eqn. (2)]:

$$k_o = k_u + k_H[H^+] \quad (2)$$

Organic solvents. Rates of tautomerization have been measured as a function of $[H^+]$ (HCl) in 70% v/v aqueous mixtures (the water concentration was equal to 16.7 M in every case) of the organic solvents dimethylsulfoxide (DMSO), 1-propanol (1-PrOH), 2-propanol (2-PrOH), methanol (MeOH), tetrahydrofuran (THF), dioxane and acetonitrile (MeCN). A moderate catalysis by H^+ according to eqn. (2) was observed. The linear least-squares fitting of k_o *versus* $[H^+]$ affords the values of k_u and k_H, which are listed in Table 1 along with some properties of the solvent. Also in Table 1 is given k_u, measured, when possible, in 96.7% v/v organic solvent–water ($[H_2O]$ = 1.85 M). In dioxane or MeCN no enolization reaction seemed to occur under these conditions (the absorbance at 291 nm remained unchanged during at least 3 h). For comparative purposes, data obtained for enol ketonization in water are also included .

As the observed process is an approach to equilibrium, k_o is the sum of the rate constants of the forward (k_o^e, enolization) and backward (k_o^k, ketonization) reactions. The separation of both rate constants is possible through eqn. (3) if the keto-enol equilibrium constant in the corresponding medium, K'_E, is known. The calculation of K'_E can be done using the appropriate combination of initial (A_0) and infinite (A_∞) absorbance values measured in the same kinetic experiment [eqn. (1)]. The expressions of eqn. (4) were used to relate these parameters with the total concentration of ACHE, where ε_{EH} represents the molar extinction coefficient of the enol and ℓ, the optical path length (= 1 cm).

$$k_o^e = k_o \frac{K'_E}{1 + K'_E} \text{ and } k_o^k = k_o \frac{1}{1 + K'_E} \quad (3)$$

$$A_0 = \varepsilon_{EH}\ell \frac{K_E}{1 + K_E}[ACHE]_0 \text{ and}$$
$$A_\infty = \varepsilon_{EH}\ell \frac{K'_E}{1 + K'_E}[ACHE]_0 \quad (4)$$

Table 1 Solvent characteristics and the uncatalyzed, k_u, and H^+-catalyzed, k_H, rate constants for the enolization of the keto tautomer of ACHE in 70% v/v organic solvent–water mixture at 25 °C

Solvent	ε^a	μ/D^b	$k_u/10^{-4}$ s^{-1}	$k_H/10^{-3}$ mol^{-1}dm^3 s^{-1}	K'_E ^{c}	k_u/ s^{-1} ^{d}
H_2O	78.5	1.8	13.9^e	5.8^e	0.72	
DMSO	46.5	4.05	5.71 ± 0.04	1.94 ± 0.06	1.8	0.84×10^{-4}
1-PrOH	20.5	1.65	6.10 ± 0.01	1.33 ± 0.02	2.8	2.74×10^{-4}
2-PrOH	19.9	1.65	6.19 ± 0.04	1.24 ± 0.05	2.8	—
MeOH	32.7	1.71	3.92 ± 0.03	2.05 ± 0.04	2.0	2.73×10^{-4}
THF	7.6	1.74	2.76 ± 0.04	1.27 ± 0.05	3.1	—
Dioxane	2.2	0.45	1.03 ± 0.05	2.74 ± 0.06	1.9	~0
MeCN	35.9	3.54	0.087 ± 0.036	2.64 ± 0.05	2.0	~0

^{a} Relative dielectric constant. ^{b} Dipole moment; D = 3.336×10^{-30} cm. ^{c} Average value of at least ten determinations. ^{d} In 96.7% solvent–water, no added acid. ^{e} Ref. 10.

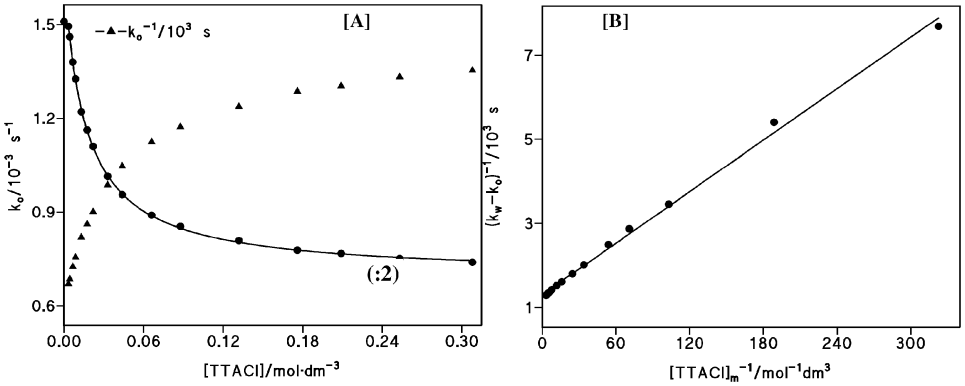


Fig. 1 (A) Variation of k_o (•) and of $1/k_o$ (▲) obtained in the keto-enol tautomerization of ACHE in aqueous micellar solutions of TTACl at $[H^+] = 0.030$ M as a function of the surfactant concentration. The solid line fits eqn. (5); for parameters see text. (B) Plot of eqn. (5) in the linear form; the straight line represents the linear regression $(1300 \pm 30) + (20.4 \pm 0.3) \times (1/[TTACl]_m)$.

To obtain K'_E, it is indispensable to know K_E, the keto-enol equilibrium constant in water. Several methods have been followed to estimate K_E. In the first one,[10] we checked the Beer–Lambert law validity in water under nonequilibrium conditions; the resulting value was $K_E = 0.72$. In a second method,[11] the effect of aqueous β-cyclodextrin solutions on the position of the keto-enol equilibrium in ACHE system was used to obtain $K_E = 0.69$. In a third method,[6] we followed the procedure developed in the case of benzoylacetone,[7] which analyzes the changes in the absorption spectrum of the substrate as a function of surfactant concentration: a fixed amount of ACHE was dissolved in aqueous micellar solutions of variable surfactant concentration; after giving the solutions enough time to reach equilibrium, the absorbance readings at 291 taken at different [surfactant] were quantitatively analyzed. The derived value was $K_E = 0.75$. Therefore, in this study we used the mean value of $K_E = 0.72$ to obtain K'_E reported in Table 1 by applying eqn. (4).

The tautomerization rates assisted by the solvent (*i.e.*, k_u) are lower than the half-value determined in water and no clear trend with the solvent polarity or the dielectric constant is observed. The bimolecular rate constant for the water-assisted tautomerization can be determined as $k_{H_2O} = k_u/[H_2O] = 2.5 \times 10^{-5}$ M^{-1} s^{-1}.[10] If one assumes the same value for the rate in 70% v/v organic solvents–water, then the expected value of k_u in these water mixtures, where $[H_2O] = 16.7$ M, is 4.2×10^{-4} s^{-1}, which is practically equal to the rate constant measured in 70% MeOH–water. In DMSO and 1-PrOH and 2-PrOH, the measured k_u is slightly higher, whereas in THF, dioxane, and MeCN, k_u values are considerably lower. In fact, the comparison between the results obtained in DMSO and in MeCN, that is, two solvents of quite similar dielectric constants and dipole moments, shows that k_u obtained in DMSO is more than 60 times that in MeCN. A key difference between both solvents is that whereas DMSO is a good hydrogen-bond acceptor, MeCN is neither a good hydrogen-bond acceptor nor donor. The alcohols are good H-bond donors and acceptors, whilst THF and dioxane are H-bond acceptors, even though their solvation capabilities are notably lower. Therefore, it can be concluded that the H-bond donor or acceptor ability of a solvent is the most important property in controlling solvent-assisted rates of tautomerization. Finally, the H^+-catalyzed tautomerization rates, that is, the k_H values, no longer depend on the solvent nature, but they are clearly lower than the value measured in pure water. By decreasing the water content, one also decreases the acidity of H_3O^+ and its solvation.

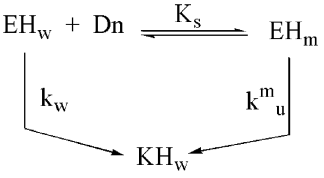
Aqueous micellar solutions. Rates of tautomerization of ACHE in aqueous micellar solutions of TTACl have been measured at fixed $[H^+]$ (0.030 M, HCl). To start the reaction, 10 μl of a stock ACHE (0.18 M) solution in dioxane were diluted into 3.0 ml of an aqueous solution containing the rest of the reagents. In dioxane, ACHE exists in the enol (EH) form; in fact, the initial absorbance ($A_0 = \varepsilon_{EH}\ell[ACHE]_0$) at 291 nm takes a constant value of around $A_0 = 0.900$, whatever the [surfactant].

Upon increasing the surfactant concentration over the cmc (critical micelle concentration), that is, the micellar pseudophase, the observed rate constant (k_o) decreases, but the reciprocal plot of k_o against [TTACl] is not a straight line; nevertheless, the values of $(k_w - k_o)^{-1}$, with k_w being the rate constant measured in the absence of surfactant, increase proportional to $1/[TTACl]_m$, see Fig. 1. These facts indicate that the reaction also goes in the micellar phase, even though the rate is lower than that in water. The corresponding reaction mechanism appears in Scheme 2, where Dn indicates micellized surfactant. Taking into account that the overall reaction rate is the sum of the rate in water and in the micellar phase, the expression of k_o derived from Scheme 2 is given in eqn. (5), originally derived by Menger and Portnoy.[16]

$$k_o = \frac{k_w + k_u^m K_s [TTACl]_m}{1 + K_s [TTACl]_m} \qquad (5)$$

The nonlinear regression analysis of the experimental points by means of eqn. (5) gives the solid curve drawn in Fig. 1(A) for $k_w = (1.51 \pm 0.01) \times 10^{-3}$ s^{-1}; $k_u^m = (6.96 \pm 0.03) \times 10^{-4}$ s^{-1}; $K_s = 51.3 \pm 0.9$ M^{-1} and the cmc $= 3.5 \times 10^{-3}$ M. The extrapolated k_w is in good agreement with that measured in water at the same $[H^+]$; likewise, k_u^m compares quite well with the k_u values determined in aqueous mixtures of DMSO or alcohols (Table 1). This rate constant measures the reactivity at the positively charged micellar interface, where $[H^+]$ would be negligible due to electrostatic repulsions and the concentration of water is also reduced. Both characteristics explain the agreement between k_u^m and k_u, the latter being measured in DMSO of alcohols.

On the other hand, the absorbance at infinite time (A_∞), that is, once the keto-enol equilibrium is established, increases with [TTACl] due to the presence of micelles. This enhances the enol concentration, which is proportional to A_∞ { $= \varepsilon_{EH}\ell[ACHE]_o$-$K_E^{ap}/(1 + K_E^{ap})$}, where K_E^{ap} is given by eqn. (6), and has been determined experimentally at each [TTACl] as the quotient of the experimental readings of A_∞ and $(A_0 - A_\infty)$. In contrast, the difference $A_0 - A_\infty$, which is proportional to the concentration



Scheme 2

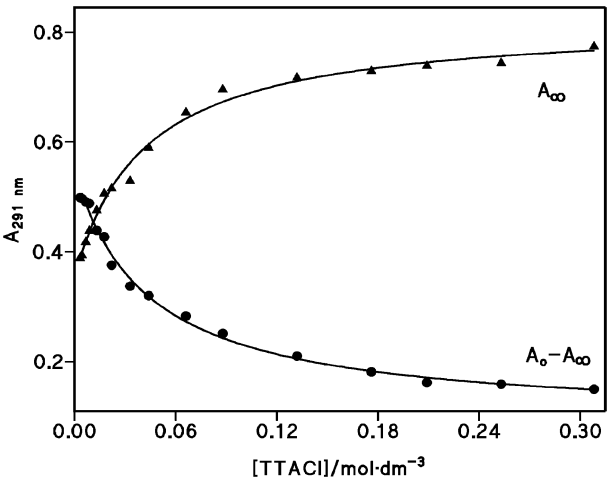


Fig. 2 Influence of [TTACl] on both experimental A_∞ and $(A_0 - A_\infty)$; solid lines fit eqns. (8) and (9), respectively; for parameters, see text.

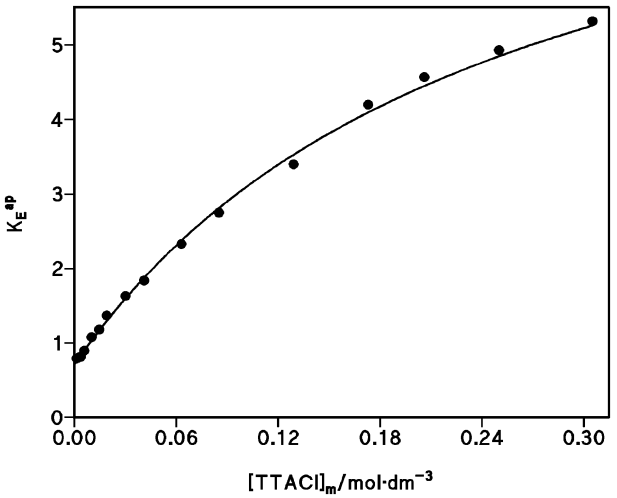


Fig. 3 Variation of K_E^{ap}, determined from $A_\infty/(A_0 - A_\infty)$, as a function of the micellized surfactant concentration. The solid line fits eqn. (7); for parameters, see text.

of the keto form, diminishes upon increasing the TTACl concentration, see Fig. 2.

$$K_E^{ap} = \frac{[EH]_w + [EH]_m}{[KH]_w + [KH]_m} = \frac{A_\infty}{A_0 - A_\infty} \qquad (6)$$

Under equilibrium conditions, the reaction scheme that considers all possible distributions is displayed in Scheme 3. From this scheme, the expression of eqn. (6) can be transformed into eqn. (7) to give the variation of K_E^{ap} as a function of micellized [TTACl]. The corresponding plot can be seen in Fig. 3, clearly displaying a curvature, meaning that the association of the keto form to the micelle is not negligible, in contrast to other cases.[7–9,15]

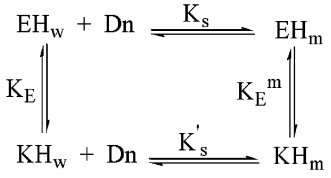
$$K_E^{ap} = \frac{K_E(1 + K_s[TTACl]_m)}{1 + K'_s[TTACl]_m} \qquad (7)$$

The curve in Fig. 3 was drawn by the fit of eqn. (7) to the experimental points with $K_E = 0.71 \pm 0.03$; $K_s = 51 \pm 2\ M^{-1}$; $K'_s = 4.0 \pm 0.3\ M^{-1}$, and correlation coefficient (cc) = 0.999. A good concordance between the K_s values determined here and in the analysis of k_o can be seen. Similarly, K_E agrees perfectly with the values determined in previous studies, *vide supra*.[6,10–11] Notice also the lower association to micelles of the keto than the enol form; the value of K'_s implies that less than 10% of the total ACHE concentration is in the micellar phase in its ketonic form. In fact, for other 1,3-dicarbonyl compounds the association of the keto form has not been detected.

Moreover, taking into account that $A_\infty = \varepsilon_{EH}\ell([EH]_w + [EH]_m)$, the expression in eqn. (7), and that $[ACHE]_0 = [EH]_w + [EH]_m + [KH]_w + [KH]_m$, it is easy to arrive at eqns. (8) and (9) to relate the variation of both A_∞ and $(A_0 - A_\infty)$ as a function of [Dn], the micellized surfactant concentration.

$$A_\infty = \frac{A_0 \frac{K_E}{1+K_E}(1 + K_s[Dn])}{1 + \frac{K'_s + K_E K_s}{1+K_E}[Dn]} \qquad (8)$$

$$A_0 - A_\infty = \frac{A_0 \frac{1}{1+K_E}(1 + K'_s[Dn])}{1 + \frac{K'_s + K_E K_s}{1+K_E}[Dn]} \qquad (9)$$



Scheme 3

The fit of eqn. (8) to the experimental points displayed in Fig. 2 draws the ascending curve with the following values of the unknown parameters: $A_0K_E/(1 + K_E) = 0.385 \pm 0.008$; $K_s = 49 \pm 6\ M^{-1}$ and $(K'_s + K_EK_s)/(1 + K_E) = 23 \pm 3\ M^{-1}$; in the same manner, the descending curve was drawn as the fit of eqn. (9) to the experimental data with $A_0/(1 + K_E) = 0.519 \pm 0.008$; $K'_s = 3.9 \pm 0.8\ M^{-1}$ and $(K'_s + K_EK_s)/(1 + K_E) = 22 \pm 2\ M^{-1}$. From these results, one gets $K_E = 0.74$ and $A_0 = 0.903$, in perfect agreement with the expected values. The good concordance in the values obtained for the same parameter from the various treatments that have been applied constitutes an indubitable proof of the validity of the proposed reaction mechanism.

Kinetic experiments at fixed [surfactant] and variable $[H^+]$ have also been performed. To start the reaction under these experimental conditions, 100 μl of a stock equilibrated solution of ACHE in water was diluted into 3 ml of a micellar solution. The increase in absorbance at 291 nm due to the neat conversion of the keto form into the enol form (mainly solubilized in the micellar phase) was monitored with time. The variation of the observed rate constant as a function of $[H^+]$ in 0.22 M of the cationic surfactants TTACl and TTABr is shown in Fig. 4. The least-squares adjustment of the experimental points yields the k_u^o and k_H^o values reported in Table 2. A similarity between these results and those determined in DMSO or in propyl alcohols can be noted, which could indicate *a priori* that, in the

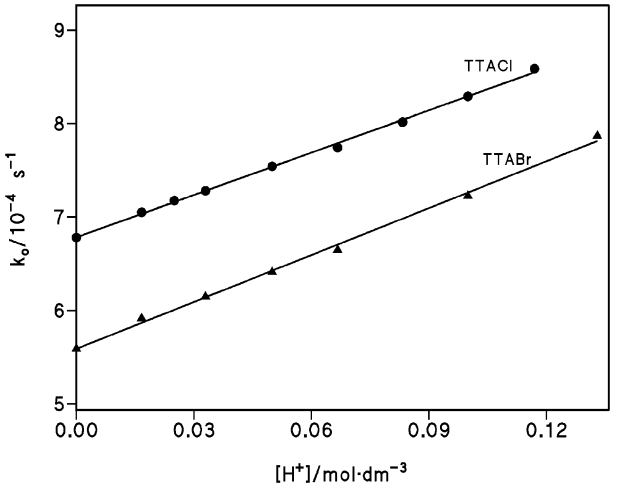
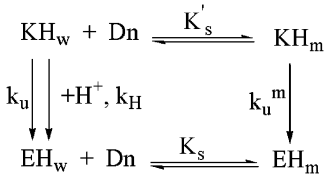


Fig. 4 Influence of $[H^+]$ on the observed rate constant obtained for the tautomerization of ACHE at a fixed surfactant concentration equal to [TTACl] = 0.22 M or [TTABr] = 0.25 M.

Table 2 Rate constants obtained in the study of the keto-enolization reaction of ACHE in aqueous micellar solutions of the indicated surfactants by investigating the variation of k_o as a function of $[H^+]$ (HCl)

Surfactant	cmc/M	k_u^o /10^{-4} s^{-1}	k_H^o /10^{-3} mol^{-1} dm^3 s^{-1}	K'_E[a]
TTACl (0.22 M)	3.5×10^{-3}	6.78 ± 0.01	1.51 ± 0.02	4.5
TTABr (0.25 M)	3.0×10^{-3}	5.60 ± 0.03	1.75 ± 0.03	4.8

[a] Average value of at least nine determinations obtained from the values of A_0 and A_∞.



Scheme 4

presence of micelles, the tautomerization reaction occurs in a region of low hydration, such as the micellar interface. Nevertheless, the H^+-catalyzed pathway cannot take place in this site due to electrostatic repulsion of H^+ ions by the positively charged micellar interface. Therefore, we consider Scheme 4 to interpret the experimental facts, which includes the fast distribution of both KH and EH between the water and micellar pseudo-phases and the slow conversion of excess keto into the enol.

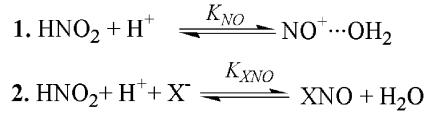
The total concentration of the initial keto form is given by: $[KH]_o = [KH]_w + [KH]_m = [ACHE]_o/(1 + K_E)$, with $K_E = 0.72$. On the other hand, rate $= (k_u + k_H[H^+])[KH]_w + k_u^m[KH]_m$. From these considerations and Scheme 4, the observed rate constant may be expressed by eqn. (10), which predicts a linear dependence of k_o *vs.* $[H^+]$, in agreement with the experiments.

$$k_o = k_u^o + k_H^o[H^+] = \frac{(k_u + k_u^m K'_s[Dn]) + k_H[H^+]}{(1 + K_E)(1 + K'_s[Dn])} \qquad (10)$$

The predicted values of k_u^o and k_H^o by application of eqn. (10) in the case of [Dn] = 0.22 M and the results previously determined for k_u, k_u^m , K'_s, K_E and k_H, affords $k_u^o = 6.2 \times 10^{-4}$ s^{-1} and $k_H^o = 1.79 \times 10^{-3}$ M^{-1} s^{-1}, in perfect agreement with the experimental results shown in Table 2.

Nitrosation

1,3-Diketones are readily nitrosated in water to yield 2-nitrosoketones, which are usually stable as oxime tautomers when an H atom is attached to the C-2.[17–19] The reaction involves enolization of the ketone, followed by electrophilic nitrosation of the enol. Therefore, the nitrosation reaction is a good method for enol detection. In aqueous acid medium of sodium nitrite (a stable salt), the nitrosating agents are generated in the protonation of HNO_2, as indicated in Scheme 5.[20] The concentration of NO^+ is very small due to the low value of $K_{NO} = 3.5 \times 10^{-7}$ M^{-1} (reaction 1 of Scheme 5); however, it is the most reactive nitrosating agent for the acid medium. In the presence of nonbasic anions, such as Cl^-, Br^-, SCN^-, *etc.*, new nitrosating agents, generally called XNO with X = Cl, Br, *etc.*, appear (reaction 2 of scheme 5). The concentration of XNO is always higher than that of NO^+, because K_{XNO} is higher than K_{NO} and equal to 1.14×10^{-3} for ClNO, 0.051 for BrNO, and 32 M^{-2} for SCNNO (all data at 25 °C).[21–23] Therefore, it is expected to observe catalysis by X^- in nitrosation reactions, even though the reactivity of XNO is lower than that of NO^+ and decreases in the order ClNO < BrNO < SCNNO, but the concentration effect overwhelms in many cases the low reactivity.



Scheme 5

The nitrosation of the enol of ACHE in the presence of micelles has been studied at $[H^+] = 0.015$ and 0.030 M and at [nitrite] = 1.7×10^{-3} M. The [ACHE] ($\sim 6 \times 10^{-5}$ M) was always much smaller than that of nitrite. To start the reaction, an aliquot (~ 10 μl) of a stock dioxane solution of ACHE was added to the sample (V = 3 ml) containing the rest of the reagents. The nitrosation of ACHE in water goes through an 'unusual' reaction mechanism for nitrosation.[11] However, under the above experimental conditions, the reaction rate shows a first-order dependence on $[H^+]$, [nitrite], and $[X^-]$, that is, $k_o = (k_1 + k_2[X^-])[H^+]$[nitrite], where k_1 and k_2 correspond to nitrosation *via* NO^+ and XNO, respectively. The reason for working under these conditions is to facilitate the interpretation of micellar effects.

Cationic surfactants. In the presence of TTACl, HCl was used to control acidity, while HBr was used in the case of TTABr, DTABr and CTABr micelles. On the other hand,

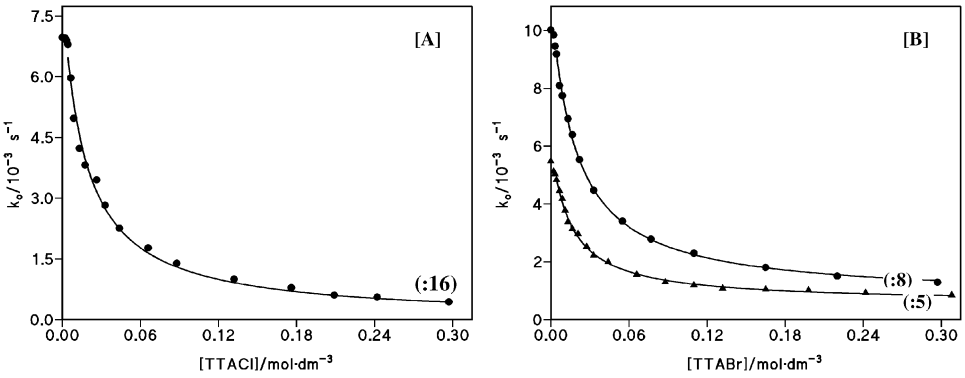


Fig. 5 Plot of k_o against (A) [TTACl], obtained in the nitrosation of ACHE in aqueous micellar solutions of TTACl at $[H^+] = 0.030$ M (HCl), and (B) [TTABr], obtained in the nitrosation of ACHE in aqueous micellar solutions of TTABr at $[H^+]$ equal to (•) 0.030 and (▲) 0.015 M, controlled with HBr, and at [nitrite] = 1.7×10^{-3} M at 25 °C.

Table 3 Experimental conditions and parameters of eqn. (11) for the nitrosation of ACHE in aqueous micellar solutions of the cationic surfactants at [nitrite] = 1.7×10^{-3} M at 25 °C (for the definition of the various terms, see text).

Surfactant	cmc/M	[acid]/M	Factor	$\delta/10^{-3}$ s^{-1}	$\delta^{cal}/10^{-3}$ s^{-1a}	$\phi/10^{-2}$ s^{-1}	$\phi^{cal}/10^{-2}$ s^{-1a}	K_s/M^{-1}
TTACl	3×10^{-3}	HCl (0.030)	16	7.0 ± 02	6.8	0.9 ± 0.6	1.0	56 ± 4
DTABr	1×10^{-2}	HBr (0.030)	4.5	9.9 ± 0.2	12.3	4.56 ± 0.15	4.2	37 ± 1
TTABr	3×10^{-3}	HBr (0.015)	8	5.2 ± 0.1	4.4	2.7 ± 0.4	2.1	58 ± 3
	3×10^{-3}	HBr (0.030)	5	9.7 ± 0.2	11.6	4.9 ± 0.2	4.2	53 ± 1
CTABr	3×10^{-4}	HBr (0.013)	$<2^b$	4.3 ± 0.3	3.6	2.3 ± 0.6	1.8	65 ± 6

[a] Rate constants used to calculate δ^{cal} and ϕ^{cal} [eqn. (11)] were taken from ref. 11: $k_1 = 110$ M^{-2} s^{-1}; $k_2 = k_{ClNO}K_{ClNO} = 787$ M^{-3} s^{-1}; $k_2 = k_{BrNO}K_{BrNO} = 4130$ M^{-3} s^{-1}; $K_{NO} = 3 \times 10^{-7}$ M^{-1}; $K_{ClNO} = 1.14 \times 10^{-3}$ M^{-2}; $K_{BrNO} = 0.051$ M^{-2}. [b] At the highest [CTABr] used, 0.02 M;

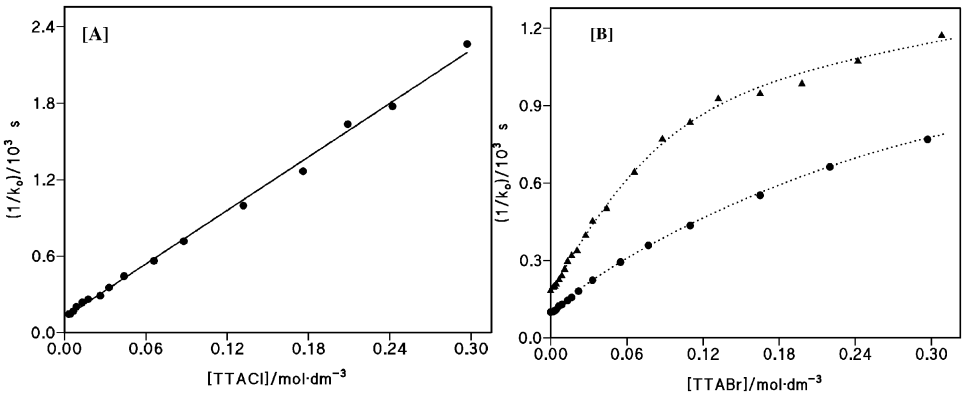
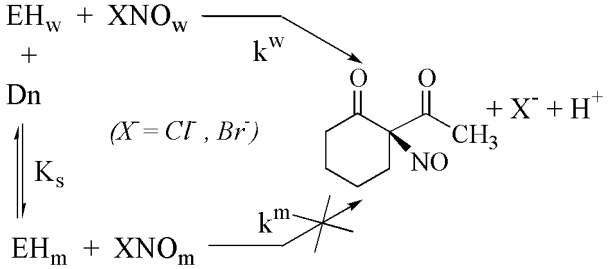


Fig. 6 Reciprocal plot of k_o against (A) [TTACl] and (B) [TTABr] obtained in the nitrosation of ACHE in aqueous micellar solutions of TTACl at [H$^+$] = 0.030 M (HCl) and of TTABr at [H$^+$] equal to (•) 0.030 M and (▲) 0.015 M, controlled with HBr, and at [nitrite] = 1.7×10^{-3} M.

under the above experimental conditions, the maximum concentration of NO_2^- is lower than 0.13×10^{-3} M, hence, one cannot expected a significant displacement of the surfactant counterions Cl^- or Br^- due to ionic exchange with NO_2^-. Whatever the cationic surfactant, k_o decreases as the [surfactant] increases (Fig. 5 shows two representative cases). However, the overall inhibition factor varies with the nature of the counterion (higher with Cl^- than with Br^-) and with the hydrocarbon chain length (Table 3). In addition, a comparison between Fig. 2 and Fig. 6 shows, firstly, that nitrosation is faster than tautomerization and, secondly, that the overall inhibition observed in nitrosation is higher than in tautomerization.

Still, the results displayed in Fig. 6 indicate that, whereas the reciprocal plot of k_o against [TTACl] makes a good straight line, in the case of TTABr the variation of $1/k_o$ is not a linear function of [TTABr]. Similar behaviour is observed with DTABr. The former finding is often attributed to the absence of reaction in the micellar phase, whereas the latter is typical of reaction occurring in both water and micellar phases.

Nevertheless, the following reasons are in opposition to any reaction in the micellar phase. Starting from Scheme 6, the distribution of the enol between the water and micellar pseudophases must be considered, with K_s being the equilibrium constant. Then the total ACHE concentration is $[ACHE]_0 = [EH]_w + [EH]_m$ ([KH] is negligible as the nitrosation is much faster than tautomerization). The nitrosation is catalyzed by



Scheme 6

Cl^- or Br^-, whose concentrations in water increase with [TTACl] and [TTABr], respectively (near 20% of the counterions are ionized), that is $[X^-]_0 = [X^-]_{ad} + cmc + \alpha[TTAX]_m$, where $[X^-]_{ad}$ is the added amount with the acid (HCl or HBr); cmc is the critical micelle concentration, and α is the degree of micelle ionization.[24,25] Therefore, considering *a priori* reaction only in the water phase, then rate = $k^w[EH]_w[XNO]_w$. The symbol XNO refers to the nitrosation agents present under the experimental conditions, that is, NO^+ and ClNO or BrNO, respectively, in the presence of Cl^- or Br^-. All these considerations lend us to eqn. (11), in which $k_1 = k_{NO}K_{NO} = 110$ M^{-2} s^{-1} has been determined for the nitrosation by NO^+ in water in the absence of micelles; in the same manner, $k_2 = k_{XNO}K_{XNO}$, equal to 787 or 4130 M^{-3} s^{-1} when $X^- = Cl^-$ or Br^-, respectively, refers to nitrosation *via* ClNO or BrNO; K_s is the binding constant of the enol to micelles and $[TTAX]_m$ is the micellized surfactant concentration.

$$k_o = \frac{(k_1 + k_2[X^-]_{ad}) + k_2\alpha[TTAX]_m}{1 + K_s[TTAX]_m}[H^+][\text{nitrite}]$$

$$= \frac{\delta + \phi[TTAX]_m}{1 + K_s[TTAX]_m} \quad (11)$$

The plot of k_o against $[TTAX]_m$ has been fit to this equation by using nonlinear regression analysis. Full lines in Fig. 5(A) and 5(B) were constructed by application of eqn. (11) and the values of δ {$= (k_1 + k_2[X^-]_{ad})[H^+][\text{nitrite}]$}, ϕ ($= k_2\alpha$ [H$^+$][nitrite]) and K_s listed in Table 3. These values are compared with the calculated ones, δ^{cal} and ϕ^{cal}, relative to our experimental conditions and using k_1 and k_2 determined in water and reported in the table. The good agreement between ϕ and ϕ^{cal} rules out any possibility of reaction in the micellar phase, or, at the least, indicates a very low contribution of this reaction pathway. To understand this, one should keep in mind the very low [XNO] in water and, consequently, in the micellar interface, as well as the slower rate of nitrosation in the micellar interface than in water. Moreover, the agreement of the K_s values obtained here and in the previous section on the study of tautomerization is in favour of the mechanistic treatment. In

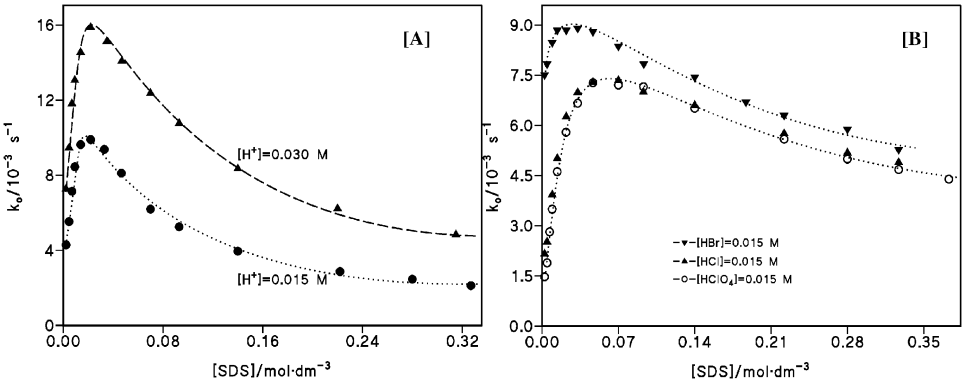


Fig. 7 Plots of k_o against [SDS] for the nitrosation of (A) 2-acetylcyclohexanone at [nitrite] = 1.7 mM in the presence of $HClO_4$ and of (B) 2-acetylcyclopentanone at [nitrite] = 1.7 mM and 0.015 M of the indicated strong acid.

conclusion, the inhibition effect of cationic micelles in the nitrosation of the enol by XNO is a consequence of the reactants' separation; the increase of the enol bound to micelles parallels the increase of XNO in water. The different degree of inhibition observed between TTACl and TTABr is because in the latter the inhibition, due to separation of the reagents, is in part overwhelmed by the increase in the concentration of BrNO ($K_{BrNO} > K_{ClNO}$) parallel with TTABr.

Anionic surfactants. The influence of SDS on the nitrosation rates of ACHE was analyzed under the same experimental conditions as for cationic surfactants, except that the acid used was $HClO_4$. The results are compared with those obtained in the nitrosation of 2-acetylcyclopentanone (ACPE),[9] in which the keto-enol tautomerization is fast but the kinetic features of the nitrosation reaction in water are the same as for ACHE.[11]

Fig. 7 displays typical results of the variation of k_o as a function of [SDS]. The maxima in the k_o–[SDS] profiles are for nonsolvolytic reactions carried out in the presence of surfactants with inert counterions. The rate equation for enol nitrosation under the experimental conditions of the present study is rate = $k[H^+][\text{nitrite}][\text{EH}]$. Binding of the enol (EH) and H^+ to SDS micelles begins at the cmc, hence the concentration of both reagents in the small volume of the micelle explains the sharp increase in k_o; however, the continuous dilution of the reaction within the micellar interface with the increase in [SDS] causes a decrease in k_o.

The qualitative analysis of the data shows that the maximum catalytic effect is higher for ACPE (~5 fold) than for ACHE (~2.5 fold) and that the [SDS] at which k_o reaches its highest value is, approximately, 0.07 M for ACPE but only 0.02 M for ACHE. These two kinetic features reflect the importance of reactant dilution. The enol of ACHE binds to SDS micelles (K_s = 78 M^{-1})[6] stronger than the enol of ACPE (K_s = 23.7 M^{-1});[9] moreover, the initial amount of ACHE added to the reaction sample is in the enol form ($[\text{ACHE}]_0 = [\text{EH}]$), whereas in the case of ACPE, less that 30% of $[\text{ACPE}]_0$ is in the enol form {$[\text{EH}] = [\text{ACPE}]_0 K_E/(1 + K_E)$ with $K_E = 0.40$};[9] in fact, the initial absorbance readings, A_0, are independent of [SDS] in the case of ACHE, but increase with the [SDS] in the case of ACPE [Fig. 8(A)].

The quantitative analysis of the k_o–[SDS] profiles can be accomplished by means of the simple pseudo-phase ion-exchange model developed by Romsted.[26] This treatment considers the distribution of the EH between aqueous and micellar pseudo-phases; the selective ion-exchange between the reactive H^+ ions and the inert Na^+ ions of the surfactant, eqn. (12) with K_I = 0.6–1,[27] and the independent reactivities in the micellar (k^m) and aqueous (k^w) phases.

$$Na^+_w + H^+_m \overset{K_I}{\rightleftharpoons} Na^+_m + H^+_w \qquad (12)$$

By defining $m_H = [H^+]_m/[\text{SDS}]_m$, the molar ratio of H^+ bound to micelles from the micellized surfactant can be determined at each [SDS] at constant $[H^+]_t$ (= $[H^+]_w$ + $[H^+]_m$) by solving the quadratic equation in m_H given in eqn. (13); then, the variation of k_o as a function of $[\text{SDS}]_m$ can be described by eqn. (14).

$$m_H^2 + m_H\left\{\frac{K_I[Na^+]_t + [H^+]_t}{(K_I - 1)[\text{SDS}]_m} - \beta\right\} - \frac{\beta[H^+]_t}{(K_I - 1)[\text{SDS}]_m} = 0 \qquad (13)$$

$$k_o = \frac{\left\{k^w[H^+]_t + \left(\frac{k^m}{V^2}K_s^N K_s - k^w\right)m_H[\text{SDS}]_m\right\}}{1 + K_s[\text{SDS}]_m}[\text{nitrite}] \qquad (14)$$

In these equations, β is the degree of micelle neutralization and equals $([H^+]_m + [Na^+]_m)/[\text{SDS}]_m$ (= $m_H + m_{Na}$); $[Na^+]_t$ = [SDS] + [nitrite]. In the case of ACPE, the numerator of eqn. (14) appears multiplied by $K_E/(1 + K_E)$ and the denominator

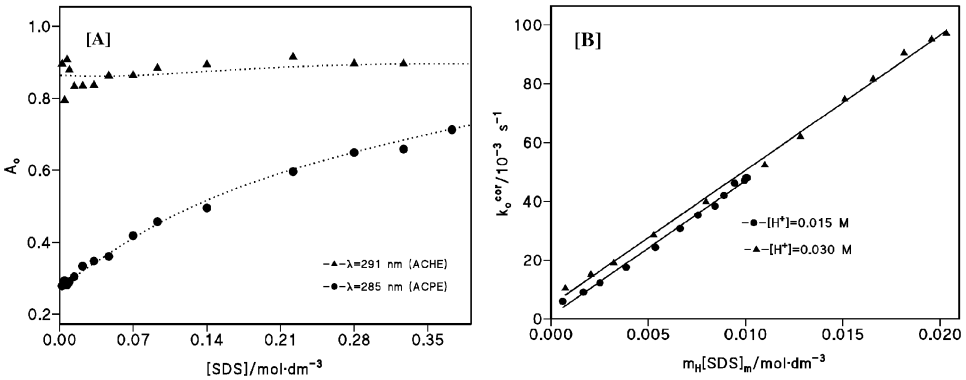


Fig. 8 (A) Variation of A_0 as a function of [SDS] for ACHE (at λ 291 nm) and for ACPE (at λ 285 nm). (B) Plots of k_o^{cor} against the product $m_H[\text{SDS}]_m$ according to eqn. (13); $k_o^{cor} = k_o(1 + K_s[\text{SDS}]_m)$ corresponding to ACHE. See Table 4 for plot parameters.

Table 4 Experimental conditions and rate and equilibrium constants obtained for the nitrosation of ACHE and ACPE in aqueous SDS micellar solutions at [nitrite] = 1.67 mM at 25 °C

Parameter		2-Acetylcylohexanone	2-Acetylcyclopentanone
$[H^+]$ = 0.015 M ($HClO_4$ or HCl)	Intercept/10^{-3} s^{-1}	2.56 ± 0.07	1.25 ± 0.02
	Slope/mol^{-1} dm^3 s^{-1}	4.41 ± 0.05	1.06 ± 0.02
$[H^+]$ = 0.030 M ($HClO_4$)	Intercept/10^{-3} s^{-1}	4.7 ± 0.9	—
	Slope/mol^{-1} dm^3 s^{-1}	4.59 ± 0.07	—
K_s/mol^{-1} dm^3		78	23.7
K_E		0.72	0.40
k^w/mol^{-2} dm^6 s^{-1}		94–102 (131[11])	170 (220[9])
k^m/mol^{-2} dm^6 s^{-1}		3.45–3.6	3.3
K_s^N/mol^{-1} dm^3		0.20[28]	0.20[28]
K_I		0.75[27]	0.75[27]

of eqn. (14) changes to $1 + [SDS]_m K_E K_s/(1 + K_E)$ in order to account for the fraction of the substrate in the enol form, which is the reactive species towards nitrosation. K_s^N represents the equilibrium constant for the association of HONO to SDS micelles, whose value was estimated as 0.20 mol^{-1} dm^3 from the variation of the free energy of transfer of HONO through the water–micelle interface;[28] V is the volume of the micellar phase where the reaction takes place and equals 0.14 dm^3 mol^{-1},[29] and K_s and K_E have been previously determined from direct measurements.[6,9]

Fig. 8(B) shows the linearization of eqn. (14) by plotting k^{cor}, determined as $k_o(1 + K_s[SDS]_m)$, against the product $m_H[SDS]_m$. As expected, the plot is a straight line, from whose slope one determines the reactivity in the micellar phase, k^m. The results are listed in Table 4. The rate constant in the micellar pseudo-phase is much smaller than the rate constant in water due to the lower polarity of the micellar interface. Therefore, the catalysis observed at low SDS concentrations is the consequence of the concentration of the reactants in the small volume of the micelle.

Conclusions

The keto-enol tautomerization of 2-acetylcyclohexanone is retarded in mixtures of organic solvents–water of 70% v/v. The highest effect is observed in acetonitrile whereas the lowest is in dimethylsulfoxide. Between them lie the cases of dioxane, THF and alcohols. Aqueous micellar solutions of cationic surfactants also retard the rates of tautomerization. The overall effect increases with the concentration of micelles and is due to the distribution of the enol between the water and micellar interface, where the reaction is slower than in the bulk water phase; moreover, the H^+-catalyzed pathway is not possible in the micellar interface due to electrostatic repulsions. The association of the keto tautomer is also detected, but the binding constant is 20-fold lower than that of the enol. Rates of nitrosation of the enol in aqueous acid medium are also reduced by the presence of cationic micelles. Kinetic profiles are satisfactorily explained by assuming that the reaction goes only in the water phase; the increase in the concentration of the nitrosating agent XNO parallels [TTAX] and the decrease of [enol] in water is due to its partition between both pseudo-phases. By contrast, the presence of anionic micelles of SDS enhances the rate of nitrosation at low surfactant concentrations due to the increase of the reactants' concentration in the micellar interface, because the reactivity in this region is much lower than that in the bulk water phase.

Acknowledgements

Financial support from the Dirección General de Investigación (Ministerio de Ciencia y Tecnología) of Spain (Projects BQU2000-0239-C02-01 and BQU2003-04775-C02-01) is gratefully acknowledged.

References

1 E. J. Fendler and J. H. Fendler, *Catalysis in Micellar and Macromolecular Systems*, Academic Press, New York, 1975.
2 G. Savelli, R. Germany and L. Brinchi, in *Reactions and Synthesis in Surfactant Systems* (Surfactant Science Series) ed. J. Texter, Marcel Dekker, New York, 2001, vol. 100, ch. 8, pp. 175–246.
3 C. A. Bunton and G. Savelli, *Adv. Phys. Org. Chem.*, 1986, **22**, 231.
4 C. A. Bunton, F. J. Nome, F. H. Quina and L. S. Romsted, *Acc. Chem. Res.*, 1991, **24**, 357.
5 F. H. Quina and H. Chaimovich, *J. Phys. Chem.*, 1979, **83**, 1844.
6 E. Iglesias, *Curr. Org. Chem.*, 2004, **8**, 1.
7 E. Iglesias, *J. Phys. Chem.*, 1996, **100**, 12592.
8 E. Iglesias, *Langmuir*, 2000, **16**, 8438.
9 E. Iglesias, *New J. Chem.*, 2002, **26**, 1353.
10 E. Iglesias, *J. Org. Chem.*, 2003, **68**, 2680.
11 E. Iglesias, *J. Org. Chem.*, 2003, **68**, 2689.
12 E. Iglesias and D. L. H. Williams, *J. Chem. Soc., Perkin Trans. 2*, 1988, 1035.
13 (*a*) A. Graham and D. L. H. Williams, *J. Chem. Soc., Perkin Trans. 2*, 1992, 747; (*b*) D. L. H. Williams and A. Graham, *Tetrahedron*, 1992, **48**, 7973.
14 P. Hervés-Beloso, P. Roy and D. L. H. Williams, *J. Chem. Soc., Perkin Trans. 2*, 1991, 17.
15 E. Iglesias, *J. Chem. Soc., Perkin Trans. 2*, 1997, 431.
16 F. M. Menger and C. E. Portnoy, *J. Am. Chem. Soc.*, 1967, **89**, 4698.
17 D. L. H. Williams, *Nitrosation*, Cambridge University Press, Cambridge, UK, 1998.
18 E. Iglesias, L. García-Río, J. R. Leis and J. Casado, *Recent Res. Devel. Phys. Chem.*, 1997, **1**, 403.
19 J. March, *Advanced Organic Chemistry. Reactions, Mechanisms, and Structure*, John Wiley & Sons, New York, 4th edn., 1992, p. 592.
20 J. H. Ridd, *Adv. Phys. Org. Chem.*, 1978, **16**, 1.
21 H. Schmid and E. Hallaba, *Monatsh. Chem.*, 1956, **87**, 560.
22 H. Schmid and E. Fouad, *Monatsh. Chem.*, 1957, **88**, 631.
23 G. Stedman and P. A. E. Whincup, *J. Chem. Soc.*, 1963, 5796.
24 (*a*) E. Iglesias, *Langmuir*, 1998, **14**, 5764; (*b*) A. Domínguez, A. Fernández, N. González, E. Iglesias and L. Montenegro, *J. Chem. Educ.*, 1997, **74**, 1227.
25 N. M. van Os, J. R. Haak and L. A. M. Rupert, *Physico-Chemical Properties of Selected Anionic, Cationic, and Nonionic Surfactants*, Elsevier Science Publishers, Amsterdam, The Netherlands, 1993.
26 (*a*) L. S. Romsted, in *Micellization, Solubilization and Microemulsions*, ed. K. L. Mittal, Plenum Press, New York, 1977, vol. 2, p. 489; (*b*) L. S. Romsted, in *Surfactants in Solution*, eds. K. L. Mittal and B. Lindman, Plenum Press, New York, 1984, vol. 2, p. 1015.
27 C. A. Bunton and B. Wolfe, *J. Am. Chem. Soc.*, 1973, **95**, 3742.
28 L. García-Río, E. Iglesias, J. R. Leis and M. E. Peña, *Langmuir*, 1993, **9**, 1263.
29 C. A. Bunton, N. Carrasco, S. K. Huang, C. H. Paik and L. S. Romsted, *J. Am. Chem. Soc.*, 1978, **100**, 5420.