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Solvent effects *versus* concentration effects in determining rates of base-catalyzed keto-enol tautomerization

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Solvent effects of homogeneous media (such as solvent–water mixtures) on chemical reactivity may be interpreted as due to solvent polarity and/or molecular structure of solvent molecules. In microheterogeneous media (such as aqueous micellar solutions), solvent effects on reaction rates must include concentration effects, in addition to changes in the solvent polarity of the micelle interface where the reaction is assumed to occur. In this work, we measured the rates of keto-enol tautomerization of the 2-acetylcyclohexanone (ACHE) and 2-acetyl-1-tetralone (ATLO) systems in dimethylsulfoxide (DMSO)–water mixtures and in aqueous micellar solutions with both anionic and cationic surfactants and in the presence of buffers. The results appear as an ideal framework to understand the paramount importance of the specific molecular structure of solvent molecules in determining chemical reactivity *versus* solvent polarity or even concentration effects.

Introduction

Most chemical reactions are carried out in solution. The role of the solvent in governing a chemical reaction is far from passive.[1,2] Therefore, a proper understanding of solvent effects is essential to any model of chemical reactivity.[3,4] The simplest one considers only the polarity of the solvent,[5] as measured by its dielectric constant ε, in which case the solvent is treated as a continuous medium. Nevertheless, the specific molecular structure of the solvent molecules cannot be ignored in any detailed interpretation of solvent effects on reactivity.

In the last few years, many studies have been devoted to investigating chemical reactivity in aqueous micellar solutions.[6–9] Unlike homogeneous solvents or continuous media, the inherently microheterogeneous micellar solutions provide a variety of solubilization environments, ranging from "hydrocarbon-like cores" to bulk water. Indeed, the distinctive feature of aqueous micellar solutions as solvents is that they can offer different microenvironments not only for different molecules, but also for different parts of the same molecule. In homogeneous or continuous media, solvent effects on reactivity are explained in terms of the specific interactions between solvent and substrate molecules and between solvent and transition states.[10–12] These two effects may be distinguished as reactant, or initial state, and transition state solvation, respectively. Solvated reactants cannot approach close enough to react unless some desolvation occurs, a process that requires considerable energy if a reactant is ionic; Similarly, transition state solvation may induce changes in the orientation of molecules within the solvation shell that affects its stability.[13] Nevertheless, in microheterogeneous micellar solutions the concentration effects of the two reactants of a bimolecular reaction in the small volume of the micelle can be decisive in the analysis of solvent effects.

This paper provides a comparative study of solvent effects *versus* concentration effects on chemical reactivity. For this purpose, we report results obtained in the kinetic study of keto-enol tautomerism in both homogeneous and heterogeneous solvents. For the former, we chose dimethylsulfoxide (DMSO)–water mixtures, while for the latter, we used aqueous micellar solutions of anionic and cationic surfactants; as substrates, we analyzed the keto-enol conversion of 2-acetylcyclohexanone (ACHE) and 2-acetyl-1-tetralone (ATLO).

The keto-enol tautomerism of both ACHE and ATLO occurs at slow rates that, as a result, are strongly influenced by the nature of the solvent as well as the relative proportions of both the keto and enol tautomers. In other words, the position of the keto-enol equilibrium in 1,3-diketones, as measured by K_E (the equilibrium constant in water), is largely determined by the type of solvent.[14,15] Rates of tautomerization are also influenced by acids and bases. Here, the base-catalyzed tautomerization reaction is studied in both DMSO–water mixtures and aqueous micellar solutions; the results are compared with those of solvent-assisted rates and acid-catalyzed rates.[16]

Experimental

2-Acetylcyclohexanone and 2-acetyl-1-tetralone were commercially available and used without further purification. Dioxane, DMSO, and acetonitrile of spectrophotometric grade were purchased from Merck. All inorganic reagents (salts, acids or bases) were used as received. Surfactants, sodium dodecyl sulfate (SDS) and tetradecyltrimethylammonium bromide (TTABr), of the highest purity from Sigma or Aldrich, were used without further purification. Aqueous solutions were prepared with doubly distilled water from a permanganate solution. Freshly prepared solutions were used in all experiments.

Kinetic measurements were recorded with a double beam spectrophotometer provided with a thermostatted cell holder. The pH was measured with a Crison pH meter equipped with a GK2401B combined glass electrode. The glass electrode was standardized by using commercial standard pH 4.01 and 7.01 buffers.

Kinetic measurements were carried out under pseudo-first-order conditions, the ketone being the limiting reagent. Stock solutions of either ACHE or ATLO were prepared in dry dioxane. Tautomerization rates were measured by following two procedures. In the first one, a small volume ($\sim$100 μl) of

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an aqueous concentrated solution of the substrate (previously equilibrated to the keto-enol equilibrium composition) was diluted into a large volume (3.0 ml) of a solvent–water mixture or of a micellar solution; the increase in absorbance at $\lambda = 291$ nm (for ACHE) or 343 nm (for ATLO) was registered as a function of time and the experimental data $A(t)$ was fitted to eqn. (1) by nonlinear regression analysis to obtain the fittable parameters A_∞, A_o, and k_o.

$$A = A_\infty + (A_o - A_\infty)e^{-k_o t} \text{ with } k_o = k_o^e + k_o^c \qquad (1)$$

In the second procedure, a small volume (~ 10 μl) of a dioxane concentrated solution of either ACHE or ATLO was diluted into a large volume of water containing the other reagents; the rates of the approach to equilibrium corresponding to enol-ketonization were measured by registering the decrease in absorbance, also at 291 and 343 nm for ACHE and ATLO, respectively, and fitting the experimental data to eqn. (1). Under the same experimental conditions, the values of k_o determined from eqn. (1) were independent of the procedure used.

With the first procedure, $A_o = \epsilon_{EH}\ell[S]_o K_E/(1 + K_E)$ (with S representing the ketone, ACHE or ATLO), and $A_\infty = \epsilon_{EH}\ell [S]_o K/(1 + K)$ with $K = K'_E$ in solvent–water mixtures, or $K = K_E^{ap}$ in aqueous micellar solutions, *vide infra*. When the second procedure was followed, $A_o = \epsilon_{EH}\ell[S]_o$, but A_∞ is equivalent to the previous one.

Results

The keto-enol equilibrium of both ACHE and ATLO has been studied in water.[17,18] The two tautomers are present in an aqueous equilibrated solution of the substrate. The content of the enol is lower than that of the keto form, but in apolar aprotic solvents, the enol form predominates over the keto form, as depicted in Scheme 1. In contrast to other 1,3-diketones,[19] the keto-enol interconversion in ACHE or ATLO occurs slowly, and catalysis by H^+ and buffers, according to eqns. (2) and (3), was observed.

$$k_o^1 = k_u + k_H [H^+] \qquad (2)$$

$$k_o = k_o^1 + k_{buf} [\text{buffer}] \qquad (3)$$

1. Keto-enol tautomerization in DMSO–water mixtures

The k_o values for keto-enol tautomerization were obtained in buffers prepared from acetic acid and sodium acetate. The rates have been measured in DMSO aqueous mixtures by following the first procedure (see Experimental). Fig. 1 shows the effect of increasing the percentage of DMSO in the reaction medium at low buffer concentration for the ratio $[AcOH]/[AcO^-] = 1$ (henceforth 1 : 1, where AcOH is acetic acid and AcO^- the acetate anion). For comparison purpose, the rates of H^+ (HCl) catalyzed tautomerization measured as a function of the percentage of DMSO for ACHE are also included. First, increasing the percentage of DMSO has opposite effects on k_o in acid- and base-catalyzed reactions, and second, much higher rates are observed for the buffer-catalyzed reactions compared to the H^+ catalyzed reactions above, approximately, 60% DMSO.

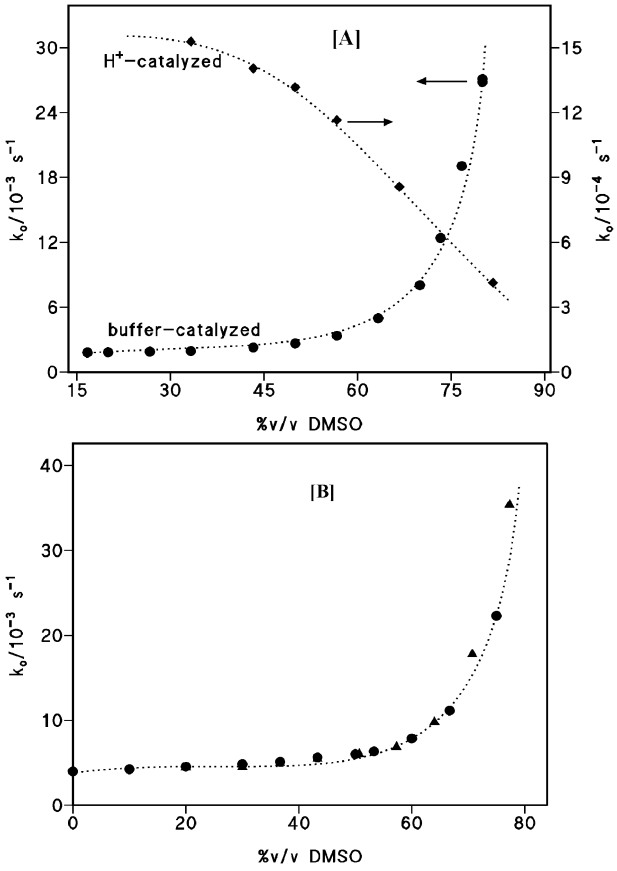
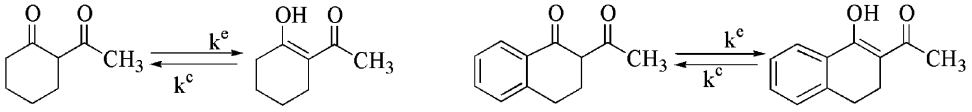


Fig. 1 Influence of the percentage of DMSO on the pseudo-first-order rate constant for keto-enol tautomerization. (A) 2-Acetylcyclohexanone in (◆) aqueous hydrochloric acid $[H^+] = 0.075$ M and (●) aqueous solutions of acetic acid–acetate ($AcOH : AcO^-$, 1 : 1) at [buffer] = 3.3 mM. (B) 2-Acetyl-1-tetralone in aqueous solutions of acetic acid–acetate ($AcOH : AcO^-$, 1 : 1) at [buffer] = 1.0 mM for (●) enol-ketonization and (▲) keto-enolization.

The effect of increasing buffer concentration at a fixed percentage of DMSO on k_o values is displayed in Fig. 2. k_o values measured at 1 : 1 and 1.4 : 1 ratios of $AcOH : AcO^-$ are also included. In every case, a linear relationship as expressed by eqn. (3) and observed in water is also fulfilled in DMSO–water mixtures. It can be seen that k_{buf} increases with the percentage of DMSO, but decreases when the ratio of $AcOH : AcO^-$ increases, that is, when the concentration of the basic form of the buffer diminishes; by contrast, k_o^1, the solvent-assisted tautomerization reaction, is faster at low DMSO percentages. For comparison purposes, Fig. 3 displays the values of k_o measured as a function of buffer concentration in water, by application of the second procedure, that is, for the enol-ketonization of ACHE, and in 60% acetonitrile (for the keto-enolization of ATLO).



$K_E = k^e/k^c = 0.70$ (in water)

$K_E >> 1$ (in solvents)

$k^e \sim 0.6 \times 10^{-3}$ s^{-1} in water, 25 °C

$k^c \sim 0.8 \times 10^{-3}$ s^{-1} in water, 25 °C

$K_E = k^e/k^c = 0.90$ (in water)

$K_E >> 1$ (in solvents)

$k^e \sim 1.7 \times 10^{-3}$ s^{-1} in water, 25 °C

$k^c \sim 1.8 \times 10^{-3}$ s^{-1} in water, 25 °C

Scheme 1 Characteristics of the keto-enol equilibrium in ACHE and ATLO measured in water.

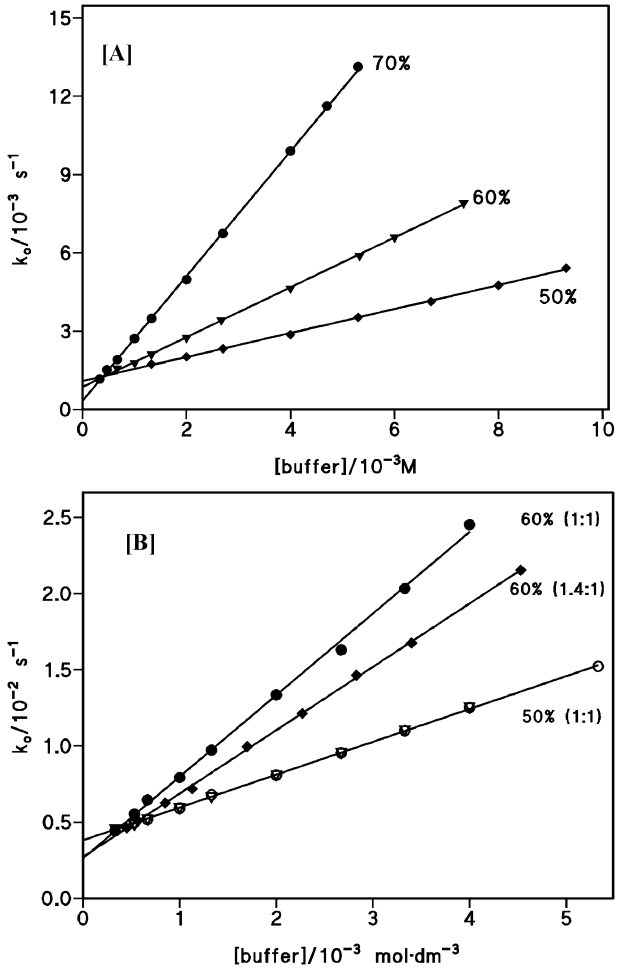


Fig. 2 Pseudo-first-order rate constants, k_o, for keto-enol tautomerization of (A) ACHE determined as a function of buffer concentration at 70%, 60% and 50% DMSO and a 1 : 1 ratio of AcOH : AcO$^-$, and (B) ATLO determined at 60% and 50% DMSO , and at ratios of AcOH : AcO$^-$ equal to 1 : 1 and 1.4 : 1 for (●,◆,○) keto-enolization and (▽) enol-ketonization.

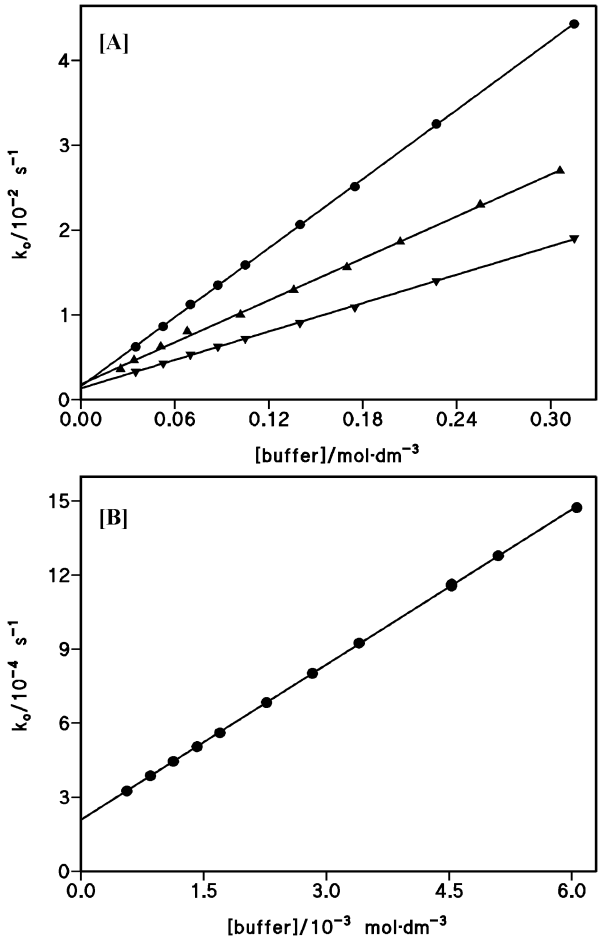


Fig. 3 Variation of k_o as a function of acetic acid–acetate buffer concentration for (A) enol-ketonization of ACHE in water at pH (●) 5.08; (▲) 4.60, and (▼) 4.28, and for (B) keto-enolization of ATLO in 60% acetonitrile at [AcOH] : [AcO$^-$] of 1.4 : 1.

The inspection of Figs. 2(A) and 3(A) reveals that, in order to obtain similar rates of reaction in water and in, for example, 70% DMSO, one needs to work in water with a buffer concentration that is more than 25-fold that used in DMSO. Similarly, a comparison of Figs. 2(B) and 3(B) indicates that, even though DMSO and MeCN have similar dipole moments (μ = 4.05 and 3.54 D, respectively) and dielectric constants (ε = 46.5 and 35.9, respectively),[1] the reaction rate in MeCN is almost 20-fold lower than that observed in DMSO under the same experimental conditions. These findings point to important solvent effects in controlling the rates of keto-enol tautomerization, which are strictly related to the specific molecular structure of the solvent molecules.

The linear-square adjustment of eqn. (3) to the experimental points yields the results depicted in Table 1 for k_o^1 and k_{buf} and correspondingly to both ACHE and ATLO obtained at fixed percentages of DMSO. For the sake of comparison, the results obtained in 60% acetonitrile and in water (for the study of enol-ketonization) are also included.

The overall catalytic effect increases with both the percentage of DMSO and the buffer concentration; moreover, at a given DMSO percentage and buffer concentration, the k_o values decrease when the ratio [AcOH] : [AcO$^-$] increases. The latter finding evidences general base catalysis; in other words, k_{buf} is due to the reaction by the acetate anion. By contrast, the uncatalyzed pathway, k_o^1, decreases parallel to the water content in the reaction medium; for example, $k_u = 1.4 \times 10^{-3}$ s^{-1} in water, whereas in 70% DMSO it is ~4-fold lower (0.3×10^{-3} s^{-1}).

2. Keto-enol tautomerization in micelles

Pseudo-first-order rate constants k_o of keto-enol tautomerization in aqueous micellar solutions have been measured following the first procedure under different experimental conditions. Fig. 4 shows the plots of k_o against [SDS] (for [SDS] > cmc (which, under the experimental conditions, is of the order of 7 mM) obtained in the kinetic study of keto-enol tautomerization of both ACHE and ATLO in the presence of acetic acid–acetate at a 1 : 1 ratio of AcOH : AcO$^-$. It should be noted that the buffer concentration used in the case of ACHE is 100-fold higher than that used with ATLO. In Fig. 4(A), the effect of increasing [buffer] at constant [SDS] can also be seen: k_o increases with [buffer] according to the linear relationship in eqn. (3).

For ATLO however, k_o remains almost constant on varying [buffer] at [SDS] = 0.22 M [see Fig. 5(B)]. On the other hand, the reciprocal plot of k_o against [SDS] describes downward curved lines. Therefore, eqn. (4):

$$k_o = \frac{k_o^w + \alpha[SDS]_m}{1 + \delta[SDS]_m} \quad (4)$$

was used to fit the experimental points. The solid lines obtained in the fitting process are drawn, with the adjustable parameters k_o^w, α and δ being those listed in Table 2. This behaviour is typical of micellar effects due to a separation of the reagents by the micelles. Either ACHE or ATLO associate to micelles whereas the AcO$^-$ ions are repelled from the interface due to electrostatic effects. ATLO is more hydrophobic than ACHE and associates to SDS micelles stronger than ACHE does.

Table 1 Keto-enol tautomerization rate constants obtained in aqueous-dimethylsulfoxide (or acetonitrile) mixtures of different compositions for solvent-assisted (k_o^1) and for buffer-catalyzed (k_{buf}) reactions at 25 °C (the buffer is acetic acid–acetate at concentration ratios of 1 : 1 or 1.4 : 1)

		2-Acetylcyclohexanone		2-Acetyl-1-tetralone	
% Solvent	[AcOH] : [AcO$^-$]	k_o^1/ 10^{-3} s^{-1}	k_{buf}/ M^{-1} s^{-1}[b]	k_o^1/ 10^{-3} s^{-1}	k_{buf}/ M^{-1} s^{-1}[b]
70% DMSO	1 : 1	0.32 ± 0.04	2.39 ± 0.015	—	—
60% DMSO	1 : 1	0.86 ± 0.03	0.955 ± 0.006	2.62 ± 0.02	5.35 ± 0.08
60% DMSO	1.4 : 1	—	—	2.71 ± 0.08	4.16 ± 0.03
50% DMSO	1 : 1	1.08 ± 0.03	0.460 ± 0.005	3.80 ± 0.04	2.15 ± 0.02
50% DMSO[a]	1 : 1	—	—	3.81 ± 0.02	2.19 ± 0.01
60% MeCN	1.4 : 1	0.009 ± 0.004	?	0.208 ± 0.002	0.210 ± 0.005
Water	—	1.4 ± 0.1	—	3.61 ± 0.02	—

[a] Corresponding to enol-ketonization; [b] M^{-1} s^{-1} is the same as mol^{-1} dm^3 s^1.

Therefore, a reduction factor of approximately 10-fold is obtained at high [SDS] with ATLO, whereas the reduction in k_o is approximately half with ACHE. The greatest reduction in k_o is observed at [SDS] < 0.06 M in the case of ATLO, whereas for ACHE, the minimum value of k_o is obtained at [SDS] close to 0.18 M.

Nevertheless, similar k_o–[SDS] profiles are observed for the H^+ catalyzed tautomerization (data not shown), even when the H^+ ions are concentrated in the micellar interface at low values of [SDS]. This means that the overall reduction in k_o is due to solvent polarity effects that overwhelm the rate increase by concentration effects of enol and H^+ in the small volume of the micellar interface. At fixed [SDS] we analyzed the effect of increasing both [H^+] and [buffer]. Representative results can be seen in Fig. 5. Linear least-squares fits of the data to eqn. (2) and (3), respectively, yield the results presented in Table 3.

The buffer-catalyzed reaction was also studied in aqueous micellar solutions of cationic surfactants. The buffer-catalyzed reaction is more important in the presence of cationic micelles than in that of anionic micelles. The k_o–[surfactant] profiles observed with both substrates, working at fixed [buffer], are depicted in Fig. 6. The observed rate constant sharply increases at low [TTABr] (cmc < 4 × 10^{-3}M), passes through a maximum value, then decreases at higher surfactant concentrations. This experimental behaviour is typical for micellar effects of cationic micelles in reactions between hydrophobic neutral substrates and anions, just as in our case: reaction between acetate ions and the ketones ACHE or ATLO. In other words, the qualitative reason for the catalysis on the

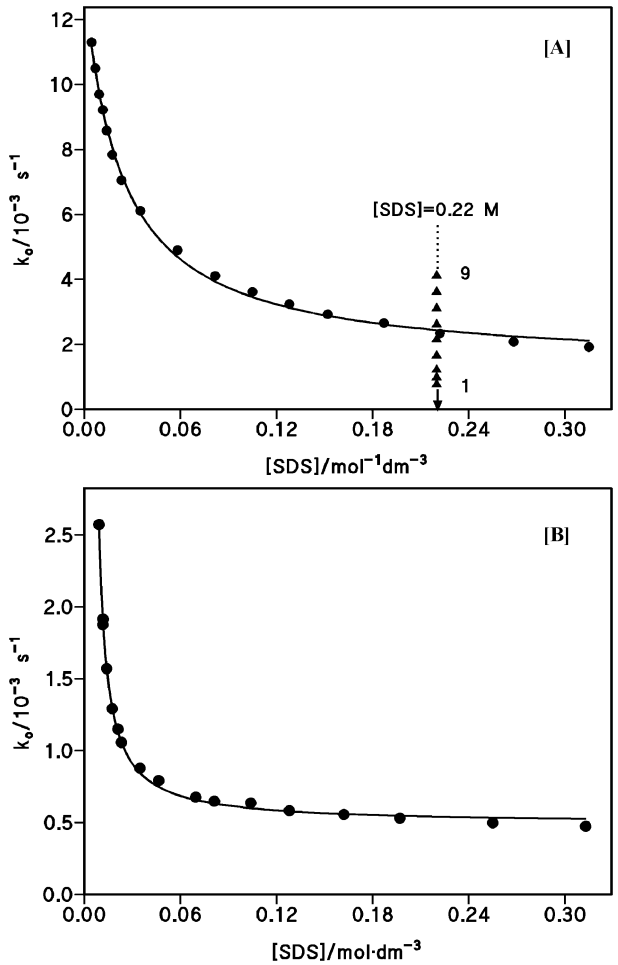


Fig. 4 Influence of the SDS concentration on rates of keto-enol tautomerization of (A) 2-acetylcyclohexanone at (●) [buffer] = 0.133 M and at (▲) fixed [SDS] = 0.22 M and variable [buffer] ranging between [9] = 0.24 M and [1] = 0.030 M, and of (B) 2-acetyl-1-tetralone at [buffer] = 1.33 mM.

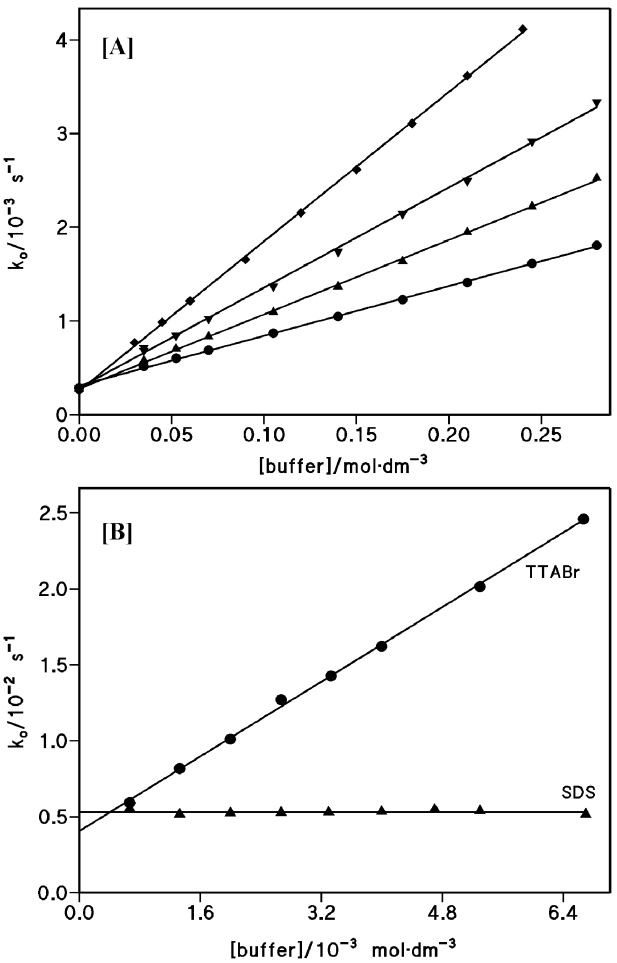


Fig. 5 Variation of k_o as a function of [buffer] for keto-enol tautomerization of (A) ACHE in 0.25 M of SDS at pH (◆) 4.85, (▼) 4.60, (▲) 4.40 and (●) 4.15, and (B) ATLO in 0.22 M aqueous micellar solutions of (●) TTABr and (▲) SDS.

Table 2 Kinetic parameters obtained from the fit of eqn. (4) to the experimental data obtained in the kinetic study of the buffer-catalyzed keto-enol tautomerization of ACHE and ATLO in aqueous micellar solutions of SDS

Ketone	[buffer]/M	k_o^w /10^{-3} s^{-1}	α /mol^{-1} dm^3 s^{-1}	δ/mol^{-1} dm^3
ACHE	1.33×10^{-1}	11.6 ± 0.1	0.048 ± 0.005	37 ± 1
ATLO	1.33×10^{-3}	3.62 ± 0.02	0.103 ± 0.008	227.5 ± 9

base-catalyzed pathway is concentration effects due to the presence of micelles. Also included in Fig. 6, the k_o values measured at constant [TTABr] and variable [buffer] show linear relationships according to eqn. (3).

Discussion

The kinetic features observed for the tautomerization reaction in either DMSO–water mixtures or in aqueous micellar solutions indicate that the reaction mechanism in these media is the same as in water.[17] Therefore, on this basis, the following points are commented.

1. Solvent effects

The rates of H^+ catalyzed keto-enol tautomerization are reduced in DMSO–water mixtures; in contrast, the buffer-catalyzed rates are strongly enhanced at high DMSO percentages. On the other hand, data in Figs. 2 to 4 indicate that the catalysis by buffer is due to the basic component of the buffer, that is, to the acetate ion. Scheme 2 presents the reaction mechanisms for acid- and base-catalyzed keto-enol tautomerization.

Both reaction pathways can be seen as a reaction between a neutral substrate and an ion. By considering only the solvent polarity, the solvent effects should be similar, firstly, for both reaction pathways, and secondly, in water mixtures of both DMSO and acetonitrile. It is evident that the polarity of the solvent does not suffice to explain the experimental observations. If one considers also the specific molecular structure of the solvent molecules, it is possible to explain not only the different behaviour of DMSO in the acid- and base-catalyzed pathways, but also the different reactivities in DMSO and acetonitrile solvents.

Dimethylsulfoxide is a dipolar aprotic solvent that solvates cations much more strongly than anions as a consequence of its molecular structure (Fig. 7). The sulfone oxygen atom has a partial negative charge localized in the small volume of the O atom, but the positive pole of the dipole is diffused over the methyl groups in such a way that attraction to anions is small. In addition, DMSO is a good hydrogen-bond acceptor, but cannot act as a hydrogen-bond donor; therefore, DMSO stabilizes the enol better than the keto tautomer.

The previous considerations allow us to propose the 2D energy diagrams of Fig. 7 that, on the basis of the solvation of the reagents, predict a considerable lowering of the activation energy for the base-catalyzed tautomerization carried out in DMSO–water mixtures whereas the contrary should be observed for the H^+ catalyzed pathway. These facts should explain the variation of the kinetic rate constants reported in Table 1 as a function of the nature of the reaction medium.

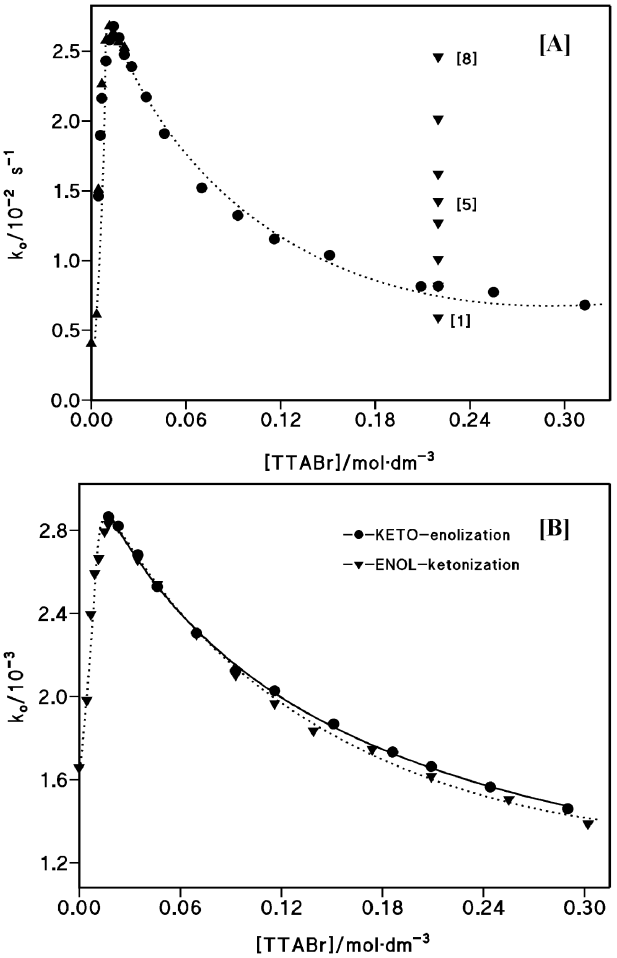


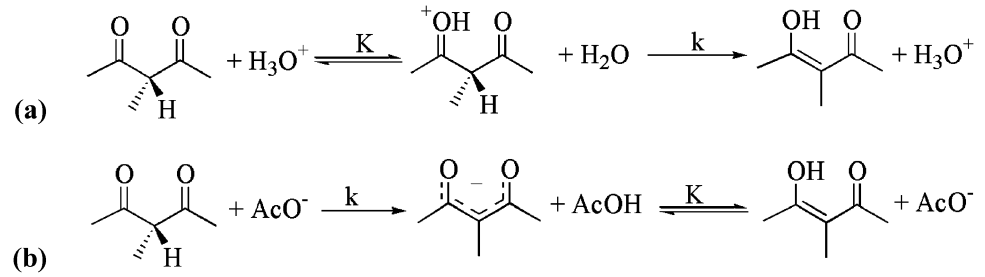
Fig. 6 Rates of keto-enol tautomerization measured in aqueous micellar solutions of TTABr for (A) 2-acetylcyclohexanone at [buffer] = 2.67 mM (acetic acid : acetate in a 1 : 1 ratio) and (B) 2-acetyl-1-tetralone at (●) [buffer] = 1.33 mM and (▼) 0.22 M of TTABr and variable buffer concentrations (*e.g.*, [8] 6.7 mM; [5] 3.3 mM, and [1] 0.67 mM).

2. Concentration effects

Aqueous micellar solutions are the most adequate media to investigate concentration effects on bimolecular reactions.

Table 3 Rates of keto-enol tautomerization measured in aqueous micellar solutions of 0.22 M SDS for 2-acetylcyclohexanone in the presence of either HCl or buffers

H^+ catalyzed [eqn. (2)]			Buffer-catalyzed [eqn. (3)]			
T /°C	$k_u/10^{-4}$ s^{-1}	k_H /$mol^{-1}dm^3$ s^{-1}	Buffer	pH	$k_o^1/10^{-4}$ s^{-1}	$k_{buf}/10^{-3}$ mol^{-1} dm^3 s^{-1}
40	13.3 ± 0.2	$(37.6 \pm 0.3) \times 10^{-3}$	Acetic acid–acetate; 25 °C	4.85	2.54 ± 0.02	15.9 ± 0.1
35	8.6 ± 0.1	$(25.2 \pm 0.2) \times 10^{-3}$		4.60	2.85 ± 0.23	10.7 ± 0.1
30	6.1 ± 0.2	$(15.6 \pm 0.3) \times 10^{-3}$		4.40	2.76 ± 0.10	7.94 ± 0.08
25	4.0 ± 0.2	$(10.2 \pm 0.2) \times 10^{-3}$		4.15	3.01 ± 0.06	5.30 ± 0.05
20	2.50 ± 0.08	$(6.6 \pm 0.2) \times 10^{-3}$	Chloroacetic acid–chloroacetate; 25 °C	3.23	3.31 ± 0.05	2.60 ± 0.03
15.8	1.67 ± 0.06	$(4.22 \pm 0.07) \times 10^{-3}$		2.99	3.54 ± 0.04	2.15 ± 0.02
				2.65	3.78 ± 0.01	1.75 ± 0.01
				2.50	3.99 ± 0.02	1.40 ± 0.02
				2.25	4.40 ± 0.03	1.04 ± 0.02
				2.11	4.75 ± 0.04	0.81 ± 0.03



Scheme 2 (a) Reaction mechanism of H^+ catalyzed enolization and (b) base-catalyzed enolization.

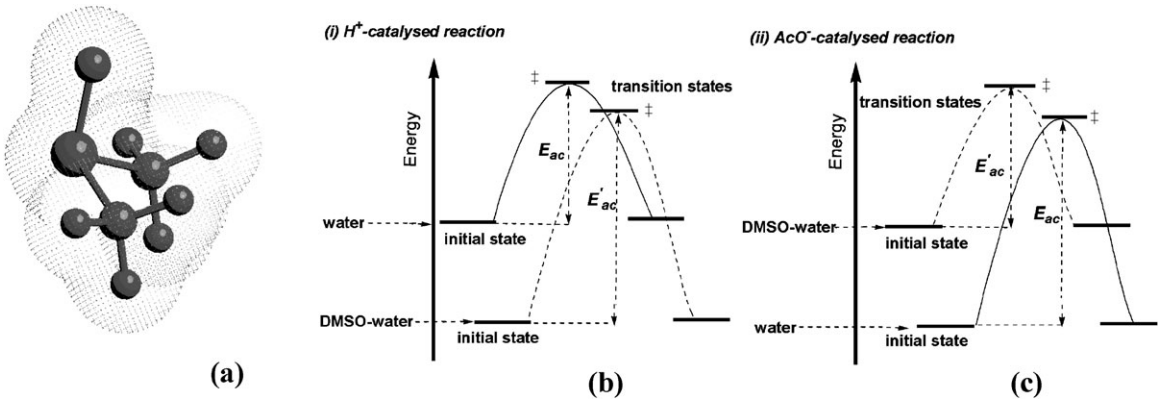
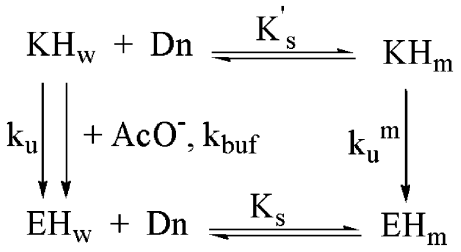


Fig. 7 (a) Charge density surface of DMSO; (b) schematic 2D energy diagram for acid-catalyzed keto-enol conversion; (c) schematic 2D energy diagram for base-catalyzed keto-enol tautomerization.

However, solvent effects cannot be ruled out but must only consider the solvent polarity, since the reagents concentrate in the micellar interface where the water content is lower than in the bulk water phase (this micellar water is involved in solvation of surfactant head groups and counterions, as well as in solvation of reagents and transition states). Therefore, the comparison between rates obtained in micellar media and in, for example, DMSO–water mixtures, reflects the paramount importance of the molecular structure of solvent molecules.

For nonsolvolytic bimolecular reactions, the first-order rate constant k_o should reach a limiting value at high surfactant concentration when the substrate is fully micelle-bound. If only one reagent binds to micelles, the limiting value of k_o is lower than that measured in water. This is the case of buffer-catalyzed tautomerization in the presence of SDS micelles. By contrast, when the two reagents bind to micelles, k_o increases with the surfactant concentration and reaches a constant value when the surfactant counterions are not inert.[20–22] With inert counterions, and on the basis of the original assumption that a substrate in one micelle does not react with a reactant in another and that equilibrium is maintained between aqueous and micellar pseudo-phases, rate maxima are observed as a consequence of the dilution of the reagents in the micellar interface at high micelle concentration.[23,24] This is the situation of the buffer-catalyzed tautomerization in TTABr micellar solutions or the H^+ catalyzed tautomerization in SDS micelles.



Scheme 3 Equilibrium and kinetic processes that occur in the presence of micelles.

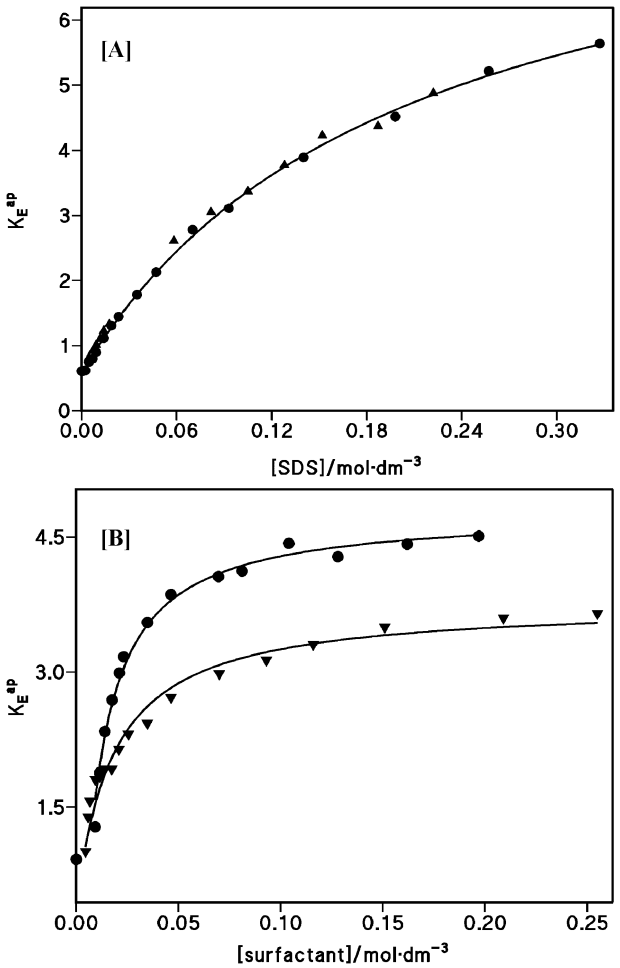


Fig. 8 Plots of K_E^{ap} against [surfactant] corresponding to (A) ACHE determined in (●) 0.030 M HCl; (▲) 0.13 M acetic acid–acetate, 1 : 1, and (B) ATLO in 1.33 mM acetic acid–acetate, 1 : 1, in (●) SDS and (▼) TTABr. The lines are fits from eqn. (6); for results, see Table 4.

Table 4 Values obtained for the binding constants of the enol (K_s) and keto (K'_s) tautomers of both ACHE and ATLO from an analysis of the variation of K_E^{ap} as a function of [surfactant] according to eqn. (6)

Surfactant	Parameter	2-Acetylcyclohexanone	2-Acetyl-1-tetralone
Anionic micelles of SDS	K_E	0.71 ± 0.02	0.92 ± 0.03
	K_s/mol^{-1} dm^3	71 ± 3	443 ± 16
	K'_s /mol^{-1} dm^3	6.6 ± 0.6	87 ± 4
	k^m /s^{-1}	7.3×10^{-3}	1.2×10^{-3}
	δ^{calcd} /mol^{-1} dm^3	33.3	257
Cationic micelles of TTABr	K_E	0.71 ± 0.03	0.92 ± 0.02
	K_s/mol^{-1} dm^3	51 ± 2	149 ± 8
	K'_s /mol^{-1} dm^3	4.0 ± 0.3	31 ± 2
	k_u^m /s^{-1}	0.696×10^{-3} (ref. 16)	1.1×10^{-3}
	k_B^m /mol^{-1} dm^3 s^{-1}	0.043	0.92
Water	k_B^w /mol^{-1} dm^3 s^{-1}	0.18 (ref. 17)	1.79
60% DMSO–water	$k_B^{60\%}$ /mol^{-1} dm^3 s^{-1}	1.9	10.7

The quantitative analysis of the k_o *versus* [SDS] profiles in Fig. 4 can be done through Scheme 3, where KH and EH refer to the keto and enol tautomers, respectively; Dn represents the micellized surfactant, and subscripts w and m indicate respectively the water and micellar pseudo-phases. From this scheme, one can derive eqn. (5):

$$k_o = \frac{\left(k_o^w + k^m K'_s[SDS]_m\right)}{1 + \frac{K'_s + K_E K_s}{1 + K_E}[SDS]_m} \quad (5)$$

which matches eqn. (4) if $\alpha = k^m K'_s$ and $\delta = (K'_s + K_E K_s)/(1 + K_E)$. In this equation, $k_o^w = k_u + k_{buf}$ [buffer] and $k^m = k_u^m/V$, where V is the molecular volume of the interface[25] and is equals to 0.14 dm^3 mol^{-1}.

In order to separate the k^m values, it is necessary to know K'_s. This was done from the analysis of the variation of A_o and A_∞ as a function of [SDS] to obtain values of K_E^{ap} [$= A_\infty/(A_o - A_\infty)$], as described in our previous paper.[16] Hence, the definition of K_E^{ap} as stated in eqn. (6):

$$K_E^{ap} = \frac{K_E\left(1 + K_s[SDS]_m\right)}{1 + K'_s[SDS]_m} \quad (6)$$

allows the determination of the association constants of both the enol (K_s) and the keto (K'_s) tautomers to micelles. The quantitative analysis of the experimental results displayed in Fig. 8 yields the values of K_E, K_s, and K'_s reported in Table 4, along with the values of k^m, obtained from α, and the expected δ values (δ^{calcd}), which compare quite well with the experimental ones, and the same parameters obtained in the presence of TTABr micelles, *vide infra*. Even though ATLO is more reactive than ACHE, k^m values calculated for ATLO are lower than the k^m of ACHE. This rate constant refers to the uncatalyzed rate constant in the micellar interface and reflects the polarity of the location of the substrate inside the micellar interface. The overall reduction is greater for ATLO than for ACHE, as expected, due to the higher hydrophobicity of ATLO; it resides deeper inside the micellar interface, in a region of lower polarity than ACHE.

The quantitative analysis of the k_o *versus* [TTABr] profiles in Fig. 6 was accomplished on the bases of the simple pseudo-phase ion-exchange model. The observed catalysis indicates a reaction involving anions, that is, the reaction of AcO^- ions and the enol. For micellar binding of AcO^- to a cationic micelle with Br^- as the counterion the approach of the ion-exchange model can be expressed by eqn. (7) with an equilibrium constant $K_I = [AcO^-]_w[Br^-]_m/[AcO^-]_m[Br^-]_w = 10$.[26]

$$AcO^-_m + Br^-_w \overset{K_I = 10}{\rightleftharpoons} AcO^-_w + Br^-_m \quad (7)$$

Setting $m_{AcO} = [AcO^-]_m/[TTABr]_m$ and proceeding in a similar way as that in the previous work[16] for the catalysis by anionic SDS micelles in the presence of H^+ ions, the pseudo-first-order rate constant for keto-enolization is given by eqn. (8), where $k_o^w = k_o^1 + k_B^w[AcO^-]_t$:

$$k_o = \frac{k_o^w + \left(\frac{k_B^m}{V}K_s - k_B^w\right)m_{AcO}[TTABr]_m + k_u^m K_s[TTABr]_m}{1 + \frac{K'_s + K_E K_s}{1 + K_E}[TTABr]_m} \quad (8)$$

The experimental kinetic results can be adapted to eqn. (8) by simulation of k_o with surfactant and AcO^- concentrations or following the procedure adopted in the preceding paper.[16] In the latter method, we determined for each [TTABr] a new constant, k_o^{corr}, from the known values of K_E, K_s, K'_s, and k^m reported in Table 4 as $k_o^{corr} = k_o(1 + \delta[TTABr]_m) - k_u^m K_s[TTABr]_m$. As expected, the plots of k_o^{corr} *versus* [TTABr]$_m$ give good straight lines, from whose slope can be obtained k_B^m, the reactivity in the micellar interphase. The obtained values are also listed in Table 4, along with the results obtained in water, k_B^w, and in 60% DMSO–water mixtures, $k_B^{60\%}$. Notice the small values for the water solvent in comparison with those corresponding to the micellar interface or DMSO–water mixtures. The importance of solvent polarity in determining base-catalyzed reaction rates can be obtain by comparing k_B^m and k_B^w (factors of 2–4, depending on the substrate) but the effect of the molecular structure of the solvent molecules is of paramount importance, which can be noted in the comparison between k_B^m and $k_B^{60\%}$.

Conclusions

Rates of keto-enol tautomerization of both ACHE and ATLO are strongly enhanced in DMSO–water mixtures above approximately 60% DMSO. The effect is not due to a change in the reaction mechanism, thus the kinetic features are the same as in water. On the contrary, the experimental findings are indicative of remarkable solvent effects, which, in homogenous solvents, can be due to a change in the solvent polarity or in the molecular structure of solvent molecules, while, in microheterogeneous solvents such as micellar solutions, concentration effects cannot be ignored. The present results show the paramount importance of the molecular structure of solvent molecules in determining the magnitude of solvent effects in the base-catalyzed keto-enol tautomerization. For media of similar polarity, such as (70–80)% DMSO–water mixtures and the micellar interface of TTABr micelles, where for ACHE, for example, the rates in the former medium are enhanced by more than 15 times, the effect of concentration at the micellar interface approximately doubles only the observed rate. On the other hand, so as to obtain concentration effects comparable to the effect of the molecular structure of solvent molecules, with ATLO, for example, it is necessary to work with [buffer] near 7-fold that used in 70% DMSO–water mixtures. Therefore, the role of the solvent, seen as the specific solvation

of reagents or transition state in governing a chemical reaction, is many times decisive but never passive, and one must look not only at the polarity parameters of the solvent, but also at the structure of solvent molecules.

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