

Keto–enol interconversion of 2-phenacylfuran in aqueous solution and in the presence of surfactant micelles

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Dedicated to Professor Domenico Spinelli on the occasion of his 70th birthday
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Abstract

The equilibrium constants for the keto–enol tautomerism of 2-phenacylfuran (2PF), $K_T = [\text{enol}]/[\text{ketone}]$, have been determined in water and in aqueous solutions of CTAB (cetyltrimethylammonium bromide) by combining the $\text{p}K_a^{\text{KH}}$ for ionization of the ketone, directly measured in aqueous NaOH solutions, and the $\text{p}K_a^{\text{EH}}$ for ionization of the enol, obtained from the corresponding rate profile of ketonization. Comparison of these equilibrium constants with those reported for some previously studied phenylacetyl- and phenacyl- heterocycles highlights the effect of an adjacent furyl group on keto–enol tautomerism. Moreover, it has been shown that micelles from cationic (CTAB) and zwitterionic [3-N,N-(dimethyl-N-myristylammonium)propanesulfonate] surfactants decrease the rate of ketonization of the enolate of 2PF and/or increase the apparent acidity of the keto form. These effects have been related to the affinity of the surfactant micelles for the enolate of 2PF. To the contrary, anionic surfactants (SDS: sodium dodecyl sulfate) do not display appreciable effects on the acidity of the keto form or on the kinetics of ketonization of the enol form of 2PF.

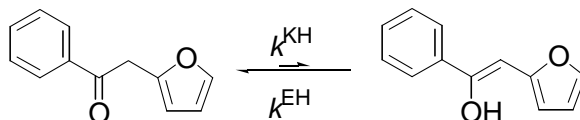
Keywords: Keto–enol tautomerism, acid–base catalysis, micellar catalysis, 2-phenacylfuran

Introduction

The keto–enol interconversions of 2-phenylacetylthiophene,¹ **2PAF**, and 2-phenylacetylthiophene,² **2PAT**, have been studied kinetically in aqueous solutions by combining their rates of enolisation (k^{KH}) with the reverse rates of ketonization of the enol, k^{EH} , or the enolate, k^{E} . For the latter

compound it turned out that the presence of micelles from a cationic surfactant (CTAB: cetyltrimethylammonium bromide) produces a number of interesting effects on rates and/or equilibria of the investigated processes. In particular, a significant increase (of about 2.2 pK_a units) in the acidity of the keto form of **2PAT**, as a carbon acid, was observed on passing from water to an aqueous solution of CTAB, owing to the interaction of the hydrophobic enolate of **2PAT** with the cationic micelles of the surfactant. This increase of acidity has recently allowed us to perform³ alkylation reactions of some hydrophobic ketones with alkyl halides in aqueous micellar solutions of a number of cationic-, zwitterionic-, and anionic surfactants. The advantage of carrying out the alkylation reactions in aqueous micellar solutions rather than in organic solvents by conventional methods⁴ has been outlined.³

In this paper we report our investigation of the keto–enol interconversion (Scheme 1) of 2-phenacylfuran (**2PF**) at 25°C in aqueous solution at different pHs in order to compare the results with those obtained previously¹ for its structural isomer 2-phenylacetyl-furan (**2PAF**) and some other structurally related ketones.



Scheme 1

In addition we have studied the effect produced by surfactants on the rates of ketonization of the enol and/or enolate of **2PF** at 0.5 mol dm⁻³ ionic strength (NaCl), as well as the effect on the apparent acid dissociation constants of the two tautomeric forms of **2PF**. Finally, we have compared the results with those obtained previously² for **2PAT**.

Results and Discussion

Ketonization reactions in buffer solutions

Reaction rates were measured in glycolate-, acetate-, phosphate-, and borate buffers in the absence of surfactant, and in cyanoacetate-, glycolate-, acetate-, cacodylate-, and propionate buffers in the presence of CTAB.

The meaning of pH, and the role of buffers in aqueous surfactants are not fully understood. However, little change in pH, even with a relatively low buffer concentration (acetate), was observed⁵ in aqueous CTAB if the ionic strength was maintained high with NaCl as in the present work. In addition it is known⁶ that changes in the ionic equilibria of buffers, owing to the presence of cationic surfactants, can be minimized by using hydrophilic buffers such as those used in this work.

The observed pseudo-first-order rate-constant, k_e , was of the form shown in Eq. (1), in which B represents the basic component of the buffer acid BH.

$$k_e = k_o^{\text{EH}} + k_B^{\text{EH}} \times [\text{B}] \quad (1)$$

Experiments⁷ at constant buffer ratio, $r = [\text{B}]/[\text{BH}]$, and different concentrations of B show the absence of a general-acid-catalysis contribution by the acidic component of the buffers. Therefore k_B^{EH} represents the second order rate constant for the general-base catalyzed ketonization reaction and k_o^{EH} represents the first order rate constant independent of buffer concentration. The obtained results in water and in aqueous CTAB are reported in Table 1 and 2, respectively.

Table 1. Buffer ratios, r , calculated pH, slopes k_B^{EH} (= rate constants for general base catalysis), and intercepts k_o^{EH} , from the plot of the experimental pseudo-first-order rate constants (k_e/s^{-1}) against concentration of buffer base B, in aqueous solution at 25°C, and ionic strength 0.5 mol dm^{-3} (NaCl)

Base	r	pH	$k_o^{\text{EH}} / \text{s}^{-1}$	$k_B^{\text{EH}} / \text{dm}^3 \text{mol}^{-1} \text{s}^{-1}$
HOCH ₂ COO ⁻	1	3.65	0.027 (\pm 0.010)	2.11 (\pm 0.05)
	5	4.35	0.019 (\pm 0.018)	2.31 (\pm 0.06)
CH ₃ COO ⁻	1	4.58	0.022 (\pm 0.016)	8.98 (\pm 0.09)
	5	5.28	0.022 (\pm 0.05)	9.17 (\pm 0.44)
HPO ₄ ²⁻	1	7.02	0.24 (\pm 0.36)	66.8 (\pm 4.9)
B(OH) ₄ ⁻	0.25	8.46	1.98 (\pm 0.52)	96.7 (\pm 7.5)
	0.5	8.76	3.09 (\pm 0.26)	82.9 (\pm 8.5)
	1	9.06	4.46 (\pm 0.41)	91.4 (\pm 8.4)

Table 2. Buffer ratios, r , calculated pH, slopes k_B^{EH} (= rate constants for general base catalysis) and intercepts k_o^{EH} from the plot of the experimental pseudo-first-order rate constants (k_e/s^{-1}) against concentration of buffer base B, in the presence of CTAB (0.01 mol dm^{-3}) at 25°C and ionic strength 0.5 mol dm^{-3} (NaCl)

Base	r	pH	$k_o^{\text{EH}} / \text{s}^{-1}$	$k_B^{\text{EH}} / \text{dm}^3 \text{mol}^{-1} \text{s}^{-1}$	
NCCH ₂ COO ⁻	0.5	1.99	0.014 (\pm 0.004)	0.269 (\pm 0.024)	
	1	2.29	0.015 (\pm 0.005)	0.244 (\pm 0.030)	
	3	2.77	0.014 (\pm 0.005)	0.296 (\pm 0.032)	
	5	2.99	0.016 (\pm 0.005)	0.273 (\pm 0.030)	
HOCH ₂ COO ⁻	0.5	3.35	0.018 (\pm 0.004)	0.542 (\pm 0.018)	
	CH ₃ COO ⁻	1	4.58	0.044 (\pm 0.022)	6.02 (\pm 0.14)
		3	5.06	0.050 (\pm 0.078)	7.21 (\pm 0.42)
CH ₃ CH ₂ COO ⁻	5	5.28	0.059 (\pm 0.073)	7.31 (\pm 0.43)	
	8	5.60	0.076 (\pm 0.129)	8.56 (\pm 0.60)	
(CH ₃) ₂ AsO ₂ ⁻	5	6.79	0.39 (\pm 0.01)	8.95 (\pm 0.09)	
	B(OH) ₄ ⁻	1	9.06	1.78 (\pm 0.24)	28.6 (\pm 3.2)
3		9.54	1.39 (\pm 0.86)	26.2 (\pm 11.7)	

Ketonization reaction in dilute sodium hydroxide

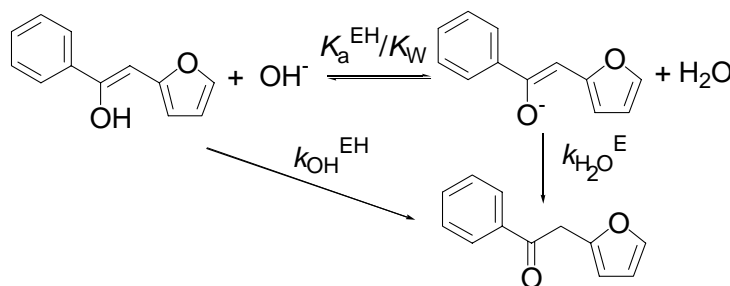
Reaction rates were measured with a concentration of **2PF** about $2.5 \times 10^{-4} \text{ mol dm}^{-3}$. The following k_e values were obtained at different NaOH concentrations (mol dm^{-3} , in brackets):

$$k_e/\text{s}^{-1} = 14.1 (0.001); 15.4 (0.005); 14.9 (0.015).$$

The corresponding results in the presence of 0.01 mol dm^{-3} CTAB were:

$$k_e/\text{s}^{-1} = 1.34 (0.001); 1.24 (0.005); 1.20 (0.01); 1.34 (0.025).$$

The experimental rate of ketonization is apparently independent of the concentration of OH^- and this is understandable in view of the fact that there is a change in reactant from the enol at lower pH to enolate anion at high pH according to the following scheme (and the pH profiles of Figure 1).



Scheme 2

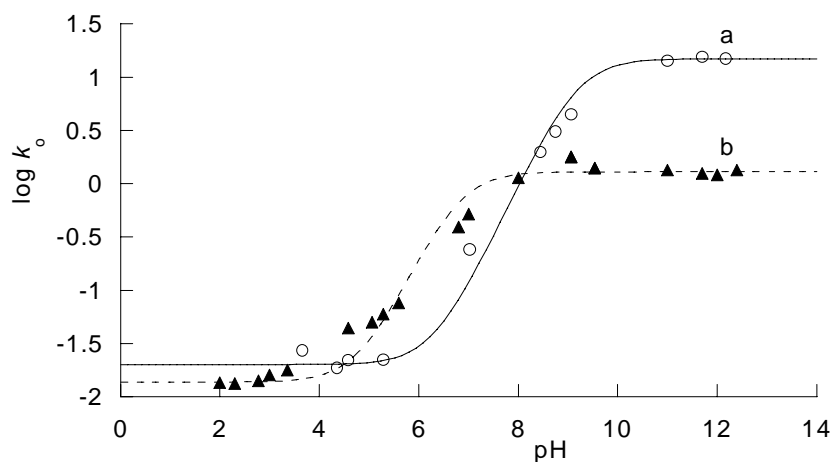


Figure 1. pH- Profiles for the ketonization reaction of the enol of **2PF** in water (open circles, \circ : curve a) and in aqueous solutions of 0.01 mol dm^{-3} CTAB (full triangles, \blacktriangle : curve b). For the significance of $\log k_o$ see the 'pH- profiles' section in the text. pH Values are calculated values corrected for the ionic strength, 0.5 mol dm^{-3} .

Thus, the k_e values above correspond to the rate constant $k_{\text{H}_2\text{O}}^{\text{E}}$ for the spontaneous (water catalyzed) ketonization of the enolate anion, which is kinetically indistinguishable from the OH^- catalyzed ketonization of the enol, $k_{\text{OH}}^{\text{EH}}$. The two rate constants are related by the expression: $k_{\text{H}_2\text{O}}^{\text{E}} = k_{\text{OH}}^{\text{EH}} K_{\text{W}}/K_{\text{a}}^{\text{EH}}$. The rate of ketonization of the enolate anion, $k_{\text{H}_2\text{O}}^{\text{E}}$, in aqueous NaOH solutions was also studied at different concentrations of CTAB and SDS. The obtained results are presented in Figure 2.

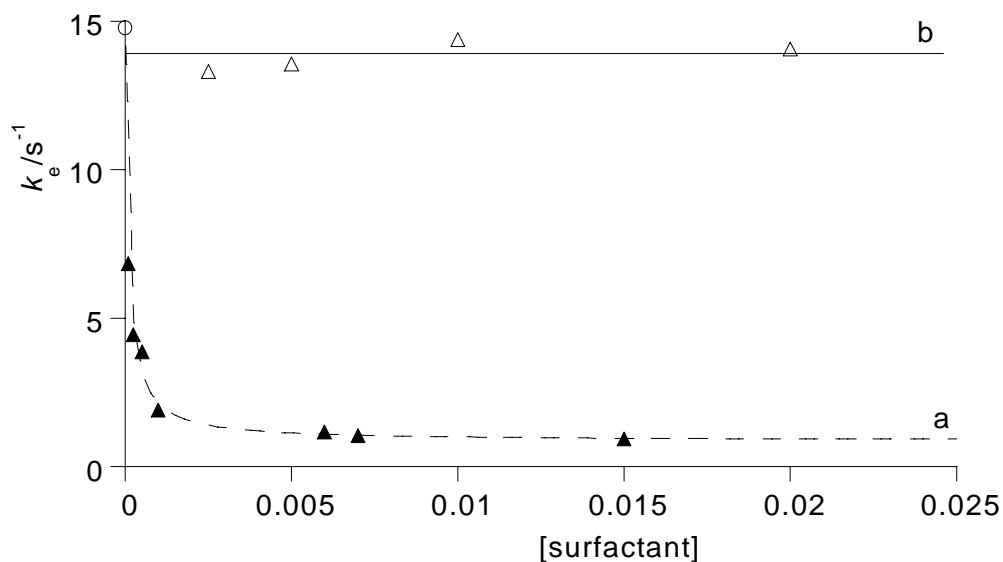


Figure 2. Effect of the addition of CTAB (full triangles, \blacktriangle : curve (a) and SDS (open triangles, \triangle : line (b) on the rate of ketonization of the enolate of **2PF** ($5 \times 10^{-5} \text{ mol dm}^{-3}$) in aqueous NaOH (0.01 and $0.001 \text{ mol dm}^{-3}$, respectively), ionic strength 0.5 mol dm^{-3} (NaCl) at $25.0 \pm 0.1^\circ\text{C}$. The curve (a) is the best-fit non-linear regression described by Eq. (7). The line (b) is drawn as a visual guide. The open circle, \circ , is the average experimental value in water. The reported c.m.c. values in water are $9.2 \times 10^{-4} \text{ mol dm}^{-3}$ and $8.1 \times 10^{-3} \text{ mol dm}^{-3}$ for CTAB⁸ and SDS,⁹ respectively.

Enolisation reactions in acetate buffers

Rates of iodination were measured with **2PF** concentration about $2.5 \times 10^{-4} \text{ mol dm}^{-3}$ in acetate buffer ($r=1$). All reactions were strictly zero-order with respect to the halogen concentration, with the rate-determining step being the formation of the enol.

The following pseudo-first-order rate constants, k_e , were obtained at different AcO^- concentrations (mol dm^{-3} , in brackets):

$$k_e/\text{s}^{-1} = 2.49 \times 10^{-5} (0.01); 4.01 \times 10^{-5} (0.025); 7.18 \times 10^{-5} (0.05); 1.00 \times 10^{-4} (0.075); 1.23 \times 10^{-4} (0.1).$$

The obtained second-order rate constant, $k^{\text{KH}}_{\text{AcO } r=1}$, for the acetate-catalyzed enolisation reaction was $1.11 (\pm 0.04) \times 10^{-3} \text{ mol}^{-1} \text{ dm}^3 \text{ s}^{-1}$.

Calculation of the tautomeric constant, K_T

The tautomeric constant, $K_T = [\text{enol}]/[\text{ketone}]$ can be calculated¹ by combining the second-order rate constants for the enolisation, k^{KH} , and the ketonization, k^{EH} , reactions, measured under the same conditions. Our measurements in acetate buffer ($r = 1$) gave $K_T 1.24 \times 10^{-4}$ ($\text{p}K_T 3.91$). The enolisation and ketonization rate constants were not corrected for the 0.5 mol dm^{-3} ionic strength and, even if ionic strength effects should not substantially affect K_T values, the above-determined tautomeric constant should not correspond to the proper thermodynamic value.

pH-Profile

The profile for the ketonization reaction in aqueous solutions is reported in Figure 1 (curve a) as a plot of values of $\log k_{\text{O}}^{\text{EH}}$ from Table 1 and of $\log k_e (= \log k_{\text{H}_2\text{O}}^{\text{E}}$ for reaction in aqueous NaOH solutions) against pH. A similar profile obtained in the presence of 0.01 mol dm^{-3} CTAB for the corresponding values of $\log k_{\text{O}}^{\text{EH}}$ from Table 2 and $\log k_e$ is reported in Figure 1 (curve b). For the significance of pH in aqueous solutions of CTAB see ref. 5. Each profile shows two regions in which the reaction is pH-independent and a region for OH^- catalysis. The pH-independent region at lower pH can be attributed to the uncatalyzed (water) reaction in which the enol initially ionizes to the enolate anion and H_3O^+ which then recombine to form the ketone and H_2O .¹⁰ On the other hand, in the pH-independent region at higher pH, the reactant is the enolate anion which is protonated by H_2O to form the ketone. The region for OH^- catalysis represents the change in reactant from the enol at lower pH to the enolate anion at high pH. The points of inflections of the curves a and b of Figure 1 correspond to the $\text{p}K_{\text{a}}^{\text{EH}}$ values of the enol in the absence and in the presence of CTAB respectively. These $\text{p}K_{\text{a}}^{\text{EH}}$ values may be obtained from a best fit of experimental rate constants to Eq. (2)

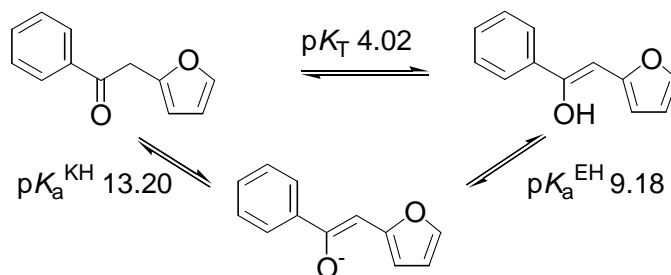
$$k_e = k_{\text{H}_2\text{O}}^{\text{EH}} + (k_{\text{H}_2\text{O}}^{\text{E}} \times K_{\text{a}}^{\text{EH}} / K_{\text{W}}) [\text{OH}^-] / (1 + (K_{\text{a}}^{\text{EH}} / [\text{H}^+])) \quad (2)$$

in which $k_{\text{H}_2\text{O}}^{\text{EH}} = 0.02 \text{ s}^{-1}$ and 0.01 s^{-1} , and $k_{\text{H}_2\text{O}}^{\text{E}} = 14.8$ and 1.28 s^{-1} , are rate constants for the uncatalyzed (water) ketonizations of the enol (EH) and of the enolate (E) in the absence and in the presence of CTAB, respectively. These rate constants are the averages of the values obtained experimentally in the two pH-independent regions of the pH-profile mentioned above. The calculated $\text{p}K_{\text{a}}^{\text{EH}}$ values are $9.18 (\pm 0.08)$ in aqueous solution and $6.79 (\pm 0.08)$ in the presence of CTAB.

Discussion

2-Phenacylfuran, **2PF**, is acidic enough for its acid ionization constant to be directly measured in aqueous solution ($\text{p}K_{\text{a}}^{\text{KH}} = 13.2$, see Experimental Section) and this means that the rates of

ketonization of the enol form can be determined by quenching the enolate anion in acid or buffer solutions, following a previously reported procedure.^{1,2} The relaxation of the enol- to its more stable keto- tautomer was monitored by stopped-flow spectrophotometry (at a wavelength near the absorption peak of the enol or enolate anion). The value of pK_a^{EH} , 9.18, obtained from the rate profile of Figure 2 (curve a), can be combined with the measured acid dissociation constant of the ketone, pK_a^{KH} , to obtain the tautomeric constant $pK_T = -\log ([\text{enol}]/[\text{keto}]) = pK_a^{KH} - pK_a^{EH} = 4.02$ in aqueous solution at 25°C. This pK_T is in quite good agreement with that ($pK_T = 3.91$) determined as the ratio of rate constants for enolisation and ketonization (see Results Section), especially taking into account that only the former is a true thermodynamic value. In fact, the pK_a^{KH} value is extrapolated to 0 mol dm⁻³ NaOH concentration and the pK_a^{EH} derives from Eq. (2) in which $[H^+]$ and $[OH^-]$ allow for activity coefficients at the ionic strength, I , of 0.5 mol dm⁻³ (see Experimental). These results are summarized in Scheme 3.



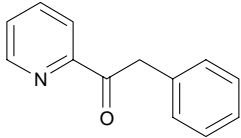
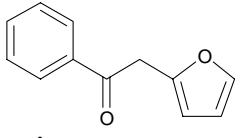
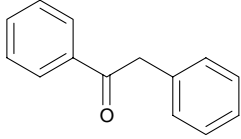
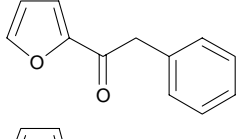
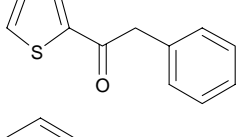
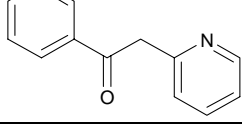
Scheme 3

As expected, the acidity of both the enol and keto forms, as well as the enol-content of **2PF**, are considerably higher than those of simple ketones such as, for example, acetone ($pK_a^{KH} = 19.16$, $pK_a^{EH} = 10.94$, $pK_T = 8.22$)¹¹ or acetophenone ($pK_a^{KH} = 18.24$, $pK_a^{EH} = 10.34$, $pK_T = 7.90$)¹² and are of an order expected from other aryl benzyl ketones¹.

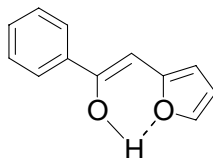
Equilibrium constants for the ionization and tautomerization of **2PF** and some previously studied aryl benzyl ketones are summarized in Table 3 as their pK values.

The higher acidity (pK_a^{KH}) of **2PF** than that of deoxybenzoin can be attributed to the electron- withdrawing effect of the furyl group ($\sigma = 1.10$)¹⁶ compared with the phenyl group ($\sigma = 0.06$)¹⁷ which renders the benzyl hydrogens of **2PF** more easily removable by a base. For the same reason the enol of **2PF** is more acidic (lower pK_a^{EH}) than the enol of deoxybenzoin, but the acidity difference between the two enol forms is smaller than that between the two keto forms. Consequently, the enol content at equilibrium (pK_T) is lower for deoxybenzoin, as can be expected from the destabilization of the keto form of **2PF** by the electron-withdrawing effect of the furyl group.

Table 3. Tautomeric constants and acid dissociation constants for the keto- and the enol- forms of some phenylacetyl- and phenacyl- heterocycles

Substrate	pK_T	pK_a^{KH}	pK_a^{EH}	Ref.
	3.35	12.0	8.67	13
	4.02	13.2	9.18	This work
	5.15	14.8	9.60	14,15
	5.88	14.4	8.50	1
	6.45	14.6	8.15	2
	2.00	13.3	11.3	15

On the other hand, the enol form of **2PF** can be stabilized by delocalization of the furyl oxygen lone electron pair into the phenyl ring. Some stabilization of the enol by hydrogen-bonding to the furyl oxygen (see Scheme 4) is also possible, but almost certainly is less relevant than in the case of the enol of 2-phenacylpyridine¹¹ (pK_T 2.00). A destabilization of the keto form, owing to a β -oxygen substituent effect, has recently been discussed¹⁸ in detail for the isochroman-2-one with reference to α -tetralone. Noteworthy are the parallelism observed for the substitution of an oxygen atom for the β -CH₂ of α -tetralone and the substitution of a furfuryl for a benzyl group in deoxybenzoin. In both cases there is a reduction in the pK_T value, and an increase in the enol and the ketone acidities [$(\Delta pK_T, \Delta pK_a^{EH}, \Delta pK_a^{KH})_{(\alpha\text{-tetralone}\rightarrow\text{isochroman-2-one})} = 2.1, 0.7, 2.7$ and $(\Delta pK_T, \Delta pK_a^{EH}, \Delta pK_a^{KH})_{(\text{deoxybenzoin}\rightarrow\mathbf{2PF})} = 1.1, 0.4, 1.6$]. Obviously, the interpretation of the above ΔpK values should be qualitatively the same for isochroman-2-one and **2PF** although the values observed for **2PF** are smaller, owing to the fact that the oxygen atom is in a γ rather than in a β -position with respect to the enolizable carbonyl group.



Scheme 4

Interestingly, the enol contents of **2PAF** and **2PAT** are considerably lower than that of **2PF**: this can probably be attributed to external conjugation with the lone pair of electrons on the oxygen- and sulfur atoms which stabilizes the carbonyl groups of the keto forms of **2PAF** and **2PAT**, as previously suggested.^{1,2} Of course, an analogous stabilization of the keto form of **2PF** is not possible.

Let us then discuss the major effects produced by the investigated surfactants on the keto–enol interconversion of **2PF**. From the practical point of view, the most interesting effect is the reduction in pK_a^{KH} observed on passing from the aqueous- to a 10^{-2} mol dm^{-3} solution of CTAB ($\Delta pK_a^{KH} = 2.3$).

We have recently shown³ that one can take advantage of similar ΔpK_a^{KH} values, together with the hydrophobic association of the enolate anions with micelles from suitable surfactants, in performing C–C and C–O bond-formation reactions of synthetic interest in aqueous solution near room temperature. This increase in the apparent acidity of the ketone should be ascribed to the stabilization of the enolate of **2PF** by the CTAB micelles, as is shown by the large difference between the binding constants, K_s , of the carbon acid and its conjugate base (see Experimental Section). This stabilization is also apparent from the bathochromic shift in the UV–vis spectrum of the enolate of **2PF** upon transfer from water to CTAB micelles (see below).

Besides the above-mentioned hydrophobic effect, two other factors might be responsible for the increased acidity of the ketone and the strong association of the enolate of **2PF** with the cationic micelles. The first effect is the electrostatic attraction between the ammonium head groups of CTAB micelles and the OH^- ions (some OH^- ions might eventually substitute for Br^- as the counterions in the Stern layer of the micelle of CTAB). The second effect is a similar electrostatic attraction between the enolate anion and the ammonium head groups. The importance of these electrostatic effects can be appreciated by comparing the value of pK_a^{KH} in the presence of CTAB with those obtained in the presence of a zwitterionic [3-(dimethyltetradecylammonium)propane sulfonate: SB3-14] and of an anionic (sodium dodecyl sulfate: SDS) surfactant. The apparent ΔpK_a^{KH} values are 2.3, 1.1, and zero, respectively showing that the hydrophobic association with the micelle is impossible when the enolate anion is repelled by the negative head groups of the SDS micelles. These ΔpK_a^{KH} values are nicely paralleled by the observed bathochromic shifts of the λ_{max} (339 nm) of the enolate on passing from water to 0.01 mol dm^{-3} CTAB ($\Delta\lambda = 18$ nm), 0.01 mol dm^{-3} SB3-14 ($\Delta\lambda = 15$ nm), and 0.03 mol dm^{-3} SDS (no shift observed).

Equally significant are some kinetic effects attributable to the presence of micelles. The rate of the “water” ketonization of the enolate of **2PF** (which is kinetically equivalent to the OH⁻ catalyzed ketonization of the enol) is about 12 times slower in the presence of 10⁻² mol dm⁻³ CTAB (compare the plateau values at higher pH of the profiles a and b of Figure 1). Average $k_{\text{H}_2\text{O}}^{\text{E}}$ values ($k_{\text{H}_2\text{O}}^{\text{E}} = k_{\text{e}}$ values in aqueous sodium hydroxide) are 14.8 s⁻¹ in the absence-, and 1.28 s⁻¹ in the presence-, of CTAB. The progressive decrease of $k_{\text{H}_2\text{O}}^{\text{E}}$ with increasing amounts of CTAB can be seen in Figure 2. A similar trend with CTAB concentration was observed previously² and discussed in detail for the rate of ketonization of the enolate of **2PAT**. The main effect responsible for this rate decrease upon micellisation for the water catalyzed ketonization of the enolate anion is probably the decreased water availability within the micellar aggregates of CTAB by which the enolate is stabilized. Interestingly the same rate constant ($k_{\text{H}_2\text{O}}^{\text{E}}$) remains essentially unchanged in the presence of SDS (see Figure 2), again owing to electrostatic repulsion.

A closer insight into the pH profile in the presence of micelles of CTAB (curve b of Figure 1) highlights the consistency of kinetic rate constants obtained over a wide range of “pH” in several overlapping buffers. As suggested by Bunton⁶ this approach is reminiscent of that used by Hammett in developing his H₀ acidity scale and warrants to the reliability of our rate constants in CTAB solutions. Moreover, a comparison of the pH profiles obtained in water (curve a of Figure 1) and in the presence of micelles of CTAB (curve b of Figure 1) shows that the micellar effect on the uncatalyzed (water) ketonization of the enolate, $k_{\text{H}_2\text{O}}^{\text{E}}$, is much higher than that on the rate of uncatalyzed ketonization of the enol, $k_{\text{H}_2\text{O}}^{\text{EH}}$. Average $k_{\text{H}_2\text{O}}^{\text{EH}}$ values are 0.02 s⁻¹ in the absence-, and 0.01 s⁻¹ in the presence of CTAB. Apparently the micelles of the cationic surfactant stabilize more effectively the negatively charged enolate anion than the neutral molecule of the corresponding enol. There is a shift to lower pHs of the profile obtained in the presence of CTAB and this is due to the above discussed decrease of pK_a^{EH} on passing from water (pK_a^{EH} = 9.18) to CTAB solutions (apparent pK_a^{EH} = 6.79).

Experimental Section

Instruments

The kinetic experiments were carried out with a Jasco V-550 UV/Vis spectrophotometer or with a Varian–Cary 1E spectrophotometer. The stopped-flow spectrophotometer was a model VI Tri-Tech Dynamic Instruments. A 93 Radiometer pH-meter was used for the pH measurements. ¹H- and ¹³C- NMR spectra were recorded on a Bruker AC 200 E spectrometer.

Materials

All inorganic salts (KCl, NaCl, KI, KH₂PO₄, Na₂HPO₄), I₂, cetyltrimethylammonium bromide (CTAB), 3-(N,N-dimethyl-N-myristylammonium) propanesulfonate (SB3-14), sodium dodecyl sulfate (SDS), iodine and buffer acids [CNCH₂COOH, HOCH₂COOH, CH₃COOH,

CH₃CH₂COOH, (CH₃)₂AsO₂H, H₃BO₃] were commercial samples of Analar grade (Aldrich, Merck or Carlo Erba) and were used without further purification except for CTABr, which was recrystallized from acetone. The solvents used in extraction and purification procedures were distilled prior to use.

2-Phenacylfuran (2PF). 2-(2-Furyl)-benzoylacetate^{19a} was prepared following a previously described procedure. Acetic acid (2.5 mL) and LiCl (2.76 g, 65.2 mmol) were added at room temperature to a solution of ethyl 2-(2-furyl)-benzoylacetate (6 g, 23.2 mmol) in NMP (N-methyl-2-pyrrolidone) (7 mL). The reaction mixture was refluxed for 1h and poured after cooling into a biphasic system formed by a saturated aqueous solution of NaHCO₃ (100 mL) and diethyl ether (100 mL). The organic layer was then separated and the aqueous phase was extracted twice with diethyl ether. The combined organic phases, dried over Na₂SO₄, were evaporated to dryness. The crude material was purified by flash chromatography eluting with 90/10 (v/v) *n*-hexane/ethyl acetate mixture to give the desired 2-phenacylfuran, **2PF** (4.31g, 86% yield).^{19b} The identity of the product was confirmed by ¹H- and ¹³C-NMR spectra.

Kinetic measurements

Rates of ketonization of the enol of **2PF**, both in water and in the presence of surfactant, were measured by stopped-flow spectrophotometry upon quenching a freshly prepared solution of the enolate anion in 0.2 mol dm⁻³ aqueous NaOH with 0.2 mol dm⁻³ HCl plus the desired concentration of the buffer. The initial reaction that will occur on neutralization is the protonation of the enolate, resulting in a solution containing enol far in excess of its equilibrium concentration. In the case of the OH⁻ catalyzed reaction, NaOH was only partially neutralized. The kinetics associated with the return to the equilibrium position were monitored at λ_{max} = 339 nm in aqueous solutions and in aqueous SDS, and at λ_{max} = 357 nm in aqueous CTAB.

The enolisation reactions were followed by halogen-trapping as previously described²⁰ with 2.5·10⁻⁴ mol dm⁻³ **2PF** and acetate buffer (r = 1) in the concentration range 0.01 ≤ [AcO⁻] ≤ 0.1 mol dm⁻³.

All kinetic measurements were made at 25.0 ± 0.1 °C and at an ionic strength (*I*) of 0.5 mol dm⁻³ by the addition of NaCl.

pH Values in buffer solution were calculated at 0.5 mol dm⁻³ ionic strength using Eq. (3)²¹ in which *I* is the ionic strength, *K*_a is the ionization constant, and *r* is the ratio of base- to acid-concentrations of the buffer.

$$\text{pH} = \text{p}K_a + \log r + (0.512 \times \sqrt{I}) / (1 + 1.5 \times \sqrt{I}) \quad (3)$$

Acid ionization constants

The p*K*_a^{KH} values of **2PF**, in water and in aqueous surfactants, were determined spectrophotometrically in solutions of increasing concentration of sodium hydroxide. The p*K*_a^{KH}

values in the presence of SB3-14 and SDS surfactants were also measured for sake of comparison.

pK_a^{KH} in water. The concentration of NaOH was varied in the range 0.1–4 mol dm⁻³ while the concentration of the substrate was kept constant at 5 × 10⁻⁵ mol dm⁻³. The absorbance measurements were treated using Eq. (4)

$$K_a^{KH} = K_W / K_b^{KH} = K_W / \{(A_{\max} - A) \times [OH^-]\} / (A - A_0) \quad (4)$$

where A, A₀ (0.009) and A_{max} (0.652) are absorbances at λ = 339 nm at the specified [OH⁻], in water and at the highest [OH⁻], respectively. A thermodynamic pK_a^{KH} value of 13.2 (± 0.1) was obtained by extrapolation to zero [OH⁻] of a linear plot of pK_a^{KH} vs. [OH⁻]²² assuming that this dependence becomes linear²⁴ below *ca.* 2 mol dm⁻³.

pK_a^{KH} in aqueous surfactants. The concentrations of the substrate, CTAB, SB3-14 and SDS were kept constant (5 × 10⁻⁵, 0.01, 0.01 and 0.03 mol dm⁻³, respectively) while the concentration of NaOH was varied in the range 0.001 – 0.7 mol dm⁻³. The absorbance measurements were treated with Eq. (4) using A₀ and A_{max} obtained at λ_{max} values 357, 354 and 336 nm for CTAB, SB3-14 and SDS, respectively. The thermodynamic acid dissociation constants, pK_a^{KH} (CTAB) = 10.9 (± 0.1), pK_a^{KH} (SB3-14) = 12.1 (± 0.1) and pK_a^{KH} (SDS) = 13.4 (± 0.1), were obtained by extrapolation to zero [OH⁻] of the linear plots of pK_a^{KH} vs. [OH⁻].

Binding constants

Thanks to the bathochromic shift of λ_{max} of the enolate due to the association of **2PF** with the surfactant (S) (see Figure 2), it was possible to measure directly the binding constants (K_S^E) of the enolate form of **2PF** by UV–VIS spectroscopy. In the presence of CTAB the change in absorbance at λ 357 nm was measured as a function of the concentration of the surfactant in 0.2 mol dm⁻³ NaOH assuming that both the free and the associated enolate contribute to the observed absorbance, A. Equation (5) was derived accordingly, where [**2PF**]_i is the initial concentration of the substrate and ε_{E-CTAB} (12504 dm³mol⁻¹cm⁻¹) and ε_E (6916 dm³mol⁻¹cm⁻¹) are the molar absorptivities of the associated and free enolate respectively.

$$A = \{[2PF]_i \times K_S^E \times [S] / (1 + K_S^E \times [S])\} \times \epsilon_{E-S} + \{[2PF]_i / (1 + K_S^E \times [S])\} \times \epsilon_E \quad (5)$$

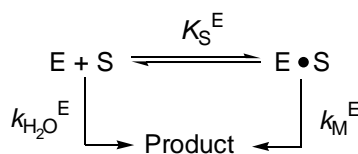
From a best fit of experimental A values to Eq. (5) a value is obtained of $K_{CTAB}^E = 7900 (\pm 1300) \text{ dm}^3\text{mol}^{-1}$.

Analogously the binding constant, $K_{CTAB}^{KH} = 690 (\pm 110)$, of the keto form with the surfactant was determined in aqueous solution of CTAB at λ_{max} = 246 nm.

Micellar effects upon ketonization reactions under the adopted experimental conditions can be treated^{2,25,26} quantitatively in terms of an equilibrium distribution of the enolate, E, between water and micelles as distinct reaction regions (Scheme 5) using Eq. (6), derived from Eq. (7), where the subscripts H₂O and M refer to aqueous- and micellar pseudophases, respectively.

$$1/k_e = \{(1/k_{\text{H}_2\text{O}}^{\text{E}}) + (K_{\text{S}}^{\text{E}} \times [\text{S}]/k_{\text{H}_2\text{O}}^{\text{E}})\} / \{1 + (k_{\text{M}}^{\text{E}} \times K_{\text{S}}^{\text{E}} \times [\text{S}]/k_{\text{H}_2\text{O}}^{\text{E}})\} \quad (6)$$

$$k_e = \{k_{\text{H}_2\text{O}}^{\text{E}} + (k_{\text{M}}^{\text{E}} \times K_{\text{S}}^{\text{E}} \times [\text{S}])\} / \{1 + (K_{\text{S}}^{\text{E}} \times [\text{S}])\} \quad (7)$$



Scheme 5

A multiple-regression analysis of Eq. (6) by using experimental k_e , $k_{\text{H}_2\text{O}}^{\text{E}}$ and $[\text{CTAB}]$ values (Figure 3) affords the following results: $K_{\text{CTAB}}^{\text{E}} = 9990 (\pm 1480) \text{ dm}^3 \text{ mol}^{-1}$; $k_{\text{M}}^{\text{E}} = 0.87 (\pm 0.04) \text{ s}^{-1}$, in quite good agreement with the value of $K_{\text{CTAB}}^{\text{E}} = 7900 (\pm 1300) \text{ dm}^3 \text{ mol}^{-1}$ calculated by Eq. (5) from results in aqueous solutions of CTAB in the absence of external NaCl.

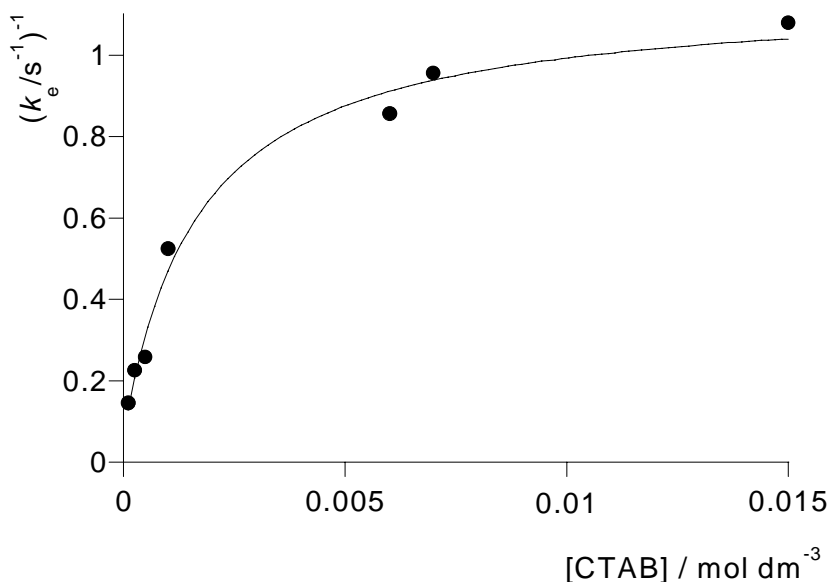


Figure 3. Plot of the experimental first-order rate constants for ketonization of the enolate of **2PF** in NaOH (0.01 mol dm⁻³) against the stoichiometric concentration of CTAB, fitted into Eq. (6) (solid line).

A similar spectrophotometric determination of the binding constants ($K_{\text{SB3-14}}^{\text{E}}$) of the enolate form of **2PF** with the zwitterionic surfactant SB3-14 gave a $K_{\text{SB3-14}}^{\text{E}} = 845 (\pm 82) \text{ dm}^3 \text{ mol}^{-1}$ while the absorbance of **2PF** solution decreases on addition of SDS allowing no determination of the corresponding binding constant. A value of $K_{\text{SB3-14}}^{\text{KH}} = 701 (\pm 95) \text{ dm}^3 \text{ mol}^{-1}$ was determined at $\lambda_{\text{max}} = 247 \text{ nm}$ for the keto form.

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