Determination of keto–enol equilibrium constants and the kinetic study of the nitrosation reaction of β-dicarbonyl compounds

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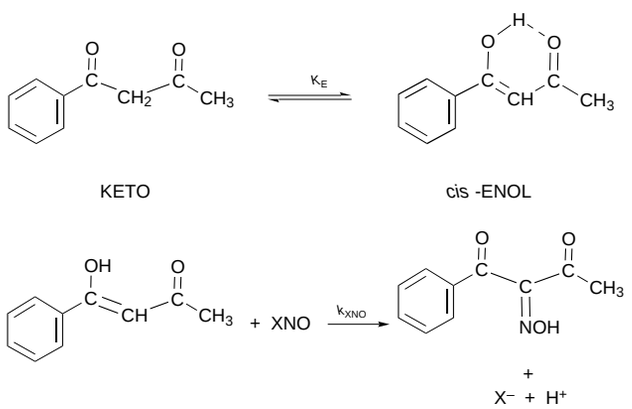
The keno–enol equilibrium constants of acetylacetone, ethyl acetoacetate and ethyl benzoylacetate in water at 25 °C are determined by studying the influence of surfactants on their UV–VIS spectra, following the method applied to benzoylacetone published recently. These measured equilibrium constants are used to obtain the reactivity of the ketones towards several nitrosating agents. For this end, the nitrosation reaction of benzoylacetone, acetylacetone, ethyl acetoacetate and ethyl benzoylacetate are studied in aqueous acidic solution in the presence and absence of Cl^-, Br^- or SCN^-. Analysis of the kinetic data indicates that the rate-limiting step is, in every case, the reaction of the enol.

Introduction

β-Diketones and other β-dicarbonyl compounds or related structures, are readily nitrosated to yield nitroso ketones, which are usually stable as oxime tautomers.[1] Detailed studies of the mechanism of this reaction in water have been carried out recently by Williams and co-workers.[2–4] The reaction, analogous to other electrophilic substitutions, involves enolization of the ketone (or, more generally, tautomerisation), followed by electrophilic nitrosation of the enol, important intermediates in many reactions. In some cases there is evidence of the involvement of enolates or carbanions[5] as the effective substrates, the latter being the only route detected for malononitrile both in acid[6] and in basic[7] conditions. The process is typified by the reaction of benzoylacetone in Scheme 1.



Scheme 1

The most commonly used nitrosating agents have been aqueous acidic solutions of sodium nitrite.[8] In the presence of nucleophilic species (X^-), such as Cl^-, Br^- or SCN^- reaction by the nitrosyl compounds (XNO) can also take place; then, a catalysis usually linear, becomes observable because of the presence of these nucleophiles.

Depending on the nature of the ketone and on the experimental conditions, the reaction may be first-order in both [ketone] and [H^+], and zero-order or first-order in the nitrosating agent concentration,[3] meaning that the rate-limiting step may be either the enolization of the ketone or the attack of the nitrosating agent on the enol. This change in the mechanism of the reaction can be effected for the nitrosation of those ketones with low enol content by adjusting the experimental conditions, particularly both [X^-] and [nitrite].

When nitrosation is the rate-limiting step, as is the case for the 1,3-diketones studied here, the rate constants corresponding to the attack of the different nitrosating species on the enolic form that can be determined from the kinetic data depend directly on the value of the keto–enol equilibrium constant (K_E) of the ketone.

In this context, keto–enol tautomerism in β-dicarbonyl compounds has been the object of extensive investigation and much debate.[9,10] The enol tautomer may predominate at equilibrium; it is stabilized relative to the keto tautomer *via* resonance through the conjugated π-system and by intramolecular hydrogen bonding. In protic solvents (water, alcohols) the intramolecular H-bond is broken and replaced by association with solvent by intermolecular hydrogen bonding, which better stabilizes the keto form. Consequently, as the polar carbonyl compounds are progressively diluted with non-polar or aprotic solvents, the enol content of the system increases. Likewise, at constant concentrations, the differences in polarity between these 'inert' solvents also produce predictable shifts in the keto–enol equilibrium.

Surfactants with hydrocarbon chains attached to ionic or polar head groups self-assemble in water at concentrations above the critical micelle concentration (cmc) to yield aqueous micellar solutions.[11] These aqueous micellar solutions influence reaction rates and equilibria by providing a submicroscopic reaction or solubilization medium different from that of the bulk solvent.[12]

In a previous paper,[13] a novel method was proposed to determine keto–enol equilibrium constants of β-dicarbonyl compounds in water and was applied to the case of benzoylacetone (1-phenylbutane-1,3-dione, BZA). Basically, the method is based on the property of micelles to offer a different medium inside the bulk water solvent and on the extremely solvent-sensitive character of the keto–enol tautomerism of β-dicarbonyl compounds.[14] The present work applies the aforementioned method further to determine the keto–enol equilibrium constants in water of acetylacetone (AcAc), ethyl acetoacetate (EAA) and ethyl benzoylacetate (EBZA). The enolization constants determined in this manner were used to calculate, from the experimental kinetic results obtained in water, the reactivities of these ketones towards the nitrosating agents NO^+, ClNO, BrNO and SCNNO. Some discrepancies have been found between the data of this study and the K_E values in the literature.

Experimental

Materials

BZA and EAA (Aldrich), products of the maximum purity, were used as supplied. AcAc (Merck) was purified by fractional low-pressure distillation and EBZA, which decomposes by fractional low-pressure distillation (at 60 °C), was purified by chromatography. The surfactants sodium dodecyl sulfate (SDS), tetradecyltrimethylammonium bromide (TTABr), cetyltrimethyl ammonium bromide (CTABr) and polyoxyethylene, 9-dodecyl ether ($C_{12}E_9$) (Aldrich and Sigma), were used without further purification. The remaining reagents ($NaNO_2$, $HClO_4$, NaCl, NaBr, NaSCN, HCl) (Merck) were used as received. All solutions were prepared with doubly distilled water obtained from a permanganate solution.

Methods

The pure ketones were dissolved in dioxane (spectrophotometric grade). From these stock solutions, the working solution was prepared daily by diluting the appropriate volume (between 0.2–0.4 ml) in 25 ml final volume to produce an aqueous solution of the required concentration for each case.

The stability of the dicarbonyl compound in the aqueous medium under the experimental conditions was examined by looking at the possible changes which could be observed in the absorption spectra (obtained by adding the dicarbonyl compound in dioxane solution directly to the water mixture),† or by carrying out kinetic experiments with the same ketone aqueous solution at several different time intervals. Under the experimental conditions of the present work, the aqueous solutions of the ketones studied were completely stable, at least during the time of analysis.

UV–VIS absorption spectra and kinetic measurements were recorded with Kontron-Uvikon (models 941 or 942) double-beam spectrophotometers, both provided with multiple cell carriers thermostatted by circulating water. All experiments were performed at 25 °C.

The procedure followed to obtain the UV–VIS spectra of a ketone aqueous solution in the presence of surfactants, in order to determine the keto–enol equilibrium constants in water (K_E), has been reported previously.[13] The measurements were taken in acidic media ([HCl] *ca*. 0.03 mol dm^{-3}), as some studies[15] refer to the slow interconversion between the keto and enol tautomers, which is catalysed by H^+. Nevertheless, as we shall see, the results obtained in the present work are the same for the case of EAA working in acidic and neutral media. There are a number of examples in the literature where enolization is not acid catalysed. This is interpreted as base-catalysed (solvent in this case) ionization leading to the carbanion ⟷ enolate intermediate.

All kinetic studies were carried out under pseudo-first-order conditions, with the [nitrite] at least 10 times greater than the concentration of the ketone, except in the case of EAA, for which the [EAA] was always in excess over the nitrosating agent concentration. In every kinetic experiment, the $NaNO_2$ aqueous solution, previously thermostatted at the same temperature as the rest of the reaction mixture, was added (0.10–0.20 ml) to start the reaction; this procedure guarantees that keto–enol equilibrium is achieved before the reaction starts. In each case the integrated method was followed, fitting the experimental absorbance–time date to the first-order integrated equation and obtaining satisfactory correlation coefficients (>0.999) and residuals. The reaction spectra were clean in every case. In this connection, the spectra of the reaction between BZA (7×10^{-5} mol dm^{-3}) and $NaNO_2$ (1.7×10^{-3} mol dm^{-3}) in acid media (0.03 mol dm^{-3} of HCl) were clean, with an isosbestic point at 280 nm; all reactions were observed by recording the decrease in absorbance due to enol consumption at 312 nm. The reaction spectra between AcAc (1.5×10^{-4} mol dm^{-3}) and $NaNO_2$ (3×10^{-3} mol dm^{-3}) in aqueous acid media (0.03 mol dm^{-3} $HClO_4$) displayed clear isosbestic points at *ca*. 256 and 305 nm; the kinetic studies were made by recording the decrease in absorbance at 274 nm, due to enol consumption, or the increase in absorbance at 245 nm due to oxime formation; in both cases the same value, within experimental error, was obtained for the rate constant. For the experimental conditions of $[NaNO_2] = 5 \times 10^{-3}$, $[EBZA] = 1 \times 10^{-4}$ and $[HCl] = 0.16$ mol dm^{-3} the spectra of the nitrosation reaction of EBZA exhibited clear isosbestic points at 237, 256 and 320 nm; the nitrosation reaction was noted by recording the increase in absorbance at 280 nm. Finally, the spectra of the reaction between EAA (0.04 mol dm^{-3}) and $NaNO_2$ (2.5×10^{-3} mol dm^{-3}) at 0.03 mol dm^{-3} of $HClO_4$ showed an isosbestic point at 320 nm; the reaction was studied by recording the decrease in absorbance at 371 nm (ε *ca*. 55 dm^3 mol^{-1} cm^{-1}) due to consumption of nitrite.

Results and discussion

Keto–enol equilibrium studies

The method followed to determine the keto–enol equilibrium constants in water of 1,3-dicarbonyl compounds was reported for the case of BZA in a previous paper.[13] The method is based on the use of surfactant solutions that generate micelles in water. The presence of micelles alters the keto–enol equilibria of β-dicarbonyl compounds by taking up the enolic form, which is stabilized by intramolecular hydrogen bonding and therefore increasing the percentage of the enol tautomer in non-polar or in non-hydrogen bond donor solvents.

Fig. 1 shows the absorption spectra of AcAc and EAA in water and cyclohexane (CyH). As shown, the absorption band due to the enolic form of AcAc and centred at *ca*. 275 nm increases strongly in CyH; similarly, the UV-absorption band centred at 245 nm in the case of EAA increases in CyH; meanwhile, the band at 211 nm, mainly resulting from the keto form, does not appear in CyH. In the case of EBZA, strong absorption in water occurs at 248 nm and weak absorption appears at 284 nm; in CyH solvent, a strong decrease in the absorption band at 248 nm (mainly due to the keto form) is observed and an increase in the absorption band centred at 284 nm (due to the enol form) appears.

Fig. 2 shows the relationship between the absorbance (A_λ) of the diketone solution, in water and in CyH solvent and [ketone]. Except for the case of EBZA at the wavelength absorption of the enol tautomer in CyH, a perfectly linear correlation between A_λ and [ketone] was observed, thereby indicating negligible association of the dicarbonyl compound molecules in both the enol and keto forms. In the case of EAA, this behaviour was observed even up to 0.16 mol dm^{-3} of EAA [see Fig. 2(*b*)], whereas the enol form of EBZA in CyH solvent shows important association at ketone concentrations higher than 10^{-4} mol dm^{-3}. Least-squares fitting of the data A_λ *versus* [ketone] yielded the results listed in Table 1 for the slopes of the corresponding lines; also reported is the wavelength at which the absorbance readings were taken and the range of ketone concentration used.

In water, both the keto (KH) and enol (EH) tautomers are in equilibrium in measurable proportions. Therefore, since [ketone] = [KH] + [EH], eqn. (1) may be applied to express the

$$A_\lambda = \frac{\varepsilon_{EH}\, l\, K_E}{1 + K_E}\,[\text{Ketone}] \qquad (1)$$

variation of the absorbance of the solution (read at a wavelength where only the enol form absorbs) as a function of [ketone]. In this equation, l (= 1.0 cm) is the pathlength of the

† In some cases (BZA, AcAc), a rapid decrease in absorbance at starting was observed as a consequence of the tautomerization of the enol form (high content in dioxane) to the keto form (more prevalent in water).

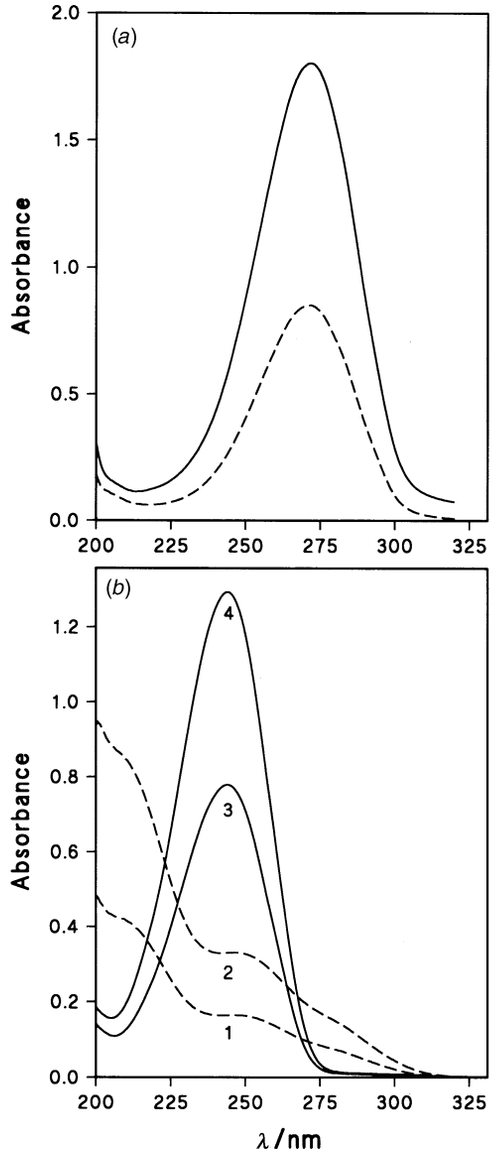


Fig. 1 Absorption spectra of (*a*) AcAc in (——) CyH at 1.7×10^{-4} mol dm^{-3} and in (– – –) water at 3.9×10^{-4} mol dm^{-3}, and of (*b*) EAA in water at 4.1×10^{-3} (1) and 6.2×10^{-3} (2), and in (——) CyH at 2.7×10^{-4} (3) and 4.3×10^{-4} (4), in mol dm^{-3}

light, ε_{EH} is the extinction coefficient of the enol at λ (see Table 1) and K_E refers to the keto–enol equilibrium constant. The values of the slopes in Table 1, then, depend both on ε_{EH} and K_E. If the enol were the only species present under any experimental condition, then the slope of the line A_λ *vs.* [ketone] would be equal to ε_{EH}.

The value of the extinction coefficient of the enolic form of a dicarbonyl compound is assumed to be of the order of (16–12) $\times 10^3$ dm^3 mol^{-1} cm^{-1}; it depends on the compound[16] and on the solvent.[17] For the enol form of BZA we have measured a value of 13 900 dm^3 mol^{-1} cm^{-1} at $\lambda = 312$ nm.[13] Judging from the data in Table 1, either the percentage of enolization is lower than 100% in every case, even in CyH solvent, or the extinction coefficient of the enol varies from one dicarbonyl compound to another.

Regarding the above, previous studies of keto–enol tautomerization of β-dicarbonyl compounds[18–21] have demonstrated that the enolization equilibrium constant of a given β-dicarbonyl compound increases as both the solvent polarity and the β-dicarbonyl compound concentration decrease. For example, in the case of AcAc, $K_E = 0.34$ in water and to 42 in CyH and K_E in THF (tetrahydrofuran) is equal to 4.3 at [AcAc] = 0.1 mol dm^{-3} and to 7.2 at [AcAc] = 2×10^{-3} mol dm^{-3}; in the same way, for the case of EAA, $K_E = 0.053$ in water and to 0.98 in CyH and K_E in CyH solvent is equal to 0.98 at 0.1 mol dm^{-3} of EAA and equal to 1.65 at 2×10^{-3} mol dm^{-3}. Nevertheless, the advantages of our proposed method for measuring keto–enol equilibrium constants are founded on the use of small ketone concentrations and it is not necessary to assume the extinction coefficient of the enol form.

Table 1 Experimental conditions and slopes of the plots of absorbance readings at the indicated wavelength *vs.* ketone concentration

Ketone	Solvent	λ/nm	Slope/ dm^3 mol^{-1}	Range [Ketone]/ mol dm^{-3}
AcAc	Water–HCl	274	1 899 ± 21	(0.06–1) × 10^{-3}
AcAc	CyH	274	10 966 ± 214	(0.25–2.5) × 10^{-4}
EAA	Water–HCl	211	136 ± 1	(1–9.3) × 10^{-3}
EAA	Water–HCl	245	53.2 ± 0.4	(1–9.3) × 10^{-3}
EAA	Water–HCl	300	6.7 ± 0.1	(0.02–0.16)
EAA	CyH	245	3 364 ± 32	(0.9–8) × 10^{-4}
EBZA	Water–HCl	248	12 250 ± 28	(0.12–1.5) × 10^{-4}
EBZA	Water–HCl	284	1 450 ± 6	(0.12–1.5) × 10^{-4}
EBZA	Water–HCl	300	625 ± 5	(0.12–1.5) × 10^{-4}
EBZA	CyH	248	9 232 ± 96	(0.13–1.3) × 10^{-4}
EBZA	CyH	284	5 305 ± 73	(0.13–1.3) × 10^{-4}
EBZA	CyH	300	3 912 ± 59	(0.13–1.3) × 10^{-4}

Fig. 3 shows the effect of surfactants on the keto–enol equilibrium of EAA and EBZA. At constant [ketone] in acid medium, an increase in the surfactant concentration above the cmc (critical micelle concentration) is accompanied by an increase in the absorption band related to the enol tautomer. Typical results for the variation in the A_λ of aqueous EAA, AcAc and EBZA solutions with the [surfactant] are shown in Fig. 4. The solid lines correspond to the theoretical fits of eqn. (2) to the experimental points of A_λ *vs.* $[D_n]$; D_n being the micellized surfactant, *i.e.* $[D_n] = [\text{surfactant}]_t - \text{cmc}$; A_λ^0 means the UV-absorption of the aqueous ketone solution in the absence of surfactant [see eqn. (1)]; and K_s is the association constant of the enol form to the micelle, *i.e.* $K_s = [EH]_m/[EH]_w [D_n]$ (the subscripts m and w refer to the micelle and aqueous pseudo-phases, respectively).

$$A_\lambda = \frac{A_\lambda^0 (1 + K_s [D_n])}{1 + \dfrac{K_E K_s}{1 + K_E} [D_n]} \qquad (2)$$

The values of K_s and $K_E/(1 + K_E)$ were calculated by fitting the experimental data to eqn. (2), using both values as adjustable parameters and A_λ^0 as input. The results obtained are presented in Table 2. The experimental conditions and the calculated values of K_E are also reported.

The values of K_s do not correlate with the hydrophobicity of the micelles; *i.e.* this value is greater for the case of SDS micelles, the least hydrophobic, than for the case of CTABr micelles, the most hydrophobic. This situation has not been found with BZA; here, the results were quantitatively explained under the assumption that the enolic form associates to micelles by hydrophobicity, since a satisfactory correlation was observed between K_s and the number of C-atoms in the hydrocarbon chain of the surfactant. On the other hand, the absence of a bathochromic shift in the maximum wavelength absorptions of BZA, on an increase in the polarity and/or in the dielectric properties of the solvent (by comparing the spectrum in water and in micellar medium), indubitably indicates that BZA-enol is dissolved in the micellar interface. The different behaviour observed between BZA and the ketones studied here, can be ascribed to the less hydrophobic character of these ketones, which causes them to reside inside the micellar interface in a more exterior zone, where interaction with the head groups is possible. Therefore, it is easy to explain the higher association of these ketones with the SDS-micelles, where the interaction of

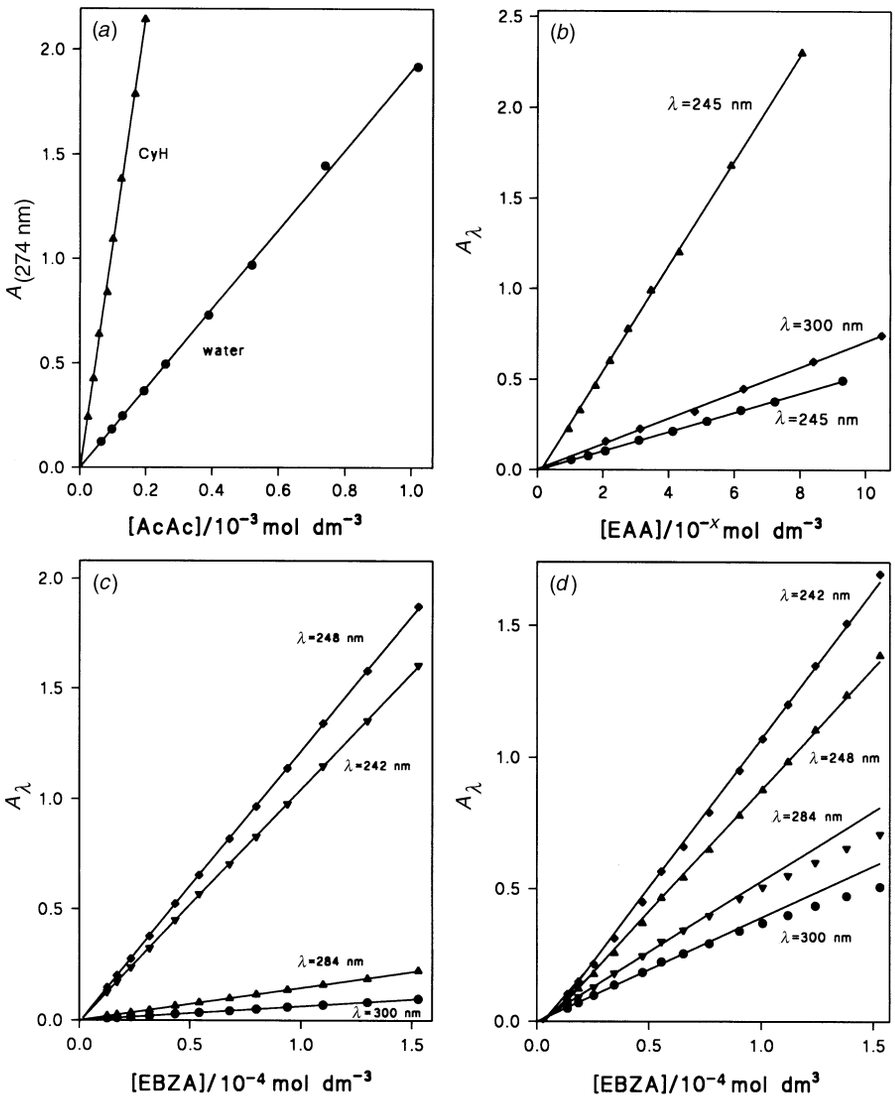


Fig. 2 Relationship between the absorbance and ketone concentrations in aqueous and cyclohexane solutions (*a*) AcAc in (▲) CyH and in (●) water at [HCl] = 0.017 mol dm^{-3}; (*b*) EAA in (▲) CyH, $x = 4$ and in water (◆) $x = 2$, (●) $x = 3$ at [HCl] = 0.03 mol dm^{-3}; (*c*) EBZA in water at [HCl] = 0.017 mol dm^{-3}; (*d*) EBZA in CyH

the enolic form is due not only to hydrophobicity, but also to reformation of hydrogen bonds with the sulfate head groups; this interaction is not possible with the tetramethylammonium head groups. In this context, we may observe the lower difference of K_s of EAA (or EBZA) as compared to AcAc, a consequence of the greater hydrophobic character of those compounds, which causes these substrates to be located in a deeper zone of micellar interface, where the interactions with the surfactant head groups are poorer.

We can also say, judging from the small values of K_s and K_E, that a high percentage of the keto form is in equilibrium with the enol form, even at high surfactant concentration; *i.e.* in the micellar solution the enolization is lower than 100%.

There is some difference between the K_E values obtained in this work and those determined with other methods; the most important discrepancy is found with EAA. As we shall see from the kinetic results, the values of K_E determined here seem to be more appropriate for explaining the reactivity of these ketones.

Finally, the influence of surfactant on the absorption spectra of EBZA demonstrates a rapid increase in the absorption band due to the enol tautomer at low surfactant concentrations [see insert of Fig. 4(*b*)], to then become independent of surfactant concentration; nevertheless, the band centred at 248 nm—due mainly to the keto tautomer—does not disappear even at high [surfactant] [see Fig. 3(*b*)]. This effect could be explained if the keto form of EBZA also solubilizes in the micellar phase; in fact, one can see in Fig. 3(*b*) a bathochromic shift of the absorption bands in the presence of micelles—more pronounced for the band centred at *ca.* 248 nm; at the same time, the clear isosbestic points which were observed with BZA—indicative of the conversion of the keto into the enol tautomer—are not observed here. Therefore, when one takes into account that the keto form of the EBZA is also solubilized in the micelles, the denominator of eqn. (2) would have to include the association constant of the keto form to the micelles; thus the denominator of eqn. (2) changes to $1 + (K_s' + K_E K_s)/(1 + K_E)$, with K_s' being the corresponding binding constant. Obviously, this simple expression is applicable only for the absorbance readings at 300 nm, where the keto form does not absorb. Consequently, to obtain the entire equilibrium constant, we must assume a value of $K_E = 0.20$, by comparison with the equilibrium and kinetic (see below) results obtained with EAA. With this assumption, we arrived at the following: $K_s' = 65$ and 27 dm^3 mol^{-1} for the association of the keto form of EBZA to SDS and TTABr micelles, respectively. The differing values, contrary to the micelle hydrophobicity, indicate that the EBZA–keto is located in the micellar interface and since the SDS micelles are more hydrated, the stronger interactions with the solvent molecules and sulfate head groups in this region make for an increase in the solubility of this tautomer in the SDS micelles, as compared with that of TTABr micelles.

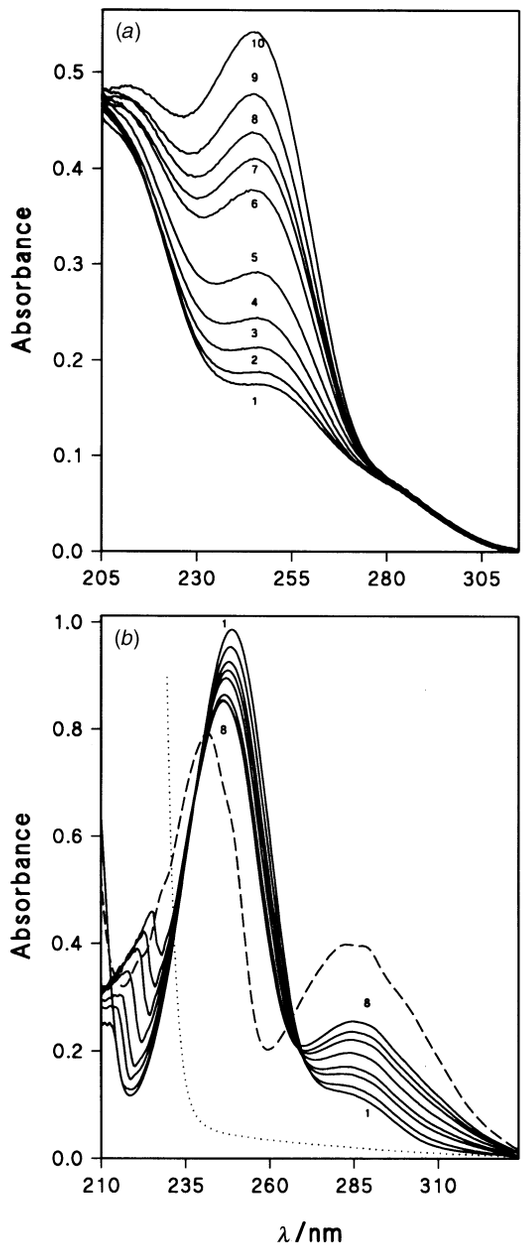


Fig. 3 (*a*) Absorption spectra of EAA (3.1×10^{-3} mol dm^{-3}) at [HCl] = 0.031 mol dm^{-3} as a function of [SDS] of (1) 5.5; (2) 11; (3) 22; (4) 33; (5) 55; (6) 110; (7) 132; (8) 154; (9) 198; (10) 275 mmol dm^{-3}; and (*b*) absorption spectra of EBZA (– – –) 7.4×10^{-5} mol dm^{-3} in CyH; (——) 7.7×10^{-5} mol dm^{-3} at [HCl] = 0.017 mol dm^{-3} as a function of [TTABr] of (1) 0; (2) 4.4; (3) 8.8; (4) 13.2; (5) 26.4; (6) 66; (7) 132; (8) 297 mmol dm^{-3}; (····) aborption spectra of aqueous TTABr

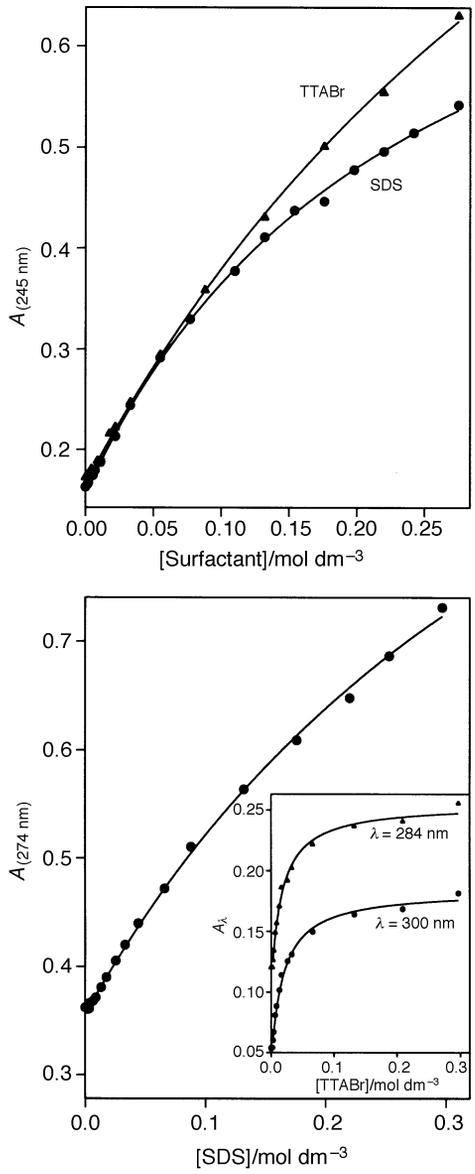


Fig. 4 (*a*) Influence of (●) [SDS] at [HCl] = 0.033 mol dm^{-3} and of (▲) [TTABr] at [NaCl] = 0.067 mol dm^{-3} on the absorbance intensity at 245 nm of EAA (3.1×10^{-3} mol dm^{-3}); (*b*) AcAc (1.95×10^{-4} mol dm^{-3}) at [HCl] = 0.013 mol dm^{-3}; the insert shows the variation of the absorbance of EBZA (7.7×10^{-5} mol dm^{-3}) at [HCl] = 0.017 mol dm^{-3} as a function of [TTABr] at two wavelength values

Kinetic studies

Ketones react with a variety of nitrosating agents, including nitrous acid ($H_2NO_2^+$ or NO^+), nitrosyl halides (XNO), alkyl nitrites and others, to produce nitroso ketones, which are usually stable as the oxime tautomers. The nitrosation reactions of BZA, AcAc, EAA and EBZA in aqueous acid medium were studied in the absence and presence of nucleophiles.

In the absence of nucleophiles, the nitrosation of BZA, AcAc and EBZA was carried out with [nitrite] ≫ [ketone]; in the case of EAA, [EAA] greatly exceeded [nitrite]. In all cases, the experimental absorbance–time data perfectly fit the first-order integrated equation.

The influence of [nitrite] or [EAA] was studied in aqueous perchloric acid at constant [H^+]. The influence of [H^+] has been studied at a constant nitrite concentration. The ketone concentrations and the experimental conditions used in each case are reported in Table 3. The variations of the observed pseudo-first-order rate constant, k_o, with both [nitrite] or [EAA] and [H^+] are shown in Figs. 5 and 6, respectively. With BZA and AcAc, good straight lines with no significant intercept at the origin were attained; in contrast, in the case of their ethyl esters, EBZA and EAA, a small but significant intercept at [nitrite] or [EAA] = 0, respectively, was observed.

These results are consistent with a mechanism in which the rate-limiting step is the nitrosation reaction of the enol tautomer of the ketone. In the absence of nucleophiles the only possible nitrosating agent is the NO^+ ($H_2NO_2^+$) that is formed from the protonation of nitrous acid: $HNO_2 + H^+ \rightleftharpoons NO^+ + H_2O$, K_{NO} being the corresponding equilibrium constant whose value is reported[22] as 3.5×10^{-7} dm^3 mol^{-1}; as well as at this [H^+], all the nitrite is in the form of HNO_2 (pK_a = 3.1[23]). All these considerations lead to the expression in eqn. (3) for the reaction rate, namely, first-order in both substrates (ketone and nitrite) and first-order in [H^+].

Table 2 Values of the optimized parameters for the binding constants of the enolic form of ketones (K_s), and the keto–enol equilibrium constants in water (K_E) obtained by studying the influence of [surfactant] on the absorption spectra of ketones under the indicated experimental conditions

[Ketone][a]/10^{-3} mol dm^{-3}	Medium[b]	λ/nm	A^0	K_s/dm^{-3} mol	$K_E/(1 + K_E)$	K_E	K_E[c]
AcAc (0.19)	SDS	274	0.3605	7.7 ± 0.3	0.28 ± 0.01	0.38	0.34[15(b)]
AcAc (0.19)	TTABr	274	0.3592	4.5 ± 0.3	0.30 ± 0.02	0.43	0.23[15(a)]
AcAc (0.19)	CTABr	274	0.3566	5.4 ± 0.6	0.32 ± 0.06	0.47	0.19[14]
AcAc (0.20)	$C_{12}E_9$	274	0.3696	5.2 ± 0.1	0.29 ± 0.03	0.40	0.21[16]
EAA (3.1)	SDS	245	0.1632	21.5 ± 0.6	0.185 ± 0.004	0.23	0.057[15(b)]
EAA (3.1)	SDS[d]	245	0.1685	24.1 ± 0.5	0.194 ± 0.003	0.24	0.07[15(a)]
EAA (3.1)	TTABr	245	0.1700	16.1 ± 0.4	0.111 ± 0.005	0.12	0.005[16]
EAA (3.1)	TTABr[d]	245	0.1720	16.6 ± 0.4	0.115 ± 0.005	0.13	
EAA (3.1)	CTABr	245	0.1720	23 ± 1	0.15 ± 0.01	0.16	
EBZA(0.11)	SDS	300	0.0760	161 ± 10	81 ± 5[e]	0.20[f]	0.23[18g]
EBZA (0.11)	SDS	284	0.170	126 ± 9	86 ± 7[e]	0.20[f]	0.58[18h]
EBZA (0.076)	TTABr	300	0.0540	169 ± 16	50 ± 5[e]	0.20[f]	0.54[25h]
EBZA (0.076)	TTABr	284	0.1204	115 ± 8	54 ± 4[e]	0.20[f]	

[a] Values in parentheses are [ketone]. [b] Hydrochloric aqueous solutions of the indicated surfactant. [c] Literature values in water. [d] With NaCl instead HCl. [e] Values determined for the expression $(K_s' + K_sK_E)/(1 + K_E)$. [f] Assumed value. [g] For the neat liquid. [h] In CCl_4.

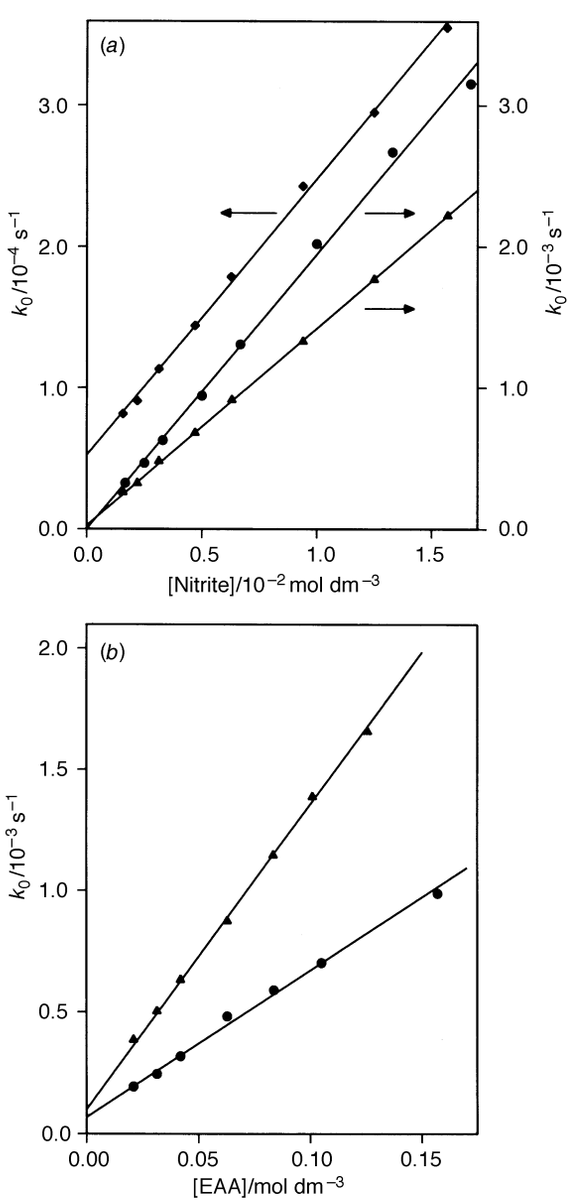


Fig. 5 Influence of [nitrite] on the nitrosation of (●) BZA and of (▲) AcAc at $[H^+] = 0.031$ mol dm^{-3}, and (◆) EBZA at $[H^+] = 0.10$ mol dm^{-3}; and of [EAA] on the nitrosation of EAA at $[H^+]$ of (▲) 0.065 and (●) 0.031 mol dm^{-3}

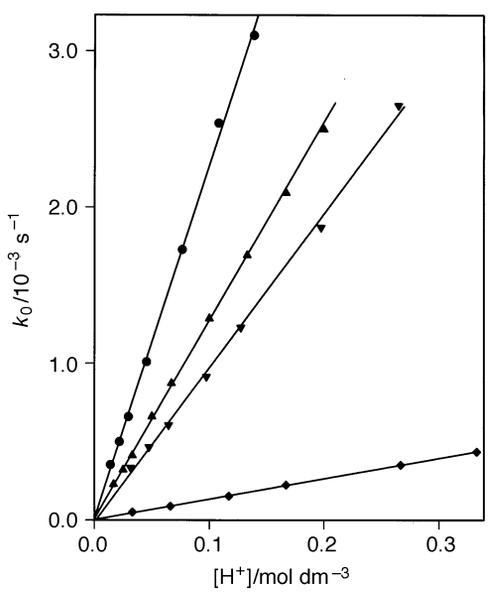


Fig. 6 Influence of $[H^+]$ on the nitrosation of (●) BZA 7.5×10^{-5} mol dm^{-3}, [Nitrite] = 3.1×10^{-3} mol dm^{-3}; (▲) AcAc 1.7×10^{-4} mol dm^{-3}, [Nitrite] = 3.1×10^{-3} mol dm^{-3}; (▼) EAA 0.044 mol dm^{-3}, [Nitrite] = 2.5×10^{-3} mol dm^{-3}, and of (◆) EBZA 1.15×10^{-4} mol dm^{-3}, [Nitrite] = 4.7×10^{-3} mol dm^{-3}

$$\text{Rate} = k_{NO} K_{NO} \frac{K_E}{1 + K_E} [\text{Ketone}] [\text{Nitrite}] [H^+] = k_1 [\text{Ketone}] [\text{Nitrite}] [H^+] = k_o [\text{Ketone}] (= k_o [\text{Nitrite}]) \quad (3)$$

With BZA and AcAc there is no kinetic evidence of the reversibility of the reaction, primarily because of the small oxime concentration that can be formed; in the case of EBZA and EAA, the small intercept at the origin of the k_o *vs.* [nitrite] plot, in the former case and k_o *vs.* [EAA], in the latter, whose value increases with the $[H^+]$, suggests that the overall reaction is reversible,‡ and that $k_o = (k_1 [\text{nitrite}] + k_{-1}) [H^+]$, or $k_o = (k_1 [\text{EAA}] + k_{-1}) [H^+]$, where k_1 is the rate constant for the forward reaction and k_{-1} is the rate constant for the reverse reaction. Values of the overall equilibrium constants K ($= k_1/k_{-1}$) were found to be 350 and 370 dm^3 mol^{-1} for EBZA and 120 and 128

‡ The other possibility of the decomposition of nitrous acid can be ruled out. Direct measurements of this reaction at 3.1×10^{-3} mol dm^{-3} of $NaNO_2$ in the range of $[HClO_4]$ from 0.03 to 0.24 mol dm^{-3} shown no acidity dependence and a decrease in absorbance of 30% in 7 h. The slowest kinetic experiment conducted with EAA was completed in approximately 1.5 h.

Table 3 Experimental conditions and results obtained in the nitrosation of ketones in aqueous perchloric acid medium in the absence of nucleophiles

[Ketone][a]	$[H^+]$[a]	[Nitrite][a]	k_1[b]	k_{-1}[c]	K_E	$k_{NO}K_{NO}$[b]
BZA (0.075)	0.031	Variable	6.26	—	0.60	16.7
BZA (0.075)	Variable	1.7×10^{-3}	7.27	—	0.60	19.4
AcAc (0.17)	0.031	Variable	4.22	—	0.40	14.8
AcAc (0.17)	Variable	3.1×10^{-3}	4.02	—	0.40	14.1
EBZA (0.15)	0.10	Variable	0.195	5.2×10^{-4}	0.20	1.17
EBZA (0.15)	0.15	Variable	0.175	5.0×10^{-4}	0.20	1.05
EBZA (0.12)	Variable	4.7×10^{-3}	0.28	—	0.20	1.68
EAA (variable)	0.031	2.5×10^{-3}	0.19	1.64×10^{-3}	0.17	1.31
EAA (variable)	0.065	2.5×10^{-3}	0.19	1.52×10^{-3}	0.17	1.31
EAA (44)	Variable	2.5×10^{-3}	0.22	—	0.17	1.51

[a] Concentration in 10^{-3} mol dm^{-3}. [b] In dm^6 mol^{-2} s^{-1}. [c] In dm^3 mol^{-1} s^{-1}.

Table 4 Experimental conditions and values of the intercepts (= $k_1[H^+][Nitrite]$ or [EAA]) and slopes (= $k_2[H^+][Nitrite]$ or [EAA]) of the linear plots of k_o *vs.* $[X^-]$ [see eqn. (4)] obtained in the nitrosation of β-diketones at 25 °C

X^-	$[H^+]$/ mol dm^{-3}	[Nitrite]/ mol dm^{-3}	Intercept/ 10^{-4} s^{-1}	slope/10^{-3} dm^3 mol^{-1} s^{-1}	k_1/dm^6 mol^{-2} s^{-1}	k_2/dm^9 mol^{-3} s^{-1}
BZA (7.4×10^{-5} mol dm^{-3})						
Cl^-	0.031	1.67×10^{-3}	3.6 ± 0.1	1.12 ± 0.02	6.86	21.7
Br^-	0.031	1.67×10^{-3}	4.3 ± 0.3	5.4 ± 0.1	8.38	94
Br^{-1}	0.065	1.67×10^{-3}	8.2 ± 0.1	10.3 ± 0.3	7.44	104
SCN^-	0.023	1.67×10^{-3}	2.84 ± 0.07	401 ± 9	7.23	10 220
AcAc (1.5×10^{-4} mol dm^{-3})						
Cl^-	0.030	3.1×10^{-3}	4.59 ± 0.07	2.40 ± 0.02	4.49	23.5
Br^-	0.030	3.1×10^{-3}	4.75 ± 0.05	13.2 ± 0.4	4.64	104
SCN^-	0.030	3.1×10^{-3}	4.09 ± 0.04	661 ± 16	4.55	7 100
EAA (0.044 mol dm^{-3})						
Cl^-	0.031	2.5×10^{-3}	3.43 ± 0.05	2.9 ± 0.1	0.22[a]	2.2
Br^-	0.031	2.5×10^{-3}	3.9 ± 0.1	19.4 ± 0.2	0.25[a]	14.5
SCN^-	0.031	2.5×10^{-3}	4.1 ± 0.2	420 ± 4	0.26[a]	318
EBZA (1.15×10^{-4} mol dm^{-3})						
Cl^-	0.05	4.7×10^{-3}	0.73 ± 0.01	0.133 ± 0.003	0.20[a]	0.629
Br^-	0.05	4.7×10^{-3}	0.91 ± 0.02	0.363 ± 0.009	0.28[a]	2.2
SCN^-	0.05	4.7×10^{-3}	0.80 ± 0.02	27.2 ± 5	0.23[a]	129

[a] These values have been corrected from the value of k_{-1} which are included in the intercept value.

dm^3 mol^{-1} for EAA, as taken from two sets of measurements made at two difference acidities. Thus, oxime formation is very much favoured over its decomposition under these experimental conditions.

Least-squares fitting of the data to eqn. (3) yielded the results for k_1 [$= k_{NO}K_{NO}K_E/(1 + K_E)$] listed, along with the experimental conditions and the value of K_E used to obtain the value of $k_{NO}K_{NO}$, in Table 3. From $K_{NO} = 3.5 \times 10^{-7}$ dm^3 mol^{-1}, it is possible to estimate the bimolecular rate constant for the nitrosation by NO^+ *ca.* 4×10^7 dm^3 mol^{-1} s^{-1} in the case of BZA and AcAc and *ca.* 10 times lower in the case of their ethyl esters. This means that BZA and EAA show practically the same reactivity towards NO^+, but that the value is lower for the corresponding encounter limit and *ca.* 10 times more reactive than their respective ethyl esters. The former observation seems very logical if one takes into account the following: first, that the reaction centre (=CH–) is not directly attached to the different substituents (–CH_3 in AcAc, phenyl ring in BZA); and second, that the Taft inductive effects of both substituents are of a similar degree and that the resonance effect is more important through the carbonyl groups. Therefore the difference in k_1 (see Tables 3 and 4) could only be attributable to the distinct value of K_E.

On the other hand, the lower reactivity of EAA and EBZA, as compared to AcAc and BZA, could be due to the ethoxide substituent, which has an electron-withdrawing inductive effect; and the nitrosation reaction is an eletrophilic substitution. Nevertheless, if one takes $K_E = 0.20$[3] for AcAc, this ketone would show a reactivity towards NO^+ of nearly double that found with BZA; likewise, if K_E of EAA were taken as 0.005,[5] the corresponding enol would be even more reactive than the enol of BZA. Thus, these kinetic results are in total agreement with the results of K_E obtained in the present work.

In the presence of the nucleophiles Cl^-, Br^- and SCN^-, the nitrosation of BZA, AcAc, EBZA and EAA was studied at constant $[H^+]$, [Nitrite] and [Ketone]. The experimental conditions are presented in Table 4.

As expected, the reaction is notably catalysed by the presence of those nucleophiles. In all cases, good straight lines were obtained in the plots of k_o *vs.* $[X^-]$ (X = Cl, Br or SCN) with non-zero intercepts at $[X^-] = 0$. This non-zero intercept respresents reaction *via* the NO^+ and the catalysis results from the presence of the new nitrosating species, the nitrosyl halides (generally represented by XNO) which are formed in aqueous acid solutions of $NaNO_2$ in the presence of X^-, through the equilibrium process of $X^- + HNO_2 + H^+ \rightleftharpoons XNO + H_2O$. The corresponding equilibrium constants K_{XNO}, have been measured[24–26] and are reported in Table 5. Therefore in the presence of nucleophiles the reaction rate equation can be represented by eqn. (4). with $k_1 = k_{NO}K_{NO}K_E/(1 + K_E)$ and $k_2 =$

$$\text{Rate} = (k_1 + k_2[X^-])[\text{Ketone}][\text{Nitrite}][H^+] \qquad (4)$$

$k_{XNO}K_{XNO}K_E/(1 + K_E)$. This equation predicts linear behaviour for k_o *versus* $[X^-]$, as was experimentally observed in all cases. Fig. 7 shows typical results. The intercepts at the origin and the

Table 5 Average values of the bimolecular rate constants k_{XNO}, in $dm^3\ mol^{-1}\ s^{-1}$, for the reaction of the corresponding enol tautomer of each ketone with the nitrosating agents XNO, determined from the kinetic results obtained in the nitrosation of these β-diketones and the values of the equilibrium constants K_E and K_{XNO}

			Substrate			
Reagent	K_{XNO}[a]		BZA	AcAc	EBZA	EAA
—	—	K_E[b]	0.60[13]	0.40	0.20	0.17
NO^+[a]	3.5×10^{-7}[22]	k_{NO^+}[c]	5.5×10^7	4.4×10^7	3.9×10^6	3.7×10^6
ClNO	1.14×10^{-3}[24]	k_{ClNO}[c]	1.9×10^4	7.2×10^4	3.3×10^3	1.3×10^4
BrNO	0.051[25]	k_{BrNO}[c]	5.1×10^3	7.1×10^3	0.26×10^3	2.0×10^3
SCNNO	30[26]	k_{SCNNO}[c]	797	731	23	64

[a] In $dm^6\ mol^{-2}$, except K_{NO}, in $dm^3\ mol^{-1}$. [b] Determined in this work. [c] In $dm^3\ mol^{-1}\ s^{-1}$.

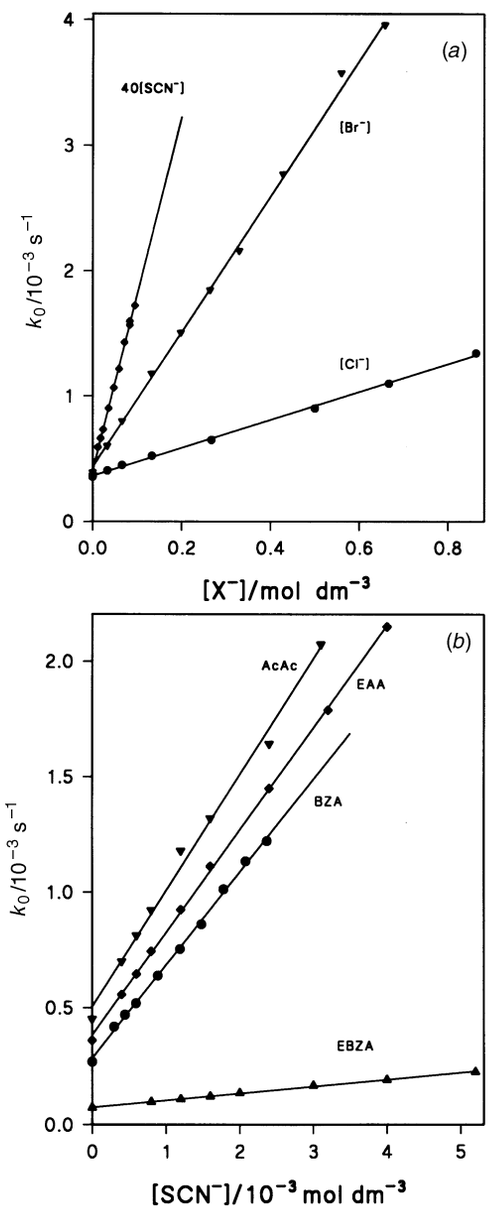


Fig. 7 (*a*) Influence of $[X^-]$ in the nitrosation reaction of BZA at [Nitrite] = 1.7×10^{-3} mol dm^{-3} and $[HClO_4]$ = 0.031 mol dm^{-3}; and (*b*) of $[SCN^-]$ on the nitrosation of (▼) AcAc at [Nitrite] = 3.1×10^{-3} mol dm^{-3} and $[H^+]$ = 0.031 mol dm^{-3}; (◆) EAA at [EAA] = 0.044 mol dm^{-3} and $[H^+]$ = 0.031 mol dm^{-3}; (●) BZA at [Nitrite] = 1.7×10^{-3} mol dm^{-3} and $[H^+]$ = 0.022 mol dm^{-3}, and (▲) EBZA at [Nitrite] = 4.7×10^{-3} mol dm^{-3} and $[H^+]$ = 0.045 mol dm^{-3}

slope of the corresponding plots imply the values of k_1 and k_2, respectively, which are reported in Table 4.

From the values of the rate constants k_1 and k_2 and of the equilibrium constant K_E and K_{XNO}, the reactivity of the four diketones towards the different nitrosating agents can be calculated and these are reported in Table 5 along with the equilibrium constants K_E and K_{XNO} used to calculated the values of k_{XNO}. For any one substrate, the reactivity sequence is clearly $NO^+ > NOCl > NOBr > NOSCN$. This is the expected sequence for the reactivity in water and it has been observed frequently in several nitrosation reactions,[3–5,27–30] whether N-, O-, S- or C-nitrosation. For each nitrosating agent the enol reactivity of BZA and AcAc is greater than the reactivity of their corresponding ethyl ester, as has been previously explained for the case of NO^+ and this is a consequence of the nature of the reaction being studied, an electrophilic addition to alkenes.

Conclusions

In the present study the keto–enol equilibrium constants in water of acetylacetone, ethyl acetoacetate and ethyl benzoylacetate have been determined by quantitatively analysing the effect of aqueous micellar solutions in their UV-absorption spectra. The presence of micelles shifts the keto–enol equilibrium to the enol form, which is trapped by the micelles, but the presence of micelles does not alter the equilibrium in the bulk water phase, thus micelles do not modify the properties of the bulk solvent. The K_E constants obtained in this manner differ, in some cases substantially, from literature values. The reactivity of these compounds towards several nitrosating agents shows that the 1,3-diketo compounds are more reactive than their corresponding ethyl esters; the differences observed in the third-order rate constant, k_1, being attributable to the distinct values of the keto–enol equilibrium constants. The reactivity results on the nitrosation reaction are in total accordance with the keto–enol equilibrium results determined in this work.

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