Similar catalytic behaviour of oximate and phenoxide bases in the ionization of bis(2,4-dinitrophenyl)methane in 50% water–50% Me_2SO. Revisiting the role of solvational imbalances in determining the nucleophilic reactivity of α-effect oximate bases

Gilles Moutiers,[a] Eric Le Guével,[b] Luc Villien[b] and François Terrier *,[a]

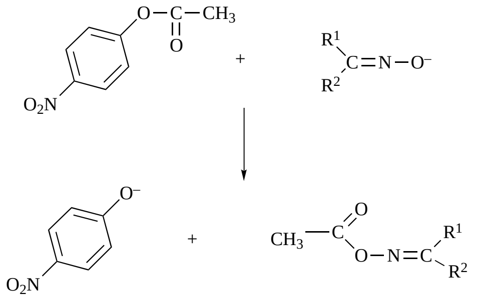
[a] *University of Versailles, Department of Chemistry, Sircob (EP CNRS No. 102),*
Bâtiment Lavoisier, 45 Avenue des Etats Unis 78035 Versailles Cedex, France
[b] *Centre d'Etudes du Bouchet, BP 3, 91710 Vert Le Petit, France*

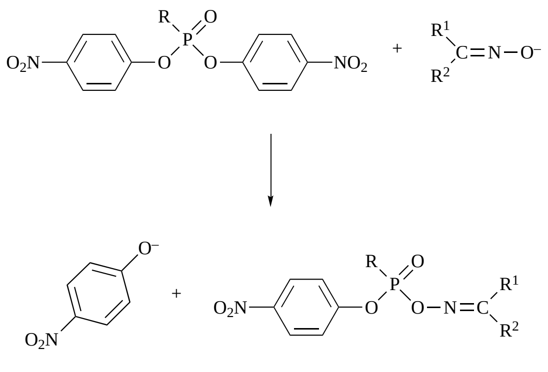
Rates of proton abstraction from bis(2,4-dinitrophenyl)methane 1 by a series of oximate bases and of reprotonation of the related diphenylmethyl carbanion C-1 by the conjugate oxime acids have been measured in a 50 : 50 (v/v) H_2O–Me_2SO mixture at 25 °C. The results reveal an essentially identical behaviour of oximate (Ox^-) and phenoxide (ArO^-) bases in these proton transfer reactions. The Brønsted lines for the two types of catalysts are nearly the same, showing no tendency to level off at high pK_a and providing very similar values for the intrinsic reactivity of 1: log $k_0^{Ox} = 0.9 \pm 0.1$; log $k_0^{ArO} = 0.5 \pm 0.1$. A comparison with previous results obtained with carboxylate ions as well as primary and secondary amines indicates that solvational imbalances due to the catalysts are important in determining the intrinsic reactivity of 1. This conclusion implies that ArO^- and Ox^- bases undergo comparable solvation changes along the coordinate of the ionization reactions of 1, a result which is indirectly supported by the finding that a transfer from water to H_2O–Me_2SO mixtures rich in Me_2SO induces similar variations in the acidity of oximes and phenols of similar p$K_a^{H_2O}$. The identical behaviour of ArO^- and Ox^- bases in the ionization of 1 is in marked contrast with the situation observed in nucleophilic addition or substitution reactions. In agreement with their α-effect character, oximates are much more reactive than phenoxides in these processes but a typical feature is that the nucleophilic reactivity of Ox^- species is subject to a very rapid levelling off at pK_a *ca.* 8.5. Based on the information obtained in this work, this peculiar behaviour is re-examined and suggested to be a reflection of especially large solvational imbalances in the transition states for nucleophilic reactions.

Introduction

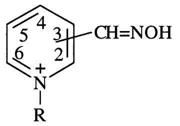
Like other nucleophiles containing an atom with an unshared pair of electrons adjacent to the reaction site, oximate bases are known to exhibit a much higher reactivity than common oxyanionic nucleophiles of similar basicities (ArO^-, $RCOO^-$) in many substitution processes, a phenomenon known as the α-effect.[1–12] A noteworthy feature, however, is that the nucleophilic reactivity of oximate bases of p$K_a > 8$ is subject to a rapid levelling off in aqueous solution, thereby causing a marked decrease in the α-effect with increasing basicity.[13] The reactions of oximate bases (Ox^-) with *p*-nitrophenylacetate [reaction (1)] and bis(*p*-nitrophenyl) methyl- and phenylphosphonates [reaction (2)] are representative systems where such a saturation effect is operating.[13,14] In these instances, we have shown that the observation of a non-linear free energy relationship cannot be the result of a change in the rate-limiting step in a two-step elimination process.[15] Accordingly, we suggested that the most reasonable explanation for the observed behaviour is in terms of a requirement for desolvation of the oximate functionality prior to nucleophilic attack which would become more difficult with increasing basicity. As suggested by Jencks, Hupe and Bernasconi, this desolvation will occur ahead of bond formation in the transition states of the reactions.[12,16–19] In other words, the observed levelling off in the Brønsted plots for reactions (1) and (2) would be the reflection of solvational imbalances in these transition states.

Transition state imbalances of solvational nature have been previously invoked to account for the observation of curved

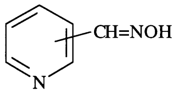

(1)


(2)

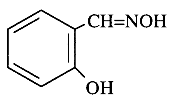
R = CH_3, C_6H_5



2 R=CH_3, 2-CH=NOH
4 R=C_8H_{17}, 4-CH=NOH
5 R=CH_3, 4-CH=NOH



8 4-CH=NOH
9 2-CH=NOH
10 3-CH=NOH



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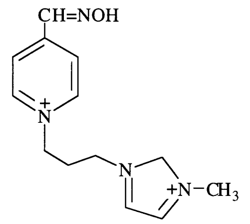

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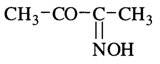


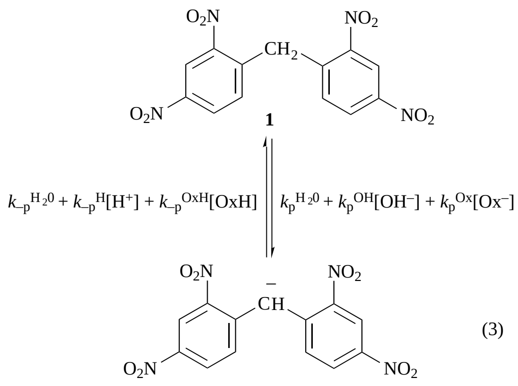
$CH_3–CO–\underset{NOH}{\underset{\|}{C}}–CH_3$

7

Brønsted correlations in a number of reactions involving common oxyanionic nucleophiles like phenoxide, hydroxide or alkoxide ions.[12,16,17,20,21] In these instances, however, the curvature was found to appear only when relatively basic or strongly basic reagents (pK_a > 10–11) were used and it developed rather smoothly with increasing basicity. Similar situations have been reported in studies of the ionization of some carbon acids.[18,19,22] For these reasons, the drastic saturation effect observed in the reactivity of the oximate functionality in reactions (1) and (2) remains a unique and very intriguing result which requires further investigation.

A type of reaction which is especially sensitive to transition state imbalances, including those due to solvation, is the ionization of carbon acids giving rise to strongly resonance-stabilized carbanions.[18,19,23–28] Prototype examples for such carbon acids are nitroalkanes, *e.g.* nitromethane and phenylnitromethane, and polynitro-substituted benzyl derivatives, *e.g.* bis(2,4-dinitrophenyl)methane **1**, whose deprotonation by oxyanionic bases (ArO^-, $RCOO^-$) or nitrogen bases (amines) is characterized by very large imbalance effects and therefore low intrinsic reactivities in aqueous or aqueous dimethyl sulfoxide solutions.[19,24,25,29,30]

In this paper, we report rate data obtained for the ionization of the bis(dinitrophenyl)methane **1** by a series of oximate bases (**2**–**10**) in 50:50 (v/v) $H_2O–Me_2SO$ [equilibrium (3)]. When conducting these experiments we hoped that they would reveal significant differences in the behaviour of oximate and phenoxide bases, contributing to clarify the reasons for the particular reactivity of the former reagents in nucleophilic processes. As will be seen, both of these species were found to exhibit a similar catalytic behaviour in equilibrium (3), confirming some observations made by Hupe and Wu in an early study of the enolisation of 4-(*p*-nitrophenoxy)butan-2-one in aqueous solution.[22] Possible explanations accounting for the different behaviour of oximate bases in nucleophilic and proton-transfer processes will be suggested.



(3)

C–1

Results

Due to the extremely low solubility of **1** in water, all rate measurements pertaining to the ionization of this carbon acid in the series of oximate buffers studied were made in a 50:50 (v/v) $H_2O–Me_2SO$ mixture at 25 °C. Pseudo-first-order conditions were used throughout with a large excess of the buffer reagent over the substrate concentration ([**1**] *ca.* 3×10^{-5} mol dm^{-3}). The ionic strength was kept constant at 0.5 mol dm^{-3}. In a general way, the ionization reactions can be represented by equilibrium (3) where $k_p^{H_2O}$, k_p^{OH} and k_p^{Ox} are the rate constants referring to the deprotonation of **1** by water, hydroxide ion and the oximate base species (Ox^-), respectively, while k_{-p}^{H}, $k_{-p}^{H_2O}$ and k_{-p}^{OxH} are the rate constants referring to the reprotonation of the conjugate carbanion **C-1** by hydronium ion, water and the oxime acid species (OxH), respectively.

In view of the pK_a^{CH} value of **1** in 50:50 (v/v) $Me_2SO–H_2O$ ($pK_a^{CH} = 10.90$),[25a] the ionization rates were measured as follows. In oximate buffers of pH $\leqslant pK_a^{CH}$, equilibrium (3) was approached from pH-jump experiments. These were carried out by mixing a freshly prepared 10^{-3} mol dm^{-3} NaOH solution of **C-1** (λ_{max} 678 nm; ε 28 700 dm^3 mol^{-1} cm^{-1}) with oximate buffers made up so as to obtain the desired final pH. At pH $\geqslant pK_a^{CH}$, the equilibrium was approached in the opposite direction by mixing a neutral solution of **1** with the appropriate buffer. In the case of buffers **7–10** where the equilibrium could be readily approached from both reactant and product sides, the rate data obtained in the two series of experiments for a given buffer were identical within experimental error. In agreement with a direct equilibrium approach according to equilibrium (3), oscilloscope pictures obtained in stopped-flow experiments revealed that only one relaxation time is associated with the interconversion of **1** and **C-1** in all oximate buffers studied. Accordingly, the general expression for the observed first-order rate constant k_{obs}, pertaining to the process is given by eqn. (4).[19,25a,b] All k_{obs}

$$k_{obsd} = k_p^{H_2O} + k_p^{Ox}[Ox^-] + k_p^{OH}[OH^-] + k_{-p}^{H_2O} + k_{-p}^{OxH}[OxH] + k_{-p}^{H}[H^+] \quad (4)$$

values obtained at 25 °C are summarized in Supplementary Table S_1.†

As expected from the values of the k_p^{OH}, $k_p^{H_2O}$, k_{-p}^{H} and $k_{-p}^{H_2O}$ rate constants, which were known from previous studies,[25a,b] a standard analysis of the rate data of Table S_1 showed that only the buffer pathways of equilibrium (3) are important in determining k_{obs} in the pH range of 8.13–11.73 covered by the various oximate buffers employed in this work, *i.e.* eqn. (4) reduces to eqn. (5). In buffers of $10.6 < pK_a^{OxH} < 11.43$, all

$$k_{obs} = k_p^{Ox}[Ox^-] + k_{-p}^{OxH}[OxH] \quad (5)$$

$$k_{obs} = (pk_p^{Ox} + k_{-p}^{OxH})[OxH] \quad (6)$$

plots of k_{obs} *vs.* [OxH] at constant pH (constant buffer ratio $p = [Ox]/[OxH]$) were linear with negligible intercepts but the

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† Table S_1 has been deposited with the British Library, Suppl. Pub. 57185 (7 pp.). For details of the supplementary publication scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 2*, 1997, Issue No. 1.

Table 1 Rate constants for the proton transfer reactions of bis(2,4-dinitrophenyl)methane **1** with hydroxide ion, water and oximate base species in 50:50 (v/v) H_2O–Me_2SO at 25 °C[a]

Entry	pK_a^{BH}	BH Species	k_p^B/dm^3 mol^{-1} s^{-1}	k_{-p}^{BH}/dm^3 mol^{-1} s^{-1}
1	−1.44	H_3O^+	7.92×10^{-9}[b,c]	17 500[c]
2	8.38	2-(Hydroxyiminomethyl)pyridinium	0.51	172.2
3	8.68	CEB 1574 (**3**)	0.51	85
4	9.04	4-(Hydroxyiminomethyl)-*N*-octylpyridinium	1.26	91.5
5	9.22	4-(Hydroxyiminomethyl)pyridinium	1.47	70.3
6	10.12	Salicylaldehyde oxime	5.48	28.3
7	10.62	Butane-2,3-dione monoxime	4.71	22.3
8	10.98	4-(Hydroxyiminomethyl)pyridine	8.85	6.35
9	11.19	2-(Hydroxyiminomethyl)pyridine	9.47	4.87
10	11.43	3-(Hydroxyiminomethyl)pyridine	10.60	3.18
11	17.34	H_2O	46.6[c]	1.98×10^{-5}[b,c]

[a] *I* 0.5 mol dm^{-3}. [b] $k_p^{H_2O}/27.6$ and $k_p^{H_2O}/27.6$. [c] Values taken from ref. 25(*b*).

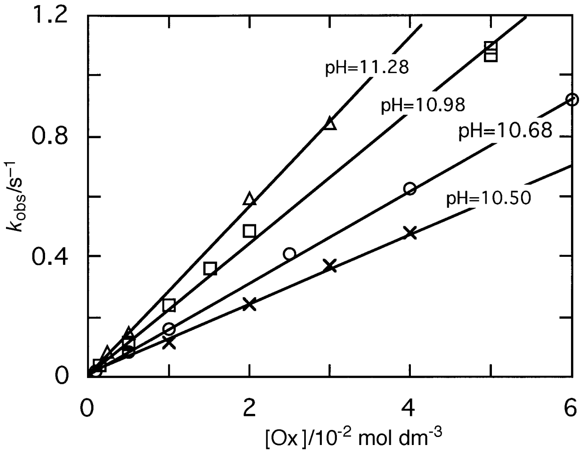


Fig. 1 Observed first-order rate constants, k_{obs}, for the ionization of **1** by pyridine-4-carbaldehyde oxime buffers, 50:50 (v/v) H_2O–Me_2SO *T* 25 °C, *I* 0.5 mol dm^{-3}

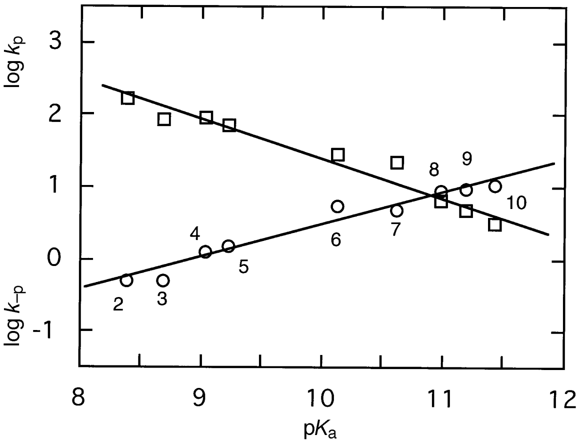


Fig. 2 Brønsted plots for the ionization of **1** by oxime buffers in 50:50 (v/v) H_2O–Me_2SO. The numbering is given in Table 1. *T* 25 °C, *I* 0.5 mol dm^{-3}

slopes of these plots decreased with decreasing pH. This situation is illustrated in Fig. 1 for the ionization of **1** in pyridine-4-carbaldehyde oximate buffers. For each of the buffers **7–10**, the k_{-p}^{OxH} and k_p^{Ox} values were thus determined by working out data obtained at three or more buffer ratios (Table S_1). In all other buffers with $pK_a^{OxH} \leqslant 10.12$, experimental conditions could be readily designed where the k_p^{Ox}[Ox] contribution to eqn. (5) was negligible, *i.e.* $k_{obs} = k_{-p}^{OxH}$[OxH]. Thus, a unique straight line was obtained for each of the buffers **2–6** when the k_{obs} values measured at different pH were plotted *versus* the oxime concentration; this allowed a facile determination of k_{-p}^{OxH} from the slopes and the corresponding k_p^{Ox} rate constants were subsequently calculated by means of eqn. (7).

$$k_p^{Ox} = \frac{K_a^{CH}}{K_a^{Ox}}\ k_{-p}^{OxH} \qquad (7)$$

All rate constants k_p^{Ox} and k_{-p}^{OxH} for ionization of **1** by the buffer base and acid species of **2–10** are summarized in Table 1, along with related parameters for the OH^-, H^+ and water pathways.

The pK_a values of oximes **2–10** in the 50:50 (v/v) H_2O–Me_2SO mixture containing 0.5 mol dm^{-3} NMe_4Cl were measured by potentiometry at 25 °C.[21,32] For an assessment of solvation effects, the acidity of some of these oximes was similarly measured in water (*I* 0.1 mol dm^{-3} KCl) and H_2O–Me_2SO mixtures containing 30 and 50% Me_2SO (*I* 0.5 mol dm^{-3} NMe_4Cl). The corresponding pK_a values are given in Table 2 together with those previously measured for various phenols under similar experimental conditions.[21]

Discussion

Brønsted behaviour and intrinsic reactivity of 1

Fig. 2 shows that the rate constant k_p^{Ox} and k_{-p}^{OxH} pertaining, respectively, to the deprotonation of **1** by oximate bases and reprotonation of **C-1** by the conjugate acids define satisfactorily linear Brønsted relationships. The related β_{Ox} and α_{OxH} values ($\beta_{Ox} = 0.45$; $\alpha_{OxH} = 0.55$) are in the range 0.5 ± 0.1 commonly found for these parameters in the ionization of carbon acids by oxyanionic bases like phenoxide or carboxylate ions.[18,19,24–31] For example, β_B values of 0.53 and 0.46 have been found for ionization of indane-1,3-dione ($pK_a^{CH} = 6.35$) and picrylacetophenone ($pK_a = 7.80$), respectively, by $RCOO^-$ in 50:50 (v/v) H_2O–Me_2SO.[19*b*,26*b*] Keeping with the traditional view that β_B is a good measure of the degree of proton transfer in the transition state,[18,19,33] the measured β_β value of 0.45 for equilibrium (3) suggests that the process is about half complete at the corresponding transition states. On the other hand, the intersection of the two Brønsted plots in Fig. 2 allows a direct determination of the intrinsic rate constant, k_0, of Marcus theory, defined as $k_0 = k_{-p}^{BH}/p = k_p^B/q$ when $pK_a^{BH} + \log(p/q) - pK_a^{CH} = 0$ ($p = q = 1$ for $B = $ Ox, BH = OxH).[18,33] One thus obtains log $k_0^{Ox} = 0.9 \pm 0.1$. As can be seen in Table 3, which summarises a number of log k_0 values for some representative structures, this log k_0 value ranks amongst the lowest log k_0 values so far measured for ionization of nitrosubstituted carbon acids by oxyanionic as well as nitrogen bases.[18,19,24–26,30,31]

Why a low intrinsic reactivity for 1?

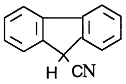
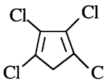
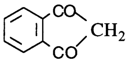
It is now well recognized that high intrinsic barriers, *i.e.* low log k_0 values, are found in ionization reactions of carbon acids provided that the formation of the conjugate carbanions is accom-

Table 2 pK_a Values of some phenols and oximes in various H_2O–Me_2SO mixtures[a]

Acid	Me_2SO(%) 0	30	50	70	ΔpK[c]
2-Cyanophenol	7.22	7.54	7.97	8.88	1.66
4-Cyanophenol	7.80	8.17	8.45	9.31	1.51
2-(Hydroxyiminomethyl)pyridinium	7.75[b]	8.28	8.38	9.00	1.25
3,5-Dichlorophenol	8.03	8.27	8.53	9.38	1.35
CEB 1574 (**3**)	8.05	8.58	8.68	9.47	1.42
4-(Hydroxyiminomethyl)pyridinium	8.27[b]	8.70	9.22	10.16	1.89
3,4-Dichlorophenol	8.51	8.78	9.10	10.08	1.57
Butanedione monoxime	9.30	9.97	10.62	12.07	2.77
4-Chlorophenol	9.35	9.85	10.18	11.52	2.17
4-(Hydroxyiminomethyl)pyridine	9.55[b]	—	10.98	12.40	2.85
3-Methoxyphenol	9.65	10.35	11.05	12.24	2.59
2-(Hydroxyiminomethyl)pyridine	9.85	—	11.19	12.96	3.11
Phenol	9.88	10.62	11.21	12.44	2.56
4-Methoxyphenol	10.27	10.70	11.47	12.90	2.63

[a] I 0.1 mol dm^{-3} in water; I 0.5 mol dm^{-3} in 30, 50, 70% Me_2SO. [b] Ref. 13(*c*). [c] ΔpK $pK_a^{70\% Me_2SO} - pK_a^{H_2O}$.

Table 3 Comparison of intrinsic rate constants for deprotonation of **1** and some representative carbon acid structures in 50:50 (v/v) H_2O–Me_2SO. Effect of structure of the base catalyst

CH-Acid	Base catalyst	log k_0
$RCH(CN)_2$	RR′ NH	*ca.* 7[a]
	RR′NH	4.58[b,c]
	RNH_2	3.76[b,c]
$CH_3COCH_2COCH_3$	$RCOO^-$	3.80[b,d]
	RR′NH	2.75[b,d]
	RNH_2	2.06[b,d]
	RR′NH	3.59[b,e]
	RNH_2	2.50[b,e]
	ArO^-	4[b,f]
	$RCOO^-$	3.18[b,f]
	RR′NH	3.13[b,f]
	RNH_2	2.44[b,f]
CH_3NO_2	ArO^-	(1.5)[h]
	RR′NH	0.73[b,g]
$C_6H_5CH_2NO_2$	ArO^-	(0.10)[h]
	RR′NH	−0.25[b,g]
	$RCOO^-$	−0.57[b,g]
1	Ox^-	0.90[i,j]
	ArO^-	0.50[k]
	RR′NH	−0.10[k]
	$RCOO^-$	−0.60[k]
	RNH_2	−0.65[k]

[a] Ref. 18(*c*); in water. [b] T 20 °C. [c] Ref. 35(*a*). [d] Ref. 19(*a*). [e] Ref. 35(*b*). [f] Ref. 19(*b*). [g] Ref. 24. [h] Estimated value; see ref. 26(*b*). [i] T 20 °C. [j] This work. [k] Ref. 25(*a*),(*b*).

panied by an extensive structural–electronic and solvational reorganization of the carbon skeleton and that the development of this reorganization occurs behind proton transfer at the transition state.[18,19,23–31] The data in Table 3 are illustrative in this regard. Thus, the two criteria are not met with carbon acids such as nitriles because the conjugate carbanions, even though not totally devoid of resonance, derive most of their stabilization from the polar effect of the cyano group.[18,35] The corresponding reactions go through essentially balanced transition states and are characterized by high log k_0 values.[18] In contrast, reactions of carbon acids whose ionizable site is activated by substituents like a carbonyl group or a fluorenyl or cyclopentadienyl moiety which can provide a substantial resonance stabilization of the anion are characterized by notably imbalanced transition states and log k_0 values in the mid-range of the scale.[18,19,36] However, it is with compounds like nitroalkanes that large imbalance effects and large intrinsic barriers are found.[18,23,24,30,31] Due to the strong capability of a NO_2 group to absorb a negative charge, the conjugate carbonions exist as nitronate ions, implying that a very important rearrangement of the carbon skeleton occurs upon ionization.[18]

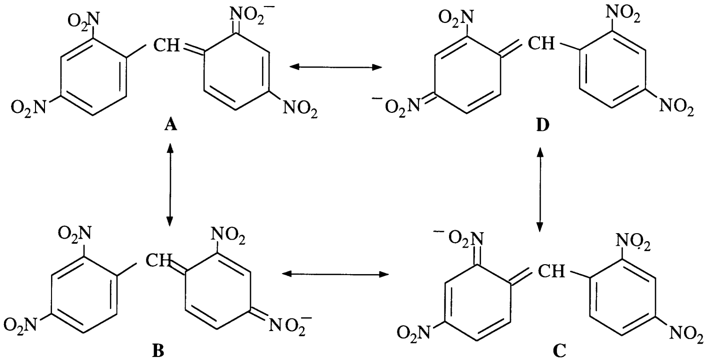
As we have previously demonstrated,[25*a*,*b*,37] there is no doubt that the two criteria required to have low log k_0 values are fulfilled in the case of **1**. First, the ionization affords an essentially planar carbanion **C-1**, with a high dispersion of the negative charge over the two 2,4-dinitrophenyl rings, as illustrated in resonance structures **A–D** (Scheme 1).

This implies a number of significant changes in bond lengths and bond angles and therefore a very important structural and electronic reorganization.[37] Concomitantly, the shift of negative charge onto the oxygen atoms of the NO_2 groups may favour some hydrogen bonding solvation in aqueous solution. On the other hand, previous studies of the ionization of **1** and other benzylic-type carbon acids (CH) by various bases ($B = ArO^-$, $RCOO^-$, RR′NH) have revealed that the rate constants k_p^B and k_{-p}^{BH} suffer very different variations when one induces similar changes in the equilibrium constant K_p of equilibrium (8) by

$$CH + B^{(-)} \underset{k_{-p}^{BH}}{\overset{k_p^B}{\rightleftharpoons}} C^- + BH^{(+)}\ (K_p) \qquad (8)$$

varying the strength of the base catalyst ($\Delta\log K_p = \Delta pK_a^{BH}$; $\beta_B = 0.48$) or that of the carbon acid ($\Delta\log K_p = \Delta pK_a^{CH}$; $\alpha_{CH} = 0.99$). Such a large inequality between the Brønsted β_B and α_{CH} values is known to be good evidence for a considerable lag in structural–electronic solvational reorganization behind proton transfer in the transition state.[18] Since such reorganization features are associated with the carbon acid structure, they will necessarily operate in the ionization of **1** by any deprotonating reagent, so that one can reasonably expect log k_0 values falling in the same range of the intrinsic reactivity scale whatever the nature of the base catalyst may be.

Clearly the data in Table 3 fit this expectation but a significant feature is that the intrinsic reactivity of **1** depends appreciably upon the structure of the catalyst. There is an approximately 30-fold increase in k_0 on going from carboxylate ions or primary amines to oximate bases. Interestingly, log k_0^{Ox} is found to be only 0.4 unit higher than log k_0^{ArO} and this similarity goes along with a similar β_B value and with



Scheme 1

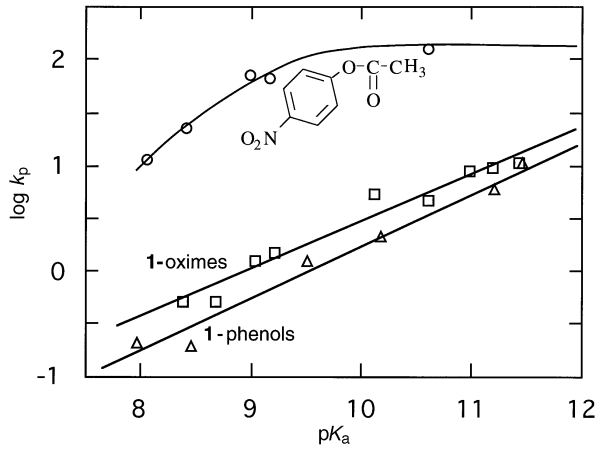


Fig. 3 Relative reactivities of oximate and phenoxide bases towards **1** and *p*-nitrophenylacetate in 50 : 50 (v/v) $H_2O–Me_2SO$, *T* 25 °C

the fact that both Brønsted plots are linear over the entire pK_a range (Fig. 3).

Effect of structure of the catalyst on reactivity. The identical behaviour of ArO^- and Ox^- bases in reactions (3)

Variations within log k_0 values determined for a given acid by using different catalysts are often interpreted in terms of imbalanced solvation effects pertaining to the base reagent and/or the resulting conjugate acid.[18] Thus, the reduced intrinsic rate constant for primary amines compared to secondary amines is part of a general pattern that has been observed in numerous systems.[19,24,25*a*,31,36,38] It has been commonly attributed to a stronger solvation of the ammonium ions derived from primary amines and the fact that this solvation will develop behind proton transfer at the transition state.[18,19,25*a*,38] Similarly, the weaker catalytic efficiency of $RCOO^-$ relative to ArO^- ions has been attributed to the fact that at least a partial desolvation of these bases must develop ahead of the proton transfer along the reaction coordinate.[25,26] In agreement with the finding that $RCOO^-$ ions are more strongly solvated than similarly basic ArO^- ions in aqueous solution,[39] the cost of desolvation is greater for the former bases, accounting for the pattern: $\log k_0^{RCOO} < \log k_0^{ArO^-}$. Costly desolvation is also the explanation as to why the points for OH^- and other strong RO^- bases with $pK_a \geqslant 11$ display generally large deviations from Brønsted plots defined by less basic catalysts in the ionization of carbon acids, thereby resulting in a substantial curvature of these plots at high pK_a.[18–20,22–31,33]

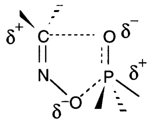
Based on the above ideas, the finding that ArO^- and oximate bases exhibit an identical Brønsted behaviour suggest that these oxyanionic bases undergo comparable solvation changes along the reaction coordinate of equilibrium (3). To test this assumption, a comparison of the pK_a values of oximes and phenols over a whole range of $H_2O–Me_2SO$ mixtures is of interest. In agreement with the well known feature that Me_2SO has a low ability to provide hydrogen bond solvation, thereby destabilizing anionic centres with a localized or a relatively localized negative charge,[19,40,41] the acidity of the various oximes listed in Table 2 is found to decrease upon addition of increasing amounts of Me_2SO to aqueous solutions. Interestingly, the solvent effect is roughly the same for phenols and oximes of similar $pK_a^{H_2O}$ values. For example, for a change from water to 70% Me_2SO, we have $\Delta pK_a = pK_a^{70\%\ Me_2SO} - pK_a^{H_2O} = 1.35$ for 3,5-dichlorophenol ($pK_a^{H_2O} = 8.03$) and $\Delta pK_a = 1.42$ for the oxime **3** ($pK_a = 8.05$). In addition, the dependence of the ΔpK_a values upon the acidity measured in aqueous solution is the same for the two functionalities. These increase regularly from the most acidic substrate, *e.g.* ΔpK_a *ca.* 1.50 ± 0.2 for compounds with $pK_a^{H_2O}$ *ca.* 7.8–8 to $\Delta pK_a = 2.8 \pm 0.3$ for compounds with $pK_a^{H_2O}$ *ca.* 9.5–10. This trend is similar to the one observed by Bernasconi for the ionization of carboxylic acids in $H_2O–Me_2SO$ mixtures.[19]

Inasmuch as they are primarily the reflection of the desolvation of the oxyanion caused by the addition of Me_2SO to aqueous solutions,[40,41] it may be reasonably assumed that the ΔpK_a values in Table 2 give a good picture of the relative degrees of solvation of the anions in aqueous solution. Accordingly, the similarity of the solvent effects suffered by the pK_a^{Ox} and pK_a^{ArO} values is consistent with the finding that the two corresponding functionalities exhibit a nearly identical Brønsted behaviour in equilibrium (3). In addition, the regular increase observed in the ΔpK_a values with increasing $pK_a^{H_2O}$ fits well the idea that desolvation requirements become energetically more expensive when the basicity is increased.[16,17,19,22] Should the cost of the desolvation in the transition state become the major factor determining the reactivity in a given process, the points for the basic reagents will deviate more and more from the Brønsted line drawn at low pK_a and a curved correlation will develop.

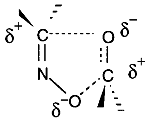
Comparison of the reactivity of oximate bases in proton transfer reactions and nucleophilic processes

Based on the above conclusions, the known behaviour of oximates bases in nucleophilic processes raises two major questions: (*i*) why these reagents are much stronger nucleophiles than aryloxide ions but similarly efficient proton transfer catalysts; (*ii*) why the reactivity of the oximate functionality levels off so rapidly [*i.e.* at pK_a *ca.* 8 in aqueous solution and pK_a *ca.* 9 in a 50 : 50 (v/v) $Me_2SO–H_2O$ mixture] in nucleophilic reactions but not in the proton-transfer reactions of equilibrium (3). This situation is illustrated by Fig. 3 where the Brønsted plots for reactions (1) and (3) in 50% Me_2SO are compared.

Regarding the enhanced reactivity of oximate species, and more generally α-effect reagents in nucleophilic processes, several studies have suggested that it is most probably the result of an extra stabilization of the transition state rather than of a ground-state destabilization or solvation effects.[2,4,10,42–45] Various suggestions have been made which involve the possibility of having cyclic transition states, especially in reactions of nucleophiles like HOO^- or oximates with organophosphorus esters or carbonyl compounds, as shown in **11** or **12**.[4,10b,42] If intramolecular catalysis is actually the key for the observation of an α-effect for an oximate functionality, the absence of any enhanced reactivity of reagents **2–10** in the ionization of **1** can be accounted for by the difficulty of visualizing reasonable cyclic transition states in proton transfer reactions at carbon.

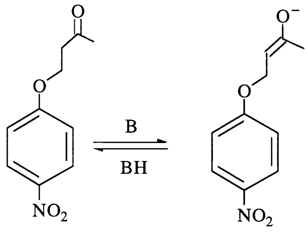


11



12

At first, a possible explanation of why solvational imbalances associated with Ox^- species of pK_a *ca.* 8–10 do not cause any levelling off in the Brønsted plots for equilibrium (3) is that their contribution to the enthalpy of activation is minor compared to that of the imbalance effects associated with the extensive reorganization of the carbon skeleton of **1**. It turns out, however, that this idea is not very attractive since Hupe and Wu have reported an identical and classical Brønsted behaviour for a few oximate and phenoxide bases with pK_a values up to 10.6 in the enolization of 4-(*p*-nitrophenoxy)butan-2-one **13** in aqueous solution [equilibrium (9)].[22] As previously discussed, reorganization features pertaining to the formation of an enolate-type carbanion like **C-13** are much less important than those associated with the formation of carbanions like **C-1**. This should reinforce the weight of solvational imbalances due to the catalysts and favour the appearance of a different Brønsted behaviour for ArO^- and Ox^- species. This expectation is clearly not borne out by experiments. Similarly, the more basic hydroperoxide ion (HOO^-; $pK_a = 11.60$) is found to behave as other similarly basic oxyanions in equilibrium (9) as well as in the general-base catalysed detritiation of *tert*-butylmalonitrile—a carbon acid whose ionization proceeds through low intrinsic barriers.[46] All these results add to the evidence accumulated that ArO^- and Ox^- functionalities exhibit a truly similar catalytic behaviour in the ionization of carbon acids.



(9)

13 **C–13**

We would like to suggest that the rapid levelling off observed in the reactivity of oximate species with electrophilic carbon or phosphorus centres is a reflection of especially large imbalances in the transition states for these nucleophilic reactions. In other words, there is a need that desolvation of the oximate functionality develops much further ahead of bond formation in transition states of type **11** and **12** than ahead of proton transfer in transition states for C–H bond breaking. In this regard, Bernasconi has suggested that the effect of decoupling between desolvation and bond formation on reactivity in a given process may be expressed in terms of eqn. (10).[19] In this equation, $\Delta\log k$

$$\Delta\log k = (\alpha_d - \beta)\log K_d \qquad (10)$$

measures the decrease in reactivity caused by desolvation of a 'basic' reagent with reference to the Brønsted line of slope β drawn at low pK_a while K_d is the equilibrium constant for partial desolvation of the base and $1 \geqslant \alpha_d \geqslant 0$ measures the progress of desolvation in the transition state. Eqn. (10) predicts that, as desolvation becomes energetically more expensive, the increasingly more negative $\log K_d$ values will render $\Delta\log k$ more negative as well, provided that $\alpha_d > \beta$, *i.e.* desolvation occurs ahead of bond formation in the transition state. Eqn. (10) shows that, in this case, the curvature will occur more rapidly if α_d is markedly greater than β, than if α_d is not very different from β. It follows from this model that nucleophilic reactions of type (1) and (2) must proceed through much more strongly imbalanced transition states ($\alpha_d \gg \beta_{nuc}$) than proton transfer reactions of the type shown in equilibrium (3).

Experimental

Materials

With the exception of oximes **3** (CEB 1574) and **4** [4-(hydroxyiminomethyl)-*N*-octylpyridinium] which were generous gifts from the Centre d'Etudes du Bouchet, all the oximes used in this work were of the highest quality commercially available and were recrystallised before use. Bis(2,4-dinitrophenyl)methane **1** was available from previous studies[25] (mp 179 °C, lit.,[47] mp 182 °C). Dimethyl sulfoxide was refluxed over calcium hydride and distilled, and the fractions of bp 32–35 °C (at 2 mmHg) were collected and stored under nitrogen. Me_2SO–water solutions were prepared as described previously.[21,25] Only freshly prepared solutions were used in kinetic and potentiometric studies.

Acidity measurements

The acidity constants of the various oximes (OxH) were measured by potentiometry at 25 °C, using a Tacussel Isis 2000 electronic pH meter.[21] The pK_a^{OxH} values were determined from buffer solutions with $[Ox^-]/[OxH]$ ratios equal to 1/3, 1/1 and 3/1. As previously described for the measurements of pK_a^{ArOH} values for phenols, these buffer solutions were prepared so that the molarity of the Ox^- species was in all cases equal to 10^{-2} mol dm^{-3}. The ionic strength was kept constant at 0.1 mol dm^{-3} KCl in aqueous solution and 0.5 mol dm^{-3} NMe_4Cl in H_2O–Me_2SO mixtures containing 30, 50 and 70% Me_2SO. Under these experimental conditions, the pK_a^{OxH} values at the corresponding ionic strength were obtained in each solvent from the measured pH values of the buffers by means of eqn. (11).

$$pK_a^{OxH} = pH - \log([Ox^-]/[OxH]) \qquad (11)$$

Calibration of the cell used to obtain the pH measurements was carried out as previously described.[32]

Kinetic measurements

Pseudo-first-order rate constants, k_{obs}, for attainment of equilibrium (3) were determined spectrophotometrically following the appearance or the disappearance of the strongly coloured carbanion **C-1** at its absorption maximum in 50:50 (v/v) H_2O–Me_2SO (λ_{max} 678 nm; ε 28 700 dm^3 mol^{-1} cm^{-1}). The reactions were carried out at 25 °C with use of oximate buffers, varying the concentration of the oximate base between 5×10^{-4} and 6×10^{-2} mol dm^{-3} at a given $[Ox^-]/[OxH]$ ratio; *i.e.* a given pH. The concentration of the substrate or its conjugate carbanion **C-1** was always $\leqslant 3 \times 10^{-5}$ mol dm^{-3} and the ionic strength maintained constant at 0.1 mol dm^{-3} in aqueous solution and 0.5 mol dm^{-3} in H_2O–Me_2SO mixtures. Usually at least six values of $[Ox^-]$ were employed and each individual experiment was made in triplicate. In all cases, the reactions were found to be kinetically first-order in **1** up to at least 90% of the overall reaction.

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