Rapid Marcus Curvature Due to Extremely Strong Solvational Imbalances in the Deprotonation of a Trinitrobenzylic Carbon Acid by Oximate Bases

François Terrier,*[a] Gilles Moutiers,*[a] Sandrie Pelet,[a] and Erwin Buncel*[a][+]

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We report the first instance of the levelling of oximate reactivity in a deprotonation process, which is shown to have as origin the desolvation of the oximate ion prior to actual proton transfer, in accord with the large predominance of the work term (w_r) far exceeding the intrinsic barrier term in the Marcus formulation.

Traditional applications of Marcus theory to proton transfers between acid and base pairs requires the separation of the overall rate processes into three different components (Equation 1) and leads to the derivation of the general Equation (2), which is commonly used in the simplified form of Equation (3).[1−8] This is because the work terms W_r and W_p, which represent the free energy changes required to bring the reactants together to form an encounter complex and to separate the product encounter complex, are generally assumed to be very similar within a series of reactions between a given carbon acid and a number of structurally similar bases B^- of different p*K*a′s.

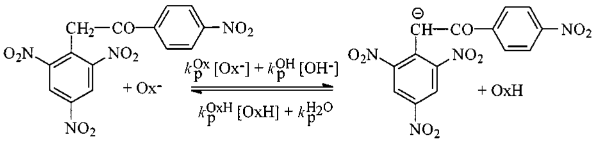
$$\mathrm{AH + B^-} \xrightleftharpoons{W_r} \mathrm{AH \cdot B^-} \rightleftharpoons \mathrm{A^- \cdot HB} \xrightleftharpoons{W_p} \mathrm{A^- + HB} \qquad (1)$$

$$\Delta G^{\neq} = W_r + \gamma \cdot \left(1 + \frac{\Delta G^\circ - W_r + W_p}{4\gamma}\right)^2 \qquad (2)$$

$$\Delta G^{\neq} = W_r + \gamma \cdot \left(1 + \frac{\Delta G^\circ}{4\gamma}\right)^2 \qquad (3)$$

$$\Delta G^{\neq}{}_0 = W_r + \gamma \qquad (4)$$

In Equations (2) and (3), $\Delta G^{\neq}$ and ΔG° refer, respectively, to the free energy of activation and the free energy change pertaining to the overall process, while γ is the intrinsic barrier corresponding to the free energy barrier for the proton transfer within the encounter complex in the identity reaction ($\Delta G^\circ = 0$). In this instance, Equation (3) becomes Equation (4), which shows that the readily measurable standard free energy barrier for the overall identity reaction is actually the combination of γ and the work term. In the past, it has proven difficult to discriminate between these two terms in most studies of proton transfers at carbon;[7,9−12] however, as seen in Equation (3), the fastest rate will correspond to the situation in which the intrisic barrier term is negligible relative to W_r. In this communication, we describe a system, namely the deprotonation of the picryl acetophenone **1** by a series of oximate bases (Ox^-) to give the carbanion **C-1** (Equation 5), where the w_r term is so predominant that a dramatic levelling off in reactivity of these catalysts is observed.



(5)

1

C-1

Results

Rates of proton transfer according to Equation (5) have been measured in 50:50 (v/v) H_2O/Me_2SO at 25 °C and constant ionic strength of 0.5 mol L^{-1} (KCl). Experiments were carried out over a large pH range (8.38−11.43) in buffers made up from a set of oximes, maintaining pseudo-first-order conditions with the buffer being the excess reagent throughout. Under these conditions and in view of the pK_a value of **1** in this medium (pK_a = 5.72), formation of the carbanion **C-1** was essentially complete with only the oximate and hydroxide ion pathways contributing to the observed first-order rate constant for the approach to equilibrium, i.e. k_{obs} is given by Equation (6). The k_{obs} values measured in each buffer system studied, varying the concentration of the oximate base between $5 \cdot 10^{-4}$ and 0.01 mol L^{-1} at constant pH, are collected in Table S1, given as Supporting Material. From these data, the second-order rate constants k_p^{Ox} were readily obtained as the slopes of the various k_{obs} vs. [Ox^-] plots, which were all linear at a given pH. These rate constants are given in Table 1, together with the related k_{-p}^{OxH} values calculated from $k_{-p}^{OxH} = k_p^{Ox} K_a^{OxH}/K_a^1$.

$$k_{obs} = k_p^{Ox}\,[Ox^-] + k_p^{OH}\,[OH^-] \qquad (6)$$

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[a] SIRCOB (EP CNRS 102), Université de Versailles, Bâtiment Lavoisier,
45 avenue des Etats-Unis, 78035 Versailles Cedex, France
E-mail: moutiers@chimie.uvsq.fr;
terrier@chimie.uvsq.fr
[+] Visiting Professor from Queen′s University, Kingston, Ontario K7L 3N6, Canada

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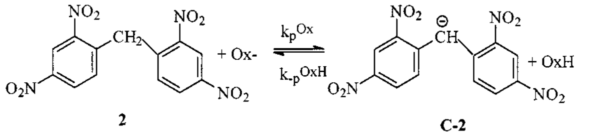
Discussion

Figure 1 provides a revealing comparison of the oximate reactivity with that of a series of phenoxides studied previously.[13] The striking result is that a rapid levelling of the oximate catalytic efficiency is seen, while the phenoxide reactivity follows a normal pattern with linear Brønsted behaviour ($\beta = 0.49$).

While the levelling in oximate reactivity has been previously found in nucleophilic processes,[14–16] this has not been the case in deprotonation of carbon acids.[17] In fact, two linear and essentially superimposable Brønsted plots describe the behaviour of phenoxide and oximate bases in the ionization of 2,2′,4,4′-tetranitrodiphenylmethane **2**, a compound with a much lower acidity ($pK_a = 10.50$) but an intrinsic reactivity comparable with **1** [$\Delta G_0^{\neq}(\mathbf{1}) = 62.8\ \mathrm{kJ{\cdot}mol^{-1}}$; $\Delta G_0^{\neq}(\mathbf{2}) = 70.2\ \mathrm{kJ{\cdot}mol^{-1}}$ for a phenoxide reference] in 50:50 (v/v) H_2O/Me_2SO.[13][17] In this instance there is no evidence at all of levelling in the oximate reactivity (Equation 7).[17]



(7)

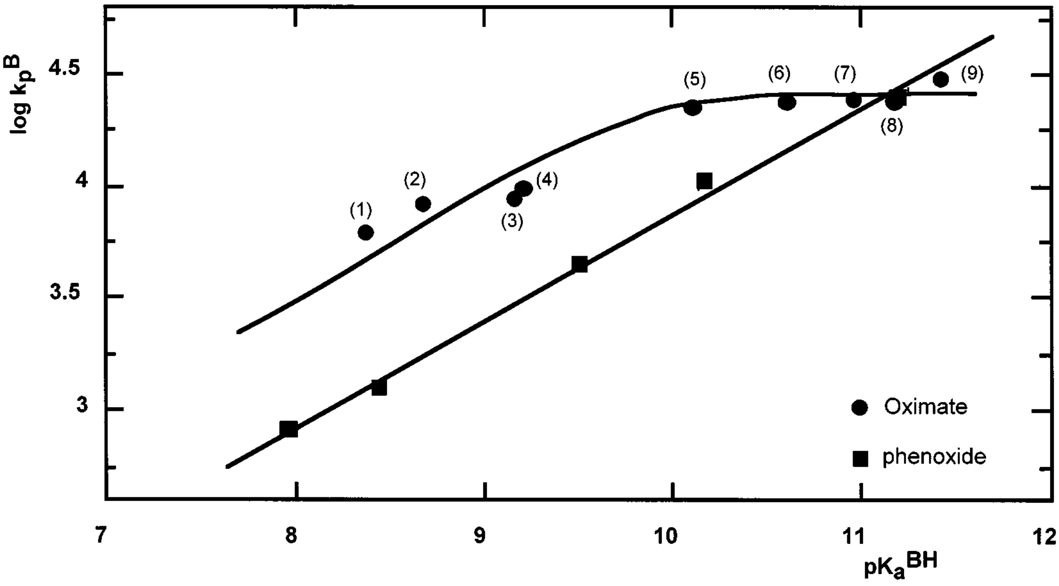


Figure 1. Brønsted plot for reactions (5) in 50:50 (v/v) H_2O/Me_2SO at 25°C; $I = 0.5\ \mathrm{mol{\cdot}L^{-1}}$ KCl. The numbering of the oximate catalysts is given in Table 1. Data for phenoxide bases are taken from ref.[17]

Solvational imbalances have been shown to be the major factor determining the occurrence of rapid levelling in the reactivity of oximates in nucleophilic processes.[14][15] In such instances, there is a requirement for desolvation of the oximate functionality prior to nucleophilic attack, which becomes more and 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, and in the extreme, the desolvation process could become energetically predominant.[18–22] We propose that this is actually the situation met in Equation (5).

Taking into account that the deprotonation of **1** and **2** by phenoxide ions is associated with $\Delta G_0^{\neq}$ values of the same order of magnitude, the two contrasting situations observed for reactions (5) and (7) can be understood by returning to the Marcus Equation (3) and considering the relative magnitude of the w_r and intrinsic barriers terms with respect to changes in $\Delta G°$. In the case of **1**, the deprotonation by the series of oximates studied always occurs under highly thermodynamically favorable conditions. (Due to the low pK_a value of **1**, no common oximates were available for study of the ionization process in the reverse direction, corresponding to $\Delta G° \geq 0$ for reaction (5); this would have provided an initially increasing rate plot prior to the observed levelling.)

Hence, the W_r term, which will reflect mainly the energetic cost of desolvation of the oximate reagent, will be the predominant factor and the intrinsic barrier term will contribute only slightly, if at all, to the measured $\Delta G^{\neq}$ value, i.e. $\Delta G^{\neq} \approx W_r$. Hence, the desolvation step will be fully rate-limiting. In contrast, the deprotonation of **2** is achieved either under thermodynamically unfavorable or under ergoneutral conditions. In this instance, the intrinsic barrier term of Equation (3) will contribute markedly to $\Delta G^{\neq}$; consequently, the actual proton transfer step now appears to be the rate-limiting step. The corresponding reaction profiles in Figure 2 are calculated on the reasonable assumption that the two systems involve rather similar W_r terms. It is noteworthy that the high estimate of the W_r term ($\approx 50\ \mathrm{kJ{\cdot}mol^{-1}}$) deduced from the plateau in Figure 1 and the related low γ value ($10-12\ \mathrm{kJ{\cdot}mol^{-1}}$) estimated from the data at $pK_a^{Ox} < 9.5$ are of the same order of magnitude as the W_r and γ values reported by Kreevoy and Oh for the hydrolysis of diazoacetate by trialkylammonium cations.[10]

So far, this reaction has been highlighted as one of the few systems giving rise to considerable curvature in a Brønsted plot describing a proton transfer at carbon.[9−12]

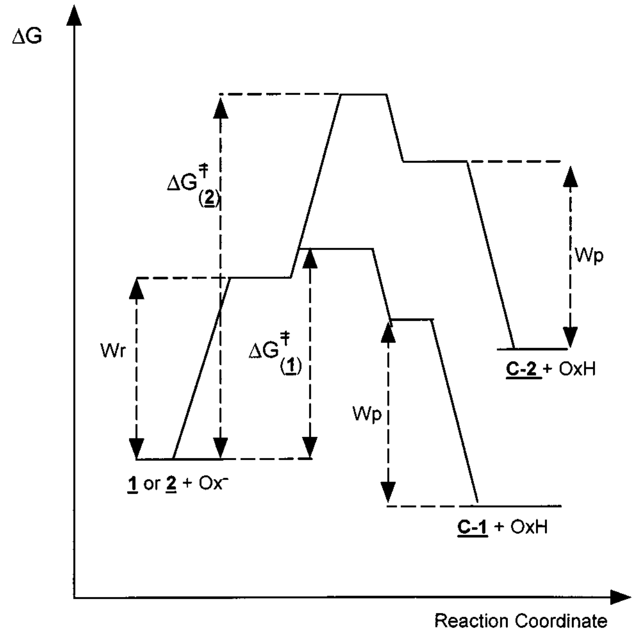


Figure 2. Proposed Marcus reaction profiles for the thermodynamically favorable and unfavorable ionization processes of **1** and **2**, respectively, assuming for clarity that the W_r and W_p values are closely similar in the two reactions and that the initial states are of equal energy or almost so

Thus the present deprotonation reaction (Equation 5) represents not only the first instance of the occurrence of levelling of oximate reactivity in proton transfer processes but also a new prototype example for the occurrence of rapid Marcus curvature in Brønsted plots for deprotonation of carbon acids. Moreover, the results emphasize the importance of desolvation as the origin of imbalances in chemical processes in general and clarify the role of the W_r term in Marcus theory. On the other hand, the results relate well to previous observations of oximate reactivity levelling in nucleophilic addition or substitution processes, thereby resulting in a marked decrease in the α-effect of oximate catalysts.[14−16] Another interesting point is that our work also relates very well to two recent studies which have involved measurements of equilibrium acidity coefficients of various oximates.[23][24] These studies have shown that the negative charge of oximate bases is not much prone to delocalization and remains therefore largely localized on the oxygen atom irrespective of the structure bearing the C=NO⁻ functionality. Because of this charge localization, the most basic oximates would behave rather similarly to the 10^6-10^7-fold more basic OH^- ion in terms of desolvation requirements.[23][24] In this regard, it is a significant finding that the rate constant k_p^{OH} for the ionization of **1** by OH^- appears to be nearly the same as the k_p^{Ox} values defining the plateau in Figure 1 (see Table 1). Since it is well known that the reactivity of OH^- is considerably reduced relative to that of normal oxyanions, e.g. ArO^- ions, in most proton transfer reactions at carbon,[6,7,13,21] the observed similarity of the k_p^{OH} and $k_{p,\,max}^{Ox}$ values for **1** further highlights the importance of the levelling off in the reactivity of oximate species. Obviously, this factor must be kept in mind when considering use of these catalysts for detoxification.[25][26]

Experimental Section

Buffer oximes and compound **1** were available from previous studies.[14][15] Solvents were purified and solutions made up as described previously.[22]

Pseudo-first-order rate constants, k_{obs}, for attainment of equilibrium (5) were determined spectrophotometrically following the appearance of the strongly coloured carbanion **C-1** at its λ_{max} = 528 nm in 50:50 (V/V) H_2O/Me_2SO. The reactions were carried out at 25 °C with use of oximate buffers, varying the concentration of the oximate base between $5 \cdot 10^{-4}$ mol·L^{-1} and 10^{-2} mol·L^{-1} at a given [Ox⁻]/[OxH] ratio, i.e. a given pH. The concentration of **1** was always lower than $3 \cdot 10^{-5}$ mol·L^{-1} and the ionic strength maintained constant at 0.5 mol·L^{-1} by KCl. Usually six values of [Ox⁻] were employed and each individual experiment was kinetically first order in **1** up to at least 90% of the overall reaction. All rates reported in Table S1 were measured with an Applied Photophysics stopped flow spectrophotometer and found to be reproducible to within ±5%.

Table 1. Rate constants for reaction (5) in 50:50 (v/v) H_2O/Me_2SO at 25 °C[a]

Entry	Buffer acid specie (BH)[b]	pK_a^{BH} [c]	k_p^B L mol^{-1}s^{-1}	k_{-p}^{BH}[d] L mol^{-1}s^{-1}
1	2-(hydroxyiminomethyl) pyridinium	8.38	6180	12.33
2	CEB 1574[e]	8.68	8280	8.87
3	2-oxopropanal oxime	9.17	8715	3.02
4	4-(hydroxyiminomethyl) pyridinium	9.22	9650	2.98
5	salicylaldoxime[f]	10.12	22600	0.88
6	butane-2,3-dione monoxime	10.62	23700	0.29
7	4-(hydroxyiminomethyl) pyridine	10.98	24200	0.13
8	2-(hydroxyiminomethyl) pyridine	11.19	23900	0.079
9	3-(hydroxyiminomethyl) pyridine	11.43	30400	0.058
10	H_2O	17.34	55600	$1.3 \cdot 10^{-7}$

[a] I = 0.5 mol·L^{-1} KCl; experimental error in the rate constants: ±4% or better; in pKa ±0.05 pK units. − [b] BH = OxH or H_2O. − [c] pK_a^{BH} values taken from ref.[17] − [d] $k_{-p}^{OXH} = (k_p^{Ox} K_a^{OXH})/K_a^{1}$. − [e] ref.[27] − [f] A titration curve shows that the pK_{a2} value for the ionization of the OH group of salicylaldoxime is 13±0.1 in H_2O/Me_2SO (50:50, v/v); this makes a possible contribution of the dianionic form to the reactivity at pH ≈ 10 negligeable.

Acknowledgments

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