Nonlinear Brönsted Relationships in the Reactions of Phenoxide Ions with Bis(4-nitrophenyl) Phenylphosphonate in H_2O-Me_2SO Mixtures. Solvation Effects

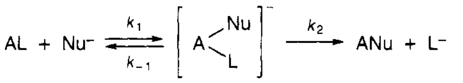
François Terrier,*,† Gilles Moutiers,† Lan Xiao,† Eric Le Guével,† and Frédéric Guir‡

URA CNRS 403, Department of Chemistry, The University of Versailles, 45 Avenue des Etats Unis, 78035 Versailles Cedex, France, and Centre d'Etudes du Bouchet, BP 3, 91710 Vert-le-Petit, France

Received November 3, 1994⊗

The second-order rate constants (k^{ArO}) for reaction of substituted phenoxide ions with bis(4-nitrophenyl) phenylphosphonate in aqueous as well as various aqueous dimethyl sulfoxide (Me_2SO) mixtures are reported. Traditional Brönsted plots of log k^{ArO} vs $\mathrm{p}K_a^{\mathrm{ArOH}}$ are linear at low $\mathrm{p}K_a^{\mathrm{ArOH}}$ but show very strong downward curvature at high $\mathrm{p}K_a^{\mathrm{ArOH}}$. In each solvent, the break point in the Brönsted plot occurs at a $\mathrm{p}K_a^{\mathrm{ArOH}}$ value which is much higher than that corresponding to the basicity of the leaving *p*-nitrophenoxide ion, suggesting that the observed levelling off does not reflect a change in the identity of the rate-determining step in a two-step process involving formation of a pentacoordinate intermediate. An analysis of the data on the basis of a novel strategy recently designed by Buncel and co-workers for the construction of Brönsted plots in solvent mixtures confirms this conclusion. It is proposed that the curvature in the traditional Brönsted plots is the reflection of strong imbalances in the transition states of the reactions, and it is suggested that these imbalances are essentially of solvational nature.

Structure−reactivity correlations have played an important role in determining the structure of the transition states in nucleophilic substitution reactions of carbon-, phosphorus-, and sulfur-based esters that possess good leaving functionalities in aqueous solution.[1-3] The two major mechanisms for these reactions are shown in eqs 1 and 2.


(1)

$$\mathrm{AL} + \mathrm{Nu}^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \left[\mathrm{A}\genfrac{}{}{0pt}{}{\diagup \mathrm{Nu}}{\diagdown \mathrm{L}}\right]^- \xrightarrow{k_2} \mathrm{ANu} + \mathrm{L}^- \qquad (1)$$

$$\mathrm{AL} + \mathrm{Nu}^- \rightleftharpoons [\mathrm{L}\cdots\mathrm{A}\cdots\mathrm{Nu}]^{-\ddagger} \rightleftharpoons \mathrm{ANu} + \mathrm{L}^- \qquad (2)$$

In principle, the distinction between the two mechanisms can be readily obtained from a study of substituent effects on the nucleophile.[1-3] For the addition−elimination mechanism of eq 1, a change in rate-limiting step may be expected when the reactivity of the nucleophile is varied. This change will be from rate-limiting leaving group departure with weak nucleophiles (k_2:k_{-1} > k_2) to rate-limiting nucleophilic addition with strong nucleophiles (k_1:k_2 > k_{-1}). Since the two conditions correspond to two transition states of different structures, the situation will be normally reflected by a change in the slope of the structure−reactivity correlation pertaining to eq 1 and, therefore, by the finding of nonlinear Brönsted or Hammett plots.[1-9] As a matter of fact, many reactions of transfer of general acyl groups between nucleophiles have been successfully interpreted as occurring via a stepwise process on the basis of the observation of nonlinear free energy correlations. These include especially systems involving displacement of leaving groups by nucleophiles of similar structures where the break point in the correlation occurs, as expected, when $\Delta\mathrm{p}K = \mathrm{p}K_a^{\mathrm{Nu}} - \mathrm{p}K_a^{\mathrm{L}} = 0$. Representative examples of such "symmetrical" systems are the reactions of a series of thiol anions with *p*-nitrothiophenyl acetate in aqueous solution.[5] Interestingly, the reasoning has proved to be also appropriate in various systems involving nucleophiles and leaving groups of different structures where a prediction of the pK_a at which the change in rate-determining step must occur is not normally possible. Reactions of aminolysis of aryl acetates belong to the latter category.[7]

In contrast with eq 1, no abrupt change is expected to occur in the transition state structure for eq 2 when the reactivity of the nucleophile is varied. Accordingly, the observation of a linear free energy plot will be excellent evidence for a concerted mechanism provided that the correlation is established with such a wide range of basicities of the nucleophiles that a change in rate-limiting step for a putative stepwise process would necessarily be detected.[1,2] Amongst representative systems where such meaningful linear correlations have been obtained are the transfers of acetyl, phosphoryl, and

---

† The University of Versailles.

‡ Centre d'Etudes du Bouchet.

⊗ Abstract published in *Advance ACS Abstracts*, March 1, 1995.

(1) (a) Jencks, W. P. *Acc. Chem. Res.* **1976**, *9*, 425; **1980**, *13*, 161. (b) Jencks, W. P. In *Nucleophilicity*; Harris, J. M., McManus, S. P., Eds.; ACS Advances in Chemistry Series; American Chemical Society: Washington, D.C., 1987; p 155 and references therein. (c) Jencks, W. P. *Bull. Soc. Chim. Fr.* **1988**, 218.

(2) (a) Williams, A. *Acc. Chem. Res.* **1989**, *22*, 387; (b) *Adv. Phys. Org. Chem.* **1992**, *27*, 1 and references therein.

(3) Buncel, E.; Wilson, H. *J. Chem. Educ.* **1987**, *64*, 475.

(4) (a) Knier, B. L.; Jencks, W. P. *J. Am. Chem. Soc.* **1980**, *102*, 6789. (b) Jencks, W. P.; Gilchrist, M. *Ibid.* **1968**, *90*, 2622. (c) Shoog, M. T.; Jencks, W. P. *Ibid.* **1984**, *106*, 7597.

(5) Hupe, D. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 451.

(6) Hupe, D. J.; Wu, D. *J. Am. Chem. Soc.* **1977**, *99*, 7653.

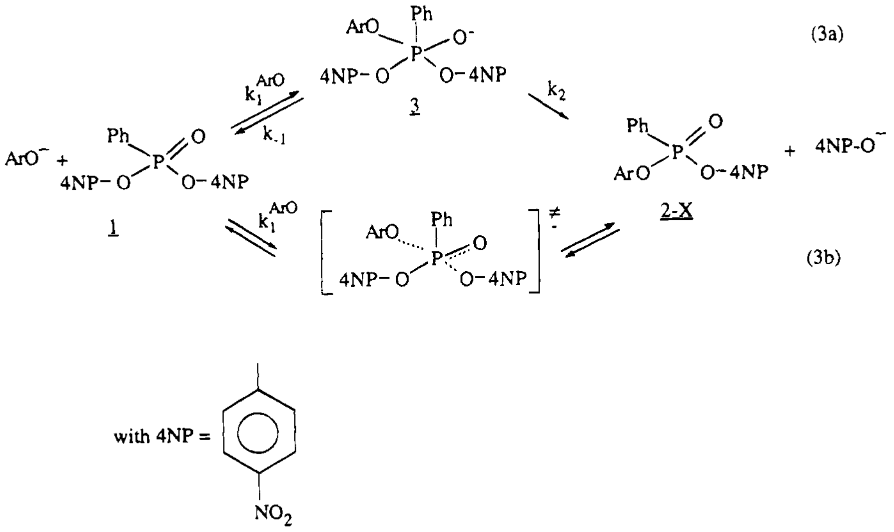
(7) (a) Castro, E. A.; Ureta, C. *J. Org. Chem.* **1989**, *54*, 2153. (b) Castro, E. A.; Freudenberg, M. *Ibid.* **1980**, *45*, 906.

(8) (a) Ba-Saif, S.; Luthra, A. K.; Williams, A. *J. Am. Chem. Soc.* **1987**, *109*, 6362. (b) Bourne, N.; Chrystiuk, E.; Davis, A. M.; Williams, A. *Ibid.* **1988**, *110*, 1890. (c) Ba-Saif, S.; Luhra, A. K.; Williams, A. *Ibid.* **1989**, *111*, 2647. (d) Ba-Saif, S.; Waring, M. A.; Williams, A. *Ibid.* **1990**, *112*, 8115. (e) D'Rozario, P.; Smith, R. L.; Williams, A. *Ibid.* **1984**, *106*, 5027.

(9) Gallis, D. E.; Acken, B. J.; Warshaw, J. A.; Richardson, A. L.; Crist, D. R.; Cichra, D. A. *J. Org.Chem.* **1990**, *55*, 5510.

0022-3263/95/1960-1748$09.00/0

Scheme 1



phosphinoyl groups between phenoxide ions,[8,10] of a sulfonyl group between oxyanions,[8c] and of sulfonyl and phosphoryl groups between pyridines.[11]

Although the presence or the absence of curvature in free energy plots is in most instances understandable within the above reasonings, it remains that some other factors may be important in determining the shape of a correlation. In particular, Jencks and co-workers have shown that nonlinear Brönsted correlations pertaining to acyl group transfers are in some instances best interpreted in terms of solvation effects rather than in terms of a change in rate-limiting step in a process of type (1).[4b,5,6,12–14] In this paper, we report a study of the reaction of bis(4-nitrophenyl) phenylphosphonate *1* with a series of phenoxide ions (ArO^-) in H_2O-Me_2SO media at 25 °C (Scheme 1, eq 3). We will show that traditional Brönsted plots for these reactions are subject to strong downward curvature in all solvent mixtures studied, and we will show that this behavior is more consistent with a need for partial desolvation of the phenoxide anions before nucleophilic attack than with a change in rate-determining step in an addition–elimination process.

Results

The rates of the reactions (3) were measured by using phenoxide buffers, varying the concentration of the acid and basic buffer components at constant pH in each H_2O-Me_2SO mixture studied, and following spectrophotometrically the appearance of the resulting *p*-nitrophenoxide ion ($4NPO^-$) at 410–425 nm. The reactions were conducted at 25 °C with a large excess of the base reagent, i.e., $[1] \leq 5 \times 10^{-5}$ mol L^{-1}, $[ArO^-] = 10^{-3}-10^{-2}$ mol L^{-1}, keeping the ionic strength constant at $I = 0.1$ mol L^{-1} in aqueous solution and $I = 0.5$ mol L^{-1} NMe_4Cl in H_2O-Me_2SO solutions. If one excepts the 4-chlorophenoxide, 3-methoxyphenoxide, phenoxide, and 4-methoxyphenoxide buffers in 50 and 70% Me_2SO, excellent first-order kinetics up to about 90% of the total release of $4NPO^-$ were observed in all buffer systems studied. Plots of the corresponding observed rate constants k_{obsd} versus the phenoxide concentration were linear with negligible intercepts, indicating no appreciable contribution of hydroxide ion and/or water to the rates and suggesting that k_{obsd} is simply given by eq 4. Determination of the second-order rate constants k_1^{ArO} from the slopes of the various buffer plots was straightforward.

$$k_{obsd} = k_1^{ArO}[ArO^-] \qquad (4)$$

With the most basic reagents mentioned above, reaction (3) was found to be followed by the analogous but much slower displacement of $4NPO^-$ from the resulting monosubstituted product **2-X** (eq 5) in 50 and 70% Me_2SO.

$$\mathbf{2\text{-}X} + ArO^- \xrightarrow{k_2^{ArO}} \underset{\mathbf{4\text{-}X}}{(ArO)_2P(O)Ph} + 4NPO^- \qquad (5)$$

In these instances, the k_{obsd} values for reactions (3) were obtained by recording the increase in absorbance at λ_{max} of $4NPO^-$ as a function of time up to about 50% of the release of the first mole of this anion. In this way, excellent first-order kinetics were obtained with the k_{obsd} values fitting eq 4 nicely. The kinetics of reactions (5) were similarly followed by recording the changes in the absorbance of $4NPO^-$ after about 30% completion of these processes, i.e., after displacement of 1.3 mol of $4NPO^-$. The k_{obsd} values thus obtained also obeyed eq 4, allowing a facile determination of the second-order rate constants k_2^{ArO}.

The derived parameters k_1^{ArO} and k_2^{ArO} are summarized in Table 1. Also given in Table 1 are the rate constants k_1^{OH} for monosubstitution of *1* by hydroxide ion which were measured in dilute hydroxide ion solutions ($10^{-3}-10^{-2}$ mol L^{-1}).

Discussion

Brönsted Relationships. Figures 1 and 2 show that the second-order rate constants k_1^{ArO} for the reactions of phenoxide ions with *1*, resulting in displacement of *p*-nitrophenoxide ion ($4NPO^-$), follow a nonlinear Brön-

---

[10] (a) Ba-Saif, S.; Waring, M. A.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1991**, 1653. (b) Ba-Saif, S.; Colthurst, M.; Waring, M. A.; Williams, A. *Ibid.* 1901.

[11] (a) Bourne, N.; Williams, A. *J. Am. Chem. Soc.* **1984**, *106*, 7591. (b) Bourne, N.; Hopkins, A.; Williams, A. *Ibid.* **1985**, *107*, 4327.

[12] Jencks, W. P.; Brant, S. R.; Gandler, J. R.; Friedrich, G.; Nakamura, C. *J. Am. Chem. Soc.* **1982**, *104*, 7045.

[13] Jencks, W. P.; Gilchrist, M. *J. Am. Chem. Soc.* **1962**, *84*, 2910.

[14] Jencks, W. P.; Haber, M. T.; Herschlag, D.; Nazaretian, K. L. *J. Am. Chem. Soc.* **1986**, *108*, 479.

Table 1. pK_a^{ArOH} **Values and Rate Constants for Nucleophilic Substitution of Bis(4-nitrophenyl) Phenylphosphonate (1) by Phenoxide Ions in Various H_2O–DMSO Mixtures**[a]

		H_2O		70% H_2O–30% Me_2SO		50% H_2O–50% Me_2SO		30% H_2O–70% Me_2SO	
	phenoxide	pK_a^{ArOH}	k_1, L mol^{-1} s^{-1}	pK_a^{ArOH}	k_1, L mol^{-1} s^{-1}	pK_a^{ArOH}	k_1, L mol^{-1} s^{-1} (k_2, s^{-1})	pK_a^{ArOH}	k_1, L mol^{-1} s^{-1} (k_2, s^{-1})
1	2-cyanophenoxide	7.22	0.1	7.54	0.09	7.97	0.18	8.88	0.84
2	3,4,5-trichlorophenoxide	7.68	0.28	7.85	0.18	8.01	0.20	8.77	0.69
3	2,4-dichlorophenoxide	7.65	0.21	8.01	0.20	8.31	0.26	9.08	1.16
4	4-cyanophenoxide	7.80	0.33	8.17	0.28	8.45	0.46	9.31	1.20
5	3,5-dichlorophenoxide	8.03	0.54	8.27	0.395	8.53	0.43	9.38	1.78
6	3,4-dichlorophenoxide	8.51	1.13	8.78	0.95	9.10	1.56	10.08	4.34
7	4-chlorophenoxide	9.35	2.77	9.85	2.64	10.18	4.77 (0.61)	11.52	19.42 (2.27)
8	3-methoxyphenoxide	9.65	2.90	10.35	2.55	11.05	4.86 (0.24)	12.24	17.86 (0.72)
9	phenoxide	9.88	3.08	10.62	2.58	11.21	5.83 (0.31)	12.44	20.41 (0.73)
10	4-methoxyphenoxide	10.27	2.75	10.70	3.03	11.47	6.39 (0.60)	12.90	27.43 (1.04)
11	4-nitrophenoxide	7.12		7.22		7.29		7.72	
12	OH^-	15.74	30.48		39.63		63.52		289

[a] $T = 25$ °C; $I = 0.5$ mol L^{-1} NMe_4Cl.

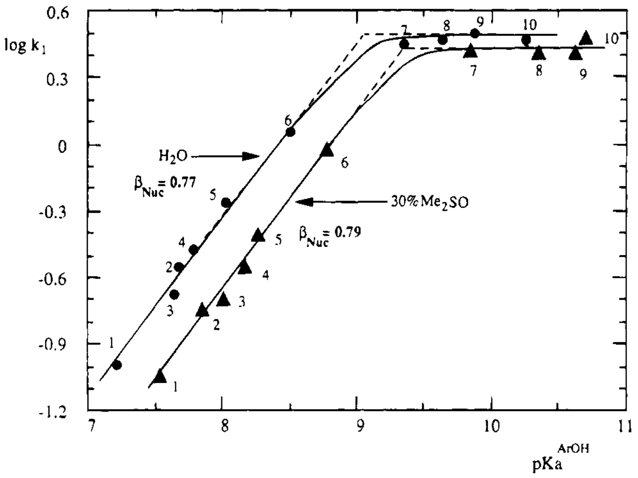


Figure 1. Brönsted plots for reactions of phenoxide ions with bis(4-nitrophenyl) phenylphosphonate in aqueous solution ($I = 0.1$ mol L^{-1} KCl) and in 70% H_2O–30% Me_2SO (v/v) mixture ($I = 0.5$ mol L^{-1} NMe_4Cl) at 25 °C. See Table 1 for the numbering of the catalysts.

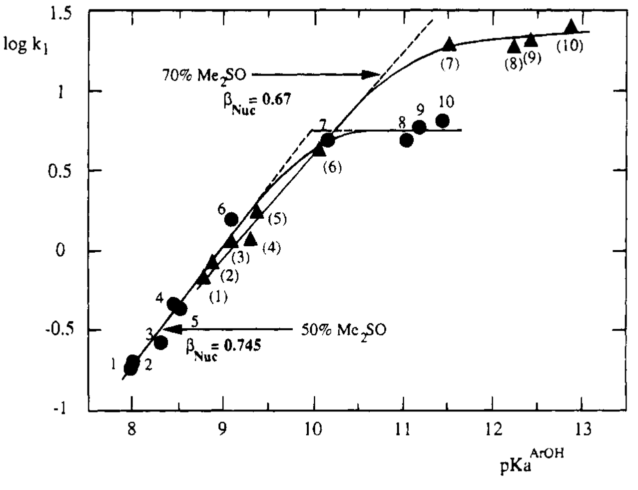


Figure 2. Brönsted plots for reactions of phenoxide ions with bis(4-nitrophenyl) phenylphosphonate in 50% H_2O–50% Me_2SO and in 30% H_2O–70% Me_2SO (v/v) mixture at 25 °C and $I = 0.5$ mol L^{-1} NMe_4Cl. See Table 1 for the numbering of the catalysts.

sted-type correlation in aqueous solution as well as in the three water–Me_2SO mixtures studied. This behavior is in marked contrast with recent reports by Williams that the second-order rate constants k_1^{ArO} for the analogous displacements of $4NPO^-$ from two related phosphorus electrophiles, namely 4-nitrophenyl diphenylphosphinate (*5*) and 4-nitrophenyl diphenyl phosphate (*6*), obey good linear relationships in aqueous solution.[8b,d] In these instances, the phenoxide nucleophiles employed had pK_a values ranging well above and below that of the leaving $4NPO^-$ anion so that the observed linearity was taken as evidence that reactions (6) and (7) proceed through a concerted mechanism.

$$\mathrm{ArO^- + \underset{\mathbf{5}}{Ph_2P(O)O4NP}} \xrightarrow{k_1^{\mathrm{ArO}}} \mathrm{Ph_2P(O)OAr + 4NPO^-} \tag{6}$$

$$\mathrm{ArO^- + \underset{\mathbf{6}}{(PhO)_2P(O)O4NP}} \xrightarrow{k_1^{\mathrm{ArO}}} \mathrm{(PhO)_2P(O)OAr + 4NPO^-} \tag{7}$$

In the case of reactions (3), the curvature in Figures 1 and 2 may at first suggest a two-step transacylation process (eq 3a) with a rate-determining step changing from the decomposition (k_2) to the formation (k_1^{ArO}) of the pentacoordinate intermediate *3* when the basicity of the attacking aryloxide anion is increased.[1,2] However, such an explanation is difficult to reconcile with our results, simply because the phenoxides used in our study are all more basic than the leaving $4NPO^-$ ion. As a matter of fact, the break points in the observed biphasic Brönsted plots of Figures 1 and 2 occur at pK_a^{ArOH} values (9.05 in water, 9.35 in 30% Me_2SO, 10.20 in 50% Me_2SO, 10.60 in 70% Me_2SO) which are much greater than the pK_a values of $4NPO^-$ in the corresponding solvents (7.12, 7.22, 7.29, and 7.72, respectively). On this ground, it seems more reasonable to consider that reactions (3) involve rate-determining nucleophilic attack, coupled (eq 3b) or not (eq 3a) with leaving group departure, under the experimental conditions employed. It follows that the curvature of the Brönsted plots in Figures 1 and 2 must have another origin than a change in the identity of the rate-determining step in a transacylation process proceeding according to eq 3a. This conclusion is supported by recent results pertaining to the substitution of the phosphinate *5* by phenoxide ions in H_2O–Me_2SO mixtures which have been reported after the completion of this work.[15]

Imbalanced Transition States. In contrast with the situation observed by Williams et al. in aqueous solution,[8b] Buncel, Tarkka, and Hoz have found that plots of log

---

(15) Buncel, E.; Tarkka, R.; Hoz, S. *Chem. Commun.* **1993**, 109.

k_1^{ArO} vs $\mathrm{p}K_a^{\mathrm{ArOH}}$ for reactions (6) give curved Brönsted plots of the same type as those found for reactions (3) in the various solvents studied.[15] In these instances, the conclusion that the observed curvature cannot be attributed to change in rate-determining step was supported by use of a new methodology developed by the same authors for the construction of Brönsted-type plots.[16] While in the classical approach, the $\mathrm{p}K_a$ of the nucleophile is changed by variation of substituents, in the new method $\mathrm{p}K_a$ variations are brought about by gradual changes in the solvent composition, namely by increasing the Me_2SO content of the solvent mixtures, while the identity of the nucleophile is retained. When applied to acyl-transfer reactions such as the reactions of phenoxide ions with 4-nitrophenyl acetate or 4-nitrophenyl benzenesulfonate, in which rate-determining nucleophilic attack goes along with a linear dependence of the traditional Brönted plots built in each H_2O-Me_2SO mixture employed, the novel method afforded a single linear correlation that extends over a large range of $\mathrm{p}K_a$ and log k values.[16] Although the fundamental basis for such linear correlations is not yet very well understood, the interesting point is that they defined β_{nuc} values which nicely average the individual β_{nuc} values obtained from the classical Brönsted plots.

Following these observations, Buncel et al. looked at how the curvature seen in the log k_1^{ArO} vs $\mathrm{p}K_a^{\mathrm{ArOH}}$ plots drawn for reactions (6) in each H_2O-Me_2SO mixture studied is reflected in their new approach of the Brönsted behavior.[15] Interestingly, this analysis resulted neither in the formation of a single line nor in two distinct Brönsted lines, as required for a division of the nucleophiles into two groups according to their basicity relative to the leaving group. Instead, the results appeared to fit a set of individual nonoverlapping straight lines, each belonging to a different nucleophile, with slopes that decrease with increasing $\mathrm{p}K_a^{\mathrm{ArOH}}$, supporting the idea that the curvature of the classical Brönsted plots is not due to a change in rate-limiting step. In the light of Jencks' results,[5,12-14] it was therefore concluded that the curvature was most reasonably the result of a need for desolvation of the phenoxide ions before nucleophilic attack that becomes more and more energetically costly with increasing basicity.

Figure 3 shows the Brönsted plot obtained when Buncel's strategy is applied to reactions (3) in 30, 50, and 70% Me_2SO. The data in aqueous solution have not been used to draw the correlation because it is well known that the addition of small quantities of dimethyl sulfoxide to aqueous solutions results in important changes in the physical properties of the media, often causing unpredictable changes in reactivity.[16-22] In the present case, there is a decrease in k_1^{ArO} on going from water to 30% Me_2SO as opposed to a regular increase of these rate constants on going to higher Me_2SO concentrations. As can be seen in Figure 3, a good straight line of slope $\beta_{\mathrm{nuc}} = 0.74$ is obtained provided that only the k_a^{ArO} and $\mathrm{p}K_a^{\mathrm{ArOH}}$ values for the less basic phenoxide ions are considered. On the other hand, the data for the phenoxides with $\mathrm{p}K_a^{\mathrm{ArO}} >$ 9–9.5 do not define a second Brönsted line. In Figure 3 two lines of slopes 0.495 and 0.43 have been arbitrarily drawn which correspond to moderately or very basic nucleophiles, respectively.

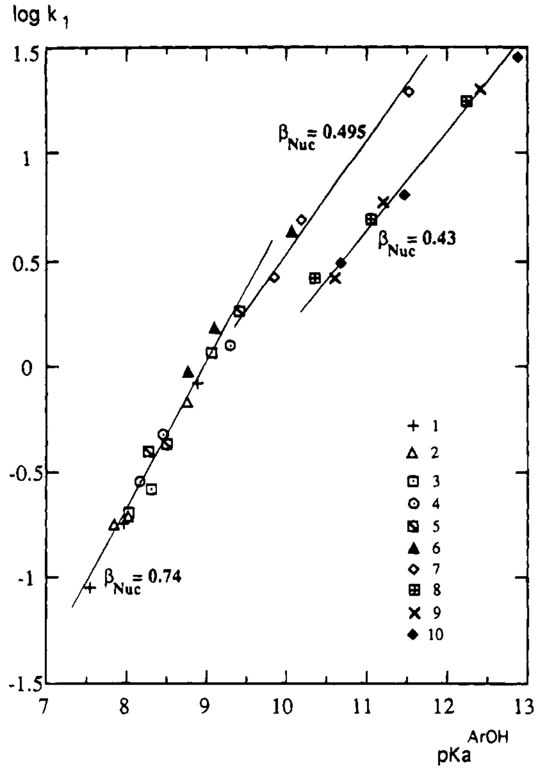


Figure 3. Buncel-type plots for reactions of phenoxide ions with bis(4-nitrophenyl) phenylphosphonate in various mixtures (H_2O, 70% H_2O–30% Me_2SO, 50% H_2O–50% Me_2SO, 30% H_2O–70% Me_2SO (v/v)) at 25 °C.

Even though our data for reactions (3) refer to H_2O-Me_2SO mixtures of somewhat lower Me_2SO content than those used by Buncel et al., they resemble in many aspects those reported for substitution of the phosphinate *5*.[15] First, the linear parts of the Brönsted plots of Figures 1 and 2 afford β_{nuc} values which decrease notably with increasing the Me_2SO concentration ($\beta_{\mathrm{nuc}} = 0.77$, 0.745, and 0.67 in water and 50% and 70% Me_2SO, respectively). This suggests, in agreement with the Hammond postulate[23] and the reactivity–selectivity principle,[3,24-28] that the transition state occurs earlier along the reaction coordinate as the system becomes more reactive. On the other hand, a comparable but unique

---

(16) (a) Buncel, E.; Um, I. H.; Hoz, S. *J. Am. Chem. Soc.* **1989**, *111*, 971. (b) Tarkka, R. M.; Park, W. K. C.; Liu, P.; Buncel, E.; Hoz, S. Submitted for publication.

(17) Buncel, E.; Wilson, H. *Adv. Phys. Org. Chem.* **1977**, *14*, 133 and references therein.

(18) Francks, F., Ed. *Water—A comprehensive Treatise*; Plenum: New York, 1972–1982; Vols. 1–7.

(19) Rallo, F.; Rodante, R.; Silverstroni, P. *Thermochim. Acta* **1970**, *1*, 311.

(20) Haak, J. R.; Engberts, J. B. F. N. *J. Am. Chem. Soc.* **1986**, *108*, 705.

(21) Symons, E. A. *Can. J. Chem.* **1971**, *24*, 8940 and references therein.

(22) Larn, S. Y.; Benoît, R. L. *Can. J. Chem.* **1974**, *52*, 718.

(23) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334.

(24) (a) Pross, A. *Adv. Phys. Org. Chem.* **1977**, *14*, 69. (b) Giese, B. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 125. (c) Hoz, S. *J. Org. Chem.* **1982**, *47*, 3545.

(25) Hoz, S.; Buncel, E. *Isr. J. Chem.* **1985**, *26*, 313.

(26) Buncel, E.; Wilson, H. *J. Chem. Educ.* **1987**, *64*, 475.

(27) Exner, O. *J. Chem. Soc., Perkin Trans. 2* **1993**, 973.

(28) (a) Jencks, W. P. *Chem. Rev.* **1985**, *85*, 511. (b) Pross, A. *Adv. Phys. Org. Chem.* **1985**, *21*, 99. (c) Williams, I. H.; Hammond, R. B. *J. Chem. Soc., Perkin Trans. 2* **1989**, 59. Lewis, E. J. *J. Phys. Org. Chem.* **1990**, *3*, 1. (e) Hoz, S. *Acc. Chem. Res.* **1993**, *26*, 69.

(29) Bernasconi, C. F.; Bunnell, R. D. *Isr. J. Chem.* **1985**, *26*, 420.

(30) Bernasconi, C. F.; Paschalis, P. *J. Am. Chem. Soc.* **1986**, *108*, 2969.

(31) (a) Bernasconi, C. F. *Tetrahedron* **1985**, *41*, 3219. (b) *Acc. Chem. Res.* **1987**, *20*, 301. (c) *Adv. Phys. Org. Chem.* **1992**, *27*, 119.

β_{nuc} value is obtained upon treatment of the data for the phenoxides of low pK_a by the Buncel method (Figure 3), *suggesting that the transition state structure does not vary significantly with changing solvent composition*. Thus, as previously found for the reactions of phenoxide ions with p-nitrophenyl acetate and *p*-nitrophenyl benzenesulfonate[15,16] the two methods of analysis lead to somewhat conflicting conclusions regarding the transition state structure of reactions (3). In the present system, *the most interesting result is that the two methods lead to a clear distinction between the behavior of weakly basic* (p$K_{a(H_2O)}$ < 8.5) *and more basic* (p$K_{a(H_2O)}$ > 8.5) *phenoxides*. Interestingly, such a differentiation within the reactivity of these oxyanions is unprecedented in pure aqueous solution but it is reminiscent of that which we have previously observed for oximate ions.[32,33] At that time we suggested that it may most reasonably be assigned to the occurrence of solvational imbalance phenomena in the transition states of the reactions.[12,13,29-33]

The Nature of the Imbalance:Solvational Effects. Imbalanced transition states in rate-determining nucleophilic attacks have been previously observed in reactions of oxyanions like phenoxide, alkoxide, or oximate anions with esters, proceeding via eq 1 in aqueous solution.[32-34] In these instances, curvature in the traditional plots was attributed by Jencks to a need for partial desolvation of the anions before nucleophilic attack that is less important for weakly basic than for more basic anions.[12] Such desolvation will occur ahead of bond formation in the transition state leading to the tetrahedral intermediate involved in these reactions, and it will become more and more energetically expensive with increasing basicity, thus causing a decrease in the observed Brönsted slope, β_{nuc}, for basic nucleophiles. Subsequently, a similar explanation was proposed by Bernasconi to account for the finding that Brönsted plots for the deprotonation of some carbon acids, e.g., acetylacetone or 1,3-indandione, by carboxylate ions are also subject to downward curvature in some H_2O-Me_2SO mixtures.[29-31]

In an attempt to illustrate his ideas, Jencks proposed a simple model based on the assumption that partial desolvation of the oxyanion occurs in a preequilibrium step, as shown in eq 8.[12]

$$\mathrm{RO}^-_{\mathrm{sol}} \overset{K_d}{\rightleftharpoons} \mathrm{RO}^-_{\mathrm{desol}} \xrightarrow{\mathrm{ArL}} [\ ]^{\ddagger} \tag{8}$$

$$\Delta \log k_1^{\mathrm{RO}} = (1 - \beta_{\mathrm{nuc}}) \log K_d \tag{9}$$

Using the straight line of slope β_{nuc} defined in a given solvent by the points at low pK_a^{RO} as reference, the negative deviation of the points at high basicity from the "normal" Brönsted correlation may then be expressed by eq 9 where K_d is the equilibrium constant for partial desolvation of the oxygen base. Equation 9 predicts that, as desolvation becomes energetically more expensive, the increasingly more negative log K_d value renders Δ log k_1^{RO} more negative as well, accounting for the observed levelling off in nucleophilic reactivity. It appears, however, that the situation is better visualized in terms of a more sophisticated but more general model which has been the subject of considerable discussion in the context of the imbalances encountered in proton transfer reactions on carbon atoms.[29-31] Instead of assuming that desolvation and bond formation occur in two different steps, this model considers that the two events take place in the same step but that desolvation has progressed further than bond formation in the transition state. Then, the change in log k_1^{RO} is described by an equation of the form

$$\Delta \log k_1^{\mathrm{RO}} = (\alpha_d - \beta_{\mathrm{nuc}}) \log K_d \tag{10}$$

where $1 \geq \alpha_d \geq 0$ measures the progress of desolvation in the transition state. If desolvation is ahead of bond formation, we have $\alpha_d > \beta_{nuc}$ so that Δ *log* k_1^{RO} *is again negative*. For $\alpha_d \approx 1$, the situation becomes simply identical to that depicted by Jencks' model.

A major advantage of eqs 9 and 10 is to clearly emphasize that a primary requirement for observation of curved Brönsted plots due to solvation effects is not only that partial desolvation of the nucleophile becomes energetically more expensive with increasing pK_a but that this desolvation occurs ahead of bond formation in the transition state.[31] For a series of nucleophiles with different log K_d values reacting with various electrophiles in a given solvent, linear or curved Brönsted relationships may thus be expected depending upon whether $\alpha_d = \beta_{nuc}$ or $\alpha_d \neq \beta_{nuc}$, respectively. In the latter case, the curvature will be detectable at low pK_a if α_d is markedly greater than β_{nuc} but only at high pK_a if α_d is not very different from β_{nuc}. On this ground, it is a significant result that the curvature appears very early in the Brönsted plots of Figures 1 and 2 compared to previously reported examples involving phenoxide ions.[12] This suggests that reactions (3) proceed through strongly imbalanced transition states. A similar situation was recently encountered in the reactions of oximate ions with 4-nitrophenyl acetate in aqueous solution.[32,33]

Solvational imbalances pertaining to late solvation of developing charged species have also been shown to affect the reactivity.[35] Although our data for reactions (3) did not allow us to establish whether rate-limiting nucleophilic attack results in the formation of the negatively charged intermediate *3* (Scheme 1, eq 3a) or leads directly to formation of the substituted phosphonate **2-X** and the $4NPO^-$ anion (Scheme 1, eq 3b), it seems reasonable to exclude a major contribution of these potential imbalances to the observed differences in reactivity with increasing pK_a^{ArOH}. In eq 3a, the negative charge in the resulting intermediate *3* is so much localized on the oxygen atom of the P → O bond that the energetics of its solvation cannot reasonably depend a lot on the nature of the attacking phenoxide. On the other hand, the concerted mechanism of eq 3b (Scheme 1) implies that all reactions involve the release of the same $4NPO^-$ ion. Thus, should late solvation of the developing anionic species *3* and *4* occur, the corresponding energetic contribution must be very similar in all phenoxide systems studied.

Solvent Effect on pK_a^{ArOH}. Due to their poor ability to provide hydrogen-bond solvation, dipolar aprotic solvents are expected to strongly destabilize anionic species with a localized or relatively localized negative charge

---

(32) Terrier, F.; Degorre, F.; Kiffer, D.; Laloi, M. *Bull. Soc. Chim. Fr.* **1988**, 415.

(33) Terrier, F.; McCormack, P.; Kizilian, E.; Hallé, J. C.; Demerseman, P.; Guir, F.; Lion, C. *J. Chem. Soc., Perkin Trans. 2*, **1991**, 153.

(34) Hupe, D. J.; Wu, D.; Shepperd, P. *J. Am. Chem. Soc.* **1977**, *99*, 7659.

(35) Bernasconi, C. F.; Terrier, F. *J. Am. Chem. Soc.* **1988**, *110*, 6514.

compared to protic solvents.[17,36−38] In accord with this idea, the acidity of oxygen acids like carboxylic acids and phenols has been reported to decrease upon addition of increasing amounts of Me_2SO to aqueous solutions.[17,30,38−44] The pK_a^{ArOH} values listed in Table 1 confirm this behavior but they also reveal a most significant feature, namely that the solvent effect on pK_a^{ArOH} is a function of the acidity measured in aqueous solutions. For example, for the change from water to 70% Me_2SO, the $\Delta pK_a = pK^{ArOH}_{a(70\% Me_2SO)} - pK^{ArOH}_{a(H_2O)}$ values increase from the most acidic phenols, e.g., $\Delta pK_a = 0.60$ for 4-nitrophenol, ($pK_{a(H_2O)} = 7.12$), $\Delta pK_a = 1.09$ for 3,4,5-trichlorophenol ($pK_{a(H_2O)} = 7.68$), to the less acidic phenols, e.g., $\Delta pK_a = 2.17$ for 4-chlorophenol ($pK^{ArOH}_{a(H_2O)} = 9.35$), $\Delta pK_a = 2.59$ for 3-methoxyphenol ($pK_{a(H_2O)} = 9.65$), with a tendency to a saturation effect beyond the latter compound ($\Delta pKa = 2.56$ for phenol ($pK_{a(H_2O)} = 9.88$) and $\Delta pK_a = 2.63$ for 4-methoxyphenol ($pK_{a(H_2O)} = 10.27$). This trend is similar to the one reported by Bernasconi for the ionization of carboxylic acids[30] but due to the greater basic character of phenoxide ions relative to carboxylate ions, the ΔpK_a^{ArOH} values are, for a given solvent transfer, notably greater than the ΔpK_a^{RCOOH} values.

Inasmuch as they are primarily the reflection of the desolvation of phenoxide ions caused by the addition of Me_2SO to aqueous solutions,[17,32,38] the ΔpK_a values may be considered as giving a good idea of the relative degrees of solvation of the anions in aqueous solution. Then, the regular increase in ΔpK_a with increasing pK_a^{ArOH} fits well Jencks and Hupe's proposal that desolvation requirements in the transition states of some nucleophilic substitution processes of type 1 or 2 become energetically more expensive when the basicity of the nucleophile is increased.[1,12,34] As well, the fact that ΔpK_a no longer increases with pK_a^{ArOH} beyond 3-methoxyphenol can account for the observed plateaus in Figures 1 and 2 if the cost of the desolvation is the major factor determining the reactivity. The division of the phenoxide ions in several classes in Figure 3 can be equally understood along similar lines, Buncel's methodology being apparently more appropriate than the traditional Brönsted approach to discriminate between the requirements for desolvation of the various phenoxide ions.[16]

The fact that the addition of Me_2SO decreases the solvation of phenoxide ions also suggests that desolvation requirements should become less and less important in determining the reactivity of these species on going from water-rich to Me_2SO-rich solvents. On this ground, one might reasonably expect that the curvature of the Bronsted plots is attenuated or even disappears in solvents of high Me_2SO content. Obviously, the results obtained in this work do not allow us to test this assumption because the H_2O-Me_2SO mixtures studied cover a relatively narrow range of molar fractions in Me_2SO (0−0.356). In contrast, data for reactions (6) have been obtained by Buncel et al. in a larger composition range (0−90 mol % Me_2SO), but in all solvents studied, significantly curved Bronsted plots were drawn.[15] The role of solvation thus remains very unclear, and further studies on this particular aspect of solvent effects on the reactivity are clearly needed.

Experimental Section

Materials. The various phenols used in this study were of the highest quality commercially available and were recrystallized before used. The phosphonate *1* was prepared according to standard literature methods[45,46] (mp = 104−105 °C (lit.[45] mp 102 °C)). Dimethyl sulfoxide was refluxed over calcium hydride and distilled, and the fractions of 32−35 °C (under 2 mmHg) were collected and stored under nitrogen. Me_2SO–water solutions were prepared as described previously.[39] Only freshly prepared solutions were used in the kinetic and potentiometric studies.

Acidity Measurements. The acidity constants of the various phenols (ArOH) were measured by potentiometry at 25 °C, using an electronic pH meter (Tacussel Isis 20000). The pK_a^{ArOH} values were determined from buffer solutions with $[ArO^-]/[ArOH]$ ratios equal to 1/2, 1/1, and 2/1. These solutions were prepared so that the molarity of the ArO^- species was in all cases equal to 10^{-2} mol L^{-1}. The ionic strength was maintained constant at 0.1 mol L^{-1} in aqueous solution and 0.5 mol L^{-1} in H_2O-Me_2SO mixtures. Under these experimental conditions, the pK_a^{ArOH} values at the corresponding ionic strength were in each solvent obtained from the measured pH values of the buffers by mean of eq 11.

$$pK_a^{ArOH} = pH - \log \frac{[ArO^-]}{[ArOH]} \qquad (11)$$

Calibration of the cell used to obtain the pH measurements was carried out as previously described.[39]

Kinetic Measurements. Pseudo-first-order rate constants for the reaction of the phenoxide ions with *1* were determined spectrophotometrically following the appearance of the generated 4-nitrophenoxide ion ($4NPO^-$) at its absorption maximum in each solvent (410−425 nm). The reactions were carried out at 25 °C with use of phenoxide buffers, varying the concentration of the phenoxide base between 0.001 and 0.01 mol L^{-1} at constant pH. The concentration of *1* was always $\leq 5.10^{-5}$ mol L^{-1} and the ionic strength maintained constant at 0.1 mol L^{-1} in aqueous solution and 0.5 mol L^{-1} in H_2O-Me_2SO mixtures. Usually at least six values of ArO^- were employed, and replicate values of k_{obsd} were determined to obtain the second-order rate constants from the linear k_{obsd} vs $[ArO^-]$ plots. As mentionned in the Results, some interference between the first and second substitution processes of *1* (eqs 3 and 5) was observed in the most basic buffers in 50 and 70% Me_2SO, but this interference was never appreciable before at least 50 or 60% completion of the first substitution. Accordingly, the k_{obsd} values for reactions (3) were readily obtained by recording the changes in absorbance at $\lambda_{max}^{4\text{-}NPO}$ as a function of time up to 50% of the release of the first mole of *p*-nitrophenoxide ion. Similarly, the k_{obsd} values for reactions (5) were readily determined by recording absorbance changes after displacement of ≥ 1.3 mol of $4\text{-}NPO^-$. In these instances, the infinity

---

(36) Jencks, W. P. In *Catalysis in Chemistry and enzymology*; McGraw Hill: New York, 1968; p 178.

(37) (a) Bell, R. P. In *The proton in Chemistry*, 2nd ed.; Cornwell University Press: Thaco, 1973; Chapter 10. (b) Bell, R. P.; Trotman-Dickerson, A. F. *J. Chem. Soc.* **1949**, 1288.

(38) (a) Ritchie, C. D. In *Solute−Solvent Interactions*; Coetzee, J. F., Ritchie, C. D., Eds.; Dekker: New York, 1966; p 216. (b) Parker, A. *J. Chem. Rev.* **1969**, *69*, 1.

(39) (a) Hallé, J. C.; Gaboriaud, R.; Schaal, R. *Bull. Soc. Chim. Fr.* **1970**, 2047. (b) Sorkhabi, H. A.; Hallé, J. C. Terrier, F. *J. Chem. Res., Synop.* **1978**, 196.

(40) Chantooni, M. K., Jr.; Kolthoff, I. M. *J. Phys. Chem.* **1976**, *80*, 1306.

(41) Bordwell, F. G.; McCallum, R. J.; Olmstead, W. N. *J. Org. Chem.* **1984**, *49*, 1424.

(42) Laloi-Diard, M.; Verchère, J. F.; Gosselin, P.; Terrier, F. *Tetrahedron Lett.* **1984**, *25*, 1267.

(43) Kolthoff, I. M.; Chantooni, M. K., Jr.; Blowmick, S. *J. Am. Chem. Soc.* **1976**, *90*, 23.

(44) Farrell, P. G.; Terrier, F.; Schaal, R. *Tetrahedron Lett.* **1985**, *26*, 2435.

(45) Belskii, V. E.; Kudryavtsva, L. A.; Ilina, D. M.; Ivanov, B. E. *Zh. Obsh. Khim.* **1979**, 49, 2470 and references therein.

(46) Loran, J. S.; Naylor, R. A.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1977**, 418.

absorbance measured after complete release of $4NPO^-$ in monosubstitution processes was used as the reference to work out the spectrophotometric data.

Product analysis was carried out for some reactions of phenols with *1*. A solution of *1* (0.640 g in 10 mL of acetonitrile) was added during 3 h at −80 °C to a mixture of 1 equiv of *p*-chlorophenol and 1 equiv of butyllithium in 8 mL of acetonitrile. The resulting reaction mixture was then allowed to slowly warm to room temperature and then extracted with dichloromethane (25 mL). The solution was then dried and evaporated under vacuum to give 0.353 g of an oil. This oil was shown to contain a mixture of the monosubstituted ($\geq 80\%$) and disubstituted ($\leq 20\%$) products **2-X** and **4-X** by comparison of its TLC and NMR spectra with those of authentic samples of the products. Although it proved impossible to obtain quantitative product analysis data under conditions approximating those of the kinetic experiments, the formation of **2-X** and **4-X** at the preparative scale leaves no doubt that our kinetic studies deal with reactions (3) and (5) in aqueous as well as aqueous Me_2SO mixtures.

JO9418487