Origin of the Bell-Shaped α-Effect—Solvent Composition Plots. pKa—Solvent Dependence of the α-Effect at a Phosphorus Center

Richard M. Tarkka and Erwin Buncel*

Contribution from the Department of Chemistry, Queen's University, Kingston, Canada K7L 3N6

Received June 16, 1994[⊗]

Abstract: The rates of reaction of the "α" nucleophile, 2,3-butanedione monoximate (Ox⁻), and the "normal" nucleophile, 4-chlorophenoxide (4-ClPhO⁻), with the phosphorus ester, *p*-nitrophenyl diphenylphosphinate (PNPDPP), were measured in DMSO—H_2O mixtures at 25.0 °C. Addition of small quantities of DMSO (up to *ca.* 10 mol %) to the aqueous solvent led to a decrease in the second-order rate constants of reaction for both nucleophiles. Additional increases in the DMSO content above 20 mol % resulted in smooth and regular increases in the rate for 4-ClPhO⁻, but for Ox⁻ the corresponding increase in reaction rate upon increase of DMSO content is not linear, being best described as either curved or composed of two intersecting linear portions in the log *k* vs mole percent DMSO plot. The magnitude of the α-effect, $k_{Ox^-}/k_{4\text{-}ClPhO^-}$, shows a bell-shaped dependence on solvent composition, with a maximum value of *ca.* 40 at *ca.* 50 mol % DMSO. The data is analyzed in terms of the recently developed novel procedure for Brønsted-type plots, in which changes in basicity and reactivity of the nucleophile are brought about through changes in solvent composition rather than changes of remote substituent. This analysis suggests that the bell-shaped dependence of the α-effect magnitude upon solvent composition may stem from the effect of advanced desolvation of the Ox⁻ nucleophile at the transition state relative to bond formation, i.e., imbalance or nonperfect synchronization effects.
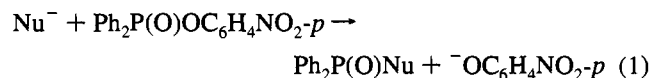
Introduction

Nucleophiles which bear nonbonding pairs of electrons at the position α to the nucleophilic center are called α-nucleophiles and characteristically deviate upwardly on Brønsted-type plots; i.e., the reactivity is greater than would be expected on the basis of the pKa values.[1] Typical α-nucleophiles include peroxides, hydroxamates, and hydrazines. The unusually high reactivity of α-nucleophiles was first described in 1947,[2] although it was not until 1962 that Edwards and Pearson[3] first characterized and named the α-effect. Since then, significant efforts have been made to account for the source of the α-effect, though a clear explanation of this phenomenon is not apparent even today.[1]

The relative reduction in the free energy of activation ($\Delta G^{\ddagger}$) for reaction of α-nucleophiles relative to normal nucleophiles arises from some combination of ground state (GS) destabilization and transition state (TS) stabilization.[4] Factors which have been postulated to account for these changes in the relative energies of the GS and TS include lone pair—lone pair repulsion in the α-nucleophile, enhanced stability of the α-product,[5] and solvent effects, to name just a few. Evidence which points to solvent effects being responsible for the α-effect includes gas phase experiments by DePuy[6a] and *ab initio* calculations by Jorgensen[6b] and Wolfe.[6c]

We recently showed[7] that the magnitude of the α-effect for the reaction of *p*-nitrophenyl acetate (PNPA) with *p*-chlorophenoxide anion (4-ClPhO⁻, pKa = 9.35) and 2,3-butanedione monoximate anion (Ox⁻, pKa = 9.44) as the normal and α-nucleophiles, respectively, is very sensitive to the quantity of DMSO in the binary DMSO—H_2O solvent.[7] The magnitude of the α-effect, $k_{Ox^-}/k_{4\text{-}ClPhO^-}$, showed a bell-shaped dependence on solvent composition, with values ranging from *ca.* 90 in 10 and 90 mol % DMSO to a maximum of almost 300 in 50 mol % DMSO. On the other hand, Moss[8] reported that using the α-nucleophile *o*-iodosylbenzoate (pKa = 7.1 in H_2O) did not lead to a bell-shaped α-effect for reaction with PNPA in DMSO—H_2O mixtures at 25.0 °C when compared to 4-ClPhO⁻, but instead the α-effect magnitude decreased steadily. However, in the absence of information on the variation of pKa with mole percent of DMSO for *o*-iodosylbenzoate, it is difficult to draw conclusions as to the generality of this finding.[8]

In the present work we have extended our studies of the effect of solvent on the magnitude of the α-effect for nucleophiles Ox⁻ and 4-ClPhO⁻ with the phosphinate ester, *p*-nitrophenyl diphenylphosphinate (PNPDPP) (eq 1). The second-order rates

$$Nu^- + Ph_2P(O)OC_6H_4NO_2\text{-}p \longrightarrow$$

$$Ph_2P(O)Nu + {}^-OC_6H_4NO_2\text{-}p \quad (1)$$

$$Nu^- = 4\text{-ClPhO}^- \text{ or } Ox^-$$

of reaction were measured in DMSO—H_2O mixtures at 25.0 °C using the usual pseudo-first-order kinetic technique.

⊗ Abstract published in *Advance ACS Abstracts*, January 15, 1995.
(1) Hoz, S.; Buncel, E. *Isr. J. Chem.* **1985**, *26*, 313.
(2) Fina, N. J.; Edwards, J. O. *Int. J. Chem. Kinet.* **1973**, *5*, 1.
(3) Edwards, J. O.; Pearson, R. G. *J. Am. Chem. Soc.* **1962**, *84*, 16.
(4) (a) Buncel, E.; Wilson, H. *Acc. Chem. Res.* **1979**, *12*, 42. (b) Buncel, E.; Wilson, H. *J. Chem. Educ.* **1987**, *64*, 475.
(5) (a) Herschlag, D.; Jencks, W. P. *J. Am. Chem. Soc.* **1990**, *112*, 1951. (b) Dixon, J. E.; Bruice, T. C. *J. Am. Chem. Soc.* **1971**, *93*, 3248, 6592. (c) Buncel, E.; Chuaqui, C.; Wilson, H. *J. Org. Chem.* **1980**, *45*, 3621. (d) Buncel, E.; Wilson, H.; Chuaqui, C. *J. Am. Chem. Soc.* **1982**, *104*, 4896. (e) Hoz, S.; Buncel, E. *Tetrahedron Lett.* **1984**, *25*, 3411. (f) Laloi-Diard, M.; Verchere, J. F.; Gosselin, P.; Terrier, F. *Tetrahedron Lett.* **1984**, *25*, 1267.

(6) (a) DePuy, C. H.; Della, E. W.; Filley, J.; Grabowski, J. J.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1983**, *105*, 2481. (b) Evanseck, J. D.; Blake, J. F.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1987**, *109*, 2349. (c) Wolfe, S.; Mitchell, D. J.; Schlegel, H. B.; Minot, C.; Eisenstein, O. *Tetrahedron Lett.* **1982**, *23*, 615.
(7) Buncel, E.; Um, I. H. *J. Chem. Soc., Chem. Commun.* **1986**, 595.
(8) Moss, R. A.; Swarup, S.; Ganguli, S. *J. Chem. Soc., Chem. Commun.* **1987**, 860.

Table 1. Dependence upon Solvent Composition of the Second-Order Rates of Reaction of 4-ClPhO$^-$ and Ox$^-$ with PNPDPP at 25.0 °C and the Magnitude of the α-Effect

mol % DMSO	pK_a Ox$^-$	k_{Ox^-} (M^{-1} s^{-1})	pK_a 4-ClPhO$^-$	$k_{4\text{-}ClPhO^-}$ (M^{-1} s^{-1})	α-effect ($k_{Ox^-}/k_{4\text{-}ClPhO^-}$)
2.5	9.56	5.03	9.47	0.341	14.7
10	10.04	4.56	9.94	0.236	19.3
20	10.68	8.40	10.58	0.303	27.7
30	11.33	23.9	11.21	0.726	32.9
40	12.06	70.9	11.93	1.81	39.2
50	12.86	194.8	12.73	4.89	39.8
60	13.69	367	13.54	11.89	30.9
70	14.51	709	14.34	30.2	23.5
80	15.32	1640	15.14	78.9	20.7
90	16.14	3390	15.95	235	13.8

Our recently developed methodology for Brønsted-type LFERs is employed to analyze the data.[9-11] The principle of nonperfect synchronization (PNS)[12] provides important clues toward explanation of the bell-shaped dependence of the α-effect magnitude on solvent composition observed in this system.

Results

The pseudo-first-order rates of reaction of the α-nucleophile, 2,3-butanedione monoximate (Ox$^-$), and the reference nucleophile, 4-chlorophenoxide (4-ClPhO$^-$), with the phosphinate ester, *p*-nitrophenyl diphenylphosphinate (PNPDPP), were measured spectrophotometrically in various DMSO—H$_2$O mixtures at 25.0 °C by following the appearance of the *p*-nitrophenoxide ion leaving group. Excellent first-order kinetics were obtained with the nucleophile concentration in large excess. Second-order rate constants were calculated from the slopes of plots of *k* vs [Nu]; results for the various solvent compositions are presented in Table 1. The pseudo-first-order rate constants and the corresponding regression analysis used to obtain the second-order rate constants and the intercepts are presented as supplementary data in Tables 1—20 in the supplementary material. The pK_a values of *p*-chlorophenol and 2,3-butanedione monoxime as functions of solvent composition are also given in Table 1.[5f,13]

Discussion

1. Solvent Behavior of the α-Effect. It is seen from the data in Table 1 and Figure 1 that the reaction rates exhibit a marked though nonuniform dependence on solvent composition. For both nucleophiles, there is an initial decrease in rate with a shallow minimum occurring at 10 mol % DMSO, while the rate increases from 20 to 90 mol % DMSO, the limit of the present measurements. The overall solvent rate-enhancing effect is about 10^3 for both nucleophiles. Importantly, the α-nucleophile, Ox$^-$, is more reactive than the normal nucleophile, 4-ClPhO$^-$, by a factor of *ca.* 15—40 depending on the solvent composition, with the rate enhancement having a maximum value in *ca.* 50 mol % DMSO.

A number of studies have observed nonuniform behavior of reaction rates in DMSO—H$_2$O mixtures, usually in the region of high H$_2$O content, and this has been attributed to specific
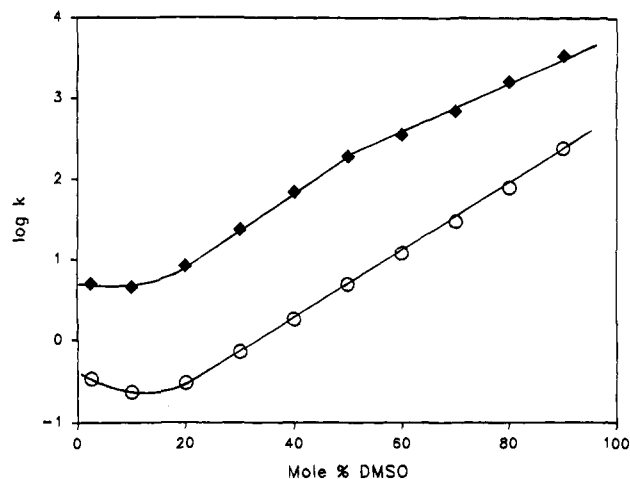
(9) Buncel, E.; Um, I. H.; Hoz, S. *J. Am. Chem. Soc.* **1989**, *111*, 971.
(10) Buncel, E.; Tarkka, R. M.; Hoz, S. *J. Chem. Soc., Chem. Commun.* **1993**, 109.
(11) Tarkka, R. M.; Park, W. K. C.; Liu, P.; Buncel, E.; Hoz, S. *J. Chem. Soc., Perkin Trans. 2* **1994**, 2439.
(12) (a) Bernasconi, C. F. In *Nucleophilicity*; Harris, J. M., McManus, S. P., Eds.; Advances in Chemistry 215; American Chemical Society: Washington, DC, 1987; p 115. (b) Bernasconi, C. F. *Adv. Phys. Org. Chem.* **1992**, *27*, 119. (c) Bernasconi, C. F. *Acc. Chem. Res.* **1987**, *20*, 301.
(13) (a) Sorkhabi, H. A.; Halle, J. C.; Terrier, F. *J. Chem. Res., Synop.* **1978**, 196. (b) Tarkka, R.; Buncel, E. To be published.

Figure 1. Plot of log *k* vs mole percent DMSO for the reaction of 2,3-butanedione monoximate (Ox$^-$, ◆) and 4-chlorophenoxide (4-ClPhO$^-$, O) with 4-nitrophenyl diphenylphosphinate (PNPDPP) at 25.0 °C.

solvent—solvent as well as solute—solvent interactions.[14] Hydrogen bonding between DMSO and H$_2$O is known to be strong, and evidence points to formation of 1:2 and 1:3 complexes between DMSO and water molecules. A number of physical properties of DMSO—water mixtures show extrema, including adiabatic compressibility[14d] and excess free energy of mixing,[14h] to name just a few. The solubility of dihydrogen exhibits a minimum at *ca.* 20% DMSO.[14g] Hydrophobic interactions induced by addition of small quantities of DMSO to water induce "rigidification" of hydrogen bonds between H$_2$O molecules.[14a] The "irregular" behavior of these solvent mixtures appears to vanish at higher DMSO concentrations. In view of this, our ensuing discussion will focus on the kinetic data obtained in media containing ≥20 mol % DMSO.

Examination of the plots of log *k* vs mole percent DMSO (Figure 1) shows that the 4-ClPhO$^-$ plot is linear in media containing ≥20 mol % DMSO, whereas the Ox$^-$ plot is best described as being either curved or, as shown, consisting of two intersecting linear portions. Between 20 and 50 mol % DMSO, the slope of the Ox$^-$ plot is steeper than that of the 4-ClPhO$^-$ plot, and the plots diverge as the DMSO content increases. This, of course, leads to a net increase in the magnitude of the α-effect, the $k_{Ox^-}/k_{4\text{-}ClPhO^-}$ ratio. At 50 mol % DMSO, the gap between the Ox$^-$ plot and the 4-ClPhO$^-$ plot is at a maximum, as is the magnitude of the α-effect. Between 60 and 90 mol % DMSO, the slope of the Ox$^-$ plot is smaller than that of the 4-ClPhO$^-$ plot and the plots head toward convergence. The magnitude of the α-effect thus decreases.

It is apparent that if each plot in Figure 1 were linear with identical slope, the magnitude of the α-effect would be independent of solvent composition. The nonlinearity of the Ox$^-$ plot in >20 mol % DMSO thus appears to lead to the bell-shaped α-effect plot obtained on plotting the ratio $k_{Ox^-}/k_{4\text{-}ClPhO^-}$ vs mole percent DMSO (Figure 2). This phenomenological account of the bell-shaped α-effect plot, however, cannot explain what *molecular*-level phenomena are responsible for the individual trends (linearity of the 4-ClPhO$^-$ plot vs nonlinearity of

(14) (a) Franks, F., Ed. *Water. A Comprehensive Treatise*; Plenum: New York, 1974; Vol. 4, pp 1—94. (b) Franks, F. *Water*; The Royal Society of Chemistry: London, 1983. (c) Rallo, F.; Rodante, R.; Silverstroni, P. *Thermochim. Acta* **1970**, *1*, 311. (d) Bowen, D. E.; Priesand, M. A.; Eastman, M. P. *J. Phys. Chem.* **1974**, *78*, 2611. (e) Vaisman, I. I.; Berkowitz, M. L. *J. Am. Chem. Soc.* **1992**, *114*, 7889. (f) Lindberg, J. J.; Kenttamaa, J. *Suom. Kemistil. B* **1960**, *33*, 104. (g) Symons, E. A. *Can. J. Chem.* **1971**, *24*, 3940. (h) Lam, S. Y.; Benoit, R. L. *Can. J. Chem.* **1974**, *52*, 718. (i) Buncel, E.; Wilson, H. *Adv. Phys. Org. Chem.* **1977**, *14*, 133.
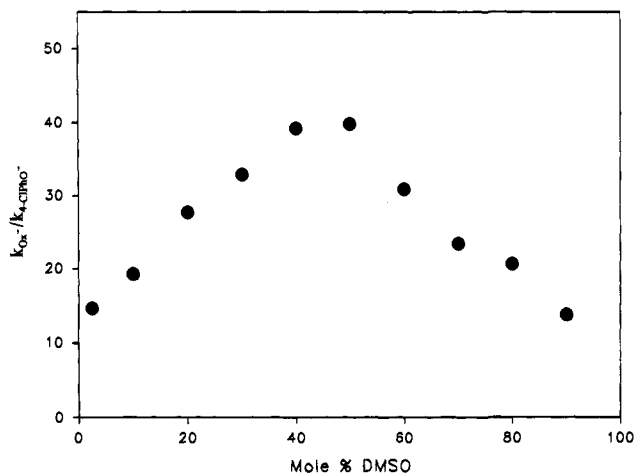
pKₐ—Solvent Dependence of the α*-Effect*

J. Am. Chem. Soc., Vol. 117, No. 5, 1995 1505

Figure 2. Plot of the magnitude of the α-effect ($k_{Ox^-}/k_{4\text{-}ClPhO^-}$) vs mole percent DMSO for reaction with PNPDPP at 25.0 °C.

the Ox⁻ plot), and a more in-depth analysis is required to explain the results. Possible reasons why the Ox⁻ plot is not linear while the 4-ClPhO⁻ plot is linear are discussed below.

2. Is a Change in Mechanism Responsible for the Bell-Shaped α-Effect? In a previous study[7] of the reaction of Ox⁻ and 4-ClPhO⁻ with *p*-nitrophenyl acetate (PNPA) in DMSO—H_2O mixtures, we observed a bell-shpaed dependence of the α-effect, similar to the present study with PNPDPP. However, the magnitude of the α-effect is 7-fold higher in the case of PNPA, ranging from *ca.* 90 in 10 and 90 mol % DMSO to *ca.* 300 in 50 mol % DMSO.

It is well established that the magnitude of the α-effect is dependent on the mechanism of reaction and on the hybridization state of the electrophilic center.[1] For example, S_N2 reactions at sp³ (tetrahedral) carbon centers exhibit α-effects that are 2—3 orders of magnitude smaller than corresponding α-effects at sp² carbon centers.[5d] It might thus be argued that the source of the large differences between the PNPA and PNPDPP α-effect magnitudes lies in a difference of mechanism. Williams[14a] showed that the reaction of phenoxide anions with PNPDPP is concerted, $S_N2(P)$, in aqueous media. Evidence for this claim was deduced from the linearity of a Brønsted-type plot for the reaction of PNPDPP with a series of substituted phenoxide nucleophiles whose pK_a values straddled that of the 4-NO_2PhO^- leaving group. A stepwise addition—elimination mechanism would have resulted in a "break" in the Brønsted-type plot with a discontinuity occurring at $pK_{nuc} = pK_{LG}$.

The mechanism of displacement of substituted phenoxide leaving groups by other substituted phenoxide nucleophiles from esters such as PNPA is still controversial. Results of an LFER study (Hammett plots)[9] are consistent with a stepwise addition—elimination mechanism for the reactions in DMSO—H_2O media. On the other hand, the Brønsted-type plot for the reaction of PNPA in H_2O with a series of substituted phenoxide nucleophiles whose pK_a values straddled that of the 4-NO_2PhO^- leaving group is again linear, suggesting that the reaction is concerted.[15b] Other results consistent with a concerted mechanism for PNPA include cross-interaction LFER plots,[16] isotope effects,[17] and consideration of Marcus effects,[18] though these studies do not extend to H_2O—DMSO media.

(15) (a) Bourne, N.; Chrystiuk, E.; Davis, A. M.; Williams, A. *J. Am. Chem. Soc.* **1988**, *110*, 1890. (b) Ba-Saif, S.; Luthra, A. K.; Williams, A. *J. Am. Chem. Soc.* **1987**, *109*, 6362.

(16) Stefanidis, D.; Cho, S.; Dhe-Paganon, S.; Jencks, W. P. *J. Am. Chem. Soc.* **1993**, *115*, 1650.

(17) Hengge, A., *J. Am. Chem. Soc.* **1992**, *114*, 6575.

(18) Guthrie, J. P. *J. Am. Chem. Soc.* **1991**, *113*, 3941.
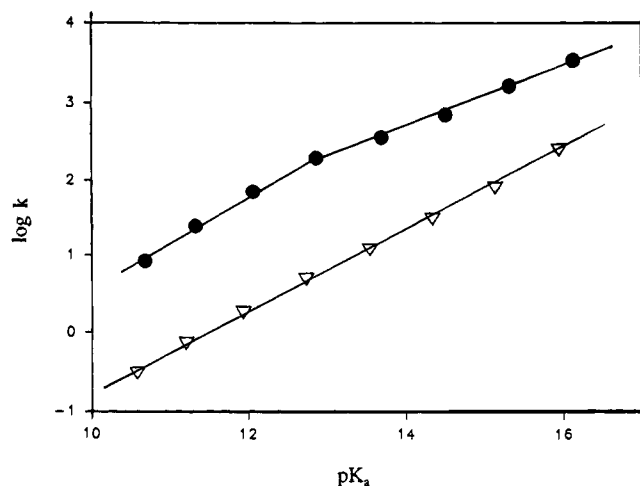
We showed in our previous study with PNPA, from a constancy in β_{nuc} as a function of DMSO—H_2O composition when using novel Brønsted-type plots, that the transition state of the PNPA—ArO⁻ reaction remained invariant with changing solvent composition.[9] However, application of this method to PNPDPP[10] gave quite different behavior *(vide infra)*. The uncertainty of the mechanism of displacement for PNPDPP and PNPA as a function of solvent composition makes any analysis of α-effect magnitudes in terms of changing reaction mechanisms inconclusive.

3. Nonlinear Brønsted Plots and the α-Effect. A new methodology for constructing Brønsted-type plots was developed recently. The pK_a values of Brønsted acids, specifically phenols, increase in a regular manner as DMSO is added to DMSO—H_2O mixtures.[5f,12] In fact, the pK_a values are essentially a linear function of mole percent DMSO. This suggested that it would be possible to plot log *k* values vs pK_a(nucleophile) for the reaction of a *single* nucleophile with a given substrate, with variations in the pK_a and log *k* terms being brought about through changes in the solvent composition, as contrasted to traditional Brønsted-type plots in which basicity and nucleophilicity are varied through changes in remote substituent while solvent identity is maintained.[9] These novel Brønsted-type plots were constructed for the reaction of PNPA with phenoxide, 4-cyanophenoxide, 4-chlorophenoxide, and 4-methylphenoxide at 25.0 °C in 40, 50, 70, and 90 mol % DMSO. On a composite Brønsted-type plot of log *k* vs pK_a, all 16 data points fell on a single line and yielded a β_{nuc} value which was statistically more reliable than the values obtained from the four traditional Brønsted-type plots (one for each of the four solvent compositions). These traditional Brønsted-type plots were also linear but gave slightly varying β_{nuc} values (0.67—0.59) as the DMSO composition was increased.

On the other hand, it was recently found that, for the reaction of phenoxide anions with PNPDPP in DMSO—H_2O mixtures, the novel Brønsted-type plots (changing solvent, constant substituent) yielded quite different information compared to the traditional (constant solvent, varying substituent) Brønsted-type plots.[10] The traditional Brønsted-type log *k* vs pK_a plots are now nonlinear with the extent of curvature increasing with increasing DMSO content. However, construction of the novel Brønsted-type plots leads to an array of straight lines. Each nucleophile yields a linear Brønsted-type plot, with the slope of the plot decreasing as the basicity of the nucleophile increases.

We have now constructed the novel Brønsted-type plots for the reaction of Ox⁻ and 4-ClPhO⁻, excluding the data points that represent reactions in H_2O-rich solvent mixtures (<20 mol % DMSO) because of the aforementioned complications in these solvent systems. As seen in Figure 3, the 4-ClPhO⁻ plot is linear, with slope $\beta_{nuc} = 0.53$ ($r^2 = 0.999$), while the Ox⁻ plot is nonlinear. In a manner similar to the plot of log *k* vs mole percent DMSO (Figure 1), the gap between the two novel Brønsted-type plots (at a given pK_a value) increases with increasing pK_a values up to *ca.* $pK_a = 12.8$. The slope of the Ox⁻ plot is larger than that of 4-ClPhO⁻ as the plots diverge, and the magnitude of the α-effect increases until a maximum value of around 40 is reached at *ca.* $pK_a = 12.8$. As the pK_a of the nucleophile is increased further, the slope of the Ox⁻ plot becomes smaller than that of 4-ClPhO⁻, the gap between the plots decreases, and the magnitude of the α-effect decreases.

In the context of the definition of the α-effect being a positive deviation from the Brønsted-type plot (from reference nucleophiles),[1] the bell shape of the α-effect plot thus results from the bell-shaped gap between the two Brønsted-type plots. This is analogous to the result obtained by Terrier[19] for the reaction

Figure 3. Novel Brønsted-type plots of log k vs pK_a for the reaction of 2,3-butanedione monoximate (Ox⁻, ●) and 4-chlorophenoxide (4-ClPhO⁻, ▽) with 4-nitrophenyl diphenylphosphinate (PNPDPP) at 25.0 °C.

of PNPA in aqueous media with a series of substituted oximate anions relative to a series of substituted phenoxide anions. Brønsted-type plots constructed from the data set revealed two types of behavior. For the oximate set an initial linear portion was followed by a plateau for oximate nucleophiles with pK_a values ≥8. For the phenoxide series the plot was linear over the entire pK_a region studied (7.7—10.2). The α-effect, k_{Ox^-}/k_{ArO^-}, increased from 220 at pK_a 6.5 to 260 at pK_a 7.5 and then decreased steadily to 30 at pK_a 9.8. The steep decrease in the α-effect with increasing pK_a is the direct result of the plateau in the oximate curve.[19]

The present study has obtained a similar result through use of the novel Brønsted-type plots to the results obtained by Terrier,[19] who used traditional Brønsted-type plots. In both cases, a bell-shaped α-effect is obtained due to the differential nature of the Brønsted-type plots: the reference series of phenoxide nucleophiles give rise to plots that are linear in both studies, whereas the oximate series of α-nucleophiles yield nonlinear plots in both studies.

4. Role of Nonperfect Synchronization (Imbalance) in Desolvation. The requirement for desolvation of anions in nucleophilic bond formation with an electrophilic center has been a long-accepted dogma.[20,21] Jencks[22] ascribed curvature in Brønsted-type plots observed for carbonyl centers to the progressively more difficult desolvation of anions as their basicity increases and considered that this desolvation would occur ahead of bond formation, leading to TS "imbalance". More recently, the idea of imbalance has been quantified by Bernasconi[12] as the "principle of nonperfect synchronization (PNS)", which can be applied to the present system.[23]

Considering the effect on reaction rate of increasing the basicity of a nucleophile, an empirical quantification of the PNS is given by eq 2, where $\partial \log k_0$ is the decrease in reaction rate

$$\partial \log k_0 = (\alpha_{DES} - \beta_{nuc}^{norm}) \, \partial \log K_{DES} \qquad (2)$$

from the reference reaction induced by enhanced desolvation. The $\partial \log K_{DES}$ term represents the change in the equilibrium constant for desolvation of the nucleophile, while nucleophilic bond formation to the substrate is measured by β_{nuc}^{norm} and the extent of anion desolvation by α_{DES}. If a perturbation is made to the nucleophile and the extent of synchronicity between bond formation and nucleophile desolvation (the $\alpha_{DES} - \beta_{nuc}^{norm}$ term) remains constant, and if the $\partial \log K_{DES}$ term also remains constant, then the rate does not differ from that of the reference reaction. On the other hand, if the $(\alpha_{DES} - \beta_{nuc}^{norm})$ term increases in magnitude, the reaction rate will decrease.

The nonlinearity of the novel Brønsted-type plot for the reaction of Ox⁻ with PNPDPP finds explanation in terms of the PNS model as follows. The deviation in reaction rate (the $\partial \log k_0$ term in eq 2) from the reference reaction is nonlinear, which would arise if the $(\alpha_{DES} - \beta_{nuc}^{norm})$ term or the $\partial \log K_{DES}$ term or both terms were nonlinear functions of pK_a. In the case of nonlinear Brønsted-type plots it is concluded that the $(\alpha_{DES} - \beta_{nuc}^{norm})$ term is the source of the nonlinearity, specifically that the α_{DES} term varies while the β_{nuc}^{norm} term remains constant.[19] This would indicate that nonsynchronicity between bond formation and desolvation exists for reaction of the oximate, and *the extent of nonsynchronicity varies as the solvent composition is changed.* In other words, the ($\alpha_{DES} - \beta_{nuc}^{norm}$) term varies with changes in the solvent composition. In the case of the phenoxide anions, the $(\alpha_{DES} - \beta_{nuc}^{norm})$ term is constant (but not necessarily 0) for changes in solvent composition.[24]

It is suggested that the nonlinearity of the Brønsted-type plot for the reaction of Ox⁻ with PNPDPP in DMSO—H₂O mixtures may arise from variation in the desolvation term for Ox⁻. For the reference nucleophile the TS structure remains constant, leading to a linear Brønsted-type plot. The bell-shaped dependence on solvent composition of the α-effect magnitude hence originates from changes in the extent of desolvation at the TS for reaction of Ox⁻.

Terrier[19a,b] also accounted for his results by considering PNS effects. In his case, though, the extent of desolvation of the nucleophile increases as the basicity of the *substituted* oximate nucleophile increases. It appears, then, that not only the results but also the significance of PNS effects are common to this and Terrier's study. The contrast between these studies is that, while Terrier's study, based on traditional Brønsted-type plot analysis, requires use of a family of oximates and of aryloxides, the novel Brønsted-type plots in conjunction with solvent pK_a variation enable analogous conclusions to be reached with a single oximate and phenoxide.

In discussing the origin of the α-effect we have previously presented evidence that transition state stabilization is a more important factor than ground state destabilization.[5c,d] The Jencks-More—O'Ferrall diagram for reaction at an sp³ center signified a tight transition structure with bond formation more advanced than bond rupture in the case of the α-nucleophile as compared to the normal nucleophile which did not show this tightness. In the present study, i.e., nucleophilic reaction at a

(19) (a) Terrier, F.; Degorre, F.; Kiffer, D.; Laloi, M. *Bull. Soc. Chim. Fr.* **1988**, 415. (b) Terrier, F.; MacCormack, P.; Kizilian, E.; Halle, J. C.; Demerseman, P.; Guir, F.; Lion, C. *J. Chem. Soc., Perkin Trans. 2* **1991**, 153.

(20) Ritchie, C. D. *Can. J. Chem.* **1986**, *64*, 2239.

(21) Jencks, W. P. *Catalysis in Chemistry and Enzymology*; McGraw-Hill: New York, 1969.

(22) (a) Hupe, D. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 451. (b) Jencks, W. P.; Brant, S. R.; Gandler, J. R.; Fendrich, G.; Nakamura, C. *J. Am. Chem. Soc.* **1982**, *104*, 7045. (c) Jencks, W. P.; Haber, M. T.; Herschlag, D.; Nazaretian, K. L. *J. Am. Chem. Soc.* **1986**, *108*, 479.

(23) A similar argument can be based on the Kurz model: Kurz, J. L. *J. Am. Chem. Soc.* **1989**, *111*, 8631.

(24) A referee has pointed out that it is equally possible that variation in the $\partial \log K_{DES}$ term for the α-nucleophile could be the cause of the curvature. While this would be expected to hold in general, in the present case the similarities of the pK_a values (oximate vs p-chlorophenoxide) imply that the $\partial \log K_{DES}$ term is not the cause of this curvature. This term is dependent on the basicity, and if the basicity of the nucleophiles varies in a similar way, this term should also vary in a similar way in the DMSO—H₂O mixtures. This would imply that the $(\alpha_{DES} - \beta_{nuc}^{norm})$ term is responsible for the curvature. Nevertheless, we concur with the referee that one cannot conclude with certainty which of the terms is the cause of the nonlinearity.

phosphoryl center, a two-stage mechanism with rate-determining formation of a pentacoordinate intermediate and a one-step concerted mechanism are possible, but in the latter case it is highly probable that bond formation would be more advanced than bond rupture by analogy with the previous study.[5c,d] Taken together with the present analysis of the effect of solvent on the α-effect, it is clear that the TS structure for reaction of the α-nucleophile is very different from the TS structure for reaction of the normal nucleophile, in terms of the extent of *both* nucleophilic bond formation (β_{nuc}^{norm}) and anion desolvation (α_{DES}) at the TS. As such, the source of the α-effect appears to lie in variations in the entire ensemble of parameters used to describe TS structures rather than in a single parameter.

Experimental Section

Materials. *p*-Nitrophenyl diphenylphosphinate (PNPDPP) was prepared by the following modification of Williams's procedure.[15a] To a stirred solution of 2.8 mL of triethylamine (0.02 mol) and 2.8 g of *p*-nitrophenol (0.02 mol) in 25 mL of CH_2Cl_2 was added dropwise over the course of 20 min a solution of 4.8 g of diphenylphosphinic chloride (Aldrich, 0.02 mol) in 25 mL of CH_2Cl_2. The mixture was stirred at ambient temperature for 2 days, after which it was filtered to remove precipitated Et_3NHCl. The filtrate was washed with 0.1 M aqueous HCl (2 × 50 mL) and then distilled water until the washings were neutral. The CH_2Cl_2 solution was dried ($CaSO_4$) and concentrated under reduced pressure to give a crude product, which was recrystallized from ethanol. The product, uncorrected mp 149−150 °C, was characterized by IR and ¹H NMR.

The 4-ClPhOH and OxH (Aldrich) were recrystallized prior to use (from 30/60 petroleum ether and chloroform, respectively) and stored under argon in a glovebox. Doubly distilled deionized water was boiled and cooled under nitrogen prior to use. DMSO was refluxed over CaH_2 at reduced pressure (64−66 °C/6−7 mmHg) for 16 h and distilled, and the middle fraction was collected and stored under nitrogen. DMSO−water mixtures of various compositions were prepared by weight prior to use.

Preparation of Nucleophilic Stock Solutions. (a) Solvent Compositions with ≥40 mol % DMSO. Nucleophilic stock solutions of *ca.* 0.2 M were prepared in a 25.0 mL volumetric flask in a glovebox under an argon atmosphere by adding 2 equiv of the appropriate phenol to 1 equiv of $NMe_4OH\cdot5H_2O$. One equivalent each of the phenol and the corresponding phenoxide resulted, ensuring a self-buffering solution which inhibited attack by hydroxide ion on the substrate during the kinetic run. Six equivalents of H_2O was also formed, and hence the appropriate quantity of pure DMSO was added to the flask as a correction for this H_2O, after which the flask was filled to the mark with the appropriate freshly prepared DMSO−H_2O binary solvent.

(b) Solvent Composition with ≤40 mol % DMSO. A stock NaOH solution prepared by dissolving NaOH pellets (BDH) in doubly distilled deionized H_2O was standardized by titration against potassium hydrogen

phthalate using phenolphthalein as an indicator. A quantity of the conjugate acid of the nucleophile was added to a 25 mL volumetric flask so that addition of ¹/₂ equiv of the NaOH stock solution and the appropriate amount of compensating DMSO and dilution to mark with freshly prepared binary solvent resulted in a buffer solution of *ca.* 10^{-2} M.

Reactions were initiated by injecting with a syringe 5 μL of 0.02 M PNPDPP in dry dioxane into a 10 mm quartz UV cell containing 2.5 mL of solvent and an aliquot of the nucleophile stock solution. The cell was placed into the thermostated cell holder of the Perkin-Elmer Lambda 5 spectrophotometer for reactions with $t_{1/2}$ > 3 h or the Hewlett-Packard 8452A diode array spectrophotometer for reactions with $t_{1/2}$ < 3 h. The reactions were followed spectrophotometrically by monitoring the appearance of *p*-nitrophenoxide ion at the appropriate fixed wavelength (λ_{max} 400 nm in H_2O, 410 nm in 10% DMSO, 414 nm in 20% and 30% DMSO, 420 nm in 50% DMSO, 426 nm in 70% DMSO, and 432 nm in 90% DMSO). First-order (k_{obs}) rate constants were calculated from at least 20 points spanning 3 half-lives, the infinity value being taken after at least 10 half-lives. All reactions were carried out under pseudo-first-order conditions with the concentration of phenoxide ion in at least 25-fold excess over the substrate. The concentration of nucleophile ranged over (1−25) × 10^{-3} M while the substrate concentration was generally 2 × 10^{-5} M.

Rate constants (k_{obs}) from data obtained on the Perkin-Elmer spectrophotometer were derived using the standard linear least-squares method of obtaining the slope of a plot of $\ln(A_\infty - A_t)$ *vs* time, while those derived from the Hewlett-Packard spectrophotometer were obtained by a nonlinear least-squares fit to the experimental data. It is estimated from replicate runs that the error in any particular measured rate constant is not greater than ±3%. Second-order rate constants were obtained from the slope of a plot of k_{obs} *vs* nucleophile concentration, which had negligible intercepts, showing that the reaction with solvent did not occur to an appreciable extent. All plots of k_{obs} *vs* nucleophile concentration were satisfactorily linear. Homoconjugation effects, which would have led to downward curvature in the plots of k_{obs} *vs* nucleophile concentration, were not observed.

Supplementary Material Available: Pseudo-first-order rate constants for the normal and α-nucleophiles in DMSO−H_2O mixtures of different compositions (Tables 1−20) (7 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JA941900G