Medium effects on the α -effect in DMSO-H₂O mixtures — Comparative studies of *p*-nitrophenyl benzoate and acetate — Dissection of ground-state and transition-state effects

Ik-Hwan Um, Young-Hee Shin, Jeong-Yoon Han, and Erwin Buncel

Abstract: In a study of the origin of the α -effect and its dependence on the nature of the reaction medium as well as structural effects, we report herein a kinetic study of the reactions of *p*-nitrophenyl benzoate (PNPB) with butan-2,3-dione monoximate (Ox⁻, α -nucleophile) and *p*-chlorophenoxide (*p*-ClPhO⁻, the reference nucleophile) in dimethyl sulfoxide (DMSO)–H₂O mixtures of varying compositions at 25.0 ± 0.1 °C. The second-order rate constants (k_N) decrease modestly on addition of DMSO to the medium up to 10 mol% DMSO but increase significantly beyond that point for both nucleophiles. Ox⁻ is more reactive than *p*-ClPhO⁻ in all solvent mixtures studied (i.e., the α -effect). The α -effect increases as the DMSO content in the medium increases up to 40 mol% DMSO and then decreases beyond that point resulting in a bell-shaped α -effect profile. The bell-shaped α -effect profile obtained for the current reaction is similar to that found previously for the corresponding reaction of *p*-nitrophenyl acetate (PNPA), differing notably however, in the magnitude of the α -effect beyond 40 mol% DMSO. The PNPB/*p*-ClPhO⁻ reaction gains greater rate enhancement than the PNPA/*p*-ClPhO⁻ reaction in the DMSO-rich region, resulting in the smaller α -effect for PNPB beyond 40 mol% DMSO. It is proposed that the observed modulation of the α -effect by the solvent medium is explicable as a ground-state effect in the H₂O-rich region and a transition-state effect in the DMSO-rich region.

Key words: medium effect, the α -effect, ground state, transition state, solvation, desolvation.

Résumé : Dans le cadre d'une étude sur l'origine de l'effet α et de sa dépendance sur la nature du milieu réactionnel ainsi que des effets structuraux, on a réalisé une étude cinétique des réactions du benzoate de p-nitrophényle (BPNP) avec le monoximate de la butane-2,3-dione (Ox^- , α -nucléophile) et le *p*-chlorophénolate (*p*-ClPhO⁻, le nucléophile de référence), dans des mélanges de diméthylsulfoxyde (DMSO)-eau (H₂O) de compositions variables, à 25,0 ± 0,1 °C. Jusqu'à une concentration de 10 mole %, les constantes de vitesse du deuxième ordre (k_N) diminuent légèrement par addition de DMSO; au-delà de ce point, elles augmentent toutefois d'une façon significative pour les deux nucléophiles. Le nucléophile Ox⁻ est plus réactif que le p-ClPhO⁻ dans tous les mélanges de solvant étudiés, c'est-à-dire qu'il présente l'effet a. Jusqu'à une concentration de 40 mole % de DMSO, l'effet a augmente avec une augmentation de la concentration de DMSO; au-delà de ce point, il diminue ce qui conduit à un profil d'effet α qui est en forme de cloche. Le profil d'effet α en forme de cloche qui est obtenu pour cette réaction est semblable à celui qui a été observé antérieurement pour la réaction correspondante de l'acétate de p-nitrophényle (APNP); il diffère toutefois dans l'amplitude de l'effet α au-delà de la concentration de 40 mole % en DMSO. Dans la région riche en DMSO comportant plus de 40 mole % de DMSO, la réaction du BPNP-p-ClPhO- conduit à une augmentation beaucoup plus grande de la vitesse que celle observée pour la réaction du APNP-p-ClPhO⁻. On propose donc que la modulation observée de l'effet α par la nature du solvant (figure 2) peut être expliquée par un effet de l'état fondamental dans la région riche en eau et un effet de l'état de transition dans la région riche en DMSO.

Mots clés : effet de solvant, effet α , état fondamental, état de transition, solvatation, désolvatation.

[Traduit par la Rédaction]

Received 14 August 2006. Accepted 10 October 2006. Published on the NRC Research Press Web site at http://canjchem.nrc.ca on 16 November 2006.

I.-H. Um,¹ Y.-H. Shin, and J.-Y. Han. Division of Nano Sciences and Department of Chemistry, Ewha Womans University, Seoul 120–750, Korea.

E. Buncel.² Department of Chemistry, Queen's University, Kingston, ON K7L 3N6, Canada and Division of Nano Sciences and Department of Chemistry, Ewha Womans University, Seoul 120–750, Korea.

¹Corresponding author (e-mail: ihum@ewha.ac.kr). ²Corresponding author (e-mail: buncele@queensu.ca)



Nu⁻: Ox⁻ and *p*-ClPhO⁻ Solvent : 0, 10, 20, 30, 40, 50, 60, 70, 80, 90 mol % DMSO in H₂O

Introduction

Nucleophiles possessing one or more nonbonding electron pairs at the position α to the nucleophilic center exhibit enhanced reactivity compared with reference nucleophiles of similar basicity (the α -effect) (1). Various proposals have been advanced to account for the α -effect phenomenon, including destabilization of the ground state (GS) through electronic repulsion between nonbonding electron pairs, stabilization of product (thermodynamic α -effect), stabilization of the transition state (TS), a TS having aromatic or radicaloid character, as well as a solvent medium effect (1–11). However, up to this time there is no general agreement as to which factor(s) are predominant as the origin(s) of this phenomenon. Our studies have been largely directed toward elucidating the role of the solvent medium (7–10).

In the best known protic polar solvent, water, anionic nucleophiles are expected to be highly solvated through Hbonding (12, 13). Transfer to an aprotic polar solvent such as DMSO should result in loss of H-bonding, however, iondipole and polarizability interactions could become dominant (12, 13). The generally observed increased nucleophilic reactivity of small (hard) anions in DMSO with respect to water was first highlighted in studies by Parker (13). However, this effect may operate differentially when comparing two nucleophiles, as must be the case when considering the α -effect. Differential solvation could be exhibited in imbalanced transition states as well as in differences in ground state solvation and desolvation (14). To probe such differential effects, we have combined kinetic and thermodynamic studies for α -effect systems as a function of incremental modulation of the solvent medium from pure water to DMSO (7, 9).

The definition of the α -effect adopted recently is a positive deviation exhibited by an α -nucleophile from a Brønsted-type nucleophilicity plot (1*a*, 1*b*). According to this definition, the reference nucleophile is one which possesses the same basicity as the α -nucleophile but does not deviate from the Brønsted-type plot.

Some years ago, we performed nucleophilic substitution reactions of *p*-nitrophenyl acetate (PNPA) with butan-2,3dione monoximate (Ox⁻, α -nucleophile) and *p*-chlorophenoxide (*p*-ClPhO⁻, the reference nucleophile) in dimethyl sulfoxide (DMSO)–H₂O mixtures at 25.0 ± 0.1 °C (7*a*). The *pK*_a of the conjugate acids of the two nucleophiles has been reported to vary in a parallel manner in the DMSO–H₂O mixtures studied. Unexpectedly, we found that the α -effect increases as the DMSO content in the medium increases up to ca. 50 mol% DMSO and then decreases on further addition of DMSO, resulting in a bell-shaped α -effect profile (7*a*). Such a bell-shaped α -effect profile cannot be accounted for in terms of basicity changes with solvent variation and was also found for the corresponding reactions of substrates with different electrophilic centers (i.e., *p*-nitrophenyl diphenylphosphinate and benzenesulfonate) and with different leaving groups (i.e., substituted phenyl acetates) (7c-7e).

However, a contrasting result was reported by Moss et al. (11) for the reactions of PNPA with o-iodosylbenzoate as the α -effect nucleophile and *p*-ClPhO⁻ as reference nucleophile, i.e., the α -effect decreased steadily as the mol% DMSO was increased. Since the basicity of *o*-iodosylbenzoate was not determined in the DMSO-H₂O mixtures, one cannot exclude the possibility that the decreasing α -effect trend could be due to variation in pK_a for the conjugate acid of *o*-iodosylbenzoate with mol% DMSO. In fact, we have recently shown that variation of the basicity of the α -nucleophile is an important factor in determining the magnitude of the α effect in the reactions of PNPA with Ox⁻ and p-ClPhO⁻ in MeCN-H₂O mixtures (8). While the α -effect increases continuously as the mol% MeCN in the medium increases, Ox^- becomes more basic than p-ClPhO⁻ with increasing mol% MeCN in the medium. Accordingly, the increasing basicity difference between Ox⁻ and p-ClPhO⁻ was held responsible for the increasing α -effect in MeCN–H₂O mixtures (8).

There has been an upsurgence of interest in recent years in studies of solvent effects on reaction kinetics, equilibria, and chemistry more generally (12). For example, renewed interest has been engendered by studies into environmentally benign or "green" solvents including ionic solvents and supercritical water (15). Any practical use of such new media will require an in-depth examination of the physical organic chemistry of these systems. DMSO has emerged as the prototypical aprotic solvent of choice for a wide range of reactions (12, 13). One may cite a few landmark studies: those of Cram in the area of stereocontrol in isotopic H exchange and carbanion chemistry more generally (16), Cox and Stewart on the H_{_} basicity scale (17), and Parker (13) on nucleophilic reactivity, as well as the extensive investigations of Bordwell (18) into acidities in DMSO. Studies of mixed solvent systems have yielded a wealth of information on structure-reactivity relationships (19). In this context, we have focused on DMSO-H2O mixed media and more recently on MeCN-H₂O media (7-9).

As mentioned above, one key difference between H₂O and DMSO is the enhanced polarizability of the latter solvent, which may be expected to extend to DMSO-rich media as well. To test the significance of this factor we have extended our study to *p*-nitrophenyl benzoate (PNPB) as the substrate. Here, a change of a methyl in PNPA for a phenyl group in PNPB provides a test compound that should exhibit greater polarizability interactions with the DMSO solvent component. The reaction studied is that of PNPB with Ox⁻ and *p*-CIPhO⁻ anions (Scheme 1) as part of the α -effect phenomenon, as modulated by systematic change of mol% DMSO in DMSO-H₂O mixtures.

DMSO (mol%)	pK _a (OxH)	$k_{\text{Ox-}}$ ((mol/L) ⁻¹ s ⁻¹)	p <i>K</i> _a (<i>p</i> -ClPhOH)	$k_{p-\text{CIPhO}-}$ ((mol/L) ⁻¹ s ⁻¹)	α -effect $k_{Ox-}/k_{p-ClPhO-}$
0	9.44	22.5	9.38	0.255	88
10	10.04	20	9.94	0.144	139
20	10.68	34.2	10.58	0.185	185
30	11.33	75.7	11.21	0.347	218
40	12.06	186	11.93	0.814	229
50	12.86	455	12.73	2.21	206
60	13.69	1070	13.54	5.73	187
70	14.51	2360	14.34	15.5	152
80	15.32	5360	15.14	44.8	120
90	16.14	11700	15.95	162	72

Table 1. Summary of second-order rate constants for reactions of PNPB with Ox^- and *p*-ClPhO⁻ in various DMSO-H₂O mixtures at 25.0 ± 0.1 °C.

Note: The pK_a data were taken from ref. 7*b*.

Results

The kinetic study was performed spectrophotometrically under pseudo-first-order conditions with the nucleophile in excess. All the reactions in this study obeyed pseudo-firstorder kinetics and pseudo-first-order rate constants (k_{obsd}) were obtained from plots of ln $(A_{\infty}-A_t)$ vs. t, which were linear over 90% of the total reaction. Second-order rate constants (k_{Nu}) were determined from the slopes of the linear plots of k_{obsd} vs. the nucleophile concentration. These plots had only small intercept values, indicating that the contribution of hydroxide and (or) water to k_{obsd} is negligible (see Supplementary data for detailed kinetic data).³ It is estimated from replicate runs that the uncertainty in the rate constants is less than $\pm 3\%$. The $k_{\rm Nu}$ values determined are summarized in Table 1 for the reactions of PNPB with Oxand p-ClPhO⁻ in DMSO-H₂O mixtures of varying compositions.

Discussion

Effect of medium on reactivity

The rate data presented in Table 1 and exhibited in Fig. 1 show a nonuniform behaviour as the DMSO content of the medium is varied. Now, it is well-known that the properties of DMSO-H₂O mixtures exhibit anomalous behavior up to 33 mol% DMSO (7, 12, 20). This has been interpreted as resulting from rigidification of water–water H bonding induced by the addition of DMSO or the strong tendency of DMSO to form complexes with two water molecules (7, 12, 20). In the present system we have observed that the reactivity of *p*-ClPhO⁻ and Ox⁻ decreases modestly in the low DMSO region (<20 mol% DMSO) but increases significantly in the high DMSO region. This initial decline in reactivity is more significant for *p*-ClPhO⁻ than for Ox⁻.

Focusing on the high DMSO region, it is generally accepted that GS destabilization of anionic nucleophiles is responsible for the rate enhancement in this region relative to pure water (12, 13). Loss of H bonding in going to DMSO-rich media will effectively destabilize the anionic nucleo-

Fig. 1. Logarithmic plots of relative rate constants, $\log k^{(DMSO-H_2O)}/k^{(H_2O)}$, vs. mol% DMSO for reactions of PNPB

log $k^{(DMSO-H_2O)}/k^{(H_2O)}$, vs. mol% DMSO for reactions of PNPB (and PNPA in inset) with Ox⁻ (\bullet) and *p*-ClPhO⁻ (\bigcirc) at 25.0 ± 0.1 °C. The data for reactions of PNPA were taken from ref. 7*a*.



phile (see Introduction). This desolvation of the anion enhances reactivity. For *p*-ClPhO⁻ and Ox⁻, in fact, we have recently found through calorimetric measurements that these anions become desolvated to the extent of 10.2 and 13.2 kcal/mol (1 cal = 4.184 J), respectively, as the medium is changed from pure water to 90 mol% DMSO (7*b*).

The effect of medium change on reactivity can be expressed as the ratio of the second-order rate constant in DMSO–H₂O mixtures over the corresponding rate constant in pure H₂O, i.e., $k^{(DMSO-H_2O)}/k^{(H_2O)}$. As shown in Fig. 1, this rate constant ratio decreases as the medium changes from H₂O to 10 mol% DMSO with both Ox⁻ and *p*-ClPhO⁻. Beyond 10 mol% DMSO the relative rate for Ox⁻ increases linearly as the mol% DMSO increases, while *p*-ClPhO⁻ exhibits slightly upward curvature resulting in a crossover.

³ Supplementary data for this article are available on the journal Web site (http://canjchem.nrc.ca) or may be purchased from the Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, ON K1A 0R6, Canada. DUD 5097. For more information on obtaining material refer to http://cisti-icist.nrc-cnrc.gc.ca/irm/unpub_e.shtml.

Fig. 2. Plots of the α -effect $(k_{Ox}-/k_{p-CIPhO}-)$ vs. mol% DMSO for reactions of PNPA with Ox⁻ and *p*-CIPhO⁻ (\bullet) and PNPB with Ox⁻ and *p*-CIPhO⁻ (\bigcirc) at 25.0 ± 0.1 °C. The data for reactions of PNPA were taken from ref. 7*a*.



Recalling that our calorimetric study has shown that Ox^- is more destabilized than *p*-ClPhO⁻ throughout the range of DMSO-H₂O mixtures studied, we conclude that destabilization of the anionic nucleophile GS cannot be solely responsible for the rate enhancement in the high DMSO region.

The bell-shaped α -effect

As shown in Table 1, Ox^- exhibits much larger k_N values than *p*-ClPhO⁻ for the reaction of PNPB in all the medium compositions investigated (i.e., the α -effect). Interestingly, as illustrated in Fig. 2 up to 40 mol% DMSO the magnitude of the α -effect ($k_{Ox-}/k_{p-ClPhO_-}$) increases as the DMSO content in the medium increases. Beyond that point there is a decrease in the α -effect, resulting in a bell-shaped α -effect profile. The bell-shaped α -effect profile found for PNPB is similar to that found previously for the comparable reactions of PNPA, differing notably however in the magnitude of the α -effect beyond 40 mol% DMSO; the PNPB system exhibits a much smaller α -effect than the PNPA system in this DMSO-rich region.

The origin of the bell-shaped α -effect

A further striking aspect of the α -effect plots in Fig. 2 is that up to 30 mol% DMSO the plots for PNPB and PNPA are virtually superimposable but diverge thereafter; the PNPB curve reaches a maximum at 40 mol% DMSO while the maximum for PNPA is found at 50 mol% DMSO. Also the α -effect maximum occurs at 230 for PNPB and at 285 for PNPA. While the advent of the maximum in the bell-shaped α -effect profile at a lower DMSO content with PNPB, relative to PNPA, is concordant with the higher polarizability associated with the change from Me to Ph, the different response of the two systems to medium change beyond 40 mol% DMSO bears further analysis.

Dissection of medium effect into GS and TS contributions

Studies of the relationship between the magnitude of the α -effect, Brønsted basicity, and medium effects have revealed a remarkable behaviour of oximate reactivity that is, however, still not fully understood (2, 21). Terrier et al. (2a)studied the reaction of PNPA with a series of pyridinium carbaldoximates in H₂O and found that the Brønsted-type plot is linear for reactions of low basic oximates ($pK_a < -8$), but levels off for more basic oximates $(pK_a \ge 8)$. In a study of reactions of PNPB with a series of acetophenone oximates in 20 and 90 mol% DMSO, we observed that in 20 mol% DMSO the Hammett plot is linear with $\rho = +0.20$, but in 90 mol% DMSO $\rho = -0.15$ (21). The positive ρ value obtained for the reactions in 20 mol% DMSO is striking since it corresponds to a decrease in reactivity of the oximate with a stronger base strengthening substituent. A similar result has recently been found by Terrier and coworkers (2b) for reactions of bis(p-nitrophenyl)phenylphosphonate with a series of oximates in H₂O. The Brønsted-type plot exhibited a negative β_{nuc} value in the region of $pK_a > \sim 9$, indicating that more basic oximates become less reactive.

We have recently reported (7b) from a calorimetric study that both Ox⁻ and p-ClPhO⁻ become desolvated on addition of DMSO to water and the former experiences higher desolvation than the latter. The difference in desolvation energy between Ox^- and p-ClPhO⁻ ($\Delta\Delta H_{sol}$) became large as the DMSO content in the medium increased up to 40 mol% DMSO and then remained nearly constant beyond that point. Thus, $\Delta\Delta H_{sol}$ increased from 0 to 0.6, 1.8, and 3.2 kcal/mol as the medium changes from pure water to 10, 20, and 40 mol% DMSO, in turn, but remained nearly constant on further addition of DMSO (7b). The increasing trend in $\Delta\Delta H_{sol}$ up to 40 mol% DMSO was found to parallel the increasing α -effect trend observed over that medium range, indicating that the difference in GS desolvation between Ox^- and p-ClPhO⁻ may be responsible for the increasing α -effect trend for the reactions of PNPA in this solvent region. However, since $\Delta\Delta H_{sol}$ remains constant beyond 40 mol% DMSO the GS effect cannot account for the decreasing α -effect trend in that medium range.

Previously, we introduced a methodology for the dissection of medium effects into GS and TS contributions (see also refs. 12, 13, 22, 23). Figure 3 shows a qualitative two-dimensional energy profile for a reaction carried out in two different media, H₂O and a DMSO–H₂O mixture. δG_{tr}^{T} can be evaluated from the measurable transfer free energies of reactants (δG_{tr}^{R}) and the kinetic activation parameters (δG_{tr}^{\ddagger}) as given by eq. [1].

$$[1] \qquad \delta \Delta G_{tr}^{\ddagger} = \delta G_{tr}^{T} - \delta G_{tr}^{R}$$

This methodology can be applied to enthalpy and entropy parameters as well. This allows the dissection of the effect of medium on the α -effect into GS and TS effects through the combination of the calorimetrically measured enthalpies of solution (ΔH_{sol}) and the kinetically determined activation parameters. For the reaction of PNPA with Ox⁻ and *p*-ClPhO⁻, we have found that in the DMSO-rich region the TS becomes more stabilized for *p*-ClPhO⁻ than for Ox⁻ resulting in a smaller α -effect (7*b*). Accordingly, differential solvation of the two TSs was proposed to be responsible for the de-



creasing α -effect trend for the reactions of PNPA beyond the break point of 40–50 mol% DMSO (7*b*). For the current PNPB system, one can also conclude that the origin of the increasing and decreasing α -effect trend found with medium change can be attributed to the same factors as for the PNPA system, i.e., dominant GS effect in the H₂O-rich region and TS effect in the DMSO-rich region, which demonstrates the generality of this methodology.

The effect of medium change on reactivity can be illustrated in a different way via Fig. 4, showing a plot of the logarithmic relative rate constants for the reactions of PNPA and PNPB with Ox^- and p-ClPhO⁻ vs. the transfer enthalpies from H₂O to DMSO-H₂O mixtures ($\Delta\Delta H_{tr}$) for the two nucleophiles (Table 2). $\Delta\Delta H_{tr}$ represents the extent of GS desolvation for Ox⁻ and p-ClPhO⁻ ions as the medium changes from H₂O to DMSO-H₂O mixtures (7b). Accordingly, if the GS effect were solely responsible for the relative rate constants one should have observed a linear correlation between $\Delta\Delta H_{\rm tr}$ and log $k^{\rm (DMSO-H_2O)}/k^{\rm (H_2O)}$. Contrariwise, Fig. 4 exhibits nonlinear correlations, i.e., the increase in the relative rate constant is small on changing $\Delta\Delta H_{tr}$ from 0 to 8 kcal/mol for *p*-ClPhO⁻ and from 0 to 11 kcal/mol for Ox⁻. However, for p-ClPhO⁻ the relative rate constant increases significantly as $\Delta\Delta H_{tr}$ changes from 8 to 10 kcal/mol while for Ox⁻ the change is from 11 to 13 kcal/mol. These results further emphasize that the GS effect is not solely responsible for the medium effect on reactivity but that a TS effect also contributes to the rate enhancement in the DMSO-rich region.

Notably in Fig. 4, the curved lines for the reactions of PNPA and PNPB with *p*-ClPhO⁻ cross over those for the corresponding reactions for Ox^- at $\Delta\Delta H_{tr} = 6-7$ kcal/mol. The points for the reactions of *p*-ClPhO⁻ lie below those for the reactions with Ox^- up to $\Delta\Delta H_{tr} = -6$ kcal/mol but exceed them beyond that point. Such a crossover indicates that in the DMSO-rich region the reactions with *p*-ClPhO⁻ attain almost the same rate enhancements as those with Ox^- but with smaller $\Delta\Delta H_{tr}$ values.

Interestingly, further scrutiny of Fig. 4 reveals that the points for the reactions of PNPA with Ox^{-} fall above

Fig. 4. Plots of log $k^{(DMSO-H2O)}/k^{(H2O)}$ vs. transfer enthalpies $(\Delta A H_{tr})$ for reactions of PNPA (\bigcirc) and PNPB (\bigcirc) with Ox⁻ and *p*-ClPhO⁻ at 25.0 ± 0.1 °C. The data for reaction of PNPA were taken from ref. 7*b*.



Table 2. Transfer enthalpies ($\Delta\Delta H_{tr}$, kcal/mol) from 0 to 90 mol% DMSO for single ions of *p*-ClPhO⁻ and Ox⁻ at 25.0 °C.

	$\Delta\Delta H_{\rm tr}$ (kcal/mol)		
DMSO (mol%)	p-ClPhO ⁻	Ox-	
0	0	0	
10	0.8	1.4	
20	3.3	5.1	
30	5.4	8.3	
40	6.7	9.9	
50	8.0	11.4	
60	8.6	11.9	
70	9.0	12.4	
80	9.5	12.7	
90	10.2	13.2	

Note: Data were taken from ref. 7b.

those for the reactions of PNPB with Ox^- throughout the whole $\Delta\Delta H_{tr}$ range. However, a contrasting result is shown for the reactions with *p*-ClPhO⁻, i.e., the points for the reactions of PNPA lie above those for the reactions of PNPB up to $\Delta\Delta H_{tr} = ~7$ kcal/mol, but are situated below beyond that point. This result indicates that the reactions of PNPB with *p*-ClPhO⁻ gain greater rate enhancement than the corresponding reactions of PNPA with the same $\Delta\Delta H_{tr}$ value in the DMSO-rich medium. The contrasting α -effect behaviour for the PNPB and PNPA systems, as exhibited in Fig. 2 for the DMSO-rich region, is therefore accounted for.

Conclusions

Through the combination of kinetic data with calorimetrically determined GS solvation of Ox^- and *p*-ClPhO⁻, which allowed dissection of the medium effect on TS and GS contributions, the present study leads to the following conclusions. (i) The bell-shaped α -effect profile obtained for the reaction of PNPB with Ox⁻ and p-ClPhO⁻ is similar to that previously found for the corresponding reaction with PNPA, differing notably however, in the magnitude of the α -effect beyond 40 mol% DMSO; the PNPB system exhibits a much smaller α -effect than the PNPA system in this DMSO-rich region. (ii) The dominant GS effect in the H₂O-rich region and TS effect in the DMSO-rich region are proposed to be responsible for the origin of the increasing and decreasing α effect trends, respectively. (iii) The effect of medium change on reactivity is more significant for the reaction with p-ClPhO⁻ than for that with Ox⁻ in DMSO-rich region. (*iv*) The reaction of PNPB with p-ClPhO⁻ gains greater rate enhancements than the corresponding reaction of PNPA in DMSO-rich region, which is responsible for the smaller α effect found for the reaction of PNPB beyond 40 mol% DMSO. (v) Concordant with the increased polarizability effected on going from PNPA to PNPB with the change Me \rightarrow Ph, is the advent of the maximum in the bell-shaped α -effect profile (Fig. 2) at a lower DMSO content with PNPB than with PNPA (40 vs. 50 mol% DMSO) and similarly the smaller magnitude of the α -effect (230 vs. 285).

Experimental section

Materials

PNPB was readily prepared from the reaction of benzoyl chloride with *p*-nitrophenol in the presence of triethyl amine in anhydrous ether. Butan-2,3-dione monoxime and phenols used are of the highest quality available and were recrystallized before use. DMSO was refluxed over calcium hydride, distilled, collecting the fraction of bp 64–66 °C (6–7 mm Hg, 1 mm Hg = 133.322 4 Pa) and stored under nitrogen. Doubly glass distilled water was further boiled and cooled under nitrogen just before use.

Kinetics

Kinetic studies were performed with a UV-vis spectrophotometer for slow reactions $(t_{1/2} \ge 10 \text{ s})$ and a stopped-flow spectrophotometer for fast reactions ($t_{1/2}$ < 10 s) with a constant temperature circulating bath at 25.0 \pm 0.1 °C. Typically, the reaction was initiated by adding 5 µL of ca. 0.02 mol/L of substrate solution in MeCN by 10 μL gastight syringe to a 10 mm quartz UV cell containing 2.50 mL of the thermostated reaction mixture made up of reaction medium and an aliquot of the nucleophile stock solution. The nucleophile stock solution of ca. 0.2 mol/L was prepared by dissolving 2 equiv. of oxime (or phenol) and 1 equiv. of standardized NaOH solution to make a self buffered solution. Generally, the nucleophile concentration was varied over the range, $1-100 \times 10^{-3}$ mol/L, while the substrate concentration was 4×10^{-5} mol/L. All the solutions were transferred by gastight syringes under nitrogen. The reactions were followed by monitoring the appearance of pnitrophenoxide ions at 410 nm.

Product analysis

p-Nitrophenoxide ion was liberated quantitatively and identified as one of the reaction products in the reactions of PNPB by comparison of the UV–vis spectra after comple-

tion of the reactions with those of the authentic samples under the same reaction conditions.

Acknowledgement

The authors are grateful for the financial support from Korea Science and Engineering Foundation (KOSEF-F01– 2005–000–10033–0) and Natural Sciences and Engineering Research Council of Canada (NSERC) (EB). Y.H. Kim is also grateful for the BK 21 Fellowship.

References

- For reviews see: (a) E. Buncel and I.H. Um. Tetrahedron, 60, 7801 (2004); (b) E. Buncel and S. Hoz. Isr. J. Chem. 26, 313 (1985); (c) A.P. Grekov and V.Y. Veselov. Usp. Khim. 47, 1200 (1978); (d) N.J. Fina and J.O. Edwards. Int. J. Chem. Kinet. 5, 1 (1973).
- (a) F. Terrier, E. Le Guevel, A.P. Chatrouse, G. Moutiers, and E. Buncel. Chem. Commun. (Cambridge), 600 (2003); (b) E. Buncel, C. Cannes, A.P. Chatrousse, and F. Terrier. J. Am. Chem. Soc. 124, 8766 (2002); (c) A.P. Moutiers, E. Le Guevel, L. Villien, and F. Terrier. J. Chem. Soc. Perkin Trans. 2, 7 (1997); (d) F. Terrier, G. Moutiers, L. Xiao, E. Le Guvel, and F. Guir. J. Org. Chem. 60, 1748 (1995); (e) F. Terrier, P. McCormack, E. Kizilian, J.C. Halle, P. Demerseman, F. Guir, and C. Lion. J. Chem. Soc. Perkin Trans. 2, 153 (1991); (f) G. Moutiers, E. Le Guevel, C. Cannes, F. Terrier, and E. Buncel. Eur. J. Org. Chem. 17, 3279 (2001).
- (a) C.F. Bernasconi and C. Murray. J. Am. Chem. Soc. 108, 5251 (1986); (b) C.F. Bernasconi and A. Leyes. J. Am. Chem. Soc. 117, 1703 (1995); (c) C.F. Bernasconi and M. Stronach. J. Org. Chem. 56, 1993 (1991); (d) D. Herschlag and W. P. Jencks. J. Am. Chem. Soc. 112, 1951 (1990); (e) D.J. Palling and W.P. Jencks. J. Am. Chem. Soc. 106, 4869 (1984); (f) H.J. Dixon, and T.C. Bruice. J. Am. Chem. Soc. 94, 2052 (1972); (g) H.J. Dixon and T.C. Bruice. J. Am. Chem. Soc. 93, 6592 (1971).
- (a) K.R. Fountain. J. Phys. Org. Chem. 18, 481 (2005);
 (b) K.R. Fountain, C.J. Felkerson, J.D. Driskell, and B.D. Lamp. J. Org. Chem. 68, 1810 (2003); (c) K.R. Fountain, D.B. Tad-y, T.W. Paul, and M.V. Golynskiy. J. Org. Chem. 64, 6547 (1999); (d) K.R. Fountain, and K.D. Patel. J. Org. Chem. 62, 4795 (1997).
- (a) Y. Ren and H. Yamataka. Org. Lett. 8, 119 (2006); (b) J.D. Evanseck, J.F. Blake, and W.L. Jorgensen. J. Am. Chem. Soc. 109, 2349 (1987); (c) S. Hoz and E. Buncel. Tetrahedron Lett. 25, 3411 (1984); (d) E. Buncel and S. Hoz. Tetrahedron Lett. 24, 4777 (1983); (e) S. Hoz. J. Org. Chem. 47, 3545 (1982).
- (a) C.H. DePuy, E.W. Della, J. Filley, J.J. Grabowski, and V.M. Bierbaum. J. Am. Chem. Soc. **105**, 2481 (1983); (b) S. Wolfe, D.J. Mitchell, and H.B. Schlegel. J. Am. Chem. Soc. **103**, 7694 (1981).
- (a) E. Buncel and I.H. Um. J. Chem. Soc. Chem. Commun. 595 (1986); (b) I.H. Um and E. Buncel. J. Org. Chem. 65, 577 (2000); (c) R.M. Tarkka and E. Buncel. J. Am. Chem. Soc. 117, 1503 (1995); (d) I.H. Um, J.Y. Hong, and E. Buncel. Chem. Commun. (Cambridge), 27 (2001); (e) I.H. Um, S.J. Hwang, and E. Buncel. J. Org. Chem. 71, 915 (2006).
- (a) I.H. Um, Y.M. Park, and E. Buncel. Chem. Commun. (Cambridge), 1917 (2000); (b) I.H. Um, E.J. Lee, and E. Buncel. J. Org. Chem. 66, 4859 (2001).
- 9. I.H. Um and E. Buncel. J. Am. Chem. Soc. 123, 11111 (2001).

- (a) I.H. Um, J.S. Lee, and S.M. Yuk. J. Org. Chem. 63, 9152 (1998); (b) I.H. Um, H.W. Lee, J.S. Lee, H.J. Moon, and D.S. Kwon. J. Org. Chem. 62, 5939 (1997).
- 11. R.A. Moss, S. Swarup, and S. Ganguli. J. Chem. Soc. Chem. Commun. 860 (1987).
- (a) E. Buncel, R. Stairs, and H. Wilson. The role of the solvent in chemical reactions. Oxford University Press, Oxford, UK. 2003. (b) E. Buncel and H. Wilson. Adv. Phys. Org. Chem. 14, 133 (1977); (c) E. Buncel and H. Wilson. Acc. Chem. Res. 12, 42 (1979).
- 13. A.J. Parker. Chem. Rev. 69, 1 (1969).
- 14. C.F. Bernasconi. Adv. Phys. Org. Chem. 27, 119 (1992).
- 15. (a) R.D. Rogers and K.R. Seddon. Ionic liquid IIIA: fundamentals, progress, challenges, and opportunities — Properties and structure. Adv. Chem. Ser. 901, American Chemical Society, Washington D.C. 2005; (b) R.D. Rogers and K.R. Seddon. Ionic liquid *IIIB*: fundamentals, progress, challenges, and opportunities-transformations and processes. Adv. Chem. Ser. 902, American Chemical Society, Washington D.C. 2005

- (a) D.J. Cram. Pure Appl. Chem. 7, 155 (1963); (b) E. Buncel and J.M. Dust. Carbanion chemistry. Structures and mechanisms. Oxford University Press-ACS, Oxford and Washington D.C. 2003.
- 17. R.A. Cox and R. Stewart. J. Am. Chem. Soc. 98, 488 (1976).
- 18. F.G. Bordwell. Acc. Chem. Res. 21, 456 (1988).
- (a) E. Grunwald and S. Winstein, J. Am. Chem. Soc. 70, 846 (1948); (b) T.W. Bentley and P.v.R. Schleyer, Adv. Phys. Org. Chem. 14, 1 (1977).
- (a) D.E. Bowen, M.A. Priesand, and M.P. Eastman. J. Phys. Chem. 78, 2611 (1974); (b) E.A. Symons. Can. J. Chem. 24, 3940 (1971), and refs. therein.
- 21. I.H. Um, S.J. Oh, and D.S. Kwon. Tetrahedron Lett. 36, 6903 (1995).
- 22. P. Harberfied, J. Friedman, and M.F. Pinkston. J. Am. Chem. Soc. **94**, 71 (1972).
- 23. C.D. Ritchie. *In* Solute-solvent interactions. *Edited by* J.F. Coetzee and C.D. Ritchie. Marcel Dekker, New York. 1969.