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Solvent-Independent Transition-State Structure for Acyl-Transfer Reactions. A Novel Strategy for Construction of a Brønsted Correlation

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Abstract: The effect of changing solvent (DMSO-water) composition on the rate of the acyl-transfer reaction, for substituted phenoxides reacting with *p*-nitrophenyl acetate and *p*-chlorophenoxide reacting with substituted phenyl acetates, has been studied. A correlation of log k with σ° in preference to σ^-, for leaving group substituent changes, supports a reaction pathway involving a tetrahedral intermediate, contrary to recent proposals of a concerted mechanism. The results are further analyzed by means of two kinds of Brønsted type correlations: the traditional method (A), where the pK_a of the nucleophile is changed via substituent changes, and a novel method (B), where the change in pK_a is brought about by changes in the reaction medium, in this case by changing the DMSO-water composition. Method B was found to be applicable only over the range of 40-90 mol % DMSO in water where the physical properties of the media do not show any abrupt changes. It is shown that application of method A, which leads to the conclusion (via β_{nuc} values) that the transition-state structure changes with changing solvent composition (in accord with the RSP and Hammond's postulate), is inconsistent with the conclusion of a constant transition-state structure based on application of method B. The latter is shown to be the more reliable by independent criteria. It is proposed that this novel strategy for construction of Brønsted type plots could be applied to other reactions and different solvent systems.

Deciphering transition-state (TS) structure in a chemical reaction has been and still is a major goal in mechanistic chemistry. Only recently a method that enables a direct spectroscopic observation of transition states was devised.[1] However, for many years and for most reactions still today, TS structures are only indirectly inferred. The common and probably the most popular probes for the determination of TS structure are linear free energy relationships (LFERs) of various kinds.[2] The last decade, however, has seen many papers questioning the validity of the traditional interpretation of linear free energy relationships,[3] namely, whether the slopes of these correlations could be directly correlated with structural parameters and charge densities of the transition state.

As evidenced from the enormous amount of data compiled over the years and regardless of the different points of view adopted by researchers belonging to the different schools, it is clear that the linearity observed in these correlations is not merely fortuitous. Moreover, and regardless of the ways of interpretation, it is obvious that the slopes of these correlations convey important information regarding the transition state.

Among LFERs, one of the most important correlations is a variation of the original Brønsted equation[4] in which log k represents nucleophilic attack rather than proton-transfer reaction (eq 1).[5] This correlation has been widely employed in studies

$$\log k = \beta_{nuc} pK_a + C \qquad (1)$$

of nucleophilic reactions, especially in reactions of biological importance such as transesterification and transamidation reactions.[6] The usual and, up to now, probably the only way by which the pK_a of the nucleophile was varied for the purpose of construction of Brønsted type plots was by varying substituents on the nucleophile at a position remote from the attacking atom. This paper focuses on a new strategy for the construction of Brønsted type correlations and its chemical implications. For the sake of simplicity we have chosen to analyze the data in the traditional way, that is, to assume that the slope (β_{nuc}) of Brønsted type plots can be interpreted as the degree of bond formation at the transition state.[5,6]

Table I. Summary of Second-Order Rate Constants for the Reaction of *p*-Chlorophenoxide Ion with Substituted Phenyl Acetates [$CH_3C(O)OC_6H_4Y$] in DMSO-H_2O Mixtures at 25.0 °C

	k, M^{-1} s^{-1}				
DMSO, mol %	4-NO_2	3-NO_2	4-CHO	3-CHO	4-$COCH_3$
0	0.685	0.320	0.302	0.091	0.171
10	0.653	0.230	0.224	0.050	0.127
20	0.760	0.241	0.232	0.038	0.117
40	2.80	0.562	0.465	0.052	0.191
50	5.90	1.09	0.922	0.085	0.353
70	34.7	4.88	4.72	0.312	1.47
90	335	38.8	36.4	1.97	10.3

Table II. Summary of Second-Order Rate Constants for the Reaction of Substituted Phenoxides ($XC_6H_4O^-$) with *p*-Nitrophenyl Acetate in DMSO-H_2O Mixtures at 25.0 °C

	k, M^{-1} s^{-1}			
DMSO, mol %	4-CN	4-Cl	H	4-CH_3
0	0.030	0.685	1.13	2.13
10	0.019	0.653	1.29	2.33
20	0.021	0.761	1.82	3.85
40	0.062	2.80	8.02	18.2
50	0.120	5.90	19.0	40.5
70	0.462	34.7	108	257
90	2.87	334	1210	2620

Results

Reactions of the phenoxides with the aryl acetates in DMSO-water mixtures were studied spectrophotometrically by following the appearance of the absorption due to the generated aryl oxide ion. The reactions were conducted under pseudo-first-order conditions with the phenoxide concentration in excess of the aryl acetate. An equivalent amount of the free phenol was added in

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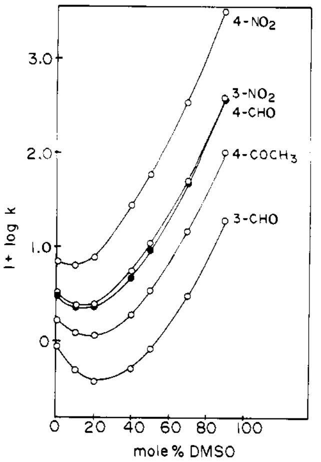

Figure 1. Plot showing dependence of log k on solvent composition for the reaction of *p*-chlorophenoxide ion with substituted phenyl acetates $CH_3C(O)OC_6H_4Y$.

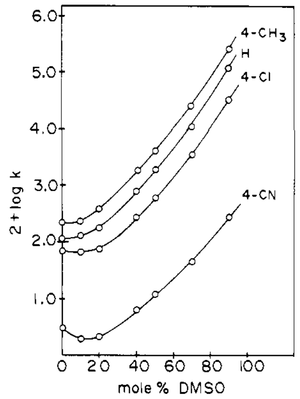

Figure 2. Plot showing dependence of log k on solvent composition for the reaction of substituted phenoxides ($XC_6H_4O^-$) with *p*-nitrophenyl acetate.

order to suppress formation of hydroxide ion by solvolysis. Pseudo-first-order rate constants were obtained from plots of ln $(A_\infty - A_t)$ vs t, which were linear over ca. 90% reaction. Second-order rate constants were obtained from the slopes of the linear plots of k_{obsd} vs the phenoxide concentration. These plots had only small intercept values indicating that the contribution of hydroxide ion and/or water to the rate was negligible.

In Table I are presented the second-order rate constants at 25 °C for the reactions of *p*-chlorophenoxide ion with the series of substituted phenyl acetates in media of various DMSO-water compositions. The corresponding data for reactions of substituted phenoxides with *p*-nitrophenyl acetate are given in Table II. The data are shown graphically in Figures 1 and 2.

For the construction of Brønsted type log k vs pK_a(NuH) plots, the required pK_a values of the phenols as a function of DMSO-water composition were obtained by interpolation of literature pK_a data at specific solvent compositions. These data were available for 4-chloro- and 4-cyanophenol, as well as for the unsubstituted phenol itself.[7a] For 4-methylphenol, only the pK_a values in 0 and 100% DMSO are known,[7a] but since the other pK_a-mole percent DMSO curves are smooth functions showing no extrema, a parallel curve was constructed for 4-methylphenol from which the relevant pK_a values were obtained. In the absence of σ^- values for some of the phenols, these pK_a values were plotted directly versus their pK_a values in water (plots not shown) and were found to give a very good correlation (correlation coefficients ranging between 0.9967 and 0.9985). The resulting pK_a values for the four phenols at various DMSO–water compositions are given in Table III. The error introduced in the determination of the pK_a values by the interpolation procedure is estimated to be smaller than 0.1 pK_a unit, which can be considered negligible for purposes of the present discussion.

Table III. pK_a Values of Phenols (XC_6H_4OH, Table II) in DMSO–H_2O Mixtures at 25.0 °C

	pK_a			
DMSO, mol %	4-CN	4-Cl	H	4-CH_3
0	7.73[a]	9.35[b]	9.95[f]	10.07[e]
10	8.1	9.9	10.6	10.9
20	8.6	10.5	11.3	11.7
40	9.6	11.8	12.8	13.2
50	10.1	12.5	13.5	14.0
70	11.0	13.8	15.0	15.5
90	12.2	15.3	16.6	17.2
100	13.1[c]	16.74[d]	18.03[d]	18.86[d]

[a] Reference 7e. [b] Reference 7a. [c] Reference 7d. [d] Reference 7c. [e] Reference 7b. [f] Reference 7f.

Table IV. Hammett ρ Values for the Reaction of *p*-Chlorophenoxide with Substituted Phenyl Acetates in DMSO–H_2O Mixtures at 25.0 °C [using the σ° (ρ°) and σ^- (ρ^-) Substituent Constants and the Normalized (ρ_n^0) Values Relative to Substituted Benzoic Acids (ρ_{ArCO_2H})]

DMSO, mol %	ρ°	ρ^-	ρ_{ArCO_2H}[b]	ρ_n°
0	1.62 (0.925)[a]	0.781 (0.849)[a]	1.00	1.62
10	1.96 (0.910)	1.00 (0.882)	1.14	1.72
20	2.31 (0.913)	1.17 (0.878)	1.30	1.77
40	3.15 (0.929)	1.53 (0.857)	1.60	1.97
50	3.37 (0.932)	1.63 (0.861)	1.75	1.93
70	3.66 (0.914)	1.84 (0.874)	2.05	1.79
90	3.99 (0.917)	1.99 (0.871)	2.35	1.70

[a] Correlation coefficient in the plot of log k vs σ° or σ^-. [b] Reference 29.

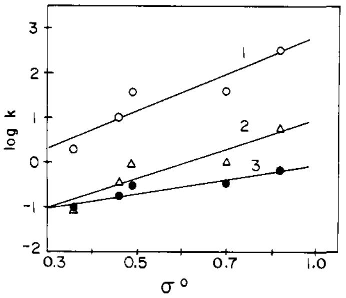

Figure 3. Hammett type plot (log k vs σ°) for the reaction of *p*-chlorophenoxide ion with substituted phenyl acetates $CH_3C(O)OC_6H_4Y$ in 90 (1), 50 (2), and 0 mol % DMSO (3).

Discussion

Reaction Pathways. Transacylation reactions are usually interpreted as two-step reactions in which nucleophilic attack and leaving group departure are separated by a tetrahedral intermediate.[6] The identity of the rate-determining step in this mechanism is governed by the relative nucleofugalities of the nucleophile and the leaving group from this intermediate, which can usually be equated with their relative pK_a's. The alternative view is that the reaction proceeds, similar to S_N2 reactions, via a single transition state. The latter mechanism was suggested, for example, by Haberfield[8] for the reaction of ArCOCl with 2-naphthoxide and

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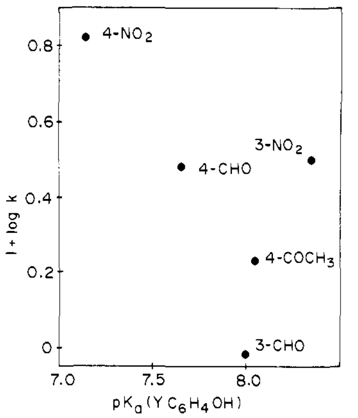

Figure 4. Plot showing the absence of a Brønsted correlation (log k vs pK_a) for the reaction of p-chlorophenoxide ion with substituted phenyl acetates in water at 25 °C (pK_a values from ref 7f).

more recently by Blake and Jorgensen[9] for the reaction of Cl^- with AcCl (ab initio calculations), as well as by Williams and coworkers[10] for the reaction of phenoxides with p-nitrophenyl acetate.

As part of the present study, we have investigated the acyl-transfer reaction for p-chlorophenoxide reacting with a series of substituted phenyl acetates (Table I). A Hammett type treatment for variation of substituents on the leaving group, at various DMSO–water compositions, although showing a relatively high degree of scatter, gave a much better correlation with σ^0 (Figure 3) than with σ^- (Table IV). Furthermore, the Brønsted type plot of log k vs pK_a, where pK_a refers to the substituted phenols of the leaving group (values only known in water[7f]), shows no obvious linear correlation (Figure 4) as would have been expected if leaving group departure occurred concertedly with nucleophilic attack. These results obviously lend more credence to the proposal that the bond to the leaving group is cleaved only to a small extent (if at all) at the TS of the rate-determining step.

For purposes of the present paper, it is essential to note that both schools would concur that under the conditions employed, i.e., pK_a (leaving group) < pK_a (nucleophile), the nucleophilic attack, coupled or not with leaving group departure, takes place at the rate-determining step.

Solvent Behavior. In Figures 1 and 2 is shown the effect of varying the DMSO–water composition on the rate constants of the acyl-transfer reaction when changing the leaving group and nucleophile, respectively. Inspection of the figures clearly indicates two distinguishable reactivity zones, one rich in water and one in DMSO. This behavior is not specific to the present reaction but is, rather, a characteristic feature of water–DMSO mixtures.[11,12] Hydrophobic interactions effected by addition of small quantities of DMSO (or any other organic solute) induce "rigidification" of water–water hydrogen bonds.[12] This is manifested, for example, in the decrease of the rotational correlation rate constant for water up to 30 mol % DMSO.[13] A study of the partial molar enthalpies of the solution of water in water–DMSO mixtures also confirms this view.[14] The "capricious"[15] behavior of these solvent mixtures seems to vanish at higher concentrations of DMSO. Thus, a plot of energy–volume coefficient data vs solvent composition, for example, shows a sharp increase in the water-rich region which nearly levels off in the DMSO-rich zone.[16,17] Another example is the solubility of molecular hydrogen in this solvent system, for which partial molal entropies and heats of solution level off in the DMSO-rich region after an initial sharp increase in the water-rich zone.[16] The borderline between the two zones seems to be located around 30 mol % DMSO, where the aforementioned and other phenomena such as the adiabatic compressibility[18] and the excess free energy of mixing[19] show a break in a continuous pattern of behavior. Most likely this phenomenon stems from the strong tendency of DMSO to form complexes with two and with three water molecules.[16] Since at 33.3 mol % DMSO the stoichiometric ratio of 1:2 for DMSO:water is achieved and since it is known that water hydrogen bonds more strongly to DMSO than to itself,[20,21] it is clear that in the DMSO-rich region the concentration of "free" water is exceedingly small. In fact it has been suggested that solvent structure remains essentially constant in that region.[22] Therefore, in the present paper we will focus largely on the data obtained at DMSO concentrations ≥40 mol %.

Table V. Brønsted β_{nuc} Values for the Reaction of Substituted Phenoxides with p-Nitrophenyl Acetate as a Function of Solvent Composition in DMSO–H_2O Mixtures (Method A)

DMSO, mol %	β_{nuc}	corr coeff	DMSO, mol %	β_{nuc}	corr coeff
0	0.75	0.993	50	0.65	0.998
10	0.74	0.996	70	0.60	0.997
20	0.72	0.996	90	0.59	0.997
40	0.67	0.996			

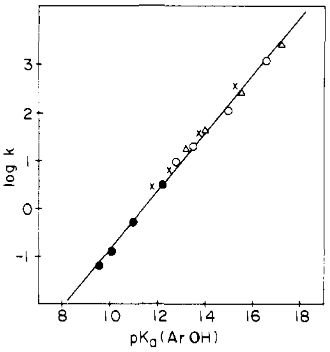

Figure 5. Brønsted type log k vs pK_a plot constructed by method B for the reaction of substituted phenoxides, $XC_6H_4O^-$, with p-nitrophenyl acetate using pK_a values over the solvent composition range 40–90 mol % DMSO with X = p-CH_3 (△), H (○), p-Cl (×), and p-CN (●).

Brønsted Correlations. From the rate dependence in the reaction of the substituted phenoxides with p-nitrophenyl acetate on the DMSO–water composition (Table II) and the pK_a values of the phenols (Table III), one can construct Brønsted type log k vs pK_a plots. The resulting β_{nuc} values for various solvent compositions are listed in Table V. It can be seen that as the medium becomes less polar the β_{nuc} values decrease. Traditionally interpreted, this would mean that the transition state is achieved earlier as the system becomes more reactive. It should be pointed out, however, that in contrast to this hypothesis, which is consistent with the Hammond postulate[23] and the reactivity–selectivity principle (RSP),[24] the initially added amounts of DMSO induce a rate decrease rather than an increase (Figures 1 and 2).

In general, and as illustrated by the above, β_{nuc} is the slope of the plot of log k for a given nucleophilic reaction versus the pK_a

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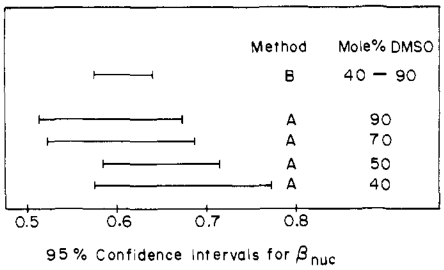

Figure 6. Bar diagram showing the 95% confidence intervals in Brønsted β_{nuc} values determined by method A for each of 40, 50, 70, and 90 mol % DMSO and by method B for the overall range 40–90 mol % DMSO and all the nucleophiles.

of the conjugate acid of the nucleophile. This pK_a is usually varied by changing a substituent in a position remote from the nucleophilic atom. The assumption involved is that these variations in the nucleophile entail only a small perturbation and the TS structure remains essentially constant. In the following we will refer to this procedure as method A.

However, as inspection of the data in Table III shows, in order to vary the pK_a of the nucleophile one need not necessarily vary the substituents. Instead, one can use the same phenol and vary the solvent composition. This procedure will be referred to as method B. Obviously, in the present case this cannot be employed in the water-rich region where the medium properties vary in drastic fashion and cannot be viewed as causing merely a perturbation in the TS structure. Therefore, only the data for DMSO ≥40 mol % will be treated by this method.

A Brønsted type plot constructed by using method B for the kinetic data in Table II for ≥40 mol % DMSO is presented in Figure 5. It is seen that by combining the variation in both solvent and substituent a linear correlation is obtained that extends over nearly 8 pK_a units and 4.5 orders of magnitude in rate constant. The slope of this line (β_{nuc}) is 0.61 with a correlation coefficient of 0.9962. The linearity of the line immediately suggests that, within this range of solvent composition, the TS structure remains by and large constant. This conclusion does not conform with the previous one based on method A which suggested a somewhat decreasing degree of bond formation with decrease in polarity of the medium.

Since the difference in the β_{nuc} values determined by methods A and B is rather small, one has to be concerned foremost with the reliability of the β_{nuc} values obtained by the different methods. Needless to say, correlation coefficients cannot serve as a useful measure of the reliability of the slopes (r will be 1.0000, for example, for a line based on two points, yet the reliability of the slope in this case could be very low). An unbiased statistical criterion is the T-test.[25] Application of this analysis at the 95% confidence level to the data at hand is graphically depicted in Figure 6. This clearly shows that the unique β_{nuc} value obtained by method B is by far more reliable than the several different values obtained by method A. Thus, with method A, at the 95% confidence level, the average $\Delta\beta_{nuc}$ value is ±0.081, whereas $\Delta\beta_{nuc}$ for method B is only ±0.033. Hence, it is clear that the slope value obtained by method B is significantly more reliable than those derived by method A.

It is important to note that the β_{nuc} value derived by method B is indeed unique and is not simply the result of a complex procedure for averaging the individual β_{nuc} values obtained by method A (the average value of the latter over the 40–90 mol % DMSO range is 0.627). This conclusion becomes immediately apparent if method B is extended to the water-rich region. In this region, the variations in the individual β_{nuc} values obtained by method A (Table V) span 0.08 β_{nuc} unit, which is identical with the range of variation of β_{nuc} in the DMSO-rich region. However, application of method B to the 0–40 mol % DMSO range clearly does not result in any kind of averaging as is demonstrated in Figure 7.

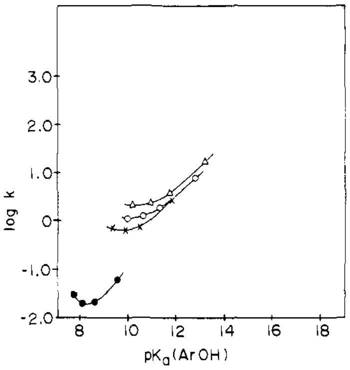

Figure 7. Application of method B to the water-rich region (0–40 mol % DMSO); symbols are identical with those of Figure 5.

Transition-State Structure. Having established the greater reliability of the unique β_{nuc} value determined by method B (Figure 5), we will now turn to discussion of the chemical consequences of this outcome. It is generally believed that the existence of a LFER implies that the TS structure remains constant over the whole range of the correlation.[26] In light of the linearity of the plot in Figure 5 and the high reliability of its slope, it can be concluded that the TS structure does not vary significantly with variation of the substituents on the nucleophile and over the solvent range 40–90 mol % DMSO. In the following discussion, evidence supporting the validity of this conclusion will be presented.

A constant structure of the transition state would imply that the same amount of charge will be developed on the substrate at the transition state over the whole range of the correlation.[27] In the present case, this conclusion is subjected to further verification by examination of the leaving group substituent effect on the reaction rates at the various solvent compositions. The ρ values given in Table IV increase progressively from 3.15 to 3.99 as the DMSO content of the solvent increases from 40 to 90 mol %. However, the proper procedure for determining TS structure involves normalization[28] of these ρ values by dividing them by the ρ values for the related equilibrium reactions. Unfortunately, these values are not available and we are obliged to seek a different model for the normalization procedure. Such a model should fulfill two conditions. The first is that the negative charge in the model equilibrium reaction will not interact by resonance directly with the ring substituents. The second condition is that suitable data will be available for this equilibrium process for the various water–DMSO composition mixtures. We have chosen to use the ionization of substituted benzoic acids[29] as the model equilibrium reaction. This procedure, of course, will not provide the absolute magnitude of charge developed on the substrate at the transition state as a fraction of unit charge developed in the equilibrium reaction. However, since at this stage we are only interested to ascertain whether the "normalized" ρ values vary with solvent composition or remain constant on solvent variation, we find this model to be satisfactory.

In the last column of Table IV are given the normalized ρ values, ρ_n°, obtained by dividing the raw ρ° values by the corresponding ρ values for the ionization of ArCOOH. It is evident that the ρ_n° values vary only to a small extent, and in light of the relatively large scattering of points (Figure 3), these values can be considered as representing a transition state with a nearly constant structure, thus supporting the above conclusion.

The fact that the TS structure remains essentially constant despite changing the solvent composition from 40 to 90 mol % DMSO receives additional support from other studies. Very recently, Jencks and co-workers[30] have shown that, in transphosphorylation reactions, metal cations such as Ca^{2+} and Mg^{2+}

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induce rate enhancement by virtue of coordination to the phosphoryl oxygen atoms. However, β_{nuc} for the catalyzed processes (0.21 and 0.17, respectively) was found to be practically identical with that of the uncatalyzed reaction (0.18). It was therefore concluded that both reactions have essentially the same TS structure. Similarly, the work of Jorgensen and Buckner[31] showed that, for the reaction of chloride ion with methyl chloride, the TS structure remains essentially constant on going from the gas phase to aqueous medium. Thus, it is not surprising that in the present case variation in the intensity of solvent interactions with the transition state, e.g., by hydrogen bonding, while changing its energy does not affect its structure.

Finally, it should be pointed out that the magnitude of β_{nuc} cannot be used to deduce the degree of nucleophile–substrate bond formation at the transition state. This parameter can be obtained from the normalized β_{nuc} value, i.e., $\beta_{\mathrm{nuc}}/\beta_{\mathrm{eq}}$, where β_{eq} refers to the equilibrium for the formation of the tetrahedral intermediate. The latter, however, is not available for the present system.

Conclusions. Two goals were achieved in this study: (a) we have shown that, under certain conditions, the TS structure of the title reaction is insensitive to variation in the reaction medium, and (b) a novel strategy for the construction of Brønsted type plots was devised. The latter involves *variation of the pK_a of the nucleophile by changing the solvent composition rather than by variation of substituents*. This method is applicable in cases where no drastic and capricious changes of solvent properties occur. In water–DMSO mixtures, the range 40–90 mol % DMSO was found to comply with this requirement.

Using a statistical analysis it was shown that the unique β_{nuc} value obtained by the method proposed herein is by far more reliable than the individual values derived by the traditional method. The linearity obtained in this case, together with the nearly constant value of the normalized ρ values for substituent variation on the leaving group, indicates a nearly constant structure of the transition state. This conclusion derives strong support from the aforementioned studies by Jencks[30] and Jorgensen.[31]

The major advantage of this novel method for construction of Brønsted type plots is that it enables an extension of the pK_a range beyond the one set by the limited number of substituents and that within this range more data points can be obtained. These two features increase significantly the reliability of the derived β_{nuc} parameter, providing a more solid basis for mechanistic interpretation. We believe that this strategy is of general nature and can be applied to other systems as well.

Experimental Section

The aryl acetates in this study were prepared by literature procedures and their purity was checked by means of their physical constants and IR and ^{1}H NMR characteristics. The phenols were of the highest quality available and were generally recrystallized before use. Doubly glass-distilled water was boiled and cooled under nitrogen just before use. Dioxane was first refluxed and distilled from anhydrous stannous chloride and then from metallic sodium. Dimethyl sulfoxide was refluxed over calcium hydride, distilled, collecting the fraction of bp 64–66 °C (6–7 mmHg), and stored under nitrogen. All solutions were prepared and stored under nitrogen and transferred by means of syringes. DMSO–water solutions of various mol % DMSO compositions were prepared by weight. Only freshly prepared solutions were used in the kinetic studies.

The rates of relatively slow reactions ($T_{1/2} > 10$ s) were followed spectrophotometrically with a Beckman 25, Acta IV, or Perkin-Elmer 552 spectrophotometer equipped with thermostated cell holders. Generally, reactions were followed at a fixed wavelength ($\lambda_{\max}$ of ArO$^-$). Typically, reaction was initiated by adding 5 μL of a 0.02 M solution of the aryl acetate in dioxane by syringe to a 10-mm quartz cuvette containing the reaction mixture made up of DMSO–water, the phenol, and 0.5 equiv of aqueous NaOH or aqueous Me_4NOH for DMSO-rich media. Generally, the phenoxide concentration was varied over the range $(1-30) \times 10^{-3}$ M while the ester concentration was 2×10^{-5}–2×10^{-4} M, depending on $\lambda_{\max}$ and molar extinction values, with the nucleophile concentration at least 15 times that of the substrate. Usually, five values of [ArO$^-$] were employed and replicate values of k_{obsd} were determined to obtain the second-order rate coefficients from linear k_{obsd} vs [ArO$^-$] plots. For reactions with $T_{1/2} < 10$ s, a stopped-flow technique was used with a Can-Tech module, spectral traces being displayed on an oscilloscope and data stored on a transient recorder coupled to a computer to yield the pseudo-first-order rate constant k_{obsd}.

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Registry No. 4-$ClC_6H_4^-$, 24573-38-4; 4-$CNC_6H_4^-$, 14609-76-8; PhO$^-$, 3229-70-7; 4-$CH_3C_6H_4O^-$, 22113-51-5; $CH_3C(O)OC_6H_4$-4-NO_2, 830-03-5; $CH_3C(O)OC_6H_4$-3-NO_2, 1523-06-4; $CH_3C(O)OC_6H_4$-4-CHO, 878-00-2; $CH_3C(O)OC_6H_4$-3-CHO, 34231-78-2; $CH_3C(O)OC_6H_4$-4-C-OCH_3, 13031-43-1.

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Rearrangement of 4-Alkynylcyclobutenones. A New Synthesis of 1,4-Benzoquinones

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Abstract: A new convergent synthesis of 1,4-benzoquinones from 4-alkynyl-4-alkoxy(or hydroxy or trimethylsilyloxy)cyclobutenones is described. The required cyclobutenones are prepared from squaric acid and converted to the quinones upon mild thermolysis. The reaction proceeds via electrocyclic ring opening of the required cyclobutenones to (2-alkynylethenyl)ketenes, which then ring close to unique diradical intermediates. These then give the quinone products. The scope and mechanism of this unusual rearrangement are discussed.

Reported here are details of a new reaction having significant utility for the synthesis of substituted 1,4-benzoquinones **6** and 2-alkylidene-1,3-cyclopentenediones **7** (Scheme I).[2,3] These products arise from 4-alkynylcyclobutenones **2** which are envisaged to undergo a remarkably selective electrocyclic ring opening upon mild thermolysis to generate (2-alkynylethenyl)ketenes **3**. These reactive ketenes then undergo ring closure to produce the unique diradicals (or zwitterions) **4** and **5**, which, in turn, proceed to

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[1] This work was taken primarily from the Ph.D. Dissertation research of L.D.F.

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