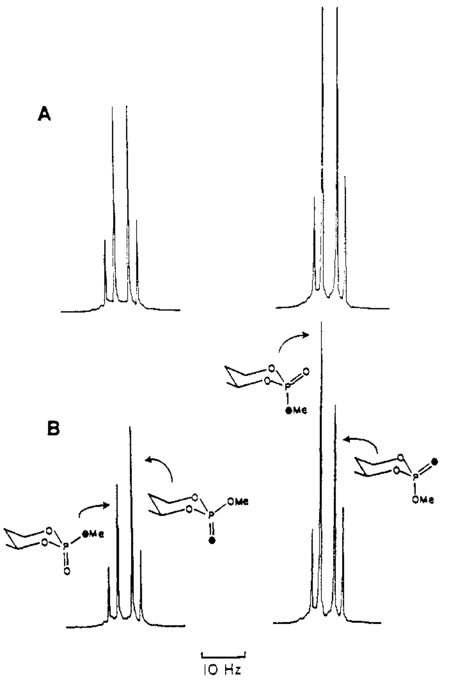

Figure 2. ^{31}P NMR spectra of the phosphate triesters provided from stereochemical analysis of (A) the *tert*-butyl [^{16}O,^{17}O,^{18}O]phosphate product and (B) the recovered *p*-nitrophenyl [^{16}O,^{17}O,^{18}O]phosphate substrate from the solvolysis of *p*-nitrophenyl (R_P)-[^{16}O,^{17}O,^{18}O]phosphate in neat *tert*-butyl alcohol at 30 °C. The spectra were taken as described in the legend to Figure 1, except that a Gaussian multiplication with Gaussian broadening of 0.05 Hz was applied. The remaining substrate [in (B)] is 85% R_P, and the product [in (A)] is completely racemic.

In a recent investigation, Cullis and Rous have attempted to increase the effective lifetime of monomeric metaphosphate by lowering the concentration of the trapping nucleophile in the medium.[37] The phospho group donor P^1-*O*-ethyl-P^1-thio-[P^2-^{16}O,^{17}O,^{18}O]pyrophosphate was labilized by S methylation in dichloromethane solution containing a primary alcohol. The phospho group transfer proceeded with partial racemization (30% inversion) at phosphorus. This result, while not consistent with a completely free metaphosphate species, does suggest that most of the phospho group transfers in this experiment involve a metaphosphate intermediate. In another study, Cullis and Nicholls have looked at the rate of positional isotope exchange in the reaction of adenosine 5′-[α,β-^{18}O]diphosphate trianion in acetonitrile, in acetonitrile/*tert*-butyl alcohol, and in neat *tert*-butyl alcohol.[38] In each case, some scrambling of the ^{18}O label between the "bridge" and "nonbridge" positions was evident in the reisolated starting material, this finding being consistent with the transient formation of monomeric metaphosphate. It should be noted, however, that positional isotope exchange only requires rotation around one P–O bond within the solvent cage and that this reaction could proceed stereospecifically with retention or inversion of the configuration at the terminal (transferred) phospho group. Racemization of the transferred phospho group is, therefore, a more demanding requirement for monomeric metaphosphate. In any case, it is gratifying that the isotope exchange and stereochemical studies are in agreement.

The conclusion from the present work is that metaphosphate *can* be a viable, liberated, intermediate in the solvolytic reactions of phosphate monoesters. If the intermediate is trapped by ambient nucleophiles before the leaving group has diffused away, inversion of the configuration at phosphorus is seen, while if the nucleophilicity of the available nucleophiles is low, racemization of chiral phospho groups can be observed. In these cases, we must conclude that a metaphosphate intermediate is formed and that it survives long enough so that collapse to an acceptor nucleophile is equally probable from each face of the planar species.

Acknowledgment. This work was supported by the National Institutes of Health and the Science and Engineering Research Council. We are grateful to David Hansen for his development of the stereoanalytical method using butane-1,3-diol and to John Rose, Shaw Huang, and Phil Briggs for technical assistance.

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A Theoretical Treatment of Nucleophilic Reactivity in Additions to Carbonyl Compounds. Role of the Vertical Ionization Energy

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Abstract: In water solvent, experimental $\Delta G^{\ddagger}$ values for attack of X:$^-$ upon several esters correlate with the *vertical* ionization potentials of X:$^-$. Two kinds of nucleophiles are discerned in this way, delocalized nucleophiles (AcO^-, N_3^-, NO_2^-, etc.) exhibiting a larger slope than localized nucleophiles (F^-, HO^-, CH_3O^-, etc.). In terms of the state correlation diagram model, the existence of a $\Delta G^{\ddagger}$ versus $IP(X^-)^*$ correlation implies that an important aspect of the activation process is the single electron switch from X:$^-$ to the substrate that occurs during the nucleophilic attack.

The rationalization of nucleophilic reactivities has been a longstanding goal in physical organic chemistry.[2-4] Theoretical approaches to this problem have been found to be increasingly fruitful, but these have been largely limited to nucleophilic sub-

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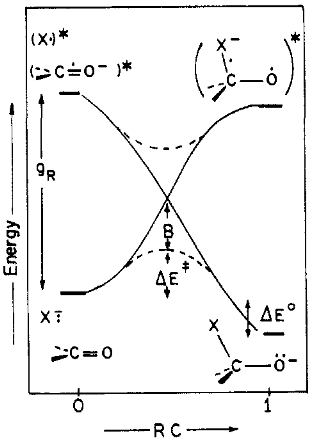

Figure 1. State correlation diagram for nucleophilic attack on a carbonyl compound. The asterisks denote vertical states. The dark circles symbolize electrons.

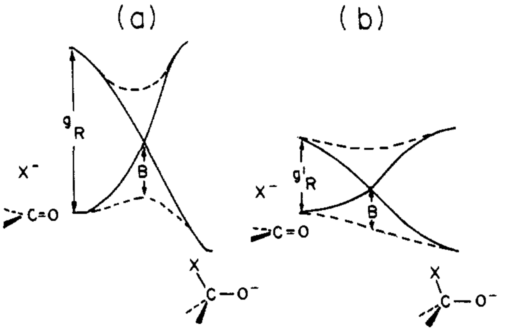

Figure 2. (a) State correlation diagram for a nucleophilic carbonyl addition that contains a barrier. (b) State correlation diagram for a barrierless nucleophilic carbonyl addition.

stitution at saturated (sp^3) carbon centers and, in particular, S_N2 type processes.[4h,l,m,5] Recently, several publications have appeared focusing on the problem of nucleophilic reactivity at carbonyl centers,[6] including ab initio studies on the addition of amines to model carbonyl compounds in the gas phase,[6d] theoretical studies on the simulation of addition reactions in aqueous solutions,[6e,f] and calculations of substituent effects.[6g]

In the present study we apply the state correlation diagram (SCD) model, developed in previous papers in this series,[7-9] to the problem of nucleophilic reactivity of anionic nucleophiles toward esters in aqueous solution. Kinetic data for such reactions are available in the literature.

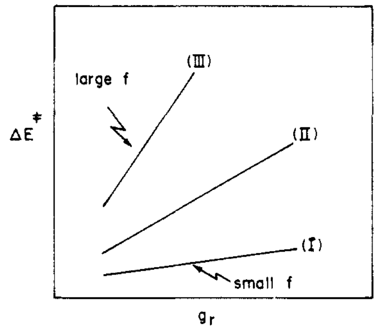

Figure 3. Schematic diagram showing variation of free energy of activation with the parameter f in eq 2 for a series of related processes.

Theoretical Model

The addition step (a) in nucleophilic substitution of esters (eq 1) possesses a barrier whose origin can be described by the state

$$X:^- + R(R'O)C{=}O \underset{-a}{\overset{a}{\rightleftharpoons}} R(R'O)C(X) - \ddot{O}^- \xrightarrow{b} R(X)C{=}O + R'O:^- \quad (1)$$

correlation diagram of Figure 1.[7a,10] The barrier is, phenomenologically, the energy of the crossing point minus the avoided crossing resonance interaction, B. The energy of the crossing point can be expressed as a fraction (f) of the electron-transfer energy gap, g_R, between the curves. The resulting barrier expression is

$$\Delta E^{\ddagger} = fg_R - B \quad (2)$$

Since this equation describes the energy of the crossing point, after avoided crossing, relative to the reactants, eq 2 also encompasses the situation in which the avoided crossing leads to no barrier.[11] For example, when the gap g_R is large, as in Figure 2a, the avoided crossing results in a barrier; when the gap is small, as in Figure 2b, the avoided crossing leads to a barrierless reaction profile. Equation 2 therefore characterizes both activated and unactivated processes. In the gas phase, some nucleophilic carbonyl additions seem to proceed without a barrier, while others have barriers ranging from small to significant.[12,13] All carbonyl addition reactions in solution have a significant barrier.[14] This spectrum of behavior depends on the electron-transfer energy gap, g_R, as is discussed below.

In the form in which it appears in eq 2, f is a parameter that can be shown[15] to depend on the curvatures of the two intersecting surfaces, on the energy change for the reaction ($\Delta E°$ in Figure 1), and on g_P, the gap on the product side.[5,7,10,11,15] An important

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[1] (a) Queen's University. (b) Ben-Gurion University.

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[9] (a) For the related EVB approach, see: Warshel, A.; Russell, S. T. *Rev. Biophys.* **1984**, *17*, 3. Warshel, A. *Acc. Chem. Res.* **1981**, *14*, 284. (b) For the related MO-VB approach, see: Epiotis, N. D. *Lect. Notes Chem.* **1983**, *34* (e.g., p 115).

[10] Cohen, D.; Bar, R.; Shaik, S. S. *J. Am. Chem. Soc.* **1986**, *108*, 231.

[11] See, for example, discussions of avoided crossings in: Shaik, S. S.; Hiberty, P. C. *J. Am. Chem. Soc.* **1985**, *107*, 3089.

[12] (a) For experimental studies of nucleophilic carbonyl additions in the gas phase, see, e.g.; Bowie, J. H. *Acc. Chem. Res.* **1980**, *13*, 76. Asubiojo, O. I.; Brauman, J. I. *J. Am. Chem. Soc.* **1979**, *101*, 3715. Bartmess, J. E.; Hays, R. L.; Caldwell, G. *Ibid.* **1981**, *103*, 1338. Kleingeld, J. C.; Nibbering, M. M.; Grabowski, J. J.; De Puy, C. H.; Fukuda, E. K.; McIver, R. T., Jr. *Tetrahedron Lett.* **1982**, *23*, 4755. McDonald, R. N.; Chowdhury, A. K. *J. Am. Chem. Soc.* **1983**, *105*, 198, 7267. Takashima, K.; Jose, S. M.; do Amaral, A. T.; Riveros, J. M. *J. Chem. Soc., Chem. Commun.* **1983**, 1255. Johlmann, C. L.; Wilkins, C. L. *J. Am. Chem. Soc.* **1985**, *107*, 327. (b) A small barrier is computed for $HO^- + CH_2O$ at the 6-31+G* level.[6e] (c) A significant barrier is computed for $NC^- + CH_2O$ at the 4-31G level.[13]

[13] Mitchell, D. J. Ph.D. Thesis, Queen's University, 1981, pp 120–129.

[14] March, J. In *Advanced Organic Chemistry: Reactions, Mechanisms and Structures*, 2nd ed.; McGraw-Hill: New York, 1977; pp 349–353.

[15] See Appendix A of ref 5 and pp 214–216. See also: Shaik, S. S.; Schlegel, H. B.; Mitchell, D. J.; Wolfe, S. *Theoretical Physical Organic Chemistry*; Wiley: New York, in preparation.

contributor to the curvature is the extent of odd-electron delocalization in the charge-transfer state.[5,10] Such delocalization weakens the bond coupling interaction between $X^\bullet$ and $(>C{=}O)^-$, leads to a shallow descent of the charge-transfer state, and results in a large *f*. Although, without additional information, eq 2 does not provide absolute values of *f* for a particular reaction, trends in *f* can be predicted. For example, delocalized charge-transfer states will have higher *f* values than localized charge-transfer states. Since, when the nucleophile $X{:}^-$ is delocalized, the radical $X^\bullet$ is also delocalized, a higher *f* value should be expected.

To specify *f* precisely would require a priori knowledge of all factors that determine this quantity, but this is not practical when the number of reactions to be analyzed or correlated is large. Therefore, a useful strategy is to rely upon correlations that lead to *f* values associated with different reaction families.

In terms of the foregoing analysis, a reaction family is characterized by the existence of a constant *f*, and families generated from delocalized nucleophiles should have larger *f* values than families generated from localized nucleophiles. It can, therefore, be predicted that a plot of barriers versus the gap g_R (eq 2) will lead to series of lines characteristic of different families. This is envisaged schematically in Figure 3, using three hypothetical families (I, II, and III), characterized by an increasing degree of radical anion delocalization, and, hence, increasing *f*. Such structure–reactivity plots, if they are found, would have obvious mechanistic significance.

Analysis of Nucleophilic Reactivity

Consider a nucleophilic attack of X^- upon an ester *in solution*. The gap of the diagram in Figure 1 is the vertical electron-transfer energy expressed in eq 3:

$$g_R = \mathrm{IP}(X^-)^* - \mathrm{EA}(\text{ester})^* \qquad (3)$$

Here IP and EA are, respectively, the ionization potential and electron affinity; the asterisk refers to a vertical process in which all geometric features are frozen.[16] For a constant substrate the electron affinity term is constant and $\mathrm{IP}(X^-)^*$ is the only variable of g_R.

Vertical ionization potentials of nucleophiles in aqueous solution are known experimentally in some cases.[17] Other values can be estimated[5,16,17] by using the Marcus theory of nonequilibrium polarization,[18] with the aid of the thermochemical cycle of eq 4.

$$X{:}^-(\text{s, equil}) \rightarrow X{:}^-(\text{g});\quad \Delta G^\circ_1 = -\Delta G_S(X^-) \qquad (4a)$$

$$X{:}^-(\text{g}) \rightarrow X^\bullet(\text{g}) + e^-;\quad \Delta G^\circ_2 = \mathrm{EA}(X^\bullet) \qquad (4b)$$

$$X^\bullet(\text{g}) \rightarrow X^\bullet(\text{s, equil});\quad \Delta G^\circ_3 = \Delta G_S(X^\bullet) \qquad (4c)$$

$$X^\bullet(\text{s, equil}) \rightarrow X^\bullet(\text{s}^*, \text{nonequil});\quad \Delta G^\circ_4 = \Delta G_{SR} \qquad (4d)$$

$$X{:}^-(\text{s, equil}) \rightarrow X^\bullet(\text{s}^*, \text{nonequil}) + e^-;\quad \Delta G^\circ = \mathrm{IP}(X^-)^* \qquad (4e)$$

The fourth step of the cycle (eq 4d) refers to the reorganization of the solvent orientations about $X^\bullet$ to the orientations that pertain to $X{:}^-$.[19] This causes the solvent molecules to be in a state of disequilibrium with $X^\bullet(\text{s}^*)$, as denoted by the asterisk.

The components of the cycle lead to eq 4e, which describes the loss of an electron from $X{:}^-$ under *frozen solvent orientations*. The vertical ionization potential is then given by eq 5 and involves three

$$\mathrm{IP}(X^-)^* = \mathrm{EA}(X^\bullet) - \Delta G_S(X^-) + \Delta G_S(X^\bullet) + \Delta G_{SR} \qquad (5)$$

main contributions: the intrinsic energy change caused by electron loss from $X{:}^-$, the loss of the solvation energy of $X{:}^-$, and the solvent reorganization energy caused by the disequilibrium orientations of the solvent molecules.[19]

Table I. Vertical Ionization Potential, Gas-Phase Electron Affinities, and Free Energy of Activation Data (kcal/mol) for Reactions of Nucleophiles with Esters **1**–**3**

Nu: (X^-)	$\mathrm{IP}(X^-)^*$	$\mathrm{EA}(X^\bullet)$	$\Delta G^\ddagger$		
			1	**2**	**3**
PrS^-	164.8	46.1	15.5	14.1	11.0
HOO^-	171.0	27.4	12.6	11.8	8.8
ClO^-	176.4	64.0	15.5		
CH_3O^-	177.2	36.7	13.8	12.7	9.9
$CF_3CH_2O^-$	179.2	51.2	15.0	14.0	11.1
CN^-	200.0	88.1	18.5	17.9	15.0
HO^-	195.0[a]	42.1	16.2	15.1	12.1
F^-	237.6[a]	78.4	23.8	21.0	16.7
PhO^-	161.1	48.9	17.5	16.0	12.6
PhS^-	160.0	56.9	18.1	15.9	12.8
ONO^-	174.6[a]	53.0	23.8	20.3	16.2
N_3^-	172.0[a]	60.1	19.6	17.5	14.0
AcO^-	180.3[a]	73.0	24.6	21.9	17.4

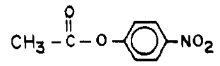
[a] Experimental value, ref 17. The other values of $\mathrm{IP}(X^-)^*$ have been calculated via eq 4e; see text and footnote 19.

Consider now the *family* that results from the reaction of an ester with a series of nucleophiles. Having a common ester, the reaction family will possess a gap, g_R, whose only variable is $\mathrm{IP}(X^-)^*$, because $\mathrm{EA}(\text{ester})^*$ is constant. From eq 2, the barrier for the series will be

$$\Delta E^\ddagger = f\{\mathrm{IP}(X^-)^*\} - C$$
$$C = B + f[\mathrm{EA}(\text{ester})^*] \qquad (6)$$

Here *C* is a constant that depends on *B* as well as on the identity of the ester. The only variable for the reaction family of eq 6 is then $\mathrm{IP}(X^-)^*$. From the components of $\mathrm{IP}(X^-)^*$ (eq 5), it is evident that two properties contribute to the barrier in solution (eq 6). One is $\mathrm{EA}(X^\bullet)$, i.e., the gas-phase ionization potential of $X{:}^-$. The second arises from the solvation effects expressed by the ΔG_S and ΔG_{SR} terms of eq 5, and the relative contributions of the two will depend upon the nature of X^-.[20] For example, as can be seen from the data of Table I, solvation effects make the dominant contribution to the barriers in the case of HO^-. However, for CN^-, the two effects are approximately the same.

Experimental $\Delta G^\ddagger$ data in water solvent for the three related esters **1**–**3** are available in the literature[21a–c] and are included in Table I. In each case, the reactions of these substrates with 13 anionic nucleophiles obey second-order kinetics, and nucleophilic addition to the carbonyl group is believed to be rate determining



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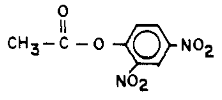

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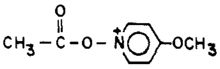

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[16] Shaik, S. S. *J. Am. Chem. Soc.* **1984**, *106*, 1227.

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[19] ΔG_{SR} is estimated by using the relationship $\Delta G_{SR} = -\rho\Delta G_S(X^-)$; $\rho = 0.56$ in H_2O at 298 K. This relation is appropriate for aqueous solutions at 298 K and leads to values close to the experimental data in the known cases, see ref 5 and 16.

[20] For a separation of the barrier into gas-phase and solvent contributions, see ref 5, 16, and: Shaik, S. S. *Isr. J. Chem.* **1985**, *26*, 367.

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(step a in eq 1). Other possibilities consistent with the kinetics must also be considered, e.g., a change in mechanism or a change in rate-determining step, as the nucleophile is varied with each of the substrates. A change in rate-determining step, from formation (eq 1, step a) to decomposition (step b) of the tetrahedral intermediate, would be anticipated when the pK_a of the nucleophile is less than that of the leaving group of the ester. For esters **1**, **2**, and **3**, the leaving group pK_a's are 7.1, 4.1, and 2.1, respectively. A change in rate-determining step is, therefore, not expected in the case of ester **3** but cannot be excluded, on the basis of such pK_a arguments, for esters **1** and **2** when the nucleophiles are weakly basic (AcO^-, N_3^-, NO_2^-, and F^-).

However, studies of nucleophilic substitution at carbonyl centers[21a–i] have shown that a simple relationship between pK_a's and a change in rate-determining step will be strictly valid only when the nucleophile and the leaving group are structurally similar (OR_1/OR_2, OAr_1/OAr_2, SAr_1/SAr_2, etc.), but not in other cases. Since the nucleophiles and leaving groups of the present systems are quite dissimilar, it is, therefore, not required to invoke a change in rate-determining step on the basis of a pK_a argument. The fact that AcO^-, NO_2^-, and F^- are found on the linear portions of the Brønsted type log k versus pK_a plots also argues against a change in rate-determining step with these nucleophiles. Azide ion shows a positive deviation on such plots but this deviation is probably related to the exalted polarizability of N_3^-.[21j] A curvature in some Brønsted plots which occurs in the region as one passes from aryl oxides to alkoxides as the nucleophiles has been ascribed by Jencks and Hupe to differential solvation rather than a change in the rate-determining step.[21d–g]

More plausible than a change in rate-determining step is the possibility of a change in mechanism with the weakly basic nucleophiles, from direct nucleophilic attack to general-base-catalyzed attack of H_2O at the carbonyl center. The energetics of such a protolytically catalyzed hydrolysis have been discussed in detail by Schowen,[21k] and Gold has demonstrated[21l,m] that the nucleophilic pathway in the reaction of AcO^- with **1** occurs to the extent of 57%, and with **2** to 98%, the balance being a general-base-catalyzed attack of H_2O at the carbonyl center. The general-base-catalyzed pathway could conceivably occur to some extent (<50%) in the reactions of **1** with N_3^-, NO_2^-, and F^-, but this would be negligible in the cases of **2** and **3** provided that a relationship exists between leaving-group ability (nucleofugacity) and pK_a.[21d–j] We have made no correction for the general-base-catalyzed pathway in the present work since the correction factor (≤ 0.2 on the $\Delta G^\ddagger$ scale for **1** and negligible for **2** or **3**) would not significantly alter the nature of the plots (Figure 4) and resulting correlations.[22a]

Each of the three substrates exhibits the same kind of $\Delta G^\ddagger$ versus $IP(X^-)^*$ behavior. One of these plots is shown in Figure 4 and illustrates the point.[22a] In these figures, with the exception of PrS^-, the nucleophiles are seen to fall into two distinct groups. The first comprises localized nucleophiles (F^-, HO^-, etc.), and the second, delocalized nucleophiles (AcO^-, N_3^-, NO_2^-, etc.). Although the number of data points for the second group is small, it is apparent that reactivity in this group is more sensitive to changes in $IP(X^-)^*$ than reactivity in the first group. The data thus appear to behave in conformity with the theoretical plots of Figure 3.

The linear correlations of Figure 4 correspond to eq 7a,b, which,

$$\Delta G^\ddagger = 0.14\,IP(X^-)^* - 11\ \text{kcal/mol} \qquad (7a)$$

$$\Delta G^\ddagger = 0.29\,IP(X^-)^* - 31\ \text{kcal/mol} \qquad (7b)$$

together with eq 6, can be used to obtain values for the resonance interaction B, in the transition state (Figure 1). Values of EA(ester)* can be reasonably bracketed between −4 and +28 kcal/mol using gas-phase EA and solvation energy data.[22b] Using this range of EA(ester)* leads to B values of 10 ± 3 and 27 ± 5 kcal/mol for the two families of eq 7a and 7b, respectively. A similar distinction between the two families is obtained in each case for the esters **1**–**3**.

However, because of the limited data set for the delocalized family, it does not follow that the two families have characteristically different transition-state resonance energies. Indeed, if it is required that the two families share the same B values (e.g., 12 kcal/mol), the delocalized family of Figure 4 can be fit to eq 8. Although this equation has a poor correlation coefficient (0.70),

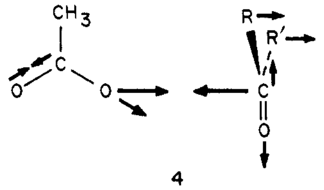
$$\Delta G^\ddagger = 0.21\,IP(X^-)^* - 18\ \text{kcal/mol} \qquad (8)$$

its predictions of barrier trends and their absolute magnitudes are reasonable. Thus, while a distinction between the two families in terms of slopes appears to be reliable, a more detailed discussion of the relative B values of the two families should await additional data for the second family.

Discussion

According to Figure 1, nucleophilic attack upon a carbonyl group involves a *single* electron switch synchronized to all of the molecular deformations and motions that convert reactants to products.[5,7,10] These include skeletal reorganization of the reacting species as well as reorganization of the solvent molecules which attempt to maintain equilibrium with the migrating charge.[5,16] The correlations of $\Delta G^\ddagger$ with $IP(X^-)^*$ reflect the reorganizational effort that promotes the electron switch and bond coupling.

Further insight into the physical significance of the correlation requires a more explicit discussion of the factors that, according to the model, contribute to the geometry of the transition state,[5,10,23] which corresponds approximately to the crossing point of the ground state and the charge-transfer state of Figure 1.[7b] Since the two states are initially separated by the vertical electron-transfer energy gap g_R (eq 3), molecular deformations are required to overcome this gap, and these are illustrated schematically in **4** for the reaction of acetate ion with a general carbonyl compound.



4

The heavy arrows imply that the deformations involve distortions of both reactants, as well as their mutual approach. The distortions lower the ionization potential of $X:^-$ and improve the electron affinity of the carbonyl substrate; the mutual approach gradually couples the two odd electrons of the charge-transfer state into a nucleophile–substrate bond. All of these effects, together with solvent reorganization, operate to stabilize the charge-transfer state and destabilize the ground state until they cross. At the crossing point, mixing of the two states lowers the energy and endows the transition state with a resonance energy, B. The barrier is then manifested as a deformation and solvent reorganization energy which is proportional to the vertical electron-transfer energy gap (eq 3) that must be overcome in order to achieve a transition state.[5,10,23]

It is the relative contributions of the gas-phase and solvent terms to $IP(X^-)^*$ (eq 5) that determine the relative proportions of

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(22) (a) The three plots exhibit the two families with similar slope information. The worst pair of correlation coefficients is 0.931 and 0.948 for substrate **3**. Though these correlation coefficients are mediocre, the reactivities follow the order of $IP(X^-)^*$. The other correlation coefficients are 0.975, 0.924 (**1**); and 0.964, 0.947 (**2**). The second correlation coefficient in each case corresponds to the second family (AcO^-, N_3^-, etc.). (b) A cycle analogous to eq 4 leads (see ref 5, p 296) to EA (ester)* = EA(ester − $\Delta G_S(\text{ester}^{\cdot -})$ − ΔG_{SR} + ΔG_S(ester). EA(ester) is the gas-phase vertical electron affinity of the carbonyl group. Using the data of ref 22c, it is possible to estimate EA(ester) values in the range −0.5 to −1.5 eV. $\Delta G_S(\text{ester}^{\cdot -})$ is the solvation energy of the carbonyl radical anion and can be estimated as −70 to −90 kcal/mol. ΔG_{SR} is the solvent reorganization energy and can be estimated as $-\rho\Delta G_S(\text{ester}^{\cdot -}$; $\rho = 0.56$. ΔG_S(ester) is the solvation energy of the neutral ester and is taken as zero. (c) Modelli, A.; Jones, D.; Rossini, S.; Distefano, G. *Chem. Phys. Lett.* **1986**, *123*, 375. Modelli, A.; Jones, D.; Rossini, S.; Distefano, G. *Tetrahedron* **1984**, *40*, 3257.

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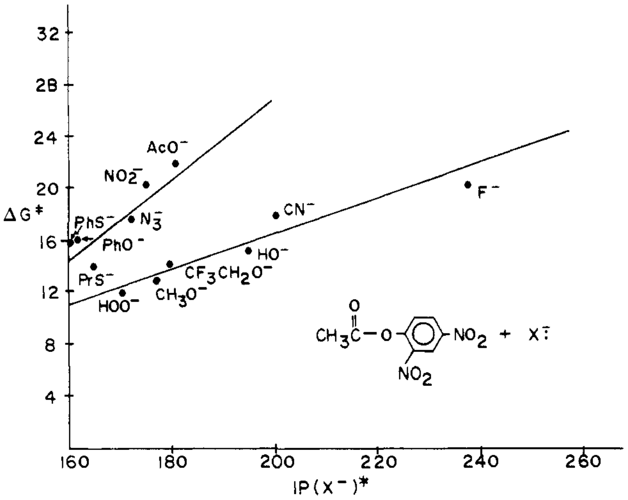

Figure 4. A plot of $\Delta G^{\ddagger}$ data against IP(X^-) for substrate **2**.

molecular distortion and solvent reorganization for a given reaction. For example, in the case of HO^-, for which the solvent terms make the main contribution to IP(X^-)* (Table I), solvation changes are predicted to make the main contribution to the transition state, and molecular deformations are predicted to be relatively unimportant. On the other hand, for reactions of NC^-, molecular deformation is expected to be significant in the transition state, in accord with the increased contribution of EA($X^\bullet$) to IP(X^-)*. On the basis of theoretical calculations of $HO^- + H_2CO$[6e] and $NC^- + H_2CO$,[13] these predictions appear to be reasonable. However, additional tests are needed.

For a given degree of odd-electron delocalization, an increase in the electron-transfer energy gap will require a greater extent of deformation and solvent reorganization in the transition state.[10] This statement is related to the variations within each of the reaction families of Figure 4. In each of the families, the transition states are predicted to become increasingly distorted as IP(X^-)* increases. This increasing distortion is comprised of molecular deformations and solvent reorganization. The relative contributions of the two cannot at present be stated but may become known[10,23] when additional gas-phase reactivity data[6c-f] or empirical VB calculations[9a] become available.

For a given vertical electron-transfer energy gap, the deformation and solvent reorganization required to achieve a transition state are also predicted to increase as the odd electrons in the charge-transfer state become increasingly delocalized.[10,23] The reaction families of the delocalized nucleophiles in Figure 4 are, therefore, expected to possess more distorted transition states (in both molecular and solvent senses) than those for the reaction families of the localized nucleophiles. In this respect we are in agreement with the conclusions of Schowen and co-workers[21k] concerning the role of electron delocalization in the activation process.

An increase in the slope of a correlation line implies that the reaction family is more sensitive to IP(X^-)* and thereby experiences a proportionally greater increase in transition-state deformation as IP(X^-)* increases.[23b] Thus the relative slopes of the family lines in Figure 4 reveal that electronic delocalization is a factor that imposes higher barriers and larger extents of molecular deformations and solvent reorganization in the transition states. The same behavior has already been demonstrated in other nucleophilic processes.[10,23,24]

Interestingly, we find phenyl acetate to provide the same type of correlation as is exhibited by esters **1**–**3**, and the plot of $\Delta G^{\ddagger}$ versus IP(X^-)* for this ester (not shown) is qualitatively analogous to that displayed in Figure 4. This should not have been expected, because the mechanism of hydrolysis of phenyl acetate with AcO^- and, possibly, other delocalized nucleophiles (NO_2^-, N_3^-) is thought to involve a general-base-catalyzed attack by H_2O (proteolytic catalysis).[21a,k-m] Since the behavior of phenyl acetate does not differ from those of **1**–**3** in our plots, the reaction of AcO^- with this ester appears also to involve a rate-determining electron switch from the nucleophile. A proteolytic mechanism that involves an electron switch to the proton of a water molecule would exhibit a correlation with IP(X^-)*. Within the context of the model developed here, more work is evidently needed to clarify the factors that cause a proteolytic pathway to be preferred over nucleophilic catalysis in some systems.

Summary

Within restricted series, the "nucleophilicity" of $X:^-$ toward carbonyl compounds correlates with the vertical ionization potential of the nucleophile, IP(X^-)*. Using the state correlation diagram model, one may interpret this empirical correlation to mean that an important aspect of the activation process is the total deformation associated with the single electron switch from $X:^-$ to the substrate that occurs during the nucleophilic attack.[5,10]

Analogous correlations of "nucleophilicity" have been suggested previously by Hoz[6a] and by Ritchie.[6b] Their treatments employed adiabatic ionization potentials of $X:^-$ rather than the vertical ionization potentials used here. A more detailed examination of these and other correlations of nucleophilic reactivity is under way.[25,26]

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Registry No. 1, 122-79-2; **2**, 830-03-5; **3**, 4232-27-3; PrS^-, 20733-14-6; HOO^-, 14691-59-9; ClO^-, 14380-61-1; CH_3O^-, 3315-60-4; $CF_3CH_2O^-$, 24265-37-0; CN^-, 57-12-5; HO^-, 14280-30-9; F^-, 16984-48-8; PhO^-, 3229-70-7; PhS^-, 13133-62-5; ONO^-, 14797-65-0; N_3^-, 14343-69-2; AcO^-, 71-50-1.

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[26] For example, linear correlations, analogous to those seen here in Figure 4, are obtained for the gas-phase data of ref 6d and 6g.