transition state for the cation–anion combination reactions is such that part of this outer shell solvation around the cation has been released into bulk solvent, we then expect a negative entropy contribution to ΔS^*. Similarly, on going from the neutral product, Ar_3CX, to the transition state, the solvation around the developing cation and anion is largely electrostrictive, and the full second-shell solvation disorder has not been attained.

These postulates may ultimately help in understanding the relative reactivities of the cations, a topic which has caused some difficulties arising from the previously[1] postulated nature of the transition states.

Acknowledgments. This work has been supported by grants from the National Science Foundation (GP-29164x), and National Institutes of Health—Public Health Service (GM-12832). Acknowledgment is also made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. We also express our appreciation to Mrs. S. V. McKinley for sending us samples of several of the carbonium ions used in the present study.

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Cation–Anion Combination Reactions. XIII.[1] Correlation of the Reactions of Nucleophiles with Esters

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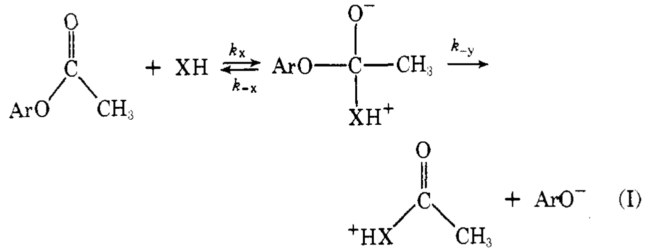
Abstract: The N_+ correlation of nucleophilic reactivities, previously shown to apply to the reactions of nucleophiles with organic cations, is now shown to apply to the reactions of nucleophiles with esters when explicit consideration of a two-step mechanism is included. The consideration of this mechanism requires that leaving-group abilities of attacking nucleophiles relative to leaving-group abilities of the ester leaving group be evaluated. This evaluation is accomplished by empirical data fitting under the stringent restriction that the leaving-group ability of a given group is assumed to be independent of other groups present in the intermediate. The new correlations extend previous observations to include reactions of 26 electrophiles and 52 nucleophiles. Interpretations of the correlations considerably extend and slightly modify earlier conclusions regarding the mechanisms of nucleophilic reactions with esters. The range of applicability of the N_+ equation documented in the present paper is far greater than could be anticipated on the basis of current theories of nucleophilic reactivity. Our own earlier rationalizations of these correlations are, at best, incomplete and need thorough reexamination.

The reactions of nucleophiles with acetate esters have been the subject of numerous experimental studies. The rate constants obtained in these studies, particularly those obtained by Jencks and his coworkers,[2-4] probably furnish the most extensive body of data obtained under a standard set of conditions that is available for any class of reactions. These data furnish a unique opportunity for testing of hypotheses concerning the effects of structure on reactivity.

Figure 1 shows plots of log *k* for reactions of nucleophiles with phenyl acetate (PA) *vs.* log *k* for reactions of the same nucleophiles with other acetate esters. Quite obviously, no simple general linear correlation is shown by these data. Previous interpretations of the rate data have relied on the application of the Brϕnsted catalysis relationship,[2-4] in which limited "structural families" of nucleophiles, such as primary amines, are examined individually.

The complexity of the general picture indicated in Figure 1 almost certainly has its origin in mechanisms of the reactions, and interpretations of the Brϕnsted relationships have centered on this point. Early discussions of the mechanisms of these reactions postulated the existence of a tetrahedral reaction intermediate. Somewhat later, strong arguments against the existence of the tetrahedral intermediate were advanced.[2] These arguments were based on the apparently reasonable assumption that such an intermediate would have to be at equilibrium with respect to proton-transfer reactions. Recently, it has been shown that this assumption is not valid for at least some cases.[5] In the most recent work,[3-5] the reactions of nucleophiles with aryl acetates are postulated to proceed by a simple two-step mechanism uncomplicated by proton-transfer reactions of the intermediate (eq I).



Application of the Bodenstein approximation to this reaction scheme gives:

$$k_{\text{obsd}} = k_x/[1 + k_{-x}/k_{-y}] \qquad (1)$$

for the observed second-order rate constant of the reaction.

In our own work,[1,6] we have demonstrated that the reactions of a wide range of nucleophiles with various types of organic cations are well correlated by the equation:

$$\log k = \log k_0 + N_+ \qquad (2)$$

where k is the observed second-order rate constant for the reaction of a given nucleophile with a given cation in a given solvent, k_0 is dependent solely on the identity of the cation, and N_+ is dependent on the identity of the nucleophile and on the solvent in which the rate is measured. We noted that eq 2 gives a very good correlation for the rates of reactions of nucleophiles with *N*-acetoxy-4-methoxypyridinium ion (AMPP) and with several substituted *N*-acetylpyridinium ions. These esters had been studied by Jencks[2,4] as examples of esters with extremely good leaving groups. If the two-step mechanism applies to these reactions, the k_x step should be rate determining at least for the most basic nucleophiles. The good correlation of data by eq 2 suggests, in fact, the the k_x step is rate determining for reactions of nearly all nucleophiles.

When we attempted[6] to apply eq 2 to reactions of nucleophiles with aryl acetates, we found reasonable correlation for reactions of 2,4-dinitrophenyl acetate (DNPA), but poor correlations for reactions of *p*-nitrophenyl acetate (PNPA) and of phenyl acetate (PA). The correlation for reactions of DNPA showed rather large deviations for weakly basic nucleophiles. At this point, it was not clear whether the deviations from eq 2 were due to mechanistic changes in the reactions or simply due to inapplicability of the equation to reactions of neutral electrophiles.

Kice's observation[7] that the reactions of nucleophiles with phenyl α-disulfone (PDS) correlated well with reactions of the same nucleophiles with AMPP, and, therefore, must be correlated by eq 2, suggested strongly that the N_+ equation might apply to reactions of nucleophiles with neutral electrophiles *if the attack of nucleophile is rate determining.*

We hypothesize, then, that the rate constants, k_x, in the above mechanism for reactions of nucleophiles with esters are correlated by eq 2. Substitution of eq 2 into eq 1 gives

$$\log k_{\text{obsd}} = \log k_0 + N_+ - \log [1 + k_{-x}/k_{-y}] \qquad (3)$$

In order to test the validity of the hypothesis and the resulting eq 3, it is necessary to have some way of evaluating the quantities k_{-x}/k_{-y} for various nucleophiles and esters. The only available methods for this purpose appear to involve data fitting. If the k_{-x} parameters were allowed to vary for different esters, the parameterization would involve enough adjustable quantities that even perfect data fits would not be valid tests of our hypothesis.

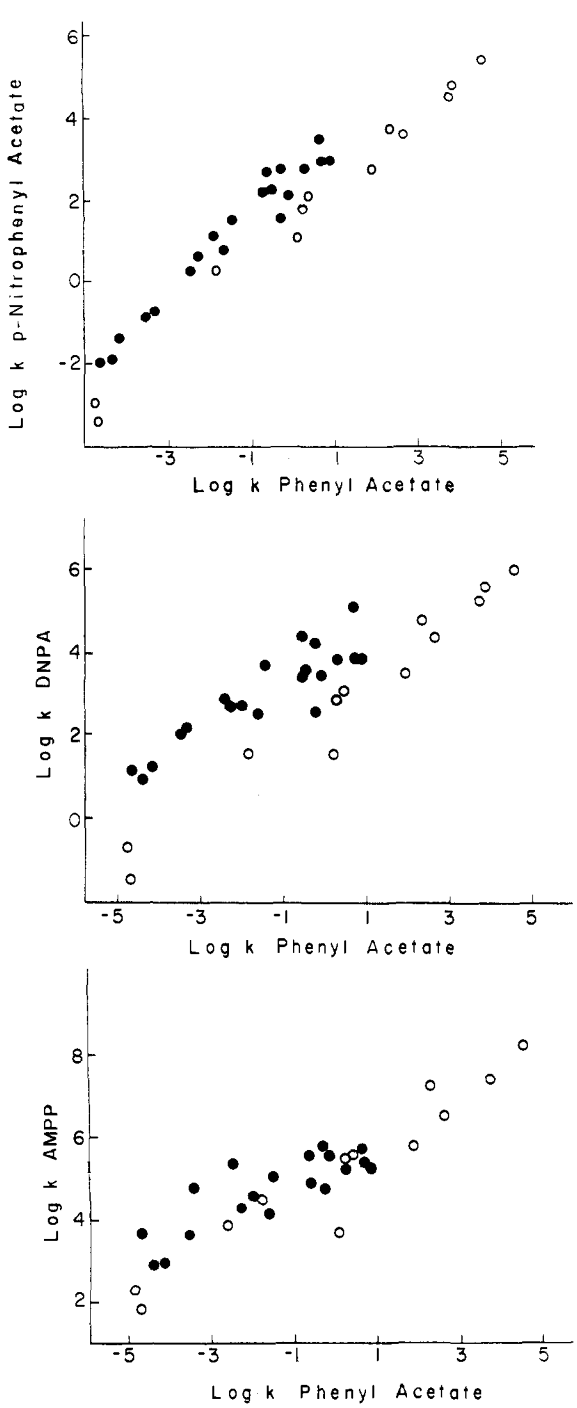


Figure 1. Log-log plots of rate constants for reactions of nucleophiles with phenyl acetate *vs.* those for reactions of other acetate esters. Open circles are for reactions of anionic nucleophiles; closed circles are for reactions of amines. DNPA is 2,4-dinitrophenyl acetate; AMPP is *N*-acetoxy-4-methoxypyridinium ion.

The most restrictive condition imaginable for the evaluation of the k_{-x} and k_{-y} parameters is that relative values of k_{-x} be required to be independent of the identity of the ester (*i.e.*, k_{-x} is independent of k_{-y}). This condition is quite drastic. It requires, for example, that k_{-y} be independent of the attacking nucleophile. Thus, if the k_{-y} step is rate determining, the observed rate constant will be directly proportional to the equilibrium constant for formation of the tetrahedral intermediate. It also requires that the relative value of log k_{-x} for an attacking nucleophile be identical with the relative value of log k_{-y} when the nucleophile is

Table I. Nucleophilic Parameters

No.	Nucleophile (solvent)	N_+	Log k_{-x} rel	Rms[a] dev	Electrophiles studied[a]
1	H_2O (water)	0	5.20	0.40	1,2,*3*,4,11,12,*13*,14,15,18,19,20,21,23,(**16**,**22**,**24**,**25**,**26**)
2′	CH_3OH (methanol)	1.18		0.38	*1*,11.12,13,14,15
3	$DabcoH^+$ (water)[b]	1.4	4.5	0.08	18,23,24,(**25**)
4′	$CF_3CH_2NH_2$ (water)	2.89	3.47	0.21	2,14,15,18,19,20,21,23,24,25,26
5′	$H_2NCONHNH_2$ (water)	3.17	4.22	0.27	2,14,15,18,19,23,24,25
6′	PiperazineH^+ (water)	3.18	3.14	0.33	17,*18*,19,20,23,24,25,26,(**22**)
7	Imidazole (water)	3.66	1.42	0.29	16,17,26,27(**18**,*23*,*24*,**25**)
8′	$C_6H_5SO_2^-$ (methanol)	3.67		0.06	4,5,6,7,8,9
9′	CN^- (water)	3.67	≪0	0.31	1,2,3,4,5,6,7,8,9,11,*16*,17,18,23,24,25,27
10′	CH_3ONH_2 (water)	3.88	3.20	0.12	1,2,26,(*14*,*15*)
11′	$H_2NCH_2CH_2NH_3^+$ (water)	3.91	1.95	0.23	2,14,15,17,18,23,24,25
12	p-$O_2NC_6H_4O^-$ (water)	4.05	2.00	0.27	18,19,26,(**25**)
13	Aniline (water)	4.10	5.20	0.15	18,23,24,25
14′	$H_2NCH_2CO_2C_2H_5$ (water)	4.21	2.86	0.27	2,14,15,*17*,18,19,20,21,23,24,25
15′	$C_6H_5NHNH_2$ (water)	4.38		0.18	2,15
16′	$H_2NCH_2CONHCH_2CO_2^-$ (water)	4.48	2.81	0.12	1,2,14,15.18,23,24,25
17′	OH^- (water)	4.75	≪0	0.19	1,2,3,4,5,6,7,8,9,11,12,13,14,15,16,(**17**,**18**,*19*,*20*,*21*,**22**,23,*24*,*25*,**26**,*27*)
18	Pyridine (water)	5.00	4.94	0.19	18,23,24,25
19′	$CH_3OCH_2CH_2NH_2$ (water)	5.05	1.93	0.13	18,23,24,25,27
20′	H_2NOH (water)	5.05	1.57	0.34	2,*17*,*18*,23,24,25,27
21′	$H_2NCH_2COO^-$ (water)	5.22	2.09	0.19	2,15,16,23,24,25,26,27
22′	Morpholine (water)	5.25	3.02	0.16	16,17,18,19,20,21,23,24,25,26,27,(*22*)
23	Dabco[b] (water)	5.3	3.8	0.27	18,23,24,25
24′	$C_2H_5NH_2$ (water)	5.31	0.82	0.27	2,15,16,18,23,24,25,26
25′	$H_2NCH_2CH_2NH_2$ (water)	5.37	1.52	0.18	2,15,17,18,23,24,25,27
26	4-Methylpyridine (water)	5.40	4.48	0.13	18.23,24,25
27	Quinuclidinol (water)	5.5	3.4	0.33	18,23,24,25
28′	$CH_3CH_2CH_2NH_2$ (water)	5.55	1.21	0.12	16,18,19,20,21,23,24,25
29	$C_6H_5O^-$ (water)	5.6	(0)	0.27	16,18,19,26,(**23**,**24**,**25**)
30′	H_2NNH_2 (water)	5.66	2.41	0.28	1,2,*16*,17,18,19,23,24,25,27,(*14*,*15*)
31	p-$CH_3C_6H_4O^-$ (water)	5.8	(0)	0.40	*16*,18,26,(**23**,**24**,**25**)
32′	CH_3NHNH_2 (water)	5.78		0.22	2,15
33′	CN^- (methanol)	5.94		0.12	4,5
34′	Piperazine (water)	5.94	2.75	0.23	16,17,18,29,20,23,24,25,26
35′	Piperidine (water)	6.11	1.75	0.26	15,16,17,18,19,20,21,23,24,25,26,(**22**)
36′	$CF_3CH_2O^-$ (water)	6.42	≪0	0.15	17,18,19,20,23,24,25,26,27(22)
37′	CH_3CONHO^- (water)	6.94	1.00	0.30	17,18,23,24,25,26
38′	OCl^- (water)	7.13			2
39′	CH_3O^- (water)	7.28	≪0	0.17	18,19,20,23,24,25,(22)
40′	CH_3O^- (methanol)	7.68		0.26	1,2,3,4,5,11,12,13,15
41′	SO_3^{2-} (water)	7.90		0.24	1,2,3,4,5,7,15
42′	HOO^- (water)	8.08	≪0	0.28	2,17,18,19,20.23,24,25,26
43′	CN^- (dimethyl sulfoxide)	8.60		0.39	1,2,3,*4*,5,7,*9*,10
44′	N_3^- (methanol)	8.85		0.22	1,4,5,6,7,8,9,(*10*)
45′	CN^- (dimethylformamide)	9.33		0.19	1,2,3
46′	N_3^- (dimethyl sulfoxide)	10.07		0.26	4,5,6,7,8,9,10
47′	$C_6H_5S^-$ (methanol)	10.51		0.38	1,2,4[c],5[c],6[c],7,8,9,10,*15*
48′	$C_6H_5S^-$ (dimethyl sulfoxide)	12.83			3
49	NO_2^- (water)	3.04	5.37	0.10	17,18,23,24
50	F^- (water)	>3.45	>6.20	0.04	18,23,(**17**,*24*,**25**)
51	CH_3COO^- (water)	>2.95	>6.20	0.27	17,18,19,20,23,26,(24,25)
52	N_3^- (water)	7.6	8.3	0.20	16,17,18,23,(*24*,**25**)

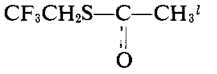
[a] Numbers correspond to the electrophiles identified in Table 11. Those electrophiles whose identifications are within parentheses are not included in the calculation of the root-mean-square deviation (rms dev). An italic number indicates that the difference between calculated and observed log k is 0.5–1.0 unit. A boldface number indicates that the difference between calculated and observed log k is greater than 1.0 unit. [b] Dabco is diazabicyclo[2.2.2]octane. [c] The calculated rate constants are above diffusion-controlled limits; observed rate constants are diffusion controlled.

the leaving group of the ester. For example, log k_{-x} must equal log k_{-y} for the attack of phenoxide ion on PA. We shall examine this condition in more detail in the Discussion section. For the moment, the important point is that the condition is sufficiently restrictive that fortuitous correlations of data by use of eq 3 and a single set of log k_{-x} values are extremely unlikely.

Treatment of Data

Reevaluation of N_+ Parameters. Before proceeding with a consideration of the reactions of esters, we wished to have a reliable set of N_+ values for as many nucleophiles as possible. In our previous work,[1,6] we have defined N_+ values directly from the measured rate constants for reactions of nucleophiles with either Malachite Green [bis(p-dimethylaminophenyl)phenylmethyl cation] or p-nitro(Malachite Green) [bis(p-dimethylaminophenyl)-p-nitrophenylmethyl cation]. For the present purposes, we have chosen a basic data set to allow a statistical evaluation of the parameters in eq 2.

Table II. Electrophilic Parameters

No.	Electrophile	Log k_0[a]	Log k_{-y}[b] rel	Rms[c] dev	Range[d]	Nucleophiles studied[e]
1	*p*-Nitro(Malachite Green)	−3.91	Inf	0.24	10.7	1,2′,9′,10′,16′,17′,30′,40′, 41′,43′,44′,45′,47′
2	Malachite Green	−4.13	Inf	0.26	9.7	1,4′,5′,9′,10′,11′,14′,15′, 16′,17′,20′,21′,24′,25′, 30′,32′,38′,40′,41′,42′, 43,′45′,47′
3	Crystal Violet	−5.42	Inf	0.36	12.1	1,9′,17′,40′,41′,43′,45′,48′
4	*p*-Nitrobenzenediazonium ion	0.68	Inf	0.29	10.4	1,8′,9,′17′,33′,40′,41′,*43*′, 44′,46′,47
5	*p*-Cyanobenzenediazonium ion	0.49	Inf	0.26	6.1	8′,9′,17′,33′,40′,41′,43′, 44′,46:,47
6	*m*-Chlorobenzenediazonium ion	−0.12	Inf	0.24	6.8	8′,9′,17′,44′,46′,47
7	*p*-Chlorobenzenediazonium ion	−0.62	Inf	0.14	7.0	8′,9′,17′,41′,43′,44′,46′,47′
8	Benzenediazonium ion	−1.20	Inf	0.15	6.8	8′,9′,17′,44′,46′,47′
9	*p*-Toluenediazonium ion	−1.54	Inf	0.28	7.2	8′,9′,17′,*43*′,44′,46′,47′
10	*p*-Methoxybenzenediazonium ion	−1.84	Inf	0.30	2.6	43′,46′,47′,(**44**)
11	*p*-Chlorophenyltropylium ion	0.43	Inf	0.34	8.2	1,2′,9′,17′,40′
12	Phenyltropylium ion	0.46	Inf	0.32	8.3	1,2′,17′,40′
13	*p*-Methoxyphenyltropylium ion	−0.02	Inf	0.30	8.4	1,2′,17′,40′
14	Tropylium ion	0.68	Inf	0.28	5.1	1,2′,4′,1**1**′,14′,16′,17′ (*10*,*30*)
15	*p*-Dimethylaminophenyltropylium ion	−1.46	Inf	0.31	11.5	1,2′,4′,5′,11′,14′,15′,16′, 17′,21′,24′,25′,32′,35′, 40′,41′,*47*′,(*10*,*30*)
16	Tri-*p*-anisylmethyl cation[f]	−0.91	Inf	0.35	4.0	7,*9*′,17′,21′,22′,24′,28′,29, *30*,*31*,34′,35′,52,(**1**)
17	$C_6H_5SO_2SO_2C_6H_5$[g]	−4.19	5.00	0.26	6.2	6′,7,9′,11′,*14*′,*20*′,22′,25′, 30,34′,35′,36′,37′,42′, 49,51,52,(**17**,**50**)
18	*N*-Acetoxy-4-methoxypyridinium ion[h]	−1.85	5.20	0.20	8.3	1,3,4′,5′,*6*′,9′,11′,12′,13′, 14′,16′,18′,19′,*20*′,22′, 23,24′,25′,26,27,28′,29, 30,31,34′,35′,36′,37′,39′, 42′,49,50,51,52,(**7**,**17**)
19	*N*-Acetyl-4-methylpyridinium ion[i]	0.78	4.50	0.26	8.9	1,4′,6′,12′,14′,22′,28′,29, 30,34′,35′,36′,39′,42′,51, (*17*)
20	*N*-Acetyl-3,4-lutidinium ion[i]	0.62	4.74	0.22	7.8	1,4′,6′,14′,22′,28′,34′,35′, 36′,39′,51,(*17*)
21	*N*-Acetyl-4-methoxypyridinium ion[i]	0.09	4.50	0.24	6.7	1,4′,14′,22′,28′,35′,(*17*)
22	*N*,*O*-Trimethylenephthalimidium ion[j]	0.74		0.85	4.9	**6**,7,*22*,**35**,36,40,(**1**,**17**)
23	2,4-Dinitrophenyl acetate[h]	−3.45	3.80	0.25	12.7	1,3,4,*6*,9′,11′,13,14′,16′,**18**, 19′,20′,21′,22′,23,24′,25′, 26,27,28′,30,34′,35′,36′, 37′,39′,42′,49,50,51,52, (*7*,17,**29**,**31**)
24	*p*-Nitrophenyl acetate[h]	−4.46	2.00	0.19	12.6	3,4,5,6,9′,11,13,14,16,18,19, 20,21,22,23,24,25,26,27, 28′,30,34,35′,36′,37′,39′, 42′,49,(**1**,*7*,*17*,**29**,**31**,*50*, 51,*52*)
25	Phenyl acetate[h]	−5.41	(0)	0.11	14.0	4,5,6,9,11,13,14,16,18,19, 20,21,22,23,24,25,26,27, 28,30,34,35,36,37,39,42, (**1**,**3**,**12***17*,**29**,**31**,**50**,51, **52**)
26	*N*-Acetylimidazolium ion[k]	−0.38	1.42	0.27	9.6	4,6,7,10,12,21,22,24,29,31, 34,35,36,37,39,51,(**1**,**17**)
27	 $CF_3CH_2S\text{—}\underset{\underset{O}{\|}}{C}\text{—}CH_3$[l]	−4.99	2.07	0.21	2.4	7,9,17,19,20,21,22,25,30,36

[a] Second-order rate constants in units of M^{-1} sec^{-1}; rate constants for reactions of water and methanol are pseudo-first-order constants in units of sec^{-1}. [b] See eq 4. [c] Root-mean-squaie deviation of calculated and observed log k's. [d] Range of log k observed. [e] Numbers correspond to the identification of the nucleophiles given in Table I. Those numbers marked with a "prime" indicate reactions included in the basic data set discussed in the text. Those numbers in parentheses were not included in the calculation of the root-mean-square deviation. An italic number indicates a deviation of 0.5–1.0 unit between calculated and observed log k; a boldface number indicates a deviation of greater than 1 unit. [f] Data from C. A. Bunton and S. K. Huang, *J. Amer. Chem. Soc.*, **94**, 3436 (1972); **95**, 2701 (1973); **96**, 515 (1974). [g] Data from J. L. Kice and E. Legan, *ibid.*, **95**, 3912 (1973). [h] Data from W. P. Jencks and M. Gilchrist, *ibid.*, **90**, 2622 (1968). [i] Data from A. R. Fersht and W. P. Jencks, *ibid*, **92**, 5442 (1970). [j] Data from N. Gravetz and W. P. Jencks, *ibid.*, **96**, 489, 499, 507 (1974). [k] Data from A. R. Fersht and W P. Jencks, *ibid.*, **93**, 178 (1971). [l] Data from M. J. Gregory and T. C. Bruice, *ibid.*, **89**, 2121 (1967).

The basic data set was chosen by examination of plots according to eq 2 using previously evaluated N_+ parameters. Points clearly deviating from the plots were excluded from the data set. The reactions chosen for inclusion are indicated in Tables I and II by primed numbers. The log k_0 value for Malachite Green was arbitrarily set equal to −4.13 to preserve the magnitudes of the numbers previously reported.

Starting with approximate values of N_+ and log k_0 obtained from the plots mentioned above, iterative averaging of, first, log k_0 for each electrophile, then, N_+ values for each nucleophile was carried out until further iterations led to no changes greater than 0.01 unit in any of the parameters.

The basic data set consisted of 204 rate constants for which the final log k_0 and N_+ parameters employed in eq 2 gave a correlation with an average deviation of 0.20 unit, a root-mean-square deviation of 0.25 unit, and a maximum deviation of 0.66 unit. The nucleophiles included in the basic data set are referred to as "prime nucleophiles" in the remaining discussion. Their identification numbers are marked by primes in Table I.

Evaluation of Relative Log k_{-x} for Prime Nucleophiles. The empirical evaluation of relative log k_{-x} parameters requires initial estimates of log k_0 for DNPA, PNPA, and PA. The values for DNPA and PNPA were obtained from the basic data set described above. The log k_0 value for PA was obtained by comparing rates of reactions of hydroxide, peroxide, methoxide, and trifluoroethoxide ions with PA with those for reactions of the same ions with DNPA and PNPA. Since these nucleophiles are expected to be much poorer leaving groups than any of the phenoxides, the relative rates of reactions of the three esters should depend only on their log k_0 values.

The log k_{-x} (and, therefore, the log k_{-y}) value for phenoxide ion is arbitrarily set equal to zero. Initial estimates of log k_{-x} for other nucleophiles were obtained by application of eq 3 to the data for reactions of PA, using the N_+ values for the prime nucleophiles and the initial estimate of log k_0 for PA.

From this point, an iterative procedure was employed to obtain the final log k_{-x} values for the nucleophiles, the log k_0 values for DNPA, PNPA, and PA, and the log k_{-y} values for DNPA and PNPA, as follows.

(1) Obtain log k_{-y} values for DNPA and PNPA by application of eq 3 using the current values of log k_{-x} for the nucleophiles and log k_0 for the esters.

(2) Increment the log k_{-x} value of each nucleophile so that the sums of the squares of the deviations of eq 3 applied to reactions of PA, PNPA, and DNPA are minimized.

(3) Iterate steps 1 and 2 until further iterations lead to no changes greater than 0.05 unit in any log k_{-x} or log k_{-y} values.

(4) Obtain new values of log k_0 for PA, PNPA, and DNPA by averaging deviations from eq 3.

(5) Repeat steps 1 through 4.

The final values obtained are shown in Tables I and II.

Reactions of Nucleophiles with Acetylimidazolium Ion[4] (AcImH$^+$) and with Trifluoroethyl Thiolacetate[8] (TFSAc). With the values of N_+ and log k_{-x} for the prime nucleophiles, values of log k_0 and log k_{-y} for AcImH$^+$ and TFSAc were obtained by iterative adjustment and application of eq 3 to minimize the sums of squares of deviations between observed and calculated values of log k_{obsd}. The values obtained are shown in Table II.

Reactions of Aniline, Pyridine, 4-Picoline, Quinuclidinol, and Dabco with Esters. Rate constants for reactions of the listed amines with AMPP, DNPA, PNPA, and PA have been reported.[2] The values of N_+ and log k_{-x} for these nucleophiles were obtained by iterative incrementation of values to minimize sums of squares of deviations from eq 3, subject to the restriction that log k_{-y} for AMPP be equal to log k_{-x} + 0.3 for pyridine. This somewhat arbitrary, but reasonable, restriction assumes that the leaving group ability of 4-methoxypyridine *N*-oxide is twice that of pyridine and is found to be consistent with all the data available.

The parameters obtained are reported in Table I. Values of log k_{-y} for *N*-acetyl-4-methylpyridinium ion (AMeP) and for *N*-acetyl-4-methoxypyridinium ion (AMeOP) were set equal to log k_{-x} for 4-picoline.

Reactions of Imidazole and of Azide Ion. Rate constants for reactions of these two nucleophiles with tri-*p*-anisylmethyl cation[9] (TAM) and with several esters[2-5] have been reported. The N_+ values for both nucleophiles, reported in Table I, are based only on the reactions with TAM. The log k_{-x} value for imidazole is set equal to the log k_{-y} value for AcImH$^+$. The log k_{-x} value for azide ion is obtained from the reported rate constant for reaction with AMPP by application of eq 3.

Reactions of DabcoH$^+$, Acetate, Fluoride, and Nitrite Ions. Values of N_+ and log k_{-x} for these four nucleophiles were obtained in a manner analogous to that described above for aniline, pyridine, etc., except that the reactions of PA were excluded from the data considered. The reaction of acetate ion with PA is known to be a case of general base catalysis of the water reaction rather than nucleophilic attack,[10] and the other nucleophiles considered here have p*K*'s similar to that of acetate ion. The reported rate constants for reactions of acetate ion with DNPA and PNPA have been corrected for the general base catalysis contribution[10] in the present analysis.

Since the log k_{-x} values found for fluoride ion and acetate ion are greater than the log k_{-y} values for any of the esters, the only meaningful quantities for these nucleophiles which are obtainable by application of eq 3 are the values of [N_+ − log k_{-x}]. Thus, the N_+ and log k_{-x} values found for these nucleophiles are only lower limits.

The log k_{-y} value for PDS was obtained by application of eq 3 to the measured rate constant for reaction of PDS with nitrite ion using the N_+ and log k_{-x} values found for this nucleophile.

Reactions of Phenoxide Ions. Rate constants for the reactions of phenoxide and *p*-toluoxide ions with TAM, AMPP, DNPA, PNPA, PA, and AcImH$^+$ have been reported. The log k_{-x} value for phenoxide ion is set by the log k_{-y} value for PA, and we assume that the log k_{-x} for *p*-toluoxide ion is roughly equal to that for phenoxide ion. The values of N_+ for these nucleophiles, reported in Table I, are based on the reactions with TAM, AMPP, and AcImH$^+$, but the calculated rate constants for reactions with the aryl acetates are seriously above the observed values when these N_+ values are used in eq 3.

Similarly, the N_+ value for *p*-nitrophenoxide ion reported in Table I is based on the rate constants for reactions with AMPP, AMeP, and AcImH$^+$. This value, along with the log k_{-x} value which is equal to the log k_{-y} for PNPA, gives calculated rate constants for reactions of the aryl acetates which are seriously above the observed values.

Reactions of *N,O*-Trimethylenephthalimidium Ion[11] (PHTH). The rate constants for reactions of several nucleophiles with PHTH are correlated very poorly by eq 2. Use of the parameters shown in Table II for PHTH gives calculated log k values which are more than 1 unit off from the observed values for four of the eight reactions studied.

Discussion

A summary of the reactions considered and the parameters found and an indication of the quality of the correlations are given in Tables I and II. In general, the correlations are quite remarkable. Of the 382 rate constants included in the present examination, only 24 show deviations of more than 1 log unit between calculated and observed values: another 23 show deviations of between 0.5 and 1.0 log unit.

Most of these large deviations are associated with particular reagents rather than being randomly distributed among the data, and many of them have rational explanations in terms of known mechanistic detail. We shall consider these deviant cases before proceeding to a general discussion of the nucleophilic and electrophilic parameters.

Reactions of Water and Hydroxide Ion. The reactions of water and of hydroxide ion account for nine of the deviations of more than 1 log unit and for eight of the deviations of between 0.5 and 1.0 log unit.

We have previously commented at length on the unique nature of the reactions of water as a nucleophile.[1,6] In every case that has been closely examined, the reaction of water with an organic cation involves general base catalysis and is not, therefore, a simple nucleophilic reaction analogous to the reactions of other nucleophiles. The surprising fact in the present examination is that most of the reactions of water, even several of those with esters, are correlated by eq 2 and 3. Perhaps this is indicative of a similarity of mechanisms for these reactions.

The reactions of hydroxide ion in aqueous solution are also likely to be unusual types of reactions. For other nucleophiles, it is obviously necessary that the nucleophile and electrophile come into direct contact before formation of the combination product can occur. In the case of the reaction of hydroxide ion, however, a proton transfer from water separating the electrophile from hydroxide ion, simultaneously with formation of a bond between the solvent molecule and the electrophile, could furnish a unique reaction path. This postulated path, of course, is nothing more than general base catalysis of the water reaction by hydroxide ion. We have commented earlier[12] that the Brφnsted relationship applied to the general base catalysis of the reaction of water with Malachite Green makes it appear reasonable that hydroxide ion may be acting as a general base catalyst.

The reaction of acetate ion with PA is known[10] to proceed essentially completely by general base catalysis of the water reaction and has $\log k = -6.42$.[2] The rate constant for reaction of hydroxide ion with PA gives $\log k = 0.10$. Thus, the hydroxide reaction could easily be general base catalysis with a Brφnsted slope of 0.6. The same conclusion results from examination of the data for reactions of PNPA[2,10] and is not inconsistent with the data for reactions of the other esters.

The postulate that hydroxide ion is acting as a general base catalyst for the reaction of water with electrophiles is not in accord with "the rule" formulated by Jencks[13] without some modification of that rule. According to the strict application of this rule, since the reaction of hydroxide ion with water in a simple proton exchange does not involve an unfavorable free-energy change, general base catalysis would not be expected to occur. We believe, however, that this interpretation is naive for the present cases.

The simple proton transfer between water and catalyzing base which is pertinent to the application of Jencks' rule to the present case can be written

$$[\mathrm{HO^-\ H_2O\ E}] \rightleftharpoons [\mathrm{H_2O\ HO^-\ E}]$$

where E is the electrophile. Essentially, this exchange of a proton places the electrophile in a position which was originally occupied by the solvation shell of the hydroxide ion. Thus, the free-energy change for the process is expected to be very unfavorable. General base catalysis would avoid formation of the unstable intermediate $[\mathrm{H_2O\ HO^-\ E}]$. Thus, the postulated general base catalysis by hydroxide ion is in accord with the *basis* of Jencks' rule.

Reactions of DabcoH$^+$, Fluoride, and Azide Ions. The reactions of these three ions with PA give more than 1 log unit deviation from eq 3, and the reactions of the two anions with PNPA give deviations of more than 0.5 log unit.

We have already pointed out above that the reaction of acetate ion with PA is known to involve general base catalysis and gives $\log k = -6.46$. Both DabcoH$^+$ and fluoride ion have basicities quite similar to that of acetate ion, and the log k's for reactions of these ions with PA are -6.60 and -6.50, respectively. The similarity of rate constants to that for acetate ion strongly suggests that these reactions are also general base catalysis rather than nucleophilic attack.

In view of the smaller, but still significant, contribution of general base catalysis to the reaction of acetate ion with PNPA,[10] we also expect some general base catalysis contribution to the observed rate constants for reactions of DabcoH$^+$ and of fluoride ion with this ester. A 50% component of such catalysis would bring the observed rate constants into reasonable agreement with the calculated values.

The reported values of log k for reactions of azide ion with PA and PNPA are -3.63 and -1.52, respectively. These values are more than 3 units higher than those for reactions of acetate ion with the same esters. Since acetate ion and azide ion have similar basicities, it appears that the large deviations from eq 3 for the reaction of azide ion with PA (calculated $\log k = -6.11$) and with PNPA (calculated $\log k = -3.16$) do not result from operation of the general base catalysis mechanism. We can offer no reasonable explanation for these deviations at this time.

For analogous reasons, it does not appear that the large deviation between observed and calculated values of log k (observed value $= -0.75$; calculated value $= -1.97$) for the reaction of fluoride ion with PDS can be attributed to operation of the general base catalysis mechanism. It does seem reasonable to suppose, however, that the intermediate resulting from attack of fluoride ion on PDS has a greater stability, relative to the one resulting from attack of oxygen and nitrogen nucleophiles, than in the corresponding reactions of the acetate esters. This could lead to the $\log k_{-\mathrm{x}}$ value for fluoride ion being smaller for attack on sulfur than for attack on carbon.

Reactions of Imidazole and Phenoxide Ions. Use of the parameters shown in Table I gives poor results when applied to the reactions of phenoxide ion with DNPA, PNPA, and PA; the reactions of *p*-toluoxide ion with TAM, DNPA, PNPA, and PA; the reaction of *p*-nitrophenoxide ion with PA; and the reactions of imidazole with AMPP, DNPA, PNPA, and PA. For all the reactions of the phenoxides with aryl acetates, the observed log k's are approximately 1 unit lower than the calculated values. Similarly, the observed log k's for reactions of imidazole with the four esters listed are appreciably lower than the calculated values. No other choice of parameters for these nucleophiles would appreciably improve the situation even if we relaxed the restriction that $\log k_{-\mathrm{x}}$ for the phenoxides must be equal to the $\log k_{-\mathrm{y}}$ for the aryl acetate with the corresponding phenoxide as leaving group.

Several of the rate constants above have been determined by indirect methods which depend on interrelationships among the rate and equilibrium constants for reactions of phenoxide ions with AcImH$^+$ and those for reactions of imidazole with aryl acetates. It is easily conceivable that some of the rate constants could be in error by as much as a factor of 2. For example, the pK_a of AcImH$^+$, which is directly used in the calculation of many of the rate constants, was taken to be 3.6 in the original paper[14] reporting rate constants for reactions of phenoxides with AcImH$^+$ but was reported as 3.86, under similar conditions, in a later paper.[4] We have used the later value to recalculate these rate constants for our present examination. It is most unlikely, however, that the errors could account for the large deviations found between observed and calculated values.

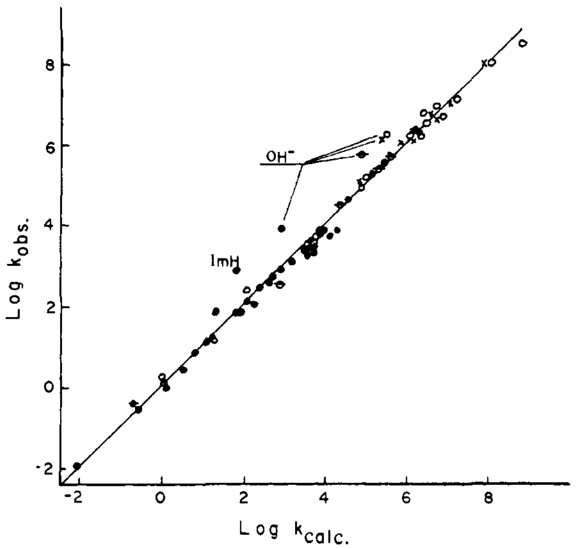


Figure 2. Data for reactions of nucleophiles with cationic esters as correlated by eq 3. Data for reactions of the different esters are identified as follows: (●) AMPP; (○) AMeP; (⊖) AMeOP; (X) *N*-acetyl-3,4-lutidinium ion. See text for other abbreviations.

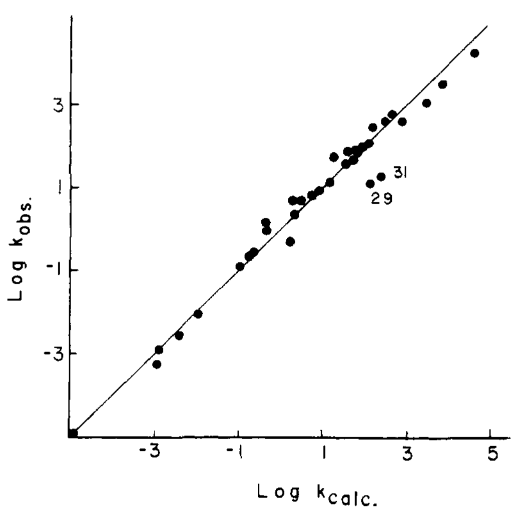


Figure 3. Data for reactions of DNPA with nucleophiles as correlated by eq 3. Identification numbers on the plot correspond to those given in Table 1.

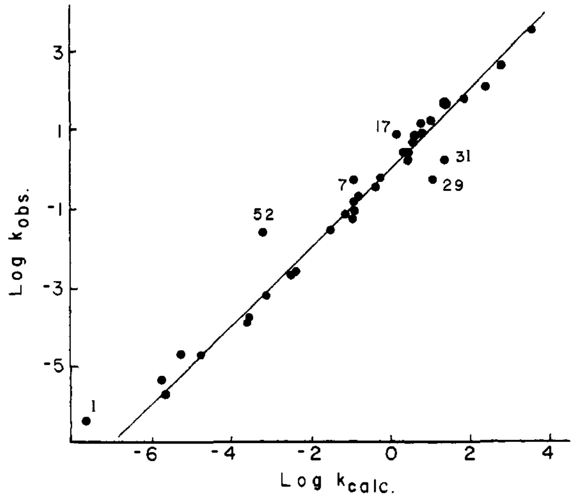


Figure 4. Data for reactions of PNPA with nucleophiles as correlated by eq 3. Identification numbers on the plot correspond to those given in Table 1.

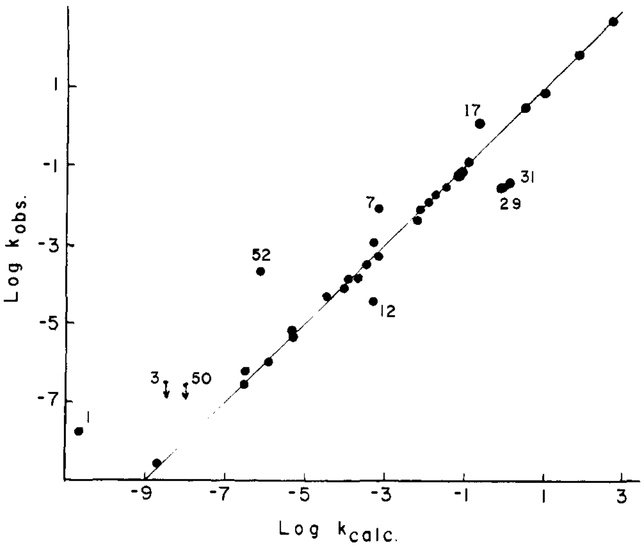


Figure 5. Data for reactions of PA with nucleophiles as correlated by eq 3. Identification numbers on the plot correspond to those given in Table 1. See text for explanation of limiting points shown for DabcoH$^+$ and fluoride ion.

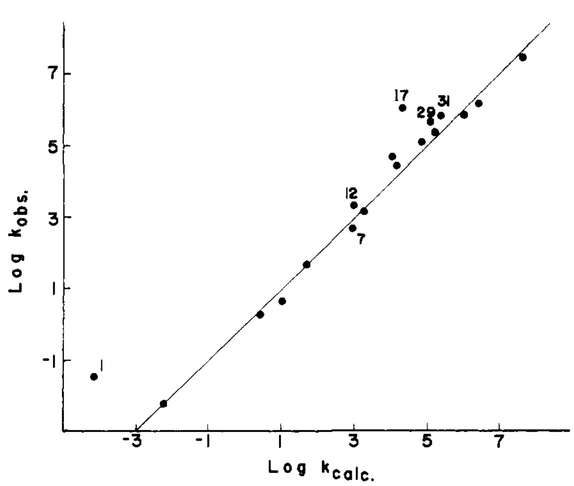


Figure 6. Data for reactions of acetylimidazolium ion with nucleophiles as correlated by eq 3. Identification numbers on the plot correspond to those in Table 1.

There is little doubt that these reactions involve direct nucleophilic attack since the substitution products have been directly observed in several cases. Also, the rate measurement for the reaction of phenoxide ion with PA was made by observing the incorporation of ^{14}C-labeled phenoxide into PA.[15]

At the present time, we can offer no rational explanation for these deviations. In view of the excellent correlations obtained for other reactions, however, it does not appear that these deviations can be ascribed to a general breakdown of the hypothesis that the relative values of log k_{-x} for nucleophiles are independent of the leaving group of the ester.

Reactions of *N*,*O*-Tetramethylenephthalimidium Ion. The reactions of PHTH with nucleophiles are simply not correlated by the N_+ equation even though the pK_R (*ca.* −0.1)[11] and reactivity of this cation are within the range shown by other cations considered here. A particularly striking illustration of the odd pattern of reactivity of PHTH is furnished by comparisons with reactions of AMeP. For reaction of methoxide ion, log k for PHTH is 0.4 unit lower than that for AMeP, and for reaction of piperidine, log k for PHTH is 1.3 units lower than that for AMeP, but for reaction of piperazineH$^+$, log k for PHTH is 1 unit *greater* than that for AMeP.

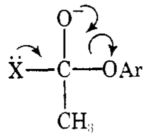
It is rather disappointing that the reactions of this cation are not correlated with reactions of esters since some data are available which give estimates of leaving-group abilities of nucleophiles from the tetrahedral addition product with PHTH. From the measured rates of breakdown (acid catalyzed) of the adducts of PHTH with secondary amines and estimates of the p*K*'s of the adducts, rate constants for the formation of amine plus PHTH were estimated[11] as follows: piperidine, log $k = 1.52$; *N*-methylpiperazine, log $k = 3.56$; morpholine, log $k = 3.92$; imidazole, log $k = 1.22$; and piperazineH$^+$, log $k = 6.5$. The qualitative order of leaving-group abilities, piperazineH$^+$ > morpholine > piperazine > piperidine > imidazole, is the same as that given by the log k_{-x} values in Table I, but the quantitative agreement is rather poor.

In view of the poor correlation of the forward reaction, the qualitative agreement for the reverse reactions is probably all that could be expected.

Correlations and Mechanisms of the Reactions of Nucleophiles with Esters. The correlations of ester reactions by eq 3 using the parameters reported in Tables I and II are shown graphically in Figures 2-6. All the data, including the deviant points discussed above, are shown in these plots. These figures may be compared with Figure 1 in which no account of mechanism is taken.

We believe that the quality of these correlations provide strong support for the validity of the mechanism assumed, for the hypothesis that the attack of nucleophiles on esters are governed by the N_+ equation, and for the supplementary assumption that the relative leaving-group abilities of nucleophiles are independent of the ester leaving group. The simplicity and lack of flexibility of eq 3 make it most unlikely that these correlations are fortuitous.

We have already mentioned in the introductory section that the assumption that relative leaving-group abilities of nucleophiles are independent of the ester leaving group is quite drastic. Jencks[11] has argued, for example, that the leaving-group ability of an aryl oxide would be expected to depend on the driving force which might be exerted by lone pairs of another group in the tetrahedral intermediate:



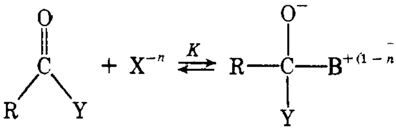
Such an effect would, of course, invalidate the assumption that we have used to allow evaluation of a single scale of log k_{-x} values. The fact that a single scale of log k_{-x} values works so well in the present correlations, then, argues against the operation of the effect. In particular, the fact that log k_{-x} values which work for the reactions of aryl acetates also work for the AMPP reactions is quite striking. For reactions of aniline, pyridine, nitrite ion, and acetate ion with both AMPP and the aryl acetates, the log k_{-y} terms contribute significantly to the calculated values of log k_{obsd}. All these reactions are well correlated by eq 3, indicating strongly that the log k_{-y} terms are not dependent on nucleophile. Similarly, it is difficult to understand how the reactions of both TFSAc and the reactions of PA with a range of nucleophiles could be so well correlated by a single scale of log k_{-x} values if the sulfur and oxygen lone pairs provided differential driving forces for leaving of the nucleophile.

Table III. Comparison of Nucleophilic Parameters

Nucleophile	$[N_+ - \log k_{-x}]$	pK_a[a]	p$K_a - [N_+ - \log k_{-x}]$
	Simple Primary Amines		
$CF_3CH_2NH_2$	−0.6	5.8	6.4
$H_2NCH_2CH_2NH_3^+$	1.9	7.4	5.5
$H_2NCH_2CO_2C_2H_5$	1.3	7.9	6.3
$H_2NCH_2CONHCH_2COO^-$	1.7	8.2	6.4
$CH_3OCH_2CH_2NH_2$	3.1	9.7	6.6
$C_2H_5NH_2$	4.5	11.0	6.5
$H_2NCH_2COO^-$	3.1	9.8	6.7
$H_2NCH_2CH_2NH_2$	3.9	10.2	6.3
$CH_3CH_2CH_2NH_2$	4.4	10.9	6.5
Aniline	−1.1	4.8	5.9
	Simple Secondary Amines		
PiperazineH$^+$	0.1	6.0	5.9
Morpholine	2.3	8.9	6.6
Piperazine	3.2	10.1	6.9
Piperidine	4.4	11.4	7.0
	Tertiary Amines		
Quinuclidinol	2.1	10.1	8.0
Dabco	1.5	9.2	7.7
DabcoH$^+$	−3.1	3.5	6.6
Imidazole	2.3	7.2	4.9
Pyridine	0.1	5.5	5.4
4-Picoline	1.0	6.3	5.3
	"α-Effect" Nucleophiles		
$H_2NCONHNH_2$	−1.0	3.9	4.9
CH_3ONH_2	0.7	4.6	3.9
$HONH_2$	3.4	6.2	2.8
H_2NNH_2	3.3	8.2	4.9
CH_3CONHO^-	5.9	9.4	3.5
	Anions		
CH_3COO^-	−3.2	4.7	7.9
F^-	−2.8	3.1	5.9
NO_2^-	−2.3	3.4	5.7
p-Nitrophenoxide	2.0	7.1	5.1
Phenoxide	5.6	10.0	4.4
p-Toluoxide	5.8	10.1	4.3
N_3^-	−0.7	4.0	4.7

[a] The pK_a values are taken from ref 2.

Another indication of the validity of the log k_{-x} scale can be gained by an examination of the quantities $[N_+ - \log k_{-x}]$ for the various nucleophiles. On the basis of the two-step mechanism for ester reactions, these quantities are directly related to the relative values of log *K* for the equilibrium addition of the nucleophile to the ester to form the tetrahedral intermediate:



$$RC(=O)Y + X^{-n} \overset{K}{\rightleftarrows} R{-}C(O^-)(Y){-}B^{+(1-n)}$$

For a "structural family" of nucleophiles, such as a series of primary or secondary amines, we expect that the equilibrium constants for this reaction will be linear functions of the basicities of the nucleophiles. Jencks has argued,[3] for example, that a β_{nuc} of close to unity (he actually uses a value of 0.9) indicates that the k_{-y} step is rate determining. Table III shows a comparison of the quantities $[N_+ - \log k_{-x}]$ and p*K*'s for various types of nucleophiles.

The data for primary and secondary amines show, as expected, a reasonably constant difference between pK_a and $[N_+ - \log k_{-x}]$, except for the two monoprotonated amines.

Even more striking is the fact that the differences between pK_a and $[N_+ - \log k_{-x}]$ for "α-effect" nucleophiles are much smaller than those for primary and secondary amines. Thus, the equilibrium constants for formation of tetrahedral intermediates from "α-effect" nucleophiles are unusually high relative to those for primary and secondary amines of similar basicity. This conclusion is in agreement with previous observations[6,16] on the equilibrium constants for reactions of amines and "α-effect" nucleophiles with organic cations.[17]

According to the present analysis, the attack of nucleophile on ester is rate determining for those cases where log k_{-y} is greater than log k_{-x}, and the breakdown of the tetra-

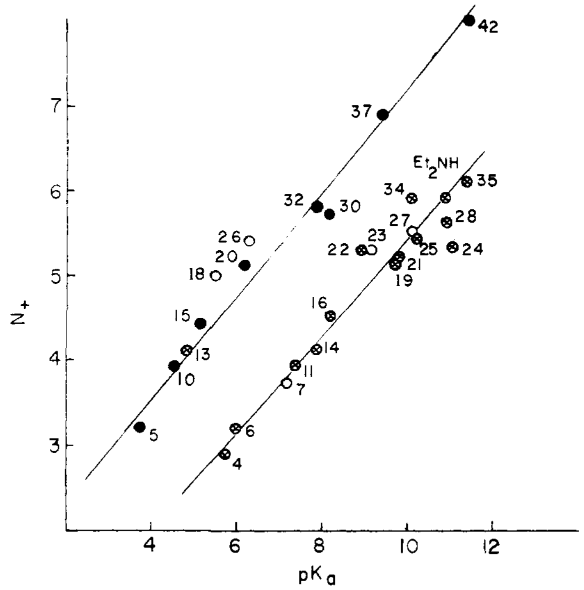


Figure 7. Brϕnsted plot of N_+ values for amines. Identification numbers are from Table I. (⊗) Primary and secondary amines; (○) tertiary amines; (●) "α-effect" nucleophiles.

hedral intermediate is rate determining in those cases where log k_{-x} is greater than log k_{-y}. The general conclusions concerning the identity of the rate-determining step which result from examination of the parameters in Tables I and II are in agreement with conclusions reached by Jencks[2-5] from analysis of the application of the Brϕnsted relationship. There are, however, some minor disagreements. Jencks concludes, for example, that the reactions of weakly basic amines, such as trifluoroethylamine, with AMPP involve rate-determining breakdown of the intermediate, while the parameters in Tables I and II indicate that the reactions of all the amines with AMPP involve rate-determining attack. Only in the cases of acetate, nitrite, fluoride, and azide ions do the log k_{-x} parameters exceed the log k_{-y} for AMPP. These minor disagreements result from disagreements concerning the interpretations of curved Brϕnsted plots given by Jencks.[2-5]

Nucleophilic Parameters and Brϕnsted Relationships. A plot of N_+ parameters *vs.* pK_a for the conjugate acids of amines and "α-effect" nucleophiles is shown in Figure 7. The points for aliphatic primary, secondary, and tertiary amines define a moderately good straight line with a slope, β_{nuc}, of 0.56. If the primary amines are considered alone, the Brϕnsted slope is 0.49. Both of these values are considerably greater than those considered by Jencks as indicative of rate-determining attack of nucleophiles on esters.[5,11] In most of the cases examined by Jencks, however, the Brϕnsted plots are fitted by curved lines with only the most basic amines falling on the portion with small slope. The most convincing data to support the contention of very small Brϕnsted slope for rate-determining amine attack are derived from Jencks' study of the reactions of PHTH.[11] In this case, four amines, methylpiperazineH$^+$, piperazineH$^+$, morpholine, and piperidine, gave a Brϕnsted slope of 0.1. We have already noted that these reactions are not correlated by eq 2.

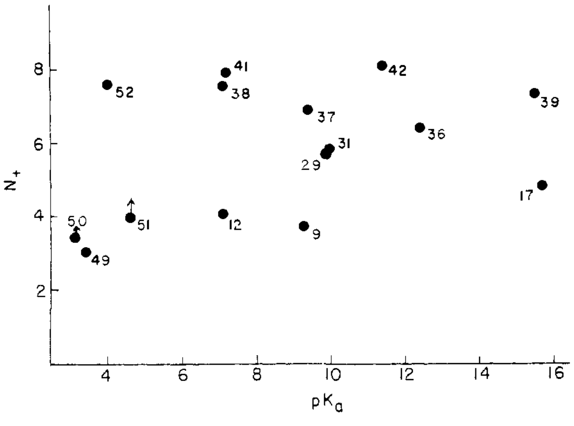


Figure 8. Brϕnsted plot of N_+ values for anions. Identification numbers are from Table I.

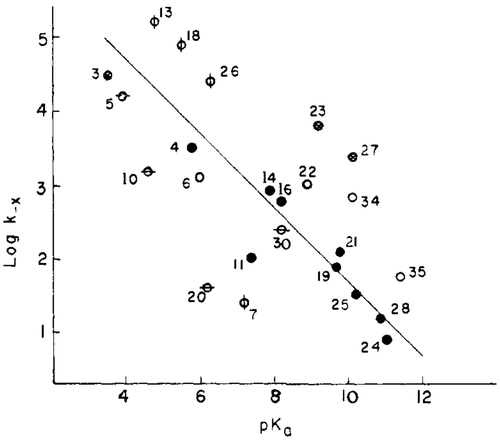


Figure 9. Brϕnsted plot of leaving-group abilities for amines. Identification numbers are from Table I. (●) Primary amines; (○) secondary amines; (⊗) tertiary amines; (ϕ) aromatic amines; (⊖) "α-effect" amines.

Since the N_+ values shown in Table I correlate the reactions of amines with several organic cations when employed in eq 2,[6] these reactions must give a Brϕnsted slope of *ca.* 0.5. We do not understand why this slope is so far different from that for reactions of PHTH but note that many more amines are included in the N_+ correlation than in the Brϕnsted correlation for reactions of PHTH. It seems to us to be most unlikely that the N_+ values would give such a good correlation for reactions of AMPP (by use of the simple eq 2 for all the amines) if some of these reactions involved rate-determining attack, while others involved rate-determining breakdown. Thus, we believe that the data for reactions of PHTH are misleading in showing the small Brϕnsted slope, and that rate-determining attack of amines on esters will generally be characterized by Brϕnsted slopes of *ca.* 0.5, consistent with the correlations given in the present paper.

It is interesting to note in Figure 7 that the data for "α-effect" nucleophiles give quite a good Brϕnsted correlation with a slope of 0.62. Even the anionic reagents HOO$^-$ and CH$_3$CONHO$^-$ are included in this plot. It is surprising to note that aniline, pyridine, and 4-picoline appear to behave as "α-effect" nucleophiles in this respect, while imidazole appears with the aliphatic amines.

The Brϕnsted plot of N_+ values for anionic nucleophiles is shown in Figure 8. There is certainly no simple relationship between reactivity and basicity for these nucleophiles.

A plot of log k_{-x} *vs.* pK_a for amine nucleophiles is shown in Figure 9. Close inspection of Figures 7 and 9 makes several conclusions obvious. (1) Imidazole (no. 7) is a much poorer leaving group than expected from its pK value and the behaviors of other tertiary amines. (2) Aniline (no. 13), pyridine (no. 18), and 4-picoline (no. 26) are both better entering and better leaving groups than expected from their pK values relative to primary and secondary amines. The leaving-group abilities of these amines, however, follow the pattern of aliphatic tertiary amines. (3) The "α-effect" nucleophiles are better entering groups but poorer leaving groups than expected from their pK's relative to primary and secondary amines. The very good Brønsted plot for entering "α-effect" nucleophiles does not appear for the leaving-group abilities of these amines. (4) The monoprotonated diamines piperazineH$^+$ (no. 6) and ethylenediamineH$^+$ (no. 11) have entering-group abilities about as expected but are poorer leaving groups than expected from their pK's relative to other primary and secondary amines. (5) The simple alkoxide ions are much poorer leaving groups than amines of similar pK, but the generalization does not apply to acetate, fluoride, or nitrite ions.

Conclusions 1 and 5 are in agreement with results obtained by Jencks[11] concerning leaving-group abilities from the tetrahedral intermediate formed from PHTH. Conclusion 3 is not in agreement with the results obtained from reactions of PHTH. In this latter connection, however, we may note from Figure 9 that the "α-effect" nucleophiles show a rather variable behavior. Hydrazine (no. 30) is quite comparable to primary amines as a leaving group, but the other "α-effect" nucleophiles are much poorer leaving groups than other amines of similar pK.

General Features of the N_+ Correlations. The success of the present application of eq 2 indicates a much greater generality than we had anticipated. In fact, the observed generality forces us to retract and reexamine virtually all our earlier postulates concerning the fundamental factors which give rise to such simple behavior.

At the present time, we are unable to formulate a consistently rational model which will accommodate all the empirical observations. In the following discussion, what appear to us to be some of the more important and confusing of these observations are listed, and apparent paradoxes are brought out.

(a) **Rate *vs.* Equilibrium Behavior.** In general, there is no correlation between rate and equilibrium constants for the nucleophile–electrophile reactions. There is also little or no correlation of the equilibrium constants for reactions of a series of nucleophiles with one electrophile *vs.* those for another electrophile.[18-21] The conclusion seems obvious that steric and specific bonding effects which are present in the products of the reactions are not present at the transition states. The implication, then, is that the nucleophile and electrophile are separated by rather large distances at the transition states for the reactions.

This implication appears to be contradicted by the observation of fairly large Brønsted slopes for reactions of amine nucleophiles as discussed above. Similarly, the Hammett ρ values for reactions of a series of aryldiazonium ions with a given nucleophile or for reaction of a series of arylsulfinates with a given aryldiazonium ion[22,23] show that substituent effects on rates are approximately one-half of the effects on equilibria.

(b) **Solvent Effects.** The relative rates of reactions of cations are remarkably independent of solvent, even though the relative equilibrium constants are appreciably solvent dependent.[19] We have previously argued[21] that this indicates that the solvation shell of the cationic moiety at the transition state is essentially the same as that of the reactant cation. It is difficult to understand, however, why different cations would react at such different rates if there is so little change on going from reactant to transition state.

In earlier papers,[21] we have rationalized this behavior by assuming that interactions between electrophile and nucleophile at the transition state are relatively long-range coulombic attractions. This rationalization is certainly incorrect. Anionic, neutral, and cationic nucleophiles reacting with both neutral and cationic electrophiles show the same orders of reactivity, as given by eq 2.

(c) **Relative Reactivities of Nucleophiles.** From the limited amount of data presently available, it appears that the relative reactivities of nucleophiles are solvent dependent. This observation, along with those already mentioned above, led us to postulate[18,21] that the N_+ values are determined by the energy required to partially desolvate the nucleophile. This postulate is not consistent with the observed Brønsted slopes for reactions of amines nor with the observation that amines are relatively unreactive when compared with anions of similar basicity. One would expect the opposite behavior if solvation effects dominated.

It may be pertinent to note in this connection that the entropy of activation for reactions of amines are much more negative than those for reactions of anions.[1] Thus, the low reactivity of amines may be ascribed, at least in part, to unfavorable entropy factors.

Acknowledgment. I am particularly grateful to Professor W. P. Jencks for furnishing me with preprints of his recent work, for valuable comments and suggestions on early drafts of this paper, and for several useful discussions.

References and Notes

(1) (a) For previous papers in this series, see C. D. Ritchie, D. J. Wright, D. Huang, and A. Kamego, *J. Amer. Chem. Soc.*, **97**, 1759 (1975). (b) This work was supported by grants from the National Science Foundation (No. 29164x) and from National Institutes of Health—Public Health Service (GM-12832). Acknowledgment is also made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this work.

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