

Nucleophilic Reactivities toward Cations

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Although the Lewis concept of acid–base reactions has been extremely useful for the qualitative understanding of chemical reactions, it has been difficult to place the concept on a quantitatively useful basis. The general observation that the relative reactivities of Lewis bases (acids) depend on the reference Lewis acid (base) has led to extensive study of the factors responsible for this behavior. The problem encompasses a major portion of current organic and inorganic chemistry.

The quantitative aspects of Brønsted acid–base theory are relatively well, although incompletely, understood. Since the proton is the constant reference acid for all Brønsted bases, the equilibrium constants for formation of conjugate acids from Brønsted bases and proton provide a unique quantitative scale of basicity, or acidity, so long as all of the reactions are referred to the same standard states. The incomplete quantitative understanding of Brønsted acid–base reactions arises solely from the variations in activity coefficients, relative to a common standard state, of the various acids and their conjugate bases. Thus, the fact that methoxide ion is a far weaker base than is fluorenyl ion in methanol solution, while the reverse is true in dimethyl sulfoxide solution,¹ is directly attributable to the different solvent interactions with the two different pairs of acid and conjugate base.

Although one should not be overly complacent about the problem of understanding this variation in relative strengths of Brønsted bases, at least the variation can be traced to a single source. The situation with respect to relative strengths of Lewis acids and bases is far more complex. For example, ammonia and cyanide ion, in water, have nearly the same basicity toward the proton, but cyanide ion, in water, is more than six powers of ten more basic toward methylmercuric ion than is ammonia, in water.²

The same general disparity in understanding between Brønsted and Lewis acid–base reactions occurs with respect to the rates of reactions. Brønsted acid–base reactions are frequently correlated by the Brønsted linear log–log relationship between rates and basicities, or acidities. Even in more general cases, it is usually observed that a monotonic relationship exists between

rates and basicities, and a great deal of progress has been made in delineating important factors governing the rates of such reactions.³ Much less progress has been made with respect to Lewis acid–base reactions. Some of the attempts to understand the rates and equilibria of these reactions are summarized below. Qualitatively, it has appeared that several factors, including Brønsted basicity, polarizability, and solvation, are important, although attempts to assess the quantitative importances of the various factors have met with limited success, at best.

In order to distinguish between Brønsted and Lewis bases and acids, the terms nucleophile and electrophile, respectively, are commonly used for the Lewis species, with the unmodified terms base and acid reserved for the Brønsted species. This usage will be followed throughout the rest of this paper.

The first attempt at a quantitative treatment of nucleophilic reactivities, primarily concerned with the S_N2 reactions of organic compounds, resulted in the Swain–Scott equation⁴

$$\log k_x/k_{\text{H}_2\text{O}} = sn_x \quad (1)$$

where n_x is a parameter characteristic of the nucleophilic reagent, and s is a parameter characteristic of the electrophile. This equation had some success in correlating the reactions of various nucleophilic reagents, including solvents, with alkyl halides. A resurgence of interest in the equation, as applied to solvolysis reactions, has taken place in recent months as the result of new work by Peterson⁵ and Schleyer⁶ allowing clearer distinctions between S_N1 and S_N2 reactions.

A more general equation, proposed by Edwards,⁷ attempted to correlate the rates and equilibria of an extremely wide variety of nucleophilic substitution reactions, including reactions of inorganic complexes, nucleophilic aromatic substitution, carbonyl addition, and S_N2 substitution reactions. Equation 2 relates the basicity, H , and the oxidation potential, E , both

$$\log k_x/k_{\text{H}_2\text{O}} = \beta H + \alpha E \quad (2)$$

(1) C. D. Ritchie, "Solute-Solvent Interactions," J. F. Coetzee and C. D. Ritchie, Ed., Marcel Dekker, New York, N. Y., 1969, Chapter 4.

(2) R. G. Pearson, H. Sobel, and J. Songstad, *J. Amer. Chem. Soc.*, **90**, 319 (1968).

(3) See, for example: M. Eigen, *Angew. Chem., Int. Ed. Engl.*, **3**, 1 (1964); C. D. Ritchie, *J. Amer. Chem. Soc.*, **91**, 6749 (1969).

(4) C. G. Swain and C. B. Scott, *ibid.*, **75**, 141 (1953).

(5) P. E. Peterson and F. J. Waller, *ibid.*, **94**, 991 (1972).

(6) T. W. Bentley, F. L. Schadt, and P. Schleyer, *ibid.*, **94**, 992 (1972).

(7) J. O. Edwards, *ibid.*, **76**, 1540 (1954); **78**, 1819 (1956).

Calvin D. Ritchie was born in Arlington, Va., in 1930. He received his undergraduate and graduate education at The George Washington University. He spent 4 years (1956–1960) with the Food and Drug Administration, and then 1 year at Rice University as a Welch Post-doctoral Fellow. Following that, he joined the staff at the State University of New York at Buffalo, where he is now Professor. His research centers on the effects of solvent and structure on reactivity of organic compounds.

relative to water, of the nucleophilic reagent to its reactivity. The parameters α and β are measures of the sensitivity of the electrophile to the two properties of the nucleophile.

A later modification⁸ of eq 2 substituted the polarizability of the nucleophile for the oxidation potential. The resulting equation was capable of correlating a large body of data, and some order was perceived in the values of α and β required by various electrophiles.

Even this four-parameter equation, however, was insufficient to correlate much of the available data, and Pearson² has preferred to use the more qualitative principle of "soft and hard acids and bases" in more recent work. The failures of eq 2 have been discussed thoroughly by Pearson.²

Largely as a result of the original observations by Winstein⁹ and the extensive studies by Parker,¹⁰ it has become clear that relative reactivities of nucleophilic reagents are solvent dependent, and that equations such as (1) and (2) are bound to fail when reactions in different solvents are considered. It might be supposed that these equations would be more successful if the nucleophilic parameters were obtained from studies in the same solvent as that in which the reactions to be correlated are carried out. Unfortunately, not enough data are available to test this suggestion, although indications are that the failings of the equations are at a more fundamental level.

Another concept that is frequently employed in discussions of nucleophilic reactivity is that of selectivity-reactivity relationships. It is commonly believed, although one is hard-pressed to find unambiguous examples, that the selectivity of a reagent toward a series of reaction partners decreases as the reactivity of the reagent increases. The relationship is most frequently interpreted as being the result of the transition state increasingly "resembling" reactants as the energies of reactants and transition states become more nearly equal. We shall refer further to this concept in the discussion of our own work below. It is worth noting here, however, that although this relationship can accommodate quantitative changes in nucleophilic reactivities with variation in electrophile, it cannot accommodate the qualitative reversals in nucleophilic reactivity orders which are frequently observed.

Cation-Nucleophile Reactions

The reactions of cations with anions to form covalent molecules are among the simplest reaction types of organic chemistry, and are elementary steps in many more complex reactions such as the common S_N1 solvolysis reaction. In our early work,¹¹ we had relied on the simplicity of these reactions to allow us to delve into the complex problems of solvent and structural

effects on nucleophilic reactivities without worries concerning changes in mechanism which frequently frustrate the interpretations of data dealing with such effects. We were considerably surprised by the data for reactions of triarylmethyl cations with anions, which fail to give rate-equilibrium correlations, and which give the unique nucleophilic reactivity sequence: $N_3^- > CH_3O^- > CN^-$. Since cyanide ion is both more basic and more polarizable than azide ion, no combination of these factors can explain the observed sequence of reactivity, and such a sequence has not been reported for any other reaction.

The appearance of the common problem of differences in kinetic and thermodynamic orders of reactivity in such simple reactions appeared to us to offer an unusual opportunity to gain general insight into factors affecting reactivity, if the proper approach could be made.

The proper approach was not immediately obvious. The experimental situation was simply that the kinetic order of reactivity of various nucleophiles did not correlate with any known thermodynamic or physical properties of the nucleophiles nor with reactivities of the nucleophiles in other reactions which had been studied. It finally occurred to us that the unique feature of our reactions is simply that the nucleophile is attacking a positive center without the necessity of displacing any leaving group. If this is indeed the important feature, then it should be possible to observe the same kinetic order in reactions of other cations with nucleophiles. The problem then became one of finding cations as dissimilar as possible to the triarylmethyl cations, but which would still undergo the simple combination reactions.

Some time passed before a suggestion by Professor E. S. Lewis, in a casual conversation, led us to look at the reactions of aryldiazonium ions with nucleophiles. Although these reactions are complex and often lead to products which are not those of the direct combination reaction,¹² there was some evidence^{13,14} to indicate that the first step of these reactions is usually the simple combination, and that this step is, in at least some cases, rate determining. Our initial experiments with *p*-nitrobenzenediazonium ion reactions with hydroxide, azide, and cyanide ions in aqueous solution gave the qualitative rate order: $N_3^- > OH^- > CN^-$, similar to that already mentioned for the triarylmethyl cations, and raised our hopes that we were on the right track. Immediately thereafter, however, our hopes were thoroughly dampened on finding that other aryldiazonium ions in aqueous solution showed azide ion reacting more slowly than hydroxide ion.¹⁵ By that

(8) J. O. Edwards and R. G. Pearson, *J. Amer. Chem. Soc.*, **84**, 16 (1962).

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(12) E. S. Lewis and H. Suhr, *ibid.*, **80**, 1367 (1958); *Chem. Ber.*, **92**, 3043 (1959); I. Ugi and R. Huisgen, *ibid.*, **90**, 2914 (1957); J. F. Bunnett and H. Takayama, *J. Amer. Chem. Soc.*, **90**, 5173 (1968); A. Hantsch and A. Freese, *Chem. Ber.*, **28**, 3237 (1895); H. Zollinger, "Azo and Diazo Chemistry," Wiley-Interscience, New York, N. Y., 1961.

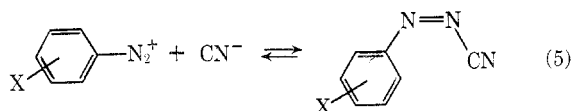
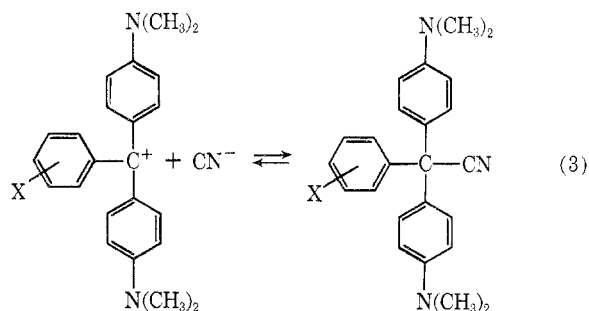
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(14) J. S. Littler, *Trans. Faraday Soc.*, **59**, 2296 (1963).

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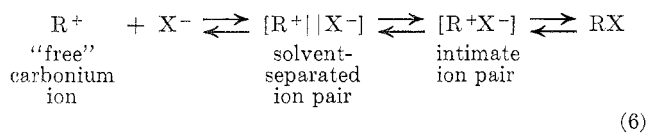
time, fortunately, we had collected enough data to indicate that the rate-determining step for the azide ion reaction in aqueous solution is not the combination step, but the decomposition of the diazoazide to aryl-pentazole and aryl azide.¹⁶ The first step, in all probability, has the above rate order for all of the diazonium ions in water, and in methanol solution, where the first step is indeed rate determining, we observe $N_3^- > CH_3O^- > CN^-$ in all cases.¹⁷

Our studies have now included reactions of triarylmethyl cations,^{11,17} aryldiazonium ions,^{13,15-18} and tropylium ions^{19,20} with a variety of nucleophiles in several solvents. The reactions studied are illustrated in eq 3-5, using the example of cyanide ion as nucleophile. These reactions and the remarkable correlations of reactivities of nucleophiles toward the different cations form the subject matter of the present paper. The results provide some unusual insights into the problems of nucleophilic reactivities and of solvent effects on organic reactions.



Background

A large portion of the literature pertinent to reactions of organic cations with nucleophiles is concerned with the S_N1 solvolysis reaction, involving the presence of steady-state concentrations of the cations. Winstein's mechanism for the S_N1 reaction,²¹ shown in reverse in eq 6, appears to be well substantiated with the possible



exception of one point. Work by Eigen²² and by

Atkinson²³ on the ion-pairing reactions of inorganic salts indicates that two types of solvent-separated ion pairs are probable. These are postulated²³ to involve one and two molecules of solvent separating the two ions. It is particularly noteworthy that Atkinson has concluded that the conversion of the two-solvent-separated ion pair into the one-solvent-separated ion pair is very anion dependent, while the conversion of the one-solvent-separated ion pair into the intimate ion pair is strongly cation dependent but anion independent.

It might seem that previous studies of trapping of S_N1 solvolysis intermediates²⁴ with added nucleophiles would provide direct information concerning cation-anion combination reactions. The fact that trapping of more than one intermediate can occur, and that the proportions of products derived from the different intermediates vary with structure of the substrate, the nature of the trapping agent, and even with the concentration of the trapping agent,²⁵ make the interpretation of such data very difficult, at best. This subject is discussed in detail in a later section.

Until very recently, direct kinetic studies of the reactions of organic cations with nucleophiles have been reported only for relatively stable triarylmethyl cations^{11,26} and for tropylium ion reacting with water and hydroxide ion.³ Recent studies of reactions of tri-*p*-anisylmethyl cation with azide ion,²⁷ and of Malachite Green with a variety of nucleophiles,²⁸ will be discussed in a later section.

Correlation of Cation-Nucleophile Reactions

The entire body of data which we have obtained, involving Crystal Violet [tris(*p*-dimethylaminophenyl)methyl tetrafluoroborate], Malachite Green [bis(*p*-dimethylaminophenyl)phenylmethyl tetrafluoroborate], *p*-nitro(Malachite Green) [bis(*p*-dimethylaminophenyl)-*p*-nitrophenylmethyl tetrafluoroborate], a wide range of substituted aryldiazonium ions, tropylium ion, phenyl-tropylium ion, *p*-chlorophenyltropylium ion, and *p*-dimethylaminophenyltropylium ion, reacting with the nucleophilic systems listed in Table I, can be correlated by eq 7, where k_n is the rate constant for reaction of a

$$\log [k_n/k_{H_2O}] = N_+ \quad (7)$$

cation with a given nucleophilic system (*i.e.*, a given nucleophile in a given solvent), k_{H_2O} is the rate constant for reaction of the same cation with water in water, and N_+ is a parameter characteristic of the nucleophilic system and *independent* of the cation. We use the convention that rate constants for reactions of solvents are in units of sec^{-1} and those for reactions of other nucleophiles are in units of $M^{-1} \text{sec}^{-1}$.

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Table I
 N_+ Values for Nucleophilic Systems at 23°

Nucleophile (solvent)	N_+	Nucleophile (solvent)	N_+
H ₂ O (H ₂ O)	0.0	CH ₃ O ⁻ (MeOH)	7.5
MeOH (MeOH)	0.5	N ₃ ⁻ (MeOH)	8.5
CN ⁻ (H ₂ O)	3.8	CN ⁻ (Me ₂ SO)	8.6
C ₆ H ₅ SO ₂ ⁻ (MeOH)	3.8 ^a	CN ⁻ (DMF)	9.4
OH ⁻ (H ₂ O)	4.5	N ₃ ⁻ (Me ₂ SO)	10.7 ^c
N ₃ ⁻ (H ₂ O)	5.4(?) ^{a,b}	C ₆ H ₅ S ⁻ (MeOH)	10.7
CN ⁻ (MeOH)	5.9 ^a	C ₆ H ₅ S ⁻ (Me ₂ SO)	13.1

^a Evaluated from reactions of *p*-nitrobenzenediazonium ion.

^b This value should be regarded as a lower limit since it is quite possible that the rate-determining step in the reaction of azide ion with *p*-nitrobenzenediazonium ion in water is not the combination step. See ref 16 and 17. ^c Evaluated from reactions of benzenediazonium ion.

Table II
Equilibrium Constants for Cation-Nucleophile Reactions^a

Nucleophile	Cation	
	PNMG ^b	<i>p</i> -CNPhN ₂ ⁺ ^c <i>p</i> -DMAPhTr ⁺ ^d
N ₃ ⁻ (MeOH)	1.6 × 10 ³	1.9 × 10 ³
OH ⁻ (H ₂ O)	3.1 × 10 ⁸	4.5 × 10 ⁸
CH ₃ O ⁻ (MeOH)	1.3 × 10 ¹⁰	8.6 × 10 ⁸ 1.7 × 10 ¹⁰
C ₆ H ₅ S ⁻ (MeOH)	1.6 × 10 ⁶	1.8 × 10 ¹⁰ 9.1 × 10 ⁸

^a Equilibrium constants at 23° in units of M⁻¹. ^b *p*-Nitro-(Malachite Green). ^c *p*-Cyanobenzenediazonium ion. ^d *p*-Dimethylaminophenyltropylium ion.

The N_+ values are defined by the rate constants for reactions of *p*-nitro(Malachite Green) wherever possible, but other cation reactions have been utilized where data for *p*-nitro(Malachite Green) cannot be obtained. The N_+ values are reported in Table I, and the quality of the correlations is illustrated in Figure 1, which is representative of the more extensive data available.¹⁸

Early in this Account, we commented that the rate and equilibrium constants for the reactions of Malachite Green type cations showed no correlation with each other. The same observation is valid for the other cations studied, and, moreover, there is no correlation of equilibrium constants for reactions of one cation with those for reactions of another. Data illustrating this last point are shown in Table II.

The good correlation of rate data by eq 7 in the absence of either rate-equilibrium or equilibrium-equilibrium relationships forces the conclusion that the transition states for these reactions do not resemble products in any feature responsible for the variations in equilibrium constants. We infer, then, that the transition states for the cation-nucleophile reactions are characterized by rather large separations of cationic and anionic moieties and by the cationic moiety having a solvation shell little perturbed from that of the reactant cation.¹⁸ The latter part of this inference is virtually forced by the observation that, although the relative equilibrium constants for the various cations reacting with hydroxide ion in water are different from those for reactions with methoxide ion in methanol, the relative rate constants for the two reactions are the same.²⁰ This observation is valid even for the series of

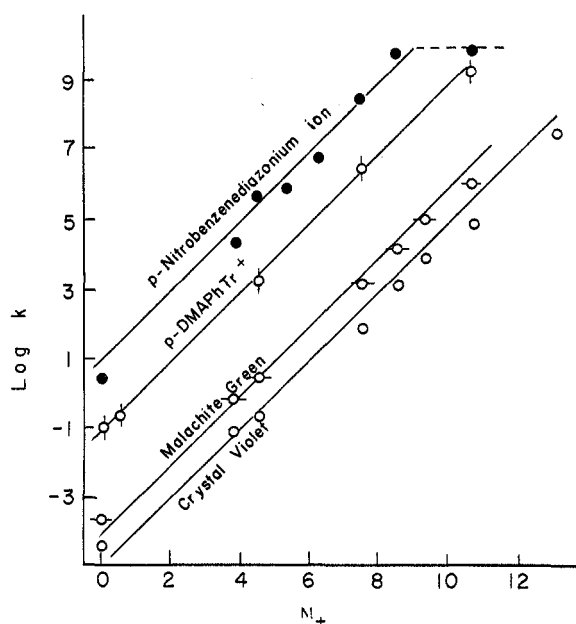


Figure 1. The correlation of rates of cation-nucleophile reactions by eq 7.

aryltropylium ions where steric influences must remain constant for the series.

In terms of the ion-pair mechanism for cation-anion combination reactions (*i.e.*, eq 6), the above conclusions indicate that the transition state for the rate-determining step is either between the intimate and solvent-separated ion pairs, or, with the modification of the mechanism suggested by Atkinson,²³ between the two-solvent-separated and one-solvent-separated ion pairs. If the former, the transition state must be very close in structure to the one-solvent-separated ion pair, since the cation solvation shell is virtually intact.

Some further information concerning the transition state can be gained by examination of the Hammett equation correlations of rate and equilibrium constants within the three series of cation types. For all three series, the ρ values for the combination rates are between 0.5 and 0.7 of the ρ values for equilibria. This information, as well as the fact that the rates of reaction of, for example, Crystal Violet and phenyltropylium ion with any given nucleophile differ by six powers of ten, makes it appear unlikely that the cation and nucleophile are separated by more than a single solvent molecule at the transition state. Even if the rate-determining step of the reaction is the conversion of the two-solvent-separated to one-solvent-separated ion pairs, then, the transition state must be very close in structure to that of the one-solvent-separated ion pair. It is worth noting that, in the cases studied by Atkinson,²³ the one-solvent-separated ion pair is less stable than either the two-solvent-separated or intimate ion pairs. If the same situation applies to the present cases, the Hammond postulate²⁵ would indicate that either transformation would have a transition state similar in structure to that of the one-solvent-separated ion pair.

The single fact of the existence of the correlation by eq 7, wherein the relative reactivities of the nucleophiles

Table III
Comparison of N_+ Values with Parker's Solvation Values

Anion	$\Delta \log k_2^a$	N_+
$C_6H_5S^-$	4.0	10.7
N_3^-	4.6	8.5
CN^-	5.7	5.9

^a $\Delta \log k_2$ is the difference in the logs of the rate constants for the reaction of the anion with methyl iodide in methanol and dimethylformamide solutions; see ref 10.

Table IV
Relative Reactivities of Cations

Cation	$\log k_{R^+}/k_{PNMG}^a$
Crystal Violet	-1.4
Malachite Green	-0.4
<i>p</i> -Nitrobenzenediazonium ion	4.5
<i>p</i> -Cyanobenzenediazonium ion	4.1
Benzenediazonium ion	2.6
<i>p</i> -Tolyldiazonium ion	2.1
Tropylium ion	4.5
Phenyltropylium ion	4.2
<i>p</i> -Dimethylaminophenyltropylium ion	2.3

^a k_{R^+}/k_{PNMG} is the rate constant for R^+ relative to that for *p*-nitro(Malachite Green) reacting with any given nucleophilic system. Values are averaged.

are independent of the structure and reactivity of the cation, forces the conclusion that the N_+ values are measures of some "inherent" property of the nucleophilic systems. *A priori*, one immediately suspects that this property must be associated with the solvation of the nucleophile. The above reasoning concerning the nature of the transition states strengthens the suspicion to a reasonably based hypothesis. Thus, the higher N_+ values are associated with the lower solvation energies of the nucleophiles.

This hypothesis can be subjected to one test with data already available. Parker¹⁰ has argued convincingly that the changes in rate constants for nucleophilic attack on methyl iodide on changing solvent from methanol to dimethylformamide can be used to evaluate the "hydrogen-bonding solvation energies" of the nucleophiles in methanol solution. We should, then, expect to find that the N_+ values of the anions in methanol solution are related to Parker's values for the changes in rate constants with change in solvent for the methyl iodide reaction. The data for the three anionic nucleophiles, N_3^- , CN^- , and $C_6H_5S^-$, for which data are available for comparison are shown in Table III. The qualitative agreement found is all that could be hoped for, and is particularly striking when it is realized that the rate constants for reactions of these anions with methyl iodide and our cations in either solvent alone give no correlation.¹⁸

The large variation in rates of reactions of the different cations with any given nucleophilic system must have its origin in nonspecific interactions, such as electrostatic effects, if our postulates concerning the transition states for these reactions are correct. The cationic reactivities relative to Malachite Green are shown in Table IV.

A crude electrostatic model involving the interaction of a uniformly charged circular disk with a point charge through an effective dielectric constant of 2.0 results in eq 8 for the energy of interaction, where z is the distance

$$E \text{ (kcal/mole)} = [334/a^2][z - (z^2 + a^2)^{1/2}] \quad (8)$$

of the point charge from the disk, along the axis of the disk, and a is the radius of the disk, both expressed in ångströms. Taking the radius of the Crystal Violet model disk as 5.6 Å, the distance between the central carbon and the nitrogen of the *p*-dimethylamino group, and the radius of the tropylium ion model disk as 2.9 Å, computed from aromatic bond lengths and the planar geometry of the ion, the observed rate difference for the two cations requires that z be between 3 and 4 Å. This appears quite consistent with the postulate of a one-solvent-separated species for the transition state.

At this point in our research, two apparent conflicts with current concepts of physical-organic chemistry became apparent. First, the fact that hydroxide ion in water and methoxide ion in methanol both react faster than cyanide ion in the respective solvents appeared inconsistent with the fact that the lyate ions are more strongly solvated than any other ions in their respective solvents. Second, the constant selectivities of the cations involved in our studies appeared inconsistent with the frequent observations of selectivity-reactivity relationships in solvolysis reaction trapping studies.²⁴

The first problem, that of the unexpectedly high rates of reactions of hydroxide and methoxide ions, can be rationalized away by recognizing the possibility of a unique reaction path available in these cases where a proton transfer across solvent molecules can accomplish the same transformation that must be accomplished by removal of solvent molecules in other cases. Deeper thought, however, shows that this possibility implies the existence of general base catalysis for the reaction of the cation with solvent, whereas it is generally believed that this type of reaction is not subject to such catalysis.^{26,27} For example, the reverse reaction, formation of carbonium ion from an alcohol, is frequently cited as a prime example of a reaction involving specific acid catalysis, which directly implies that reaction of carbonium ion with water is not base catalyzed. Since existing data on this point were hardly conclusive, however, we instituted a careful search for general base catalysis in the reaction of Malachite Green with water. A direct dependence of the rate of this reaction on buffer concentration, using triethylenediamine buffers, was found.³⁰ Moreover, the extrapolation of the Brønsted relationship for triethylenediamine and triethylamine to hydroxide ion gave close agreement with the observed rate constant for reaction of hydroxide ion with Malachite Green.

The second problem, involving the interpretation of data associated with the trapping of solvolysis inter-

mediates, presents a complex situation. Since any trapping agent can, in principle, serve as a general base catalyst for reaction of solvent, even the simplest case of trapping of a single intermediate must be interpreted with care. The rate of formation of trapped product will be directly proportional to concentration of trapping agent, but the rate of formation of solvolysis product will be linear in concentration of trapping agent, rather than independent as has been assumed in earlier studies.

The experiments are even further complicated by the possibility of trapping both ion pairs and free cations. If the different species have different selectivities toward solvent and added trapping agent, the observed product ratio from any given reaction will result from a weighted average of the different selectivities, the weighting factor being the relative steady-state concentrations of the species being trapped. The complexity is multiplied by the fact that the relative steady-state concentrations of the intermediates will depend on the concentration of the added trapping agent.

A series of experiments involving trapping of solvolysis intermediates in the methanolysis of *p,p'*-dimethoxybenzhydrylmesitoate were carried out²⁵ to test the idea that different intermediates would show different selectivities. The product ratios found at very low ($9.7 \times 10^{-6} M$) and very high ($5.0 \times 10^{-3} M$) concentrations of added azide appear well outside of experimental error from those required for trapping of a single intermediate even in the presence of general base catalysis, and provide strong support for the essential correctness of the idea. The detailed interpretation of the data in terms of the individual selectivities of the trapped species, however, involves too many adjustable parameters to warrant any attempt in that direction.

Current Work

Within the past year, three papers from other laboratories have appeared which are directly pertinent to our studies and raise interesting points. Bunton²⁷ has reported studies of the reactions of tri-*p*-anisylmethyl cation with water, hydroxide ion, and azide ion in aqueous solution, with particular emphasis on salt effects on the rates of these reactions, and Bruce²⁸ has reported studies of the reactions of Malachite Green with a number of amines, peroxide ion, hypochlorite ion, and bisulfite ion in aqueous solution, with particular emphasis on the operation of the " α effect" in these reactions. Both studies have generally employed ionic strengths much higher than those used in our studies (*i.e.*, 1 *M* as compared to our studies at less than $10^{-2} M$), and Bruce's studies have been carried out at a slightly higher temperature than that of our studies.

Bunton reports $k_{H_2O} = 12 \text{ sec}^{-1}$; $k_{OH} = 8.2 \times 10^3 M^{-1} \text{ sec}^{-1}$; and $k_{N_3} = 5 \times 10^6 M^{-1} \text{ sec}^{-1}$, for reactions of tri-*p*-anisylmethyl cation at an ionic strength of $5 \times 10^{-2} M$. The rate constant ratio for reaction of hydroxide ion and water is only $680 M^{-1}$, while the value found in our studies is $3 \times 10^4 M^{-1}$. It may be misleading to compare the azide ion data with our studies

since the only data we have for aqueous solution are based on the questionable assumption that the combination step is rate determining in the reaction of *p*-nitrobenzenediazonium ion with azide ion. Nevertheless, the ratio $k_{N_3}/k_{H_2O} = 10^{5.6}$ reported by Bunton is in good agreement with the value of $10^{5.4}$ found in our study. At this time, then, it appears that the rate constant for reaction of hydroxide ion with the tri-*p*-anisylmethyl cation is unusually low in comparison with our cation reactions.

Swain has reported a rate constant ratio of *ca.* $10^8 M^{-1}$ for the reactions of hydroxide ion and water with trityl cation.³¹ Although this value was obtained from trapping studies of the sort discussed above, it is hard to see how the carbonium ion could give a lower selectivity than that observed, although a higher value is quite likely. Thus, Bunton's observation of an even lower rate constant ratio for the reaction of tri-*p*-anisylmethyl cation is quite surprising. Clearly, further studies of this system, with particular emphasis on the possibility of general base catalysis, are called for.

Bruce's studies of the " α effect" in reactions of nucleophiles with Malachite Green have led to conclusions which need reexamination in light of our studies. In the reactions of amines with Malachite Green, Bruce finds that those amines which have a lone pair of electrons on an atom α to the nucleophilic atom exhibit greater kinetic and thermodynamic reactivity than other amines of comparable basicity. He concludes that the enhanced rates of the " α -effect" nucleophiles result from the same factors which cause enhanced product stability. In the cases of the reactions of peroxide and hypochlorite ions, however, he finds enhanced rates without enhanced equilibria over those for other anions with comparable basicities. He concludes that the " α effect" on rates in these cases must arise from a different source than in the case of amines, and may be due to solvation effects.³²

We are presently engaged in a study of the reactions of amine nucleophiles with the three cationic classes involved in our other work. Although space limitations prevent a detailed discussion of our results here, we may state that all of the nucleophiles studied by Bruce, with the two exceptions of methoxyamine and hydrazine, give reaction rates correlated by eq 7.

Future Directions

Among the many extensions, elaborations, and testings of the concepts developed in this work, a high priority will be placed on the collection of data for the reactions of some of the common nucleophiles, such as halide ions, used in other types of nucleophilic substitution reactions. When enough data are available, we are hopeful that the N_+ values will allow solvation effects on nucleophilic reactivities to be separated

(31) C. G. Swain, C. B. Scott, and K. H. Lohmann, *J. Amer. Chem. Soc.*, **75**, 136 (1953).

(32) In a more recent paper, Bruce appears to be dubious of this distinction between neutral and anionic " α -effect" nucleophiles. See: J. E. Dixon and T. C. Bruce, *ibid.*, **94**, 2052 (1972).

from other effects so that these other effects may be identified and evaluated. Perhaps the use of N_+ values in an equation of the form of eq 2 will be useful.

The successful application of the concepts already developed to the clarification of the selectivity-reactivity problem and to the problem of general base catalysis in cation reactions have served as demonstra-

tions of the general scientific value of these concepts. Undoubtedly, the concepts will be found to have some limitations, and it is the goal of much of our present work to define these limitations as closely as possible.

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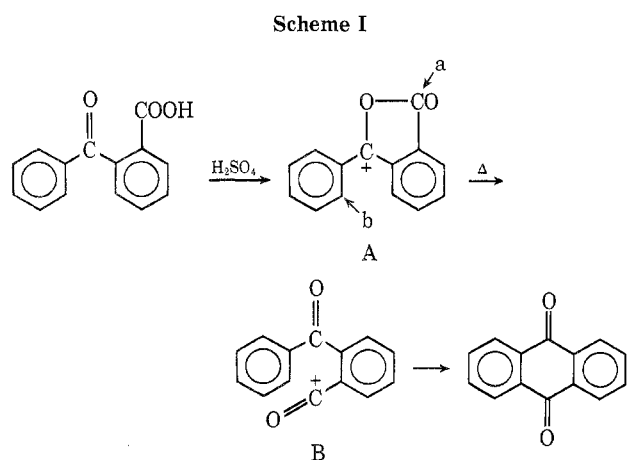
Spirocyclic Intermediates in Organic Reactions

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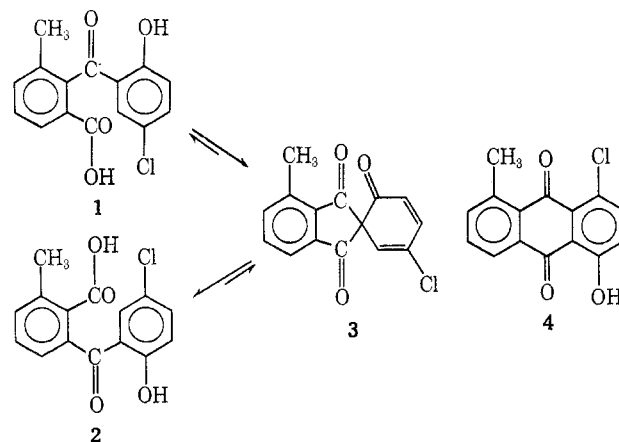
My interest in spirocyclic reaction mechanisms arose from early work on the mechanism of anthraquinone formation from *o*-benzoylbenzoic acid.¹ The proposed mechanism is shown in Scheme I.



It was pointed out¹ that cyclic ion A was undoubtedly produced first.² Ion A is stable at temperatures up to about 70°. Cyclization to anthraquinone cannot occur because carbons a and b cannot approach within bond-forming distance. However, at temperatures above 70° opening of A to B occurs readily and cyclization to anthraquinone may result.

Later, my attention was drawn to the fact that certain keto acids of the *o*-benzoylbenzoic type give rise to isomeric keto acids and to anthraquinone-type molecules which could not be explained solely by the

above mechanism. Hayashi had shown³ that 2-(2-hydroxy-5-chlorobenzoyl)-3-methylbenzoic acid (**1**) rearranges to 6-(2-hydroxy-5-chlorobenzoyl)-2-methylbenzoic acid (**2**) on warming in sulfuric acid. The rearrangement was postulated to go through the cyclohexadienone **3** shown. Both **1** and **2** give the same quinone (**4**) on warming in sulfuric acid.



The species **3** represents a spirocyclic compound and, presumably, the phenolic hydroxyl in **1** or **2** is necessary for its formation, although this point was not mentioned in Hayashi's discussion.³ In the present discussion, however, I do not cover reactions which yield spirocyclic compounds, rather, reactions which may proceed through a *spirocyclic intermediate* (nonisolable).

The spirocyclic mechanism for anthraquinone formation is best illustrated by the work done on 3-nitro-2-(2-thenoyl)benzoic acid (**5**)⁴ (Scheme II). On

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(1) M. S. Newman, *J. Amer. Chem. Soc.*, **64**, 2324 (1942).

(2) D. S. Noyce and P. A. Kittle, *J. Org. Chem.*, **30**, 1899 (1965), give uv data in favor of A in 100% H₂SO₄.

(3) M. Hayashi, *J. Chem. Soc.*, 2516 (1927); see also M. Hayashi, *ibid.*, 1513, 1520, 1524 (1930).

(4) M. S. Newman and K. G. Ihrman, *J. Amer. Chem. Soc.*, **80**, 3652 (1958).