Cation–Anion Combination Reactions. 14.[1] Reactions of *p*-Dimethylaminophenyltropylium Ion with Nucleophiles in Water and Methanol

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Abstract: Rate and equilibrium constants for reactions of *p*-dimethylaminophenyltropylium ion with primary, secondary, and α-effect amines in water and methanol solution, and the p*K*s of the amines in methanol solution, are reported. Although the change in p*K* of an amine on change from water to methanol is different for the different types of amines, the change in rates of reactions of the amines with the cation is the same for all amine types. Thus, the "α effect" on rates of reactions is solvent dependent. We also report here studies of the general base catalysis of the reactions of aryltropylium cations with water, rate constants for reactions of several anionic nucleophiles with *p*-dimethylaminophenyltropylium ion in water, and a comparison of both forward and reverse rates of reactions of amines with cations and esters.

In our continuing conviction that the problem of nucleophilic reactivities can best be approached through the study of simple reactions, we have exploited the reactions of relatively stable organic cations with nucleophiles in combination reactions. The *p*-dimethylaminophenyltropylium ion (DMAPTr$^+$) is particularly well suited for such studies. The pK_R of 7.35[2] in aqueous solution, strong color, relatively low reactivity (k_{H_2O} = 1.7×10^{-2} s^{-1} at 25 °C),[2] and small steric effects on equilibria (i.e., the cation reacts appreciably with secondary amines[3]) provide the opportunity for study of a very wide range of nucleophiles.

The present paper reports some rate and equilibrium studies of reactions of DMAPTr$^+$ in both water and methanol solutions. As part of this study, the p*K*s of primary, secondary, and α-effect[4] amines in methanol solutions have been measured, and the general base catalysis of the reaction of water with aryltropylium cations has been demonstrated. The results bear importantly on the questions of the generality of the N_+ scale of nucleophilicity,[1] the origins and operation of the α effect,[4] and leaving group abilities in reversible nucleophilic addition reactions.

Experimental Section

The purifications and standardizations of reagents and the general techniques for the stop-flow kinetic studies have been detailed in previous papers.[1]

The determinations of the p*K*s of the ammonium ions in methanol solution utilized the glass and methanolic calomel electrodes, and followed the general methods, which we have previously described.[5] The electrodes were standardized in methanol solution with tribenzylamine–tribenzylammonium ion buffers (pK_a = 6.40[6]) and the standardization was routinely checked immediately before or after each titration with potassium hydrogen phthalate buffer[6] at pH 8.987. Either the amine was titrated with standard methanolic perchloric acid[5] or the amine hydrochloride was titrated with standard methanolic potassium methoxide.[5] Initial concentrations of the amine or its hydrochloride were $1-1.5 \times 10^{-3}$ M in all cases. The p*K*s were determined from the potentiometric titration curves utilizing points corresponding to 25–75% equivalence. Each value reported in Table I is the average of two independent titrations in each of which 20 points were included in the calculations.

The experimental conditions and derived rate and equilibrium constants for reactions of cations with nucleophiles are reported in Table II. The p*K*s used in the calculations were those reported in Table I or in the footnotes to Table II.

Pertinent data concerning the studies of general base catalysis of the reactions of water with DMAPTr$^+$ and with *p*-methoxyphenyltropylium ion are reported in Table III. In all of these experiments, the solutions were carefully buffered at pH 8.49 ± 0.01 with Dabco buffers, and the pH was measured with a pH meter equipped with glass and saturated calomel electrodes. Ionic strength was maintained at 0.10 M by the addition of NaCl.

Results

p*K*s in Methanol Solution. The p*K* values of the ammonium ions determined in the present study and a few values from the literature are shown in Table I. The present values are based on at least two independent titrations, and all titrations gave good agreement between observed and calculated end points. The precision of the results was better than 0.02 p*K* unit between titrations and for 20 points between 25 and 75% equivalence in each titration. We have previously discussed the accuracy of such determinations, and believe that the values are accurate to approximately 0.02 units.[5,6]

All values were obtained at low concentrations and low ionic strengths. Debye–Hückel theory gives a value of −0.05 for the logarithm of the activity coefficient of the ammonium ion at 10^{-3} M ionic strength and leads to p*K* values at infinite dilution which are 0.05 units lower than those reported in Table I. Since this correction is barely outside experimental error, we have not included it in the reported values.

Cation–Nucleophile Reactions. All of the reactions reported in Table II were studied in solutions buffered by the nucleophile and its conjugate acid. Ionic strengths were kept as low as possible consistent with the concentration of nucleophile required to give appreciable reactions with the cations. From our previous work,[6] we believe that ionic strength effects on the rate constants are negligible when the ionic strength is kept below 10^{-1} M in water or ca. 10^{-2} M in methanol. The results obtained were consistent with this belief. In only two cases, those for reactions of $CF_3CH_2NH_2$ with DMAPTr$^+$ and of ethylglycine with malachite green, was it necessary to exceed these limits on ionic strength. In these cases, only one concentration of amine was studied, chosen to give the most favorable compromise between low ionic strength and favorable rate and equilibrium constants.

For aqueous solution reactions, the pH of the reaction solutions was measured and the concentration of nucleophile was calculated from the total concentration of nucleophile plus conjugate acid and the known p*K* of the conjugate acid. The values of concentration of nucleophile obtained were in good agreement with those calculated from the known makeup of the solutions. For methanol solutions, the pH of the solution was calculated from the known concentrations of nucleophile and conjugate acid added and the p*K* values reported in Table I.

Under the conditions shown in Table II, the reactions of nucleophiles with cations were much faster than reaction of

Table I. p*K*s of Ammonium Ions in Methanol and Water at 25 °C

	pK_{MeOH}	pK_{water}	ΔpK
	Primary Amines		
$C_6H_5NH_2$	5.90^{b}	4.57^{a}	1.23
$CF_3CH_2NH_2$	6.68	5.59^{k}	1.09
$C_2H_5O_2CH_2NH_2$	9.15	7.90^{h}	1.25
$H_2NCH_2CH_2NH_2$	10.90	9.87^{a}	1.03
n-$C_4H_9NH_2$	11.7^{c}	10.55^{a}	1.15
$^{+}H_3NCH_2CH_2NH_2$	7.34	6.81^{a}	0.53
	Secondary Amines		
$C_6H_5NHCH_3$	5.27^{b}	4.85^{b}	0.42
Morpholine	8.69^{d}	8.45^{a}	0.24
	Tertiary Amines		
$C_6H_5N(CH_3)_2$	5.02^{b}	5.15^{b}	−0.13
4-$CH_3C_5H_4N$	6.09^{e}	6.02^{g}	0.07
$N(CH_2CH_2)_3N$	8.99	8.80^{f}	0.19
$(C_2H_5)_3N$	10.88^{l}	10.66^{a}	0.22
	α-Effect Amines		
$H_2NCONHNH_2$	5.80	3.86^{h}	1.94
CH_3ONH_2	6.41	4.60^{i}	1.81
$C_6H_5NHNH_2$	7.30	5.27^{j}	2.03
NH_2NH_2	9.84	7.91^{a}	1.93

[a] J. W. Larson and L. G. Hepler in "Solute-Solvent Interactions", J. F. Coetzee and C. D. Ritchie, Ed., Marcel Dekker, New York, N.Y., 1969. [b] A. L. Bacarella, E. Grunwald, H. P. Marshall, and E. L. Purlee, *J. Org. Chem.*, **20**, 747 (1955). [c] L. D. Goodhue and R. M. Hixson, *J. Am. Chem. Soc.*, **56**, 1329 (1934). [d] N. A. Izmailov and H. Mayharova, *Russ. J. Phys. Chem.* (*Engl. Transl.*), **34**, 814 (1960). [e] Reference 5. [f] C. P. Paoletti, J. H. Stern, and A. Vacca, *J. Phys. Chem.*, **69**, 3759 (1965). [g] H. C. Brown and X. R. Mihm, *J. Am. Chem. Soc.*, **77**, 1723 (1955). [h] W. P. Jencks and M. Gilchrist, *ibid.*, **90**, 2622 (1968); values obtained at an ionic strength of 1 M. [i] H. K. Hall, Jr., *J. Am. Chem. Soc.*, **79**, 5441 (1957). [j] H. Stroh and G. Westphal, *Chem. Ber.*, **96**, 189 (1963). [k] P. Love, R. B. Cohen, and R. W. Taft, Jr., *J. Am. Chem. Soc.*, **90**, 2455 (1968). [l] Reference 6.

solvent[2,3] and the observed pseudo-first-order rate constants were converted to second-order rate constants in the standard manner for reversible reactions. Estimated experimental errors in the second-order rate constants are shown in Table II and are generally within the ±10% range expected for the usual stop-flow studies.

For the reaction of thioglycollate ion with malachite green in water, Bruice[8] has reported a second-order rate constant of $1.8 \times 10^4\ M^{-1}\ s^{-1}$ at 30 °C and 1 M ionic strength. The discrepancy with the value shown in Table II could be an ionic strength effect. This is the only nucleophile shown for which previous data are available.

The calculations of the equilibrium constants shown in Table II involve several assumptions. All of the reactions were studied at pH equal to the p*K* of the conjugate acid of the nucleophile. If we assume that the reaction product has a lower p*K* than that of the conjugate acid of the nucleophile,[9] then the reaction observed is

$$R^+ + R'NH_2 \rightleftarrows RNHR' + H^+$$

and the pertinent equilibrium constant can be calculated from the equation

$$K_{eq} = \frac{[RNHR'][H^+]}{[R^+][R'NH_2]} = \frac{[A_0 - A_{eq}][H^+]}{A_{eq}[R'NH_2]} \qquad (1)$$

where A_0 is the absorbance of the cation before any reaction and A_{eq} is the absorbance of the cation at equilibrium with the amine but before any appreciable reaction with solvent.

The use of eq 1 also assumes that there is no appreciable protonation at other sites on the product such as the dimethylamino group or the "nonreacted" nitrogen of the hydrazine-type moieties. Since the p*K* of dimethylanilinium ion in methanol is 5.02, as shown in Table I, and since the p*K*s of all of the ammonium ions in this study are considerably greater, the protonation of the dimethylamino group is unlikely. The assumption may be incorrect, however, regarding protonation of the alternate nitrogen of the products of the hydrazine derivative reactions. Thus, for these latter cases, the equilibrium constants reported in Table II may be in considerable error. In the other cases, we did not concentrate on accurate measurements of the equilibrium constants, but did obtain consistent values with fair reproducibility. We estimate that the values are accurate to better than a factor of 2.

General Base Catalysis of Water Reactions. Upon mixing solutions of either $DMAPTr^+$ or *p*-methoxyphenyltropylium ion with solutions buffered with Dabco there is a rapid decrease in absorbance of the solutions which has reached equilibrium before the first observation can be made on the stop-flow spectrophotometer. There follows a much slower first-order decrease in absorbance which, at final equilibrium, shows the presence of extremely small concentrations of the cation consistent with equilibrium with solvent. In these experiments, the initially observed absorbance, A_{mix}, depends on the concentration of Dabco in a manner consistent with the reaction

$$ArTr^+ + N(CH_2CH_2)_3N \rightleftarrows ArTr\text{-}N^+(CH_2CH_2)_3N$$

having reached equilibrium. The appropriate equilibrium constant expression is

$$K = \frac{[A_0 - A_{mix}]}{A_{mix}[\mathrm{Dabco}]} \qquad (2)$$

where A_0 is the absorbance of the cation solution mixed with dilute acid in the stop-flow.

Appropriate data for these experiments are shown in Table III, and are seen to be consistent with the reaction scheme

$$ArTr^+ + B \underset{\text{equil}}{\overset{\text{fast}}{\rightleftarrows}} ArTrB^+$$

$$ArTr^+ + H_2O \xrightarrow{k_{H_2O}} ArTrOH + H^+$$

which leads to the rate constant equation

$$k_{H_2O} = k_\psi[1 + K(B)] \qquad (3)$$

where k_ψ is the observed pseudo-first-order rate constant for slow disappearance of absorbance.

In Table III, it is seen that the values of k_{H_2O} obtained from eq 2 and 3 depend on the concentration of Dabco, and are consistent with the equation

$$k_{H_2O} = k_w + k_{\mathrm{Dabco}}[\mathrm{Dabco}] \qquad (4)$$

where k_w is the rate constant for "water-catalyzed" water reaction and k_{Dabco} is the rate constant for Dabco-catalyzed water reaction.

The values of k_w and k_{Dabco} shown in Table III were obtained by linear least-squares treatment according to eq 4. Repetition of the experiments indicated a precision of ca. ±5% for the values of k_w and k_{Dabco} for both cations.

The values of k_w obtained in the present study are in reasonable agreement with the values obtained in an earlier study[2] employing borate and triethylamine buffers. Apparently, the equilibrium reaction of the cations with triethylamine is quite small at the 10^{-2} M concentrations of amine employed.

Discussion

α-Effect Nucleophiles. The postulate of the existence of an α effect in nucleophilic reactivities is based on the Brønsted

Table II. Reactions of Cations with Nucleophiles at 25.0 ± 0.1 °C[a]

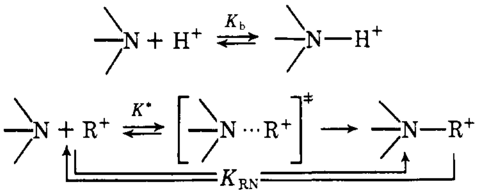
Nucleophile	Concn range, M	Ionic strength, M	k_2, $M^{-1}\ s^{-1}$	K_{eq}[b]
		p-Dimethylaminophenyltropylium Ion		
$CF_3CH_2O^-$, H_2O	$3\text{-}27 \times 10^{-3}$	3×10^{-2}	$1.4 \pm 0.1 \times 10^4$	
HOO^-, H_2O	$6\text{-}53 \times 10^{-5}$	6×10^{-3}	$4.8 \pm 0.7 \times 10^5$	
$^-O_2CCH_2S^-$, H_2O	$1\text{-}5 \times 10^{-6}$	7.5×10^{-3}	$5.5 \pm 0.4 \times 10^7$	
CN^-, H_2O	$1\text{-}10 \times 10^{-2}$	1.0×10^{-1}	$3.5 \pm 0.3 \times 10$	
Morpholine, H_2O	$1\text{-}15 \times 10^{-4}$	1.0×10^{-2}	$1.9 \pm 0.3 \times 10^4$	3.0×10^{-5}
Piperazine, H_2O	$1\text{-}5 \times 10^{-3}$	1.0×10^{-1}	$7.2 \pm 0.5 \times 10^4$	
CH_3ONH_2, MeOH[d,e]	$9\text{-}96 \times 10^{-4}$	2.0×10^{-2}	$6.5 \pm 0.3 \times 10^2$	2.4×10^{-3}
$C_2H_5O_2CCH_2NH_2$, MeOH[d]	$1\text{-}96 \times 10^{-4}$	2.0×10^{-2}	$4.2 \pm 0.3 \times 10^3$	$7. \times 10^{-6}$
Morpholine, MeOH[d]	$9\text{-}91 \times 10^{-5}$	2.0×10^{-2}	$1.4 \pm 0.1 \times 10^5$	1.8×10^{-4}
H_2NNH_2, MeOH[d]	$1\text{-}96 \times 10^{-4}$	2.0×10^{-2}	$2.6 \pm 0.2 \times 10^4$	
$CF_3CH_2NH_2$, MeOH[c]	5.0×10^{-2}	1.0×10^{-1}	2.1×10^2	3.5×10^{-6}
$C_6H_5NHNH_2$, MeOH[d]	$1\text{-}96 \times 10^{-4}$	2.0×10^{-2}	$6.0 \pm 0.8 \times 10^3$	3.0×10^{-4}
$H_2NCONHNH_2$, MeOH	$9\text{-}93 \times 10^{-4}$	1×10^{-1}	$5.3 \pm 0.5 \times 10^2$	4.0×10^{-4}
		Malachite Green		
$^-O_2CCH_2S^-$, H_2O	$1\text{-}10 \times 10^{-4}$	2.0×10^{-3}	$4.8 \pm 0.2 \times 10^4$	
$C_2H_5O_2CCH_2NH_2$, MeOH	7.7×10^{-2}	1.0×10^{-1}	5.3 ± 0.5[c]	1.3×10^{-9}
H_2NNH_2, MeOH	$9\text{-}96 \times 10^{-4}$	2.0×10^{-2}	$3.0 \pm 0.3 \times 10^2$	6.0×10^{-7}

[a] The p*K*s used in the calculations were as follows: $CF_3CH_2NH_2$, 12.4 (ref 7); HOOH, 11.65 (ref 7); $HSCH_2CO_2^-$, 10.01 (ref 8); HCN, 9.14 (ref 11); piperazinium ion, 10.1 (ref 7); or are from Table I. [b] See Results section. [c] Only a single concentration of the amine was used because of the unfavorable equilibrium. [d] Ionic strength maintained with $NaClO_4$. [e] For the reaction of methoxylamine, an increase in ionic strength to 4.0×10^{-2} M ($NaClO_4$) caused an increase of ca. 5% in the observed rate constants. This change is not believed to be significantly outside the expected experimental error.

Table III. Dabco General Base Catalysis of Reaction of Water with Aryltropylium Cations: $\mu = 0.10$ M (NaCl), $T = 25$ °C, pH 8.49 ± 0.01

[Dabco] × 10^3, M	A_{mix}	$[A_0 - A_{mix}]/A_{mix}$	K_{eq}, M^{-1}	$10^2\ k_\psi$, s^{-1}	$10^2\ k_{H_2O}$, s^{-1}
		p-Dimethylaminophenyltropylium Ion $A_0 = 1.240$			
50.0	0.661	0.876	17.5	1.54	2.89
40.0	0.760	0.630	15.7	1.55	2.52
30.1	0.842	0.471	15.7	1.57	2.31
20.1	0.887	0.397	19.7	1.54	2.15
10.1	1.011	0.225	22.3	1.60	1.96
5.07	1.123	0.103	20.3	1.63	1.80
2.62	1.184	0.046	17.6	1.66	1.73
0.65	1.227	0.010	14.9	1.66	1.67
		$k_w = 1.68 \times 10^{-2}\ s^{-1}$; $k_{Dabco} = 2.26 \times 10^{-1}\ M^{-1}\ s^{-1}$			
		p-Methoxyphenyltropylium Ion $A_0 = 1.686$			
20.1	0.097	12.5	625	3.03	40.9
10.0	0.162	7.12	709	4.74	38.5
5.04	0.293	3.48	690	7.87	35.3
3.05	0.437	2.00	656	11.2	33.7
2.05	0.592	1.22	593	14.7	32.5
1.06	0.817	0.607	574	20.3	32.6
		$k_w = 3.16 \times 10^{-1}\ s^{-1}$; $k_{Dabco} = 6.9\ M^{-1}\ s^{-1}$			

Scheme I



relationship[4] in which rates of electrophile-nucleophile reactions are compared with basicities of the nucleophiles. Those nucleophiles having a lone pair of electrons on the atom adjacent to the site of electrophilic attack are found generally to be more reactive than "comparable" nucleophiles which do not have the adjacent lone pair. This type of Brønsted relationship is, of course, a comparison of the effects of amine structure on the two "equilibrium" constants, K_b and K^* (see Scheme I). The behavior of the α-effect nucleophiles could be attributed to "unusual" effects of structure on either K_b or K^*, or both.

In the present case of reactions of amines with carbonium ions, Bruice[9] has pointed out that the α-effect amines, relative to primary amines, give larger values of both K^* and K_{RN} than expected from their K_bs. That is, the α-effect amines appear more "normal" when K^* is compared with K_{RN} than when K^* is compared with K_b. This fact, coupled with the data in Table I, strongly indicates that the α effect in these cases lies in an "unusual" effect of structure on K_b, and implicates the conjugate acids of the α-effect amines as the source of at least part of the "unusual" Brønsted behavior. The assumption that the

Table IV. Leaving Group Abilities of Nucleophiles[a]

Nucleophile	Log k_f[b]	Log K_f[c]	Log k_r[d]	pK_a[e]	Log k_{-1}[f]	Log k_{-x}[g]
OH^-, H_2O	3.23	6.65	−3.4		−3.4	0.0
CH_3O^-, MeOH	6.36	10.2	−3.8		−3.8	
$C_6H_5S^-$, MeOH	9.81	9.0	0.8		0.8	
$^-O_2CCH_2NH_2$, H_2O	3.71	−5.1	8.8	9.8	0.0	2.09
$^+H_3NCH_2CH_2NH_2$, H_2O	2.32	−4.9	7.2	6.8	1.4	1.95
$^-O_2CCH_2NHCOCH_2NH_2$, H_2O	3.18	−5.1	8.3	8.2	1.1	2.81
$C_2H_5O_2CCH_2NH_2$, H_2O	2.74	−5.1	7.8	7.9	0.9	2.86
$CF_3CH_2NH_2$, H_2O	1.57	−5.6	7.2	5.6	2.6	3.47
Morpholine, H_2O	4.28	−4.5	8.8	8.5	1.3	3.02
Dabco, H_2O	3.8[h]	1.2	2.6		2.6	3.80
CH_3ONH_2, H_2O	1.70	−3.3	5.0	4.6	1.4	3.20
$C_6H_5NHNH_2$, H_2O	2.79	−3.6	6.4	5.3	2.1	
$H_2NCONHNH_2$, H_2O	1.98	−4.2	6.0	3.9	3.1	4.22
$C_2H_5O_2CCH_2NH_2$, MeOH	3.62	−5.2	8.8	9.2	1.4	
$CF_3CH_2NH_2$, MeOH	2.32	−5.5	7.8	6.7	2.1	
Morpholine, MeOH	5.15	−3.7	8.8	8.7	1.1	
CH_3ONH_2, MeOH	2.81	−2.6	5.4	6.4	0.0	
$H_2NCONHNH_2$, MeOH	2.72	−3.4	6.1	5.8	1.3	
$C_6H_5NHNH_2$, MeOH	3.78	−3.5	7.3	7.3	1.0	

[a] See text for methods of evaluation. [b] k_f is the forward rate constant for the cation–nucleophile association. [c] For anions and tertiary amines, K_f is the equilibrium constant for the simple association reaction. For other amines, $K_f = K_1K_2$, where K_1 and K_2 are defined in eq 5. [d] For anions and tertiary amines, k_r is the rate constant for dissociation of the adduct. For other amines, $k_r = k_{-1}/K_2$ (see eq 5). [e] pK_a of the conjugate acid of the nucleophile. [f] In every case, k_{-1} is the rate constant for dissociation of simple adduct. [g] k_{-x} is the relative rate constant for dissociation of tetrahedral intermediate in aryl acetate reactions. [h] Rate constant estimated from the N_+ correlation.

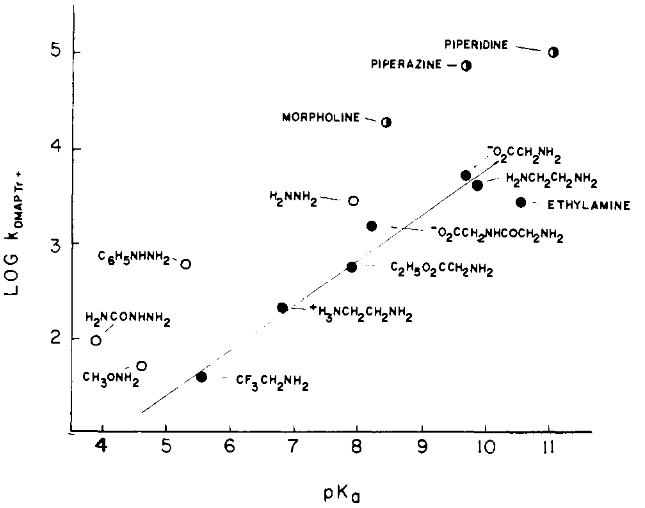


Figure 1. Brønsted plot for the reactions of amines with *p*-dimethylaminophenyltropylium ion in water. Data are from the present study and from ref 3.

conjugate acids of the α-effect amines are destabilized by some factor not operative on ordinary ammonium ions, and, therefore, that the pKs are lower than "normal", would be consistent with all observations. Some unusually unfavorable solvation of the conjugate acids of the α-effect amines in water is suggested, conceivably originating from an unfavorable interaction of the solvation shells of the lone pair and protonated sites.

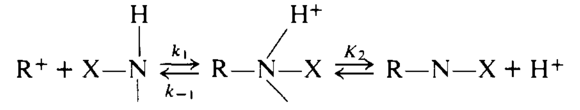
We would like to emphasize that we do not believe that the α effect can be attributed in every case solely to this solvation effect. As Jencks[19] has argued, it seems likely that the α effect has a variety of sources with the importance of different factors varying from case to case. Even in the simple cation-nucleophile combination reactions, as discussed further below, it appears that steric effects, for example, contribute to some of the α-effect behavior.

Whether or not the above suggestions are correct, the fact that the pKs and rates change by different amounts for change of solvent depending on amine type directly shows that the α effect in the present reactions is a solvent-dependent phenomenon.

In connection with the above discussion and with the following discussion of the reactions of nucleophiles with esters, it should be noted that the Brønsted relationship for the amine-DMAPTr$^+$ reactions is not very good even if we limit attention to the primary amines. The Brønsted plot is shown in Figure 1. We note particularly that the more basic amines show little variation in rate with change in basicity, and that the rate constants for reactions of secondary amines are approximately a factor of 10 greater than those for primary amines of the same pK. The plots become even more confused when the data for methanol solution reactions are included: secondary amines become more reactive, and α-effect amines become less reactive, relative to primary amines of equal pK, in methanol than in water solution.

Dissociation of Electrophile-Nucleophile Adducts. In a number of cases, we now have values for both rate and equilibrium constants of reactions of nucleophiles with carbonium ions. The available data for DMAPTr$^+$ are shown in Table IV. For anionic nucleophiles, the data shown lead directly to the rate constants for the dissociation of the electrophile-nucleophile adducts.

For amine nucleophiles, the measured equilibrium constants are for formation of product amine plus proton; i.e., $K_{obsd} = K_1K_2$ in the scheme



$$R^+ + X-\overset{\displaystyle H}{\overset{|}{N}} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} R-\overset{\displaystyle H^+}{\overset{/}{N}}-X \overset{K_2}{\rightleftarrows} R-N-X + H^+ \tag{5}$$

$K_1 = k_1/k_{-1}$; $k_{f(obsd)} = k_1$; $K_{obsd} = K_1K_2 = k_{f(obsd)}/k_{r(obsd)}$; $k_{r(obsd)} = k_{-1}/K_2$. In these cases, as shown in eq 5, the observed forward rate constant divided by the observed equilibrium constant gives the rate constant for specific acid catalyzed dissociation of the product amine, $k_{r(obsd)}$. In order to obtain the desired values of k_{-1}, we need to know the values for K_2.

For simple primary amines reacting with either DMAPTr$^+$ or with malachite green, the observed equilibrium constants are very nearly independent of the identity of the amine. The data for DMAPTr$^+$ are shown in Table IV. For malachite green reactions,[3,9] the values are (amine, pK_{obsd}) $^-O_2CCH_2NH_2$, 8.0; $C_2H_5NH_2$, 8.3; $H_2NCH_2CH_2NH_2$, 8.4; glycylglycinate, 7.9; $^+H_3NCH_2CH_2NH_2$, 8.6; $CF_3CH_2NH_2$, 8.6. The most reasonable explanation of this constancy is that the product ammonium ions have pK_2 lower than pK_a of the conjugate acids of the reactant amines by a constant amount. This is exactly what is expected on the basis of linear free energy relationships, the result being that change in X of eq 5 influences log K_1 and pK_a by the same amount as long as we deal with a related series of amines. Direct measurements of K_2 for malachite green reactions,[9] although not very precise, indicate that the adducts are approximately 1 pK unit more acidic than the conjugate acids of the reactant amines. We expect a similar effect for the adducts from aryltropylium ions, and show values of K_1 of eq 5 calculated on this basis in Table IV. These values, together with K_{obsd} and k_1, then lead to the values of k_{-1} shown in the sixth column of Table IV.

In the previous paper of this series,[1] we reported a correlation of the rates of reactions of nucleophiles with esters. For aryl acetates, the correlation depended upon an evaluation of relative leaving group abilities of nucleophiles from the tetrahedral intermediates formed in the first steps of the reactions. The evaluation was based on the stringent assumption that the relative leaving group abilities of the nucleophiles are independent of the identity of the aryloxy group. Data fitting to the N_+ equation then yielded a single scale of relative leaving group abilities, denoted log k_{-x}. The values obtained for the nucleophiles shown in Table IV are in the last column of the table, and are shown plotted vs. the log k_{-1} values from the present study in Figure 2.

With the single exception of the monoprotonated ethylenediamine leaving group, there is a reasonable relationship between the two quantities. Linear least-squares treatment of the data gives

$$\log k_{-1} = 1.55 \log k_{-x} - 3.32 \qquad (6)$$

Both the deviation of the point for protonated ethylenediamine and the slope of the correlation are easily rationalized. The tetrahedral intermediate resulting from attack of protonated ethylenediamine on aryl acetates has the opportunity of a favorable intramolecular hydrogen bond between the ammonium group and the anionic oxygen which could either stabilize the intermediate or cause rapid proton transfer to trap the intermediate.

The presence of the formal negative charge on the oxygen of the tetrahedral intermediate is also expected to cause the equilibrium constants for its formation to be less susceptible to structure (i.e., variation of X in eq 5) of the amine than the equilibrium constants for addition of a carbonium ion to the amine. Since, as we discuss below, these effects do not operate on the forward rate constants, they must operate on the reverse rate constants, leading to the slope shown in eq 6.

Correlations of Nucleophilic Reactivity. In our previous reports[1,3] of the reactions of nucleophiles with aryltropylium and triarylmethyl cations, we have noted that there is a generally good correlation of reactions by the simple equation

$$\log k = \log k_0 + N_+ \qquad (7)$$

with significant deviations of the points for methoxylamine and hydrazine reacting with both DMAPTr$^+$ and tropylium ion.[3] In addition to these deviations, three of the presently studied nucleophiles show rather large deviations from eq 7. The points for cyanide ion, peroxide ion, and hydrazine in methanol reacting with DMAPTr$^+$ fall about 1 log unit below the correlation line for other nucleophiles.

From the present study, the results in the accompanying paper on nucleophilic aromatic substitution,[12] and recent reports from other laboratories,[13-15] it is becoming obvious that the N_+ correlations do not generally have high precision. The use of the averaged N_+ values which we have listed[1] gives reasonable correlations in nearly all cases, but there are frequent moderate deviations of up to 1 log unit. We believe that we are beginning to see some patterns emerging in these deviations, but there are a number of cases where deviations have no apparent explanations. We can add very little to Kice's general summary of the situation,[13] but there are several specific points which merit some discussion.

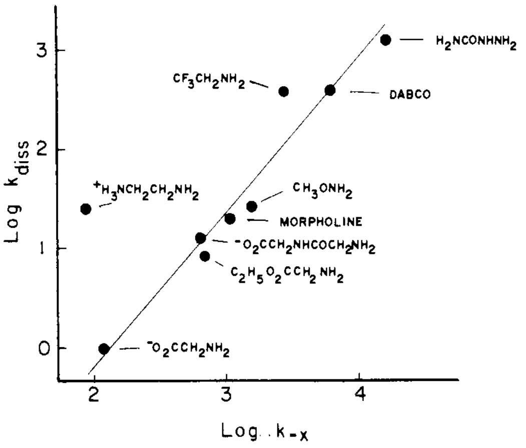


Figure 2. Dissociation of aryltropylammonium ions (k_{diss}) compared with dissociations of amine–aryl acetate adducts (k_{-x}). See Table IV and text for data.

First, we believe that steric effects are beginning to show up in these reactions. Since reactions of a number of nucleophiles with DMAPTr$^+$ and with tropylium ion are well correlated, we believe that the reaction center of DMAPTr$^+$ is similar to that of tropylium ion and is relatively unhindered sterically. (See also the comparison of DMAPTr$^+$ with aryl halides in the accompanying paper.[12]) A comparison of DMAPTr$^+$ with tri-p-anisylmethyl cation (TAM$^+$)[14,17] reactions gives the following results (nucleophile, log $k_{\mathrm{TAM}}/k_{\mathrm{DMAPTr}}$): ethylamine, 0.95; glycinate, 1.01; morpholine, −0.11; piperazine, −0.08; piperidine, −0.22; methoxylamine, 2.14; hydrazine, 2.02; cyanide ion, 1.90. The order of these values (methoxylamine ≈ hydrazine ≈ cyanide > primary amines > secondary amines) is what one would expect from steric effects for the TAM reactions. Quite similar effects of nearly the same relative magnitude are seen in the comparison of DMAPTr$^+$ and N-acetoxy-4-methoxypyridinium ion (AMPP) reactions, as shown in Figure 5.

If we choose the apparently unhindered nucleophiles methoxylamine, hydrazine, cyanide ion, and peroxide ion as standards (these nucleophiles show a range of 10^4 in rate constants for reactions with any given electrophile) and compare reactions of other electrophiles with those of DMAPTr$^+$, primary amines are 1 unit less reactive with triarylmethyl cations, 0.4 unit less reactive with 2,4-dinitrophenyl acetate, and 0.7 unit less reactive with methyl chloroformate,[18] than expected.

The same comparison indicates that sulfite ion reacts ca. 1 log unit too slowly with triarylmethyl cations, and that hydroxide and alkoxide ions react more than 1 log unit too slowly with triarylmethyl cations. Obviously, if these are steric effects, the solvation of the nucleophiles, and perhaps of the electrophiles, needs to be considered.[15]

The second point which we wish to discuss concerns the absence of a slope parameter in eq 7. Scott[14] has recently suggested that the precision of the N_+ correlation can be improved by allowing for a nonunit slope by the addition of another adjustable parameter making eq 7 identical in form with

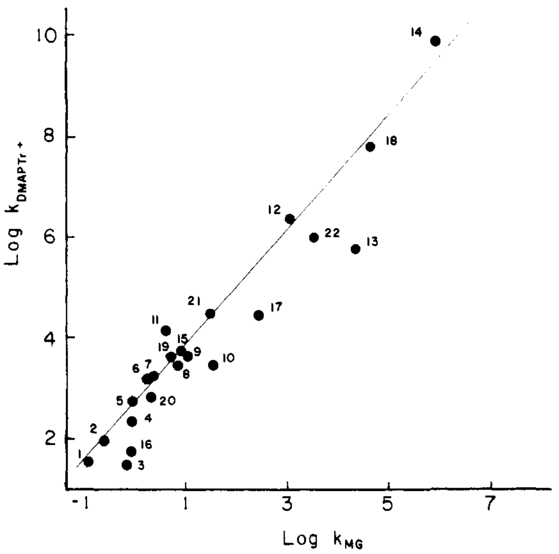


Figure 3. Comparison of rate constants for reactions of nucleophiles with *p*-dimethylaminophenyltropylium ion and with malachite green. The rate constant for reaction of trifluoroethoxide ion with malachite green is from ref 17; other data are from the present study and ref 2, 3, and 6. Point numbering is as follows: (1) $CF_3CH_2NH_2$, H_2O; (2) $H_2NCONHNH_2$, H_2O; (3) CN^-, H_2O; (4) $^+H_3NCH_2CH_2NH_2$, H_2O; (5) $C_2H_5O_2CCH_2NH_2$, H_2O; (6) $^-O_2CCH_2NHCOCH_2NH_2$, H_2O; (7) OH^-, H_2O; (8) $C_2H_5NH_2$, H_2O; (9) $H_2NCH_2CH_2NH_2$, H_2O; (10) H_2NNH_2, H_2O; (11) $CF_3CH_2O^-$, H_2O; (12) CH_3O^-, methanol; (13) HOO^-, H_2O; (14) $C_6H_5S^-$, methanol; (15) $^-O_2CCH_2NH_2$, H_2O; (16) CH_3ONH_2, H_2O; (17) H_2NNH_2, methanol; (18) $^-O_2CCH_2S^-$, H_2O; (19) $C_2H_5O_2CCH_2NH_2$, methanol; (20) $C_6H_5NHNH_2$, H_2O; (21) CH_3NHNH_2, H_2O; (22) SO_3^{2-}, H_2O.

the Swain-Scott equation.[16] Scott particularly makes the point that a comparison of reactions of nucleophiles with malachite green and with TAM shows the more reactive cation (TAM) to have a smaller selectivity than the less reactive one (malachite green). Although the slope is only slightly different from unity (1.2), it is in the direction "expected" from the selectivity-reactivity relationship. The improvement in correlation by the use of nonunit slope in this case is largely due to the inclusion of the point for reaction of water. We have previously[1] pointed out that the reaction of water with cations is a general-base-catalyzed reaction, and cannot be fairly compared with reactions of other nucleophiles. If this point for water reaction is excluded from consideration, the quantity log k_{TAM}/k_{MG} varies from 3.80 for ammonia (log $k_{MG} = -0.52$) and 3.56 for CN^- (log $k_{MG} = -0.16$) to 3.11 for SO_3^{2-} (log $k_{MG} = 3.60$). The best least-squares line still has a slope greater than unity, but the deviations of the points from a line of unit slope are quite small.

A direct comparison of the rates of reactions of nucleophiles with $DMAPTr^+$ and with malachite green is shown in Figure 3. If the badly deviant points for cyanide, peroxide, methoxylamine, and hydrazine are excluded, least-squares treatment of the data gives the correlation equation

$$\log k_{DMAPTr} = 1.12 \log k_{MG} + 2.69 \qquad (8)$$

with a correlation coefficient of 0.988 and a standard deviation of 0.318. Note that the slope here is such that the less reactive malachite green is also the less selective cation. It is also obvious from the plot, however, that deviations are large enough that a unit slope can accommodate the data nearly as well. If we limit attention to the "unhindered" nucleophiles methoxylamine, hydrazine, cyanide ion, and peroxide ion, the values of log k_{DMAPTr}/k_{MG} are 1.68, 1.82, 1.88, and 1.87, respectively, with log k for either electrophile spanning 4 units.

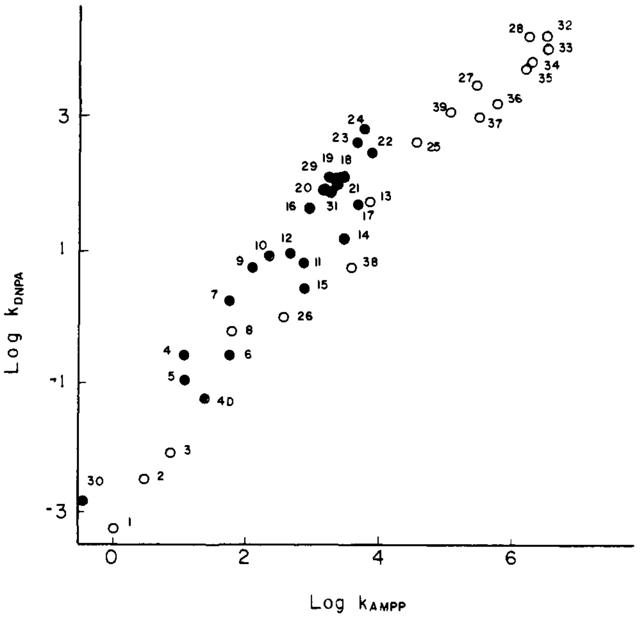


Figure 4. Comparison of rate constants for reactions of nucleophiles with 2,4-dinitrophenyl acetate (DMPA) and with *N*-acetoxy-4-methoxypyridinium ion (AMPP) in water solution. Data from ref 7 and 15. Point numbering is as follows: (1) acetate; (2) fluoride; (3) nitrite; (4) $CF_3CH_2NH_2$; (5) $H_2NCONHNH_2$; (6) $C_6H_5NH_2$; (7) piperazine H^+; (8) CN^-; (9) $^+H_3NCH_2CH_2NH_2$; (10) $C_2H_5O_2CCH_2NH_2$; (11) imidazole; (12) $^-O_2CCH_2NHCOCH_2NH_2$; (13) OH^-; (14) 4-methylpyridine; (15) pyridine; (16) $CH_3OCH_2CH_2NH_2$; (17) $HONH_2$; (18) *n*-$C_3H_7NH_2$; (19) $C_2H_5NH_2$; (20) morpholine; (21) $H_2NCH_2CH_2NH_2$; (22) H_2NNH_2; (23) piperazine; (24) piperidine; (25) $CF_3CH_2O^-$; (26) N_3^-; (27) CH_3O^-; (28) HOO^-; (29) 4-hydroxyquinuclidine; (30) Dabco H^+; (31) Dabco; (32) *n*-$C_3H_7S^-$; (33) $C_2H_5S^-$; (34) $HOCH_2CH_2S^-$; (35) $CH_3OCH_2CH_2S^-$; (36) $CF_3CH_2S^-$; (37) $C_6H_5S^-$; (38) 2,3,5,6-$F_4C_6HS^-$; (39) $HC{\equiv}CCH_2O^-$; (40) nicotinamide. ● = neutral; ○ = anionic.

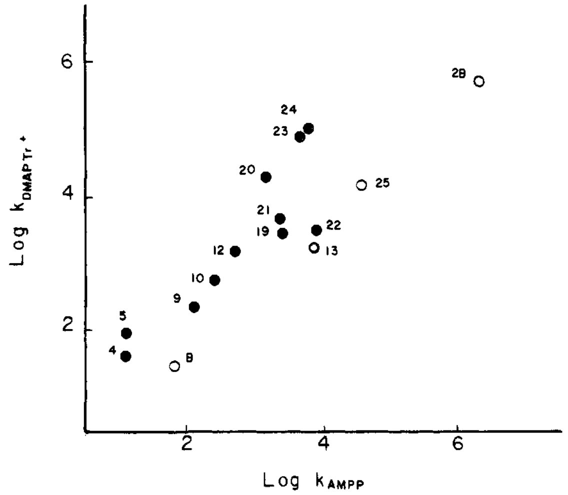


Figure 5. Comparison of rate constants for reactions of nucleophiles with *p*-dimethylaminophenyltropylium ion and with *N*-acetoxy-4-methoxypyridinium ion in water solution. Data from the present study and ref 2, 3, and 7. Point numbering is as given for Figure 4. ● = neutral; ○ = anionic.

There is no question that the addition of another adjustable parameter to eq 7 improves correlations. There is, however, considerable question about the significance of the added parameter in either a statistical or chemical sense. This question of selectivity-reactivity relationships is discussed further in the accompanying paper on nucleophilic aromatic substitution.[12]

The final point in this connection on which we would like to comment concerns the use of the Brønsted relationship in attempts to understand nucleophilic reactivity. The most frequent use of this relationship is in attempts to decide the rate-determining step in multistep reactions.[7,10,15] In cases where rate-determining attack of nucleophile occurs, a small slope is expected, whereas in cases of fast equilibrium formation of nucleophile-electrophile adduct followed by a rate-determining step, a slope near unity is expected.

As seen in Figure 1, for the reactions of amines with $DMAPTr^+$, where nucleophilic attack is certainly rate determining, the Brønsted relationship shows considerable scatter even for the simple primary amines. In particular, the more basic amines show little variation in reactivity with change in basicity.

As can be seen for one specific case in Figure 3, eq 7 is quite precise when attention is limited to structurally similar nucleophiles. The same behavior is seen in reactions of nucleophiles with 2,4-dinitrophenyl halides,[12] and is shown in Figures 4 and 5 for reactions of AMPP and of 2,4-dinitrophenyl acetate. We suggest that a precise adherence of rates of reactions of "families" of nucleophiles to eq 7 is the best indication of rate-determining attack of nucleophile. In most cases, the conclusions from this approach will coincide with those from the Brønsted approach. In cases where the less basic amines might just be showing changeover in rate-determing step, however, the conclusions will be different. For example, our approach indicates that attack of $CF_3CH_2NH_2$ on AMPP is rate determining while Jencks[7] assigns intermediate breakdown as rate determining.

As a side point in connection with Figures 4 and 5, it is seen that the points for anionic nucleophiles fall below the correlation line for primary amines in both cases. Since Figure 5 involves the comparison of a carbonium ion with a cationic ester, whereas a neutral and a cationic ester are compared in Figure 4, it does not seem reasonable that the deviations of the anionic points in Figure 4 can be ascribed to a coulombic effect. One might object that the use of $DMAPTr^+$ in these comparisons has the fault that the positive charge on this cation may be largely on the *p*-dimethylamino group, and thus far enough away from the reaction site that there is no coulombic effect. The direct comparison of reactions of $DMAPTr^+$ and tropylium ion, however, indicates that this objection is not valid. Hydroxide ion and trifluoroethylamine show precisely the same value (2.26) for $\log k_{Tr}/k_{DMAPTr}$, and the value for monoprotonated ethylenediamine (2.08) is only slightly different. We also note the absence of appreciable coulombic effects in the comparison of reactions of aryl halides with those of $DMAPTr^+$.[12]

General Base Catalysis of Reactions of Water. The data presented in Table III and discussed in the Results section clearly show the existence of general base catalysis for the reactions of water with aryltropylium ions. The ratios of the "water-catalyzed" and Dabco-catalyzed rate constants are 0.075 M for $DMAPTr^+$ and 0.046 M for the *p*-methoxyphenyltropylium ion. These values are quite similar to those of 0.06-0.2 M for reactions of water with triarylmethyl cations.[11]

The complicating factor in the present studies is the direct reaction of the aryltropylium ions with Dabco to form quaternary ammonium ions. At the concentrations of Dabco necessary to give appreciable equilibrium reaction, the establishment of equilibrium was fast enough that it could not be observed on the stop-flow. From our observations, we can set a lower limit of ca. $5 \times 10^3\ M^{-1}\ s^{-1}$ on the second-order rate constant for the amine-$DMAPTr^+$ combination reaction. On the basis of reactions of Dabco with esters, we had assigned[1] an N_+ value of 5.3 to Dabco. Equation 7 then leads to a predicted rate constant of $7 \times 10^3\ M^{-1}\ s^{-1}$ for the present reaction. This value, combined with the measured value of the equilibrium constant, leads to the reverse rate constant shown in Table IV. As seen in Figure 2, the value is in accord with expectations from data for the ester reactions.

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