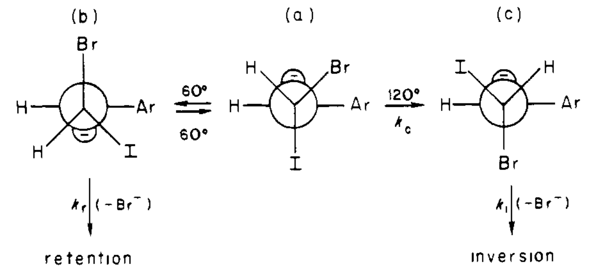
Scheme II



the addition of CH_3O^- to p-$NO_2PhCH{=}CF_2$.[96]

On the other hand the E2 path may be enforced by insufficient stability of the carbanion intermediate toward loss of halide. There are pertinent results in the literature, but as the following argument shows, only a rough estimate of this barrier can be made at the present time. Miller and Yonan found that reaction of iodide ions with *cis-p*-nitro-β-bromostyrene (in butyl carbitol at 196 °C) gives (prior to equilibration) substitution with retention of configuration faster than either isomerization or substitution with inversion.[97] The result may be rationalized by postulating the formation of an intermediate, p-$NO_2C_6H_4^-CHCHBrI$, which must assume a conformation in which a carbon-halogen bond is coplanar with the orbital containing the electron pair before expulsion of halide. On this basis the dominance of retention occurs because the suitable conformation is achieved through a small, 60° rotation during which only the eclipsing of a pair of hydrogens is necessary. Isomerization and inversion require more rotation and the eclipsing of larger groups. The competition is illustrated in Scheme II, beginning with the conformation (a) first formed by attack of iodide perpendicular to the double-bond plane. If we assume hyperconjugative stabilization of the anions[69,98] and that (a) is more stable than (b), then the preference for retention *also* requires that $k_r \gg k_c$. Molecular orbital calculations indicate that the barrier for k_c can be substantial,[98] but would be lowered by the electron-withdrawing p-nitrophenyl group.[98c] It is possible to say only that expulsion of bromide from a suitable conformation of p-$NO_2C_6H_4^-CHCH_2Br$ probably has a barrier considerably less than ca. 10 kcal/mol.

Similarly, Marchese, Naso, and Modena have shown that nucleophilic substitution of benzenethiolate for chloride or bromide in the isomeric p-nitro-β-halostyrenes (CH_3OH, 25 °C) occurs with complete retention of configuration.[99] In contrast, the kinetically controlled substitution of benzenethiolate for fluoride in *cis*- or *trans-p*-nitro-β-fluorostyrene gives the thermodynamically more stable trans product in both cases.[99]

In summary it can be said that of the p-nitrophenethyl halides, only the fluoride has been demonstrated to be capable of giving a carbanion that is not impossibly short-lived. It will be interesting to see whether the fluoride uses the E2 or the E1cB mechanism. If it is the former it will mean that elimination is concerted even though it is not required to be by the impossibility of intermediate formation, i.e., that concertedness is not enforced. It remains to be determined whether the unusual stability of p-nitrobenzyl anions can be accounted for by the large σ value of the p-nitro group or whether it reflects a special barrier for protonation of a delocalized nitrocarbanion.[26,65a,96]

Acknowledgment. We are grateful to the National Science Foundation (Grant PCM 77-08369) and the National Institutes of Health (Grant GM 20888) for financial support of this work. We also thank James Tropp and Professor A. Redfield for assistance with the 270-MHz NMR measurements.

Registry No. **1**·Br$^-$, 73997-48-5; **2**·ClO$_4^-$, 83967-66-2; **3**·2ClO$_4^-$, 83967-68-4; **4**·Br$^-$, 73997-50-9; **5**·Br$^-$, 83967-69-5; **6**·2I$^-$, 83967-70-8; **7**·Cl$^-$, 83967-71-9; p-nitrophenethyl fluoride, 56153-06-1; p-nitrophenethyl chloride, 20264-95-3; p-nitrophenethyl bromide, 5339-26-4; p-nitrophenethyl iodide, 20264-96-4; 1,2-dibromo-1-(p-nitrophenethyl)ethane, 21086-34-0; acetohydroxamate, 41879-86-1; deuterium, 7782-39-0; N-methyl-3-oxoquinuclidinium iodide, 6659-51-4; 3-oxoquinuclidinium chloride, 1193-65-3; (2-(p-nitrophenyl)ethyl-$\beta,\beta,$-d_2)trimethylammonium perchlorate, 83967-73-1.

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[96] Koch, H. F.; Koch, J. G.; Kim, S. W.; Koch, N. H.; Koch, A. S., personal communication.

[97] Miller, S. I.; Yonan, P. K. *J. Am. Chem. Soc.* **1957**, *79*, 5931-5936.

[98] (a) Hoffmann, R.; Radom, L.; Pople, J. A.; Schleyer, P. v. R.; Hehre, W. J.; Salem, L. *J. Am. Chem. Soc.* **1972**, *94*, 6221-6223. (b) Apeloig, Y.; Rappoport, Z. *Ibid.* **1979**, *101*, 5095-5098. (c) Rappoport, Z. *Acc. Chem. Res.* **1981**, *14*, 7-15.

[99] Marchese, G.; Naso, F.; Modena, G. *J. Chem. Soc. B* **1968**, 958-962; **1969**, 290-293.

Cation-Anion Combination Reactions. 22.[1] Rate and Equilibrium Constants for Reactions of Pyronin and Thiopyronin with Nucleophiles

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Contribution from the Department of Chemistry, State University of New York at Buffalo, Buffalo, New York 14214. Received June 1, 1982

Abstract: Rate and equilibrium constants for the reactions of Pyronin, 3,6-bis(dimethylamino)xanthylium cation, and of Thiopyronin, 3,6-bis(dimethylamino)thioxanthylium cation, with several anionic and amine nucleophiles in water and methanol solutions have been determined. Rate and equilibrium constants for corresponding reactions of the two cations are quite similar, but small effects that may be attributed to polarizability interactions can be distinguished. Comparisons with earlier data for reactions of triarylmethyl cations clearly show the existence of large steric effects in the triarylmethyl systems. Simple relationships between rate and equilibrium constants do not exist for any of these systems, and it is shown that Marcus theory cannot be applied to electrophile-nucleophile combination reactions. Conclusions drawn from such attempted applications are without foundation.

An understanding of the fundamental factors affecting the reactivities of electrophiles and nucleophiles in simple combination reactions is a long-sought goal throughout chemistry. For organic electrophiles and many common nucleophiles, our previous work

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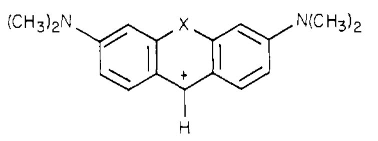
has shown that unexpectedly general patterns such as that expressed in the N_+ relationship[2] exist (with a number of exceptions[3-6]) but any relationship between reactivities and more fundamental properties of the electrophiles and nucleophiles remain obscure.[3]

The concepts of "intrinsic barriers" and rate–equilibrium relationships, which are a part of Marcus theory,[7] have aided the understanding of other reaction types. For electron-transfer reactions, there is ample evidence[7-9] for the validity of the theory, and, for proton-transfer[10] and S_N2 exchange reactions,[11] there is reasonable promise that the same concepts can be applied. There have also been reports of the application of Marcus theory to electrophile–nucleophile combination reactions.[12-14]

For reasons to be presented in the Discussion section, we do not believe that the application of Marcus theory to electrophile–nucleophile combination reactions can be justified. We have, nevertheless, been interested in obtaining equilibrium constants for such reactions. It seems reasonable to believe that the underlying forces that determine equilibrium constants must operate to some extent at the transition states, even though they may be masked by other effects. The equilibrium constants are also of considerable importance in themselves, for example, in attempts to understand thermodynamics of complex molecules in terms of group contributions and group–group interactions.[15]

We have found two cationic electrophiles, Pyronin (Ia), 3,6-bis(dimethylamino)xanthylium cation, and Thiopyronin (Ib), 3,6-bis(dimethylamino)thioxanthylium cation, that provide unusually wide opportunities for the measurements of rate and equilibrium constants for reactions with nucleophiles. These two cations are of further interest since their reactions should be relatively free of the steric effects probably present for triarylmethyl cation reactions[3] and of the possibility of isomeric product formation present in the aryltropylium cation reactions, which have made the latter systems less than ideal in our previous work. There is also the obvious interest in the effects of the change from X = O to X = S on the rate and equilibrium constants for various types of nucleophiles.



Ia, X = O
Ib, X = S

Experimental Section

Materials. Pyronin-Y, Certified Stain, Baker Analyzed Reagent, was commercially available as the chloride salt. The chloride salt was dissolved in hot ethanol and filtered while hot, and then a hot concentrated solution of sodium fluoroborate in ethanol was added. On cooling, shiny green needles of Pyronin fluoroborate precipitated and were filtered off. The fluoroborate salt was recrystallized from acetonitrile until the molar absorbance of the material at 547 nm (aqueous solution) showed no increase on further recrystallizations: λ_{max} = 547 nm ($\epsilon = 9.7 \times 10^4$ M^{-1} cm^{-1}); ^1H NMR (Me_2SO-d_6) δ 3.25 (s, 12 H), 6.76 (d, J = 3 Hz, 2 H), 7.15 (dd, J = 3 and 9 Hz, 2 H), 7.80 (d, J = 9 Hz, 2 H), 8.65 (s, 1 H).

Thiopyronin, as the zinc chloride double salt, was obtained as described by Nealy.[16] The crude product was dissolved in hot water, the hot solution was filtered, and a hot concentrated solution of sodium fluoroborate was added to the filtrate. On cooling, Thiopyronin fluoroborate precipitated as dark green needles. The fluoroborate salt was repeatedly recrystallized from acetonitrile until the molar absorbance of the salt, dissolved in water, at 563 nm did not increase on further recrystallizations: λ_{max} = 563 nm $\epsilon = 9.0 \times 10^4$ M^{-1} cm^{-1}); ^{1} H NMR (Me_2SO-d_6 δ 3.25 (s, 12 H), 7.20 (d, J = 9 Hz, 2 H), 7.24 (s, 2 h), 7.90 (d, J = 9 Hz, 2 H), 8.25 (s, 1 H).

Water used for the preparation of reaction solutions was house-distilled water, further purified by distillation from basic $KMnO_4$. Methanol was reagent-grade commercial material used without further purification.

Glycine and hydrazine hydrochlorides were commercial materials purified by recrystallization as described in earlier papers.[1,2] Commerical n-butylamine was distilled from KOH under a nitrogen atmosphere; the hydrochloride was prepared from the purified amine by treatment with concentrated aqueous HCl in ethanol and was recrystallized from ethanol. Purity of the salt was verified by potentiometric titration with $AgNO_3$ in water.

Master solutions of sodium sulfite in water were prepared from reagent-grade material to be ca. 1 M and were standardized by titration with $KMnO_4$, which, in turn, had been standardized by titration of oxalic acid. These master solutions were stable for periods of at least several days, but more dilute solutions used in the reactions appeared to decompose rapidly. The dilute solutions were stabilized by the addition of ca. 10^{-4} M hydroquinone in order to overcome this problem.

Master solutions of hydrogen peroxide in water were prepared from 30% reagent to be ca. 1 M and were standardized by titration with $KMnO_4$.

Commercial propanethiol was distilled and stored under a nitrogen atmosphere.

Sodium methoxide solutions were prepared by the reaction of sodium metal with methanol and were standardized by titration with aqueous HCl, which, in turn, had been standardized by titration with standard NaOH (Dilut-It reagent).

All other materials were commercial reagent-grade samples used without further purification.

Procedures. Master solutions of Pyronin and of Thiopyronin were prepared in acetonitrile to be ca. 10^{-3} M. These solutions were diluted into water to be ca. 10^{-5} M for the reaction studies. The master solutions were stable for at least 1 week, but the dilute aqueous solutions showed appreciable decreases in absorbance after 1 day.

The measurements of the pK_R's of the cations utilized carbonate–bicarbonate buffers up to pH of ca. 10.7 and dilute solutions of sodium hydroxide for higher pH. The pH of each reaction solution was measured by using a glass vs. saturated calomel electrode system that had been standardized at pH 12.45 with saturated $Ca(OH)_2$ at 25.0 °C. Spectra of the solutions were obtained by using 1.0-cm cells in a Cary Model 14 spectrophotometer. The spectral measurements were made within a few minutes after preparation of the solutions and showed good isosbestic points in the UV region. After longer times, strong absorbance develops at ca. 400 nm and the isosbestic points are badly degraded.

The kinetics of the hydroxide ion reactions were studied by stop-flow spectrophotometry, using both single-wavelength and rapid-scanning instruments.[17] The side reaction mentioned above was too slow to cause any difficulties in the kinetic measurements, and the reactions accurately followed pseudo-first-order behavior and gave "infinity" readings in good agreement with the measured pK_R's for at least eight half-lives.

The reactions of the cations with cyanide ion, studied at pH of ca. 10.3, were complicated by the simultaneous reaction of hydroxide ion, the extent of which was sufficient to cause observable deviations from strict pseudo-first-order behavior. At the concentrations of cyanide ion reported in Table I, the reactions resulted in complete disappearance of the cations. The kinetic data for these reactions were analyzed according to the scheme for simultaneous reversible first-order reactions. Since the rate and equilibrium constants for the hydroxide ion reactions were known from the study described above, the only unknown parameter in the scheme is the rate constant for the cyanide ion reaction, which was then obtained by nonlinear least-squares fitting. Attempts to extend these studies to lower cyanide ion concentrations gave such slow reactions that the side reaction mentioned above, producing absorbance at 390–400 nm, interfered.

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(1) Previous paper in this series: Ritchie, C. D.; Van Verth J. E.; Virtanen, P. O. I. *J. Am. Chem. Soc.* **1982**, *104*, 3491.

(2) Ritchie, C. D.; Virtanen, P. O. I. *J. Am. Chem. Soc.* **1972**, *94*, 4966. Ritchie, C. D. *Acc. Chem. Res.* **1972**, *5*, 348; *J. Am. Chem. Soc.* **1975**, *97*, 1170.

(3) Ritchie, C. D. *Pure Appl. Chem.* **1978**, *50*, 1281.

(4) Ritchie, C. D.; Gandler, J. *J. Am. Chem. Soc.* **1979**, *101*, 7318.

(5) Ritchie, C. D.; Kawasaki, A. *J. Org. Chem.* **1981**, *46*, 4704.

(6) Ritchie, C. D.; Kamego, A. A.; Virtanen, P. O. I.; Kubisty, C. *J. Org. Chem.* **1981**, *46*, 1957.

(7) Marcus, R. A. *J. Phys. Chem.* **1968**, *72*, 891.

(8) Marcus, R. A. *Discuss. Faraday Soc.* **1960**, *29*, 21.

(9) Marcus, R. A. *Annu. Rev. Phys. Chem.* **1964**, *15*, 155.

(10) Marcus, R. A. *Symp. Faraday Soc.* **1975**, *10*, 60.

(11) Albery, W. J.; Kreevoy, M., *Adv. Phys. Org. Chem.*, **1978**, *16*, 87. Albery, W. J. *Pure Appl. Chem.* **1979**, *51*, 949.

(12) Hine, J. *J. Am. Chem. Soc.* **1971**, *93*, 3701.

(13) Albery, W. J. *Annu. Rev. Phys. Chem.* **1980**, *31*, 227.

(14) Guthrie, J. P. *J. Am. Chem. Soc.* **1973**, *95*, 6999; **1974**, *96*, 3608; **1978**, *100*, 5892; **1980**, *102*, 5177; *Can. J. Chem.* **1976**, *54*, 202.

(15) Hine, J. "Structural Effects on Equilibria in Organic Chemistry" Wiley: New York, 1975; particularly pp 225–229 and 263–265.

(16) Nealy, R. H.; Driscoll, J. S. *J. Heterocycl. Chem.* **1966**, *3*, 228.

(17) Ritchie, C. D.; Hofelich, T. C. *J. Am. Chem. Soc.* **1980**, *102*, 7039.

Table I. Summary of Experimental Conditions Used[a]

nucleophile (solvent)	nucleophile × 10^3 range, M	ionic strength, M	buffer	pH range
A. Pyronin Reactions				
OH^- (H_2O)	1.0-36	0.05	OH^- or HCO_3^--CO_3^{2-}	10.9-12.6
CN^- (H_2O)	2.4-96	0.4	OH^- or HCO_3^--CO_3^{2-}	10.2-11.1
n-$BuNH_2$ (H_2O)	100-300	0.3	*n*-$BuNH_2$-*n*-$BuNH_3^+$	10.1-10.6
glycinate (H_2O)	200-450	0.6	Gly:$GlyH^+$	10.5
SO_3^{2-} (H_2O)	0.035-0.66[b]	0.01[b]	OH^- or HOAc-AcO^-	4.9 and 11.0
HOO^- (H_2O)	1.7-5.4	0.01	OH^- or HCO_3^--CO_3^{2-}	10.4-11.4
n-PrS^- (H_2O)	0.004-0.03	0.01	Dabco-$DabcoH^+$	8.72
CH_3O^- (MeOH)	0.002-0.006[c]	0.001	Et_3N-Et_3NH^+	11.2-11.7[c]
n-$BuNH_2$ (MeOH)	1.0-20	0.001	*n*-$BuNH_2$-*n*-$BuNH_3^+$	11.7-13.0[c]
B. Thiopyronin Reactions				
OH^- (H_2O)	0.4-200	0.05-0.2[d]	OH^- or HCO_3^--CO_3^{2-}	10.7-13.3
CN^- (H_2O)	0.1-1.0	0.05	HCO_3^--CO_3^{2-}	10.06
n-$BuNH_2$ (H_2O)	100-700	0.3-0.6[d]	*n*-$BuNH_2$-*n*-$BuNH_3^+$	9.9-11.3
glycinate (H_2O)	100-300	0.6	Gly-$GlyH^+$	10.5
SO_3^{2-} (H_2O)	0.0001-2.4[b]	0.02-0.05[b]	OH^- or HOAc-AcO^-	3.97, 4.68, 11.0
HOO^- (H_2O)	2.0-20	0.01	OH^-	11.0-11.7
n-PrS^- (H_2O)	0.0006-0.009	0.01	Dabco-$DabcoH^+$	8.74
CH_3O^- (MeOH)	0.003-0.010[c]	0.001	Et_3N-Et_3NH^+	11.4-11.9[c]
NH_2NH_2 (MeOH)	1.0-5.0	0.001	NH_2NH_2-$NH_2NH_3^+$	10.84[c]
n-$BuNH_2$ (MeOH)	10-100	0.001-0.03[d]	*n*-$BuNH_2$-*n*-$BuNH_3^+$	11.7-12.7[c]

[a] All measurements at 23 ± 1 °C. Pertinent pK_a values used for aqueous solutions are: HCO_3^-, 10.33; $DabcoH^+$, 8.72; HCN, 9.21; *n*-$BuNH_3^+$, 10.55; $GlyH^+$, 9.78; HSO_3^-, 7.18; HOOH, 11.65; *n*-PrSH, 10.78. [b] The Debye-Hückel limiting law was used to calculate the activity of SO_3^{2-}. [c] pK_a's from ref 22. [d] The variation in ionic strength caused no observable change in rates.

Table II. Data Obtained in This Study (23 ± 1 °C)

	Pyronin		Thiopyronin	
nucleophile (solvent)	log K[a]	log K[b]	log K[a]	log K[b]
n-PrS^- (H_2O)	6.60	5.11	6.85	6.11
CH_3O^- (MeOH)	5.18	5.43	4.46	5.26
SO_3^{2-} (H_2O)[c]	4.77	6.64	4.65	6.40
HOO^- (H_2O)	4.20	2.48	3.66	2.48
H_2NNH_2 (MeOH)			3.04	0.68
n-$BuNH_2$ (MeOH)	3.41	−0.26	3.04	0.15
n-$BuNH_2$ (H_2O)	2.98	0.24	2.49	0.37
glycinate (H_2O)	2.66	−1.39	2.18	−1.10
HO^- (H_2O)	1.62	2.49[d]	0.97	2.45[d]
CN^- (H_2O)	0.02	>4	−0.02	>5

[a] Rate constants in units of M^{-1} s^{-1}. [b] Equilibrium constants in units of M^{-1}. Values for the amine reactions are from eq 3; see text. [c] Activities, calculated by the Debye-Hückel limiting law, were used for the evaluation of both rate and equilibrium constants for sulfite reactions. [d] From $pK_R = 11.51$ for Pyronin and 11.55 for Thiopyronin.

The reaction of Pyronin with *n*-butamine in both water and methanol solutions were also complicated by the sumultaneous reactions of hydroxide or methoxide ion. Kinetic data were treated as described above for cyanide ion reactions. For Thiopyronin, the *n*-butylamine reaction reached equilibrium before appreciable reaction of hydroxide or methoxide ions and gave simple pseudo-first-order kinetics.

The remainder of the reactions studied were straightforward, and the procedures used were analogous to those reported in earlier work.[1] The experimental conditions used are summarized in Table I, and the rate and equilibrium constants obtained are reported in Table II.

Results

The measurements of the pK_R values for the cations showed maximum deviations of 0.05 unit from the reported values over the pH range of 10.97-12.58 for Pyronin and of 10.66-12.30 for Thiopyronin. There is no reason to expect the accuracies of these values to be less than this precision.

There is a literature report of a pK_R of 11.55 determined for Pyronin,[18] which is in surprising agreement with trhe present value since the authors report the appearance of absorbance at ca. 390 nm as the absorbance of the cation at 546 nm decreases. Our studies show quite clearly that the absorbance at 390-400 nm is due to a side reaction, probably a disproportionation of the cation and carbinol to form ketone and leuco base.

As in our previous studies, the precisions of the second-order rate constants determined for all reactions are better than ±10%, and the accuracies are expected to be comparable. Equilibrium constants for the reactions, other than the hydroxide ion reaction, are less precise than the corresponding rate constants. Maximum deviations of a factor of 2 were occasionally observed, but average deviations were more generally ±25% over reasonable extents of reactions. The accuracies should be better than ±50%.

The reactions of sulfite ion with the cations have several features requiring attention. These reactions were studied at pH 11, where the concentration of bisulfite ion is negligible, and at pH less than 5, where the concentration of bisulfite is much greater than that of sulfite ion. The kinetics show clearly that bisulfite ion, even at pH 3.97 for the reaction with Thiopyronin, does not contribute observably to the reactions. At the low pH necessary for the equilibrium studies, the equilibria, but not the kinetics, are complicated by protonation of the dimethylamino groups of products. For the reactions of Thiopyronin, the measurements at pH 3.97 and 4.68 were brought into agreement by assuming a pK_a of 4.7 for the monoprotonated product and of 4.1 for the diprotonated product. These are the same pK_a values that we have found in previous work for protonated dimethylamino-substituted triarylmethanols.[19] For the Pyronin reaction, we have simply assumed that the same pK_a's apply.

Reactions of amines with the cations give equilibrium behavior that is consistent with the expected reaction scheme:

$$Pyr^+ + RNH_2 \underset{K_{app}}{\rightleftharpoons} PyrNHR + H^+ \qquad (1)$$

In previous work with triarylmethyl cations, we[20] and others[21] have found that the pK_a's of $Ar_3CNH_2R^+$ products are approximately one unit less than the pK_a's of the corresponding RNH_3^+ ions, and we expect quite similar behavior for the $PyrNH_2R^+$ products. In the present study of the reactions of *n*-butylamine in water, we were able to use pH as low as 0.5 unit below the pK_a of *n*-butylammonium ion and did not observe any deviations from the reaction scheme (1). The pK_a of the $PyrNH_2R^+$ product must,

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(18) Fujiki, K.; Iwanaga, C.; Kioizumi, M. *Bull. Chem. Soc. Jpn.* **1962**, *35*, 185.

(19) Ritchie, C. D.; Wright, D. J.; Huang, D-S.; Kamego, A. A. *J. Am. Chem. Soc.* **1975**, *97*, 1163.

(20) Ritchie C. D.; Virtanen, P. O. I. *J. Am. Chem. Soc.* **1973**, *95*, 1882.

(21) Dixon J. E.; Bruice, T. C. *J. Am. Chem. Soc.* **1971**, *93*, 3248.

(22) Ritchie, C. D.; Minasz, R. J.; Kamego, A. A.; Sawada, M. *J. Am. Chem. Soc.* **1977**, *99*, 3747.

Table III. Reactions of Aryltropylium and Triarylmethyl Cations[a]

	DMAPTr[b]		MG[b]		CV[b]	
nucleophile (solvent)	log *k*	log *K*	log *k*	log *K*	log *k*	log *K*
n-PrS$^-$ (H_2O)	8.18[c]	8.85[c]	4.52	6.7[d]	3.35[d]	4.2[d]
CH_3O^- (MeOH)	6.36	10.24	3.10	8.11	1.81	4.64
SO_3^{2-} (H_2O)	5.98		3.60		2.67	3.90
HOO^- (H_2O)	5.68		4.11			
H_2NNH_2 (MeOH)	4.41		2.48	2.50		
n-BuNH_2 (H_2O)	3.64[e]	4.6[f]	0.87	2.2[g]		
glycinate (H_2O)	3.71	3.10	0.95	0.69		
HO^- (H_2O)	3.23	6.65	0.34	7.06	−0.70	4.61
CN^- (H_2O)	1.53		−0.29		−1.27	

[a] All data are from previous papers in this series, and units and conditions are comparable to those used in the present study. [b] DMAPTr is *p*-(dimethylamino)phenyltropylium ion; MG is Malachite Green cation; and CV is Crystal Violet cation. [c] The values given are actually for ethanethiolate reactions. [d] Values are estimated from those for reactions of 2-hydroxyethanethiolate and the relationships noted in ref 4. [e] Measured in the present work. [f] Value is estimated from the value for glycinate reaction; see ref 20. [g] Value is actually that for ethylamine reaction.

therefore, be appreciably more than 0.5 unit less than that of *n*-butylammonium ion, as expected.

The equilibrium constants reported in Table II for the reactions of amines are those estimated from the measured K_{app} of scheme 1 and the assumption, discussed above, that the pK_a's of the ammonium ion products are one unit less than the pK_a's of the conjugate acids of the reactant amines for the addition reactions

$$\mathrm{Pyr}^+ + \mathrm{RNH}_2 \underset{K_{add}}{\rightleftharpoons} \mathrm{PyrNH_2R}^+ \qquad (2)$$

by use of eq 3.

$$\log K_{add} = \log K_{app} + pK_{a(RNH_3^+)} - 1.0 \qquad (3)$$

The only nucleophile in the present study for which we were not able to determine equilibrium constants is cyanide ion. Because of the low rate constants for reactions of cyanide ion with both cations, the side reaction discussed above for hydroxide ion (or one similar to it in producing absorbance at 390–400 nm) interferes with studies at low cyanide ion concentrations. At the lowest cyanide ion concentration for which we could neglect the side reaction (1.0×10^{-4} M for Thiopyronin), the disappearance of cation was complete at infinity readings. This sets a lower limit of ca. 10^5 M^{-1} on the equilibrium constant for the Thiopyronin plus cyanide ion reaction. We suspect, from Hine's[15] evaluation of the "methyl basicity" of the cyanide ion, that the equilibrium constant is much greater than this lower limit.

Discussion

A comparison of the equilibrium constants for reactions of Pyronin with those for the corresponding reactions of Thiopyronin shows that the change from X = O to X = S in structure I has only small effects on the equilibrium reactivities of the cations. The largest difference for the two cations is the factor of 10 in the equilibrium constant for reaction of propanethiolate, with Thiopyronin having the larger value. This, of course, is what might have been expected from polarizability arguments.[23]

The data for the reactions of the two cations of the present study may be compared with corresponding data from our earlier studies of triarylmethyl and aryltropylium cations.[1] Some of the pertinent data are shown in Table III. The relative log *K*'s for reactions of DMAPTr ((*p*-(dimethylamino)phenyl)tropylium cation) with nucleophiles are quite similar to those for reactions of Pyronin. Log *K* values for the DMAPTr reactions are ca. 4.3 units greater than the corresponding ones for Pyronin reactions. As mentioned in the introduction, the positions of attack of the nucleophiles on the tropylium ring are not known and could be different for different nucleophiles. If this is the case, there is no indication of any appreciable effects on the equilibrium constants.

The comparisons of the relative log *K* values for reactions of the nucleophiles with the triarylmethyl cations to those for the corresponding reactions of Pyronin do indicate sizable steric effects in the triarylmethyl cation reactions. For reaction with hydroxide ion, log *K* for Malachite Green is 4.5 units greater than that for Pyronin. For reactions of all other nucleophiles, an appreciably smaller difference is seen in the log *K*'s for the two cations. Similar variations can be seen in the comparisons for Pyronin and Crystal Violet reactions. Log *K* for reaction of hydroxide ion is 2.1 units greater for Crystal Violet than for Pyronin, while for reaction of sulfite ion, log *K* for Crystal Violet is 2.7 units *less* than that for Pyronin. Close inspection of the data shows that these variations closely follow expectations based on the sizes of the nucleophiles and strongly supports the suggestion that these are indeed steric effects.

Hines[15] has pointed out that carbon basicities of nucleophiles are not invariant even in the absence of steric effects; in particular, relative equilibrium constants for reactions of nucleophiles at phenyl, methyl, and 1-hydroxyalkyl carbons show large variations. We emphasize, therefore, that the equilibrium constant found in the present work should not be used indiscriminately as general measures of relative carbon basicities.

The differences in rate constants for corresponding reactions of Pyronin and Thiopyronin are quite small but do appear to follow a pattern, indicating some influence of polarizability. For the oxygen and nitrogen nucleophiles, log *k*s are 0.5–0.7 unit greater for reactions with Pyronin than for the corresponding ones with Thiopyronin. Log *k* for reaction of propanethiolate with Pyronin is 0.2 unit *less* than that with Thiopyronin, and the log *k*s for reactions of sulfite ion and cyanide ion are nearly equal for the two cations.

There is an excellent unit slope correlation of the log *k*s for reactions of Pyronin with those for reactions of DMAPTr, the log *k*'s for DMAPTr being 1.3 ± 0.3 units greater than those for Pyronin with no recognizable pattern of deviations. This average difference in log *k*'s is less than one-third of the average difference in log *K*'s discussed above.

There is a poor correlation of the log *k*'s for reactions of Pyronin with those for reactions of either Malachite Green or Crystal Violet, and the patterns of behavior are not consistent with steric effects that were seen in the comparisons of equilibrium constants. For example, both hydroxide ion and sulfite ion have log *k* greater by 1.2 units for Pyronin than for Malachite Green reactions. It is also worth noting that the equilibrium constants for reactions of nucleophiles with Malachite Green are invariably greater than those for the corresponding reactions with Pyronin, while the rate constants for Pyronin reactions are greater than those for Malachite Green reactions with all nucleophiles except peroxide and cyanide ions, where the rates are nearly equal for the two electrophiles.

It is immediately obvious from the data in Table II that there is no simple, direct relationship between the equilibrium and kinetic reactivities of the various nucleophiles. It should also be obvious from the above discussion that no simple relationship exists between the kinetic and equilibrium reactivities of the electrophiles, nor is there any simple parallel between steric effects on rates and equilibria. In recent work,[1] we have also pointed out that solvent effects on rates do not parallel those on equilibria.

Marcus theory, which offers a rather indirect relationship between kinetic and equilibrium behavior in terms of "intrinsic barriers", is a tempting refuge from this unsettling state.[7-14] We have concluded, however, that this refuge is a mirage, and that attempts[12-14] to use the Marcus equations for electrophile–nucleophile combination reactions are completely without foundation.

The conclusion follows from a close examination of Marcus theory. Since the theory may be rationalized by the use of several quite different models, we will avoid the use of any specific model in the following examination and focus on the general formulation of the theory that Marcus[7] has presented.

This general formulation is based on several assumptions: (1) for the reactions treated, there must be some extent of reaction

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(23) Bunnett, J. F.; Kato, T.; Nudelman, S. *J. Org. Chem.* **1969**, *34*, 785. Bartoli, G.; Todesco, P. E. *Acc. Chem. Res.* **1977**, *10*, 125.

parameter, n, such that all contributions to the energy of the reacting system vary smoothly as functions of n;[24] (2) the energy of a general reacting system must consist of effectively additive contributions from identifiable moieties of the system;[25] and (3) there must be some method for evaluating the energy contributions from the moieties at some known value of n that is not too far different from the value of n at the transition state for any reaction considered.

Assumption (3) is not necessary for a functional formulation of the theory, but it will become clear, below, that the practical use of the theory does require it.

With the first two assumptions, Marcus writes the equation[26]

$$\Delta G = n\Delta G^\circ + G_1'g_1(n) + G_2'g_2(1-n) \qquad (4)$$

where ΔG is the energy of the reaction, ΔG° is the standard energy change for the reaction considered. The functions $g_1(n)$ and $g_2(1-n)$ give the dependence of the energy contributions from moieties 1 and 2, respectively, on the parameter n, and G_1' and G_2' are the energy contributions at the point where $g_1(n) = g_2(1-n) = 1$.

In order to make eq 4 practically useful, the following steps are carried out: (i) we find G_1' and G_2' for a value of n not too far different from its value at the transition state for the reaction under consideration; (ii) we expand eq 4 as a Taylor series in n about this value of n; (iii) we find $n^\dagger$, the value of n at the transition state for the reaction, by setting the partial derivative of ΔG with respect to n equal to zero; (iv) this solution for $n^\dagger$ is substituted into the Taylor expansion of eq 4 to give $\Delta G^\dagger$; and, finally, (v) we use some model to evaluate the first and second derivatives of g_1 and g_2 that appear in this final equation for $\Delta G^\dagger$. In step (v), we have assumed that the Taylor series was truncated at second-order terms, as Marcus does; this is the reason for the proviso that G_1' and G_2' be evaluated for n not too far different from its value at the transition state for the reaction under consideration.

It should be specially noted here that the value of n about which the Taylor expansion is carried out determines, among other things, the numerical coefficient of ΔG° in the final expression for $\Delta G^\dagger$.

In order to make the discussion slightly less abstract and to emphasize the necessity for some degee of symmetry in the reactions treated by the theory, let us consider a general exchange reaction

$$\text{A–X} + \text{B} \rightleftarrows \text{A} + \text{X–B} \qquad (5)$$

and the two related "identity" reactions

$$\text{A–X} + \text{A} \rightleftarrows \text{A} + \text{X–A} \qquad (6a)$$

$$\text{B–X} + \text{B} \rightleftarrows \text{B} + \text{X–B} \qquad (6b)$$

If the energy of the reaction system eq 5 can be expressed as effectively additive contributions from A, X, and B and if these contributions vary smoothly with some single reaction parameter n, then eq 4 applies, with ΔG being the energy of the A, X, B system and ΔG° being the standard energy change for reaction 5.

If the energy surfaces for these reactions contain a single saddle point, then, by symmetry, the value of n at the saddle point for reactions 6a and 6b must be 0.5. If A and B are not too far different, we may reasonably expect that the value of n at the saddle point for reaction 5 will be close to 0.5. It should be obvious, then, that we can identify G_1' in eq 4 as $0.5\Delta G^\dagger$ for reaction 6a and G_2' as $0.5\Delta G^\dagger$ for reaction 6b and that the Taylor expansion of eq 4 will be about the point $n = 0.5$.

We emphasize the point that it is the symmetry of reactions 6 and of analogous identity reactions for electron transfer, that allows the assignment of $n = 0.5$ at the transition states for these "base reactions" having $\Delta G^\circ = 0$.

We may note in passing that these systems (eq 5 and 6) provide an example of the qualifier "effective" in the addditivity of the energy contributions of the reaction moieties. The group X is common to all of the reactions, and there is no reason to expect its energy contribution to be completely independent of A and B. So long as the substitution of B for one of the A's, in reaction 6a to obtain reaction 5, does not influence the interaction of X with the other A, then effectively the energy of the A, X, B system is the average of those for the A, X, A and B, X, B systems. Even less restrictive conditions may apply, as recently discussed by Murdoch.[27]

In order to proceed further with eq 4, even for these exchange reactions, we must have some way of evaluating the first and second derivatives of g_1 and g_2. Models that give these g's as quadratics in n (actually parabolas[7]) lead to the simple form, neglecting work terms, used by Albery[13]

$$\Delta G^\dagger{}_5 = 0.5\Delta G^\circ{}_5 + 0.5(\Delta G^\dagger{}_{6a} + \Delta G^\dagger{}_{6b}) + \Delta G^\circ{}_5{}^2/8(\Delta G^\dagger{}_{6a} + \Delta G^\dagger{}_{6b}) \qquad (7)$$

where the subscripts refer to reactions 5 and 6 above and the other notations are as already defined. The coefficient 0.5 of $\Delta G^\circ{}_5$ arises from the fact that the Taylor expansion was about $n = 0.5$, and the coefficient of 8 appearing in the denominator of the last term arises from the assumed quadratic form of the g's. This last coefficient (8) is different if one uses a BEBO model for the g's[7] (it is 8(ln 2)) and is obviously dependent on the model.

Two problems are encountered in attempts to apply the general theory to electrophile–nucleophile combination reactions of the type

$$\text{E} + \text{N} \rightleftarrows \text{E–N} \qquad (8)$$

The first problem, involving standard states, has been handled in a reasonable manner by Hine.[12] The problem arises from the entropy associated with the conversion of two reactant species into a single product species. Hine[12] uses a simple model to calculate the equilibrium constant for the formation of a noninteracting encounter complex of E and N and then uses this with the experimental equilibrium constants to obtain the dimensionless equilibrium constants for conversion of the encounter complex to product. Albery[13] ignores the problem.

The second, and presently insurmountable, problem arises from the lack of symmetrical "base reactions" to serve the function of reactions 6 discussed above. There is, of course, no identity reaction analogous to reaction 8. If one chooses an example of reaction 8 with $\Delta G^\circ = 0$, or with the value of ΔG° such that the conversion of encounter complex to product has $\Delta G^\circ = 0$, there is no symmetry requiring that $n = 0.5$ at the transition state for the reaction. If we attempt to visualize an intersecting parabolic well model for the reaction, for example, there is no reason to expect the curvatures of the reactant and product wells to be even similar.

One might hope to approach this last problem from an empirical standpoint. If we could find a series of nucleophiles, or a series of electrophiles, with constant intrinsic barrier contributions in reaction 8, with ΔG° close to zero, then, if eq 4 is valid for the reactions, the slope of the ΔG° vs. $\Delta G^\dagger$ plot would give $n^\dagger$ for a reaction 8, with $\Delta G^\circ = 0$. Unfortunately, the experimental data presently available are, at best, ambiguous. A series of alkoxides gives a different Brønsted slope than does a series of phenoxides in reactions with carbonyl compounds.[28] A series of alkylthiolates[4] gives a different slope than does a series of alkylamines[2] in reactions with cations. We do not know which, if any, of these series

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[24] The importance of this assumption is implicit in the entire development of the theory and is clearly stated by Marcus in ref 7. The requirement for the "smoothness" of the functions is discussed in the section headed Remarks on Eq. (4) in ref 7.

[25] This assumption is made implicitly in each of the models discussed by Marcus and in the general eq 16 of ref 7. It is stated explicitly following eq A5 of ref 7.

[26] In order to keep the present discussion as simple as possible, we use the symbols for free energy but neglect the work terms that appear in Marcus' equations of ref 7. The work terms present an added problem in the actual application of the theory; they are, essentially, terms that do not vary smoothly with n.

[27] Murdoch, J. R.; Magnoli, D. E. *J. Am. Chem. Soc.* **1982**, *104*, 3792 and the earlier papers cited there.

[28] Jencks, W. P.; Gilchrist, M. *J. Am. Chem. Soc.* **1962**, *84*, 2910. Hupe, D. J.; Jencks, W. P. *Ibid.* **1977**, *99*, 451.

have constant intrinsic barriers.

In addition to these difficulties, there is at least a reasonable doubt that the conditions for the validity of eq 4 are met by electrophile–nucleophile combination reactions. If, as we believe probable,[2] extensive desolvation of reactants occurs before any appreciable bond formation, then there is no single extent of reaction variable and work terms[26] must be considered. There is a further indication of complications arising from different extents of reaction measured by resonance and polar effects[29] in some of these reactions. The additivity condition[30] is probably less troublesome.

It is clearly naive and speculative, at best, to attempt the application of eq 7 to reactions of the type of eq 8. Until some theory of reasonable origin is developed that at least gives the coefficient of ΔG° in some rate–equilibrium relationship, attempts such as Albery's[13] to derive intrinsic properties from the measured rate and equilibrium constants by rearrangement of eq 7 are completely meaningless.

We suspect, on the basis of the approximately invariant orders of reactivities of nucleophiles and electrophiles seen in a number of studies of the combination reactions,[2,3] that some intrinsic contributions to the reaction barriers exist. We also believe, as stated in the introduction, that the free energies of activation contain some contributions from the same factors that influence the free energies of reaction. At present, however, we have no way of separating these contributions.

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[29] Young, P. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1979**, *101*, 3288. Young, P. R.; McMahon, P. E. *Ibid.* **1979**, *101*, 4678.

[30] Such additivity, at least at the transition states, is clearly implied by the N_+ relationship (ref 2). There can be no doubt that additivity applies to the reactants, where E and N are independent entities.

Effects of Through-Bond and Through-Space Interactions on Singlet–Triplet Energy Gaps in Localized Biradicals

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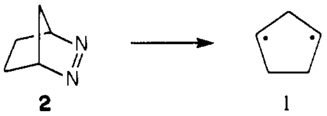
Abstract: Singlet–triplet energy gaps in localized 1,3 biradicals have been investigated by using ab initio electronic structure theory. Analysis of both the molecular orbital and generalized valence bond wave functions allows one to follow the complex interplay between through-bond and through-space interactions. When the two effects are of similar magnitude, a triplet ground state is possible. However, when one significantly dominates the other, a singlet ground state is expected. Extension of the analysis to other systems and the implications of the results for experimental studies of localized biradicals are discussed.

Biradicals have long been postulated as intermediates in a variety of thermal and photochemical reactions.[1] More recently, direct observations of such species has become possible, and ESR studies of several highly delocalized biradicals have been reported over the last 15 years.[2] In 1975, Closs[3] photolyzed azoalkane **2** at 5.5 K and observed the ESR spectrum of the triplet state of 1,3-cyclopentanediyl (**1**). This landmark result promised to remove simple *localized*[4] biradicals from the realm of "permissible intermediate" and "theoretical model" to that of thermodynamically and kinetically characterized reactive intermediate. However, extension of the Closs experiment to other fundamental localized biradical systems has thus far not been possible. This failure is certainly not for want of effort,[3,5,6] and it suggests that insights into the factors that make the observation of **1** successful would be useful.[7]



2 **1**

Several lines of experimental evidence[3] and theoretical calculation[8] indicate that **1** has a triplet ground state. It seems certain that this is a major factor that facilitates its direct observation by ESR. Direct observation of the singlet state of a localized biradical has not yet been accomplished, and in most cases the lifetimes of such species must be quite short. If a biradical has a triplet ground state, however, the spin forbiddeness of the normal unimolecular decomposition pathways (e.g., ring closure) can increase the biradical lifetime. If the singlet–triplet energy gap is substantial, an additional enthalpic barrier to the T → S conversion may also be operative. It is quite possible that a triplet ground state is a necessary criterion for ESR observation of certain types of nonconjugated biradicals. In the general case, however, one would not expect a triplet ground state for a localized biradical. Hund's rule does not apply to structures such as **1**, since the atomic orbitals containing the unpaired electrons are not orthogonal.[9]

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[1] (a) Berson, J. A. In "Rearrangements in Ground and Excited States"; de Mayo, P., Ed.; Academic Press: New York, 1980; Vol. I, pp 311–390. (b) Gajewski, J. J. "Hydrocarbon Thermal Isomerizations"; Academic Press: New York, 1981. (c) Wagner, P. J. In "Rearrangements in Ground and Excited States"; de Mayo, P., Ed.; Academic Press, New York, 1980; Vol. III, pp 381–444. (d) Borden, W. T., Ed. "Diradicals"; Wiley-Interscience: New York, 1982.

[2] (a) Dowd, P. *J. Am. Chem. Soc.* **1966**, *88*, 2587–2589. (b) Closs, G. L.; Kaplan, L. R., Bendall, V. I. *Ibid.* **1967**, *89*, 3376–3377. (c) Arnold, D. R.; Evnin, A. B.; Kasai, P. H. *Ibid.* **1969**, *91*, 784–785. (d) Berson, J. A.; Bushby, R. J.; McBride, J. M.; Tremelling, M. *Ibid.* **1971**, *93*, 1544–1546. (e) Roth, W. R.; Erker, G. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 503–504. (f) Pagni, R. M.; Watson, C. R., Jr.; Boor, J. E.; Dodd, J. R. *J. Am. Chem. Soc.* **1974**, *96*, 4064–4066.

[3] Buchwalter, S. L.; Closs, G. L. *J. Am. Chem. Soc.* **1979**, *101*, 4688–4694.

[4] The term "localized" is used here in a classical sense, implying that the radical centers are not part of a conventional π system. Of course, a major point of this work is that the radical centers do delocalize via the CH_2 groups.

[5] Goldberg, A. H.; Dougherty, D. A., unpublished results.

[6] Closs, G. L., personal communication.

[7] Of course, one must have a suitable photochemicl precursor, and it is quite possible that in some cases the photochemistry of the biradical precursor undermines the experiment (see below).

[8] Conrad, M. P.; Pitzer, R. M.; Schaefer, H. F., III *J. Am. Chem. Soc.* **1979**, *101*, 2245–2246.

0002-7863/83/1505-0284$01.50/0