The Thermodynamic and Kinetic Acidity Properties of Nitroalkanes. Correlation of the Effects of Structure on the Ionization Constants and the Rate Constants of Neutralization of Substituted 1-Phenyl-1-nitroethanes[1a]

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Abstract: Electron-withdrawing substituents in *meta* and *para* positions increase whereas electron-donating substituents decrease the dissociation constants and the second-order rate constants for neutralization of 1-phenyl-1-nitroethanes by hydroxide ion in 50% (vol) dioxane–water. The ionization constants (pK_a) and the neutralization rate constants (log k_2) correlate with σ constants for aqueous and for 50% (vol) dioxane–water systems. There is linear correlation of the rate constants (log k_2) for neutralization and the ionization constants (pK_a) of the 1-phenyl-1-nitroethanes with a Brønsted coefficient of 1.17–1.20. The Brønsted coefficient of greater than unity stems from the fact that as the electron-withdrawing capacity of the substituent is increased, the relative effects on the rate constants of neutralization of substituted 1-phenyl-1-nitroethanes are greater than on the ionization constants. *meta* and *para* electron acceptor groups accelerate and electron donor groups retard reversal of 1-phenyl-1-ethanenitronates to 1-phenyl-1-nitroethanes. The Brønsted coefficient for correlation of the logarithms of the rate constants of hydrolysis of 1-phenyl-1-ethanenitronates and the pK_a's of their 1-phenyl-1-nitroethanes is $-0.17 - (-0.20)$. Electron-withdrawing *meta* and *para* substituents in a 1-phenyl-1-ethanenitronate result in electronic absorption at longer wavelengths. The long wavelength ultraviolet maximum of a 1-phenyl-1-ethanenitronate is shifted bathochromically in poor hydrogen bonding and in aprotic polar solvents. The rate of reversal of a 1-phenyl-1-ethanenitronate upon introduction of an electron donor *meta* or *para* substituent may be retarded because the carbonitronate behaves relatively electron deficiently at α carbon as a result of increased hydrogen bonding at oxygens of enhanced nucleophilicity and because of the increased work involved in breaking the hydrogen bonds. For salts of simple nitroalkanes there is a shift in the infrared absorption for C=N to longer wavelength as the charge density of the cation is decreased. Replacement of methyl groups for hydrogen in nitronates results in maximum ultraviolet absorption at shorter wavelengths; solvents of diminished hydrogen-bonding ability or of increased polarity lead to absorption at longer wavelengths. The effects of structure and environment on the properties of alkanenitronates are analogous to those for 1-phenyl-1-ethanenitronates.

Neutralization of acidic mononitro compounds is subject to general base catalysis and there is Brønsted correlation between the rates of neutralization of such nitro compounds and the strengths of unhindered bases.[2] Previous studies of the rates of neutralization (or ionization) and the dissociation constants of nitroalkanes have been limited. The results are of interest however in that nitro compounds which are weaker (or stronger) may neutralize (or ionize) faster (slower) than their stronger (or weaker) homologs. Thus the order of acid strengths[3a] of the following nitroalkanes is 2-nitropropane (2100,[4a] 1780[4b]) > nitroethane (350,[4a] 252[4b]) > nitromethane (6.2,[4a] 6.0[4b]), whereas for neutralization by hydroxide ion,[3b,4c] nitromethane (238) > nitroethane (39.1) > 2-nitropropane (2.08). The effects of structure on the thermodynamic acidities of these nitro compounds are opposite that for their neutralization and the systems do not give a linear inverse Brønsted correlation. Comparison of isomers reveals that 1-nitropropane is weaker (105[3a,4b]) but neutralizes (29.2[3b,4d]) more rapidly than 2-nitropropane; similarly 1-nitrobutane has a smaller ionization constant (10[3c,4e]) but is neutralized faster (~130[3d,4f]) than 2-nitrobutane (39.8,[3c,4e] 3.82[3d,4g]).

The kinetic reactivity orders for neutralization (and thus ionization) of the above series of nitroalkanes are understandable on the basis of conventional electrical and steric effects. The thermodynamic acidic properties of the nitro compounds compared however are opposite that expected from electronic factors in carbon acids, and it is apparent that the striking acidity

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[2] (a) K. J. Pederson, *Kgl. Dan. Vidensk. Selsk. Mat. Fys. Medd.*, **12**, 1 (1932); (b) R. G. Pearson, *J. Amer. Chem. Soc.*, **70**, 204 (1948); (c) R. G. Pearson and F. V. Williams, *ibid.*, **75**, 3073 (1953); (d) R. G. Pearson and F. V. Williams, *ibid.*, **76**, 258 (1954); (e) M. J. Gregory and T. C. Bruice, *ibid.*, **89**, 2327 (1967).

[3] (a) $K_A \times 10^{11}$, H_2O, 25°; (b) k_2, l./mol min, H_2O, 0°; (c) $K_A \times 10^{11}$, 50% (vol) aqueous ethanol, 25°; (d) k_2, l./mol min, 50% (vol) aqueous dioxane, 0°; (e) $k_2 \times 10^{-8}$, H_2O, 25°; (f) relative rates of reversal.

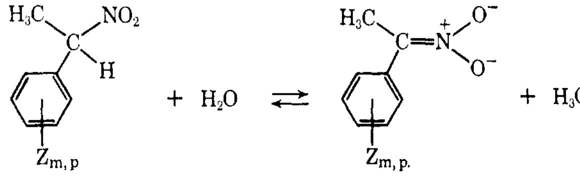
[4] (a) D. Turnbull and S. H. Maron, *J. Amer. Chem. Soc.*, **65**, 212 (1943); (b) G. W. Wheland and J. Farr, *ibid.*, **65**, 1433 (1943); (c) S. H. Maron and V. K. La Mer, *ibid.*, **60**, 2588 (1938); (d) R. Junell, *Arkiv. Kemi*, **11B**, No. 34 (1934); R. Junell, Dissertation, Uppsala, 1935; (e) N. Kornblum, R. Blackwood, and J. Powers, *J. Amer. Chem. Soc.*, **79**, 2508 (1957); (f) estimated from the data of ref 1c; (g) J. G. Traynham, The Ohio State University, Columbus, Ohio, 1952.

orders of these nitroalkanes stem from remarkable kinetic effects in hydrolytic reversal of the alkanenitronates.[5] The rate constants or the relative reactivities for protonation of alkanenitronates to nitroalkanes are: methanenitronate (39,470[3e]) > ethanenitronate (112[3e]) > 2-propanenitronate (1[3e]), 1-propanenitronate (163[3e]) > 2-propanenitronate (1[3e]), and 1-butanenitronate (~135[3f]) > 2-butanenitronate (1[3f]). Although the unusual thermodynamic properties of nitroalkanes and the nucleophilicities of alkanenitronates have been discussed in terms of dielectric,[4b] electronic,[5] steric,[6a] and solvation[6b] effects, the paradoxes of these systems have been largely unresolved. It is also clear that the relative behavior of nitroethane and 1-nitropropane obeys traditional theory in that nitroethane is stronger and neutralizes more rapidly, and the rate of reversal of 1-propanenitronate is greater than of ethanenitronate.[5]

The previous investigations of proton transfer and the equilibria of nitroalkanes have involved substrates which differ sterically at the neutralization and the ionization sites. A study is now reported of the ionization constants and the kinetics of neutralization of *meta*- and *para*-substituted 1-phenyl-1-nitroethanes, a system in which the steric factor is essentially constant.[7] The effects of structure and environment on the spectral properties of *meta*- and *para*-substituted 1-phenyl-1-ethanenitronates and of various alkanenitronates have also been investigated. The objective of this study is to provide additional insight into the intriguing thermodynamic and kinetic properties of various nitroalkanes and alkanenitronates.

Results and Discussion

Ionization Constants of Substituted 1-Phenyl-1-nitroethanes. The ionization constants (K_A) of highly purified *meta*- and *para*-substituted 1-phenyl-1-nitroethanes (eq 1) were determined potentiotitrimetrically in 50% (vol) dioxane–water at 20°.[8] Decomposition of the substituted 1-phenyl-1-ethanenitronates was limited



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and the equilibrium data were highly reproducible upon effecting partial or total neutralization of the nitro compounds with sodium hydroxide at 0° in the absence of oxidants and then equilibrating the mixtures at 20° just prior to determination of their acidities.[9]

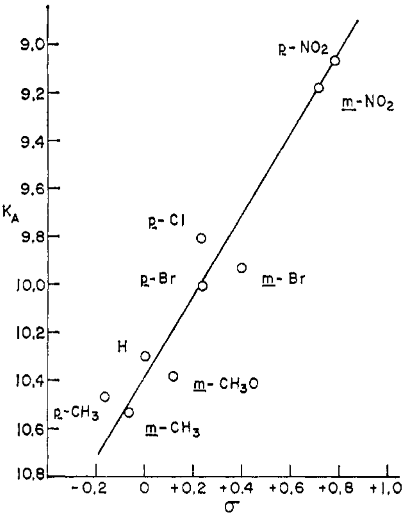

Figure 1. Hammett correlation of the ionization constants (pK_a) of *meta*- and *para*-substituted 1-phenyl-1-nitroethanes at 20° in 50% (vol) dioxane-water with σ constants; $\rho = 1.62$; correlation coefficient 0.977.

The ionization constants reported[10] (Table I) have been corrected thermodynamically[8c] and are the average for at least five (and usually many more) separate determinations for each nitro compound. The pK_A value obtained in any single experiment varied by no more than ±0.03 pH unit from the average values for each compound in Table I; all experiments were included in the statistical average.

Of the systems studied, 1-*p*-nitrophenyl-1-nitroethane is the strongest acid and 1-*m*-tolyl-1-nitroethane is the weakest; the ratio of acid strengths of the two nitro compounds is ~26:1. In general, electron-withdrawing substituents increase whereas electron-donating substituents in *meta*- and *para*-positions decrease the dissociation constants of 1-phenyl-1-nitroethanes. Hammett correlation of the pK_a's of the nitroalkanes with σ substituent values is satisfactory (Figure 1; correlation coefficient 0.966)[11a] and gives a ρ of 1.62; linearity is improved (correlation coefficient 0.977), and the reaction constant (ρ') is lowered to 1.06 upon correlating the acid strengths of the nitro compounds with σ values of substituted benzoic acids as presently determined potentiotitrimetrically in 50% (vol) dioxane–water at 30°.[11b,c]

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(5) (a) H. M. E. Cardwell, *J. Chem. Soc.*, 2442 (1951); (b) R. G. Pearson and R. L. Dillon, *J. Amer. Chem. Soc.*, **75**, 2439 (1953).

(6) (a) G. S. Hammond in M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley & Sons, Inc., New York, N. Y., 1963, p 441; (b) F. T. Williams, Jr., P. W. K. Flanagan, W. J. Taylor, and H. Shechter, *J. Org. Chem.*, **30**, 2674 (1965).

(7) The complications involved in analysis of the effects of structure on the rates of neutralization and the ionization constants of homologous nitrocycloalkanes have been summarized recently: P. W. K. Flanagan, H. W. Amburn, H. W. Stone, J. G. Traynham, and H. Shechter, *J. Amer. Chem. Soc.*, **91**, 2797 (1969).

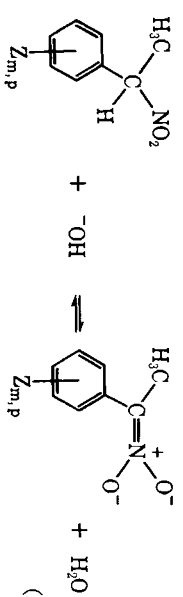
(8) The method used is an adaptation (see Experimental Section) of that of (a) ref 4a; (b) J. D. Farr, Ph.D. Dissertation, University of Chicago, Chicago, Ill., 1939, and (c) P. D. Schickedantz, Ph.D. Dissertation, The Ohio State University, Columbus, Ohio, 1959.

(9) (a) There is appreciable decomposition of the substituted 1-phenyl-1-ethanenitronates if they are kept excessively at 20°; (b) the reactions of oxygen with alkanenitronates have been studied by G. A. Russell, *J. Amer. Chem. Soc.*, **76**, 1595 (1954).

(10) (a) The apparent ionization constants (K_{app}) presently measured are related to the ionization constants (K_A) of the 1-phenyl-1-nitroethanes by the equation $K_{app} = (H^+)(\text{anion}^-)/[(\text{nitro form}) + (\text{aci form})] = K_A/(1 + K_i)$, where $K_A = (H^+)(\text{anion}^-)/(\text{nitro form})$ and $K_i = (\text{aci form})/(\text{nitro form})$. K_{app} is equal, within less than the experimental error, to K_A when K_i is sufficiently small. Nmr analysis of 1-*p*-tolyl-1-nitroethane and 1-*p*-nitrophenyl-1-nitroethane, respectively, in methanol did not indicate detectable quantities of their nitronic acids.[10b] More significantly plots of the resistances of neutralizing kinetic solutions back to zero reaction times gave R_0 values essentially identical with those determined experimentally before initiating the kinetic experiments. (b) The isomerization constants (K_i)[4a] for nitromethane, nitroethane, and 2-nitropropane in water at 25° are 1.1×10^{-7}, 8.9×10^{-5}, and 2.75×10^{-3}, respectively. *p*-Nitrophenylnitromethane contains 0.18% nitronic acid in ethanol and 0.79% in dilute aqueous methanol; K. H. Meyer and P. Wertheimer, *Chem. Ber.*, **47**, 2374 (1914).

(11) (a) H. H. Jaffé (*Chem. Rev.*, **53**, 191 (1953)), in evaluating linear free-energy relations of the Hammett type, indicates a standard correlation coefficient of >0.99 to be excellent and >0.95 satisfactory. (b) Hammett σ values are based on the ionization constants of substituted benzoic acids in water at 25°. (c) The ionization constants of substituted benzoic acids were presently determined in 50% (vol) di-

Rate Constants for Neutralization of Substituted 1-Phenyl-1-nitroethanes. The rates of neutralization of the substituted 1-phenyl-1-nitroethanes by sodium hydroxide in 50% (vol) dioxane–water (eq 2) were then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investigated as second-order processes at various temperatures using rapid conductometric methods.[12] Under the kinetic conditions the conductivities of the ionic species present, sodium hydroxide and sodium-substituted 1-phenyl-1-ethanenitronates, are additive and vary linearly with concentration. Satisfactory reproducible data were obtainable for a variety of different kinetic methods if oxygen and peroxides were excluded from the kinetic systems.

The initial kinetic studies were effected at 20, 10, and 0°, respectively, using the reactants in equivalent concentrations. Under these conditions, because of hydrolysis, the neutralizations were from 94.4 to 99.5% complete.[13] The infinite resistances (R_∞), which are necessary in the kinetic analysis (see Experimental Section), were determined by adding excess nitro compound at the end of a kinetic run and/or by calculation from the resistances measured during a kinetic experiment.[14] Plots of the kinetic data for determination of the rate constants (k_2, l./mol min) from pairs of experiments for each nitro compound at each temperature as summarized in Table I (series A) and for the enthalpies of activation ($\Delta H^{\ddagger}$, kcal/mol) were of excellent linearity.

Studies were then made of the rate constants of neutralization at 20, 10, and 0°, respectively, using the substituted 1-phenyl-1-nitroethanes in sufficient excess to ensure that the neutralizations were essentially complete (>99.5%) during the actual kinetic runs. Reactions of relatively weak acids such as 1-*p*-tolyl-1-nitroethane with hydroxide were thus conducted at mole ratios of ~10:1; a relatively strong acid, 1-*p*-nitrophenyl-1-nitroethane was studied at a mole ratio to base of >2:1.[15] At least two kinetic experiments at different concentrations were conducted for each compound at each temperature; 1-phenyl-1-nitroethane and 1-*p*-nitrophenyl-1-nitroethane were studied in much greater depth to check the reproducibility of the results. The data obtained were highly reproducible and quite satisfactory for determining the

Table I. Ionization Constants and Rate Constants of Neutralization of *meta*- and *para*-Substituted 1-Phenyl-1-nitroethanes. Ionization Constants of *meta*- and *para*-Substituted Benzoic Acids

	Series A						Series B					
	$ZC_6H_4CHNO_2CH_3$[a]		$ZC_6H_4CO_2H$[a]	$ZC_6H_4CHNO_2CH_3$[a,b]			$ZC_6H_4CHNO_2CH_3$[a,b]					
Substituent	K_A, 20°	pK_A, 30°	pK_A, 20°	k_2, 0°	k_2, 10°	k_2, 20°	k_2, 0°	k_2, 10°	k_2, 20°	$\Delta H^{\ddagger}$[c,d]	$-\Delta S^{\ddagger}$[d,e]	$k_{-1} \times 10^3$, 20°
p-CH_3	3.39×10^{-11}	10.47	6.46	55.2 ± 2.3	117.5 ± 2.5	264.5 ± 2.5	54.2 ± 0.4	117 ± 3	252 ± 0.2	11.67	15.9	0.93;[f] 0.98[d]
m-CH_3	2.95×10^{-11}	10.53	6.38	64.0 ± 1.0	133 ± 7	254	60.6 ± 0.6	136 ± 1	289 ± 3	10.79	18.7	1.22; 1.08
m-CH_3O	4.17×10^{-11}	10.38	6.16	92.4 ± 0.9	201.5 ± 1.5	446 ± 1.0	91.2 ± 0.5	201 ± 3	450 ± 4	12.12	13.2	1.35; 1.34
H	5.08×10^{-11}	10.30	6.29	86.0 ± 0.3	193	386	84.2 ± 2.1	188 ± 3	395 ± 6	11.75	14.7	0.94; 0.97
p-Cl	1.55×10^{-10}	9.81	5.90	336 ± 2	637 ± 4	1,497.5 ± 7.5	307 ± 3	644 ± 4	1,500 ± 50	12.04	10.2	1.21; 1.21
p-Br	1.00×10^{-10}	10.00	5.87	327 ± 9	636 ± 23	1,335 ± 15	307 ± 5	646 ± 6	1,360 ± 60	11.28	13.9	1.70; 1.67
m-Br	1.17×10^{-10}	9.93	5.73	412 ± 0.5	835 + 9	1,670	386 ± 3	851 ± 2	1,698 ± 3	11.22	13.5	1.81; 1.78
m-NO_2	6.61×10^{-10}	9.18	5.26	2045 ± 15	4200 ± 150	9,370	1873 ± 2	4080 ± 70	8,760 ± 70	11.72	8.68	1.66; 1.62
p-NO_2	8.71×10^{-10}	9.06	5.09	3250	7110	15,500	3150 ± 130	7140 ± 200	14,770 ± 270	11.75	7.45	2.12; 2.22

[a] Solvent: 50% (vol) dioxane–water. [b] k_2, l./mol min. [c] Kcal/mol. [d] Based on the rate constants of series B in which excess compound was used. [e] Entropy units. [f] Based on the rate constants series A in which equivalent amounts of reactants were used.

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oxane–water using the same technique and instrument as used for the 1-phenyl-1-nitroethanes; the effects of experimental and solvent differences on the Hammett correlation were thus minimized. Correlation of the ionization constants of the benzoic acids in dioxane–water with σ values gave a ρ of 1.48. The electrical effect of substituents on this system is thus greater in the mixed solvent than in water.

(12) The kinetic method is that of ref 4c as modified by P. W. K. Flanagan,[10] F. W. Williams, Jr.,[4f] and the demands of the present study in which the reaction half-lives were as short at 20 sec.

(13) The extents of hydrolysis were calculated from the K_A's presently determined for the substituted 1-phenyl-1-nitroethanes and K_W of 1.249 × 10^{-16} for 50% (vol) dioxane–water at 20°; H. S. Harned and L. D. Fallon, *J. Amer. Chem. Soc.*, **61**, 2374 (1939).

(14) There was excellent agreement for R_∞ as determined experimentally or by mathematical analysis.

(15) (a) A large excess of nitro compound was not needed if it was a sufficiently strong acid. (b) It was of advantage to keep the ratios of the stronger nitro compounds to base relatively small because of the great reactivities of these derivatives.

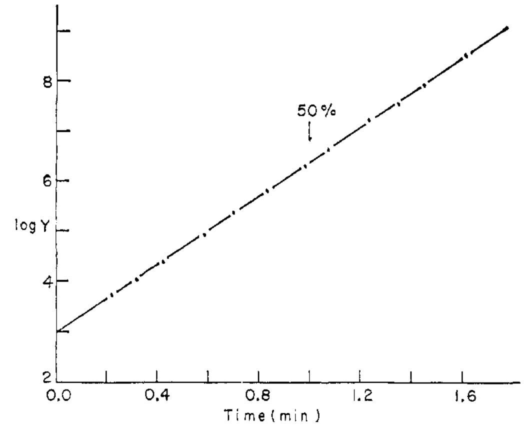

Figure 2. Plot (eq 7) of log Y *vs.* t (min) for neutralization of 1-*p*-nitrophenyl-1-nitroethane (4.829 × 10^{-4} mol/l.) by hydroxide ion (2.421 × 10^{-4} mol/l.) in 50% (vol) dioxane–water at 0°.

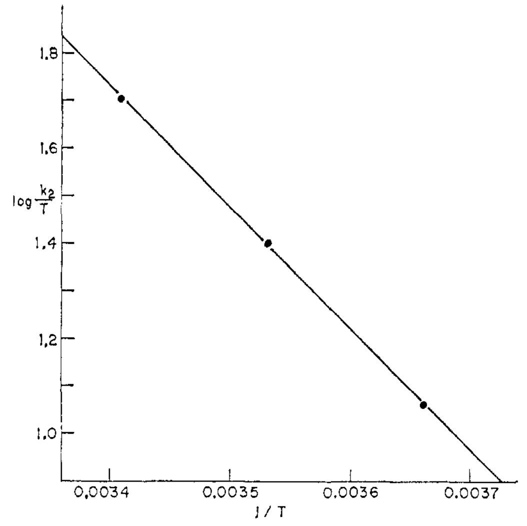

Figure 3. Enthalpy of activation plot (log k_2/T *vs.* $1/T$) for neutralization of 1-*p*-nitrophenyl-1-nitroethane (excess) at 0, 10, and 20°, respectively.

rate constants and the kinetic parameters (Table I, series B) for neutralization of the substituted 1-phenyl-1-nitroethanes. A plot (Figure 2) typical and illustrative of *all* of the systems of this study is illustrated for neutralization of 1-*p*-nitrophenyl-1-nitroethane, the fastest and most difficult of all the compounds studied. A typical plot indicative of the reliability of the rate constants for neutralization of the substituted 1-phenyl-1-nitroethanes over the temperature range 0–20° is shown for 1-*p*-nitrophenyl-1-nitroethane in Figure 3. There is good agreement between the rate constants (series A) as determined from R_∞ as corrected for hydrolysis and those (series B) obtained upon use of the substituted 1-phenyl-1-nitroethanes in excess. As inherent in the two kinetic methods the rate constants obtained upon use of excess substituted 1-phenyl-1-nitroethane are slightly smaller than those from the reactants in equivalent quantities.

Electron-withdrawing substituents accelerate and electron-donating substituents retard neutralization of substituted 1-phenyl-1-nitroethanes. The relative rate of reaction of 1-*p*-nitrophenyl-1-nitroethane as compared to 1-*m*-tolyl-1-nitroethane is ~51:1. Satisfactory Hammett correlations of the logarithms of the rates of neutralization result from use of σ values for *meta*- and *para*-substituents. The ρ values, correlation coefficients, and standard deviations for neutralization in experimental series A and B at the various temperatures (0–20°) range (Table II) from 1.90 to 1.94, 0.984 to 0.987, and 0.110 to 0.123, respectively. Improved correlations (correlation coefficient ~0.992; see Figure 4) having a smaller reaction constant (ρ' = ~1.49) were obtained between the rates of neutralization of the 1-phenyl-1-nitroethanes (log k_2) and σ' values derived from the ionization constants (pK_a) of substituted benzoic acids in 50% (vol) dioxane–water (Table I).[16] Solvent effects are thus important in neutralization of the 1-phenyl-1-nitroethanes.

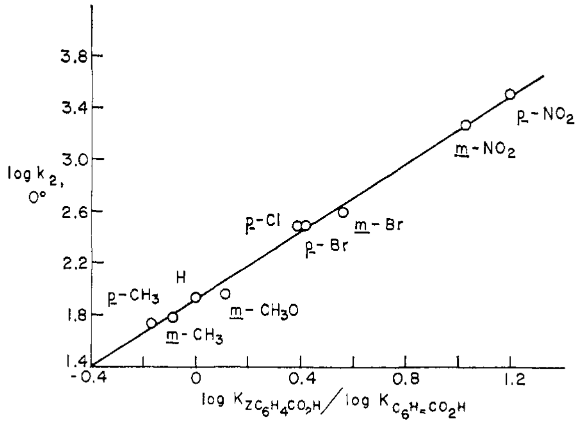

Figure 4. Hammett correlation of the rate constants (log k_2) for neutralization of *meta*- and *para*-substituted 1-phenyl-1-nitroethanes at 0° with σ'; constants (log $K_{ZC_6H_4CO_2H}$/log $K_{C_6H_5CO_2H}$) as presently determined from the ionization constants of substituted benzoic acids in 50% (vol) dioxane–water at 30°; ρ' = ~1.49; correlation coefficient ~ 0.992.

Table II. Correlation of the Rate Constants of Neutralization of *meta*- and *para*-Substituted 1-Phenyl-1-nitroethanes with Hammett σ Values

Log k_2	ρ	Standard correlation coefficient	Standard deviation
20°, series A	1.940	0.984	0.123
10°, series A	1.917	0.987	0.110
0°, series A	1.924	0.985	0.120
20°, series B	1.898	0.986	0.114
10°, series B	1.913	0.987	0.111
0°, series B	1.908	0.986	0.116

Correlations of the Ionization Constants and the Rate Constants for Neutralization of Substituted 1-Phenyl-1-nitroethanes. The equilibrium and kinetic data of Table I reveal in general that, as the *meta*- and *para*-substituents become more electron demanding, the rates of neutralization of the substituted 1-phenyl-1-nitroethanes respond more to the effects of a substituent than do the ionization constants of the substituted 1-phenyl-1-nitroethanes. There is excellent linear correlation of the logarithms of the rate constants for neutralization (log k_2, series A and B; 20, 10, and 0°, respectively)

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[16] (a) 1-(*p*-Nitrophenyl)-1-nitroethane is neutralized considerably slower than predicted by the σ_p^- constant for the nitro group. (b) The Hammett correlations are very poor upon using σ^+ constants.

and the average ionization constants (pK_a, 20°) of the 1-phenyl-1-nitroethanes yielding Brønsted coefficients of 1.17–1.20. The results of the six individual correlations, the correlation coefficients, the standard deviations, and the probabilities that the Brønsted coefficient is greater than 1 are summarized in Table III. A Brønsted plot (log k_2, 20°, series B *vs.* pK_a, 20°) typical of those yielding the results in Table III is exhibited in Figure 5. The linear Brønsted correlations in which the coefficients are greater than one are the first to have been found[17] between the rates of neutralization (log k_2) and the ionization constants (pK_a) of acidic mononitroalkanes.[18, 19] Brønsted coefficients usually range from 0 to 1.[20]

Table III. Brønsted Correlations of the Rate Constants (Log k_2) and the Ionization Constants (Log pK_a) of *meta*- and *para*-Substituted 1-Phenyl-1-nitroethanes[a]

Log k_2	Brønsted slope, β	Standard correlation coefficient	Standard deviation	% probability $\beta > 1.0$
20°, series A	1.198	0.993	0.049	>99.99
10°, series A	1.177	0.990	0.058	99.88
0°, series A	1.184	0.990	0.060	99.89
20°, series B	1.167	0.991	0.054	>99.90
10°, series B	1.174	0.989	0.061	>99.78
0°, series B	1.173	0.990	0.059	99.84

[a] A seventh correlation of the pK_a's of Table I with the log k_2's of the 1-phenyl-1-nitroethanes as originally observed by P. W. K. Flanagan[1c] resulted in a Brønsted coefficient of 1.24.

The Brønsted coefficient greater than unity is a necessary consequence of the observations that ρ for neutralization (1.91–1.94) is larger than for ionization (1.62) of the *meta*- and *para*-substituted 1-phenyl-1-nitroethanes.

The rate constants (k_{-1}, min^{-1}) for reversal (protonation) of the substituted 1-phenyl-1-ethanenitronates to substituted 1-phenyl-1-nitroethanes (Table I) have been calculated from the ionization constants and the rate constants (series A and B) for neutralization of the 1-phenyl-1-nitroethanes at 20°.[21] It is thus seen that the reversal reaction, as the forward reaction, is facilitated by electron-withdrawing and slowed by electron-donating substituents. The Brønsted coefficients for correlation of the logarithms of the rates of hydrolysis of the substituted 1-phenyl-1-ethanenitronates (log k_{-1}) and the ionization constants of their 1-phenyl-1-nitroethanes (pK_a) are −0.17 – (−0.20). Brønsted coefficients for reversible reactions must total one. The overall effects of substituents on the rates of protonation of substituted 1-phenyl-1-ethanenitronates are formally analogous to the findings that the relative rates of reversal of methanenitronate, ethanenitronate, and 2-propanenitronate are 39,470:112:1[4,5] and the rate of conversion of nitromethanenitronate ion ($O_2NCH{=}NO_2^-$) to dinitromethane ($O_2NCH_2NO_2$) is ~5 times that for methanenitronate ion to nitromethane even though the rate of ionization of dinitromethane is 1.9×10^7 times that of nitromethane.[5b]

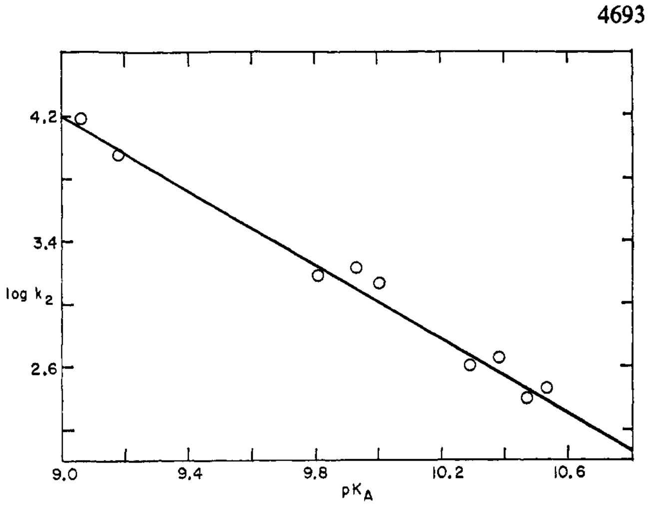

Figure 5. Brønsted correlation of the neutralization constants (log k_2, 20°) and the ionization constants (pK_a, 20°) of substituted 1-phenyl-1-nitroethanes; series B, β = 1.167, standard correlation coefficient 0.991, standard deviation 0.054, >99.90% probability $\beta > 1.0$.

Electronic Spectra of Substituted 1-Phenyl-1-ethanenitronates. The paradox of present concern is that *meta*- and *para*-electron acceptor groups increase whereas electron donor groups decrease the rates of conversion of substituted 1-phenyl-1-ethanenitronates to 1-phenyl-1-nitroethanes. Electronegatively substituted 1-phenyl-1-ethanenitronates (**1a–c**) thus express greater carbanionic character (**1a** > **2a**) than do electropositively substituted 1-phenyl-1-ethanenitronates (**2a–c**). In an attempt to understand the effects of substituents on the kinetic basicities of 1-phenyl-1-ethanenitronates, the electronic spectra of the various nitronates were studied. Since the longest wavelength absorption maximum of such ions involves $\pi \rightarrow \pi^*$ transition in which there is intramolecular charge transfer from the oxygens

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(17) The observations of a coefficient greater than one (1.16–1.20) for Brønsted correlation of the ionization constants and the rate constants for neutralization of substituted 1-phenyl-1-nitroethanes in 50% (vol) dioxane–water were first reported by M. Fukuyama to the U. S. Army Research Office (Final Report, DA-ORD-31-124-61-G22) on March 31, 1962. These experiments are also summarized in the Ph.D. Dissertation of H. W. Amburn, ref 1e. Submittal for publication of the observations and the above discussion of Brønsted coefficients of >1 for the 1-phenyl-1-nitroethane system and <0 for the 1-phenyl-1-ethanenitronate system was delayed from late July 1968 in anticipation of simultaneous reporting of our research and that being carried out at Northwestern University.[18]

(18) F. G. Bordwell, W. C. Boyle, Jr., J. A. Hautula, and K. C. Yee (*J. Amer. Chem. Soc.*, **91**, 4002 (1969)), recently communicated that the Brønsted coefficient for the neutralization and the ionization constant of *meta* and *para*-substituted 1-phenyl-1-nitroethanes in 50% (vol) methanol–water is 1.31.

(19) Lines drawn with slopes of 1.0 through any points of the Brønsted plots of Table III lead to the conclusion that the rate constants and the ionization constants measured are quite different than predicted if the Brønsted coefficients were indeed 1.0. Thus for Figure 8 with a line drawn with a slope of 1.0 through the midpoint of the Brønsted plot, on the basis of the measured ionization constants, the predicted rate constant for 1-*p*-nitrophenyl-1-nitroethane is 10,000 (Found: 14,770) and for 1-*p*-tolyl-1-nitroethane is 403 (Found: 252). On the basis of the rate constants actually measured the predicted pK_a for 1-*p*-nitrophenyl-1-nitroethane is 8.91 (Found: 9.06) and for 1-*p*-tolyl-1-nitroethane is 10.55 (Found: 10.47). Similar analyses of all of the present Brønsted correlations reveal that the measured and the predicted values are much beyond the experimental precision and accuracy (see Experimental Section).

(20) M. Eigen, *Angew. Chem. Int. Ed. Engl.*, **3**, 1 (1964), and references therein.

(21) Calculated for

$$HA + OH^- \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} A^- + H_2O$$

where $[A^-]/([HA][OH^-]) = K_A/K_{H_2O} = k_2/(k_{-2}[H_2O]) = k_2/k_{-1}$ and K_{H_2O} in 50% (vol) aqueous dioxane is 1.249×10^{-16}.

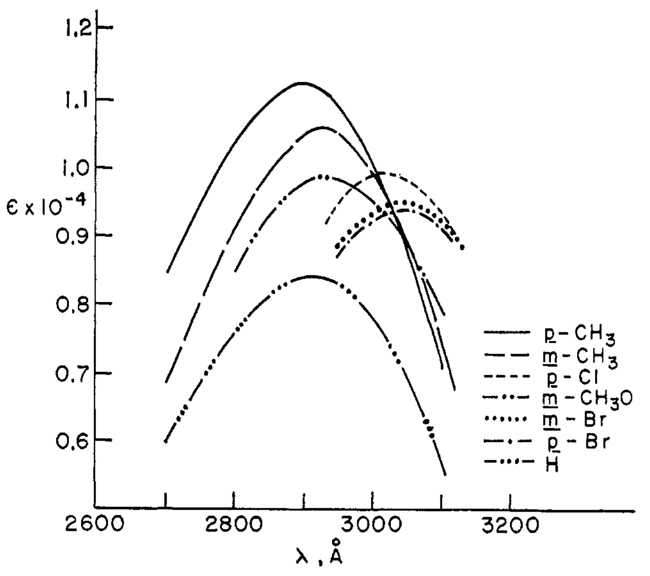
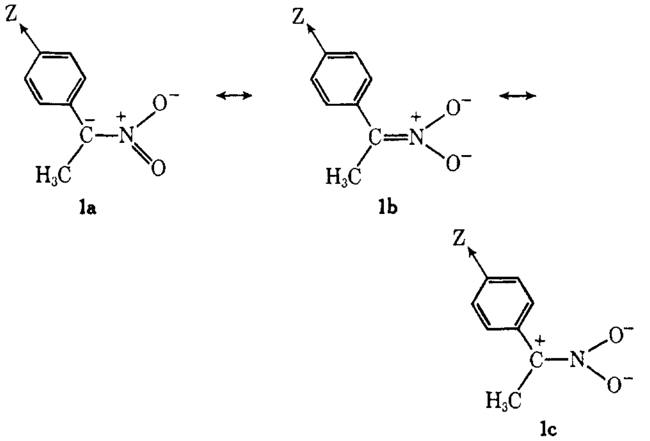
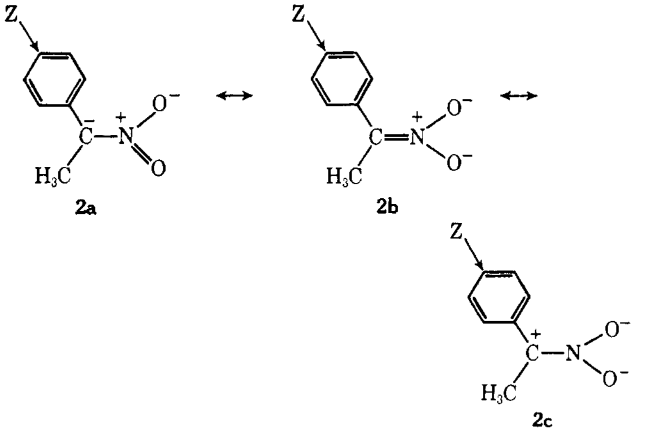


Figure 6. Ultraviolet absorption of *meta*- and *para*-substituted 1-phenyl-1-ethanenitronates in 50% (vol) dioxane–water.

increasing the electron density on the α carbon of the carbonitronate,[6b] it was of interest to investigate correlation of the abilities of 1-phenyl-1-ethanenitronates to function as electron donors for proton transfer with the abilities of the 1-phenyl-1-ethanenitronates to acquire carbanionic character by electronic excitation.



1a **1b** **1c**



2a **2b** **2c**

The ultraviolet absorption spectra of substituted 1-phenyl-1-ethanenitronates were thus determined in 50% (vol) dioxane–water. As a 1-phenyl-1-ethanenitronate is substituted by groups of increasing electron-withdrawing ability, absorption occurs at longer wavelengths (Figure 6). The ultraviolet maximum of a 1-phenyl-1-ethanenitronate increases from 2895 to 3070 Å (Table IV) as the electron-acceptor ability of the phenyl substituent is increased from *para*-methyl to *meta*-nitro.[22] A *para*-nitro group results in much longer wavelengths of absorption (λ_{max} 4065 Å) of a 1-phenyl-1-ethanenitronate.[23] There is general correlation between (1) the ultraviolet absorption maxima (log λ_{max}) of the various salts and the σ values of the substituents of the 1-phenyl-1-ethanenitronate derivatives and (2) the effect of a substituent in increasing the kinetic basicity of a 1-phenyl-1-ethanenitronate and in lowering the electronic transition energy for increasing the negative charge on carbon of a 1-phenyl-1-ethanenitronate.

Table IV. Ultraviolet Absorption Spectra of Substituted 1-Phenyl-1-ethanenitronates in 50% (vol) Dioxane–Water

Substituent	Absorption	
	λ_{max}, Å	$\epsilon_{max} \times 10^{-4}$
p-CH_3	2895	1.10
m-CH_3	2925	1.09
H	2915	0.915
m-OCH_3	2930	0.976
p-Cl	3020	0.976
m-Br	3040	0.989
p-Br	3050	1.10
m-NO_2	3070[a–c]	1.20
p-NO_2	4065	1.05

[a] Determined in methanol. [b] The maximum is not sharply defined because of broad absorption. [c] See ref 23a.

The ultraviolet absorption of substituted 1-phenyl-1-ethanenitronates was then studied in solvents of different hydrogen bonding abilities and polarities. The absorptions and the ultraviolet maxima (Table V) of the long wavelength bands of 1-*p*-tolyl-1-ethanenitronate (**4**), 1-*m*-nitrophenyl-1-ethanenitronate (**5**), and 1-*p*-nitrophenyl-1-ethanenitronate (**6**) shift to longer wavelengths for the solvent series: methyl, ethyl, isopropyl, and *t*-butyl alcohols.[6b,22] Thus as the hydrogen bonding ability of an alcohol is decreased, coordination of the solvent with a 1-phenyl-1-ethanenitronate is diminished and less energy is required for excitation of the 1-phenyl-1-ethanenitronate that results

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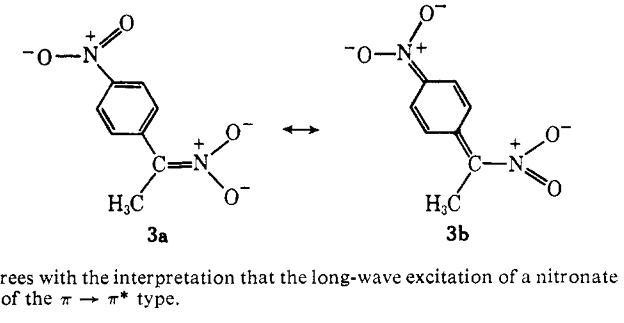
[22] R. C. Kerber and A. Porter (*J. Amer. Chem. Soc.*, **91**, 366 (1969)) have reported the effects of hydrogen bonding, aprotic solvents, and cationic coordination on the electronic and nmr spectra of salts of 1-nitroindene and 9-nitrofluorene.

[23] (a) Extensive absorption of 1-*m*-nitrophenyl-1-ethanenitronate occurs over a much broader range (up to 3600 Å) than do the 1-ethanenitronates in which the 1-phenyl groups contain substituents which are less electronically delocalizing than is the *meta*-nitro group. (b) The very large shift in the ultraviolet absorption maximum upon introducing a *para*-nitro group into 1-phenyl-1-ethanenitronate presumably is derived from the first-order conjugative effect (**3a–b**) of the substituent and agrees with the interpretation that the long-wave excitation of a nitronate is of the π → π* type.



3a **3b**

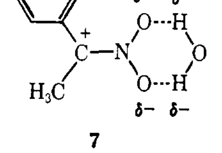
Table V. Effect of Solvents on the Ultraviolet Absorption Maxima of 1-Phenyl-1-ethanenitronates

Sodium 1-*p*-tolyl-1-ethanenitronate Solvent	λ_{max} (Å)	Sodium 1-*m*-nitrophenyl-1-ethanenitronate Solvent	λ_{max} (Å)	Sodium 1-*p*-nitrophenyl-1-ethanenitronate Solvent	λ_{max} (Å)
MeOH	2925	MeOH	3070	MeOH	3940
EtOH	2935	EtOH	3145	EtOH	4025
i-PrOH	2945	*i*-PrOH	3150	*i*-PrOH	4055
t-BuOH	2975	*t*-BuOH	3165	*t*-BuOH	4065
		$(CH_3)_2C{=}O$	3220	$(CH_3)_2C{=}O$	4555
		CH_3CN	3360	CH_3CN	4970
		$PrCO_3$[a]	3500	$PrCO_3$	5180
		HMP[b]	3765	HMP[b]	5575

[a] Propylene carbonate. [b] Hexamethylphosphoramide.

in increased electron density on carbon of the delocalized anion. The differences in the transition energies for **4**–**6** over the range of alcohols studied are approximately 1.6, 3.8, and 1.8 kcal/mol, respectively, and it is likely that these effects arise from the strengths of the hydrogen bonding of the solvents[24] with the oxygens of the nitronates. The influence of a solvent on the properties of a 1-phenyl-1-ethanenitronate is indicated further by the very large shifts in the absorptions of **5** and **6** to longer wavelengths in propylene carbonate and in hexamethylphosphoramide (Table V). In these polar aprotic solvents, hydrogen bonding is prevented and **5** and **6** are not tightly associated with sodium ions. Nitronates **5** and **6** thus have increased anionic character in these environments and their $\pi \rightarrow \pi^*$ transitions occurs at considerably lower energies.

Structural and Solvent Effects on the Rates of Reversal of Substituted 1-Phenyl-1-ethanenitronates. Analysis of the structure of a carbonitronate[6b] reveals that its carbon is electron deficient because of the electrical demands of its nitrogen and oxygen atoms. In 1-phenyl-1-ethanenitronate derivatives (**1** and **2**) there is presumably extensive contribution of **1c** and **2c**. If indeed hybridization and delocalization in a nitronate in its ground state results in greater cationic character of its α carbon than does the corresponding transition state for proton transfer yielding nitro compound, electron donor groups can retard and electron acceptor groups can accelerate reversal of a nitronate to a nitroalkane. This interpretation for the abilities of substituted 1-phenyl-1-ethanenitronates to undergo reversal appears oversimplified, however, in that the role of the solvent is not included. It is thus suggested (as in general agreement with the results in Table I) that 1-*p*-tolyl-1-ethanenitronate in aqueous solvents (**7**) reverses more slowly than 1-phenyl-1-ethanenitronate because the *p*-tolyl derivative behaves relatively electron deficiently at carbon of the carbonitronate as a result of increased hydrogen bonding at oxygens of electronically enhanced nucleophilicity and because of the greater work involved in breaking the hydrogen bonds. Conversely the 1-*p*-nitrophenyl-1-ethanenitronate ion in aqueous solution (**8**) should be less tightly hydrogen bonded at nitronate, its nitronate carbon will express greater carbanionic character, and rupture of its hydrogen bonds is less difficult.[25,26]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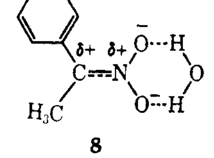
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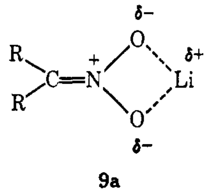
Electronic Spectra of Alkanenitronates. The influences of cations and of hydrogen bonding and aprotic polar solvents on the spectral properties of simpler alkanenitronates were then studied. The infrared spectra of lithium, sodium, and potassium salts of nitroethane and 2-nitropropane, as potassium bromide wafers, revealed shifts in the principal absorption band (C=N vibration) in the 1575–1650 cm^{-1} region (Table VI). For salts of a specific nitroalkane, there is a shift to longer wavelength as the charge density (charge/radius) of the cation is decreased. These results are interpretable on the basis that lithium salts are more covalent because of tighter coordination of the nitronate oxygens with a cation of relatively high charge density (**9a,b**), whereas the sodium and potassium salts are more ionic and have greater charge separation.

Table VI. Principal Infrared Absorption of Alkanenitronates[a,b]

Alkanenitronate	Li$^+$	Na$^+$	K$^+$
$CH_2NO_2^-$		1623[c]	
$CH_3CHNO_2^-$	1621	1610	1584
$(CH_3)_2CNO_2^-$	1637	1613	1603

[a] Values are in cm^{-1}. [b] For C=N. [c] Damp because of hazard.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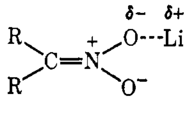
9b

Lithium salts of nitronates may thus be more localized and have greater carbon–nitrogen double bond character than do the salts of the larger cations. Although the effects are not regular, replacement of hydrogens by methyl groups leads to C=N absorption at shorter wavelengths. These results are consistent with the

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(24) G. J. Brealey and M. Kasha, *J. Amer. Chem. Soc.*, **77**, 4462 (1955).

(25) The present interpretation, the near-maximal kinetic isotope effect (k_H/k_D) for neutralization of nitro compounds,[1c,26] and the Brønsted coefficient of near zero for reversal of 1-phenyl-1-ethanenitronates are consistent with the supposition that in the transition state for neutralization (or reversal) the C–H bond of the nitro compound is highly broken and that being formed from protium and hydroxide ion is poorly developed.

(26) O. Reitz, *Z. Elektrochem.*, **42**, 582 (1936).

previous interpretation in that electron release by the methyl groups allows a larger electron density on nitronate oxygens, tighter coordination with cations, and thus a higher double bond order between carbon and nitrogen.

The electronic spectra of sodium salts of nitromethane, nitroethane, and 2-nitropropane in water reveal maximum ultraviolet absorption ($\pi \rightarrow \pi^*$) at 2320, 2290, and 2230 Å, respectively.[27] Methyl groups are electron donors and result in hypsochromic shifts in the absorption of alkanenitronates. These effects are analogous to those observed upon introduction of *meta*- or *para*-methyl substituents in 1-phenyl-1-ethanenitronates and, as for the substituted 1-phenyl-1-ethanenitronates, are derived from stabilization of the ground states relative to their excited states.

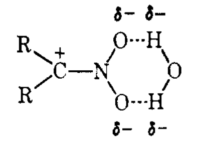
Sodium ethanenitronate and sodium 2-propanenitronate exhibit marked spectral changes in solvents of varied hydrogen bonding abilities and polarities (Table VII). The shift in the ultraviolet maximum to longer wavelengths for sodium ethanenitronate on progression from water to the poorer hydrogen bonding solvent, triethylcarbinol, represents a decrease in transition energy of approximately 7.9 kcal. The absorption difference in propylene carbonate, an aprotic, very polar solvent, represents a lessening of the $\pi \rightarrow \pi^*$ transition energy of almost 20 kcal from that required in water. The effect of solvents on absorption is smaller with sodium 2-propanenitronate than with sodium ethanenitronate. The difference in excitation energies for maximum absorption of sodium 2-propanenitronate in water and in propylene carbonate is ~17.6 kcal.

Table VII. Ultraviolet Absorption Maxima (Å) of Alkanenitronates in Various Solvents

Solvent	Na^+CH_3-$CHNO_2^-$	$Na^+(CH_3)_2$-CNO_2^-
CF_3CH_2OH		2165
H_2O	2265	2220
MeOH	2305	2260
EtOH	2325	2265
i-PrOH	2345	2270
t-BuOH	2365	2280
Et_3COH	2395	
MeCN	2640	2560
PC[a]	2690	2570

[a] Propylene carbonate.

The shifts in absorption of alkanenitronates to longer wavelengths as the hydrogen-bonding abilities of solvents are decreased are analogous to those for substituted 1-phenyl-1-ethanenitronates. The effects however on an energy basis are considerably larger with the simpler alkanenitronates. The alkanenitronates are stronger electron donors for hydrogen bonding than are the 1-phenyl-1-ethanenitronates and thus coordinate more tightly with excellent acceptor solvents such as trifluoroethanol and water to give adducts such as **10** which are relatively difficult to excite at long wavelengths. As a solvent is less able to hydrogen bond these nitronates, less negative charge is transferred to the solvent and the electronic structures of such weak complexes may more closely resemble **11**.



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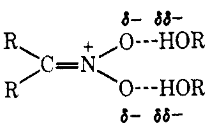

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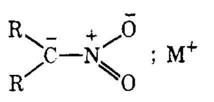

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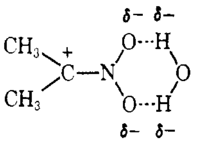
In propylene carbonate the nitronates are barer, more highly delocalized carbanions (**12**) with increased electron density on α carbon, and are excitable at lower energies. The transition energy for maximum excitation of ethanenitronate in water as compared to 2-propanenitronate is 1.6 kcal; in propylene carbonate the difference is increased to 5.0 kcal. It thus appears that as a result of electron donation by methyl groups to nitronate oxygens in solution, the sodium ion is more highly associated with 2-propanenitronate than with ethanenitronate.[28]

Structural and Solvent Effects on the Rates of Reversal of Alkanenitronates. The results of the present investigation allow more complete explanation[6b] of the facts that the rates of reversal of the specific alkanenitronates in water are $CH_2{=}NO_2^- > CH_3CH{=}NO_2^- > (CH_3)_2C{=}NO_2^-$ and the ionization constants in water are: $(CH_3)_2CHNO_2 > CH_3CH_2NO_2 > CH_3NO_2$. It is thus theorized that 2-propanenitronate ion in aqueous solution (**13**) is relatively highly hydrogen bonded on oxygen, its nitronate carbon is of reduced nucleophilicity (less carbanionic; more cationic) and sterically shielded, and rupture of its hydrogen bonds during protonation is relatively difficult. Methanenitronate ion is relatively poorly hydrogen bonded (**15**), and as a result of electronic and steric factors and less extensive solvation is a carbanion of enhanced reactivity with respect to protonation. From the ideas of the present manuscript, the greater rate of reversal of 1-propanenitronate than ethanenitronate, though correlative simply on the basis of inductive effects, stems from combination of significant electrical, steric, and solvent effects. It is of particular note that the greater rate of proton transfer to the dinitromethane anion ($O_2NCH{=}NO_2^-$) than to nitromethane anion ($CH_2NO_2^-$)[5b] can be rationalized on the basis that, because of the extensive hydrogen bonding of methanenitronate, its kinetic basicity is enormously depressed.



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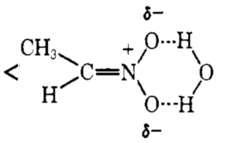

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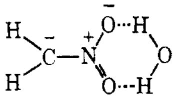

15

Experimental Section

Substituted 1-Phenyl-1-nitroethanes. The various substituted 1-phenyl-1-nitroethanes were prepared from the appropriate bromides[29] and sodium nitrite in dimethylformamide. The procedure used is an extension of that reported.[30] Synthesis of 1-(*m*-tolyl)-1-

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[27] The transition energy for maximum absorption of methanenitronate in water is ~5.6 kcal less than that for 2-propanenitronate.

[28] The chemical shifts for the proton magnetic resonance of nitroalkanes and their various salts in solvents of different hydrogen bonding and polar abilities are in excellent agreement with the present interpretations based on spectral effects and will be the subject of a detailed manuscript from this laboratory.

[29] Obtained from the respective alcohols and phosphorus tribromide (20% excess) at ~15°.

[30] The reactions of alkyl halides and sodium nitrite are summarized by N. Kornblum, *Org. React.*, 12, 101 (1962).

Table VIII. Substituted 1-Phenyl-1-nitroethanes

$ZC_6H_4CH-NO_2CH_3$ Z	Yield,[a] %	Bp, °C	$n^{20}D$	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
p-CH_3		78 (0.5)	1.5288	$C_9H_{11}NO_2$	65.43	6.70	8.48	65.65	6.73	8.53
m-CH_3	59	86–89 (1)	1.5208	$C_9H_{11}NO_2$	65.43	6.70	8.48	65.43	6.71	8.53
H[b]	42	82 (0.8)	1.5220	$C_8H_9NO_2$						
m-CH_3O	47	84–85 (0.3)		$C_9H_{11}NO_3$	59.66	6.12	7.73	59.85	6.27	7.88
p-Cl	53	83 (0.3)	1.5403	$C_8H_8ClNO_2$	51.77	4.34	7.55	52.02	4.34	7.50
p-Br	58	84 (0.2)	1.5640	$C_8H_8BrNO_2$	41.76	3.50	6.09	41.94	3.48	6.08
m-Br	36	100 (0.45)	1.5648	$C_8H_8BrNO_2$	41.76	3.50	6.09	42.06	3.51	6.25
m-NO_2	43	79.5–80.0[c]		$C_8H_8N_2O_4$	48.98	4.11	14.28	49.05	4.17	14.30
p-NO_2	20	66–67[c]		$C_8H_8N_2O_4$	48.98	4.11	14.28	49.13	4.23	14.18

[a] In the present experiments purity of the nitro compounds rather than yields was emphasized. [b] Prepared previously; L. F. Fieser, "Experiments in Organic Chemistry," 2nd ed, D. C. Heath & Co., 1961, p 368. [c] Melting points of white crystalline solids.

nitroethane is described since it is typical for the products summarized in Table VIII. The substituted 1-phenyl-1-nitroethanes were scrupulously purified and handled in the subsequent potentiotitrimetric and kinetic experiments.

1-(*m*-Tolyl)-1-nitroethane. 1-Bromo-1-*m*-tolylethane (69.7 g, 0.35 mol) was added to a stirred solution of urea (47.4 g, 0.79 mol), phloroglucinol (44.4 g, 0.35 mol; the dihydrate was rendered anhydrous by heating at 110° for several hours), and anhydrous sodium nitrite (35.6 g, 0.53 mol) in dimethylformamide (550 ml, dried over calcium hydride) at −18° and protected from light. After 18 hr at −18°, a negative test for the parent halide was obtained. The mixture was then poured into ice-water (1 l.) layered with benzene (400 ml). The aqueous phase was extracted with benzene and with ether. The combined organic extract was washed with water, sodium bicarbonate solution (5%), and water, and then dried ($MgSO_4$). After evaporation of the benzene and the ether, the combined residue was rectified through a glass helix column (20 cm) to give, after removal of (1-*m*-tolyl)-1-ethyl nitrite, 1-(*m*-tolyl)-1-nitroethane (34.1 g, 59%). The product was distilled four times to give a kinetic sample of the properties indicated in Table VIII. The infrared spectrum of the nitro compound showed no absorption bands for functional groups other than the nitro group. The experimental samples were kept cold and in darkness and were vacuum distilled again prior to use.

Determination of Ionization Constants. The ionization constants of the 1-aryl-1-nitroethanes were determined from pH measurements at 20° upon equilibration after (partially) neutralizing the nitro compounds with standardized sodium hydroxide at 0°. The measurements were made with a pH meter (Beckman, Model G) equipped with a glass electrode (Beckman 40495, type E-2 for measurements at high pH) and an asbestos-fiber calomel electrode. The pH meter was standardized before and after each measurement with buffers (U. S. Bureau of Standards) at pH 4.00, 6.88, and 9.22 at 20°.

The experimental technique involved weighing the nitro compound and diluting the sample to volume with dioxane–water at room temperature. The nitro compound (5 aliquots) was pipetted into glass-stoppered flasks purged with pure nitrogen, additional fresh solvent was added, and the mixtures were equilibrated at 0.0°. At 0°, 0.25, 0.50 (three samples), and 0.75 equiv of sodium hydroxide solution were added to the previous individual aliquots; two of the solutions containing 0.50 equiv of base were used to measure the pH at various reaction times to check on decomposition of the nitronate formed. After an appropriate reaction time (5–10 hr for 1-*p*-nitrophenyl-1-nitroethane and 10–24 hr for 1-*p*-tolyl-1-nitroethane), the flask was transferred to a constant temperature bath at 20°, equilibrated, and the pH was determined under nitrogen.

Carrying out an entire equilibration, neutralization, and measurement at 20° over a 5–24-hr period led to some decomposition of the 1-aryl-1-ethanenitronate solutions. Upon use of this technique the pH of a partially neutralized mixture continued to fall slowly after neutralization should have been completed, and it was difficult to determine a true equilibrium value. This problem was essentially eliminated and the precision was improved by effecting the prior equilibrations and neutralizations at 0° and then determining the pH of a neutralized sample after rapid equilibration (1 hr) at 20°.

Table IX. Determination of pK_a of 1-*p*-Chlorophenyl-1-nitroethane, 20°

Expt	Degree of neutralization	Equil time, hr	pH[a]	pK_a
1	0.25	24	9.28	9.80
2	0.50	24	9.72	9.78
3	0.75	24	10.20	9.79
4	0.50	10	9.80	9.86
5	0.50	48	9.78	9.83
			Mean pK_a	9.81 ± 0.03

[a] Measured.

Table X. Determination of pK_a of 1-*m*-Nitrophenyl-1-nitroethane, 20°

Expt	Degree of neutralization	Equil time, hr	pH[a]	pK_a
1	0.25	10	8.68	9.20
2	0.50	10	9.11	9.16
3	0.75	10	9.57	9.16
4	0.50	5	9.15	9.20
5	0.50	20	9.11	9.16
			Mean pK_a	9.18 ± 0.02

[a] Measured.

The ionization constants were determined in moderately dilute solution (5 × 10^{-3} to 10^{-2} mol/l.) and the pK_a's were calculated from eq 3 in which the Debye–Hückel limiting law (eq 4) was applied.[8] Typical data are illustrated (Tables IX and X) for determination of the pK_a's of 1-*p*-chlorophenyl-1-nitroethane and 1-*m*-nitrophenyl-1-nitroethane.

$$pK_a = pH - \log([A^-]/[HA]) - \log \gamma_\pm \qquad (3)$$

$$-\log \gamma_\pm = 0.920\mu^{1/2}; \ \mu = {}^1/_2\sum C_iZ_i^2 \qquad (4)$$

Kinetic Techniques. a. Conductometric Equipment. A 2000-cps signal from an oscillator (Jackson Electrical Equipment Co. Model 652; output ~1 V) was led by shielded wire to a 1:1 isolation transformer and then to a modified Jones–Joseph bridge (Leeds and Northrup; range, 0–60,000 ohms). The signal from the bridge was led through another isolation transformer to a preamplifier (a voltage amplifier, a RC coupled 6SN7 twin-triode amplifier tube, producing a 240-fold voltage gain). Two leads from the bridge contacted the conductivity cell. The signal was led from the preamplifier to the Y input of an oscilloscope (Dumont, Model 208-B) used as a null point indicator. When the 2000-cps trace on the oscilloscope disappeared, the bridge was in balance.

b. Conductivity Cells. The conductivity cell designed for this investigation is diagramed in Figure 7. Vertical placement of the platinum electrodes in this cell virtually eliminated accumulation of bubbles. The second reactant could be introduced rapidly through the slanted inlet tube and led to excellent mixing. The volume of the solution (~30 ml) adequately covered the electrodes and yet left sufficient gas space in the cell to allow the contents to be thoroughly mixed by shaking the cell in the bath. The ground-glass stoppers effectively eliminated absorption of oxygen and carbon dioxide from the air.

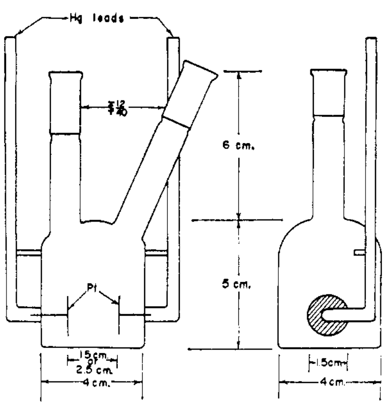

Figure 7. Conductivity cell for kinetic experiments.

c. Solvent and Solutions. The solvent in all experiments was a mixture of 1,4-dioxane and water (50:50 by volume at 25°). Purified dioxane[31] was passed through an alumina column to remove peroxides and then distilled through a glass helix column just prior to a kinetic run. The dioxane was then mixed with water (nonmetallic doubly distilled water which had been freshly boiled and then redistilled) immediately after the distillation and the solution was flushed with highly purified nitrogen. The substituted 1-phenyl-1-ethanenitronate ions are sensitive to peroxides. Proper purification and handling of the solvent are important in order to obtain satisfactory rate constants for neutralization of the nitro compounds. Use of dioxane–water which had been saturated with oxygen resulted in an increase in rate constant of ~6% in neutralization of 1-phenyl-1-nitroethane. Addition of benzoyl peroxide caused a decrease in the resistance of neutralized kinetic solutions.

A concentrated solution of carbonate-free sodium hydroxide was prepared from sodium hydroxide pellets and highly purified water. A small portion of the solution was diluted with freshly prepared dioxane–water solvent and the mixture was standardized. The sodium hydroxide solutions were kept carbonate free.

Solutions of the nitro compounds for a kinetic experiment were prepared from a known weight of material, adding freshly prepared dioxane–water, and equilibrating the resulting mixture.

d. Execution of a Kinetic Experiment. Fresh dioxane–water was added to a scrupulously clean conductivity cell which had been rinsed with distilled ethanol, dried, and flushed with pure nitrogen. The air space in the conductivity cell was purged with purified nitrogen and an appropriate known volume of standardized sodium hydroxide in dioxane–water was added. The cell was suspended in a constant temperature bath and the volume of the solvent and the standard sodium hydroxide solution was corrected to the kinetic temperature by use of appropriate expansion coefficients.[32]

A hypodermic syringe was filled with slightly more than the required volume of the dioxane–water solution of the nitro compound. After the needle had been removed, the syringe was capped with a small rubber ampoule and then suspended top down in the constant temperature bath. The kinetic cell and the syringe were equilibrated (~45 min).

At the start of a run, the syringe was removed from the bath, wiped rapidly with cotton, and adjusted to volume. The time for this operation ranged from 5 to 10 sec. The solution of nitro compound was injected (~1 sec, the syringe was used without needle) into the conductivity cell, timing was initiated, and the cell was shaken in the bath for 2–3 sec. Resistances were determined within 6–10 sec after beginning an experiment.

Prior to starting a kinetic experiment, the bridge was set at a resistance approximately 10% higher than the expected R_0; the capacitance was reduced slightly from that required to balance the kinetic sodium hydroxide solution. During a run, as soon as the resistance bridge was balanced, the time was noted and the bridge was advanced to the next higher predetermined resistance. In order to obtain a sharp null point, it was necessary to adjust the capacitance periodically. The kinetic reactions were usually followed to 80% completion; the resistance upon completion of an experiment (R_∞) was determined after 7–8 half-lives of reaction.

Kinetic Methods and Calculations. Neutralization of nitro compounds by hydroxide, a bimolecular process of the type A + B → C + D, is expressed as a second-order kinetic reaction by eq 5 where $a = [\mathrm{A}]_0$, $na = [\mathrm{B}]_0$, $x = [\mathrm{C}]_t$, and $n = [\mathrm{B}]_0/[\mathrm{A}]_0$. Since the

$$2.303 \log \frac{na - x}{a - x} = a(n - 1)k_2t + 2.303 \log n \quad (5)$$

conductivities of the ionic species in the reaction system, hydroxide and nitronate, are additive and vary linearly (Figure 6[33]), where R,

$$\left(\frac{R_\infty - R_0}{R_0}\right)\left(\frac{R}{R_\infty - R}\right) = \frac{a}{a - x} \quad (6)$$

R_0, and R_∞ are the resistances of the reaction mixture at time t, $t = 0$, and $t = \infty$, respectively. Substituting eq 6 into eq 5 gives

$$\log Y = \log\left[(n - 1)\left(\frac{R_\infty - R_0}{R_0}\right)\left(\frac{R}{R_\infty - R}\right) + 1\right] = \frac{a(n - 1)k_2t}{2.303} + \log n \quad (7)$$

for the general second-order process with the reactants in different concentrations. When equal concentrations of reactants are used ($n = 1$)

$$t(R_\infty - R) = \frac{R_\infty R}{ak_2R_0} - \frac{R_\infty}{ak_2} \quad (8)$$

and k_2 can be evaluated from the intercept of the plot without knowledge of R_0.

In kinetic experiments with one of the reactants in excess and to use eq 7, it is necessary to know R_0. This resistance could not be measured directly because of the rapid rates of neutralization of the nitro compounds. The initial resistance, R_0, was thus determined (1) from kinetic samples which did not contain the nitro compounds (the 1-phenyl-1-nitroethanes are nonconductors and thus do not affect R_0) and (2) by linear extrapolation of the initial points from a kinetic experiment to t_0. The values of R_0 as determined by both methods were in excellent agreement and are deemed highly accurate. The more convenient and usual technique was to evaluate R_0 by extrapolation.

For use of eq 7 or eq 8, R_∞ is required. At the outset of this investigation a series of kinetic neutralizations by hydroxide was effected at 0, 10, and 20°, respectively, using equal initial concentrations of reactants. The results were plotted according to eq 8 and rate constants were calculated. The experimental points deviated from a straight line at the later stages of reaction and, at the completion of a kinetic experiment (the resistance of the solution ceased rising), addition of a drop of the nitro compound to the reaction mixture resulted in an increase in resistance (50–400 ohms), indicating neutralization of the nitro compound was incomplete. In a portion of the kinetic experiments, R_∞ was determined upon addition of excess nitro compound after initial neutralization. From the ionization constants of the substituted 1-phenyl-1-nitroethanes and K_W (1.249×10^{-16}) for 50% (vol) dioxane–water at 20°, the degree of neutralization (α) was calculated in each kinetic experiment from eq 9 where C_0 is the initial concentration of either

$$\frac{\alpha}{(1 - \alpha)^2C_0} = \frac{K_\mathrm{ion}}{K_\mathrm{W}} \quad (9)$$

reactant. The extent of neutralization ranged from 95.4 to 99.5% in the various kinetic runs. There is a linear relation between concentration and conductivity of the individual ions in the present systems, and thus the conductivity of a kinetic solution is a linear function of α (eq 10). At $\alpha = 0$, α, and 1, $R = R_0$, R_obsd, and R_∞, respectively, and R_∞ for complete neutralization can be calculated

$$1/R = \lambda_\mathrm{OH}(1 - \alpha)c_0 + \lambda_{\mathrm{RNO_2}} - \alpha c_0 \quad (10)$$

from eq 11. There was excellent agreement for R_∞ as calculated

$$\frac{1}{R_\infty} = \frac{1}{R_0} - \frac{[(1/R_0) - (1/R_\mathrm{obsd})]}{\alpha} \quad (11)$$

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[31] See Table VIII, footnote *b*.

[32] J. A. Geddes, *J. Amer. Chem. Soc.*, **55**, 4834 (1933).

[33] A. A. Frost and R. T. Pearson, "Kinetics and Mechanism," John Wiley & Sons, Inc., New York, N. Y., 1953, pp 28–29, 35–37.

and as determined experimentally. Plots of $t(R_\infty - R_{obsd})$ *vs.* R_{obsd} for each kinetic experiment are of excellent linearity, and the rate constants as calculated by this method are summarized in Table I.

A detailed kinetic study was then made under conditions in which one of the reactants in each experiment was in sufficient excess to ensure greater than 99.5% neutralization of the minor component. As an example, for neutralization of 1-phenyl-1-nitroethane to be 99.5% complete under the kinetic conditions (eq 7), n must be 1.4; for $n = 10$, neutralization occurs to almost 100%. For use of eq 7 effectively, R_∞ of accuracy is required. It was more reliable and convenient to use excess nitro compound than excess hydroxide ion in each kinetic experiment. Excess hydroxide ion did not lead to a totally constant R_∞ value in any system; with time R_∞ as measured experimentally increased slowly. Excess hydroxide ion could be used reliably upon measuring R_∞ at times corresponding to 8–10 half-lives for neutralization. It was more convenient to use excess nitro compound (n = 1.4–10) because R_∞ stabilized more satisfactorily by this method; upon prolonged storage of the kinetic solutions the resistance of a neutralized solution began to drop slowly but this did not lead to serious inconvenience or experimental complication. A further advantage in using excess nitro compound is that the resistance change is larger than when the base is the reactant in excess. This technique also reduces the effect of any error introduced by approximation of R_0. The rate constants and the kinetic parameters for neutralization of the nitro compounds by this method are summarized in Table I.

Infrared Spectra of Alkanenitronates. Nitromethane, nitroethane, and 2-nitropropane were fractionated and stored over Linde 5A Molecular Sieves. The pure nitroalkanes (1.0 g) were dissolved in pentane (25 ml) and treated, respectively, with 0.5 equiv of butyllithium (Foote Chemical Co., 1 *M* in hexane), sodium methoxide powder (sublimed), and potassium *t*-butoxide powder (MSA Research Corp.). The salts precipitated almost immediately and the mixtures began refluxing. The slurries were stirred for 5 min, filtered, washed with fresh pentane (3 × 25 ml), and vacuum dried.[34]

The white salts were ground with anhydrous potassium bromide crystals (Fisher Chemical Co.) and pressed under vacuum in a pellet die to give clear, transparent wafers. The infrared spectra of each salt were immediately determined on a Perkin-Elmer Infracord spectrophotometer. This position of the major band near 1650 cm^{-1} is reported in Table VI.

Ultraviolet Spectra of Alkanenitronates. For determining the wavelengths ($\pi \rightarrow \pi^*$) of maximum absorption of the various alkanenitronates (Tables V and VII), each nitro compound was treated with excess sodium methoxide or pure sodium salts of the nitronates were dissolved in the various hydrogen bonding or aprotic solvents to give alkaline solutions approximately 10^{-4} *M* in nitro compound. The solutions were always blanketed with nitrogen and analyzed within 0.25 hr after preparation. Cary (Model 14) and Beckman (DU) spectrophotometers were used for the measurements.

For the data in Table IV and Figure 7, solutions from kinetic runs at 0° were used in which the initial concentrations of the reactants were the same. After the resistance of a solution had reached a constant or a maximum value, an aliquot was taken and diluted with 50% (vol) dioxane–water so that the final concentration of the nitronate was $\sim 7.5 \times 10^{-5}$ M. The spectra of the anions were determined immediately with a Beckmann (DU) spectrophotometer. The extinction coefficients are only approximate since neutralization was not complete (>94%) and there was no correction for hydrolysis of the spectral samples upon dilution. Use of excess sodium hydroxide resulted in solutions whose absorptions were time dependent in which the extinction coefficients became less.

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(34) Methanenitronates are very dangerous and were used as slightly damp powders.

Models of Ribonuclease Action. II. Specific Acid, Specific Base, and Neutral Pathways for Hydrolysis of a Nucleotide Diester Analog[1,2]

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Abstract: The rate of production of phenol from the phenyl ester I has been measured as a function of pH at 50° and ionic strength 0.1. The cyclic phosphate III is the sole initial product at pH values above 4, and it is considered likely that this is also true for the reaction in acid. Four kinetically distinct terms appear in the rate equation: k_1(HEH)(H); k_2(EH)(H); k_3(EH); k_4(EH)(OH), and the four rate constants and the acid dissociation constant of the phosphate were obtained by a weighted nonlinear least squares analysis. A large specific salt effect was shown by k_4. The kinetic pK_a of the neighboring hydroxyl group of I has been measured by stopped-flow kinetics in strong base. Plausible mechanisms for these reactions are considered, and it is shown that these results can be useful in considering some of the elementary steps of ribonuclease action.

Since 1920, when Jones recorded[6] in the *American Journal of Physiology* his recent discovery that a boiled aqueous extract of pig pancreas was able to hydrolyze yeast nucleic acid, ribonucleases from many different sources have come under the close scrutiny of a large number of workers in several disciplines, and today one of the most studied of all enzymes is a member of this group.[7]

Enormous progress has been made since the first crystallization[8] of bovine pancreatic ribonuclease in 1940.

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(2) A preliminary report of a part of this work has appeared: D. G. Oakenfull, D. I. Richardson, Jr., and D. A. Usher, *J. Amer. Chem. Soc.*, **89**, 5491 (1967).

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(4) Predoctoral N. I. H. Trainee, 2T01-GM00834.

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(6) W. Jones, *Amer. J. Physiol.*, **52**, 203 (1920).

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