terms with smaller isotope effects would reduce the gross isotope effect substantially in the aqueous ethanol system. We therefore are inclined to weight the new large isotope more heavily than the old in aqueous ethanol and do not feel that a large isotope effect near a factor of 20 in the aqueous ethanol is necessarily excluded. The minimization of all these complications in aqueous *t*-butyl alcohol is doubtless related to the lower basicity and acidity of this solvent and its resistance to halogenation. It was indeed the unreliability of the lowest rates in the aqueous ethanol solution that prompted us to reinvestigate this reaction in aqueous *t*-butyl alcohol.

Experimental Section

Materials. 2-Nitropropane and 2-nitroproane-2-*d* were prepared as before;[3] the protium content of the deuterated species was 1.3% in the 2 position, as measured by the nuclear magnetic resonance spectrum. The substituted pyridines were prepared and purified as described before, and several new ones were commercial materials purified by distillation. Impurity by gas chromatography, which was able to resolve all the compounds available, amounted to no more than 1%. 2,4,6-Trimethylpyridine was purified by distillation from its boron fluoride complex as described before for 2,6-dimethylpyridine[3] to remove unhindered isomers. Tertiary butyl alcohol was a commercial material of good melting point.

Rate Measurements. The solvent was usually made by diluting 1.26 ml of 0.119 *M* aqueous perchloric acid with 30 ml of *t*-butyl alcohol. The carefully weighed appropriate amount of pyridine base (often about 0.4 g) was mixed with the *t*-butyl alcohol solution which was then diluted to 50 ml with water, giving a solution about 0.003 *M* in perchloric acid and 0.1 *M* in pyridine.

The reactions were started by adding a concentrated solution of iodine in aqueous *t*-butyl alcohol to this base solution until the absorbance reached a preselected value (about 0.48) and allowed to come to the thermostat temperature. 2-Nitropropane, about 0.5 g carefully weighed, was diluted to 50 ml with the above base and iodine solution and the resulting solution was placed in a 10-cm absorption cell placed in a recording spectrophotometer set at 468 mμ as rapidly as possible. Since temperatures in the cell compartment were slightly closer to room temperature than the thermostat, because of heat transfer in the circulating system, the temperature changes in dilution and cell filling were in part compensated and the times taken for the cell to come adequately close to the compartment temperature were in fact rather small.

In order to demonstrate absence of serious error from the conversion of absorbances to concentration, the results for 2,4,6-trimethylpyridine were repeated at 360 mμ, using 1-cm cells instead of 10 to compensate for the higher extinction coefficients. The results agreed within 2%.

Controls showed that uncertainty about the reaction temperature was not a significant source of error. Temperatures were measured with a thermistor in the cell compartment with the thermostat itself used frequently as a reference to compensate for drift. The thermostat temperature was determined with a Bureau of Standards calibrated thermometer. Absolute temperatures are probably not accurate to better than ±0.1°, but relative temperatures are limited primarily by reading accuracy and by the precision of bore of the thermometer, leading to an error probably ±0.02°, since the calibration was smooth.

Solutions of known concentration of the base, iodine, and iodide ion in the solvent simulating various extents of reaction were made up, to determine the relation between absorbance and concentration of iodine in all its various complexed states. The record of absorbance *vs.* time from the rates was then converted to a concentration *vs.* time plot, which was linear up to large extents of completion confirming the zero order in iodine and its complexes. There was a residual iodine absorption because of the reversibility of the reaction, but this complication was avoided by using only the linear portion of the curve. The reported second-order rate constants are the slopes of these linear plots, less a blank correction amounting in the largest case to 10% of the observed rate (measured in a solution containing everything but 2-nitropropane and not followed to complete consumption of iodine, since it is so slow) and then divided by the base and nitropropane concentrations. Blank runs with the pyridine base omitted showed negligible reaction, and the measured rates were unchanged by the omission of the small amount of perchloric acid, usually added.

The Importance of the "α Effect" in Amine General Base Catalyzed Ionization of Nitroethane

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Abstract: The conversion of nitroethane to its ion by amine general-base catalysis ($k_{2,\mathrm{B}}$) and the retrograde general-acid neutralization of the anion ($k_{2,\mathrm{A}}$) have been investigated. Both $k_{2,\mathrm{B}}$ and $k_{2,\mathrm{A}}$ are correlated by the Brønsted equations for general-acid and general-base catalysis, respectively. Though the log of the rate constants for tertiary, secondary, and primary amines lie on separate Brønsted plots of parallel slope (presumably due to differences of solvation), hydrazine, N-methylhydrazine, hydroxylamine, and methoxylamine show no positive deviations from these plots. Therefore, the so-called α effect does not appear to be operative in the breaking or making of the C–H bond of nitroethane.

The term "α effect" has been used[3] to describe the high reactivity of nucleophiles possessing an unshared pair of electrons adjacent (α) to the nucleophilic atom. This high reactivity is generally noted as a large positive deviation of the log k_{rate} for a nucleophile from a Brønsted plot for nucleophilic displacements by a series of like nucleophiles in aqueous solution. Therefore, the α effect amounts to a nucleophilic (kinetic) parameter not predicted by the thermodynamic affinity of nucleophile for a proton. The various rationales for this kinetic effect have recently been summarized and discussed.[4] They include intramolecular hydrogen

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

(4) T. C. Bruice, A. Donzel, R. W. Huffman, and A. R. Butler, *ibid.*, **89**, 2106 (1967).

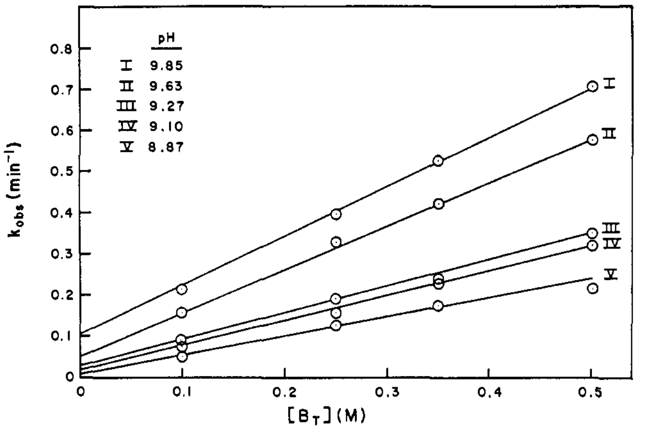

Figure 1. The linear dependence of the pseudo-first-order rate constants for the reaction of glycine with nitroethane on the concentration of glycine at five pH's.

bonding to a carbonyl or similar group,[5,6] intramolecular general-base catalysis,[6] stabilization of the transition state due to overlap of the orbitals of the α lone pair of electrons,[3] lessened solvation of nucleophiles exhibiting the α effect relative to other nucleophiles of the same series,[7] destabilization of the nucleophile by repulsion of the nonbonding electrons,[8,9] high polarizability, and stabilization of the products of reaction.

Substrates upon which this effect has been noted to operate are all valence states of carbon, peroxides, and tetrahedral phosphorus (see ref 3). The question arises as to whether the α effect is of importance in nucleophilic displacement on hydrogen (*i.e.*, general-base catalysis). It has been reported[10] that oxime anions show an enhanced effectiveness in the dehydration of acetaldehyde hydrate. The present work is concerned with the neutralization of nitroethane with a series of aliphatic amines. This reaction has received some attention by Pearson and co-workers.[11]

Experimental Section

Apparatus. Absorbance measurements were made on Gilford Model 2000 or 220 recording spectrophotometers. Kinetic solutions were maintained at 30 ± 0.1° by circulating water at this temperature through Beckman double thermospacers. pH Measurements were made with a Radiometer Model 22 pH meter with a PHA 630 scale expander, using a combined glass-calomel electrode (Radiometer G.K. 2021C). The electrode was thermostated at the temperature of the kinetic runs.

Materials. Nitroethane (Matheson Coleman and Bell) was distilled twice through a 9-in. Vigreux column; bp 113°. Concentrated ammonia solution (Baker and Adamson, CP) and ethylamine (Eastman White Label) were appropriately diluted with water. Diethylamine (Eastman) and piperidine (Matheson Coleman and Bell) were distilled from barium oxide, bp 55 and 103–104°, respectively. Morpholine (Eastman) was refluxed over sodium for 24 hr and distilled under nitrogen, bp 125–126°. Methoxylamine, glycine ethyl ester (Eastman), and hydrazine (Matheson Coleman and Bell) hydrochlorides were crystallized from ethanol–ether mixtures. Tris(hydroxymethyl)aminomethane (Matheson Coleman and Bell), glycine (Fisher reagent), and hydroxylamine hydrochloride (Baker Analyzed Reagent) were used without further purification. Methylhydrazine hydrochloride was prepared by passing dry hydrogen chloride into an ethereal solution of the amine (Matheson Coleman and Bell). The precipitate was crystallized from ethanol–ether mixtures.

Kinetics. The rate of disappearance of nitroethane in various buffers was followed by measuring the variation in absorbance at 240 mμ. Stock solutions of nitroethane in peroxide-free dioxane were prepared. One drop of these solutions in 2 ml of buffer gave a solution approximately 10^{-5} to 10^{-4} *M* in nitroethane. Freshly distilled water was used to prepare buffer solutions and serial dilutions were made with 1.0 *M* potassium chloride solution stored under nitrogen. The reactions were carried out in ₮ cuvettes. Absorption due to the various buffers was compensated for by using a reference cell containing only the buffer solution. The concentration of buffer was always in large excess over that of nitroethane, resulting in pseudo-first-order kinetics. Reactions were routinely followed to four half-lives or more. The pH's of solutions were determined before and after each run. Pseudo-first-order rates were obtained from the slopes of plots of log (OD_∞ − OD_t) *vs.* time.

Results[12]

The reaction studied is of the type

$$AH + B \underset{k_{2,A}}{\overset{k_{2,B}}{\rightleftharpoons}} BH^+ + A^- \qquad (1)$$

If [B] and [BH$^+$] are in large excess over [A$_T$], this equilibrium can be treated as a unimolecular equilibrium

$$AH \underset{k_{2,A}[BH^+]}{\overset{k_{2,B}[B]}{\rightleftharpoons}} A^- \qquad (2)$$

(2), for which the rate expression is given by[13]

$$-\ln([AH]_0 - [AH]_e)/([AH] - [AH]_e) = (k_{2,B}[B] + k_{2,A}[BH^+])t \qquad (3)$$

where [AH]$_0$, [AH], and [AH]$_e$ represent concentrations of AH at $t = 0$, at any time t, and at equilibrium, respectively. As the measured absorbance is that of the nitroethane anion, ($OD_\infty - OD_t$) is proportional to ([AH] − [AH]$_e$)

$$-\ln([AH]_0 - [AH]_e) + \ln(OD_\infty - OD_t) = (k_{2,B}[B] + k_{2,A}[BH^+])t \qquad (4)$$

Thus the slope of a plot of log ($OD_\infty - OD_t$) *vs.* t is equal to $0.434(k_{2,B}[B] + k_{2,A}[BH^+]) = k_{obsd}$. As the neutralization is also catalyzed by hydroxide ion this term is included in k_{obsd} which is then equal to $(k_{2,B}[B] + k_{2,A}[BH^+] + k_{OH}[OH^-])$. Thus, a plot of k_{obsd} *vs.* [B$_T$] is linear, of slope k_2' and intercept $k_{OH}[OH^-]$ (Figure 1)

$$k_2' = k_{2,B}([B]/[B_T]) + k_{2,A}([BH^+]/[B_T]) \qquad (5)$$

and

$$k_2' = k_{2,B}[K_a'/(K_a' + a_H)] + k_{2,A}[a_H/(K_a' + a_H)] \qquad (6)$$

A plot of $k_2'(K_a' + a_H)$ *vs.* a_H is linear of slope $k_{2,A}$ and intercept $k_{2,B}K_a'$ (Figure 2). For amines of high

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[5] J. Epstein, M. M. Demek, and D. H. Rosenblatt, *J. Org. Chem.*, 21, 796 (1956).

[6] W. P. Jencks, *J. Am. Chem. Soc.*, **80**, 4585 (1958).

[7] C. A. Bunton in "Peroxide Reaction Mechanisms," J. O. Edwards, Ed. Interscience Publishers, Inc., New York, N. Y., 1962, p 25.

[8] K. M. Ibne-Rasa and J. O. Edwards, *J. Am. Chem. Soc.*, 84, 763 (1962).

[9] C. K. Ingold, 150th National Meeting of the American Chemical Society, J. F. Norris Award Address, Atlantic City, N. J., Sept 1965.

[10] R. P. Bell, *J. Phys. Chem.*, **55**, 885 (1959).

[11] R. G. Pearson and F. V. Williams, *J. Am. Chem. Soc.*, **76**, 258 (1954). This paper gives leading references to previous papers.

[12] Abbreviations used in this study are: $[B_T] = [B] + [BH^+]$

$$BH^+ \overset{K_a'}{\rightleftharpoons} B + H^+$$

where B and BH$^+$ represent amine and its conjugate acid; k_{obsd}, pseudo-first-order rate constant at constant pH and [B$_T$]; k_2', apparent second-order rate constant at a fixed pH; $k_{2,A}$, $k_{2,B}$, pH-independent second-order rate constants for general acid and general base catalyzed reactions, respectively; a_H, hydrogen ion activity as determined by the glass electrode, $[OH^-] = 1.48 \times 10^{-14}/a_H$.

[13] A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1961, p 186.

Table I. Experimentally Determined Rate Constants and Equilibria Constants for the Reaction of Amines with Nitroethane in Water at 30°, $\mu = 1.0$

	Base	Min^{-1} M^{-1}		$K'_{\text{aNE}} \times 10^{-9}$	No. of k_{obsd}	pH range	No. of pH's	Concn range, M	pK_a'[a]
		$k_{2,\text{A}}$	$k_{2,\text{B}}$						
1	Ethylamine	...	7.7	...	20	10.26–11.10	5	0.448–0.090	10.69[b]
2	Ethylenediamine	...	6.7	...	20	9.63–11.18	5	0.5–0.1	10.10[c]
3	Glycine	0.22	1.71	4.4	24	8.87–10.26	6	0.5–0.1	9.63[c]
4	Ammonia	...	0.56	...	20	8.64–9.85	5	0.380–0.076	9.33[b]
5	Methylhydrazine	1.65	1.32	6.3	16	7.36–8.40	4	0.5–0.1	8.14[d]
6	Hydrazine	0.72	0.35	3.7	20	7.42–8.60	5	0.5–0.1	8.11[c]
7	Tris(hydroxymethyl)aminomethane	0.56	0.31	3.7	20	7.52–8.87	5	0.5–0.1	8.15[c]
8	Hydroxylamine	...	5.7×10^{-2}	...	5	8.95	1	1.0–0.1	6.04[c]
9	Glycine ethyl ester	1.00	0.23	4.0	20	6.99–8.47	5	0.5–0.1	7.75[d]
10	Methoxylamine	...	1.35×10^{-2}	...	3	8.80	1	1.0–0.2	4.81[c]
11	Diethylamine	...	49.5	...	16	10.61–11.27	4	0.3–0.06	11.08[d]
12	Piperidine	...	39.2	...	16	10.20–11.32	4	0.5–0.04	11.10[c]
13	Morpholine	1.38	3.45	6.4	20	8.28–9.67	5	0.5–0.1	8.59[c]
14	Hydroxide	...	990	...	11	9.63–11.18	11	...	...

[a] $\mu = 1.0$, 30°. [b] See ref 4. [c] See T. C. Bruice, J. J. Bruno, and W. S. Chou, *J. Am. Chem. Soc.*, **85**, 1659 (1963). [d] This study, by half-neutralization.

pK_a' the acid-catalyzed rate constant is small and $k_2'(K_a' + a_{\text{H}})$ was a constant equal to $k_{2,\text{B}}K_a'$. Kinetic runs using methoxylamine and hydroxylamine were carried out in 0.1 M borate buffer to maintain constant pH. Rate constants for these amines were determined as the slopes of plots of k_{obsd} *vs.* $[\text{B}_\text{T}]$. In all other cases the nucleophile and its conjugate acid were used to maintain a constant pH.

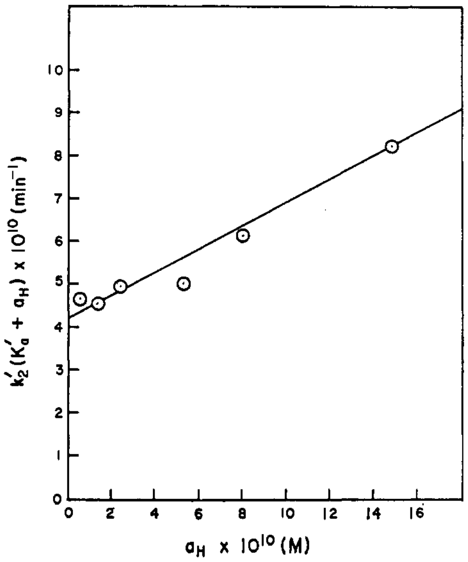

Figure 2. The linear dependence of the product $k_2'(K_a + a_{\text{H}})$ on the hydrogen ion activity for the reaction of glycine with nitroethane.

The rate constants for the reaction of 13 amines with nitroethane derived by these methods are given in Table I. The rate constant for hydroxide was obtained by plotting the intercepts at $[\text{B}_\text{T}] = 0$ from buffer dilution plots *vs.* [OH$^-$]. The buffers used were ethylamine, glycine, and ammonia.

The equilibrium constants K_e for (1) are given by

$$K_e = k_{2,\text{B}}/k_{2,\text{A}} = [\text{BH}^+]_e[\text{A}^-]_e/[\text{AH}]_e[\text{B}]_e \tag{7}$$

where the concentration terms refer to equilibrium concentrations

$$K_e = [\text{A}^-]_e a_{\text{H}}/[\text{AH}]_e K_a' = K'_{\text{aNE}}/K_a' \tag{8}$$

and K'_{aNE} is the calculated dissociation constant of nitroethane. The calculated constant as obtained for each amine is given in Table I.

Discussion

The rate constants for the general-base neutralization of nitroethane by 13 amines are given as a Brønsted plot in Figure 3. Comparison of this Brønsted plot with that of Pearson and Williams[11] shows that the behavior of the various classes of amines are essentially the same, the only difference being in the slope used for primary amines (0.50 *vs.* 0.65 for Pearson and Williams' estimate).

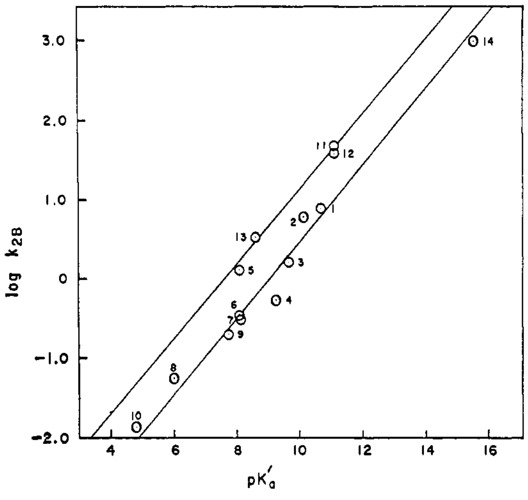

Figure 3. Brønsted plot for the reactions of 14 bases with nitroethane. The numbers refer to the compounds in Table I. No statistical corrections have been made.

The dissociation constants (K'_{aNE}) for nitroethane determined from the rate constants for primary amines are in good agreement with that found by half-neutralization (3.6×10^{-9} at 30°).[14] However, the values derived from rate constants with secondary amines differ considerably from those obtained by half-

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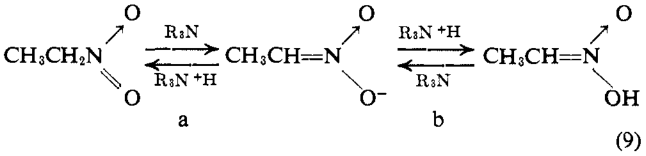
[14] D. Turnbull and S. H. Maron, *J. Am. Chem. Soc.*, **65**, 212 (1943).

neutralization. This is believed to be due to a statistical factor, and that the true equilibrium constant should be expressed in terms of the number of equivalent protons on the conjugate acid of the amine. In order to correlate the equilibrium constants found with secondary amines (two protons) with those for primary amines and hydronium ion (three protons), the former constants were multiplied by a factor of $^2/_3$. This correction gave a value for the K_a' of nitroethane of 4.1×10^{-9}, which is close to the value found with primary amines (3.9×10^{-9}).

The possibility that the rates obtained were for reaction of the amine species with the tautomeric *aci*-nitro forms of nitroethane and its anion (9) was discounted, as the pK_a' obtained from the kinetic data is that for nitroethane whereas the pK_a' of *aci*-nitroethane is approximately 5. In the pH range studied (7–11) the equilibrium concentration of *aci*-nitroethane would be so small that equilibrium 9b can be ignored.

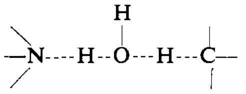


(9)

The order of catalytic efficiency for amines in this reaction (*i.e.*, tertiary > secondary > primary) has been attributed to solvation effects by Pearson and Williams.[11] The same order of nucleophilicity of amines (*i.e.*, tertiary > secondary > primary) has also been noted with phosphate[15] and sulfate[16] esters and has also been attributed to solvation effects. It is interesting to note that these substrates are sensitive to the α effect. However, toward phenyl acetate primary and secondary amines lie on a single Brønsted plot whereas tertiary amines exhibit a negative deviation from this plot.[4] A possible explanation for this apparent anomaly is found in the fact that the bond from nucleophile to substrate is little formed in the transition states for substrate equals phosphate or sulfate esters whereas when the substrate is phenyl acetate the bond is much more completely formed. This suggestion is supported by the small Brønsted α constants for the former substrates (0.20 and 0.13, respectively) as compared to the large value for the latter substrate (1.05). Therefore, steric effects outweigh solvation effects for phenyl acetate while steric effects are of little importance for phosphate and sulfate esters. This contention finds support in the much greater nucleophilicity of azetidines and aziridine toward phenyl acetate as compared to acyclic secondary amines.[17]

The rate constants for the general base catalyzed reactions of hydrazine, hydroxylamine, and methoxylamine with nitroethane do not deviate significantly from the Brønsted plot for primary amines (Figure 3). The rate constant for methylhydrazine lies on the Brønsted plot for secondary amines, in agreement with Condon's[18] suggestion that protonation of alkylhydrazines occurs at the nitrogen bearing the greater number of alkyl groups. We can therefore find no evidence for an α effect for hydrazine, methylhydrazine, hydroxylamine, or methoxylamine in this reaction. The value of 0.5 for the slope of the Brønsted plot suggests that the proton has moved considerably in the transition state, and that any effect operating on the ground state of either products or reactants should be observable. This confirms that the reactivity in proton abstraction of these amines is adequately related to their pK_a''s.

General base catalyzed proton abstraction differs from nucleophilic displacement reactions on other elements on two points. Whereas the latter must involve direct attack of the nucleophile on the substrate molecule or capture of carbonium ion, etc., the former may operate through a water molecule in a manner analogous to proton transfer in water.[19] Regardless of the mechanism of the proton abstraction, the unshared pair of electrons of the base are not considered[3] to be greatly perturbed in the transition state, whereas considerable perturbation of these electrons occurs in other nucleophilic displacements. Thus proton abstraction and nucleophilic displacements are not strictly analogous in that proton abstraction is insensitive to polarizability of the nucleophile.



(10)

As amines which exhibit the α effect are similar in polarizability (as measured by molar refractivity) to those which do not, the α effect must be a kinetic parameter which is not described by the E_n or P terms of Edwards.[20] Our results eliminate such ground-state phenomena as diminished solvation as a cause of the α effect in amines such as hydrazine since amine-catalyzed ionization of nitroethane is sensitive to solvation changes at the basic nitrogen.

The attribution of the high reactivity of oxime anions in the dehydration of aldehyde and ketone hydrates to an α effect[3] is probably not valid, as this too could be caused by solvation differences between these anions and the carboxylate and phenolate anions used as references. This is supported by the fact that water exhibits an equally great positive deviation from the Brønsted plot. However, for the general base catalyzed hydrolysis of ethyl trifluorothiolacetate[21] and the self-assisted general base catalyzed aminolysis of phenyl acetate[4] the α effect is probably of importance and for the latter process of greater kinetic significance than for simple nucleophilic attack of amine on ester. These reactions differ from the neutralization of nitroethane in that they involve an actual nucleophilic attack on an unsaturated center and in addition proton transfer from nitrogen or oxygen rather than from carbon. It is possible that work in process may provide a rationale for these observations.

Acknowledgment. This research was supported by a grant from the National Institutes of Health.

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[15] A. J. Kirby and W. P. Jencks, *J. Am. Chem. Soc.*, **87**, 3209 (1965).

[16] S. J. Benkovic and P. A. Benkovic, *ibid.*, **88**, 5504 (1966).

[17] L. R. Fedor, T. C. Bruice, K. L. Kirk, and J. Meinwald, *ibid.*, **88**, 108 (1966).

[18] F. E. Condon, *ibid.*, **87**, 4481 (1965).

[19] Private discussions with Professor F. A. Long and Professor M. M. Krevoy [See *Discussions Faraday Soc.*, **39**, 101 (1965)].

[20] J. O. Edwards, *J. Am. Chem. Soc.*, **76**, 1540 (1954); **78**, 1819 (1956).

[21] L. R. Fedor and T. C. Bruice, *ibid.*, **87**, 4138 (1965).