a laser intensity of 2.1 J/cm^2 and 5-Torr total pressure, the observed CPF(ethylene)$_{\text{total}}$ = 19% and CPF(propylene) = 28%. For a thermal rate constant ratio of 0.08, this yields a CPF(ethylene)$_{\text{laser}}$ of 12%, indicating 64% of the ethylene produced was via the nonthermal, laser-augmented pathway under these conditions.

Summary

Our results demonstrate that under appropriate conditions a moderate-sized organic molecule can be induced to undergo a nonequilibrium reaction by multiple photon absorption from a high energy infrared laser pulse. The need to conduct such experiments at lower pressure and rather high laser intensities to minimize V–V and V–T,R intermolecular relaxation may be a general requirement particularly for large polyatomic molecules for which V–V relaxation rates are ≥ 0.1 of the gas kinetic collision frequency. Since the nonequilibrium laser-induced reaction pathway follows the unimolecular pathway of lowest energy and since the laser pathway is competitive with collisional relaxation in the 1-Torr range, *intramolecular* relaxation of the absorbed laser energy is implied.[6,10]

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References and Notes

(1) Many authors use the terms "heat", "thermal reaction", etc., without a clear definition. For unimolecular reactions we find it convenient to choose the point at which the vibrational energy has reached equilibrium among all modes of all molecules as the differentiation point between nonequilibrium, laser-induced chemistry and thermal chemistry.

(2) See "Laser Photochemistry, Tunable Lasers, and Other Topics", "Physics of Quantum Electronics", Vol. 4, S. F. Jacobs, M. Sargent III, M. O. Scully, and D. T. Walker, Ed., Addison-Wesley, Reading, Mass., 1976, for a review of laser isotope separation processes.

(3) (a) R. V. Ambartzumian and V. S. Letokhov, *Acc. Chem. Res.*, **10,** 61 (1977); (b) S. Mukamel and J. Jortner, *J. Chem. Phys.*, **65,** 5204 (1976), and references therein; (c) M. F. Goodman, J. Stone, and D. A. Daws, *ibid.*, **65,** 5052, 5062 (1976).

(4) (a) H. Glatt and A. Yogev, *J. Am. Chem. Soc.*, **98,** 7087 (1976); (b) A. Yogev and R. M. J. Benmair, *Chem. Phys. Lett.*, **46,** 290 (1977); (c) A. Yogev and R. M. J. Loewenstein-Benmair, *J. Am. Chem. Soc.*, **95,** 8487 (1973); (d) J. M. Preses, R. E. Weston, Jr., and G. W. Flynn, *Chem. Phys. Lett.*, **46,** 69 (1977).

(5) (a) S. W. Benson and H. E. O'Neal, Report NSRDS-NBS 21, National Bureau of Standards, Washington, D.C., 1970, p 158; (b) p 95.

(6) Chemical activation studies[7] indicate that intramolecular vibrational energy relaxation occurs in polyatomic organic type molecules at rates of $\sim 10^{12}$ s^{-1}. Dever and Grunwald[8] have recently interpreted their laser-induced data as indicating that reaction largely takes place while the excitation energy still resides in the vibrational mode into which it was deposited. Our results suggest that, under the present experimental conditions, intramolecular vibrational relaxation has begun, and may well be complete, before the rearrangement reaction occurs.[10]

(7) A. N. Ko, B. S. Rabinovitch, and K. J. Chao, *J. Chem. Phys.*, **66,** 1374 (1977).

(8) D. F. Dever and E. Grunwald, *J. Am. Chem. Soc.*, **98,** 5055 (1976).

(9) Focusing was accomplished with a germanium lens of focal length 40 cm. The measured cross-sectional area of the beam at various distances from the lens agreed with the area expected from simple geometric considerations.

(10) RRKM calculations of the statistical rate constant for reaction of ethyl acetate indicate an energy of $\sim$70 kcal/mol is required to produce a decomposition rate of 10^7 s^{-1}. This energy requires the absorption of a significant number of infrared photons over and above that needed to achieve the classical activation energy of 48 kcal/mol. This will be a general result for large molecules with sizable activation energies if energy is randomized[3] and if the unimolecular rate is specified to be comparable to the collision frequency at 1 Torr.

Ester Aminolysis. Structure–Reactivity Relationships and the Rate-Determining Step in the Aminolysis of Substituted Diphenyl Carbonates[1]

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Abstract. The rates of reaction of quinuclidines with substituted diphenyl carbonates in aqueous solution increase sharply with increasing amine basicity ($\beta_{\text{nuc}} = 1.0$) until the amine is 3–5 units more basic than the leaving aryl oxide ion and then break to a small dependence on amine basicity ($\beta_{\text{nuc}} = 0.3$); corresponding breaks, with $\beta_{\text{lg}} = -1.3$ and -0.2, are found with changing pK of the leaving group. This behavior is interpreted in terms of a change in rate-determining step from breakdown to formation of the addition intermediate, as in the similar reactions of substituted phenyl acetates. The structure–reactivity data are described in terms of "effective charges" on the reacting groups and it is shown that the pK difference at which the change in rate-determining step occurs is a function of the absolute basicity of the attacking and leaving groups. In the reactions of phenyl acetates the kinetic partitioning of the intermediate through the transition states for expulsion of amine and aryl oxide reflects the thermodynamic partitioning of the reaction products at equilibrium.

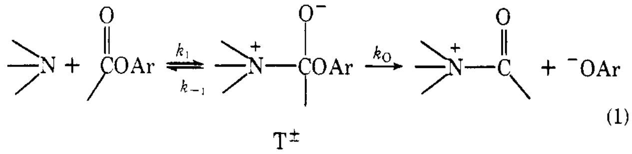
Structure–reactivity relationships in acyl transfer reactions are of interest in themselves and for the light they shed on the mechanism of the reactions. Structure–reactivity correlations for the reactions of primary, secondary, and tertiary amines with substituted phenyl acetates show a break from a large ($\beta_{\text{nuc}} = 0.9 \pm 0.1$) to a small ($\beta_{\text{nuc}} = 0.2 \pm 0.2$) dependence of the rate on the basicity of the attacking amine when the amine becomes some 4–5 pK units more basic than the leaving aryl oxide ion.[2] This break has been interpreted as a consequence of a change in rate-determining step, from rate-determining amine attack with the most basic amines ($\beta_{\text{nuc}} \sim 0.2$) to rate-determining aryl oxide expulsion from an addition intermediate, T$^{\pm}$, with less basic amines ($\beta_{\text{nuc}} \sim 0.9$) (eq 1).[3,4]

The experiments reported in this and the subsequent paper were directed toward the goal of testing this interpretation directly in the closely related reactions of substituted diphenyl carbonates by generating the tetrahedral intermediate T$^{\pm}$ from

Table I. Experimental Conditions for the Determination of Rates of Reactions of Substituted Quinuclidines with Nitrophenyl Phenyl Carbonates[a]

Amine	Concentration, M (free base)	pH	No. of runs
p-Nitrophenyl Phenyl Carbonate			
Quinuclidine	$0.22-0.63 \times 10^{-3}$	9.47-9.50	5
3-Quinuclidinol	$0.57-1.7 \times 10^{-2}$	9.62-9.66	5
3-Chloroquinuclidine	$0.14-0.43 \times 10^{-1}$	9.47-9.48	4
3-Quinuclidinone	$0.58-1.94 \times 10^{-1}$	9.04	5
m-Nitrophenyl Phenyl Carbonate			
Quinuclidine	$0.076-0.57 \times 10^{-2}$	10.23-10.36	5
3-Quinuclidinol	0.033-0.086	10.33-10.34	5
3-Chloroquinuclidine	$0.18-3.1 \times 10^{-2}$	9.09-9.11	5
3,4-Dinitrophenyl Phenyl Carbonate			
Quinuclidine	$0.012-0.24 \times 10^{-5}$	7.20-7.22	6
3-Quinuclidinol	$0.029-0.34 \times 10^{-4}$	6.97-7.19	6
3-Chloroquinuclidine	$0.24-4.3 \times 10^{-4}$	7.14-7.19	6
3-Quinuclidinone	$0.121-2.42 \times 10^{-3}$	7.15-7.17	9
2,4-Dinitrophenyl Phenyl Carbonate			
Quinuclidine	$0.012-0.22 \times 10^{-5}$	7.19-7.22	6
3-Quinuclidinol	$0.029-0.42 \times 10^{-4}$	5-7.19	6
3-Chloroquinuclidine	$0.12-2.0 \times 10^{-4}$	7.12-7.19	6
3-Quinuclidinone	$0.06-0.484 \times 10^{-3}$	7.17	6

[a] The experiments were done at 25 °C, 4% tetrahydrofuran by volume, and ionic strength maintained at 1.0 M with tetramethylammonium chloride. Sodium salts of carbonate, borate, and phosphate were used as buffers at pH 10, 9, and 7, respectively. Buffer concentrations were 0.01 M.



(1)

another reaction pathway and determining its preferred direction of breakdown as a function of the p*K* of the amine and aryl oxide leaving groups. The rate-determining step in the aminolysis reaction is the step that occurs least readily in the partitioning of T±. As background for these experiments it was desirable to determine the structure-reactivity relationships for the aminolysis of diphenyl carbonates with polar substituents in one phenyl group and compare them to the behavior of phenyl acetates. Substituted quinuclidines were selected as the amine nucleophile in order to avoid any possible ambiguities from proton transfer and variable steric effects in the series of substituted amines; however, the structure-reactivity behavior of primary, secondary, and tertiary amines does not differ significantly in the uncatalyzed aminolysis of phenyl acetates.[2] The observed structure-reactivity correlations have been described in terms of the "effective charge" on the attacking and leaving groups in the two transition states for rate-determining amine attack and leaving group expulsion. These effective charges determine the effect of polar substituents on the partitioning of the addition intermediate and the change in rate-determining step.

Experimental Section

Materials. Aryl phenyl carbonates were prepared by a modification of a procedure for *m*-methylphenyl phenyl carbonate.[5] For illustration, the preparation of 2,4-dinitrophenyl phenyl carbonate is described in detail.

2,4-Dinitrophenyl Phenyl Carbonate. 2,4-Dinitrophenol (1.17 g, 6.4 mmol) was added to 1.0 g (6.4 mmol) of phenyl chloroformate in 75 mL of dry toluene (distilled from calcium hydride). The mixture was cooled in an ice bath and 0.775 g (6.4 mmol) of *N*,*N*-dimethylaniline (freshly distilled from calcium hydride under vacuum) in 10 mL of dry toluene was added over 15 min with stirring. Moisture was carefully excluded. After stirring overnight at room temperature the solution was mixed with 50 g of ice and shaken and the ice was filtered off. The organic phase was washed with 5% hydrochloric acid and 10% sodium chloride (three times), dried over anhydrous calcium sulfate, and evaporated to dryness. The yellow solid thus obtained was crystallized from ethyl ether to give white flakes, mp 108-110 °C. Anal. Calcd for $C_{13}H_8O_7N_2$: C, 51.32; H, 2.65; N, 9.21. Found: C, 51.32; H, 2.66; N, 9.20 (Galbraith Laboratories, Inc.).

3,4-Dinitrophenyl phenyl carbonate, mp 118-119 °C, ***p*-nitrophenyl phenyl carbonate,** mp 128-129 °C, and ***m*-nitrophenyl phenyl carbonate,** mp 95-96.5 °C, were prepared similarly and gave satisfactory analyses.

All other reagents used were commercially available and were purified by standard procedures to give melting or boiling points in agreement with the literature, except that carbonate, phosphate, and borate salts were used as received. Acetonitrile and tetrahydrofuran were distilled through a Vigreux column from calcium hydride and lithium aluminum hydride, respectively, and stored under dry nitrogen. Quinuclidines or their hydrochlorides were purchased from Aldrich Chemical Co. and were purified by recrystallization.

Kinetics. The reactions were initiated by injecting a tetrahydrofuran solution of the substrate from a Hamilton CR 700-200 spring-loaded syringe into a 3-mL, 1-cm square cuvette containing the other components of the reaction solution which had been thermostated at 25 °C. This technique was used in order to avoid the possibility that some of the relatively insoluble substrates might come out of solution before mixing was complete. The cuvette was then stoppered, inverted a few times to complete mixing, and inserted into the thermostated cell compartment of a Gilford or Cary 118 spectrophotometer. The release of aryl oxide was followed at 400 nm. Pseudo-first-order rate constants were determined in the usual manner from semilogarithmic plots of absorbance change against time. The plots were linear to at least 5 half-lives. Second-order rate constants were determined from linear plots of pseudo-first-order rate constants against free amine concen-

Table II. Second-Order Rate Constants for the Reactions of Substituted Quinuclidines with *m*-Nitrophenyl Phenyl Carbonate (MNPPC), *p*-Nitrophenyl Phenyl Carbonate (PNPPC), 3,4-Dinitrophenyl Phenyl Carbonate (3,4-DNPPC), and 2,4-Dinitrophenyl Phenyl Carbonate (2,4-DNPPC) at 25 °C, Ionic Strength 1.0 M,[a] 4% THF

		$k_2/M^{-1}\ s^{-1}$			
Amine	pK_{amine}[b]	MNPPC (8.31[c])	PNPPC (7.14[c])	3,4-DNPPC (5.33[c])	2,4-DNPPC (4.00[c])
Quinuclidine	11.45	6.26	1.07×10^2	2.62×10^3	1.27×10^3
3-Quinuclidinol	10.02	2.50×10^{-1}	5.13	5.55×10^2	4.12×10^2
3-Chloroquinuclidine	9.03	2.27×10^{-2}	5.2×10^{-1}	1.07×10^2	2.45×10^2
3-Quinuclidinone	7.53		1.41×10^{-2}	3.34	4.45×10

[a] The ionic strength was maintained with tetramethylammonium chloride. [b] The pK_a values of the conjugate acids of amines were determined from titration curves under the conditions of the rate measurements, with the exception that the rates were measured in 4% tetrahydrofuran, and the titration curves were not. [c] The p*K* of leaving group. pK_a values of the conjugate acids of leaving aryl oxides were estimated from pH measurements of solutions of the substituted phenol half-neutralized with sodium hydroxide, ionic strength maintained at 1.0 M with KCl. Glass-distilled, degassed water was used.

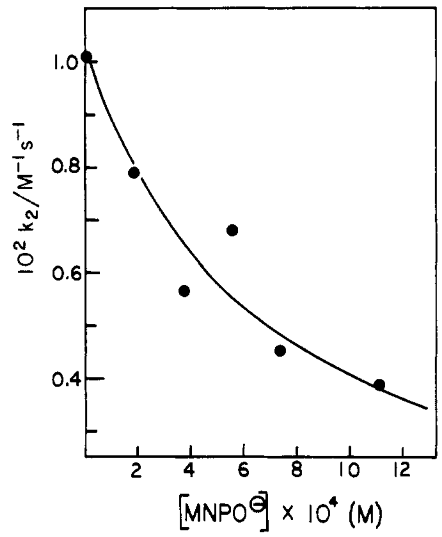


Figure 1. The observed second-order rate constants for the reaction of 3-chloroquinuclidine with *m*-nitrophenyl phenyl carbonate in the presence of added *m*-nitrophenoxide ion (MNPO$^-$). The solid line is calculated from eq 2 with $k_{-1}/k_2 = 10^{3.2}$ M^{-1}. The rates were measured at 25 °C, ionic strength 1.0 M maintained with tetramethylammonium chloride, $[\text{3-Cl-Q}]_{\text{free base}} = 0.04$ M, pH 9.01.

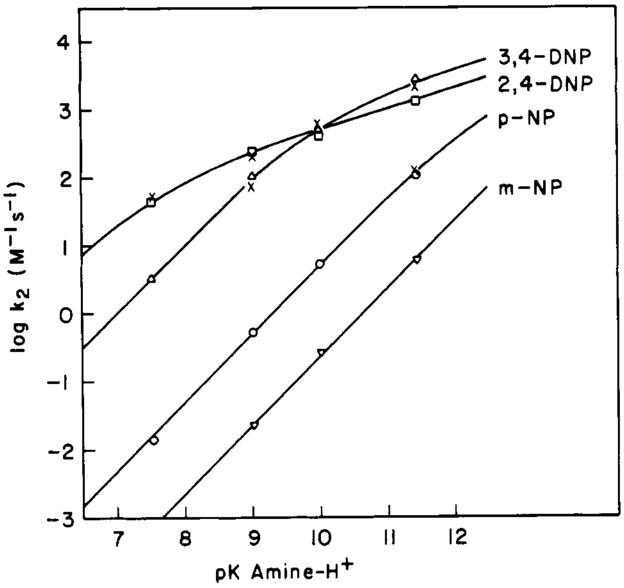


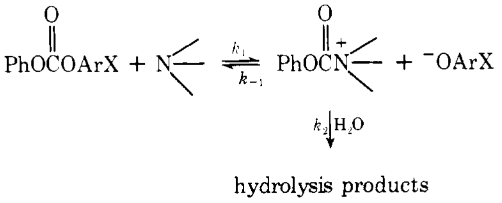
Figure 2. Logarithmic plot of the rate constants for reactions of *m*-nitrophenyl phenyl carbonate, ▽; *p*-nitrophenyl phenyl carbonate, ○; 3,4-dinitrophenyl phenyl carbonate, △; and 2,4-dinitrophenyl phenyl carbonate, □, with substituted quinuclidines as a function of amine basicity at 25 °C and ionic strength 1.0 M (tetramethylammonium chloride). The solid lines were calculated from eq 5–7. The crosses were calculated based on the observed partitioning ratios for the addition intermediate, T$^\pm$.[20]

tration. Conditions were chosen such that inhibition by the leaving group did not become significant during the reaction. The substrate concentrations used were such that the optical density at 400 nm at t_∞ was 0.2 or less with 2,4-dinitrophenyl phenyl carbonate, 3,4-dinitrophenyl phenyl carbonate, and *p*-nitrophenyl phenyl carbonate and 0.05 or less with *m*-nitrophenyl phenyl carbonate. Measurements of pH were made with a Radiometer Model 26 pH meter and a GK2321C electrode. Experimental conditions for the rate measurements are shown in Table I.

Results

Second-order rate constants, k_2, for the reactions of a series of substituted quinuclidines with a series of aryl phenyl carbonates, XArOC(=O)OPh, are shown in Table II. The two slowest reactions studied, those of 3-quinuclidinone with *p*-nitrophenyl phenyl carbonate and 3-chloroquinuclidine with *m*-nitrophenyl phenyl carbonate, were also studied in the presence of various concentrations of added aryl oxide ion in order to demonstrate that the measured rates represent nucleophilic catalysis. Inhibitions of 30% for the former reaction by 3.2×10^{-4} M *p*-nitrophenoxide ion and 60% for the latter reaction by 1.1×10^{-3} M *m*-nitrophenoxide ion demonstrate that the second-order rate constants determined for these two reactions represent at least substantially nucleophilic catalysis. These experiments also allowed conditions for the rate constant determinations to be chosen such that inhibition by aryl oxide released during the runs was not important. The inhibition of the reaction of 3-chloroquinuclidine with *m*-nitrophenyl phenyl carbonate by added *m*-nitrophenoxide ion is shown in Figure 1. Approximate values of $k_{-1}/k_2 = 10^{3.2}$ M^{-1}, for this reaction and $10^{3.3}$ M^{-1} for inhibition by added *p*-nitrophenoxide ion of the reaction of 3-chloroquinuclidine with *p*-nitrophenyl phenyl carbonate were calculated from eq 2, based on the mechanism shown in eq 3.

$$k_{\text{obsd}} = k_1k_2/(k_2 + k_{-1}[^-\text{OAr}]) \tag{2}$$



$$\text{PhOC(=O)OArX} + \text{N}{<} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{PhOC(=O)N}^+{<} + {}^-\text{OArX} \xrightarrow{k_2,\ \text{H}_2\text{O}} \text{hydrolysis products} \tag{3}$$

Discussion

The dependence of the reaction rate on the basicity of the attacking amine for the different carbonate esters is shown in the Brønsted-type plots of Figure 2. The data fall on lines with a slope, β_{nuc}, of 1.0 or 0.3, depending on the basicity of the amine and the leaving aryloxide anion. The lines for the two most reactive esters cross because of a relatively slow reaction of the 2,4-dinitrophenyl ester with basic amines. The dependence of the reaction rate on the pK of the leaving aryl oxide is shown in Figure 3. The limiting slopes, β_{lg}, of the lines in Figure 3 are −0.2 and −1.3.

This pattern of reactivity of substituted diphenyl carbonates is similar to that for phenyl acetates.[2,6] A large dependence of the rate on amine basicity, with $\beta_{\text{nuc}} = 1.0$, is observed for most of the reactions, even with amines that are more basic than the leaving aryl oxide anions. However, when the amine becomes more basic than the leaving group by 4 to 5 pK units, there is a break to a smaller dependence on the basicity of the nucleophile, with a slope of $\beta_{\text{nuc}} = 0.3$. These two types of reaction are assigned to rate-determining breakdown of the addition intermediate, which requires a large amount of bond formation and charge development on the attacking amine, and to rate-determining amine attack, which requires less bond formation and charge development, respectively.[3] The corresponding dependencies on the pK of the leaving group (Figure 3) are $\beta_{\text{lg}} = -1.3$ for rate-determining aryl oxide expulsion and an approximate value of $\beta_{\text{lg}} = -0.2$ for rate-determining amine attack.

The structure-reactivity data alone do not prove the existence of an addition intermediate with a finite lifetime. They demonstrate a change in the *nature* of the rate-determining step with changing reactant structure and could be accommodated either by a two-step reaction with an intermediate or by a reaction coordinate with a plateau rather than a potential well near the center.[7] The rate constant for breakdown to reactants of the intermediate that is formed from the addition of methylamine to *p*-tolyl acetate has been estimated[4] to be ~3×10^9 s^{-1}. This rate constant may be increased by electron-withdrawing substitutents on the amine, by electron

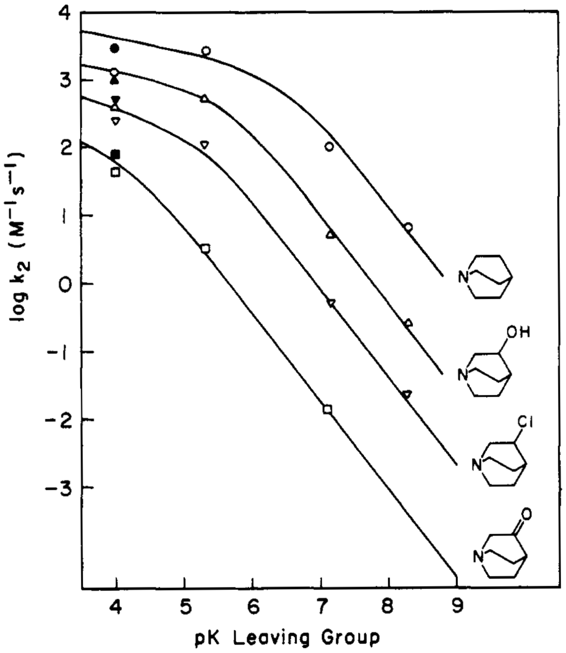


Figure 3. The dependence of the rate constants for the reactions of carbonate esters with substituted quinuclidines on the pK of the conjugate acid of the leaving aryloxide ion, at 25 °C and ionic strength 1.0 M (tetramethylammonium chloride). Open symbols: observed rate constants. Closed symbols: corrected for the rate-retarding effect of the *o*-nitro group, as described in the text. The solid lines were calculated from eq 7–9.

donation from the additional phenolic oxygen atom, and by steric effects in the series of phenyl carbonate reactions.

It is useful to describe the effects of polar substituents on the aminolysis of carbonate and other esters in terms of the "effective charges" on the reacting groups in the ground and transition states.[2,8,9] The effective charge serves as a kind of shorthand for describing the change in charge at a particular position in going from a ground state to a transition state or product, as measured by the effect of polar substituents on rate or equilibrium constants. The effective charge has the following properties.

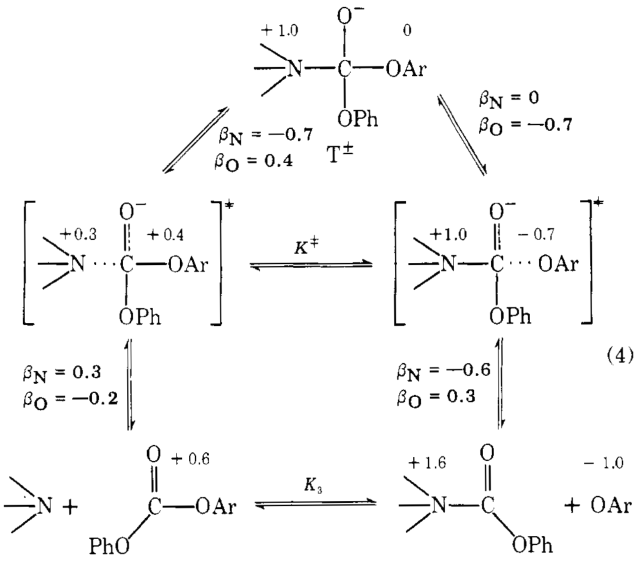
(a) The change in effective charge in a reaction is defined by the slope, β, of log k or log K against the pK of the reacting atom or its conjugate acid in a Brønsted-type plot, defining the change in charge in the reference ionization reaction as +1.0 or −1.0. Thus, one can say that a reaction which follows a slope, β_{nuc}, of 0.3 is 0.3 as sensitive to polar substituents in the nucleophile as is the protonation of the nucleophile so that, as far as substituent effects are concerned, the reaction behaves *as if* there is a development of +0.3 charge on the nucleophile in the transition state.

(b) The changes in effective charge on a given group are additive in the sense that the changes in charge in going from reactants to a transition state and then to products are equal to the change in charge in the equilibrium reaction. Thus, $\beta_{\mathrm{eq}} = \beta_{\mathrm{f}} - \beta_{\mathrm{r}}$ where β_{eq} refers to the effect of substituents on the equilibrium constant of the overall reaction and β_{f} and β_{r} refer to the forward and reverse rate constants of a reaction; for example, $\beta_{\mathrm{eq}} = \beta_{\mathrm{nuc}} - \beta_{\mathrm{lg}}$ when the substituents are on the nucleophile in the forward reaction and on the leaving group in the reverse reaction.

(c) The effective charges on different groups in a molecule are *not* necessarily additive. Neither the effective charges nor their sum is a measure of the *absolute* charge on a particular atom or group, although there is certainly some relationship to the absolute charge. This nonadditivity results in large part from the imbalance in the extent to which various processes have taken place in going from reactants to transition state to products and, in fact, provides a measure of this imbalance. For example, incomplete development of solvation of the charge on a leaving oxy anion in the transition state can result in a large negative effective charge on this oxygen atom, as measured by substituent effects, that is not balanced by changes in charge on other atoms of a reacting ester or nucleophile.[8,9]

(d) The change in effective charge can serve as a useful measure of how far toward completion a reaction has proceeded in the transition state. However, this measure will not be the same for different substituted atoms in the reactants if there is imbalance of different processes in the transition state, as just indicated. In a few instances, particularly for substituents on a central reacting atom, the change in charge is not monotonic during the reaction; i.e., it is larger in the transition state than in reactants or products, so that it is necessary to determine on which side of the maximum in charge development a given transition state lies in order to define its position along the reaction coordinate.

The data shown in Figures 2 and 3 permit us to make a tentative assignment of the "effective charge" distribution for the reactions of tertiary amines with carbonate esters (eq 4).



(4)

From the values of $\beta_{\mathrm{nuc}} = +0.3$ for the reactions of basic amines with esters that have a good leaving group and $\beta_{\mathrm{nuc}} = +1.0$ for reactions of less basic amines with esters that have less good leaving groups (Figure 2), the effective charges on the attacking nitrogen atom are +0.3 in the transition state for rate-determining attack and +1.0 in the transition state for rate-determining breakdown of the tetrahedral intermediate, taking the charge on the free amine as zero. The values of β_{nuc} are 0.15 and 0.93 for the attack of substituted pyridines on methyl chloroformate under conditions of rate-determining attack and breakdown, respectively,[10] and a value of $\beta_{\mathrm{nuc}} = 0.4$ has been reported for the reactions of primary amines with ethyl pyrocarbonate.[11] A charge of +1.0 is assigned to the nitrogen atom in the tetrahedral intermediate $T^{\pm}$.[12] The charge of +1.6 on the cationic nitrogen atom of the reaction product is assigned by analogy with acylpyridinium compounds, the equilibrium formation of which exhibits a value of $\beta_{\mathrm{eq}} = +1.6$; the same value of +1.6 ± 0.1 is found for amides and anilides if allowance is made for conversion to the cation by N-protonation.[16-18]

The solid lines in Figure 2 are calculated from the Brønsted-type equations, 5 and 6, for rate-determining amine attack and aryl oxide expulsion, respectively, based on the values of C_1 and C_b in Table III, and on the steady-state eq 7 for the region in which both steps are partially rate determin-

Table III. Constants that Describe the Reaction of Quinuclidines with Substituted-Aryl Phenyl Carbonates at 25 °C, Ionic Strength 1.0 M

	C_1	C_b	p$K°$	ΔpK Obsd	ΔpK Calcd
m-Nitrophenyl[a]		−10.66	>12.5[b]	>5.3	
p-Nitrophenyl[a]	−0.59	−9.31	12.5[b]	5.3	5.6
3,4-Dinitrophenyl[a]	−0.02	−6.96	9.9[b]	4.6	4.6
2,4-Dinitrophenyl[a]	−0.30	−5.58	7.5[b]	3.5	3.8
Quinuclidine[b]	4.43	11.55	6.5[c]	5.0	5.2
3-Hydroxyquinuclidine[b]	3.95	10.10	5.6[c]	4.4	4.7
3-Chloroquinuclidine[b]	3.42	9.02	5.1[c]	3.9	4.4
3-Quinuclidinone[b]	2.82	7.40	4.2[c]	3.4	3.9

[a] Aryl group. [b] Amine. [c] Phenol.

ing; the calculated lines show a satisfactory fit to the experimental data.

$$\log k_1 = 0.3\ \mathrm{p}K_N + C_1 \tag{5}$$

$$\log k_b = 1.0\ \mathrm{p}K_N + C_b \tag{6}$$

$$k_{obsd} = k_1 k_b/(k_1 + k_b) \tag{7}$$

The slower rates for the 2,4-dinitrophenyl than for the 3,4-dinitrophenyl ester (Figures 2 and 3) mean that there is a specific inhibitory effect of the o-nitro group on the rate that is sufficient to overcome the rate increase that is expected from the greater acidity of the 2,4-dinitrophenyl group under conditions of rate-determining amine attack. Possible explanations for this inhibitory effect include steric hindrance and special resonance effects of the o-nitro group. An approximate correction for this effect was applied to the observed rate constants[19] and the corrected rate constants are indicated by the solid symbols in Figure 3. The solid lines in Figure 3 are calculated from eq 7-9, in which pK_{lg} is the pK of the conjugate acid of the leaving phenol, and the values of C_1 and C_b in Table III; they show a satisfactory fit to the data.

$$\log k_1 = -0.2\ \mathrm{p}K_{lg} + C_1 \tag{8}$$

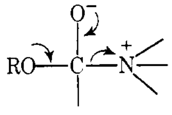
$$\log k_b = -1.3\ \mathrm{p}K_{lg} + C_b \tag{9}$$

The corrected rate constants for the 2,4-dinitrophenyl esters are clearly less accurate than the measured rate constants for the other esters, but they do serve to indicate that the value of β_{lg} for rate-determining attack is small. A more reliable value of $\beta_{lg} = -0.21$ for rate-determining amine attack is available from the rate constants for the reaction of pyridine with substituted phenyl chloroformates.[21]

The effective charge of +0.6 on the phenolic oxygen atom of the starting ester (eq 4) was obtained from the value of $\beta_{eq} = +0.4$ for the equilibrium formation of carbonate half-ester anions, $ROCO_2^-$, and a correction of +0.2 for the effect of the negative charge.[13,22] Essentially the same value, $\beta_{eq} = 0.7$, has been found for the equilibrium formation of acetate esters from substituted alcohols and phenols.[23] A charge of +0.4 is then assigned to the oxygen atom in the transition state for amine attack, based on the value of $\beta_{lg} = -0.2$, and a charge of −0.7 is assigned to this atom in the transition state for rate-determining aryl oxide expulsion, based on the value of $\beta_{lg} = -1.3$. A charge of 0 is assigned to the oxygen atom in the addition intermediate $T^\pm$ and −1.0 to the aryl oxide anion product.

The position of the break in the structure–reactivity correlation for the reactions of 3,4-dinitrophenyl phenyl carbonate with substituted quinuclidines (Figure 2) shows that the change in rate-determining step occurs when the amine is 4.6 units more basic than the leaving aryl oxide ion; i.e., the amine is expelled faster than the aryl oxide ion from the tetrahedral intermediate unless it is more than 4.6 pK units more basic than the oxy anion. The change in rate-determining step occurs when $k_1 = k_b$ (eq 7) and the pK values of the amine and leaving aryl oxide ion at which this occurs, p$K°$, were calculated from the observed rate constants and eq 5-9 and are given in Table III. The values of ΔpK, the difference in the pK values of the attacking amine and the leaving aryl oxide anion at which the change in rate-determining step occurs and the rates of expulsion of amine and aryl oxide from $T^\pm$ are equal are also given in Table III. The results suggest that this difference becomes larger as the amine and aryl oxide become more basic.

The effect of polar substituents on the partitioning of the addition intermediate, $T^\pm$, can be evaluated from the effective charges on $T^\pm$ and on the nitrogen and oxygen leaving groups in the transition states for the breakdown of $T^\pm$ with amine and aryl oxide expulsion (eq 4). The difference in the effective charge on the leaving group in the tetrahedral intermediate and the transition state gives a value of $\beta_N = -0.7$ for amine expulsion with the rate constant k_N and $\beta_O = -0.7$ for oxy anion expulsion with the rate constant k_O, so that the dependence of leaving ability on basicity is similar for these two leaving groups. However, the rate of expulsion of a group depends on the *push* provided by the groups that remain behind as well as the *pull* provided by the leaving group. The *push* provided by the aryl oxide oxygen atom (**1**) is measured by the value of β_O = +0.4 for amine expulsion, whereas the value of $\beta_N = 0 \pm 0.1$ for aryl oxide expulsion means that there has been little or no electron donation from the cationic amine to push out the leaving oxy anion. This difference is consistent with electron donation from oxygen by resonance to help expel the leaving group and stabilize the ester product and the absence of such electron donation from the cationic nitrogen atom.



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The effects of substituents on the relative rates of leaving of aryl oxide and amine, k_O/k_N, may be evaluated more directly from their effects on the equilibrium constant $K^\ddagger$ for the interconversion of the transition states for these two processes (eq 4). A plot of log $K^\ddagger$ against the pK of substituted amines has a slope that is given by the difference in the effective charges on the nitrogen atoms in the two transition states, $\beta_N = 1.0 - 0.3 = 0.7$. The corresponding slope for substituted aryloxides is $\beta_O = -0.7 - 0.4 = -1.1$. Thus, the preferred leaving group is more sensitive to polar substituents on oxygen than on nitrogen and a plot of log $K^\ddagger$ or log k_O/k_N against pK will have a slope of $\beta = 0.7 - 1.1 = -0.4$ when the basicities of the amine and aryl oxide are increased by equal amounts. It should be noted that the partitioning depends only on the relative stability of the two transition states, not on the properties of the intermediate $T^\pm$. Qualitatively, the conclusion is that *the partitioning of the tetrahedral intermediate will favor amine expulsion and the value of* Δp*K, at which amine and oxyanion expulsion are equal, will increase as the basicity of the leaving groups is increased.*

The dependence of the partitioning ratio on the basicities of the aryl oxide and amine leaving groups, based on these effective charges, is given by eq 10.

$$\log(k_O/k_N) = -1.1\ \mathrm{p}K_O + 0.7\ \mathrm{p}K_N + C_t \tag{10}$$

For the aminolysis of the 3,4-dinitrophenyl ester the value of pK_N − pK_O = 4.6 for equal partitioning at the change in rate-determining step, when $k_N = k_O$, gives a value for C_t of −1.09. This equation indicates that, with an amine and aryl oxide with an equal pK of 5, the amine will be expelled faster by a factor of $k_N/k_O = 10^3$; with equal pKs of 10 the ratio of k_N/k_O is 10^5.

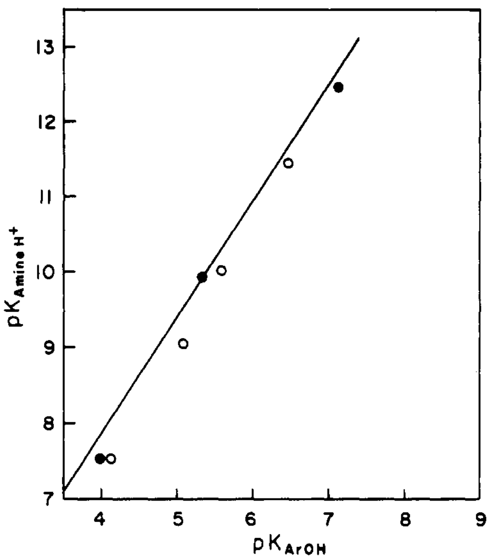
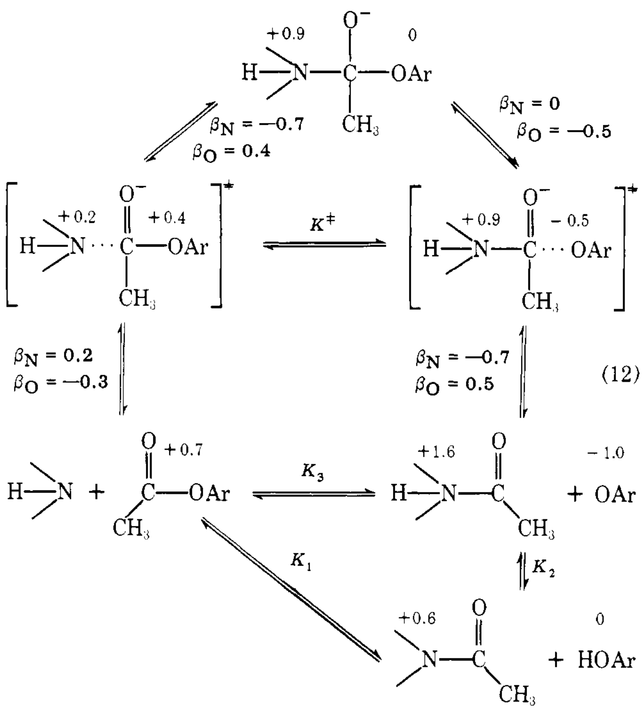


Figure 4. The pK values of amine and aryl oxide at which the addition intermediate T$^\pm$ breaks down equally in both directions and the reaction undergoes a change in rate-determining step. Closed circles: varying amine pK for a constant ester (Figure 2 and eq 5 and 6). Open circles: varying aryloxide leaving group with a given amine (Figure 3 and eq 8 and 9). The solid line is calculated from eq 11.

The difference in pK at which the change in rate-determining step occurs, ΔpK, for the aminolysis of other esters is determined by eq 10 when $k_O = k_N$ and is given by eq 11.

$$\Delta pK = pK_N - pK_O = 1.51 + 0.57\,pK_O \qquad (11)$$

The values of ΔpK calculated from eq 11 are compared in Table III with the values estimated directly from the observed changes in rate-determining step (Figures 2 and 3). In Figure 4 the pK values at which the change in rate-determining step occurs are plotted as a function of the pK of the amine nucleophile and the aryl oxide leaving group and compared with the values calculated from eq 11, shown as the solid line. Although the available data permit only an approximate analysis at this time, the agreement is surprisingly good and the data summarized by Figure 4, Table III, and eq 11 provide strong support for the qualitative conclusion that ΔpK increases with increasing basicity of the aryl oxide ion. Direct evidence for this conclusion is provided by the partitioning data in the accompanying paper.[20]



(12)

$$CH_3\overset{\overset{O}{\|}}{C}OR \overset{K_E}{\rightleftharpoons} CH_3COOH + HOR \qquad (13)$$

$$H\overset{\overset{O}{\|}}{C}N\!< \overset{K_A}{\rightleftharpoons} CH_3COOH + HN\!< \qquad (14)$$

$$\log K_E = +12.1 - 0.70\,pK_O \qquad (15)$$

$$\log K_A = -0.50 - 0.51\,pK_N \qquad (16)$$

$$XArOH \overset{K_O}{\rightleftharpoons} XArO^- + H^+ \qquad (17)$$

$$R\underset{|}{\overset{|}{N}}H^+ \overset{K_N}{\rightleftharpoons} RN\!< + H^+ \qquad (18)$$

$$CH_3\overset{\overset{O}{\|}}{C}\underset{|}{N}HR^+ \overset{K_{am}}{\rightleftharpoons} CH_3\overset{\overset{O}{\|}}{C}\underset{|}{N}R + H^+ \qquad (19)$$

$$pK_{am} = -18.6 + 1.04\,pK_N \qquad (20)$$

Reactions of Acetate Esters. It is of interest to compare the *kinetic* partitioning of T$^\pm$ through the transition states for amine or aryl oxide expulsion with the *thermodynamic* partitioning of the products, in which expulsion of the leaving groups is complete. Sufficient data are not available for such an analysis of the carbonate reactions, but an approximate analysis is possible for derivatives of acetic acid and the data reported here as well as the similarity of the two reactions suggest that the results will not be grossly different for the carbonate derivatives. The kinetic and equilibrium partitioning are given by $K^\ddagger$ and K_3, respectively, in eq 4 and 12. The value of K_3 for amine and phenol leaving groups of the same pK in the acetate series is approximately $10^{-7.5}$, calculated from K_1 and K_2 as follows. The values of K_E and K_A (eq 13 and 14) for a phenol and an amine of pK 10 are $10^{5.1}$ and $10^{-5.6}$, respectively, based on the relationships of eq 15–18.[16–18,23] Since the equilibrium constants for the formation of thiosemicarbazides from formic and acetic acid are the same,[17] we assume that this equivalence will hold for other derivatives of these acids. The value of K_1 is then $K_E/K_A = 10^{10.7}$. The value of K_{am} (eq 19) is estimated as $10^{8.2}$ from eq 20[17] and, with a value of $K_O = 10^{-10}$, K_2 is given by $K_{am}/K_O = 10^{18.2}$. The value of K_3 is then given by $K_1/K_2 = 10^{-7.5}$. Since the effects of substituents in the leaving group on the stability of esters and cationic amides are the same within experimental error, as shown by values of $\beta_{eq} = 1.6 \pm 0.1$ for the formation of these compounds from substituted phenolate ions and amines, respectively,[16–18,23] the value of K_3 should not change significantly with changing pK of the leaving groups as long as the pK of the two leaving groups is the same. If the pK of one leaving group is varied, the value of K_3 will change with a β value of ± 1.6 according to eq 21. Thus, if the amine is held constant at pK = 10, the value of K_3 will be 1.0 when the pK of the phenol is ~10.0 − 7.5/1.6 = 5.3; it will also be 1.0 for any amine-phenol pair in which the pK of the phenol is 4.7 units less than that of the amine.

$$\log K_3 = -7.5 + 1.6\,(pK_N - pK_O) \qquad (21)$$

The *kinetic partitioning* of T$^\pm$ for acetates can be estimated from the effective charges in the transition state in the same manner as for carbonates. The results are summarized in eq 12. The charge of +0.2 on the attacking amine is based on the small dependence of the rate of ester aminolysis on amine basicity, with $\beta_{nuc} = 0.2 \pm 0.2$, under conditions of rate-determining amine attack.[2,3,24] The charge of +0.9 and $\beta_{nuc} = 0.9 \pm 0.1$ for rate-determining aryl oxide expulsion are firmly established[2,3,6,10,16,18,24,25] and the same charge is assigned to the nitrogen atom in T$^\pm$. The value of β_{nuc} is the same or slightly smaller for the uncatalyzed aminolysis as for general base catalyzed aminolysis, which is believed to involve the equilibrium formation of $T^{\pm}$ followed by proton transfer from $T^{\pm}$ to a second molecule of amine.[3,6,25,26] The charge of +1.6 in the product is based on equilibrium measurements.[16-18] The charge of +0.7 on oxygen in the starting ester is also based on equilibrium measurements[23] and an uncertain value of +0.4 for rate-determining amine attack is consistent with the limited available data[2] and analogy with the carbonate reaction. A formal charge of 0 on oxygen in $T^{\pm}$ is consistent with the observed value of $\beta_{lg} = -0.6$ for the general base catalyzed aminolysis of phenyl acetates under conditions in which the observed rate is believed to depend mainly on the equilibrium concentrations of the addition intermediate.[3] The charge of −0.5 in the transition state for aryl oxide expulsion is based on values of $\beta_{lg} = -1.2 \pm 0.2$ for ester aminolysis[27] and is consistent with a value of $\beta_{nuc} = 0.6$ for the attack of two phenoxides on two acetylpyridinium ions in the reverse direction.[28] The product aryl oxide ion is assigned a charge of −1.0.

As described for the carbonate reactions, the dependence of log $K^{\ddagger}$ on the pK of the two leaving groups is given by $\beta_N = 0.9 - 0.2 = 0.7$ and $\beta_O = -0.5 - 0.4 = -0.9$, and the partitioning ratio is given by eq 22.

$$\log(k_O/k_N) = \log K^{\ddagger} = -0.9\ pK_O + 0.7\ pK_N + C_t \quad (22)$$

The change in rate-determining step for the reactions of 2,4-dinitrophenyl acetate with amines occurs when the amine is 4–5 pK units more basic than the aryl oxide, as in the carbonate series.[2,29] Thus, both the kinetic and the thermodynamic partitioning are equal ($K^{\ddagger} = 1.0$, $K_3 = 1.0$) when the phenolate is 4–5 pK units less basic than the amine. Taking $\Delta pK = 4.5$, the value of C_t is −2.4. For amine and aryl oxide leaving groups with an equal pK of 5, the calculated ratio of the rate constants for aryl oxide and amine expulsion, k_O/k_N, is $10^{-3.4}$; for groups with an equal pK of 10 the ratio of k_O/k_N is $10^{-4.4}$. Comparing this with the value of $K_3 = 10^{-7.5}$, it is apparent that the kinetic partitioning is roughly half of the thermodynamic partitioning of the products.

Although this analysis is far from exact, it does permit the conclusion that the greater leaving ability from $T^{\pm}$ of amines than of aryl oxide leaving groups with a given pK reflects the greater stability of the ester compared with the cationic amide that is the immediate product of the reaction. One of the reasons for this difference is that electron donation by resonance from the oxygen atom stabilizes both the transition state for nitrogen expulsion and the ester product, whereas there is no such stabilization from the nitrogen atom. Thus, the assumption[30] that the rate constant for leaving group expulsion from $T^{\pm}$ is independent of the nature of the attacking nucleophile is not unreasonable for nitrogen nucleophiles, as indicated by the absence of a significant change in the effective charge on nitrogen in $T^{\pm}$ and in the transition state for aryl oxide expulsion, but for oxygen nucleophiles there appears to be significant assistance to leaving group expulsion by electron donation from oxygen, as manifested in the development of a partial positive charge on this atom in going from $T^{\pm}$ to the transition state for amine expulsion in the carbonate and acetate series. The "effective charges" on the alcohol oxygen atom in the reactions of esters with oxy anions and thiol anions also require significant electron donation from oxygen (but not sulfur) to aid the expulsion of alcohol and thiol anion leaving groups[8] and the value of $\beta_{nuc} = 1.3$ for the reactions of aryl oxide anions with acetylimidazole is larger than expected for the equilibrium formation of $T^{\pm}$, suggesting that electron donation from the aryl oxide assists the rate-determining expulsion of imidazole anion in this reaction also.[31]

The values of log (k_O/k_N) = log $K^{\ddagger}$ for the reactions of pyridine and 4-methylpyridine with phenyl acetate and for the corresponding reactions with p-nitrophenyl acetate are −7.5, −7.0, −4.9, and −4.4, respectively, as calculated from eq 22. The values of log K_3 for these reactions are available from the ratio of the directly measured rate constants in the forward and reverse directions and are −12.4, −11.0, −8.0, and −6.5, respectively.[2,28] Again these results suggest that the kinetic partitioning reflects the thermodynamic partitioning of the products. The values of log K_3 calculated from eq 21 are −14.7, −13.5, −10.1, and −8.7, respectively; these values are about 2 log units smaller than those obtained from observed rate constants. The difference may reflect resonance stabilization of the acetylpyridinium ion product (which is not available to acylated aliphatic amines), solvation effects, or error. It must be emphasized that the equations given here, while useful for estimating the magnitude and direction of substituent effects over a large range of reactivity, are no more than a crude approximation to a quantitative treatment.

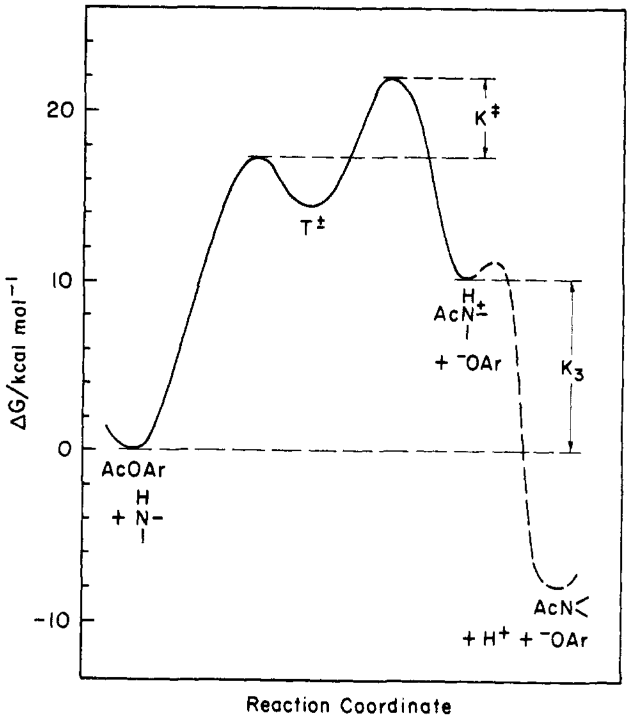


Figure 5. Semiquantitative reaction coordinate diagram for the aminolysis of an ester with $pK_{nuc} = pK_{lg} = 5.0$, to show the relationship between the Gibbs free energy differences of the two transition states ($K^{\ddagger}$) and the two ground states (K_3). The dashed line on the right refers to proton loss from an N-protonated amide product.

The structure-reactivity behavior of the acetate esters is generally similar to, although not identical with, that of the carbonate esters. The calculated values of log (k_O/k_N) for the reactions of quinuclidine with 2,4-dinitrophenyl, p-nitrophenyl, and phenyl acetates of 1.0, −1.8, and −4.4, respectively, are similar to those for the corresponding carbonate esters of 1.6, −1.7, and −5.0 and may be compared with values of 0.4, −1.4, and −3.4 calculated for acetates from a correlation based on the N^+ parameter for nucleophilic reactivity.[30] The fact that the structure-reactivity behavior of primary, secondary, and tertiary amines is almost identical in their uncatalyzed reactions with phenyl acetates[2] shows that the proton is not removed from the attacking amine in the transition state or immediate product and that this analysis is applicable to the different classes of amine.

A semiquantitative reaction coordinate diagram for the aminolysis of an acetate ester with an amine and aryl oxide of pK = 5, based on the estimates reported here and elsewhere,[2,4] is shown in Figure 5. The Gibbs free energy differences for $K^{\ddagger}$ and K_3 are indicated, showing how the kinetic and thermodynamic partitioning are related. In the case of primary and secondary amines the initial cationic amide product rapidly loses a proton to give the uncharged amide in a reaction that makes the overall reaction strongly exergonic.

References and Notes

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(2) W. P. Jencks and M. Gilchrist, *J. Am. Chem. Soc.*, **90,** 2622 (1968).

(3) A. Satterthwait and W. P. Jencks, *J. Am. Chem. Soc.*, **96,** 7018 (1974).

(4) A. Satterthwait and W. P. Jencks, *J. Am. Chem. Soc.*, **96,** 7031 (1974).

(5) G. G. Smith and B. Kösters, *Chem. Ber.*, **93,** 2400 (1960).

(6) T. C. Bruice, A. Donzel, R. W. Huffman, and A. R. Butler, *J. Am. Chem. Soc.*, **89,** 2106 (1967).

(7) J. F. Kirsch and W. P. Jencks, *J. Am. Chem. Soc.*, **86,** 837 (1964).

(8) D. J. Hupe and W. P. Jencks, *J. Am. Chem. Soc.*, **99,** 451 (1977).

(9) J. M. Sayer and W. P. Jencks, *J. Am. Chem. Soc.*, **99,** 464 (1977).

(10) P. M. Bond, E. A. Castro, and R. B. Moodie, *J. Chem. Soc., Perkin Trans. 2*, 68 (1976).

(11) S. Osterman-Golkar, L. Ehrenberg, and F. Solymosy, *Acta Chem. Scand.*, **B28,** 215 (1974).

(12) An effective charge of 0.8 has been assigned to the nitrogen atom in the intermediate $T^{\pm}$ formed from amines and aromatic aldehydes; this value is below 1.0 because of the electron-donating effect of the negative charge on the oxygen atom of $T^{\pm}$, as modified by a falloff factor of 0.2 for transmission to the nitrogen atom.[13] However, in carbonates this electron-donating effect is offset by the electron-withdrawing effect of the two aryloxy groups so that the effective charge is expected to equal the formal charge of +1.0 on nitrogen (two phenoxy groups are expected to decrease the pK of $T^{\pm}$ by $2\ \sigma_I\rho_I = 2 \times 0.38 \times 8.4 = 7.4$ units, compared with an increase in pK of 4.7 units for the negative charge on oxygen).[13-15] A value of $\beta_{nuc} = 1.08$ has been reported for the general base catalyzed aminolysis of phenyl acetates,[6] which is believed to involve the equilibrium formation of $T^{\pm}$ followed by proton transfer from $T^{\pm}$ to a second molecule of amine.[3]

(13) J. M. Sayer and W. P. Jencks, *J. Am. Chem. Soc.*, **95,** 5637 (1973).

(14) J. P. Fox and W. P. Jencks, *J. Am. Chem. Soc.*, **96,** 1436 (1974).

(15) C. D. Ritchie and W. F. Sager, *Prog. Phys. Org. Chem.*, **2,** 323 (1964).

(16) A. R. Fersht and W. P. Jencks, *J. Am. Chem. Soc.*, **92,** 5432 (1970).

(17) A. R. Fersht and Y. Requena, *J. Am. Chem. Soc.*, **93,** 3499 (1971); A. R. Fersht, *ibid.*, **93,** 3504 (1971).

(18) W. P. Jencks, B. Schaffhausen, K. Tornheim, and H. White, *J. Am. Chem. Soc.*, **93,** 3917 (1971).

(19) A correction of 0.12 log units for log k_b was estimated from the negative deviation of 0.12 units in the value of log k_b for the reaction of 3-quinuclidinone with 2,4-dinitrophenyl acetate below the line of slope −1.3 that describes log k_b (Figure 3); k_b was calculated from k_{obsd} and the partitioning ratio in the following paper.[20] The change in rate-determining step for the 2,4-dinitrophenyl ester, based on the data in Figure 2 and the following paper,[20] occurs with a ΔpK of 3.53 units, 0.26 units smaller than the value of $\Delta pK = 3.79$ calculated from eq 11 (see later). This shift is a measure of an additional rate-retarding effect of the *o*-nitro group under conditions of rate-determining amine attack and, since $\beta_{nuc} = 1.0$ for k_b, the correction for log k_1 is $0.12 + 0.26 = 0.38$ log units. These corrections were applied to k_{obsd} based on eq 5 and the experimental partitioning ratios.[20]

(20) M. J. Gresser and W. P. Jencks, *J. Am. Chem. Soc.*, following paper in this issue.

(21) A. R. Butler, I. H. Robertson, and R. Bacaloglu, *J. Chem. Soc., Perkin Trans. 2*, 1733 (1974). The value of $\beta_{1g} = -0.21$ is the ratio of the ρ values of 0.47 for log k and −2.2 for the pK of substituted phenols (G. H. Parsons and C. H. Rochester, *J. Chem. Soc., Faraday Trans. 1*, **71,** 1058 (1975)). There is evidence that the reaction of pyridine with chloroformates involves rate-determining attack.[10]

(22) C. K. Sauers, W. P. Jencks, and S. Groh, *J. Am. Chem. Soc.*, **97,** 5546 (1975).

(23) J. Gerstein and W. P. Jencks, *J. Am. Chem. Soc.*, **86,** 4655 (1964).

(24) The rate constants for the reaction of piperidine and morpholine with succinic anhydride in 10% dioxane (W. E. Hall, T. Higuchi, I. H. Pitman, and K. Uekama, *J. Am. Chem. Soc.*, **94,** 8153 (1972)) give a value of $\beta_{nuc} = 0.19$; for the reaction of substituted anilines $\beta = 0.78$.

(25) The values of $\beta_{eq} = 1.6$ for product formation and $\beta_{1g} = -0.6$ for the attack of phenolate and *p*-nitrophenolate ions on two acetylpyridinium compounds are consistent with the value of $\beta_{nuc} = 0.9 \pm 0.1$ for pyridine attack in the reverse direction. M. Novak and G. M. Loudon (*J. Am. Chem. Soc.*, **98,** 3591 (1976)) have reported $\beta_{nuc} = 1.1$ for the aminolysis of an enol acetate.

(26) S. L. Johnson, *Adv. Phys. Org. Chem.*, **5,** 237 (1967).

(27) Values of β_{1g} (number of points) were calculated from published rate constants for the aminolysis of substituted phenyl esters, excluding *p*-NO_2– and *p*-CH_2CO–: piperidine, −1.33 (2); morpholine, −1.0 (2); glycine ethyl ester, −1.15 (3) (L. do Amaral, K. Koehler, D. Bartenbach, T. Pletcher, and E. H. Cordes, *J. Am. Chem. Soc.*, **89,** 3537 (1967)); aziridines, −1.20 ± 0.05 (5);[6] ammonia −1.14 (4) (T. C. Bruice and M. F. Mayahi, *ibid.*, **82,** 3067 (1960)); hydrazine, −1.4 (4) (T. C. Bruice and S. J. Benkovic, *ibid.*, **86,** 418 (1964)); trimethylamine, −1.03 (3) (T. C. Bruice and S. J. Benkovic, *ibid.*, **85,** 1 (1963)).

(28) A. R. Fersht and W. P. Jencks, *J. Am. Chem. Soc.*, **92,** 5442 (1970).

(29) The break occurs at $pK_N - pK_O = 4.5 \pm 0.1$ units; if the 2,4-dinitrophenyl group shows the same deviation for acetate esters as for carbonate esters, this value is too small by ~0.26 units.

(30) C. D. Ritchie, *J. Am. Chem. Soc.*, **97,** 1170 (1975).

(31) D. G. Oakenfull and W. P. Jencks, *J. Am. Chem. Soc.*, **93,** 178 (1971).

Ester Aminolysis. Partitioning of the Tetrahedral Addition Intermediate, $T^{\pm}$, and the Relative Leaving Ability of Nitrogen and Oxygen[1]

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Abstract. The tetrahedral addition intermediate $T^{\pm}$ that is presumably formed in the aminolysis of unsymmetrical carbonate esters was generated from two different reactions: (a) reaction of an aryl chloroformate with a tertiary amine followed by addition of phenoxide ion and (b) reaction of a symmetrical bis(aryl) carbonate with amine followed by trapping with phenoxide ion. The partitioning between amine and aryl oxide expulsion is the same when $T^{\pm}$ is generated by these two paths. It also agrees with the partitioning estimated from kinetic data, confirming that the nonlinear Brønsted-type plot for aminolysis represents a change in rate-determining step from amine attack to aryl oxide expulsion. Equal partitioning with the 3,4-dinitrophenoxide leaving group occurs with amines that are 4.4 pK units more basic. The results provide evidence that $T^{\pm}$ is a discrete intermediate with a lifetime that is adequate for equilibration of solvation and rotation around the central carbon atom; there is no evidence that stereoelectronic control affects the partitioning ratio. The ΔpK for equal partitioning increases with increasing pK of the aryl oxide and aryl oxide expulsion is favored by increasing pK of the "acyl" substituent that is not expelled. These results suggest that electron donation by resonance from oxygen contributes significantly to leaving group expulsion. Amine expulsion is favored by addition of aprotic solvent. *N*-Methylimidazole and 4-*N*,*N*-dimethylaminopyridine are less good leaving groups than aliphatic amines of the same pK. The results show that relative leaving group ability is controlled by the electron-donating ability of the remaining group, polar substituents on the "acyl" group, solvent, and probably electrostatic effects, as well as by the pK of the leaving group.

The first problem in the analysis of the mechanism of acyl transfer reactions, such as ester aminolysis (eq 1), is to determine whether the rate-determining step is the attack of the nucleophilic reagent on the acyl compound (k_1) or the expulsion of the leaving group from a tetrahedral intermediate, $T^{\pm}$, that is formed in a rapid, equilibrium addition reaction (k_O,