Kinetics of Dialkylaminium Cation Radical Reactions: Radical Clocks, Solvent Effects, Acidity Constants, and Rate Constants for Reactions with Hydrogen Atom Donors

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Abstract: Dialkylaminium cation radical kinetics were studied directly by laser flash photolysis methods. Irradiation of *N*-hydroxypyridine-2-thione carbamates with 355-nm light gave dialkylaminyl radicals that were protonated to produce dialkylaminium cation radicals. Fragmentation of the *N*-ethyl-2,2-diphenylethylaminium cation radical (**2A**) and cyclizations of the *N*-methyl-5,5-diphenyl-4-pentenaminium cation radical (**6A**) and the *N*-methyl-6,6-diphenyl-5-hexenaminium cation radical (**9A**) were studied. In organic solvents, these reactions are several orders of magnitude faster than analogous reactions of their neutral dialkylaminyl radical precursors and faster than reactions of isostructural carbon radical analogs. In acetonitrile and in THF with carboxylic acids as proton sources, reactions of **2A** and **9A** displayed saturation kinetics from which rate constants for reaction and apparent equilibrium constants for protonation could be determined by regression analysis of observed rate constants as a function of acid normality. In ethanol with perchloric acid, **9A** was completely protonated. In aqueous solutions, the observed kinetics for reactions of **2A** and **9A** were dependent on the pH of the solutions which permitted determinations of both the rate constants for the reactions and the pK_a values for the dialkylaminium cation radicals. Large kinetic solvent effects and a counterion effect when oxalic acid was the proton source in acetonitrile were observed. Arrhenius functions for **2A** in acetonitrile and in THF and for **9A** in acetonitrile, THF, and ethanol were determined. A rate constant for the 5-*exo* cyclization of **6A** in acetonitrile at 20 °C was estimated by comparing the apparent second-order rate constants for reactions of the aminyl radical precursors to **6A** and **9A** with various carboxylic acids; with strong carboxylic acids, rate limiting protonation for the precursor to **6A** apparently occurred. Second-order rate constants at ambient temperature for reactions of octanethiol and triphenylstannane with radical **2A** were determined directly, and that for reaction of thiophenol with radical **9A** was determined by indirect methods; the stannane, with an electron rich hydrogen, reacts much more rapidly with the aminium cation radical than with carbon radicals, whereas the thiols react less rapidly.

Aminium cation radicals are useful in synthesis,[1−3] are known or purported intermediates in biological oxidations of amines by enzymes,[4−6] and are produced in chemical, electrochemical, and photochemical electron transfer reactions of amines.[7−9] Sophisticated kinetic and pK_a studies of anilinium radical cations,[10−14] trialkylaminium cation radicals,[15−17] and radical cations of NADH analogs[18,19] have been reported recently, but kinetic studies of dialkylaminium cation radical reactions are less well developed. Most of the absolute kinetic studies of these species have involved total rates of disappearance of dialkylaminium cation radicals generated by photolysis of *N*-chloroamines or *N*-nitrosoamines in acidic aqueous solutions.[20]

Advances in the development of alkyl radical kinetic scales[21] have necessarily paralleled the explosive growth in radical-based synthetic applications because most useful methods involve chain reactions wherein the desired processes must, by design, compete with side reactions. Therefore, the lack of a kinetic scale of dialkylaminium cation radical reactions is a serious limitation for synthetic applications despite the fact that useful radical-chain entries to dialkylaminyl radicals from *N*-hydroxypyridine-2-thione (PTOC) carbamates,[22−24] sulfenamides,[25−28]

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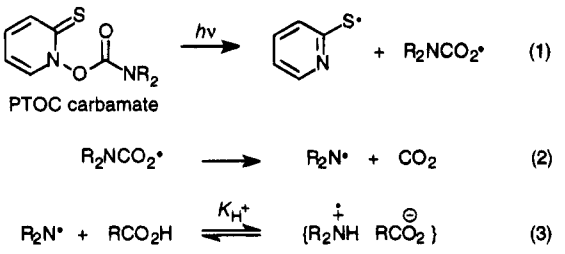
Scheme 1



and aziridines[29-31] have been developed recently which compliment the classical production of aminyl and aminium radicals from *N*-chloroamines.[1-3] The problem is further compounded by the fact that reactive, electrophilic dialkylaminium radical cations equilibrate with much less reactive, nucleophilic aminyl radicals by simple proton exchange which requires some knowledge of the acidities of the intermediates. We report here applications of a method for direct kinetic measurements of dialkylaminium cation radical reactions employing laser-flash photolysis (LFP) which establish the beginnings of a kinetic scale for dialkylaminium cation radical reactions including calibrations of dialkylaminium radical cation clocks, determinations of solvent effects on kinetics, kinetic titrations of dialkylaminium cation radicals in aqueous media, and measurements of second-order rate constants for hydrogen atom transfers to dialkylaminium cation radicals from representative trapping agents. In their paper, Wagner *et al.* report a different experimental design employing LFP and its application in the measurement of several second-order rate constants for reactions of dialkylaminium cation radicals.[32]

Results and Discussion

Method, Precursors, and Products. The method is a modification of that we have recently reported for kinetic studies of alkyl radical reactions[33-35] and aminyl radical reactions[36] (Scheme 1). An *N*-hydroxypyridine-2-thione (PTOC is an acronym for pyridine-2-thioneoxycarbonyl) carbamate[37] serves as the radical precursor. Irradiation with 355-nm light from a Nd-YAG laser cleaves the weak N–O bond to give the 2-pyridylthiyl radical and an acyloxy radical (eq 1) that decarboxylates within the duration of the 7-ns laser pulse to give a dialkylaminyl radical (eq 2). In the presence of a carboxylic acid, the dialkylaminyl radical can be protonated to give a dialkylaminium cation radical–carboxylate ion pair (eq 3). As in previous studies,[33-36] the radicals employed here were designed such that a fragmentation or cyclization reaction would give a diphenylalkyl radical product that could be monitored readily by its characteristic long wavelength absorbance at ca. 330 nm, and kinetics were measured by following the growth of this signal by UV spectroscopy with a 2 ns resolution digital oscilloscope.

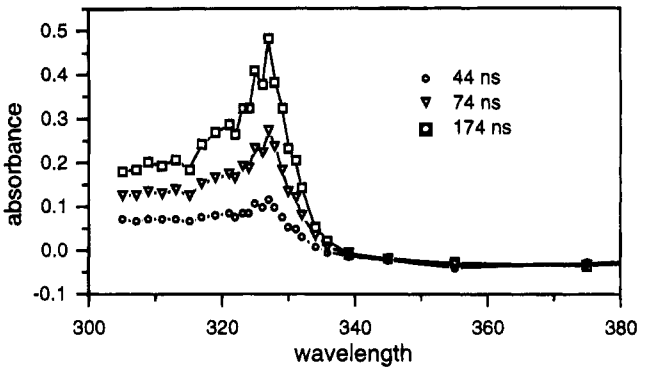
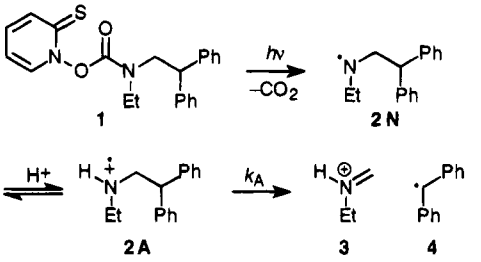


Figure 1. Time-resolved spectrum of the diphenylmethyl radical from photolysis of PTOC carbamate **1** in CH_3CN in the presence of 0.175 M CF_3CO_2H at 22 °C.

Scheme 2



The PTOC carbamates employed in this work were readily prepared from the corresponding dialkylamines by a previously described method.[23] Because these compounds are thermally unstable and sensitive to visible light, they were characterized only by NMR spectroscopy, but their precursors were known or were characterized.

Photolysis of PTOC carbamate **1** gave aminyl radical **2N** which was protonated to give aminium cation radical **2A**. Fragmentation of **2A** gave iminium ion **3** and the diphenylmethyl radical (**4**) (Scheme 2). In time-resolved LFP studies of **1** in the presence of acid, the UV spectrum of the diphenylmethyl radical[38] was observed to grow in smoothly (Figure 1). When acid was not present in LFP studies of **1**, the fragmentation of neutral aminyl radical **2N** was too slow to observe, but Bowman has reported formation of diphenylmethane in 67% yield from reaction of a closely related aminyl radical, *N*-(2,2-diphenylethyl)-3-phenylpropylaminyl, in the presence of Bu_3SnH.[27]

In reactions similar to those in Scheme 2, photolysis of PTOC carbamates **5** and **8** produced aminyl radicals **6N** and **9N** that could be protonated. A very rapid 5-*exo* cyclization of aminium cation **6A** to pyrrolidinium radical **7** was expected because (1) norphenyl analogs of **6A** (*i.e.* *N*-alkyl-4-pentenaminium ions) cyclize efficiently,[1-3,23] (2) diphenyl substitution on the terminus of the double bond results in about a two order of magnitude acceleration in 5-*exo* cyclizations of carbon radicals,[33-35] and (3) neutral aminyl radical **6N** has already been found to cyclize to the neutral (2-pyrrolidinyl)diphenylmethyl radical fast enough to be observed in LFP studies.[36] In LFP studies of PTOC

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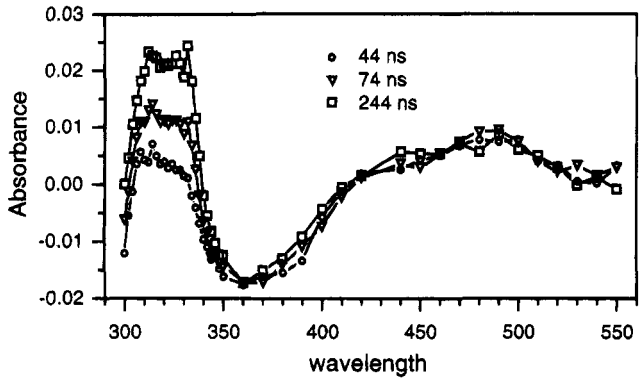
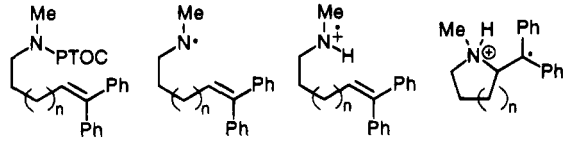


Figure 2. Time-resolved spectrum from photolysis of PTOC carbamate **8** in CH_3CN in the presence of 0.01 M CF_3CO_2H at 20 °C. The diphenylalkyl radical product (**10**) has λ_{max} at ca. 325 nm. The 2-pyridylthiyl radical has λ_{max} at ca. 490 nm; note that it is formed instantly and does not decay noticeably on the time scale of our studies.

carbamate **5** in the presence of an acid, the UV spectrum of a diphenylalkyl radical was produced quite rapidly. When PTOC carbamate **5** was allowed to react in acetonitrile in the presence of oxalic acid and thiophenol, *N*-methyl-2-(diphenylmethyl)-pyrrolidine was isolated in 33% yield.



5: n = 1 **8**: n = 2 **6N**: n = 1 **9N**: n = 2 **6A**: n = 1 **9A**: n = 2 **7**: n = 1 **10**: n = 2

Efficient 6-*exo* cyclization of aminium cation **9A** to the distonic piperidinium cation radical **10** also was expected. LFP studies of PTOC carbamate **8** in the presence of acid showed growth of a diphenylalkyl radical (Figure 2). An authentic sample of *N*-methyl-2-(diphenylmethyl)piperidine was obtained in 73% isolated yield from reaction of PTOC **8** in THF in the presence of Bu_3SnH. This piperidine was also produced when **8** was allowed to react in CH_3CN in the presence of CF_3CO_2H in competition kinetic studies for determining the rate constant of reaction of PhSH with radical **9A** (see below).

Unimolecular Kinetics. The first point to address involves which unimolecular reactions were observed in LFP studies. Both the neutral and charged species can fragment (**2**) or cyclize (**6** and **9**) to give diphenylalkyl radicals. However, aminium cation radicals are known to be considerably more reactive than aminyl radicals.[3] In practice, the two routes to rearrangement were readily differentiated. Because LFP studies of PTOC carbamate **1** performed with no acid present showed no formation of the diphenylmethyl radical, one can state unequivocally that the fragmentation of **2N** occurs with a rate constant $< 1 \times 10^4$ s^{-1}.[39]

The aminyl radical **6N** cyclizes with a rate constant of 4×10^5 s^{-1} at 25 °C,[36] and when PTOC carbamate **8** was irradiated in LFP studies at 20 °C in solutions containing no acid, a diphenylalkyl radical signal from 6-*exo* cyclization of **9N** grew in slowly ($k < 1 \times 10^4$ s^{-1}). However, irradiation of PTOC carbamates **5** and **8** in solutions containing a carboxylic acid resulted in much more rapid formation of diphenylalkyl radical signals. In the case of PTOC carbamate **5**, the dynamic resolution of our instrument ($k > 1 \times 10^8$ s^{-1}) was exceeded even with dilute acid concentrations. For the 6-*exo* cyclization of system **9**, rate constants at room temperature in the range of $(2-8) \times 10^7$ s^{-1} ultimately were obtained in organic solvent solutions containing carboxylic acids. Thus, the aminium cation radicals **6A** and **9A** cyclize at least three orders of magnitude faster than their neutral counterparts **6N** and **9N**. If at equilibrium only 1% of the neutral aminyl radicals were protonated, the observed kinetics would be mainly from reactions of the aminium cation radicals.

Solutions of the PTOC carbamate precursors in acetonitrile and in THF in the presence of varying concentrations of carboxylic acids were studied by LFP. The kinetics of reactions of radicals **2A**, **6A**, and **9A** were observed to be dependent on the concentration and identity of carboxylic acid. For aminium cation radicals **2A** and **9A**, saturation kinetic behavior was observed. In the case of aminium cation radical **6A**, acid concentration dependent kinetics were observed at low concentrations of carboxylic acids, but the dynamic resolution of the instrument was exceeded at such low concentrations of acids that saturation kinetic behavior could not be demonstrated for this 5-*exo* cyclization reaction; that is, the rate constants for reaction of **6A** were linearly dependent on acid concentration for the accessible dynamic range of our nanosecond kinetic unit.

For cases in which saturation kinetic behavior was observed, one can interpret the data in terms of a prior equilibrium between neutral aminyl radical and protonated aminium cation radical. In this model, the protonation equilibrium in eq 3 (Scheme 1) is established with an equilibrium constant K_{H^+} defined by eq 4 where **N** represents the aminyl radical and $\mathbf{A}\cdot RCO_2^-$ denotes an aminium cation radical−carboxylate ion pair. The observed kinetics in LFP studies are the sums of the kinetics of reactions of **N** and **A** (eq 5 where F_X represents the fraction of species X), but because $k_N \ll k_A$, eq 5 reduces to eq 6. Substituting the equilibrium constant in eq 4 into eq 6 gives eq 7a which can be rewritten in the inverse form of eq 7b.

$$K_{H^+} = [\mathbf{A}\cdot RCO_2^-]/([\mathbf{N}][RCO_2H]) \quad (4)$$

$$k_{obs} = k_A F_A + k_N F_N \quad (5)$$

$$k_{obs} = k_A F_A \quad (6)$$

$$k_{obs} = k_A K_{H^+}[RCO_2H]/(1 + K_{H^+}[RCO_2H]) \quad (7a)$$

$$1/k_{obs} = 1/k_A + 1/(k_A K_{H^+}[RCO_2H]) \quad (7b)$$

The above formalism provides a convenient method for analyzing saturation kinetics by either nonlinear regression analysis according to eq 7a or the more conventional linear analysis of the inverse form in eq 7b. In practice, we consistently employed nonlinear regressions (eq 7a) in order to minimize errors due to the assumption that the aminyl radical is unreactive; the linear regression of eq 7b is strongly influenced by results at low acid concentrations.

One must note that the assumption that a protonation equilibrium is rapidly established was not verified directly in this work and, in fact, apparently was not the case in some reactions. The aminium cation radical rearrangements we studied are fast, and analysis of the data for strong carboxylic acids indicates that *deprotonation* of the aminium cation radicals by the weak carboxylate anions was only marginally competitive (and in some cases non-competitive) with these reactions. When the deprotonation reaction is marginally competitive with the follow-up reaction of the aminium cation radical, the reactions will still display saturation kinetic behavior as long as protonation is faster than rearrangement, but the apparent equilibrium constant from regression analysis of eqs 7 will not be a true

(39) The lower kinetic limit in the LFP study results from residual oxygen in degassed solutions which reacts with radicals at diffusion control.

Table 1. Kinetics of Fragmentation of Aminium Cation Radical **2A** in Acetonitrile at 22 °C[a]

acid	k_A (s^{-1})	K_{H^+} (N^{-1})	pK_a[b]
CF_3CO_2H	2.5×10^7	30	0.19
CCl_3CO_2H	2.5×10^7	26	0.70
$CHCl_2CO_2H$	3.5×10^7	11	1.48
	2.5×10^7 [c]	24	
oxalic	2.2×10^7	14	1.23
malonic	2.5×10^7 [c]	3.3	2.83
acetic	2.5×10^7 [c]	0.023	4.75

[a] Results from regression analysis via eq 7a. Temperature was 22 ± 1 °C. [b] Aqueous pK_a value of the carboxylic acid. [c] Assumed value for k_A.

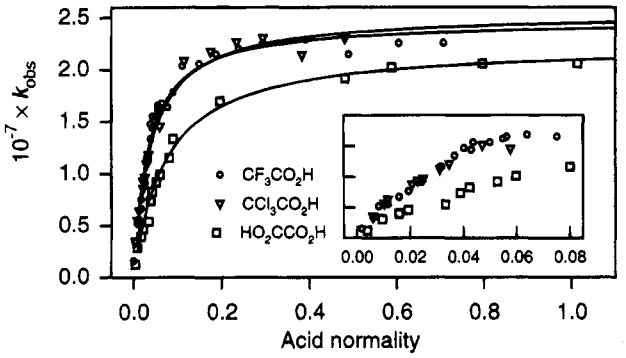


Figure 3. Observed rate constants for fragmentation of aminium cation radical **2A** in acetonitrile at 22 °C in the presence of carboxylic acids. The lines are calculated fits for the values of k_A and K_{H^+} for the respective acids listed in Table 1. The inset is an expansion of the low concentration data.

equilibrium constant but will be equal to $k_{H^+}/(k_{-H^+} + k_A)$. Because k_{H^+} and k_{-H^+} are correlated, the two cannot be solved independently by three-variable analysis via eqs 7; however, one can make some reasonable estimates regarding the values of k_{-H^+} by comparing the apparent K_{H^+} values for aminyl radicals of similar structure whose aminium cation radicals react at different rates. Because saturation kinetics are solved in terms of two variables, the precisions of the values of k_A obtained typically are poorer than those of the actual kinetic measurements (k_{obs}) which often had standard deviations of only a few percent, and considerable systematic errors are introduced when the data collected at the extremes contain errors.

When the rearrangement of the aminium cation radical is much faster than the deprotonation, saturation kinetics will not be observed. The reactions will be sequential either with rate-limiting protonation or complex kinetics due to comparable velocities of the protonation step and the subsequent rearrangement reaction. Such kinetic behavior obviously was not the case for **2A** and **9A**. For radical **6A**, we will argue below that rate-limiting protonation of **6N** occurred with strong carboxylic acids; sigmoidal kinetic traces indicative of accumulation of an intermediate were not observed.

Protonation Equilibrium Constants and Rate Constants. Kinetic studies with PTOC carbamate **1** were conducted in acetonitrile at 22 °C with varying concentrations of carboxylic acids, and the results are collected in Table 1. Figure 3 shows the results for fragmentation of aminium cation radical **2A** in acetonitrile at 22 °C with three of the carboxylic acids. For the stronger carboxylic acids in acetonitrile, nearly complete protonation was achieved as indicated by the slight changes in k_{obs} at higher acid concentrations. In these cases, the kinetic data were analyzed by nonlinear regression (eq 7a) to give best fits of k_A and K_{H^+} that are listed in Table 1. For the weaker carboxylic acids, malonic acid and acetic acid, the values of k_{obs} increased with acid concentration but did not approach a limiting value; we assumed that saturation kinetics applied and used a value of k_A at 22 °C of 2.5×10^7 s^{-1} to analyze the data via eq 7a in order to calculate apparent protonation equilibrium constants, K_{H^+}. The limited data collected at high concentrations of dichloroacetic acid resulted in apparently erroneous values for K_{H^+} and k_A, so Table 1 also contains an apparent K_{H^+} for this acid calculated with k_A set at 2.5×10^7 s^{-1}.

Three of the rate constants for fragmentation of **2A** in acetonitrile at 22 °C, those obtained with CF_3CO_2H, CCl_3CO_2H, and oxalic acid, were firmly established by conducting the reactions at high acid concentrations where protonation was nearly complete (Figure 3). These reactions apparently occur for **2A** in an ion pair. The slight decrease in the rate constant when oxalic acid was the proton source appears to be a real effect, and a similar slight rate reduction with oxalate counterion was also observed in the cyclization of **9A**. The kinetics of fragmentation of aminium cation radical **2A** displayed considerable solvent effects (see below), and it is possible that the oxalate counterion in the ion pair with **2A** presented a localized donor solvent effect leading to a slight kinetic reduction not observed with the monoprotic carboxylic acids.

Inspection of the calculated values of K_{H^+} for protonation of **2N** in acetonitrile in Table 1 shows that the protonation equilibrium constant generally increased as a function of the strength of the carboxylic acids as expected, but these values are not linearly correlated with the aqueous pK_a values of the acids. In analogy to a solvent leveling effect, we are observing a kinetic leveling effect for the stronger acids because the rearrangement reaction is competitive with deprotonation of the aminium cation radical **2A** by the weaker carboxylate ions as suggested above. That the effect was not due to traces of water in the acetonitrile was confirmed by running a series of reactions with CF_3CO_2H in "anhydrous" acetonitrile and in acetonitrile solutions containing 1% and 2% water by volume; no differences in kinetic behavior were observed. Irrespective of the origin of the leveling effect and any resulting differences between the apparent and true values of K_{H^+}, the values of k_A derived from the analyses are not affected.

The 6-*exo* cyclization of radical **9A** in acetonitrile with CF_3CO_2H or oxalic acid and in THF with CF_3CO_2H also demonstrated saturation kinetic behavior with a maximum value of k_{obs} that was within the dynamic range of a nanosecond kinetic spectrometer. The results with **9A** are presented and discussed below in the section concerning activation parameters and solvent effects, but we note here that for CF_3CO_2H in acetonitrile at 20 °C, k_A was 9×10^7 s^{-1} and K_{H^+} was 12.8 M^{-1}; that is the rate constant for rearrangement of **9A** was 3.5 times as large as that for **2A**, whereas the K_{H^+} value for **2N** was 2.5 times as large as that for **9N**. These results are consistent with our interpretation that deprotonations of the aminium cation radicals by trifluoroacetate are only marginally competitive with the rearrangement rate constants. Specifically, if the rate constants for protonation and deprotonation of the two systems are nearly equal and if the rearrangement reactions are competitive with deprotonation, then the apparent K_{H^+} value should be smaller for the system that rearranges more rapidly.

The very rapid 5-*exo* cyclization of aminium cation radical **6A** precluded studies with high concentrations of carboxylic acids because the dynamic resolution of our kinetic spectrometer was exceeded even with low concentrations of acids. In order to study this reaction, we performed matched sets of experiments with PTOC carbamates **5** and **8**. The reasoning was that the two aminyl radicals **6N** and **9N** are so similar that protonation rate constants and equilibrium constants should be the same for the two. Observed rate constants for cyclizations of radicals

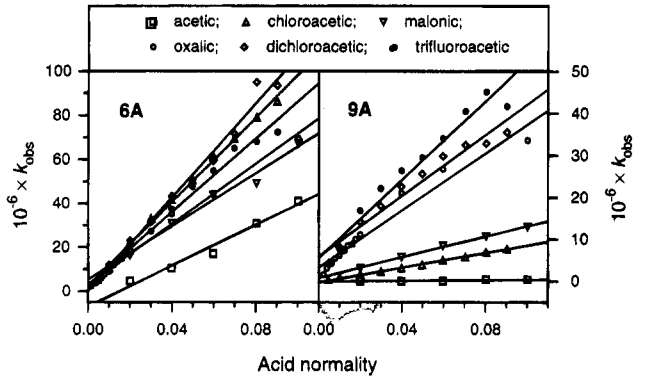


Figure 4. Observed rate constants for cyclization of aminium cation radicals **6A** and **9A** in acetonitrile at 20 °C in the presence of low concentrations of carboxylic acids. Regression lines show the best linear fits. The acetic acid concentrations are 2.5 times those shown on the X axes. Note that the two Y axes are not equal.

Table 2. Apparent Second-Order Rate Constants for Reactions of **6N** and **9N**[a]

acid	$10^{-8}k_{9N}$ (N^{-1} s^{-1})	$10^{-8}k_{6N}$ (N^{-1} s^{-1})	k_{9N}/k_{6N}
acetic acid	1.8	0.015	120
malonic acid	6.0	1.2	5.0
CH_2ClCO_2H	9.6	0.87	11.0
oxalic acid	9.2	5.0	1.8
$CHCl_2CO_2H$	10.6	6.4	1.6
CF_3CO_2H	9.3	8.5	1.1

[a] In acetonitrile at 20 °C.

6A and **9A** in acetonitrile at 20 °C in the presence of varying (but low) concentrations of several carboxylic acids were measured. At the low concentrations of acids employed in these studies, k_{obs} for both reactions were linearly dependent on the concentration of carboxylic acid (Figure 4), and apparent second-order rate constants were calculated for both systems (Table 2).

In order to analyze the data in Table 2, we first make the reasonable assumption that the true equilibrium constants K_{H^+} for protonation and the rate constants for protonation (k_{H^+}) of the very similar aminyl radicals **6N** and **9N** by a specific carboxylic acid should be nearly equal. Next, we note that, if a rapid protonation equilibrium is established, the values of k_{obs} will be proportional to $k_A K_{H^+}$. Therefore, under the conditions of rapid equilibration, the ratios of the (apparent) second-order rate constants for reactions of **6A** and **9A** at low acid concentrations for each carboxylic acid should be the same. However, this clearly is not the case; for the weak acetic acid, the cyclization of **6A** appears to be 120 times faster than that of **9A** (final column in Table 2), but the ratios of the (apparent) second-order rate constants for the 5-*exo* and 6-*exo* reactions decrease as a function of increasing strength of the acid until, ultimately, cyclization of **6A** appears to be only 1.1 times as fast as cyclization of **9A** when CF_3CO_2H is the acid.

For reactions at room temperature of several pairs of carbon radicals that are isostructural with radicals **6A** and **9A**, the 5-*exo* cyclization reactions have been found to be about 100 times faster than the 6-*exo* cyclizations.[34,35] From this fact and the determined value for k_A for **9A** in acetonitrile at 20 °C (9×10^7 s^{-1}), the rate constant for cyclization of **6A** in acetonitrile at 20 °C would be predicted to be about 1×10^{10} s^{-1}. For the acetic acid results in Table 2, one calculates that k_A for **6A** at 20 °C is 120 times greater than that of **9A** or 1.1×10^{10} s^{-1}. Thus, it would appear that the protonation equilibrium for aminyl radical **6N** is achieved or nearly achieved for acetic acid. That is, the relatively strong acetate ion deprotonated aminyl radical cation **6A** with a rate constant at least competitive with that for cyclization of **6A**. We note in passing that the approximate rate constant for cyclization of **6A** of 1×10^{10} s^{-1} at 20 °C is 25 000 times greater than that for cyclization of the neutral aminyl radical **6N**.[36]

For the strong carboxylic acids, the predicted rate constants for the cyclization of **6A** obtained by the above procedure are completely unreasonable. In fact, the value of k_A for **6A** that would be calculated from the CF_3CO_2H results is within the dynamic range of our unit and could have been measured were it correct, but at CF_3CO_2H concentrations greater than 0.1 M, the k_{obs} for **6A** was above our upper limit. The measured second-order rate constants for reactions of **6A** in the presence of the strong acids must be the actual rate constants for protonation of **6N**. They appear to converge at a rate about an order of magnitude smaller than the diffusional limit in acetonitrile (Table 2), but these values derive from the normalities of the acids and no correction for aggregation has been made.

A value for the second-order *protonation* rate constant (k_{H^+}) for CF_3CO_2H in acetonitrile at 20 °C of *ca.* 9×10^8 M^{-1} s^{-1} (and also the assertion that rate-limiting protonation occurred for **6N**) can be tested in the following manner. Assume that this value is also the rate constant for protonation of aminyl radical **9N** in the same solvent and at the same temperature. If this is the case, then the measured apparent second-order rate constant for protonation of **9N** (equal to 0.9 times that for **6N**) requires that deprotonation of **9A** by trifluoroacetate (k_{-H^+}) was 0.1 times as fast as the cyclization of **9A**. (The conclusion that deprotonation by trifluoroacetate is slow relative to the cyclization of **9A** is supported by the kinetic leveling effect in the K_{H^+} values for **2N** as discussed above.) Accordingly, the apparent K_{H^+} value for CF_3CO_2H with **9A** at 20 °C is actually equal to $k_{H^+}/(1.1k_A)$, and one can now calculate k_A for **9A** from the second-order rate constant k_{H^+} (9×10^8 M^{-1} s^{-1}) and the apparent equilibrium constant K_{H^+} (12.8 M^{-1}, see below). The value for k_A for **9A** thus calculated is 6×10^7 s^{-1} which compares quite well with the value of 9×10^7 s^{-1} obtained for the cyclization of **9A** at this temperature.

Activation Parameters and Solvent Effects. A series of studies at varied temperatures were performed with PTOC carbamate **8** in order to determine the activation parameters for cyclization of aminium cation radical **9A**. Typically, one ignores solvent effects in radical reactions, but for the positively charged aminium cation radicals, solvent effects should be important. Therefore, we conducted the studies in three distinctly different solvents: the high dielectric, weak donor solvent acetonitrile; the low dielectric, strong donor solvent THF; and the high dielectric, strong donor solvent ethanol. Rate constants for cyclization of radical **9A** were measured in acetonitrile with CF_3CO_2H and oxalic acid, in THF employing CF_3CO_2H as the acid, and in ethanol using perchloric acid. The kinetics were investigated from the lower practical limit for our unit, 0 °C, to an upper temperature determined by the point at which the kinetics exceeded the dynamic resolution of the instrument. The results are in Table 3.

In the protic solvent ethanol with perchloric acid, equilibration of the aminyl radical **9N** and aminium cation radical **9A** was rapid, and **9A** was essentially the only species present. In a series of studies conducted at 20 °C, the perchloric acid concentration was varied from 0.1 to 0.4 M, but no change in k_{obs} was found. Therefore, variable-temperature studies were performed with 0.3 M perchloric acid, and the measured values of k_{obs} gave k_A directly.

Although the values of k_{obs} for cyclization of **9A** in acetonitrile and in THF did not display a plateau region at high concentra-

Table 3. Rate and Equilibrium Constants for Reactions of **9A**

solvent	acid	temp (°C)	K_{H^+} (M^{-1})	$10^{-7}k_A$ (s^{-1})
EtOH	perchloric	0.0		2.48 ± 0.18
		10.0		3.29 ± 0.36
		20.0		4.23 ± 0.40
		30.0		4.86 ± 0.44
		40.0		5.48 ± 0.58
		50.0		7.11 ± 0.13
CH_3CN	CF_3CO_2H	0.0	14.9 ± 1.4	5.5 ± 0.2
		10.0	13.1 ± 0.8	7.3 ± 0.2
		20.0	12.8 ± 1.2	8.8 ± 0.3
CH_3CN	oxalic	−1.0	12.8 ± 0.9	4.05 ± 0.1
		9.3	12.4 ± 0.4	5.07 ± 0.06
		20.0	12.0 ± 0.5	5.97 ± 0.09
		30.4	13.1 ± 1.0	6.69 ± 0.18
		41.4	13.4 ± 0.8	7.16 ± 0.15
THF	CF_3CO_2H	0.0	7.3 ± 0.5	2.5 ± 0.1
		10.0	6.2 ± 0.7	3.1 ± 0.2
		20.0	5.7 ± 0.7	3.9 ± 0.3
		30.0	7.1 ± 0.6	4.3 ± 0.2
		40.0	5.0 ± 0.3	5.9 ± 0.2
		50.0	5.8 ± 0.5	6.1 ± 0.3

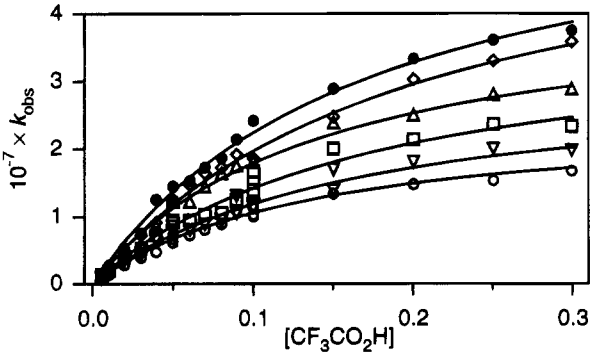


Figure 5. Observed rate constants for cyclization of radical **9A** in THF in the presence of CF_3CO_2H at 0, 10, 20, 30, 40, and 50 °C (from bottom to top). The lines are the fits calculated with the values of k_A and K_{H^+} in Table 3.

tions of acid from which k_A could be determined directly, saturation kinetic behavior was apparent, and it was clear that the protonated aminium cation radical **9A** largely predominated at the higher acid concentrations (Figure 5). The kinetic data were solved by nonlinear regression analysis to give values of k_A and K_{H^+} that are listed in Table 3. We note that the estimated rate constant for protonation of dialkylaminyl radicals by CF_3CO_2H in acetonitrile (ca. 1×10^9 M^{-1} s^{-1} at ambient temperature) discussed above provides assurance that rate-limiting protonation of **9N** did not occur.

The fragmentation of aminium cation radical **2A** also was studied at varying temperatures in acetonitrile and in THF with CF_3CO_2H (Table 4). For reactions in THF, we noted apparent phase separations in solutions with CF_3CO_2H concentrations exceeding 0.3 M. For the reactions in acetonitrile, we could employ high concentrations of acid to obtain a plateau region in the kinetics (see Figure 1), but the results of the regression analyses indicate random errors which appear to be significant from inspection of the K_{H^+} values. In principle, one can minimize the random errors by treating an entire variable-temperature data set as a whole. Specifically, if one assumes that K_{H^+} varies smoothly as a function of $1/T$, the experimental K_{H^+} values can be employed to determine this temperature-dependent behavior, and the resulting function can be used to calculate new K_{H^+} values at each temperature that are then entered as constants in the regression analyses of the data. When this procedure was employed for the CH_3CN data in Table 4, the values of k_A changed slightly, but the activation parameters

Table 4. Rate and Equilibrium Constants for Reactions of **2A** in the presence of CF_3CO_2H

solvent	temp (°C)	K_{H^+} (M^{-1})	$10^{-7}k_A$ (s^{-1})[a]
CH_3CN	8.0	38.2 ± 3.9	1.22 ± 0.03 (1.29)
	11.4	18.0 ± 2.4	1.78 ± 0.08 (1.60)
	16.0	26.7 ± 3.1	2.04 ± 0.08 (2.06)
	22.0	26.8 ± 1.7	2.60 ± 0.06 (2.84)
	38.7	12.3 ± 1.3	6.16 ± 0.14 (5.96)
THF	8.8	12.0 ± 1.0	1.60 ± 0.06
	17.3	12.7 ± 0.7	1.86 ± 0.04
	25.5	10.1 ± 0.9	2.21 ± 0.09
	33.5	9.2 ± 0.8	2.73 ± 0.10

[a] The values in parentheses for the CH_3CN data result from the assumption that K_{H^+} varies smoothly as a function of $1/T$; see text.

Table 5. Activation Parameters for Reactions of **9A** and **2A**

radical	solvent	acid	Arrhenius function[a]	k_{20} (s^{-1})[b]
9A	CH_3CN	CF_3CO_2H	$(10.7 \pm 0.6) - (3.7 \pm 0.7)/\theta$	8.9×10^7
		oxalic	$(9.5 \pm 0.3) - (2.3 \pm 0.5)/\theta$	5.7×10^7
	THF	CF_3CO_2H	$(10.0 \pm 0.3) - (3.3 \pm 0.5)/\theta$	3.8×10^7
	EtOH	perchloric	$(10.2 \pm 0.3) - (3.5 \pm 0.4)/\theta$	4.0×10^7
2A	CH_3CN	CF_3CO_2H	$(13.9 \pm 0.9) - (8.7 \pm 1.2)/\theta$	2.5×10^7
	c		$(13.8 \pm 0.3) - (8.6 \pm 0.4)/\theta$	2.4×10^7
	THF	CF_3CO_2H	$(10.1 \pm 0.4) - (3.7 \pm 0.6)/\theta$	2.0×10^7

[a] $\theta = 2.3RT$ in kcal/mol. Errors are 2σ. [b] Calculated rate constant at 20 °C. [c] Temperature-dependent function calculated from the adjusted values of k_A in Table 4; see text.

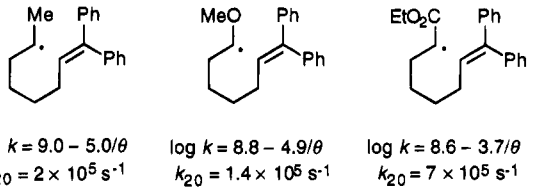


Figure 6. Temperature-dependent functions and rate constants at 20 °C for 6-*exo* cyclizations of carbon-centered radicals.

of the resulting Arrhenius function were virtually unaffected, and the standard errors in the activation parameters were reduced by a factor of 3. The corrected k_A values are listed in the final column of Table 4.

The activation parameters for the cyclization of **9A** and fragmentation of **2A** in the various solvents are listed in Table 5. The relatively narrow temperature ranges employed resulted in slightly poorer precision for the Arrhenius functions in Table 5 in comparison to those obtained for unimolecular reactions of related carbon radical systems obtained by the same method under optimal conditions.[34,35] Nevertheless, minor solvent effects are apparent in the cyclization of radical **9A**, and a dramatic solvent effect was present for the fragmentation of **2A**. In addition, we note the counterion effect for cyclization of **9A** in acetonitrile between trifluoroacetate and oxalate which leads to a rate reduction with oxalate that is similar to that observed in the fragmentation of **2A**. On the basis of the observations in fragmentation of **2A**, we believe it is likely that oxalate represents the special case in which the counterion provides an additional donor at the molecular level that would be expected to be important in the poor donor solvent acetonitrile.

The activation parameters for cyclization of aminium cation radical **9A** can be compared to those obtained for 6-*exo* cyclizations of isostructural carbon-centered radicals which are shown in Figure 6. The rate constants for cyclization of **9A** are greater than those of its carbon-radical analogs due to a reduced activation energy and a slightly more favorable entropy of activation for the aminium cation radical. The solvent effects in the cyclization of **9A** are relatively minor despite the large differences in the properties of the solvents employed. This is

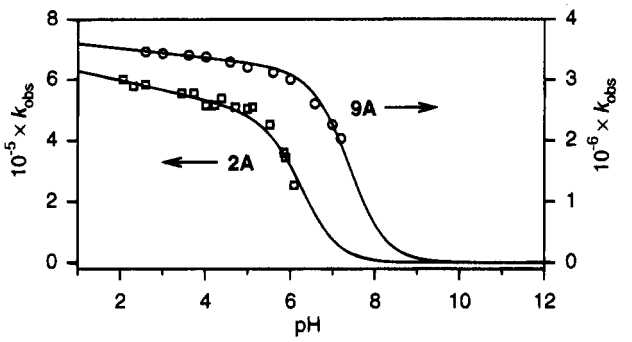


Figure 7. Observed rate constants for reactions of aminium cation radicals **2A** (in water) and **9A** (in water–acetonitrile; 71.29 (v:v)) at various pH. The lines are calculated rate constants from eq 10 using the values of k_A and pK_a listed in the text with ionic strength effect adjustments of k_A as described in the text.

perhaps not an unexpected result because in this cyclization reaction the educt radical with localized positive charge is converted into a distonic radical cation product in which charge remains localized on nitrogen. An interpretation of the trends in the solvent effects which is the same as that given below for **2A**, where the effects were much larger, is possible. The important point, however, is that one is observing the effects of charge dispersal in the transition state of the cyclization, and this must be relatively small in comparison to that in the fragmentation of **2A** (see below) as deduced from the slight differences in the activation energy terms in the three solvents. In addition, the similarities of the log *A* values for **9A** in the three solvents and the fact that the entropy of activation for cyclization of **9A** is less unfavorable than those of its analogous carbon radicals indicate that substantial solvent reorganization is not required for the cyclization of **9A**, consistent with the conclusion that little charge dispersal occurs in the transition state.

In contrast to the results with **9A**, the solvent effect on the fragmentation of radical **2A** was dramatic. In the transition state for fragmentation of **2A**, charge is being dispersed as the localized aminium cation radical progresses toward the delocalized iminium cation product **3** (Scheme 2). Thus, the educt radical cation is better stabilized relative to the transition state by the solvent with the higher dielectric constant, acetonitrile, and the activation energy for fragmentation is much higher than that in THF. However, the rate constants for fragmentation of **2A** in the two solvents are coincidentally similar at room temperature because the log *A* term in THF is considerably smaller than that in acetonitrile. Apparently, in the donor solvent THF, solvent molecules are highly organized around the aminium cation radical **2A**, and reorganization of this solvent shell in the transition state results in a negative entropy of activation despite the fact that a fragmentation is occurring. In acetonitrile, the entropy of activation is positive as one expects for a fragmentation reaction.

Acidity Constants in Aqueous Solutions. PTOC carbamate **1** was slightly soluble in water and PTOC carbamate **8** could be dissolved in an acetonitrile–water mixture. The amounts soluble were sufficient to permit LFP studies in buffered aqueous solutions between pH 2 and 7. Observed rate constants for reactions of **2A** and **9A** at various pH at 20 °C were measured (Figure 7). In basic aqueous solutions, the PTOC carbamates were destroyed as determined by monitoring the UV spectra of the solutions; apparently the activated carbamic acid derivatives were hydrolyzed by base.

The observed rate constants in aqueous solutions for both **2A** and **9A** were considerably smaller than those obtained in organic solvents. A reduction in the rate constant for fragmentation of **2A** by nearly two orders of magnitude is consistent with the results obtained for this radical in acetonitrile and in THF. Specifically, with water one has both a high dielectric constant which should increase E_a and strong donor properties that should reduce log *A*. A decrease in the rate constant for cyclization of **9A** in water–acetonitrile by about an order of magnitude from that observed in the organic solvents is perhaps unexpected, but the kinetic reduction in aqueous solution is consistent with higher activation energy found for **9A** in acetonitrile with CF_3CO_2H and the smaller log *A* terms for **9A** obtained with the donor solvents.

Because the rate constants of the rearrangement reactions of the aminium cation radicals were reduced in water relative to those in organic solvents and because the solvent is protic, there is little doubt that the protonation equilibrium for the aminyl and aminium cation radicals was rapidly established. The reactions are specific acid catalyzed, and the kinetics should be described by eq 8 where we have again assumed that reactions of the neutral aminyl radicals are unimportant. In eq 8, K_A is the acidity constant of the aminium cation radical, and k_A is the rate constant for its rearrangement reaction.

$$k_{obs} = (k_A[H^+])/(K_A + [H^+]) \quad (8)$$

According to eq 8, one should expect that plots of k_{obs} versus pH will be kinetic titration plots with a midpoint in the titration at a pH corresponding to the aminium cation radical pK_a value. In general, the plots of k_{obs} vs pH demonstrate such behavior (Figure 7), but another minor kinetic effect is apparent. Specifically, in the low-pH regions where the aminium cation radicals were essentially completely protonated, a minor decrease in k_{obs} with increasing pH is seen. This effect is due to the increasing ionic strength of the citric acid–dipotassium phosphate buffer solutions which is essentially a linear function of pH in the pH range 1 to 7.[40] Confirmation of an ionic strength effect was obtained for cyclization of **9A** by running a series of reactions at pH 3 with 0, 0.1, 0.2, 0.25, and 0.3 M NaCl; the observed rate constant decreased with increasing NaCl concentration in a manner which, although not linear, was reasonably well described by the linear function $k_{obs} = \{(3.3 \pm 0.2) - (8.8 \pm 0.9)[NaCl]\} \times 10^6\ s^{-1}$. An ionic strength effect on the kinetics of fragmentation of **2A** is highly likely as deduced from the strong solvent effect found in organic solvents for this reaction, but attempts to confirm such an effect were precluded by the low solubility of PTOC carbamate **1** in aqueous solutions containing added salts.

In order to treat the effect of ionic strength changes due to the buffer, we modified eq 8 in the following manner. For pH values below 4.5, essentially complete protonation for both **2A** and **9A** occurred. The values of k_{obs} measured in this region were solved as a linear function of k_A and pH according to eq 9 where *C* is a negative constant. The derived values for k_A and *C* from eq 9 were then incorporated into eq 8 to give eq 10, and the values of K_a were determined by regression analysis.

$$k_{obs} = k_A C(pH) \quad (9)$$

$$k_{obs} = ((k_A C(pH)[H^+])/(K_A + [H^+]) \quad (10)$$

The solid lines in Figure 7 are predicted rate constants for reactions of **2A** and **9A** calculated from eq 10 employing values of k_A and pK_a obtained by the above data analysis. For the

(40) The ionic strength is described by $\mu = 0.392 + 0.181$ (pH) over this pH range.

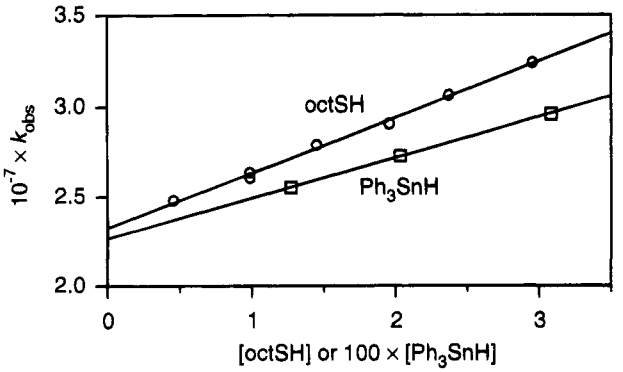


Figure 8. Observed rate constants for fragmentation of aminium cation radical **2A** in acetonitrile in the presence of 0.3 M CF_3CO_2H and octanethiol (at 24.5 °C) or triphenylstannane (at 22 °C).

fragmentation of aminium cation radical **2A** in water at 22 °C, the rate constant at zero ionic strength is $(6.6 \pm 0.4) \times 10^5$ s^{-1}, and the pK_a of **2A** is 6.3 ± 0.1. For the cyclization of radical **9A** in water–acetonitrile (71:29 (v:v)) at 20 °C, the rate constant at zero ionic strength is $(3.7 \pm 0.1) \times 10^6$ s^{-1}, and the pK_a of **9A** is 7.41 ± 0.06 (stated errors are at 2σ). We have already noted the significant rate retardations relative to those observed in organic solvents. The pK_a values in the 6.5 to 7.5 range are consistent with the pK_a values for dimethylaminium cation radical of 6.5–7.5 and 7.0 determined by ESR methods.[41,42]

Bimolecular Reactions. For planning synthetic applications of radical chain reactions, one needs to know rate constants of bimolecular processes, and hydrogen atom transfer reactions from reactive donors are among the most commonly employed in synthesis. We have briefly studied second-order reactions of aminium cation radicals with three donors, triphenylstannane, octanethiol, and thiophenol. Our objective was not to characterize the trapping reactions completely but to determine the order of reactivity of these distinctly different hydrogen atom donors with the charged aminium cation radicals and the relative magnitudes of the rate constants.

Octanethiol and triphenylstannane are essentially transparent at 330 nm, and the kinetics of reactions of aminium cation radical **2A** with these agents could be determined by direct LFP. Reactions were conducted in acetonitrile with 0.3 M CF_3CO_2H in the presence of varying amounts of the donors. At this acid concentration, the **2N**–**2A** system is about 90% protonated, and the observed kinetics give the total rate of reaction of **2A** according to eq 11 where k_A is the fragmentation rate constant, k_T is the second-order trapping rate constant, and [Y–H] is the concentration of the hydrogen atom donor. Plots of k_{obs} versus [Y–H] (Figure 8) had slopes of $(3.1 \pm 0.2) \times 10^6$ M^{-1} s^{-1} for reaction of **2A** with octanethiol in acetonitrile at 24.5 °C and $(2.2 \pm 0.1) \times 10^8$ M^{-1} s^{-1} for reaction of **2A** with triphenylstannane in acetonitrile at 22 °C. The intercepts of both plots were 2.3×10^7 s^{-1} which confirms the 90% protonation noted above. Accordingly, the slopes are multiplied by 1.1 to give rate constants for the second-order trapping reactions of 3.4×10^6 M^{-1} s^{-1} for octanethiol and 2.4×10^8 M^{-1} s^{-1} for triphenylstannane.

$$k_{obs} = 0.9(k_A + k_T[Y–H]) \quad (11)$$

Direct LFP studies with thiophenol were not possible due to the absorbance of PhSH in the region of interest in the UV, but a rate constant for reaction of this hydrogen atom donor with aminium cation radical **9A** was determined by the indirect method.[21] Reactions of PTOC carbamate **8** in acetonitrile in the presence of 0.3 M CF_3CO_2H and 0.5 to 4.1 M PhSH at 20 °C were conducted, and the product mixtures were analyzed by GC to determine the ratio of acyclic amine to piperidine product **10**. A plot of this ratio against [PhSH] (Figure 9 and eq 12) gave a value of k_T/k_A of (0.49 ± 0.04) M^{-1} which can be combined with the value of k_A for **9A** in acetonitrile at 20 °C to give a value for k_T of $(4.3 \pm 0.7) \times 10^7$ M^{-1} s^{-1} for reaction of PhSH with **9A** at 20 °C.

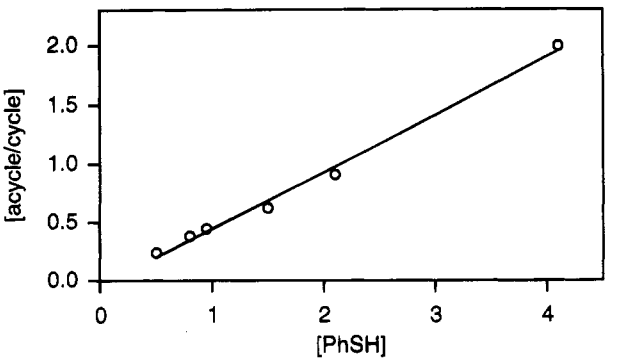


Figure 9. Ratios of acyclic to cyclic products formed from reactions of aminium cation radical **9A** in acetonitrile in the presence of 0.3 M CF_3CO_2H and thiophenol.

Table 6. Rate Constants for Reactions of Hydrogen Atom Donors with Radicals at Ambient Temperature[a]

donor	$RCH_2^•$	$R_2N^•$	$R_2HN^{•+}$
PhSH	1.4×10^8	1×10^8	4.3×10^7
t-BuSH	8×10^6	5.6×10^6	
$C_8H_{17}SH$			3.4×10^6
Ph_3SnH	5×10^6		2.4×10^8
Bu_3SnH	2.4×10^6	1×10^5	

[a] Rate constants in units of M^{-1} s^{-1}. See text for references.

$$k_T/k_A = ([\text{amine}]/[\mathbf{10}])(1/[\text{PhSH}]) \quad (12)$$

The rate constants for reactions of the hydrogen atom donors with dialkylaminium cation radicals are listed in Table 6 along with those for reactions of the same or similar donors with other radicals. The rate constants for reactions of alkyl radicals have been compiled previously.[21] Those for reactions of dialkylaminyl radicals with *t*-BuSH and with Bu_3SnH were known,[36] and a crude rate constant for reaction of PhSH with dialkylaminyl radical **6N** was determined by competition kinetics using the reported rate constant for cyclization of this radical.[36] The trends in the kinetics are readily rationalized by considering the X–H bond energies of the donors and the character of the radicals. For example, PhSH consistently reacts faster than RSH with any radical as one would predict from bond energies. Dialkylaminyl radicals are nucleophilic, and a favorable polarization in the transition states for reactions of these radicals with the electron deficient hydrogen donor thiols results in rate constants similar to those for the alkyl radicals, which might be considered "neutral", but a marked reduction in the rate constant for reaction with the electron rich hydrogen in tin hydride in comparison to that for the alkyl radical. The dialkylaminium cation radicals are electrophilic and display the opposite trend; reaction with the electron rich hydrogen atom of the tin hydride apparently enjoys a favorable polarization in the transition state and is much faster than the similar alkyl radical reaction, but the reactions with the thiols are now slower than those of alkyl radicals despite the generally increased reactivity of the aminium versus the carbon radical systems. Similar, although attenuated, kinetic effects have been observed

(41) Fessenden, R. W.; Neta, P. *J. Phys. Chem.* **1972**, *76*, 2857–2859.
(42) See also the discussion in ref 8.

Table 7. Rate Constants for Reactions of Dialkylaminium Cation Radicals at 20 °C

radical	solvent	k_{20} (s^{-1})
2A	CH_3CN	2.5×10^7
	CH_3CN (with oxalate)	2.2×10^7
	THF	2.0×10^7
	water[a]	6×10^5
9A	CH_3CN	9×10^7
	CH_3CH (with oxalate)	5.7×10^7
	THF	3.8×10^7
	EtOH	4.0×10^7
	water–CH_3CN (79:21)[a]	3.7×10^6
6A	CH_3CN	1×10^{10}

[a] At zero ionic strength.

previously in reactions of "nucleophilic" α-methoxy and "electrophilic" α-ethoxycarbonyl radicals with hydrogen atom donors.[34,35] One obvious conclusion from the results in Table 6 is that one should attempt to employ thiols rather than tin hydrides in a chain reaction of a dialkylaminium cation radical in which the desired conversion involves an N–C bond forming reaction followed by a hydrogen atom transfer step.

Conclusion

The rate constants for reactions of dialkylaminium cation radicals at 20 °C are collected in Tables 6 and 7. They provide a foundation for a kinetic scale for dialkylaminium cation radical reactions that can be elaborated by indirect kinetic methods as has been accomplished with alkyl radicals[21] and as is demonstrated here by the determination of the rate constant for reaction of PhSH with **9A**. Dialkylaminium cation radicals were known to be more reactive than their neutral dialkylaminyl radical counterparts, and the kinetic values provide quantitative data supporting the previous qualitative observations. Specifically, the dialkylaminium cation radicals appear to react more than 4 orders of magnitude faster in cyclization reactions conducted in organic solvents. However, unlike the case with simple alkyl radicals, the kinetics of dialkylaminium cation radicals can be highly sensitive to solvent effects.

One important conclusion from the studies in this work is that the use of dialkylaminium cation radical reactions as qualitative mechanistic probes or quantitative radical clocks in enzyme-catalyzed reactions will be complicated for two reasons. Because the pK_a values of the dialkylaminium cation radicals are about 7 and the reactivities of the aminyl and aminium cation radicals differ by several orders of magnitude, the local pH within an enzyme's active site will strongly influence the overall reaction rates of a given system. Even if the local pH in the enzyme is known, the solvent effects on the kinetics of the aminium cation radicals will add a further level of complexity to any studies. Thus, meaningful applications of mechanistic probe or quantitative radical clock precursors as substrates in enzyme-catalyzed oxidation reactions might require both characterization of the probe systems' acidity and rate constants and information about the local environment in an enzyme's active site. In principle, however, the sensitivity of the kinetics of a particular aminyl/aminium system to acidity and solvent character might be used to explore the details of an enzyme's active site when structural information is not available.

Experimental Section

Preparations of PTOC carbamates were accomplished by the method of Newcomb *et al.*[23,24] The crude PTOC carbamates were purified by silica gel chromatography and characterized by NMR spectroscopy. The NMR spectra of PTOC carbamates are complicated due to the presence of slowly interconverting conformations.[24] The supporting information contains the synthetic details for preparation of the requisite amines.

1-[(Ethyl(2,2-diphenylethyl)carbamoyl)oxy]-2(1*H*)-pyridinethione (1) was prepared from 0.9 g (4 mmol) of *N*-ethyl-2,2-diphenylethylamine, 0.84 g (4.5 mmol) of 1-oxa-2-oxo-3-thiaindolizinium chloride,[43] and 0.56 mL of Et_3N in 40 mL of benzene. Crude PTOC carbamate **1** was purified by silica gel chromatography (hexanes–ethyl acetate; 60:40 (v:v)) which gave **1** (0.96 g, 2.5 mmol, 63%) as a gummy oil that was >95% pure by NMR spectroscopy. ^1H NMR: δ 1 (m, 3 H), 3 (q, J = 7.2 Hz, 1.2 H), 3.1 (q, J = 6.9 Hz, 0.8 H), 3.9 (d, J = 7.8 Hz, 0.9 H), 4 (d, J = 7.8 Hz, 1.1 H), 4.4 (t, J = 7.8 Hz, 0.45 H), 4.5 (t, J = 7.8 Hz, 0.55 H), 6.4 (m, 1 H), 7–7.3 (m, 11 H), 7.4 (bm, 0.7 H), 7.5 (m, 1.3 H). ^{13}C NMR: δ 12.083, 13,342, 43.037, 44.208, 48.753, 49.165, 52.033, 53.656, 101.833, 112.123, 126.586, 126.862, 128.075, 128.160, 128.366, 133.398, 136.633, 136.760, 138.305, 138.434, 141.398, 141.793, 150.964, 151.636, 175.894, 175.988.

1-[(Methyl(5,5-diphenyl-4-pentenyl)carbamoyl)oxy]-2(1*H*)-pyridinethione (5) was prepared from 2.51 g (10 mmol) of *N*-methyl-5,5-diphenyl-4-pentenamine, 2.10 g (11 mmol) of 1-oxa-2-oxo-3-thiaindolizinium chloride, and 1.10 g (10 mmol) of Et_3N in 60 mL of benzene. The crude product was purified by column chromatography on silica gel (hexanes–ethyl acetate; 60:40 (v:v)) to give **5** as a yellow gummy oil (2.74 g, 6.8 mmol, 68%) that was >95% pure by NMR spectroscopy. ^1H NMR: δ 1.75 (pent, 1.2 H), 1.9 (pent, 0.8 H), 2.2 (pent, 2 H), 3.0 (s, 1.2 H), 3.17 (s, 1.8 H), 3.35 (t, J = 6.6 Hz, 1.2 H), 3.5 (t, J = 6.6 Hz, 0.8 H), 6.05 (t, J = 7.2 Hz, 1 H), 6.6 (t, J = 6.9 Hz, 1 H), 7.1–7.4 (m, 11 H), 7.5 (m, 1 H), 7.6 (d, J = 9.0 Hz, 1 H). ^{13}C NMR: δ 26.59, 26.79, 26.98, 27.86, 34.36, 35.64, 49.01, 50.05, 112.13, 126.80, 126.99, 127.90, 128.07, 129.60, 133.43, 136.66, 136.77, 138.51, 139.70, 142.21, 142.25, 151.35, 176.10.

1-[(Methyl(6,6-diphenyl-5-hexenyl)carbamoyl)oxy]-2-(1*H*)-pyridinethione (8) was prepared from 2.91 g (11.0 mmol) of *N*-methyl-6,6-diphenyl-5-hexenamine, 2.29 g (12 mmol) of 1-oxa-2-oxo-3-thiaindolizinium chloride, and 1.5 mL of Et_3N in 60 mL of benzene. The crude product was purified by column chromatography on silica gel (hexanes–ethyl acetate; 60:40 (v:v) to give **8** as a yellow gummy oil (2.34 g, 5.69 mmol, 51%) that was >95% pure by NMR spectroscopy. ^1H NMR: δ 1.4–1.6 (m, 4 H), 2.1 (m, 2 H), 2.9 (s, 1.2 H), 3 (s, 1.8 H), 3.2 (t, J = 6.9 H, 1.2 Hz), 3.4 (t, J = 7.5 Hz, 0.8 H), 6 (t, J = 7.5 Hz, 1 H), 6.5 (m, 1 H), 7–7.3 (m, 11 H), 7.5 (d, J = 6.9 Hz, 0.4 H), 7.55 (d, J = 9.3 Hz, 1.6 H). ^{13}C NMR: δ 26.54, 26.72, 26.82, 27.30, 29.21, 34.38, 35.74, 49.35, 50.35, 112.16, 126.73, 126.81, 127.08, 127.97, 128.08, 129.06, 129.23, 129.75, 133.44, 136.86, 136.95, 138.62, 139.97, 141.85, 142.50, 151.54, 175.99.

***N*-Methyl-2-(diphenylmethyl)pyrrolidine.** A solution of oxalic acid (6.34 g, 0.05 mol) in acetonitrile (200 mL) in a 500-mL 3-necked flask was deoxygenated for 20 min with a flow of nitrogen. Thiophenol (2.0 mL, 0.019 mol) was added. Nitrogen gas was bubbled briefly through a solution of PTOC carbamate **5** (1.05 g, 0.0026 mol) in acetonitrile (50 mL). The solution of PTOC carbamate was then added to the solution of oxalic acid and thiophenol. The resulting solution was irradiated for 2 h with a 150 W tungsten filament lamp. The solution was washed with NaOH (20%) and saturated aqueous NaCl solutions and dried over $MgSO_4$. After removal of solvent at reduced pressure, crude product was acidified with 10% HCl. The aqueous layer was washed with Et_2O, basified with 20% NaOH solution, and extracted with Et_2O. The Et_2O extracts were dried over $MgSO_4$, and solvent was removed at reduced pressure to give 0.386 g of a 92:8 mixture of cyclic:acyclic amines in 65% total yield. Chromatography on alumina (90:10, hexane–ethyl acetate (v:v) gave the pure amine (0.216 g, 33%). ^1H NMR (500 MHz): δ 1.55 (m, 1 H), 1.64 (m, 2 H), 1.90 (dq, J = 12.3, 8.0 Hz, 1 H), 2.30 (dt, J = 9.1, 7.7 Hz, 1 H), 3.10 (m, 2 H), 3.94 (d, J = 8.3 Hz, 1 H), 7.2 to 7.4 (m, 10 H). ^{13}C NMR (75 MHz): δ 22.71, 31.09, 42.74, 57.65, 58.53, 69.05, 126.01, 126.19, 128.19, 128.36, 128.54, 144.13. Mass spectrum: *m/e* (rel intensity) 250 (0.3), 167 (2.2), 84 (100). HRMS for $(M - 1)^+$: calcd for $C_{18}H_{20}N$, 250.1595; found, 250.1599.

***N*-Methyl-2-(diphenylmethyl)piperidine.** A dry round-bottomed flask under nitrogen was wrapped in aluminum foil and then placed in

(43) Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron* **1985**, *41*, 3901–3924.

a −78 °C bath. A solution of PTOC carbamate **8** (0.1815 g, 0.434 mmol) in 25 mL of THF was transferred *via* syringe into the reaction flask, followed by a solution of Bu_3SnH (0.1515 g, 0.52 mmol) in 20 mL of THF. The reaction then was allowed to equilibrate at room temperature. The aluminum foil was removed, and the reaction was irradiated with a 150 W tungsten filament lamp. After 1 h a solution of I_2 in CH_2Cl_2 was added until a red color persisted. The organic solution was then washed with an aqueous solution of KF and a 1 M aqueous solution of $Na_2S_2O_3$. The ethereal layer was acidified with 50 mL of 10% aqueous HCl, and the aqueous layer was separated and neutralized with 10% aqueous NaOH. Diethyl ether (50 mL) was added, and the organic layer was separated, washed with brine, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the product was purified by column chromatography on neutral alumina (95:5, hexanes−ethyl acetate) to give *N*-methyl-2-(diphenylmethyl)piperidine as a light yellow oil (0.082 g, 0.308 mmol, 73%). ^{1}H NMR: δ 1.3−1.8 (m, 6 H), 2.3 (s, 3 H), 2.4 (m, 1 H), 2.9 (m, 1 H), 3 (dt, J = 3.3 Hz, 8.7, 1 H), 4 (d, J = 9 Hz, 1 H), 7−7.3 (m, 10 H). ^{13}H NMR: δ 22.20, 24.45, 24.92, 39.77, 54.57, 55.77, 64.60, 125.96, 126.00, 128.25, 128.30, 128.42, 129.84, 143.42, 143.94. Mass spectrum: *m/e* (rel intensity) 265 (0.2), 264 (0.8), 165 (8), 98 (100), 70 (10). HRMS for $(M - 1)^+$: calcd for $C_{19}H_{22}N$, 264.1752; found, 264.1746.

Kinetic Methods. Direct kinetic studies were performed with an Applied Photophysics LK-50 kinetic spectrometer employing a Spectron Nd-YAG laser using the third harmonic (355 nm) of the laser for radical production from the PTOC carbamates. All studies involved solutions that flowed from a temperature regulated addition funnel through a flow cell contained in a temperature regulated block. Temperatures were measured with a thermocouple contained in the flowing stream immediately above the irradiation zone of the cell. The method has been described in detail.[33−35] The kinetic results were supplied to the referees and are available from the authors upon request.

Indirect kinetic studies involved conventional competition experiments.[21] Reactions of PTOC carbamate **8** and an internal standard of pentadecane in acetonitrile with 0.3 M CF_3CO_2H and varying concentrations of PhSH were conducted in a temperature regulated bath held at 20 °C. The reaction mixtures were irradiated with a 150 W tungsten filament lamp at a distance of 0.5 m for ca. 60 min. The reaction mixtures were analyzed on an FID equipped GC employing a wide-bore DB-5 capillary column (J&W Scientific); yields were calculated with response factors measured with authentic samples. The identity of the products was confirmed by GCMS (Carbowax) by comparison of the retention times and mass spectra to those of authentic samples.

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Supporting Information Available: Experimental procedures for preparation of the amine precursors to PTOC carbamates **1**, **5**, and **8** (4 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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