A Curve-Crossing Model for Oxidative Decarboxylation. Kinetics of Anilino Carboxylate Fragmentations

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The kinetics of oxidative decarboxylation of a series of anilino carboxylates have been measured. These compounds find use in the recently described two-electron sensitization process for silver halide photography, and control of their fragmentation kinetics is essential to be useful in this application. The measured rate constants vary over 5 orders of magnitude. The decarboxylation rate constants decrease substantially with increasing solvent polarity, an effect that results in misleading Arrhenius analysis of temperature effect measurements. The rate constants also depend on the product radical stability and the oxidation potential of the aniline precursor. A valence bond curve-crossing model is proposed that provides a combined picture of this and the related decarboxylation of acyloxy radicals. The model is able to explain the substitution and solvent polarity effects. Consistent with this model, manipulation of solvation via changes in substituents (hydrophilic vs hydrophobic) around the reaction site is shown to strongly influence the decarboxylation rate constants. In this way, the decarboxylation rate constants can be altered by nearly 3 orders of magnitude at constant solvent polarity and precursor oxidation potential.

Introduction

Decarboxylation reactions of organic radical cations have been widely studied in mechanistic and synthetic chemistry[1] and have been implicated in several important biological processes (reaction A, Scheme 1).[2] A closely related process is the electrochemical Kolbe reaction, where oxidation of (usually) an aliphatic carboxylate leads to an acyloxy radical that decarboxylates to form an alkyl radical (reaction B, Scheme 1).[3] Also related is the decarboxylation reaction of acyloxy radicals (e.g., reaction C, Scheme 1), which plays a central role in the chemistry of peroxides.[4]

Oxidative decarboxylation also represents an example of a photoinduced electron transfer/fragmentation reaction, which have proved to be the most technologically important processes in electron-transfer photochemistry.[5] In this regard, we recently reported a new technological application of electron transfer/fragmentation in silver halide photography, as part of a novel sensitization process called two-electron sensitization (TES).[6,7] The central idea behind TES is that the oxidized form of the photographic sensitizing dye (formed upon light exposure and electron transfer to silver halide[8]) further oxidizes a fragmentable electron donor (X−Y) to form $X-Y^{\bullet+}$. Cleavage of $X-Y^{\bullet+}$ yields a radical $X^{\bullet}$, which is designed to be a powerful reducing agent capable of injecting another electron into the conduction band of silver halide. In this way, two electrons are transferred per absorbed photon, thus doubling the photographic efficiency. Decarboxylation of $X-Y^{\bullet+}$ proved to be one of the most useful of the fragmentation reactions in the TES process, providing the motivation for the present work.[6,9]

An important issue in the TES process is control over the rate constant for fragmentation (decarboxylation) of the oxidized donor, $X-Y^{\bullet+}$.[6] Because of their wide importance (see above), a number of studies of the kinetics of oxidative decarboxylation and the related acyloxy radical decarboxylation have appeared, from which a number of broad generalizations can be made.[10] The rate of acyloxy radical decarboxylation depends on the stability of the radical formed in the fragmentation process and can occur with very high rate constants ($>10^{10}$ s^{-1}).[10c,j] The rate of radical cation fragmentation tends to be slower and varies considerably depending upon the structure of the aryl group and radical stability. The relationship between the acyloxy radical and radical cation decarboxylation processes has been little discussed, except by Saveant in his work delineating the mechanism of the Kolbe reaction,[11] and in some cases the difficulty in assigning the structure of the intermediate to the radical cation or acyloxy radical has been pointed-out.[12]

Despite this prior work, some confusion remains regarding the quantification of the factors that controlled the rate constants for fragmentation. For example, some of the most detailed previous work on the kinetics of radical cation decarboxylation is reported in ref 10n and p. In these papers, however, the radical cation fragmentation rate constants were reported to be both strongly[10n] and also weakly[10p] dependent upon the oxidation potential of the aryl group. Although decarboxylation of acyloxy radicals is clearly faster when more stable radicals are formed, it was reported that this was not generally the case for radical cation decarboxylation.[10p] Solvent effects had been studied in very few cases,[10e] and virtually no reports of the magnitudes of the reaction barriers are available. Thus, we initiated a quantitative study of the factors that control the rate constants for oxidative decarboxylation and sought a qualitative theoretical description that would accommodate all of the important observations and factors that control the rates. The reactions

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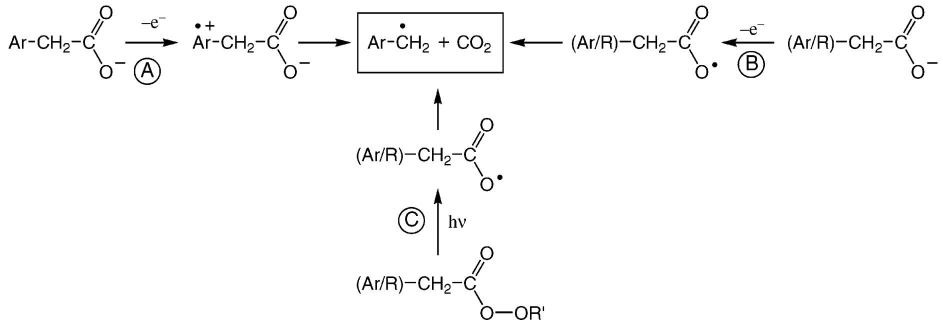
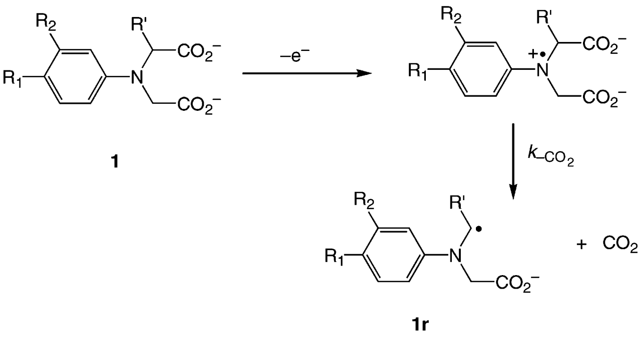
SCHEME 1



SCHEME 2



that we studied are best described as radical cation decarboxylations, but the simple theoretical description results in a combined picture of the three types of reaction shown in Scheme 1. Our goal was a comprehensive description of the factors controlling the rate of reaction, so that suitable TES donors could be designed.

Results and Discussion

To be useful in a TES application, the radicals formed upon decarboxylation must be strongly reducing. We have shown previously that α-amino radicals are appropriately reducing, which means that most useful TES donors are amines.[6] We have found bis-carboxylates of aniline derivatives of the general formula **1** (Scheme 2) to be particularly useful because of their high thermal stability and the ease of synthesis of several derivatives.

The effect of reaction exothermicity on the decarboxylation rate constant, k_{-CO_2}, was explored by varying the ring substituents R_1 and R_2. Variations in these substituents result in corresponding variations in the oxidation potential of the aniline derivative, and in turn this changes the reaction exothermicity (see ref 13 and further below). The effect of the stability of the product radical was examined by changing the side chain substituent R′. In addition to substituent effects, we also examined the effect of solvent and of temperature on the decarboxylation rate constants of the radical cations.

Determination of Rate Constants

The radical cations of the aniline derivatives, $\mathbf{1}^{\bullet+}$, were generated and characterized as described previously, from the reaction of excited 9,10-dicyanoanthracene (DCA) with a cosensitizer, biphenyl (BP), which leads to formation of free $DCA^{\bullet-}$ and $BP^{\bullet+}$ in a high yield.[6a,9b] Secondary electron transfer from **1** to $BP^{\bullet+}$ yields $\mathbf{1}^{\bullet+}$. Experiments were performed in nitrile solvents and in acetonitrile−water mixtures, and the radical cations were characterized in these solvents as described previously.[6a,9b] Representative absorption spectra are shown in Figure 1. The radical cation absorptions are somewhat red-shifted compared to the aniline radical cations from which they are derived.[14] As illustrated in the figure, the spectra also exhibit a dependence on the water content of the medium. The carboxylates are hydrogen-bonded in water, and in its absence, an intramolecular interaction with the radical cation anilino moiety may be responsible for the observed changes in the absorption spectra. Only a small amount of water is required to effect the observed spectral changes, presumably due to efficient hydration of the carboxylates, and the spectra in a 19:1 acetonitrile−water mixture are close to those in a 4:1 mixture.[15]

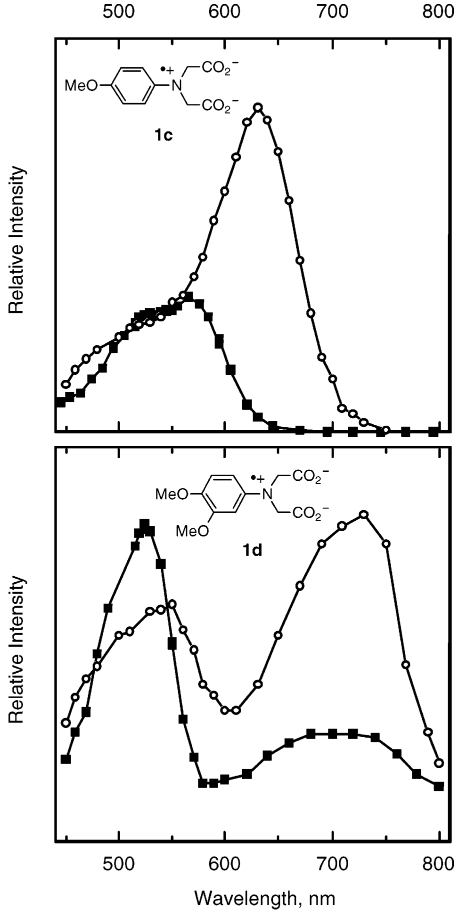
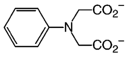
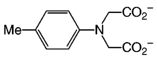
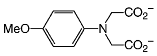
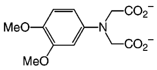
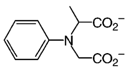
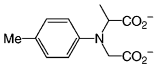
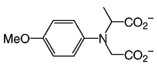
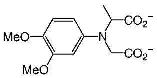


Figure 1. Transient absorption spectra of the radical cations of anilinodicarboxylates **1c** and **1d**, at room temperature in (■) 4:1 acetonitrile/water and (○) 100% acetonitrile.

Rate constants for decarboxylation of the different derivatives of $\mathbf{1}^{\bullet+}$ were obtained in conventional nanosecond transient absorption experiments, by monitoring the decay in absorbance of the radical cations as a function of time, as described in detail previously for a closely related system.[9b] In all cases the absorption decays were well-described by exponential kinetics

TABLE 1: Rate Constants (at Room Temperature), Oxidation Potentials, and Apparent Arrhenius Activation Parameters for Decarboxylation of Aniline Radical Cations in 4:1 Acetonitrile/Water

Compound		k_{-CO_2}	$(E_p)^a$	E_{ox}^b	Apparent E_a	Apparent Log A
		(s^{-1})	(V vs SCE)		(kcal/mol)	
	**1a**	1.7×10^7	*(0.535)*	0.709	8.1	13.3
	**1b**	1.6×10^6	*(0.460)*	0.604	13.7	16.3
	**1c**	9.3×10^3	*(0.375)*	0.454	19.9	18.8
	**1d**	$\sim 2 \times 10^3$	*(0.357)*	0.416	~21	~19
	**1e**	$\geq 1 \times 10^8$	*(0.500)*	≥ 0.70	[c]	[c]
	**1f**	8.1×10^6	*(0.460)*	0.625	12.9	16.4
	**1g**	9.0×10^4	*(0.355)*	0.463	16.8	17.4
	**1h**	9.7×10^3	*(0.326)*	0.405	18.9	18.0

[a] Peak potentials measured at a carbon electrode at a scan rate of 0.1 V/s in 4:1 acetonitrile/water containing 0.1 M $LiClO_4$. [b] Oxidation potentials derived from the peak potentials and the decarboxylation rate constants according to eqs 1. [c] The decarboxylation rate constant of the radical cation of compound **1e** is too high to measure accurately.

over more than two lifetimes. Competing second-order recombination with the $DCA^{\bullet-}$ was ensured to be negligible by using low pulsed laser energies, resulting in low concentrations of radical ions in solution. The reactions were assigned to decarboxylation based on the facts that the products were reducing α-amino radicals.[6] Deprotonation at the α-methylene is a possible competing reaction; however, we and others have shown elsewhere that this process occurs with pseudo-first-order rate constants that are orders of magnitude lower than those observed here.[16] Most of the experiments were performed in 4:1 acetonitrile−water. This solvent mixture was initially selected both to ensure solublization of all of the amine carboxylates and to provide an appropriate model environment for the mainly aqueous photographic environment.[6] Monitoring wavelengths around 530−630 nm were generally found to be useful for measuring the decay kinetics of the radical cations, Figure 1.

Summarized in Table 1 are the rate constants for decarboxylation measured at 22 °C in 4:1 acetonitrile−water. The results of temperature-dependent experiments included in Table 1 in the form of *apparent* activation energies and the logarithms of the preexponentials obtained from least-squares linear fits to Arrhenius plots.

Also given in Table 1 are the oxidation potentials of the donors, E_{ox}. The method by which these were obtained is described in detail elsewhere.[17a] Cyclic voltammetry of compounds with reactive radical cation such as these gives irreversible oxidation waves, from which only peak potentials were determined, E_p. Combination of such peak potentials with the measured decarboxylation rate constants, however, can provide

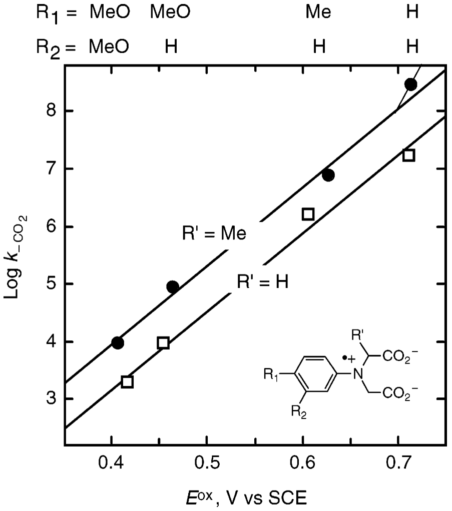


Figure 2. Plot of the logarithms of the rate constant for decarboxylation of the radical cations of anilinodicarboxylates as a function of the oxidation potential in 4:1 acetonitrile/water at room temperature for (□) aniline diacetates, **1a**-**1d**, and (●) aniline acetate-propionates, **1e**−**1h**.

thermodynamically meaningful oxidation potentials via the well-known eq 1a.[17b] Here, a is equal to $\nu F/RT$, where F is the Faraday constant, ν is the scan rate in V/s, and R and T have their usual meanings. At 22 °C and a scan rate of 0.1 V/s, eq 1a reduces to eq 1b.

$$E_{ox} = E_p + (RT/2F)\{\ln(k_{-CO_2}/a) - 1.56\} \tag{1a}$$

$$E_{ox} = E_p + 0.0127\ \{\ln(k_{-CO_2}/3.93) - 1.56\} \tag{1b}$$

Dependence of Decarboxylation Rate Constants on Reaction Energetics

As mentioned above, the dependence of the decarboxylation rate constants on the reaction energetics was examined by varying (a) the oxidation potential of the aniline derivatives, **1**, (b) the stability of the resultant radicals, **1r**, and (c) the medium polarity.

As illustrated in Figure 2, the rate constants are found to depend strongly on the oxidation potential for both the radical cations of the diacetate derivatives (R′ = H) and the acetate−propionate derivatives (R′ = Me). In both cases, the rate constants decrease by roughly 4 orders of magnitude as the oxidation potential decreases by ∼0.32 V, which compares reasonably well with the data of Candeias et al..[10n] In addition, all rate constants of the derivatives with R′ = Me are displaced by ∼0.8 on the logarithmic scale above those with R′ = H (Figure 2), i.e., are higher by an average factor of ∼6.

Shown in Figure 3 are some typical Arrhenius plots. The slopes and intercepts of these plots are given as “apparent” activation energies and preexponential factors in Table 1. Although the plots appear linear, the activation parameters are unusual in that the preexponential factors are all significantly greater than 10^{13} s^{-1}, which is much larger than normally observed for simple unimolecular reactions.[18] In addition, there appears to be a relationship between the magnitude of the apparent activation energies and the preexponential factors; see Table 1. The most reasonable explanation for the high preexponential factors is that although the Arrhenius plots appear to be linear *over the experimental temperature range*, they are actually curved, with the slope increasing with decreasing reciprocal temperature. The reactions with the higher temper-

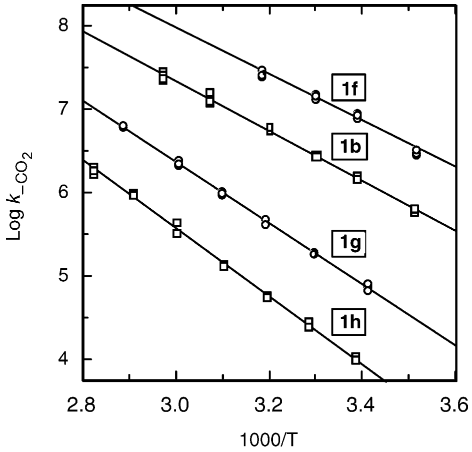


Figure 3. Arrhenius plots for decarboxylation of the radical cations of **1b**, **1f**, **1g**, and **1h** in 4:1 acetonitrile/water. The straight lines represent best linear fits to the data; see Table 1 for the parameters.

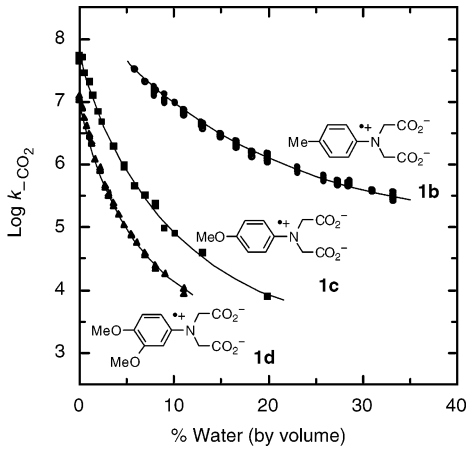


Figure 4. Plots of the logarithms of the rate constants for decarboxylation of the radical cations of anilino dicarboxylates (●) **1b**, (■) **1c**, and (▲) **1d**, showing a dramatic decrease in rate constant with added water.

ature dependencies extrapolate to larger preexponential factors because the experimental data are on the “lower” part of the curve.

These experiments were performed in a 4:1 acetonitrile−water mixture. For the donors **1b**, **1c**, and **1d**, the decarboxylation rate constants were also determined as a function of the water content in the solvent mixture, Figure 4. The dependence of the rate constants on the amount of added water is dramatic. For the radical cations of **1c** and **1d**, the decarboxylation rate constants decrease by ∼3 orders of magnitude with the addition of 10% water. For **1b** the decrease is somewhat less severe but still substantial. Part of the water effect is presumably due to the carboxylate hydration effect that results in the spectral changes observed in Figure 1. However, continued addition of water continues to decrease the reaction rate constant after the spectra have stopped changing, implying an additional effect of medium polarity.

This effect might explain the unusual Arrhenius plots discussed above. It is known that the bulk polarity of solvents decreases with increasing temperature.[19] Thus, as the temperature is raised, an additional increase in the decarboxylation rate constant could be due to the decrease in medium polarity, resulting in overall nonlinear Arrhenius plots. It was important, therefore, to test whether the dependence of the solvent dielectric constant was a significant factor for the present reactions.

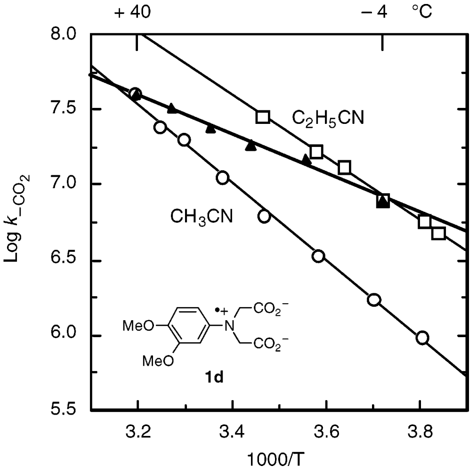


Figure 5. Arrhenius plot for decarboxylation of the radical cation of anilio diacetate **1d** in (○) acetonitrile, (□) propionitrile, and (▲) acetonitrile/propionitrile solvent mixtures that give a dielectric constant of 33.1 at all temperatures measured. The Arrhenius parameters in the solvent mixture are log $A = 11.8$ and $E_a = 5.9$ kcal/mol.

The dielectric constant (ϵ) of acetonitrile is 36 at room temperature but decreases to 33.1 at 40 °C.[20] Propionitrile, although a lower polarity solvent (at room temperature, $\epsilon = 27$), also has a dielectric constant of 33.1 °C at −4 °C, the same as acetonitrile at 40 °C.[20] This allows an experiment to be performed, in which the temperature is varied, but ϵ is kept constant. Rate constants were measured at different temperatures in acetonitrile−propionitrile mixtures of varying proportions such that the bulk dielectric constant remained at 33.1. The results for the aniline derivative **1d** are shown in Figure 5, together with the corresponding data for experiments performed in pure acetonitrile and in pure propionitrile. Similar to the results in the 4:1 acetonitrile−water mixtures mentioned above, the apparent preexponential factors for the reactions in pure acetonitrile and in pure propionitrile are again in the range $\sim 10^{15}$ to 10^{16} s^{-1}. However, the acetonitrile−propionitrile mixed-solvent experiment in which ϵ was maintained constant gave a preexponential factor (log $A = 11.8$) much closer to the expected range for a simple unimolecular reaction.[18] Also the apparent activation barriers of 11.9 and 9.5 kcal/mol obtained from the reactions in pure acetonitrile and in pure propionitrile are now replaced by an activation barrier of only 5.9 kcal/mol in the constant ϵ experiment. The obvious conclusion, then, is that the Arrhenius plots in the pure solvents and in the 4:1 acetonitrile−water mixtures are unusual as a result of the extreme sensitivity of the present reactions to solvent polarity, and when this is corrected for, reasonable Arrhenius behavior is restored.

Decarboxylation Mechanism

For an aryl-substituted carboxylate, the product of oxidation is expected to be an acyloxy radical, unless the oxidation potential of the aryl moiety is less than that of carboxylate (estimated to be ∼1.9 V vs SCE[21]), as in the present cases. The products of cleavage of the radical cation of an anilino carboxylate are a neutral α-amino radical and carbon dioxide, Scheme 2. The reaction thus involves charge annihilation; i.e., at some stage in the course of the reaction a transfer of charge must take place. This is one way in which the current reactions differ from decarboxylation of an acyloxy radical (reaction C, Scheme 1). Charge neutralization could occur by intramolecular electron transfer from the carboxylate group ($-CO_2^-$) to the anilino radical cation ($An^{\bullet+}-$) to yield the acyloxy radical

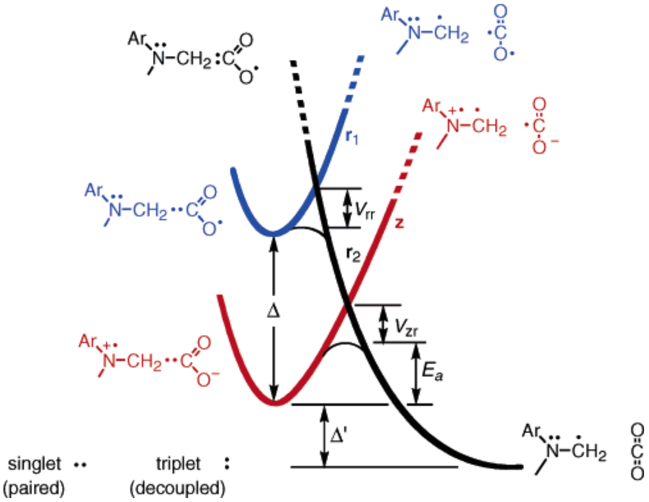
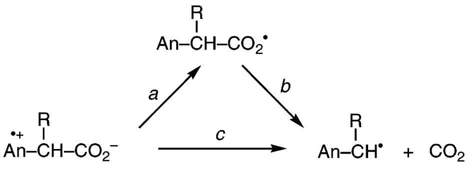


Figure 6. Qualitative valence bond energy curves for the (z, red) zwitterionic radical cation/carboxylate state, (r_1, blue) the acyloxy radical state, and (r_2, black) C−C bond decoupled acyloxy radical state, which are involved in the oxidative cleavage of anilino carboxylates. The r_1 and r_2 states experience avoided crossing characterized by a matrix element V_{rr}, and the z state experiences avoided crossing with the mixed r state, V_{zr}.

(reaction a, eq 2), followed by homolytic bond cleavage to form the products (reaction b, eq 2). Under these conditions, the intramolecular electron transfer would presumably become the rate-determining step, since decarboxylation of acyloxy radicals is so rapid. A minimum activation energy for this reaction is given by the difference in oxidation potential between the aniline and carboxylate. Even though the carboxylate potential is not known accurately, it is clear that this cannot be the mechanism, since, as mentioned above, the activation barrier for decarboxylation of the radical cation of **1d** in nitrile solvents is ∼6 kcal/mol, whereas the energy difference in oxidation potentials is estimated to be >30 kcal/mol.[21] Thus, an alternative mechanism to the "stepwise" processes (reactions a and b, eq 2), i.e., a "direct path" (reaction c, eq 2), is required to explain the data.



(2)

The dependence on oxidation potential is expected, based on the simple thermodynamic cycle argument that a lower bond dissociation energy results when the oxidation potential of the precursor is decreased;[13] however, we sought a more detailed model in terms of the important orbital and state correlations for the reactions that could qualitatively account for all of the *structural* observations. We have found the valence bond (VB) approach of Shaik and Pross to be useful.[22−24] Shown in Figure 6 is an energy curve as a function of C−C bond length for the radical cation (zwitterionic) state of an anilino carboxylate, z. Stretching the C−C bond raises the energy of the spin-paired electrons in the bond. In the VB formalism, the electrons are paired even at large C−C distances, and a cation and a radical anion of carbon dioxide is formed. Corresponding bond stretching in the acyloxy radical state, r_1, again raises the energy of the spin-paired electrons in the C−C bond while maintaining their pairing, preventing bonding with the odd electron on the carboxylate oxygen. An excited state of carbon dioxide is formed, in a singlet configuration (to maintain overall doublet spin character). A state in which the electrons in the C−C bond are decoupled in a triplet configuration is repulsive with respect to bond stretching (r_2, Figure 6).

Furthermore, one of these unpaired electrons can now undergo a bonding interaction with the unpaired electron on oxygen, and the ground state of the products is formed. The acyloxy radical state r_1 and r_2 are charge-transfer excited states of the ground z state. In addition to decoupling the electrons, a spin flip of the odd electron is required to maintain doublet character in r_2, which thus represents a double-excitation of the r_1 state.

Cleavage of either the radical cation or the acyloxy radical states thus involves an electronic barrier due to an avoided crossing with r_2. The matrix element that splits the r_1 and r_2 curves, V_{rr}, is an energy transfer type[25] and is likely to be large, and thus the barrier to reaction in the acyloxy radical is small.[10c,10j,24] The matrix element that splits the z and (now mixed) r curves, V_{zr}, is an electron-transfer type.[26] V_{zr} may be somewhat smaller than V_{rr};[27] however being intramolecular it is still expected to be substantial.

This reaction model can explain all of the observed effects on the decarboxylation rate constant of the anilino carboxylate radical cations. The model is redrawn in Figure 7 to illustrate the lowest energy adiabatic reaction surface formed as a result of the avoided crossings for three important cases.

The reaction activation energy, E_a, is given by the energy required to reach the crossing point of the z and r curves minus the matrix element V_{zr} (Figure 6). It is clear that the energy required to form the acyloxy radical from the anilino radical cation, Δ, is much larger than E_a, as observed. The decarboxylation rate constants decrease with increasing electron-donating ability of the substituents on the benzene ring, i.e., with decreasing oxidation potential of the anilino moiety (Table 1). Such substituents stabilize (i.e., lower the energy of) the zwitterionic state, which increases the energy difference Δ (energy diagram B relative to A, Figure 7). This increase in vertical displacement of the curves causes the energy required to reach the curve crossing point to be larger for the more stabilized donor radical cation, thus increasing the reaction activation barrier and decreasing the rate constant. This is in agreement with the data given in Table 1.

Stabilization of the zwitterionic state as a result of decreasing oxidation potential also lowers the exothermicity of the reaction, Δ′. The diagram thus provides a connection between the kinetics of the reaction and the predictions from thermodynamic cycles, i.e., that decreasing oxidation potential is related to a decrease in reaction exothermicity.[13]

Figure 7 also provides an explanation for the effect of the substituent R′ (H vs Me, i.e., *N*-acetate vs *N*-propionate) on the decarboxylation rate constant. The decarboxylation rate constants are higher for the propionate derivatives **1e**−**1h**, compared to the corresponding acetate derivatives **1a**−**1d**. The decarboxylation product of a propionate derivative is a secondary radical, which is more stable than the corresponding primary radical from the reaction of an acetate derivative (i.e., larger exothermicity, Δ′).

Increasing the radical stability lowers the energy of all of the bond breaking correlations in Figure 6, resulting in a lower energy for curve crossing (energy diagram C relative to A, Figure 7), a smaller activation energy, and a larger reaction rate constant.

The mechanism also explains the solvent effects. More polar solvents (for example, acetonitrile versus propionitrile) stablize the zwitterionic state, decreasing the rate (energy diagram B relative to A, Figure 7). This again will increase the energy

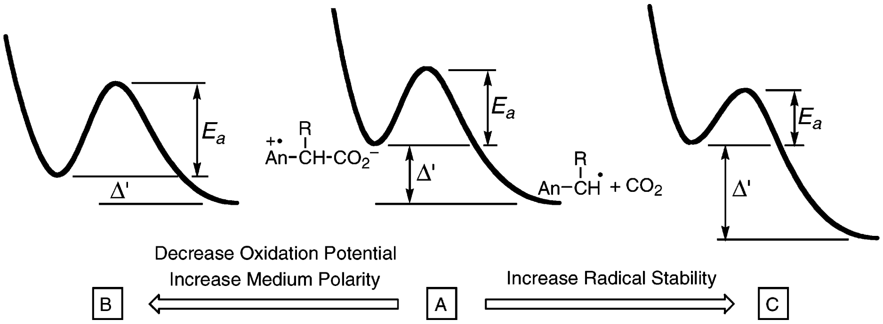


Figure 7. Adiabatic reaction energy curves for decarboxlyation of anilino carboxlyate radical cations. Curve A shows that the activation energy for reaction via avoided crossing with the radical states, E_a, is smaller than the energy difference between the radical cation and acyloxy radical states, Δ (defined in Figure 6). Curve B shows the increase in activation energy and decrease in reaction exothermicity, Δ′, in more polar solvents and for lower oxidation potential aniline moieties as a result of stabilization of the zwitterionic state. Curve C shows the decrease in activation energy and increase in reaction exothermicity as a result of formation of a more stable radical product.

gap Δ, causing an increase in the activation energy and a decrease in the rate constant (Figure 5). It is also well-known that the oxidation potential of the carboxylate anion (and most anions) is much higher in water than in acetonitrile due to stronger solvation and H-bonding.[21b,28] This provides an explanation of the dramatic water effect on decarboxylation rate constant (Figure 4), although the water must also be influencing the structure of the reactive radical cations, as observed by the changes in absorption spectra (Figure 1).

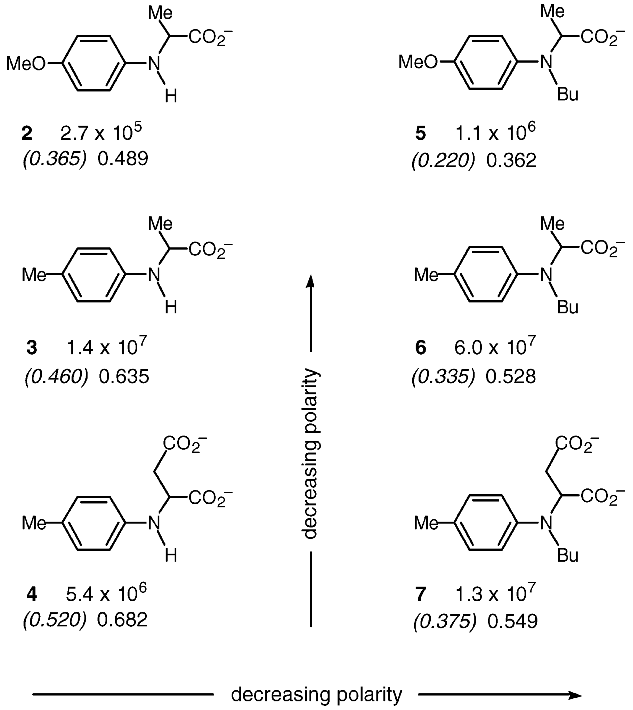
The model of Figure 6 has other interesting features. The reactions of the radical cations occur by stretching the C−C bond to the point of crossing with the radical state, at which point mixing causes electron transfer and a decrease in energy toward the ground state products. The reaction thus proceeds via only one transition state, is concerted, and fits Saveant's definition of, and provides an intramolecular example of, a dissociative electron-transfer reaction.[11,23,29] Dissociative electron-transfer reactions in turn are an example of bond-coupled electron-transfer reactions that are becoming increasingly recognized as common processes.[30,31] A final point is that electron-transfer reactions (in the adiabatic limit) are understood as examples of *radiationless transitions* whose rates depend on the value of an electronic coupling matrix element (squared),[26] whereas this and other bond-coupled electron-transfer reactions represent examples of *chemical* processes whose rates are determined by the magnitude of an electron-transfer matrix element.

Control of the Decarboxylation Rate Constant

The combined experimental results and the theoretical model clearly illustrate that solvation effects (either via bulk polarity or specific solvation) can have a very strong effect on the decarboxylation rate constant. This suggested a method of controlling the rate constant without changing the bulk medium, which is clearly not possible in the TES application, and without changing the oxidation potential of the aniline, by varying the solvation *at the reaction site*.

In the acetate/propionate derivatives (**1e**−**1h**) discussed above, decarboxylation occurs on the propionate group to yield a secondary radical. The molecular solvation in the vicinity of this reactive group was altered by substitution with other hydrophobic and hydrophilic groups, while maintaining decarboxylation to give an equivalent secondary radical. In one set of compounds, the acetate group on the nitrogen was replaced by a simple hydrogen, as in compounds **2**−**4** of Scheme 3. In another set, the acetate was replaced by a hydrophobic butyl group, as in compounds **5**−**7** of Scheme 3. A third set of compounds were obtained by replacement of the propionate on nitrogen with the presumably more hydrophilic succinate group, compounds **4** and **7**. To determine whether any effects of the fragmentation rate constant were genuinely due to changes in solvation, adjustments for corresponding changes in oxidation potential were required. The oxidation potentials of these new compounds were determined as described above from the peak potentials of irreversible cyclic voltammetry experiments and the corresponding decarboxylation rate constants, according to eqs 1.

SCHEME 3: *N*-H (2−4) and *N*-butyl (5−7) Aniline Derivatives; Decarboxylation Rate Constants (in s^{-1}) of Their Radical Cations in at 22 °C; Peak Potentials (in Parentheses) from Irreversible Oxidations (V vs SCE at Scan Rate of 0.1 V/s), Also in 4:1 Acetonitrile/Water; and the Oxidation Potentials Calculated According to Eqs 1 (V vs SCE)



The rate constant data are summarized in Scheme 3 and are illustrated graphically in Figure 8. From these, a number of conclusions can be drawn. Replacement of the acetate by hydrogen (compounds **2** and **3**) does not significantly affect the rate of decarboxylation, as these points fall on the same curve for compounds **1e**−**1h**. This is presumably a consequence of balancing solvation effects. The acetate is obviously larger than

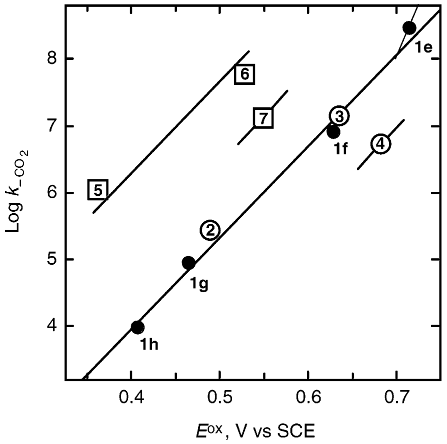


Figure 8. Plots of the logarithms of rate constants for decarboxylation of radical cations vs oxidation potentials illustrating the effect of micropolarity. The closed circles represent the *N*-acetate-*N*-propionate derivatives **1e**−**1h**, shown in Figure 2. The open circles represent *N*-H derivatives, **2**−**4**, and the open squares, *N*-butyl derivatives, **5**−**7**. In compounds **4** and **7**, the propionate group is replaced by a succinate (Scheme 3).

hydrogen, reducing solvent interaction at the reaction site for simple steric reasons. However, acetate is also much more hydrophilic, which may increase the effective water concentration at the reactive site. On the other hand, replacement of acetate or hydrogen with a butyl group (compounds **5** and **6**) leads to an increase in the decarboxylation rate constant by ca. 2 orders of magnitude, after correcting for oxidation potential, Figure 8. Presumably the hydrophobic group decreases the effective water concentration at the reactive site. Increasing the number of hydrophilic groups by replacing the propionate by a succinate (compare compound **4** to **2** and **3** and also **7** to **5** and **6**) decreases the rate constant for fragmentation by nearly an order of magnitude, Figure 8.

These data clearly demonstrate that varying the hydrophobic/hydrophilic nature of substituent groups can be used to control specific solvation, and thus the rate constant for fragmentation over almost 3 orders of magnitude, at constant oxidation potential.

Summary

Decarboxylation of the radical cations of aryl carboxylates is related to decarboxylation of acyloxy radicals via a valence bond curve-crossing model. Both reactions involve an avoided crossing and an electronic barrier to reaction. The rate constants of the radical cation reactions depend strongly upon the oxidation potential of the amine, the stability of the radical product, and, most importantly, solvent polarity. Making use of this information, we have been able to design a series of molecules in which the decarboxylation rate constants, adjusted for differences in oxidation potential, could be dramatically varied by changing the molecular micropolarity.

Experimental Section

The solvents were spectrograde and used as received. Water was deionized and distilled. The anilino-dicarboxylates **1a**−**1h** and **2**−**7** were prepared by alkylation of the anilines with the appropriate bromo-reagent as described in detail in ref 7b. An illustrative example is reproduced here for compound **1a**.

Synthesis of 1a. A suspension of 21.4 g of aniline, 50 g of ethyl 2-bromopropionate, 4.6 g of potassium iodide, and 60 g of anhydrous potassium carbonate in 300 mL of acetonitrile was refluxed under nitrogen for 2 days. The mixture was cooled and filtered, and the filterate was dissolved in dichloromethane and extracted with aqueous sodium bicarbonate solution and then with water. The solution was dried over anhydrous sodium sulfate and filtered, and the solvent was distilled off. The residue was distilled (108−115 °C at 0.05 mm) to give 31.9 g (72%) of ethyl 2-phenylaminopropionate as colorless crystals.

To a solution of 24.6 g of this propionate ester and 31.9 g of ethyl bromoacetate in 200 mL of acetonitrile 4.2 g potassium iodide and 35 g anhydrous potassium carbonate were added, and the mixture was refluxed under nitrogen for 6 days. The mixture was cooled and filtered, and the filtrate was taken into dichlormethane and washed with aqueous sodium bicarbonate and with water. The residue after stripping off the solvent was distilled (138−142 °C at 0.028 mm) to yield 20.8 g (50%) of ethyl 2-(ethoxycarbonylmethylphenylamino)propionate (the diethyl ester analogue of **1a**).

A solution of 11.4 g of this diester and 3.3 g of sodium hydroxide in a mixture of 10 mL of water, 10 mL of ethanol, and 14 mL of tetrahydrofuran was refluxed for 15 h and cooled, and the precipitated salt was collected and recrystallized from ethanol to give 7.5 g (69%) of **1a**, as colorless crystals. ^{1}H NMR (D_2O): δ 1.42 (d, 3), 3.78 (d, 1), 4.05 (d, 1), 4.15 (q, 1), 6.58 (m, 2), 6.70 (m, 1), 7.25 (m, 2).

All other materials were available from previous work.[6,9b]

The aniline radical cations were formed using the DCA/biphenyl cosensitization system in acetonitrile.[32] Using DCA/biphenyl, the aniline radical cations were formed with constant and high yield, and we have used this method for studying the kinetics of a wide variety of radical cation reactions using transient absorption spectroscopy.[6,9,30] The experimental details for determining the rate constants for fragmentation of aniline radical cations using this method have been described in detail in a previous publication.[9b] The observed transient species were assigned to radical cations, since their formation occurred in concert with decay of the precursor biphenyl radical cation, their lifetimes did not vary with dissolved oxygen, and their fragmentation kinetics varied with structure as expected. As discussed above, the actual absorption maxima of the radical cations varied somewhat with reaction conditions (Figure 1) and were not determined in all cases. In addition, the wavelength chosen for observation of the decay kinetics was not necessarily the maximum but that which gave the most easily analyzed signal, which was typically between 530 and 630 nm. In all cases the decays of the radical cations fit well to pseudo-first-order kinetics over at least two lifetimes.

The details of the electrochemical measurements will be given elsewhere.[17a]

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