

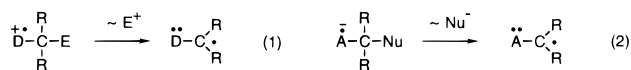
The Dynamics of α -Anilino Carboxylate and Related Cation Radical α -Heterolytic Fragmentations

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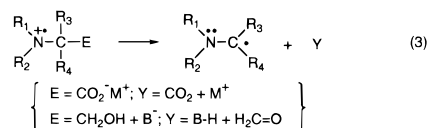
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α -Heterolytic fragmentation reactions of ion-radicals play a major role in governing the chemoselectivities and efficiencies of a wide variety of redox processes. The function of these reactions (eqs 1 and 2) in SET-photochemistry is pivotal since departure of an electrofugal or nucleofugal group from a respective cation or anion radical often occurs in competition with back electron transfer or alternative reaction modes. As a result, knowledge about the dynamics of ion radical fragmentation reactions and their dependence on substrate structures and redox potentials as well as the medium and additives is crucial to the design of efficient SET-photochemical processes.



The importance of this information is evidenced by the expanding number of investigations in which the rates of ion radical reactions have been directly measured.² Our initial efforts^{2h} in this area focused on the α -deprotonation reactions of tertiary amine cation radicals and the related α -silylamine cation radical desilylation process.³ We demonstrated that laser flash irradiation of solutions containing 1,4-dicyanobenzene (DCB) and *N,N*-dialkylanilines generates spectroscopically detectable anilinium radicals which decay by (1) back electron transfer with DCB^{•-} at diffusion controlled rates, (2) base induced α -deprotonation with second order rate constants that are dependent on base strength and the nature of α - and arene ring-substituents, or (3) silophile induced α -desilylation. Recently, we initiated a more broad study of aminium radical α -heterolytic fragmentation reactions in order to determine if the trends noted earlier are general. Our plan was to determine the rates of the known,³ but relatively unstudied,⁴ unimolecular decarboxylation reactions of α -amino carboxylates (eq 3), to compare these rates to the bimolecular rates of the related deprotonation,^{2h} desilylation,^{2h} and retro-aldol fragmentation (eq 3),^{5,2b} and, finally, to ascertain if substituent effects on the rates of these aminium radical fragmentation can be generalized.



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Scheme 1

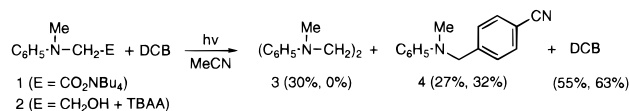


Table 1. Rate Constants for Decarboxylation and Retro-Aldol Cleavage of Anilinium Radicals [*p*-X-C₆H₄NMeCHRE]^{•+}

anilinium radical			solvent	fragmentation rates k_{dec} (s ⁻¹) ^a or k_{ra} (M ⁻¹ s ⁻¹) ^{b,c}
E	X	R		
CO ₂ NBu ₄	H	H	MeCN	1.7 ± 0.2 × 10 ⁶
CO ₂ NBu ₄	H	H	EtOH	2.5 × 10 ⁶
CO ₂ NBu ₄	H	H	MeOH	2.8 × 10 ⁶
CO ₂ NBu ₄	MeO	H	MeCN	8.1 ± 0.3 × 10 ⁵
CO ₂ NBu ₄	CF ₃	H	MeCN	1.2 ± 0.2 × 10 ⁷
CO ₂ NBu ₄	H	Me	MeCN	1.3 × 10 ⁶
CO ₂ NBu ₄	H	Ph	MeCN	2.6 × 10 ⁶
CH ₂ OH	H	H	60% MeOH–MeCN	4.1 ± 0.6 × 10 ⁴
CH ₂ OH	MeO	H	60% MeOH–MeCN	2.0 ± 0.3 × 10 ⁴
CH ₂ OH	CF ₃	H	60% MeOH–MeCN	3.1 × 10 ⁵
CH ₂ OH	H	Me	60% MeOH–MeCN	3.3 × 10 ⁴
CH ₂ OH	H	Ph	60% MeOH–MeCN	3.3 ± 0.7 × 10 ⁵

^a 25 °C. ^b 25 °C with *n*BuNOAc as base. ^c Errors were obtained by evaluating data from 3–5 independent experiments.

To evaluate the dynamics of the aminium radical decarboxylation and the related retro-aldol cleavage, we explored the SET-photochemistry of precursors of these transients in order to ensure that the respective fragmentation reaction pathways were followed cleanly in these systems. Preparative irradiation (Pyrex ($\lambda > 300$ nm N₂, MeCN) of the anilino carboxylate **1** (2.5 mM) and DCB (2.5 mM) leads to clean production of a mixture the diamine **3** (30%), adduct **4** (27%), and recovered DCB (55%) (Scheme 1). Likewise, adduct **4** (32%) and recovered DCB (63%) are produced when an MeCN solution containing the anilino alcohol **2** (2.4 mM), DCB (2.4 mM) and tetra-*n*-butylammonium acetate (TBAA) (0.3 M) is irradiated (Scheme 1). The results demonstrate that α -amino radical formation by decarboxylation and retro-aldol cleavage is dominant for anilino carboxylate and anilino alcohol cation radical decay.

Time-resolved laser spectroscopy was used to determine the dynamics of these α -fragmentation reactions. Laser excitation (308 nm, 6 ns, 50–60 mJ) of solutions containing (Table 1) tetra-*n*-butylammonium anilino carboxylates (ANC, 0.5 mM) and DCB (50 mM) in each case leads to initial generation (Figure 1) of a 1:1 (known^{2h} molar absorptivities) of two transients characterized as DCB^{•-} (340(s), 430(w) nm) and ANC^{•+} (ca. 460 nm).^{2h,6} Analysis of the decay profiles for ANC^{•+} employed a kinetic treatment which takes into account competitive diffusion controlled^{2h} SET between ANC^{•+} and DCB^{•-} and unimolecular decarboxylation of ANC^{•+}. This analysis when combined with the known^{2h,6} molar absorptivities of the transients yields the unimolecular rate constants (k_{dec}) for ANC^{•+} decarboxylation. Decarboxylation rates were measured for a series ring- and α -substituted systems and in aprotic and protic solvents (Table 1). In addition, counter cation effects on the rates of ANC^{•+} decarboxylation were evaluated. Representative data for the metal cation type dependence of k_{dec} are given in Table 2.

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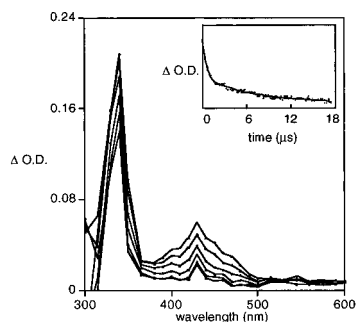


Figure 1. Transient absorption spectra following (1–40 μs) 308 mM excitation of $\text{PhNMeCH}_2\text{CO}_2\text{NBu}_4$ and DCB in MeCN at 25 $^\circ\text{C}$. (Insert: Transient absorption at 460 nm, experimental data (points) and fit (line)).

Table 2. Salt Effects on $[\text{PhNMeCH}_2\text{CO}_2\text{NBu}_4]^+$ Decarboxylations

added salt ^a	$k_{\text{dec}} \times 10^6 \text{ (s}^{-1}\text{)}$	added salt	$k_{\text{dec}} \times 10^6 \text{ (s}^{-1}\text{)}$
none	1.7	RbClO ₄	2.8
LiClO ₄	1.1	CsClO ₄	2.9
NaClO ₄	1.9	Mg(ClO ₄) ₂	0.12
KClO ₄	2.5	Ca(ClO ₄) ₂	0.08

^a 25 $^\circ\text{C}$, MeCN with $[\text{PhNMeCH}_2\text{CO}_2\text{NBu}_4] = 0.5 \text{ mM}$ and $[\text{MClO}_4] = 10 \text{ mM}$.

By use of similar methods, the rates of TBAA promoted retro-aldol fragmentation (k_{ra}) of photogenerated cation radicals derived from the anilinoalcohols (ANA) (Table 1) were measured. Plots of the observed rates of ANA^{•+} decay (treated as two competitive bimolecular decay routes) *vs* TBAA concentration (0.1–0.5 M) provide k_{ra} values for cleavage. Additional data supporting the proposal that TBAA induced retro-aldol fragmentation is the major, if not exclusive, pathway for decay of ANA^{•+} are an OH/OD isotope effect of 2.2⁷ and an NCH₃/NCD₃ isotope effect of 1.3 for $\text{PhN}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{OH}$.⁸

A number of interesting features of anilinium radical α -fragmentation reactions can be gleaned by inspection of the accumulated data. Firstly, ANC^{•+} decarboxylations are among the most rapid of amine cation radical fragmentation processes.⁹ Owing to their large rate constants (*ca.* 10^6 – 10^7 s^{-1}) and unimolecular nature, decarboxylations dominate other modes of aminium radical decay when high concentrations of bases or silophiles are absent. For comparison purposes, the rate constant for TBAA deprotonation of $[\text{PhN}(\text{Me})_2]^+$ is $2.0 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$ and for MeCN (solvent) desilylation of $[\text{PhN}(\text{Me})\text{CH}_2\text{TMS}]^+$ is $2.0 \times 10^4 \text{ s}^{-1}$.

Secondly, the decarboxylation rates are moderately sensitive to solvent, nearly doubling in moving from the less polar/aprotic MeCN ($E_{\text{T}} = 47$) to the more polar/protic MeOH ($E_{\text{T}} = 56$). This effect can be attributed to greater solvation by MeOH of the butylammonium cation and carboxylate anion components resulting in a greater rate of free carboxylate decarboxylation. This simple reasoning is compatible with the observed metal cation effects (Table 2). Metal perchlorate salts appear to influence the decarboxylation rates in two ways. Addition of perchlorates of non-oxophilic metal cations such as Rb⁺ and Cs⁺ leads to an increase in the decarboxylation rates, a likely result of a general salt effect. In contrast, the presence of highly oxophilic metal cations results in a modest (Li⁺) to dramatic

(7) Retro-aldol cleavage of related anilino-alcohol cation radicals has been analyzed from this same perspective by Schanze and his co-workers (ref 2b).

(8) Even though the rates of TBAA induced α -CH deprotonations of $[\text{PhNMeCH}_2\text{R}]^+$ are in the range of those measured for retro-aldol fragmentation, the current data show that α -CH deprotonation is not competitive in decay of $[\text{PhNMeCH}_2\text{CH}_2\text{OH}]^+$.

(9) (a) Earlier (ref 9b) we observed that the rates of α -heterolytic fragmentation of benzylic cation radicals varies in the order $\text{CO}_2\text{H} > \text{TMS} > \text{CO}_2\text{H} > \text{H}$. (b) d'Alessandro, N.; Albini, A.; Mariano, P. S. *J. Org. Chem.* **1993**, *58*, 937.

(Mg²⁺, Ca²⁺) decrease in k_{dec} . Thus, tight-coordination of the carboxylate moiety to cations, brought about by the use of less polar/protic solvents or more oxophilic metals, slows ANC^{•+} decarboxylation.

Finally, substituents influence the rates of α -heterolytic fragmentation reaction of anilium radicals. In earlier efforts,^{2h} we showed that the rate of TBAA-induced α -deprotonation of $[\text{p-X-C}_6\text{H}_4\text{NMe}_2]^+$ is a sensitive function of the para-substituent ($k_{\text{deprot}} \times 10^{-5} = 2.0$ (X = H), 0.8 (X = MeO), and 8.9 (X = CF₃)). The data in Table 1 demonstrate that this trend holds for decarboxylation and retro-aldol cleavage. Linear free energy treatments of the rate data give $\rho_{\text{deprot}} = 1.5$, $\rho_{\text{dec}} = 1.8$, and $\rho_{\text{ra}} = 1.6$ which suggest that anilium radical deprotonation, decarboxylation, and retro-aldol cleavage⁷ reactions occur *via* early transition states which have similar electronic character in the anilino-moiety region. As discussed earlier,^{2h,10} the rates of anilinium radical deprotonation parallel their thermodynamic acidities which are known to be inversely related to aniline oxidation potentials. Thus, the current results show that this relationship (increasing rate with increasing precursor oxidation potential) also exists for amine cation radical decarboxylation and retro-aldol cleavage reactions.¹¹

Equally interesting is the observation that the amine cation radical α -heterolytic fragmentation processes show the same α -substituent dependence. Accordingly, replacement of one of the α -hydrogens in $[\text{C}_6\text{H}_5\text{N}(\text{Me})\text{CH}_2\text{E}]^+$ by methyl causes a decrease in the rate of loss of the electrofugal group, while a rate increase is engendered by phenyl substitution.¹² The rationale presented earlier by Lewis and his co-workers¹³ for α -substituent effects on aminium radical deprotonations, based upon both stereoelectronic and C–E bond dissociation energy effects, appear to be generally applicable to other α -heterolytic fragmentation processes.^{2h,14}

In summary, results presented here demonstrate that aminium radicals generated from α -aminocarboxylate undergo fast decarboxylation to produce α -amino radicals and that the decarboxylation rates as well as those for related deprotonation, desilylation, and retro-aldol cleavage can be significantly altered by changes in solvent, counter cation, and N- and α -substituents.¹⁵

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(10) We showed earlier (ref 2e) that $\log k_{\text{deprot}}$ is well correlated with both σ and $E_{1/2}(+)$ values of para-substituted anilines.

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(12) For comparison purposes, the rate constants of deprotonation of $[\text{Ph}_2\text{N-CH}_2\text{R}]^+$ by TBAA are 9.5×10^5 (R = H), 2.3×10^5 (R = Me), and 3.2×10^6 (R = Ph) $\text{M}^{-1} \text{ s}^{-1}$ (ref 2h).

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(15) An example of how this knowledge can lead to the design of efficient SET-photochemical processes is seen in the results of a laser spectroscopic study (unpublished) which show that a change in the N-substituent Z in $[\text{PhN}(\text{Z})\text{CH}_2\text{TMS}]^+$ from Me to CO₂Et causes the rate of MeOH promoted desilylation to increase from $7.0 \times 10^5 \text{ s}^{-1}$ to $1.8 \times 10^7 \text{ s}^{-1}$, and those of a parallel photochemical study which show that the quantum yield for SET-photochemical cyclization of the phthalimides (**i** \rightarrow **ii**) increases from 0.05 to 0.22 when Z is changed from Me to Ac.

