•OH Radical Induced Decarboxylation of Amino Acids. Decarboxylation vs Bond Formation in Radical Intermediates

L. Kraig Steffen,[†] Richard S. Glass,*[,†] Mahmood Sabahi,[†] George S. Wilson,[†,‡] Christian Schöneich,[§] Sabine Mahling,[§,⊥] and Klaus-Dieter Asmus*[,§]

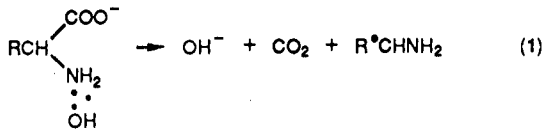
Contribution from the Department of Chemistry, University of Arizona, Tucson, Arizona 85721, and Hahn-Meitner Institut Berlin, Bereich S, Abteilung Strahlenchemie, Postfach 39 01 28, 1000 Berlin 39, Germany. *Received May 3, 1990*

Abstract: The •OH radical reaction with *exo*-2-amino-*endo*-6-(methylthio)bicyclo[2.2.1]heptane-*endo*-2-carboxylic acid primarily affords oxidation of the sulfur center in the molecule. The subsequent pathway strongly depends on pH. A transient radical with interaction between the sulfur and the carboxylate moieties is stabilized particularly in acid solutions with maximum yield at pH 3. It is characterized by a sulfur–carboxyl bond, which exhibits typical features of $2\sigma/1\sigma^*$ three-electron bonds. It exhibits an optical absorption (λ_{max} 340 nm) and decays with $t_{1/2} \approx 26$ μs via deprotonation to an α-thioalkyl carbon-centered radical. This transient bond formation between the carboxyl group and the oxidized sulfur at low pH successfully prevents a competing process, namely, decarboxylation, which takes over at pH > 4. The underlying mechanism is considered to be a concerted action involving an electron transfer from the anionic carboxylate to the oxidized sulfur atom, homolytic carbon–carboxyl bond breakage, and deprotonation of the amino group. Related studies indicate that this kind of radical-induced decarboxylation can be generalized and receives its driving force to a significant extent from the resonance stabilization of the α-amino radical remaining after CO_2 cleavage.

Introduction

The radical-induced decarboxylation of amino acids has been the subject of a number of investigations.[1-5] It is evident that this process is of great significance for biological systems considering many well-established enzymatic or metabolic pathways of radical generation "in vivo".[6,7] Chemically, decarboxylation seems to be initiated mainly by oxidative attack and has only been observed for α-amino acids. Involvement of the amino group appears to be essential.[2-5,8]

The mechanistic details of the radical-induced decarboxylation are still under debate. Oxidation takes place at either the nitrogen of the amino function or the carboxyl group itself, with the amino nitrogen seemingly being the preferred target. Evidence for this has been provided by, for example, a study on •OH radical reactions with a large number of α-amino acids $RCH(NH_2)COOH$.[3-5] The most favorable conditions for decarboxylation are achieved if the amino group is deprotonated and directly available for oxidative attack. The mechanism proposed includes an •OH adduct at nitrogen and a, probably concerted, electronic rearrangement[5] as shown in eq 1. The immediate chemical outcome



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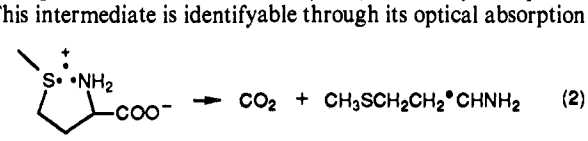
of the radical-induced decarboxylation is the formation of α-amino radicals, which are known to be strongly reducing species.[5,9,10] The decarboxylation process thus drastically changes the redox properties of the system.

Direct evidence for the involvement of the amino nitrogen has been observed in the radical-induced oxidation of methionine $(CH_3S(CH_2)_2CH(NH_2)COOH)$.[3-5] In this case, the initial oxidation takes place at the sulfur atom, which then coordinates with the nitrogen in a three-electron ($2\sigma/1\sigma^*$) bond to yield species **1**. This intermediate is identifyable through its optical absorption



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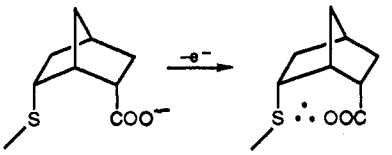
(λ_{max} 400 nm). Its lifetime is very short ($t_{1/2} \approx 200$ ns, in aqueous solution), and it seemingly decays directly into CO_2 and an α-amino radical.[2-4] As the S∴N bond exhibits oxidizing properties,[11] it is likely that it attracts electron density from the carboxylate and thus initiates a pseudo-Kolbe-type decarboxylation mechanism.[12]

Direct oxidation of the carboxyl group appears to be much less efficient. Practically no decarboxylation is observed for amino acids lacking the α-amino group, e.g., β-alanine.[5] An interesting and instructive situation prevails in sulfur-containing amino acids such as 3-(methylthio)propanoic acid,[13] *S*-methylcysteine,[3,8] or the *endo*-6-(methylthio)bicyclo[2.2.1]heptane-*endo*-2-carboxylic acid (**2**).[13-16] In these compounds, oxidation occurs initially at sulfur and the oxidized sulfur function may then directly interact with the carboxyl group, exemplified in reaction 3. The driving



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[†] University of Arizona.
[‡] Present address: Department of Chemistry, University of Kansas, Lawrence, KS 66045.
[§] Hahn-Meitner Institut Berlin.
[⊥] Present address: Umweltbundesamt, Bismarckplatz 1, D-1000 Berlin 33, FRG.

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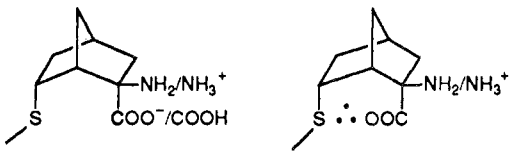
force in all these cases is the establishment of sterically favorable 5- or 6-membered rings in the species with sulfur–carboxylate interaction. Transient **3**, incidentally, exhibits an optical absorption (λ_{max} 390 nm) and a considerable lifetime in aqueous solutions ($t_{1/2}$ = 30–60 μs, depending on pH).[13-15] Its electronic structure has been discussed in detail in an earlier publication.[13] In many respects, it resembles features typical for two-center–three-electron ($2\sigma/1\sigma^*$) bonds justifying the commonly used "∴" notation for describing this bond in **3** and similar species. (A different notation (>S$^{\bullet+}$ ↔ $^-$OOC–) just indicating an unspecified interaction between the oxidized sulfur function and the carboxylate is equally reasonable.[13]

Decarboxylation is only observed from *S*-methylcysteine, i.e., the only compound in this group that is an amino acid. In this case, the α-amino substituent participates indirectly as an activating function.[8]

Considering all the information gathered so far, there are still many open questions concerning the detailed mechanism of decarboxylation. It seems that structure plays a significant role. This applies in particular to amino acids, like the above-mentioned sulfur-containing molecules, in which the initial oxidative attack does not directly occur at either the α-amino or the carboxyl function. One-electron oxidation of the conformationally constrained methionine derivative **4**, which is the *exo*-amino derivative



4 **5**

of **2**, provided unique insight into the decarboxylation mechanism of α-amino acids as deliniated in this paper. This compound was synthesized and characterized and its electrochemical behavior investigated previously.[17] It can be expected that the sulfur–carboxylate interaction species **5** is one of the intermediates generated in the oxidation of **4** (in analogy to **2** → **3**). But is this the species that actually decarboxylates, or are there other intermediates and processes that are responsible for decarboxylation? The answer to these questions is provided by radiation chemical pulse- and γ-radiolysis investigations. The conclusions derived from this structurally very defined system will be compared with literature data and, in particular with a complementary study (with details in a separate paper) on a much more complex system, namely, the •OH radical induced decarboxylation of methionine-containing peptides.[18]

Experimental Section

All radiolysis experiments were performed with aqueous solutions of **4**. The water was purified and deionized by "Millipore" filtration. Solutions were generally prepared in 0.2–0.5-dm^3 samples at amino acid concentrations of 5 × 10^{-5}–10^{-3} M. Deoxygenation was achieved by bubbling with N_2 for at least 0.5 h for each solution. Subsequently, the solutions were saturated with N_2O. This additive converts hydrated electrons (generated with about the same yield as •OH as primary radiolysis product of water)[19] into hydroxyl radicals via $e_{aq}^- + N_2O \rightarrow {}^\bullet OH + OH^- + N_2$, i.e., doubles the available concentration of •OH radicals. Under these conditions, the •OH radicals account for 90% of all reactive primary species in the irradiated solution; the remainder are hydrogen atoms. The pH of the solutions was adjusted by either $HClO_4$ or NaOH.

All time-resolved experiments (pulse radiolysis) were carried out by applying short pulses of high-energy electrons from either a 3.8 or 1.5-MeV van de Graaff accelerator with typical pulse widths of 50 ns and 1 μs, respectively. Absorbed doses were on the order of 1–5 Gy (1 Gy = 1 J/kg). On the basis of the radiation chemical yield $G(^\bullet OH) \approx 6$ in N_2O-saturated solutions, this corresponds to a total radical concentration

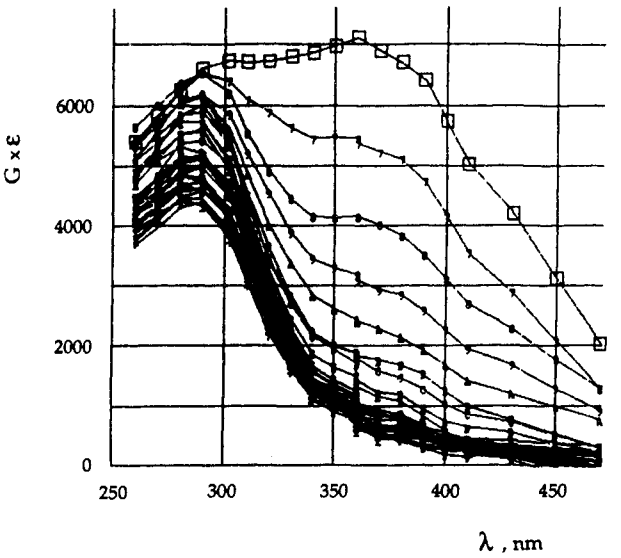


Figure 1. Optical absorption spectra recorded at time intervals of 10 μs after a 50-ns pulse given to a N_2O-saturated, aqueous, pH 2.6 solution of 10^{-4} M amino acid **4** (□, initial trace immediately after pulse).

of (0.6–3) × 10^{-6} M/pulse. (The radiation chemical yield (G) is defined as the number of species formed, destroyed, or converted per 100 eV of absorbed energy.) Further details on the technique of pulse radiolysis, the dosimetry, and in particular the evaluation of data from the experimental results have been described.[19]

Decarboxylation was initiated by irradiation in the field of a ca. 6000-Ci ^{60}Co γ-source. Total absorbed doses were on the order of 50–200 Gy at a dose rate of ca. 700 Gy/h. Analysis for CO_2 was achieved by ion chromatography with a Dionex 2010i machine equipped with an HPICE-AS1 column in conjunction with a conductivity detector. The underlying procedures have been described previously.[5]

The synthesis of *exo*-2-amino-*endo*-6-(methylthio)bicyclo[2.2.1]heptane-*endo*-2-carboxylic acid has been reported in a separate publication.[17] All experiments have been carried out at room temperature.

Results

Time-Resolved Optical Measurements. The •OH radical induced oxidation of the amino acid **4** leads to the formation of several optically absorbing transients. This is demonstrated in Figure 1, which shows a series of spectra recorded at time intervals of 10 μs after a 50-ns pulse given to a N_2O-saturated, aqueous, pH 2.6, 10^{-4} M solution of **4**. The overall spectrum recorded immediately after the pulse (□) shows a broad absorption extending from the UV into the visible. Two different species can clearly be distinguished, a short-lived one absorbing in the 300–500-nm range and disappearing practically within ca. 100 μs and a long-lived one with an absorption peaking at 280 nm. The latter decays comparatively slowly, and at the final recording time of our experiment (400 μs after the pulse) it is still present at more than half its original yield.

The spectrum of the short-lived transient (difference spectrum between recordings immediately and 100 μs after the pulse) is displayed in Figure 2. It exhibits a maximum at 340 nm and is attributed to the radical **5** formed upon interaction of the oxidized sulfur with the carboxylate. This assignment is based on several experimental observations and arguments displayed and discussed below and the resemblance of the essential features with the findings for the oxidation of other carboxylic acids with sulfide functions.[3,13-15]

The longer lived UV absorption is assigned to the carbon-centered α-thioalkyl radicals **6a** and **6b** in analogy with the corresponding findings during the oxidation of other organic sulfides.[20,21] A distinction between **6a** and **6b** cannot be made on the grounds of the absorption characteristics.

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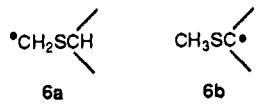


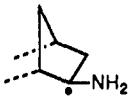
6a 6b

The kinetic stability of the short-lived transient **5** is shown in Figure 3. The absorption–time trace has been recorded at 360 nm upon pulse irradiation of a N_2O-saturated, pH 3.1 solution of 10^{-4} M of **4**. The signal is seen to be fully developed at the end of the pulse, substantiating previous findings that the reactions of •OH radicals with organic sulfides are diffusion-controlled processes.[20]

The decay of **5** occurs exponentially with a half-life of 26 μs corresponding to a first-order rate constant of 2.7×10^4 s^{-1}. The solid curve represents a best fit computer calculation. The decay kinetics stayed essentially constant (within error limits) over the pH 2–6 range. At higher pH, shorter lifetimes are indicated possibly due to base-catalyzed reaction of **5** with OH^- ions. Such a reaction has been found to occur for practically all sulfur-centered radical cations and the sulfur–carboxylate intermediate **3** in basic solutions.[13,20] (The hydroxyl ion is considered to displace the carboxylate at the oxidized sulfur.) The low yield of **5** at higher pH prevented more accurate kinetic measurements precluding quantitative conclusions.

The carbon-centered radicals **6a,b** exhibit a much longer lifetime. Their decay seems to proceed predominantly by a second-order process, and a bimolecular rate constant on the order of $2k \approx 10^9$ M^{-1} s^{-1} can be estimated. The underlying process could be radical–radical combination as well as ionic disproportionation. Both processes have been found to occur for many similar species from other organic sulfides.[20,22]

With increasing pH, the maximum at 280 nm becomes less and less pronounced. Also, the absorption attains a lower value as compared with the spectrum of **6a,b** at all wavelengths ≤325 nm, while at higher wavelengths it becomes relatively stronger. The following $G\epsilon$ values have been measured at 100 μs after the pulse: at 280 nm, 4300 M^{-1} cm^{-1} (pH 2.6) vs 3300 (pH 5.9); at 325 nm, 2000 (pH 2.6 and 5.9); and at 400 nm, 300 (pH 2.6) vs 800 (pH 5.9). The spectral characteristics at higher pH more and more resemble the features of α-amino radicals,[9,10] in our case of species **7**. Formation of this species requires decarboxylation.



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The yield of the short-lived transient **5**, as measured from the optical experiments and given in terms of $G\epsilon$ at 360 nm, is displayed in curve a of Figure 4. At low pH (i.e., <3), the experimentally obtained yields were normalized to the actual •OH radical concentration. (With decreasing pH, the reaction $e_{aq}^- + H_{aq}^+ \rightarrow H^•$ has to be taken into account.) The curve shows a relatively pronounced maximum at pH 2–3. At higher and lower pH, the measurable yields become increasingly lower and no **5** is observable above pH 9.5. It should be noted that the decrease in yield at pH >3 does not correlate with the kinetic stability of **5**. A correlation is apparent only in the very acidic region at pH <2 where the decay of the transient becomes considerably faster. At pH 1, for example, the half-life of **5** drops to 8 μs as compared to ca. 30 μs at pH 2–8.

Time-Resolved Conductivity Experiments. The above observations are corroborated by time-resolved conductivity experiments. The transient conductivity signal, which is presented in Figure 5 for example, has been recorded upon pulse irradiation of a N_2O-saturated, 10^{-4} M solution of **4** at pH 3.6. The conductivity is seen to decrease with the pulse to a minimum value of $G\Delta\Lambda = -440$ Ω^{-1} cm^2. This initial process is followed by an exponential increase to a final, still negative value of -100 Ω^{-1} cm^2 at the end of the experimental time scale (ca. 200 μs). The half-life of this increase is 24 μs and thus corresponds to the kinetics for the decay of the short-lived transient optical absorption. The change in conductivity is therefore associated with species **5**.

The interpretation of time-resolved conductivity measurements has been described in detail in other publications,[19,23] and only the essential features shall be mentioned for the analysis of the present data. The initial decrease of the signal is indicative for a replacement of a highly conducting H^+ by a less conducting

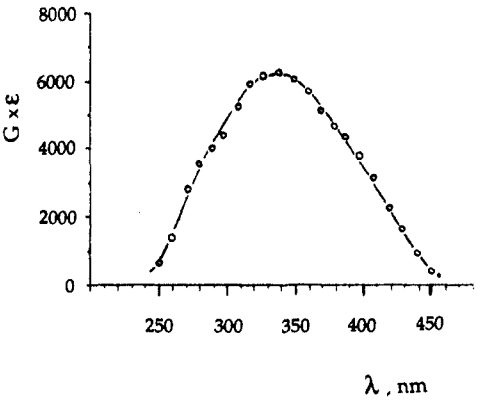

Figure 2. Optical absorption spectrum of radical **5** extracted from Figure 1 (subtraction of long-lived from initial short-lived absorption).

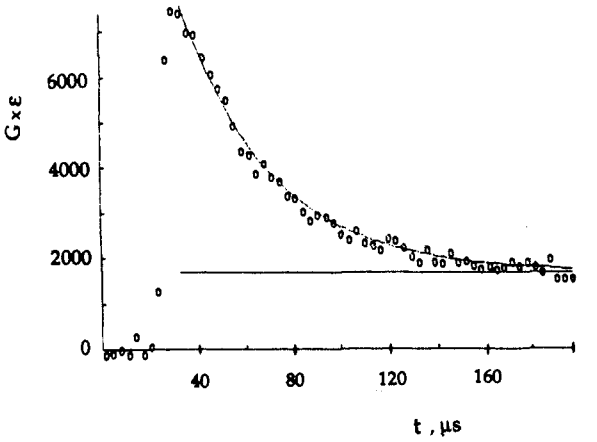

Figure 3. Optical absorption vs time trace recorded at 360 nm from a N_2O-saturated, aqueous, pH 3.1 solution of 10^{-4} M amino acid **4** (horizontal bar indicates long-lived absorption).

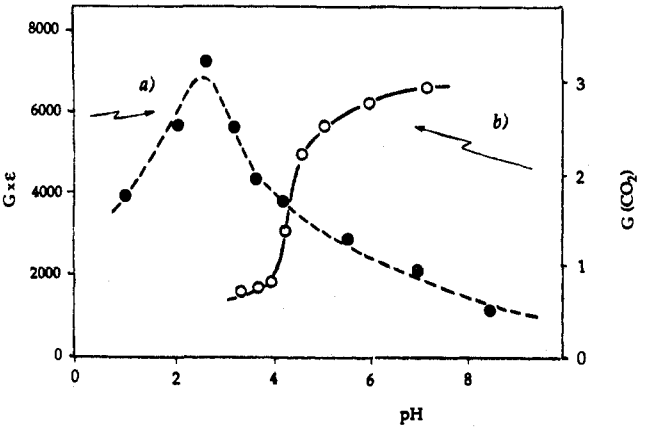

Figure 4. Yield of radical **5** expressed in terms of $G\epsilon$ measured at 360 nm (curve a) and yield of CO_2 measured in terms of G (curve b) as a function of pH, obtained from N_2O-saturated, aqueous solutions of 10^{-4} M (a) and 3×10^{-4} M (b) amino acid **4**.

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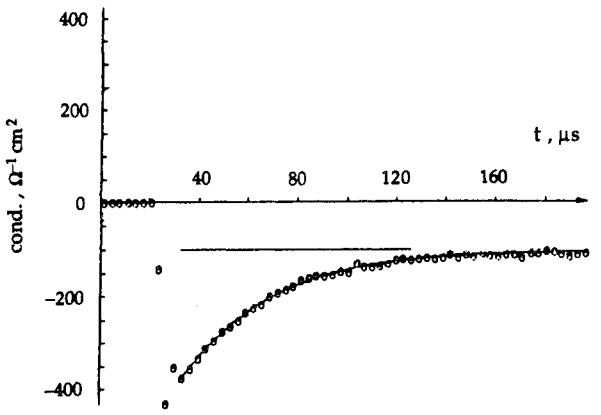


Figure 5. Conductivity vs time trace recorded from a N_2O-saturated, aqueous, pH 3.6 solution of 10^{-4} M amino acid **4** (horizontal bar indicates long-lived change in conductivity).

"normal" cationic species in the overall reaction sequence in an acidic solution as shown in eqs 4 and 5. At the pH of the experiment, compound **4** is an overall neutral zwitterion (COO^-, NH_3^+); after oxidation, it becomes overall singly positively charged (NH_3^+) since the carboxylate is now "neutralized" in the >S∴OOC– bond. Based on the known specific conductivity of the proton (Λ = 315 Ω^{-1} cm^2 at 18 °C) and an assumed $\Lambda \approx 45$ Ω^{-1} cm^2 for the oxidized amino acid (i.e., $\Delta\Lambda = -270$ Ω^{-1} cm^2), the actual yield of **5** is calculated to G = 1.5 (corresponding to ca. 25% with respect to •OH).

$$\text{•OH} + \mathbf{4}\ (COO^-, NH_3^+) \rightarrow \mathbf{5}\ (NH_3^+) + OH^- \quad (4)$$

$$OH^- + H^+ \rightarrow H_2O \quad (5)$$

A corresponding experiment conducted at pH 4.2 gave a measured value of $G\Delta\Lambda = -300$ Ω^{-1} cm^2 for the initial decrease and an actual yield of G = 1.1 for **5** at this pH (ca. 20% yield with respect to •OH). This is lower than that at pH 3.6 and in accord with the trend obtained from the optical measurements.

The increase in conductivity following the initial decrease is compatible with a liberation of a proton at the expense of a "normal" cationic charge and therefore indicates that the decay of **5** is associated with a deprotonation process. In analogy to the decay of sulfur-centered radical cations,[20] this is assumed to yield the carbon-centered radical **6a,b**.

The long-lived negative conductivity change cannot be assigned unambiguously to a particular species. It may in part be due to a nonstoichiometric deprotonation of **5** (or a consecutive product) or to an ionic disproportionation of the carbon-centered radicals **6a,b**. Cationic species that are stable within the millisecond to second time range have, in fact, been observed to result from the latter type process in the radical-induced oxidation of many organic sulfides.[20,24]

The absolute yields derived from the conductivity measurements allow the calculation of extinction coefficients for the transient **5**. From $G\epsilon$ = 5000 at pH 3.6 and 3500 at pH 4.2, almost identical values of $\epsilon \approx 3350$ and 3150 M^{-1} cm^{-1}, respectively, are calculated. The average of ϵ = 3250 ± 500 M^{-1} cm^{-1} agrees well, within magnitude, with ϵ = 3900 M^{-1} cm^{-1} derived for the corresponding species **3** from the *endo*-carboxylic acid that lacks the amino group.[13]

Decarboxylation. Curve b in Figure 4 shows the CO_2 yields obtained upon γ-irradiation of N_2O-saturated solutions of 3 × 10^{-4} M **4** as a function of pH. The curve is sigmoidal and shows a break point around pH 4. It complements the pH dependence of the yields of **5** shown in curve a of Figure 4. The CO_2 yield decreases with increasing solute concentration, e.g., to $G \approx 0.8$ at pH 4.4 for a 10^{-3} M solution of **4**.

Discussion

Reaction Mechanism and pH Dependence. Any discussion of possible reaction mechanisms must take into account that the optically absorbing intermediate **5**, characterized by a three-electron sulfur–carboxyl bond cannot be the species that undergoes decarboxylation. The most obvious and convincing argument, among others, for this is that the kinetic lifetime of **5** does not change over the pH range in which the yields of **5** and CO_2 show their dramatic and complementary pH dependence. Mechanistic considerations must also take into account the acid/base properties of the carboxyl and the amino group both in the unoxidized molecule as well as in the radicals generated from them.

The minimal mechanism based on these premises and generally accepted prior precedents from the radical-induced oxidation of organic sulfides, in general, postulates a sulfur–hydroxyl adduct **8** as first-formed intermediate.[3,20,25] The fate of this species then depends on pH and solute concentration. In very acidic solutions,

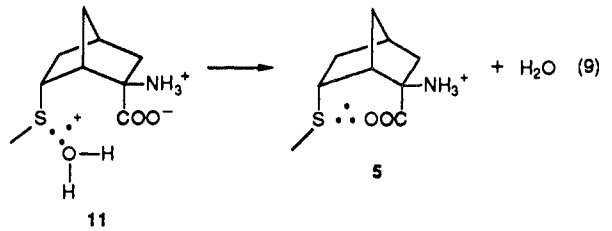
$$\underset{\mathbf{8}}{>S.\therefore OH} + H^+ \rightarrow \underset{\mathbf{9}}{(>S.\therefore OH_2)^+} \quad (6)$$

i.e., under conditions where both the amino and the carboxyl groups are protonated ($-NH_3^+$ and –COOH), **8** is protonated by reaction with free H^+ from the solution to yield the radical cation **9**, which is probably best characterized as molecular sulfide radical cation (>S$^{\bullet+}$) complexed with one water molecule[26-28] and with a sulfur–oxygen three-electron bond. This radical cation undergoes predominantly either of two reactions: deprotonation at carbon α to sulfur to yield the carbon-centered radicals **6a,b** (absorbing at 280 nm) as shown in eq 7 and a displacement reaction with

$$\mathbf{9} \rightarrow H^+ + \mathbf{6a,b} \quad (7)$$

a second unoxidized sulfide molecule to give the dimeric sulfur–sulfur three-electron-bonded radical cation **10** as shown in eq 8.

$$\mathbf{9} + \mathbf{4} \rightleftarrows \underset{\mathbf{10}}{(>S.\therefore S<)^+} + H_2O \quad (8)$$



Formation of **10** is therefore favored both at low pH but also at high solute concentrations and indicated by a characteristic optical absorption in the 500-nm range. This has been demonstrated, for example, in an extensive study on the oxidation of methionine.[2]

As the pH is increased, sufficient carboxylate is present so that reaction 9 becomes important. In this reaction, nucleophilic carboxylate displaces water from sulfur, thereby forming an *intra*molecular sulfur–oxygen three-electron bond. The yield of species **5** reaches a maximum at pH ≈ 2.5, which is consistent with ionization of the carboxylic acid moiety as suggested above. The pK_a of the carboxyl group in **4** is probably close to that of the carboxyl group in methionine, which is 2.4.[17] It should be noted that **11** and **5** are structurally completely different species.

Species **5** does not decarboxylate because it has a constant lifetime over the pH 2.5–8 range in which the CO_2 yield dramatically increases at the expense of a corresponding decrease in the yield of **5**. This implies that it must be the precursor of **5**, namely, species **11**, which undergoes a pH-dependent decarboxylation in competition with the formation of **5** via reaction 9. The common break points of the yield curves suggest deprotonation with a pK_a in the range of 4–5 as the underlying reason. This cannot be simply deprotonation of the amino group in the

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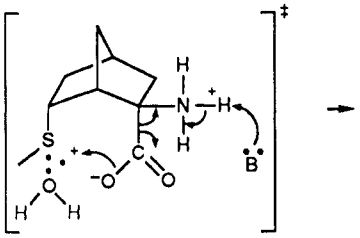
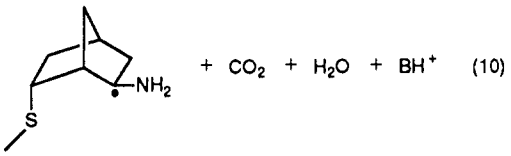
unoxidized molecule **4** nor in a radical species in which the oxidized-sulfur function remains entirely isolated from the amino acid moiety because the respective pK_as of the amino group are much higher at ca. 9. The observed break point is, however, close to the pK_a of an α-amino radical, that is, the radical remaining after the decarboxylation (e.g., pK_a = 3.85 for the α-amino radical from methionine[9]). Consequently, deprotonation of **11** in concert with decarboxylation to directly form the α-amino radical **7** (as shown in eq 10) would fully account for the observed pH de-



11



7

pendence (B = base, e.g., H_2O). The transition state for this process involves a one-electron transfer from carboxylate to the sulfur radical cation/water complex, homolysis of the carbon–carbon bond involving the carboxylate group, and deprotonation of the ammonium group by water (or hydroxide ion). The simultaneous occurrence of these three processes with their stereoelectronic constraints would be expected to require a high degree of ordering. This may be achievable because of the preorganization built into the norbornane-based amino acid **4**. Irrespective of structural consideration, reaction 10 receives an energetic driving force from the resonance stabilization of the unpaired electron in **7** with the free electron pair at nitrogen.[9,10] This clearly signifies the importance of the amino pK_a in the α-amino radical. The electron transfer itself resembles features of an indirect Kolbe mechanism.[12] The proposed mechanism is also in accord with the lack of decarboxylation of **2**, that is, the carboxylic acid that does not contain an α-amino group.[13]

Comparison with Methionine. The characteristics of the short-lived transient **5** differ significantly from those of the intermediate **1** observable during the •OH-induced oxidation of methionine.[2,3] The latter absorbs at 400 nm as compared to 340 nm of **5**. With respect to stability, **1** is not formed at all in very acidic solution and exists only at pH >3, completely contrary to the pH dependence of the stability of **5**. Furthermore, the lifetime of **1** ($t_{1/2}$ = 220 ns) is shorter by ca. 2 orders of magnitude than that of **5**. In fact, pulse radiolysis of the *endo*-amino/*exo*-carboxylate isomer of **4**[29] yields a transient, which with respect to the absorption (λ_{max} 400 nm) and lifetime ($t_{1/2}$ = 0.5–2 μs depending on pH) closely resemble the S∴N-bonded intermediate from methionine.[9]

It can thus be concluded that the general structures of the two species must be distinctly different, and this, in turn, can be taken as additional support for sulfur–nitrogen interaction in the methionine-derived transient.[2-4] Indeed, the properties of **5** resemble much more those of the corresponding transient derived from *S*-methylcysteine[3,8] and thus can serve as supporting evidence for sulfur–oxygen (sulfur–carboxylate) interaction in both species.

The position of λ_{max} of **5** (340 nm) is blue-shifted by 50 nm compared to that of the corresponding sulfur–carboxylate intermediate **3** (390 nm), which does not contain the amino function.[13-15] This is plausibly explained by the electronic structure of the sulfur–carboxylate interaction system, which despite a probably strong delocalization of electron density toward the more electronegative oxygen may be viewed in terms of a $2\sigma/1\sigma^*$ bond. For three-electron bonds, in general, it has been established that the visible optical absorption band in first approximation is due to a $\sigma \rightarrow \sigma^*$ transition and thus reflects the overall strength of the three-electron bond.[20,24,25,30-35] The latter depends mainly on the electron density in the antibonding orbital, and any change thereof induced by electron-releasing or -withdrawing substituents shows up as a red or blue shift of the absorption, respectively. The strong electron-withdrawing effect of the protonated amino group in **5** thus provides a most reasonable rationale for the observed spectral shift.

Conclusion

The most important conclusion that can be deduced from our present experiments is that the sulfur-centered radical cation/water adduct (species **11**) can undergo a pH-dependent decarboxylation in competition with a collapse to the sulfur–decarboxylate three-electron-bonded species **5**. This mechanistic scheme may apply in general to any radical-induced oxidation of carboxylic acids with an α-positioned heteroatom as indicated, for example, in the •OH radical induced decarboxylation of α-hydroxyl carboxylic acids[8] or methionine-containing di- and tripeptides.[18,36]

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Registry No. 4, 131486-46-9; **5**, 131407-10-8; HO•, 3352-57-6.

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