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Spectroscopic Detection, Reactivity, and Acid−Base Behavior of Ring-Dimethoxylated Phenylethanoic Acid Radical Cations and Radical Zwitterions in Aqueous Solution

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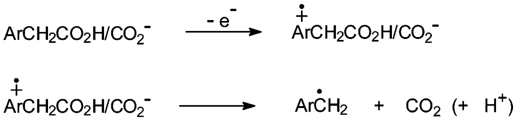
A product and time-resolved kinetic study of the one-electron oxidation of ring-dimethoxylated phenylethanoic acids has been carried out at different pH values. Oxidation leads to the formation of aromatic radical cations or radical zwitterions depending on pH, and pK_a values for the corresponding acid−base equilibria have been measured. The radical cations undergo decarboxylation with first-order rate constants (k_{dec}) ranging from $<10^2$ to 5.6×10^4 s^{-1} depending on radical cation stability. A significant increase in k_{dec} (between 10 and 40 times) is observed on going from the radical cations to the corresponding radical zwitterions. The results are discussed in terms of the ease of intramolecular side chain to ring electron transfer required for decarboxylation, in both the radical cations and radical zwitterions.

The oxidative decarboxylation of carboxylic acids represents an important reaction in both chemistry and biology.[1−4] In particular, the oxidation of arylethanoic acids has attracted considerable attention. The involvement of aromatic radical cations following the one-electron oxidation of arylethanoic acids has been proposed in several studies,[5,6] but clear evidence in this respect has been obtained only for relatively electron-rich substrates such as 1-naphthylethanoic acid,[7] 4-dimethylaminophenylethanoic acid and its α-methyl and α-hydroxy derivatives, and 2,4,5-trimethoxymandelic acid.[3] With these substrates a mechanism proceeding through a direct electron transfer from the aromatic ring with formation of an intermediate radical cation (or radical zwitterion) has been proposed. The radical cation then undergoes rapid decarboxylation leading to the corresponding benzylic-type radicals as described in Scheme 1.

SCHEME 1



With a less electron-rich substrate such as 4-methoxyphenylethanoic acid (**1**), a number of product studies led to the conclusion that one-electron oxidation proceeds through an analogous mechanism with formation of **1**$^{•+}$.[5a,e,6] The same mechanism was also proposed in a laser flash photolysis (LFP) study of the one-electron oxidation of 4-methoxy- and 4-methylphenylethanoic acids (**1** and **2**, respectively) in aqueous solution, even though no direct evidence for the formation of an intermediate radical cation but only of the 4-methoxy and 4-methylbenzyl radicals was provided.[7] In the same study, it was also shown that the decarboxylation rate constants, measured by following the formation of the corresponding benzyl radicals, increase by increasing pH, indicating that decarboxylation is faster when the carboxyl group is ionized.

Additional information comes from a recent indirect kinetic study of the effect of pH on the oxidation of **1** induced by potassium 12-tungstocobalt(III)ate (from now on simply indicated as Co(III)W).[8] This study led to the conclusion that no aromatic radical cation is formed as a reaction intermediate, electron removal from the aromatic ring being instead concerted with an intramolecular side chain to ring electron transfer, directly leading to a carboxyl radical that then undergoes rapid decarboxylation to give the 4-methoxybenzyl radical (Scheme 2).

Along this line, to obtain more information on the actual role of aromatic radical cations in these processes,

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[1] Kraeutler, B.; Jaeger, C. D.; Bard, A. J. *J. Am. Chem. Soc.* **1978**, *100*, 4903−4905 and references therein.

[2] Budac, D.; Wan, P. *J. Photochem. Photobiol. A: Chem.* **1992**, *67*, 135−166.

[3] Gould, I. R.; Lenhard, J. R.; Muenter, A. A.; Godleski, S. A.; Farid, S. *J. Am. Chem. Soc.* **2000**, *122*, 11934−11943.

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[5] (a) Maki, Y.; Sako, M.; Oyabu, I.; Murase, T.; Kitade, Y.; Hirota, K. *J. Chem. Soc., Chem. Commun.* **1989**, 1780−1782. (b) Gilbert, B. C.; Scarratt, C. J.; Thomas, C. B.; Young, J. *J. Chem. Soc., Perkin Trans. 2* **1987**, 371−380. (c) Walling, C.; El-Taliawi, G. M.; Amarnath, K. *J. Am. Chem. Soc.* **1984**, *106*, 7573−7578. (d) Walling, C.; Camaioni, D. M. *J. Org. Chem.* **1978**, *43*, 3266−3271. (e) Dessau, R. M.; Heiba, E. I. *J. Org. Chem.* **1975**, *40*, 3647−3649.

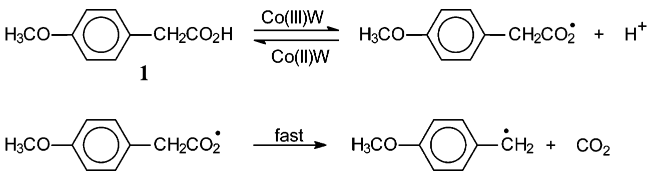
[6] (a) Jönsson, L. *Acta Chem. Scand.* **1983**, *B37*, 761−768. (b) Jönsson, L. *Acta Chem. Scand.* **1981**, *B35*, 683−689. (c) Trahanovsky, W. S.; Cramer, J.; Brixius, D. W. *J. Am. Chem. Soc.* **1974**, *96*, 1077−1081.

[7] Steenken, S.; Warren, C. J.; Gilbert, B. C. *J. Chem. Soc., Perkin Trans. 2* **1990**, 335−342.

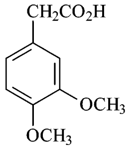
[8] Baciocchi, E.; Bietti, M. *J. Chem. Soc., Perkin Trans. 2* **2002**, 720−722.

10.1021/jo035492n CCC: $27.50

SCHEME 2



and in view of the observation that decarboxylation is faster when the carboxyl group is ionized, we have carried out a product and time-resolved kinetic study at different pH values on the one-electron oxidation of ring dimethoxylated phenylethanoic acids (**3**−**6**), substrates characterized by oxidation potentials which are intermediate between that of **1**,[9] and those of 4-dimethylaminophenylethanoic acid and its α-methyl and α-hydroxy derivatives described above.[3]



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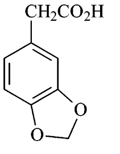

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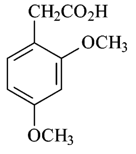

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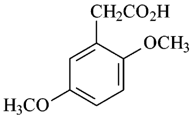

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Results and Discussion

Spectral Properties and Acid−Base Behavior. Argon-saturated aqueous solutions of substrates **3**−**6** (0.5−2 mM) were photolyzed (248 nm) in the presence of 0.1 M $K_2S_2O_8$ at pH ≈2 and pH ≈7. Under these conditions $SO_4^{\bullet-}$ is formed (eq 1).[7]

$$S_2O_8^{\ 2-} \xrightarrow[248\text{ nm}]{h\nu} 2SO_4^{\ \bullet-} \tag{1}$$

Alternatively, $SO_4^{\bullet-}$ was generated by pulse radiolysis (PR) of argon saturated aqueous solutions containing substrates **3**−**6** (0.2−2 mM), $K_2S_2O_8$ (10 mM), and 2-methyl-2-propanol (0.1 M), according to eqs 2−4.

$$H_2O \rightsquigarrow H^+, {}^\bullet OH, e_{aq}^{\ -} \tag{2}$$

$${}^\bullet OH + CH_3C(CH_3)_2OH \rightarrow H_2O + {}^\bullet CH_2C(CH_3)_2OH \tag{3}$$

$$e_{aq}^{\ -} + S_2O_8^{\ 2-} \rightarrow SO_4^{\ 2-} + SO_4^{\ \bullet-} \tag{4}$$

Radiolysis of water leads to the formation of the hydroxyl radical (${}^\bullet OH$) and the hydrated electron (e_{aq}^-) (eq 2). The former is scavenged by 2-methyl-2-propanol (eq 3; $k = 6 \times 10^8$ M^{-1} s^{-1}),[11] while e_{aq}^- reacts with the peroxydisulfate anion leading to the formation of $SO_4^{\bullet-}$ (eq 4; $k = 1.2 \times 10^{10}$ M^{-1} s^{-1}).[11] $SO_4^{\bullet-}$ is a strong oxidant that is able to react with ring-methoxylated aromatic substrates via electron transfer to yield the corresponding radical cations with $k \geq 5 \times 10^9$ M^{-1} s^{-1} (eq 5).[12−14]

$$SO_4^{\ \bullet-} + ArR \rightarrow SO_4^{\ 2-} + Ar^{\bullet+}R \tag{5}$$

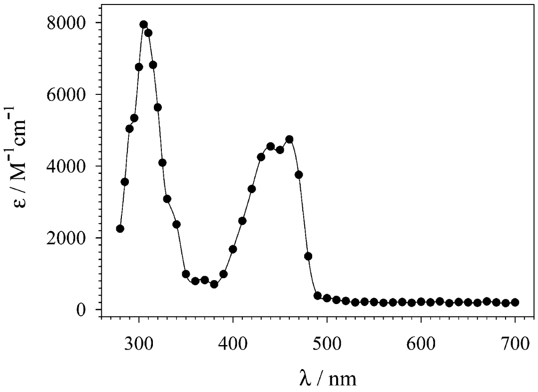

FIGURE 1. Time-resolved absorption spectrum observed on reaction of $SO_4^{\bullet-}$ with **6** (0.2 mM) recorded after pulse radiolysis of an argon-saturated aqueous solution (pH 1.7), containing 0.1 M 2-methyl-2-propanol and 10 mM $K_2S_2O_8$, at 8 μs after the 300-ns, 10-MeV electron pulse. For the determination of the extinction coefficient, *G*(radical cation) = *G*($SO_4^{\bullet-}$) = 3.1 × 10^{-7} mol J^{-1} was used.[19,20]

In acid solution, Tl^{2+} was also used as the oxidant, produced by PR of N_2O saturated aqueous solutions. The function of N_2O is to scavenge e_{aq}^-, leading to the formation of an additional hydroxyl radical (eq 6), with $k = 9.1 \times 10^9$ M^{-1} s^{-1}.[15] Tl^{2+} is then produced by oxidation of Tl^+ by ${}^\bullet OH$ (eq 7) with $k = 1.2 \times 10^{10}$ M^{-1} s^{-1}.[16] Also Tl^{2+} reacts with ring methoxylated aromatic substrates by electron transfer to give the corresponding radical cations (eq 8) with $k \approx 5 \times 10^8$ M^{-1} s^{-1}.[14]

$$e_{aq}^{\ -} + N_2O + H_2O \rightarrow N_2 + {}^\bullet OH + {}^-OH \tag{6}$$

$${}^\bullet OH + T1^+ + H^+ \rightarrow T1^{2+} + H_2O \tag{7}$$

$$T1^{2+} + ArR \rightarrow T1^+ + Ar^{\bullet+}R \tag{8}$$

The transients produced after LFP or PR of acidic aqueous solutions (pH ≤2) containing **3**−**6** showed UV and visible absorption bands centered around 270−310 and 420−480 nm which are analogous to those observed for the corresponding ring dimethoxylated aromatic radical cations.[14,17,18] As an example, Figure 1 shows the time-resolved absorption spectrum observed after PR of

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[9] The following one-electron oxidation potentials have been determined in aqueous solution for anisole, 1,2-, 1,3-, and 1,4-dimethoxybenzene respectively 1.62, 1.44, 1.58, and 1.30 V/NHE,[10] substrates which can be taken as models for **1**, **3** (and **4**), **5**, and **6**, respectively.

[10] Jonsson, M.; Lind, J.; Reitberger, T.; Eriksen, T. E.; Merényi, G. *J. Phys. Chem.* **1993**, *97*, 11278−11282.

[11] Buxton, G. V.; Greenstock, C. L.; Helman, W. P.; Ross, A. B. *J. Phys. Chem. Ref. Data* **1988**, *17*, 513−886.

[12] Baciocchi, E.; Bietti, M.; Putignani, L.; Steenken, S. *J. Am. Chem. Soc.* **1996**, *118*, 5952−5960.

[13] Neta, P.; Madhavan, V.; Zemel, H.; Fessenden, R. W. *J. Am. Chem. Soc.* **1977**, *99*, 163−164.

[14] O'Neill, P.; Steenken, S.; Schulte-Frohlinde, D. *J. Phys. Chem.* **1975**, *79*, 2773−2779.

[15] Janata, E.; Schuler, R. H. *J. Phys. Chem.* **1982**, *86*, 2078−2084.

[16] Schwarz, H. A.; Dodson, R. W. *J. Phys. Chem.* **1984**, *88*, 3643−3647. Asmus, K.-D.; Bonifacic, M.; Toffel, P.; O'Neill, P.; Schulte-Frohlinde, D.; Steenken, S. *J. Chem. Soc., Faraday Trans. 1* **1978**, *74*, 1820−1826.

[17] Baciocchi, E.; Bietti, M.; Gerini, M. F.; Manduchi, L.; Salamone, M.; Steenken, S. *Chem. Eur. J.* **2001**, *7*, 1408−1416.

[18] No direct evidence for the formation of the ring-dimethoxylated benzyl radicals was obtained. It is, however, possible that under oxidative conditions, due to their very low oxidation potential, these radicals are rapidly oxidized to the corresponding cations. See for example: Wayner, D. D. M.; Sim, B. A.; Dannenberg, J. J. *J. Org. Chem.* **1991**, *56*, 4853−4858.

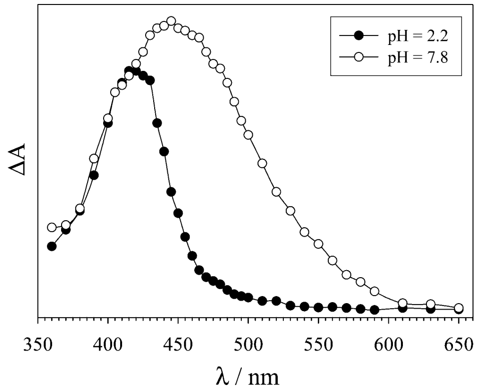

FIGURE 2. Time-resolved absorption spectra observed after 248-nm LFP of argon-saturated aqueous solutions containing 0.1 M $K_2S_2O_8$ and 2 mM **3**, recorded at pH 2.2 (solid circles) and pH 7.8 (open circles), 1 μs after the 20-ns, 5-mJ laser flash. For the experiment at pH 2.2 the pH was adjusted with $HClO_4$, while 1 mM Na_2HPO_4 was added to the solution and the pH was adjusted with NaOH for the experiment at pH 7.8.

an argon-saturated aqueous solution (pH 1.7) containing **6** (0.2 mM), 2-methyl-2-propanol (0.1 M), and $K_2S_2O_8$ (10 mM). Two bands are visible, centered around 310 and 450 nm. An identical spectrum was obtained after 248-nm LFP of an argon-saturated aqueous solution (pH 2.0) containing $K_2S_2O_8$ (0.1 M) and **6** (0.4 mM).

On the basis of these observations, the transients described above can be reasonably assigned to the dimethoxylated phenylethanoic acid radical cations $\mathbf{3}^{\bullet+}$–$\mathbf{6}^{\bullet+}$, formed by $SO_4^{\bullet-}$ or Tl^{2+} induced one-electron oxidation of the neutral substrates as described in eq 9.

$$SO_4^{\bullet-}(T1^{2+}) + ArCH_2CO_2H \rightarrow SO_4^{2-}(T1^{+}) + Ar^{\bullet+}CH_2CO_2H \quad (9)$$

By increasing the pH of the solution to ≈7, the spectra obtained after $SO_4^{\bullet-}$ induced one-electron oxidation of **3**–**6** were similar to those obtained in acidic solution. However, a broadening of the radical cation visible absorption band accompanied in some cases by a slight red shift of its position (between 15 and 30 nm) was observed, a behavior that is attributed to the formation of the radical zwitterions $^{-}\mathbf{3}^{\bullet+}$–$^{-}\mathbf{6}^{\bullet+}$.[21] As an example, Figure 2 shows the time-resolved absorption spectra observed after 248-nm LFP of argon-saturated aqueous solutions containing **3** (2 mM) and $K_2S_2O_8$ (0.1 M) at pH 2.2 (solid circles) and pH 7.8 (open circles). The broadening of the visible absorption band is accompanied by a 30-nm red shift of its position on going from $\mathbf{3}^{\bullet+}$ to $^{-}\mathbf{3}^{\bullet+}$.

By measuring the absorption at a suitable wavelength (where the difference in absorption between radical cation and radical zwitterion is sufficiently large) as a function of pH, the pK_a values for the acid–base equilibria between the radical cations and the corresponding radical zwitterions (eq 10) were determined.

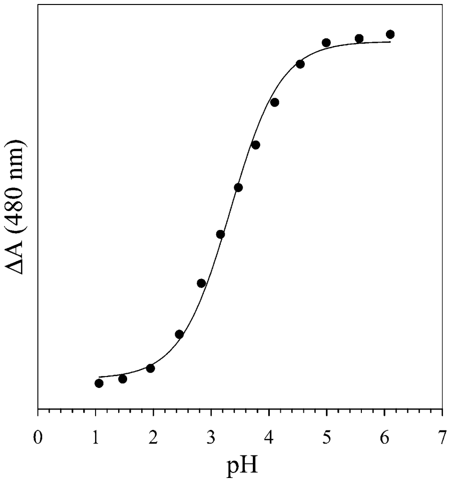

FIGURE 3. Plot of ΔA monitored at 480 nm vs pH for $\mathbf{6}^{\bullet+}$, generated after 248-nm LFP of an argon-saturated aqueous solution containing 0.1 M $K_2S_2O_8$ and 0.4 mM **6**. From the curve fit pK_a = 3.33 ± 0.04 (r = 0.997).

TABLE 1. Visible Absorption Band Maxima for Radical Cations and Radical Zwitterions Generated from Substrates 3–6,[a] and Corresponding pK_a Values for Their Acid–Base Equilibria, Measured at Room Temperature

substrate	λ_{max}(vis)[b] (nm)	λ_{monit}[c] (nm)	[substrate] (mM)	pK_a[d]
3	420 (450)	460	2	3.49 ± 0.05
4	430 (450)	470	2	3.67 ± 0.07
5	455, 480 (480)[e]	[f]		
6	450 (450)	480	0.4	3.34 ± 0.02

[a] Generated by 248-nm LFP as described above. [b] Visible absorption band maxima for radical cations $\mathbf{3}^{\bullet+}$–$\mathbf{6}^{\bullet+}$. The values for the corresponding radical zwitterions are given in parentheses. [c] Monitoring wavelength for pK_a determination. [d] Based on the average of two or three independent measurements. [e] Shoulder at 455 nm. [f] The radical zwitterion $^{-}\mathbf{5}^{\bullet+}$ is not sufficiently stable (see later) to allow a reliable pK_a determination.

$$Ar^{\bullet+}CH_2CO_2H + H_2O \rightleftharpoons ArCH_2CO_2^{-} + H_3O^{+} \quad (10)$$

Figure 3 shows the plot of ΔA (monitored at 480 nm) vs pH for the acid–base equilibrium between $\mathbf{6}^{\bullet+}$ and $^{-}\mathbf{6}^{\bullet+}$.

The pK_a values thus obtained for $\mathbf{3}^{\bullet+}$–$\mathbf{6}^{\bullet+}$ are collected in Table 1, together with the visible absorption band maxima for the radical cations and radical zwitterions.

With the exception of the equilibrium between $\mathbf{5}^{\bullet+}$ and $^{-}\mathbf{5}^{\bullet+}$ where the latter was too reactive (see later) to allow a reliable pK_a determination, similar pK_a values (between 3.34 and 3.67) were obtained for $\mathbf{3}^{\bullet+}$, $\mathbf{4}^{\bullet+}$, and $\mathbf{6}^{\bullet+}$. On the basis of a pK_a value of 4.33 measured for **3**,[22] it appears that in $\mathbf{3}^{\bullet+}$ the increased electron withdrawing effect caused by the presence of an electron hole on the aromatic ring leads to an increase in acidity of almost one pK_a unit. In this context, the slight difference observed between $\mathbf{3}^{\bullet+}$ (and $\mathbf{4}^{\bullet+}$) and $\mathbf{6}^{\bullet+}$ may reflect the fact that the 2-methoxy group (in $\mathbf{6}^{\bullet+}$) is closer to the acidic center than the 3-methoxy group (in $\mathbf{3}^{\bullet+}$).

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(19) Faria, J. L.; Steenken, S. *J. Phys. Chem.* **1992**, *96*, 10869–10874.

(20) Where G is the radiation chemical yield defined as the number of radicals produced by 100 eV of absorbed radiation (1 molecule/100 eV = 1.036 × 10^{-7} mol J^{-1}). For further details see: Spinks, J. W. T.; Woods, R. J. *An Introduction to Radiation Chemistry*, 3rd ed.; Wiley: New York, 1990.

(21) This notation represents an oversimplification since, as compared to the radical cations, the corresponding radical zwitterions lack the presence of the carboxylic proton.

(22) Kortüm, G.; Vogel, W.; Andrussow, K. *Dissociation Constants of Organic Acids in Aqueous Solution*; Butterworth: London, UK, 1961.

SCHEME 3

$$ArCH_2^{\bullet} \xrightarrow[2)\ H_2O,\ -\ H^+]{1)\ ox} ArCH_2OH \longrightarrow \longrightarrow ArCHO$$

It is also interesting to compare the values collected in Table 1 with those reported in the literature for monosubstituted acetic acids, showing that the increase in acidity determined by the positively charged ring is significantly smaller than that determined by α-chloro ($pK_a = 2.86$) and α-cyano ($pK_a = 2.46$) groups, being instead comparable with that resulting from the presence of an α-methoxy group ($pK_a = 3.54$).[23] An even more pronounced effect is observed when the comparison is made with a positively charged acid such as the protonated form of the α-amino acid glycine, $H_3N^+CH_2CO_2H$, for which $pK_{a1} = 2.35$.[23] This large difference in acidity is likely to reflect the fact that in the radical cations the positive charge is delocalized over a relatively large dimethoxyphenyl system and the resulting electron withdrawing effect is relatively weak, while in $H_3N^+CH_2$-CO_2H the extent of charge delocalization is instead limited resulting in a much stronger electron withdrawing effect.

Product Studies. The oxidation reactions of substrates **3**−**6** were carried out in argon saturated aqueous solution (pH 1.0 and 6.7) at room temperature, employing Co(III)W or $SO_4^{\bullet-}$ (generated by steady state 254-nm photolysis as described in eq 1) as the oxidant. Co(III)W is a well-known one-electron oxidant able to oxidize methoxybenzene derivatives via outer-sphere electron transfer.[8,24] For all substrates product analysis, at both pH 1.0 and 6.7, showed the formation of the corresponding benzyl alcohol accompanied by smaller amounts of benzaldehyde, and similar results were obtained with the two oxidants. Experiments carried out varying the substrate/Co(III)W ratio showed that the aldehyde is formed by oxidation of the first-formed alcohol.

These results, together with those of the time-resolved experiments described above, are consistent with the mechanism shown in Scheme 1: formation of an intermediate radical cation or zwitterion followed by decarboxylation to give a benzyl radical. Oxidation of the benzyl radical in the reaction medium leads to the benzyl alcohol, which eventually can be further oxidized to give the corresponding benzaldehyde, as described in Scheme 3.[8,12,24b]

Thus, differently than with the monomethoxylated derivative **1**, the increased electron density derived from the presence of an additional methoxy group on the aromatic ring induces a mechanistic changeover with formation of an intermediate radical cation.

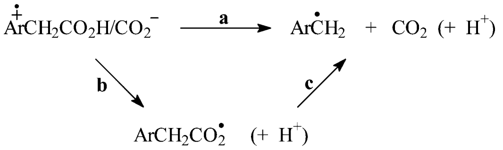
Kinetic Studies. These were carried out by using the pulse radiolysis technique. The decay rates of the radical cations $\mathbf{3}^{\bullet+}$−$\mathbf{6}^{\bullet+}$ and zwitterions $^{-}\mathbf{3}^{\bullet+}$−$^{-}\mathbf{6}^{\bullet+}$ were measured spectrophotometrically, following the decrease in optical density at the visible absorption band maxima (420−480 nm), and were found to follow first-order kinetics in a reaction which, on the basis of product analysis results, is assigned to decarboxylation. All the rate constants for decarboxylation of the radical cations and radical zwitterions (k_{dec}) measured at different pH values are collected in Table 2.

TABLE 2. First-Order Rate Constants (k_{dec}) for the Decarboxylation of Radical Cations $\mathbf{3}^{\bullet+}$−$\mathbf{6}^{\bullet+}$ and Radical Zwitterions $^{-}\mathbf{3}^{\bullet+}$−$^{-}\mathbf{6}^{\bullet+}$ Generated by Pulse Radiolysis of the Parent Substrates in Aqueous Solution, Measured at Room Temperature

substrate	pH	transient	oxidant	$\lambda_{det}{}^a$ (nm)	k_{dec} (s^{-1})
3	1.7	$\mathbf{3}^{\bullet+}$	$SO_4^{\bullet-}$	425	5.2×10^3
	1.7	$\mathbf{3}^{\bullet+}$	Tl^{2+}	425	5.2×10^3
	7.1−10.2	$^{-}\mathbf{3}^{\bullet+}$	$SO_4^{\bullet-}$	450	6.5×10^4
4	1.7	$\mathbf{4}^{\bullet+}$	Tl^{2+}	425	3.8×10^3
	7.0−10.2	$^{-}\mathbf{4}^{\bullet+}$	$SO_4^{\bullet-}$	450	6.6×10^4
5	1.4	$\mathbf{5}^{\bullet+}$	$SO_4^{\bullet-}$	460	5.6×10^4
	6.3	$^{-}\mathbf{5}^{\bullet+}$	$SO_4^{\bullet-}$	480	2.0×10^6 [b]
6	1.7	$\mathbf{6}^{\bullet+}$	Tl^{2+}	450	$<10^2$ [c]
	7.4−10.8	$^{-}\mathbf{6}^{\bullet+}$	$SO_4^{\bullet-}$	450	$<10^2$ [c]

[a] Monitoring wavelength. [b] Generated by LFP of an argon saturated aqueous solution (pH 6.3) containing **5** (10 mM) and $K_2S_2O_8$ (0.1 M), as described above (eqs 1 and 5). [c] The time resolution of the instrument did not allow the measurement of the decarboxylation rate constant and only an upper limit is provided ($k_{dec} < 10^2\ s^{-1}$).

SCHEME 4



Interestingly, reactivity parallels radical cation stability,[9,10] k_{dec} increasing in the following order: $\mathbf{6}^{\bullet+} \ll \mathbf{3}^{\bullet+} \cong \mathbf{4}^{\bullet+} < \mathbf{5}^{\bullet+}$. This reactivity order can be rationalized in terms of the ease of the intramolecular side chain to ring electron transfer required for decarboxylation, which is influenced by the extent of stabilization of the positive charge on the aromatic ring and hence by the number and relative position of methoxy groups.

Thus, $\mathbf{6}^{\bullet+}$ displays the lower reactivity in line with the greater stabilization of the positive charge in the 2,5-dimethoxyphenyl system as compared to the 2,4- and 3,4-dimethoxyphenyl ones.[9,10] In other words the intramolecular side chain to ring electron transfer is significantly more costly in $\mathbf{6}^{\bullet+}$ as compared to $\mathbf{3}^{\bullet+}$, $\mathbf{4}^{\bullet+}$, and $\mathbf{5}^{\bullet+}$, and accordingly its reactivity is strongly depressed.

For **3**, **4**, and **5** a significant increase in k_{dec} was observed on going from the radical cation (pH ≤1.7) to the corresponding radical zwitterion (pH >6), and no significant difference in reactivity was observed between pH 6 and 10. The lower decarboxylation rate constants measured for $Ar^{\bullet+}CH_2CO_2H$ as compared to $Ar^{\bullet+}CH_2CO_2^-$ can be again rationalized in terms of the kinetic barrier for intramolecular side chain to ring electron transfer, which should be higher for the former, since in this case an additional proton transfer to the medium is required.[8]

Unfortunately, these data do not provide any information on whether decarboxylation occurs directly from the radical cation or zwitterion (Scheme 4, path **a**) or if an intermediate arylacetoxyl radical is involved (paths **b** and **c**), as previously shown in the case of benzoic acids.[25]

Accordingly, rate constants $k \geq 1.5 \times 10^9\ s^{-1}$ have been measured for the decarboxylation of a series of phenyl-

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(23) Streitwieser, A.; Heathcock, C. H.; Kosower, E. M. *Introduction to Organic Chemistry*, 4th ed.; Prentice Hall: Upper Saddle River, NJ, 1998.

(24) (a) Weinstock, I. A. *Chem. Rev.* **1998**, *98*, 113−170. (b) Baciocchi, E.; Bietti, M.; Mattioli, M. *J. Org. Chem.* **1993**, *58*, 7106−7110. (c) Eberson, L. *J. Am. Chem. Soc.* **1983**, *105*, 3192−3199.

acetoxyl radicals,[26,27] showing moreover that no significant effect on reactivity results from the presence of ring substituents,[27] values which are at least 3 orders of magnitude higher than those reported in Table 2 for decarboxylation of the radical cations and radical zwitterions. Thus, the extremely fast rate constants measured independently for reaction **c** do not allow us to distinguish between the concerted (path **a**) or stepwise (through paths **b** and **c**) nature of the conversion of the radical cation (zwitterion) into the benzyl radical.[28]

In conclusion this work clearly shows that aromatic radical cations and radical zwitterions are intermediates in the one-electron oxidation of ring-dimethoxylated phenylethanoic acids, providing moreover for the first time pK_a values for their acid−base equilibria. The radical cations undergo decarboxylation with rate constants which depend on the stabilization of the positive charge on the aromatic ring, i.e., on the height of the kinetic barrier for side chain to ring intramolecular electron transfer, and a significant increase in reactivity is observed for the corresponding radical zwitterions. More importantly, these results provide a more complete mechanistic picture for the one-electron oxidation of arylethanoic acids in aqueous solution, a process that is governed by the interplay between electron removal from the aromatic ring and intramolecular side chain to ring electron transfer required for decarboxylation. With **1** (and with less electron rich arylethanoic acids such as **2**), electron removal is relatively costly and is thus coupled with the intramolecular electron transfer, i.e., no radical cation intermediate is formed. By increasing ring electron density (as in substrates **3**−**6**), electron removal becomes easier while the rate of intramolecular electron transfer is depressed and a stepwise mechanism, proceeding through the formation of a radical cation (or radical zwitterion) followed by decarboxylation, occurs.

Experimental Section

Reagents. Potassium peroxydisulfate, sodium hydroxide, disodium tetraborate decahydrate, disodiumhydrogen phosphate, perchloric acid, and 2-methyl-2-propanol were of the highest commercial quality available. Potassium 12-tungstocobalt(III)ate (Co(III)W) was prepared as described previously.[24b] Milli-Q-filtered (Millipore) water was used for all solutions.

Commercial samples of (3,4-dimethoxyphenyl)acetic acid (**3**), (3,4-methylenedioxy)phenylacetic acid (**4**), (2,4-dimethoxyphenyl)acetic acid (**5**), and (2,5-dimethoxyphenyl)acetic acid (**6**) were used as received.

Product Studies. (a) Oxidations with Co(III)W. A 5-mL sample of an argon-saturated aqueous solution (pH 1.0 or 6.7) containing the substrate (5 mM) and Co(III)W (substrate/Co(III)W ratio = 0.5−2) was stirred at $T = 25$ °C until complete conversion of the oxidant.

(b) Oxidations with $SO_4^{\bullet-}$. A 20-mL sample of an argon-saturated aqueous solution (pH 1.0 or 6.7) containing the substrate (2 mM) and $K_2S_2O_8$ (0.1 M) was irradiated at room temperature for 0.5 min employing a Photochemical Multirays Reactor (Helios Italquartz) equipped with 10 × 15 W 254 nm lamps.

With both oxidizing systems, the reaction mixture was acidified with 2 N HCl (only for the experiments at pH 6.7), extracted with ethyl ether, and dried over anhydrous Na_2SO_4 and the reaction products were identified by GC and GC-MS (comparison with authentic samples).

Time-Resolved Studies. (a) Pulse Radiolysis. The pulse radiolysis experiments were performed by using a 10 MeV electron linear accelerator that supplied 300-ns pulses with doses such that 1−3 μM radicals were produced. Experiments were performed at room temperature with argon-saturated aqueous solutions containing the substrate (0.5−2.0 mM), peroxydisulfate (2−10 mM), and 2-methyl-2-propanol (0.1 M). Alternatively, N_2O-saturated aqueous solutions (pH ≤ 2) containing the substrate (0.5 mM) and thallium(I) sulfate (2.0 mM) were employed. The pH of the solutions was adjusted with NaOH or $HClO_4$. For the experiments at pH ≈ 7 and ≈ 10, 2 mM Na_2HPO_4 or 1 mM $Na_2B_4O_7$, respectively, was added. A flow system was employed in all the experiments. The rate constants (k_{dec}) were obtained by averaging 4 to 8 values, each consisting of the average of 3 to 10 shots, and were reproducible to within 5%.

(b) Laser Flash Photlysis. The radical cations of interest were generated at room temperature by direct laser flash photolysis (LFP) of argon-saturated aqueous solutions, containing the substrate (0.4−2 mM) and $K_2S_2O_8$ (0.1 M), using a 248 nm excimer laser (KrF*, Lambda Physik EMG103MSC) providing 20-ns pulses with energies between 2 and 10 mJ/pulse (output power of the laser). The concentration of $K_2S_2O_8$ was such that this species absorbed most of the 248-nm radiation. The solutions were flowed through a 2 mm (in the direction of the laser beam) by 4 mm (in the direction of the analyzing light, 90° geometry) Suprasil quartz cell. All experiments were carried out at about 22 ± 2 °C. Optical detection was employed, with a pulsed xenon lamp as analyzing light. Wavelengths were selected with a monochromator. The time-dependent optical changes were recorded with Tektronix 7612 and 7912 transient recorders, interfaced with a DEC LSI 11/73$^+$ computer, which also controlled the other functions of the instrument and preanalyzed the data.[29]

pK_a values for the acid−base equilibria between the radical cations and corresponding radical zwitterions were determined by plotting ΔA as a function of pH at a fixed wavelength (where the difference in absorption between radical cation and radical zwitterion is sufficiently large) in the pH range 1−7, making sure that the measurements are conducted in the linear range of the detector. The ΔA vs pH curve was fitted to the following equation: $\Delta A = [\Delta A_0 + \Delta A_1 \times 10^{(\mathrm{pH}-\mathrm{p}K_a)}]/1 + 10^{(\mathrm{pH}-\mathrm{p}K_a)}$). Two or three independent pK_a determinations were carried out for every radical cation.

In the kinetic studies, $^{-}\mathbf{5}^{\bullet+}$ was generated by LFP of an argon-saturated aqueous solution (pH 6.3) containing **5** (10 mM) and $K_2S_2O_8$ (0.1 M), and the decay rate was measured spectrophotometrically, following its decrease in optical density at 480 nm.

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(28) In light of this observation, in the mechanism shown in Scheme 2 the possibility that decarboxylation is concerted with electron removal from the aromatic ring, bypassing 4-methoxyphenylacetoxyl radical formation, should also be considered.

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