Oxygen Versus Carbon Acidity in the Side-Chain Fragmentation of 2-, 3-, and 4-Arylalkanol Radical Cations in Aqueous Solution: The Influence of the Distance between the OH Group and the Aromatic Ring[1]

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Abstract: The decay of 2-, 3-, and 4-(4-methoxyphenyl) alkanol radical cations in water has been kinetically investigated by pulse radiolysis, the reaction products being determined either by steady-state γ-radiolysis experiments or by reactions promoted by potassium 12-tungstocobalt(III)ate, a bona fide one-electron oxidant. It was found that all 2-arylalkanol radical cations react with $^-$OH at a diffusion-controlled rate leading to $C_\alpha-C_\beta$ bond cleavage products. This suggests a reaction induced by deprotonation at the alcoholic OH group. In acidic medium (pH = 4), the rates of decay of these radical cations are much lower leading to $C_\alpha-$H deprotonation (for 2-(4-methoxyphenyl)ethanol ($1^{\bullet+}$) and 1-(4-methoxyphenyl)-2-propanol ($4^{\bullet+}$)) or $C_\alpha-C_\beta$ bond cleavage products (for 1-phenyl-2-(4-methoxyphenyl)ethanol ($5^{\bullet+}$) and 2-methyl-1-phenyl-3-(4-methoxyphenyl)-2-propanol ($6^{\bullet+}$)). The 3-(4-methoxyphenyl)propanol radical cation ($2^{\bullet+}$) reacts in acidic medium (pH = 4) at a rate close to that of $1^{\bullet+}$, undergoing $C_\alpha-$H deprotonation. In contrast, in basic medium (pH = 10) $2^{\bullet+}$ produces 3-(4-methoxyphenyl)propanal, with a rate ~5-fold lower than that of $1^{\bullet+}$, again indicating a reaction promoted by O$-$H deprotonation. With 4-(4-methoxyphenyl)-1-butanol radical cation ($3^{\bullet+}$), products of $C_\alpha-$H deprotonation were observed both in the presence and in the absence of $^-$OH. These results are discussed in terms of a mechanistic dichotomy, that is, carbon versus oxygen acidity, which appears to be operating for 2- and 3-arylalkanols whereas with 4-arylalkanol radical cations only carbon acidity is observed.

Recently, we have discovered that 1-(4-methoxyphenyl)-alkanol, (4-MeOC$_6$H$_4$CH(OH)R, R = H, alkyl) radical cations in aqueous solution can exhibit a very interesting mechanistic dichotomy (Scheme 1, An = 4-MeOC$_6$H$_4$).[3]

In the absence of added base, these species display the expected carbon acids behavior, undergoing $C_\alpha-$H (from now on simply indicated as C$-$H) deprotonation (path **a**); however, in the presence of $^-$OH the deprotonation site shifts from carbon to oxygen and the radical cations behave as oxygen acids (path **b** or **d**). It was suggested that deprotonation at the α-OH group leads to the formation of a benzyloxyl radical, either directly (intramolecular electron transfer coupled to proton transfer, path **d**) or via a radical zwitterion (path **b**) which can undergo an intramolecular electron transfer (path **c**). The benzyloxyl radical can then undergo a formal 1,2-hydrogen atom shift forming an α-hydroxybenzyl-type radical (path **e**) or a β-fragmentation reaction leading to R$^\bullet$ and 4-methoxybenzaldehyde (path **f**). The competition between the two pathways was found to depend on the nature of R: for R = H or Me only the 1,2-H shift was observed and for R = *t*Bu only $C_\alpha-C_\beta$ (from now on simply indicated as C$-$C) bond cleavage occurs. Intermediate situations hold for R = Et and *i*Pr.[4] Direct evidence for the formation of

Scheme 1
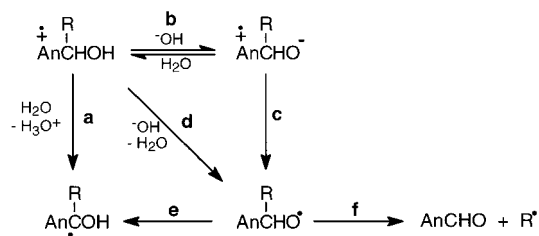
the benzyloxyl radical was indeed obtained in a pulse radiolysis study of the $^-$OH-induced decay of 4-methoxycumyl alcohol radical cation on its way to form 4-methoxyacetophenone and Me$^\bullet$.[5]

To gather additional information about the generality and the scope of the mechanistic dichotomy illustrated in Scheme 1, and about the factors which may influence the oxygen acidity of arylalkanol radical cations, we have investigated the role of the distance of the OH group from the aromatic ring. Thus, in this paper we report on a pulse radiolysis study of the reactivity in aqueous solution of the radical cations generated from 2-, 3-, and 4-(4-methoxyphenyl)-alkanols **1**−**6**, where the OH group is separated from the aromatic ring by an increasing number

(1) Dedicated to Dr. Keith U. Ingold on the occasion of his 70th birthday.
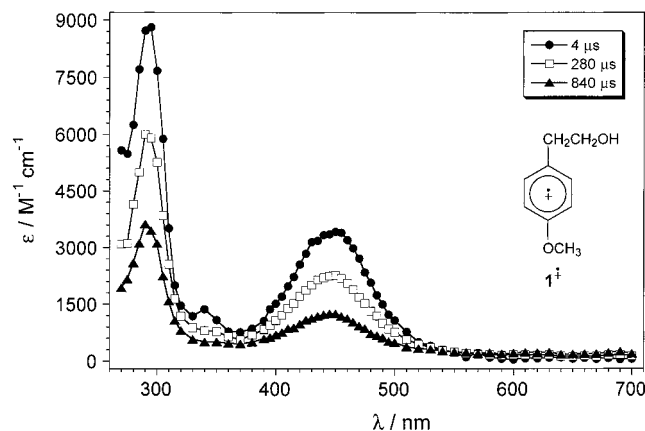
(2) (a) Universitá "La Sapienza"; (b) Universitá "Tor Vergata"; (c) Max-Planck-Institut.

(3) Baciocchi, E.; Bietti, M.; Steenken, S. *J. Am. Chem. Soc.* **1997**, *119*, 4078−4079.

(4) Baciocchi, E.; Bietti, M.; Steenken, S. *Chem. Eur. J.* **1999**, *5*, 1785−1793.

(5) Baciocchi, E.; Bietti, M.; Lanzalunga, O.; Steenken, S. *J. Am. Chem. Soc.* **1998**, *120*, 11516−11517.

(from 2 to 4) of carbon atoms. For comparison, the radical cations of the methyl ethers of **2**, **3**, and **4** (respectively **8**, **9**, and **7**) and that of 4-methoxytoluene (**10**) have also been investigated.

1: (n = 2)   **4**: (R = Me)   **6**   **7**   **8**: (n = 3)   **10**
2: (n = 3)   **5**: (R = Ph)   **9**: (n = 4)
3: (n = 4)

Some information about analogous arylalkanol radical cations, lacking however the methoxy ring substituent, has already been provided by Snook and Hamilton in their pioneering work[6] and later by Gilbert[7] and Walling[8] and their associates. However, in no case were the radical cations detected nor was any direct kinetic information provided.

Results

Radical cations of substrates **1**−**10** were generated in aqueous solution either by pulse radiolysis or by steady-state γ-radiolysis, employing sulfate radical anion ($SO_4^{\bullet-}$; method 1) or Tl^{2+} (method 2) as the oxidant.[9] Both oxidants are known to react with aromatic compounds by electron transfer, leading to the formation of the corresponding radical cation (eq 1).[9−11]

$$SO_4^{\bullet-}(Tl^{2+}) + ArOMe \rightarrow SO_4^{2-}(Tl^+) + Ar^{\bullet+}OMe \quad (1)$$

Product analysis of the reactions of radical cations **1**•+−**10**•+ was carried out after steady-state γ-radiolysis, generating the radical cations through method 1. Argon-saturated aqueous solutions containing 0.5−1.0 mM substrate, 0.2−0.5 mM $K_2S_2O_8$, and 0.2 M 2-methyl-2-propanol (added to scavenge the OH radicals produced on radiolysis of aqueous solutions) were irradiated at room temperature with a ^{60}Co γ-source at dose rates of 0.5 Gy s^{-1} for the time necessary to obtain a 40% conversion with respect to peroxydisulfate. To minimize over-oxidation of the first formed products, we carried out all experiments with a substrate/oxidant ratio of 2. The product distribution was studied at pH ≈ 4 and 10. In some experiments the radical cations were generated by oxidation of the neutral substrates with potassium 12-tungstocobalt(III)ate (Co(III)W),[10,12] a bona fide one-electron oxidant.[15,16]

(6) Snook, M. E.; Hamilton, G. A. *J. Am. Chem. Soc.* **1974**, *96*, 860−869.

(7) Davies, M. J.; Gilbert, B. C. *Adv. Detailed React. Mech.* **1991**, *1*, 35−81 and references therein.

(8) Walling, C.; El-Taliawi, G. M.; Zhao, C. *J. Org. Chem.* **1983**, *48*, 4914−4917.

(9) For a description of this technique see: O'Neill, P.; Steenken, S.; Schulte-Frohlinde, D. *J. Phys. Chem.* **1975**, *79*, 2773−2777.

(10) Baciocchi, E.; Bietti, M.; Putignani, L.; Steenken, S. *J. Am. Chem. Soc.* **1996**, *118*, 5952−5960.

(11) Neta, P.; Madhavan, V.; Zemel, H.; Fessenden, R. W. *J. Am. Chem. Soc.* **1977**, *99*, 163−164.

(12) When dealing with sufficiently long-lived radical cations (lifetime ≥ 0.1 ms) such as several of those reported in this study, we observed a very low conversion of the parent substrate in some steady-state γ-radiolysis experiments carried out in acid solution. On the basis of previous observations,[13,14] this behavior can be attributed to an electron-transfer reaction between the radical cation and $^{\bullet}CH_2C(CH_3)_2OH$ (formed by H-atom abstraction from 2-methyl-2-propanol by the OH radical), leading to the parent substrate and a carbocation. Thus in some cases the product study was carried out by generating the radical cation by reaction of the substrate with Co(III)W.

(13) Baciocchi, E.; Bietti, M.; Steenken, S. *J. Chem. Soc., Perkin Trans. 2* **1996**, 1261−1263.

Steady-State γ-Radiolysis. In basic solution (pH = 10) the reaction of **1** led to 4,4′-dimethoxybibenzyl (**11**) and 2-methyl-4-(4-methoxyphenyl)-2-butanol (**12**) as main products. A small amount of 4-methoxybenzyl alcohol was also formed together with traces of 4-methoxybenzaldehyde. These products clearly indicate that the radical cation undergoes C−C bond cleavage, as illustrated in Scheme 2 ($R_1 = R_2 = H$), leading to the 4-methoxybenzyl radical and $H_2C=O$.

Scheme 2

The benzyl radical can then follow different pathways: get oxidized by $S_2O_8^{2-}$ finally leading to 4-methoxybenzyl alcohol (path **a**) which, under the experimental conditions, can be oxidized to 4-methoxybenzaldehyde (path **b**); dimerize giving **11** (path **c**); react with the radical $^{\bullet}CH_2C(CH_3)_2OH$ (formed by H-atom abstraction from 2-methyl-2-propanol by the OH radical) forming **12** (path **d**).

Under the same reaction conditions, the oxidation of **2** led to the exclusive formation of 3-(4-methoxyphenyl)propanal (**13**).

13   **14**

The γ-radiolysis of **3** was studied at pH = 4 and 10. In both cases, 2-(4-methoxyphenyl)tetrahydrofuran (**14**) was the exclusive product. The proposed mechanism for the formation of the products from **2**•+ and **3**•+ will be presented later.

At pH = 10 the reaction of **4** led to **11**, **12**, and 4-methoxybenzyl alcohol together with traces of 4-methoxybenzaldehyde, indicating that the radical cation undergoes C−C bond cleavage, leading to the 4-methoxybenzyl radical and CH_3CHO (Scheme 2; $R_1 = H$, $R_2 = Me$).

The reaction of **5** at pH = 4 led to **11** and **12** together with 4-methoxybenzyl alcohol and benzaldehyde. A small amount of 4-methoxybenzyl phenyl ketone and traces of 4-methoxybenzaldehyde were also detected. At pH = 10, the products were the same, but the amount of 4-methoxybenzyl alcohol was significantly decreased. Also in this case there is almost exclusive C−C bond cleavage in the radical cation and the

(14) Bietti, M.; Baciocchi, E.; Steenken, S. *J. Phys. Chem. A* **1998**, *102*, 7337−7342.

(15) Eberson, L. *J. Am. Chem. Soc.* **1983**, *105*, 3192−3199.

(16) Baciocchi, E.; Bietti, M.; Mattioli, M. *J. Org. Chem.* **1993**, *58*, 7106−7110.

Figure 1. Time-resolved absorption spectra observed on reaction of $SO_4^{\bullet-}$ with **1** (0.2 mM) recorded on pulse radiolysis of an Ar-saturated aqueous solution (pH = 4.2), containing 0.1 M 2-methyl-2-propanol and 2 mM $K_2S_2O_8$, at 4 (●), 280 (□), and 840 μs (▲) after the 300 ns, 3 MeV electron pulse. For the determination of the extinction coefficient, G(radical cation) = G($SO_4^{\bullet-}$) = 3.0×10^{-7} mol J^{-1} was used.[18]

products can be rationalized as for the case of **1•+** according to Scheme 2 (R_1 = H, R_2 = Ph).[17]

From **6** (pH = 4), phenylacetone and **12** were the main products together with small amounts of **11** and 4-methoxy-benzyl alcohol. Under basic conditions (pH = 10) the product distribution was very similar although 4-methoxybenzyl alcohol was detected only in traces while the amount of **11** increased. Again these products indicate C–C bond cleavage in **6•+** (Scheme 2, R_1 = Me, R_2 = Bz).

Under both acidic and basic conditions the radical cation generated from 4-methoxytoluene (**10**) gave exclusively products deriving from C_α–H deprotonation: **11**, **12**, 4-methoxybenzyl alcohol, and 4-methoxybenzaldehyde (formed by oxidation of 4-methoxybenzyl alcohol).

Oxidations Induced by Co(III)W. The experiments were carried out in 55/45 (w/w) AcOH/H_2O mixed solvents at T = 50 °C, a compromise to dissolve both Co(III)W and the substrate. Under these conditions the radical cations generated from substrates **1** and **2** gave exclusively products deriving from C_α–H deprotonation. From **1**, 1-(4-methoxyphenyl)-1,2-ethanediol, its oxidation product, 4-methoxybenzaldehyde, and the corresponding α-acetate; from **2**, 1-(4-methoxyphenyl)-1,3-propanediol and the corresponding α-acetate. For **4** and **7**, the formation of products of C_α–H deprotonation by reaction with Co(III)W has already been reported in a previous work.[10]

Kinetic Studies. These were carried out using the technique of pulse radiolysis. A 300 ns, 3 MeV electron pulse was employed, the radical cations being produced with both methods 1 and 2. In all cases they exhibited the characteristic UV and visible absorption bands, centered around 290 and 440–450 nm, of anisole-type radical cations.[9,10] The decay rates of the radical cations were measured by monitoring the production of H^+, using the ac conductance technique, or spectrophotometrically by measuring the decrease in optical density at 440–450 nm. A typical time-resolved spectrum obtained by oxidation of **1** at pH 4.2, showing the absorption bands due to **1•+** centered at 290 and 440 nm, is displayed in Figure 1.

In acidic solution (pH ≤ 4), the radical cations were found to decay by a reaction that is predominantly first-order. The

(17) A possible way to 4-methoxybenzyl phenyl ketone could be a 1,2-hydride shift in the α-substituted benzylic carbocation obtained by oxidation of the benzylic radical formed by C–H deprotonation of **5•+**.[8]

Table 1. Rate Constants for the Uncatalyzed (k_{dec}) and $^-$OH-Catalyzed (k_{-OH}) Decay of Radical Cations **1•+**–**10•+** Generated by Pulse Radiolysis of the Parent Substrate in Aqueous Solution, Measured at T = 25 °C (An = 4-$MeOC_6H_4$)

substrate	radical cation	k_{dec} $(s^{-1})^a$	k_{-OH} $(M^{-1}s^{-1})^b$
$AnCH_2OH$	c	1.5×10^4	1.2×10^{10}
$An(CH_2)_2OH$	**1•+**	5.2×10^2	8.3×10^9
$AnCH_2CH(OH)Me$	**4•+**	5.5×10^2	7.6×10^9
$AnCH_2CH(OMe)Me$	**7•+**	5.4×10^2	9.6×10^7
$AnCH_2CH(OH)Ph$	**5•+**	1.3×10^4	8.5×10^9
$AnCH_2C(OH)MeCH_2Ph$	**6•+**	4.5×10^3 ^{d,e}	8.1×10^9
$An(CH_2)_3OH$	**2•+**	1.8×10^3	1.7×10^9
$An(CH_2)_3OMe$	**8•+**	5×10^2 ^{e}	6.9×10^7
$An(CH_2)_4OH$	**3•+**	1.4×10^3	9.7×10^7
$An(CH_2)_4OMe$	**9•+**	1.2×10^3 ^{e}	5.5×10^7
$AnCH_3$	**10•+**	4.0×10^2	5.5×10^7

^{a} The radical cations were generated by method 2 from N_2O-saturated aqueous solutions (pH ≤ 3.5) containing 0.1 mM substrate and 0.5 mM thallium(I) sulfate, using doses such that <1 μM radicals were produced. The rates of decay were measured by monitoring the increase in conductance. ^{b} The radical cations were generated by method 1 from Ar-saturated aqueous solutions containing 0.2–1.0 mM substrate, 10 mM $K_2S_2O_8$, and 0.1 M 2-methyl-2-propanol, using doses such that ≤3 μM radicals were produced. $Na_2B_4O_7$ (1 mM) was added to avoid undesired pH changes upon irradiation. The observed rates were measured by monitoring the decay of optical absorption at 440–450 nm. The pH of the solution was varied between 8.5 and 11 (when possible), and the second-order rate constants for reaction of the radical cations with $^-$OH were obtained from the slope of the plots of the observed rate (k_{obs}) versus NaOH concentration. ^{c} Reference 4. ^{d} In this case, the substrate was not stable below pH = 4 and thus the radical cation was generated by method 1 from Ar-saturated aqueous solutions, containing 0.2 mM substrate, 5.0 mM $K_2S_2O_8$, and 0.1 M 2-methyl-2-propanol, adjusting the pH at 5.8 by addition of 1 mM KH_2PO_4.^{e} The rate of decay was measured by monitoring the decrease of optical absorption at 440–450 nm, using doses such that <1 μM radicals were produced.

values of the first-order rate constants (k_{dec}) for the decay of radical cations **1•+**–**10•+** are reported in column 3 of Table 1.

In the presence of $^-$OH, the radical cations decayed at a much faster rate, showing a linear dependence upon the concentration of added base, which indicates the occurrence of a second-order reaction. By plotting the observed rate (k_{obs}) against the concentration of $^-$OH, we determined the second-order rate constants for reaction of $^-$OH with the radical cations (k_{-OH}), which are displayed in column 4 of Table 1. In the same table also the corresponding data (k_{dec} and k_{-OH}) for 4-methoxybenzyl alcohol radical cation are presented.

Discussion

We begin to discuss the behavior of 2-(4-methoxyphenyl)-alkanol radical cations (β-OH), first considering the radical cations **1•+** and **4•+**. The data in Table 1 show that **1•+** and **4•+** decay very slowly in H_2O (pH ≤ 4), with a reactivity ($k_{dec} \approx 5 \times 10^2$ s^{-1} for both substrates) very close to that of 4-methoxytoluene radical cation **10•+** (k_{dec} = 4.0×10^2 s^{-1}). Clearly, it is reasonable to suggest that, under these conditions, **1•+** and **4•+** behave as carbon acids undergoing C–H deprotonation. Support for this suggestion comes from the observation that **7•+**, the methyl ether of **4•+**, undergoes C–H deprotonation at an almost identical rate (k_{dec} = 5.4×10^2 s^{-1}), and from the finding that in the oxidation of **1** and **4** with Co(III)W in aqueous acetic acid,[10] only products of α-C–H substitution are formed.[19] A

(18) Faria, J. L.; Steenken, S. *J. Phys. Chem.* **1992**, *96*, 10869–10874.
(19) The carbon acidity appears absent in phenethyl alcohol radical cation since this compound undergoes C–C bond cleavage in acid media.[20] We have previously observed that the presence of a *p*-methoxy group favors C_α–H deprotonation with respect to C_α–C_β bond cleavage in alkylaromatic radical cations.[10]

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larger reactivity in acid medium is observed for the other 2-arylalkanol radical cations **5•+** and **6•+**; however, product studies clearly indicate that both undergo unimolecular C−C bond cleavage and not C−H deprotonation.[21]

When the decay of **1•+** and **4•+** is studied in the presence of ⁻OH, a completely different situation holds. The ⁻OH promoted decay of **1•+** and **4•+** occurs at a very fast rate (k_{-OH} = 8.3 and 7.6 × 10⁹ M⁻¹ s⁻¹, respectively), which is similar to that of 4-methoxybenzyl alcohol radical cation (k_{-OH} = 1.2 × 10¹⁰ M⁻¹ s⁻¹)[4] and very close to the diffusion limit. Moreover, in basic solution **4•+** is about 80 times more reactive than its corresponding methyl ether **7•+**. Thus a shift from carbon to oxygen acidity on moving from acidic to basic aqueous solution can be reasonably suggested also when the OH group is in the β-position. Such a shift leads to reaction products different than those observed at pH = 4. Accordingly, under steady-state γ-radiolysis conditions at pH = 10, **1•+** and **4•+** undergo C−C bond cleavage, leading to products deriving from the 4-methoxybenzyl radical as already discussed (Scheme 2, R₁ = H, R₂ = H, Me). Products of C−C bond cleavage are also observed with **5•+** and **6•+**, which react with ⁻OH at practically the same rate as **1•+** and **4•+** (Table 1). Clearly, in basic media also **5•+** and **6•+** exhibit oxygen acidity.

Thus, for the ⁻OH-promoted reactions of 2-arylalkanol radical cations, a mechanism resembling the one described in Scheme 1 for 1-arylalkanol radical cations can be proposed (Scheme 3: An = 4-MeOC₆H₄).

Scheme 3
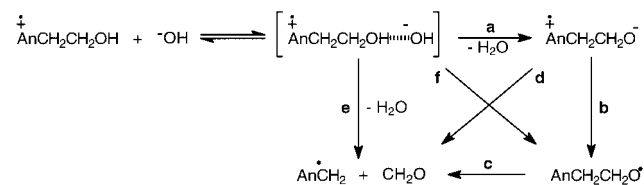
An encounter complex between the radical cation and ⁻OH is first formed, which may lead to the formation of an alkoxyl radical, either directly (path **f**) or via a radical zwitterion (paths **a** and **b**), which then undergoes C−C bond cleavage forming the 4-methoxybenzyl radical (the precursor of 4-methoxybenzyl alcohol in the steady-state γ-radiolysis experiments) and CH₂O (path **c**). Alternatively, O−H deprotonation in the complex can be coupled to C−C bond cleavage (Grob-type fragmentation, path **e**).

The fact that the rate for reaction of 2-arylalkanol radical cations with ⁻OH is close to the diffusion limit is noteworthy as it indicates that in the radical cation the acidity of the β-OH group is higher than that of H₂O (pK_a = 15.7) and hence significantly higher than that of the parent compound (the pK_a of benzyl alcohol is around 17).[22] This relatively high O−H acidity in the radical cation, even when the OH group is separated by 2 carbon atoms from the positively charged aromatic ring, is very remarkable.

We have already mentioned that, when **1•+** and **4•+** react with ⁻OH, C−C bond cleavage and not C−H deprotonation occurs. That the presence of a β-OH group favors side-chain C−C bond cleavage in aromatic radical cations is a well-known phenom-

enon studied in detail, first by Whitten[23] and then by Schanze[24] and their associates for the radical cations of 2-(4-*N*,*N*-dimethylaminophenyl)-1-phenylethanol and of a series of 2-(phenylamino)-1,2-diphenylethanols, respectively, where the positive charge mainly resides on the nitrogen atom. These studies were carried out in MeCN as the solvent and under conditions where the rate constants for reaction of the radical cation with the base were generally below the diffusion limit. It was proposed that OH deprotonation and C−C bond cleavage are concerted, but more recently Schanze also discussed the possibilty that OH deprotonation precedes C−C bond cleavage (E1cB mechanism).[24]

In our case, a similar distinction is made difficult by the diffusion control of the initiating ⁻OH reaction. Accordingly, as already noted, all β-OH-substituted radical cations, **1•+**, **4•+**, **5•+**, and **6•+**, react with ⁻OH at almost the same rate, although the scissible C−C bond is made weaker, particularly in **5•+** and **6•+** by the presence on the β-carbon of alkyl or phenyl substituents.[25]

Significant information in this respect is, however, provided by the nature of the products formed in the ⁻OH-induced decay of **6•+**. Indeed, for this radical cation, different products are expected depending on whether or not an alkoxyl radical is formed as reaction intermediate. Namely, if deprotonation in the encounter complex or the intramolecular electron transfer in the zwitterion are coupled to C−C bond cleavage, only C$_\alpha$−C$_\beta$ bond cleavage should be observed with formation of phenylacetone and products deriving from the 4-methoxybenzyl radical. On the other hand, if the alkoxyl radical **15** forms, in addition to the above products we should also find 4-methoxyphenylacetone and products deriving from the benzyl radical since two energetically very similar C−C β-cleavage reactions are possible for **15**, as shown in Scheme 4.

Scheme 4

15
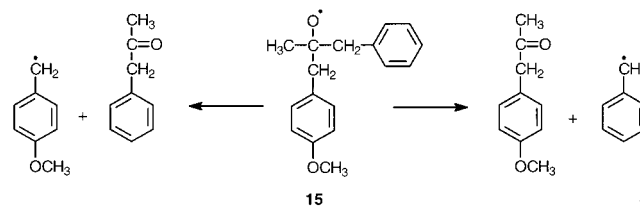
Since the base-induced decay of **6•+** leads only to phenylacetone and products deriving from the 4-methoxybenzyl radical (see results), a reasonable conclusion is that alkoxyl radicals are not involved in the base-catalyzed fragmentation of β-OH-substituted alkylaromatic radical cations. Very likely the encounter complex decomposes through path **e** or paths **a** and **d** in Scheme 3.

Surprisingly enough, the mechanistic dichotomy between C−H and O−H acidity appears to extend also to substrates bearing the OH group in the γ-position, which we would expect to be significantly less acidic than the β-OH group in **1•+**. Thus, **2•+** in acid medium undergoes C$_\alpha$−H deprotonation, as indicated by the products study (see results) and by the reactivity which

(20) Gilbert, B. C.; Warren, C. J. *Res. Chem. Intermed.* **1989**, *11*, 1−17.

(21) The C−C bond cleavage reactivity of arylalkanol radical cations in acid media is discussed elsewhere.[10]

(22) Estimated on the basis of a pK_a value of 17.4 for 2,4,6-trimethylbenzyl alcohol: Deno, N. C.; Jaruzelski, J. J.; Schriesheim, A. *J. Am. Chem. Soc.* **1955**, *77*, 3044−3051.

(23) Ci, X.; Whitten, D. G. *J. Am. Chem. Soc.* **1989**, *111*, 3459−3461. See also: Gaillard, E. R.; Whitten, D. G. *Acc. Chem. Res.* **1996**, *29*, 292−297.

(24) Burton, R. D.; Bartberger, M. D.; Zhang, Y.; Eyler, J. R.; Schanze, K. S. *J. Am. Chem. Soc.* **1996**, *118*, 5655−5664 and references therein.

(25) For example, the difference in BDE between **1•+** and **4•+** can be estimated to be around 5 kcal mol⁻¹, on the basis of the difference in reduction potentials of ⁺CH₂OMe and ⁺CH(CH₃)OEt.[26]

(26) Wayner, D. D. M.; McPhee, D. J.; Griller, D. *J. Am. Chem. Soc.* **1988**, *110*, 132−137.

is close to that of the radical cation of its methyl ether **8**[•+] (Table 1). However, in the presence of ⁻OH the reactivity of **2**[•+] (1.7 × 10⁹ M⁻¹ s⁻¹) is significantly higher (∼25-fold) than that of **8**[•+] and ∼30-fold higher than that of 4-methoxytoluene radical cation **10**[•+] (Table 1). Clearly, these results again indicate a reaction where the OH group of **2**[•+] has to play a key role.[27] Moreover, that this group is the reaction site for the reaction of **2**[•+] with ⁻OH is also nicely confirmed by the formation of 3-(4-methoxyphenyl)propanal (**13**) in the steady-state γ-radiolysis of **2**. Accordingly, the formation of this product can be accounted for as shown in Scheme 5 (An = 4-MeOC₆H₄), where

Scheme 5
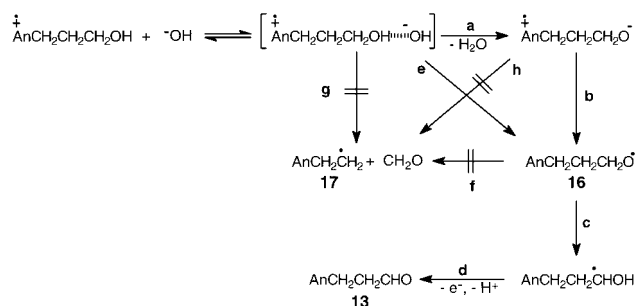
⁻OH deprotonation may lead directly (path **e**) or via a radical zwitterion (paths **a** and **b**) to an alkoxyl radical **16**, which then undergoes a 1,2-H atom shift (path **c**) producing an α-hydroxy carbon radical from which the aldehyde **13** can be easily formed (path **d**).

The suggestion that an alkoxyl radical is an intermediate in the base-induced decay of 3-arylalkanol radical cations would appear to be in contrast with our previous conclusion that such radicals are not involved in the base-catalyzed decay of 2-arylalkanol radical cations. Probably, this different behavior is due to the fact that in **2**[•+] the paths avoiding the formation of the alkoxyl radical (C−C bond cleavage concerted with O−H deprotonation in the encounter complex (path **g**) or concerted C−C bond cleavage and intramolecular electron transfer in the zwitterion (path **h**)) would form the primary unactivated 2-(4-methoxyphenyl)ethyl radical (**17**). For the same reason, in the alkoxyl radical **16**, the 1,2-H atom shift to produce 3-(4-methoxyphenyl)propanal (**13**) (paths **c** and **d**) overcomes the β-C−C bond cleavage (path **f**).

A further point of interest is that the reaction rate for reaction of **2**[•+] with ⁻OH is lower than that found with **1**[•+] and quite below the diffusion-controlled limit, thus indicating that the formation of the encounter complex is no longer the rate-determining step. Two factors may play a role in this respect, both related to the increased distance of the OH group from the charged aromatic ring. First, the OH group is certainly less acidic in **2**[•+] than in **1**[•+], which can slow the deprotonation rate. Second, the intramolecular electron transfer, either in the zwitterion (Scheme 5; path **b**) or coupled with proton transfer (Scheme 5; path **e**), should be energetically more costly in **2**[•+] than in **1**[•+]. For each CH₂ group interposed between the ring and the −O⁻ group a lowering of the intramolecular electron-transfer rate by a factor of 4−5 can be predicted,[30] a factor

which is substantially in line with the observed decrease in rate as we move from **1**[•+] to **2**[•+].

It is also possible, in analogy to a mechanism proposed by Gilbert[20] for the 3-phenyl-propanol radical cation, that in the reaction of **2**[•+] the intramolecular electron transfer takes place by an inner sphere mechanism, via a sequence of ring-closing/ring-opening equilibria as illustrated in Scheme 6. However,

Scheme 6
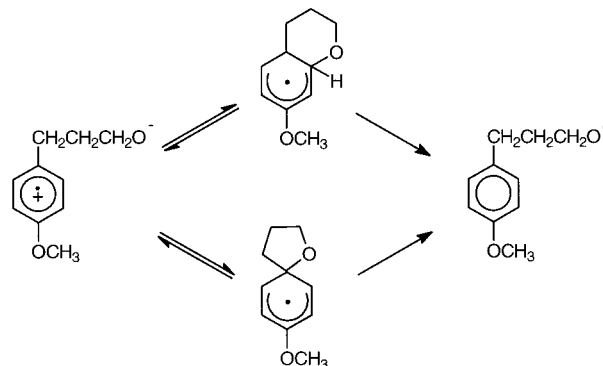
our present results do not allow any conclusion in this respect.[31]

The oxygen acidity completely disappears when the OH group is in the δ-position, that is when four CH₂ groups are interposed between the ring and the OH group. Accordingly, **3**[•+] reacts with ⁻OH at a rate close to those of the radical cations of its methyl ether **9**[•+] and 4-methoxytoluene, **10**[•+] (Table 1), thus suggesting that in this case carbon acidity is in play also in basic medium. Moreover, steady-state γ-radiolysis experiments showed that **3** gave the same product, namely, 2-(4-methoxyphenyl)-tetrahydrofuran (**14**), both in acid and basic media. The formation of **14** is in line with the deprotonation at the C_α−H bond leading to the formation of a carbon-centered radical which is oxidized to the corresponding carbocation followed by ring closure to form **14** (Scheme 7).

Scheme 7
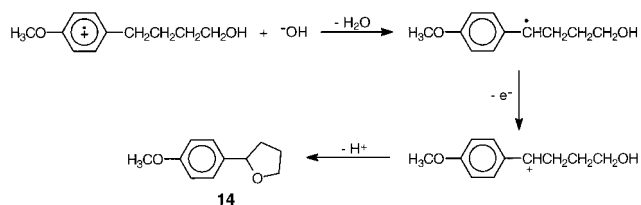
Clearly, in **3**[•+], the interposition of an additional CH₂ group between the alcoholic OH and the aromatic ring has further lowered the OH reactivity with respect to **2**[•+] in such a way that oxygen acidity can no longer compete with carbon acidity.

Summary and Conclusions

It has been clearly shown that the mechanistic dichotomy (carbon acidity in acidic media and oxygen acidity in basic media) observed for 1-(4-methoxyphenyl)-alkanol radical cations

(27) It is highly unlikely that 3-(4-methoxyphenyl)propanal derives from an oxygen-centered radical cation, in view of the fact that the ionization potential of ethanol (10.48 eV)[28] is much higher than that of 4-methoxytoluene (8.18 eV).[29]

(28) See for example: Kiser, R. W. *Introduction to Mass Spectrometry and its Applications*; Prentice Hall: Englewood Cliffs, 1965; pp 308−320.

(29) Fukuzumi, S.; Kochi, J. K. *J. Am. Chem. Soc.* **1981**, *103*, 7240−7252.

(30) Mehta, L. K.; Porssa, M.; Parrick, J.; Candeias, L. P.; Wardman, P. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1487−1491.

(31) Interestingly, when the *p*-OMe group is absent in the radical cation, the mechanistic dichotomy is observed at a much lower pH than in our case. Thus, 3-phenylpropanol radical cation is C−H deprotonated at pH < 1 but exhibits the reactivity associated with the OH group at pH < 3.[20] Probably, when the radical cation is *p*-methoxy substituted a significant portion of the charge resides on the OMe group. Thus, the intramolecular electron transfer, either outer- or inner-sphere, associated to the oxygen acidity, requires more energy and hence can efficiently occur only if there is deprotonation at the OH group.

in aqueous solution also extends to 2- and 3-(4-methoxyphenyl)-alkanol radical cations. 2-(4-Methoxyphenyl)-alkanol radical cations react with $^-$OH at a rate very close to the diffusion limit, forming products of C_α–C_β bond cleavage. Evidence is presented showing that either O–H deprotonation is coupled to C–C bond cleavage or a radical zwitterion is first formed which undergoes intramolecular electron transfer coupled to C–C bond cleavage. It does not seem that an oxyl radical intermediate is involved in these processes.

The intermediacy of an oxyl radical is instead suggested for the base-catalyzed decay of 3-(4-methoxyphenyl)-propanol radical cation. This radical undergoes a 1,2-H atom shift, leading to the formation of 3-(4-methoxyphenyl)propanal. The rate for reaction of the radical cation with $^-$OH is below the diffusion limit, which is probably due to the increased distance between the OH group and the aromatic ring (compared to 1- and 2-arylalkanols). This may lower the acidity of this group as well as make energetically costly the intramolecular electron transfer.

The oxygen acidity disappears when four carbon atoms are interposed between the OH group and the aromatic ring. These systems behave as carbon acids both in acidic and in basic aqueous solution.

Experimental Section

Reagents. Potassium peroxydisulfate, sodium hydroxide, disodium tetraborate decahydrate, potassium thiocyanate, thallium(I) sulfate, 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.[16] Milli-Q-filtered (Millipore) water was used for all solutions.

4-Methoxybenzyl alcohol, 2-(4-methoxyphenyl)ethanol (**1**), 3-(4-methoxyphenyl)propanol (**2**), 4-(4-methoxyphenyl)-1-butanol (**3**), and 4-methoxytoluene (**10**) (Aldrich) were used as received. 1-(4-Methoxyphenyl)-2-propanol (**4**), 1-phenyl-2-(4-methoxyphenyl)ethanol (**5**), and 1-(4-methoxyphenyl)-2-methoxypropane (**7**) were avalable from a previous work.[10]

2-Methyl-1-phenyl-3-(4-methoxyphenyl)-2-propanol (**6**) was prepared by reaction of benzylmagnesium chloride with 4-methoxyphenylacetone in anhydrous tetrahydrofuran, purified by column chromatography (silica gel, eluent hexane/ethyl acetate 5:1), and identified by GC-MS. ^{1}H NMR (CDCl$_3$) δ 1.05 (s, 3H, CH_3), 1.44 (s, 1H, OH), 2.68–2.88 (m, 4H, 2CH_2), 3.79 (s, 3H, OCH_3), 6.83–7.13 (m, 4H, 4-MeOC$_6H_4$), 7.17–7.36 (m, 5H, C$_6H_5$).

Methyl ethers **8** and **9** were prepared by reaction of the corresponding alcohols (**2** and **3**, respectively) with methyl iodide and sodium hydride in anhydrous tetrahydrofuran and identified by GC-MS. ^{1}H NMR (CDCl$_3$) **8**: δ 1.78–1.94 (m, 2H, β-CH_2), 2.63 (t, 2H, γ-CH_2), 3.34 (s, 3H, OCH_3), 3.40 (t, 2H, α-CH_2), 3.79 (s, 3H, OCH_3), 6.79–7.14 (m, 4H, 4-MeOC$_6H_4$). **9**: δ 1.54–1.74 (m, 4H, 2CH_2), 2.57 (t, 2H, δ-CH_2), 3.32 (s, 3H, OCH_3), 3.38 (t, 2H, α-CH_2), 3.78 (s, 3H, OCH_3), 6.78–7.14 (m, 4H, 4-MeOC$_6H_4$).

Product Analysis. γ-Irradiations were carried out with a panorama ^{60}Co γ-source (Nuclear Engineering) at dose rates of 0.5 Gy s^{-1}. In a typical experiment, 5 mL of an argon-saturated aqueous solution containing the substrate (0.5–1.0 mM), potassium peroxydisulfate (0.2–0.5 mM), and 2-methyl-2-propanol 0.2 M was irradiated at room temperature ($T \approx 25$ °C) for the time necessary to obtain a 40% conversion of peroxydisulfate. Reaction products were identified by GC-MS and HPLC (comparison with authentic samples). Blank experiments were performed under every condition and showed the presence of negligible amounts of products.

Oxidations induced by Co(III)W were performed at $T = 50$ °C in AcOH/H$_2$O 55:45 (w/w). In a typical experiment, 5 mL of an argon-saturated solution containing the substrate (0.05 M), Co(III)W (0.05 M), and AcOK (0.30 M) was stirred until complete conversion of the oxidant. Workup was performed as described previously.[16] Reaction products were identified by GC and GC-MS (comparison with authentic samples). The stability of the substrates to reaction conditions was shown by blind reactions in AcOH/H$_2$O 55:45 at 50 °C.

Pulse Radiolysis. The pulse radiolysis experiments were performed using a 3-MeV van de Graaff accelerator which supplied 300 ns pulses with doses such that 0.5–3 μM radicals were produced. A thermostatable continuous flow cell was employed in all experiments. The pulse radiolysis setup and the methods of data handling have been described elsewhere.[32] Dosimetry was performed with N$_2$O-saturated 10 mM KSCN aqueous solutions taking G($^\bullet$OH) = 6.0×10^{-7} mol J^{-1} and ϵ [(SCN)$_2$$^{\bullet-}$] = 7600 M^{-1} cm^{-1} at 480 nm.[33] Experiments were performed using argon-saturated aqueous solutions containing the substrate (0.1–1.0 mM), peroxydisulfate (2–10 mM), and 2-methyl-2-propanol (0.1 M). Alternatively, N$_2$O-saturated aqueous solutions (pH $\leq$ 3.5) containing the substrate (0.1–0.2 mM) and thallium(I) sulfate (0.5–2.0 mM) were employed. The pH of the solutions was adjusted with NaOH or HClO$_4$. The temperature of the solutions was kept constant at 25 $\pm$ 0.2 °C. Rate constants were obtained by averaging 8–14 values, each consisting of the average of 10–30 shots and were reproducibile to within 3%.

The second-order rate constants for reaction of the radical cations with $^-$OH (k_{-OH}) were obtained from the slopes of the plots of the observed rates (k_{obs}) versus the concentration of NaOH. For these experiments the solution containing 0.2–1.0 mM substrate, 10 mM potassium peroxydisulfate, and 0.1 M 2-methyl-2-propanol was saturated with argon or oxygen and 1 mM sodium tetraborate was added to avoid undesired pH variations upon irradiation.

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(33) Schuler, R. H.; Hartzell, A. L.; Behar, B. *J. Phys. Chem.* **1981**, *85*, 192–199.