11516 *J. Am. Chem. Soc.* **1998,** *120,* 11516−11517

Oxygen Acidity of 1-Arylalkanol Radical Cations. 4-Methoxycumyloxyl Radical as $-C(Me)_2-O^-$-to-Nucleus Electron-Transfer Intermediate in the Reaction of 4-Methoxycumyl Alcohol Radical Cation with OH^-

Enrico Baciocchi,*[,1a] Massimo Bietti,[1b]
Osvaldo Lanzalunga,[1c] and Steen Steenken*[,1d]

Dipartimento di Chimica and
Centro CNR di Studio sui Meccanismi di Reazione
Universitá “La Sapienza”
P.le A. Moro, 5 I-00185 Rome, Italy
Dipartimento di Scienze e Tecnologie Chimiche
Universitá “Tor Vergata”
Via della Ricerca Scientifica, I-00133 Rome, Italy
Max-Planck-Institut für Strahlenchemie
D-45413 Mülheim, Germany

Received February 26, 1998

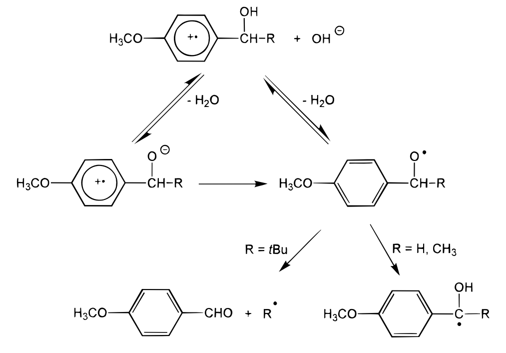
We have recently shown that 1-arylalkanol radical cations,[2] e.g., $[4\text{-MeOPhCH(OH)R}]^{\bullet+}$, in aqueous solution can exhibit oxygen acidity in addition to the expected and well-known carbon acidity, depending on pH. Thus, whereas at pH ≤ 5 $4\text{-MeOPhCH(OH)R}]^{\bullet+}$ radical cations undergo α-C−H deprotonation ($R = H$, $k = 1.5 \times 10^4$; $R = Me = 7.0 \times 10^3\ s^{-1}$, determined by conductance),[3] at pH = 10, a very fast OH^--induced reaction ($k \approx 5 \times 10^9\ M^{-1}\ s^{-1}$) takes place involving deprotonation *at the OH group*. It was suggested that a benzyloxyl radical forms (either directly (*concerted* with OH^- attack) or via an *intermediate* radical zwitterion) which then undergoes a formal 1,2-hydrogen atom shift[4] (R = H, Me) converting the oxyl radical into a carbon-centered radical or a β-fragmentation reaction (R = *t*Bu) leading to 4-methoxybenzaldehyde and the radical $R^\bullet$ (Scheme 1). However, the oxyl radical postulated in Scheme 1 has so far not been seen.

Since decisive support for the suggested OH deprotonation consists of the *direct* observation of the benzyloxyl radical in the reaction with OH^- of a suitable 1-arylalkanol radical cation precursor, we have now studied the reaction of 4-methoxycumyl alcohol (MCA) radical cation in acidic and basic solutions. If this species is indeed deprotonated at the OH group by OH^-, the cumyloxyl radical should form, and there should be a good chance to detect it since the only reaction of this radical is β-fragmentation leading to $^\bullet CH_3$ (the least stable alkyl radical), a process expected to be relatively slow.

Along these lines, the radical cation of MCA was generated by pulse radiolysis in water using $SO_4^{\bullet-}$ or Tl^{2+} as the oxidant.[5] Under acidic conditions (pH = 4.1), at 4 μs after the pulse, the complete formation of $MCA^{\bullet+}$ was observed which exhibits the characteristic[6,7] anisole-type absorption bands centered at ∼290 and 440 nm.

The radical cation, as generated with Tl^{2+}, decayed with the (*low*) rate constant $2.9 \times 10^2\ s^{-1}$ by formation of H^+, as measured by time-resolved AC-conductance. On this time scale, *products* of this decay were not visible with *optical* detection.[8]

Scheme 1



However, when the reaction was performed at pH = 10, a *fast* decay of the radical cation was observed, resulting in the formation of 4-methoxyacetophenone ($\lambda_{max} = 280$ nm).[10] The rate constant $5.1 \times 10^9\ M^{-1}\ s^{-1}$ was measured for the OH^--induced reaction, a value almost identical to those previously obtained for the reaction of other 4-MeOPhCH(OH)R radical cations under similar conditions.[2] It is therefore reasonable to assume that $MCA^{\bullet+}$ also[2] is deprotonated by OH^- at the alcoholic OH group with or followed by electron transfer to yield the intermediate 4-methoxycumyloxyl radical which subsequently forms 4-methoxyacetophenone by β-cleavage[11] (Scheme 1).

Full support of this hypothesis was obtained when the reaction was carried out at pH = 11 where the rate of decay of the radical cation is 10 times larger than that at pH = 10.

Under these conditions, the spectra presented in Figure 1 were obtained which clearly show that the product of the radical cation decay at 440 nm (see also inset a) is a species characterized by a broad absorption band centered at ∼660 nm which subsequently decays (inset b, the “spike” after the pulse is due to the removal of e_{aq}^- by $S_2O_8{}^{2-}$) giving rise, with the same rate, to 4-methoxyacetophenone (inset c).[12]

On the basis of these observations, the 660-nm absorption band is assigned to the 4-methoxycumyloxyl radical, for which a λ_{max} of 590 nm was reported for acetonitrile as solvent.[13,14] In these studies, it was found that the visible absorption band of cumyloxyl radicals is solvent-*in*sensitive when measured in a large variety of *non*aqueous solvents. We felt, however, that a red-shift of

---

(1) (a) Dipartimento di Chimica, Universitá “La Sapienza”; (b) University “Tor Vergata”; (c) Dipartimento di Chimica and Centro CNR di Studio sui Meccanismi di Reazione, Universitá “La Sapienza”; (d) Max-Planck-Institut.

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

(3) As expected, this reaction shows a significant kinetic isotope effect, i.e., for $[4\text{-MeOPhCH}_2\text{OH}]^{\bullet+}/[\text{MeOPhCD}_2\text{OH}]^{\bullet+}$, $k_H/k_D = 4.5$, and, for the corresponding methyl ethers, $k_H/k_D = 5.7$.

(4) Gilbert, B. C.; Laue, H. A. H.; Norman, R. O. C.; Sealy, R. C. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1040. Dobbs, A. J.; Gilbert, B. C.; Laue, H. A. H.; Norman, R. O. C. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1044. Gilbert, B. C.; Holmes, R. G. G.; Laue, H. A. H.; Norman, R. O. C. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1047.

(5) For details on this technique, see ref 6 or ref 2 or 7.

(6) O’Neill, P.; Steenken, S.; Schulte-Frohlinde, D. *J. Phys. Chem.* **1975**, *79*, 2773.

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

(8) Some steady state γ-radiolysis experiments[9] were carried out at pH = 4.0, using $SO_4^{\bullet-}$ to generate the radical cation. Under these conditions the only observed product was 4-methoxyacetophenone, but its yield (based on the initial concentration of radical cation, calculated from the radiation dose) was only 3.5%. A reasonable explanation is that the long-lived radical cation reacts with the radical $^\bullet CH_2C(CH_3)_2OH$ (formed through H-atom abstraction from 2-methyl-2-propanol by $^\bullet$OH), thus leading to the regeneration of MCA. In agreement with this hypothesis is the observation of a 4-fold acceleration in the rate of decay of $MCA^{\bullet+}$ when 2-methyl-2-propanol was added in a concentration sufficient to scavenge 50% of the initially produced $OH^\bullet$ radicals, which leads to the production of $^\bullet CH_2C(CH_3)_2OH$ instead of Tl^{2+}. The details of the mechanism of the decay of $MCA^{\bullet+}$ in acid medium are currently under investigation.

(9) Irradiations were carried out on Ar-saturated aqueous solutions containing 1 mM MCA, 0.5 mM $K_2S_2O_8$, and 0.2 M 2-methyl-2-propanol, at room temperature, using 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. The pH of the solution was adjusted to 4 or 10 with $HClO_4$ or NaOH, respectively; in the latter case, 1 mM $Na_2B_4O_7 \times 10H_2O$ was added to avoid undesired pH changes upon irradiation. Products were identified and quantitatively determined by HPLC (comparison with authentic samples).

(10) Steady-state experiments confirmed that under these conditions, 4-methoxyacetophenone is produced from $MCA^{\bullet+}$ in quantitative yield.

(11) The methyl radical was in fact detected via EPR by trapping with $CH_2{=}NO_2^-$ (We thank Dr. K. Hildenbrandt for performing this experiment at pH = 11).

10.1021/ja980645n CCC: $15.00

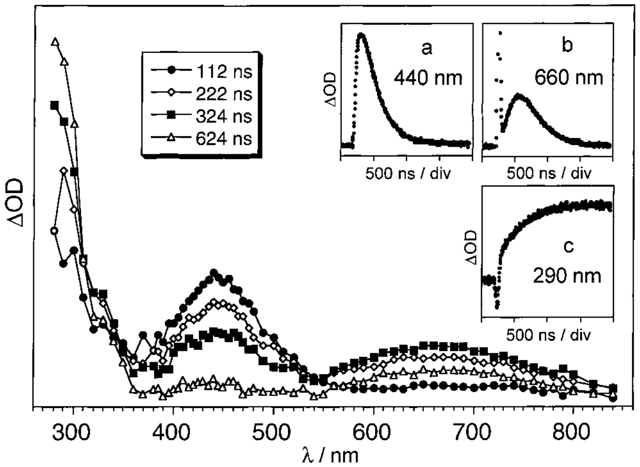


Figure 1. Time-resolved absorption spectra observed on reaction of $SO_4^{\bullet-}$ with MCA (1 mM) recorded on pulse radiolysis of an Ar-saturated aqueous solution (pH = 11.0), containing 0.1 M 2-methyl-2-propanol, 1 mM $Na_2B_4O_7$ and 10 mM $K_2S_2O_8$, at 112 (●), 222 (◇), 324 (■) and 624 ns (△) after the 20 ns, 10-MeV electron pulse. Insets: (a) decay of $MCA^{\bullet+}$ monitored at 440 nm; (b) buildup and subsequent decay, monitored at 660 nm assigned to the 4-methoxycumyloxyl radical; visible is also the fast decay of the electron, due to eq 3; (c) buildup at 290 nm assigned to 4-methoxyacetophenone.

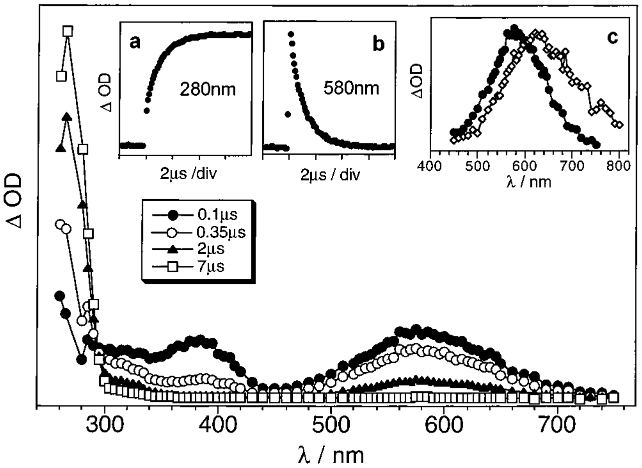


Figure 2. Absorption spectra of transients obtained after 248-nm laser flash photolysis of an Ar-saturated CH_3CN solution containing 5 mM 4-methoxycumyl-*t*butyl peroxide, recorded 0.1, 0.35, 2, and 7 μs after the laser flash. Insets: (a) buildup of 4-methoxyacetophenone monitored at 280 nm; (b) decay of the 4-methoxycumyloxyl radical monitored at 580 nm;. (c) comparison between the transient absorption spectra of $MeOCumO^\bullet$ generated by 248-nm LFP in CH_3CN (●) and in CH_3CN/H_2O 1:1 (◇).

λ_{max} could not be excluded *in water* in view of the special characteristics of this solvent, which should stabilize the excited state of the 4-methoxycumyloxyl radical, suggested to be characterized by a quite large charge separation.[14]

To test this hypothesis, we synthesized 4-methoxycumyl-*t*-butyl peroxide ($4\text{-}MeOPhC(CH_3)_2OOC(CH_3)_3$)[15] and produced the 4-methoxycumyloxyl radical, $4\text{-}MeOPhC(CH_3)_2O^\bullet$ ($MeOCumO^\bullet$), by 248-nm photolysis of the peroxide in CH_3CN and in CH_3CN/H_2O 1:1 (v/v).[16] Figure 2 displays the spectrum of $MeOCumO^\bullet$ recorded in CH_3CN at 100 ns after the laser flash. The spectrum, with a λ_{max} of 580 nm for the visible absorption band, is in excellent agreement with that[13,14] previously reported.[14a] $MeOCumO^\bullet$, the species responsible, undergoes a first-order change, such that at 7 μs after the flash is present, the spectrum of 4-methoxyacetophenone whose buildup at 280 nm (inset a) occurs with the same rate ($k = 1.0 \times 10^6\ s^{-1}$) as the decay of $MeOCumO^\bullet$ at 580 nm (inset b).

In inset c, the visible absorption band of the 4-methoxycumyloxyl radical in CH_3CN (●) is compared with that in CH_3CN/H_2O 1:1 (open diamonds). It is evident that the presence of water results in a red-shift of ~45 nm. This observation supports the attribution of the 660 nm absorption in water to the 4-methoxycumyloxyl radical since an even larger red-shift should occur on going from CH_3CN/H_2O 1:1 to *pure* water. Analogous results were obtained with the *unsubstituted* cumyloxyl radical where a red shift of 30 nm was observed for the same solvent change, thus showing the generality of the phenomenon.[17]

In conclusion, we have obtained for the first time *direct* evidence that 1-arylalkanol radical cations can be deprotonated at the OH group to finally form a highly reactive alkoxyl radical. Apparently, the oxygen acidity of these radical cations is displayed only in fairly basic media, and this can be rationalized in terms of the oxygen-bonded hydrogen being a hard acid center, requiring a hard base (OH^-) to react. With the neutral base water (at pH ≤ 5), the *normal* (weak) C−H acidity prevails, as concluded from systems containing an α-hydrogen.[2] There is an interesting theoretical aspect in this oxygen acidity as it finally leads to an intramolecular electron transfer from the side-chain ($-O^-$ or $-OH$, depending on whether the zwitterion (see Scheme 1) is an intermediate rather than a transition state) to the aromatic π-system of the radical cation, involving orbitals which, different from those of the C_α-H bond, do not directly overlap. Finally, another novel observation reported in this paper is that the visible absorption band of cumyloxyl radicals undergoes a significant red-shift on going from *non*aqueous to aqueous solvents. This effect of wateris in contrast to the solvent *in*sensitivity[13,14] with respect to nonaqueous solvents.[18]

Acknowledgment. E.B., M.B., and O. L. thank the Ministry of University and Technological Research (MURST) and the National Research Council (CNR) for financial support. Some of the experiments were performed at the Paterson Institute for Cancer Research Free Radical Research Facility, Manchester, U.K. with the support of the European Commission through the Access to Large-Scale Facilities activity of the TMR Program.

JA980645N

---

[12] On the basis of the values of the extinction coefficients of $MCA^{\bullet+}$ ($\epsilon_{440} \approx 3600\ M^{-1}\ cm^{-1}$) and of $MeOCumO^\bullet$ ($\epsilon_{590} \approx 1550\ M^{-1}\ cm^{-1}$, as measured in MeCN[14]) and taking account of the buildup and decay kinetics, the spectral data (Figure 1) are interpreted in terms of ≥90% of $MCA^{\bullet+}$ being converted into $MeOCumO^\bullet$. At pH 11, $MCA^{\bullet+}$ decays and $MeOCumO^\bullet$ is produced with $k \approx 7 \times 10^6\ s^{-1}$ (at pH 11.5, $k \geq 1.2 \times 10^7\ s^{-1}$), and from inset b it is evident that the rate of buildup of $MeOCumO^\bullet$ is larger than that of its decay. Furthermore, the decay kinetics of the 660 nm species matches the buildup of the 290 nm one ($k \approx 3 \times 10^6\ s^{-1}$ at pH 11). Thus, we are dealing with the 440 → 660 → 290 nm sequence.

[13] Avila, D. V.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1992**, *114*, 6576.

[14] Avila, D. V.; Ingold, K. U.; Di Nardo, A. A.; Zerbetto, F.; Zgierski, M. Z.; Lusztyk, J. *J. Am. Chem. Soc.* **1995**, *117*, 2711. (a) The band at ~400 nm is mainly due to the $4\text{-}HOC(Me)_2C_6H_4O^\bullet$ radical which is a side-product (by O−Me bond rupture) of the photolysis of the peroxide precursor.

[15] Hendrickson, W. H.; Nguyen, C. C.; Nguyen, J. T.; Simons, K. T. *Tetrahedron Lett.* **1995**, *36*, 7217.

[16] In pure water, the peroxide is not sufficiently soluble.

[17] The cumyloxyl radical, $PhC(CH_3)_2O^\bullet$, was produced by 248-nm photolysis of (commercially available) dicumylperoxide in CH_3CN and in CH_3CN/H_2O 1:1 (v/v).[16] The spectrum recorded in CH_3CN is in perfect agreement with that previously reported, with a λ_{max} of 485 nm for the visible absorption band.[13,14] This band shifts to 515 nm in CH_3CN/H_2O 1:1 (v/v).

[18] Since AcOH and EtOH behave the same way as *a*protic solvents,[13,14] the remarkable effect of water on the visible band of benzyloxyl radicals is probably not (exclusively) related to hydrogen-bond formation: Thus, other solvent properties (e.g., the dielectric constant) must play a role.