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Side-Chain Fragmentation of Arylalkanol Radical Cations. Carbon−Carbon and Carbon−Hydrogen Bond Cleavage and the Role of α- and β-OH Groups

Enrico Baciocchi,*,[1a] Massimo Bietti,[1a] Lorenza Putignani,[1a] and Steen Steenken*,[1b]

Contribution from the Dipartimento di Chimica, Università "La Sapienza", P. le A. Moro, 5 00185 Rome, Italy, and Max-Planck-Institut für Strahlenchemie, D-45413 Mülheim, Germany

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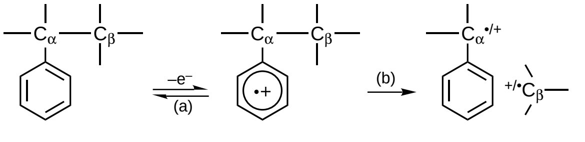
Abstract: A product analysis and kinetic study of the one-electron oxidation of a number of 1-arylpropanols, 1,2-diarylethanols, and some of their methyl ethers by potassium 12-tungstocobaltate(III) (abbreviated as Co(III)W) in aqueous acetic acid was carried out and complemented by pulse radiolysis experiments. The oxidations occur via radical cations which undergo side-chain fragmentation involving the C_α−H and/or C_α−C_β bond. With 1-(4-methoxyphenyl)-2-methoxypropane (**1**), only deprotonation of the radical cation is observed. In contrast, removing the ring methoxy group leads to exclusive C−C bond cleavage in the radical cation. Replacing the side-chain β-OMe by β-OH, the radical cation undergoes both C−C and C−H bond cleavage, with both pathways being base catalyzed. C−C bond breaking in the radical cation is also enhanced by an α-OH group, as shown by 1-(4-methoxyphenyl)-2,2-dimethyl-1-propanol (**7**), where this pathway, which is also base catalyzed, is the only one observed. Interestingly, α- and β-OH groups exhibit a very similar efficiency in assisting the C−C bond cleavage route in the radical cations, as is evident from the kinetic and products study of the oxidation of 1-phenyl-2-(4-methoxyphenyl)ethanol (**5**) and 1-(4-methoxyphenyl)-2-phenylethanol (**6**) by Co(III)W, and from pulse radiolysis experiments on **5** and **6**. C−C bond cleavage is the main reaction for both radical cations which exhibit a very similar rate of fragmentation (k = 2.0 and 3.2 × 10^4 s^{-1}, respectively). In both fragmentation reactions a small solvent isotope effect, $k(H_2O)/k(D_2O)$ (1.4 for $\mathbf{5}^{\bullet+}$ and 1.2 for $\mathbf{6}^{\bullet+}$) and negative activation entropies are observed. These data suggest that a key role in the assistance by α- or β-OH groups to C−C bond cleavage is played by hydrogen bonding or specific solvation of these groups. The kinetic study of the oxidations promoted by Co(III)W has also shown that when only one group, OH or OMe, is present in the side chain (either on C_α or C_β), the fragmentation step or both the electron transfer and fragmentation steps contribute to the overall oxidation rate. However, with an OH group on both carbons of the scissile bond, as in 1-(4-methoxyphenyl)-1,2-propanediol (**9**), the rate of C−C bond cleavage is so fast that the electron transfer step becomes rate determining.

Formation of a radical cation followed by the cleavage of a side-chain C_α−C_β bond (eq 1) is an important pathway through which the oxidative fragmentation reactions of a large variety of aromatic compounds (i.e. arylalkanols and their ethers, tri- and tetraarylethanes, bicumyls, arylpinacols and pinacol ethers, 1,2-amino alcohols) take place. The cleavage can be heterolytic or homolytic depending on whether the positive charge is transferred to the leaving fragment or remains on the C_α carbon.



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These reactions have been the subject of intensive investigation in the last decade from both the practical and theoretical points of view. On the practical side, for example, reaction 1 appears to play a fundamental role in the chemical and enzymatic oxidative degradation of lignine to lower and useful aromatics, a process of industrial importance.[2−6]

From the mechanistic point of view, the step involving the cleavage of the C_α−C_β bond (hereafter abbreviated as the C−C bond for the sake of simplicity) in the radical cation (step b in eq 1) is the one attracting most attention. Interestingly, such a cleavage is strongly helped by the presence of +R electron releasing substituents on C_α and/or C_β,[7] which, at least in part, can be ascribed to a decreased strength of the C−C bond in the radical cation. However, another important factor is that these substituents can stabilize the positive charge which has to be transferred to the scissile bond in the transition state of the cleavage reaction. The importance of through bond delocalization has been clearly shown by Maslak and his associates[8] and has also received the support of theoretical calculations.[9,10]

Arnold and his group have investigated the role of the C−C bond strength in the radical cation with respect to reaction 1 in a study where the radical cations were generated by photoinduced electron transfer (PET). They concluded that only if the C−C bond dissociation energy in the radical cation is lower than ca. 10−15 kcal mol^{-1} could the scission of this bond compete with back electron transfer from the photoreduced

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(1) (a) University of Rome. (b) Max-Planck-Institut für Strahlenchemie, Mülheim.

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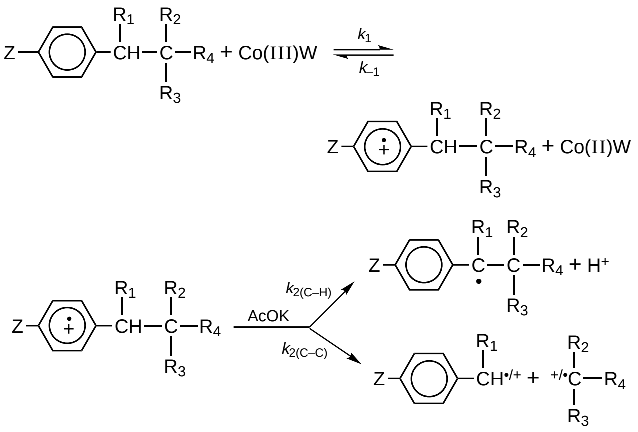
sensitizer.[11] It has to be noted, however, that in PET reactions the back electron transfer (which involves the ground state molecules) is generally highly exoergonic. In comparison, the competition between C−C bond cleavage and back electron transfer is likely to be more favorable in electron transfer reactions involving ground state oxidants rather than photoexcited species.

The studies by Arnold also provided information on the problem of how the charge is apportioned between the two fragments formed in the C−C bond cleavage (heterolytic or homolytic rupture?). By examining the cleavage products of 1,1,2-triaryl- and 1,1,2,2-tetraarylalkane radical cations, it was found that the type of apportionment is determined by the relative oxidation potentials of the two radical fragments.[11] However, this might not be the only factor of importance since Maslak and co-workers have recently shown that there is some kinetic advantage for the heterolytic type of cleavage of a β-bond in an alkylaromatic radical cation[12] which allows regioconservation of the spin, as already observed with radical anions.[13] Moreover, the situation would be further complicated if the C−C bond cleavage, depicted as unimolecular in eq 1, were nucleophilically assisted, as is actually found in the C−C bond cleavage reaction of diphenylcyclopropane radical cations.[14]

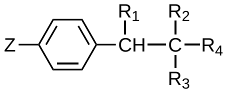
Finally, conformational factors in the radical cation can play a decisive role with respect to the energetics of C−C bond cleavage. In particular, overlap of this bond with the singly occupied molecular orbital (SOMO), generally localized in the aromatic ring, is necessary for the cleavage to occur (stereoelectronic effect). Evidence supporting the role of stereoelectronic effects in the cleavage of the C−C bond has been provided by Arnold and his associates.[15] On the other hand, Gilbert and Davies have found similar rates of C−C bond cleavage for $PhCH_2CH_2OH^{\bullet+}$ and for the radical cation of 2-indanol in spite of the fact that in the latter no overlap between the scissile C−C bond and the SOMO in the aromatic ring is possible.[16]

It appears very surprising that in spite of the considerable amount of work carried out on this subject, no detailed kinetic study of reaction 1 has hitherto been carried out. Most of the kinetic information concerns the cleavage step, but the interconnections of this step with the electron transfer step are unknown. Likewise, little is known about the role of the aromatic structure and the side chain on the competition between C−C bond and C_α−H bond (from now on simply indicated as the C−H bond) cleavage. A quantitative assessment of the relative effects of OH and OR groups on the carbon atoms of the scissile bond on the cleavage rate is also lacking. Information of this type would be highly desirable, especially with respect to the possibility of a specific assistance to the cleavage exerted by the OH group.[17,18]

Scheme 1



We have considered it of interest to address at least parts of the above problems, and to this purpose we have exploited the already tested ideal properties of potassium 12-tungstocobaltate(III) ($K_5[Co(III)W_{12}O_{40}]$; from now on indicated as Co(III)W) for the kinetic investigations of *bona fide* one-electron oxidations.[19−21] Thus, we have performed a detailed kinetic and products study of the reactions of a number of 1-arylpropanols, 1-aryl-1,2-propanediols and their corresponding methyl ethers (compounds **1**−**4** and **7**−**10**) and 1,2-diarylethanols (compounds **5** and **6**) with Co(III)W in aqueous acetic acid, in the presence and in the absence of a base (AcOK).



1: Z = R_2 = OCH_3; R_1 = R_3 = H; R_4 = CH_3
2: Z = OCH_3; R_1 = R_3 = H; R_2 = OH; R_4 = CH_3
3: Z = R_1 = R_3 = H; R_2 = OH; R_4 = CH_3
4: Z = R_1 = R_3 = H; R_2 = OCH_3; R_4 = CH_3
5: Z = OCH_3; R_1 = R_3 = H; R_2 = OH; R_4 = C_6H_5
6: Z = OCH_3; R_2 = R_3 = H; R_1 = OH; R_4 = C_6H_5
7: Z = OCH_3; R_1 = OH; R_2 = R_3 = R_4 = CH_3
8: Z = R_1 = OCH_3; R_2 = R_3 = R_4 = CH_3
9: Z = OCH_3; R_1 = R_2 = OH; R_3 = H; R_4 = CH_3
10: Z = R_1 = R_2 = OCH_3; R_3 = H; R_4 = CH_3

For these reactions, the mechanism shown in Scheme 1 can reasonably be expected. In this scheme the C−C bond cleavage path is indicated as a base-induced process, since as we will see, this is the situation found with the substrates under investigation. It should also be noted that since the $E°$ value for the Co(III)W/Co(II)W couple is 1.00 V vs NHE,[19] the kinetic investigation is meaningful with and has been applied only to the more reactive 4-methoxy-substituted substrates (compounds **1**, **2**, and **5**−**10**), whose oxidation potential should be around 1.8−1.9 V vs NHE.[22] For compounds **3** and **4**, with much higher oxidation potential, only the products study has been carried out. For compounds **5** and **6**, this study has been supplemented with pulse radiolysis experiments to obtain direct information on the radical cation fragmentation step. The results of this investigation are described in this paper.

Results

(a) Oxidations Induced by Co(III)W. The reactions of compounds **1**, **2**, and **5**−**10** with Co(III)W were studied under

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[22] In non-aqueous solvents, based on the reasonable assumption that 4-methoxyphenylalkanols have an oxidation potential quite close to that of 4-methoxytoluene.[21] In water the $E°$ values should be lower by 0.2−0.3 V (Jonsson, M.; Lind, J.; Reitberger, T.; Eriksen, T. E.; Merényi, G. *J. Phys. Chem.* **1993**, *97*, 11278−11282).

Scheme 2

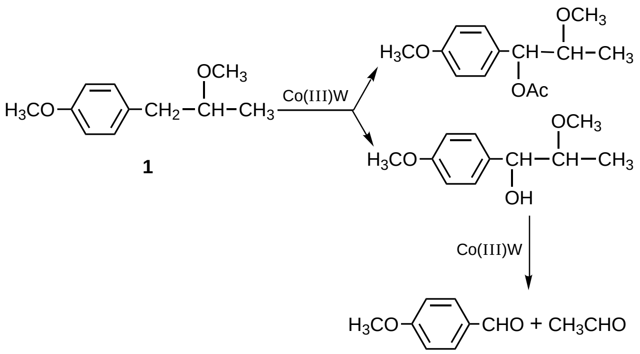

Table 1. Ratio between 4-Methoxybenzaldehyde (*A*) and the Sum of 4-Methoxybenzyl Alcohol (*B*) and 4-Methoxybenzyl Acetate (*C*) as a Function of the Concentration of AcOK for the Reaction of **2** with Co(III)W in AcOH/H_2O (55:45 (w/w) at 50 °C

[AcOK] (M)	$A/(B+C)^a$
0.00	>20
0.25	1.94
0.47	1.11
1.00	0.63

[a] Determined by GLC analysis.

argon, in 55/45 (w/w) AcOH/H_2O mixed solvents at 50 °C in the presence and in the absence of AcOK. Compounds **1**−**4** were also investigated in 4/1 (v/v) AcOH/H_2O at 110 °C with no AcOK added. The concentrations ranged from 0.038 to 0.094 M for Co(III)W and from 0.050 to 0.108 M for the substrate. AcOK concentration was varied from 0.25 to 1.00 M. Generally, equal concentrations of Co(III)W and substrate were used for reactions at 50 °C, whereas those at 110 °C were carried out with a substrate/Co(III)W molar ratio of 2. Products were identified by GLC (comparison with authentic specimen) and by GC-MS analysis, and quantitatively determined by GLC. Acetaldehyde was detected by formation and characterization of its 2,4-dinitrophenylhydrazone, and 2-methylpropene by conversion into 1,2-dibromo-2-methylpropane.

The reactions of 1-(4-methoxyphenyl)-2-methoxypropane (**1**), both in the presence and in the absence of AcOK, led to the formation of 4-methoxybenzaldehyde and the acetate of 1-(4-methoxyphenyl)-2-methoxy-1-propanol) (*erythro*−*threo* mixture), in a molar ratio (*ca*. 2.5) which remains constant during the reaction. Acetaldehyde is also formed together with small amounts of 1-(4-methoxyphenyl)-2-methoxy-1-propanol (*erythro*−*threo* mixture). It is very likely that 4-methoxybenzaldehyde derives from the oxidation of the latter diastereomeric mixture. Indeed, in an independent experiment, the mixture was rapidly converted into 4-methoxybenzaldehyde by Co(III)W. The reaction of **1** with Co(III)W should therefore occur as described in Scheme 2, leading to side-chain-substituted derivatives as the primary reaction products. The same product distribution was observed when **1** was reacted with Co(III)W at 110 °C.

In the absence of AcOK as a base, at 50 °C, the reaction of 1-(4-methoxyphenyl)-2-propanol (**2**) with Co(III)W afforded as products only 4-methoxybenzaldehyde and acetaldehyde. In the presence of AcOK, the formation of 4-methoxybenzyl alcohol and 4-methoxybenzyl acetate was additionally observed, whereby the amount of benzylic products increased with increasing [AcOK], as shown in Table 1.

In comparison, in the absence of AcOK, at 110 °C, the major product still was 4-methoxybenzaldehyde (76%), but substantial amounts of 4-methoxybenzyl acetate (18%) were also observed, together with 4-methoxyphenylacetone (6%).

Replacement of the 4-methoxy group by H led to a substantial decrease in reactivity. Thus, both 1-phenyl-2-propanol (**3**) and its methyl ether (**4**) reacted very slowly with Co(III)W (ca. 20% conversion after 280 h) and the only reaction products observed were benzyl acetate and acetaldehyde.

The reaction of 1-phenyl-2-(4-methoxyphenyl)ethanol (**5**), both in the presence and in the absence of AcOK, led to the following ring-methoxylated products: 4-methoxybenzaldehyde (10%), and 4-methoxybenzyl alcohol and 4-methoxybenzyl acetate (together 90%). In addition, benzaldehyde was formed in an amount corresponding to that of the ring-methoxylated products.

1-(4-Methoxyphenyl)-2-phenylethanol (**6**) gave 4-methoxybenzaldehyde (85%) and 4-methoxyphenyl benzyl ketone (15%) as the only ring-methoxylated products. Benzyl alcohol and benzyl acetate, in amounts corresponding to that of 4-methoxybenzaldehyde, were also formed. The products distribution was the same in the presence and in the absence of AcOK.

With 1-(4-methoxyphenyl)-2,2-dimethyl-1-propanol (**7**), its methyl ether (**8**), *threo*-1-(4-methoxyphenyl)-1,2-propanediol (**9**), and its dimethyl diether (**10**), 4-methoxybenzaldehyde was the only observed aromatic product. However, it was found that compounds **8** and **10** are first hydrolyzed to **7** and 1-(4-methoxyphenyl)-2-methoxy-1-propanol, respectively, which then react with Co(III)W to give the aldehyde: thus no further study was carried out with **8** and **10**.

The stoichiometry of the reaction was determined for compounds **7** and **9**, which lead to stable oxidation products. With these compounds, 2 mol of Co(III)W are required to oxidize 1 mol of substrate, in line with previous observations.[19−21] For compounds **1**, **2**, and **5**, the stoichiometry was not determined since the first oxidation products (diols or methoxy alcohols) react further with Co(III)W.

(b) Kinetic Studies. Kinetics were carried out spectrophotometrically, at 50 °C, by following the decrease of the absorption due to Co(III)W at 390 nm. The concentration of Co(III)W (between 5×10^{-4} and 2.5×10^{-3} M) was at least 15-fold smaller than that of the substrate (ranging from 0.015 to 0.20 M). Under these conditions, any complication due to further oxidation of the reaction products is also minimized (see above).

On the basis of the mechanism in Scheme 1, the complete rate expression for the reactions under investigation is that reported in eq 2, where k_1 and k_{-1} are the rate constants for the forward and the back electron transfer step, respectively, and k_2 is the rate constant for the fragmentation step ($k_{2(C-C)}$, $k_{2(C-H)}$, or $k_{2(C-C)} + k_{2(C-H)}$ depending on the fragmentation pattern). The factor 2 takes into account the fact that 2 mol of Co(III)W are needed to form the first oxidation products.

$$\frac{-d[\mathrm{Co(III)W}]}{dt} = \frac{2k_1k_2[\mathrm{Co(III)W}][\mathrm{AcOK}][\mathrm{subst}]}{k_{-1}[\mathrm{Co(II)W}] + k_2[\mathrm{AcOK}]} \quad (2)$$

When $k_{-1}[\mathrm{Co(II)W}] \gg k_2[\mathrm{AcOK}]$ eq 2 can be rewritten as in eq 3, whereas if the reverse situation holds, i.e. $k_{-1}[\mathrm{Co(II)W}] \ll k_2[\mathrm{AcOK}]$, a simple second-order reaction is expected.

$$\frac{-d[\mathrm{Co(III)W}]}{dt} = \frac{2k_1k_2[\mathrm{subst}][\mathrm{Co(III)W}][\mathrm{AcOK}]}{k_{-1}[\mathrm{Co(II)W}]} \quad (3)$$

The kinetic study showed that the reactions of compounds **5**−**7** with Co(III)W require the complete rate expression (eq 2) to be conveniently described. This means that $k_{-1}[\mathrm{Co(II)W}]$ cannot be disregarded with respect to $k_2[\mathrm{AcOK}]$ and *vice versa*. Thus, the kinetic data were subjected to the mathematical

Table 2. Kinetic Data for the Oxidation of **5**, **6**, and **7** by Co(III)W in AcOH/H_2O (55:45) at 50 °C in the Presence of 0.3 M AcOK

compd	[Co(III)W] (M)	[subst] (M)	k_1 (M^{-1} s^{-1})[a]	k_{-1}/k_2[b]
5	1.0×10^{-3}	5.0×10^{-2}	5.7×10^{-2}	1.1×10^{3}
6	1.0×10^{-3}	5.0×10^{-2}	9.9×10^{-3}	6.9×10^{2}
7	5.0×10^{-4}	5.0×10^{-2}	1.8×10^{-2}	7.5×10^{2}
7	1.0×10^{-3}	5.0×10^{-2}	1.8×10^{-2}	6.0×10^{2}
7	1.0×10^{-3}	7.5×10^{-2}	1.9×10^{-2}	5.1×10^{2}
7[c]	1.0×10^{-3}	5.0×10^{-2}	1.7×10^{-2}	7.1×10^{2}

[a] Rate constant for the electron transfer step, calculated as described in ref 21. [b] Ratio between the rate constant for the back electron transfer and the one for the fragmentation step, calculated as described in ref 21. [c] In the presence of 0.1 M AcOK.

Table 3. Kinetic Data for the Oxidation of **1** and **2** by Co(III)W in AcOH/H_2O (55:45) at 50 °C in a Variety of Conditions

compd	[Co(III)W] (M)	[subst] (M)	[AcOK] (M)	k_1k_2/k_{-1} (M^{-1} s^{-1})[a]
1	1.0×10^{-3}	5.0×10^{-2}	0.30	1.5×10^{-6}
1	9.4×10^{-4}	4.7×10^{-2}	0.47	1.9×10^{-6}
1	1.0×10^{-3}	1.0×10^{-1}	0.50	2.0×10^{-6}
2	1.0×10^{-3}	5.0×10^{-2}	0.10	3.2×10^{-6}
2	1.0×10^{-3}	5.0×10^{-2}	0.30	3.9×10^{-6}

[a] Calculated as described in the text.

Table 4. Kinetic Data for the Oxidation of *threo*-**9** by Co(III)W in AcOH/H_2O (55:45) at 50 °C in the Presence of 0.30 M AcOK

[Co(III)W] (M)	[subst] (M)	k_1 (M^{-1} s^{-1})[a]
1.0×10^{-3}	1.5×10^{-2}	1.21×10^{-2}
1.0×10^{-3}	5.0×10^{-2}	1.21×10^{-2}
1.0×10^{-3}	1.0×10^{-1}	1.15×10^{-2}
1.0×10^{-3}	2.0×10^{-1}	1.08×10^{-2}
5.0×10^{-4}	1.0×10^{-1}	1.18×10^{-2}
2.5×10^{-3}	1.0×10^{-1}	1.13×10^{-2}
1.0×10^{-3}	5.0×10^{-2}	2.32×10^{-2} [b]
1.0×10^{-3}	5.0×10^{-2}	2.07×10^{-2} [b,c]

[a] Rate constant for the electron transfer step, calculated as described in the text. [b] No AcOK added. [c] Mixture of *threo*- and *erythro*-**9**.

analysis provided by Kochi and co-workers for the one-electron oxidation of methylbenzenes by iron(III) phenanthrolines, which is also described by eq 2, with pyridine as the base in the place of AcOK.[23] By such analysis it was possible to calculate the values of k_1 and k_{-1}/k_2 for the reactions of **5**–**7**. These values are reported in Table 2.

Equation 3 appeared, instead, to be more appropriate than eq 2 to describe the kinetic behavior of the reactions of **1** and **2**, thus indicating that in these reactions k_{-1}[Co(II)W] is much larger than k_2[AcOK] and the rate determining step is the fragmentation of the radical cation. When eq 3 holds, the kinetic analysis allowed only the calculation of k_1k_2/k_{-1}. The values are in Table 3.

A different kinetic behavior was found for the reactions of *threo*-**9**. Working with an excess of substrate excellent first-order plots were obtained up to 90% of reaction. No base catalysis was observed; in fact, the reaction rate was faster when no AcOK was added. From the first-order rate constants, obtained by fitting the kinetic data to eq 4 by a nonlinear regression analysis, the second-order rate constants k_1 were calculated. Clearly, in the reaction of *threo*-**9** the situation holds where $k_{-1}[\mathrm{Co(II)W}] \ll k_2[\mathrm{AcOK}]$, the electron transfer step being rate determining.

$$[\mathrm{Co(III)W}] = [\mathrm{Co(III)W}]_0 \exp(-k_{\mathrm{obs}}t) \qquad (4)$$

Some experiments were also carried out by using a mixture of *threo*- and *erythro*-**9** as the substrates. The rate constant found is very close to that with *threo*-**9**; thus no significant difference in reactivity exists between the two diastereoisomers. All data are collected in Table 4.

(c) Pulse Radiolysis Experiments. In order to gain further insight into the reaction pattern of the radical cations, compounds **5** and **6** were studied using the pulse radiolysis technique. For this purpose, in aqueous solution at pH ≈4 containing 0.02–0.2 mM **5** or **6**, the oxidizing radicals $SO_4^{\bullet-}$ or Tl^{2+} were produced by 400-ns pulses of 3-MeV electrons, as shown in eq 5–7.

$$H_2O \rightarrow H^+, OH^\bullet, e^-_{aq} \qquad (5)$$

$$S_2O_8^{2-}\ (2\ \mathrm{mM}) + e^-_{aq} \rightarrow SO_4^{2-} + SO_4^{\bullet-} \qquad (6)$$

$$Tl^+\ (2\ \mathrm{mM}) + OH^\bullet + H^+ \rightarrow Tl^{2+} + H_2O \qquad (7)$$

Tl^{2+} ($E°$ = 2.2 V vs NHE) and $SO_4^{\bullet-}$ (E° = 2.7 V vs NHE) have been shown to react with anisole derivatives by one-electron transfer to yield the corresponding radical cations;[24] eq 8.

$$SO_4^{\bullet-}(Tl^{2+}) + \mathrm{ArOMe} \rightarrow SO_4^{2-}\ (Tl^+) + \mathrm{Ar}^{\bullet+}\mathrm{OMe} \qquad (8)$$

As expected on this basis, in solutions containing **5** or **6** the radical cations $\mathbf{5}^{\bullet+}$ and $\mathbf{6}^{\bullet+}$ were formed[25,26] as depicted in Figures 1 and 2. The spectra recorded at 30 μs after the pulse correspond to completion of the formation reaction (eq 8). Visible are the characteristic[24] bands at ~290 and ~445 nm.

It was found that the concentration of $\mathbf{5}^{\bullet+}$ and $\mathbf{6}^{\bullet+}$, as monitored by the absorbance at 440 nm, decreased in an exponential fashion (see Figures 1 and 2, insets a). In the case of $\mathbf{6}^{\bullet+}$, there was a *buildup* of optical density in the range 280–300 nm with the same rate as that for the decrease of the 440-nm band (see inset a′ of Figure 2), indicating that at this wavelength a product of the decomposition of the radical cation absorbs more strongly than the radical cation itself (at ~300 nm there is an isosbestic region). From the fact that the rate of the process responsible for the OD changes was independent of [**5**] or [**6**] (in the range 0.02–0.2 mM) or of the initial concentrations of the radical cations (in the range 0.5–5 μM) we conclude that $\mathbf{5}^{\bullet+}$ and $\mathbf{6}^{\bullet+}$ undergo a *uni*molecular transformation reaction. As shown by time-resolved conductance experiments (for example, see inset a′ of Figure 1), this reaction, which leads to an *in*crease in conductance in acidic solution (pH 3.5–6) and a stoichiometrically equal *de*crease of conductance in basic solution (pH 8–9) with the same rate as observed optically, consists of the production of H^+ with the same yield as that of the radical cations, $\mathbf{5}^{\bullet+}$ or $\mathbf{6}^{\bullet+}$, based on the initial yield of $SO_4^{\bullet-}$ and its complete reaction via eq 8. On the basis of the product analysis results (see Results, section a), this

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[23] Schlesener, C. J.; Amatore, C.; Kochi, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 7472–7482.

[24] O'Neill, P.; Steenken, S.; Schulte-Frohlinde, D. *J. Phys. Chem.* **1975**, *79*, 2773–2779. Steenken, S.; O'Neill, P.; Schulte-Frohlinde, D. *J. Phys. Chem.* **1977**, *81*, 26–30.

[25] The rate constants for reaction with $SO_4^{\bullet-}$ are ≈5×10^9 M^{-1} s^{-1} and those for Tl^{2+} are ≈1×10^9 M^{-1} s^{-1}, similar to those for reaction of $SO_4^{\bullet-}$ and Tl^{2+} with other anisole derivatives (see ref 24).

[26] The *yield* of the radical cations was found to be independent of whether they were produced by $SO_4^{\bullet-}$ or by Tl^{2+}. For Tl^{2+}, reaction with only the methoxylated ring in **5** or **6** is expected. However, with $SO_4^{\bullet-}$ both the methoxylated and the non-methoxylated ring are expected to be attacked (on the basis of the rate constants for reaction with anisole and benzene see ref 24 and: Neta, P.; Madhavan, V.; Zemel, H.; Fessenden, R. W. *J. Am. Chem. Soc.* **1977**, *99*, 163–164. If this occurs, the equality of the yields from reaction with (a) the selective and (b) the nonselective oxidant indicates rapid intramolecular electron transfer from the methoxylated to the "electron hole" at the non-methoxylated ring.

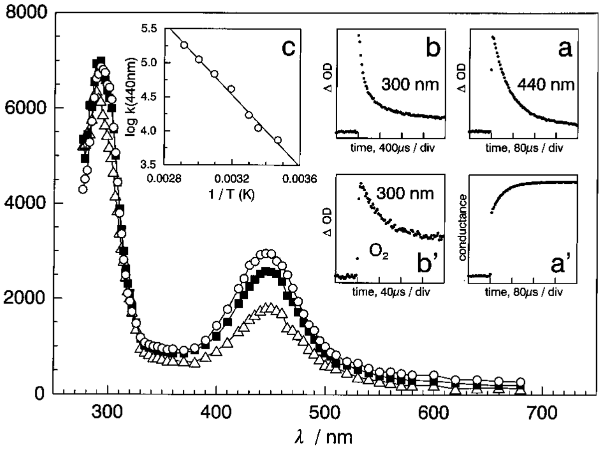


Figure 1. Time-resolved absorption spectra observed on reaction of $SO_4^{\bullet-}$ with **5** (0.1 mM) in an argon-saturated aqueous solution (pH 5.4) containing 0.1 M *tert*-butyl alcohol and 10 mM $K_2S_2O_8$ at 10 (circles), 28 (squares), and 80 μs (triangles) after the 400 ns 3-MeV electron pulse. Insets: (a) First-order decay of $\mathbf{5}^{\bullet+}$ as monitored at 440 nm; (a′) buildup of conductance resulting from decay of $\mathbf{5}^{\bullet+}$. (b) Decay (second-order) of absorption at 300 nm, assigned to mainly $4MeOC_6H_4CH_2^{\bullet}$ and to $4MeOC_6H_4CH^{\bullet}CH(OH)Ph$ (see text). (b′) Decay at 300 nm in the presence of O_2 (1 mM). In the case of b′ the signal amplitude is only half of that in b. Note that in b′ the time scale is 10 times shorter than that in b. (c) Arrhenius plot for the decay of $\mathbf{5}^{\bullet+}$.

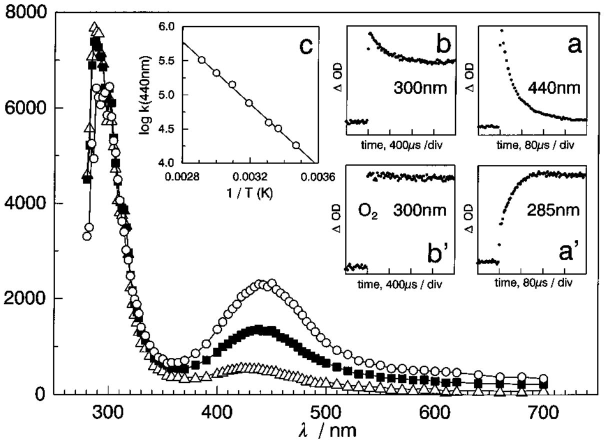
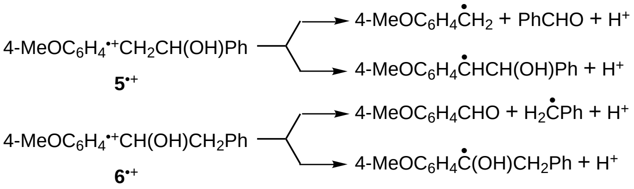


Figure 2. Time-resolved absorption spectra observed on reaction of $SO_4^{\bullet-}$ with **6** (0.1 mM) in an argon-saturated aqueous solution (pH 5.4) containing 0.1 M *tert*-butyl alcohol and 10 mM $K_2S_2O_8$ at 10 (circles), 30 (squares), and 80 μs (triangles) after the 400-ns 3-MeV electron pulse. Insets: (a) First-order decay of $\mathbf{6}^{\bullet+}$ as monitored at 440 nm. (a′) Corresponding buildup of absorption at 285 nm due to the formation of $4MeOC_6H_4CHO$. In this experiment, $\mathbf{6}^{\bullet+}$ was produced by oxidation with Tl^{2+} (eq 8). (b) Decay (partial) of absorption at 300 nm. The decay is assigned to $4MeOC_6H_4C^{\bullet}(OH)CH_2Ph$, which is scavenged by O_2 (inset b′). The remaining absorption is due to $4MeOC_6H_4CHO$ (see text). (c) Arrhenius plot for the decay of $\mathbf{6}^{\bullet+}$.

Scheme 3



reaction is identified as fragmentation of the $C_\alpha-C_\beta$ bond together with deprotonation of the $C_\alpha-H$ bond (Scheme 3).

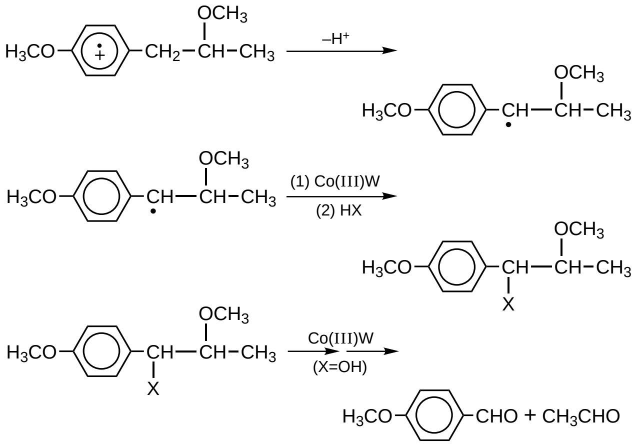
In the case of $\mathbf{6}^{\bullet+}$, one of the aromatic products of the $C_\alpha-C_\beta$ bond cleavage is 4-methoxybenzaldehyde, which has a strong absorption at ~280 nm. The observed first-order increase of absorption in the 280−300-nm range (inset a′ of Figure 2) is thus in support of the product analysis data which show 4-methoxybenzaldehyde to be the major product. In agreement with the above assignment, the decay at 300 nm[27] (inset b of Figure 2) is *not* to zero and an apparently stable species, which does not react with O_2, remains after 0.8 ms (inset b′ of Figure 2). The (small) decay observed up to 0.8 ms is assigned to $4MeOC_6H_4C^{\bullet}(OH)CH_2Ph$ formed in minor proportion. This is again in agreement with the product analysis results. In contrast, in the case of $\mathbf{5}^{\bullet+}$, the optical density at 300 nm (inset b Figure 1) decays (by second-order kinetics) to almost zero in the 1.6-ms period after generation of the radical cation, suggesting that the species responsible are benzyl radicals, most probably $4MeOC_6H_4CH_2^{\bullet}$ and $4MeOC_6H_4CH^{\bullet}CH(OH)Ph$. In agreement with this assumption is the fact that the decay is accelerated by O_2 (see inset b′ of Figure 1).

Table 5. Kinetic Data for the Fragmentation Reactions of $\mathbf{5}^{\bullet+}$ and $\mathbf{6}^{\bullet+}$ Obtained from Pulse Radiolysis Experiments[a]

compd	k (s^{-1})[b]	$\Delta H^{\#}$ (kJ mol^{-1})	$\Delta S^{\#}$ (J K^{-1})	$k(H_2O)/k(D_2O)$
$\mathbf{5}^{\bullet+}$	2.0×10^4	48	−6	1.4
$\mathbf{6}^{\bullet+}$	3.2×10^4	41	−21	1.2

[a] The reaction is mainly C−C bond cleavage (see text). [b] Decay rate of the radical cation.

Scheme 4



The rate of disappearance of the radical cations by cleavage (Scheme 3) increased with increasing temperature, and from this dependence (see insets c in Figures 1 and 2) the Arrhenius parameters at 298 K were obtained. The decays of the radical cations $\mathbf{5}^{\bullet+}$ and $\mathbf{6}^{\bullet+}$ were also studied in D_2O, where the rate constants for transformation were found to be lower, i.e., $k(H_2O)/k(D_2O)$ was 1.4 and 1.2 for $\mathbf{5}^{\bullet+}$ and $\mathbf{6}^{\bullet+}$, respectively. All kinetic data are collected in Table 5.

Discussion

As shown in the Results, section a, the primary products in the oxidation of **1** at 50 °C are 1-(4-methoxyphenyl)-2-methoxy-1-propanol and its acetate (both diastereomeric mixtures). Whereas the latter is stable under the reaction conditions, the former is rapidly converted into 4-methoxybenzaldehyde and acetaldehyde by reaction with Co(III)W. These findings clearly suggest that the exclusive pathway of $\mathbf{1}^{\bullet+}$ is deprotonation to form an α-substituted benzyl radical from which products are obtained as shown in Scheme 4 (X = OH, OAc).

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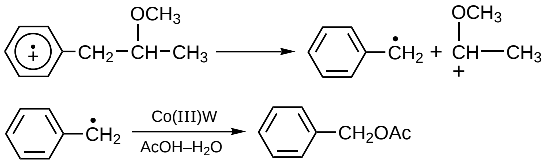
(27) In the insets b of Figures 1 and 2 are shown traces reflecting the optical density change at 300 nm in a time range extending to 1.6 ms after generation of the radical cations by reaction described in eq 8.

Scheme 5



The kinetic study of this reaction (see Results, section b) indicates that the radical cation is formed in a fast equilibrium and that the cleavage of the C−H bond is the step which determines the rate of the overall oxidation.

The reaction of **1** with Co(III)W at 110 °C leads to the same products, i.e., the large increase in the temperature does not modify the outcome of the reaction, C−H bond cleavage remaining the only path available to $\mathbf{1}^{\bullet+}$. Conversely, a dramatic effect is observed upon the removal of the 4-methoxy group (that is, passing from **1** to **4**). Accordingly, in the oxidation of **4** the major product is benzyl acetate, which derives from C−C bond cleavage in $\mathbf{4}^{\bullet+}$, which should occur in a heterolytic fashion (Scheme 5) since the oxidation potential of $^{\bullet}CH(OCH_3)CH_3$ (−0.45 V)[28,29] is significantly more negative than that of the benzyl radical (0.73 V).[28]

The drastically different behavior of $\mathbf{4}^{\bullet+}$ and $\mathbf{1}^{\bullet+}$ with respect to the competition between C−H and C−C bond cleavage is in full agreement with our results concerning the photooxidation of **4** and **1** sensitized by TiO_2 in the presence of Ag^+: **1** gave only products of C−H bond cleavage, whereas from **4** only products of C−C bond cleavage were observed.[30] It should be noted that exclusive C−C bond cleavage in $\mathbf{4}^{\bullet+}$ has also been observed by Arnold in the photooxidation of **4** sensitized by 1,4-dicyanobenzene.[31]

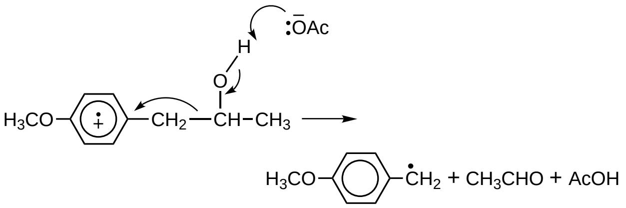
The relative weight of C−H vs C−C bond cleavage significantly decreases on going from $\mathbf{1}^{\bullet+}$ to $\mathbf{4}^{\bullet+}$, indicating the existence of different electronic requirements for the two pathways.

Probably, the extent of positive charge, which accumulates on the scissile bond in the transition state of the cleavage process, is larger for the scission of the C−C bond than for that of the C−H bond. Thus, the 4-methoxy group, which stabilizes the positive charge by its +R effect and therefore opposes the charge transfer from the ring to the β bond, may exert an unfavorable effect more on the cleavage of the C−C bond than on C−H deprotonation.

In the oxidation of 1-(4-methoxyphenyl)-2-propanol (**2**) the products are 4-methoxybenzaldehyde, 4-methoxybenzyl alcohol, and 4-methoxybenzyl acetate. Thus, $\mathbf{2}^{\bullet+}$ undergoes both C−H and C−C bond cleavage, the former leading to 4-methoxybenzaldehyde (by a mechanism analogous to that reported in Scheme 4), the latter to 4-methoxybenzyl alcohol and acetate, formed by Co(III)W induced oxidation of the 4-methoxybenzyl radical. Thus, replacing the β-methoxy group with the hydroxyl group leads to a significant increase in the relative weight of the C−C bond cleavage.

Interestingly, both fragmentation paths of $\mathbf{2}^{\bullet+}$ are catalyzed by AcOK. In fact, the proportion of C−C bond cleavage products increases on increasing the concentration of AcOK, as clearly shown by the data reported in Table 1. Accordingly, when the reaction is carried out in the absence of AcOK, only products of C−H bond cleavage are observed!

Scheme 6



The favorable effect of a β-OH group on the C−C bond cleavage rate in a radical cation has already been observed by Whitten and his associates in the photoinduced oxidation of 1,2-amino alcohols.[17,18] They suggested that C−C bond cleavage is concerted with the breaking of the O−H bond and such a suggestion should also hold in the present case (Scheme 6) where it is further supported by the observation of base catalysis. Certainly, this hypothesis nicely accounts for the largely different behaviors of $\mathbf{1}^{\bullet+}$ and $\mathbf{2}^{\bullet+}$ with respect to the importance of the C−C bond cleavage path. However, the situation may be more complex than that depicted in Scheme 6, as will be discussed later on.[32]

As expected,[34] on increasing the temperature, the rate of C−C bond cleavage is enhanced relative to that of the C−H bond. Thus, at 110 °C in the absence of AcOK, the reaction of **2** with Co(III)W leads to 4-methoxybenzyl acetate (product of C−C bond cleavage in the radical cation) in addition to 4-methoxybenzaldehyde (C−H bond breaking), which is the major product. This result has to be compared with that obtained at 50 °C, in the absence of AcOK, where only the product of C−H bond breaking (4-methoxybenzaldehyde) was obtained. In the reaction at 110 °C, small amounts of 4-methoxyphenylacetone were also formed. Probably, it also derives from the C−H bond cleavage pathway; the possibility of a 1,2-hydrogen shift in the α-substituted benzyl carbocation, obtained by oxidation of the radical $4\text{-MeOPhCH}^{\bullet}CH(OH)CH_3$ formed in the deprotonation step, has been suggested by Walling and co-workers.[35]

The oxidation of **2** exhibits the same kinetic behavior as that of **1**, the fragmentation reaction of the radical cation (this time involving both C−H and C−C bond breaking) occurring in the rate determining step. The values of k_1k_2/k_{-1} for the two compounds (Table 3) are very similar as expected.

Removal of the 4-methoxy group from **2** (that is of passing from **2** to **3**) has the same effect as that observed with the corresponding methyl ether, leading to an increased role of the C−C bond cleavage pathway. Thus, at 110 °C, in the absence of AcOK 1-phenyl-2-propanol (**3**) reacts with Co(III)W to form only benzyl acetate which derives from C−C bond cleavage in the radical cation, whereas, as reported above, under the same reaction conditions, **2** undergoes C−H bond cleavage as the major reaction pathway, predominantly forming 4-methoxybenzaldehyde.

In view of the results obtained with **1** and **2**, it seemed of interest also to look at the effect of α-OH and α-OCH_3 groups on the rate of C−C bond cleavage in the radical cation; thus,

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[28] Wayner, D. D. M.; McPhee, D. J.; Griller, D. *J. Am. Chem. Soc.* **1988**, *110*, 132−137.

[29] Actually, in ref 28 the oxidation potential of $CH_3CH^{\bullet}OC_2H_5$ is reported, which should be very close to that of $CH_3CH^{\bullet}OCH_3$.

[30] Baciocchi, E.; Rol, C.; Sebastiani, G. V.; Taglieri, L. *J. Org. Chem.* **1994**, *59*, 5272−5276.

[31] Arnold, D. R.; Lamont, L. J. *Can. J. Chem.* **1989**, *67*, 2119−2127.

[32] An additional factor making OH more effective than OCH_3 in favoring C−C bond cleavage when located on one of the two carbon atoms of the bond might be that the OH group ($\sigma^+ = -0.92$)[33] is a better +R electron donor than the OCH_3 group ($\sigma^+ = -0.78$).[33] Thus, the former group should be more effective than the latter in stabilizing the positive charge which, as already mentioned, should accumulate on the scissile bond in the transition state leading to the cleavage.

[33] Chapman, N. B.; Shorter, J. *Correlation Analysis in Chemistry*; Plenum Press: New York, 1979; Table 10.2.

[34] Okamoto, A.; Snow, M. S.; Arnold, D. R. *Tetrahedron* **1986**, *42*, 6175−6187.

[35] Walling, C.; El Taliawi, G. M.; Zhao, C. *J. Org. Chem.* **1983**, *48*, 4914−4917.

we have studied the oxidations of 1-(4-methoxyphenyl)-2,2-dimethyl-1-propanol (**7**) and its methyl ether (**8**).

In the reaction of **7** with Co(III)W, 4-methoxybenzaldehyde is the exclusive aromatic product, clearly indicating that in $\mathbf{7}^{\bullet+}$ only C−C bond cleavage takes place. In this case, however, the cleavage should occur in a homolytic way forming the *tert*-butyl radical, since the latter ($E° = 0.09$ V)[28] is much more difficult to oxidize than the α-hydroxy-4-methoxybenzyl radical ($E° = -0.51$ V).[36,37] Once formed the *tert*-butyl radical is oxidized under the reaction conditions to the corresponding carbocation, which is predominantly deprotonated to yield 2-methylpropene.

Kinetically, the oxidation of **7** follows eq 2, since contrary to the oxidation of **1** and **2**, k_2[AcOK] could not be disregarded with respect to k_{-1}[Co(II)W]. Thus, the fragmentation reaction competes better with the back electron transfer in $\mathbf{7}^{\bullet+}$ than in $\mathbf{2}^{\bullet+}$. It is reasonable to assume that k_{-1}[Co(II)W] is approximately the same in both systems (k_{-1} should be diffusion controlled). On this basis, the rate of the base-catalyzed C−C bond cleavage is significantly faster for $\mathbf{7}^{\bullet+}$ than for $\mathbf{2}^{\bullet+}$. For the oxidation of **7**, k_1, the rate constant for the electron transfer step, and the k_{-1}/k_2 ratios were calculated. From the data in Table 2, $k_1 \approx 1.8 \times 10^{-2}$ M^{-1} s^{-1} and $k_{-1}/k_2 \approx 6.6 \times 10^2$.

With the corresponding methyl ether (**8**), the process observed was only the slow conversion of **8** into **7**. Whereas the result did not allow any further study of **8**, it clearly shows that an OH group is much more effective than an OCH_3 group in promoting C_α−C_β bond cleavage in an alkylaromatic radical cation *also* when the groups are located on the α-carbon.

In order to acquire information on the relative efficiency of α- and β-OH groups in assisting C−C bond cleavage in the radical cations, the oxidations of **5** (β-OH) and **6** (α-OH) were studied. The product distribution shows that C−C bond cleavage, leading to 4-methoxybenzyl alcohol and the corresponding acetate, is the main pathway for $\mathbf{5}^{\bullet+}$. Deprotonation of the radical cation forming 4-methoxybenzaldehyde accounts for only 10% of the overall process. A similar situation holds for the oxidation of **6**. The main product (85%) is 4-methoxybenzaldehyde coming from C−C bond cleavage in $\mathbf{6}^{\bullet+}$. Deprotonation of $\mathbf{6}^{\bullet+}$ is a minor reaction (15%) leading to 4-methoxyphenyl benzyl ketone. Thus, a similar extent of C−C bond cleavage is observed for $\mathbf{5}^{\bullet+}$ and $\mathbf{6}^{\bullet+}$.

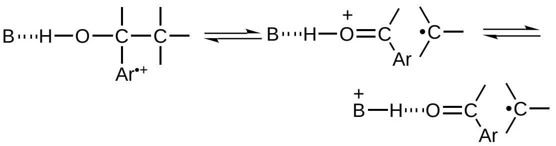
Kinetically, **5** and **6** behave like **7**, with the term k_2[AcOK] not negligible with respect to k_{-1}[Co(II)W]. The pertinent k_1 and k_{-1}/k_2 values are reported in Table 2.

The electron transfer step (k_1) is faster with **5** than with **6**, probably due to the slightly lower oxidation potential of the former compound (β-OH group) than that of the latter (α-OH group).[21] In contrast, the k_{-1}/k_2 ratios are very similar for the two substrates, which suggests very similar values of k_2 and, in view of the results of the product analysis, of the C−C bond cleavage rate in the corresponding radical cations. In conclusion, these observations indicate that in our system an OH group assists C−C bond cleavage when on the α carbon of the aromatic radical cation and the efficiency of this assistance is not very different from that provided by the β-OH group.

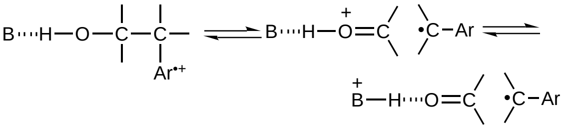
This conclusion is fully supported by the pulse radiolysis experiments, since the data in Table 5 indicate that $\mathbf{5}^{\bullet+}$ and $\mathbf{6}^{\bullet+}$ decay with a comparable rate (in fact $\mathbf{6}^{\bullet+}$ decays slightly faster than $\mathbf{5}^{\bullet+}$) to mainly form $4MeOC_6H_4CH_2^\bullet$ and $4MeOC_6H_4CHO$, respectively, as the main products. This agreement between the results of pulse radiolysis experiments (a *direct* approach to the study of radical cations) and of the kinetic study of the oxidation by Co(III)W (an *indirect* approach) is very rewarding, as it provides a convincing proof of the general reliability of the latter approach, which some of us have already used for other reactions.[21]

The finding of a similar efficiency for α- and β-OH groups in assisting the C−C bond cleavage in the radical cations requires some comments, since the idea of a Grob-type fragmentation (Scheme 6), used to rationalize the effect of the β-OH group, cannot be applied to the α-OH group, since in this case the C−C bond cleavage is of the homolytic type.

A significant insight into the nature of α- and β-OH group assistance to C−C bond cleavage is provided by the kinetic solvent isotope effect data for the fragmentation reactions of $\mathbf{5}^{\bullet+}$ and $\mathbf{6}^{\bullet+}$ (mainly C−C bond cleavage), obtained in the pulse radiolysis experiments (Table 5). In the first place, the similar $k(H_2O)/k(D_2O)$ values for the two reactions suggest a similar mechanism for the two processes and, therefore, also cast doubts on the adequacy of Scheme 6 to describe the assistance to C−C bond cleavage provided by the β-OH group. In the second place, the observed values (1.4 for $\mathbf{5}^{\bullet+}$ and 1.2 for $\mathbf{6}^{\bullet+}$) are very small, indicating that the proton does not participate to any considerable degree to the reaction coordinate, as it generally occurs for those base-catalyzed reactions where the proton transfers from and to the electronegative atom as part of an overall process also involving heavy atom motions.[38]



(9)



(10)

Since it has been suggested that for these reactions the catalytic effect of the base is due to hydrogen bonding or specific solvation, it seems reasonable to propose that the assistance of the O−H group to C−C bond cleavage may consist of the sequence of events described in eqs 9 (α-OH) and 10 (β-OH), where the reacting species do not diffuse apart between the individual steps. If the cleavage of the C−C bond is the slow step, this interpretation rationalizes the small kinetic solvent isotope effect (only a secondary effect is expected) as well as the similar efficiency of α- and β-OH in assisting the cleavage of the C−C bond, the main driving force in both cases being provided by the formation of the carbonyl group. Probably, some energetic disadvantage of the homolytic way of cleavage actually exists,[12] but in this case it is compensated by the formation of a more stable C═O double bond (conjugation with the p-OCH_3 group) in the C−C bond cleavage of $\mathbf{6}^{\bullet+}$. The negative entropies of activation for the fragmentation reactions of $\mathbf{5}^{\bullet+}$ and $\mathbf{6}^{\bullet+}$, as determined in the pulse radiolysis experiments (Table 5), are in support of this picture ($B = H_2O$ in eqs 9 and 10) as they indicate (partial) immobilization of water molecules in the transition state of the cleavage process.[39]

It should be mentioned, however, that at variance with our observations, only deprotonation was observed for the radical cation of 1-(4-(dimethylamino)phenyl)-2-phenylethanol, a system with an α-OH group, whereas C−C bond cleavage is the exclusive reaction for the radical cation of 2-(4-(dimethylamino)-phenyl)-1-phenylethanol where the OH group is instead located

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(36) Wayner, D. D. M.; Sim, B. A.; Dannenberg, J. J. *J. Org. Chem.* **1991**, *56*, 4853−4858.

(37) Actually, in ref 36 the oxidation potential value refers to $4\text{-MeOPhCH}^\bullet\text{-OCH}_3$. We reasonably assume a very similar value for $4\text{-MeOPhCH}^\bullet\text{OH}$.

(38) Schowen, R. L. *Prog. Phys. Org. Chem.* **1972**, *9*, 275−332.

on the β carbon.[17] We have no explanation for this discrepancy apart from the fact that in the above systems most of the charge should reside on the nitrogen atom, whereas in the radical cations of **5**−**7**, the charge is predominantly located on the aromatic ring. Differences in charge distribution in the radical cations may result in the different structural response of the C−H *vs* C−C bond cleavage competition in the two systems. It may also be relevant that the reactions of the amino alcohols were carried out in a non-aqueous solvent.

We now discuss the results of the reaction of *threo*-1-(4-methoxyphenyl)-1,2-propanediol (*threo*-**9**) with Co(III)W. The radical cation undergoes exclusive C−C bond cleavage with formation of 4-methoxybenzaldehyde. Kinetically, the oxidation of *threo*-**9** displays clean second-order kinetics (Table 4), different from the substrates discussed above. Clearly, the cleavage of the C−C bond in the radical cation is sufficiently fast as to make the electron transfer rate determining. As a result, no effect of AcOK on the reaction rate is observed. We also found that the reactivity of *threo*-**9** is identical to that of a mixture of *threo*- and *erythro*-**9**, which indicates identical reactivity for the two diastereomers, in perfect line with a rate determining electron transfer step (the two diastereoisomers should have the same oxidation potential). It is rewarding to note that the directly determined rate constant for the oxidation of *threo*-**9** (1.2×10^{-2} M^{-1} s^{-1}), which refers to the electron transfer step (k_1), is very similar to that calculated by eq 2 for the electron transfer step in the oxidation of **7**, as expected.

For the dimethyl ether of **9**, the study was hampered by the conversion of the α-OCH_3 group into an OH group, which occurs with a rate at least comparable with that of the oxidation process. Thus, it can only be estimated that the oxidation of **10** (an *erythro*−*threo* mixture) with Co(III)W is at *least* 20 times slower than that of **9**. This strong decrease in reactivity is in line with the role of the OH group (α or β) in assisting the cleavage of the C−C bond, as already discussed (see eqs 9 and 10).

Finally, it is noted that with metal-induced oxidative fragmentations of alcohols, the observation that the alcohol (or the diol) is more reactive than the corresponding ether is often taken as evidence for complexation of the substrate with the oxidant involving the OH group.[43] On this basis, a radical cation mechanism is generally discarded. However, this conclusion is probably not justified since the results presented here clearly show that C−C bond cleavage in α- and (or) β-OH substituted alkylaromatic radical cations is much faster than in the corresponding OCH_3 substituted species, due to the possibility for O−H deprotonation and, more importantly, formation of carbonyl products.

Summary and Conclusions

The results reported in this paper provide insight into the effects of structure upon the competition between C_α−H and C_α−C_β bond cleavage in arylalkanol radical cations and on the role of the side-chain OH groups in assisting the cleavage of the C_α−C_β bond. The path leading to the cleavage of the C−C bond is strongly disfavored when a 4-methoxy group is present in the *ring*, probably because it opposes the accumulation of positive charge on the scissile C−C bond in the transition state leading to the cleavage. The presence of an OH group on C_α or C_β enhances the rate of C−C bond cleavage, the effect being much larger than that of the OCH_3 group, and the efficiency of such assistance is almost the same for α- and β-OH groups, in spite of the fact that the C−C bond breaking is homolytic in the former case and heterolytic in the latter. On the basis of the kinetic solvent isotope effect values, $k(H_2O)/k(D_2O)$, for the fragmentation reactions of $\mathbf{5}^{\bullet+}$ and $\mathbf{6}^{\bullet+}$, obtained by pulse radiolysis experiments, hydrogen bonding or specific solvation in conjunction with carbonyl group formation appear to be the key factors determining the enhancing effect of the α- and β-OH groups on the rate of C−C bond cleavage.

Finally, information has been obtained on how substituents on the scissile C−C bond influence the relative importance of the electron transfer and fragmentation steps with respect to the rate of the oxidation induced by Co(III)W. When only one group (OH or OCH_3) is present in the side chain (either on C_α or C_β) the fragmentation step or both the electron transfer and fragmentation steps contribute to the overall oxidation rate. However, with an OH group on both carbons of the scissile bond, the rate of C−C bond cleavage becomes so fast that the electron transfer step is rate determining.

Experimental Section

Potassium 12-tungstocobaltate(III) was prepared as described previously.[19] **1-(4-Methoxyphenyl)-2-propanol (2)** was prepared by reaction of 4-methoxyphenylacetone with $NaBH_4$ in 2-propanol: bp 98−99 °C (0.26 mbar) (lit.[44] bp 119 °C (4 mmHg)).

1-(4-Methoxyphenyl)-1,2-propanediol (9). The *threo* isomer was prepared by reaction of *trans*-anethole with potassium permanganate in CH_2Cl_2 in the presence of benzyltriethylammonium chloride[45] and identified by ^{1}H-NMR[46] and GC-MS; mp 61.5−62.5 °C (lit.[46] mp 63−64 °C). The *erythro*−*threo* mixed diols were prepared as described previously.[47]

1-(4-Methoxyphenyl)-2-methoxy-1-propanol (*erythro*−*threo* mixture) was prepared by a three-step synthesis. 2-Methoxypropionitrile was prepared by reaction of trimethylsilyl cyanide with acetaldehyde dimethylacetal in the presence of boron trifluoride-etherate:[48] bp 110−115 °C (lit.[49] 110−113 °C). 2-Methoxypropionitrile was reacted with 4-methoxyphenyl magnesium bromide in anhydrous tetrahydrofuran to yield 4-methoxyphenyl 1-methoxyethyl ketone. The ketone was reduced with $NaBH_4$ in 2-propanol to yield 1-(4-methoxyphenyl)-2-methoxy-1-propanol (*erythro*−*threo* mixture). For ^{1}H-NMR,[50] ^{13}C-NMR, EIMS, and elemental analysis data see the supporting information.

1-(4-Methoxyphenyl)-2-methoxy-1-propanol acetate (*erythro*−*threo* mixture) was prepared by reaction of the corresponding alcohol with acetic anhydride in pyridine. For ^{1}H-NMR,[50] ^{13}C-NMR, EIMS, and elemental analysis data see the supporting information.

1-Phenyl-2-(4-methoxyphenyl)ethanol (5), 1-(4-methoxyphenyl)-2-phenylethanol (6), and **1-(4-methoxyphenyl)-2,2-dimethyl-1-pro-**

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[39] Another possibility might be that the α-hydroxy-substituted radical cation is first deprotonated to form a benzyloxy radical, which then undergoes a fast β-fragmentation reaction, as also proposed by Albini[40] and Kochi[41] to rationalize the C−C bond cleavage in photogenerated pinacol radical cations. However, there is clear evidence that benzyl alcohol radical cations undergo C_α−H and not O−H deprotonation,[42] and moreover we cannot envisage any mechanism by which the charge can be transferred from the aromatic ring to the oxygen atom since there is no direct interaction between the π system and the O−H bond.

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panol (7) were prepared by reaction of the corresponding ketones with $NaBH_4$ in 2-propanol. The ketones were prepared by reaction of the appropriate Grignard reagent (4-methoxyphenylmagnesium or phenylmagnesium bromide) and acid chloride (4-methoxyphenylacetyl, phenylacetyl, and trimethylacetyl, respectively) in anhydrous tetrahydrofuran.[51] **5**: mp 57−58 °C. **6**: mp 55−57 °C (lit.[52] mp 58 °C). **7**: identified by ^{1}H NMR.[53]

The methyl ethers of **2**, **3**, **7**, and **9** (respectively **1**, **4**, **8**, and **10**) were prepared by reaction of the corresponding alcohol with methyl iodide and sodium hydride in anhydrous tetrahydrofuran. All the methyl ethers had the expected ^{1}H-NMR and MS spectra.

Product Analysis. Products were generally identified by GLC (comparison with authentic specimens) and by GC-MS analysis. For the detection of acetaldehyde and 2-methylpropene see the supporting information.

All oxidation reactions were performed under an inert atmosphere of argon. With the exception of substrates **3** and **4**, all reactions were carried out until complete conversion of Co(III)W. The oxidations at 50 °C were performed in $AcOH/H_2O$ 55:45 (w/w) as described previously[19] using equal amounts of substrate and Co(III)W. Oxidations at 110 °C were performed as described previously,[54] for substrates **1**−**4** in $AcOH/H_2O$ 4:1 (v/v) using a 2-fold substrate excess.

Kinetics. All kinetic experiments were carried out as previously described.[21] The kinetic analysis for compounds **5**, **6**, and **7** is analogous to the one described previously.[23] The values of k_1k_2/k_{-1} for compounds **1** and **2** were obtained by fitting the kinetic data up to 90% of conversion to eq **3** (see text). Second-order rate constants for compound **9** were obtained by fitting the kinetic data up to 90% of conversion to eq **4** (see text).

Pulse Radiolysis. The pulse radiolysis experiments were performed using a 3 MeV van de Graaff accelerator which supplied 400-ns pulses with doses such that 0.5−3 μM radicals were produced. The temperature of the solutions under study was kept constant to ≈0.1 °C by using a cell that is an integral part of a heat exchanger, as described previously.[55]

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Supporting Information Available: Complete experimental section with spectral data, details on synthetic procedures, oxidation reactions, and kinetics (6 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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