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Substituent Effects in the Reaction of OH Radicals with Aromatics: Toluene

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The relative rates for addition of •OH radical to toluene at its ortho, meta, and para sites have been shown to be in the ratios of 0.84:0.41:1. These ratios provide a quantitative basis for considering the effects of alkyl substituents in determining the site of •OH attack on other aromatics. Because •OH is a strong electrophile, the relative yields of •OH adducts provide a measure of the effect of the methyl group on the distribution of negative charge in toluene's aromatic system. Comparison of the partial rate constants observed for reaction at the different sites of toluene, biphenyl, and phenol with theoretical estimates of the distribution of charge in the valence shell indicates that factors other than charge also play some role.

Introduction

Because of the electrophilic character of the •OH radical,[1] studies in aqueous solutions of the relative frequency for its addition to the different positions of a substituted aromatic provide information on the distribution of electronic charge in the aromatic. Previous studies have shown, for example, that •OH preferentially adds to the electron-rich ortho and para sites of phenol[2−5] and that the electron withdrawing carboxyl group of benzoic acid has the opposite effect on directing •OH addition to the meta position.[6] In this report, hydroxyl's role as an electrophile dominates its role as a radical so that it behaves in much the same way as a closed-shell electrophile familiar from physical organic chemistry.[7] The early studies of Eberhardt and Martinez[8] showed qualitatively that the methyl group directs •OH addition to the ortho and para positions of toluene. The present study on the distribution of the methyl-hydroxycyclohexadienyl radicals produced in the radiolytic oxidation of toluene has been undertaken to provide a quantitative basis for a discussion of the concerted effects of methyl and OH substitution on charge distribution in the cresols.

In previous studies of the radiolytic oxidation of benzene, it has been shown that ferricyanide present during radiolysis oxidizes the initially produced hydroxylcyclohexadienyl radicals to phenol quantitatively.[9] In their studies on toluene, Eberhardt and Martinez[8] examined a number of inorganic radical oxidants and found somewhat different yields of the cresol isomers by the different oxidants. Reducing radicals were also present in their studies so that the cresol yields observed were less than quantitative. In the present study on toluene, we use ferricyanide to convert the hydroxylcyclohexadienyl radicals produced to cresols in an oxidizing environment. The total yield of cresols is found to be essentially quantitative so that one can take the observed distribution of cresol isomers as representing the relative frequency for •OH attack at the different positions of toluene.

The present study was carried out using radiolytic methods to produce •OH under well-controlled conditions. N_2O was used to convert the hydrated electrons produced in the radiolysis to •OH. The distribution of cresols produced on oxidation of the intermediate methyl-hydroxycyclohexadienyl radicals was determined by micellar electrophoretic capillary chromatography (MECC). The data presented below show that the methyl substituent in toluene has a significant effect on the charge distribution that results in a preferential addition of •OH to its ortho and para sites. The effect observed is considerably less than that of an OH substituent, but comparable to that of a phenyl substituent.

To the extent that the addition site is directed by the electrophilic nature of •OH, it should be possible to correlate the distribution of radicals produced with the electronic properties of the target molecules. Bader and Chang,[10] using the theory of atoms in molecules,[11] demonstrated how the properties of the electron density of substituted benzenes could be used to explain their relative susceptibilities to electrophilic attack. They focused attention on the Laplacian of the electron density ($\nabla^2\rho$)-that indicates regions of electron concentration and correlated computed quantities with Hammett σ-ρ parameters for electrophilic substitution. In the present study we apply their approach to examine correlation of the partial rate constants for addition of •OH to toluene with $\nabla^2\rho$. We also consider phenol and biphenyl, for which the partial rate constants for •OH addition have been determined in a consistent manner.[2−5, 12]

Experimental Section

Aqueous solutions were outgassed and saturated with toluene (5.8 mM) and nitrous oxide (25 mM). They contained 2.7 mM potassium ferricyanide as a radical oxidant. Irradiations were in a ^{60}Co source at a dose rate determined by Fricke dosimetry of 4.7 krads/min. At this dose rate, •OH is produced in N_2O-saturated solutions at a rate of 28 μM/min. Yields are given in the following as *G*-values in units of molecules per 100 eV of absorbed energy. Samples were analyzed immediately after irradiation using a Hewlett-Packard 1600 3-D CE capillary electrophoresis system having a diode array detector and an extended-path-length (1.1 mm) optical cell. The electrophoretic buffer was 10 mM phosphate (pH 11.54) containing 75 mM sodium dodecyl sulfate. Electrophoretic data were recorded in 3-D format. Areas representing the individual components were

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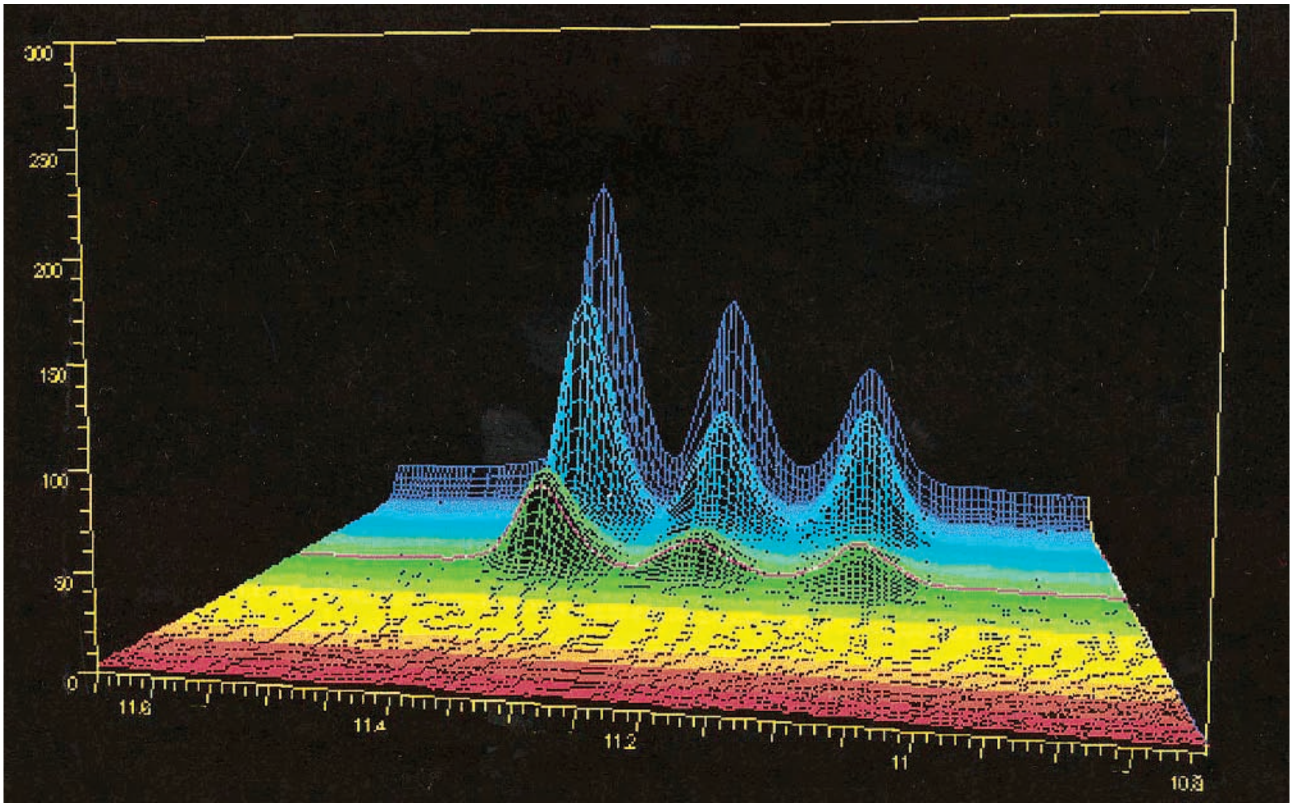

Figure 1. 3-D presentation illustrating the resolution of *o*-, *m*-, and *p*-cresol using micellar electrophoretic capillary chromatography.

determined from electropherograms extracted at appropriate wavelengths. Comparison of these areas with those of reference samples of the cresols (Aldrich) provided a quantitative measure of each of the products. Proper identification of the peaks was assured by comparison of their electrophoretic times and spectra extracted at the peak maxima with reference samples.

Theoretical Methods

Wave functions for toluene, phenol, biphenyl, and benzene were determined using second-order perturbation theory[13] and correlation-consistent polarized valence double-ζ basis sets.[14] Molecular geometries were established by optimization at the MP2/cc-pVDZ level, using the Gaussian 98 program.[15] Extrema in the Laplacian of the molecular electron densities **(**$\nabla^2\rho$) were located with the AIMPAC suite of programs.[16] Each ring carbon has a pair of $\nabla^2\rho$ extrema above and below the molecular plane that control the site of electrophilic attack due to the relative concentrations of associated ring π electrons. Bader and Chang[10] refer to these as secondary valence shell charge concentrations. We will denote them here as $\nabla^2\rho$**VSCC.** In the present study, we apply their approach to examine correlation between observed partial rate constants and $\nabla^2\rho$VSCC.

Results

It was not found possible to resolve the meta and para isomers of cresol by HPLC or by conventional electrophoretic methods using borate as the buffer. As illustrated in Figure 1, resolution of the three cresol isomers was attained using micellar electrophoretic methods. The separations noted in the figure, however, required careful tuning of the pH of the electrophoretic buffer to take advantage of the slight difference in the acid dissociation constants of *m*- and *p*-cresol (pK_a of 10.09 and 10.26, respectively). A typical electropherogram, extracted from the 3-D data at 235 nm, where all three cresols have a significant absorption, is illustrated in Figure 2. At 235 nm, the sensitivities of *p*- and *m*-cresol are similar and 10% lower than that of *o*-cresol, so this figure shows quite directly that the yield of *m*-cresol is considerably less than that of *o*-cresol. As indicated in the figure, this electropherogram could be fitted quite well by Gaussian dependences representing the three cresols. Taking into account the relative sensitivities of the cresols at 235 nm, the relative yields determined from these Gaussian fits are in the ratios 1.60:0.89:1.

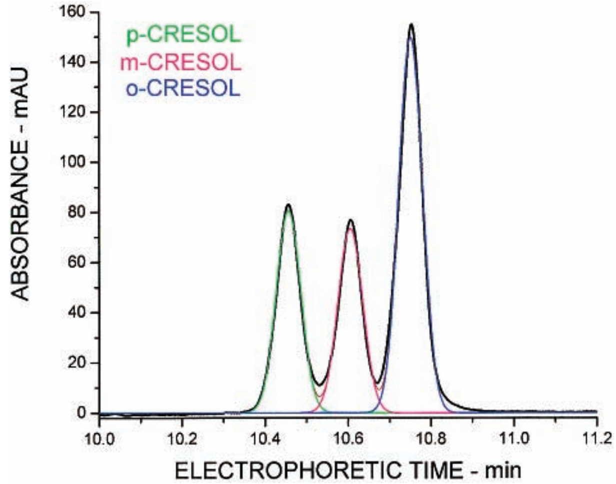

Figure 2. Electropherogram recorded at 235 nm for a 5.8 mM toluene solution (containing 2.7 mM ferricyanide and saturated with N_2O) irradiated to a dose of 9.4 krads. The peaks due to *p*-, *m*-, and *o*-cresol at, respectively, 10.47, 10.61, and 10.77 min are fitted by the colored Gaussians in the figure. These Gaussians have widths of 3.5 s and are separated by 8 and 10 s.

The dependences for production of each of the cresols on dose, determined from the areas under the peaks and the known sensitivities, are given in Figure 3. It is seen that, as the result

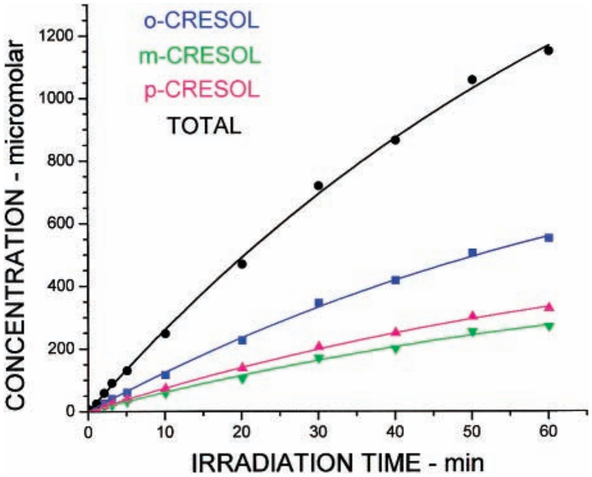

Figure 3. Dose dependence of the cresol concentrations produced at a dose rate of 4.7 krads/min. The solid curves in the figure represent optimized fits to eq 1 of the text. The initial slopes of these fits correspond to radiation chemical yields of 2.76, 1.34, and 1.73 for *o*-, *m*-, and *p*-cresol.

TABLE 1: Initial Slopes, Radiation Chemical Yields, and Partial Rate Constants for the Reaction of ·OH with Toluene

	initial slope (μM/min)	yield (G)	k_p[a] partial rate constant	k_p/k_b[b]	$\nabla^2\rho$VSCC
o-cresol	13.31	2.73	1.91	1.45	−0.177189
m-cresol	6.49	1.33	0.93	0.72	−0.160289
p-cresol	7.88	1.62	2.27	1.75	−0.170287
benzyl alcohol	0.54	0.11			
Total	28.22	5.79			
ipso-adduct	- - -	<0.2	<0.3	<0.2	−0.156534
benzene		6.0	1.3	(1)	−0.164258

[a] k_p per position $\times$ 10^{-9} M^{-1} s^{-1}. [b] k_b the partial rate constant for reaction at each of the 6 ring positions of benzene (1.3×10^9 M^{-1} s^{-1}).[20]

of competition of the radiolytic products with the toluene, the slope of these dependences decreases with dose. The solid curves in the figure represent a fit of the data to a function of the form

$$[\mathrm{Ci}]_D = \mathrm{d}[\mathrm{Ci}]_0/\mathrm{d}D\{2\ (\ln(1 + QD)/Q) - D\} \qquad (1)$$

In eq 1, $[\mathrm{Ci}]_D$ is the concentration of a cresol isomer at dose D, $\mathrm{d}[\mathrm{Ci}]_0/\mathrm{d}D$ is the initial slope of its dose dependence, and Q is given by

$$Q = k_2/k_1\ (\mathrm{d}[\mathrm{C}]_0/\mathrm{d}D)/[T] \qquad (2)$$

where k_1 and k_2 are, respectively, the rate constants for the reaction of ·OH with toluene and the cresols produced, ($\mathrm{d}[\mathrm{C}]_0/\mathrm{d}D$) is the initial rate for production of products, and [T] is the toluene concentration. Equation 1 takes into account the loss of the cresols in the secondary reactions[17] (see Appendix A in ref 17). Determination of the initial yields for production of each of the cresol isomers in this way avoids problems that might be associated with selectivity in the secondary reactions and should give an accurate measure of the relative rates for reaction of ·OH at the different positions of toluene.

Equation 1 is an approximation that is applicable to the initial stages of the radiolysis where tertiary reactions are of minor importance. The initial yields of *o*-, *m*-, and *p*-cresol, determined from the initial slopes of the dependences of Figure 3, are given in Table 1. The ratios of these initial yields are essentially the same as the ratios determined from the areas in Figure 2. Taking into account the 2-fold greater number of ortho and meta positions than the unique para position, the relative rates for ·OH attack at the ortho, meta, and para positions are in the ratios of 0.84:0.41:1, as given in Table 2.

TABLE 2: Relative Yields for ·OH Addition to Ortho, Meta, and Para Sites[a,b]

	toluene[c]	biphenyl[d]	phenol[e,f]
ortho	0.84	0.72	0.68
meta	0.41	0.36	0.13
para	1	1	1

[a] Normalized for the number of equivalent sites in the aromatic. [b] Computed values of $\nabla^2\rho$**VSCC** are as follow: for biphenyl −0.161404, −0.169727, −0.161794, and −0.165780, and for phenol −0.190429, −0.213007, −0.152661, and −0.187989 at, respectively, the ipso, ortho, meta, and para positions. [c] In ref 8, ortho:meta:para ratios of 0.96:0.45:1 are reported for toluene solutions containing 5 mM ferricyanide and 1.18:0.45:1 for solutions containing 5 mM dichromate as the radical oxidant. [d] Ref 12. [e] Ref 5. Relative yields determined by MECC analysis. [f] Ye (ref 4) reported relative yields of 0.72:0.09:1 obtained in liquid chromatographic studies. Yields approximately in the ratios of 0.66:0.04:1, obtained by analysis of the growth of the signals in pulse radiolysis studies of solutions containing quinones as the radical oxidant, were reported in ref 3.

In addition to the three cresols, benzyl alcohol was observed to be produced in small yield (G(benzyl alcohol) ∼ 0.11). Other products are absent initially, as is the case for ·OH oxidation of benzene where radiochemical studies show that products other than phenol are absent.[9] In the present study, no product that might result from addition of ·OH to the ipso carbon of toluene was detected. However, intermediate radicals so produced are not expected to be converted readily to measurable products, so one depends on a comparison of the total yield of measurable products with the total expected to give an estimate of the upper limit of ∼0.2 for reaction at the ipso position.

The total initial yield of 5.8 is only slightly less than the phenol yield of 6.0 observed in similar studies of the radiolyic oxidation of benzene[2,8] and is essentially the yield of ·OH expected for N_2O-saturated solutions (25 mM) at a toluene concentration of 5.8 mM.[19] This shows that oxidation of the intermediate methyl-hydroxycyclohexadienyl radicals is essentially quantitative and leaves little room for any appreciable yield of other products, particularly for those that might result from ·OH addition to the ipso position. Because there is only a low valence shell charge concentration at the ipso position (see below), one does not expect significant reaction at that position.

In their studies, Eberhardt and Martinez[8] did not use N_2O to convert the hydrated electrons produced in water radiolysis to ·OH radicals. As a result the yields of cresols they reported were considerably lower than those found in the present study and did not represent quantitative conversion of the intermediate radicals to cresols. The ratios of the cresols that they found were approximately as given by the present study but depended on the radical oxidant and its concentration. The best radical oxidants were found to be ferricyanide and dichromate (cf., footnote c in Table 2).

The total rate constant for reaction of ·OH with toluene is 8.1×10^9 M^{-1} s^{-1}.[20] Based on this value and the product distribution the partial rate constants for ·OH attack at the different positions of toluene are given in Table 1. These partial rate constants take into account the 2:2:1 ratio of the number of ortho, meta, and para sites in toluene. They can be compared to a partial rate constant of 1.3×10^9 M^{-1} s^{-1} for reaction of ·OH at each of the six equivalent sites in benzene.[20] Because of the chemical similarity of these two systems, the ratios given in the table for the reaction of ·OH with toluene and benzene

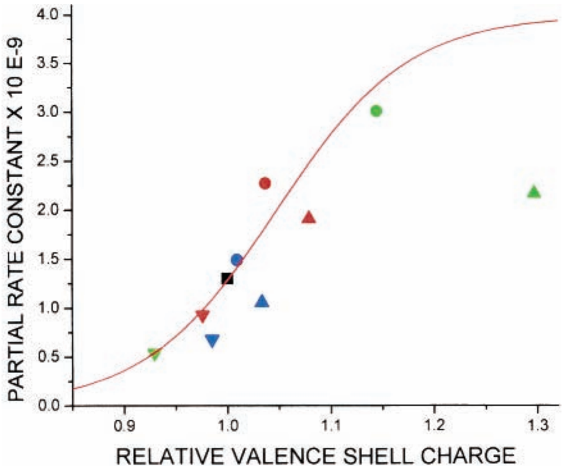

Figure 4. Partial rate constants for ·OH attack on the aromatic ring as a function of the ratio of valence shell charge concentration ($\nabla^2\rho_{\mathrm{VSCC}}$) located at the reaction site to the value of $\nabla^2\rho_{\mathrm{VSCC}}$ for benzene. Benzene is indicated by the black symbol. The data for toluene are in red, for phenol in green, and for biphenyl in blue; upright triangles are for reaction at an ortho site, inverted triangles at a meta site, and circles at a para site. The solid curve is a fit of the data for the para and meta positions to a sigmoidal dependence with lower and upper limits of 0 and 4×10^9 M^{-1} s^{-1}.

clearly indicate that the methyl substituent enhances the rate for attack at the ortho and para positions at the expense of a decrease in the rate for attack at the meta and ipso positions.

Figure 4 represents an attempt to correlate the partial rate constants obtained in the present study with the values of $\nabla^2\rho$**VSCC** computed for the different ring positions of toluene**.** Partial rate constants obtained in previous studies on phenol[5] and biphenyl[12] are also included in the figure. These latter values take into account the 40% greater overall rate constants for reaction of ·OH with phenol and biphenyl than for reaction with benzene and toluene. The solid curve in Figure 4 is an optimized sigmoidal fit of the partial rate constants for ·OH attack on benzene and at the para and meta positions of the three substituted aromatics. It is seen that the values for attack at the ortho positions all fall well below this curve (see discussion).

Discussion

The yields for ·OH attack at each of the ring positions of toluene, phenol,[2-5] and biphenyl[12] are compared in Table 2. It is seen that the directing effect of methyl is somewhat less than that of phenyl and considerably less than that of OH. In Table 1, comparison of the partial rate constants with that for benzene (1.3×10^9 M^{-1} s^{-1})[20] shows that methyl increases the rates for attack at the para and ortho positions by factors of 1.83 and 1.45 while lowering that for attack at the meta position by a factor of 0.71. These differences clearly manifest the shift of negative charge away from the meta position and toward the para and ortho positions.

While Figure 4 indicates that there is only limited correlation between $\nabla^{2}\rho$**VSCC** and the partial rate constants, the patterns for the three substrates are similar. The computed values of $\nabla^2\rho$**VSCC** show that in each case the negative charge concentration at the ortho and para positions is greater than that of benzene and less at the meta position, in qualitative agreement with the observed directing effect. The computed values, however, indicate that the ortho positions have a greater charge concentration than the para positions, in contrast to the observed preference for attack at the para position. It is also noted in Table 2 that the directing effects of phenyl and methyl substituents are similar, although the differences in the computed values of $\nabla^2\rho$**VSCC** are considerably greater for methyl substitution. Either $\nabla^2\rho$**VSCC** does not contain sufficient information on the electron distribution to differentiate rates at the ortho and para sites or the reaction rates of the processes that compete within the reaction complex are partially governed by factors other than the distribution of electronic charge. Steric hindrance may, for example, play some role in the attack of ·OH at the ortho position. It is also possible that spin polarization of the type suggested by Bader and Gangi,[21] brought about by hydroxyl's unpaired electron, may play a role in determining the reaction pathway. However, it is beyond the scope of the present treatment to address this question.

The directing effect observed for biphenyl[12] is of particular interest in that, because of its symmetry, the observed effect cannot be ascribed to charge transfer. It is clear from both the experimental and the theoretical results that even in the absence of charge transfer the electronic distribution in the aromatic system is severely perturbed by a phenyl substituent. In the case of phenol, the values of $\nabla^{2}\rho$**VSCC** given in Table 2 indicate that the observed directing effect is dominated by charge transfer, as is usually assumed to be the case. Whether viewed experimentally or theoretically, toluene is intermediate between biphenyl and phenol, and generally closer to biphenyl. This suggests that the structural effect seen in biphenyl and the charge-transfer effect seen in phenol both play roles in determining the observed directing effect in toluene.

The total rate constants for reaction of ·OH with the four aromatics under consideration are all of the magnitude of 10^{10} M^{-1} s^{-1}, indicating that they are essentially diffusion-controlled. Because of this, the partial rate constants that represent the fraction of the total are limited so that their absolute values cannot be directly correlated with $\nabla^2\rho$**VSCC**. The observed differences in yields largely reflect the relative rates for addition to the ring within the reaction complex. It is clear that as the ·OH radical approaches the aromatic system, it senses the charge distribution in the aromatic and preferentially attacks the more negative sites. As a result, as indicated in the Introduction, the distribution of radicals produced, as measured by the observed distribution of cresols, provides information on the charge distribution in the aromatic.

The results presented here are important in providing basic information required for understanding the concerted effects of OH and alkyl substituents observed in studies of the radiolytic oxidation of alkylated phenols by other approaches capable of producing ·OH radical as a reactive intermediate.

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