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On the Addition of $^{\bullet}$OH Radicals to the Ipso Positions of Alkyl-Substituted Aromatics: Production of 4-Hydroxy-4-methyl-2,5-cyclohexadien-1-one in the Radiolytic Oxidation of *p*-Cresol

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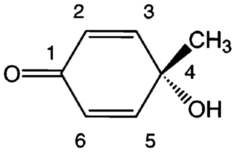
4-Hydroxy-4-methyl-2,5-cyclohexadien-1-one has been conclusively identified by its ^{1}H and ^{13}C NMR spectra as a significant initial product in the radiolysis of aqueous solutions of *p*-cresol. This product is formed as the result of oxidation of the hydroxycyclohexadienyl radicals produced by addition of ∼12% of the $^{\bullet}$OH radicals to the aromatic ring at the ipso position adjacent to the methyl group. It has a strong absorption band at 228 nm that is similar to the 246 nm band of *p*-benzoquinone. Its proton NMR spectrum exhibits strong coupling between two pairs of ring protons. A quartet is observed in the spectrum of the methyl-^{13}C labeled product, confirming that a methyl group is attached to the dienone ring.^{13}C chemical shifts and ^{13}C−H spin−spin splittings of the dienone are reported. Although DFT calculations of the proton NMR parameters are in very good agreement with the experimental values, the calculated chemical shifts of the ring ^{13}C carbons are 4−8 ppm too high, indicating that the DFT calculations do not properly take into account the dienone π system. This conclusion is confirmed by parallel experimental and theoretical studies of 4*H*-pyran-4-one that provides a model system closely related to the dienone. The observation of 4-hydroxy-4-methyl-2,5-cyclohexadien-1-one as a product in the radiolysis of aqueous solutions is important in demonstrating that addition of $^{\bullet}$OH radicals to aromatic rings at positions substituted with alkyl groups can be of appreciable importance in the $^{\bullet}$OH oxidation of aromatic substrates.

Introduction

Chromatographic and capillary electrophoretic studies of the radiolytic oxidation of *p*-cresol at low doses show that four products are formed initially as the result of attack of $^{\bullet}$OH radicals on the cresol.[1] Of these, three are readily identified as 4-methyl catechol, 4-methyl resorcinol, and *p*-hydroxybenzyl alcohol by comparison of their absorption spectra and elution times with reference samples. The first two are expected as the result of oxidation of the hydroxycyclohexadienyl radicals initially produced by addition of $^{\bullet}$OH to the unsubstituted positions of the cresol. The third indicates that abstraction of a methyl hydrogen atom is also of some importance. However, in these studies the identity of the fourth product, that has a strong absorption band at 228 nm, was not immediately evident. Its ^{1}H and ^{13}C NMR spectra reported below conclusively show that this product is 4-hydroxy-4-methyl-2,5-cyclohexadien-1-one (subsequently referred to as dienone). The observation of this product is of general importance in demonstrating the importance of addition of $^{\bullet}$OH at ipso positions of alkyl-substituted aromatics.



In the following, the radiolytic preparation, spectral properties, and theoretical studies of 4-hydoxy-4-methyl-2,5-cyclohexadien-1-one and its methyl-^{13}C labeled analogue are described in some detail. Parallel experimental and theoretical NMR studies on 4*H*-pyran-4-one (O═CC$_4$H$_4$O), also reported below, provide comparative data on a ring system closely related to the dienone.

Experimental Section

Radiolytic Preparation of the Dienone. Aqueous solutions 20 mM in *p*-cresol (Aldrich), also containing 20 mM potassium ferricyanide and saturated with N$_2$O (∼25 mM), were irradiated to a dose of ∼1.5 megarads (15 kGy) in a ^{60}Co source at a dose rate of ∼1 megarad/h (10 kGy/h). The N$_2$O served to convert the hydrated electrons produced in water radiolysis to $^{\bullet}$OH radicals and the ferricyanide to oxidize the hydroxycyclohexadienyl radicals initially resulting from the addition of $^{\bullet}$OH to the cresol. At this dose ∼50% of the cresol was consumed and numerous secondary products were formed in addition to the initial products. The irradiated samples were extracted four times with an equal volume of diethyl ether and the extract concentrated to a volume ∼1 mL. The dienone was then isolated chromatographically (see below) by collecting samples from individual injections of 100 μL. These samples were combined and extracted with ether. After evaporation of the ether the resultant dienone fraction was shown to be free of products other

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than a small contribution of *p*-hydroxybenzyl alcohol. Irradiation of 250 mL of the cresol solution yielded 2 mg of the purified dienone. This sample, dissolved in 0.3 cm^3 of Aldrich dichloromethane-d_2 (99.95% D), was used for the NMR analysis.

The dienone having the methyl group labeled with ^{13}C was prepared similarly from a 100 mg sample of 4-methylphenol-^{13}C (99% enrichment of CH_3) obtained from Isotec Inc. Although the amount of this labeled dienone was less than 1 mg, it was adequate for observation of the additional splittings resulting from the methyl-^{13}C substituent. It is pointed out that the radiolytic approach used here made it possible to synthesize the labeled dienone from the limited quantity of labeled cresol available.

Chromatography. A Waters Millennium system with a 996 diode array detector was used to record liquid chromatographic (LC) data in 3-D format. Product separation was with a 5μ Phenomenex Luna C-8 column using gradient elution, initially with 70:30 water−methyl alcohol, followed by a gradual increase of the alcohol to 100%. The alcohol cleared the column of the other products formed in the radiolysis. The dienone was well separated from all radiolytic products except for *p*-hydroxybenzyl alcohol that eluted immediately in front of the dienone. Appropriate chromatograms and absorption spectra were extracted from the recorded 3-D data. Chromatographic sensitivities were determined from the areas of the recorded peaks and the extinction coefficients determined spectrophotometrically.

Electrophoretic Studies. Capillary electrophoretic (CE) studies were with a Hewlett-Packard G1600 3-D CE system. A micellar buffer (10 mM phosphate at pH 7 containing 50 mM SDS) was used to optimize resolution. With this buffer the dienone appears immediately after the water plug but is well resolved from all other components. These electrophoretic studies complemented the chromatography in tracking the isolation of the dienone.

Spectrophotometry. Absorption spectra were recorded with a Hewlett-Packard 4865 spectrophotometer. The dienone spectrum recorded spectrophotometrically was essentially identical to those extracted from the LC and CE data. For reference purposes spectra of known concentrations of 4-methyl catechol and *p*-benzoquinone were also recorded. In the radiolytic experiments the signal of the catechol provided an internal reference against which to compare the dienone. The extinction coefficient of the dienone determined spectrophotometrically is 11 600 M^{-1} cm^{-1} at 228 nm. This value compares with values of 2400 M^{-1} cm^{-1} for 4-methyl catechol at 280 nm and 17 300 M^{-1} cm^{-1} for *p*-benzoquinone at 246 nm. The initial dienone yield[1] was determined at low doses, taking the relative sensitivities as proportional to these extinction coefficients. Because only 2 mg of the purified dienone was available, its LC and CE sensitivities are estimated to be accurate to only ∼10%.

NMR Spectra. ^1H and ^{13}C NMR spectra were recorded on a three-channel Varian Unity*Plus* spectrometer using a 3 mm Nalorac dual $^1H/^{13}C$ probe: ^1H NMR spectra (^1H, DQF-COSY, HMBC) at 599.98 MHz and ^{13}C spectra (^{13}C, DEPT, HETCOR, HMBC) at 150.86 MHz. All experiments were run at ambient temperature (20 °C) in deuterated methylene chloride. Chemical shifts (δ) are reported in ppm relative to TMS as an internal standard. Values of scalar spin−spin couplings (*J*, i.e., NMR splittings) are reported in hertz.

Proton connectivities were determined by DQF-COSY experiments.[2] These experiments were run in the phase sensitive mode. The 512 t_1 increments of 88 scans each were sampled in 2048 complex data points for each of the increments. Zero-filling the F_1 domain to 2048 and a Gaussian weighting function were applied in both F_1 and F_2 domains prior to double Fourier transformation.

The DEPT experiment allowed classification of the carbon signals as representing methyl, methylene, methine, and quaternary carbons. Specific assignments of the signals of carbons with directly attached protons were made using HETCOR spectra.[3] The HETCOR spectrum was obtained using 4096 complex data points in the F_2 domain and 128 t_1 increments (320 scans each), which were zero-filled to 1024 in the F_1 domain. A sine-bell weighting function was applied in both domains prior to double Fourier transformation.

Finally, the HMBC spectrum obtained using the pulse sequence of Bax and Summers[4] was used to assign quarternary carbons and to check the correctness of the connectivities established by the interpretation of the other spectra. Low-pass *J*-filtering was used to suppress correlations due to one-bond couplings. Delay Δ_2 was set to 62.5 ms corresponding to the average long range (through two or three bonds) carbon−proton coupling constant of 8 Hz. In this experiment, 512 t_1 increments were sampled in 2048 complex data points using 196 scans for each of the t_1 increments. Data in the F_1 domain were zero-filled to 2048, and a Gaussian weighting function was applied in both F_1 and F_2 domains prior to double Fourier transformation.

For comparison purposes the NMR spectra of 4*H*-pyran-4-one, obtained from Aldrich, were recorded under conditions similar to the above.

Computational Details. Geometries were computed by density functional theory (DFT) using the popular B3LYP functional[5] and a modest polarized split-valence basis set (6-31G*).[6] Chemical shifts were estimated relative to TMS from calculations at the B3LYP/6-311+G(2d,p) level,[7] using gauge-including atomic (London) orbitals.[8] Computed shifts at the ring carbons were further refined by comparison to calculations on benzene and toluene. Optical absorption spectra were evaluated from time-dependent DFT adding a set of diffuse functions to the heavy-atom basis (6-31+G*). All of these calculations were performed with the Gaussian 98 series of quantum chemistry codes.[9] Indirect NMR spin−spin coupling constants were calculated using finite (Fermi-contact) field double perturbation theory[10] and a specifically designed augmented double-ζ basis ([5s2p1d,3s1p])[11] with a modified version of the Gaussian suite.[12]

Results

As indicated in the Introduction, the LC and CE studies have shown that a product having a strong absorption at 228 nm is formed in the radiolysis of aqueous solutions of *p*-cresol.[1] The intensity of this absorption increases with radiation dose in parallel with the intensities of the products formed by addition of $^{\bullet}OH$ to the ortho and meta positions of the cresol so it is clear that this product is also produced as an initial product in the reaction of $^{\bullet}OH$ with the cresol.

Comparison in Figure 1 of this product's absorption spectrum with that of *p*-benzoquinone indicates that it has structural features closely resembling those of the quinone.

Although this product was initially thought to be the quinone methide ($O{=}C_6H_4{=}CH_2$), it proved to be quite stable, suggesting otherwise. The NMR studies described below conclusively identify this product as having the structure indicated in the Introduction, i.e., that it is 4-methyl-4-hydroxy-2,5-cyclohexadien-1-one. Presumably, it is produced by addition of $^{\bullet}OH$ at the methyl position of the aromatic ring followed by loss of

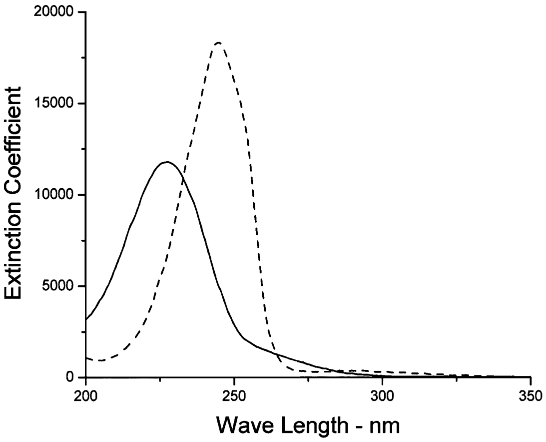

Figure 1. Absorption spectra of 4-methyl-4-hydroxy-2,5-cyclohexadien-1-one (solid spectrum) and of *p*-benzoquinone (dashed spectrum).

the phenolic proton on oxidation of the resultant hydroxycyclohexadienyl radical.

$$HOC_6H_4CH_3 + {}^{\bullet}OH \xrightarrow{-e^-} [HOC_6H_4\,(OH)CH_3]^{\bullet} \qquad (I)$$

$$[HOC_6H_4\,(OH)CH_3]^{\bullet} \xrightarrow{-H^+} [HOC_6H_4\,(OH)\,CH_3]^{+} \qquad (II)$$

$$[HOC_6H_4\,(OH)\,CH_3]^{+} \rightarrow O{=}C_6H_4(OH)CH_3 \qquad (III)$$

The radiation chemical yield of this product, determined from the initial slopes of its production in LC and CE experiments,[1] is 0.7 molecules per 100 eV of absorbed energy, i.e., ~12% of the ${}^{\bullet}OH$ radicals formed in the radiolysis of N_2O saturated solutions add at the methyl position of *p*-cresol. Clearly its production in significant yield demonstrates that, in general, addition of ${}^{\bullet}OH$ to aromatic rings at positions substituted with aliphatic groups can be of importance.

NMR Spectra of the Dienone. The structure of the isolated dienone was determined by analysis of one- and two-dimensional ^1H and ^{13}C NMR spectra. The ^1H NMR spectrum showed a singlet at δ 1.456 that, from its intensity, is assignable to the methyl protons (see also below) and to two multiplets at δ 6.086 and 6.870. These multiplets are assignable to the two pairs of ring protons. Although the latter patterns, illustrated in Figure 2, are quite complex, they are virtually superimposeable, so they clearly represent strong coupling among the ring protons. The complexity noted in Figure 2 is similar to that in the case of 1,1-difluorethylene where a less than obvious spectrum was observed for both hydrogen and fluorine as the result of a strongly coupled AA′XX′ spin system.[13] The values of δ and J for the ring protons, given in Table 1, were obtained by spin simulation using the program PERCH.[14] Figure 2 shows the quality of agreement between the experimental spectra (black) and the simulated one (red). Coupling constants are fitted to better than 0.02 Hz and chemical shifts are accurate to 0.001 ppm.

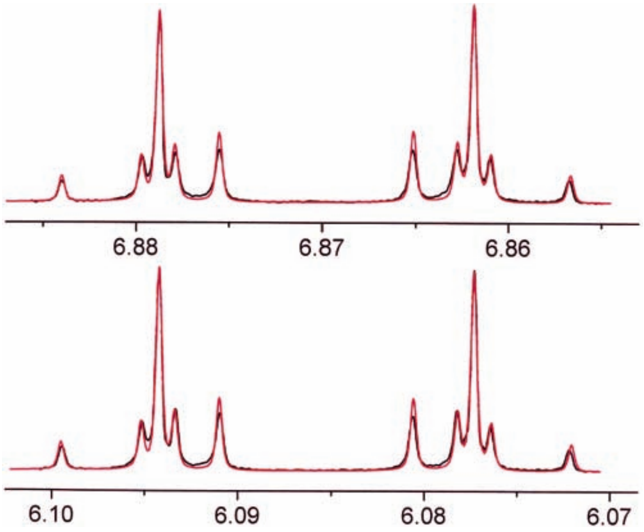

Figure 2. Proton NMR spectra of the dienone for the groups centered at chemical shifts of 6.870 and 6.086 ppm: the experimental spectrum is given in black, and the red spectrum is that simulated (see text) using the parameters of Table 1.

TABLE 1: Dienone ^1H NMR Parameters[a,b]

	experimental[a]	calculated[a,b]
$\delta_{2,6}$	6.086	6.3
$\delta_{3,5}$	6.870	7.0
δ_{CH_3}	1.456	1.4
$J_{2,6}$	2.00	1.9
$J_{3,5}$	3.09	3.0
$J_{2,3} = J_{5,6}$	10.12	10.4
$^1J(C_{me}H_{me}$	129.24[c]	132
$^3J(C_{me}H3) = {}^3J(C_{me}H5)$	2.17[d]	2.6
$^4J(C_{me}H2) = {}^4J(C_{me}H6)$	(−)0.76[e]	−0.9

[a] Chemical shifts (δ) of the unlabeled dienone in ppm relative to TMS; spin−spin coupling constants (J) are in hertz. [b] In the ^{13}C-methyl labeled dienone the spin−spin coupling constants are not observably affected by the isotopic substitution, but the chemical shifts are marginally affected (see text). [c] The one-bond spin−spin coupling between ^{13}C and the methyl protons in the ^{13}C-methyl labeled dienone. [d] The three-bond spin−spin coupling between ^{13}C and the ring protons at C_3 and C_5 in the ^{13}C-methyl labeled dienone. [e] The four-bond spin−spin coupling between ^{13}C and the ring protons at C_2 and C_6 in the ^{13}C-methyl labeled dienone.

TABLE 2: Dienone ^{13}C NMR Parameters[a]

	experimental[a]	calculated
δ_1	185.65	191
$\delta_2 = \delta_6$	127.57	135
$\delta_3 = \delta_5$	152.54	160
δ_4	67.62	73.2
δ_{CH_3}	27.16	27.4

[a] Chemical shifts (δ) relative to TMS in the unlabeled dienone in ppm.

The ^{13}C DEPT experiment at a natural abundance level revealed a total of five carbon resonance signals having the chemical shifts reported in Table 2. From its intensity, the signal at δ 27.16 can be assigned to the methyl carbon and is observed as a quartet in the sample having the methyl carbon enriched in ^{13}C (see below). The unique signal at δ 185.65 is readily assignable to the carbonyl carbon. The HETCOR spectrum showed that the carbon signal at δ 127.57 correlates with the proton multiplet at δ 6.087 and that at δ 152.54 with the multiplet at δ 6.870. They are assignable, respectively, to the methine pairs at C2 and C6 and at C3 and C5. The HETCOR spectrum also showed that the proton signal at 1.456 correlates with the methyl carbon signal at δ 27.16, confirming its assignment to the methyl protons.

The HMBC spectrum showed that the carbon signal at δ 152.54 correlates with the methyl proton signal, allowing its assignment to the carbon pair at C3 and C5. The HMBC spectrum also allows the carbon signal at δ 67.62 to be assigned to the C4 carbon as it exhibits cross-peaks with the methyl proton signal at δ 1.45 due to two-bond linkage and with the proton signal at δ 6.086 due to three-bond linkage. Finally, the

TABLE 3: Dienone ^{13}C-^{1}H Coupling Constants[a]

	experimental	calculated
^{1}J(C2H2)	166.15	171
^{1}J(C3H3)	162.64	167
^{2}J(C2H3)	<1	0.2
^{4}J(C2H5)	<1	−1.0
^{3}J(C2H6)	3.44	3.9
^{2}J(C3H2)	<1	0.4
^{4}J(C3H6)	<1	−0.9
^{3}J(C3H5)	5.5	5.9
^{2}J(C3Hme)	3.9	4.0
^{2}J(C1H2)	n.o.[b]	1.4
^{3}J(C1H3)	n.o.	10.1
^{2}J(C4H3)	n.o.	2.0
^{3}J(C4H2)	n.o.	9.1
^{3}J(C4Hme)	n.o.	−2.9

[a] Spin−spin coupling constants observed in the spin uncoupled mode. Ring positions of the C and H are given parenthetically. [b] no: not observed. Signals of C1HX and C4HX were too weak to be observed in the uncoupled mode.

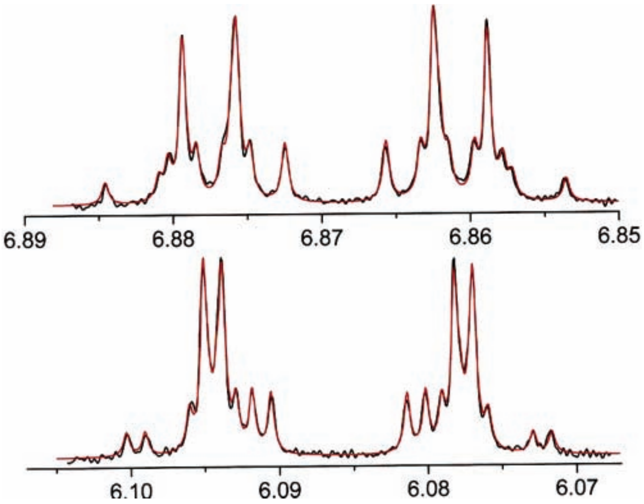

Figure 3. Proton NMR spectra of the methyl-^{13}C labeled dienone illustrating the additional ^{13}C splittings of 2.17 Hz for the group at δ 6.870 and 0.76 Hz for the group at δ 6.086. The red spectrum gives the fit to the experimental spectrum in black.

HMBC spectrum shows that the carbon signal at δ 185.65 correlates with the proton multiplet at δ 6.870, confirming its assignment to the carbonyl carbon at C1.

These various correlations permit unequivocal assignment of the chemical shifts observed in the ^{13}C spectrum to the five different types of carbon atoms in the dienone. These assignments are further substantiated by the DFT calculations reported below.

In addition to the above, in uncoupled spectra, the ^{13}C signals of the two pairs of methine carbons are split by the protons adjacent to the carbons. Additionally, the signals of the C2 carbons are observed as doublets because of couplings to the protons at C6 and the signals of C3 appear as a doublet of quartets corresponding to coupling to the proton at C5 and the methyl protons. The other protons broaden these observed lines somewhat but are not resolved. At natural abundance levels the ^{13}C signals of the methyl carbon and those at C1 and C4 were too weak in the uncoupled spectra to manifest additional structure. The observed ^{13}C−^{1}H coupling constants are summarized in Table 3.

NMR Spectra of the ^{13}C-Methyl Labeled Dienone. The product produced from a sample of *p*-cresol enriched with ^{13}C at the methyl position exhibits a ^{13}C 129.24 Hz quartet centered at a chemical shift of δ 27.14. The observation of this quartet additionally confirms the identity of the ^{13}C line with a similar chemical shift in the unlabeled dienone as representing the methyl carbon. Each of the lines in the quartet also shows unresolved structure resulting from coupling to the ring protons. The observation of this quartet, which clearly demonstrates that a methyl group is attached to the ring system, was crucial in the initial identification of the product as the dienone.

In the case of the methyl-^{13}C labeled dienone, the proton line at δ 1.456 in the spectrum of the unlabeled dienone is observed as a doublet split by 129.24 Hz. The agreement of this splitting with the proton splitting of the ^{13}C quartet, noted above, allows unequivocal assignment of the line at δ 1.456 in the proton spectrum to the methyl protons. In the labeled dienone its chemical shift is slightly lower at δ 1.454.

In Figure 3 the proton spectrum of the ^{13}C labeled sample shows line groups corresponding to those in Figure 2 in which each pattern has been additionally split, as indicated in Table 1, by 2.17 Hz for the group at δ 6.870 and by 0.76 Hz for the group at δ 6.086. The experimental spectra accurately depict the superposition of two patterns of Figure 2 separated by the above splittings, indicating that the methyl-^{13}C group has a negligible effect on the splittings by the ring protons. Taking into account the additional splittings indicated above, the spectral simulations in Figure 3 gave values for the proton splittings identical to those of the unlabeled compound. The optimized spectra obtained with PERCH are superimposed on the experimental spectra in Figure 3. In the optimization, changing the sign of either or both of these spin−spin splittings had no effect. Slight differences between the chemical shifts of the labeled and unlabeled dienones are, however, noted. The chemical shift of the protons at C3 and C5 is 0.0013 ppm (0.77 Hz) lower for the labeled than for the unlabeled compound. This difference is evident by comparing the upper spectra in Figures 2 and 3. It may be caused by differing vibrational amplitudes in the ^{12}C- and ^{13}C-containing compounds. An even smaller difference is observed the patterns of the C2 and C6 protons, where the shift of the labeled dienone is marginally (0.12 Hz) higher than that of the unlabeled dienone.

Theoretical Studies. Initial theoretical attempts to identify the carrier of the 228 nm absorption band were guided by its similarity to the well-known benzoquinone band at 246 nm. Time dependent DFT calculations on quinone methide, with a structure optimized at the B3LYP/6-31G* level of theory, gave an absorption maximum at 276 nm as compared to a calculated maximum of 253 nm for *p*-benzoquinone. This comparison essentially ruled out the methide as a candidate. Similar calculations for the dienone, for which some significant structural parameters are displayed in Figure 4, predict an absorption maximum at 231 nm, in excellent agreement with the experimental value (228 nm). Also the calculated oscillator strength, 70% of that of the corresponding band in *p*-benzoquinone, is comparable to that determined from the ratio of the extinction coefficients.

The structure for the dienone given in Figure 4 shows a C_s equilibrium structure with the OH bond located under the ring (anti- to the exocyclic CC bond). A barrier of 14.5 kJ mol^{-1} is predicted to inhibit free rotation of the OH. Local minima at +11.1 kJ mol^{-1} exist when the OH bond is approximately anti- to either CC ring bond. The calculated harmonic frequency for OH torsion in this potential well is 396 cm^{-1}.

The DFT calculations of the proton NMR parameters given in Table 1 confirm the experimental assignments of the chemical shifts and spin−spin coupling constants. Whereas the computed shifts are slightly larger (∼0.2 ppm) than the experimental ones,

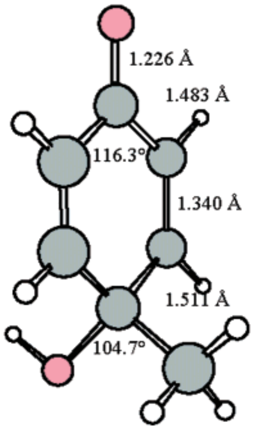

Figure 4. Computed (B3LYP/6-31G*) structural parameters.

the indirect nuclear spin−spin coupling constants are in close accord with those deduced from the analysis presented above. Also, the DFT calculations for the methyl-^{13}C labeled dienone gave values for the couplings between the methyl carbon and the methyl and ring protons, in good agreement with the experimental values. We note here that the theoretical work indicates that the sign of the spin−spin coupling between the methyl carbon and the protons at C2 and C6 is negative, as expected for four bond coupling.

The calculated values of the chemical shifts of the methyl and ring ^{13}C carbons are given in Table 2. Whereas the value for the methyl carbon is very close to that observed, the computed values for the ring carbons are in the range 5.5−7.5 ppm too high. This difference is discussed below. The calculated ^{13}C−^{1}H splittings given in Table 3 permit the specific assignments indicated in the table. We note that these calculations show three-bond C3Hme, C3H5 and C2H6 couplings to be responsible for the additional structure observed experimentally, that the two-bond C2H3 and C3H2 couplings are very small, and that the four-bond C3H6 and C3H5 couplings are somewhat larger than the two-bond couplings but negative.

Discussion

The NMR results reported here conclusively identify the dienone as the product of the $^{\bullet}$OH oxidation of *p*-cresol that absorbs at 228 nm and allow specific assignments of the observed chemical shifts and coupling constants. As indicated above 12% of the $^{\bullet}$OH radicals add to the ring at the methyl position of the cresol. This yield indicates that attack of $^{\bullet}$OH on the ring at the methyl position is approximately statistical. Wipf and Kim have previously prepared the dienone by chemical oxidation of *p*-cresol.[15] They reported that the dienone was produced in a 61% yield. Such a high yield indicates that chemical oxidation must involve a mechanism other than $^{\bullet}$OH radical attack on the cresol.

In their study Wipf and Kim examined the proton NMR spectrum of this dienone in deuterated chloroform and reported a singlet at δ 1.39 that they assigned to the methyl protons, in agreement with the assignment given above for the line observed in deuterated methylene chloride at δ 1.456 in the present study. They also found lines at δ 5.98 and 6.83 that they interpreted as doublets of doublets. Their analysis of these structures differs from that given in Table 1 in indicating splittings of 8.4 and 1.8 Hz for the signals at δ 5.98 and 8.4 and 1.6 Hz for those at δ 6.83. Wipf and Kim also observed a singlet at δ 3.95 that is likely assignable to the hydroxyl proton. In our experiments this latter signal was not observed, probably because it is very broad, as is frequently the case in solvents such as methylene chloride. Wipf and Kim also examined the ^{13}C spectrum at natural abundance and reported five carbons with ^{13}C chemical shifts of δ 186.0. 153.1, 126.6, 66.9, and 26.7. Although these shifts were unassigned, the values are very similar to those in Table 2.

TABLE 4: Comparative NMR Parameters for Dienone and Pyranone[a]

dienone		pyranone	
	Proton Parameters		
δ_2	6.086	δ_3	6.283
δ_3	6.870	δ_2	7.727
J(H2H6)	2.00	*J*(H3H5)	2.9
J(H3H5)	3.09	*J*(H2H6)	1.0
J(H2H5)	10.12	*J*(H2H5)	5.9
	^{13}C Parameters		
δ_1	185.65	δ_4	178.04
δ_2	127.57	δ_3	118.15
δ_3	152.54	δ_2	155.44
J(C2H2)	166.15	*J*(C3H3)	168.6
J(C3H3)	162.64	*J*(C2H2)	198.6
J(C2H3)	<1	*J*(C3H2)	7.46
J(C2H6)	3.44	*J*(C3H5)	3.55
J(C3H2)	<1	*J*(C2H3)	7.7
J(C3H5)	5.5	*J*(C2H6)	7.4

[a] Because the ring carbons of dienone are referenced to the carbonyl position and those of pyranone to the ring oxygen C2, C3, and C4 of the dienone correspond to C3, C2, and C1 of the pyranone.

As mentioned above, attempts to directly compute the chemical shifts produced values for the carbonyl and C2 and C6 carbons 5.5 ppm and those for C3 and C5 carbon 7.5 ppm higher than the experimental. To better calibrate this method for chemical shifts, we have compared the DFT predictions with experiment in a number of related systems. For example, the calculated values are 5−9 ppm too high for the ring carbons of benzoquinone, 2-cyclopenten-1-one (a model for the enone motif), cyclopenta-1,3-diene, benzene, toluene, phenol, and *p*-cresol. Similar discrepancies can therefore be expected for other aromatic like systems.

We have also examined 4*H*-pyran-4-one (subsequently called pyranone) as a model system more closely related to the present case. In pyranone, oxygen replaces the dienone C4 carbon and the conjugated structure of the dienone ring is preserved. Its optical spectrum is similar to that of the dienone with, however, a shift of the absorption maximum to 250 nm. Because pyranone has only four protons and five ring carbons, its NMR spectra are considerably simpler than those of the dienone. The various experimental and theoretical parameters of its proton spectrum are given in Table S1 of the Supporting Information and the ^{13}C chemical shifts and ^{13}C−^{1}H splittings are given in Table S2. Assignments, made here on the basis of comparison with values from the DFT calculations, are discussed in the Supporting Information.

Selected NMR values are compared with those at the corresponding positions of the dienone in Table 4. Though the overall patterns are similar, these comparisons show that the ring oxygen has an appreciable effect on the proton parameters related to its adjacent carbons. In pyranone, for example, there is a large increase in δ_2 and an appreciable decrease in the coupling between adjacent ring protons ($J_{2,3}$). These increases manifest a significant effect of the ring oxygen on the electronic distribution. This effect is also manifest in the ^{13}C chemical shifts and ^{13}C−H splittings associated with the nuclei adjacent to the oxygen. There are relatively small differences in the chemical shifts of the carbonyl carbon and the adjacent carbons that indicate that the effects of the ring oxygen are to a large extent localized in the region of the oxygen.

In Table 2S we particularly note that the ^{13}C chemical shifts of the ring carbons are, as for the dienone, somewhat higher than those predicted by the DFT calculations. Clearly, the DFT calculations, which are optimized for alkyl-like carbons, do not produce reliable values for the ring carbons. As mentioned above, similar discrepancies are noted for other aromatic systems. We stress here that TMS is an inappropriate computational reference for the DFT calculations of the chemical shifts of ring carbons in aromatic like systems. Apparently, at the level used, these calculations do not adequately take into account the π electrons.

Summary

The present example represents a special case in that addition of $^\bullet$OH radical at the methyl position of the cresol results in a readily observable product. Addition of $^\bullet$OH radicals at ipso positions of most other alkyl-substituted aromatics produces intermediates that are not readily converted to products that retain information pertaining to the site of addition. For example, no product other than the expected cresols was found in a detailed study of the radiolytic oxidation of toluene.[17] There currently is no quantitative information on the importance of addition of $^\bullet$OH to alkyl-substituted positions of aromatics from either time-resolved or product analysis studies. Attack of $^\bullet$OH at positions of aromatics substituted with groups other than alkyls clearly must also be of some importance, but such processes are frequently masked by complicating secondary reactions. For example, in the case of phenol the intermediate radical produced by $^\bullet$OH addition at the hydroxyl position rapidly loses H_2O to produce a phenoxyl radical. The observation that reaction I occurs to a significant extent is of particular importance in radiolytic studies of aqueous solutions because $^\bullet$OH radicals frequently dominate the oxidation processes. In a more general sense similar processes must also be considered in chemical studies where oxidation occurs via the reactions of hydroxyl radicals.

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Supporting Information Available: NMR properties of 4*H*-pyran-4-one as a model for the dienone system are described in the Supporting Information. Included are Tables S1, listing the proton chemical shifts and coupling constants, and Table S2, the ^{13}C chemical shifts and ^{13}C$-$^{1}H coupling constants. This material is available free of charge via the Internet at http://pubs.acs.org.

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