Photoisomerization of Phenyl Alkyl Ethers. II. The Mechanism for the Formation of Meta Alkylphenols

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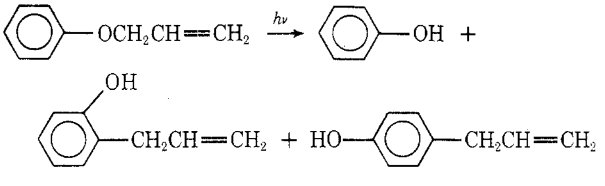
In the photoisomerization of anisole to the three isomeric cresols, evidence is presented for a common precursor to *m*- and *p*-cresol. The intermediate is presumed to be 4-methylcyclohexa-2,5-dienone, which subsequently is photoisomerized to 6-methylbicyclo[3.1.0]hex-3-en-2-one. This, on further irradiation, isomerized to *m*-cresol. Strong evidence for this mechanism is provided by the irradiation of 2,4,6-trideuterioanisole, and the isolation from the photolysate of a dideuterio-*m*-cresol showing the predicted location of the deuterons.

The photo-Claisen rearrangement (eq 1) serves as a model for the photoisomerization of most diaryl, aryl allyl, and aryl benzyl ethers.[1-4] As we previously reported,[5] however, the photoisomerization of phenyl alkyl ethers exhibits the complication that meta alkylphenols are formed, in addition to the ortho and para isomers predicted by eq 1. It is the purpose of this paper to describe the probable mechanism by which meta alkylphenols are formed. The most significant aspect of the proposed mechanism is that it requires an unhindered 2,5-cyclohexadienone to aromatize slowly enough that a prior photoisomerization can occur.



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Results and Discussion

Characteristics of the Reaction. The photoisomerization of phenyl alkyl ethers is best carried out in methanol, ethanol, or 2-propanol. Other solvents, such as cyclohexane, cyclohexene, and *tert*-butyl alcohol, have also been used, but these lead to decreased yields of the desired phenols and an increased yield of tar (Table I).

A 450-W Hanovia medium-pressure mercury arc in a quartz dipping well was used in these studies. Experiments with Corex, Vycor, and Pyrex sleeves lead us to conclude that the wavelength at which the yield is maximized is about 220 nm. Quantum yields were not measured, owing to the difficulty of isolating wavelengths in this region of the spectrum, but Table II gives the absolute yields of the phenolic products from four phenyl alkyl ethers, irradiated for 24 hr as 0.10 *M* solutions in methanol.

That the photoisomerization is unimolecular may be seen from the absence of "crossover" products in the photolysate of a mixture of phenetole and *p*-methylanisole.[5] At present, by analogy to Pinhey's work[2] on phenyl allyl ethers, we are inclined toward a mechanism whereby initially formed alkyl and phenoxy radicals combine within a solvent cage to produce 2,4- and 2,5-cyclohexadienones, but we cannot yet rule out a concerted pathway from the ether to the cyclohexadienones. It is certain, however, that photochemical interconversion of alkylphenols is not intervening, since, when *o*-, *m*-, and *p*-cresol were irradiated separately in methanol under the usual conditions, no products except the original cresol and tar were obtained.

Formation of Meta Alkylphenol. There are two plausible mechanisms by which meta alkylphenols could be formed in these reactions, and these are illustrated in Schemes I and II. In the first scheme, a "direct attack" of the alkyl radical at the meta position of the phenoxy radical yields a diradical (**1**) which is transformed into meta alkylphenol by the (formal) transfer of a hydrogen from the meta carbon to the oxygen. Scheme II involves the photoisomerization of an initially formed 4-alkylcyclohexa-2,5-dienone (**2**) to a 6-alkylbicyclo[3.1.0]hex-3-en-2-one (**3**)—a process with ample precedent in the literature.[6]

The latter mechanism, we feel, is favored by evidence, derived from the photolysis of anisole, which links the for-

Table I
Solvent Effect on Photolysis of Anisole[a]

Solvent	Conversion to phenolic products, %	Phenol, %	*o*-Cresol, %	*m*-Cresol, %	*p*-Cresol, %
Methanol	30.1	11.50	10.99	3.65	3.96
Ethanol	31.2	12.65	10.40	2.45	5.70
2-Propanol	19.0	8.10	7.53	0.83	2.54
tert-Butyl alcohol	22.7	7.58	9.29	1.40	4.44
Cyclohexane	0.65	0.10	0.33	0.17	0.05
Cyclohexene	0.95	0.16	0.53	0.08	0.19

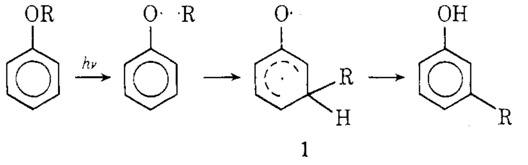
[a] Initial concentration of anisole 0.10 *M*; irradiated for 24 hr with a 450-W medium-pressure Hg lamp.

Table II
Per Cent Yield of Photoproduct after 24 Hr[a]

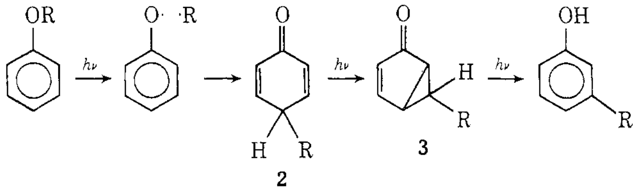
Registry no.	Starting ether	Phenol	Ortho isomer	Meta isomer	Para isomer
100-66-3	PhOMe	2.81	2.38	0.28	1.61
103-73-1	PhOEt	2.85	2.19	0.44	1.97
2741-16-4	PhOPr-*i*	9.10	2.06	0.77	2.32
6669-13-2	PhOBu-*t*	41.30	7.40	1.11	9.81

[a] Initial concentration of starting ether was 1.35 *M*; irradiated for 24 hr with a 450-W medium-pressure Hg lamp.

Scheme I
Formation of Meta Alkylphenol *via* "Direct Attack" Mechanism



Scheme II
Formation of Meta Alkylphenol *via* a Secondary Photolysis



mation of meta and para alkylphenols. The first piece of evidence is found in the concentration dependence of the relative yields of *m*- and *p*-cresol (Table III).

While the relative yields of phenol, *o*-cresol, and *m*- plus *p*-cresol are invariant, within experimental error, *m*-cresol increases in yield at the expense of *p*-cresol when the more dilute solution of anisole is irradiated. This suggests that *m*- and *p*-cresol have a common precursor. In the absence of knowledge of the mechanism by which the cyclohexadienones are formed, however, the concentration effect on the meta to para ratio cannot be explained. This aspect is currently under investigation.[7]

Secondly, Stern-Volmer plots were obtained for the quenching of the anisole photolysis by *cis*-dichloroethylene (Figure 1). The plots for *m*- and *p*-cresol formation are nearly coincident ($k_q\tau$ = 169 and 176 l. mol^{-1}, respectively) and are clearly separated from the *o*-cresol plot ($k_q\tau$ = 270 l. mol^{-1}). It is not as yet clear which entity or entities in the reaction scheme are being quenched, anisole or an anisole eximer being the most likely candidates. A common precursor for *m*- and *p*-cresol is clearly implied, however.[8]

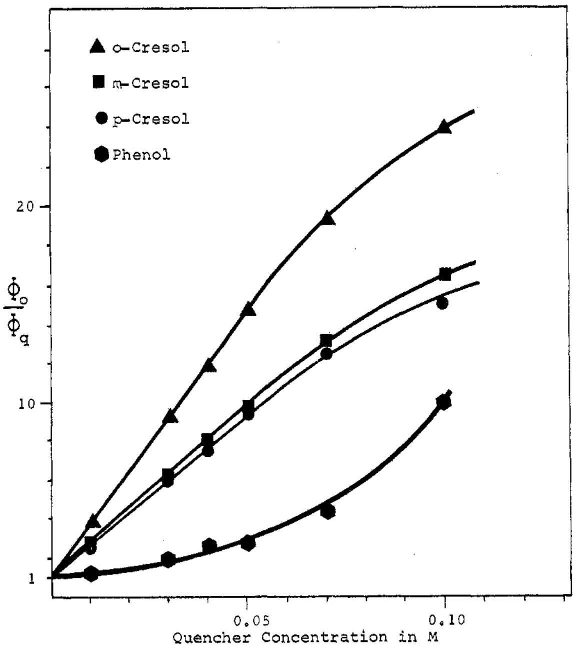


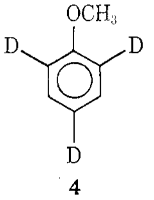
Figure 1. Stern-Volmer plots for the quenching of the anisole photoisomerization by *cis*-dichloroethylene, initial anisole concentration 0.10 *M* in methanol.

Table III
Composition of the Phenolic Photoproduct from the Irradiation of Anisole at two Different Initial Concentrations[a]

Product	Per cent formed at 1.35 *M*[b]	Per cent formed at 0.10 *M*[c]
Phenol	39.7	38.2
o-Cresol	33.6	36.5
m-Cresol	4.0 } 26.7	12.1 } 25.3
p-Cresol	22.7	13.2

[a] For 24 hr in methanol. [b] Absolute yield of phenolic photoproduct was 7.08%. [c] Absolute yield of phenolic photoproduct was 30.1%.

Labeling Studies. In order to distinguish between Schemes I and II, 2,4,6-trideuterioanisole (4) was prepared and photolyzed in methanol under the usual conditions. The phenolic products were partially separated by preparative gas chromatography, and the *m*-cresol fraction was collected. The aromatic region of a 300-MHz nmr spectrum of this fraction appears in Figure 2. If the mechanism of formation of *m*-cresol from anisole is as outlined in Scheme I, the deuterated *m*-cresol isolated will be **5**. If Scheme II is correct, **6** will be the expected deuterated *m*-cresol. Figure 3 shows the aromatic region of a 300-MHz spectrum of a mixture of undeuterated *m*- and *p*-cresol. Using the chemical shifts and coupling constants obtained from Figures 2 and 3 and from 60-MHz spectra, the 300-MHz spectra of **6** and **7** were simulated on an IBM 350/70 computer, using the LAOCOON III program and a suitable plotting program. The presumed genesis of Figure 2, then, is given in Figure 4. The small peaks in the δ 7.1-7.2 region in Figure 2 are considered to be due to impurities. Figure 4A is the simulated spectrum of a mixture of 17.5% *m*-cresol, 48.8% **6**, 3.5% *p*-cresol, and 30.2% **7**. The presence of **5** in the mixture would simply add to the intensity of the peak at δ 7.028. While the correspondence of relative areas between Figures 2 and 4A is not perfect, owing to some impurities in the collected sample, we can say that **5** cannot be present to the extent of more than a few per cent.



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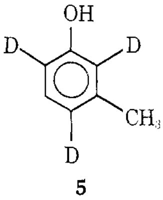

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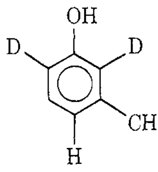

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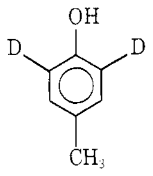

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Tautomerization *vs.* Photoisomerization. A remarkable feature of this reaction, as outlined in Scheme II, is that a 4-alkyl-2,5-cyclohexadienone (**2**), unsubstituted in the 2 and 6 positions, is capable of being photoisomerized before it can tautomerize to a 4-alkylphenol. In a series of papers, Miller[9] has shown that, in 4-alkyl-2,5-cyclohexadienones substituted with bulky alkyl groups in the 2, 3, and 6 positions, photoisomerization to the bicyclo[3.1.0]hex-3-en-2-one proceeds to the virtual exclusion of tautomerization. This phenomenon, however, does not appear to have been reported for less hindered systems.

On the assumption that tautomerization should be subject to acid and base catalysis, anisole was photolyzed

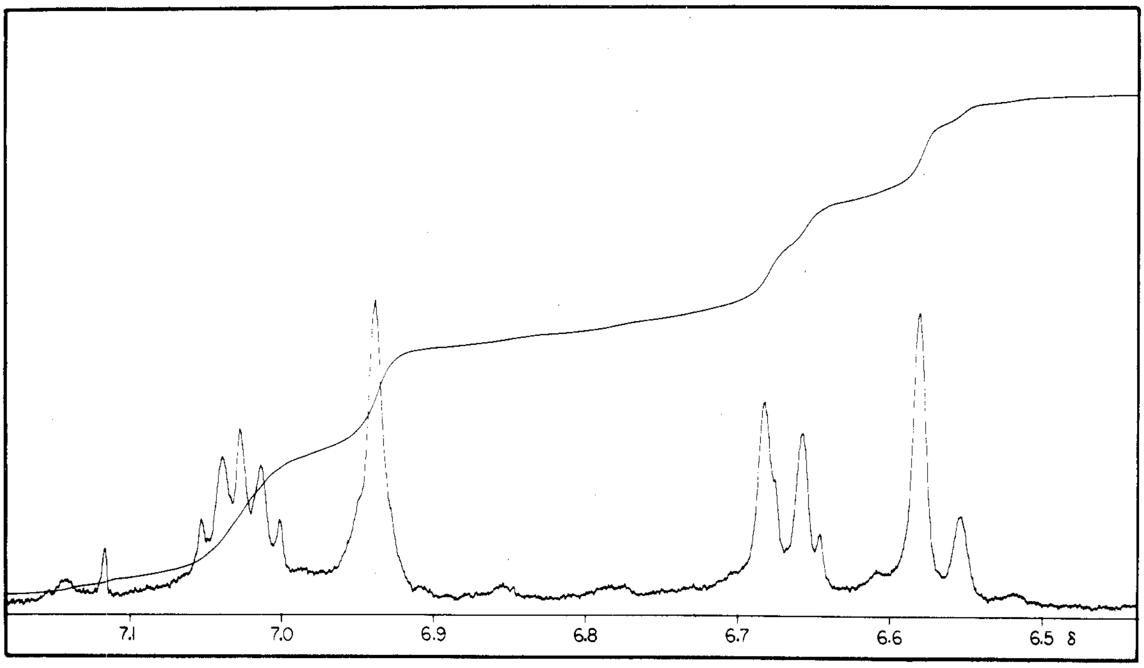

Figure 2. Partial 300-MHz spectrum of the *m*-cresol fraction from the photolysate of 2,4,6-trideuterioanisole, solvent $CDCl_3$.

in methanol containing minute amounts of HCl or $NaOCH_3$. As expected, in both cases, *m*-cresol formation was completely eliminated and *p*-cresol formation increased. Conversely, if C–H bond breaking at C-4 were retarded, *m*-cresol formation should increase as photoisomerization competed more successfully with tautomerization. To this end, 4-deuterioanisole was irradiated under the usual conditions, and the photolysate was examined by gas chromatography. It was observed that the yield of *m*-cresol had been increased by a factor of 2 to 3, while that of *p*-cresol had been correspondingly reduced. Though these data are only semiquantitative, they are completely in accord with the operation of a primary kinetic isotope effect on the tautomerization of the 2,5-cyclohexadienone.

Irradiation of Phenyl Ether. As stated at the outset, the photolysis of phenyl ether, phenyl benzyl ether, and phenyl allyl ether have been reported to yield ortho- and para-substituted phenols, but none of the meta isomer. Because we had observed both that meta alkylphenols tend to be formed in smaller amounts than the ortho and para isomers and that on most gas chromatographic columns meta and para alkylphenols cannot be separated from each other, we irradiated phenyl ether in methanol, and separated the photolysate on a column which had a demonstrated ability to separate the three phenylphenols.

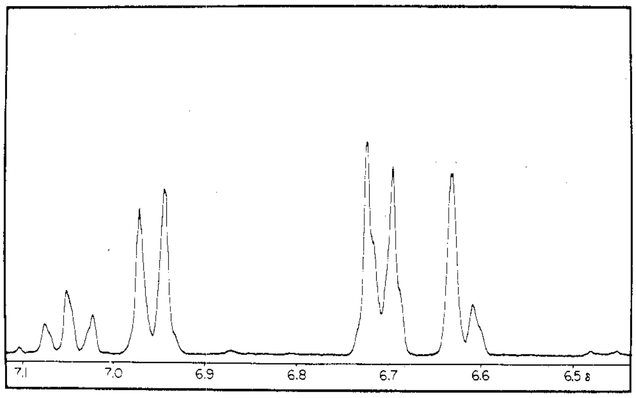

Figure 3. Partial 300-MHz spectrum of a mixture of *m*- and *p*-cresol in $CDCl_3$.

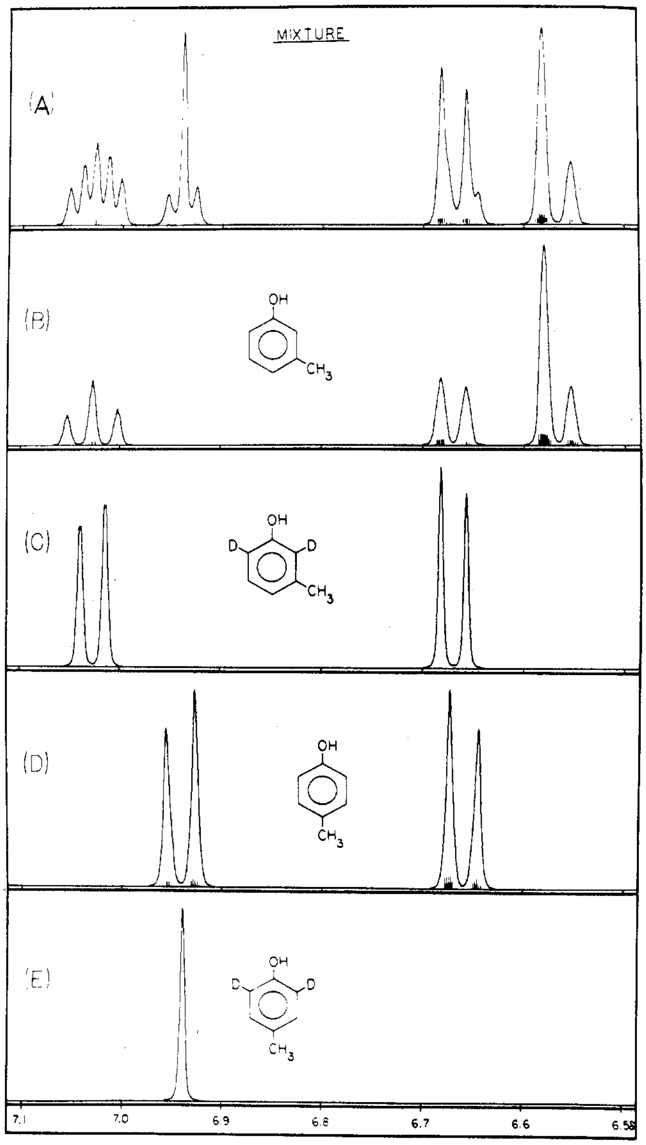

Figure 4. Computer simulation of the 300-MHz spectra of several cresols from the photolysate of 2,4,6-trideuterioanisole in methanol.

In this experiment, *m*-phenylphenol could not be detected in the photolysate. We conclude, then, that a phenyl, benzyl, or allyl group in the 4 position of a 2,5-cyclohexadienone promotes tautomerization by electron withdrawal, rendering the C-4 proton more acidic.

Experimental Section

Materials. Anisole, phenetole, *p*-methylanisole, phenyl ether, phenol, *cis*-dichloroethylene, and all solvents were obtained commercially as reagent or Spectrograde materials, and were used as received. All alkylated phenols were commercial materials, and were recrystallized or vacuum distilled before use.

Isopropyl phenyl ether and *tert*-butyl phenyl ether were prepared by the dicyclohexylcarbodiimide-promoted condensation of phenol with the corresponding alcohol according to the method of Vowinkel[10] and purified by vacuum distillation. Isopropyl phenyl ether had bp 62° (12 Torr); nmr τ 8.75 (doublet, J = 6.2 Hz, rel area 6), 5.55 (septet, J = 6.2 Hz, rel area 1), and 3.0 (multiplet, rel area 5). *tert*-Butyl phenyl ether had bp 68–69° (11 Torr); nmr τ 8.7 (singlet, rel area 1) and 3.0 (multiplet, rel area 5).

Sodium 2,4,6-trideuteriophenoxide was prepared by dissolving sodium phenoxide, freshly prepared from phenol and sodium hydroxide, in D_2O with a small chip of sodium added to ensure basicity. The solution was refluxed overnight, and the D_2O was distilled off *in vacuo*. Fresh D_2O was then added, the solution was again refluxed for several hours, and the D_2O was distilled off. A final refluxing with D_2O yielded sodium 2,4,6-trideuteriophenoxide which, by nmr analysis, contained only about 9% of undeuterated and partially deuterated phenoxide. To the D_2O solution of this product was added 2 equiv of methyl sulfate, and the resulting mixture was refluxed overnight. The trideuterioanisole was extracted from this solution, washed, dried, and distilled at atmospheric pressure. Its purity was confirmed by ir and nmr spectroscopy.

4-Deuterioanisole was prepared by quenching 4-methoxyphenylmagnesium bromide in D_2O. The product was then extracted with ether, dried, and distilled at atmospheric pressure. The purity of the compound was confirmed by its nmr spectrum.

Irradiation. Photolyses were typically carried out in a 250-ml cylindrical Pyrex irradiation vessel equipped with a nitrogen inlet tube and standard taper joints for a condenser and the water-cooled dipping well. High-purity tank nitrogen was bubbled vigorously through the solution for 30–40 min prior to irradiation, and a slow stream of nitrogen was maintained during the irradiation. Phenolic products were isolated from the photolysate by extraction with dilute base, followed by acidification and ether extraction. The products in all cases were separated and collected by preparative gas chromatography, and were identified by comparison of their ir and nmr spectra with those of authentic samples. In the quenching experiment, the 0.10 M solutions of anisole in methanol were sealed in quartz tubes after three freeze-pump-thaw degassing cycles, and were arranged around the dipping well, in contact with it. Because of the long irradiation time (24 hr) the tubes were not continuously rotated, but were moved around the dipping well every few hours. At high quencher concentrations (above 0.07 M) a yellow, insoluble material began to be deposited on the walls of the sample tubes, thereby reducing the light input. In the attempted photoisomerization of *o*-, *m*-, and *p*-cresol, these compounds were irradiated separately for 24 hr as 0.05 M solutions in methanol.

Gas Chromatographic Separation. Phenol and the isomeric alkylphenols were separated on a 0.25 in. × 20 ft column containing 15% SE-52 and 5% Bentone 34 on 60–80 mesh Gas-Chrom Z, at a column temperature of 160–180°. This column could not separate *o*-cresol from phenol, however; so the anisole photolysate was analyzed both on the SE-52/Bentone 34 column and on a 0.25 in. × 10 ft column containing 10% SE-30 on 60–80 mesh Chromosorb W, at a column temperature of 105°. For the preparative chromatographic analysis of the trideuterioanisole photolysate, a 0.25 in. × 10 ft column containing 20% Carbowax 2000 on 60–80 mesh Chromosorb W was plced in tandem with the SE-52/Bentone 34 column, and the column temperature was 160°.

Spectroscopic Analysis. Infrared spectra were obtained with a Perkin-Elmer Model 337 spectrophotometer; nmr spectra were obtained with either a Varian A-60 or a Varian HR-300 spectrometer.

Computer Simulation of Nmr Spectra. The chemical shifts (in parts per million from TMS) and coupling constants (in hertz) used in the simulation of the 300-MHz spectrum of *m*-cresol were $\delta_{o'}$, 6.581, δ_o 6.566, δ_m 7.028, δ_p 6.670, δ_{Me} 2.201, $J_{o,o'}$ = 1.4, $J_{o',m}$ = 1.7, $J_{o',p}$ = 1.5, $J_{o,m}$ = 8.0, $J_{o,p}$ = 1.2, $J_{m,p}$ = 7.5, $J_{o',\mathrm{Me}}$ = 0.6, $J_{o,\mathrm{Me}}$ = 0.6, $J_{m,\mathrm{Me}}$ = 0.7, $J_{p,\mathrm{Me}}$ = 0.6 Hz. The parameters for the simulation of the *p*-cresol spectrum were δ_o 6.669, δ_m 7.028, δ_{Me} 2.201, $J_{o,m}$ = 8.6, $J_{o,\mathrm{Me}}$ = 0.6, $J_{m,\mathrm{Me}}$ = 0.7 Hz. The values for $J_{o',m}$, $J_{o,m}$, and $J_{m,p}$ in the case of *m*-cresol are known to be somewhat in error. However, the appearance of the simulated 300-MHz spectrum does not change materially when these coupling constants are varied over a reasonable range. In both the *m*- and *p*-cresol cases, the values of δ_o and δ_p are sensitive to concentration. In plotting the simulations, the nmr Spectra Plot Program III—Variable Peak Height was used as adapted by B. L. Bruner (the University of Kentucky) for use with a Calcomp plotter. To simulate the spectrum of the cresol mixture, the intensities of the spectral lines of the individual components were multiplied by the appropriate factors, and the resulting data were combined and plotted.

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Registry No.—*m*-Cresol, 108-39-4; *p*-cresol, 106-44-5.

References and Notes

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(6) See, for example, P. J. Kropp in "Organic Photochemistry," Vol. I, Marcel Dekker, New York, N. Y., 1962, pp 1–90.

(7) A possible explanation is autocatalysis of the tautomerization of **2** by the phenolic photoproducts, since the absolute final concentration of phenols in the 1.35 M case is roughly three times that in the 0.10 M case. A study of the *m*- to *p*-cresol yield ratio as a function of solution acidity is in progress.

(8) (a) We are examining the possibility that more than one excited state of the ether may be involved. When the photolyses of 0.10 M methanolic anisole solutions were quenched at 254 nm with *cis*-dichloroethylene, the slope of the Stern–Volmer plot for *o*-cresol was now lower than those for the *m*- or *p*-cresol plots. These latter were, as above, nearly coincident. Moreover, at 254 nm, the ratio of phenol yield to total cresol yield (1.8) was higher than the ratio observed with the medium-pressure lamp (0.62). (b) A referee has suggested that the fact that the yield of phenol decreases less rapidly with increasing quencher concentration than does the yield of any cresol implies that the dichloroethylene, in addition to quenching excited states, is capturing a methyl radical from the $PhO\cdot\cdot CH_3$ radical pair. We feel that an equally plausible explanation involves the production of phenol from two different excited species which are quenched with different efficiencies. This would also account for the curvature of the Stern–Volmer plot for phenol.

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