Photo-induced Reaction. II.[1),*1]
The Photo-sensitized Oxidation of Hindered Phenols

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It is well known that a phenol produces a phenoxy radical by oxidation with so-called "one electron transfer oxidizing agents" and that the radical couples to form various types of products.2) Since the type of the product largely depends upon the oxidant and the starting phenol employed, it is rather difficult to predict the structures of such products. It has been suggested that a large number of natural products may be formed by the oxidative coupling of their phenol precursors in vivo.2,3) It may also be supposed that such phenol precursors can be oxidized photochemically in the presence of natural pigments serving as sensitizers, particularly in plants. We expected that the photo-sensitized oxidation of phenols might give some specific products, and so we investigated the photo-oxidation of several hindered phenols.

In general, phenols are destructively oxidized under the influence of ultrasonic radiation.4) Arnow has reported that when an aqueous solution of tyrosine is irradiated with an ultraviolet light 3, 4-dihydroxyphenylalanine is formed.5) Several investigators have reported that the primary reaction in the irradiation of phenols with an ultraviolet light or a visible light in the presence of a photo-sensitizer is the formation of phenoxy radicals,6-8) but they did not describe the subsequent behavior of the radicals in detail. Very recently Johnson and Tam have reported that some simple phenols dimerize on ultraviolet irradiation under bubbling oxygen.9)

As a preliminary experiment, we examined the photochemical oxidation of 2, 6-di-*t*-butylphenol (I) using various photo-sensitizers: eosin Y, erythrosin, methylene blue, chlorophyllin, methyl orange, riboflavin tetraacetate, and 2, 5-di-*t*-butyl-*p*-benzoquinone. Eosin Y and

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1) Part I. T. Matsuura, This Bulletin, **37**, 564 (1964).

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2) H. Musso, *Angew. Chem.*, **75**, 965 (1963).

3) a) D. H. R. Barton and T. Cohen, "Festschrift Arthur Stoll," Birkhäuser, Basel (1957), p. 117; b) H. Erdtman and C. A. Wachtmeister, ibid., p. 144.

4) B. Robert, R. O. Prudhomme and P. Grabar, *Bull. soc. chim. biol.*, **37**, 897 (1955).

5) L. E. Arnow, *J. Biol. Chem.*, **120**, 151 (1937).

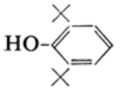
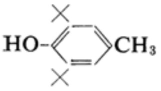
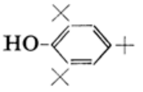
6) L. I. Grossweiner and E. F. Zwicker, *J. Phys. Chem.*, **67**, 549 (1963).

7) E. J. Land and G. Porter, *Trans. Faraday Soc.*, **59**, 2061 (1963).

8) J. O. Roebber, *J. Chem. Phys.*, **37**, 1974 (1962).

9) A. W. Johnson and S. W. Tam, *Chem. & Ind.*, **1964**, 1425.

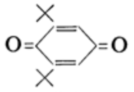
TABLE I. PHOTOSENSITIZED OXIDATION OF HINDERED PHENOLS[a]

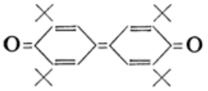
Phenol	Sensitizer	Tungsten lamp, W.	Irradiation period, hr.	Recovered phenol, %	Non-volatile products, g.	Peoduct isolated or identified (yield[b])
2, 6-Di-*t*-butylphenol	Eosin Y	200	50	41	1.02	IV (11%) V (18%)
	Erythrosin	500	30	23	1.01	IV (12%) V (33%)
	Erythrosin[c]	500	30	16	0.86	IV (11%) V (42%)
(I)	Methylene blue	500	32	64	0.32	IV (12%) V (15%)
2, 6-Di-*t*-butyl-*p*-cresol  (II)	Eosin Y	200	20	16	—	VI (4.2%) VII (2.8%)
2, 4, 6-Tri-*t*-butylphenol  (III)	Eosin Y	500	30	53	—	IV (13%) VIII(1.1%)

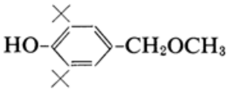
a) A solution of 3.00 g. of the starting phenol and 0.30 g. of the sensitizer in 100 ml. of methanol was irradiated under bubbling oxygen.

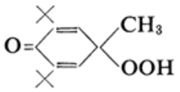
b) Yields were based on consumed starting phenol.

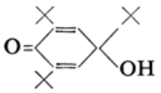
c) Crystals of 3, 5, 3′, 5′-tetra-*t*-butyl-4, 4′-diphenoquinone deposited in the course of the reaction were collected time to time.


(IV)


(V)


(VI)


(VII)


(VIII)

erythrosin were found to be most effective (see Experimental). A solution of a hindered phenol and a sensitizer in methanol was irradiated with a tungsten lamp under bubbling oxygen. The products were either isolated by column chromatography or analyzed by infrared and ultraviolet spectra and vapor phase chromatography. Three hindered phenols, 2, 6-di-*t*-butylphenol (I), 2, 6-di-*t*-butyl-*p*-cresol (II) and 2, 4, 6-tri-*t*-butylphenol (III), were oxidized under these conditions. The results are shown in Table I.

The photo-sensitized oxidation of 2, 6-di-*t*-butylphenol (I) with eosin Y yielded 2, 6-di-*t*-butyl-*p*-benzoquinone (IV) and 3, 5, 3′, 5′-tetra-*t*-butyl-4, 4′-diphenoquinone (V).[10] When erythrosin wasused as the sensitizer, the yield of the diphenoquinone V was considerably increased, but the yield of the benzoquinone IV was not altered. In both cases, some of the starting phenol I was recovered, and non-volatile products, probably several polymerized substances, were formed.

The reaction with 2, 6-di-*t*-butyl-*p*-cresol (II) seems to be rather complicated, giving many products. Among them, two crystalline products, a phenol and a hydroperoxide, were isolated in low yields. The NMR spectrum[*2] of the former phenol showed five singlets, at τ 8.57, 6.73, 5.75, 4.99, and 3.03, which were assigned to two *t*-butyl, a methoxyl, a hydroxyl, a benzyl, and two aromatic protons respectively. The structure VI was suggested for the compound; this was confirmed by comparing it with an authentic sample of VI.[11,12] The hydroperoxide was shown to have the structure VII by comparing it with an authentic sample.[13]

2, 4, 6-Tri-*t*-butylphenol was somewhat resistant to the photo-oxidation under these conditions. 2, 6-Di-*t*-butyl-*p*-benzoquinone (IV) was isolated as the main product, and 2, 4, 6-tri-*t*-butyl-4-hydroxy-2, 5-cyclohexadien-1-one (VIII),

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[10] C. D. Cook, E. S. English and B. J. Wilson, *J. Org. Chem.*, **23**, 755 (1958).

[*2] The NMR spectrum was kindly measured at the Faculty of Pharmaceutical Science of this University.

[11] D. H. Kim and F. A. Kummerow, *J. Am. Oil Chem. Soc.*, **39**, 150 (1962).

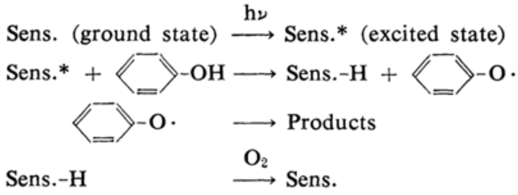
[12] T. Fujisaki, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zassi*), **77**, 727 (1956).

[13] M. S. Kharasch and B. S. Joshi, *J. Org. Chem.*, **22**, 1439 (1957).

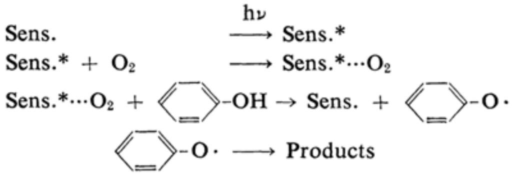
as the minor product. The formation of IV can be explained in terms of the thermal[14] or photochemical[1] conversion of the peroxide, XII, which is formed from the tri-*t*-butylphenoxy radical X (R=*t*-butyl) and oxygen.

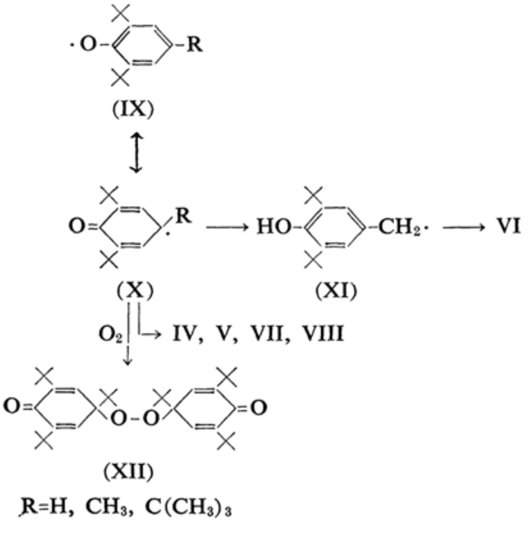
When the photo-oxidation reaction was carried out without irradiation or in the absence of the sensitizer, all the startiug phenols, I, II and III, were recovered unchanged. It appears, therefore, that the formation of a phenoxy radical in the primary process of this reaction requires both the irradiation and the presence of the sensitizer. The radical may be formed by hydrogen abstraction from the phenolic hydroxyl group by the excited photosensitizer molecule (Scheme 1), as has been suggested by Grossweiner and Zwicker.[6] Another possible mechanism, that the excited sensitizer-oxygen complex, proprosed by Schenck[15] in connection with the photosensitized addition of oxygen to olefins, can remove a hydrogen atom from the phenolic hydroxyl group, may also be taken into consideration (Scheme 2). In any case, the phenoxy radical, IX, can give various products via either its mesomeric form X or its tautomeric form XI.

Scheme 1



Scheme 2





R=H, CH_3, $C(CH_3)_3$

A large number of reports on the oxidation of these three phenols, I, II, and III, with one electron-transfer oxidizing agents have recently been published. The oxidation of 2,6-di-*t*-butylphenol gives mainly 2,6-di-*t*-butyl-*p*-benzoquinone (IV) and the diphenoquinone V,[10,13,16-18] in accordance with the results we obtained in the photo-sensitized oxidation. Because of the capability of the formation of the benzyl radical XI the oxidation of 2,6-di-*t*-butyl-*p*-cresol (II) with various oxidants is complicated and the products are obtained usually in low yields.[13,16,19-22] The oxidation of 2,4,6-tri-*t*-butylphenol (III) gives the stable free radical IX (R=*t*-butyl), under a nitrogen atmosphere, while it forms the peroxide XII and other products in the presence of oxygen.[16,20,23,24]

An unhindered phenol, *p*-cresol, was submitted to photosensitized oxidation using erythrosin under the same conditions. From the reaction mixture, some non-volatile products were also obtained besides volatile products, including the starting material. The analysis of the volatile products by vapor phase chromatography showed a pattern similar to that[25] of the products obtained from *p*-cresol by the oxidation with alkaline ferricyanide, except for the appearance of a new peak in the former case. Further studies of the photosensitized oxidation of *p*-cresol and of other unhindered phenols are in progress.

Experimental

The Photo-sensitized Oxidation of 2,6-Di-*t*-butylphenol (I).—A typical procedure using eosin Y as the sensitizer will be described below. A solution of 3.00 g. (15 mmol.) of 2,6-di-*t*-butylphenol and 0.30 g. (0.43 mmol.) of eosin Y in 100 ml. of methanol was placed in a 300-ml. flask and irradiated with a 200 W. tungsten lamp under bubbling oxygen at the reflux temperature. After it had been irradiated for 50 hr., the mixture was concentrated

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[14] C. D. Cook, R. C. Woodworth and P. Fianu, *J. Am. Chem. Soc.*, **78**, 4159 (1956).

[15] G. O. Schenck, *Angew. Chemie*, **69**, 579 (1957).

[16] H. R. Gersman and A. F. Bickel, *J. Chem. Soc.*, **1959**, 2711.

[17] A. S. Hay, H. S. Blanchard, G. F. Endres and J. W. Eustance, *J. Am. Chem. Soc.*, **81**, 6335 (1959).

[18] H. Hart and F. A. Cassis, ibid., **73**, 3179 (1951).

[19] G. R. Yohe et al., ibid., **75**, 2688 (1953); *J. Org. Chem.*, **21**, 1829 (1956); ibid., **24**, 1251 (1959).

[20] C. D. Cook, ibid., **18**, 261 (1953).

[21] J. I. Wasson and W. M. Smith, *Ind. Eng. Chem.*, **45**, 197 (1953).

[22] C. D. Cook, N. G. Nash and H. R. Flanagan, *J. Am. Chem. Soc.*, **77**, 1783 (1955).

[23] C. D. Cook and R. C. Woodworth, ibid., **75**, 6242 (1953).

[24] E. Müller and K. Ley, *Chem. Ber.*, **87**, 922 (1954).

[25] Unpublished data from this laboratory.

to a small volume. The crystals (0.29 g.) which formed were collected by filtration and recrystallized from methanol and ethanol to give reddish brown crystals, m. p. 235—237°C. The infrared spectrum was identical with that of an authentic sample (m. p. 238°C) of 3, 5, 3′, 5′-tetra-*t*-butyl-4,4′-diphenoquinone (V),[10] lit. m. p. 240—241°C.

The filtrate was then evaporated to dryness, and the residue was treated with petroleum ether to remove the eosin Y. The insoluble eosin Y (quantitatively recovered) was filtered off. The evaporation of the filtrate left a reddish-orange liquid which, on distillation, yielded 1.43 g. of a yellow liquid, b. p. 100—140°C/1 mmHg. The residue weighed 1.04 g. The distillate consisted of 2, 6-di-*t*-butylphenol (I) and 2, 6-di-*t*-butyl-*p*-benzoquinone (IV). The two components in the distillate were measured i) by vapor phase chromatographic analysis (conditions: stationary phase, silicone D. C. 550 on celite; carrier gas, helium; gas pressure, 0.8 kg./cm^2; temperature, 178°C), ii) by analysis of the intensity of the infrared bands, 750 cm^{-1} of I and 1660 cm^{-1} of IV, and iii) by analysis of the ultraviolet maxima, 255.5 mμ (log ε 4.25) of IV and 278.5 mμ (log ε 3.29) of I in cyclohexane, as 85.3% of I and 14.7% of IV. The amount (0.07 g.) of the diphenoquinone V in the residue was estimated from the intensity of its ultraviolet maximum, 403 mμ (log ε 4.74) in cyclohexane. Therefore, the amounts of IV, V, and I were found to be 0.21 g., 0.35 g., and 1.22 g. respectively.

Photo-sensitized oxidation reactions of I with erythrosin, and methylene blue were carried out in a similar manner; the results are summarized in Table I.

A solution of 3.00 g. of 2, 6-di-*t*-butylphenol (I) in 150 ml. of methanol was heated under reflux and bubbled with oxygen for 55 hr. The reaction mixture was evaporated to dryness and then treated with petroleum ether and filtered. The evaporation of the filtrate gave a residue whose infrared spectrum was identical with that of the starting phenol I, except for very small bands at 1600 and 1660 cm^{-1}.

The Photo-sensitized Oxidation of 2, 6-Di-*t*-butyl-*p*-cresol (II).—A solution of 3.00 g. (14 mmol.) of the phenol II and 0.30 g. of eosin Y in 100 ml. of methanol was irradiated for 20 hr., as has been described above. The residual liquid (2.46 g.), which was obtained by the removal of the sensitizer, was dissolved in petroleum ether and passed through a column containing 80 g. of silica gel. Elution with petroleum ether yielded 0.48 g. of the starting phenol II, which was identified by infrared spectrum and vapor phase chromatography. Elution with benzene yield 0.12 g. of crystals. Recrystallization from petroleum ether gave colorless crystals, m. p. 98—100°C, which were identical with 3, 5-di-*t*-butyl-4-hydroxybenzyl methyl ether (VI)[11,12] (infrared spectrum and mixed melting point).

Elution with benzene-ether (9 : 1) yielded 80 mg. of yellow crystals, m. p. 106—111°C. The infrared spectrum was identical with that of an authentic sample (m. p. 112—114°C) of 2, 6-di-*t*-butyl-4-methyl-4-hydroperoxy-2, 5-cyclohexadien-1-one (VII).[13]

Elution with methanol yielded 0.87 g. of a yellow liquid which showed several peaks in vapor phase chromatography but which was not further investigated.

A solution of the phenol II (3.00 g.) and eosin Y (0.30 g.) in methanol (100 ml.) was placed in a brown flask and heated under reflux with bubbling oxygen for 50 hr. The product 2.60 g. was obtained as colorless crystals, m. p. 64—65°C. The infrared spectrum was identical with that of the starting phenol II, m. p. 66—68°C.

The Photosensitized Oxidation of 2, 4, 6-Tri-*t*-butylphenol (III).—A solution of 3.00 g. (11 mmol.) of 2, 4, 6-tri-*t*-butylphenol[*3] and 0.30 g. of eosin Y in 100 ml. of methanol was irradiated with a 500 W. tungsten lamp for 50 hr., as has been described above. The mixture was then treated in the same manner. The residual liquid (2.90 g.) was dissolved in petroleum ether and passed through a column containing 110 g. of neutralized alumina (grade I). Elution with petroleum ether yielded 1.76 g. of pale yellow crystals which were found, by vapor phase chromatographic analysis, to be a mixture of the starting phenol III, 2, 6-di-*t*-butyl-*p*-benzoquinone (IV) and a minor product (ratio, 91 : 7 : 2). The analysis was carried out under the following conditions: stationary phase, silicon D.C. 550 on celite; carrier gas, helium; gas pressure, 0.8 kg./cm^2; temperature, 240°C. Elution with petroleum ether-benzene (1 : 1) yielded 145 mg. of a semi-solid, from which 16 mg. of colorless crystals, m. p. 102—123°C, were obtained. The infrared spectrum was identical with that of 2, 4, 6-tri-*t*-butyl-4-hydroxy-2, 5-cyclohexadien-1-one (VIII),[26] m. p. 133—134°C.

A solution of the phenol III (3.00 g.) in methanol (1.00 ml.) was irradiated with a 500 W. tungsten lamp under bubbling oxygen for 31 hr. The evaporation of the mixture left colorless crystals, which were identified as pure 2, 4, 6-tri-*t*-butylphenol by infrared and vapor phase chromatographic analyses.

The Photo-sensitized Oxidation of *p*-Cresol.—A solution of 1.20 g. (11 mmol.) of *p*-cresol and 0.20 g. of erythrosine in 100 ml. of methanol was irradiated with a 500 W. tungsten lamp, as has been described above. The distillation of the products gave 0.40 g. of a distillate, b. p. 120—180°C/10^{-1} mmHg, and 0.35 g. of a residue. The pattern of the vapor phase chromatographic analysis of the distillate was almost identical with that of the products obtained from *p*-cresol by oxidation with alkaline ferricyanide,[25] except for one unknown peak.

On irradiation without a sensitizer, *p*-cresol was recovered unchanged.

A Comparison of the Effect of Sensitizers in the Oxidation of 2, 6-Di-*t*-butylphenol (I).—Solutions of the phenol I and 0.05 mmol. of each of the following sensitizers in 10 ml. of methanol were irradiated with a 200 W. tungsten lamp under bubbling oxygen for 6.5 hr.: eosin Y (35 mg.) erythrosin (44 mg.), methylene blue (19 mg.), riboflavin tetraacetate (29 mg.), chlorophyllin (36 mg.), methyl orange (16 mg.), and 2, 5-di-*t*-butyl-*p*-benzoquinone (11 mg.). After the removal of the sensitizer, the intensities of the infrared bands, 1660 cm^{-1} (characteristic of

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[*3] Kindly supplied by the Koppers Co., Inc.

[26] E. Müller and K. Ley, *Chem. Ber.*, **88**, 601 (1955).

2, 6-di-*t*-butyl-*p*-benzoquinone (IV)) and 1600 cm^{-1} (characteristic of V), of the products in each case were compared. This comparison showed that eosin Y and erythrosin are most effective.

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