5,5′-diphenyldiphenoquinone, 31 g (0.137 mol) of 2-*t*-butyl-6-phenylphenol, and 10 g of pyridine under a nitrogen atmosphere. The reaction was slowly heated to 200° over a 55-min period and then heated for an additional 65 min at 220°. The initially deep red solution was now a light brown color. The reaction mixture was cooled to about 100° and diluted with 200 ml of acetic acid. When this mixture cooling to room temperature there was deposited 57 g (0.126 mol, 94% yield) of 2,2′-di-*t*-butyl-6,6′-diphenyl-*p*,*p*′-biphenol. After one recrystallization from aqueous alcohol, colorless crystals, mp 161°, were obtained.

Anal. Calcd for $C_{32}H_{34}O_2$: C, 85.29; H, 7.61. Found: C, 85.28, 85.16; H, 7.57, 7.63.

2,2′-Diphenyl-*p*,*p*′-biphenol.—The previous product could be dealkylated directly or preferably several steps in the procedure could be combined as follows. To a 500-ml three-necked flask equipped with a gas inlet tube, Dry Ice condenser, thermometer, and magnetic stirrer was added 90 g (0.40 mol) of 2-*t*-butyl-6-phenylphenol and 88 g (0.196 mol) of 3,3′-di-*t*-butyl-5,5′-diphenyl-4,4′-diphenoquinone. The reaction mixture was heated to 182° for 1 hr while trimethylamine was slowly bubbled through. The reaction mixture was then cooled and the trimethylamine was replaced with nitrogen. There was added 0.3 g of aluminum and 50 g of *p*-*t*-butylphenol. The reaction mixture was heated to 220° and after 1.5 hr a total of 45 ml of isobutylene was collected. The products were distilled directly from the pot. There was obtained 95.9 g (0.28 mol, 72.0% yield) of 2,2′-diphenyl-*p*,*p*′-biphenol, bp 270–285° (0.5 mm), mp 140°.

Anal. Calcd for $C_{24}H_{18}O_2$: C, 85.18; H, 5.36. Found: C, 84.79, 85.11; H, 5.42, 5.39.

2-Phenyl-*p*,*p*′-biphenol.—Oxygen was passed through a vigorously stirred solution consisting of 0.2 g of copper(I) chloride and 0.4 ml of N,N,N′,N′-tetramethylenediamine in 200 ml of isopropyl alcohol. Over 30 min there was added dropwise a solution of 25.8 g (0.125 mol) 2,6-di-*t*-butylphenol and 28.2 g (0.125 mol) of 2-*t*-butyl-6-phenylphenol dissolved in 100 ml of isopropyl alcohol. The reaction was continued for 40 min and then the red precipitate was isolated by filtration and washed with a small amount of isopropyl alcohol and dried. The products from four identical reactions were combined to give a total yield of 161.7 g. This product was suspended in hot acetic acid and titrated with hydrazine until the red color disappeared. The mixture of biphenols was isolated by adding an equivalent volume of water and the product was removed by filtration and dried. To a 500-ml three-necked flask equipped with a magnetic stirrer, condenser, and thermometer was added 150 g of *p*-cresol and 0.3 g of aluminum foil. The aluminum was dissolved by heating and to this solution was added the mixture of biphenols. The reaction mixture was heated to 194° and over a 155-min period 101 ml of isobutylene was evolved. The reaction mixture was cooled and diluted with an equal volume of toluene. There was deposited 24.1 g (0.129 mol, 25.8% yield) of *p*,*p*′-biphenol. The filtrate was washed with dilute hydrochloric acid, then dried, and distilled. After removal of toluene and *p*-cresol, two fractions were obtained.

The first fraction consisted of 39.5 g (0.150 mol, 30% yield) of 2-phenyl-*p*,*p*′-biphenol, bp 225–30° (0.5 mm). Recrystallization from ethanol gave mp 185–186°.

Anal. Calcd for $C_{18}H_{14}O_2$: C, 82.4; H, 5.4. Found: C, 82.3; H, 5.4.

The second consisted of 24.1 g (0.07 mol, 14% yield) of 2,2′-diphenyl-*p*,*p*′-biphenol.

2,6-Diisopropyl-*p*,*p*′-biphenol.—Following a procedure similar to the preceding, there was obtained from 30.9 g (0.15 mol) of 2,6-di-*t*-butylphenol and 26.7 g (0.15 mol) of 2,6-diisopropylphenol 11.2 g (0.04 mol, 27.6% yield) of 2,6-diisopropyl-*p*,*p*′-biphenol, mp 185–186.5°.

Anal. Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 79.8; H, 7.9.

The other products, *p*,*p*′-biphenol and 2,2′,6,6′-tetraisopropyl-*p*,*p*′-biphenol, were not isolated.

Registry No.—*p*,*p*′-biphenol, 92-88-6; 2-*t*-butyl-6-phenylphenol, 2416-98-0; 3,3′-di-*t*-butyl-5,5′-diphenyldiphenoquinone, 2416-99-1; 2,2′-di-*t*-butyl-6,6′-diphenyl-*p*,*p*′-biphenol, 2401-41-4; 2,2′-diphenyl-*p*,*p*′-biphenol, 2401-43-6; 2-phenyl-*p*,*p*′-biphenol, 18801-72-4; 2,6-diisopropyl-*p*,*p*′-biphenol, 18801-73-5.

The Radiolytic Oxidation of Cysteine[1]

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A recent communication by Packer[2] on the radiolysis of cysteine in neutral solution has prompted us to report our observations of its behavior in more acidic buffer solutions. It is well known that cysteine in aqueous solution is oxidized to cystine upon exposure to ionizing radiations. In aerated solution more thiol is destroyed than would be expected, and chain reactions involving dissolved oxygen have been postulated by several workers.[3]

The sequence given in eq 1–7 seemed plausible to us.

initiation

$$H_2O \rightsquigarrow e^- + \cdot OH + H^+ \tag{1}$$

$$e^- + O_2 + H^+ \rightarrow \cdot O_2H \tag{2}$$

$$RS\text{–}H + \cdot O_2H \text{ or } \cdot OH \rightarrow RS\cdot + H_2O_2 \text{ or } H_2O \tag{3}$$

propagation and product formation

$$RS\cdot + O_2 \rightarrow RS\text{–}O\text{–}O\cdot \tag{4}$$

and

$$RS\text{–}O\text{–}O\cdot + RSH \rightarrow RS\text{–}O\text{–}O\text{–}H + RS\cdot \tag{5a}$$

$$RS\text{–}O\text{–}O\text{–}H + RSH \rightarrow RSSR + H_2O_2 \tag{5b}$$

or

$$RS\text{–}O\text{–}O\cdot + RSH \rightarrow RSSR + \cdot O_2H \tag{6a}$$

$$\cdot O_2H + RSH \rightarrow H_2O_2 + RS\cdot \tag{6b}$$

termination

$$2RS\cdot \rightarrow RSSR \tag{7}$$

with minor contributions from other reactions such as

$$RS\cdot + \cdot O_2H \rightarrow RS\text{–}O\text{–}O\text{–}H$$

$$RS\cdot + e^- + H^+ \rightarrow RSH$$

The scheme is compatible with previously published data. The propagation steps (5 and 6) are reasonable reactions of sulfenyl compounds[4] and would be expected to occur cleanly in the presence of a large excess of thiol. They require the production of cystine and hydrogen peroxide in amounts which should be approximately equal and should increase with increasing thiol concentration. The results in Table I are consistent with these requirements.

The chain obviously is very short. At the highest cysteine concentration studied (30 mM), the yield of destruction of thiol was only three times the yield of primary radicals from water, and the yields of both cystine and hydrogen peroxide in 1 mM cysteine (pH ~3) were such that they could have resulted from the initiating and terminating steps alone.

Much higher yields of oxidation have been reported to result upon radiolysis of aerated neutral or alkaline, as opposed to acidic, thiol solutions. The most recent report, for example, records values for cysteine oxidation at pH 7 some five times as great as those at pH ~3 and similar concentrations observed by us. Such

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[1] Financial support from the Division of Radiological Health, B. S. S. (EH), Public Health Service, Research Grant RH 379, is gratefully acknowledged.

[2] J. E. Packer and R. V. Winchester, *Chem. Commun.*, 826 (1968).

[3] A. J. Swallow, *J. Chem Soc.*, 1334 (1952); J. E. Packer, *Nature*, **194**, 81 (1962); *J. Chem. Soc.*, 2320 (1963).

[4] See, *e.g.*, N. Kharasch, "Sulfenium Ions and Sulfenyl Compounds," in "Organic Sulfur Compounds," N. Kharasch, Ed., Pergamon Press, Inc., New York, N. Y., 1961.

Table I

Yields of Cystine and Hydrogen Peroxide upon X-Irradiation of Aqueous Cysteine Solutions[a]

[Cysteine], m*M*	[H_2SO_4], m*M*	pH	G_0 (cystine)	G_0 (H_2O_2)
30		~2.5	8.0	6.7
30		2.2	9.9	7.6
10		~2.5	6.6	5.6
10		2.4	8.4	5.6
3		~3	4.9	3.9
3	1.5	~3	4.8	3.7
3		2.8	5.3	3.5
3	3.0	2.5	4.6	3.4
1		3	3.1	2.9
1		3.25	3.0	2.3
1	1.0	3.0	2.7	2.6
1	0.5	3.2	2.4	2.7

[a] See Experimental Section for conditions.

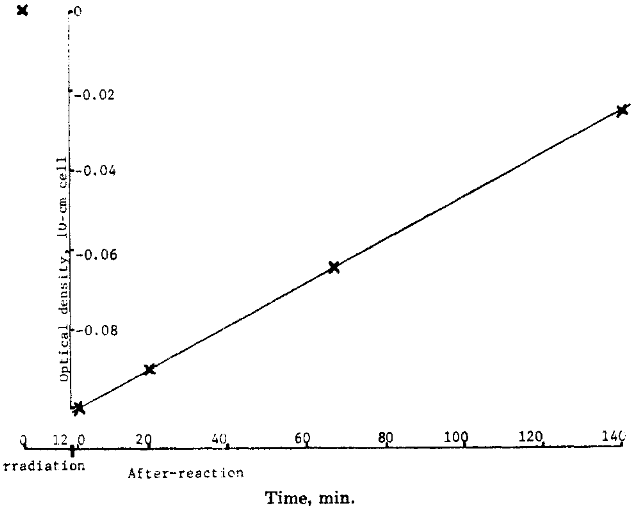

Figure 1.

results are not unequivocal; thiols are susceptible to oxidation by hydrogen peroxide and even by dissolved oxygen at pH 7 or above. In attempts to clarify the situation, we have examined solutions irradiated at intermediate pH (4–5). Moderately concentrated cysteine solutions (30 m*M*, pH 4) gave disulfide and peroxide yields little, if at all, greater than those obtained at pH 3. More dilute solutions, however, showed quite anomalous behavior. Thus, the optical densities at 255 mμ of 1 m*M* solutions (pH 4.5) *decreased* markedly during irradiation and then increased steadily, albeit slowly, when the solutions were allowed to stand after irradiation (Figure 1). However, when such irradiated solutions were acidified to pH 3 or below, the optical densities rose immediately to values which would have been observed had the irradiations been effected at pH 3. Yields of hydrogen peroxide were similar to those obtained at pH 3. The values may not represent the quantities actually present at pH 4.5, however, since the determination of peroxide involves acidification of the solution.

Clearly, little cystine is produced during irradiation in 1 m*M* solution at pH 4.5. Tentatively, we suggest that consumption of thiol (reactions, 3, 4, and 5a) proceeds readily, but that production of disulfide and peroxide (reactions 5b and 6a) is suppressed, plausibly because protonation of an oxygen atom of the sulfenyl peroxide must occur concomitantly with nucleophilic attack by the undissociated thiol (rate $\alpha[RSH][H^+]$).

The product under these conditions, then, would be the sulfenyl hydroperoxide. It is reasonable to suppose that this, like cysteic acid and cysteinesulfinic acid, might be even more transparent than the thiol at 255 mμ. First-order dependence of reaction 5b on hydrogen ion and thiol would then account for the nonproduction of disulfide, the slow after-reaction, and the disappearance of the anomaly at pH 3 and 1 m*M*, at pH 4 and 30 m*M*, and upon acidification. In more basic solution, the slow acid-dependent process would be superseded by rapid acid-independent reaction of the sulfenyl peroxide with the powerful nucleophile, thiolate ion (rate $\alpha[RS^-]$). The termination reaction (7) should be essentially pH independent, and the nucleophilic substitution step is probably rate determining in the propagating sequence. Thus, the chain length and the yield of disulfide should increase with increasing alkalinity, as they are reported to do.

Experimental Section

A General Electric Co. Maximar II X-ray apparatus operated at 125 kV and 15 mA, unfiltered, was used for irradiations. Dose rates, determined by ferrous dosimetry and corrected for sulfuric acid concentration effects, were 1300–1400 rads min^{-1}. Typical times of irradiation were 4, 8, 12 and 20 min. All initial rates (G_0) were derived from three- or four-point yield *vs.* dose curves, all of which were linear from the origin. Optical densities of solutions were determined using a Bausch and Lomb "Precision" spectrophotometer.

Water for solutions to be irradiated was distilled successively from alkaline permanganate and a sodium dichromate–phosphoric acid mixture through 30-in. Vigreux columns. Vessels were preirradiated until brown while filled with such water. Cysteine solutions (chloride free) were prepared afresh for each experiment and were adjusted to about the desired pH with 50 m*M* sulfuric acid. The final acid concentrations in some of the solutions are recorded in Table I.

Eisenberg's[5] titanium sulfate procedure was used to determine hydrogen peroxide. Control experiments demonstrated fair reliability and no significant reaction of hydrogen peroxide (10 m*M*) with cysteine (50 m*M*) at pH 5 or below. Determinations of cysteine by the phosphotungstate color reaction were unreliable at thiol concentrations above 5 m*M*, presumably because of reaction with peroxide in the acetate buffer. However, the ultraviolet spectrum of cystine (like most simple disulfides) shows a strong shoulder at 255 mμ (ε 290) in the rising end absorbance, and so cystine production was measured directly. The extinction of cysteine, although variable owing to small amounts of cystine, is less than one-tenth of that of cystine at 255 mμ. Plausible minor radiolysis products (cysteic acid, cysteinesulfinic acid, and hydrogen sulfide) are essentially transparent.

Registry No.—Cysteine, 52-90-4.

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[5] G. E. Eisenberg, *Ind. Eng. Chem. Anal. Ed.*, **15**, 327 (1943).

Aromatic o-Diisocyanates. A New Class of Compounds

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All recorded attempts to prepare representatives of the yet unknown class of aromatic *o*-diisocyanates by