

Quinone studies. Part III. Metal ion-catalysed oxidation of halophenols and halonaphthols by peroxidisulphate

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Abstract. Oxidation of representative halophenols and halonaphthols by peroxidisulphate has been examined. The influence of metallic ions, viz. Cu^{2+} , Fe^{3+} , Ag^+ , on the above reaction has been studied. Cu^{2+} ion-catalyzed oxidation gives halo-1, 4-quinones in excellent yield. Potassium *bis*(biureto)cuprate(III) complex also oxidises halophenols to halo-1, 4-quinones.

Keywords. Metal ion-catalysed oxidation; halophenols; halonaphthols; peroxidisulphate; halo-1, 4-quinones.

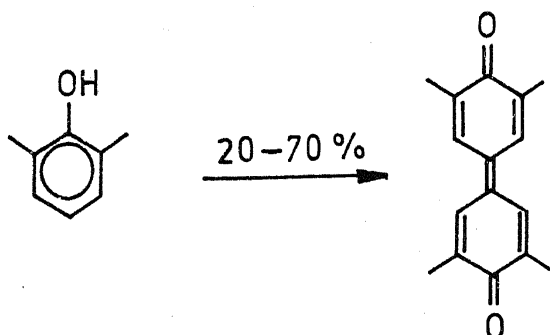
1. Introduction

Oxidation of phenols and phenolic derivatives is a reaction which takes place in a wide variety of environments and conditions in nature – in plants (Mayer and Harel 1979), and in animal and human tissues (Kuczenski 1973). Many complex natural products are biosynthesized through the oxidation of phenolic precursors (Woolf 1963; Taylor and Battersby 1967). Phenolic oxidation by a number of reagents has been the subject of sustained interest. With most oxidants phenols give a mixture of products, viz., quinones (Woolf 1963; Bacon and Izzat 1966; Taylor and Battersby 1967; Finkbeiner and Toothaker 1968), dihydroxy derivatives (Baker and Brown 1948; Woolf 1963; Ogata and Akada 1970), dimeric compounds (Albert 1954; Bacon and Munro 1960; Woolf 1963) and polymeric materials (Bacon *et al* 1954; Inove *et al* 1962; Woolf 1963; Taylor and Battersby 1967; Finkbeiner and Toothaker 1968). The yields of single compounds in most cases are poor. Fremy's salts (Teuber and Rau 1953; Teuber and Staiger 1955) thallium trifluoro acetate (McKillop *et al* 1970), hydrogen peroxide hydrochloric acid (Perumal and Bhatt 1979), periodic acid (Perumal and Bhatt 1979), cerium IV oxide-hydrogen peroxide (Barton *et al* 1975), and diphenyl seleninic anhydride (Barton *et al* 1976, 1977) are reagents which give quinones.

Ortho-blocked phenols like 2, 6-dimethyl phenol have been reacted with chromic acid (Horswill and Ingold 1966), hydrogen peroxide-copper(II) salt (Walling and Hodgdon 1958), *t*-butyl hydro-peroxide (Moore and Waters 1952), alkaline ferricyanide (Haynes *et al* 1956) and peroxysulphate-silver (I) salt (Bacon and Munro 1960) to give the corresponding diphenoquinone.

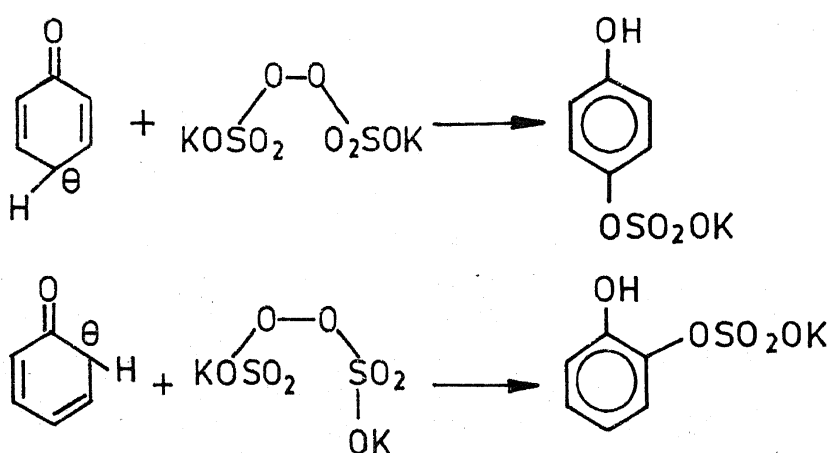
Oxidation of phenols with potassium peroxidisulphate under alkaline conditions (Baker and Brown 1948) constitutes the well-known Elbs oxidation reaction of

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conversion of phenols to the dihydroxy compound. Although the reaction was discovered in 1893 (Elbs 1893) it was only after 1960, that serious mechanistic work has been carried out (Behrman 1963; Ogata and Akada 1970). Evidence has been provided for the formation of sulphate esters of dihydroxy phenols (Baker and Brown 1948; Bacon *et al* 1954; Behrman 1963; Ogata and Akada 1970) through nucleophilic attack of phenoxide ions on the peroxy O-O bond.

There is little mechanistic investigation on the oxidation by potassium peroxydisulphate in neutral medium or in the presence of metal salts (Bacon and Izzat 1966; Bacon and Munro 1960).



We are reporting in this paper a study of reactions of halophenols with potassium peroxydisulphate in the presence of metallic salts. We have confined ourselves to product analysis and have attempted to optimise the yields of the single products. Ortho- and para-blocked halophenols are easily accessible. These substituents serve to slow down dimerization and polymerization of the initially formed radicals.

2. Results and discussion

The main product of the oxidation of halophenols are the halo-1, 4-quinones (table 1). Of the metal salts, Ag⁺ and Fe³⁺ have a marginally beneficial effect in improving the yield. In the case of the Ag⁺ ion, its ready conversion to silver bromide probably renders it unavailable for catalyzing the oxidation reaction. The most noteworthy result is the role of the Cu²⁺ ion. Under favourable conditions, the yield of haloquinones is increased to above 80%. In fact a highly efficient method for the preparation of halo-1, 4-quinones consists of using a copper salt as a catalyst. In all

Table 1. Oxidation of halophenols and halonaphthols with peroxydisulphate^a.

Substrate	Catalyst ^b	Reaction conditions		Product ^c	Yield (%)	m.p. (°C)	Lit. m.p. (°C)
		Time (h)	Temp (°C)				
4,6-Dibromo- <i>o</i> -cresol 1	Nil	5	70-80	2-Bromo-6-methyl-1, 4-benzoquinone	53	93	94-95 (Zincke and Janney 1913)
	Ag	1	70-80		54		
	Cu	1	70-80		80		
	Cu	1/3	70-80		74		
	Cu	12	30		67		
2,4,6-Tribromo-phenol 2	Fe	5	70-80	2,6-Dibromo-1, 4-benzoquinone	66	130	131-132 (Heinichen 1889)
	Nil	5	70-80		40		
	Ag	1	70-80		57		
	Cu	1	70-80		70		
	Cu	1/3	70-80		60		
2,4-Dibromothymol 3	Cu	12	30	2-Bromo-3-methyl-6-isopropyl-1, 4-benzoquinone	41	46	47-48 (Kehrmann 1889)
	Fe	5	70-80		61		
	Nil	5	70-80		75		
	Ag	1	70-80		76		
	Cu	1	70-80		85		
	Cu	1/3	70-80		81		
	Cu	12	30		71		
	Fe	5	70-80		55		
	Nil	5	70-80		55		
	Ag	1	70-80		114		
2,4-Dibromo-6-chlorophenol 4	Ag	1	70-80	2-Bromo-6-chloro-1, 4-benzoquinone	66	114-115 (Ling 1892)	
	Cu	1	70-80		67		
	Cu	1/3	70-80		54		
	Cu	12	30		46		
	Fe	5	70-80		62		

(Continued)

Table 1. (Continued)

Substrate	Catalyst ^b	Reaction conditions		Product ^c	Yield (%)	m.p. (°C)	Lit. m.p. (°C)
		Time (h)	Temp (°C)				
2,4,6-Tribromo- <i>m</i> -cresol <u>5</u>	Nil	5	70-80	2,6-Dibromo-3-methyl-1,4-benzoquinone	64	116	117 (Raiford 1911)
	Ag	1	70-80		60		
	Cu	1	70-80		80		
	Cu	1/3	70-80		76		
	Cu	12	30		70		
	Fe	5	70-80		68		
2,4-Dibromo-carvacrol <u>6</u>	Nil	5	70-80	2-Bromo-6-methyl-3-isopropyl-1,4-benzoquinone	64	52	53-54 (Kehrmann and Kruger 1900)
	Ag	1	70-80		70		
	Cu	1	70-80		70		
	Cu	1/3	70-80		64		
	Cu	12	30		60		
	Fe	5	70-80		62		
2,4-Dibromo-1-naphthol <u>7</u>	Nil	5	70-80	2-Bromo-1, 4-naphthoquinone	60	130	131 (McElavin and Engelhardt 1944)
	Ag	1	70-80		52		
	Cu	1	70-80		56		
	Cu	1/3	70-80		45		
	Cu	12	30		50		
	Fe	5	70-80		61		

^a The mol ratio of peroxodisulphate was 2.

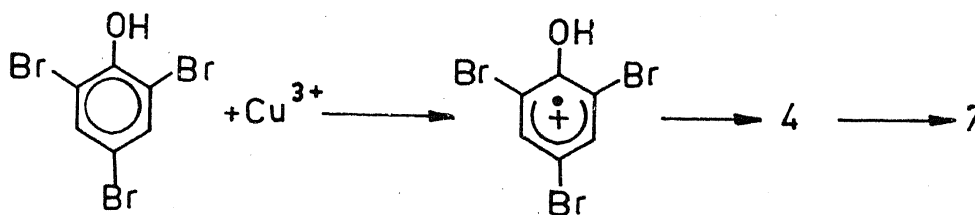
^b The mol ratio of catalysts was (i) Ag: silver nitrate 1; (ii) Cu: copper sulphate 0.11; (iii) Fe: ferric ammonium sulphate 0.1.

^c Product isolated by preparative TLC using 1:1 chloroform/hexane (40-60°) and identified by NMR, IR and m.p. data.

these metal-catalysed oxidations besides the halo-1, 4-quinones, some unreacted starting materials and polymeric materials could be recovered (table 2). It is clear that the system copper(II) salt-potassium peroxydisulphate is superior to peroxydisulphate itself.

Our results do not enable us to suggest a unique mechanism. More data is necessary before a mechanism can be advanced. Two possibilities, however, can be outlined (path A and path B, see scheme 1).

Oxidation of halophenols with potassium *bis*(biureto)-cuprate(III) (Gadd *et al* 1977) gave the corresponding halo quinones (table 3). These results clearly lend support to the electron transfer mechanism of path A.



However, the question of whether all the oxidation takes place exclusively by path A or whether concurrent paths operate has to be answered.

Table 2. Recovery (%) of materials other than quinones.

Starting materials ^a	Phenols ^c						Polymers ^d					
	A ^b	B	C	D	E	F	A	B	C	D	E	F
1	22	23	9	15	6	6	25	23	11	11	23	28
2	30	14	12	23	26	12	30	29	18	17	33	27
3	12	5	6	10	13	13	13	19	9	9	16	32
4	10	12	9	28	26	10	35	22	24	18	28	28
5	14	10	5	9	20	12	22	30	15	15	10	20
6	10	4	8	15	14	8	26	24	22	21	26	30
7	0	0	0	0	0	0	40	48	46	45	50	39

^a For the identity of the phenols see table 1

^b A-F represent the methods used as follows:

A. Without catalyst; B. Ag, 1 h; C. Cu, 1 h; D. Cu, 1/3 h; E. Cu, 12 h; F. Fe, 5 h

^c Isolated by preparative TLC

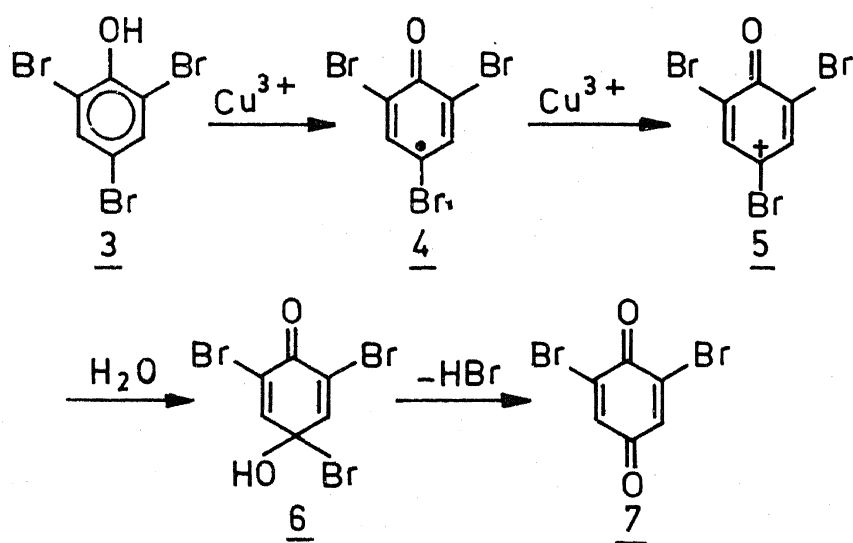
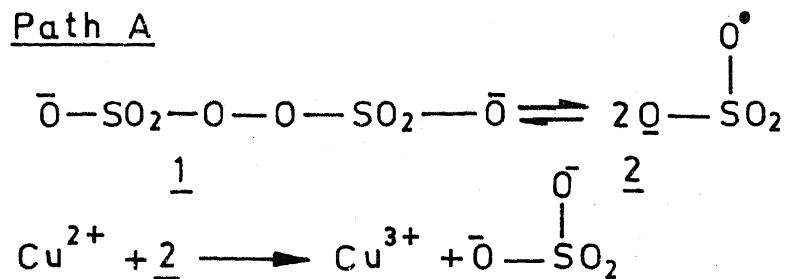
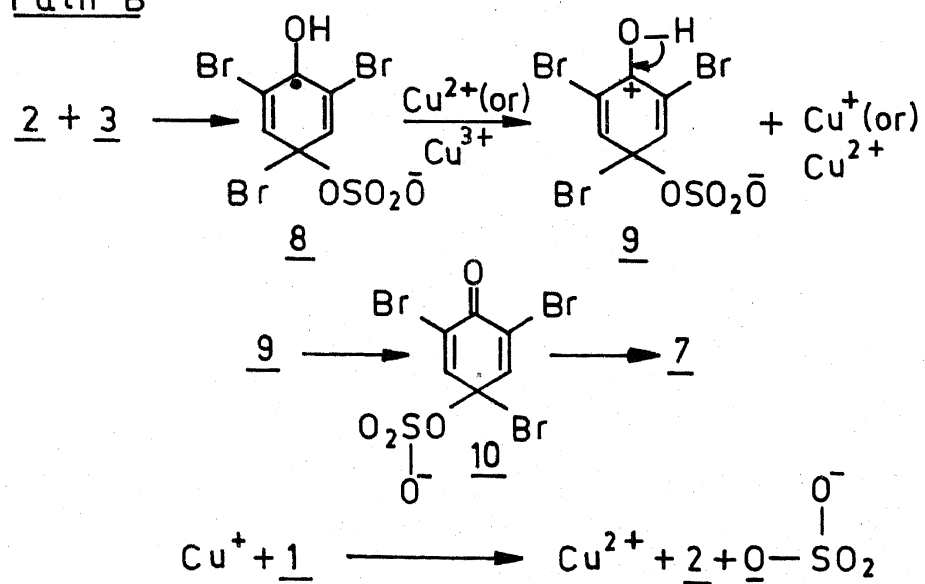
^d Yield calculated by difference

Table 3. Oxidation of halophenols with potassium *bis*(biureto)cuprate(III)^a.

Substrate	Product ^b	Yield (%)	m.p. (°C)
4,6-Dibromo- <i>o</i> -cresol (1)	2-Bromo-6-methyl-1, 4-benzoquinone	56	93
2,4,6-Tribromophenol (2)	2,6-Dibromo-1, 4-benzoquinone	30	130
2,4-Dibromothymol (3)	2-Bromo-3-methyl-6-isopropyl-1, 4-benzoquinone	67	46
2,4,6-Tribromo- <i>m</i> -cresol (5)	2,6-Dibromo-3-methyl-1, 4-benzoquinone	21	116

^a 4 mmol of K Cu (biureto)₂ and 1 mmol of phenol in 50 ml of 60% aqueous acetonitrile were stirred at 70–80°C for 2 h

^b The products were isolated by preparative TLC on silica gel using 1:1 chloroform-hexane (40–60°C) as eluent

Path APath B

Scheme 1.

3. Experimental

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. The identity of the compounds was confirmed by comparison of the IR and NMR spectra. IR spectra were recorded by the normal nujol mull techniques on a Perkin-Elmer model 700 spectrometer and NMR spectra were recorded in CDCl_3 or CCl_4 solutions on a Varian T-60 spectrometer.

The halophenols were prepared by a modified procedure (Meldola and Hughes 1890). To the phenol (0.25 mol) dissolved in glacial acetic acid (100 ml), was added bromine (0.5 mol or 0.75 mol depending upon the phenol) in 50 ml of glacial acetic acid. It was refluxed for 2 h in a fume hood. The reaction mixture was then poured into 250 ml of cold water. The product was collected by filtration if solid, then washed with water, dried and crystallized from suitable solvents. When the product was a liquid, it was extracted from the aqueous suspension with ether and washed four times with water. It was dried over sodium sulphate and the ether removed. The product was distilled under reduced pressure. The yields of the crude products were 90–95%. Melting and boiling points, and spectral data of the compounds matched with those of the authentic compounds 1 (Claus and Jackson 1888), 2 (Orton *et al* 1907), 3 (Kehrmann 1889), 4 (Ling 1892), 5 (Jost and Richter 1923), 6 (Kehrmann and Kruger 1900), 7 (Meldola and Hughes 1890).

3.1 Preparative scale general procedure for the preparation of quinones: Oxidation of 4,6-dibromo-*o*-cresol

4,6-Dibromo-*o*-cresol (1) (10.64 g, 0.04 mol) in 200 ml of acetonitrile was added to a solution of potassium peroxydisulphate (21.6 g, 0.08 mol) in 150 ml of water and copper sulphate (1.1 g, 0.0044 mol). The resulting yellow mixture was stirred at 70–80° for 1 h. The reaction mixture was then extracted with ether and the ether extracts were washed with water and then dried over sodium sulphate. Concentration of the solution gave the crude quinone, which was purified by passing through a short column of silica gel using 1:1 chloroform and hexane (40–60°) as eluent. Concentration of the eluate and crystallization of the product gave 2-bromo-6-methyl-1, 4-benzoquinone; yield 6.45 g (80%), m.p. 93°.

3.2 Oxidation of 2, 4, 6-tribromo-*m*-cresol: Typical small scale procedure

A solution of 2, 4, 6-tribromo-*m*-cresol (5) (0.69 g, 2 m mol) in 30 ml of acetonitrile is added to the solution of potassium peroxydisulphate (1.08 g, 4 m mol) in 20 ml of water and copper sulphate (0.055 g, 0.22 m mol). The resulting yellow mixture is stirred at 70–80° for 1 h. The reaction mixture is extracted with ether. The extract, after drying, is distilled to remove the solvent. The product is separated by TLC using 1:1 chloroform/hexane (40–60°C); yield 448 mg (80%), m.p. 116°.

3.3 Oxidation of 2,4-dibromothymol with potassium bis(biureto)-cuprate(III) ($\text{KCu}(\text{NH}.\text{CO}.\text{NH}.\text{CO}.\text{NH})_2$): Typical small-scale procedure

A solution of 2, 4-dibromothymol (3) (0.3 g, 1 m mol) in 30 ml of acetonitrile is added to the solution of potassium bis-(biureto)cuprate(III) (1.24 g, 4 m mol) in 20 ml of water.

The resulting brown colour mixture is stirred at 70–80°C for 2 h. The reaction mixture is extracted with ether. The extract, after drying, is distilled to remove the solvent. The product is separated by TLC using 1:1 chloroform/hexane (40–60°C); yield 163 mg (67%), m.p. 46°.

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