Persulfate/Copper(II): A Mild and Efficient Oxidising System for the Conversion of Dihydroxybenzenes to Quinones

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Sodium persulfate in the presence of copper(II) ions efficiently oxidises a number of *o*- and *p*-diphenols to the corresponding quinones under mild conditions.

The preparation of quinones by oxidation of *o*- and *p*-dihydroxybenzenes has traditionally been an active issue in synthetic organic chemistry.[1-3] Virtually all most common oxidising systems have been exploited to bring about such a conversion, including sodium dichromate,[4] chromium trioxide,[5] periodic acid,[6,7] iodic acid,[8] hypervalent iodine oxides,[9] iron(III) chloride,[10] silver oxide,[11] sodium chlorate,[12] manganese dioxide,[13] *N*-chlorosuccinimide/triethylamine,[14] sodium hypochlorite,[15] cerium(IV) sulfate,[16] benzeneseleninium(VI) anhydride,[17] and hydrogen peroxide/iodine.[18] Improved procedures involving supported reagents, such as silver carbonate/Celite (Fetizon's reagent)[19], cerium(IV) ammonium nitrate/silica[20] and periodate/silica[21] have recently been added to the relevant literature.

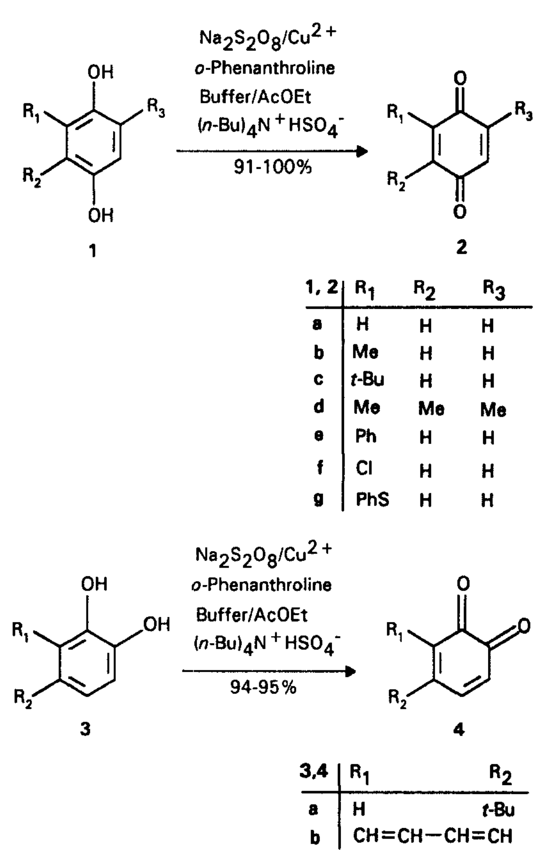
One oxidant that has not yet been given credit as a quinone forming reagent is persulfate.[22,23] We have now found that persulfate can effect the fast and quantitative conversion of a range of dihydroxybenzenes to the corresponding quinones in the presence of catalytic amounts of copper(II) ions. Copper(II), which has only sporadically been described in the literature for the activation of persulfate,[23-26] is apparently specific for promoting the oxidation of diphenols, since Fe^{2+} and Ag^{+}, the most efficient catalysts for persulfate oxidations, as well as Fe^{3+}, Pb^{2+}, Ni^{2+}, Co^{2+}, and Mn^{2+} were virtually ineffective.

The method was initially employed for the oxidation of water-soluble catechol substrates, e.g. dopa and dopamine. Using sodium persulfate (4 molar equivalents with respect to the catechol) and copper(II) acetate (0.05 molar equivalents) in tris buffer, pH 7.5, afforded the expected aminochromes[27,28] in about 80 % yield (data not shown). A more general procedure for the oxidation of water-insoluble substrates was then developed, involving reaction with sodium persulfate and catalytic copper(II) acetate/*o*-phenanthroline in ethyl acetate–(or dichloromethane)–phosphate buffer, pH = 6.5, in the presence of tetrabutylammonium hydrogen sulfate as phase transfer catalyst (Scheme). The oxidation is usually complete within 15 minutes at room temperature [a longer reaction time is required only for phenylthiohydroquinone (**1g**)] and the desired quinone can be obtained as chromatographically homogeneous crystals by simply evaporating the organic solvent. Impurities do not exceed 5 %, as judged by ^1H NMR and/or HPLC, and can be removed by crystallization. Failure to add the phase transfer catalyst results in lower yields and longer oxidation times.

Table. Oxidation of Dihydroxybenzenes **1** and **3**

Substrate	Solvent	Reaction time (min)	Yield[a] (%)	Mp[b] (°C)	Lit. mp (°C)	Ref
1a	EtOAc	5	100	102–107	115	29, 30
1b	EtOAc	5	91	[c]	66–68	15
1c	CH_2Cl_2	5	97	48–51	52–55	31
1d	EtOAc	15	91	[c]	29–30	15
1e	CH_2Cl_2	15	100	112	114–115	29, 30
1f	EtOAc	15	92	53–55	57	32
1g	EtOAc	400	100	108–110	114	33
3a	CH_2Cl_2	15	94	64–66	67–70	31
3b	EtOAc	10	95	130	121–122 145–147	34 35

[a] Isolated yield.
[b] Crude; nor recrystallized.
[c] Oil.



1, 2	R1	R2	R3
a	H	H	H
b	Me	H	H
c	*t*-Bu	H	H
d	Me	Me	Me
e	Ph	H	H
f	Cl	H	H
g	PhS	H	H

3,4	R1	R2
a	H	*t*-Bu
b	CH=CH–CH=CH	

Scheme

The parent *o*-quinone, as well as 4-methyl-*o*-quinone, can not be obtained in satisfactory yields due to rapid polymerisation, even at low temperatures. *O*-Alkylcatechols and hydroquinones, e.g. 4-methoxyphenol, are completely oxidised to mixtures of products, but no quinone is formed. Monophenols, e.g. tyrosine and anthrone, however, remain unchanged. In conclusion, the persulfate/copper(II) system provides a new convenient oxidising agent for the quantitative and selective conversion of dihydroxybenzenes to quinones. Salient features of the method include fast reaction time, ease of operation and suitability for large scale preparations.

Oxidation of Phenylhydroquinone (1e) to Phenylbenzoquinone (2e); Typical Procedure:

To a solution of sodium persulfate (2.8 g, 1.2×10^{-2} mol) in 0.5 M phosphate buffer, pH 6.5 (40 mL), containing tetrabutylammonium hydrogen sulfate (25 mg, 7.6×10^{-5} mol), *o*-phenanthroline (26 mg, 1.3×10^{-4} mol) in methanol (0.5 mL) was added followed by copper(II) acetate monohydrate (30 mg, 1.5×10^{-4} mol). The resulting mixture was vigorously stirred with a solution of **1e** (558 mg, 3×10^{-3} mol) in $CHCl_2$ (40 mL). Stirring was continued until TLC analysis showed complete disappearance of the starting material (15 min). The organic layer was separated, dried (Na_2SO_4) and evaporated to dryness to give **2e** as a yellow solid; yield: 550 mg (100%); mp 111°C (Ref,[29,30] mp 114–115°C).

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(1) Cason, J. *Org. React.* **1948**, *4*, 305.
(2) Thomson, R.H. In *The Chemistry of Quinonoid Compounds, Part I;* Patai, S., Ed.; Wiley: New York, 1974; p111.
(3) Naruta, Y.; Maruyama, K. In *The Chemistry of the Quinonoid Compounds*; Patai, S.; Rappoport, Z., Eds.; Wiley: New York, 1988, pp241–402.
(4) Kvalnes, D.E. *J. Am. Chem. Soc.* **1934**, *6*, 2487.
(5) Kohn, M.; Sussmann, J.J. *Monatsh. Chem.* **1927**, *48*, 203.
(6) Pennington, D.E.; Ritter, D.M. *J. Am. Chem. Soc.* **1946**, *68*, 1391.
(7) Pennington, D.E.; Ritter, D.M. *J. Am. Chem. Soc.* **1947**, *69*, 187.
(8) Evans, F.J.; Wilgus, H.S.; Gates, J.W. *J. Org. Chem.* **1955**, *30*, 1655.
(9) Takata, T.; Tajima, R.; Ando, W. *J. Org. Chem.* **1983**, *48*, 4764.
(10) Jempty, T.C.; Gogins, K.A.Z.; Mazur, Y.; Miller, L.L. *J. Org. Chem.* **1981**, *46*, 4545.
(11) Willstätter, R.; Pfannenstiel, A. *Chem. Ber.* **1904**, *37*, 4744.
(12) Billmann, J.H.; Wolnak, B.; Barnes, D.K. *J. Am. Chem. Soc.* **1944**, *66*, 652.
(13) Cassis, R.; Valderrama, J.A. *Synth. Commun.* **1983**, *13*, 347.
(14) Durst, H.D.; Mack, M.P.; Wudl, F. *J. Org. Chem.* **1975**, *40*, 268.
(15) Ishii, F.; Kishi, K.-I. *Synthesis*, **1980**, 706.
(16) Brockhaus, R. *Liebigs Ann. Chem.* **1968**, *712*, 214.
(17) Barton, D.H.R.; Brewster, A.G.; Ley, S.V.; Read, C.M.; Rosenfeld, M.N. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1473.
(18) Minisci, F.; Citterio, A.; Vismara, E.; Fontana, F.; De Bernardinis, S. *J. Org. Chem.* **1989**, *54*, 728.
(19) Balogh, V.; Fetizon, M.; Golfier, M. *J. Org. Chem.* **1971**, *36*, 1339.
(20) Fischer, A.; Henderson, G.N. *Synthesis* **1985**, 641.
(21) Gupta, D.N.; Hodge, P.; Davis, J.E. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2970.
(22) Minisci, F.; Citterio, A. *Acc. Chem. Res.* **1983**, *16*, 27.
(23) House, D.A. *Chem. Rev.* **1962**, *62*, 185.
(24) Hingorani, H.; Goal, H.C.; Chandra, G.; Srivastava, S.N. *Z. Phys. Chem. (Leipzig)* **1990**, *271*, 823.
(25) Walling, C.; El-Taliawi, G.M.; Amarnath, K. *J. Am. Chem. Soc.* **1984**, *106*, 7573.
(26) Perumal, P.T.; Bhatt, M.V. *Proc. Indian. Acad. Sci., Sect. B* **1989**, *101*, 2532; *Chem. Abstr.* **1989**, *112*, 54662s.
(27) Heacock, R.A. *Adv. Heterocycl. Chem.* **1965**, *5*, 205.
(28) Sobotka, H.; Barsel, N.; Chanley, J.D. *Fortschr. Chem. Org. Naturst.* **1957**, *14*, 217.
(29) Teuber, H.; Rau, W. *Chem. Ber.* **1953**, *86*, 1036.
(30) Zimmer, H.; Lanken, D.C.; Morgan, S.W. *Chem. Rev.* **1971**, *71*, 229.
(31) Buben, I.; Pospisil, J. *Collect Czech. Chem. Commun.***1969**, *34*, 1991.
(32) McKillop, A.; Ray, S.J. *Synthesis* **1977**, 847.
(33) Dimroth, O.; Kraft, L.; Aichinger, K. *Liebigs Ann. Chem.* **1940**, *545*, 124.
(34) Teuber, H.J.; Gotz, N. *Chem. Ber.* **1954**, *87*, 1236.
(35) Fieser, L.; Fieser, M. *J. Am. Chem. Soc.* **1935**, *57*, 491.