

INDIRECT HYDROXYLATION OF PHENOLS: A NEW ROUTE TO HYDROQUINONES

Durvasula V. Rao* and Fred A. Stuber

The Upjohn Company, Donald S. Gilmore Research Laboratories
North Haven, Connecticut 06473

Summary: Hydroquinone and alkyl hydroquinones are obtained from the corresponding phenols by alkylation with cyclopentadiene followed by isomerization and oxidation.

There are several methods to achieve direct hydroxylation of phenols to hydroquinones. They are oxidation with (i) hydrogen peroxide catalyzed by ferrous sulfate (Fenton's Reagent)¹ (ii) hydrogen peroxide in the presence of carbonyl compounds² (iii) peracids³ and (iv) persulfate (Elbs oxidation)⁴. In all these methods the yields are moderate and often accompanied by by-products. We wish to report an indirect method of introducing a hydroxyl function in the para position of phenol under mild conditions in excellent yields.

The starting materials used in these studies are 4-(cyclopenten-2-yl)phenol (1a), 4-(cyclopenten-2-yl)-o-cresol (1b), 4-(cyclopenten-2-yl)-2,6-dimethylphenol (1c). They were readily obtained by alkylation of phenol, o-cresol, and 2,6-dimethylphenol with cyclopentadiene in the presence of 85% phosphoric acid at room temperature in better than 80% yield.^{5,6,7}

The isomerization of allylic to propenyl double bond can be effected with several transition metal catalysts^{9,10} and metal carbonyls.¹¹ We have found that the best catalyst to achieve this isomerization was dichlorobis(benzonitrile)palladium(II). 1a readily isomerizes to 4-(cyclopenten-1-yl)phenol (2a) in practically quantitative yield. Similarly 1b and 1c yielded 2b and 2c respectively.

The oxidation of 2a to hydroquinone was effected with 30% hydrogen peroxide in acetonitrile in the presence of conc. hydrochloric acid at 50^o

in 91.6% yield. The co-product, cyclopentanone was not isolated but co-distilled with acetonitrile. By a similar oxidation, 2b and 2c produced 2-methylhydroquinone and 2,6-dimethylhydroquinone, respectively.

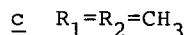
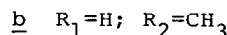
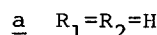
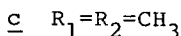
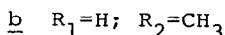
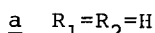
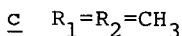
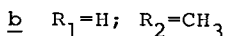
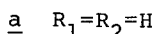
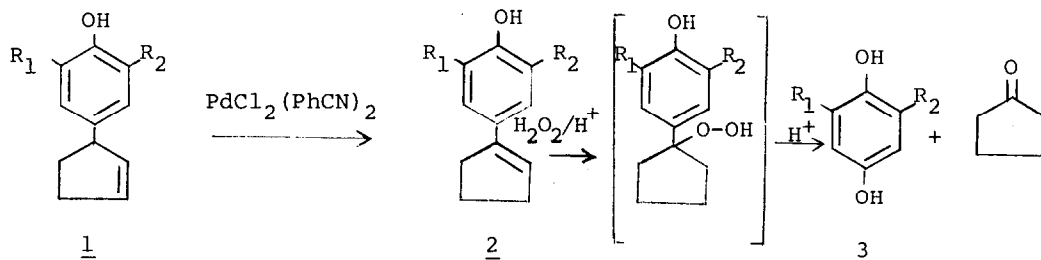


Table. Hydroquinones by Isomerization Followed by Oxidation

	<u>1</u>	<u>2</u>		<u>3</u>
	B.P. ($^{\circ}\text{C}/0.1\text{mm}$) (m.p., $^{\circ}\text{C}$)	Yield (%)	m.p., $^{\circ}\text{C}$	Yield of Hydroquinones (%)
<u>a</u>	90-110 $^{\circ}$ (64-66 $^{\circ}$)	90.6	148-149 $^{\circ}$	91.6
<u>b</u>	110-115 $^{\circ}$ (55-56 $^{\circ}$)	92.0*	88-89 $^{\circ}$	70.3
<u>c</u>	95-100 $^{\circ}$	100*	92-94 $^{\circ}$	60.0

*2b and 2c on standing turned dark and sticky. The oxidation was carried out immediately after they were isolated.

The acid-catalyzed rearrangement of cumene hydroperoxide to phenol and acetone is a well known reaction.^{12,13} In the present work the reaction occurs via a similar hydroperoxide formed from 2 and hydrogen peroxide in the

presence of acid. The resulting hydroperoxide rapidly undergoes acid-catalyzed rearrangement to yield hydroquinone and cyclopentanone.

General Procedure

Isomerization: To 1a (30.0g; 0.1875 mole) in 300 ml of dry benzene was added $\text{PdCl}_2(\text{PhCN})_2$ (1.2g) and heated under reflux. In one hour the isomerization was complete (followed by $^1\text{H-NMR}$; disappearance of multiplet at $\delta 3.50-4.00$ corresponding to $1-\text{CH}$ of cyclopentene). After another hour of reaction, the reaction mixture was filtered while hot from the dark precipitate to yield 2a (18.0g) as a pale yellow crystalline solid. Further concentration of filtrate to 1/3 volume yielded another crop of 2a (9.2g). Total yield amounted to 90.6%. After one recrystallization from chloroform 2a melted at $148-149^\circ\text{C}$ (lit.⁵ $149-150^\circ\text{C}$). $^1\text{H NMR}$ (CDCl_3): $\delta 5.90-6.10$ [1,m, C(2)-H].

Oxidation: To 2a (10.0g; 0.0624 mole) in 100 ml of acetonitrile was added 30% H_2O_2 (9.5g; 0.084 mole) followed by conc. HCl (1.0g). The solution was kept at 50°C under stirring and in two hours the reaction was complete (monitored by $^1\text{H-NMR}$). After another hour the reaction mixture was cooled, neutralized with sodium bicarbonate (2.0g) and the excess of H_2O_2 was reduced by catalytic hydrogenation in a Parr shaker at 45 psi using 10% Pd-C (0.1g). The solution was filtered from the catalyst and solids, and evaporated in vacuo to give a crystalline solid which after recrystallization from boiling chlorobenzene yielded hydroquinone (6.3g) in 91.6% yield, mp $168-170^\circ\text{C}$.

References and Notes

1. A. Chwala and M. Pailer, J. Prakt. Chem., 152, 46 (1939); (CA., 33, 3348⁹ (1939)).
2. U. S. Patent, 4,208,536 (1980) (To Rhône-Poulenc Industries, Paris).
3. U. S. Patent, 4,223,165 (1980) (To Rhône-Poulenc Industries, Paris).
4. W. Baker and N. C. Brown, J. Chem. Soc., 2303 (1948).
5. A. Bader, J. Am. Chem. Soc., 75, 5967 (1953).

6. The reaction can be completed in 2-4 hrs. by using Vibromixer during the addition of cyclopentadiene.
7. We have found that the alkylation of these phenols can also be carried out with 2,2'-dicyclopentenyl ether⁸ under these conditions to yield la, lb, and lc in better than 80% yields.
8. K. Alder and F. H. Flock, Chem. Ber., 89, 1733 (1956).
9. P. Golborn and F. Scheinmann, J. Chem. Soc. (Perkin I), 2870 (1973).
10. H. A. J. Carless and D. J. Haywood, J. Chem. Soc. (Chem. Comm.), 980(1980)
11. R. Damico, J. Org. Chem., 33, 1550 (1968).
12. H. Hock and S. Lang, Chem. Ber., 77, 257(1944).
13. M. S. Kharasch, A. Fono, and W. Nudenberg, J. Org. Chem., 15, 748 (1950).

(Received in Japan 12 February 1981)