Quinones. I. The Syntheses of Acetyl-p-benzoquinone Derivatives and 2-Acetylnaphthoquinone

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Acetyl-*p*-benzoquinone derivatives are expected to show interesting chemical and biological properties, owing to the presence of an acetyl carbonyl group conjugated to quinone double bond. However, only acetyl-*p*-benzoquinone has been reported in the literature[1].

An attempt was made as described below to synthesize several acetyl-*p*-benzoquinone derivatives, e. g., 2-methyl-5-acetyl-*p*-benzoquinone (acetyltoluquinone), 2, 3-dimethyl-5-acetyl-*p*-benzoquinone (acetyl-*o*-xyloquinone) and 2-acetyl-1, 4-naphthoquinone by the oxidation of corresponding acetylhydroquinone derivatives with silver oxide.

Acetylhydroquinone has been synthesized by several methods: viz., i) by the action of zinc chloride on hydroquinone in glacial acetic acid[2], ii) by the Fries migration of hydroquinone diacetate[3], and iii) by the action of acetyl chloride on hydroquinone dimethyl ether in the presence of aluminum chloride followed by demethylation[1]. But because of the complicated procedures or low yield, these methods did not give good results.

It has been found that these acetylhydroquinone derivatives are obtained in good yield as a result of the action of boron trifluoride on hydroquinone derivatives in glacial acetic acid[4]. Acetylation was carried out by the saturation of boron trifluoride to the suspension of hydroquinone derivatives in excess glacial acetic acid. 2-Acetylhydroquinone (III, $R=R'=H$) was obtained directly by this method from hydroquinone (I, $R=R'=H$) in an almost quantitative yield. But in the cases of 2-methyl- and 2, 3-dimethylhydroquinone and naphthohydroquinone, there were obtained mono- or diacetates of corresponding acetyl derivatives. For example, acetylation of 2-

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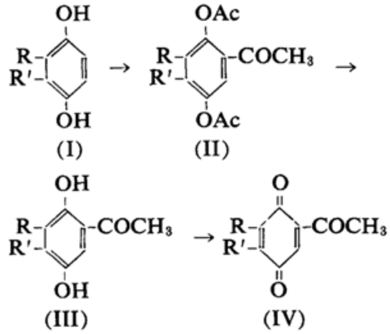
[1] T. Irie and E. Kurosawa, presented at the 7th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1954; M. C. Kloetzel, R. P. Dayton and B. Y. Abadir, *J. Org. Chem.*, **20**, 38 (1955); N. N. Vorozhtsov and V. P. Makaev, *D. I. Statei obschei Khim. Akad. Nauk, U. S. S. R.*, **1**, 553 (1953).

[2] M. Nencki and W. Schmidt, *J. Prakt. Chem.*, **23**, 546 (1881).

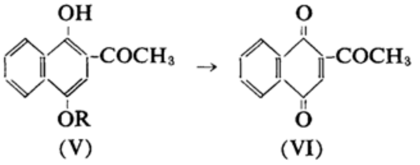
[3] "Organic. Syntheses," Vol. 28, New York (1948), p. 42; R. D. Desai and C. K. Mavani, *Proc. Indian Acad. Sci.*, **29A**, 267 (1949); P. S. Rao and K. L. Gakhar, ibid., **30A**, 327 (1949).

[4] E. Kurosawa, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **78**, 312 (1957).

methylhydroquinone (I, R=H, R′=CH_3) afforded pale yellow crystals, then after several recrystallizations from dilute ethanol, colorless crystals were obtained. This material melted at 112°C and exhibited no coloration with ferric chloride in ethanol.



After saponification of this diacetate (II, R=H, R′=CH_3) with aqueous sodium hydroxide containing a small amount of sodium hydrosulfite, 2-methyl-5-acetylhydroquinone (III, R=H, R′=CH_3) was obtained; it melted at 145°C. Similarly, there was obtained 2,3-dimethyl-5-acetylhydroquinone diacetate (II, R=R′=CH_3), m. p. 98°C, which was hydrolyzed to corresponding hydroquinone (III, R=R′=CH_3), m. p. 151°C. In the case of acetylation of naphthohydroquinone, 2-acetyl-4-acetoxynaphthol (V, R=$COCH_3$), m. p. 101°C, was obtained and it was hydrolyzed to 2-acetylnaphthohydroquinone (V, R=H).



2-Methyl-5-acetylhydroquinone was oxidized quantitatively to 2-methyl-5-acetyl-*p*-benzoquinone (IV, R=H, R′=CH_3) by being shaken with silver oxide and anhydrous potassium carbonate in dry benzene. When 2,3-dimethyl-5-acetylhydroquinone was oxidized under the same conditions, an oily product was obtained. It gave the stimulative odor characteristic to quinone derivative and it was easily reduced to 2,3-dimethyl-5-acetylhydroquinone by shaking its chloroform solution with aqueous sodium hydrosulfite. In infrared spectrum, this compound showed the band attributed to quinone carbonyl at 1640 cm^{-1} as shown in Fig. 1, but no band in the region of about 3300 cm^{-1}. Similarly, 2-acetylnaphthohydroquinone was oxidized to 2-acetyl-1,4-naphthoquinone (VI), m. p. 83~84°C, in good yield.

2-Acetyl-*p*-benzoquinone and 2-methyl-5-acetyl-*p*-benzoquinone have the bands attributed to quinone carbonyl at 1645 cm^{-1} and 1635 cm^{-1} in infrared spectrum as shown in Fig. 1. Likewise, 2,3-dimethyl-5-acetyl-*p*-benzoquinone and 2-acetyl-1,4-naphthoquinone have the bands attributed to quinone carbonyl at 1640 cm^{-1} and 1662 cm^{-1}, respectively. In general, it has been reported[5], that *p*-benzoquinone has the band attributed to quinone carbonyl at 1663 cm^{-1}; when the substituent is a negative group as chlorine or bromine, the quinone carbonyl band shifts to a higher frequency, and when the substituent is positive, the band shifts to a lower frequency. The position of the absorption maximum can be qualitatively interpreted by the sum of I-effect and M-effect. Contrary to expectation that acetyl-*p*-benzoquinone derivatives would show the band attributed to quinone carbonyl at a higher frequency than that of *p*-benzoquinone, due to the influence of the acetyl carbonyl group, these compounds show the bands at a considerable lower frequency as shown in Fig. 1.

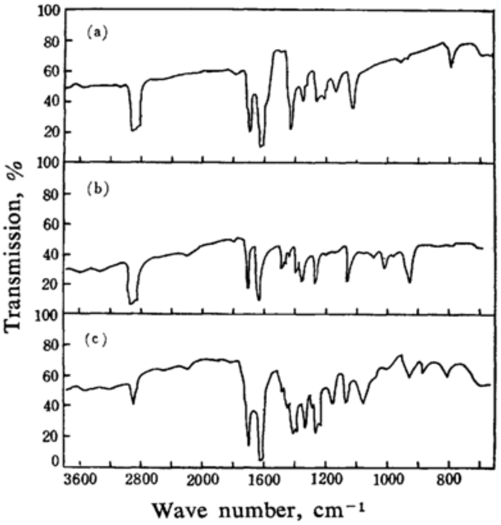


Fig. 1. IR spectra.
(a) Acetylbenzoquinone (Nujol)
(b) Acetyltoluquinone (Nujol)
(c) Acetyl-*o*-xyloquinone (direct)

These results indicate the existence of a large M-effect in the molecules of acetyl-*p*-benzoquinone derivatives. For the confirmation of this fact, the author attempted to find the relationship between the frequency of quinone carbonyl in infrared spectrum and the other properties of quinone derivatives. L. J. Bellamy[6] reported the existence of a straight lineal relationship between the sum of electronegativity of substituents of ethylene derivatives and frequency of CH_2-deformation (δCH_2), and between the molecular refractions of

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[5] P. Yates, M. I. Ardao and L. F. Fieser, *J. Am. Chm. Soc.*, **78**, 650 (1956).

[6] L. J. Bellamy, *J. Chem. Soc.*, **1955**, 4221.

functional derivatives and frequencies of the carbonyl band of carboxylic acids. The author gave attention to the oxidation-reduction potential of quinone derivatives which is one of the important properties of these compounds. It has been suggested that certain quinones, e. g., ubiquinone, play a part in the oxidation-reduction process of living matter[7] and the feature of the reactions is interpreted with the oxidation-reduction potential[8].

The oxidation-reduction potentials and the frequencies of quinone carbonyl bands of some benzoquinone derivatives are listed in Table I. When the oxidation-reduction potentials are plotted against the frequency of quinone carbonyl bands, the resulting curve is a nearly straight line as shown in Fig. 2.

This result indicates that the hypsochromic shift of the quinone carbonyl band resultant from the effect of the substituent linearly depends on the elevation of oxidation-reduction potential of the quinones.

TABLE I. CARBONYL FREQUENCIES AND OXIDATION-REDUCTION POTENTIALS OF BENZOQUINONE DERIVATIVES

Benzoquinone	Frequency cm^{-1}[a]		Potential V.[b]
	in CS_2	Nujol	
Chlorobenzoquinone	1678		0.736[c]
Benzoquinone	1668	1663	0.711
Toluquinone	1663	1663	0.656
o-Xyloquinone	1660	1660	0.588
p-Xyloquinone	1660	1668	0.597
m-Xyloquinone	1657	1653	0.592
Thymoquinone	1660		0.589[c]
Pseudocumoquinone	1657*	1650	0.536
Duroquinone	1642	1639	0.471
Ubiquinone[d]	1653		0.542

a) P. Yates, M. I. Ardao and L. F. Fieser, *J. Am. Chem. Soc.*, **78**, 650 (1956).
b) See Ref. 8.
c) Conant and Fieser, *J. Am. Chem. Soc.*, **45**, 2194 (1923).
d) J. F. Pennock, R. Ruegg, U. Schwieter and O. Wiss, *Helv. Chim. Acta*, **41**, 3243 (1958).
* Inflection.

TABLE II. CARBONYL FREQUENCIES AND OXIDATION-REDUCTION POTENTIALS OF ACETYL-*p*-BENZOQUINONE DERIVATIVES

Benzoquinone	Frequency, cm^{-1}		Potential V.
	in CS_2	Nujol	
Acetylbenzoquinone	1668	1645	0.564
Acetyltoluquinone	1662	1645	0.539
Acetyl-*o*-xyloquinone	1654	1640	0.504

TABLE III. CARBONYL FREQUENCIES AND OXIDATION-REDUCTION POTENTIALS OF 1,4-NAPHTHOQUINONE DERIVATIVES

Substituent	Frequency, cm^{-1} in CCl_4	Potential V.[a]
2-Chloro-	1684	0.510
2-Bromo-	1686	0.509
2,3-Dichloro-	1687	0.498
None	1675	0.483
2-Methyl-	1670	0.422
2,3-Dimethyl-	1660	0.340
2,6-Dimethyl-	1668	0.405
2,7-Dimethyl-	1673	0.407
2-Methoxy-	1660	0.369

a) W. Mansfield Clark, "Oxidation-Reduction Potentials of Organic Systems", The Williams & Wilkins Company, Baltimore (1960), p. 376.

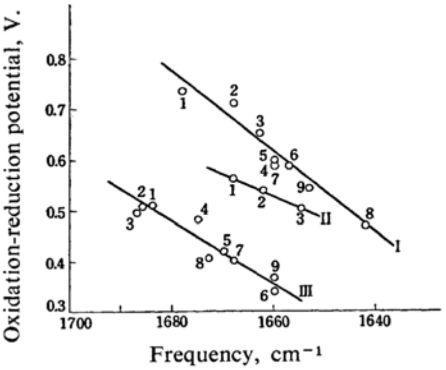

Fig. 2. Carbonyl frequency vs. oxidation-reduction potential.

I: Benzoquinone derivatives (in CS_2)
1. Chlorobenzoquinone
2. Benzoquinone
3. Toluquinone
4. *o*-Xyloquinone
5. *p*-Xyloquinone
6. *m*-Xyloquinone
7. Thymoquinone
8. Duroquinone
9. Ubiquinone

II: Acetylbenzoquinone derivatives (in CS_2)
1. Acetylbenzoquinone
2. Acetyltoluquinone
3. Acetyl-*o*-xyloquinone

III: Naphthoquinone derivatives (in CCl_4)
1. 2-Chloronaphthoquinone
2. 2-Bromonaphthoquinone
3. 2,3-Dichloronaphthoquinone
4. Naphthoquinone
5. 2-Methylnaphthoquinone
6. 2,3-Dimethylnaphthoquinone
7. 2,6-Dimethylnaphthoquinone
8. 2,7-Dimethylnaphthoquinone
9. 2-Methoxynaphthoquinone

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[7] R. H. Thomson, "Naturally Occurring Quinones", Butterworths Scientific Publications, London (1957), p. 1; W. Mansfield Clark, "Oxidation-Reduction Potentials of Organic Systems", The Williams and Wilkins Company, Baltimore (1960).

[8] Fausto Ramirez, et al., *J. Am. Chem. Soc.* **81**, 4338 (1959).

The author determined the oxidation-reduction potentials of acetylbenzoquinone derivatives by the polarographic method. The buffer solution used was that of Smith et al.⁹⁾ The results, given in Table II and Fig. 2, show that these acetyl benzoquinone derivatives have relatively low potentials, but the quinone carbonyl frequencies are slightly higher than the other benzoquinone derivatives as compared with the potentials.

In general, the effect of substituents upon the oxidation-reduction potential has not been interpreted sufficiently, but in this case, the following explanation is possible. When the substituent of benzoquinone derivative gives a fairly large inductive effect in comparison with the M-effect against quinone carbonyl, a straight linear relationship between quinone-carbonyl frequency in the infrared spectrum and oxidation-reduction potential exists as shown in Fig. 2.

In the case of naphthoquinone and anthraquinone, however, relatively high frequencies of quinone carbonyl-bands against the oxidation-reduction potentials were observed as shown in Table III and Fig. 2. This fact is interpreted as due to the influence of the M-effect of an aromatic ring against quinone carbonyl.

Similarly, it is possible that in the cases of acetylbenzoquinone derivatives, deviation from the above linear relationship, as shown in Fig. 2, may be interpreted as due to the fairly large M-effect of the acetyl group against quinone carbonyl in comparison with the inductive effect.

From these results, it is expected that the interesting properties may be gained about acetylquinone derivatives by reason of the low oxidation-reduction potential and the lack of substituent in β-position toward quinone carbonyl and acetyl carbonyl.

Further investigation concerning the effect of the substituent upon the oxidation-reduction potential and the reactivity of acetylbenzoquinone derivatives is in progress.

Experimental

2-Methyl-5-acetylhydroquinone. — Methylhydroquinone (5 g.) was suspended in glacial acetic acid (30 cc.) and warmed on a water bath. Boron trifluoride was passed into the mixture. The suspension slowly dissolved and a red color appeared. The saturation of boron trifluoride afforded a clear red solution which was heated for further 5 hr. on a water bath. The reaction mixture was then poured into ice water. The crystals thus separated (crude product) were collected by filtration and dried. After repeated recrystallizations from dilute ethanol, colorless needles were obtained, m. p. 112°C. (Found: C, 62.35; H, 5.78%). This material was found to be identical with 2-methyl-5-acetylhydroquinone diacetate¹⁰⁾ by use of the mixed melting point method.

The above crude product was treated with 2 N sodium hydroxide containing a small amount of sodium hydrosulfite for half an hour and then the alkaline solution was neutralized with 2 N hydrochloric acid. The crystals thus obtained were filtered and recrystallized from dilute ethanol. 2-Methyl-5-acetylhydroquinone was obtained as yellow needles, m. p. 145°C. (Found: C, 65.10; H, 6.17%).

2-Methyl-5-acetylbenzoquinone. — 2-Methyl-5-acetylhydroquinone (5 g.), anhydrous potassium carbonate (5 g.) and freshly prepared silver oxide (15 g.) were shaken in dry benzene (50 cc.) for 5 min. at 40°C. The reaction mixture was filtered and the solids were shaken with fresh benzene. On evaporation of the combined solution under reduced pressure, orange yellow crystals were obtained. After sublimation in vacuo or recrystallization from carbon disulfide, this substance melted at 79.5°C, yield 94%.

Found: C, 65.90; H, 4.95. Calcd. for $C_9H_8O_3$: C, 65.85; H, 4.88%.

2, 3-Dimethyl-5-acetylhydroquinone. — *o*-Xylohydroquinone (5 g.) was suspended in glacial acetic acid (30 cc.) and warmed on a water bath. Boron trifluoride was passed into the mixture. The suspension slowly dissolved and a yellow color appeared. After saturation of boron trifluoride, the reaction mixture was heated for further 5 hr. on a water bath. After the solution was poured into ice water, the resulting crystals (crude product) were collected and dried. After repeated recrystallizations from dilute ethanol, colorless needles were obtained, m. p. 97~98°C. This material exhibited no coloration with ferric chloride in ethanol and gave positive result to the iodoform test; by the mixed melting point method, it was found to be identical with 2, 3-dimethyl-5-acetylhydroquinone diacetate (see below).

The above crude product was treated with 2 N alcoholic sodium hydroxide for 5 min. and then the alkaline solution was neutralized with 2 N hydrochloric acid. The crystals thus obtained were recrystallized from dilute ethanol. Yellow needles were obtained, m. p 151°C, yield 5.9 g. (91%).

Found: C, 66.83; H, 6.92. Calcd. for $C_{10}H_{12}O_3$: C, 66.67; H, 6.67%.

This material exhibited green coloration with ferric chloride in ethanol and a positive result to the iodoform test.

Acetylation of 2,3-Dimethyl-5-acetylhydroquinone. —2, 3-Dimethyl-5-acetylhydroquinone (0.5 g.) was refluxed for 2 hr. in acetic anhydride (2 cc.). The solvent was removed under reduced pressure and the residue was sublimated in vacuo. Diacetate m. p. 97~98°C, was obtained as colorless needles.

Found: C, 63.64; H, 5.94. Calcd. for $C_{14}H_{16}O_5$: C, 63.64; H, 6.06%.

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9) L. I. Smith, I. M. Kolthoff, S. Wawzonek and P. M. Ruoff, *J. Am. Chem. Soc.*, **63**, 1018 (1941).

10) R. D. Desai and C. K. Mavani, *Proc. Indian Acad. Sci.*, **29A**, 269 (1949).

2,4-Dinitrophenylhydrazone of 2,3-Dimethyl-5-acetylhydroquinone. — 2, 3-Dimethyl-5-acetylhydroquinone and 2,4-dinitrophenylhydrazine reacted in ethanol in the presence of a few drops of concentrated sulfuric acid. Crystals deposited were collected and recrystallized from butanol. Orange red needles were obtained, m. p. 271°C.

Found: C, 53.26; H, 4.55. Calcd. for $C_{16}H_{16}O_6N_4$: C, 53.33; H, 4.45%.

2,3-Dimethyl-5-acetylbenzoquinone. — 2,3-Dimethyl-5-acetylhydroquinone (5 g.), anhydrous potassium carbonate (5 g.) and freshly prepared silver oxide (15 g.) were shaken in dry benzene (50 cc.) for 5 min. at 35°C. The reaction mixture was filtered and the solid was shaken with fresh benzene. On evaporation of combined solution under reduced pressure, 2,3-dimethyl-5-acetylbenzoquinone was obtained in yellow brown oily state, yield 92%.

Found: C, 67.52; H, 5.68. Calcd. for $C_{10}H_{10}O_3$: C, 67.41; H, 5.62%.

2-Acetylnaphthohydroquinone. — Naphthohydroquinone (5 g.) was suspended in glacial acetic acid (30 cc.) and under water cooling, boron trifluoride was passed into the suspension. Under heat evolution, hydroquinone dissolved slowly and a clear red-brown solution was obtained. After saturation with boron trifluoride the reaction mixture was immediately poured into ice water. The orange red product (crude product) was filtered; after repeated recrystallizations from dilute ethanol, it melted at 101°C.

Found: C, 68.96; H, 5.00. Calcd. for $C_{14}H_{12}O_4$: C, 68.85; H, 4.93%.

In the infrared spectrum, this material has the bands attributed to OH at 3300 cm^{-1} (broad), acetate carbonyl at 1750 cm^{-1} and carbonyl (bonded) at 1630 cm^{-1}. It exhibited greenish blue coloration with ferric chloride in ethanol solution and a positive result to the iodoform test.

The above crude product was dissolved in 2 N aqueous sodium hydroxide containing a small amount of sodium hydrosulfite. After 20 min., the insoluble materials were filtered off, the solution was neutralized with 2 N hydrochloric acid and the resulting crystals collected by filtration. After repeated recrystallizations from dilute ethanol, yellow crystals were obtained, m.p. 206~208°C, yield 3.5 g. (56%).

Found: C, 70.92; H, 4.96. Calcd. for $C_{12}H_{10}O_3$: C, 71.29; H, 4.96%.

This material exhibited yellow brown coloration with ferric chloride in an ethanol solution and a positive result to the iodoform test. In the infrared spectrum, it has the bands attributed to OH at about 3300 cm^{-1} (bonded) and acetyl carbonyl at 1618 cm^{-1} (bonded.).

2-Acetylnaphthoquinone[11]. — 2-Acetylnaphthohydroquinone (1 g.), anhydrous potassium carbonate (1 g.) and freshly prepared silver oxide (3 g.) were shaken in dry benzene at 40°C for 15 min. The reaction mixture was filtered and the solvent was removed under reduced pressure. The residue was recrystallized from light petroleum; golden yellow needles were obtained, m. p. 83~84°C, yield 0.84 g. (85%). (Found: C, 71.85; H, 3.87%).

Determinations of Oxidation-Reduction Potential by Polargroaphic Method. — Oxidation-reduction potential measurement was carried out by preparing 0.001 M solution of quinone derivatives in a buffer solution containing 0.1 N sodium acetate and 0.1 N acetic acid in 50% ethanol at pH 5.4. In order to find the standard normal hydrogen electrode the potentials were calculated for pH of zero, using 0.246 V. as the standard potential of the saturated calomel electrode.

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[11] P. Friedländer, *Ber.*, **28**, 1950 (1895).