

Hypervalent Iodine Oxidation of *p*-Alkoxy- and Related Phenols: A Facile and Efficient Synthesis of *p*-Quinones

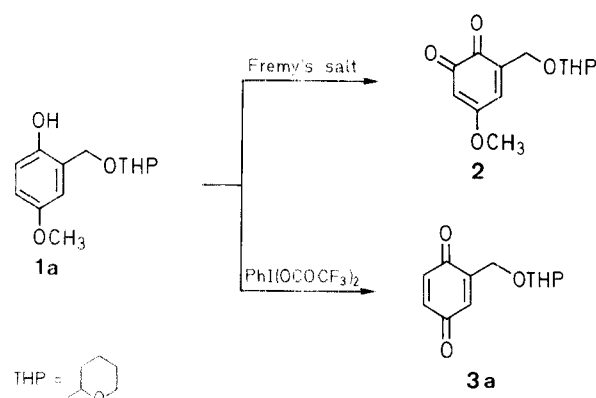
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(Ditrifluoroacetoxyiodo)benzene oxidizes *p*-alkoxy- and related phenols to the corresponding *p*-quinones in excellent yields under mild conditions.

The synthesis of *p*-quinones and *p*-quinone derivatives is an important synthetic aspect in organic chemistry, because they are not only useful intermediates, but also many are pharmacologically active compounds.¹ Although there are many oxidation methods for the preparation of *p*-quinones from phenol derivatives such as, metal oxidants,² Fremy's salt,³ silver oxide,⁴ 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ),⁵ ammonium cerium(IV) nitrate,⁶ they have some limitations especially in the case of phenol derivatives with an acid-sensitive group. For certain reagents, the acidic conditions used resulted in decomposition or hydrolysis of the acid-sensitive group. Thus, attempted oxidation of 4-methoxy-2-(tetrahydropyranyloxy)methylphenol (**1a**) with DDQ in methanol gave a complex mixture, and oxidation with Fremy's salt in potassium dihydrogen phosphate solution did not give the *p*-quinone but the *o*-quinone derivative **2** selectively. Oxidation of **1a** with ammonium cerium(IV) nitrate in acetonitrile/water gave hy-

drolyzed *p*-quinone, and with ammonium cerium(IV) nitrate in the presence of potassium carbonate gave the desired *p*-quinone **3a**, but in unsatisfactory yield (69% yield).



In continuation of our study on the hypervalent iodine compounds,⁷ we recently described a general synthetic method for *p*-benzoquinone monoacetals from *p*-alkoxyphenols by the hypervalent iodine reagent, (ditrifluoroacetoxyiodo)benzene,⁸ and now found that oxidation of **1a** with (ditrifluoroacetoxyiodo)benzene in acetonitrile/water in the presence of potassium carbonate gave **3a** in excellent yield. Similar results were obtained in the oxidation of 4-methoxy-2-(methoxymethyl)oxy-methylphenol (**1b**). The present hypervalent iodine oxidation using (ditrifluoroacetoxyiodo)benzene was found to be quite useful not only for the preparation of acid-sensitive *p*-quinones,

Table. *p*-Quinones **3** and 1,4-Naphthoquinones **5** Prepared

Product	Yield ^a (%)	mp (°C) ^b (solvent)	Molecular Formula ^c or Lit. mp (°C)	IR (KCl) ^d ν (cm ⁻¹)	¹ H-NMR (CDCl ₃ /TMS) ^e δ, J (Hz)
3a	86	67–69 (<i>n</i> -hexane)	C ₁₂ H ₁₄ O ₄ (222.2)	3050; 2925; 2850; 1655; 1645; 1600	1.45–2.1 (m, 6H); 3.45–4.1 (m, 2H); 4.53 (m, 2H); 4.75–4.9 (m, 1H); 6.8–7.1 (m, 3H)
3b	99	yellow oil	C ₉ H ₁₀ O ₄ (182.2)	2950; 2875; 1660; 1600 ^f	3.36 (s, 3H); 4.43 (d, 2H, J = 2); 4.69 (s, 2H); 6.7–6.9 (m, 3H)
3c	100 ^g 93 ^h	115–116 (C ₆ H ₆ / <i>n</i> -hexane)	115–116 ¹¹	1660; 1640; 1630; 1585	6.76 (s, 4H)
3d	86	140–142 (C ₆ H ₆)	140 ¹²	1675; 1645; 1620; 1590	3.82 (s, 3H); 5.9–6.0 (m, 1H); 6.65–6.75 (m, 2H)
3e	100	250–252 (C ₆ H ₆)	250–252 ¹¹	1690; 1640; 1620; 1590	3.82 (s, 6H); 5.83 (s, 2H)
3f	94	76–77 (CH ₂ Cl ₂ / <i>n</i> -hexane)	74–75 ¹³ 75–76 ¹⁴	3500–3100; 1655; 1640; 1590	2.57 (br s, 1H); 4.56 (d, 2H, J = 2); 6.7–6.9 (m, 3H)
3g	98	123–125 (CH ₂ Cl ₂ / <i>n</i> -hexane)	C ₁₀ H ₈ F ₃ NO ₃ (247.2)	3375; 1710; 1655; 1600; 1550; 1540	2.69 (t, 2H, J = 7); 3.55 (dd, 2H, J = 13, 6); 6.55–6.9 (m, 3H)
3h	98	90–93 (CH ₂ Cl ₂ / <i>n</i> -hexane)	C ₁₀ H ₈ O ₃ (176.2)	1700; 1655; 1645; 1585	2.05–2.3 (m, 2H); 2.5–2.9 (m, 4H); 6.66 (d, 1H, J = 10); 6.82 (d, 1H, J = 10)
5a	100	182–185 (C ₆ H ₆ / <i>n</i> -hexane)	180–185 ¹⁵	1655; 1615; 1580	4.00 (s, 3H); 6.82 (s, 2H); 7.2–7.8 (m, 3H)
5b	96	153–155 (CH ₂ Cl ₂ / <i>n</i> -hexane)	154–155 ¹⁵	1670; 1645; 1635; 1610; 1595; 1580	4.01 (s, 3H); 7.15–7.7 (m, 4H)

^a Yield of isolated products. R¹, R², and R³ correspond to R¹, R², and R³ in **1a–h**. The products were identified by comparison of their physical data with the literature data and by their spectral data.

^b Uncorrected, measured with a Yanagimoto micro melting point apparatus.

^c The microanalyses or high-resolution MS data were in satisfactory agreement with the calculated values: C ± 0.22, H ± 0.30, N ± 0.29; *m/z* = 0.0017 (M⁺).

^d Recorded on a JASCO HPIR-102 IR spectrophotometer.

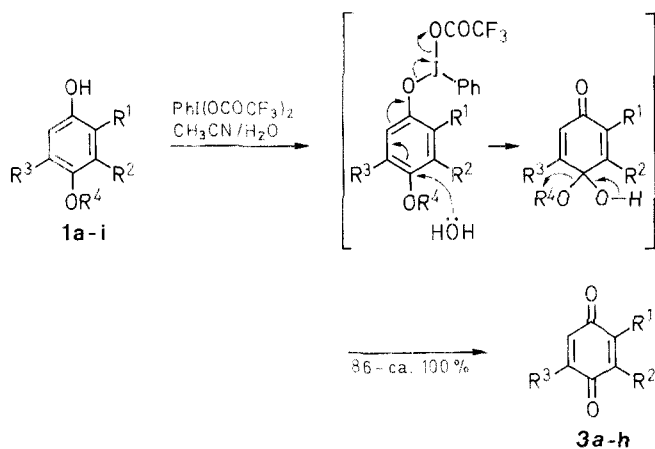
^e Obtained on a Hitachi R-22 (90 MHz) spectrometer.

^f Measured in CHCl₃ solution.

^g Obtained from **Ic**.

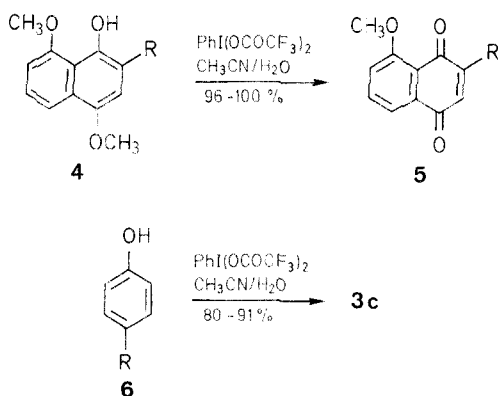
^h Obtained from **Ii**.

but also for other *p*-quinones **3c-i** and 1,4-naphthoquinones **5a, b** from the corresponding *p*-alkoxyphenols **1c-i** and 1,4-alkoxynaphthols **4a, b**, respectively.



I	R ¹	R ²	R ³	R ⁴
a	CH ₂ OTHP	H	H	CH ₃
b	CH ₂ OCH ₂ OCH ₃	H	H	CH ₃
c	H	H	H	CH ₃
d	H	OCH ₃	H	CH ₃
e	H	OCH ₃	OCH ₃	CH ₃
f	CH ₂ OH	H	H	CH ₃
g	(CH ₂) ₂ NHCOCF ₃	H	H	CH ₃
h	-CO(CH ₂) ₃ -	H	H	CH ₃
i	H	H	H	C ₂ H ₅

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4, 5	R	6	R
a	H	a	OH
b	Br	b	NHCOCF ₃

The oxidation reaction can be carried out under mild conditions. Thus, treatment of **1a** or **1b** with (ditrifluoroacetoxy)iodobenzene in acetonitrile/water in the presence of an equimolar amount of potassium carbonate at room temperature for 10 minutes gave *p*-benzoquinone **3a** or **3b** in 86% or 99% yield, respectively. Oxidation of other *p*-alkoxyphenols **1c-i** and 1,4-alkoxynaphthols **4a, b** proceeded rapidly under similar conditions, except for the absence of potassium carbonate, to give the corresponding *p*-quinones **3c-h** and 1,4-naphthoquinones **5a, b**, respectively, in excellent yields. Hydroquinone **6a** and *p*-trifluoroacetylaminophenol (**6b**) were also oxidized with (ditrifluoroacetoxy)iodobenzene to **3c** in 91% and 80% yield,

respectively. All known products were identified by comparison with authentic samples and new compounds were characterized by microanalyses and IR and ¹H-NMR spectral data. The results are summarized in the Table.

p-Quinones **3** and 1,4-Naphthoquinones **5**; General Procedure:

To a solution of the phenol **1, 4**, or **6** (0.5 mmol) in CH₃CN/H₂O (2:1, 1.5 mL) is added a solution of (ditrifluoroacetoxy)iodobenzene (215 mg, 0.5 mmol) in CH₃CN/H₂O (2:1, 1.5 mL). The mixture is stirred at room temperature for 10 min, neutralized with aq. NaHCO₃ solution, and extracted with CH₂Cl₂ (2 × 15 mL). The combined organic layer is washed with brine, dried (MgSO₄), and evaporated to give the quinone **3** or **5**. Pure samples are obtained by recrystallization from the solvent indicated in the Table, except for the quinone **3b**. The crude sample of **3b** is purified by column chromatography on silica gel (EtOAc/*n*-hexane, 1:1). For the oxidation of *p*-alkoxyphenols **1a, b** having acid-sensitive groups such as tetrahydropyranloxy (THPO) and (methoxymethyl)oxy in the molecule, K₂CO₃ (0.5 mmol) is added to the reaction mixture.

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Concurrent with this work, Lewis⁹ and Pelter¹⁰ independently reported a similar phenolic oxidation with (diacetoxy)iodobenzene.
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