The Oxidation of *p*-Substituted Phenols Using a *t*-Butyl Hydroperoxide-Heteropolyacid System

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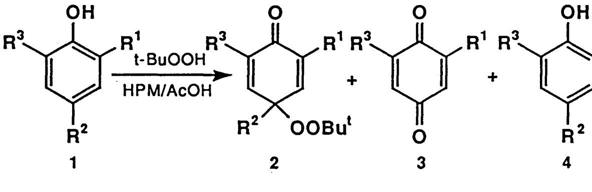
Synopsis. The oxidation of *p*-substituted phenols with *t*-BuOOH in the presence of heteropolyacids was carried out. 4-*t*-Butylperoxy-2,5-cyclohexadien-1-ones were obtained in good yields by the oxidation of 2,4,6-trialkylsubstituted phenols in this oxidation system.

Heteropolyacids are useful catalysts for the oxidation of hydrocarbons since they possess both oxidizing ability and acid catalyst center.[1] Hydrogen peroxide oxidation of various organic substrates has been done by use of heteropolyacid as catalyst[2] since aqueous hydrogen peroxide is inexpensive, environmentally clean, and easy to handle. Meanwhile, it is well-known that *t*-butyl hydroperoxide is also a convenient oxidizing agent, especially for highly selective oxygenation of olefins and acetylenes.[3] However, there have been few reports on the oxidation with *t*-butyl hydroperoxide catalyzed by heteropolyacids. It was reported that secondary alcohols were selectively oxidized to ketones using a *t*-BuOOH–hexadecylpyridinium molybdophosphate system.[4]

We previously reported that 2,6-di-*t*-butyl-4-hydroperoxy-4-methyl-2,5-cyclohexadien-1-one was determined as an intermediate in the oxidation of 2,6-di-*t*-butyl-4-methylphenol to 2,6-di-*t*-butyl-*p*-benzoquinone with a H_2O_2–heteropolyacid system.[5] Here, we report the oxidation of several *p*-substituted phenols with a *t*-BuOOH–heteropolyacid system.



HPM=$H_3PMo_{12}O_{40}\cdot nH_2O$

Results and Discussion

When 2,6-di-*t*-butyl-4-methylphenol (**1a**) was stirred with 80% *t*-butyl hydroperoxide in the presence of 12-molybdophosphoric acid at 30 °C in acetic acid for 5 h, 2,6-di-*t*-butyl-4-*t*-butylperoxy-4-methyl-2,5-cyclohexadien-1-one (**2a**) was obtained in 44% yield. This product is analogous to the compound obtained in the oxidation of **1a** with the H_2O_2–heteropolyacid system.[5] 2,6-Di-*t*-butyl-*p*-benzoquinone (**3a**) was also obtained in 9% yield as a by-product. The oxidations of **1a** with *t*-butyl hydroperoxide were carried out using other heteropolyacid as catalyst (Table 1). Molybdic compounds showed higher catalytic activities than tungstic ones. Although carboxylic acids such as acetic and propionic acids were employed as a solvent to afford **2a** in good yields, the oxidation did not proceed efficiently in alcohols such as methanol and ethanol; this tendency is similar to that obtained with the H_2O_2–heteropolyacid system.[5]

Table 1. Oxidation of **1a** Using *t*-BuOOH–Heteropolyacid[a)]

Catalyst	Conv./%	Yield/%	
		2a	**3a**
$H_3PMo_{12}O_{40}\cdot nH_2O$	99.0	47.9	8.6
$H_3PW_{12}O_{40}\cdot nH_2O$	46.7	26.2	0.8
$H_4SiMo_{12}O_{40}\cdot nH_2O$	99.9	41.6	9.3
$H_4SiW_{12}O_{40}\cdot nH_2O$	58.1	27.4	3.3
H_2MoO_4	17.1	14.1	—
None	17.5	17.1	—

a) Reaction conditions: **1a**, 2 mmol; *t*-BuOOH (80%), 1 ml; catalyst, 100 mg; AcOH, 10 ml; 30 °C, 5 h.

Table 2. Oxidation of Phenols Using *t*-BuOOH–Heteropolyacid[a)]

	R¹	R²	R³	Yield/%		
				2	3	4
a	*t*-Bu	Me	*t*-Bu	61.6	12.7	—
b	Me	Me	Me	31.4	—	—
c	*t*-Bu	Me	Me	33.5	11.5	—
d	H	*t*-Bu	*t*-Bu	—	—	26.3
e	H	Me	*t*-Bu	—	—	3.9
f	*t*-Bu	$AcOCH_2$	*t*-Bu	—	64.9	—
g	*t*-Bu	MeO	*t*-Bu	—	91.2	—

a) Reaction conditions: phenol, 2 mmol; *t*-BuOOH (80%), 1 ml; $H_3PMo_{12}O_{40}\cdot nH_2O$, 100 mg; AcOH, 10 ml; 30 °C, 3 h.

When 2,4,6-trialkylsubstituted phenols were oxidized with the *t*-BuOOH–heteropolyacid system, peroxides were obtained as main products (Table 2). However, the quinone (**3a**) became as a main product when the phenols which have more eliminative substituents than methyl group on the para positions, such as **1f** and **1g**, were treated with *t*-butyl hydroperoxide. In the reactions of 2,4-disubstituted phenols, no peroxide formed but dimerized products at the ortho position of the phenol rings were obtained.

From the above results, the oxidation mechanism is considered as follows. When the 6-unsubstituted phenols were oxidized in the *t*-BuOOH–heteropolyacid system, the corresponding dimers were formed. This result suggests that the oxidations proceed by way of phenoxyl radical intermediates. Although two 6-unsubstituted phenols couple each other at the ortho position of the phenol rings to afford dimers, 2,4,6-trisubstituted phenols are difficult to dimerize due to sterical hindrance. The radicals generated from the 2,4,6-trisubstituted phenols react with *t*-butyl hydroperoxide at the para position of the phenyl rings to afford the peroxides. *p*-Benzoquinones were formed by decomposition of the peroxides. A similar reaction mechanism from the peroxide to the *p*-benzoquinone under acidic conditions was reported.[6] As previously reported,[5] a 4-hydroperoxy-2,5-cyclohexadien-1-one was obtained as a main product from 2,6-di-*t*-butyl-4-methylphenol with H_2O_2–heteropolyacid oxidation system. It seems that the first step of the phenol oxidation with the H_2O_2–heteropolyacid system is similar to that with the present system.

Consequently, 4-*t*-butylperoxy-2,5-cyclohexadien-1-ones were obtained in good yield by the oxidation of 2,4,6-trialkylsubstituted phenols with the *t*-BuOOH–heteropolyacid system. Cobalt(II) salts have usually been used as catalyst for synthesis of the peroxide. This is one of rare examples of peroxide synthesis with other metal species than cobalt as catalyst.[7]

Experimental

Melting points were determined on a Yanagimoto micromelting apparatus. ^{1}H NMR spectra were recorded on a Hitachi R-40 High Resolution NMR Spectrometer (90 MHz). IR spectra were recorded on a JASCO FT/IR-7000 Fourier Transfer Infrared Spectrometer. Gas chromatograph analyses were performed on a Shimadzu GC-7A gas chromatograph using a Thermon 3000 column. *t*-Butyl hydroperoxide (about 80% solution in di-*t*-butyl peroxide, Merck-Schuchardt) was used without further purification.

General Procedure for the Oxidation of a Phenol Using a *t*-BuOOH-Heteropolyacid System. *t*-Butyl hydroperoxide (2 ml) was added dropwise to a solution of a phenol (2 mmol) and a catalyst (100 mg) in acetic acid (10 ml) . The reaction mixture was stirred at 30 °C under nitrogen atmosphere. Water was added to the solution and products were extracted with dichloromethane three times. The organic layer was washed with water and dried over anhydrous magnesium sulfate. Yields of the products were determined by an internal standard technique using the GC method for **2a**, and by isolation for the others.

2,6-Di-*t*-butyl-4-*t*-butylperoxy-4-methyl-2,5-cyclohexadien-1-one (2a). The crude product was chromatographed on silica gel using benzene–hexane (1 : 3) mixture as eluent. The product was recrystallized from hexane; mp 84—85 °C (lit,[6] mp 85.5—86.5 °C). ^{1}H NMR ($CDCl_3$) δ=1.15 (s, 9H), 1.22 (s, 18H), 1.30 (s, 3H), 6.55 (s, 2H); IR (KBr) 1665, 1644, 1364, 1247, 1199, 1162, 1058, 884, 872 cm^{-1}.

4-*t*-Butylperoxy-2,4,6-trimethyl-2,5-cyclohexadien-1-one (2b). The crude product was chromatographed on silica gel using dichloromethane as eluent. Bp 28 °C (1.33 Pa); ^{1}H NMR ($CDCl_3$) δ=1.17 (s, 9H), 1.33 (s, 3H), 1.86 (s, 6H), 6.57 (s, 2H); IR ($CHCl_3$) 1680, 1640, 1450, 1365, 1065, 909 cm^{-1}. Found: C, 69.96; H, 9.11%. Calcd for $C_{13}H_{20}O_3$: C, 69.64; H, 8.93%.

2-*t*-Butyl-4-*t*-butylperoxy-4,6-dimethyl-2,5-cyclohexadien-1-one (2c). The crude product was chromatographed on silica gel using benzene as eluent. Bp 35 °C (1.33 Pa); ^{1}H NMR ($CDCl_3$) δ=1.17 (s, 9H), 1.22 (s, 9H), 1.32 (s, 3H), 1.83 (s, 3H), 6.60 (m, 2H); IR ($CHCl_3$) 1644, 1458, 1360, 1065, 903 cm^{-1}. Found: C, 72.78; H, 10.04%. Calcd for $C_{16}H_{26}O_3$: C, 72.18; H, 9.77%.

3,3′,5,5′-Tetra-*t*-butyl-2,2′-biphenyldiol (4d). The crude product was chromatographed on silica gel using benzene as eluent. The product was recrystallized from methanol; mp 193—194 °C (lit,[8] mp 200—201 °C). ^{1}H NMR ($CDCl_3$) δ=1.29 (s, 18H), 1.44 (s, 18H), 5.17 (s, 2H), 7.10 (d, 2H, J=2.5 Hz), 7.40 (d, 2H, J=2.5 Hz); IR (KBr) 3528, 1479, 1437, 1363, 1334, 1284, 1238, 1203, 1170, 1096, 882, 816 cm^{-1}.

3,3′-Di-*t*-butyl-5,5′-dimethyl-2,2′-biphenyldiol (4e). The crude product was chromatographed on silica gel using benzene as eluent. This compound was obtained as glass.[9] ^{1}H NMR ($CDCl_3$) δ=1.42 (s, 18H), 2.27 (s, 6H), 5.11 (s, 2H), 6.90 (br s, 2H), 7.15 (br s, 2H); IR ($CHCl_3$) 3536, 1435, 1394, 1365, 1328, 1276, 1172, 1096, 870 cm^{-1}.

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