Oxidation by Cobalt(III) Acetate. Part 13.[1] Oxidation of Substituted Phenols with Cobalt(III) Acetate in Acetic Acid

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Synopsis. The oxidation of 2,6-di- and 2,4,6-tri-substituted phenols with cobalt(III) acetate has been investigated in acetic acid under an inert atmosphere; the former gave the corresponding diphenoquinones in excellent yields, and the latter yielded side-chain or nuclear acetoxylated products in moderate to good yields.

In connection with natural organic products and antioxidants, phenols enjoy important and specific positions in organic chemistry. The oxidation of phenols has also been of considerable significance in the synthesis of a variety of organic chemicals, especially for the biogenetic syntheses of natural products. Thus, fairly extensive methodologies have been demonstrated for the phenol oxidations using ample chemical and biological processes; viz. oxidation with metal oxidants (particularly with iron(III) salts), organic and inorganic peroxides (or peroxy acids), halides, quinones, and Fremy's salt, and electrolytic, enzymatic, auto-, and photo-oxidations and so on.[2]

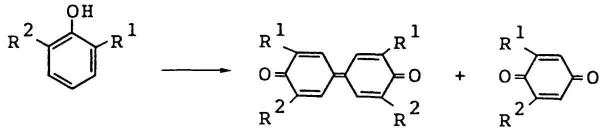
Although cobalt(III) acetate (**1**) is a potent and versatile one-electron oxidant and has been successfully used for the transformation of various functional groups, especially for the selective oxidation of alkylbenzenes[3] and olefins[1,4] via an electron-transfer mechanism, little attention has been paid to the oxidation of the hydroxyl compounds. We have thus recently examined product and/or kinetic studies concerning the catalytic[5] and stoichiometric oxidations of alcohols[6] and glycols[7] with **1** in acetic acid. Nevertheless, since there have been no data on the oxidation of phenols, the validity of **1** for the hydroxyl compounds has not been fully established. In this article we wish to describe some observations concerning the phenol oxidation with **1**. This is the first case in which **1** has been utilized for this objective.

Results and Discussion

The oxidation of phenols with **1** in acetic acid was carried out under nitrogen in order to exclude any influence of autoxidation. The reaction was stopped at a time in which the dark-green color of the reaction solution disappeared, a clear indication of the complete reduction of the cobalt(III) species into cobalt(II). After the conventional work-up procedures (see the Experimental section), the oxidation products formed were isolated and/or analyzed by GLC.

2,6-Dimethylphenol (**2a**) was readily oxidized at 70 °C, giving 3,3′,5,5′-tetramethyl-4,4′-diphenoquinone (**3a**) as the main product, along with a minor amount of 2,6-dimethyl-*p*-benzoquinone (**4a**). The other 2,6-disubstituted phenols (**2b**—**e**) exclusively afforded the corresponding diphenoquinones **3b**—**e** in fairly good yields, while the benzoquinones **4b**—**e** were absent (Table 1). Thus, *para-para* coupling predominates in the oxidation of the 2,6-disubstituted phenols. On the other hand, the oxidation of 2,4-di-*t*-butylphenol (**5**) at ambient temperature for 15 h ([**1**]/[**5**]=1.2; mole ratio) yielded solely the 2,2′-biphenyldiol (**6**) in 87 mol% GLC yield at 94% conversion, as a result of exclusive *ortho-ortho* coupling.[8]

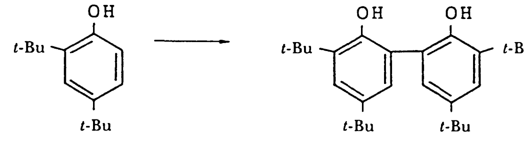
Table 1. Oxidation of 2,6-Disubstituted Phenols[a)]



2 **3** **4**

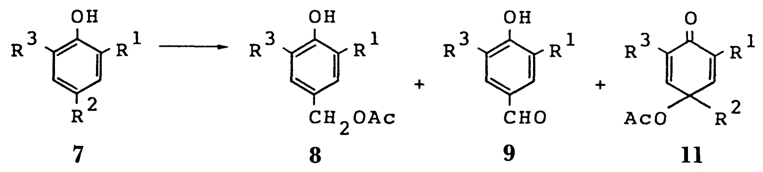
Phenols 2		Temp	Time	[1]/[2]	Isolated yields/%	
R¹	R²	°C	h	Mole ratio	3	4
(a) Me	Me	70	5.5	2.5	75	23
(b) Me	*t*-Bu	70	15	2.5	97	
(c) *i*-Pr	*i*-Pr	50	15	5.0	91	
(d) *t*-Bu	*t*-Bu	70	72	2.5	95	
(e) MeO	MeO	Ambient	24	2.5	95	

a) Under nitrogen, $[Co(OAc)_3]=0.420$ mol dm^{-3}; 8.4 mmol of phenols were used in every run.



5 **6**

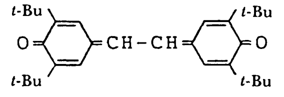
These results are of considerable interest in considering the steric and electronic effects of the substituents on the reactivity of the phenols, as well as product selectivity. As compared with "less" hindered phenols, **2a**—**c**, a steric hindrance of the *t*-Bu groups of **2d** is prominent; they may severely limit the initial attack of **1** on the "more" hindered hydroxyl group. For example, when oxidations of **2a**—**d** were conducted at 50 °C ([**1**]/[**2**]=2.5), the reaction times required for complete reduction of **1** were 16, 20, 24, and 72 h, respectively. These results are well consistent with the previous observation that oxidation with **1** is highly sensitive to steric factors.[3c—e,4a—c] The selectivity of the products can also be explained in terms of a steric hindrance of the substituents; thus, carbon-



Scheme 1. (a); R^1=Me, R^2=Me, R^3=Me: (b); R^1=*t*-Bu, R^2=Me, R^3=*t*-Bu: (c); R^1=*t*-Bu, R^2=*t*-Bu, R^3=*t*-Bu.

carbon couplings occurred at the unhindered *para*- of **2a**—**e** and *ortho*-position of **5**. Smooth oxidation of **2e**, even at room temperature, evidently indicates that the electron-donating group contributes to promote the reaction. A similar electronic effect has been observed in the oxidations of alkylbenzenes[3a,b] and olefins.[4d,e]

The oxidation of 2,4,6-trisubstituted phenols (**7a**—**c**) was conducted in a manner analogous to that of **2** in acetic acid (Scheme 1). The oxidation of **7a**, **b** ([**1**]/[**7**]=2.5) at 50 °C for 1 and 15 h, respectively, afforded 49 and 73 mol% of the benzyl acetates (**8**), and 27 and 7 mol% of the benzaldehydes (**9**) (GLC yields), respectively. In the latter case, a small amount of 3,3′,5,5′-tetra-*t*-butyl-4,4′-stilbenequinone (**10**) was formed (3 mol% by GLC).[9] Control experiments showed that upon treatment of **8a**, **b** with **1** ([**1**]/[**8**]=2.5) at 50 °C for 1 and 15 h, respectively, **9a**, **b** were formed as the sole products in 67 and 47 mol% yields, respectively, implying that **9** was derived from a consecutive oxidation of **8**, as expected. The difference in the reactivity of **7a** and **7b** can also be explained by the difference in the steric effect of the Me and the *t*-Bu groups, as noted above. The oxidation of **7c**, having no labile hydrogen on the side-chains, with 2.5 equiv of **1** at 50 °C for 15 h, gave 4-acetoxy-2,4,6-tri-*t*-butyl-2,5-cyclohexadien-1-one (**11**) in 83% yield, along with only a trace amount of the 2-acetoxylated derivative (**12**). It has been comparatively rare that such a *p*-acetoxylated product as **11** is selectively formed in high yield. In fact, it has been reported that a mixture of **11** and **12** is obtained from **7c**, where **12** is formed (≈60%) in preference to **11** (<30%) as typically observed in Pb oxidations.[10]



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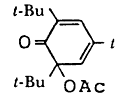

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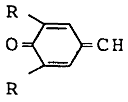
In order to obtain some information on the possible route leading to **8**, close GLC as well as GC-MS analyses of the product mixtures obtained from **7a**, **b** were carried out, where components (<10%; GLC selectivities) assignable to the 4-methylene-2,5-cyclohexadien-1-ones (**13**) were detected. Although the isolation of **13a**, **b** from the product mixtures of **7a**, **b** failed because of their extreme instability, these facts may be suggestive of a reaction pathway via the 4-aryloxy-2,5-cyclohexadien-1-ones (**14**) as key intermediates, as proposed in the oxidations with Pb, Mn, and DDQ.[11]



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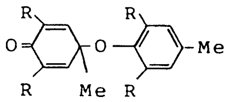

14 [(**a**); R=Me, (**b**); R=*t*-Bu]

The oxidation of phenol and *p*-cresol only afforded amorphous solids, which were infusible upon heating over 350 °C; possibly, polymeric materials were formed.

Experimental

^{1}H NMR spectra were measured with a JEOL JNM-C-HL model spectrometer for solutions in carbon tetrachloride or deuteriochloroform. The IR spectra were recorded for KBr disks or nujol mull on a JASCO DS-403G spectrophotometer. GLC was carried out on a Shimadzu GC-4CM instrument, with a 2 m column packed with 1.5% Silicone OV-17 on Shimalite WAW-DMCS, with temperature programming. The mass spectra were determined on a Shimadzu GC-MS 7000 spectrometer which was coupled via a heated 2 m column packed with 1.5% Silicone OV-17 on Shimalite WAW-DMCS to a GLC apparatus. Melting points were measured on a Yamato capillary mp apparatus and were uncorrected.

Starting Materials. All phenols were commercially available and were purified by recrystallization just before use. Cobalt(III) acetate in acetic acid was prepared by the oxidation of cobalt(II) acetate tetrahydrate with ozone in acetic acid containing acetic anhydride.[12]

Oxidation Procedures. The typical oxidation procedures are as follows: 2,6-Dimethylphenol (**2a**, 1.02 g, 8.4 mmol) was mixed with a solution of cobalt(III) acetate (2.5 mole equiv) in acetic acid in a reaction vessel. The vessel was then flushed with dry nitrogen gas, sealed with a glass stopper, and maintained at a controlled temperature in a thermostat without agitation. After a given period, the reaction mixture was poured into water to precipitate a dark-red solid. Separation of the solid by filtration, followed by recrystallization from acetic acid, afforded dark-purple needles **3a**: 1.51 g, 75%; mp 203—204 °C (lit,[13] 206 °C).

The aqueous filtrate was extracted three times with ether; the combined ether was successively washed with water, 10% aqueous sodium carbonate, and water and then dried (Na_2SO_4). Removing the ether on a rotary evaporator left a red solid, which was chromatographed on silica gel with chloroform as an eluent to give crude **4a**. Upon recrystallization from petroleum ether, the solid yielded yellow needles of pure **4a**: 0.263 g, 23%; mp 71—72 °C(lit,[14] 70—72 °C).

All products thus obtained were known compounds, and were identified by the mps as well as comparisons of the NMR and IR spectra and/or GLC retention times with those of authentic samples prepared independently. For the measurement of the GLC yields of the products, biphenyl or benzophenone was added to the reaction mixture as an internal standard; they were found to be intact under the reaction conditions employed.

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