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Oxidation of 2,6-Dialkyl-*p*-cresols by Metal Acetates

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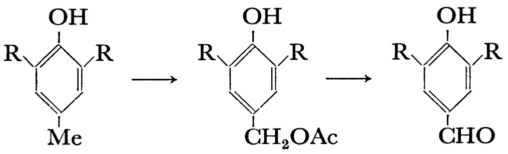
Synopsis. The oxidation of 2,6-dialkyl-*p*-cresols by silver(I) and palladium(II) acetate afforded the corresponding *p*-hydroxybenzyl acetates and *p*-hydroxybenzaldehydes.

Recently much attention has been focused on the selective oxidation of the methyl group of *p*-cresols. However, the selective side-chain oxidation of alkylphenols is generally attained with difficulty, *e.g.*, coupling reactions predominantly occur when 2,6-di-*t*-butyl-*p*-cresol (**1a**) is oxidized by metal salts,[1] although the oxidation of **1a** to 3,5-di-*t*-butyl-4-hydroxybenzaldehyde (**3a**) using bromine,[2] 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ),[3] or oxygen in alkaline medium[4] has been reported. The oxidation of toluenes to benzyl acetates or benzaldehydes by palladium(II) acetate is however well known.[5] These observations and an interest in metal salt-catalyzed oxidations of aromatic compounds[6] led to this examination of the oxidation of *p*-cresols with palladium(II) acetate and other metal acetates. The side-chain oxidations of *p*-cresol itself and 2,4-dimethylphenol led to failure,[7] however, it was found that the *p*-methyl group of **1a** and 2,4,6-trimethylphenol (**1b**) were oxidized by silver(I) acetate and palladium(II) acetate in acetic acid. There appears to be no other reports that the products from the side-chain oxidation of *p*-cresols change depending on the amount of the oxidant used, although the oxidation of **1b** with $S_2O_8^{2-}$–Ag^+ gives 3,5-dimethyl-4-hydroxybenzylalcohol[8] and with DDQ[3] or with oxygen[4] gives 3,5-dimethyl-4-hydroxybenzaldehyde (**3b**).

Treatment of **1a** and **1b** with silver(I) acetate in acetic acid under nitrogen at 118 °C afforded 3,5-di-*t*-butyl-4-hydroxybenzyl acetate (**2a**) and 3,5-dimethyl-4-hydroxybenzyl acetate (**2b**), respectively, in good yields. When the oxidation was conducted with an excess of the metal acetate, **3** was obtained in good yield. Furthermore, the oxidation of **2** gave the corresponding **3**. The oxidation of **1** by palladium(II) acetate also resulted in the formation of **2** and **3**, but the yield of **2b** from **1b** was reduced. These results are summarized in Table 1. The attempted oxidations with other metal acetates, listed in Table 1, were unsuccessful.



(1) (2) (3)

a: R = *t*-Bu
b: R = Me

Experimental

*Oxidation of **1a** by Metal Acetates.* A solution of **1a** (1 mmol) and the metal acetate (0.5—4.0 mmol) in acetic acid (30 ml) was heated at 118 °C under a nitrogen atmosphere for 5—15 h. The reaction mixture was evaporated to dryness under reduced pressure and chromatographed on a silica-gel plate (chloroform/petroleum ether) to give **1a** (recovered), **2a**, identical with a sample which was prepared according to the method described by Coppinger and Campbell,[9] and **3a**, identical with an authentic sample.[4]

*Oxidations of **1b**, **2a**, and **2b** by Metal Acetates.* The

TABLE 1. THE OXIDATION OF **1a**, **1b**, **2a**, AND **2b** BY METAL ACETATES

Substrate (1 mmol)	Metal acetate (mmol)	Reaction time (h)	Conversion (%)	Product yield (%)
1a		14	0	—
	AgOAc (1)	7	88	**2a**(78)[a]
	AgOAc (4)	14	100	**3a**(71)[a]
	$Pd(OAc)_2$ (1/2)	7	85	**2a**(69), **3a**(6)[a]
	$Pd(OAc)_2$ (1)	10	100	**2a**(40), **3a**(50)[b]
	$Pd(OAc)_2$ (2)	5	85	**2a**(35), **3a**(55)[b]
	$Cu(OAc)_2$ (1/2)	14	3	**3a**(80)[a]
	$Co(OAc)_2 4H_2O$ (1/2)	14	0	—
	$Ni(OAc)_2 4H_2O$ (1/2)	14	0	—
	$Mn(OAc)_2 4H_2O$ (1/2)	14	0	—
1b	AgOAc (1)	7	92	**2b**(77), **3b**(6)[a]
	AgOAc (4)	14	100	**2b**(20), **3b**(70)[b]
	$Pd(OAc)_2$ (1/2)	7	80	**2b**(20), **3b**(60)[b]
2a	AgOAc (1)	7	85	**3a**(70)[b]
	$Pd(OAc)_2$ (1/2)	4	100	**3a**(60)[b]
2b	AgOAc (1)	7	60	**3b**(80)[b]
	$Pd(OAc)_2$ (2)	2	87	**3b**(70)[b]

a) Isolated yield. b) Yield determined by NMR spectroscopy.

phenol **1b** was oxidized by the metal acetate and worked up as described above to yield **1b** (recovered), **2b**, mp 73—75 °C (lit,[10] 76 °C), and **3b**, identical with an authentic sample.[4]

Similar procedures were applied to the oxidations of **2a** and **2b**, the results of which are summarized in Table 1.

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