Choice of Manganese(III) Complexes for the Synthesis of 4,4′-Biphenyldiols and 4,4′-Diphenoquiones

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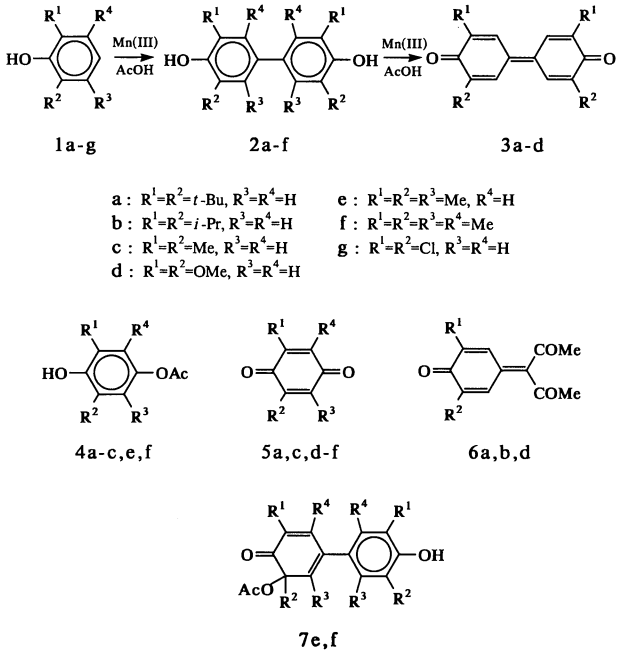
Synopsis. 2,6-Disubstituted phenols are oxidized with tris(2,4-pentanedionato)manganese(III), [Mn(acac)$_3$], in glacial acetic acid to give the corresponding 4,4′-biphenyldiols in high yields, whereas similar reactions using manganese(III) acetate, [Mn(OAc)$_3$], instead of [Mn(acac)$_3$] quantitatively yield the corresponding 4,4′-diphenoquinones. Cross-coupling reactions of 2,6-di-*t*-butylphenol and other substituted phenols afford the corresponding cross-coupled 4,4′-biphenyldiols and 4,4′-diphenoquinones together with oxidation products derived from the starting phenols themselves. The advantageous use of [Mn(acac)$_3$] and [Mn(OAc)$_3$] in the ubiqitous phenol coupling reaction is discussed.

There is a significant number of reports concerning the oxidation of phenols with molecular oxygen catalyzed by metals, metal salts or metal complexes, and peroxides[1] in the study of charge-transfer complexes[2] and polymer science.[3] It is generally known that oxidation of phenols gives benzoquinones, biphenyldiols, diphenoquinones, and/or poly(phenylene ethers). The primary product must be a phenoxyl radical and thus the phenoxyl radicals obtained from the reactions of 2′-hydroxychalcones with manganese(III) acetate, [Mn(OAc)$_3$], eventually add to the olefinic double bond to yield the corresponding aurones.[4] Although some coupling reactions involving simple phenols such as 2,6-di-*t*-butyl- or 2,6-dimethylphenol using tris(2,4-pentanedionato)manganese(III), [Mn(acac)$_3$], or [Mn(OAc)$_3$] in carbon disulfide or acetonitrile have been reported,[5] there are few reports for the reactions using manganese(III) complexes in glacial acetic acid as a solvent. We applied the oxidation of some simple phenols with [Mn(acac)$_3$] in glacial acetic acid to obtain the corresponding 4,4′-biphenyldiols in high yields. On the other hand, similar oxidations with [Mn(OAc)$_3$] in glacial acetic acid quantitatively gave the corresponding 4,4′-diphenoquinones. In order to prepare 4,4′-biphenyldiols and 4,4′-diphenoquiones having different substituents, we also examined the cross-coupling reactions between 2,6-di-*t*-butylphenol and other substituted phenols under similar reaction conditions. In this note, we report the results of our study in detail.

Results and Discussion

Oxidation of Simple Phenols. When 2,6-di-*t*-butylphenol (**1a**) was oxidized with [Mn(acac)$_3$] *in glacial acetic acid at room temperature,* we were surprised that the yield of the corresponding 4,4′-biphenyldiol (**2a**; 93%) was significantly improved, although **2a** (71%) has been obtained by a similar reaction *in carbon disulfide at reflux temperature.*[5d] The oxidations of 2,6-diisopropyl- (**1b**), 2,6-dimethyl- (**1c**), 2,6-dimethoxy- (**1d**), and 2,3,6-trimethylphenol (**1c**) were conducted under similar reaction conditions and the corresponding 4,4′-biphenyldiols (**2b**—**e**) were obtained in good yields. The oxidation of **1a**—**d** using [Mn(OAc)$_3$] instead of [Mn(acac)$_3$] did not stop at the stage of biphenyldiols, but did produce the corresponding 4,4′-diphenoquinones (**3a**—**d**). While **1e** or 2,3,5,6-tetramethylphenol (**1f**) was oxidized with [Mn(OAc)$_3$] to predominantly yield the corresponding 4,4′-biphenyldiol (**2e** or **2f**), no diphenoquinones were formed. Although the biphenyldiols (**2e** and **2f**) were subjected to further oxidation with [Mn(OAc)$_3$], the reaction failed probably because of the steric hindrance of the methyl groups at the C-3, 3′, 5, 5′ positions. The reaction of 2,6-dichlorophenol (**1g**) with [Mn(acac)$_3$] and [Mn(OAc)$_3$] gave a polymeric product (Found: C, 48.11; H, 1.90%) and any biphenyldiols and diphenoquinones were not isolated at all. The oxidation of **1a** with hexakis(dimethyl sulfoxide)manganese(III) perchlorate, [Mn(dmso)$_6$](ClO$_4$)$_3$,[6] in glacial acetic acid for 1 min yielded **2a** and **3a** in moderate yields. The same reaction was run in dichloromethane since [Mn(dmso)$_6$](ClO$_4$)$_3$ is soluble in dichloromethane. However, only half of **1a** was consumed even after 9 h and only **3a** was obtained. The results are summarized in Scheme 1 and Table 1.

The formation of 4-diacetylmethylene-2,5-cyclohexadien-1-ones (**6a,b,d**) deserves comments. It is known that [Mn(acac)$_3$] readily decomposes in acetic acid to produce diacetylmethyl radicals, ·CH$_2$(COCH$_3$)$_2$, which are trapped by radical-trapping reagents such as xanthenes or 2,6-di-*t*-buryl-4-methylphenol.[7] Therefore, it is considered that the diacetylmethyl radicals attack the phenoxyl radicals formed by the electron transfer



1a-g 2a-f 3a-d

a : R^1=R^2=*t*-Bu, R^3=R^4=H
b : R^1=R^2=*i*-Pr, R^3=R^4=H
c : R^1=R^2=Me, R^3=R^4=H
d : R^1=R^2=OMe, R^3=R^4=H
e : R^1=R^2=R^3=Me, R^4=H
f : R^1=R^2=R^3=R^4=Me
g : R^1=R^2=Cl, R^3=R^4=H

4a-c,e,f 5a,c,d-f 6a,b,d

7e,f

Scheme 1.

Table 1. Oxidation of Substituted Phenols (**1a**—**g**) with Mn(III) Complexes in AcOH

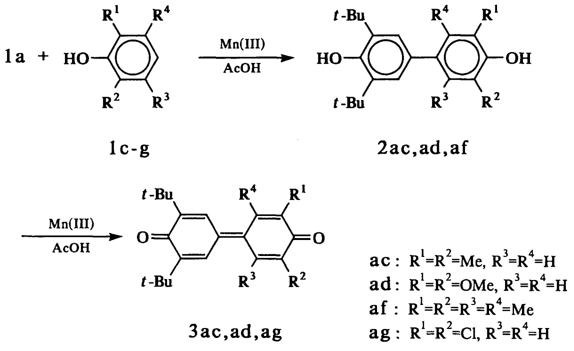
Entry	Phenol	Manganese(III) complex	Molar	Temperature	Time	Conversion	Product (yield/%)[b]
				°C	min	%	
1	**1a**	$[\mathrm{Mn(acac)_3}]$	1:1	R.t.	40	100	**2a**[10] (93)
2			1:4	Reflux	1	100	**3a**[10] (63) **6a (15)**
3		$[\mathrm{Mn(OAc)_3}]$	1:2	100	5	100	**3a** (98)
4		$[\mathrm{Mn(dmso)_6}](\mathrm{ClO_4})_3$	1:2	Reflux	1	90	**2a** (44) **3a** (35)
5	**1b**	$[\mathrm{Mn(acac)_3}]$	1:1	R.t.	1	95	**2b**[10] (65) **3b**[10] (18)
6			1:4	Reflux	1	100	**3** (68) **6b** (8)
7		$[\mathrm{Mn(OAc)_3}]$	1:3	100	5	100	**2b** (1) **3b** (95) **4b**[10] (1)
8	**1c**	$[\mathrm{Mn(acac)_3}]$	1:1	R.t.	1	83	**2c**[9] (32) **3c**[9] (16)
9			1:4	Reflux	1	100	**3c** (78)
10		$[\mathrm{Mn(OAc)_3}]$	1:2[c]	100	20	97	**3c** (84)**4c** (6) **5c**[9] (2)
11	**1d**	$[\mathrm{Mn(acac)_3}]$	1:2	Reflux	1	94	**2d**[11] (80) **3d**[12] (3) **5d**[12] (11)
12			1:4	Reflux	1	100	**2d** (65) **5d** (26) **6d** (4)
13		$[\mathrm{Mn(OAc)_3}]$	1:4	100	10	100	**3d** (79) **5d** (9)
14	1e	$[\mathrm{Mn(acac)_3}]$	1:4	Reflux	3	100	**2e**[13] (63) **5e**[12] (15)
15		$[\mathrm{Mn(OAc)_3}]$	1:2	100	5	100	**2e** (52) **4e**[14] (5) **5e** (17) **7e** (7)
16	1f	$[\mathrm{Mn(OAc)_3}]$	1:2	100	10	100	**2f**[13] (36) **4f**[15] (9) **5f**[12] (21) **7f** (14)

a) Phenol (1 mmol): Mn(III) complex. b) The yields based on the amounts of phenols added. c) $\mathrm{NH_4Cl}$ (10 mmol).

from phenols to $[\mathrm{Mn(acac)_3}]$, giving **6a**,**b**,**d**.

We also examined the oxidative coupling reaction of *p*-substituted phenols such as *p*-cresol, *p*-chlorophenol, *p*-*t*-butylphenol, and 2,4,6-tribromophenol using $[\mathrm{Mn(OAc)_3}]$. However, most of the oxidations gave polymeric products and other coupling products were not isolated except for Pummerer's ketone[8] (1%) from *p*-cresol and 2,6-bis(4-chlorophenoxy)-1,4-benzoquinone (**5h**; 5%) from *p*-chlorophenol.

Cross-Coupling Reactions. In order to synthesize unsymmetrical 4,4′-biphenyldiols and 4,4′-diphenoquinones, cross-coupling reactions of **1a**, which were selected because of their easy separation by TLC, and other substituted phenols (**1c**—**g**) were carried out under similar reaction conditions (Scheme 2). The reactions actually afforded cross-coupled 4,4′-biphenyldiols (**2ac**, **2ad**, **2af**) and 4,4′-diphenoquinones (**3ac**, **3ad**, **3ag**) except for the cases of **1a** and **1e**. However, oxidation products of the starting phenols themselves were also obtained at the same time. The yields and the reaction conditions are summarized in Table 2.



Scheme 2.

In closing, we demonstrated that the proper use of $[\mathrm{Mn(acac)_3}]$ and $[\mathrm{Mn(OAc)_3}]$ in glacial acetic acid was advantageous for the ubiquitous phenol coupling reactions in the laboratory. The formation of phenoxyl radicals and the subsequent para-para coupling of the phenoxyl radicals are generally accepted. However, the product distribution depends on the used oxidants.[9] In the present reactions, the electron donor-aceptor complex of Mn(III) with phenols and the corresponding phenoxyl radicals might be formed at the first stage and

Table 2. Cross-Coupling Reaction of 2,6-Di-*t*-butylphenol (**1a**) and Substituted Phenols (**1c**—**g**) with Mn(III) Complexes in AcOH at 100 °C

Entry	Phenol	Manganese(III) complex	Molar	Time	Conversion		Product (yield %)[b]
				min	1a	1c—g	
24[c]	**1a**, **c**	$[\mathrm{Mn(acac)_3}]$	1:1:4	1	96	100	**2ac** (7) **3ac** (12) **2c** (11) **3a** (28) **4c** (4) **5c** (8) **6a** (5)
25		$[\mathrm{Mn(OAc)_3}]$	1:1:8[d]	30	100	100	**3ac** (26) **3a** (25) **3c** (14) **5a**[12] (10) **5c** (8)
26[c]	**1a**, **1d**	$[\mathrm{Mn(acac)_3}]$	1:1:8	1	100	100	**2ad** (14) **3ad**[16] (10) **3a** (21) **5d** (39) **6a** (9)
27		$[\mathrm{Mn(OAc)_3}]$	1:1:8	10	100	100	**3ad** (11) **2d** (3) **3a** (41) **3d** (11) **5a** (2) **5d** (33)
28	**1a**, **1e**	$[\mathrm{Mn(OAc)_3}]$	1:1:4[e]	10	96	100	**2a** (7) **3a** (30) **4a** (3) **5a** (4) **2e** (19) **4e** (9) **5e** (10)
29	**1a**, **1f**	$[\mathrm{Mn(OAc)_3}]$	1:1:4	10	97	97	**2af** (10) **2a** (3) **3a** (15) **4a** (1) **5a** (20) **2f** (13) **4f** (24) **5f** (4)
30	**1a**, **1g**	$[\mathrm{Mn(OAc)_3}]$	1:1:4[f]	10	100	100	**3ag** (14) **3a** (33) **4a** (4) **5a** (9)

a) **1a** (1 mmol): Substituted phenol (1 mmol): Manganese(III) complex. b) The yields based on the amounts of phenols added. c) The reaction at the reflux temperature. d) Acetic anhydride (50 mmol) was added. e) 2-Acetoxymethyl-5,6-dimethyl-1,4-benzoquinone (**5i**; 7%) was formed along with **3a** (10%), **5a** (40%), and **5e** (29%), when the reaction was run at the molar ratio of 1:1:8 for 20 min. f) Ammonium chloride (10 mmol) was added.

might affect the product distribution.

Experimental

Oxidation of Simple Phenols. A typical procedure for the oxidation of phenols with [Mn(acac)$_3$] or [Mn(OAc)$_3$] was as follows. A mixture of a phenol (1 mmol) and [Mn(acac)$_3$] (1—4 mmol) was stirred at room temperature in glacial acetic acid (30 cm^3) or [Mn(acac)$_3$] was added to a heated solution of a phenol in glacial acetic acid. The reactions proceeded until the solutions turned transparent. The solvent was removed in vacuo, and the residue was triturated with 2 M (1 M=1 mol dm^{-3}) hydrochloric acid (30 cm^3) and then extracted with chloroform. The products were separated by TLC (Wakogel B-10) using chloroform as the developing solvent. While in the [Mn(OAc)$_3$] oxidation, a phenol (1 mmol) and [Mn(OAc)$_3$] (1—4 mmol) were added to glacial acetic acid (20 cm^3) and then the mixture was heated at 100 °C. After the solution turned colorless, hot water (50 cm^3) was added. The aqueous solution was extracted with chloroform three times. When a 4,4′-diphenoquinone crystallized after adding hot water, the 4,4′-diphenoquione was filtered using a glass filter and then the filtrate was extracted with chloroform. The products were separated by TLC.

Oxidation Products. 6a: Mp 86—87 °C; IR (CHCl$_3$) 1680, 1630; ^{1}H NMR δ=1.10 (18H, s), 2.43 (6H, s), 7.10 (2H, s). Anal. ($C_{19}H_{26}O_3$) C, H.

4c: Mp 96.04—96.5 °C; IR (CHCl$_3$) 3590, 3460, 1755; ^{1}H NMR δ=2.19 (6H, s), 2.21 (3H, s), 4.49 (1H, s), 6.55 (2H, s). Found: *m*/*z* 180.07575. Calcd for $C_{10}H_{12}O_3$: M, 180.07864.

7e: This product was presumed to be a mixture of three isomers, 6-acetoxy-4-(4-hydroxy-2,3,5-trimethylphenyl)-2,5,6-trimethyl-2,4-cyclohexadien-1-one, 6-acetoxy-4-(4-hydroxy-2,3,5-trimethylphenyl)-2,3,6-trimethyl-2,4-cyclohexadien-1-one, and 4-acetoxy-4-(4-hydroxy-2,3,5-trimethylphenyl)-2,3,6-trimethyl-2,5-cyclohexadien-1-one, based on the analysis of the ^{13}C NMR spectrum. Mp 177.5—179.5 °C; IR (CHCl$_3$) 3580, 3400, 1745, 1680; ^{1}H NMR δ=1.49 (s), 1.57 (s), 1.93 (s), 2.05 (m), 2.12 (s), 2.18 (s), 5.05 (s), 6.68 (s); ^{13}C NMR δ=200.16, 199.97, 198.01, 169.45, 151.61, 151.43, 148.81, 144.42, 144.18, 143.45, 138.64, 136.50, 136.02, 132.82, 131.27, 130.17, 129.99, 128.28, 127.37, 122.62, 122.49, 120.61, 82.23, 82.05, 78.09, 24.18, 20.47, 18.46, 16.67, 16.39, 15.96, 15.77, 14.98, 14.50, 14.38, 12.18, 11.51. Found: *m*/*z* 328.16618. Calcd for $C_{20}H_{24}O_4$: M, 328.16746.

7f: Mp 228—229 °C; IR (CHCl$_3$) 3570, 3400, 1740, 1665; ^{1}H NMR δ=1.39 (3H, s), 1.47 (3H, s), 1.58 (3H, s), 1.99 (9H, s), 2.13 (3H, s), 2.21 (6H, s), 4.71 (1H, s); ^{13}C NMR δ=198.88, 169.34, 150.88, 150.03, 143.20, 133.16, 131.87, 130.23, 128.28, 127.87, 119.51, 119.27, 81.38, 24.12, 20.59, 18.40, 16.44, 16.20, 14.13, 12.30, 11.57. Found: *m*/*z* 356.19816. Calcd for $C_{22}H_{28}O_4$: M, 356.19876.

2ac: Mp 198.5—200 °C; IR (CHCl$_3$) 3620, 3590; ^{1}H NMR δ=1.47 (18H, s), 2.26 (6H, s), 4.54 (1H, s), 5.16 (1H, s), 7.09 (2H, s), 7.27 (2H, s). Found: *m*/*z* 326.22474. Calcd for $C_{22}H_{30}O_2$: M, 326.22458.

3ac: Mp 176—177 °C; IR (CHCl$_3$) 1635, 1595; ^{1}H NMR δ=1.37 (18H, s), 2.16 (6H, s), 7.68 (2H, s), 7.70 (2H, s). Anal. ($C_{22}H_{28}O_2$) C, H.

4a: Mp 89.5—90.5 °C; IR (CHCl$_3$) 3620, 1760; ^{1}H NMR δ=1.42 (18H, s), 2.22 (3H, s), 5.05 (1H, s), 6.83 (2H, s). Anal. ($C_{16}H_{24}O_3$) C, H.

2ad: Mp 201.0—201.5 °C; IR (CHCl$_3$) 3615, 3525; ^{1}H NMR δ=1.47 (18H, s), 3.90 (6H, s), 5.21 (1H, s), 5.52 (1H, s), 6.72 (2H, s), 7.29 (2H, s). Anal. ($C_{22}H_{30}O_4$) C, H.

2af: Mp 199—200 °C; IR (CHCl$_3$) 3620, 3590; ^{1}H NMR δ=1.46 (18H, s), 1.95 (6H, s), 2.21 (6H, s), 4.72 (1H, s), 5.11 (1H, s), 6.87 (2H, s). Found: *m*/*z* 354.26410. Calcd for $C_{24}H_{34}O_2$: M, 354.25588.

3ag: Mp 203—205 °C; IR (CHCl$_3$) 1645, 1630, 1615; ^{1}H NMR δ=1.35 (18H, s), 7.53 (2H, s), 8.04 (2H, s). Found: *m*/*z* 364.09991. Calcd for $C_{20}H_{22}O_2{}^{35}Cl_2$: M, 364.09969.

5i (R^1=CH$_2$OAc, R^2=R^3=Me, R^4=H): Mp 56.5—57.5 °C; IR (CHCl$_3$) 1745, 1645, 1615; ^{1}H NMR δ=2.02 (6H, s), 2.13 (3H, s), 4.92 (2H, d, *J*=1.6 Hz), 6.65 (1H, t, *J*=1.6 Hz). Found: *m*/*z* 208.07205. Calcd for $C_{11}H_{12}O_4$: M, 208.07356.

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