

Notes

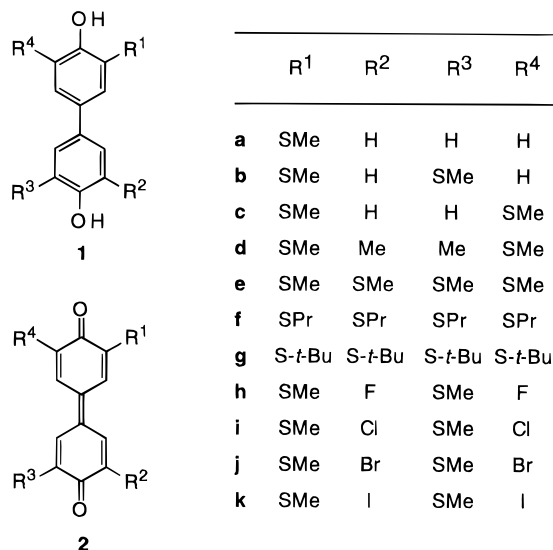
**First Synthesis of Alkylthio-Substituted
4,4'-Biphenylquinones and
4,4'-Biphenylhydroquinones
(4,4'-Biphenyldiols)**

Yasushi Morita,* Atsushi Kashiwagi, and
Kazuhiro Nakasuji*

Department of Chemistry, Graduate School of Science,
Osaka University, Toyonaka, Osaka 560, Japan

Received November 4, 1996 (Revised Manuscript Received
July 7, 1997)

1,4-Benzoquinhydrone is a hydrogen-bonded charge-transfer (CT) complex between quinone and hydroquinone. Since a new phase transition of the complex was found under high pressure, we have been interested in chemical modification of the quinhydrone-type CT complexes to explore new molecular materials having interesting solid state properties.¹ Our recent studies on the 1,4-benzoquinones with donor and acceptor substituents made clear their amphoteric redox nature and the substituent effects of π -donor groups.³ In the present study, we have designed and synthesized new extended conjugated quinones and hydroquinones having the donor and acceptor substituents to decrease the intermolecular CT gap.^{2,4} In this paper, we report the first synthesis of 11 new 4,4'-biphenylquinone derivatives **2** and 11 new 4,4'-biphenylhydroquinone derivatives **1** with alkylthio and halogen substituents.



* To whom correspondence should be addressed: fax, 81-06-850-5392.

(1) (a) Nakasuji, K.; Sugiura, K.; Kitagawa, T.; Toyoda, J.; Okamoto, H.; Okaniwa, K.; Mitani, T.; Yamamoto, H.; Murata, I. *J. Am. Chem. Soc.* **1991**, *113*, 1862. (b) Mitani, T.; Saito, G.; Urayama, H. *Phys. Rev. Lett.* **1988**, *60*, 2299. (c) Sugiura, K.; Toyoda, J.; Okamoto, H.; Okaniwa, K.; Mitani, T.; Kawamoto, A.; Tanaka, J.; Nakasuji, K. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 852.

(2) Viehe, H. G.; Janousek, Z.; Merenyi, R.; Stella, L. *Acc. Chem. Res.* **1985**, *18*, 148.

(3) Kitagawa, T.; Toyoda, J.; Nakasuji, K.; Yamamoto, H.; Murata, I. *Chem. Lett.* **1990**, 897.

The key steps for the synthesis of new 4,4'-biphenylhydroquinones **1** and new 4,4'-biphenylquinones **2** are as follows: for **1**, direct methylthiolation of 4,4'-biphenyldiol, cross-coupling reaction of aryl bromide with arylstannane, and bromine–sulfur exchange reaction of a tetrabromo compound with thiolate nucleophile; and for **2**, oxidative coupling reaction of phenols.

As reported by Ranken and McKinnie,⁵ methylthio-substituted phenols are conveniently prepared by direct methylthiolation from the corresponding phenols and (MeS)₂. We utilized this method for the preparation of methylthio-substituted 4,4'-biphenylhydroquinones. Mono- and bis(methylthio) derivatives **1a,b** were obtained as main products by treating 4,4'-biphenyldiol with a large excess of (MeS)₂ in the presence of 1 and 2 equiv of AlCl₃ in 17% and 22% yields, respectively. Oxidation of **1a** using 2 equiv of CAN⁶ in a mixture of CH₂Cl₂–H₂O and of **1b** using excess of K₃Fe(CN)₆ in benzene–KOH (aq) gave mono- and bis(methylthio)biphenylquinones **2a,b**⁷ as reddish-black powders in 73% and 84% yields, respectively.

In addition, synthesis of unsymmetrical derivatives **1c,d** and **2c,d** has been accomplished by the palladium-catalyzed coupling reaction of aryl bromide with arylstannane (the Stille reaction⁸) as a key step. The preparation of the starting aryl bromide and arylstannanes **3b–d** is summarized in Table 1 (entries 1–3). Cross-coupling reactions of **3b** with arylstannanes **3c,d** were conducted in the presence of 6 equiv of LiCl, 10 mol % Pd(PPh₃)₄, and 4 mol % 2,6-di-*tert*-butyl-4-methylphenol (BHT) in 1,4-dioxane. The coupling products **4a,b** were obtained in 46% and 27% yields, respectively. Deprotection of these compounds by TsOH·H₂O in MeOH afforded the desired 4,4'-biphenylhydroquinone derivatives **1c,d** in 93% and 77% yields, respectively. The biphenylquinones **2c,d** were obtained from **1c,d** by using 5 equiv of K₃Fe(CN)₆ in 52% and 56% yields, respectively.

(4) CT complexes based on the tetrachloro- or tetrabromo-4,4'-biphenylquinones are reported: (a) Iida, Y. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 105. (b) Matsunaga, Y.; Narita, Y. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 408. (c) Golovkina, I. F.; Krivoshei, I. V.; Starodub, V. A.; Aleshin, V. G.; Gella, I. M.; Nemoshkalenko, V. V.; Senkevich, A. I.; Surov, Y. N. *Teor. Eksp. Khim.* **1979**, *15*, 181. (d) Starikova, Z. A.; Shchegoleva, T. M.; Trunov, V. K.; Lantratova, O. B.; Pokrovskaya, I. E. *Zh. Strukt. Khim.* **1980**, *21*, 73. (e) Shchegoleva, T. M.; Starikova, Z. A.; Trunov, V. K.; Lantratova, O. B.; Pokrovskaya, I. E. *Zh. Strukt. Khim.* **1981**, *22*, 93. (f) Starodub, V. A.; Gluzman, E. M.; Golovkina, I. F.; Zaslavskaya, G. S.; Krivoshei, I. V. *Zh. Obshch. Khim.* **1981**, *51*, 2306. (g) Lau, C.-P.; Singh, P.; Cline, S. J.; Seiders, R.; Brookhart, M.; Marsh, W. E.; Hodgson, D. J.; Hatfield, W. E. *Mol. Cryst. Liq. Cryst.* **1982**, *86*, 131. (h) Starodub, V. A.; Gluzman, E. M.; Golovkina, I. P. *Zh. Obshch. Khim.* **1983**, *53*, 1127. (i) Akutagawa, T.; Saito, G. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1753.

(5) (a) Ranken, P. F.; McKinnie, B. G. *Synthesis* **1984**, 117. (b) McKinnie, B. G.; Ranken, P. F. Eur. Patent 122,203, 1984; *Chem. Abstr.* **1985**, *102*, 28149d.

(6) CAN is known as an effective oxidizing agent for both hydroquinone and sulfide to the quinone and sulfoxide, respectively; see for review: Ho, T.-L. In *Cerium(IV) Oxidation of Organic Compounds*; Mijs, W. J., de Jonge, C. R. H. I., Eds.; Plenum Press: New York, 1986; Chapter 11, p 569.

(7) This biphenylquinone was obtained as a mixture of stereoisomers.

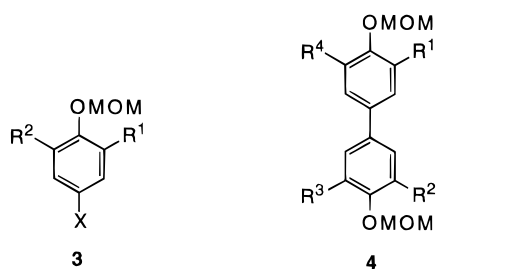
(8) Reviews: (a) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508. (b) Mitchell, T. N. *Synthesis* **1992**, 803.

(9) This MOM-protected phenol was prepared from the corresponding phenol, MOMCl (1.1–1.5 equiv), and NaH (1.1–1.8 equiv) in THF at rt in quantitative yield; see: Supporting Information.

Table 1. Preparation of Alkylthio-Substituted Phenol Derivatives^a

entry	products	starting materials	reagents and conditions	yield, %
1	3b	3a^b	a. 5 equiv of <i>n</i> -BuLi, pentane, -20 °C ^c b. 5 equiv of (MeS) ₂ , -30-0 °C	41
2	3c	4-bromophenol MOM ether ^d	a. <i>n</i> -BuLi, THF, -78 °C b. Bu ₃ SnCl, -78 °C	89
3	3d	4-bromo-2,6-dimethylphenol MOM ether ^e	a. 2 equiv of <i>t</i> -BuLi, THF, -95 °C b. Bu ₃ SnCl, -95 °C	85
4	5a^f	phenol	excess (MeS) ₂ cat. Al powder, 110 °C, 5 days	16
5	5b	2,6-dibromophenol ^g	3 equiv of Cu(I)SPr ^h quinoline-pyridine, 160 °C, 5.5 h	83
6	5c	2,6-dibromophenol ^g	4 equiv of Cu(I)S- <i>t</i> -Bu ^k quinoline-pyridine, 160 °C, 6 h	79
7	5d	2-fluorophenol	excess (MeS) ₂ AlCl ₃ , 100 °C, 4 h	15
8	5eⁱ	2-chlorophenol	excess (MeS) ₂ AlCl ₃ , 110 °C, 5 h	16
9	5f^j	6c	cat. TsOH·H ₂ O MeOH, 65 °C, 8 h	92
10	5g	6d	cat. TsOH·H ₂ O MeOH, 65 °C, 2 h	98
11	6c	6a^b	a. 2 equiv of <i>t</i> -BuLi, THF, -95 °C b. (MeS) ₂ , 0.5 h	72
12	6d	6b^b	a. 2 equiv of <i>t</i> -BuLi, THF, -95 °C b. (MeS) ₂ , 0.5 h	40

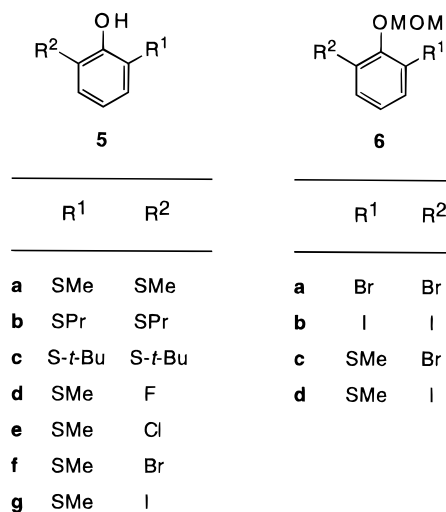
^a See Supporting Information for full details. ^b Reference 9. ^c Reference 10. ^d Reference 11. ^e Reference 12. ^f Reference 5. ^g Reference 16. ^h Reference 17. ⁱ Reference 15. ^j Reference 18. ^k Reference 20.



	R ¹	R ²	X		R ¹	R ²	R ³	R ⁴
a	Br	Br	Br	a	SMe	H	H	SMe
b	SMe	SMe	Br	b	SMe	Me	Me	SMe
c	H	H	SnBu ₃					
d	Me	Me	SnBu ₃					

Synthesis of tetrasubstituted biphenoquinones **2e,f,h-k** has been accomplished by the oxidative coupling reaction of phenols. Alkyl, phenyl, and methoxy derivatives of 4,4'-biphenoquinones were prepared from the corresponding substituted phenols by using a variety of reagents, such as metal oxidants and organic oxidants, and by electrochemical oxidation.¹³ However, the products are mostly complex mixtures of compounds such as the 1,4-benzoquinone, 4,4'-biphenohydroquinone, and polymeric phenol ether as well as the desired 4,4'-biphenoquinone.¹³ Furthermore, in the case of alkylthio-substituted phenol as substrate, sulfoxide compounds are also produced under the oxidative coupling condi-

tions. In such circumstances we have found that DDQ¹⁴ is a very effective and convenient oxidant for the synthesis of the desired 4,4'-biphenoquinones **2e,f,h-k** from the alkylthio-substituted phenols **5a,b,d-g** in good yield.



The preparation of the starting phenols **5a,b,d-g** is shown in Table 1 (entries 4, 5, 7-12). These phenols were treated with 1 equiv of DDQ in MeOH at rt, and then the resulting black precipitate was filtered and washed with MeOH to afford the desired, analytically pure 4,4'-biphenoquinones **2e,f,h⁷-k⁷** as bluish-black

(10) For ortho-selective lithiation of 2,4,6-tribromophenyl methyl ether, see: Green, K. *J. Org. Chem.* **1991**, *56*, 4325.

(11) Kipping, F. B.; Wren, J. J. *J. Chem. Soc.* **1957**, 3246.

(12) Borrer, A. L.; Cincotta, L.; Ellis, E. W.; Foley, J. W.; Kampe, M. M. U.S. 4,181,660, 1980; *Chem. Abstr.* **1980**, *92*, 146747.

(13) For review: (a) Boldt, P. In *Methoden der Organischen Chemie (Houben-Weyl)*; Müller, E., Bayer, O., Eds.; Georg Thieme Verlag: Stuttgart, 1979; Bd. 7, 3b, p 188. (b) Whiting, D. A. In *Comprehensive Organic Synthesis*; Pattenden, G., FRS, Ed.; Pergamon Press: Oxford, 1991; Vol. 3, Chapter 2.9, p 659.

(14) Only a limited number of reports are known about DDQ as a phenol oxidative coupling agent: (a) Becker, H.-D. *J. Org. Chem.* **1965**, *30*, 982. (b) Boldt, P.; Michaelis, W.; Lackner, H.; Krebs, B. *Chem. Ber.* **1971**, *104*, 220. (c) Cardillo, G.; Cricchio, R.; Merlini, L. *Tetrahedron* **1971**, *27*, 1875. For DDQ review: (d) Walker, D.; Hiebert, J. D. *Chem. Rev.* **1967**, *67*, 153.

(15) Winkler, A. DE 2644591, 1978; *Chem. Abstr.* **1978**, *89*, 23960q.

(16) Pearson, D. E.; Wysong, R. D.; Breder, C. V. *J. Org. Chem.* **1967**, *32*, 2358.

(17) Ford, P. W.; Davidson, B. S. *J. Org. Chem.* **1993**, *58*, 4522.

(18) Lertratanangkoon, K.; Horning, M. G. *Drug Metab. Dispos.* **1987**, *15*, 1.

Table 2. Selected Physical and Cyclic Voltammetric Data (V vs SCE)^a of Biphenoquinones 2

	2a	2b	2c	2d	2e	2f	2g	2h	2i	2j	2k
IR, ^b cm ⁻¹	1621, 1580, 1559	1612, 1594, 1543	1623, 1592, 1509	1587, 1559, 1508	1588, 1513	1605, 1592, 1510	2960, 1625, 1508	1611, 1526	1619, 1519	1616, 1514	1610, 1509
UV, ^c nm	274, 402, 512	266, 402, 564	250, 288, 326, 492	248, 288, 332, 496	256, 304, 562	258, 308, 570	262, 304, 428, 568	266, 422, 572	242, 284, 452, 582	244, 288, 462, 582	248, 298, 494, 576
E ₁ ^{red}	-0.22	-0.23	-0.21	-0.31	-0.25	-0.37	-0.10	-0.07	-0.02	-0.01	-0.02
E ₂ ^{red}	-0.45	-0.50	-0.45	-0.55	-0.52		-0.39	-0.33	-0.29	-0.30	-0.28

^a Measured against the saturated calomel electrode (SCE) in CH₃CN with 0.1 M *n*-Bu₄NClO₄ as supporting electrolyte at rt. ^b KBr pellet. ^c CH₂Cl₂ solution.

powders in 80%, 60%, 52%, 70%, 64%, and 84% yields, respectively. Na₂S₂O₄ reduction of **2e,f,h-k** gave the corresponding biphenohydroquinones **1e,¹⁹f,h-k** in 73%, 42%, 79%, 94%, 96%, and 99% yields, respectively. Since oxidation of 2,6-bis(*tert*-butylthio)phenol (**5c**) (Table 1, entry 6) with DDQ did not give the desired **2g**, we prepared tetrakis(*tert*-butylthio) derivative (**1g**) by treating 3,3',5,5'-tetrabromo-4,4'-biphenohydroquinone²¹ with excess of Cu(I)S-*t*-Bu²⁰ in 14% yield. Oxidation of **1g** using excess of K₃Fe(CN)₆ gave tetrakis(*tert*-butylthio)-biphenoquinone **2g** in 86% yield.

The biphenoquinones **2** are stable in the solid state. The tetrasubstituted derivatives **2d-f** are stable in solution. The monosubstituted derivative **2a** is not stable in CDCl₃: for example, it decomposed to the extent of more than 50% within several days. Selected physical data and redox potentials of these biphenoquinones are shown in Table 2.

In conclusion, our synthetic procedures provide a simple and convergent approach for the preparation of 4,4'-biphenoquinones and 4,4'-biphenohydroquinones substituted with alkylthio and halogen groups. We are currently investigating further applications of these methods for the synthesis of new bipheno compounds.

Experimental Section

General. ¹H and ¹³C NMR spectra were recorded at 270 and 68 MHz, respectively, with CDCl₃, acetone-*d*₆, or DMSO-*d*₆ as solvent and Me₄Si or residual solvent as an internal standard. Infrared spectra were recorded using KBr plates or Cl₂C=CCl₂ solution. Electronic spectra were recorded using CH₃CN or CH₂Cl₂ solution. Mass spectra analyses were recorded by electron impact at 70 eV. The cyclic voltammeteries were carried out at rt under argon. Melting points were measured with a hot-stage apparatus and are uncorrected. Elemental analyses were performed at the Graduate School of Science at Osaka University. Silica gel 60 (100–200 mesh) was used for column chromatography. Deactivated silica gel was prepared by mixing with 6% water. Solvents were dried (drying agent in parentheses) and distilled under argon prior to use: THF (Na-benzophenone ketyl), 1,4-dioxane (Na), MeOH (Mg(OMe)₂), CH₃CN, CH₂Cl₂ (CaH₂), Cl₂C=CCl₂ (P₄O₁₀), quinoline (Na₂SO₄ then Zn powder). All reactions requiring anhydrous conditions were conducted under argon atmosphere.

3-(Methylthio)-4,4'-biphenohydroquinone (1a). 4,4'-Biphenyldiol (2.09 g, 11.2 mmol), (MeS)₂ (20.2 mL, 225 mmol), and AlCl₃ (1.50 g, 11.2 mmol) were placed in a 100-mL round-bottomed flask, and this mixture was heated at 110 °C. After being stirred at this temperature for 0.5 h, this reaction mixture was cooled to rt and then poured into a chilled 1 M HCl aqueous solution (100 mL) and ether (50 mL). The organic layer was separated, and the aqueous layer was extracted with ether (50 mL). The combined organic extracts

were dried over Na₂SO₄, then filtered, and concentrated under reduced pressure. The residual white powder was subjected to silica gel column chromatography with a 10:1 to 2:1 mixture of hexane and ethyl acetate as eluant, yielding crude **1a**. This crude product was further purified by silica gel column chromatography with CH₂Cl₂ as eluant, to give **1a** (433 mg, 17%) as a white powder: mp 105 °C; ¹H NMR (DMSO-*d*₆) δ 2.42 (s, 3, SMe), 6.80 (d, 2, *J* = 8.6 Hz, 3'-, 5'-H), 6.82 (d, 1, *J* = 8.1 Hz, 5-H), 7.16 (dd, 1, *J* = 2.1, 8.1 Hz, 6-H), 7.22 (d, 1, *J* = 2.1 Hz, 2-H), 7.39 (d, 2, *J* = 8.6 Hz, 2'-, 6'-H), 9.37 (s, 1, OH), 9.76 (s, 1, OH); IR (KBr) 3300, 1494 cm⁻¹; UV (CH₃CN) 252 nm; MS *m/z* 232 (M⁺, 100). Anal. Calcd for C₁₃H₁₂O₂S: C, 67.21; H, 5.21. Found: C, 66.87; H, 5.16.

3-(Methylthio)-4,4'-biphenoquinone (2a). Hydroquinone **1a** (100.3 mg, 0.432 mmol) was placed in a 50-mL round-bottomed flask and dissolved in CH₂Cl₂ (15 mL) and H₂O (15 mL) at rt. To this mixture was added CAN (473.7 mg, 0.864 mmol) in one portion, and the mixture was stirred at rt for 3 min. The dark-red-colored organic layer was separated, washed with H₂O (15 mL × 2), and then dried over Na₂SO₄. After being filtered and washed with CH₂Cl₂, the resulting dark-red solution was concentrated under reduced pressure and dried *in vacuo* at rt to give crude **2a** as a reddish-black powder. This crude product was subjected to deactivated silica gel column chromatography with a 2:1 to 1:1 mixture of hexane and ethyl acetate as eluant, yielding biphenoquinone **2a** (72.4 mg, 73%) as a reddish-black powder: mp 165–168 °C dec; ¹H NMR (CDCl₃) δ 2.49 (s, 3), 6.60–6.75 (m, 3), 7.34 (d, 1, *J* = 2.6 Hz), 7.85–8.00 (m, 3); MS *m/z* 232 (M⁺ + 2H, 100); HRMS *m/z* calcd for C₁₃H₁₂O₂S (M⁺ + 2H) 232.0559, found 232.0533.

3,3'-Bis(methylthio)-4,4'-biphenohydroquinone (1b). This compound was prepared by a similar procedure as for the synthesis of **1a** using 4,4'-biphenyldiol (2.14 g, 11.5 mmol), (MeS)₂ (41.4 mL, 460 mmol), and AlCl₃ (3.07 g, 23.0 mmol): grayish-yellow-green powder, yield 22%; mp 68 °C; ¹H NMR (CDCl₃) δ 2.38 (s, 6), 6.64 (s, 2), 7.03 (d, 2, *J* = 8.3 Hz), 7.42 (dd, 2, *J* = 8.3, 2.3 Hz), 7.66 (d, 2, *J* = 2.3 Hz); IR (KBr) 3320, 1421 cm⁻¹; UV (CH₃CN) 248, 275(sh), 305(sh) nm; MS *m/z* 278 (M⁺, 100). Anal. Calcd for C₁₄H₁₄O₂S₂: C, 60.40; H, 5.07. Found: C, 60.18; H, 4.83.

3,3'-Bis(methylthio)-4,4'-biphenoquinone (2b).⁷ Hydroquinone **1b** (221.8 mg, 0.797 mmol) was placed in a 100-mL round-bottomed flask and mixed with benzene (30 mL). To this mixture was added a solution of K₃Fe(CN)₆ (2651 mg, 7.97 mmol) and KOH (2634 mg, 39.9 mmol) in H₂O (30 mL) in one portion, and the mixture was stirred at rt for 5 min. The black precipitate was filtered and washed with H₂O (300 mL) and MeOH (100 mL), successively. The resulting reddish-black powder was dried *in vacuo* at rt for 4 h, yielding biphenoquinone **2b** (186.0 mg, 84%) as a reddish-black powder: mp >300 °C; ¹H NMR (CDCl₃) δ 2.56 (s, 6), 2.60 (s, 6), 6.61 (br s, 4), 7.70 (br dd, 4, *J* = 8.9, 2.3 Hz), 8.23 (d, 2, *J* = 8.1 Hz), 8.37 (d, 2, *J* = 8.1 Hz); MS *m/z* 278 (M⁺ + 2H, 100). Anal. Calcd for C₁₄H₁₂O₂S₂: C, 60.84; H, 4.38. Found: C, 60.68; H, 4.24.

3,5-Bis(methylthio)biphenyl-4,4'-diyl Bis(methoxy-methyl) Ether (4a). Bromophenol derivative **3b** (1.29 g, 4.18 mmol), arylstannane **3c** (1.78 g, 4.18 mmol), Pd(PPh₃)₄ (483 mg, 0.418 mmol), BHT (37.7 mg, 0.171 mmol), and LiCl (1.06 g, 25.0 mmol) were placed in a 500-mL round-bottomed flask and suspended in 1,4-dioxane (150 mL). This mixture was stirred at 110–115 °C for 8.5 h and then cooled to rt. To this reaction mixture was added satd aqueous KF solution (50 mL), and the resulting suspension was filtered. The organic layer was separated, and the aqueous layer was extracted with

(19) This hydroquinone was also obtained by the homocoupling reaction of **3b** (NiCl₂(PPh₃)₂ (1 equiv), active Zn powder (1 equiv), and PPh₃ (1.7 equiv) in DMF at -20–0 °C, yield 28%) and subsequent deprotection of MOM groups (cat. TsOH·H₂O in THF–MeOH at 60 °C, yield 89%); see: Supporting Information.

(20) Adams, R.; Ferretti, A. *J. Am. Chem. Soc.* **1959**, *81*, 4927.

(21) Magatti, G. *Chem. Ber.* **1880**, *13*, 224.

ether. The combined organic extracts were washed with satd aqueous NaCl solution (50 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residual oil was subjected to silica gel column chromatography with a 100:1 to 10:1 mixture of hexane and ethyl acetate as eluant, yielding coupling product **4a** (706 mg, 46%) as a pale-yellow oil: ¹H NMR (CDCl₃) δ 2.47 (s, 6), 3.51 (s, 3), 3.74 (s, 3), 5.18 (s, 2), 5.22 (s, 2), 7.09 (s, 2), 7.11 (br d, 2, *J* = 8.9 Hz), 7.46 (br d, 2, *J* = 8.9 Hz). The product was used without further purification in the following reaction.

3,5-Bis(methylthio)-4,4'-biphenohydroquinone (1c). Bis-(MOM)-protected biphenol derivative **4a** (706 mg, 1.93 mmol) was placed in a 300-mL round-bottomed flask and dissolved in THF (50 mL) and MeOH (50 mL). To this mixture was added TsOH·H₂O (20.0 mg, 0.105 mmol), and the mixture was stirred at rt for 14 h and then at 90 °C for 28 h. After being cooled to rt, most of the solvent was removed *in vacuo* at rt. pH 7.0 phosphate buffer solution (0.1 M solution, 20 mL) and ethyl acetate (20 mL) were added to this residual oil. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (10 mL × 2). The combined organic extracts were dried over MgSO₄, filtered, and concentrated under reduced pressure. The residual oil was subjected to deactivated silica gel column chromatography with a 100:1 to 5:1 mixture of hexane and ethyl acetate as eluant, yielding **1c** (446 mg, 83%) as a yellowish-gray powder: mp 126–127 °C; ¹H NMR (CDCl₃) δ 2.44 (s, 6), 4.83 (s, 1), 6.89 (d, 2, *J* = 8.8 Hz), 7.04 (s, 1), 7.41 (d, 2, *J* = 8.8 Hz), 7.41 (s, 1); IR (KBr) 3441, 3332, 1450, 1435 cm⁻¹; UV (CH₃CN) 254, 320 nm; MS *m/z* 278 (M⁺, 100). Anal. Calcd for C₁₄H₁₄O₂S₂: C, 60.40; H, 5.07. Found: C, 59.99; H, 5.01.

3,5-Bis(methylthio)-3',5'-dimethylbiphenyl-4,4'-diyl Bis(methoxymethyl) Ether (4b). This compound was prepared by a similar procedure as for the synthesis of **4a** using **3b** (524 mg, 1.67 mmol), **3d** (772 mg, 1.67 mmol), Pd(PPh₃)₄ (196 mg, 0.170 mmol), BHT (18.7 mg, 0.085 mmol), and LiCl (431 mg, 10.2 mmol): yield 27%; ¹H NMR (CDCl₃) δ 2.36 (s, 6), 2.48 (s, 6), 3.64 (s, 3), 3.73 (s, 3), 5.00 (s, 2), 5.18 (s, 2), 7.08 (s, 2), 7.17 (s, 2); MS *m/z* 394 (M⁺, 52), 349 (M⁺ - SCH₃ + 2H, 100). The product was used without further purification in the following reaction.

3,5-Bis(methylthio)-3',5'-dimethyl-4,4'-biphenohydroquinone (1d). This compound was prepared by a similar procedure as for the synthesis of **1c** using **4b** (403 mg, 1.02 mmol) and TsOH·H₂O (13.9 mg, 0.073 mmol): yield 64%; mp 108–111 °C; ¹H NMR (CDCl₃) δ 2.31 (s, 6), 2.45 (s, 6), 7.02 (s, 2), 7.14 (s, 2), 7.41 (s, 2); IR (KBr) 3475, 3316, 1456 cm⁻¹; UV (CH₃CN) 256, 320(sh) nm; MS *m/z* 306 (M⁺, 100). Anal. Calcd for C₁₆H₁₈O₂S₂: C, 62.71; H, 5.92. Found: C, 62.24; H, 5.81.

3,5-Bis(methylthio)-4,4'-biphenoquinone (2c). This compound was prepared by a similar procedure as for the synthesis of **2b** using **1c** (136 mg, 0.488 mmol), K₃Fe(CN)₆ (803 mg, 2.44 mmol), and KOH (548 mg, 9.76 mmol): brownish-black powder, yield 56%; mp 195–199 °C dec; ¹H NMR (CDCl₃) δ 2.49 (s, 6), 6.66 (d, 2, *J* = 9.9 Hz), 7.34 (d, 2, *J* = 13.9 Hz), 7.95 (d, 2, *J* = 9.9 Hz); MS *m/z* 278 (M⁺ + 2H, 100). Anal. Calcd for C₁₄H₁₂O₂S₂: C, 60.84; H, 4.38. Found: C, 60.80; H, 4.38.

3,5-Bis(methylthio)-3',5'-dimethyl-4,4'-biphenoquinone (2d). This compound was prepared by a similar procedure as for the synthesis of **2b** using **1d** (177 mg, 0.579 mmol), K₃Fe(CN)₆ (953 mg, 2.90 mmol), and KOH (650 mg, 11.6 mmol): dark-grayish-olive powder, yield 88%; mp 158–160 °C dec; ¹H NMR (CDCl₃) δ 2.18 (s, 6), 2.50 (s, 6), 7.35 (s, 2), 7.69 (s, 2); MS *m/z* 304 (M⁺, 64), 306 (M⁺ + 2H, 54). Anal. Calcd for C₁₆H₁₆O₂S₂: C, 63.13; H, 5.30. Found: C, 63.23; H, 5.46.

General Procedure for the Tetrasubstituted 4,4'-Biphenoquinones from 2,6-Disubstituted Phenols: 3,3',5,5'-Tetrakis(methylthio)-4,4'-biphenoquinone (2e). DDQ (2.59 g, 11.4 mmol) was placed in a 100-mL round-bottomed flask and dissolved in MeOH (25 mL). To this mixture was added a solution of 2,6-bis(methylthio)phenol (**5a**) (2.12 g, 11.4 mmol) in MeOH (10 mL) in one portion, and the mixture was rinsed with MeOH (10 mL). The resulting bluish-black suspension

was stirred at rt for 75 min and then filtered, washed with MeOH, and dried *in vacuo* at rt for 4 h, yielding biphenoquinone **2e** (1.67 g, 80%) as a bluish-black powder: mp 220–222 °C dec; ¹H NMR (acetone-*d*₆) δ 2.43 (s, 12), 6.38 (s, 4); MS *m/z* 370 (M⁺ + 2H, 100). Anal. Calcd for C₁₆H₁₆O₂S₄: C, 52.14; H, 4.38. Found: C, 51.88; H, 4.33.

3,3',5,5'-Tetrakis(propylthio)-4,4'-biphenoquinone (2f): bluish-black powder, yield 60%; mp 192–194 °C dec; ¹H NMR (CDCl₃) δ 1.12 (t, 12, *J* = 7.3 Hz), 1.82 (sextet, 8, *J* = 7.3 Hz), 2.91 (t, 8, *J* = 7.4 Hz), 7.35 (s, 4); MS *m/z* 482 (M⁺ + 2H, 100). Anal. Calcd for C₂₄H₃₂O₂S₄: C, 59.96; H, 6.71. Found: C, 59.88; H, 6.65.

3,3'-Difluoro-5,5'-bis(methylthio)-4,4'-biphenoquinone (2h): dark-grayish-blue powder, yield 52%; mp > 300 °C; ¹H NMR (DMSO-*d*₆) δ 2.57 (s, 6), 2.59 (s, 6), 7.49 (s, 2), 7.64 (s, 2), 8.16 (d, 2, *J* = 10.8 Hz), 8.34 (d, 2, *J* = 10.8 Hz); MS *m/z* 314 (M⁺ + 2H, 100). Anal. Calcd for C₁₄H₁₀F₂O₂S₂: C, 53.83; H, 3.23. Found: C, 53.27; H, 3.25.

3,3'-Dichloro-5,5'-bis(methylthio)-4,4'-biphenoquinone (2i): bluish-black powder, yield 70%; mp > 300 °C; ¹H NMR (acetone-*d*₆) δ 2.63 (s, 6), 2.66 (s, 6), 7.74 (d, 2, *J* = 2.6 Hz), 7.75 (d, 2, *J* = 2.6 Hz), 8.56 (d, 2, *J* = 2.6 Hz), 8.58 (d, 2, *J* = 2.6 Hz); MS *m/z* 346 (M⁺ + 2H, 100). Anal. Calcd for C₁₄H₁₀Cl₂O₂S₂: C, 48.70; H, 2.92. Found: C, 48.60; H, 2.95.

3,3'-Dibromo-5,5'-bis(methylthio)-4,4'-biphenoquinone (2j): grayish-black powder, yield 64%; mp > 300 °C dec; ¹H NMR (acetone-*d*₆) δ 2.63 (s, 6), 2.65 (s, 6), 7.74 (d, 2, *J* = 2.6 Hz), 7.77 (d, 2, *J* = 2.6 Hz), 8.79 (d, 2, *J* = 3.0 Hz), 8.81 (d, 2, *J* = 3.0 Hz); MS *m/z* 436 (M⁺ + 2H, 2.2). Anal. Calcd for C₁₄H₁₀Br₂O₂S₂: C, 38.73; H, 2.32. Found: C, 39.13; H, 2.41.

3,3'-Diiodo-5,5'-bis(methylthio)-4,4'-biphenoquinone (2k): black powder, yield 84%; mp > 300 °C; ¹H NMR (DMSO-*d*₆) δ 2.56 (s, 6), 2.58 (s, 6), 7.62 (s, 4), 9.06 (d, 2, *J* = 2.3 Hz), 9.13 (d, 2, *J* = 2.3 Hz); MS *m/z* 530 (M⁺ + 2H, 43). Anal. Calcd for C₁₄H₁₀I₂O₂S₂: C, 31.84; H, 1.91. Found: C, 32.28; H, 1.90.

General Procedure for the 3,3',5,5'-Tetrasubstituted 4,4'-Biphenohydroquinones from the Corresponding 4,4'-Biphenoquinones: 3,3',5,5'-Tetrakis(methylthio)-4,4'-biphenohydroquinone (1e). Biphenoquinone **2e** (539 mg, 1.46 mmol) was placed in a 200-mL round-bottomed flask and suspended in ether (50 mL). A solution of Na₂S₂O₄ (3.56 g, 20.5 mmol) in 1 M NaOH (75 mL) was added to this mixture in one portion. After being stirred at rt for 30 min, the reaction mixture was acidified by slow addition of concd HCl. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (50 mL × 2). The combined organic extracts were dried over MgSO₄, filtered, and concentrated under reduced pressure at 40 °C. The residual yellowish-pink powder was subjected to silica gel column chromatography with a 10:1 to 2:1 mixture of hexane and ethyl acetate as eluant, yielding **1e** (393 mg, 73%) as a beige-white powder: mp 128–129 °C; ¹H NMR (CDCl₃) δ 2.45 (s, 12), 7.08 (s, 2), 7.40 (s, 4); IR (KBr) 3367, 2916, 1443 cm⁻¹; UV (CH₃CN) 252, 310 nm; MS *m/z* 370 (M⁺, 100). Anal. Calcd for C₁₆H₁₈O₂S₄: C, 51.86; H, 4.90. Found: C, 51.85; H, 4.86.

3,3',5,5'-Tetrakis(propylthio)-4,4'-biphenohydroquinone (1f): colorless oil, 42% yield; ¹H NMR (CDCl₃) δ 1.03 (t, 12, *J* = 7.3 Hz), 1.66 (sextet, 8, *J* = 7.3 Hz), 2.84 (t, 8, *J* = 7.3 Hz), 7.19 (s, 2), 7.44 (s, 4); IR (Cl₂C=CCl₂) 3388, 2964, 2932, 1432 cm⁻¹; UV (CH₃CN) 256, 310 nm; MS *m/z* 482 (M⁺, 100). Anal. Calcd for C₂₄H₃₄O₂S₄: C, 59.71; H, 7.10. Found: C, 60.11; H, 7.18.

3,3'-Difluoro-5,5'-bis(methylthio)-4,4'-biphenohydroquinone (1h): pale-beige powder, 79% yield; mp 128–130 °C; ¹H NMR (CDCl₃) δ 2.44 (s, 6), 6.26 (s, 2), 7.20 (br dd, 2, *J* = 2.3, 11.2 Hz), 7.35 (br t, 2); IR (KBr) 3423, 1473 cm⁻¹; UV (CH₃CN) 250, 300(sh) nm; MS *m/z* 314 (M⁺, 100). Anal. Calcd for C₁₄H₁₂F₂O₂S₂: C, 53.49; H, 3.85. Found: C, 53.59; H, 3.93.

3,3'-Dichloro-5,5'-bis(methylthio)-4,4'-biphenohydroquinone (1i): pale-yellow powder, 94% yield; mp 116–117 °C; ¹H NMR (CDCl₃) δ 2.45 (s, 6), 6.61 (s, 2), 7.42 (d, 2, *J* = 2.3 Hz), 7.44 (d, 2, *J* = 2.3 Hz); IR (KBr) 3346, 2923, 1456 cm⁻¹; UV (CH₃CN) 254, 305(sh) nm; EI-MS *m/z* 346 (M⁺, 100).

Anal. Calcd for $C_{14}H_{12}Cl_2O_2S_2$: C, 48.42; H, 3.48. Found: C, 48.42; H, 3.50.

3,3'-Dibromo-5,5'-bis(methylthio)-4,4'-biphenohydroquinone (1j): beige-white powder, 96% yield; mp 122–123 °C; 1H NMR ($CDCl_3$) δ 2.44 (s, 6), 6.69 (s, 2), 7.48 (d, 2, J = 2.3 Hz), 7.57 (d, 2, J = 2.0 Hz); IR (KBr) 3424, 3333, 2919, 1455 cm^{-1} ; UV (CH_3CN) 256, 305(sh) nm; MS m/z 436 (M^+ , 100). Anal. Calcd for $C_{14}H_{12}Br_2O_2S_2$: C, 38.55; H, 2.77. Found: C, 38.87; H, 2.85.

3,3'-Diiodo-5,5'-bis(methylthio)-4,4'-biphenohydroquinone (1k): yellowish-white powder, 99% yield; mp 178–180 °C; 1H NMR ($CDCl_3$) δ 2.42 (s, 6), 6.93 (s, 2), 7.54 (d, 2, J = 2.3 Hz), 7.78 (d, 2, J = 2.0 Hz); IR (KBr) 3356, 2923, 1429 cm^{-1} ; UV (CH_3CN) 234, 260, 305(sh) nm; MS m/z 530 (M^+ , 100). Anal. Calcd for $C_{14}H_{12}I_2O_2S_2$: C, 31.71; H, 2.28. Found: C, 32.08; H, 2.31.

3,3',5,5'-Tetrakis(*tert*-butylthio)-4,4'-biphenohydroquinone (1g). 3,3',5,5'-Tetrabromo-4,4'-biphenohydroquinone (5.57 g, 11.1 mmol) and $Cu(I)S-t-Bu$ (13.6 g, 88.8 mmol) were placed in a 500-mL round-bottomed flask and mixed with quinoline (75 mL) and pyridine (25 mL). This mixture was warmed up to 160 °C and stirred at this temperature for 2.5 h. After being cooled to rt, the resulting suspension was poured into a chilled 2 M HCl aqueous solution (100 mL). After addition of ethyl acetate (100 mL) to this mixture, the organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic extracts were washed with 2 M HCl aqueous solution (100 mL \times 2), dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residual brown oil was subjected to silica gel column

chromatography with a 100:1 to 10:1 mixture of hexane and ethyl acetate as eluant, yielding **1g** (813 mg, 14%) as a white powder: mp 176–178 °C; 1H NMR ($CDCl_3$) δ 1.36 (s, 36), 7.47 (s, 2), 7.66 (s, 4); IR (KBr) 3375, 3341, 2973, 1422 cm^{-1} ; UV (CH_3CN) 220, 266, 310(sh) nm; MS m/z 538 (M^+ , 9), 450 (M^+ – S-*t*-Bu + H, 18). Anal. Calcd for $C_{28}H_{42}O_2S_4$: C, 62.40; H, 7.86. Found: C, 62.34; H, 7.82.

3,3',5,5'-Tetrakis(*tert*-butylthio)-4,4'-biphenohydroquinone (2g). This compound was prepared by a similar procedure as for the synthesis of **2b** using **1g** (398 mg, 0.739 mmol), $K_3Fe(CN)_6$ (2.40 g, 7.39 mmol), and KOH (2.07 g, 37.0 mmol): dark-grayish-violet powder, yield 86%; mp 190–191 °C dec; 1H NMR ($CDCl_3$) δ 1.51 (s, 36), 7.97 (s, 4); MS m/z 538 (M^+ + 2H, 25). Anal. Calcd for $C_{28}H_{40}O_2S_4$: C, 62.64; H, 7.51. Found: C, 62.57; H, 7.46.

Acknowledgment. This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture, Japan.

Supporting Information Available: Spectroscopic data (1H NMR, IR, MS, and Anal. Calcd) and experimental procedures for the preparation of compounds **3a–d**, **5b–g**, and **6a–d** and homocoupling reaction of **3b** (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO962058V