JOC Article

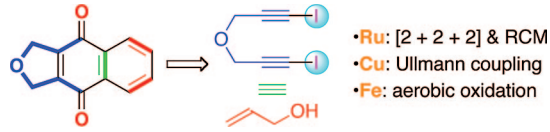
Synthesis of 2,5-Dihydrofuran-Fused Quinones from Ether-Tethered Diiododiyne

Yoshihiko Yamamoto,*,† Ryousuke Takuma, Tomitaka Hotta, and Ken Yamashita

Department of Applied Chemistry, Graduate School of Science and Engineering, Tokyo Institute of Technology, Ookayama, Meguro-ku, Tokyo 152-8552, Japan

omyy@apc.titech.ac.jp; yamamoto@apchem.nagoya-u.ac.jp

Received March 20, 2009



Biologically interesting 2,5-dihydrofuran-fused quinones were synthesized via the ruthenium-catalyzed [2 + 2 + 2] cycloaddition of an ether-tethered diiododiyne with alkynes, copper-catalyzed Ullmann coupling of the resultant fused *p*-diiodobenzenes with methanol or allyl alcohol, and subsequent oxidation of phenol derivatives. The double Claisen rearrangement of the bis(allyl) ether product furnished a diallylhydroquinone derivative, which underwent iron-catalyzed oxidation, ring-closing metathesis, and dehydrogenation to deliver 1,3-dihydronaphtho[2,3-*c*]furan-4,9-dione.

Introduction

Naphtho[2,3-*c*]furan-4,9-dione has received much attention, because this compound with an intriguing structure is found in biologically interesting natural products, and its reactivity is almost comparable to that of *o*-quinodimethide.[1] In contrast, its 1,3-dihydro analogue **1** has not received significant attention, even though it is also found in several natural products such as ventilones C−E (**2**) (isolated from the root bark of *V. maderaspatana*),[2] cerdarin **3a** (an antifungal metabolite isolated from the coprophilous fungus *C. sordarioides*),[3] and its demethoxy analogue **3b** (derived from the ascomycete *G. pseudoreticulata*) (Figure 1).[4] The latter two closely related derivatives have been reported to exhibit anti-*Candida* activity and monoamine oxidase inhibitory activity, respectively. The development of a feasible synthetic route to 1,3-dihydronaphtho[2,3-*c*]furan-4,9-dione (**1**) and its related structures is an important task, but it remains to be explored.

Results and Discussion

Our research group has developed efficient methods to synthesize highly substituted benzenes via ruthenium-catalyzed [2 + 2 + 2] cycloaddition of diiododiynes and subsequent transition metal-catalyzed couplings of the resulting *p*-diiodobenzenes.[5] On the basis of these results, we envisioned that if previously obtained phthalan derivative **4a** undergoes copper-catalyzed Ullmann coupling with alcohols,[6] 2,5-dihydrofuran-fused quinones can be synthesized after appropriate transformations and/or oxidation of diether intermediates (Scheme 1). However, to the best of our knowledge, no example of 2-fold Ullmann coupling reaction of fused *p*-diiodobenzenes with alcohols affording *p*-hydroquinone diethers has been reported thus far.[7]

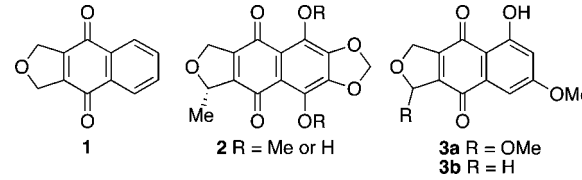


FIGURE 1. 1,3-Dihydronaphtho[2,3-*c*]furan-4,9-diones.

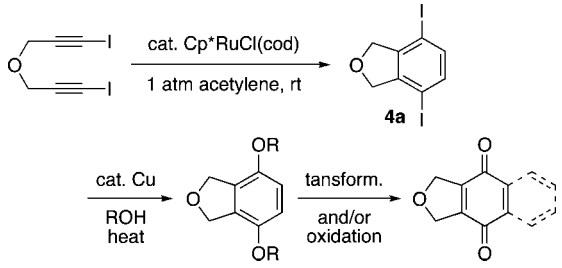
To implement the above strategy, we first optimized the 2-fold Ullmann coupling reaction of **4a** with MeOH using microwave

† Current address: Department of Applied Chemistry, Graduate School of Engineering, Nagoya University, Chikusa-ku, Nagoya 464-8603, Japan.

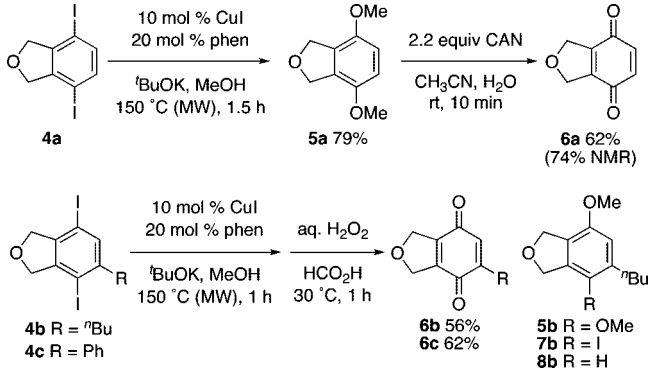
(1) Piggott, M. J. *Tetrahedron* **2005**, *61*, 9929–9954.
(2) Hanumaiah, T.; Rao, G. S. R.; Rao, C. P.; Rao, K. V. J.; Cowe, H. J.; Cox, P. J.; Howie, R. A.; Marshall, D. S.; Thomson, R. H. *Tetrahedron* **1985**, *41*, 635–642.
(3) Whyte, A. C.; Gloer, K. B.; Gloer, J. B.; Koster, B.; Malloch, D. *Can. J. Chem.* **1997**, *75*, 768–772.
(4) Fujimoto, H.; Okuyama, H.; Motohashi, Y.; Yoshida, E.; Yamazaki, M. *Mycotoxins* **1995**, 61–66.
(5) Yamamoto, Y.; Hattori, K.; Nishiyama, H. *J. Am. Chem. Soc.* **2006**, *128*, 8336–8340. (b) Yamamoto, Y.; Yamashita, K.; Hotta, T.; Hashimoto, T.; Kikuchi, M.; Nishiyama, H. *Chem. Asian J.* **2007**, *2*, 1388–1399. (c) Yamamoto, Y.; Hattori, K. *Tetrahedron* **2008**, *64*, 847–855.
(6) For reviews, see: (a) Finet, J.-P.; Fedorov, A. Y.; Combes, S.; Boyer, G. *Curr. Org. Chem.* **2002**, *6*, 597–626. (b) Kunz, K.; Scholz, U.; Ganzer, D. *Synlett* **2003**, 2428–2439. (c) Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400–5449. (d) Monnier, F.; Taillefer, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 3096–3099.

10.1021/jo9005975 CCC: $40.75
Published on Web 04/29/2009

SCHEME 1. Proposed Synthetic Route to 2,5-Dihydrofuran-Fused Quinones



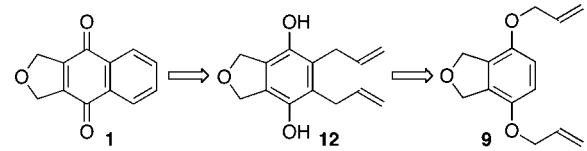
SCHEME 2. Synthesis of Isobenzofuran-4,7(1*H*,3*H*)-diones



(MW) irradiation.[8] Thus, **4a** was treated with 10 mol % of CuI, 20 mol % of 1,10-phenanthroline (phen) as a ligand, and 2.4 equiv of *t*BuOK as a base in MeOH at 150 °C for 1.5 h. The purification of the crude product by silica gel column chromatography afforded **5a** in 79% yield (Scheme 2). The reaction was sluggish when ligands such as 2,2′-bipyridyl or *N*,*N*′-dimethylethylenediamine[9] were employed instead of phen. When Cs_2CO_3 or K_3PO_4 was used as a base, the yield decreased slightly (75% and 77%, respectively). In contrast, *t*BuONa was found to be less effective: the conversion rate was low under the same reaction conditions. The oxidation of **5a** was then carried out by using a single-electron oxidant $Ce(NH_4)_2(NO_3)_6$ (CAN). A solution of **5a** in CH_3CN was treated with an aqueous solution of CAN (2.2 equiv) at ambient temperature to afford the desired quinone **6a** in 74% yield as estimated by ^{1}H NMR. Because **6a** partly decomposed during purification by chromatography, an analytically pure sample was obtained in 62% yield by recrystallization from AcOEt.

We then attempted to synthesize substituted derivatives of **6a** from previously synthesized diiodobenzenes **4b** and **4c** (Scheme 2).[5] However, the Ullmann coupling reaction of **4b** with MeOH was sluggish under the MW heating conditions,

SCHEME 3. Retrosynthetic Analysis of the Synthesis of 1



producing a complex mixture including desired product **5b**, monocoupling adduct **7b**, and **8b** formed by the reduction of **7b**. This probably occurred because of the steric congestion around the C−I bond α to the *n*-butyl substituent. Because methoxybenzenes **5b**, **7b**, and **8b** were assumed to yield a single quinone product upon oxidation, we examined the direct oxidation of the crude mixture with the aim of obtaining desired **6b** without tedious separation. The crude mixture obtained after MW irradiation for 1 h (**5b**:**7b**:**8b** = 63:33:4) was treated with CAN in a similar manner as **5a**. However, the reaction was not completed. Next, we carried out oxidation using aqueous H_2O_2 in formic acid at 30 °C for 1 h.[10] As a result, expected quinone product **6b** was obtained in a two-step yield of 56%. It was confirmed that neither diiodide **4b** nor parent 5-*n*-butyl-1,3-dihydroisobenzofuran yielded **6b** under the same oxidation conditions. Similarly, phenyl-substituted **4c** was successfully converted to the corresponding quinone **6c** in 62% yield by using this two-step protocol.

The next goal was to establish the synthetic route to 1,3-dihydronaphtho[2,3-*c*]furan-4,9-dione (**1**) from **4a**. To this end, we designed the synthetic route outlined in Scheme 3. The tricyclic framework of **1** would be generated by the ring-closing metathesis (RCM) of diallylhydroquinone **12** and subsequent oxidation. In turn, **12** would be obtained from the Claisen rearrangement of diallyl ether **9**. Although a related tandem Ullmann coupling/Claisen rearrangement reaction of allylic alcohols with vinyl iodides has been carried out by Nordmann and Buchwald,[11] our strategy is intriguing because it includes the challenging 2-fold Ullmann coupling reaction with allyl alcohol,[7] leading to **9**, a promising intermediate for the synthesis of polycyclic quinones. In fact, diallyl ethers of hydroquinones have been transformed into polycyclic quinones by Claisen rearrangement and subsequent RCM.[12]

Our endeavor starts with the Ullmann coupling of **4a** with allyl alcohol. However, the use of allyl alcohol posed problems; under the same MW heating conditions as those employed in the case of MeOH, the reaction of **4a** with allyl alcohol was found to be sluggish, and it produced a complex product mixture including intact **4a** and a trace amount of monocoupling product **10**. The use of Cs_2CO_3 as a base increased the yield of **10** only marginally. Therefore, we reoptimized the Ullmann coupling of **4a** by employing mild conventional heating conditions (Table 1). In the presence of 30 mol % of CuI, 60 mol % of phen, and 2.4 equiv of *t*BuOK, **4a** was heated in allyl alcohol at 110 °C in a sealed tube for 24 h (entry 1). As a result, **4a** was completely consumed and **9** was obtained in 31% yield along with **10** as the major product (61% yield). Increasing the amount of *t*BuOK to 4 equiv improved the yield of **9** up to 47%, but further

(7) For examples of 2-fold Ullmann coupling of *p*-dibromobenzene with aryl or aliphatic alcohols, see: (a) Sax, K. J.; Saari, W. S.; Mahoney, C. L.; Gordon, J. M. *J. Org. Chem.* **1960**, *25*, 1590−1595. (b) Bacon, R. G. R.; Rennison, S. C. *J. Chem. Soc. C* **1969**, 312–315. (c) Wang, L. Y.; Xi, H. T.; Sun, X. Q.; Shen, Y. Z.; Yang, Y.; Pan, Y.; Hu, H. W. *Synth. Commun.* **2000**, *30*, 227–234. For selected examples of the Ullmann coupling of *p*-methoxyphenyl halides with aliphatic alcohols, see: (d) Wolter, M.; Nordmann, G.; Job, G. E.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 973–976. (e) Zhang, H.; Ma, D.; Cao, W. *Synlett* **2007**, 243–246. (f) Altman, R. A.; Shafir, A.; Choi, A.; Lichtor, P. A.; Buchwald, S. L. *J. Org. Chem.* **2008**, *73*, 284–286. (g) Niu, J.; Zhou, H.; Li, Z.; Xu, J.; Hu, S. *J. Org. Chem.* **2008**, *73*, 7814–7817. (h) Naidu, A. B.; Sekar, G. *Tetrahedron Lett.* **2008**, *49*, 3147–3151.

(8) For an example of the MW-promoted Ullmann coupling with aliphatic alcohols, see: Manbeck, G. F.; Lipman, A. J.; Stockland, R. A., Jr.; Freidl, A. L.; Hasler, A. F.; Stone, J. J.; Guzei, I. A. *J. Org. Chem.* **2005**, *70*, 244–250.

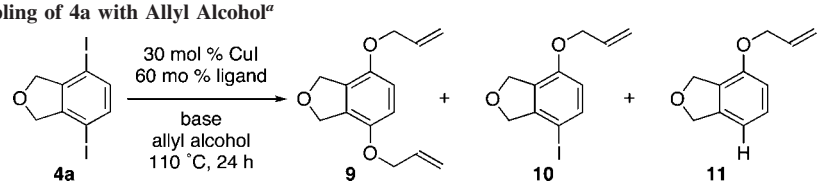
(9) Klapars, A.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 7421–7428.

(10) Orita, H.; Shimizu, M.; Hayakawa, T.; Takehira, K. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 1652–1657.

(11) Nordmann, G.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 4978–4979.

(12) For selected examples, see: (a) Chattopadhyay, S. K.; Pal, B. K.; Maity, S. *Chem. Lett.* **2003**, 1190–1191. (b) Kotha, S.; Mandal, K. *Tetrahedron Lett.* **2004**, *45*, 2585–2588. (c) Kotha, S.; Mandal, K.; Deb, A. C.; Banerjee, S. *Tetrahedron Lett.* **2004**, *45*, 9603–9605. (d) Kotha, S.; Shah, V. R.; Mandal, K. *Adv. Synth. Catal.* **2007**, *349*, 1159–1172.

TABLE 1. Ullmann Coupling of 4a with Allyl Alcohol[a]

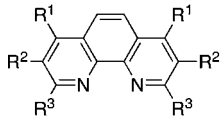


entry	ligand/base (equiv)	yields **4a/9/10/11** (%)
1	**A**/^{t}BuOK (2.4)	0/31/61/0
2	**A**/^{t}BuOK (4)	0/47/28/11
3	**A**/^{t}BuOK (6)	0/46/27/15
4	**A**/K_2CO_3 (4)	12/13/69/0
5	**A**/Cs_2CO_3 (4)	0/53/0/20
6	**A**/K_3PO_4 (4)	0/42/32/11
7	**B**/^{t}BuOK (4)	0/50/19/14
8	**C**/^{t}BuOK (4)	0/27/0/50
9	**D**/^{t}BuOK (4)	1/8/28/21[b]
10	**E**/^{t}BuOK (4)	35/0/56/6

[a] **4a** (0.3 mmol), CuI (30 mol %), ligand (60 mol %), allyl alcohol (4 mL), 110 °C, 24 h. [b] 4-Iodo-1,3-dihydroisobenzofuran was also formed in 18% yield.

increase in the amount of this base also yielded a similar result (entries 2 and 3). When Cs_2CO_3 was used instead of ^{t}BuOK, **10** was completely consumed, but in this case, undesired **11** was produced in a significant yield of 20% (entry 5). Other bases such as K_2CO_3 and K_3PO_4 were less efficient (entries 4 and 6), while no reaction occurred in the case of Et_3N and Ag_2CO_3.

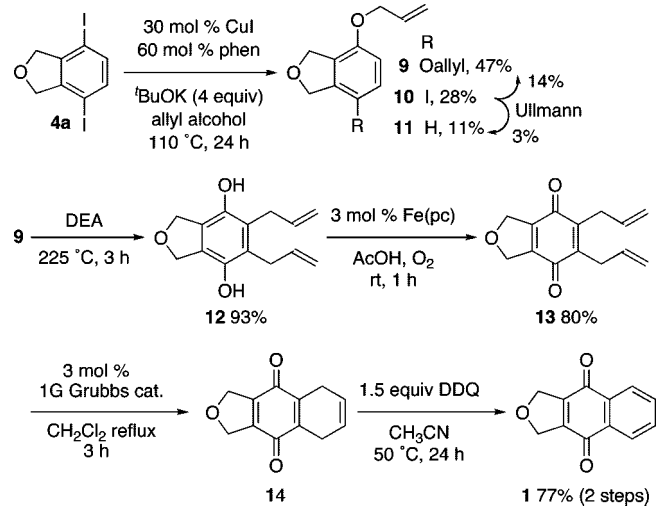
Substituted phenanthroline derivatives were then examined as ligands. A 3,4,7,8-tetramethyl derivative **B** gave a similar result as phen **A** (entry 7).[7f,11,13] Electron-rich 4,7-dimethoxy analogue **C** increased the conversion rate of **10**, but undesired **11** was formed as a major product in 50% yield (entry 8).[14] In contrast, electron-deficient 4,7-dichloro analogue **D** hardly furnished **9** and undesired products were produced along with **10** (entry 9). The reaction was very sluggish in the case of neocuproine **E** (entry 10).[13,15] None of the other Cu−ligand systems improved the yield of **9** (see the Supporting Information).



A: $R^1 = R^2 = R^3 = H$ (phen)
B: $R^1 = R^2 = Me$, $R^3 = H$
C: $R^1 = OMe$, $R^2 = R^3 = H$
D: $R^1 = Cl$, $R^2 = R^3 = H$
E: $R^1 = R^2 = H$, $R^3 = Me$

Because neither increased catalyst loading nor long reaction time improved the yield of **9**, we subjected isolated **10** to Ullmann coupling reaction with allyl alcohol to obtain **9** in 49% yield along with **10** and **11** in 25% and 10% yields, respectively. Consequently, a total yield of 61% of **9** was obtained in the two cycles of the Ullmann coupling reaction (Scheme 4). The Claisen rearrangement of **9** was carried out in *N*,*N*-diethylaniline (DEA) at 225 °C for 3 h according to the report,[12a] producing hydroquinone **12** in 93% yield. The use of Lewis acid catalysts such as BCl_3 or $Bi(OTf)_3$ resulted in partial deallylation or decomposition.[16] The RCM of hydroquinones similar to **12** with Grubbs catalysts proved to be unsuccessfull.[12b] Thus, the

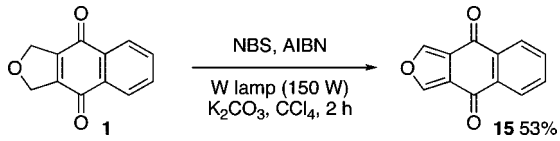
SCHEME 4. Synthesis of 1,3-Dihydronaphtho[2,3-*c*]-furan-4,9-dione 1



protection or oxidation of hydroxy groups should precede RCM.[12] From the viewpoint of improving the atom economy,[17] we decided to examine the aerobic oxidation of **12**, rather than its protection. However, **12** proved to be reluctant to undergo oxidation under air or an O_2 atmosphere. We then employed iron catalysis for the activation of O_2, according to the report of Grennberg and Bäckvall.[18] In the presence of 3 mol % of iron phthalocyanine [Fe(pc)], **12** was stirred in AcOH under an O_2 atmosphere for 1 h. As a result, desired quinone **13** was obtained in 80% yield. Finally, the RCM of **13** was carried out by using first generation (1G) Grubbs catalyst[19] (3 mol %) in refluxing CH_2Cl_2 for 3 h to afford cyclohexadiene product **14**, which was slowly dehydrogenated in the air. The formation of **14** was inferred from its ^{1}H NMR spectrum showing three singlet peaks at δ 3.09, 5.02, and 5.82 ppm with an integral ratio of 2:2:1. The complete aromatization of **14** was conducted with DDQ in acetonitrile at 50 °C for 24 h to afford **1** in a two-step yield of 77%.

(13) Kelkar, A. A.; Patil, N. M.; Chaudhari, R. V. *Tetrahedron Lett.* **2002**, *43*, 7143–7146.
(14) (a) Altman, R. A.; Buchwald, S. L. *Org. Lett.* **2006**, *8*, 2779–2782. (b) Altman, R. A.; Koval, E. D.; Buchwald, S. L. *J. Org. Chem.* **2007**, *72*, 6190–6199.
(15) Gujadhur, R. K.; Bates, C. G.; Venkataraman, D. *Org. Lett.* **2001**, *3*, 4315–4317.
(16) For a review of catalytic Claisen rearrangement, see: Majumdar, K. C.; Alam, S.; Chattopadhyay, B. *Tetrahedron* **2008**, *64*, 597–643.
(17) (a) Trost, B. M. *Science* **1991**, *254*, 1471–1477. (b) Trost, B. M. *Angew. Chem., Int. Ed.* **1995**, *34*, 259–281.
(18) Grennberg, H.; Bäckvall, J. E. *Acta Chem. Scand.* **1993**, *47*, 506–508.
(19) Schwab, P.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1996**, *118*, 100–110.

SCHEME 5. Dehydrogenation of 1 Leading to Naphtho[2,3-*c*]furan-4,9-dione 15



Finally, we carried out the dehydrogenation of **1** leading to naphtho[2,3-*c*]furan-4,9-dione **15** (Scheme 5).[20] This compound has been synthesized only once by Karichiappan and Wege,[20a] although it has a parent framework found in naturally occurring products such as ventilone A, monosporascone, or arthoniafurone A (Figure 2).[1]

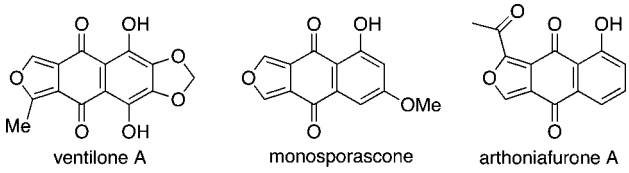


FIGURE 2. Naturally occurring naphtho[2,3-*c*]furan-4,9-diones.

According to the reported procedure,[20b] **1** was treated with NBS and K_2CO_3 in the presence of a small amount of AIBN in CCl_4 under irradiation with a 150-W tungsten lamp for 2 h. Although the chromatographic separation was hampered due to its diminished solubility in common organic solvents, **15** was isolated by recrystallization from hot CH_2Cl_2 in 53% yield. The formation of **15** was corroborated from the following observations: the singlet signal of the methylene protons on the dihydrofuran ring in **1** (δ 5.16 ppm) disappeared, but instead, a new singlet peak of the furan ring of **15** appeared at δ 8.23 ppm. Other analytical data were also in good agreement with those previously reported.[20a]

Conclusion

In conclusion, we have developed the synthetic route to isobenzofuran-4,7(1*H*,3*H*)-diones and 1,3-dihydronaphtho[2,3-*c*]-furan-4,9-dione. In this method, we employed diiodophthalan derivatives that were readily obtained from the Cp*RuCl(cod)-catalyzed [2 + 2 + 2] cycloaddition of an ether-tethered diiododiyne with alkynes. One of the key transformations was the Ullmann coupling of the diiodophthalans with alcohols with use of the CuI/phen catalyst system. The Ullmann coupling reaction of methanol was conveniently carried out under MW heating conditions, and the resulting methoxydation products were oxidized by CAN or H_2O_2 to afford isobenzofuran-4,7(1*H*,3*H*)-diones. On the other hand, Ullmann coupling with allyl alcohol was carried out under conventional heating conditions by a two-batch process. The obtained diallyl ether was transformed into 1,3-dihydronaphtho[2,3-*c*]furan-4,9-dione by means of Claisen rearrangement, Fe-catalyzed aerobic oxidation, RCM with 1G Grubbs catalyst, and aromatization with DDQ.

Experimental Section

General Considerations. Column chromatography was performed on silica gel with mixed solvents. ^{1}H and ^{13}C NMR spectra were obtained for samples in $CDCl_3$ solutions at 25 °C. ^{1}H NMR chemical shifts are reported in terms of chemical shift (δ, ppm) relative to the singlet at 7.26 ppm for chloroform. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; sept, septet; m, multiplet. Coupling constants are reported in hertz. ^{13}C NMR spectra were fully decoupled and are reported in terms of chemical shift (δ, ppm) relative to the triplet at 77.0 ppm for $CDCl_3$. Elemental analyses were performed at the Center for Advanced Materials Analysis of the Tokyo Institute of Technology. Melting points were obtained in capillary tubes. Microwave irradiation experiments were carried out with a single-mode microwave reactor (CEM Discover Lab-Mate). Closed reaction vessels were used, and the temperature was monitored by an online IR detector. *p*-Diiodobenzenes **4a**−**c** were obtained according to the previous report.[5]

Synthesis of Isobenzofuran-4,7(1*H*,3*H*)-diones 6a−c. Synthesis of Dimethoxyphthalan 5a. In a 6-mL reaction tube, diiodobenzene **4a** (111.6 mg, 0.30 mmol), CuI (5.8 mg, 0.030 mmol), phen·H_2O (12.1 mg, 0.060 mmol), and ^{t}BuOK (80.7 mg, 0.72 mmol) were mixed with methanol (1 mL) at room temperature. The reaction tube was sealed with a Teflon cap and heated in a microwave reactor at 150 °C for 1.5 h. After cooling to room temperature, the solution was diluted with AcOEt (3 mL) and filtered through a pad of Celite. The insoluble materials were further washed with AcOEt (10 mL). The filtrate was concentrated in vacuo. The residue was purified by silica gel flash column chromatography (eluent hexane−AcOEt 30:1) to give dimethoxyphthalan **5a** (43.0 mg, 79%) as a white solid (mp 88−89 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.79 (s, 6 H), 5.11 (s, 4 H), 6.68 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.7, 72.6, 109.8, 128.9, 148.2; MS (EI) *m*/*z* (%) 180 (100) $[M]^+$, 151 (59) $[MH - CH_2O]^+$, 137 (52) $[MH - CH_2OCH_2]^+$, 121 (61) $[M - Me - CH_2OCH_2]^+$/ EA calcd (%) for $C_{10}H_{12}O_3$ (180.20): C 66.65, H 6.71. Found: C 66.38, H 6.80.

Synthesis of Isobenzofuran-4,7(1*H*,3*H*)-dione 6a. In a 50-mL round-bottomed flask, to a solution of dimethoxyphthalan **5a** (145.0 mg, 0.80 mmol) in CH_3CN (8 mL) was added dropwise a solution of $Ce(NH_4)_2(NO_3)_6$ (970.2 mg, 1.77 mmol) in H_2O (8 mL) at room temperature. After being stirred for 10 min, the solution was diluted with H_2O (10 mL) and extracted with AcOEt (4 × 10 mL). The combined organic layer was washed with H_2O (15 mL) and brine (10 mL), then dried over $MgSO_4$. The solvent was removed in vacuo, and the crude yield of 74% was estimated by ^{1}H NMR. Analytically pure isobenzofuran-4,7(1*H*, 3*H*)-dione **6a** (74.3 mg, 62%) was obtained as an orange solid by recrystallization from AcOEt (mp 130−132 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.04 (s, 4 H), 6.74 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 73.4, 136.8, 144.2, 183.6; MS (EI) *m*/*z* (%) 150 (38) $[M]^+$, 148 (50) $[M - 2H]^+$, 121 (100) $[MH - CH_2O]^+$. EA calcd (%) for $C_8H_6O_3$ (150.13): C 64.00, H 4.03. Found: C 63.84, H 4.19.

Representative Procedures for Synthesis of Isobenzofuran-4,7(1*H*,3*H*)-diones 6b and 6c: Synthesis of 6b. In a 6-mL reaction tube, diiodobenzene **4b** (128.3 mg, 0.30 mmol), CuI (5.7 mg, 0.030 mmol), phen·H_2O (12.0 mg, 0.060 mmol), and ^{t}BuOK (80.8 mg, 0.72 mmol) were mixed with methanol (1 mL) at room temperature. The reaction tube was sealed with a Teflon cap and heated in a microwave reactor at 150 °C for 1 h. After cooling to room temperature, the solution was diluted with AcOEt (3 mL), then was filtered through a pad of Celite. The insoluble materials were further washed with AcOEt (10 mL). The filtrate was concentrated in vacuo. The residue was dissolved in HCO_2H (3 mL) and degassed at −78 °C. To this solution was added aqueous H_2O_2 (30%, 0.31 mL, 3.0 mmol) at 30 °C and the reaction mixture was stirred at this temperature for 1 h. This solution was diluted with AcOEt (10 mL) and washed with H_2O (10 mL). The product was further extracted with AcOEt (3 × 10 mL), and the combined organic layer was washed with H_2O (15 mL) and brine (10 mL), then dried over $MgSO_4$. After concentration in vacuo, the residue was purified by silica gel flash column chromatography (eluent hexane−AcOEt 150:1−120:1) to give **6b** (34.8 mg, 56%) as a reddish-brown oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, J = 7.2 Hz, 3 H), 1.33−1.53

(20) (a) Karichiappan, K.; Wege, D. *Aust. J. Chem.* **2000**, *53*, 743–747. (b) Buttery, J. H.; Wege, D. *Aust. J. Chem.* **1998**, *51*, 409–419.

(m, 4 H), 2.44 (dt, J = 7.2, 1.2 Hz, 2 H), 5.01 (s, 4 H), 6.50 (t, J = 1.2 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.7, 22.4, 28.3, 30.2, 73.3, 73.4, 132.6, 144.2, 144.4, 150.3, 183.9, 184.0; MS (EI) m/z (%) 206 (32) $[M]^+$, 204 (15) $[M - 2H]^+$, 177 (100) $[MH - CH_2O]^+$, 164 (93) $[M - CH_2{=}CHCH_3]^+$, 149 (44) $[M - (CH_2)_3CH_3]^+$. EA calcd (%) for $C_{12}H_{14}O_3$ (206.24): C 69.88, H 6.84. Ffound: C 69.81, H 6.94.

Analytical data for 6c: orange solid (recrystallization from hexane−AcOEt; mp 158−160 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.09 (s, 4 H), 6.80 (s, 1 H), 7.45−7.47 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 73.4, 73.6, 128.6, 129.3, 130.2, 132.3, 133.2, 144.3, 144.6, 146.7, 183.1, 183.7; MS (EI) m/z (%) 226 (100) $[M]^+$, 198 (26) $[MH - CO - CH_2O]^+$, 141 (49) $[MH - 2CO - CH_2O]^+$. EA calcd (%) for $C_{14}H_{10}O_3$ (226.23): C 74.33, H 4.46. Found: C 74.24, H 4.55.

Synthesis of 1,3-Dihydronaphtho[2,3-*c*]furan-4,9-dione 1. Procedures for Ullmann Coupling of 4a with Allyl Alcohol. In a 40-mL sealed reaction tube, diiodobenzene **4a** (111.6 mg, 0.30 mmol), CuI (17.2 mg, 0.090 mmol), phen·H_2O (35.7 mg, 0.180 mmol), and ^{t}BuOK (134.7 mg, 1.20 mmol) were mixed with allyl alcohol (4 mL) at room temperature. The reaction mixture was stirred on an oil bath at 110 °C for 24 h. After cooling to room temperature, the solution was diluted with AcOEt (5 mL), then filtered through a pad of Celite. The insoluble materials were further washed with AcOEt (15 mL). The filtrate was concentrated in vacuo, and the residue was purified by silica gel flash column chromatography (eluent hexane−AcOEt 600:1) to give **10** (25.4 mg, 28%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.54 (dt, J = 5.2, 1.5 Hz, 4 H), 4.98−5.00 (m, 2 H), 5.24−5.26 (m, 2 H), 5.29 (dq, J = 10.5, 1.5 Hz, 2 H), 5.37 (dq, J = 17.4, 1.5 Hz, 2 H), 6.00 (ddt, J = 17.4, 10.5, 5.2 Hz, 2 H), 6.53 (d, J = 8.4 Hz, 1 H), 7.50 (d, J = 8.4 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 68.9, 73.8, 75.7, 78.1, 112.8, 117.8, 128.5, 132.6, 137.4, 145.1, 153.4; MS (EI) m/z (%) 302 (78) $[M]^+$, 272 (8) $[M - CH_2O]^+$, 260 (100) $[M - H - CH_2CH{=}CH_2]^+$. EA calcd (%) for $C_{11}H_{11}IO_2$ (302.11): C 43.73, H 3.67. Found: C 43.87, H 3.72.

Further elution (hexane−AcOEt 500:1) to give **11** (5.7 mg, 11%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.57 (dt, J = 5.1, 1.5 Hz, 4 H), 5.12 (s, 2 H), 5.13 (s, 2 H), 5.28 (dq, J = 10.5, 1.5 Hz, 2 H), 5.39 (dq, J = 17.4, 1.5 Hz, 2 H), 6.04 (ddt, J = 17.4, 10.5, 5.1 Hz, 2 H), 6.73 (d, J = 7.8 Hz, 1 H), 6.83 (d, J = 7.5 Hz, 1 H), 7.22 (dd, J = 7.8, 7.5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 68.7, 72.1, 74.1, 110.0, 113.3, 117.5, 127.3, 129.0, 133.1, 141.2, 153.2; MS (EI) m/z (%) 176 (37) $[M]^+$, 147 (13) $[M - H - CH_2O]^+$, 134 (100) $[M - H - CH_2CH{=}CH_2]^+$. EA calcd (%) for $C_{11}H_{12}O_2$ (176.21): C 74.98, H 6.86. Found: C 74.86, H 6.98.

Further elution (hexane−AcOEt 100:1) to give **9** (33.1 mg, 47%) as a white solid (mp 53−54 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.50 (dt, J = 5.2, 1.5 Hz, 4 H), 5.13 (s, 4 H), 5.26 (dq, J = 10.5, 1.5 Hz, 2 H), 5.37 (dq, J = 17.2, 1.5 Hz, 2 H), 6.02 (ddt, J = 17.2, 10.5, 5.2 Hz, 2 H), 6.66 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 69.3, 72.7, 111.4, 117.3, 129.4, 133.4, 147.3; MS (EI) m/z (%) 232 (53) $[M]^+$, 191 (47) $[M - CH_2CH{=}CH_2]^+$, 149 (100) $[M - 2\,CH_2CH{=}CH_2 - H]^+$. EA calcd (%) for $C_{14}H_{16}O_3$ (232.28): C 72.39, H 6.94. Found: C 72.21, H 7.19.

Procedures for Claisen Rearrangememt of 9. In a 100-mL round-bottomed flask, a solution of **9** (465.4 mg, 2.00 mmol) in *N*,*N*-diethylaniline (27 mL) was stirred on an oil bath at 225 °C under Ar atmosphere for 3 h. After cooling to room temperature, the solution was concentrated in vacuo, then the residue was purified by short column chromatography (eluent hexane−AcOEt 3:1) to give diallylhydroquinone **12** (434.0 mg, 93%) as a brown solid (mp 99−101 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.40 (dt, J = 5.7, 1.5 Hz, 4 H), 4.59−4.62 (br m, 2 H), 5.05 (dq, J = 17.2, 1.5 Hz, 2 H), 5.13 (s, 4 H), 5.13 (dq, J = 10.2, 1.5 Hz, 2 H), 5.96 (ddt, J = 17.2, 10.2, 5.7 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.8, 72.4, 116.3, 124.0, 126.0, 135.7, 142.5; MS (EI) m/z (%) 232 (100) $[M]^+$, 203 (62) $[M - H - CH_2O]^+$, 187 (22) $[M - H - CH_2OCH_2]^+$, 161 (40) $[M - CH_2O - CH_2CH{=}CH_2]^+$. EA calcd (%) for $C_{14}H_{16}O_3$ (232.28): C 72.39, H 6.94. Found: C 72.36, H 6.97.

Procedures for Oxidation of 12. In a 100-mL round-bottomed flask, hydroquinone **12** (434.0 mg, 1.87 mmol) and iron(II) phthalocyanine (34.1 mg, 0.060 mmol) were mixed in AcOH (20 mL) at room temperature under O_2. After stirring for 1 h at room temperature, the solution was diluted with AcOEt (5 mL) and filtered through a pad of Celite. The insoluble materials were further washed with AcOEt (15 mL). The filtrate was concentrated in vacuo, and the obtained residue was purified by silica gel flash column chromatography (eluent hexane−AcOEt 200:1) to give diallylquinone **13** (344.3 mg, 80%) as an orange oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.28 (dt, J = 6.3, 1.5 Hz, 4 H), 5.02 (s, 4 H), 5.08 (dq, J = 17.4, 1.5 Hz, 2 H), 5.08 (dq, J = 9.6, 1.5 Hz, 2 H), 5.78 (ddt, J = 17.4, 9.6, 6.3 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.0, 73.5, 117.1, 133.4, 142.9, 144.0, 183.5; MS (EI) m/z (%) 229 (28) $[M - H]^+$, 201 (100) $[MH - CH_2O]^+$, 187 (38) $[MH - CH_2OCH_2]^+$, 173 (43) $[M - CH_2OCH_2 - CH{=}CH_2]^+$. EA calcd (%) for $C_{14}H_{14}O_3$ (230.26): C 73.03, H 6.13. Found: C 72.96, H 6.20.

Procedures for Synthesis of 1. In a 50-mL round-bottomed flask, Grubbs 1G catalyst (3.43 mg, 0.0042 mmol) and **12** (31.9 mg, 0.139 mmol) were refluxed in degassed dichloromethane (3.5 mL) under Ar atmosphere for 3 h. After concentration in vacuo, the obtained residue was dissolved in acetonitrile (2.7 mL) and to this solution was added DDQ (47.6 mg, 0.210 mmol). This solution was degassed and stirred at 50 °C under Ar atmosphere for 24 h. After evaporation of the solvent, the residue was purified by silica gel flash column chromatography (eluent hexane $CHCl_3$ 1:1−0:1) to give quinone **1** (21.4 mg, 77%) as a light-brown solid (mp 203−205 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.16 (s, 4 H), 7.76 (dd, J = 5.5, 3.3 Hz, 2 H), 8.11 (dd, J = 5.5, 3.3 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 73.8, 126.4, 132.9, 133.9, 146.5, 181.4; MS (EI) m/z (%) 200 (100) $[M]^+$, 172 (45) $[M - CO]^+$, 144 (49) $[M - 2\,CO]^+$. EA calcd (%) for $C_{12}H_8O_3$ (200.19): C 72.00, H 4.03. Found: C 72.15, H 3.88.

Procedures for Synthesis of 15. In a 30-mL round-bottomed flask, **1** (37.91 mg, 0.189 mmol), NBS (37.0 mg, 0.208 mmol), K_2CO_3 (52.1 mg, 0.377 mmol), and AIBN (3.79 mg, 0.023 mmol) were dissolved in CCl_4 (11 mL) and the solution was degassed at −78 °C. The reaction mixture was irradiated by a 150-W tungsten lamp under Ar atmosphere for 2 h. The solution was diluted with CH_2Cl_2 (10 mL) and poured into H_2O (20 mL). The product was extracted with CH_2Cl_2 (3 × 20 mL) and the combined organic layer was dried over $MgSO_4$. After concentration in vacuo, the crude product was purified by recrystallization from hot CH_2Cl_2 to give isofuranonaphthoquinone **15** (20.0 mg, 53%) as an orange needle (mp 275−280 °C dec). The following analytical data are in good agreement with those reported;[5] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (dd, J = 6.0, 3.6 Hz, 2 H), 8.23 (s, 2 H), 8.31 (dd, J = 6.0, 3.6 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 123.0, 127.5, 134.1, 135.4, 145.9, 179.4; MS (EI) m/z (%) 198 (100) $[M]^+$, 170 (19) $[M - CO]^+$, 142 (48) $[M - 2\,CO]^+$.

Acknowledgment. This research was partially supported by the Ministry of Education, Science, Sports and Culture, Grant-in-Aid for Scientific Research (B) (20350045), Scientific Research on Priority Area "Chemistry on Concerto Catalysis" (20037018), and the Sumitomo Foudation. We thank Prof. K. Tomooka (Kyushu University) for use of a NMR spectrometer and Profs. H. Suzuki and T. Takao (Tokyo Instituted of Technology) for use of mass spectrometers.

Supporting Information Available: Ligand-screening experiments for Ullmann coupling of **4a** with allyl alcohol and ^{1}H and ^{13}C NMR data for products. This material is available free of charge via the Internet at http://pubs.acs.org.

JO9005975