negative logarithm of k/T vs. $1/T$ based on the absolute reaction rate theory equation, from which ΔS^*(intercept) and ΔH^*(slope) were determined for the five absorption bands of CBDA and the four absorption bands of CPDA used in this work, are presented in Figure 1.

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Registry No.—Cyclobutane-1,1-dicarboxylic acid, 5445-51-2; cyclopropane-1,1-dicarboxylic acid, 598-10-7; diethyl cyclopropane-1,1-dicarboxylate, 1559-02-0; α-carboxy-γ-butyrolactone, 4360-91-2.

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Synthesis of the 1-, 2-, 3-, and 4-Hydroxy Isomers of Benz[*a*]anthracene-7,12-dione, Benz[*a*]anthracene, and 7,12-Dimethylbenz[*a*]anthracene[1]

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Studies on the mechanisms of chemical carcinogenesis require the use of potential metabolites of known carcinogens. The 1-, 2-, 3-, and 4-hydroxy isomers of benz[*a*]anthracene-7,12-dione (**4a–d**), of benz[*a*]anthracene (**6a–d**), and of 7,12-dimethylbenz[*a*]anthracene (**8b–d**) have been synthesized. A Diels–Alder reaction between the appropriate methoxystyrene (**2a–c**) and 1,4-naphthoquinone (**1**) produced the respective methoxybenz[*a*]anthracene-7,12-diones (**3a–d**). These methoxy diones were demethylated to yield the hydroxydiones **4a–d**, reduced and demethylated to yield the hydroxybenz[*a*]anthracenes (**6a–d**), and converted via the classical Grignard procedure followed by demethylation to the hydroxy-7,12-dimethylbenz[*a*]anthracenes (**8b–d**).

Current interest in the metabolism of carcinogenic polycyclic aromatic hydrocarbons (PAH), such as the potent carcinogen 7,12-dimethylbenz[*a*]anthracene (DMBA) and the weaker carcinogen benz[*a*]anthracene[2] (BA), has led to renewed efforts to synthesize potential metabolites of these compounds. Since recent studies have suggested that the angular ring is the site of metabolic activation for these compounds, our initial efforts were directed toward the synthesis of the A ring (1, 2, 3, 4 positions) phenols of BA and DMBA. Some of these compounds have been previously synthesized by tedious multistep routes.[3–10] We describe here a new, relatively simple, and direct approach to the preparation of these compounds by a general synthetic procedure from readily available starting materials.

Results and Discussion

The key intermediates in the synthesis of the phenolic isomers of BA and DMBA were the 1-, 2-, 3-, and 4-methoxybenz[*a*]anthracene-7,12-diones (**3a–d**) shown in Scheme I. Our recent report that a Diels–Alder reaction between 1,4-naphthoquinone and substituted styrenes produced 1-, 2-, 3-, 4-, and 5-substituted BADs[11,12] indicated that **3a–d** could be prepared easily, in one step. From these diones, the BA derivatives could be obtained in one additional step,[13] and the DMBA derivatives could be obtained in two steps using the classical Grignard procedure.[8,14,15]

The 1- and 3-MeOBADs (**3a** and **3c**) were obtained as a

Scheme I

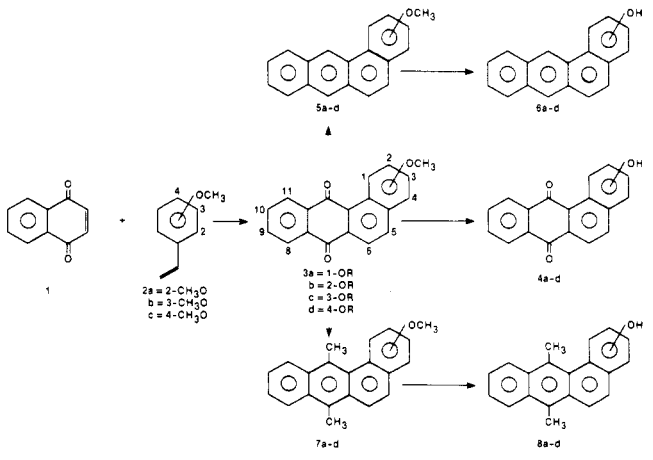

Table I. Characteristic Infrared Bands from the Fingerprint Region of the Spectra of Isomeric Hydroxy Derivatives

compd	IR bands (1000–600 cm^{-1})
4a	962, 884, 853, 848, 786, 753, 718, 693, 657
4b	945, 890, 885, 860, 850, 832, 781, 718, 639
4c	994, 870, 841, 809, 789, 718, 692, 650, 625
4d	997, 839, 795, 785, 752, 719, 683, 656
6a	894, 889, 879, 818, 761, 753, 740
6b	877, 864, 835, 830, 751, 739
6c	957, 903, 888, 870, 832, 828, 750, 739, 690
6d	933, 892, 804, 748
8b	839, 829, 752
8c	875, 867, 828, 753, 748
8d	907, 803, 770, 744

mixture of isomers from the reaction of naphthoquinone (**1**) and *m*-methoxystyrene[16] (**2b**) in the presence of chloranil. The isomers were easily separated by column chromatography and after recrystallization yielded 3% of **3a** and 45% of **3c.** The reaction of **1** and *o*-methoxystyrene (**2a**) in the presence of chloranil gave **3d** in a 43% yield. A modified procedure using 2 mol of **1** and 1 mol of *p*-methoxystyrene (**2c**) was used to prepare **3b.** The crude reaction mixture was oxygenated prior to column chromatography purification. The yield of **3b** was 19%. Demethylation of the four MeOBAD iosmers, **3a–d,** using 48% HBr/HOAc[8] under nitrogen gave the respective 1-, 2-, 3-, and 4-HOBADs (**4a–d**).

Aluminum tricyclohexoxide was used to reduce the MeOBADs to the respective BA analogues where the substituents were not located near the carbonyl moiety.[13] The reductions of **3b,c,d** to **5b,c,d** were accomplished in good yields by this method. The sterically crowded **5a** was obtained in 10% yield by this method. The reduction of **3a** to **5a** using zinc/acetic acid/pyridine was accomplished in 32% yield. Demethylation of each of the MeOBA isomers in 48% HBr/acetic acid[8] under nitrogen gave the respective HOBAs (**6a–d**).

The 2-, 3-, and 4-MeODMBAs (**7b–d**) were obtained by the classical Grignard procedure[8,14,15] from the corresponding BADs (**3b–d**) in good yields. Several attempts at preparing **7a** by this method led to numerous products of which a minor component was thought to be **7a.** Demethylation of **7b–d** to yield the phenols **8b–d** was accomplished using either 48% HBr/acetic acid,[8] boron tribromide/benzene,[18] or sodium ethylmercaptide/dimethylformamide.[9,19,20] The latter procedure gave the best yields for compounds **8b** and **8c,** while 48% HBr/acetic acid gave the best yield for **8d.** The 1-methoxy and 1-HODMBAs (**7a** and **8a**) were not isolated in sufficient quantities to be identified.[21]

Spectral Properties

The mass spectra of the hydroxy compounds **4a–d, 6a–d,** and **8b–d** were characterized by the molecular ions as the base peak. The hydroxy diones (**4a–d**) gave characteristic losses of $M^{+\cdot} - 17$ ($HO^{\cdot}$) and $M^{+\cdot} - 56$ (2CO) as would be expected for compounds of this structure.[22] The BA phenols (**6a–d**) showed a loss of $M^{+\cdot} - 29$ typical of phenols,[22] whereas the DMBA phenols showed a characteristic $M^{+\cdot} - 15$ ($CH_3^{\cdot}$) loss.

The infrared bands from the fingerprint region of the isomeric hydroxyl derivatives spectra showed significant differences for each isomer. In each of the three series, **4a–d, 6a–d,** and **8b–d,** the position of hydroxyl substitution was characteristically different for each isomer, and the differences are readily discernible as shown in Table I.

The proton magnetic resonance spectra of **3a–d** and **4a–d** were particularly useful in establishing the positions of substitution in the angular benzene ring. Compound **4a** showed the absence of a proton resonance signal in the region of δ 9–10 ($CDCl_3$) assignable to H_1. The hydroxyl proton in **4a** was observed at δ 11.3 ($CDCl_3$) due to hydrogen bonding to the C_{12} carbonyl oxygen and should not be confused with an H_1. The spectrum of **4b** was characterized by a doublet (2–3 Hz) for H_1 at δ 9.3, while **4c** showed a doublet (9–10 Hz) centered at δ 9.6 and **4d** showed a complex doublet (9–10 Hz) centered at δ 9.3. In all cases, line broadening was observed because of unresolved spin–spin coupling. The proton magnetic resonance spectra of **3a–d** and **4a–d** were found to be consistent with the assigned positions of substitution. The NMR spectra of **6a–d** and **8b–d** were too complex to assign the aromatic protons. However, the respective isomer positions were established by literature melting points.

Table II. Ultraviolet Absorption Data[23] for the Phenols (95% Ethanol)

compd	λ_{max}, nm (log ϵ), phenols
4a	311 (4.36), 250 (4.35), 222 (4.61)
4b	290 (4.33), 254 (4.63), 224 (4.61), 211 (4.52)
4c	304 (4.43), 222 (4.47)
4d	306 (4.38), 244 (4.36), 218 (4.61)
6a	309 (4.54), 282 (4.84), 273 (4.81), 255 (4.70), 227 (**4.65**)
6b	298 (4.64), 287 (4.68), 278 (4.67), 270 (4.68), 263 (**4.64**), 227 (4.71)
6c	288 (4.81), 244 (4.54)
6d	313 (4.39), 287 (4.79), 277 (4.71), 257 (4.69), 245 (**4.71**), 230 (4.64), 204 (4.42)
8b	302 (4.55), 291 (4.59), 277 (4.52), 267 (4.51), 226 (**4.44**)
8c	298 (4.82), 244 (4.15)
8d	322 (4.61), 292 (4.74), 281 (4.78), 265 (4.68), 228 (4.62)

Ultraviolet absorption data for the phenols in 95% ethanol were characteristically different for each isomer (**6a–d** and **8b–d**). These differences are easily discernible as shown in Table II.

Experimental Section

All melting points were determined using a Fisher–Johns hot-stage apparatus and are uncorrected. Mass spectra were taken on a Finnigan 3300 mass spcetrometer equipped with a Finnigan 6000 data system. The UV spectra[23] were obtained on a Cary 17 and Gilford 250 UV–vis spectrophotometers. The fluorescence data given in the Supplementary Material were obtained on a Perkin-Elmer Model MPF-3 fluorescence spectrophotometer. Proton magnetic resonance spectra were taken on a Varian XL-100 spectrometer using $CDCl_3$ (0.5% Me_4Si) as solvent, while the IR spectra were obtained on a Perkin-Elmer 467 spectrophotometer as KBr pellets. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn. All new compounds gave elemental analyses within ±0.4% of theoretical.

General Procedure for Methoxybenz[*a*]anthrace-7,12-diones (3a,c,d). To 5–10 mL of toluene was added 5 to 50 mmol of 1,4-naphthoquinone (**1**) and equimolar amounts of methoxystyrenes[16] (**2a** or **2b**) and chloranil. The mixture was placed in an oil bath (at 80–85 °C) for 1 to 4 weeks. When little or no naphthoquinone remained, as observed by TLC on silica gel GF plates using benzene as solvent, the reaction mixture was chromatographed on Silicar CC-7 (Mallinckrodt) by elution with hexane and then benzene–hexane (1:1). The progress of the components through the column was followed by observing the red-orange colors of the diones with long wavelength UV light. The MeOBADs isolated were recrystallized from either benzene or benzene–hexane.

1-MeOBAD (3a) was isolated in 3% yield (150 mg) after chromatography and recrystallization from benzene–hexane, mp 133–134 °C.

3-MeOBAD (3c) was isolated from the same reaction mixture as 1-MeOBAD in 45% yield (2.3 g) after chromatography and recrystallization from benzene–hexane, mp 169–169.5 °C (lit.[9,10] mp 145, 162–163 °C).

4-MeOBAD (3d) was obtained in 43% yield (1.25 g) after chromatography and recrystallization from benzene, mp 219–220 °C (lit.[8] mp 220–221 °C).

2-MeOBAD (3b) was prepared by the addition of 50 mmol of naphthoquinone and 25 mmol of 4-methoxystyrene (**2c**) to 5–10 mL of toluene and heating at 80–85 °C for 3–4 weeks. The mixture was then reduced to dryness on a rotary evaporator, and 500 mL of a 5% solution of alcoholic potassium hydroxide (95% ethanol) was added to the dark material. The flask was fitted with a reflux condenser, and oxygen was bubbled through for 24 h. After neutralization with concentrated hydrochloric acid, the crude product was extracted with benzene and dried. The solvent was removed by evaporation and the residue was chromatographed as above. After recrystallization from

benzene–hexane, 2.8 g (19% yield) was obtained, mp 200–201 °C(lit.[4] mp 200–201 °C).

General Procedure for Demethylation of MeOBADs to HOBADs (4a–d). To 0.52–1.0 mmol of the methoxybenz[*a*]anthracene-7,12-dione in 2–3 mL of glacial acetic acid under a nitrogen atmosphere was added 0.3–0.7 mL of 48% hydrobromic acid.[8] The mixture was heated under reflux and after 2 h an additional 0.3–0.7 mL of 48% hydrobromic acid was added. The mixture was refluxed under nitrogen for a total of 16–20 h. The progress of the reaction was monitored by TLC using silica gel GF plates and chloroform as solvent. (An exception to the above reflux time was the demethylation of 1-MeOBAD to **4a** which was completed in less than 1 h.) The reaction mixture was poured into water, filtered, washed with water, and dried. The crude product was chromatographed on Silicar CC-7 (Mallinckrodt) and eluted with chloroform.

1-HOBAD (4a) was obtained in 95% yield after chromatography and recrystallization from benzene, mp 235–236 °C.

2-HOBAD (4b) was obtained in 73% yield after chromatography and recrystallization from ethanol, mp 249–252 °C (lit.[3] mp 253–253.5 °C).

3-HOBAD (4c) was obtained in 68% yield after chromatography, mp 252–254.5 °C.

4-HOBAD (4d) was obtained in 20% yield after chromatography and recrystallization from benzene, mp 227–229 °C (lit.[7] mp 224–5 °C).

General Procedure for the Reduction of MeOBADs to MeOBAs (5a–d). Aluminum tricyclohexoxide[13] was prepared by the addition of 1.5 g of aluminum wire, 1 mL of carbon tetrachloride, and 5–10 mg of mercuric chloride to 15–20 mL of distilled cyclohexanol. This mixture was refluxed under nitrogen for 2 h.

To the freshly prepared aluminum tricyclohexoxide solution was added 0.2–1 mmol of the methoxybenz[*a*]anthracene-7,12-dione. This mixture was refluxed under nitrogen until the starting material had disappeared as observed by TLC using silica gel GF plates and benzene as eluting solvent. The hot reaction mixture was poured into ice–water and acidified with stirring to pH 1–3 over 3 h. The aqueous mixture was extracted with benzene. The organic materials were back extracted with water, 5% sodium bicarbonate, and saturated sodium chloride solution and dried ($MgSO_4$). Removal of the benzene gave a solution of the MeOBA in cyclohexanol, from which the MeOBA slowly crystallized upon cooling. Final purification was accomplished by chromatography on Silicar CC-7 and elution with benzene.

1-MeOBA (5a) was obtained in 10% yield after chromatography and recrystallization from benzene–hexane, mp 134–135 °C (lit.[5] mp 131–132 °C).

2-MeOBA (5b) was obtained in 47% yield after chromatography and recrystallization from benzene, mp 165–167 °C (lit.[4] mp 165–166 °C).

3-MeOBA (5c) was obtained in 73% yield after chromatography and recrystallization from benzene, mp 162–163.5 °C (lit.[24] mp 161–162 °C).

4-MeOBA (5d) was obtained in 59% yield after chromatography and recrystallization from benzene, mp 164–166 °C (lit.[5,7] mp 163 °C).

To a mixture of 70 mg of 1-MeOBAD (**3a**), 200 mg of activated zinc, and 5 mL of pyridine was added 20 mL of 80% aqueous acetic acid while the temperature was kept at 80 °C. The mixture was refluxed for 4 h with 10 mL of 80% aqueous acetic acid added at 30-min intervals. The reaction mixture was cooled, the excess zinc was filtered off, and the total volume of filtrate was reduced to approximately 15 mL by rotary evaporation. Water (60 mL) was added and the mixture was extracted with three 20-mL volumes of benzene. Removal of benzene gave a crude product that was chromatographed on Silicar CC-7 using 20% benzene–hexane as eluting solvent. A total of 21 mg (32% yield) of **5a** was obtained, mp 134–135 °C.

General Procedure for the Demethylation of MeOBAs to HOBAs (6a–d). The reaction procedures and conditions for the demethylation of MeOBAs were as stated above for the MeOBADs. The solvent system used to elute the TLC plates for monitoring the progress of the reactions was benzene.

1-HOBA (6a) was obtained in 66% yield after chromatography, mp 168–169 °C (lit.[5] mp 168–170 °C).

2-HOBA (6b) was obtained in 87% yield after chromatography and recrystallization from benzene, mp 198–199 °C (lit.[4] mp 191.5–193.5 °C).

3-HOBA (6c) was obtained in 34% yield after chromatography and recrystallization from benzene, mp 218–219 °C.

4-HOBA (6d) was obtained in 66% yield after chromatography and recrystallization from benzene, mp 235–236 °C (lit.[6] mp 231.5–232.5 °C).

General Procedure for Methoxy-7,12-dimethylbenz[*a*]anthracenes (7a–d). To a solution of 0.3–1.7 mmol of the methoxybenz[*a*]anthracene-7,12-dione (**3a–d**) in 25 mL of dry benzene was added an excess of freshly prepared methylmagnesium iodide in ether. During the initial addition, each reaction mixture turned a characteristic color, and near completion of the Grignard addition, the solution became transparent. This mixture was stirred at room temperature for 1 h and then added dropwise to 50 mL of methanol and 25 mL of 57% hydroiodic acid at 0–5 °C with vigorous stirring. Cold acetic acid (50–100 mL) was added to precipitate the iodomethyl intermediate which was immediately collected by filtration. The yellow-orange intermediate was dissolved with 25 mL of purified dioxane (Al_2O_3 purified) containing 1 mL of concentrated hydrochloric acid. This solution was added to a mixture of 2 g of anhydrous stannous chloride, 5 mL of concentrated hydrochloric acid, and 25 mL of purified dioxane and refluxed for 20–30 min. The reaction mixture was poured into ice-water and extracted with benzene. The organic solution was washed with water, 5% sodium bicarbonate solution, and saturated sodium chloride and dried ($MgSO_4$). Removal of the solvent gave a crude product that was purified by column chromatography on Silicar CC-7 using benzene as the eluting solvent.

1-MeODMBA (7a). Numerous products were obtained after preparative thin-layer chromatography of the crude reaction mixture. A minor component had a mass spectrometry parent ion *m/e* of 286, an NMR spectrum showing three methyl groups at δ 2.8, 3.0, and 3.9, and aromatic protons along with unknown absorptions. Amounts of this component large enough for further purification and analyses were not obtained.

2-MeODMBA (7b) was obtained in 72% yield (450 mg) after chromatography, mp 131–132.5 °C (lit.[9,25] mp 131–132.5, 131–132 °C).

3-MeODMBA (7c) was obtained in 53% yield (144 mg) after chromatography, mp 128–129 °C (lit.[9] mp 131–132 °C).

4-MeODMBA (7d) was obtained in 63% yield (125 mg) after chromatography, mp 118–120 °C (lit.[8,9] mp 121, 120–121 °C).

General Procedures for the Demethylation of MeODMBA to HODMBA (8a–d). a. 48% Hydrobromic Acid/Acetic Acid.[8] The conditions were identical with those stated above for HOBAs. The yields were 55% for **8b,** 80% for **8c,** and 63% for **8d.**

b. Boron Tribromide/Benzene.[18] To 0.27–0.7 mmol of the methoxy-7,12-dimethylbenz[*a*]anthracene (**7b–d**) in 10 mL of dry benzene was added dropwise 1–1.5 mL of boron tribromide in 5 mL of dry benzene under a nitrogen atmosphere. Upon completion of the addition, the mixture was refluxed for 1 h and poured into 50 mL of ice-water. Ethyl acetate extraction, washing of the organic layer with water, drying ($MgSO_4$), and removal of the solvent gave a crude product. Chromatography on Silicar CC-7 using benzene as eluting solvent gave the purified compound that was recrystallized from benzene–hexane. The yields obtained by this method were 64% for **8b,** 56% for **8c,** and 34% for **8d.**

c. Sodium Ethylmercaptide/Dimethylformamide.[19,20] A solution of 0.15–0.5 mmol of **7b–d** in DMF was added to 0.5 to 1 g of sodium ethylmercaptide in DMF. The mixture was placed in an oil bath (at 160 °C) for 1–2 h. The cooled reaction mixture was poured into 2 N hydrochloric acid and extracted four times with methylene chloride, and the organic material was washed with water and saturated sodium chloride solution. After being dried (Na_2SO_4) and removed from the solvent, the crude products were chromatographed on Silicar CC-7 and eluted with benzene.

1-HODMBA (8a). The crude 1-MeODMBA that was obtained in a minor amount was demethylated as above to give a crude product that had a mass spectrometry ion at *m/e* of 272. Amounts of material necessary for other types of analyses were not obtained.

2-HODMBA (8b) was obtained in 97% yield (131 mg) after chromatography, mp 120–121.5 °C (lit.[9] mp 122–124 °C).

3-HODMBA (8c) was obtained in 95% yield (38 mg) after chromatography, mp 166–168 °C (lit.[9] mp 167–168 °C).

4-HODMBA (8d) was obtained in 65% yield (31 mg) after chromatography, mp 163–164 °C (lit.[8,9] mp 164–165 °C).

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Registry No.—1, 130-15-4; **2a,** 612-15-7; **2b,** 626-20-0; **2c,** 637-69-4; **3a,** 69847-20-7; **3b,** 63216-10-4; **3c,** 63216-11-5; **3d,** 16277-48-8; **4a,** 60549-34-0; **4b,** 69847-21-8; **4c,** 60549-33-9; **4d,** 69847-22-9; **5a,** 69847-23-0; **5b,** 69847-24-1; **5c,** 69847-25-2; **5d,** 63020-56-4; **6a,**

69847-26-3; **6b**, 69847-27-4; **6c**, 4834-35-9; **6d**, 5133-12-0; **7a**, 66240-14-0; **7b**, 66240-30-0; **7c**, 66240-02-6; **7d**, 16277-49-9; **8a**, 66240-13-9; **8b**, 66240-31-1; **8c**, 57266-83-8; **8d**, 14760-53-3; methyl iodide, 74-88-4; aluminum tricyclohexoxide, 1971-69-3.

Supplementary Material Available: Complete proton magnetic resonance spectra, UV data, Infrared spectra, and tables summarizing mass spectra, fluorescence, and phenolate ultraviolet absorption data (21 pages). Ordering information is given on any current masthead page.

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Synthesis of Bromonaphthoquinones from 1,5-Dimethoxynaphthalene

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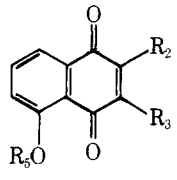
New regiospecific syntheses of 2-bromo-5-methoxy-1,4-naphthoquinone and 3-bromo-5-methoxy-1,4-naphthoquinone have been developed via 4,8-dimethoxy-1-naphthalenecarboxaldehyde, prepared by formylation of 1,5-dimethoxynaphthalene. The naphthaldehyde, on oxidation with *m*-chloroperbenzoic acid and hydrolysis of the intermediate formate, gave 4,8-dimethoxy-1-naphthol. Bromination followed by oxidation of the bromonaphthol gave 3-bromo-5-methoxy-1,4-naphthoquinone in 58% overall yield from 1,5-dimethoxynaphthalene. The naphthol may also be oxidized to 5-methoxy-1,4-naphthoquinone (juglone methyl ether), which was then brominated to give 2-bromo-5-methoxy-1,4-naphthoquinone in 49% overall yield from 1,5-dimethoxynaphthalene. These syntheses offer the advantages of ease of manipulation, increased yields, and purity.

2- and 3-Halo-1,4-naphthoquinones have recently been utilized effectively in the synthesis of naturally occurring anthraquinones because of their regiospecific reaction with ketene acetals.[1-4] The halonaphthoquinones of particular interest are derivatives of 5-hydroxy-1,4-naphthoquinine (**1a**, juglone), a natural product isolated from walnut shells, and include 2-bromo-5-methoxy-1,4-naphthoquinone (**1b**, 2-bromojuglone methyl ether) and 3-bromo-5-methoxy-1,4-naphthoquinone (**1c**, 3-bromojuglone methyl ether) as well as the corresponding hydroxyquinones 2-bromo-5-hydroxy-1,4-naphthoquinone (**1d**, 2-bromojuglone) and 3-bromo-5-hydroxy-1,4-naphthoquinone (**1e**, 3-bromojuglone) which are efficiently methylated to the corresponding ethers. Reported syntheses of the four bromoquinones give poor yields, contamination by the wrong isomer, and/or contamination by compounds containing more than one bromine; these objections led us to seek new syntheses.



1a, $R_5 = H; R_2 = H; R_3 = H$
b, $R_5 = CH_3; R_2 = Br; R_3 = H$
c, $R_5 = CH_3; R_2 = H; R_3 = Br$
d, $R_5 = H; R_2 = Br; R_3 = H$
e, $R_5 = H; R_2 = H; R_3 = Br$
f, $R_5 = CH_3; R_2 = H; R_3 = H$

The reported procedure for the synthesis of 2-bromojuglone methyl ester (**1b**, Scheme I) requires 5-methoxy-1-naphthol (**3**). The production of **3** directly from the cheap and readily available 1,5-dihydroxynaphthalene (**2**) under alkaline[5] or acidic conditions gives a mixture of all three possible products, naphthol, monoether **3**, and 1,5-dimethoxynaphthalene (**4**), with the desired monoether in less than 30% yield. A recently reported[6] synthesis of **3** by total methylation of **2** to **4** followed by monocleavage with sodium thioethoxide in DMF offered a much more attractive route to **3**, and we found that a slight excess of thioethoxide in DMF at 100 °C cleanly demethylated **4** to **3** in 91% yield; neither sodium thiophenoxide nor potassium hydroxide in diethylene glycol was as selective in its cleavage.

Even with a convenient preparation of 5-methoxy-1-naphthol in hand, the ultimate conversion to 2-bromojuglone methyl ether (**1b**) is poor. Naphthol **3** has been reported[7] to be brominated in refluxing CCl_4 (18 h) in 33% yield to 2-bromo-5-methoxy-1-naphthol (**5**). In our hands this reaction proceeds rapidly even at 0 °C in 97% yield; care must be taken, however, as excess bromine leads to polybromination and subsequent contamination of the quinone product. Oxidation of **5** with CrO_3–HOAc gives **1b** in 43% yield from **5** according to the report;[7] however, in our experience this oxidation proceeds poorly to give **1b** in an overall yield of about 15%. We

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