One-Step Preparation of Some 2-Isopropenyl-2,3-dihydronaphtho-[2,3-*b*]furan-4,9-diones

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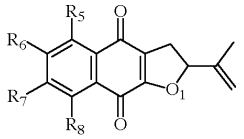
Received May 5, 2000

Some 2-isopropenyl-2,3-dihydronaphtho[2,3-*b*]furan-4,9-diones **1a-f,b',f'** were prepared by one-step cyclizations of 2-hydroxy-1,4-naphthoquinones **2a-f** with 1,4-dibromo-2-methyl-2-butene (**3**).

J. Heterocyclic Chem., **38**, 511 (2001).

Our recent interests were focused on the effective preparation of natural 2-isopropenyl-2,3-dihydrobenzofuran derivatives [1]. Some dehydroiso-α-lapachones **1a,b,b',f,** having a 2-isopropenyl-2,3-dihydronaphtho-[2,3-*b*]furan-4,9-dione structure, were isolated from *Cresentia cujete*, and showed interesting mutagenic activities [2]. In this paper, one-step preparation of 2-isopropenyl-2,3-dihydronaphtho[2,3-*b*]furan-4,9-diones **1** are described.

Chart 1

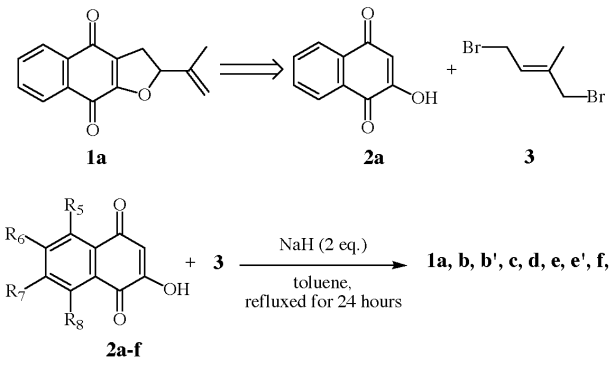


1a) $R_5 = R_6 = R_7 = R_8 = H$ (dehydroiso-α-lapachone)
1b) R_5 = OMe, $R_6 = R_7 = R_8 = H$ (5-methoxydehydroiso-α-lapachone)
1b') R_5 = OH, $R_6 = R_7 = R_8 = H$ (5-hydroxydehydroiso-α-lapachone)
1c) $R_5 = R_7 = R_8 = H$, R_6 = OMe
1d) $R_5 = R_6 = R_8 = H$, R_7 = OMe
1e) $R_5 = R_6 = R_7 = H$, R_8 = OMe
1e') $R_5 = R_6 = R_7 = H$, R_8 = OH
1f) $R_5 = R_6$ = OMe, $R_7 = R_8 = H$ (5,6-dimethoxydehydroiso-α-lapachone)
1f') R_5 = OH, R_6 = OMe, $R_7 = R_8 = H$

Nickl reported the first one-step preparation of 2-isopropenyl-2,3-dihydrobenzofuran derivatives; cyclization of 2',4',6'-trihydroxyacetophenone with 1,4-dibromo-2-methyl-2-butene **3** effectively gave 7-acetyl-2-isopropenyl-2,3-dihydrobenzofuran-4,6-diol in ethanol/sodium ethoxide solution [3]. But, the similar cyclization of general phenols with **3** generates only *O*-alkylation products in ethanol/sodium ethoxide solution. We found that the cyclization of general phenols with **3** was effective in non-polar solvents, such as ether or toluene with sodium metal or sodium hydride [1], and the cyclization of 1,3-diketones with **3** was effective in acetone with potassium carbonate [4].

For the preparation of **1**, a one-step cyclization of 2-hydroxy-1,4-naphthoquinones **2** with **3** was planned. The one-step cyclization was studied under several conditions using commercially available 2-hydroxy-1,4-naphthoquinone (**2a**), and the results are summarized in table 1. Cyclization of **2a** with **3** gives none of the cyclized product in polar conditions, such as ethanol/sodium

Chart 2



ethoxide or acetone/potassium carbonate, but gives the desired cyclized product **1a** under non-polar conditions. Cyclizations using sodium hydride (2 equivalents) in refluxing ether or tetrahydrofuran, calcium hydride (2 equivalents) in refluxing toluene, and *n*-butyl lithium (1 equivalent) in refluxing toluene, show low yields (<4%). But, cyclization using sodium hydride (2 equivalents) in refluxing toluene shows the best yield of 16% after 24 hours. Use of equal (1 equivalent) or excess (3 equivalents) amounts of sodium hydride decreases the yields (1 equivalent gives 0%, 3 equivalents give 1%), and longer reaction time also decreases the yield (48 hours gives < 1%).

Table 1
One-Step Cyclization of **2a** with **3**

Base	(eq.)	Solvent	Temperature	Time (hours)	Yields of **1a** (%)
Na	(3.5)	MeOH	room temp.	2	0
K_2CO_3	(3)	acetone	refluxing temp.	7	0
NaH	(2)	ether	refluxing temp.	24	<1
NaH	(2)	THF	refluxing temp.	24	4
NaH	(2)	toluene	refluxing temp.	24	16
NaH	(2)	toluene	refluxing temp.	48	<1
NaH	(1)	toluene	refluxing temp.	24	0
NaH	(3)	toluene	refluxing temp.	24	1
CaH_2	(2)	toluene	refluxing temp.	24	<1
n-BuLi	(1)	toluene	refluxing temp.	24	4

For a preparation of the corresponding 2-hydroxy-1,4-naphthoquinones **1b-f**, five methoxy-substituted 2-hydroxy-1,4-naphthoquinones **2b-f** were prepared according to reported procedures [5a-e]. Four methoxy-substituted 2-hydroxy-1,4-naphthoquinones (**2b-e**) and

one dimethoxy-substituted 2-hydroxy-1,4-naphthoquinones (**2f**), thus prepared, were subjected to a similar one-step cyclization by treatment with **3** and sodium hydride (2 equivalents) in refluxing toluene for 24 hours; the results are summarized in table 2. Cyclizations of 6-methoxy **2c** and 7-methoxy **2d** with **3** give the corresponding isopropenylfuronaphthoquinones **1c** and **1d** in 21% and 10% yield, respectively. In cyclizations of 5-methoxy **2b**, 8-methoxy **2e**, and 5,6-dimethoxy **2f** the corresponding isopropenylfuronaphthoquinones **1b** (11%), **1e** (8%), and **1f** (9%) are obtained, as well as the partial demethylation products 5-hydroxy **1b'** (5%), 8-hydroxy **1e'** (trace), and 5-hydroxy-6-methoxy **1f'** (5%). The spectral data of the cyclized products **1a,b,b',f**, thus obtained, is identical to that of the corresponding natural dehydroiso-α-lapachones.

Table 2
One-Step Cyclization of **2a-f** with **3**

Substrate	Cyclized Product (Yield/%)
2a	**1a** (16)
2b	**1b** (11) and **1b'** (5)
2c	**1c** (21)
2d	**1d** (10)
2e	**1e** (8) and **1e'** (trace)
2f	**1f** (9) and **1f'** (5)

For another preparation of isopropenylfuronaphthoquinones, Diels-Alder reactions of 2-isopropenyl-2,3-dihydrobenzofuran-4,7-dione **4** with the corresponding dienes was planned. Furoquinone **4** might be prepared by one-step cyclization of 2,5-dimethoxyphenol with **3** to 4,7-dimethoxy-2-isopropenyl-2,3-dihydrobenzofurane **5a** followed by oxidative demethylation with ceric ammonium nitrate. However, one-step cyclizations of 2,5-dimethoxyphenol with **3** did not give the desired 4,7-dimethoxy-2-isopropenyl-2,3-dihydrobenzofurane **5a** under any conditions [6]. As a result, the conversion of 2-isopropenyl-2,3-dihydrobenzofuran-4-ol **7** to **4** *via* **5b** was then planned. According to the reported method [4a], benzofuranol **7** was prepared by one-step cyclization of 1,3-cyclohexandione with **3** followed by dehydrogenation of **6** with DDQ, and persulfate oxidation of **7** gave 2-isopropenyl-2,3-dihydrobenzofuran-4,7-diol **5b** in 72% yield by treating with potassium persulfate in aqueous tetramethylammonium hydroxide solution. However, the conversion of hydroquinone **5b** to quinone **4** was unsuccessful because of the instability of **5b**, and the conversion of hydroquinone **5b** to dimethyl ether **5a** also gives low yield (15%) [7].

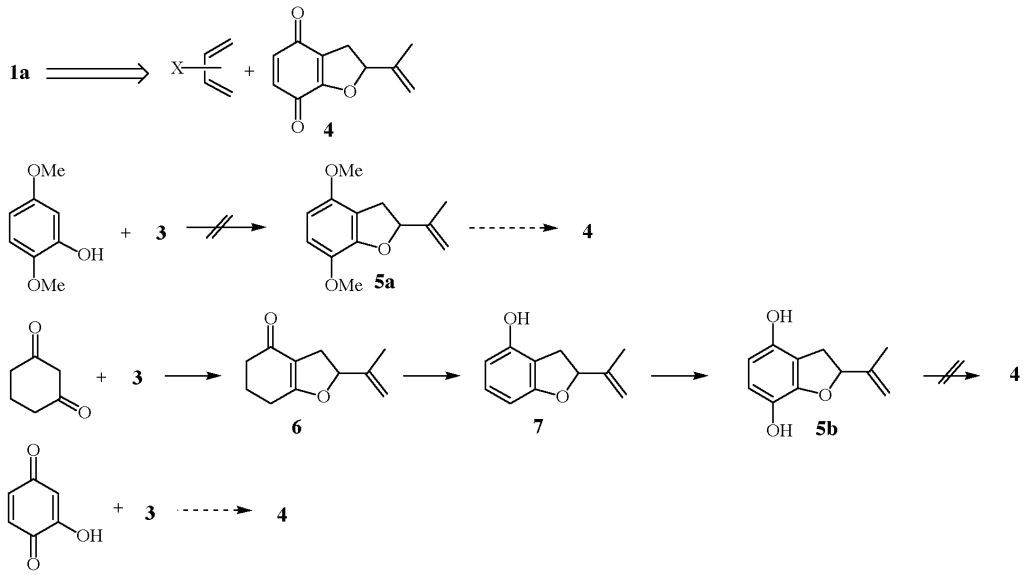
EXPERIMENTAL

Melting points were measured on a Yanagimoto micro melting point apparatus and are uncorrected. The ir spectra were recorded on a JASCO FT/IR spectrometer in liquid films or potassium bromide disks, the uv spectra were recorded on a Hitachi 220A spectrophotometer, the pmr spectra were recorded on a JEOL MAC-FX (90 MHz) or A440 (400 MHz) spectrometer in deuteriochloroform solution, and the mass spectra were recorded on a JEOL JMS-OISG-2 spectrometer.

General Procedure for Cyclization of **2a-f** with **3** to **1a-f**.

To a solution of **2a-f** (1.0 mmol) in dry toluene (10 ml) was added sodium hydride (2.0 mmol) and **3** (1.5 mmol) at room temperature, and the mixture was refluxed with stirring for 24 hours. The mixture was treated with water, acidified with 10% hydrochloric acid, and extracted with ether. The organic layer was washed with saturated sodium hydrogen carbonate solution and brine, and then dried over anhydrous sodium sulfate. After removal of the solvent, the residual oil was chromatogramed on a silica-gel column to give the corresponding isopropenylfuronaphthoquinones **1a-f** and demethylated **1b'**, **1f'**.

Chart 3



2-Isopropenyl-2,3-dihydronaphtho[2,3-*b*]furan-4,9-dione (**1a**).

Compound **1a** was isolated as fractions eluted with hexane:benzene (1:1); ir: ν_{CO} 1683 cm^{-1}; uv: λ 252 (log ε 3.74), 290 (log ε 3.42), 315 (sh, log ε 3.05), 332 (log ε 2.89), 345 nm (sh, log ε 3.74); ^{1}H nmr: δ 1.81 (br s, 3H, CH_3), 3.04 (dd, 1H, 3-H_a, J = 8.7 and 17.2 Hz), 3.36 (dd, 1H, 3-H_b, J = 10.8 and 17.2 Hz), 5.01 (br s, 1H, C=C$H_a$$H_b$), 5.14 (br s, 1H, C=C$H_a$$H_b$), 5.42 (dd, 1H, 2-$H_x$, J = 8.7 and 10.8 Hz), 7.67-7.75 (m, 2H, 6-H and 7-H), 8.07-8.11 ppm (m, 2H, 5-H and 8-H); ms: m/z 240 (M^+); high resolution ms: M^+ 240.0786 (Calcd. for $C_{15}H_{12}O_3$: 240.0783). This sample was identical to natural dehydroiso-α-lapachone in all reported spectral data [2].

2-Isopropenyl-5-methoxy-2,3-dihydronaphtho[2,3-*b*]furan-4,9-dione (**1b**).

Compound **1b** was isolated as fractions eluted with hexane:ethyl acetate (9:1); mp 121-126°C; ir: ν_{CO} 1654 cm^{-1}; uv: λ 231 (sh, log ε 3.87), 280 (sh, log ε 3.38), 286 (sh, log ε 3.33), 295 (log ε 3.33), 323 (log ε 3.18), 336 (log ε 3.20), 350 nm (sh, log ε 3.10); ^{1}H nmr δ 1.80 (br s, 3H, CH_3), 3.00 (dd, 1H, 3-H_a, J = 8.7 and 17.5 Hz), 3.31 (dd, 1H, 3-H_b, J = 10.9 and 17.5 Hz), 4.00 (s, 3H, 5-OMe), 4.98 (br s, 1H, C=C$H_a$$H_b$), 5.12 (br s, 1H, C=C$H_a$$H_b$), 5.37 (dd, 1H, 2-$H_x$, J = 8.7 and 10.9 Hz), 7.31 (dd, 1H, 6-H, J = 1.2 and 8.5 Hz), 7.62 (dd, 1H, 7-H, J = 7.6 and 8.5 Hz), 7.77 ppm (dd, 1H, 8-H, J = 1.2 and 7.6 Hz); ms: m/z 270 (M^+), 255 (M^+-CH_3); high resolution ms: M^+ 270.0890 (Calcd. for $C_{16}H_{14}O_4$: 270.0888). This sample was identical to natural 5-methoxydehydroiso-α-lapachone in all reported spectral data [2].

5-Hydroxy-2-isopropenyl-2,3-dihydronaphtho[2,3-*b*]furan-4,9-dione (**1b'**).

Compound **1b'** was isolated as fractions eluted with hexane:ethyl acetate (9:1); ir: ν_{OH} 2926 cm^{-1}, ν_{CO} 1636 cm^{-1}; uv: λ 247 (log ε 3.86), 289 (log ε 3.65), 300 (sh, log ε 3.61), 400 (sh, log ε 3.21), 412 (log ε 3.21), 428 nm (log ε 3.21); ^{1}H-nmr: δ 1.81 (br s, 3H, CH_3), 3.02 (dd, 1H, 3-H_a, J = 8.5 and 17.1 Hz), 3.34 (dd, 1H, 3-H_b, J = 11.0 and 17.1 Hz), 5.02 (br s, 1H, C=C$H_a$$H_b$), 5.14 (br s, 1H, C=C$H_a$$H_b$), 5.44 (dd, 1H, 2-$H_x$, J = 8.5 and 11.0 Hz), 7.25 (dd, 1H, 6-H, J = 1.2 and 8.3 Hz), 7.64 (dd, 1H, 7-H, J = 1.2 and 7.6 Hz), 12.23 ppm (s, 1H, 5-OH); ms: m/z 256 (M^+); high resolution ms: M^+ 256.0759 (Calcd. for $C_{15}H_{12}O_4$: 256.0732). This sample was identical to natural 5-hydroxydehydroiso-α-lapachone in all reported spectral data [2].

2-Isopropenyl-6-methoxy-2,3-dihydronaphtho[2,3-*b*]furan-4,9-dione (**1c**).

Compound **1c** was isolated as fractions eluted with hexane:ethyl acetate (19:1); ir: ν_{CO} 1651 cm^{-1}; uv: λ 240 (sh, log ε 3.82), 293 (sh, log ε 3.44), 310 (sh, log ε 3.30), 321 (sh, log ε 3.13), 335 nm (sh, log ε 3.00); ^{1}H nmr: δ 1.81 (br s, 3H, CH_3), 3.02 (dd, 1H, 3-H_a, J = 8.7 and 17.0 Hz), 3.33 (dd, 1H, 3-H_b, J = 10.9 and 17.0 Hz), 3.95 (s, 3H, 6-OMe), 5.00 (br s, 1H, C=C$H_a$$H_b$), 5.13 (br s, 1H, C=C$H_a$$H_b$), 5.41 (dd, 1H, 2-$H_x$, J = 8.5 and 10.9 Hz), 7.01 (dd, 1H, 7-H, J = 2.5 and 8.8 Hz), 7.54 (d, 1H, 5-H, J = 2.5 Hz), 8.03 ppm (d, 1H, 8-H, J = 8.8 Hz); ms: m/z 270 (M^+), 255 (M^+-CH_3); high resolution ms: M^+ 270.0875 (Calcd. for $C_{16}H_{14}O_4$: 270.0888).

Anal. Calcd. for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 70.93; H, 5.37.

2-Isopropenyl-7-methoxy-2,3-dihydronaphtho[2,3-*b*]furan-4,9-dione (**1d**).

Compound **1d** was isolated as fractions eluted with hexane:benzene (1:1); ir: ν_{CO} 1644 cm^{-1}; uv: λ 263 (log ε 4.18), 296 (log ε 3.79), 340 nm (log ε 3.49); ^{1}H nmr: δ 1.80 (br s, 3H, CH_3), 3.00 (dd, 1H, 3-H_a, J = 8.8 and 17.3 Hz), 3.32 (dd, 1H, 3-H_b, J = 10.7 and 17.3 Hz), 3.91 (s, 3H, 7-OMe), 4.99 (br s, 1H, C=C$H_a$$H_b$), 5.12 (br s, 1H, C=C$H_a$$H_b$), 5.39 (dd, 1H, 2-$H_x$, J = 8.8 and 10.7 Hz), 7.15 (dd, 1H, 6-H, J = 2.4 and 8.5 Hz), 7.51 (d, 1H, 8-H, J = 2.4 Hz), 7.97 (d, 1H, 5-H, J = 8.5 Hz); ms: m/z 270 (M^+), 255 (M^+-CH_3); high resolution ms: M^+ 270.0883 (Calcd. for $C_{16}H_{14}O_4$: 270.0888).

Anal. Calcd. for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 71.03; H, 5.35.

2-Isopropenyl-8-methoxy-2,3-dihydronaphtho[2,3-*b*]furan-4,9-dione (**1e**).

Compound **1e** was isolated as fractions eluted with hexane:ethyl acetate (4:1); ir: ν_{CO} 1645 cm^{-1}; uv: λ 228 (sh, log ε 3.84), 267 (sh, log ε 3.43), 282 (log ε 3.43), 296 (sh, log ε 3.34), 312 (sh, log ε 3.15), 322 (log ε 3.09), 328 (log ε 3.09), 345 nm (log ε 3.00); ^{1}H nmr: δ 1.78 (br s, 3H, CH_3), 2.99 (dd, 1H, 3-H_a, J = 8.6 and 16.8 Hz), 3.33 (dd, 1H, 3-H_b, J = 11.0 and 16.8 Hz), 4.01 (s, 3H, 8-OMe), 4.97 (br s, 1H, C=C$H_a$$H_b$), 5.11 (br s, 1H, C=C$H_a$$H_b$), 5.39 (dd, 1H, 2-$H_x$, J = 8.6 and 11.0 Hz), 7.25 (dd, 1H, 7-H, J = 1.2 and 7.6 Hz), 7.66 (t, 1H, 6-H, J = 7.6 Hz), 7.75 (dd, 1H, 5-H, J = 1.2 and 7.6 Hz), 11.08 ppm (s, 1/30H, for 8-OH of **1e**); ms: m/z 270 (M^+), 255 (M^+-CH_3); high resolution ms: M^+ 270.0876 (Calcd. for $C_{16}H_{14}O_4$: 270.0888).

Anal. Calcd. for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 70.99; H, 5.48.

2-Isopropenyl-5,6-dimethoxy-2,3-dihydronaphtho[2,3-*b*]furan-4,9-dione (**1f**).

Compound **1f** was isolated as fractions eluted with hexane-ethyl acetate (9:1); mp 103-108°C; ir: ν_{CO} 1651 cm^{-1}; uv: λ 268 (log ε 4.03), 298 (log ε 3.85), 347 (log ε 3.47), 356 (log ε 3.47), 365 nm (log ε 3.48); ^{1}H nmr: δ 1.80 (br s, 3H, CH_3), 3.00 (dd, 1H, 3-H_a, J = 8.7 and 17.2 Hz), 3.31 (dd, 1H, 3-H_b, J = 10.7 and 17.2 Hz), 3.92 and 3.97 (two s, 6H, 5-OMe and 6-OMe), 4.99 (br s, 1H, C=C$H_a$$H_b$), 5.12 (br s, 1H, C=C$H_a$$H_b$), 5.38 (dd, 1H, 2-$H_x$, J = 8.7 and 10.7 Hz), 7.10 (d, 1H, 7-H, J = 8.5 Hz), 7.94 ppm (d, 1H, 8-H, J = 8.5 Hz); ms: m/z 300 (M^+), 285 (M^+-CH_3); high resolution ms: M^+ 300.1009 (Calcd. for $C_{17}H_{16}O_5$: 300.0993). This sample is identical to natural 5,6-dimethoxydehydroiso-α-lapachone in all reported spectral data [2].

5-Hydroxy-2-isopropenyl-6-methoxy-2,3-dihydronaphtho-[2,3-*b*]furan-4,9-dione (**1f'**).

Compound **1f'** was isolated as fractions eluted with hexane-ethyl acetate (9:1); mp 146-151°C; ir: ν_{OH} 3443 cm^{-1}, ν_{CO} 1629 cm^{-1}; uv: λ 249 (sh, log ε 3.95), 310 (log ε 3.70), 416 (sh, log ε 3.42), 435 nm (log ε 3.44); ^{1}H nmr: δ 1.81 (br s, 3H, CH_3), 3.02 (dd, 1H, 3-H_a, J = 8.6 and 16.8 Hz), 3.33 (dd, 1H, 3-H_b, J = 11.0 and 16.8 Hz), 3.99 (s, 3H, 6-OMe), 5.01 (br s, 1H, C=C$H_a$$H_b$), 5.13 (br s, 1H, C=C$H_a$$H_b$), 5.44 (dd, 1H, 2-$H_x$, J = 8.6 and 11.0 Hz), 6.99 (d, 1H, 7-H, J = 8.4 Hz), 7.68 (d, 1H, 8-H, J = 8.4 Hz); 12.79 ppm (s, 1H, 5-OH); ms: m/z 286 (M^+), 271 (M^+-CH_3); high resolution ms: M^+ 286.0847 (Calcd. for $C_{16}H_{14}O_5$: 286.0837).

Anal. Calcd. for $C_{16}H_{14}O_5$: C, 67.12; H, 4.93. Found: C, 66.97; H, 4.97.

Persulfate Oxidation of **7** to **5b**.

According to the reported procedure [4a], **7** was prepared by cyclization of cyclohexane-1,3-dione with **3** followed by dehydrogenation. To a solution of potassium persulfate (952 mg, 3.52 mmol) in 5% aqueous tetramethylammonium hydroxide solution (40 ml) was added **7** (456 mg, 2.59 mmol), and the mixture was stirred at room temperature for 5 hours. The mixture was poured onto aqueous saturated potassium dihydrogenphosphate solution, acidified with 10% hydrochloric acid, and stirred at room temperature for 4 hours. The mixture was then extracted with ethyl acetate, and the organic layer was washed with brine and dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure gave crude hydroquinone **5b** (356 mg, crude 72%); ir: ν_{OH} 3347 cm^{-1}; ^1H nmr: δ 1.79 (br s, 3H, CH_3), 3.03 (dd, 1H, 3-H_a, J = 9.3 and 8.5 Hz), 3.34 (dd, 1H, 3-H_b, J = 9.3 and 9.1 Hz), 4.94 (br s, 1H, C=C$H_a$$H_b$), 5.10 (br s, 1H, C=C$H_a$$H_b$), 5.26 (dd, 1H, 2-$H_x$, J = 8.5 and 9.1 Hz), 6.21 (d, 1H, 5-H, J = 8.5 Hz), 6.63 (d, 1H, 6-H, J = 8.5 Hz); ms: m/z 192 (M^+). Hydroquinone **12b** was unstable, and used without further purification.

Methylation of **5b** to **5a**.

To a solution of crude **5b** (314 mg, 1.63 mmol) in dry acetone (30 ml) was added dimethyl sulfate (516 mg, 4.08 mmol) and anhydrous potassium carbonate (504 mg, 3.59 mmol), and the mixture was refluxed for 8 hours. After removal of most of the acetone, the mixture was treated with water and extracted with ether. The ether layer was washed with brine and dried over anhydrous sodium sulfate. After removal of the solvent, the residual oil was chromatograhed on a silica-gel column to give **5a** (55 mg, 15%) as fractions eluted with hexane:benzene (3:1); ^1H nmr: δ 1.77 (br s, 3H, CH_3), 3.08 (dd, 1H, 3-H_a, J = 9.0 and 15.6 Hz), 3.41 (dd, 1H, 3-H_b, J = 8.5 and 15.6 Hz), 3.80 (s, 3H, 4-OMe), 3.90 (s, 3H, 7-OMe), 4.90 (br s, 1H, C=C$H_a$$H_b$), 5.08 (br s, 1H, C=C$H_a$$H_b$), 5.14 (dd, 1H, 2-$H_x$, J = 8.5 and 9.0 Hz), 6.45 (d, 1H, 5-H, J = 8.5 Hz), 6.68 (d, 1H, 6-H, J = 8.5 Hz); ms: m/z 220 (M^+), 205 (M^+-CH_3).

Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.93; H, 7.37.

REFERENCES AND NOTES

[1a] Y. Kawase, S. Yamaguchi, S. Kondo, and K. Shimokawa, *Chem. Lett.*, **1978**, 253; [b] S. Yamaguchi, S. Kondo, K. Shimokawa, O. Inoue, M. Sannnomiya, and Y. Kawase, *Bull. Chem. Soc. Jpn.*, **55**, 253 (1982); [c] S. Yamaguchi, A. Miyata, M. Ueno, T. Hase, K. Yamamoto, and Y. Kawase, *Bull. Chem. Soc. Jpn.*, **57**, 617 (1984); [d] S. Yamaguchi, K. Sugiura, R. Fukuoka, K. Okazaki, M. Takeuchi, and Y. Kawase, *Bull. Chem. Soc. Jpn.*, **57**, 3607 (1984); [e] S. Yamaguchi, A. Saitoh, and Y. Kawase, *Bull. Chem. Soc. Jpn.*, **59**, 3983 (1986); [f] S. Yamaguchi, M. Takai, I. Hanazome, Y. Okada, and Y. Kawase, *Bull. Chem. Soc. Jpn.*, **60**, 3603 (1987); [g] S. Yamaguchi, T. Nitta, T. Hosoka, Y. Nishino, and Y. Kawase, *Bull. Chem. Soc. Jpn.*, **63**, 3230 (1990).

[2] C. E. Heltzel, A. A. Gunatilaka, E. Glass, and G. I. Kingston, *J. Natural Products.*, **56**, 1500 (1993).

[3] J. Nickl, *Chem. Ber.*, **91**, 553 (1958).

[4a] F. Bigi, G. Gasiraghi, G. Gasnati, and Sartori, *Tetrahedron*, **39**, 169 (1983); [b] S. Yamaguchi, R. Miyakawa, S. Yonezawa, and Y. Kawase, *Bull. Chem. Soc. Jpn.*, **62**, 3593 (1989); [c] S. Yamaguchi, Y. Sugioka, M. Ishida, H. Yokoyama, and Y. Hirai, *J. Heterocyclic Chem.*, **34**, 1329 (1997).

[5a] K. A. Parker and M. E. Sworin, *J. Org. Chem.*, **46**, 3218 (1981); [b] K. Mayor and H. S. Bloch, *Org. Synth.* Coll. Vol. 3, 637 (1955); [c] J. E. Davies, F. E. King, and J. C. Roberts, *J. Chem. Soc.*, , 2782 (1955); [d] A. C. Baillie and R. H. Thomson, *J. Chem. Soc.* (C), , 2184 (1966); [e] O. Soga, A. Takuwa, and H. Doi, *Nippon Kagaku Zasshi*, **1976**, 1735.

[6] One-step cyclization needs the *ortho-C*-alkylation at the first step, but the methoxy group in one *ortho* position of the phenolic hydroxyl group might chelate with the sodium ion and it disturbs the *ortho-C*-alkylation to give *O*-alkylation products.

[7] These might be due to the instability of the hydroquinone **5b** and any *C*-alkylation.