Regiospecific Synthesis of 2-Substituted Furanonaphthoquinones

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Dedicated to the memory of Professor Raymond N. Castle

The naturally-occurring furanonaphthoquinones **1a-d** have been synthesized from 3-furancarboxylic acid and 2,3-dimethoxybenzaldehyde *via* the Birch reduction-elimination.

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Plants belonging to the family *Bignoniaceae* are sources of furanonaphthoquinones which have shown several biological and pharmacological effects [1]. Recently, some furanonaphthoquinones were isolated from *Tabebuia* species (*ochracea* [2] [3], and *incana* [2]) by two groups. These compounds were characterized as 2-substituted (acetyl or hydroxyethyl)-7,8-disubstituted (8-hydroxy-7-methoxy or 7,8-dimethoxy)naphtho[2,3-*b*]-furan-4,9-diones **1a-d** on the basis of spectral data, respectively. We now describe an efficient regiospecific synthesis of **1a-1d** [4] [5] as a further application [6] of the Birch reduction-elimination and for the purpose of biological evaluation.

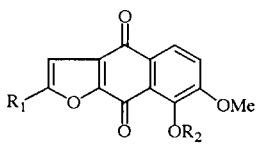
Acylation of furan-3-carboxylic acid with acetic anhydride in the presence of boron trifluoride etherate afforded 5-acetylfuran-3-carboxylic acid [7], which, upon subsequent ketalization, was converted into the ketal acid **2** in 62% yield. Base-catalyzed coupling [8] [9a] of **2** with 2,3-dimethoxybenzaldehyde using lithium diisopropylamide, followed by treatment with dimethylsulfoxide and iodomethane, furnished the methoxy methyl ester **3** in 64% yield. Hydrolysis of the ketal ester **3** and subsequent reductive elimination [9] of the aliphatic methoxyl of **4** with two equivalent atoms of sodium in liquid ammonia gave the keto acid **5** in 84% yield. Though a small amount of starting material was recovered, no side products were obtained.

The Friedel-Crafts cyclization of **5** with trifluoroacetic anhydride in trifluoroacetic acid at room temperature yielded the diketone **6k** as a single and stable product in 93% yield. The nmr spectrum of **6** was obtained in both deuteriochloroform and dimethylsulfoxide-d_6. The presence of the keto form **6k** in deuteriochloroform was confirmed by the apperance of a sharp singlet (2H) δ 4.24 in the methylene region, and no indication of any enolic material was found in both nmr and ir spectrum. The nmr spectrum in dimethylsulfoxide-d_6, however, indicated the presence of the enol form **6e** by the apperance of a singlet (1H) δ 11.23 in the enolic proton region and a singlet (1H) δ 8.06 in the aromatic region with disappearance of the sharp signal at δ 4.24. Since keto-enol tautomerism in the thiophene analogs of anthrone [10] have been studied by means of nmr spectroscopy and solvent effects [11], it should be noted [12] that the nmr spectrum of **6** in deuteriochloroform indicated only the keto form **6k**, while that in dimethylsulfoxide-d_6 indicated only the enol form **6e**. On the other hand, cyclization of **5** with zinc chloride and acetic anhydride in acetic acid afforded the enol acetate **7** and **8** (**7**:**8** =7:1). The acylated compound **8** was found to be derived from **7** under the same reaction condition, and hydrolysis of **7** with benzyltrimethylammonium hydroxide in methanol gave **6k** in quantitative yield. The formation of products analogous to the phenol acetate [13] **7** and the 9-acylated [14] **8** is known in other synthesis of furanonaphthoquinones.

Oxidation of **6** with chromium trioxide in acetic acid gave the quinone **1a** in 77% yield, which was further converted into the 8-hydroxyquinone **1b** by demethylation with boron tribromide. Reduction of 2-acetylfuranonaphthoquinones **1a** and **1b** with sodium borohydride afforded the 2-hydroxyethyl-furanonaphthoquinones **1c** and **1d**, respectively. These synthetic compounds **1a-d** were found to be identical with the natural products by comparing its mp, ir, ^1H and ^{13}C nmr spectra with those reported [2] [3].

Thus, this synthesis is regiospecific and efficient yielding **1a** in an overall yield 33% from **2** (5 steps). In conclusion, the present work illustrates a further application of the Birch reduction-elimination of 5-acyl-3-furancarboxylic acid derivative to the synthesis of 2-substituted furanonaphthoquinones.

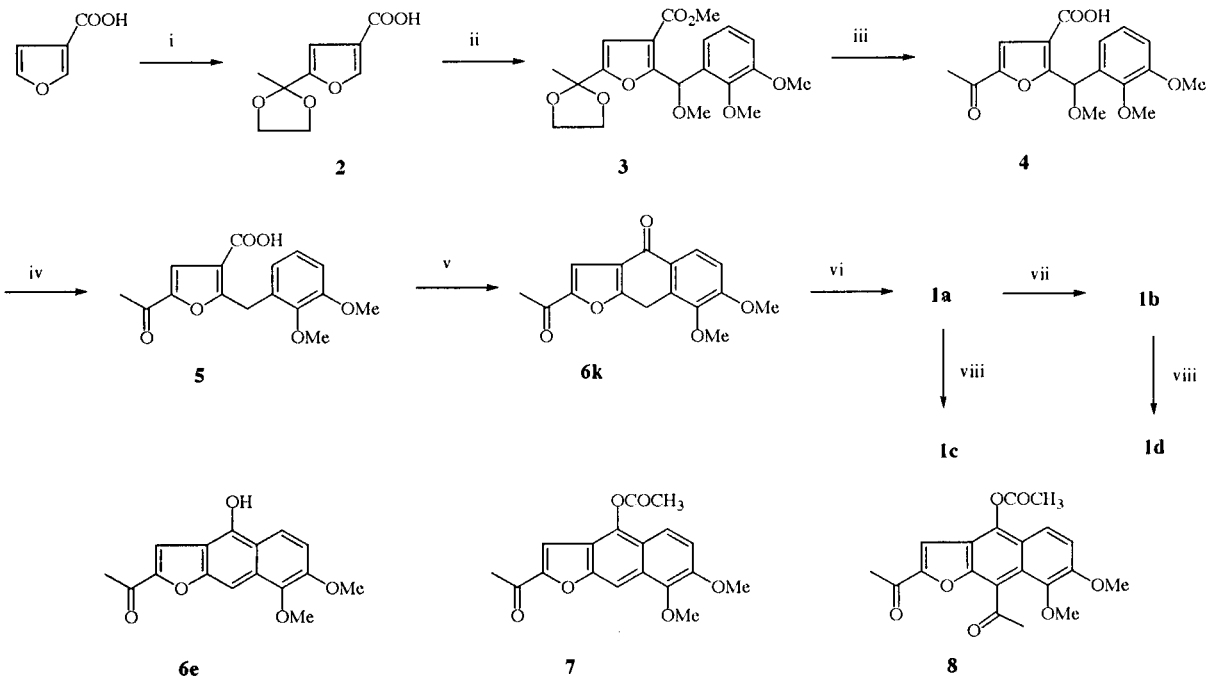
Figure



1

a R_1=CH_3CO, R_2=CH_3
b R_1=CH_3CO, R_2=H
c R_1=CH_3CHOH, R_2=CH_3
d R_1=CH_3CHOH, R_2=H

Scheme



Reagents and conditions :i, (a) BF_3Et_2O, Ac_2O, 60°; (b) CH_3COCl, EtOH, rt, 65% (2 steps); (c)$HO(CH_2)_2OH$, *p*-TsOH, benzene, reflux; (d) NaOH, MeOH-H_2O, 40°; 95% (2 steps); ii, 2 equivalents of lithium diisopropylamide, 2,3-dimethoxybenzaldehyde, tetrahydrofuran, -78°, then, dimethylsulfoxide, CH_3I, reflux, 64%; iii, NaOH, MeOH-H_2O, rt, then HCl, 85%; iv, 2 Na, liq NH_3, tetrahydrofuran, -33°, 84%; v, $(CF_3CO)_2O$, CF_3COOH, rt, 93%; vi, CrO_3, SiO_2, CH_3COOH, rt, 77%; vii, BBr_3, CH_2Cl_2, -78°, 1 h and -40°, 3 h, 57%;viii, $NaBH_4$, MeOH, rt, 86% (for **1c**) and 72% (for **1d**).

EXPERIMENTAL

Melting points were measured with Yanagimoto MP apparatus and are uncorrected. Ir spectra were taken on a JASCO A-102 IR spectrophotometer. The ^1H and ^{13}C nmr were recorded on a JEOL LA-300 (300 MHz) in deuteriochloroform solution, unless stated otherwise. Chemical shifts (ppm) are given downfield of tetramethylsilane. The mass spectra were recorded on a JEOL AX-500 spectrometer. All reagents were commercially available (reagent grade) and purified by distillation. Dichloromethane was distilled from phosphorous pentoxide. Diisopropylamine and dimethylsulfoxide were distilled from calcium hydride. Tetrahydrofuran was dried by distillation from sodium benzophenone ketyl prior to use. Column chromatography was performed with silica gel (Merck NO. 7734; 63-200 μm), and thin layer chromatography was performed on a glass plate coated with Kieselgel 60 GF_{254} (Merck). Organic solutions were dried over anhydrous sodium sulfate. Ether refers to diethyl ether.

5-(2-methyl-[1,3]dioxolane-2-yl)furan-3-carboxylic acid (**2**).

The acylation of 3-furancarboxylic acid was carried out using a modification of the procedure reported by Eugster and Waser [7]. To a mixture of 3-furancarboxylic acid (33.6 g, 0.3 mole) in acetic anhydride (40 ml) was added boron trifluoride etherate (4 ml) at 60°, and the mixture was heated at reflux for 20 minutes. To the cooled mixture in an ice-bath was added acetic acid (20 ml), and the precipitate was filtered off. The filtrate was concentrated *in vacuo*. The resulting residue was esterified according to the procedure described previously [15] to give ethyl 5-acetylfuran-3-carboxylate (35.5 g, 65%); bp 135-140°/10 mm Hg); mp 75° (*n*-hexane and ethyl acetate); ^1H nmr: δ 1.37 (t, 3H, J = 7.1 Hz, CH_3), 2.50 (s, 3H, $COCH_3$), 4.33 (q, 2H, J = 7.1 Hz, CH_2), 7.46 (d, 1H, J = 0.7 Hz, 4-H), 8.12 (d, 1H, J = 0.7 Hz, 2-H); ^{13}C nmr: δ 14.2, 26.0, 60.9, 116.3, 121.5, 150.0, 153.1, 161.9, 186.4.

Anal. Calcd. for $C_9H_{10}O_4$: C, 59.34; H, 5.53. Found: C, 59.40; H, 5.52.

A mixture of the acetylfuran carboxylate (30.4 g, 0.17 mole), ethyleneglycol (95 ml) and *p*-toluenesulfonic acid (320 mg) in benzene (650 ml) was boiled at reflux for 17 hours with a Dean-Stark separator. The cooled reaction mixture was washed with saturated sodium bicarbonate and brine. The solution was dried and concentrated to give an oil, which was hydrolyzed with sodium hydroxide in aqueous ethanol at 40° for 2 hours to afford **2** (31.2 g, 95%); mp 123-124° (*n*-hexane and ethyl acetate); ^1H nmr: δ 1.74 (s, 3H, CH_3), 4.04 (m, 4H, CH_2), 6.69 (d, 1H, J = 0.7 Hz, 4-H), 8.05 (d, 1H, J = 0.7 Hz, 2-H); ^{13}C nmr: δ 24.1, 65.2 (t) (-OCH_2- x 2), 104.2, 106.5, 118.9, 148.7, 156.3, 168.3.

Anal. Calcd. for $C_9H_{10}O_5$: C, 54.55; H, 5.09. Found: C, 54.42; H, 5.04.

Methyl 2-[(2,3-dimethoxyphenyl)methoxymethyl]-5-[2-methyl-[1,3]dioxolane-2-yl]-furan-3-carboxylate (**3**).

A solution of lithium diisopropylamide was prepared by the addition of *n*-butyllithium (1.6 *M* in *n*-hexane, 32.5 ml, 52 mmoles) to a stirred and cooled solution of diisopropylamine (8 ml, 52 mmoles) in dry tetrahydrofuran (100 ml) at -78° under

nitrogen. To this was added a solution of **2** (4.1 g, 21 mmoles) in tetrahydrofuran (50 ml). After 1 hour, a solution of 2,3-dimethoxybenzaldehyde (4.5 g, 27 mmoles) in tetrahydrofuran (15 ml) was added to the mixture and stirring was continued for additional 4 hours at -78°. To the reaction mixture was added dry dimethylsulfoxide (100 ml), and the low boiling point organic solvents (*n*-hexane and tetrahydrofuran) were removed *in vacuo*. A large amount of iodomethane (30 g) was added to the mixture and stirred for 5 hours at room temperature. The reaction was quenched by the addition of water (150 ml) at 0°, and extracted with ether (3 x 100 ml). The combined organic solution was dried and concentrated *in vacuo*. The residue was purified by chromatography (*n*-hexane-ethyl acetate; 4:1) to give **3** as an oil (5.2 g, 64%); ir (potassium bromide): 2900, 1720, 1610, 1590, 1490, 1440, 1370, 1270, 1230, 1070, 1040, 950 cm^{-1}; ^1H nmr: δ 1.67 (s, 3H, CH_3), 3.40 (s, 3H, OMe), 3.71 (s, 3H, OMe), 3.84 (s, 3H, OMe), 3.86 (s, 3H, OMe), 3.86-3.91 (m, 2H, CH_2), 3.93-4.03 (m, 2H, CH_2), 6.43 (s, 1H, 6-H), 6.59 (s, 1H, 4-H), 6.86 (dd, 1H, J = 1.2 Hz, J = 8.1 Hz, 4'-H), 7.09 (t, 1H, J = 7.9 Hz, 5'-H), 7.26 (dd, 1H, J = 1.1 Hz, J = 7.9 Hz, 6'-H); ^{13}C nmr: δ 23.9, 51.6, 55.7, 57.2, 60.6, 65.1, 65.2, 70.6, 104.1, 107.3, 112.0, 116.0, 119.9, 124.0, 132.1, 146.7, 152.4, 154.2, 157.7, 163.6. hrms: Calcd. for $C_{20}H_{24}O_8$: (M^+) 392.1471. Found: m/z 392.1469.

5-Acetyl-2-[(2,3-dimethoxyphenyl)methoxymethyl]furan-3-carboxylic acid (**4**).

To a solution of **3** (5.7 g, 14.6 mmoles) in methanol (60 ml) was added a solution of sodium hydroxide (1.0 g) in water (20 ml), and the mixture was stirred overnight at room temperature. After acidification (pH~1) with 3 *M* hydrochloric acid, the reaction mixture was extracted with ether (3 x 100 ml). The organic layer was washed with water and brine, dried and concentrated *in vacuo* to give **4** as white crystals (4.2 g, 86 %); mp 153-154° (*n*-hexane and ethyl acetate); ir (nujol): 3000, 1725, 1655, 1650, 1590, 1090, 730 cm^{-1}; ^1H nmr: δ 2.47 (s, 3H, $COCH_3$), 3.48 (s, 3H, OMe), 3.79 (s, 3H, OMe), 3.86 (s, 3H, OMe), 6.44 (s, 1H, 6-H), 6.91 (dd, 1H, J = 1.5 Hz, J = 8.0 Hz, 4'-H), 7.12 (t, 1H, J = 8.0 Hz, 5'-H), 7.22 (dd, 1H, J = 1.5 Hz, J = 7.9 Hz, 6'-H), 7.49 (s, 1H, 4-H); ^{13}C nmr: δ 26.1, 55.7, 57.6, 60.7, 71.8, 112.7, 117.3, 117.7, 119.6, 124.3, 130.5, 146.8, 151.5, 152.5, 161.5, 166.1, 186.5.

Anal. Calcd. for $C_{17}H_{18}O_7$: C, 61.07; H, 5.43. Found: C, 61.03; H, 5.43.

5-Acetyl-2-(2,3-dimethoxybenzyl)furan-3-carboxylic acid (**5**).

To a solution of **4** (4.0 g, 12 mmoles) in tetrahydrofuran (30 ml) and liquid ammonia (500 ml) was added 2.0 equivalent atoms of sodium (552 mg) little by little with constant stirring under reflux. The mixture was stirred for 30 minutes and excess of ammonium chloride (1.6 g, 40 mmoles) was added. After evaporation of ammonia at room temperature, the residue was acidified with hydrochloric acid and extracted with ether (3 x 100 ml). The combined organic extracts were washed with water and brine, and dried. Removal of solvent afforded **5** (3.04 g, 84%); mp 152-153° (*n*-hexane and ethyl acetate); ir (nujol): 1720, 1640, 1580, 1270, 1210, 1070, 990 cm^{-1}; ^1H nmr: δ 2.42 (s, 3H, $COCH_3$), 3.86 (s, 6H, C-2 OMe and C-3 OMe), 4.49 (s, 2H, 6-H), 6.78 (d, 1H, J = 8.0 Hz, 4'-H), 6.84 (d, 1H, J = 8.0 Hz, 6'-H), 6.98 (t, 1H, J = 8.0 Hz, 5'-H), 7.47 (s, 1H, 4-H); ^{13}C nmr: δ 25.9, 28.2, 55.7, 60.6, 111.6, 115.4, 118.1, 121.9, 124.0, 129.6, 147.2, 150.8, 152.8, 165.4, 167.9, 186.2.

Anal. Calcd. for $C_{16}H_{16}O_6$: C, 63.15; H, 5.30. Found: C, 63.10; H, 5.31.

2-Acetyl-4,9-dihydro-7,8-dimethoxynaphtho[2,3-*b*]furan-4-one (**6**).

To a stirred solution of **5** (2.0 g, 6.6 mmoles) in trifluoroacetic acid (60 ml) was added trifluoroacetic anhydride (1.0 ml, 6.7 mmoles), and the mixture was stirred at room temperature for 1 hour. After addition of water (10 ml) and dichloromethane (150 ml) at 0° and stirring for 15 minutes, the organic phase was washed with water and brine, dried and concentrated. The residue was purified by chromatography (dichloromethane-ethyl acetate; 20:1) to afford **6** (1.75 g, 93%) as a colorless crystal; mp 202-203° (dec.); ir (potassium bromide): 1640, 1560, 1270, 1070 cm^{-1}; **6k** (keto-form): ^1H nmr: δ 2.54 (s, 3H, $COCH_3$), 3.95 (s, 3H, OMe), 3.99 (s, 3H, OMe), 4.24 (s, 2H, 9-H), 7.09 (d, 1H, J = 8.6 Hz, 6-H), 7.62 (s, 1H, 3-H), 8.13 (d, 1H, J = 8.8 Hz, 5-H); ^{13}C nmr: δ 24.8, 26.1, 56.0, 60.2, 111.5, 114.2, 122.1, 124.2, 126.0, 130.4, 146.0, 152.4, 156.1, 166.0, 180.2, 186.5. **6e** (enol-form): ^1H nmr (dimethylsulfoxide-d_6): δ 2.54 (s, 3H, $COCH_3$), 3.86 (s, 3H, OMe), 3.94 (s, 3H, OMe), 7.35 (d, 1H, J = 9.5 Hz, 6-H), 7.50 (s, 1H, 3-H), 7.83 (d, 1H, J = 9.5 Hz, 5-H), 8.06 (s, 1H, 9-H), 11.23 (s, 1H, OH); ^{13}C nmr (dimethylsulfoxide-d_6): δ 26.3, 56.5, 60.3, 91.0, 111.9, 112.6, 112.7, 116.5, 119.4, 130.6, 141.2, 148.8, 149.5, 150.8, 155.0, 187.4.

Anal. Calcd. for $C_{16}H_{14}O_5$: C, 67.13; H, 4.93. Found: C, 66.76; H, 4.69.

Cyclization of **5** to (**7**) and (**8**).

A solution of **5** (3.1 g, 10 mmoles), acetic anhydride (1.02 g, 10 mmoles) and zinc chloride (1.36 g) in acetic acid (40 ml) was heated at reflux for 2 hours. The cooled reaction mixture was quenched by addition of water (30 ml), and extracted with dichloromethane (3 x 100 ml). The combined organic layers were washed with water and brine, dried and concentrated. The residue was purified by chromatography (*n*-hexane-ethylacetate; 4:1) to give **7** (660 mg, 20 %), **8** (110 mg, 3%) and recovered **5** (1.3 g, 42%), respectively. 4-Acetoxy-2-acetyl-7,8-dimethoxynaphtho[2,3-*b*]furan **7**: mp 161-162°; ir (potassium bromide): 1760, 1660, 1540, 1260, 1160, 1050 cm^{-1}; ^1H nmr: δ 2.57 (s, 3H, $OCOCH_3$), 2.65 (s, 3H, $COCH_3$), 4.02 (s, 3H, OMe), 4.03 (s, 3H, OMe), 7.33 (d, 1H, J = 9.5 Hz, 6-H), 7.43 (d, 1H, J = 1.1 Hz, 3-H), 7.75 (d, 1H, J = 9.4 Hz, 5-H), 8.16 (s, 1H, 9-H); ^{13}C nmr: δ 20.8, 26.6, 56.9, 61.0, 100.1, 109.8, 115.2, 118.0, 119.2, 120.1, 130.7, 140.6, 142.4, 148.6, 153.6, 154.4, 168.7, 188.7.

Anal. Calcd. for $C_{18}H_{16}O_6$: C, 65.85; H, 4.91. Found: C, 65.81; H, 4.84.

4-Acetoxy-2,9-diacetyl-7,8-dimethoxynaphtho[2,3-*b*]furan **8**: ^1H nmr: δ 2.56 (s, 3H, $OCOCH_3$), 2.62 (s, 3H, $COCH_3$), 2.71 (s, 3H, $COCH_3$), 3.81 (s, 3H, OMe), 4.04 (s, 3H, OMe), 7.36 (d, 1H, J = 9.5 Hz, 6-H), 7.41 (s, 1H, 3-H), 7.79 (d, 1H, J = 9.5 Hz, 5-H). hrms: Calcd. for $C_{20}H_{18}O_7$: (M^+) 370.1052. Found: m/z 370.1044.

Hydrolysis of **7** to (**6k**).

To a solution of **7** (474 mg, 1.44 mmoles) in dichloromethane (10 ml) was added a solution of benzyltrimethylammonium hydroxide (Triton B) (40% in methanol, 6.0 g, 14.4 mmoles) in methanol (20 ml), and the mixture was stirred at room temperature for 30 minutes. After acidification (pH~3) by addition of 3 *M* hydrochloric acid and water, the mixture was extracted with

dichloromethane (3 x 100 ml). The organic phase was washed with water, dried and concentrated. A white crystal (405 mg, 98%) was obtained, which was identical with the keto form **6k** by comparing its ^1H and ^{13}C nmr spectra in deuteriochloroform.

2-Acetyl-7,8-dimethoxynaphtho[2,3-*b*]furan-4.9-dione (**1a**).

To a stirred suspension of chromium trioxide (1.34 g, 14 mmoles) and silica gel (500 mg) in acetic acid (30 ml) was added dropwise a solution of **6** (1.0 g, 3.5 mmoles) in acetic acid (50 ml), and the mixture was stirred for 2 hours at room temperature. After quenching by addition of 2-propanol (20 ml) and dichloromethane (500 ml), the mixture was filtered through celite, and the filtrate was washed with water and saturated sodium bicarbonate and dried. The solvent was removed *in vacuo* and the residual product was purified by chromatography (dichloromethane-ethyl acetate; 20:1) to give **1a** (810 mg, 77%); mp 240-243°, [lit [2a] [2b] 240-244°]; ir (potassium bromide): 1690, 1665, 1560, 1260, 985 cm^{-1}; ^1H nmr: δ 2.65 (s, 3H, $COCH_3$), 3.98 (s, 3H, OMe), 4.00 (s, 3H, OMe), 7.22 (d, 1H, J = 8.6 Hz, 6-H), 7.55 (s, 1H, 3-H), 8.07 (d, 1H, J = 8.6 Hz, 5-H); ^{13}C nmr (dimethylsulfoxide-d_6): δ 26.7, 56.5, 61.4, 112.0, 115.7, 125.4, 125.8, 127.0, 128.8, 129.5, 150.9, 155.2, 159.6, 173.4, 178.7, 187.6. hrms: Calcd. for $C_{16}H_{12}O_6$: (M^+) 300.0634. Found: m/z 300.0621.

2-Acetyl-8-hydroxy-7-methoxynaphtho[2,3-*b*]furan-4,9-dione (**1b**).

To a stirred solution of **1a** (136 mg, 0.45 mmole) in dry dichloromethane (100 ml) at -78° was added dropwise boron tribromide (0.84 ml) and the solution was stirred for 1 hour. The reaction mixture was slowly allowed to reach -40° and was stirred for an additional 3 hours. Water (20 ml) and dichloromethane (200 ml) was added and the mixture stirred for 30 minutes. The organic phase was washed with water and brine, dried and concentrated. The residue was purified by chromatography (dichloromethane-ethyl acetate; 20:1) to give **1b** (78 mg, 57 %) as orange needles; mp 206-209°, [lit [3] 206-210°]; ir (potassium bromide): 3400, 1700, 1670, 1640, 1470, 1260, 1240 cm^{-1}; ^1H nmr: δ 2.66 (s, 3H, $COCH_3$), 4.02 (s, 3H, OMe), 7.11 (d, 1H, J = 8.8 Hz, 6-H), 7.59 (s, 1H, 3-H), 7.81 (d, 1H, J = 8.8 Hz, 5-H), 12.39 (s, 1H, OH); ^{13}C nmr: δ 26.7, 56.5, 112.6, 115.2, 122.1, 125.4, 127.0, 129.5, 132.1, 153.7, 155.9, 159.6, 172.0, 179.2, 187.3. hrms: Calcd. for $C_{15}H_{10}O_6$: (M^+) 286.0477. Found: m/z 286.0495.

2-(1-Hydroxyethyl)-7,8-dimethoxynaphtho[2,3-*b*]furan-4,9-dione (**1c**).

To a solution of **1a** (430 mg, 1.43 mmoles) in methanol (30 ml) was added sodium borohydride (22 mg, 0.6 mmole), and the mixture was stirred at room temperature for 4 hours. After acidification with 3 *M* hydrochloric acid and water (30 ml), the mixture was extracted with dichloromethane (3 x 100 ml) and washed with water, dried and concentrated. The residue was purified by chromatography (dichloromethane-ethyl acetate; 4:1) to give **1c** (338 mg, 86%) and recovered **1a** (73 mg); mp 167-168° (recrystallized three times from dichloromethane), [lit [2b] 180-182° for optically active form]; ir (potassium bromide): 3420, 2980, 2940, 1668, 1658, 1577, 1330, 1265, 1050, 985 cm^{-1}; ^1H nmr: δ 1.63 (d, 3H, J = 7.0 Hz, CH_3), 3.95 (s, 3H, OMe), 3.98 (s, 3H, OMe), 5.02 (q, 1H, J = 7.0 Hz, CH), 6.76 (d, 1H, J = 0.8 Hz, 3-H), 7.16 (d, 1H, J = 8.6 Hz, 6-H), 7.99 (d, 1H, J = 8.6 Hz, 5-H), hydroxyl proton could not be observed; ^{13}C nmr: δ 21.4, 56.3, 61.3, 63.7, 103.2, 115.1, 125.0, 125.4, 127.0, 129.8, 150.5, 152.5, 159.3, 164.7, 173.1, 179.6. hrms: Calcd. for $C_{16}H_{14}O_6$: (M^+) 302.0790. Found: m/z 302.0806.

2-(1-Hydroxyethyl)-8-hydroxy-7-methoxynaphtho[2,3-*b*]furan-4,9-dione (**1d**).

The similar reaction of **1b** as in the synthesis of **1c**, after chromatography, gave **1d** as orange crystals in 72% yield; mp 153-154°, [lit [2c] 152-154°]; ir (potassium bromide): 3550, 3440, 1670, 1645, 1530, 1470, 1440, 1270, 1230, 1070, 980, 760 cm^{-1}; ^1H nmr: δ 1.58 (d, 3H, J = 6.7 Hz, CH_3), 3.93 (s, 3H, OMe), 4.97 (q, 1H, J = 6.7 Hz, CH), 6.78 (s, 1H, 3-H), 6.98 (d, 1H, J = 8.4 Hz, 6-H), 7.68 (d, 1H, J = 8.4 Hz, 5-H), 12.42 (s, 1H, 8-OH); ^{13}C nmr: δ 21.5, 56.4, 63.9, 104.3, 114.5, 115.0, 121.6, 125.1, 132.8, 151.2, 153.3, 154.6, 165.9, 178.7, 178.9. hrms: Calcd. for $C_{15}H_{12}O_6$: (M^+) 288.0634. Found: m/z 288.0622.

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