A New Synthetic Route to 2-Substituted Naphtho[2,3-*b*]furan-4,9-dione

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4,9-Dimethoxynaphtho[2,3-*b*]furan **9** was obtained in 91% yield *via* the reductive methylation of naphtho[2,3-*b*]furan-4,9-dione **2**. After treatment of **9** with butyllithium, the mixture was allowed to react with *N,N*-dimethylacetamide, followed by oxidization with cerium(IV) diammonium nitrate to give 2-acetylnaphtho[2,3-*b*]furan-4,9-dione **1**. 2-Formylnaphtho[2,3-*b*]furan-4,9-dione **13** and 2-trimethylsilylnaphtho[2,3-*b*]furan-4,9-dione **14** were also obtained from **9** by a similar method. The halodesilylations of **14** easily gave 2-iodonaphtho[2,3-*b*]furan-4,9-dione **16**, 2-bromonaphtho[2,3-*b*]furan-4,9-dione **17**, and 2-chloronaphtho[2,3-*b*]furan-4,9-dione **18** in 82%, and 93% and 83% yield, respectively. Furthermore, the nitrodesilylation of **14** gave 2-nitronaphtho[2,3-*b*]furan-4,9-dione **3** in 77% yield.

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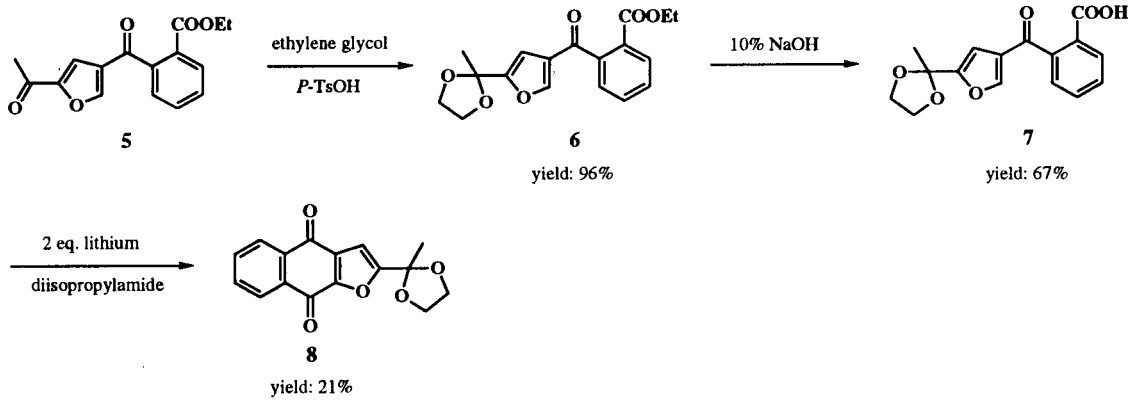
A number of naphtho[2,3-*b*]furan-4,9-diones, which have interesting biological activities, have been isolated from various plants [1]. For example, 2-acetylnaphtho-[2,3-*b*]furan-4,9-dione **1** isolated from *Tabebuia Cassinoides* (Lam.) DC (*Bignoniaceae*) exhibit cytotoxic activity [2]. Hayashi *et al.* [3] have reported that the cytotoxic activity of 2-methylnaphtho[2,3-*b*]furan-4,9-dione is three times that of **1**. As mentioned above, the activities of the 2-substituted naphtho[2,3-*b*]furan-4,9-diones vary with the type of substituent on the parent naphtho[2,3-*b*]-furan-4,9-dione **2**. Therefore, organic chemists have an interest in the syntheses of these compounds. Hitherto, a convenient method to directly introduce various substituents into the 2-position of **2** has not been reported. Recently, we also became interested in the synthesis of the 2-substituted compounds, and reported a short-step synthesis of **2** [4]. Furthermore, the reactions of **2** with various electrophiles were studied, but 2-nitronaphtho-[2,3-*b*]furan-4,9-dione **3** was obtained only in small amounts during nitration [5]. Accordingly, 2-(2-acetyl-4-furanoyl)benzoic acid **4**, previously introduced with the acetyl group on the α-position of the furan ring, was treated with lithium diisopropylamide for cyclization, however, **1** was obtained only in 25% yield [5]. In the present paper, we wish to report a new route, which used **2** as the starting material to prepare 2-substituted naphthofuranquinones.

First, in order to protect the carbonyl group on **4**, ethyl 2-(2-acetyl-4-furanoyl)benzoate **5** [5] was allowed to react with ethylene glycol in the presence of *p*-toluenesulfonic acid to give ethyl 2-[2-(2-methyl-1,3-dioxolan-2-yl)-4-furanoyl]benzoate **6** in almost quantitative yield, and followed by the saponification of **6**, gave the desired 2-[2-(2-methyl-1,3-dioxolan-2-yl)-4-furanoyl]benzoic acid **7**. Compound **5** was unstable under basic conditions in marked contrast to **6**, and only an intractable mixture was formed during the saponification of **5** [5]. This may be due to the acetyl group of **5** being changed into the 1,3-dioxolane ring, and decreasing its strong electron-withdrawing property. Compound **7** was treated with lithium diisopropylamide at -78° for thirty minutes in a manner similar to the preparation of **1** [5], but 2-(2-methyl-1,3-dioxolan-2-yl)naphtho[2,3-*b*]furan-4,9-dione **8** was obtained in only 10% yield. Because **7** does not have a acetyl group on the furan ring, it may be difficult to form the lithio compound as compared with **4**.

Scheme 1

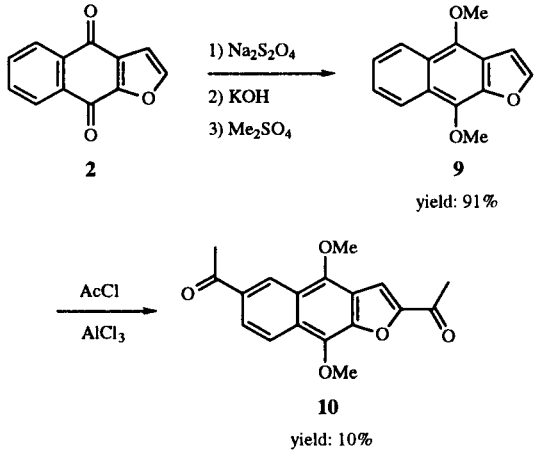


Compound **7** was then treated with lithium diisopropylamide for four hours to give **8** in 21% yield. By using this method, the yield was slightly increased (Scheme 1).

Furonaphthoquinone **8** was obtained from **7**, but the yield was not satisfactory. Thus, it was desired to develop an efficient route to prepare the 2-substituted naphtho[2,3-*b*]furan-4,9-diones. The synthesis of **1** was planned by a new route in which 4,9-dimethoxynaphtho-[2,3-*b*]furan **9** was first prepared by the reductive methylation of **2** in order to accelerate the reactivity of the furan ring for the electrophilic substitution, then the acetylation of **9** was carried out, and the acetylated compound was oxidized to **1**. That is, **2** gave **9** by the reductive methylation as reported by Kraus and Man [6], in good yield. Next the acetylation of **9** was carried out using acetyl chloride in the presence of a Lewis acid [boron trifluoride, tin(IV) chloride], but only a complex mixture was formed. Next, **9** was treated with acetyl chloride in the presence of aluminum chloride to give yellow needles **10** in a small amount (Scheme 2). The pmr spectrum of **10** showed the presence of two kinds of acetyl groups. It was apparent that one of the acetyl groups was introduced into the 2-position of **9**, but the position of the other one could not be determined from the data. It was determined that the proton signal at δ 4.31 (s, 3H) corresponded to the 4-position methoxy protons since the 3-position proton at δ 7.79 (s, 1H) and δ 4.31 proton showed a nuclear overhauser effect (NOE) (8.4%). The signal that appeared at δ 8.86 (d, 1H) was assigned to the 5-position proton on the basis of the NOE (3.3%) between the signal of δ 8.86 and the 4-position methoxy proton signal. The δ 8.86 signal did not exhibit NOE toward other aromatic protons but showed NOE (10.8%) toward the proton signal of the acetyl group at δ 2.71 (s, 3H). From these results, **10** was determined to be 2,6-diacetyl-4,9-dimethoxynaphtho[2,3-*b*]-furan. The structure was supported by ir and ms data and the results of elemental analyses. In addition, to obtain the 2-acetyl-4,9-dimethoxynaphtho[2,3-*b*]furan **11** having an acetyl group in only the 2-position, **9** was treated with an acetylating agent in the mole ratio of 1:1, but an intractable complex was only obtained. The reaction of **9** with acetic anhydride in the presence of aluminum chloride was also attempted, but the decomposition of **9** predominated. As already mentioned, it seems that **9** is unstable under acidic conditions.

Next, the acetylation of **9** under basic conditions was carried out. Compound **9** was treated with butyllithium, then *N,N*-dimethylacetamide was added to the mixture to give **11** in 50% yield. The compound **11** was oxidized by cerium(IV) diammonium nitrate [7], which is generally used as an oxidizing agent for the hydroquinone dimethyl ethers, to give **1** in 79% yield (Scheme 3). Thus, a new efficient synthetic route to **1** was established.

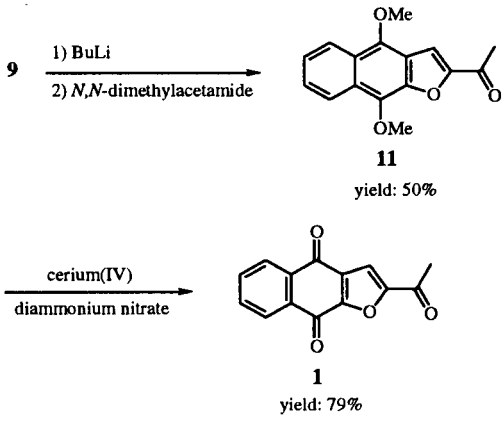
Scheme 2



2 **9** yield: 91%

10 yield: 10%

Scheme 3



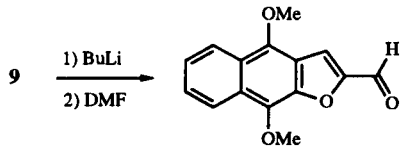
9 **11** yield: 50%

1 yield: 79%

In a similar manner, 2-formyl-4,9-dimethoxynaphtho-[2,3-*b*]furan **12** was obtained from the reaction of the 2-lithio compound of **9** with *N,N*-dimethylformamide in 63% yield. Also, the Vilsmeier-Hacck reaction of **9** was attempted, but an intractable complex mixture was only obtained. The reason is that **9** is susceptible to decomposition under acidic conditions. The cerium(IV) diammonium nitrate oxidation of **12** easily gave 2-formylnaphtho-[2,3-*b*]furan-4,9-dione **13** in 57% yield (Scheme 4). On the other hand, Scholl and Zinke [8] have suggested the participation of **13** as an intermediate when 2-carboxy-naphtho[2,3-*b*]furan-4,9-dione was prepared from 2-methoxalylnaphtho[2,3-*b*]furan-4,9-dione. However, they have not isolated **13**. Compound **13** is an important material for the syntheses of the 2-substituted naphtho-[2,3-*b*]furan-4,9-diones.

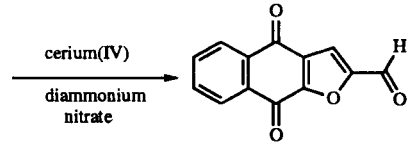
On the other hand, we have reported that the trimethylsilyl group of the 2-trimethylsilylfurans, having an electron-withdrawing group on the furan ring, is very useful as a leaving group during electrophilic substitutions [9]. For

Scheme 4



12

yield: 63%

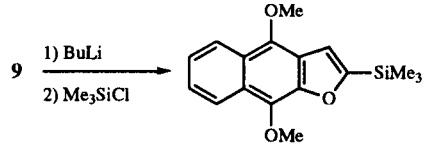


13

yield: 57%

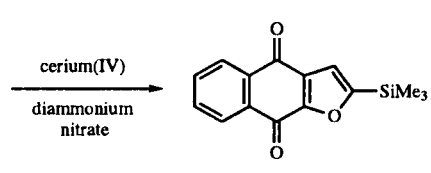
example, the halodesilylations of 3,4-bis(methoxycarbonyl)-2-trimethylsilylfuran [9a] and ethyl 5-trimethylsilyl-2-furancarboxylate [9b] easily yielded the corresponding halofurans. Therefore, we were interested in the reactivity of the trimethylsilyl group on 2-trimethylsilylnaphtho[2,3-*b*]furan-4,9-dione **14** having two carbonyl groups, in connection with this study. The preparation of **14** was then planned. After treatment of **9** with butyllithium, chlorotrimethylsilane was added to the solution of the lithio-compound to give 4,9-dimethoxy-2-trimethylsilylnaphtho[2,3-*b*]furan **15** in almost quantitative yield. The cerium(IV) diammonium nitrate oxidation of **15** gave **14** in 82% yield (Scheme 5).

Scheme 5



15

yield: 95%

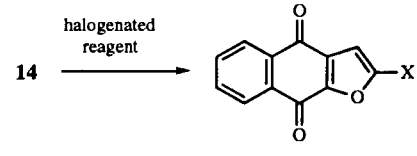


14

yield: 82%

Next, the halodesilylations of **14** were carried out. Compound **14** was allowed to react with one equimolar amount of iodine monochloride in acetonitrile at room temperature for twenty-four hours to give a mixture of **14** and 2-iodonaphtho[2,3-*b*]furan-4,9-dione **16** in a ratio of *ca.* 3:1 (based on gas chromatography-mass spectrometry), but the mixture could not be separated by fractional crystallization. Furthermore, upon increasing the quantities of iodine monochloride by five fold, **14** disappeared for eighteen hours, and **16** was isolated in 82% yield. In the reaction of **14** with bromine, **14** disappeared for thirty minutes, and 2-bromonaphtho[2,3-*b*]-furan-4,9-dione **17** was obtained in 93% yield. The reaction of **14** with sulfuryl chloride gave 2-chloronaphtho[2,3-*b*]furan-4,9-dione **18** in 83% yield for one and a half hours (Scheme 6). In order to substantiate the effect of the trimethylsilyl group on **14**, **2** was treated with five equimolar amounts of bromine in acetonitrile at room temperature for twenty-four hours; however, no product could be detected, and only **2** was recovered. There is only one old report by Scholl and Zinke [8] concerning the synthesis of 2-halonaphtho[2,3-*b*]furan-4,9-diones. They reported that when **2** was treated with excess amounts of bromine in carbon disulfide 2,3-dibromo-2,3-dihydronaphtho[2,3-*b*]furan-4,9-dione was produced, followed by boiling the dibromo compound with acetic acid to yield a mixture of **17** and 3-bromonaphtho[2,3-*b*]furan-4,9-dione. They tried to separate the mixture to obtain a compound of mp 167-168°, but they could not determine whether the compound was the 2-bromo compound or the 3-bromo compound. Our method is very useful for preparing three kinds of 2-halonaphtho[2,3-*b*]furan-4,9-diones from **14** because it is simple and provides a good yield.

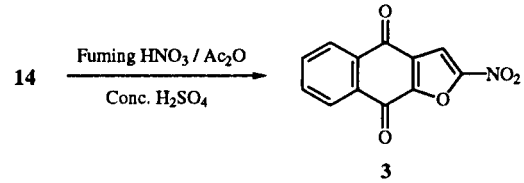
Scheme 6



16: X = I yield: 82%
17: X = Br yield: 93%
18: X = Cl yield: 83%

Hitherto, reports with respect to the electrophilic substitution of **2** can not be found except for the nitration which we reported [5]; the nitration gave **3** only in 20% yield. But, the nitration of **14** was carried out in a manner similar to that of **2** to give **3** in 77% yield (Scheme 7). It was found that the trimethylsilyl group on **14** also behaved as an excellent leaving group during the nitration.

Scheme 7



3

yield: 77%

In conclusion, the very useful intermediates **1**, **13** and **14** used to prepare the new 2-substituted naphtho[2,3-*b*]-furan-4,9-diones were easily obtained *via* **9**. It was demonstrated that the trimethylsilyl group on **14** is an excellent leaving group during the electrophilic substitutions. From this clue, many 2-substituted naphthofuranquinones could be prepared from **14**. Further work on the nucleophilic substitutions of 2-halonaphthofuranquinones with carbanions is in progress. These results will be reported in due course. We established a new synthetic route to naphthofuranquinones from **2**.

EXPERIMENTAL

All melting points (open capillaries) were determined using a Yamato MP-21 and are uncorrected. The pmr spectra were determined at 60 MHz with a Nippon Denshi JNM PMX-60 SI spectrometer with tetramethylsilane as the internal reference. The pmr spectra of **10** was determined at 500 MHz with a Nippon Denshi A 500 spectrometer. The ir spectra were measured with a JASCO IR-810 spectrometer. The mass spectra were obtained on a Nippon Denshi DX-300 spectrometer at 70 ev. Tetrahydrofuran (THF) was distilled from lithium aluminum hydride immediately prior to use. Chromatography was carried out using silica gel (Wakogel C-300, Wako Pure Chemical Industries, Ltd.).

Ethyl 2-[2-(2-Methyl-1,3-dioxolan-2-yl)-4-furanoyl]benzoate **6**.

Ethylene glycol (7.5 ml) and *p*-toluenesulfonic acid (0.2 g) were added to **5** [5] (6.0 g, 21.0 moles) in ethyl orthoformate (15 ml), then the mixture was heated at 165° for 20 hours. The mixture was cooled to room temperature and diluted with ether. The ether layer was washed with brine and dried over anhydrous sodium sulfate, then the solvent was evaporated. The residue was purified by chromatography on silica gel with (hexane: ethyl acetate = 2:1) to give 6.6 g (96%, Rf = 0.26) of **6** as yellow needles, mp 48-51°; ir (potassium bromide): 1730 (COOEt), 1670 (C=O) cm^{-1}; pmr (deuteriochloroform): δ 7.97 (1H, m, Ph), 7.61~7.30 (3H, m, Ph), 7.50 (1H, s, F-5), 6.73 (1H, s, F-3), 4.18 (2H, q, CH_2, 7 Hz), 4.00 (4H, s, CH_2-CH_2), 1.73 (3H, s, CH_3), 1.20 (3H, t, CH_3, 7 Hz); ms: m/z 330 (M^+), 315 (M^+-Me).

Exact Mass Calcd. for $C_{18}H_{18}O_6$ 330.1103. Found 330.1130.

2-[2-(2-Methyl-1,3-dioxolan-2-yl)-4-furanoyl]benzoic Acid **7**.

An aqueous solution of 10% sodium hydroxide (24 g) was added to **6** (2.0 g, 6.1 mmoles) in dioxane (15 ml) with stirring at a room temperature. The mixture was allowed to react for 1 hour and then was poured into ice-cold water. The solution was made acidic with 10% hydrochloric acid and extracted with ether. The ether layer was washed with brine and dried over anhydrous sodium sulfate. The solution was evaporated and the residue was recrystallized from benzene-hexane to give 1.2 g (67%) of **7** as white needles, mp 150-152°; ir (potassium bromide): 1685 (COOH), 1665 (C=O) cm^{-1}; pmr (deuteriochloroform): δ 8.50 (1H, bs, OH, exchangeable proton), 7.93 (1H, m, Ph), 7.60~7.22 (3H, m, Ph), 7.38 (1H, s, F-5), 6.63 (1H, s, F-3), 3.95 (4H, s, CH_2-CH_2), 1.68 (3H, s, CH_3); ms: m/z 302 (M^+), 287 (M^+-Me).

Anal. Calcd. for $C_{16}H_{14}O_6$: C, 63.58; H, 4.67. Found: C, 63.35; H, 4.80.

2-(2-Methyl-1,3-dioxolan-2-yl)naphtho[2,3-*b*]furan-4,9-dione **8**.

Butyllithium (6.1 ml of 1.66 *M*-solution in hexane, 10.1 mmoles) was added to diisopropylamine (1.4 ml, 10.0 mmoles, freshly distilled from solid potassium hydroxide) with stirring at -10° in an atmosphere of argon. After 15 minutes, the resulting viscous oil was diluted with THF (20 ml), cooled to -78° and **7** (1.5 g, 5.0 mmoles) in THF (15 ml) was added. The mixture was stirred at -78° for 4 hours, then the mixture was warmed to 0° for 15 minutes and poured into ice-cold water. The solution was made acidic with 10% hydrochloric acid and extracted with ether. The ether layer was washed with 5% sodium bicarbonate solution then brine and dried over anhydrous sodium sulfate. The solution was evaporated and the residue was recrystallized from ethanol-water to give 0.3 g (21%) of **8** as yellowish needles, mp 170~171° (mp, pmr, ir and mass data were not described by Koyama *et al.* [10]); ir (potassium bromide): 1680 (C=O) cm^{-1}; pmr (deuteriochloroform): δ 8.10 (2H, m, Ph), 7.65 (2H, m, Ph), 6.82 (1H, s, F-3), 4.05 (4H, s, CH_2-CH_2), 1.80 (3H, s, CH_3); ms: m/z 284 (M^+), 269 (M^+-Me).

Anal. Calcd. for $C_{16}H_{12}O_5$: C, 67.60; H, 4.25. Found: C, 67.63; H, 4.38.

4,9-Dimethoxynaphtho[2,3-*b*]furan **9**.

Sodium hydrosulfite (21.2 g) in water (100 ml) was added to **2** [4] (4.0 g, 20.2 mmoles) and tetrabutylammonium bromide (0.8 g) in THF (52 ml) and water (20 ml) with stirring at room temperature. After 15 minutes, potassium hydroxide (26 g) in water (52 ml) was added. After 5 minutes, dimethyl sulfate (40 ml) was added and the mixture was stirred for 12 hours. The product was extracted with dichloromethane. The organic layer was washed with brine and dried over anhydrous sodium sulfate. The solvent was evaporated and the residue was purified by chromatography on silica gel with (hexane-ethyl acetate, 4:1) to give 4.2 g (91%, Rf = 0.60) of **9** as white needles, mp 42-43°; pmr (deuteriochloroform): δ 8.15 (2H, m, Ph), 7.50 (1H, d, F-2, 2 Hz), 7.35 (2H, m, Ph), 6.90 (1H, d, F-3, 2 Hz), 4.20 (3H, s, OCH_3), 4.10 (3H, s, OCH_3); ms: m/z 228 (M^+), 213 (M^+-Me).

Exact Mass Calcd. for $C_{14}H_{12}O_3$: 228.0786. Found: 228.0784.

2,6-Diacetyl-4,9-dimethoxynaphtho[2,3-*b*]furan **10**.

Acetyl chloride (0.75 g, 9.6 mmoles) in anhydrous dichloromethane (6 ml) was added to a suspension of anhydrous aluminum chloride (1.2 g, 9.0 mmoles) in anhydrous dichloromethane (6 ml) with stirring at 0-5°. To this mixture, **9** (0.7 g, 3.1 mmoles) in anhydrous dichloromethane (6 ml) was added at 0-5°; the mixture was stirred for 24 hours at room temperature and poured into ice-cold water. The solution was extracted with dichloromethane. The organic layer was washed with 5% sodium bicarbonate solution and brine, and then dried over anhydrous sodium sulfate. The solution was evaporated and the residue was recrystallized from ethanol-water to give 0.1 g (10%) of **10** as yellow needles, mp 198-199°; ir (potassium bromide): 1675 (COMe) cm^{-1}; pmr (deuteriochloroform): δ 8.86 (1H, d, 5-position, 1.74 Hz), 8.25 (1H, d, 8-position, 8.97 Hz), 8.01 (1H, dd, 7-position, 1.74 and 8.97 Hz), 7.79 (1H, s, 3-position), 4.31 (3H, s, OCH_3, 4-position), 4.27 (3H, s, OCH_3, 9-position), 2.71 (3H, s, $COCH_3$, 6-position), 2.65 (3H, s, $COCH_3$, 2-position); ms: m/z 312 (M^+), 297 (M^+-Me).

Anal. Calcd. for $C_{18}H_{16}O_5$: C, 69.22; H, 5.16. Found: C, 69.09; H, 5.28.

2-Acetyl-4,9-dimethoxynaphtho[2,3-*b*]furan **11**.

Butyllithium (3.9 ml of 1.57 *M*-solution in hexane, 6.1 mmoles) was diluted with THF (6 ml) at -15° in an atmosphere of argon. To this mixture, **9** (0.7 g, 3.1 mmoles) in THF (30 ml) was added at -15°. The mixture was stirred at the same temperature for 4 hours, and then *N,N*-dimethylacetamide (0.6 ml, 6.5 mmoles) in THF (5 ml) was added. The mixture was stirred at room temperature for 3 hours and poured into ice-cold water. The solution was acidified with 10% hydrochloric acid and extracted with ether. The ether layer was washed with brine and dried over anhydrous sodium sulfate. The solution was evaporated and the residue was recrystallized from ethanol-water to give 0.4 g (50%) of **11** as yellow needles, mp 142-143°; ir (potassium bromide): 1670 (COMe) cm^{-1}; pmr (deuteriochloroform): δ 8.20 (2H, m, Ph), 7.70 (1H, s, F-3), 7.42 (2H, m, Ph), 4.28 (3H, s, OCH_3), 4.20 (3H, s, OCH_3), 2.63 (3H, s, $COCH_3$); ms: m/z 270 (M^+), 255 (M^+-Me).

Anal. Calcd. for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 70.82; H, 5.29.

2-Acetylnaphtho[2,3-*b*]furan-4,9-dione **1**.

A solution of cerium(IV) diammonium nitrate (1.4 g) in acetonitrile (2.5 ml) and water (2.5 ml) was added to a suspension of **11** (270 mg, 1.0 mmole) in acetonitrile (8 ml) and water (1.5 ml) with vigorous stirring at 0-5° for 20 minutes. The mixture was allowed to react for 20 minutes at the same temperature and then poured into ice-cold water. The solution was extracted with dichloromethane; the organic layer was washed with brine and dried over anhydrous sodium sulfate. The solution was evaporated and the residue was recrystallized from ethanol-water to give 190 mg (79%) of **1** as yellow needles, mp 219-220° (mp 218-219° [5]).

2-Formyl-4,9-dimethoxynaphtho[2,3-*b*]furan **12**.

Butyllithium (3.6 ml of 1.69 *M*-solution in hexane, 6.1 mmoles) was diluted with THF (6 ml) at -15° in an atmosphere of argon. To the above, **9** (0.7 g, 3.1 mmoles) in THF (30 ml) was added at -15°. The mixture was stirred at the same temperature for 4 hours, and then *N,N*-dimethylformamide (0.3 ml, 3.9 mmoles) in THF (5 ml) was added over 5 minutes. The mixture was stirred at room temperature for 1 hour and poured into ice-cold water. The solution was acidified with 10% hydrochloric acid and extracted with ether. The ether layer was washed with brine and dried over anhydrous sodium sulfate. The solution was evaporated and the residue was recrystallized from ethanol-water to give 0.5 g (63%) of **12** as yellow needles, mp 129-130°; ir (potassium bromide): 1675 (CHO) cm^{-1}; pmr (deuteriochloroform): δ 9.77 (1H, s, CHO), 8.15 (2H, m, Ph), 7.70 (1H, s, F-3), 7.38 (2H, m, Ph), 4.25 (3H, s, OCH_3), 4.20 (3H, s, OCH_3); ms: m/z 256 (M^+), 241 (M^+-Me).

Anal. Calcd. for $C_{15}H_{12}O_4$: C, 70.31; H, 4.72. Found: C, 70.06; H, 4.90.

2-Formylnaphtho[2,3-*b*]furan-4,9-dione **13**.

A solution of cerium(IV) diammonium nitrate (1.4 g) in acetonitrile (2.5 ml) and water (2.5 ml) was added to a suspension of **12** (260 mg, 1.0 mmole) in acetonitrile (8 ml) and water (1.5 ml) with vigorous stirring at 0-5° over 20 minutes. The mixture was allowed to react for 20 minutes at the same temperature and poured into ice-cold water. The solution was extracted with dichloromethane; the organic layer was washed with brine and dried over anhydrous sodium sulfate. The solution was evaporated and the residue was recrystallized from ethanol-water to give 130 mg (57%) of **13** as yellow needles, mp 190-191°; ir (potassium bromide): 1685 (CHO, C=O) cm^{-1}; pmr (deuteriochloroform): δ 9.78 (1H, s, CHO), 8.10 (2H, m, Ph), 7.72 (2H, m, Ph), 7.53 (1H, s, F-3); ms: m/z 226 (M^+).

Anal. Calcd. for $C_{13}H_6O_4$: C, 69.03; H, 2.67. Found: C, 68.84; H, 2.91.

4,9-Dimethoxy-2-trimethylsilylnaphtho[2,3-*b*]furan **15**.

Butyllithium (21.6 ml of 1.69 *M*-solution in hexane, 36.5 mmoles) was diluted with THF (36 ml) at -15° in an atmosphere of argon. To the above, **9** (4.2 g, 18.4 mmoles) in THF (180 ml) was added at -15°. The mixture was stirred at the same temperature for 4 hours, and then chlorotrimethylsilane (3.0 ml, 23.6 mmoles) was added. The mixture was stirred at room temperature for 1 hour and poured into ice-cold water. The solution was acidified with 10% hydrochloric acid and extracted with ether. The ether layer was washed with brine and dried over anhydrous sodium sulfate. The solution was evaporated and the residue was purified by chromatography on silica gel with (hexane: ethyl acetate = 15:1) to give 5.2 g (95%, Rf = 0.47) of **15** as yellow needles, mp 44-46°; ir (potassium bromide): 845 (TMS) cm^{-1}; pmr (deuteriochloroform): δ 8.15 (2H, m, Ph), 7.32 (2H, m, Ph), 7.10 (1H, s, F-3), 4.22 (3H, s, OCH_3), 4.07 (3H, s, OCH_3), 0.38 (9H, s, CH_3 x 3); ms: m/z 300 (M^+), 285 (M^+-Me).

Exact Mass Calcd. for $C_{17}H_{20}O_3Si$: 300.1182. Found: 300.1178.

2-Trimethylsilylnaphtho[2,3-*b*]furan-4,9-dione **14**.

A solution of cerium(IV) diammonium nitrate (11.2 g) in acetonitrile (20 ml) and water (20 ml) was added to a suspension of **15** (2.4 g, 8.0 mmoles) in acetonitrile (32 ml) and water (12 ml) with vigorous stirring at 0-5° over 30 minutes. The mixture was allowed to react for 20 minutes at the same temperature and poured into ice-cold water. The solution was extracted with dichloromethane; the organic layer was washed with brine and dried over anhydrous sodium sulfate. The solution was evaporated and the residue was recrystallized from ethanol-water to give 1.8 g (82%) of **14** as yellow needles, mp 129-130°; ir (potassium bromide): 1680 (C=O), 845 (TMS) cm^{-1}; pmr (deuteriochloroform): δ 8.08 (2H, m, Ph), 7.62 (2H, m, Ph), 7.17 (1H, s, F-3), 0.38 (9H, s, CH_3 x 3); ms: m/z 270 (M^+), 255 (M^+-Me).

Anal. Calcd. for $C_{15}H_{14}O_3Si$: C, 66.64; H, 5.22. Found: C, 66.67; H, 5.33.

2-Iodonaphtho[2,3-*b*]furan-4,9-dione **16**.

A solution of iodine monochloride (4.2 g, 26 mmoles) in acetonitrile (25 ml) was added to **14** (1.4 g, 5.2 mmoles) in acetonitrile (50 ml) with stirring at room temperature. The mixture was allowed to react for 18 hours and was then poured into ice-cold water. The solution was extracted with dichloromethane, and the organic layer was washed with 10% sodium thiosulfate solution, then brine, and dried over anhydrous sodium sulfate. The solution was evaporated, and the residue was recrystallized from ethanol-water to give 1.4 g (82%) of **16** as yellow needles, mp 172-173°; ir (potassium bromide): 1685, 1665 (C=O) cm^{-1}; pmr (deuteriochloroform): δ 8.07 (2H, m, Ph), 7.67 (2H, m, Ph), 7.05 (1H, s, F-3); ms: m/z 324 (M^+), 197 (M^+-I).

Anal. Calcd. for $C_{12}H_5IO_3$: C, 44.48; H, 1.56. Found: C, 44.52; H, 1.78.

2-Bromonaphtho[2,3-*b*]furan-4,9-dione **17**.

A solution of bromine (4.1 g, 26 mmoles) in acetonitrile (25 ml) was added to **14** (1.4 g, 5.2 mmoles) in acetonitrile (50 ml) with stirring at room temperature. The mixture was allowed to react for 30 minutes, and the product was worked up in the same manner as for **16** to give **17** 1.3 g (93%) as yellow needles, mp 175-176°; ir (potassium bromide): 1685, 1670 (C=O) cm^{-1}; pmr (deuteriochloroform): δ 8.05 (2H, m, Ph), 7.65 (2H, m, Ph), 6.80 (1H, s, F-3); ms: m/z 278 (M^++2), 276 (M^+).

Anal. Calcd. for $C_{12}H_5BrO_3$: C, 52.02; H, 1.82. Found: C, 51.81; H, 2.01.

2-Chloronaphtho[2,3-*b*]furan-4,9-dione **18**.

A solution of sulfuryl chloride (2.1 ml, 26 mmoles) in acetonitrile (25 ml) was added to **14** (1.4 g, 5.2 mmoles) in acetonitrile (50 ml) with stirring at room temperature. The mixture was allowed to react for 1.5 hours, and the product was worked up in the same manner as for **16** to give **18** 1.0 g (83%) as yellow needles, mp 176-177°; ir (potassium bromide): 1685 (C=O) cm^{-1}; pmr (deuteriochloroform): δ 8.07 (2H, m, Ph), 7.68 (2H, m, Ph), 6.68 (1H, s, F-3); ms: m/z 234 (M^++2), 232 (M^+), 197 (M^+-Cl).

Anal. Calcd. for $C_{12}H_5ClO_3$: C, 61.96; H, 2.17. Found: C, 61.78; H, 2.40.

2-Nitronaphtho[2,3-*b*]furan-4,9-dione **3**.

Fuming nitric acid (3.5 ml, d = 1.52) was added to acetic anhydride (8 ml) at -5° with stirring, and five drops of sulfuric acid were added. To the above, **14** (1.4 g, 5.2 mmoles) was slowly added at -5° and the mixture was stirred for 3 hours at the same temperature and poured into ice-cold water. The resulting product was collected by filtration and purified by recrystallization from acetonitrile-water to give 1.0 g (77%) of **3** as yellow needles, mp 227-228° (mp 226-227° [5]).

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