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Introduction of a 3-Alkoxycarbonyl-2-propenyl Group at the *ortho* Position of Phenol and Naphthol *via* α-Aryloxy-γ-butyrolactone. Application to Syntheses of (±)-Nanaomycin A and a 1-Anthracenone

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Introduction of a (γ-alkoxycarbonyl)allyl group at the 2 position of 1-naphthol was achieved by a sequence of reactions involving a Claisen rearrangement, as illustrated in Chart 1, in overall yields of 62% (*via* **2a**) and 50% (*via* **2b**). By using the same technique, 5-methoxy- and 4,5-isopropylidenedioxy-1-naphthols and 4-methoxyphenol were converted to the corresponding 4-aryl-2-butenoates (**6a**, **b** and **10**), which underwent base-catalyzed cyclization to give dihydrofurans (**7a**, **b** and **11**). Compounds **7a**, **b** were readily transformed into (±)-nanaomycin A (**14**). 8,10-Dimethoxy-1-anthracenone (**19**) was prepared from **6a** in 77% yield by a standard method.

Keywords——dihydro-1(2*H*)-anthracenone; bromobutyrolactone; Claisen rearrangement; nanaomycin; naphthol; phenol; naphthoquinone; selenophenolate; thiophenoxide

In a recent communication reporting an efficient synthesis of (±)-nanaomycin A (**14**),[1] we presented a new methodology for the introduction of the (γ-alkoxycarbonyl)allyl group at the *ortho*-position of 1-naphthols as exemplified in Chart 1. This paper describes the reaction sequence in detail, including additional examples and some synthetic applications of the products.

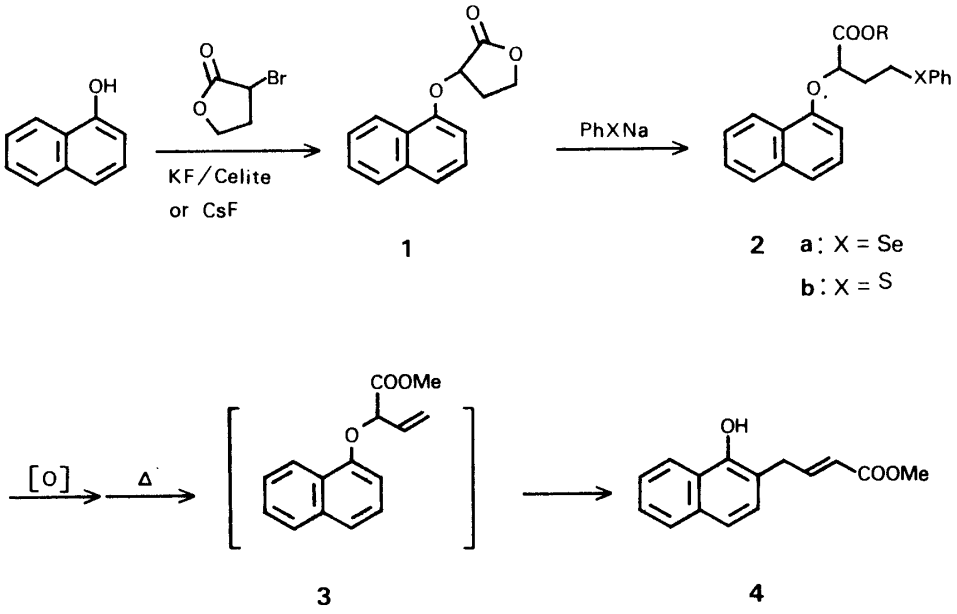

Chart 1

The first step, *O*-alkylation of 1-naphthol with α-bromo-γ-butyrolactone, has been most satisfactorily carried out in the presence of either KF on Celite[2] in acetonitrile at 60 °C or CsF in *N*, *N*-dimethylformamide (DMF)[3] at 120 °C, giving **1** in excellent yield (92 or 84%). Use of sodium hydride as a base in DMF or tetrahydrofuran resulted in a decrease of the yield (60—70%), with concurrent dehydrobromination of the bromolactone occurring to an appreciable extent. Nucleophilic fission of the γ-lactone at the alkyl-oxygen bond with sodium selenophenolate[4] proceeded smoothly on heating in DMF to afford the carboxylic acid **2a** (R=H), which was esterified with diazomethane or methanolic sulfuric acid to give the key compound **2a** (R=Me) in yields of more than 90%. Treatment of the ester with hydrogen peroxide followed by heating of the product **3** (not characterized)[4] at 90 °C under reduced pressure for 1 h afforded 4-(1-hydroxy-2-naphthyl)-2-butenoate (**4**) in 76% yield. Here, it should be noted that the [3,3]-sigmatropic rearrangement occurred at remarkably low temperature, in contrast to the Claisen rearrangement of allyl 1-naphthyl ethers that requires higher temperatures.[5] The facile rearrangement observed with **3** could be rationalized by consideration of the transition state, the ester group being conjugated with the developing double bond. The sulfur analog **2b** (R=Me) was also readily prepared in 92% yield by the reaction of **1** with sodium thiophenoxide[6] followed by esterification. Transformation of the corresponding sulfoxide obtained by oxidation with *m*-chloroperbenzoic acid (MCPBA) into compound **4** was, however, rather sluggish. Heating at 170—200 °C (neat, or better in dimethyl sulfoxide) was required, giving *ca.* 60% yield of **4**. The reaction temperature, higher than that for the selenide **2a** (R=Me), should be due to the desulfenylation step, not the subsequent rearrangement.

The reaction sequence described above was next applied to two functionalized 1-naphthols, 5-methoxy-1-naphthol and 4,5-*O*-isopropylidene-1,4,5-trihydroxynaphthalene, and 4-methoxyphenol. The naphthyloxybutyrolactones **5a**, **b** prepared by the KF–Celite method were smoothly transformed into 4-naphthyl-2-butenoates (**6a**, **b**) in the following overall yields: **6a**, 64% (*via* selenide) or 51% (*via* sulfide); **6b**, 58% (*via* selenide). In the case of 4-methoxyphenol, however, although condensation with α-bromo-γ-butyrolactone to give **8** and subsequent lactone cleavage with thiophenoxide and selenophenolate proceeded nicely

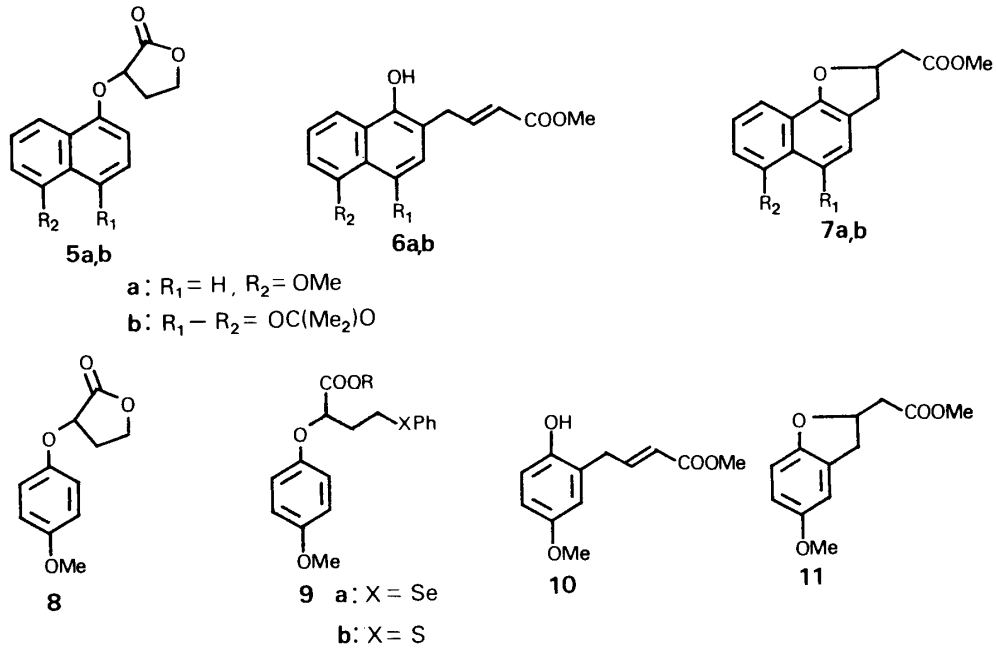

Chart 2

again, giving **9a**, **b** in high yields, rearrangement of the (γ-methoxycarbonyl)allyl ether intermediate generated from **9a** (R = Me) was extremely slow at the temperature (90 °C) employed in the naphthyl series. This step was most effectively carried out by heating the oxidation product of **9a** (R = Me) in dimethyl sulfoxide at 170 °C for 1 h, affording **10** in 67% yield. Transformation of the sulfoxide of **9b** (R = Me) to **10** could be achieved under the same conditions in 62% yield.

The 4-(*ortho*-hydroxyaryl)-2-butenoates (**6a**, **b** and **10**) obtained above underwent intramolecular Michael addition readily on brief treatment with alcoholic sodium carbonate to give dihydrofurans (**7a**, **b** and **11**) quantitatively.

The regiospecific introduction of the 2-butenoate group described above was originally developed in a study on the synthesis of nanaomycins. Oxidation of compound **7b** with silver (II) oxide generated the juglone derivative **12**, which was then readily transformed into nanaomycin A (**14**).[1] An alternative and attractive approach to **14** employing **7a** has also been accomplished. The Vilsmeier reaction of **7a** using a combination of DMF and phosphoryl chloride produced a mixture of two isomeric aldehydes **15** and **16** in a ratio of *ca.* 9 : 1, from which **15** was isolated in 71% yield by recrystallization. Treatment of **15** with MCPBA followed by alkaline hydrolysis of the resulting formate produced the corresponding naphthol **17** in 57% yield. Oxidation of **17** to naphthoquinone **13** was cleanly effected with ceric ammonium nitrate in 93% yield. Conversion of **13** to nanaomycin A (**14**) has been reported by Li and Ellison.[7]

Finally, application of the title methodology to the synthesis of a dimethoxyanthracenone (**19**), an intermediate that we required in another project,[8] is described. An initial attempt to prepare the precursor **18** starting with naphthyl hydrogen succinate (**20**) was

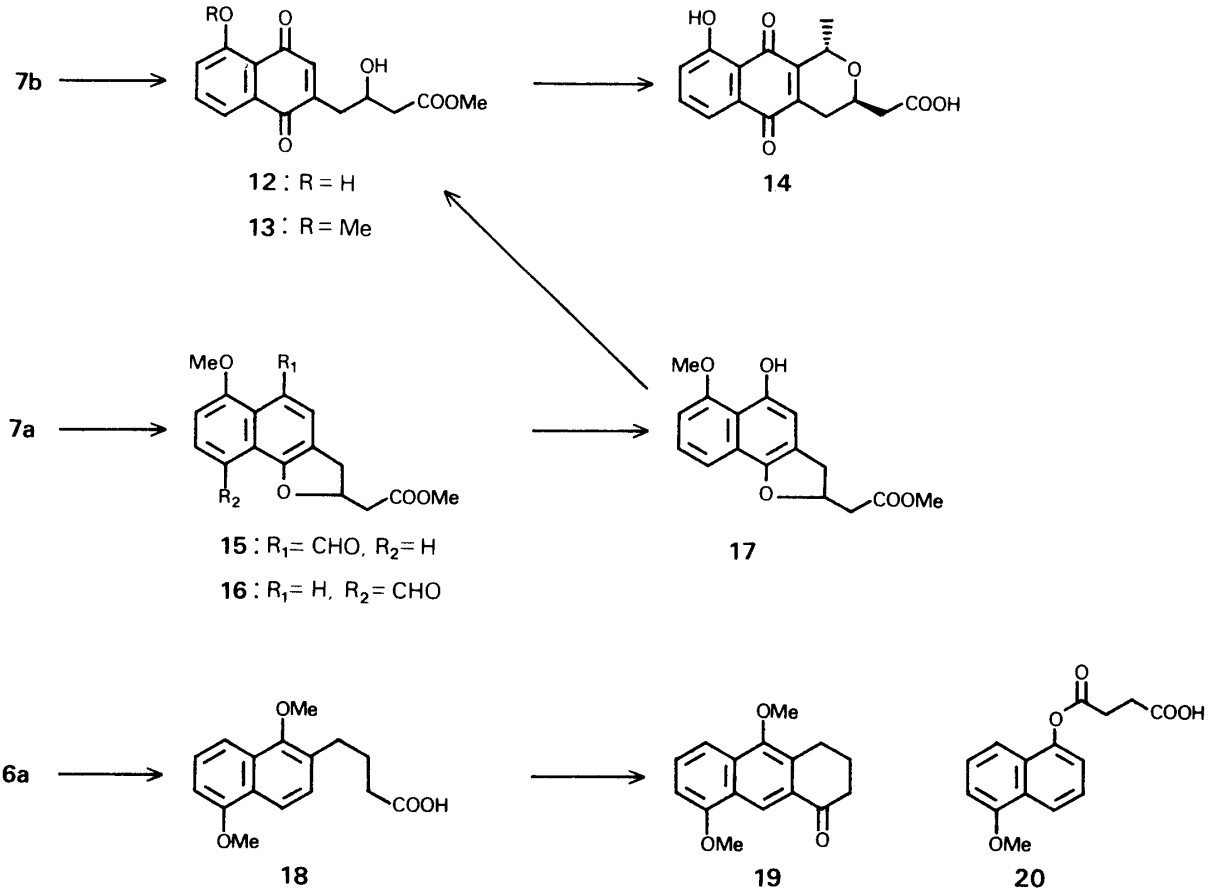

Chart 3

unsuccessful, since Lewis acid-catalyzed Fries rearrangement of **20** ($ZnCl_2$, $AlCl_3$, $BF_3 \cdot Et_2O$) produced a complex mixture of unidentified products. Therefore, compound **18** was prepared from **6a** by catalytic hydrogenation with Pd/C, *O*-methylation with dimethyl sulfate under phase transfer conditions, and then ester hydrolysis. Intramolecular acylation of **18** was effected with polyphosphoric acid to afford 8,10-dimethoxyanthracenone (**19**) in an overall yield of 77% from **6a**.

Experimental

Infrared spectra (IR) were recorded on a Hitachi 215 or a Jasco IRA-1 spectrometer and were calibrated with 1601 cm^{-1} absorption of polystyrene. Proton nuclear magnetic resonance spectra (^{1}H-NMR) were taken on a JEOL PMX-60 (60 MHz), a JEOL MH-100 (100 MHz), or a Varian XL-200 (200 MHz) spectrometer in deuteriochloroform. Chemical shifts are reported in parts per million relative to tetramethylsilane as an internal standard. Resonance patterns are described as s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. Mass spectra (EI) were obtained on a Hitachi RMU-6MG or a JEOL JMS-D300 spectrometer. A Büchi Kugelrohr apparatus was used for vacuum distillation and all boiling points are uncorrected. Melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. Most reactions were followed by thin-layer chromatography (TLC) with Merck precoated plates (Silica gel 60 F_{254}). Merck Silica gel 60 (70—230 or 230—400 mesh) was used for column chromatography. Elemental analyses were performed by the Microanalytical Laboratory of this university. Dry solvents were obtained by using standard procedures. Anhydrous magnesium sulfate was used for drying all organic solvent extracts in work-up, and removal of the solvents was performed with a rotary evaporator.

2-(1-Naphthyloxy)-4-butanolide (1)——a) 2-Bromo-4-butanolide (277 mg, 1.68 mmol) was added to a stirred suspension of 1-naphthol (200 mg, 1.4 mmol) and 50% KF on Celite (812 mg, 7 mmol) in acetonitrile (3 ml), and the mixture was heated at 60 °C. After 6 h, the dark-colored reaction mixture was allowed to cool, then it was filtered, and the filtrate was concentrated. The crystalline residue was recrystallized from ether to give **1** (291 mg, 92%) as colorless crystals, mp 76—77 °C. *Anal.* Calcd for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30. Found: C, 73.77; H, 5.39. IR (KBr): 1780 cm^{-1}. ^{1}H-NMR (100 MHz) δ: 2.30—2.90 (2H, m, 3-H), 4.10—4.50 (2H, m, 4-H), 4.95 (1H, t, J=8 Hz, 2-H), 6.92 (1H, d, J=8 Hz, ArH), 7.20—7.50 (4H, m, ArH), 7.70 (1H, m, ArH), 8.15 (1H, m, ArH). MS *m/e* (relative intensity): 228 (M^+, 100), 144 (35), 143 (98), 115 (35).

b) Cesium fluoride (1.06 g, 7 mmol) was added to a solution of 1-naphthol (200 mg, 1.4 mmol) in DMF (5 ml), and the mixture was stirred at 100 °C for 5 min. 2-Bromo-4-butanolide (460 mg, 2.8 mmol) was then added and stirring at 120 °C was continued for 1 h. The reaction mixture was diluted with water and extracted with AcOEt. The extract was washed with water, dried, and concentrated. The residue was crystallized from ether to give **1** (267 mg, 84%), which was identical with the sample obtained above.

2-(5-Methoxy-1-naphthyloxy)-4-butanolide (5a)——This compound was obtained in 87% yield by the reaction of 5-methoxy-1-naphthol with 2-bromo-4-butanolide in the presence of KF on Celite as described for **1**: colorless needles from EtOH, mp 119.5—121 °C. *Anal.* Calcd for $C_{15}H_{14}O_4$: C, 69.76; H, 5.46. Found: C, 70.04; H, 5.50. ^{1}H-NMR (60 MHz) δ: 2.2—2.9 (2H, m, 3-H), 3.97 (3H, s, OMe), 4.1—4.7 (2H, m, 4-H), 5.00 (1H, t, J=7 Hz, 2-H), 6.80 (1H, d, J=8 Hz, ArH), 7.00 (1H, d, J=8 Hz, ArH), 7.35 (2H, t, J=8 Hz, ArH), 7.68 (1H, d, J=8 Hz, ArH), 7.92 (1H, d, J=8 Hz, ArH).

2-(4,5-Isopropylidenedioxy-1-naphthyloxy)-4-butanolide (5b)——a) A solution of 5-hydroxy-1,4-naphthoquinone (juglone) (1.0 g, 5.75 mmol) in AcOEt (150 ml) was vigorously shaken with a saturated aqueous solution of $Na_2S_2O_4$ (100 ml) for 10 min. The organic layer was separated, washed with water, dried, and concentrated to give 1,4,5-naphthalenetriol. The crude triol was dissolved in acetone (50 ml) under a nitrogen atmosphere and the stirred solution was treated at room temperature with 2,2-dimethoxypropane (5 ml) and $BF_3 \cdot Et_2O$ (0.1 ml) for 1 h. The reaction mixture was concentrated under reduced pressure and the residue was dissolved in DMF (15 ml), and then CsF (4.37 g, 28.8 mmol) was added. The mixture was heated at 100 °C for 5 min under a nitrogen atmosphere, then 2-bromo-4-butanolide (1.90 g, 11.5 mmol) was added to the stirred mixture and heating at 120 °C was continued for 1 h. The reaction mixture was allowed to cool, diluted with water and extracted with AcOEt. The extract was washed with water, dried, and concentrated to give crude **5b**, which after chromatography (silica gel, 30 g; solvent, benzene) was distilled to afford pure **5b** (1.27 g, 74%) as a colorless oil, bp 200—210 °C/1 Torr. IR (film): 1780 cm^{-1}. ^{1}H-NMR (100 MHz) δ: 1.57 (3H, s, Me), 1.60 (3H, s, Me), 2.40—2.75 (2H, m, 3-H), 4.20—4.60 (2H, m, 4-H), 4.91 (1H, t, J=8 Hz, 2-H), 6.64 (1H, d, J=8 Hz, ArH), 6.80 (1H, d, J=8 Hz, ArH), 6.93 (1H, d, J=8 Hz, ArH), 7.33 (1H, t, J=8 Hz, ArH), 7.66 (1H, d, J=8 Hz, ArH).

b) Crude 4,5-isopropylidene-1,4,5-naphthalenetriol obtained from juglone (0.5 g, 2.87 mmol) by the method described above was dissolved in acetonitrile (10 ml), then 50% KF on Celite (1.67 g, 14.4 mmol) and 2-bromo-4-butanolide (711 mg, 4.3 mmol) were added to the solution. The mixture was stirred and heated at 60 °C for 14 h, and then subjected to the same work-up as described above to give **5b** (603 mg, 70%).

2-(4-Methoxyphenyloxy)-4-butanolide (8)——This compound, obtained by the KF–Celite method in 98% yield, showed the following properties. mp 63—64 °C (EtOH). *Anal.* Calcd for $C_{11}H_{12}O_4$: C, 63.46; H, 5.81. Found: C, 63.25; H, 5.98. IR (KBr): 1760 cm^{-1}. ^{1}H-NMR (60 MHz) δ: 2.0—2.9 (2H, m, 3-H), 3.75 (3H, s, OMe), 4.0—4.6 (2H, m, 4-H), 4.80 (1H, t, J=8 Hz, 2-H), 6.90 (4H, m, ArH).

Methyl 2-(1-Naphthyloxy)-4-phenylselenobutanoate (2a, R=Me)——A solution of diphenyldiselenide (222 mg, 0.71 mmol) in DMF (3 ml) was stirred under a nitrogen atmosphere and treated with $NaBH_4$ (61 mg, 1.6 mmol). The mixture was heated to 100 °C during a period of 20 min, and after addition of a solution of **1** (300 mg, 1.3 mmol) in DMF (2 ml), it was kept at 120 °C for 2.5 h. The reaction mixture was allowed to cool to room temperature, acidified by addition of 10% HCl, and extracted with AcOEt. The extract was washed with water, dried, and concentrated. The residual oil (**2a**, R=H) was subjected to esterification with excess ethereal diazomethane (or with MeOH : H_2SO_4 = 20 : 1 in v/v at room temperature for 3.5 h) in the usual manner, and the crude methyl ester was purified by chromatography (silica gel, 15 g; solvent, benzene) followed by distillation to give **2a** (R=Me) as a pale yellow oil (467 mg, 89%), bp 150—155 °C/0.5 Torr. *Anal.* Calcd for $C_{21}H_{20}O_3Se$: C, 63.16; H, 5.05. Found: C, 62.89; H, 5.14. IR (neat): 1755 cm^{-1}. ^{1}H-NMR (100 MHz) δ: 2.2—2.6 (2H, m, 3-H), 3.08 (2H, t, J=7 Hz, 4-H), 3.61 (3H, s, OMe), 4.90 (1H, dd, J=8, 5 Hz, 2-H), 6.52 (1H, d, J=8 Hz, ArH), 7.0—7.5 (9H, m, ArH), 7.70 (1H, m, ArH), 8.20 (1H, m, ArH). MS *m/e* (relative intensity): 400 (M^+, 28), 398 (16), 257 (100), 255 (52).

Methyl 2-(1-Naphthyloxy)-4-phenylthiobutanoate (2b, R=Me)——A suspension of NaH (60% dispersion in mineral oil, 69 mg, previously washed with petroleum ether) in DMF (2 ml) was stirred under a nitrogen atmosphere, and a solution of thiophenol (189 mg, 1.7 mmol) in DMF (0.5 ml) was added dropwise by a syringe. When hydrogen evolution had ceased, a solution of **1** (300 mg, 1.3 mmol) in DMF (1 ml) was added to the mixture and heating at 120 °C was continued for 1 h. The reaction mixture was allowed to cool, acidified by addition of 10% HCl, and extracted with AcOEt. The extract was washed with water, dried, and concentrated to give a solid residue, which was recrystallized from MeOH to give **2b** (R=H) (409 mg, 92%): mp 147—147.5 °C. *Anal.* Calcd for $C_{20}H_{18}O_3S$: C, 70.98; H, 5.36. Found: C, 71.08; H, 5.49. This carboxylic acid was treated with an excess of ethereal diazomethane to give **2b** (R=Me) as a colorless oil (408 mg), bp 160—170 °C/1 Torr. *Anal.* Calcd for $C_{21}H_{20}O_3S$: C, 71.57; H, 5.72. Found: C, 71.87; H, 5.63. IR (neat): 1750 cm^{-1}. ^{1}H-NMR (100 MHz) δ: 2.1—2.55 (2H, m, 3-H), 3.13 (2H, t, J=7 Hz, 4-H), 3.60 (3H, s, OMe), 4.94 (1H, dd, J=7, 5 Hz, 2-H), 6.56 (1H, d, J=8 Hz, ArH), 7.0—7.5 (9H, m, ArH), 7.70 (1H, m, ArH), 8.24 (1H, m, ArH). MS *m/e* (relative intensity): 352 (M^+, 36), 209 (100), 123 (38).

Methyl 4-(1-Hydroxy-2-naphthyl)-2-butenoate (4)——a) A stirred solution of **2a** (R=Me) (450 mg, 1.13 mmol) in tetrahydrofuran (THF) (9 ml) was treated with 30% hydrogen peroxide (1.75 ml) at room temperature for 3 h. The reaction mixture was diluted with water, and extracted with AcOEt. The extract was washed with 10% Na_2CO_3 and water, then dried, and concentrated. The residue was heated at 90 °C under reduced pressure (*ca.* 20 Torr) for 1 h, and the resulting red-brown oil was subjected to chromatography (silica gel, 20 g; solvent, benzene : AcOEt=98 : 2). The solid eluate was crystallized from ether to give **4** as colorless crystals (207 mg, 76%), mp 109—110 °C. *Anal.* Calcd for $C_{15}H_{14}O_3$: C, 74.36; H, 5.82. Found: C, 74.29; H, 5.84. IR (KBr): 3480, 1705 cm^{-1}. ^{1}H-NMR (100 MHz) δ: 3.60 (2H, m, 4-H), 3.63 (3H, s, OMe), 5.56 (1H, s, OH), 5.73 (1H, dt, J=15, 1.5 Hz, 2-H), 6.9—7.5 (5H, m, 3-H and ArH), 7.70 (1H, m, ArH), 7.95 (1H, m, ArH).

b) A stirred solution of **2b** (R=Me) (67 mg, 0.19 mmol) in dichloromethane (8 ml) was cooled with ice-water and treated with MCPBA (33 mg, 0.19 mmol) for 0.5 h. The reaction mixture was washed with 10% $Na_2S_2O_3$, 5% $NaHCO_3$ and water, then dried, and concentrated. The residue was heated to 200 °C for 1 h, and the resulting dark oil was purified by chromatography as described above to give **4** (27 mg, 59%).

Methyl 4-(1-Hydroxy-5-methoxy-2-naphthyl)-2-butenoate (6a)——a) Compound **5a** (903 mg) was transformed to 2-(5-methoxy-1-naphthyloxy)-4-phenylselenobutanoate (1.33 g, 89%) by the procedure described for **1**. mp 75—78 °C (EtOH). ^{1}H-NMR (60 MHz) δ: 2.2—2.6 (2H, m, 3-H), 3.10 (2H, t, J=7 Hz, 4-H), 3.68 (3H, s, OMe), 3.95 (3H, s, OMe), 4.95 (1H, dd, J=7, 5 Hz, 2-H), 6.63 (1H, d, J=8 Hz, ArH), 6.80 (1H, d, J=8 Hz, ArH), 7.0—7.55 (7H, m, ArH), 7.85 (2H, d, J=8 Hz, ArH). This selenide (3.70 g) was treated with 30% H_2O_2 (9.8 ml) in THF (50 ml) for 3 h, and the oxidation product (isolated by AcOEt extraction) was heated at 90 °C under reduced pressure (aspirator) for 1 h. Chromatography (silica gel, 50 g; solvent, benzene : AcOEt=98 : 2) of the crude product afforded **6a** (1.68 g, 72%), which was recrystallized from AcOEt–hexane to give colorless needles, mp 95—99 °C. *Anal.* Calcd for $C_{16}H_{16}O_4$: C, 70.58; H, 5.92. Found: C, 70.62; H, 5.98. IR (KBr): 3470, 1705, 1645 cm^{-1}. ^{1}H-NMR (200 MHz) δ: 3.69 (2H, dd, J=6.3, 1.8 Hz, 4-H), 3.70 (3H, s, OMe), 4.00 (3H, s, OMe), 5.29 (1H, s, OH), 5.82 (1H, dt, J=15.5, 1.8 Hz, 2-H), 6.83 (1H, d, J=7.5 Hz, ArH), 7.20 (1H, dt, J=15.5, 6.3 Hz, 3-H), 7.20 (1H, d, J=8.5 Hz, ArH), 7.42 (1H, dd, J=8.5, 7.5 Hz, ArH), 7.60 (1H, dt, J=8.5, 0.5 Hz, ArH), 7.85 (1H, dd, J=8.5, 0.5 Hz, ArH).

b) Methyl 2-(5-methoxy-1-naphthyloxy)-4-phenylthiobutanoate (8.1 g, 93%), mp 87—89 °C, was obtained from **5a** (6.0 g). ^{1}H-NMR (60 MHz) δ: 2.2—2.6 (2H, m, 3-H), 3.20 (2H, dd, J=8, 7 Hz, 4-H), 3.70 (3H, s, OMe), 3.95 (3H, s, OMe), 5.00 (1H, dd, J=7, 6 Hz, 2-H), 6.74 (2H, t, J=8 Hz, ArH), 7.1—7.5 (7H, m, ArH), 7.90 (2H, d, J=9 Hz, ArH). This sulfide (3.33 g) was treated with MCPBA, and the resulting sulfoxide was dissolved in dimethyl sulfoxide (35 ml) and the solution was heated at 170 °C for 1.5 h. After removal of *ca.* 15 ml of the solvent under reduced pressure, the dark solution was diluted with AcOEt and washed with brine, dried, and concentrated. The residue was subjected to chromatography to give **6a** (1.3 g, 55%).

Methyl 4-(1-Hydroxy-4,5-isopropylidenedioxy-2-naphthyl)-2-butenoate (6b)——Methyl 2-(4,5-isopropylidenedioxy-1-naphthyloxy)-4-phenylselenobutanoate was obtained from **5b** in 81% yield by the same procedure as described for **1**: bp 210—220 °C/1 Torr, a pale yellow oil. *Anal.* Calcd for $C_{24}H_{24}O_5Se$: C, 61.15; H, 5.13. Found: C, 60.86; H, 5.33. IR (neat): 1755 cm^{-1}. ^{1}H-NMR (100 MHz) δ: 1.60 (6H, s, Me), 2.2—2.6 (2H, m, 3-H), 3.15 (2H, t, J=7 Hz, 4-H), 3.68 (3H, s, OMe), 4.92 (1H, dd, J=8, 5 Hz, 2-H), 6.58 (1H, d, J=8 Hz, ArH), 6.70 (1H, d, J=8 Hz, ArH), 6.92 (1H, d, J=8 Hz, ArH), 7.15—7.6 (6H, m, ArH), 7.94 (1H, d, J=8 Hz, ArH). MS *m/e* (relative intensity): 472 (M^+, 55), 257 (100), 215 (86). This seleno-ester was subjected to the oxidation–rearrangement sequence applied in the case of **2a** to give **6b** as a pale red oil in 72% yield. ^{1}H-NMR (100 MHz) δ: 1.60 (6H, s, Me), 3.63 (2H, m, 4-H), 3.69 (3H, s, OMe), 5.56 (1H, s, OH), 5.83 (1H, dt, J=15, 1.5 Hz, 2-H), 6.60 (1H, s, ArH), 6.83 (1H, d, J=8 Hz, ArH), 7.0—7.65 (3H, m, 3-H and ArH). MS *m/e* (relative intensity): 314 (M^+, 100), 254 (76).

Methyl 4-(2-Hydroxy-5-methoxyphenyl)-2-butenoate (10)——a) A solution of sodium selenophenolate was prepared by reduction of diphenyldiselenide (1.2 g) with $NaBH_4$ (325 mg) in DMF, and it was reacted with **8** (1.45 g) at 90 °C for 35 min. The crude carboxylic acid **9a** (R=H) isolated in the usual way was treated with MeOH (25 ml) and H_2SO_4 (1 ml) at room temperature for 3.5 h, and the resulting neutral product was purified by chromatography (silica gel, 80 g; solvent, hexane : AcOEt=2 : 1) to give **9a** (R=Me) (2.40 g, 91%) as a pale yellow oil. ^{1}H-NMR (60 MHz, CCl_4) δ: 1.95—2.40 (2H, m, 3-H), 3.03 (2H, t, J=7 Hz, 4-H), 3.63 (3H, s, OMe), 3.70 (3H, s, OMe), 4.60 (1H, t, J=6 Hz, 2-H), 6.72 (4H, s, ArH), 7.05—7.60 (5H, m, ArH). MS *m/e* (relative intensity): 366 (M^+, 30), 364 (15), 243 (100), 241 (50). A sample of **9a** (R=Me) (200 mg) was treated with 30% H_2O_2 (0.8 ml) in THF (4 ml) at room temperature for 3 h. The oxidation product was dissolved in dimethyl sulfoxide (0.5 ml) under a nitrogen atmosphere, and the solution was heated at 170 °C for 1 h. It was then diluted with water and extracted with AcOEt. The extract was washed with water, dried, and concentrated. The residue was subjected to chromatography (silica gel, 5 g; solvent, hexane : AcOEt=98 : 2) to give **10** (78 mg, 67%), mp 64—68 °C, colorless needles from AcOEt–hexane. *Anal.* Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.68; H, 6.32. IR (KBr): 3375, 1695, 1650 cm^{-1}. ^{1}H-NMR (60 MHz) δ: 3.47 (2H, dd, J=7, 1.5 Hz, 4-H), 3.72 (6H, s, OMe), 5.81 (1H, dt, J=15, 1.5 Hz, 2-H), 6.07 (1H, s, OH), 6.65 (3H, br s, ArH), 7.15 (1H, dt, J=15, 7 Hz, 3-H).

b) Methyl 2-(4-methoxyphenyloxy)-4-phenylthiobutanoate (**9b**, R=Me) was obtained from **8** in >80% yield: bp 220—225 °C/0.2 Torr. *Anal.* Calcd for $C_{18}H_{20}O_4S$: C, 65.04; H, 6.06. Found: C, 64.81; H, 6.04. MS *m/e* (relative intensity): 332 (M^+, 20), 209 (80), 149 (30), 123 (100). It was treated with MCPBA to give the corresponding sulfoxide in 95% yield. The sulfoxide was subjected to pyrolysis at 170 °C in dimethyl sulfoxide for 3.5 h and the product was purified by chromatography to give **10** in 62% yield.

Dihydrofuran Derivatives (7a, b and 11)——Treatment of the corresponding butenoates (0.8—1 mmol) with 10% Na_2CO_3 : MeOH=1 : 50 (20 ml) at room temperature until the starting materials were no longer detectable on TLC (hexane : AcOEt=2 : 1) (1—2 h) afforded the dihydrofurans quantitatively; the properties were as follows.

7a: bp 150—160 °C/0.05 Torr. *Anal.* Calcd for $C_{16}H_{16}O_4$: C, 70.58; H, 5.92. Found: C, 70.70; H, 6.02. ^{1}H-NMR (200 MHz) δ: 2.73 (1H, dd, J=16, 7 Hz), 2.98 (1H, dd, J=16, 7 Hz), 3.08 (1H, dd, J=16, 7 Hz), 3.59 (1H, dd, J=16, 9.5 Hz), 3.74 (3H, s), 3.97 (3H, s), 5.37 (1H, dq, J=9.5, 7 Hz), 6.76 (1H, d, J=7 Hz), 7.29 (1H, d, J=8.5 Hz), 7.30 (1H, t, J=8.5 Hz), 7.36 (1H, d, J=7 Hz), 7.52 (1H, d, J=8.5 Hz), 7.79 (1H, d, J=8.5 Hz). MS *m/e* (relative intensity): 272 (M^+, 100), 240 (65), 211 (50), 198 (90), 169 (30), 115 (45).

7b: bp 160—165 °C/1 Torr. *Anal.* Calcd for $C_{18}H_{18}O_5$: C, 68.78; H, 5.77. Found: C, 68.68; H, 5.91. ^{1}H-NMR (100 MHz) δ: 1.60 (6H, s), 2.72 (1H, dd, J=15, 7 Hz), 2.99 (1H, dd, J=15, 7 Hz), 3.08 (1H, dd, J=16, 7 Hz), 3.58 (1H, dd, J=16, 9 Hz), 5.1—5.6 (1H, m), 6.72 (1H, s), 6.81 (1H, d), 7.3—7.5 (2H, m). MS *m/e* (relative intensity): 314 (M^+, 100), 254 (25).

11: bp 150—160 °C/0.45 Torr. *Anal.* Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.67; H, 6.34. ^{1}H-NMR (200 MHz) δ: 2.68 (1H, dd, J=16, 6.5 Hz), 2.86 (1H, t, J=7 Hz), 2.94 (1H, t, J=7 Hz), 3.40 (1H, dd, J=16, 9 Hz), 3.74 (3H, s), 3.76 (3H, s), 5.14 (1H, dq, J=9, 7 Hz), 6.68 (2H, br s), 6.67 (1H, br s). MS *m/e* (relative intensity): 222 (M^+, 70), 190 (65), 162 (73), 161 (100), 148 (60), 75 (90).

Methyl 5-Formyl-2,3-dihydro-6-methoxynaphtho[1,2-*b*]furan-2-ylacetate (15)——A solution of **7a** (352 mg, 1.3 mmol) in toluene (4 ml) was cooled with ice-water, and DMF (0.3 ml, 3.9 mmol) and $POCl_3$ (0.3 ml, 3.3 mmol) were added with stirring. After 10 min, the reaction mixture was heated under reflux for 30 min. It was then allowed to cool to room temperature, treated with crushed ice and 10% NaOH (2 ml), and extracted with AcOEt. The extract was washed with water, dried, and concentrated under reduced pressure to give a pale yellow solid (350 mg), which showed a single spot on TLC (^{1}H-NMR analysis indicated it to be a *ca.* 9 : 1 mixture of **15** and **16**[9]). Recrystallization of the product from acetone–ether afforded **15** (276 mg, 71%) as colorless needles, mp 106—108 °C. *Anal.* Calcd for $C_{17}H_{16}O_5$: C, 67.99; H, 5.37. Found: C, 68.09; H, 5.39. IR (KBr): 1740, 1660 cm^{-1}. ^{1}H-NMR (200 MHz) δ: 2.80 (1H, dd, J=16, 7 Hz, 10-H), 3.01 (1H, dd, J=16, 7 Hz, 10-H), 3.14 (1H, dd, J=16, 7 Hz, 3-H), 3.65 (1H, dd, J=16, 7 Hz, 3-H), 3.78 (3H, s, OMe), 4.03 (3H, s, OMe), 5.50 (1H, m, 2-H), 7.01 (1H, d, J=8 Hz, ArH), 7.44 (1H, t, J=8 Hz, ArH), 7.67 (1H, d, J=8 Hz, ArH), 8.08 (1H, s, 4-H), 10.74 (1H, s, CHO). MS *m/e* (relative intensity): 300 (M^+, 100), 187 (38), 186 (58).

Methyl 2,3-Dihydro-5-hydroxy-6-methoxynaphtho[1,2-*b*]furan-2-ylacetate (17)——A stirred solution of **15** (100 mg, 0.33 mmol) in dichloromethane (5 ml) was treated with MCPBA (115 mg, 0.67 mmol) at room temperature

for 2 h. The solution was successively washed with 10% $NaHSO_3$, 5% $NaHCO_3$ and water, then dried. The formate of **17**, obtained by evaporation of the solvent, was dissolved in MeOH : THF = 1 : 1 (4 ml). The solution was cooled with ice-water and flushed with N_2 gas for 5 min, then treated with degassed 10% methanolic KOH (1 ml) for 15 min. The mixture was acidified with 5% HCl and diluted with AcOEt. The organic layer was washed with brine, dried, and concentrated. The residue was subjected to chromatography (silica gel, 5 g; solvent, benzene) to give **17** (55 mg, 57%) as a pale yellow oil. IR (neat): 3430, 1740 cm^{-1}. ^1H-NMR (200 MHz) δ: 2.58 (1H, dd, J = 16, 7 Hz, 10-H), 2.84 (1H, dd, J = 16, 8 Hz, 10-H), 2.91 (1H, dd, J = 16, 8 Hz, 3-H), 3.43 (1H, dd, J = 16, 8 Hz, 3-H), 3.60 (3H, s, OMe), 3.87 (3H, s, OMe), 5.12 (1H, m, 2-H), 6.50 (1H, d, J = 8 Hz, ArH), 6.54 (1H, s, 4-H), 7.05 (1H, t, J = 8 Hz, ArH), 7.30 (1H, d, J = 8 Hz, ArH), 8.70 (1H, s, OH). MS *m/e* (relative intensity): 288 (M^+, 100), 228 (53).

5-Methoxy-2-[(3-methoxycarbonyl-2-hydroxy)propyl]-1,4-naphthoquinone (13)——Ceric ammonium nitrate (314 mg, 0.57 mmol) in water (1 ml) was added to a stirred solution of **17** (55 mg, 0.19 mmol) in MeCN (1 ml) at room temperature. After 5 min, the reaction mixture was diluted with water and extracted with AcOEt. The extract was washed with 5% $NaHCO_3$ and water, then dried, and concentrated under reduced pressure to give **13** (54 mg, 93%) as a yellow crystalline solid. An analytical sample was obtained by recrystallization from MeOH as yellow needles, mp 130—132 °C. *Anal.* Calcd for $C_{16}H_{16}O_6$: C, 63.15; H, 5.30. Found: C, 63.31; H, 5.26. IR (KBr): 3490, 1740, 1660, 1625 cm^{-1}. ^1H-NMR (200 MHz) δ: 2.45—2.70 (4H, m), 3.20 (1H, br s, OH), 3.60 (3H, s, OMe), 3.85 (3H, s, OMe), 4.20 (1H, m), 6.86 (1H, s, 3-H), 7.32 (1H, d, J = 8 Hz, ArH), 7.70 (1H, t, J = 8 Hz, ArH), 7.78 (1H, d, J = 8 Hz, ArH). MS *m/e* (relative intensity): 304 (M^+, 1.5), 286 (6), 272 (22), 254 (9), 230 (25), 202 (100).

8,10-Dimethoxy-3,4-dihydro-1(2*H*)-anthracenone (19)——Catalytic hydrogenation of **6a** (3.63 g, 13.3 mmol) in EtOH (200 ml) in the presence of 5% Pd/C (1.2 g) at atmospheric pressure afforded methyl 4-(1-hydroxy-5-methoxy-2-naphthyl)butanoate as pale yellow needles from iso-Pr_2O, mp 102—103 °C. ^1H-NMR (60 MHz) δ: 1.65—2.15 (2H, m, CH_2), 2.37 (2H, br t, J = 6 Hz, CH_2), 2.77 (2H, br t, J = 7 Hz, CH_2), 3.70 (3H, s, OMe), 3.95 (3H, s, OMe), 6.68 (1H, d, J = 8 Hz, ArH), 7.17 (1H, t, J = 8 Hz, ArH), 7.35 (1H, d, J = 8 Hz, ArH), 7.68 (1H, d, J = 8 Hz, ArH), 7.78 (1H, d, J = 8 Hz, ArH). The dihydro compound of **6a** obtained here was dissolved in dichloromethane (50 ml), and to the solution were added Me_2SO_4 (6.6 ml, 66.5 mmol), Bu_4NBr (0.43 g, 1.3 mmol) and 5% NaOH (50 ml). The mixture was vigorously stirred under a nitrogen atmosphere at room temperature for 12 h. The organic layer was separated and concentrated. The residue was dissolved in 10% methanolic KOH (25 ml) and the solution was heated at 60 °C for 30 min. It was acidified with 10% HCl, and diluted with AcOEt. The organic solution was washed with brine, dried, and concentrated to give **18** as a viscous oil. IR (neat): 1710 cm^{-1}. The sample was added to polyphosphoric acid prepared from H_3PO_4 (83%, 18.5 g) and P_2O_5 (17.4 g), and the mixture was heated at 45 °C with stirring for 3.5 h. The reaction mixture was diluted with water and extracted with AcOEt. The extract was washed with water, dried, and concentrated. The residual oil was distilled to give **19** (2.60 g, 77% from **6a**) as a pale yellow solid, bp 160 °C/0.03 Torr. An analytical sample was obtained by recrystallization from iso-Pr_2O as colorless prisms, mp 95—97 °C. *Anal.* Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.82; H, 6.28. IR (KBr): 1675 cm^{-1}. ^1H-NMR (60 MHz) δ: 1.8—2.3 (2H, m, CH_2), 2.68 (2H, br t, J = 6 Hz, CH_2), 3.08 (2H, br t, J = 6 Hz, CH_2), 3.89 (3H, s, OMe), 3.93 (3H, s, OMe), 6.70 (1H, dd, J = 8, 1.5 Hz, ArH), 7.38 (1H, t, J = 8 Hz, ArH), 7.58 (1H, d, J = 8 Hz, ArH), 8.77 (1H, s, ArH). MS *m/e* (relative intensity): 256 (M^+, 17), 241 (7), 213 (6), 199 (5), 32 (100), 28 (100).

References and Notes

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9) Although compound **16** could not be isolated in a pure state, its formation, which can be reasonably interpreted from mechanistic considerations of the reaction, was supported by 200 MHz ^1H-NMR analysis of the sample (**15** : **16** = *ca.* 1 : 10) obtained from the mother liquor of recrystallization. The NMR signals attributable to **16**: δ 2.78 (1H, dd, J = 16, 7 Hz, 10-H), 2.98 (1H, dd, J = 16, 7 Hz, 10-H), 3.15 (1H, dd, J = 16, 7 Hz, 3-H), 3.63 (1H, dd, J = 16, 7 Hz, 3-H), 3.74 (3H, s, OMe), 4.06 (3H, s, OMe), 5.43 (1H, m, 2-H), 6.87 (1H, d, J = 8 Hz, 7-H), 7.37 (1H, d, J = 8 Hz, 4-H), 7.94 (1H, d, J = 8 Hz, 5-H), 8.26 (1H, d, J = 8 Hz, 8-H), 10.74 (1H, s, CHO).