Antiviral activity of arylnaphthalene and aryldihydronaphthalene lignans

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Abstract: A practical method for large scale synthesis of 1-arylnaphthalene and 1-aryl-1,2-dihydronaphthalene lignans is described. The method makes use of the classic Stobbe condensation followed by regioselective reactions that provide access to both the common and retrolactone lignans, e.g., **2** and **3**. A total of 25 compounds, many of which are known natural products, were prepared and their antiviral activity against human cytomegalovirus measured.

Key words: lignan, Stobbe, arylnaphthalene, antiviral.

Résumé : On décrit une méthode pratique de réaliser des synthèses à grande échelle de 1-arylnaphtalène et de 1-aryl-1,2-dihydronaphtalène lignanes. La méthode fait appel à la condensation classique de Stobbe suivie de réactions régiosélectives qui conduisent aussi bien aux lignanes normales que rétrolactoniques, par exemple **2** et **3**. On a ainsi préparé vingt-cinq composés, dont plusieurs sont des produits naturels connus, et on a mesuré leur activité antivirale vis-à-vis le cytomégalovirus humain.

Mots clés : lignane, Stobbe, arylnaphtalène, antiviral.

[Traduit par la Rédaction]

Introduction

Lignans are natural products that are well known for their broad spectrum of medicinal properties (1–4). They are found in many plant species and are believed to be derived from the dimerization of two phenyl propanoid units at the central carbons of their side chains (see Scheme 1) (4).

Further cyclization of lignans can lead to cyclolignans, such as 1-arylnaphthalenes, **1**, (as well as reduced 1-arylnaphthalenes and dibenzocyclooctadienes). Natural 1-arylnaphthalene lignans often feature a γ-lactone ring at the 2,3-position most commonly oriented as in structure **2**, but also found as in **3** (retrolactone) (see Scheme 1) (4).

A recent review of the antiviral activity of lignans (5) prompted us to carry out a more extensive study of the antiviral activity of several 1-arylnapthalene and 1-aryl-1,2-dihydronaphthalene lignans, and their analogs. Although several excellent methods for the synthesis of arylnaphthalene lignans have been published (1–4, 6, 7), we sought a simple method that would yield both 1-arylnaphthalene and 1-aryl-1,2-dihydronaphthalene compounds. The general method that we have used is shown in Scheme 2.

The method is short, convergent, and the purification of intermediates is relatively straightforward. Although the classic Stobbe condensation (first step) is well known (8), it appears that the route from the Stobbe diester **5** to the 1-aryl-1,2-dihydroanthracenes **7** has not previously been investigated. DDQ oxidation of **7** led to the arylnaphthalene diesters **8** that could be regioselectively hydrolysed and reduced to form the lactones **2** or **3**. The dihydrodiesters **7** and **8,** and the lactones **2** and **3**, were tested for antiviral activity against human cytomegalovirus using a standard plaque reduction assay.

Received October 20, 1999. Published on the NRC Research Press website on May 8, 2000.

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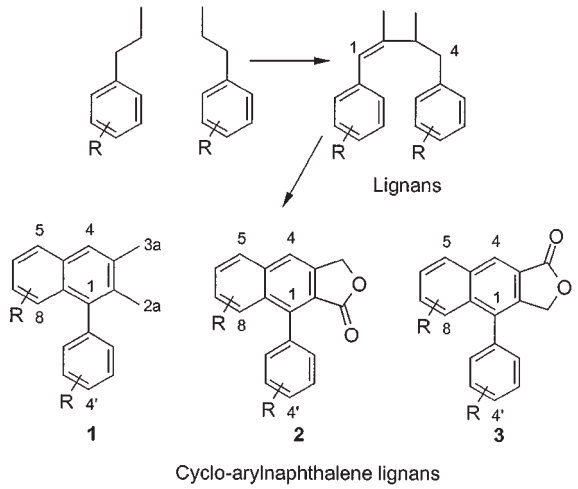
Results and discussion

The classic Stobbe condensation of diethyl succinate with piperonal (3,4-methylenedioxybenzaldehyde) (**a**), veratraldehyde (3,4-dimethoxybenzaldehyde) (**b**) and 3,4,5-trimethoxybenzaldehyde (**c**) was used to prepare the corresponding mono-acids **4a**–**c** (8, 9) The crude mono-acids were esterified to the diethyl esters **5a**–**c** (9) followed by short path distillation under vacuum. Each of the diesters was treated with strong base (LDA) and condensed with each of the three aromatic aldehydes (except for the reaction of **5c** with veratraldehyde) to provide a library of eight alcohols, **6aa**–**6ca**, and **6cc**. It was necessary to quench the condensations with acetic acid at low temperature to prevent lactonization and elimination reactions from occurring. The alcohols were not purified or characterized but were immediately dissolved in trifluoroacetic acid and stirred at room temperature for one hour to form the eight 1-aryl-1,2-dihydronaphthalenes **7aa**–**7ca** and **7cc**. Although there are many methods for the preparation of 1-aryltetralin and 1-aryldihydronaphthalene lignans in the literature, we could find no precedent for this direct and relatively straightforward preparation of 1-aryl-1,2-dihydronaphthalenes from the Stobbe diesters **5**.

Aromatization of the dihydronaphthalenes **7** was accomplished using dicyanodichloro-*p*-benzoquinone (DDQ) in refluxing toluene. This worked well for compounds **7aa**–**7bc** but did not work for the more hindered derivatives **7ca** and

Scheme 1.



7cc, presumably due to steric crowding. The naphthalenes **8aa**–**8bc** could all be recrystallized from the crude reaction mixtures using $CHCl_3$–hexanes as solvent.

The selective hydrolysis of 1-arylnaphthalene diesters similar to **8** has been described in the literature (6). We found that hydrolysis using KOH in methanol–water gave the six mono-acids **9aa**–**9bc** in good yield. Formation of the lactones **2** was accomplished by reducing **9** using borane–dimethylsulfide in THF followed by lactonization in acid. In this way, lactones **2aa** (Taiwanin C), **2ab** (Chinensin), **2ac** (dehydroanhydropodophyllotoxin), **2ba** (Justicidin B), **2bb,** and **2bc** (7-deoxydiphyllin) were prepared. Formation of the retrolactones **3** was accomplished by reducing the ester group using sodium borohydride – lithium chloride in diglyme at 120°C followed by lactonization in acid. The lactones **3aa** (Justicidin E), **3ab** (Retrochinensin), **3ac** (5′-methoxyretrocinensin), **3ba** (Retrojusticidin B), **3bb,** and **3bc** were prepared.

Most of the compounds represented by structures **2**, **3**, **7**, and **8** were tested for their ability to inhibit human cytomegalovirus virus using a standard plaque reduction assay. The cytotoxicities of the compounds were also measured using a tetrazolium salt MTT (10). Seven compounds had EC_{50}s in the low micromolar range (EC_{50}/TC_{50}: **7aa** 25/ >37 μM; **7ac** 1.4/ >25 μM; **7bc** 22/ >33 μM; **2aa** 1.2/ >19 μM; **2ac** 1.4/ >2.0 μM; **3ab** 63/50 μM; **3ba** 7.2/ >65 μM). Most of the remaining compounds did not show substantial antiviral activity at their solubility limit (ca. 50 μM).

Conclusions

A simple, convergent procedure has been developed for the synthesis of 1-arylnaphthalene and 1-aryl-1,2-dihydronaphthalene lignans and lignan analogs. The compounds prepared were screened for activity against human cytomegalovirus using a standard plaque reduction assay. While antiviral activity was found, the activity did not extend into the nanomolar range and was often paired with high cytotoxicity. Only **2aa** (Taiwanin C) and **3ba** (Retrojusticidin B) had a clear antiviral window.

Experimental

General methods

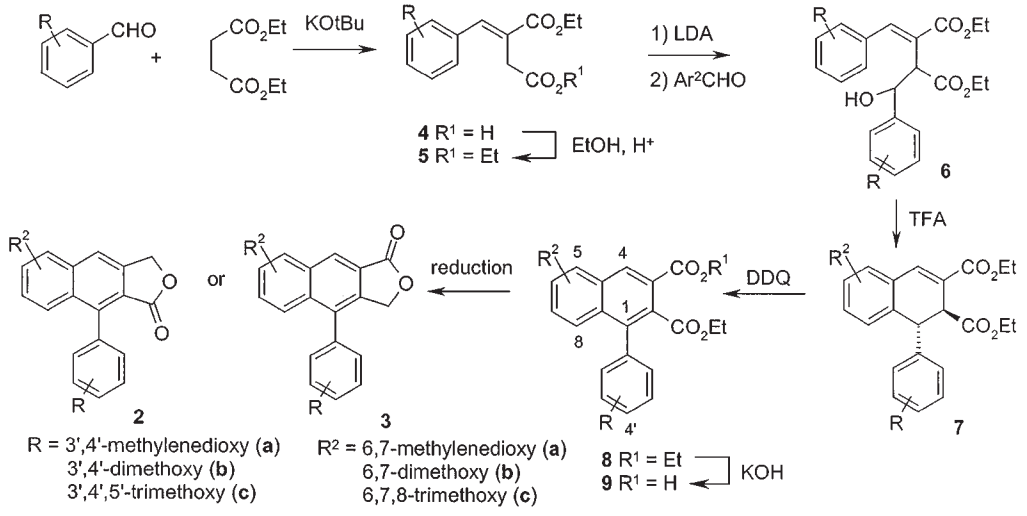
The general experimental procedures and instrumentation have been described in a previous publication (12).

Stobbe condensation – general procedure

tert-Butyl alcohol was charged to a 500 mL flask, and then potassium metal (1.2 equiv., ca. 0.5 M) was cut into pieces and added to the flask. The mixture was heated at reflux until the potassium metal had disappeared (ca. 1 h), and then was cooled to room temperature. Diethyl succinate (2.0 equiv.) and the substituted benzaldehyde (1.0 equiv.) were dissolved in *tert*-butyl alcohol (30 mL), and this mixture added, with stirring, via a dropping funnel over 20 min. The dropping funnel was rinsed with *tert*-butyl alcohol, and the reaction mixture stirred at room temperature for 3 h, during which time a yellow precipitate formed.

The mixture was poured into 10% HCl (100 mL) in a separatory funnel and extracted with EtOAc (3 × 100 mL). The organic layers were combined and washed with satu-

Scheme 2.



rated aqueous $NaHCO_3$ (3 × 100 mL). The basic extracts were combined, acidified with concentrated HCl, and extracted into fresh EtOAc (3 × 50 mL). This second organic extract was washed with water (10 mL), dried over anhydrous magnesium sulfate, filtered, and evaporated to give crude product, which was reacted in the next step without further purification.

*Stobbe acid – **4a***

Piperonal (3,4-methylenedioxybenzaldehyde, 15 g, 100 mmol), potassium metal (4.7 g, 120 mmol), *tert*-butyl alcohol (250 mL), and diethyl succinate (33 mL, 200 mmol), following the general procedure gave a crude product as a light yellow oil (14.0 g, 50% yield).

*Stobbe acid – **4b***

Veratraldehyde (3,4-dimethoxybenzaldehyde, 20 g, 120 mmol), potassium metal (5.6 g, 144 mmol), *tert*-butyl alcohol (250 mL), and diethyl succinate (42 mL, 240 mmol), following the general procedure gave a crude product as a light yellow oil (29.7 g, 77% yield).

*Stobbe acid – **4c***

3,4,5-Trimethoxybenzaldehyde (20 g, 102 mmol), potassium metal (4.8 g, 123 mmol), *tert*-butyl alcohol (250 mL), and diethyl succinate (34 mL, 204 mmol), following the general procedure gave crude product as a yellow oil (27.2 g, 82% yield).

Esterification reaction – general procedure

The crude acid-ester **4** was dissolved in anhydrous EtOH (100 mL, ca. 0.4 M), concentrated H_2SO_4 was added (catalytic amount) and the mixture was heated at reflux for 16 h. The majority of the ethanol was removed on a rotary evaporator, the mixture poured into saturated aqueous NaCl (150 mL) and extracted with EtOAc (3 × 50 mL). The organic extracts were combined and washed with saturated aqueous $NaHCO_3$ (3 × 50 mL) and water (50 mL). The mixture was dried over anhydrous magnesium sulfate, filtered, and evaporated to give a yellow oil. This crude oil was purified by short path, high vacuum (0.01 mm Hg) distillation to give the product.

*Stobbe diester – **5a***

Crude acid **4a** (14.0 g, 50.3 mmol), concentrated H_2SO_4 (2.5 mL), and ethanol (100 mL) gave **5a** as a clear pale yellow distillate (10.7 g, 70% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (s, 1H, Ar-C*H*=C), 6.8–6.9 (m, 3H, Ar-*H*), 5.99 (s, 2H, O-CH_2-O), 4.26 (q, 2H, *J* = 7.1 Hz, CH=C-CO_2-C$H_2$$CH_3$), 4.19 (q, 2H, *J* = 7.1 Hz, CO_2-C$H_2$$CH_3$), 3.53 (s, 2H, C$H_2$-$CO_2$Et), 1.32 (t, 3H, *J* = 7.1 Hz, $CO_2CH_2CH_3$), 1.26 (t, 3H, *J* = 7.1 Hz, $CO_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.1 (*C*=O), 167.4 (*C*=O), 148.2, 147.9, 141.4, 128.9, 124.9, 123.9, 109.1, 108.5, 101.4, 61.0, 60.9, 33.8, 14.3, 14.2; EIMS *m*/*z* = 306 [M^+] (base), 261, 232, 203, 175, 159; HRMS calcd. for $C_{16}H_{18}O_6$: 306.1103, found: 306.1084.

*Stobbe diester – **5b***

Crude acid **4b** (19.0 g, 64.5 mmol), concentrated H_2SO_4 (2.5 mL), and ethanol (100 mL) gave **5b** as a clear yellow distillate (16.0 g, 77% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (s, 1H, Ar-C*H*=C), 6.7–7.0 (m, 3H, Ar-*H*), 4.22 (q, 2H, *J* = 7.1 Hz, CH=C-CO_2-C$H_2$$CH_3$), 4.14 (q, 2H, *J* = 7.2 Hz, CO_2-C$H_2$$CH_3$), 3.85 (s, 3H, OC$H_3$), 3.83 (s, 3H, OC$H_3$), 3.53 (s, 2H, C$H_2$), 1.29 (t, 3H, *J* = 7.1 Hz, $CO_2CH_2CH_3$), 1.22 (t, 3H, *J* = 7.2 Hz, $CO_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.1 (*C*=O), 167.3 (*C*=O), 149.5, 148.6, 141.4, 127.5, 124.2, 122.4, 112.0, 110.9, 60.8, 60.7, 55.7, 55.6, 33.7, 14.1, 14.0; EIMS *m*/*z* = 322 [M^+] (base), 276, 249, 175; HRMS calcd. for $C_{17}H_{22}O_6$: 322.1416, found: 322.1436. The preparation of this compound has been previously reported (8).

*Stobbe diester – **5c***

Crude acid **4c** (27.2 g, 83.8 mmol), concentrated H_2SO_4 (4.0 mL), and ethanol (100 mL) gave **5c** as a clear pale yellow distillate (15.7 g, 53% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (s,1H, Ar-C*H*=C), 6.59 (s, 2H, Ar-*H*), 4.24 (q, 2H, *J* = 7.13 Hz, CO_2-CH_2-CH_3), 4.14 (q, 2H, *J* = 7.13 Hz, CO_2-CH_2-CH_3), 3.83 (s, 3H, *p*-O-CH_3), 3.81 (s, 6H, *m*-O-CH_3), 3.52 (s, 2H, CH_2-CO_2), 1.30 (t, 3H, *J* = 7.12 Hz, O-CH_2CH_3), 1.22 (t, 3H, *J* = 7.13 Hz, O-CH_2CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ171.0 (*C*=O), 167.1 (*C*=O), 153.0, 141.6, 138.5, 130.3, 125.5, 106.2, 60.9, 60.8, 60.6, 55.9, 33.8, 14.0_3, 14.0_1; EIMS *m*/*z* = 352 [M^+] (base), 278, 263, 205; HRMS calcd. for $C_{18}H_{24}O_7$: 352.1522, found: 352.1509. The preparation of this compound has been previously reported (8).

Dihydronaphthalene diesters – general method

Lithium diisopropylamide (1.2 equiv.) was prepared by addition of *n*-BuLi (1.2 equiv., 2.5 M in hexanes) to diisopropylamine (1.3 equiv.) in freshly distilled THF at –70°C. The solution was warmed briefly to 0°C, then recooled to –70°C. A solution of the diester **5** (1 equiv.) in THF was added dropwise through a plug (ca. 1 g) of activated alumina, which was then rinsed with THF. On addition of the diester, the solution turns orange to deep red; this colour persists until the reaction is quenched. The mixture was stirred for 10 min, then a solution of the aldehyde (**a**, **b**, or **c**) in THF was added, and stirring was continued for 1 h. The reaction was quenched with glacial acetic acid at –70°C, then warmed to room temperature.

The mixture was extracted with EtOAc (3 × 20 mL), washed with water (20 mL), dried over anhydrous magnesium sulfate, filtered, and evaporated on the rotary evaporator at 30–40°C. The residue was subjected to high vacuum for 1/2 h to remove solvent, then excess trifluoroacetic acid (TFA) (3–4 mL) was added and the solution stirred at room temperature for 1 h. The reaction was poured into saturated aqueous $NaHCO_3$ and extracted into EtOAc (3 × 20 mL). The organic extracts were washed with saturated aqueous $NaHCO_3$ (3 × 10 mL) and water (10 mL), dried over anhydrous magnesium sulfate, filtered and evaporated. The products were isolated by flash column chromatography on silica gel using 20–30% (depending on the polarity of the final product) EtOAc–hexane as the eluant. The product appears as a fluorescent spot on thin layer chromatography (silica) under UV light.

*Dihydronaphthalene diester – **7aa***

Diester **5a** (1.00 g, 3.28 mmol), diisopropylamine (597 μL, 4.26 mmol), *n*-BuLi (1.79 mL of 2.2 M, 3.94 mmol), piperonal (516 mg, 3.44 mmol), and TFA

(3 mL) were used in the general method above. Flash column chromatography on silica gel using 20% EtOAc–hexanes gave diester **7aa** (684 mg, 48% yield) as a yellow oil, which foamed under vacuum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (s, 1H, Ar-C*H*=C), 6.81 (s, 2H, Ar-*H*), 6.67 (d, 1H, *J* = 7.5 Hz, Ar-*H*), 6.60 (s, 1H, Ar-*H*), 6.53 (dd, 1H, *J* = 1.9, 7.5 Hz, Ar-*H*), 6.52 (s, 1H, Ar-*H*), 5.95 (s, 2H, O-CH_2-O), 5.88 (m (AB), 2H, O-CH_2-O), 4.56 (d, 1H, *J* = 3.0 Hz, C*H*-CO_2Et), 4.21 (m (2 overlapping doublets of quartets), 2H, *J* = 7.1 Hz, CH=C-CO_2C$H_2$$CH_3$), 4.08 (m (2 overlapping doublets of quartets), 2H, *J* = 7.2 Hz, CH-CO_2C$H_2$$CH_3$), 3.93 (d, 2H, *J* = 3.1 Hz, C*H*-Ar), 1.29 (t, 3H, *J* = 7.1 Hz, CH_2CH_3), 1.16 (t, 3H, *J* = 7.1 Hz, CH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.2 (*C*=O), 166.6 (*C*=O), 149.4, 147.7, 147.1, 146.4, 137.1, 136.3, 132.0, 125.5, 123.2, 120.8, 109.7, 108.9, 108.2, 108.1, 101.5, 101.0, 61.2, 60.8, 47.4, 46.2, 14.3, 14.1; EIMS *m*/*z* = 438 [M^+], 410, 364 (base), 319, 292; HRMS calcd. for $C_{24}H_{22}O_8$: 438.1315, found: 438.1311.

*Dihydronaphthalene diester – **7ab***

Diester **5a** (1.26 g, 4.1 mmol), diisopropylamine (692 μL, 4.9 mmol), *n*-BuLi (1.8 mL of 2.5 M, 4.5 mmol), 3,4-dimethoxybenzaldehyde (814 mg, 4.9 mmol), and TFA (4 mL) were used in the general method above. Flash column chromatography on silica gel using 30% EtOAc–hexanes gave diester **7ab** (1.01 g, 54% yield) as a yellow oil, which foamed under vacuum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (s, 1H, Ar-C*H*=C), 6.82 (s, 2H, Ar-*H*), 6.70 (d, 1H, *J* = 8.4 Hz, Ar-*H*), 6.66 (d, 1H, *J* = 2.0 Hz, Ar-*H*), 6.61 (s, 1H, Ar-*H*), 6.50 (dd, 1H, *J* = 2.0, 8.1 Hz, Ar-*H*), 5.96 (s, 2H, O-CH_2-O), 4.58 (d, 1H, *J* = 3.4 Hz, C*H*-CO_2Et), 4.21 (m (2 overlapping doublets of quartets), 2H, *J* = 7.0 Hz, CH=C-CO_2C$H_2$$CH_3$), 4.08 (m (2 overlapping doublets of quartets), 2H, *J* = 7.7 Hz, CH-CO_2C$H_2$$CH_3$), 3.98 (d, 1H, *J* = 3.4 Hz, C*H*-Ar), 3.82 (s, 3H, O-CH_3), 3.80 (s, 3H, O-CH_3), 1.29 (s, 3H, *J* = 7.0 Hz, CH_2CH_3), 1.15 (s, 3H, *J* = 7.0 Hz, CH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.3 (*C*=O), 166.5 (*C*=O), 149.3, 148.9, 147.9, 146.9, 136.9, 134.7, 132.2, 125.5, 123.5, 119.8, 111.1, 110.9, 109.7, 108.7, 101.4, 61.1, 60.7, 55.9, 55.8, 47.3, 46.1, 14.3, 14.1; EIMS *m*/*z* = 454 [M^+], 380 (base), 335, 308; HRMS calcd. for $C_{25}H_{26}O_8$: 454.1628, found: 454.1647.

*Dihydronaphthalene diester – **7ac***

Diester **5a** (751 mg, 2.4 mmol), diisopropylamine (446 μL, 3.2 mmol), *n*-BuLi (1.3 mL of 2.5 M, 2.9 mmol), 3,4,5-trimethoxybenzaldehyde (483 mg, 2.5 mmol), and TFA (4 mL) were used in the general method above. Flash column chromatography on silica gel using 30% EtOAc–hexanes gave diester **7ac** (495 mg, 42% yield) as a yellow oil, which foamed under vacuum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (s, 1H, Ar-C*H*-C), 6.81 (s, 1H, Ar-*H*), 6.61 (s, 1H, Ar-*H*), 6.26 (s, 2H, Ar-*H*), 5.96 (m (AB), 2H, O-CH_2-O), 4.55 (d, 1H, *J* = 4.0 Hz, C*H*-CO_2Et), 4.21 (m (2 overlapping doublets of quartets), 2H, *J* = 7.0 Hz, CH=C-CO_2C$H_2$$CH_3$), 4.08 (m (2 overlapping doublets of quartets), 2H, *J* = 7.4 Hz, CH-CO_2C$H_2$$CH_3$), 3.98 (d, 2H, *J* = 3.7 Hz, C*H*-Ar), 3.78 (s, 3H, *p*-OCH_3), 3.75 (s, 6H, 2 × *m*-OCH_3) 1.29 (t, 3H, *J* = 7.1 Hz, CH_2CH_3), 1.14 (t, 3H, *J* = 7.1 Hz, CH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.3 (*C*=O), 166.5 (*C*=O), 153.1, 149.3, 146.8, 137.8, 136.9, 136.8, 131.9, 125.4, 123.6, 109.7, 108.7, 104.9, 101.5, 61.1, 60.7 (both ethyl CH_2 carbons), 56.1, 47.2, 46.5, 14.3, 14.0; EIMS *m*/*z* = 484 [M^+], 410 (base), 365, 338; HRMS calcd. for $C_{26}H_{28}O_9$: 484.1733, found: 484.1718.

*Dihydronaphthalene diester – **7ba***

Diester **5b** (1.70 g, 5.31 mmol), diisopropylamine (1.04 mL, 7.4 mmol), *n*-BuLi (2.98 mL of 2.5 M, 6.86 mmol), piperonal (911 mg, 6.07 mmol), and TFA (4 mL) were used in the general method above. Flash column chromatography on silica gel using 20% EtOAc–hexanes gave diester **7ba** (1.08 g, 42% yield) as a yellow oil, which foamed under vacuum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (s, 1H, Ar-C*H*=C), 6.86 (s, 1H, Ar-*H*), 6.66 (d, 1H, *J* = 8.0 Hz, Ar-*H*), 6.62 (s, 1H, Ar-*H*), 6.50 (dd, 1H, *J* = 1.7, 8.0 Hz, Ar-*H*), 6.48 (d, 1H, *J* = 1.7 Hz, Ar-*H*), 5.88 (m (AB), 2H, O-CH_2-O), 4.60 (d, 1H, *J* = 2.7 Hz, C*H*-CO_2Et), 4.21 (q, 2H, *J* = 7.0 Hz, CH=C-CO_2C$H_2$$CH_3$), 4.10 (m (2 overlapping doublets of quartets), 2H, *J* = 7.0 Hz, CH-CO_2C$H_2$$CH_3$), 3.94 (d, 2H, *J* = 2.7 Hz, C*H*-Ar), 3.90 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3) 1.30 (t, 3H, *J* = 7.0 Hz, CH_2CH_3), 1.16 (t, 3H, *J* = 7.0 Hz, CH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.3 (*C*=O), 166.6 (*C*=O), 150.8, 148.2, 147.7, 146.4, 137.1, 136.7, 130.1, 124.3, 122.9, 120.8, 112.0, 111.8, 108.2, 108.1$_6$ 101.0, 61.2, 60.7, 56.1, 56.0, 47.6, 45.8, 14.3, 14.1; EIMS *m*/*z* = 454 [M^+], 380 (base), 335, 308); HRMS calcd. for $C_{25}H_{28}O_8$: 454.1627, found: 454.1624

*Dihydronaphthalene diester – **7bb***

Diester **5b** (1.00 g, 3.11 mmol), diisopropylamine (611 μL, 4.36 mmol), *n*-BuLi (1.8 mL of 2.5 M, 4.03 mmol), 3,4-dimethoxybenzaldehyde (574 mg, 3.45 mmol), and TFA (4 mL) were used in the general method above. Flash column chromatography on silica gel using 30% EtOAc–hexanes gave diester **7bb** (694 mg, 46% yield) as a yellow oil, which foamed under vacuum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (s, 1H, Ar-C*H*=C), 6.87 (s, 1H, Ar-*H*), 6.69 (d, 1H, *J* = 8.4 Hz, Ar-*H*), 6.64 (s, 2H, Ar-*H*), 6.47 (dd, 1H, *J* = 2.0, 8.1 Hz, Ar-*H*), 4.62 (d, 1H, *J* = 3.0 Hz, C*H*-CO_2Et), 4.18 (m (2 overlapping doublets of quartets), 2H, *J* = 7.0 Hz, CH=C-CO_2C$H_2$$CH_3$), 4.06 (m (2 overlapping doublets of quartets), 2H, *J* = 7.0 Hz, CH-CO_2C$H_2$$CH_3$), 3.96 (d, 2H, *J* = 3.0 Hz, C*H*-Ar), 3.90 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 1.29 (t, 3H, *J* = 7.1 Hz, CH_2CH_3), 1.15 (t, 3H, *J* = 7.2 Hz, CH_2CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.5 (*C*=O), 166.6 (*C*=O), 150.7, 148.9, 148.1, 147.9, 137.0, 135.1, 130.4, 124.4, 123.2, 119.8, 111.7, 111.3, 110.6, 110.3, 61.2, 60.8, 56.1, 56.0, 55.9, 55.8$_8$, 47.5, 45.8, 14.3, 14.1; EIMS *m*/*z* = 470 [M^+], 396 (base), 351, 324; HRMS calcd. for $C_{26}H_{30}O_8$: 470.1941, found: 470.1965.

*Dihydronaphthalene diester – **7bc***

Diester **5b** (1.10 g, 3.11 mmol), diisopropylamine (672 μL, 4.79 mmol), *n*-BuLi (2.0 mL of 2.2 M, 4.43 mmol), 3,4,5-trimethoxybenzaldehyde (724 mg, 3.69 mmol), and TFA (5 mL) were used in the general method above. Flash column chromatography on silica gel using 30% EtOAc–hexanes gave diester **7bc** (804 mg, 44% yield) as a yellow

oil, which foamed under vacuum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (s, 1H, Ar-C*H*=C), 6.88 (s, 1H, Ar-*H*), 6.66 (s, 1H, Ar-*H*), 6.24 (s, 2H, Ar-*H*), 4.62 (d, 1H, *J* = 3.4 Hz, C*H*-CO_2Et), 4.23 (m (2 overlapping doublets of quartets), 2H, *J* = 6.8 Hz, CH=C-$CO_2CH_2CH_3$), 4.09 (m (2 overlapping doublets of quartets), 2H, *J* = 7.4 Hz, CH-$CO_2CH_2CH_3$), 4.00 (d, 2H, *J* = 3.0 Hz, C*H*-Ar), 3.92 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 3.73 (s, 6H, 2 × *m*-OCH_3), 1.30 (t, 3H, *J* = 7.1 Hz, CH_2CH_3), 1.16 (t, 3H, *J* = 7.2 Hz, CH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4 (*C*=O), 166.6 (*C*=O), 153.1, 150.7, 148.3, 138.2, 136.9, 130.0, 124.4, 123.4, 112.1, 111.6, 104.9, 61.2, 60.8, 60.7, 56.1, 56.0_6 (2 × OCH_3), 47.5, 46.3, 14.3, 14.1 (one quaternary carbon not observed, may be obscured by peak at 136.9); EIMS *m*/*z* = 500 [M^+], 426 (base), 381, 354; HRMS calcd. for $C_{27}H_{32}O_9$: 500.2046, found: 500.2049.

*Dihydronaphthalene diester – **7ca***

Diester **5c** (1.01 g, 2.87 mmol), diisopropylamine (523 μL, 3.73 mmol), *n*-BuLi (1.9 mL of 1.76 M, 3.44 mmol), piperonal (443 mg, 2.95 mmol), and TFA (4 mL) were used in the general method above. Flash column chromatography on silica gel using 30% EtOAc–hexanes gave diester **7ca** (498 mg, 36% yield) as a yellow oil, which foamed under vacuum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (s, 1H, Ar-C*H*=C), 6.70 (s, 1H, Ar-*H*), 6.49–6.62 (m, 3H), 5.85 (m (AB), 2H, O-CH_2-O), 4.93 (bs, 1H, C*H*-CO_2Et), 4.19 (q, 2H, *J* = 7.0 Hz, CH=C-$CO_2CH_2CH_3$), 4.09 (m (2 overlapping doublets of quartets), 2H, *J* = 7.1 Hz, CH-$CO_2CH_2CH_3$), 3.94 (d, 2H, *J* = 1.0 Hz, C*H*-Ar), 3.90 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 3.61 (s, 3H, OCH_3), 1.28 (t, 3H, *J* = 7.0 Hz, CH_2CH_3), 1.18 (t, 3H, *J* = 7.0 Hz, CH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8 (*C*=O), 166.5 (*C*=O), 152.7, 151.3, 147.5, 146.2, 144.3, 137.0, 136.9, 127.1, 124.5, 123.3, 120.5, 108.4, 108.1, 108.0, 100.9, 61.2, 60.9, 60.8, 56.1, 56.0, 46.9, 39.3, 14.3, 14.1; EIMS *m*/*z* = 484 [M^+], 410, 352 (base), 278, 263, 205; HRMS calcd. for $C_{26}H_{28}O_9$: 484.1733, found: 484.1753.

*Dihydronaphthalene diester – **7cc***

Diester **5c** (3.01 g, 8.50 mmol), diisopropylamine (1.55 mL, 11.05 mmol), *n*-BuLi (6.0 mL of 1.76 M, 10.2 mmol), 3,4,5-trimethoxybenzaldehyde (1.68 g, 8.56 mmol), and TFA (5 mL) were subjected to the general method above. Flash column chromatography on silica gel using 30% EtOAc–hexanes gave diester **7cc** (704 mg, 16% yield) as a yellow oil, which foamed under vacuum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (s, 1H, C*H*=C-CO_2Et), 6.71 (s, 1H, Ar-*H*), 6.28 (s, 2H, 2 × Ar-*H*), 5.00 (d, 1H, *J* = 1.2 Hz, C*H*-CO_2Et), 4.23 (2 overlapping quartets, 2H, *J* = 7.1 Hz, CO_2-CH_2CH_3), 4.12 (2 overlapping quartets, 2H, *J* = 7.2 Hz, CO_2-CH_2CH_3), 4.06 (d, 1H, *J* = 1.2 Hz, C*H*-Ar), 3.89 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 3.72 (s, 6H, 2 × *m*-OCH_3), 3.67 (s, 3H, OCH_3), 1.31 (t, 3H, *J* = 7.1 Hz, CH_2CH_3), 1.19 (t, 3H, *J* = 7.2 Hz, CH_2CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.7 (*C*=O), 166.5 (*C*=O), 152.9, 152.7, 151.4, 144.2, 138.4, 136.7, 127.1, 124.9, 123.2, 108.2, 104.6, 61.2, 60.8_4, 60.7_7, 60.7_1, 56.0 (4 × OCH_3), 46.2, 39.4, 14.3, 14.1 (one quaternary carbon not observed); EIMS *m*/*z* = 530 [M^+], 456 (base), 411, 384, 196; HRMS calcd. for $C_{28}H_{34}O_{10}$: 530.2152, found: 530.2129.

Aromatization – formation of arylnapthalene diesters – general procedure

The dihydronaphthalene diesters **7** were dissolved in toluene (ca. 0.015 M), then dicyanodichloroquinone (DDQ, 1.2 equiv.) was added, and the mixture was heated at reflux for 2–5 h. The reaction mixture was cooled to room temperature, and quenched by addition of 100 mL 0.1 M KOH. The product was extracted into 60 mL EtOAc (60 mL) and washed with aqueous KOH (0.1 M, 2 × 50 mL). The aqueous layer was extracted with additional EtOAc (2 × 50 mL), the organic layers combined and washed with water (20 mL) and saturated aqueous NaCl (20 mL). The solution was dried over anhydrous magnesium sulfate, filtered, and evaporated. The resulting red-brown residue was dissolved in the minimum amount of dichloromethane, then passed through a filter column of silica gel using 30% EtOAc–hexanes as the eluant and evaporated. Further purification, to get better than 95% purity by HPLC, required recrystallization from $CHCl_3$–hexanes.

*Arylnaphthalene diester – **8aa***

Diester **7aa** (656 mg, 1.5 mmol), DDQ (409 mg, 1.8 mmol) was heated at reflux in toluene (20 mL) for 5 h, and worked up as in the general method above to give **8aa** (571 mg, 87% yield) as off-white crystals; mp = 171–172°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.38 (s, 1H, C*H*=C-CO_2Et), 7.23 (s, 1H, Ar-*H*), 6.8–6.9 (m, 4H, Ar-*H*), 6.06 (s, 2H, O-CH_2-O), 6.03 (m (AB), 2H, O-CH_2-O), 4.39 (q, 2H, *J* = 7.1 Hz, CO_2-CH_2CH_3), 4.12 (q, 2H, *J* = 7.1 Hz, CO_2-CH_2CH_3), 1.40 (t, 3H, *J* = 7.1 Hz, CO_2-CH_2CH_3), 1.11 (t, 3H, *J* = 7.1 Hz, CO_2-CH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.9 (*C*=O), 166.0 (*C*=O), 150.3, 148.7, 147.3, 136.9, 132.3, 130.6_4, 130.5_9, 129.9, 129.8_6, 123.9, 123.4, 111.0, 108.1, 104.9, 103.3, 101.7, 101.2, 61.5, 61.1, 14.3, 13.9 (one quaternary carbon not detected; perhaps under 147.3); EIMS *m*/*z* = 436 [M^+] (base), 391, 363; HRMS calcd. for $C_{24}H_{20}O_8$: 436.1158, found: 436.1140.

*Arylnaphthalene diester – **8ab***

Diester **7ab** (838 mg, 1.85 mmol), DDQ (503 mg, 2.21 mmol) was heated at reflux in toluene (10 mL) for 3 h, and worked up as in the general method above to give **8ab** (826 mg, 99% yield) as off-white crystals. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.37 (s, 1H, C*H*=C-CO_2Et), 7.21 (s, 1H, Ar-*H*), 6.94 (d, 1H, *J* = 8.0 Hz, Ar-*H*), 6.87 (dd, 1H, *J* = 2.0, 8.0 Hz, Ar-*H*), 6.86 (s, 1H, Ar-*H*), 6.85 (s, 1H, Ar-*H*), 6.04 (s, 2H, O-CH_2-O), 4.38 (q, 2H, *J* = 7.0 Hz, CO_2-CH_2CH_3), 4.07 (2s, 2H, *J* = 7.0 Hz, CO_2-CH_2CH_3), 3.94 (s, 3H, OCH_3), 3.84 (s, 3H, O-CH_3), 1.39 (t, 3H, *J* = 7.1 Hz, CO_2-CH_2CH_3), 1.03 (t, 3H, *J* = 7.1 Hz, CO_2-CH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0 (*C*=O), 165.9 (*C*=O), 150.1, 148.6, 148.5_9, 148.4, 137.1, 132.3, 130.5, 129.8, 129.4, 123.3, 122.7, 113.6, 110.7, 104.8, 103.3, 101.6, 61.4, 61.0, 55.9 (2 × OCH_3), 14.2, 13.8 (one quaternary carbon not detected); EIMS *m*/*z* = 452 [M^+] (base), 407, 379, 363, 335; HRMS calcd. for $C_{25}H_{24}O_8$: 452.1471, found: 452.1470.

*Arylnaphthalene diester – **8ac***

Diester **7ac** (464 mg, 0.96 mmol), DDQ (260 mg, 1.15 mmol) was heated at reflux in toluene (10 mL) for 3 h,

and worked up as in the general method above to give **8ac** (414 mg, 90% yield) as off-white crystals; mp = 178–182°C; ^{1}H (300 MHz, $CDCl_3$) δ 8.39 (s, 1H, C*H*=C-CO_2Et), 7.24 (s, 1H, Ar-*H*), 6.91 (s, 1H, Ar-*H*), 6.55 (s, 2H, Ar-*H*), 6.07 (s, 2H, O-CH_2-O), 4.39 (q, 2H, *J* = 7.1 Hz, CO_2-CH_2CH$_3$), 4.10 (q, 2H, *J* = 7.2 Hz, CO_2-CH_2CH$_3$), 3.92 (s, 3H, *p*-OCH_3), 3.83 (s, 6H, 2 × *m*-OCH_3), 1.40 (t, 3H, *J* = 7.2 Hz, CO_2-CH$_2$CH_3), 1.03 (t, 3H, *J* = 7.1 Hz, CO_2-CH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0 (*C*=O), 165.9 (*C*=O), 152.9, 150.2, 148.8, 137.6, 137.3, 132.5, 132.0, 130.3, 130.0, 129.9, 123.4, 107.7, 104.9, 103.3, 101.8, 61.5, 61.1, 61.0, 56.2, 14.3, 13.9; EIMS *m*/*z* = 482 [M^+] (base), 410, 393, 365; HRMS calcd. for $C_{26}H_{26}O_9$: 482.1576, found: 482.1566.

*Arylnaphthalene diester – **8ba***

Diester **7ba** (914 mg, 2.01 mmol), DDQ (548 mg, 2.4 mmol) was heated at reflux in toluene (10 mL) for 5 h, and worked up as in the general method above to give **20** (878 mg, 97% yield) as off-white crystals; mp = 195–197°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.43 (s, 1H, C*H*=C-CO_2Et), 7.24 (s, 1H, Ar-*H*), 6.79–6.92 (m, 4H, Ar-*H*), 6.02, 6.07 (2s, 2H, O-CH_2-O, hindered rotation), 4.39 (q, 2H, *J* = 7.1 Hz, CO_2-CH_2CH$_3$), 4.13 (q, 2H, *J* = 7.1 Hz, CO_2-CH_2CH$_3$), 4.03 (s, 3H, OCH_3), 3.79 (s, 3H, O-CH_3), 1.40 (t, 3H, *J* = 7.1 Hz, CO_2-CH$_2$CH_3), 1.10 (t, 3H, *J* = 7.1 Hz, CO_2-CH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.1 (*C*=O), 166.1 (*C*=O), 151.7, 150.5, 147.4, 147.3, 136.4, 130.7, 130.6, 130.4, 129.5, 128.5, 123.9, 123.2, 110.9, 108.1, 107.3, 105.3, 101.2, 61.4, 61.1, 56.1, 55.9, 14.3, 13.9; EIMS *m*/*z* = 452 [M^+] (base), 407, 379; HRMS calcd. for $C_{25}H_{24}O_8$: 452.1471, found: 452.1525.

*Arylnaphthalene diester – **8bb***

Diester **7bb** (594 mg, 1.33 mmol), DDQ (363 mg, 1.59 mmol) was heated at reflux in toluene (10 mL) for 3 h, and worked up as in the general method above to give **8bb** (586 mg, 99% yield) as off-white crystals; mp = 127–128°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.43 (s, 1H, C*H*=C-CO_2Et), 7.24 (s, 1H, Ar-*H*), 6.85–7.00 (m, 4H, Ar-*H*), 4.39 (q, 2H, *J* = 7.1 Hz, CO_2-CH_2CH$_3$), 4.09 (dq, 2H, *J* = 2.4, 7.1 Hz, CO_2-CH_2CH$_3$), 4.03 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 3.76 (s, 3H, O-CH_3), 1.40 (t, 3H, *J* = 7.1 Hz, CO_2-CH$_2$CH_3), 1.05 (t, 3H, *J* = 7.1 Hz, CO_2-CH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.3 (*C*=O), 166.1 (*C*=O), 151.7, 150.5, 148.6, 148.5, 136.6, 130.6, 129.6, 129.4, 128.5, 123.2, 122.7, 113.6, 110.8, 107.3, 105.4, 61.4, 61.1, 56.1, 56.0, 55.9$_4$, 55.8$_7$, 14.3, 13.9 (one quaternary carbon not observed; perhaps under 129.4); EIMS *m*/*z* = 468 [M^+] (base), 423, 395; HRMS calcd. for $C_{26}H_{28}O_8$: 468.1784, found: 468.1794.

*Arylnaphthalene diester – **8bc***

Diester **7bc** (538 mg, 1.08 mmol), DDQ (293 mg, 1.29 mmol) was heated at reflux in toluene (20 mL) for 2 h, and worked up as in the general method above to give **8bc** (535 mg, 100% yield) as off-white crystals; mp = 148–149°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.44 (s, 1H, C*H*=C-CO_2Et), 7.24 (s, 1H, Ar-*H*), 6.93 (s, 1H, Ar-*H*), 6.61 (s, 2H, Ar-*H*), 4.39 (q, 2H, *J* = 7.1 Hz, CO_2-CH_2CH$_3$), 4.12 (q, 2H, *J* = 7.1 Hz, CO_2-CH_2CH$_3$), 4.03 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 3.84 (s, 6H, 2 × *m*-OCH_3), 3.79 (s, 3H, O-CH_3), 1.40 (t, 3H, *J* = 7.1 Hz, CO_2-CH$_2$CH_3), 1.04 (t, 3H, *J* = 7.1 Hz, CO_2-CH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2 (*C*=O), 166.0 (*C*=O), 152.9, 151.8, 150.6, 137.6, 136.7, 132.6, 130.2, 130.0, 129.5, 128.5, 123.2, 107.6, 107.3, 105.4, 61.4, 61.1, 61.0, 56.2, 56.1, 56.0, 14.3, 13.9; EIMS *m*/*z* = 498 [M^+], 425, 409, 322, 196 (base); HRMS calcd. for $C_{27}H_{30}O_9$: 498.1890, found: 498.1899.

Formation of arylnapthalene mono-acids – general procedure

The arylnaphthalene diesters **8** were dissolved in MeOH (20 mL, ca. 0.05 M), aqueous KOH (0.4 M, 1.2 equiv.) was added, and the mixture was heated at reflux for 3 h. The mixture was cooled, quenched by addition of 10% HCl until precipitation occurred (pH of <2), then the mixture extracted into EtOAc (3 × 20 mL). The organic layers were combined and extracted with 3 × 20 mL (sat.) $NaHCO_3$. This basic extract was washed with EtOAc (20 mL), then acidified and extracted with ethyl acetate (3 × 10 mL), backwashing with 10 mL of water. The mixture was dried over anhydrous magnesium sulfate, filtered, and evaporated to give a powdery white solid.

*Acid – **9aa***

Arylnaphthalene diester **8aa** (356 mg, 0.82 mmol) and KOH (6 mL, 0.4 M, 2.4 mmol) were subjected to the general procedure described above, producing **9aa** (291 mg, 87% yield) as a fine white powder. ^{1}H NMR (300 MHz, acetone-d_6) δ 11.40 (br. s, 1H, CO_2*H*), 8.49 (s, 1H, C*H*=C-CO_2H), 8.00 (s, 1H, Ar-*H*), 7.48 (s, 1H, Ar-*H*), 6.97 (d, 1H, *J* = 7.7 Hz, Ar-*H*), 6.83 (s, 1H, Ar-*H*), 6.80 (d, 1H, *J* = 1.3 Hz, Ar-*H*), 6.76 (dd, 1H, *J* = 1.7, 7.7 Hz, Ar-*H*), 6.18 (2s, 2H, O-CH_2-O, hindered rotation), 6.09 (m (AB), 2H, O-CH_2-O), 4.02 (q, 2H, *J* = 7.1 Hz, CO_2-CH_2CH$_3$), 1.05 (t, 3H, *J* = 7.1 Hz, CO_2-CH$_2$CH_3); ^{13}C NMR (75 MHz, acetone-d_6) δ 168.5 (*C*=O), 166.9 (*C*=O), 151.2, 149.6, 148.2, 137.4, 132.7, 131.9, 131.4, 130.6$_2$, 130.5$_5$, 124.5, 124.3, 111.5, 108.5, 105.4, 103.1, 102.9, 102.1, 60.9, 14.0 (one quaternary carbon not observed); EIMS *m*/*z* = 408 [M^+], 362 (base), 290, 260, 232, 174; HRMS calcd. for $C_{22}H_{16}O_8$: 408.0845, found: 408.0823.

*Acid – **9ab***

Arylnaphthalene diester **8ab** (602 mg, 1.33 mmol) and KOH (4 mL, 0.4 M, 1.6 mmol) were subjected to the general procedure described above, producing **9ab** (491 mg, 87% yield) as a fine white powder. ^{1}H NMR (300 MHz, $CDCl_3$) 8.49 (s, 1H, C*H*=C-CO_2H), 7.25 (d, 1H, *J* = 2.8, Ar-*H*), 6.8–7.0 (m, 5H, Ar-*H*), 6.07 (s, 2H, O-CH_2-O), 4.09 (2 overlapping quartets, 2H, *J* = 7.1 Hz, CO_2-CH_2CH$_3$), 3.95 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 1.09 (t, 3H, *J* = 7.1 Hz, CO_2-CH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7 (*C*=O), 169.1 (*C*=O), 150.9, 149.1$_0$ 149.0$_9$, 148.8, 137.7, 131.3, 131.2, 130.1, 129.6, 123.1, 122.1, 113.9, 111.1, 105.4, 103.8, 101.8, 61.6, 56.3 (2 × OCH_3), 14.2 (one quaternary carbon not observed); EIMS *m*/*z* = 424 [M^+], 378 (base), 335, 291, 248; HRMS calcd. for $C_{23}H_{20}O_8$: 424.1158, found: 424.1152.

*Acid – **9ac***

Arylnaphthalene diester **8ac** (840 mg, 1.74 mmol) and KOH (6 mL, 0.4 M, 2.4 mmol) were subjected to the general procedure described above, producing **9ac** (644 mg, 82% yield) as a fine white powder. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.48 (s, 1H, C*H*=C-CO_2H), 6.92 (s, 1H, Ar-*H*), 6.56 (s, 2H, Ar-*H*), 6.08 (s, 2H, O-CH_2-O), 4.10 (2 overlapping quartets, 2H, *J* = 7.1 Hz, CO_2-CH_2CH$_3$), 3.93 (s, 3H, *p*-OCH_3), 3.83 (s, 6H, 2 × *m*-OCH_3), 1.07 (t, 3H, *J* = 7.1 Hz, CO_2-CH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9 (*C*=O), 168.7 (*C*=O), 150.6, 152.9, 148.8, 137.7, 137.5, 132.6, 132.2, 131.0, 130.5, 129.7, 107.7, 105.0, 103.4, 101.8, 61.3, 61.0, 56.2, 13.8 (one quaternary carbon not detected); EIMS *m*/*z* = 454 [M$^+$], 408 (base), 393, 380, 365; HRMS calcd. for $C_{24}H_{22}O_9$: 454.1264, found: 454.1285.

*Acid – **9ba***

Arylnaphthalene diester **8ba** (877 mg, 1.94 mmol) and KOH (6 mL, 0.4 M, 2.4 mmol) were subjected to the general procedure described above, producing **9ba** (613 mg, 74% yield) as a fine white powder. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.52 (s, 1H, C*H*=C-CO_2H), 6.92 (d, 1H, *J* = 8.0 Hz, Ar-*H*), 6.88 (s, 1H, Ar-*H*), 6.86 (d, 1H, *J* = 1.0 Hz, Ar-*H*), 6.83 (dd, 1H, *J* = 1.3, 8.0 Hz, Ar-*H*), 6.04 (m (AB), 2H, O-CH_2-O, hindered rotation), 4.14 (q, 2H, *J* = 7.1 Hz, CO_2-CH_2CH$_3$), 4.03 (s, 3H, O-CH_3), 3.80 (s, 3H, O-CH_3), 1.15 (t, 3H, *J* = 7.1 Hz, CO_2-CH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9 (*C*=O), 168.8 (*C*=O), 152.1, 150.5, 147.4, 147.3, 136.5, 131.2, 130.6, 130.5, 130.4, 128.4, 123.8, 121.6, 110.9, 108.1, 107.5, 105.4, 101.2, 61.2, 56.1, 55.9, 13.9; EIMS *m*/*z* = 424 [M$^+$], 378 (base), 306, 291, 276; HRMS calcd. for $C_{23}H_{20}O_8$: 424.1158, found: 424.1159.

*Acid – **9bb***

Arylnaphthalene diester **8bb** (906 mg, 1.94 mmol) and KOH (6 mL, 0.4 M, 2.4 mmol) were subjected to the general procedure described above, producing **9bb** (763 mg, 90% yield) as a fine white powder. ^{1}H NMR (300 MHz, acetone-d_6) δ 11.32 (br. s, 1H, CO_2*H*), 8.51 (s, 1H, C*H*=C-CO_2H), 7.55 (s, 1H, Ar-*H*), 7.06 (d, 1H, *J* = 8.0 Hz, Ar-*H*), 6.96 (s, 1H, Ar-*H*), 6.93 (d, 1H, *J* = 2.0 Hz, Ar-*H*), 6.88 (dd, 1H, *J* = 2.0, 8.0 Hz, Ar-*H*), 4.01 (q, 2H, *J* = 7.1 Hz, CO_2-CH_2CH$_3$), 4.00 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 1.02 (t, 3H, *J* = 7.2 Hz, CO_2-CH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3 (*C*=O), 169.0 (*C*=O), 152.0, 150.5, 148.6, 148.4, 136.7, 131.2, 130.5, 130.4, 129.3, 128.3, 122.7, 121.6, 113.5, 110.7, 107.4, 105.4, 61.2, 56.0, 55.9, 55.7 (2 × OCH$_3$), 13.8; EIMS *m*/*z* = 440 [M$^+$], 394 (base), 307; HRMS calcd. for $C_{24}H_{24}O_8$: 440.1471, found: 440.1469.

*Acid – **9bc***

Arylnaphthalene diester **8bc** (621 mg, 1.25 mmol) and KOH (6 mL, 0.4 M, 2.4 mmol) were subjected to the general procedure described above, producing **9bc** (516 mg, 88% yield) as a fine white powder. ^{1}H NMR (300 MHz, acetone-d_6) δ 11.25 (br. s, 1H, CO_2*H*), 8.54 (s, 1H, C*H*=C-CO_2H), 7.56 (s, 1H, Ar-*H*), 7.03 (s, 1H, Ar-*H*), 6.64 (s, 2H, Ar-*H*), 4.03 (q, 2H, *J* = 7.0 Hz, CO_2-CH_2CH$_3$), 4.01 (s, 3H, OCH_3), 3.84 (s, 6H, 2 × *m*-OCH_3), 3.81 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 1.03 (t, 3H, *J* = 7.0 Hz, CO_2-CH$_2$CH_3); ^{13}C NMR (75 MHz, acetone-d_6) δ 168.9, 167.1, 153.9, 152.9, 151.8, 138.7, 137.3, 133.3, 130.6, 130.0, 129.3, 124.1, 108.7, 108.3, 106.0, 61.0, 60.6, 56.4, 56.0, 55.7, 14.0 (one quaternary carbon not observed); EIMS *m*/*z* = 470 [M$^+$], 424 (base), 409, 381, 363; HRMS calcd. for $C_{25}H_{26}O_9$: 470.1577, found: 470.1568.

Formation of arylnaphthalene lactones – general procedure

The arylnaphthalene mono-acids **9** were dissolved in dry THF (ca. 0.05 M) under nitrogen, a borane-dimethylsulfide solution (2.0 M in ether, 10 equiv.) added, and the mixture stirred at room temperature for 2 h. The reaction was quenched with 3% HCl–EtOH (prepared by addition of 0.5 mL acetyl chloride to 9.5 mL of anhydrous ethanol), then the solvent removed on a rotary evaporator. Anhydrous ethanol (20 mL) was added and evaporated, the solid residue dissolved in chloroform and washed with saturated aqueous $NaHCO_3$ (3 × 10 mL) to remove any remaining acid. The organic extract was washed with water (10 mL), dried over anhydrous magnesium sulfate, filtered, and evaporated to give a white powder. Further purification, to get better than 95% purity by HPLC, involved recrystallization from $CHCl_3$–hexanes.

*Taiwanin C – **2aa***

Arylnaphthalene acid **9aa** (99 mg, 0.24 mmol) and BH_3–DMS (1.2 mL, 2.4 mmol) were subjected to the above conditions to give taiwanin C (**2aa**) (70 mg, 82% yield) as a white powder. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (s, 1H, C*H*=C-CH_2O), 7.19 (s, 1H, Ar-*H*), 7.11 (s, 1H, Ar-*H*), 6.95 (d, 1H, *J* = 7.7 Hz, Ar-*H*), 6.80 (s, 1H, Ar-*H*), 6.77 (d, 1H, *J* = 1.3, 7.7 Hz, Ar-*H*), 6.08 (s, 2H, O-CH_2-O), 6.06 (2 s, 2H, O-CH_2-O, hindered rotation), 5.37 (s, 2H, CH_2-O-C=O); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7 (*C*=O), 149.9, 148.6, 147.6, 147.5, 140.1, 139.8, 134.6, 130.5, 123.5, 128.3, 119.0, 118.9, 110.5, 108.2, 103.7 (broad, 2 carbons), 101.8, 101.2, 68.0; EIMS *m*/*z* = 348 [M$^+$] (base), 319, 289, 261; HRMS calcd. for $C_{20}H_{12}O_6$: 348.0634, found: 348.0629. ^{1}H NMR data identical to that published previously (12, 13).

*Chinensin – **2ab***

Arylnaphthalene acid **9ab** (198 mg, 0.47 mmol) and BH_3–DMS (2.3 mL, 4.7 mmol) were subjected to the above conditions to give Chinensin (**2ab**) (166 mg, 97% yield) as a white powder. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (s, 1H, C*H*=C-CH_2O), 7.20 (s, 1H, Ar-*H*), 7.12 (s, 1H, Ar-*H*), 7.02 (d, 1H, *J* = 8.0 Hz, Ar-*H*), 6.88 (dd, 1H, *J* = 1.7, 8.4 Hz, Ar-*H*), 6.86 (d, 1H, *J* = 1.7 Hz, Ar-*H*), 6.07 (s, 2H, O-CH_2-O), 5.37 (2s, 2H, CH_2-O-C=O), 3.97 (s, 3H, O-CH_3), 3.87 (s, 3H, O-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7 (*C*=O), 149.9, 148.9, 148.6, 148.5, 140.5, 139.8, 134.6, 130.5, 127.2, 122.5, 118.9, 118.8, 113.4, 110.8, 103.7, 103.6, 101.8, 67.9, 55.9, 55.8; EIMS *m*/*z* = 364 [M$^+$] (base); HRMS calcd. for $C_{21}H_{16}O_6$: 364.0947, found: 364.0958. ^{1}H NMR data identical to that published previously (12).

*Dehydroanhydropodophyllotoxin – **2ac***

Arylnaphthalene acid **9ac** (201 mg, 0.44 mmol) and BH_3–DMS (2.2 mL, 4.4 mmol) were subjected to the above conditions to give dehydroanhydropodophyllotoxin (**2ac**)

(122 mg, 70% yield) as a white powder. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (s, 1H, C*H*=C-CH_2O), 7.20 (s, 1H, Ar-*H*), 7.12 (s, 1H, Ar-*H*), 6.55 (s, 2H, Ar-*H*), 6.09 (s, 2H, O-CH_2-O), 5.38 (2s, 2H, CH_2-O-C=O), 3.97 (s, 3H, *p*-OCH_3), 3.84 (s, 6H, 2 × *m*-OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.6 (*C*=O), 152.9, 150.0, 148.6, 140.4, 139.8, 137.8, 134.6, 130.3 (broad, 2 carbons), 119.1, 118.7, 107.3, 103.7, 103.6, 101.8, 68.0, 60.9, 56.1; EIMS *m*/*z* = 394 [M^+] (base), 379; HRMS calcd. for $C_{22}H_{18}O_7$: 394.1052, found: 394.1041. ^{1}H NMR data identical to that published previously (14).

Justicidin B – ***2ba***

Arylnaphthalene acid **9ba** (273 mg, 0.65 mmol) and BH_3–DMS (3.2 mL, 6.5 mmol) were subjected to the above conditions to give justicidin B (**2ba**) (223 mg, 95% yield) as a white powder. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (s, 1H, C*H*=C-CH_2O), 7.18 (s, 1H, Ar-*H*), 7.10 (s, 1H, Ar-*H*), 6.96 (d, 1H, *J* = 7.7 Hz, Ar-*H*), 6.84 (d, 1H, *J* = 2.0 Hz, Ar-*H*), 6.83 (dd, 1H, *J* = 2.0, 7.7 Hz, Ar-*H*), 6.08, 6.03 (2s, 2H, O-CH_2-O, hindered rotation), 5.37 (2s, 2H, CH_2-O-C=O), 4.04 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9 (*C*=O), 151.7, 150.0, 147.4$_9$, 147.4$_6$, 139.5$_5$, 139.4$_6$, 133.1, 128.8, 128.3, 123.4, 118.4, 118.2, 110.5, 108.1, 106.0, 105.8, 101.2, 68.0, 56.0, 55.8; EIMS *m*/*z* = 364 [M^+] (base); HRMS calcd. for $C_{21}H_{16}O_6$: 364.0947, found: 364.0958. ^{1}H NMR data identical to that published previously (15).

Lactone – ***2bb***

Arylnaphthalene acid **9bb** (304 mg, 0.69 mmol) and BH_3–DMS (3.4 mL, 6.9 mmol) were subjected to the above conditions to give lactone **2bb** (250 mg, 95% yield) as a white powder. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (s, 1H, C*H*=C-CH_2O), 7.19 (s, 1H, Ar-*H*), 7.15 (s, 1H, Ar-*H*), 7.04 (d, 1H, *J* = 8.4 Hz, Ar-*H*), 6.96 (dd, 1H, *J* = 2.0, 8.2 Hz, Ar-*H*), 6.93 (dd, 1H, *J* = 2.0 Hz, Ar-*H*), 5.38 (2s, 2H, CH_2-O-C=O), 4.05 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9 (*C*=O), 151.8, 150.0, 148.9, 148.5, 139.9, 139.6, 133.1, 128.8, 127.1, 122.6, 118.3, 118.1, 113.4, 110.8, 106.0 (broad, 2 carbons), 68.0, 56.0$_5$, 55.9$_6$, 55.8$_0$, 55.7$_7$; EIMS *m*/*z* = 380 [M^+] (base), 365; HRMS calcd. for $C_{22}H_{20}O_6$: 380.1260, found: 380.1256. ^{1}H NMR data identical to that published previously (13).

7-Deoxydiphyllin – ***2bc***

Arylnaphthalene acid **9bc** (191 mg, 0.41 mmol) and BH_3–DMS (2.0 mL, 4.1 mmol) were subjected to the above conditions to give lactone **2bc** (233 mg, 80% yield) as a white powder. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (s, 1H, C*H*=C-CH_2O), 7.20 (s, 1H, Ar-*H*), 7.15 (s, 1H, Ar-*H*), 6.62 (s, 2H, 2 × Ar-*H*), 5.40 (2s, 2H, CH_2-O-C=O), 4.06 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 3.85 (s, 6H, 2 × *m*-OCH_3), 3.80 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7 (*C*=O), 152.9, 151.9, 150.1, 139.9, 139.5, 137.8, 133.2, 130.2, 128.6, 118.3, 118.2, 107.4 (broad, 2 carbons), 106.0, 68.0, 61.0, 56.2, 56.1, 55.9; EIMS *m*/*z* = 410 [M^+] (base), 395; HRMS calcd. for $C_{23}H_{22}O_7$: 410.1365, found: 410.1376. ^{1}H NMR data identical to that published previously (16).

Formation of arylnaphthalene retrolactones – general procedure

The arylnaphthalene mono-acids, **9**, sodium borohydride (10–15 equiv.), and lithium chloride (10–15 equiv.) were charged to a 25 mL flask as powders, then diglyme (10 mL) was added and the resulting mixture was heated at ~120°C for 3–16 h. The mixture was cooled and quenched with 10% HCl (10 mL), which was stirred for 1.5 h. The product was extracted into EtOAc (3 × 20 mL) and washed with saturated aqueous $NaHCO_3$ (3 × 10 mL) to remove any remaining acid. The organic extract was washed with water (10 mL), dried over anhydrous magnesium sulfate, filtered, and evaporated to give a white powder. Recrystallization from $CHCl_3$–hexanes provided a white powder, which was a mixture of the desired lactone and the corresponding diol as a side product from over-reduction. The lactone was purified by recrystallization from hot EtOH (95%), providing crystals that were >90% pure by HPLC.

Justicidin E – ***3aa***

Arylnaphthalene acid **9aa** (125 mg, 0.31 mmol), $NaBH_4$ (174 mg, 4.6 mmol), LiCl (194 mg, 4.6 mmol) were used in the general procedure above (16 h reflux time) to give justicidin E (**3aa**) (20.5 mg, 19.2% yield) as colourless crystals. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (s, 1H, C*H*=C-CO_2), 7.30 (s, 1H, Ar-*H*), 7.09 (s, 1H, Ar-*H*), 6.97 (d, 1H, *J* = 8.4 Hz, Ar-*H*), 6.80 (s, 1H, Ar-*H*), 6.79 (dd, 1H, *J* = 1.6, 8.4 Hz, Ar-*H*), 6.09 (s, 2H, O-CH_2-O), 6.08 (2s, 2H, O-CH_2-O, hindered rotation), 5.20 (AB doublet, 2H, Δδ = 17.6 Hz, *J* = 15.0 Hz, C-CH_2-O); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4 (*C*=O), 150.5, 148.4, 148.2, 147.7, 138.4, 133.4, 132.7, 131.3, 129.6, 124.7, 122.7, 121.6, 109.6, 109.0, 105.2, 102.0, 101.8, 101.4, 69.4; EIMS *m*/*z* = 348 [M^+] (base), 319, 233; HRMS calcd. for $C_{20}H_{12}O_6$: 348.0634, found: 348.0604. ^{1}H NMR spectral properties identical with those previously reported (6,12).

Retrochinensin – ***3ab***

Arylnaphthalene acid **9ab** (311 mg, 0.73 mmol), $NaBH_4$ (277 mg, 7.3 mmol), LiCl (309 mg, 7.3 mmol) were used in the general procedure above (5 h reflux time) to give retrochinensin (**3ab**) (165.7 mg, 62.3%; 86.2 mg, 32.4% yield after recrystallization from 95% EtOH) as colourless crystals. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23 (s, 1H, C*H*=C-CO_2), 7.28 (s, 1H, Ar-*H*), 7.09 (s, 1H, Ar-*H*), 7.03 (d, 1H, *J* = 8.2 Hz, Ar-*H*), 6.89 (dd, 1H, *J* = 1.9, 8.1 Hz, Ar-*H*), 6.84 (d, 1H, *J* = 1.9 Hz, Ar-*H*), 6.08 (s, 2H, O-CH_2-O), 5.19 (AB doublet, 2H, Δδ = 17.8 Hz, *J* = 14.8 Hz, C-CH_2-O), 3.97 (s, 3H, O-CH_3), 3.88 (s, 3H, O-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4 (*C*=O), 150.4, 149.3, 148.9, 148.3, 138.3, 133.4, 132.9, 131.2, 128.5, 124.5, 121.6, 112.2, 111.7, 105.2, 102.0, 101.8, 69.5, 56.0$_4$, 55.9$_9$ (one quaternary carbon not observed); EIMS *m*/*z* = 364 [M^+] (base), 350, 335, 319; HRMS calcd. for $C_{21}H_{16}O_6$: 364.0947, found: 364.0927. ^{1}H NMR spectral properties identical with those previously reported (17).

5′-Methoxyretrochinensin – ***3ac***

Arylnaphthalene acid **9ab** (407 mg, 0.89 mmol), $NaBH_4$ (334 mg, 8.9 mmol), LiCl (378 mg, 8.9 mmol) were used in the general procedure above (5 h reflux time) to give 5′-

methoxyretrochinensin (**3ac**) (250.7 mg, 71.5%; 163 mg, 46.5% yield after recrystallization from 95% EtOH) as colourless crystals. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (s, 1H, C*H*=C-CO_2), 7.30 (s, 1H, Ar-*H*), 7.10 (s, 1H, Ar-*H*), 6.54 (s, 2H, Ar-*H*), 6.10 (s, 2H, O-CH_2-O), 5.22 (s, 2H, CH_2-O-C=O), 3.96 (s, 3H, *p*-OCH_3), 3.86 (s, 6H, 2 × *m*-OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3 (*C*=O), 153.7, 150.5, 148.4, 138.1, 137.9, 133.2, 133.0, 131.6, 131.2, 124.7, 121.6, 106.2, 105.2, 102.0, 101.9, 69.4, 61.0, 56.3; EIMS *m*/*z* = 394 [M^+] (base), 379, 363; HRMS calcd. for $C_{22}H_{18}O_7$: 394.1052, found: 394.1060. ^{1}H NMR spectral properties identical with those previously reported (18).

*Retrojusticidin B – **3ba***

Arylnaphthalene acid **9ba** (152 mg, 0.36 mmol), $NaBH_4$ (203 mg, 5.4 mmol), LiCl (226 mg, 5.4 mmol) were used in the general procedure above (16 h reflux time) to give retrojusticidin B (**3ba**) (139.9 mg, 83%; 52.8 mg, 40.3% yield after recrystallization from 95% EtOH) as colourless crystals. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (s, 1H, C*H*=C-CO_2), 7.28 (s, 1H, Ar-*H*), 7.09 (s, 1H, Ar-*H*), 6.98 (d, 1H, *J* = 8.2 Hz, Ar-*H*), 6.84 (s, 1H, Ar-*H*), 6.83 (d, 1H, *J* = 8.2 Hz, Ar-*H*), 6.10, 6.07 (2s, 2H, O-CH_2-O, hindered rotation), 5.22 (s, 2H, CH_2O-C=O), 4.04 (s, 3H, O-CH_3), 3.86 (s, 3H, O-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5 (*C*=O), 151.9, 150.0, 148.2, 147.6, 137.9, 131.8, 131.5, 129.8, 129.7, 124.1, 122.7, 121.3, 109.4, 109.0, 107.6, 104.0, 101.4, 69.4, 56.0, 55.9; EIMS *m*/*z* = 364 [M^+] (base), 335; HRMS calcd. for $C_{21}H_{16}O_6$: 364.0947, found: 364.0943. ^{1}H NMR spectral properties identical with those previously reported (19).

*Retrolactone – **3bb***

Arylnaphthalene acid **9bb** (187 mg, 0.54 mmol), $NaBH_4$ (203 mg, 5.4 mmol), LiCl (227 mg, 5.4 mmol) were used in the general procedure above (16 h reflux time) to give retrolactone **3bb** (105.2 mg, 51%; 60.1 mg, 29.3% yield after recrystallization from 95% EtOH) as colourless crystals. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (s, 1H, C*H*=C-CO_2), 7.29 (s, 1H, Ar-*H*), 7.12 (s, 1H, Ar-*H*), 7.06 (d, 1H, *J* = 8.1 Hz, Ar-*H*), 6.95 (d, 1H, *J* = 8.2 Hz, Ar-*H*), 6.91 (s, 1H, Ar-*H*), 5.22 (d, 2H, *J* = 6.2 Hz, CH_2O-C=O), 4.05 (s, 3H, O-CH_3), 4.00 (s, 3H, O-CH_3), 3.89 (s, 3H, O-CH_3), 3.83 (s, 3H, O-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5 (*C*=O), 151.9, 150.0, 149.3, 148.9, 137.8, 132.1, 131.6, 129.8, 128.6, 124.0, 121.5, 121.3, 112.2, 111.6, 107.6, 104.1, 69.5, 56.0 (2 carbons, OCH_3), 55.9, 55.8; EIMS *m*/*z* = 380 [M^+] (base), 351; HRMS calcd. for $C_{22}H_{20}O_6$: 380.1260, found: 380.1267. ^{1}H NMR spectral properties identical with those previously reported (13).

*Retrolactone – **3bc***

Arylnaphthalene acid **9bc** (310 mg, 0.66 mmol), $NaBH_4$ (250 mg, 6.6 mmol), and LiCl (280 mg, 6.6 mmol) were used in the general procedure above (3 h reflux time) to give retrolactone **3bc** (230.5 mg, 85.1%; 143.6 mg, 53.0% yield after recrystallization from 95% EtOH) as colourless crystals. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (s, 1H, C*H*=C-CO_2), 7.27 (s, 1H, Ar-*H*), 7.13 (s, 1H, Ar-*H*), 6.60 (s, 2H, Ar-*H*), 5.24 (s, 1H, CH_2O-C=O), 4.04 (s, 3H, O-CH_3), 3.96 (s, 3H, O-CH_3), 3.86 (s, 6H, 2 × O-CH_3), 3.84 (s, 3H, O-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 153.7, 152.0, 150.1, 137.8, 137.6, 132.2, 131.6, 131.3, 129.8, 124.1, 121.3, 107.6, 106.2, 104.1, 69.5, 60.9, 56.3, 56.0, 55.9; EIMS *m*/*z* = 410 [M^+] (base), 395, 379; HRMS calcd. for $C_{23}H_{22}O_7$: 410.1365, found: 410.1382. ^{1}H NMR spectral properties identical with those previously reported (13).

Acknowledgements

We are grateful to the Natural Sciences and Engineering Research Council of Canada, Boehringer Ingelheim (Canada) Ltd., Bio-Méga Research Division, and the University of Manitoba for financial support of this project. We also thank Nathalie Dansereau for assaying the compounds in cell culture.

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