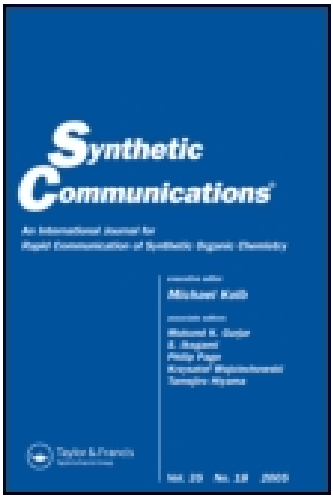

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Synthetic Approaches to Sporochnols A-C

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Synthetic Approaches to Sporochnols A–C

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Abstract: Formal total synthesis of sporochnols A–C, hydroxyphenyl substituted monoterpenes isolated from the Caribbean brown alga *Sporochnus bolleanus* exhibiting feeding deterrent property toward herbivorous fish, is described.

Keywords: Sporochnols, sesquiterpene, Claisen rearrangement

In a variety of marine organisms, chemical defense is common phenomenon as part of the self-defense mechanism to protect themselves from higher animals. During their investigations on the families of chemically defended tropical marine algae, Shen et al.[1] have reported the isolation and structure elucidation of one major, sporochnol A **1**, and two minor, sporochnols B **2** and C **3**, metabolites from the brown alga *Sporochnus bolleanus*, which was found to be rejected by the Caribbean surgeon fish. It was found that the major metabolite sporochnol A **1**, when incorporated into a palatable food, deterred feeding by a mixed species group of herbivorous Caribbean parrotfishes. Structures of sporochnols A–C **1–3** were established from their spectral data, and compounds **2** and **3** were found to be 1:1 mixtures of diastereomers. Feeding deterrence toward herbivorous fish exhibited by sporochnol A made the compounds **1–3** interesting

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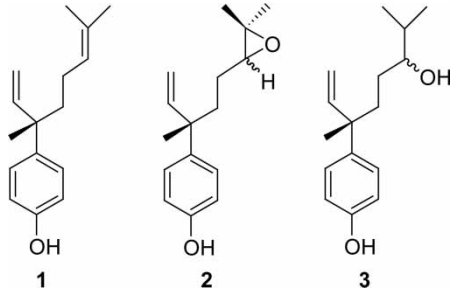
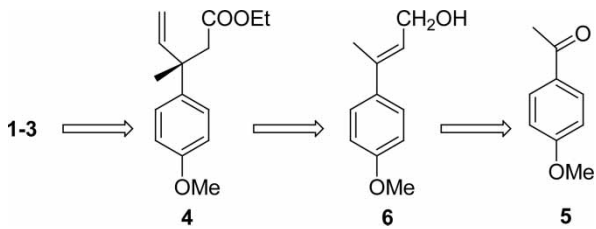
synthetic targets.[2] Herein, we report our approaches toward the synthesis of sporochnols A–C **1–3**.

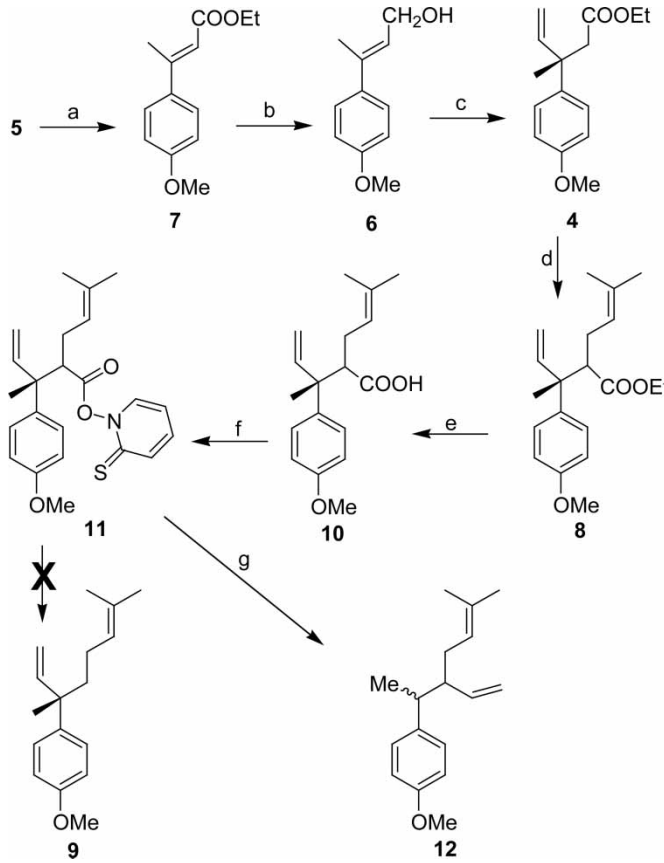


It was contemplated that sporochnols A–C **1–3** could be obtained from the pentenoate **4** via alkylation with dimethylallyl bromide followed by decarboxylation and hydrolysis of the methyl ether. The pentenoate **4**, containing the requisite quaternary carbon atom, could be obtained from the acetophenone **5** via the cinnamyl alcohol **6** employing a Claisen rearrangement–based methodology, Scheme 1.

The synthetic sequence starting from 4-methoxyacetophenone **5** is depicted in Schemes 2 and 3. First, synthesis of the pentenoate **4** was accomplished via the alcohol **6**. Thus, Horner–Wadsworth–Emmons reaction of the acetophenone **5** with triethyl phosphonoacetate and sodium hydride in refluxing THF furnished a 9:1 *E,Z*-mixture of the cinnamate **7** in 95% yield. Regioselective reduction with lithium aluminium hydride (LAH) in ether at a low temperature transformed the cinnamate **7** into the allyl alcohol **6** in 97% yield. Johnsons' one-pot ortho ester variation[3] of the Claisen rearrangement was employed for the conversion of the allyl alcohol **6** into the pentenoate **4**. Thermal activation of the allyl alcohol **6** with triethyl orthoacetate and a catalytic amount of propionic acid in a sealed tube at 180°C for 48 h furnished the pentenoate **4** in 69% yield, creating the requisite quaternary carbon atom, whose structure was established from its spectral data. Generation of enolate of the ester **4** with lithium diisopropylamide (LDA) in THF at −70°C and alkylating with dimethylallyl bromide furnished the hexenoate **8** in 74%

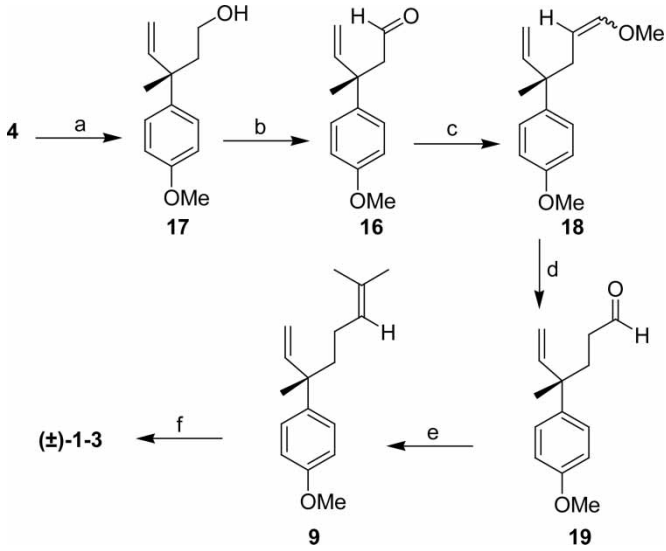


Scheme 1.



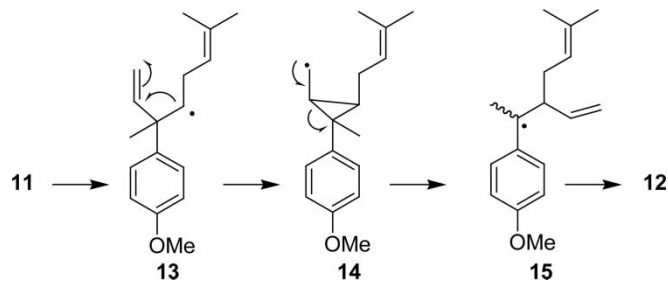
Scheme 2. Reagents, conditions, and yields: (a) $(EtO)_2P(O)CH_2COOEt$, NaH, THF, reflux, 10 h, 95%; (b) LAH, Et_2O, $-70°C \rightarrow -20°C$, 1 h, 97%; (c) $CH_3C(OEt)_3$, EtCOOH, sealed tube, 180°C, 48 h, 69%; (d) LDA, THF, $-70°C \rightarrow$ RT, $Me_2C{=}CHCH_2Br$, 16 h, 74%; (e) 20% KOH in MeOH, reflux, 48 h; (f) i. $(COCl)_2$, C_6H_6, RT, 2 h; ii. *N*-hydroxypyridine-2-thione Na salt, C_6H_6, DMAP, reflux, 1 h; (g) $^nBu_3SnH$, C_6H_6, AIBN, reflux, 14 h; 36% (from the ester **8**).

yield. Next, attention was turned to decarboxylation for the conversion of the hexenoate **8** into the methyl ether **9** of sporochnol A, and Barton's radical-mediated decarboxylation method[4] was chosen. Base-catalyzed hydrolysis of the hexenoate **8** furnished the acid **10**, which was converted into the N-hydroxypyridinethione ester **11** via the corresponding acid chloride. Treatment of the ester **11** with tributyltin hydride in the presence of azobisisobutyronitrile (AIBN) in refluxing benzene, however, failed to produce the expected product **9**, and generated the rearrangement product **12**, whose structure was deduced from the spectral data, in particular ^1H and ^{13}C NMR.



Scheme 3. Reagents, conditions, and yields: (a) LAH, Et_2O, 0°C, 1 h, 92%; (b) PCC, silica gel, CH_2Cl_2, RT, 0.5 h, 88%; (c) $Ph_3P{=}CHOMe$, THF, 0°C → RT, 40 min, 70%; (d) 3 *N* HCl, THF, RT, 1.5 h, 87%; (e) $Ph_3P{=}CMe_2$, THF, RT, 1 h, 78%; (f) reference 2 g.

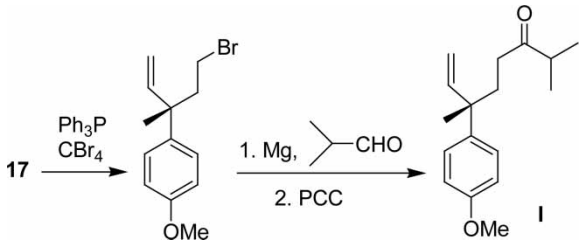
Formation of the diene **12** from the ester **11** can be readily explained as shown in Scheme 4. The homoallyl radical **13** formed from the ester **11** undergoes 3-*exo* trig cyclization to generate the cyclopropylmethyl radical **14**. Opening of the cyclopropylmethyl radical **14** generates the more stable benzylic radical **15**, which abstracts hydrogen from tinhydride leading to the diene **12**.[5] Generation of the rearranged product **12** in the radical-mediated decarboxylation prompted us to alter the strategy, and a homologation and Wittig reaction was contemplated for the conversion of the pentenoate **4** into the diene **9**, which is depicted in Scheme 3. The ester **4** was converted into the aldehyde **16** employing a two-step protocol. Thus,



Scheme 4.

reduction of the pentenoate **4** with LAH in ether furnished the alcohol **17**, which upon oxidation with pyridinium chlorochromate (PCC) and silica gel in methylene chloride generated the pentenal **16** in 81% yield. Wittig reaction of the aldehyde **16** with methoxymethylenetriphenylphosphorane followed by hydrolysis of the resultant enol ether **18** with 3*N* hydrochloric acid furnished the hexenal **19** in 61% yield. Finally, Wittig reaction with isopropylidinetriphenylphosphorane in THF transformed the hexenal **19** into sporochnol A methyl ether **9** in 78% yield, which exhibited spectral data identical to that reported in the literature. Because the conversion of the ether **9** into sporochnols A–C **1–3** has already been reported,[2g] the present sequence constitutes the formal total synthesis of sporochnols A–C.

In conclusion, we have developed an efficient methodology for the synthesis of sporochnols A–C, which can be extended to several analogues.[1]



EXPERIMENTAL

IR spectra were recorded on a Jasco FTIR 410 spectrophotometer. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded on JNM λ-300 spectrometer, using 1:1 mixture of $CDCl_3$ and CCl_4 as solvent. The chemical shifts (δ ppm) and coupling constants (Hz) are reported in the standard fashion with reference to either internal tetramethylsilane (for ^{1}H) or the central line (77.0 ppm) of $CDCl_3$ (for ^{13}C). In the ^{13}C NMR spectra,

[1]Synthesis of a keto analogue **I** of sporochnols has also been accomplished in ≈35% yield starting from the alcohol **17** via the bromide as depicted. Spectral data for the ketone **I**: IR (neat): ν_{max}/cm^{-1} 1712, 1609, 1512, 915. ^{1}H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 7.16 (2 H, d, *J* 8.7 Hz, H-2′ and 6′), 6.78 (2 H, d, *J* 8.7 Hz, H-3′ and 5′), 5.94 (1 H, dd, *J* 17.7 and 10.8 Hz, H-7), 5.07 (1 H, dd, *J* 10.8 and 0.9 Hz), and 5.02 (1 H, dd, *J* 17.7 and 0.9 Hz) [H-8], 3.77 (3 H, s, OCH_3), 2.47 (1 H, septet, *J* 6.9 Hz), 2.35–2.10 (2 H, m, H-4), 2.10–1.85 (2 H, m, H-5), 1.32 (3 H, s, *tert*-CH_3), 1.01 (3 H, d, *J* 6.9 Hz), and 1.02 (3 H, d, *J* 6.9 Hz) [$CH(CH_3)_2$]. ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 213.4 (C, C-3), 157.8 (C, C-4′), 146.7 (CH, C-7), 138.4 (C, C-1′), 127.6 (2 C, CH, C-2′ and 6′), 113.6 (2 C, CH, C-3′ and 5′), 112.1 (CH_2, C-8), 55.0 (CH_3, OMe), 43.3 (C, C-6), 40.9 (CH, C-2), 36.0 (CH_2), 34.2 (CH_2, *tert*-CH_3), 25.5 (CH_3), 18.4 [2 C, CH_3, $CH(CH_3)_2$].

the nature of the carbons (C, CH, CH_2, or CH_3) was determined by recording DEPT-135 spectra and is given in parentheses. Low-resolution mass spectra were recorded using Shimadzu QP-5050A GCMS instrument using direct inlet mode. Relative intensities are given in parentheses. High-resolution mass spectra were recorded on a Micromass Q-TOF micromass spectrometer using electron spray ionization mode.

Ethyl *E*-3-(4-methoxyphenyl)but-2-enoate (7): A suspension of sodium hydride (667 mg, 60% dispersion in oil, 16.7 mmol) in hexanes under nitrogen atmosphere was magnetically stirred for 10 min and the solvent was syringed out. The oil-free NaH was then suspended in dry THF (4 ml) and cooled in an ice bath. Triethyl phosphonoacetate (3.43 ml, 17.3 mmol) was added dropwise and the reaction mixture was stirred for 30 min at rt. A solution of 4-methoxyacetophenone **5** (1 g, 6.7 mmol) in dry THF (2 ml) was added dropwise to the reaction mixture and refluxed for 10 h. It was cooled, quenched by careful addition of saturated aqueous NH_4Cl solution, and extracted with ether (4 × 5 ml). The ether extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica-gel column using ethyl acetate–hexane (1:20) as eluent furnished 9:1 diastereomers of the cinnamate **7** (1.4 g, 95%) as oil. IR (neat): ν_{max}/cm^{-1} 1711, 1626, 1604, 1574, 1513. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): peaks resulting from the major isomer δ 7.42 (2 H, d, *J* 8.7 Hz, H-2′ and 6′), 6.84 (2 H, d, *J* 8.7 Hz, H-3′ and 5′), 6.06 (1 H, s, H-2), 4.18 (2 H, q, *J* 7.2 Hz, OCH_2CH_3), 3.81 (3 H, s, OCH_3), 2.55 (3 H, s, H-4), 1.31 (3 H, t, *J* 7.2 Hz, OCH_2CH_3). Peaks resulting from the minor isomer: δ 7.14 (2 H, d, *J* 8.7 Hz, H-2′ and 6′), 6.82 (2 H, d, *J* 8.7 Hz, H-3′ and 5′), 5.82 (1 H, s, H-2), 4.02 (2 H, q, *J* 7.2 Hz, OCH_2CH_3), 3.80 (3 H, s, OCH_3), 2.16 (3 H, s, H-4), 1.14 (3 H, t, *J* 7.2 Hz, OCH_2CH_3). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 166.5 (C, OC=O), 160.4 (C, C-3), 154.7 (C, C-4′), 134.4 (C, C-1′), 127.6 (2 C, CH, C-2′ and 6′), 115.4 (CH, C-2), 113.8 (2 C, CH, C-3′ and 5′), 59.4 (CH_2, OCH_2CH_3), 55.1 (CH_3, OMe), 17.7 (CH_3, C-4), 14.5 (CH_3, OCH_2CH_3). Peaks resulting from the minor isomer: δ 165.7 (C, OC=O), 159.5 (C, C-3), 154.5 (C, C-4′), 132.6 (C, C-1′), 128.6 (2 C, CH, C-2′ and 6′), 117.2 (CH, C-2), 113.2 (2 C, CH, C-3′ and 5′), 59.5 (CH_2, OCH_2CH_3), 55.0 (CH_3, OMe), 27.4 (CH_3, C-4), 14.3 (CH_3, OCH_2CH_3). Mass: m/z 220 (M^+, 97%), 175 (100), 174 (45), 148 (82), 115 (28), 103 (20), 91 (32).

***E*-3-(4-methoxyphenyl)but-2-enol (6):** To a cold (−90°C), magnetically stirred solution of the cinnamate **7** (1.05 g, 4.8 mmol) in dry ether (10 ml) was added LAH (181 mg, 4.8 mmol) and stirred for 1 h. The reaction mixture was then diluted with ether (30 ml) and carefully quenched with water (5 ml). The organic layer was separated and the aqueous phase extracted with ether (20 ml). The combined organic phase was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the

residue over a silica-gel column using ethyl acetate–hexane (1:20 to 1:5) as eluent furnished the alcohol **6** (848 mg, 99%) as a colorless solid.[6] Mp 51–53°C. IR (neat): ν_{max}/cm^{-1} 3340, 3247, 1607, 1514, 1029. ^{1}H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 7.28 (2 H, d, *J* 8.7 Hz, H-2′ and 6′), 6.78 (2 H, d, *J* 8.7 Hz, H-3′ and 5′), 5.86 (1 H, t, *J* 6.6 Hz, H-2), 4.28 (2 H, d, *J* 6.6 Hz, C*H*$_2$OH), 3.78 (3 H, s, OCH_3), 2.02 (3 H, s, H-4), 1.86 (1 H, brs). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 159.0 (C, C-4′), 137.2 (C), 135.3 (C), 126.8 (2 C, CH, C-2′ and 6′), 125.0 (CH, C-2), 113.6 (2 C, CH, C-3′ and 5′), 59.8 (CH_2, OCH_2), 55.0 (CH_3, OMe), 16.0 (CH_3, C-4). Mass: 178 (M^+, 31%), 163 (21), 136 (10), 135 (100), 121 (15), 105 (15), 91 (20).

Ethyl 3-methyl-3-(4-methoxyphenyl)pent-4-enoate (4): A solution of the allyl alcohol **6** (1 g, 5.6 mmol), triethyl orthoacetate (5 ml, 28.1 mmol), and a catalytic amount of propionic acid was placed in a sealed tube and heated to 180°C for 2 days in an oil bath. The reaction mixture was then cooled, diluted with ether (10 ml), washed with 3 N of aqueous HCl (10 ml), followed by saturated $NaHCO_3$ solution (10 ml) and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica-gel column using ethyl acetate–hexane (1:50) as eluent furnished the pentenoate **4** (960 mg, 69%) as oil. IR (neat): ν_{max}/cm^{-1} 1734, 1609, 1512, 917. ^{1}H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 7.18 (2 H, d, *J* 8.7 Hz, H-2′ and 6′), 6.77 (2 H, d, *J* 8.7 Hz, H-3′ and 5′), 6.10 (1 H, dd, *J* 17.4 and 10.5 Hz, H-4), 5.08 (1 H, d, *J* 10.5 Hz) and 5.02 (1 H, d, *J* 17.4 Hz) [H-5], 3.96 (2 H, q, *J* 7.2 Hz, OC*H*$_2$CH$_3$), 3.75 (3 H, s, OCH_3), 2.72 and 2.66 (2 H, AB q, *J* 13.8 Hz, H-2), 1.52 (3 H, s, *tert*-CH_3), 1.10 (3 H, t, *J* 7.2 Hz, OCH_2CH_3). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 170.8 (C, OC=O), 157.9 (C, C-4′), 146.0 (CH, C-4), 137.9 (C, C-1′), 127.4 (2 C, CH, C-2′ and 6′), 113.4 (2 C, CH, C-3′ and 5′), 112.0 (CH_2, C-5), 59.8 (CH_2, OCH_2), 54.9 (CH_3, OMe), 45.7 (CH_2, C-2), 42.9 (C, C-3), 25.7 (CH_3, *tert*-CH_3), 14.2 (CH_3, OCH_2CH_3). Mass: 248 (M^+, 8%), 162 (12), 161 (100), 91 (14). HRMS: m/z calcd. for $C_{15}H_{20}O_3Na$ (M + Na): 271.1310. Found: 271.1306.

Ethyl 2-[2-(4-methoxyphenyl)but-3-en-2-yl]-5-methylhex-4-enoate (8): To a cold (−70°C), magnetically stirred solution of LDA [prepared from diisopropylamine (0.28 ml, 2.03 mmol) and ^{n}BuLi (2.4 *M* in hexane, 0.81 ml, 1.9 mmol)] in dry THF (3 ml) was added a solution of the ester **4** (100 mg, 0.4 mmol) in dry THF (2 ml), and the reaction mixture stirred for 40 min at the same temperature. The enolate thus formed was treated with prenyl bromide (0.24 ml, 2.03 mmol) and stirred for 16 h at rt. It was then diluted with water (5 ml) and extracted with ether (2 × 10 ml). The combined ether extract was washed with 3 N of HCl, followed by brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica-gel column using ethyl acetate–hexane (1:49) as eluent furnished a 2:1 diastereomeric mixture of the ester **8** (70 mg, 74% based on starting material consumed). IR (neat): ν_{max}/cm^{-1} 1732, 1726, 1611, 1513, 919. ^{1}H

NMR (300 MHz, $CDCl_3 + CCl_4$, 2:1 mixture of diastereomers): δ 7.26–7.18 (2 H, m, H-2″ and 6″), 6.60–6.40 (2 H, m, H-3″ and 5″), 6.35 (dd, *J* 17.7 and 10.8 Hz) and 6.15 (dd, *J* 17.1 and 10.5 Hz) [1 H, H-3′], 5.22–4.90 (3 H, m, H-4 and 4′), 4.10–3.60 (2 H, m, OCH_2), 3.76 and 3.75 (3 H, s, OCH_3), 2.82–2.60 (1 H, m), 2.42–1.50 (2 H, m), 1.63 (3 H, s) and 1.47 (3 H, s) [2 × olefinic CH_3], 1.47 (3 H, s, *tert*-CH_3), 1.09 (t, *J* 7.2 Hz) and 0.97 (t, *J* 6.9 Hz) [3 H, OCH_2CH_3]. ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 173.8 and 173.7 (C, OC=O), 157.8 and 157.9 (C, C-4″), 144.4 and 144.0 (CH, C-3′), 137.9 and 137.8 (C), 133.1 and 133.0 (C), 127.7 and 127.8 (2 C, CH, C-2″ and 6″), 121.8 and 121.9 (CH, C-4), 113.4 and 113.3 (2 C, CH, C-3″ and 5″), 112.6 (CH_2, C-4′), 59.6 (CH_2, OCH_2CH_3), 55.6 and 55.7 (CH, C-2), 55.0 (CH_3, OMe), 45.8 and 45.7 (C, C-2′), 27.2 (CH_2, C-3), 25.9 (CH_3), 21.2 and 21.3 (CH_3), 17.7 and 17.8 (CH_3), 14.1 and 14.3 (CH_3, OCH_2CH_3). Mass: 316 (M^+, 2%), 162 (14), 161 (100), 160 (4), 159 (4), 146 (5). HRMS: m/z calcd. for $C_{20}H_{28}O_3Na$ (M + Na): 339.1936. Found: 339.1938. Further elution furnished starting material (26 mg).

3-[1-(4-Methoxyphenyl)ethyl]-6-methylhepta-1,5-diene (12): To a magnetically stirred solution of 20% KOH in methanol (3 ml) was added the ester **8** (55 mg, 0.17 mmol) and refluxed for 50 h. The reaction mixture was cooled, taken in water (10 ml), and washed with CH_2Cl_2 (5 ml). The aqueous layer was acidified with 3 N of HCl and extracted with CH_2Cl_2 (3 × 5 ml). The organic extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent furnished the acid **10** (50 mg, 99%). To a magnetically stirred solution of the acid **10** (50 mg, 0.17 mmol) in dry benzene (2 ml) at 0°C was added oxalyl chloride (0.11 ml, 1.22 mmol) and stirred for 2 h at rt. Evaporation of the solvent and excess oxalyl chloride under reduced pressure afforded the acid chloride, which was taken in dry benzene (2 ml), added to a magnetically stirred solution of 2-thiopyridine-1-oxide sodium salt (39 mg, 0.26 mmol) and a catalytic amount of DMAP in dry benzene (3 ml), and the resulting reaction mixture was refluxed for 1 h. To the ester **11** thus formed was added dropwise a solution of tributyltin hydride and a catalytic amount of AIBN in dry benzene (5 ml) over a period of 5 min and refluxed for 14 h. The reaction mixture was cooled, washed with 1% ammonia solution, and extracted with ether (3 × 5 ml). The combined ether extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica-gel column using hexane as eluent furnished a 3:2 diastereomeric mixture of the diene **12** (15 mg, 36%) as oil. IR (neat): ν_{max}/cm^{-1} 1511, 910. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$, 3:2 mixture of the diastereomers): δ 7.10–6.95 (2 H, m) and 6.85–6.72 (2 H, m) [Ar-H], 5.43 (ddd, *J* 18.9, 10.2 and 8.4 Hz) and 5.57 (ddd, *J* 19.2, 9.9 and 9.0 Hz) [1 H, H-2], 5.11–4.80 (3 H, m, H-1 and 5), 3.77 (3 H, s, OCH_3), 2.56 (quintet, *J* 6.9 Hz) and 2.70 (d of q, *J* 6.9 and 5.7 Hz) [1 H], 2.20–1.60 (3 H, m), 1.64 and 1.68 (3 H, s), 1.42 and 1.53 (3 H, s) [2 × olefinic CH_3], 1.15 (d, *J* 7.5 Hz) and 1.23 (d, *J* 7.5 Hz) [3 H, *sec*-CH_3].

^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$, 3:2 mixture of the diastereomers): δ 157.8 (C, C-4″), 140.4 and 141.2 (CH, C-2), 136.6 and 138.5 (C), 131.8 and 131.7 (C), 129.2 and 128.4 (2 C, CH, C-2″ and 6″), 123.1 and 122.8 (CH, C-5), 115.5 and 115.6 (CH_2, C-1), 113.2 and 113.6 (2 C, CH, C-3″ and 5″), 55.1 (CH_3, OMe), 50.9 and 51.7 (CH), 42.0 and 42.6 (CH), 30.7 and 31.4 (CH_2), 25.9 (CH_3), 19.3 and 19.9 (CH_3), 17.9 and 18.0 (CH_3). Mass: 244 (M^+, 2%), 221 (3), 136 (10), 135 (100), 105 (9), 91 (7). HRMS: m/z calcd. for $C_9H_{11}O$ (M-C_8H_{13}): 135.0810. Found: 135.0815.

3-Methyl-3-(4-methoxyphenyl)pent-4-en-1-ol (17): To an ice-cold, magnetically stirred solution of the ester **4** (645 mg, 2.6 mmol) in dry ether (10 ml) was added LAH (99 mg, 2.6 mmol) and stirred for 1 h. The reaction mixture was then diluted with ether (20 ml) and carefully quenched with water (5 ml). The organic layer was separated and the aqueous phase was extracted with ether (15 ml). The combined organic phase was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica-gel column using ethyl acetate–hexane (1:20 to 1:5) as eluent furnished the alcohol **17** (494 mg, 92%). IR (neat): ν_{max}/cm^{-1} 3370, 1634, 1609, 1580, 1513, 916. ^{1}H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 7.16 (2 H, d, *J* 8.7 Hz, H-2′ and 6′), 6.77 (2 H, d, *J* 8.7 Hz, H-3′ and 5′), 5.96 (1 H, dd, *J* 17.4 and 10.5 Hz, H-4), 5.06 (1 H, d, *J* 10.5 Hz) and 5.02 (1 H, d, *J* 17.4 Hz) [H-5], 3.74 (3 H, s, OCH_3), 3.60–3.35 (2 H, m, H-1), 2.20–1.90 (3 H, m, H-2 and OH), 1.34 (3 H, s, *tert*-CH_3). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 157.7 (C, C-4′), 146.9 (CH, C-4), 138.7 (C, C-1′), 127.3 (2 C, CH, C-2′ and 6′), 113.5 (2 C, CH, C-3′ and 5′), 111.6 (CH_2, C-5), 59.5 (CH_2, C-1), 54.9 (CH_3, OMe), 43.3 (CH_2, C-2), 42.5 (C, C-3), 25.6 (CH_3). Mass: m/z 206 (M^+, 8%), 162 (12), 161 (100), 146 (11), 135 (9), 121 (9), 115 (10), 91 (20). HRMS: m/z calcd. for $C_{13}H_{18}O_2Na$ (M + Na): 229.1204. Found: 229.1206.

3-(4-Methoxyphenyl)-3-methylpent-4-enal (16): To a magnetically stirred solution of the primary alcohol **17** (404 mg, 2.0 mmol) in dry CH_2Cl_2 (3 ml) was added a homogeneous mixture of PCC (1.3 g, 5.9 mmol) and silica gel (1.3 g) and stirred vigorously for 30 min at RT. The reaction mixture was then filtered through a small silica-gel column and the column was eluted with excess CH_2Cl_2. Evaporation of the solvent and purification of the residue over a silica-gel column using ethyl acetate–hexane (1:40 to 1:20) as eluent furnished the pentenal **16** (352 mg, 88%) as an oil.[7] IR (neat): ν_{max}/cm^{-1} 2737, 1719, 1677, 1635, 1608, 1510, 920. ^{1}H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 9.51 (1 H, t, *J* 3 Hz, CHO), 7.20 (2 H, d, *J* 8.7 Hz, H-2′ and 6′), 6.81 (2 H, d, *J* 8.7 Hz, H-3′ and 5′), 6.05 (1 H, dd, *J* 17.7 and 10.5 Hz, H-4), 5.16 (1 H, d, *J* 10.5 Hz) and 5.07 (1 H, d, *J* 17.7 Hz) [H-5], 3.76 (3 H, s, OCH_3), 2.75 and 2.66 (2 H, d of AB q, *J* 15.0 and 3.0 Hz, H-2), 1.48 (3 H, s, *tert*-CH_3). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 201.7 (CH, CHO), 158.1 (C, C-4′), 145.4 (CH, C-4), 137.2 (C, C-1′), 127.3 (2 C,

CH, C-2′ and 6′), 113.8 (2 C, CH, C-3′ and 5′), 112.7 (CH_2, C-5), 54.9 (CH_3, OMe), 53.3 (CH_2, C-2), 42.2 (C, C-3), 26.3 (CH_3).

4-(4-Methoxyphenyl)-4-methylhexa-1,5-dienyl methyl ether (18): To a magnetically stirred suspension of methoxymethyltriphenylphosphonium chloride (984 mg, 2.9 mmol) in dry THF (4 ml) at 0°C was added a solution of ^{n}BuLi (1.95 *M* in hexane, 1.12 ml, 2.2 mmol) dropwise and the resulting dark red solution was stirred for 15 min at rt. To a magnetcially stirred solution of the aldehyde **16** (178 mg, 0.87 mmol) in dry THF (1 ml) at 0°C was added the dark-red-colored solution of methoxymethylenetriphenlyphosphorane and stirred for 40 min at rt. Saturated aq. NH_4Cl solution (5 ml) was added to the reaction mixture and extracted with ether (2 × 10 ml). The combined ether extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica-gel column using hexane as eluent furnished the enol ether **18** (141 mg, 70%) as oil. IR (neat): ν_{max}/cm^{-1} 1664, 1654, 1609, 1511, 915. ^{1}H NMR (300 MHz, $CDCl_3 + CCl_4$, 5:4 mixture of *E,Z*-isomers): δ 7.21 and 7.19 (2 H, d, *J* 9.0 Hz, H-2′ and 6′), 6.79 and 6.80 (2 H, d, *J* 9.0, Hz, H-3′ and 5′), 6.20 (d, *J* 12.9 Hz) and 5.84 (m of d, *J* 6.0 Hz) [1 H, H-1], 6.00 (dd, *J* 17.4 and 10.8 Hz) and 5.99 (dd, *J* 17.4 and 10.8 Hz) [1 H, H-6], 5.13–4.80 (2 H, m, H-6), 4.45 (t of d, *J* 12.9 and 7.8 Hz) and 4.15 (quintet, *J* 6.9 Hz) [1 H, H-2], 3.77 and 3.76 (3 H, s), 3.53 and 3.40 (3 H, s), 2.50 (d of AB q *J* 12.9 and 7.5 Hz) and 2.32 (1 H, dd, *J* 7.5 and 2.7 Hz) [H-3], 1.32 and 1.30 (3 H, s, *tert*-CH_3). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 157.6 (C, C-4′), 148.6 and 147.2 (CH), 147.0 (CH), 139.2 and 139.1 (C, C-1′), 127.7 and 127.6 (2 C, CH, C-2′ and 6′), 113.3 and 113.2 (2 C, CH, C-3′ and 5′), 111.7 and 111.6 (CH_2, C-6), 103.1 and 98.7 (CH, C-2), 59.3 and 55.7 (CH_3, OCH_3), 55.0 (CH_3, ArOMe), 43.8 (C), 39.6 and 35.1 (CH_2, C-3), 25.3 and 24.9 (CH_3).

4-(4-Methoxyphenyl)-4-methylhex-5-enal (19): A solution of the enol ether **18** (141 mg, 0.6 mmol) in THF (3 ml) and 3 N of HCl (3 ml) was magnetically stirred for 1.5 h at rt. The reaction mixture was diluted with water (5 ml) and extracted with ether (3 × 7 ml). The combined ether extract was washed with aqueous $NaHCO_3$ and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of residue over a silica-gel column using ethyl acetate–hexane (1:49 to 1:20) as eluent furnished the aldehyde **19** (115 mg, 87%) as oil. IR (neat): ν_{max}/cm^{-1} 2721, 1723, 1634, 1609, 1580, 1512, 917. ^{1}H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 9.67 (1 H, s, CHO), 7.18 (2 H, d, *J* 8.7 Hz, H-2′ and 6′), 6.81 (2 H, d, *J* 8.7 Hz, H-3′ and 5′), 5.96 (1 H, dd, *J* 17.1 and 10.5 Hz, H-5), 5.11 (1 H, d, *J* 10.5 Hz) and 5.04 (1 H, d, *J* 17.1 Hz) [H-6], 3.77 (3 H, s, OCH_3), 2.40–2.19 (2 H, m, H-2), 2.19–1.70 (2 H, m, H-3), 1.34 (3 H, s, *tert*-CH_3). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 201.6 (CH, CHO), 157.9 (C, C-4′), 146.2 (CH, C-5), 138.0 (C, C-1′),

127.5 (2 C, CH, C-2′ and 6′), 113.6 (2 C, CH, C-3′ and 5′), 112.3 (CH_2, C-6), 55.0 (CH_3, OMe), 43.0 (C, C-4), 39.9 (CH_2), 32.5 (CH_2), 25.1 (CH_3).

3-(4-Methoxyphenyl)-3,7-dimethylocta-1,6-diene (methyl ether of sporochnol A 9): To a cold (0°C), magnetically stirred suspension of isopropyltriphenylphosphonium bromide (420 mg, 1.1 mmol) in dry THF (3 ml) was added a solution of ^{n}BuLi (1.9 *M* in hexane, 0.41 ml, 0.78 mmol) dropwise and the resulting red-colored solution was stirred for 15 min at rt. The isopropylidene-triphenylphosphorane thus formed was added to a magnetically stirred solution of the aldehyde **19** (34 mg, 0.15 mmol) in THF (1 ml) and the reaction mixture was stirred for 1 h at rt. Saturated aq. ammonia solution (3 ml) was added to the reaction mixture and extracted with ether (3 × 5 ml). The combined ether extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of residue over silver nitrate–impregnated silica-gel column using hexane as eluent furnished the diene **9** (30 mg, 77%) as oil. IR (neat): ν_{max}/cm^{-1} 3081, 1633, 1609, 1580, 1512, 913. ^{1}H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 7.18 (2 H, d, *J* 8.7 Hz, H-2′ and 6′), 6.78 (2 H, d, *J* 8.7 Hz, H-3′ and 5′), 5.98 (1 H, dd, *J* 17.4 and 10.8 Hz, H-2), 5.05–5.00 (1 H, m), 5.04 (1 H, d, *J* 10.8 Hz) and 4.99 (1H, d, *J* 17.4 Hz) [H-1], 3.77 (3 H, s, OCH_3), 2.00–1.50 (4 H, m), 1.64 (3 H, s) and 1.50 (3 H, s) [2 × olefinic-CH_3], 1.34 (3 H, s, *tert*-CH_3). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 157.6 (C, C-4′), 147.3 (CH, C-2), 139.3 (C, C-7), 131.0 (C, C-1′), 127.6 (2 C, CH, C-2′ and 6′), 125.0 (CH, C-6), 113.4 (2 C, CH, C-3′ and 5′), 111.5 (CH_2, C-1), 55.0 (CH_3, OMe), 43.7 (C, C-3), 41.3 (CH_2, C-4), 25.8 (CH_3), 25.3 (CH_3), 23.4 (CH_2, C-5), 17.7 (CH_3). Mass: 244 (M^+, 5%), 162 (20), 161 (100), 146 (8), 134 (8), 121 (9), 91 (11).

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