

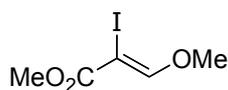
## Total Synthesis of Strobilurin B using a Hetero-*bis*-metallated Linchpin

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### Supplementary Information

**General.** Proton (400 MHz) and  $^{13}\text{C}$  (100 MHz) NMR spectra were recorded on a Bruker DRX-400 spectrometer in  $\text{CDCl}_3$  using  $\text{CHCl}_3$  ( $^1\text{H}$   $\delta$  7.27) and  $\text{CDCl}_3$  77.0 ( $^{13}\text{C}$   $\delta$  77.0) as internal standards. High resolution mass spectra were recorded on a Micromass Q-TOF2 instrument at The Ohio State University Chemistry Mass Spectrometry Facility. All reactions were conducted in either oven-dried (120 °C) glassware or flame-dried glassware, under an argon atmosphere when necessary. Tetrahydrofuran (THF) was distilled from benzophenone ketyl. Triethylamine and dichloromethane were distilled from calcium hydride prior to use. Cesium fluoride was ground to a fine powder using a mortar and pestle and then dried under high vacuum at 100 °C for 4 h. All other chemicals were used as received.

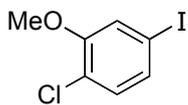


**Methyl (Z)-2-Iodo-3-methoxypropenoate (3).** A mixture of methyl

(*E*)-3-methoxypropenoate (1.16 g, 10.0 mmol), *N*-iodosuccinimide (2.70 g, 12.0 mmol), glacial acetic acid (1.5 mL, 20 mmol), and dichloromethane (20 mL) was stirred at room temperature for 24 h. Triethylamine (4.2 mL, 30 mmol) was added, and the reaction mixture was stirred at room temperature for 12 h before water (30 mL) was added. The organic layer was separated, and the aqueous layer was extracted with ether (2 x 20 mL). The combined organic extracts were washed with saturated aqueous sodium thiosulfate (2

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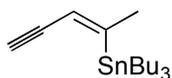
x 20 mL), saturated aqueous sodium bicarbonate (2 x 20 mL), and water (2 x 20 mL), and were dried (MgSO<sub>4</sub>) and concentrated. The residue was purified by flash chromatography (silica, 1:5 ether/hexane) to afford **3** (1.87 g, 77%) as a white solid: mp 51.0-51.5 °C (hexane) (lit.<sup>7</sup> 47-48 °C; lit.<sup>6</sup> 66-67 °C); IR (thin film)  $\nu_{\max}/\text{cm}^{-1}$  3001, 1699, 1620, 1136, 752; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  7.69 (1 H, s), 4.01 (3 H, s), 3.80 (3 H, s); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  164.4, 164.3, 64.9, 62.0, 52.9; HRMS (ESI),  $m/z$  264.9333 (C<sub>5</sub>H<sub>7</sub>IO<sub>3</sub>Na requires 264.9338).



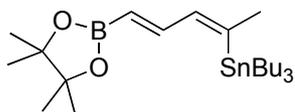
**2-Chloro-5-iodoanisole (4)**. A solution of sodium nitrite (0.380 g, 5.50 mmol) in water (3 mL) was added over 30 min to a mixture of 4-chloro-3-methoxyaniline (0.788 g, 5.00 mmol), concentrated aqueous hydrochloric acid (10 mL), and water (10 mL) at 0 °C. The reaction mixture was stirred for 30 min at this temperature, and was added over 30 min via cannula to a solution of potassium iodide (8.35 g, 50.0 mmol) in water (15 mL) at 0 °C. The reaction mixture was stirred at room temperature for 3 d and was warmed at reflux for 1 h before it was allowed to cool to room temperature and was diluted with ether (100 mL). The organic layer was separated, and the aqueous layer was extracted with ether (2 x 20 mL). The combined organic extracts were washed with 1 M aqueous sodium hydroxide (2 x 20 mL), saturated aqueous NaCl (2 x 20 mL), and were dried (MgSO<sub>4</sub>) and concentrated. The residue was purified by flash chromatography (silica, 100:2 hexane/ethyl acetate) to afford **4** (1.12 g, 84%) as a white solid: mp 39-40 °C; IR (thin film)  $\nu_{\max}/\text{cm}^{-1}$  3001, 2926, 1573, 835, 799; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  7.23-7.18 (2 H, m), 7.06 (1 H, d,  $J = 8.1$  Hz), 3.88 (3 H, s); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)

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$\delta$  155.5, 131.4, 130.3, 122.7, 121.3, 91.4, 56.3; HRMS (ESI),  $m/z$  290.9039 ( $C_7H_6ClIOna$  requires 290.9050).



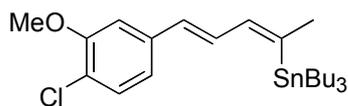
**(Z)-4-Tri-*n*-butylstannyl-3-penten-1-yne (12)**. A mixture of (Z)-1-trimethylsilyl-4-tri-*n*-butylstannyl-3-penten-1-yne (**11**) (1.19 g, 2.79 mmol), potassium fluoride (1.62 g, 27.9 mmol), and methanol (10 mL) was warmed at 50 °C for 24 h. After cooling to room temperature, water (10 mL) and ether (10 mL) were added. The aqueous layer was separated and was extracted with ether (2 x 10 mL). The combined organic extracts were washed with water (2 x 15 mL), and were dried ( $Na_2SO_4$ ) and concentrated to afford **12** (0.98, 99%) as a colorless liquid, which was used without further purification: IR (thin film)  $\nu_{max}/cm^{-1}$  3311, 2955, 2097, 1461, 835;  $^1H$  NMR ( $CDCl_3$ , 400 MHz)  $\delta$  6.10 (1 H, quintet,  $J = 1.6$  Hz,  $^3J_{Sn-H} = 112$  Hz), 2.78 (1 H, d,  $J = 2.0$  Hz), 2.02 (3 H, d,  $J = 1.6$  Hz,  $^3J_{Sn-H} = 40.0$  Hz), 1.58-1.48 (6 H, m), 1.33 (6 H, sextet,  $J = 7.2$  Hz), 1.04 (6 H, t,  $J = 8.0$  Hz), 0.91 (9 H, t,  $J = 7.2$  Hz);  $^{13}C$  NMR ( $CDCl_3$ , 100 MHz)  $\delta$  162.0, 118.5, 80.6, 75.6, 29.1 ( $^3J_{Sn-C} = 20.1$  Hz), 27.4 ( $^2J_{Sn-C} = 57.3$  Hz), 27.3 ( $^2J_{Sn-C} = 29.1$  Hz), 13.7, 9.87 ( $^1J_{Sn-C} = 340.1/324.0$  Hz); MS (EI),  $m/z$  298.6 ( $M^+ - C_4H_8$ ), 242.9, 184.5, 144.5.



**2-((1E,3Z)-4-((Tri-*n*-butylstannyl)penta-1,3-dienyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2)**. A flame-dried flask was charged with sodium borohydride (0.157 g, 4.14 mmol), 2,5-dimethyl-2,4-hexadiene (1.20 mL, 8.28 mmol),

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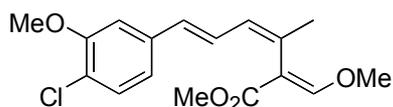
and 2 mL of anhydrous diglyme. The mixture was cooled to 0 °C and dimethyl sulfate (0.4 mL, 4.14 mmol) was added over 30 min. The reaction mixture was stirred at 0 °C for 3 h, when enyne **12** (0.980 g, 2.76 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 1 h and was allowed to warm to room temperature. Water (0.4 mL) was added and the reaction mixture was stirred for 30 min, and was treated with an aqueous solution of formaldehyde (0.4 mL, 37 wt%, 4.14 mmol). After stirring for 1 h, pinacol (0.359 g, 3.04 mmol) was added. The reaction mixture was stirred at room temperature for 24 h before water (10 mL) and ether (10 mL) were added. The aqueous layer was separated and was extracted with ether (3 x 10 mL). The combined organic extracts were washed with water (2 x 15 mL), and were dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated. Purification of the residue by flash chromatography (silica, 100:6 hexane/ether) afforded **2** (1.01 g, 75%) as a pale yellow liquid: IR (thin film)  $\nu_{\max}/\text{cm}^{-1}$  2925, 2853, 1614, 1145, 850; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  6.98 (1 H, dd,  $J = 17.1, 10.6$  Hz), 6.75 (1 H, dd,  $J = 10.8, 1.2$  Hz), 5.43 (1 H, d,  $J = 17.2$  Hz), 2.04 (3 H, s,  $^3J_{\text{Sn-H}} = 41.4$  Hz), 1.55-1.48 (6 H, m), 1.34 (6 H, sextet,  $J = 7.3$  Hz), 1.26 (12 H, s), 1.00 (6 H, t,  $J = 8.2$  Hz), 0.91 (9 H, t,  $J = 7.3$  Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  153.8, 151.7, 142.8, 82.9, 29.7 ( $^3J_{\text{Sn-C}} = 20.0$  Hz), 27.5, 27.3 ( $^2J_{\text{Sn-C}} = 55.0$  Hz), 24.8, 13.6, 10.2 ( $^1J_{\text{Sn-C}} = 331.0/316.0$  Hz) [Note: the carbon attached to boron was not observed due to quadrupole broadening caused by the boron nucleus]; HRMS (ESI),  $m/z$  507.2444 (C<sub>23</sub>H<sub>45</sub>BO<sub>2</sub>SnNa requires 507.2432).



**Vinylstannane 14.** A flame-dried flask was charged with (t-Bu<sub>3</sub>P)<sub>2</sub>Pd (19.1 mg, 0.0373 mmol) in a dry box. Anhydrous THF (4 mL) was added to

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the flask. Under an argon atmosphere, solid 2-chloro-5-iodoanisole (**4**) (0.100 g, 0.373 mmol) was added to the flask. After 5 min, a solution of 2-((1*E*,3*Z*)-4-((tri-*n*-butylstannyl)penta-1,3-dienyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2**) (0.200 g, 0.414 mmol) in 8 mL of THF was added via cannula. Solid sodium hydroxide (44.8 mg, 1.12 mmol) and water (20  $\mu$ L, 1.12 mmol) were added in sequence under the protection of an argon atmosphere. The reaction mixture was warmed at 60 °C for 5 h before it was allowed to cool to room temperature, when water (10 mL) and ether (10 mL) were added. The aqueous layer was separated and extracted with ether (3 x 10 mL). The combined organic extracts were washed with water (2 x 10 mL), and were dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated. Purification of the residue by flash chromatography (silica, 100:3 hexane/ether) provided **14** (0.137 g, 74%) as a pale yellow liquid: IR (thin film)  $\nu_{\text{max}}/\text{cm}^{-1}$  3001, 2956, 1590, 1067, 801;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.29 (1 H, d,  $J = 8.0$  Hz), 6.91 (1 H, d,  $J = 1.6$  Hz), 6.88 (1 H, dd,  $J = 8.0$  and 1.6 Hz), 6.83 (1 H, dd,  $J = 10.8$  and 1.6 Hz), 6.68 (1 H, dd,  $J = 15.2$  and 10.4 Hz), 6.40 (1 H, d,  $J = 15.2$  Hz), 3.93 (3 H, s), 2.09 (3 H, s,  $^3J_{\text{Sn-H}} = 42.8$  Hz), 1.61–1.50 (6 H, m), 1.34 (6 H, sextet,  $J = 7.4$  Hz), 1.05 (6 H, t,  $J = 8.0$  Hz), 0.90 (9 H, t,  $J = 7.4$  Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  155.0, 149.8, 140.4, 137.9, 131.4, 130.2, 129.8, 121.0, 119.2, 109.2, 55.9, 29.2 ( $^3J_{\text{Sn-C}} = 29.2$  Hz), 27.6, 27.4 ( $^2J_{\text{Sn-C}} = 55.9$  Hz), 13.6, 10.4; HRMS (ESI),  $m/z$  521.1615 ( $\text{C}_{24}\text{H}_{39}\text{ClOSnNa}$  requires 521.1609).



**Strobilurin B (1).** A flame-dried flask was charged with

(*t*-Bu<sub>3</sub>P)<sub>2</sub>Pd (5.2 mg, 0.0102 mmol), cuprous iodide (3.9 mg, 0.0204 mmol), and cesium fluoride (34.1 mg, 0.224 mmol) in a dry box. Anhydrous DMF (2 mL) was added to the flask. Under the protection of an argon atmosphere, solid (*Z*)-2-iodo-3-methoxypropenoate (**3**) (24.8 mg, 0.102 mmol) was added. After 5 min, a solution of compound **14** (60 mg, 0.120 mmol) in DMF (2 mL) was added via cannula. The reaction mixture was warmed at 90 °C for 2 hr. After cooling to room temperature, water (10 mL) and ether (10 mL) were added. The aqueous layer was separated and extracted with ether (3 x 10 mL). The combined organic extracts were washed with water (2 x 10 mL), and were dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated. Purification of the residue by flash chromatography (silica, 2:1 hexane/ether) provided strobilurin B (**1**) as a cream white solid (15 mg, 45%): mp 92-93 °C (lit.<sup>22</sup> 95 °C); IR (thin film)  $\nu_{\max}/\text{cm}^{-1}$  2920, 1705, 1627, 1460, 1237, 1119, 804; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  7.45 (1 H, s), 7.27 (1 H, d, *J* = 8.4 Hz), 6.92 (1 H, d, *J* = 8.4 Hz), 6.86 (1 H, s), 6.59 (1 H, dd, *J* = 15.6, 10.8 Hz), 6.45 (1 H, d, *J* = 15.6 Hz), 6.26 (1 H, d, *J* = 10.4), 3.92 (3 H, s), 3.87 (3 H, s), 3.76 (3 H, s), 2.00 (3 H, s); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  167.7, 158.9, 154.9, 137.9, 132.1, 130.2, 130.1, 129.5, 127.2, 121.1, 119.1, 110.7, 110.0, 61.9, 56.1, 51.6, 23.7; HRMS (ESI), *m/z* 345.0857 (C<sub>17</sub>H<sub>19</sub>ClO<sub>4</sub>Na requires 345.0870).