# A Synthesis of the Welwistatin Core (supporting information)

Ryan Lauchli and Kenneth J. Shea\*

Department of Chemistry, 1102 Natural Sciences II, University of California, Irvine, Irvine, CA 92697-2025

**Instrumentation:** NMR measurements were conducted with Bruker instruments at 500 MHz for proton spectra and 125 MHz for carbon spectra. Chemical shifts are given in ppm values referenced to residual solvent peaks.

**General Procedures:** Toluene, THF, and dichloromethane were purified by passage through alumina columns. Isopropanol, triethylamine, and benzene were distilled from CaH<sub>2</sub>. Methanol was distilled from its magnesium alkoxide. DMF was dried over 4Å molecular sieves. All reactions were performed under N<sub>2</sub> using flame dried glassware and standard syringe and septa techniques. Removal of solvent *in vacuo* refers to use of a Büchi rotary evaporator. Reagents were purchased from VWR, Fisher, or Aldrich and generally used without purification. TLC was performed with aluminum-backed silica gel 60 F<sub>254</sub> analytical plates from EMD. Visualization of compound spots was done with a short wave UV lamp followed by staining with either anisaldehyde or Seebach's stain (phosphomolybdic acid and Ce<sub>2</sub>(SO<sub>4</sub>)<sub>3</sub>). Flash chromatography was performed on Geduran silica gel 60 (40-63 µm) from EMD.

#### 4-bromo-1*H*-indole-3-carbaldehyde (6)



A round bottom flask was charged with 6 mL of dry DMF, and the flask was cooled in an ice bath. The liquid was magnetically stirred under  $N_2$  and POCl<sub>3</sub> (0.98 mL, 10.5 mmol) was added dropwise. The solution was stirred for 2 min, and then a solution of 4-

bromoindole<sup>1</sup> (0.94 g, 4.7 mmol) in 5 mL of DMF was added dropwise. The ice bath was removed and the reaction mixture was left to stir for 1 h at ambient temp. The reaction mixture became a heavy suspension, and was slowly quenched with 2.66 g KOH in 10 mL of water. The quench was done slowly enough to keep the reaction mixture just below boiling. The reaction mixture was left to cool overnight, and was then partitioned between EtOAc and saturated aqueous NaHCO<sub>3</sub>. The organic layer was washed with saturated aqueous NaCl, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo* to give an off-white solid. Yield: 1.11 g, quantitative. NMR spectral data matched literature values.<sup>2</sup>

## 4-Trimethylsilanylethynyl-1H-indole-3-carbaldehyde (7)



4-bromo-1*H*-indole-3-carbaldehyde (305 mg, 1.36 mmol), Pd(PPh<sub>3</sub>)<sub>4</sub> (62.5 mg, 0.05 mmol), and CuI (19 mg, 0.10 mmol, 99.999% purity) were combined in a resealable glass flask in an Ar atmosphere using a glovebox. The flask was taken out of the glovebox, and triethylamine (6.5 mL) and trimethylsilylacetylene (0.30 mL, 0.20 mmol) were added via syringe. A magnetic stir bar was added and the reaction was sealed. The reaction was heated to 100 °C with an oil bath and stirring was maintained. After 22 h, the now dark reaction was allowed to cool and then diluted with EtOAc (100 mL). The mixture was filtered through celite 545. The organic solution was washed with saturated aqueous NH<sub>4</sub>Cl (3x30 mL), water (3x30 mL), and brine (30 mL). The organics were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, adsorbed on celite 545, and the solvents were removed *in vacuo*. The impregnated celite was placed on top of a SiO<sub>2</sub> flash chromatography column and eluted with 2:1 hexanes:EtOAc. The product was collected as a tan solid. Yield: 321 mg, 98 %. Mp: 148.8-149.8 °C

<sup>1</sup>H NMR (*d*6-DMSO, 500 MHz) 12.48 (s.br., 1 H), 10.75 (s, 1 H), 8.26 (s, 1 H), 7.59 (dd, J = 8.2, 0.8 Hz, 1 H), 7.37 (dd, J = 6.8, 0.98 Hz, 1 H), 7.23 (app.t, J = 7.8 Hz, 1 H), 0.27 (s, 9 H). <sup>13</sup>C NMR (*d*6-DMSO, 125 MHz) 185.0, 136.7, 132.4, 126.8, 125.7, 122.5, 118.0, 114.3, 112.5, 105.5, 97.8, -0.28. IR (KBr, cm<sup>-1</sup>): 3267, 3117, 3050, 2959, 2895, 2848, 2157, 2144, 1652, 1636, 1606, 1514, 1504, 1446, 1385, 1338, 1322, 1300, 1250, 1121, 865, 844, 785, 760, 731, 652. HRMS (TOF ES+) calculated for C<sub>14</sub>H<sub>15</sub>OSiNNa (M+Na)<sup>+</sup> 264.0821, observed 264.0825.

<sup>&</sup>lt;sup>1</sup> Available commercially, but made in this case according to: Moyer, M. P.; Shiurba, J. F.; Rapoport, H. J. Org. Chem. **1986**, *51*, 5106.

<sup>&</sup>lt;sup>2</sup> Somei, M.; Kizu, K.; Kunimoto, M.; Yamada, F. Chem. Pharm. Bull. 1985, 33, 3696.

#### 4-Ethynyl-1*H*-indole-3-carbaldehyde



A mixture of 4-trimethylsilanylethynyl-1*H*-indole-3-carbaldehyde (321 mg, 1.33 mmol) and  $K_2CO_3$  (25 mg) was stirred in 6 mL of methanol under  $N_2$  for 18 h. The solvent was then removed *in vacuo*, and the residue was partitioned between EtOAc (45 mL) and saturated aqueous NaHCO<sub>3</sub>. The organic layer was washed with water and brine, dired over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated *in vacuo* to give the product as a tan solid. Yield: 193 mg, 86 %.

Mp: 158.0-158.9 °C.

<sup>1</sup>H NMR (*d6*-DMSO, 500 MHz) 12.49 (s.br., 1 H), 10.73 (s, 1 H), 8.27 (s, 1 H), 7.60 (dd, J = 8.3, 0.73 Hz, 1 H), 7.40 (dd, J = 7.3, 0.73 Hz, 1 H), 7.24 (app.t, J = 7.8 Hz, 1 H), 4.50 (s, 1 H). <sup>13</sup>C NMR (*d6*-DMSO, 125 MHz) 185.0, 136.8, 132.5, 127.2, 125.8, 122.6, 117.9, 114.2, 112.1, 84.2, 83.7. IR (KBr, cm<sup>-1</sup>): 3286, 3272, 3231, 3117, 3091, 3049, 3006, 2944, 2890, 2869, 1656, 1638, 1519, 1503, 1389, 1335, 1300, 1131, 788, 737. HRMS (TOF ES+) calculated for C<sub>11</sub>H<sub>7</sub>ONNa (M+Na)<sup>+</sup> 192.0425, observed 192.0419.

## 4-Ethynyl-1-(toluene-4-sulfonyl)-1*H*-indole-3-carbaldehyde (8)



In a round bottom flask under N<sub>2</sub>, 4-ethynyl-1*H*-indole-3-carbaldehyde (100 mg, 0.59 mmol), *p*TSCl (133 mg, 0.70 mmol), DMAP (5 mg), and triethylamine (123  $\mu$ L, 0.92 mmol) were dissolved in 5 mL of CH<sub>2</sub>Cl<sub>2</sub>, and the solution was stirred for 2.5 h. The reaction mixture was diluted with more CH<sub>2</sub>Cl<sub>2</sub>, and the organics were washed with 1 N HCl. The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, adsorbed onto celite 545, and the solvents were removed *in vacuo*. The product was isolated by SiO<sub>2</sub> flash chromatography using 3:1 hexanes:EtOAc to give the product as an off-white solid. Yield: 163 mg, 85 %.

Mp: 162.0-163.1 °C.

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) 10.90 (s, 1 H), 8.39 (s, 1 H), 8.04 (d, J = 8.3 Hz, 1 H), 7.83 (d, J = 8.6 Hz, 2 H), 7.52 (d, J = 7.6 Hz, 1 H), 7.34 (t, J = 8.0 Hz, 1 H), 7.29 (d, J = 8.1 Hz, 2 H), 3.43 (s, 1 H), 2.37 (s, 3 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz) 186.9, 146.5, 135.3, 134.4, 131.4, 130.5, 130.2, 128.2, 127.5, 125.3, 122.2, 114.8, 114.4, 82.7, 21.8. IR (KBr, cm<sup>-1</sup>): 3278, 3136, 2871, 1676, 1594, 1531, 1485, 1423, 1405, 1381, 1372, 1289, 1273,

1189, 1181, 1174, 1146, 1096, 1085, 1061, 1043, 878, 821, 787, 745, 704, 689, 666, 639, 600, 577, 549. HRMS (TOF ES+) calculated for  $C_{18}H_{14}O_3NS (M+H)^+$  324.0694, observed 324.0699.

#### 4-(1-Methylene-allyl)-1-(toluene-4-sulfonyl)-1*H*-indole-3-carbaldehyde (9)



A 2-dram vial with a magnetic stir bar was introduced into the glovebox under  $N_2$ , and was charged with 4-ethynyl-1-(toluene-4-sulfonyl)-1*H*-indole-3-carbaldehyde (49 mg, 0.15 mmol)and Grubb's 2<sup>nd</sup> generation catalyst (6 mg, 0.0076 mmol). The septum-sealed vial was taken out of the glovebox and an ethylene balloon was used to provide positive ethylene pressure. Toluene (2.5 mL) was added, and an outlet needle was used to briefly purge the atmosphere with ethylene. The solution was heated to 75-80 °C for 40 min, in which time the solution became slightly darker. The reaction was quenched with 5 drops of ethylvinyl ether, and the solvents were removed *in vacuo*. The residue was purified by SiO<sub>2</sub> flash chromatography using 3:1 hexanes:EtOAc to give the diene as a brown oil. Yield: 50 mg, 94%.

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) 10.10 (s, 1 H), 8.32 (s, 1 H), 7.98 (dd, J = 8.5, 0.98 Hz, 1 H), 7.88 (d, J = 8.3 Hz, 2 H), 7.38 (dd, J = 8.3, 7.3 Hz, 1 H), 7.32 (d, J = 8.3 Hz, 2 H), 7.15 (dd, J = 7.3, 0.98 Hz, 1 H), 6.67 (dd, J = 17.4, 10.5 Hz, 1 H), 5.49 (d, J = 0.98 Hz, 1 H), 5.28 (s, 1 H), 5.16 (d, J = 10.3 Hz, 1 H), 4.68 (d, J = 17.4 Hz, 1 H), 2.39 (s, 3 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz) 187.3, 148.0, 146.3, 138.4, 135.2, 134.6, 133.4, 131.3, 130.5, 127.6, 125.99, 125.89, 125.59, 121.9, 119.9, 118.7, 113.0, 21.9. IR (NaCl, cm<sup>-1</sup>): 3134, 3090, 3053, 3036, 3006, 2924, 2872, 1682, 1596, 1531, 1488, 1406, 1378, 1286, 1274, 1190, 1177, 1161, 1139, 1096, 1088, 1041, 1026, 991, 912, 815, 798, 755, 738, 703, 687, 665, 629. HRMS (TOF ES+) calculated for C<sub>20</sub>H<sub>17</sub>O<sub>3</sub>NSNa (M+Na)<sup>+</sup> 374.0827, observed 374.0828.

1-[4-(1-Methylene-allyl)-1-(toluene-4-sulfonyl)-1H-indol-3-yl]-prop-2-en-1-ol (10)



The aldehyde (96 mg, 0.27 mmol) was dissolved in 0.5 mL of THF under  $N_2$  in a 2-dram vial, and was magnetically stirred. The solution was cooled in an ice bath as vinyl-magnesium bromide (0.35 mL of a 1 M solution in THF, 0.35 mmol) was added dropwise. The reaction mixture was stirred at ambient temp for 10 min, and then was quenched with saturated aqueous NH<sub>4</sub>Cl. The product was extracted into EtOAc, washed with brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. The organics were concentrated *in vacuo*, and the residue was purified by SiO<sub>2</sub> flash chromatography using 3:1 hexanes:EtOAc to give the product as a yellow tinted tar. Yield: 84 mg, 81%.

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) 7.96 (dd, J = 8.4, 1.0 Hz, 1 H), 7.80 (d, J = 8.5 Hz, 2 H), 7.57 (s, 1 H), 7.30 (dd, J = 8.3, 7.3 Hz, 1 H), 7.26 (d, J = 8.3 Hz, 2 H), 7.00 (dd, J = 7.3, 0.98 Hz, 1 H), 6.75 (dd, J = 17.4, 10.5 Hz, 1 H), 6.12 (ddd, J = 15.4, 10.5, 4.9 Hz, 1 H), 5.52 (d, J = 0.98 Hz, 2 H), 5.50 (s, 1 H), 5.40 (d, J = 17.4 Hz, 1 H), 5.18-5.27 (m, 3 H), 4.68 (d, J = 17.4 Hz, 1 H), 2.37 (s, 3 H), 2.14 (d, J = 3.9 Hz, 1 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz) 145.3, 139.6, 138.3, 135.7, 135.5, 132.6, 130.2, 127.2, 125.3, 125.1, 125.0, 124.6, 118.9, 115.5, 113.0, 66.8, 21.8. IR (NaCl, cm<sup>-1</sup>): 3550, 3089, 3033, 2980, 2922, 1596, 1411, 1369, 1292, 1246, 1188, 1174, 1138, 1094, 1026, 1016, 990, 921, 812, 795, 757, 705, 664. HRMS (TOF ES+) calculated for C<sub>22</sub>H<sub>21</sub>O<sub>3</sub>NSNa (M+Na)<sup>+</sup> 402.1140, observed 402.1137.

#### Cycloadduct (13)



The alcohol (20 mg) was dissolved in 17 mL of  $CH_2Cl_2$ . The reaction mixture was magnetically stirred under N<sub>2</sub> and about 100 mg of activated MnO<sub>2</sub> was added. After 1 h, the reaction mixture was filtered through celite 545, and concentrated *in vacuo* to give the enone as a colorless tar. The enone (it is possible to isolate the enone in 64% at this stage) was dissolved in 45 mL of toluene and the solution was placed in a 450 mL Parr high pressure reactor. The solution was sparged with N<sub>2</sub> for 10 min, and the reactor was sealed. The reaction was heated to 120 °C for 1 h, and then the solvents were removed *in vacuo*. The colorless residue was purified by SiO<sub>2</sub> flash chromatography using 3:1 hexanes:EtOAc to give the product as a white solid. Yield: 10 mg, 50%. Mp: 112.3-119.3 °C.

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) 8.24 (s, 1 H), 7.87 (app.d, J = 8.6 Hz, 2 H), 7.81 (dd, J = 8.6, 0.73 Hz, 1 H), 7.27-7.34 (m, 3 H), 7.16 (dd, J = 7.2, 0.61 Hz, 1 H), 6.09-6.13 (m, 1 H), 3.25-3.30 (m, 1 H), 2.80 (app.d, J = 13.2 Hz, 1 H), 2.46-2.54 (m, 1 H), 2.39 (s, 3 H), 2.29-2.36 (m, 2 H), 1.97-2.06 (m, 1 H), 1.47-1.55 (m, 1 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz)

202.8, 146.0, 139.8, 135.0, 133.9, 132.5, 131.0, 130.4, 127.51, 127.47, 126.2, 125.7, 123.5, 117.8, 111.7, 47.3, 31.5, 29.2, 23.3, 21.9. IR (KBr, cm<sup>-1</sup>): 3119, 3091, 3031, 2947, 2894, 2870, 1658, 1596, 1513, 1481, 1422, 1377, 1189, 1178, 1132, 1096, 1025, 995, 856, 761, 704, 668, 579, 550. HRMS (TOF ES+) calculated for  $C_{22}H_{19}O_3NSNa$  (M+Na)<sup>+</sup> 400.0983, observed 400.0986.

#### 4-Furan-3-yl-1*H*-indole-3-carbaldehyde (14)



A 15 mL flask was fitted with a condenser, Ar inlet, and magnetic stir bar. This set-up was charged with 4-bromo-1*H*-indole-3-carbaldehyde (300 mg, 1.36 mmol), Pd(PPh<sub>3</sub>)<sub>4</sub> (62.5 mg, 0.05 mmol), furan-3-boronic acid (200 mg, 1.8 mmol), DME (5 mL), and Na<sub>2</sub>CO<sub>3</sub> (1.5 mL of a saturated solution in water). This heterogeneous mixture was heated to reflux for 3.5 h, cooled, and then partitioned between EtOAc and water. The organic layer was washed three times with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, adsorbed onto about 3 g of celite 545, and concentrated *in vacuo*. The material was purified via SiO<sub>2</sub> flash chromatography using 2:1 hexanes:EtOAc as the eluent to give the product as a semisolid.

Yield: 0.30 g (100%).

<sup>1</sup>H NMR (DCCl<sub>3</sub>):  $\delta$  9.97 (s, 1 H), 9.78 (br.s, 1 H), 8.04 (d, J = 3.2 Hz, 1 H), 7.62 (dd, J = 1.6, 0.8 Hz, 1 H), 7.54 (t, J = 1.7 Hz, 1 H), 7.45 (dd, J = 8.1, 1.0 Hz, 1 H), 7.30 (app.t, J = 7.6 Hz, 1 H), 7.21 (dd, J = 7.1, 1.0 Hz, 1 H), 6.64 (dd, J = 1.7, 0.7 Hz, 1 H). <sup>13</sup>C NMR (DCCl<sub>3</sub>):  $\delta$  187.3, 143.3, 140.2, 137.3, 131.6, 126.20, 126.16, 124.8, 124.6, 123.6, 119.6, 112.1, 111.8. IR (NaCl, cm<sup>-1</sup>): 3243, 3056, 3000, 2963, 2940, 2091, 2863, 2850, 2767, 1651, 1514, 1494, 1422, 1387, 1356, 1332, 1290, 1266, 1234, 1184, 1158, 1138, 1120, 1062, 1046, 1022, 988, 873, 832, 788, 749, 663, 646, 599. HRMS (TOF ES+) calculated for C<sub>14</sub>H<sub>9</sub>O<sub>2</sub>N (M+H)<sup>+</sup> 212.0712, observed 212.0705.

4-Furan-3-yl-1-(toluene-4-sulfonyl)-1H-indole-3-carbaldehyde (15)



A 2-dram vial was charged with a solution of 4-furan-3-yl-1*H*-indole-3-carbaldehyde (274 mg, 1.3 mmol) in 10 mL of CH<sub>2</sub>Cl<sub>2</sub>. The solution was magnetically stirred under N<sub>2</sub> as DMAP (about 20 mg, 0.16 mmol), triethylamine (265  $\mu$ L, 1.9 mmol), and *p*TSCl (292 mg, 1.5 mmol) were added. The resulting yellow solution was stirred for 1h 40 min, and then was quenched with 1 N HCl and diluted with more CH<sub>2</sub>Cl<sub>2</sub>. The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, adsorbed onto celite 545, and purified via SiO<sub>2</sub> flash chromatography using 4:1 to 3:1 hexanes:EtOAc to give the product as an orange-tinted semi-solid. Rf = 0.23 in 3:1 hexanes:EtOAc (UV active and stained grey-green with anisaldehyde). Yield: 400 mg (84%).

<sup>1</sup>H NMR (DCCl<sub>3</sub>):  $\delta$  9.85 (s, 1 H), 8.35 (s, 1 H), 8.01 (dd, J = 8.5, 0.8 Hz, 1 H), 7.88 (app.d, J = 8.6 Hz, 2 H), 7.55 (dd, J = 1.5, 1.0 Hz, 1 H), 7.53 (t, J = 1.7 Hz, 1 H), 7.39 (dd, J = 8.5, 7.5 Hz, 1 H), 7.31 (app.d, J = 8.5 Hz, 2 H), 7.25 (dd, J = 7.3, 1.0 Hz, 1 H), 6.53 (dd, J = 1.7, 1.0 Hz, 1 H), 2.39 (s, 3 H). <sup>13</sup>C NMR (DCCl<sub>3</sub>):  $\delta$  186.8, 146.4, 143.7, 140.2, 135.6, 134.6, 131.6, 130.5, 127.6, 127.0, 126.56, 126.49, 125.50, 125.35, 122.6, 113.2, 111.9, 21.9. IR (NaCl, cm <sup>-1</sup>): 3133, 3055, 2923, 2870, 1677, 1596, 1527, 1506, 1406, 1378, 1276, 1192, 1175, 1160, 1125, 1096, 1087, 1030, 1006, 930, 874, 834, 813, 801, 788, 752, 737, 703, 679, 661, 615, 579. HRMS (TOF ES+) calculated for C<sub>20</sub>H<sub>15</sub>O<sub>4</sub>NSNa (M+Na)<sup>+</sup> 388.0620, observed 388.0603.

## 1-[4-Furan-3-yl-1-(toluene-4-sulfonyl)-1H-indol-3-yl]-prop-2-en-1-ol (16)



4-Furan-3-yl-1-(toluene-4-sulfonyl)-1*H*-indole-3-carbaldehyde (175 mg, 0.48 mmol) was dissolved in 1.0 mL of dry THF under N<sub>2</sub> in a 2-dram vial. The solution was magnetically stirred and cooled in a dry ice-acetone bath as vinylmagnesium bromide (0.60 mL of a 1.0 M solution in THF) was added dropwise. The mixture was stirred in the cool bath for 15 min, and then the dry ice bath was replaced with an ice bath and stirring was continued for 15 additional minutes. The reaction mixture was quenched with saturated aqueous NH<sub>4</sub>Cl and extracted into EtOAc. The organic layer was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The residue was purified via SiO<sub>2</sub> flash chromatography using 3:1 to 2:1 hexanes:EtOAc to give the product as an oil. The product eluted between the starting material and the reduction product. Yield: 190 mg (100%).

<sup>1</sup>H NMR (DCCl<sub>3</sub>):  $\delta$  8.06 (d, J = 8.3 Hz, 1 H), 7.86 (d, J = 8.3 Hz, 2 H), 7.68 (s, 1 H), 7.58 (app. s, 1 H), 7.57 (t, J = 1.7 Hz, 1 H), 7.37 (t, J = 7.9 Hz, 1 H), 7.31 (app. d, J = 9.5 Hz, 2 H), 7.17 (d, J = 7.3 Hz, 1 H), 6.63-6.64 (m, 1 H), 6.05 (ddd, J = 17.1, 10.5, 5.4 Hz,

1 H), 5.35 (app. t, J = 4.5 Hz, 1 H), 5.21-5.27 (m, 2 H). IR (NaCl, cm<sup>-1</sup>): 3550, 3418, 3146, 3090, 3070, 3035, 2983, 2924, 1644, 1596, 1557, 1505, 1494, 1479, 1446, 1414, 1372, 1308, 1291, 1245, 1189, 1172, 1127, 1095, 1031, 1006, 937, 908, 874, 813, 788, 757, 737, 704, 666, 617, 600, 579. HRMS (TOF ES+) calculated for C<sub>22</sub>H<sub>19</sub>O<sub>4</sub>NSNa (M+Na)<sup>+</sup> 416.0933, observed 416.0928.

## Cylcoadduct (18)



The alcohol (19.7 mg) was dissolved in 15 mL of  $CH_2Cl_2$ . The reaction mixture was magnetically stirred under N<sub>2</sub> and 80 mg of activated MnO<sub>2</sub> was added. After 40 min, the reaction mixture was filtered through celite 545, and concentrated *in vacuo*. The residue was dissolved in 45 mL of toluene, and the solution was placed in a 450 mL Parr high pressure reactor. The solution was sparged with N<sub>2</sub> for 10 min. The reactor was sealed and heated at 120 °C for 3 h. The solvent was then removed *in vacuo* at less than 35 °C, and the brown residue was purified by SiO<sub>2</sub> flash chromatography using 3:1 hexanes:EtOAc. The product (Rf = 0.1) was collected as a tan solid. Yield: 13.5 mg (69%).

## Mp: 185-190 °C, decomp.

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) 8.27 (s, 1 H), 7.85-7.91 (m, 3 H), 7.37 (t, J = 7.8 Hz, 1 H), 7.31 (d, J = 8.6 Hz, 2 H), 7.23 (d, J = 7.3 Hz, 1 H), 6.31 (d, J = 1.5 Hz, 1 H), 5.14-5.18 (m, 2 H), 3.42 (dt, J = 10.1, 4.3 Hz, 1 H), 2.71 (ddd, J = 11.5, 10.1, 4.4 Hz, 1 H), 2.39 (s, 3 H), 1.51 (dd, J = 11.5, 4.4 Hz, 1 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz) 196.6, 146.3, 143.7, 134.7, 133.9, 133.2, 132.2, 130.5, 130.0, 127.6, 126.0, 124.2, 122.8, 120.6, 112.7, 80.02, 79.97, 50.1, 35.4, 21.9. IR (KBr, cm<sup>-1</sup>): 3145, 3085, 3064, 3047, 3031, 2995, 2981, 2951, 1644, 1596, 1517, 1484, 1426, 1376, 1287, 1191, 1182, 1160, 1096, 922, 818, 813, 788, 757, 704, 694, 665, 612, 576, 549.