# Total Synthesis of Diverse Carbogenic Complexity within the Resveratrol Class from a Common Building Block

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## Supporting Information

### Experimental Data for Compounds

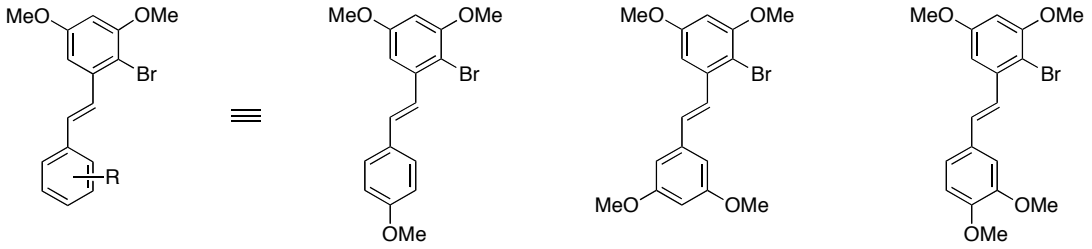
**General Procedures.** All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dry tetrahydrofuran (THF), acetonitrile (MeCN), toluene, benzene, diethyl ether ($Et_2O$) and methylene chloride ($CH_2Cl_2$) were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Yields refer to chromatographically and spectroscopically ($^1H$ and $^{13}C$ NMR) homogeneous materials, unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reactions were magnetically stirred and monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and an ethanolic solution of phosphomolybdic acid and cerium sulfate, and heat as developing agents. SiliCycle silica gel (60, academic grade, particle size 0.040–0.063 mm) was used for flash column chromatography. Preparative thin-layer chromatography (PTLC) separations were carried out on 0.50 mm E. Merck silica gel plates (60F-254). NMR spectra were recorded on Bruker DRX-300, DRX-400, DMX-500 instruments and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, br = broad, AB = AB quartet, app = apparent. IR spectra were recorded on a Perkin-Elmer 1000 series FT-IR spectrometer. High-resolution mass spectra (HRMS) were recorded in the Columbia University Mass Spectral Core facility on a JOEL HX110 mass spectrometer using the FAB (fast atom bombardment) and APCI (atmospheric pressure chemical ionization) techniques.

**Abbreviations.** NBS = *N*-bromosuccinimide, TFA = trifluoroacetic acid, KHMDS = potassium bis(trimethylsilyl)amide, *p*-TsOH = *para*-toluenesulfonic acid, *m*CPBA = *meta*-chloroperoxybenzoic acid, 9-I-BBN = 9-iodo-9-borabicyclo[3.3.1]nonane, AIBN = 2,2'-azobisisobutyronitrile, TMS = trimethylsilyl, NaHMDS = sodium bis(trimethylsilyl)amide, EDTA = ethylenediaminetetraacetic acid.

**Diethyl 2-bromo-3,5-dimethoxybenzylphosphonate (24)**. $NaBH_4$ (25.0 g, 676 mmol, 2.0 equiv) was added slowly to a solution of 3,5-dimethoxybenzaldehyde (55.0 g, 338 mmol, 1.0 equiv) in MeOH (0.7 L) at 0 °C. After 30 min of stirring at 0 °C, the reaction contents were quenched by the slow addition of water (400 mL), poured into water (300 mL), and extracted with EtOAc (3 × 2 L). The combined organic layers were then washed with water (300 mL) and brine (300 mL), dried ($MgSO_4$), and concentrated to afford the desired alcohol intermediate (54.7 g, 99% yield) as a white solid which was carried forward without further purification. Next, pyridine (1.19 mL, 14.8 mmol,

0.05 equiv) and $PBr_3$ (28.0 mL, 297 mmol, 1.0 equiv) were added sequentially and slowly to a portion of this newly-formed alcohol (50.0 g, 297 mmol, 1.0 equiv) in $Et_2O$ (1.5 L) at 25 °C, and the resultant mixture was heated at 40 °C for 3 h. Upon completion, the reaction contents were quenched carefully with ice water (500 mL), poured into water (500 mL), and extracted with $Et_2O$ (3 × 2 L). The combined organic layers were then washed with water (300 mL) and brine (300 mL), dried ($MgSO_4$), and concentrated to afford the desired alkyl halide (105 g, 94% yield) as an amorphous white solid which was carried forward without additional purification. $R_f$ = 0.66 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3002, 2960, 2838, 1597, 1465, 1429, 1348, 1325, 1300, 1264, 1206, 1158, 1064, 992, 931, 836, 693, 650 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.54 (d, *J* = 2.1 Hz, 2 H), 6.39 (t, *J* = 2.1 Hz, 1 H), 4.42 (s, 2 H), 3.80 (s, 6 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 160.9, 139.7, 107.0 (2 C), 100.6, 55.4 (2 C), 33.6; HRMS (FAB) calcd for $C_9H_{11}BrO_2^+$ [$M^+$] 229.9942, found 229.9937. To a solution of the newly formed alkyl bromide (50.0 g, 216 mmol, 1.0 equiv) in $CH_2Cl_2$ (2 L) at 0 °C was added solid NBS (19.3 g, 108 mmol, 0.5 equiv) in multiple portions. After stirring the resultant solution for 30 min at 0 °C, a second portion of NBS was added (19.3 g, 108 mmol, 0.5 equiv) and the reaction was stirred for an additional 30 min at 0 °C. Upon completion, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (400 mL), poured into water (200 mL), and extracted with $CH_2Cl_2$ (3 × 1.5 L). The combined organic layers were then washed with water (500 mL) and brine (500 mL), dried ($MgSO_4$), and concentrated to give the desired halogenated intermediate (63.4 g, 95% yield) as a white solid which was carried forward without additional purification. Next, a portion of this newly formed aryl bromide (80.0 g, 258 mmol, 1.0 equiv) was dissolved in THF (400 mL) and added dropwise at 0 °C to a THF solution of the anion of diethylphosphite which had been prepared by adding KHMDS (928 mL, 0.5 M in toluene, 464 mmol, 1.8 equiv) to a solution of diethylphosphite (66.4 mL, 515 mmol, 2.0 equiv) in THF (1.6 L) at 0 °C and stirring for 30 min. After 25 min of stirring at 0 °C, the reaction contents were warmed to 25 °C and stirred for 12 h. Upon completion, the reaction mixture was quenched with saturated aqueous $NH_4Cl$ (0.8 L), poured into water (500 mL), and extracted with EtOAc (3 × 2 L). The combined organic layers were then washed with water (400 mL) and brine (400 mL), dried ($MgSO_4$), and concentrated. The resultant light yellow product was left under high vacuum for 24 h to remove any residual diethylphosphite, ultimately affording phosphonate **24** (86.0 g, 91% yield) as a white solid. **24**: $R_f$ = 0.15 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2981, 2938, 2907, 2837, 1592, 1456, 1418, 1331, 1253, 1204, 1165, 1079, 1052, 1024, 961, 852, 782, 650 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.67 (t, *J* = 2.7 Hz, 1 H), 6.39 (t, *J* = 2.4 Hz, 1 H), 4.15 (dd, *J* = 6.9, 6.0 Hz, 2 H), 4.06 (dd, *J* = 6.9, 6.0 Hz, 2 H), 3.86 (s, 3 H), 3.80 (s, 3 H), 3.43 (d, *J* = 22.2 Hz, 2 H), 1.36 (t, *J* = 6.9 Hz, 3 H), 1.27 (t, *J* = 6.9 Hz, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 159.3, 156.8, 133.7, 133.6, 107.4, 107.3, 99.8, 62.3, 62.2, 56.3, 55.5, 34.7, 16.4, 16.3; HRMS (FAB) calcd for $C_{13}H_{21}BrO_5P^+$ [M + $H^+$] 367.0310, found 367.0301.

**Horner–Wadsworth–Emmons Olefination Products (25)**. KO*t*-Bu (57.1 mL, 1.0 M in THF, 57.1 mmol, 1.05 equiv) was added dropwise over the course of 5 min to a solution of phosphonate **24** (20.0 g, 54.4 mmol, 1.0 equiv) in THF (250 mL) at –78 °C. After 20 min of stirring at –78 °C, a solution of the desired aldehyde (7.04 g, 51.7 mmol, 0.95 equiv) in THF (50 mL) was added at –78 °C. The resultant solution was stirred at –78 °C for 1 h, and then at 25 °C for 12 h. Upon completion, the reaction mixture was quenched with saturated aqueous $NH_4Cl$ (150 mL), poured into water (100 mL), and extracted with EtOAc (3 × 500 mL). The combined organic layers were then washed with water (100 mL) and brine (100 mL), dried ($MgSO_4$), and concentrated to give resveratrol derivatives **25** (all in 98% yield) as white powders which were carried forward without additional purification.




**S1**: $R_f$ = 0.61 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3002, 2937, 2836, 1719, 1589, 1511, 1454, 1415, 1341, 1286, 1252, 1203, 1163, 1082, 1023, 962, 827 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.7 Hz, 2 H), 7.41 (d, *J* = 16.2 Hz, 1 H), 6.98 (d, *J* = 16.2 Hz, 1 H), 6.91 (d, *J* = 9.0 Hz, 2 H), 6.80 (d, *J* = 2.7 Hz, 1 H), 6.42 (d, *J* = 2.7 Hz, 1 H), 3.88 (s, 3 H), 3.86 (s 3 H), 3.83 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 159.6, 159.5, 156.8, 138.9, 131.1, 129.7, 128.1, 125.8, 114.1, 104.9, 102.4, 98.7, 56.3, 55.5, 55.3; HRMS (FAB) calcd for $C_{17}H_{17}BrO_3^+$ [$M^+$] 348.0361, found 348.0362.

**S2**: $R_f$ = 0.55 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3001, 2957, 2938, 2837, 1592, 1457, 1418, 1353, 1288, 1230, 1204, 1155, 1083, 1022, 959, 829, 650 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.50 (d, *J* = 15.9 Hz, 1 H), 6.94 (d, *J* = 15.9 Hz, 1 H), 6.80 (d, *J* = 2.7 Hz, 1 H), 6.71 (d, *J* = 2.4 Hz, 2 H), 6.43 (d, *J* = 2.7 Hz, 1 H), 6.42 (t, *J* = 2.1 Hz, 1 H), 3.88 (s, 3 H), 3.85 (s, 3 H), 3.83 (s, 6 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 160.9, 159.5, 156.8, 138.9, 138.5, 131.5, 128.4, 104.9, 102.7, 100.3, 99.1, 56.3, 55.5, 55.3; HRMS (FAB) calcd for $C_{18}H_{19}BrO_4^+$ [$M^+$] 378.0467, found 378.0484.

**S3**: $R_f$ = 0.53 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2951, 2923, 1578, 1511, 1454, 1226, 1157, 1021 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.38 (d, *J* = 16.1 Hz, 1 H), 7.08 (m, 2 H), 6.96 (d, *J* = 16.1 Hz, 1 H), 6.86 (d, *J* = 8.7 Hz, 1 H), 6.79 (d, *J* = 2.3 Hz, 1 H), 6.41 (d, *J* = 1.9 Hz, 1 H), 3.95 (s, 3 H), 3.90 (s, 3 H), 3.87 (s, 3 H), 3.85 (s, 6 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 159.5, 156.8, 149.3, 149.1, 138.8, 131.4, 130.0, 126.0, 120.3, 111.2, 109.1, 104.8, 102.4, 98.7, 56.3, 55.9, 55.8, 55.5; HRMS (FAB) calcd for $C_{18}H_{19}O_4^+$ [$M^+$] 378.0467, found 378.0473.

**General procedure to access key triaryl intermediates (26).** *n*-BuLi (37.7 mL, 1.6 M in THF, 60.3 mmol, 1.05 equiv) was added slowly over the course of 5 min to a solution of resveratrol derivative **25** (20.0 g, 57.4 mmol, 1.0 equiv) in THF (400 mL) at –78 °C, ultimately yielding a light yellow solution. After 20 min of stirring at –78 °C, a solution of the appropriate aldehyde (9.52 g, 57.4 mmol, 1.0 equiv) in THF (200 mL) was added slowly at –78 °C, and the resultant mixture was stirred for 1 h at –78 °C, warmed slowly to 25 °C, and stirred for an additional 4 h at 25 °C. Upon completion, the reaction contents were quenched with saturated aqueous $NH_4Cl$ (250 mL), poured into water (100 mL), and extracted with EtOAc (3 × 1 L). The combined organic layers were then washed with water (300 mL) and brine (300 mL), dried ($MgSO_4$), and concentrated. The resultant light yellow oils crystallized upon standing and were then triturated with EtOAc (3 × 10 mL) to give the desired triaryl intermediates as white solids.

**(*E*)-[2,4-dimethoxy-6-(4-methoxystyryl)phenyl]-(3,5-dimethoxyphenyl)methanol (27)**: 83% yield, $R_f$ = 0.40 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3509, 3001, 2938, 2837, 1604, 1511, 1458, 1307, 1244, 1204, 1175, 1153, 1059, 1032, 966, 930, 833, 736 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.7 Hz, 2 H), 7.28 (d, *J* = 16.2 Hz, 1 H), 6.88 (d, *J* = 16.2 Hz, 1 H), 6.86 (d, *J* = 8.7 Hz, 2 H), 6.74 (d, *J* = 2.1 Hz, 1 H), 6.54 (d, *J* = 2.0 Hz, 2 H), 6.45 (d, *J* = 2.1, 1 H), 6.33 (t, *J* = 2.4, 1 H), 6.22 (d, *J* = 9 Hz, 1 H), 3.86 (s, 3 H), 3.80 (s, 3 H), 3.78 (s, 1 H), 3.74 (s, 6 H), 3.72 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 160.5, 159.8, 159.4, 158.6, 147.5, 138.7, 131.5, 129.9,

127.8, 124.4, 121.7, 114.0, 103.8, 103.1, 98.6, 98.3, 70.0, 55.7, 55.3, 55.1; HRMS (FAB) calcd for $C_{26}H_{28}O_6^+$ [$M^+$] 436.1886, found 436.1870.

**(*E*)-[2,4-dimethoxy-6-(3,5-dimethoxystyryl)phenyl]-(3,5-dimethoxyphenyl)methanol (28)**: 88% yield, $R_f$ = 0.45 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3508, 3001, 2938, 2837, 1599, 1510, 1459, 1425, 1323, 1283, 1246, 1203, 1152, 1064, 1035, 964, 835, 799, 736 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.36 (d, *J* = 15.9 Hz, 1 H), 7.24 (d, *J* = 8.4 Hz, 2 H), 6.84 (d, *J* = 15.9 Hz, 1 H), 6.82 (d, *J* = 8.7 Hz, 2 H), 6.74 (d, *J* = 2.4 Hz, 1 H), 6.56 (d, *J* = 2.1 Hz, 2 H), 6.48 (d, *J* = 2.4 Hz, 1 H), 6.38 (t, *J* = 2.1 Hz, 1 H), 6.23 (d, *J* = 9.9 Hz, 1 H), 3.87 (s, 3 H), 3.80 (s, 6 H), 3.77 (s, 3 H), 3.73 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 160.9, 159.8, 158.8, 158.3, 139.1, 138.2, 136.8, 132.0, 127.1, 126.9, 122.3, 113.4, 104.6, 103.3, 100.3, 99.1, 69.8, 55.7, 55.4, 55.3, 55.2; HRMS (FAB) calcd for $C_{26}H_{28}O_6^+$ [$M^+$] 436.1886, found 436.1870.

**(*E*)-[2,4-dimethoxy-6-(3,4-dimethoxystyryl)phenyl]-(3,5-dimethoxyphenyl)methanol (29)**: 68% yield, $R_f$ = 0.26 (silica gel, EtOAc/hexanes, 1:2); IR (film) $\nu_{max}$ 3003, 2955, 2917, 1590, 1508, 1454, 1258, 1204, 1150 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.31 (s, 1 H), 7.01 (m, 2 H), 6.90 (d, *J* = 16.1 Hz, 1 H), 6.88 (app s, 1 H), 6.78 (d, *J* = 2.3 Hz, 1 H), 6.57 (m, 2 H), 6.50 (d, *J* = 2.4 Hz, 1 H), 6.37 (app t, *J* = 2.3 Hz, 1 H), 6.27 (d, *J* = 9.5 Hz, 1 H), 3.95 (s, 3 H), 3.94 (s, 3 H), 3.92 (s, 3 H), 3.79 (s, 3 H), 3.78 (s, 6 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 161.0, 160.4, 159.2, 149.5, 148.1, 139.1, 132.2, 130.7, 125.1, 122.3, 120.6, 111.5, 109.1, 104.4, 103.6, 99.2, 98.6, 70.3, 56.4, 56.3, 56.2, 55.8, 55.6; HRMS (MALDI-FTMS) calcd for $C_{27}H_{30}O_7^+$ [$M^+$] 466.1992, found 466.1995.

**(*E*)-[2,4-dimethoxy-6-(3,5-dimethoxystyryl)phenyl]-(3,4-dimethoxyphenyl)methanol (30)**: 75% yield, $R_f$ = 0.47 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3487, 2987, 2930, 2830, 1591, 1511, 1455, 1200, 1136, 1026 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.35 (d, *J* = 15.9 Hz, 1 H), 7.03 (d, *J* = 1.5 Hz, 1 H), 6.83 (d, *J* = 15.9 Hz, 1 H), 6.74 (d, *J* = 10.2 Hz, 1 H), 6.73 (app s, 1 H), 6.68 (ddd, *J* = 8.4, 1.7, 0.9 Hz, 1 H), 6.55 (d, *J* = 2.4 Hz, 2 H), 6.48 (d, *J* = 2.4 Hz, 1 H), 6.37 (t, *J* = 2.4 Hz, 1 H), 6.21 (d, *J* = 10.2 Hz, 1 H), 3.87 (s, 3 H), 3.83 (s, 3 H), 3.82 (s, 3 H), 3.78 (s, 6 H), 3.75 (d, *J* = 10.2 Hz, 1 H), 3.73 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 161.4, 160.3, 159.2, 149.1, 148.1, 139.5, 138.7, 137.8, 132.4, 127.7, 122.5, 118.1, 109.8, 105.1, 103.7, 100.6, 99.5, 70.3, 56.2, 55.8, 55.7; HRMS (FAB) calcd for $C_{27}H_{30}O_7^+$ [$M^+$] 466.1992, found 466.1983.

**3-(3,5-dimethoxyphenyl)-4,6-dimethoxy-2-(4-methoxyphenyl)-2,3-dihydro-1*H*-inden-1-ol (33)**. To a solution of key intermediate **27** (25.0 g, 57.3 mmol, 1.0 equiv) in $CH_2Cl_2$ (1.5 L) at –78 °C was added in a single portion a solution of TFA (4.5 mL, 57.3 mmol, 1.0 equiv) in $CH_2Cl_2$ (10 mL). The resultant dark purple reaction mixture was then warmed slowly to –20 °C over the course of 30 min and stirred for 5 h at –20 °C. Upon completion, the reaction mixture was quenched sequentially with solid $K_2CO_3$ (79.2 g, 573 mmol, 10 equiv) and MeOH (700 mL), warmed to 25 °C, and stirred for 30 min at 25 °C. The reaction contents were then poured into water (200 mL) and extracted with EtOAc (3 × 2 L). The combined organic layers were washed with water (300 mL) and brine (300 mL), dried ($MgSO_4$), and concentrated. The resultant brown oil was purified by flash column chromatography (silica gel, EtOAc/hexanes, 2:1) to give alcohol **33** (18.8 g, 75% yield) as an amorphous white solid. **33**: $R_f$ = 0.41 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2935, 1597, 1512, 1463, 1304, 1248, 1203, 1151, 1060, 829 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.7 Hz, 2 H), 6.83 (d, *J* = 8.7 Hz, 2 H), 6.65 (d, *J* = 2.1 Hz, 1 H), 6.42 (d, *J* = 2.1 Hz, 1 H), 6.27 (t, *J* = 2.3 Hz, 1 H), 6.17 (d, *J* = 2.4 Hz, 2 H), 5.13 (app t, *J* = 5.7 Hz, 1 H), 4.19 (d, *J* = 6.9 Hz, 1 H), 3.86 (s, 3 H), 3.79 (s, 3 H), 3.68 (s, 3 H), 3.59 (s, 3 H), 3.18 (d, *J* = 6.6 Hz, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 161.7, 160.4, 158.5, 157.1, 146.9, 146.3, 134.0, 128.7, 122.9, 113.9, 105.5, 99.7, 99.4, 99.3, 98.0, 82.5, 66.1, 55.6, 55.3, 55.2, 54.7; HRMS (FAB) calcd for $C_{26}H_{28}O_6^+$ [$M^+$] 436.1886, found 436.1870.

**Paucifloral F (10).** Dess–Martin periodinane (0.152 g, 0.358 mmol, 1.2 equiv) was added in a single portion to a solution of alcohol **33** (0.130 g, 0.298 mmol, 1.0 equiv) in $CH_2Cl_2$ (8 mL) at 25 °C, and the resultant slurry was stirred for 1 h at 25 °C. Upon completion, the reaction contents were quenched with saturated aqueous $Na_2SO_3$ (1.5 mL) followed by stirring the resultant biphasic system vigorously for 5 min at 25 °C. The reaction contents were then poured into saturated aqueous $NaHCO_3$ (5 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated to afford permethylated paucifloral F (**48**, 0.122 g, 97% yield) as a light yellow oil which was carried forward without additional purification. **48**: $R_f$ = 0.45 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 1696, 1614, 1514, 1474, 1347, 1155, 1082, 1005, 842 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.02 (d, *J* = 8.7 Hz, 2 H), 6.90 (d, *J* = 2.1 Hz, 1 H), 6.84 (d, *J* = 8.7 Hz, 2 H), 6.70 (d, *J* = 2.1 Hz, 1 H), 6.32 (app t, *J* = 2.4 Hz, 1 H), 6.16 (d, *J* = 2.4 Hz, 2 H), 4.44 (d, *J* = 2.7 Hz, 1 H), 3.88 (s, 3 H), 3.78 (s, 3 H), 3.71 (s, 3 H), 3.69 (s, 3 H), 3.65 (d, *J* = 3.0 Hz, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 205.9, 162.0 (2 C), 160.8, 158.6, 157.8, 145.9, 138.7, 137.6, 131.5, 128.8, 114.2 (2 C), 106.4, 105.1 (2 C), 98.1, 96.4, 64.1, 55.8, 55.6, 55.2, 51.9. Finally, a solution of this newly synthesized ketone (0.035 g, 0.081 mmol, 1.0 equiv) in $CH_2Cl_2$ (3 mL) was added dropwise to a commercially-prepared solution of $BBr_3$ (0.770 mL, 1.0 M in $CH_2Cl_2$, 0.810 mmol, 10 equiv) at 0 °C, and the resultant solution was stirred for 6 h at 0 °C. Upon completion, the reaction mixture was quenched with water (5 mL), poured into water (10 mL), and extracted with EtOAc (3 × 20 mL). The combined organic layers were then washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. The resultant light pink product was purified by flash column chromatography (silica gel, $CH_2Cl_2$/MeOH, 9:1) to give paucifloral F (0.025 g, 86% yield) as an amorphous white solid. **10**: $R_f$ = 0.06 (silica gel, $CH_2Cl_2$/MeOH, 9:1); IR (film) $\nu_{max}$ 3334, 1696, 1614, 1514, 1474, 1347, 1155, 1082, 1005, 842 $cm^{-1}$; $^1H$ NMR (300 MHz, Acetone-$d_6$) δ 8.75 (s, 1 H), 8.49 (s, 1 H), 8.27 (s, 1 H), 8.07 (s, 2 H), 6.96 (d, *J* = 8.7 Hz, 2 H), 6.78 (d, *J* = 8.7 Hz, 2 H), 6.72 (s, 2 H), 6.19 (app t, *J* = 2.1 Hz, 1 H), 6.02 (d, *J* = 2.1 Hz, 2 H), 4.38 (d, *J* = 2.7 Hz, 1 H), 3.50 (d, *J* = 2.7, 1 H); $^{13}C$ NMR (75 MHz, Acetone-$d_6$) δ 205.5, 160.2, 159.5, 157.2, 156.7, 147.3, 140.0, 134.8, 131.8, 129.6, 116.3, 110.2, 106.3, 101.6, 100.5, 65.3, 52.1; HRMS (FAB) calcd for $C_{21}H_{17}O_6^+$ [M + $H^+$] 365.1025, found 365.1055. All spectroscopic data for this synthetic material match those reported by Ito and co-workers for natural paucifloral F (**10**).[1]

**Sulfide 35.** Solid *p*-TsOH (0.039 g, 0.229 mmol, 1.0 equiv) was added in a single portion to a solution of key intermediate **27** (0.100 g, 0.229 mmol, 1.0 equiv) in $CH_2Cl_2$ (10 mL) at –50 °C. The resultant mixture was then warmed slowly to –30 °C over the course of 20 min and stirred for an additional 5 h at –30 °C. Once this operation was complete, the reaction contents were warmed to 0 °C, *p*-methoxy-α-toluenethiol (**34**, 0.096 mL, 0.687 mmol, 3.0 equiv) was added in a single portion, and the resultant mixture was concentrated to a minimum volume (approximately 0.2 mL). The resultant solution was then stirred for 12 h at 25 °C. Upon completion, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (5 mL), poured into water (5 mL), and extracted with EtOAc (3 × 10 mL). The combined organic layers were then washed with water (10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated. The resultant yellow solid was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give sulfide **35** (0.075 g, 57%) as a light yellow oil. Alternatively, *p*-methoxy-α-toluenethiol (**34**, 9.6 mL, 68.6 mmol, 3.0 equiv) and *p*-TsOH (3.96 g, 22.9 mmol, 1.0 equiv) were added to a highly concentrated solution of alcohol **33** (10.0 g, 22.9 mmol, 1.0 equiv) in $CH_2Cl_2$ (2 mL) at 25 °C. The resulting yellow-green solution was stirred for 48 h at 25 °C under the strict exclusion of light. Upon completion, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (30 mL), poured into water (30 mL), and extracted with EtOAc (3 × 200 mL). The combined organic layers were then washed with water (50 mL) and

brine (30 mL), dried ($MgSO_4$), and concentrated. The resultant light green product was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:3) to give a sulfide **35** (10.8 g, 82%) as a light yellow oil. **35**: $R_f$ = 0.71 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2995, 2934, 2831, 1607, 1512, 1463, 1421, 1326, 1303, 1249, 1203, 1175, 1154, 1061, 1035, 934, 830 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$, 1:1 mixture of diastereomers) δ 7.13 (d, *J* = 8.4 Hz, 2 H), 7.07 (d, *J* = 8.7 Hz, 2 H), 7.04 (d, *J* = 9.0 Hz, 2 H), 7.03 (d, *J* = 8.4 Hz, 2 H), 6.84 (d, *J* = 2.4 Hz, 2 H), 6.80 (d, *J* = 2.7 Hz, 2 H), 6.79 (s, 1 H), 6.77 (s, 1 H), 6.74 (d, *J* = 8.7 Hz, 2 H), 6.53 (d, *J* = 1.5 Hz, 1 H), 6.45 (d, *J* = 1.5 Hz, 1 H), 6.36 (br m, 3 H), 6.28 (br m, 2 H), 6.18 (br m, 4 H), 4.55 (s, 1 H), 4.53 (d, *J* = 2.7 Hz, 1 H), 4.22 (app t, *J* = 7.2 Hz, 3 H), 3.82 (s, 3 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 3.79 (s, 3 H), 3.77 (s, 3 H), 3.76 (s, 3 H), 3.69 (s, 3 H), 3.68 (s, 6 H), 3.61 (s, 3 H), 3.57 (s, 6 H); $^{13}C$ NMR (75 MHz, $CDCl_3$, 1:1 mixture of diastereomers) δ 161.5, 161.3, 160.5, 160.3, 158.5, 157.0, 156.8, 147.1, 146.5, 146.2, 145.3, 135.7, 133.5, 130.3, 130.0, 129.8, 128.6, 124.1, 123.7, 113.9, 113.8, 113.7, 113.3, 105.5, 100.8, 100.4, 98.9, 98.5, 98.1, 97.9, 64.6, 60.3, 57.2, 56.7, 55.5, 55.2, 54.0, 53.7, 36.0, 34.9; HRMS (FAB) calcd for $C_{34}H_{35}O_6S^+$ [M – $H^+$] 571.2154, found 571.2168.

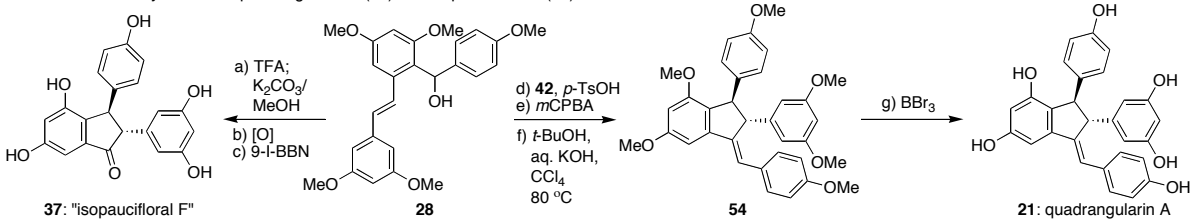
**Ampelopsin D (5).** Solid $NaHCO_3$ (7.34 g, 87.4 mmol, 5.0 equiv) and *m*CPBA (77%, 9.06 g, 52.5 mmol, 3.0 equiv) were added sequentially to a solution of sulfide **35** (10.0 g, 17.5 mmol, 1.0 equiv) in $CH_2Cl_2$ (150 mL) at 0 °C to give a milk-colored slurry. After warming this mixture to 25 °C and stirring for 15 min, the reaction contents were quenched with saturated aqueous $NaHCO_3$ (150 mL), poured into water (100 mL), and extracted with $CH_2Cl_2$ (3 × 300 mL). The combined organic layers were then washed with water (100 mL) and brine (100 mL), dried ($MgSO_4$), and concentrated. The resultant off-white solid was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give the desired sulfone intermediate (8.26 g, 78%) as a yellow-pink oil. Next, finely powdered KOH (18.6 g, 331 mmol, 20 equiv) was added in a single portion to a solution of a portion of this newly synthesized adduct (10.0 g, 16.6 mmol, 1.0 equiv) in a mixture of $CCl_4$/t-BuOH/$H_2O$ (5/5/1, 380 mL/380 mL/79 mL) at 25 °C. The resultant slurry was then stirred for 12 h at 80 °C. Upon completion, the reaction mixture was quenched with saturated aqueous $NH_4Cl$ (500 mL), poured into water (200 mL), and extracted with EtOAc (3 × 1.5 L). The combined organic layers were then washed with water (200 mL) and brine (200 mL), dried ($MgSO_4$), and concentrated. The resultant light yellow oil was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give both the desired alkene (**61**, 4.2 g, 52%) as a yellow oil along with a small and separable portion of its exocyclic olefinic regioisomer (1.3 g, 15%) as a light yellow oil. **61**: $R_f$ = 0.53 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2995, 2934, 2836, 1606, 1509, 1463, 1288, 1248, 1203, 1175, 1152, 1065, 1036, 827 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.7 Hz, 2 H), 7.18 (d, *J* = 8.4 Hz, 2 H), 7.09 (s, 1 H), 6.85 (d, *J* = 1.8 Hz, 1 H), 6.80 (d, *J* = 8.4 Hz, 2 H), 6.72 (d, *J* = 8.7 Hz, 2 H), 6.33 (d, *J* = 1.8 Hz, 1 H), 6.29 (d, *J* = 2.1 Hz, 1 H), 6.27 (d, *J* = 2.1 Hz, 1 H), 4.36 (s, 1 H), 4.25 (s, 1 H), 3.93 (s, 3 H), 3.76 (s, 3 H), 3.73 (s, 3 H), 3.71 (s, 6 H), 3.62 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 161.5, 160.6, 158.4, 158.0, 157.6, 148.1, 145.6, 142.7, 137.3, 130.0, 129.6, 127.9, 126.0, 122.1, 114.1, 113.7, 105.3, 99.1, 97.5, 94.9, 58.0, 57.9, 55.6, 55.2 (2 C); HRMS (FAB) calcd for $C_{34}H_{34}O_6^+$ [$M^+$] 538.2355, found 538.2357. Finally, permethylated ampelopsin D (**61**, 0.050 g, 0.090 mmol, 1.0 equiv) was added as a solution in $CH_2Cl_2$ (5 mL) at 25 °C to a freshly-prepared solution of $BBr_3$ [made by dissolving solid $BBr_3$ (0.271 g, 1.08 mmol, 12 equiv) in $CH_2Cl_2$ (5 mL) at 25 °C in a glove box], and the resulting solution was stirred for 6 h at 25 °C. Upon completion, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (15 mL), poured into water (15 mL), and extracted with EtOAc (3 × 15 mL). The combined organic layers were then washed with water (20 mL) and brine (20 mL), dried ($MgSO_4$), and concentrated. The resultant light yellow solid was purified by flash column chromatography (silica gel, $CH_2Cl_2$/MeOH, 9:1) to afford a 5/1 mixture of ampelopsin D and isoampelopsin D (**5**/**36**,

0.041 g combined, 89% overall) as colorless oils. These regioisomers were obtained individually in near quantitative yield (95%) following acetylation [$Ac_2O$, pyridine], chromatographic separation via flash column chromatography, and acetate hydrolysis [cat. KCN, MeOH]. **5**: $R_f$ = 0.03 (silica gel, $CH_2Cl_2$/MeOH, 9:1); IR (film) $\nu_{max}$ 3339, 1604, 1511, 1465, 1374, 1335, 1238, 1147, 1010, 834, 650 $cm^{-1}$; $^1H$ NMR (300 MHz, acetone-$d_6$) δ 8.30 (br s, 1 H), 8.20 (br s, 1 H), 8.11 (br s, 1 H), 7.97 (br s, 2 H), 7.85 (br s, 1 H), 7.18 (d, *J* = 8.7 Hz, 2 H), 7.12 (d, *J* = 8.7 Hz, 2 H), 7.04 (app t, *J* = 0.6 Hz, 1 H), 6.81 (d, *J* = 1.8 Hz, 1 H), 6.75 (d, *J* = 8.4 Hz, 2 H), 6.66 (d, *J* = 8.7 Hz, 2 H), 6.30 (d, *J* = 2.1 Hz, 1 H), 6.11 (m, 3 H), 4.29 (s, 1 H), 4.15 (s, 1 H); $^{13}C$ NMR (75 MHz, acetone-$d_6$) δ 159.7, 159.3, 157.3, 156.7, 156.1, 149.3, 147.6, 143.1, 137.4, 131.0, 129.7, 128.8, 123.8, 122.7, 116.3, 116.0, 106.5, 103.8, 101.3, 98.4, 59.5, 58.7; HRMS (FAB) calcd for $C_{28}H_{22}O_6^+$ [$M^+$] 454.1416, found 454.1448. All spectroscopic data for this synthetic material match those reported by Niwa and co-workers for natural ampelopsin D (**5**).[2]

**Isoampelopsin D (36)**. Concentrated HCl (50 μL, 0.600 mmol, 5.5 equiv.) was added to a solution of ampelopsin D (**5**, 5.0 mg, 0.110 mmol, 1.0 equiv) in MeOH (0.5 mL) at 25 °C, and the resultant mixture was stirred at 80 °C for 12 h. Upon completion, the reaction mixture was quenched with water (3 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were then washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. The resultant light yellow product was purified by flash column chromatography (silica gel, $CH_2Cl_2$/MeOH, 9:1) to give isoampelopsin D (**36**, 4.8 mg, 96%) as a colorless oil. **36**: $R_f$ = 0.13 (silica gel, $CH_2Cl_2$/MeOH, 9:1); IR (film) $\nu_{max}$ 3411, 2810, 1680, 1628, 1511, 1443, 1371, 1333, 1206, 1149, 1055, 1006, 833 $cm^{-1}$; $^1H$ NMR (300 MHz, methanol-$d_4$) δ 7.11 (d, *J* = 8.4 Hz, 2 H), 7.07 (d, *J* = 8.7 Hz, 2 H), 6.73 (d, *J* = 8.7 Hz, 2 H), 6.66 (d, *J* = 8.7 Hz, 2 H), 6.17 (d, *J* = 2.1 Hz, 1 H), 6.06 (d, *J* = 1.5 Hz, 1 H), 6.06 (d, *J* = 2.1 Hz, 2 H), 5.99 (t, *J* = 2.1 Hz, 1 H), 4.80 (s, 1 H), 3.84 (s, 2 H); $^{13}C$ NMR (75 MHz, methanol-$d_4$) δ 158.9, 158.7, 157.5, 156.5, 154.0, 150.4, 149.9, 144.0, 136.6, 132.1, 131.1, 130.2, 128.9, 125.4, 116.3, 115.8, 108.1, 101.4, 100.7, 56.7, 32.2; HRMS (FAB) calcd for $C_{28}H_{22}O_6^+$ [$M^+$] 454.1416, found 454.1428. All spectroscopic data for this synthetic material match those reported by Niwa and co-workers for natural isoampelopsin (**36**).[2]

**Total Synthesis of Quadrangularin A (21) and Isopaucifloral F (37).** These two natural products were synthesized from intermediate **28** exactly as described above for ampelopsin D (**5**) and paucifloral F (**10**). Only the final deprotection leading to isopaucifloral F (**45**) is fundamentally different from the steps outlined above, so only this procedure is defined specifically below.

***Scheme S1***. Total synthesis of quadrangularin A (**21**) and isopaucifloral F (**37**).[a]




[a]Reagents and conditions: (a) TFA (1.0 equiv), $CH_2Cl_2$, -30→-20 °C, 5 h; then $K_2CO_3$ (10 equiv), MeOH, 25 °C, 5 min, 93%; (b) Dess-Martin periodinane (1.2 equiv), $NaHCO_3$ (5.0 equiv), $CH_2Cl_2$, 25 °C, 3 h, 98%; (c) 9-I-BBN (1.0 M in hexanes, 10 equiv), $CH_2Cl_2$, 40 °C, 30 min, 72%; (d) *p*-TsOH (1.0 equiv), $CH_2Cl_2$, -30→-20 °C, 5 h; *p*-methoxybenzenethiol (3.0 equiv), then concentration to near dryness, 25 °C, 12 h, 65%; (e) *m*CPBA (3.0 equiv), $NaHCO_3$ (10 equiv), $CH_2Cl_2$, 0→25 °C, 3 h, 70%; (f) *t*-BuOH/$H_2O$/$CCl_4$ (5/1/5), KOH (powder, 20 equiv), 80 °C, 12 h, 55%; (g) $BBr_3$ (1.0 M in $CH_2Cl_2$, 12 equiv), $CH_2Cl_2$, 25 °C, 6 h, 75% of **21**, 14% of internal alkene isomer. 9-I-BBN = 9-iodo-9-borabicyclo[3.3.1]nonane.

**Isopaucifloral F (37).** 9-I-BBN (1.61 mL, 1.0 M in hexanes, 1.61 mmol, 7.0 equiv) was added dropwise to a solution of permethylated isopaucifloral F (0.100 g, 0.240 mmol, 1.0 equiv) in $CH_2Cl_2$ (10 mL) at 25 °C. The reaction solution turned a red color immediately, and was immediately heated at 40 °C for 30 min with continued stirring. Upon completion, the reaction mixture was cooled to 25 °C, quenched with water (15 mL), and extracted with EtOAc (3 × 20 mL).

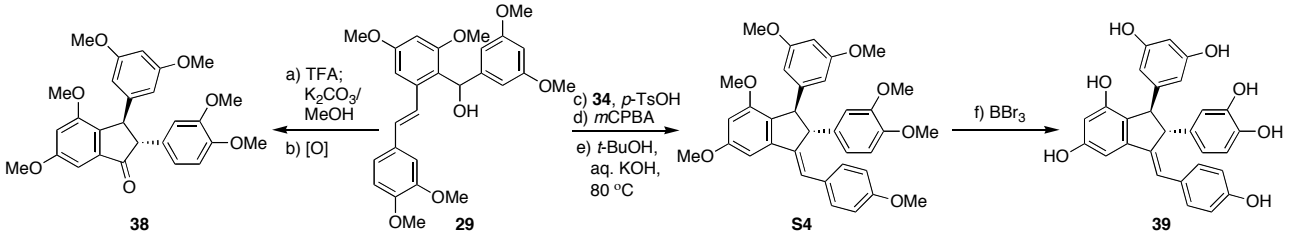
The combined organic layers were then washed with water (15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated. The resultant red oil was purified by flash column chromatography (silica gel, $CH_2Cl_2$/MeOH, 9:1) to afford isopaucifloral F (**37**, 0.063 g, 72%) as colorless oil. **37**: $R_f$ = 0.06 (silica gel, $CH_2Cl_2$/MeOH, 9:1); IR (film) $\nu_{max}$ 3349, 1691, 1602, 1512, 1418, 1342, 1251, 1149 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 8.13 (s, 3 H), 7.35 (s, 2 H), 6.89 (d, *J* = 8.7 Hz, 2 H), 6.74 (d, *J* = 8.7 Hz, 2 H), 6.71 (d, *J* = 2.1 Hz, 1 H), 6.24 (t, *J* = 2.1 Hz, 1 H), 6.11 (d, *J* = 2.1 Hz, 2 H), 4.48 (d, *J* = 2.4 Hz, 1 H), 3.42 (d, *J* = 2.7 Hz, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 205.1, 160.2, 159.6, 156.8, 156.6, 143.3, 140.1, 135.7, 135.3, 128.9, 116.1, 110.3, 107.0, 102.1, 100.7, 66.3, 51.4; HRMS (FAB) calcd for $C_{21}H_{16}O_6^+$ [$M^+$] 364.0947, found 364.0961.

**Permethylated quadrangularin A (54)**: $R_f$ = 0.50 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2995, 2925, 2831, 1593, 1509, 1462, 1246, 1202, 1151, 1061, 1035 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.24 (d, *J* = 9.0 Hz, 2 H), 7.12 (s, 1 H), 7.05 (d, *J* = 8.7 Hz, 2 H), 6.85 (d, *J* = 2.1 Hz, 1 H), 6.77 (d, *J* = 8.7 Hz, 2 H), 6.75 (d, *J* = 8.7 Hz, 2 H), 6.45 (d, *J* = 2.1 Hz, 2 H), 6.33 (d, *J* = 2.1 Hz, 1 H), 6.31 (app t, *J* = 2.1 Hz, 1 H), 4.32 (d, *J* = 4.2 Hz, 2 H), 3.93 (s, 3 H), 3.75 (s, 3 H), 3.74 (s, 3 H), 3.74 (s, 6 H), 3.61 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 161.4, 160.9, 158.4, 157.8, 157.4, 147.7, 145.2, 142.2, 137.9, 130.0, 129.7, 127.8, 126.8, 122.4, 113.7, 105.3, 99.1, 97.6, 94.8, 59.2, 56.8, 55.5, 55.2 (3 C); HRMS (FAB) calcd for $C_{34}H_{34}O_6^+$ [M – $2H^+$] 538.2374, found 538.2355.

**Quadrangularin A (21)**: $R_f$ = 0.03 (silica gel, $CH_2Cl_2$/MeOH, 9:1); IR (film) $\nu_{max}$ 3306, 1603, 1511, 1459, 1339, 1242, 1149, 1004, 833, 650 $cm^{-1}$; $^1H$ NMR (300 MHz, MeOH-$d_3$) δ 7.13 (d, *J* = 8.7 Hz, 2 H), 6.98 (s, 1 H), 6.88 (d, *J* = 8.7 Hz, 2 H), 6.70 (d, *J* = 1.8 Hz, 1 H), 6.62 (d, *J* = 8.7 Hz, 2 H), 6.60 (d, *J* = 8.7 Hz, 2 H), 6.22 (d, *J* = 2.1 Hz, 2 H), 6.17 (d, *J* = 1.8 Hz, 1 H), 6.09 (t, *J* = 2.1 Hz, 1 H), 4.17 (br s, 1 H), 4.03 (br s, 1 H); $^{13}C$ NMR (75 MHz, MeOH-$d_3$) δ 159.7 (2 C), 157.4, 156.5, 156.2, 149.7, 147.7, 143.4, 138.5, 131.2 (2 C), 130.3, 128.9 (2 C), 125.4, 123.1, 116.0 (4 C), 106.6 (2 C), 103.8, 101.5, 98.4, 61.2, 58.1; HRMS (FAB) calcd for $C_{28}H_{22}O_6^+$ [$M^+$] 454.1416, found 454.1440. All spectroscopic data for this synthetic material match those reported by Païs and co-workers for natural quadrangularin A (**21**).[3]

**Synthesis of Natural Product-Like Compounds 38 and 39.** These two compounds were synthesized from intermediate **29** exactly as described above for ampelopsin D (**5**) and paucifloral F (**10**); as such, only data for selected compounds is provided.

***Scheme S2***. Synthesis of natural product-like architectures **38** and **39**.[a]




[a]Reagents and conditions: (a) TFA (1.0 equiv), $CH_2Cl_2$, -30→-20 °C, 5 h; then $K_2CO_3$ (10 equiv), MeOH, 25 °C, 5 min, 93%; (b) Dess-Martin periodinane (1.2 equiv), $NaHCO_3$ (5.0 equiv), $CH_2Cl_2$, 25 °C, 3 h, 98%; (c) *p*-TsOH (1.0 equiv), $CH_2Cl_2$, -30→-20 °C, 5 h; *p*-methoxybenzenethiol (3.0 equiv), then concentration to near dryness, 25 °C, 12 h, 65%; (d) *m*CPBA (3.0 equiv), $NaHCO_3$ (10 equiv), $CH_2Cl_2$, 0→25 °C, 3 h, 70%; (e) *t*-BuOH/$H_2O$/$CCl_4$ (5/1/5), KOH (powder, 20 equiv), 80 °C, 12 h, 55%; (f) $BBr_3$ (1.0 M in $CH_2Cl_2$, 12 equiv), $CH_2Cl_2$, 25 °C, 6 h, 75% of **39**, 14% of internal alkene isomer.

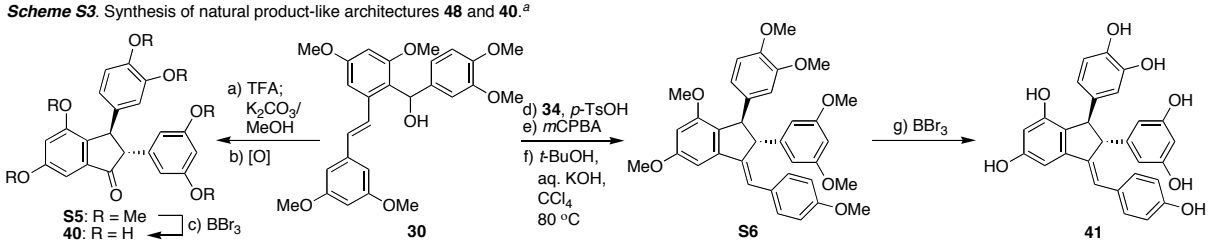
**38**: $R_f$ = 0.39 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2998, 2935, 2835, 2056, 1733, 1593, 1511, 1486, 1463, 1428, 1329, 1300, 1251, 1236, 1202, 1177, 1154, 1095, 1066, 1030, 935, 827, 757, 733, 694 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.7 Hz, 2 H), 7.09 (s, 1 H), 6.83 (d, *J* = 1.8 Hz, 1 H), 6.79–6.70 (m, 5 H), 6.32–6.26 (m, 4 H), 4.34 (app s, 1 H), 4.26 (app s, 1 H), 3.92 (s, 3 H), 3.82 (s, 3 H), 3.79 (s, 6 H), 3.73 (s, 3 H), 3.70 (s, 6 H), 3.62 (s, 3 H); $^{13}C$ NMR (75

MHz, $CDCl_3$) δ 161.5, 160.7, 160.6, 158.4, 157.5, 149.0, 148.2, 147.4, 145.5, 142.7, 137.7, 130.0, 129.7, 126.2, 122.2, 118.7, 113.7, 111.4, 110.6, 105.3, 99.1, 97.6, 95.0, 58.4, 57.9, 55.9, 55.8, 55.6, 55.3, 55.1; HRMS (FAB) calcd for $C_{35}H_{35}O_7^+$ [$M^+$] 568.2461, found 568.2479.

**39**: $R_f$ = 0.03 (silica gel, MeOH/$CH_2Cl_2$, 1:9); IR (film) $\nu_{max}$ 3317, 2923, 2851, 1660, 1651, 1604, 1511, 1462, 1455, 1373, 1338, 1248, 1153, 1111, 1008, 832, 693, 662 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.7 Hz, 2 H), 7.02 (s, 1 H), 6.78 (d, *J* = 1.8 Hz, 1 H), 6.74–6.72 (m, 2 H), 6.66 (d, *J* = 8.7 Hz, 2 H), 6.30 (d, *J* = 1.8 Hz, 1 H), 6.14 (d, *J* = 2.4 Hz, 1 H), 6.11–6.09 (m, 3 H), 4.21 (app s, 1 H), 4.16 (app s, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 159.9, 158.3, 157.1, 150.4, 148.7, 147.1, 145.4, 144.1, 139.4, 132.2, 131.1, 123.8, 120.4, 117.4, 117.3, 117.0, 115.7, 108.8, 107.5, 104.8, 102.3, 99.4, 60.9, 59.8; HRMS (FAB) calcd for $C_{27}H_{27}O_7^+$ [$M^+$] 470.1366, found 470.1375.

**Synthesis of Natural Product-Like Compounds 40 and 41.** These two compounds were synthesized from intermediate **30** exactly as described above for ampelopsin D (**5**) and paucifloral F (**10**); as such, only data for selected compounds is provided.

***Scheme S3***. Synthesis of natural product-like architectures **48** and **40**.[a]




[a]Reagents and conditions: (a) TFA (1.0 equiv), $CH_2Cl_2$, -30→-20 °C, 5 h; then $K_2CO_3$ (10 equiv), MeOH, 25 °C, 5 min, 93%; (b) Dess-Martin periodinane (1.2 equiv), $NaHCO_3$ (5.0 equiv), $CH_2Cl_2$, 25 °C, 3 h, 98%; (c) $BBr_3$ (1.0 M in $CH_2Cl_2$, 12 equiv), $CH_2Cl_2$, 25 °C, 12 hr, 72%; (d) *p*-TsOH (1.0 equiv), $CH_2Cl_2$, -30→-20 °C, 5 h; *p*-methoxybenzenethiol (3.0 equiv), then concentration to near dryness, 25 °C, 12 h, 65%; (e) *m*CPBA (3.0 equiv), $NaHCO_3$ (10 equiv), $CH_2Cl_2$, 0→25 °C, 3 h, 70%; (f) *t*-BuOH/$H_2O$/$CCl_4$ (5/1/5), KOH (powder, 20 equiv), 80 °C, 12 h, 55%; (g) $BBr_3$ (1.0 M in $CH_2Cl_2$, 12 equiv), $CH_2Cl_2$, 25 °C, 6 h, 75% of **41**, 14% of internal alkene isomer.

**S5**: $R_f$ = 0.46 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3002, 2936, 2837, 1710, 1593, 1513, 1460, 1304, 1203, 1148, 1028, 730 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.89 (d, *J* = 2.0 Hz, 1 H), 6.73 (d, *J* = 8.8 Hz, 1 H), 6.68 (d, *J* = 2.0 Hz, 1 H), 6.53 (dd, *J* = 8.8, 2.0 Hz, 1 H), 6.53 (d, *J* = 2.8 Hz, 1 H), 6.35 (t, *J* = 2.4 Hz, 1 H), 6.23 (d, *J* = 2.4 Hz, 2 H), 4.48 (d, *J* = 2.8 Hz, 1 H), 3.86 (s, 3H), 3.83 (s, 3 H), 3.87 (s, 3 H), 3.83 (s, 3 H), 3.75 (s, 3 H), 3.72 (s, 6 H), 3.65 (s, 3 H), 3.61 (d, *J* = 2.8 Hz, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 205.8, 162.5, 161.4, 158.2, 149.3, 148.0, 141.9, 139.0, 138.6, 136.4, 119.3, 111.5, 110.8, 107.0, 106.5, 99.4, 96.9, 65.7, 56.2, 56.0, 55.71, 55.70. HRMS (FAB) calcd for $C_{27}H_{28}O_7^+$ [$M^+$] 464.1835, found 464.1842.

**40**: $R_f$ = 0.13 (silica gel, DCM/MeOH, 9:1); IR (film) $\nu_{max}$ 3418, 1683, 1615, 1495, 1374, 1154; $^1H$ NMR (400 MHz, acetone-$d_6$) δ 6.74 (d, *J* = 2.1 Hz, 1 H), 6.73 (d, *J* = 3.1 Hz, 1 H), 6.72 (d, *J* = 8.0 Hz, 1 H), 6.51 (d, *J* = 2.4 Hz, 1 H), 6.43 (dd, *J* = 8.1, 2.1 Hz, 1 H), 6.25 (t, *J* = 2.4 Hz, 1 H), 6.13 (d, *J* = 2.4 Hz, 2 H), 4.44 (d, *J* = 2.4 Hz, 1 H), 3.43 (d, *J* = 2.4 Hz, 1 H); $^{13}C$ NMR (75 MHz, acetone-$d_6$) δ 205.8, 165.8, 163.0, 158.9, 154.0, 145.0, 143.8, 142.0, 140.5, 124.8, 120.5, 115.2, 109.6, 102.5, 102.1, 100.1, 97.8, 60.0, 47.9; HRMS (FAB) calcd for $C_{21}H_{16}O_7^+$ [$M^+$] 380.0896, found 380.0884. [Note: this compound decomposes relatively quickly even under an Argon atmosphere, precluding several attempts at obtaining a $^{13}C$ spectrum].

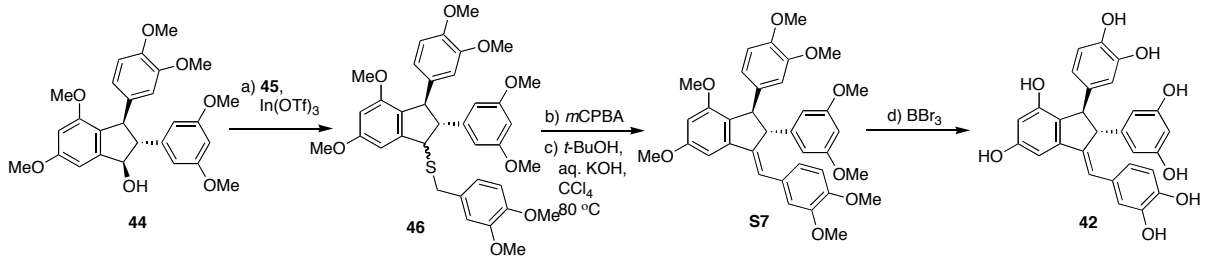
**S6**: $R_f$ = 0.51 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2960, 2919, 2850, 1595, 1463, 1426, 1261, 1117, 1094, 1027 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.7 Hz, 2 H), 7.09 (s, 1 H), 6.82 (d, *J* = 1.8 Hz, 1 H), 6.73 (d, *J* = 8.7 Hz, 2 H), 6.69 (s, 1 H), 6.67 (d, *J* = 1.8 Hz, 1 H), 6.64 (d, *J* = 1.8 Hz, 1 H), 6.61 (d, *J* = 2.1 Hz, 1 H), 6.41 (d, *J* = 2.1 Hz, 2 H), 6.30 (d, *J* = 2.1 Hz, 1 H), 6.28 (t, *J* = 2.1 Hz, 1 H), 4.31 (app s, 1 H), 4.28 (app s, 1 H), 3.91 (s, 3 H), 3.80 (s, 3 H), 3.75 (s, 3 H), 3.73 (s, 3 H), 3.72 (s, 6 H), 3.65 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ161.9, 161.4, 158.9,

157.9, 149.1, 148.1, 147.7, 145.6, 142.9, 138.9, 130.4, 130.1, 127.2, 122.8, 119.1, 114.2, 111.6, 110.9, 105.8, 99.6, 98.1, 95.4, 59.5, 57.5, 56.2, 56.0, 55.6; HRMS (FAB) calcd for $C_{35}H_{37}O_7^+$ [M+H$^+$] 569.2539, found 569.2520.

**41**: $R_f$ = 0.03 (silica gel, $CH_2Cl_2$/MeOH, 9:1); IR (film) $\nu_{max}$ 3394, 2956, 2917, 2849, 1363, 1260; $^1$H NMR (300 MHz, acetone-$d_6$) δ 7.22 (d, *J* = 8.7 Hz, 2 H), 7.04 (s, 1 H), 6.79 (d, *J* = 2.1 Hz, 1 H), 6.69 (d, *J* = 8.7 Hz, 2 H), 6.67 (d, *J* = 8 Hz, 1 H), 6.53 (d, *J* = 1.8 Hz, 2 H), 6.50 (dd, *J* = 8.1, 2.4 Hz, 1 H), 6.31 (app t, *J* = 2.4 Hz, 3 H), 6.20 (t, *J* = 2.1 Hz, 1 H), 4.22 (app s, 1 H) 4.15 (app. s, 1 H); $^{13}$C NMR (75 MHz, acetone-$d_6$) δ 159.20, 159.16, 156.8, 156.7, 155.4, 148.6, 146.9, 145.2, 143.7, 142.2, 138.3, 130.5, 124.0, 122.4, 118.7, 115.5, 115.4, 114.3, 105.8, 103.3, 101.1, 97.9, 60.2, 57.3; HRMS (FAB) calcd for $C_{28}H_{22}O_7^+$ [M$^+$] 470.1366, found 470.1366.

**Synthesis of Natural Product-Like Compound 42.** This compound was synthesized from intermediate **44** (prepared in the above sequence) exactly as described above for ampelopsin D (**5**) and paucifloral F (**10**) except for the step incorporating the sulfide fragment and the final deprotection, so only these procedures are defined specifically below. The synthesis of sulfide **45** is also described, along with physical data for the starting material (i.e. **44**).

***Scheme S4***. Synthesis of natural product-like compound **42**.[a]




[a]Reagents and conditions: (a) In(OTf)$_3$ (1.0 equiv), **45** (2.6 equiv), 25 °C, 90 min, 85%, 100% based on recovered **44**; (b) *m*CPBA (3.0 equiv), $NaHCO_3$ (10 equiv), $CH_2Cl_2$, 0 °C, 15 min, 94%; (c) *t*-BuOH/$H_2O$/$CCl_4$ (5/1/5), KOH (powder, 20 equiv), 80 °C, 12 h, 55%; (d) $BBr_3$ (1.0 M in $CH_2Cl_2$, 12 equiv), $CH_2Cl_2$, 25 °C, 6 h, 82%.

**44:** $R_f$ = 0.24 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3495, 3000, 2937, 2937, 1594, 1513, 1461, 1201, 1147, 1045, 1027, 729 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 6.69 (d, *J* = 8.1 Hz, 1 H), 6.64 (d, *J* = 1.8 Hz, 1 H), 6.57 (d, *J* = 1.8 Hz, 1 H), 6.41 (d, *J* = 2.1 Hz, 1 H), 6.33 (t, *J* = 2.1 Hz, 1 H), 6.31 (d, *J* = 2.1 Hz, 2 H), 5.18 (t, *J* = 6.6 Hz, 1 H), 4.23 (d, *J* = 7.2 Hz, 1 H), 3.85 (s, 3 H), 3.83 (s, 3 H), 3.72 (s, 6 H), 3.55 (s, 3 H), 3.13 (t, *J* = 6.9 Hz, 1 H), 2.25 (d, *J* = 6.6 Hz, 1 H),; $^{13}$C NMR (75 MHz, $CDCl_3$) δ 162.0, 161.2, 157.5, 148.9, 147.6, 146.6, 144.6, 137.3, 123.5, 119.8, 111.4, 111.0, 107.5, 106.3, 100.1, 99.8, 99.0, 82.4, 67.8, 56.2, 56.0, 55.7 (2 C), 54.3; HRMS (FAB) calcd for $C_{27}H_{30}O_7^+$ [M$^+$] 466.1992, found 466.1983.

**3,4-dimethoxytoluenethiol (45)**: $NaBH_4$ (0.455 g, 12.0 mmol, 1.95 equiv) was added slowly to a solution of 3,4-dimethoxybenzaldehyde (1.00 g, 6.15 mmol, 1.0 equiv) in MeOH (10 mL) at 0 °C. After 30 min of stirring at 0 °C, the reaction contents were quenched by the slow addition of water (10 mL), poured into water (10 mL), and extracted with EtOAc (3 × 15 mL). The combined organic layers were then dried ($MgSO_4$) and concentrated to afford desired alcohol intermediate (1.00 g, 99% yield) as a colorless liquid. Moving forward without any additional purification, this intermediate (1.00 g, 5.95 mmol, 1.0 equiv) was dissolved in water/acetone (1:1, 15 mL). Thiourea (0.910 g, 12.0 mmol, 2.0 equiv) was then added at 25 °C, the solution was acidified by addition of 5 N HCl (7 mL), and the resultant mixture was stirred at 25 °C for 12 h. Upon completion, the contents were poured into water and extracted with EtOAc (3 × 15 mL) to remove excess thiourea. Following separation of the aqueous layer, it was brought to an alkaline pH by the addition of crushed NaOH (~1 g), transferred to a sealed tube, and heated at 100 °C for 3 h. Upon completion, the contents were cooled to 25 °C and acidified with concentrated HCl (~2

mL), poured into water (10 mL) and extracted with EtOAc (3 × 15 mL). The combined organic layers were then washed with water (15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated to give **45** (1.06 g, 97%) as a colorless oil which was used without further purification. **45**: $R_f$ = 0.57 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3000, 2934, 2834, 1514, 1464, 1263, 1027 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.87 (s, 1 H), 6.86 (app d, *J* = 8.1 Hz, 1 H), 6.80 (d, *J* = 8.1 Hz, 1 H), 3.89 (s, 3 H), 3.72 (d, *J* = 7.2 Hz, 2 H), 1.76 (t, *J* = 7.2 Hz, 1 H), $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 149.3, 148.3, 133.9, 120.4, 111.7, 111.6, 56.0, 55.9, 28.9. HRMS (FAB) calcd for $C_9H_{12}O_2S^+$ [$M^+$] 184.0558, found 184.0567.

**Sulfide 46**: To a neat mixture of **44** (0.100 g, 0.214 mmol, 1.0 equiv) and $In(OTf)_3$ (0.120 g, 0.214 mmol, 1.0 equiv) at 25 °C was added thiol **45** (0.10 mL, 0.617 mmol, 2.6 equiv) in a single portion. The resultant viscous red mixture was protected from light and stirred for 90 min at 25 °C. Upon completion, the reaction contents were dissolved in EtOAc (2.0 mL), quenched with saturated aqueous $NaHCO_3$ (15 mL), filtered through Celite, and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with water (15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated. The resultant yellow solid was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:9→1:1) to give recovered **44** (0.150 g) along with sulfide **46** (0.118 g, 87% yield, 100% yield based on recovered s.m.) as a white amorphous solid. **46**: $R_f$ = 0.39 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2997, 2935, 2835, 1595, 1514, 1463, 1261, 1150 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$, 3:2 mixture of diastereomers) major diastereomer δ 6.72 (d, *J* = 1.8 Hz, 1 H), 6.70 (d, *J* = 9.6 Hz, 1H), 6.68 (d, *J* = 8.1 Hz, 1 H), 6.64 (d, *J* = 2.1 Hz, 1 H), 6.55 (dd, *J* = 9.6, 2.8 Hz, 1 H) 6.54 (dd, *J* = 8.1, 1.5 Hz, 1 H), 6.46 (d, *J* = 2.1 Hz, 1 H), 6.42 (d, *J* = 2.1 Hz, 2 H), 6.35 (t, *J* = 2.1 Hz, 1 H), 6.32 (d, *J* = 2.1 Hz, 2 H), 4.27 (d, *J* = 6.0 Hz, 2 H), 3.84 (s, 3 H), 3.84 (s, 3 H), 3.83 (s, 3 H), 3.76 (s, 3 H), 3.73 (s, 3 H), 3.72 (s, 6 H), 3.63 (m, 2 H), 3.55 (s, 3 H), 3.38 (app t, *J* = 6.0 Hz, 1 H); $^1H$ NMR (300 MHz, $CDCl_3$, 3:2 mixture of diastereomers) minor diastereomer δ 6.73 (d, *J* = 1.8 Hz, 1 H), 6.69 (d, *J* = 7 Hz, 1H), 6.69 (d, *J* = 2.1 Hz, 1 H), 6.63 (d, *J* = 2.1 Hz, 1 H), 6.62 (dd, *J* = 7.1, 2.1 Hz, 1 H), 6.56 (dd, *J* = 8.1, 1.8 Hz, 1 H), 6.56 (d, *J* = 8.1 Hz, 1 H), 6.35 (d, *J* = 2.1 Hz, 2 H), 6.34 (t, *J* = 3.0 Hz, 1 H), 6.24 (d, *J* = 3.0 Hz, 1 H), 4.59 (d, *J* = 6.0 Hz, 1 H), 4.49 (d, *J* = 6.0 Hz, 1 H), 3.58 (app t, *J* = 9.0 Hz, 1 H), 3.83 (s, 3 H), 3.82 (s, 3 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 3.73 (s, 6 H), 3.72 (s, 3 H), 3.56 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$, 3:2 mixture of diastereomers) δ 159.5, 159.2, 158.8, 158.3, 155.0, 146.9, 146.8, 146.4, 145.9, 145.3, 145.1, 143.9, 143.2, 141.3, 135.3, 134.3, 128.8, 128.7, 122.3, 122.0, 119.1. 117.4, 117.0, 109.9, 108.7, 108.6, 108.5, 105.4, 103.7, 98.8, 98.4, 96.9, 96.5, 64.1, 59.6, 54.8, 53.8, 53.7, 53.4, 52.3, 50.7, 34.6, 33.8; HRMS (FAB) calcd for $C_{36}H_{40}O_8S^+$ [$M^+$] 632.2444, found 632.2441.

**S7**: $R_f$ = 0.50 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2952, 2923, 2851, 1732, 1593, 1514, 1463, 1261, 1151 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.11 (s, 1 H), 6.87 (dd, *J* = 8.4, 1.6 Hz, 1 H), 6.83 (d, *J* = 1.6 Hz, 1 H), 6.76 (d, *J* = 1.6 Hz, 1 H), 6.71 (d, *J* = 8.4 Hz, 1 H), 6.63 (d, *J* = 8.4 Hz, 1 H), 6.68 (d, *J* = 2.0 Hz, 1 H), 6.64 (dd, *J* = 8.2, 2.0 Hz, 1 H), 6.43 (d, *J* = 2.4 Hz, 2 H), 6.31 (d, *J* = 2.0 Hz, 1 H), 6.28 (t, *J* = 2.4 Hz, 1 H), 4.32 (app s, 1 H), 4.29 (app s, 1 H), 3.91 (s, 3 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 3.76 (s, 3 H), 3.70 (s, 6 H), 3.60 (s, 3 H), 3.54 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 161.4, 161.1, 157.4, 148.6, 148.5, 148.0, 147.6, 147.3, 145.1, 142.3, 138.4, 130.0, 126.7, 122.8, 122.2, 110.9, 110.5, 105.4, 99.2, 97.6, 949, 59.2, 57.1, 55.7, 55.5, 55.2; HRMS (FAB) calcd for $C_{36}H_{38}O_8^+$ [$M^+$] 598.2567, found 598.2573.

**Gnetulin analog (42)**. To a solution of **S7** (11.0 mg, 0.023 mmol, 1.0 equiv) in $CH_2Cl_2$ (1mL) at –78 °C was added dropwise a commercial solution of $BBr_3$ (0.330 mL, 1.0M in $CH_2Cl_2$, 0.330 mmol, 14.3 equiv). After 10 min of stirring at –78 °C, the solution was quickly warmed to 25 °C and stirred for an additional 2 h. Upon completion, the reaction mixture was quenched with water (5 mL), poured into water (10 mL), and extracted with EtOAc (3 × 10 mL). The combined

organic layers were washed with water (10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated. The resultant pale pink solid was purified by preparative TLC on $Et_3N$-deactivated plates ($CH_2Cl_2$/MeOH, 9:1) to give **42** along with a small, and inseparable, amount of its internal alkene regioisomer (7.4 mg, 83% yield) as a pale yellow oil. [Note: under the reaction conditions, almost no alkene isomerization was observed; this event occurs only upon final purification]. **42**: $R_f$ = 0.06 (silica gel, $CH_2Cl_2$/MeOH, 9:1); IR (film) $\nu_{max}$ 3416, 2919, 2847, 1630, 1384, 1105, 1064 $cm^{-1}$; $^1H$ NMR (300 MHz, acetone-$d_6$) δ 6.97 (s, 1H), 6.93 (d, *J* = 2.1 Hz, 1 H), 6.78 (d, *J* = 1.8 Hz, 1 H), 6.74 (m, 1 H), 6.67 (d, *J* = 7.5 Hz, 1 H), 6.57 (d, *J* = 8.7 Hz, 1 H), 6.49 (dd, *J* = 8.1, 2.1 Hz, 1 H), 6.39 (d, *J* = 2.1 Hz, 1 H), 6.33 (d, *J* = 2.4 Hz, 2 H), 6.30 (d, *J* = 2.1 Hz, 1 H), 6.18 (t, *J* = 2.1 Hz, 1 H), 4.22 (s, 1 H), 4.19 (s, 1 H); $^{13}C$ NMR (75 MHz, acetone-$d_6$) δ 161.4, 160.8, 157.7, 150.7, 147.4, 147.2, 144.5, 140.6, 133.8, 132.2, 125.1, 124.0, 122.3, 120.9, 117.6 (2 C), 116.7, 108.2, 105.5, 103.4, 100.1, 62.4, 59.7; HRMS (FAB) calcd for $C_{28}H_{22}O_8^+$ [$M^+$] 486.1315, found 486.1327.

**Chloride 43**. Solid $BiCl_3$ (0.076 g, 0.240 mmol, 1.05 equiv) was added in a single portion to a solution of alcohol **33** (0.100 g, 0.229 mmol, 1.0 equiv) in $CH_2Cl_2$ (10 mL) at –78 °C. The resultant reaction mixture was then warmed slowly to –30 °C over the course of 1 h and stirred for 3 h at –30 °C. Upon completion, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (10 mL), poured into water (10 mL), and extracted with EtOAc (3 × 20 mL). The combined organic layers were then washed with water (20 mL) and brine (20 mL), dried ($MgSO_4$), and concentrated. The resultant yellow oil was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:4) to give chloride **43** (0.090 g, 86% yield) as a light yellow oil. **43**: $R_f$ = 0.58 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2924, 2853, 1727, 1608, 1596, 1514, 1490, 1463, 1428, 1332, 1305, 1251, 1203, 1179, 1146, 1095, 1066, 1035, 927, 827, 788, 699 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.08 (d, *J* = 8.7 Hz, 2 H), 6.84 (d, *J* = 9.0 Hz, 2 H), 6.64 (d, *J* = 1.8 Hz, 1 H), 6.42 (d, *J* = 2.1 Hz, 1 H), 6.30 (t, *J* = 2.4 Hz, 1 H), 6.22 (d, *J* = 2.4 Hz, 2 H), 5.27 (d, *J* = 6.0 Hz, 1 H), 4.28 (d, *J* = 6.3 Hz, 1 H), 3.87 (s, 3 H), 3.79 (s, 3 H), 3.69 (s, 6 H), 3.59 (s, 3 H), 3.56 (t, *J* = 6.6 Hz, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 161.8, 160.4, 158.7, 156.9, 146.3, 144.5, 133.6, 128.4, 123.7, 114.1, 105.6, 100.1, 98.3, 77.2, 68.4, 65.7, 56.1, 55.6, 55.4, 55.2; HRMS (FAB) calcd for $C_{26}H_{26}O_5Cl^+$ [$M^+$] 454.1547, found 454.1554.

**Sulfide 47**. 4-methoxytoluene-α-thiol (**34**, 0.014 mL, 0.100 mmol, 3.0 equiv) and $In(OTf)_3$ (0.019 g, 0.033 mmol, 1.0 equiv) were added sequentially in single portions to a solution of biaryl alcohol **27** (0.015 g, 0.033 mmol, 1.0 equiv) in $CH_2Cl_2$ (0.5 mL) at –50 °C. The resultant mixture was then warmed to –10 °C over the course of 5 min with constant stirring. Upon completion, the reaction contents were quenched with saturated aqueous $NaHCO_3$ (2 mL), poured into water (2 mL), and extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. The resultant yellow solid was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:9→1:1) to give **47** (0.018 g, 96% yield) as a white amorphous solid. **47**: $R_f$ = 0.63 (silica gel, EtOAc/hexanes, 1:2); IR (film) $\nu_{max}$ 3000, 2935, 2835, 1597, 1511, 1250, 1154 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.4 Hz, 2 H), 7.21 (d, *J* = 15.9 Hz, 1 H), 7.20 (d, *J* = 8.4 Hz, 2 H), 6.85 (d, *J* = 8.4 Hz, 2 H), 6.78 (d, *J* = 8.4 Hz, 2 H), 6.75 (d, *J* = 15.9 Hz, 1 H), 6.69 (d, *J* = 2.4 Hz, 1 H), 6.65 (dd, *J* = 2.1, 0.6 Hz, 2 H), 6.38 (d, *J* = 2.4 Hz, 1 H), 6.28 (t, *J* = 2.1 Hz, 1 H), 5.70 (br s, 1 H), 3.84 (s, 3 H), 3.82 (s, 3 H), 3.76 (s, 3 H), 3.71 (s, 6 H), 3.69 (s, 3 H), 3.68 (s, 2H); $^{13}C$ NMR (75 MHz, $CDCl_3$) 160.9, 159.8, 159.7, 159.0, 144.8, 139.5, 130.9, 130.8, 130.5, 129.7, 128.3, 126.1, 121.7, 114.4, 114.2, 114.1, 106.8, 103.2, 98.6, 98.4, 56.2, 55.7, 55.7 (4 C), 37.2; HRMS (FAB) calcd for $C_{34}H_{36}O_6S^+$ [$M^+$] 572.2233, found 572.2225.

**Ketone 49**. To a solution of permethylated paucifloral F (**48**, 0.150 g, 0.345 mmol, 1.0 equiv) in THF (20 mL) at –78 °C was added a solution of KHMDS (0.759 mL, 0.5 M in toluene

0.380 mmol, 1.1 equiv) in a single portion. The resultant bright yellow reaction mixture was then warmed slowly to 25 °C over the course of 3 h and stirred for 12 h at 25 °C. Upon completion, the reaction mixture was quenched with water (15 mL), poured into water (15 mL), and extracted with EtOAc (3 × 25 mL). The combined organic layers were washed with brine (15 mL), dried ($MgSO_4$), and concentrated. The resultant dark purple oil was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:3) to give ketone **49** (0.123 g, 82% yield) as light yellow oil. **49**: $R_f$ = 0.43 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3002, 2938, 2837, 1717, 1610, 1512, 1496, 1463, 1430, 1358, 1309, 1249, 1204, 1180, 1154, 1066, 1039, 965, 934, 834, 807, 791, 736, 702 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.99 (d, *J* = 1.8 Hz, 1 H), 6.92 (d, *J* = 9.0 Hz, 2 H), 6.74 (d, *J* = 2.1 Hz, 1 H), 6.57 (d, *J* = 9.0 Hz, 2 H), 6.07 (t, *J* = 2.1 Hz, 1 H), 5.82 (br s, 2 H), 4.62 (s, 1 H), 3.91 (s, 3 H), 3.67 (s, 3 H), 3.64 (s, 3 H), 3.55 (s, 6 H), 2.99 (s, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 206.9, 161.9, 159.8, 158.7, 158.3, 141.6, 137.3, 135.5, 132.3, 128.1, 112.8, 107.4, 107.2, 98.5, 96.8, 85.5, 77.2, 56.6, 55.8, 55.7, 55.2; HRMS (MALDI-FTMS) calcd for $C_{26}H_{25}O_6^+$ [$M^+$] 433.1651, found 433.1667.

**Monobrominated intermediate 55.** Solid NBS (3.2 mg, 0.018 mmol, 1.0 equiv) was added in a single portion to a solution of permethylated quadrangularin A (**54**, 10.0 mg, 0.018 mmol, 1.0 equiv) in THF (5 mL) at –78 ºC. The resultant solution was stirred for 5 min at –78 ºC and then was slowly warmed to 25 ºC over the course of 3 h. Upon completion, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (5 mL), poured into water (5 mL), and extracted with EtOAc (3 × 5 mL). The combined organic layers were then washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. The resultant brown residue was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to afford bromide **55** (8.0 mg, 72%) as a light yellow oil. **55**: $R_f$ = 0.50 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2934, 1592, 1511, 1460, 1330, 1252, 1204, 1177, 1157, 1034, 829, 732 $cm^{-1}$; $^1H$ NMR (300 MHZ, $CDCl_3$): 8.07 (s, 1 H), 7.16 (d, *J* = 8.7 Hz, 2 H), 7.05 (d, *J* = 8.7 Hz, 2 H), 6.75 (d, *J* = 3.9 Hz, 2 H), 6.72 (d, *J* = 3.9 Hz, 2 H), 6.44 (d, *J* = 2.1 Hz, 2 H), 6.34 (s, 2 H), 6.31 (m, 1 H), 4.26 (s, 2 H), 3.93 (s, 3 H), 3.74 (s, 3 H), 3.74 (s, 6 H), 3.72 (s, 3 H), 3.64 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 161.0, 158.7, 157.9, 157.0, 156.0, 147.9, 142.0, 141.2, 137.0, 136.8, 130.3, 130.1, 129.8, 129.0, 128.4, 127.8, 113.7, 105.2, 98.0, 97.3, 96.3, 59.0, 56.9, 56.3, 55.9, 55.5, 55.2; HRMS (FAB) calcd for $C_{34}H_{33}BrO_6^+$ [$M^+$] 616.1461, found 616.1439.

**Dibrominated intermediate 56.** A solution of $Br_2$ (2.9 μL, 0.056 mmol, 1.0 equiv) in $CH_2Cl_2$ (0.5 mL) was added dropwise to a solution of permethylated quadrangularin A (**54**, 0.030 g, 0.056 mmol, 1.0 equiv) in $CH_2Cl_2$ (3.0 mL) at –78 ºC. The resultant solution was stirred at –78 ºC for 2 h, warmed slowly to 25 ºC over the course of 1 h, and stirred for an additional 1 h at 25 ºC. Upon completion, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (5 mL), poured into water (5 mL), and extracted with EtOAc (3 × 15 mL). The combined organic layers were then washed with water (15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated. The resultant product was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give bromide **56** (0.033 g, 83%) as a light yellow oil. **56**: $R_f$ = 0.50 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2954, 1586, 1511, 1460, 1330, 1252, 1177, 1034 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 8.08 (s, 1 H), 7.27 (d, *J* = 2.4 Hz, 1 H), 7.16 (d, *J* = 8.7 Hz, 2 H), 7.10 (d, *J* = 8.7 Hz, 2 H), 6.76 (d, *J* = 8.7 Hz, 2 H), 6.70 (d, *J* = 8.7 Hz, 2 H), 6.38 (d, *J* = 2.7 Hz, 1 H), 6.33 (d, *J* = 1.8 Hz, 2 H), 4.71 (s, 1 H), 4.15 (s, 1 H), 3.92 (s, 3 H), 3.91 (s, 3 H), 3.74 (s, 3 H), 3.72 (s, 3 H), 3.62 (s, 3 H), 3.60 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 159.6, 158.9, 157.8, 157.0, 156.9, 156.0, 146.1, 142.2, 141.4, 136.8, 130.2, 129.6, 129.2, 128.4, 113.9, 113.3, 105.3, 104.4, 98.0, 97.1, 96.5, 58.3, 56.9, 56.3, 55.5, 55.2, 55.1, 54.3; HRMS (FAB) calcd for $C_{34}H_{32}Br_2O_6^+$ [$M^+$] 694.0566, found 694.0540.

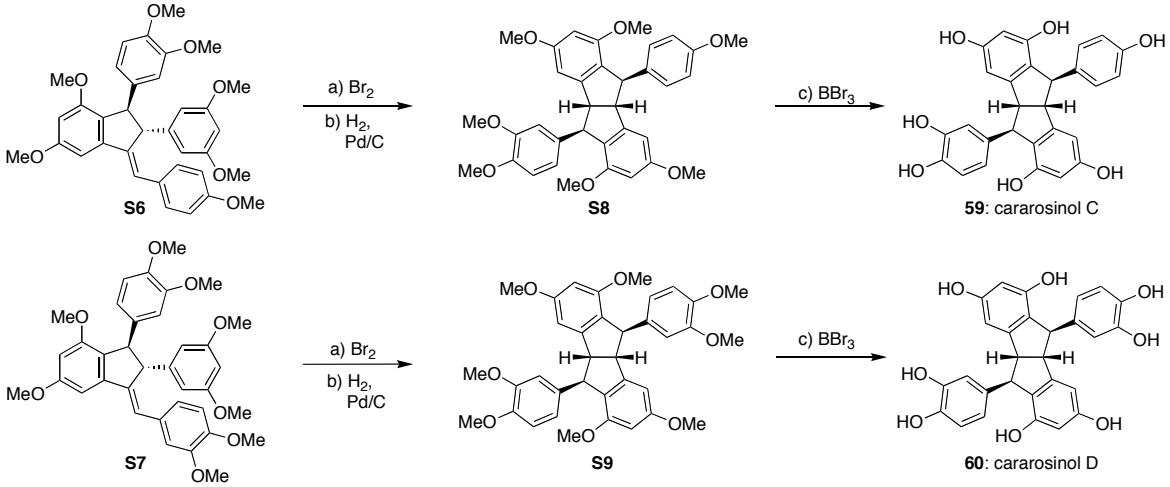
**Cascade Product 58.** A solution of $Br_2$ (8.60 μL, 0.167 mmol, 2.0 equiv) in $CH_2Cl_2$ (0.1 mL) was added dropwise to a solution of permethylated quadrangularin A (**54**, 0.045 g, 0.083 mmol, 1.0 equiv) in $CH_2Cl_2$ (4.5 mL) at –78 ºC. The resultant solution was stirred at –78 ºC for 2 h, warmed slowly to 25 ºC over the course of 1 h, and stirred for an additional 1 h at 25 ºC. Upon completion, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (3 mL), poured into water (5 mL), and extracted with EtOAc (3 × 5 mL). The combined organic layers were then washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. The resultant yellow-orange oil was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give trihalogenated adduct **58** (0.052 g, 81%) as a pale yellow oil. Alternatively, to a solution of permethylated quadrangularin A (**54**, 10 mg, 0.018 mmol, 1.0 equiv) in $CH_2Cl_2$ (0.5 mL) at 25 °C was added solid NBS (9 mg, 0.054 mmol, 3.0 equiv) in a single portion. The resultant solution was stirred at 25 °C for 5 h. Upon completion, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (2 mL), poured into water (2 mL), and extracted with EtOAc (3 × 15 mL). The combined organic layers were then washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), concentrated and purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give the desired halogenated intermediate (8.70 mg, 80% yield) as a light yellow oil. **58**: $R_f$ = 0.40 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3434, 2956, 2919, 2862, 2091, 1643, 1511, 1462, 1330, 1247, 1211, 1175, 1149, 1111, 1083, 1036, 998 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.7 Hz, 2 H), 6.80 (br d, *J* = 8.7 Hz, 6 H), 6.39 (s, 1 H), 6.27 (s, 1 H), 5.59 (s, 1 H), 5.10 (s, 1 H), 4.53 (s, 1 H), 3.91 (s, 3 H), 3.87 (s, 3 H), 3.77 (s, 6 H), 3.62 (s, 3 H), 3.55 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 158.2, 157.9, 157.5, 156.9, 155.8, 155.3, 145.9, 144.3, 136.3, 135.4, 129.7, 126.5, 126.2, 113.0, 99.5, 98.4, 97.1, 96.2, 78.1, 70.9, 56.8, 56.6, 55.6, 55.1, 51.5; HRMS (FAB) calcd for $C_{34}H_{32}Br_3O_6^+$ [M + H$^+$] 772.9746, found 772.9756.

**Pallidol (7).** Activated Pd/C (10%, 13.7 mg, 0.013 mmol, 0.5 equiv) was added in a single portion to a solution of tribromide **58** (20.0 mg, 0.026 mmol, 1.0 equiv) in MeOH (2.5 mL) at 25 ºC, and then $H_2$ gas was bubbled slowly and continuously through the solution for 24 h. Upon completion, the reaction mixture was filtered through Celite to remove insoluble particulates (using several washes of EtOAc to ensure quantitative transfer), poured into water (5 mL), and extracted with EtOAc (3 × 5 mL). The combined organic layers were then washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. The resultant colorless oil was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give permethylated pallidol (10.6 mg, 76%) as an amorphous white solid. All spectroscopic data for this synthetic material in DMSO-$d_6$ match those reported by Zaman and co-workers for the same derivative prepared from natural material.[4] Next, a portion of this newly synthesized adduct (5.0 mg, 0.009 mmol, 1.0 equiv) was dissolved in $CH_2Cl_2$ (0.5 mL) and treated with $BBr_3$ (0.108 mL, 1.0 M solution in $CH_2Cl_2$, 0.108 mmol, 12 equiv) at 0 ºC. The resultant red mixture was stirred for 4 h at 0 ºC, and then stirred for an additional 20 h at 25 ºC. Upon completion, the reaction mixture was quenched with water (5 mL), poured into water (5 mL), and extracted with EtOAc (3 × 5 mL). The combined organic layers were then washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. The resultant product was purified by preparative TLC (silica gel, $CH_2Cl_2$/MeOH, 9:1) to give pallidol (3.4 mg, 83%) as an off-white solid. **7**: $R_f$ = 0.01 (silica gel, $CH_2Cl_2$/MeOH, 9:1); IR (film) $\nu_{max}$ 3368, 2957, 2919, 2850, 1601, 1512, 1459, 1333, 1244, 1168, 1124, 1036, 985, 833 $cm^{-1}$; $^1H$ NMR (300 MHz, acetone-$d_6$) δ 8.03 (app d, *J* = 5.7 Hz, 4 H), 7.79 (s, 2 H), 6.98 (d, *J* = 8.4 Hz, 4 H), 6.70 (d, *J* = 8.4 Hz, 4 H), 6.62 (s, 2 H), 6.19 (d, *J* = 1.5 Hz, 2 H), 4.56 (br s, 2 H), 3.79 (br s, 2 H); $^{13}C$ NMR (75 MHz, acetone-$d_6$) δ 159.3, 156.3, 155.3, 150.3, 137.7, 129.0, 123.2, 115.8, 103.3, 102.5, 60.5, 53.9; HRMS (MALDI-FTMS) calcd for $C_{28}H_{22}O_6^+$ [M$^+$] 454.1414, found 454.1416. $^1H$ NMR

data for the natural product was consistent with material prepared by Sun, X.; Lin, G.; Hu, C.; Dong, J. CN 2004-100067215.

**Total Synthesis of Cararosinol C (59) and Cararosinol D (60).** These two compounds were synthesized from intermediates **S6** and **S7** exactly as described above for pallidol (**7**) with some alteration in solvent and reaction times as noted below; as such, only data for selected compounds are provided.

***Scheme S5***. Total synthesis of cararosinol C (**59**) and cararosinol D (**60**).[a]




[a] Reagents and conditions: (a) $Br_2$ (2.0 equiv), oxygen atmosphere, $CH_2Cl_2$, -78 °C, 10 min, 81%; (b) $H_2$, Pd/C (20%, 0.2 equiv), $CH_2Cl_2$/MeOH (1:1), 25 °C, 12 h, 94% for **S8**, 83% for **S9**; (c) $BBr_3$ (1.0 M in $CH_2Cl_2$, 12 equiv), $CH_2Cl_2$, -78 °C, 10 min, then warm to 25 °C, 3 h, 83%.

**S8**: $R_f$ = 0.32 (silica gel, EtOAc/hexanes, 1:1 IR (film) $\nu_{max}$ 2928, 2934, 1602, 1508, 1141 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.06 (d, *J* = 8.7 Hz, 2 H), 6.79 (d, *J* = 8.4 Hz, 2 H), 6.71 (d, *J* = 2.1 Hz, 1 H), 6.68 (app s, 1 H), 6.62 (dd, *J* = 8.1, 1.5 Hz, 2 H), 6.49 (d, *J* = 8.4 Hz, 1 H), 6.26 (app d, *J* = 1.8 Hz, 2 H), 4.59 (app d, *J* = 3.3 Hz, 1 H), 4.00 (app dd, *J* = 10.5, 6.3 Hz, 1 H), 3.85 (s, 6 H), 3.83 (s, 3 H), 3.82 (s, 3 H), 3.76 (s, 3 H), 3.62 (s, 3 H), 3.60 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) 161.7, 161.6, 157.4, 149.2, 149.1, 148.9, 138.9, 138.4, 138.3, 128.6, 128.5, 125.3, 119.3, 114.1, 111.6, 111.4, 101.0, 100.8, 100.7, 98.1, 98.0, 60.1, 56.5, 56.4, 56.3, 56.1, 56.0, 55.8, 55.6, 54.2, 53.9; HRMS (FAB) calcd for $C_{35}H_{36}O_7^+$ [$M^+$] 568.2567, found 568.2472.

**Cararosinol C (59)**: $R_f$ = 0.11 (silica gel, $CH_2Cl_2$/MeOH, 9:1); IR (film) $\nu_{max}$ 3285, 2933, 1698, 1599, 1512, 1463, 1355, 1257, 1129, 1043, 838 $cm^{-1}$; $^1H$ NMR (300 MHz, acetone-$d_6$) δ 6.95 (d, *J* = 8.4 Hz, 2 H), 6.68 (d, *J* = 8.4 Hz, 2 H), 6.67 (d, *J* = 8.7 Hz, 1 H), 6.58 (d, *J* = 2.1 Hz, 2 H), 6.57 (d, *J* = 2.0 Hz, 1 H), 6.16 (br s, 2 H), 4.53 (s, 1 H), 4.48 (s, 1 H), 3.79 (d, *J* = 6.0 Hz, 1 H), 3.76 (d, *J* = 6.6 Hz, 1 H) $^{13}C$ NMR (75 MHz, acetone-$d_6$) 159.3 (2 C), 156.3, 155.3 (2 C), 150.3 (2 C), 145.6, 143.9, 138.7, 137.8, 129.0, 123.2 (2 C), 119.5, 115.9, 115.8, 115.1, 103.3, 103.2, 102.5 (2 C), 60.6, 60.5, 54.1, 54.0; LRMS (FAB) calcd for $C_{28}H_{22}O_7Na^+$ [M+$Na^+$] 493.13, found 493.33. All spectroscopic data for this synthetic material in acetone-$d_6$ match those reported by Yang and co-workers for the same naturally-derived compound.[5]

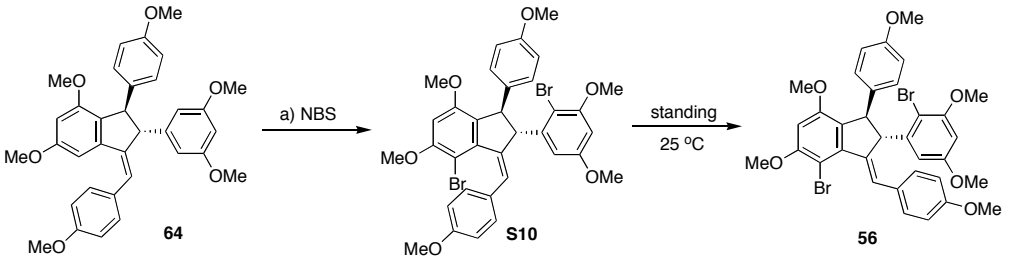
**S9**: $R_f$ = 0.31 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3003, 2935, 1595, 1508, 1460, 1265, 1141; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.74 (d, *J* = 8 Hz, 2 H), 6.72 (d, *J* = 2.0 Hz, 2 H), 6.68 (d, *J* = 1.6 Hz, 2 H), 6.63 (dd, *J* = 8 Hz, 2.0 Hz, 2 H), 6.26 (d, *J* = 1.6 Hz, 2 H), 4.58 (s, 2 H), 4.01 (s, 2 H), 3.85 (s, 6 H), 3.823 (s, 6 H), 3.818 (s, 6 H), 3.43 (s, 6 H), $^{13}C$ NMR (75 MHz, $CDCl_3$) 157.4, 149.0, 138.8, 128.6, 125.1, 119.3, 111.5, 111.4, 102.4, 100.8, 98.0, 89.2, 60.0, 56.3, 56.0, 55.7, 54.3, 50.0; HRMS (FAB) calcd for $C_{36}H_{38}O_8^+$ [$M^+$] 598.2567, found 598.2596.

**Cararosinol D (60)**: $R_f$ = 0.01 (silica gel, $CH_2Cl_2$/MeOH, 9:1); IR (film) $\nu_{max}$ 3399, 2923, 1604, 1462, 1378, 1260, 1103, 1023, 801; $^1$H NMR (300 MHz, acetone-$d_6$) δ 6.67 (d, *J* = 7.8 Hz, 2 H), 6.58 (d, *J* = 1.8 Hz, 2 H), 6.52 (dd, *J* = 7.8, 1.8 Hz, 2 H), 6.16 (d, *J* = 1.8 Hz, 2 H), 4.47 (s, 1 H), 3.76 (s, 1 H); $^{13}$C NMR (75 MHz, acetone-$d_6$) 159.2, 155.4, 150.3, 145.6, 143.9, 138.8, *123.2*, 119.4, 115.9, 115.1, 103.2, 102.5, 60.5, 54.1. All spectroscopic data for this synthetic material in acetone-$d_6$ match those reported by Yang and co-workers for the same naturally-derived compound.[5]

**Ampelopsin F (8)**. A solution of $Br_2$ (2.87 μL, 0.056 mmol, 2.0 equiv) in $CH_2Cl_2$ (0.1 mL) was added dropwise to a solution of permethylated ampelosin D (**61**, 15.0 mg, 0.028 mmol, 1.0 equiv) in $CH_2Cl_2$ (1.5 mL) at –78 ºC. The resultant solution was stirred at –78 ºC for 2 h, warmed slowly to 25 ºC over the course of 1 h, and stirred for an additional 1 h at 25 ºC. Upon completion, the reaction was quenched with saturated aqueous $NaHCO_3$ (3 mL), poured into water (3 mL), and extracted with EtOAc (3 × 5 mL). The combined organic layers were then washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. The resultant light yellow residue was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to afford tribromide **63** (11.5 mg, 53%) as a light yellow oil. Alternatively, to a solution of permethylated ampelosin D (**61**, 20.0 mg, 0.036 mmol, 1.0 equiv) in $CH_2Cl_2$ (0.5 mL) at 25 °C was added solid NBS (19.0 mg, 0.108 mmol, 3.0 equiv) in a single portion. The resultant solution was stirred at 25 °C for 5 h. Upon completion, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (2 mL), poured into water (2 mL), and extracted with EtOAc (3 × 15 mL). The combined organic layers were then washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), concentrated and purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give the desired halogenated intermediate (25 mg, 89% yield) as a light yellow oil. Next, solid AIBN (0.8 mg, 0.005 mmol, 1.0 equiv) was added in a single portion at 25 ºC to a solution of tribromide **63** (4.0 mg, 0.005 mmol, 1.0 equiv) and $(TMS)_3SiH$ (0.014 mL, 0.046 mmol, 9.0 equiv) in toluene (0.7 mL) that had been carefully degassed by bubbling argon for 20 min directly into the solvent. The resultant solution was then heated at 100 ºC for 8 h. Upon completion, the reaction contents were cooled to 25 ºC, concentrated, and purified directly by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to afford permethylated ampelopsin F (2.4 mg, 89%) as a light yellow oil. Finally, after repeating the previous reaction, this newly synthesized adduct (3.0 mg, 0.006 mmol, 1.0 equiv) was dissolved in $CH_2Cl_2$ (0.5 mL) and treated with $BBr_3$ (0.083 mL, 1.0 M solution in $CH_2Cl_2$, 0.083 mmol, 12 equiv) at 0 ºC. The resultant red mixture was stirred for 4 h at 0 ºC, and then stirred for an additional 15 h at 25 ºC. Upon completion, the reaction mixture was quenched with water (3 mL), poured into water (3 mL), and extracted with EtOAc (3 × 5 mL). The combined organic layers were then washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. The resultant orange-red residue was purified by flash column chromatography (silica gel, $CH_2Cl_2$/MeOH, 9:1) to afford ampelopsin F (2.5 mg, 90%) as an off-white solid. **8**: $R_f$ = 0.13 (silica gel, $CH_2Cl_2$/MeOH, 9:1); IR (film) $\nu_{max}$ 3361, 2953, 2920, 2847, 1598. 1496, 1471, 1330, 1240, 1165, 1121, 1035, 985, 833 cm$^{-1}$; $^1$H NMR (300 MHz, acetone-$d_6$) δ 8.04 (s, 1 H), 7.98 (s, 1 H), 7.97 (s, 1 H), 7.91 (s, 1 H), 7.83 (s, 1 H), 7.40 (s, 1 H), 7.09 (d, *J* = 8.4 Hz, 2 H), 6.78 (d, *J* = 8.4 Hz, 2 H), 6.76 (d, *J* = 8.4 Hz, 2 H), 6.57 (d, *J* = 8.7 Hz, 2 H), 6.52 (d, *J* = 1.8 Hz, 1 H), 6.44 (d, *J* = 1.8 Hz, 1 H), 6.15 (d, *J* = 2.1 Hz, 1 H), 6.07 (d, *J* = 1.8 Hz, 1 H), 4.19 (d, *J* = 0.6 Hz, 1 H), 4.13 (d, *J* = 0.6 Hz, 1 H), 3.65 (br s, 1 H), 3.36 (br s, 1 H); $^{13}$C NMR (75 MHz, acetone-$d_6$) δ 158.6, 157.8, 157.2, 156.2, 156.0, 153.1, 147.6, 147.4, 138.4, 135.5, 129.9, 129.3, 127.8, 115.6, 115.5, 113.4, 105.7, 104.2, 101.9, 101.6, 58.2, 50.5, 49.7, 47.2; HRMS (FAB) calcd for $C_{28}H_{22}O_6^+$ [$M^+$] 454.1416, found 454.1402. All spectroscopic data for this synthetic material match those reported by Niwa and co-workers for natural ampelopsin F (**8**).[2]

**Alkene 64**: $R_f$ = 0.49 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2995, 2924, 2831, 1593, 1508, 1465, 1247, 1201, 1151, 1059, 1037 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.7 Hz, 2 H), 7.06 (d, *J* = 8.7 Hz, 2 H), 6.88 (d, *J* = 8.7 Hz, 2 H), 6.80 (d, *J* = 8.7 Hz, 2 H), 6.51 (d, *J* = 1.8 Hz, 1 H), 6.39 (s, 1 H), 6.34 (d, *J* = 1.8 Hz, 2 H), 6.33 (app t, *J* = 2.1 Hz, 1 H), 6.29 (d, *J* = 2.1 Hz, 1 H), 4.32 (d, *J* = 2.7 Hz, 1 H), 3.92 (d, *J* = 2.7 Hz, 1 H), 3.83 (s, 3 H), 3.78 (s, 3 H), 3.75 (s, 6 H), 3.58 (s, 3 H), 3.55 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 160.7, 160.2, 158.6, 157.8, 157.1, 148.4, 144.9, 141.5, 137.7, 130.2, 130.0, 129.7, 128.0, 124.9, 113.6, 113.5, 105.8, 99.7, 99.5, 97.8, 63.2, 55.2, 54.9, 54.5; HRMS (FAB) calcd for $C_{34}H_{34}O_6^+$ [M – 2H$^+$] 538.2374, found 538.2355.

***Scheme S6***. Exploration into alkene geometry effects in brominative cyclizations.[a]




[a]Reagents and conditions: (a) NBS (2.0 equiv), THF, -78 °C, 30 min, 99%.

**Transient dibrominated intermediate S10.** Solid NBS (1.6 mg, 0.009 mmol, 2.0 equiv) was added in a single portion to a solution of permethylated quadrangularin A derivative **64** (5.0 mg, 0.009 mmol, 1.0 equiv) in THF (2 mL) at –78 ºC. The resultant solution was stirred for 30 min at –78 ºC. Upon completion, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (2 mL) at –78 ºC, poured into water (2 mL), and extracted with EtOAc (3 × 5 mL). The combined organic layers were then washed with water (3 mL) and brine (3 mL), dried ($MgSO_4$), and concentrated. The resultant brown residue was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to afford bromide **S10** (6.4 mg, 99%) as a light yellow oil. **S10**: $R_f$ = 0.35 (silica gel, EtOAc/hexanes, 1:2); IR (film) $\nu_{max}$ 2926, 2849, 1776, 1710, 1591, 1510, 1461, 1432, 1327, 1294, 1248, 1201, 1176, 1035 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.7 Hz, 2 H), 7.23 (d, *J* = 8.7 Hz, 2 H), 6.85 (d, *J* = 9.0 Hz, 2 H), 6.81 (d, *J* = 8.7 Hz, 2 H), 6.68 (s, 1H), 6.35 (s, 1H) 6.34 (d, *J* = 2.7 Hz, 1 H), 6.28 (d, *J* = 2.7 Hz, 1 H), 4.44 (s, 1 H), 4.27 (s, 1 H), 3.88 (s, 3 H), 3.86 (s, 3 H), 3.82 (s, 3 H), 3.76 (s, 3 H), 3.66 (s, 3 H), 3.60 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 159.3, 158.8, 158.1, 157.1, 156.6, 156.0, 145.8, 143.5, 139.9, 135.7, 131.2, 130.8, 129.5, 128.7, 128.4, 128.2, 113.9, 113.6, 113.5, 113.3, 105.3, 98.5, 96.7, 64.6, 56.9, 56.3, 55.6, 55.2, 55.1, 53.7. Upon standing at 25 ºC neat or in solution, **S10** converted quantitatively into alkene isomer **56**.

**7-Membered Ring Bromide 67.** Solid $NaHCO_3$ (3.30 g, 39.4 mmol, 10 equiv) and Dess–Martin periodinane (1.67 g, 3.94 mmol, 1.0 equiv) were added sequentially in single portions to a solution of alcohol **27** (1.72 g, 3.94 mmol, 1.0 equiv) in $CH_2Cl_2$ (30 mL) at 25 °C, and the resultant slurry was stirred for 2 h at 25 °C. Upon completion, the reaction contents were quenched with saturated aqueous $Na_2SO_3$ (10 mL) followed by stirring the resultant biphasic system vigorously for 5 min at 25 °C. The reaction contents were then poured into saturated aqueous $NaHCO_3$ (10 mL) and extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with water (30 mL) and brine (30 mL), dried ($MgSO_4$), and concentrated to afford the desired ketone (**73**, 1.66 g, 97% yield) as a white solid. **73**: $R_f$ = 0.45 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3003, 2938, 2838, 1668, 1595, 1512, 1456, 1426, 1351, 1316, 1301, 1273, 1252, 1204, 1175, 1157, 1118, 1080, 1065, 1032, 989, 971, 928, 831, 782, 765, 736, 703 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.7 Hz, 2 H), 6.99 (d, *J* = 2.4 Hz, 2 H), 6.98 (d, *J* = 16.2 Hz, 1 H), 6.84 (d, *J* = 2.1 Hz, 1 H),

6.80 (d, $J$ = 8.7 Hz, 2 H), 6.74 (d, $J$ = 15.9 Hz, 1 H), 6.63 (app t, $J$ = 2.4 Hz, 1 H), 6.42 (d, $J$ = 2.4 Hz, 1 H), 3.91 (s, 3 H), 3.79 (s, 6 H), 3.78 (s, 3 H), 3.68 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 197.3, 161.3, 160.8, 159.5, 158.4, 140.4, 137.7, 131.0, 129.6, 128.0, 123.1, 121.4, 114.0, 107.3, 105.7, 101.1, 97.7, 55.8, 55.5 (2 C), 55.3; HRMS (FAB) calcd for $C_{26}H_{26}O_6^+$ [$M^+$] 434.1729, found 434.1725. Next, a solution of $Br_2$ (0.024 mL, 0.460 mmol, 1.0 equiv) in $CH_2Cl_2$ (0.4 mL) was added dropwise to a solution of the newly-formed ketone (**73**, 0.200 g, 0.460 mmol, 1.0 equiv) in $CH_2Cl_2$ (0.2 mL) at –78 °C. The reaction mixture was then stirred for 1 h at –78 °C, warmed slowly to 0 °C over the course of 1 h, and then stirred for 3 h at 0 °C and an additional 12 h at 25 °C. Upon completion, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (2 mL), poured into water (1 mL), and extracted with EtOAc (3 × 10 mL). The combined organic layers were then washed with water (10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated to afford bromide **67** (0.118 g, 50%) as a white solid that was utilized immediately in subsequent chemistry. [Note: this product is especially light sensitive, so it must be kept away from sunlight at all times]. **67**: $R_f$ = 0.36 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2932, 2829, 1659, 1602, 1511, 1450, 911, 832 $cm^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, $J$ = 2.7 Hz, 1 H), 6.75 (d, $J$ = 8.7 Hz, 2 H), 6.57 (d, $J$ = 8.7 Hz, 2 H), 6.57 (d, $J$ = 2.7 Hz, 1 H), 5.74 (d, $J$ = 2.1 Hz, 1 H), 5.25 (d, $J$ = 5.1 Hz, 1 H), 5.12 (d, $J$ = 5.4 Hz, 1 H), 3.90 (s, 3 H), 3.83 (s, 3 H), 3.69 (s, 3 H), 3.58 (s, 3 H), 3.53 (s, 3 H).

**7-Membered Ring Acetate 70.** Solid AgOAc (0.073 g, 0.438 mmol, 3.0 equiv) was added in a single portion to a solution of bromide **67** (0.075 g, 0.146 mmol, 1.0 equiv) in neat AcOH (5 mL) at 25 °C. The reaction flask was then wrapped with aluminum foil to protect its contents from light, and stirring was continued at 25 °C for 3 h. Upon completion, the reaction mixture was neutralized with saturated aqueous $NaHCO_3$ (3 mL), poured into water (3 mL), and extracted with EtOAc (3 × 10 mL). The combined organic layers were then washed with water (10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated. The resultant yellow oily residue was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give acetate **70** (0.045 g, 62%) as a crystalline white solid. This compound was recrystallized from dichloromethane and hexanes. **70**: $R_f$ = 0.25 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3001, 2939, 2837, 1732, 1669, 1600, 1512, 1460, 1315, 1235, 1152, 1100, 1059, 1034, 963, 834, 792, 735 $cm^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 6.87 (d, $J$ = 5.4 Hz, 1 H), 6.83 (d, $J$ = 7.5 Hz, 2 H), 6.82 (d, $J$ = 2.7 Hz, 1 H), 6.63 (d, $J$ = 8.7 Hz, 2 H), 6.47 (d, $J$ = 2.4 Hz, 1 H), 6.45 (d, $J$ = 2.1 Hz, 1 H), 6.30 (d, $J$ = 2.1 Hz, 1 H), 4.81 (d, $J$ = 5.4 Hz, 1 H), 3.84 (s, 3 H), 3.81 (s, 3 H), 3.79 (s, 3 H), 3.69 (s, 3 H), 3.67 (s, 3 H), 1.95 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 194.2, 170.3, 162.2, 160.6, 159.5, 158.9, 158.0, 143.1, 141.3, 131.2, 129.3, 122.6, 115.0, 113.4, 107.8, 103.2, 101.8, 97.9, 69.7, 56.0, 55.6, 55.4, 55.1, 51.6, 21.2; HRMS (FAB) calcd for $C_{28}H_{29}O_8^+$ [M + $H^+$] 493.1862, found 493.1847.

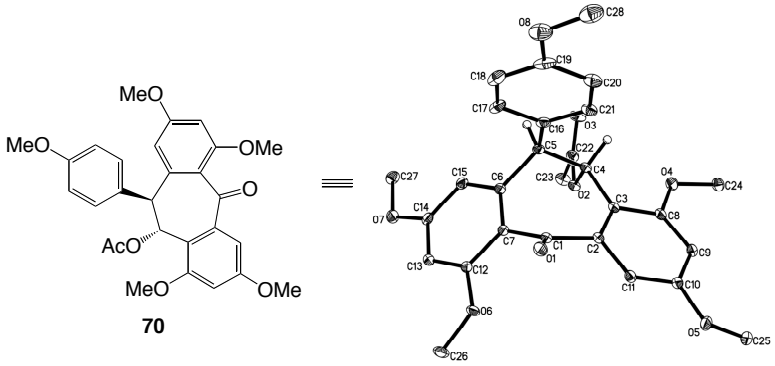
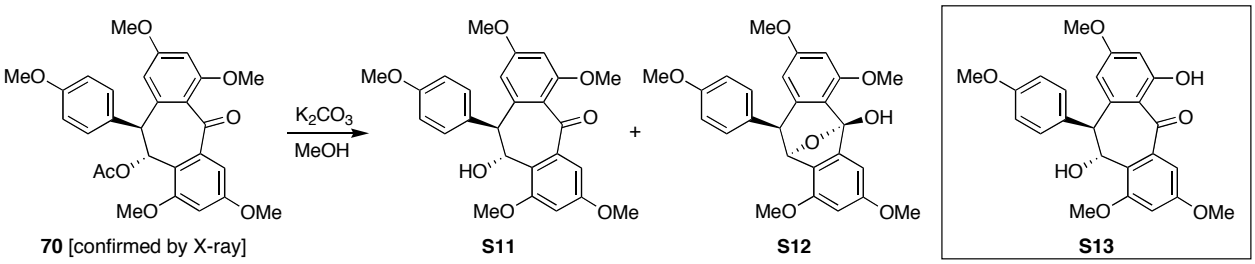



**Figure S1**. X-ray crystal structure of acetate **70**.

***Scheme S7.*** Generation of a mixture of both open, as well as lactol, forms of the acetate cleavage product of **70**.[a]




[a] Interestingly, if the phenol adjacent to the carbocyclic ketone is unprotected, the lactol is not observed under the same cleavage conditions (i.e. **S13** was formed cleanly). As such, this step highlights an element of unique reactivity instigated entirely by protecting groups.

**Permethylated Hemsleyanol E Analog S11/S12.** Finely powdered $K_2CO_3$ (0.121 g, 0.873 mmol, 10 equiv) was added in a single portion to a solution of acetate **70** (0.043 g, 0.087 mmol, 1.0 equiv) in MeOH (8 mL) at 25 °C, and the resultant slurry was stirred for 12 h at 25 °C. Upon completion, the reaction contents were neutralized with saturated aqueous $NH_4Cl$ (5 mL), poured into water (5 mL), and extracted with EtOAc (3 × 10 mL). The combined organic layers were then washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. The resultant colorless residue was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give an inseparable mixture of alcohol **S11** and lactol **S12** (2.5/1, 0.039 g, 78% combined). **S11** and **S12**: $R_f$ = 0.16 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3469, 2933, 2839, 1664, 1600, 1511, 1460, 1312, 1249, 1211, 1149, 1096, 1057, 1036, 987, 935, 833, 735 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.89 (d, *J* = 8.7 Hz, 2.8 H), 6.85 (d, *J* = 2.4 Hz, 1 H), 6.67 (d, *J* = 8.7 Hz, 2.8 H), 6.60 (d, *J* = 2.4 Hz, 1 H), 6.52 (d, *J* = 2.1 Hz, 1.8 H), 6.44 (d, *J* = 2.1 Hz, 1 H), 6.32 (d, *J* = 2.1 Hz, 0.4 H), 6.04 (d, *J* = 1.8 Hz, 0.8 H), 5.88 (d, *J* = 5.4 Hz, 1 H), 5.54 (d, *J* = 5.7 Hz, 0.4 H), 4.76 (d, *J* = 6.0 Hz, 0.4 H), 4.66 (d, *J* = 6.0 Hz, 1 H), 3.96 (s, 1.2 H), 3.87 (s, 3 H), 3.85 (s, 3 H), 3.81 (s, 3 H), 3.78 (s, 4.2 H), 3.71 (s, 1.2 H), 3.69 (s, 4.2 H), 3.58 (s, 1.2 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 194.3, 162.0, 161.6, 160.1, 159.8, 159.2, 158.7, 158.4, 157.8, 155.4, 154.3, 151.8, 141.1, 140.8, 140.4, 131.9, 131.5, 128.9, 123.3, 120.9, 119.8, 117.8, 113.5, 108.2, 107.8, 104.8, 103.5, 102.5, 97.8, 97.2, 97.0, 94.8, 79.3, 67.5, 56.1, 55.9, 55.4, 55.3, 55.2, 55.0, 54.7, 53.6, 47.8; HRMS (FAB) calcd for $C_{26}H_{27}O_7^+$ [M + $H^+$] 451.1757, found 451.1756.

**Tetramethylated Hemsleyanol E Analog S13.** Acetate **70** (0.050 g, 0.102 mmol, 1.0 equiv) was dissolved in neat AcOH (8 mL) at 25 °C, and the resultant solution was stirred for 12 h at 25 °C. Upon completion, the reaction mixture was quenched with water (5 mL), poured into water (5 mL), and extracted with EtOAc (3 × 15 mL). The combined organic layers were then washed with brine (10 mL), dried ($MgSO_4$), and concentrated to afford the desired mono-deprotected intermediate (0.045 g, 93%) as a colorless oil which was carried forward without any additional purification. Next, solid KCN (0.6 mg, 0.009 mmol, 0.1 equiv) was added in a single portion to a solution of newly-formed compound (0.045 g, 0.090 mmol, 1.0 equiv) in MeOH (8 mL) at 25 °C, and then resultant mixture was heated at 65 °C for 3 h. Upon completion, the reaction was quenched with water (5 mL), poured into water (5 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were then washed with brine (5 mL), dried ($MgSO_4$), and concentrated. The resultant light yellow product was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give alcohol **S13** (0.037 g, 89%) as a colorless oil. **S13**: $R_f$ = 0.19 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3468, 3001, 238, 2831, 1606, 1579, 1511, 1462, 1416, 1351, 1298, 1253, 1206, 1151, 1055, 1035, 935, 841, 796, 726 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 13.70 (s, 1 H), 6.95 (d, *J* = 2.4 Hz, 1 H), 6.71 (d, *J* = 8.7 Hz, 2 H), 6.58 (d, *J* = 8.7 Hz, 2 H), 6.42 (d, *J* = 2.7 Hz, 1 H), 6.29 (d, *J* = 2.4 Hz, 1 H), 6.27 (dd, *J* = 2.7, 0.6 Hz, 1 H), 5.76 (dd, *J* = 5.7, 2.4 Hz,

1 H), 4.88 (d, $J$ = 6.1 Hz, 1 H), 3.81 (s, 3 H), 3.77 (s, 3 H), 3.68 (s, 3 H), 3.45 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 198.2, 166.6, 165.0, 160.0, 157.9, 156.8, 143.6, 141.0, 132.7, 129.5, 121.5, 115.0, 113.2, 112.6, 105.7, 102.2, 100.0, 67.0, 57.3, 55.9, 55.4, 55.3, 55.2, 55.1; HRMS (FAB) calcd for $C_{25}H_{24}O_7^+$ [$M^+$] 436.1522, found 436.1544.

**Diptoindonesin D Analog 71.** Dess–Martin periodinane (0.049 g, 0.115 mmol, 1.0 equiv) and solid $NaHCO_3$ (0.097 g, 1.15 mmol, 10 equiv) were added sequentially in single portions to a solution of alcohol **S10** and lactol **S11** (0.052 g, 0.115 mmol, 1.0 equiv) in $CH_2Cl_2$ (10 mL) at 25 °C, and the resultant slurry was stirred for 1.5 h at 25 °C. Upon completion, the reaction contents were quenched with saturated aqueous $Na_2SO_3$ (3 mL) followed by stirring the resultant biphasic system vigorously for 5 min at 25 °C, poured into water (5 mL), and extracted with EtOAc (3 × 15 mL). The combined organic layers were then washed with saturated aqueous $NaHCO_3$ (3 × 10 mL), dried ($MgSO_4$), and concentrated to give the desired permethylated diptoindonesin A analog **71** (0.051 g, 99%) as a light yellow oil. **71**: $R_f$ = 0.33 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3008, 2939, 2837, 1668, 1592, 1512, 1462, 1327, 1295, 1250, 1211, 1157, 1070, 1023, 974, 928, 832, 732 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 6.98 (d, $J$ = 2.4 Hz, 1 H), 6.91 (d, $J$ = 8.1 Hz, 2 H), 6.69 (d, $J$ = 9.2 Hz, 2 H), 6.64 (d, $J$ = 2.4 Hz, 1 H), 6.52 (d, $J$ = 2.1 Hz, 1 H), 6.47 (d, $J$ = 2.1 Hz, 1 H), 5.18 (s, 1 H), 3.90 (s, 3 H), 3.86 (s, 3 H), 3.85 (s, 3 H), 3.81 (s, 3 H), 3.70 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 195.3, 192.5, 163.0, 162.6, 161.1, 159.9, 158.4, 141.9, 136.7, 129.9, 129.4, 122.5, 116.8, 113.8, 105.8, 105.4, 104.0, 98.8, 66.7, 56.8, 56.1, 55.7, 55.5, 55.1; HRMS (FAB) calcd for $C_{26}H_{25}O_7^+$ [M + $H^+$] 449.1556, found 449.1619.

**Alkene 72.** To a solution of bromide **67** (0.119 g, 0.231 mmol, 1.0 equiv) in THF (10 mL) at 25 °C was sequentially added finely powdered KOH (0.129 g, 2.31 mmol, 10.0 equiv) and 18-crown-6 (0.006 g, 0.023 mmol, 0.1 equiv) in single portions; the reaction was then wrapped in aluminum foil to protect the contents from light. The resultant mixture was heated at 40 °C for 12 h. Upon completion, the reaction contents were quenched with saturated aqueous $NH_4Cl$ (15 mL), poured into water (10 mL), and extracted with EtOAc (3 × 20 mL). The combined organic layers were then washed with water (10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated. The resultant yellow oily residue was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give alkene **72** (0.092 g, 92%) as an amorphous white solid. **72**: $R_f$ = 0.39 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2996, 2932, 1669, 1593, 1565, 1508, 1454, 1328 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, $J$ = 8.8 Hz, 2 H), 6.95 (s, 1 H), 6.84 (d, $J$ = 8.7 Hz, 2 H), 6.83 (d, $J$ = 2.1 Hz, 1 H), 6.50 (app d, $J$ = 1.8 Hz, 2 H), 6.46 (d, $J$ = 1.5 Hz, 1 H), 3.90 (s, 3 H), 3.86 (s, 3 H), 3.85 (s, 3 H), 3.82 (s, 3 H), 3.47 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 195.2, 161.4, 161.1, 158.7, 158.6, 157.6, 147.4, 140.0, 137.5, 137.2, 127.5, 116.6, 113.2, 103.6, 101.9, 100.3, 98.7, 56.1, 55.8, 55.7, 55.5, 55.3; HRMS (FAB) calcd for $C_{26}H_{25}O_6^+$ [M + $H^+$] 433.1651, found 433.1659.

**Cyclized alcohol 74**. A solution of ketone **73** (0.500 g, 1.15 mmol, 1.0 equiv) in MeCN (10 mL) at 25 °C was treated sequentially with an aqueous solution of the disodium salt of EDTA (6 mL, 0.0004 M), excess 1,1,1-trifluoroacetone (2 mL), Oxone® (3.50 g, 5.75 mmol, 5.0 equiv), and solid $NaHCO_3$ (0.774 g, 11.5 mmol, 8.0 equiv). The resulting suspension was allowed to stir at 25 °C for 3 h. Upon completion, the reaction mixture was quenched with saturated aqueous $NH_4Cl$ (15 mL), poured into water (30 mL), and extracted with $Et_2O$ (3 × 30 mL). The combined organic layers were then washed with water (10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated. The resultant red oily residue was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give **74** (0.176 g, 34%) as a pale yellow solid. [Note: this compound exists as an equilibrium mixture of both alcohol and lactol forms in a 6:1 ratio, respectively]. **74**: $R_f$ = 0.14 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3442, 2996, 2955, 2939, 1666, 1651, 1650,

1600, 1511, 1454, 1153 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 2.4 Hz, 1 H), 6.72 (d, *J* = 8.8 Hz, 2 H), 6.61 (d, *J* = 8.0 Hz, 2 H), 6.54 (d, *J* = 2.8 Hz, 1 H), 6.35 (d, *J* = 2.0 Hz, 1 H), 5.79 (d, *J* = 1.8 Hz, 1 H), 4.99 (dd, *J* = 6.3, 1.8 Hz, 1 H), 4.87 (d, *J* = 6.3 Hz, 1 H), 3.88 (s, 3 H), 3.82 (s, 3 H), 3.71 (s, 3 H), 3.59 (s, 3 H), 3.52 (s, 3 H), 2.37 (d, *J* = 2.0 Hz, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 195.7, 161.5, 159.2, 158.1, 157.8, 141.5, 141.1, 133.6, 129.2, 121.8, 119.9, 113.2, 112.8, 104.1, 103.4, 98.7, 78.4, 56.1, 56.0, 55.5, 55.4, 55.1, 49.6; HRMS (FAB) calcd for $C_{26}H_{27}O_7^+$ [M + $H^+$] 451.1757, found 451.1768.

**Alkene 76**. To a solution of alcohol **74** (10.0 mg, 0.222 mmol, 1.0 equiv) in toluene (3 mL) was added solid *p*-TsOH (0.422 g, 2.22 mmol, 10.0 equiv) as a single portion and the resultant mixture was heated at 65 °C for 12 h. Upon completion, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (10 mL), poured into water (10 mL), and extracted with EtOAc (3 × 10 mL). The combined organic layers were then washed with water (10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated to afford pure alkene **76** (9.6 mg, 96%) as a white solid. **76:** $R_f$ = 0.37 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2927, 2908, 1682, 1651, 1594, 1594, 1559, 1505, 1454 $cm^{-1}$; $^1H$ NMR (300 MHz, $CCl_3$) δ 7.39 (d, *J* = 8.4 Hz, 2 H), 7.37 (s, 1 H), 6.92 (d, *J* = 8.3 Hz, 2 H), 6.84 (d, *J* = 2.0 Hz, 1 H), 6.58 (d, *J* = 2.0 Hz, 1 H), 6.54 (d, *J* = 2.0 Hz, 1 H), 6.28 (d, *J* = 2.0 Hz, 1 H), 3.90 (app s, 9 H), 3.85 (s, 3 H), 3.64 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 195.3, 160.9, 160.5, 159.0, 157.8, 157.3, 144.7, 138.9, 138.6, 136.7, 130.4, 123.5, 117.6, 116.3, 113.6, 105.0, 100.9, 99.9, 99.2, 56.3, 56.0, 55.7, 55.3 (2 C); HRMS (FAB) calcd for $C_{26}H_{25}O_6^+$ [M + $H^+$] 433.1651, found 433.1645.

**Permethylated diptoindonesin D (75).** Dess–Martin periodinane (0.113 g, 0.266 mmol, 1.2 equiv) and solid $NaHCO_3$ (0.093 g, 1.11 mmol, 5.0 equiv) were added sequentially in single portions to a solution of alcohol **74** (0.100 g, 0.222 mmol, 1.0 equiv) in $CH_2Cl_2$ (10 mL) at 25 °C, and the resultant slurry was stirred for 1 h at 25 °C. Upon completion, the reaction contents were quenched with saturated aqueous $Na_2SO_3$ (3 mL) followed by stirring the resultant biphasic system vigorously for 5 min at 25 °C, poured into water (5 mL), and extracted with EtOAc (3 × 15 mL). The combined organic layers were then washed with saturated aqueous $NaHCO_3$ (3 × 10 mL), dried ($MgSO_4$), and concentrated to give permethylated diptoindonesin D (**75**, 0.095 g, 96%) as a light yellow oil. **75**: $R_f$ = 0.25 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2932, 2834, 1676, 1650, 1593, 1460, 1508 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 2.4 Hz, 1 H), 6.81 (d, *J* = 8.8 Hz, 2 H), 6.67 (d, *J* = 8.8 Hz, 2 H), 6.66 (d, *J* = 2.4 Hz, 1 H), 6.60 (d, *J* = 2.4 Hz, 1 H), 6.58 (d, *J* = 2.4 Hz, 1 H), 5.97 (s, 1 H), 3.89 (s, 3 H), 3.85 (app s, 6 H), 3.81 (s, 3 H), 3.69 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 196.4, 193.7, 162.9, 160.6, 159.6, 158.4, 157.9, 146.2, 137.0, 129.9, 128.7, 120.8, 113.9, 111.8, 106.2, 103.6, 103.3, 101.0, 56.7, 56.2, 55.7, 55.6, 55.1, 54.9 ; LRMS (APCI+) calcd for $C_{21}H_{16}O_6^+$ [M + $H^+$] 449, found 449.

**Cyclized product 82**. Dess–Martin periodinane (0.109 g, 0.258 mmol, 1.2 equiv) and solid $NaHCO_3$ (0.180 g, 2.15 mmol, 10 equiv) were added sequentially in single portions to a solution of alcohol **29** (0.100 g, 0.215 mmol, 1.0 equiv) in $CH_2Cl_2$ (10 mL) at 25 °C, and the resultant slurry was stirred for 1 h at 25 °C. Upon completion, the reaction contents were quenched with saturated aqueous $Na_2SO_3$ (3 mL) followed by stirring the resultant biphasic system vigorously for 5 min at 25 °C, poured into water (5 mL), and extracted with EtOAc (3 × 15 mL). The combined organic layers were then washed with saturated aqueous $NaHCO_3$ (3 × 10 mL), dried ($MgSO_4$), and concentrated to give the desired ketone (0.098 g, 96%) as a white solid. $R_f$ = 0.46 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2923, 2948, 2857, 1647, 1559, 1505, 1454 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.99 (d, *J* = 2.4 Hz, 1 H), 6.93 (m, 2 H), 6.80 (d, *J* = 1.8 Hz, 1 H), 6.78 (d, *J* = 1.8 Hz, 1 H), 6.61 (m, 1 H), 6.63 (app t, *J* = 2.4 Hz, 1 H), 6.42 (d, *J* = 1.8 Hz, 1 H), 3.91 (s, 3 H), 3.86 (s, 3 H), 3.83 (s, 3 H), 3.79 (s, 6 H), 3.69 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 197.1, 161.2,

160.7, 158.3, 149.1, 148.9, 140.4, 137.5, 131.1, 129.9, 123.3, 121.2, 120.0, 111.0, 109.1, 107.1, 105.4, 101.1, 97.7, 55.7 (2 C), 55.6 (2 C), 55.4 (2 C). Next, *p*-TsOH (0.082 g, 0.860 mmol, 2.0 equiv) was added in a single portion to a solution of the newly-generated ketone (0.200 g, 0.43 mmol, 1.0 equiv) in toluene (10 mL) at 25 °C and the resultant mixture was heated at 60 °C for 48 h. Upon completion, the reaction contents were quenched with saturated aqueous $NaHCO_3$ (20 mL), poured into water (20 mL), and extracted with EtOAc (3 × 20 mL). The combined organic layers were then washed with water (15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated. The resultant brown oily residue was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give cyclized ketone **82** (0.454 g, 85%) as a white crystalline solid. This compound was recrystallized from hexanes and chloroform. **82**: $R_f$ = 0.24 (silica gel, EtOAc/hexanes, 1:1); m.p. = 80–82 °C; IR (film) $\nu_{max}$ 3002, 2930, 1653, 1600, 1514, 1458, 1340, 1207, 1138 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.15 (d, *J* = 2.4 Hz, 1 H), 6.60 (d, *J* = 8.4 Hz, 2 H), 6.53 (d, *J* = 2.9 Hz, 1 H), 6.41 (dd, *J* = 8.1, 1.8 Hz, 1 H), 6.28 (d, *J* = 2.1 Hz, 1 H), 5.71 (d, *J* = 2.1 Hz, 1 H), 4.64 (dd, *J* = 6.9, 2.7 Hz, 1 H), 3.89 (s, 3 H), 3.79 (s, 3 H), 3.78 (s, 3 H), 3.58 (app s, 6 H), 3.54 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 196.7, 161.8, 158.8, 158.6, 157.8, 148.0, 146.7, 141.1, 138.9, 136.3, 125.1, 123.4, 119.8, 111.1, 110.3, 105.9, 103.9, 103.2, 97.1, 55.9, 55.6, 55.4, 55.3, 43.1, 40.9; HRMS (FAB) calcd for $C_{27}H_{29}O_7^+$ [M + $H^+$] 465.1913, found 465.1924.

**Cyclized ketone 84.** Solid *p*-TsOH (0.655 g, 3.448 mmol, 8.0 equiv) was added in a single portion to solution of the ketone derived from **29** (0.200 g, 0.431 mmol, 1.0 equiv) in toluene (10 mL) at 25 °C and the resultant was mixture heated to 60 °C for 48 h. Upon completion, the reaction contents were quenched with saturated aqueous $NaHCO_3$ (20 mL), poured into water (20 mL), and extracted with EtOAc (3 × 20 mL). The combined organic layers were then washed with water (15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated. The resultant brown oily residue was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give cyclized ketone **84** (0.454 g, 83%) as a white crystalline solid. This compound was recrystallized from hexanes and chloroform. **84**: $R_f$ = 0.36 (silica gel, EtOAc/hexanes, 1:1); m.p. = 167–168 °C; IR (film) $\nu_{max}$ 2951, 2925, 1650, 1598, 1508, 1459, 1267, 1207 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.66 (s, 1 H), 7.34 (d, *J* = 1.6 Hz, 1 H), 6.74 (d, *J* = 2.4 Hz, 1 H), 6.35 (s, 1 H), 6.26 (t, *J* = 2.0 Hz, 1 H), 5.89 (d, *J* = 2.0 Hz, 2 H), 4.56 (dd, *J* = 8.4, 3.6 Hz, 1 H), 3.99 (s, 3 H), 3.96 (s, 3 H), 3.91 (s, 3 H), 3.70 (s, 3 H), 3.63 (s, 6 H); 3.31 (dd, *J* = 12.8, 3.6 Hz, 1 H), 2.55 (dd, *J* = 12.8, 8.4 Hz, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 183.3, 160.2, 159.4, 157.1, 152.2, 148.2, 141.1, 139.3, 133.7, 127.1, 125.2, 110.4, 108.3, 107.8, 103.4, 100.2, 98.6, 56.0, 55.9, 55.7 (2 C), 55.2, 53.4, 46.0, 39.3; HRMS (FAB) calcd for $C_{27}H_{29}O_7^+$ [M + $H^+$] 465.1913, found 465.1917.

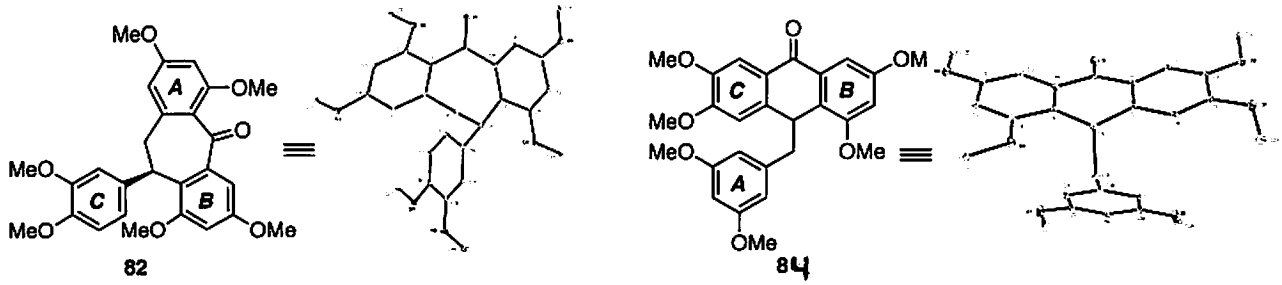



**Figure S2.** X-ray crystal structures of **82** and **84**.

**Permethylated cassigarol B (86).** Solid $LiAlH_4$ (0.041 g, 1.08 mmol, 5.0 equiv) was added in a single portion to a solution of cyclized ketone **82** (0.100 g, 0.22 mmol, 1.0 equiv) in THF (10 mL) at 0 °C. The resulting slurry was stirred at 0 °C for 1 h, then slowly warmed to 25 °C and

stirred for an additional 1 h. Upon completion, the reaction contents were quenched with 1 N HCl (10 mL) and stirred vigorously for an additional 2 h at 25 °C. Next, saturated aqueous $NaHCO_3$ (15 mL) was added, and the reaction mixture poured into water (10 mL) and extracted with EtOAc (3 × 20 mL). The combined organic layers were then washed with water (15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated. The resultant light yellow oily residue was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give permethylated cassigarol B (**97**, 0.088 g, 91%) as a white solid. Alternatively, permethylated cassigarol B could be prepared in 73% yield by the identical procedure starting from biaryl ketone **80**. Additionally, permethylated cassigarol B (**86**) could be prepared by the slow, dropwise addition of HBr (33% in HOAc, 7.8 μL, 0.043 mmol, 1.0 equiv) to a solution of alcohol **29** (0.020 g, 0.043 mmol, 1.0 equiv) in $CH_2Cl_2$ (2 mL) at –78 °C. The solution was stirred at –78 °C for 1 h, then slowly warmed to 25 °C and stirred for an additional 12 h. Upon completion, the reaction contents were quenched by the addition of saturated aqueous $NaHCO_3$ (10 mL), poured into water (10 mL), and extracted with EtOAc (3 × 20 mL). The combined organic layers were then washed with water (15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated. The resultant dark oily residue was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give permethylated cassigarol B (**86**, 0.016 g, 74%) as a white solid. Finally, permethylated cassigarol B (**86**) could also be prepared by the addition of $PBr_3$ (4.0 μL, 0.043 mmol, 1.0 equiv) to a solution of alcohol **29** (0.020 g, 0.043 mmol, 1.0 equiv) in $CH_2Cl_2$ (2 mL) at 25 °C. The resultant red solution was warmed to 40 ºC and then stirred for an additional 3 h at 40 ºC. Upon completion, the reaction mixture was quenched with water (5 mL), poured into water (5 mL), and extracted with EtOAc (3 × 5 mL). The combined organic layers were then washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. The resultant dark oily residue was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give permethylated cassigarol B (**86**, 0.012 g, 58%) as a white solid. Importantly, permethylated Cassigarol B could be prepared on large scale (up to 0.750 g) by this procedure without loss of yield. **86**: $R_f$ = 0.39 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3005, 2932, 2828, 1606, 1508, 1444, 1207, 1138 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.94 (s, 1 H), 6.87 (s, 1 H), 6.53 (d, *J* = 2.2 Hz, 1 H), 6.29 (d, *J* = 2.2 Hz, 1 H), 6.24 (d, *J* = 2.4 Hz, 1 H), 6.02 (d, *J* = 2.3 Hz, 1 H), 5.52 (s, 1 H), 4.57 (dd, *J* = 6.9, 3.5 Hz, 1 H), 3.91 (s, 3 H), 3.86 (s, 3 H), 3.85 (s, 3 H), 3.83 (s, 3 H), 3.77 (s, 3 H), 3.65 (s, 3 H), 3.14 (d, *J* = 3.4 Hz, 2 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 158.9, 158.5, 156.2, 155.9, 147.7, 147.1, 146.9, 137.3, 137.2, 134.0, 123.0, 121.4, 109.9, 109.2, 107.8, 102.1, 96.4, 96.3, 56.1, 55.5, 55.4, 55.1, 41.9, 36.4, 36.2; HRMS (FAB) calcd for $C_{27}H_{28}O_6^+$ [$M^+$] 448.1886, found 448.1882.

**Cassigarol B (77).** Permethylated cassigarol B (**86**, 15.0 mg, 0.0334 mmol, 1.0 equiv) was dissolved in $CH_2Cl_2$ (1.0 mL) and treated with $BBr_3$ (0.40 mL, 1.0 M in $CH_2Cl_2$, 0.40 mmol, 12 equiv) at –78 ºC. The resultant red solution was stirred for 1 h at –78 ºC, allowed to warm slowly to 25 ºC and then stirred for an additional 10 h at 25 ºC. Upon completion, the reaction mixture was quenched with water (5 mL), poured into water (5 mL), and extracted with EtOAc (3 × 5 mL). The combined organic layers were then washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. The resultant product was purified by preparative TLC (silica gel, $CH_2Cl_2$/MeOH, 9:1) to give cassigarol B (**77**, 10.6 mg, 87%) as an off-white solid. **77**: $R_f$ = 0.11 (silica gel, $CH_2Cl_2$/MeOH, 9:1); IR (film) $\nu_{max}$ 3300, 2945, 2927, 1682, 1600, 1454, 1328, 1296 $cm^{-1}$; $^1H$ NMR (300 MHz, DMSO-$d_6$) δ 9.13 (s, 1 H), 9.12 (s, 1 H), 8.87 (s, 1 H), 8.74 (s, 1 H), 8.56 (br s, 1 H), 8.52 (br s, 1 H), 6.67 (s, 1 H), 6.55 (s, 1 H), 6.09 (d, *J* = 2.0 Hz, 1 H), 6.04 (d, *J* = 2.0 Hz, 1 H), 6.00 (d, *J* = 2.0 Hz, 1 H), 5.70 (d, *J* = 2.0 Hz, 1 H ), 5.03 (s, 1 H), 4.18 (m, 1 H), 2.79 (m, 2 H); $^{13}C$ NMR (75 MHz, acetone-$d_6$) δ 155.5, 155.2, 153.3, 153.2, 147.9, 142.5, 142.2, 136.9, 136.0, 132.8, 120.3, 117.9, 113.4, 112.4, 108.7, 103.2, 99.6, 99.5, 41.1, 36.2, 35.4; HRMS (FAB) calcd for

$C_{21}H_{16}O_6^+$ [$M^+$] 364.0947, found 364.0964. All spectroscopic data for the free phenol form of this synthetic material in DMSO-$d_6$ match those reported by Kozawa and co-workers for the same naturally-derived compound.[6]

**Methyl ether 90**. NaH (60% dispersion in mineral oil, 0.086 g, 2.14 mmol, 2.0 equiv) was added in a single portion to a solution of alcohol **29** (0.500 g, 1.07 mmol, 1.0 equiv) in THF (15 mL) at 0 ºC. After stirring for 30 min at 0 ºC, MeI (0.33 mL, 5.35 mmol, 5.0 equiv) was added dropwise at 0 ºC. The resulting mixture was then warmed slowly to 25 ºC and stirred for an additional 4 h. Upon completion, the reaction contents were quenched with saturated aqueous $NH_4Cl$ (15 mL), poured into water (10 mL), and extracted with EtOAc (3 × 20 mL). The combined organic layers were then washed with water (10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated. The resultant oil was then triturated with hexanes (3 × 10 mL) to remove residual mineral oil, yielding **90** (0.494 g, 98%) as a pale yellow solid. **90**: $R_f$ = 0.34 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2999, 2955, 2933, 1670, 1591, 1514, 1451, 1261, 1157 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.42 (d, *J* = 16.1 Hz, 1 H), 6.86 (m, 2 H), 6.78 (app t, *J* = 2.6 Hz, 2 H), 6.74 (d, *J* = 16.1 Hz, 1 H), 6.57 (m, 2 H), 6.44 (d, *J* = 2.3 Hz, 1 H), 6.27 (app t, *J* = 2.2 Hz, 2 H), 6.10 (s, 1 H), 3.89 (s, 3 H), 3.87 (app s, 6 H), 3.85 (s, 3 H), 3.69 (s, 6 H), 3.33 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 160.5, 159.9, 159.5, 149.0, 148.7, 146.1, 139.4, 131.1, 128.4, 126.4, 120.1, 119.7, 111.0, 108.6, 104.2, 102.5, 97.9, 97.4, 75.9, 56.4, 55.9, 55.7, 55.3, 55.1 (2 C); HRMS (FAB) calcd for $C_{28}H_{32}O_7^+$ [$M^+$] 480.2148, found 480.2151.

**Alcohol 96**. A solution of $Br_2$ (10.7 μL, 0.200 mmol, 1.0 equiv) in $CH_2Cl_2$ (1.0 mL) was added dropwise to a solution of methyl ether **90** (0.100 g, 0.200 mmol, 1.0 equiv) in $CH_2Cl_2$ (5.0 mL) at –78 ºC. The resultant dark green solution was stirred at –78 ºC for 2 h, warmed slowly to 25 ºC over the course of 6 h, and stirred for an additional 6 h at 25 ºC. Upon completion, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (15 mL), poured into water (5 mL), and extracted with EtOAc (3 × 15 mL). The combined organic layers were then washed with water (10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated. The resultant crude brown oil was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give cyclized alcohol **96** (0.047 g, 52% yield) as a white solid. **96**: $R_f$ = 0.18 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 3471, 2996, 2948, 2927, 1606, 1587, 1458, 1268, 1194, 1151 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.90 (s, 1 H), 6.82 (s, 1 H), 6.67 (d, *J* = 2.1, 1 H), 6.56 (d, *J* = 2.1, 1 H), 6.34 (d, *J* = 2.1, 1 H), 6.31 (d, *J* = 2.1, 1 H), 5.10 (s, 1 H), 4.78 (m, 2 H), 3.93 (s, 3 H), 3.86 (app s, 6 H), 3.82 (s, 3 H), 3.79 (s, 3 H), 3.77 (s, 3 H), 1.79 (d, *J* = 11.4 Hz, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 159.4, 159.1, 157.2, 155.4, 148.0, 147.8, 147.4, 138.5, 134.7, 129.5, 126.1, 117.5, 115.6, 110.2, 105.8, 102.2, 97.1, 96.2, 69.4, 56.0, 55.9, 55.6, 55.5, 55.3, 45.8, 45.5; HRMS (FAB) calcd for $C_{27}H_{29}O_7^+$ [M + $H^+$] 465.1913, found 465.1928.

**Permethylated cassigarol B analog #1 (97)**. To a solution of alcohol **96** (6.5 mg, 0.014 mmol, 1.0 equiv) in $CH_2Cl_2$ (4.7 mL) at 0 °C was added $NaCNBH_3$ (0.089 mg, 1.42 mmol, 100 equiv) in a single portion to give a cloudy suspension. A solution of TFA in $CH_2Cl_2$ (0.132 mL TFA diluted with $CH_2Cl_2$ to a final volume of 0.6 mL, 0.084 mmol, 6.0 equiv) was added dropwise over the course of 10 min. The resultant suspension was stirred at 0 °C for 30 min and then slowly warmed to 25 °C and stirred for an additional 1 h. Upon completion, the reaction contents were quenched with saturated aqueous $NaHCO_3$ (5 mL), poured into water (5 mL), and extracted with EtOAc (3 × 5 mL). The combined organic layers were then washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. The resultant oil yellow oil was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give **97** (5.5 mg, 87%) as a white crystalline solid. This compound was recrystallized from hexanes and chloroform. **97**: $R_f$ = 0.43 (silica gel, EtOAc/hexanes, 1:1); m.p. = 220–221 °C; IR (film) $\nu_{max}$ 2923, 2911, 1609, 1587, 1518, 1315, 1141

$cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.84 (s, 1 H), 6.57 (d, *J* = 2.3 Hz, 1 H), 6.54 (d, *J* = 2.2 Hz, 1 H), 6.36 (s, 1 H), 6.30 (d, *J* = 2.3 Hz, 1 H), 6.28 (d, *J* = 2.2 Hz, 1 H), 3.89 (s, 3 H), 3.83 (s, 3 H), 3.82 (s, 3 H), 3.78 (s, 3 H), 3.77 (s, 3 H), 3.70 (s, 3 H), 3.10 (d, *J* = 3.6 Hz, 2 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 159.1, 159.0, 156.2, 155.0, 147.7, 147.5, 146.3, 143.5, 133.4, 126.7, 125.2, 120.2, 115.1, 111.4, 102.9, 101.9, 96.4, 96.3, 56.1, 55.8, 55.6, 55.4, 55.3, 45.3, 37.4, 35.0; HRMS (FAB) calcd for $C_{27}H_{28}O_6^+$ [$M^+$] 448.1886, found 448.1896.

**Cassigarol B analog #1 (78)**. Permethylated cassigarol B analog #1 (**97**, 15.0 mg, 0.033 mmol, 1.0 equiv) was dissolved in $CH_2Cl_2$ (1.0 mL), and the resultant solution was degassed by bubbling argon through it for 20 min. The solution was then cooled to –78 ºC and treated with $BBr_3$ (0.40 mL, 1.0 M solution in $CH_2Cl_2$, 0.400 mmol, 12 equiv). The resultant red mixture was stirred for 1 h at –78 ºC, allowed to warm slowly to 25 ºC over 1 h, and then stirred for an additional 2 h at 25 ºC. Upon completion, the reaction mixture was quenched with water (5 mL), poured into water (5 mL), and extracted with EtOAc (3 × 5 mL). The combined organic layers were then washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. The resultant crude brown oil was purified by preparative TLC (silica gel, $CH_2Cl_2$/MeOH, 9:1) to give cassigarol B analog #1 (**78**, 9.4 mg, 78%) as a clear oil. **78**: $R_f$ = 0.11 (silica gel, $CH_2Cl_2$/MeOH, 9:1); IR (film) $\nu_{max}$ 3377, 2914, 1592, 1490, 1365 $cm^{-1}$; $^1H$ NMR (400 MHz, acetone-$d_6$) δ 8.16 (s, 1 H), 8.09 (s, 1 H), 7.92 (s, 1 H), 7.90 (s, 1 H), 7.43 (s, 1 H), 7.39 (s, 1 H), 6.76 (s, 1 H), 6.40 (d, *J* = 2.0 Hz, 1 H), 6.37 (d, *J* = 2.4 Hz, 1 H), 6.30 (s, 1 H), 6.20 (d, *J* = 2.0 Hz, 1 H), 6.18 (d, *J* = 2.0 Hz, 1 H), 4.91 (s, 1 H), 4.46 (t, *J* = 3.6 Hz, 1 H), 2.96 (d, *J* = 2.8 Hz, 2 H); $^{13}C$ NMR (75 MHz, acetone-$d_6$) δ 156.6, 156.5, 154.0, 152.9, 148.8, 144.9, 143.8, 142.4, 134.1, 126.4, 123.1, 118.8, 118.0, 115.5, 105.0, 104.3, 100.4, 100.3, 45.6, 37.9, 35.8; LRMS (APCI+) calcd for $C_{21}H_{16}O_6^+$ [M + $H^+$] 365, found 365.

**Permethylated cassigarol B analog #2 (99)**. To a solution of alcohol **96** (15.0 mg, 0.032 mmol, 1.0 equiv) in $CH_2Cl_2$ (2.0 mL) was added concentrated TFA (0.303 mL, 0.19 mmol, 12 equiv) at 0 °C to give a brown solution. After 10 minutes of stirring at 0 °C, the solution was warmed slowly to 25 °C and stirred for an additional 3 h. Solid $NaCNBH_3$ (42.0 mg, 0.64 mmol, 20 equiv) was then added in a single portion and the reaction contents were stirred vigorously for 10 min. Upon completion, the reactions contents were quenched with saturated aqueous $NaHCO_3$ (5 mL), poured into water (5 mL), and extracted with EtOAc (3 × 5 mL). The combined organic layers were then washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. The resultant brown oil was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to give **99** (12.6 mg, 83%) as a white crystalline solid. This compound was recrystallized from chloroform and hexanes. **99**: $R_f$ = 0.43 (silica gel, EtOAc/hexanes, 1:1); m.p. = 108–109 °C; IR (film) $\nu_{max}$ 2941, 2825, 1597, 1508, 1321, 1196, 1143 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.92 (s, 1 H), 6.91 (s, 1 H), 6.56 (app t, 2 H), 6.29 (d, *J* = 2.4 Hz, 1 H), 6.21 (d, *J* = 2.4 Hz, 1 H), 5.09 (s, 1 H), 4.14 (t, *J* = 3.8 Hz, 1 H), 3.86 (s, 3 H), 3.85 (s, 3 H), 3.82 (s, 3 H), 3.81 (s, 3 H), 3.78 (s, 3 H), 2.95 (d, *J* = 3.6 Hz, 2 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 159.5, 159.3, 158.1, 155.1, 147.3, 147.1, 143.7, 142.5, 136.6, 133.0, 124.8, 115.1, 109.9, 109.2, 104.8, 102.8, 96.3, 95.9, 56.2, 56.0, 55.6, 55.4, 55.3, 55.1, 45.6, 45.4, 31.2; HRMS (FAB) calcd for $C_{27}H_{28}O_6^+$ [$M^+$] 448.1886, found 448.1880.

**Cassigarol B Analog #2 (79)**. Permethylated cassigarol B analog #2 (**99**, 15.0 mg, 0.033 mmol, 1.0 equiv) was dissolved in $CH_2Cl_2$ (1.0 mL), and the resultant solution was degassed by bubbling argon through it for 20 min. The solution was then cooled to –78 ºC and treated with $BBr_3$ (0.40 mL, 1.0 M solution in $CH_2Cl_2$, 0.400 mmol, 12 equiv). The resultant red mixture was stirred for 1 h at –78 ºC, allowed to warm slowly to 25 ºC over 1 h, and then stirred for an additional 2 h at 25 ºC. Upon completion, the reaction mixture was quenched with water (5 mL), poured into water (5 mL), and extracted with EtOAc (3 × 5 mL). The combined organic layers were then washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. The resultant crude brown oil

was purified by preparative TLC (silica gel, $CH_2Cl_2$/MeOH, 9:1) to give cassigarol B analog #2 (**79**, 9.8 mg, 81%) as a brown solid. [Note: this compound is highly sensitive to oxygen, so all operations must be performed under an argon atmosphere and conducted as quickly as possible]. **79**: $R_f$ = 0.11 (silica gel, $CH_2Cl_2$/MeOH, 9:1); IR (film) $\nu_{max}$ 2303, 2891, 2993, 1686, 1605, 1249, 1139 $cm^{-1}$; $^1H$ NMR (300 MHz, acetone-$d_6$) δ 8.10 (s, 1 H), 7.92 (s, 1 H), 7.82 (s, 1 H), 7.78 (s, 1 H), 7.55 (s, 1 H), 7.52 (s, 1 H), 6.86 (s, 1 H), 6.81 (s, 1 H), 6.41 (d, *J* = 1.8 Hz, 1 H), 6.39 (d, *J* = 2.7 Hz, 1 H), 6.19 (d, *J* = 1.0 Hz, 1 H), 6.12 (d, *J* = 2.1 Hz, 1 H), 4.93 (s, 1 H), 4.00 (t, *J* = 3.6 Hz, 1 H), 2.85 (d, *J* = 3.6 Hz, 2 H); $^{13}C$ NMR (75 MHz, acetone-$d_6$) δ 159.8, 157.3, 165.7, 152.9, 145.0, 143.3, 142.9, 122.6, 118.8, 115.4, 113.5, 112.8, 107.1, 106.7, 104.9, 100.3, 96.7, 54.5, 45.5, 32.3; LRMS (APCI+) calcd for $C_{21}H_{16}O_6^+$ [M+H$^+$] 365, found 365.

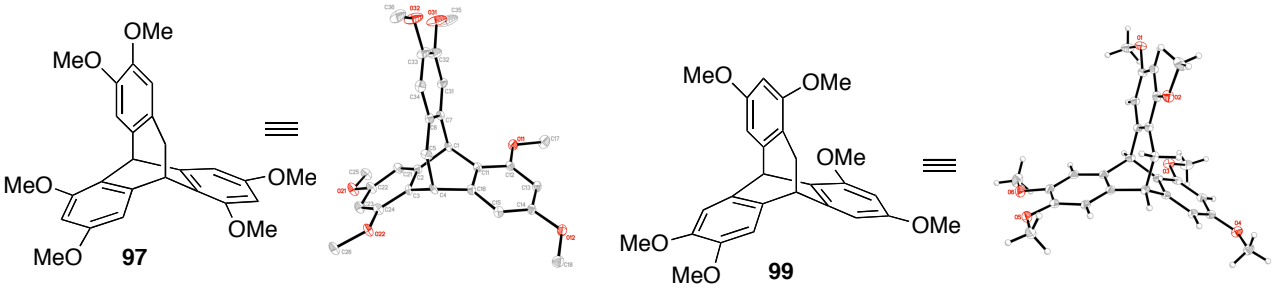



**Figure S3**. X-ray crystal structures of **97** and **99**.

**Enol Ether 100**. Palladium (II) chloride *bis*-benzonitrile (8.2 mg, 0.0214 mmol, 0.20 equiv) and $CuCl_2$ (2.8 mg, 0.0214 mmol, 0.20 equiv) were added sequentially in single portions to a solution of alcohol **27** (0.050 g, 0.107 mmol, 1.0 equiv) in DMF (5 mL) at 25 ºC under an oxygen atmosphere. The reaction solution was then warmed to 50 ºC and stirred for 3 h. Upon completion, the reaction contents were concentrated directly to give a crude oil that was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to afford a mixture of regioisomers **100** (0.037 g, 75%) and **102** (0.011 g, 22%) as a white crystalline solid and clear oil, respectively. [Note: due to the instability of **102**, it was not characterized but rather utilized immediately in subsequent chemistry]. Compound **100** was recrystallized from dichloromethane and methanol. **100**: $R_f$ = 0.55 (silica gel, EtOAc/hexanes, 1:1); m. p. = 123–124 °C; IR (film) $\nu_{max}$ 2905, 2790, 1601, 1512, 1161, 851 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.67 (d, *J* = 9.0 Hz, 2 H), 6.87 (d, *J* = 9.0 Hz, 2 H), 6.62 (s, 1 H), 6.49 (app d, *J* = 1.8 Hz, 2 H), 6.36 (d, *J* = 2.1 Hz, 1 H), 6.31 (app d, *J* = 2.1 Hz, 2 H), 6.22 (s, 1 H), 3.84 (s, 3 H), 3.82 (s, 3 H), 3.79 (s, 3 H), 3.68 (s, 6 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 160.6, 160.4, 160.2, 156.2, 151.9, 143.5, 133.1, 127.3, 126.6, 113.6, 109.8, 105.2, 100.5, 99.4, 96.7, 73.4, 55.5, 55.4, 55.3, 55.1; HRMS (FAB) calcd for $C_{26}H_{26}O_6^+$ [M$^+$] 434.1729, found 434.1715.

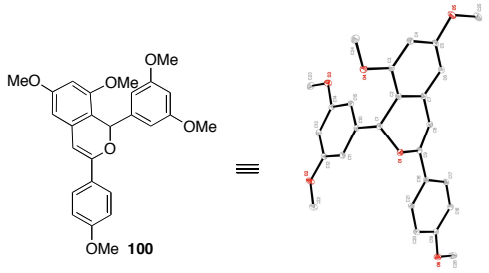



**Figure S4**. X-ray crystal structure of compound **100**.

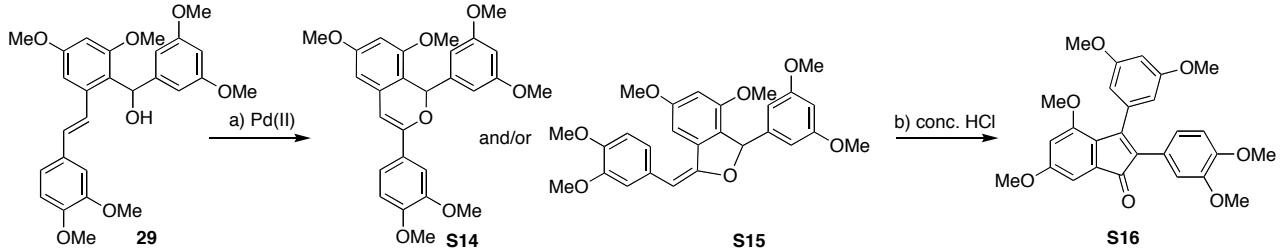
**Cyclization product 106**. $Pd(OAc)_2$ (0.048 g, 0.0214 mmol, 0.20 equiv) and $Cu(OAc)_2$ (4.0 mg, 0.0214 mmol, 0.20 equiv) were added sequentially in single portions to a suspension of alcohol **27** (0.050 g, 0.107 mmol, 1.0 equiv) in 2-propanol (5 mL) at 25 °C. The reaction flask was then purged of air, kept under an $O_2$ atmosphere, and warmed to 60 °C and stirred vigorously for 5 h or until palladium black was observed on the walls of the flask. At this time (when **102** had been formed cleanly *in situ*), the reaction contents were cooled to 25 °C and concentrated HCl (5 mL) was added dropwise. The resultant black solution was stirred for 16 h at 25 °C. Upon completion, the reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ (15 mL), poured into water (10 mL), and extracted with EtOAc (3 × 10 mL). The combined organic layers were then washed with water (15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated. The resultant black residue was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to afford **106** (0.033 g, 72%) as a purple solid. [Note: this compound is an extremely effective chromophore, and trace amounts of it can turn any solution deep red]. Alternatively, this cyclization product **106** could be prepared by the dropwise addition of concentrated HCl (1 mL) to a solution of **100** and **102** (3.3/1, 0.050 g, 0.115 mmol) in MeOH (5 mL) at 25 ºC. After 15 min of stirring, the solution turned purple; the reaction contents were stirred for a total of 16 h at 25 ºC. Upon completion, the reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ (15 mL), poured into water (10 mL), and extracted with EtOAc (3 × 10 mL). The combined organic layers were then washed with water (15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated. The resultant black residue was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to afford unreacted **100** (34.8 mg, 93% recovery) alongside **106** (11.9 mg, 90% yield based on initial amount of **102**). **106**: $R_f$ = 0.52 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2932, 2834, 1704, 1605, 1455, 1308, 1156 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.4 Hz, 2 H), 6.86 (d, *J* = 1.8 Hz, 1 H), 6.74 (d, *J* = 8.7 Hz, 2 H), 6.49 (app d, *J* = 2.1 Hz, 2 H), 6.43 (app d, *J* = 2.1 Hz, 2 H), 3.86 (s, 3 H), 3.76 (s, 3 H), 3.70 (s, 6 H), 3.60 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 196.6, 162.5, 160.2, 158.7, 156.6, 154.7, 137.0, 134.1, 131.0, 130.6, 123.6, 122.7, 113.4, 106.6, 104.1, 102.8, 101.0, 55.9, 55.8, 55.3, 55.2; HRMS (FAB) calcd for $C_{26}H_{24}O_6^+$ [$M^+$] 432.1573, found 432.1571. It is significant to note that **106** has previously been reported in the literature by Pan and co-workers;[7] however, their published carbon data did not fully match at two signals (108.0 ppm versus our observed value of 106.6 ppm and 114.2 ppm versus our observed value of 113.4 ppm) and they are missing another signal entirely (our observed value of 122.7 ppm). As such, **106** was prepared via an alternate method from the previously confirmed permethylated paucifloral F (**48**). To a solution of **48** (0.010 g, 0.023 mmol, 1.0 equiv) in THF (2 mL) at –78 °C was added NaHMDS (1.07 mL, 1.0 M in THF, 1.07 mmol, 3.0 equiv) and the resulting yellow solution was stirred at –78 °C for 30 min. Next, TMSCl (4.4 μL, 0.035 mmol, 1.5 equiv) was added dropwise, the solution was warmed slowly to 25 °C, and was then stirred for an additional 1 h at 25 °C. Upon completion, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (10 mL), poured into water (5 mL), and extracted with EtOAc (3 × 15 mL). The combined organic layers were then washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated to afford the desired silyl enol ether intermediate. Pressing forward without any additional purification, this material was dissolved immediately in MeCN (2 mL) at 25 °C and then treated with $Pd(OAc)_2$ (5.6 mg, 0.0253 mmol, 1.1 equiv). The resulting dark solution was stirred for 12 h at 25 °C. Upon completion, the reaction contents were concentrated directly and the resultant oily brown residue purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:1) to afford **106** (5.0 mg, 48%), material that matched that obtained via the previously described cyclization product in all respects.

**Natural product analog 107.** Cyclization product **106** (15.0 mg, 0.0347 mmol, 1.0 equiv) was dissolved in $CH_2Cl_2$ (1.0 mL) and treated with $BBr_3$ (0.40 mL, 1.0 M solution in $CH_2Cl_2$, 0.40 mmol, 12 equiv) at –78 ºC. The resultant red mixture was stirred for 1 h at –78 ºC, allowed to warm slowly to 25 ºC over 1 h, and then stirred for an additional 2 h at 25 ºC. Upon completion, the reaction mixture was quenched with water (5 mL), poured into water (5 mL), and extracted with EtOAc (3 × 5 mL). The combined organic layers were then washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. The resultant brown crude oil was purified by preparative TLC (silica gel, $CH_2Cl_2$/MeOH, 9:1) to give phenol **107** (12.4 mg, 88%) as a purple solid. **107**: $R_f$ = 0.08 (silica gel, $CH_2Cl_2$/MeOH, 9:1); IR (film) $\nu_{max}$ 3190, 2954, 2923, 1686, 1605, 1437, 1201, 1152 $cm^{-1}$; $^1H$ NMR (400 MHz, acetone-$d_6$) δ 7.08 (d, $J$ = 9.0 Hz, 2 H), 6.68 (d, $J$ = 8.4 Hz, 2 H), 6.62 (d, $J$ = 2.0 Hz, 1 H), 6.39 (d, $J$ = 2.4 Hz, 2 H), 6.36 (t, $J$ = 2.4 Hz, 1 H ), 6.34 (d, $J$ = 2.0 Hz, 1 H); $^{13}C$ NMR (75 MHz, acetone-$d_6$) δ 197.8, 161.7, 160.50, 160.47, 158.3, 158.2, 154.1, 136.1, 132.5, 130.9, 124.5, 120.4, 116.2, 109.6, 107.8, 106.5, 104.5; LRMS (APCI+) calcd for $C_{21}H_{14}O_6^+$ [M+H$^+$] 363, found 363.

**Diketone 105.** Osmium tetroxide (0.58 mL of 2.5 wt % solution in *t*-BuOH, 0.0115 mmol, 0.10 equiv) was added to a stirring solution of ketone **73** (50.0 mg, 0.115 mmol, 1.0 equiv) and 4-methylmorpholine *N*-oxide (41.0 mg, 0.350 mmol, 3.0 equiv) in acetone (12 mL) and water (6 mL). The resulting solution was stirred for 3 h at 25 °C at which point it was quenched with saturated aqueous $Na_2SO_3$ (20 mL) and stirred for 10 min at 25 °C. The reaction contents were then diluted with water (10 mL) and extracted with EtOAc (5 × 20 mL). The combined organic layers were washed with water (25 mL) and brine (25 mL), dried ($MgSO_4$), and concentrated to afford the crude diol intermediate, which was carried forward without purification due to its relative instability. This material (54.0 mg, 0.115 mmol, 1.0 equiv) was then dissolved in $CH_2Cl_2$ (1 mL) and cooled to 0 °C. Pyridine (28 μL, 0.347 mmol, 3.0 equiv) and *p*-TsCl (24.0 mg, 0.126 mmol, 1.1 equiv) were added sequentially at 0 °C and the resulting solution was warmed to 25 °C over the course of 4.5 h. Upon completion, the reaction contents were quenched with saturated aqueous $NH_4Cl$ (3 mL), diluted with water (5 mL) and extracted with $CH_2Cl_2$ (3 × 5 mL). The combined organic layers were washed with water (5 mL) and brine (5 mL) and concentrated. The resultant yellow product was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:3) to afford diketone **105** (20.0 mg, 39%) as a clear oil. **105**: $R_f$ = 0.30 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2938, 2838, 1674, 1596, 1513, 1460, 1320, 1300, 1248, 1203, 1155, 1034 $cm^{-1}$; $^1H$ NMR (300 MHz, $C_6D_6$) δ 7.40 (d, $J$ = 2.1 Hz, 2 H), 6.97 (d, $J$ = 8.7 Hz, 2 H), 6.82 (d, $J$ = 2.1 Hz, 1 H), 6.66 (d, $J$ = 8.7 Hz, 2 H), 6.63 (t, $J$ = 2.1 Hz, 1 H), 6.30 (d, $J$ = 2.1 Hz, 1 H), 3.80 (s, 2 H), 3.27 (s, 3 H), 3.23 (s, 3 H), 3.22 (s, 6 H), 2.99 (s, 3 H). This material cyclized to **106** instantly upon exposure to concentrated HCl in MeOH as described above.

**Synthesis of cyclization analog product S16.** This compound was synthesized from intermediate **29** exactly as described above. Intermediates **S14** and **S15** were prepared in exactly the same manner as well.

***Scheme S7.*** Extension of the cascade cyclization processes to an additional substrate.



**S14**: $R_f$ = 0.40 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2999, 2952, 2933, 1594, 1515, 1458, 1423, 1271, 1201, 1150 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 7.5, 2.0 Hz, 1 H), 7.21 (d, *J* = 2.0 Hz, 1 H), 6.84 (d, *J* = 7.8 Hz, 1 H), 6.63 (s, 1 H), 6.48 (d, *J* = 2.2 Hz, 2 H), 6.37 (d, *J* = 2.0 Hz, 1 H), 6.32 (d, *J* = 2.2 Hz, 1 H), 6.31 (app t, *J* = 2.2 Hz, 1 H), 6.23 (s, 1 H), 3.92 (s, 3 H), 3.89 (s, 3 H), 3.84 (s, 3 H), 3.79 (s, 3 H), 3.68 (s, 6 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 160.6, 160.4, 156.2, 151.8, 149.7, 148.6, 143.3, 133.0, 127.6, 118.2, 110.7, 109.9, 108.2, 105.2, 100.4, 99.8, 99.3, 96.7, 73.4, 55.9, 55.8, 55.5, 55.4, 55.1; HRMS (FAB) calcd for $C_{26}H_{25}O_7^+$ [M + $H^+$] 464.1835, found 464.1850.

**S15**: [Note: This compound is not stable and must be reacted immediately]. $R_f$ = 0.40 (silica gel, EtOAc/hexanes, 1:1); $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 1.2 Hz, 1 H), 7.28 (d, *J* = 2.0 Hz, 1 H), 6.83 (d, *J* = 8.5 Hz, 1 H), 6.63 (d, *J* = 2.0 Hz, 1 H), 6.54 (d, *J* = 2.0 Hz, 2 H), 6.48 (s, 1 H), 6.39 (t, *J* = 2.0 Hz, 1 H), 6.36 (d, *J* = 2.0 Hz, 1 H), 5.86 (s, 1 H), 3.88 (s, 3 H), 3.87 (s, 3 H), 3.83 (s, 3 H), 3.74 (s, 6 H), 3.72 (s, 3 H).

**Cyclization Product S16**: $R_f$ = 0.40 (silica gel, EtOAc/hexanes, 1:1); IR (film) $\nu_{max}$ 2993, 2955, 2929, 1701, 1587, 1511, 1461, 1416, 1302, 1252 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.92 (dd, *J* = 8.4, 2.0 Hz, 1 H), 6.86 (d, *J* = 2.0 Hz, 1 H), 6.67 (d, *J* = 8.4 Hz, 1 H), 6.66 (d, *J* = 2.0 Hz, 1 H), 6.51 (d, *J* = 2.0 Hz, 2 H), 6.43 (app d, *J* = 1.0 Hz, 1 H), 3.86 (s, 3 H), 3.84 (s, 3 H), 3.71 (s, 6 H), 3.61 (s, 3 H), 3.59 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 196.5, 162.6, 160.4, 156.7, 154.7, 148.2, 148.0, 137.3, 134.0, 130.3, 123.8, 122.6, 112.7, 110.6, 106.4, 104.0, 102.8, 100.8, 55.9, 55.7 (2 C), 55.4 (3 C); HRMS (FAB) calcd for $C_{26}H_{25}O_7^+$ [M + $H^+$] 463.1757, found 463.1746.

## References


[1] Ito, J.; Tanaka, T.; Iinuma, M.; Nakaya, K.; Takahashi, Y.; Sawa, R.; Murata, J.; Darnaedi, D. *J. Nat. Prod.* **2004**, *67*, 932–937.

[2] Takaya, Y.; Yan, K.-X.; Terashima, K.; Ito, J.; Niwa, M. *Tetrahedron* **2002**, *58*, 7259–7265.

[3] Adesanya, S. A.; Nia, R.; Martin, M.-T.; Boukamcha, N.; Montagnac, A.; Païs, M. *J. Nat. Prod.* **1999**, *62*, 1694–1695.

[4] Khan, M. A.; Nabi, S. G.; Prakash, S.; Zaman, A. *Phytochemistry* **1986**, *25*, 1945–1948.

[5] Yang, G.; Zhou, J.; Li, Y.; Hu, C. *Planta Medica* **2005**, *71*, 569–571.

[6] Baba, K.; Maeda, K.; Tabata, Y.; Doi, M.; Kozawa, M. *Chem. Pharm. Bull.* **1988**, *36*, 2977–2983.

[7] Chen, B.; Xie, X.; Lu, J.; Wang, Q.; Zhang, J.; Tang, S.; She, X.; Pan, X. *Synlett* **2006**, 259–262.