

Supporting Information

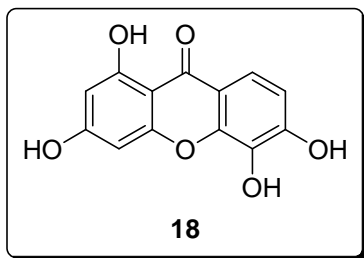
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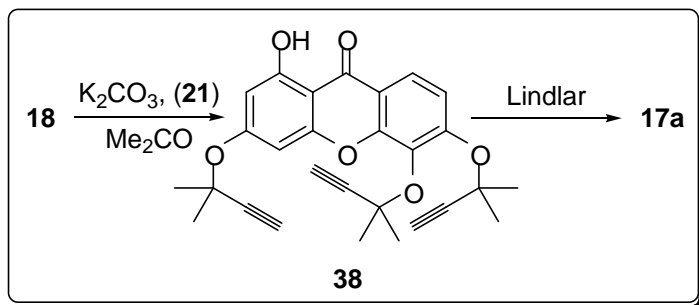
General Notes

All reagents were commercially obtained (Aldrich, Acros) at the highest commercial quality and used without further purification except where noted. Air- and moisture-sensitive liquids and solutions were transferred via syringe or stainless steel cannula. Organic solutions were concentrated by rotary evaporation below 45 °C at approximately 20 mmHg. All non-aqueous reactions were carried out under anhydrous conditions, *i.e.* they were performed using flame-dried glassware, under an argon atmosphere and in dry, freshly distilled solvents, unless otherwise noted. Tetrahydrofuran (THF), diethyl ether (Et₂O), dichloromethane (DCM), toluene (PhCH₃) and benzene (PhH) were purified by passage through a bed of activated alumina. Pyridine, triethylamine (TEA) and boron trifluoride etherate (BF₃•Et₂O) were distilled from calcium hydride prior to use. Dimethyl sulfoxide (DMSO) and dimethylformamide (DMF) were distilled from calcium hydride under reduced pressure (20 mmHg) and stored over 4Å molecular sieves until needed. Phloroglucinol (**19**) and 2,3,4-trihydroxybenzoic acid (**20**) were commercially available and used without any additional purification. Yields refer to chromatographically and spectroscopically (¹H NMR, ¹³C NMR) homogeneous materials, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) and visualized under UV light and/or developed by dipping in solutions of 10% ethanolic phosphomolybdic acid (PMA) or *p*-anisaldehyde and applying heat. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash chromatography. Preparative thin-layer chromatography separations were carried out on 0.25 or 0.50 mm E. Merck silica gel plates (60F-254). NMR spectra were recorded on Varian Mercury 300, 400 and/or Unity 500 MHz instruments and calibrated using the residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded on a Nicolet 320 Avatar FT-IR spectrometer and values are reported in cm⁻¹ units. Optical rotations were recorded on a Jasco P-1010 polarimeter and values are reported as follows: [α]_D^T (c: g/100 mL, solvent). High-resolution mass spectra (HRMS) were recorded on a VG 7070 HS mass spectrometer under chemical ionization (CI) conditions or on a VG ZABZSE mass spectrometer under fast atom bombardment (FAB) conditions.

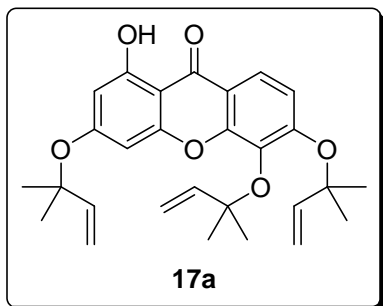
Experimental Details



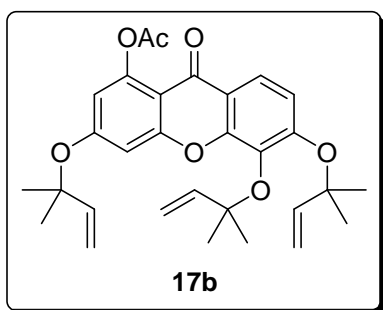
To a round-bottomed flask containing phloroglucinol (**19**) (1.0 g, 7.93 mmol), 2,3,4-trihydroxybenzoic acid (**20**) (1.35 g, 7.93 mmol) and ZnCl_2 (7.00 g, 51.5 mmol) was added POCl_3 (15.0 mL). The reaction vessel was then equipped with a reflux condenser and stirred under argon at 65 °C. The onset of a red color indicated the formation of the xanthone product. After 3 hours, the reaction was complete by TLC (80% Et_2O /hexane). It was cooled to 25 °C and poured into a beaker of ice. The reaction mixture was then partitioned between water and EtOAc . The water layer was back-extracted several times and the combined EtOAc layers dried over MgSO_4 , filtered and concentrated. The crude material was column chromatographed (65–70% Et_2O /hexane) to yield 1,3,5,6-tetrahydroxyxanthone (**18**) (0.94 g, 46%). **18**: yellow solid; $R_f = 0.25$ (80% Et_2O /hexane); IR (film) ν_{max} 3482, 3145, 1655, 1611, 1593, 1515, 1459, 1341, 1293, 1212, 1161, 1096, 1059, 1011, 962, 891, 808, 786, 683 cm^{-1} ; ^1H NMR (400 MHz, d_6 -acetone) δ 13.10 (s, 1H), 9.14 (br s, 3H), 7.57 (d, $J = 9.2$ Hz, 1H), 6.93 (d, $J = 9.2$ Hz, 1H), 6.37 (d, $J = 2.0$ Hz, 1H), 6.18 (d, $J = 2.0$ Hz, 1H); ^{13}C NMR (100 MHz, d_6 -acetone) δ 180.68, 165.44, 164.41, 158.34, 151.77, 146.55, 132.92, 117.17, 114.54, 113.42, 102.87, 98.64, 94.53; HRMS calc. for $\text{C}_{13}\text{H}_9\text{O}_6$ (MH^+) 261.0394, found 261.0389.



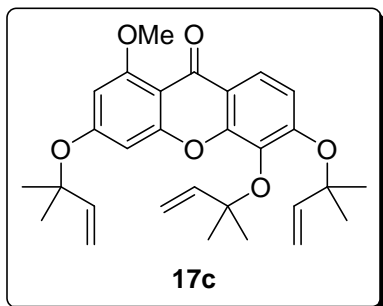
To a round-bottomed flask containing xanthone **18** (95.9 mg, 0.36 mmol), KI (197.4 mg, 1.19 mmol), K_2CO_3 (164.3 mg, 1.19 mmol) and CuI (7.0 mg, 36.9 μmol) was added dry acetone (5.00 mL) and 2-chloro-2-methylbut-3-yne (**21**) (0.21 mL, 1.84 mmol). The reaction vessel was then equipped with a reflux condenser and the reaction stirred under argon while heating at 45 °C. The reaction was monitored by TLC (30 and 80% Et_2O /hexane) until it was complete. After 6 hours, the reaction mixture was cooled to 25 °C and acidified with AcOH . The reaction mixture was then partitioned between EtOAc and water. The water layer was back-extracted once and the combined EtOAc layers dried over MgSO_4 , filtered and concentrated. The crude material was column chromatographed (5% Et_2O /hexane) to yield alkyne **38** (42.2 mg, 25%). **38**: yellow solid; $R_f = 0.4$ (30% Et_2O /hexane); IR (film) ν_{max} 3542, 3474, 3412, 3292, 2990, 2937, 2116, 1649, 1600, 1564, 1501, 1439, 1383, 1363, 1335, 1285, 1215, 1183, 1132, 1102, 1069, 1021, 991, 949, 909, 873, 818, 734 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 12.82 (s, 1H), 7.95 (d, $J = 8.8$ Hz, 1H), 7.63 (d, $J = 8.8$ Hz, 1H), 6.81 (d, $J = 2.0$ Hz, 1H), 6.71 (d, $J = 2.0$ Hz, 1H), 2.71 (s, 1H), 2.68 (s, 1H), 2.34 (s, 1H), 1.82 (s, 6H), 1.79 (s, 6H), 1.77 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 180.3, 162.6, 162.5, 156.6, 156.1, 152.1, 135.2, 120.8, 115.8, 115.6, 103.8, 101.1, 97.5, 85.0, 84.7, 77.4, 75.2, 75.0, 74.0, 73.7, 73.6, 72.6, 30.5, 29.68, 29.65; HRMS calc. for $\text{C}_{28}\text{H}_{27}\text{O}_6$ (MH^+) 459.1802, found 459.1819.



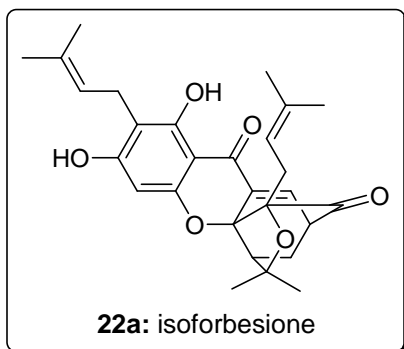
To a solution of alkyne **38** (96.5 mg, 0.21 mmol) in EtOAc (4.00 mL) was added 10% Pd/BaSO₄ (9.7 mg) and quinoline (3.5 μL, 29.6 μmol). The reaction mixture was then degassed and stirred under an atmosphere of H₂. To decrease the reaction time, an additional amount of 10% Pd/BaSO₄ (9.7 mg) was added to the reaction mixture every hour until the reaction was complete by TLC (20% Et₂O/hexane). After five additions and a total of 6 hours, the reaction mixture was filtered through a plug of silica gel and concentrated under reduced pressure. The crude material was column chromatographed (5% Et₂O/hexane) to yield alkene **17a** (73.4 mg, 75%). **17a**: yellow oil; *R_f* = 0.55 (30% Et₂O/hexane); IR (film) ν_{\max} 3086, 2982, 2935, 1650, 1597, 1562, 1497, 1436, 1379, 1362, 1334, 1285, 1212, 1128, 1102, 1068, 999, 926, 908, 868, 817, 705 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 12.79 (s, 1H), 7.80 (d, *J* = 8.8 Hz, 1H), 7.09 (d, *J* = 9.2 Hz, 1H), 6.53 (d, *J* = 2.4 Hz, 1H), 6.42 (d, *J* = 2.0 Hz, 1H), 6.27–6.13 (m, 3H), 5.30–5.16 (m, 5H), 5.02 (dd, *J* = 10.8, 0.8 Hz, 1H), 1.581 (s, 6H), 1.577 (s, 6H), 1.56 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 180.3, 163.6, 162.5, 156.9, 156.6, 152.1, 143.5, 143.4, 143.2, 135.4, 120.0, 116.5, 115.6, 114.1, 114.0, 112.9, 103.3, 101.3, 97.4, 83.5, 82.2, 81.1, 27.4, 27.3, 27.0; HRMS calc. for C₂₈H₃₃O₆ (MH⁺) 465.2272, found 465.2278.



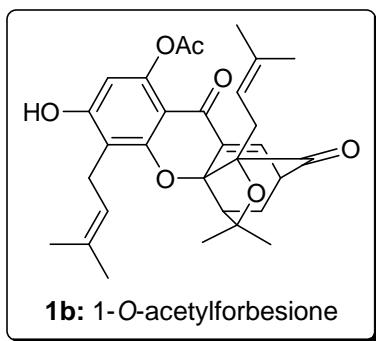
To a magnetically stirred solution of **17a** (259.5 mg, 0.56 mmol) in CH₂Cl₂ (10.0 mL) at 0 °C was added pyridine (1.13 mL, 14.0 mmol), DMAP (6.8 mg, 55.9 μmol) and acetic anhydride (1.32 mL, 14.0 mmol). After the addition, the reaction mixture was warmed to 35 °C. After 24 h, the reaction was complete by TLC (30% Et₂O/hexane). The reaction mixture was partitioned between Et₂O and saturated NaHCO₃ (aq). The Et₂O layer was then washed with brine, dried over MgSO₄, filtered and concentrated. The crude material was purified by column chromatography (15% Et₂O/hexane) to yield acetate **17b** (239.4 mg, 85%). **17b**: colorless oil; *R_f* = 0.6 (70% Et₂O/hexane); IR (film) ν_{\max} 3086, 2981, 2934, 1775, 1655, 1624, 1598, 1558, 1430, 1366, 1328, 1283, 1199, 1126, 1085, 1023, 1001, 925, 900, 863, 791 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.78 (d, *J* = 9.2 Hz, 1H), 7.03 (d, *J* = 8.8 Hz, 1H), 6.95 (d, *J* = 2.8 Hz, 1H), 6.58 (d, *J* = 2.4 Hz, 1H), 6.28–6.13 (m, 3H), 5.32–5.15 (m, 5H), 5.02 (dd, *J* = 10.8, 1.2 Hz, 1H), 2.46 (s, 3H), 1.56 (s, 6H), 1.55 (s, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 174.5, 169.5, 161.2, 157.7, 156.1, 151.4, 150.5, 143.41, 143.36, 143.2, 135.4, 120.6, 117.5, 116.9, 114.3, 113.9, 112.8, 110.6, 108.6, 104.0, 83.4, 82.1, 81.4, 27.3, 27.2, 27.0, 21.4; HRMS calc. for C₃₀H₃₅O₇ (MH⁺) 507.2377, found 507.2391.



To a magnetically stirred solution of **17a** (45.0 mg, 0.10 mmol) in DMF (1.00 mL) was added Cs_2CO_3 (157.8 mg, 0.48 mmol) and MeI (30.2 μL , 0.48 mmol). TLC (80% Et_2O /hexane) of the reaction mixture 15 minutes after the addition indicated the reaction was complete. The reaction mixture was then acidified with AcOH and partitioned between Et_2O and water. The Et_2O layer was washed with brine, dried over MgSO_4 , filtered and concentrated. The crude material was then column chromatographed (65% Et_2O /hexane) to give methyl ether **17c** (28.3 mg, 61%). **17c**: colorless oil; $R_f = 0.2$ (70% Et_2O /hexane); IR (film) ν_{max} 3086, 2980, 2934, 1657, 1617, 1596, 1561, 1463, 1438, 1419, 1379, 1365, 1326, 1283, 1226, 1204, 1118, 1056, 1000, 924, 900, 864, 827, 792 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.84 (d, $J = 8.4$ Hz, 1H), 7.03 (d, $J = 8.8$ Hz, 1H), 6.68 (d, $J = 2.0$ Hz, 1H), 6.38 (d, $J = 2.0$ Hz, 1H), 6.29–6.15 (m, 3H), 5.33–5.15 (m, 5H), 5.01 (dd, $J = 10.4, 0.8$ Hz, 1H), 3.93 (s, 3H), 1.60 (s, 6H), 1.55 (s, 12H); ^{13}C NMR (100 MHz, CDCl_3) δ 175.8, 175.2, 161.7, 161.1, 158.4, 155.5, 150.9, 143.7, 143.4, 143.3, 135.0, 120.8, 118.2, 116.7, 113.8, 112.6, 106.5, 98.3, 98.2, 83.2, 81.9, 80.9, 56.1, 27.2, 27.1, 26.8; HRMS calc. for $\text{C}_{29}\text{H}_{35}\text{O}_6$ (MH^+) 479.2428, found 479.2431.

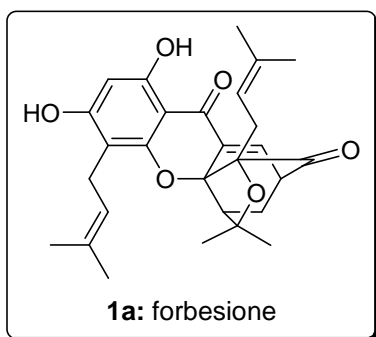


A solution of **17a** (27.3 mg, 58.8 μmol) in DMF (1.00 mL) was heated at 120 $^\circ\text{C}$ and continuously monitored by TLC (50% Et_2O /hexane). While heating, the reaction mixture turned yellow providing a qualitative indication of the reaction's progress. After 1 hour, the reaction mixture was diluted with toluene and concentrated several times at 60 $^\circ\text{C}$ under reduced pressure to remove DMF by azeotropic distillation. The crude material was purified by preparative TLC (30% Et_2O /hexane; same plate several times) to yield forbesione (**1a**) (13.4 mg, 49%) and isoforbesione (**22a**) (9.6 mg, 35%). **1a**: *vide infra*. **22a**: yellow foam; $R_f = 0.15$ (50% Et_2O /hexane); IR (film) ν_{max} 3293, 2972, 2924, 1739, 1637, 1599, 1453, 1383, 1330, 1280, 1231, 1188, 1168, 1142, 1085, 1062, 1038, 983, 893, 813, 737 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 12.81 (s, 1H), 7.41 (d, $J = 6.8$ Hz, 1H), 6.41 (br s, 1H), 6.04 (s, 1H), 5.26–5.22 (m, 1H), 4.45–4.41 (m, 1H), 3.49 (dd, $J = 6.8, 4.4$ Hz, 1H), 3.37 (d, $J = 7.2$ Hz, 2H), 2.60 (d, $J = 7.6$ Hz, 2H), 2.41 (d, $J = 9.6$ Hz, 1H), 2.32 (dd, $J = 13.2, 4.4$ Hz, 1H), 1.82 (s, 3H), 1.77 (s, 3H), 1.67 (s, 3H), 1.39 (s, 3H), 1.34 (dd, $J = 12.4, 9.6$ Hz, 1H), 1.29 (s, 3H), 1.10 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 202.8, 179.1, 164.2, 161.7, 158.8, 135.8, 135.0, 133.8, 133.4, 121.1, 118.1, 107.0, 100.9, 95.3, 89.8, 84.4, 83.5, 48.8, 46.8, 30.4, 29.12, 29.08, 26.0, 25.7, 25.3, 21.2, 18.1, 17.1; HRMS calc. for $\text{C}_{28}\text{H}_{33}\text{O}_6$ (MH^+) 465.2272, found 465.2288.



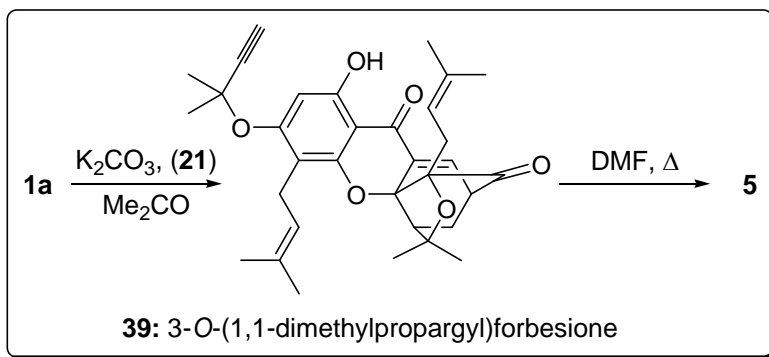
A solution of acetate **1b** (204.0 mg, 0.40 mmol) in DMF (4.00 mL) was heated at 120 °C and the reaction continuously monitored by TLC (80% Et₂O/hexane). While heating, the reaction mixture yellowed providing a qualitative indication of the reaction's progress. After 1 hour, the reaction mixture was diluted with toluene and concentrated several times at 60 °C under reduced pressure to remove DMF by azeotropic distillation. The crude material was purified by column chromatography (10–40% Et₂O/hexane) to yield 1-O-acetylforbesione

(**1b**) (150.2 mg, 79%). **1b**: off-white powder; $R_f = 0.25$ (70% Et₂O/hexane); IR (film) ν_{\max} 3279, 2966, 2925, 1771, 1737, 1662, 1612, 1501, 1417, 1368, 1319, 1301, 1203, 1162, 1144, 1128, 1107, 1056, 952, 908, 869, 843, 733 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.34 (d, $J = 6.8$ Hz, 1H), 6.51 (br s, 1H), 6.25 (s, 1H), 5.29–5.26 (m, 1H), 4.48–4.44 (m, 1H), 3.56–3.44 (m, 3H), 2.62–2.57 (m, 1H), 2.55 (d, $J = 9.6$ Hz, 1H), 2.48 (d, $J = 9.2$ Hz), 2.39 (s, 3H), 2.31 (dd, $J = 13.2, 4.4$ Hz, 1H), 1.83 (s, 3H), 1.78 (s, 3H), 1.69 (s, 3H), 1.40 (s, 3H), 1.32 (dd, $J = 13.2, 10.0$ Hz, 1H), 1.29 (s, 3H), 1.07 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 203.5, 174.2, 169.9, 159.7, 150.0, 135.2, 134.8, 134.4, 133.3, 120.6, 117.6, 112.9, 106.0, 105.9, 90.8, 84.5, 83.1, 49.1, 47.0, 30.2, 29.2, 28.9, 25.9, 25.8, 25.5, 22.7, 21.3, 18.2, 16.9; HRMS calc. for C₃₀H₃₅O₇ (MH⁺) 507.2377, found 507.2388.



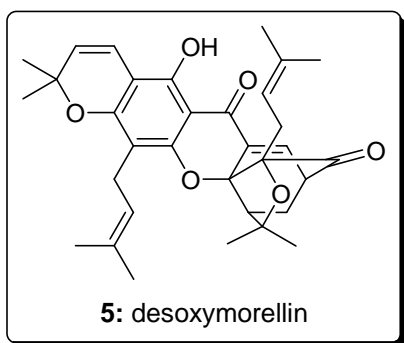
To a solution of **1b** (71.5 mg, 0.14 mmol) in MeOH (6.00 mL) at room temperature was added 0.25 mL of 0.5 M K₂CO₃ (aq) turning the reaction mixture yellow. This addition was repeated every hour for 5 hours, until a total of 1.50 mL of 0.5 M K₂CO₃ (aq) had been added. The reaction was monitored by TLC (70% Et₂O/hexane) and was complete after 6 hours. The mixture was then acidified with AcOH, diluted with EtOAc and washed twice with water and once with brine. The EtOAc layer was dried over MgSO₄, filtered and concentrated. The

crude material was then purified by column chromatography (10–40% Et₂O/hexane) to yield forbesione (**1a**) (59.7 mg, 91%). **1a**: yellow solid; $R_f = 0.19$ (50% Et₂O/hexane); IR (film) ν_{\max} 3197, 2914, 1732, 1636, 1593, 1502, 1425, 1384, 1333, 1285, 1250, 1208, 1174, 1140, 1123, 1084, 1051, 989, 954, 886, 871, 849, 825, 779, 732 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 12.59 (s, 1H), 7.46 (d, $J = 6.8$ Hz, 1H), 6.20 (br s, 1H), 6.04 (s, 1H), 5.26–5.23 (m, 1H), 4.45–4.41 (m, 1H), 3.51 (dd, $J = 6.8, 4.4$ Hz, 1H), 3.48–3.37 (m, 2H), 2.59–2.56 (m, 2H), 2.50 (d, $J = 9.2$ Hz, 1H), 2.35 (dd, $J = 13.6, 4.8$ Hz, 1H), 1.82 (s, 3H), 1.77 (d, $J = 1.2$ Hz, 3H), 1.70 (s, 3H), 1.39 (s, 3H), 1.36 (dd, $J = 13.6, 10.0$ Hz, 1H), 1.30 (s, 3H), 1.06 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 203.1, 179.4, 163.9, 163.0, 157.9, 135.4, 134.9, 133.9, 133.3, 121.1, 117.7, 105.6, 101.0, 97.0, 90.5, 84.5, 83.2, 49.2, 47.0, 30.3, 29.2, 29.0, 25.9, 25.7, 25.6, 22.3, 18.2, 16.9; HRMS calc. for C₂₈H₃₃O₆ (MH⁺) 465.2272, found 465.2275.



To a round-bottomed flask containing forbesione (**1a**) (71.6 mg, 0.15 mmol), KI (38.4 mg, 0.23 mmol), K₂CO₃ (63.9 mg, 0.46 mmol) and CuI (2.9 mg, 15.4 μmol) was added dry acetone (5.00 mL) and 2-chloro-2-methylbut-3-yne (**21**) (0.35 mL, 3.08

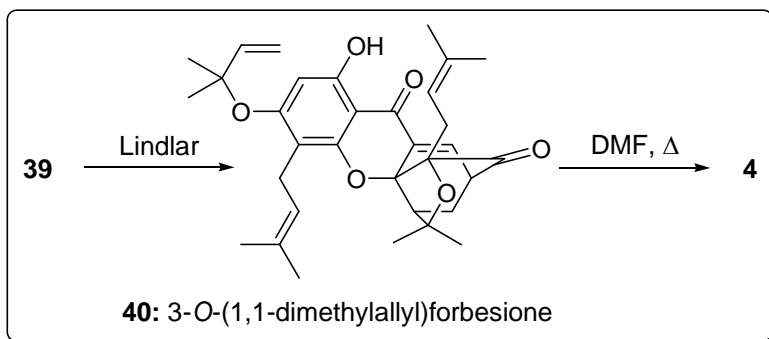
mmol). The reaction vessel was equipped with a reflux condenser and the mixture stirred under argon while heating at 55 °C. The reaction was monitored by TLC (70% Et₂O/hexane) until complete. After 4 hours, the reaction mixture was cooled to 25 °C and acidified with AcOH. The reaction mixture was then partitioned between Et₂O and water. The water layer was back-extracted once and the combined Et₂O layers were dried over MgSO₄, filtered and concentrated. The crude material was column chromatographed (10–80% CH₂Cl₂–hexane) to yield 3-O-(1,1-dimethylpropargyl)forbesione (**39**) (54.8 mg, 67%). **39**: yellow solid; *R_f* = 0.6 (70% Et₂O–hexane); IR (film) ν_{max} 3271, 2985, 2926, 1737, 1639, 1592, 1427, 1382, 1366, 1322, 1273, 1230, 1199, 1172, 1125, 1057, 992, 907, 865, 829, 732 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 12.59 (s, 1H), 7.45 (d, *J* = 6.8 Hz, 1H), 6.89 (s, 1H), 5.22–5.18 (m, 1H), 4.42–4.38 (m, 1H), 3.50 (dd, *J* = 6.4, 4.8, 1H), 3.37–3.25 (m, 2H), 2.70 (s, 1H), 2.58 (d, *J* = 7.6 Hz, 2H), 2.49 (d, *J* = 9.6 Hz, 1H), 2.35 (dd, *J* = 13.6, 4.4 Hz, 1H), 1.742 (s, 3H), 1.736 (s, 6H), 1.71 (s, 3H), 1.68 (s, 3H), 1.38 (s, 3H), 1.34 (dd, *J* = 8.4, 4.4 Hz, 1H), 1.29 (s, 3H), 0.99 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 203.2, 179.6, 162.7, 162.1, 157.4, 134.9, 133.9, 133.6, 131.4, 122.3, 117.8, 110.6, 101.1, 98.1, 90.3, 84.7, 84.6, 83.2, 75.2, 72.7, 49.2, 47.0, 30.2, 29.6, 29.2, 28.9, 25.8, 25.7, 25.6, 22.2, 18.4, 16.7; HRMS calc. for C₃₃H₃₉O₆ (MH⁺) 531.2741, found 531.2748.



A round-bottomed flask containing **39** (25.5 mg, 48.1 μmol) in DMF (1.00 mL) was heated at 125 °C and the reaction continuously monitored by TLC (70% Et₂O/hexane). After 4 hours, the reaction mixture was diluted with toluene and concentrated several times at 60 °C under reduced pressure to remove DMF by azeotropic distillation. The crude material was then purified by column chromatography (10–80% CH₂Cl₂–hexane) to yield desoxymorellin (**5**) (23.1 mg, 91%).

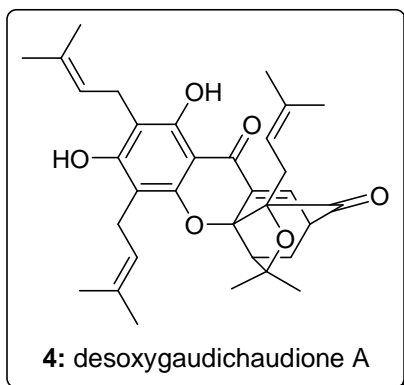
5: yellow solid; *R_f* = 0.64 (70% Et₂O/hexane); IR (film) ν_{max} 3454, 2973, 2925, 1737, 1634, 1594, 1438, 1400, 1382, 1330, 1302, 1214, 1186, 1165, 1141, 1047, 960, 875, 842, 754 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 12.87 (s, 1H), 7.44 (d, *J* = 6.8 Hz, 1H), 6.64 (d, *J* = 10.0 Hz, 1H), 5.53 (d, *J* = 9.6 Hz, 1H), 5.24–5.21 (m, 1H), 4.45–4.42 (m, 1H), 3.50 (dd, *J* = 6.4, 4.8 Hz, 1H), 3.38–3.26 (m, 2H), 2.58 (d, *J* = 8.0 Hz, 2H), 2.50 (d, *J* = 9.2 Hz, 1H), 2.35 (dd, *J* = 13.2, 4.0 Hz, 1H), 1.78 (s, 3H), 1.72 (s, 3H), 1.69 (s, 3H), 1.46 (s, 6H), 1.38 (s, 3H), 1.36 (dd, *J* = 13.2, 9.6 Hz, 1H), 1.30 (s, 3H), 1.04 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 203.2, 179.3, 160.3, 157.6, 157.2,

134.8, 133.58, 133.55, 131.5, 126.0, 122.0, 117.7, 115.5, 108.2, 102.9, 100.5, 90.4, 84.6, 83.2, 78.4, 49.2, 47.0, 30.2, 29.2, 28.9, 28.4, 28.3, 25.9, 25.7, 25.6, 21.8, 18.3, 16.8; HRMS calc. for C₃₃H₃₉O₆ (MH⁺) 531.2741, found 531.2741.



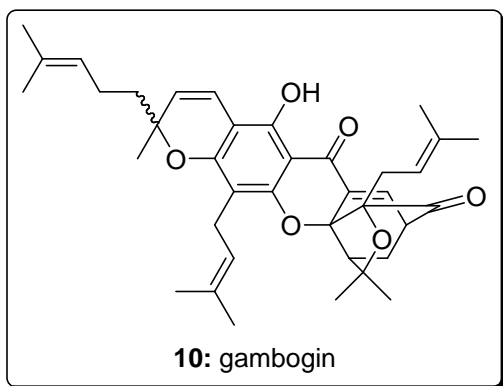
To a solution of alkyne **39** (15.4 mg, 29.0 μmol) in EtOAc (1.00 mL) was added 10% Pd/BaSO₄ (0.5 mg) and quinoline (0.5 μL , 4.3 μmol). The reaction mixture was degassed, and then stirred under an atmosphere of H₂. TLC (50%

Et₂O/hexane) indicated the reaction was complete in 15 minutes. The reaction mixture was filtered through a plug of silica gel and concentrated under reduced pressure. The crude material was purified by preparative TLC (50% Et₂O/hexane) to yield 3-O-(1,1-dimethylallyl)forbesione (**40**) (10.2 mg, 66%). **40**: yellow foam; $R_f = 0.26$ (50% Et₂O/hexane); IR (film) ν_{max} 2980, 2926, 1738, 1638, 1591, 1426, 1366, 1321, 1273, 1206, 1173, 1122, 1057, 995, 927, 864, 828, 731 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 12.58 (s, 1H), 7.44 (d, $J = 6.8$ Hz, 1H), 6.33 (br s, 1H), 6.12 (dd, 17.6, 11.2 Hz, 1H), 5.26-5.21 (m, 3H), 4.43-4.39 (m, 1H), 3.49 (dd, $J = 6.8, 4.8$ Hz, 1H), 3.40-3.28 (m, 2H), 2.58 (d, $J = 8.4$ Hz, 2H), 2.49 (d, $J = 9.6$ Hz, 1H), 2.34 (dd, $J = 13.6, 4.8$ Hz, 1H), 1.76 (s, 3H), 1.72 (s, 3H), 1.69 (s, 3H), 1.58 (s, 3H), 1.57 (s, 3H), 1.38 (s, 3H), 1.35 (dd, $J = 13.6, 9.6$ Hz, 1H), 1.30 (s, 3H), 1.00 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 203.3, 179.4, 163.7, 162.1, 157.3, 143.3, 134.8, 133.7, 133.6, 131.3, 122.5, 117.8, 114.1, 110.5, 100.7, 98.3, 90.3, 84.7, 83.2, 81.4, 49.2, 47.0, 30.2, 29.2, 28.9, 27.7, 27.6, 25.8, 25.67, 25.66, 22.3, 18.4, 16.7; HRMS calc. for C₃₃H₄₁O₆ (MH⁺) 533.2903, found 533.2919.



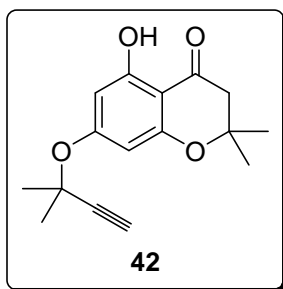
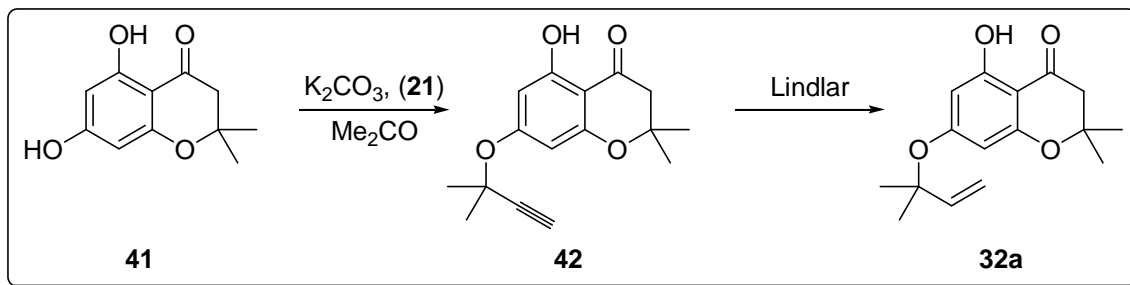
A round-bottomed flask containing **40** (13.4 mg, 25.2 μmol) in DMF (1.00 mL) was heated at 125 °C and the reaction continuously monitored by TLC (50% Et₂O/hexane). After 2 hours, the reaction mixture was diluted with toluene and concentrated several times at 60 °C under reduced pressure to remove DMF by azeotropic distillation. The crude material was then purified by preparative TLC (50% Et₂O/hexane) to yield desoxygaudichaudione A (**4**) (10.5 mg, 78%). **4**: yellow foam; $R_f = 0.41$ (50% Et₂O/hexane); IR (film) ν_{max} 3416, 2968, 2923, 2854, 1738, 1634, 1601, 1441, 1403, 1380, 1334, 1276, 1220, 1181, 1135, 1099, 1065, 1046, 985, 960, 824 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 12.92 (s, 1H), 7.44 (d, $J = 6.8$ Hz, 1H), 6.46 (br s, 1H), 5.23-5.20 (m, 2H), 4.45-4.41 (m, 1H), 3.50 (dd, $J = 6.4, 5.2$ Hz, 1H), 3.42-3.36 (m, 4H), 2.57-2.55 (m, 2H), 2.47 (d, $J = 9.2$ Hz, 1H), 2.34 (dd, $J = 13.2, 4.8$ Hz, 1H), 1.83 (s, 3H), 1.80 (s, 3H), 1.77 (s, 3H), 1.75 (s, 3H), 1.69 (s, 3H), 1.38 (s, 3H), 1.35 (dd, $J = 12.4, 6.8$ Hz, 1H), 1.29 (s, 3H), 1.03 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 203.3, 179.4, 162.7,

160.0, 156.0, 135.1, 134.8, 134.3, 133.7, 133.6, 121.6, 121.4, 117.7, 107.2, 106.0, 100.7, 90.2, 84.5, 83.1, 49.1, 47.0, 30.2, 29.2, 29.0, 26.0, 25.9, 25.7, 25.6, 22.3, 21.4, 18.2, 18.1, 16.9; HRMS calc. for $C_{33}H_{41}O_6$ (MH^+) 533.2898, found 533.2910.

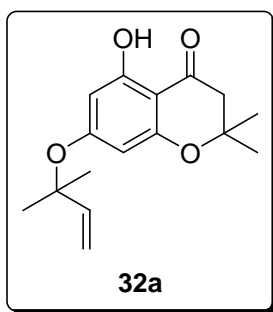


To a sealed tube containing forbesione (**1a**) (33.7 mg, 72.4 μ mol) in MeOH (2.50 mL) was added freshly prepared citral (**24**) (33.1 mg, 0.22 mmol), $CaCl_2 \cdot H_2O$ (21.3 mg, 0.14 mmol) and triethylamine (33.3 μ L, 0.22 mmol). The reaction mixture was then heated for a period of 3 hours. After cooling to room temperature, the reaction mixture was poured into a separatory funnel and partitioned between Et_2O and water, then Et_2O and brine. The ethereal extract was dried over $MgSO_4$, filtered and

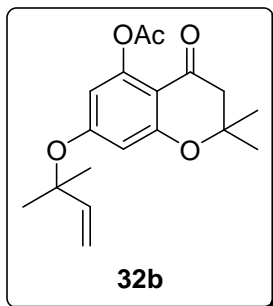
concentrated. The crude material was then column chromatographed (15% Et_2O /hexane) to yield gambogin (**10**) (27.5 mg, 75%). **10**: yellow foam; $R_f = 0.40$ (30% Et_2O /hexane); IR (film) ν_{max} 2969, 2925, 1738, 1634, 1595, 1438, 1401, 1380, 1331, 1224, 1174, 1139, 1086, 1048, 984, 960, 871, 840, 758 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 12.89 (s, 1H), 7.43 (d, $J = 7.2$ Hz, 1H), 6.69 (d, $J = 10.4$ Hz, 1H), 5.464/5.456 (d, $J = 9.6/10.4$ Hz, 1H), 5.24-5.19 (m, 1H), 5.08 (m, 1H), 4.45 (m, 1H), 3.49 (dd, $J = 6.4, 4.4$ Hz, 1H), 3.38-3.26 (m, 2H), 2.58 (d, $J = 7.2$ Hz, 2H), 2.49 (d, $J = 9.2$ Hz, 1H), 2.35 (dd, $J = 13.2, 4.4$ Hz, 1H), 2.12-2.06 (m, 2H), 1.84-1.64 (m, 2H), 1.77 (s, 3H), 1.72 (s, 3H), 1.68 (s, 6H), 1.58 (s, 3H), 1.422/1.418 (s, 3H), 1.36 (dd, 13.2, 9.6 Hz, 1H), 1.39 (s, 3H), 1.30 (s, 3H), 1.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.20/203.17, 179.2, 160.7/160.6, 157.6, 157.2, 134.81/134.77, 133.6, 133.53/133.51, 131.8/131.7, 131.50/131.46, 124.62/124.56, 123.7/123.6, 122.1/122.0, 117.7, 115.9/115.8, 107.8/107.7, 102.5, 100.4, 90.4, 84.61/84.58, 83.2, 81.1/81.0, 49.2, 47.0, 42.0/41.9, 30.23/30.20, 29.2, 28.9, 27.5/27.4, 25.82, 25.76, 25.7, 25.6, 22.9/22.8, 21.8, 18.3, 17.7, 16.9/16.8; HRMS calcd for $C_{38}H_{47}O_6$ (MH^+) 599.3367, found 599.3375.



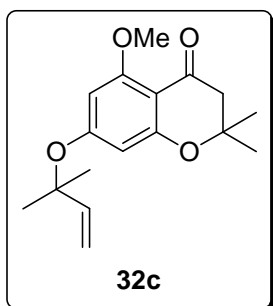
To a round-bottomed flask containing 5,7-dihydroxy-2,2-dimethyl-2,3-dihydrochromen-4-one (**41**) (251.3 mg, 1.21 mmol) [*J. Med. Chem.* **2001**, *44*, 664-671], KI (300.5 mg, 1.81 mmol), K_2CO_3 (500.4 mg, 3.62 mmol) and CuI (23.0 mg, 0.12 mmol) was added dry acetone (12.0 mL) and 2-chloro-2-methylbut-3-yne (**21**) (0.68 mL, 3.62 mmol). The reaction vessel was then equipped with a reflux condenser and the mixture stirred under argon and refluxed. The reaction was monitored by TLC (50% Et_2O /hexane) until complete. After 3 hours, the reaction mixture was cooled to 25 °C and acidified with AcOH. The reaction mixture was then partitioned between EtOAc and water. The water layer was back-extracted once and the combined EtOAc layers were dried over MgSO_4 , filtered and concentrated. The crude material was column chromatographed (5% Et_2O /hexane) to yield alkyne **42** (248.3 mg, 75%). **42**: white solid; $R_f = 0.52$ (50% Et_2O /hexane); IR (film) ν_{max} 3286, 2984, 1642, 1572, 1499, 1441, 1373, 1355, 1319, 1281, 1257, 1231, 1203, 1160, 1134, 1088, 1018, 868, 835, 645 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 11.88 (s, 1H), 6.34 (d, $J = 2.4$ Hz, 1H), 6.20 (d, $J = 2.4$ Hz, 1H), 2.66 (s, 1H), 2.64 (s, 2H), 1.67 (s, 6H), 1.42 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 196.1, 164.4, 163.0, 160.8, 102.6, 98.6, 98.3, 84.6, 78.8, 75.1, 72.2, 47.6, 29.5, 26.6; HRMS calc. for $\text{C}_{16}\text{H}_{19}\text{O}_4$ (MH^+) 275.1283, found 275.1295.



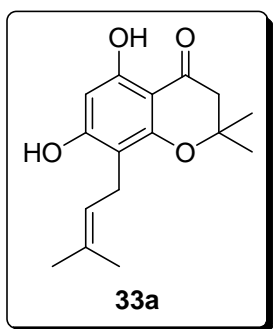
To a solution of **42** (206.7 mg, 0.75 mmol) in EtOAc (7.50 mL) was added 10% Pd/BaSO₄ (10.3 mg) and quinoline (94.6 μL , 0.80 mmol). The reaction mixture was then degassed and stirred under an atmosphere of H_2 for 1.5 hours, at which point the reaction was found to be complete by TLC (50% Et_2O /hexane). The reaction mixture was filtered through a plug of silica gel and concentrated under reduced pressure. The crude material was column chromatographed (5% Et_2O /hexane) to yield alkene **32a** (196.2 mg, 94%). **32a**: white solid; $R_f = 0.54$ (50% Et_2O /hexane); IR (film) ν_{max} 3086, 2981, 2936, 1640, 1570, 1499, 1440, 1373, 1354, 1319, 1280, 1255, 1207, 1160, 1128, 1087, 1013, 961, 927, 865, 834, 790, 736, 688 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 11.88 (s, 1H), 6.10 (dd, $J = 17.6, 10.8$ Hz, 1H), 6.09 (d, $J = 2.0$ Hz, 1H), 5.99 (d, $J = 2.4$ Hz, 1H), 5.24 (d, $J = 17.6$ Hz, 1H), 5.20 (d, $J = 10.8$ Hz, 1H), 2.67 (s, 2H), 1.53 (s, 6H), 1.45 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 195.7, 165.4, 162.8, 160.6, 143.3, 114.0, 102.3, 98.8, 98.6, 80.9, 78.7, 47.8, 27.5, 26.9; HRMS calc. for $\text{C}_{16}\text{H}_{21}\text{O}_4$ (MH^+) 277.1440, found 277.1458.



To a magnetically stirred solution of **32a** (65.4 mg, 0.24 mmol) in CH_2Cl_2 (2.50 mL) at 0 °C was added pyridine (95.7 μL , 1.18 mmol), DMAP (2.9 mg, 23.7 μmol) and acetic anhydride (0.11 mL, 1.18 mmol). After the addition, the reaction mixture was warmed to room temperature. After 24 hours, the reaction was complete by TLC (50% Et_2O /hexane). The reaction mixture was then partitioned between Et_2O and saturated NaHCO_3 (aq), Et_2O and H_2O , then Et_2O and 10% CuSO_4 (aq). The Et_2O layer was then washed with brine, dried over MgSO_4 , filtered and concentrated. The crude material was purified by column chromatography (20% Et_2O /hexane) to yield acetate **32b** (68.1 mg, 90%). **32b**: white solid; $R_f = 0.27$ (50% Et_2O /hexane); IR (film) ν_{max} 2980, 2936, 1771, 1682, 1615, 1562, 1434, 1368, 1321, 1283, 1252, 1199, 1155, 1128, 1072, 1054, 1020, 930, 888, 863, 817, 730, 686 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.39 (d, $J = 2.0$ Hz, 1H), 6.23 (d, $J = 2.8$ Hz, 1H), 6.11 (dd, $J = 17.6, 10.8$ Hz, 1H), 5.26 (d, $J = 17.6$ Hz, 1H), 5.23 (d, $J = 11.2$ Hz, 1H), 2.59 (s, 2H), 2.36 (s, 3H), 1.54 (s, 6H), 1.43 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 189.1, 169.2, 162.6, 161.7, 150.6, 143.1, 114.2, 107.3, 107.1, 104.5, 80.9, 79.0, 49.4, 27.3, 26.5, 21.2; HRMS calc. for $\text{C}_{18}\text{H}_{23}\text{O}_5$ (MH^+) 319.1545, found 319.1562.

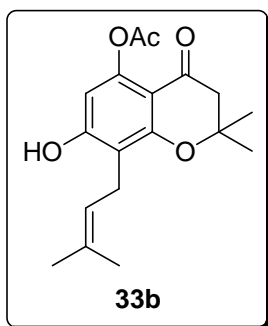


To a magnetically stirred solution of **32a** (65.4 mg, 0.24 mmol) in DMF (2.50 mL) was added Cs_2CO_3 (385.6 mg, 1.18 mmol) turning the reaction mixture yellow. The addition of MeI (73.7 μL , 1.18 mmol) returned the reaction mixture to a colorless state. TLC (50% Et_2O /hexane) of the reaction mixture 2 hours after the MeI addition ensured the reaction was complete. The reaction mixture was then acidified with AcOH and partitioned between Et_2O and water. The Et_2O layer was washed with brine, dried over MgSO_4 , filtered and concentrated. The crude material was then column chromatographed (40% Et_2O /hexane) to give methyl ether **32c** (59.2 mg, 86%). **32c**: white solid; $R_f = 0.14$ (50% Et_2O /hexane); IR (film) ν_{max} 2977, 2934, 1680, 1604, 1567, 1461, 1420, 1370, 1322, 1281, 1248, 1223, 1197, 1158, 1123, 1108, 1058, 1028, 927, 865, 832 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.141 (dd, $J = 17.2, 10.8$ Hz, 1H), 6.136 (d, $J = 2.4$ Hz, 1H), 6.07 (d, $J = 2.0$ Hz, 1H), 5.25 (d, $J = 17.2$ Hz, 1H), 5.22 (d, $J = 10.8$ Hz, 1H), 3.84 (s, 3H), 2.62 (s, 2H), 1.55 (s, 6H), 1.42 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 189.6, 163.1, 162.3, 161.1, 143.6, 113.8, 99.3, 95.7, 80.6, 78.5, 56.0, 50.1, 27.4, 26.6; HRMS calc. for $\text{C}_{17}\text{H}_{23}\text{O}_4$ (MH^+) 291.1596, found 291.1608.

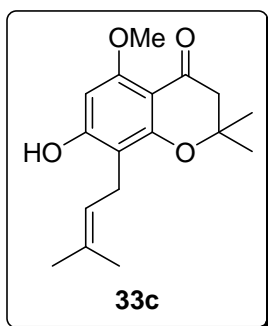


A round-bottomed flask containing **32a** (22.8 mg, 82.5 μmol) in DMF (1.00 mL) was heated at 125 °C and the reaction continuously monitored by TLC (50% Et_2O /hexane). After 1 hour, the reaction mixture was diluted with toluene and concentrated several times at 60 °C under reduced pressure to remove DMF by azeotropic distillation. The crude material was then purified by preparative TLC (50% Et_2O /hexane) to yield **33a** (9.3 mg, 41%) and **34a** (8.9 mg, 39%). **33a**: white solid; $R_f = 0.45$ (50% Et_2O /hexane); IR (film) ν_{max} 3303, 2977, 2924, 1635,

1596, 1502, 1436, 1373, 1302, 1258, 1234, 1165, 1106, 1076, 945, 902, 865, 796, 733 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 11.96 (s, 1H), 6.51 (br s, 1H), 5.96 (s, 1H), 5.21-5.17 (m, 1H), 3.28 (d, $J = 7.2$ Hz, 2H), 2.69 (s, 2H), 1.80 (s, 3H), 1.74 (s, 3H), 1.46 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 196.3, 163.5, 161.6, 158.2, 133.7, 121.8, 106.8, 102.3, 96.0, 78.8, 47.5, 26.9, 25.9, 21.7, 18.0; HRMS calc. for $\text{C}_{16}\text{H}_{21}\text{O}_4$ (MH^+) 277.1440, found 277.1454.



A round-bottomed flask containing **32b** (17.6 mg, 55.3 μmol) in DMF (1.00 mL) was heated at 125 $^\circ\text{C}$ and the reaction continuously monitored by TLC (80% Et_2O /hexane). After 1 hour, the reaction mixture was diluted with toluene and concentrated several times at 60 $^\circ\text{C}$ under reduced pressure to remove DMF by azeotropic distillation. The crude material was then purified by preparative TLC (80% Et_2O /hexane) to yield **33b** (13.2 mg, 75%). **33b**: colorless oil; $R_f = 0.50$ (80% Et_2O /hexane); IR (film) ν_{max} 3326, 2977, 2921, 1772, 1737, 1677, 1612, 1501, 1419, 1371, 1324, 1299, 1255, 1232, 1204, 1181, 1166, 1103, 1075, 1053, 961, 913, 842, 733 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.13 (s, 1H), 6.04 (s, 1H), 5.24-5.20 (m, 1H), 3.36 (d, $J = 7.2$ Hz, 2H), 2.61 (s, 2H), 2.37 (s, 3H), 1.83 (s, 3H), 1.77 (s, 3H), 1.45 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 190.0, 170.4, 160.7, 159.5, 148.7, 133.8, 121.1, 113.5, 106.8, 104.4, 79.1, 49.2, 26.7, 25.9, 22.3, 21.4, 18.0; HRMS calc. for $\text{C}_{18}\text{H}_{23}\text{O}_5$ (MH^+) 319.1545, found 319.1558.



A round-bottomed flask containing **32c** (19.7 mg, 67.8 μmol) in DMF (1.00 mL) was heated at 125 $^\circ\text{C}$ and the reaction continuously monitored by TLC (80% Et_2O /hexane). After 1 hour, the reaction mixture was diluted with toluene and concentrated several times at 60 $^\circ\text{C}$ under reduced pressure to remove DMF by azeotropic distillation. The crude material was then purified by preparative TLC (80% Et_2O /hexane) to yield **33c** (16.2 mg, 82%). **33c**: white solid; $R_f = 0.31$ (Et_2O); IR (film) ν_{max} 3217, 2973, 2922, 1646, 1590, 1503, 1448, 1413, 1368, 1336, 1301, 1260, 1214, 1166, 1093, 990, 939, 902, 837, 728 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.42 (br s, 1H), 6.03 (s, 1H), 5.25-5.21 (m, 1H), 3.82 (s, 3H), 3.33 (d, $J = 7.6$ Hz, 2H), 2.64 (s, 2H), 1.83 (s, 3H), 1.76 (s, 3H), 1.44 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 190.3, 161.4, 160.0, 159.9, 134.4, 121.7, 107.0, 105.0, 92.5, 78.5, 55.9, 49.9, 26.7, 25.9, 22.1, 18.0; HRMS calc. for $\text{C}_{17}\text{H}_{23}\text{O}_4$ (MH^+) 291.1596, found 291.1610.

