Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Differentiation of Nonconventional "Carbanions" – The Total Synthesis of Nemorosone and Clusianone

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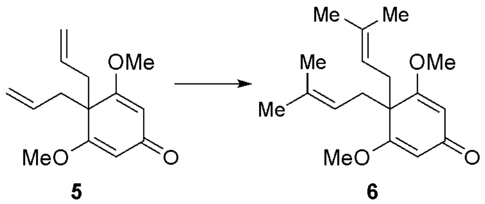
General Methods. All reactions sensitive to air or moisture were carried out in oven-dried glassware fitted with rubber septa under a positive pressure of nitrogen atmosphere, unless otherwise noted. Air- and moisture-sensitive liquids and solutions were transferred via syringe or stainless steel cannula. Where necessary solutions were deoxygenated by alternative freeze (liquid nitrogen)/evacuation/ thaw cycles (≥ three iterations). Organic solutions were concentrated by rotary evaporation at 40-60 Torr. Flash column chromatography was performed as described by Still et al. (Still, W. C.; Kahn, M.; Mitra, A. J. *J. Org. Chem*. 1978, 43, 2923-2925.) Analytical thin layer chromatography was performed using glass plates pre-coated with 0.25 mm 230-400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light and/or exposure to ceric ammonium molybdate, phosphomolybdic acid, or an acidic solution of *p*-anisaldehyde followed by heating on a hot plate.

Materials. Commercial reagents and solvents were used as received with the following exceptions. Chlorotrimethylsilane, triethylamine, and diisopropylamine were distilled from calcium hydride at 760 Torr under nitrogen atmosphere. Tetrahydrofuran was distilled from sodium benzophenone ketyl. Benzene, dichloromethane, ethyl ether and toluene were purified using Solv-Tek, Inc. solvent purification systems. The molarity of *n*-butyllithium was determined by titration against menthol.

Instrumentation. Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) were recorded with Bruker AMX-500 spectrometer. Chemical shifts for protons are reported in parts per million scale (δ scale) downfield from tetramethylsilane and are referenced to residual proton in the NMR solvents ($CHCl_3$: δ 7.24, C_6D_5H: δ 7.15, CD_2HOD: δ 3.31). Chemical shifts for carbon are reported in parts per million (δ scale) downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent ($CDCl_3$: δ 77.0, C_6D_6: δ 128.0, CD_3OD: δ 49.0). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), integration, coupling constant in Hz, and assignment. Infrared (IR) spectra were obtained using a Perkin-Elmer 1600 FT-IR spectrophotometer referenced to a polystyrene standard. Data are represented as follows: frequency of the absorption (cm^{-1}), intensity of absorption (s = strong, sb = strong broad, m = medium, w = weak, br =broad), and assignment (where appropriate).

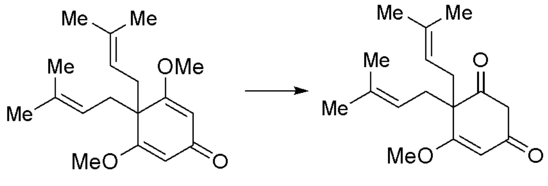


5 6

Compound **6**

To a solution of compound **5** (11.71 g, 50.0 mmol) in CH_2Cl_2/2-methyl-2-butene (1:1, 200mL) was added Grubbs catalyst 2nd generation (837.2 mg, 0.99 mmol). The resulting solution was refluxed at 40 °C for 30 h. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (0-50% ethyl acetate/hexane) to afford compound **6** (11.44 g, 79%) as a white.

6: $R_f \approx 0.41$ (50% ethyl acetate/hexanes); IR (film) 2974, 2914, 1663, 1593, 1391, 1200, 1163, 1084 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.44 (s, 2H, CH x2), 4.67 (t, J = 7.5 Hz, 2H, CH x2), 3.62 (s, 6H, OCH_3 x2), 2.48 (d, J = 7.5 Hz, 4H, CH_2 x2), 1.52 (s, 6H, CH_3 x2), 1.48 (s, 6H, CH_3 x2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.9, 173.8 (x2), 134.2 (x2), 117.9 (x2), 102.9 (x2), 55.5 (x2), 51.5, 35.6 (x2), 25.7 (x2), 17.5 (x2); HRMS calcd for $C_{18}H_{27}O_3$ [$(M+H)^+$] 291.1960, found 291.1967.

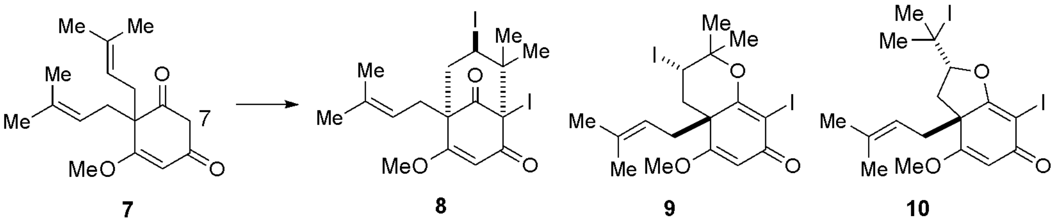


6 7

Diketone **7**

To a solution of compound **6** (11.44 g, 39.4 mmol) in 2,4,6-collidine (80 mL) was added lithium iodide (26.51 g, 198 mmol). The reaction mixture was stirred at 140 °C for 19 h and then cooled to room temperature. The resultant mixture was diluted with ethyl acetate/hexane (1:1), washed with 1 M HCl, water and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (10-75% ethyl acetate/hexane) to afford diketone **7** (8.91 g, 82%) as a white solid.

7: $R_f \approx 0.19$ (50% ethyl acetate/hexanes); IR (film) 2969, 2915, 1650, 1556, 1454, 1381, 1212, 1195, 1080 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.71 (s, 1H, CH), 4.80 (dd, J = 8.1, 7.3 Hz, 2H, CH x2), 3.76 (s, 3H, CH_3), 3.20 (s, 2H, CH_2), 2.63 (dd, J = 13.8, 8.1 Hz, 2H, CH_2 x2), 2.45 (d, J = 13.8, 7.3 Hz, 2H, CH_2 x2), 1.59 (s, 6H, CH_3 x2), 1.54 (s, 6H, CH_3 x2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.6, 192.3, 178.0, 136.0 (x2), 117.8 (x2), 105.0, 58.7, 56.4, 52.8, 35.8 (x2), 25.9 (x2), 17.7 (x2); HRMS calcd for $C_{17}H_{25}O_3$ [$(M+H)^+$] 277.1804, found 277.1808.



7 8 9 10

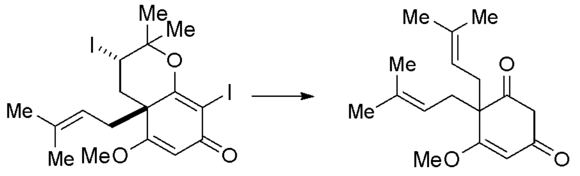
Diiodide **8**, **9** and **10**

To a solution of diketone **7** (6.38 g, 23.1 mmol) in THF/water (3:1, 160 mL) was added $KHCO_3$ (6.94 g, 69.3 mmol), potassium iodide (11.50 g, 69.3 mmol) and iodide (17.61 g, 69.4 mmol). The reaction mixture was stirred at room temperature for 50 min and quenched with saturated aqueous $Na_2S_2O_3$. The resultant mixture was diluted with ethyl acetate, washed with water and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (10-30% ethyl acetate/hexane) to afford diiodide **8** (3.87 g, 32%) as a white solid, diiodide **9** (3.58 g, 29%) as a white solid and diiodide **10** (2.90 g, 24%) as a white solid.

8: $R_f \approx 0.31$ (20% ethyl acetate/hexanes); IR (film) 2977, 1738, 1657, 1596, 1451, 1372, 1226 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.82 (s, 1H, CH), 5.00 (t, J = 7.0 Hz, 1H, CH), 4.47 (dd, J = 12.7, 5.2 Hz, 1H, CH), 3.78 (s, 3H, CH_3), 2.58 (dd, J = 14.6, 7.0 Hz, 1H, CH_2), 2.48 (dd, J = 14.6, 7.0 Hz, 1H, CH_2), 2.42 (dd, J = 12.7, 5.2 Hz, 1H, CH_2), 2.36 (t, J = 12.7 Hz, 1H, CH_2), 1.64 (s, 6H, CH_3 x2), 1.39 (s, 3H, CH_3), 1.19 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.9, 188.8, 175.0, 135.3, 118.2, 103.7, 79.2, 59.2, 57.4, 48.6, 44.3, 31.5, 30.5, 30.1, 26.0, 24.1, 18.0; HRMS calcd for $C_{17}H_{23}O_3I_2$ $[(M+H)^+]$ 528.9737, found 528.9747.

9: $R_f \approx 0.25$ (20% ethyl acetate/hexanes); IR (film) 2976, 1639, 1373, 1224, 1079, 834 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 5.47 (s, 1H, CH), 4.70 (t, J = 7.9 Hz, 1H, CH), 4.23 (dd, J = 13.5, 4.5 Hz, 1H, CH), 2.82 (s, 3H, CH_3), 2.44 (dd, J = 13.3, 7.9 Hz, 1H, CH_2), 2.40 (dd, J = 13.5, 4.5 Hz, 1H, CH_2), 2.16 (t, J = 13.5 Hz, 1H, CH_2), 1.97 (dd, J = 13.3, 7.9 Hz, 1H, CH_2), 1.45 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.31 (s, 3H, CH_3); ^{13}C NMR (125 MHz, C_6D_6) δ 181.1, 172.4, 168.2, 138.2, 128.5, 116.7, 100.4, 94.1, 86.0, 55.3, 50.7, 41.7, 35.7, 30.1, 29.2, 25.8, 21.2, 17.7; HRMS calcd for $C_{17}H_{23}O_3I_2$ $[(M+H)^+]$ 528.9737, found 528.9749.

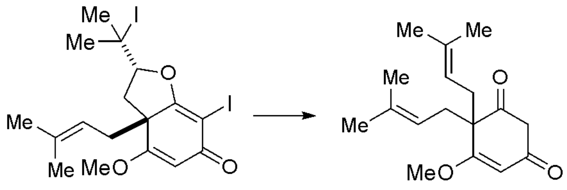
10: $R_f \approx 0.16$ (20% ethyl acetate/hexanes); IR (film) 2967, 2933, 1614, 1454, 1384, 1231, 1105 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.50 (s, 1H, CH), 4.83 (t, J = 7.9 Hz, 1H, CH), 4.44 (dd, J = 9.6, 5.8 Hz, 1H, CH), 3.69 (s, 3H, CH_3), 2.58 (dd, J = 12.9, 5.8 Hz, 1H, CH_2), 2.51 (d, J = 7.9 Hz, 2H, CH_2), 2.21 (dd, J = 12.9, 9.6 Hz, 1H, CH_2), 2.00 (s, 3H, CH_3), 1.92 (s, 3H, CH_3), 1.62 (s, 3H, CH_3), 1.51 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 183.8, 176.5, 171.6, 138.2, 116.2, 100.2, 91.0, 71.3, 56.2, 54.3, 47.2, 38.3, 37.9, 34.3, 31.4, 25.9, 17.7; HRMS calcd for $C_{17}H_{23}O_3I_2$ $[(M+H)^+]$ 528.9737, found 528.9739.



9 **7**

Reduction of compound **9**

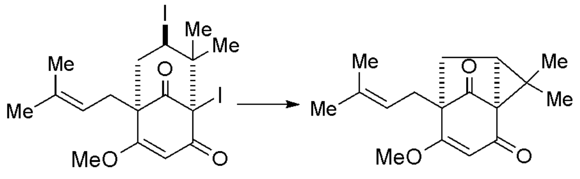
To a solution of diiodide **9** (1.5445 g, 2.93 mmol) in THF/water (20:1, 21 mL) was added zinc dust (972.8 mg, 14.9 mmol). The reaction mixture was stirred at 65 °C for 4.5 h and cooled to room temperature. The resultant mixture was diluted with ethyl acetate, washed with 1 M HCl, water and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (10-75% ethyl acetate/hexane) to afford diketone **7** (633.1 mg, 78%) as a white solid.



10 **7**

Reduction of compound **10**

To a solution of diiodide **10** (1.2635 g, 2.39 mmol) in THF/water (20:1, 21 mL) was added zinc dust (1.1754 g, 18.0 mmol). The reaction mixture was stirred at 65 °C for 7 h and cooled to room temperature. The resultant mixture was diluted with ethyl acetate, washed with 1 M HCl, water and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (10-75% ethyl acetate/hexane) to afford diketone **7** (576.4 mg, 87%) as a white solid.

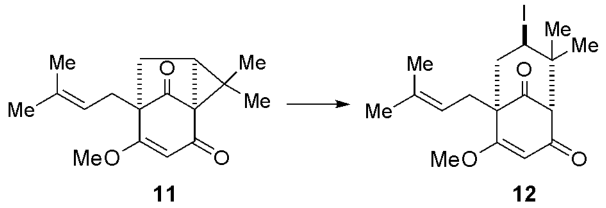


8 **11**

Compound **11**

To a solution of diiodide **8** (3.8734 g, 7.33 mmol) in THF/ether (1:1, 75 mL) at -78 °C was added *i*-PrMgCl (2.0 M in THF, 4.40 mL, 8.80 mmol). The reaction mixture was stirred at -78 °C for 40 min and warmed to 0 °C. After 10 min, the reaction mixture was quenched with saturated aqueous NH_4Cl, diluted with ethyl acetate, washed with water and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (10-20% ethyl acetate/hexane) to afford compound **11** (1.8684 g, 93%) as a light yellow solid.

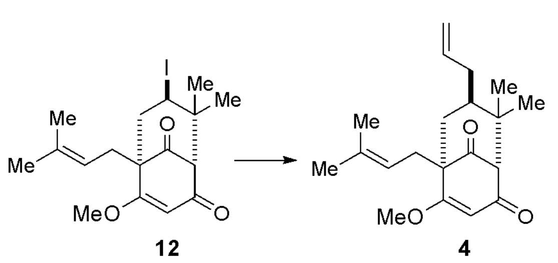
11: $R_f \approx 0.19$ (20% ethyl acetate/hexanes); IR (film) 2964, 2922, 1759, 1666, 1555, 1378, 1216 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.48 (s, 1H, CH), 5.17 (dd, *J* = 8.0, 6.7 Hz, 1H, CH), 3.70 (s, 3H, CH_3), 2.50 (dd, *J* = 15.0, 8.0 Hz, 1H, CH_2), 2.37 (dd, *J* = 15.0, 6.7 Hz, 1H, CH_2), 2.05 (dd, *J* = 14.1, 8.0 Hz, 1H, CH_2), 1.85 (dd, *J* = 14.1, 5.3 Hz, 1H, CH_2), 1.68 (s, 3H, CH_3), 1.62 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.20 (dd, *J* = 8.0, 5.3 Hz, 1H, CH), 1.13 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.3, 191.6, 177.9, 134.7, 118.7, 106.9, 72.4, 57.0, 55.9, 43.8, 39.3, 27.0, 25.8, 25.6, 23.,2 19.1, 17.8; HRMS calcd for $C_{17}H_{23}O_3$ [$(M+H)^+$] 275.1647, found 275.1634.



Iodide **12**

To a solution of compound **11** (370.1 mg, 1.35 mmol) in CH_2Cl_2 (14 mL) at -78 °C was added TMSI (0.21 mL, 1.54 mmol). The reaction mixture was stirred at -78 °C for 10 min and warmed to 0 °C. After 20 min, the reaction mixture was quenched with saturated aqueous $NaHCO_3$, diluted with ethyl acetate, washed with water and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (20% ethyl acetate/hexane) to afford iodide **12** (529.5 mg, 98%) as a colorless oil.

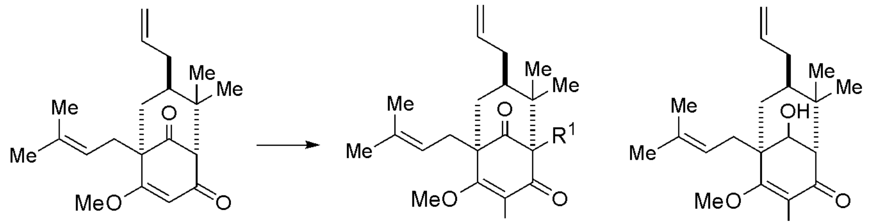
12: $R_f \approx 0.22$ (20% ethyl acetate/hexanes); IR (film) 2969, 1735, 1656, 1593, 1371, 1224 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.74 (s, 1H, CH), 4.95 (t, *J* = 6.7 Hz, 1H, CH), 4.35 (dd, *J* = 13.4, 4.9 Hz, 1H, CH), 3.75 (s, 3H, CH_3), 3.17 (s, 1H, CH), 2.47 (dd, *J* = 14.5, 6.7 Hz, 1H, CH_2), 2.43 (dd, *J* = 13.4, 4.9 Hz, 1H, CH_2), 2.38 (dd, *J* = 14.5, 6.7 Hz, 1H, CH_2), 2.28 (t, *J* = 13.4 Hz, 1H, CH_2), 1.62 (s, 6H, CH_3 x2), 1.12 (s, 3H, CH_3), 1.05 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.2, 192.4, 176.2, 134.6, 118.4, 106.2, 70.9, 59.1, 57.0, 44.9, 43.9, 35.5, 29.3, 28.9, 25.9, 24.0, 17.9; HRMS calcd for $C_{17}H_{23}O_3I$ [$(M+H)^+$] 403.0764, found 403.0766.



Compound **4**

To a solution of iodide **12** (529.5 mg, 1.32 mmol) in benzene/allyltributylstannane (1:2, 15 mL) was added AIBN (24.8 mg, 0.151 mmol). The resultant mixture was degassed by flozen-thow method. The reaction mixture was stirred at 80 °C for 15 h, cooled to room temperature and diluted with CH_3CN. The acetonitrile layer was collected, washed with hexanes and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (10-20% ethyl acetate/hexane) to afford compound **4** (310.9 mg, 75%) as a colorless oil.

4: $R_f \approx 0.21$ (20% ethyl acetate/hexanes); IR (film) 2967, 2935, 1732, 1654, 1594, 1226 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.68 (s, 1H, CH), 5.60 (m, 1H, CH), 4.97-4.90 (m, 3H), 3.70 (s, 3H, CH_3), 2.79 (s, 1H, CH), 2.42 (dd, J = 14.5, 7.6 Hz, 1H, CH_2), 2.33 (dd, J = 14.5, 7.6 Hz, 1H, CH_2), 2.24 (m, 1H, CH_2), 1.91 (dd, J = 13.4, 4.4 Hz, 1H, CH_2), 1.71 (m, 1H, CH), 1.63 (m, 1H, CH_2), 1.60 (s, 3H, CH_3), 1.58 (s, 3H, CH_3), 1.33 (t, J = 13.4 Hz, 1H, CH_2), 1.04 (s, 3H, CH_3), 0.82 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.4, 193.5, 177.6, 136.7, 133.7, 119.2, 116.6, 106.1, 74.5, 56.9, 56.8, 42.7, 39.6, 39.0, 33.5, 29.5, 26.5, 25.8, 20.5, 17.8; HRMS calcd for $C_{20}H_{29}O_3$ [$(M+H)^+$] 317.2117, found 317.2124.



4

15 : R^1 = H
16 : R^1 = I

17

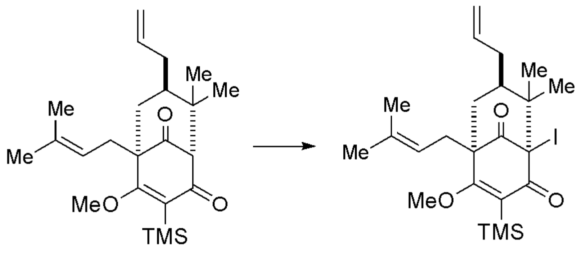
Compound **16**

To a solution of compound **4** (44.5 mg, 0.141 mmol) in THF (1.5 mL) was added TMSCl (0.18 ml, 1.42 mmol) at room temperature and then added freshly prepared LDA solution (0.25 M in THF, 2.8 mL, 0.70 mmol). After stirring for 10 min at -78 °C, the reaction mixture was allowed to warm to 0 C. After stirring for 1 min at 0 °C, to the resultant solution was added iodide (127.1 mg, 0.501 mmol) in THF (1.2 mL) via cannula. The resultant solution was stirred for 20 min at 0 °C, quenched with saturated aqueous $Na_2S_2O_3$, diluted with ethyl acetate, washed with water and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (5-30% ethyl acetate/hexane) to afford iodide **16** (36.8 mg, 51%) as a colorless oil, compound **15** (6.7 mg, 12%) as a colorless oil and alcohol **17** (18.0 mg, 33%) as a colorless oil.

16: $R_f \approx 0.25$ (5% ethyl acetate/hexanes); IR (film) 2972, 2940, 1733, 1652, 1558, 1237, 845 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.63 (m, 1H, CH), 5.05-4.99 (m, 3H), 3.87 (s, 3H, CH_3), 2.59 (dd, J = 14.5, 6.5 Hz, 1H, CH_2), 2.47 (dd, J = 14.5, 7.3 Hz, 1H, CH_2), 2.38 (m, 1H, CH_2), 1.95 (dd, J = 14.0, 3.4 Hz, 1H, CH_2), 1.78-1.71 (m, 2H, CH and CH_2), 1.61 (s, 6H, CH_3 x2), 1.33 (dd, J = 14.0, 12.3 Hz, 1H, CH_2), 1.24 (s, 3H, CH_3), 0.87 (s, 3H, CH_3), 0.20 (s, 9H, CH_3 x3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.6, 194.5, 184.5, 136.5, 134.3, 125.8, 119.1, 117.1, 87.7, 64.3, 59.9, 48.1, 39.7, 37.8, 35.5, 31.4, 27.8, 25.9, 20.8, 18.0, 0.5 (x3); HRMS calcd for $C_{23}H_{36}O_3SiI$ [$(M+H)^+$] 515.1479, found 515.1483.

15: $R_f \approx 0.19$ (5% ethyl acetate/hexanes); IR (film) 2965, 2935, 1732, 1646, 1558, 1247, 1213, 842 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.64 (m, 1H, CH), 5.05-4.95 (m, 3H), 3.84 (s, 3H, CH_3), 2.81 (s, 1H, CH), 2.51 (dd, J = 14.6, 6.2 Hz, 1H, CH_2), 2.37 (dd, J = 14.6, 7.4 Hz, 1H, CH_2), 2.26 (m, 1H, CH_2), 2.01 (dd, J = 13.9, 2.9 Hz, 1H, CH_2), 1.69-1.62 (m, 2H, CH and CH_2), 1.62 (s, 3H, CH_3), 1.59 (s, 3H, CH_3), 1.37 (dd, J = 13.9, 12.3 Hz, 1H, CH_2), 1.03 (s, 3H, CH_3), 0.81 (s, 3H, CH_3), 0.21 (s, 9H, CH_3 x3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.2, 198.3, 186.4, 136.8, 133.7, 119.5, 116.9, 75.7, 64.0, 59.6, 43.0, 40.6, 38.8, 33.4, 29.8, 26.6, 25.8, 20.5, 18.0, 0.6 (x3); HRMS calcd for $C_{23}H_{37}O_3Si$ [$(M+H)^+$] 389.2506 found 389.2479.

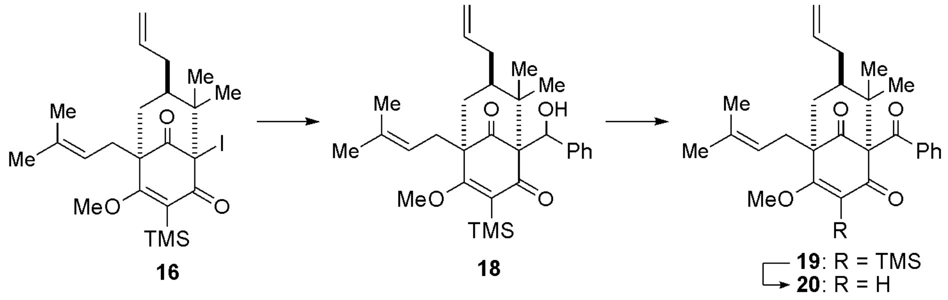
17: $R_f \approx 0.05$ (5% ethyl acetate/hexanes); IR (film) 3447, 2962, 2930, 1636, 1558, 1248, 1055, 842 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.64 (m, 1H, CH), 5.02-4.98 (m, 2H), 4.93 (br t, J = 7.6 Hz, 1H, CH), 3.95 (dd, J = 3.3, <1 Hz, 1H, CH), 3.78 (s, 3H, CH_3), 2.36 (br d, J = 7.6 Hz, 2H, CH_2), 2.27 (m, 1H, CH_2), 2.26 (d, J = 3.3 Hz, 1H, CH), 1.71 (m, 1H, CH_2), 1.65 (s, 3H, CH_3), 1.63 (s, 3H, CH_3), 1.55 (dd, J = 13.3, 9.4 Hz, 1H, CH_2), 1.53 (br s, 1H, OH), 1.49 (dd, J = 13.3, 3.7 Hz, 1H, CH_2), 1.40 (m, 1H, CH), 1.06 (s, 3H, CH_3), 0.88 (s, 3H, CH_3), 0.20 (s, 9H, CH_3 x3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.5, 189.6, 137.8, 134.4, 126.4, 119.1, 116.4, 70.0, 63.5, 63.4, 49.6, 41.5, 34.5, 33.8, 31.2, 30.3, 28.5, 26.0, 24.1, 17.9, 0.8 (x3); HRMS calcd for $C_{23}H_{39}O_3Si$ [$(M+H)^+$] 391.2668, found 391.2683.



15 **16**

Compound **16**

To a solution of compound **15** (18.4 mg, 0.0474 mmol) in THF (0.50 mL) was added TMSCl (0.03 ml, 0.236 mmol) at room temperature and then added freshly prepared LDA solution (0.25 M in THF, 0.66 mL, 0.165 mmol). After stirring for 10 min at -78 °C, the reaction mixture was allowed to warm to 0 C. After stirring for 1 min at 0 °C, to the resultant solution was added iodine (35.0 mg, 0.138 mmol) in THF (0.70 mL) via cannula. The resultant solution was stirred for 15 min at 0 °C, quenched with saturated aqueous $Na_2S_2O_3$, diluted with ethyl acetate, washed with water and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (0-20% ether/hexane) to afford iodide **16** (14.2 mg, 41%) as a colorless oil and starting material **15** (8.4 mg, 46%) as a colorless oil.



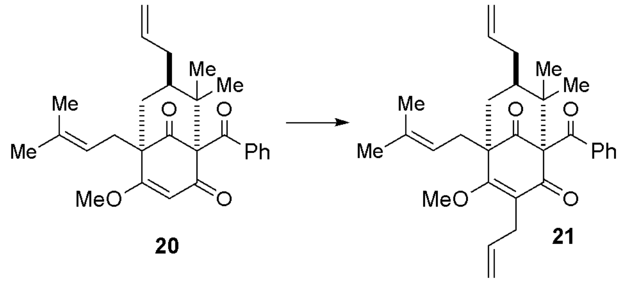
Compound **20**

To a solution of iodide **16** (57.4 mg, 0.112 mmol) in THF (4.0 mL) was added *i*-PrMgCl (2.0 M in THF, 0.11 mL, 0.22 mmol) at -78 °C. After stirring for 4 min at -78 °C, the resultant yellow solution was treated with PhCHO (0.05 mL, 0.492 mmol) at -78 °C and stirred for 4 min at -78 °C. The resultant solution was allowed to warm to 0 °C and stirred for 7 min at 0 °C. The reaction mixture was quenched with saturated aqueous NH_4Cl, diluted with ethyl acetate, washed with water and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford crude alcohol **18** (73.4 mg), which was used for the next reaction without further purification.

To a solution of the above alcohol **18** (73.4 mg) in CH_2Cl_2 (5.0 mL) was added Dess-Martin periodinane (143.0 mg, 0.337 mmol) at room temperature. After stirring for 3 h at room temperature, the reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$, diluted with ethyl acetate, washed with water and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford crude triketone **19**, which was used for the next reaction without further purification.

To a solution of the above triketone **19** in THF (6.0 mL) was added TBAF (1.0 M in THF, 0.48 mL, 0.48 mmol) at room temperature. After stirring for 3 h at room temperature, the reaction mixture was diluted with ether and washed with water and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (1-5% ether/benzene) to afford compound **20** (34.3 mg, 61%) as a colorless oil and compound **15** (14.1 mg, 14%) as a colorless oil.

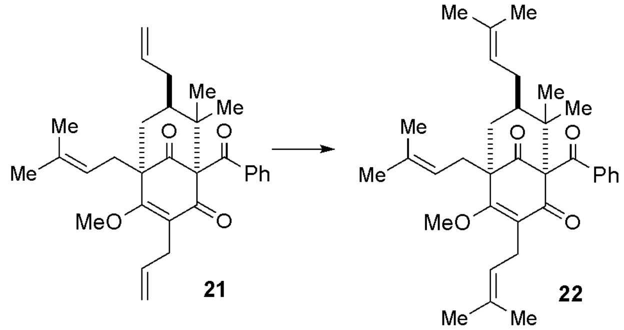
20: $R_f \approx 0.22$ (20% ethyl acetate/hexanes), 0.52 (10% ether/benzene); IR (film) 2938, 1721, 1697, 1642, 1599, 1446, 1370, 1233 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.4 Hz, 2H, CH), 7.38 (t, *J* = 7.4 Hz, 1H, CH), 7.25 (t, *J* = 7.4 Hz, 2H, CH), 5.96 (s, 1H, CH), 5.62 (m, 1H, CH), 5.02-4.98 (m, 3H), 3.85 (s, 3H, CH_3), 2.56 (dd, *J* = 14.2, 6.4 Hz, 1H, CH_2), 2.46 (dd, *J* = 14.2, 7.5 Hz, 1H, CH_2), 2.34 (m, 1H, CH_2), 2.00 (dd, *J* = 13.7, 4.3 Hz, 1H, CH_2), 1.80 (m, 1H, CH), 1.72 (m, 1H, CH_2), 1.65 (s, 3H, CH_3), 1.63 (s, 3H, CH_3), 1.46 (dd, *J* = 13.7, 12.8 Hz, 1H, CH_2), 1.37 (s, 3H, CH_3), 1.10 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.8, 193.2, 193.1, 176.8, 136.8, 136.3, 134.9, 132.1, 128.4 (x2), 128.3, 127.9 (x2), 118.8, 116.8, 106.0, 79.3, 58.2, 57.1, 48.5, 42.1, 40.4, 33.0, 29.1, 26.0, 23.4, 18.0, 15.8; HRMS calcd for $C_{27}H_{33}O_4$ [$(M+H)^+$] 421.2379, found 421.2400.



Compound **21**

To a solution of compound **20** (34.3 mg, 0.0682 mmol) in THF (3.0 mL) was added freshly prepared LDA solution (0.25 M in THF, 0.85 mL, 0.213 mmol) at -78 °C. After stirring for 10 min at -78 °C, to the reaction solution was added lithium 2-thienylcyanocuprate (0.25 M in THF, 0.55 mL, 0.138 mmol) at -78 °C. The reaction solution was stirred at -78 °C for 20 min and treated with allyl bromide (0.10 mL, 1.16 mmol) at -78 °C. After stirring for 20 min at -78 °C, the reaction mixture was quenched with saturated aqueous NH_4Cl, diluted with ethyl acetate, washed with water and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (0-10% ethyl acetate/hexane) to afford compound **21** (27.6 mg, 88%) as a colorless oil.

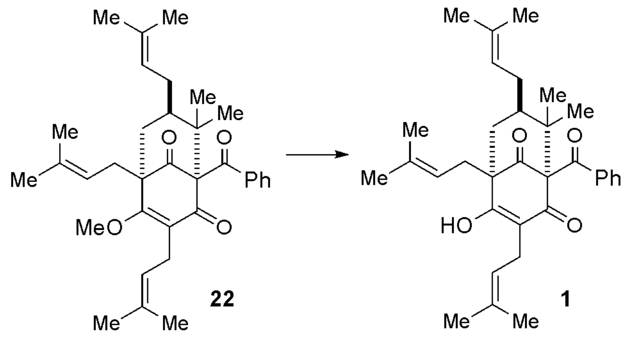
$R_f \approx$ 0.49 (20% ethyl acetate/hexanes); IR (film) 2920, 1718, 1698, 1645, 1638, 1594, 1340, 1239, 1222 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 7.4, 0.9 Hz, 2H, CH), 7.36 (td, *J* = 7.4, 0.9 Hz, 1H, CH), 7.21 (t, *J* = 7.4 Hz, 2H, CH), 5.82 (m, 1H, CH), 5.63 (m, 1H, CH), 5.07-5.02 (m, 5H), 4.04 (s, 3H, CH_3), 3.39 (ddt, *J* = 16.1, 6.0, 1.5 Hz, 1H, CH_2), 3.21 (ddt, *J* = 16.1, 5.7, 1.7 Hz, 1H, CH_2), 2.58 (dd, *J* = 14.3, 6.5 Hz, 1H, CH_2), 2.44 (dd, *J* = 14.3, 7.4 Hz, 1H, CH_2), 2.34 (m, 1H, CH_2), 2.06 (dd, *J* = 13.6, 4.0 Hz, 1H, CH_2), 1.76-1.70 (m, 2H, CH and CH_2), 1.66 (s, 3H, CH_3), 1.63 (s, 3H, CH_3), 1.47 (dd, *J* = 13.6, 12.1 Hz, 1H, CH_2), 1.32 (s, 3H, CH_3), 1.11 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.1, 193.8, 192.9, 173.7, 136.8, 136.2, 135.4, 134.6, 132.0, 128.5 (x2), 127.8 (x2), 123.2, 119.4, 116.9, 115.6, 79.0, 62.2, 59.9, 48.8, 42.5, 40.3, 32.8, 29.8, 28.1, 26.0, 23.4, 18.1, 15.8; HRMS calcd for $C_{30}H_{37}O_4$ [$(M+H)^+$] 461.2692, found 461.2699.



Compound **22**

Compound **21** (25.7 mg, 0.0600 mmol) and Grubbs' 2nd cat (15.9 mg, 0.0187 mmol) was added to a 35 mL Fischer-Porter bottle. Isobutylene (5 mL) was condensed into the bottle at -78 °C. The bottle was sealed, and allowed to slowly warm to 40 °C. After stirring for 12 h, the bottle was removed from the oil bath and allowed to cool to room temperature. The isobutylene was slowly vented off at room temperature. The residue was purified by column chromatography on silica gel (1-10% ethyl acetate/hexane) to afford compound **22** (28.3 mg, 91%) as a colorless oil.

22: $R_f \approx 0.66$ (20% ethyl acetate/hexanes); IR (film) 2966, 2915, 1722, 1698, 1648, 1597, 1446, 1337, 1220 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.42 (br d, J = 7.4, 2H, CH), 7.35 (br t, J = 7.4 Hz, 1H, CH), 7.20 (br t, J = 7.4 Hz, 2H, CH), 5.01 (m, 2H, CH x2), 4.98 (m, 1H, CH), 3.98 (s, 3H, CH_3), 3.23 (dd, J = 15.2, 7.0 Hz, 1H, CH_2), 3.14 (dd, J = 15.2, 6.5 Hz, 1H, CH_2), 2.57 (dd, J = 14.2, 6.6 Hz, 1H, CH_2), 2.42 (dd, J = 14.2, 7.2 Hz, 1H, CH_2), 2.15 (m, 1H, CH_2), 2.00 (dd, J = 13.6, 3.7 Hz, 1H, CH_2), 1.74-1.64 (m, 2H, CH and CH_2), 1.67 (s, 3H, CH_3), 1.66 (s, 3H, CH_3), 1.63 (s, 6H, CH_3 x2), 1.61 (s, 3H, CH_3), 1.56 (s, 3H, CH_3), 1.45 (dd, J = 13.6, 12.2 Hz, 1H, CH_2), 1.33 (s, 3H, CH_3), 1.11 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.3, 194.1, 193.0, 173.1, 136.2, 134.4, 133.5, 133.0, 131.9, 128.6 (x2), 127.7 (x2), 126.7, 122.6, 121.3, 119.5, 79.2, 62.4, 59.8, 48.8, 43.7, 40.2, 29.8, 26.7, 26.0, 25.8, 25.7, 23.4, 23.3, 18.1, 17.9 (x2), 15.7; HRMS calcd for $C_{34}H_{45}O_4$ $[(M+H)^+]$ 517.3318, found 517.3328.

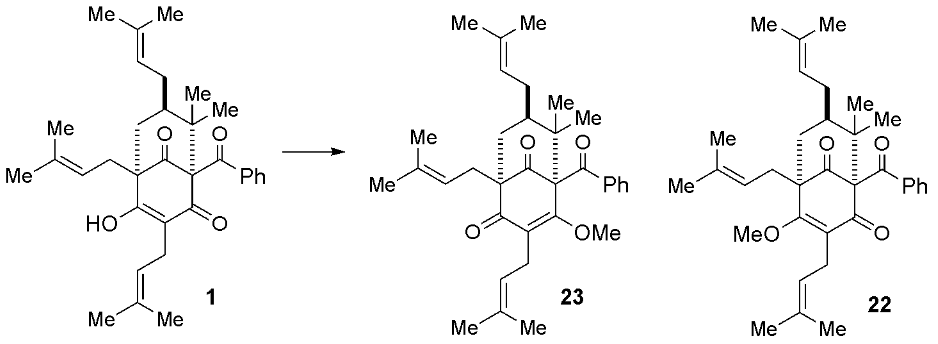


Nemorosone **1**

To a solution of compound **22** (34.5 mg, 0.0669 mmol) in degassed 2,4,6-collidine (1.0 mL) was added lithium iodide (25.3 mg, 0.189 mmol). The reaction mixture was stirred at 140 °C for 1 h and then cooled to room temperature. The resultant mixture was diluted with ether, washed with 1 M HCl, water and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (0-33% ethyl acetate/hexane) to afford nemorosone **1** (11.9 mg, 35%) as a light yellow oil.

$R_f \approx 0.21$ (20% ethyl acetate/hexanes); IR (film) 3363, 2971, 2915, 1724, 1698, 1597, 1446, 1372, 1222 cm^{-1}; ^1H NMR (500 MHz, CD_3OD with 0.7 eq NH_4CO_2H) δ 7.67 (d, J = 7.4 Hz, 2H, CH), 7.39 (t, J = 7.4 Hz, 1H, CH), 7.23 (t, J = 7.4 Hz, 2H, CH), 5.17 (m, 1H, CH), 5.03 (m, 1H, CH), 5.02 (m, 1H, CH), 3.11 (dd, J = 14.2, 7.0 Hz, 1H, CH_2), 3.06 (dd, J = 14.2, 7.0 Hz, 1H, CH_2), 2.46 (d, J = 6.9 Hz, 2H, CH_2), 2.13 (m, 1H, CH_2), 1.99 (dd, J = 13.2, 4.5 Hz, 1H, CH_2), 1.85 (m, 1H, CH), 1.72 (m, 1H, CH_2), 1.674 (s, 3H, CH_3), 1.670 (s, 3H, CH_3), 1.63 (s, 9H, CH_3x3), 1.58 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.35 (t, J = 13.2 Hz, 1H, CH_2), 1.08 (s, 3H, CH_3); ^1H NMR (500 MHz, CD_3OD without NH_4CO_2H) δ 7.54 (d, J = 7.4 Hz, 2H, CH), 7.44 (t, J = 7.4 Hz, 1H, CH), 7.26 (t, J

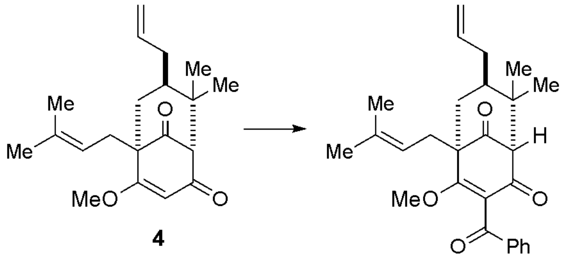
= 7.4 Hz, 2H, CH), 5.08 (m, 1H, CH), 5.02 (m, 1H, CH), 5.01 (m, 1H, CH), 3.13 (dd, *J* = 14.6, 7.3 Hz, 1H, CH_2), 3.08 (dd, *J* = 14.6, 7.3 Hz, 1H, CH_2), 2.51 (m, 1H, CH_2) 2.49 (dd, *J* = 14.1, 7.0 Hz, 1H, CH_2), 2.16 (m, 1H, CH_2), 2.02 (m, 1H, CH_2), 1.75-1.69 (m, 2H, CH and CH_2), 1.69 (s, 3H, CH_3), 1.65 (s, 12H, CH_3x4), 1.60 (s, 3H, CH_3), 1.44 (t, *J* = 13.0 Hz, 1H, CH_2), 1.34 (s, 3H, CH_3), 1.11 (s, 3H, CH_3); ^{13}C NMR (125 MHz, CD_3OD with 0.7 eq NH_4CO_2H) δ 212.3, 196.7, 186.5, 186.2, 139.1, 133.8, 133.6, 132.6, 131.4, 129.7 (x2), 128.5 (x2), 124.6, 124.5, 122.2, 119.5, 78.9, 63.0, 48.1, 44.4, 42.4, 30.8, 28.5, 26.2, 26.1, 26.0, 25.5, 23.1, 18.3, 18.2, 18.0, 16.5; ^{13}C NMR (125 MHz, CD_3OD without NH_4CO_2H) δ 209.2 (br), 194.9, 175.4 (br), 170.9 (br), 138.2, 135.3, 134.2, 133.7, 133.1, 129.6 (x2), 128.8 (x2), 124.0, 121.8, 121.2, 120.8, 82.9 (br), 61.6 (br), 44.6, 44.3 (br), 40.4 (br), 30.4, 28.2 (br), 26.3, 26.1, 26.0, 24.3 (br), 22.3, 18.3, 18.1, 18.0, 16.2; HRMS calcd for $C_{33}H_{43}O_4$ [$(M+H)^+$] 503.3155, found 503.3164; HRMS calcd for $C_{33}H_{41}O_4$ [$(M-H)^-$] 501.3010, found 501.3023.



Re-methylation of nemorosone **1**

To a solution of nemorosone **1** (1.3 mg, 0.0026 mmol) in ether (3.0 mL) was added CH_2N_2 ether solution (1.0 mL, large excess) at 0 °C. After stirring for 10 min at 0 °C, the resultant solution was allowed to warm to room temperature. After stirring for 20 min at room temperature, the reaction mixture was quenched with saturated aqueous $NaHCO_3$, diluted with ether and washed with brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (0-20% ether/hexane) to afford compound **23** (0.8 mg, 60%) as a colorless oil and compound **22** (0.1 mg, 7%) as a colorless oil.

23: $R_f \approx 0.70$ (20% ethyl acetate/hexanes); IR (film) 2966, 2914, 1720, 1700, 1653, 1603, 1446, 1241, 1218 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.6 Hz, 2H, CH), 7.41 (t, *J* = 7.6 Hz, 1H, CH), 7.28 (t, *J* = 7.6 Hz, 2H, CH), 4.99 (m, 1H, CH), 4.98 (m, 1H, CH), 4.90 (m, 1H, CH), 3.44 (s, 3H, CH_3), 3.32 (dd, *J* = 15.4, 6.1 Hz, 1H, CH_2), 3.21 (dd, *J* = 15.4, 5.7 Hz, 1H, CH_2), 2.55 (dd, *J* = 13.9, 7.0 Hz, 1H, CH_2), 2.46 (dd, *J* = 13.9, 7.6 Hz, 1H, CH_2), 2.08 (m, 1H, CH_2), 1.93 (dd, *J* = 13.3, 3.8 Hz, 1H, CH_2), 1.68-1.62 (m, 2H, CH and CH_2), 1.66 (s, 3H, CH_3), 1.65 (s, 12H, CH_3 x4), 1.53 (s, 3H, CH_3), 1.42 (m, 1H, CH_2), 1.33 (s, 3H, CH_3), 1.16 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.9, 197.2, 193.2, 170.0, 137.0, 134.5, 133.2, 133.0, 132.1, 128.4 (x2), 127.9 (x2), 123.2, 122.5, 121.5, 119.7, 74.0, 65.2, 61.6, 47.9, 42.5, 30.3, 29.5, 27.7, 26.0, 25.9, 25.7, 24.5, 23.3, 18.2, 18.0, 17.9, 16.2; HRMS calcd for $C_{34}H_{44}O_4$ [$(M+H)^+$] 517.3318, found 517.3304.



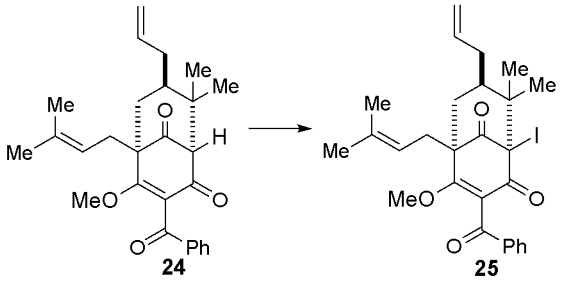
4 **24**

Compound 24

To a solution of compound **4** (36.7 mg, 0.116 mmol) in THF (1.0 mL) was added freshly prepared LDA solution (0.25 M in THF, 0.93 mL, 0.232 mmol) at -78 °C. After stirring for 10 min at -78 °C, the resultant yellow solution was treated with PhCHO (0.02 mL, 0.197 mmol) at -78 °C and stirred for 15 min at -. The reaction mixture was quenched with saturated aqueous NH_4Cl, diluted with ethyl acetate, washed with water and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford crude alcohol (49.6 mg), which was used for the next reaction without further purification.

To a solution of the above alcohol (49.6 mg) in CH_2Cl_2 (5.0 mL) was added Dess-Martin periodinane (53.1 mg, 0.125 mmol) at 0 °C. After stirring for 30 min at 0 °C, the reaction mixture was allowed to warm to room temperature. After stirring for 30 min at room temperature, the reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$, diluted with ethyl acetate, washed with water and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (0-20% ethyl acetate/hexanes) to afford compound **24** (28.0 mg, 57% for two steps) as a colorless oil.

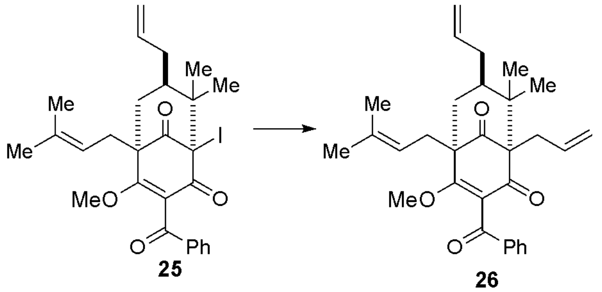
24: $R_f \approx 0.51$ (20% ethyl acetate/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, J = 7.9 Hz, 2H, CH), 7.54 (t, J = 7.9 Hz, 1H, CH), 7.43 (t, J = 7.9 Hz, 2H, CH), 5.74 (m, 1H, CH), 5.12 (m, 1H, CH), 5.06 (br d, J = 9.4 Hz, 1H, CH_2), 5.05 (br d, J = 17.6 Hz, 1H, CH_2), 3.65 (s, 3H, CH_3), 2.91 (s, 1H, CH), 2.54 (dd, J = 14.2, 5.3 Hz, 1H, CH_2), 2.42 (dd, J = 14.2, 8.6 Hz, 1H, CH_2), 2.33 (m, 1H, CH_2), 2.13 (dd, J = 13.4, 4.5 Hz, 1H, CH_2), 2.05 (m, 1H, CH), 1.73 (m, 1H, CH_2), 1.69 (s, 3H, CH_3), 1.62 (s, 3H, CH_3), 1.43 (t, J = 13.4 Hz, 1H, CH_2), 1.08 (s, 3H, CH_3), 0.85 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.7, 195.4, 192.7, 174.1, 137.8, 136.7, 134.3, 133.8, 129.2 (x2), 128.9, (x2), 121.3, 119.4, 116.9, 74.8, 60.7, 58.7, 43.7, 40.0, 39.8, 33.7, 30.2, 26.5, 26.0, 20.6, 17.9; HRMS calcd for $C_{27}H_{33}O_4$ [$(M+H)^+$] 421.2373, found 421.2369.



Compound **25**

To a solution of compound **24** (28.4 mg, 0.0667 mmol) in THF (1.0 mL) was added TMSCl (0.04 ml, 0.315 mmol) at room temperature and then added freshly prepared LDA solution (0.25 M in THF, 0.95 mL, 0.238 mmol) at -78 °C. After stirring for 10 min at -78 °C, the reaction mixture was allowed to warm to 0 °C. After stirring for 1 min at 0 °C, to the resultant solution was added iodine (49.9 mg, 0.197 mmol) in THF (1.0 mL) via cannula. The resultant solution was stirred for 15 min at 0 °C, quenched with saturated aqueous $Na_2S_2O_3$, diluted with ethyl acetate, washed with water and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (0-20% ether/hexane) to afford iodide **25** (17.3 mg, 48%) as a colorless oil.

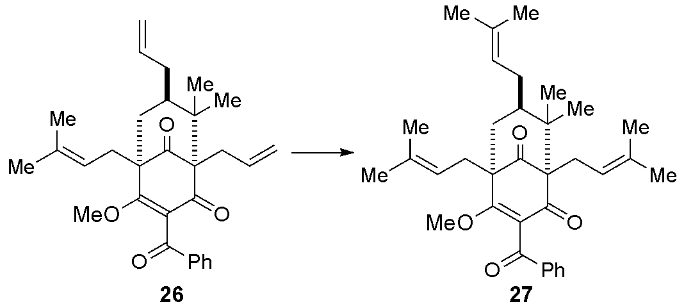
25: $R_f \approx 0.46$ (20% ethyl acetate/hexanes); IR (film) 2975, 2940, 1736, 1676, 1647, 1582, 1448, 1330, 1277 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.4 Hz, 2H, CH), 7.55 (t, *J* = 7.4 Hz, 1H, CH), 7.43 (t, *J* = 7.4 Hz, 2H, CH), 5.74 (m, 1H, CH), 5.12 (m, 1H, CH), 5.09 (br d, *J* = 6.4 Hz, 1H, CH_2), 5.06 (br d, *J* = 16.2 Hz, 1H, CH_2), 3.65 (s, 3H, CH_3), 2.61 (dd, *J* = 14.4, 6.0 Hz, 1H, CH_2), 2.54 (dd, *J* = 14.2, 7.9 Hz, 1H, CH_2), 2.44 (m, 1H, CH_2), 2.17-2.10 (m, 2H, CH and CH_2), 1.78 (m, 1H, CH_2), 1.68 (s, 3H, CH_3), 1.64 (s, 3H, CH_3), 1.53 (t, *J* = 12.9 Hz, 1H, CH_2), 1.22 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.2, 194.2, 189.4, 173.4, 137.4, 136.5, 134.7, 133.9, 129.1 (x2), 128.9, (x2), 119.13, 119.11, 117.2, 86.3, 61.4, 59.0, 48.8, 39.3, 38.9, 35.8, 31.7, 27.6, 25.9, 21.0, 18.0; HRMS calcd for $C_{27}H_{32}O_4I$ [$(M+H)^+$] 547.1339, found 547.1334.



Compound **26**

To a solution of iodide **25** (17.2 mg, 0.0317 mmol) in benzene (5 mL) was added allyltributylstannane (0.05 mL, 0.161 mmol) and Et_3B (1.0 M in hexane, 0.09 mL, 0.09 mmol). The reaction mixture was stirred at room temperature for 2 h. The resultant solution was directly purified by column chromatography on silica gel (0-10% ether/hexanes) to afford compound **26** (10.3 mg, 71%) as a colorless oil.

26: $R_f \approx 0.56$ (20% ethyl acetate/hexanes); IR (film) 2977, 2943, 1724, 1675, 1638, 1596, 1338, 1280 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, J = 7.4 Hz, 2H, CH), 7.53 (t, J = 7.4 Hz, 1H, CH), 7.40 (t, J = 7.4 Hz, 2H, CH), 5.72 (m, 1H, CH), 5.54 (m, 1H, CH), 5.08-5.01 (m, 3H), 4.98 (br d, J = 17.8 Hz, 1H, CH_2), 4.95 (br d, J = 10.6 Hz, 1H, CH_2), 3.60 (s, 3H, CH_3), 2.60 (dd, J = 13.0, 7.2 Hz, 1H, CH_2), 2.58-2.52 (m, 2H, CH_2), 2.45 (dd, J = 14.4, 8.2 Hz, 1H, CH_2), 2.33 (m, 1H, CH_2), 2.11 (dd, J = 13.4, 4.5 Hz, 1H, CH_2), 1.98 (m, 1H, CH_2), 1.69 (m, 1H, CH), 1.67 (s, 3H, CH_3), 1.63 (s, 3H, CH_3), 1.44 (t, J = 13.4 Hz, 1H, CH_2), 1.01 (s, 3H, CH_3), 0.71 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.8, 195.5, 194.8, 173.1, 137.8, 136.9, 134.4, 133.8, 133.6, 129.3 (x2), 128.6 (x2), 122.6, 119.8, 119.0, 116.7, 71.3, 60.8, 57.7, 47.1, 40.8, 40.1, 34.0, 30.7, 29.7, 25.9, 22.4, 18.0, 15.9; HRMS calcd for $C_{30}H_{37}O_4$ $[(M+H)^+]$ 461.2686, found 461.2696.

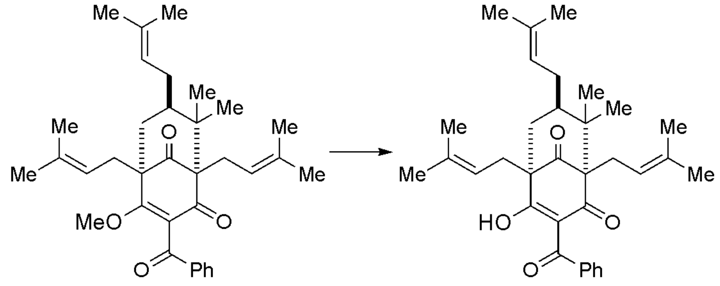


26 **27**

Compound **27**

Compound **26** (12.9 mg, 0.0280 mmol) and Grubbs' 2nd cat (7.7 mg, 0.0091 mmol) was added to a 35 mL Fischer-Porter bottle. Isobutylene (5 mL) was condensed into the bottle at -78 °C. The bottle was sealed, and allowed to slowly warm to 40 °C. After stirring for 8 h, the bottle was removed from the oil bath and allowed to cool to room temperature. The isobutylene was slowly vented off at room temperature. The residue was purified by column chromatography on silica gel (0-20% ether/hexanes) to afford compound **27** (13.6 mg, 94%) as a colorless oil.

27: $R_f \approx 0.71$ (20% ethyl acetate/hexanes); IR (film) 2973, 2915, 1726, 1674, 1643, 1598, 1448, 1336, 1279 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, J = 7.4 Hz, 2H, CH), 7.52 (t, J = 7.4 Hz, 1H, CH), 7.40 (t, J = 7.4 Hz, 2H, CH), 5.08 (m, 1H, CH), 5.05 (m, 1H, CH), 4.80 (m, 1H, CH), 3.60 (s, 3H, CH_3), 2.56-2.51 (m, 2H, CH_2), 2.47-2.41 (m, 2H, CH_2), 2.12 (m, 1H, CH_2), 2.05 (dd, J = 13.8, 4.5 Hz, 1H, CH_2), 1.87 (m, 1H, CH_2), 1.72 (s, 3H, CH_3), 1.68 (m, 1H, CH), 1.67 (s, 3H, CH_3), 1.63 (s, 3H, CH_3), 1.57 (s, 6H, CH_3 x2), 1.51 (s, 3H, CH_3), 1.40 (t, J = 13.8 Hz, 1H, CH_2), 1.02 (s, 3H, CH_3), 0.72 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.7, 195.6, 195.5, 172.9, 137.9, 134.2, 133.6, 133.4, 133.1, 129.2 (x2), 128.6 (x2), 122.64, 122.56, 120.1 (x2), 71.0, 60.7, 57.7, 47.0, 41.8, 40.2, 30.7, 28.0, 26.1, 26.0, 25.9, 24.6, 22.4, 18.04, 17.98, 17.92, 15.9; HRMS calcd for $C_{34}H_{45}O_4$ $[(M+H)^+]$ 517.3312, found 517.3311.



27 **2**

Clusianone **2**

To a solution of compound **27** (9.7 mg, 0.0188 mmol) in dioxane (1.0 mL) was added 2M aq. NaOH (1.0 mL) at room temperature. The reaction mixture was heated to 90 °C and stirred for 4h. After the solution was cooled to room temperature, 1M aq. HCl (2.0 mL) was added to the reaction mixture. The mixture was diluted with ethyl acetate, washed with water, 1M aq.$NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (20-40% ethyl acetate/hexanes) to afford clusianone **2** (6.4 mg, 68%).

2: $R_f \approx 0.45$ (20% ethyl acetate/hexanes); IR (film) 2972, 2912, 1728, 1667, 1557, 1447, 1395, 1376 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.53-7.48 (m, 3H), 7.37-7.33 (m, 2H), 5.17-5.11 (m, 1H), 5.00 (m, 0.4H), 4.95 (br t, *J* = 6.8 Hz, 0.4H), 4.88 (br t, *J* = 7.2 Hz, 0.6H), 4.80 (br t, *J* = 6.8 Hz, 0.6H), 2.72-2.68 (m, 1.6H), 2.61 (m, 0.8H), 2.53 (dd, *J* = 9.2, 14.0 Hz, 0.6H), 2.46-2.38 (m, 1H), 2.13 (dd *J* = 13.6, 4.2 Hz, 0.4H), 2.11-2.04 (m, 1H), 1.99 (dd *J* = 13.2, 4.0 Hz, 0.6H), 1.76 (s, 1.2H), 1.74 (s, 1.8H), 1.68 (s, 4.8H), 1.67 (s, 1.2H), 1.64 (s, 1.2H), 1.62 (s, 1.8H), 1.60-1.56 (s, 3.8H), 1.54 (s, 1.2H), 1.50 (s, 1.8H), 1.50 (m, 0.6H), 1.36 (t *J* = 13.1 Hz, 0.6H), 1.21 (s, 1.8H), 1.03 (s, 1.2H), 0.82 (s, 1.8H), 0.71 (s, 1.2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ major 207.4, 197.5, 194.7, 193.9, 137.2, 134.62, 134.5, 133.3, 132.50, 128.9 (x2), 127.8 (x2), 122.2, 119.9, 119.11, 116.9, 67.3, 64.6, 48.6, 42.9, 42.3, 30.6, 28.5, 26.07, 26.0, 25.7, 24.9, 23.7, 18.14, 18.11, 17.9, 16.4, minor 207.6, 197.8, 195.5, 192.6, 137.2, 134.60, 134.5, 133.3, 132.53, 129.0 (x2), 127.7 (x2), 122.3, 120.4, 119.07, 116.1, 71.0, 59.6, 47.6, 42.9, 41.5, 29.9, 28.1, 26.14, 26.0, 25.8, 25.5, 22.6, 18.2, 18.07, 17.9, 16.2; HRMS calcd for $C_{33}H_{41}O_4$ $[(M+H)^-]$ 517.3010, found 501.3008.