An Approach to the Synthesis of Tricholomalide A: An Effective Means for Achieving Homo-Robinson Annulation

Sun-Joon Min[a] and Samuel J. Danishefsky [a,b,*]

[a]*Department of Chemistry, Columbia University, 3000 Broadway, New York, NY 10027, USA*

[b]*Laboratory for Bioorganic Chemistry, Sloan-Kettering Institute for Cancer Research, 1275 York Avenue, New York, NY 10065, USA,*

Supporting Information

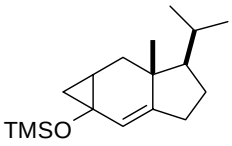
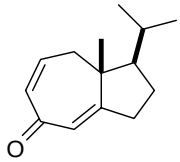
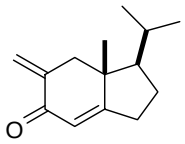
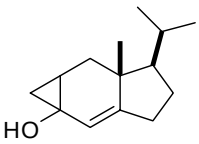
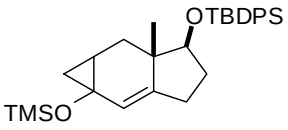
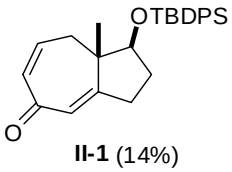
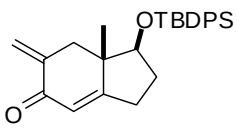
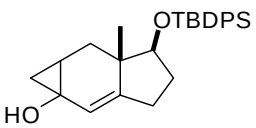
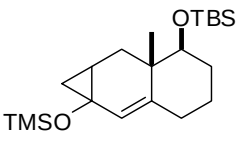
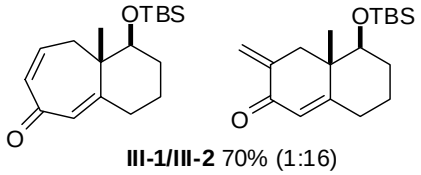
Experimental Procedure

General. All non-aqueous reactions were carried out in oven-dried glassware under a slight positive pressure of argon unless otherwise noted. All reagents were commercially available and used without further purification from Sigma-Aldrich and TCI America, unless indicated otherwise. Solvents were reagent grade and purified by standard techniques: THF was distilled from Na-benzophenone or filtered through a dry-solvent system; CH_2Cl_2 was distilled from CaH_2 or filtered through a dry-solvent system; all other solvents were Aldrich "anhydrous" grade solvents, unless indicated otherwise. Reactions were magnetically stirred and monitored by thin layer chromatography on Merck silica gel 60-F254 coated 0.25 mm plates. Preparative thin layer chromatography was performed with Merck silica gel 60-F254 coated 0.50 mm plates. Flash

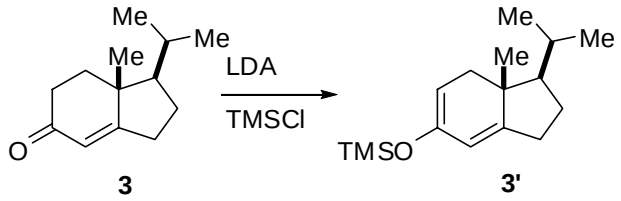
* Corresponding author. Tel.: +1-212-639-5501; fax: +1-212-772-8691; e-mail: danishes@mskcc.org

chromatography was performed with Sorbent Technology silica gel 60 (particle size 32-63 μm), unless indicated otherwise. Yields reported are for isolated, spectroscopically pure compounds. Melting points are uncorrected. $CDCl_3$ was allowed to stand over K_2CO_3 and 4Å MS to neutralize and dry prior to NMR sample preparation. NMR spectra were recorded on Bruker DRX 300, DRX 400 or DMX 500MHz spectrometers. ^1H and ^{13}C chemical shifts were referenced to residual solvent peaks. IR spectra were recorded on a Perkin-Elmer Paragon 1000 FTIR spectrometer. High resolution mass spectra were acquired in the Columbia University Mass Spectral Core facility on a JEOL HX110 spectrometer.

Table. Examination of ring expansion protocol described in the original literature[1]

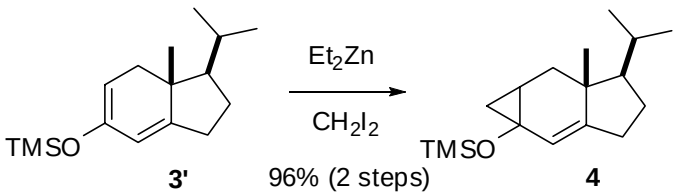
Substrates	Results		
 **4**	 **I-1** (11%)	 **I-2** (45%)	 **I-3** (12%)
 **II**	 **II-1** (14%)	 **II-2** (27%)	 **II-3** (44%)
 **III**	 **III-1/III-2** 70% (1:16)		

[1] Yun, H.; Danishefsky S. J. *Tetrahedron Lett*. **2005**, *46*, 3879–3882.



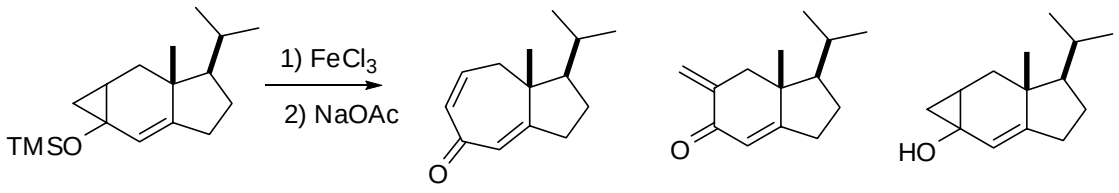
Silyloxydiene (3′). To a solution of diisopropylamine (2.04 mL, 14.5 mmol) in tetrahydrofuran (20 mL) cooled to –78 °C was added *n*-butyllithium (5.20 mL, 2.5 M in hexane). After 5 min, the solution was warmed to 0 °C and stirred for 30 min. The mixture was cooled to –78 °C again and then a solution of enone **3** (1.00 g, 5.20 mmol) in tetrahydrofuran (6 mL) was added. After 30 min, chlorotrimethylsilane was added and the mixture was stirred for 40 min. The reaction mixture was quenched with aqueous ammonium chloride (30 mL), extracted with diethyl ether (3 x 30 mL), washed with brine and buffer solution (pH 7), and dried over magnesium sulfate. The solution was concentrated under reduced pressure to give the silyl enol ether **3′** (1.38 g, quantitative) as yellowish oil, which was directed used for the next step without further purification.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.37 (m, 1H), 4.60 (m, 1H), 2.43 (m, 1H), 2.32-2.22 (m, 3H), 1,96-1.89 (m, 1H), 1.57 (dqq, J = 9.3, 6.6, 6.6 Hz, 1H), 1.41-1.27 (m, 2H), 0.93 (d, J = 6.6 Hz, 3H), 0.90 (d, J = 6.6 Hz, 3H), 0.90 (s, 3H), 0.18 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 156.2, 148.2, 115.9, 89.3, 58.5, 43.7, 37.4, 29.5, 28.4, 27.2, 23.0, 22.4, 15.4, 0.2.



Silyloxycyclopropane (4). To a solution of crude silyl enol ether **3′** (1.38 g, 5.20 mmol) in diethyl ether (25 mL) were added diethylzinc (10.4 mL, 1.0 M in hexane) and

diiodomethane (1.05 mL, 13.0 mmol) at 0 °C. The reaction was allowed to warm up to 23 °C. After 24 h, the reaction mixture was cooled to 0 °C and quenched with aqueous ammonium chloride (30 mL). After separation, the ether layer was filtered through a short pad of silica gel, which was washed with a 20:1 solution of ether and pentane. The combined filtrates were washed with aqueous ammonium chloride and brine. The solution was dried over magnesium sulfate and concentrated under reduced pressure. The resulting crude oil was purified by flash column chromatography on silica gel (20:1 hexane/diethyl ether) to afford silyloxycyclopropane **4** (1.39 g, 96% from **3**) as yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.56 (dd, J = 3.4, 1.9 Hz, 1H), 2.52 (dd, J = 13.5, 8.6 Hz, 1H), 2.35 (br dd, J = 17.8, 9.8 Hz, 1H), 2.09 (dddd, J = 17.8, 11.0, 9.2, 2.2 Hz, 1H), 1.81 (dddd, J = 12.6, 8.7, 6.5, 1.4 Hz, 1H), 1.56 (dqq, J = 9.4, 6.6, 6.6 Hz, 1H), 1.32 (dddd, J = 12.4, 12.4, 10.4, 10.4, 1H), 1.24-1.11 (m, 2H), 1.09 (s, 3H), 0.98 (ddd, J = 12.2, 9.2, 6.5 Hz, 1H), 0.92 (d, J = 6.6 Hz, 3H), 0.88 (d, J = 6.6 Hz, 3H), 0.29 (dd, J = 4.5, 4.4 Hz, 1H), 0.14 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 153.9, 119.4, 57.9, 56.4, 45.5, 43.9, 29.4, 28.9, 27.6, 23.0, 22.8, 19.6, 17.1, 1.5.



4 **I-1** (11%) **I-2** (45%) **I-3** (12%)

Dieneones (I-1) and (I-2). To a solution of iron(III) chloride (146 mg, 0.90 mmol) in DMF (3 mL) cooled to 0 °C was slowly added silyloxycyclopropane **4** (100 mg, 0.36 mmol) in DMF (2 mL) over 2 h via syringe pump and then stirred at 23 °C for 16 h. The

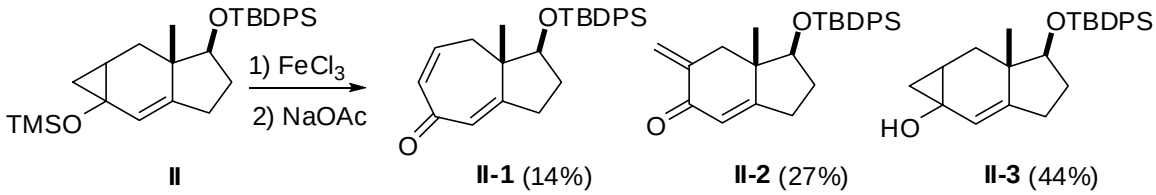
mixture was poured into ice cold 1N HCl solution (15 mL). The aqueous solution was extracted with diethyl ether (3 x 15 mL). The combined organic extracts were washed with 1N HCl, aqueous sodium bicarbonate, and brine, dried over magnesium sulfate, and concentrated under reduced pressure. The resulting crude materials were treated with saturated sodium acetate in methanol (3 mL) and stirred at 80 °C for 3 h. The reaction was cooled to 23 °C and quenched with water (15 mL). The solution was extracted with diethyl ether (3 x 15 mL), washed with brine, dried over magnesium sulfate, and concentrated under reduced pressure. The crude products were purified by column chromatography on silica gel (15:1 hexane/ethyl acetate) to give **I-1** (8 mg, 11%), **I-2** (33 mg, 45%) and **I-3** (9 mg, 12%). The spectral data of **I-1** was identical to that published in the literature[2].

I-2: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.07 (dd, J = 2.2, 2.2 Hz, 1H), 5.89 (br s, 1H), 5.30 (dd, J = 2.1, 2.1 Hz, 1H), 2.95 (d, J = 13.8 Hz, 1H), 2.67 (dddd, J = 20.0, 10.5, 2.1, 2.1 Hz, 1H), 2.60 (br d, J = 13.8 Hz, 1H), 2.48 (dddd, J = 20.0, 9.0, 9.0, 1.7 Hz, 1H), 2.04 (dddd, J = 12.8, 9.2, 6.9, 2.1 Hz, 1H), 1.69 (dqq, J = 9.3, 6.6, 6.6 Hz, 1H), 1.55 (dddd, J = 12.8, 12.8, 10.4, 9.0 Hz, 1H), 1.41 (ddd, J = 11.9, 7.0, 9.3 Hz, 1H), 1.04 (d, J = 6.6 Hz, 3H), 1.01 (s, 3H), 0.97 (d, J = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 187.7, 180.2, 141.0, 121.6, 121.1, 57.3, 46.6, 46.3, 29.6, 29.0, 27.4, 22.8, 22.5, 18.0. HRMS (FAB) *m/z* found for $(M+H)^+$ 205.1583 calcd for $C_{14}H_{21}O$ 205.1592.

I-3: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.60 (dd, J = 3.6, 2.0 Hz, 1H), 2.53 (dd, J = 13.7, 8.6 Hz, 1H), 2.37 (dddd, J = 18.0, 9.8, 1.5, 1.5 Hz, 1H), 2.12 (dddd, J = 18.0, 11.0, 9.1, 2.3 Hz, 1H), 1.86-1.79 (m, 2H), 1.57 (dqq, J = 9.2, 6.6, 6.6 Hz, 1H), 1.33 (dddd, J = 12.5,

[2] Mandal, M.; Yun, H.; Dudley, G. B.; Lin, S.; Tan, D. S.; Danishefsky, S. J. *J. Org. Chem*. **2005**, *70*, 10619-10637.

12.5, 10.7, 9.8 Hz, 1H), 1.30-1.19 (m, 2H), 1.15-1.07 (m, 1H), 1.07 (s, 3H), 1.00 (ddd, *J* = 12.6, 9.4, 6.5 Hz, 1H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.38 (dd, *J* = 4.8, 4.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*:. HRMS (FAB) *m/z* found for $(M+H)^+$ 207.1059 calcd for $C_{14}H_{23}O$ 207.1749.



II **II-1** (14%) **II-2** (27%) **II-3** (44%)

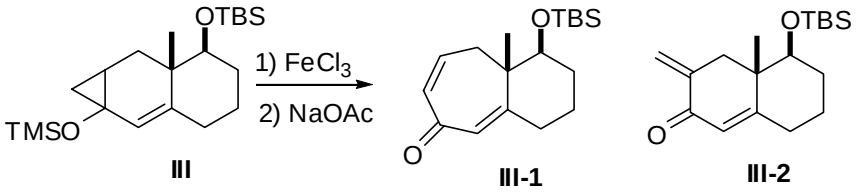
Dieneones (II-1) and (II-2). Following the same procedure as that used for the ring opening reaction of **4**, the reaction of silyloxycyclopropane **II** (140 mg, 0.29 mmol) and iron (III) chloride (116 mg, 0.72 mmol) in DMF (5 mL) followed by treatment of saturated sodium acetate in methanol (3 mL) gave **II-1** (32 mg, 27%), **II-2** (17 mg, 14%), and **II-3** (52 mg, 44%) after purification by column chromatography on silica gel (12:1 hexane/ethyl acetate).

II-1: ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 7.70-7.66 (m, 4H), 7.48-7.37 (m, 6H), 6.39 (ddd, *J* = 12.1, 8.6, 2.9 Hz, 1H), 6.09 (ddd, *J* = 12.1, 3.0, 2.1, 1H), 5.89 (dd, *J* = 4.0, 2.0 Hz, 1H), 3.83 (dd, *J* = 10.7, 6.7 Hz, 1H), 2.52-2.45 (m, 1H), 2.49 (dd, *J* = 16.7, 8.7 Hz, 1H), 2.27-2.17 (m, 2H), 1.83-1.63 (m, 2H), 1.23 (s, 3H), 1.09 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 190.5, 167.2, 140.3, 135.9, 134.0, 129.9, 129.8, 127.7, 127.6, 126.4, 81.7, 49.4, 37.3, 29.8, 28.7, 27.0, 19.4, 16.5. HRMS (FAB) *m/z* found for $(M+H)^+$ 417.2252 calcd for $C_{27}H_{33}O_2Si$ 417.2250.

II-2: ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 7.74-7.65 (m, 4H), 7.47-7.35 (m, 6H), 3.87 (dd, *J* = 10.1, 7.4 Hz, 1H), 6.05 (dd, *J* = 2.2, 2.2 Hz, 1H), 5.82 (s, 1H), 5.25 (dd, *J* = 2.0, 2.0 Hz,

1H), 2.61 (dddd, J = 20.0, 10.9, 2.2, 2.2 Hz, 1H), 2.59 (d, J = 13.8 Hz, 1H), 2.24 (dddd, J = 20.0, 9.3, 9.3, 1.6 Hz, 1H), 2.19 (br d, J = 13.8 Hz, 1H), 1.91-1.72 (m, 2H), 1.16 (s, 3H), 1.11 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 187.9, 174.7, 140.5, 135.9, 134.8, 134.0, 133.5, 130.0, 129.8, 127.7, 127.6, 123.3, 121.5, 80.9, 47.4, 43.4, 29.7, 27.0, 26.5, 19.3, 17.3. HRMS (FAB) *m/z* found for $(M+H)^+$ 417.2261 calcd for $C_{27}H_{33}O_2Si$ 417.2250.

II-3: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.69-7.66 (m, 4H), 7.45-7.35 (m, 6H), 5.58 (dd, J = 3.5, 2.0 Hz, 1H), 3.55 (dd, J = 10.5, 6.8 Hz, 1H), 2.35 (dd, J = 13.6, 8.8 Hz, 1H), 2.31 (dddd, J = 18.2, 10.2, 1.8, 1.8 Hz, 1H), 1.95-1.85 (m, 2H), 1.66 (dddd, J = 12.3, 12.3, 10.4, 10.4, 1H), 1.51 (dddd, J = 12.3, 8.7, 6.9, 1.7 Hz, 1H), 1.33-1.27 (m, 1H), 1.24 (s, 3H), 1.20 (dd, J = 9.8, 4.6 Hz, 1H), 1.08 (s, 9H), 0.84 (dd, J = 13.2, 5.1 Hz, 1H), 0.30 (dd, J = 5.1, 5.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 150.5, 135.93, 135.88, 134.6, 133.9, 129.6, 129.5, 127.5, 127.4, 120.0, 81.8, 55.6, 45.2, 42.4, 29.9, 28.3, 27.0, 24.8, 19.4, 19.2, 17.8. HRMS (FAB) *m/z* found for $(M+H)^+$ 419.2415 calcd for $C_{27}H_{35}O_2Si$ 419.2406.



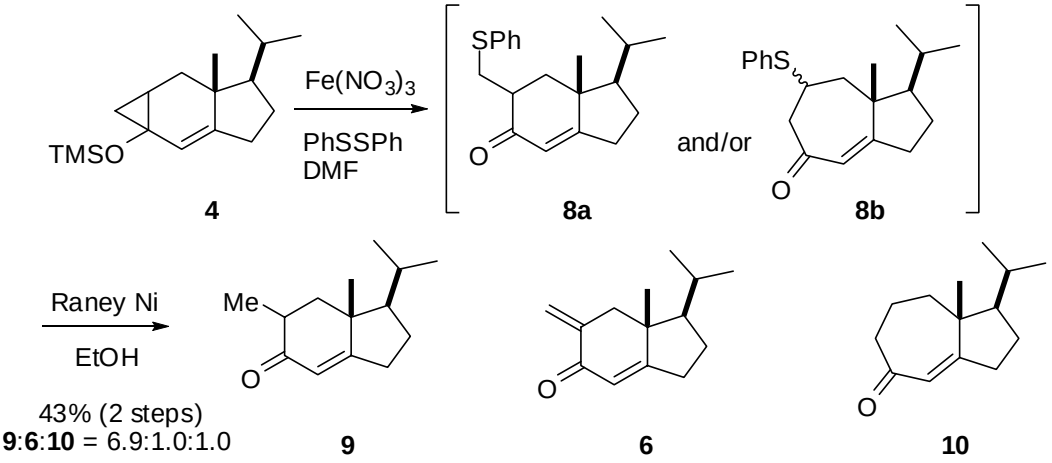
III **III-1** **III-2**

70% (1:16)

Dienones (III-1) and (III-2). Following the same procedure as that used for the ring opening reaction of **4**, the reaction of silyloxycyclopropane **III** (150 mg, 0.39 mmol) and iron (III) chloride (160 mg, 1.00 mmol) in DMF (5 mL) followed by treatment of saturated sodium acetate in methanol (3 mL) gave a 16:1 inseparable mixture of **III-1** and **III-2** (85 mg, 70%) after purification by column chromatography on silica gel (15:1 hexane/ethyl acetate).

III-1: Partial ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.46 (ddd, J = 11.2, 9.1, 4.7 Hz, 1H), 6.16 (ddd, J = 11.2, 2.1, 2.1 Hz, 1H), 5.98 (dd, J = 1.8, 1.8 Hz, 1H).

III-2: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5. 95 (dd, J = 2.1, 2.1 Hz, 1H), 5.87 (d, J = 1.6 Hz, 1H), 5.23 (m, 1H), 3.43 (dd, J = 11.2, 4.5 Hz, 1H), 2.74 (d, J = 14.2, 1H), 2.45 (br d, J = 14.2 Hz, 1H), 2.33 (dddd, J = 15.2, 13.3, 5.7, 2.1 Hz, 1H), 2.27-2.23 (m, 1H), 1.84 (dddd, J = 13.3, 5.7, 5.7, 3.2 Hz, 1H), 1.77-1.70 (m, 1H), 1.65 (dddd, J = 13.2, 13.2, 11.3, 3.8 Hz, 1H), 1.39 (dddd, J = 13.2, 13.2, 4.5, 4.5 Hz, 1H), 1.08 (s, 3H), 0.91 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 188.9, 169.5, 141.2, 125.8, 120.4, 78.4, 44.1, 44.0, 31.9, 30.7, 25.8, 22.9, 18.0, 16.7, -3.9, -4.9. HRMS (FAB) *m/z* found for $(M+H)^+$ 307.2100 calcd for $C_{18}H_{31}O_2Si$ 307.2093.



4 **8a** **8b** **9** **6** **10**

α-Methyl enone (9). To a solution of silyloxypropane **4** and diphenyldiselenide in DMF (0.5 mL) was added a solution of iron (III) nitrate in DMF (prepared by treatment of iron (III) nitrate nonahydrate with 4Å molecular sieves for 12 h) at 0 °C over 30 min. The orange/red solution was stirred at 0 °C for a further 1 h and then allowed to warm to 23 °C. The reaction mixture was poured into water and extracted with ethyl acetate (4 x 10 mL). The combined organic extracts were washed with water and brine, dried over

magnesium sulfate, filtrated and the solvent was removed under reduced pressure. The resultant oil was purified by column chromatography to remove the disulfide residue.

The mixture of the previous sulfides was dissolved in ethanol (1 mL) and then treated with excess Raney-Nickel (washed with water and ethanol three times) under vigorous magnetic stirring. After being stirred at 23 °C for 24 h, the reaction was filtered through a pad of Celite. The filtrate was treated with ammonium chloride and extracted with diethyl ether (3 x 10 mL). The organic layer was washed with brine, dried over magnesium sulfate and concentrated under reduced pressure. The crude material was purified by column chromatography to give a 6.9:1.0:1.0 mixture of **9**, **6**, and **10** (16 mg, 43%, 2 steps). The spectral data of **10** was identical to that published in the literature[1].

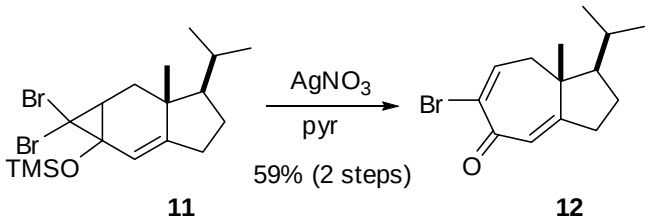
9: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.70 (dd, J = 1.8, 1.8 Hz, 1H), 2.60 (dddd, J = 19.5, 11.3, 2.2, 2.2 Hz, 1H), 2.52 (dddd, J = 20.2, 6.7, 6.7, 4.9 Hz, 1H), 2.36 (dddd, J = 17.8, 9.6, 8.3, 1.6 Hz, 1H), 2.23 (dd, J = 13.0, 4.8 Hz, 1H), 1.97 (dddd, J = 13.4, 9.8, 7.6, 2.7 Hz, 1H), 1.67 (dqq, J = 9.4, 6.6, 6.6 Hz, 1H), 1.59 (dd, J = 13.3, 13.2 Hz, 1H), 1.51 (dddd, J = 13.2, 11.4, 11.4, 8.2 Hz, 1H), 1.27 (ddd, J = 11.6, 9.5, 7.7 Hz, 1H), 1.12 (d, J = 6.8 Hz, 1H), 1.10 (s, 3H), 0.99 (d, J = 6.6 Hz, 3H), 0.93 (d, J = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 201.5, 178.6, 121.1, 57.7, 46.4, 45.5, 36.6, 29.8, 28.6, 26.8, 22.8, 22.5, 16.6, 15.9. HRMS (FAB) *m/z* found for $(M+H)^+$ 207.1741 calcd for $C_{14}H_{23}O$ 207.1749.

3 **11**

Dibromocyclopropane (11). Following the same procedure as that used for the formation of **3′**, the reaction of enone **3** (6.00 g, 31.2 mmol) and LDA (prepared from diisopropylamine (12.2 mL, 87.0 mmol) and *n*-buthyllithium (31.2 mL, 2.5 M in hexane)) in THF (150 mL) followed by addition of chlorotrimethylsilane (7.89 mL, 62.4 mmol) gave silyloxydienone **3′**, which was used for the next step without further purification.

To a solution of crude silyloxydienone **3′** and potassium *tert*-butoxide (5.35 g, 47.7 mmol) in pentane (100 mL) cooled to 0°C was added bromoform (3.96 mL, 45.3 mmol) over a period of 1.5 h. Then the mixture was allowed to warm to 23 °C, stirring was continued for 3 h, and the mixture was filtered through a pad of Celite. The precipitate was washed with pentane and the combined filtrate and washings were evaporated under reduced pressure to give a mixture of the starting material **3′** and dibromocyclopropane **11**. Repeating the procedure one more time afforded crude dibromocycloproprane **11**, which was used for the next step without further purification.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.41 (dd, J = 4.0, 2.0 Hz, 1H), 2.63 (dd, J = 14.1, 10.2 Hz, 1H), 2.39 (br dd, J = 18.2, 9.6 Hz, 1H), 1.90-1.82 (m, 2H), 1.62-1.50 (m, 2H), 1.33 (dddd, J = 12.4, 12.4, 10.8, 9.8 Hz, 1H), 1.11 (ddd, J = 12.2, 9.3, 6.4 Hz), 1.02 (s, 3H), 0.96 (d, J = 6.6 Hz, 3H), 0.91 (d, J = 6.6 Hz, 3H), 0.25 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 159.3, 115.0, 62.0, 57.2, 51.6, 43.4, 41.2, 34.8, 29.3, 28.0, 25.2, 23.0, 22.6, 20.6, 1.2.

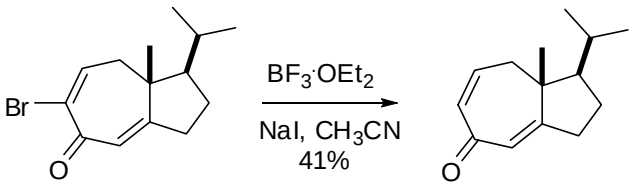


11 **12**

Bromodienone (12). To a solution of **11** in ethanol (125 mL) were added pyridine (3.02 mL, 37.3 mmol) and silver(I) nitrate (6.36 g, 37.4 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 1.5 h and concentrated under reduced pressure. The mixture was dissolved in a solution of hexane/ethyl acetate (10:1) and filtered through a pad of silica gel. The solid residue was washed with a solution of hexane/ethyl acetate (10:1) and then the combined filtrate and washings were evaporated and dried under high vacuum. The crude black oil was purified by column chromatography on silica gel (15:1 hexane/ethyl acetate) to give bromodienone **12** (5.17 g, 59%, 3 steps) as a white solid.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.19 (dd, J = 9.7, 3.5 Hz, 1H), 6.11 (dd, J = 1.9, 1.9 Hz, 1H), 2.73 (dd, J = 17.0, 9.7 Hz, 1H), 2.62-2.48 (m, 2H), 2.49 (dd, J = 11.6, 3.5 Hz, 1H), 1.97-1.93 (m, 1H), 1.69 (dqq, J = 6.7, 6.7, 6.6 Hz, 1H), 1.57-1.44 (m, 2H), 1.08 (s, 3H), 1.02 (d, J = 6.7 Hz, 3H), 0.95 (d, J = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 182.7, 173.4, 142.0, 128.1, 122.3, 57.8, 47.6, 40.1, 32.6, 28.2, 26.4, 23.7, 22.3, 17.3. HRMS (FAB) *m/z* found for M^+ 283.0707 calcd for $C_{14}H_{20}OBr$ 283.0698.

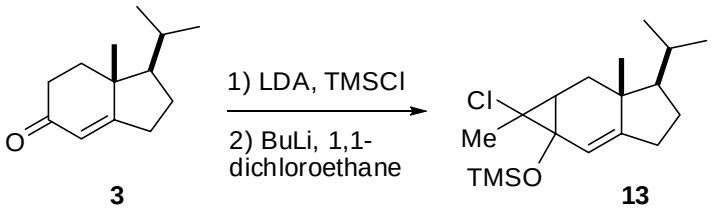
Structure determination of **12**



12 **8**

To a solution of **12** (20 mg, 0.071 mmol) and sodium iodide (29 mg, 0.19 mmol) in acetonitrile (1 mL) cooled to 0 °C was added BF_3•Et_2O (22 mL, 0.18 mmol). After 4.5 h,

the reaction mixture was quenched with 10% sodium thiosulfate and extracted with dichloromethane. The combined organic layer was washed with brine, dried over magnesium sulfate, and concentrated under reduced pressure. The crude oil was purified by column chromatography to give **8** (6 mg, 41%), of which the spectral data was identical to that published in the literature[2].

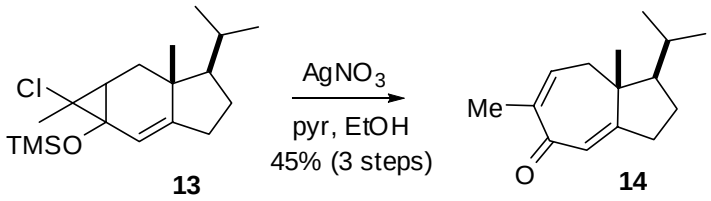


3 **13**

Chloromethylclopropane (13). Following the same procedure as that used for the formation of **3′**, the reaction of enone **3** (500 mg, 2.60 mmol) and LDA (prepared from diisopropylamine (1.02 mL, 7.28 mmol) and *n*-buthyllithium (2.60 mL, 2.5 M in hexane)) in THF (18 mL) followed by addition of chlorotrimethylsilane (0.66 mL, 5.22 mmol) gave silyloxydienone **3′**, which was used for the next step without further purification.

To a stirred solution of crude silyloxydienone **3′** and 1,1-dichloroethane (0.44 mL, 5.25 mmol) in diethyl ether (5 mL) cooled to -35 °C was added *n*-butyllithium (1.13 mL, 2.5 M in hexane) over a period of 12 h. The mixture was allowed to warm to 0 °C and stirred for additional 2 h. The precipitate was filtered off through a pad of Celite and the filtrate was concentrated under reduced pressure to give a mixture of the starting material **3′** and dibromocyclopropane **13**. Repeating the procedure afforded the crude chloromethylcyclopropane **13**, which was used for the next step without further purification.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.41-5.39 (m, 1H and 1H′), 2.43-2.32 (m, 2H and 2H′), 2.26-2.13 (m, 1H and 1H′), 1.88-1.79 (m, 1H and 1H′), 1.68 (s, 3H), 1.63-1.42 (m, 3H and 3H′), 1.40 (s, 3H′), 1.35-1.21 (m, 1H and 1H′), 1.15-1.10 (m, 1H and 1H′), 1.04 (s, 3H), 1.03 (s, 3H′), 0.95 (d, J = 6.7 Hz, 3H), 0.93 (d, J = 6.8 Hz, 3H′), 0.90 (d, J = 6.6 Hz, 3H), 0.89 (d, J = 6.6 Hz, 3H′).

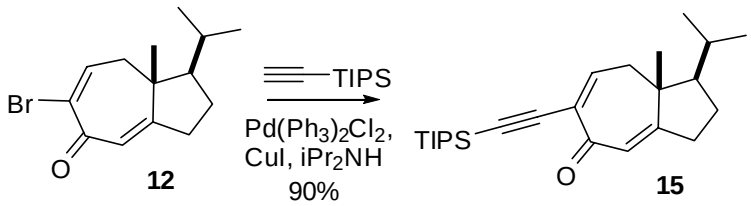


13 **14**

α-Methyldienone (14). To a solution of **13** in ethanol (10 mL) were added pyridine (0.25 mL, 3.09 mmol) and silver(I) nitrate (530 mg, 3.12 mmol) at 23 °C. The reaction mixture was stirred at 60 °C for 3.5 h, cooled to 23 °C and concentrated under reduced pressure. The mixture was dissolved in a solution of hexane/ethyl acetate (10:1) and filtered through a pad of silica gel. The solid residue was washed with a solution of hexane/ethyl acetate (10:1) and then the combined filtrate and washings were evaporated and dried under high vacuum. The crude black oil was purified by column chromatography on silica gel (15:1 hexane/ethyl acetate) to give α-methyldienone **14** (258 mg, 45%, 3 steps) as a yellowish oil along with desilylated alcohol (92 mg, 14%) and exo dieneone (39 mg, 6%).

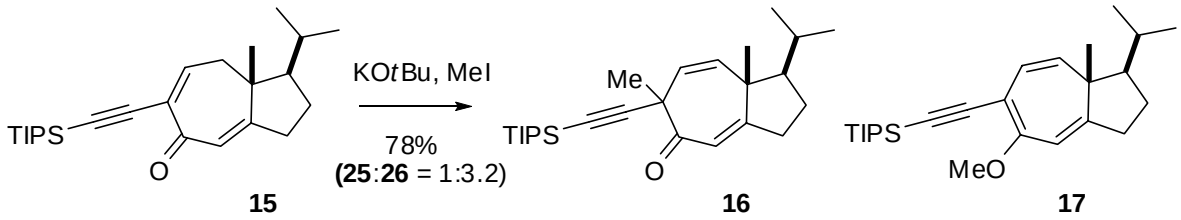
^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.36 (ddq, J = 9.0, 3.5, 1.4 Hz, 1H), 5.96 (dd, J = 2.0, 2.0 Hz, 1H), 2.63 (dd, J = 16.7, 9.0 Hz, 1H), 2.56-2.45 (m, 3H), 1.96-1.90 (m, 1H), 1.90 (dd, J = 2.0, 1.4 Hz, 3H), 1.69 (dqq, J = 6.7, 6.6, 6.4 Hz, 1H), 1.56-1.42 (m, 2H), 1.04 (s, 3H), 1.02 (d, J = 6.4 Hz, 3H), 0.94 (d, J = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 190.7,

171.8, 138.3, 135.9, 124.3, 57.4, 47.1, 38.5, 31.8, 27.8, 26.2, 23.3, 21.9, 19.8, 16.4. HRMS (FAB) *m/z* found for $(M+H)^+$ 219.1759 calcd for $C_{15}H_{23}O$ 219.1749.



To a solution of bromodienone **12** (185 mg, 0.65 mmol) in tetrahydrofuran (3 mL) cooled at 0 °C was added $PdCl_2(PPh_3)_2$ (23 mg, 0.032 mmol), copper (I) iodide (12 mg, 0.063 mmol), TIPS-acetylene (0.17 mL, 0.77 mmol) and diisopropylamine (0.28 mL, 1.98 mmol). The reaction mixture was allowed to warm to 23 °C and stirred for 12 h. The reaction mixture was quenched with 1N HCl (10 mL) and extracted with diethyl ether (3 x 15 mL). The combined organic layer was washed with brine, dried over magnesium sulfate, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (15:1 hexane/ethyl acetate) to give α-ethynyl dienone **15** (226 mg, 90%) as an oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.94 (dd, J = 9.2, 3.8 Hz, 1H), 5.96 (dd, J = 1.9, 1.9 Hz, 1H), 2.74 (dd, J = 17.0, 9.2 Hz, 1H)., 2.61-2.43 (m, 2H), 2.55 (dd, J = 17.0, 3.9 Hz, 1H), 1.97-1.97 (m, 1), 1.69 (dqq, J = 6.7, 6.7, 6.7 Hz, 1H), 1.55-1.43 (m, 2H), 1.09 (m, 21H), 1.07 (s, 3H), 1.00 (d, J = 6.7 Hz, 3H), 0.93 (d, J = 6.7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 186.8, 172.7, 145.9, 128.7, 124.3, 104.4, 90.8, 57.7, 47.9, 39.4, 32.4, 28.2, 26.5, 23.7, 22.3, 18.6, 17.3, 11.3. HRMS (FAB) *m/z* found for $(M+H)^+$ 385.2919 calcd for $C_{25}H_{41}OSi$ 385.2927.

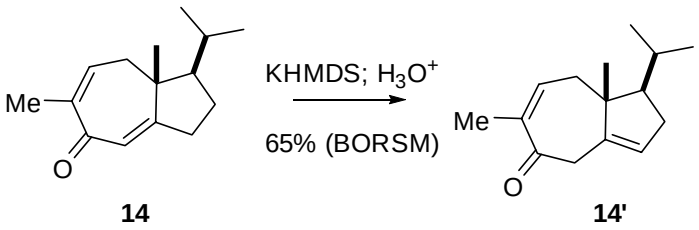


15 **16** **17**

Methylenone (16) and methyl enol ether (17). To a solution of α-ethynyl dienone **15** (13 mg, 0.034 mmol) in tetrahydrofuran (0.3 mL) cooled to 0 °C was added a solution of potassium *tert*-butoxide (40 μL, 1.0 M in THF). After 30 min, methyl iodide (11 μL, 0.18 mmol) was added and stirring was continued at 0 °C for 1.5 h. The reaction mixture was allowed to warm to 23 °C for 1.5 h and then quenched with ammonium chloride (3 mL). The solution was extracted with diethyl ether (3 x 5 mL), washed with brine, dried over magnesium sulfate, and concentrated under reduced pressure. The crude mixture was purified by preparative TLC (50:1 hexane/ethyl acetate) to give **16** (2.5 mg, 19%) and **17** (8 mg, 59%).

16: ^{1}H NMR ($CDCl_3$, 400 MHz) δ:6.05 (d, J = 11.4 Hz, 1H), 5.91 (dd, J = 1.8, 1.8 Hz, 1H), 5.35 (d, J = 11.4 Hz, 1H), 2.66 (dddd, J = 18.5, 10.2, 2.2, 2.2 Hz, 1H), 2.45 (dddd, J = 18.5, 9.2, 9.2 1.6 Hz, 1H), 1.94-1.86 (m, 1H), 1.77 (dqq, J = 6.8, 6.8, 6.6 Hz, 1H), 1.65-1.58 (m, 1H), 1.53 (s, 3H), 1.51-1.45 (m, 1H), 1.43 (s, 3H), 1.04 (d, J = 6.8 Hz, 3H), 1.03 (s, 21H), 0.96 (d, J = 6.6 Hz, 3H).

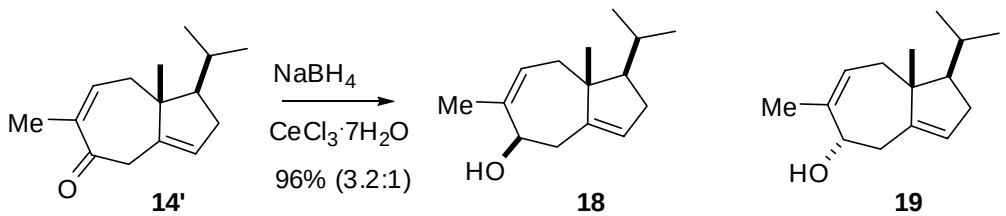
17: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.02 (dd, J = 1.8, 1.8 Hz, 1H), 0.98 (d, J = 10.3 Hz, 1H), 5.14 (d, J = 10.3 Hz, 1H), 3.76 (s, 3H), 2.55-2.50 (m, 2H), 1.96-1.90 (m, 1H), 1.74 (dqq, J = 9.6, 6.5, 6.5 Hz, 1H), 1.60-1.42 (m, 2H), 1.11 (s, 21H), 1.05 (d, J = 6.5 Hz, 3H), 0.96 (d, J = 6.5 Hz, 3H), 0.73 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ:. HRMS (FAB) *m/z* found for M^+ 398.3003 calcd for $C_{26}H_{42}OSi$ 398.3005.



14 **14'**

Deconjugated dienone (14′). To a solution of methhyldienone **14** (210 mg, 0.96 mmol) in tetrahydrofuran (5 mL) cooled to –78 °C was added potassium hexamethyldisilazane (KHMDS, 2.31 mL, 0.5 M in THF). The reaction was stirred at –78 °C for 1 h and then quenched with saturated aq. ammonium chloride (10 mL). The solution was extracted with diethyl ether (3 x 15 mL), washed with brine, dried over magnesium sulfate, and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel (15:1 hexane/ethyl acetate) to give deconjugated dienone **14′** (111 mg, 53%) along with the starting material **14** (38 mg, 18%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.36 (ddq, J = 9.3, 4.4, 1.4 Hz, 1H), 5.45 (m, 1H), 3.25 (d, J = 16.4 Hz, 1H), 2.95 (br d, J = 16.4 Hz, 1H), 2.53 (dd, J = 14.7, 9.3, 1H), 2.26-2.18 (m, 2H), 1.98 (dddd, J = 15.8, 10.2, 1.7, 1.7 Hz, 1H), 1.79 (dd, J = 1.7, 1.7 Hz, 3H), 1.76 (dqq, J = 10.2, 6.5, 6.5 Hz, 1H), 1.56 (ddd, J = 10.2, 10.2, 7.7 Hz, 1H), 1.03 (d, J = 6.5 Hz, 3H), 0.94 (s, 3H), 0.88 (d, J = 6.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 201.3, 145.2, 139.12, 139.06, 125.9, 54.6, 51.0, 43.1, 36.7, 35.5, 29.5, 22.8, 22.6, 19.4, 18.7.

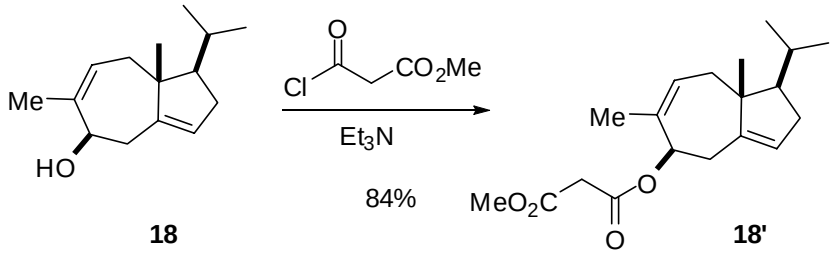


14' **18** **19**

Alcohols (18) and (19). To a solution of dienone **14′** (111 mg, 0.51 mmol) in methanol (3 mL) cooled to 0 °C were added $CeCl_3 \cdot 7H_2O$ (284 mg, 0.76 mmol) and $NaBH_4$ (29 mg, 0.77 mmol) successively. The reaction mixture was stirred at 0 °C for 20 min and then quenched with saturated ammonium chloride (10 mL). The aqueous layer was extracted with ethyl acetate (3 x 15 mL), washed with brine, and dried over magnesium sulfate. The solvent was removed under reduced pressure to give the crude oil, which was purified by column chromatography on silica gel (12:1 hexane/ethyl acetate) to afford the alcohol **18** (83 mg, 74%) and its epimer **19** (26 mg, 23%).

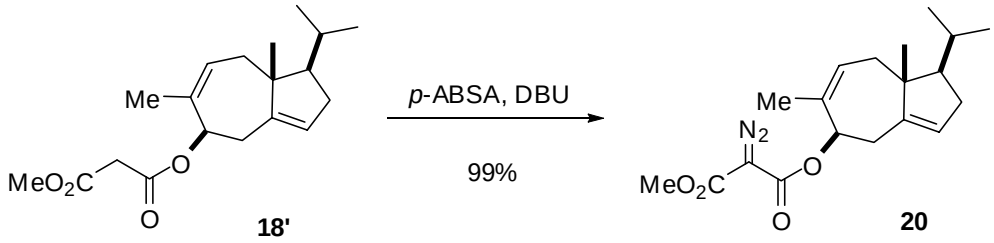
18: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.41 (dddd, J = 7.4, 7.4, 1.4, 1.4 Hz, 1H), 5.30 (dd, J = 1.2, 1.2 Hz, 1H), 4.21 (dd, J = 10.9, 3.4 Hz, 1H), 2.95 (br d, J = 16.4 Hz, 1H), 2.49 (dd, J = 13.0, 4.3, 1H), 2.27-2.18 (m, 3H), 2.02 (dd, J = 14.7, 7.4 Hz, 1H), 1.98 (br s, 1H), 1.89 (dddd, J = 15.7, 10.2, 2.7, 1.7 Hz, 1H), 1.79 (s, 3H), 1.76 (dqq, J = 9.8, 6.6, 6.6 Hz, 1H), 1.50 (ddd, J = 10.0, 8.0, 8.0 Hz, 1H), 0.99 (d, J = 6.6 Hz, 3H), 0.88 (d, J = 6.6 Hz, 3H), 0.83 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 149.0, 141.4, 123.5, 121.9, 72.9, 55.7, 50.0, 37.4, 36.3, 34.7, 29.5, 23.1, 22.9, 20.6, 17.3. HRMS (FAB) *m/z* found for $(M\text{-}H)^+$ 219.1745 calcd for $C_{15}H_{23}O$ 219.1749.

19: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.42 (br s, 1H), 5.38 (ddd, J = 7.6, 6.2, 1.4 Hz, 1H), 4.12 (m, 1H), 2.53 (br d, J = 14.0 Hz, 1H), 2.42 (dd, J = 14.0, 4.4 Hz, 1H), 2.29-2.22 (m, 1H), 2.25 (dd, J = 14.9, 7.8 Hz, 1H), 2.09 (dddd, J = 15.1, 5.9, 1.2, 1.2 Hz), 1.98-1.92 (m, 2H), 1.78 (s, 3H), 1.72 (dqq, J = 9.7, 6.5, 6.5 Hz, 1H), 1.59 (ddd, J = 9.8, 9.8, 7.8, 1H), 0.99 (d, J = 6.5 Hz, 3H), 0.89, (s, 3H), 0.88 (d, J = 6.5, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 148.8, 139.9, 124.6, 122.9, 71.1, 54.5, 52.3, 36.7, 35.1, 33.2, 29.4, 23.3, 22.9, 22.8, 18.6. LRMS (APCI) *m/z* found for $(M\text{-}H)^+$ 219.0 calcd for $C_{15}H_{23}O$ 219.2.



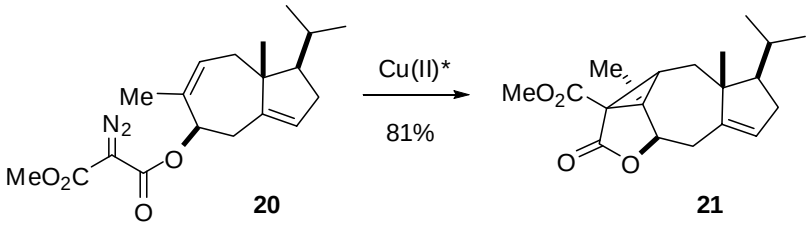
Malonic ester (18′). To a solution of alcohol **18** (319 mg, 1.45 mmol) in dichloromethane (7 mL) cooled to 0 °C were added triethylamine (0.40 mL, 2.87 mmol) and methyl malonyl chloride (0.31 mL, 2.89 mmol). The reaction was allowed to warm to 23 °C. After 2 h, the reaction mixture was quenched with water (20 mL), extracted with diethyl ether (3 x 25 mL), washed with brine and dried over magnesium sulfate. The solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (10:1 hexane/ethyl acetate) to give malonic ester **18′** (389 mg, 84%) as a colorless oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.51 (m, 1H), 5.38 (m, 1H), 5.32 (dd, J = 11.2, 4.3 Hz, 1H), 3.75 (s, 3H), 3.41 (s, 2H), 2.55 (dd, J = 13.0, 4.3 Hz, 1H), 2.31-2.24 (m, 1H), 2.28 (dd, J = 14.5, 8.0 Hz, 1H), 2.23 (ddd, J = 15.8, 7.9, 2.9 Hz, 1H), 2.11 (dd, J = 14.5, 7.5 Hz, 1H), 1.93-1.87 (m, 1H), 1.71 (dqq, J = 9.8, 6.6, 6.5 Hz, 1H), 1.69 (s, 3H), 1.52 (ddd, J = 10.0, 10.0, 8.0 Hz, 1H), 1.00 (d, J = 6.5 Hz, 3H), 0.88 (d, J = 6.6 Hz, 3H), 0.84 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 167.0, 165.8, 147.4, 137.3, 124.9, 124.3, 75.8, 55.6, 52.5, 49.3, 41.5, 37.3, 34.7, 32.1, 29.5, 23.0, 22.9, 20.6, 17.4. HRMS (FAB) *m/z* found for $(M-H)^+$ 319.1918 calcd for $C_{19}H_{27}O_4$. 319.1909.



Diazomalonate (20). To a solution of **18′** (360 mg, 1.12 mmol) and *p*-acetaminobenzenesulfonyl azide (324 mg, 1.35 mmol) in acetonitrile (10 mL) cooled to 0 °C was added DBU (0.20 mL, 1.34 mmol). After stirred for 1 h, saturated ammonium chloride solution was then added, and the mixture was extracted twice with dichloromethane. The organic layer was dried over magnesium sulfate, filtered and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (8:1 hexane/ethyl acetate) to give diazomalonate **20** (385 mg, 99%) as a yellow oil.

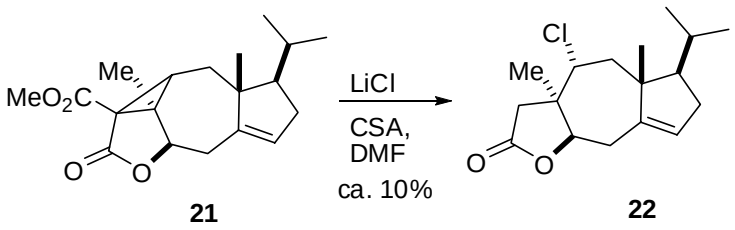
^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.53-5.49 (m, 1H), 5.41 (dd, J = 11.2, 3.9 Hz, 1H), 5.39 (m, 1H), 3.84 (s, 3H), 2.59 (dd, J = 13.0, 4.1 Hz, 1H), 2.35-2.27 (m, 1H), 2.29 (dd, J = 11.4, 7.9 Hz, 1H), 2.23 (ddd, J = 15.8, 7.7, 3.0 Hz, 1H), 2.10 (dd, J = 14.4, 7.3 Hz, 1H), 1.93-1.86 (m, 1H), 1.71 (s, 3H), 1.70 (dqq, J = 9.8, 6.6, 6.5 Hz, 1H), 1.52 (ddd, J = 9.9, 9.9, 8.0 Hz, 1H), 1.00 (d, J = 6.5 Hz, 3H), 0.88 (d, J = 6.6 Hz, 3H), 0.85 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 161.6, 160.2, 147.4, 137.4, 125.0, 124.2, 75.6, 55.6, 52.5, 49.1, 37.5, 34.6, 32.6, 29.5, 23.1, 22.8, 20.6, 17.3 (one C's not shown). HRMS (FAB) *m/z* found for $(M-H)^+$ 345.1825 calcd for $C_{19}H_{25}O_4N_2$ 345.1814.



Cu(II)*: copper (II) bis(salicylidene-*tert*-butylamine)

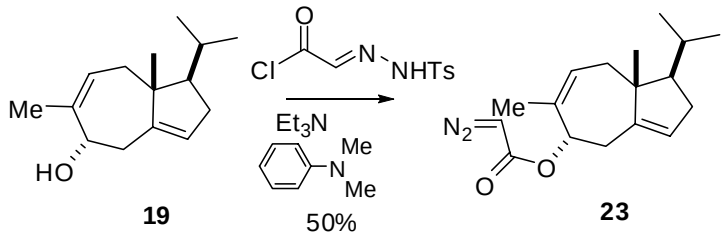
Lactone (21). A solution of diazomalonate **20** (375 mg, 1.08 mmol) in toluene (23 mL) was added slowly to a stirred refluxing solution of copper (II) bis(salicylidene-*tert*-butylamine) (22 mg, 0.053 mmol) in toluene (20 mL) via syringe pump over a period of 3h. After completion of addition, the solution was stirred at 110 °C for additional 30 min, cooled, concentrated in vacuo and the residue was purified by column chromatography on silica gel (6:1 hexane/ethyl acetate) to give lactone **21** (278 mg, 81%) as a white solid along with the staring material **20** (17 mg, 5%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.42 (dd, J = 1.3, 1.3 Hz, 1H), 4.57 (d, J = 8.8 Hz, 1H), 3.80 (s, 3H), 2.80 (dd, J = 16.1, 8.8 Hz, 1H), 2.43 (br d, J = 16.1 Hz, 1H), 2.36-2.28 (m, 3H), 2.10-1.95 (m, 1H), 1.82 (ddd, J = 9.9, 9.9, 7.6 Hz, 1H), 1.77 (dqq, J = 10.0, 6.4, 6.3 Hz, 1H), 1.29 (s, 3H), 1.20 (dd, J = 17.3, 13.2 Hz, 1H), 1.03 (d, J = 6.3 Hz, 3H), 0.92 (d, J = 6.4 Hz, 3H), 0.88 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 170.1, 167.0, 146.8, 127.2, 79.4, 53.5, 52.7, 51.4, 41.2, 41.1, 35.4, 33.9, 32.6, 29.7, 29.6, 22.9, 22.7, 19.0, 16.4. HRMS (FAB) *m/z* found for $(M+H)^+$ 319.1916 calcd for $C_{19}H_{27}O_4$ 319.1909.



Chlorolactone (22). To a solution of latone **21** (10 mg, 0.031 mmol) in dimethylformamide (0.3 mL) were added lithium chloride (13 mg, 0.31 mmol) and camphorsulfonic acid (7.3 mg, 0.031 mmol). The reaction mixture was stirred at 145 °C for 7 h and cooled to 23 °C. The mixture was quenched with 1N HCl (1 mL), extracted with ethyl acetate (3 X 5 mL), washed with brine and water, and dried over magnesium sulfate. After filtration, the solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (10:1 hexane/ethyl acetate, then 15:1 dichloromethane/methanol) to give chlorolactone **22** (1 mg, 11%) along with hydrolyzed acid (8 mg, 84%).

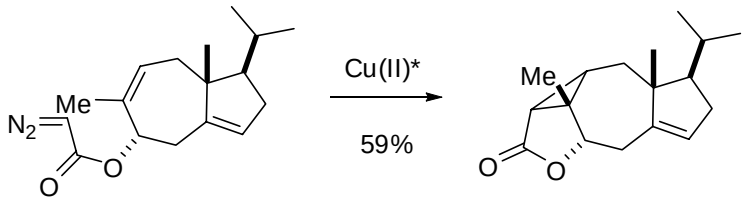
^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.46 (s, 1H), 4.44 (d, J = 10.6 Hz, 1H), 4.01 (dd, J = 10.0, 2.6 Hz, 1H), 2.67 (d, J = 17.9 Hz, 1H), 2.57 (dd, J = 13.8, 2.6 Hz, 1H), 2.48 (d, J = 17.9 Hz, 1H), 2.34-2.26 (m, 2H), 2.32 (d, J = 14.9 Hz, 1H), 2.00-1.92 (m, 1H), 1.97 (dd, J = 14.9, 10.6 Hz, 1H), 1.76 (dqq, J = 9.8, 6.6, 6.6 Hz, 1H), 1.52-1.47 (m, 1H), 1.35 (s, 3H), 1.06 (s, 3H), 0.99 (d, J = 6.6 Hz, 3H), 0.91 (d, J = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 174.4, 145.0, 128.0, 87.9, 62.9, 59.5, 49.5, 48.4, 46.9, 43.0, 35.4, 31.7, 29.4, 23.1, 22.9, 21.0, 17.0. HRMS (FAB) *m/z* found for $(M+H)^+$ 297.1613 calcd for $C_{17}H_{26}O_2Cl$ 297.1621.



Diazo ester (23). To a solution of alcohol **19** (26 mg, 0.12 mmol) in dichloromethane (1 mL) cooled to 0 °C were added tosyl hydrazone (62 mg, 0.24 mmol) and *N,N*-

dimethylaniline (29 μL, 0.23 mmol). After 15 min, triethylamine (39 μL, 0.28 mmol) was added and the resulting orange suspension was stirred for 10 min at 0°C, and then for 15 min at 23°C. Water (2 mL) was added and then saturated citric acid (3 mL) was added. The mixture was extracted with 10% ethyl acetate in hexane (3 x 10 mL), washed with brine, dried over magnesium sulfate and concentrated under reduced pressure. The crude oil was purified by column chromatography on silica gel (15:1 hexane/ethyl acetate) to give diazo ester **23** (17 mg, 50%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.56 (m, 1H), 5.30 (br s, 1H), 5.29 (dd, J = 5.8, 3.5 Hz, 1H), 4.74 (br s, 1H), 2.57 (dd, J = 14.8, 5.8 Hz, 1H), 2.44 (dddd, J = 14.8, 5.2, 3.6, 1.9, 1H), 2.31 (dd, J = 13.7, 5.8 Hz, 1H), 2.24 (dddd, J = 15.7, 7.9, 3.0, 1.2 Hz, 1H), 2.12 (dd, J = 14.5, 7.8 Hz, 1H), 1.87 (dddd, J = 15.7, 10.1, 3.3, 1.6 Hz, 1H), 1.77 (s, 3H), 1.72 (dqq, J = 9.6, 6.6, 6.5 Hz, 1H), 1.56 (ddd, J = 9.8, 9.8, 8.0 Hz, 1H), 1.00 (d, J = 6.5 Hz, 3H), 0.90 (s, 3H), 0.89 (d, J = 6.6 Hz, 3H).



23 **24**

Lactone (24). A solution of diazo ester **23** (17 mg, 0.059 mmol) in toluene (0.5 mL) was added slowly to a stirred refluxing solution of copper (II) bis(salicylidene-*tert*-butylamine) (1.2 mg, 0.003 mmol) in toluene (0.5 mL) via syringe pump over a period of 1 h. After completion of addition, the solution was stirred at 110 °C for additional 20 min, cooled, concentrated *in vacuo* and the residue was purified by column chromatography on silica gel (6:1 hexane/ethyl acetate) to give lactone **24** (9 mg, 59%) as a white solid.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.32 (m, 1H), 4.47 (d, J = 5.4 Hz, 1H), 2.88 (d, J = 16.1, 5.6 Hz, 1H), 1.53 (dddd, J = 16.1, 6.0, 3.9, 2.2 Hz, 1H), 2.39 (dd, J = 15.0, 8.6 Hz, 1H), 2.27 (dddd, J = 16.0, 8.3, 2.4, 2.4 Hz, 1H), 2.02 (d, J = 8.8 Hz, 1H), 1.89 (dddd, J = 16.0, 9.4, 4.7, 1.8 Hz, 1H), 1.73 (dqq, J = 9.2, 6.6, 6.5 Hz, 1H), 1.51 (ddd, J = 9.4, 9.3, 8.3 Hz, 1H), 1.43 (ddd, J = 8.8, 8.7, 8.6 Hz, 1H), 1.39 (s, 3H), 1.17 (dd, J = 15.0, 8.6 Hz, 1H), 1.08 (s, 3H), 1.00 (d, J = 6.5 Hz, 3H), 0.87 (d, J = 6.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 174.9, 145.9, 127.1, 81.4, 56.3, 51.1, 38.6, 35.1, 31.8, 31.7, 29.8, 29.4, 26.3, 23.4, 23.4, 22.2, 18.3, 15.7. HRMS (FAB) *m/z* found for $(M+H)^+$ 261.1853 calcd for $C_{17}H_{25}O_2$ 261.1855.