SUPPORTING INFORMATION

For

Synthesis of a 2,9-Dioxabicyclo[3.3.1]nonane via Double Intramolecular Hetero-Michael Addition: Entry to the F-G Ring System of the Azaspiracids

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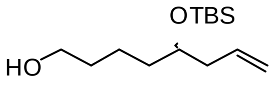
CONTENTS: full experimental procedures and characterization data for compounds **7**, **8**, **11**, **13**, **15-22** and **24-26**.

EXPERIMENTAL SECTION

General methods. Unless otherwise noted, all reactions were carried out under nitrogen or argon atmosphere using oven-dried glassware and standard syringe, cannula and septa techniques. THF, benzene and Et_2O were distilled over Na / benzophenone ketyl under nitrogen immediately prior to use. CH_2Cl_2, CH_3CN, Et_3N and *i*-Pr_2NEt were distilled from CaH_2 under nitrogen prior to use. Flash chromatography was performed using Baker Flash silica gel 60 (40 µm) and the solvents indicated. After chromatography, solvents were evaporated by using a Büchi rotary evaporator, followed by further treatment under high vacuum, unless otherwise indicated. Analytical and preparative TLC was performed using 0.25 mm or 0.50 mm EM silica gel 60 F_{254} plates that were analyzed by fluorescence upon 254 nm irradiation or by staining with anisaldehyde reagent (450 mL of 95% EtOH, 25 mL of conc. H_2SO_4, 15 mL of glacial acetic acid and 25 mL of anisaldehyde). NMR spectra were obtained in $CDCl_3$ with an INOVA 500 MHz Varian instrument. High resolution mass spectrometric data was performed by the University of Minnesota Mass Spectrometry Laboratory using CI or FAB techniques.

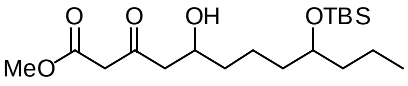


13

Alcohol (±) 13. To a stirred solution of aldehyde **12** (8.30 g, 38.3 mmol) in DMF (150 mL) was added allyl bromide (4.64 mL, 53.7 mmol) and the resulting solution was cooled to 0 °C. Zn powder (3.76 g, 57.5 mmol) was added slowly over a period of 10 min. The resulting suspension was allowed to warm to rt and was sonicated for 2 h, after which no remaining **12** was observed by TLC (**12**: R_f 0.55 (hexanes-ethyl acetate, 5:1, v/v), **12a**: R_f 0.30 (hexanes-ethyl acetate, 5:1, v/v)). Saturated aqueous NH_4Cl (150 mL) was added and the reaction mixture diluted with Et_2O (150 mL). The layers were separated and the aqueous phase was extracted with Et_2O (3 x 100 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography (hexanes-ethyl acetate, 5:1, v/v) to yield the homoallylic alcohol **12a** (5.08 g, 19.7 mmol, 51%) as a clear, colorless oil.

To a magnetically stirred rt solution of **12a** (5.01 g, 19.3 mmol) in CH_2Cl_2 (100 mL) was added Et_3N (4.57 mL, 32.8 mmol), TBSCl (3.78 g, 25.1 mmol) and DMAP (236 mg, 1.93 mmol). After stirring at rt for 24 h, saturated aqueous NH_4Cl (100 mL) was added and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (3 x 50 mL) and the combined organic phases were dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography (hexanes-ethyl acetate, 20:1, v/v) to afford the corresponding silyl ether **12b** (5.07 g, 13.6 mmol, 70%): R_f 0.82 (hexanes-ethyl acetate, 5:1, v/v).

To a stirred solution of **12b** (3.64 g, 9.70 mmol) in THF (45 mL) was added HF·Pyr (1.2 mL). After 4 h, saturated aqueous $NaHCO_3$ (50 mL) was added slowly and the mixture was diluted with Et_2O (30 mL). The two phases were separated and the aqueous phase was extracted with Et_2O (3 x 25 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography on silica gel (hexanes-ethyl acetate, 5:1, v/v) to yield alcohol **13** (1.90 g, 7.31 mmol, 77%) as a clear, colorless oil: R_f 0.35 (hexanes-ethyl acetate, 5:1, v/v); IR (neat): 3338, 2930, 2857, 1641, 1361, 1255, 1057 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 5.80 (dddd, J = 17.0, 10.0, 7.5, 7.5 Hz, 1H), 5.05 (dt, *J* = 17.0, 1.7 Hz, 1H), 5.03 (dt, *J* = 10.5, 1.5 Hz, 1H), 3.77 (pentet, *J* = 6.0 Hz, 1H), 3.71-3.58 (m, 2H), 2.26 (broad t, *J* = 6.0 Hz, 2H), 1.96 (broad s, 1H), 1.67-1.60 (m, 3H), 1.58-1.52 (m, 3H), 0.90 (s, 9H), 0.07 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 135.0, 116.9, 71.8, 63.1, 41.5, 33.1, 28.3, 25.9, 21.4, 18.1, -4.5; HRCIMS calcd for $C_{14}H_{30}O_2Si$ $[M+H]^+$ 259.2093, found 259.2106.



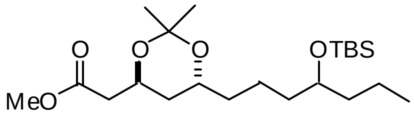
15

Ketoester 15. A mixture of alcohol **13** (500 mg, 1.93 mmol) and Pd (10% on carbon, 203 mg, 0.193 mmol) in ethyl acetate (15 mL) was stirred vigorously under H_2 (1 atm) for 1 h. The suspension was filtered through celite with ethyl acetate and the filtrate was concentrated under vacuum to yield the crude saturated alcohol **13a** (451 mg, 1.73 mmol) as a colorless oil: R_f 0.31 (hexanes-ethyl acetate, 5:1, v/v).

To a stirred, –78 °C solution of DMSO (0.41 mL, 5.8 mmol) in CH_2Cl_2 (15 mL), was added oxalyl chloride (0.25 mL, 2.9 mmol). After 30 min, a solution of **13a** (451 mg, 1.73 mmol) in CH_2Cl_2 (4 mL) was added via cannula. The resulting mixture was stirred for 1 h before Et_3N (2.45 mL, 19.3 mmol) was added. The reaction mixture was warmed to rt, diluted with Et_2O (40 mL) and water (40 mL) was added. The aqueous phase was extracted with Et_2O (3 x 30 mL) and the combined organic extracts were washed with H_2O and saturated aqueous NaCl (30 mL each). The organic phase was dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (hexanes-ethyl acetate, 5:1, v/v) of the residue provided the aldehyde **13b** (423 mg, 1.63 mmol, 85%) as a pale yellow oil: R_f 0.62 (hexanes-ethyl acetate, 5:1, v/v).

To a stirred, 0 °C solution of diisopropylamine (0.780 mL, 5.55 mmol) in THF (16 mL) was added *n*-butyllithium (1.99 mL of a 2.60 M solution in hexanes, 5.23 mmol). The resulting solution was stirred for 30 min and cooled to –78 °C before methyl acetoacetate (0.260 mL, 2.45 mmol) was added dropwise. After 30 min, a solution of the aldehyde (423 mg, 1.63 mmol) in THF (1 mL) was added and the reaction mixture was stirred at –78 °C for an additional 30 min. Saturated aqueous NH_4Cl (15 mL) was added and the reaction mixture diluted with Et_2O (15 mL). The aqueous phase was extracted with Et_2O

(3 x 10 mL) and the combined organic extracts were dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography (hexanes-ethyl acetate, 5:1, v/v) to yield **15** (435 mg, 1.16 mmol, 71%) as a clear, colorless oil: R_f 0.13 (hexanes-ethyl acetate, 5:1, v/v); IR (neat): 3476, 2943, 2901, 1747, 1698, 1651, 1632, 1462, 1325, 1246 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz, mixture of diastereomers): δ 4.09-3.99 (m, 1H), 3.74 (s, 3H), 3.72-3.67 (m, 1H), 3.50 (s, 1H), 3.49 (s, 1H), 2.87 (d, J = 4.0 Hz, 1H), 2.74-2.63 (m, 2H), 1.66-1.60 (m, 1H), 1.60-1.46 (m, 4H), 1.46-1.36 (m, 3H), 1.36-1.24 (m, 2H), 0.89 (t, J = 7.5 Hz, 3H), 0.88 (s, 9H), 0.06-0.03 (m, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz, mixture of diastereomers): δ 203.4, 203.2, 167.5, 72.0, 71.7, 68.1, 67.6, 52.5, 52.3, 50.0, 49.7, 49.6, 39.3, 39.1, 38.8, 36.7, 33.0, 32.3, 32.2, 31.7, 25.9, 21.1, 18.7, 18.6, 18.1, 14.3, -4.4, -4.5; HRFABMS calcd for $C_{19}H_{38}O_5Si$ $[M+Na]^+$ 397.2387, found 397.2369.

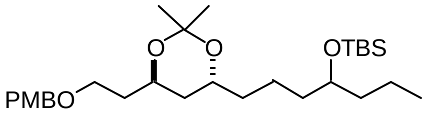


16

Ester 16. To a stirred, 0 °C solution of $Me_4NBH(OAc)_3$ (1.60 mg, 6.10 mmol) in CH_3CN : AcOH (18 mL, 1:1 v/v) was added via cannula a solution of ketoester **15** (765 mg, 2.03 mmol) in CH_3CN (2 mL). After 50 min, the reaction mixture was diluted with ethyl acetate (20 mL) and a saturated aqueous solution of sodium-potassium tartrate (15 mL) was added. The separated aqueous phase was washed with ethyl acetate (3 x 20 mL), and the combined organic extracts were washed with saturated $NaHCO_3$ (3 x 20), water (15 mL) and saturated aqueous NaCl (15 mL). The organic phase was dried over Na_2SO_4, filtered, and concentrated by rotary evaporation to yield diol **15a** as a yellow oil which was carried onto the next step without further purification: R_f 0.52 (hexanes-ethyl acetate, 1:1, v/v).

To a stirred solution of crude **15a** in CH_2Cl_2 (10 mL) was added 2,2-dimethoxypropane (1.0 mL, 8.1 mmol) and PPTs (51 mg, 0.20 mmol). After 4 h, Et_3N (0.1 mL) was added and the solvent removed by rotary evaporation. The residue was purified by flash chromatography on silica gel (hexanes-ethyl acetate, 20:1, v/v) to yield **16** (667 mg, 6.42 mmol, 79%) as a clear, colorless oil: R_f 0.55 (hexanes-ethyl acetate, 10:1, v/v); IR (neat):

2955, 2856, 1744, 1462, 1436, 1379, 1252, 1224, 1077 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz, mixture of diastereomers): δ 4.28-4.22 (m, 1H), 3.76-3.70 (m, 1H), 3.68 (s, 3H), 3.66-3.62 (m, 1H), 2.53 (dd, *J* = 15.5, 8.0 Hz, 1H), 2.43 (dd, *J* = 15.5, 5.5 Hz, 1H), 1.67-1.60 (m, 2H), 1.60-1.27 (m, 10 H), 1.35 (s, 3H), 1.32 (s, 3H), 0.88 (t, *J* = 7.5 Hz, 3H), 0.87 (s, 9H), 0.03 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz, mixture of diastereomers): δ 171.4, 100.5, 72.0, 71.6, 66.8, 66.6, 63.5, 63.4, 51.6, 51.6, 40.6, 39.6, 39.2, 38.1, 38.0, 32., 32.5, 31.8, 31.0, 25.9, 24.7, 24.6, 18.5, 18.4, 18.1, 14.3, -4.4; HRFABMS calcd for $C_{22}H_{44}O_5Si$ $[M+Na]^+$ 439.2856, found 439.2850.

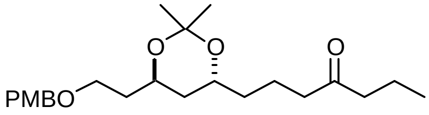


17

Acetonide 17. To a stirred, 0 °C solution of ester **16** (654 mg, 1.57 mmol) in Et_2O (10 mL) was added $LiAlH_4$ (72 mg, 1.9 mmol). After 10 min, H_2O (10 mL) was added to the reaction mixture and the separated aqueous phase was washed with Et_2O (3 x 10 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (hexanes-ethyl acetate, 3:1, v/v) of this residue yielded **16a** (610 mg, 1.57 mmol, 100%) as clear, colorless oil: R_f 0.17 (hexanes-ethyl acetate, 5:1, v/v).

To a stirred 0 °C suspension of KH (490 mg of a 30% suspension in mineral oil, 3.68 mmol) in THF (12 mL) was added a solution of **16a** (481 mg, 1.23 mmol). After 30 min, *p*-methoxybenzyl chloride (0.183 mL, 1.35 mmol) and tetrabutylammonium iodide (46 mg, 0.12 mmol) were added and the reaction mixture was allowed to warm to rt. After 5 h, saturated aqueous NH_4Cl (10 mL) was added and the mixture diluted with Et_2O (15 mL). The separated aqueous phase was extracted with Et_2O (3 x 10 mL) and the combined organic phases were dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography (hexanes-ethyl acetate, 20:1, v/v) to give **17** (574 mg, 1.13 mmol, 91%) as a clear, colorless oil: R_f 0.65 (hexanes-ethyl acetate, 5:1, v/v); IR (neat): 2955, 2946, 2857, 1612, 1513, 1462, 1378, 1248, 1171 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.25 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 4.44 (d, *J* = 11.5 Hz, 1H), 4.41 (d, *J* = 11.5 Hz, 1H), 4.00-3.94 (m, 1H), 3.80 (s, 3H), 3.76-3.70

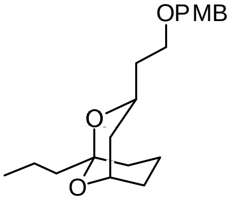
(m, 1H), 3.69-3.62 (m, 1H), 3.55-3.48 (m, 2H), 1.77-1.73 (m, 2H), 1.60-1.29 (m, 12 H), 1.35 (s, 3H), 1.34 (s, 3H), 0.89 (t, *J* = 7.0 Hz, 3H), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz, mixture of diastereomers): δ 159.1, 130.6, 129.3, 113.8, 100.2, 72.8, 72.0, 71.7, 67.0, 66.8, 66.4, 63.7, 55.3, 39.6, 39.2, 38.8, 38.7, 36.0, 32.8, 32.6, 31.9, 31.2, 25.9, 24.8, 24.7, 18.6, 18.5, 14.3, -4.4; HRFABMS calcd for $C_{29}H_{52}O_5Si$ $[M+Na]^+$ 531.3482, found 531.3451.



18

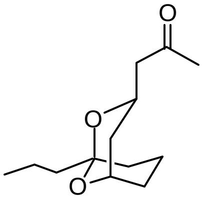
Ketone (±) 18. To acetonide **17** (97 mg, 0.19 mmol) was added TBAF (0.285 mL of a 1 M solution in THF, 0.285 mmol). After 48 h, the solvent was removed by rotary evaporation and the crude residue was purified by silica gel column chromatography (hexanes-ethyl acetate, 5:1 to 2:1, v/v) to yield the alcohol **17a** (66 mg, 0.17 mmol, 89%) as a colorless oil: R_f 0.11 (hexanes-ethyl acetate, 5:1, v/v).

To a stirred rt solution of **17a** (86 mg, 0.22 mmol) in CH_2Cl_2 (2 mL) was added crushed 4 Å molecular sieves (50 mg) and tetra-n-propylammonium perruthenate (7.4 mg, 22 μmol), followed by 4-methylmorpholine N-oxide (51 mg, 0.44 mmol). After 20 min, the reaction mixture was filtered through silica gel (ethyl acetate) and concentrated by rotary evaporation. The residue was purified by silica gel column chromatography (hexanes-ethyl acetate 5:1 v/v) to yield **18** (85.0 mg, 0.216 mmol, 99%) as a colorless oil: R_f 0.21 (hexanes-ethyl acetate, 5:1, v/v); IR (neat): 3001, 2914, 2874, 1712, 1613, 1586, 1513, 1462, 1379, 1247 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.25 (d, *J* = 8.0 Hz, 2H), 6.87 (d, *J* = 8.0 Hz, 2H), 4.43 (d, *J* = 12.0 Hz, 1H), 4.40 (d, *J* = 12.0 Hz, 1H), 3.99-3.93 (m, 1H), 3.80 (s, 3H), 3.73 (dddd, *J* = 13.5, 13.5, 6.5, 4.0 Hz, 1H), 3.54-3.47 (m, 2H), 2.55-2.40 (m, 2H), 2.38 (t, *J* = 7.0 Hz, 2H), 1.82-1.72 (m, 3H), 1.70-1.62 (m, 2 H), 1.61-1.54 (m, 4H), 1.36 (d, *J* = 16.0 Hz, 1H), 1.30 (s, 3H), 1.29 (s, 3H), 0.91 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 210.8, 159.2, 130.6, 129.3, 113.8, 100.3, 72.8, 66.3, 66.0, 63.7, 55.3, 44.8, 38.8, 38.5, 35.9, 32.8, 29.6, 24.7, 24.6, 19.9, 17.3, 13.8; HRCIMS calcd for $C_{23}H_{36}O_5$ $[M+H]^+$ 393.2641, found 393.2655, calcd for $[M+NH_4]^+$ 410.2906, found 410.2915.



8

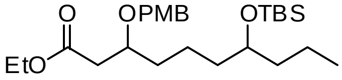
Acetal 8. To a solution of **18** (59.5 mg, 0.151 mmol) in CH_2Cl_2 : MeOH (1.5 mL, 5:1, v/v) was added camphorsulfonic acid (3.50 mg, 15.1 μmol). Upon disappearance of **18** by TLC analysis (ca. 2.5 h), the solvent was removed and the crude mixture was dissolved in benzene (3 mL) maintaining vigorous stirring. After 3 h, Et_3N (50 μL) was added and the solvent removed. The crude mixture was purified by silica gel column chromatography (hexanes-ethyl acetate 5:1 v/v) to yield **8** (41.4 mg, 0.123 mmol, 82%) as a colorless oil: R_f 0.46 (hexanes-ethyl acetate, 3:1, v/v); IR (neat): 2957, 2870, 1612, 1586, 1513, 1465, 1301, 1249 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.25 (d, *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 4.51-4.49 (m, 1H), 4.45 (d, *J* = 11.5 Hz, 1H), 4.41 (d, *J* = 11.5 Hz, 1H), 4.00 (dddd, *J* = 12.0, 8.0, 4.0, 4.0 Hz, 1H), 3.81 (s, 3H), 3.56 (ddd, *J* = 8.0, 8.0, 5.5 Hz, 1H), 3.49 (ddd, *J* = 9.5, 6.0, 6.0 Hz, 1H), 2.08-1.98 (m, 2H), 1.83-1.67 (m, 8H), 1.61 (ddd, *J* = 15.0, 11.0, 5.5 Hz, 1H), 1.49-1.35 (m, 2H), 1.30 (ddd, *J* = 13.0, 1.8, 1.8 Hz, 1H), 0.92 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 159.1, 130.7, 129.3, 113.7, 106.8, 74.9, 72.6, 65.8, 65.3, 55.3, 40.2, 37.1, 36.5, 32.8, 28.4, 17.4, 14.5; HRCIMS calcd for $C_{20}H_{30}O_4$ $[M+H-CH_2]^+$ 321.2066, found 321.2055, calcd for $[M+NH_4-CH_2]^+$ 338.2332, found 338.2328.



7

Ketone 7. To a mixture of **8** (39.0 mg, 0.117 mmol), CH_2Cl_2 (1 mL), an aqueous phosphate buffer (pH = 7, 0.1 mL) and *tert*-butyl alcohol (0.1 mL) was added DDQ (66.0 mg, 0.291 mmol). The reaction flask was placed in an aqueous bath and sonicated for 5 min, then assayed by TLC. This process was repeated again, at which point no **8** remained. Saturated aqueous $NaHCO_3$ (1 mL) was added, and the mixture was diluted with Et_2O (3 mL). The organic phase was washed with saturated aqueous $NaHCO_3$ (3 x 1 mL) and the aqueous phase was extracted with Et_2O (3 x 1 mL). The combined organic extracts were washed with H_2O and saturated NaCl (2 mL each), dried over Na_2SO_4, filtered and concentrated. The resulting residue was purified by flash chromatography on silica gel (hexanes-ethyl acetate, 5:1 to 2:1, v/v) to give the alcohol **8a** (13.6 mg, 63.7 μmol, 55%) as a colorless oil: R_f 0.12 (hexanes-ethyl acetate, 3:1, v/v).

To a solution of **8a** (13.5 mg, 63.0 μmol) in CH_2Cl_2 (0.6 mL) was added sequentially crushed 4 Å molecular sieves (~10 mg), tetra-n-propylammonium perruthenate (1.0 mg, 3.0 μmol), and 4-methylmorpholine *N*-oxide (18.3 mg, 0.157 mmol). After 20 min, TLC showed no remaining **8a**. The reaction mixture was filtered through silica gel (hexanes-ethyl acetate 1:1 v/v) and concentrated by rotary evaporation. The residue was dissolved in THF (0.6 mL) under Ar, and methylmagnesium bromide (63 μL of a 3.0 M solution in Et_2O, 0.19 mmol) was added at 0 °C. After 30 min, saturated aqueous NH_4Cl (1 mL) was added and the aqueous phase was extracted with Et_2O (3 x 1 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated. The resulting residue was dissolved in CH_2Cl_2 (0.6 mL) and crushed 4 Å molecular sieves (5 mg), tetra-n-propylammonium perruthenate (1.0 mg, 3.0 μmol), and 4-methylmorpholine *N*-oxide (18.3 mg, 0.157 mmol) were added. After 20 min, the suspension was filtered through silica gel (hexanes-ethyl acetate 1:1 v/v) and concentrated. Purification by silica gel column chromatography (hexanes-ethyl acetate, 3:1, v/v) gave ketone **7** (4.8 mg, 22 μmol, 34% over three steps) as a clear, colorless oil: R_f 0.39 (hexanes-ethyl acetate, 2:1, v/v); IR (neat): 2958, 2874, 1712, 1467, 1356, 1323, 1260, 1191, 1159 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 4.52-4.51 (m, 1H), 4.32-4.27 (m, 1H), 2.71 (dd, *J* = 15.5, 7.0 Hz, 1H), 2.42 (dd, *J* = 15.5, 5.5 Hz, 1H), 2.18 (s, 3H), 2.11-2.03 (m, 3H), 1.86-1.79 (m, 2H), 1.75-1.57 (m, 4H), 1.47-1.37 (m, 3H), 0.91 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 207.4, 107.0, 74.9, 74.8, 65.5, 49.9, 40.0, 36.8, 32.8, 31.4, 28.3, 17.3, 14.4; LRCIMS calcd for $C_{13}H_{22}O_3$ $[M+H-CH_2]^+$ 213.1, found 213.1, calcd for $[M+NH_4-CH_2]^+$ 230.2, found 230.2.



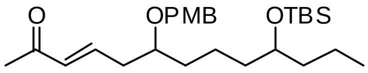
19

Ester 19. A mixture of alcohol **13** (500 mg, 1.93 mmol) and Pd (10 % on carbon, 203 mg, 0.193 mmol) in ethyl acetate (15 mL) was stirred vigorously under H_2 (1 atm) for 1 h. The suspension was filtered through celite with ethyl acetate and the filtrate was concentrated under vacuum to yield the crude saturated alcohol **13a** (451 mg, 1.73 mmol) as a colorless oil: R_f 0.31 (hexanes-ethyl acetate, 5:1, v/v).

To a stirred –78 °C solution of DMSO (0.41 mL, 5.8 mmol) in CH_2Cl_2 (15 mL), was added oxalyl chloride (0.25 mL, 2.9 mmol). After 30 min, a solution of **13a** (451 mg, 1.73 mmol) in CH_2Cl_2 (4 mL) was added via cannula. The resulting mixture was stirred for 1 h and Et_3N (2.45 mL, 19.3 mmol) was added. The reaction was warmed to rt, diluted with Et_2O (40 mL) and water (40 mL) was added. The aqueous phase was extracted with Et_2O (3 x 30 mL) and the combined organic extracts were washed with H_2O (30 mL) and saturated aqueous NaCl (30 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (hexanes-ethyl acetate, 5:1, v/v) of the residue provided the aldehyde **13b** (423 mg, 1.63 mmol, 85%) as a pale yellow oil: R_f 0.62 (hexanes-ethyl acetate, 5:1, v/v).

To a stirred 0 °C solution of diisopropylamine (0.280 mL, 1.98 mmol) in THF (13 mL) was added *n*-butyllithium (0.705 mL of a 2.60 M solution in hexanes, 1.86 mmol). The resulting solution was stirred for 30 min and cooled to –78 °C before ethyl acetate (0.160 mL, 1.61 mmol) was added dropwise. After 30 min, a solution of **13b** (319 mg, 1.23 mmol) was added via cannula, and the reaction mixture was stirred at –78 °C for an additional 30 min. Saturated aqueous NH_4Cl (5 mL) and Et_2O (5 mL) were added. The separated aqueous phase was extracted with Et_2O (3 x 5 mL) and the combined organic extracts were dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography (hexanes-ethyl acetate, 5:1, v/v) to yield the hydroxyester **13c** (378 mg, 1.09 mmol, 88%) as a clear, colorless oil: R_f 0.35 (hexanes-ethyl acetate, 5:1, v/v).

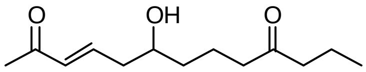
To a 0 °C solution of **13c** (542 mg, 1.56 mmol) in CH_2Cl_2 (15 mL) was added via cannula a solution of *p*-methoxybenzyl trichloroacetimidate (1.5 g, 4.7 mmol), followed by boron trifluoride diethyl etherate (0.10 mL of a 0.37 M solution in CH_2Cl_2, 37 μmol). The resulting solution was stirred for 4 h and Et_3N (50 μL, 0.40 mmol) was added. The mixture was filtered through celite and the resulting crude oil was further purified on silica gel column chromatography (hexanes-ethyl acetate 10:1 v/v) to afford **19** (677 mg, 1.46 mmol, 86%) as a colorless oil: R_f 0.50 (hexanes-ethyl acetate, 5:1, v/v); IR (neat): 2954, 2856, 1731, 1613, 1514, 1462, 1372, 1301, 1247, 1172 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.24 (d, *J* = 8.0 Hz, 2H), 6.86 (d, *J* = 8.0 Hz, 2H), 4.47 (s, 2H), 4.14 (qd, *J* = 7.0, 1.5 Hz, 2H), 3.87 (m, 1H), 3.80 (s, 3H), 3.64 (m, 1H), 2.59 (dd, *J* = 15.0, 7.5 Hz, 1H), 2.44 (ddd, *J* = 15.0, 4.5, 1.5 Hz, 1H), 1.68-1.27 (m, 10 H), 1.25 (td, *J* = 7.0, 1.0 Hz, 1H), 0.89 (t, *J* = 7.0 Hz, 3H), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz, mixture of diastereomers): δ 171.8, 159.1, 130.7, 129.3, 113.7, 76.0, 75.9, 72.0, 71.8, 71.1, 60.4, 55.3, 55.2, 40.1, 39.4, 39.3, 32.3, 32.2, 29.9, 29.7, 25.9, 18.6, 18.5, 18.1, 14.3, 14.2, -4.4; HRFABMS calcd for $[M+Na]^+$ 489.3012, found 489.3022.



20

Enone 20. To a stirred -78 °C solution of **19** (677 mg, 1.46 mmol) in toluene (15 mL) was added DIBAL (0.285 mL, 1.60 mmol). After 40 min, MeOH (1.0 mL) was added slowly followed by saturated aqueous sodium-potassium tartrate (10 mL). The aqueous phase was extracted with ethyl acetate (3 x 10 mL) and the combined organic phases were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (hexanes-ethyl acetate, 5:1, v/v) of the residue provided the aldehyde **19a** (530 mg, 1.26 mmol, 87%) as a pale yellow oil: R_f 0.47 (hexanes-ethyl acetate, 5:1, v/v).

To a stirred solution of dimethyl (2-oxopropyl)-phosphonate (0.190 mL, 1.39 mmol) in CH_3CN (8 mL) was added LiCl (106 mg, 2.52 mmol) followed by diisopropylethylamine (0.331 mL, 1.89 mmol). After stirring for 10 min, a solution of **19a** (530 mg, 1.26 mmol) in CH_3CN (4.5 mL) was added. The resulting mixture was stirred for 3 h. The solvent was removed under a stream of N_2, and the resulting residue was diluted with ethyl acetate (15 mL). Saturated aqueous NH_4Cl (15 mL) was added and the separated aqueous phase was extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (hexanes-ethyl acetate, 5:1, v/v) of the residue gave **20** (477 mg, 1.04 mmol, 82%) as a colorless oil: R_f 0.55 (hexanes-ethyl acetate, 3:1, v/v); IR (neat): 2948, 2854, 1698, 1678, 1613, 1513, 1462, 1359, 1255, 1172 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.25 (d, *J* = 7.5 Hz, 2H), 6.88 (d, *J* = 8.0 Hz, 2H), 6.80 (dddd, *J* = 16.5, 7.0, 7.0, 2.5 Hz, 1H), 6.10 (dd, *J* = 16.0, 2.0 Hz, 1H), 4.47 (d, *J* = 11.5 Hz, 1H), 4.44 (d, *J* = 11.5 Hz, 1H), 3.81 (s, 3H), 3.64 (pentet, *J* = 5.0 Hz, 1H), 3.50 (pentet, *J* = 5.5 Hz, 1H), 2.46-2.43 (m, 2H), 2.23 (t, *J* = 1.5 Hz, 3H), 1.67-1.24 (m, 10 H), 0.90 (t, *J* = 6.0 Hz, 3H), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz, mixture of diastereomers): δ 198.4, 159.2, 144.7, 133.3, 130.5, 129.4, 113.8, 72.0, 71.8, 70.7, 55.3, 39.6, 39.3, 37.1, 32.5, 32.5, 29.8, 29.3, 26.7, 25.9, 18.6, 18.5, 18.1, 14.3, -4.4; HRCIMS calcd for $[M+NH_4]^+$ 480.3509, found 480.3536.

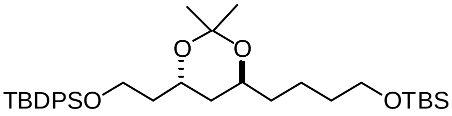


11

Hydroxyenone 11. To a stirred rt solution of enone **20** (73 mg, 0.21 mmol) in MeOH (2.1 mL) was added camphorsulfonic acid (3.6 mg, 16 μmol). After 3 h, Et_3N (50 μL) was added and the resulting mixture was concentrated by rotary evaporation. The residue was purified by silica gel column chromatography (hexanes-ethyl acetate 3:1 v/v) to yield alcohol **20a** (66 mg, 0.19 mmol, 90%) as a colorless oil: R_f 0.25 (hexanes-ethyl acetate, 1:1, v/v).

To a solution of **20a** (54.0 mg, 0.155 mmol) in CH_2Cl_2 (1.6 mL) was sequentially added $NaHCO_3$ (197 mg, 2.32 mmol) and the Dess-Martin periodinane reagent (197 mg, 0.465 mmol). The resulting mixture was stirred for 40 min before Et_2O (5 mL), saturated aqueous $NaHCO_3$ (1 mL), and saturated aqueous $Na_2S_2O_3$ (1 mL) were added. This mixture was vigorously stirred until the organic layer became clear (~15 min). The separated organic phase was washed with H_2O and saturated aqueous NaCl (2 x 2 mL each) and the aqueous phases were extracted with Et_2O (3 x 2 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated. The resulting crude aldehyde **20b** as a colorless oil: R_f 0.57 (hexanes-ethyl acetate, 1:1, v/v).

To a mixture of **20b**, CH_2Cl_2 (1.6 mL), an aqueous phosphate buffer (pH 7, 0.16 mL) and *tert*-butanol (0.16 mL) was added DDQ (105 mg, 0.465 mmol). The reaction flask was placed in an aqueous bath and was sonicated for 5 min, then assayed by TLC. This process was repeated, at which point no **20b** remained. Saturated aqueous $NaHCO_3$ (1 mL) was added, and the mixture was diluted with ethyl acetate (3 mL). The organic phase was washed with saturated aqueous $NaHCO_3$ (3 x 1 mL) and the aqueous phase was extracted with ethyl acetate (3 x 1 mL). The combined organic extracts were washed with H_2O (2 mL) and saturated NaCl (2 mL), dried over Na_2SO_4, filtered and concentrated. The resulting residue was purified by flash chromatography on silica gel (hexanes-ethyl acetate, 1:1, v/v) to give the alcohol (18.3 mg, 81.0 μmol, 52% over two steps) as a colorless oil: R_f 0.29 (hexanes-ethyl acetate, 1:1, v/v); IR (neat): 3457, 2961, 2875, 1711, 1666, 1631, 1415, 1367, 1256 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 6.86-6.79 (m, 1H), 6.12 (d, *J* = 16.5 Hz, 1H), 3.78-3.69 (m, 1H), 2.64-2.56 (m, 2H), 2.47-2.34 (m, 4H), 2.2 (s, 3H), 1.84-1.77 (m, 1H), 1.73-1.65 (m, 2H), 1.64-1.54 (m, 3H), 1.48-1.41 (m, 1H) 0.90 (t, *J* = 7.0 Hz, 3H): ^{13}C NMR ($CDCl_3$, 125 MHz, partial): δ 212.0, 144.1, 133.5, 70.2, 44.9, 42.2, 40.8, 40.4, 39.1, 36.7, 30.6, 26.9, 19.3, 17.3, 13.7; HRCIMS calcd for $[M+NH_4]^+$ 244.1913, found 244.1922.



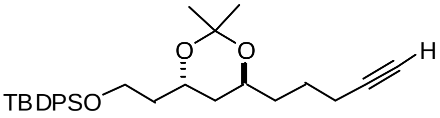
24

Acetal 24. To a stirred 0 °C solution of diisopropylamine (8.42 mL, 48.0 mmol) in THF (145 mL) was added *n*-butyllithium (21.8 mL of a 2.60 M solution in hexanes, 56.6 mmol). The resulting solution was stirred for 30 min and cooled to –78 °C before methyl acetoacetate (2.84 mL, 26.4 mmol) was added dropwise. After 30 min, a solution of aldehyde **12** (5.20 g, 24.0 mmol) was added and the reaction mixture was stirred at –78 °C for an additional 30 min. Saturated aqueous NH_4Cl (150 mL) and Et_2O (100 mL) were added. The layers were separated and the aqueous phase was extracted with Et_2O (3x50 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography (hexanes-ethyl acetate, 5:1, v/v) to yield the ketoester **12c** (4.61 g, 13.9 mmol, 58%) as a clear, colorless oil: R_f 0.35 (hexanes-ethyl acetate, 2:1, v/v); IR (neat): 3463, 2937, 2854, 1747, 1651, 1436, 1404, 1360, 1254, 1092 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 4.07 (m, 1H), 3.74 (s, 3H), 3.60 (t, *J* = 6.0 Hz, 2H), 3.49 (s, 2H), 2.77 (broad s, 1H), 2.72 (dd, *J* = 17.0, 3.0 Hz, 1H), 2.64 (dd, *J* = 17.0, 9.0 Hz, 1H), 1.54-1.34 (m, 6H), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 203.5, 167.3, 67.5, 63.0, 52.4, 49.7, 49.6, 36.2, 32.6, 26.0, 21.8, 18.4, -5.3; HRFABMS calcd for $C_{16}H_{32}O_5Si$ $[M+H]^+$ 333.2097, found 333.2090.

To a stirred 0 °C solution of $Me_4NBH(OAc)_3$ (2.3 g, 9.0 mmol) in CH_3CN : AcOH (20 mL, 1:1, v/v) was added via cannula a solution of **12c** (1.0 g, 3.0 mmol) in CH_3CN (2 mL). After 50 min, the reaction mixture was diluted with ethyl acetate (20 mL) and a saturated aqueous solution of sodium-potassium tartrate (25 mL) was added. The separated aqueous phase was extracted with ethyl acetate (3 x 25 mL), and the combined organic extracts were washed with saturated $NaHCO_3$ (3 x 30), water (25 mL) and saturated aqueous NaCl (25 mL). The organic phase was dried over Na_2SO_4, filtered, and concentrated by rotary evaporation to yield a yellow oil **12d**, which was carried onto the next step without further purification: R_f 0.52 (hexanes-ethyl acetate, 1:1, v/v).

To a stirred rt solution of **12d** in CH_2Cl_2 (20 mL) was added 2,2-dimethoxypropane (1.51 mL, 12.0 mmol) followed by PPTs (75 mg, 0.30 mmol). After 4 h, Et_3N (0.1 mL) was added and the solvent removed by rotary evaporation. The crude mixture was purified by flash chromatography on silica gel (hexanes-ethyl acetate, 20:1 to 10:1, v/v) to give **12e** (521 mg, 1.40 mmol, 47% over two steps) as a clear, colorless oil: R_f 0.75 (hexanes-ethyl acetate, 5:1, v/v); IR (neat): 2986, 2934, 2892, 1747, 1462, 1436, 1380, 1318, 1224 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 4.26 (dddd, *J* = 8.5, 8.5, 6.5, 6.5 Hz, 1H), 3.78 (m, 1H), 3.70 (s, 3H), 3.60 (t, *J* = 6.0 Hz, 2H), 2.54 (dd, *J* = 15.5, 8.5 Hz, 1H), 2.44 (dd, *J*= 15.5, 5.0 Hz, 1H), 1.69-1.59 (m, 2H), 1.57-1.49 (m, 2H), 1.47-1.39 (m, 2H), 1.36 (s, 3H), 1.33 (s, 3H), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.4, 100.5, 66.5, 63.5, 63.1, 51.6, 40.6, 38.0, 35.6, 32.7, 25.9, 24.6, 25.5, 21.7, 18.4, -5.2; HRFABMS calcd for $C_{19}H_{38}O_5Si$ $[M+H]^+$ 375.2567, found 375.2557.

To a stirred 0 °C solution of **12e** (520 mg, 1.40 mmol) in Et_2O (14 mL) was added $LiAlH_4$ (80 mg, 2.1 mmol). After 10 min, H_2O (10 mL) was added and the aqueous phase was extracted with Et_2O (3 x 10 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated. The residue was dissolved in CH_2Cl_2 (15 mL) and *tert*-butyldiphenylsilyl chloride (0.48 mL, 1.8 mmol), Et_3N (0.40 mL, 2.8 mmol) and DMAP (18 mg, 0.14 mmol) were sequentially added. After 12 h, saturated aqueous NH_4Cl (15 mL) was added and the separated aqueous phase was washed with CH_2Cl_2 (2 x 10 mL), dried over Na_2SO_4, filtered and concentrated by rotary evaporation. The crude residue was purified by silica gel column chromatography (hexanes-ethyl acetate, 20:1, v/v) to yield **24** (655 mg, 0.570 mmol, 80% over two steps) as a clear, colorless oil: R_f 0.40 (hexanes-ethyl acetate, 10:1, v/v); IR (neat): 3070, 3048, 2926, 2803, 1957, 1896, 1820, 1589, 1462, 1427, 1378, 1252 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.69-7.64 (m, 4H), 7.45-7.35 (m, 6H), 4.08 (dddd, *J* = 7.5, 7.5, 7.5, 6.5 Hz, 1H), 3.82-3.73 (m, 2H), 3.70 (pentet, *J* = 5.5 Hz, 1H), 3.61 (t, *J* = 7.0 Hz, 2H), 1.78-1.66 (m, 2H), 1.60-1.50 (m, 6H), 1.46-1.40 (m, 2H), 1.34 (s, 3H), 1.33 (s, 3H), 1.05 (s, 9H), 0.90 (s, 9H), 0.05 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 135.6, 133.9, 129.5, 127.6, 100.2, 66.6, 63.4, 63.2, 60.3, 38.9, 38.8, 37.7, 32.7, 26.8, 26.0, 24.8, 24.7, 21.7, 19.2, 16.7, -5.2; HRCIMS calcd for $C_{34}H_{56}O_4Si_2$ $[M+H]^+$585.3795, found 585.3818.

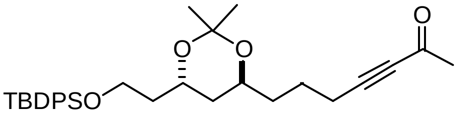


25

Alkyne 25. To a stirred solution of **24** (660 mg, 1.13 mmol) in THF (5 mL) was added HF·Pyr complex (0.17 mL). After 6.5 h, the reaction mixture was diluted with Et_2O (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) was added slowly. The organic phase was washed with saturated $NaHCO_3$ (2 x 10 mL) and the aqueous phase was extracted with Et_2O (3 x 10 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated by rotary evaporation. Silica gel column chromatography (hexanes-ethyl acetate, 5:1 to 2:1, v/v) to yield the alcohol **24a** (390 mg, 0.870 mmol, 74 %) as a clear, colorless oil: R_f 0.11 (hexanes-ethyl acetate, 5:1, v/v).

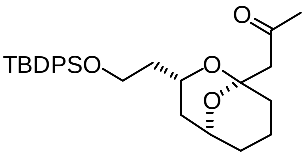
To a stirred –78 °C solution of DMSO (0.16 mL, 2.3 mmol) in CH_2Cl_2 (7 mL), oxalyl chloride (98 μL, 1.1 mmol) was added. The resulting mixture was stirred at –78 °C for an additional 30 min before a solution of **24a** (390 mg, 0.870 mmol) in CH_2Cl_2 (2 mL) was added via cannula. The resulting mixture was stirred for 1 h before Et_3N (0.55 mL, 4.4 mmol) was added. The reaction was warmed to rt, diluted with Et_2O (25 mL) and water (25 mL) was added. The separated aqueous phase was extracted with Et_2O (2 x 20 mL) and the combined organic extracts were washed with H_2O (20 mL) and saturated aqueous NaCl (20 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated. Silica gel column chromatography (hexanes-ethyl acetate, 10:1 to 5:1, v/v) of the residue provided the aldehyde **24b** (345 mg, 0.770 mmol, 89%) as a pale yellow oil: R_f 0.45 (hexanes-ethyl acetate, 5:1, v/v); IR (neat): 3070, 3049, 2934, 2857, 1960, 1892, 1820, 1727, 1589, 1472, 1427, 1379, 1224, 1111 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.78 (t, *J* = 2 Hz, 1H), 7.66 (m, 4H), 7.45-7.36 (m, 6H), 4.09 (m, 1H), 3.82-3.74 (m, 2H), 3.70 (pentet, *J* = 5.5 Hz, 1H), 2.47 (td, *J* = 7.5, 2.0 Hz, 2H), 1.81-1.62 (m, 4H), 1.58 (t, *J* = 7.5 Hz, 2H), 1.55-1.44 (m, 2H), 1.34 (s, 3H), 1.33 (s, 3H), 1.05 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 202.5, 135.5, 133.9, 129.6, 127.6, 100.2, 66.3, 63.4, 60.0, 43.7, 38.9, 38.7, 35.2, 26.8, 24.8, 24.8, 19.2, 18.3; HRFABMS calcd for $C_{28}H_{40}O_4Si$ $[M+Na]^+$ 491.2594, found 491.2581.

To a solution of **24b** (345 mg, 0.770 mmol) in MeOH (8 mL) was added K_2CO_3 (215 mg, 1.55 mmol) and dimethyl-1-diazo-2-oxopropylphosphonate (178 mg, 0.930 mmol). The suspension was stirred for 4 h before Et_2O (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) were added. The aqueous phase was extracted with Et_2O (2 x 10 mL) and the combined organic phases were dried over Na_2SO_4, filtered and concentrated by rotary evaporation. The residue was purified by flash chromatography on silica gel (hexanes-ethyl acetate, 20:1, v/v) to yield alkyne **25** (289 mg, 0.650 mmol, 84%) as a clear, colorless oil: R_f 0.80 (hexanes-ethyl acetate, 5:1, v/v); IR (neat): 3071, 3049, 2939, 2117, 1958, 1840, 1824, 1589, 1472, 1428, 1379, 1224 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.67 (tt, *J* = 6.0, 1.5 Hz, 4H), 7.46-7.36 (m, 6H), 4.10 (dddd, *J* = 7.5, 7.5, 7.5, 5.5 Hz, 1H), 3.83-3.76 (m, 2H), 3.70 (pentet, *J* = 5.5 Hz, 1H), 2.25-2.19 (m, 2H), 1.95 (t, *J* = 2.5 Hz, 1H), 1.79-1.64 (m, 3H), 1.62-1.50 (m, 5H), 1.35 (s, 3H), 1.33 (s, 3H), 1.05 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 135.6, 133.9, 129.6, 127.6, 100.2, 84.4, 68.4, 66.2, 63.4, 60.0, 38.9, 38.7, 34.9, 26.9, 24.82, 24.80, 24.6, 19.2, 18.3; HRFABMS calcd for $C_{29}H_{40}O_3Si$ $[M+Na]^+$ 487.2645, found 487.2643.



26

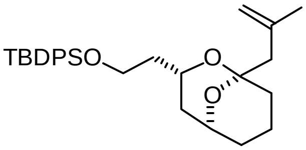
Ynone 26. To a stirred –78 °C solution of **25** (58.5 mg, 0.131 mmol) in THF (1 mL) under Ar was added *n*-butyllithium (103 µL of a 2.60 M solution in hexanes, 0.262 mmol). After the mixture was stirred for 45 min, acetaldehyde (26.5 µL, 0.654 mmol) was added. After 10 min, saturated aqueous NH_4Cl (1 mL) was added and phases were separated. The aqueous phase extracted with Et_2O (2 x 4 mL). The organic fraction was dried over Na_2SO_4, filtered and concentrated. The crude residue was dissolved in hexanes (1 mL) and MnO_2 (170 mg, 1.96 mmol) was added. After stirring for 10 h, the reaction mixture was filtered through celite and the residue was purified by silica gel column chromatography (hexanes-ethyl acetate, 10:1, v/v) to yield ynone **26** (57 mg, 0.11 mmol, 86%) as a clear, colorless oil: R_f 0.50 (hexanes-ethyl acetate, 5:1, v/v); IR (neat): 3070, 3049, 2939, 2858, 2209, 1961, 1892, 1821, 1679, 1589, 1471, 1427, 1379, 1359, 1226 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.66 (tt, *J* = 5.5, 2.0 Hz, 4H), 7.45-7.36 (m, 6H), 4.09 (dddd, *J* = 7.5, 7.5, 7.5, 5.5 Hz, 1H), 3.83-3.74 (m, 2H), 3.70 (pentet, *J* = 5.5 Hz, 1H), 2.38 (m, 2H), 2.32 (s, 3H), 1.78-1.66 (m, 3H), 1.62-1.53 (m, 5H), 1.34 (s, 3H), 1.32 (s, 3H), 1.05 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 184.9, 135.6, 133.9, 129.6, 127.6, 100.3, 93.6, 81.6, 66.1, 63.4, 60.0, 38.8, 38.7, 34.9, 32.8, 26.9, 24.8, 24.8, 23.9, 19.2, 18.9; HRFABMS calcd for $C_{31}H_{42}O_4Si$ $[M+H]^+$ 507.2930, found 507.2920.



22

Ketone 22. To a stirred solution of **26** (13.0 mg, 25.5 µmol) in CH_2Cl_2 : MeOH (0.5 mL, 5:1, v/v), camphorsulfonic acid (0.58 mg, 2.5 µmol) was added. After 35 h, the solvent was removed by rotary evaporation, the residue dissolved in benzene (1 mL), and *p*-

toluensulfonic acid monohydrate (0.50 mg, 2.5 μmol) was added. After additional stirring for 4 h, triethylamine (20.0 μL, 160 μmol) was added and the volatile components removed by rotary evaporation. The residue was purified by silica gel column chromatography (hexanes-ethyl acetate, 7:1, v/v) to give **22** (10.6 mg, 23.0 μmol, 90%) as a clear, colorless oil: R_f 0.25 (hexanes-ethyl acetate, 7:1, v/v); IR (neat): 3070, 3049, 2956, 2891, 1961, 1891, 1821, 1711, 1589, 1471, 1428, 1356, 1200 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.71-7.66 (m, 4H), 7.46-7.37 (m, 6H), 4.77 (dddd, *J* = 11.5, 8.7, 8.7, 5.0 Hz, 1H), 4.23 (t, *J* = 5.0 Hz, 1H), 3.83 (dt, *J* = 10.5, 6.5 Hz, 1H), 3.71 (pentet, *J* = 5.5 Hz, 1H), 2.61 (d, *J* = 13.0 Hz, 1H), 2.57 (d, *J* = 13.0 Hz, 1H), 2.18 (s, 3H), 2.15-2.02 (m, 2H), 1.96-1.85 (m, 3H), 1.76 (m, 1H), 1.70-1.63 (m, 3H), 1.54 (dd, *J* = 13.5, 4.0 Hz, 1H), 1.06 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 206.9, 135.5, 133.9, 129.6, 127.7, 95.6, 67.4, 66.7, 59.6, 56.5, 41.1, 35.1, 32.9, 32.1, 27.6, 26.9, 19.6, 19.2; HRFABMS calcd for $C_{28}H_{38}O_4Si$ $[M+H]^+$ 467.2617, found 467.2608.



21

Alkene 21. To a stirred –78 °C suspension of methyltriphenylphosphonium bromide (92.0 mg, 0.253 mmol) in THF (1 mL) under Ar was added *n*-butyllithium (81.0 μL of a 2.60 M solution in hexanes, 0.211 mmol). After the mixture was stirred for 30 min, it was allowed to warm to 0 °C and stir for 1 h. A solution of **22** (19.5 mg, 42.0 μmol) in THF (0.4 mL) was added and the reaction mixture was allowed to warm to rt. After stirring at rt for 12 h, the solvent was removed and silica gel column chromatography of the residue (hexanes to hexanes-ethyl acetate, 20:1, v/v) provided **21** (18.5 mg, 39.8 μmol, 95%) as a clear, colorless oil: R_f 0.30 (hexanes-ethyl acetate, 20:1, v/v); IR (neat): 3070, 3049, 2956, 2891, 1961, 1891, 1821, 1711, 1589, 1471, 1428, 1356, 1200 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.69-7.67 (m, 4H), 7.45-7.30 (m, 6H), 4.82 (q, *J* = 1.5 Hz, 1H), 4.76-4.71 (m, 1H), 4.73 (broad s, 1H), 4.22 (t, *J* = 5.5 Hz, 1H), 3.85 (dt, *J* = 9.5, 6.5 Hz, 1H), 3.73 (pentet, *J* = 5.5 Hz, 1H), 2.28 (d, *J* = 13.5 Hz, 1H), 2.24 (d, *J* = 13.5 Hz, 1H), 2.18-2.01 (m, 2H), 1.94 (ddd, J = 12.0, 12.0, 5.5 Hz, 1H), 1.86-1.82 (m, 2H), 1.76

(s, 3H), 1.78-1.61 (m, 4H), 1.52 (dd, *J* = 13.0, 4.0 Hz, 1H), 1.06 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 142.2, 135.6, 134.0, 129.5, 127.6, 114.5, 96.4, 67.3, 66.2, 59.9, 51.1, 41.3, 35.2, 31.7, 28.0, 26.9, 24.0, 19.7, 19.2; HRFABMS calcd for $C_{29}H_{40}O_3Si$ $[M+H]^+$ 465.2825, found 465.2817.