Total Synthesis of (±)-Kalihiinol C

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Material and Methods

Unless otherwise stated, reactions were performed under a nitrogen atmosphere using freshly distilled solvents. Diethyl ether (Et₂O) and tetrahydrofuran (THF) were distilled from sodium/benzophenone. Methylene chloride (CH₂Cl₂), and benzene were distilled from calcium hydride. Methanol (MeOH) was distilled from magnesium. All other commercially obtained reagents were used as received. All reactions were magnetically stirred and monitored by thin-layer chromatography (TLC) using E. Merck silica gel 60 F254 pre-coated plates (0.25-mm). Column or flash chromatography was performed with the indicated solvents using silica gel (particle size 0.032-0.063 nm) purchased from Bodman. ¹H and ¹³C NMR spectra were recorded on Bruker Advance DPX-500 or Bruker Advance DPX-400 spectrometers. Chemical shifts are reported relative to internal solvent as described by Gottlieb (i.e. chloroform ¹H δ 7.26 ppm, ¹³C δ 77.16 ppm; acetone ¹H δ 2.05 ppm, ¹³C δ 29.84 ppm; methanol ¹H δ 3.31 ppm, ¹³C δ 49.00 ppm). Melting points were obtained on a Gallenkamp variable temperature melting point apparatus and are uncorrected. Infrared spectra were recorded on a Midac M-1200 FTIR. High resolution mass spectra were acquired at The University of Illinois Mass Spectrometry Center.

Experimental Procedures

Preparation of TBS-ethers 6 and 25

TBS-ethers 6 and 25. A solution of acrolein (20.0 mL, 300 mmol, 1.0 equiv) in Et₂O (120 mL) at 0°C was treated with anhydrous HBr. After NMR had indicated the reaction was complete (ca. 10 min), the solution was neutralized with solid NaHCO₃ (ca. 3 g) and filtered. The yellow solution was diluted with pentane (150 mL) and cooled to -78°C before adding vinyl magnesium bromide (1.0 M in THF, 300 mL, 1.0 equiv). After 1 h the reaction was quenched with saturated aqueous NH₄Cl (ca. 50 mL). The mixture was washed with water (2 x 100 mL), brine (100 mL), and dried with Na₂SO₄. The solvent was removed *in vacuo* and the resulting oil taken up in CH₂Cl₂ (500 mL).

Imidazole (20.4 g, 300 mmol, 1.0 equiv) was added followed by TBSCl (45.0 g, 300 mmol, 1.0 equiv) and the mixture was allowed to stir for 16 h. After filtering, the solvent was removed *in vacuo* and the resulting residue purified by silica gel column chromatography (10:1 pentane:Et₂O) to afford a mixture of bromide **6** (26.8 g, 32% yield) and olefin **25** (6.5g, 11% yield) as a colorless oils which could be further purified by low pressure distillation.

TBS-ether 6. b.p. 69-70°C @1.5 mm Hg; ¹H NMR (500 MHz, CDCl₃) δ 5.82-5.74 (m, 1H), 5.23-5.18 (m, 1H), 5.10-5.06 (m, 1H), 4.31-4.26 (m, 1H), 3.50-3.38 (comp m, 2H), 2.08-1.92 (comp m, 2H), 0.89 (s, 9H), 0.09 (s, 3H), 0.04 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 140.7, 114.9, 71.9, 41.1, 30.1, 26.0, 18.3, -4.1, -4.7; IR (thin film/NaCl) 2955 (s), 2857 (s), 1644 (w), 1472 (m), 1361 (m), 1257 (s), 1162 (w), 1092 (s), 1027 (s), 837 (s) cm⁻¹

TBS-ether 25. b.p. 30-31°C @1.5 mm Hg; ¹H NMR (500 MHz, CDCl₃) δ 5.81 (ddd, *J*=5.3, 10.5, 17.0 Hz, 1H), 5.22 (dt, *J*=1.6, 17.2 Hz, 2H), 5.06 (dt, *J*=1.6, 16.9 Hz, 2H), 4.63-4.59 (m, 1H), 0.91 (s, 9H), 0.07 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 140.3, 113.8, 74.8, 26.0, 18.5, -2.8, -4.6; IR (thin film/NaCl) 2956 (s), 2830 (s), 2858 (s), 1638 (w), 1472 (m), 1361 (m), 1254 (s), 1126 (s), 1073 (s), 922 (s) cm⁻¹

Preparation of ester 7

Ester 7. To a solution of (±)-**5** (1.00 g, 6.24 mmol, 1.0 equiv) in THF (35 mL) and HMPA (3.2 mL, 18.7 mmol, 3.0 equiv) at -40°C, was added LDA (0.5 M in THF, 26.0 mL, 13.1 mmol, 2.1 equiv). After 20 min, a solution of **6** (2.61 g, 9.36 mmol, 1.5 equiv) in THF (5 mL) was added via syringe pump over 1 h. After an additional 2 h, the reaction was warmed to 0°C for 1h then quenched with saturated aqueous NaHCO₃ (10 mL). EtOAc (50 mL) was added and the mixture was washed with water (25 mL), brine (25 mL), and dried with Na₂SO₄. After the solvent was removed *in vacuo*, the resulting residue was purified by silica gel column chromatography (9:1 hexanes:EtOAc) to afford ester **7** (1.77 g, 79% yield) as a colorless oil. (1:1 mixture of diastereomers) ¹H NMR (400 MHz, CDCl₃) δ 5.83-5.71 (m, 1H), 5.14 (d, *J*=17.0 Hz, 1H), 5.03 (d, *J*=17.0 Hz, 1H), 4.13-4.05 (m, 1H), 3.89-3.80 (m, 1H), 2.62 (br s, 1H), 2.29-2.19 (m, 1H), 1.78-1.40 (comp m, 13H), 1.27-1.15 (comp m, 3H), 0.89 (s, 9H) 0.03 (d, *J*=8.6 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 175.1, 141.5, 141.4, 114.2, 114.1, 81.3, 73.6, 73.5, 68.6, 68.5, 53.2, 53.0, 35.5, 35.4, 28.3, 26.0, 25.2, 21.7, 21.6, 18.4, -4.2, -4.2, -4.7, -4.7; IR (thin film/NaCl) 3442 (br m), 2957 (m), 2930 (m), 2858 (m), 1728 (m), 1473 (m), 1368 (m), 1254 (m), 1156 (m), 1087 (m) cm⁻¹; HRMS (FAB) *m/z* found: 359.2618 [calc'd for C₁₉H₃₉O₄Si (M+H): 359.2618].

Preparation of benzyl ether **8**

Benzyl ether **8.** To a solution of **7** (10.4 g, 28.9 mmol, 1.0 equiv) in THF (200 mL) at 0°C was added NaH (60% in mineral oil, 1.27 g, 31.8 mmol, 1.1 equiv) followed by benzyl bromide (10.3 mL, 86.7 mmol, 3.0 equiv) and sodium iodide (1.30 g, 8.64 mmol, 0.3 equiv). The reaction was allowed to warm to rt and stirred for 12 h before quenching with water (100 mL). After diluting with hexanes (100 mL), the organic layer was separated, washed with brine (2 x 100 mL), and dried with Na₂SO₄. Removal of the solvent *in vacuo* provided a residue which was purified by silica gel column chromatography (100% hexanes then 9:1 hexanes:EtOAc) to afford **8** (12.1 g, 93% yield) as a colorless oil. (1:1 mixture of diastereomers) ¹H NMR (500 MHz, CDCl₃) δ 7.33-7.19 (comp m, 5H), 5.74 (ddd, *J*=5.9, 10.5, 16.7 Hz, 1H), 5.14-4.98 (m, 2H), 4.53 (d, *J*=11.4 Hz, 1H), 4.42 (d, *J*=11.2 Hz, 1H), 4.11-4.03 (m, 1H), 3.69 (dq, *J*=6.2, 8.3 Hz, 1H), 2.42-2.33 (m, 1H), 1.59-1.37 (comp m, 13H), 1.16-1.14 (m, 3H), 0.87-0.86 (m, 9H), 0.03- -0.03 (m, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 174.0, 173.9, 141.6, 141.5, 128.3, 127.9, 127.8, 127.5, 114.1, 114.0, 80.4, 80.3, 73.8, 73.4, 71.3, 53.1, 53.0, 35.7, 35.6, 28.3, 26.0, 24.2, 23.8, 18.4, 18.4, 17.1, -4.2, -4.2, -4.7; IR (thin film/NaCl) 2957 (s), 2857 (s), 1728 (s), 1497 (w), 1472 (m), 1455 (m), 1390 (m), 1366 (s), 1254 (s), 1156 (s) cm⁻¹; HRMS (FAB) *m/z* found: 449.7186 [calc'd for C₂₆H₄₅O₄Si (M+H): 449.7186].

Preparation of alcohol **26**

Alcohol **26.** A solution of **8** (19.6 g, 43.7 mmol, 1.0 equiv) in CH₂Cl₂ (350 mL) at -78°C was treated with DIBAL-H (17.1 mL, 96.2 mmol, 2.2 equiv). After 1 h, the reaction was quenched with 20% aqueous Rochelle's salt (100 mL). The organic layer was washed with water (100 mL), brine (100 mL) and dried with Na₂SO₄. After concentration, the resulting residue was purified by silica gel column chromatography (3:1 hexanes:EtOAc) to afford **26** (14.9 g, 90%) as a colorless oil. (1:1 mixture of diastereomers) ¹H NMR (500 MHz, CDCl₃) δ 7.40-7.25 (comp m, 5H), 5.82-5.72 (m, 1H), 5.16-5.11 (m, 1H), 4.65 (d, *J*=11.4 Hz, 1H), 4.41-4.37 (m, 1H), 4.09-4.05 (m, 1H), 3.86-3.81 (m, 1H), 3.65-3.56 (comp m, 2H), 1.58-1.35 (comp m, 6H), 1.28 (d, *J*=6.0 Hz, 3H), 0.91-0.88 (comp m, 9H), 0.04 (s, 3H), 0.03 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ

141.7, 141.6, 138.4, 128.6, 127.9, 127.9, 127.9, 114.0, 114.0, 79.3, 79.2, 74.1, 73.9, 71.2, 71.2, 63.9, 63.7, 46.3, 46.3, 35.8, 35.7, 26.0, 24.3, 24.1, 18.4, 18.4, 17.8, 17.7, -4.2, -4.7; IR (thin film/NaCl) 3446 (br m), 2954 (m), 2928 (m), 2884 (m), 2856 (m), 1471 (m), 1455 (m), 1252 (m), 1088 (m), 1028 (m) cm^{-1} ; HRMS (FAB) m/z found: 379.2669 [calc'd for $\text{C}_{22}\text{H}_{39}\text{O}_2\text{Si}$ (M+H): 379.2668].

Preparation of aldehyde 9

Aldehyde 9. A solution of oxalyl chloride (3.57 mL, 40.9 mmol, 1.1 equiv) in CH_2Cl_2 (250 mL) at -78°C was treated with DMSO (5.80 mL, 81.8 mmol, 2.2 equiv) and stirred for 10 min. A solution of **26** (14.1 g, 37.2 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was then added and stirring continued for an additional 10 min. Et_3N (25.9 mL, 186 mmol, 5.0 equiv) was added and the mixture was allowed to warm to rt. Water (100 mL) was introduced and the organic layer washed with brine (100 mL) and dried with Na_2SO_4 . After concentration, the resulting residue was purified by silica gel column chromatography (18:1 then 9:1 hexanes:EtOAc) to afford **9** (14.9 g, 89%) as a colorless oil. (1:1 mixture of diastereomers) ^1H NMR (500 MHz, CDCl_3) δ 9.68-9.66 (m, 1H), 7.36-7.26 (comp m, 5H), 5.80-5.71 (m, 1H), 5.17-5.16 (m, 1H), 5.06-5.04 (m, 1H), 4.62 (d, $J=11.5$ Hz, 1H), 4.42 (d, $J=11.5$ Hz, 1H), 4.12-4.07 (m, 1H), 3.81 (m, 1H), 2.39-2.33 (m, 1H), 1.81-1.41 (comp m, 4H), 1.27-1.24 (comp m, 3H), 0.90-0.88 (comp m, 9H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 204.7, 204.7, 141.3, 138.4, 128.5, 127.8, 127.8, 114.2, 114.2, 74.9, 74.8, 73.6, 73.4, 70.8, 57.8, 57.7, 35.4, 35.3, 26.0, 21.6, 21.5, 18.3, 17.4, -4.2, -4.7; IR (thin film/NaCl) 2955 (s), 2930 (s), 2857 (s), 1725 (s), 1497 (w), 1472 (m), 1379 (m), 1252 (s), 1091 (s), 836 (s) cm^{-1} ; HRMS (FAB) m/z found: 375.2355 [calc'd for $\text{C}_{22}\text{H}_{35}\text{O}_3\text{Si}$ (M-H): 375.2355].

Preparation of triene 4

Triene 4. A solution of methallyl phosphonic acid diethyl ester (6.92 g, 36.0 mmol, 1.3 equiv) in THF (300 mL) at -78°C was treated with $n\text{-BuLi}$ (2.3 M in hexanes, 15.7 mL, 36.0 mmol, 1.3 equiv) and the solution was stirred for 5 min. A solution of **9** (10.4 g, 27.7 mmol, 1.0 equiv) in THF (10 mL) was added and stirring continued for an additional 15 min. The reaction was warmed to rt and stirred for an additional 1 h before

quenching with water (100 mL). The mixture was diluted with hexanes (200 mL) and the organic layer was washed with water (3 x 100 mL), brine (100mL), and dried with Na₂SO₄. Concentration *in vacuo* afforded **4** (24.9 g, 90%) as a colorless oil which could be advanced without further purification. An analytical sample, however, could be obtained by silica gel column chromatography (9:1 hexanes:EtOAc, 1% Et₃N). (1:1 mixture of diastereomers) ¹H NMR (500 MHz, CDCl₃) δ 7.40-7.25 (comp m, 5H), 6.13 (d, *J*=15.4 Hz, 1H), 5.82-5.74 (m, 1H), 5.54-5.41 (m, 1H), 5.16-5.10 (m, 1H), 5.04-4.99 (m, 1H), 4.89 (s, 2H), 4.58 (d, *J*=11.2 Hz, 1H), 4.45 (d, *J*=11.9 Hz, 1H), 4.10-4.05 (m, 1H), 3.53-3.48 (m, 1H), 2.21-2.12 (m, 1H), 1.85-1.83 (m, 3H), 1.70-1.25 (comp m, 4H), 1.16-1.12 (comp m, 3H), 0.90 (s, 9H), 0.05-0.03 (comp m, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 142.3, 142.0, 141.8, 139.3, 138.5, 134.9, 134.9, 131.5, 128.6, 128.4, 128.4, 127.9, 127.8, 127.8, 127.7, 127.5, 114.7, 114.7, 113.7, 113.6, 78.0, 77.9, 74.1, 72.3, 70.9, 70.8, 49.1, 49.0, 48.9, 36.3, 36.2, 26.4, 26.3, 26.1, 18.9, 18.4, 17.2, 17.1, -4.2, -4.2, -4.6; IR (thin film/NaCl) 2955 (m), 2929 (m), 2857 (m), 1472 (w), 1454 (w), 1361 (m), 1252 (m), 1090 (m), 1028 (m), 836 (m) cm⁻¹; HRMS (FAB) *m/z* found: 415.7039 [calc'd for C₂₆H₄₃O₂Si (M+H): 415.7039].

Preparation of *cis*-decalin **10**

Note: The diastereoselectivity of the cyclization correlated with the Lewis acidity of the oxidant. Lewis acidic oxidants (Cr⁶⁺ and Mn⁴⁺) afforded high to moderate diastereoselectivity, while non-metal based oxidants (Swern conditions) led to low diastereoselectivity.

Conditions	Diastereoselectivity
Jones ox. (H ₂ SO ₄ + Cr ⁶⁺)	9:1
MnO ₂ (Mn ⁴⁺)	6:1
PCC (Cr ⁶⁺)	5:1
Swern ox.	3:1

***cis*-Decalin **10**.** A solution of **4** (6.92 g, 22.0 mmol, 1.0 equiv) in MeCN (225 mL) at 0°C was treated with 20% aqueous fluorosilicic acid (1.6 mL, 2.2 mmol, 0.1 equiv). After ca. 4 h, the reaction was quenched with K₂CO₃ (ca. 5g) and diluted with hexanes (100 mL) and water (100 mL). The organic layer was washed with water (100 mL), brine (100 mL) and dried with Na₂SO₄. Concentration *in vacuo* provided a residue which was taken up in CH₂Cl₂ (225 mL). The solution was cooled to 0°C and PCC (19.0

g, 88.0 mmol, 4.0 equiv) was added. After 1h, the reaction was warmed to rt and stirred for an additional 12 h. Celite (ca 10 g) was added and the mixture was filtered. Concentration *in vacuo* followed by silica gel column chromatography (9:1 hexanes:EtOAc) afforded **10** (4.73 g, 72% yield from **4**) as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.28-7.18 (comp m, 5H), 5.16-5.13 (m, 1H), 4.59 (d, $J=12.1$ Hz, 1H), 4.38 (d, $J=12.1$ Hz, 1H), 3.79-3.71 (m, 1H), 2.64 (br s, 1H), 2.24-2.15 (comp m, 3H), 2.05-1.75 (comp m, 5H), 1.61-1.52 (comp m, 4H), 1.43-1.35 (m, 1H), 1.18 (d, $J=6.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 214.0, 138.8, 135.6, 128.5, 127.9, 127.7, 124.0, 74.1, 70.8, 46.2, 44.3, 38.1, 37.9, 28.1, 23.8, 23.8, 22.9, 15.8; IR (thin film/NaCl) 2926 (m), 2876 (m), 1707 (s), 1496 (w), 1452 (m), 1376 (m), 1323 (w), 1121 (m), 1090 (m), 1073 (m) cm^{-1} ; HRMS (FAB) m/z found: 299.2011 [calc'd for $\text{C}_{20}\text{H}_{27}\text{O}_2$ (M+H): 299.2011].

Preparation of epoxide **27**

Epoxide 27. To a 0.09 M solution of dimethyl dioxirane in acetone (94.3 mL, 8.49 mmol, 1.5 equiv) at -78°C , was added olefin **10** (1.69 g, 5.65 mmol, 1.0 equiv) in acetone (10 mL). After 2 h, the solution was slowly warmed to 25°C before removing the solvent *in vacuo*. NMR of the resulting oil showed a mixture of diastereomers in the ratio of 94:6 which could be purified by silica gel column chromatography (9:1 then 3:1 hexanes:EtOAc) to afford **27** (1.51 g, 85% yield) as a colorless oil. ^1H NMR (500 MHz, CDCl_3) δ 7.26-7.17 (comp m, 5H), 4.61 (d, $J=11.7$ Hz, 1H), 4.35 (d, $J=11.9$ Hz, 1H), 3.65-3.59 (m, 1H), 2.59 (s, 1H), 2.57-2.53 (m, 1H), 2.24-2.16 (m, 1H), 2.13-2.01 (comp m, 2H), 1.84-1.66 (comp m, 6H), 1.23-1.13 (comp m, 7H); ^{13}C NMR (125 MHz, CDCl_3) δ 212.8, 138.5, 128.6, 128.1, 127.9, 74.6, 70.9, 63.9, 58.1, 43.8, 42.0, 38.1, 37.0, 25.9, 23.6, 23.5, 19.2, 16.3; IR (thin film/NaCl) 2957 (m), 2928 (m), 2872 (m), 1707 (s), 1495 (w), 1453 (m), 1421 (w), 1378 (m), 1330 (w), 1090 (m) cm^{-1} ; HRMS (FAB) m/z found: 315.1959 [calc'd for $\text{C}_{20}\text{H}_{27}\text{O}_3$ (M+H): 315.1959].

Preparation of olefin **11**

Olefin 11. To a solution of epoxide **27** (1.51 g, 4.80 mmol, 1.0 equiv) in MeOH (50 mL) at rt was added NaOMe (15 mg, 0.24 mmol, 0.05 equiv). After 36 h, the

solution was concentrated under reduced pressure, diluted with CH₂Cl₂ (100 mL), and washed with water (2 x 25 mL) and brine (25 mL). After drying with Na₂SO₄, concentration *in vacuo* gave a 3:2 equilibrium mixture of decalins, which could be used without further purification. A solution of DMSO (6.8 mL, 96.0 mmol, 20 equiv) in THF (20 mL) was treated with NaH (60% in mineral oil, 394 mg, 9.60 mmol, 2.0 equiv). The resulting slurry was heated at 60°C for 2 h then cooled to 25 °C before adding methyltriphenylphosphonium iodide (3.43 g, 9.60 mmol, 2.0 equiv) and THF (10 mL). The resulting yellow mixture was added in 0.1 equiv portions every 2 h to a crude solution of decalins from **27** in THF (50 mL). After reaction was complete by TLC, it was quenched with water (50 mL) and diluted with hexanes (100 mL). The aqueous layer was separated and extracted with hexanes (2 x 25 mL) and the combined organic fractions were washed with water (3 x 50 mL), dried (Na₂SO₄), and concentrated. The resulting residue was purified by silica gel column chromatography (100% hexanes then 9:1 hexanes:EtOAc) to give **11** (1.23 g, 82% from **27**) as a colorless oil. ¹H NMR (500 MHz, CDCl₃) δ 7.29-7.16 (comp m, 5H), 4.59 (s, 1H), 4.47 (q, *J*=11.1 Hz, 1H), 4.42 (s, 1H), 3.96-3.90 (m, 1H), 2.77 (s, 1H), 2.31-2.26 (m, 1H), 2.04-1.85 (comp m, 4H), 1.63-1.43 (comp m, 3H), 1.26-1.13 (comp m, 7H), 1.08 (d, *J*=6.3 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 151.9, 139.1, 128.5, 127.6, 127.6, 104.8, 74.4, 70.5, 60.9, 58.4, 45.9, 43.6, 43.2, 35.8, 30.3, 27.3, 23.7, 22.5, 14.3; IR (thin film/NaCl) 2978 (m), 2930 (m), 2880 (m), 1648 (m), 1453 (m), 1379 (m), 1135 (m), 1101 (m), 1071 (m), 887 (m) cm⁻¹; HRMS (FAB) *m/z* found: 313.2169 [calc'd for C₂₁H₂₉O₂ (M+H): 313.2168].

Preparation of alcohols **12** and **28**

Alcohols 12 and 28. To condensed ammonia (40 mL) at -78°C was added sodium (368 mg, 16 mmol, 10.0 equiv) followed by **11** (500 mg, 1.60 mmol, 1.0 equiv), which was contaminated with ca. 1% of the corresponding *cis*-decalin, in THF (4 mL). After 1 h, the reaction was quenched with solid ammonium chloride and the ammonia allowed to evaporate. The resulting residue was taken up in EtOAc (50 mL), washed with water (2 x 25 mL), brine (25 mL) and dried with Na₂SO₄. After concentration, the resulting oil was purified by silica gel column chromatography (3:1 then 1:1 hexanes:EtOAc) to afford **12** (324 mg, 91%) and **28** (7 mg, 2%) as a white solid.

Alcohol 12. ¹H NMR (400 MHz, CDCl₃) δ 4.66 (s, 1H), 4.50 (s, 1H), 4.38-4.32 (m, 1H), 2.98 (s, 1H), 2.40-2.34 (m, 1H), 2.12-1.95 (comp m, 3H), 1.83-1.76 (m, 1H), 1.71-1.51 (comp m, 4H), 1.32-1.12 (comp m, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 151.6, 104.9, 67.3, 60.9, 58.4, 46.1, 45.8, 43.5, 35.6, 30.2, 26.8, 23.7, 22.4, 17.7; IR (thin film/NaCl) 3437 (br m), 2975 (m), 2931 (m), 2878 (m), 1649 (m), 1447 (m), 1422 (w), 1379 (m), 1100 (m), 888 (m) cm⁻¹; HRMS (FAB) *m/z* found: 223.1699 [calc'd for C₁₄H₂₃O₂ (M+H): 223.1698].

Alcohol 28. m.p. 154-156°C (recrystallized from 3:1 hexanes:EtOAc); ^1H NMR (400 MHz, CDCl_3) δ 4.69 (s, 1H), 4.60 (s, 1H), 4.16-4.09 (m, 1H), 2.43 (dt, $J=3.3, 12.8$ Hz, 1H), 2.08-1.93 (comp m, 2H), 1.82-1.38 (comp m, 8H), 1.33-1.02 (comp m, 10H); ^{13}C NMR (125 MHz, CDCl_3) δ 152.3, 104.8, 69.6, 67.2, 49.0, 45.8, 43.1, 41.2, 38.2, 36.2, 31.8, 25.9, 24.4, 16.8; IR (thin film/NaCl) 3372 (m), 3081 (w), 2964 (m), 2929 (m), 2845 (m), 1644 (m), 1443 (m), 1374 (m), 1309 (w), 1264 (w) cm^{-1} ; HRMS (FAB) m/z found: 206.1668 [calc'd for $\text{C}_{14}\text{H}_{22}\text{O}$ ($\text{M}+\text{H}_2\text{O}$): 206.1671].

Preparation of ketone 3

Ketone 3. A solution of alcohol **12** (300 mg, 1.35 mmol, 1.0 equiv) in undistilled CH_2Cl_2 (20 mL) was treated with Dess-Martin periodinane (744 mg, 1.76 mmol, 1.3 equiv) and the mixture was stirred at 0°C for 2 h. Saturated aqueous NaHCO_3 (5 mL) and $\text{Na}_2\text{S}_2\text{O}_3$ (5 mL) were then added. After 30 min, the organic layer was separated and dried with Na_2SO_4 . Concentration *in vacuo* gave a residue which was purified by silica gel column chromatography (9:1 then 3:1 hexanes:EtOAc) to afford ketone **3** (253 mg, 85% yield) as a white, amorphous solid. ^1H NMR (400 MHz, CDCl_3) δ 4.72 (d, $J=1.1$ Hz, 1H), 4.57 (d, $J=1.1$ Hz, 1H), 2.57 (dt, $J=12.0, 3.4$ Hz, 1H), 2.50 (s, 1H), 2.44-2.39 (m, 1H), 2.21 (s, 3H), 2.15-2.00 (comp m, 3H), 1.78 (t, $J=12.0$ Hz, 1H), 1.72-1.57 (comp m, 2H), 1.53-1.42 (comp m, 2H), 1.36 (dt, $J=4.6, 11.7$ Hz, 1H), 1.29 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 211.4, 149.9, 106.2, 61.9, 58.3, 56.2, 44.8, 42.8, 35.4, 31.7, 30.3, 27.9, 23.4, 22.0; IR (thin film/NaCl) 2973 (w), 2932 (m), 2887 (w), 2853 (w), 1706 (m), 1650 (w), 1440 (w), 1424 (w), 1374 (w), 1183 (w) cm^{-1} ; HRMS (FAB) m/z found: 221.1543 [calc'd for $\text{C}_{14}\text{H}_{21}\text{O}_2$ ($\text{M}+\text{H}$): 221.1542].

Preparation of alcohols 13 and 12

Alcohols 13 and 12. To a solution of **3** (15 mg, 0.068 mmol, 1.0 equiv) in MeOH (5 mL) at 0°C was added NaBH_4 (8 mg, 0.204 mmol, 3.0 equiv) in one portion. After 30 min, EtOAc (25 mL) was added and the mixture was washed with water (25 mL), brine (25 mL), and dried with Na_2SO_4 . Following concentration under reduced pressure, NMR analysis of the crude residue revealed a mixture of alcohols in the ratio of ca. 91:9. Following purification of the mixture by silica gel column chromatography (3:1

hexanes:EtOAc), the major compound was revealed to be alcohol **13** (19 mg, 77%), a colorless oil, and the minor compound was identical with material obtained from benzyl deprotection of **11** and was determined to be **12**.

Alcohol 13. ^1H NMR (400 MHz, CDCl_3) δ 4.66 (s, 1H), 4.50 (s, 1H), 4.30-4.22 (m, 1H), 3.17 (s, 1H), 2.39-2.33 (m, 1H), 2.14-1.97 (comp m, 2H), 1.90-1.82 (m, 1H), 1.71-1.43 (comp m, 6H), 1.40-1.21 (comp m, 8H); ^{13}C NMR (100 MHz, CDCl_3) δ 151.5, 104.9, 67.3, 61.2, 58.6, 45.7, 44.6, 43.3, 35.7, 30.3, 27.7, 23.8, 22.6, 20.5; IR (thin film/NaCl) 3440 (s), 2974 (s), 2932 (s), 1649 (m), 1448 (m), 1422 (w), 1378 (m), 1134 (w), 1011 (w), 887 (s) cm^{-1} ; HRMS (FAB) m/z found: 223.1698 [calc'd for $\text{C}_{14}\text{H}_{23}\text{O}_2$ (M+H): 223.1698].

Preparation of ester 16

Ester 16. A solution of ethyl propiolate (28 μL , 0.272 mmol, 4.0 equiv) in THF (3 mL) at -78°C was treated with $n\text{-BuLi}$ (2.3 M in hexanes, 117 μL , 0.27 mmol, 4.0 equiv). After 5 min, **3** (15 mg, 0.068 mmol, 1.0 equiv) in THF (1 mL) was added. The temperature was maintained at -78°C for 30 min before slowly warming to 0°C for an additional 1 hr. Water (5 mL) was added followed by EtOAc (15 mL). The layers were separated and the aqueous portion was extracted with EtOAc (10 mL). The combined organic fractions were washed with brine (15 mL) and dried with Na_2SO_4 before concentrating *in vacuo*. Crude NMR showed ca. 98:2 mixture of diastereomers which could be purified by silica gel column chromatography (3:1 hexanes:EtOAc) to afford **16** (19 mg, 89%) as a colorless oil. ^1H NMR (500 MHz, CDCl_3) δ 4.68 (s, 1H), 4.54 (s, 1H), 4.24 (q, $J=7.2$ Hz, 2H), 3.93 (s, 1H), 2.42 (s, 1H), 2.39 (dt, $J=4.5, 13.1$ Hz, 1H), 2.35-2.29 (m, 1H), 2.14-1.98 (comp m, 3H), 1.73-1.51 (comp m, 7H), 1.41-1.17 (comp m 8H); ^{13}C NMR (125 MHz, CDCl_3) δ 153.7, 151.0, 105.2, 90.9, 77.0, 72.6, 62.3, 61.1, 59.0, 48.8, 45.7, 43.0, 35.7, 32.3, 30.2, 25.0, 23.6, 22.4, 14.2; IR (thin film/NaCl) 3400 (br m), 2984 (m), 2936 (m), 2237 (m), 1712 (s), 1650 (m), 1447 (m), 1368 (m), 1246 (s), 1092 (m) cm^{-1} ; HRMS (EI) m/z found: 318.1835 [calc'd for $\text{C}_{19}\text{H}_{26}\text{O}_4$ (M+): 318.1835].

Preparation of aziridines 17 and 29

Aziridines 17 and 29. A solution of ketone **3** (1.06 g, 4.80 mmol, 1.0 equiv) in dry MeCN (250 mL) with 4 Å sieves (ca. 3 g) at 25°C, was treated with *N*-tosyliminophenylidiodane (3.59 g, 9.62 mmol, 2.0 equiv). After 2 minutes, Cu(OTf)₂ (87 mg, 0.24 mmol, 0.05 equiv) was added and the mixture was vigorously stirred for 8 h. The mixture was then diluted with EtOAc (50 mL) and filtered through a short plug of silica gel. After removing the solvent *in vacuo*, the resulting residue, ca. 5:1 mixture of aziridine diastereomers, was purified by silica gel column chromatography (3:1 hexanes:EtOAc) to afford aziridine **17** (1.12 g, 60% yield) as a white solid. Mixed fractions were analyzed by HPLC to give an analytical sample of **29** (37 mg, 2% yield) as a white, amorphous solid.

Aziridine 17. m.p. 195-197°C (recrystallized from 3:1 hexanes:EtOAc); ¹H NMR (500 MHz, CDCl₃) δ 7.80 (d, *J*=8.5 Hz, 2H), 7.32 (d, *J*=8.6 Hz, 2H), 2.61 (dt, *J*=3.7, 12.1 Hz, 1H), 2.54 (s, 1H), 2.48 (s, 1H), 2.44 (s, 3H), 2.42-2.28 (comp m, 2H), 2.26 (s, 3H), 2.23-2.17 (comp m, 2H), 2.01-1.96 (m, 1H), 1.93 (t, *J*=11.8 Hz, 1H), 1.65-1.43 (comp m, 4H), 1.28 (s, 3H), 0.74 (dq, *J*=4.4, 12.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 210.5, 144.1, 137.9, 129.7, 127.4, 61.5, 58.6, 54.5, 54.0, 42.2, 42.2, 36.2, 30.6, 29.9, 29.7, 29.0, 23.2, 21.7, 18.1; IR (thin film/NaCl) 3269 (br m), 2928 (m), 2253 (w), 1708 (s), 1598 (m), 1451 (m), 1319 (s), 1159 (s), 1088 (m), 1002 (m) cm⁻¹; HRMS (EI) *m/z* found: 389.1661 [calc'd for C₂₁H₂₇NO₄S (M⁺): 389.1661].

Aziridine 29. ¹H NMR (500 MHz, CDCl₃) δ 7.84 (d, *J*=7.1 Hz, 2H), 7.32 (d, *J*=7.9 Hz, 2H), 2.55-2.41 (comp m, 8H), 2.38-2.27 (m, 1H), 2.27-2.17 (comp m, 4H), 2.10-1.93 (comp m, 3H), 1.60-1.51 (m, 1H), 1.33-1.23 (comp m, 4H), 1.12 (dq, *J*=4.4, 12.1 Hz, 1H), 0.98 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 211.6, 144.2, 137.6, 129.7, 127.7, 61.3, 58.2, 56.4, 54.9, 42.1, 40.8, 36.9, 30.0, 30.0, 27.7, 26.5, 23.2, 21.7, 18.8; IR (thin film/NaCl) 2935 (m), 2870 (m), 2251 (w), 1707 (s), 1597 (m), 1494 (w), 1451 (m), 1379 (m), 1317 (s), 1158 (s) cm⁻¹; HRMS (FAB) *m/z* found: 390.1744 [calc'd for C₂₁H₂₈NO₄S (M+H): 390.1739].

Preparation of alcohols 18 and 30

Alcohols 18 and 30. A solution of ethyl propiolate (118 μL, 1.16 mmol, 4.0 equiv) in THF (10 mL) at -78°C was treated with *n*-BuLi (2.3 M in hexanes, 0.50 mL, 1.16 mmol, 4.0 equiv). After 5 min, **17** (113 mg, 0.29 mmol, 1.0 equiv) in THF (1 mL) was added. The temperature was maintained at -78°C for 30 min before slowly warming to 0°C for an additional 1 hr. Water (10 mL) was added followed by EtOAc (30 mL). The layers were separated and the aqueous portion was extracted with EtOAc (10 mL). The combined organic fractions were washed with brine (25 mL) and dried with Na₂SO₄.

before concentrating *in vacuo*. Crude NMR showed a ~98:2 mixture of diastereomers which could be purified by silica gel column chromatography (3:1 hexanes:EtOAc) to afford **18** (125 mg, 88%) as a foam and **30** (2 mg, 1%) as a colorless oil.

Alcohol 18. ^1H NMR (400 MHz, CDCl_3) δ 7.79 (d, $J=8.0$ Hz, 2H), 7.31 (d, $J=8.0$ Hz, 2H), 4.24 (q, $J=7.2$ Hz, 2H), 3.93 (s, 1H), 2.59 (s, 1H), 2.50 (s, 1H), 2.44-2.19 (comp m, 7H), 2.00-1.91 (comp m, 2H), 1.70-1.56 (comp m, 7H), 1.49-1.42 (m, 1H), 1.34-1.25 (comp m, 6H), 0.79-0.67 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 153.5, 144.0, 138.1, 129.6, 127.4, 90.3, 77.2, 72.0, 62.4, 60.4, 59.4, 54.4, 48.1, 43.3, 42.6, 36.2, 30.8, 30.0, 29.8, 25.2, 23.4, 21.7, 18.5, 14.2; IR (thin film/NaCl) 3463 (br m), 2932 (m), 2237 (m), 1710 (s), 1598 (m), 1449 (m), 1317 (m), 1247 (s), 1158 (s), 1090 (m) cm^{-1} ; HRMS (FAB) m/z found: 488.2109 [calc'd for $\text{C}_{26}\text{H}_{34}\text{NO}_6\text{S}$ (M+H): 488.2107].

Alcohol 30. ^1H NMR (400 MHz, CDCl_3) δ 7.83 (d, $J=8.3$ Hz, 2H), 7.30 (d, $J=8.3$ Hz, 2H), 4.24 (q, $J=7.1$ Hz, 2H), 3.98 (s, 1H), 2.51-2.26 (comp m, 8H), 2.09-1.84 (comp m, 5H), 1.65-1.51 (comp m, 4H), 1.37-1.25 (comp m, 7H), 1.16 (dq, $J=4.2$, 12.7 Hz, 2H), 0.98-0.92 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 153.7, 144.0, 137.7, 129.6, 127.7, 90.4, 77.0, 73.0, 62.3, 60.4, 58.7, 55.5, 48.2, 42.3, 41.7, 36.9, 30.3, 29.8, 29.7, 24.6, 23.4, 21.7, 19.1, 14.2; IR (thin film/NaCl) 3455 (br m), 2983 (m), 2939 (m), 2240 (m), 1710 (s), 1598 (w), 1445 (w), 1451 (m), 1370 (m), 1248 (s), 1156 (s) cm^{-1} ; HRMS (FAB) m/z found: 488.2107 [calc'd for $\text{C}_{26}\text{H}_{34}\text{NO}_6\text{S}$ (M+H): 488.2107].

Preparation of ester 19

Ester 19. A solution of **18** (50 mg, 0.103 mmol, 1.0 equiv) in EtOAc (5 mL) at 0°C was treated with 10% Pd/C (5 mg) and an atmosphere of H_2 was maintained using a balloon. After 1h, the mixture was filtered through celite and concentrated. The resulting colorless oil was spectroscopically pure **19** (49 mg, 98%). ^1H NMR (400 MHz, CDCl_3) δ 7.79 (d, $J=8.3$ Hz, 2H), 7.30 (d, $J=8.6$ Hz, 2H), 4.19-4.12 (comp m, 3H), 2.55-2.18 (comp m, 9H), 1.99-1.89 (comp m, 3H), 1.81-1.54 (comp m, 6H), 1.48-1.41 (m, 1H), 1.30-1.09 (comp m, 10H), 0.79-0.68 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 175.0, 143.9, 138.2, 129.6, 127.3, 75.3, 60.9, 60.9, 59.3, 54.8, 47.5, 44.2, 42.9, 37.6, 36.4, 31.1, 29.8, 29.1, 28.4, 23.6, 23.3, 21.7, 18.6, 14.3; IR (thin film/NaCl) 3499 (m), 2976 (m), 2930 (m), 2875 (m), 2251 (w), 1730 (s), 1598 (w), 1451 (m), 1380 (m), 1317 (s) cm^{-1} ; HRMS (FAB) m/z found: 492.2420 [calc'd for $\text{C}_{26}\text{H}_{38}\text{NO}_6\text{S}$ (M+H): 492.2420].

Preparation of lactone **20**

Lactone 20. A solution of **19** (10 mg, 0.020 mmol, 1.0 equiv) in THF (10 mL) at rt was treated with LiOH (1.5 mg, 0.060 mmol, 3.0 equiv). After 12 hr, the solvent was removed *in vacuo* and the residue purified by silica gel column chromatography (1:1 hexanes:EtOAc) to give **20** (270 mg, 94%) as a white solid. m.p. 200-201°C (recrystallized from 1:1 hexanes:EtOAc); ^1H NMR (500 MHz, CDCl_3) δ 7.79 (d, $J=8.1$ Hz, 2H), 7.30 (d, $J=8.2$ Hz, 2H), 3.70 (s, 1H), 2.66-2.56 (m, 1H), 2.52-2.40 (comp m, 5H), 2.37-2.21 (comp m, 3H), 2.15-2.00 (comp m, 3H), 1.97-1.82 (comp m, 2H), 1.69-1.56 (comp m, 3H), 1.48-1.37 (comp m, 4H), 1.32-1.14 (comp m, 4H), 0.79-0.69 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 176.1, 144.0, 138.0, 129.6, 127.3, 89.2, 59.7, 59.3, 54.4, 49.3, 43.7, 42.4, 26.3, 35.2, 30.9, 29.8, 28.2, 27.9, 23.4, 21.7, 19.6, 18.4; IR (thin film/NaCl) 2959 (m), 2876 (m), 2252 (w), 1770 (s), 1598 (w), 1451 (m), 1387 (m), 1317 (m), 1209 (m), 1158 (s) cm^{-1} ; HRMS (FAB) m/z found: 446.2000 [calc'd for $\text{C}_{24}\text{H}_{32}\text{NO}_5\text{S}$ (M+H): 446.2001].

Preparation of lactol **21**

Lactol 21. To a solution of **19** (50 mg, 0.102 mmol, 1.0 equiv) in toluene (5 mL) at 0°C was added DIBAL-H (0.5 M in CH_2Cl_2 , 155 μL , 0.122 mmol, 1.2 equiv). After 10 min, the solution was warmed to rt and stirred for an additional 2 h. The reaction was quenched with 20% aqueous Rochelle's salt (10 mL) and diluted with (25 mL). The organic layer was washed with water (25 mL), brine (25 mL) and dried with Na_2SO_4 . After concentration, the resulting residue was purified by silica gel column chromatography (3:1 then 1:1 hexanes:EtOAc) to afford **21** (35 mg, 76%) as an amorphous, white solid. (2:1 mixture of lactol epimers) ^1H NMR (500 MHz, CDCl_3) δ 7.80 (d, $J=7.9$ Hz, 2H), 7.30 (d, $J=7.9$ Hz, 2H), 5.58-5.54 (comp m, 0.3H), 5.52-5.48 (comp m, 0.7H), 4.05 (s, 0.7H), 4.03 (s, 0.3H), 2.72-2.70 (m, 0.3H), 2.50-2.42 (comp m, 4.7H), 2.31-2.18 (comp m, 3H), 2.10-1.86 (comp m, 4H), 1.80-1.69 (comp m, 2H), 1.64-1.56 (comp m, 4H), 1.47-1.41 (m, 1H), 1.36 (s, 1H), 1.31-1.13 (comp m, 6H), 0.80-0.69 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 143.9, 138.3, 129.6, 127.4, 99.5, 98.4, 88.3, 87.4, 60.7, 60.6, 59.3, 59.2, 55.0, 55.0, 51.6, 50.2, 44.1, 43.9, 42.7, 42.6, 38.5, 36.5, 36.3, 36.0, 32.8, 32.3, 31.2, 31.2, 30.1, 30.0, 30.0, 29.6, 23.6, 23.6, 21.7, 21.5, 20.8, 18.6, 18.5;

IR (thin film/NaCl) 3435 (m), 2929 (m), 2871 (m), 2250 (w), 1738 (m), 1599 (w), 1453 (m), 1380 (m), 1318 (m), 1159 (m) cm^{-1} ; HRMS (FAB) m/z found: 448.2157 [calc'd for $\text{C}_{24}\text{H}_{34}\text{NO}_5\text{S}$ (M+H): 448.2158].

Preparation of olefin 22

Olefin 2. A mixture of isopropyltriphenylphosphonium iodide (116 mg, 0.268 mmol, 4.0 equiv) in THF (5 mL) at 0°C was treated with *n*-BuLi (2.3 M in hexanes, 117 μL , 0.268 mmol, 4.0 equiv). After 5 min, **21** (30 mg, 0.067 mmol, 1.0 equiv) was added as a solution in THF (1 mL). The red solution was warmed to rt and stirred for an additional 3 h before quenching with water (5 mL) and diluting with EtOAc (25 mL). The aqueous layer was extracted with EtOAc (10 mL) and the combined organic fractions were washed with brine (25 mL) and dried with Na_2SO_4 . After the solvent was removed *in vacuo*, the resulting residue was purified by silica gel column chromatography (3:1 hexanes:EtOAc) to afford **2** (26 mg, 81%) as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.79 (d, $J=8.5$ Hz, 2H), 7.30 (d, $J=8.1$ Hz, 2H), 5.12 (br t, $J=7.0$ Hz, 1H), 4.21 (s, 1H), 2.49 (s, 1H), 2.43 (s, 3H), 2.30-1.89 (comp m, 7H), 1.72-1.53 (comp m, 10H), 1.47-1.36 (comp m, 3H), 1.27 (s, 3H), 1.26 (s, 3H), 1.21-1.08 (m, 1H), 0.80-0.68 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 143.9, 138.4, 132.5, 129.6, 127.4, 124.1, 76.2, 61.0, 59.3, 55.1, 47.4, 44.3, 43.4, 43.0, 36.5, 31.3, 29.9, 29.4, 25.9, 23.7, 23.6, 21.7, 21.6, 18.6, 17.9; IR (thin film/NaCl) 3511 (br m), 2965 (s), 2925 (s), 2246 (w), 1598 (m), 1449 (m), 1379 (m), 1318 (s), 1208 (m), 1158 (s) cm^{-1} ; HRMS (FAB) m/z found: 474.2679 [calc'd for $\text{C}_{27}\text{H}_{40}\text{NO}_4\text{S}$ (M+H): 474.2678].

Preparation of tetrahydrofurans 22 and 31

Tetrahydrofurans 22 and 31. A solution of **2** (30 mg, 0.063 mmol, 1.0 equiv) in CH_2Cl_2 (5 mL) at -78°C was treated with pyridine (8 μL , 0.076 mmol, 1.2 equiv) and PhSeCl (17 mg, 0.088 mmol, 1.4 equiv). After ca. 10 minutes, saturated aqueous NaHCO_3 (1 mL) was added and the mixture was allowed to warm to rt. The organic layer was washed with brine (10 mL) and dried with Na_2SO_4 . After concentration, the resulting residue was dissolved in CH_2Cl_2 (5 mL), cooled to -78°C , and reacted with *m*-

CPBA (15 mg, 0.088 mmol, 1.4 equiv). After ca. 20 minutes, saturated aqueous NaHCO₃ (1 mL) was added and the mixture was allowed to warm to rt. The organic layer was washed with brine (10 mL), dried with Na₂SO₄, and concentrated *in vacuo*. NMR analysis of the residue showed a 3:2 mixture of tetrahydrofurans which could be separated by silica gel column chromatography (9:1 then 3:1 hexanes:EtOAc) to afford **22** (major diastereomer, 48%, 14 mg) and **31** (30%, 9 mg) as colorless oils.

Tetrahydrofuran 22. ¹H NMR (400 MHz, CDCl₃) δ 7.80 (d, *J*=8.2 Hz, 2H), 7.30 (d, *J*=8.2 Hz, 2H), 4.91 (s, 1H), 4.73 (s, 1H), 4.46-4.42 (m, 1H), 4.20 (s, 1H), 2.50 (s, 1H), 2.43 (s, 3H), 2.29-2.23 (comp m, 2H), 2.21 (s, 1H), 2.14-2.03 (m, 1H), 2.00-1.90 (comp m, 2H), 1.75-1.53 (comp m, 9H), 1.47-1.40 (m, 1H), 1.32-1.16 (comp m, 8H), 0.81-0.68 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 146.7, 143.8, 138.3, 129.6, 127.4, 109.3, 86.6, 80.7, 60.8, 59.1, 55.1, 50.4, 43.9, 43.0, 38.1, 36.5, 31.3, 30.3, 30.1, 28.7, 23.4, 21.7, 19.4, 18.9, 18.5; IR (thin film/NaCl) 2965 (m), 2878 (m), 2249 (w), 1651 (w), 1599 (m), 1495 (w), 1451 (m), 1379 (m), 1321 (s), 1159 (s) cm⁻¹; HRMS (FAB) *m/z* found: 472.2522 [calc'd for C₂₇H₃₈NO₄S (M+H): 472.2522].

Tetrahydrofuran 31. ¹H NMR (400 MHz, CDCl₃) δ 7.81 (d, *J*=8.3 Hz, 2H), 7.31 (d, *J*=8.3 Hz, 2H), 4.98 (s, 1H), 4.74 (s, 1H), 4.34 (dd, *J*=5.6, 9.6 Hz, 1H), 4.14 (s, 1H), 2.50 (s, 1H), 2.43 (s, 3H), 2.31-2.25 (comp m, 2H), 2.23 (s, 1H), 2.04-1.89 (comp m, 3H), 1.86-1.80 (comp m, 2H), 1.76-1.54 (comp m, 8H), 1.46-1.39 (m, 1H), 1.29-1.18 (comp m, 7H), 0.82-0.70 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 146.4, 143.9, 138.3, 129.6, 127.4, 109.2, 86.1, 82.5, 60.7, 59.3, 55.3, 50.8, 44.0, 42.9, 39.9, 36.6, 31.4, 30.5, 29.9, 29.9, 23.6, 21.8, 21.8, 18.8, 18.4; IR (thin film/NaCl) 2967 (m), 2931 (m), 2872 (m), 2248 (w), 1652 (w), 1598 (w), 1495 (w), 1450 (m), 1320 (m), 1159 (m) cm⁻¹; HRMS (FAB) *m/z* found: 472.2522 [calc'd for C₂₇H₃₈NO₄S (M+H): 472.2522].

Preparation of amine 32

Amine 32. To a solution of aziridine **22** (30 mg, 0.064 mmol, 1.0 equiv) in THF (5 mL) at 0°C was added a 1M solution of Li(Et)₃BH in THF (191 μL, 0.191 mmol, 3.0 equiv). The reaction mixture was stirred at 0°C for 1 h before warming to rt for an additional 2 h. The reaction was quenched with H₂O (5 mL) and diluted with EtOAc (25 mL). The organic layer was separated, washed with brine (2 x 10 mL), and dried with Na₂SO₄. After removing the solvent *in vacuo*, the resulting residue was purified by silica gel column chromatography (3:1 hexanes:EtOAc) to afford **32** (26 mg, 86% yield) as a white foam. ¹H NMR (400 MHz, CDCl₃) δ 7.77 (d, *J*=8.1 Hz, 2H), 7.27 (d, *J*=7.9 Hz, 2H), 4.88 (s, 1H), 4.82 (s, 1H), 4.71 (s, 1H), 4.43-4.38 (m, 1H), 4.11 (s, 1H), 2.42 (s, 3H), 2.10-1.90 (comp m, 2H), 1.76-1.42 (comp m, 12H), 1.30-1.19 (comp m, 5H), 1.13 (s, 3H), 1.12-0.96 (comp m, 5H); ¹³C NMR (100 MHz, CDCl₃) δ 146.7, 143.0, 140.9, 129.7, 127.0, 109.2, 86.7, 80.5, 61.5, 60.3, 58.8, 50.1, 47.2, 40.4, 39.2, 37.9, 30.7, 28.7, 26.7, 23.4, 21.7, 19.9, 19.3, 18.8, 18.7; IR (thin film/NaCl) 3267 (m), 2965 (m), 2871 (m),

1652 (w), 1599 (w), 1496 (w), 1453 (m), 1379 (m), 1326 (m), 1158 (s) cm^{-1} ; HRMS (FAB) m/z found: 474.2678 [calc'd for $\text{C}_{27}\text{H}_{40}\text{NO}_4\text{S}$ ($\text{M}+\text{H}$): 474.2678].

Preparation of azide **23**

Azide 23. To a solution of **32** (30 mg, 0.063 mmol, 1.0 equiv) in DMF (7 mL) was added NaN_3 (25 mg, 0.378 mmol, 6.0 equiv) and NH_4Cl (10 mg, 0.189 mmol, 3.0 equiv). The mixture was heated to 80°C . After ca. 72 h, the solution was cooled to rt and diluted with EtOAc (25 mL). After washing with water (25 mL) and brine (2 x 25 mL), the organic fraction was dried with Na_2SO_4 and concentrated under reduced pressure. Purification by silica gel column chromatography (3:1 hexanes:EtOAc) afforded azide **23** (27 mg, 82% yield) as an amorphous, white solid. ^1H NMR (500 MHz, CDCl_3) δ 7.76 (d, $J=8.4$ Hz, 2H), 7.27 (d, $J=8.4$ Hz, 2H), 4.93-4.91 (m, 1H), 4.74-4.71 (m, 1H), 4.46 (dd, $J=3.4, 9.5$ Hz, 1H), 4.40 (s, 1H), 4.07 (s, 1H), 2.42 (s, 3H), 2.11-2.05 (m, 1H), 1.95 (dd, $J=2.7, 11.0$ Hz, 1H), 1.85 (ddd, $J=3.3, 3.3, 12.9$ Hz, 1H), 1.72-1.50 (comp m, 11H), 1.44-1.36 (comp m, 2H), 1.32-1.22 (comp m, 4H), 1.19-1.01 (comp m, 8H); ^{13}C NMR (125 MHz, CDCl_3) δ 146.8, 143.0, 140.8, 129.6, 127.2, 111.0, 86.7, 81.6, 73.4, 69.1, 60.0, 46.8, 42.2, 39.5, 38.5, 38.0, 33.2, 29.0, 28.8, 25.5, 21.6, 21.5, 19.1, 18.3, 17.4; IR (thin film/ NaCl) 3530 (m), 3271 (m), 2966 (w), 2871 (w), 2103 (s), 1455 (w), 1383 (m), 1318 (m), 1286 (m), 1265 (m) cm^{-1} ; HRMS (FAB) m/z found: 517.2849 [calc'd for $\text{C}_{27}\text{H}_{41}\text{N}_4\text{O}_4\text{S}$ ($\text{M}+\text{H}$): 517.2849].

Preparation of (±)-kalihinol C (**1**)

(±)-Kalihinol C (1). To condensed ammonia (20 mL) at -78°C was added sodium (3 mg, 0.116 mmol, 4 equiv). After 5 min, the sodium/ammonia solution was added via cannula to a solution of **23** (15 mg, 0.029 mmol, 1.0 equiv) in THF (2 mL) and ammonia (5 mL) at -78°C . After ca. 1 h, the reaction was quenched with solid ammonium chloride and the ammonia allowed to evaporate. The resulting residue was taken up in EtOAc (30 mL), washed with 0.1 M NaOH (2 x 10 mL), brine (10 mL) and dried with Na_2SO_4 . After concentration under reduced pressure, the resulting oil was dissolved in THF (10 mL) and acetic formic anhydride (ca. 0.1 ml) was added at rt. After

6 h the solution was concentrated under reduced pressure and the resulting residue was taken up in CH₂Cl₂ (5 mL). The solution was treated with pyridine (9 µL, 0.116 mmol, 4.0 equiv) and *p*-toluenesulfonyl chloride (22 mg, 0.116 mmol, 4.0 equiv) at rt. After the reaction was complete (ca. 16 hr), the solvent was removed *in vacuo* and the resulting residue was purified by silica gel column chromatography (9:1 then 3:1 hexanes:EtOAc) to afford **1** (4 mg, 39% yield from **23**) as a colorless oil. ¹H NMR (500 MHz, CDCl₃, referenced to 77.0) δ 5.04 (s, 1H), 4.77 (s, 1H), 4.50 (br s, 1H), 4.41 (dd, *J*=3.6, 9.4 Hz, 1H), 1.73 (s, 3H), 1.43 (s, 3H), 1.34 (br s, 3H), 1.05 (s, 3H), 2.13-1.04 (complex); ¹³C NMR (125 MHz, CDCl₃) δ 146.27, 109.98, 86.23, 80.85, 70.59, 63.18 (t, *J*=5 Hz), 59.91 (t, *J*=5 Hz), 46.31, 42.18, 39.93, 38.18, 36.08, 32.65, 28.82, 28.74, 24.30, 21.65, 20.73, 18.25, 18.16; IR (thin film/NaCl) 3416 (br m), 2968 (m), 2875 (m), 2137 (m), 1653 (w), 1455 (m), 1384 (m), 1273 (w), 1189 (w), 1101 (w) cm⁻¹; HRMS (FAB) *m/z* found: 330.2433 [calc'd for C₂₁H₃₂NO₂ (M-NC)⁺: 330.2433].