SUPPORTING INFORMATION

Sulfinyl-directed Diastereoselective [5+2] Pyrone-Alkene Cycloadditions: A Practical Route to Enantiopure 8-Oxabicyclo[3.2.1]octane Derivatives

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**General Procedures.** All dry solvents were freshly distilled under argon from the appropriate drying agent before use. Toluene and THF were distilled from sodium/benzophenone. CH$_2$Cl$_2$ was distilled from P$_2$O$_5$. MeOH was distilled from Mg/I$_2$. All reactions were conducted in dry solvents under argon atmosphere unless otherwise stated. Melting points (open capillary tubes) are uncorrected. Thin-layer chromatography (TLC) was performed on silica gel plates and components were visualized by observation under UV light, or by treating the plates with a phosphomolybdic reagent followed by heating. Flash chromatography was performed on silica gel, unless otherwise stated. Dryings were performed with anhydrous Na$_2$SO$_4$. Concentrations were carried out in a rotary evaporator. $^1$H and $^{13}$C NMR spectra were recorded in CDCl$_3$, at 250 MHz and 62.9 MHz, respectively, and in some cases at 300 or 500 MHz (75.4 or 125.7 for $^{13}$C NMR). Carbon types were determined from DEPT $^{13}$C NMR experiments. The following abbreviations are used to indicate signal multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. [α]$_D$ were measured at rt (20 °C) in CHCl$_3$. Eu(hfc)$_3$ refers to tris[heptafluoropropyl-hydroxymethylene](-) camphorate]europium (III). Pr(hfc)$_3$ refers to praseodymium tris[heptafluoropropyl-hydroxymethylene](-) camphorate].

(2E, R$_S$)-3-$p$-Tolylsulfinyl-2-propenylmethanesulfonate (3).

Methanesulfonyl chloride (116 mg, 1.02 mmol) was added dropwise to an ice-water cooled solution of the alcohol 15$^{11}$ [100 mg, 0.50 mmol, ≥ 97% ee [α] = +234 (c=1); [α]$^{20}$ lit. = +233 (c=1, ee = 97%] and Et$_3$N (0.14 mL, 1.02 mmol) in CH$_2$Cl$_2$ (10 mL). The reaction mixture was warmed to rt and stirred for 1h. The resulting solution was poured into water, extracted with CH$_2$Cl$_2$, dried, filtered, and concentrated. The crude residue was flash chromatographed on silica gel (50-100% EtOAc/hexanes) to afford 133 mg of 3 as a white solid [95%, R$_f$ 0.50 (EtOAc), mp 58-60 °C]. [α] = +249 (c=1.1). $^1$H NMR δ 7.51 (2H, d, J = 7.9 Hz), 7.33 (2H, d, J = 7.9 Hz), 6.62 (2H, s), 4.90 (2H, s), 3.03 (3H, s), 2.41 (3H, s); $^{13}$C NMR δ 142.3 (CH), 139.3 (C), 138.3 (C), 130.2 (CH), 128.3 (CH), 124.8 (CH), 67.0 (CH$_2$), 37.8 (CH$_3$), 21.3 (CH$_3$); LRMS m/z 274 (M$^+$, 0.04), 226 (44), 139 (41), 131 (100), 91 (54), 65 (38); HRMS calcd. for C$_{11}$H$_{14}$O$_4$S$_2$ 274.0333, found 274.0334.
2-[(3-t-Butyldimethylsilyloxy-4-oxo-4H-2-pyranyl)methyl]-2-[(2E, RS)-3-p-tolylsulfinyl-2-propenyl]malononitrile (2a).

Malononitrile (0.83 g, 12.5 mmol) was added to a –78 °C cooled suspension of NaH (0.5 g, 60% mineral oil, 12.5 mmol) in THF (20 mL). After stirring for 15 min at rt, the reaction mixture was cooled at –78 °C, and the bromide 1 (2 g, 6.27 mmol) was added. The reaction mixture was stirred for 1 h at that temperature poured into brine, extracted with Et₂O, dried, filtered, and concentrated. The residue was flash chromatographed on silica gel (90% CH₂Cl₂/hexanes) to afford 2.2 g of 16 as a colorless viscous oil [75%, Rf 0.15 (90% CH₂Cl₂/hexanes)]: ¹H NMR δ 7.67 (1H, d, J = 5.5 Hz), 6.35 (1H, d, J = 5.5 Hz), 4.26 (1H, t, J = 7.2 Hz), 3.40 (2H, d, J = 7.2 Hz), 0.93 (9H, s), 0.26 (6H, s); ¹³C NMR δ 173.6 (C), 153.7 (CH), 147.6 (C), 144.5 (C), 115.8 (CH), 111.4 (CN), 29.3 (CH₂), 26.0 (CH₃), 20.1 (CH), 18.6 (C), -3.9 (CH₃); LRMS m/z 289 (M⁺ - CH₃, 3), 247 (79), 182 (100), 154 (12), 111 (18); HRMS calcd. for C₁₅H₂₀O₃N₂Si - CH₃ 289.1008, found 289.1015.

A solution of compound 16 (200 mg, 0.66 mmol) in THF (2 mL) was added to an ice-cooled suspension of NaH (26 mg, 0.60 mmol) in THF (10 mL). After stirring for 15 min at rt a solution of mesylate 3 (163 mg, 0.60 mmol) in THF (2 mL) was added. The reaction mixture was stirred at rt for 12 h and the reaction quenched by adding 3 mL of water. The solvent was evaporated and the residue diluted with Et₂O, washed with brine, dried, filtered, and concentrated. The crude was flash chromatographed on silica gel (35% EtOAc/hexanes) to afford 244 mg of 2a [85%, Rf 0.30 (50% EtOAc/hexanes), brown solid, mp 147-149 °C]. [α] = +160 (c=0.42); ¹H NMR δ 7.71 (1H, d, J = 5.5 Hz), 7.53 (2H, d, J = 8.1 Hz), 7.32 (2H, d, J = 8.1 Hz), 6.65 (2H, m), 6.39 (1H, d, J = 5.5 Hz), 3.41 (2H, s), 2.95 (2H, d, J = 3.6 Hz), 2.40 (3H, s), 0.95 (9H, s), 0.30 (6H, s); ¹³C NMR δ 173.6 (C), 153.6 (CH), 147.0 (C), 145.3 (C), 143.6 (CH), 142.4 (C), 139.1 (C), 130.3 (CH), 125.7 (CH), 125.0 (CH), 115.9 (CH), 113.5 (CN), 39.3 (CH₂), 35.3 (C), 34.7 (CH₂), 26.1 (CH₃), 21.4 (CH₃), 18.8 (C), -3.5 (CH₃); LRMS m/z 425 (M⁺ - C₄H₉, 42), 245 (31), 182 (100), 139 (24), 73 (25); HRMS calcd. for C₂₅H₃₀O₄SiSN₂ - C₄H₉ 425.0991, found 425.0986.

Diethylmalonate (2 g, 12.5 mmol) was added to a –78 °C cooled suspension of NaH (0.5 g, 60% mineral oil, 12.5 mmol) in THF (20 mL). After being stirred for 20 min at rt, the reaction mixture was cooled at –78 °C, and the bromide 1 (2 g, 6.27 mmol) was added. After being stirred for 2 h at rt the mixture was poured into brine, extracted with Et2O, dried, filtered, and concentrated. The crude was flash chromatographed on silica gel (10-25% EtOAc/hexanes) to afford 2.2 g of 17 as a colorless viscous oil [90%, Rf 0.15 (10% EtOAc/hexanes)]: \( ^1\)H NMR \( \delta \) 7.57 (1H, d, \( J = 5.5 \) Hz), 6.3 (1H, d, \( J = 5.5 \) Hz), 4.20 (4H, q, \( J = 7.1 \) Hz), 3.77 (1H, t, \( J = 7.7 \) Hz), 3.31 (2H, d, \( J = 7.7 \) Hz), 1.24 (6H, t, \( J = 7.1 \) Hz), 0.95 (9H, s), 0.27 (6H, s); \( ^{13} \)C NMR \( \delta \) 174.5 (C), 168.1 (C), 153.3 (C), 152.8 (CH), 143.0 (C), 115.6 (CH), 61.8 (CH2), 48.9 (CH), 27.6 (CH2), 26.0 (CH3), 18.7 (C), 14.0 (CH3), -3.7 (CH3); LRMS \( m/z \) 341 (M+-C4H9, 100), 267 (9), 239 (9), 195 (39), 165 (4); HRMS calcd. for C19H30O7Si-C4H9 341.1056, found 341.1054.

A solution of compound 17 (240 mg, 0.60 mmol) in THF (2 mL) was added to an ice-cooled suspension of NaH (24 mg, 0.60 mmol) in THF (10 mL). After stirring for 15 min at rt a solution of mesylate 3 (150 mg, 0.55 mmol) in THF (2 mL) was added. The reaction mixture was stirred at rt for 12 h and the reaction quenched by adding 3 mL of water. The solvent was evaporated and the residue diluted with Et2O, washed with brine, dried, filtered, and concentrated. The crude was flash chromatographed on silica gel (35% EtOAc/hexanes) to afford 221 mg of 2b as a colorless oil [70%, Rf 0.38 (50% EtOAc/hexanes)]: [\( \alpha \)] = +39 (c=0.72); \( ^1\)H NMR \( \delta \) 7.50 (1H, d, \( J = 4.4 \) Hz), 7.41 (2H, d, \( J = 6.6 \) Hz), 7.25 (2H, d, \( J = 6.6 \) Hz), 6.49 (1H, m), 6.26 (1H, d, \( J = 5.1 \) Hz), 6.20 (1H, d, \( J = 15.1 \) Hz), 4.10 (4H, m), 3.45 (2H, s), 2.70 (2H, m), 2.34 (3H, s), 1.15 (6H, m), 0.94 (9H, s), 0.21 (6H, s); \( ^{13} \)C NMR \( \delta \) 173.8 (C), 169.3(C), 169.2 (C), 152.9 (CH), 152.4 (C), 144.1 (C), 141.4 (C), 140.3 (C), 139.5 (CH), 133.2 (CH), 129.9 (CH), 124.5 (CH) 115.5 (CH), 61.9 (CH2), 56.3 (C), 35.9 (CH2), 31.0 (CH2), 25.9 (CH3), 21.2 (CH3), 18.6 (C), 14.8 (CH3), -3.8 (CH3); LRMS FAB\( m/z \) 577 (M++1, 16), 519 (8), 249 (27), 239 (19), 182 (100), 179 (41), 173 (74); HRMS calcd. for C29H41O8SiS 577.2291, found 577.2277.
Triphenylsilanethiol (187 mg, 0.64 mmol) was added to a solution of mesylate 3 (175 mg, 0.639 mmol), PPh₃ (168 mg, 0.64 mmol) and Cs₂CO₃ (416 mg, 1.28 mmol) in THF (7 mL), cooled at −5 °C. After stirring for 15 min, a solution of bromide 1 (510 mg, 1.6 mmol) in THF (2 ml) was added and the reaction mixture further stirred for 10 h at rt. The resulting solution was poured into brine, extracted with Et₂O, dried, filtered, and concentrated. The crude residue was flash chromatographed on silica gel (30-60% EtOAc/hexanes) to afford 201 mg of 2c as an orange-pale solid [70 %, Rf 0.33 (50 % EtOAc/hexanes), mp 83-86 °C]. [α] = +112 (c=1.8); ¹H NMR δ 7.60 (1H, d, J = 5.6 Hz), 7.50 (2H, d, J = 7.9 Hz), 7.32 (2H, d, J = 7.9 Hz), 6.45 (1H, m), 6.30 (1H, d, J = 14.9 Hz), 6.17 (1H, d, J = 5.6 Hz), 3.6 ( 2H, s,), 3.28 (2H, d, J = 6.85 Hz), 2.30 ( 3H, s), 0.9 ( 9H, s), 0.05 (6H, s); ¹³C NMR δ 173.5 (C), 153.2 (CH), 149.9 (CH), 142.4 (C), 141.4 (C), 140.0 (C), 137.4 (CH), 132.9 (CH), 129.8 (CH), 124.2 (CH), 115.2 (CH), 32.7 (CH₂), 27.6 (CH₂), 25.7 (CH₃), 21.1 (CH₃), 18.4 (C), -3.9 (CH₃); LRMS FAB m/z 451 (M++1, 77), 392 (11), 240 (32), 212 (35), 182 (33), 163 (50); HRMS calcd. for C₂₂H₃₁O₄S₂Si 451.1433, found 451.1429.

General procedure for the thermal cycloadditions (EXEMPLIFIED FOR SUBSTRATE 2a).

A solution of pyrone 2a (100 mg, 0.21 mmol) in toluene (10 mL) was heated under reflux for 10 h. The solvent was evaporated and the crude purified by flash chromatography (25-50% EtOAc/hexanes) to afford a 91:9 ratio of diastereoisomers 4a and 5a as colorless oils [98%, Rfₛ (50% EtOAc/hexanes): 4a=0.54, 5a=0.70]. The diastereoisomeric ratio was determined integrating the signals of the vinylic hydrogen of the two isomers in the ¹H NMR spectrum of the crude reaction mixture.
(IR, 5S, 6R, 7R, RS)-9-t-Butyldimethylsilyloxy-6-[p-tolylsulfinyl]-10-oxo-11-oxatricyclo[5.3.1.01,5]undec-8-ene-3,3-dicarbonitrile (4a): [α] = +108 (c=0.65); 1H NMR δ 7.61 (2H, d, J = 8.1 Hz), 7.42 (2H, d, J = 8.1 Hz), 6.63 (1H, d, J = 5.0 Hz), 5.32 (1H, t, J = 4.9 Hz), 3.73 (1H, m), 3.13 (1H, d, J = 14.5 Hz), 2.63 (1H, d, J = 14.7 Hz), 2.50 (3H, s), 2.49 (1H, m), 2.08 (1H, m), 1.68 (1H, m), 0.98 (9H, s), 0.25 (6H, s); 13C NMR δ 189.3 (C), 147.5 (C), 143.7 (C), 138.8 (C), 130.8 (CH), 124.5 (CH), 124.8 (CH), 123.8 (CH), 114.6 (CH), 114.3 (CN), 96.7 (C), 77.7 (CH), 76.5 (CH), 44.9 (CH), 41.3 (CH2), 40.4 (CH2), 34.3 (C), 25.4 (CH3), 22.6 (CH3), 18.3 (C), -4.7 (CH3); LRMS FAB m/z 483 (M+1, 95), 426 (16), 425 (56), 371 (100), 281 (29), 257 (16), 239 (23); HRMS calcd. for C25H31O4SiSN2 483.1773, found 483.1751.

(IS, 5R, 6S, 7S, R)-9-t-Butyldimethylsilyloxy-6-[p-tolylsulfinyl]-10-oxa-11-oxatricyclo[5.3.1.01,5]-undec-8-ene-3,3-dicarbonitrile (5a): [α] = +15.7 (c=0.37); 1H NMR δ 7.48 (2H, d, J = 8.1 Hz), 7.39 (2H, d, J = 8.1 Hz), 6.27 (1H, d, J = 5.0 Hz), 5.07 (1H, t, J = 5.3 Hz), 3.48 (1H, dd, J = 5.8 and 6.6 Hz), 3.29 (1H, m), 3.03 (1H, d, J = 14.6 Hz), 2.62 (1H, d, J = 14.6 Hz), 2.47 (3H, s), 2.34 (1H, dd, J = 9.9 and 14.4 Hz), 1.75 (1H, m), 0.97 (9H, s), 0.22 (6H, s); 13C NMR δ 189.5 (C), 147.2 (C), 142.8 (C), 138.6 (C), 130.6 (CH), 124.5 (CH), 123.0 (CH), 115.2 (CN), 114.5 (CN), 96.2 (C), 76.1 (CH), 74.0 (CH), 41.9 (CH2), 41.6 (CH), 40.2 (CH2), 34.1 (C), 25.5 (CH3), 21.5 (CH3), 18.3 (C), -4.7 (CH3); LRMS m/z 425 (M+-C4H9, 34), 335 (4), 285 (58), 182 (71), 139 (100); HRMS calcd. for C25H30O4SiSN2 425.0991, found 425.0974.

Diethyl (IR, 5S, 6R, 7R, RS)-9-t-Butyldimethylsilyloxy-6-[p-tolylsulfinyl]-10-oxo-11-oxatricyclo[5.3.1.01,5]-undec-8-ene-3,3-dicarboxylate (4b) and (IS, 5R, 6S, 7S, R)-9-t-Butyldimethylsilyloxy-6-[p-tolylsulfinyl]-10-oxo-11-oxatricyclo[5.3.1.01,5]-undec-8-ene-3,3-dicarboxylate (5b). The cycloaddition of 2b produces a 97:3 mixture of diastereoisomers 4b and 5b as colorless oils [99%, Rf (20% EtOAc/hexanes): 4b=0.20, 5b=0.30]. The diastereomeric ratio was determined integrating the signals of the vinylic hydrogen of the two isomers in the 1H NMR of the crude reaction mixture.

(4b): [α] = +90 (c=0.6); 1H NMR δ 7.61 (2H, d, J = 8.1 Hz), 7.36 (2H, d, J = 8.1 Hz), 6.60 (1H, d, J = 4.9 Hz), 5.10 (1H, t, J = 5.3 Hz), 4.13 (4H, m), 3.87 (1H, t, J = 5.9 Hz), 3.0 (1H, d, J = 14.8 Hz), 2.51 (1H, d, J = 14.8 Hz), 2.43 (3H, s), 2.33 (1H, m), 1.19 (6H, m), 0.97 (9H, s), 0.21 (6H, s); 13C NMR δ 191.4 (C), 170.4 (C), 170.1 (C), 147.7 (C), 142.7 (C), 139.1 (C), 130.4 (CH), 124.8 (CH), 124.3 (CH), 97.5 (C), 76.9 (CH), 76.3 (CH), 61.9 (CH2), 61.7 (CH2), 61.2 (C), 44.3 (CH), 37.1 (CH2), 36.3 (CH2), 25.5 (CH3), 21.5 (CH3), 18.3 (C), 13.9 (CH3), 13.9 (CH3), -4.7 (CH3); LRMS m/z 519 (M+-C4H9, 8), 380 (21), 333 (11), 233 (25), 173 (46), 139 (40); HRMS calcd. for C29H40O8SiS-C4H9 519.1509, found 519.1523.

(5b): [α] = +41 (c=0.2); 1H NMR δ 7.52 (2H, d, J = 7.9 Hz), 7.36 (2H, d, J = 7.9 Hz), 6.23 (1H, d, J = 5 Hz), 4.80 (1H, t, J = 5.4 Hz), 4.13 (4H, m), 3.74 (1H, t, J = 6.0 Hz), 3.1 (1H, m), 3.08 (1H, d, J = 14.85 Hz), 2.48 (1H, d, J = 14.85 Hz), 2.43 (3H, s), 1.92 (2H, m), 1.21 (6H, m), 0.96 (9H, s), 0.22 (6H, s); 13C NMR δ 192.2 (C), 171.0 (C), 169.5 (C), 147.2 (C), 142.0 (C), 139.2 (C), 130.3
(1R, 5R, 6R, 7R, R₅)-9-t-butyldimethylsilyloxy-6-[p-tolylsulfinyl-11-oxa-3-thiatricyclo[5.3.1.0₁,₅]undec-8-en-10-one (4c) and (1S, 5S, 6S, 7S, R₅)-9-t-butyldimethylsilyloxy-6-[p-tolylsulfinyl-11-oxa-3-thiatricyclo[5.3.1.0₁,₅]undec-8-en-10-one (5c).

The cycloaddition of 2c affords a 93:7 mixture of diastereoisomers 4c and 5c as colorless oils [95%, Rfₕ (30% EtOAc/hexanes): 4c=0.55, 5c=0.70]. The diastereomeric ratio was determined integrating the signals of the H-7 (t) of the two isomers in the ¹H NMR of the crude reaction mixture.

(4c): [α] = +73 (c=1.9); ¹H NMR δ 7.60 (2H, d, J = 7.9 Hz), 7.37 (2H, d, J = 7.9 Hz), 6.63 (1H, d, J = 4.8 Hz), 5.26 (1H, t, J = 5.03 Hz), 3.51 (1H, m), 3.45 (1H, m), 2.78 (1H, d, J = 12 Hz), 2.5 (1H, m), 2.45 (3H, s), 2.38 (1H, m), 1.77 (1H, dd, J = 3.2 Hz and 8.9 Hz), 1.0 (9H, s), 0.24 (6H, s); ¹³C NMR δ 191.6 (C), 147.7 (C), 143.2 (C), 139.1 (C), 130.4 (CH), 124.8 (CH), 124.2 (CH), 100.2 (C), 77.3 (CH), 75.8 (CH), 49.5 (CH), 35.7 (CH₂), 35.2 (CH₂), 25.2 (CH₃), 23.1 (CH₃), 18.4 (C), -4.6 (CH₃); LRMS FAB m/z 451 (M⁺+1, 54), 393 (13), 255 (11), 179 (100), 163 (97); HRMS calcd. for C₂₂H₃₁O₄S₂Si 451.1433, found 451.1421.

(5c): [α] = +11.5 (c=0.23); ¹H NMR δ 7.52 (2H, d, J = 7.9 Hz), 7.37 (2H, d, J = 7.9 Hz), 6.23 (1H, d, J = 4.9 Hz), 4.84 (1H, t, J = 5.16 Hz), 3.46 (1H, d, J = 13.3 Hz), 3.36 (1H, m), 3.26 (1H, m), 2.88 (1H, dd, J = 7.9 Hz and 12.5 Hz), 2.76 (1H, d, J = 13.3 Hz), 2.43 (3H, s), 2.11 (1H, d, J = 12.5 Hz), 0.97 (9H, s), 0.22 (6H, s); ¹³C NMR δ 192.3 (C), 148.0 (C), 143.1 (C), 139.1 (C), 130.8 (CH), 124.4 (CH), 123.7 (CH), 100.5 (C), 76.1 (CH), 74.1 (CH), 48.2 (CH), 36.7 (CH₂), 36.2 (CH₂), 26.0 (CH₃), 22.0 (CH₃), 18.8 (C), -4.3 (CH₃); LRMS FAB m/z 451 (M⁺+1, 61), 312 (38), 255 (31), 237 (57), 221 (38), 179 (100) 163 (54); HRMS calcd. for C₂₂H₃₁O₄S₂Si 451.1433, found 451.1413.

Procedure for the reduction of the sulfoxides to the sulfides (EXEMPLIFIED FOR 4c).

PBr₃ (0.02 mL, 0.22 mmol) was added to an ice-cooled solution of sulfoxide 4c (50 mg, 0.11 mmol) in DMF (6 ml). After 30 min, the mixture was poured into brine, extracted with Et₂O, dried, and concentrated. The crude was flash chromatographed on silica gel (10% EtOAc/hexanes) to afford 47 mg of 18c as a colorless oil [98%, Rf 0.8 (10% EtOAc/hexanes)]. ¹H NMR δ 7.34 (2H, d,
J = 8.1 Hz), 7.15 (2H, d, J = 8.1 Hz), 6.32 (1H, d, J = 4.9 Hz), 4.94 (1H, t, J = 5.2 Hz), 3.62 (1H, dd, J = 6.9 Hz and 5.5 Hz), 3.50 (1H, d, J = 13.2 Hz), 2.48 (3H, s), 0.98 (9H, s), 0.21 (6H, s); 13C NMR δ 192.1 (C), 146.6 (C), 138.0 (C), 131.5 (CH), 131.0 (C), 130.4 (CH), 125.8 (CH), 99.3 (C), 77.6 (CH), 56.0 (CH), 55.9 (CH), 53.7 (CH2), 35.6 (CH2), 25.4 (CH3), 21.1 (CH3), 18.2 (CH), -4.2 (CH3); LRMS FAB m/z 435 (M+1, 84) 377 (25), 377 (96), 308 (21), 307 (84), 289 (37), 240 (100); HRMS calcd. for C22H31O3S2Si 435.1484, found 435.1463.

18b: colorless oil [90%, Rf 0.1 (3% EtOAc/hexanes)]; [α] = +87 (c=1.4); 1H NMR δ 7.37 (2H, d, J = 8.0 Hz), 7.28 (2H, d, J = 8.0 Hz), 6.3 (1H, d, J = 5 Hz), 4.80 (1H, t, J = 5.3 Hz), 4.2 (4H, m), 3.95 (1H, t, J = 6 Hz), 3.07 (1H, t, J = 14.5 Hz), 2.65-2.40 (3H, m), 2.35 (3H, s), 2.25 (1H, m), 1.20 (6H, m), 0.95 (9H, s), 0.3 (6H, s); 13C NMR δ 192.0 (C), 170.9 (C), 170.5 (C), 146.5 (C), 137.6 (C), 131.6 (CH), 131.0 (C), 130.0 (CH), 126.2 (CH), 97.2 (C), 77.5 (CH), 61.8 (CH2), 61.6 (CH2), 61.3 (C), 56.7 (CH), 51.7 (CH), 37.2 (CH2), 36.9 (CH2), 25.5 (CH3), 21.1 (CH3), 18.3 (C), 14.0 (CH3), 13.9 (CH3), -4.7 (CH3); LRMS m/z 503 (M+-C4H9, 19), 437 (26), 240 (100), 224 (37), 130 (19), 73 (77); HRMS calcd. for C29H40O7SiS 560.2264, found 560.2285.

18a: colorless oil [90%, Rf 0.78 (15% EtOAc/hexanes)]; 1H NMR δ 7.30 (2H, d, J = 8.0 Hz), 7.15 (2H, d, J = 5.0 Hz), 5.00 (1H, t, J = 4.9 Hz), 3.80 (1H, m), 3.10 (1H, m, J = 14.5 Hz), 2.65 (3H, m), 2.50 (1H, m), 2.40 (3H, s), 0.95 (9H, s), 0.25 (6H, s); 13C NMR δ 198.9 (C), 146.3 (C), 138.9 (C), 132.3 (CH), 130.3 (CH), 129.5 (C), 125.5 (CH), 115.1 (CN), 114.8 (C), 96.2 (C), 78.2 (CH), 57.3 (CH), 52.1 (CH), 41.9 (CH2), 40.3 (CH2), 34.2 (C), 25.5 (CH3), 21.4 (CH3), 18.3 (C), -4.7 (CH3).

Diethyl (1R, 5R, 7S)-9-t-butyldimethylsilyloxy-10-oxo-11-oxatricyclo[5.3.1.01,5]undec-8-ene-3,3-dicarboxylate (6).

A solution of compound 4b (35 mg, 0.06 mmol) in THF (2 mL) was added to a suspension of activated Raney nickel (300 mg) in THF (4 mL). The reaction mixture was refluxed for 25 min, allowed to come to rt, filtered, and poured into water. Extraction with EtOAc, drying and concentration gave a residue which was purified by flash chromatography (5% EtOAc/hexanes) to afford 23 mg of 6 [85%, > 96% ee, Rf 0.33 (10% EtOAc/hexanes), colorless oil]. Enantiomeric excess was determined by 1H NMR in presence of Eu(hfc)3 (0.3 equiv) by comparison of the split signals of the vinylic proton with those of racemic 6. [α] = +43 (c=1); 1H NMR δ 6.21 (1H, d, J =
4.9 Hz), 4.81 (1H, dt, \(J = 4.8\) and 1.8 Hz), 4.17 (4H, m), 3.13 (1H, d, \(J = 14.7\) Hz), 2.60 (1H, m), 2.54 (1H, m), 2.45 (1H, m), 2.33 (1H, m), 2.14 (2H, m), 1.24 (6H, m), 0.91 (9H, s), 0.13 (6H, s);

\[\text{^13C NMR } \delta 193.4 (C), 170.9 (C), 145.6 (C), 128.7 (CH), 97.1 (C), 75.6 (CH), 61.9 (C), 61.7 (CH_2), 61.5 (CH_2), 43.4 (CH), 38.9 (CH_2), 37.7 (CH_2), 37.0 (CH_2), 25.5 (CH_3), 18.4 (C), 14.0 (CH_3), -4.321 (CH_3);\]

LRMS FAB \(m/z\) 439 (M\(^{++1}\), 100), 381 (52), 307 (79), 289 (44); HRMS calcd. for C\(_{22}\)H\(_{35}\)O\(_7\)Si 439.2152, found 439.2133.

\(\text{(1R, 2S, 5S, 7R)-9-t-Butyldimethylsilyloxy-1,7-dimethyl-8-oxabicyclo[3.2.1]octan-3-one (7).}\)

A solution of compound 4c (35 mg, 0.07 mmol) in THF (2 mL) was added to a suspension of activated Raney nickel (500 mg) in THF (6 mL) under hydrogen atmosphere (balloon). The reaction mixture was refluxed for 60 min, allowed to come to room temperature, filtered, and poured into water. Extraction with EtOAc, drying and concentration gave a residue which was purified by flash chromatography (2-7% EtOAc/hexanes) to afford 12.4 mg of 7 [65%, > 96% ee, Rf 0.30 (6% EtOAc/hexanes), colorless oil]. Enantiomeric excess was determined by \(^1\)H NMR in presence of Eu(hfc)\(_3\) (0.35 equiv) by comparison of the split signals of H-9 with those of racemic 7.\(^{6a}\) [\(\alpha\)] = -44 (c=0.25); \(^1\)H NMR \(\delta 4.5\) (1H, t, \(J = 6.1\) Hz), 3.9 (1H, s), 2.75 (1H, dd, \(J = 5.5\) and 14.7), 2.23 (2H, m), 1.97 (1H, dd, \(J = 9.1\) and 12.8), 1.59 (1H, m), 1.32 (3H, s), 0.92 (3H, d), 0.9 (9H, s), 0.14 (3H, s), 0.01 (3H, s).

Synthesis of (±6) by cycloaddition of the pyrone 24.

Allylbromide (0.28 mL, 3.21 mmol) was added to a solution of compound 17 (320 mg, 0.80 mmol) and NaH (35.4 mg, 0.88 mmol) in THF (15 mL) at rt. The mixture was stirred for 30 min and quenched by adding 3 mL of water. The solvent was evaporated and the residue diluted with Et\(_2\)O, washed with brine, dried, filtered, and concentrated. The crude was flash chromatographed on silica gel (15-25% EtOAc/hexanes) to afford 230 mg of 24 as a colorless oil [65%, Rf 0.3 (10% EtOAc/hexanes)]: \(^1\)H NMR \(\delta 7.51\) (2H, d, \(J = 5.5\) Hz), 6.26 (1H, d, \(J = 5.5\) Hz), 5.68 (1H, m), 5.12 (2H, m), 4.17 (4H, q, \(J = 7.12\) Hz), 3.41 (2H, s), 2.57 (2H, d, \(J = 7.4\) Hz), 1.22 (6H, t, \(J = 7.12\) Hz), 0.95 (9H, s), 0.23 (6H, s); \[^{13}C\text{ NMR } \delta 173.7\) (C), 169.9 (C), 153.1 (CH), 152.7 (C), 143.8 (C), 131.9 (CH), 119.4 (CH\(_2\)), 115.4 (CH), 60.8 (CH\(_2\)), 56.5 (C), 37.3 (CH\(_2\)), 30.4 (CH\(_2\)), 25.8 (CH\(_3\)),
19.2 (C), 13.9 (CH₃), -3.8 (CH₃); LRMS m/z 381 (M⁺-C₄H₉, 50), 289 (10), 233 (19), 182 (100), 179 (51), 111 (20), 75 (51); HRMS calcd. for C₂₂H₃₄O₇Si - C₄H₉ 381.1370, found 381.1373.

A solution of compound 24 (77 mg, 0.176 mmol) in toluene (10 mL) was heated under reflux for 12h. The solvent was evaporated and the crude purified by flash chromatography (10-20% EtOAc/hexanes) to afford racemic 6 as a colorless oil [97%, Rf 0.30 (10% EtOAc/hexanes)].