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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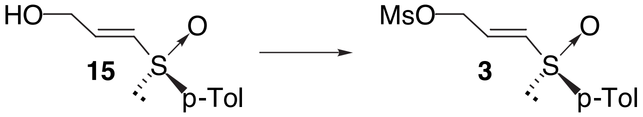
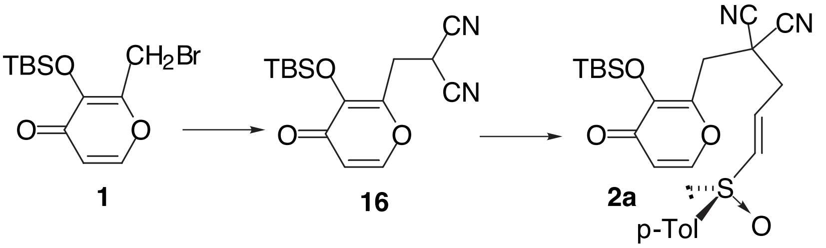
General Procedures. All dry solvents were freshly distilled under argon from the appropriate drying agent before use. Toluene and THF were distilled from sodium/benzophenone. CH_2Cl_2 was distilled from P_2O_5. MeOH was distilled from Mg/I_2. All reactions were conducted in dry solvents under argon atmosphere 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_2SO_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. $[\alpha]_D$ 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 $[\alpha] = +234$ (*c*=1); $[\alpha]^{20}$ lit. = +233 (*c*=1, ee = 97%] and Et_3N (0.14 mL, 1.02 mmol) in CH_2Cl_2 (10 mL). The reaction mixture was warmed to rt and stirred for 1h. The resulting solution was poured into water, extracted with CH_2Cl_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]. $[\alpha] = +249$ (*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 $C_{11}H_{14}O_4S_2$ 274.0333, found 274.0334.

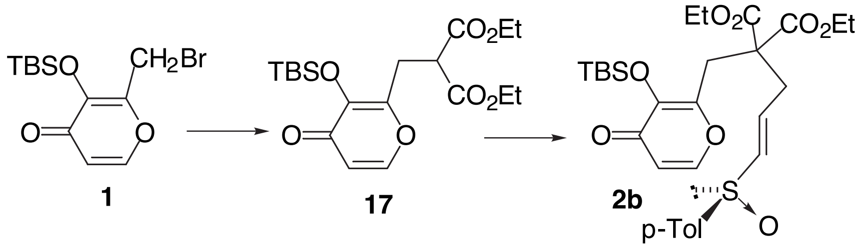
2-[(3-*t*-Butyldimethylsilyloxy-4-oxo-*4H*-2-pyranyl)methyl]-2-[(*2E*, *R*$_S$)-3-*p*-tolylsulfinyl-2-propenyl]malononitrile (2a).



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 Et_2O, dried, filtered, and concentrated. The residue was flash chromatographed on silica gel (90% CH_2Cl_2/hexanes) to afford 2.2 g of **16** as a colorless viscous oil [75%, Rf 0.15 (90% CH_2Cl_2/hexanes)]: ^{1}H 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); ^{13}C NMR δ 173.6 (C), 153.7 (CH), 147.6 (C), 144.5 (C), 115.8 (CH), 111.4 (CN), 29.3 (CH_2), 26.0 (CH_3), 20.1 (CH), 18.6 (C), -3.9 (CH_3); LRMS *m/z* 289 (M^+ - CH_3, 3), 247 (79), 182 (100), 154 (12), 111 (18); HRMS calcd. for $C_{15}H_{20}O_3N_2Si – CH_3$ 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 Et_2O, washed with brine, dried, filtered, and concenttrated. 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); ^{1}H 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); ^{13}C 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 (CH_2), 35.3 (C), 34.7 (CH_2), 26.1 (CH_3), 21.4 (CH_3), 18.8 (C), -3.5 (CH_3); LRMS *m/z* 425 (M^+- C_4H_9, 42), 245 (31), 182 (100), 139 (24), 73 (25); HRMS calcd. for $C_{25}H_{30}O_4SiSN_2$ - C_4H_9 425.0991, found 425.0986.

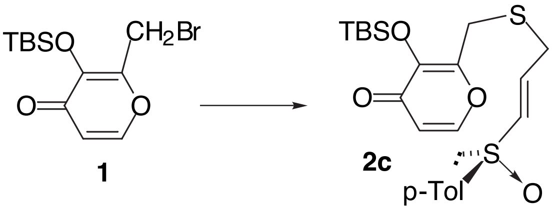
Diethyl-2-[(3-*t*-Butyldimethylsilyloxy-4-oxo-*4H*-2-pyranyl)methyl]-2-[(*2E*, R_S)-3-*p*-tolylsulfinyl-2-propenyl]malonate (2b).



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 Et_2O, 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 δ 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 δ 174.5 (C), 168.1 (C), 153.3 (C), 152.8 (CH), 143.0 (C), 115.6 (CH), 61.8 (CH_2), 48.9 (CH), 27.6 (CH_2), 26.0 (CH_3), 18.7 (C), 14.0 (CH_3), -3.7 (CH_3); LRMS *m/z* 341 (M^+-C_4H_9, 100), 267 (9), 239 (9), 195 (39), 165 (4); HRMS calcd. for $C_{19}H_{30}O_7Si–C_4H_9$ 341.1056, found 341.1054.

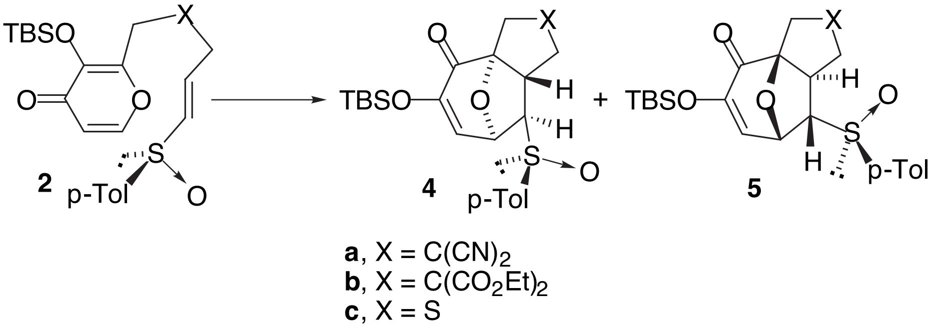
A solution of compound **17** (240 mg, 0.60 mmol) in THF (2 mL) was added to an ice-cooled suspension of NaH (24 mg, 0.60 mmol) in THF (10 mL). After stirring for 15 min at rt a solution of mesylate **3** (150 mg, 0.55 mmol) in THF (2 mL) was added. The reaction mixture was stirred at rt for 12 h and the reaction quenched by adding 3 mL of water. The solvent was evaporated and the residue diluted with Et_2O, washed with brine, dried, filtered, and concenttrated. 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)]. [α] = +39 (*c*=0.72); ^{1}H NMR δ 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 δ 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 (CH_2), 56.3 (C), 35.9 (CH_2), 31.0 (CH_2), 25.9 (CH_3), 21.2 (CH_3), 18.6 (C), 14.8 (CH_3), -3.8 (CH_3); LRMS FAB*m/z* 577 (M^++1, 16), 519 (8), 249 (27), 239 (19), 182 (100), 179 (41), 173 (74); HRMS calcd. for $C_{29}H_{41}O_8SiS$ 577.2291, found 577.2277.

3-*t*-Butyldimethylsilyloxy-2-[((2*E*,*R*$_S$)-3-*p*-tolylsulfinyl-2-propenyl)sulfanylmethyl] -4*H*-4-pyranone (2c).



Triphenylsilanethiol (187 mg, 0.64 mmol) was added to a solution of mesylate **3** (175 mg, 0.639 mmol), PPh_3 (168 mg, 0.64 mmol) and Cs_2CO_3 (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 Et_2O, 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); ^{1}H 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); ^{13}C 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 (CH_2), 27.6 (CH_2), 25.7 (CH_3), 21.1 (CH_3), 18.4 (C), -3.9 (CH_3); LRMS FAB *m/z* 451 (M^++1, 77), 392 (11), 240 (32), 212 (35), 182 (33), 163 (50); HRMS calcd. for $C_{22}H_{31}O_4S_2Si$ 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 chomatography (25-50% EtOAc/hexanes) to afford a 91:9 ratio of diastereoisomers **4a** and **5a** as colorless oils [98%, Rf$_s$ (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 ^{1}H NMR spectrum of the crude reaction mixture.

(*1R*, *5S*, *6R*, *7R*, *R*$_S$)-9-*t*-Butyldimethylsilyloxy-6-[*p*-tolylsulfinyl-10-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undec-8-ene-3,3-dicarbonitrile (4a): [α] = +108 (*c*=0.65); ^{1}H 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); ^{13}C NMR δ 189.3 (C), 147.5 (C), 143.7 (C), 138.8 (C), 130.8 (CH), 124.5 (CH), 123.8 (CH), 114.6 (CN), 114.3 (CN), 96.7 (C), 77.7 (CH), 76.5 (CH), 44.9 (CH), 41.3 (CH_2), 40.4 (CH_2), 34.3 (C), 25.4 (CH_3), 22.6 (CH_3), 18.3 (C), -4.7 (CH_3); LRMS FAB *m/z* 483 (M^++1, 95), 426 (16), 425 (56), 371 (100), 281 (29), 257 (16), 239 (23); HRMS calcd. for $C_{25}H_{31}O_4SiSN_2$ 483.1773, found 483.1751.

(*1S, 5R, 6S, 7S, R*$_S$)-9-*t*-butyldimethylsilyloxy-6-[*p*-tolylsulfinyl-10-oxa-11-oxatricyclo-[5.3.1.0^{1,5}]undec-8-en-3,3-dicarbonitrile (5a): [α] = +15.7 (*c*=0.37); ^{1}H 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 6.6Hz), 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); ^{13}C NMR δ 189.5 (C), 147.2 (C), 142.8 (C), 138.6 (C), 130.6 (CH), 123.5 (CH), 123.0 (CH), 115.2 (CN), 114.5 (CN), 96.2 (C), 76.1 (CH), 74.0 (CH), 41.9 (CH_2), 41.6 (CH), 40.2 (CH_2), 34.1 (C), 25.5 (CH_3), 21.5 (CH_3), 18.3 (C), -4.7 (CH_3); LRMS m/z 425 (M^+-C_4H_9, 34), 335 (4), 285 (58), 182 (71), 139 (100); HRMS calcd. for $C_{25}H_{30}O_4SiSN_2$ 425.0991, found 425.0974.

Diethyl (*1R*, *5S*, *6R*, *7R*, *R*$_S$)-9-*t*-butyldimethylsilyloxy-6-[*p*-tolylsulfinyl-10-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undec-8-ene-3,3-dicarboxylate (4b) and (*1S*, *5R*, *6S*, *7S*, *R*$_S$)-9-*t*-butyldimethylsilyloxy-6-[*p*-tolylsulfinyl-10-oxo-11-oxatricyclo[5.3.1.0^{1,5}]-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$_s$ (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 ^{1}H NMR of the crude reaction mixture.

(4b): [α] = +90 (*c*=0.6); ^{1}H 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), 1.68 (2H, m), 1.19 (6H, m), 0.97 (9H, s), 0.21 (6H, s); ^{13}C 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 (CH_2), 61.7 (CH_2), 61.2 (C), 44.3 (CH), 37.1 (CH_2), 36.3 (CH_2), 25.5 (CH_3), 21.5 (CH_3), 18.3 (C), 13.9 (CH_3), 13.9 (CH_3), -4.7 (CH_3); LRMS *m/z* 519 (M^+-C_4H_9, 8), 380 (21), 333 (11), 233 (25), 173 (46), 139 (40); HRMS calcd. for $C_{29}H_{40}O_8SiS$ -C_4H_9 519.1509, found 519.1523.

(5b): [α] = +41 (*c*=0.2); ^{1}H 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); ^{13}C NMR δ 192.2 (C), 171.0 (C), 169.5 (C), 147.2 (C), 142.0 (C), 139.2 (C), 130.3

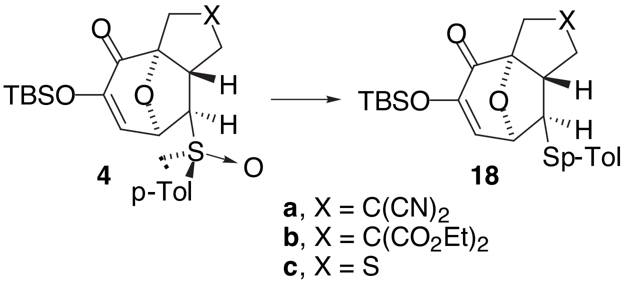
(CH), 123.7 (CH), 123.5 (CH), 97.2 (C), 75.4 (CH), 73.9 (CH), 61.8 (CH_2), 61.7 (CH_2), 61.2 (C), 41.7 (CH), 37.5 (CH_2), 37.3 (CH_2), 25.9 (CH_3), 21.8 (CH_3), 18.7 (C), 14.3 (CH_3), 14.3 (CH_3), -4.2 (CH_3); LRMS FAB*m/z* 577 (M^++1, 79), 421 (30), 363 (34), 281 (50), 233 (24), 221(66), 173 (100); HRMS calcd. for $C_{29}H_{41}O_8SiS$ 577.2291, found 577.2291.

(*1R, 5R, 6R, 7R, R_S*)-9-*t*-butyldimethylsilyloxy-6-[*p*-tolylsulfinyl-11-oxa-3-thiatricyclo[5.3.1.$0^{1,5}$]undec-8-en-10-one (4c) and (*1S, 5S, 6S, 7S, R_S*)-9-*t*-butyldimethylsilyloxy-6-[*p*-tolylsulfinyl-11-oxa-3-thiatricyclo[5.3.1.$0^{1,5}$]undec-8-en-10-one (5c). The cycloaddition of **2c** affords a 93:7 mixture of diastereoisomers **4c** and **5c** as colorless oils [95%, Rf_s (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); ^{13}C 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), 49.8 (CH), 35.7 (CH_2), 35.2 (CH_2), 25.2 (CH_3), 23.1 (CH_3), 18.4 (C), -4.6 (CH_3); LRMS FAB *m/z* 451 (M^++1, 54), 393 (13), 255 (11), 179 (100), 163 (97); HRMS calcd. for $C_{22}H_{31}O_4S_2Si$ 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); ^{13}C NMR δ 192.3 (C), 148.0 (C), 143.1 (C), 139.6 (C), 130.8 (CH), 124.4 (CH), 123.7 (CH), 100.5 (C), 76.1 (CH), 74.1 (CH), 48.2 (CH), 36.7 (CH_2), 36.2 (CH_2), 26.0 (CH_3), 22.0 (CH_3), 18.8 (C), -4.3 (CH_3); LRMS FAB*m/z* 451 (M^++1, 61), 312 (38), 255 (31), 237 (57), 221 (38), 179 (100) 163 (54); HRMS calcd. for $C_{22}H_{31}O_4S_2Si$ 451.1433, found 451.1413.

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

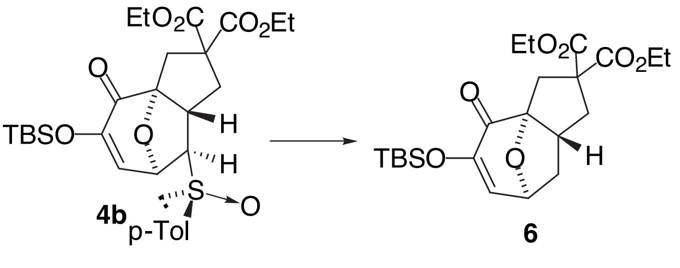


PBr_3 (0.02 mL, 0.22 mmol) was added to an ice-cooled solution of sulfoxide **4c** (50 mg, 0.11 mmol) in DMF (6 ml). After 30 min, the mixture was poured into brine, extracted with Et_2O, dried, and concentrated. The crude was flash chromatographed on silica gel (10% EtOAc/hexanes) to afford 47 mg of **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), 3.08 (1H, dd, *J* = 12.2 and 7.7 Hz), 2.78 (1H, d, *J* = 13.4 Hz), 2.66 (2H, m), 2.34 (3H, s), 0.98 (9H, s), 0.21 (6H, s); ^{13}C NMR δ 192.1 (C), 146.6 (C), 138.0 (C), 131.8 (C), 131.5 (CH), 130.4 (CH), 125.8 (CH), 99.3 (C), 77.6 (CH), 56.0 (CH), 55.9 (CH), 35.7 (CH_2), 35.6 (CH_2), 25.4 (CH_3), 21.1 (CH_3), 18.2 (C), -4.2 (CH_3); LRMS FAB*m/z* 435 (M^++1, 84) 377 (25), 377 (96), 308 (21), 307 (84), 289 (37), 240 (100); HRMS calcd. for $C_{22}H_{31}O_3S_2Si$ 435.1484, found 435.1463.

18b: colorless oil [90%, Rf 0.1 (3% EtOAc/hexanes)]: [α] = +87 (*c*=1.4); ^{1}H 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); ^{13}C 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 (CH_2), 61.6 (CH_2), 61.3 (C), 56.7 (CH), 51.7 (CH), 37.2 (CH_2), 36.9 (CH_2), 25.5 (CH_3), 21.1 (CH_3), 18.3 (C), 14.0 (CH_3), 13.9 (CH_3), -4.7 (CH_3); LRMS *m/z* 503 (M^+-C_4H_9, 19), 437 (26), 240 (100), 224 (37), 130 (19), 73 (77); HRMS calcd. for $C_{29}H_{40}O_7SiS$ 560.2264, found 560.2285.

18a: colorless oil [90%, Rf 0.78 (15% EtOAc/hexanes)]: ^{1}H NMR δ 7.30 (2H, d, *J* = 8.0 Hz), 7.15 (2H, d, *J* = 8.0 Hz), 6.30 (1H, d, *J* = 5.0 Hz), 5.00 (1H, t, *J* = 4.9 Hz), 3.80 (1H, m), 3.10 (1H, d, *J* = 14.5 Hz), 2.65 (3H, m), 2.50 (1H, m), 2.40 (3H, s), 0.95 (9H, s), 0.25 (6H, s); ^{13}C NMR δ 189.8 (C), 146.3 (C), 138.9 (C), 132.3 (CH), 130.3 (CH), 129.5 (C), 125.5 (CH), 115.1 (CN), 114.8 (CN), 96.2 (C), 78.2 (CH), 57.3 (CH), 52.1 (CH), 41.9 (CH_2), 40.3 (CH_2), 34.2 (C), 25.5 (CH_3), 21.4 (CH_3), 18.3 (C), -4.7 (CH_3).

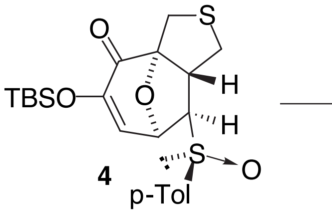
Diethyl (*1R, 5R, 7S*)-9-*t*-butyldimethylsilyloxy-10-oxo-11-oxatricyclo[5.3.1.0^{1,5}]undec-8-ene-3,3-dicarboxylate (6).



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 ^{1}H 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); ^{1}H NMR δ 6.21 (1H, d, *J* =

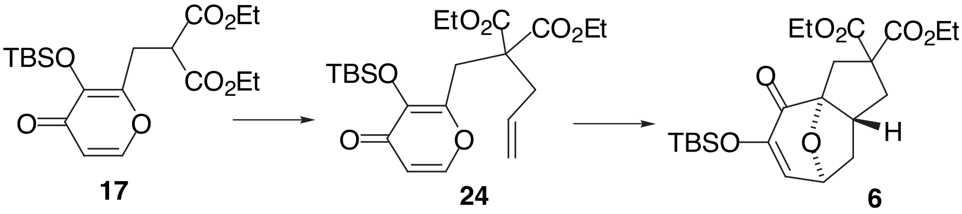
4.9 Hz), 4.81 (1H, dt, J = 4.8 and 1.8 Hz), 4.17 (4H, m), 3.13 (1H, d, J = 14.7 Hz), 2.60 (1H, m), 2.54 (1H, m), 2.45 (1H, m), 2.33 (1H, m), 2.14 (2H, m), 1.24 (6H, m), 0.91 (9H, s), 0.13 (6H, s); ^{13}C NMR δ 193.4 (C), 170.9 (C), 145.6 (C), 128.7 (CH), 97.1 (C), 75.6 (CH), 61.9 (C), 61.7 (CH_2), 61.5 (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 $C_{22}H_{35}O_7Si$ 439.2152, found 439.2133.

(*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] [α] = -44 (*c*=0.25); ^{1}H NMR δ 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_2O, 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 δ 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 NMR δ 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 (CH_3), -3.8 (CH_3); LRMS *m/z* 381 (M^+-C_4H_9, 50), 289 (10), 233 (19), 182 (100), 179 (51), 111 (20), 75 (51); HRMS calcd. for $C_{22}H_{34}O_7Si$ - C_4H_9 381.1370, 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 chomatography (10-20% EtOAc/hexanes) to afford racemic **6** as a colorless oil [97%, Rf 0.30 (10% EtOAc/hexanes)].