Theory-Guided Discovery of Unique Chemical Transformations of Cyclopropenes

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Supplementary Material

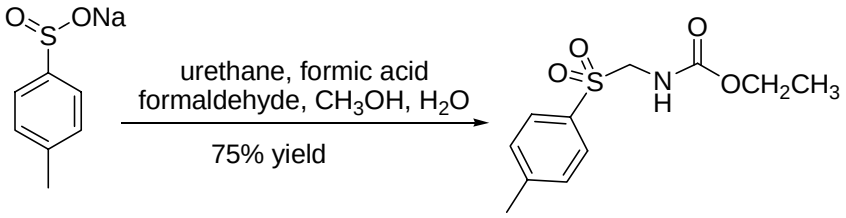
Material and Methods. Reactions were performed in flame-dried glassware under a positive pressure of nitrogen using freshly distilled solvent. Tetrahydrofuran and diethyl ether were freshly distilled from Na°/benzophenone before use. Dichloromethane, benzene, acetonitrile and cyclohexane were freshly distilled from CaH_2 before use. Commercial grade reagents and solvents were used without further purification unless otherwise stated. Thin layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 pre-coated plates (0.25 mm). Preparative thin layer chromatography separations were carried out on 0.50 mm E. Merk silica gel plates (60F-254). Column chromatography was performed using Bakerbond® silica gel (40 μm particle size). Other chromatographic methods involved using combinations of Al_2O_3 (neutral) with Celite 545®, and Bakerbond® CN capped silica gel (40 μm particle size).

Analytical high performance liquid chromatography (HPLC) was performed on an Agilent 1100 Series HPLC using the indicated analytical chiral column and conditions (solvent system, flow rate, wavelength). Preparative high performance liquid chromatography (HPLC) was performed on a Dynamax® Model SD-200 using a Daicel Chiracel OJ column (2 cm ϕ x 25 cm). One dimensional ^{1}H NMR spectra were recorded on either a on either a Varian Mercury-400 (400 MHz) or a Varian Unity/INOVA-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CHCl_3$: δ7.26). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, quin = quintuplet, sext = sextuplet), coupling constants (Hz), and integration. One dimensional ^{13}C NMR spectra were recorded on either a Varian Mercury-400 (100 MHz) or a Varian Unity/INOVA-500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CHCl_3$: δ77.0). ^{2}H-NMR spectra was recorded on a Brüker DMX-500 spectrometer. Chemical shifts are reported in ppm using residual *d*-chloroform as the internal standard ($CDCl_3$: δ7.26). One dimensional ^{1}H-NOE and two dimensional homonuclear (^{1}H-^{1}H-COSY, ^{1}H-^{1}H-NOESY) and heteronuclear (^{1}H-^{13}C-HSQC, ^{1}H-^{13}C-HMBC) NMR experiments were conducted on a Varian Unity/INOVA-500 (500 MHz) spectrometer. All Infrared spectra, with the exception of tosyl diazomethane, were recorded on an

Applied Systems (ASI) ReactIR™ 1000 spectrophotometer, ν_{max} in cm^{-1}. An IR spectra of tosyl diazomethane was obtained on an Avatar 360 FT-IR spectrophotometer, ν_{max} in cm^{-1}. Specific optical rotations were measured with a Perkin-Elmer 241 Polarimeter at the indicated temperature with a sodium lamp (D line, 589 nm). Melting points were obtained using a Büchi melting point apparatus. High resolution mass spectral analyses (ESI^+, ESI^-, CI^+, EI^+) were performed at the Bauer Laboratory Mass Spectrometry Facility, (Harvard University, Cambridge, MA). X-ray data was collected by R. A. Weatherhead-Kloster at the Bauer X-ray Diffraction Laboratory (Harvard University, Cambridge, MA) using either a Siemens 1K CCD or APEX CCD diffractometer. The x-ray structures were solved using $SAINT^+$ and Brüker SHELXTL programs.

Synthesis of Tosyl Diazomethane

(Toluene-4-sulfonylmethyl)-carbamic acid ethyl ester

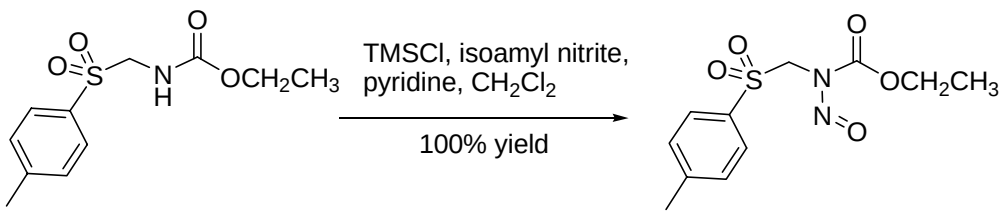


Preparation of the title compound follows the reported synthesis: [a]

Formaldehyde (37 weight % in water) (8 mL), urethane (6.3 g, 0.07 mol) and formic acid (15 mL) were added to a solution of *p*-tolylsulfinate dihydrate (15.1 g, 0.07 mol) in water (80 mL), and the reaction mixture was heated to a gentle reflux for two hours. The solution was cooled to 23 °C, and further cooled to 0°C for two hours. The white precipitate was collected by vacuum filtration and recrystallized upon standing at -22 °C for two hours from absolute ethanol. The solid was filtered and washed thoroughly with hexanes. The title compound was obtained as a crystalline white solid (13.5 g, 75% yield). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.11 (t, J = 6.8 Hz, 3 H); 2.43 (s, 3 H); 3.96 (q, J = 6.8 Hz, 2 H); 4.53 (d, J = 8.0 Hz, 2 H); 5.58 (s, 1 H); 7.33 (d, J = 8.4 Hz, 2 H); 7.77 (d, J = 8.4 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 100 MHz): δ 14.3, 21.7, 61.9, 62.3, 128.9, 129.9, 133.8, 145.4, 155.

[a] Van Leusen, A. M.; Strating, J. *Rec. Trav. Chim. Pays-Bas* **1965**, *84,* 151-164.
Van Leusen, A. M.; Strating, J. *Rec. Trav. Chim. Pays-Bas* **1965**, *84,* 140-151.
Van Leusen, A. M.; Strating, J. *Org. Synth VI* **1977**, 981-988.

N-Nitroso-(toluene-4-sulfonylmethyl)-carbamic acid ethyl ester

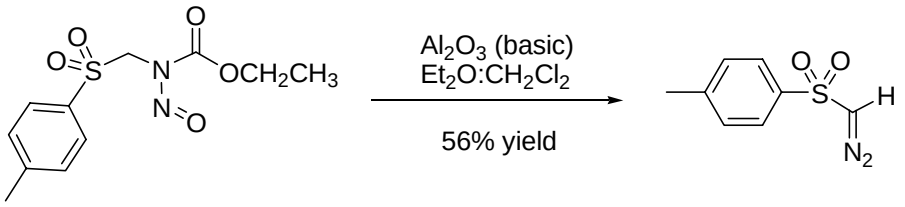


Preparation of the title compound follows the reported synthesis: [a]

To a solution of toluene-4-sulfonylmethyl)-carbamic acid ethyl ester (11.98 g, 0.05 mol) in dichloromethane (50 mL) in a flame dried flask under nitrogen was added pyridine (6.1 mL, 0.075 mol), isopentyl nitrite (10 mL, 0.075 mol) and trimethylsilyl chloride (TMSCl) (16.6 mL, 0.13 mol). The reaction, shielded from light, was monitored by thin layer chromatography for complete disappearance of starting material. After 24 hours, additional 0.2 equivalents of pyridine (0.8 mL, 0.01 mol), isopentyll nitrite (1.3 mL, 0.01 mol) and TMSCl (1.3 mL, 0.01 mol) were sequentially added to the reaction every 2-3 hours until complete conversion of starting material to product. The reaction was then slowly poured into a 10% $NaHCO_3$ (aq) solution (200 mL), and stirred for 30 minutes. The heterogenous solution was diluted with diethyl ether (500 mL) and the organic layer was washed with water (250 mL), 1 M HCl (250 mL), water (250 mL), 10% $NaHCO_3$ (aq) (250 mL), water (250 mL) and brine (250 mL). The light yellow organic phase was dried with $MgSO_4$, concentrated under reduced pressure and triturated with hexanes to a yellow solid. Upon decanting the hexanes solution, the title compound was obtained as a yellow solid (14.3 g, 100% yield).

^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.42 (t, J = 7.1 Hz, 3H); 2.46 (s, 1 H); 4.52 (q, J = 7.1 Hz, 2 H); 5.12 (s, 2 H); 7.36 (d, J = 8.4 Hz, 2 H); 7.70 (d, J = 8.4 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 100 MHz): δ 14.1, 21.7, 58.3, 65.4, 128.5, 130.1, 135.0, 145.8, 152.4.

Tosyl diazomethane[b,c]

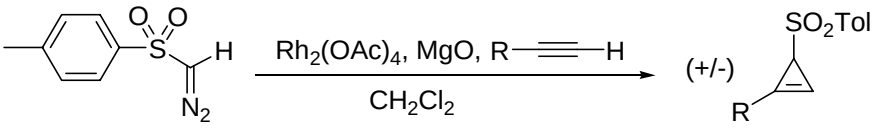


Al_2O_3 (activated, basic, Brockman 1, standard grade, 150 mesh, 58 Å) (100g), was placed under N_2 atmosphere, cooled to 0 ºC, and slurried in anhydrous diethyl ether (300 mL). To this was added N-nitroso-(toluene-4-sulfonylmethyl)-carbamic acid ethyl ester (10.7 g, 0.037 mol) in CH_2Cl_2 (30 mL). The reaction, shielded from light, was mechanically stirred at 0 °C – 5 °C for 2 hours. Over the course of the reaction, the solution became bright yellow and the Al_2O_3 slighty pinkened. The reaction was judged complete by thin layer chromatography upon complete disappearance of the starting material. The yellow solution was decanted, and the solid thoroughly washed with diethyl ether. The solution was filtered and concentrated under reduced pressure to an oil which solidified upon treatment with cold petroleum ether in a dry ice/acetone bath. The yellow solid was triturated with PET ether at -78 °C and the solution decanted from the solid. The bright yellow solid was stored at -22 °C over a 6 month period, shielded from light and moisture, without any detectable decomposition. 4.1 g, 56 % yield. mp = 36 – 37 °C. IR (film, cm $^{-1}$): 3085, 2107, 1598, 1328, 1272, 1152, 1082, 812. ^{1}H NMR ($CDCl_3$, 400MHz): δ 2.44 (s, 3 H); 5.26 (s, 1 H); 7.33 (d, J = 8.4 Hz, 2 H); 7.70 (d, J = 8.4 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 100 MHz): δ 21.5, 57.7, 126.2, 129.9, 141.2, 144.3. HRMS (CI^+) calcd for $C_8H_8N_2O_2S$ $(M+NH_4)^+$ 214.0650, found 214.0657.

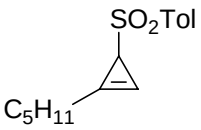
[b] Plessis, C.; Uguen, D.; DeCian, A.; Fischer, J. *Tetrahedron Letters* **2000**, *41*, 5489-5493.

[c] Decomposition of tosyl diazomethane with $Rh_2(OAc)_4$ (2 mol%) in CH_2Cl_2 (0.1 M) at 23 °C led to the formation of the expected carbene dimerization products *trans* and *cis* 1,2-bis-(p- toluene sulfonyl) ethylene as well as the unexpected product, *p*-tolyl thiosulfonate, in a 5 to 1 to 2 ratio.

Synthesis of Racemic Tosyl Cyclopropenes 2a – 2c.

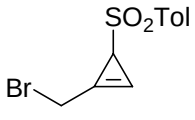


(+/-)-2-*n*-Amyl-2-cyclopropenyl-4-tolyl sulfone (**2a**)



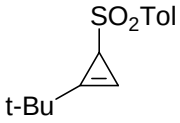
To a solution of $Rh_2(OAc)_4$ (72 mg, 2 mol%), MgO (328 mg, 8.2 mmol), and 1-heptyne (10.7 mL, 0.082 mol) in CH_2Cl_2 (3 mL) at 0 °C under N_2 atmosphere was added a solution of tosyl diazomethane (1.6 g, 8.2 mmol) in CH_2Cl_2 (16 mL) over 20 minutes. The reaction was warmed to 23 °C and an additional 0.5 mol% of $Rh_2(OAc)_4$ (20 mg) was added to the yellow reaction mixture and N_2 extrusion observed. The reaction was stirred for 20 minutes, filtered through Celite, and concentrated under reduced pressure to a crude residue. The residue was purified on a short silica column (maximum height 2.5 inches) by flash chromatography (20% Et_2O in hexanes) and the title compound was obtained as a light yellow oil which slowly solidified at -22 °C over 16 hours. The sticky solid was triturated in petroleum ether at -78 °C and the solution decanted to give the title compound (+/-)-**2a** as an off-white solid, 1.66g, 77% yield. X-ray quality crystals were obtained from an evaporating mixture of CH_2Cl_2, petroleum ether and hexanes at 23 °C. mp = 45 – 47 °C. IR (film, cm $^{-1}$): 3132, 2956, 2931, 2861, 1598, 1457, 1302, 1312, 1289, 1142, 1086, 816, 710. ^{1}H NMR ($CDCl_3$, 500MHz): δ 0.88 (t, J = 7.0 Hz, 3 H); 1.25 – 1.33 (m, 4 H); 1.55 – 1.59 (m, 2 H); 2.44 (s, 3 H); 2.45 – 2.57 (m, 2 H); 3.08 (s, 1 H), 6.48 (s, 1 H); 7.32 (d, J = 8.5 Hz, 2 H); 7.70 (d, J = 8.5 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 125 MHz): δ 13.9, 21.5, 22.2, 24.7, 26.0, 31.2, 42.2, 96.0, 119.0, 127.7, 129.7, 137.5, 143.8. HRMS (ESI$^+$) calcd for $C_{15}H_{20}O_2S$ $(M+NH_4)^+$ 282.1528, found 282.1530.

(+/-)-2-(bromomethyl)-2-cyclopropenyl-4-tolyl sulfone (**2b**)



To a solution of $Rh_2(OAc)_4$ (56 mg, 2.5 mol%) and propargyl bromide (4.5 mL, 0.050 mol) at 23 °C under N_2 atmosphere was added a solution of tosyl diazomethane (1.0 g, 5.0 mmol) in CH_2Cl_2 (10 mL) over 1.5 hours [Note: addition of MgO is not necessary]. The reaction was stirred for 30 minutes, filtered through Celite, and concentrated under reduced pressure. The crude residue was triturated with hexanes to a crude yellow solid, which was purified on a short silica column (maximum height 2.5 inches, pretreated with 1% NEt_3 in CH_2Cl_2) by flash chromatography (20% EtOAc in hexanes) in order to obtain the title compound (+/-)-**2b** as a light yellow solid (805 mg, 56 % yield). X-ray quality crystals were obtained from an evaporating mixture of MeOH and EtOAc at 5 °C. mp = 52 - 54 °C. IR (film, cm $^{-1}$): 3134, 3062, 2956, 2923, 1802, 1596, 1493, 1451, 1414, 1310, 1289, 1136, 1084, 1019, 949, 814, 721. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.44 (s, 3 H); 3.32 (s, 1 H); 4.16 (d, J = 13.6 Hz, 1 H); 4.32 (d, J = 13.6 Hz, 1 H); 6.78 (s, 1 H); 7.34 (d, J = 8.0 Hz, 2 H); 7.70 (d, J = 8.0 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 100 MHz): δ 19.6, 21.6, 44.2, 100.7, 114.8, 127.8, 129.9, 136.6, 144.3. HRMS (CI^+) calcd for $C_{11}H_{11}BrO_2S$ $(M+NH_4)^+$ 304.0007, found 303.9994.

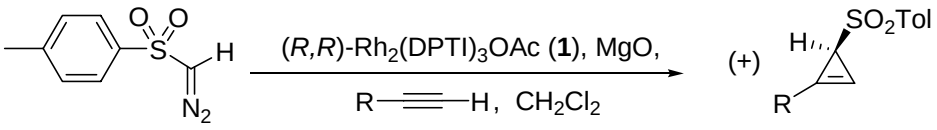
(+/-)-2-*t*-Butyl-2-cyclopropenyl-4-tolyl sulfone (**2c**)



To a solution of $Rh_2(OAc)_4$ (2.5 mg, 2 mol%), MgO (11 mg, 0.28 mmol), and 3,3-dimethyl butyne (0.35 mL, 2.8 mmol) in CH_2Cl_2 (0.05 mL) at 23 °C under N_2 atmosphere was added a solution of tosyl diazomethane (55 mg, 0.28 mmol) in CH_2Cl_2 (0.5 mL) over 10 minutes. An additional 0.8 mol% of $Rh_2(OAc)_4$ (1 mg) was added to the yellow reaction mixture and N_2 extrusion observed. The reaction was stirred for 20 minutes, filtered through Celite, and concentrated under reduced pressure. The crude residue was triturated with hexanes to a crude off white solid and was purified on a short silica column (maximum height 2.5 inches) by flash chromatography (30% Et_2O in hexanes) to obtain the title compound (+/-)-**2c** as an off-white solid (35 mg, 50% yield).

X-ray quality crystals were obtained from an evaporating CH_2Cl_2 solution at -22 °C. mp = 84 - 85 °C. IR (film, cm $^{-1}$): 3132, 2970, 1775, 1598, 1461, 1366, 1312, 1289, 1140, 1086, 1005, 918, 814, 731, 669. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.23 (s, 9 H); 2.43 (s, 3 H), 3.12 (d, J = 1.0 Hz, 1 H); 6.34 (d, J = 1.0 Hz, 1 H); 7.32 (d, J = 8.0 Hz, 2 H); 7.74 (d, J = 8.0 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 100 MHz): δ 21.6, 28.0, 31.0, 42.8, 94.0, 126.9, 127.7, 129.6, 137.8, 143.7. HRMS (CI^+) calcd for $C_{14}H_{18}O_2S$ $(M+NH_4)^+$ 268.1371, found 268.1370.

Synthesis of Chiral Tosyl Cyclopropenes (+)- 2a – 2c.

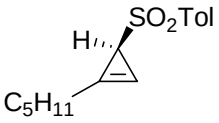


A solution of alkyne (2.2 mmol, 20 eq), MgO (0.11 mmol, 1 eq), (*R,R*)-$Rh_2(DPTI)_3OAc$ (**1**)[1] with CH_2Cl_2 (0.05 mL) under N_2 atmosphere was cooled to 0 °C, and tosyl diazomethane (0.11 mmol, 1 eq) in CH_2Cl_2 (0.15 mL) was added over a 15 minute period. The reaction mixture was stirred an additional 5 minutes at 0 °C, 5 mg of charcoal was added, and solution was stirred for another 5 minutes at 0 °C. The reaction mixture was filtered through a short pipet plug of layered (top to bottom) of Al_2O_3 (neutral) : Celite 545 ® (1:5) into a flask cooled to 0 °C, washing with CH_2Cl_2, and the filtrate concentrated under reduced pressure. The residue was slurried in cyclohexane, and filtered through a pad of Celite 545® into a flask at 23 °C. The filtrate was concentrated under reduced pressure to a residue which was dissolved in cyclohexane and flushed through a pipet plug of Bakerbond® CN capped silica gel (height = 0.5 inches). The solution was concentrated under reduced pressure in order to obtain the purified optically enriched cyclopropenyl sulfone. The product can be stored in a -78 °C freezer at over a 1 month period with little to no racemization.

NOTE:

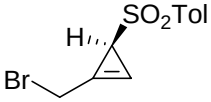
- The addition of MgO is necessary in order to prevent *in situ* racemization. Some racemization occurs with MgO added, but more slowly. For example, under identical cyclopropenation conditions with MgO as an additive, (+)-**2a** is obtained in 91% ee after 25 min, or in 79% ee after 1.75 hr. If no MgO is added to the reaction, (+)-**2a** is obtained in 85% ee (25 min).
- Cyclopropenyl sulfones (+)-**2a** and (+)-**2c** racemize readily on silia gel (*ca* within 30 minutes of exposure). Cyclopropenyl sulfone (+)-**2b** racemizes much more slowly on silica gel and can, if necessary, be purified on silica gel without significant loss to enantiomeric purity. There is no racemization observed using Bakerbond® CN capped silica gel for (+)-**2a** – **2c**, and thus this reverse phase gel is used as a standard purification tool.

(+)-2-*n*-Amyl-2-cyclopropenyl-4-tolyl sulfone (**2a**)



The reaction was conducted at 0 °C with **1** (1.5 mol%) over the 25 minute reaction period. The title chiral compound (+)-**2a** was obtained as a colorless oil (16 mg, 56% yield) in 91% ee (HPLC, Chiracel OD column, 2% i-PrOH in hexanes, 0.8 mL/min, 210 nm, major isomer 28.8 min, minor isomer 26.4 min). $[\alpha]^{23}_{D}$ = +71° (c 0.75, $CHCl_3$). Purification on silica gel (30 min time period) results in the title compound in 0% ee.

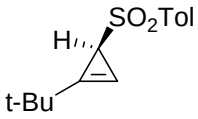
(+)-2-(bromomethyl)-2-cyclopropenyl-4-tolyl sulfone (**2b**)



The reaction was conducted at 0 °C with **1** (1 mol%) over the 25 minute reaction period. A modified workup procedure was followed: The reaction mixture was filtered through a short pipet plug of layered (top to bottom) of Al_2O_3 (neutral):Celite (1:5) into a flask cooled to 0 °C, washing with CH_2Cl_2, and the filtrate concentrated under reduced pressure. The residue was slurried in a solution of 5% CH_2Cl_2 in

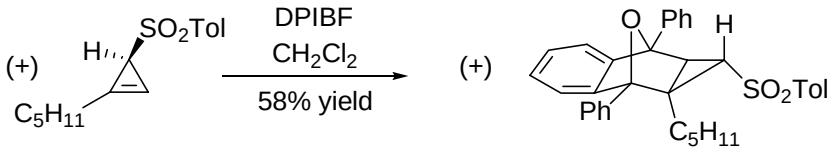
cyclohexane and flushed through a pipet plug of Bakerbond® CN capped silica gel (height = 0.5 inches). The title chiral compound (+)-**2b** was obtained as a white solid (22 mg, 59% yield) in 94 % ee (HPLC, Chiracel OJ column, 12% i-PrOH in hexanes, 1 mL/min, 210 nm, major isomer 26.8 min, minor isomer 31.3 min). $[\alpha]^{22}_{D}$ = +149° (c 1.05, $CHCl_3$). mp = 54 - 55 °C. Purification on silica gel (5g of silica, 100% CH_2Cl_2, jacketed chromatography column cooled with ice/brine, 10 min) results in the title compound in 93 % ee.

(+)-2-*t*-Butyl-2-cyclopropenyl-4-tolyl sulfone (**2c**)



The reaction was conducted at 23 °C with **1** (2.5 mol%) over the 25 minute reaction period. Following the general workup procedure, the title chiral compound (+)-**2c** was obtained as an off-white solid (16 mg, 49 % yield) in 78% ee (HPLC, Chiralpak !A column, 1% i-PrOH in hexanes, 1 mL/min, 210 nm, major isomer 29.2 min, minor isomer 26.9 min). $[\alpha]^{22}_{D}$ = +56° (c 0.6, $CHCl_3$). mp = 74 – 76 °C. Purification on silica gel (30 min time period) results in the title compound in 0% ee.

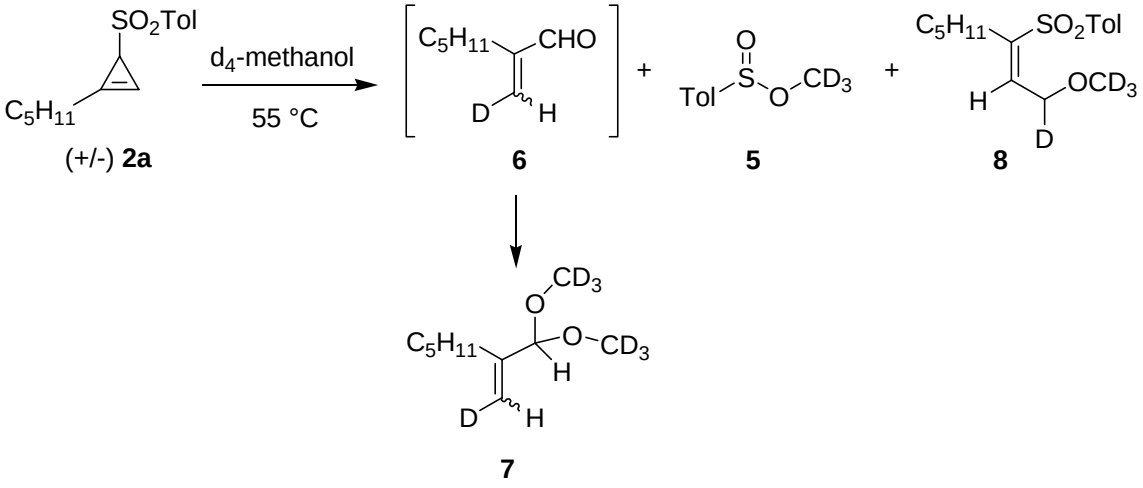
(+)- (*S*) - 1,8 -Diphenyl-11-pentyl-10-(toluene-4-sulfonyl)-12-oxa-tetracyclo-[6.3.1.0 ^{2,7}. 0 ^{9,11}]-dodeca -2, 4, 6 –triene (**3**)



To a solution of (+)-**2a** (22.0 mg, 0.083 mmol) in CH_2Cl_2 (0.5 mL) under N_2 atmosphere was added diphenyl isobenzofuran (DPIBF) (100 mg, 0.4 mmol) in one portion. The reaction was shielded from light and allowed to stir at 23 °C for 15 hours, at which time the reaction was judged complete by thin layer chromatography and the solution concentrated under reduced pressure. The DPIBF-adduct, obtained as a crude yellow

oil by flash chromatography (50% CH_2Cl_2 in hexanes), was further purified by preparative thin layer chromatography in order to obtain pure DPIBF-adduct as a white solid in 86% ee (HPLC Chiralpak IA column, 10% *i*-PrOH in hexanes, 0.8 mL/min, 210 nm, major isomer 7.5 min, minor isomer 8.1 min). 36 mg, 68% yield. Trituration of the insoluable DPIBF-adduct with hexanes and separation of the hexanes solution from the solid gave the chiral title compound (+)-**3** in 94% ee. 25 mg, 58% yield. X-ray quality crystals were obtained from an evaporating mixture of (+)-**3** in MeOH and CH_2Cl_2 at 23 °C. The x-ray crystal structure established the DPIBF-adduct as the *exo*-Diels Alder product in the *S* configuration. $[\alpha]_D^{23}$ = + 23° (c 1.03, $CHCl_3$). mp = 179 – 180 °C. IR (film, cm^{-1}): 3064, 2956, 2929, 2860, 1725, 1598, 1457, 1318, 1302, 1291, 1148, 1088, 1019, 737, 679. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.34 – 0.79 (m, 1 H); 0.71 (t, J = 7.6 Hz, 3 H); 0.88 – 0.95 (m, 1 H); 1.00 – 1.10 (m, 3 H); 1.17 – 1.22 (m, 1 H); 1.73 (ddd, J = 5.6 Hz, 12.0 Hz, 16.8 Hz, 1 H); 2.10 (ddd, J = 5.6 Hz, 12.0 Hz, 16.8 Hz, 1 H); 2.50 (s, 3 H); 2.53 (d, J = 3.2 Hz, 1 H); 3.73 (d, J = 3.2 Hz, 1 H); 7.07 – 7.10 (m, 1 H); 7.22 – 7.28 (m, 5 H); 7.31 – 7.35 (m, 3 H); 7.38 – 7.43 (m, 5 H); 7.60 (d, J = 8.0 Hz, 1 H); 7.61 (d, J = 6.0 Hz, 1 H); 7.89 (d, J = 8.0 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 100 MHz): δ 13.9, 21.6, 22.0, 24.1, 27.5, 31.6, 41.2, 50.2, 88.6, 92.8, 120.3, 121.9, 126.6, 127.0, 127.6, 128.1, 128.3, 128.7, 128.9, 129.3, 129.7, 129.8, 133.0, 134.5, 138.5, 144.4, 146.9, 149.5. HRMS (ESI^+) calcd for $C_{35}H_{34}O_3S$ $(M+H)^+$ = 535.2307, found 535.2310.

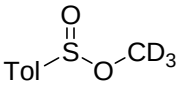
Decomposition of (+/-)-2a in d_4-methanol at 55 °C.



(+/-)-**2a** (21 mg, 0.08 mmol) was deposited to an oven and flame dried NMR tube and placed under N_2 atmosphere. d_4-Methanol (99.8% D) (0.85 mL) was injected and the tube sealed using a propane torch. The reaction was placed in an oil bath heated to 55 °C and monitored by ^{1}H and ^{13}C NMR spectroscopy. Three new compounds were observed to form over a 1.5 day period: d_3-methyl-*p*-toluene sulfinyl ester (**5**), the d_6-dimethyl acetal of 2-pentyl-1- d_1-propen-2-al (**7**), and *Z*-1-(d_3-Methoxy- d_1-methyl)-2-(sulfonyl-4-methylbenzene)-heptene (**8**) in a 1 to 1 to 3 ratio. The NMR tube was opened and the reaction mixture analyzed by GCMS. Three components were detected: the dimethyl acetal (**7**) {[M – OCD_3]$^+$ = 145}, methyl *p*-tosyl sulfinyl ester (**5**) {[M]$^+$ = 173}, and *Z* -1-(d_3-Methoxy-d_1-methyl)-2-(sulfonyl-4-methylbenzene)-heptene (**8**) {[M]$^+$ = 300}. The volatiles were removed under reduced pressure and the residue purified by preparative thin layer chromatography. The two UV active compounds were isolated and identified as d_3-methyl-*p*-toluene sulfinyl ester (**5**) and *Z*-1-(d_3-Methoxy-d_1-methyl)-2-(sulfonyl-4-methylbenzene)-heptene (**8**) (9 mg, 38% yield).

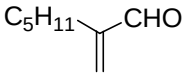
7 was identified upon comparison of the reported ^{1}H NMR values for the non-deuterated acetal[e]. Upon exposure of the NMR reaction to moisture, the d_6-dimethyl acetal (**7**) was slowly converted over a 24 hour period to 2-pentyl-1-d_1-propen-2-al (**6**), identified by ^{1}H NMR.[f]

d_3-Methyl- *p*-toluene sulfinyl ester (**5**)



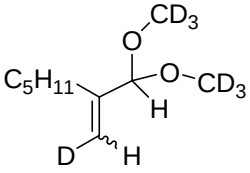
IR (film, cm^{-1}): 3041 (w), 2925 (w), 2871 (w), 2074 (C-D stretch, w), 1596 (m), 1493 (m), 1136 (s), 1082 (s), 947 (s), 812 (s), 708 (s). ^{1}H NMR ($CDCl_3$, 500MHz): δ 2.43 (s, 3 H); 7.34 (d, J = 8.5 Hz, 2 H); 7.59 (d, J = 7.5 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 125 MHz): δ 21.5, 50.2 (quin, 85 Hz), 125.4, 129.7, 141.0, 142.8. ^{2}H NMR ($CHCl_3$, 77 MHz): δ 3.45 (s, 3D). HRMS (EI^+) calcd $C_8H_7O_2SD_3$ for $(M)^+$: 173.0590, found 173.0598.

2-Pentyl propen-2-al (**6**)[d]



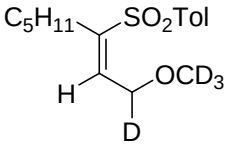
IR (film, cm^{-1}): 2958 (s), 2873 (s), 1696 (s), 1466 (m), 1266 (m), 1111(m), 941 (m), 737 (m). ^{1}H NMR ($CDCl_3$, 500MHz): δ 0.89 (t, J = 7 Hz, 3 H); 1.25 – 1.32 (m, 4 H); 1.45 (quin, J = 7.5 Hz, 2 H); 2.23 (t, J = 8 Hz, 2 H); 5.98 (s, 1 H); 6.25 (s, 1 H); 9.54 (s, 1 H). ^{13}CNMR ($CDCl_3$, 125 MHz): δ 14.0, 22.4, 27.4, 27.7, 31.4, 133.9, 150.5, 194.8.

2-Pentyl-d_1-propen-2-al d_6-dimethyl acetal (**7**)[e]



^{1}H NMR (CD_3OD, 500 MHz): 0.90 (t, J = 6.0 Hz, 3 H); 1.27 – 1.36 (m, 4 H); 1.47 (quin, J = 6.5 Hz, 2 H); 2.01 (t, J = 6.5 Hz, 2 H); 4.61 (s, 1 H); 4.99 (s, ½ H); 5.14 (s, ½ H).

Z-1-(d_3-Methoxy-d_1-methyl)-2-(sulfonyl-4-methylbenzene)-heptene (**8**)

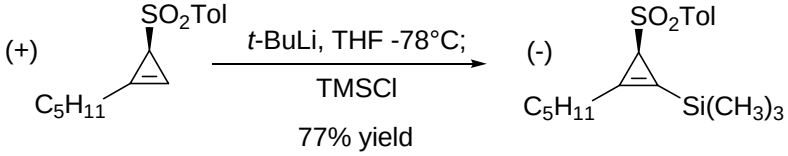


IR (film, cm^{-1}): 2956 (m), 2927 (m), 2860 (m), 2070 (C-D stretch, m), 1665 (s), 1598 (m), 1457 (m), 1314 (s), 1289 (s), 1208 (s), 1146 (s), 1109 (s), 818 (s), 719 (s), 675 (s). ^{1}H NMR ($CDCl_3$, 500MHz): δ 0.85 (t, J = 7.5 Hz, 3 H); 1.15 – 1.21 (m, 2

[d] Oku, Y. ; Ogawa, A. ; Kambe, N. ; Sonoda, N.; Murai, S. *J. Org. Chem.* **1992**, *57*, 17 – 28.
[e] Gora, J. ; Smigeilski, K. ; Kula, J. *Synthesis* **1986**, 586 – 588.

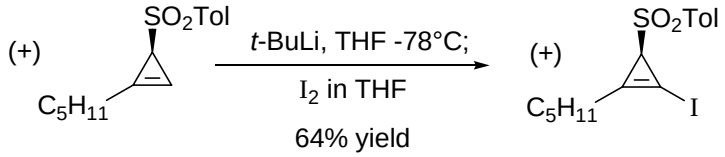
H); 1.24 – 1.31 (m, 4 H); 2.05 (t, J = 8.0 Hz, 2 H); 2.44 (s, 3 H); 3.57 (s, 1 H); 5.72 (s, 1 H); 7.33 (d, J = 7.5 Hz, 2 H); 7.72 (d, J = 8.0 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 125 MHz): δ14.0 (CH_3), 21.6 (CH_2), 22.4 (CH_2), 26.7 (CH_2), 27.0 (CH_2), 31.4 (CH_2), 58.9 (quin, J = 88 Hz, CD_3), 59.3 (t, J = 83 Hz, CHD), 106.2 (C), 128.6 (CH), 129.5 (CH), 135.7 (C), 144.4 (C), 149.9 (CH). ^{2}H NMR ($CHCl_3$, 77 MHz): δ 3.47 (s, 3 D); 3.59 (bs, 1 D). HRMS (EI^+) calcd $C_{16}H_{20}O_3SD_4$ for $(M)^+$ = 300.1697, found 300.1686.

(-)-Trimethyl-[2-pentyl-3-(toluene-4-sulfonyl)-cycloprop-1-enyl]-silane (**11**)



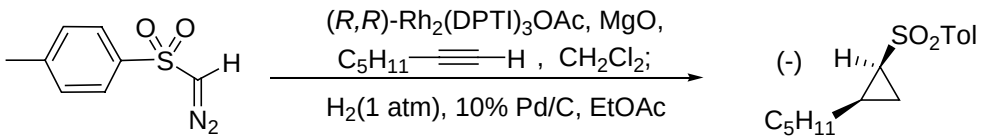
A solution of (+)-**2a** (63 mg, 0.24 mmol) (91% ee) in THF (1.0 mL) cooled to -78 °C under N_2 atmosphere was transferred by cannula to a solution of *t*-BuLi (0.29 mmol) in THF (1.5 mL) at -78 °C under N_2 atmosphere. Upon addition the solution became red. After five minutes, trimethylsilyl chloride (TMSCl) (46 μL, 0.36 mmol) was added, and the reaction was stirred for an additional 5 minutes at -78 °C, and then warmed to 0 °C for 5 minutes. The reaction mixture was quenched with brine (1 mL), diluted with Et_2O (25 mL) and washed with H_2O (25 mL) and brine (25 mL). The organic fractions were combined, dried with Na_2SO_4, decolorized with charcoal, and concentrated under reduced pressure to provide the title chiral compound **11** as a light yellow oil (62 mg, 77% yield). 91% ee by HPLC (Chiralpak IA, 2% *i*-PrOH in hexanes, 1 mL/min, 210 nm, major isomer 16.0 min, minor isomer 14.8 min). $[\alpha]_D^{20}$ = - 46° (c 0.6, $CHCl_3$). IR (film, cm^{-1}): 2958, 2931, 2860, 1808, 1598, 1459, 1312, 1287, 1140, 1086, 947, 843, 748. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.16 (s, 9 H); 0.88 (t, J = 7.0 Hz, 3 H); 1.26 – 1.31 (m, 4 H); 1.54 (quint, J = 7.0 Hz, 2 H); 2.41 (td, J = 7.0 Hz, 17.0 Hz, 1 H); 2.43 (s, 3 H); 2.51 (td, J = 7.0 Hz, 17.0 Hz, 1 H); 2.99 (s, 1 H); 7.31 (d, J = 8.0 Hz, 2 H); 7.71 (d, J = 8.0 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 125 MHz): δ -1.47, 13.9, 21.5, 22.2, 25.9, 26.4, 31.2, 43.9, 106.3, 127.6, 129.6, 129.8, 138.5, 143.4. HRMS (ESI^+) calcd $C_{18}H_{28}O_2SSi$ for $(M+NH_4)^+$ = 354.1923, found 354. 1921.

1-Pentyl-2-methyl-3-(toluene-4-sulfonyl) cyclopropene (**12)**



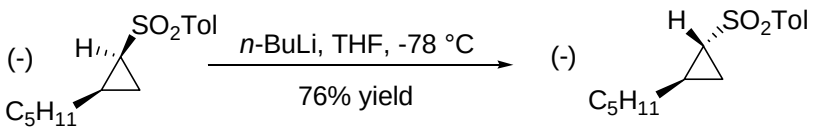
A solution of (+)-**2a** (59 mg, 0.22 mmol) (91 % ee) in THF (1 mL) cooled to -78 °C under N_2 atmosphere was transferred by cannula to a solution of *t*-BuLi (0.27 mmol) in THF (1.5 mL) at -78 °C under N_2 atmosphere. Upon addition the solution became red. After five minutes a cold solution (0 °C) of I_2 (168 mg, 0.66 mmol) in THF (2 mL) was added by cannula, and the reaction was stirred for an additional 5 minutes at -78 °C, and then warmed to 0 °C for 5 minutes. The reaction mixture was quenched with brine (1 mL), diluted with Et_2O (25 mL) and washed with H_2O (25 mL) and brine (25 mL). The organic fractions were combined, dried with Na_2SO_4, decolorized with charcoal, and concentrated under reduced pressure to provide the title chiral compound **12** as a light yellow oil (55 mg, 64% yield). 91% ee by HPLC (Chiralcel OD, 2% *i*-PrOH in hexanes, 1 mL/min, 210 nm, major isomer 20.9 min, minor isomer 27.1 min). $[\alpha]_D^{23}$ = + 9 ° (c 0.5, $CHCl_3$). IR (film, cm^{-1}): 2956, 2927, 2858, 1598, 1459, 1312, 1289, 1248, 1142, 1084, 1044, 1019, 967, 814, 746, 671. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.90 (t, J = 7.2 Hz, 3 H); 1.25 – 1.37 (m, 4 H); 1.61 – 1.66 (m, 2 H); 2.47 – 2.61 (m, 2 H); 3.30 (s, 1 H); 7.34 (d, 8.5 Hz, 2 H); 7.74 (d, 8.5 Hz, 2 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.9, 21.6, 22.2, 25.0, 25.3, 31.3, 46.8, 48.1, 128.1, 128.3, 129.8, 136.8, 144.3. HRMS (ESI^+) calcd $C_{15}H_{19}O_2SI$ for $(M+NH_4)^+$ = 408.0494**,** found 408.0491.

(-) *cis* -1-Methyl-4-(2-pentyl-cyclopropanesulfonyl)-benzene (**13**)



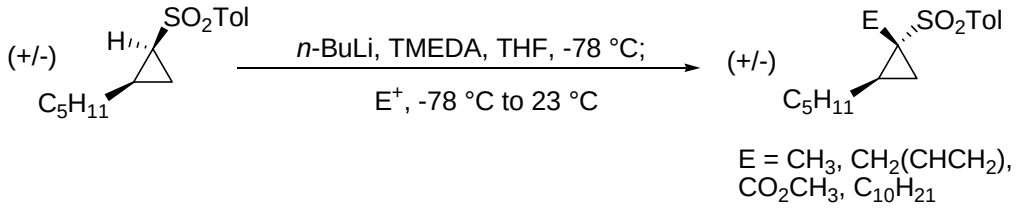
A solution of 1-heptyne (0.2 mL, 1.5 mmol, 10 eq), MgO (0.0.15 mmol, 1 eq), *R,R*-$Rh_2(DPTI)_3OAc$ (3 mg, 0.002 mmol, 1.5 mol%) with CH_2Cl_2 (0.05 mL) under N_2 atmosphere was cooled to 0 °C, and tosyl diazomethane (30 mg, 0.15 mmol, 1 eq) in CH_2Cl_2 (0.25 mL) was added over a 15 minute period. The reaction mixture was stirred an additional 5 minutes at 0 °C. The N_2 atmosphere was replaced with H_2 (1-2 atm), and a slurry of 10% Pd/C (5 mg) in EtOAc (1 mL) was added to the reaction mixture. The solution was stirred at 0 °C, warming slowly to 23 °C over 16 hrs. The reaction mixture was then filtered through Celite 545® and concentrated under reduced pressure to a crude residue. Purification by preparative thin layer chromatography provided the title compound (**13**) as a white solid. 91 % ee (HPLC Chiracel OJ, 1% *i*-PrOH in hexanes, 0.8 mL/min, 210 nm, major isomer 29.3 min, minor isomer 41.0 min). 25 mg, 56% yield. $[\alpha]_D^{21}$ = -6° (c 0.98, $CHCl_3$). mp = 54 -55 °C. IR (film, cm^{-1}): 2956, 2927, 2860, 1598, 1457, 1320, 1289, 1146, 1086, 899, 839, 715. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.88 (t, J = 7.5 Hz, 3 H); 1.21 – 1.26 (m, 2 H); 1.29 – 1.32 (m, 4 H); 1.34 – 1.44 (m, 2 H); 1.75 – 1.80 (m, 2 H); 2.39 (t, J = 8.0 Hz, 1 H); 2.40 (t, J = 8.0 Hz, 1 H); 2.44 (s, 3 H); 7.33 (d, J = 8.0 Hz, 2 H); 7.79 (d, J = 8.0 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 125 MHz): δ 12.2, 14.0, 21.6, 22.2, 22.6, 26.4, 29.6, 31.5, 38.2, 127.3, 129.7, 139.1, 144.0. HRMS (ESI^+) calcd $C_{15}H_{22}O_2S$ for $(M+H)^+$ = 267.1419, found 267.1422.

(-) *trans* -1-Methyl-4-(2-pentyl-cyclopropanesulfonyl)-benzene (**14a**)

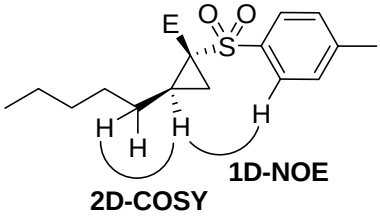


(-)-**13** (20 mg, 0.075 mmol) in THF (0.6 mL) was added to a solution of *n*-BuLi (0.05 mL, 0.11 mmol, 2.36 M in hexanes) in THF (0.4 mL) at -78 °C under N_2 atmosphere. The solution became bright yellow upon addition. The reaction was stirred at -78 °C for 40 minutes. NH_4Cl (sat) (1 mL) was added to the reaction, and the solution warmed to 23 °C. The reaction mixture was diluted with diethyl ether (20 mL) and washed with water (20 mL) and brine (20 mL), and dried with $MgSO_4$. After concentration under reduced pressure, purification by silica gel chromatography (100% CH_2Cl_2 elutant) provided the title compound (**14a**) as a colorless oil (15.1 mg, 76% yield) in 91% ee (HPLC Chiralpak IA, 0.1% *i*-PrOH / 14.9% CH_2Cl_2 / 85% hexanes, 1 mL/min, 210 nm, major isomer 31.6 min, minor isomer 29.0 min). $[\alpha]_D^{22}$ = -6.8° (c 0.75, $CHCl_3$). IR (film, cm^{-1}): 2927, 2858, 1598, 1457, 1314, 1289, 1146, 1090, 1019, 928, 801, 733. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.81 – 0.87 (m, 4 H); 1.12 – 1.25 (m, 6 H); 1.33 – 1.39 (m, 1 H); 1.48 (dt, J = 5.5 Hz, 9.5 Hz, 1 H); 1.62 – 1.69 (m, 1 H); 2.15 (dt, 4.0 Hz, 8.5 Hz, 1 H); 2.44 (s, 3H); 7.34 (d, J = 8.0 Hz, 2 H); 7.76 (d, J = 8.0 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 125 MHz): δ 13.1, 14.1, 20.6, 21.8, 22.7, 28.7, 31.4, 32.1, 39.6, 127.8, 130.0, 138.2, 144.3. HRMS (ESI^+) calcd $C_{15}H_{22}O_2S$ for $(M+H)^+$ = 267.1419, found 267.1422.

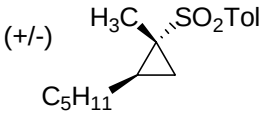
General Procedure in the α-Alkylation of (+/-)-13 to 14b – 14e.



n-BuLi (2.7 M solution in hexanes, 1.2 eq) was added to (+/-) or (-)-**13** (1 eq) and N,N,N',N'-tetramethylethylenediamine (TMEDA) (1.2 eq) in THF (0.1 M) at -78 °C under N_2 atmosphere. Upon addition of *n*BuLi, the colorless solution became bright yellow. The temperature was maintained at -78 °C for 1 hour. At that time, an excess of electrophile (10 - 20 eq) was added to the reaction mixture, and the solution stirred at -78 °C for 1 hour, and then warmed to 23 °C and stirred an additional 30 minutes. A white precipitate gradually formed. The solution was quenched upon addition of NH_4Cl (sat) (1 mL), and the reaction mixture diluted with H_2O (50 mL) and washed with CH_2Cl_2 (3 x 50 mL). The organic fractions were combined, dried with $MgSO_4$, and concentrated under reduced pressure to a crude oil. Both the desired α-alkylated product (**14b** – **14d**) and *trans* -1-methyl-4-(2-pentyl-cyclopropanesulfonyl)-benzene **14a** were isolated by preparative thin layer chromatography. The relative stereochemistry of the α-alkylated product (**14b** – **14d**) was determined by NMR spectroscopy using a combination of 1D-NOE with 2D-COSY and/or 2D-HSQC:

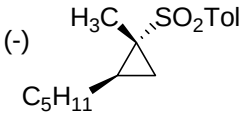


(+/-)-1-Methyl-4-(1-methyl-2-pentyl-cyclopropanesulfonyl)-benzene (**14b**)



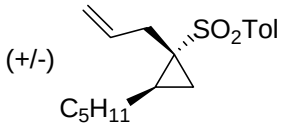
A 9 :1 mixture (by ^{1}H NMR analysis) of the title compound **14b** and *trans*-1-methyl-4-(2-pentyl-cyclopropanesulfonyl)-benzene (+/-) **14a** was obtained from the reaction of (+/-)-**13** (22.9 mg, 0.086 mmol) with *n*-BuLi (40 μL, 0.11 mmol) and TMEDA (14 μL, 0.086 mmol) in THF (0.9 mL) at -78 °C under N_2 atmosphere, with methyl iodide (54 μL, 0.86 mmol) as the electrophile. The two compounds were isolated by preparative thin layer chromatography (10% Et_2O in hexanes). **14a** was isolated as a colorless oil (1 mg). The title compound **14b** was obtained as a colorless oil (17 mg, 71 % yield). IR (film, cm^{-1}): 2956, 2929, 2860, 1598, 1457, 1382, 1312, 1301, 1287, 1194, 1140, 1084, 1044, 1019, 804, 791, 710, 677. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.47 (dd, J = 5.5 Hz, 7.0 Hz, 1 H); 0.86 (t, J = 7 Hz, 3 H); 1.25 – 1.37 (m, 14 H); 1.67 (dd, J = 5.5 Hz, 9 Hz, 1 H); 1.82 – 1.88 (m, 1H); 2.45 (s, 3 H); 7.33 (d, J = 8.5 Hz, 2 H); 7.73 (d, J = 8.0 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 125 MHz): δ 13.0, 13.9, 18.4, 21.6, 22.5, 22.9, 28.2, 29.0, 31.4, 40.9, 128.7, 129.6, 135.6, 144.0. HRMS (ESI^+) calcd $C_{16}H_{24}O_2S$ for $(M+NH_4)^+$ = 298.1841, found 298.1849.

(-)-1-Methyl-4-(1-methyl-2-pentyl-cyclopropanesulfonyl)-benzene (**14b**)



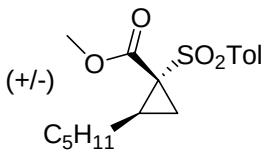
The title compound (-)-**14b** was obtained from the reaction of (-)-**13** (15.0 mg, 0.06 mmol) (91% ee) with *n*-BuLi (25 μL, 0.066 mmol) and TMEDA (10 μL, 0.066 mmol) in THF (0.6 mL) at -78 °C under N_2 atmosphere, with methyl iodide (37 μL, 0.6 mmol) as the electrophile. After preparative thin layer chromatography (10% Et_2O in hexanes), the title compound (-)-**14b** was obtained as a colorless oil (8.8 mg, 52 % yield) in 91% ee (HPLC Chiracel OJ, 2% *i*-PrOH in hexanes, 0.8 mL/min, 210 nm, major isomer 18.5 min, minor isomer 17.4 min) $[\alpha]_D^{23}$ = -8° (c 0.25, $CHCl_3$).

(+/-)-1-(1-Allyl-2-pentyl-cyclopropanesulfonyl)-4-methyl-benzene (**14c**)



A 1.6 : 1 mixture (by ^{1}H NMR analysis) of the title compound **14c** and *trans*-1-methyl-4-(2-pentyl-cyclopropanesulfonyl)-benzene (**14a**) was obtained from the reaction of (+/-)-**13** (28.7 mg, 0.11 mmol) with *n*-BuLi (44 μL, 0.13 mmol) and TMEDA (18 μL, 0.12 mmol) in THF (1.1 mL) at -78 °C under N_2 atmosphere, with allyl bromide (0.2 mL, 2.2 mmol) as the electrophile. The two compounds were isolated by preparative thin layer chromatography (20% EtOAc in hexanes). **14a** was isolated as a colorless oil (8.8 mg). The title compound **14c** was obtained as a colorless oil (19.5 mg, 58% yield). IR (film, cm^{-1}): 3078, 2956, 2927, 2858, 1640, 1598, 1457, 1312, 1287, 1173, 1140, 1086, 914, 814, 713, 688. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.58 (dd, J = 5.5 Hz, 7.5 Hz, 1 H); 0.87 (t, J = 7 Hz, 1 H); 1.26 – 1.40 (m, 8 H); 1.69 (dd, J = 5.5 Hz, 10.5 Hz, 1 H); 1.90 – 1.96 (m, 1 H); 2.19 (dd, J = 8.0 Hz, 17.0 Hz, 1 H); 2.45 (s, 3H); 2.55 (dd, J = 6.0 Hz, 17.0 Hz, 1H); 4.89 (dd, J = 1.5 Hz, 17.0 Hz, 1H); 4.93 (dd, J = 1.5 Hz, 10.0 Hz, 1 H); 5.63 – 5.71 (m, 1 H); 7.33 (d, J = 8.0 Hz, 2 H); 7.73 (d, J = 8.5 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 125 MHz): δ 14.0, 17.1, 21.6, 22.5, 24.0, 28.2, 28.9, 31.3, 31.4, 44.6, 116.9, 128.8, 129.6, 134.8, 136.1, 144.2. HRMS (ESI^+) calcd $C_{18}H_{26}O_2S$ for $(M+NH_4)^+$ = 324.1997, found 324.1992.

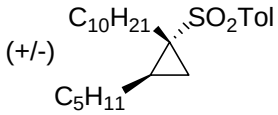
(+/-)-2-Pentyl-1-(toluene-4-sulfonyl)-cyclopropanecarboxylic acid methyl ester (**14d**)



A 4 : 1 mixture (by ^{1}H NMR analysis) of the title compound **14d** and *trans*-1-methyl-4-(2-pentyl-cyclopropanesulfonyl)-benzene (**14a**) was obtained from the reaction of (+/-)-**13** (34.6 mg, 0.13 mmol) with *n*-BuLi (58 μL, 0.16 mmol) and TMEDA (22 μL, 0.14 mmol) in THF (1.3 mL) at -78 °C under N_2 atmosphere, with methyl chloroformate (0.2 mL, 2.6 mmol) as the electrophile. The two compounds were isolated by preparative thin layer chromatography (20% EtOAc in hexanes). **14a** was isolated as

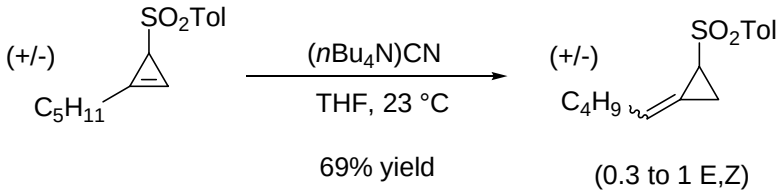
a colorless oil (4 mg). The title compound **14d** was obtained as a colorless oil (21.5 mg, 51% yield). IR (film, cm^{-1}): 2956, 2929, 2860, 1731, 1598, 1437, 1318, 1291, 1208, 1189, 1158, 1136, 1084, 889, 870, 816, 800, 758, 729, 715. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.82 (t, J = 6.8 Hz, 3 H); 1.11 – 1.53 (m, 8 H); 1.66 (dd, J = 4.8 Hz, 8.0 Hz, 1 H); 2.10 (dd, J = 4.8 Hz, 10 Hz, 1 H); 2.14 – 2.22 (m, 1 H); 2.44 (s, 3 H); 3.64 (s, 3 H); 7.32 (d, J = 8.0 Hz, 2 H); 7.80 (d, J = 8.4 Hz, 2 H). $^{13}CNMR$ ($CDCl_3$, 100 MHz): δ 13.9, 20.3, 21.6, 22.4, 27.0, 28.4, 29.9, 31.1, 50.1, 52.4, 129.0, 129.3, 137.0, 144.4, 166.0. HRMS (ESI^+) calcd $C_{17}H_{24}O_4S$ for $(M+NH_4)^+$ = 342.1739, found 342.1745.

(+/-)-1-(1-Decyl-2-pentyl-cyclopropanesulfonyl)-4-methyl-benzene (**14e**)



The title compound **14e** was obtained from the reaction of (+/-)-**13** (192 mg, 0.72 mmol) with *n*-BuLi (0.32 ml, 0.86 mmol) and TMEDA (0.13 Ml, 0.86 mmol) in THF (7.2 mL) at -78 °C under N_2 atmosphere, with decyl iodide (2.3 mL, 10.8 mmol) as the electrophile. After separation from excess decyl iodide by column chromatography (100% hexanes elutant to separate from decyl iodide, then 100% CH_2Cl_2 to collect the crude cyclopropane) **14e** was purified by preparative thin layer chromatography (20% EtOAc in hexanes) as a colorless oil (252 mg, 86% yield). IR (film, cm^{-1}): 2956, 2923, 2854, 1600, 1495, 1466, 1380, 1312, 1289, 1140, 1086, 1046, 1019, 814, 712, 681. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.53 (dd, J = 5.6 Hz, 7 Hz, 1 H); 0.86 (t, J = 6 Hz, 3 H); 0.88 (t, J = 6.4 Hz, 3 H); 1.19 – 1.39 (m, 24 H); 1.59 – 1.68 (m, 3 H); 1.84 – 1.89 (m, 1 H); 2.44 (s, 3 H); 7.33 (d, J = 8.0 Hz, 2 H); 7.72 (d, J = 8.4 Hz, 2 H).$^{13}CNMR$ ($CDCl_3$, 100 MHz): δ 13.9, 14.1, 16.9, 21.6, 22.5, 22.7, 23.9, 26.9, 27.3, 28.2, 28.9, 29.2, 29.3, 29.4, 29.5, 29.8, 31.5, 31.9, 45.2, 128.6, 129.5, 136.4, 144.0. HRMS (ESI^+) calcd $C_{25}H_{42}O_2S$ for $(M+NH_4)^+$ = 424.3249, found 424.3289.

(+/-)-1-Methyl-4-(2-pentylidene-cyclopropanesulfonyl)-benzene (**15**)



A solution of (nBu$_4$N)CN (523 mg, 2.1 mmol) in THF (7 mL) was added to a solution of (+/-)-**2a** (544 mg, 2.1 mmol) in THF (5 mL) at 23 °C under N_2 atmosphere. Upon addition, the colorless solution became bright orange and gradually darkened to a brown color. The reaction was monitored by TLC. After 3 hours, the solution was flushed through a short silica column and concentrated to a brown residue. Purification by silica gel chromatography (30% Et_2O in hexanes) provided slightly crude material as a yellow oil (437 mg). Re-purification by silica gel chromatography (50% CH_2Cl_2 in hexanes) provided the title compound **15**, a light yellow oil (373 mg, 69% yield), as a 0.3 to 1 E,Z mixture (by ^{1}H NMR analysis). The enantiomers of the major isomer were separated by preparative HPLC (Chiracel OJ, 2% *i*-PrOH in hexanes, 5 mL/min, 254 nm, 80 psi, major (-) isomer 50.4 min, major (+) isomer 62.1 min, (+/-) mixture of minor isomers 67.6 min).

(-)-Enantiomer of the major isomer

$[\alpha]_D^{22}$ = - 40° (c 1.31, $CHCl_3$). IR (film, cm^{-1}): 2958, 2929, 2873, 1598, 1304, 1316, 1291, 1148, 1088, 816, 718, 694. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.90 (t, J = 7.5 Hz, 3 H); 1.31 (sext, J = 7.5 Hz, 2 H); 1.43 (quin, J = 7.0 Hz, 2 H); 1.70 (ddt, J = 1.5 Hz, 2.5 Hz, 7.5 Hz, 1 H); 1.99 – 2.03 (m, 1 H); 2.22 (dd, J = 6 Hz, 10 Hz, 2 H); 2.45 (s, 3 H), 3.01 – 3.03 (m, 1H); 5.88 – 5.92 (m, 1 H); 7.34 (d, J = 8.0 Hz, 2 H); 7.76 (d, J = 8.0 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 125 MHz): δ 9.56, 13.8, 21.6, 22.2, 30.6, 31.1, 35.7, 115.0, 124.3, 127.8, 129.7, 137.3, 144.2. HRMS (ESI$^+$) calcd $C_{15}H_{20}O_2S$ for $(M+NH_4)^+$ =282.1528, found 282.1523.

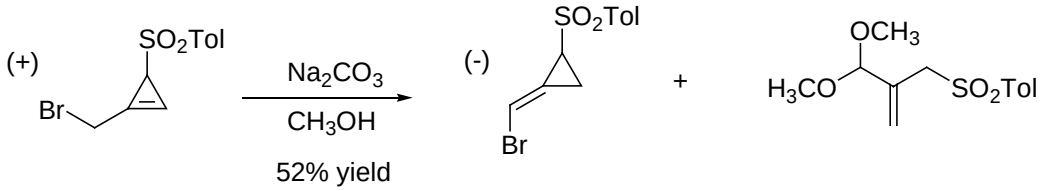
(+)-Enantiomer of the major isomer

$[\alpha]_D^{22}$ = + 41.2° (c 0.66, $CHCl_3$)

(+/-)-Minor isomer

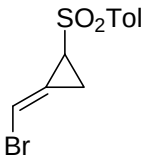
IR (film, cm^{-1}): 2958, 2927, 2858, 1598, 1457,1316, 1304, 1291, 1146, 1088, 816, 718, 693. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.89 (t, J = 7.5 Hz, 3 H); 1.21 – 1.3 (m, 2 H); 1.31 – 1.38 (m, 2H); 1.68 (ddt, J = 2 Hz, 4 Hz, 7 Hz, 1H); 1.93 – 1.97 (m, 1 H); 2.01 (sext, J = 7 Hz, 2 H); 2.45 (s, 3 H); 3.09 – 3.11 (m, 1 H); 6.01
(ddt, J = 2 Hz, 4 Hz, 7.5 Hz, 1 H); 7.34 (d, J = 8.0 Hz, 2 H); 7.79 (d, J = 8.0 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 125 MHz): δ 10.5, 14.1, 22.3, 22.7, 31.2, 31.8, 36.3, 114.6, 125.3, 127.8, 129.8, 137.7, 144.3.

Synthetic transformations of (+/-)-2b to 17 and 18a – 18d.



(2:1 ratio of **17** to acetal by ^{1}H NMR analysis)

(-) 1-Bromomethylene-2-(toluene-4-sulfonyl)-cyclopropane (**17**)



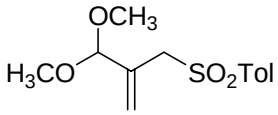
A solution of (+)-**2b** (19.4 mg, 0.068 mmol) (91% ee) and oven dried Na_2CO_3 (7.2 mg, 0.068 mmol) in methanol (1.4 mL) was stirred at 23 °C under N_2 atmosphere for 23 hours. The solution was diluted with EtOAc (25 mL), washed with water (15 mL), brine (15 mL), and the organic fraction was dried with Na_2SO_4 and concentrated to a crude oil. The residue consisted of a 1 to 0.5 mixture of the title compound **17** (17:1 ds) to 1-(2-dimethoxymethyl-prop-2-ene-1-sulfonyl)-4-methyl-benzene as judged by ^{1}H NMR analysis. The title compound (**17**), isolated by preparative thin layer

chromatography, was obtained as a colorless oil (> 20:1 ds) (10 mg, 52% yield). 89% ee (HPLC Chiracel OD, 2% *i*-PrOH in hexanes, 1 mL/min, 210 nm, major isomer 26.1 min, minor isomer 23.8 min). $[\alpha]_D^{22}$ = -38° (c 0.33, $CHCl_3$). mp = 99 – 100 °C. IR (film, cm^{-1}): 3031, 2958, 2923, 2852, 1742, 1598, 1129, 1086, 1036, 814, 725, 685. ^{1}H NMR ($CDCl_3$, 400 MHz) [major isomer]: 1.82 (ddd, J = 2.8 Hz, 8.4 Hz, 10.2 Hz, 1 H); 2.12 (ddd, J = 2.8 Hz, 4.8 Hz, 10.2 Hz, 1 H); 2.46 (s, 3 H); 3.27 (ddd, J = 2.8 Hz, 4.8 Hz, 8.4 Hz, 1 H); 6.56 – 6.58 (m, 1H); 7.36 (d, J = 8.0 Hz, 2 H); 7.76 (d, J = 8.4 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 100 MHz) [major isomer]: 12.4, 21.6, 40.8, 100.9, 121.8, 127.9, 130.0, 136.4, 145.0. HRMS (ESI^+) calcd $C_{11}H_{11}O_2SBr$ for $(M+NH_4)^+$ = 304.00007, found 304.0000.

NOTE:

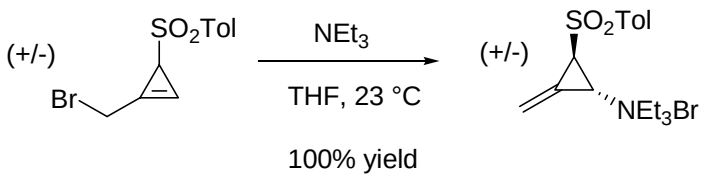
- The structure of **17** was determined by X-ray crystallographic analysis of a sample of (+/-)-**17** (mp = 99 – 100 °C, prepared as above from (+/-)-**2b**). X-ray quality crystals were obtained from an evaporating CH_2Cl_2 solution of (+/-)-**17** at – 22 °C.
- When the above reaction was conducted with (+/-)-**2b** with Cs_2CO_3 (1 equiv) in *i*-PrOH at 23 °C for 24 hr, (+/-)-**17** was isolated in 73% yield.

<u>1-(2-Dimethoxymethyl-prop-2-ene-1-sulfonyl)-4-methyl-benzene</u>



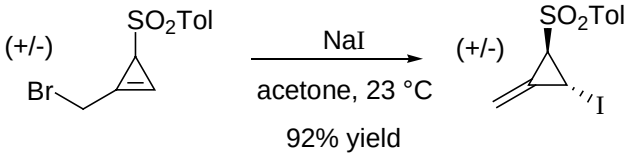
IR (film, cm^{-1}): 2956, 2931, 2833, 1598, 1449, 1318, 1291, 1152, 1129, 1109, 1086, 1054, 712. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.45 (s, 3 H); 3.24 (d, J = 1.2 Hz, 6 H); 3.85 (s, 2 H); 4.78 (s, 1 H); 5.25 (s, 1 H); 5.55 (s, 1 H); 7.34 (d, J = 7.6 Hz, 2 H); 7.75 (d, J = 7.6 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 100 MHz): δ 21.6, 53.3, 58.4, 102.3, 122.6, 128.6, 129.6, 133.3, 135.7, 144.7. HRMS (ESI^+) calcd $C_{13}H_{18}O_4S$ for $(M + NH_4)^+$ = 288.1270, found 288.1279.

(+/-)-Triethyl-[2-methylene-3-(toluene-4-sulfonyl)-cyclopropyl]-amine bromide (**18a**)



NEt_3 (0.013 mL, 0.096 mmol) was added to a solution of (+/-)-**2b** (23 mg, 0.08 mmol) in THF (0.9 mL) at 23 °C under N_2 atmosphere. A white precipitate gradually formed over 2.5 hrs. Upon complete consumption of starting material as judged by thin layer chromatography the volatiles were removed under reduced pressure to provide the title compound **18a** as a light pink oil (31 mg, 100% yield). IR (film, cm^{-1}): 3421; 2983, 2873, 2194, 2082, 1661, 1596, 1451, 1333, 1293, 1150, 1086, 922, 816, 722, 683. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.40 (t, J = 7.0 Hz, 9 H); 2.43 (s, 3 H); 3.44 (q, J = 7.0 Hz, 1 H); 3.46 (q, J = 7.0 Hz, 1 H); 3.48 (q, J = 7.0 Hz, 1 H); 3.86 (q, J = 7.0 Hz, 1 H); 3.88 (q, J = 7.0 Hz, 1 H); 3.90 (q, J = 7.0 Hz, 1 H); 4.05 (s, 1 H); 5.78 – 5.79 (m, 1 H); 5.83 – 5.84 (m, 1 H); 6.00 (s, 1 H); 7.38 (d, J = 8.0 Hz, 2 H); 7.96 (d, J = 8.0 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 100 MHz): δ 8.1, 21.7, 38.7, 46.3, 55.1, 116.2, 119.7, 128.4, 130.2, 135.1, 145.7. HRMS (ESI^+) calcd $C_{17}H_{26}NO_2SBr$ for $(M - Br)^+$ = 308.1684, found 308.1684.

(+/-)-1-Iodo-2-methylene-3-(toluene-4-sulfonyl)cyclopropane (**18b**)



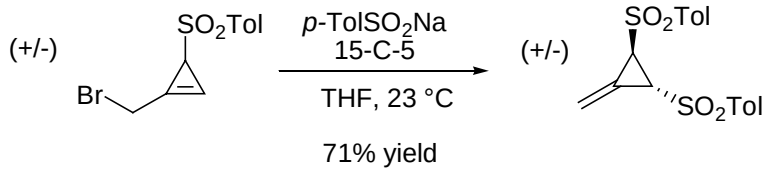
NaI (11.3 mg, 0.075 mmol) was added to a solution of (+/-)-**2b** (20.5 mg, 0.07 mmol) in acetone (1 mL) at 23 °C under N_2 atmosphere, and the heterogeneous solution vigorously stirred for 30 minutes. The solution was diluted with EtOAc (50 mL) and

washed with water (2 x 50 mL) and brine (50 mL). The organic fraction was dried with Na_2SO_4 and concentrated under reduced pressure to a light yellow oil. The title compound **18b** was obtained as a colorless oil (21 mg, 92% yield) after purification by preparative thin layer chromatography (20% EtOAc in hexanes). IR (film, cm^{-1}): 3018, 2958, 2923, 2854, 1598, 1320, 1293, 1150, 1084, 1019, 910, 827, 762, 712, 669. ^1H NMR ($CDCl_3$, 400 MHz): δ 2.47 (s, 3 H); 3.12 (dd, J = 2.4 Hz, 5.0 Hz, 1 H); 3.98 (dd, J = 2.4 Hz, 5.0 Hz, 1 H); 5.76 (m, 1 H); 5.94 (m, 1 H); 7.37 (d, J = 8.0 Hz, 2 H); 7.75 (d, J = 8.4 Hz, 2 H). ^{13}CNMR ($CDCl_3$, 100 MHz): δ 21.7, 45.2, 45.3, 111.9, 126.9, 127.8, 130.1, 136.1, 145.1. HRMS (ESI^+) calcd $C_{11}H_{11}IO_2S$ for $(M+NH_4)^+$ = 351.9868, found 351.9869.

(+)-1-Iodo-2-methylene-3-(toluene-4-sulfonyl)cyclopropane (**18b**)

NaI (5 mg, 0.033 mmol) was added to a solution of (+)-**2b** (9.1 mg, 0.032 mmol) (93% ee) in acetone (0.5 mL) at 23 °C under N_2 atmosphere, and the heterogeneous solution vigorously stirred for 20 minutes. The solution was diluted with EtOAc (50 mL) and washed with water (2 x 50 mL) and brine (50 mL). The organic fraction was dried with Na_2SO_4 and concentrated under reduced pressure to a light yellow oil. The title chiral compound (+)-**18b** was obtained as a colorless oil (6.6 mg, 62% yield) after purification by preparative thin layer chromatography (20% EtOAc in hexanes). 92% ee (HPLC, Chiracel OD, 2% *i*-PrOH in hexanes, 1 mL/min, 210 nm, major isomer 14.9 min, minor isomer 17.5 min). $[\alpha]_D^{22}$ = +182° (c 0.3, $CHCl_3$).

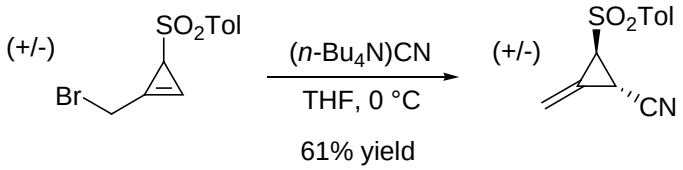
(+/-) - *trans* - 2, 3 - (toluene-4-sulfonyl) methylene cyclopropane (**18c**)



p-Toluene sulfinic acid, sodium salt (47 mg, 0.26 mmol) and 15-Crown-5 (18 μL, 0.09 mmol) were added to a solution of (+/-)-**2b** (51 mg, 0.18 mmol) in acetonitrile (2 mL) at

23 °C under N_2 atmosphere. After 20 hours, the reaction mixture was filtered through Celite 545®, and the volatiles were removed under reduced pressure to obtain a crude residue. The title compound **18c** was obtained as a white solid (46 mg, 71% yield) after purification by preparative thin layer chromatography (50% CH_2Cl_2 in hexanes). X-ray quality crystals were obtained from an evaporating mixture of **18c** in MeOH and EtOAc at 23 °C. mp = 168 – 169 °C. IR (film, cm^{-1}): 3006, 1766, 1596, 1320, 1295, 1185, 1146, 1081, 916, 816, 756, 708, 685. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.46 (s, 6 H); 3.77 (dd, J = 2.4 Hz, 5.8 Hz, 1 Hz); 5.88 (dd, J = 2.4 Hz, 5.8 Hz, 1 Hz). ^{13}CNMR ($CDCl_3$, 100 MHz): δ 21.7, 41.6, 113.0, 119.0, 127.9, 130.1, 135.8, 145.3. HRMS (ESI^+) calcd $C_{18}H_{18}O_4S_2$ for $(M+NH_4)^+$ = 380.0990, found 380.0992.

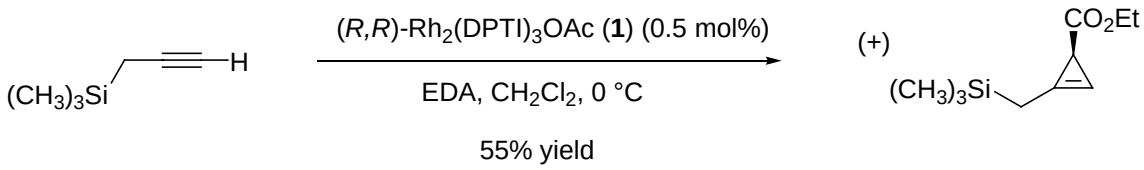
(+/-)-2-Methylene-3-(toluene-4-sulfonyl)-cyclopropanecarbonitrile (**18d**)



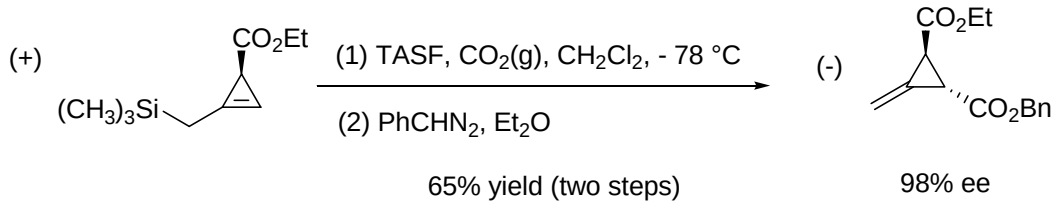
(+/-)-**2b** (54.6 mg, 0.19 mmol) in THF (1.5 mL) was added to a solution of $(nBu_4N)CN$ (59 mg, 0.23 mmol) in THF (1.5 mL) at 0 °C under N_2 atmosphere. Upon addition the colorless $(nBu_4N)CN$ solution became dark orange. After 5 minutes the solution was flushed through a SiO_2 pipet plug and concentrated to a brown residue. Upon purification by silica gel chromatography (100% CH_2Cl_2), the title compound (**18d**) was obtained as a white solid (27 mg, 61% yield). X-ray quality crystals were obtained from an evaporating mixture of **18d** in *i*-PrOH, hexanes and CH_2Cl_2 at 23 °C. mp = 129 – 130 °C. IR (film, cm^{-1}): 3014, 2250, 1598, 1328, 1291, 1148, 1084, 945, 891, 814, 706. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.49 (s, 3 H); 2.91 (dd, J = 3.0 Hz, 6.0 Hz, 1 H); 3.61 (dd, J = 3.0 Hz, 6.0 Hz, 1 H); 5.85 (dd, J = 2.0 Hz, 5.0 Hz, 1 H); 6.03 (dd, J = 2.0 Hz, 5.0 Hz, 1 H); 7.42 (d, J = 8.0 Hz, 2 H); 7.77 (d, J = 8.5 Hz, 2H). ^{13}CNMR ($CDCl_3$, 125 MHz): δ 7.74, 21.7, 41.4, 112.7, 115.4, 119.8, 128.1, 130.4, 135.3, 146.0.

Synthesis of a mixed (*S,S*)-Feist's Ester (20 – 23)

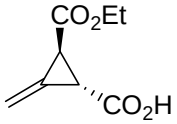
(+)-(*S*)-Ethyl 2-((trimethylsilyl)methyl)cycloprop-2-enecarboxylate (**20**)



Propargyl trimethylsilane (0.7 mL, 4.75 mmol) was added to a solution of (*R,R*)-$Rh_2(DPTI)_3OAc$ (6 mg, 0.5 mol%) in CH_2Cl_2 (40 mL) at 0 °C. A solution of ethyl diazoacetate (EDA) (0.1 mL, 0.95 mmol) in CH_2Cl_2 (10 mL) was slowly added by syringe pump to the cooled reaction mixture over a 6 hour period. After complete addition the reaction mixture was stirred an additional 30 minutes at 0 °C. The volatiles were removed under reduced pressure in order to obtain the desired product as a crude tan oil (170 mg). The residue was purified by silica gel chromatography, *using a minimal amount of silica gel* (≈ 1.5 - 2 inch height x 0.5 inch diameter, pretreated with 1% NEt_3, 100% hexanes elutant ramping to 5% Et_2O/hexanes eluant) in order to obtain the chiral title compound (+)-**20** as a colorless oil (103 mg, 55% yield). Treatment of (+)-**20** with $LiAlH_4$ in Et_2O provided the chiral (+)-**23** in 98% ee. $[\alpha]^{24}_D$ = +109°(c 0.845, $CHCl_3$). IR (film, cm^{-1}): 2981, 2958, 2902, 1721, 1368, 1337, 1250, 1177, 1030, 847, 735, 700. ^1H NMR ($CDCl_3$, 400MHz): δ 0.07 (s, 9 H); 1.25 (t, J = 7.2 Hz, 3H); 1.94 (ddd, J = 0.8 Hz, 2.8 Hz, 14.1 Hz, 2 H); 2.08 (d, 2 Hz, 1 H); 4.12 (q, 7.2 Hz, 2 H), 6.19 (d, 0.8 Hz, 1 H). ^{13}CNMR ($CDCl_3$, 100 MHz): δ -1.54, 14.4, 15.3, 20.7, 60.1, 91.6, 113.5, 176.9. HRMS (ESI^+) calcd $C_{10}H_{18}O_2Si$ for $(M + H)^+$ = 199.1154, found 199.1162.



(*1S,2S*)-2-(ethoxycarbonyl)-3-methylenecyclopropanecarboxylic acid (**21**)

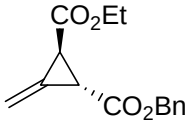


(+)-**20** (61 mg, 0.31 mmol) in CH_2Cl_2 (1.5 mL) was added over a 1 minute period to a solution of TASF (285 mg, 1.0 mmol) in CH_2Cl_2 (1.5 mL) at -78 °C under positive CO_2 (g) pressure (balloon, 1-2 atm) (see **NOTE** below). The bath temperature was maintained at -78 °C throughout the 8 hour reaction period. After 3 hrs, the solution was sparged with CO_2 (g) for 1 minute and the reaction again placed under positive CO_2(g) pressure (balloon, 1 – 2 atm). After a total of 8 hours, the reaction was carefully quenched at -78 °C by the slow addition of EtOAc (3 mL) (*careful – pressure buildup*), followed by the slow addition of a 1 M HCl solution (1.5 mL). The reaction mixture was warmed to *ca* 0 °C, transferred cold to a separatory funnel and thoroughly extracted with EtOAc (4 x 10 mL). The organic fractions were combined and dried with Na_2SO_4. The volatiles were concentrated under reduced pressure in order to obtain the title compound (**21**) as a crude oil (59 mg), 10:1 *trans* to *cis* diastereomeric mixture as judged by ^{1}H NMR analysis. Characterization of the *trans* isomer: IR (film, cm^{-1}): 3494, 2985, 2923, 2854, 1702, 1447, 1372, 1301, 1177, 1098, 1046, 1019, 960, 906, 857. ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.27 (t, J = 7.2 Hz, 3 H); 2.85 – 2.87 (m, 1 H); 2.90 – 2.93 (m, 1 H); 4.17 (q, J = 7.2 Hz, 2 H); 5.70 – 5.71 (m, 2 H). ^{13}CNMR ($CDCl_3$, 100 MHz): δ 14.1, 25.3, 26.3, 61.6, 106.9, 128.6, 168.9, 175.2. HRMS (ESI^-) calcd $C_8H_{10}O_4$for $(M - H)^-$ = 169.0501, found 169.0504.

NOTE:

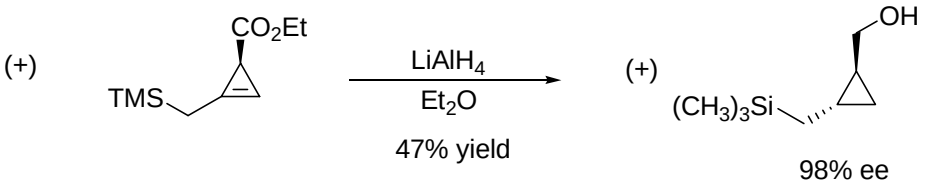
A glove bag under N_2 atmosphere was used in the storage and transfer of tris(dimethylamino)sulfonium difluorotrimethyl silicate (TASF) to a flame dried round bottomed flask. CH_2Cl_2 was sparged with CO_2(g) at 0 °C prior to use.

(-)-(*1S,2S*)-1-benzyl 2-ethyl 3-methylenecyclopropane-1,2-dicarboxylate (**22**)



A 0.016 M solution of phenyl diazomethane in benzene (15 mL, 0.24 mmol) was added to a solution of **21** (59 mg, 10:1 ds) in Et_2O (1 mL) at 23 °C and stirred for 10 minutes. At that time, all of the starting material was consumed as observed by thin layer chromatography (TLC). The reaction solution can be concentrated to *ca* 10 mL, frozen at -78 °C, and stored in a -78 °C freezer overnight. Alternatively, the reaction solution can immediately be concentrated under reduced pressure to an orange oily residue and purified by Preparative TLC (5% EtOAc in hexanes). The title compound (**22**) was obtained as a colorless oil (53 mg, 65% yield for two steps). The enantiomeric excess was determined to be 98% ee by chiral HPLC [(R,R)-Whelk-01, 1% *i*-PrOH in hexanes, 1.0 mL/min, 254 nm, 11.4 min (major), 13.7 min (minor)]. $[\alpha]^{24}_D$ = -96°(c 2.53, $CHCl_3$). IR (film, cm^{-1}): 2960, 2923, 2854, 1725, 1457, 1370, 1331, 1299, 1262, 1156, 1102, 1046, 1021, 909, 861, 749, 737, 699. ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.26 (t, J = 7.2 Hz, 3 H); 2.88 – 2.94 (m, 2 H); 4.16 (q, J = 7.2 Hz, 2 H); 5.15 (s, 2 H); 5.68 (s, 1 H); 7.32 – 7.40 (m, 5 H). ^{13}CNMR ($CDCl_3$, 100 MHz): δ 14.1, 25.7, 25.9, 106.6, 128.2, 128.4, 128.6, 128.9, 135.4, 169.15, 169.17. HRMS (ESI^+) calcd $C_{15}H_{16}O_4$for $(M + NH_4)^+$ = 278.1392, found 278.1403.

trans-(*S,S*)-(+)-2-trimethylsilylmethyl cyclopropyl methanol (**23**)

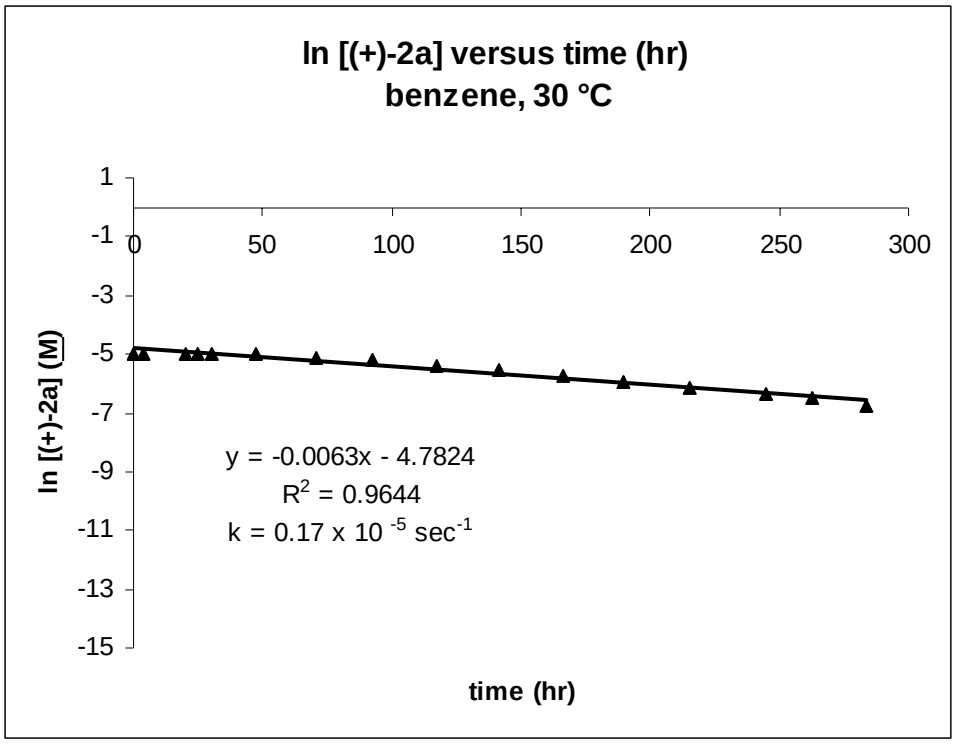


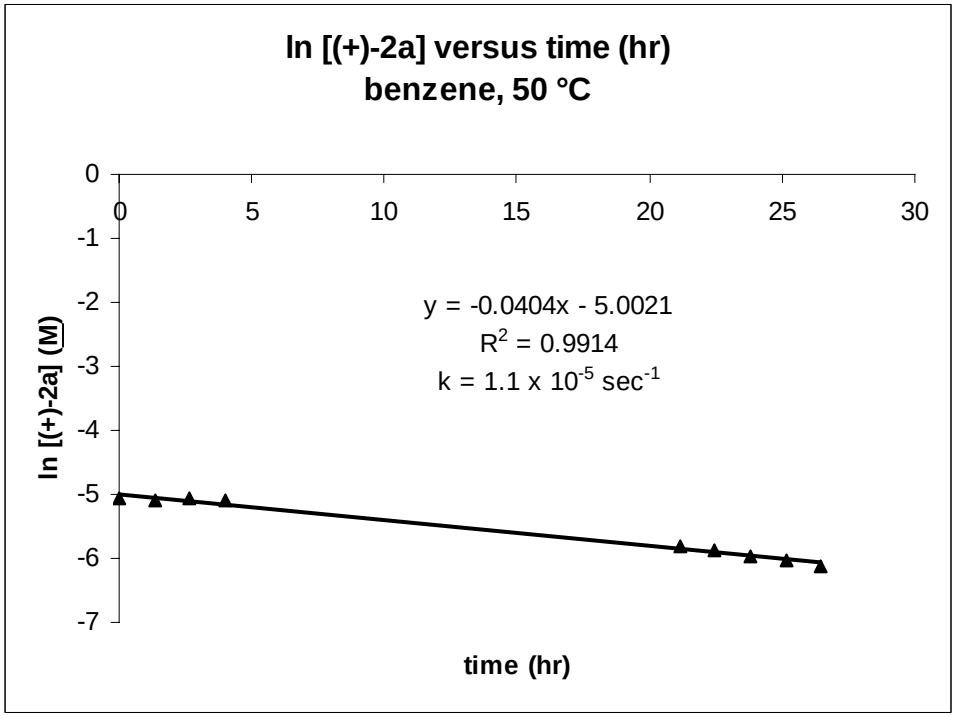
$LiAlH_4$ (8 mg, 0.21 mmol) was added in one portion to a solution of (+)-**20** (6.8 mg, 0.03 mmol) in Et_2O (1 mL), and the solution stirred at 23 °C for 30 minutes. The reaction was quenched by the addition EtOAc (0.1 mL), followed by H_2O (1 mL). The aqueous layer was extracted with Et_2O (3 x 5 mL) and the organic fractions were combined and dried

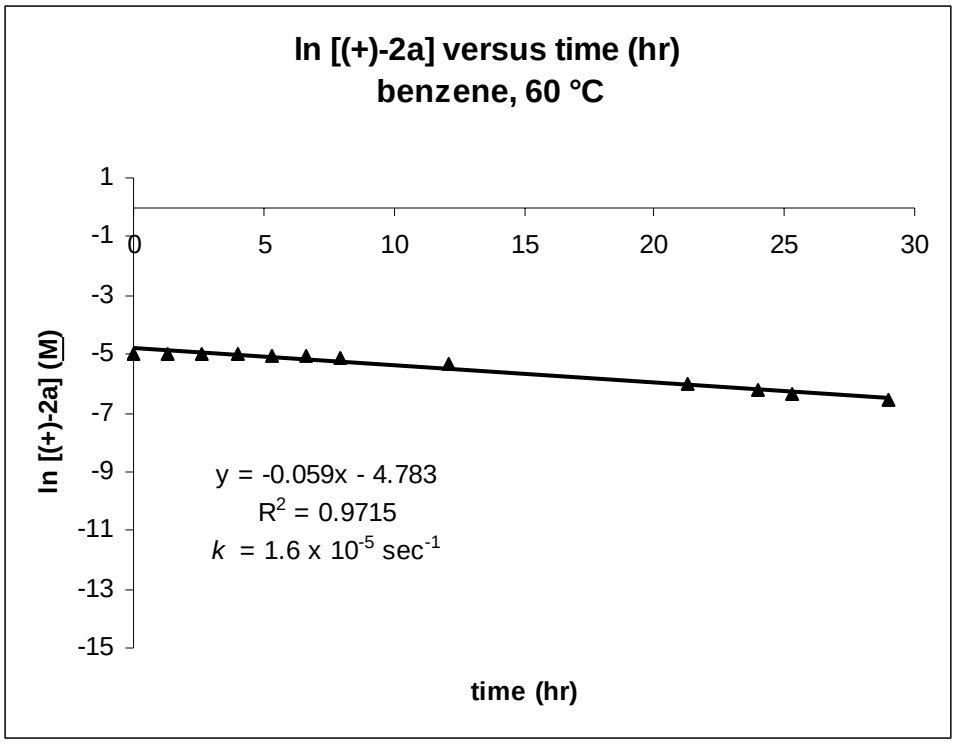
with $MgSO_4$. After filtration, the ethereal solution was passed through a silica gel pipet plug. The Et_2O solvent was removed by careful evaporation using a gentle stream of N_2 (g). The title compound (**23**) was obtained as a volatile colorless oil (2.2 mg, 47% yield). The enantiomeric excess was determined to be 98% ee by chiral GC [Chiraldex γ-TA, 45 °C isothermal, 0.8 mL/min, 3.44 min (major), 4.07 min (minor)]. $[\alpha]^{25}_D$ = +35°(c 0.11, $CHCl_3$). IR (film, cm^{-1}): 3340, 2954, 2923, 2856, 1248, 1050, 1030, 1011, 837, 693. ^{1}H NMR ($CDCl_3$, 400MHz): δ 0.02 (s, 9 H), 0.23 – 0.27 (m, 1H); 0.37 – 0.42 (m, 1 H); 0.48 – 0.60 (m, 3 H); 0.75 – 0.83 (m, 1 H); 3.35 (dd, J = 7.2 Hz, 11.2 Hz, 1 H); 3.54 (dd, J = 7.2 Hz, 11.2 Hz, 1 H). ^{13}CNMR ($CDCl_3$, 100 MHz): δ -1.44, 11.8, 12.4, 21.3, 22.9, 67.3. LRMS (GCMS) calcd $C_8H_{18}OSi$ for $(M)^+$ = 158, found 158.

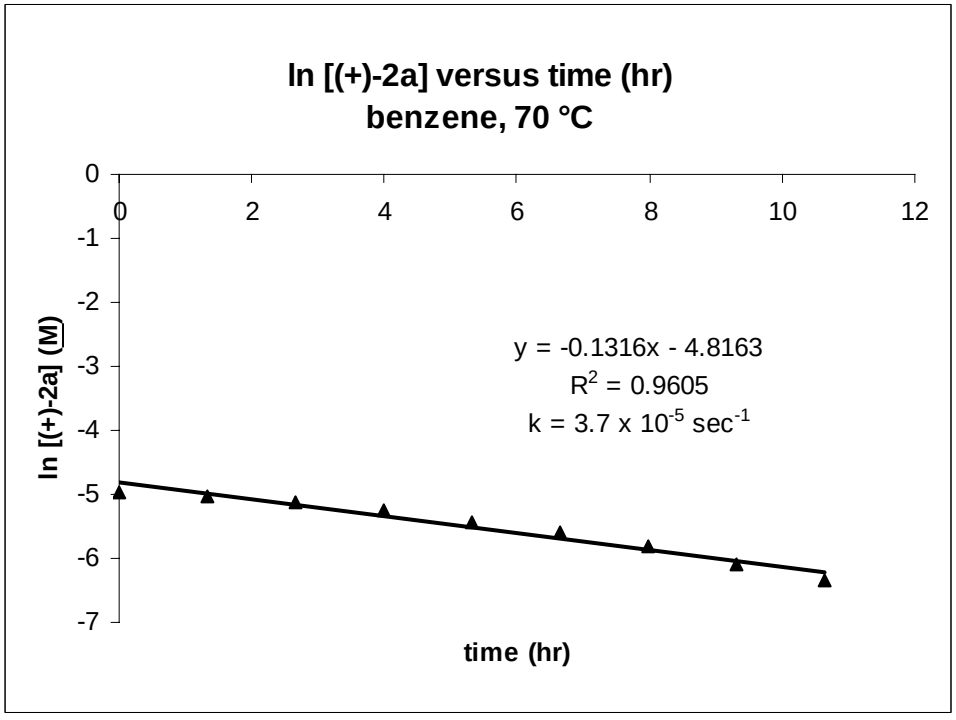
Racemization of (+)- 2a in Benzene

Stock solutions (7.5 - 7.6 mM) of (+)-**2a** were prepared in freshly distilled benzene and stored on ice. Two Pyrex ® test tubes (10 mL capacity) with 14/20 glass joints, fitted with 14/20 jointed glass adapters (one way valve), were carefully flame dried and flushed with N_2. To each of these tubes the stock solution was divided equally, with the volume of the aliquot added not exceeding 4 mL. The two test tube experiments were staggered in time such that one experiment was started 40 min ahead of the other. Each experiment was placed in a preheated oil bath (maintained at ± 1 °C) at either 30 °C, 50 °C, 60 °C or 70 °C for a 10 minute equilibration time period prior to taking the first aliquot. The rate of racemization was monitored regularly by chiral HPLC (Chiracel OD, 2% *i*-PrOH in hexanes, 0.8 mL/min, 210 nm, major enantiomer 28.8 min, minor enantiomer 26.4 min) over two half-lives, with a minimum collection of 10 data points for each experiment. At the designated collection time a 15 μL aliquot was emoved from the test tube by syringe, under positive N_2 pressure, and the solution injected to a small 1-dram vial. The volatiles were removed quickly under N_2 stream and the resulting residue was dissolved in 50 μL hexanes. 10 μl of this solution was injected to the chiral HPLC for analysis. The data taken from the two experiments were averaged and plotted as the natural log of the concentration of the major enantiomer (+)-**2a** (M) versus time (hr). The slope of the line obtained from this plot is the rate constant *k* (hr^{-1}).

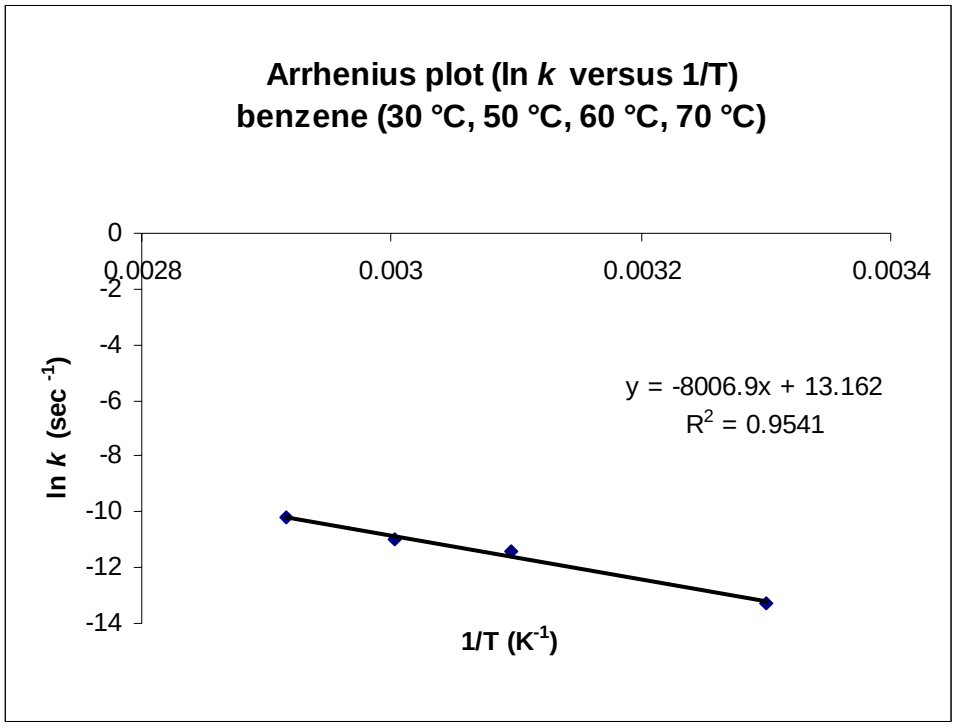

ln [(+)-2a] versus time (hr)
benzene, 30 °C
1
-1
-3
-5
-7
-9
-11
-13
-15
0
50
100
150
200
250
300
ln [(+)-2a] (M)
y = -0.0063x - 4.7824
R2 = 0.9644
k = 0.17 x 10 -5 sec-1
time (hr)


ln [(+)-2a] versus time (hr)
benzene, 50 °C
0
-1
-2
-3
-4
-5
-6
-7
0
5
10
15
20
25
30
ln [(+)-2a] (M)
y = -0.0404x - 5.0021
R2 = 0.9914
k = 1.1 x 10-5 sec-1
time (hr)


ln [(+)-2a] versus time (hr)
benzene, 60 °C
1
-1
-3
-5
-7
-9
-11
-13
-15
0
5
10
15
20
25
30
ln [(+)-2a] (M)
y = -0.059x - 4.783
R2 = 0.9715
k = 1.6 x 10-5 sec-1
time (hr)


ln [(+)-2a] versus time (hr)
benzene, 70 °C
0
-1
-2
-3
-4
-5
-6
-7
0
2
4
6
8
10
12
ln [(+)-2a] (M)
y = -0.1316x - 4.8163
R2 = 0.9605
k = 3.7 x 10-5 sec-1
time (hr)

Eyring and Arrenhius plots were derived from the rate constant *k* (sec^{-1}) at each temperature (Kelvin). From the Arrhenius plot, the equation of the line corresponds to the equation $\ln k = -(E_a/R)(1/T) + \ln A$ (Arrhenius equation). $\Delta H^{‡}$ can be calculated from E_a and an intermediate value of T (323 K) from the experimental range from the equation $\Delta H^{‡} = E_a - RT$. Entropy ($\Delta S^{‡}$) can also be calculated from E_a and an intermediate value of T (323 K) from the equation $\Delta S^{‡} = R \ln A - R \ln[(kT/h) - R]$.

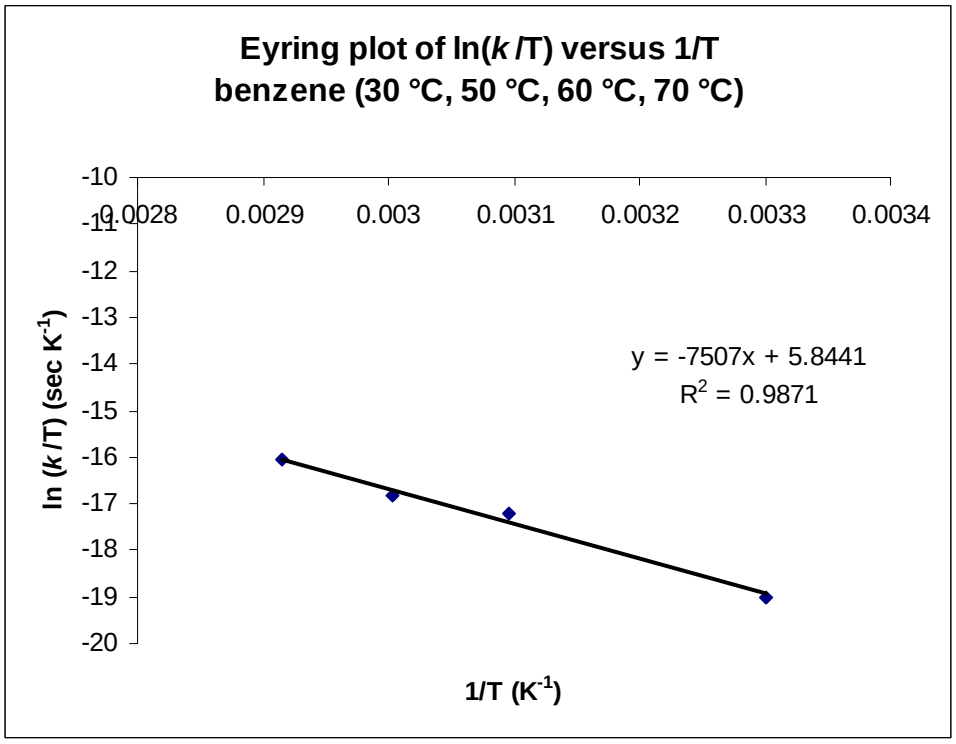


E_a = 15.9 kcal/mol and 66.6 kJ/mol

$\Delta H^{‡}$ = 15.3 kcal/mol and 63.9 kJ/mol

$\Delta S^{‡}$ = -32.5 eu and -136.2 J mol^{-1} K^{-1}

From the Eyring plot, the slope from the equation of the line is defined as $-\Delta H^{‡}/R$:



$\Delta H^{‡}$ = 14.9 kcal/mol and 62.4 kJ/mol

$K^{‡}$ can be calculated from the experimental rate *k* (sec^{-1}) for each temperature ($K^{‡}$ = *k*h/**k**T) in which h = 6.63 x 10^{-34} J sec (Planck's constant) and **k** = 1.3807 x 10^{-23} J / K (Bolzmann constant). From the calculated $K^{‡}$ the free energy $G^{‡}$ can be calculated from the equation $\Delta G^{‡} = RT\ln K^{‡}$

[C]	T	k_{obs}	$K^{‡}$	$G^{‡}$	$G^{‡}$
M	**kelvin**	**sec^{-1}**		**kcal/mol**	**kJ/mol**
0.0076	303	1.7 x 10^{-6}	2.69 x 10^{-19}	25.7	107.7
0.0076	323	1.1 x 10^{-5}	1.63 x 10^{-18}	26.3	110.0
0.0076	333	1.65 x 10^{-5}	2.38 x 10^{-18}	26.9	112.4
0.0076	343	3.65 x 10^{-5}	5.11 x 10^{-18}	27.1	113.5

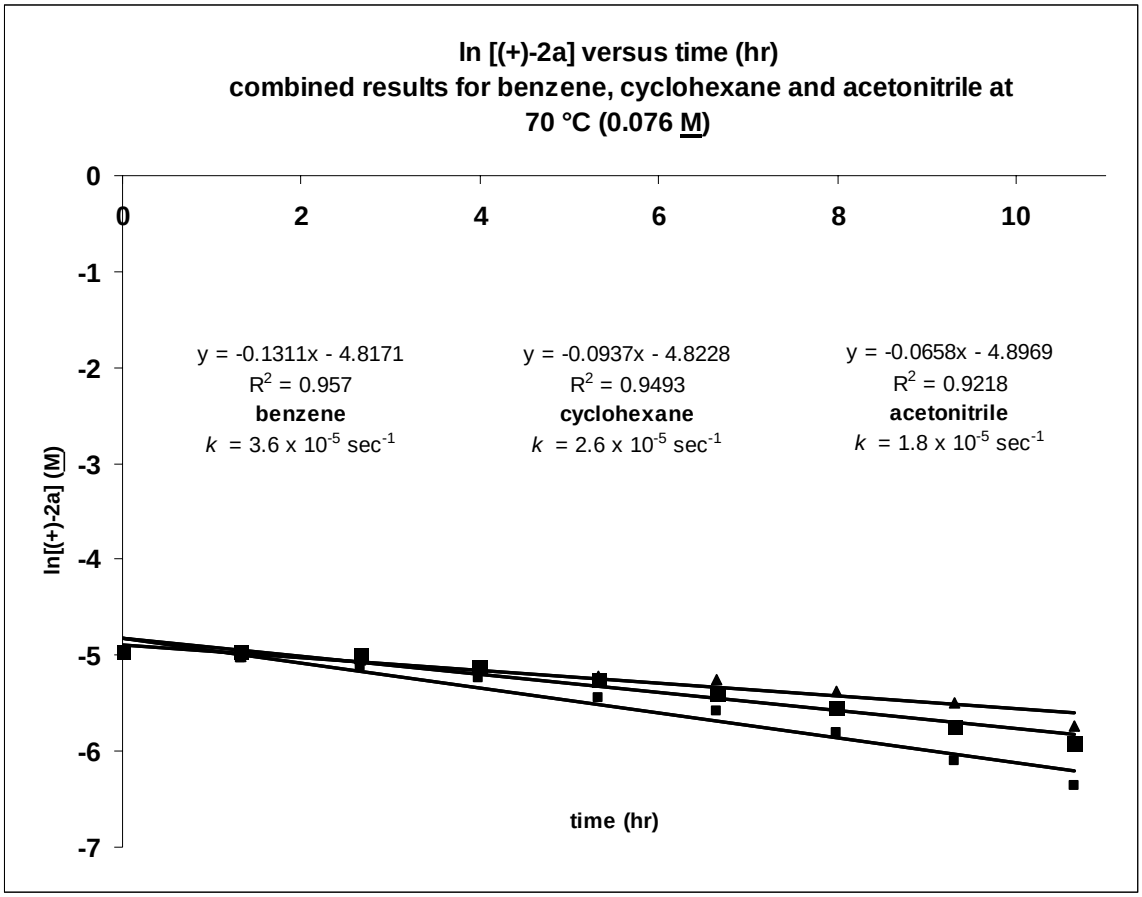
From $\Delta H^{\ddagger}$ obtained from the Eyring plot and calculated $\Delta G^{\ddagger}$, the entropy $\Delta S^{\ddagger}$ can be obtained from the equation $\Delta G^{\ddagger} = \Delta H^{\ddagger} + T\,\Delta S^{\ddagger}$

T	**$\Delta G^{\ddagger}$**	**$\Delta H^{\ddagger}$**	**$\Delta S^{\ddagger}$**
K	**kcal/mol**	**kcal/mol**	**eu (cal mol^{-1} K^{-1})**
303	25.7	14.9	-35.8
323	26.3	14.9	-35.3
333	26.9	14.9	-35.9
343	27.1	14.9	-35.7

Racemization of (+)- 2a in Acetonitrile and Cyclohexane

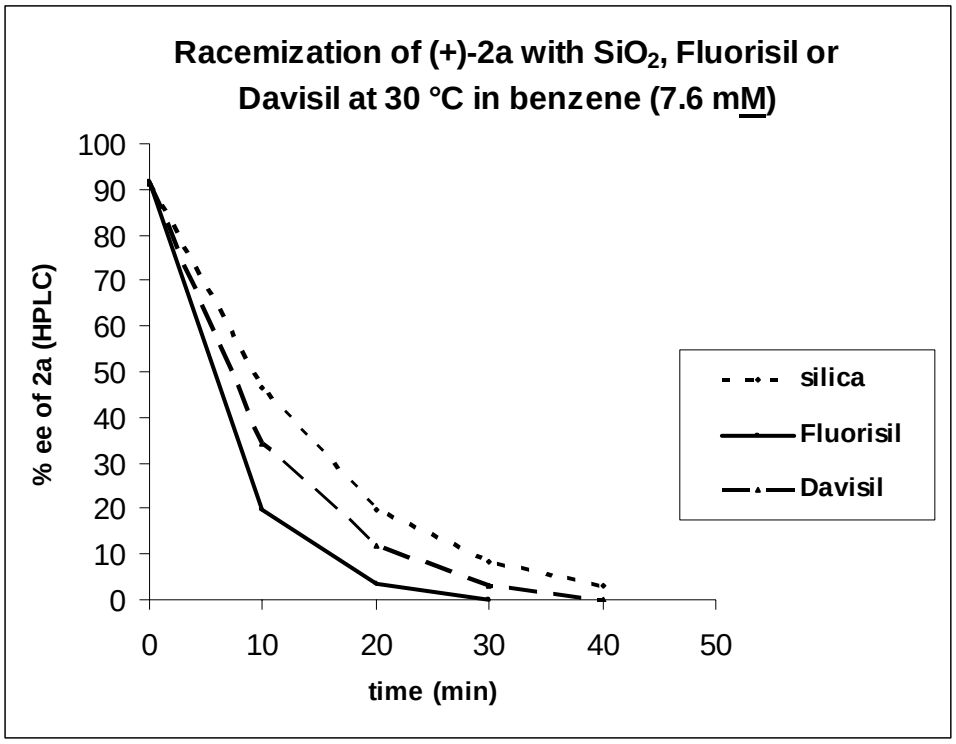
Two stock solutions (7.5 - 7.6 mM) of (+)-**2a** were prepared. One stock solution was prepared in freshly distilled benzene, and the other stock solution was prepared from either freshly distilled acetonitrile or cyclohexane. Both stock solutions were stored on ice. Two Pyrex® test tubes (10 mL capacity) with 14/20 glass joints, fitted with 14/20 jointed glass adapters (one way valve), were carefully flame dried and flushed with N_2. To one of these tubes the stock solution of either cyclohexane or acetonitrile was added, and to the other test tube the stock solution of benzene was added, with the volume added not exceeding 4 mL. The two experiments were staggered in time such that one experiment was started 40 min ahead of the other. Each experiment was placed in a preheated oil bath (maintained at ± 1 °C) at 70 °C for a 10 minute equilibration time period prior to taking the first aliquot. The rate of racemization was monitored regularly by chiral HPLC (Chiracel OD, 2% *i*-PrOH in hexanes, 0.8 mL/min, 210 nm, major enantiomer 28.8 min, minor enantiomer 26.4 min) over two half-lives, with a minimum collection of 10 data points for each experiment. At the designated collection time a 15 μL aliquot was removed from the test tube by syringe, under

positive N_2 pressure, and the solution injected to a small 1-dram vial. The volatiles were removed quickly under N_2 stream and the resulting residue was dissolved in 50 μL hexanes. 10 μl of this solution was injected to the HPLC for analysis. The racemization was monitored over a 10 hr time period. The data taken from the two experiments was plotted as the natural log of the concentration of the major enantiomer (+)-**2a** (M) versus time (hr).

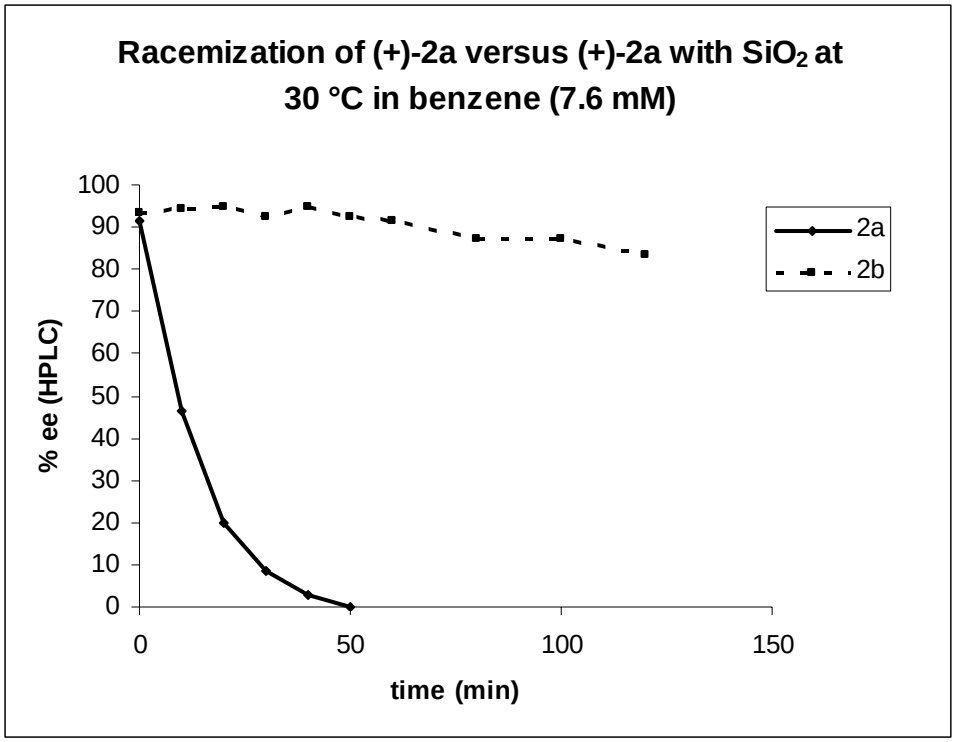


Racemization of (+)-2a and (+)-2b on Silica Gel

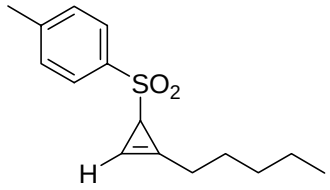
(+)-**2a** (91% ee) was stirred at 30 °C in benzene (7.6 mM) with SiO_2, Fluorisil®, or Davisil® (5.2 g of silica gel / mol of **2a**) and the change in enantiomeric excess monitored by chiral HPLC (Chiracel OD, 2 % *i*-PrOH/hexanes, 0.8 mL/min, 210 nm) every 10 minutes.



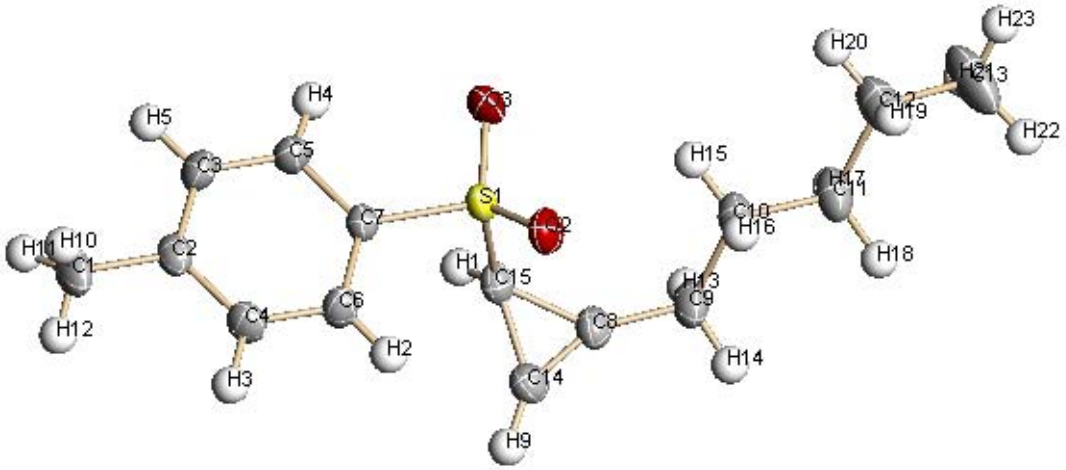
(+)-**2b** (94% ee) was stirred at 30 °C in benzene (7.6 mM) with SiO_2 (5.2 g of silica gel / mol of **2b**) and the change in enantiomeric excess monitored by chiral HPLC (Chiracel OJ, 12 % *i*-PrOH/hexanes, 1 mL/min, 210 nm). After 2 hrs reaction time the enantiomeric excess of (+)-**2b** was found to be 84% ee.



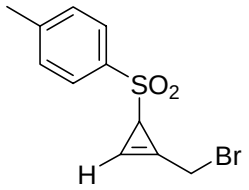
X-ray Crystal Structure (+/-)-2a



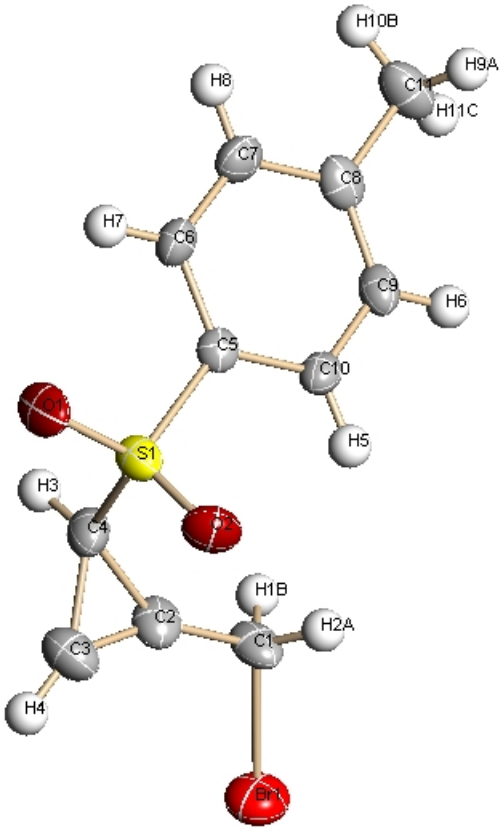
2a



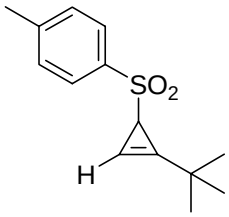
X-ray Crystal Structure (+/-)-2b



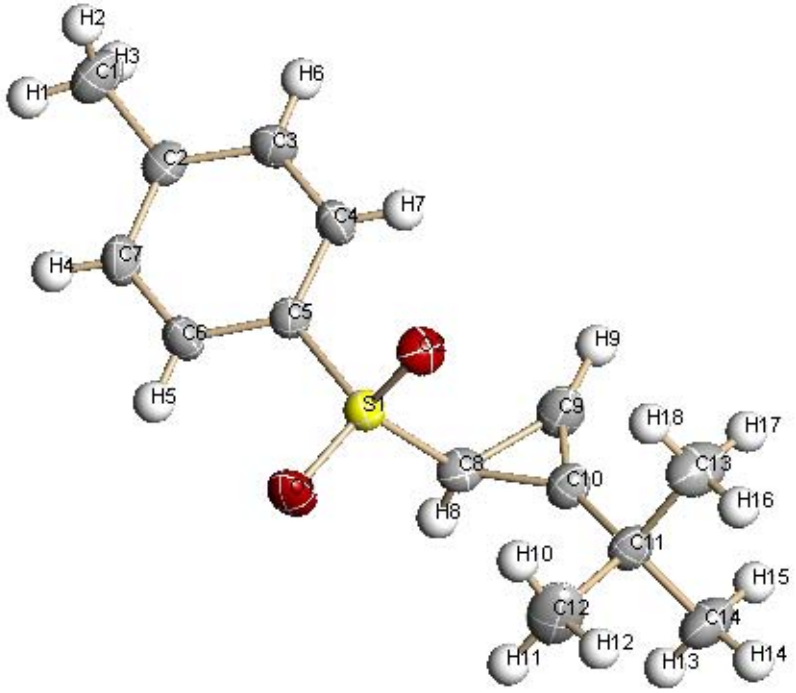
2b



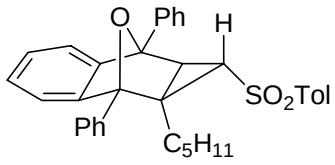
X-ray Crystal Structure (+/-)-2c



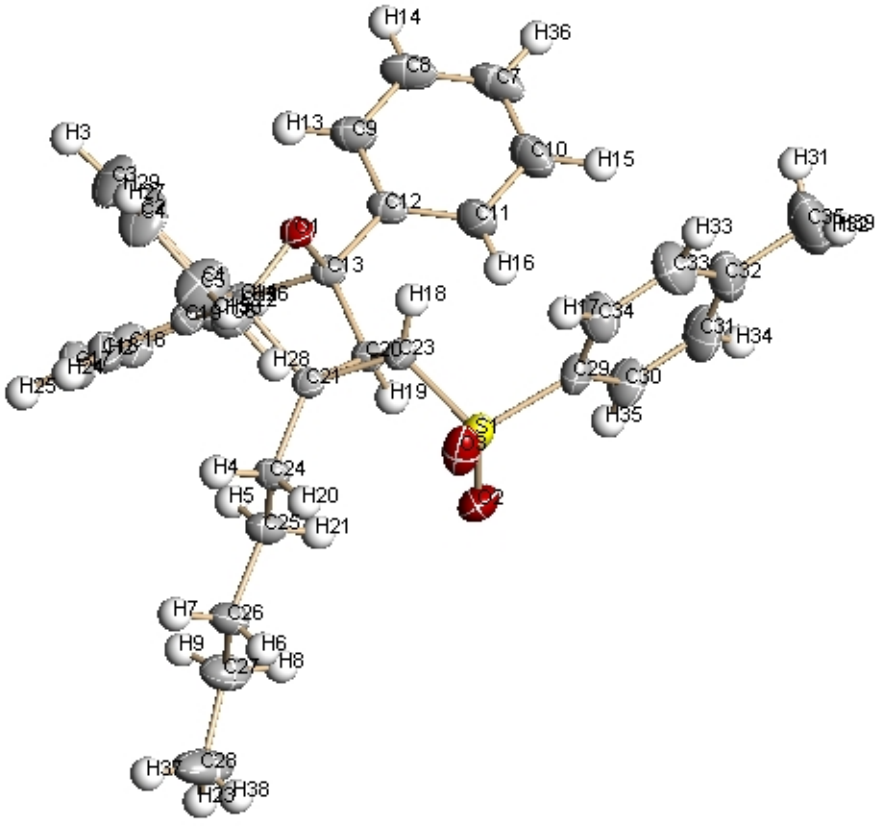
2c



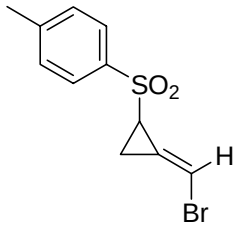
X-ray Crystal Structure (+)-3



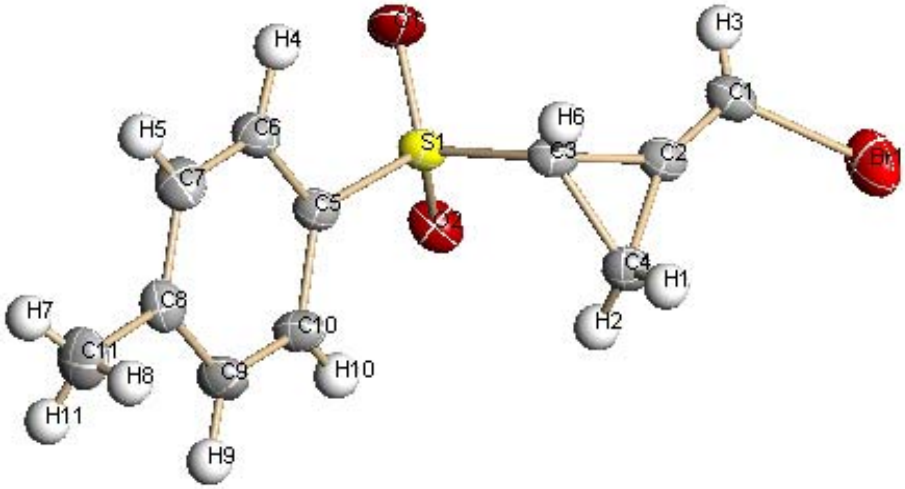
3



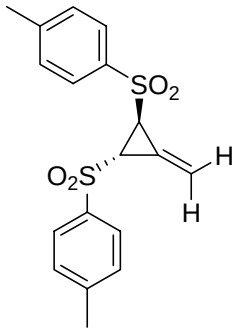
X-ray Crystal Structure (+/-)-17



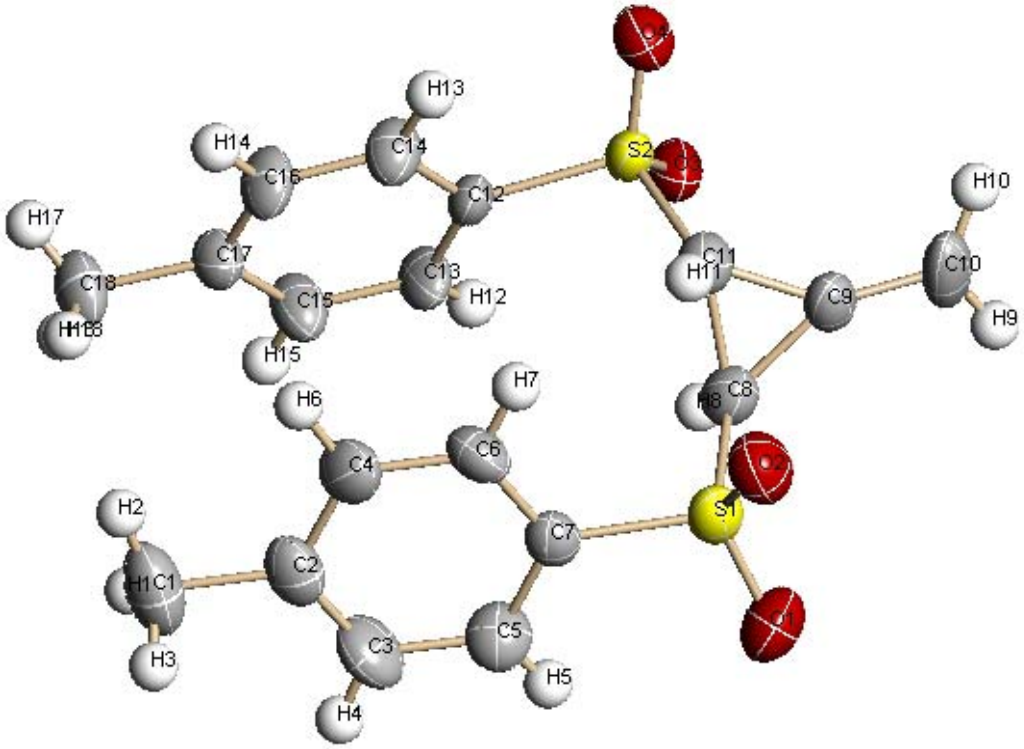
17



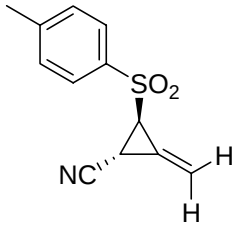
X-ray Crystal Structure (+/-)-18c



18c



X-ray Crystal Structure (+/-)-18d



18d