Supplementary material (ESI) for Chemical Communications

Intramolecular S_N2' Cyclization of an Alkyllithium Species onto a Methoxy Allyl Ether is *Syn*-Selective.

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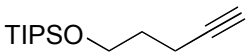
Supplementary data

General Experimental. IR spectra were recorded on a MIDAC Prospect FT-IR spectrometer. ^{1}H NMR spectra were recorded at 500 MHz and ^{13}C NMR spectra were recorded at 125 MHz on Bruker instruments. Chemical shifts of the ^{1}H NMR spectra were referenced to residual chloroform at 7.26 ppm. Chemical shifts of ^{13}C NMR spectra were referenced to $CDCl_3$ at 77.0 ppm. Optical rotations were determined on a JASCO DIP-370 digital polarimeter. Mass spectra were determined on an AE2-MS 30, a PG 7070E, or a Fisions autospec spectrometer. Tetrahydrofuran (THF), Et_2O, and CH_2Cl_2 were dried by filtration through alumina. Liquid chromatography was performed using forced flow (flash chromatography) of the indicated solvent system on E. Merk reagent silica gel 60 (230–400). Enantiomeric excess was determined by HPLC utilizing a chiralcel OD-H column. Enantiomeric ratio was determined by GC using a G-TA (β-cyclodextrin trifluoroacetyl) chiral column; 30 m x 0.25 mm; split ratio = 100:1; column flow = 1.0 mL/min; Gradient: Initial temperature = 50°C, 5 °C/min, final temperature = 150 ºC. Moisture sensitive reactions were performed under an atmosphere of argon using flame, or oven dried glassware, and standard syringe/septa techniques. Reagents bought from Aldrich were utilized with no further purification.

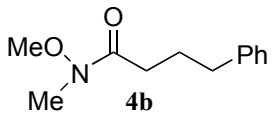
Preparation of a stock solution of LiDBB in THF (*ca*. 0.4 M). To a two-necked round-bottom flask equipped with a glass stir-bar was added 4, 4'-di-*tert*-butylbiphenyl (DBB) (0.747 g, 2.72 mmol), THF (6.80 mL), and the solution was stirred under argon. To the stirring solution of DBB was introduced 1.0 mg 1,10-phenanthroline, the mixture was cooled to 0 °C, and titrated with *n*-BuLi (2.5 M in hexanes, added to remove any residual trace of water) until a dark red end point persisted. Fresh lithium metal (0.226 g, 32.5 mmol) was prepared by submerging the wire in hexanes while scraping off the oxidized surface with an Exacto® knife. The shiny metal was then cut directly into the DBB solution under a stream of argon, forming a dark green color within 5 minutes. The resulting mixture was allowed to stir at 0 °C for 5 hours to form the desired LiDBB solution (*ca*. 0.4 M).



4a

1-(Triisopropylsilyl)oxy-4-pentyne (4a). The known title compound was synthesized from commercially available 4-pentyn-1-ol utilizing a literature procedure.[4a]

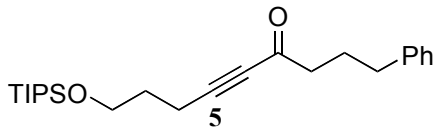
R_f = 0.71 (5% EtOAc/Hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) □ 3.77 (t, 2H, J = 6.0), 2.29 (dt, 2H, *J* = 7.2, 2.6), 1.91 (t, 1H, *J* = 2.9), 1.74 (m, 2H), 1.05 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 84.3, 68.1, 61.7, 31.8, 18.0, 14.9, 12.0; IR (neat) 3314, 2944, 2121, 1464, 1384, 1247 cm^{-1}; HRMS calcd for $C_9H_{21}OSi$ [M – iPr]$^+$ 197.1362; found 197.1359.



4b

***N*-Methoxy-*N*-Methyl-4-phenyl-butyramide (4b)**. A flask was charged with 4-phenylbutyric acid (9.00 g, 55.0 mmol), CH_2Cl_2 (274 mL) and cooled to 0 °C. To the suspension was added triethylamine (15.3 mL, 110 mmol), isobutyl chloroformate (7.80 mL, 60.0 mmol), then *N*,*O*-dimethylhydroxylamine (5.60 g, 58.0 mmol). The reaction mixture was allowed to

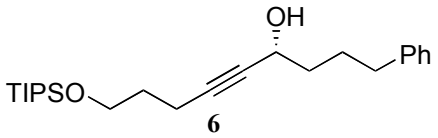
warm to room temperature and stirred for 20 hr. The excess isobutyl chloroformate was quenched with saturated aqueous $NaHCO_3$ (50 mL). The aqueous layer was extracted with ether (3 x 100 mL), and washed with brine (3 x 50 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give a yellow oil that was purified by flash chromatography (40% EtOAc/Hexanes) to afford 10.5 g (92%) of the desired amide as a colorless oil: R_f = 0.36 (40% EtOAc/Hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) 7.27 (m, 2H), 7.19 (m, 3H), 3.59 (s, 3H), 2.93 (s, 3H), 2.68 (t, 2H, *J* = 7.5), 2.43 (t, 2H, *J* = 6.7), 1.98 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) 174.0, 141.5, 128.2, 128.0, 125.4, 60.8, 35.0, 31.8, 30.8, 25.8 ppm; IR (neat) 3563, 2938, 1667, 1497, 1454, 1179, 1105 cm^{-1}; HRMS calcd for $C_{12}H_{17}NO_2$ $[M]^+$ 207.1259 found 207.1259.



5

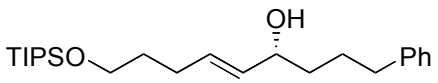
1-Phenyl-9-triisopropylsilanyloxy-non-5-yn-4-one (5). A solution of alkyne **4a** (8.00 g, 33.0 mmol) in THF (221 mL) was cooled to 0 °C at which time *n*-butyllithium (2.5 M in hexanes, 14.0 mL, 35.0 mmol) was added dropwise over a five minute period. The solution was stirred at 0 °C for 20 min, then a solution of *N*-methoxy-*N*-methyl-4-phenyl-butyramide (6.90 g, 33.3 mmol) in THF (56.0 mL) was pre cooled to 0 °C and added dropwise to the stirring solution of alkyne **21** over a 10 minute period. The colorless solution was stirred at 0 °C for 1.5 hr, the excess anion was then quenched with saturated aqueous NH_4Cl (120 mL), and the mixture was then extracted with hexanes (2 x 200 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in *vacuo*. The resulting crude was purified by flash chromatography (5% EtOAc/Hexanes) to afford 12.2 g (95% yield) of the title compound as a colorless oil: R_f = 0.39 (5% EtOAc/Hexanes); ^{1}H NMR (500 MHz, $CDCl_3$)

7.28 (m, 2H), 7.19 (m, 2H), 3.78 (t, 2H, J = 5.9), 2.65 (t, 2H, J = 7.4), 2.55 (t, 2H, J = 7.5), 2.51 (t, 2H, J = 7.1), 2.00 (dt, 2H J = 15.2, 7.7), 1.81 (m, 2H), 1.09 (m, 21H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) □ 187.7, 141.3, 128.4, 128.4, 125.9, 94.0, 80.2, 61.4, 44.6, 34.8, 30.9, 25.5, 17.9, 15.4, 11.9 ppm; IR (neat) 2944, 2213, 1675, 1463, 1383, 1238 cm^{-1}; HRMS calcd for $C_{24}H_{39}O_2Si$ $[M + H]^+$ 387.2719; found 387.2723.



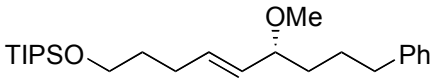
6

(*R*)-1-Phenyl-9-triiopropylsilanyloxy-non-5-yn-4-ol (6). A solution of 1-phenyl-9-triisopropylsilanyloxy-non-5-yn-4-one **5** (7.00 g, 18.1 mmol) in freshly distilled isopropanol (181 mL) was sparged with argon for 20 min. To this solution was introduced Ru[(*R*,*R*)-TsDPEN](□^{6}-*p*-cymene) (0.109 g, 0.181 mmol) at room temperature. The solution immediately turned purple then red and finally, after two hours, an orange color. At the end of the two hour period another portion of the catalyst (0.109 g, 0.181 mmol) was added to the solution and the mixture was allowed to stir for another two hours. Another portion of the catalyst was added (0.109 g 0.181 mmol) and the solution was stirred for two more hours. The resulting brown solution was then concentrated and the brown residue was purified by passing it three times through a silica gel column (10% EtOAc/Hexanes) to give 5.72 g (81% yield, 97% ee) of the title compound as a slightly yellow oil: R_f = 0.32 (10% EtOAc/Hexanes); [□]$_D$ –4.2° (*c* 0.10, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) □ 7.29 (m, 2H), 7.20 (m, 3H), 4.37 (m, 1H), 3.77 (t, 2H, J = 6.1), 2.67 (t, 2H, J = 7.6), 2.34 (dt, 2H, J = 7.1, 1.8), 1.75 (m, 7H), 1.08 (m, 21H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) □ 142.1, 128.4, 128.3, 125.7, 85.3, 81.2, 62.5, 61.8, 37.6, 35.5, 31.9, 26.9, 18.0, 15.1, 11.9 ppm; IR (neat) 3350, 2942, 1604, 1463, 1384, 1248, cm^{-1}; HRMS calcd for $C_{21}H_{33}O_2Si$ $[M - i\text{Pr}]^+$ 343.2095; found 343.2095.



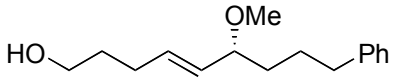
7a

(*R*)-1-Phenyl-9-triisopropylsilanyloxy-non-5-en-4-ol (7a). A flask was charged with RedAl® (65% solution in toluene, 7.67 mL, 29.9 mmol), THF (99.8 mL), and the resulting solution was cooled to 0 °C. To the cool stirring mixture was added a solution of alcohol **24** (2.91 g, 7.49 mmol) in THF (74.9 mL) drop wise over a five minute period. Once the exotherm was complete the solution was warmed to room temperature and stirred for 8 hours. The vigorously stirring mixture was cooled to 0 °C and an aqueous solution of potassium tartrate (2.0 M, 30 mL) and diethyl ether (30 mL) was introduced to the reaction vessel. The layers were separated and the inorganic layer was extracted with Et_2O (3 x 30 mL). The combined orgainc layers were washed with brine (3 x 20 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting yellow residue was purified by flash chromatography to give 2.63 g (90% yield) of the desired alcohol as a colorless oil: R_f = 0.32 (10% EtOAc/Hexanes); $[\alpha]_D$ –1.5° (*c* 0.20, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (m, 2H), 7.20 (m, 3H), 5.67 (dt, 1H, *J* = 15.1, 6.6), 5.49 (dd, 1H, *J* = 15.4, 7.1), 4.07 (m, 1H), 3.70 (t, 2H, *J* = 6.4), 2.65 (t, 2H, *J* = 7.4), 2.13 (q, 2H, J = 7.3, 6.8), 1.77–1.60 (m, 5H), 1.57–1.52 (m, 2H), 1.08 (m, 21H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.3, 133.1, 131.7, 128.4, 128.2, 125.7, 73.0, 62.6, 36.8, 35.8, 32.4, 28.5, 27.3, 18.0, 12.0 ppm; IR (neat) 3350, 2939, 1669, 1604, 1455, 1383, 1248, 1110 cm^{-1}; HRMS calcd for $C_{21}H_{35}O_2Si$ [M - *i*Pr]$^+$ 347.2077; found 347.2411.



7b

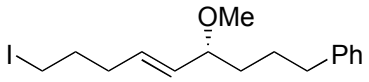
(*R*)-Triisopropyl-(6-methoxy-9-phenyl-non-4-enyloxy)-silane (7b). A stirring solution of alcohol **7a** (4.66 g, 11.9 mmol) in THF (23.6 mL) was cooled to 0 °C. Sodium hydride (60% dispersion in mineral oil, 2.06 g, 53.6 mmol), and methyl iodide (3.71 mL, 59.6 mmol) were sequentially added to the reaction mixture. The resulting grey mixture was allowed to stir for 15 hr, cooled to 0 °C, the excess sodium hydride was quenched with MeOH (20 mL), and the mixture was poured into a separatory funnel containing 50 mL of water. The aqueous layer was extracted with Et_2O (3 x 40 mL), the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash chromatograph (5% EtOAc/Hexanes) to afford 4.59 g (95 % yield) of the desired methyl ether as a colorless oil: R_f = 0.56 (5% EtOAc/Hexanes); $[\alpha]_D$ +2.6° (*c* 0.10, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (m, 2H), 7.19 (m, 3H), 5.65 (dt, 1H, *J* = 15.2, 6.7), 5.30 (dd, 1H, *J* = 15.4, 8.3), 3.73 (t, 1H, *J* = 6.5), 3.50 (m, 1H,), 3.26 (s, 3H), 2.64 (t, 2H, *J* = 7.1), 2.18 (q, 2H, J = 7.0, 6.9), 1.75–1.63 (m, 5H), 1.55–1.48 (m, 1H), 1.10 (m, 21H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.5, 133.8, 130.7, 128.4, 128.2, 125.6, 82.4, 62.7, 55.87, 35.9, 35.3, 32.5, 28.5, 27.4, 18.0, 12.0 ppm; IR (neat) 2941, 1668, 1604, 1463, 1383, 1106 cm^{-1}; HRMS calcd for $C_{24}H_{41}O_2Si$ $[M - MeO]^+$ 373.2927; found 373.2934.



7c

(*R*)-6-Methoxy-9-phenyl-non-4-en-1-ol (7c). To a solution of allyl ether **7b** (3.60 g, 8.90 mmol) in THF (44.5 mL), cooled to 0 °C, was added TBAF (1.0 M solution in THF, 2.75 mL, 11.6 mmol) in one portion. The solution was warmed to room temperature, stirred for 10 hr., and then brine (30 mL) was introduced to the reaction vessel. The mixture was extracted with Et_2O

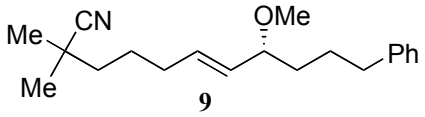
(3 x 40 mL), the combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated. The resulting oil was purified by flash chromatograph (40% EtOAc/Hexanes) to give 4.59 g of the desired alcohol as a clear oil in 95% yield: R_f = 0.51 (40% EtOAc/Hexanes); $[\alpha]_D$ +19° (*c* 0.19, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (m, 2H), 7.18 (m, 3H), 5.64 (dt, 1H, *J* = 15.4, 6.7), 5.29 (ddt, 1H, *J* = 15.4, 8.2, 1.4), 3.63 (m, 2H), 3.49 (m, 1H), 3.24 (s, 3H), 2.62 (t, 2H, *J* = 7.2), 2.15 (m, 2H), 2.00 (s, 1H), 1.70–1.61 (m, 5H), 1.52–1.47 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.4, 133.3, 130.8, 128.3, 128.2, 125.6, 82.3, 62.0, 55.7, 35.8, 35.1, 32.0, 28.4, 27.2 ppm; IR (neat) 3392, 2934, 1667, 1603, 1496, 1453, 1364, 1094 cm^{-1}; HRMS calcd for $C_{16}H_{23}O_2$ $[M - H]^+$ 247.1698; found 247.1692.



7d

(*R*)-(9-Iodo-4-methoxy-non-5-enyl)-benzene (7d). To a solution of alcohol **7c** (1.60 g, 6.44 mmol) in Et_2O (64.4 mL) at room temperature was added PPh_3 (3.38 g, 12.9 mmol), and imidazole (0.875 g, 12.9 mmol). To the reaction vessel, at room temperature, was introduced a 0.3 M solution of I_2 (1.43 g, 11.3 mmol) in Et_2O (37.6 mL) dropwise over a 10 min. period. At the end of addition of I_2 all starting material had been consumed. At this point another portion of I_2 (10 mL of a 0.3 M solution in Et_2O) was added, and the excess PPh_3 was oxidized by the addition of MeOH (10 mL) to the reaction mixture at room temperature, and excess I_2 was quenched with aqueous $NaHSO_3$ (2.0 M solution**,** 20 mL). The layers were separated, and the inorganic layer was extracted with hexanes (3 x 20 mL). The combined organic layers were washed with a saturated aqueous solution of $NaHCO_3$ (2 x 10 mL), then brine (3 x 10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the resulting oil by flash chromatography (10% EtOAc/Hexanes) gave the title compound in 97%

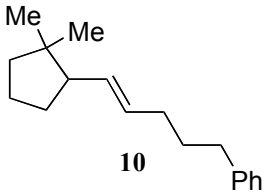
yield as a colorless oil: R_f = 0.64 (10% EtOAc/Hexanes); [□]$_D$ +12° (*c* 0.29, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) □ 7.28 (m, 2H), 7.18 (m, 3H), 5.55 (dt, 1H, *J* = 15.2, 6.7), 5.36 (ddt, 1H, *J* = 15.4, 8.0, 1.3), 3.48 (m, 1H,), 3.23 (s, 3H,), 3.18 (t, 2H, *J* = 6.9), 2.62 (t, 2H, *J* = 7.2), 2.18 (m, 2H), 1.92 (app qintet, 2H, *J* = 7.0), 1.72–1.60 (m, 3H), 1.53–1.45 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) □ 142.4, 132.1, 131.5, 128.4, 128.3, 125.7, 82.1, 55.9, 35.9, 35.2, 32.8, 32.6, 27.3, 6.2 ppm; IR (neat) 2930, 1667, 1603, 1496, 1452, 1214 cm^{-1}; HRMS calcd for $C_{16}H_{23}IO$ [M]$^+$ 358.0794; found 358.0790.



9

***R*)-8-Methoxy-2,2-dimethyl-11-phenyl-undec-6-enenitrile (9).** To a flask charged with diisopropylamine (1.01 mL, 7.19 mmol), THF (24.0 mL), and cooled to 0 °C was added *n*-butyllithium (2.5 M in Hexanes, 2.85 mL, 7.12 mmol) dropwise over a 5 min period. The solution was stirred at 0 °C for thirty minutes and then cooled to –78 °C. Isobutyronitrile (**8)** (0.660 mL, 7.26 mmol) was introduced to the reaction mixture, and stirring was continued for one hour at –78 °C. A solution of (*R*)-(9-iodo-4-methoxy-non-5-enyl)-benzene (**7d**) (1.29 g, 3.59 mmol) in THF (6.00 mL) was introduced to the reaction vessel and stirring was continued for 45 min at –78 °C. The excess isobutyronitrile anion was quenched with a saturated aqueous solution of NH_4Cl (10 mL), washed with water (10 mL), and the aqueous layer was extracted with ether (3 x 10 mL). The combined organic layers were washed with a 10% wt. aqueous solution of $NaHSO_3$ (10 mL), and the aqueous layer was back extracted with ether (1 x 20 mL). The combined organic layers were washed with saturated $NaHCO_3$ (2 x 10 mL), then brine (2 x 10), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to produce an oil that was purified by flash chromatography (15% EtOAc/Hexanes) to give 1.04 g (97%

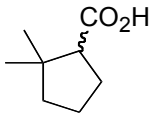
yield) of the desired compound as a colorless oil: R_f = 0.49 (15% EtOAc/Hexanes); $[\alpha]_D$ +6.1° (*c* 0.14, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (m, 2H), 7.17 (m, 3H), 5.58 (dt, 1H, *J* = 15.2, 6.6), 5.27 (ddt, 1H, *J* = 15.4, 8.2, 1.4), 3.48 (m, 1H), 3.24 (s, 3H), 2.61 (t, 2H, *J* = 6.9), 2.10 (q, 2H, *J* = 6.9), 1.72–1.61 (m, 3H), 1.59–1.55 (m, 2H), 1.53–1.45 (m, 3H), 1.32 (m, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.4, 132.8, 131.3, 128.3, 128.2, 125.6, 124.9, 82.2, 55.8, 40.4, 35.8, 35.1, 32.2, 31.9, 27.3, 26.5, 24.8 ppm; IR (neat) 2936, 2234, 1667, 1603, 1496, 1455 cm^{-1}; HRMS calcd for $C_{20}H_{29}NO$ $[M]^+$ 299.2249; found 299.2245.



10

[5-(2,2-Dimethylcyclopentyl)-pent-4-enyl] benzene (10). To a solution of nitrile **9** (0.100 g, 0.334 mmol) in THF (1.00 mL) at –78 °C was added a freshly prepared cold (–78 °C) solution of LiDBB (0.4 M in THF, 10.0 mL, 4.00 mmol), by rapid addition utilizing a glass syringe. The resulting dark green mixture was allowed to stir at –78 °C for 1 hr, and the excess LiDBB was quenched with MeOH (1 mL). The mixture was diluted with brine (3 mL), and extracted with pentane (1 x 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give a white solid (mostly DBB) that was dissolved in 1 mL of pentane and passed through a silica gel column eluting with 100% pentane to separate DBB from the other components of the mixture. The fractions containing DBB were discarded, the others were concentrated, and the resulting oil was purified by flash chromatograph (100% pentane) to give 0.030 g (37% yield) of the desired compound (97:3 *E/Z* ratio) as colorless oil. R_f = 0. 81 (pentane); $[\alpha]_D$ –3.4° (*c* 0.11, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (m, 2H), 7.19 (m, 3H), 5.41 (dt, 1H, *J* = 15.6, 6.5), 5.33 (dd, 1H, *J* = 15.2, 8.0), 2.64 (m, 2H) 2.07 (m,

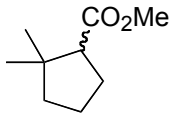
2H), 1.99 (m, 1H), 1.79 (m, 1H), 1.73–1.33 (m, 7H), 0.96 (s, 3H), 0.76 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) 142.7, 131.9, 130.3, 128.5, 128.2, 125.6, 53.5, 41.8, 41.4, 35.3, 32.3, 31.5, 30.5, 27.9, 22.2, 21.6 ppm; IR (neat) 2952, 1605, 1496, 1454, 1382, 1364 cm^{-1}; HRMS calcd for $C_{18}H_{26}$ $[M]^+$ 242.2035; found 242.2035.



11a
racemate

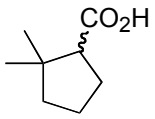
2,2-Dimethyl-cyclopentanecarboxylic acid (11a). A flask was charged with a magnetic stir bar, 2,2-Dimethyl-cyclopentanecarbonitrile(0.200 g, 1.62 mmol), aqueous NaOH (3 N, 11.6 mL), H_2O_2 (30% in water, 4.63 mL), and the resulting solution was warmed to 50 °C for two hours. Another portion of 30% H_2O_2 (4.63 mL) was added to the reaction mixture and heating to 50 °C was continued for two more hours. Another portion of 30% H_2O_2 (4.63 mL) was added, and the solution was allowed to stir at 50 °C for 10 hr. Solid KOH (4.00 g, 71.3 mmol) was then added to the reaction mixture and refluxed for 6 hr. The solution was cooled to room temperature and extracted with Et_2O (2 x 20 mL). The organic layer was discarded, the aqueous layer was acidified with 3 N HCl to pH 3–4, extracted with Et_2O (3 x 20 mL), and the combined organic layers were dried over anhydrous $MgSO_4$. The solution was filtered, concentrated under reduced pressure, and the resulting residue was purified by flash chromatograph (30% EtOAc/Hexanes) to afford 0.118 g (66% yield) of the desired compound as a colorless oil: R_f = 0.52 (30% EtOAc/Hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) 11.65 (br s, 1H), 2.42 (t, 1H, J = 8.8), 2.09–2.00 (m, 1H), 1.93–1.86 (m, 1H), 1.81–1.72 (m, 1H), 1.68–1.47 (m, 3H), 1.18 (s, 3H), 0.96 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) 181.0, 54.4, 42.9, 41.8, 29.1, 27.3, 23.7,

22.3 ppm; IR (neat) 3500–2672, 1695, 1422, 1242, 941, 724 cm^{-1}; HRMS calcd for $C_8H_{15}O_2$ [M + H]$^+$ 143.1072; found 143.1071.



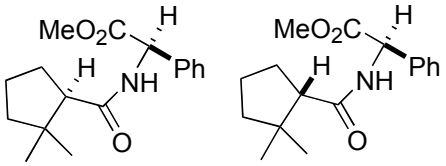
11b

Racemic methyl ester 11b. Racemic methyl ester **11b** was synthesized utilizing the following literature procedure: Covey, D. F.; Holland, K. D.; McKeon, A.; Ferrendelli, J. A. C.; Peterson, E. M.; Rothman, S. M.; Xu, K.*; J. Med. Chem*. **1994**, *37*, 275-286. CG retention times for the two enantiomers were found to be 17.001 and 18.717 min.



11

2,2-Dimethyl-cyclopentanecarboxylic acid (11). A flask was charged with hydrocarbon **10** (29 mg, 0.12mmol), CCl_4 (0.24 mL), CH_3CN (0.24 mL), and H_2O (0.36 mL). To the biphasic mixture was added $NaIO_4$ (0.105 g, 0.490 mmol), and $RuCl_3$ (2.60 mg, 0.0026 mmol). The orange colored mixture was stirred for at room temperature for 15 hr, then aqueous NaOH (2 N, 2 mL) was added to the reaction vessel, and the contents of the vessel were extracted with Et_2O (2 x 10 mL). The organic layers were discarded and the inorganic layer was acidified with 3 N HCl (3 mL) to pH 3 –4, and extracted with Et_2O (3 x 10 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated in *vacuo* to afford a yellow residue that was purified by flash chromatograph (30% EtOAc/Hexanes) to afford 0.009 g (53% yield) of the desired compound as a colorless oil. The R_f, IR, ^{1}H NMR, and ^{13}C NMR spectra of the titled compound was identical to racemic acid **11a**.



13 **14**

Amides 13 and 14. Carboxylic acid **11a** (0.0500 g, 0.352 mmol) was dissolved in DMF (1.76 mL), and to this solution was added in sequence (*R*)-(–)-2-phenylglycine methyl ester hydrochloride® (0.142 g, 0.703 mmol), *N*-methylmorpholine (0.350 mL, 3.16 mmol), PyBrOP® (0.329 g, 0.703 mmol), and HOBT® (0.0950 g, 0.703 mmol). The resulting mixture was stirred for 3 hr, diluted with EtOAc (20 mL), and benzene (10 mL). To this mixture was added 5% HCl (10 mL), the solution was allowed to stir for 2 min, and then poured into a separatory funnel containing Et_2O (40 mL). The layers were separated and the inorganic phase was extracted with diethyl ether (3 x 20 mL). The combined organic extracts were washed with saturated $NaHCO_3$ (2 x 20 mL), brine (2 x 20 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting yellow residue was purified by flash chromatograph (30% EtOAc/Hexanes) to give 0.0825 g of a 1:1 mixture of diastereomers **13** and **14** as a white solid. The diastereomers were separated by MPLC (30% EtOAc/Hexanes.) and characterized: (*R*,*R*)-amide **13**; R_f = 0.52 (30% EtOAc/Hexanes); $[\alpha]_D$ –16.4° (*c* 0.0700, $CHCl_3$); mp 102–104 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (m, 5H), 6.25 (d, 1H, *J* = 6.5), 5.60 (d, 1H, *J* = 7.0), 3.73 (s, 3H), 2.22 (t, 1H, *J* = 9.1), 2.11–2.03 (m, 2H), 1.86–1.72 (m, 2H), 1.63–1.55 (m, 1H), 1.50–1.44 (m, 1H), 1.21 (s, 3H), 0.93 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.3, 171.6, 136.7, 129.0, 128.5, 127.4, 56.4, 56.1, 52.7, 42.8, 41.8, 29.6, 27.4, 23.5, 22.1 ppm; IR (thin film) 3256, 2960, 1748, 1644, 1538, 1455 cm^{-1}; LRMS (EI) calcd for $C_{17}H_{23}NaNO_3$ $[M + Na]^+$ 312.17; found 312.18; (*S*,*R*)-amide **14**; R_f = 0.48 (30% EtOAc/Hexanes); $[\alpha]_D$ –132.9° (*c* 0.0700, $CHCl_3$); mp 107–110 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (m, 5H), 6.37 (d, 1H, *J* = 6.5), 5.60

(d, 1H, *J* = 7.1), 3.73 (s, 3H), 2.24 (t, 1H, *J* = 8.4), 2.11–2.04 (m, 1H), 1.87 (dddd, 1H, *J* = 17.3, 8.78, 8.78, 4.25), 1.79–1.72 (m, 1H), 1.66–1.59 (m, 1H), 1.56–1.52 (m, 1H), 1.47–1.41 (m, 1H), 1.09 (s, 3H), 0.76 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) 173.3, 171.7, 137.0, 128.9, 128.4, 127.3, 56.3, 56.1, 52.8, 42.8, 41.6, 29.4, 27.6, 23.5, 22.2 ppm; IR (thin film) 3259, 2956, 1748, 1653, 1540, 1496 cm^{-1}; LRMS (EI) calcd for $C_{17}H_{23}NaNO_3$ $[M + Na]^+$ 312.17 found 312.18;

Protocol for determining enantiomeric ratio and absolute configuration of hydrocarbon 10. A flask was charged with hydrocarbon **10** (29 mg, 0.12mmol), CCl_4 (0.24 mL), CH_3CN (0.24 mL), and H_2O (0.36 mL). To the biphasic mixture was added $NaIO_4$ (0.105 g, 0.490 mmol), and $RuCl_3$ (2.60 mg, 0.0026 mmol). The orange colored mixture was stirred for at room temperature for 15 hr, then aqueous NaOH (2 N, 2 mL) was added to the reaction vessel, and the contents of the vessel were extracted with Et_2O (2 x 10 mL). The organic layers were discarded and the inorganic layer was acidified with 3 N HCl (3 mL) to pH 3 –4, and extracted with Et_2O (3 x 10 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated in *vacuo* to afford 20 mg of a residue that was taken to the next step of the reaction sequence with no further purification. A portion of the residue was dissolved in 0.5 ml of Et_2O, treated with diazomethane until a bright yellow color persisted then, 050 mL MeOH was added to the reaction mixture. The enantiomeric ratio of the resulting methyl ester was evaluated by GC on a G-TA (-cyclodextrin trifluoroacetyl) chiral column and found to be 95:5 (R_t of major enantiomer 17.119, R_t of minor enantiomer 19.046. Another portion of the residue, isolated from the oxidation of hydrocarbon **10,** was dissolved in DMF (0.703 mL), and to this solution was added in sequence (*R*)-phenylglycine methyl ester (0.113 g, 0.563 mmol), *N*-methylmorpholine (0.153 mL, 1.41 mmol), PyBrOP® (0.262 g, 0.563 mmol), and HOBT® (0.0760 g, 0.563 mmol). The resulting mixture was stirred for 3 hours, diluted with EtOAc (10 mL), and benzene (5 mL).

To this mixture was added 5% HCl (5 mL), the solution was allowed to stir for 2 min., and then poured into a separatory funnel containing Et_2O (20 mL). The layers were separated and the inorganic phase was extracted diethyl ether (3 x 20 mL). The combined organic extracts were washed with saturated $NaHCO_3$ (2 x 10 mL), brine (2 x 10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting yellow residue was purified by flash chromatograph (40% EtOAc/Hexanes), then by MPLC (30% EtOAc/Hexanes.) to afford 4.1 mg of a solid composed of a mixture of diastereomers [86:14, (*R,R*):(*S,R*)]. The ^{1}H NMR spectrum of the major diastereomer was identical to ^{1}H NMR spectrum of (*R,R*)-amide **13**.