Supporting Information Experimental

Asymmetric Synthesis of Deoxypropionate Derivatives via Catalytic Hydrogenolysis of Enantioenriched *Z*-Ketene Heterodimers

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General Information.

THF was freshly distilled from benzophenone ketyl radical under nitrogen prior to use. Hünig's base (diisopropylethylamine) was distilled from calcium hydride and *N*,*N*-dimethylethylamine was distilled from potassium hydroxide under nitrogen.[1] Dichloromethane and diethyl ether were dried by passing through activated alumina columns on a solvent purification system. Zinc dust (<10 μm), *n*-butyllithium (2.5 M in hexane), Borane-THF solution (1.0 M), 2-phenylpropanoic acid, 2-phenylbutanoic acid, diphenylacetyl chloride, phenylacetic acid, and 2-pyridone were purchased from Aldrich Chemical Co. Ethylethynyl ether was purchased from GFS Chemical. Propionyl chloride, butyryl chloride, octanoyl chloride and trimethylsilyl chloride were purchased from Aldrich Chemical Co. and distilled prior to use.[1] Iatrobeads (Bioscan, 6RS-8060, 60 μ M particle size) as neutral silica gel, Silicycle (60-200 μ M particle size) as normal silica gel, and TLC plates (Sorbent Technologies, UV254, 250 μ M) were used as received. Methylphenylketene, ethylphenylketene, diphenylketene, dimethylketene and TMS-ketene were prepared according to literature procedures.[2] TMS-quinine, Me-quinidine and Me-quinine were synthesized according to literature procedure.[3] The enantioenriched *Z*-ketene heterodimers were synthesized as per previously reported procedures.[4]

NMR spectra were recorded on a Bruker Biospin AG 400 spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C). NMR chemical shifts were reported relative to TMS (0 ppm) for ^{1}H and to $CDCl_3$ (77.23 ppm) for ^{13}C spectra. High resolution mass spectra were obtained on an Agilent Technologies 6520 Accurate Mass Q-TOF LC-MS instrument (with ESI as the ionization method) at Oakland University. Low resolution mass spectra were recorded on a GC/MS Hewlett Packard HP 6890 GC instrument with a 5973 mass selective detector, and using a Restek Rtx-CL Pesticides2 GC column (30 m, 0.25 mm ID). Optical rotations were measured on Rudolph DigiPol 781 TDV automatic polarimeter. IR spectra were recorded on a Bio Rad FTS-175C spectrometer.

Analytical high performance liquid chromatography (HPLC) was performed using a Daicel Chiralpak AD column (0.46 cm × 25 cm), ODH column (0.46 cm × 25 cm), or an AS-H column (0.46 cm × 25 cm) (Daicel Chemical Ind., Ltd.) on a Perkin Elmer Flexar instrument attached with diode array detector (deuterium lamp, 190-600 nm) with HPLC-grade isopropanol and hexanes as the eluting solvents. Analytical gas chromatography (GC) was performed using an Astec CHIRALDEX^{TM} B-DM column (30 m × 0.25 mm × 0.12 um) on a Perkin Elmer Clarus 500 instrument.

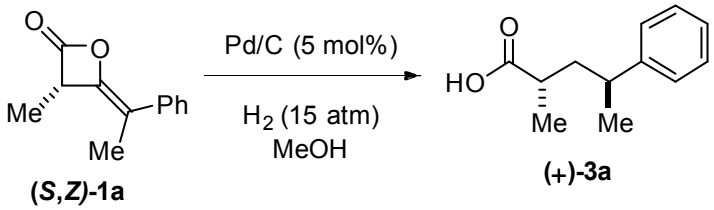
Compound Characterization and Determination of Diastereomeric Ratios and Enantiomeric Excesses: The acids **3** were purified by plug column chromatography through neutral silica or by acid-base extraction to provide samples of ≥95% purity for full characterization. Diastereomeric ratios were determined for the crude acids by GC-MS or ^{1}H NMR analysis. Enantiomeric excesses were determined by assaying the ester derivatives of acids **3a-3h** using chiral GC analysis or chiral HPLC analysis (at λ = 225 nm or 254 nm; details given for each compound). Racemic/scalemic samples for chiral HPLC or GC analysis were generated through mixing of enantiomerically enriched samples.

General procedure for catalytic hydrogenolysis: The *Z*-ketene heterodimer (1 equiv) in methanol (0.1 M) was added via pasteur pipette to the pressure device containing the 10 wt% Pd/C catalyst (0.05 equiv). While the inlet to the pressure device was closed and stirring commenced, minimum vacuum was applied to remove air inside the pressure device through its outlet. Then the outlet was closed, and hydrogen was transferred to the pressure device at 50 psi.

Minimum vacuum was applied again to remove hydrogen inside the pressure device through its outlet after the inlet was closed. This hydrogen flushing cycle was repeated twice to make sure that air was removed from the pressure device completely. Then, hydrogen was supplied at the pressure of 225 psi (15 atm) rapidly while the outlet was closed, and the inlet was also closed immediately. The reaction mixture was stirred at 1150 rpm at room temperature for the specified time for each example.

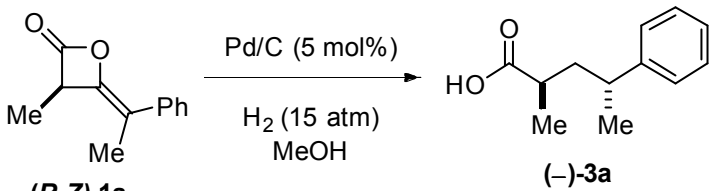
After the specified time, the pressure device was vented, and the mixture was filtered through celite (10 g), washing with dichloromethane (30-60 mL). The solvent was removed under reduced pressure. Acid-base extraction was then performed as follows: Water (10 mL/100 mg) was added to the reaction mixture and basified with aqueous NaOH (1N) solution to pH~12. The aqueous phase was extracted with dichloromethane (10 mL × 2) to remove undesired contaminants. The aqueous layer was then acidified with HCl (10N) to pH~2 and extracted with dichloromethane (20 mL × 3). The combined organic layers were washed with brine and dried over sodium sulfate. The solvent was removed under reduced pressure to afford desired product **3**.

Alternatively (instead of acid-base extraction), acid **3** was isolated after plug column chromatography (using normal 'acidic' silica; see details below).



(*S*,*Z*)-**1a** (+)-**3a**

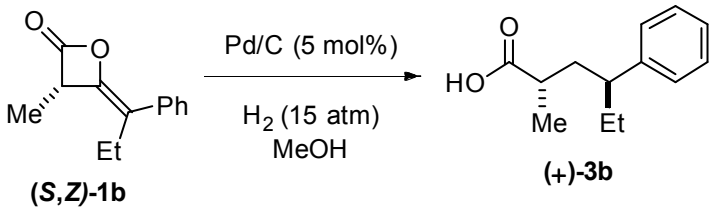
(2*S*,4*S*)-2-Methyl-4-phenylpentanoic acid [(+)-3a]: Following general procedure, the heterodimer (*S*,*Z*)-**1a** (71 mg, 0.38 mmol), of 95% ee and *Z*:*E* >20:1, in MeOH (3.8 mL) was added to the 10 wt% Pd/C catalyst (20 mg, 0.0188 mmol) (reaction time: 10 min). Acid-base extraction afforded **(+)-3a** as a colorless liquid (57 mg, 79%), dr = 4:1 (by GC-MS); GC analysis performed on methyl ester derivative from treatment with excess diazomethane solution: 96% ee [Supelco Chiraldex BDM column; GC Conditions: Split ratio: 1:20; make up flow: 25 mL/min; H_2 flow: 45 mL/min; air flow: 450 mL/min; injector temperature: 250 °C, pressure: 12.3-18.5 psi; oven temperature: 50-180 °C, 1 °C/min; detector temperature: 250 °C; retention times: 68.0 min (minor), 68.7 min (major)]; $[\alpha]_D^{24}$ = 26.0 (c = 0.08, CH_2Cl_2); IR (CH_2Cl_2): 3062, 3027, 2963, 2930, 1700, 1494, 1453, 1415, 1378, 1290, 1241, 939, 909, 761, 698, 549 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.36-7.30 (m, 2H), 7.26-7.20 (m, 3H), 2.90-2.78 (m, 1H), 2.43-2.29 (m, 1H), 2.10-1.99 (m, 1H), 1.73-1.63 (m, 1H), 1.29 (d, J = 6.9 Hz, 3H), 1.17 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.8, 146.7, 128.7, 127.3, 126.4, 42.6, 38.2, 37.9, 22.7, 18.0; $(M + H)^+$ HRMS m/z calcd for $(C_{12}H_{17}O_2)^+$: 193.1229; Found: 193.1222.



(*R*,*Z*)-**1a** (–)-**3a**

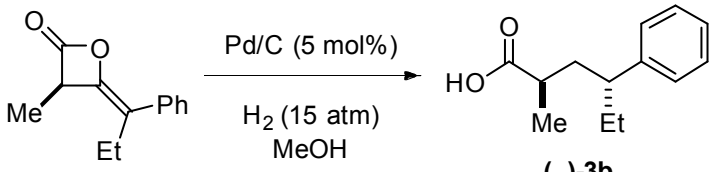
(2*R*,4*R*)-2-Methyl-4-phenylpentanoic acid [(–)-3a]: Following general procedure, the heterodimer (*R*,*Z*)-**1a** (35 mg, 0.19 mmol), of 93% ee and *Z*:*E* >20:1, in MeOH (1.9 mL) was added to the 10 wt% Pd/C catalyst (10 mg, 0.0094 mmol) (reaction time: 10 min). Acid-base extraction afforded **(–)-3a** as a colorless liquid (27 mg, 75%), dr = 4:1 (by GC-MS); GC analysis performed on methyl ester derivative from treatment with excess diazomethane solution: 94% ee [Supelco Chiraldex BDM column; GC Conditions: Split ratio: 1:20; make up flow: 25 mL/min; H_2 flow: 45 mL/min; air flow: 450 mL/min; injector temperature: 250 °C, pressure: 12.3-18.5 psi ; oven temperature: 50-180 °C, 1 °C/min; detector temperature: 250 °C; retention times: 68.2 min

(major), 68.8 min (minor)]; $[\alpha]_D^{24}$ = –40.0 (c = 0.32, CH_2Cl_2); IR (CH_2Cl_2): 3027, 2965, 2930, 1699, 1494, 1453, 1415, 1290, 1241, 1191, 938, 909, 761, 698, 549 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.33-7.26 (m, 2H), 7.23-7.15 (m, 3H), 2.87-2.73 (m, 1H), 2.40-2.25 (m, 1H), 2.06-1.95 (m, 1H), 1.70-1.58 (m, 1H), 1.25 (d, J = 7.0 Hz, 3H), 1.13 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.3, 146.7, 128.7, 127.3, 126.5, 42.6, 38.2, 37.8, 22.8, 18.0; $(M + H)^+$ HRMS m/z calcd for $(C_{12}H_{17}O_2)^+$: 193.1229; Found: 193.1221.



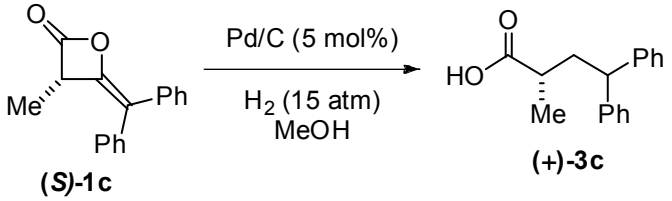
(*S*,*Z*)-1b **(+)-3b**

(2*S*,4*S*)-2-Methyl-4-phenylhexanoic acid [(+)-3b]: Following general procedure, the heterodimer (*S*,*Z*)-**1b** (23 mg, 0.11 mmol), of 98% ee and *Z*:*E* = 5:1, in MeOH (1.1 mL) was added to the 10 wt% Pd/C catalyst (6 mg, 0.0057 mmol) (reaction time: 1 h 45 min). Elution with 5%, and then 10% EtOAc/hexane through a plug column of silica gel afforded **(+)-3b** as a faint yellow gel-like liquid (17 mg, 73%), dr = 7:1 (by GC-MS); GC analysis performed on methyl ester derivative from treatment with excess diazomethane solution: 79% ee [Supelco Chiraldex BDM column; GC Conditions: Split ratio: 1:20; make up flow: 25 mL/min; H_2 flow: 45 mL/min; air flow: 450 mL/min; injector temperature: 250 °C, pressure: 12.3-18.5 psi ; oven temperature: 50-180 °C, 1 °C/min; detector temperature: 250 °C; retention times: 73.3 min (minor), 74.1 min (major)]; $[\alpha]_D^{24}$ = 29.7 (c = 0.15, CH_2Cl_2); IR (CH_2Cl_2): 3084, 3061, 3027, 2965, 2926, 2875, 1706, 1494, 1462, 1453, 1409, 1379, 1242, 1185, 1076, 1059, 757, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.39-7.26 (m, 2H), 7.26-7.12 (m, 3H), 2.60-2.47 (m, 1H), 2.36-2.23 (m, 1H), 2.18-2.04 (m, 1H), 1.80-1.52 (m, 3H), 1.14 (d, J = 7.0 Hz, 3H), 0.79 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.5, 144.9, 128.6, 128.1, 126.5, 46.1, 41.1, 37.6, 30.1, 18.5, 12.3; $(M + H)^+$ HRMS m/z calcd for $(C_{13}H_{19}O_2)^+$: 207.1385; Found: 207.1383.

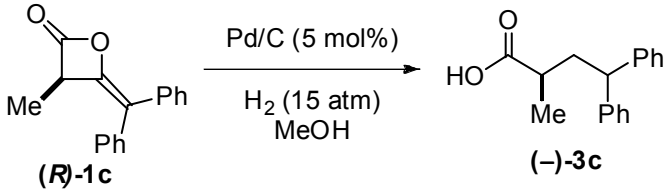


(*R*,*Z*)-1b **(–)-3b**

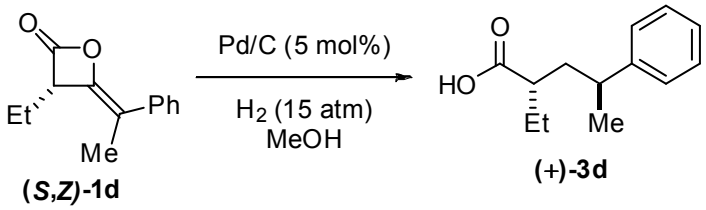
(2*R*,4*R*)-2-Methyl-4-phenylhexanoic acid [(–)-3b]: Following general procedure, the heterodimer (*R*,*Z*)-**1b** (31 mg, 0.15 mmol), of 73% ee and *Z*:*E* = 3:1, in MeOH (1.5 mL) was added to the 10 wt% Pd/C catalyst (8 mg, 0.0077 mmol) (reaction time: 2 h). Elution with 5%, and then 10% EtOAc/hexane through a plug column of silica gel afforded **(–)-3b** as a faint yellow gel-like liquid (17 mg, 55%), dr = 7:1 (by GC-MS); GC analysis performed on methyl ester derivative from treatment with excess diazomethane solution: 92% ee [Supelco Chiraldex BDM column; GC Conditions: Split ratio: 1:20; make up flow: 25 mL/min; H_2 flow: 45 mL/min; air flow: 450 mL/min; injector temperature: 250 °C, pressure: 12.3-18.5 psi ; oven temperature: 50-180 °C, 1 °C/min; detector temperature: 250 °C; retention times: 73.3 min (major), 73.9 min (minor)]; $[\alpha]_D^{24}$ = –15.0 (c = 0.01, CH_2Cl_2); IR (CH_2Cl_2): 3063, 3027, 2964, 2926, 2875, 1706, 1494, 1453, 1409, 1393, 1380, 1242, 1183, 1076, 1065, 757, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.35-7.26 (m, 2H), 7.25-7.14 (m, 3H), 2.58-2.47 (m, 1H), 2.34-2.23 (m, 1H), 2.15-2.05 (m, 1H), 1.75-1.52 (m, 3H), 1.13 (d, J = 7.0 Hz, 3H), 0.79 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.1, 144.9, 128.6, 128.1, 126.5, 46.1, 41.1, 37.5, 30.1, 18.5, 12.3; $(M + H)^+$ HRMS m/z calcd for $(C_{13}H_{19}O_2)^+$: 207.1385; Found: 207.1383.



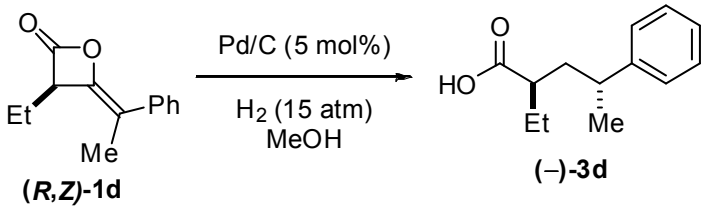
(*S*)-2-Methyl-4,4-diphenylbutanoic acid [(+)-3c]: Following general procedure, the heterodimer (*S*)-**1c** (44 mg, 0.18 mmol), of 96% ee, in MeOH (1.8 mL) was added to the 10 wt% Pd/C catalyst (9 mg, 0.0085 mmol) (reaction time: 1 h). Acid-base extraction afforded **(+)-3c** as a faint yellow gel (41 mg, 92%); HPLC analysis: 94% ee [Daicel Chiralpak AS-H column; 1.0 mL/min; solvent system: 5% isopropanol in hexane; retention time: 6.8 min (major), 10.5 min (minor)]; $[\alpha]_D^{24}$ = 30.0 (c = 0.54, CH_2Cl_2); IR (CH_2Cl_2): 3060, 3026, 2973, 2934, 1701, 1599, 1494, 1451, 1413, 1289, 1240, 1031, 915, 749, 698, 566 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.40-7.27 (m, 8H), 7.26-7.19 (m, 2H), 4.09 (t, J = 8.0 Hz, 1H), 2.66-2.54 (m, 1H), 2.48-2.37 (m, 1H), 2.20-2.09 (m, 1H), 1.27 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.1, 144.4, 144.2, 128.8, 128.8, 128.2, 128.1, 126.6, 126.6, 49.0, 39.5, 37.6, 17.4; $(M + H)^+$ HRMS m/z calcd for $(C_{17}H_{19}O_2)^+$: 255.1385; Found: 255.1362.



(*R*)-2-Methyl-4,4-diphenylbutanoic acid [(–)-3c]: Following general procedure, the heterodimer (*R*)-**1c** (45 mg, 0.18 mmol), of 96% ee, in MeOH (1.8 mL) was added to the 10 wt% Pd/C catalyst (9.6 mg, 0.009 mmol) (reaction time: 1 h). Elution with 10% EtOAc/hexane through a plug column of silica gel afforded **(–)-3c** as a colorless gel-like liquid (33 mg, 73%); HPLC analysis: 86% ee [Daicel Chiralpak AS-H column; 1.0 mL/min; solvent system: 5% isopropanol in hexane; retention time: 6.9 min (minor), 10.4 min (major)]; $[\alpha]_D^{24}$ = –34.3 (c = 0.40, CH_2Cl_2); IR (CH_2Cl_2): 3060, 3026, 2973, 2935, 1699, 1599, 1493, 1451, 1416, 1286, 1265, 1240, 1031, 916, 737, 696, 566 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.37-7.27 (m, 8H), 7.26-7.19 (m, 2H), 4.08 (t, J = 8.0 Hz, 1H), 2.65-2.53 (m, 1H), 2.48-2.35 (m, 1H), 2.20-2.08 (m, 1H), 1.26 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.0, 144.4, 144.2, 128.8, 128.8, 128.2, 128.1, 126.6, 126.6, 49.0, 39.5, 37.6, 17.4; $(M + H)^+$ HRMS m/z calcd for $(C_{17}H_{19}O_2)^+$: 255.1385; Found: 255.1377.

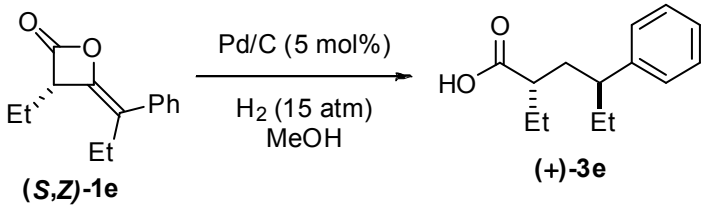


(2*S*,4*S*)-2-Ethyl-4-phenylpentanoic acid [(+)-3d]: Following general procedure, the heterodimer (*S*,*Z*)-**1d** (12 mg, 0.059 mmol), of 99% ee and *Z*:*E* >20:1, in MeOH (0.6 mL) was added to the 10 wt% Pd/C catalyst (3 mg, 0.003 mmol) (reaction time: 45 min). Acid-base extraction afforded **(+)-3d** as a faint yellow gel-like liquid (12 mg, 98%), dr = 4:1 (by ^1H NMR); GC analysis performed on methyl ester derivative from treatment with excess diazomethane solution: 96% ee [Supelco Chiraldex BDM column; GC Conditions: Split ratio: 1:20; make up flow: 25 mL/min; H_2 flow: 45 mL/min; air flow: 450 mL/min; injector temperature: 250 °C, pressure: 12.3-18.5 psi; oven temperature: 50-180 °C, 1 °C/min; detector temperature: 250 °C; retention times: 74.7 min (minor), 75.4 min (major)]; $[\alpha]_D^{24}$ = 32.1 (c = 0.24, CH_2Cl_2); IR (CH_2Cl_2): 3062, 3027, 2966, 2934, 2880, 1704, 1494, 1452, 1409, 1254, 1229, 1066, 1057, 763, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.37-7.29 (m, 2H), 7.27-7.18 (m, 3H), 2.88-2.73 (m, 1H), 2.22-2.10 (m, 1H), 2.07-1.94 (m, 1H), 1.79-1.58 (m, 2H), 1.58-1.44 (m, 1H), 1.30 (d, J = 7.0 Hz, 3H), 0.90 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 182.5, 146.6, 128.7, 127.4, 126.5, 45.2, 40.7, 38.5, 26.2, 23.2, 11.7; $(M + H)^+$ HRMS m/z calcd for $(C_{13}H_{19}O_2)^+$: 207.1385; Found: 207.1380.



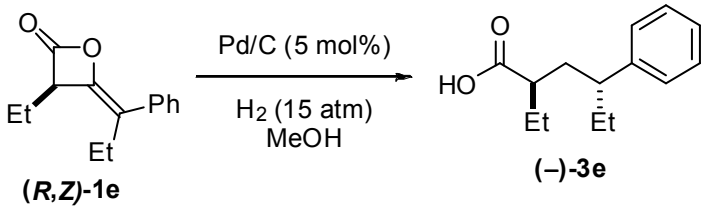
(*R*,*Z*)-**1d** (–)-**3d**

(2*R*,4*R*)-2-Ethyl-4-phenylpentanoic acid [(–)-3d]: Following general procedure, the heterodimer (*R*,*Z*)-**1d** (15 mg, 0.074 mmol), of 99% ee and *Z*:*E* >20:1, in MeOH (0.8 mL) was added to the 10 wt% Pd/C catalyst (4 mg, 0.0037 mmol) (reaction time: 30 min). Acid-base extraction afforded **(–)-3d** as a faint yellow gel-like liquid (13 mg, 87%), dr = 4:1 (by ^{1}H NMR); GC analysis performed on methyl ester derivative obtained from treatment with excess diazomethane solution: 95% ee [Supelco Chiraldex BDM column; GC Conditions: Split ratio: 1:20; make up flow: 25 mL/min; H_2 flow: 45 mL/min; air flow: 450 mL/min; injector temperature: 250 °C, pressure: 12.3-18.5 psi; oven temperature: 50-180 °C, 1 °C/min; detector temperature: 250 °C; retention times: 74.9 min (major), 75.3 min (minor)]; $[\alpha]_D^{24}$ = –40.6 (c = 0.25, CH_2Cl_2); IR (CH_2Cl_2): 3084, 3061, 3028, 2963, 2931, 2875, 1704, 1494, 1453, 1411, 1276, 1256, 1229, 1183, 763, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.38-7.29 (m, 2H), 7.27-7.18 (m, 3H), 2.87-2.73 (m, 1H), 2.21-2.09 (m, 1H), 2.06-1.94 (m, 1H), 1.79-1.68 (m, 1H), 1.68-1.57 (m, 1H), 1.57-1.45 (m, 1H), 1.29 (d, *J* = 6.9 Hz, 3H), 0.89 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 182.6, 146.7, 128.7, 127.4, 126.5, 45.3, 40.7, 38.5, 26.2, 23.2, 11.8; $(M + H)^+$ HRMS m/z calcd for $(C_{13}H_{19}O_2)^+$: 207.1385; Found: 207.1382.



(*S*,*Z*)-**1e** (+)-**3e**

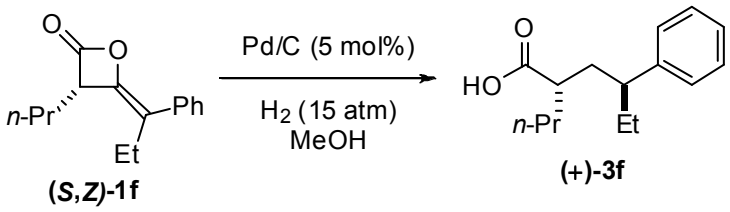
(2*S*,4*S*)-2-Ethyl-4-phenylhexanoic acid [(+)-3e]: Following general procedure, the heterodimer (*S*,*Z*)-**1e** (37 mg, 0.17 mmol), of 95% ee and *Z*:*E* = 6:1, in MeOH (1.8 mL) was added to the 10 wt% Pd/C catalyst (9 mg, 0.0086 mmol) (reaction time: 3 h 45 min). Elution with 2%, and then 5% EtOAc/hexane through a plug column of silica gel afforded **(+)-3e** as a faint yellow liquid (32 mg, 84%), dr = 9:1 (by GC-MS); GC analysis performed on methyl ester derivative obtained from treatment with excess diazomethane solution: 86% ee [Supelco Chiraldex BDM column; GC Conditions: Split ratio: 1:20; make up flow: 25 mL/min; H_2 flow: 45 mL/min; air flow: 450 mL/min; injector temperature: 250 °C, pressure: 12.3-18.5 psi ; oven temperature: 50-180 °C, 1 °C/min; detector temperature: 250 °C; retention times: 79.9 min (minor), 80.7 min (major)]; $[\alpha]_D^{24}$ = 17.1 (c = 0.04, CH_2Cl_2); IR (CH_2Cl_2): 3066, 3029, 2964, 2932, 2874, 1704, 1494, 1455, 1417, 1283, 1229, 759, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.35-7.29 (m, 2H), 7.26-7.14 (m, 3H), 2.56-2.42 (m, 1H), 2.17-1.99 (m, 2H), 1.76-1.55 (m, 4H), 1.55-1.41 (m, 1H), 0.87 (t, *J* = 7.4 Hz, 3H), 0.79 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.2, 144.9, 128.6, 128.1, 126.5, 46.3, 45.1, 39.0, 30.4, 26.4, 12.3, 11.7; $(M + H)^+$ HRMS m/z calcd for $(C_{14}H_{21}O_2)^+$: 221.1542; Found: 221.1538.



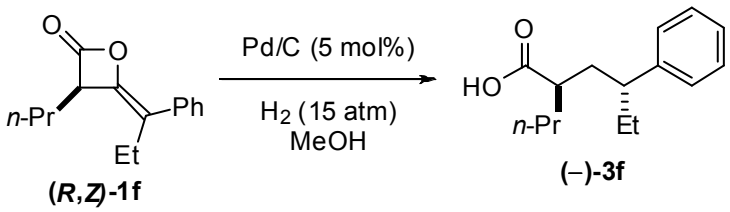
(*R*,*Z*)-**1e** (–)-**3e**

(2*R*,4*R*)-2-Ethyl-4-phenylhexanoic acid [(–)-3e]: Following general procedure, the heterodimer (*R*,*Z*)-**1e** (31 mg, 0.14 mmol), of 70% ee (*Z*) (and 86% ee for (*E*)) and *Z*:*E* = 10:1, in MeOH (1.5 mL) was added to the 10 wt% Pd/C catalyst (8 mg, 0.0075 mmol) (reaction time: 4 h 30 min). Elution with 1%, and then 5% EtOAc/hexane through a plug column of silica gel afforded **(–)-3e** as a faint yellow liquid

(26 mg, 83%), dr = 13:1 (by GC-MS); GC analysis performed on methyl ester derivative from treatment with excess diazomethane solution: 78% ee [Supelco Chiraldex BDM column; GC Conditions: Split ratio: 1:20; make up flow: 25 mL/min; H_2 flow: 45 mL/min; air flow: 450 mL/min; injector temperature: 250 °C, pressure: 12.3-18.5 psi ; oven temperature: 50-180 °C, 1 °C/min; detector temperature: 250 °C; retention times: 80.4 min (major), 80.7 min (minor)]; $[\alpha]_D^{24}$ = –7.0 (c = 0.14, CH_2Cl_2); IR (CH_2Cl_2): 3028, 2964, 2930, 2876, 1703, 1494, 1454, 1416, 1286, 1230, 949, 759, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.36-7.28 (m, 2H), 7.27-7.14 (m, 3H), 2.56-2.44 (m, 1H), 2.16-2.01 (m, 2H), 1.77-1.55 (m, 4H), 1.54-1.42 (m, 1H), 0.87 (t, J = 7.4 Hz, 3H), 0.79 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.5, 144.9, 128.6, 128.1, 126.4, 46.2, 45.1, 39.0, 30.4, 26.4, 12.3, 11.8; $(M + H)^+$ HRMS m/z calcd for $(C_{14}H_{21}O_2)^+$: 221.1542; Found: 221.1538.

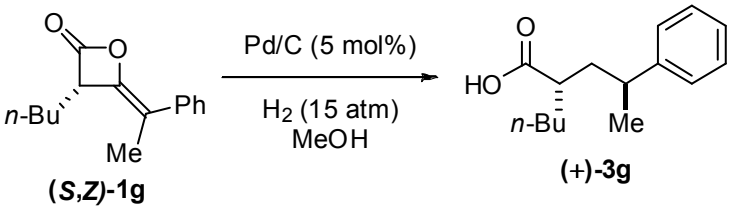


(2*S*,4*S*)-4-phenyl-2-propylhexanoic acid [(+)-3f]: Following general procedure, the heterodimer (*S*,*Z*)-**1f** (42 mg, 0.18 mmol), of 95% ee and *Z*:*E* = 4:1, in MeOH (1.9 mL) was added to the 10 wt% Pd/C catalyst (10 mg, 0.0091 mmol) (reaction time: 3 h). Elution with 2%, 3%, 4%, and then 5% EtOAc/hexane through a plug column of silica gel afforded **(+)-3f** as a faint yellow liquid (19 mg, 45%), dr > 20:1 (by GC-MS); GC analysis performed on methyl ester derivative obtained from treatment with excess diazomethane solution: 99% ee [Supelco Chiraldex BDM column; GC Conditions: Split ratio: 1:20; make up flow: 25 mL/min; H_2 flow: 45 mL/min; air flow: 450 mL/min; injector temperature: 250 °C, pressure: 14.7 psi ; oven temperature: 100 °C, isocratic; detector temperature: 250 °C; retention times: 135.8 min (minor), 140.9 min (major)]; $[\alpha]_D^{24}$ = 44.6 (c = 0.066, CH_2Cl_2); IR (CH_2Cl_2): 3062, 3028, 2959, 2930, 2874, 1702, 1494, 1453, 1284, 1243, 758, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.33-7.26 (m, 2H), 7.23-7.17 (m, 1H), 7.17-7.11 (m, 2H), 2.55-2.40 (m, 1H), 2.20-2.09 (m, 1H), 2.08-1.96 (m, 1H), 1.73-1.62 (m, 2H), 1.62-1.49 (m, 2H), 1.43-1.31 (m, 1H), 1.31-1.19 (m, 2H), 0.81 (t, J = 7.2 Hz, 3H), 0.77 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.5, 144.9, 128.6, 128.1, 126.4, 46.2, 43.3, 39.3, 35.5, 30.4, 20.5, 14.1, 12.3; $(M + H)^+$ HRMS m/z calcd for $(C_{15}H_{23}O_2)^+$: 235.1698; Found: 235.1694.

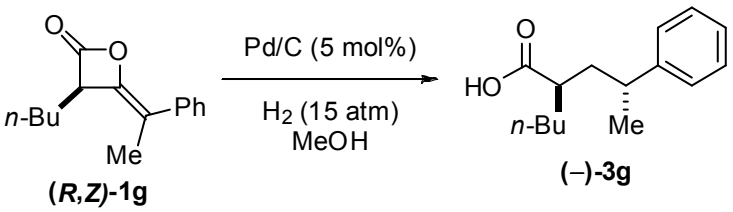


(2*R*,4*R*)-4-phenyl-2-propylhexanoic acid [(–)-3f]: Following general procedure, the heterodimer (*R*,*Z*)-**1f** (84 mg, 0.37 mmol), of 72% ee and *Z*:*E* = 6:1, in MeOH (3.7 mL) was added to the 10 wt% Pd/C catalyst (19 mg, 0.018 mmol) (reaction time: 3 h). Elution with 2%, 3%, 4%, and then 5% EtOAc/hexane through a plug column of silica gel afforded **(–)-3f** as a faint yellow liquid (56 mg, 66%), dr > 20:1 (by GC-MS); GC analysis performed on methyl ester derivative from treatment with excess diazomethane solution: 80% ee [Supelco Chiraldex BDM column; GC Conditions: Split ratio: 1:20; make up flow: 25 mL/min; H_2 flow: 45 mL/min; air flow: 450 mL/min; injector temperature: 250 °C, pressure: 14.7 psi ; oven temperature: 100 °C, isocratic; detector temperature: 250 °C; retention times: 137.6 min (major), 139.5 min (minor)]; $[\alpha]_D^{24}$ = –23.3 (c = 0.21, CH_2Cl_2); IR (CH_2Cl_2): 2959, 2928, 2873, 1702, 1453, 1283, 1240, 1216, 1181, 758, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.33-7.26 (m, 2H), 7.23-7.16 (m, 1H), 7.16-7.11 (m, 2H), 2.55-2.41 (m, 1H), 2.19-2.09 (m, 1H), 2.07-1.96 (m, 1H), 1.73-1.61 (m, 2H), 1.61-1.50 (m, 2H), 1.42-1.31 (m, 1H), 1.31-1.19 (m, 2H), 0.81 (t, J = 7.2 Hz, 3H), 0.77 (t, J = 7.4 Hz, 3H); ^{13}C

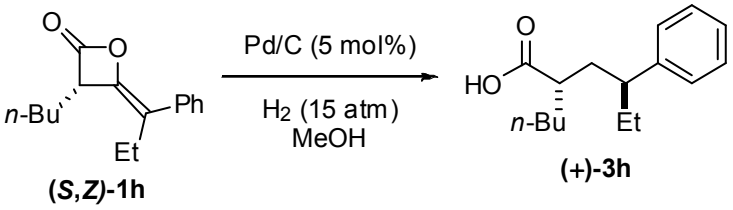
NMR (100 MHz, $CDCl_3$): δ 183.1, 144.8, 128.6, 128.1, 126.4, 46.2, 43.4, 39.3, 35.5, 30.4, 20.5, 14.1, 12.3; $(M + H)^+$ HRMS m/z calcd for $(C_{15}H_{23}O_2)^+$: 235.1698; Found: 235.1693.



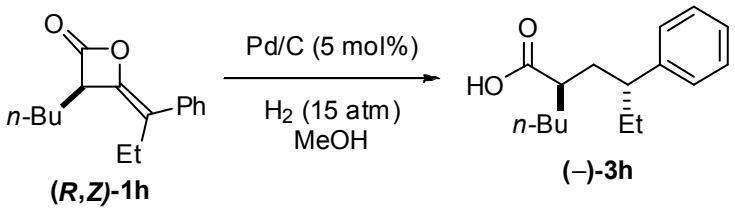
(*S*)-2-((*S*)-2-phenylpropyl)hexanoic acid [(+)-3g]: Following general procedure, the heterodimer (*S*,*Z*)-**1g** (63 mg, 0.27 mmol), of 94% ee and *Z*:*E* >20:1, in MeOH (2.8 mL) was added to the 10 wt% Pd/C catalyst (15 mg, 0.014 mmol) (reaction time: 2 h 15 min). Acid-base extraction afforded **(+)-3g** as a faint yellow liquid (51 mg, 79%), dr >20:1 (by GC-MS); $[\alpha]_D^{24}$ = 30.2 (c = 0.13, CH_2Cl_2); IR (CH_2Cl_2): 3028, 2957, 2930, 2872, 1703, 1494, 1453, 1290, 1240, 762, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.34-7.25 (m, 2H), 7.23-7.15 (m, 3H), 2.83-2.69 (m, 1H), 2.22-2.10 (m, 1H), 2.01-1.90 (m, 1H), 1.76-1.65 (m, 1H), 1.65-1.49 (m, 1H), 1.47-1.36 (m, 1H), 1.36-1.14 (m, 7H), 0.95-0.79 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.3, 146.6, 128.7, 127.4, 126.4, 43.8, 41.0, 38.5, 32.8, 29.5, 23.2, 22.8, 14.1; $(M + H)^+$ HRMS m/z calcd for $(C_{15}H_{23}O_2)^+$: 235.1698; Found: 235.1695.



(*R*)-2-((*R*)-2-phenylpropyl)hexanoic acid [(–)-3g]: Following general procedure, the heterodimer (*R*,*Z*)-**1g** (68 mg, 0.30 mmol), of 74% ee and *Z*:*E* >20:1, in MeOH (3.0 mL) was added to the 10 wt% Pd/C catalyst (16 mg, 0.015 mmol) (reaction time: 2 h 15 min). Acid-base extraction afforded **(–)-3g** as a faint yellow liquid (50 mg, 72%), dr >20:1 (by GC-MS); $[\alpha]_D^{24}$ = –23.8 (c = 0.12, CH_2Cl_2); IR (CH_2Cl_2): 3028, 2957, 2930, 2860, 1703, 1454, 1417, 1290, 1240, 762, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.34-7.25 (m, 2H), 7.23-7.15 (m, 3H), 2.83-2.69 (m, 1H), 2.23-2.11 (m, 1H), 2.02-1.90 (m, 1H), 1.76-1.64 (m, 1H), 1.64-1.49 (m, 1H), 1.47-1.36 (m, 1H), 1.36-1.16 (m, 7H), 0.93-0.79 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.5, 146.6, 128.7, 127.4, 126.5, 43.7, 41.0, 38.5, 32.8, 29.5, 23.2, 22.8, 14.1; $(M + H)^+$ HRMS m/z calcd for $(C_{15}H_{23}O_2)^+$: 235.1698; Found: 235.1693.

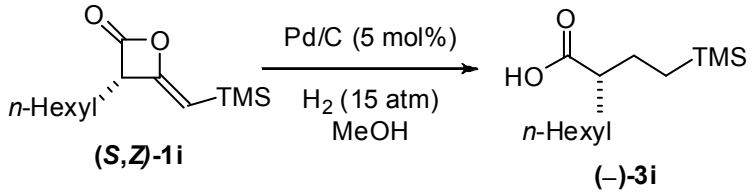


(2*S*,4*S*)-2-butyl-4-phenylhexanoic acid [(+)-3h]: Following general procedure, the heterodimer (*S*,*Z*)-**1h** (85 mg, 0.35 mmol), of 95% ee and *Z*:*E* = 4:1, in MeOH (3.5 mL) was added to the 10 wt% Pd/C catalyst (19 mg, 0.017 mmol) (reaction time: 3 h). Elution with 2%, 3%, 4%, and then 5% EtOAc/hexane through a plug column of silica gel afforded **(+)-3h** as a faint yellow liquid (59 mg, 68%), dr >20:1 (by GC-MS); $[\alpha]_D^{24}$ = 26.6 (c = 0.49, CH_2Cl_2); IR (CH_2Cl_2): 3028, 2959, 2930, 2874, 1704, 1494, 1454, 1288, 1241, 758, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.34-7.26 (m, 2H), 7.23-7.17 (m, 1H), 7.17-7.11 (m, 2H), 2.55-2.40 (m, 1H), 2.18-2.08 (m, 1H), 2.08-1.97 (m, 1H), 1.73-1.62 (m, 2H), 1.62-1.50 (m, 2H), 1.44-1.32 (m, 1H), 1.32-1.13 (m, 4H), 0.83 (t, *J* = 6.9 Hz, 3H), 0.77 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.9, 144.9, 128.6, 128.1, 126.4, 46.3, 43.6, 39.4, 33.1, 30.4, 29.5, 22.8, 14.1, 12.3; $(M + H)^+$ HRMS m/z calcd for $(C_{16}H_{25}O_2)^+$: 249.1855; Found: 249.1852.



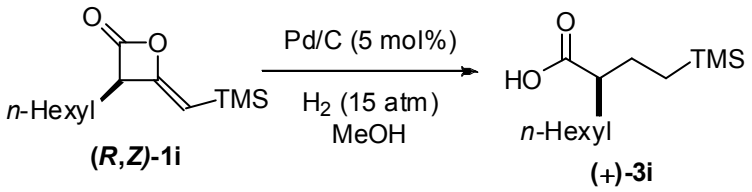
(*R*,*Z*)-**1h** (–)-**3h**

(2*R*,4*R*)-2-butyl-4-phenylhexanoic acid [(–)-3h]: Following general procedure, the heterodimer (*R*,*Z*)-**1h** (46 mg, 0.19 mmol), of 76% ee and *Z*:*E* = 4:1, in MeOH (1.9 mL) was added to the 10 wt% Pd/C catalyst (10 mg, 0.0094 mmol) (reaction time: 3 h). Elution with 2%, 3%, 4%, 5%, and then 10% EtOAc/hexane through a plug column of silica gel afforded **(–)-3h** as a faint yellow liquid (25 mg, 54%), dr >20:1 (by GC-MS); $[\alpha]_D^{24}$ = –18.3 (c = 0.06, CH_2Cl_2); IR (CH_2Cl_2): 3028, 2958, 2928, 2873, 1703, 1454, 1289, 1240, 758, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.37-7.24 (m, 2H), 7.23-7.17 (m, 1H), 7.17-7.11 (m, 2H), 2.55-2.40 (m, 1H), 2.18-2.07 (m, 1H), 2.07-1.96 (m, 1H), 1.73-1.62 (m, 2H), 1.62-1.50 (m, 2H), 1.44-1.32 (m, 1H), 1.32-1.13 (m, 4H), 0.83 (t, *J* = 6.8 Hz, 3H), 0.77 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.5, 144.9, 128.6, 128.1, 126.4, 46.3, 43.6, 39.4, 33.1, 30.4, 29.5, 22.8, 14.1, 12.3; $(M + H)^+$ HRMS m/z calcd for $(C_{16}H_{25}O_2)^+$: 249.1855; Found: 249.1851.



(*S*,*Z*)-**1i** (–)-**3i**

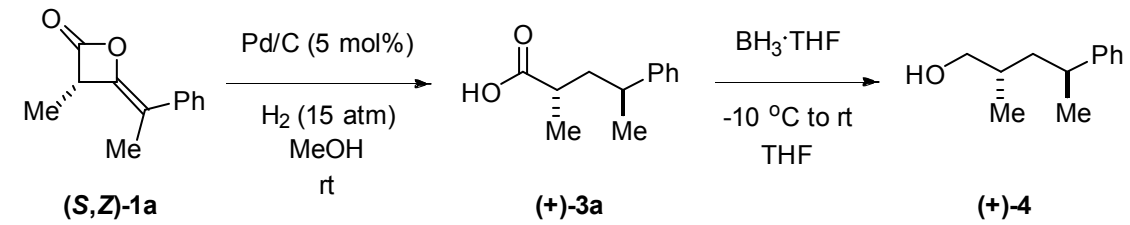
(*S*)-2-(2-(Trimethylsilyl)ethyl)octanoic acid [(–)-3i]: Following general procedure, the heterodimer (*S*,*Z*)-**1i** (24 mg, 0.10 mmol), of 95% ee and *Z*:*E* >20:1, in MeOH (1.0 mL) was added to the 10 wt% Pd/C catalyst (5 mg, 0.0047 mmol) (reaction time: 30 min). Elution with 1%, and then 5% EtOAc/hexane through a plug column of silica gel afforded **(–)-3i** as a colorless oil (17 mg, 71%); $[\alpha]_D^{24}$ = –3.1 (c = 0.03, CH_2Cl_2); IR (CH_2Cl_2): 2954, 2925, 2857, 1705, 1456, 1414, 1288, 1248, 941, 860, 836, 755, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 2.40-2.27 (m, 1H), 1.71-1.58 (m, 2H), 1.58-1.44 (m, 2H), 1.40-1.20 (m, 8H), 0.95-0.84 (m, 3H), 0.58-0.48 (m, 2H), 0.01 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.1, 48.8, 32.0, 31.9, 29.5, 27.6, 26.9, 22.8, 14.4, 14.3, -1.6; $(M + H)^+$ HRMS m/z calcd for $(C_{13}H_{29}O_2Si)^+$: 245.1937; Found: 245.1939.

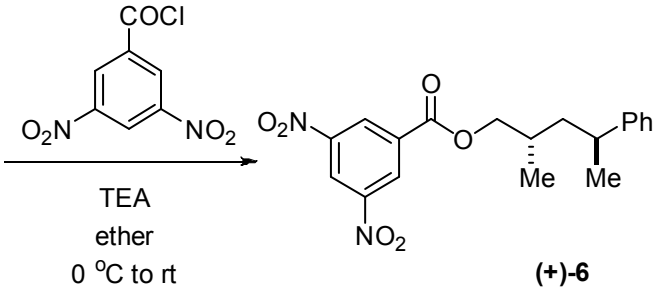


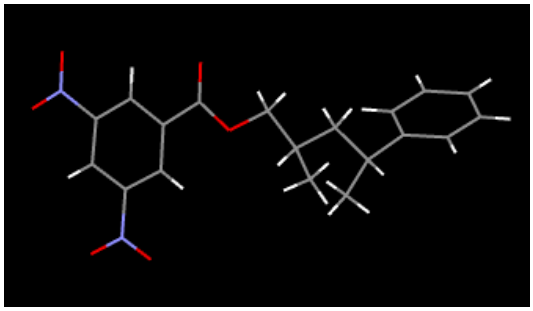
(*R*,*Z*)-**1i** (+)-**3i**

(*R*)-2-(2-(Trimethylsilyl)ethyl)octanoic acid [(+)-3i]: Following general procedure, the heterodimer (*R*,*Z*)-**1i** (36 mg, 0.15 mmol), of 97% ee and *Z*:*E* >20:1, in MeOH (1.5 mL) was added to the 10 wt% Pd/C catalyst (8 mg, 0.0075 mmol) (reaction time: 30 min). Elution with 1%, and then 5% EtOAc/hexane through a plug column of silica gel afforded **(+)-3i** as a colorless oil (26 mg, 70%); $[\alpha]_D^{24}$ = 10.7 (c = 0.04, CH_2Cl_2); IR (CH_2Cl_2): 2954, 2925, 2857, 1703, 1455, 1416, 1287, 1248, 940, 858, 835, 754, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 2.37-2.24 (m, 1H), 1.69-1.55 (m, 2H), 1.55-1.42 (m, 2H), 1.36-1.20 (m, 8H), 0.92-0.84 (m, 3H), 0.56-0.46 (m, 2H), -0.01 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.8, 48.9, 31.9, 31.9, 29.5, 27.6, 26.9, 22.8, 14.4, 14.3, -1.6; $(M + H)^+$ HRMS m/z calcd for $(C_{13}H_{29}O_2Si)^+$: 245.1937; Found: 245.1936.

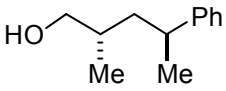
Preparation of (+)-4 and sample for X-ray structure analysis:



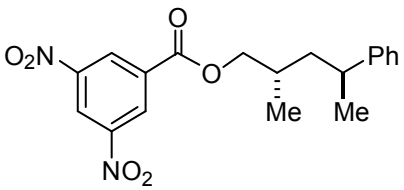




X-Ray structure of **(+)-6**



(2*S*,4*S*)-2-methyl-4-phenylpentan-1-ol [(+)-4]: BH_3·THF (0.67 mL, 1.0 M in THF) was added dropwise to an ice-salt cooled (–10 °C) solution of **(+)-3a** (82 mg, 0.43 mmol, 96% ee and dr = 4:1) in THF (1.3 mL). The reaction mixture was allowed to warm to room temperature overnight. The reaction was quenched with an aqueous solution of acetic acid (50%, 5 drops) at 0 °C, then diluted with EtOAc (100 mL), washed with saturated $NaHCO_3$ (30 mL x 2), and brine (30 mL x 2). The organic layer was dried over sodium sulfate. Removal of the solvent under reduced pressure followed by silica gel column chromatographic purification using 5% EtOAc/hexane afforded **(+)-4** as a colorless liquid (71 mg, 93%); dr = 4:1 (by GC-MS); $[\alpha]_D^{24}$ = 3.0 (c = 0.30, CH_2Cl_2); IR (CH_2Cl_2): 3346, 3083, 3061, 3026, 2959, 2923, 2871, 1493, 1452, 1377, 1092, 1035, 1007, 761, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.37-7.27 (m, 2H), 7.26-7.18 (m, 3H), 3.62-3.32 (m, 2H), 2.93-2.78 (m, 1H), 1.71-1.63 (m, 1H), 1.52-1.31 (m, 2H), 1.25 (d, J = 6.9 Hz, 3H), 0.93 (d, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 148.2, 128.6, 127.1, 126.1, 68.4, 42.2, 37.4, 33.8, 22.5, 17.2; $(M + H)^+$ HRMS m/z calcd for $(C_{12}H_{19}O)^+$: 179.1436; Found: 179.1437.



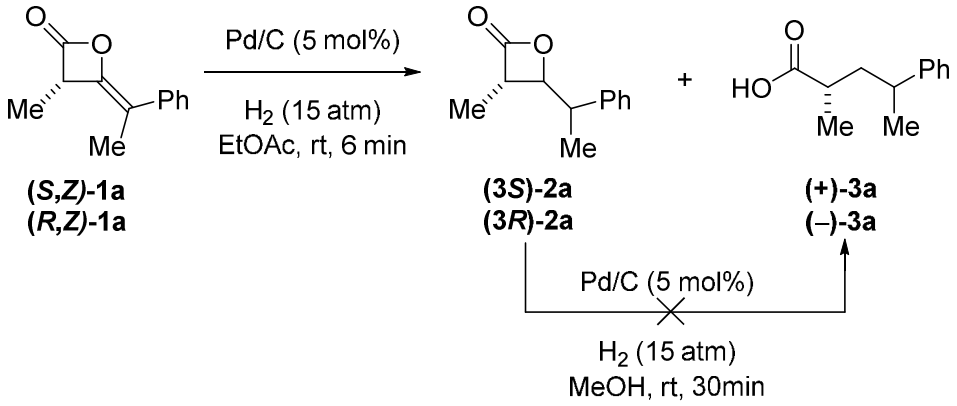
(2*S*,4*S*)-2-methyl-4-phenylpentyl 3,5-dinitrobenzoate [(+)-6]: Et_3N (15 mg, 0.15 mmol) was added to a solution of **(+)-4** (22 mg, 0.12 mmol, dr = 4:1) in ether (0.3 mL), and the mixture was cooled to 0 °C. 3,5-Dinitrobenzoyl chloride (35 mg, 0.15 mmol) in ether (0.5 mL) was added dropwise to the reaction. The reaction mixture was warmed up slowly to rt and stirred for an additional 2 h. The reaction was then diluted with EtOAc (80 mL), and washed with brine (30 mL x 2). The organic layer was dried over sodium sulfate. Removal of the solvent under reduced pressure followed by silica gel column chromatographic purification using 5%, and 10% EtOAc/hexane afforded **(+)-6** as a white solid (44 mg, 95%); mp: 92-95 °C; dr = 6:1 (by GC-MS); $[\alpha]_D^{24}$ = 6.5 (c = 0.116, CH_2Cl_2); IR (CH_2Cl_2): 2963, 1731, 1545, 1344, 1277, 1169, 765,

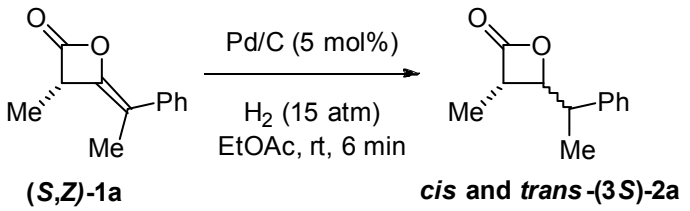
730, 721, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 9.26-9.21 (m, 1H), 9.16-9.08 (m, 2H), 7.34-7.27 (m, 2H), 7.24-7.15 (m, 3H), 4.39-4.21 (m, 2H), 2.93-2.80 (m, 1H), 2.03-1.91 (m, 1H), 1.75-1.52 (m, 2H), 1.27 (d, J = 6.9 Hz, 3H), 1.04 (d, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 162.8, 149.0, 147.3, 134.4, 129.6, 128.8, 127.1, 126.5, 122.6, 71.7, 42.3, 37.5, 30.9, 22.7, 17.8; $(M)^+$ LRMS m/z calcd for $(C_{19}H_{20}N_2O_6)^+$: 372; Found: 372, 195, 159, 145, 118 and 105.

Determination of Relative and Absolute Stereochemistry:

A colorless solution of pure **(+)-6** in acetone/hexane (1:8) was prepared. Crystals suitable for X-ray structure analysis were obtained from this on standing. The relative stereochemistry of **(+)-6** was determined by X-ray structure analysis to be the *anti*-isomer, and hence the absolute configuration was assigned to be (2*S*,4*S*). By analogy, all acids synthesized from (*S*,*Z*)-heterodimers were assigned the (2*S*,4*S*)-*anti* configuration. Similarly, all acids synthesized from (*R*,*Z*)-heterodimers were assigned the (2*R*,4*R*)-*anti* configuration.

Mechanistic experiments:

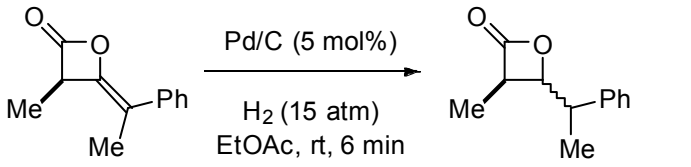




(3*S*)-3-Methyl-4-(1-phenylethyl)oxetan-2-one [(3*S*)-2a]: Following general procedure, **(*S*,*Z*)-1a** (80 mg, 0.42 mmol), of 95% ee and *Z*:*E* >20:1, in EtOAc (4.5 mL) was added to the 10 wt% Pd/C catalyst (23 mg, 0.021 mmol) (reaction time: 6 min). Crude NMR analysis showed formation of β-lactone **2a** (as a 1.3:1 isomeric mixture) and acid **3a** (as a 1.2:1 isomeric mixture) as a 1:2 mixture (favoring the acid **3a**). The crude reaction mixture was treated with excess diazomethane solution in ether to convert undesired acid to corresponding nonpolar ester for easy column purification of β-lactone. Elution with 1% to 5% EtOAc/hexane through a plug column of neutral silica gel afforded **2a** as a colorless gel-like liquid (composed of 10 mg of pure *trans*-isomer, 8 mg of pure *cis*-isomer and 6 mg of mixture of isomers, 30%)[5,6]; ***trans*-isomer**; GC analysis: 96% ee [Supelco Chiraldex BDM column; GC Conditions: Split ratio: 1:20; make up flow: 25 mL/min; H_2 flow: 45 mL/min; air flow: 450 mL/min; injector temperature: 250 °C, pressure: 12.3-18.5 psi; oven temperature: 50-180 °C, 1 °C/min; detector temperature: 250 °C; retention times: 84.55 min (major), 86.16 min (minor)]; $[\alpha]_D^{24}$ = –18.2 (c = 1.0, CH_2Cl_2); IR (CH_2Cl_2): 3030, 2969, 2932, 1822, 1454, 1121, 867 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.38-7.31 (m, 2H), 7.31-7.26 (m, 1H), 7.23-7.18 (m, 2H), 4.20 (dd, J = 9.0, 4.2 Hz, 1H), 3.25-3.15 (m, 1H), 3.04-2.94 (m, 1H), 1.43 (d, J = 6.7 Hz, 3H), 1.11 (d, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8, 140.8, 129.2,

127.7, 127.7, 83.1, 50.0, 44.6, 17.9, 12.7; $(M+H)^+$ HRMS m/z calcd for $(C_{12}H_{15}O_2)^+$: 191.1072; Found: 191.1075.

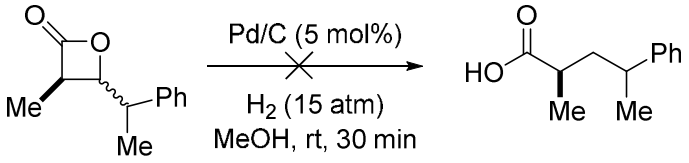
***cis*-isomer**; GC analysis: 95% ee [Supelco Chiraldex BDM column; GC Conditions: Split ratio: 1:20; make up flow: 25 mL/min; H_2 flow: 45 mL/min; air flow: 450 mL/min; injector temperature: 250 °C, pressure: 12.3-18.5 psi ; oven temperature: 50-180 °C, 1 °C/min; detector temperature: 250 °C; retention times: 94.30 min (major), 95.71 min (minor)]; $[\alpha]_D^{24}$ = +1.87 (c = 0.8, CH_2Cl_2); IR (CH_2Cl_2): 2928, 2873, 1821, 1456, 1116, 872, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.37-7.30 (m, 2H), 7.28-7.22 (m, 1H), 7.20-7.15 (m, 2H), 4.76 (dd, J = 10.8, 6.3 Hz, 1H), 3.72-3.61 (m, 1H), 3.16-3.05 (m, 1H), 1.40 (d, J = 6.8 Hz, 3H), 1.08 (d, J = 7.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.7, 141.9, 129.2, 127.6, 127.4, 78.8, 47.7, 40.9, 20.7, 9.3; $(M+H)^+$ HRMS m/z calcd for $(C_{12}H_{15}O_2)^+$: 191.1072; Found: 191.1069.



(*R*,*Z*)-**1a** *cis* and *trans*-(3*R*)-**2a**

(3*R*)-3-Methyl-4-(1-phenylethyl)oxetan-2-one [(3*R*)-2a]: Following general procedure, **(*R*,*Z*)-1a** (150 mg, 0.79 mmol), of 93% ee and *Z*:*E* >20:1, in EtOAc (8 mL) was added to the 10 wt% Pd/C catalyst (42 mg, 0.039 mmol) (reaction time: 6 min). Crude NMR showed formation of β-lactone **2a** (as a 1.5:1 isomeric mixture of diastereomers) and acid **3a** (as 1.2:1 mixture of diastereomers) as 1:3 mixture (favoring the acid **3a**). The crude reaction mixture was treated with excess diazomethane solution in ether to convert undesired acid to corresponding nonpolar ester for easy column purification of β-lactone. Elution with 1% to 5% EtOAc/hexane through a plug column of neutral silica gel afforded **2a** as a colorless gel-like liquid (21 mg of *trans*-isomer and 17 mg of *cis*-isomer, 25%)[5,6]; ***trans*-isomer**; GC analysis: 92% ee [Supelco Chiraldex BDM column; GC Conditions: Split ratio: 1:20; make up flow: 25 mL/min; H_2 flow: 45 mL/min; air flow: 450 mL/min; injector temperature: 250 °C, pressure: 12.3-18.5 psi ; oven temperature: 50-180 °C, 1 °C/min; detector temperature: 250 °C; retention times: 84.67 min (minor), 85.20 min (major)]; $[\alpha]_D^{24}$ = 37.9 (c = 2.1, CH_2Cl_2); IR (CH_2Cl_2): 3030, 2974, 2937, 2878, 1820, 1455, 1119, 870, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.37-7.31 (m, 2H), 7.30-7.24 (m, 1H), 7.23-7.18 (m, 2H), 4.20 (dd, J = 8.9, 4.0 Hz, 1H), 3.25-3.15 (m, 1H), 3.04-2.94 (m, 1H), 1.43 (d, J = 6.8 Hz, 3H), 1.11 (d, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8, 140.7, 129.1, 127.7, 127.7, 83.0, 49.9, 44.6, 17.9, 12.7; $(M+H)^+$ HRMS m/z calcd for $(C_{12}H_{15}O_2)^+$: 191.1072; Found: 191.1068.

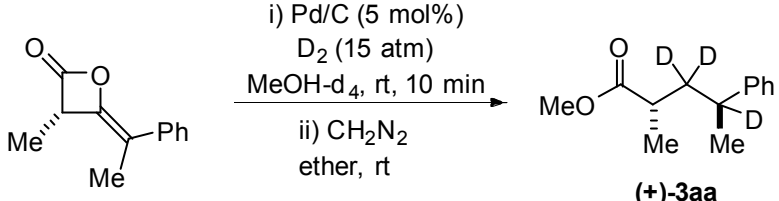
***cis*-isomer**; GC analysis: 93% ee [Supelco Chiraldex BDM column; GC Conditions: Split ratio: 1:20; make up flow: 25 mL/min; H_2 flow: 45 mL/min; air flow: 450 mL/min; injector temperature: 250 °C, pressure: 12.3-18.5 psi ; oven temperature: 50-180 °C, 1 °C/min; detector temperature: 250 °C; retention times: 94.17 min (minor), 94.63 min (major)]; $[\alpha]_D^{24}$ = –0.70 (c = 1.7, CH_2Cl_2); IR (CH_2Cl_2): 2974, 2937, 2877, 1822, 1456, 1120, 870, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.38-7.30 (m, 2H), 7.28-7.22 (m, 1H), 7.21-7.15 (m, 2H), 4.76 (dd, J = 10.9, 6.2 Hz, 1H), 3.72-3.62 (m, 1H), 3.16-3.05 (m, 1H), 1.40 (d, J = 6.8 Hz, 3H), 1.08 (d, J = 7.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.7, 141.9, 129.2, 127.6, 127.4, 78.8, 47.7, 40.9, 20.7, 9.3; $(M+H)^+$ HRMS m/z calcd for $(C_{12}H_{15}O_2)^+$: 191.1072; Found: 191.1076.



***cis* and *trans*-(3*R*)-2a** **(*R*)-3a**

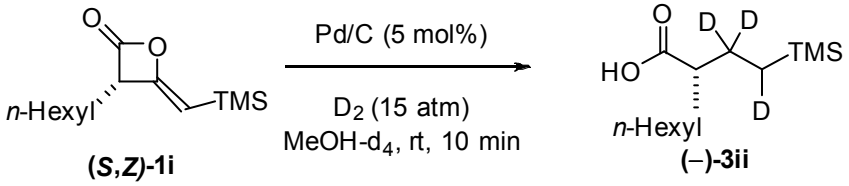
Following general procedure, ***trans*-diastereomer** of **(*3R*)-2a** (18 mg, 0.09 mmol), of 92% ee, in MeOH (1 mL) was added to the 10 wt% Pd/C catalyst (5 mg, 0.005 mmol) (reaction time: 30 min). TLC and GCMS analysis of the crude product showed presence of starting ***trans*-(*3R*)-2a**, and no desired product.

Following general procedure, ***cis*-diastereomer** of **(*3R*)-2a** (15 mg, 0.078 mmol), of 93% ee, in MeOH (0.8 mL) was added to the 10 wt% Pd/C catalyst (4 mg, 0.004 mmol) (reaction time: 30 min). TLC and GCMS analysis of the crude product showed presence of starting ***cis*-(*3R*)-2a**, and no desired product.



(*S*,*Z*)-1a **(+)-3aa**

(2*S*,4*S*)-methyl 3,3,4-trideutero-2-methyl-4-phenylpentanoate [(+)-3aa]: Following general procedure, **(*R*,*Z*)-1a** (20 mg, 0.106 mmol), of 93% ee and *Z*:*E* >20:1, in MeOH-d_4 (1 mL) was added to the 10 wt% Pd/C catalyst (6 mg, 0.005 mmol), D_2 (15 atm), (reaction time: 10 min). The crude reaction mixture (20 mg) was treated with excess of diazomethane solution in ether at room temperature. Removal of the solvent followed by silica gel column chromatographic purification using 2% EtOAc/hexane afforded **(+)-3aa** as a colorless volatile liquid (10 mg, 45% in two steps), dr = 3:1 (by NMR); $[\alpha]_D^{24}$ = 69.8 (c = 1, CH_2Cl_2); IR (CH_2Cl_2): 3025, 2958, 2933, 2875, 1735, 1435, 1198, 1170, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.32-7.26 (m, 2H), 7.22-7.14 (m, 3H), 3.66 (s, 3H), 2.35-2.24 (m, 1H), 1.22 (s, 3H), 1.09 (d, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 177.5, 147.0, 128.7, 127.3, 126.4, 51.7, 37.8, 37.6, 22.6, 18.1, 17.2; $(M+H)^+$ HRMS m/z calcd for $(C_{13}H_{16}D_3O_2)^+$: 210.1573; Found: 210.1571.



(*S*,*Z*)-1i **(–)-3ii**

(*S*)-2-(1,1,2-trideutero-2-(trimethylsilyl)ethyl)octanoic acid [(–)-3ii]: Following general procedure, the **(*S*,*Z*)-1i** (43 mg, 0.18 mmol), of 95% ee and *Z*:*E* >20:1, in MeOH-d_4 (1.8 mL) was added to the 10 wt% Pd/C catalyst (9.5 mg, 0.0089 mmol), D_2 (15 atm), (reaction time: 10 min). Elution with 1%, and then 5% EtOAc/hexane through a plug column of neutral silica gel afforded **(–)-3ii** as a colorless oil (39 mg, 88%), dr = 3:1 (by NMR); $[\alpha]_D^{24}$ = –0.708 (c = 2.4, CH_2Cl_2); IR (CH_2Cl_2): 2954, 2925, 2857, 1702, 1416, 1248, 841 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 12.02 (bs, 1H), 2.38-2.25 (m, 1H), 1.69-1.55 (m, 1H), 1.55-1.43

(m, 1H), 1.37-1.20 (m, 8H), 0.93-0.84 (m, 3H), 0.55-0.45 (m, 1H), 0.01 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 183.4, 48.8, 31.9, 31.9, 29.5, 27.6, 27.6, 22.9, 14.3, 14.3, -1.6; $(M + H)^+$ HRMS m/z calcd for $(C_{13}H_{26}D_3O_2Si)^+$: 248.2125; Found: 248.2120.

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