Enantioselective Iodolactonization to Prepare ε-Lactone Rings Using Hypervalent Iodine

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General Experimental Procedures

All reagents and solvents were commercial grade and purified prior to use when necessary. Acetonitrile (MeCN), tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), and toluene (PhMe) were dried by passage through a column of activated alumina as described by Grubbs.[1] All organic layers collected from extractions were dried over $MgSO_4$ unless otherwise indicated.

Thin layer chromatography (TLC) was performed using glass-backed silica gel (250 μm) plates and flash chromatography utilized 230–400 mesh silica gel from Sorbent Technologies. UV light, and/or the use of *para*-anisaldehyde, potassium permanganate, or phosphomolybdic acid solutions were used to visualize products.

Melting points were measured on a SRS Meltemp melting point apparatus and were not corrected. IR spectra were recorded on a Nicolet IR 200 spectrophotometer and are reported in wavenumbers (cm^{-1}) analyzed as neat films on NaCl plates (transmission). Nuclear magnetic resonance spectra (NMR) were obtained on a Bruker DRX-400 (400 MHz) or a Bruker AVIII-600 (600 MHz) spectrometer. Chemical shifts are measured to residual non-deuterated solvent as an internal standard. Mass spectra were recorded on a high resolution Thermo Electron Corporation MAT 95XP-Trap or Thermo Fisher LTQ Orbitrap XL by use of electro-spray ionization (ESI) or atmospheric pressure chemical ionization (APCI) by the Vanderbilt Mass Spectrometry Research Center (MSRC) Cores or Indiana University Mass Spectrometry Facility. Optical rotations were measured on a Perkin Elmer-341 polarimeter. Chiral HPLC analysis was conducted on an Agilent 1100 series instrument using the designated ChiralPak column. Absolute configuration was determined by X-ray analysis.

StilbPBAM (**7**) was prepared according to the previously published procedure.[2]

Additional Experiments

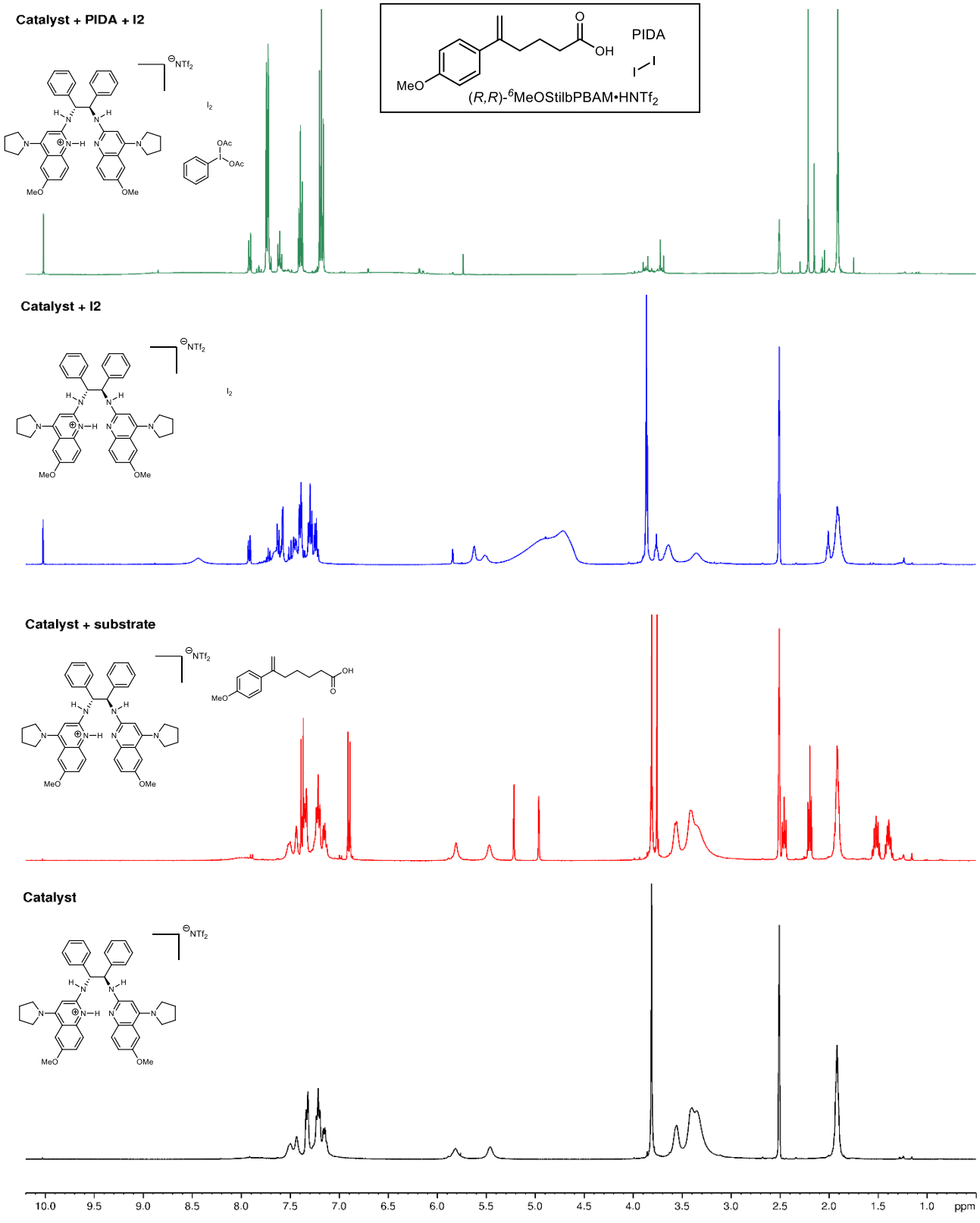
Spectroscopic examination of the catalyst with substrate and reagents

NMR experiments were carried out to prospect for new species, and to confirm that the catalyst is not modified in the reaction. No changes were observed when mixing catalyst and carboxylic acid substrate. No major differences in chemical shifts were observed between catalyst + I_2 and catalyst + PIDA + I_2. The new peaks that are formed in these two experiments are noted to be reversed by quenching with $Na_2S_2O_3$: the catalyst (72%, by mass) was recovered unchanged following chromatography.

Experiment details: One or more of the following compounds were used for each NMR experiment (using 1:1 stoichiometry): catalyst (9.5 mg, 10 μmol), 6-(4-methoxyphenyl)hept-6-enoic acid (2.3 mg, 10 μmol), PIDA (32.2 mg, 100 μmol) and I_2 (25.4 mg, 100 μmol) were dissolved in DMSO-d^6 (500 μL) and stirred at room temperature for 24 h.

[1] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.

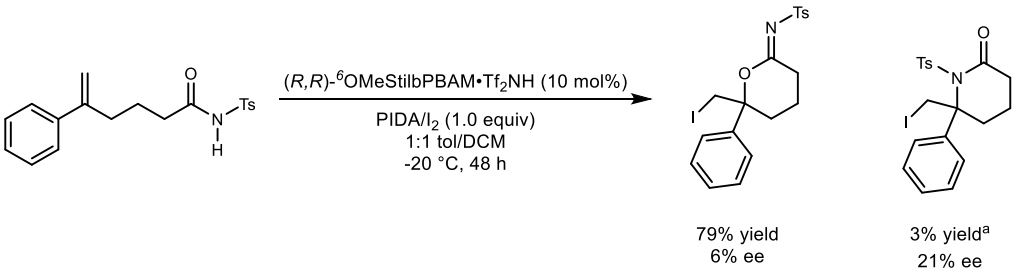
[2] Struble, T. J.; Lankswert, H. M.; Pink, M.; Johnston, J. N. *ACS Catalysis* **2018**, *8*, 11926.


Catalyst + PIDA + I2
PIDA
(R,R)-6MeOStilbPBAM•HNTf2
Catalyst + I2
Catalyst + substrate
Catalyst
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm

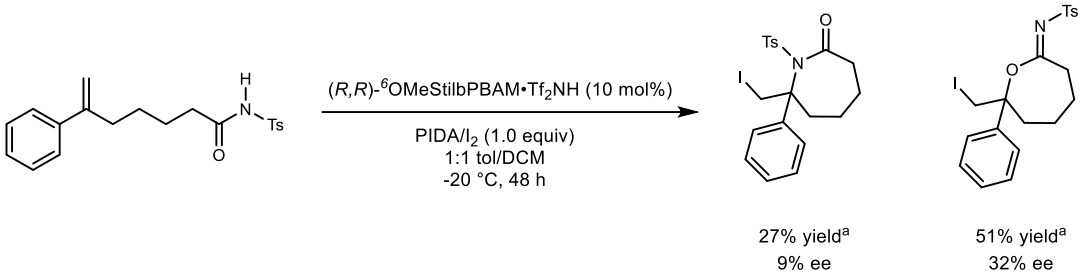
NMR

Catalyzed iodocyclizations of sulfonimide nucleophiles

6-membered ring:



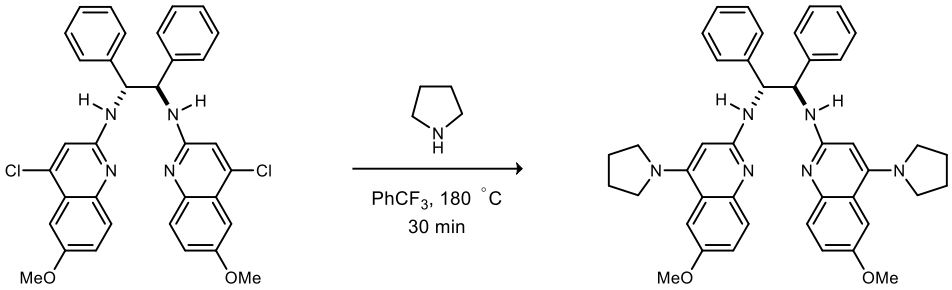
7-membered ring:



Experimental details: To a flame-dried vial equipped with a stir bar was added ^{6}MeOStilbPBAM•HNTf$_2$ (9.5 mg, 10 μmol), the tosylated amide (100 μmol), and a 1:1 mixture of anhydrous dichloromethane/toluene (1.5 mL). The reaction mixture was stirred at 750 RPM at 25 °C for 5 minutes and then cooled to -50 °C. PIDA (32 mg, 100 μmol) and I_2 (25 mg, 100 μmol) were added after 1 hour. The reaction mixture was stirred without light for a total of 48 h.

[a]The 6-membered O-cyclization product was assigned by comparison to literature values, while the *N*-isomer was assigned by exclusion. The analogous 7-membered structures were assigned by analogous chemical shifts.

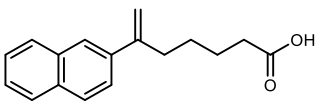
Catalyst Synthesis



^{6}MeOStilbPBAM or (1*R*,2*R*)-N1,N2-bis(6-methoxy-4-(pyrrolidin-1-yl)quinolin-2-yl)-1,2-diphenylethane-1,2-diamine (4). A 2-5 mL microwave vial equipped with a stir bar was charged with ^{4}Cl-^{6}MeOStilb-BAM (444 mg, 750 μmol), pyrrolidine (300 μL, 3.4 mmol), and trifluoromethylbenzene (2.5 mL). The vial was sealed, and the suspension was heated with stirring at 180 °C in the microwave for 30 m. The reaction mixture was diluted with dichloromethane and transferred to a round-bottomed flask for evaporation. The resulting solid was dissolved in dichloromethane and stirred with 5 M NaOH (~20 mL) overnight. The contents of the flask were then transferred to a separatory funnel where the aqueous layer was extract with DCM. The resulting organic layer was dried and concentrated to provide a light brown powder. The solid was then recrystallized from hexanes and dichloromethane to provide a light yellow solid (260 mg, 53%). Mp 162-166 °C; $[\alpha]_D^{20}$ +62.4 (*c* 1.00, $CHCl_3$); R_f = 0.1 (10% MeOH/DCM); IR (film) 3255, 2965, 1648, 1587, 1456 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* =8.5 Hz, 2H), 7.31 (d, *J* = 2.80 Hz, 2H), 7.28 (s, 2H), 7.26 (s, 2H), 7.19 (d, *J* = 6.8 Hz, 2H), 7.17 (d, *J* = 7.4 Hz, 2H), 7.15 (d, *J* = 2.8 Hz, 2H), 7.12 (d, *J* = 2.8 Hz, 2H), 5.90 (br s, 2H), 5.55 (br s, 2H), 5.51 (br s, 2H), 3.84 (s, 6H), 3.36 (br s, 4H), 3.25 (br s, 4H), 1.88 (br s, 8H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 156.9, 152.7, 144.9, 141.5, 128.1, 128.0 (2C), 127.6, 127.0, 118.6, 106.5, 92.15, 77.4, 62.6, 55.8, 51.4, 25.7; HRMS (ESI): Exact mass calcd for $C_{42}H_{45}N_6O_2$ $[M+H]^+$ 665.3500, found 665.3593.

General procedure for the synthesis of 6-aryl heptanoic acid[3]

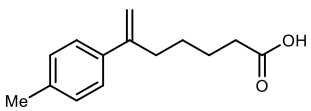
A flame-dried round-bottomed flask equipped with a stir bar was charged with $Pd(PPh_3)_4$, hept-6-ynoic acid, the aryl boronic acid, and freshly distilled 1,4-dioxane. The resulting mixture was treated with acetic acid under an argon atmosphere. Argon was bubbled through the reaction mixture for 15 min while stirring at room temperature. The round-bottomed flask was placed in an oil bath overnight at 105 °C. The reaction mixture was concentrated *in vacuo* and the crude material was dissolved in ethyl acetate. The organic layer was washed with 1 M HCl, dried, and concentrated. Flash column chromatography of the residue yielded the 6-aryl heptanoic acid.



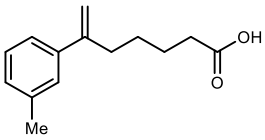
6-(Naphthalen-2-yl)hept-6-enoic acid (5b). The reaction was carried out according to the general procedure, using $Pd(PPh_3)_4$ (110 mg, 95 μmol), hept-6-ynoic acid (400 mg, 3.2 mmol), the aryl boronic acid (654 mg, 3.8 mmol), acetic acid (18 μL, 0.32

[3] Karila, D.; Leman, L.; Dodd, R. H. *Org. Lett.* **2011**, *13*, 5830.

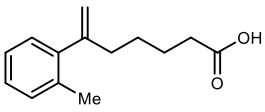
mmol), and 1,4-dioxane (12 mL). The crude material was purified by silica gel chromatography (SiO_2, 5-15% ethyl acetate in hexanes) to afford a white wax (244 mg, 30%). IR (film) 3050, 2936, 2677, 1688, 1620, 1593, 1461 cm^{-1}; R_f = 0.4 (30% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.80 (m, 4H), 7.55 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.45 (m, 2H), 5.42 (d, *J* = 1.2 Hz, 1H), 5.16 (d, *J* = 1.2 Hz, 1H); 2.64 (t, *J* = 7.4 Hz, 2H), 2.34 (t, *J* = 7.6 Hz, 2H), 1.71 (tt, *J* = 7.7, 7.6 Hz, 2H), 1.55 (tt, *J* = 7.5, 7.5 Hz, 2H) [COO*H* not observed due to broadening]; ^{13}C NMR (150 MHz, $CDCl_3$) ppm 178.7, 147.9, 138.4, 133.5, 132.9, 128.3, 128.0, 127.6, 126.2, 125.9, 124.80, 124.77, 113.3, 35.1, 33.8, 27.7, 24.4; HRMS (ESI): Exact mass calcd for $C_{17}H_{17}O_2$ $[M-H]^-$ 253.1234, found 253.1229.



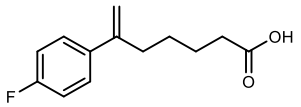
6-(*p*-Tolyl)hept-6-enoate (5c). The reaction was carried out according to the general procedure, using $Pd(PPh_3)_4$ (320 mg, 320 µmol), hept-6-ynoic acid (400 mg, 3.2 mmol), the aryl boronic acid (522 mg, 3.8 mmol), acetic acid (32 µL, 0.64 mmol), and 1,4-dioxane (12 mL). The crude material was purified by silica gel chromatography (SiO_2, 5-15% ethyl acetate in hexanes) and then recrystallized from hexanes to afford a white solid (143 mg, 20%). IR (film) 2946, 2872, 1697, 1627, 1514, 1458 cm^{-1}; R_f = 0.4 (30% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.3 Hz, 2H), 7.13 (d, *J* = 8.1 Hz, 2H), 5.24 (d, *J* = 1.5 Hz, 1H), 5.01 (d, *J* = 1.16 Hz, 1H), 2.51 (t, *J* = 7.5 Hz, 2H), 2.34 (s, 3H), 2.33 (m, 2H), 1.67 (tt, *J* = 7.6, 7.6 Hz, 2H), 1.50 (tt, *J* = 7.6, 7.5 Hz, 2H) [COO*H* not observed due to broadening]; ^{13}C NMR (150 MHz, $CDCl_3$) ppm 180.4, 147.8, 138.2, 137.2, 129.1, 126.1, 111.9, 35.0, 34.0, 27.6, 24.3, 21.2; HRMS (ESI): Exact mass calcd for $C_{14}H_{17}O_2$ $[M-H]^-$ 217.1234, found 217.1209.



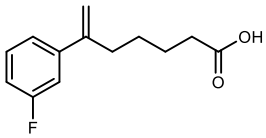
6-(*m*-Tolyl)hept-6-enoic acid (5d). The reaction was carried out according to the general procedure, using $Pd(PPh_3)_4$ (110 mg, 95 µmol), hept-6-ynoic acid (400 mg, 3.2 mmol), the aryl boronic acid (522 mg, 3.8 mmol), acetic acid (18 µL, 0.32 mmol), and 1,4-dioxane (12 mL). The crude material was purified by silica gel chromatography (SiO_2, 5-15% ethyl acetate in hexanes) to afford a yellow oil (286 mg, 40%). IR (film) 3032, 2940, 1706, 1487 cm^{-1}; R_f = 0.4 (30% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.19 (m, 3H), 7.08 (m, 1H), 5.25 (d, *J* = 1.6 Hz, 1H), 5.04 (d, *J* = 1.6 Hz, 1H), 2.51 (t, *J* = 7.3 Hz, 2H), 2.36 (s, 3H), 2.34 (t, *J* = 7.6 Hz, 3H), 1.67 (tt, *J* = 7.7, 7.5 Hz, 2H), 1.58 (tt, *J* = 7.6, 7.6 Hz, 1H) [COO*H* not observed due to broadening]; ^{13}C NMR (150 MHz, $CDCl_3$) ppm 180.1, 148.2, 141.2, 137.9, 128.3, 128.2, 127.0, 123.3, 112.4, 35.0, 33.9, 27.6, 24.3, 21.6; HRMS (ESI): Exact mass calcd for $C_{14}H_{17}O_2$ $[M-H]^-$ 217.1234, found 217.1213.



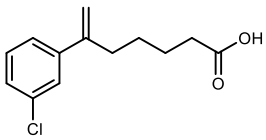
6-(*o*-Tolyl)hept-6-enoic acid (5e). The reaction was carried out according to the general procedure, using $Pd(PPh_3)_4$ (370 mg, 320 µmol), hept-6-ynoic acid (400 mg, 3.2 mmol), the aryl boronic acid (522 mg, 3.8 mmol), acetic acid (32 µL, 0.64 mmol), and 1,4-dioxane (12 mL). The crude material was purified by silica gel chromatography (SiO_2, 5-15% ethyl acetate in hexanes) to afford a yellow oil (420 mg, 60%). IR (film) 3015, 2932, 1707, 1487 cm^{-1}; R_f = 0.4 (30% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.17-7.10 (m, 3H), 7.05 (m, 1H), 5.18 (d, *J* = 1.5 Hz, 1H), 4.87 (d, *J* = 1.7 Hz, 1H), 2.34 (m, 4H), 2.28 (s, 3H), 1.66 (tt, *J* = 7.6, 7.6 Hz, 2H), 1.44 (tt, *J* = 7.7, 7.7 Hz, 2H) [COO*H* not observed due to broadening]; ^{13}C NMR (150 MHz, $CDCl_3$) ppm 180.1, 149.6, 143.0, 134.9, 130.2, 128.5, 126.9, 125.5, 114.1, 37.4, 34.0, 27.6, 24.4, 19.9; HRMS (ESI): Exact mass calcd for $C_{14}H_{17}O_2$ $[M-H]^-$ 217.1234, found 217.1218.



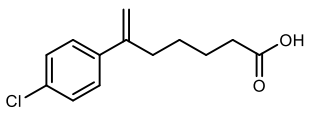
6-(4-Fluorophenyl)hept-6-enoic acid (5f). The reaction was carried out according to the general procedure, using $Pd(PPh_3)_4$ (60 mg, 52 µmol), hept-6-ynoic acid (200 mg, 1.3 mmol), the aryl boronic acid (218 mg, 1.56 mmol), acetic acid (16 µL, 0.26 mmol), and 1,4-dioxane (7 mL). The crude material was purified by silica gel chromatography (SiO_2, 15-20% ethyl acetate in hexanes) to afford a yellow oil (75 mg, 26%). IR (film) 3118 (br), 3083, 2928, 2859, 1709, 1629, 1602, 1508 cm^{-1}; R_f = 0.2 (20% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 7.3, 5.5 Hz, 2H), 7.16 (t, *J* = 8.6 Hz, 2H), 5.15 (s, 1H), 4.98 (s, 1H), 2.43 (t, *J* = 7.5 Hz, 2H), 2.28 (t, *J* = 7.5 Hz, 2H), 1.60 (tt, *J* = 7.9, 7.4 Hz, 2H), 1.42 (tt, *J* = 11.5, 7.3 Hz, 2H) [COO*H* not observed due to broadening]; ^{13}C NMR (150 MHz, $CDCl_3$) ppm 179.0, 162.5 (d, *J* = 240.5 Hz), 146.9, 137.0, 127.6 (d, *J* = 7.9, 7.5 Hz), 115.3 (d, *J* = 26.7 Hz), 112.4, 114.2 (d, *J* = 21.0 Hz), 113.5, 113.1 (d, *J* = 23.2 Hz), 35.0, 33.6, 27.3, 24.1; ^{19}F NMR (282 MHz, $CDCl_3$) ppm -115.4; HRMS (ESI): Exact mass calcd for $C_{13}H_{14}FO_2$ $[M-H]^-$ 221.0983, found 221.0979.



6-(3-Fluorophenyl)hept-6-enoic acid (5g). The reaction was carried out according to the general procedure, using $Pd(PPh_3)_4$ (80 mg, 70 µmol), hept-6-ynoic acid (268 mg, 1.7 mmol), the aryl boronic acid (266 mg, 1.9 mmol), acetic acid (10 µL, 0.17 mmol), and 1,4-dioxane (10 mL). The crude material was purified by silica gel chromatography (SiO_2, 5-15% ethyl acetate in hexanes) to afford a colorless oil (61 mg, 16%). IR (film) 3082, 3068 (br), 2940, 2878, 1709, 1611, 1580, 1487 cm^{-1}; R_f = 0.4 (30% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.34-7.27 (m, 1H), 7.19 (d, *J* = 7.9 Hz, 1H), 7.08 (dt, *J* = 10.6, 2.1 Hz, 1H), 6.98 (td, *J* = 8.3, 2.1Hz, 1H), 5.32 (s, 1H), 5.13 (s, 1H), 2.53 (t, *J* = 7.2 Hz, 2H), 2.38 (t, *J* = 7.2 Hz, 2H), 1.70 (tt, *J* = 7.7, 7.2 Hz, 2H), 1.53 (tt, *J* = 7.7, 7.2 Hz, 2H) [COO*H* not observed due to broadening]; ^{13}C NMR (150 MHz, $CDCl_3$) ppm 179.9, 163.0 (d, *J* = 259.6 Hz), 146.9, 143.5 (d, *J* = 6.8 Hz), 129.7 (d, *J* = 8.8 Hz), 121.7 (d, *J* = 2.7 Hz), 114.1 (d, *J* = 21.2 Hz), 113.5, 113.0 (d, *J* = 21.9 Hz), 34.9, 34.1, 27.4, 24.4; ^{19}F NMR (282 MHz, $CDCl_3$) ppm -113.7; HRMS (ESI): Exact mass calcd for $C_{13}H_{14}FO_2$ $[M-H]^-$ 221.0983, found 221.0973.

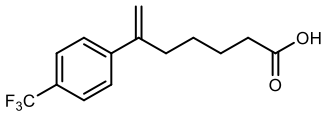


6-(3-Chlorophenyl)hept-6-enoic acid (5h). The reaction was carried out according to the general procedure, using $Pd(PPh_3)_4$ (110 mg, 95 µmol), hept-6-ynoic acid (400 mg, 3.2 mmol), the aryl boronic acid (595 mg, 3.8 mmol), acetic acid (18 µL, 0.32 mmol), and 1,4-dioxane (12 mL). The crude material was purified by silica gel chromatography (SiO_2, 5-15% ethyl acetate in hexanes) to afford a yellow oil (208 mg, 42%). IR (film) 3062, 2933, 2864, 2672, 1706, 1592, 1562, 1475 cm^{-1}; R_f = 0.4 (30% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (m, 1H), 7.26-7.23 (m, 4H), 5.28 (br s, 1H), 5.10 (d, *J* = 1.1 Hz, 1H), 2.49 (t, *J* = 7.6 Hz, 2H), 2.35 (t, *J* = 7.4 Hz, 2H), 1.86 (tt, *J* = 11.4, 7.6 Hz, 2H), 1.50 (tt, *J* = 11.2, 7.6 Hz, 2H) [COO*H* not observed due to broadening]; ^{13}C NMR (150 MHz, $CDCl_3$) ppm 180.4, 146.7, 143.0, 134.2, 129.5, 127.4, 126.3, 124.2, 113.6, 34.7, 33.8, 27.3, 24.1; HRMS (ESI): Exact mass calcd for $C_{13}H_{15}ClO_2$ $[M-H]^-$ 237.0688, found 237.0682.

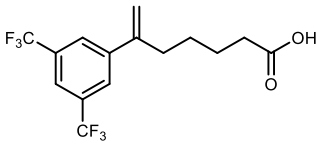


6-(4-Chlorophenyl)hept-6-enoic acid (5i). The reaction was carried out according to the general procedure, using $Pd(PPh_3)_4$ (90mg, 78 µmol), hept-6-ynoic acid (252 mg, 2.0 mmol), the aryl boronic acid (365 mg, 2.3 mmol), acetic acid (23 µL, 0.39 mmol), and 1,4-dioxane (10 mL). The crude material was purified by silica gel chromatography (SiO_2, 15-20% ethyl acetate in hexanes) to afford a yellow solid (201 mg, 42%). Mp 48-52 °C; IR (film) 3080, 3032 (br),2937, 2842, 1735, 1706, 1491 cm^{-1}; R_f = 0.2 (20% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 4.4 Hz, 2H), 7.20 (d, *J* = 4.4 Hz, 2H), 5.19 (s, 1H), 5.00 (s, 1H), 2.42 (t, *J* = 7.3 Hz, 2H), 2.27 (t, *J* = 7.3 Hz, 2H), 1.60 (tt, *J* = 7.7, 7.3 Hz, 2H), 1.41 (tt, *J* = 7.8, 7.3 Hz, 2H) [COO*H* not observed

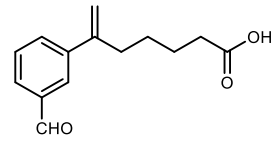
due to broadening]; ^{13}C NMR (100 MHz, $CDCl_3$) ppm 179.1, 146.8, 139.4, 128.4, 127.3, 126.8, 113.0, 34.8, 33.6, 27.3, 24.1; HRMS (ESI): Exact mass calcd for $C_{13}H_{14}ClO_2$ [M-H]$^-$ 237.0688, found 237.0667.



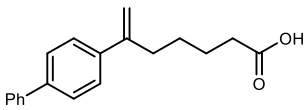
6-(4-Trifluoromethylphenyl)hept-6-enoate (5j). The reaction was carried out according to the general procedure, using $Pd(PPh_3)_4$ (90mg, 78 µmol), hept-6-ynoic acid (252 mg, 2.0 mmol), the aryl boronic acid (443 mg, 2.3 mmol), acetic acid (23 µL, 0.39 mmol), and 1,4-dioxane (10 mL). The crude material was purified by silica gel chromatography (SiO_2, 5-15% ethyl acetate in hexanes) to afford a colorless oil (117 mg, 22%). IR (film) 30788 (br),3047, 2940, 2869, 2669, 1709, 1616, 1573, 1408 cm^{-1}; R_f = 0.2 (20% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 8.4 Hz, 2H), 5.36 (s, 1H), 5.19 (s, 1H), 2.51 (t, *J* = 7.4 Hz, 2H), 2.38 (t, *J* = 7.4 Hz, 2H), 1.70 (tt, *J* = 7.5, 7.2 Hz, 2H), 1.53 (tt, *J* = 8.0, 7.5 Hz, 2H) [COO*H* not observed due to broadening]; ^{13}C NMR (100 MHz, $CDCl_3$) ppm 179.5, 146.9, 144.6, 128.2 (q, *J* = 270.1 Hz), 126.3, 125.8, 125.2 (q, *J* = 3.6 Hz) 114.4, 34.7, 33.6, 27.2, 24.0; ^{19}F NMR (282 MHz, $CDCl_3$) ppm -62.5; HRMS (ESI): Exact mass calcd for $C_{14}H_{14}F_3O_2$ [M-H]$^-$ 271.0951, found 271.0940.



6-(3,5-bis(Trifluoromethyl)phenyl)hept-6-enoate (5k). The reaction was carried out according to the general procedure, using $Pd(PPh_3)_4$ (90mg, 78 µmol), hept-6-ynoic acid (252 mg, 2.0 mmol), the aryl boronic acid (602 mg, 2.3 mmol), acetic acid (23 µL, 0.39 mmol), and 1,4-dioxane (10 mL). The crude material was purified by silica gel chromatography (SiO_2, 5-15% ethyl acetate in hexanes) to afford a colorless oil (320 mg, 48%). IR (film) 3089 (br), 2939, 2670, 1712, 1633, 1414 cm^{-1}; R_f = 0.2 (20% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 2H), 7.71 (s, 1H), 5.33 (s, 1H), 5.19 (s, 1H), 2.49 (t, *J* = 7.2 Hz, 2H), 2.30 (t, *J* = 7.2 Hz, 2H), 1.62 (tt, *J* = 7.6, 7.2 Hz, 2H), 1.45 (tt, *J* = 7.6, 7.2 Hz, 2H) [COO*H* not observed due to broadening]; ^{13}C NMR (100 MHz, $CDCl_3$) ppm 178.1, 145.5, 143.2, 131.4 (d, *J* = 30.3 Hz), 126.1, 124.7 (q, *J* = 273.6 Hz), 121.9, 115.7, 34.5, 33.0, 27.1, 24.0; ^{19}F NMR (282 MHz, $CDCl_3$) ppm -62.9; HRMS (ESI): Exact mass calcd for $C_{15}H_{13}F_6O_2$ [M-H]$^-$ 339.0825, found 339.0820.

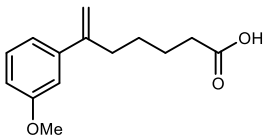


6-(3-Formylphenyl)hept-6-enoate (5l). The reaction was carried out according to the general procedure, using $Pd(PPh_3)_4$ (60 mg, 52 µmol), hept-6-ynoic acid (164 mg, 1.3 mmol), the aryl boronic acid (234 mg, 1.6 mmol), acetic acid (16 µL, 0.3 mmol), and 1,4-dioxane (7 mL). The crude material was purified by silica gel chromatography (SiO_2, 5-15% ethyl acetate in hexanes) to afford a colorless oil (125 mg, 41%). IR (film) 3072 (br), 2935, 2864, 1734, 1701, 1654, 1438 cm^{-1}; R_f = 0.3 (40% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.05 (s, 1H), 7.92 (s, 1H), 7.81 (d, *J* = 7.7 Hz, 1H), 7.68 (d, *J* = 7.7 Hz, 1H), 7.52 (t, *J* = 7.7 Hz, 1H), 5.39 (s, 1H), 5.19 (s, 1H), 2.60 (t, *J* = 7.3 Hz, 2H), 2.38 (t, *J* = 7.3 Hz, 2H), 1.71 (tt, *J* = 8.0, 7.4 Hz, 2H), 1.54 (tt, *J* = 8.0, 7.4 Hz, 2H) [COO*H* not observed due to broadening]; ^{13}C NMR (100 MHz, $CDCl_3$) ppm 192.6, 179.7, 146.8, 142.1, 136.5, 132.2, 129.1, 128.8, 127.2, 114.1, 34.8, 33.7, 27.3, 24.1; HRMS (ESI): Exact mass calcd for $C_{14}H_{15}O_3$ [M-H]$^-$ 231.1027, found 231.1011.

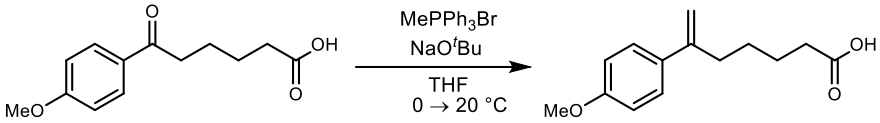


6-([1,1'-Biphenyl]-4-yl)hept-6-enoic acid (5m). The reaction was carried out according to the general procedure, using $Pd(PPh_3)_4$ (320 mg, 320 µmol), hept-6-ynoic acid (400 mg, 3.2 mmol), the aryl boronic acid (752 mg, 3.8 mmol), acetic acid (32 µL, 0.64 mmol), and 1,4-dioxane (12 mL). The crude material was purified by silica gel chromatography (SiO_2, 5-15% ethyl acetate in hexanes) and then recrystallized from hexanes to afford a white solid (143 mg, 20%). IR (film) 2926, 2856, 1697 cm^{-1}; R_f = 0.4 (30% EtOAc/hexanes); ^{1}H NMR (400

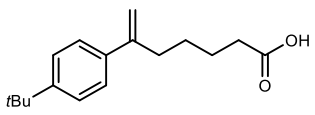
MHz, ((CD$_3$)$_2$CO) δ 7.66 (m, 4H), 7.56 (m, 2H), 7.46 (dd, *J* = 7.6, 7.6 Hz, 2H), 7.35 (m, 1H), 5.37 (d, *J* =1.4 Hz, 1H), 5.13 (d, *J* = 1.4 Hz, 1H), 2.61 (t, *J* = 7.9 Hz, 2H), 2.31 (t, *J* = 7.3 Hz, 2H), 1.66 (tt, *J* = 7.6, 7.5 Hz, 2H), 1.54 (tt, *J* = 7.9, 7.7 Hz, 2H) [COO*H* not observed due to broadening]; ^{13}C NMR (150 MHz, $CDCl_3$) ppm 178.9, 147.6, 140.9, 140.3, 140.1, 128.9, 127.4, 127.2, 127.1, 126.6, 112.7, 35.0, 33.8, 27.7, 24.4; HRMS (ESI): Exact mass calcd for $C_{19}H_{19}O_2$ [M-H]$^-$ 279.1391, found 279.1371.



6-(3-Methoxyphenyl)hept-6-enoic acid (5n). The reaction was carried out according to the general procedure, using $Pd(PPh_3)_4$ (55 mg, 48 μmol), hept-6-ynoic acid (200 mg, 1.6 mmol), the aryl boronic acid (290 mg, 1.9 mmol), acetic acid (9 μL, 0.16 mmol), and 1,4-dioxane (6 mL). The crude material was purified by silica gel chromatography (SiO_2, 5-15% ethyl acetate in hexanes) to afford a yellow oil (133 mg, 36%). IR (film) 3078, 2936, 2864, 2672, 1706, 1597, 1576, 1487 cm^{-1}; R_f = 0.4 (30% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 7.8 Hz, 1H), 6.98 (ddd, *J* = 7.7, 1.2, 0.9 Hz, 1H), 6.92 (dd, *J* = 2.3, 1.8 Hz, 1H), 6.82 (ddd, *J* = 8.2, 2.6, 0.7 Hz, 1H), 5.27 (d, *J* = 1.4 Hz, 1H), 5.06 (d, *J* = 1.2 Hz, 1H), 3.82 (s, 3H), 2.51 (t, *J* =. 7.2 Hz, 2H), 2.35 (t, *J* = 7.5 Hz, 2H), 1.68 (tt, *J* = 11.4, 7.6 Hz, 2H), 1.52 (tt, *J* = 11.2, 7.6 Hz, 2H) [COO*H* not observed due to broadening]; ^{13}C NMR (150 MHz, $CDCl_3$) ppm 180.3, 159.6, 148.0, 142.8, 129.3, 118.8, 112.8, 112.7, 112.2, 55.3, 35.1, 34.0, 27.6, 24.3; HRMS (ESI): Exact mass calcd for $C_{14}H_{18}O_3$ [M-H]$^-$ 233.1183, found 233.1178.

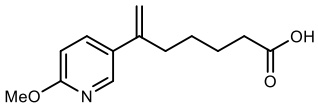


6-(4-Methoxyphenyl)hept-6-enoic acid (5o). Methyltriphenylphoshonium bromide (1.98 g, 5.55 mmol) was suspended in THF (100 mL), and cooled to 0 °C. Sodium *tert*-butoxide (1.06 g, 11.1 mmol) was added and the reaction mixture was stirred for 1 hour at room temperature. The reaction mixture was cooled to 0 °C, the carboxylic acid was added, and the reaction mixture was stirred for 48 hours at room temperature. The reaction mixture was concentrated, the residue was dissolved in 1 M aq NaOH, and washed with dichloromethane. The aqueous layer was acidified with 2 N aq HCl and extracted with dichloromethane. The combined organic layers were dried ($MgSO_4$) and concentrated to give the product as a white solid (700 mg, 70%). Mp = 97-100 °C; R_f = 0.21 (30% EtOAc/hexanes); IR (film) 3074, 2933, 2844, 1699, 1606, 1510, 1427, 1286, 1042 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.9 Hz, 2H), 6.86 (d, *J* = 8.9 Hz, 2H), 5.21 (d, *J* = 1.4 Hz, 1H), 4.98 (d, *J* = 1.4 Hz, 1H), 3.81 (s, 3H), 2.51 (t, *J* = 7.9 Hz, 2H), 2.35 (t, *J* = 7.5 Hz, 2H), 1.71-1.64 (m, 2H), 1.54-1.47 (m, 2H), [O*H* not observed]; ^{13}C NMR (100 MHz, $CDCl_3$) ppm 180.1, 159.1, 147.4, 133.6, 127.3, 113.8, 111.1, 55.4, 35.1, 34.0, 27.7, 24.4; HRMS (ESI): Exact mass calcd for $C_{14}H_{18}O_3Na$ [M+Na]$^+$ 257.1154, found 257.1149.



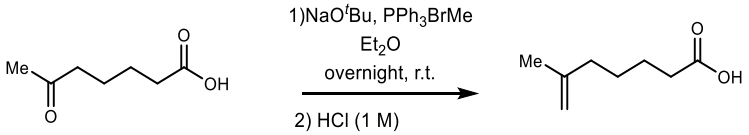
6-(4-(*tert*-Butyl)phenyl)hept-6-enoic acid (5p). The reaction was carried out according to the general procedure, using $Pd(PPh_3)_4$ (55 mg, 48 μmol), hept-6-ynoic acid (200 mg, 1.6 mmol), the aryl boronic acid (338 mg, 1.9 mmol), acetic acid (9 μL, 0.16 mmol), and 1,4-dioxane (6 mL). The crude material was purified by silica gel chromatography (SiO_2, 5-15% ethyl acetate in hexanes) to afford a yellow oil (138 mg, 35%). IR (film) 3082, 3032, 2960, 2866, 1725, 1625, 1513, 1462 cm^{-1}; R_f = 0.5 (30% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (br s, 4H), 5.27 (d, *J* = 1.1 Hz, 1H), 5.02 (d, *J* = 1.1 Hz, 1H), 2.52 (t, *J* = 7.4 Hz, 2H), 2.36 (t, *J* = 7.4 Hz, 2H), 1.70 (tt, *J* = 11.4, 7.7 Hz, 2H), 1.53 (tt, *J* = 11.5, 7.7 Hz), 1.32 (s, 9H) [COO*H* not observed due to

broadening]; ^{13}C NMR (150 MHz, $CDCl_3$) ppm 179.8, 150.5, 147.7, 138.1, 125.8, 125.3, 111.9, 35.0, 34.6, 33.9, 31.4, 27.7, 24.4; HRMS (ESI): Exact mass calcd for $C_{17}H_{23}O_2$ [M-H]$^-$ 259.1704, found 259.1697.

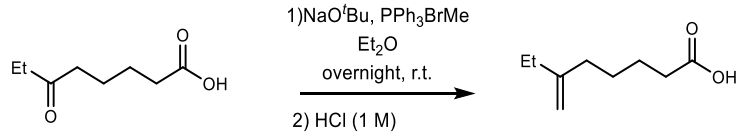


6-(6-Methoxypyridin-3-yl)hept-6-enoic acid (5q). The reaction was carried out according to the general procedure, using $Pd(PPh_3)_4$ (110 mg, 95 µmol), hept-6-ynoic acid (328 mg, 2.6 mmol), the aryl boronic acid (477 mg, 3.1 mmol), acetic acid (16 µL, 0.26 mmol), and 1,4-dioxane (12 mL). The crude material was purified by silica gel chromatography (SiO_2, 5-15% ethyl acetate in hexanes) to afford a yellow oil (336 mg, 40%). IR (film) 3110 (br), 1708, 1602, 1495 cm^{-1}; R_f = 0.3 (30% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.10 (br, 1H), 8.14 (d, *J* = 2.3 Hz, 1H), 7.54 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.64 (d, *J* = 8.8 Hz, 1H), 5.15 (s, 1H), 4.97 (s, 1H), 3.86 (s, 3H), 2.41 (t, *J* = 7.3 Hz, 2H), 2.27 (t, *J* = 7.3 Hz, 2H), 1.59 (tt, *J* = 7.6, 7.1 Hz, 2H), 1.43 (tt, *J* = 7.6, 7.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 179.2, 163.4, 144.5, 144.0, 136.6, 129.7, 112.2, 110.3, 53.5, 34.7, 33.7, 27.3, 24.1; HRMS (ESI): Exact mass calcd for $C_{13}H_{16}NO_2$ [M-H]$^-$ 234.1136, found 234.1119.

Procedure for the synthesis of 6-alkyl heptenoic acids



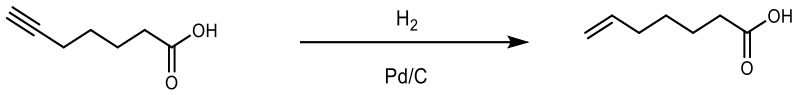
6-Methylhept-6-enoic acid (5r). Methyltriphenylphoshonium bromide (5.06 g, 14.2 mmol) was suspended in THF (100 mL), and cooled to 0 °C. Sodium *tert*-butoxide (1.36 g, 14.2 mmol) was added and the reaction mixture was stirred for 1 hour at 0 °C. The ketoacid (680 mg, 4.72 mmol) was added, and the reaction mixture was stirred for 24 hours at room temperature. The reaction was quenched with 1 M aq HCl and extracted with ethyl acetate. The combined organic layers were dried (Na_2SO_4) and concentrated to give the crude product, which was purified by silica gel chromatography (SiO_2, 15% ethyl acetate in hexanes) to afford a colorless oil (643 mg, 96%). The analytical data matched literature values.[4]



6-Methyleneoctanoic acid (5s). Methyltriphenylphoshonium bromide (542 mg, 1.5 mmol) was suspended in diethyl ether (10 mL), and cooled to 0 °C. Sodium *tert*-butoxide (146 mg, 1.5 mmol) was added and the reaction mixture was stirred for 1 hour at 0 °C. The ketoacid (80 mg, 0.5 mmol) was added, and the reaction mixture was stirred for 24 hours at room temperature. The reaction was quenched by with 1 M aq HCl and extracted with ethyl acetate. The combined organic layers were dried (Na_2SO_4) and concentrated to give the crude product, which was purified by silica gel chromatography (SiO_2, 15% ethyl acetate in hexanes) to afford a colorless oil (24 mg, 30%); R_f = 0.25 (30% EtOAc/hexanes); IR (film) 3075 (br), 2939, 2675, 1710, 1650, 1413, 1375, 1291 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.64 (d, *J* = 8.3 Hz, 2H), 2.30 (t, *J* = 6.9 Hz, 2H), 2.04-1.89 (m, 4H), 1.58

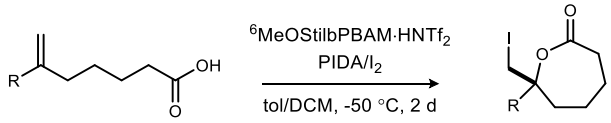
[4] Alhamadsheh, M. M.; Gupta, S.; Hudson, R. A.; Perera, L.; Tillekeratne, L. M. V. *Chem. Eur. J.* **2008**, *14*, 570.

(tt, *J* = 7.9, 7.2 Hz, 2H), 1.42 (tt, *J* = 7.9, 6.9 Hz, 2H), 0.95 (t, *J* = 7.2 Hz, 3H) [O*H* not observed]; ^{13}C NMR (100 MHz, $CDCl_3$) ppm 179.0, 150.9, 107.8, 35.7, 33.7, 28.5, 27.0, 24.3, 12.2; HRMS (ESI): Exact mass calcd for $C_9H_{15}O_2$ $[M-H]^+$ 155.1078, found 155.1062.

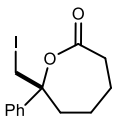


Hept-6-enoic acid (5t). The reaction was carried out according to the literature.[5] Hept-6-ynoic acid (250 mg, 2 mmol) was dissolved in MeOH under Ar in a round bottom flask, followed by addition of Lindlar's catalyst (50 mg, 100 µmol). The flask was purged and refilled by Ar for 3 times and then purged and refilled by hydrogen gas 3 times. The reaction was stirred at room temperature for 3 h. After completion, the solution was filtered through Celite and washed with EtOAc. The solvent was removed under vacuum and the residue was purified by silica gel chromatography (SiO_2, 5-10% ethyl acetate in hexanes) to afford a colorless oil (100 mg, 39%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.73 (tdd, *J* = 17.0, 10.3, 6.6 Hz, 1H), 4.95 (dd, *J* = 17.0, 1.7 Hz, 1H), 4.89 (dd, *J* = 10.3, 1.7 Hz, 1H), 2.30 (t, *J* = 7.4 Hz, 2H), 2.01 (tt, *J* = 7.4, 7.0 Hz, 2H), 1.60 (tt, *J* = 7.8, 7.4 Hz, 2H), 1.38 (tt, *J* = 7.8, 7.4 Hz, 1H).

General Procedure for Enantioselective Lactonization



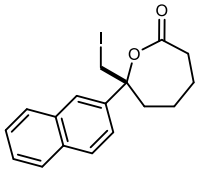
To a flame-dried vial equipped with a stir bar was added ^{6}MeOStilbPBAM•$HNTf_2$ (9.5 mg, 10 µmol), the acid(100 µmol), and a 1:1 mixture of anhydrous dichloromethane/toluene (1.5 mL). The reaction mixture was stirred at 750 RPM at 25 °C for 5 minutes and then cooled to -50 °C. PIDA (32 mg, 100 µmol) and I_2 (25 mg, 100 µmol) was added after 1 hour. The reaction mixture was stirred without light for 48 h (unless noted otherwise). To quench, the mixture was treated with 20% aq sodium thiosulfate (4 mL) and shaken vigorously. The aqueous layer was extracted twice with ethyl acetate and the organic layers were combined, dried over magnesium sulfate and concentrated in a room temperature water bath. Decomposition of lactones was observed at elevated temperatures. Flash column chromatography (SiO_2, 5-10-20% ethyl acetate in hexanes) yielded the desired product. The lactone products were stored in frozen benzene to prevent degradation. The absolute configuration of **8i** was assigned by the crystal structure from X-ray crystallography as (*R*) and the rest of the examples were assigned by analogy.



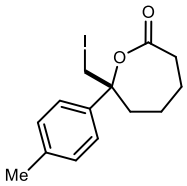
(*R*)-7-(Iodomethyl)-7-phenyloxepan-2-one (8a). The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (20.4 mg, 100 µmol) and (*R*,*R*)-^{6}MeOStilbPBAM·$HNTf_2$. The crude material was purified by silica gel chromatography to afford a colorless oil (23.0 mg, 71%) that was determined to be 88% ee by chiral HPLC (Chiralpak OD-H: 10% IPA/hexanes, 1.0 mL/min: t_r(major) = 8.81 min, t_r(minor) = 9.90 min). $[\alpha]_D^{20}$ -30.1 (*c* 1.0, $CHCl_3$); R_f = 0.4 (30%

[5] Hurtado, R. R.; Harney, A. S.; Heffern, M. C.; Holbrook, R. J.; Holmgren, R. A.; Meade, T. J. *Mol. Pharm.* **2012**, *9*, 325.

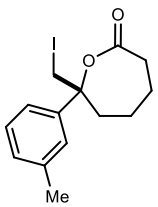
EtOAc/hexanes); IR (film) 2950, 2349, 1730, 1509, 1435, 1258, 1159 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45-7.32 (m, 5H), 3.53 (d, *J* = 10.8 Hz, 1H), 3.41 (d, *J* = 10.8 Hz, 1H), 2.70-2.63 (m, 1H), 2.60-2.53 (m, 1H), 2.40 (ddd, *J* = 3.4, 12.7, 16.0 Hz, 1H), 2.01-1.68 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 174.5, 139.1, 129.4, 128.6, 126.2, 83.1, 37.5, 36.8, 24.6, 23.0, 21.3; HRMS (ESI): Exact mass calcd for $C_{13}H_{15}INaO_2$ $[M+Na]^+$ 353.0015, found 353.0018.



(*R*)-7-(Iodomethyl)-7-(naphthalen-2-yl)oxepan-2-one (8b). The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (25.4 mg, 100 μmol) and (*R*,*R*)-^{6}MeOStilbPBAM·$HNTf_2$. The crude material was purified by silica gel chromatography to afford a colorless oil (18.3 mg, 64%) that was determined to be 87% ee by chiral HPLC (Chiralpak OJ-H: 12% IPA/hexanes, 1.0 mL/min: t_r(major) = 19.8 min, t_r(minor) = 23.4 min). $[\alpha]_D^{20}$ -34.6 (*c* 1.0, $CHCl_3$); R_f = 0.4 (30% EtOAc/hexanes); IR (film) 2928, 2859, 1728, 1434 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.8 Hz, 1H), 7.86 (m, 2H), 7.81 (d, *J* = 1.7 Hz, 1H), 7.55 (dd, *J* = 3.4, 3.4 Hz, 1H), 7.52 (dd, *J* = 3.4, 3.4 Hz, 1H), 7.42 (dd, *J* = 8.7, 2.0 Hz, 1H), 3.68 (d, *J* = 10.5 Hz, 1H), 3.50 (d, *J* = 10.6 Hz, 1H), 2.80 (ddd, *J* = 15.7, 3.4, 3.4 Hz, 1H), 2.56 (dddd, *J* = 13.9, 6.6, 1.5, 1.5 Hz, 1H), 2.47 (ddd, *J* = 15.8, 12.8, 3.1 Hz, 1H), 2.01 (m, 1H), 1.96 (m, 1H), 1.82 (m, 1H), 1.69 (m, 1H), 1.60 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 174.5, 136.4, 133.2, 132.9, 129.3, 128.3, 127.8, 127.1, 127.0, 125.8, 123.3, 83.2, 37.6, 36.7, 24.6, 22.9, 21.1; HRMS (ESI): Exact mass calcd for $C_{17}H_{18}IO_2$ $[M+H]^+$ 381.0346, found 381.0350.

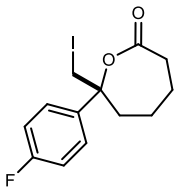


(*R*)-7-(Iodomethyl)-7-(p-tolyl)oxepan-2-one (8c). The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (21.7 mg, 100 μmol) and (*R*,*R*)-^{6}MeOStilbPBAM·$HNTf_2$. The crude material was purified by silica gel chromatography to afford a colorless oil (30.2 mg, 87%) that was determined to be 77% ee by chiral HPLC (Chiralpak IC: 12% IPA/hexanes, 1.0 mL/min: t_r(major) = 14.6 min, t_r(minor) = 16.6 min). $[\alpha]_D^{20}$ -29.1 (*c* 1.0, $CHCl_3$); R_f = 0.4 (30% EtOAc/hexanes); IR (film) 2932, 2862, 1728, 1510, 1435 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, *J* = 8.8 Hz, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 3.41 (d, *J* = 10.6 Hz, 1H), 3.29 (d, *J* = 10.6 Hz, 1H), 2.53 (ddd, *J* = 15.1, 3.5, 3.5 Hz, 1H), 3.45 (dddd, *J* = 14.2, 6.6, 1.5, 1.5 Hz, 1H), 2.28 (m, 1H), 2.26 (s, 3H), 1.82 (ddd, *J* = 13.8, 13.4, 2.6 Hz, 1H), 1.79 (m, 1H), 1.72-1.63 (m, 1H), 1.63-1.57 (m, 1H), 1.45 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 174.5, 138.4, 135.9, 130.0, 128.4, 126.0, 83.0, 37.4, 36.7, 24.6, 22.9, 21.5; HRMS (ESI): Exact mass calcd for $C_{14}H_{18}IO_2$ $[M+H]^+$ 345.0346, found 345.0346.

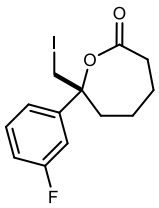


(*R*)-7-(Iodomethyl)-7-(m-tolyl)oxepan-2-one (8d). The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (21.7 mg, 100 μmol) and (*R*,*R*)-^{6}MeOStilbPBAM·$HNTf_2$. The crude material was purified by silica gel chromatography to afford a colorless oil (24.0 mg, 76%) that was determined to be 84% ee by chiral HPLC (Chiralpak IC: 12% IPA/hexanes, 1.0 mL/min: t_r(major) = 13.2 min, t_r(minor) = 16.1 min). $[\alpha]_D^{20}$ -29.9 (*c* 1.0, $CHCl_3$); R_f = 0.4 (30% EtOAc/hexanes); IR (film) 3018, 2931, 2861, 1728, 1435 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.15 (d, *J* = 7.8 Hz, 1H), 7.12 (s, 1H), 7.11 (d, *J* = 7.8 Hz, 1H), 3.51 (d, *J* = 10.6 Hz, 1H), 3.39 (d, *J* = 10.6 Hz, 1H), 2.62 (ddd, *J* = 15.3, 3.2, 3.2 Hz, 1H), 2.55 (dddd, *J* = 14.2, 6.6, 1.4, 1.4 Hz, 1H), 2.38 (m, 1H), 2.37 (s, 3H), 1.99 (ddd, *J* = 13.7, 13.7, 2.3 Hz, 1H), 1.89 (m, 1H), 1.79 (m, 2H), 1.72 (m, 1H), 1.57 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm

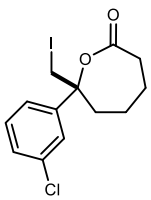
174.6, 139.2, 139.0, 129.3, 129.2, 128.4, 126.6, 123.3, 83.0, 37.54, 36.7, 24.6, 22.9, 21.4; HRMS (ESI): Exact mass calcd for $C_{14}H_{22}INO_2$ $[M+NH_4]^+$ 362.0611, found 362.0611.



(*R*)-7-(4-Fluorophenyl)-7-(iodomethyl)oxepan-2-one (8f). The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (11.1 mg, 50 μmol) and (*R,R*)-^{6}MeOStilbPBAM·$HNTf_2$. The crude material was purified by silica gel chromatography to afford a colorless oil (11.3 mg, 65%) that was determined to be 93% ee by chiral HPLC (Chiralpak OD-H: 10% IPA/hexanes, 1.0 mL/min: t_r(major) = 8.6 min, t_r(minor) = 9.6 min). [α] $^{20}_{D}$ -22.9 (*c* 0.14, $CHCl_3$); R_f = 0.2 (20% EtOAc/hexanes); IR (film) 2925, 2853, 1731, 1602, 1508 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (dd, *J* = 7.2, 5.2 Hz, 2H), 7.05 (t, *J* = 8.5 Hz, 2H), 3.43 (d, *J* = 10.6 Hz, 1H), 3.34 (d, *J* = 10.6 Hz, 1H), 2.60 (d, *J* = 15.1, 1H), 2.51 (dd, *J* = 14.3, 6.5 Hz, 1H), 2.31 (ddd, *J* = 15.7, 12.7, 3.2 Hz, 1H), 1.93-1.80 (m, 2H), 1.72-1.60 (m, 2H), 1.58-1.51 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 174.1, 163.3, 134.8, 128.2 (d, *J* = 8.3 Hz), 116.4 (d, *J* = 22.6 Hz), 82.6, 37.5, 36.6, 24.4, 22.9, 21.2; ^{19}F NMR (282 MHz, $CDCl_3$) ppm -112.9; HRMS (ESI): Exact mass calcd for $C_{13}H_{15}FIO_2$ $[M+H]^+$ 349.0095, found 349.0084.

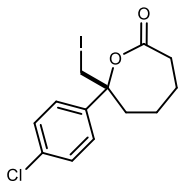


(*R*)-7-(3-Fluorophenyl)-7-(iodomethyl)oxepan-2-one (8g). The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (11.1 mg, 50 μmol) and (*R,R*)-^{6}MeOStilbPBAM·$HNTf_2$. The crude material was purified by silica gel chromatography to afford a colorless oil (9.2 mg, 53%) that was determined to be 93% ee by chiral HPLC (Chiralpak OD-H: 2% IPA/hexanes, 1.0 mL/min: t_r(major) = 17.5 min, t_r(minor) = 19.0 min). [α] $^{20}_{D}$ -25.0 (*c* 1.0, $CHCl_3$); R_f = 0.2 (20% EtOAc/hexanes); IR (film) 2926, 2852, 1730, 1613, 1588 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (ddd, *J* = 8.1, 8.1, 5.9 Hz, 1H), 7.06 (d, *J* = 7.3 Hz, 1H), 7.03-6.92 (m, 2H), 3.44 (d, *J* = 10.9 Hz, 1H), 3.35 (d, *J* = 10.9 Hz, 1H), 2.63-2.47 (m, 2H), 2.32 (ddd, *J* = 15.7, 12.7, 3.2 Hz, 1H), 1.95-1.80 (m, 2H), 1.73-1.62 (m, 2H), 1.58-1.51 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 173.8, 162.3, 141.7 , 130.9 (d, *J* = 8.7 Hz), 121.8 (d, *J* = 3.5 Hz), 115.5 (d, *J* = 21.5 Hz), 113.5 (d, *J* = 23.2 Hz), 82.5, 37.3, 36.6, 24.4, 22.7, 20.4; ^{19}F NMR (282 MHz, $CDCl_3$) ppm -110.5; HRMS (ESI): Exact mass calcd for $C_{13}H_{18}FINO_2$ $[M+NH_4]^+$ 366.0361, found 366.0366.

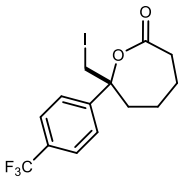


(*R*)-7-(3-Chlorophenyl)-7-(iodomethyl)oxepan-2-one (8h). The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (23.7 mg, 100 μmol) and (*R,R*)-^{6}MeOStilbPBAM·$HNTf_2$. The crude material was purified by silica gel chromatography to afford a colorless oil (7.5 mg, 21%) that was determined to be 96% ee by chiral HPLC (Chiralpak OJ-H: 12% IPA/hexanes, 1.0 mL/min: t_r(major) = 12.7 min, t_r(minor) = 13.7 min). [α] $^{20}_{D}$ -17.1 (*c* 0.58, $CHCl_3$); R_f = 0.4 (30% EtOAc/hexanes); IR (film) 2919, 2849, 1730, 1571, cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.34 (m, 2H), 7.31 (m, 1H), 7.24 (ddd, *J* = 6.8, 1.9, 1.9 Hz, 1H), 3.49 (d, *J* = 10.7 Hz, 1H), 3.41 (d, *J* = 10.7 Hz, 1H), 2.66-2.58 (m, 2H), 2.37 (ddd, *J* = 15.7, 12.7, 3.2 Hz, 1H), 1.95 (m, 2H), 1.75 (m, 2H), 1.58 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 173.8, 141.3, 135.4, 130.6, 128.8, 126.4, 124.4, 82.5, 37.3, 26.7, 24.5, 22.8, 20.6; HRMS (ESI): Exact mass calcd for $C_{13}H_{18}ClINO_2$ $[M+NH_4]^+$ 382.0065, found 382.0068.

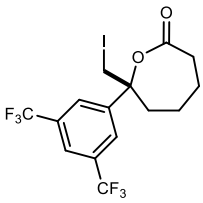
The reaction was also carried out on 1 mmol scale, using identical reaction conditions, to give the product (93.1 mg, 26%) in 96% ee.



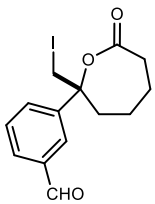
(*R*)-7-(4-Chlorophenyl)-7-(iodomethyl)oxepan-2-one (8i). The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (11.8 mg, 50 μmol) and (*R,R*)-^{6}MeOStilbPBAM·HNTf$_2$. The crude material was purified by silica gel chromatography to afford a yellow solid (12.7 mg, 70%) that was determined to be 91% ee by chiral HPLC (Chiralpak OD-H: 10% IPA/hexanes, 1.0 mL/min: t_r(major) = 10.2 min, t_r(minor) = 11.2 min). [α] $^{20}_{D}$ -20.5 (*c* 1.0, $CHCl_3$); R_f = 0.2 (20% EtOAc/hexanes); IR (film) 2934, 2864, 1730, 1593 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.8 Hz, 2H), 7.20 (d, *J* = 7.8 Hz, 2H), 3.42 (d, *J* = 11.2 Hz, 1H), 3.33 (d, *J* = 11.2 Hz, 1H), 2.60 (d, *J* = 15.7, 1H), 2.51 (dd, *J* = 14.2, 6.0 Hz, 1H), 2.31 (ddd, *J* = 15.2, 12.4, 3.1 Hz, 1H), 1.92-1.80 (m, 2H), 1.72-1.62 (m, 2H), 1.57-1.51 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 173.9, 137.6, 129.4, 128.3, 127.6, 82.6, 37.2, 36.6, 24.4, 22.8, 20.7; HRMS (ESI): Exact mass calcd for $C_{13}H_{15}ClIO_2$ $[M+H]^+$ 364.9800, found 364.9801.



(*R*)-7-(4-Trifluoromethylphenyl)-7-(iodomethyl)oxepan-2-one (8j). The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (13.6 mg, 50 μmol) and (*R,R*)-^{6}MeOStilbPBAM·HNTf$_2$. The crude material was purified by silica gel chromatography to afford a colorless oil (9.6 mg, 48%) that was determined to be 81% ee by chiral HPLC (Chiralpak OD-H: 10% IPA/hexanes, 1.0 mL/min: t_r(major) = 22.9 min, t_r(minor) = 25.8 min). [α] $^{20}_{D}$ -16.4 (*c* 0.32, $CHCl_3$); R_f = 0.2 (20% EtOAc/hexanes); IR (film) 2927, 2852, 1734, 1560 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.2 Hz, 2H), 7.41 (d, *J* = 8.2 Hz, 2H), 7.24 (ddd, *J* = 6.8, 1.9, 1.9 Hz, 1H), 3.44 (d, *J* = 10.7 Hz, 1H), 3.36 (d, *J* = 10.7 Hz, 1H), 2.66 (d, *J* = 16.1 Hz, 1H), 2.54 (dd, *J* = 14.0, 6.7 Hz, 1H), 2.35 (ddd, *J* = 15.7, 12.7, 3.2 Hz, 1H), 1.93-1.79 (m, 2H), 1.72-1.61 (m, 2H), 1.60-1.51 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 173.6, 143.2, 128.4, 126.7, 126.2 (q, *J* = 3.8 Hz) ,125.4, 82.6, 37.3, 36.6, 24.4, 22.7, 20.1; ^{19}F NMR (282 MHz, $CDCl_3$) ppm -62.8; HRMS (ESI): Exact mass calcd for $C_{14}H_{18}F_3INO_2$ $[M+NH_4]^+$ 416.0329, found 416.0325.

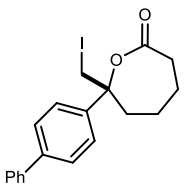


(*R*)-7-(3,5-bis(Trifluoromethyl)phenyl)-7-(iodomethyl)oxepan-2-one (8k). The reaction was carried out over 48 h at room temperature according to the general procedure, using the corresponding carboxylic acid (17.0 mg, 50 μmol) and (*R,R*)-^{6}MeOStilbPBAM·HNTf$_2$. The crude material was purified by silica gel chromatography to afford a colorless oil (3.6 mg, 10%) that was determined to be 10% ee by chiral HPLC (Chiralpak OD-H: 10% IPA/hexanes, 1.0 mL/min: t_r(major) = 9.1 min, t_r(minor) = 10.5 min). [α] $^{20}_{D}$ [undetected] (*c* 0.09, $CHCl_3$); R_f = 0.2 (20% EtOAc/hexanes); IR (film) 2920, 2850, 1733, 1372, 1166 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.34 (m, 2H), 7.84 (s, 1H), 7.72 (s, 2H), 3.44 (d, *J* = 11.0 Hz, 1H), 3.41 (d, *J* = 11.0 Hz, 1H), 2.75 (dd, *J* = 15.9, 4.3 Hz, 1H), 2.60 (dd, *J* = 14.0, 6.9 Hz, 1H), 2.35 (ddd, *J* = 15.7, 12.7, 3.2, 1H), 1.99-1.88 (m, 1H), 1.84-1.75 (m, 1H), 1.75-1.66 (m, 1H), 1.56 (m, *J* = 10.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 175.0, 141.5, 131.4 (q, $^{2}J_{CF}$ = 31.8 Hz), 125.7 (q, $^{3}J_{CF}$ = 3.8 Hz), 124.5 (q, $^{1}J_{CF}$ = 272.4 Hz), 120.3 (q, $^{3}J_{CF}$ = 3.8 Hz), 80.9, 37.8, 37.1, 24.9, 23.0, 19.5; ^{19}F NMR (282 MHz, $CDCl_3$) ppm -62.9; HRMS (ESI): Exact mass calcd for $C_{15}H_{17}F_6INO_2$ $[M+NH_4]^+$ 484.0203, found 484.0205.

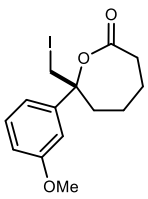


(*R*)-7-(3-Formylphenyl)-7-(iodomethyl)oxepan-2-one (8l). The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (17.9 mg, 50 μmol) and (*R,R*)-^{6}MeOStilbPBAM·HNTf$_2$. The crude material was purified by silica gel chromatography to afford a colorless oil (9.7 mg, 54%) that was determined to be 94% ee by chiral HPLC (Chiralpak OD-H: 10% IPA/hexanes, 1.0 mL/min: t_r(major) = 18.5 min, t_r(minor) =

38.8 min). [α] $^{20}_{D}$ -23.5 (*c* 1.0, $CHCl_3$); R_f = 0.2 (20% EtOAc/hexanes); IR (film) 2924, 1734, 1647 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.83 (d, *J* = 6.9, 1H), 7.76 (br s, 1H), 7.62-7.54 (m, 2H), 3.45 (d, *J* = 11.6 Hz, 1H), 3.40 (d, *J* = 11.6 Hz, 1H), 2.73 (d, *J* = 14.9 Hz, 1H), 2.54 (dd, *J* = 14.3, 6.2 Hz, 1H), 2.34 (ddd, *J* = 15.1, 12.9, 3.1 Hz, 1H), 1.92-1.86 (m, 1H), 1.83 (m, 1H), 1.70-1.63 (m, 2H), 1.58-1.54 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 191.5, 173.7, 140.7, 137.2, 132.1, 130.1, 130.0, 127.0, 82.5, 37.5, 35.7, 24.4, 22.9, 20.5; HRMS (ESI): Exact mass calcd for $C_{14}H_{16}IO_3$ $[M+H]^+$ 359.0139, found 359.0139.

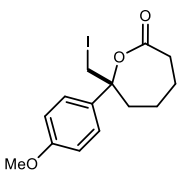


(*R*)-7-([1,1'-Biphenyl]-4-yl)-7-(iodomethyl)oxepan-2-one (8m). The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (27.9 mg, 100 μmol) and (*R,R*)-^{6}MeOStilbPBAM·$HNTf_2$. The crude material was purified by silica gel chromatography to afford a colorless oil (29.4 mg, 87%) that was determined to be 84% ee by chiral HPLC (Chiralpak AD-H: 10% IPA/hexanes, 1.0 mL/min: t_r(minor) = 14.2 min, t_r(major) = 26.8 min). [α] $^{20}_{D}$ -23.0 (*c* 1.0, $CHCl_3$); R_f = 0.4 (30% EtOAc/hexanes); IR (film) 2918, 2849, 1727, 1510, 1446 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (br d, *J* = 8.7 Hz, 2H), 7.50 (br d, *J* = 7.4 Hz, 2H), 7.36 (dd, *J* = 7.6, 7.6 Hz, 2H), 7.29 (m, 3H), 3.46 (d, *J* = 10.6 Hz, 1H), 3.35 (d, *J* = 10.6 Hz, 1H), 2.58 (ddd, *J* = 15.5, 4.2, 4.2 Hz, 1H), 2.50 (dd, *J* = 14.2, 6.6 Hz, 1H), 2.33 (ddd, *J* = 15.8, 12.6, 3.2 Hz, 1H), 1.95 (ddd, *J* = 13.8, 13.6, 2.1 Hz, 1H), 1.83 (m, 1H), 1.73 (m, 1H), 1.64 (m, 1H), 1.50 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 174.4, 141.3, 139.9, 137.9, 129.0, 128.4, 127.9, 127.1, 126.6, 82.9, 37.5, 36.8, 24.6, 22.9, 21.2; HRMS (ESI): Exact mass calcd for $C_{19}H_{20}IO_2$ $[M+H]^+$ 407.0502, found 407.0504.



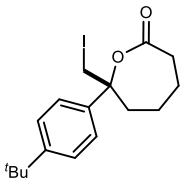
(*R*)-7-(Iodomethyl)-7-(3-methoxyphenyl)oxepan-2-one (8n). The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (25.7 mg, 100 μmol) and (*R,R*)-^{6}MeOStilbPBAM·$HNTf_2$. The crude material was purified by silica gel chromatography to afford a colorless oil (18.5 mg, 63%) that was determined to be 90% ee by chiral HPLC (Chiralpak OJ-H: 12% IPA/hexanes, 1.0 mL/min: t_r(major) = 13.5 min, t_r(minor) = 14.6 min). [α] $^{20}_{D}$ -32.2 (*c* 1.0, $CHCl_3$); R_f = 0.3 (30% EtOAc/hexanes); IR (film) 2918, 2849, 1728, 1599, 1487cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 7.9, 7.9 Hz, 1H), 6.91-6.85 (m, 3H), 3.81 (s, 3H), 3.52 (d, *J* = 10.6 Hz, 1H), 3.40 (d, *J* = 10.6 Hz, 1H), 2.58 (m, 2H), 2.38 (ddd, *J* = 15.6, 12.7, 3.5 Hz, 1H), 2.00 (ddd, *J* = 13.8, 13.8, 2.2 Hz, 1H), 1.88 (dddd, *J* = 14.3, 14.3, 3.8, 3.8 Hz, 1H), 1.79 (m, 1H), 1.75-1.68 (m, 1H), 1.57 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 174.4, 160.3, 140.6, 130.4, 118.4, 113.4, 112.3, 82.9, 55.5, 37.5, 36.7, 24.6, 22.8, 21.1; HRMS (ESI): Exact mass calcd for $C_{14}H_{17}O_3$ $[M-I]^+$ 233.1172, found 233.1170.

The reaction was also carried out on 1 mmol scale, using identical reaction conditions, to give the product (218 mg, 61%) in 87% ee.

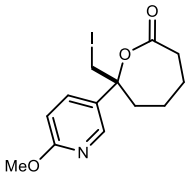


(*R*)-7-(Iodomethyl)-7-(4-methoxyphenyl)oxepan-2-one (8o). The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (25.7 mg, 100 μmol) and (*R,R*)-^{6}MeOStilbPBAM·$HNTf_2$. The crude material was purified by silica gel chromatography to afford a colorless oil (19.5 mg, 53%) that was determined to be 50% ee by chiral HPLC (Chiralpak OD-H: 2% IPA/hexanes, 1.0 mL/min: t_r(minor) = 41.06 min, t_r(major) = 47.73 min). [α] $^{20}_{D}$ -35.9 (*c* 1.0, $CHCl_3$); R_f = 0.3 (30% EtOAc/hexanes); IR (film) 2925, 2835, 1732, 1621, 1517, 1454, 1253, 1156, 1010 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.7 Hz, 2H), 6.93 (d, *J* = 8.7 Hz, 2H), 3.83 (s, 3H), 3.51 (d, *J* = 10.6 Hz, 1H), 3.38 (d, *J* = 10.6 Hz, 1H), 2.65-2.59 (m, 1H), 2.58-2.52 (m, 1H), 2.42-2.34 (m, 1H), 2.03-1.95 (m, 1H), 1.93-1.68 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 174.6,

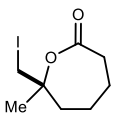
159.6, 130.9, 127.5, 114.7, 82.9, 55.5, 37.4, 36.8, 24.7, 23.0, 21.7; HRMS (ESI): Exact mass calcd for $C_{14}H_{17}IO_3$ $[M]^+$ 361.0295, found 361.0294.



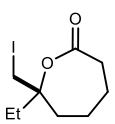
(*R*)-7-(4-(*tert*-Butyl)phenyl)-7-(iodomethyl)oxepan-2-one (8p). The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (26.0 mg, 100 μmol) and (*R,R*)-^{6}MeOStilbPBAM·$HNTf_2$. The crude material was purified by silica gel chromatography to afford a colorless oil (25.0 mg, 66%) that was determined to be 83% ee by chiral HPLC (Chiralpak OJ-H: 12% IPA/hexanes, 1.0 mL/min: t_r(major) = 10.3 min, t_r(minor) = 12.0 min). $[\alpha]_D^{20}$ -26.7 (*c* 1.0, $CHCl_3$); R_f = 0.4 (30% EtOAc/hexanes); IR (film) 2959, 2865, 1730, 1435 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.6 Hz, 2H), 7.23 (d, *J* = 8.6 Hz, 2H), 3.51 (d, *J* = 10.6 Hz, 1H), 3.36 (d, *J* = 10.6 Hz, 1H), 2.60 (ddd, *J* = 15.8, 3.8, 3.8 Hz, 1H), 2.54 (dd, *J* = 14.7, 7.2 Hz, 1H), 2.41 (ddd, *J* = 15.7, 12.6, 3.2 Hz, 1H), 1.98 (ddd, *J* = 13.7, 13.7, 2.3 Hz, 1H), 1.87 (m, 1H), 1.78 (m, 1H), 1.69 (m, 1H), 1.57 (m, 1H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 174.6, 151.6, 135.8, 128.4, 126.2, 125.8, 82.9, 37.5, 36.8, 31.3, 24.5, 22.9, 21.5; HRMS (ESI): Exact mass calcd for $C_{17}H_{23}IO_2$ $[M\text{-}I]^+$ 259.1693, found 259.1694.



(*R*)-7-(Iodomethyl)-7-(6-methoxypyridin-3-yl)oxepan-2-one (8q). The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (23.5 mg, 100 μmol) and (*R,R*)-^{6}MeOStilbPBAM·$HNTf_2$. The crude material was purified by silica gel chromatography to afford a colorless oil (17.0 mg, 47%) that was determined to be 75% ee by chiral HPLC (Chiralpak OJ-H: 10% IPA/hexanes, 1.0 mL/min: t_r(major) = 20.2 min, t_r(minor) = 24.5 min). $[\alpha]_D^{20}$ -21.2 (*c* 0.68, $CHCl_3$); R_f = 0.2 (20% EtOAc/hexanes); IR (film) 2941, 1729, 1603, 1494 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 2.6, 1H), 7.58 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.83 (d, *J* = 8.8, 6.7 Hz, 1H), 3.99 (s, 3H), 3.53 (d, *J* = 10.4 Hz, 1H), 3.44 (d, *J* = 10.6 Hz, 1H), 2.72 (d, *J* = 15.7 Hz, 1H), 2.62 (dd, *J* = 14.1, 4.4 Hz, 1H), 2.38 (ddd, *J* = 14.9, 12.7, 3.2 Hz, 1H), 2.08-1.91 (m, 2H), 1.87-1.71 (m, 2H), 1.64 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 173.6, 163.9, 145.1, 136.4, 127.3, 111.4, 81.5, 53.6, 36.9, 36.4, 24.4, 22.8, 21.0; HRMS (ESI): Exact mass calcd for $C_{13}H_{17}INO_3$ $[M+H]^+$ 362.0248, found 362.0240.

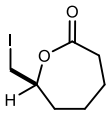


***(S)*-7-(Iodomethyl)-7-methyloxepan-2-one (8r).** The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (14.2 mg, 100 μmol) and (*R,R*)-^{6}MeOStilbPBAM·$HNTf_2$. The crude material was purified by silica gel chromatography to afford a colorless oil (11.3 mg, 42%) that was determined to be 63% ee by chiral HPLC (Chiralpak OJ-H: 10% IPA/hexanes, 1.0 mL/min: t_r(minor) = 11.3 min, t_r(major) = 12.4 min). $[\alpha]_D^{20}$ +1.4 (*c* 0.57, $CHCl_3$); R_f = 0.4 (20% EtOAc/hexanes); IR (film) 2935, 2863, 1721, 1449, 1431, 1380, 1287 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.38 (br s, 2H), 2.66-2.59 (m, 2H), 2.07-1.94 (m, 2H), 1.83-1.68 (m, 3H), 1.67-1.57 (m, 1H), 1.55 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 173.4, 80.3, 37.7, 37.0, 25.6, 24.0, 23.1, 15.6; HRMS (ESI): Exact mass calcd for $C_8H_{14}IO_2$ $[M+H]^+$ 269.0033, found 269.0036.

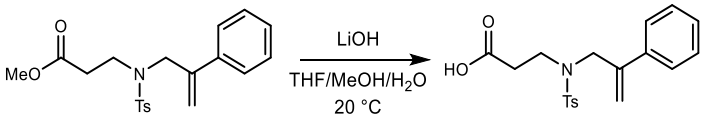


***(S)*-7-(Iodomethyl)-7-ethyloxepan-2-one (8s).** The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (7.8 mg, 50 μmol) and (*R,R*)-^{6}MeOStilbPBAM·$HNTf_2$. The crude material was purified by silica gel chromatography to afford a colorless oil (8.2 mg, 58%) that was determined to be 72% ee by chiral HPLC (Chiralpak OJ-H: 6% IPA/hexanes, 1.0 mL/min: t_r(minor) = 10.8 min, t_r(major) = 11.7 min). $[\alpha]_D^{20}$ +6.4 (*c* 0.25, $CHCl_3$); R_f = 0.4 (30%

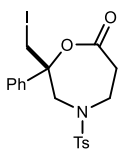
EtOAc/hexanes); IR (film) 2924, 2852, 1717, 1461, 1352, 1285, 1178 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.39 (br s, 2H), 2.68-2.54 (m, 2H), 2.08-1.82 (m, 4H), 1.78-1.70 (m, 2H), 1.70-1.62 (m, 2H), 0.89 (t, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 173.6, 80.6, 37.2, 35.9, 30.8, 29.7, 23.1, 11.6, 7.4; HRMS (ESI): Exact mass calcd for $C_9H_{16}IO_2$ $[M+H]^+$ 283.0189, found 283.0189.



(*S*)-7-(Iodomethyl)oxepan-2-one (8t). The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (23.7 mg, 100 μmol) and (*R*,*R*)-^{6}MeOStilbPBAM·$HNTf_2$. The crude material was purified by silica gel chromatography to afford a colorless oil (24%, NMR yield) that was very prone to decomposition, but determined to be 44% ee by chiral HPLC (Chiralpak OD-H: 12% IPA/hexanes, 1.0 mL/min: t_r(major) = 9.4 min, t_r(minor) = 10.1 min). The remainder of the physical data matched with literature values.[6]



3-((4-Methyl-*N*-(2-phenylallyl)phenyl)sulfonamido)propanoic acid (9). Methyl 3-((4-methyl-*N*-(2-phenylallyl)phenyl)sulfonamido)propanoate (1.70 g, 4.55 mmol) was dissolved in tetrahydrofuran/methanol/water (3:1:1, 50 mL) and treated with lithium hydroxide (550 mg, 22.8 mmol). The mixture was stirred overnight at room temperature, concentrated until the aqueous layer remained, and then diluted with 1 N aq NaOH. The aqueous layer was washed with diethyl ether, acidified using 6 M aq HCl, and extracted with dichloromethane. The organic layers were dried ($MgSO_4$), filtered, and concentrated to give the product as a white solid (890 mg, 55%). Mp = 130-133 °C; R_f = 0.43 (100% EtOAc); IR (film) 3750, 2918, 2370, 1718, 1329, 1149 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.5 Hz, 2H), 7.46-7.43 (m, 2H), 7.36-7.29 (m, 5H), 5.50 (s, 1H), 5.23 (s, 1H), 4.20 (s, 2H), 3.31-3.27 (m, 2H), 2.51-2.47 (m, 2H), 2.44 (s, 3H) [O*H* not observed]; ^{13}C NMR (100 MHz, $CDCl_3$) ppm 175.8, 143.8, 142.9, 137.0, 135.7, 130.0, 128.7, 128.4, 127.6, 126.6, 117.0, 53.2, 43.0, 33.5, 21.7; HRMS (ESI): Exact mass calcd for $C_{19}H_{22}NO_4S$ $[M+H]^+$ 360.1270, found 360.1260.



(*R*)-2-(Iodomethyl)-2-phenyl-4-tosyl-1,4-oxazepan-7-one (10). The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (36.0 mg, 100 μmol) and (*R*,*R*)-^{6}MeOStilbPBAM·$HNTf_2$ (10 mg, 10.0 μmol). The crude material was purified by silica gel chromatography to afford a colorless oil (33.6 mg, 70%) that was determined to be 87% ee by chiral HPLC analysis (Chiralcel OD-H, 20% ^{i}PrOH/hexanes, 1 mL/min, t_r(e_1, minor) = 15.46 min, t_r(e_2, major) = 20.12 min); R_f = 0.35 (30% EtOAc/hexanes); $[\alpha]_D^{20}$ -37 (*c* 1.4, $CHCl_3$); IR (film) 3755, 3041, 2385, 1735, 1369, 1253, 1156 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.7 Hz, 2H), 7.56 (d, *J* = 7.7 Hz, 2H), 7.49-7.38 (m, 5H), 4.77 (dd, *J* = 2.0, 14.4 Hz, 1H), 3.77-3.72 (m, 1H), 3.54 (d, *J* = 11.0 Hz, 1H), 3.42 (d, *J* = 11.0 Hz, 1H), 3.24 (d, *J* = 14.4 Hz, 1H), 2.66-2.61 (m, 1H), 2.55-2.49 (m, 1H), 2.47 (s, 3H), 2.37-2.29 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 171.4, 144.8, 137.5, 133.0, 130.4, 129.5, 129.2, 127.6, 126.6, 81.3, 57.3, 43.8, 36.9, 21.8, 15.7; HRMS (ESI): Exact mass calcd for $C_{19}H_{20}INaNO_4S$ $[M+Na]^+$ 508.0055, found 508.0043.

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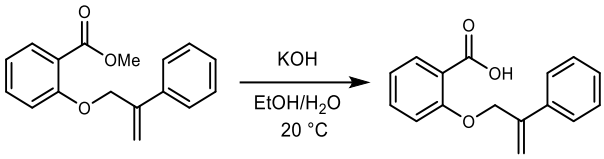
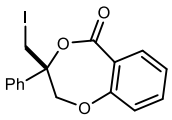
[6] Verma, A.; Jana, S.; Durga Prasad, C.; Yadav, A.; Kumar, S. *Chem. Commun.* **2016**, *52*, 4179.

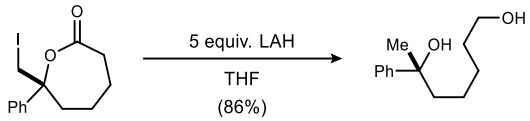


2-((2-Phenylallyl)oxy)benzoic acid (11). Methyl 2-((2-phenylallyl)oxy)benzoate (326 mg, 1.22 mmol) was dissolved in ethanol (50 mL) and water (10 mL), potassium hydroxide (342 mg, 6.10 mmol) was added, and the resulting mixture was stirred for 5 days. The reaction mixture was acidified with 5 M aq HCl and extracted with dichloromethane. The combined organic layers were dried ($MgSO_4$), filtered, and concentrated to give the product as a white solid (300 mg, 97%). Mp = 70-74 °C; R_f = 0.21 (30% EtOAc/hexanes); IR (film) 3282, 3054, 2904, 2353, 1749, 1599, 1457, 1392, 1314, 1229 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.48 (br s, 1H), 8.18 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.57 (ddd, *J* = 8.4, 7.4, 1.9 Hz, 1H), 7.44-7.35 (m, 5H), 7.17-7.11 (m, 2H), 5.68 (s, 1H), 5.50 (s, 1H), 5.17 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 165.3, 157.3, 141.9, 137.2, 135.1, 134.1, 129.1, 128.9, 126.2, 122.6, 118.1, 117.3, 113.0, 72.1; HRMS (ESI): Exact mass calcd for $C_{16}H_{14}NaO_3$ $[M+Na]^+$ 277.0841, found 277.0841.



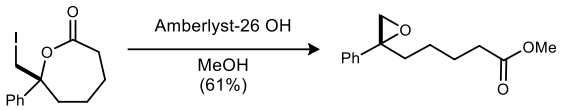
(*R*)-3-(Iodomethyl)-3-phenyl-2,3-dihydro-5H-benzo[e][1,4]dioxepin-5-one (12). The reaction was carried out over 48 h according to the general procedure, using the corresponding carboxylic acid (35.0 mg, 100 μmol) and (*R*,*R*)-^{6}MeOStilbPBAM·$HNTf_2$ (10 mg, 10.0 μmol). The crude material was purified by silica gel chromatography to afford a colorless oil (34.6 mg, 90%) that was determined to be 65% ee by by chiral HPLC analysis (Chiralcel OD-H, 10% ^{i}PrOH/hexanes, 1 mL/min, t_r(*e*$_1$, minor) = 13.76 min, t_r(*e*$_2$, major) = 16.65 min); R_f = 0.50 (30% EtOAc/hexanes); $[\alpha]_D^{20}$ +10 (*c* 1.3, $CHCl_3$); IR (film) 3050, 1711, 1614, 1498, 1439, 1291, 1129 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (dd, *J* = 1.7, 8.3 Hz, 1H), 7.42-7.38 (m, 2H), 7.34-7.27 (m, 4H), 6.98-6.94 (m, 1H), 6.80 (dd, *J* = 1.2, 8.4 Hz, 1H), 4.92 (d, *J* = 14.0 Hz, 1H), 4.79 (d, *J* = 14.0 Hz, 1H), 3.60 (d, *J* = 11.1 Hz, 1H), 3.56 (d, *J* = 11.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 165.9, 156.4, 137.0, 135.3, 135.0, 128.8 (2C), 125.9, 121.8, 119.6, 116.7, 82.1, 75.9, 12.1; HRMS (ESI): Exact mass calcd for $C_{16}H_{13}INaO_3$ $[M+Na]^+$ 402.9807, found 402.9820.

Derivatizations of ε-lactones

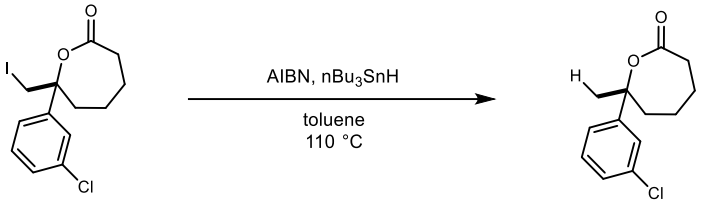


(*R*)-6-Phenylheptane-1,6-diol (13). To a microwave vial equipped with a stir bar was added $LiAlH_4$ (11.0 mg, 290 μmol), (*R*)-7-(iodomethyl)-7-phenyloxepan-2-one (19.0 mg, 58 μmol, 89% ee) and anhydrous tetrahydrofuran (1.3 mL). The reaction mixture was stirred at room temperature and monitored by TLC. Full conversion was realized after five hours, upon which the reaction was quenched with aqueous NH_4Cl. The aqueous layer was extracted twice with ethyl acetate and the organic layers were combined, dried, and concentrated. The desired product was a white oil (10.3 mg, 86%) that was determined to be 88% ee by chiral HPLC (Chiralpak AD-H: 8% IPA/hexanes, 1.0 mL/min: t_r(minor) = 16.3 min, t_r(major) = 20.4 min). $[\alpha]_D^{20}$ -18.5 (*c* 1.0, $CHCl_3$); R_f = 0.1 (50% EtOAc/hexanes); IR (film) 3391, 2929, 2850, 1556 cm^{-1}; ^1H NMR (400 MHz,

$CDCl_3$) δ 7.42 (d, *J* = 7.8 Hz, 2H), 7.34 (dd, *J* = 7.7, 7.7 Hz, 2H), 7.23 (dd, *J* = 7.4, 7.4 Hz, 1H), 3.59 (dd, *J* = 6.5, 6.5 Hz, 2H), 1.81 (m, 2H), 1.56 (s, 3H), 1.51 (ddd, *J* = 14.4, 7.3, 7.3 Hz 2H), 1.31 (m, 2H), 1.21-1.11 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 148.0, 128.2, 126.6, 124.9, 74.8, 63.0, 44.2, 32.7, 30.32, 26.12, 23.8; HRMS (ESI): Exact mass calcd $C_{13}H_{19}O$ for $[M\text{-}OH]^+$ 191.1430, found 191.1429.



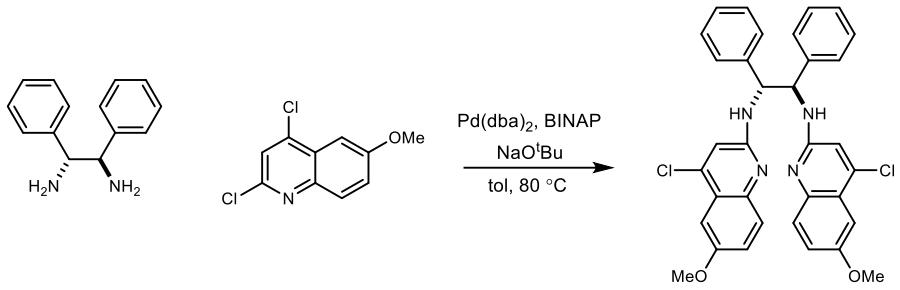
Methyl (*R*)-5-(2-phenyloxiran-2-yl)pentanoate (14). A vial backfilled with N_2 after drying was charged with a stir bar, (*R*)-7-(iodomethyl)-7-phenyloxepan-2-one (30.0 mg, 100 µmol, 90% ee) and methanol (300 µL). The reaction mixture was cooled to 0 °C and then Amberlyst A-26 hydroxide form (109 mg, 1.20 g/mmol) was added and monitored by TLC. Full conversion was realized after 90 min. The resulting mixture was filtered through a glass frit and washed with ethyl acetate. The solution was dried and concentrated to give the title compound as a colorless oil (13 mg, 61%). The product was determined to be 88% ee by chiral HPLC (Chiralpak OD-H: 10% IPA/hexanes, 1.0 mL/min: t_r(major) = 6.15 min, t_r(minor) = 7.0 min). $[\alpha]_D^{20}$ -14.5 (*c* 0.72, $CHCl_3$); R_f = 0.6 (30% EtOAc/hexanes); IR (film) 2944, 2850, 1734 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.22 (m, 4H), 7.20-7.15 (m, 1H), 3.54 (m, 3H), 2.86 (d, *J* = 5.3 Hz, 1H), 2.63 (d, *J* = 5.3 Hz, 1H), 2.18 (dd, *J* = 7.5, 7.5 Hz, 2H), 2.13 (ddd, *J* = 14.7, 10.2, 5.2 Hz, 1H), 1.64 (ddd, *J* = 14.6, 10.1, 5.5 Hz, 1H), 1.56 (ddd, *J* = 15.1, 7.6, 7.6 Hz, 2H), 1.29 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 174.0, 140.0, 128.4, 127.5, 126.0, 60.2, 55.6, 51.6, 35.2, 34.0, 25.0, 24.5; HRMS (ESI): Exact mass calcd $C_{14}H_{19}O_3$ for $[M+H]^+$ 235.1329, found 235.1330.



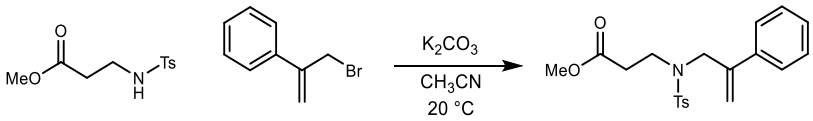
(*R*)-7-(3-Chlorophenyl)-7-methyloxepan-2-one (15). The procedure was modified from prior literature.[7] A flame dried microwave vial was charged with (*R*)-7-(3-chlorophenyl)-7-(iodomethyl)oxepan-2-one (20 mg, 54.9 µmol), ^{n}Bu$_3$SnH (42 µL, 98.9 µmol), AIBN (7.2 mg, 44.0 µmol), and anhydrous toluene (1 mL). The solution was degassed (freeze-pump-thaw) and then transferred to an oil bath that was preheated to 110 °C. The reaction was monitored by TLC and complete after 30 min. The resulting mixture was concentrated and then purified by column chromatography (10% w/w anhydrous potassium carbonate to silica) to afford a colorless oil (8.0 mg, 61%). The product was determined to be 95% ee by chiral HPLC (Chiralpak IA: 2% IPA/hexanes, 1.0 mL/min: t_r(major) = 12.8 min, t_r(minor) = 15.8 min). $[\alpha]_D^{20}$ -6.5 (*c* 0.41, $CHCl_3$); R_f = 0.5 (20% EtOAc/hexanes); IR (film) 2931, 2853, 1723 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.20 (m, 4H), 2.67-2.59 (m, 1H), 2.57 (tt, *J* = 7.1, 1.5 Hz, 1H), 2.14 (ddd, *J* = 15.5, 12.8, 3.2 Hz, 1H), 2.01 (ddd, *J* = 15.2, 12.1, 3.1, 1H), 1.91-1.82 (m, 1H), 1.79-1.69 (m, 2H), 1.60 (s, 3H), 1.59-1.55 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 175.2, 130.5, 129.1, 127.6,

[7] Viswanathan, R.; Smith, C. R.; Prabhakaran, E. N.; Johnston, J. N. *J. Org. Chem.* **2008**, *73*, 3040.

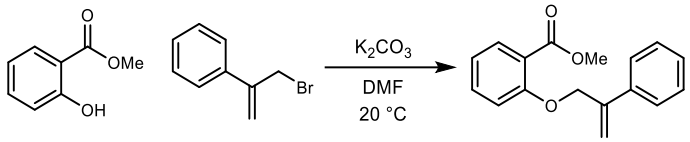
125.3, 123.1, 119.1, 83.8, 38.5, 36.8, 25.2, 24.4, 23.0; HRMS (ESI): Exact mass calcd $C_{13}H_{16}ClO_2$ for $[M+H]^+$ 239.0833, found 239.0832.



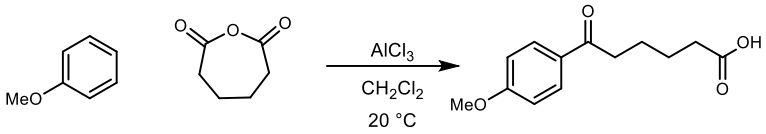
^{4}Cl-^{6}MeOStilb-BAM or (1*R*,2*R*)-*N*1,*N*2-bis(4-chloro-6-methoxyquinolin-2-yl)-1,2-diphenylethane-1,2-diamine (S1). A 25-mL, round-bottomed flask equipped with a stir bar was charged with (+)-(1*R*, 2*R*)-1,2-diphenylethylenediamine (500 mg, 2.4 mmol), $Pd(dba)_2$ (20 mg, 35 μmol), *rac*-BINAP (44 mg, 70 μmol), sodium *tert*-butoxide (565 mg, 5.8 mmol), and 2,4-dichloro-6-methoxylquinoline (1.1 g, 4.7 mmol). The reaction vessel was placed under an argon atmosphere and toluene (16 mL) was dispensed into the flask. The reaction vessel was evacuated and backfilled with argon gas three times. The round-bottomed flask was placed into an oil bath heated to 80 °C with stirring. The reaction was monitored by TLC and after 4 h nearly complete conversion was observed. The reaction was cooled to 25 °C, diluted with ethyl acetate, and filtered through a plug of Celite. Flash column chromatography (SiO_2, 15-35% ethyl acetate in hexanes) of the residue yielded a pale yellow solid (912 mg, 65%). $[\alpha]_D^{20}$ -4.1 (*c* 1.0, $CHCl_3$); R_f = 0.7 (30% EtOAc/hexanes); mp 201-205 °C; IR (film) 3241, 3062, 3027, 1600, 1491 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.79 (br d, *J* = 7.16 Hz, 2H), 7.45 (d, *J* = 9.0 Hz, 2H), 7.30 (br s, 2H), 7.29 (br s, 2H), 7.21 (dd, *J* = 8.9, 2.7 Hz, 2H), 7.18 (d, *J* = 2.7 Hz, 2H), 7.14 (dd, *J* = 7.5, 7.5 Hz, 4H), 7.04 (dd, *J* = 7.7, 7.7 Hz, 2H), 7.02 (s, 2H), 5.54 (dd, *J* = 12.6, 7.7 Hz, 2H), 3.81 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) ppm 154.9, 154.6, 143.6, 141.7, 139.5, 127.9, 127.7, 127.6, 126.5, 121.6, 120.8, 112.3, 102.6, 59.3, 55.3; HRMS (ESI): Exact mass calcd for $C_{34}H_{29}Cl_2N_4O_2$ $[M+H]^+$ 595.1662, found 595.1662.



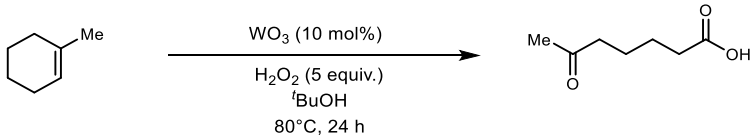
Methyl 3-((4-methyl-N-(2-phenylallyl)phenyl)sulfonamido)propanoate (S2). (3-Bromoprop-1-en-2-yl)benzene (1.30 g, 6.60 mmol) and methyl 3-((4-methylphenyl)sulfonamido)propanoate (1.70 g, 6.60 mmol) were dissolved in acetonitrile (100 mL) and treated with potassium carbonate (1.82 g, 13.2 mmol). The reaction mixture was stirred at room temperature for 3 days and then poured into 1 N aq HCl, extracted with dichloromethane, dried ($MgSO_4$), filtered, and concentrated to an oil. Flash chromatography (SiO_2, 30-50-100% ethyl acetate in hexanes) of the crude oil gave the product as a colorless oil (1.70 g, 69%). R_f = 0.40 (30% EtOAc/hexanes); IR (film) 2952, 1734, 1438, 1341, 1203, 1160, 1092 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.5 Hz, 2H), 7.38-7.36 (m, 2H), 7.28-7.18 (m, 5H), 5.42 (s, 1H), 5.16 (s, 1H), 4.13 (s, 2H), 3.52 (s, 3H), 3.26-3.23 (m, 2H), 2.41-2.37 (m, 2H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 171.9, 143.7, 142.9, 138.0, 135.8, 129.9, 128.6, 128.3, 127.5, 126.6, 116.8, 53.0, 51.7, 43.4, 33.7, 21.6; HRMS (ESI): Exact mass calcd for $C_{20}H_{23}NNaO_4S$ $[M+Na]^+$ 396.1245, found 396.1236.



Methyl 2-((2-phenylallyl)oxy)benzoate (S3). Methyl 2-hydroxybenzoate (540 mg, 3.55 mmol) was dissolved in dimethylformamide (40 mL), and then treated with (3-bromoprop-1-en-2-yl)benzene (700 mg, 3.55 mmol) and potassium carbonate (1.00 g, 7.21 mmol). The resulting mixture was stirred for 4 days and then poured over water and extracted with dichloromethane. The combined organic layers were dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (SiO_2, 20% ethyl acetate in hexanes) gave the product as an oil (326 mg, 34%). R_f = 0.51 (30% EtOAc/hexanes); IR (film) 2994, 2349, 1725, 1607, 1503, 1427, 1316, 1232, 1073 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.49-7.43 (m, 3H), 7.39-7.30 (m, 3H), 7.03-6.99 (m, 2H), 5.63 (d, *J* = 1.3 Hz, 1H), 5.60 (d, *J* = 1.3 Hz, 1H), 4.97 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 167.1, 158.0, 142.8, 138.6, 133.5, 132.0, 128.6, 128.1, 126.3, 120.9, 120.8, 114.6, 113.8, 70.4, 52.1; HRMS (ESI): Exact mass calcd for $C_{17}H_{16}NaO_3$ $[M+Na]^+$ 291.0997, found 291.0988.



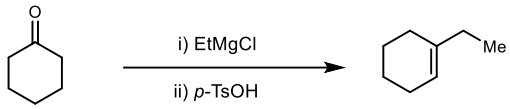
6-(4-Methoxyphenyl)-6-oxohexanoic acid (S4). Adipic anhydride (5.00 g, 39.1 mmol) was dissolved in dichloromethane (80 mL) and anisole (4.67 mL, 43.0 mmol) was added. Aluminum trichloride (11.4 g, 86.0 mmol) was added, and the reaction mixture was stirred for 18 hours, cooling as necessary. The reaction mixture was quenched with 1 N aq HCl, extracted with dichloromethane, dried (Na_2SO_4), and concentrated. The recovered solid was dissolved in dichloromethane and extracted with 1 N aq NaOH. The aqueous layer was washed with dichloromethane, acidified with 2 N aq HCl, and extracted with dichloromethane. The organic layers were dried (Na_2SO_4), and concentrated to give the product as a white solid (2.3 g, 25%). Mp = 117-122 °C; R_f = 0.06 (30% EtOAc/hexanes); IR (film) 3744, 3040, 2945, 2373, 1714, 1593, 1250, 1168 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.9 Hz, 2H) 6.93 (d, *J* = 8.9 Hz, 2H), 3.87 (s, 3H), 2.95 (t, *J* = 6.9 Hz, 2H), 2.42 (t, *J* = 6.9 Hz, 2H), 1.84-1.69 (m, 4H) [O*H* not observed]; ^{13}C NMR (100 MHz, $CDCl_3$) ppm 198.6, 178.4, 163.6, 130.4, 130.2, 113.9, 55.6, 37.9, 33.8, 24.5, 23.9; HRMS (ESI): Exact mass calcd for $C_{13}H_{16}O_4Na$ $[M+Na]^+$ 259.0946, found 259.0939.



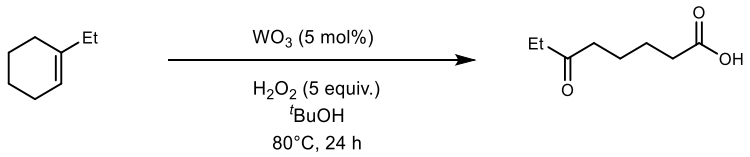
6-Oxoheptanoic acid (S5). The reaction was carried out according to literature precedence.[8] Tungsten trioxide (195 mg, 0.8 mmol) and 1-methyl-1-cyclohexene (811 mg, 8.4 mmol) were dissolved in ^{t}BuOH, followed by addition of hydrogen peroxide (42 mmol). The reaction was heated at 80 °C for 24 h. The reaction was filtered

[8] Yoshimura, Y.; Ogasawara, Y.; Suzuki, K.; Yamaguchi, K.; Mizuno, N. *Catal. Sci. Technol.* **2017**, *7*, 1662.

and washed with 1 M HCl. The organic layer was extracted with EtOAc. The solvent was removed under vacuum and the crude was purified by silica gel chromatography (SiO_2, 15% ethyl acetate in hexanes) to afford a colorless oil (815 mg, 67%). The physical data matched literature values.[8]



1-Ethylcyclohex-1-ene (S6). Cyclohexanone (980 mg, 10 mmol) was dissolved in anhydrous diethyl ether and cooled to 0 °C. Ethyl magnesium chloride (20.0 mL, 1.0 M in THF) was added dropwise by an addition funnel and stirred for 30 min. The reaction mixture was quenched with 2 N aq HCl, extracted with ethyl acetate, dried (Na_2SO_4), and concentrated. The crude oil was dissolved in 1,2-dichloroethane and *para*-toluenesulfonic acid (60 mg, 0.3 mmol) was added. The reaction was heated to reflux overnight. Sodium sulfate (5.0 g) was added to remove the water and then the reaction was filtered and concentrated. The unpurified product was used directly in the next step without further purification.



6-Oxooctanoic acid (S7). The reaction was carried out according to literature precedence.[8] Tungsten trioxide (203 mg, 0.9 mmol) and 1-ethylcyclohex-1-ene (from last procedure) were dissolved in ^{t}BuOH, followed by addition of hydrogen peroxide (34 mmol). The reaction was heated at 80 °C for 24 h. The reaction was filtered and washed with 1 M HCl. The organic layer was extracted by EtOAc. The solvent was removed under vacuum and the residue was purified by silica gel chromatography (SiO_2, 15% ethyl acetate in hexanes) to afford a colorless oil (236 mg, 15% for 3 steps). The physical data matched literature values.[9]

[9] He, T.; Chen, D.; Qian, S.; Zheng, Y.; Huang, S. *Org. Lett.* **2021**, *23*, 6525.