Supporting Information
Enantioselective Thiourea-Catalyzed Cationic Polycyclizations

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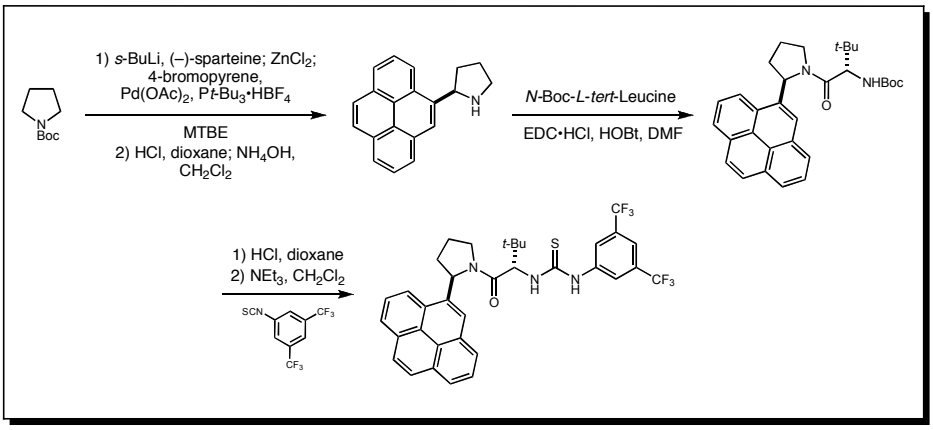
1. General Information

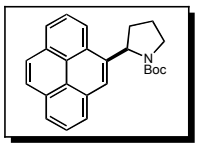
Optimization reactions were performed in oven-dried 2-dram vials; all other reactions were performed in oven-dried round bottom flasks unless otherwise noted. The vials and flasks were fitted with rubber septa and reactions were conducted under air. Stainless steel syringes were used to transfer air- and moisture-sensitive liquids. Flash chromatography was performed using silica gel 60 (230-400 mesh) from EM Science. Commercial reagents were purchased from Sigma Aldrich, Alfa Aesar, Strem, Lancaster or TCI, and used as received with the following exceptions: dichloromethane, tetrahydrofuran, diethyl ether, *t*-butyl methyl ether and methanol were dried by passing through columns of activated alumina; dimethylformamide was dried by passing through columns of activated molecular sieves. Triethylamine and chlorotrimethylsilane were distilled from CaH_2 at 760 torr. *s*-Butyllithium was titrated using diphenylacetic acid as an indicator. Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on Varian-Mercury-400 (400 MHz) and Inova-500 (500 MHz) spectrometers. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$ = δ 7.27). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent ($CDCl_3$ = δ 77.0). Data are represented as follows: chemical shift, multiplicity (br. s = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz), integration. Infrared (IR) spectra were obtained using a Bruker Optics Tensor 27 FTIR spectrometer. Optical rotations were measured using a 1 mL cell with a 0.5 dm path length on a Jasco DIP 370 digital polarimeter. The mass spectral data were obtained on an Agilent Technologies 6120 quadrupole LC/MS spectrometer. Gas chromatography (GC) analysis was performed on an Agilent Technologies 7890A gas chromatograph using an HP-5 (30 m x 0.32 mm x 0.25 μm) column. Chiral SFC analysis was performed using a Berger analytical supercritical fluid chromatograph with commercial Chiralpak columns.

Abbreviations: 9-BBN – 9-borabicyclo(3.3.1)nonane, Boc – *tert*-butyl carbamate, *s*-BuLi – *sec*-butyllithium, DBAD – di-*tert*-butyl azodicarboxylate, dppf – 1,1'-bis(diphenylphosphino)ferrocene, EDC – 1-(3-(dimethyl-amino)propyl)-3-ethyl-carbodiimide hydrochloride, EtOAc – ethyl acetate, HOBt – 1-hydroxybenzotriazole, MeOH – methanol, MTBE – *tert*-butylmethyl ether, NEt_3 –

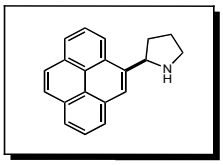
triethylamine, TBAF – tetrabutylammonium fluoride, THF – tetrahydrofuran.

General procedures for the preparation of thiourea catalysts



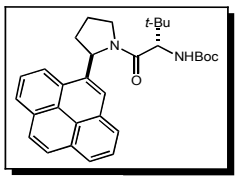


***N*-Boc-(*R*)-2-(4-pyrenyl)pyrrolidine** According to the procedure of Campos, *N*-Boc-pyrrolidine (0.77 mL, 4.4 mmol) and (−)-sparteine (1.01 mL, 4.4 mmol) were dissolved in MTBE (10 mL) and the resulting solution was cooled to −78 °C.[1] To this solution *s*-BuLi (1.1 M in cyclohexane, 4 mL, 4.4 mmol) was added dropwise via syringe pump over 40 min and the resulting solution was stirred for 3 h at −78 °C. A solution of $ZnCl_2$ (1 M in Et_2O, 4.4 mL, 4.4 mmol) was then added via syringe pump over 30 min with rapid stirring. The resulting suspension was aged at -78 °C for 30 min, and then warmed to room temperature. After 30 min, 4-bromopyrene was added, followed by $Pd(OAc)_2$ (49.4 mg, 0.22 mmol) and P*t*-Bu_3·HBF_4 (69.6 mg, 0.24 mmol) in one portion. The reaction was stirred for 16 hours at room temperature. To facilitate the filtration, ~0.3 mL NH_4OH was added, and the mixture was stirred for 1 h. The resulting slurry was filtered over Celite and rinsed with MTBE. The filtrate was washed with 1 M HCl and then twice with water. The organic layer was dried over Na_2SO_4, filtered and concentrated. The crude product was purified on the silica gel flash chromatography to obtain the desired coupling product as a pale orange gel (1.12 g, 77%), which was applied to the next step directly.

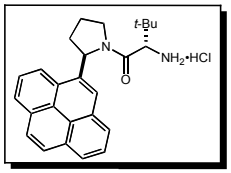


(*R*)-2-(4-pyrenyl)pyrrolidine To a solution of *N*-Boc-(*R*)-2-(4-pyrenyl)pyrrolidine (743 mg, 2 mmol) in dioxane (10 mL) was added HCl (4 M in dioxane, 7.5 mL, 30 mmol). The reaction mixture was stirred at room temperature for 6 h, then diluted with CH_2Cl_2 (30 mL), and quenched with a mixture of water (20 mL) and 33% aqueous NH_4OH (9 mL). The resulting biphasic liquid was stirred for 1 h. The organic layer was separated, dried over Na_2SO_4, and concentrated under vacuum. The crude product was purified by silica gel flash chromatography to obtain the desired amine product as pale orange crystals (0.41 g, 76%). IR (Film) 3043, 2962, 1589, 1433, 1302, 1175, 1097, 907, 824 (s), 718 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.40 (d, *J* = 8.1 Hz, 1 H), 8.32 (s, 1 H), 8.18 (dd, *J* = 2.9, 7.7 Hz, 2 H), 8.14 (dd, *J* = 1.1, 7.7 Hz, 1 H), 8.06 (s, 2 H), 7.99 (td, *J* = 7.7, 15.4 Hz, 2 H), 5.08 (t, *J* = 7.1 Hz, 1 H), 3.41 (td, *J* = 5.9, 10.2 Hz, 1 H), 3.25 (td, *J* = 7.5, 9.9 Hz, 1 H), 2.91 (br. s., 1 H), 2.57 (dt, *J* = 7.1, 13.5 Hz, 1 H), 2.10 - 1.96 (m, 2 H), 1.96 - 1.85 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 139.4, 131.5, 130.8, 129.9, 127.5, 127.2, 125.9, 125.5, 125.2, 125.1, 124.9, 124.6, 123.8, 122.8, 121.2, 58.8,

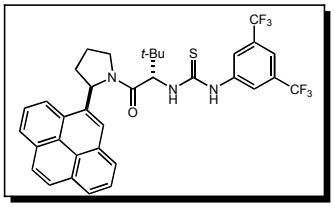
46.8, 33.3, 25.4; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{20}H_{18}N$) requires *m/z* 272.1, found *m/z* 272.1; $[\alpha]_D^{23}$ = +113.5 (*c* = 1.0, $CHCl_3$).



***tert*-butyl ((*S*)-3,3-dimethyl-1-oxo-1-((*R*)-2-(pyren-4-yl)pyrrolidin-1-yl) butan-2-yl)carbamate** A 100 mL round bottom flask was charged with (*R*)-2-(4-pyrenyl)pyrrolidine (0.81 g, 3.0 mmol), *N*-Boc-*L*-*tert*-Leucine (762 mg, 3.3 mmol), EDC·HCl (630 mg, 3.3 mmol), HOBt (446 mg, 3.3 mmol) and DMF (15 mL). The solution was stirred at room temperature for 6 h, and quenched with water. The aqueous layer was separated and extracted three times with EtOAc. The combined organic layers were washed with NH_4Cl and brine, dried over Na_2SO_4, and concentrated to obtain the crude product, which purified by to silica gel flash chromatography to give the desired amide product as pale yellow crystals (1.21 g, 83%). IR (Film) 2966 (s), 1779 (s), 1708 (s), 1647 (s), 1497, 1423, 1366, 1242, 1170 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.33 (d, *J* = 7.8 Hz, 1 H), 8.19 (d, *J* = 7.8 Hz, 1 H), 8.16 - 7.89 (m, 6 H), 7.66 (s, 1 H), 6.17 (d, *J* = 8.3 Hz, 1 H), 5.23 (d, *J* = 9.8 Hz, 1 H), 4.58 (d, *J* = 9.8 Hz, 1 H), 4.50 - 4.41 (m, 1 H), 3.95 - 3.89 (m, 1 H), 2.54 - 2.44 (m, 1 H), 2.18 - 2.06 (m, 3 H), 1.54 (s, 9 H), 1.11 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 170.8, 156.3, 136.0, 131.6, 130.8, 130.4, 128.8, 127.4, 127.2, 126.1, 125.8, 125.6, 125.4, 125.0, 124.8, 124.0, 122.4, 120.9, 79.6, 58.8, 58.3, 48.5, 34.8, 32.3, 28.5, 26.5, 23.6; MS (ESI-APCI) exact mass calculated for [M+Na] ($C_{31}H_{36}N_2NaO_3$) requires *m/z* 507.3, found *m/z* 507.2; $[\alpha]_D^{23}$ = +139.5 (*c* = 0.84, $CHCl_3$).



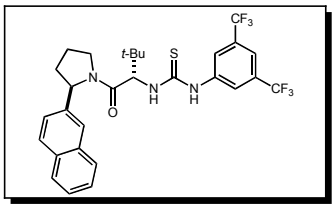
(*S*)-3,3-dimethyl-1-oxo-1-((*R*)-2-(pyren-4-yl)pyrrolidin-1-yl)butan-2-aminium chloride To a solution of *tert*-butyl ((*S*)-3,3-dimethyl-1-oxo-1-((*R*)-2-(pyren-4-yl)pyrrolidin-1-yl)butan-2-yl) carbamate (1.2 g, 2.5 mmol) in dioxane (10 mL) at 0 ^oC was added HCl (4 M in dioxane, 35 mL, 140 mmol) slowly. The reaction was warmed to room temperature and stirred until the starting material was consumed, as judged by TLC analysis. The reaction mixture was then concentrated under vacuum, yielding a yellow/brown solid that was used directly without further purification.



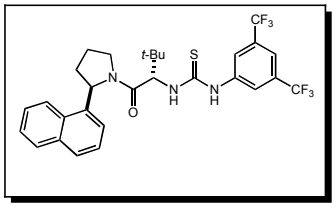
1-(3,5-bis(trifluoromethyl)phenyl)-3-((*S*)-3,3-dimethyl-1-oxo-1 -((*R*)-2-(pyren-4-yl)pyrrolidin-1-yl)butan-2-yl)thiourea (8) To a solution of crude (*S*)-3,3-dimethyl-1-oxo-1- ((*R*)-2-(pyren-4-yl) pyrrolidin-1-yl)butan-2-aminium chloride (obtained from the previous step, ~2.5 mmol) in CH_2Cl_2 was added NEt_3 (1.0 mL, 7.5 mmol) dropwise. The mixture was stirred for 15 min, and 3,5-bis(trifluoromethyl)phenyl isothiocyanate (0.50 mL, 2.75 mmol) was added dropwise. The reaction was stirred overnight, concentrated under vacuum, and purified by silica gel flash chromatography to obtain the desired thiourea as yellow crystals (1.16 g, 71% over two steps). IR (Film) 3319, 2970, 1610 (s), 1523, 1473, 1443, 1382 (s), 1274 (s), 1173 (s), 1130 (s), 961, 883, 826, 754 (s), 722 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.67 (br. s., 1 H), 8.19 (d, *J* = 7.8 Hz, 1 H), 8.14 (d, *J* = 7.8 Hz, 1 H), 8.12 - 8.08 (m, 2 H), 8.02 (s, 2 H), 8.00 - 7.92 (m, 1 H), 7.89 - 7.80 (m, 2 H), 7.70 (br. s., 2 H), 7.49 (br. s., 1 H), 6.99 (br. s., 1 H), 6.10 (d, *J* = 7.3 Hz, 1 H), 5.60 (d, *J* = 9.8

Hz, 1 H), 4.86 (t, *J* = 9.0 Hz, 1 H), 3.95 (dd, *J* = 9.8, 17.1 Hz, 1 H), 2.52 (td, *J* = 10.0, 19.5 Hz, 1 H), 2.16 (d, *J* = 10.7 Hz, 1 H), 2.14 - 2.06 (m, 2 H), 1.18 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) d = 180.9, 170.3, 139.3, 134.4, 131.9, 131.6, 131.4, 130.6, 130.3, 128.4, 127.7, 127.4, 127.2, 125.8, 125.5, 125.3, 125.0, 124.9, 124.8, 124.1, 123.8, 123.6, 122.9, 122.7, 121.6, 120.5, 118.1, 63.2, 60.4, 58.8, 48.8, 47.5, 35.9, 35.3, 32.2, 27.1, 26.8, 23.4, 21.0, 14.1; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{35}H_{32}F_6N_3OS$) requires *m/z* 656.2, found *m/z* 656.3; $[\alpha]_D^{23}$ = +66.0 (c = 1.1, $CHCl_3$).

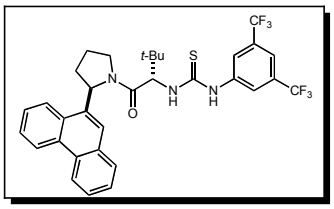
Characterization data for all novel catalysts in Table 1



1-(3,5-bis(trifluoromethyl)phenyl)-3-((*S*)-3,3-dimethyl-1-((*R*)-2-(naphthalen-2-yl)pyrrolidin-1-yl)-1-oxobutan-2-yl)thiourea (5). IR (Film) 3323 (br), 2965, 1614, 1528, 1474, 1444, 1382, 1276 (s), 1175, 1133 (s), 961, 885, 754 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.48 (br. s., 1 H), 7.88 - 7.76 (m, 2 H), 7.68 - 7.42 (m, 4 H), 7.42 - 7.21 (m, 3 H), 7.06 (d, *J* = 8.1 Hz, 1 H), 5.55 (d, *J* = 8.4 Hz, 1 H), 5.26 (d, *J* = 7.3 Hz, 1 H), 4.63 (br. s., 1 H), 3.91 - 3.76 (m, 1 H), 2.38 - 2.23 (m, 1 H), 2.06 - 1.86 (m, 3 H), 1.16 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 181.3, 170.5, 138.5, 133.0, 132.1, 131.7, 128.7, 128.0, 127.9, 127.7, 127.3, 126.5, 126.1, 125.9, 125.6, 125.5, 124.4, 124.3, 123.8, 123.5, 123.2, 118.2, 63.1, 61.2, 48.7, 35.4, 33.7, 26.8, 23.0; MS (ESI-APCI) exact mass calculated for [M-H] ($C_{29}H_{28}F_6N_3OS$) requires *m/z* 580.2, found *m/z* 580.2; $[\alpha]_D^{24}$ = +39.5 (c = 1.0, $CHCl_3$).



1-(3,5-bis(trifluoromethyl)phenyl)-3-((*S*)-3,3-dimethyl-1-((*R*)-2-(naphthalen-1-yl)pyrrolidin-1-yl)-1-oxobutan-2-yl)thiourea (6). IR (Film) 3335 (br), 2963, 1699, 1609, 1525, 1474, 1445, 1384, 1275 (s), 1175, 1131 (s), 961, 884, 777 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.86 - 7.67 (m, 3 H), 7.55 - 7.35 (m, 4 H), 7.18 - 7.01 (m, 2 H), 5.83 (d, *J* = 8.1 Hz, 1 H), 5.55 (d, *J* = 9.5 Hz, 1 H), 4.63 (t, *J* = 9.0 Hz, 1 H), 3.88 (dd, *J* = 10.2, 17.6 Hz, 1 H), 2.45 - 2.26 (m, 1 H), 2.02 - 1.87 (m, 3 H), 1.16 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 181.3, 170.3, 139.4, 137.4, 136.0, 133.7, 132.1, 131.8, 129.7, 128.8, 127.3, 126.6, 125.8, 125.3, 124.8, 123.7, 122.8, 121.7, 118.5, 63.1, 58.7, 48.7, 35.6, 32.8, 27.1, 26.9, 23.3; MS (ESI-APCI) exact mass calculated for [M-H] ($C_{29}H_{28}F_6N_3OS$) requires *m/z* 580.2, found *m/z* 580.2; $[\alpha]_D^{24}$ = -61.5 (c = 1.0, $CHCl_3$).



1-(3,5-bis(trifluoromethyl)phenyl)-3-((*S*)-3,3-dimethyl-1-oxo-1-((*R*)-2-(phenanthren-9-yl)pyrrolidin-1-yl)butan-2-yl)thiourea (7). IR (Film) 3328 (br), 2963, 1611, 1529, 1474, 1447, 1383, 1276 (s), 1177, 1134 (s), 962, 885, 749 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$) δ = 9.66 (br. s., 1 H), 8.56 (d, *J* = 8.1 Hz, 1 H), 8.47 (d, *J* = 8.4 Hz, 1 H), 7.74 (br. s., 10 H), 5.82 (d, *J* = 8.1 Hz, 1 H), 5.60 (d, *J* = 9.1 Hz, 1 H), 4.84 (t, *J* = 9.1 Hz, 1 H), 3.88 (dd, *J* = 9.9, 17.6 Hz, 1 H), 2.48 - 2.31 (m, 1 H), 2.10 - 1.92 (m, 3 H), 1.16 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) d = 181.1, 170.6, 139.6, 133.4, 131.8, 131.5, 131.2, 130.7, 129.5, 129.1, 128.6, 126.6, 126.4, 126.4, 126.0, 123.5, 123.3, 122.7,

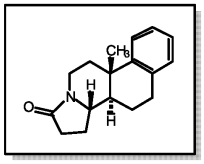
122.1, 118.0, 63.1, 58.7, 48.8, 35.3, 32.2, 26.7, 23.3; MS (ESI-APCI) exact mass calculated for [M-H] ($C_{33}H_{30}F_6N_3OS$) requires *m/z* 630.2, found *m/z* 630.2; $[\alpha]_D^{24}$ = +20.7 (c = 1.0, $CHCl_3$).

General procedures for thiourea-catalyzed polycyclization

Method A (reaction optimization):
An oven-dried vial was charged with starting material (0.033 mmol, 1.0 equiv), thiourea catalyst (0.00495 mmol, 0.15 equiv), 4Å molecular sieves (20 mg) and MTBE (1.3 mL). The flask was cooled to –78 °C and HCl (2 M in diethyl ether, 0.00825 to 0.0165 mmol, 0.25 to 0.50 equiv) was added dropwise. The reaction was placed in a -30 °C cryocool, stirred for 48 h, and then quenched at that temperature by addition of pre-cooled NEt_3 (~0.1 mL of 20% v/v solution in EtOAc). The reaction was diluted with acetone, filtered through a pipette containing ¾ inch of silica gel, and rinsed with acetone. The solvent was removed by rotary evaporation under reduced pressure to give the crude residue, which was purified by preparative silica gel thin layer chromatography.

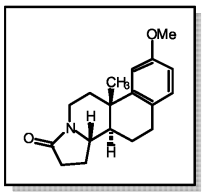
Method B (hydroxylactam substrate scope):
An oven-dried round bottom flask (25 mL) was charged with starting material (0.25 mmol, 1.0 equiv), thiourea catalyst (0.375 mmol, 0.15 equiv), 4Å molecular sieves (160 mg) and MTBE (10 mL). The flask was cooled to –78 °C and HCl (2 M in diethyl ether, 0.0625 to 0.125 mmol, 0.25 to 0.50 equiv) was added dropwise. The reaction was placed in a -30 °C cryocool, stirred for 72-96 h, and then quenched at that temperature by addition of pre-cooled NEt_3 (~1 mL of 20% v/v solution in EtOAc). The reaction was filtered through a pipette containing 1 inch of silica gel, and rinsed with acetone. The solvent was removed by rotary evaporation under reduced pressure to give the crude residue, which was purified by silica gel chromatography.

Method C (for acyloxylactam 13):
An oven-dried round bottom flask (25 mL) was charged with starting material (0.25 mmol, 1.0 equiv), CH_2Cl_2 (2.5 mL) and NEt_3 (0.78 mmol, 3.1 equiv). The solution was cooled to 0 ^oC, and acetyl chloride (0.73 mmol, 2.9 equiv) was added dropwise with stirring. The reaction was aged at room temperature for 1.5 h. The resulting light yellow suspension was filtered through a short neutral alumina plug, rinsed with acetone, and then subjected to vacuum to remove the remaining reagents and solvent. To the oily residue was added thiourea catalyst (0.375 mmol, 0.15 equiv), 4Å molecular sieves (160 mg) and MTBE (10 mL). The flask was cooled to –78 °C and TMSCl (0.50 mmol, 2.0 equiv) was added dropwise. The reaction was placed in a -30 °C cryocool, stirred for 117 h, and then quenched at that temperature by addition of pre-cooled NEt_3 (~1 mL of 20% v/v solution in EtOAc). The reaction was filtered through a pipette containing 1 inch of silica gel, and rinsed with acetone. The solvent was removed by rotary evaporation under reduced pressure to give the crude residue, which was purified by silica gel chromatography.



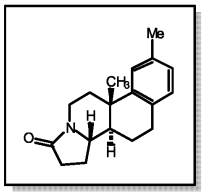
(4b*S*,10a*S*,10b*R*)-4b-methyl-5,6,9,10,10a,10b,11,12-octahydrobenzo[*f*]pyrrolo[2,1-*a*]isoquinolin-8(4b*H*)-one (10)
Followed method B from **9** (68.3 mg, 0.25 mmol), with 0.25 equiv HCl (31.3 μL, 0.0625 mmol), for 96 h, and purified using silica gel chromatography to give 32.5 mg (51% yield) of **10** as a colorless gel. This material was

determined to be 89% ee by chiral SFC analysis (ChiralPak AS, 30% MeOH, 3 mL/min, 225 nm, t_r(major) = 3.6 min, t_r(minor) = 5.6 min). IR (Film): 2931, 1685 (s), 1420, 1275, 762, 668 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.31 - 7.26 (m, 1 H), 7.22 - 7.13 (m, 2 H), 7.10 (d, *J* = 7.3 Hz, 1 H), 4.18 (ddd, *J* = 1.5, 5.4, 13.7 Hz, 1 H), 3.49 (ddd, *J* = 7.3, 8.3, 10.7 Hz, 1 H), 3.08 (dt, *J* = 3.9, 13.4 Hz, 1 H), 2.98 - 2.91 (m, 2 H), 2.45 - 2.38 (m, 2 H), 2.34 - 2.24 (m, 2 H), 1.84 - 1.76 (m, 1 H), 1.72 - 1.54 (m, 3 H), 1.42 (ddd, *J* = 2.9, 10.7, 13.2 Hz, 1 H), 1.23 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 173.5, 145.5, 134.7, 129.4, 126.0, 126.0, 124.6, 56.7, 48.7, 36.4, 36.2, 35.8, 30.7, 28.7, 24.9, 21.4, 19.6; MS (APCI) exact mass calculated for [M+H] ($C_{17}H_{22}NO$) requires *m/z* 256.2, found *m/z* 256.2; $[\alpha]_D^{23}$ = +6.5 (c = 1.2, $CHCl_3$).



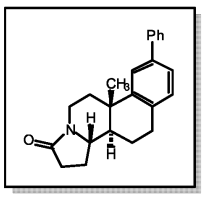
(4b*S*,10a*S*,10b*R*)-3-methoxy-4b-methyl-5,6,9,10,10a,10b,11,12-octahydrobenzo[*f*]pyrrolo[2,1-*a*]isoquinolin-8(4b*H*)-one (2)

Followed method B from **1** (76 mg, 0.25 mmol), with 0.25 equiv HCl (31.3 μL, 0.0625 mmol), for 72 h, and purified by silica gel chromatography to give 51 mg (72% yield) of **2** as a white solid. This material was determined to be 94% ee by chiral SFC analysis (ChiralPak AD-H, 25% MeOH, 3 mL/min, 210 nm, t_r(major) = 3.8 min, t_r(minor) = 4.8 min). IR (Film): 2932, 2870, 1686 (s), 1610, 1502, 1285, 1245, 1214, 1067, 1041, 911, 853, 807, 735 cm^{-1}; ^1H NMR: (500 MHz, $CDCl_3$) δ 7.02 (d, 1H, J = 8.5 Hz), 6.81 (d, 1H, J = 2.5 Hz), 6.81 (dd, 1H, J = 2.5, 8.5 Hz), 4.16 (dd, 1H, 5.0, 13.5 Hz), 3.80 (s, 3H), 3.48 (dt, 1H, J = 10.5, 7.6 Hz), 3.06 (td, 1H, 13.5, 3.0 Hz), 2.88 (m, 2H), 2.41 (m, 1H), 2.40 (d, 1H, J = 10 Hz), 2.29 (m, 1H), 2.23 (dd, 1H, J = 2.5, 13.5 Hz), 1.77 (m, 1H), 1.62 (m, 3H), 1.39 (m, 1H), 1.22 (s, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 173.8, 158.1, 147.0, 130.5, 127.1, 11.4, 110.7, 57.0, 55.5, 49.0, 36.9, 36.5, 36.1, 31.0, 28.2, 25.1, 21.6, 20.0; MS (APCI) exact mass calculated for [M+H] ($C_{18}H_{24}NO_2$) requires *m/z* 286.2, found *m/z* 286.2; $[\alpha]_D^{23}$ = +30.2 (c = 0.86, $CHCl_3$).



(4b*S*,10a*S*,10b*R*)-3,4b-dimethyl-5,6,9,10,10a,10b,11,12-octahydrobenzo[*f*]pyrrolo[2,1-*a*]isoquinolin-8(4b*H*)-one (12)

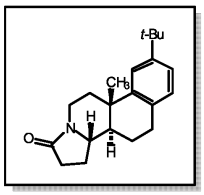
Followed method B from **11** (72 mg, 0.25 mmol), with 0.25 equiv HCl (31.3 μL, 0.0625 mmol), for 96 h, and purified using silica gel chromatography to give 42.0 mg (62% yield) of **12** as a colorless gel. This material was determined to be 91% ee by chiral SFC analysis (ChiralPak AD-H, 10% MeOH, 3 mL/min, 210 nm, t_r(major) = 6.9 min, t_r(minor) = 8.8 min). IR (Film): 2931, 2870, 1686 (s), 1419, 1299 (s), 1184 (s), 1104, 973, 852, 808, 731, 666 cm^{-1}; ^1H NMR: (500 MHz, $CDCl_3$) δ 7.06 (s, 1H), 6.96 (app. q, 2H, *J* = 8.0 Hz), 4.15 (ddd, 1H *J* = 1.5, 5.5, 14.0 Hz), 3.46 (m, 1H), 3.05 (td, 1H, *J* = 4.0, 14.0), 2.88 (m, 2H), 2.38 (m, 2H), 2.31 (s, 3H), 2.27 (dd, 2H, *J* = 4.0, 12.0 Hz), 1.75 (m, 1H), 1.60 (m, 3H), 1.38 (m, 1H), 1.20 (s, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 173.8, 145.5, 135.6, 131.9, 129.5, 127.1, 125.5, 57.0, 49.1, 36.6, 36.5, 36.1, 31.0, 28.6, 25.2, 21.6, 21.5, 19.9; MS (APCI) exact mass calculated for [M+H] ($C_{18}H_{24}NO$) requires *m/z* 270.2, found *m/z* 270.2; $[\alpha]_D^{23}$ = +18.2 (c = 2.28, $CHCl_3$).



(4b*S*,10a*S*,10b*R*)-4b-methyl-3-phenyl-5,6,9,10,10a,10b,11,12-octahydrobenzo[*f*]pyrrolo[2,1-*a*]isoquinolin-8(4b*H*)-one (14)

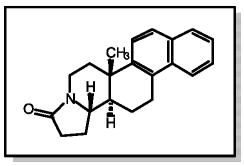
Followed method C from **13** (87.9 mg, 0.25 mmol), with 2.0 equiv TMSCl (63.5 μL, 0.50 mmol), for 117 h, and purified using silica gel chromatography

to give 44.9 mg (54% yield) of **14** as a white foam. This material was determined to be 91% ee by chiral SFC analysis (ChiralPak AS-H, 20% MeOH, 3 mL/min, 210 nm, t_r(major) = 4.9 min, t_r(minor) = 6.0 min). IR (Film): 2930 (s), 1676 (s), 1482, 1420, 1274, 1184, 909, 760, 727 (s), 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.58 - 7.54 (m, 2 H), 7.47 (d, *J* = 2.0 Hz, 1 H), 7.43 (t, *J* = 7.8 Hz, 2 H), 7.39 - 7.31 (m, 2 H), 7.16 (d, *J* = 7.8 Hz, 1 H), 4.18 (ddd, *J* = 1.7, 5.6, 13.7 Hz, 1 H), 3.50 (ddd, *J* = 6.8, 8.8, 10.7 Hz, 1 H), 3.08 (dt, *J* = 3.9, 13.4 Hz, 1 H), 3.00 - 2.93 (m, 2 H), 2.44 - 2.34 (m, 3 H), 2.30 (dtd, *J* = 4.4, 6.8, 11.2 Hz, 1 H), 1.84 - 1.78 (m, 1 H), 1.73 - 1.60 (m, 3 H), 1.44 (ddd, *J* = 2.9, 10.5, 12.9 Hz, 1 H), 1.26 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 173.6, 145.8, 141.3, 139.1, 133.9, 129.9, 128.7, 127.1, 127.0, 124.9, 123.5, 56.7, 48.7, 36.7, 36.3, 35.8, 30.7, 28.5, 24.9, 21.5, 19.6; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{23}H_{25}NO$) requires *m/z* 332.2, found *m/z* 332.2; $[\alpha]_D^{23}$ = +85.5 (c = 0.6 $CHCl_3$).



(4b*S*,10a*S*,10b*R*)-3-(tert-butyl)-4b-methyl-5,6,9,10,10a,10b,11,12-octahydrobenzo[*f*]pyrrolo[2,1-*a*]isoquinolin-8(4b*H*)-one (16)

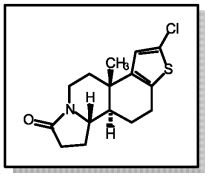
Followed method B from **15** (82.4 mg, 0.25 mmol), with 0.25 equiv HCl (31.3 μL, 0.0625 mmol), for 96 h, and purified using silica gel chromatography to give 55.3 mg (71% yield) of **16** as a colorless gel. This material was determined to be 91% ee by chiral SFC analysis (ChiralPak OD-H, 10% MeOH, 3 mL/min, 225 nm, t_r(minor) = 5.5 min, t_r(major) = 6.0 min). IR (Film) 2961 (s), 2868, 1685 (s), 1499, 1419, 1313, 1270, 1185, 909, 819, 729 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.29 (d, *J* = 2.0 Hz, 1 H), 7.26 (s, 1 H), 7.18 (dd, *J* = 2.2, 8.1 Hz, 1 H), 7.03 (d, *J* = 8.3 Hz, 1 H), 4.16 (ddd, *J* = 1.5, 5.4, 13.7 Hz, 1 H), 3.47 (ddd, *J* = 6.8, 8.3, 10.7 Hz, 1 H), 3.07 (dt, *J* = 3.7, 13.6 Hz, 1 H), 2.91 - 2.86 (m, 2 H), 2.43 - 2.36 (m, 2 H), 2.33 - 2.23 (m, 2 H), 1.79 - 1.72 (m, 1 H), 1.68 - 1.53 (m, 3 H), 1.44 - 1.36 (m, 1 H), 1.31 (s, 9 H), 1.22 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 173.6, 148.8, 144.9, 131.8, 129.0, 123.2, 121.3, 56.7, 48.9, 36.7, 36.3, 35.8, 34.5, 31.4, 30.7, 28.3, 25.0, 21.4, 19.6; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{21}H_{29}NO$) requires *m/z* 312.2, found *m/z* 312.1; $[\alpha]_D^{23}$ = +34.7 (c = 1.0, $CHCl_3$).



(6a*S*,14a*R*,14b*S*)-6a-methyl-1,5,6,6a,13,14,14a,14b-octahydronaphtho[2,1-*f*]pyrrolo[2,1-*a*]isoquinolin-3(2*H*)-one (18)

Followed method B from **17** (80.9 mg, 0.25 mmol), with 0.50 equiv HCl (62.5 μL, 0.125 mmol), for 72 h, and purified using silica gel chromatography to give 57.2 mg (75% yield) of **18** as a white solid. This material was determined to be 92% ee by chiral SFC analysis (ChiralPak AD-H, 30% MeOH, 3 mL/min, 225 nm, t_r(minor) = 10.4 min, t_r(major) = 12.5 min). IR (Film) 2931, 1675 (s), 1508, 1421, 1380, 1285, 1264, 1162, 813, 732 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.97 (d, *J* = 8.3 Hz, 1 H), 7.80 (d, *J* = 8.3 Hz, 1 H), 7.71 (d, *J* = 8.8 Hz, 1 H), 7.51 (ddd, *J* = 1.5, 6.8, 8.3 Hz, 1 H), 7.49 - 7.42 (m, 2 H), 4.19 (ddd, *J* = 1.7, 5.5, 13.8 Hz, 1 H), 3.55 (ddd, *J* = 6.5, 8.4, 10.5 Hz, 1 H), 3.38 (dd, *J* = 6.3, 17.6 Hz, 1 H), 3.23 - 3.16 (m, 1 H), 3.12 (dt, *J* = 3.9, 13.7 Hz, 1 H), 2.46 - 2.37 (m, 3 H), 2.37 - 2.29 (m, 1 H), 1.99 (dd, *J* = 7.8, 13.2 Hz, 1 H), 1.78 (ddd, *J* = 6.8, 11.7, 13.2 Hz, 1 H), 1.69 (dtd, *J* = 8.3, 10.3, 12.2 Hz, 1 H), 1.58 (dt, *J* = 5.4, 13.2 Hz, 1 H), 1.51 (ddd, *J* = 2.4, 10.7, 13.2 Hz, 1 H), 1.31 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 173.5, 142.3, 132.2, 131.8, 129.5, 128.3, 126.6, 126.1, 125.3, 123.1, 123.1, 56.6, 48.7, 36.8, 36.2, 36.1, 30.7, 25.8, 24.8, 20.9, 19.4; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{21}H_{24}NO$) requires *m/z* 306.2, found *m/z*

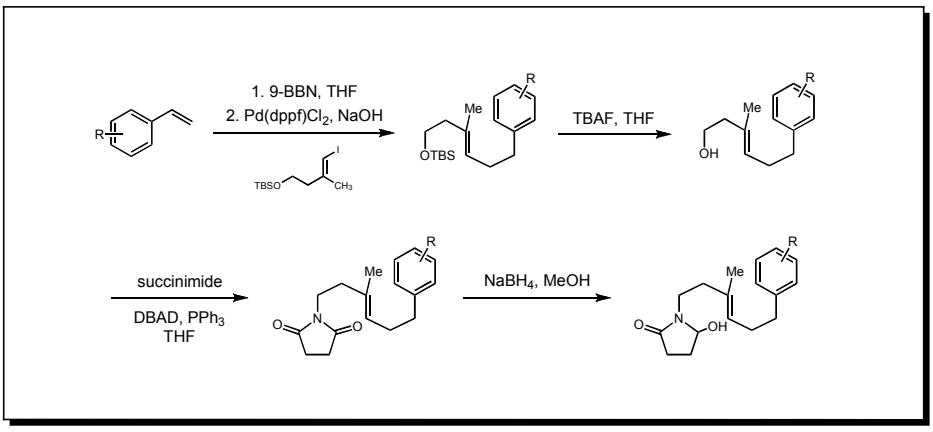
306.2; $[\alpha]_D^{23}$ = -16.1 (c = 1.0, $CHCl_3$).



(3b*S*,9a*S*,9b*R*)-2-chloro-3b-methyl-4,5,8,9,9a,9b,10,11-octahydropyrrolo[2,1-*a*]thieno[3,2-*f*]isoquinolin-7(3b*H*)-one (20)

Followed method B from **19** (78.5 mg, 0.25 mmol), with 0.25 equiv HCl (31.3 μL, 0.0625 mmol), at -10 °C for 72 h, and purified using silica gel chromatography to give 57.3 mg (77% yield) of **20** as a white solid. This material was determined to be 91% ee by chiral SFC analysis (ChiralPak OD-H, 15% MeOH, 3 mL/min, 254 nm, t_r(minor) = 7.8 min, t_r(major) = 8.5 min). IR (Film) 2936, 1666 (s), 1455, 1283, 1183, 967 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) d = 6.64 (s, 1 H), 4.11 (ddd, *J* = 1.5, 5.6, 13.9 Hz, 1 H), 3.45 (ddd, *J* = 6.8, 8.3, 10.7 Hz, 1 H), 3.01 (dt, *J* = 3.9, 13.4 Hz, 1 H), 2.82 (ddd, *J* = 1.5, 6.3, 16.6 Hz, 1 H), 2.78 - 2.69 (m, 1 H), 2.43 - 2.35 (m, 2 H), 2.30 - 2.20 (m, 1 H), 1.95 (ddd, *J* = 1.5, 3.9, 13.2 Hz, 1 H), 1.79 (tdd, *J* = 2.0, 6.8, 13.2 Hz, 1 H), 1.73 - 1.49 (m, 4 H), 1.38 (ddd, *J* = 2.4, 10.7, 12.7 Hz, 1 H), 1.17 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 173.6, 143.9, 133.1, 127.1, 123.0, 56.0, 49.0, 35.9, 35.7, 30.6, 24.8, 24.5, 20.1, 19.8; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{15}H_{18}ClNOS$) requires *m/z* 296.1, found *m/z* 296.0; $[\alpha]_D^{23}$ = +34.7 (c = 1.0, $CHCl_3$).

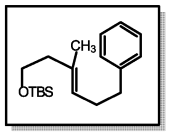
General procedure for the synthesis of hydroxylactam substrates



***B*-Alkyl Suzuki-Miyaura coupling of vinyl iodide and styrenes**

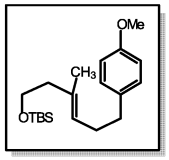
A round bottom flask was charged with a solution of vinylarene (6.1 mmol, 2.0 equiv) in THF (3 mL), flushed with N_2, and cooled to 0 °C. A solution of 9-BBN (0.5 M in THF, 13.5 mL, 6.75 mmol, 2.2 equiv) was added slowly. The homogeneous solution was warmed to room temperature and stirred for 6 hours. (White precipitates occasionally formed upon addition of 9-BBN, but disappeared during as the reaction warmed). When the hydroboration was complete, the reaction was cooled to 0 °C, and aqueous NaOH (3 M, 6 mL, 18.4 mmol, 6 equiv), $Pd(dppf)Cl_2 \cdot 2CH_2Cl_2$ (253 mg, 0.31 mmol, 0.10 equiv), and (*E*)-(4-iodo-3-methylbut-3-en-1-yl) *tert*-butyldimethylsilylether (1.0 g, 3.07 mmol, 1.0 equiv) were added sequentially.[2] The reaction mixture was moved to a 4 °C refrigerated reactor and stirred overnight. Saturated aqueous NH_4Cl solution was added to neutralize NaOH, and separated from the organic layer. The aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over

$NaSO_4$, concentrated, and the crude extracts were purified by silica gel column chromatography (gradient from 100% hexane to 10% EtOAc/hexane) to obtain the coupling product.



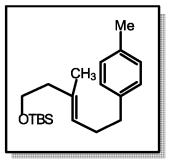
(*E*)-*tert*-butyldimethyl((3-methyl-6-phenylhex-3-en-1-yl)oxy)silane

Followed general procedure from 4-methylstyrene on 4.6 mmol scale and purified using silica gel chromatography to give 1.26 g (90% yield) of (*E*)-*tert*-butyldimethyl((3-methyl-6-phenylhex-3-en-1-yl)oxy)silane as a pale yellow oil. IR (Film): 2953, 2982, 2856, 1462, 1252, 1091 (s), 833 (s), 773 (s), 697 (s) cm^{-1}; ^1H NMR: (500 MHz, $CDCl_3$) δ 7.30 (app t, 2H, *J* = 7.5 Hz), 7.21 (app d, 3H, *J* = 7.5 Hz), 5.26 (t, 1H, *J* = 7.0 Hz), 3.68 (t, 2H, *J* = 7.0 Hz), 2.67 (t, 2H, *J* = 8.0 Hz), 3.33 (dt, 2H, *J* = 7.0, 8.0 Hz), 2.29 (t, 2H, *J* = 7.0 Hz), 1.60 (s, 3H), 0.93 (s, 9H), 0.08 (s, 6H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 142.6, 133.1, 128.7, 128.5, 125.9, 125.8, 62.8, 43.3, 36.3, 30.3, 26.2, 18.6, 16.6, -5.0; MS (APCI) exact mass calculated for [M+H] ($C_{19}H_{33}OSi$) requires *m/z* 305.2, found *m/z* 305.3.



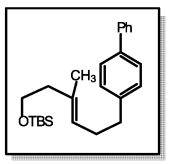
(*E*)-*tert*-butyl((6-(4-methoxyphenyl)-3-methylhex-3-en-1-yl)oxy)dimethylsilane

Followed general procedure from 4-vinylanisole on 4.6 mmol scale and purified using silica gel chromatography to give 1.54 g (>99% yield) of (*E*)-*tert*-butyl((6-(4-methoxyphenyl)-3-methylhex-3-en-1-yl)oxy)dimethylsilane as a pale yellow oil. IR (Film): 2952, 2929, 2856, 1512, 1436, 1246 (s), 1093 (br), 1040, 835, 775 cm^{-1}; ^1H NMR: (500 MHz, $CDCl_3$) δ 7.10 (d, 2H, *J* = 8.7 Hz), 6.82 (d, 2H, *J* = 8.7 Hz), 7.10 (d, 2H, *J* = 8.7 Hz), 5.21 (td, 1H, *J* = 1.0, 7.1 Hz), 3.79 (s, 3H), 3.64 (t, 2H, *J* = 7.0 Hz), 2.58 (t, *J* = 8.0 Hz), 2.26 (dt, 2H, *J* = 7.1, 8.0 Hz), 2.19 (t, 2H, *J* = 7.0 Hz), 1.57 (s, 3H), 0.89 (s, 9H), 0.05 (s, 6H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 157.8, 134.5, 132.8, 129.4, 125.7, 113.8, 62.6, 55.2, 43.2, 35.2, 30.4, 26.1, 26.0, 18.4, 16.5, –5.2; MS (APCI) exact mass calculated for [M+H] ($C_{20}H_{35}O_2Si$) requires *m/z* 335.2, found *m/z* 335.3.



(*E*)-*tert*-butyldimethyl((3-methyl-6-(p-tolyl)hex-3-en-1-yl)oxy)silane

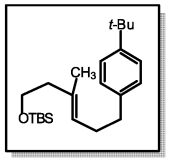
Followed general procedure from 4-methylstyrene on 3.8 mmol scale and purified using silica gel chromatography to give 1.27 g (>99% yield) of (*E*)-*tert*-butyldimethyl((3-methyl-6-(p-tolyl)hex-3-en-1-yl)oxy)silane as a pale yellow oil. IR (Film) 2927 (s), 1471, 1252, 1091 (s), 833 (s), 807, 773 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.10 (d, *J* = 5.5 Hz, 4 H), 5.24 (t, *J* = 7.3 Hz, 1 H), 3.67 (dt, *J* = 5.0, 7.1 Hz, 2 H), 2.61 (t, *J* = 7.8 Hz, 2 H), 2.34 (s, 3 H), 2.32 - 2.26 (m, 2 H), 2.22 (t, *J* = 6.9 Hz, 2 H), 1.60 (s, 3 H), 0.92 (s, 9 H), 0.08 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 139.3, 135.0, 132.7, 128.9, 128.3, 125.7, 62.5, 43.0, 35.6, 30.1, 26.0, 21.0, 18.3, 16.4, -5.3; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{20}H_{35}OSi$) requires *m/z* 319.3, found *m/z* 319.2.



(*E*)-((6-([1,1'-biphenyl]-4-yl)-3-methylhex-3-en-1-yl)oxy)(*tert*-butyl)dimethylsilane

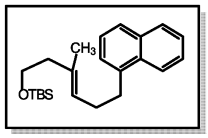
Followed general procedure from 4-vinyl-1,1'-biphenyl on 3.6 mmol scale and purified using silica gel chromatography to give 1.69 g (>99% yield) of (*E*)-((6-([1,1'-biphenyl]-4-yl)-3-methylhex-3-en-1-yl)oxy)(*tert*-butyl)dimethylsil

ane as a pale yellow oil. FTIR (Film) 2927, 1486, 1252, 1090 (s), 832 (s), 760 (s), 695 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.58 (d, *J* = 7.3 Hz, 2 H), 7.51 (d, *J* = 8.3 Hz, 2 H), 7.43 (t, *J* = 7.6 Hz, 2 H), 7.33 (d, *J* = 7.3 Hz, 1 H), 7.27 (d, *J* = 7.3 Hz, 2 H), 5.25 (t, *J* = 7.6 Hz, 1 H), 3.66 (t, *J* = 7.1 Hz, 2 H), 2.71 - 2.65 (m, 2 H), 2.34 (dd, *J* = 7.3, 15.6 Hz, 2 H), 2.21 (t, *J* = 7.1 Hz, 2 H), 1.59 (s, 3 H), 0.89 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 141.4, 141.1, 138.6, 132.9, 128.8, 128.7, 127.0, 126.9, 125.5, 62.5, 43.0, 35.7, 30.0, 25.9, 18.3, 16.4, -5.3; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{25}H_{37}OSi$) requires *m/z* 381.3, found *m/z* 381.2.



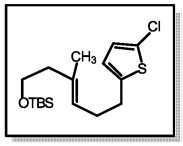
(*E*)-*tert*-butyl((6-(4-(*tert*-butyl)phenyl)-3-methylhex-3-en-1-yl)oxy)dimethylsilane

Followed general procedure from 4-*tert*-butylstyrene on 3.1 mmol scale and purified using silica gel chromatography to give 0.94 g (85% yield) of (*E*)-*tert*-butyl((6-(4-(*tert*-butyl)phenyl)-3-methylhex-3-en-1-yl)oxy)dimethylsilane as a pale yellow oil. IR (Film) 2955 (s), 2857, 1471, 1362, 1253, 1093 (s), 833 (s), 774 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.30 (d, *J* = 8.2 Hz, 2 H), 7.13 (d, *J* = 8.2 Hz, 2 H), 5.23 (t, *J* = 6.6 Hz, 1 H), 3.65 (t, *J* = 7.3 Hz, 2 H), 2.61 (t, *J* = 7.3 Hz, 2 H), 2.29 (dd, *J* = 7.3, 15.6 Hz, 2 H), 2.20 (t, *J* = 7.3 Hz, 2 H), 1.58 (s, 3 H), 1.31 (s, 9 H), 0.89 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 148.4, 139.3, 132.7, 128.0, 125.7, 125.1, 62.5, 43.0, 35.5, 34.3, 31.4, 30.0, 26.0, 16.4, -5.3; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{23}H_{41}OSi$) requires *m/z* 361.3, found *m/z* 361.2.



(*E*)-*tert*-butyldimethyl((3-methyl-6-(naphthalen-1-yl)hex-3-en-1-yl)oxy)silane

Followed general procedure from 1-vinylnaphthalene on 3.8 mmol scale and purified using silica gel chromatography to give 1.26 g (94% yield) of (*E*)-tert-butyldimethyl((3-methyl-6-(naphthalen-1-yl)hex-3-en-1-yl)oxy)silane as a pale yellow oil. IR (Film) 2928, 1461, 1251, 1091 (s), 833 (s), 773 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.06 (d, *J* = 8.8 Hz, 1 H), 7.86 (d, *J* = 7.3 Hz, 1 H), 7.71 (d, *J* = 8.3 Hz, 1 H), 7.55 - 7.43 (m, 2 H), 7.40 (t, *J* = 7.6 Hz, 1 H), 7.33 (d, *J* = 6.8 Hz, 1 H), 5.32 (t, *J* = 7.6 Hz, 1 H), 3.65 (t, *J* = 7.1 Hz, 2 H), 3.10 (t, *J* = 7.8 Hz, 2 H), 2.45 (q, *J* = 7.3 Hz, 2 H), 2.22 (t, *J* = 7.1 Hz, 2 H), 1.56 (s, 3 H), 0.91 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 138.6, 134.1, 132.1, 129.0, 126.7, 126.2, 125.9, 125.9, 125.7, 125.6, 124.0, 62.7, 43.3, 33.3, 29.5, 26.2, 18.6, 16.7, -5.0; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{23}H_{35}OSi$) requires *m/z* 355.3, found *m/z* 355.2.



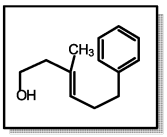
(*E*)-*tert*-butyl((6-(5-chlorothiophen-2-yl)-3-methylhex-3-en-1-yl)oxy)dimethylsilane

Followed general procedure from 2-chloro-5-vinylthiophene on 3.1 mmol scale and purified using silica gel chromatography to give (*E*)-*tert*-butyl ((6-(5-chlorothiophen-2-yl)-3-methylhex-3-en-1-yl)oxy)dimethylsilane as a pale yellow oil. IR (Film) 2927 (s), 2855, 1456, 1252 (s), 1092 (s), 1005, 833 (s), 774 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 6.72 (d, *J* = 3.7 Hz, 1 H), 6.56 (d, *J* = 3.7 Hz, 1 H), 5.21 (t, *J* = 7.1 Hz, 1 H), 3.68 (t, *J* = 7.1 Hz, 2 H), 2.77 (t, *J* = 7.3 Hz, 2 H), 2.33 (dd, *J* = 7.5, 15.0 Hz, 2 H), 2.22 (t, *J* = 6.9 Hz, 2 H), 1.62 (s, 3 H), 0.91 (s, 9 H), 0.07 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 144.0, 134.0, 126.7, 125.5, 124.5, 123.4, 62.4, 43.0, 30.4, 29.8, 25.9, 18.3, 16.5, -5.3; MS (ESI-APCI) exact mass

calculated for [M+H] ($C_{17}H_{30}ClOSSi$) requires *m/z* 345.2, found *m/z* 345.1.

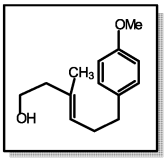
Deprotection of *tert*-butyl dimethylsilyl group

To a solution of (*E*)-*tert*-butyldimethyl((3-methyl-6-arylhex-3-en-1-yl)oxy)silane (3.5 mmol, 1.0 equiv) in THF (6 mL) was added TBAF (1 M in THF, 4.6 mmol, 1.2 equiv) at room temperature. After the reaction was complete, the reaction was diluted with a saturated aqueous NH_4Cl solution. The biphasic mixture was separated and the aqueous layer was extracted with EtOAc once. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The crude extracts were purified by silica gel column chromatography to obtain the alcohol product.



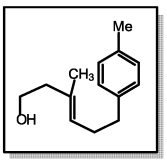
(*E*)-3-methyl-6-phenylhex-3-en-1-ol

Followed general procedure on 4.04 mmol scale and purified using silica gel chromatography to give 721 mg (94% yield) of (*E*)-3-methyl-6-phenylhex-3-en-1-ol as a pale yellow oil. IR (Film): 3334 (br), 2927, (s), 1495, 1426 1383, 1044 (s), 747 (s), 698 (s) cm^{-1}; ^1H NMR: (500 MHz, $CDCl_3$) δ 7.29 (m, 2H), 7.20 (m, 3H), 5.28 (t, 1H, *J* = 7.0 Hz), 3.61 (t, 2H, *J* = 5.5 Hz), 2.68 (t, 2H, *J* = 7.5 Hz), 2.37 (dt, 2H, *J* = 7.0, 7.5 Hz), 2.23 (t, 2H, *J* = 5.5 Hz), 1.56 (s, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 142.2, 132.3, 128.7, 128.6, 127.4, 126.1, 60.2, 42.9, 36.1, 30.1, 15.9; MS (APCI) exact mass calculated for [M+Na] ($C_{13}H_{18}ONa$) requires *m/z* 213.1, found *m/z* 213.1.



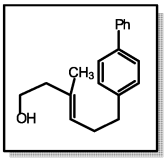
(*E*)-6-(4-methoxyphenyl)-3-methylhex-3-en-1-ol

Followed general procedure on 4.6 mmol scale and purified using silica gel chromatography to give 880 mg (87% yield) of (*E*)-6-(4-methoxyphenyl)-3-methylhex-3-en-1-ol as a pale yellow oil. IR (Film): 3369 (br), 2932, 1611, 1510 (s), 1441, 1298, 1243 (s), 1177, 1036 (s), 825 cm^{-1}; ^1H NMR: (500 MHz, $CDCl_3$) δ 7.10 (dd, 2H, *J* = 2.0, 6.5 Hz), 6.84 (dd, 2H, *J* = 2.0, 6.5 Hz), 7.10 (d, 2H, *J* = 8.7 Hz), 5.27 (t, 1H, *J* = 7.5 Hz), 3.78 (s, 3H), 3.62 (t, 2H, *J* = 6.5 Hz), 2.62 (t, *J* = 8.0 Hz), 2.26 (dt, 2H, *J* = 7.5, 8.0 Hz), 2.19 (t, 2H, *J* = 6.5 Hz), 2.0 (br s, 1H), 1.57 (s, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 158.0, 134.4, 132.3, 129.6, 127.1, 114.0, 60.5, 55.4, 42.9, 35.2, 30.4, 16.0; MS (APCI) exact mass calculated for [M+H] ($C_{14}H_{21}O_2$) requires *m/z* 221.1, found *m/z* 221.1.



(*E*)-3-methyl-6-(*p*-tolyl)hex-3-en-1-ol

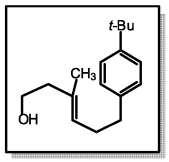
Followed general procedure on 3.8 mmol scale and purified using silica gel chromatography to give 708 mg (91% yield) of (*E*)-3-methyl-6-(*p*-tolyl) hex-3-en-1-ol as a pale yellow oil. IR (Film) 3345 (br), 2922 (s), 1514, 1445, 1043 (s), 806 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.08 (dd, *J* = 8.2, 12.4 Hz, 4 H), 5.27 (t, *J* = 7.1 Hz, 1 H), 3.61 (t, *J* = 6.2 Hz, 2 H), 2.63 (t, *J* = 7.6 Hz, 2 H), 2.32 (s, 3 H), 2.34 (dd, *J* = 7.8, 15.1 Hz, 2 H), 2.23 (t, *J* = 6.0 Hz, 2 H), 1.56 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 138.9, 135.2, 129.0, 128.3, 128.2, 127.3, 59.9, 42.6, 35.4, 30.0, 20.8, 15.6; MS (ESI) exact mass calculated for [M+Na] ($C_{14}H_{20}NaO$) requires *m/z* 227.1, found *m/z* 227.2.



(*E*)-6-([1,1'-biphenyl]-4-yl)-3-methylhex-3-en-1-ol

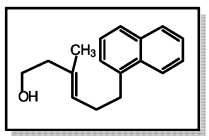
Followed general procedure on 3.8 mmol scale and purified using silica gel

chromatography to give 1.0 g (>99% yield) of (*E*)-3-methyl-6-(*p*-tolyl) hex-3-en-1-ol as a white solid. IR (Film) 3352 (br), 2924 (s), 1486, 1448, 1051 (s), 820, 757 (s), 689 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.61 - 7.57 (m, 2 H), 7.55 - 7.50 (m, 2 H), 7.46 - 7.40 (m, 2 H), 7.36 - 7.31 (m, 1 H), 7.29 - 7.24 (m, 2 H), 5.31 (t, *J* = 7.1 Hz, 1 H), 3.64 (t, *J* = 6.1 Hz, 2 H), 2.72 (t, *J* = 7.3 Hz, 2 H), 2.40 (dd, *J* = 7.3, 14.6 Hz, 2 H), 2.25 (t, *J* = 6.1 Hz, 2 H), 1.58 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 141.1, 141.0, 138.8, 132.1, 128.8, 128.7, 127.1, 127.0, 127.0, 127.0, 60.0, 42.6, 35.5, 29.9, 15.7; MS (ESI) exact mass calculated for [M+Na] ($C_{19}H_{22}NaO$) requires *m/z* 289.2, found *m/z* 289.2.



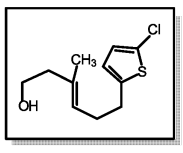
(*E*)-6-(4-(*tert*-butyl)phenyl)-3-methylhex-3-en-1-ol

Followed general procedure on 0.4 mmol scale and purified using silica gel chromatography to give 90 mg (91% yield) of (*E*)-6-(4-(*tert*-butyl)phenyl) -3-methylhex-3-en-1-ol as a colorless oil. IR (Film) 3342 (br), 2959 (s), 1514, 1462, 1363, 1046 (s), 830 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.31 (d, *J* = 8.2 Hz, 2 H), 7.12 (d, *J* = 8.2 Hz, 2 H), 5.29 (t, *J* = 6.9 Hz, 1 H), 3.62 (t, *J* = 6.2 Hz, 2 H), 2.64 (t, *J* = 7.8 Hz, 2 H), 2.35 (dd, *J* = 7.8, 15.6 Hz, 2 H), 2.24 (t, *J* = 6.2 Hz, 2 H), 1.57 (s, 3 H), 1.31 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 148.6, 138.9, 131.8, 128.0, 127.3, 125.1, 60.0, 42.7, 35.3, 34.3, 31.4, 29.9, 15.6; MS (ESI) exact mass calculated for [M+Na] ($C_{17}H_{26}NaO$) requires *m/z* 269.2, found *m/z* 269.2.



(*E*)-3-methyl-6-(naphthalen-1-yl)hex-3-en-1-ol

Followed general procedure on 3.5 mmol scale and purified using silica gel chromatography to give 805 mg (95% yield) of (*E*)-3-methyl-6-(naphthalen-1-yl)hex-3-en-1-ol as a pale yellow oil. IR (Film) 3348 (br), 2932 (s), 1665, 1596, 1509, 1440, 1394, 1043 (s), 776 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.08 (d, *J* = 8.2 Hz, 1 H), 7.87 (d, *J* = 7.8 Hz, 1 H), 7.73 (d, *J* = 8.2 Hz, 1 H), 7.61 - 7.47 (m, 2 H), 7.41 (t, *J* = 7.8 Hz, 1 H), 7.32 (d, *J* = 7.3 Hz, 1 H), 5.39 (t, *J* = 7.3 Hz, 1 H), 3.62 (t, *J* = 6.9 Hz, 2 H), 3.15 (t, *J* = 6.4 Hz, 2 H), 2.52 (dd, *J* = 7.3, 15.6 Hz, 2 H), 2.25 (t, *J* = 6.9 Hz, 2 H), 1.51 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) d = 138.0, 133.8, 132.2, 131.8, 128.8, 127.1, 126.6, 125.9, 125.7, 125.4, 125.4, 123.7, 60.0, 42.6, 32.9, 29.2, 15.6; MS (ESI) exact mass calculated for [M+Na] ($C_{17}H_{20}NaO$) requires *m/z* 263.1, found *m/z* 263.1.

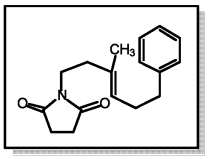


(*E*)-6-(5-chlorothiophen-2-yl)-3-methylhex-3-en-1-ol

Followed general procedure on 3.1 mmol scale and purified using silica gel chromatography to give 704 mg (99% yield over two steps) of (*E*)-6-(5-chlorothiophen-2-yl)-3-methylhex-3-en-1-ol as a pale yellow oil. IR (Film) 3332 (br), 2925 (s), 1454 (s), 1060 (s), 981, 790 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.72 (d, *J* = 3.7 Hz, 1 H), 6.56 (d, *J* = 3.7 Hz, 1 H), 5.27 (t, *J* = 7.1 Hz, 1 H), 3.67 (t, *J* = 6.2 Hz, 2 H), 2.80 (t, *J* = 7.3 Hz, 2 H), 2.38 (dd, *J* = 7.2, 14.4 Hz, 2 H), 2.27 (t, *J* = 6.2 Hz, 2 H), 1.63 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 143.7, 133.1, 126.9, 126.0, 125.6, 123.6, 60.0, 42.6, 30.4, 29.8, 15.8; MS (ESI) exact mass calculated for [M+Na] ($C_{11}H_{15}ClNaOS$) requires *m/z* 253.0, found *m/z* 253.1.

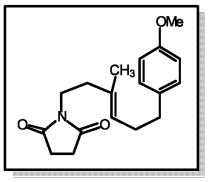
Mitsunobu reaction between homoallylic alcohols and succinimide

A solution of (*E*)-3-methyl-6-arylhex-3-en-1-ol (3.4 mmol, 1.0 equiv), succinimide (3.7 mmol, 1.1 equiv) and PPh_3 (3.7 mmol, 1.1 equiv) in THF (20 mL) was cooled to 0 ^oC. To this solution was added a solution of DBAD (3.7 mmol, 1.1 equiv) in THF (5 mL) dropwise by syringe. The resulting yellow solution was warmed to room temperature and aged for 6 h. Saturated aqueous NH_4Cl solution was added to quench the reaction. The aqueous layer was separated, extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography to obtain the desired succinimide product.



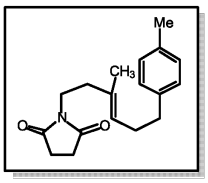
(*E*)-1-(3-methyl-6-phenylhex-3-en-1-yl)pyrrolidine-2,5-dione

Followed general procedure on 3.8 mmol scale and purified using silica gel chromatography to give 945 mg (91% yield) of (*E*)-1-(3-methyl-6-phenylhex-3-en-1-yl)pyrrolidine-2,5-dione as a pale yellow oil. IR (Film): 2940, 1697 (s), 1434, 1399, 1350, 1303, 1159 (s), 819, 749, 700, 663 cm^{-1}; ^1H NMR: (500 MHz, $CDCl_3$) δ 7.27 (m, 2H), 7.18 (m, 3H), 5.28 (td, 1H, J = 1.0, 7.0 Hz), 3.57 (t, 2H, J = 7.5 Hz), 2.60 (t, 2H, J = 7.0 Hz), 2.57 (s, 4H), 2.28 (dt, 2H, J = 7.0, 7.5 Hz), 2.23 (t, 2H, J = 7.0 Hz), 1.62 (s, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 177.3, 142.2, 132.5, 128.6, 128.5, 126.8, 126.0, 37.5, 37.4, 35.9, 29.9, 28.3, 15.9; MS (APCI) exact mass calculated for [M+H] ($C_{17}H_{22}NO_2$) requires *m/z* 272.2, found *m/z* 272.2.



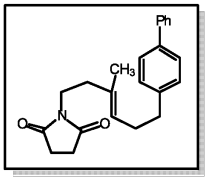
(*E*)-1-(6-(4-methoxyphenyl)-3-methylhex-3-en-1-yl)pyrrolidine-2,5-dione

Followed general procedure on 4.0 mmol scale and purified using silica gel chromatography to give 1.07 g (89% yield) of (*E*)-1-(6-(4-methoxyphenyl)-3-methylhex-3-en-1-yl)- pyrrolidine-2,5-dione as a pale yellow oil. IR (Film): 2939, 1698 (s), 1511, 1437, 1400, 1349, 1300, 1244, 1160, 1034, 818 cm^{-1}; ^1H NMR: (500 MHz, $CDCl_3$) δ 7.07 (d, 2H, *J* = 9.0 Hz), 6.81 (dd, 2H, *J* = 2.0, 8.0 Hz), 5.12 (t, 1H, *J* = 6.5 Hz), 3.77 (s, 3H), 3.56 (t, 2H, *J* = 7.0 Hz), 2.57 (s, 4H), 2.53 (m, 2H, *J* = 7.5 Hz), 2.22 (m, 4H), 1.61 (s, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 177.3, 158.0, 134.3, 132.4, 129.5, 126.9, 113.9, 55.5, 37.5, 37.4, 35.0, 30.2, 28.3, 16.0; MS (APCI) exact mass calculated for [M+H] ($C_{18}H_{24}NO_3$) requires *m/z* 302.2, found *m/z* 302.1.



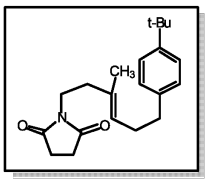
(*E*)-1-(3-methyl-6-(p-tolyl)hex-3-en-1-yl)pyrrolidine-2,5-dione

Followed general procedure on 2.3 mmol scale and purified using silica gel chromatography to give 568 mg (88% yield) of (*E*)-1-(3-methyl-6-phenylhex -3-en-1-yl)pyrrolidine -2,5-dione as a pale yellow oil. IR (Film) 2940, 1702 (s), 1436, 1400, 1161, 810, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.07 (dd, *J* = 7.7, 11.7 Hz, 4 H), 5.14 (t, *J* = 7.0 Hz, 1 H), 3.58 (t, *J* = 7.1 Hz, 2 H), 2.58 (s, 4 H), 2.56 (t, *J* = 7.7 Hz, 2 H), 2.31 (s, 3 H), 2.22 (t, *J* = 7.7 Hz, 2 H), 2.26 (dd, *J* = 7.3, 15.7 Hz, 2 H), 1.63 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.0, 138.9, 135.2, 132.1, 128.9, 128.2, 126.7, 37.2, 37.2, 35.2, 29.8, 28.0, 21.0, 15.7; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{18}H_{24}NO_2$) requires *m/z* 286.2, found *m/z* 286.2.



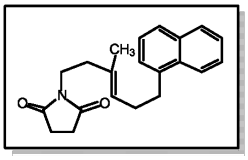
(*E*)-1-(6-([1,1'-biphenyl]-4-yl)-3-methylhex-3-en-1-yl)pyrrolidine-2,5-dione

Followed general procedure on 3.4 mmol scale and purified using silica gel chromatography to give 1.1 g (93% yield) of (*E*)-1-(6-([1,1'-biphenyl]-4-yl)-3-methylhex-3-en-1-yl)pyrrolidine-2,5-dione as a pale yellow solid. FTIR (Film) 2937, 1696 (s), 1402, 1160 (s), 820, 763, 732, 697 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$) δ = 7.58 (d, *J* = 8.1 Hz, 2 H), 7.51 (d, *J* = 7.7 Hz, 2 H), 7.43 (t, *J* = 7.7 Hz, 2 H), 7.35 - 7.30 (m, 1 H), 7.24 (s, 2 H), 5.17 (t, *J* = 7.1 Hz, 1 H), 3.59 (t, *J* = 7.0 Hz, 2 H), 2.65 (t, *J* = 8.1 Hz, 2 H), 2.57 (s, 4 H), 2.32 (dd, *J* = 7.3, 14.6 Hz, 2 H), 2.24 (t, *J* = 7.1 Hz, 2 H), 1.65 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.1, 141.1, 141.0, 138.8, 132.4, 128.8, 128.7, 127.0, 127.0, 126.9, 126.5, 37.3, 37.2, 35.3, 29.6, 28.1, 28.0, 15.8; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{23}H_{26}NO_2$) requires *m/z* 348.2, found *m/z* 348.2.



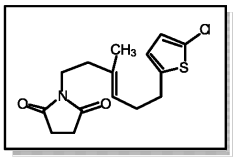
(*E*)-1-(6-(4-(*tert*-butyl)phenyl)-3-methylhex-3-en-1-yl)pyrrolidine-2,5-dione

Followed general procedure on 2.7 mmol scale and purified using silica gel chromatography to give 820 mg (93% yield) of (*E*)-1-(6-(4-(*tert*-butyl)phenyl)-3-methylhex-3-en-1-yl)pyrrolidine-2,5-dione as a pale yellow oil. IR (Film) 2958, 1699 (s), 1435, 1399, 1362, 1160 (s), 822 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.32 (d, *J* = 8.2 Hz, 2 H), 7.13 (d, *J* = 8.2 Hz, 2 H), 5.17 (t, *J* = 7.1 Hz, 1 H), 3.60 (t, *J* = 6.9 Hz, 2 H), 2.59 (t, *J* = 7.8 Hz, 2 H), 2.56 (s, 4 H), 2.30 (dd, *J* = 7.3, 14.6 Hz, 2 H), 2.25 (t, *J* = 7.1 Hz, 2 H), 1.66 (s, 3 H), 1.33 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 176.9, 148.5, 138.8, 132.0, 127.9, 126.7, 125.1, 37.2, 37.0, 35.0, 34.2, 31.3, 29.5, 27.9, 15.6; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{21}H_{30}NO_2$) requires *m/z* 328.2, found *m/z* 328.2.



(*E*)-1-(3-methyl-6-(naphthalen-1-yl)hex-3-en-1-yl)pyrrolidine-2,5-dione

Followed general procedure on 3.4 mmol scale and purified using silica gel chromatography to give 1.0 g (93% yield) of (*E*)-1-(3-methyl-6-(naphthalen-1-yl)hex-3-en-1-yl)pyrrolidine-2,5-dione as a pale yellow oil. IR (Film) 2940, 1698 (s), 1399, 1349, 1159 (s), 779 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.03 (d, *J* = 8.2 Hz, 1 H), 7.85 (d, *J* = 8.0 Hz, 1 H), 7.71 (d, *J* = 8.0 Hz, 1 H), 7.52 (t, *J* = 7.6 Hz, 1 H), 7.47 (t, *J* = 8.0 Hz, 1 H), 7.40 (t, *J* = 7.6 Hz, 1 H), 7.31 (d, *J* = 6.9 Hz, 1 H), 5.26 (t, *J* = 7.1 Hz, 1 H), 3.58 (t, *J* = 7.1 Hz, 2 H), 3.06 (t, *J* = 7.5 Hz, 2 H), 2.55 (s, 4 H), 2.43 (q, *J* = 7.3 Hz, 2 H), 2.24 (t, *J* = 7.1 Hz, 2 H), 1.62 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 177.3, 138.2, 134.1, 132.6, 132.1, 129.0, 126.9, 126.9, 126.1, 126.0, 125.7, 125.7, 123.9, 77.5, 77.5, 77.3, 77.0, 37.6, 37.5, 33.1, 29.3, 28.3, 16.0; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{21}H_{24}NO_2$) requires *m/z* 322.2, found *m/z* 322.2.

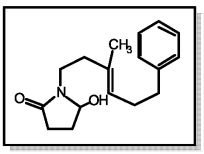


(*E*)-1-(6-(5-chlorothiophen-2-yl)-3-methylhex-3-en-1-yl)pyrrolidine-2,5-dione

Followed general procedure on 3.1 mmol scale and purified using silica gel chromatography to give 776 mg (80% yield) of (*E*)-1-(6-(5-chlorothiophen-2-yl)-3-methylhex-3-en-1-yl)pyrrolidine-2,5-dione as a pale yellow oil. IR (Film) 2940, 1696 (s), 1435, 1400, 1159 (s), 1062, 796 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.69 (d, *J* = 3.7 Hz, 1 H), 6.53 (d, *J* = 3.7 Hz, 1 H), 5.12 (t, *J* = 6.4 Hz, 1 H), 3.59 (t, *J* = 7.1 Hz, 2 H), 2.72 (t, *J* = 7.6 Hz, 2 H), 2.62 (s, 4 H), 2.29 (dd, *J* = 7.3, 14.7 Hz, 2 H), 2.24 (t, *J* = 7.1 Hz, 2 H), 1.64 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 177.0, 143.7, 133.3, 126.8, 125.6, 125.5, 123.5, 110.6, 37.3, 37.1, 30.2, 29.6, 28.1, 15.8; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{15}H_{19}ClNO_2S$) requires *m/z* 312.2, found *m/z* 312.1.

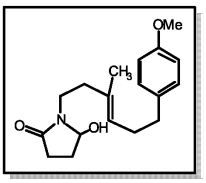
Reduction of *N*-alkyl succinimides

To a solution of (*E*)-1-(3-methyl-6-arylhex-3-en-1-yl)pyrrolidine-2,5-dione (3.1 mmol, 1.0 equiv) in MeOH (31 mL) at 0 ^{o}C was added $NaBH_4$ (9.3 mmol, 3 equiv) over 2 min. The reaction was sealed with a needle-pierced rubber septa and stirred vigorously at the same temperature. After 30 min, a second portion of $NaBH_4$ (9.3 mmol, 3 equiv) was added over 2 min. The reaction solution was further stirred for 1 h, and then poured into a mixture of CH_2Cl_2 (~50 mL) and saturated $NaHCO_3$ (~50 mL). The resulting white biphasic liquid was stirred vigorously for 15 min and separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The crude extracts were purified by silica gel column chromatography to obtain the hydroxylactam product.



(*E*)-5-hydroxy-1-(3-methyl-6-phenylhex-3-en-1-yl)pyrrolidin-2-one (9)

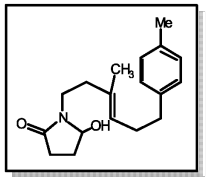
Followed general procedure on 3.49 mmol scale and purified using silica gel chromatography to give 720 mg (76% yield) of (*E*)-5-hydroxy-1-(3-methyl-6-phenylhex-3-en-1-yl)pyrrolidin-2-one. IR (Film): 3306 (br), 2929, 1658 (s), 1453, 1421, 1329, 1283, 1162, 1069, 984, 909, 748, 698, 669 cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.27 (m, 2H), 7.18 (m, 3H), 5.21 (t, 1H, *J* = 6.5 Hz), 5.11 (t, 1H, *J* = 6.5 Hz), 3.57 (dt, 1H, *J* = 7.0, 7.0 Hz), 3.21 (dt, 1H, *J* = 7.0, 6.5 Hz), 2.62 (t, 2H, *J* = 9.0 Hz), 2.49 (m, 1H), 2.30 (m, 2H), 2.21 (m, 4H), 1.83 (m, 1H), 1.61 (s, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 175.0, 142.2, 133.2, 128.6, 128.5, 126.3, 126.0, 88.5, 38.5, 37.8, 36.0, 30.0, 29.1, 28.5, 16.0; MS (APCI) exact mass calculated for [M+Na] ($C_{17}H_{23}NNaO_2$) requires *m/z* 296.2, found *m/z* 296.2.



(*E*)-5-hydroxy-1-(6-(4-methoxyphenyl)-3-methylhex-3-en-1-yl)pyrrolidin-2-one (1)

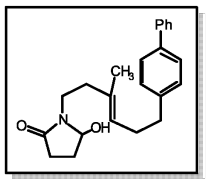
Followed general procedure on 2.33 mmol scale and purified using silica gel chromatography to give 550 mg (78% yield) of (*E*)-5-hydroxy-1-(6-(4-methoxyphenyl)-3-methylhex-3-en-1-yl)pyrrolidin-2-one as a white solid. IR (Film): 3306 (br), 2933, 1660 (s), 1612, 1511, 1463, 1298, 1244, 1177, 1069, 1036, 984, 827, 669 cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.09 (d, 2H, *J* = 8.5 Hz), 6.82 (d, 2H, *J* = 8.5 Hz), 5.20 (t, 1H, *J* = 7.0 Hz), 5.11 (t, 1H, *J* = 6.0 Hz), 3.78 (s, 3H), 3.57 (dt, 1H, *J* = 7.5, 7.5 Hz), 3.23 (dt, *J* = 7.5, 7.0 Hz), 2.88 (d, 1H, *J* = 8.5 Hz), 2.57 (t, 2H, *J* = 7.5 Hz), 2.50 (m, 1H), 2.25 (m, 5H), 1.82 (m, 1H), 1.61 (s, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 174.8, 158.0, 143.3, 133.3, 129.5, 126.4,

113.9, 83.6, 55.5, 38.7, 37.9, 35.1, 30.2, 29.0, 28.7, 16.1; MS (APCI) exact mass calculated for [M+Na] ($C_{18}H_{25}NNaO_3$) requires *m/z* 326.2, found *m/z* 326.1.



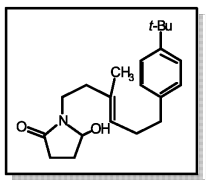
(*E*)-5-hydroxy-1-(3-methyl-6-(p-tolyl)hex-3-en-1-yl)pyrrolidin-2-one (11)

Followed general procedure on 2.0 mmol scale and purified using silica gel chromatography to give 388 mg (68% yield) of (*E*)-5-hydroxy-1-(3-methyl-6-(p-tolyl)hex-3-en-1-yl)pyrrolidin-2-one as a white solid. IR (Film) 3308 (br), 2924, 1663 (s), 1456, 1284, 1163, 1069, 985, 807 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.08 (dd, *J* = 8.2, 11.9 Hz, 4 H), 5.22 (dt, *J* = 1.4, 6.9 Hz, 1 H), 5.12 (ddd, *J* = 1.8, 6.0, 7.8 Hz, 1 H), 3.58 (td, *J* = 7.3, 14.2 Hz, 1 H), 3.25 (td, *J* = 6.7, 13.6 Hz, 1 H), 2.91 (br. s., 1 H), 2.60 (t, *J* = 7.8 Hz, 2 H), 2.55 - 2.46 (m, 1 H), 2.32 (s, 3 H), 2.30 (dd, *J* = 6.0, 13.7 Hz, 2 H), 2.27 - 2.18 (m, 4 H), 1.87 - 1.79 (m, 1 H), 1.63 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 174.5, 138.9, 135.2, 133.0, 128.9, 128.2, 126.2, 83.3, 38.4, 37.6, 35.3, 29.8, 28.8, 28.4, 21.0, 15.8; MS (ESI-APCI) exact mass calculated for [M-H_2O+H] ($C_{18}H_{24}NO$) requires *m/z* 270.2, found *m/z* 270.2.



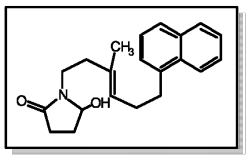
(*E*)-1-(6-([1,1'-biphenyl]-4-yl)-3-methylhex-3-en-1-yl)-5-hydroxypyrrolidin-2-one (13)

Followed general procedure on 3.2 mmol scale and purified using silica gel chromatography to give 500 mg (45% yield) of (*E*)-1-(6-([1,1'-biphenyl]-4-yl) -3-methylhex-3-en-1-yl)-5-hydroxypyrrolidin-2-one as a white solid (the starting material wasn't completely soluble in MeOH, and ~50% of it was recovered). IR (Film) 3307 (br), 2930, 1663 (s), 1486, 1450, 1283, 1163, 1070, 985, 833, 762 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.58 (d, *J* = 6.8 Hz, 2 H), 7.52 (d, *J* = 8.3 Hz, 2 H), 7.43 (t, *J* = 7.1 Hz, 2 H), 7.33 (t, *J* = 6.8 Hz, 1 H), 7.25 (d, *J* = 6.3 Hz, 2 H), 5.25 (dt, *J* = 1.2, 7.0 Hz, 1 H), 5.12 (ddd, *J* = 2.2, 6.0, 7.9 Hz, 1 H), 3.57 (td, *J* = 7.8, 14.6 Hz, 1 H), 3.28 (td, *J* = 6.7, 13.9 Hz, 1 H), 2.68 (t, *J* = 7.8 Hz, 2 H), 2.55 - 2.46 (m, 1 H), 2.36 (dd, *J* = 7.3, 15.1 Hz, 2 H), 2.30 - 2.18 (m, 4 H), 2.10 (br. s., 1 H), 1.84 - 1.75 (m, 1 H), 1.65 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 174.5, 141.1, 141.0, 138.8, 133.2, 128.8, 128.7, 127.0, 127.0, 126.9, 126.0, 83.3, 38.4, 37.6, 35.4, 29.6, 28.8, 28.4, 15.9; MS (ESI-APCI) exact mass calculated for [M-H_2O+H] ($C_{23}H_{26}NO$) requires *m/z* 332.2, found *m/z* 332.2.



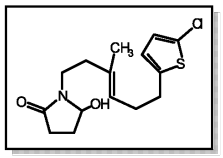
(*E*)-1-(6-(4-(*tert*-butyl)phenyl)-3-methylhex-3-en-1-yl)-5-hydroxypyrrolidin-2-one (15)

Followed general procedure on 2.5 mmol scale and purified using silica gel chromatography to give 745 mg (90% yield) of (*E*)-1-(6-([1,1'-biphenyl]-4-yl) -3-methylhex-3-en-1-yl)-5-hydroxypyrrolidin-2-one as a white solid. IR (Film) 3325 (br), 2960, 1666 (s), 1459, 1270, 1164, 1070, 829 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.36 - 7.29 (m, 2 H), 7.13 (d, *J* = 8.3 Hz, 2 H), 5.24 (dt, *J* = 1.2, 7.0 Hz, 1 H), 5.12 (ddd, *J* = 2.0, 5.9, 7.8 Hz, 1 H), 3.58 (td, *J* = 7.3, 14.2 Hz, 1 H), 3.27 (td, *J* = 6.8, 13.7 Hz, 1 H), 2.61 (t, *J* = 7.8 Hz, 2 H), 2.56 - 2.46 (m, 1 H), 2.40 - 2.19 (m, 7 H), 1.86 - 1.77 (m, 1 H), 1.64 (s, 3 H), 1.32 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 174.4, 162.1, 148.6, 138.9, 128.0, 126.3, 125.2, 83.4, 38.5, 37.6, 35.2, 34.3, 31.4, 29.6, 28.7, 28.5, 15.8; MS (ESI-APCI) exact mass calculated for [M-H_2O+H] ($C_{21}H_{30}NO$) requires *m/z* 312.2, found *m/z* 312.2.



(*E*)-5-hydroxy-1-(3-methyl-6-(naphthalen-1-yl)hex-3-en-1-yl)pyrrolidin-2-one (17)

Followed general procedure on 3.1 mmol scale and purified using silica gel chromatography to give 880 mg (86% yield) of (*E*)-5-hydroxy-1-(3-methyl-6-(naphthalen-1-yl)hex-3-en-1-yl)pyrrolidin-2-one as a colorless gel, which turned into a white solid slowly after stored at room temperature for weeks. IR (Film) 3306 (br), 2934, 1660 (s), 1458, 1282, 1163, 1068, 984, 778 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.06 (d, *J* = 8.2 Hz, 1 H), 7.87 (d, *J* = 7.8 Hz, 1 H), 7.73 (d, *J* = 8.2 Hz, 1 H), 7.51 (td, *J* = 7.3, 22.0 Hz, 2 H), 7.41 (t, *J* = 7.3 Hz, 1 H), 7.33 (d, *J* = 6.9 Hz, 1 H), 5.34 (t, *J* = 6.9 Hz, 1 H), 5.14 (t, *J* = 6.4 Hz, 1 H), 3.59 (td, *J* = 7.8, 14.7 Hz, 1 H), 3.24 (td, *J* = 6.9, 13.7 Hz, 1 H), 3.10 (t, *J* = 7.8 Hz, 2 H), 3.06 (br. s, 1 H), 2.56 - 2.41 (m, 3 H), 2.33 - 2.16 (m, 4 H), 1.89 - 1.78 (m, 1 H), 1.62 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 174.5, 138.0, 133.8, 133.2, 131.8, 128.7, 126.6, 126.1, 125.9, 125.7, 125.5, 125.4, 123.6, 83.3, 38.5, 37.6, 32.8, 29.1, 28.8, 28.4, 15.8; MS (ESI-APCI) exact mass calculated for [M-H_2O+H] ($C_{21}H_{24}NO$) requires *m/z* 306.2, found *m/z* 306.2.



(*E*)-1-(6-(5-chlorothiophen-2-yl)-3-methylhex-3-en-1-yl)-5-hydroxypyrrolidin-2-one (19)

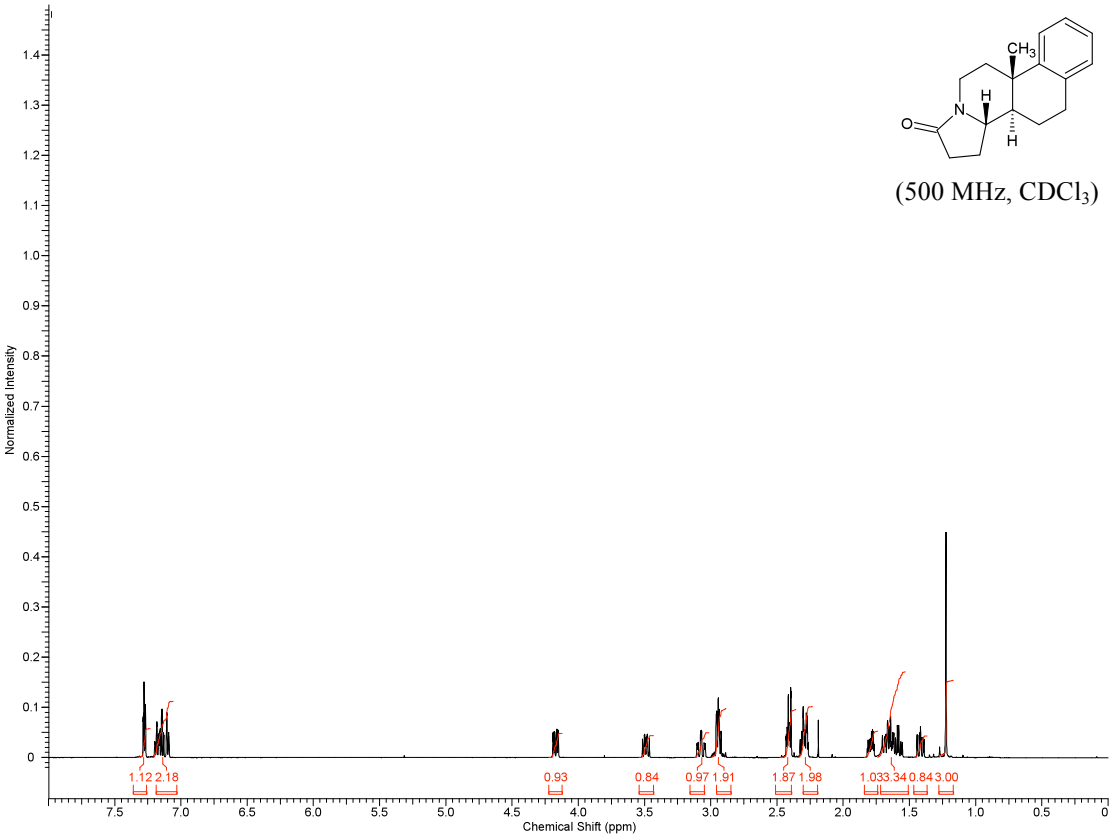
Followed general procedure on 2.5 mmol scale and purified using silica gel chromatography to give 760 mg (98% yield) of (*E*)-1-(6-(5-chlorothiophen-2-yl)-3-methylhex-3-en-1-yl)-5-hydroxypyrrolidin-2-one as a pale brown solid. IR (Film) 3306 (br.), 2930, 1660 (s), 1454 (s), 1283, 1163, 1062, 984, 791 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.70 (d, *J* = 3.7 Hz, 1 H), 6.54 (d, *J* = 3.7 Hz, 1 H), 5.18 (t, *J* = 6.9 Hz, 1 H), 5.13 (br. s., 1 H), 3.58 (td, *J* = 7.8, 14.7 Hz, 1 H), 3.24 (td, *J* = 6.7, 13.6 Hz, 1 H), 3.04 (br. s., 1 H), 2.74 (t, *J* = 7.3 Hz, 2 H), 2.55 - 2.46 (m, 1 H), 2.31 (dd, *J* = 7.3, 14.7 Hz, 2 H), 2.28 - 2.18 (m, 4 H), 1.90 - 1.80 (m, 1 H), 1.64 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) d = 174.5, 143.7, 134.1, 126.8, 125.6, 125.0, 123.5, 83.3, 38.3, 37.6, 30.2, 29.6, 28.8, 28.4, 15.9; MS (ESI-APCI) exact mass calculated for [M-H_2O+H] ($C_{15}H_{19}ClNOS$) requires *m/z* 296.1, found *m/z* 296.1.

References:

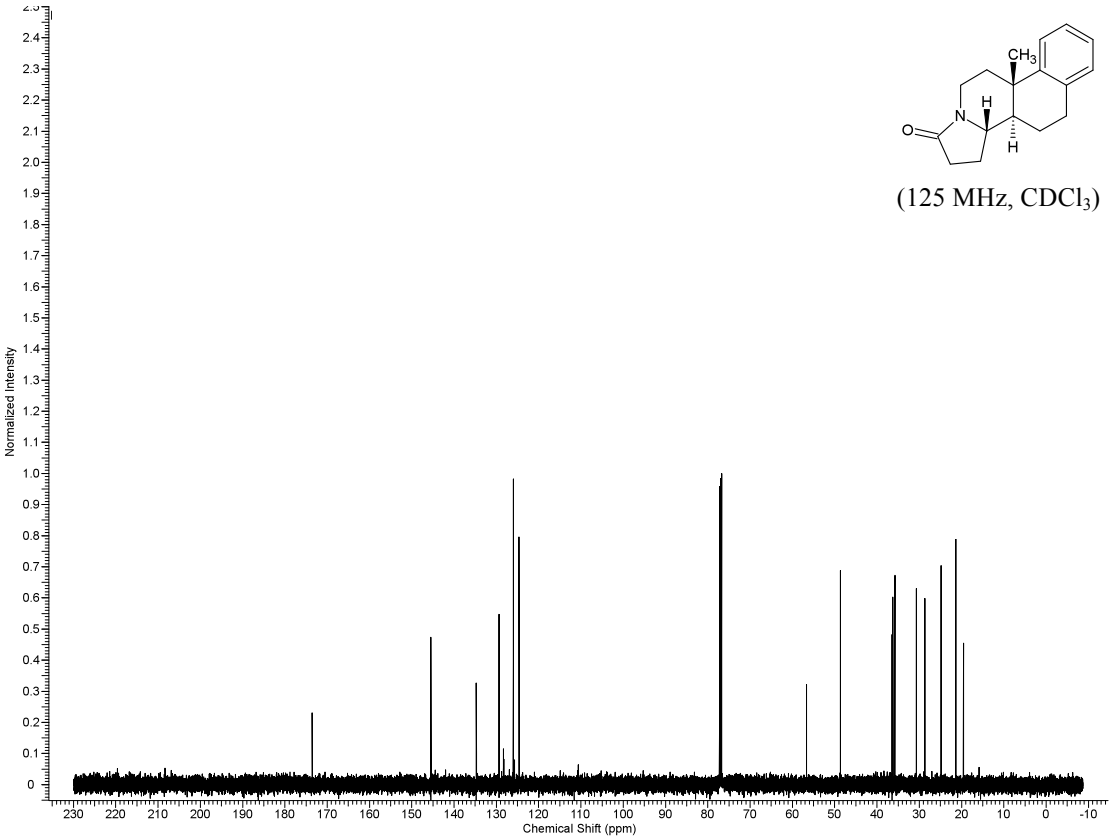
1. For the enantioselective synthesis of 2-aryl pyrrolidines, see: Campos, K. R.; Klapars, A.; Waldman, J. H.; Dormer, P. G.; Chen, C.-Y. *J. Am. Chem. Soc*. **2006**, *128*, 3538.

2. For the synthesis of (*E*)-(4-iodo-3-methylbut-3-en-1-yl) *tert*-butyldimethylsilylether, see: Wipf, P.; Lim, S. *Angew. Chem. Int. Ed.* **1993**, *32*, 1068.

2. NMR Spectra of bicyclization products



(500 MHz, $CDCl_3$)



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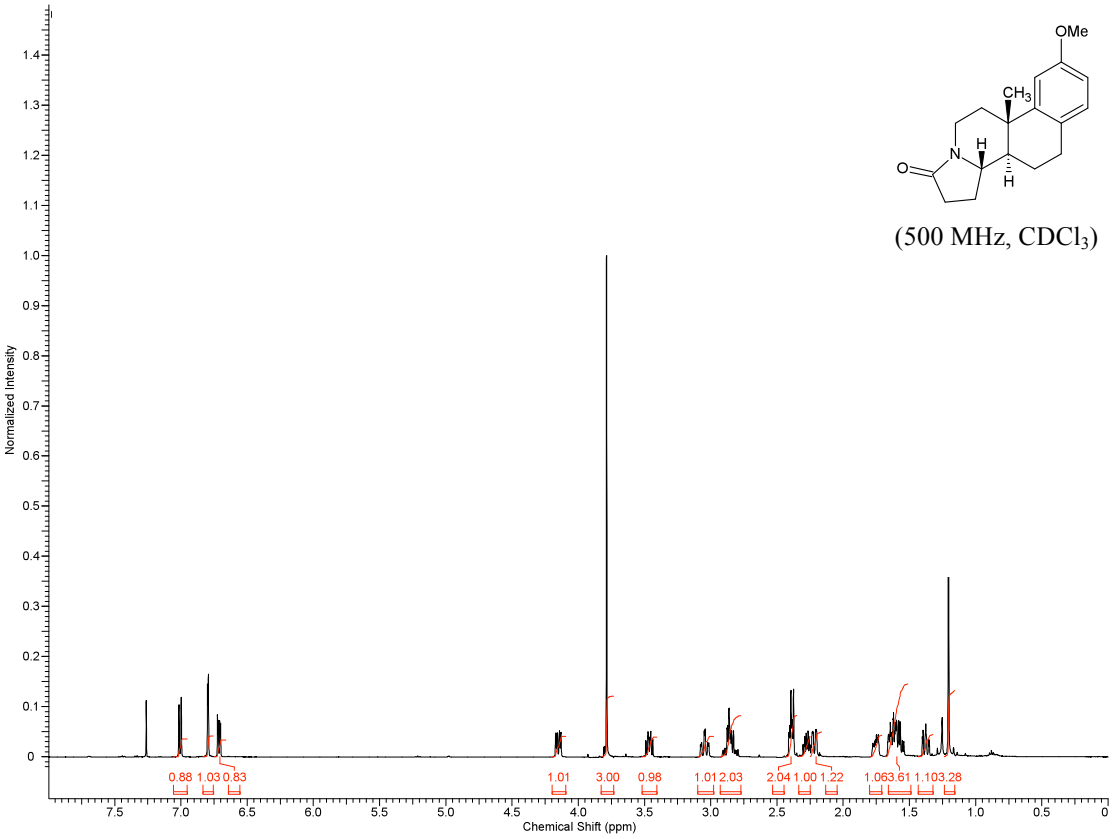
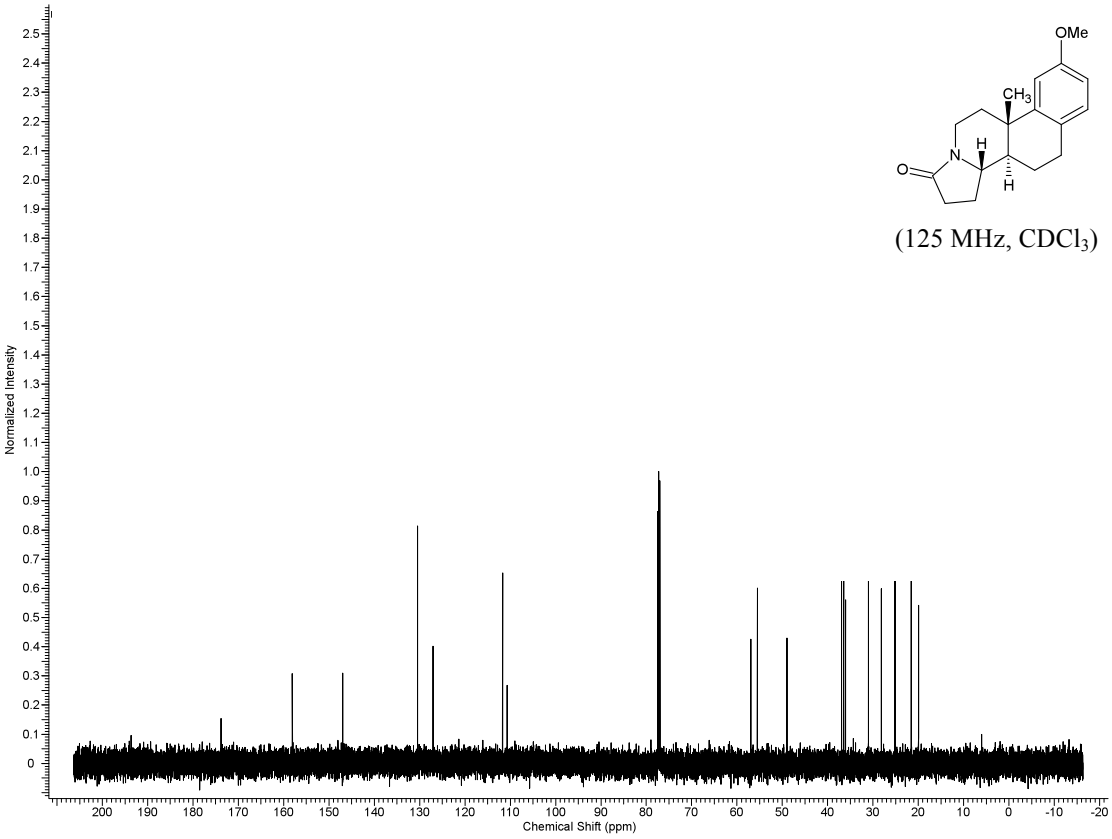
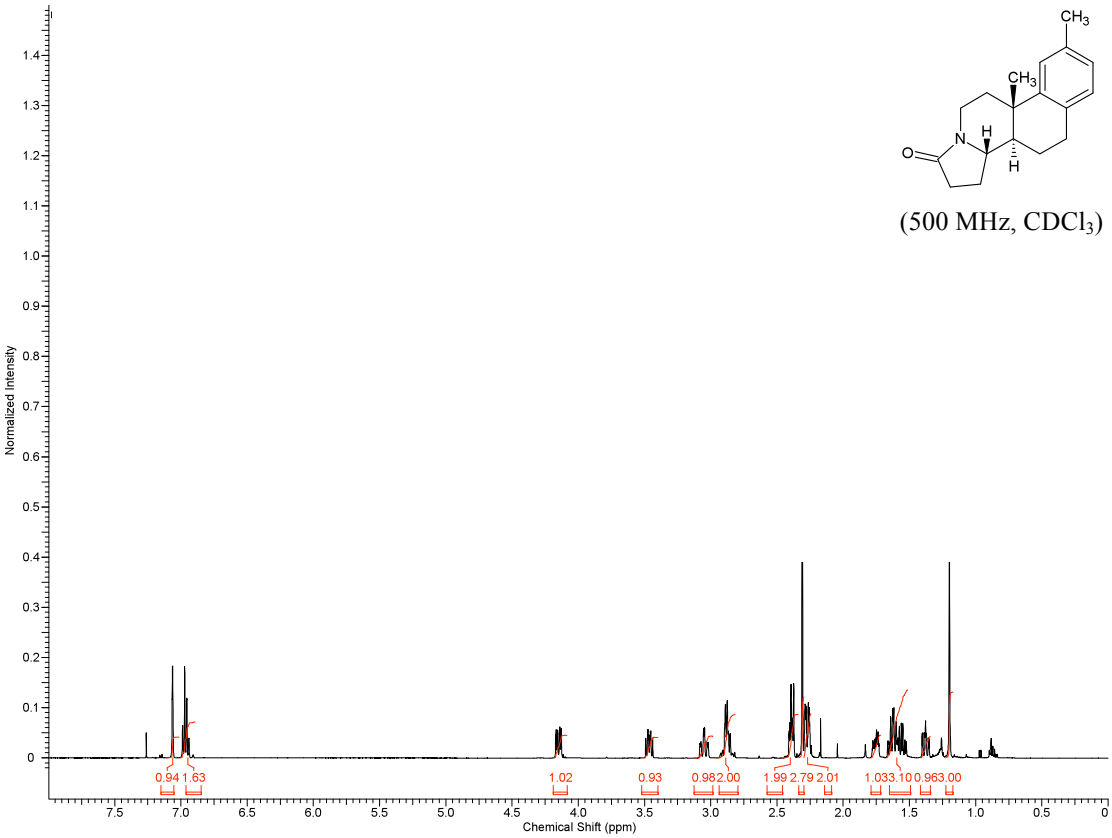


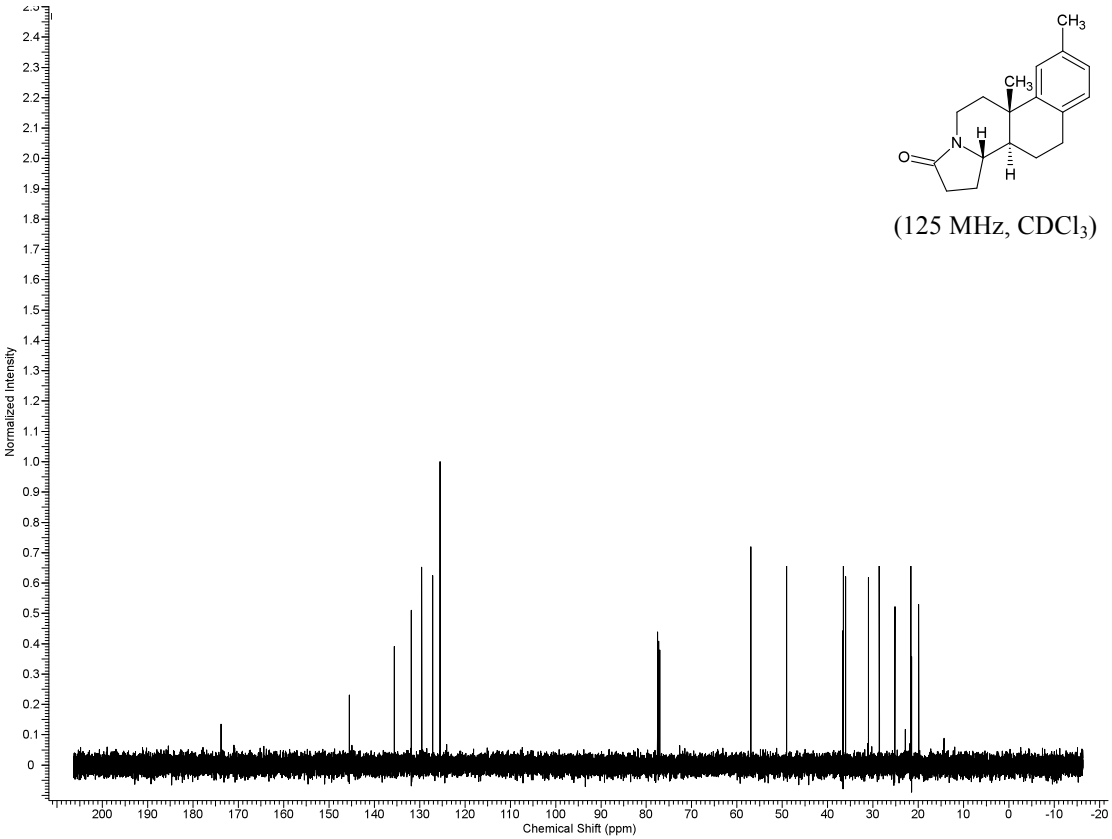
(500 MHz, $CDCl_3$)



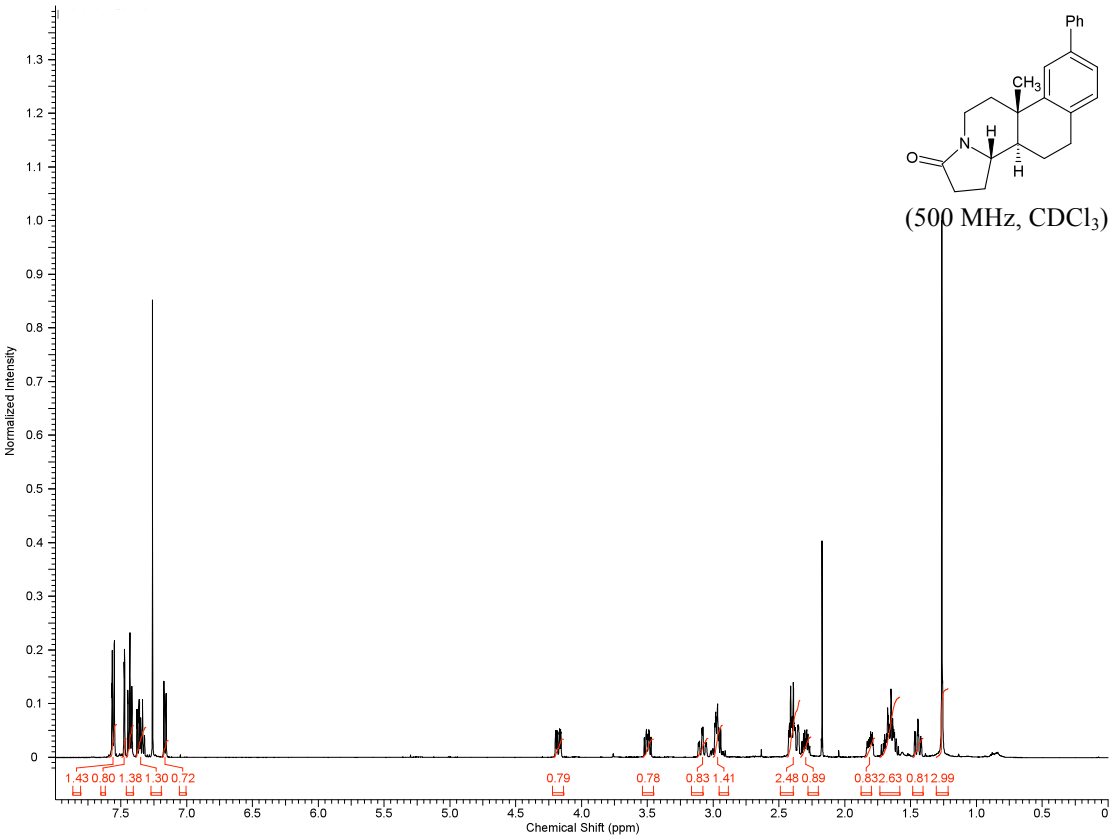
(125 MHz, $CDCl_3$)

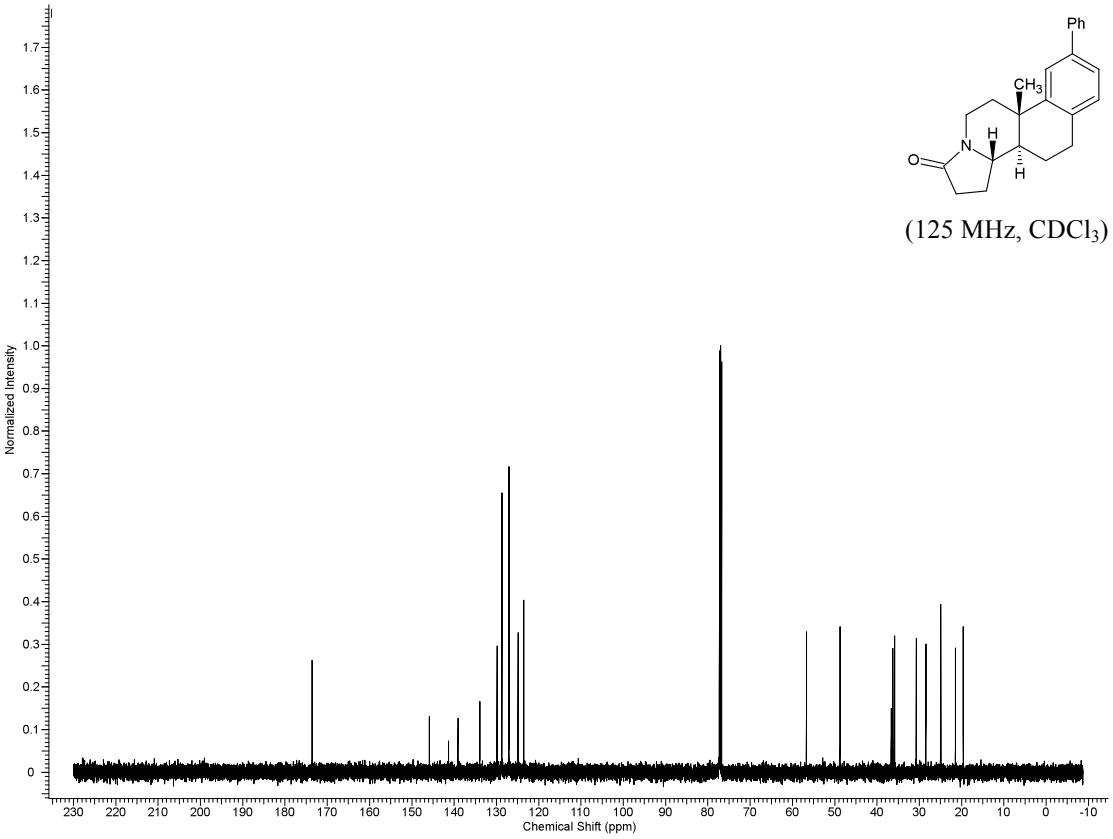


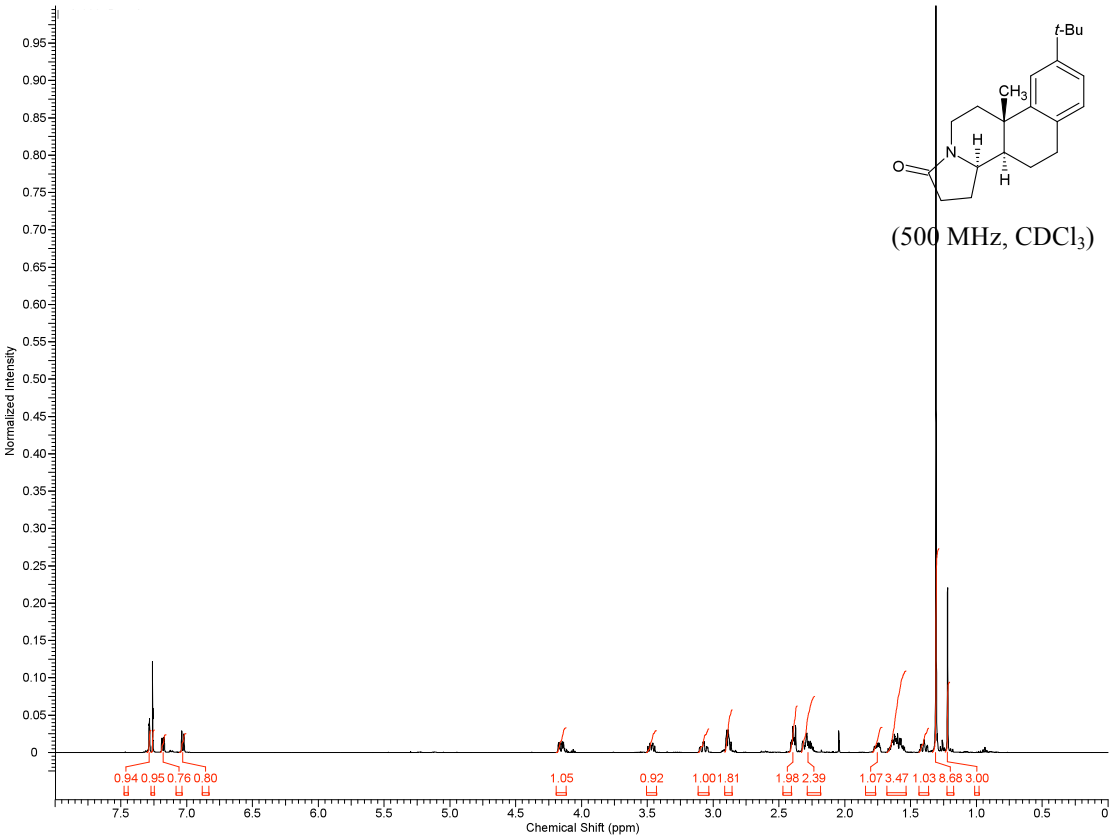
(500 MHz, $CDCl_3$)



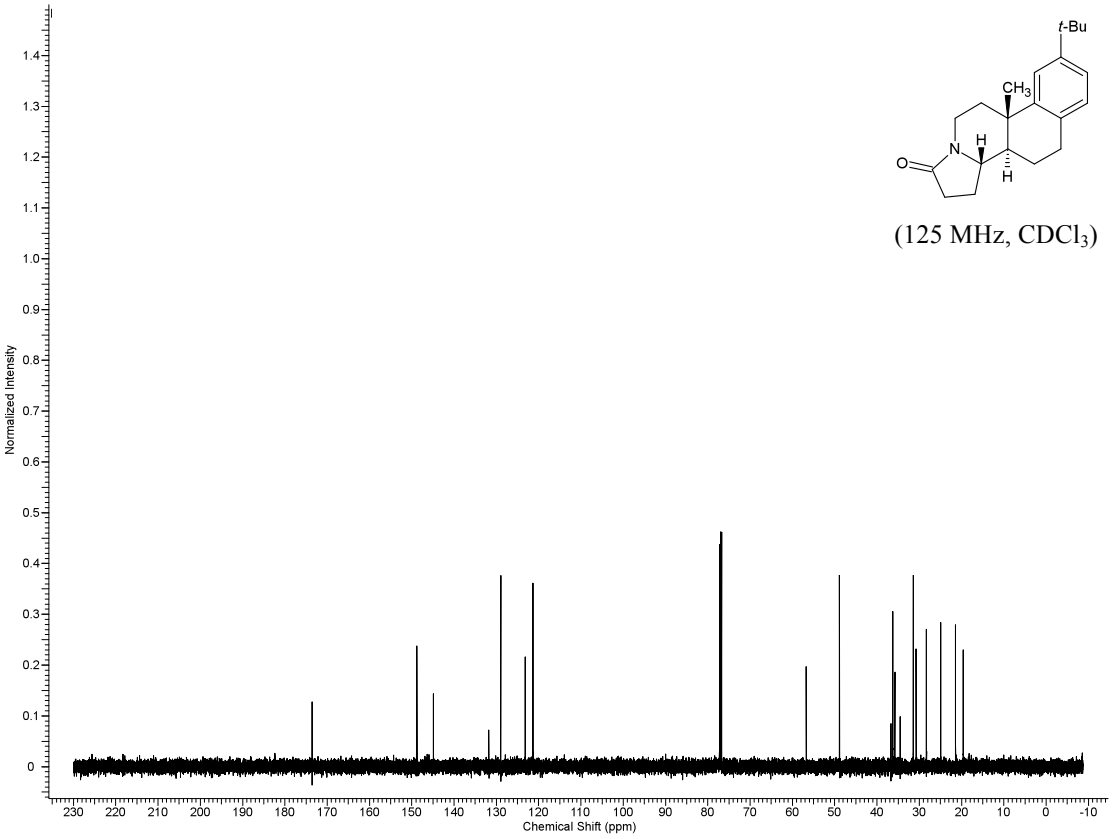
(125 MHz, $CDCl_3$)


Ph
CH3
H
N
O
H
(500 MHz, CDCl3)
Normalized Intensity
1.43 0.80 1.38 1.30 0.72
0.79
0.78
0.83 1.41
2.48 0.89
0.83 2.63 0.81 2.99
Chemical Shift (ppm)

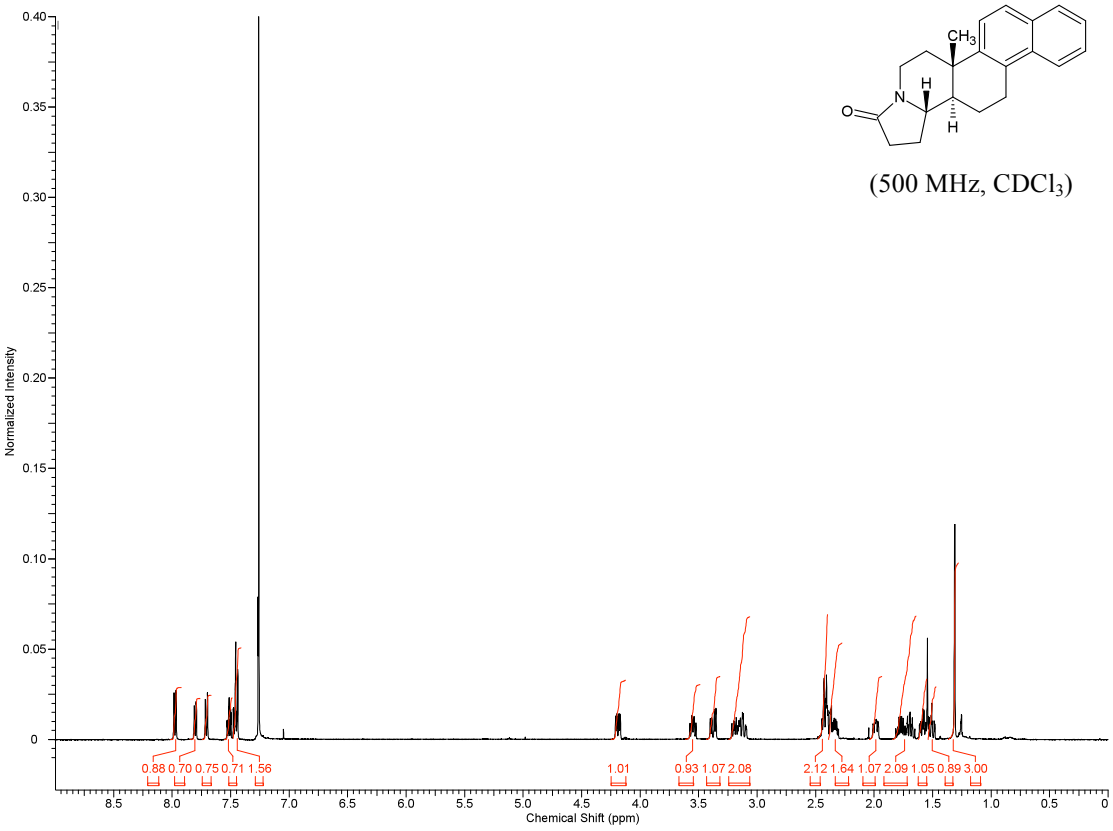

Ph
CH3
H
N
O
H
(125 MHz, CDCl3)
Normalized Intensity
Chemical Shift (ppm)



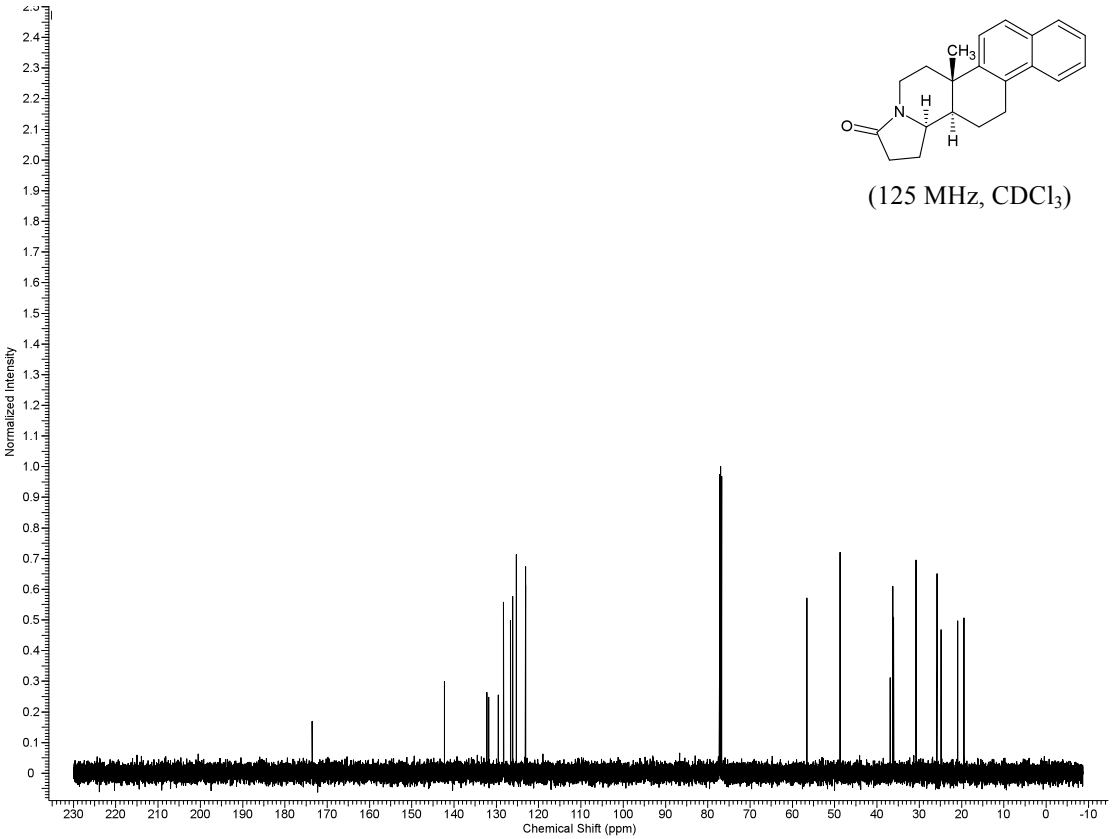
(500 MHz, $CDCl_3$)



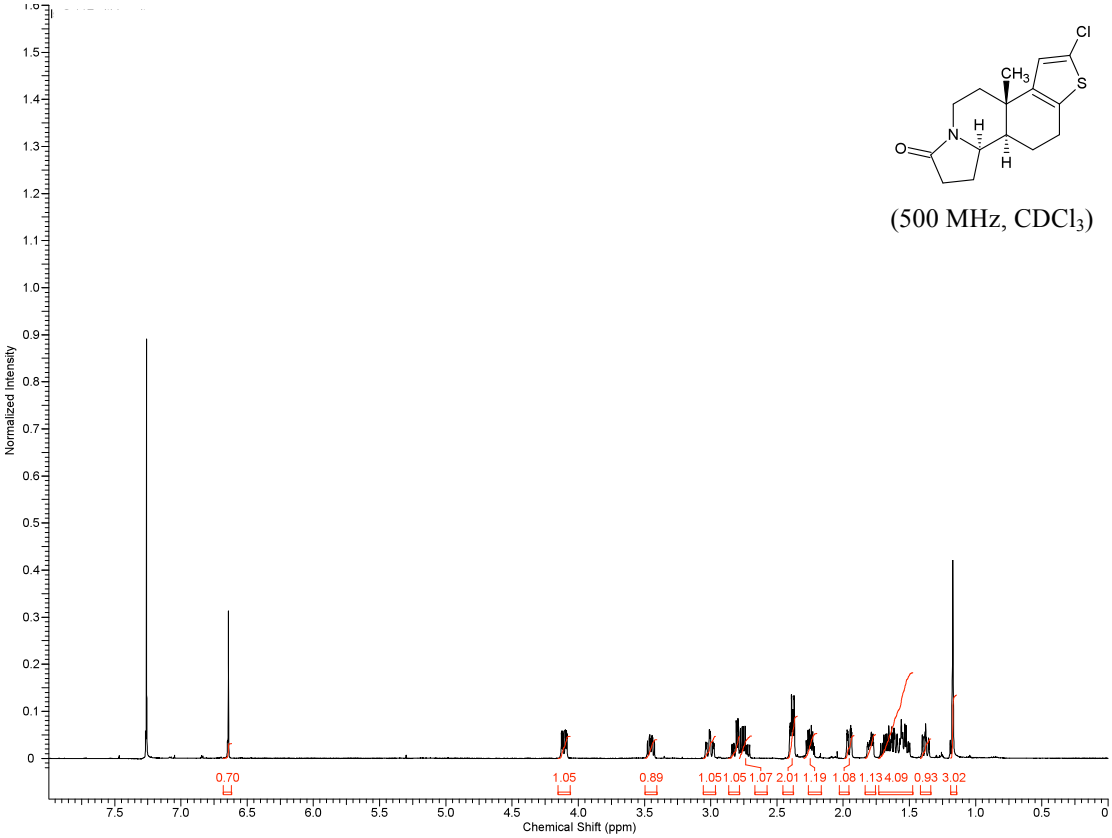
(125 MHz, $CDCl_3$)



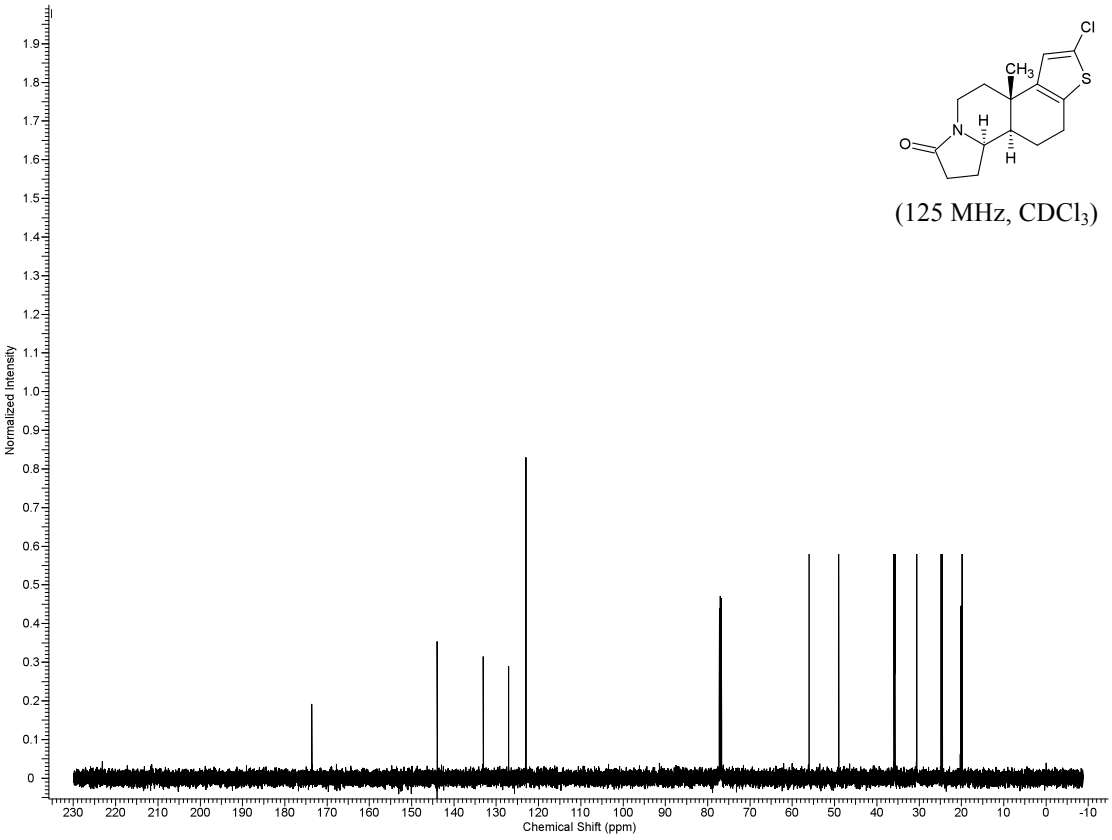
(500 MHz, $CDCl_3$)



(125 MHz, $CDCl_3$)



(500 MHz, $CDCl_3$)

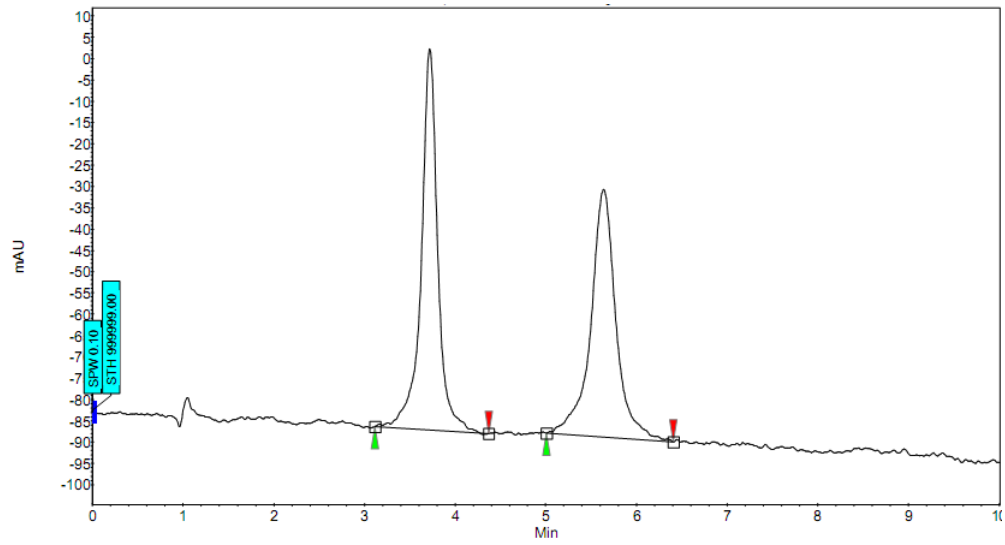


(125 MHz, $CDCl_3$)

3. SFC traces for enantioenriched bicyclization products

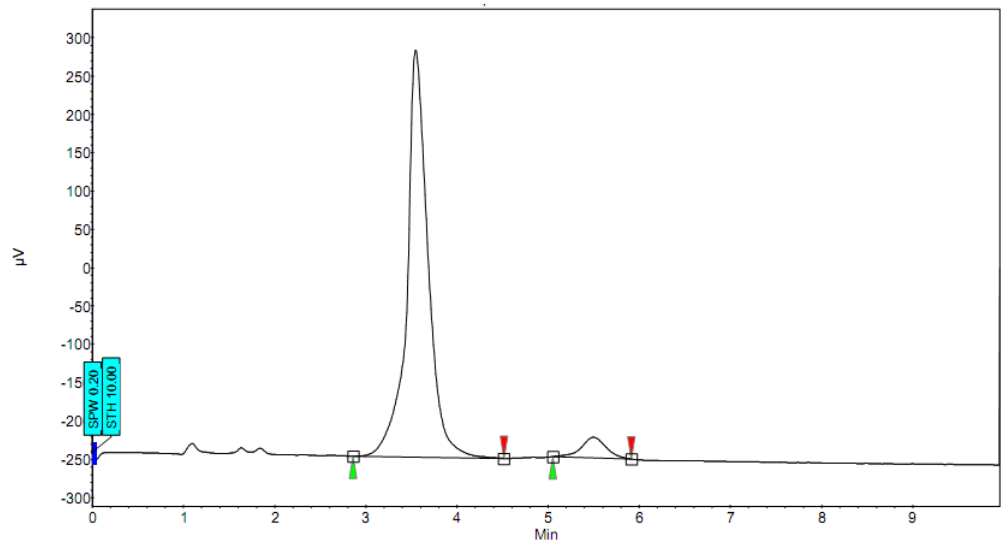
Phenyl product (10)

Racemic sample: SFC (ChiralPak AS, 30% MeOH, 3 mL/min, 225 nm)



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.11	3.72	4.37	0.00	50.31	89.4	18.9	50.313
2	UNKNOWN	5.01	5.64	6.41	0.00	49.69	58.1	18.7	49.687
Total						100.00	147.5	37.6	100.000

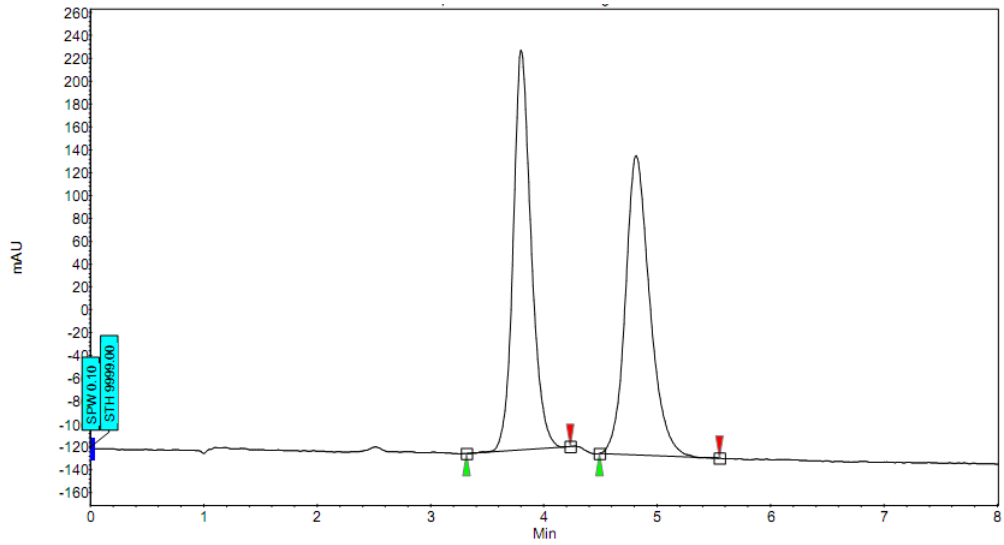
Enantioenriched sample: SFC (ChiralPak AS, 30% MeOH, 3 mL/min, 225 nm), **88.8% ee**



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	2.86	3.55	4.51	0.00	94.42	530.8	142.8	94.423
2	UNKNOWN	5.05	5.50	5.91	0.00	5.58	26.8	8.4	5.577
Total						100.00	557.6	151.2	100.000

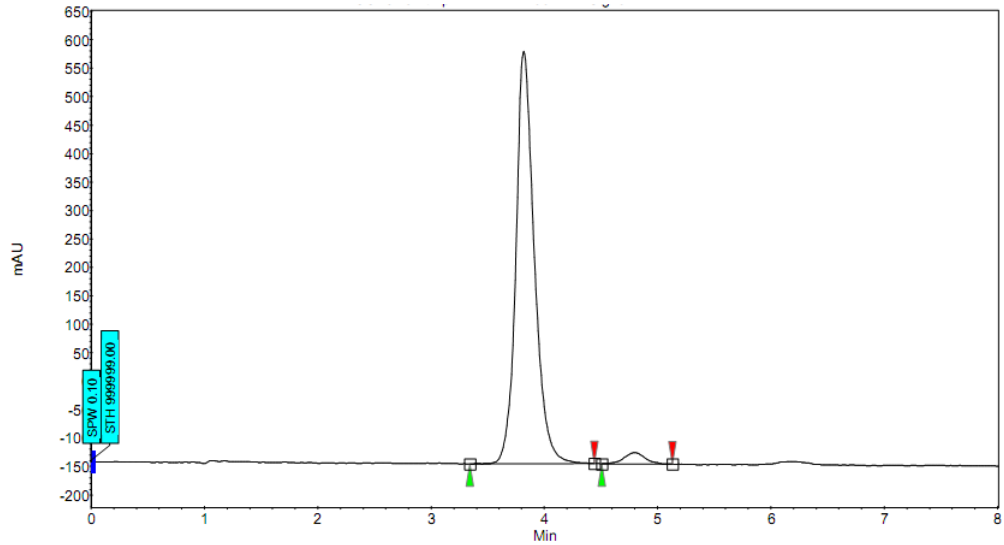
***p*-Methoxy product (2)**

Racemic sample: SFC (ChiralPak AD-H, 25% MeOH, 3 mL/min, 210 nm)



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	3.32	3.80	4.23	0.00	50.09	349.5	65.5	50.086
1	UNKNOWN	4.49	4.81	5.55	0.00	49.91	261.8	65.3	49.914
Total						100.00	611.4	130.8	100.000

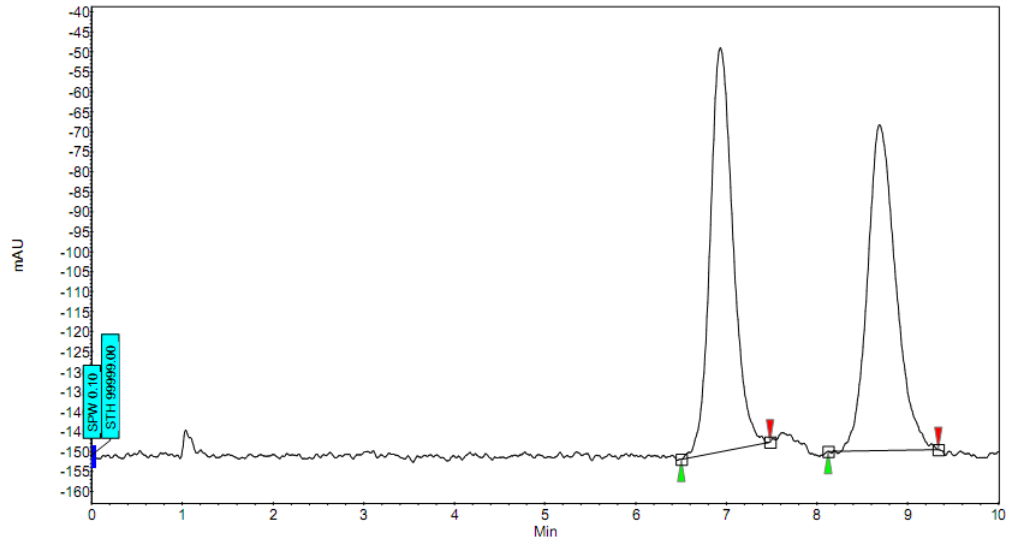
Enantioenriched sample: SFC (ChiralPak AD-H, 25% MeOH, 3 mL/min, 210 nm), **94.1% ee**



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.34	3.82	4.44	0.00	97.03	724.6	138.7	97.034
2	UNKNOWN	4.51	4.79	5.13	0.00	2.97	19.9	4.2	2.966
Total						100.00	744.5	142.9	100.000

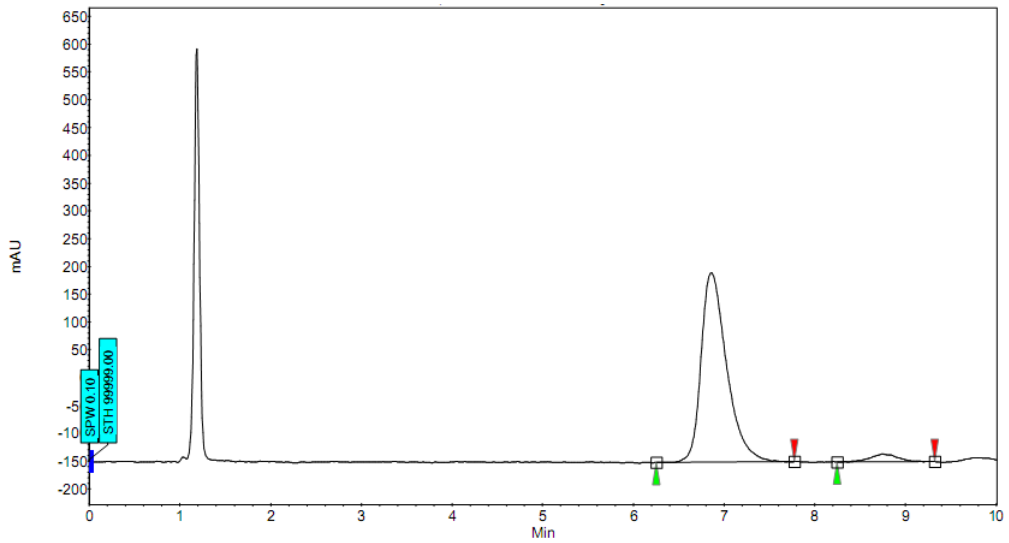
***p*-Methyl product (12)**

Racemic sample: SFC (ChiralPak AD-H, 10% MeOH, 3 mL/min, 210 nm)



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.50	6.93	7.48	0.00	50.09	101.1	29.5	50.085
2	UNKNOWN	8.12	8.69	9.34	0.00	49.91	81.5	29.4	49.915
Total						100.00	182.6	58.9	100.000

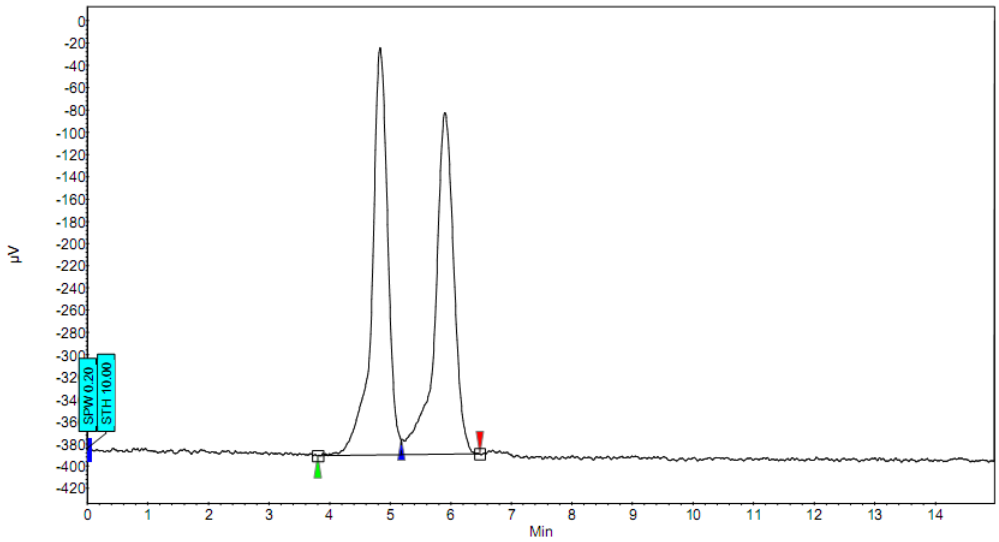
Enantioenriched sample: SFC (ChiralPak AD-H, 10% MeOH, 3 mL/min, 210 nm), **91.4% ee**



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.25	6.86	7.77	0.00	95.68	340.8	111.1	95.682
2	UNKNOWN	8.24	8.75	9.32	0.00	4.32	14.0	5.0	4.318
Total						100.00	354.8	116.1	100.000

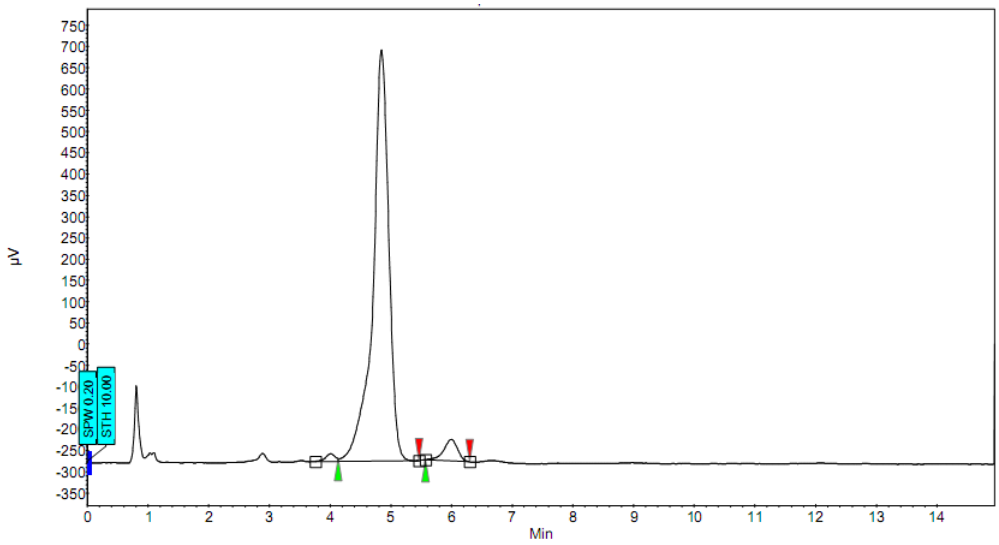
***p*-Phenyl product (14)**

Racemic sample: SFC (ChiralPak AS-H, 20% MeOH, 3 mL/min, 220 nm)



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.80	4.83	5.18	0.00	50.24	366.0	111.6	50.236
2	UNKNOWN	5.18	5.90	6.47	0.00	49.76	306.8	110.6	49.764
Total						100.00	672.8	222.2	100.000

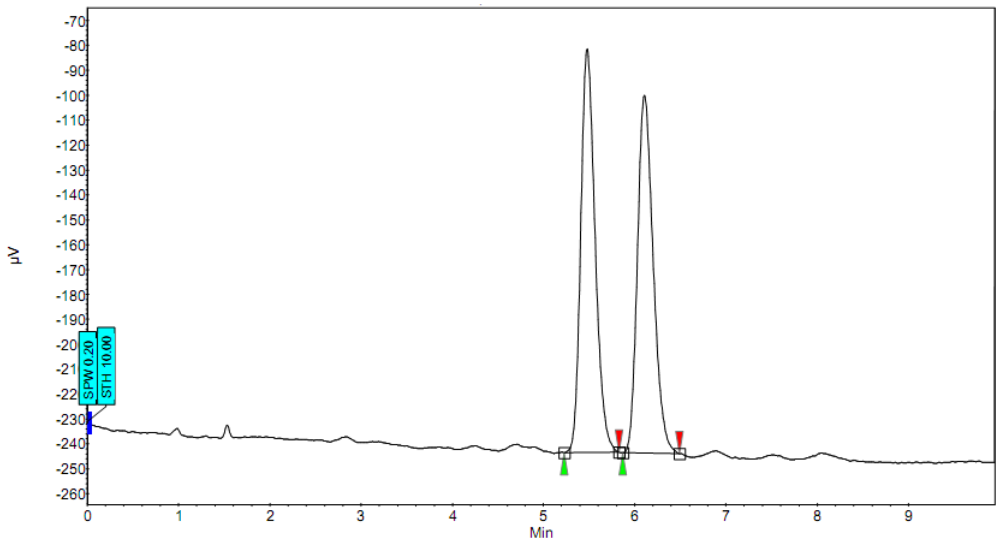
Enantioenriched sample: SFC (ChiralPak AS-H, 20% MeOH, 3 mL/min, 220 nm), **91.4% ee**



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.13	4.85	5.46	0.00	95.67	965.7	292.5	95.672
2	UNKNOWN	5.57	5.99	6.30	0.00	4.33	50.3	13.2	4.328
Total						100.00	1016.0	305.7	100.000

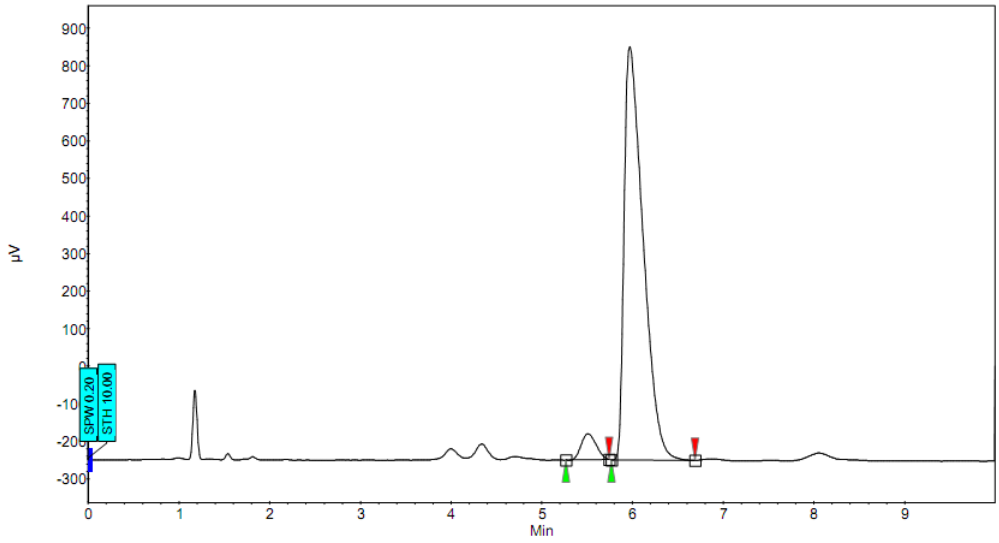
***p*-tert-Butyl product (16)**

Racemic sample: SFC (ChiralCel OD-H, 10% MeOH, 3 mL/min, 225 nm)



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.23	5.48	5.83	0.00	50.65	162.0	29.5	50.651
2	UNKNOWN	5.87	6.11	6.49	0.00	49.35	143.6	28.8	49.349
Total						100.00	305.6	58.3	100.000

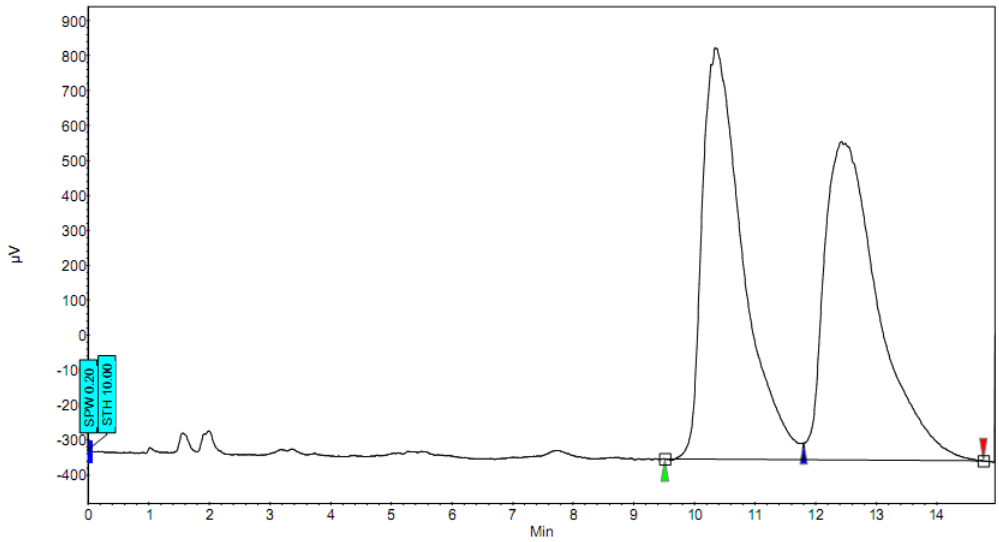
Enantioenriched sample: SFC (ChiralCel OD-H, 10% MeOH, 3 mL/min, 225 nm), **90.6% ee**



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.27	5.51	5.74	0.00	4.73	69.2	13.2	4.726
2	UNKNOWN	5.77	5.97	6.69	0.00	95.27	1100.0	265.8	95.274
Total						100.00	1169.3	279.0	100.000

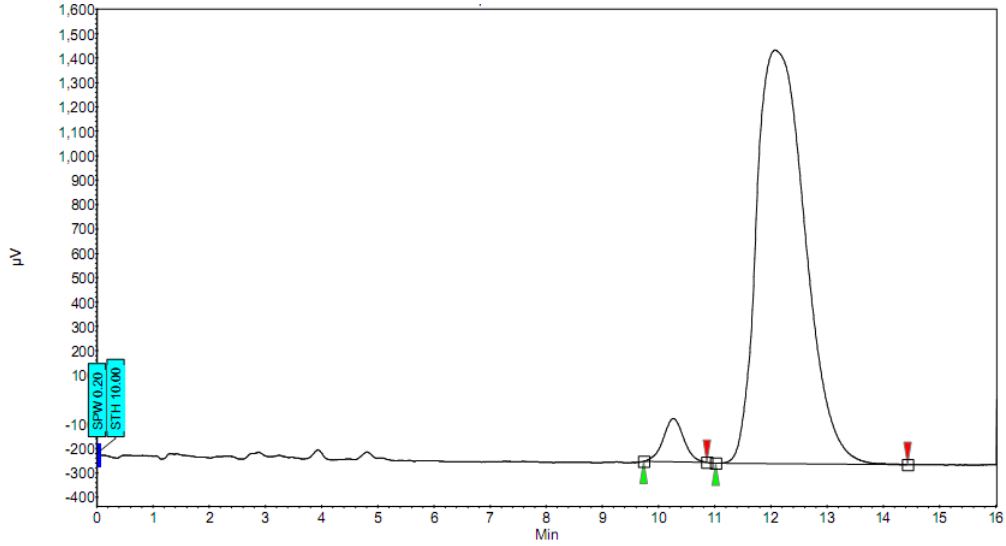
1-Naphthyl product (18)

Racemic sample: SFC (ChiralPak AD-H, 30% MeOH, 3 mL/min, 225 nm)



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	9.51	10.34	11.80	0.00	49.34	1177.5	916.0	49.343
2	UNKNOWN	11.80	12.42	14.77	0.00	50.66	910.7	940.4	50.657
Total						100.00	2088.3	1856.4	100.000

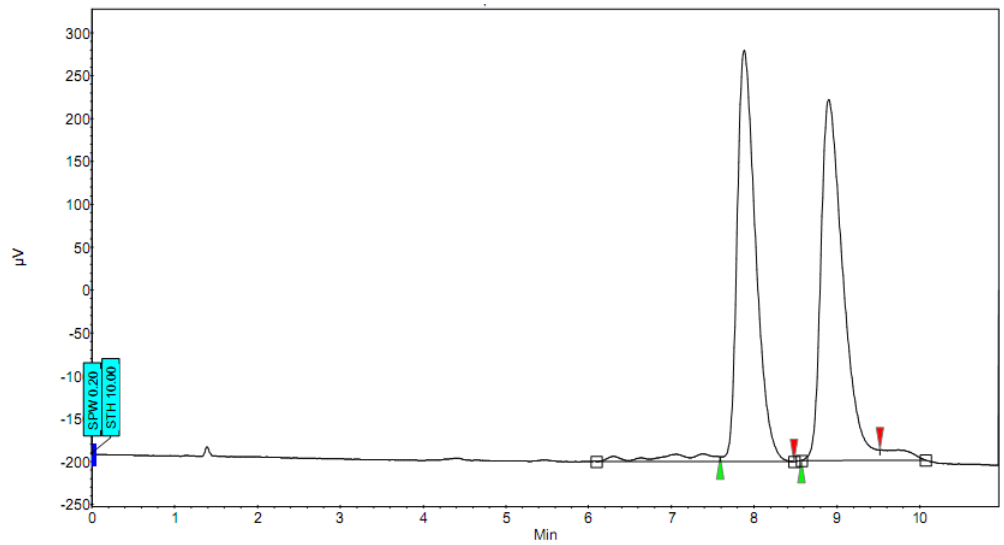
Enantioenriched sample: SFC (ChiralPak AD-H, 30% MeOH, 3 mL/min, 225 nm), **91.5% ee**



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	9.74	10.27	10.86	0.00	4.25	177.4	75.0	4.254
1	UNKNOWN	11.02	12.07	14.43	0.00	95.75	1694.4	1687.0	95.746
Total						100.00	1871.8	1761.9	100.000

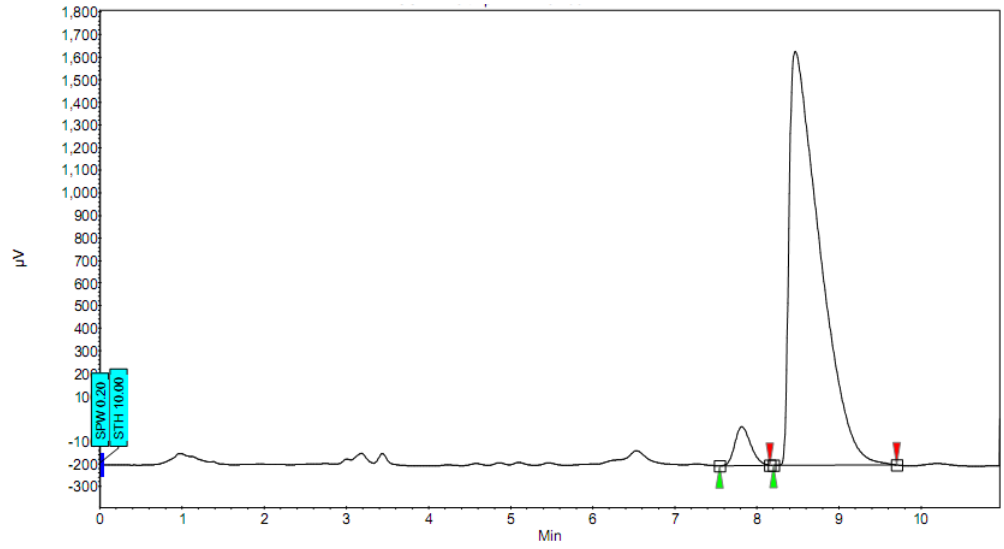
Chlorothiophene product (20)

Racemic sample: SFC (ChiralCel OD-H, 15% MeOH, 3 mL/min, 254 nm)



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	7.59	7.88	8.48	0.00	48.91	479.5	124.1	48.907
2	UNKNOWN	8.57	8.90	9.52	0.00	51.09	420.9	129.7	51.093
Total						100.00	900.5	253.8	100.000

Enantioenriched sample: SFC (ChiralCel OD-H, 15% MeOH, 3 mL/min, 254 nm), **90.7% ee**

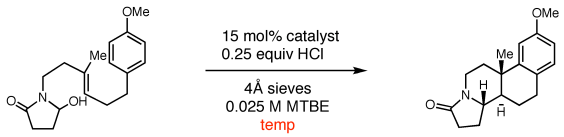


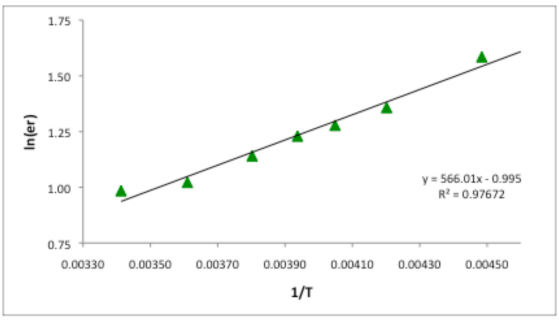
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	7.55	7.81	8.16	0.00	4.63	171.6	38.3	4.635
2	UNKNOWN	8.20	8.47	9.70	0.00	95.37	1832.0	788.3	95.365
Total						100.00	2003.5	826.6	100.000

4. Eyring Analysis of Enantioselectivity for catalysts 6, 7, and 8

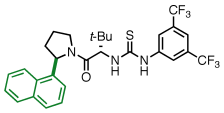
Procedure: An oven-dried vial was charged with starting material (0.033 mmol, 1.0 equiv), thiourea catalyst (0.00495 mmol, 0.15 equiv), 4Å molecular sieves (20 mg) and MTBE (1.3 mL). The flask was cooled to the indicated temperature in cryogenic bath and HCl (2 M in diethyl ether, 0.00825 mmol, 0.25 equiv) was added in one portion. The reaction was stirred for 24-48 h, and then quenched at that temperature by addition of pre-cooled NEt_3 (~0.1 mL of 20% v/v solution in EtOAc). The reaction was diluted with acetone, filtered through a pipette containing ¾ inch of silica gel, and rinsed with acetone. The solvent was removed by rotary evaporation under reduced pressure and the crude residue was purified by preparative silica gel thin layer chromatography (100% EtOAc).The enantiomeric excess was determined by chiral SFC analysis (ChiralPak AD-H, 25% MeOH, 3ml/min, t_1 = 3.80 min, t_2 = 4.81 min). The differential activation parameters were calculated using the following relationship:

ln(er) = $-\Delta\Delta H^{\ddagger}/RT + \Delta\Delta S^{\ddagger}/RT$ (where R = 1.986 cal/mol•K)



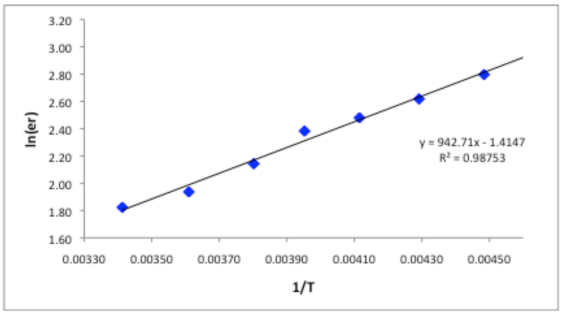


Temp °C	ee
+20	45.6
+4	47.1
–10	51.6
–19	54.8
–26	56.4
–35	59.1
–50	66.0

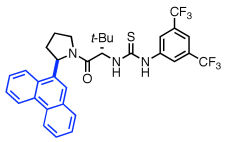


6

$\Delta\Delta H^{\ddagger}$ = –1.12 ± 0.07 kcal/mol
$\Delta\Delta S^{\ddagger}$ = –2.0 ± 0.3 cal/mol•K

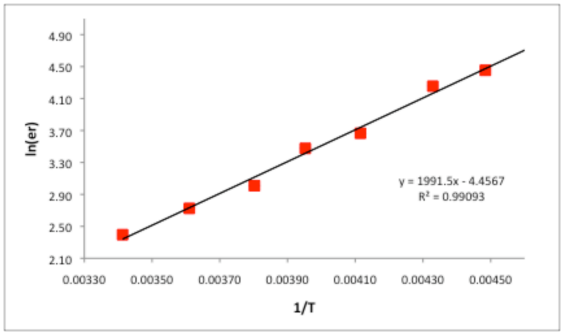


Temp °C	ee
+20	72.2
+4	74.8
–10	79.0
–20	83.1
–30	84.6
–40	86.4
–50	88.5

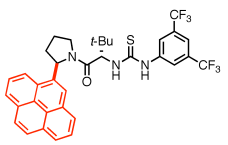


7

$\Delta\Delta H^{\ddagger}$ = –1.87 ± 0.08 kcal/mol
$\Delta\Delta S^{\ddagger}$ = –2.8 ± 0.3 cal/mol•K



Temp °C	ee
+20	83.3
+4	87.7
–10	90.6
–20	94.0
–30	95.0
–42	97.2
–50	97.7

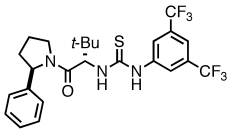


8

$\Delta\Delta H^{\ddagger}$ = –3.95 ± 0.17 kcal/mol
$\Delta\Delta S^{\ddagger}$ = –8.9 ± 0.7 cal/mol•K

4b. Correlation of arene properties with enantioselectivity for catalysts 4, 6, 7, and 8

Procedure: An oven-dried vial was charged with starting material (0.033 mmol, 1.0 equiv), thiourea catalyst (0.00495 mmol, 0.15 equiv), 4Å molecular sieves (20 mg) and MTBE (1.3 mL). The flask was cooled to –78 °C and HCl (2 M in diethyl ether, 0.00825 mmol, 0.25 equiv) was added in one portion. The reaction was then moved to a –30 °C cryogenic bath and stirred for 24-48 h, and then quenched at that temperature by addition of pre-cooled NEt_3 (~0.1 mL of 20% v/v solution in EtOAc). The reaction was diluted with acetone, filtered through a pipette containing ¾ inch of silica gel, and rinsed with acetone. The solvent was removed by rotary evaporation under reduced pressure and the crude residue was purified by preparative silica gel thin layer chromatography (100% EtOAc).The enantiomeric excess was determined by chiral SFC analysis (ChiralPak AD-H, 25% MeOH, 3ml/min, t_1 = 3.80 min, t_2 = 4.81 min).



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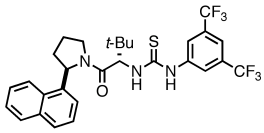

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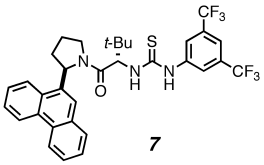

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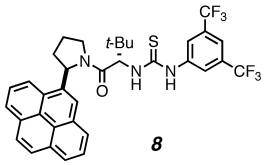

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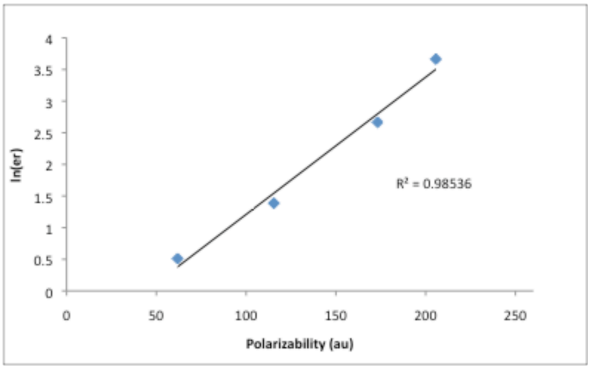
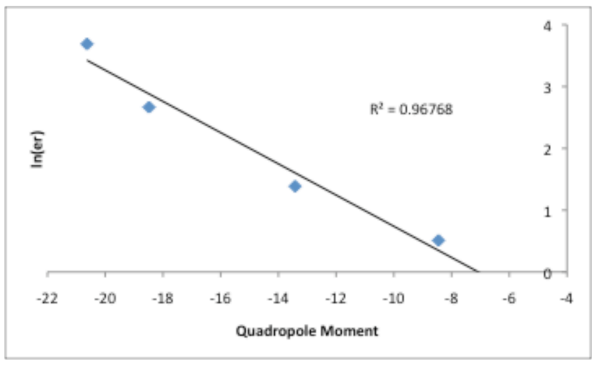


Arene	Polarizability	catalyst	ee
Benzene	61.9	**4**	25
Napthalene	115.5	**6**	60
Phenanthrene	173.2	**7**	87
Pyrene	205.7	**8**	95

Polarizabilities: Waite et al. *J. Chem. Phys.* **1982**, *77*, 2536

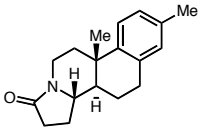


Arene	quad. mom.	catalyst	ee
Benzene	-8.45	**4**	25
Napthalene	-13.42	**6**	60
Phenanthrene	-18.48	**7**	87
Pyrene	-20.63	**8**	95

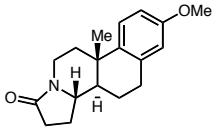
Quadropole moments: Boyd et al. *J. Phys. Chem. A* **1997,** *101,* 5374

4c. Sub-optimal Substrates

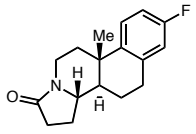
General Procedure: An oven-dried vial was charged with hydroxylactam (0.033 mmol, 1.0 equiv), thiourea catalyst **8** (0.00495 mmol, 0.15 equiv), 4Å molecular sieves (20 mg) and MTBE (1.3 mL). The flask was cooled to –78 °C and HCl (2 M in diethyl ether, 0.00825 mmol, 0.25 equiv) was added in one portion. The reaction was then moved to a cryogenic bath and stirred for 24-48 h, and then quenched by the addition of pre-cooled NEt_3 (~0.1 mL of 20% v/v solution in EtOAc). The reaction was diluted with acetone, filtered through a pipette containing ¾ inch of silica gel, and rinsed with acetone. The solvent was removed by rotary evaporation under reduced pressure and the crude residue was purified by preparative silica gel thin layer chromatography (100% EtOAc). Yields were obtained by GC analysis relative to an internal dodecane standard. The enantiomeric excess was determined by chiral SFC analysis on commercial chiral columns.



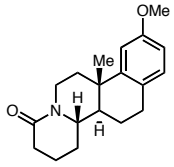
51%
77% ee
>10:1 rr



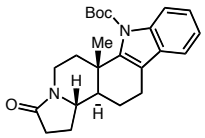
53%
79% ee
6.7:1 rr



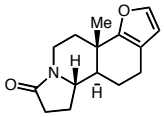
28%
92% ee
11:1 rr



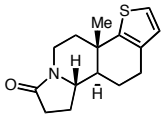
19%
82% ee



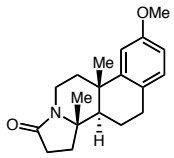
45%
37% ee



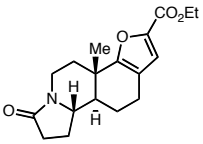
56%
59% ee



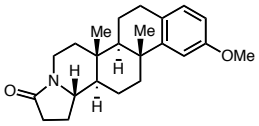
80%
80% ee
11:1 rr



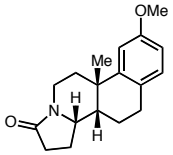
no reaction



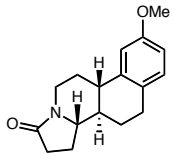
28%
83% ee



8%
89% ee



15%
21% ee



15%
64% ee