Thiourea-catalysed ring opening of episulfonium ions with indole derivatives by means of stabilising, non-covalent interactions

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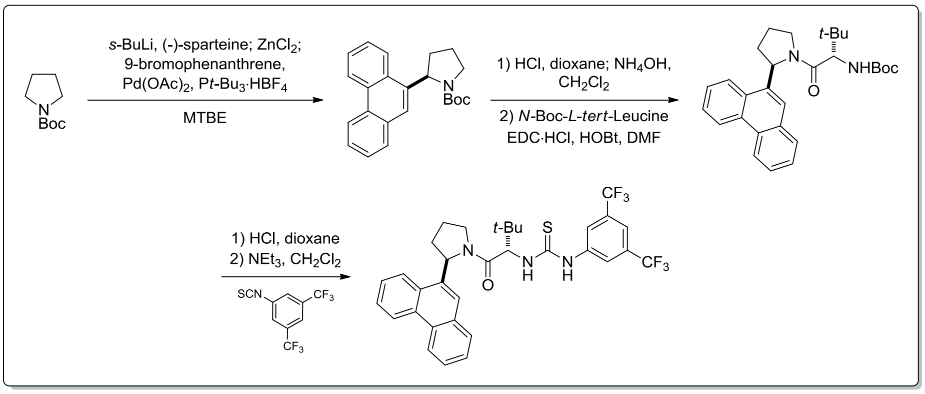
Contents

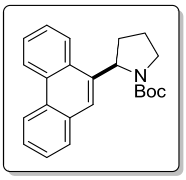
1. General information

All reactions were performed in oven-dried 1.5-dram vials unless otherwise noted. The vials 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: toluene, 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 were distilled from CaH_2 at 760 torr. *s*-Butyllithium was titrated using diphenylacetic acid as an indicator. Proton nuclear magnetic resonance (^1H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on Inova-500 (500 MHz) and Inova-600 (600 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, toluene -CH_3 = δ 2.09). 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. Chiral HPLC analysis was performed using a Shimadzu VP series instrument or an Agilent Technologies 1200 series instrument with commercial Chiralpak columns.

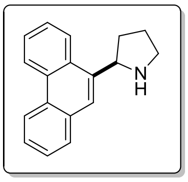
Abbreviations: Boc – *tert*-butyl carbamate, *s*-BuLi – *sec*-butyllithium, DCM – dichloromethane, EDC – 1-(3-(dimethyl-amino)propyl)-3-ethyl-carbodiimide hydrochloride, EtOAc – ethyl acetate, HOBt – 1-hydroxybenzotriazole, MeOH – methanol, MTBE – *tert*-butylmethyl ether, NBSA – nitrobenzenesulfonic acid, NEt_3 – triethylamine, *i*-PrOH – isopropyl alcohol, THF – tetrahydrofuran.

2. Preparation and characterization of thiourea catalysts 3e, 3g and 4e

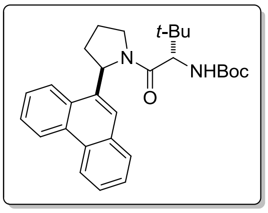




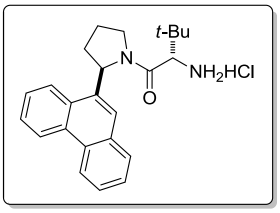
***N*-Boc-(*R*)-2-(9-phenanthryl)pyrrolidine** According to the procedure of Campos, *N*-Boc-pyrrolidine (0.75 mL, 4.3 mmol) and (–)-sparteine (0.98 mL, 4.3 mmol) were dissolved in MTBE (10 mL) and the resulting solution was cooled to –78 °C.[1] To this solution *s*-BuLi (1.4 M in cyclohexane, 3.1 mL, 4.3 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, 4.3 mL, 4.3 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, 9-bromophenanthrene (1.00 g, 3.9 mmol) was added, followed by $Pd(OAc)_2$ (47.0 mg, 0.21 mmol) and P*t*-Bu$_3$ ·HBF_4 (69.6 mg, 0.24 mmol) in one portion. The reaction was stirred for 28 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 yellow solid (0.70 g, 52%). IR (Film) 2974, 1689 (s), 1390 (s)1248, 1162 (s), 1121, 907, 725 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, exists as rotamers, resonances of the minor rotamer are shown with *) δ = 8.80 - 8.74 (m, 1H), 8.69 (d, *J*=7.8 Hz, 1H), 8.08 (d, *J*=7.3 Hz, 1H), 7.87 (d, *J*=7.8 Hz, 1H), 7.72 - 7.59 (m, 4H), 7.52 - 7.47 (m, 1H), 5.81* (d, *J*=7.8 Hz, 0.3H), 5.67 (d, *J*=7.8 Hz, 0.7H), 3.93 - 3.88 (m, 0.7H), 3.85* (m, 0.3H), 3.75 - 3.71 (m, 0.7H), 2.63 - 2.69* (m, 0.3H), 2.55 - 2.49 (m, 1H), 2.04 - 1.91 (m, 3H), 1.55* (s, 3H), 1.17 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.7, 137.4, 131.4, 130.8, 129.7, 128.4, 126.7, 126.4, 126.2, 126.0, 124.0, 123.6, 123.3, 122.3, 122.2, 79.2, 58.3, 47.3, 46.9, 33.7, 32.8, 28.5, 28.1, 23.4, 22.8; MS (ESI-APCI) exact mass calculated for [M+Na] ($C_{23}H_{25}NNaO_2$) requires *m/z* 370.2, found *m/z* 370.1; $[\alpha]_D^{24}$ = +141.8 (c = 1.0, CH_2Cl_2).



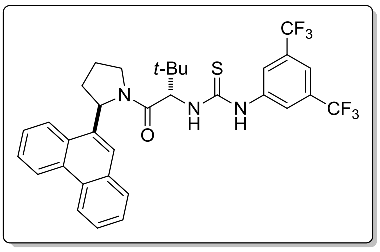
(*R*)-2-(phenanthren-9-yl)pyrrolidine. To *N*-Boc-(*R*)-2-(9-phenanthryl)pyrrolidine (0.70 g, 2.0 mmol) was added HCl (4 M in dioxane, 6 mL). The reaction mixture was stirred at room temperature for 2 h, then diluted with EtOAc (ca. 10 mL), and quenched with a mixture of water (10 mL) and 33% aqueous NH_4OH (5 mL). The resulting biphasic liquid was stirred for 10 min. The aqueous layer was separated and extracted with EtOAc twice. The combined organic layers were then dried over Na_2SO_4, and concentrated under vacuum in a 100 mL round bottom flask to afford (*R*)-2-(9-phenanthryl)pyrrolidine as a pale yellow gel. This crude product was used directly without further purification.



***tert*-butyl ((*S*)-3,3-dimethyl-1-oxo-1-((*R*)-2-(phenanthren-9-yl) pyrrolidin-1-yl)butan-2-yl)carbamate.** A 100 mL round bottom flask was charged with (*R*)-2-(phenanthren-9-yl)pyrrolidine (494 mg, 2.0 mmol), *N*-Boc-*L*-*tert*-Leucine (508 mg, 2.2 mmol), EDC ·HCl (420 mg, 2.2 mmol), HOBt (297 mg, 2.2 mmol) and DMF (10 mL). The solution was stirred at room temperature overnight, 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 was purified by silica gel flash chromatography to give the desired amide product as pale yellow crystals (750 mg, 83% over two steps). IR (Film) 3444, 2971, 1706 (s), 1645 (s), 1495, 1421 (s), 1365, 1245, 1164 (s), 1061, 1004, 906, 748 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, exists as rotamers, resonances of the minor rotamer are shown with *) δ = 8.86 - 8.54 (m, 2H), 8.09 (d, *J*=7.8 Hz, 1H), 7.80 (d, *J*=7.8 Hz, 1H), 7.94 - 7.49 (m, 4H), 7.33 (s, 1H), 6.43* (d, *J*=8.3 Hz, 0.2H), 6.02 (d, *J*=8.3 Hz, 0.8H), 5.25 (d, *J*=10.3 Hz, 0.8H), 5.11* (d, *J*=10.3 Hz, 0.2H), 4.56 (d, *J*=9.8 Hz, 1H), 4.39 (m, 1H), 3.95 - 3.77 (m, 1H), 2.41 (m, 1H), 2.20 - 1.95 (m, 3H), 1.68 - 1.52 (m, 9H), 1.21 - 1.05 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 170.43, 156.09, 134.90, 131.29, 131.03, 129.89, 129.49, 128.76, 128.44, 126.57, 126.35, 126.27, 126.15, 126.08, 124.62, 124.18, 123.95, 123.22, 122.43, 122.24, 122.12, 79.54, 58.56, 57.94, 48.29, 47.00, 34.78, 34.42, 33.68, 32.17, 28.45, 28.30, 26.41, 23.43, 21.55; MS (ESI-APCI) exact mass calculated for [M+Na] ($C_{29}H_{36}N_2NaO_3$) requires *m/z* 483.3, found *m/z* 483.3; $[\alpha]_D^{24}$ = +93.4 (*c* = 1.0, CH_2Cl_2).

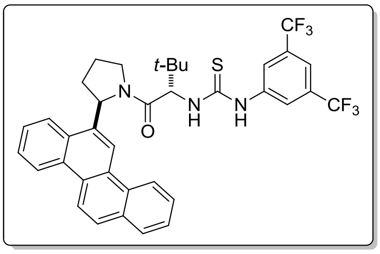


(*S*)-3,3-dimethyl-1-oxo-1-((*R*)-2-(phenanthren-9-yl)pyrrolidin-1-yl)butan-2-aminium chloride. To a solution of *tert*-butyl ((*S*)-3,3-dimethyl-1-oxo-1-((*R*)-2-(phenanthren-9-yl)pyrrolidin-1-yl) butan-2-yl) carbamate (950 mg, 2.1 mmol) at 0 ^{o}C was added HCl (4 M in dioxane, 10 mL) slowly. The reaction was warmed to room temperature and stirred until the starting material was consumed, as judged by TLC analysis (ca. 4 h). The reaction mixture was then concentrated under vacuum, yielding a yellow oil that was used directly without further purification.

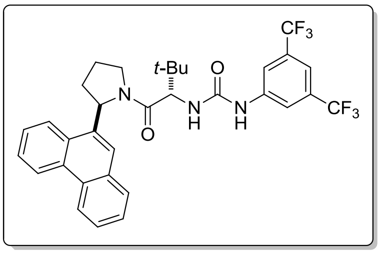


1-(3,5-bis(trifluoromethyl)phenyl)-3-((*S*)-3,3-dimethyl-1-oxo-1-((*R*)-2-(phenanthren-9-yl)pyrrolidin-1-yl)butan-2-yl)thiourea (3e). To a solution of crude (*S*)-3,3-dimethyl-1-oxo-1-((*R*)-2-(phenanthren-9-yl)pyrrolidin-1-yl)butan-2-aminium chloride (obtained from the previous step, ~2.1 mmol) in CH_2Cl_2 (14 mL) was added NEt_3 (860 μL, 6.2 mmol) dropwise. The mixture was stirred for 15 min, and 3,5-bis(trifluoromethyl)phenyl isothiocyanate (414 μL, 2.3 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 pale yellow crystals (940 mg, 72% over two steps). 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, $CHCl_3$).

Characterization data for all novel catalysts in Table 1



1-(3,5-bis(trifluoromethyl)phenyl)-3-((S)-1-((R)-2-(chrysen-6-yl)pyrrolidin-1-yl)-3,3-dimethyl-1-oxobutan-2-yl)thiourea (3g). IR (Film) 3327 (br), 2980, 1607 (s), 1525 (s), 1473, 1443, 1383 (s), 1275 (s), 1175 (s), 1133 (s), 961, 885, 758 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.32 (br. s., 1H), 8.83 - 8.76 (m, 1H), 8.70 (d, *J*=8.3 Hz, 1H), 8.54 (d, *J*=9.3 Hz, 1H), 8.21 - 8.13 (m, 1H), 8.02 - 7.83 (m, 3H), 7.77 - 7.22 (m, 8H), 6.00 (d, *J*=8.3 Hz, 1H), 5.95 (d, *J*=10.2 Hz, 1H), 4.86 (t, *J*=6.6 Hz, 1H), 4.12 - 4.00 (m, 1H), 2.53 - 2.46 (m, 1H), 2.14 - 2.01 (m, 3H), 1.18 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 181.08, 170.71, 140.56, 139.88, 135.79, 134.36, 132.30, 132.11, 131.84, 131.58, 131.31, 130.44, 129.15, 128.98, 128.49, 127.71, 127.44, 127.04, 126.52, 124.63, 124.14, 123.66, 122.63, 122.04, 121.19, 120.91, 118.12, 116.61, 62.84, 58.98, 49.41, 47.45, 36.31, 33.60, 32.88, 27.28, 27.00, 23.59, 21.30; MS (ESI-APCI) exact mass calculated for [M+Na] ($C_{37}H_{33}F_6N_3NaOS$) requires *m/z* 704.2, found *m/z* 704.2; $[\alpha]_D^{24}$ = +107.4 (c = 1.0, CH_2Cl_2).



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)urea (4e). IR (Film) 3348 (br), 2979, 1701, 1610, 1568, 1474, 1443, 1387, 1275 (s), 1174 (s), 1128 (s), 949, 879, 747 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.69 - 8.26 (m, 3H), 8.04 - 6.95 (m, 10H), 5.94 (d, *J*=7.8 Hz, 1H), 4.92 (d, *J*=9.3 Hz, 1H), 4.50 (t, *J*=8.5 Hz, 1H), 3.91 (q, *J*=8.3 Hz, 1H), 2.46 (d, *J*=6.8 Hz, 1H), 2.17 - 1.93 (m, 3H), 1.17 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 172.06, 155.68, 154.97, 141.02, 135.46, 133.96, 132.19, 131.92, 131.14, 130.82, 130.34, 129.73, 129.32, 128.57, 127.24, 126.72, 126.59, 126.44, 125.02, 124.55, 123.59, 123.42, 122.77, 122.38, 119.98, 118.33, 115.48, 58.63, 57.57, 49.04, 47.42, 35.29, 34.84, 33.38, 32.35, 26.85, 23.60, 21.50; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{33}H_{32}F_6N_3O_2$) requires *m/z* 616.2, found *m/z* 616.2; $[\alpha]_D^{23}$ = +146.3 (c = 1.0, CH_2Cl_2).

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*. **128**, 3538 (2006).

3. General procedures for thiourea-catalyzed ring opening of episulfonium ions

Method A (for condition optimization):

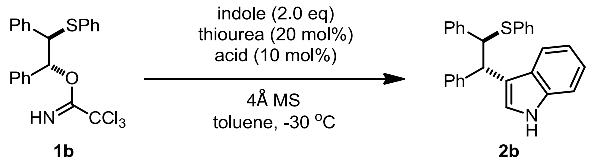
An oven-dried 1.5 dram vial was charged with substrate **1a** (0.05 mmol, 1.0 equiv), thiourea catalyst (0.0050 mmol, 0.10 equiv), indole (0.10 mmol, 2.0 equiv) and 4Å molecular sieves (25 mg, powder, activated) under an atmosphere of N_2. The vial was cooled to –30 ℃, and toluene (1 mL) was added with stirring. Once the reactants and catalyst were fully dissolved, the mixture was cooled to –78 ℃, and acid (0.0050 mmol, 0.10 equiv) was added via a 10 μL syringe (for liquid acid), or directly into the solution at once against a counterflow of N_2 (for solid acid). The resulting solution was stirred at –30 ℃ for 12 h, and NEt_3 (~10 μL) was added at –30 ℃. The resulting mixture was applied directly to a pipette column containing 4-5 cm of silica gel, and product was isolated by eluting hexanes/EtOAc (20:1 to 10:1) and solvent removal under reduced pressure.

Method B (for substrate scope):

An oven-dried 1.5 dram vial was charged with substrate **1** (0.05 mmol, 1.0 equiv), thiourea catalyst (0.0050 mmol, 0.10 equiv), nucleophile (0.10 mmol, 2.0 equiv) and 4Å molecular sieves (25 mg, powder, activated). The vial was cooled to –30 ℃, and toluene (1 mL) was added with stirring. Once the reactants and catalyst were fully dissolved, the mixture was cooled to –78 ℃, and solid 4-NBSA (0.7 mg, 0.0035 mmol, 0.07 equiv) was added at once against a counterflow of N_2. The resulting solution was stirred at –30 ℃ and the progress of the reaction was monitored by TLC.[a] When the progress of the reaction was determined to be complete (see SI-15 for reaction time), NEt_3 (~10 μL) was added at –30 ℃. The resulting mixture was applied directly to a pipette column containing 4-5 cm of silica gel, and product was isolated by eluting hexanes/EtOAc (20:1 to 10:1) and solvent removal.

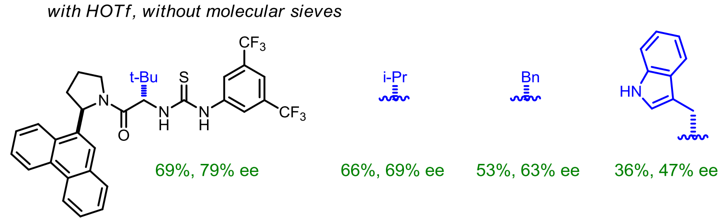
[a] Retired GC column was cut into pieces and used as the capillary tubes. A properly sized needle containing a piece of GC column inside was used to pierce the septa of the reaction vial, and an aliquot for TLC analysis was taken using the GC column and applied directly on the silica gel TLC place.

4. Catalyst structure investigations

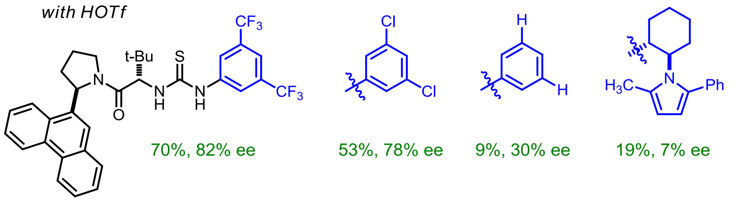


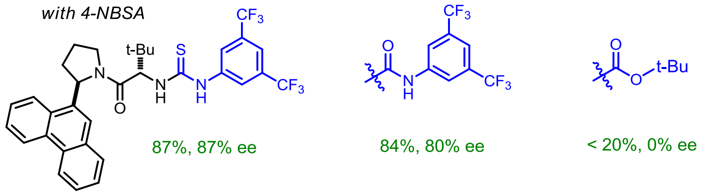
Investigation of the arylpyrrolidine moiety has been presented in the main text.

Investigation of the amino acid linker:

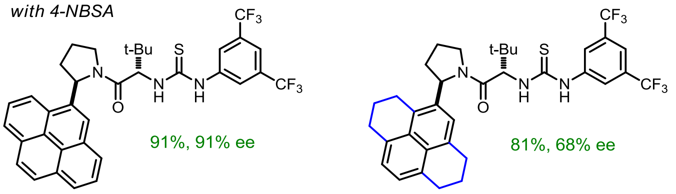


Investigation of the thiourea unit:

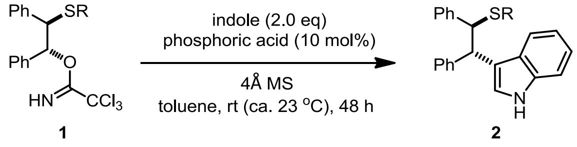


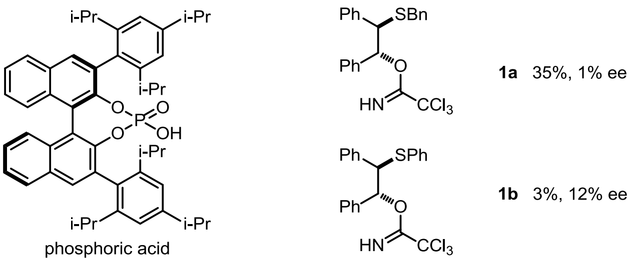


Investigation of the aryl substituent on the pyrrolidino amide portion:



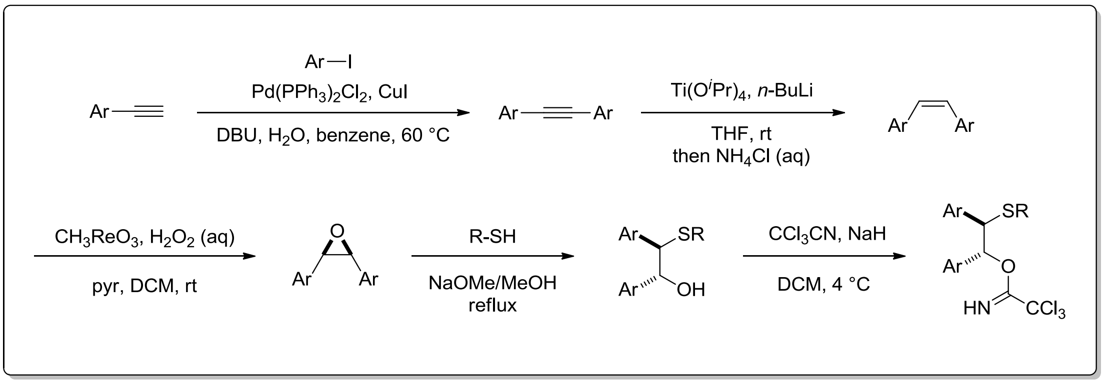
The chiral phosphoric acid that Toste and coworkers used in their episulfonium ion ring opening with alcohols does not work well in this indole alkylation reaction:





Note: at -30 °C, no desired product was observed (by TLC) after 48 h.

5. Preparation and characterization of substrates 1a-1z



Sonogashira coupling

A oven-dried round bottom flask was charged with CuI (10 mol%), $Pd(PPh_3)_2Cl_2$ (2 mol%) and flushed with N_2. Aryl iodide (1.1 equiv) in anhydrous benzene (0.2 M) was added, followed by water (0.4 equiv) and DBU (6.0 equiv) sequentially. Arylacetylene (1.0 equiv) was added at last. The flask was packaged with aluminum foil and heated to 60 ^{o}C. After TLC showed complete conversion of arylacetylene, the reaction was cooled down to room temperature, and quenched by saturate NH_4Cl (aq). After diluted with EtOAc, the mixture was stirred for 5 min before partition of the aqueous and organic layers. The aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over $NaSO_4$, concentrated, and the crude extracts were purified by silica gel column chromatography to obtain the coupling product.

Ti-mediated reduction of diarylacetylene

An oven-dried flask was charged with diarylacetylene (1.0 equiv) and flushed with N_2. THF (0.23 M) was added and the solution was cooled down to -78 ^{o}C. Freshly distilled titanium tetraisopropoxide (2.0 equiv) was added, followed by *n*-butyllithium (2.5 M in hexanes, 4 equiv) via syringe pump over 10 min. The resulting yellow/orange solution was warmed to room temperature and stirred for 2–4 h until the starting material was consumed. Saturated NH_4Cl (aq) was added slowly and carefully to quench the reaction (ice bath may be necessary). The mixture was diluted with EtOAc and stirred for 10 min. The aqueous layer was separated and extracted with EtOAc. The combined organic layers were washed with brine, dried over $NaSO_4$, concentrated, and the crude extracts were purified by silica gel column chromatography to obtain the reduction product.

Epoxidation of *cis*-diarylethene

A round bottom flask was charged with *cis*-diarylethene (1.0 equiv) and DCM (0.4 M). The mixture was cooled to 0 ^{o}C, and methylrhenium trioxide (2.5-10%, electron-deficient substrate required more rhenium catalyst) was added. Pyridine (13 mol%) and hydrogen peroxide (30% wt. aqueous solution, 1.5-5.0 equiv, electron-deficient substrate required more oxidant). The resulting yellow biphasic mixture was warmed to room temperature and stirred vigorously until TLC showed complete conversion of the alkene (usually 24-120 h). Manganese dioxide (~10 mg) was added carefully to decompose remaining hydrogen peroxide and the mixture was allowed to age for 20 min. Peroxides test sticks were use to evaluate the amount of remaining peroxide. The aqueous layer was separated and extracted with DCM. In case there was a detectable amount of peroxide residue, the combine organic layers after extraction were washed with aqueous sodium thiosulfate solution until no peroxide was detected. Otherwise, the combined organic layers were washed with brine, dried over $NaSO_4$, concentrated, and the crude extracts were purified by silica gel column chromatography to obtain the epoxidation product.

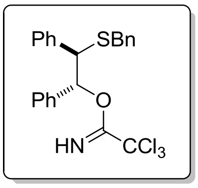
Epoxide opening with thiol

An oven-dried flask was charged with benzyl mercaptan (1.6 equiv), sodium methoxide (0.5 M in methanol, 1.5 equiv) and a refluxing condenser. The solution was heated to reflux and stirred for 10 min. After cooling down to room temperature, *cis*-diarylepoxide (1.0 equiv) was added to the resulting sodium benzylthiolate solution neat or as a stock solution in methanol (~2 M). The mixture was again brought to 60 ℃ and stirred for ca. 4 h until all starting material was consumed. The reaction was cooled down to room temperature, diluted with EtOAc, and quenched by addition of water. The aqueous layer was separated and extracted with EtOAc. The combined organic layers were washed with brine, dried over $NaSO_4$, concentrated, and the crude extracts were purified by silica gel column chromatography to obtain the sulfanyl alcohol product.

Trichloroacetimidate synthesis

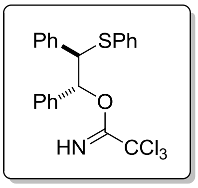
To a solution of 1,2-diaryl-2-sulfanylethanol (1.0 equiv) in DCM (0.5 M) at 0 ^{o}C was added trichloroacetonitrile (2.0 equiv) followed by sodium hydride (20 mol%). The reaction was stirred at that temperature overnight before quenched by addition of water. The resulting mixture was separated, and the 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 (hexanes/EtOAc with 1% NEt_3) to obtain the trichloroacetimidate product.

Characterization data for substrates 1a-1z



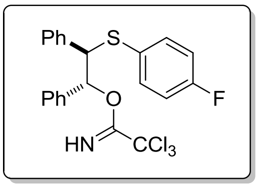
2-(benzylthio)-1,2-diphenylethyl 2,2,2-trichloroacetimidate (1a)

IR (Film): 3337, 3029, 1663 (s), 1583, 1493, 1453, 1322, 1287 (s), 1071 (s), 991, 793 (s), 696 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.41 - 7.17 (m, 11H), 7.17 - 7.01 (m, 4H), 6.14 (d, *J*=7.3 Hz, 1H), 4.18 (d, *J*=7.3 Hz, 1H), 3.72 (d, *J*=13.2 Hz, 1H), 3.57 (d, *J*=13.2 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 161.06, 137.97, 137.67, 137.21, 129.16, 129.05, 128.34, 128.11, 128.04, 127.76, 127.48, 127.04, 126.96, 83.32, 54.64, 36.16; MS (ESI-APCI) exact mass calculated for [M-(CCl_3C=NHO)] ($C_{21}H_{19}S$) requires *m/z* 303.1, found *m/z* 303.1.



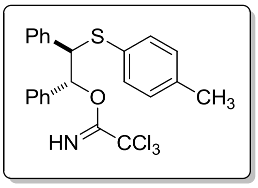
1,2-diphenyl-2-(phenylthio)ethyl 2,2,2-trichloroacetimidate (1b)

IR (Film): 3338, 3031, 1663 (s), 1583, 1479, 1453, 1322, 1288 (s), 1071 (s), 992, 835, 794 (s), 696 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.37 (br. s., 1H), 7.28 (d, *J*=7.3 Hz, 4H), 7.23 (m, 5H), 7.20 - 6.96 (m, 6H), 6.23 (d, *J*=6.8 Hz, 1H), 4.74 (d, *J*=7.3 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 161.07, 137.89, 136.78, 134.81, 131.69, 129.13, 128.69, 128.20, 127.90, 127.79, 127.43, 127.27, 126.90, 82.48, 58.82; MS (ESI-APCI) exact mass calculated for [M-(CCl_3C=NHO)] ($C_{20}H_{17}S$) requires *m/z* 289.1, found *m/z* 289.0.



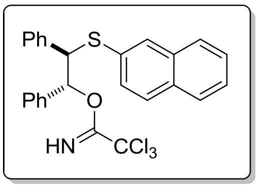
1,2-diphenyl-2-(*p*-tolylthio)ethyl 2,2,2-trichloroacetimidate (1c)

IR (Film): 3339, 3032, 1663 (s), 1588, 1489 (s), 1453, 1322, 1289 (s), 1226 (s), 1156, 1071 (s), 991, 829, 793 (s), 696 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.43 - 7.19 (m, 7H), 7.19 - 7.12 (m, 3H), 7.12 - 7.02 (m, 2H), 6.95 - 6.76 (m, 2H), 6.22 (d, *J*=7.8 Hz, 1H), 4.62 (d, *J*=7.3 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 163.34, 161.37, 161.08, 137.78, 136.87, 135.10, 135.04, 129.11, 128.25, 127.96, 127.88, 127.50, 127.25, 115.87, 115.69, 82.31, 60.05; MS (ESI-APCI) exact mass calculated for [M-(CCl_3C=NHO)] ($C_{20}H_{16}FS$) requires *m/z* 307.1, found *m/z* 307.0.



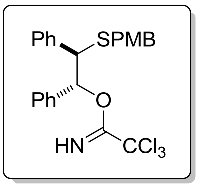
2-((4-fluorophenyl)thio)-1,2-diphenylethyl 2,2,2-trichloroacetimidate (1d)

IR (Film): 3338, 3031, 1663 (s), 1492, 1453, 1322, 1288 (s), 1073 (s), 991, 794 (s), 697 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.33 - 7.09 (m, 12H), 6.99 (d, *J*=8.3 Hz, 2H), 6.22 (d, *J*=6.8 Hz, 1H), 4.66 (d, *J*=7.3 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 161.09, 138.11, 137.18, 136.85, 132.44, 130.97, 129.51, 129.19, 128.15, 127.85, 127.77, 127.33, 82.39, 59.35, 21.04; MS (ESI-APCI) exact mass calculated for [M-(CCl_3C=NHO)] ($C_{21}H_{19}S$) requires *m/z* 303.1, found *m/z* 303.1.



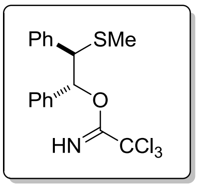
2-(naphthalen-2-ylthio)-1,2-diphenylethyl 2,2,2-trichloroacetimidate (1e)

IR (Film): 3336, 3056, 1664 (s), 1586, 1497, 1453, 1322, 1290(s), 1072 (s), 992, 794 (s), 697 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.76 (s, 2H), 7.71 - 7.59 (m, 2H), 7.52 - 7.38 (m, 2H), 7.35 (dd, *J*=1.7, 8.5 Hz, 1H), 7.31 - 7.22 (m, 5H), 7.22 - 7.09 (m, 5H), 6.29 (d, *J*=7.3 Hz, 1H), 4.86 (d, *J*=6.8 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 161.12, 137.91, 136.83, 133.53, 132.31, 132.10, 130.26, 129.13, 129.06, 128.24, 128.20, 127.98, 127.84, 127.56, 127.52, 127.31, 126.31, 125.95, 82.55, 58.78; MS (ESI-APCI) exact mass calculated for [M-(CCl_3C=NHO)] ($C_{24}H_{19}S$) requires *m/z* 339.1, found *m/z* 339.1.



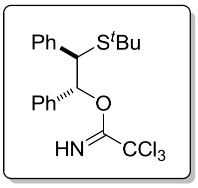
2-((4-methoxybenzyl)thio)-1,2-diphenylethyl 2,2,2-trichloroacetimidate (1f)

IR (Film): 3338, 2980 (s), 2889, 1663 (s), 1609, 1510, 1453, 1382, 1299, 1249 (s), 1174, 1073 (s), 991, 825, 794 (s), 697 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.35 - 7.17 (m, 6H), 7.17 - 7.05 (m, 6H), 6.80 (d, *J*=8.8 Hz, 2H), 6.12 (d, *J*=7.3 Hz, 1H), 4.17 (d, *J*=7.3 Hz, 1H), 3.80 (s, 3H), 3.67 (d, *J*=13.2 Hz, 1H), 3.52 (d, *J*=13.2 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 161.34, 158.85, 138.34, 137.52, 130.41, 129.45, 128.36, 128.31, 128.02, 127.72, 127.33, 114.02, 83.62, 55.53, 54.80, 35.84; MS (ESI-APCI) exact mass calculated for [M-(CCl_3C=NHO)] ($C_{22}H_{21}OS$) requires *m/z* 333.1, found *m/z* 333.1.



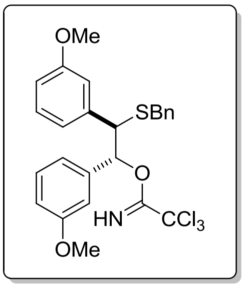
2-(methylthio)-1,2-diphenylethyl 2,2,2-trichloroacetimidate (1g)

IR (Film): 3338, 3031, 2916, 1663 (s), 1492, 1453, 1288 (s), 1072 (s), 793 (s), 696 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.35 (s, 1H), 7.37 - 7.15 (m, 10H), 6.14 (d, *J*=7.8 Hz, 1H), 4.29 (d, *J*=7.8 Hz, 1H), 1.98 (s, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 161.09, 137.67, 137.29, 129.08, 128.14, 128.11, 127.82, 127.49, 127.05, 83.25, 57.31, 15.22; MS (ESI-APCI) exact mass calculated for [M-(CCl_3C=NHO)] ($C_{15}H_{15}S$) requires *m/z* 227.1, found *m/z* 227.1.



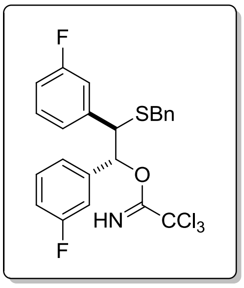
2-(*tert*-butylthio)-1,2-diphenylethyl 2,2,2-trichloroacetimidate (1h)

IR (Film): 3340, 3030, 2960, 1663 (s), 1493, 1453, 1322, 1290 (s), 1159, 1074 (s), 988, 853, 795 (s), 698 (s) cm^{-1}; ^{1}H NMR: (500 MHz, CDCl$_3$) δ 8.31 (s, 1H), 7.29 - 7.07 (m, 10H), 6.12 (d, *J*=5.4 Hz, 1H), 4.31 (d, *J*=5.4 Hz, 1H), 1.20 (s, 9H); ^{13}C NMR: (125 MHz, CDCl$_3$) δ 161.49, 141.04, 137.26, 129.79, 128.28, 128.23, 128.04, 127.90, 127.80, 127.60, 127.22, 127.11, 83.80, 52.68, 44.48, 31.46; MS (ESI-APCI) exact mass calculated for [M-(CCl$_3$C=NHO)] ($C_{20}H_{17}S$) requires *m/z* 289.1, found *m/z* 289.0.



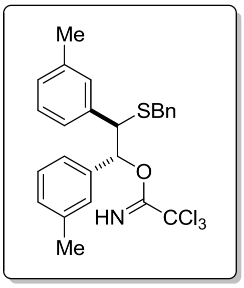
2-(benzylthio)-1,2-bis(3-methoxyphenyl)ethyl 2,2,2-trichloroacetimidate (1r)

IR (Film): 3337, 2980, 2835, 1664 (s), 1600 (s), 1491 (s), 1285, 1262 (s), 1153, 1071 (s), 994, 832, 794 (s), 695 (s) cm^{-1}; ^{1}H NMR: (500 MHz, CDCl$_3$) δ 8.35 (s, 1H), 7.40 - 7.19 (m, 5H), 7.19 - 7.02 (m, 2H), 6.86 - 6.71 (m, 4H), 6.71 - 6.55 (m, 2H), 6.09 (d, *J*=6.8 Hz, 1H), 4.12 (d, *J*=6.8 Hz, 1H), 3.70 (s, 3H), 3.71 (d, *J*=12.7 Hz, 5H), 3.66 (s, 3H), 3.58 (d, *J*=13.2 Hz, 1H); ^{13}C NMR: (125 MHz, CDCl$_3$) δ 161.00, 159.36, 159.03, 139.53, 138.73, 137.69, 129.08, 128.78, 128.33, 126.97, 121.64, 119.39, 114.40, 114.05, 113.47, 112.07, 91.45, 83.05, 55.18, 55.07, 54.67, 36.23; MS (ESI-APCI) exact mass calculated for [M-(CCl$_3$C=NHO)] ($C_{23}H_{23}O_2S$) requires *m/z* 363.1, found *m/z* 363.1.



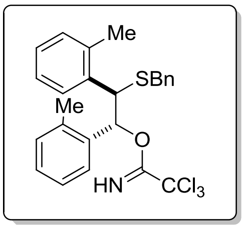
2-(benzylthio)-1,2-bis(3-fluorophenyl)ethyl 2,2,2-trichloroacetimidate (1s)

IR (Film): 3340, 3029, 1665 (s), 1614, 1591 (s), 1488 (s), 1449 (s), 1300, 1282, 1253, 1140, 1069 (s), 1000, 912, 879, 833, 794 (s), 739, 691 (s), 648 cm^{-1}; ^{1}H NMR: (500 MHz, CDCl$_3$) δ 8.38 (s, 1H), 7.38 - 7.15 (m, 7H), 7.09 - 6.85 (m, 6H), 6.08 (d, *J*=6.8 Hz, 1H), 4.10 (d, *J*=6.8 Hz, 1H), 3.72 (d, *J*=13.2 Hz, 1H), 3.56 (d, *J*=13.2 Hz, 1H); ^{13}C NMR: (125 MHz, CDCl$_3$) δ 163.55, 163.32, 161.59, 160.90, 140.45, 139.43, 137.20, 129.67, 129.61, 129.44, 129.00, 128.45, 127.18, 124.78, 122.71, 116.14, 115.96, 115.29, 115.12, 114.79, 114.62, 114.00, 113.82, 91.13, 82.12, 53.89, 36.16; MS (ESI-APCI) exact mass calculated for [M-(CCl$_3$C=NHO)] ($C_{21}H_{17}F_2S$) requires *m/z* 339.1, found *m/z* 339.1.



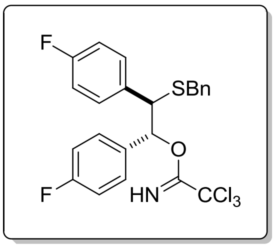
2-(benzylthio)-1,2-di-*m*-tolylethyl 2,2,2-trichloroacetimidate (1t)

IR (Film): 3338, 3027, 2919, 1663 (s), 1606, 1491, 1453, 1287 (s), 1071 (s), 988, 832, 794 (s), 697 (s) cm^{-1}; ^{1}H NMR: (500 MHz, CDCl$_3$) δ 8.32 (s, 1H), 7.38 - 7.16 (m, 5H), 7.16 - 7.05 (m, 2H), 7.05 - 6.85 (m, 6H), 6.08 (d, *J*=6.8 Hz, 1H), 4.11 (d, *J*=6.8 Hz, 1H), 3.68 (d, *J*=13.7 Hz, 1H), 3.55 (d, *J*=13.2 Hz, 1H), 2.24 (s, 3H), 2.27 (s, 3H); ^{13}C NMR: (125 MHz, CDCl$_3$) δ 161.36, 138.33, 137.52, 130.11, 129.32, 129.02, 128.55, 128.45, 128.13, 127.91, 127.86, 127.15, 126.52, 124.26, 83.62, 54.99, 36.46, 21.62, 21.56; MS (ESI-APCI) exact mass calculated for [M-(CCl$_3$C=NHO)] ($C_{23}H_{23}S$) requires *m/z* 331.2, found *m/z* 331.2.



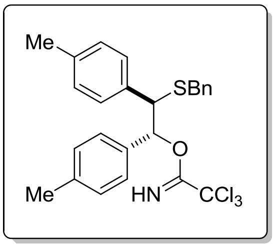
2-(benzylthio)-1,2-di-*o*-tolylethyl 2,2,2-trichloroacetimidate (1u)

IR (Film): 2980 (s), 2888, 3031, 1662 (s), 1491, 1461, 1382 (s), 1251, 1152 (s), 1073 (s), 954 (s), 829, 795, 739 cm^{-1}; ^{1}H NMR: (500 MHz, CDCl$_3$) δ 8.33 (s, 1H), 7.61 (d, *J*=7.3 Hz, 1H), 7.52 (d, *J*=7.3 Hz, 1H), 7.40 - 7.20 (m, 5H), 7.20 - 7.07 (m, 3H), 7.05 (t, *J*=7.6 Hz, 1H), 6.89 (d, *J*=7.3 Hz, 1H), 6.84 (d, *J*=7.8 Hz, 1H), 6.28 (d, *J*=9.3 Hz, 1H), 4.47 (d, *J*=9.8 Hz, 1H), 3.98 (d, *J*=13.2 Hz, 1H), 3.65 (d, *J*=13.7 Hz, 1H), 2.00 (s, 3H), 1.43 (s, 3H); ^{13}C NMR: (125 MHz, CDCl$_3$) δ 160.90, 138.33, 136.59, 136.36, 135.92, 130.08, 129.81, 129.31, 129.18, 128.42, 128.04, 127.24, 126.97, 126.78, 126.03, 125.55, 81.33, 48.59, 36.99, 19.06, 18.68; MS (ESI-APCI) exact mass calculated for [M-(CCl$_3$C=NHO)] (C$_{23}$H$_{23}$S) requires *m/z* 331.2, found *m/z* 331.2.



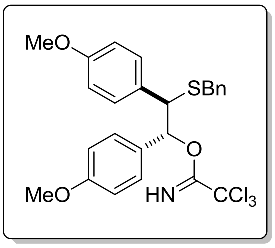
2-(benzylthio)-1,2-bis(4-fluorophenyl)ethyl 2,2,2-trichloroacetimidate (1v)

IR (Film): 3339, 1727 (s), 1665 (s), 1603 (s), 1508 (s), 1453, 1295, 1225 (s), 1158, 1071 (s), 994, 832 (s), 796 (s) cm^{-1}; ^{1}H NMR: (500 MHz, CDCl$_3$) δ 8.35 (s, 1H), 7.36 - 7.12 (m, 5H), 7.12 - 6.95 (m, 4H), 6.95 - 6.72 (m, 4H), 6.06 (d, *J*=6.8 Hz, 1H), 4.13 (d, *J*=6.8 Hz, 1H), 3.71 (d, *J*=13.7 Hz, 1H), 3.55 (d, *J*=13.7 Hz, 1H); ^{13}C NMR: (125 MHz, CDCl$_3$) δ 165.24, 163.06, 160.91, 137.37, 133.32, 132.57, 130.87, 130.80, 130.22, 128.99, 128.87, 128.81, 128.43, 127.13, 115.13, 114.96, 114.91, 114.73, 82.31, 53.54, 36.08; MS (ESI-APCI) exact mass calculated for [M-(CCl$_3$C=NHO)] (C$_{21}$H$_{17}$F$_2$S) requires *m/z* 339.1, found *m/z* 339.1.



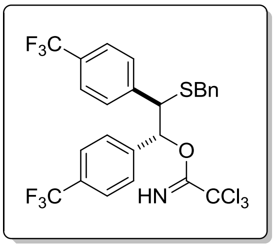
2-(benzylthio)-1,2-di-*p*-tolylethyl 2,2,2-trichloroacetimidate (1w)

IR (Film): 3338, 3027, 2920, 1664 (s), 1513, 1453, 1320, 1288 (s), 1073 (s), 985, 832, 794 (s), 741, 701, 646 (s) cm^{-1}; ^{1}H NMR: (500 MHz, CDCl$_3$) δ 8.31 (s, 1H), 7.39 - 7.16 (m, 5H), 7.16 - 6.92 (m, 8H), 6.08 (d, *J*=7.3 Hz, 1H), 4.14 (d, *J*=7.3 Hz, 1H), 3.69 (d, *J*=13.2 Hz, 1H), 3.55 (d, *J*=13.2 Hz, 1H), 2.27 (s, 3H), 2.30 (s, 3H); ^{13}C NMR: (125 MHz, CDCl$_3$) δ 161.10, 137.85, 137.69, 137.03, 134.95, 134.30, 129.08, 129.04, 128.82, 128.49, 128.31, 127.03, 126.89, 91.53, 83.32, 54.33, 36.13, 21.20, 21.12; MS (ESI-APCI) exact mass calculated for [M-(CCl$_3$C=NHO)] (C$_{23}$H$_{23}$S) requires *m/z* 331.1, found *m/z* 331.2.



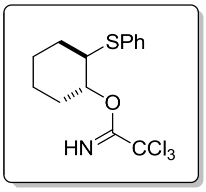
2-(benzylthio)-1,2-bis(4-methoxyphenyl)ethyl 2,2,2-trichloroacetimidate (1x)

IR (Film): 3336, 2980 (s), 1662 (s), 1633, 1610 (s), 1511 (s), 1454, 1381, 1302, 1248 (s), 1175 (s), 1072 (s), 1032 (s), 970, 829, 793 (s), cm^{-1}; ^{1}H NMR: (500 MHz, CDCl$_3$) δ 8.32 (s, 1H), 7.37 - 7.17 (m, 5H), 7.04 (d, *J*=8.8 Hz, 2H), 7.02 (d, *J*=8.8 Hz, 2H), 6.74 (d, *J*=8.8 Hz, 2H), 6.72 (d, *J*=8.8 Hz, 2H), 6.05 (d, *J*=7.3 Hz, 1H), 4.16 (d, *J*=7.3 Hz, 1H), 3.85 - 3.76 (m, 5H), 3.76 - 3.72 (m, 3H), 3.70 (d, *J*=13.2 Hz, 1H), 3.56 (d, *J*=13.2 Hz, 1H); ^{13}C NMR: (125 MHz, CDCl$_3$) δ 161.04, 159.20, 158.75, 137.84, 130.32, 129.81, 129.24, 129.04, 128.44, 128.31, 126.89, 113.42, 113.11, 91.53, 83.06, 55.14, 55.06, 53.91, 36.02; MS (ESI-APCI) exact mass calculated for [M-(CCl$_3$C=NHO)] (C$_{23}$H$_{23}$O$_2$S) requires *m/z* 363.1, found *m/z* 363.1.



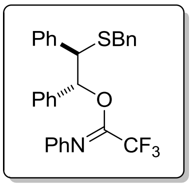
2-(benzylthio)-1,2-bis(4-(trifluoromethyl)phenyl)ethyl 2,2,2-trichloroacetimidate (1y)

IR (Film): 3342, 2980, 1667 (s), 1619, 1419, 1323 (s), 1165 (s), 1124 (s), 1067 (s), 1001, 992, 834, 796 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.48 (dd, *J*=4.4, 8.3 Hz, 4H), 7.40 - 7.19 (m, 7H), 7.14 (dd, *J*=1.7, 7.6 Hz, 2H), 6.16 (d, *J*=5.9 Hz, 1H), 4.15 (d, *J*=5.9 Hz, 1H), 3.72 (d, *J*=13.7 Hz, 1H), 3.53 (d, *J*=13.7 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 160.77, 141.83, 140.57, 136.91, 129.57, 128.94, 128.49, 127.26, 125.17, 124.92, 122.78, 90.97, 81.86, 53.65, 36.16; MS (ESI-APCI) exact mass calculated for [M-(CCl_3C=NHO)] ($C_{23}H_{17}F_6S$) requires *m/z* 439.1, found *m/z* 439.0.



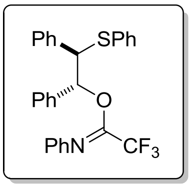
2-(benzylthio)cyclohexyl 2,2,2-trichloroacetimidate (1z)

IR (Film): 3343, 2938, 2860, 1660 (s), 1584, 1480, 1439, 1322, 1298 (s), 1073 (s), 1015, 975, 829, 794 (s), 645 cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.62 - 7.40 (m, 2H), 7.40 - 7.20 (m, 3H), 4.99 (dt, *J*=3.9, 7.8 Hz, 1H), 3.42 (dt, *J*=4.4, 8.1 Hz, 1H), 2.43 - 2.19 (m, 2H), 2.19 - 2.00 (m, 1H), 1.93 - 1.71 (m, 3H), 1.71 - 1.53 (m, 3H), 1.53 - 1.32 (m, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 162.10, 134.70, 132.44, 129.04, 127.20, 78.72, 49.16, 30.94, 28.84, 24.06, 22.80; MS (ESI-APCI) exact mass calculated for [M-(CCl_3C=NHO)] ($C_{13}H_{17}S$) requires *m/z* 191.1, found *m/z* 191.1.



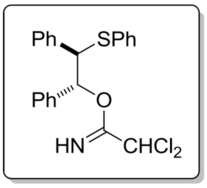
2-(benzylthio)-1,2-diphenylethyl 2,2,2-trifluoro-*N*-phenylacetimidate (1a')

IR (Film): 3031, 1707 (s), 1598, 1490, 1453, 1310, 1207 (s), 1137 (s), 1073, 1028, 968, 913, 695 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.44 - 7.20 (m, 13H), 7.20 - 6.97 (m, 5H), 6.61 (d, *J*=7.8 Hz, 2H), 6.25 (br. s., 1H), 4.21 (d, *J*=7.8 Hz, 1H), 3.76 (d, *J*=13.3 Hz, 1H), 3.62 (d, *J*=13.3 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 143.93, 137.82, 137.59, 136.97, 129.09, 129.00, 128.54, 128.41, 128.23, 128.11, 127.86, 127.55, 127.25, 127.05, 123.78, 119.33, 81.90, 54.17, 36.36; MS (ESI-APCI) exact mass calculated for [M-(CCl_3C=NHO)] ($C_{21}H_{19}S$) requires *m/z* 303.1, found *m/z* 303.1.



1,2-diphenyl-2-(phenylthio)ethyl 2,2,2-trifluoro-*N*-phenylacetimidate (1b')

IR (Film): 3032, 1706 (s), 1597, 1489, 1453, 1308, 1205 (s), 1135 (s), 1073, 1026, 964, 912, 794, 692 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.55 - 7.31 (m, 5H), 7.31 - 7.12 (m, 12H), 7.11 - 7.07 (m, 1H), 6.88 - 6.65 (m, 2H), 6.37 (br. s., 1H), 4.76 (d, *J*=7.8 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 144.20, 138.17, 136.91, 135.03, 132.34, 129.22, 129.06, 128.86, 128.53, 128.37, 128.19, 127.80, 127.77, 127.45, 124.10, 119.62, 81.36, 59.28; MS (ESI-APCI) exact mass calculated for [M-(CCl_3C=NHO)] ($C_{20}H_{17}S$) requires *m/z* 289.1, found *m/z* 289.1.



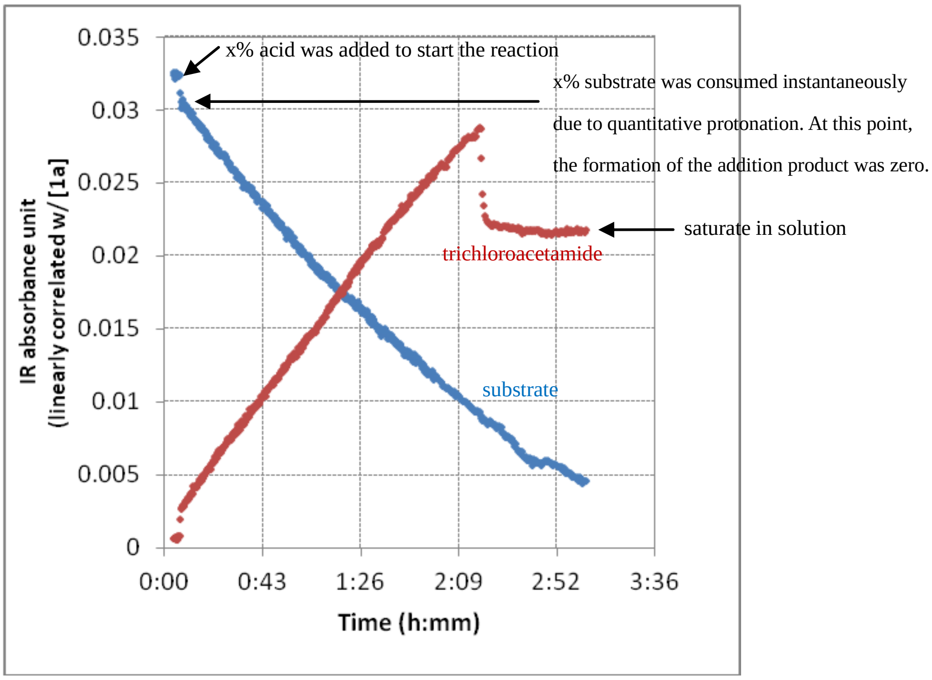
1,2-diphenyl-2-(phenylthio)ethyl 2,2-dichloroacetimidate (1b'')

IR (Film): 3323, 3031, 2980, 1667 (s), 1583, 1479, 1453, 1337, 1216, 1072 (s), 987, 798, 746, 695 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.33 (dd, *J*=1.2, 8.1 Hz, 2H), 7.29 - 7.06 (m, 13H), 6.27 (d, *J*=7.8 Hz, 1H), 5.74 (s, 1H), 4.71 (d, *J*=8.3 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 163.64, 137.70, 137.22, 135.26, 131.72, 128.96, 128.72, 128.53, 128.07, 127.85, 127.51, 127.23, 126.94, 81.76, 65.60, 58.66; MS (ESI-APCI) exact mass calculated for [M-($CCl_3C{=}NHO$)] ($C_{20}H_{17}S$) requires *m/z* 289.1, found *m/z* 289.1.

6. Data for kinetic analysis with in situ IR spectroscopy and derivation of the rate laws

Kinetic analysis by in situ infrared spectroscopy

Representative procedure: An oven-dried two-necked reaction vessel equipped with a 1/8” long stir bar was charged with indole (23.4 mg, 0.20 mmol), thiourea **3** (6.3 mg, 10.0 μmol) and molecular sieves (4Å, beads, 50 mg). It was capped with a rubber septum, and anhydrous toluene (1.5 mL) was added to dissolve the reactants. The vessel was then attached to an in situ infrared (IR) spectroscopy probe that had been dried with a heat gun. An ice bath was applied to cool the reaction mixture down to 0 ℃ with stirring, and a background IR spectrum was collected (256 scans) after 5 min. Continuous data collection was started (4 spectra/min, 50 scans/spectrum) at 0 ℃. A freshly prepared stock solution of **1a** (44.6 mg, 0.10 mmol) in toluene (0.5 mL) was added by syringe to the vessel. When the IR absorbance of the trichloroacetimidate C=N bond (height to two-point baseline, 1670 cm^{-1} to 1698/1648 cm^{-1}) had become level (ca. 3 min). A freshly prepared stock solution of 4-NBSA (4 μL of a solution of 101.6 mg 4-NBSA in 1 mL THF, 2.0 μmol) was added to start the reaction. The reaction was monitored until the absorbance of **1a** at 1670 cm^{-1} had become level or, in several cases when the reaction was slow ($t_{1/2}$ > 10 hours), until the absorbance of **1a** had reached < 30% of its initial value.

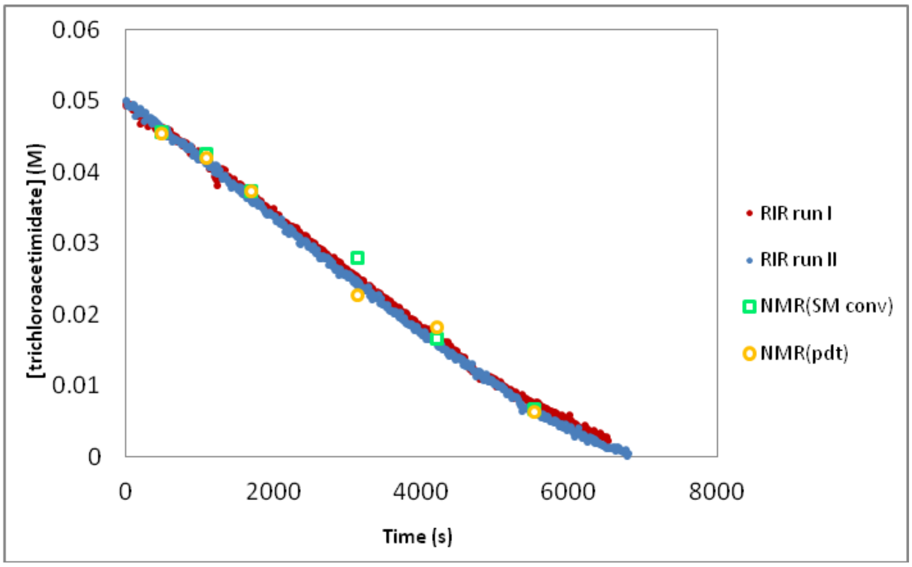


The trichloroacetamide (a by-product of the reaction) C=O bond appeared as a doublet peak (1745 and 1733 cm^{-1}) close to the monitored **1a** absorbance on all the spectrums collected after the reaction was started. Due to the partial solubility of trichloroacetamide in toluene at 0 ℃, it usually reached saturation point (at ca. 50% conversion), went supersaturated, and finally precipitated from the solution and became leveled at the saturation point (usually at ca. 60-80% conversion, depending on the rate of the reaction). The resulted IR spectrum after this by-product precipitation could be relatively messy and the absorbance of the **1a** trichloroacetimidate peak could be influenced in some cases. In order to obtain accurate data information, the reaction progress after precipitation of the amide by-product was disposed during data analysis.

After 4-NBSA was added to the reaction mixture, an immediate decrease of the monitored acetimidate absorbance and a concurrent increase of the amide by-product peak were observed, and the amount of decrease/increase, after converted to the concentration change by the beers law plot, is equivalent to the amount of acid added. This shows that after acid addition, **1a** is immediately quantitatively protonated and forms the epi-sulfonium ion and trichloroacetamide. If this step is prior to the rate limiting process (this is proved later by different access experiments, see data analysis below), at the point when x% **1a** was consumed (x% = the amount of 4-NBSA added), the formation of the desired addition product is about zero. Therefore, when data was analyzed, the first x% conversion of **1a** was not considered as part of the reaction progress, and the "0% conversion point" and "zero time point" was placed at [**1a**] = (1-x%)•[**1a**]$_{\text{initial}}$.

Data under steady state conditions (5–60% conversion) were used in the kinetic analysis. Acid-catalyzed addition reaction (i.e., racemic background reaction) does not contribute substantially to the overall reaction rate under thiourea-catalyzed conditions; the initial rate of the racemic background reaction is ~2% of the initial rate of the asymmetric reaction. The enantiomeric excess of the reaction under the standard in situ IR condition was 80-85%.

The figure below depicts a representative plot of [trichloroacetimidate (**1a**)] versus time. The red and blue data points are two independent ReactIR (RIR) reaction progress monitoring at the same condition (except that RIR run II also had added dibromomethane as NMR internal standard). The green and orange data points are ^{1}H NMR analysis of RIR run II by taking aliquots at certain time points to validate that the RIR data represents both consumption of starting material (SM) and accumulation of product **2a** (pdt) (the orange data points were applied to equation: conversion(M) = [**1a**]$_{\text{initial}}$ – yield(M), so that it could overlay with the RIR data). Concentration versus time data were converted to rate versus concentration data by analytical differentiation of a seventh-order polynomial fit to the concentration versus time data using methods described in the following reference: Zuend, S. J. & Jacobsen E. N. *J. Am. Chem. Soc.* **129**, 15872–15883 (2007).



Rates of epi-sulfonium ring opening with indole catalyzed by 4-NBSA at different [**1a**], [indole] and [4-NBSA]. Rates are provided in M s^{-1} (x 10^{-6}).

Reaction condition: [**1a**]$_i$ = 0.050 M, [indole]$_i$ = 0.10 M.

conversion of **1a** (%)	[**1a**] (M)	[indole] (M)	[4-NBSA]$_T$ = 2.5 mM	[4-NBSA]$_T$ = 5.0 mM	[4-NBSA]$_T$ = 7.5 mM	[4-NBSA]$_T$ = 10 mM
10	0.045	0.095	4.84	7.24	9.32	12.6
20	0.040	0.090	4.53	7.93	9.29	13.4
30	0.035	0.085	4.27	8.11	9.30	13.6
40	0.030	0.080	4.04	7.98	9.26	13.4
50	0.025	0.075	3.82	7.96	9.05	13.2
60	0.020	0.070	3.54	8.08	8.67	12.8
70	0.015	0.065	3.15	7.86	8.31	12.5

Reaction condition: [**1a**]$_i$ = 0.050 M, [4-NBSA]$_T$ = 0.0050 M.

conversion of **1a** (%)	[**1a**] (M)	[indole]$_i$ = 0.050 M	[indole]$_i$ = 0.10 M	[indole]$_i$ = 0.20 M	[indole]$_i$ = 0.30 M
10	0.045	3.48	6.65	16.1	26.1
20	0.040	3.19	6.55	17.8	30.7
30	0.035	2.94	6.30	18.5	33.7
40	0.030	2.70	6.18	18.7	35.1
50	0.025	2.45	6.13	19.1	36.1
60	0.020	2.18	5.94	19.9	37.6
70	0.015	1.84	5.49	20.3	39.5

Reaction condition: [indole]$_i$ = 0.10 M, [4-NBSA]$_T$ = 0.0050 M.

conversion of indole (%)	[indole] (M)	[**1a**]$_i$ = 0.050 M	[**1a**]$_i$ = 0.025 M
5	0.095	6.65	5.19
10	0.090	6.55	5.20
15	0.085	6.30	4.95
20	0.080	6.18	
25	0.075	6.13	
30	0.070	5.94	
35	0.065	5.49	

Reaction condition: [**1a**]$_i$ = 0.050 M, [indole]$_i$ = 0.10 M, [4-NBSA]$_T$ = 0.0050 M.

conversion of **1a** (%)	[indole] (M)	[TCAA]$_i$ = 0[a]	[TCAA]$_i$ = 0.010 M	[TCAA]$_i$ = ca. 0.025 M[b]
10	0.045	6.68	8.67	10.5
20	0.040	7.21	8.91	9.87
30	0.035	7.36	9.04	8.94
40	0.030	7.14	8.76	8.01
50	0.025	6.82	8.09	7.23

60	0.020	6.66	7.09	6.55
70	0.015	6.58	6.01	5.79

[a] TCAA = trichloroacetamide.

[b] Pre-saturated with TCAA. The saturation concentration of TCAA in toluene at 0 ℃ is ca. 0.025 M.

Rates of epi-sulfonium opening with indole catalyzed by 4-NBSA and chiral thiourea **3e** at different [indole], [4-NBSA] and [**3e**]. Rates are provided in M s^{-1} (x 10^{-5}).

Reaction condition: [**1a**]$_\mathrm{i}$ = 0.050 M, [indole]$_\mathrm{i}$ = 0.10 M, [**3e**]$_\mathrm{T}$ = 0.0050 M.

conversion of **1a** (%)	[**1a**] (M)	[indole] (M)	[4-NBSA]$_\mathrm{T}$ = 0.5 mM	[4-NBSA]$_\mathrm{T}$ = 1.0 mM	[4-NBSA]$_\mathrm{T}$ = 2.5 mM	[4-NBSA]$_\mathrm{T}$ = 5.0 mM
10	0.045	0.095	2.79	6.06		
20	0.040	0.090	1.90	4.50	10.4	19.4
30	0.035	0.085	1.20	3.10	8.20	14.7
40	0.030	0.080	0.86	2.13	6.42	10.8
50	0.025	0.075	0.72	1.68	4.76	8.23
60	0.020	0.070	0.54	1.42	3.87	6.72
70	0.015	0.065	0.45	1.10	3.40	5.59

Reaction condition: [**1a**]$_\mathrm{i}$ = 0.050 M, [indole]$_\mathrm{i}$ = 0.10 M, [4-NBSA]$_\mathrm{T}$ = 0.0010 M.

conversion of **1a**(%)	[**1a**] (M)	[indole] (M)	[**3e**]$_\mathrm{T}$ = 0.5 mM	[**3e**]$_\mathrm{T}$ = 1.0 mM	[**3e**]$_\mathrm{T}$ = 2.5 mM	[**3e**]$_\mathrm{T}$ = 5.0 mM
10	0.045	0.095	0.67	1.13	3.18	6.06
20	0.040	0.090	0.41	0.71	2.16	4.50
30	0.035	0.085	0.32	0.55	1.38	3.10
40	0.030	0.080	0.26	0.39	1.00	2.13
50	0.025	0.075	0.20	0.32	0.84	1.68
60	0.020	0.070			0.62	1.42
70	0.015	0.065			0.50	1.10

Reaction condition: [**1a**]$_\mathrm{i}$ = 0.050 M, [4-NBSA]$_\mathrm{T}$ = 0.0010 M, [**3e**]$_\mathrm{T}$ = 0.0025 M.

conversion of **1a** (%)	[**1a**] (M)	[indole]$_\mathrm{i}$ = 0.050 M	[indole]$_\mathrm{i}$ = 0.10 M	[indole]$_\mathrm{i}$ = 0.15 M	[indole]$_\mathrm{i}$ = 0.20 M
10	0.045	1.57	3.18	4.48	5.96
20	0.040	0.97	2.16	3.03	3.89
30	0.035	0.56	1.38	2.08	2.66
40	0.030	0.41	1.00	1.66	2.25
50	0.025	0.26	0.84	1.35	1.91
60	0.020	0.16	0.62	1.06	1.55
70	0.015		0.50	9.23	1.40

Reaction condition: [indole]$_{\text{i}}$ = 0.10 M, [**3e**]$_{\text{T}}$ = 0.0050 M.

conversion of indole (%)	[indole] (M)	[4-NBSA]$_{\text{T}}$ = 0.0010 M		[4-NBSA]$_{\text{T}}$ = 0.0025 M	
		[**1a**]$_{\text{i}}$ = 0.050 M	[**1a**]$_{\text{i}}$ = 0.075 M	[**1a**]$_{\text{i}}$ = 0.050 M	[**1a**]$_{\text{i}}$ = 0.075 M
5	0.095	5.85	5.23		
10	0.090	4.29	3.50		
15	0.085	2.94	2.18		
20	0.080	2.05	1.63	6.81	6.15
25	0.075	1.65	1.42	5.05	4.88
30	0.070	1.40	1.08	3.95	3.76
35	0.065	1.09	0.92	3.43	3.02

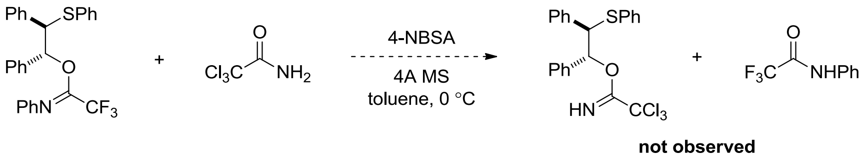
Derivation of empirical rate law

Rate dependence on starting material **1a**: 0th order – formation of epi-sulfonium ion from **1a** is quantitative. This is based on:

1) Kinetic data by in situ IR study showed that the rate of the reaction is independent on the concentration of **1a** in both racemic and asymmetric conditions.

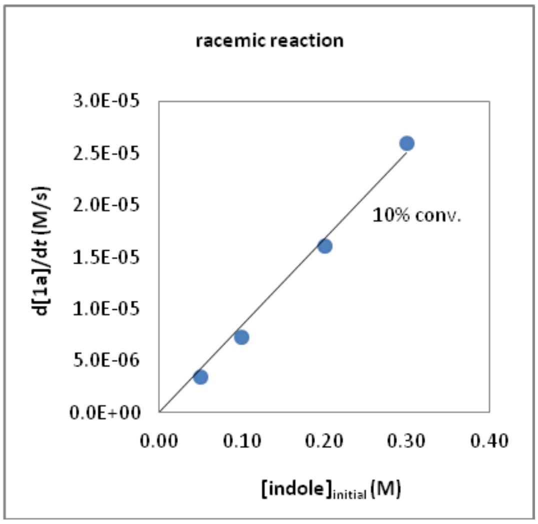
2) An inverse rate dependence on trichloroacetamide – a by-product generated during the decomposition of **1a** to form epi-sulfonium ion, was NOT observed.

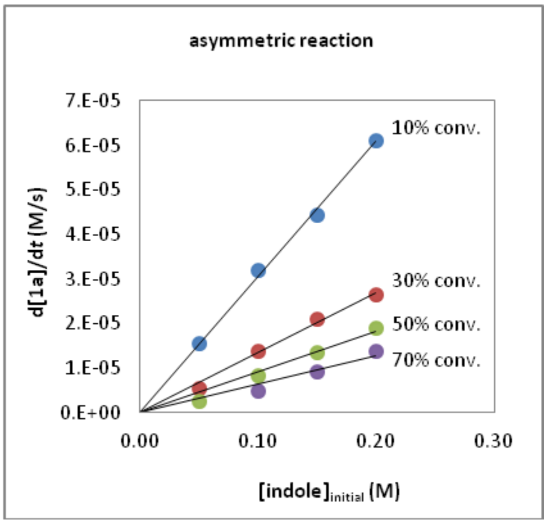
3) Treatment of **1a’** with trichloroacetamide under acid-catalyzed condition did not furnish anion-metathesis product **1a** (see equation below).



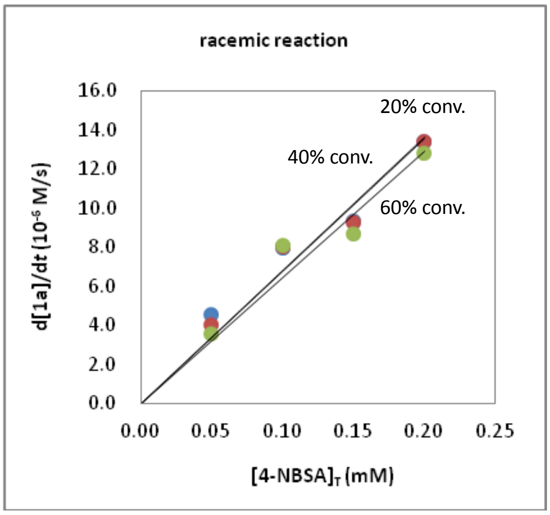
4) During in situ IR study, an immediate decrease of the monitored acetimidate absorbance and a concurrent increase of the amide by-product peak were observed after 4-NBSA was added to the reaction mixture. The amount of decrease/increase of absorbance, after converted to the concentration change by the beers law plot, is equivalent to the amount of acid added.

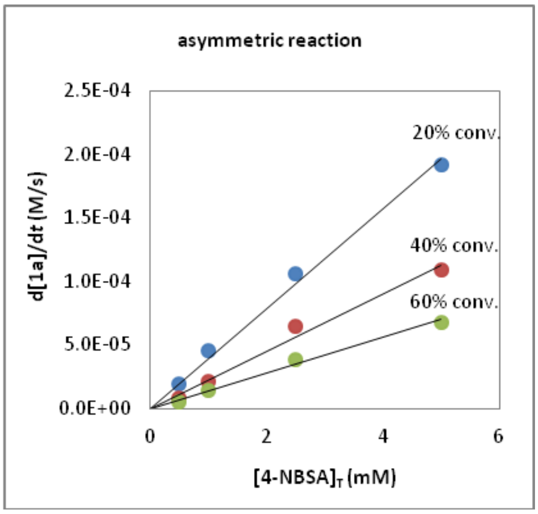
Rate dependence on indole: 1st order.

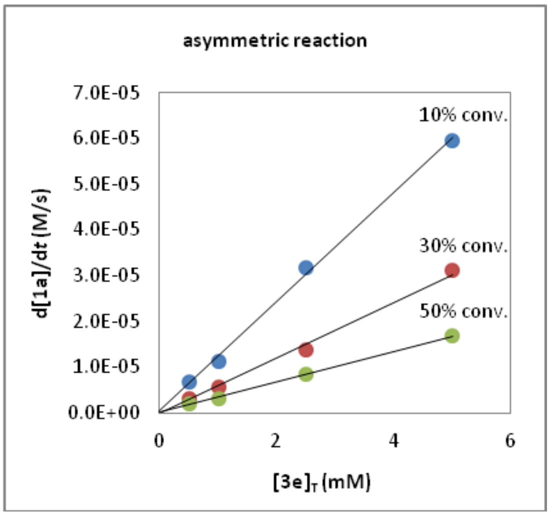




Rate dependence on acid and catalyst: 1st order.







Empirical rate laws:

For racemic reaction (catalyzed by 4-NBSA only):

$d[\mathbf{1a}]/dt = k_{rac}\,[\text{4-NBSA}]_T\,[\text{indole}]$.

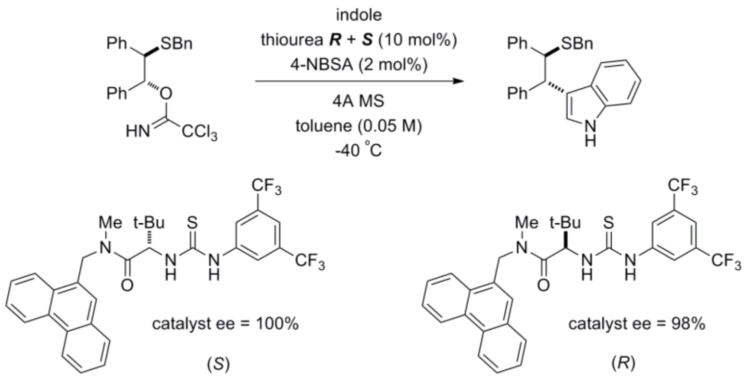
For asymmetric reaction (catalyzed by thiourea and 4-NBSA):

$d[\mathbf{1a}]/dt = k_{asym,observed}\,[\text{4-NBSA}]_T\,[\mathbf{3e}]_T\,[\text{indole}]$.

7. Non-linear effect study

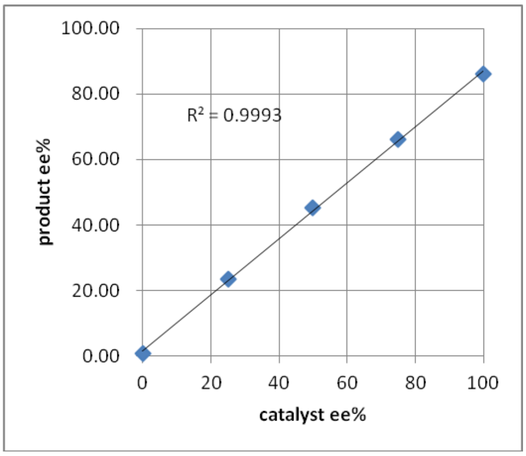
General information:

Non-linear effect study was conducted with a thiourea catalyst structurally analogues to **3e**, shown in the scheme below. This catalyst gives 85% ee under the model reaction condition (when **3e** provides 93% ee). The similar levels of stereo-induction and analogues structures led us to assume that the two catalysts induce selectivity in the same manner. The non-linear effect study was done at –40 ℃, a decreased temperature compared to the model condition in order to further exclude the effect of any background reaction. Otherwise, the procedure can refer to section 5.



cat ee% (*R*)[a]	pdt ee%[b]
0	0.67
25	23.63
50	45.40
75	66.14
100	86.18

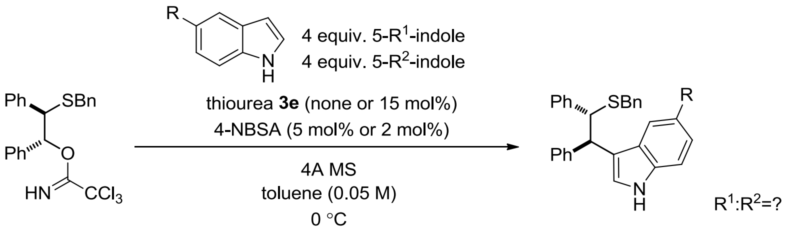
[a] The *R* and *S* catalysts are premixed with a ratio between 1:1 and 1:0, and the catalyst ee was calculated assuming that both enantiomeric catalysts have perfect ee (100%). [b] product ee was determined by HPLC, and the values presented are the average of the readouts at three different UV wavelength (210, 230 and 250 nm).



Conclusion: No non-linear effect was seen. This is consistent with the reaction transition state involving only one molecule of the thiourea catalyst.

8. Date for linear free energy relationship study with Mayr's reactivity parameters

General procedure for competition experiments:



An oven-dried vial was charged with **1a** (11.6 mg, 0.025 mmol), thiourea catalyst (none for a racemic reaction or, 2.4 mg, 3.75 μmol of **3e** for an asymmetric reaction), nucleophile I (0.10 mmol, 4.0 equiv), nucleophile II (0.10 mmol, 4.0 equiv) and 4Å molecular sieves (15 mg, powder, activated). The vial was cooled to –78 ℃, and toluene was added with stirring. The vial was then placed in a 0 ℃ ice bath until all the reactants and catalyst were fully dissolved. 4-NBSA (freshly prepared stock solution, 0.5 M in THF, 10 μL, 5 mol% for a racemic reaction or, 4 μL, 2 mol% for an asymmetric reaction) was added to the solution via syringe. The reaction mixture was stirred at 0 ℃ for 4 h, and then quenched at the same temperature by addition of NEt_3 (~10 μL). The reaction was filtered through a short silica plug, and the plug was washed with small amounts of toluene and DCM sequentially. The combined organic solutions were concentrated under vacuum to yield the crude products mixture, which was dissolved in $CDCl_3$, and analyzed with ^{1}H NMR spectroscopy (the two adjacent benzylic protons α and β to the indole ring and the methylene protons in the benzylsulfanyl group were integrated, if well resolved from the rest of the NMR resonances). The relative rate constant k_{rel} for 5-substituted indoles are with respect to the rate constant of *H*-indole ($k_{rel} = 1$). The absolute rate constant k (k_{rac} and k_{asym}) for 5-R-indoles are calculated with the equation: $k = k_{rel} \times k_{H\text{-indole}}$, assuming that the kinetic profiles of substituted indoles are the same as *H*-indole.

General procedure for in situ IR study: Followed the procedure described in section 6. Rates of indole derivatives were measured independently, and the relative rate was calculated with reference to indole.

N is the Mayr nucleophilicity parameter, s_N is the nucleophile-specific parameter, both obtained from the Mayr database of reactivity parameter:
http://www.cup.uni-muenchen.de/oc/mayr/reaktionsdatenbank/

Based on equation: $\log(k) = s_E s_N(N+E)$, a LFER is established between the logarithm of the rates of indole derivatives – $\log(k_{rac})$, and the Mayr nucleophilicity parameter – $s_N N$ (equivalent to $\log(k)$ of reactions between these indole derivatives and an electrophile with $E = 0$, e.g. dimethoxybenzhydrylium ion). For a reference describing the use of the equation, see: Phan, T. B., Breugst, M. & Mayr, H. *Angew. Chem., Int. Ed.* **45**, 3869-3874 (2006).

For the racemic background reaction:

R	***N***	s_N	$s_N N$	$k_{rel} = k_{R\text{-indole}}/k_{indole}$ [a]				**log**k_{rel}	k_{rel} [b] **(RIR)**
				I	**II**	**III**	**average**		
MeO	6.22	1.12	6.97	1.97	1.94	1.79	1.90	0.29	1.92
Me	6.00	1.10	6.60	1.44	1.32	-	1.38	0.15	-
H	5.55	1.09	6.05	1	-	-	1	0	1
F	-	-	-	0.505	0.532	0.505	0.514	-0.30	-
Cl	4.42	1.10	4.86	0.342	-	-	0.342	-0.47	-
Br	4.38	1.10	4.82	0.348	-	-	0.348	-0.46	-

[a] Obtained from competition experiments.

[b] Obtained from independent in situ IR study, and standardized with $k_{rel,indole} = 1$.

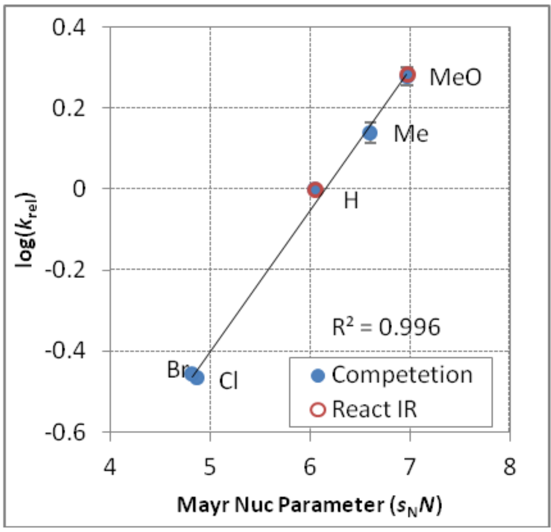
This decent correlation ($R^2 = 0.996$) between $\log(k)$ and $s_N N$ allowed us to calculate the electrophilicity parameter for the *S*-benzyl-1,2-diphenylepisulfonium ion. According to equation: $\log(k) = s_E s_N(N+E)$, the slope of the plot = $s_E = 0.36$. Given $\log(k) = 2.1$ for indole ($s_N N = 6.05$), one can figure out that the electrophilicity parameter $E = -10.3$.

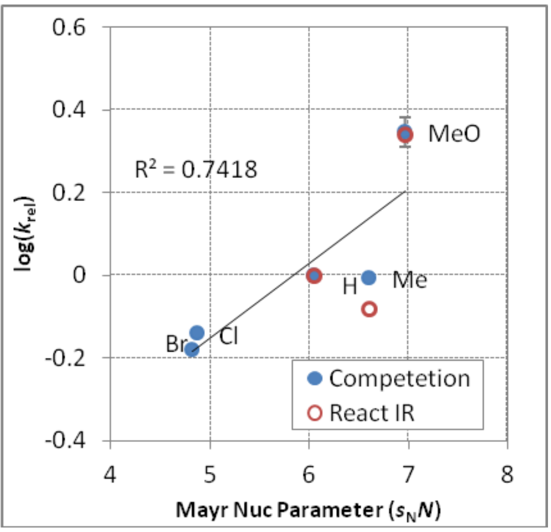
For thiourea **5**-catalyzed asymmetric reaction:

R	***N***	s_N	$s_N N$	$k_{rel} = k_{R\text{-}indole}/k_{indole}$ [a]				$\log k_{rel}$	k_{rel} [b] (RIR)
				I	**II**	**III**	**average**		
MeO	6.22	1.12	6.97	2.23	2.41	2.02	2.22	0.35	2.19
Me	6.00	1.10	6.60	0.98	0.99	-	0.98	0.003	0.83
H	5.55	1.09	6.05	1	-	-	1	0	1
F	-	-	-	1.01	1.04	0.94	1.00	0.008	1.16
Cl	4.42	1.10	4.86	0.73	-	-	0.73	-0.14	-
Br	4.38	1.10	4.82	0.66	-	-	0.66	-0.18	0.70

[a] Obtained from competition experiments.

[b] Obtained from independent in situ IR study, and standardized with $k_{rel,indole} = 1$.

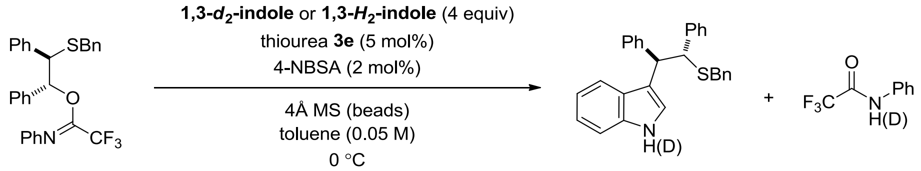




9. Data for kinetic isotope effect study

General information:

The KIE analysis was conducted using in situ IR spectroscopy with 1,3-d_2-indole/1,3-h_2-indole and a modified substrate **1e** bearing an *N*-phenyltrifluoroacetimidate leaving group (**1a’**). This was to avoid rapid H-D exchange at the 3-position of indole in the presence of other proton sources.



The KIE study was performed with in situ IR spectroscopy. 1,3-d_2-indole was synthesized according to the procedure below, and the deuterium incorporation ratio were determined by ^{1}H NMR to be 96% (position 3) and >99% (position 1). A modified substrate **1a** with *N*-phenyltrifluoroacetimidate was used to avoid rapid isotope scrambling between the acidic protons on substrate **1a** and the deuteron at 3-position of 1,3-d_2-indole catalyzed by Brønsted acid. It has been demonstrated that the acetimidate substrate undergoes quantitative protonation and decomposition to form epi-sulfonium 4-nitrobenzene-sulfonate, and thereby the structure of the leaving group does not affect the reaction kinetic profile. Therefore, the KIE of the modified **1a** can represent that of **1a** under the same condition. Although the other proton sources (thiourea and 4-NBSA) were not precluded, a large excess of 1,3-d_2-indole (4 equiv) and a relatively small amount of thiourea and acid (5 mol% and 2 mol%, respectively) were used to make sure the total isotopic concentration of exchangeable H was less than 3%.

Procedure of KIE study with in situ IR monitoring:

An oven-dried two-necked reaction vessel equipped with an 1/8” long stir bar was charged with indole (35.1 mg, 0.30 mmol) or 1,3-d_2-indole (35.7 mg, 0.30 mmol) in a glove-box under dry nitrogen atmosphere (H_2O < 0.1 ppm), and sealed with rubber septum. Thiourea **3e** (freshly prepared stock solution 0.015 M in toluene, 667 μL, 10.0 μmol), molecular sieves (4Å, beads, 40 mg, activated) and anhydrous toluene (433 μL) were transferred into the vessel quickly under air atmosphere and the vessel was purge with dry nitrogen several times before it was attached to an in situ infrared (IR) spectroscopy probe that had been dried with a heat gun. An ice bath was applied to cool the reaction mixture down to 0 ℃ with stirring for 5 min, and a background IR spectrum was collected (256 scans). Continuous data collection was started (4 spectra/min, 50 scans/spectrum). A freshly prepared stock solution of **1a’** (36.9 mg, 0.075 mmol) in toluene (0.4 mL) was added by syringe to the vessel. When the IR absorbance of the trichloroacetimidate C=N bond (height to baseline, 1713 cm^{-1}) had become level. A freshly prepared stock solution of 4-NBSA (4 μL of a solution of 101.6 mg 4-NBSA in 1 mL THF, 2.0 μmol) was added to start the reaction. The reaction was monitored until the absorbance of **1a’** at 1670 cm^{-1} had become level. Data was processed analogous to previously described in section 6.

Kinetic isotope effect data

Rates of independent KIE reactions catalyzed by 4-NBSA and chiral thiourea **3e**. Rates are provided in M s^{-1} (x 10^{-5}). Rate data become unreliable after 40% conversion due to peak overlap, and so only data from first 40% converstion are used here.

conversion of **1a’** (%)	[**1a’**] (M)	1,3-H_2-indole		1,3-d_2-indole (exp. I)		1,3-d_2-indole (exp. II)	
		[**1a’**][a]	[amide][b]	[**1a’**]	[amide]	[**1a’**]	[amide]
15	0.043	3.66	3.84	4.30	5.00	3.60	4.34
30	0.035	2.51	2.50	3.05	3.59	2.43	2.82
40	0.030	1.39	1.30	1.76	2.15	1.33	1.42

[a] based on the N=C IR peak in the substrate **1a’**.

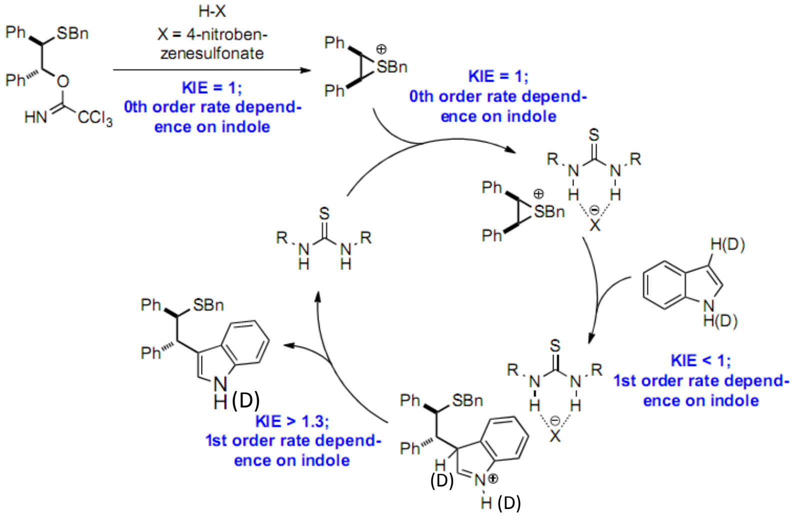
[b] based on the O=C IR peak in the by-product *N*-phenyltrifluoroacetamide.

conversion (%)	r_H/r_D			
	experiment I		experiment II	
	[**1a’**]	[amide]	[**1a’**]	[amide]
15	0.85	0.76	1.02	0.88
30	0.82	0.70	1.03	0.89
40	0.80	0.60	1.05	0.91

KIE (k_H/k_D) = 0.93 ± 0.12 (based on [**1a’**]) or, KIE (k_H/k_D) = 0.86 ± 0.13 (based on both [**1a’**] and [amide]). (**an inverse secondary kinetic isotope effect**)

The statistical value indicates an inverse secondary KIE. This is in consistence with indole addition being the rds (sp^2 to sp^3). However, since the error bar for this type of in situ IR analysis is usually about 10-15%, the saying that no primary KIE was observed would be a more rigorous conclusion.

Discussion about the rate-limiting step of thiourea-catalyzed epi-sulfonium ion opening with indole



As shown in the scheme above, the 1st order rate dependence on indole (see section 6) has suggested that the rate limiting step for the reaction is either nucleophilic ring opening or re-aromatization. The pK_a-corrected Mayr analysis (see section 13) supports the indole addition (ring opening) being the rds. A KIE study would be able to further verify this assumption if the absence of a primary KIE was observed at 3 position of indole.

If ring opening is the rds, besides the bond formation event in the indole addition to epi-sulfonium ion, another factor that can contribute to the KIE value is any interaction involving indole N-H(D) bond in the rate-limiting step. If indole N-H is broken during the rate-limiting step, a primary KIE (> 1.3) should be observed; otherwise, a non-primary KIE should be observed (~ 1.0). In either case, if re-aromatization is rate-determining, meaning that the C-H(D) at position 3 is broken during this event, an overall primary KIE (> 1.3) should be obtained. The absence of this observation excludes the possibility of re-aromatization being the rate-limiting step, and supports the indole nucleophilic addition being the rate-limiting step when taken together with other experimental results discussed in the previous paragraph.

Synthesis of *N*-phenyltrifluoroacetimidate:

To a solution of 2-(benzylthio)-1,2-diphenylethanol (300 mg, 0.94 mmol, see section 5 for synthesis) and 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (216 mg, 169 μL, 1.0 mmol) in DCM (5.0 mL) at 0 ℃ was added sodium hydride (60% suspension in mineral oil, 41.6 mg, 1.0 mmol). The mixture was stirred at room temperature for 2 h. Water and ethyl acetate were added to quench and dilute the reaction mixture. The aqueous layer was separated and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, concentrated and applied to flash column chromatography to obtain the product as a pale yellow gel (>90% yield). Characterization data are shown in section 5.

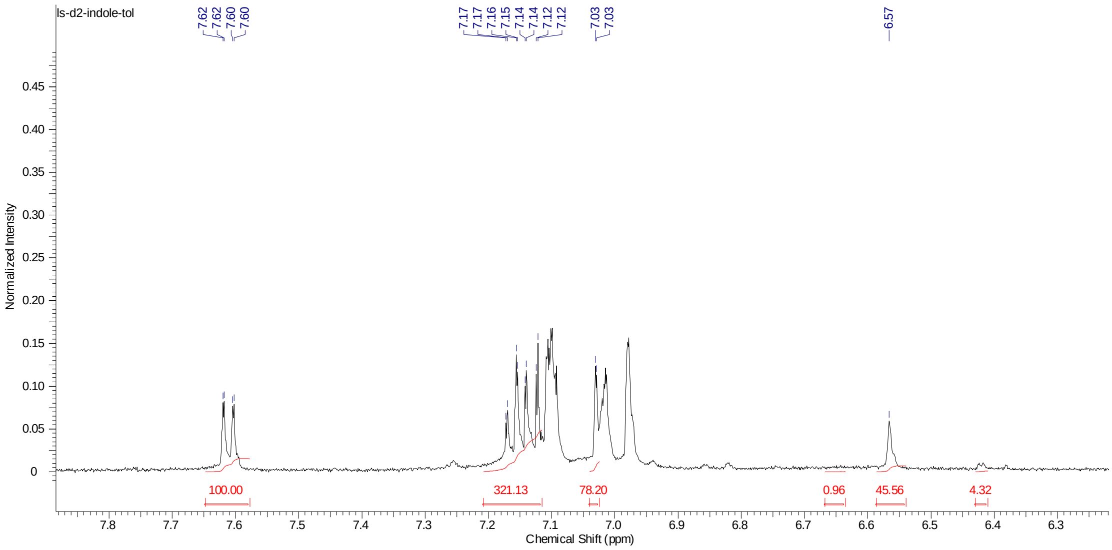
Synthesis of 1,3-d_2-indole:

The mixture of indole (585 mg, 5 mmol) and d_2-sulfuric acid (D_2SO_4, 0.001 M in D_2O, 1 mL) was refluxed under nitrogen atmosphere for 48 h. The reaction was then cooled to room temperature, and extracted with anhydrous EtOAc (dried over 4Å MS overnight). The extract was washed with D_2O

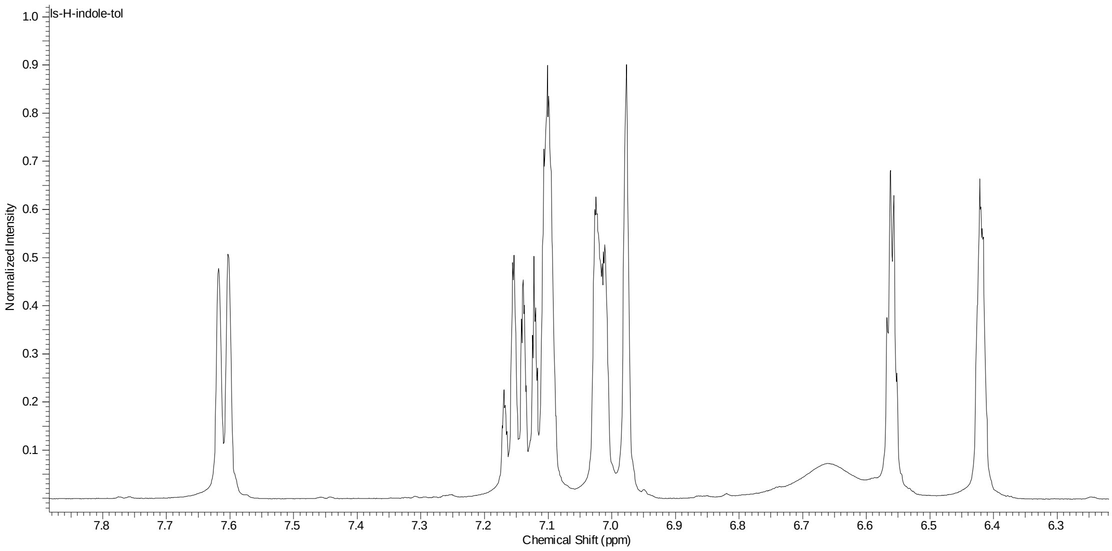
twice, dried over Na_2SO_4, concentrated and applied to flash column chromatography to yield 3-*d*-indole as white crystals. (^{1}H NMR showed partial incorporation of deuterium into the 2 position of indole under this relatively harsh condition.)

The obtained 3-*d*-indole was then dissolved in d_4-methanol (CD_3OD, 1 mL) and stirred under nitrogen atmosphere for 1 h. The solvent was then removed under vacuum, and the resulting solid was re-dissolved in d_4-methanol (CD_3OD, 1 mL) and stirred overnight under nitrogen atmosphere. The solvent was removed under vacuum to yield the desired 1,3-d_2-indole as white/pale pink crystals. The isotope incorporation ratio of the product was determined by ^{1}H NMR (in d_8-toluene) to be 96% (position 3), 54% (position 2) and >99% (position 1).

1,3-d_2-indole:



indole:



10. Data sets for Eyring analysis

Procedure: An oven-dried vial was charged with **1a** (0.025 mmol, 1.0 equiv), thiourea catalyst (0.0025 mmol, 0.10 equiv), indole (0.05 mmol, 2.0 equiv) and 4Å molecular sieves (15 mg, powder, activated). The flask was cooled to –30 ℃, and toluene was added with stirring. Once the reactants and catalyst were fully dissolved, the mixture was cooled to the desired temperature (–30 to –75 ℃), and 4-NBSA (0.5 M in THF, 0.00125 mmol, 0.05 equiv) was added directly into the solution via a 10 μL syringe. The reaction mixture was stirred at that temperature until TLC showed full conversion of the starting material, and then quenched at the same temperature by addition of NEt_3 (~10 μL). The resulting mixture was applied directly to a pipette column containing 4-5 cm of silica gel, and product was isolated by eluting hexanes/EtOAc (20:1 to 10:1) and solvent removal under reduced pressure. The enantiomeric excess was determined by chiral HPLC analysis (ChiralPak AD-H, 10% *i*-PrOH, 1 ml/min, t_1 = 24 min, t_2 = 33 min). The differential activation parameters were calculated using the following relationship:

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

catalyst	ee (%) (temperature (℃))					$\Delta\Delta H^{\ddagger}$ (kcal/mol)	$\Delta\Delta S^{\ddagger}$ (eu)	calc. ee (%) at 0 ℃
3e	91.8 (-30.0)	93.0 (-40.7)	93.5 (-48.9)	95.1 (-58.4)	95.7 (-72.1)	-1.57 ±0.19	-0.18 ±0.85	88.6
3f	89.1 (-30.0)	90.5 (-41.5)	91.1 (-50.0)	92.6 (-58.8)	93.7 (-72.3)	-1.33 ±0.09	0.22 ±0.40	85.6
3g	86.4 (-30.0)	88.3 (-41.8)	89.6 (-50.0)	89.9 (-58.7)	91.6 (-73.7)	-1.08 ±0.11	0.82 ±0.49	83.4
3d	83.5 (-30.0)	85.0 (-41.6)	n.d.	87.7 (-59.7)	89.1 (-79.5)	-1.08 ±0.03	0.33 ±0.11	79.3
3c	83.4 (-30.0)	85.0 (-40.4)	86.4 (-50.0)	88.3 (59.0)	89.9 (-73.2)	-1.23 ±0.06	-0.28 ±0.29	78.6
3b	71.8 (-30.0)	75.1 (-41.2)	77.1 (-50.5)	77.3 (-58.5)	80.3 (-73.8)	-0.84 ±0.11	0.19 ±0.50	67.8
3a	11.7 (-30.3)	11.0 (-41.7)	n.d.	9.7 (-59.6)	n.d.	0.14 ±0.41	1.03 ±1.81	13.2

The differential activation parameters ($\Delta\Delta H^{\ddagger}$) revealed that the enantioselectivity of the reaction was enthalpically controlled and that the magnitude of the differential enthalpy increased markedly as the catalyst arene increased in size. These data are consistent with that an attractive interaction between the aryl substituents on the thiourea derivatives and the cationic transition state, likely being cation-π interaction, contributes to the stereoinduction.

11. Data kinetic analysis of reactions catalyzed by thiourea 3a-3g

General information: Following the same procedure as described in section 6, reactions with thiourea **3a**-**3g** were analyzed with in situ IR spectroscopy. Plotting ln($r_{\text{asym,observed}}$) vs. ln(er) of catalysts **3**-**7** at different fractional conversion (10-60%) of reaction provided a set of nearly parallel linear correlations. This suggests that the series of catalysts follow the same rate law.

Upon gaining the raw rate data, the rate constants of the pathways in the asymmetric reaction leading to the major and minor enantiomeric products ($k_{\text{asym,major}}$ and $k_{\text{asym,minor}}$, respectively) are derived from the empirical rate laws and the equations below:

(1) $r_{\text{asym,observed}} = r_{\text{asym}} + r_{\text{rac}} = (r_{\text{asym,major}} + r_{\text{asym,minor}}) + r_{\text{rac}}$; and,

(2) $r_{\text{asym,major}}/r_{\text{asym,minor}}$ = er.

Rates measured directly with in situ IR are provided in the table below, in M s^{-1} (x 10^{-5}). Data for thiourea **3e**-catalyzed reaction and the racemic reaction are shown in section 6, and therefore not presented in the section.

Reaction condition: [**1a**]$_i$ = 0.050 M, [indole]$_i$ = 0.1 M, [4-NBSA]$_T$ = 0.0010 M, [thiourea]$_T$ = 0.0050 M.

conv. of **1a**	[**1a**] (M)	**3a** I	**3a** II	**3b** I	**3b** II	**3c** I	**3c** II	**3d** I	**3d** II	**3g** I	**3g** II	**3f** I	**3f** II
10%	0.045	0.56	0.55	1.16	1.08	2.23	2.41	2.31	2.92	2.31	2.42	4.75	5.68
20%	0.040	0.36	0.28	0.73	0.68	1.49	1.57	1.64	1.89	1.53	1.50	3.22	3.85
30%	0.035	0.22	0.15	0.39	0.34	0.85	0.92	1.00	1.16	0.97	0.96	2.09	2.49
40%	0.030	0.14	0.09	0.26	0.22	0.56	0.62	0.73	0.85	0.73	0.78	1.53	1.87
50%	0.025	0.09	0.08	0.18	0.15	0.42	0.46	0.55	0.63	0.59	0.57	1.33	1.54
60%	0.020	0.03		0.17		0.29	0.39	0.44	0.51	0.49	0.45	1.01	1.26

The following rate data are based on initial rates taken at 10% conversion of **1a**, and calculated with the equations shown above in this section.

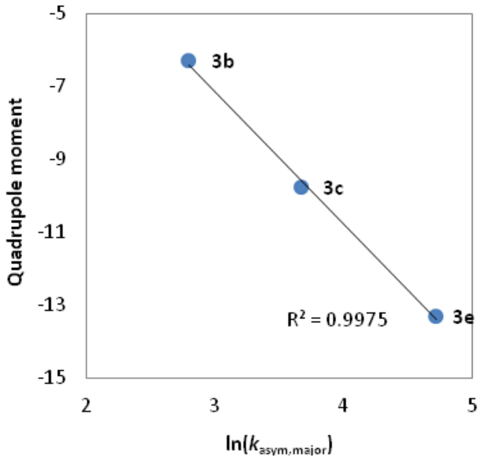
thiourea	**3a**	**3b**	**3c**	**3d**	**3g**	**3f**	**3e**^{b}
$r_{\text{asym,observed}}$ (10^{-5} M s^{-1})	0.56 ±0.01	1.12 ±0.06	2.32 ±0.10	2.62 ±0.43	2.36 ±0.06	5.22 ±0.66	6.08 ±0.36
r_{rac} (10^{-6} M s^{-1})	1.40 ±1.4						
ln($k_{\text{asym,major}}$)	1.55 ±0.03	2.79 ±0.07	3.67 ±0.05	3.79 ±0.17	3.71 ±0.03	4.54 ±0.13	4.72 ±0.09
ln($k_{\text{asym,minor}}$)	1.28 ±0.03	1.16 ±0.07	1.54 ±0.05	1.63 ±0.17	1.34 ±0.03	1.99 ±0.13	1.91 ±0.09
ln(er)^{a}	0.27	1.65	2.12	2.16	2.40	2.55	2.81

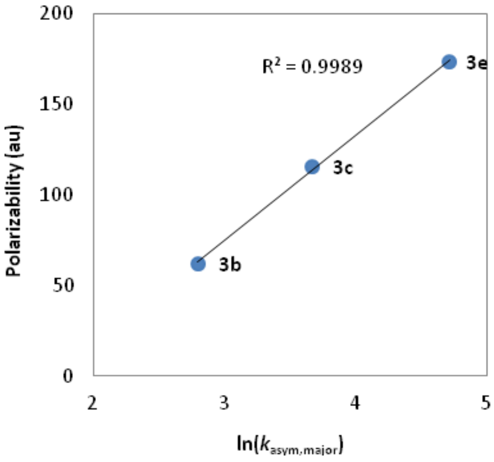
^{a} Enantiomeric ratio data at 0 ℃ were calculated based on the Eyring analysis in section 9. The direct experimental measurement of reaction ee at 0 ℃ does not provide accurate data for the intrinsic enantioselectivity of the catalysts due to the competing racemic background reaction at this temperature. ^{b} Rate data for catalyst **3e** was calculated on the basis of over 6 reactions under the standard in situ IR condition, most of which are presented in section 6.

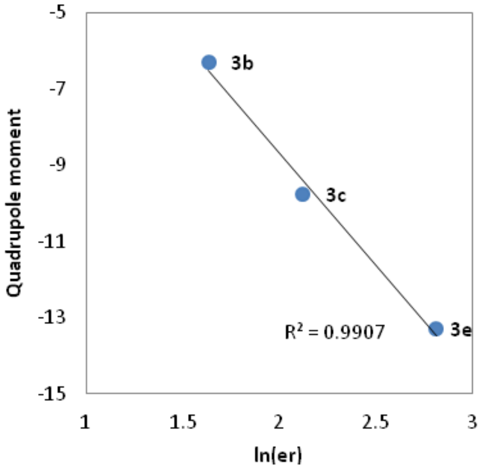
12. Correlations of arene properties with rate and enantioselectivity for catalysts 3b-3g

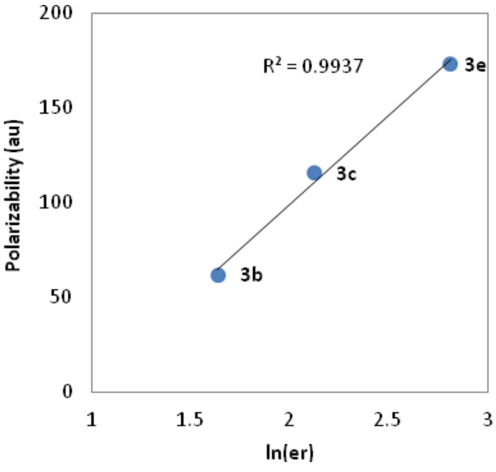
The rate and enantioselectivity data were obtained in the same manner as in section 10. The ee's at 0 ℃ were calculated on the basis of the Eyring plots (section 9). The rates were measured by in situ IR spectroscopy. Quadrupole moments of different arenes were obtained from: Ng, K. M., Ma, N. L. & Tsang, C. W. *Rapid Commun. Mass Spectrom.* **12**, 1679–1684 (1998). Polarizabilities of different arenes were obtained from: Waite, J., Papadopoulos, M. G. & Nicolaides, C. A. *J. Chem. Phys.* **77**, 2536–2539 (1982), and the website of theoretical spectral database of polycyclic aromatic hydrocarbons (http://astrochemistry.ca.astro.it/database/pahs.html).

arene	polarizability	quadrupole moment	catalyst	$\ln(k_{\mathrm{asym,major}})$	ln(er)
benzene	61.9	-6.29	**3b** (phenyl)	2.79	1.64
naphthalene	115.5	-9.77	**3c** (1-naphthyl)	3.67	2.12
phenthrene	173.2	-13.30	**3e** (9-phenanthryl)	4.72	2.81
pyrene	205.7	-14.69	**3f** (4-pyrenyl)	4.54	2.55
chrysene	239.0	-16.96	**3g** (6-chrysenyl)	3.71	2.37







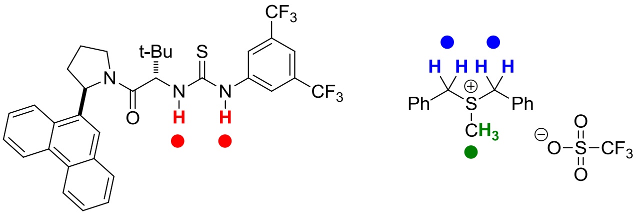


Note: Pyrenyl catalyst **3f** and chrysenyl catalyst **3g** can't fit into these correlations. An explanation has been provided in the main text. However, we can't fully understand this completely on this stage.

13. NMR binding study of thiourea 3e/3a and dibenzylmethylsulfonium triflate

General information: Attempts to isolate or observe the episulfonium salt were unsuccessful requiring theinvestigation of an analogous sulfonium triflate salt. Under the model reaction condition, the combination triflic acid (HOTf) and **3e** provided **2a** in 71% yield and 73% ee.

General procedure: An oven-dried vial was charged with thiourea **3e** (3.2 mg, 5.0 μmol), dibenzylmethylsulfonium triflate (4.0 mg, excess), and anhydrous d_8-toluene (0.5 mL). The suspension was place in an ultrasound sonicator for 2-3 min. The mixture was filtered through a short plug with cotton to remove the insoluble white solid after sonication, and the cotton was washed with a small amount of d_8-toluene. The final concentration of the thiourea-sulfonium salt solution is ca. 0.0010 M. The composition of the complex is 1.05:1 (thiourea : sulfonium triflate) by ^{1}H NMR analysis. The chemical shift of the diagnostic resonances are shown below (toluene -CH_3 $\delta = 2.09$ as reference).

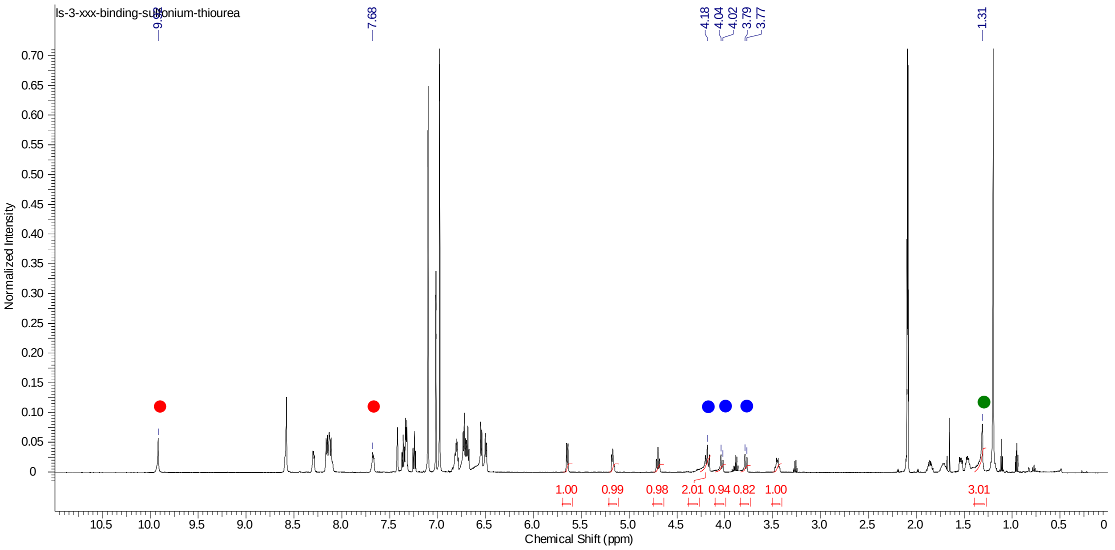


	thiourea N-H (ppm) (red dots)	benzyl protons (ppm) (blue dots)	methyl protons (ppm) (green dots)
thiourea **3e**	8.68, 7.25	-	-
dibenzylmethyl sulfonium triflate	-	4.80, 4.59	2.09
1:1 complex	9.92, 7.68	4.18, 4.03, 3.78	1.31

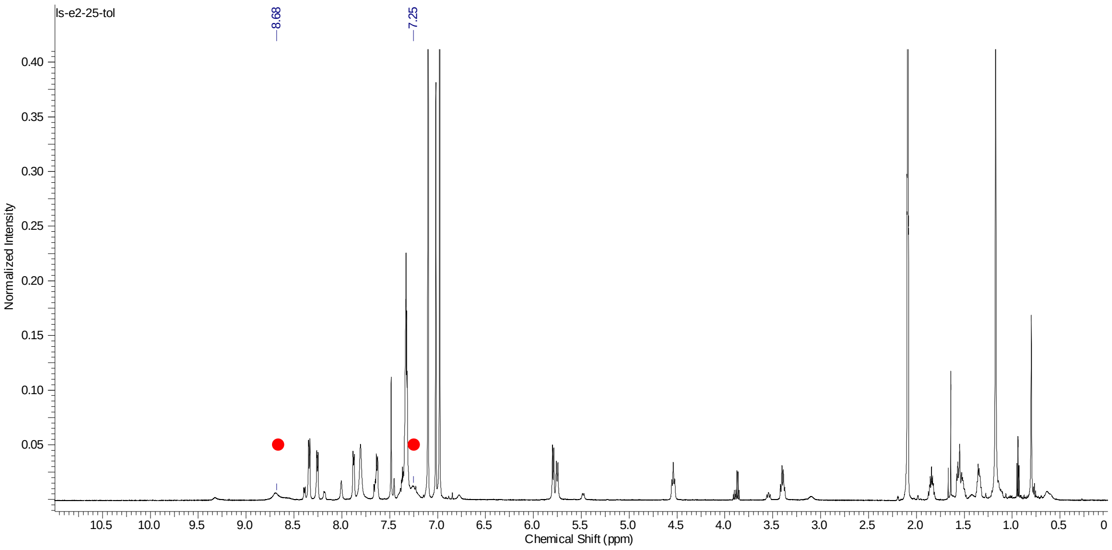
For the synthesis of dibenzylsulfonium triflate salt, see: Miyatake, K., Yamamoto, K., Endo, K. & Tsuchida, E. *J. Org. Chem.* **63**, 7522–7524 (1998).

(See below for the NMR spectrum, displayed on the same scale of chemical shift 0-11 ppm)

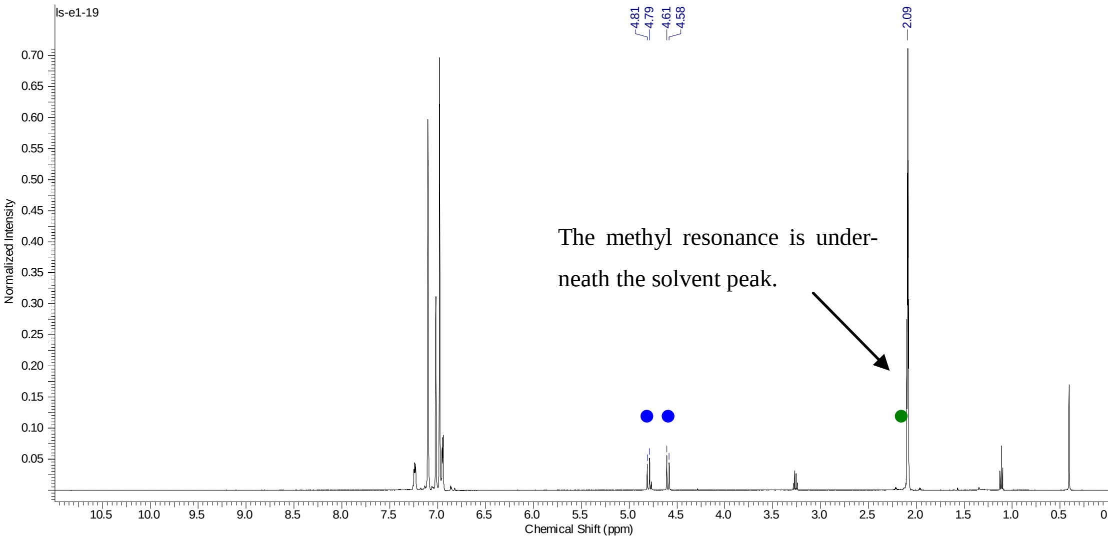
Thiourea **3e**-sulfonium triflate complex:



Thiourea **3e**:

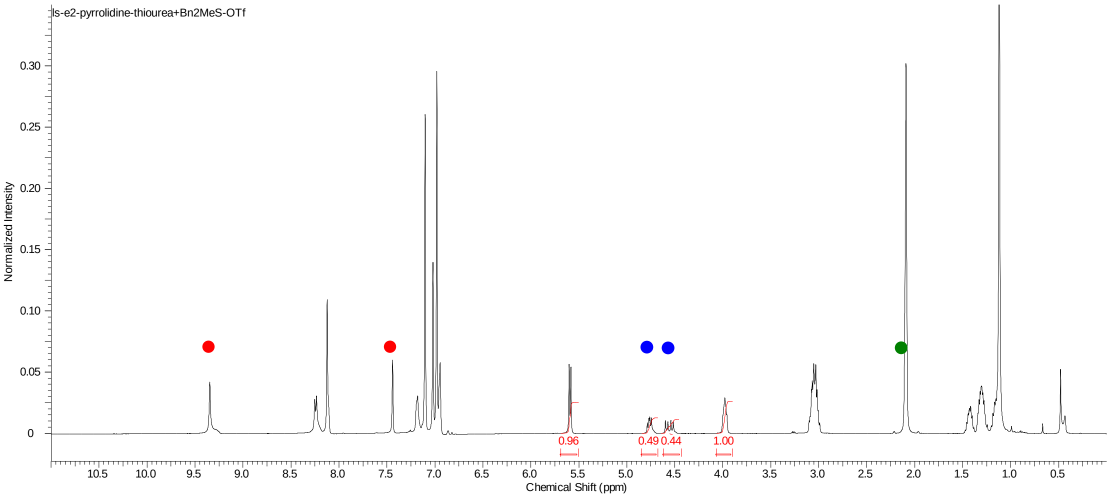


Dibenzylmethylsulfonium triflate:



The methyl resonance is underneath the solvent peak.

Thiourea **3a**-sulfonium triflate complex:



14. Correlation of indole N-H acidity with the reaction rate, and structure-reactivity, and -selectivity relationship of π-nucleophiles

General information: The pK_a values of indole derivatives used in the structure-reactivity analysis were calculated by Advanced Chemistry Development, Inc. (ACD/Labs) Software V12.01. The absolute or relative values of these calculated numbers were validated by literature reports, DFT calculations, experimental pK_a measurements via the Bordwell method, and Hammett analysis (see table below). For a reference evaluating the accuracy of pK_a calculation by ACD labs, see: Meloun, M. & Bordovská, S. *Anal. Bioanal. Chem.* **389**, 1267-1281 (2007).

Indoles pK_a, inductive Hammett constant, calculated hydrogen bond energy involving indole N-H bond

R	k_{asym}/k_{rac} [a] (10^3)	pK_a				σ_I [e]	calc. H-bond energy (kcal/mol) [f]	
		calc. by ACD labs	exp. In H_2O [b]	exp. In DMSO [c]	exp. In DMSO [d]		to benzene	to DMA [g]
H	8.7	17.00	16.97	20.82 ±0.01	20.95	0.00	2.65	8.17
Me	6.1	17.17		20.95 ±0.06		-0.04	2.61	8.02
MeO	9.8	16.70		20.71 ±0.04		0.27	2.66	8.18
F	16.5	16.16	16.30			0.52	2.88	8.56
Cl	18.4	16.09				0.47	2.97	8.92
Br	17.5	16.04	16.13			0.50	2.97	8.92

[a] For H-indole, the value was obtained from reaction progress study by in situ IR spectroscopy (conditions: 0.050 mmol **1a**, 0.10 mmol indole, 0.0050 mmol **3e**, 0.0010 mmol 4-NBSA, 50 mg 4Å MS in 2 mL toluene at 0 ℃; see section 6 for procedure), and initial rates were taken at 10% conversion of **1a**. For the indole derivatives, the values were measured on the basis of competition experiments with indole under pseudo-zeroth order conditions (see section 8), and calculated using the following equations:

$k_{asym,R\text{-}indole} = k_{rel,asym,R\text{-}indole} \text{ x } k_{asym,indole}$; $k_{rac,R\text{-}indole} = k_{rel,rac,R\text{-}indole} \text{ x } k_{rac,indole}$;

[b] See: Yagil, G. *J. Phys. Chem.* **71**, 1034-1044 (1967).

[c] Conducted using Bordwell method with 2-naphthylacetonitrile as indicator. For detailed procedure, see: Matthews, W. S. *et. al. J. Am. Chem. Soc.* **97**, 7006-7014 (1975).

[d] See: Bordwell, F. G., Drucker, G. E. & Fried, H. E. *J. Org. Chem.* **46**, 632-635 (1981).

[e] The inductive Hammett constants are obtained from Hansch, C. & Leo, A. *Substituent Constants for Correlation Analysis in Chemistry and Biology* (Wiley-Interscience: 1979).

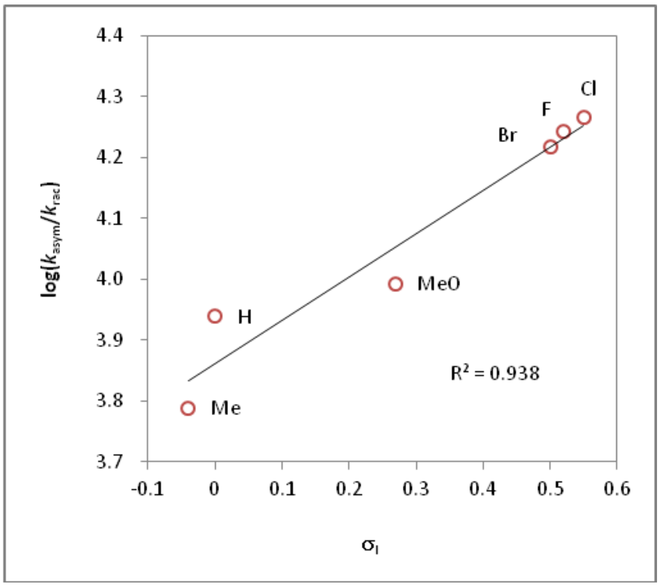
[f] Conducted using Gaussian 09, DFT B3LYP 6-31G(d).

[g] DMA = dimethylacetamide; amide oxygen as H-bond donor.

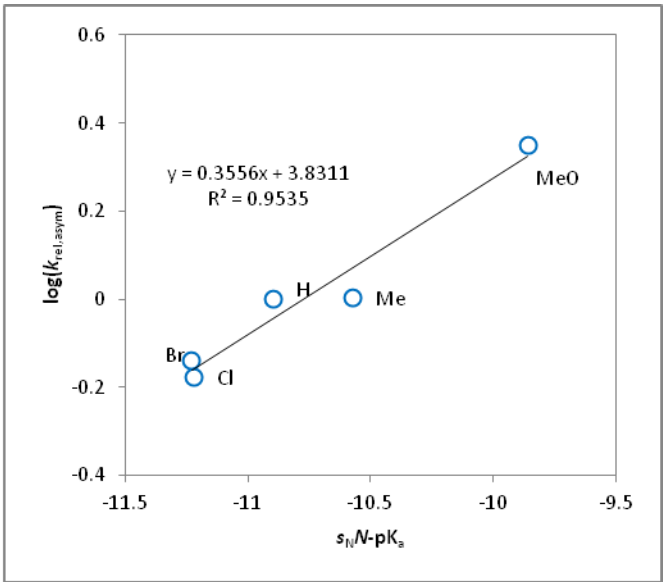
A LFER could also be generated between log(k_{asym}/k_{rac}) and the inductive Hammett parameter (σ_I). See the first figure below. The σ_I values represent the inductive ability of the substituents on indole, which is separated from their electronic properties associated with conjugation through the π-system. Since the indole N-H is on the plane of the π face and thus its acidity is only under the influence of inductive effects, σ_I can be use here to quantify the strength of an H-bond involving indole N-H.

In the main text and in section 7 of the Supplemental Information, we observed that in the thiourea-catalyzed condition, the linear relationship between log(k_{asym}) and Mayr nucleophilicity parameter $s_N N$ was poor ($R^2 = 0.757$). This was explained by the possibility of an indole N-H hydrogen bonding interaction with the thiourea catalyst, which resulted in change of nucleophilicity of indole derivatives. In fact, if $\log(k_{asym})$ of these 5-substituted indoles are plotted against ($s_N N$ – pK_a), a parameter linearly combining the Mayr nucleophilicity and the acidity of the nucleophiles, an improved correlation is obtained ($R^2 = 0.953$). See the second figure below. This is consistent with that the "actual" nucleophilicity of indole derivatives in the thiourea-catalyzed reactions is under the control of both its intrinsic reactivity and the activation effect by the catalyst via H-bond. Therefore, it explains why the Mayr nucleophilicity plot of the asymmetric reaction was scattered.

Correlation between $\log(k_{asym}/k_{rac})$ and σ_I of indole derivatives



pK_a-corrected Mayr analysis of the asymmetric reaction



Structure-reactivity-selectivity study of π-nucleophiles

General procedure:

For competition experiments: Following the procedure described in section 7, a second nucleophile was applied to a competition experiment with indole, and the relative rate with respect to indole was determined with ^1H NMR spectroscopy. The relative rate of indole is set to 1.

For reaction kinetic study with in situ IR spectroscopy: Followed the procedure described in section 6. The reaction stoichiometry is shown below –

Azulene – 0.075 mmol **1a**, 0.15 mmol azulene, 7.5 μmol **3e** or none, 7.5 μmol 4-NBSA (0.5 M in THF), 50 mg 4Å MS, 1.5 mL toluene.

Pyrrole – 0.075 mmol **1a**, 0.15 mmol azulene, 7.5 μmol **3e** or none, 3.75 μmol 4-NBSA (0.5 M in THF), 50 mg 4Å MS, 1.5 mL toluene.

N-methylindole – 0.10 mmol **1a**, 0.20 mmol azulene, 10.0 μmol **3e** or none, 5.0 μmol 4-NBSA (0.5 M in THF), 50 mg 4Å MS, 1.5 mL toluene.

NuH	$r_{\mathrm{rel,asym}}$[a,b]	$r_{\mathrm{rel,rac}}$[a,b]	$(r_{\mathrm{asym}}/r_{\mathrm{rac}})_{\mathrm{rel}}$ (compt.)[b]	r_{asym}[c] (10^{-6} M/s)	r_{rac}[c] (10^{-6} M/s)	$r_{\mathrm{asym}}/r_{\mathrm{rac}}$ (RIR)[c]
indole	1	1	1	1.40	60.8	43.4
benzotriazole	9.5	10.3	0.92	n/d[d]	n/d[d]	n/d[d]
azulene	0.038	0.26	0.15	4.10	13.2	3.2
pyrrole	0.21	2.03	0.11	1.17	3.69	3.2
N-methylindole	0.13	0.99	0.13	1.03	3.92	3.8

[a] Rate relative to reaction with indole under the same condition.

[b] Obtained from competition experiments with 1:1 nucleophile to indole.

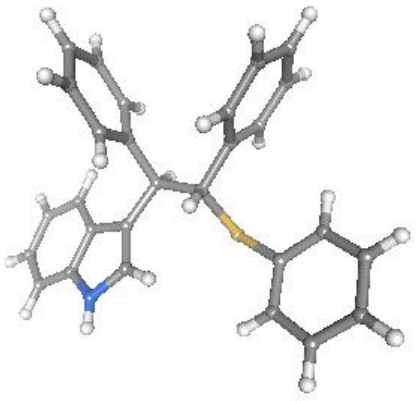
[c] Obtained from reaction kinetic study with in situ IR, and initial rates taken at 10% conversion of **1a**.

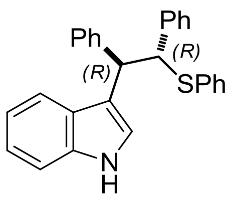
[d] The rate of benzotriazole-involving reaction is not determined because kinetic analysis was complicated by the poor solubility of benzotriazole in the reaction solvent – toluene.

15. Crystallographic data of compounds 2b, 2g and 2q

General information: The crystallographic data have been included in the *.cif files as part of the Supplementary Information. In this section are presented the crystal structures, absolute configuration assignments and conditions for growing the crystals.

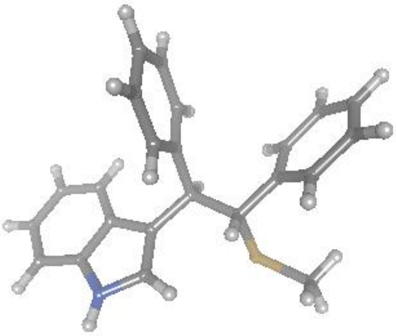
2b: (grew in hexanes/*i*-PrOH at room temperature, as a single enantiomer)

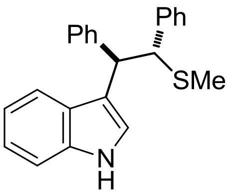




Ortep-Plot (thermal ellipsoids shown at 50% probability level)

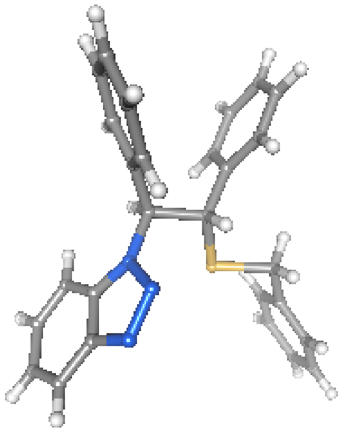
2g: (grew in hexanes/MeOH at room temperature, as a 1:1 mixture of enantiomers)

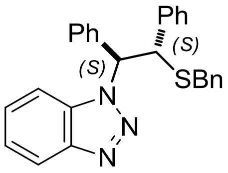




Ortep-Plot (thermal ellipsoids shown at 50% probability level)

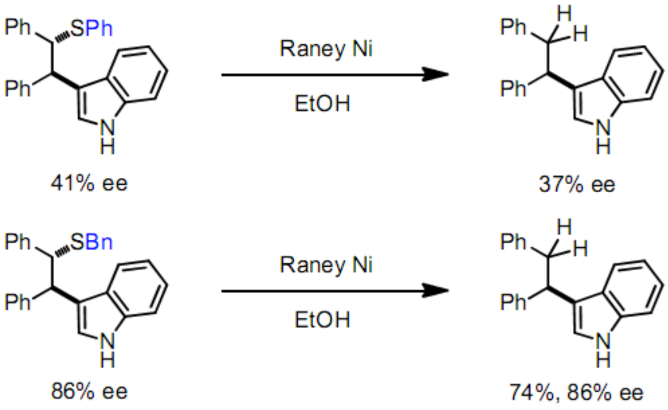
2q: (grew in hexanes/*i*-PrOH at room temperature, as a single enantiomer)





Ortep-Plot (thermal ellipsoids shown at 50% probability level)

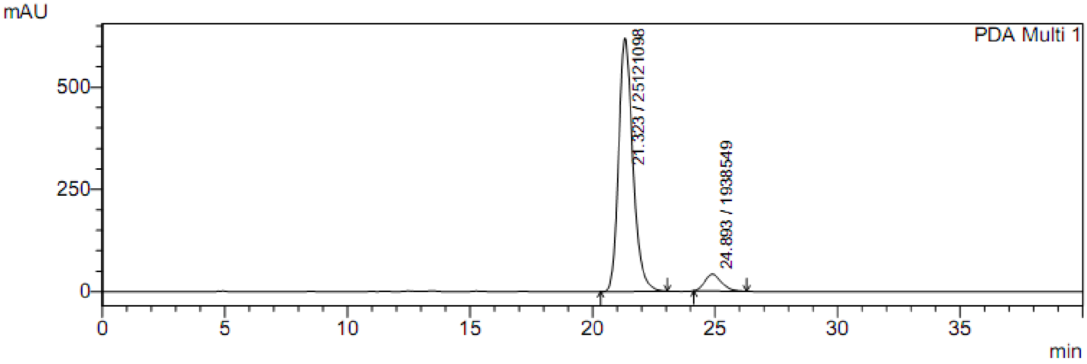
The absolute stereochemistry of product **2a** was determined by derivatization (reductive removal of the sulfanyl group –SBn) and comparison with product **2b**, as (*R*, *R*).



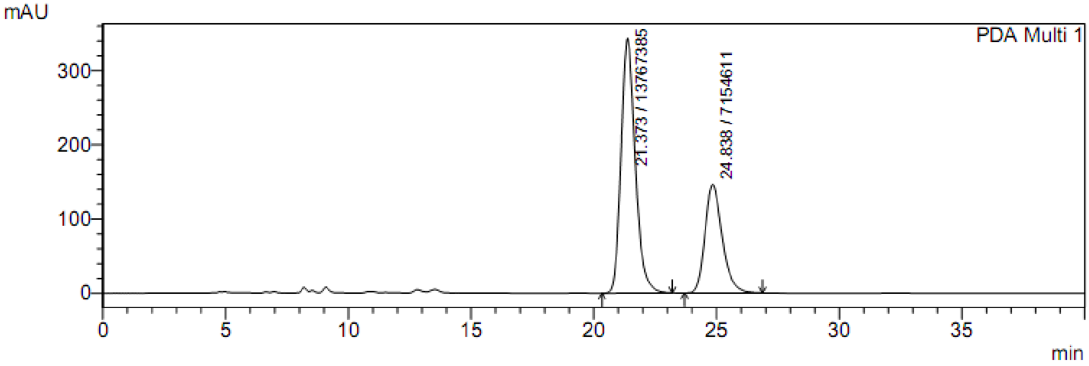
Procedure for Raney Ni promoted reduction of products **1a** and **1b**:

To a solution of the freshly prepared sulfide product (1 equiv) in ethanol (0.05 M) at room temperature was added Raney 2800 nickel (slurry in water, about the same volume as ethanol). The biphasic mixture was stirred vigorously until TLC showed complete consumption of the starting material. The mixture was then filtered through a celite plug, and diluted with water and DCM. The aqueous layer was separated and extracted with DCM. The combined organic layers were dried over Na_2SO_4, concentrated on vacuum, and applied to flash column chromatography. The product was obtained as a white solid, and ^{1}H NMR and mass spectroscopic data matched literature report perfectly. The enantiomeric excess was determined by chiral HPLC analysis (ChiralPak OD-H, 10% *i*-PrOH, 1 mL/min, 220 nm, t_r(major) = 21 min, t_r(minor) = 25 min).

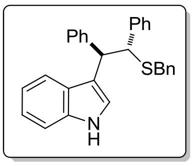
Reduction product from **1a**:



Reduction product from **1b**:

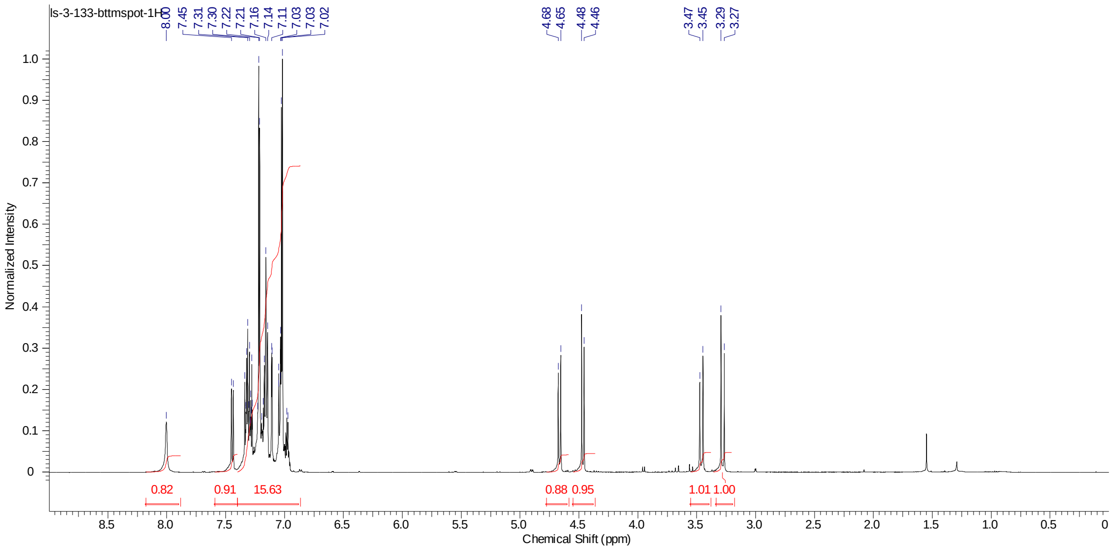


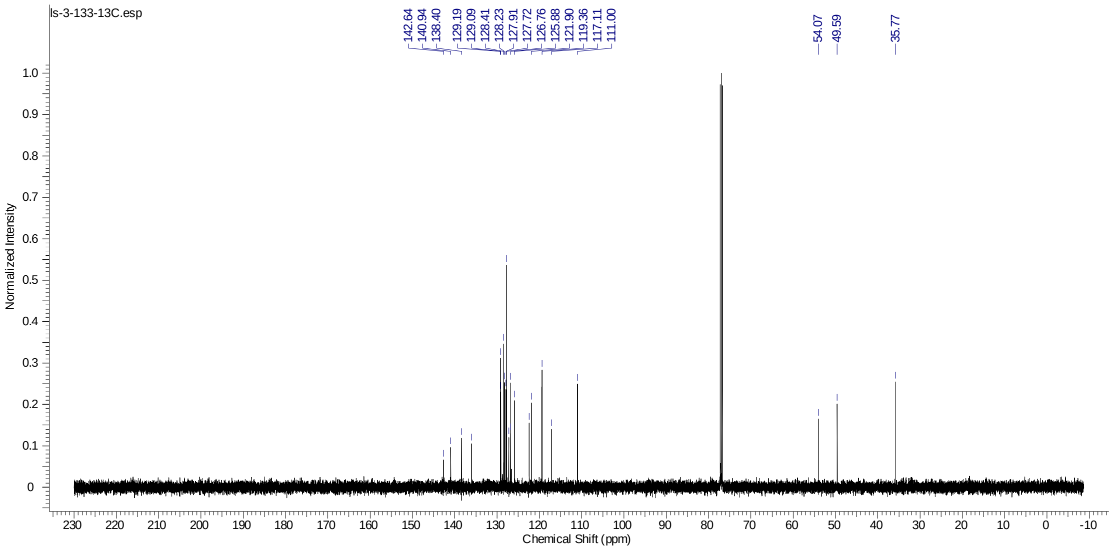
16. Characterization of products 2a-2z



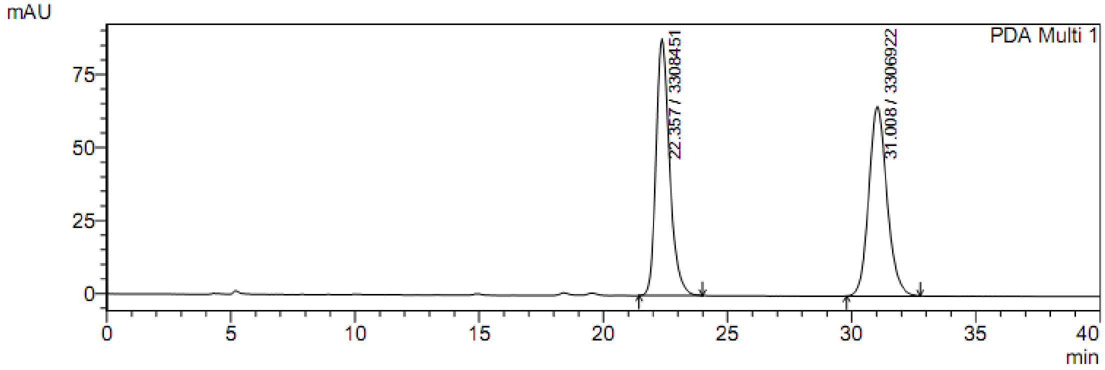
3-((1*R*,2*R*)-2-(benzylthio)-1,2-diphenylethyl)-1*H*-indole (2a)

Followed method B from **1a** (23.2 mg, 0.05 mmol), for 45 h, and purified using silica gel chromatography to give 20.8 mg (99% yield) of **2a** as a white solid. This material was determined to be 93% ee by chiral HPLC analysis (ChiralPak AD-H, 10% *i*-PrOH, 1 mL/min, 240 nm, t_r(major) = 24 min, t_r(minor) = 33 min). IR (Film): 3419 (s), 3026, 1599, 1491, 1453 (s), 1417, 1336, 1264, 1071, 736 (s), 694 (s) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ = 8.02 (br. s., 1H), 7.44 (d, *J*=7.8 Hz, 1H), 7.37 - 6.90 (m, 19H), 4.66 (d, *J*=10.5 Hz, 1H), 4.46 (d, *J*=10.5 Hz, 1H), 3.45 (d, *J*=13.7 Hz, 1H), 3.28 (d, *J*=13.7 Hz, 1H); ^{13}C NMR (125 MHz, CDCl$_3$) δ = 142.64, 140.94, 138.40, 136.00, 129.19, 129.09, 128.45, 128.41, 128.23, 127.91, 127.72, 127.25, 126.80, 126.76, 125.88, 122.38, 121.90, 119.44, 119.36, 117.11, 111.00, 54.07, 49.59, 35.77; MS (ESI-APCI) exact mass calculated for [M-SBn] ($C_{22}H_{18}N$) requires *m/z* 296.1, found *m/z* 296.1; $[\alpha]_D^{23}$ = +130.6 (c = 0.5, CH_2Cl_2).





Racemic sample:



PDA Ch1 240nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
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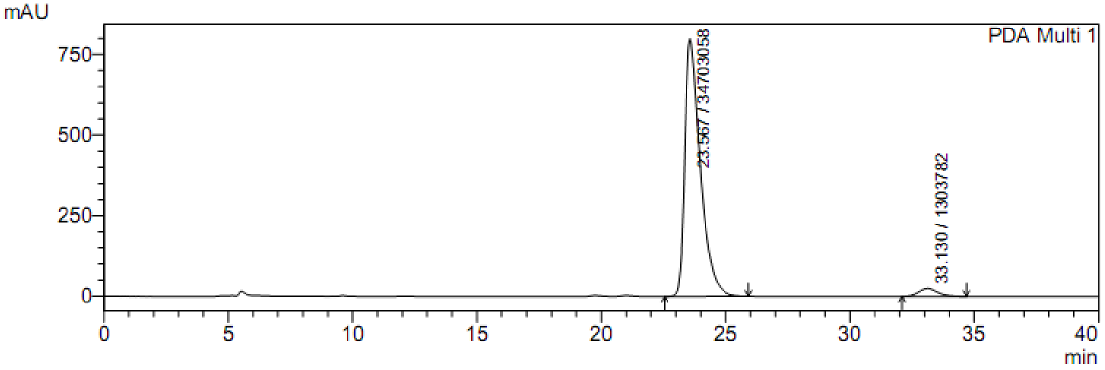
Total		6615373	152277	100.000	100.000

Enantioenriched sample:



PDA Ch1 240nm 4nm

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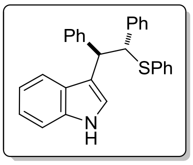
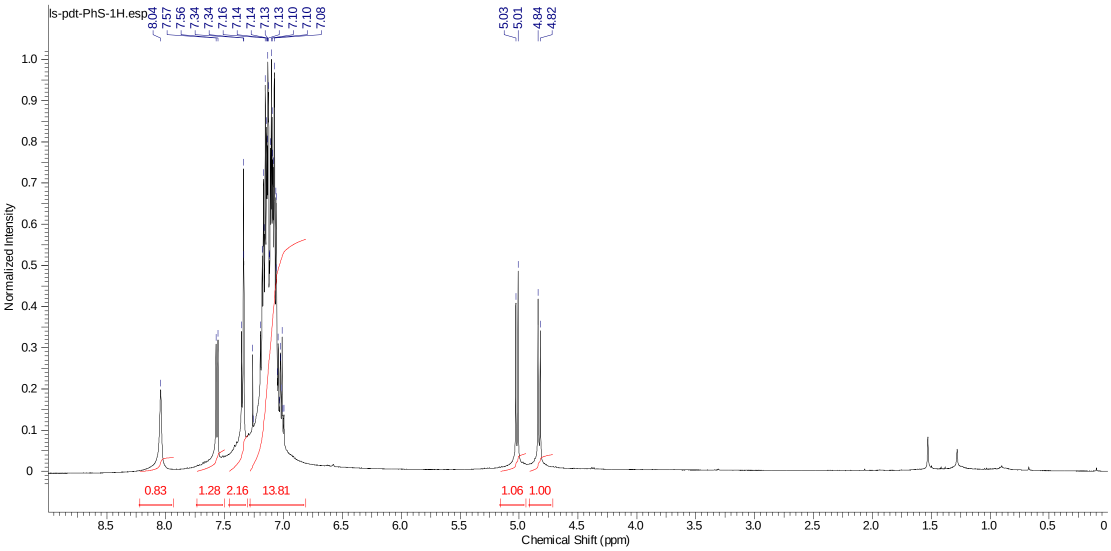
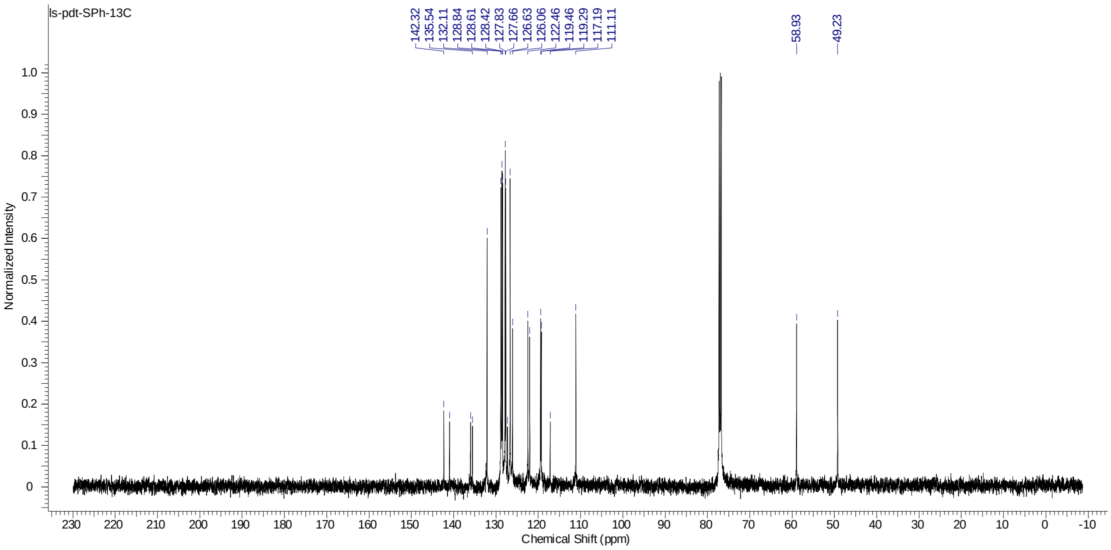
2	33.130	1303782	24397	3.621	2.963
Total		36006841	823468	100.000	100.000



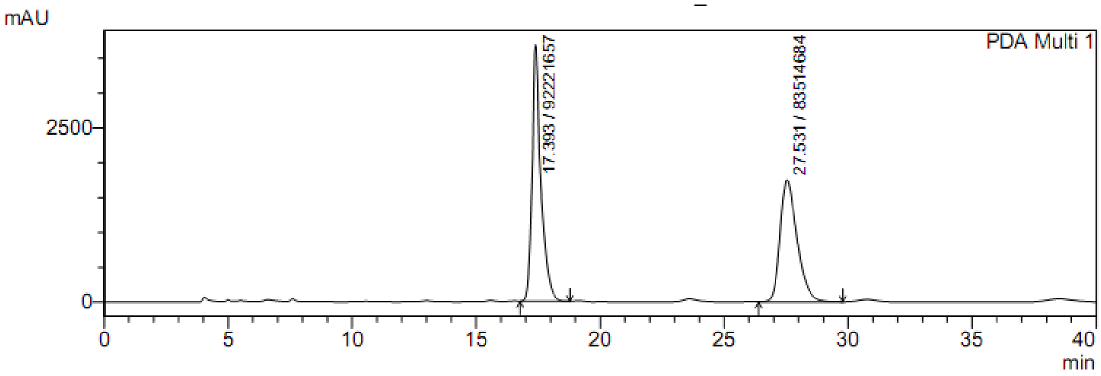
3-((1*R*,2*R*)-1,2-diphenyl-2-(phenylthio)ethyl)-1*H*-indole (2b)

Followed method B from **1b** (22.6 mg, 0.05 mmol), for 63 h, and purified using silica gel chromatography to give 16.8 mg (83% yield) of **2b** as a white solid. This material was determined to be 85% ee by chiral HPLC analysis (ChiralPak AD-H, 10% *i*-PrOH, 1 mL/min, 220 nm, t_r(major) = 29 min, t_r(minor) = 18 min). IR (Film): 3412 (s), 3058, 3027, 1582, 1490, 1454 (s), 1418, 1337, 1098, 1026, 740 (s), 695 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.04 (br. s., 1H), 7.57 (d, *J*=8.3 Hz, 1H), 7.46 - 7.30 (m, 2H), 7.23 - 7.01 (m, 17H), 5.02 (d, *J*=9.3 Hz, 1H), 4.83 (d, *J*=9.8 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 142.32, 140.98, 136.02, 135.54, 132.10, 128.84, 128.61, 128.42, 127.83, 127.66, 127.26, 126.63, 126.06, 122.46, 122.01, 119.46, 119.29, 117.19, 111.11, 58.93, 49.23; MS (ESI-APCI) exact mass calculated for [M-SPh] ($C_{22}H_{18}N$) requires *m/z* 296.1, found *m/z* 296.2; $[\alpha]_D^{25}$ = +38.6 (c = 1.0, CH_2Cl_2).





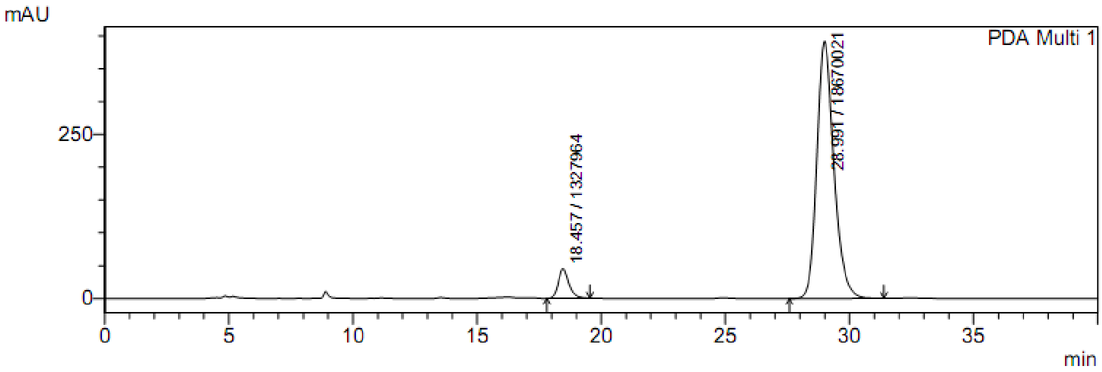
Racemic sample:



PDA Ch1 220nm 4nm

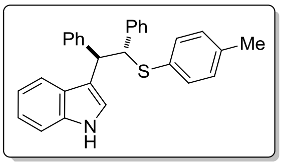
Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.393	92221657	3686825	52.477	67.826
2	27.531	83514684	1748846	47.523	32.174
Total		175736342	5435672	100.000	100.000

Enantioenriched sample:



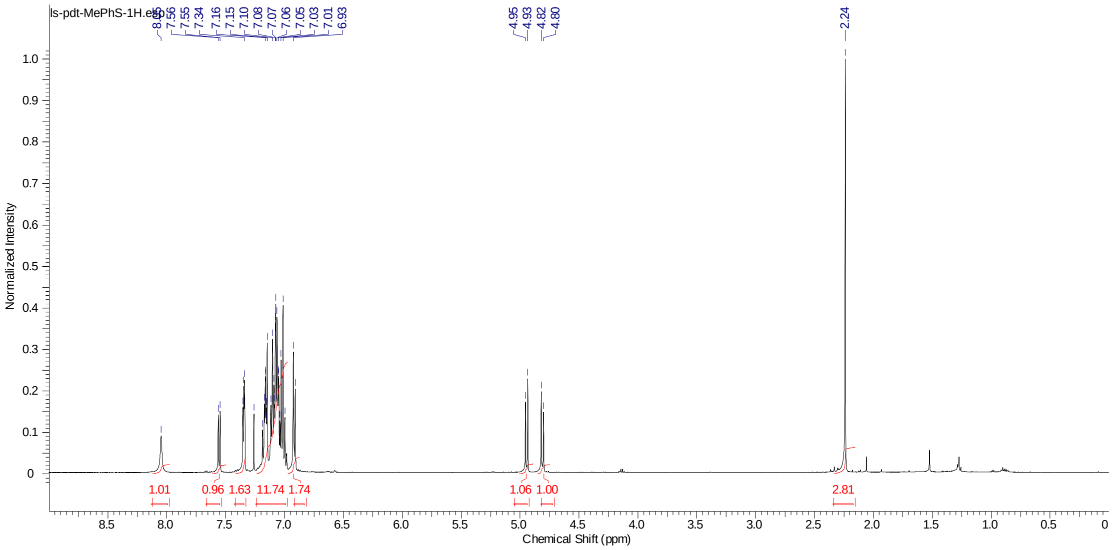
PDA Ch1 220nm 4nm

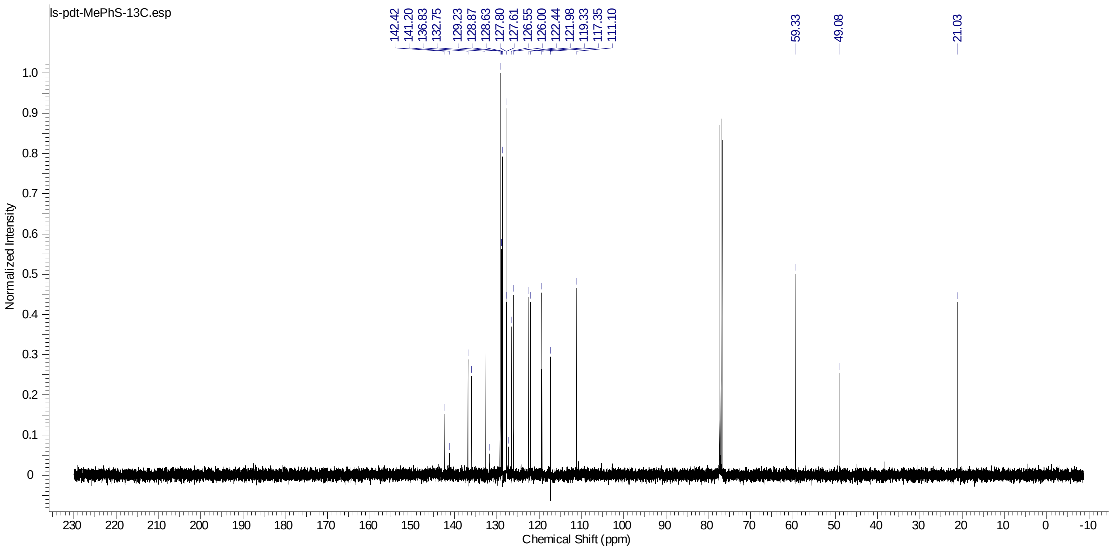
Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.457	1327964	44652	6.640	10.220
2	28.991	18670021	392252	93.360	89.780
Total		19997986	436904	100.000	100.000



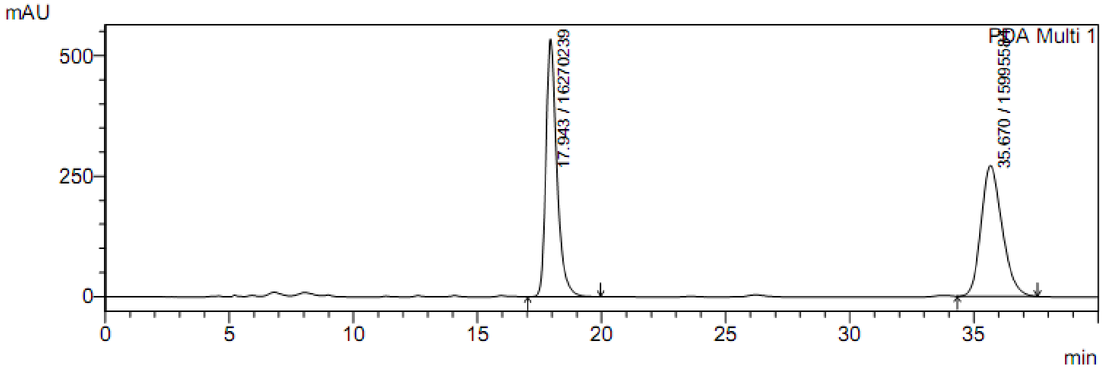
3-((1*R*,2*R*)-1,2-diphenyl-2-(*p*-tolylthio)ethyl)-1*H*-indole (2c)

Followed method B from **1c** (23.2 mg, 0.05 mmol), for 63 h, and purified using silica gel chromatography to give 16.0 mg (76% yield) of **2c** as a colorless gel. This material was determined to be 87% ee by chiral HPLC analysis (ChiralPak AD-H, 10% *i*-PrOH, 1 mL/min, 220 nm, t_r(major) = 33 min, t_r(minor) = 16 min). IR (Film): 3421 (br, s), 3026, 1491, 1454 (s), 1418, 1337, 1098, 1030, 909, 808, 739 (s), 696 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.05 (br. s., 1H), 7.55 (d, *J*=8.2 Hz, 1H), 7.42 - 7.33 (m, 2H), 7.21 - 6.98 (m, 14H), 6.92 (d, *J*=7.8 Hz, 2H), 4.94 (d, *J*=9.6 Hz, 1H), 4.81 (d, *J*=9.6 Hz, 1H), 2.24 (s, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 142.42, 141.20, 136.83, 136.04, 132.75, 131.66, 129.23, 128.87, 128.63, 127.80, 127.61, 127.29, 126.55, 126.00, 122.44, 121.98, 119.44, 119.33, 117.35, 111.10, 59.33, 49.08, 21.03; MS (ESI-APCI) exact mass calculated for [M-SAr] ($C_{22}H_{18}N$) requires *m/z* 296.1, found *m/z* 296.1; $[\alpha]_D^{24}$ = +56.2 (c = 1.0, CH_2Cl_2).





Racemic sample:



PDA Ch1 220nm 4nm

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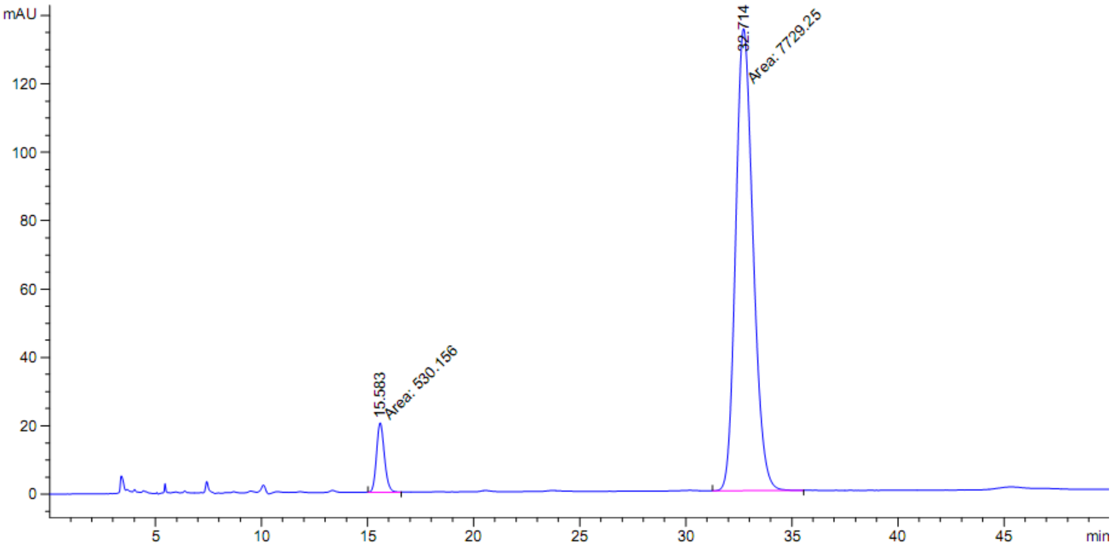
Enantioenriched sample:



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Peak RetTime Type  Width     Area      Height     Area  
  #   [min]         [min]   [mAU*s]     [mAU]       %   
----|-------|----|-------|----------|----------|--------|
   1  15.583 MM    0.4344  530.15643   20.34227   6.4188
   2  32.714 MM    0.9529 7729.24707  135.18980  93.5812
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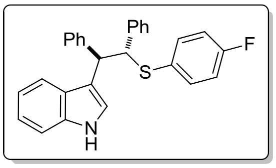
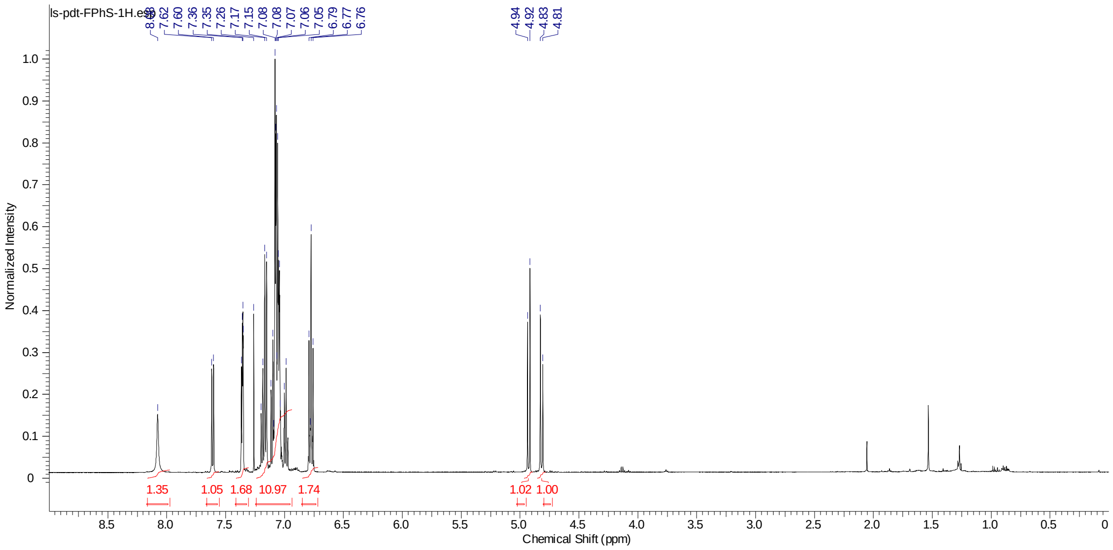
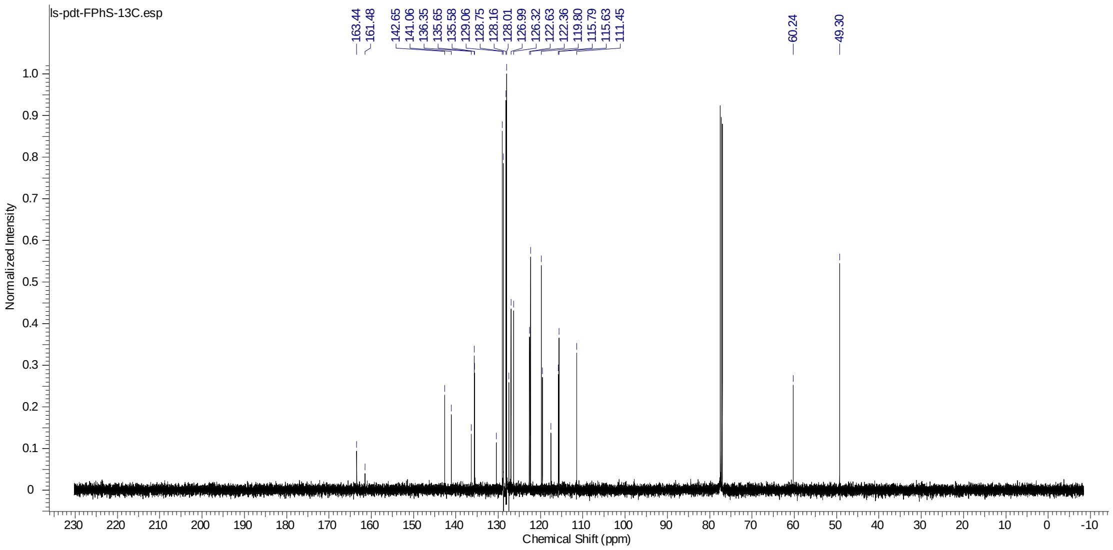
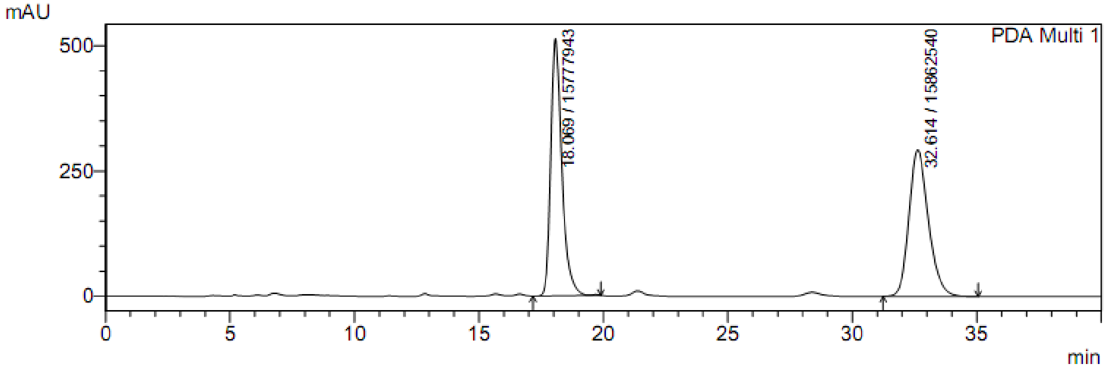


3-((1*R*,2*R*)-2-((4-fluorophenyl)thio)-1,2-diphenylethyl)-1*H*-indole (2d) Followed method B from **1d** (23.4 mg, 0.05 mmol), for 63 h, and purified using silica gel chromatography to give 15.4 mg (73% yield) of **2d** as a colorless gel. This material was determined to be 81% ee by chiral SFC analysis (ChiralPak AD-H, 10% *i*-PrOH, 1 mL/min, 220 nm, t_r(major) = 16 min, t_r(minor) = 30 min). IR (Film): 3422 (s), 3059, 1588, 1488 (s), 1454, 1337, 1223, 1155, 1096, 1012, 829, 740 (s), 698 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.08 (br. s., 1H), 7.61 (d, *J*=7.8 Hz, 1H), 7.41 - 7.31 (m, 2H), 7.24 - 6.93 (m, 14H), 6.85 - 6.72 (m, 2H), 4.93 (d, *J*=10.1 Hz, 1H), 4.82 (d, *J*=10.5 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 162.46 (d, *J*=246.3 Hz, 1C), 142.65, 141.06, 136.35, 135.65, 135.58, 130.44, 129.06, 128.75, 128.16, 128.01, 127.48, 126.99, 126.32, 122.63, 122.36, 119.80, 119.57, 117.56, 115.79, 115.63, 111.45, 60.24, 49.30; MS (ESI-APCI) exact mass calculated for [M-SAr] ($C_{22}H_{18}N$) requires *m/z* 296.1, found *m/z* 296.1; $[\alpha]_D^{24}$ = +58.0 (c = 1.0, CH_2Cl_2).





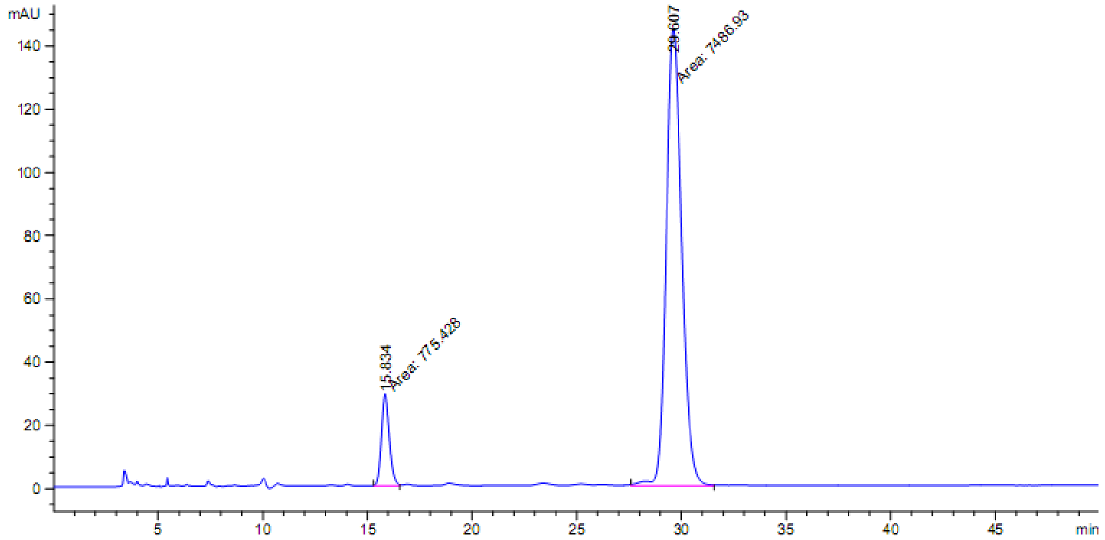
Racemic sample:



PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.069	15777943	513623	49.866	63.667
2	32.614	15862540	293112	50.134	36.333
Total		31640483	806735	100.000	100.000

Enantioenriched sample:



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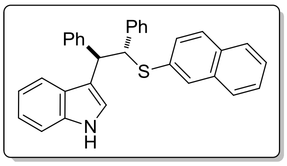
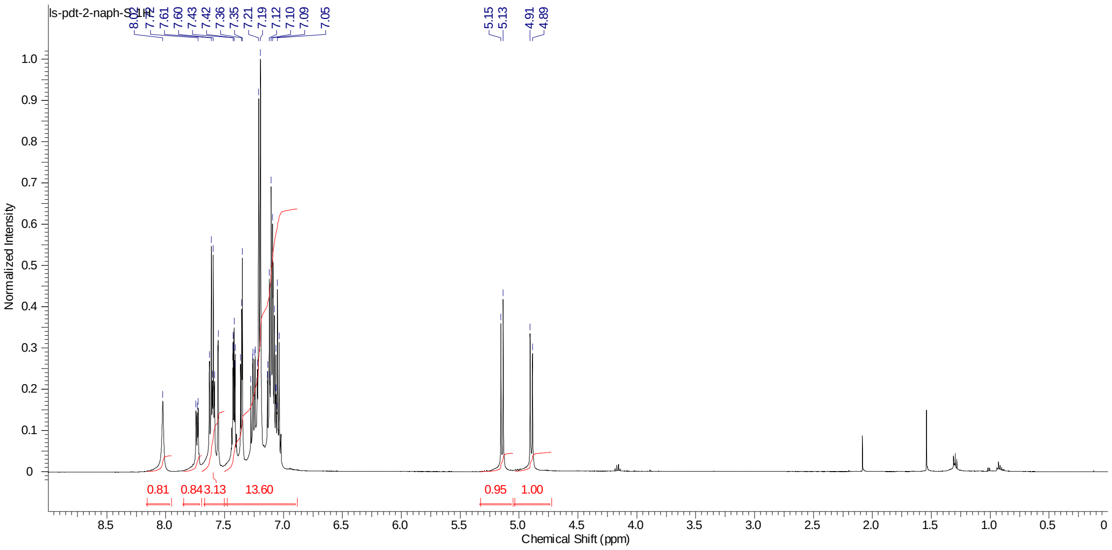
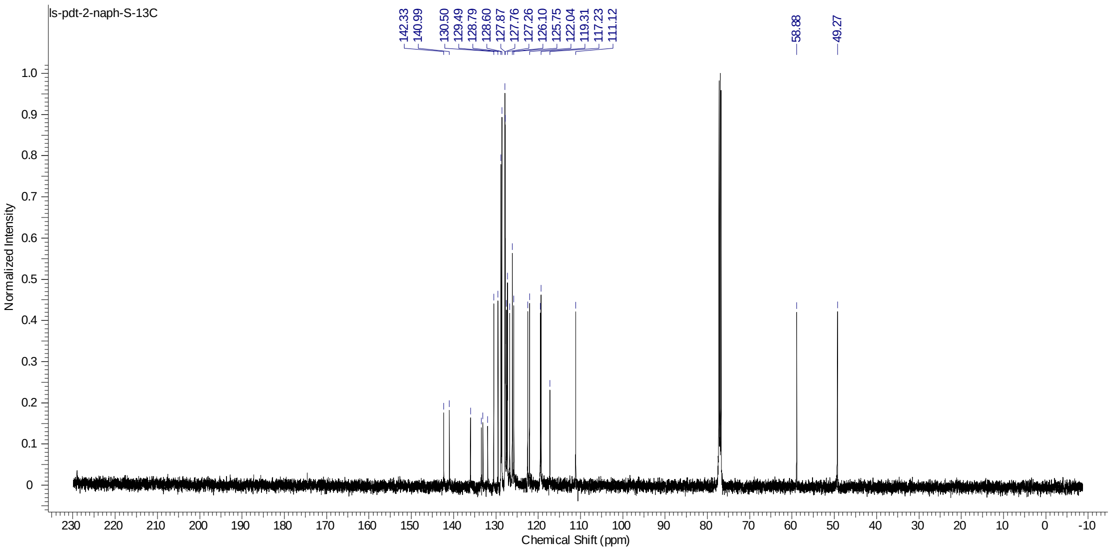
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  15.834 MM    0.4436  775.42773   29.13649   9.3851
   2  29.607 MM    0.8621 7486.93164  144.73430  90.6149
```



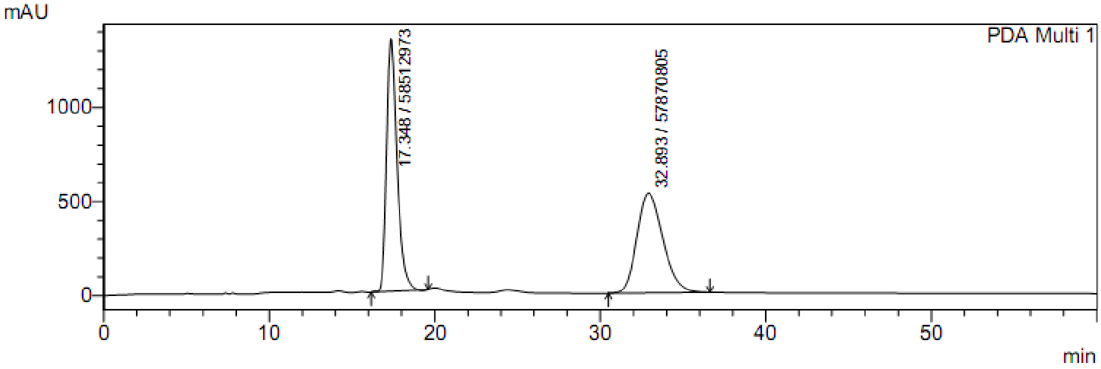
3-((1*R*,2*R*)-2-(naphthalen-2-ylthio)-1,2-diphenylethyl)-1*H*-indole (2e)

Followed method B from **1e** (25.0 mg, 0.05 mmol), for 63 h, and purified using silica gel chromatography to give 20.5 mg (90% yield) of **2e** as a white solid. This material was determined to be 88% ee by chiral HPLC analysis (ChiralPak AS-H, 10% *i*-PrOH, 1 mL/min, 220 nm, t_r(major) = 16 min, t_r(minor) = 31 min). IR (Film): 3422 (s), 3055, 1585, 1491, 1454 (s), 1337, 1098, 1073, 907 (s), 813, 738 (s), 697 (s) cm^{-1}; ^{1}H NMR: (500 MHz, CDCl$_3$) δ 8.02 (br. s., 1H), 7.88 - 7.68 (m, 1H), 7.68 - 7.52 (m, 3H), 7.52 - 7.39 (m, 2H), 7.39 - 7.31 (m, 2H), 7.31 - 7.17 (m, 5H), 7.17 - 6.93 (m, 6H), 5.14 (d, *J*=9.8 Hz, 1H), 4.90 (d, *J*=9.8 Hz, 1H); ^{13}C NMR: (125 MHz, CDCl$_3$) δ 142.33, 140.99, 136.01, 133.43, 133.06, 131.94, 130.50, 129.49, 128.79, 128.60, 127.87, 127.80, 127.76, 127.50, 127.30, 127.26, 126.72, 126.10, 126.08, 125.75, 122.47, 122.04, 119.49, 119.31, 117.23, 111.12, 58.88, 49.27; MS (ESI-APCI) exact mass calculated for [M-SAr] ($C_{22}H_{18}N$) requires *m/z* 296.1, found *m/z* 296.1; $[\alpha]_D^{24}$ = +40.9 (c = 1.0, CH_2Cl_2).





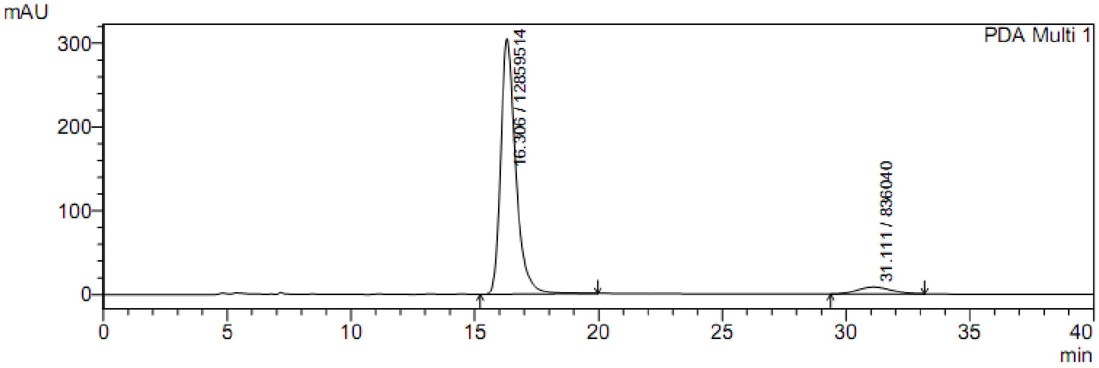
Racemic sample:



PDA Ch1 220nm 4nm

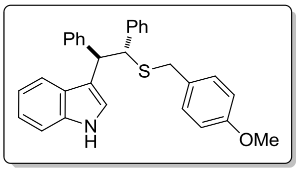
Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.348	58512973	1342223	50.276	71.677
2	32.893	57870805	530380	49.724	28.323
Total		116383778	1872604	100.000	100.000

Enantioenriched sample:



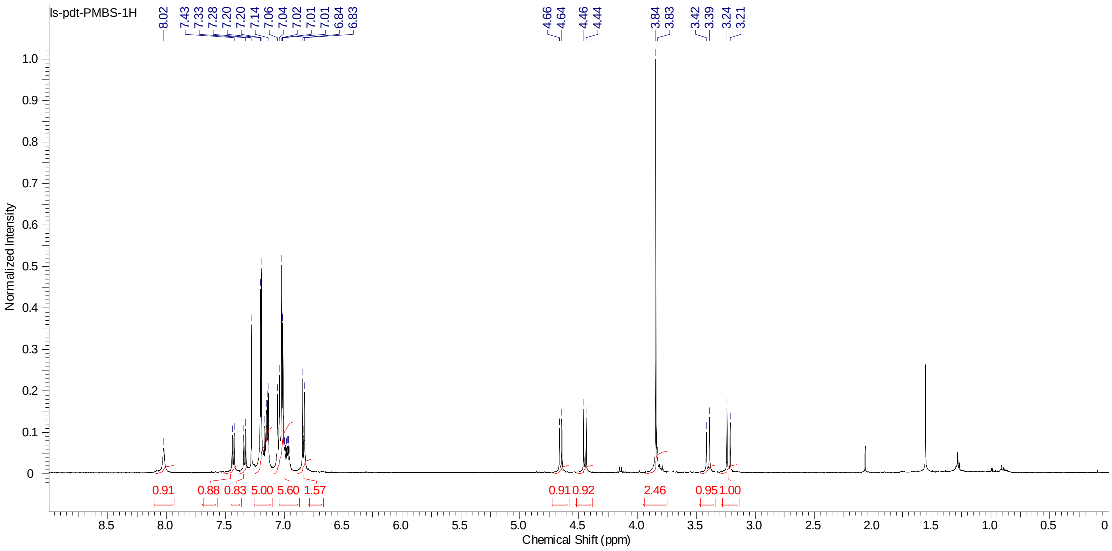
PDA Ch1 220nm 4nm

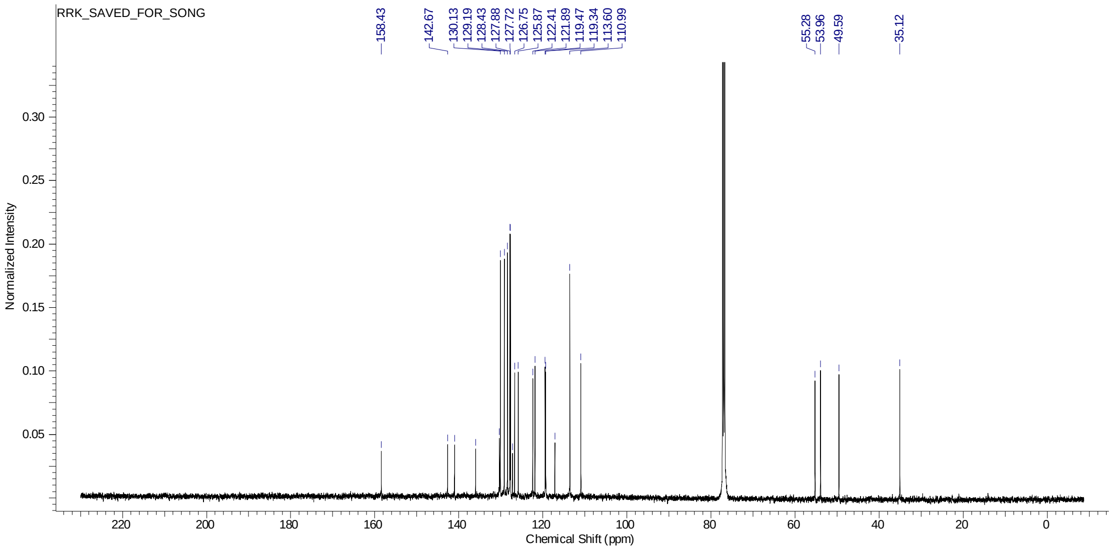
Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.306	12859514	305249	93.896	97.243
2	31.111	836040	8654	6.104	2.757
Total		13695554	313902	100.000	100.000



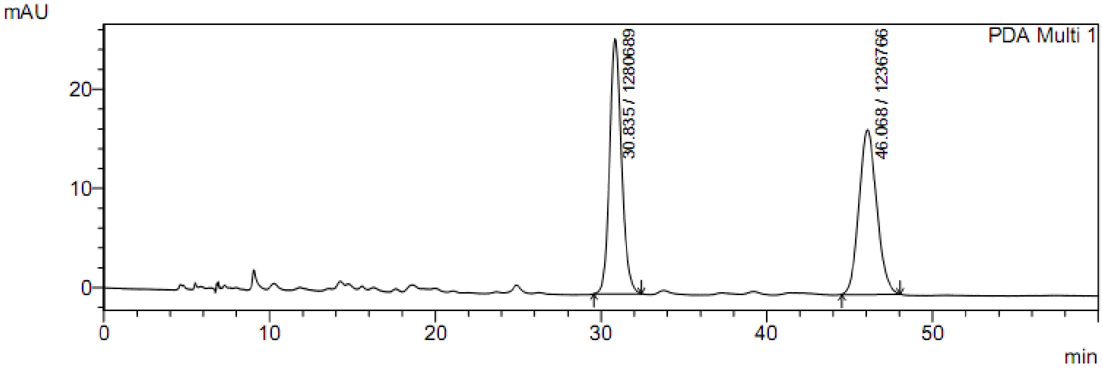
3-((1*R*,2*R*)-((4-methoxybenzyl)thio)-1,2-diphenylethyl)-1*H*-indole (2f)

Followed method B from **1f** (24.7 mg, 0.05 mmol), for 45 h, purified using silica gel chromatography to give 22.7 mg (>99% yield) of **2f** as a colorless gel. This material was determined to be 94% ee by chiral HPLC analysis (ChiralPak AD-H, 10% *i*-PrOH, 1 mL/min, 240 nm, t_r(major) = 30 min, t_r(minor) = 45 min). IR (Film): 3420 (s), 3027, 2910, 1609, 1510 (s), 1454, 1249 (s), 1175, 1032, 741 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.02 (br. s., 1H), 7.43 (d, *J*=8.2 Hz, 1H), 7.33 (d, *J*=8.2 Hz, 1H), 7.25 - 7.10 (m, 7H), 7.09 - 6.92 (m, 8H), 6.89 - 6.77 (m, 2H), 4.65 (d, *J*=10.5 Hz, 1H), 4.45 (d, *J*=10.1 Hz, 1H), 3.84 (s, 3H), 3.40 (d, *J*=13.7 Hz, 1H), 3.23 (d, *J*=13.3 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 158.43, 142.67, 141.02, 136.02, 130.34, 130.13, 129.19, 128.43, 127.88, 127.72, 127.26, 126.75, 125.87, 122.41, 121.89, 119.47, 119.34, 117.18, 113.60, 110.99, 55.28, 53.96, 49.59, 35.12; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{30}H_{28}NOS$) requires *m/z* 450.2, found *m/z* 450.2; $[\alpha]_D^{23}$ = +134.5 (c = 0.4, CH_2Cl_2).





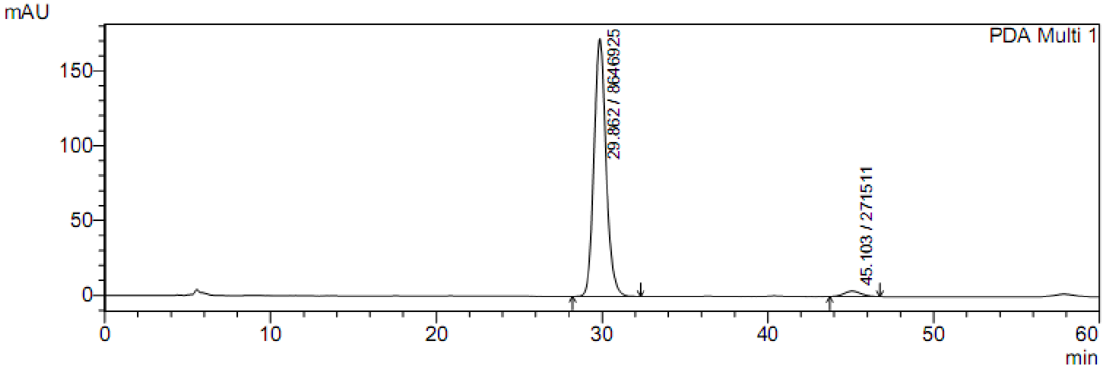
Racemic sample:



PDA Ch1 240nm 4nm

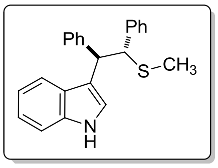
Peak#	Ret. Time	Area	Height	Area %	Height %
1	30.835	1280689	25745	50.872	60.772
2	46.068	1236766	16618	49.128	39.228
Total		2517455	42362	100.000	100.000

Enantioenriched sample:



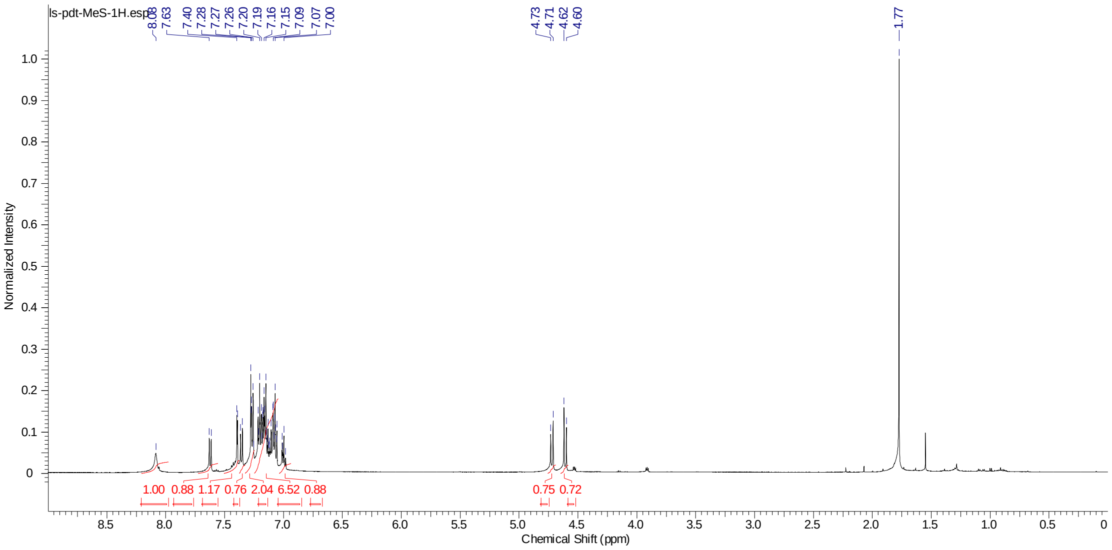
PDA Ch1 240nm 4nm

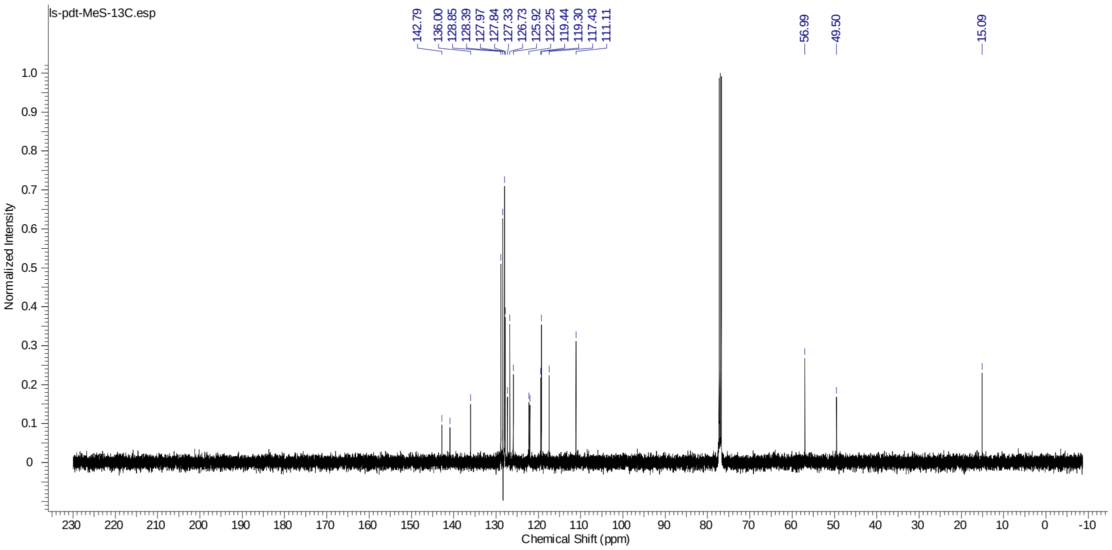
Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.862	8646925	172159	96.956	97.860
2	45.103	271511	3765	3.044	2.140
Total		8918435	175924	100.000	100.000



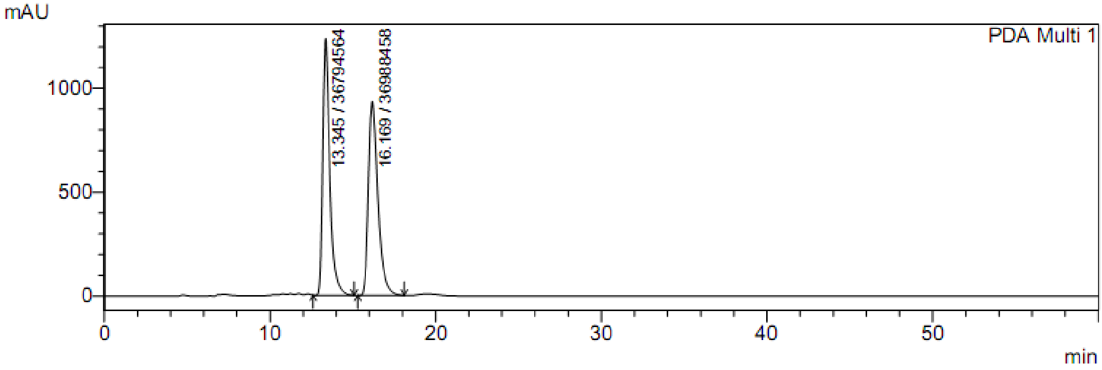
3-((1*R*,2*R*)-2-(methylthio)-1,2-diphenylethyl)-1*H*-indole (2g)

Followed method B from **1g** (19.4 mg, 0.25 mmol), for 45 h, and purified using silica gel chromatography to give 12.3 mg (72% yield) of **2g** as a colorless gel. This material was determined to be 84% ee by chiral HPLC analysis (ChiralPak AS-H, 10% *i*-PrOH, 1 mL/min, 220 nm, t_r(major) = 14 min, t_r(minor) = 17 min). IR (Film): 3419 (s), 3027, 2913, 1714, 1600, 1490, 1454 (s), 1420, 1337, 1276, 1098, 1012, 740 (s), 697 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.08 (br. s., 1H), 7.62 (d, *J*=8.2 Hz, 1H), 7.39 (d, *J*=2.7 Hz, 1H), 7.36 (d, *J*=7.8 Hz, 1H), 7.33 - 7.25 (m, 2H), 7.25 - 7.05 (m, 9H), 7.04 - 6.94 (m, 1H), 4.72 (d, *J*=10.5 Hz, 1H), 4.61 (d, *J*=10.1 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 142.79, 140.89, 136.00, 128.85, 128.39, 127.97, 127.84, 127.33, 126.73, 125.92, 122.25, 122.00, 119.44, 119.30, 117.43, 111.11, 56.99, 49.50, 15.09; MS (ESI-APCI) exact mass calculated for [M-SMe] ($C_{22}H_{18}N$) requires *m/z* 296.1, found *m/z* 296.1; $[\alpha]_D^{24}$ = +39.7 (c = 0.62, CH_2Cl_2).





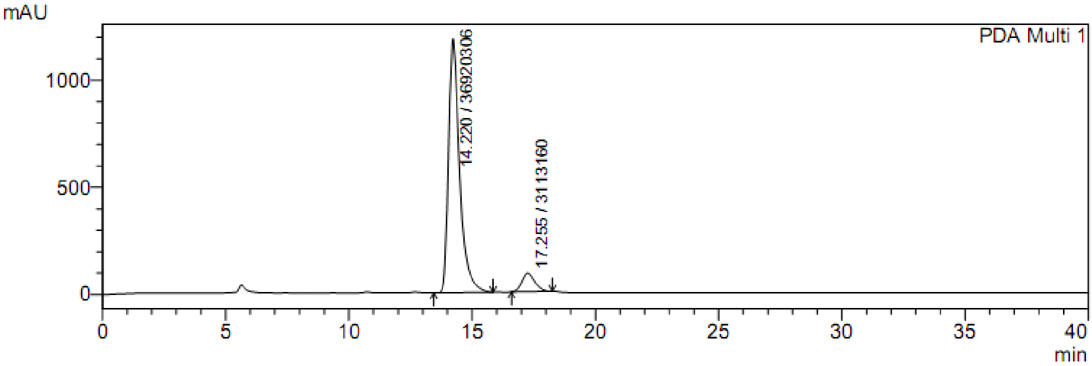
Racemic sample:



PDA Ch1 220nm 4nm

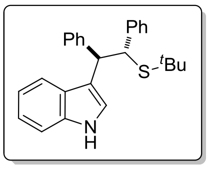
Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.345	36794564	1234936	49.869	56.924
2	16.169	36988458	934504	50.131	43.076
Total		73783021	2169440	100.000	100.000

Enantioenriched sample:



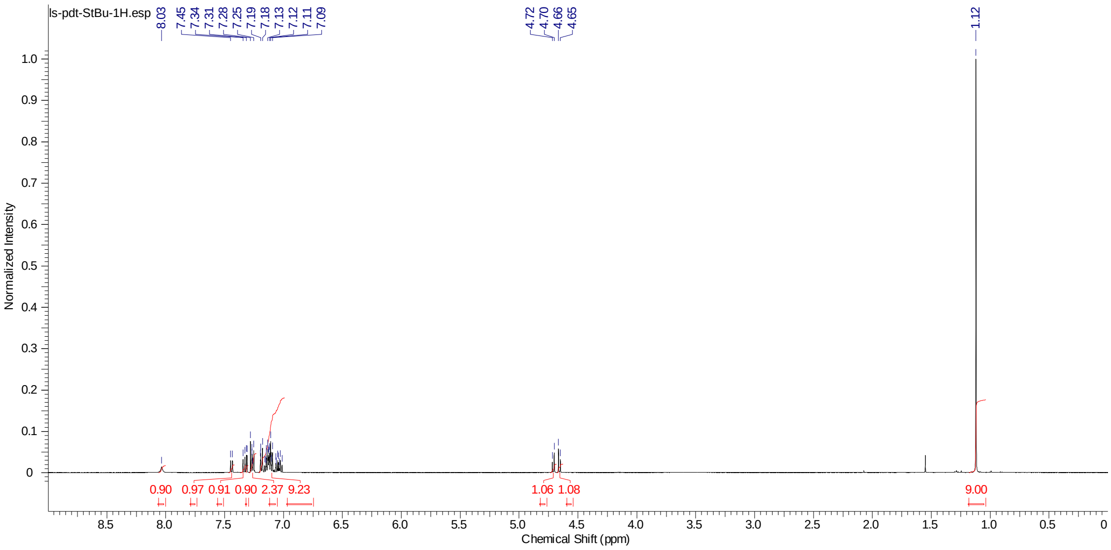
PDA Ch1 220nm 4nm

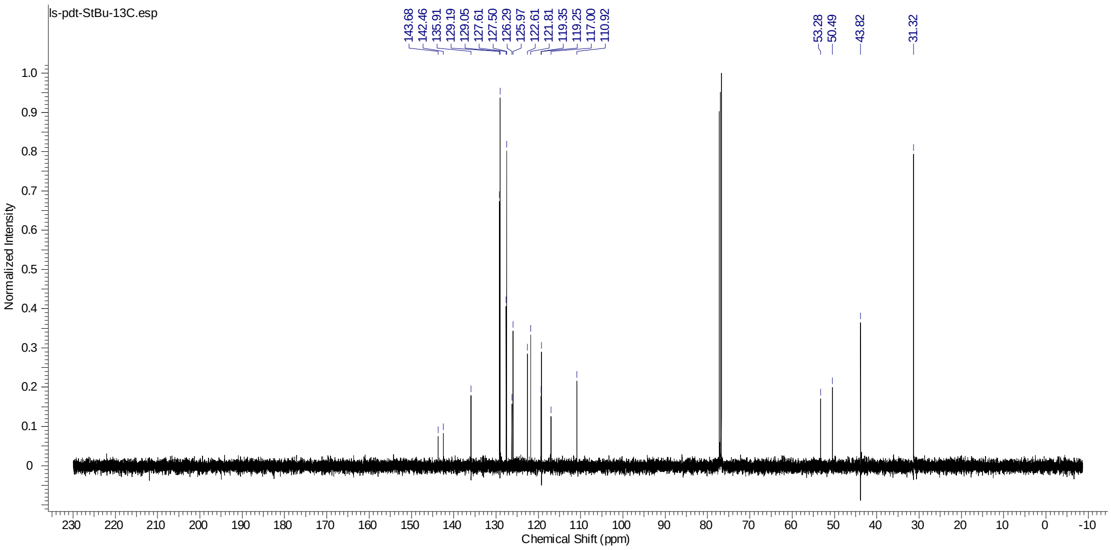
Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.220	36920306	1183736	92.224	93.232
2	17.255	3113160	85937	7.776	6.768
Total		40033466	1269673	100.000	100.000



3-((1*R*,2*R*)-2-(tert-butylthio)-1,2-diphenylethyl)-1*H*-indole (2h)

Followed method B from **1h** (21.5 mg, 0.05 mmol), for 45 h, and purified using silica gel chromatography to give 17.2 mg (89% yield) of **2h** as a colorless gel. This material was determined to be 87% ee by chiral HPLC analysis (ChiralPak AD-H, 5% *i*-PrOH, 1 mL/min, 300 nm, t_r(major) = 9 min, t_r(minor) = 10 min). IR (Film): 3419 (s), 3026, 2960, 1600, 1491, 1455 (s), 1363, 1161, 1098, 909 (s), 738 (s), 697 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.03 (br. s., 1H), 7.44 (d, *J*=7.8 Hz, 1H), 7.34 (d, *J*=8.2 Hz, 1H), 7.31 (d, *J*=2.3 Hz, 1H), 7.29 - 7.23 (m, 2H), 7.21 - 6.99 (m, 10H), 4.71 (d, *J*=7.8 Hz, 1H), 4.66 (d, *J*=7.8 Hz, 1H), 1.12 (s, 9H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 143.68, 142.46, 135.91, 129.19, 129.05, 127.61, 127.50, 126.29, 125.97, 122.61, 121.81, 119.35, 119.25, 117.00, 110.92, 53.28, 50.49, 43.82, 31.32; MS (ESI-APCI) exact mass calculated for [M-S^{t}Bu] ($C_{22}H_{18}N$) requires *m/z* 296.1, found *m/z* 296.1; $[\alpha]_D^{25}$ = +2.9 (c = 0.1, CH_2Cl_2).





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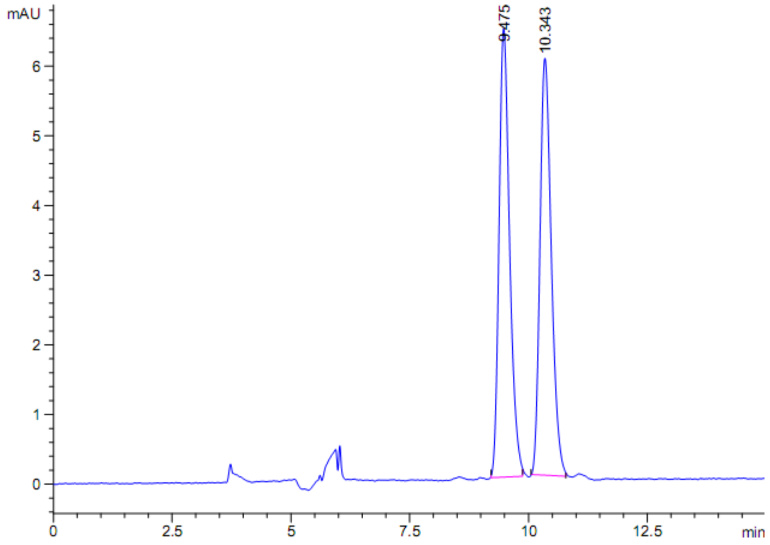

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Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   9.475 BB    0.2364   99.76691    6.45246  50.0814
   2  10.343 BB    0.2516   99.44263    5.99192  49.9186
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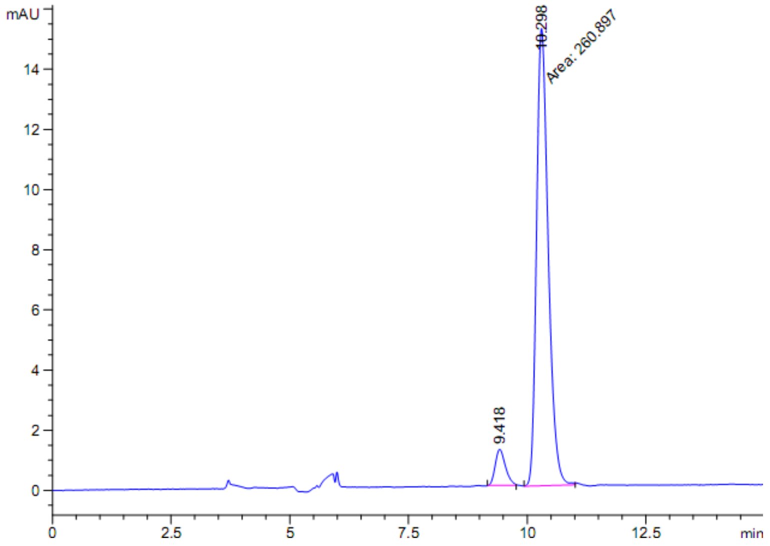
Enantioenriched sample:



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Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   9.418 BB    0.2278   18.20502    1.20843   6.5227
   2  10.298 MM    0.2859  260.89713   15.20989  93.4773
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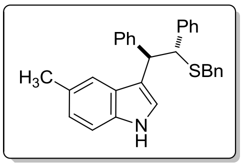
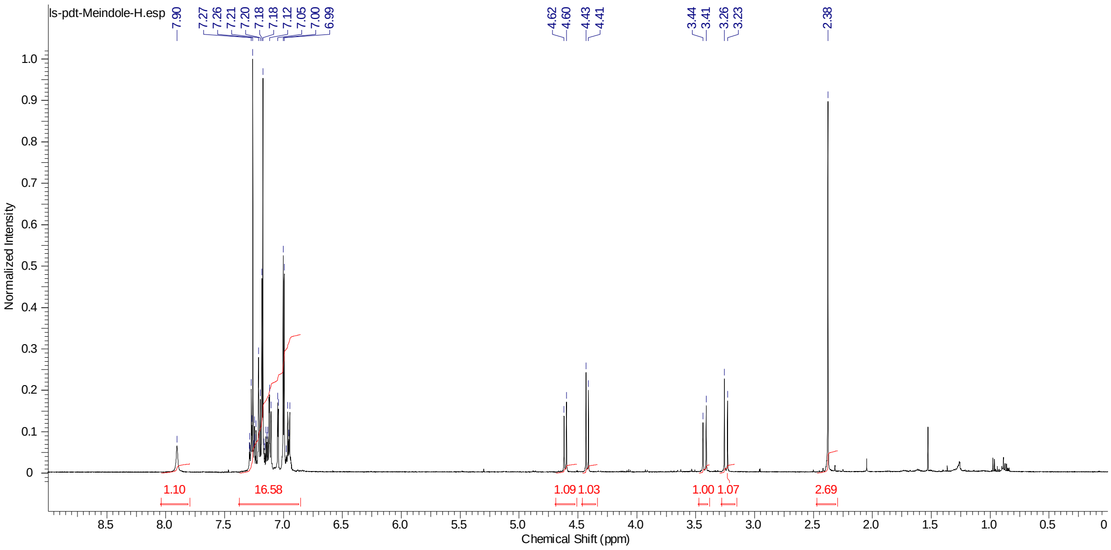
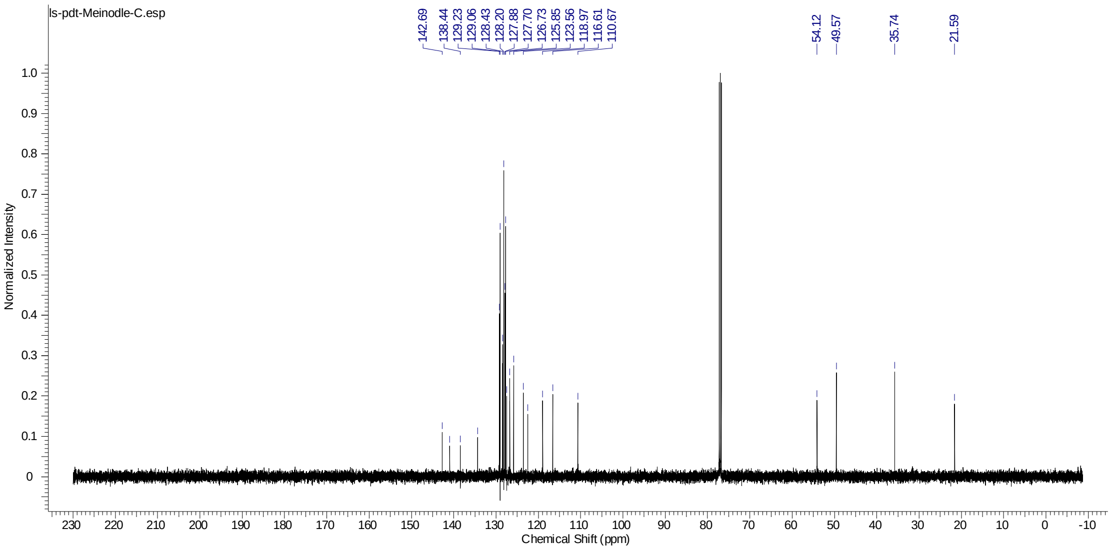


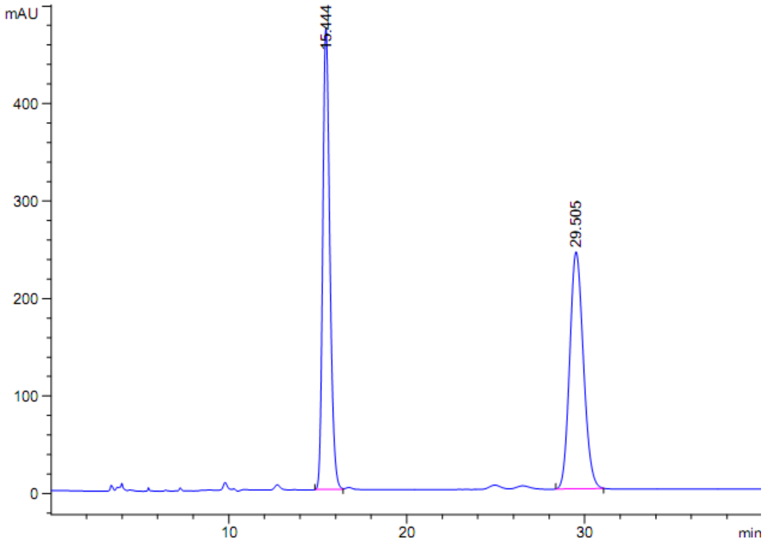
3-((1*R*,2*R*)-2-(benzylthio)-1,2-diphenylethyl)-5-methyl-1*H*-indole (2i)

Followed method B from **1a** (23.2 mg, 0.05 mmol), for 40 h, and purified using silica gel chromatography to give 20.3 mg (97% yield) of **2i** as a colorless gel. This material was determined to be 91% ee by chiral HPLC analysis (ChiralPak AD-H, 10% *i*-PrOH, 1 mL/min, 230 nm, t_r(major) = 15 min, t_r(minor) = 30 min). IR (Film): 3422 (s), 3026, 2914, 1492, 1452, 1098, 1072, 1029, 909, 696 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.90 (br. s., 1H), 7.31 - 7.08 (m, 12H), 7.05 (d, *J*=2.3 Hz, 1H), 7.02 - 6.86 (m, 5H), 4.61 (d, *J*=10.5 Hz, 1H), 4.42 (d, *J*=10.1 Hz, 1H), 3.42 (d, *J*=13.7 Hz, 1H), 3.24 (d, *J*=13.7 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 153.80, 142.61, 140.96, 138.43, 131.16, 129.19, 129.05, 128.40, 128.23, 127.93, 127.74, 126.81, 126.77, 125.90, 123.24, 116.80, 111.91, 111.61, 101.48, 55.80, 54.03, 49.47, 35.80; MS (ESI-APCI) exact mass calculated for [M-SBn] ($C_{23}H_{20}N$) requires *m/z* 310.2, found *m/z* 310.1; $[\alpha]_D^{23}$ = +137.7 (c = 1.0, CH_2Cl_2).





Racemic sample:



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Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  15.444 BB    0.4258 1.31458e4  473.62302  50.2057
   2  29.505 BB    0.8314 1.30381e4  243.23105  49.7943
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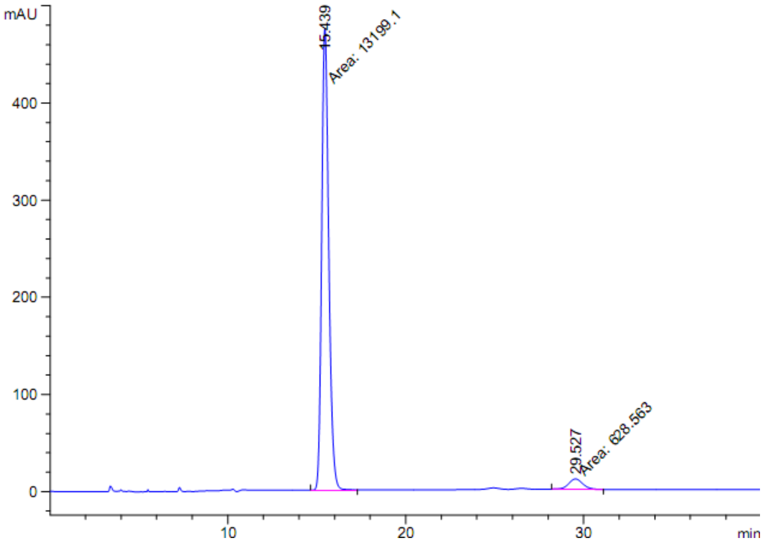
Enantioenriched sample:



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Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  15.439 MM    0.4625 1.31991e4  475.67935  95.4543
   2  29.527 MM    0.9583  628.56317  10.93136   4.5457
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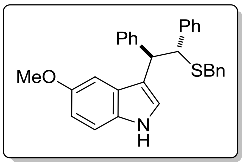
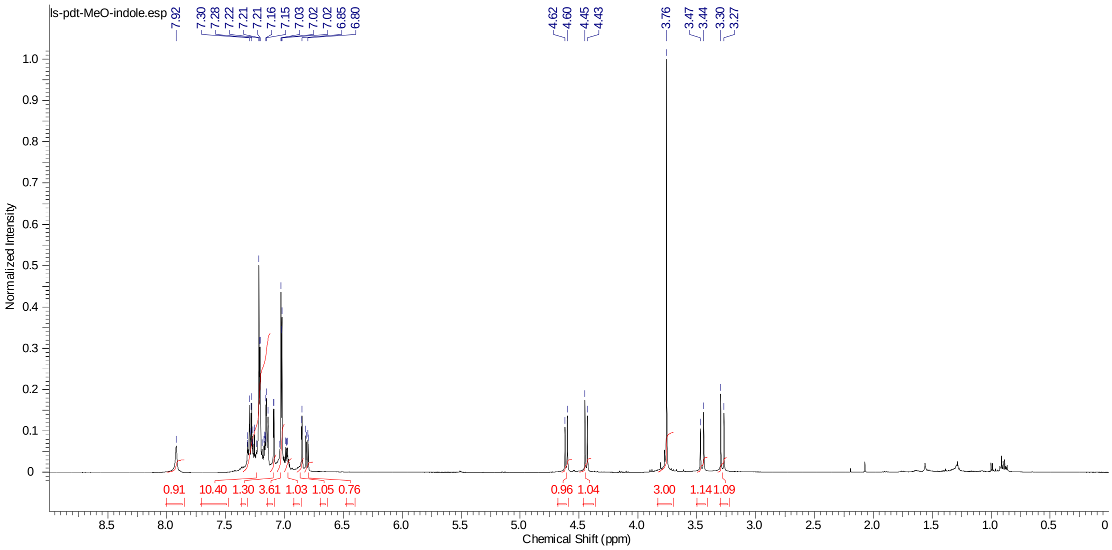
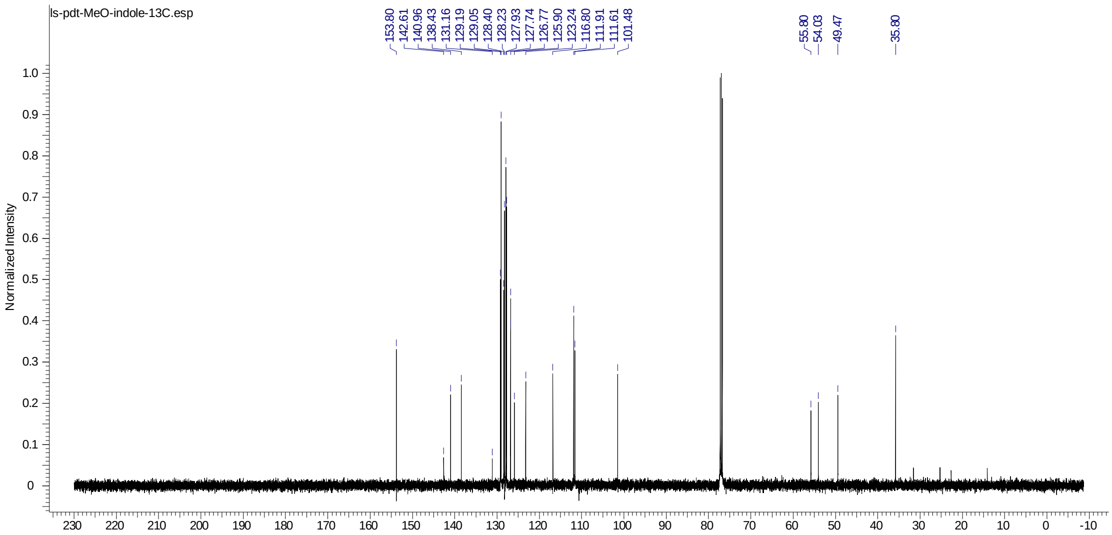


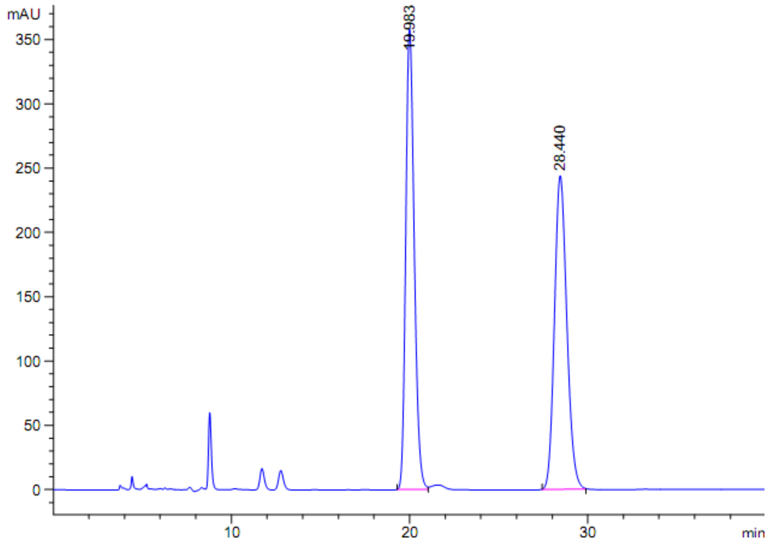
3-((1*R*,2*R*)-2-(benzylthio)-1,2-diphenylethyl)-5-methoxy-1*H*-indole (2j)

Followed method B from **1a** (23.2 mg, 0.05 mmol), for 40 h, and purified using silica gel chromatography to give 21.0 mg (93% yield) of **2j** as a colorless gel. This material was determined to be 93% ee by chiral HPLC analysis (ChiralPak AD-H, 15% *i*-PrOH, 1 mL/min, 230 nm, t_r(major) = 19 min, t_r(minor) = 27 min). IR (Film): 3421 (br), 3026, 2916, 1624, 1583, 1483, 1452 (s), 1208 (s), 1169, 1060, 1028, 929, 696 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.92 (br. s., 1H), 7.35 - 7.12 (m, 11H), 7.09 (d, *J*=2.4 Hz, 1H), 7.06 - 7.00 (m, 4H), 6.98 (dd, *J*=3.9, 4.9 Hz, 1H), 6.85 (d, *J*=2.4 Hz, 1H), 6.81 (dd, *J*=2.4, 8.8 Hz, 1H), 4.61 (d, *J*=10.3 Hz, 1H), 4.44 (d, *J*=9.8 Hz, 1H), 3.76 (s, 3H), 3.46 (d, *J*=13.7 Hz, 1H), 3.28 (d, *J*=13.7 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 153.80, 142.61, 140.96, 138.43, 131.16, 129.19, 129.05, 128.40, 128.23, 127.93, 127.74, 126.81, 126.77, 125.90, 123.24, 116.80, 111.91, 111.61, 101.48, 55.80, 54.03, 49.47, 35.80; MS (ESI-APCI) exact mass calculated for [M-SBn] ($C_{23}H_{20}NO$) requires *m/z* 326.2, found *m/z* 326.1; $[\alpha]_D^{24}$ = +155.4 (c = 1.0, CH_2Cl_2).





Racemic sample:



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Peak RetTime Type  Width     Area       Height     Area
 #    [min]        [min]   [mAU*s]      [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  19.983 BB    0.5118 1.18664e4  358.87903  50.1918
   2  28.440 BB    0.7468 1.17757e4  244.10435  49.8082
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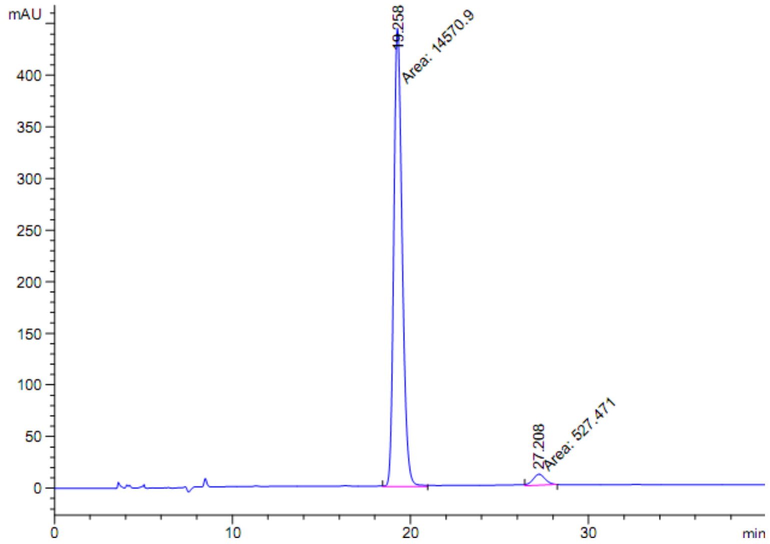
Enantioenriched sample:



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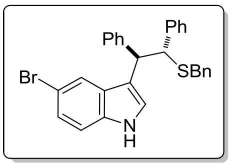
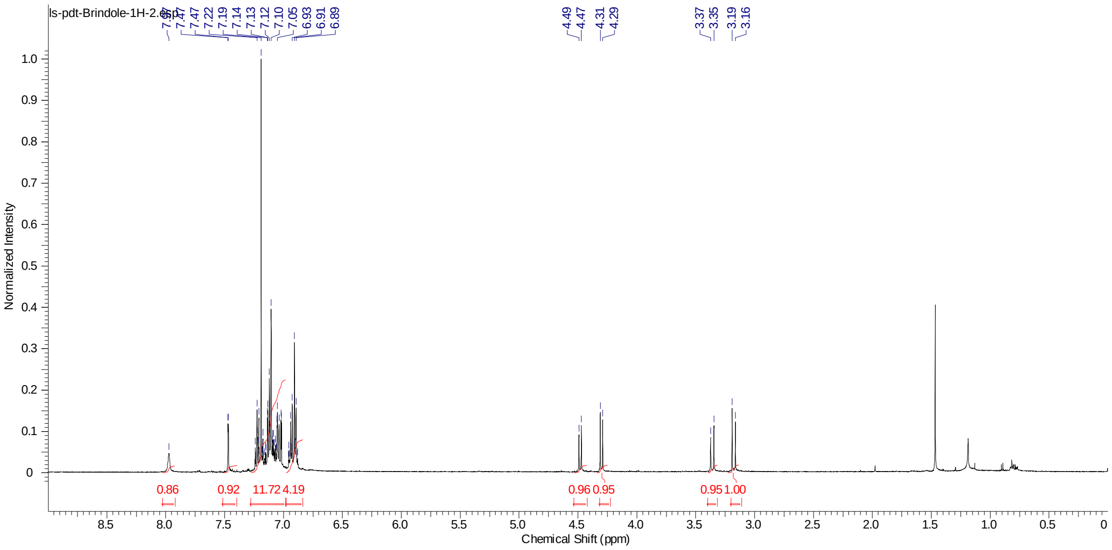
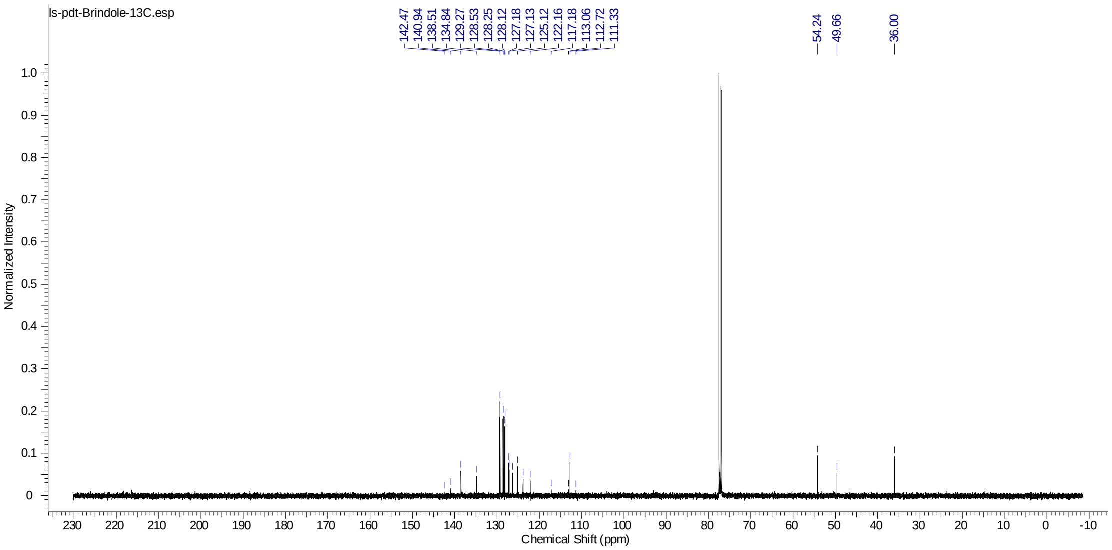


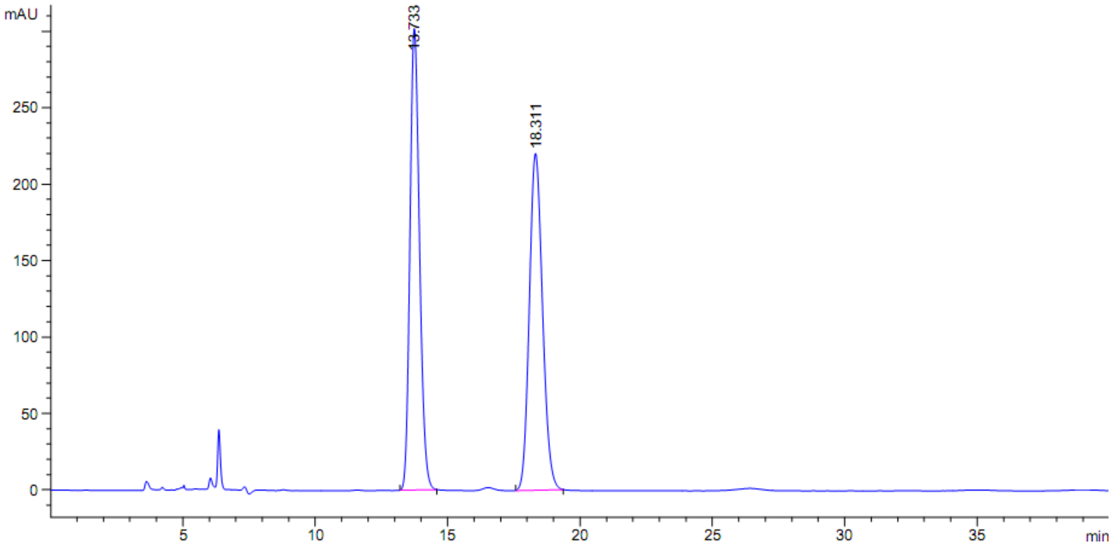
3-((1*R*,2*R*)-2-(benzylthio)-1,2-diphenylethyl)-5-bromo-1*H*-indole (2k)

Followed method B from **1a** (22.3 mg, 0.05 mmol), for 45 h, and purified using silica gel chromatography to give 20.8 mg (83% yield) of **2k** as a colorless gel. This material was determined to be 92% ee by chiral HPLC analysis (ChiralPak AD-H, 10% *i*-PrOH, 1 mL/min, 230 nm, t_r(major) = 14 min, t_r(minor) = 19 min). IR (Film): 3426 (s) 3027, 1492, 1453 (s), 1100, 909 (s) 727 (s), 696 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.97 (br. s., 1H), 7.47 (d, *J*=1.8 Hz, 1H), 7.24 - 7.00 (m, 14H), 6.98 - 6.83 (m, 4H), 4.48 (d, *J*=10.1 Hz, 1H), 4.30 (d, *J*=10.1 Hz, 1H), 3.36 (d, *J*=13.7 Hz, 1H), 3.18 (d, *J*=13.7 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 142.47, 140.94, 138.51, 134.84, 129.38, 129.27, 128.57, 128.53, 128.25, 128.12, 127.18, 127.13, 126.35, 125.12, 123.86, 122.16, 117.18, 113.06, 112.72, 111.33, 54.24, 49.66, 36.00; MS (ESI-APCI) exact mass calculated for [M-SBn] ($C_{27}H_{17}BrN$) requires *m/z* 374.1 and 376.1, found *m/z* 374.0 and 376.1; $[\alpha]_D^{25}$ = +96.4 (c = 1.0, CH_2Cl_2).





Racemic sample:



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Peak RetTime Type  Width     Area      Height     Area
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----|-------|----|-------|----------|----------|--------|
  1  13.733 BB    0.3870 7585.60254  302.04462  49.8001
  2  18.311 BB    0.5368 7646.50195  220.39206  50.1999
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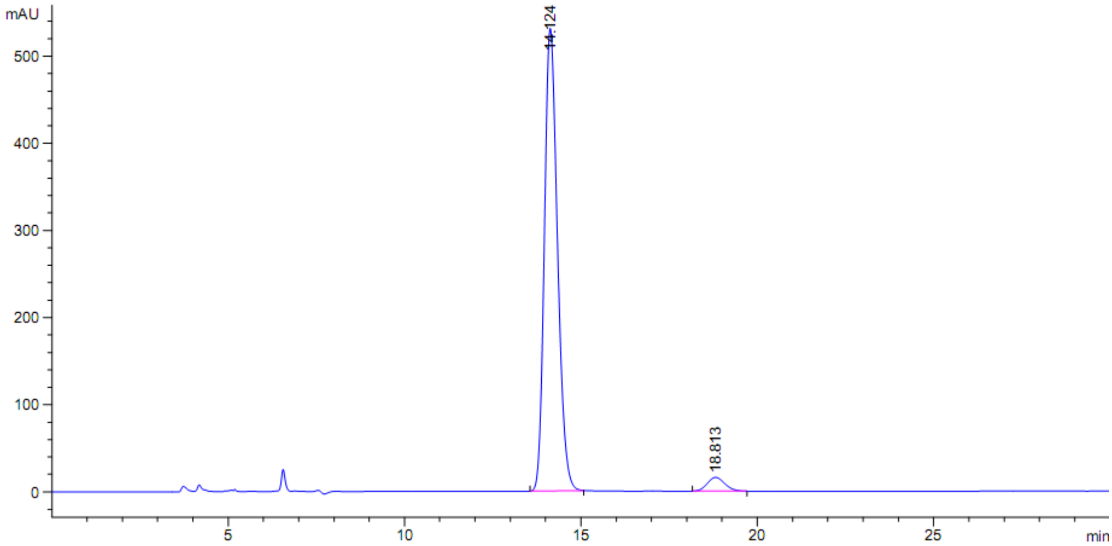
Enantioenriched sample:



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Peak RetTime Type  Width     Area      Height     Area
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----|-------|----|-------|----------|----------|--------|
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  2  18.813 BB    0.5280  553.57196   15.90586   3.8927
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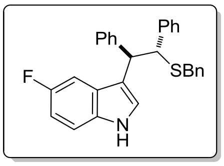
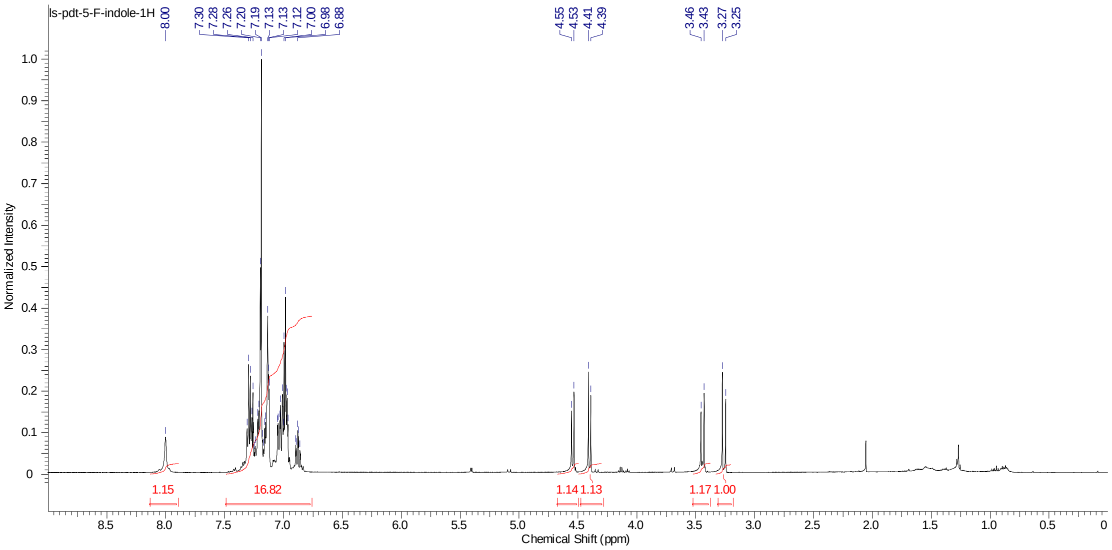
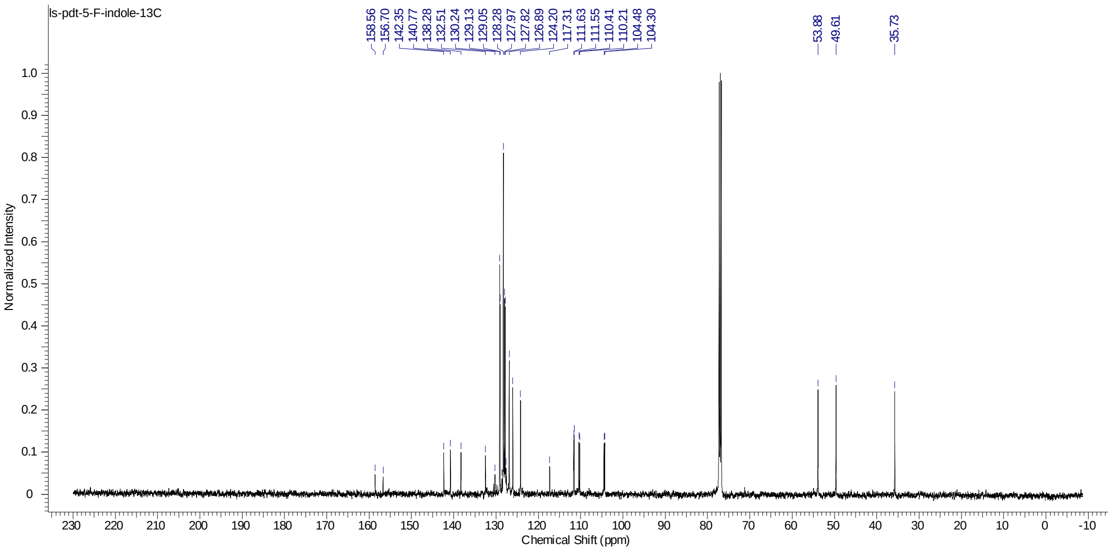


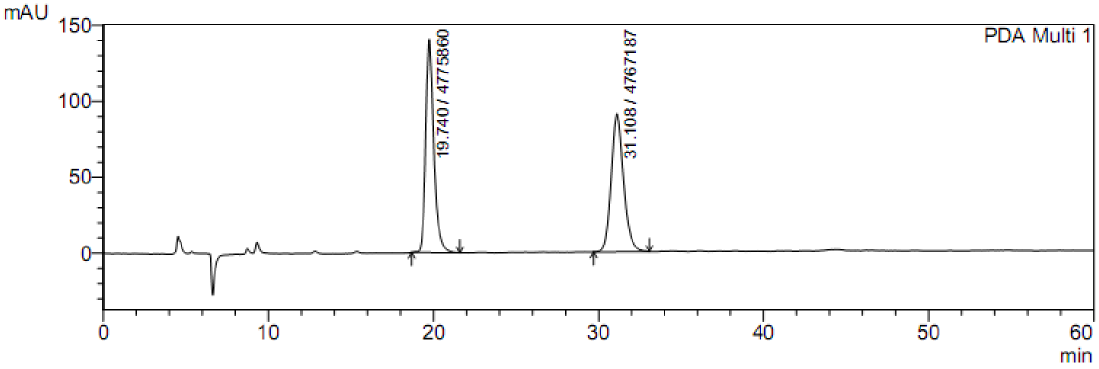
3-((1*R*,2*R*)-2-(benzylthio)-1,2-diphenylethyl)-5-fluoro-1*H*-indole (2l)

Followed method B from **1a** (23.2 mg, 0.05 mmol), for 45 h, and purified using silica gel chromatography to give 19.3 mg (88% yield) of **2l** as a colorless gel. This material was determined to be 95% ee by chiral HPLC analysis (ChiralPak AD-H, 10% *i*-PrOH, 1 mL/min, 205 nm, t_r(major) = 21 min, t_r(minor) = 33 min). IR (Film): 3425 (br), 3027, 2919, 1628, 1581, 1484 (s), 1452 (s), 1242, 1162 (s), 1029, 939, 848, 796, 695 (s) cm^{-1}; ^{1}H NMR: (500 MHz, CDCl$_3$) δ 8.00 (br. s., 1H), 7.35 - 7.11 (m, 12H), 7.09 - 6.93 (m, 6H), 6.93 - 6.76 (m, 1H), 4.54 (d, *J*=10.1 Hz, 1H), 4.40 (d, *J*=10.1 Hz, 1H), 3.44 (d, *J*=13.7 Hz, 1H), 3.26 (d, *J*=13.7 Hz, 1H); ^{13}C NMR: (125 MHz, CDCl$_3$) δ 157.54 (d, *J*=236.2 Hz, 1C), 142.35, 140.77, 138.28, 132.51, 130.24, 129.13, 129.05, 128.28, 127.97, 127.82, 127.62, 126.89, 126.86, 126.03, 124.19, 117.27, 111.63, 111.55, 110.41, 110.20, 104.48, 104.30, 53.87, 49.61, 35.73; MS (ESI-APCI) exact mass calculated for [M-SBn] ($C_{22}H_{17}FN$) requires *m/z* 314.1, found *m/z* 314.1; $[\alpha]_D^{23}$ = +103 (c = 1.0, CH_2Cl_2).





Racemic sample:



PDA Ch1 205nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
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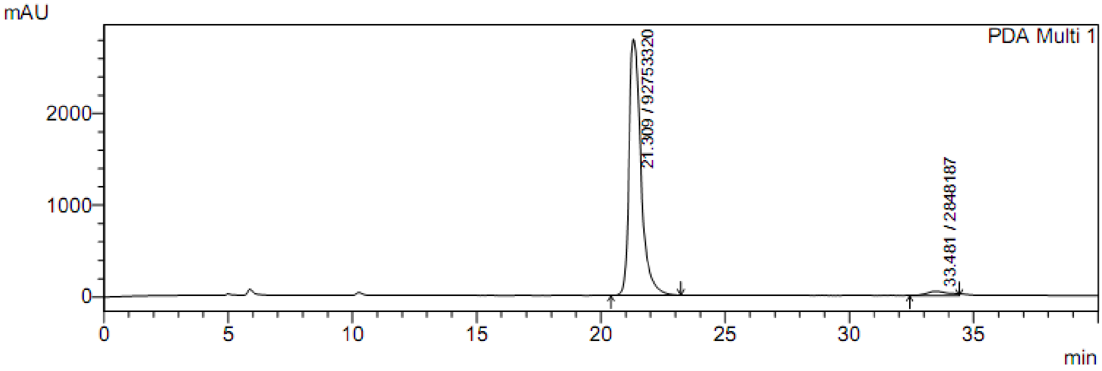
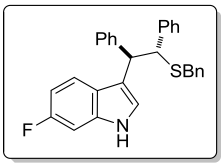
Enantioenriched sample:



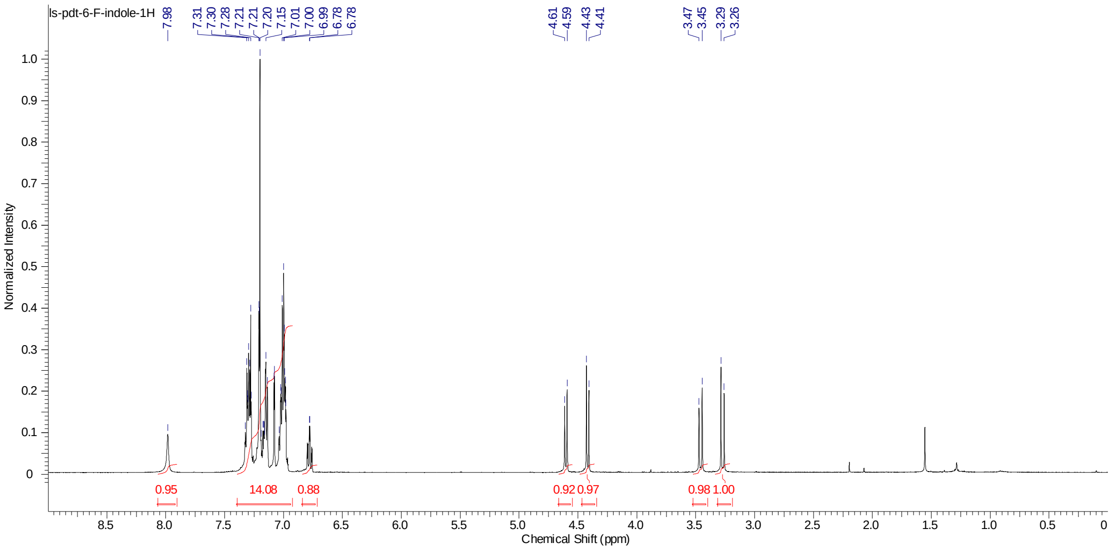
PDA Ch1 205nm 4nm

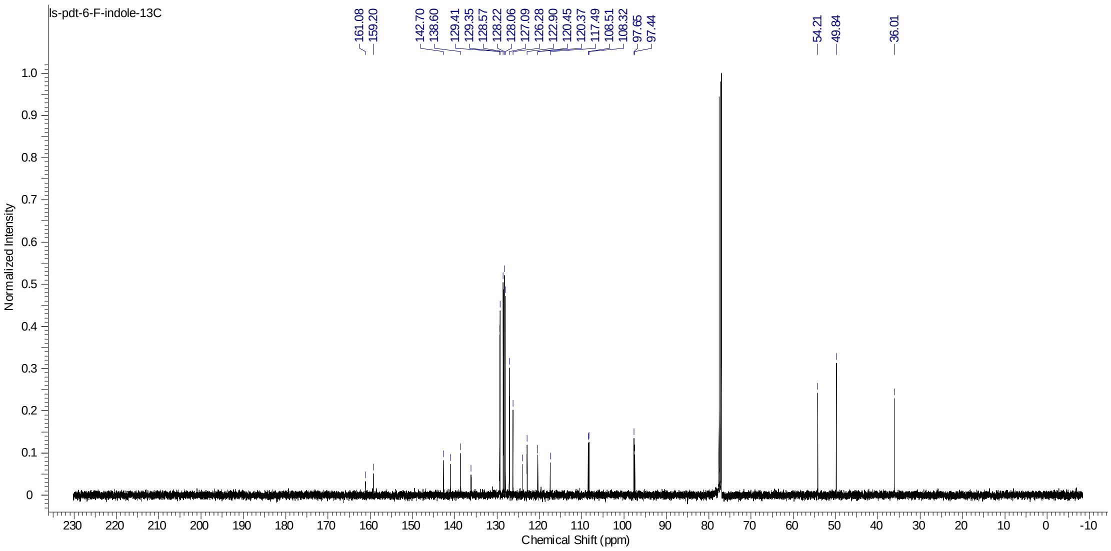
Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.309	92753320	2793174	97.021	98.399
2	33.481	2848187	45438	2.979	1.601
Total		95601507	2838612	100.000	100.000



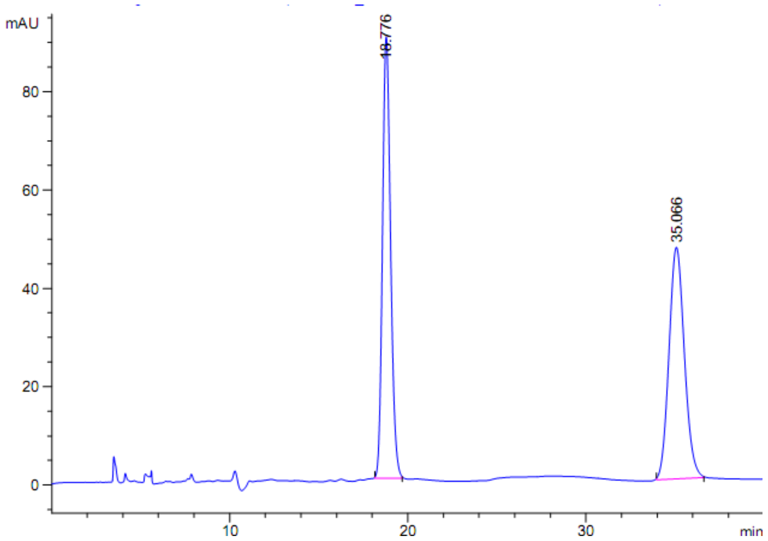
3-((1*R*,2*R*)-2-(benzylthio)-1,2-diphenylethyl)-6-fluoro-1*H*-indole (2m)

Followed method B from **1a** (23.2 mg, 0.25 mmol), for 43 h, and purified using silica gel chromatography to give 20.2 mg (92% yield) of **2m** as a colorless gel. This material was determined to be 85% ee by chiral HPLC analysis (ChiralPak AD-H, 10% *i*-PrOH, 1 mL/min, 230 nm, t_r(major) = 19 min, t_r(minor) = 36 min). IR (Film): 3425 (s), 3027, 2916, 1627, 1600, 1548, 1494 (s), 1453 (s), 1343, 1255, 1138, 909, 801, 697 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.98 (br. s., 1H), 7.39 - 7.24 (m, 4H), 7.24 - 7.11 (m, 7H), 7.11 - 6.93 (m, 7H), 6.84 - 6.71 (m, 1H), 4.60 (d, *J*=10.5 Hz, 1H), 4.42 (d, *J*=10.1 Hz, 1H), 3.46 (d, *J*=13.3 Hz, 1H), 3.27 (d, *J*=13.3 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 160.13 (d, *J*=236.2 Hz, 1C), 142.70, 141.05, 138.60, 136.21, 136.12, 129.41, 129.35, 128.57, 128.53, 128.22, 128.06, 127.14, 127.09, 126.28, 124.08, 122.93, 122.90, 120.45, 120.37, 117.49, 108.51, 108.32, 97.65, 97.44, 54.21, 49.84, 36.01; MS (ESI-APCI) exact mass calculated for [M-SBn] ($C_{22}H_{17}FN$) requires *m/z* 314.1, found *m/z* 314.1; $[\alpha]_D^{25}$ = +115 (c = 1.0, CH_2Cl_2).





Racemic sample:



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Peak RetTime Type  Width     Area      Height     Area
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----|-------|----|-------|----------|----------|--------|
   1  18.776 BB    0.4888 2839.37500   89.82629  50.1542
   2  35.066 BB    0.9190 2821.91846   47.10143  49.8458
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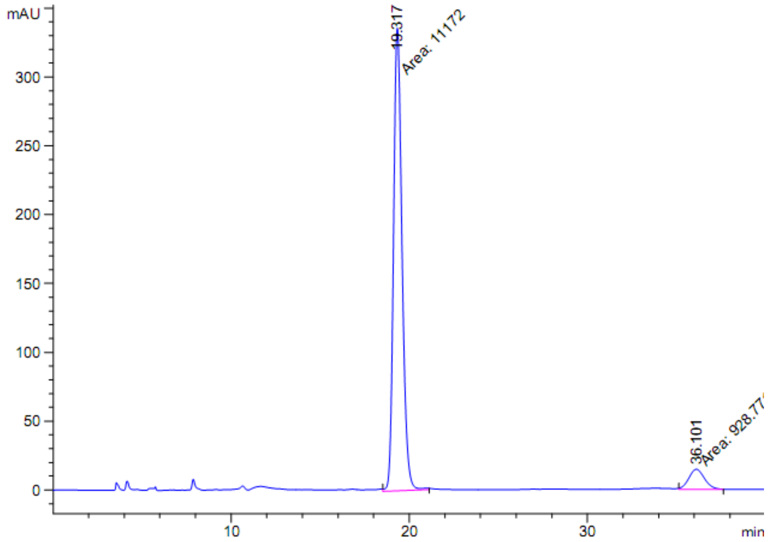
Enantioenriched sample:



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Peak RetTime Type  Width     Area      Height     Area
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----|-------|----|-------|----------|----------|--------|
   1  19.317 MM    0.5537 1.11720e4  336.29120  92.3247
   2  36.101 MM    1.0444  928.77069   14.82167   7.6753
```
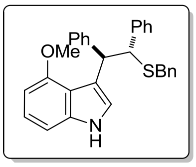
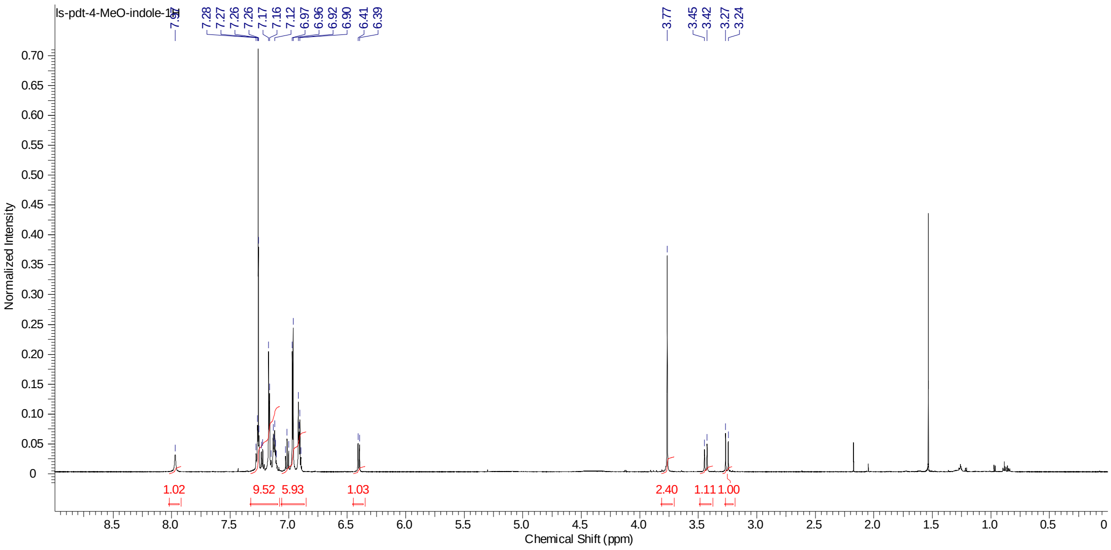
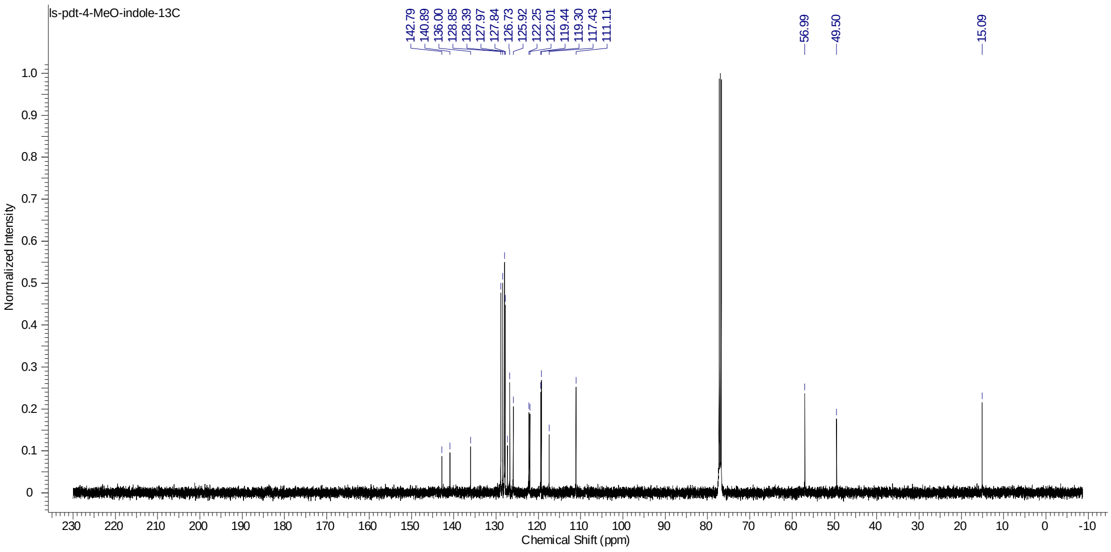



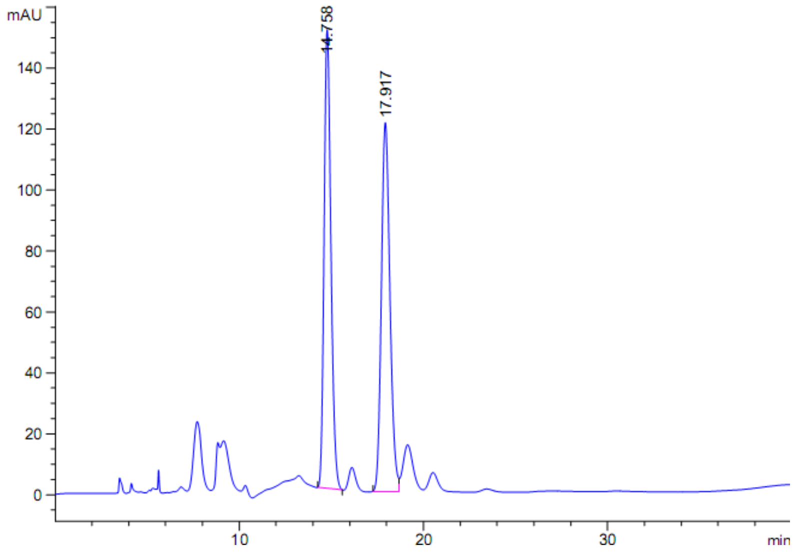
3-((1*R*,2*R*)-2-(benzylthio)-1,2-diphenylethyl)-4-methoxy-1*H*-indole (2n)

Followed method B from **1a** (23.2 mg, 0.05 mmol), for 43 h, and purified using silica gel chromatography to give 18.6 mg (83% yield) of **2n** as a colorless gel. This material was determined to be 91% ee by chiral HPLC analysis (ChiralPak AD-H, 10% *i*-PrOH, 1 mL/min, 230 nm, t_r(major) = 15 min, t_r(minor) = 19 min). IR (Film): 3422 (s), 3027, 2929, 1584, 1507, 1452, 1361, 1261 (s), 1091 (s) 1029, 732, 697 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.97 (br. s., 1H), 7.32 - 7.20 (m, 6H), 7.20 - 7.08 (m, 8H), 7.01 (s, 1H), 6.96 (s, 2H), 6.94 - 6.85 (m, 2H), 6.40 (d, *J*=7.9 Hz, 1H), 3.77 (s, 2H), 3.44 (d, *J*=13.8 Hz, 1H), 3.26 (d, *J*=13.8 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 142.79, 140.89, 136.00, 128.85, 128.39, 127.97, 127.84, 127.33, 126.73, 125.92, 122.25, 122.01, 119.44, 119.30, 117.43, 111.11, 56.99, 49.50, 15.09; MS (ESI-APCI) exact mass calculated for [M-SBn] ($C_{23}H_{20}NO$) requires *m/z* 326.2, found *m/z* 326.1; $[\alpha]_D^{25}$ = +162.8 (c = 1.0, CH_2Cl_2).





Racemic sample:



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Peak RetTime Type  Width     Area      Height     Area
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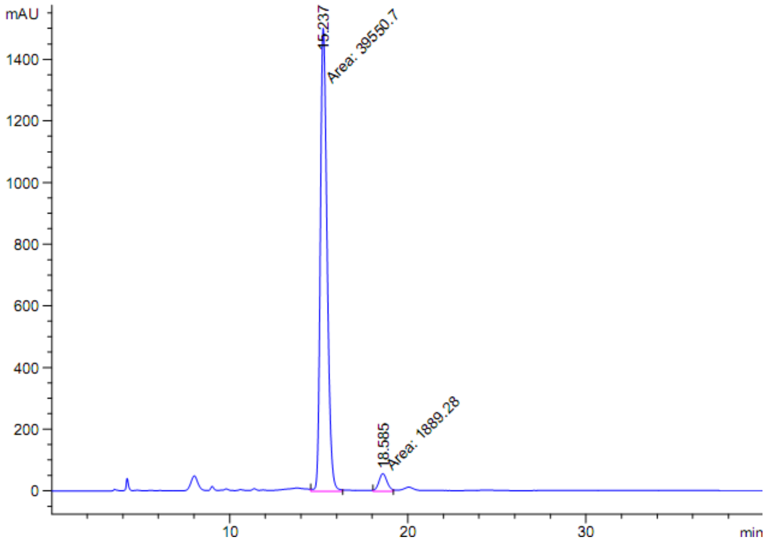
----|-------|----|-------|----------|----------|--------|
   1  14.758 BB    0.3964 3877.78442  150.61403  49.7003
   2  17.917 BV    0.4999 3924.55688  121.16393  50.2997
```

Enantioenriched sample:



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Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  15.237 MM    0.4385 3.95507e4 1503.13428  95.4409
   2  18.585 MM    0.5456 1889.28296  57.71386   4.5591
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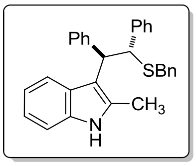
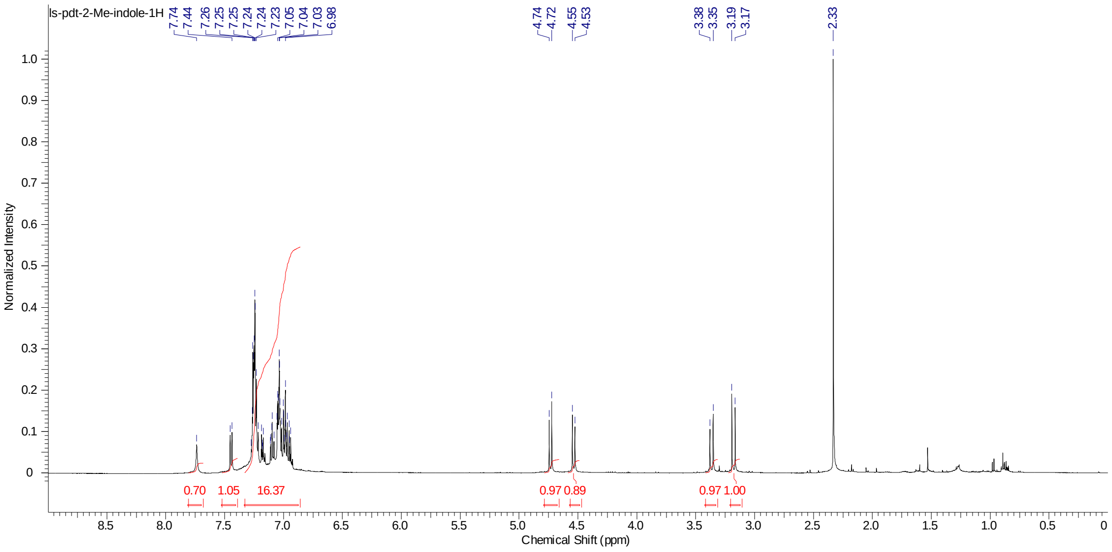
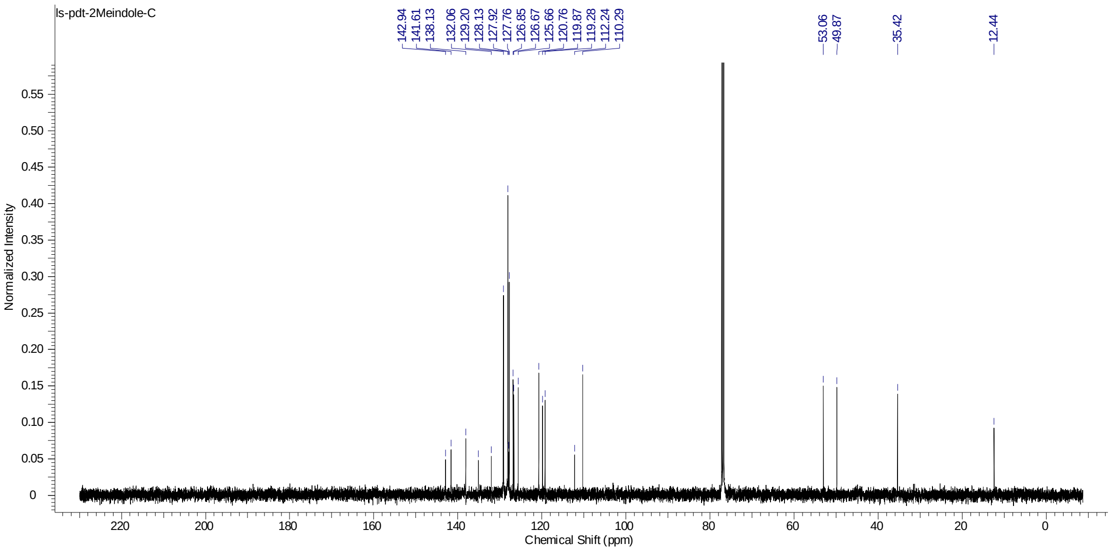


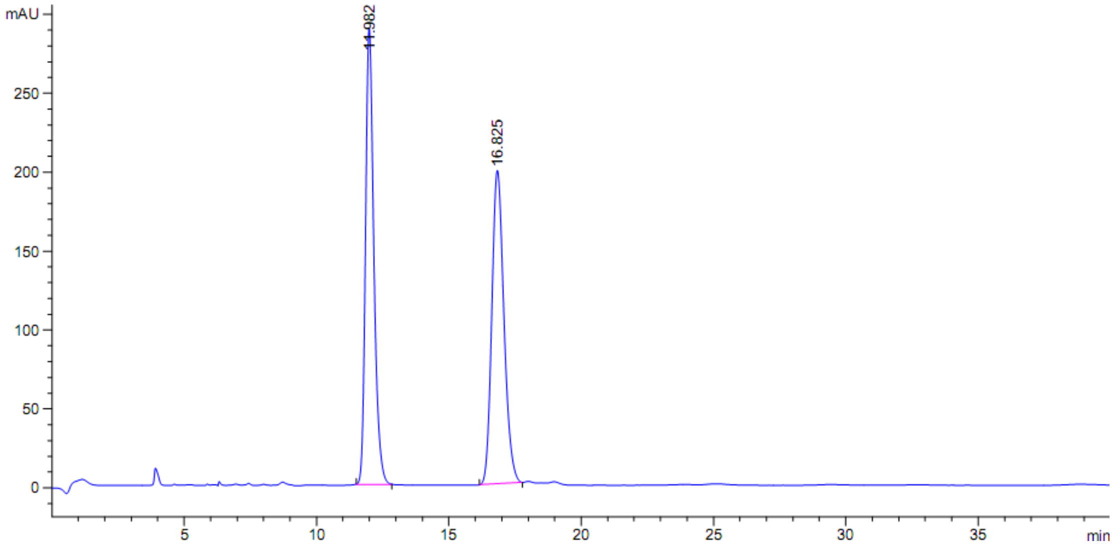
3-((1*R*,2*R*)-2-(benzylthio)-1,2-diphenylethyl)-2-methyl-1*H*-indole (2o)

Followed method B from **1a** (23.2 mg, 0.05 mmol), for 63 h, and purified using silica gel chromatography to give 20.5 mg (95% yield) of **2o** as a colorless gel. This material was determined to be 78% ee by chiral HPLC analysis (ChiralPak AD-H, 10% *i*-PrOH, 1 mL/min, 230 nm, t_r(major) = 12 min, t_r(minor) = 17 min). IR (Film): 3407 (br), 3026, 2972, 2921, 1492, 1453 (s), 1379, 1303, 1163, 950, 740, 697 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.74 (br. s., 1H), 7.44 (d, *J*=8.3 Hz, 1H), 7.37 - 7.14 (m, 9H), 7.14 - 6.90 (m, 9H), 4.73 (d, *J*=10.7 Hz, 1H), 4.54 (d, *J*=10.7 Hz, 1H), 3.37 (d, *J*=13.7 Hz, 1H), 3.18 (d, *J*=13.7 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 142.94, 141.60, 138.12, 135.14, 132.05, 129.19, 129.12, 128.12, 128.11, 128.07, 127.91, 127.75, 126.84, 126.67, 125.65, 120.75, 119.86, 119.27, 112.23, 110.29, 53.06, 49.86, 35.41, 12.44; MS (ESI-APCI) exact mass calculated for [M-SBn] ($C_{23}H_{20}N$) requires *m/z* 310.2, found *m/z* 310.1; $[\alpha]_D^{25}$ = +57.5 (c = 0.65, CH_2Cl_2).





Racemic sample:



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Peak RetTime Type  Width     Area      Height     Area
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----|-------|----|-------|----------|----------|--------|
   1  11.982 BB    0.3332 6328.65430  289.30783  50.0511
   2  16.825 BB    0.4890 6315.72803  198.62007  49.9489
```
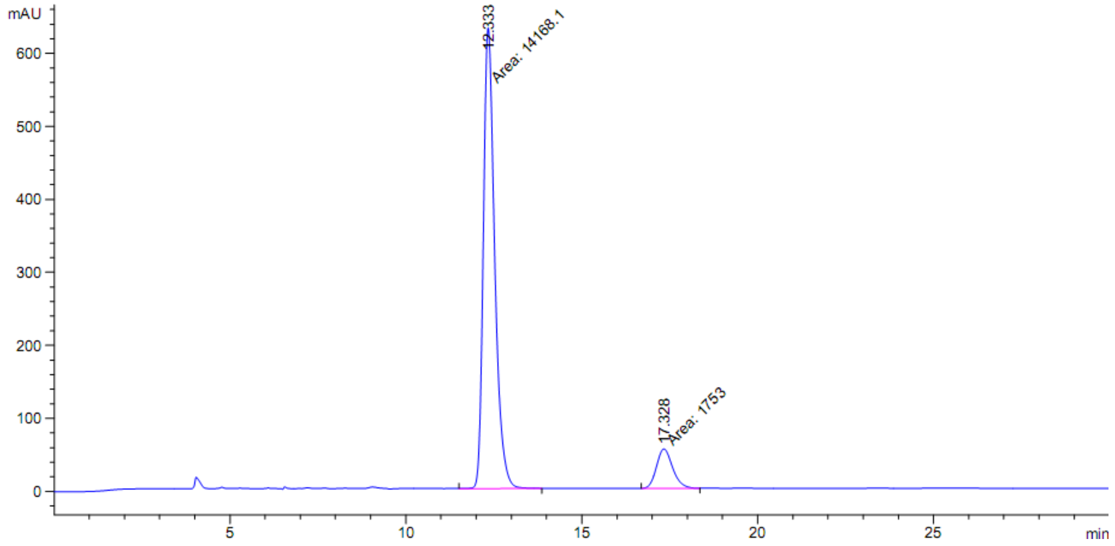

Enantioenriched sample:



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Peak RetTime Type  Width     Area      Height     Area
 #    [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  12.333 MM    0.3741 1.41681e4   631.17719  88.9894
   2  17.328 MM    0.5380 1753.00061   54.30894  11.0106
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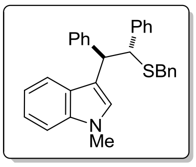
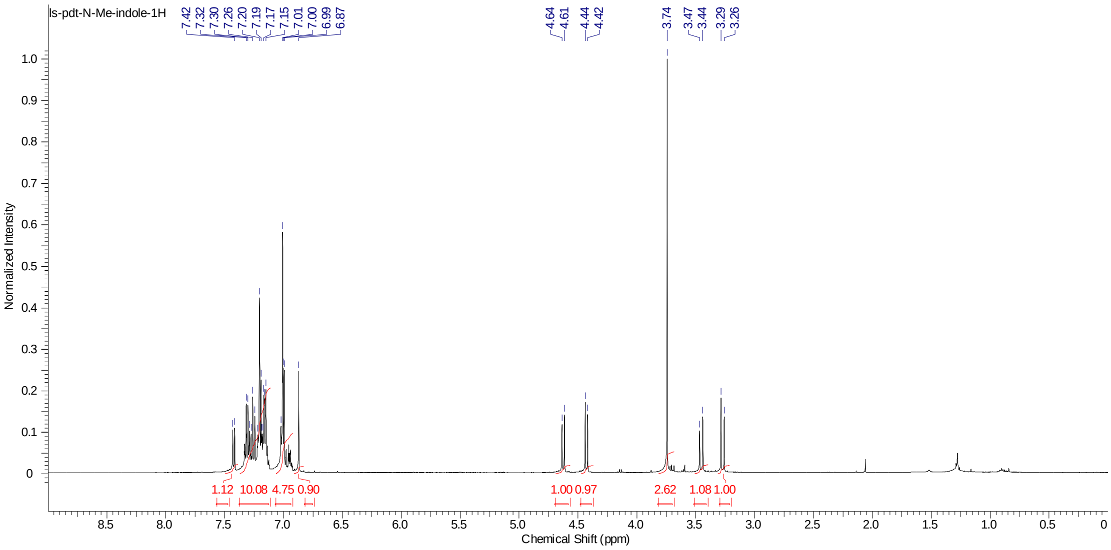
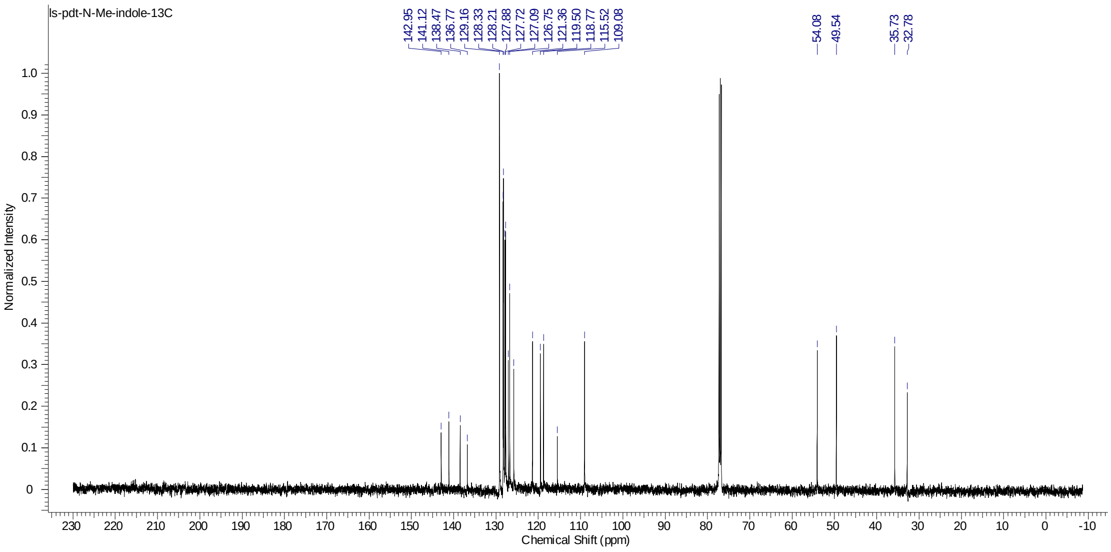


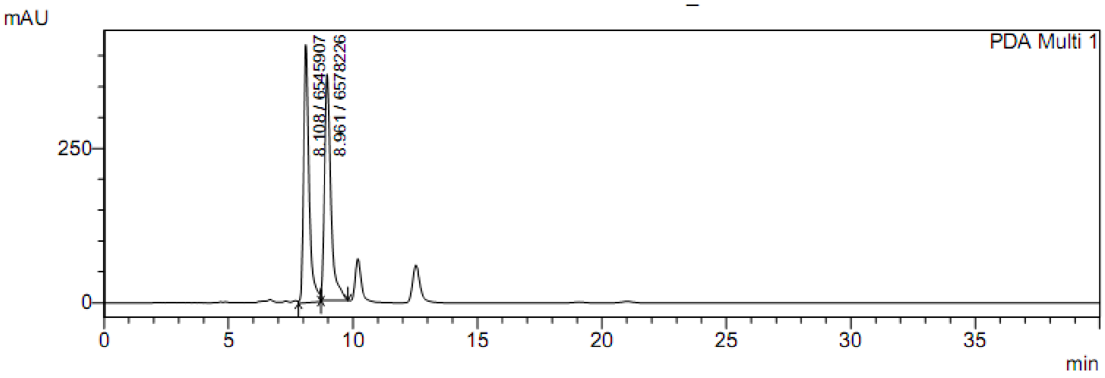
3-((1*R*,2*R*)-2-(benzylthio)-1,2-diphenylethyl)-1-methyl-1*H*-indole (2p)

Followed method B from **1a** (23.2 mg, 0.05 mmol), for 45 h, and purified using silica gel chromatography to give 11.8 mg (54% yield) of **2p** as a colorless gel. This material was determined to be 3% ee by chiral HPLC analysis (ChiralPak OD-H, 5% *i*-PrOH, 1 mL/min, 220 nm, t_r(major) = 9 min, t_r(minor) = 10 min). IR (Film): 3062, 2915, 1599, 1491, 1452, 1373, 1329, 1154, 1071, 1029, 735 (s), 697 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.42 (d, *J*=7.8 Hz, 1H), 7.36 - 7.12 (m, 12H), 7.06 - 6.92 (m, 6H), 6.87 (s, 1H), 4.62 (d, *J*=10.5 Hz, 1H), 4.43 (d, *J*=10.5 Hz, 1H), 3.74 (s, 3H), 3.45 (d, *J*=13.7 Hz, 1H), 3.27 (d, *J*=13.7 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 142.95, 141.12, 138.47, 136.77, 129.16, 128.33, 128.21, 127.88, 127.72, 127.68, 127.09, 126.75, 125.79, 121.36, 119.50, 118.77, 115.52, 109.08, 54.08, 49.54, 35.73, 32.78; MS (ESI-APCI) exact mass calculated for [M-SBn] ($C_{23}H_{20}N$) requires *m/z* 310.2, found *m/z* 310.2.





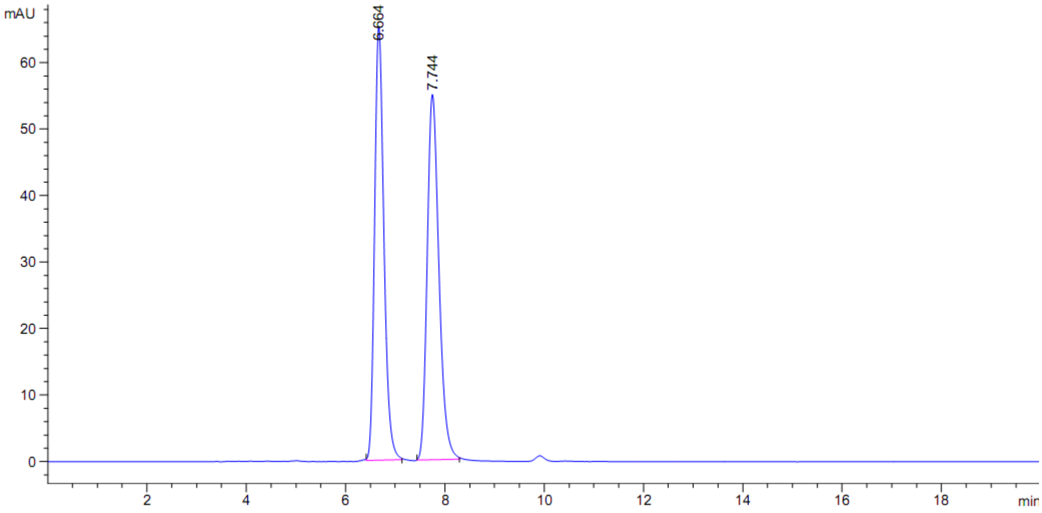
Racemic sample:



PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.108	6545907	417951	49.877	53.336
2	8.961	6578226	365664	50.123	46.664
Total		13124133	783616	100.000	100.000

Enantioenriched sample:



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Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.664 BB    0.1999  850.01630   65.27489  48.4316
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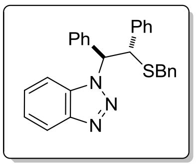
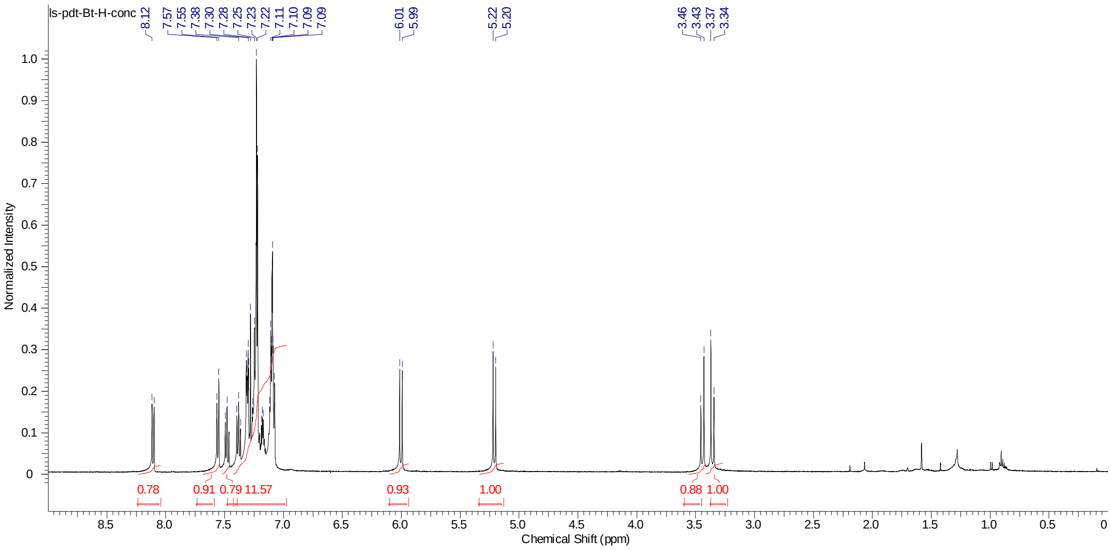
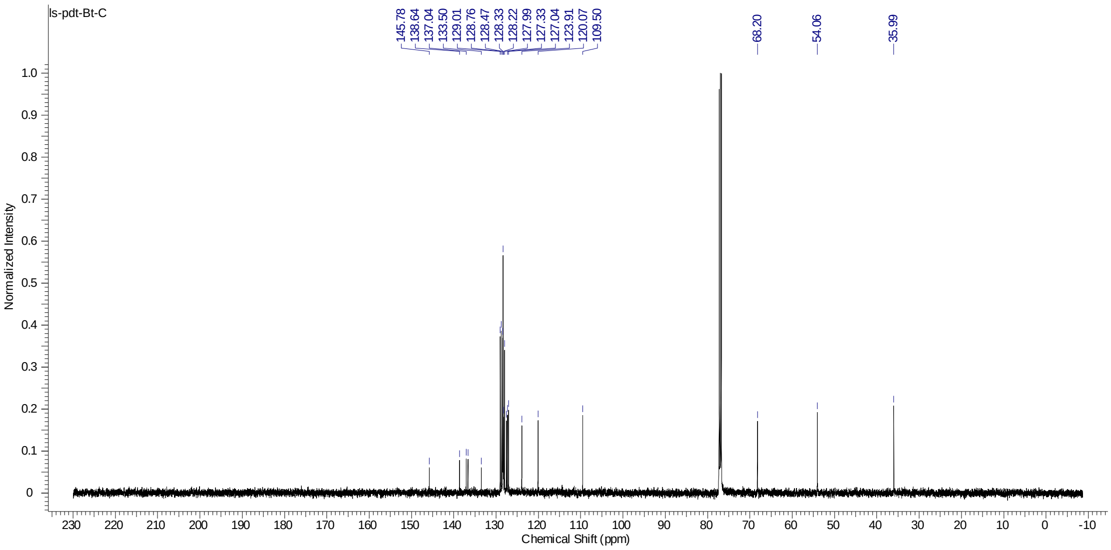
```



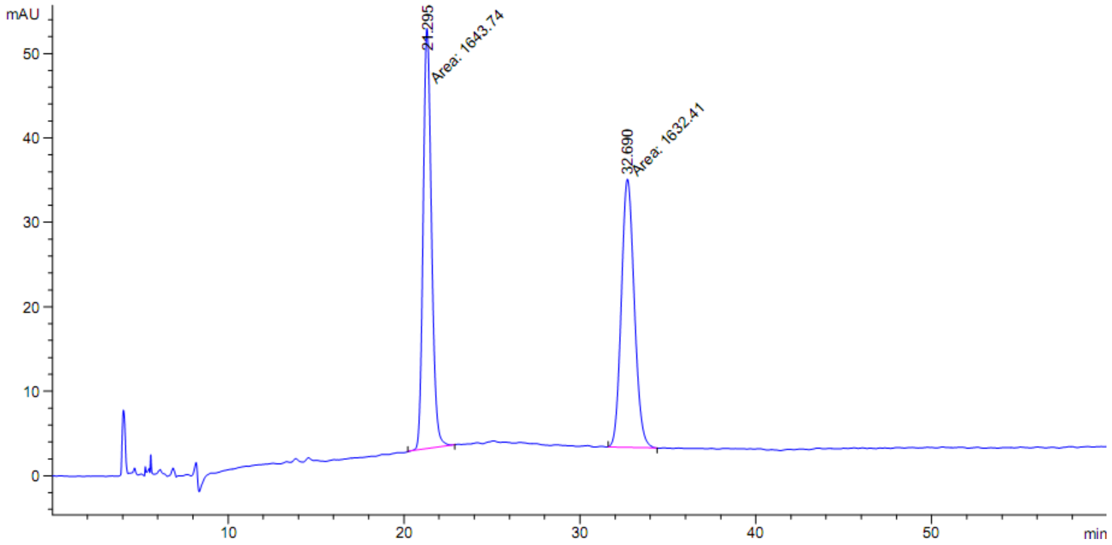
1-((1*S*,2*S*)-2-(benzylthio)-1,2-diphenylethyl)-1*H*-benzo[*d*][1,2,3]triazole (2q)

Followed method B from **1a** (22.3 mg, 0.05 mmol), for 63 h, and purified using silica gel chromatography to give 19.3 mg (92% yield) of **2q** as a colorless gel. This material was determined to be 80% ee by chiral HPLC analysis (ChiralPak AD-H, 15% *i*-PrOH, 1 mL/min, 230 nm, t_r(major) = 33 min, t_r(minor) = 21 min). IR (Film): 3029, 2923, 1492, 1452 (s), 1241, 1070, 910, 743, 723, 695 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.11 (d, *J*=8.2 Hz, 1H), 7.56 (d, *J*=8.2 Hz, 1H), 7.49 (d, *J*=7.3 Hz, 1H), 7.43 - 7.34 (m, 1H), 7.34 - 7.14 (m, 10H), 7.14 - 6.97 (m, 5H), 6.00 (d, *J*=11.4 Hz, 1H), 5.21 (d, *J*=11.4 Hz, 1H), 3.44 (d, *J*=13.3 Hz, 1H), 3.36 (d, *J*=13.3 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 145.78, 138.64, 137.04, 136.66, 133.50, 129.01, 128.76, 128.47, 128.33, 128.22, 127.99, 127.55, 127.33, 127.04, 123.91, 120.07, 109.50, 68.20, 54.06, 35.99; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{27}H_{24}N_3S$) requires *m/z* 422.1, found *m/z* 422.1; $[\alpha]_D^{25}$ = +74.2 (c = 0.6, CH_2Cl_2).





Racemic sample:



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Peak RetTime Type  Width     Area      Height     Area
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----|-------|----|-------|----------|----------|--------|
  1  21.295 MM    0.5504 1643.73926   49.77459  50.1729
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```
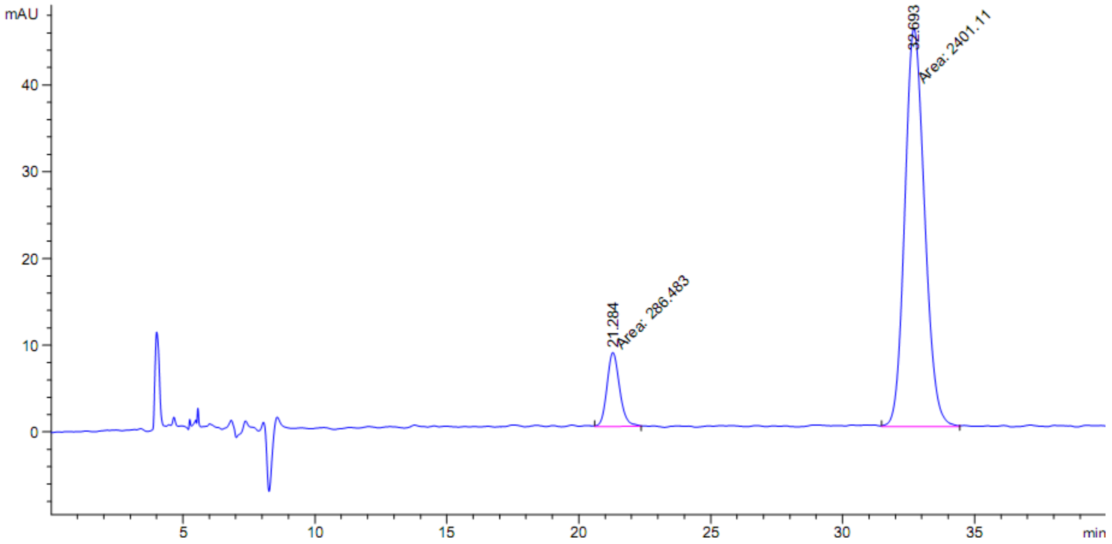

Enantioenriched sample:



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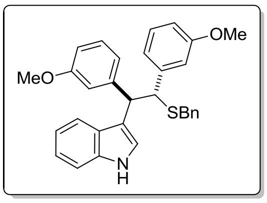
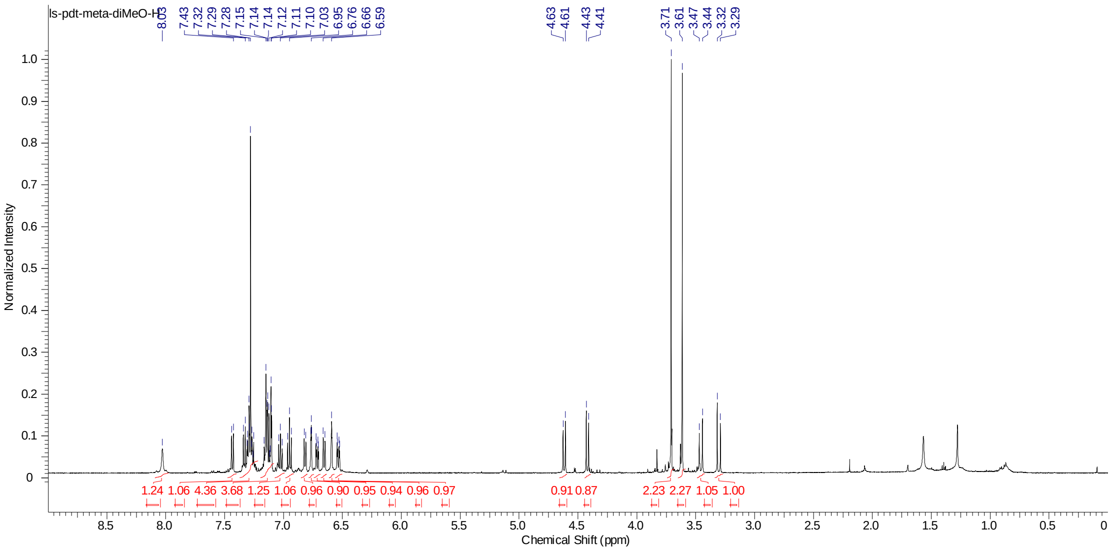
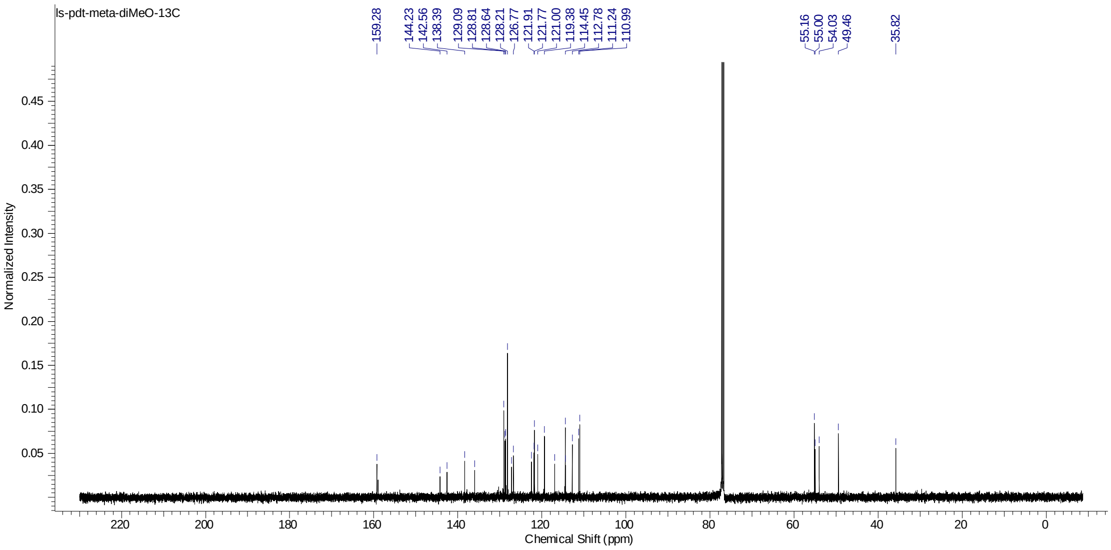
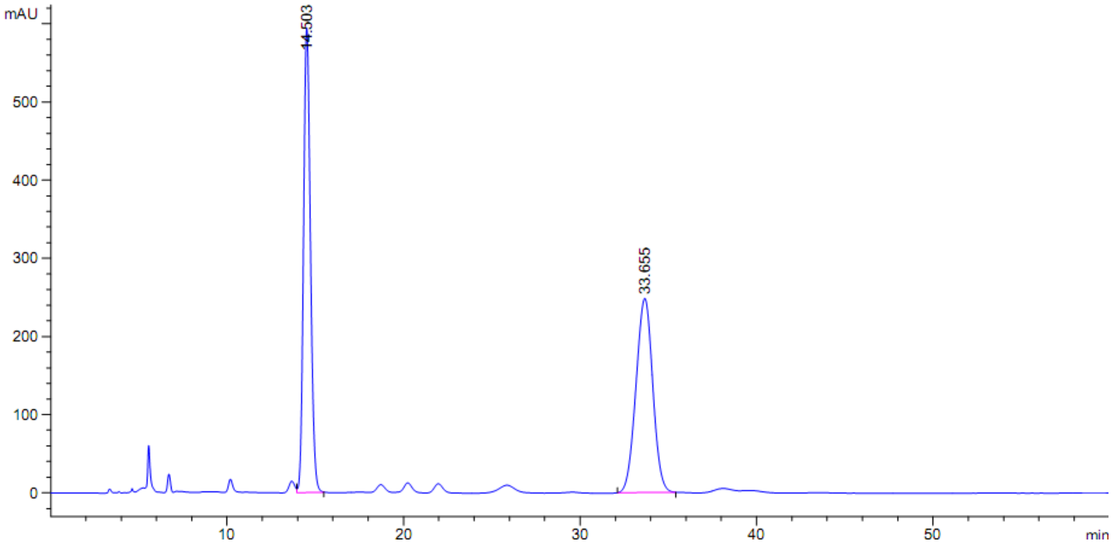


3-((1*R*,2*R*)-2-(benzylthio)-1,2-bis(3-methoxyphenyl)ethyl)-1*H*-indole (2r) Followed method B from **1r** (26.2 mg, 0.05 mmol), for 40 h, and the yield of **2r** was determined by ^{1}H NMR to be 85%. The chromatographically isolated material usually contained a small amount of **3e** and/or trichloroacetamide. Analytically pure sample could be obtained through additional flash column chromatography purification at the expense of loss of yield. This material was determined to be 93% ee by chiral HPLC analysis (ChiralPak AD-H, 15% *i*-PrOH, 1 mL/min, 230 nm, t_r(major) = 14 min, t_r(minor) = 33 min). IR (Film): 3374, 1724, 1693 (s), 1599 (s), 1489, 1455, 1264 (s), 1048, 910 (s), 738 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.03 (br. s., 1H), 7.43 (d, *J*=8.2 Hz, 1H), 7.37 - 7.22 (m, 4H), 7.20 - 7.08 (m, 5H), 7.03 (t, *J*=7.3 Hz, 1H), 6.95 (t, *J*=8.0 Hz, 1H), 6.82 (d, *J*=7.3 Hz, 1H), 6.79 - 6.74 (m, 1H), 6.74 - 6.68 (m, 1H), 6.65 (d, *J*=7.8 Hz, 1H), 6.59 (d, *J*=1.8 Hz, 1H), 6.56 - 6.50 (m, 1H), 4.62 (d, *J*=10.1 Hz, 1H), 4.42 (d, *J*=10.1 Hz, 1H), 3.71 (s, 2H), 3.61 (s, 2H), 3.46 (d, *J*=13.7 Hz, 1H), 3.30 (d, *J*=13.7 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 159.28, 144.23, 142.56, 138.39, 136.00, 129.09, 128.81, 128.64, 128.21, 127.26, 126.77, 122.47, 121.91, 121.77, 121.00, 119.44, 119.38, 116.94, 114.45, 114.42, 112.78, 111.24, 110.99, 55.16, 55.00, 54.03, 49.46, 35.82; MS (ESI-APCI) exact mass calculated for [M-SBn] ($C_{24}H_{22}NO_2$) requires *m/z* 356.2, found *m/z* 356.2; $[\alpha]_D^{24}$ = -6.7 (c = 0.06, CH_2Cl_2).





Racemic sample:



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  2  33.655 BB    1.0259 1.64501e4  248.63231  50.3759
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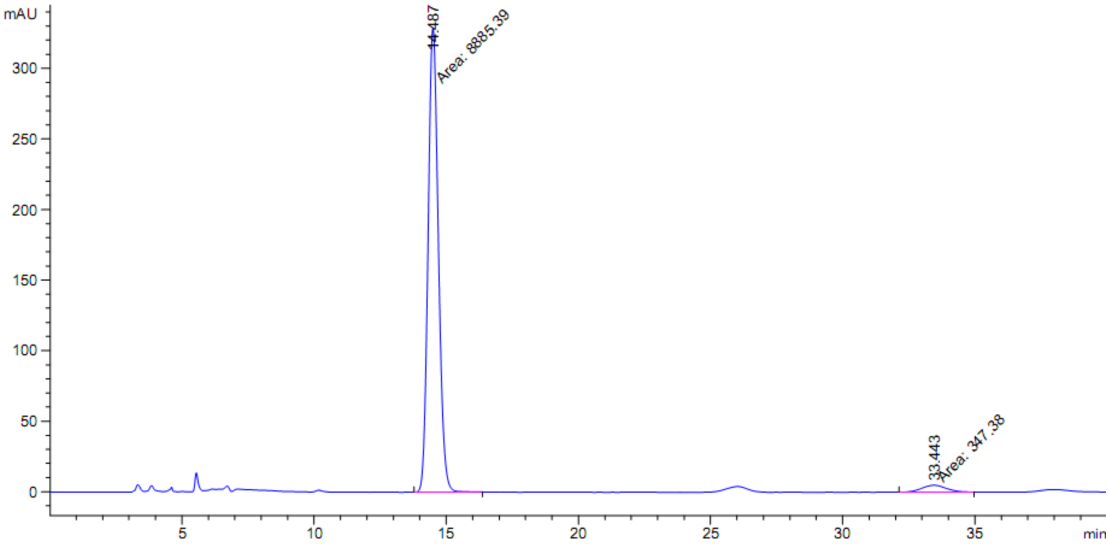
Enantioenriched sample:



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Peak RetTime Type  Width     Area      Height     Area
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----|-------|----|-------|----------|----------|--------|
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  2  33.443 MM    1.1409  347.38004    5.07454   3.7625
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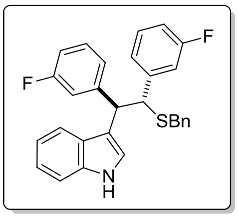
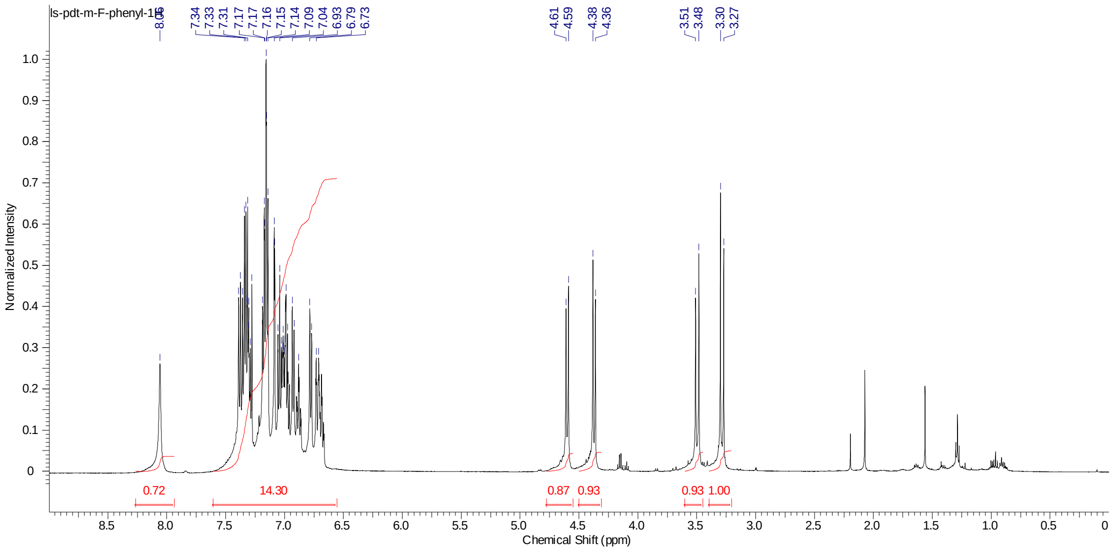
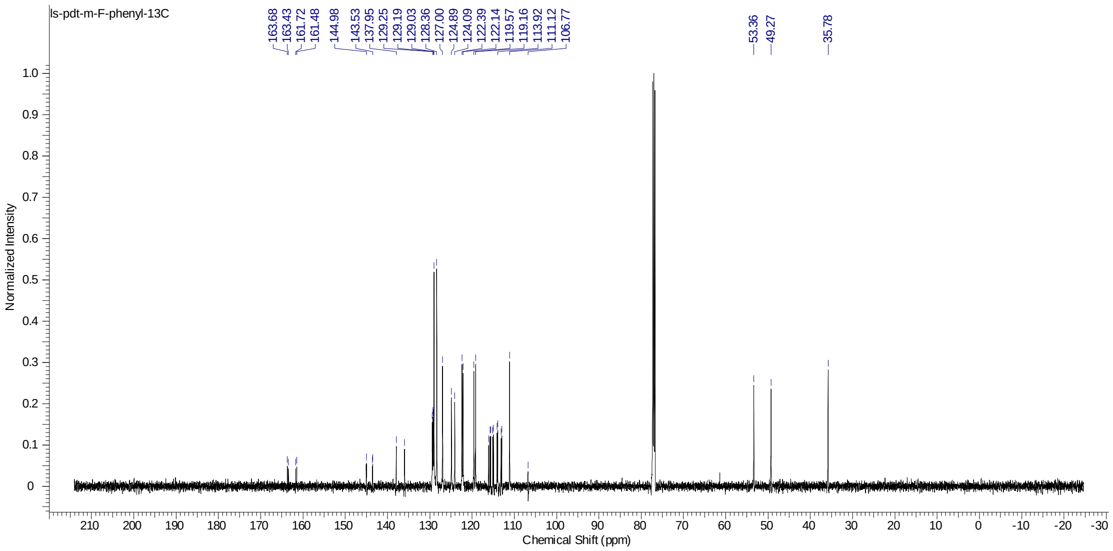


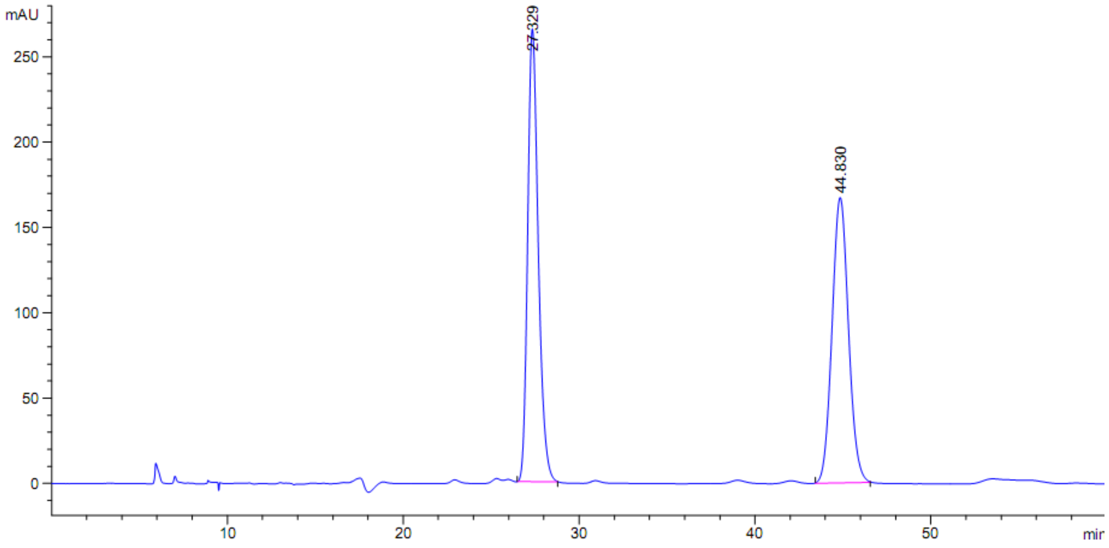
3-((1*R*,2*R*)-2-(benzylthio)-1,2-bis(3-fluorophenyl)ethyl)-1*H*-indole (2s)

Followed method B from **1s** (25.0 mg, 0.05 mmol), for 45 h, and purified using silica gel chromatography to give 22.2 mg (97% yield) of **2s** as a colorless gel. This material was determined to be 95% ee by chiral HPLC analysis (ChiralPak AD-H, 10% *i*-PrOH, 1 mL/min, 230 nm, t_r(major) = 27 min, t_r(minor) = 45 min). IR (Film): 3419 (s), 3059, 2917, 1613, 1588 (s), 1487 (s), 1449 (s), 1249 (s), 1134, 909, 739 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.06 (br. s., 1H), 7.47 - 7.23 (m, 6H), 7.23 - 7.11 (m, 4H), 7.11 - 6.95 (m, 4H), 6.95 - 6.83 (m, 2H), 6.83 - 6.60 (m, 2H), 4.60 (d, *J*=10.3 Hz, 1H), 4.37 (d, *J*=10.3 Hz, 1H), 3.50 (d, *J*=13.7 Hz, 1H), 3.28 (d, *J*=13.7 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 162.70 (d, *J*=246.3 Hz, 1C), 162.44 (d, *J*=245.3 Hz, 1C), 144.98, 143.59, 143.53, 137.95, 135.99, 129.44, 129.37, 129.25, 129.19, 129.03, 128.36, 127.00, 124.89, 124.09, 122.39, 122.14, 119.57, 119.16, 116.12, 115.79, 115.61, 115.10, 114.94, 114.09, 113.92, 113.14, 112.98, 111.12, 106.77, 53.36, 49.27, 35.78; MS (ESI-APCI) exact mass calculated for [M-SBn] ($C_{22}H_{16}F_2N$) requires *m/z* 332.1, found *m/z* 332.1; $[\alpha]_D^{22}$ = +83.9 (c = 1.0, CH_2Cl_2).





Racemic sample:



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----|-------|----|-------|----------|----------|--------|
  1  27.329 BB    0.6396 1.11361e4  265.38040  50.6236
  2  44.830 BB    1.0016 1.08617e4  167.27299  49.3764
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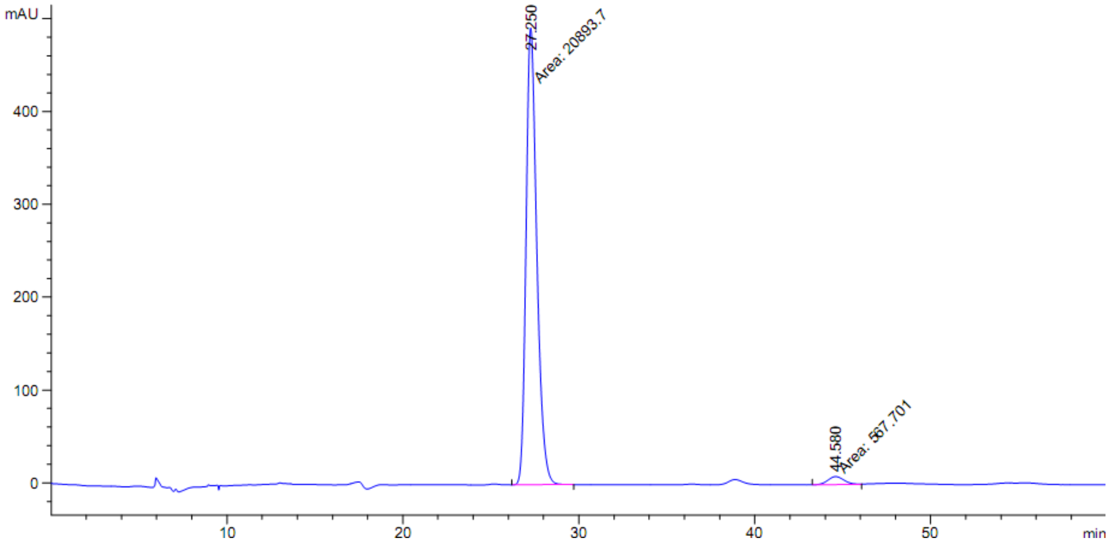
Enantioenriched sample:



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  1  27.250 MM    0.7080 2.08937e4  491.83978  97.3548
  2  44.580 MM    1.0845  567.70099   8.72422   2.6452
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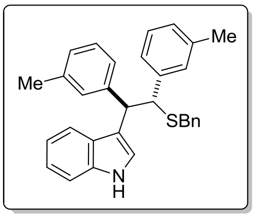
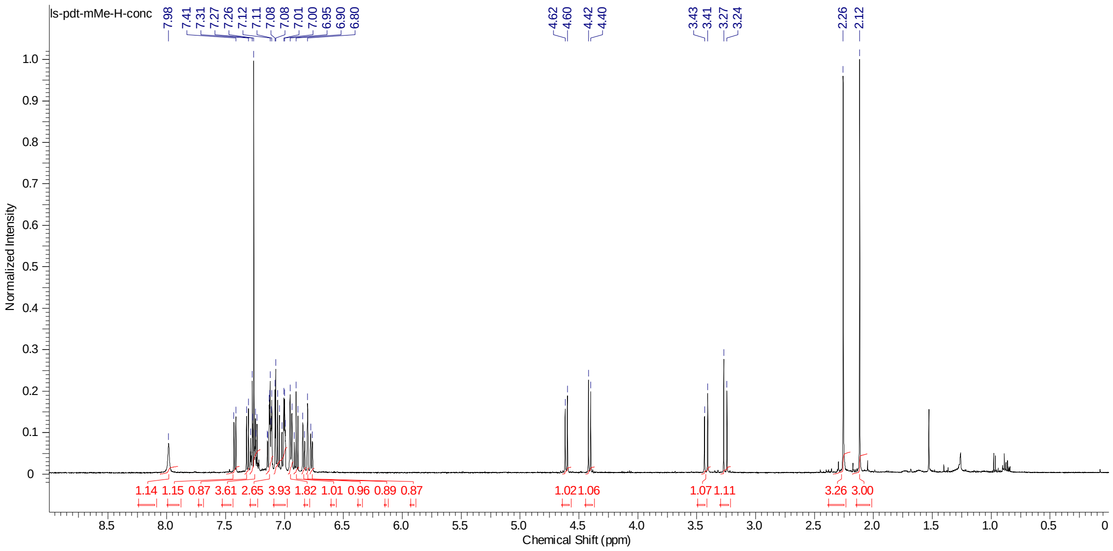
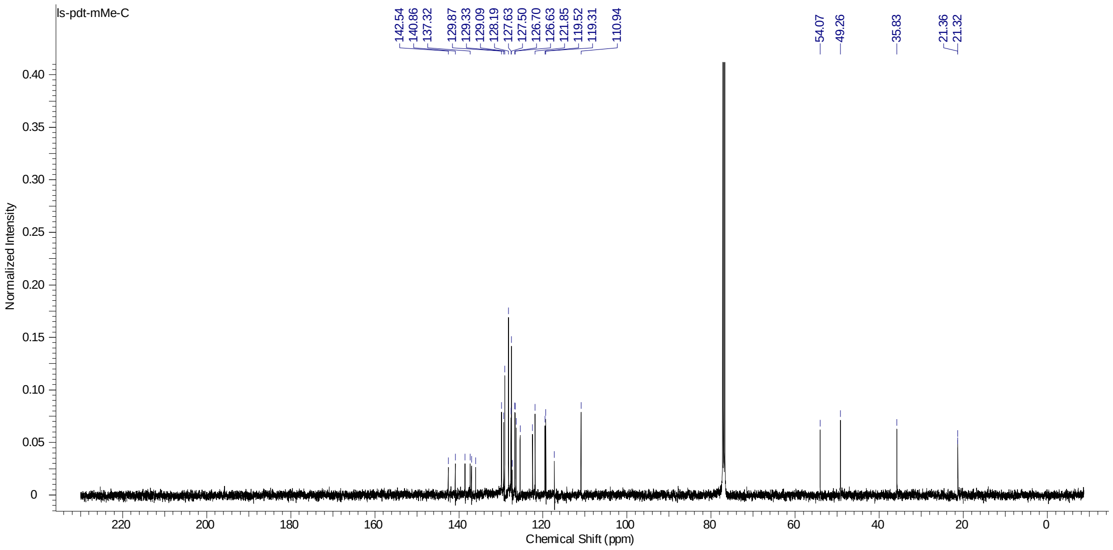


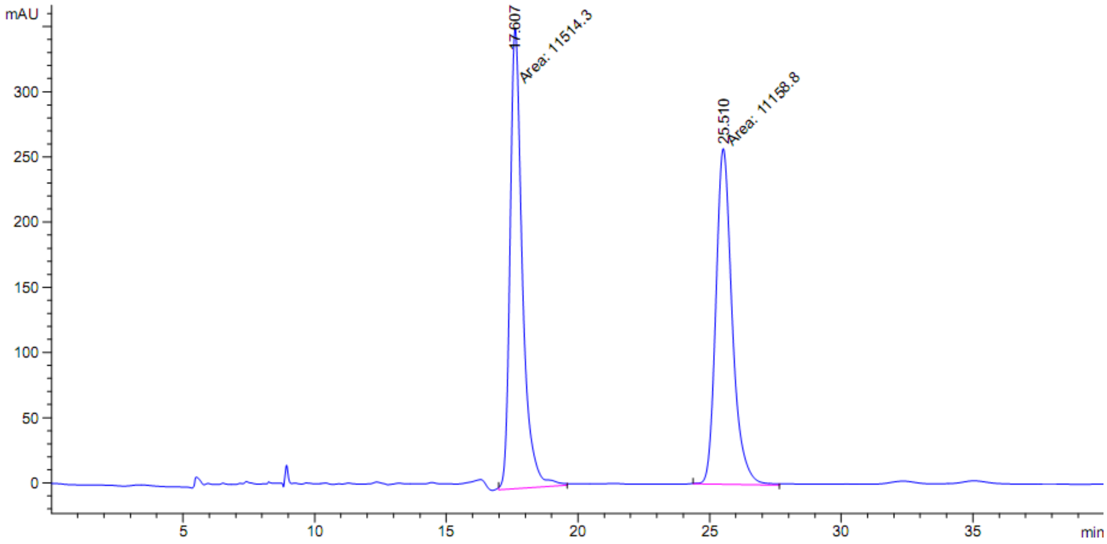
3-((1*R*,2*R*)-2-(benzylthio)-1,2-di-*m*-tolylethyl)-1*H*-indole (2t)

Followed method B from **1t** (24.6 mg, 0.05 mmol), for 45 h, and purified using silica gel chromatography to give 21.3 mg (95% yield) of **2t** as a colorless gel. This material was determined to be 93% ee by chiral HPLC analysis (ChiralPak AD-H, 10% *i*-PrOH, 1 mL/min, 230 nm, t_r(major) = 16 min, t_r(minor) = 23 min). IR (Film): 3420 (s), 3027, 2918, 1604, 1489, 1455, 1418, 1096, 909 (s), 738 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.98 (br. s., 1H), 7.42 (d, *J*=8.2 Hz, 1H), 7.31 (d, *J*=7.8 Hz, 1H), 7.30 - 7.21 (m, 3H), 7.16 - 7.10 (m, 3H), 7.09 - 6.98 (m, 4H), 6.94 (d, *J*=7.3 Hz, 2H), 6.90 (t, *J*=7.3 Hz, 1H), 6.84 (d, *J*=7.8 Hz, 1H), 6.80 (s, 1H), 6.77 (d, *J*=7.3 Hz, 1H), 4.61 (d, *J*=9.6 Hz, 1H), 4.41 (d, *J*=9.6 Hz, 1H), 3.42 (d, *J*=13.3 Hz, 1H), 3.26 (d, *J*=13.7 Hz, 1H), 2.26 (s, 3H), 2.12 (s, 2H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 142.54, 140.86, 138.52, 137.32, 137.02, 135.98, 129.87, 129.33, 129.09, 128.19, 127.63, 127.50, 127.37, 126.70, 126.63, 126.35, 125.44, 122.47, 121.85, 119.52, 119.31, 117.29, 110.94, 54.07, 49.26, 35.83, 21.36, 21.32; MS (APCI) exact mass calculated for [M-SBn] ($C_{24}H_{22}N$) requires *m/z* 324.2, found *m/z* 324.1; $[\alpha]_D^{24}$ = +13.0 (c = 0.1, CH_2Cl_2).





Racemic sample:



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Peak RetTime Type  Width      Area       Height      Area
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----|-------|----|-------|----------|----------|--------|
   1  17.607 MM    0.5430 1.15143e4  353.43860  50.7840
   2  25.510 MM    0.7215 1.11588e4  257.78049  49.2160
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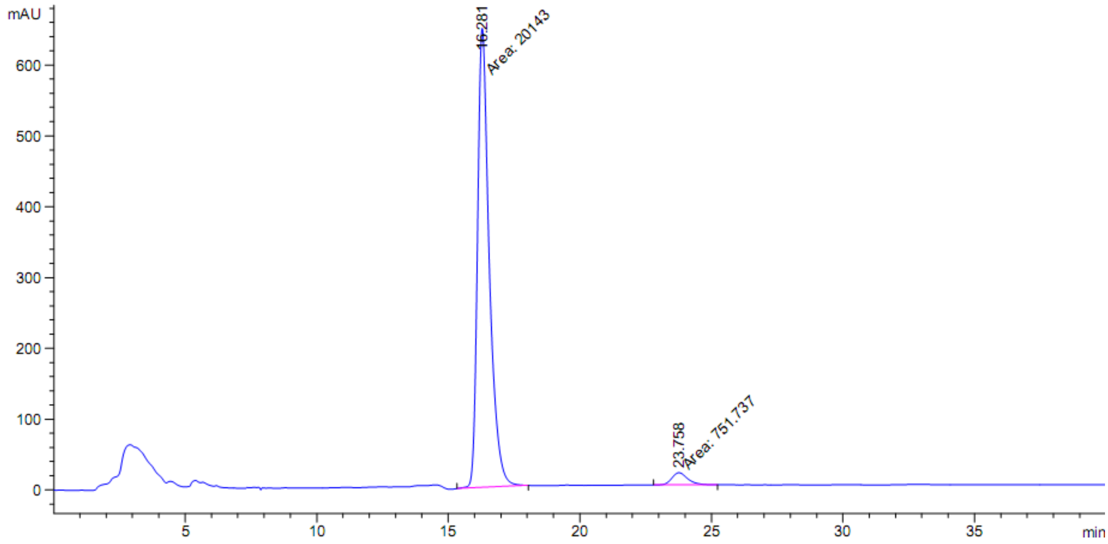
Enantioenriched sample:



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Peak RetTime Type  Width      Area       Height      Area
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----|-------|----|-------|----------|----------|--------|
   1  16.281 MM    0.5177 2.01430e4  648.44629  96.4023
   2  23.758 MM    0.7181  751.73743  17.44797   3.5977
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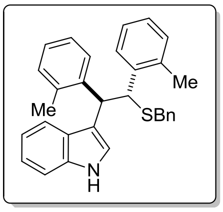
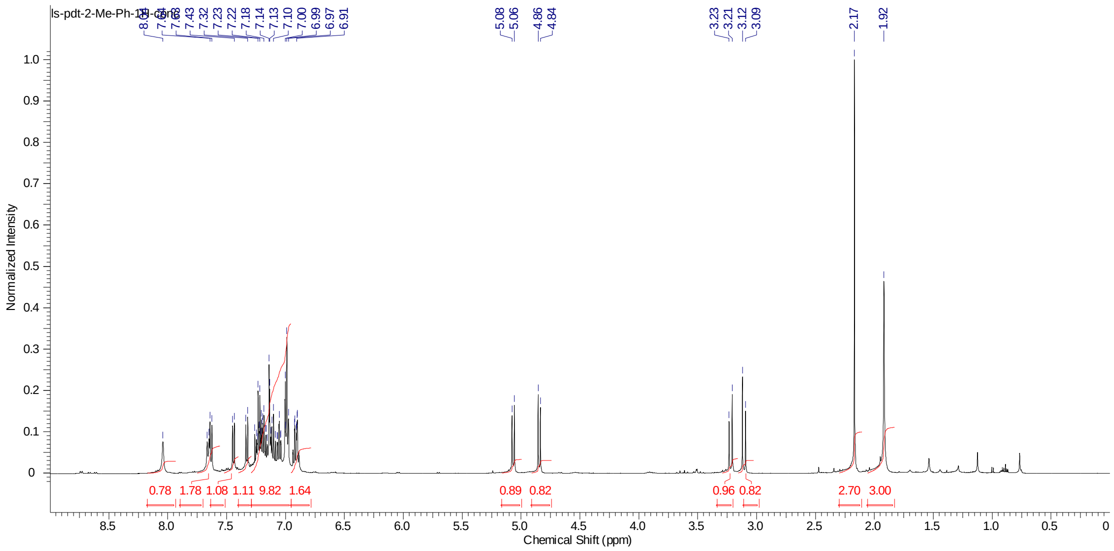
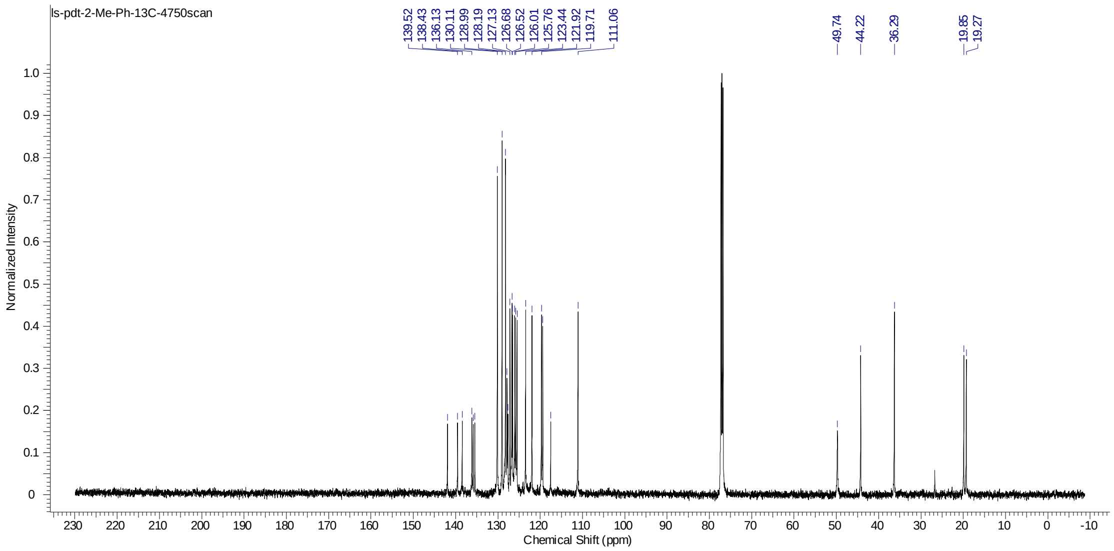


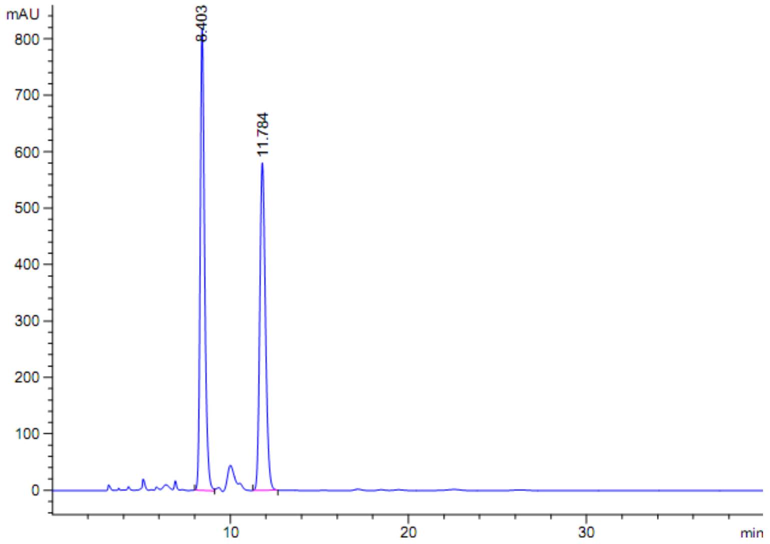
3-((1*R*,2*R*)-2-(benzylthio)-1,2-di-*o*-tolylethyl)-1*H*-indole (2u)

Followed method B from **1u** (24.6 mg, 0.05 mmol), for 40 h, and purified using silica gel chromatography to give 22.5 mg (>99% yield) of **2u** as a colorless gel. This material was determined to be 79% ee by chiral HPLC analysis (ChiralPak AD-H, 10% *i*-PrOH, 1 mL/min, 230 nm, t_r(major) = 8 min, t_r(minor) = 12 min). IR (Film): 3148 (s), 3059, 1600, 1489, 1455 (s), 1419, 1380, 1277, 1176, 1133, 1097, 1011, 737 (s) cm^{-1}; ^{1}H NMR: (500 MHz, CDCl$_3$) δ 8.04 (br. s., 1H), 7.75 - 7.56 (m, 2H), 7.44 (d, *J*=7.8 Hz, 1H), 7.33 (d, *J*=8.3 Hz, 1H), 7.26 - 7.03 (m, 9H), 7.02 - 6.97 (m, 3H), 6.95 - 6.78 (m, 2H), 5.07 (d, *J*=9.8 Hz, 1H), 4.85 (d, *J*=9.8 Hz, 1H), 3.22 (d, *J*=13.7 Hz, 1H), 3.11 (d, *J*=13.2 Hz, 1H), 2.17 (s, 3H), 1.92 (s, 3H); ^{13}C NMR: (125 MHz, CDCl$_3$) δ 141.90, 139.52, 138.43, 136.13, 135.84, 135.43, 130.11, 128.99, 128.19, 127.83, 127.62, 127.13, 126.68, 126.52, 126.01, 125.76, 125.47, 123.44, 121.92, 119.71, 119.38, 117.51, 111.06, 49.74, 44.22, 36.29, 19.85, 19.27; MS (ESI-APCI) exact mass calculated for [M-SBn] ($C_{23}H_{23}S$) requires *m/z* 324.2, found *m/z* 324.2; $[\alpha]_D^{23}$ = +129 (c = 1.0, CH_2Cl_2).





Racemic sample:



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Peak RetTime Type  Width     Area      Height     Area
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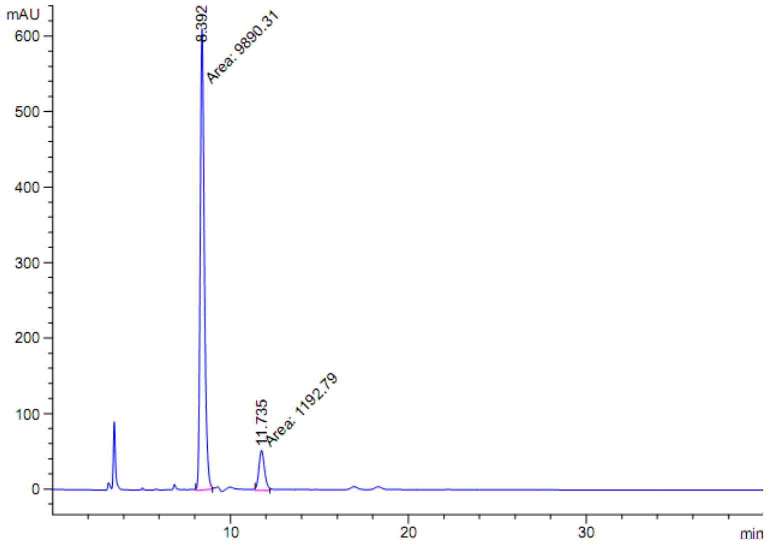
----|-------|----|-------|----------|----------|--------|
   1   8.403 BV    0.2600 1.41769e4  818.90674  52.4842
   2  11.784 BB    0.3420 1.28349e4  580.34973  47.5158
```

Enantioenriched sample:



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----|-------|----|-------|----------|----------|--------|
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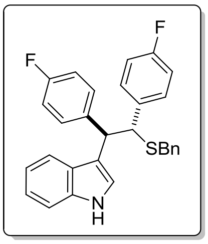
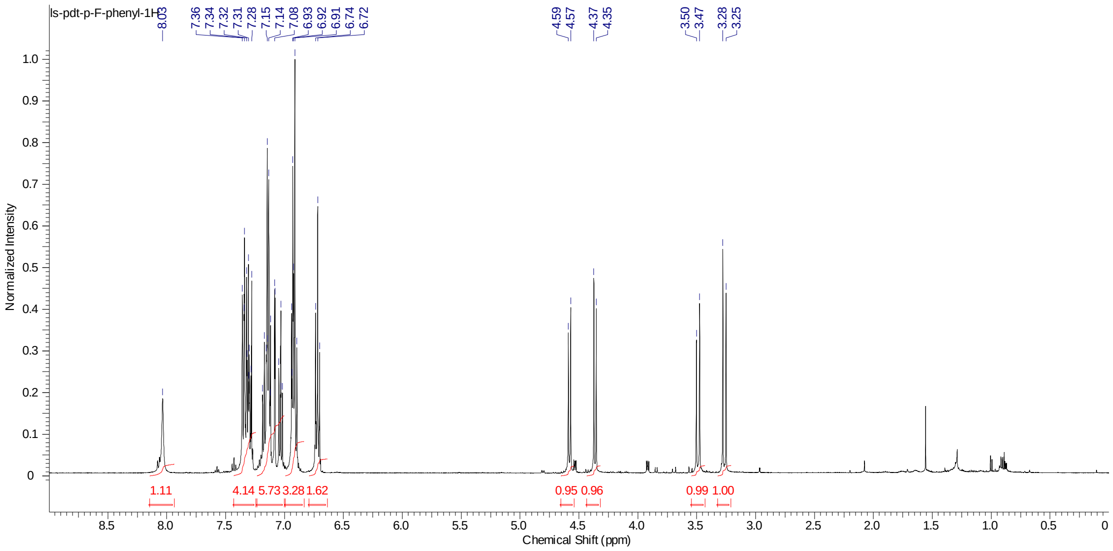
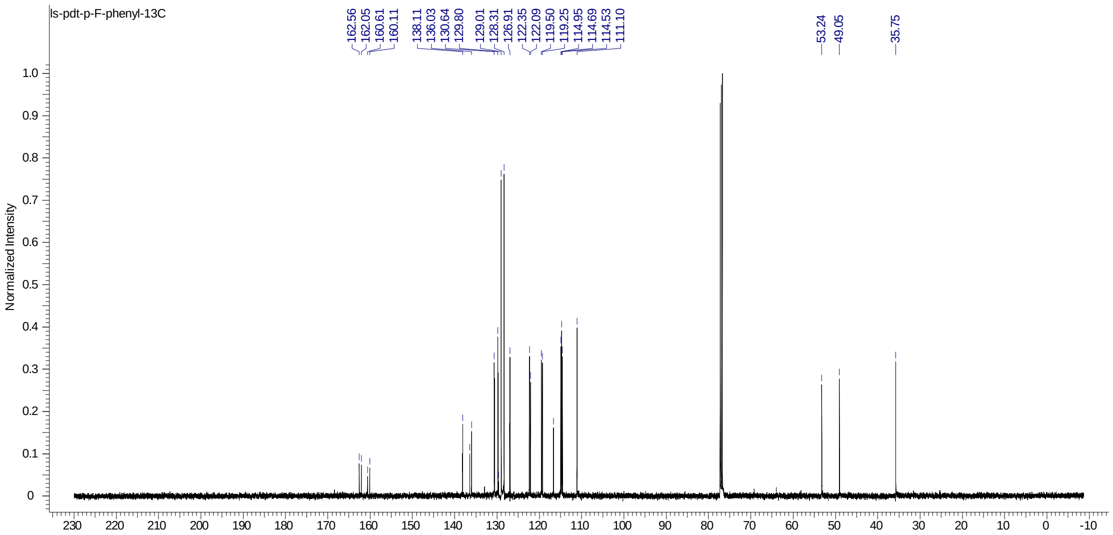


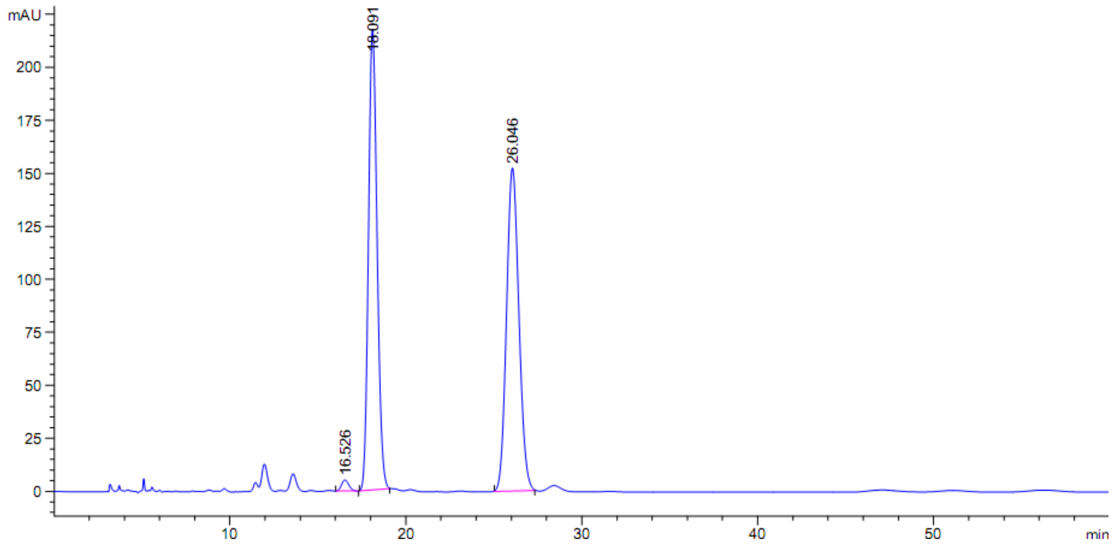
3-((1*R*,2*R*)-2-(benzylthio)-1,2-bis(4-fluorophenyl)ethyl)-1*H*-indole (2v)

Followed method B from **1v** (25.0 mg, 0.05 mmol), for 47 h, and purified using silica gel chromatography to give 20.8 mg (91% yield) of **2v** as a colorless gel. This material was determined to be 45% ee by chiral HPLC analysis (ChiralPak AD-H, 10% *i*-PrOH, 1 mL/min, 230 nm, t_r(major) = 18 min, t_r(minor) = 26 min). IR (Film): 3418 (s), 3060, 2915, 1602, 1505 (s), 1455, 1417, 1218 (s), 1157, 1095, 908, 736 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.03 (br. s., 1H), 7.43 - 7.24 (m, 5H), 7.23 - 7.00 (m, 7H), 6.99 - 6.83 (m, 4H), 6.79 - 6.64 (m, 2H), 4.58 (d, *J*=10.1 Hz, 1H), 4.36 (d, *J*=10.1 Hz, 1H), 3.49 (d, *J*=13.7 Hz, 1H), 3.26 (d, *J*=13.7 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 161.59 (d, *J*=246.3 Hz, 1C), 161.09 (d, *J*=245.3 Hz, 1C), 138.15, 138.11, 136.44, 136.42, 136.03, 130.64, 130.58, 129.80, 129.74, 129.65, 129.01, 128.31, 126.99, 126.91, 122.35, 122.09, 119.50, 119.25, 116.63, 114.95, 114.78, 114.69, 114.53, 111.10, 53.24, 49.05, 35.75; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{29}H_{23}F_2NS$) requires *m/z* 456.2, found *m/z* 456.1; $[\alpha]_D^{25}$ = +42.8 (c = 1.0, CH_2Cl_2).





Racemic sample:



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----|-------|----|-------|----------|----------|--------|
  1  16.526 BB    0.4538  154.63104    5.24775   1.0303
  2  18.091 BB    0.5275 7405.12695  217.31786  49.3390
  3  26.046 BB    0.7598 7448.91064  152.50339  49.6307
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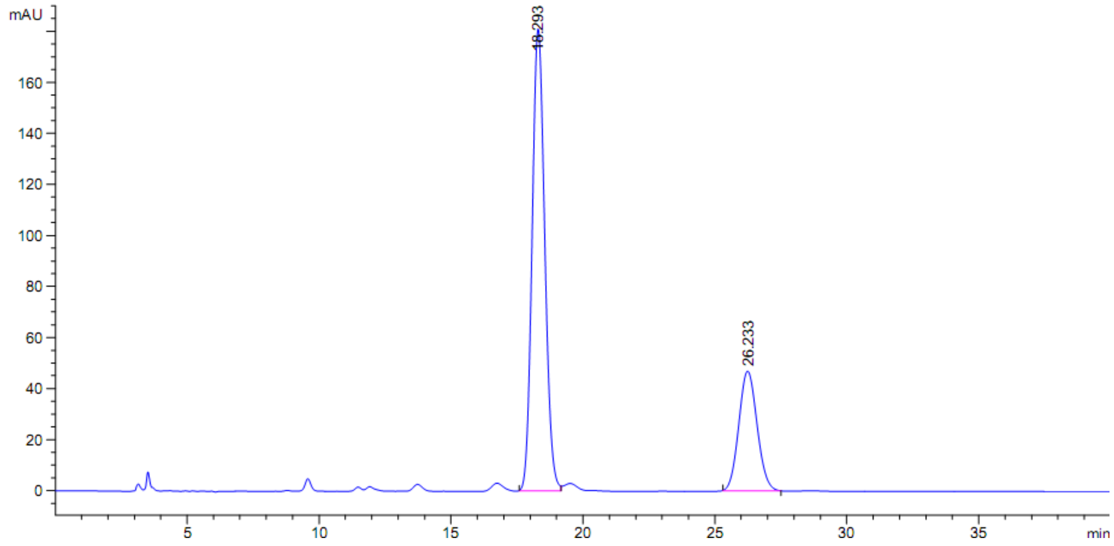
Enantioenriched sample:



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Peak RetTime Type  Width     Area      Height     Area
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----|-------|----|-------|----------|----------|--------|
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  2  26.233 BB    0.7505 2273.27417   46.98168  27.3410
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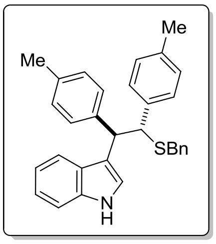
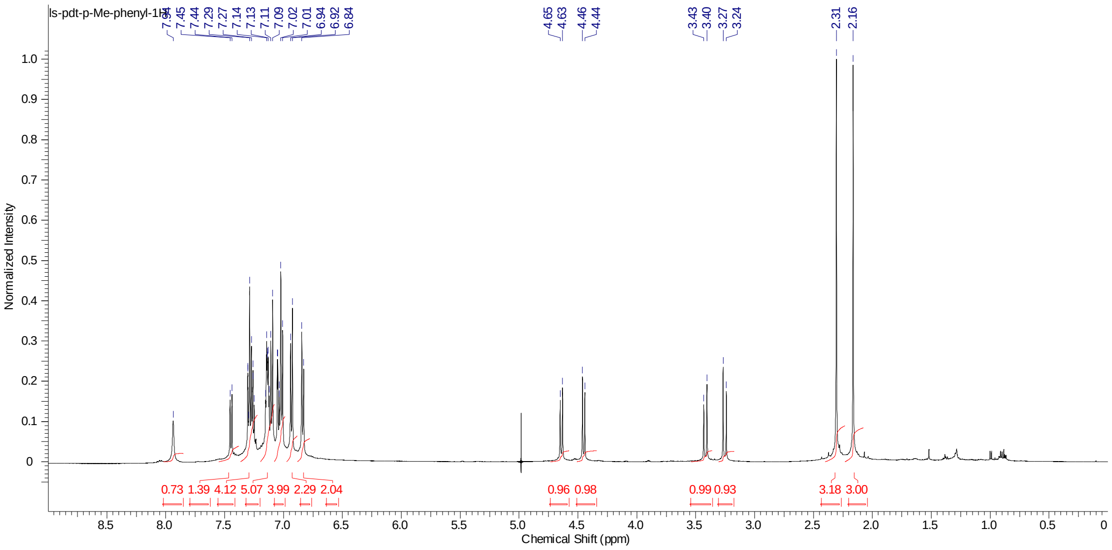
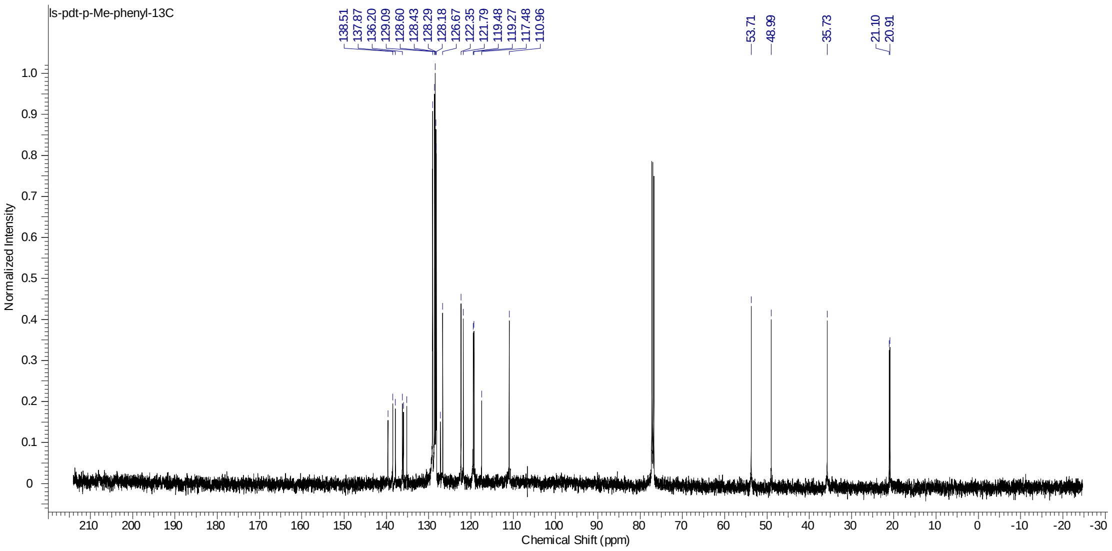


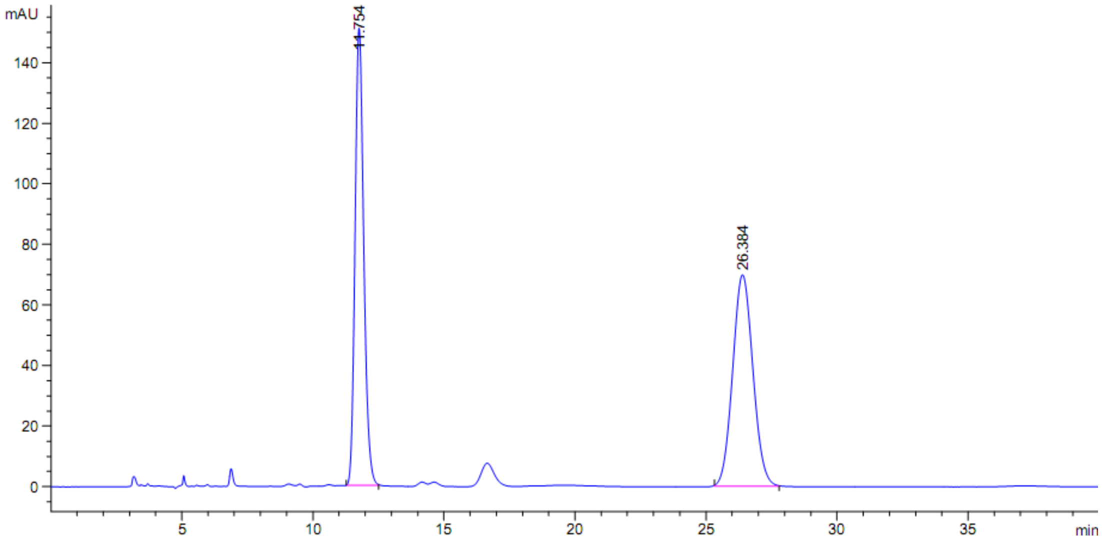
3-((1*R*,2*R*)-2-(benzylthio)-1,2-di-*p*-tolylethyl)-1*H*-indole e (2w)

Followed method B from **1w** (24.6 mg, 0.05 mmol), for 47 h, and purified using silica gel chromatography to give 20.0 mg (89% yield) of **2w** as a colorless gel. This material was determined to be 60% ee by chiral HPLC analysis (ChiralPak AD-H, 10% *i*-PrOH, 1 mL/min, 230 nm, t_r(major) = 12 min, t_r(minor) = 26 min). IR (Film): 3420 (br), 3025, 2929, 1510, 1454, 1417, 1337, 1096, 907 (s), 731 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.94 (br. s., 1H), 7.45 (d, *J*=8.1 Hz, 1H), 7.37 - 7.22 (m, 4H), 7.20 - 7.08 (m, 5H), 7.08 - 6.99 (m, 4H), 6.93 (d, *J*=8.1 Hz, 2H), 6.84 (d, *J*=8.1 Hz, 2H), 4.64 (d, *J*=10.0 Hz, 1H), 4.45 (d, *J*=10.0 Hz, 1H), 3.42 (d, *J*=13.4 Hz, 1H), 3.25 (d, *J*=13.7 Hz, 1H), 2.31 (s, 3H), 2.16 (s, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 139.66, 138.51, 137.87, 136.20, 135.99, 135.18, 129.09, 129.06, 128.60, 128.43, 128.29, 128.18, 127.21, 126.67, 122.35, 121.79, 119.48, 119.27, 117.48, 110.96, 53.71, 48.99, 35.73, 21.10, 20.91; MS (ESI-APCI) exact mass calculated for [M-SBn] ($C_{24}H_{22}N$) requires *m/z* 324.2, found *m/z* 324.2; $[\alpha]_D^{25}$ = +91.2 (c = 1.0, CH_2Cl_2).





Racemic sample:



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Peak RetTime Type  Width     Area      Height     Area
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----|-------|----|-------|----------|----------|--------|
   1  11.754 BB    0.3548 3480.52808  151.08057  48.1467
   2  26.384 BB    0.8364 3748.47632   69.81534  51.8533
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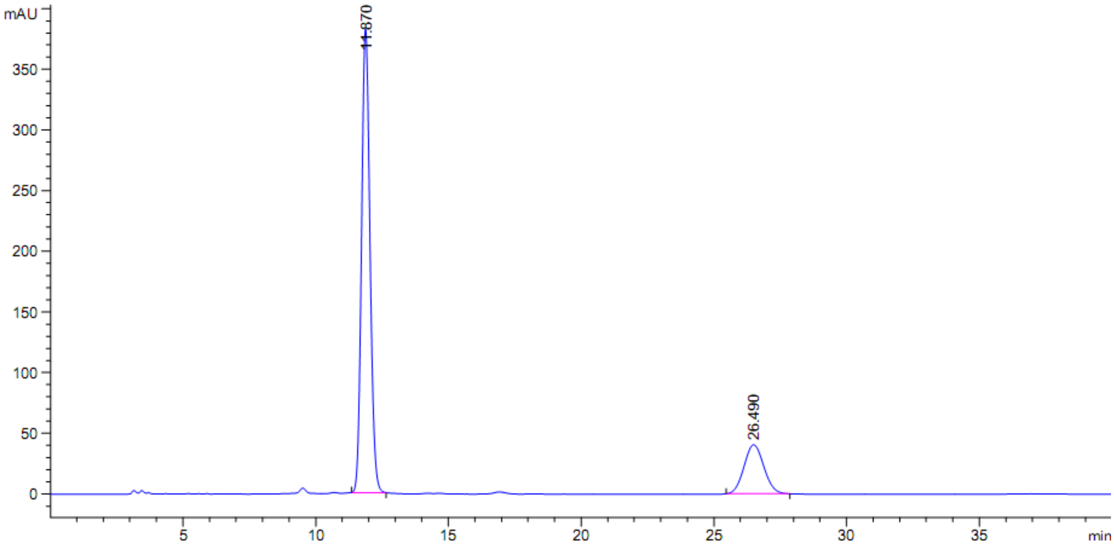
Enantioenriched sample:



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Peak RetTime Type  Width     Area      Height     Area
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----|-------|----|-------|----------|----------|--------|
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   2  26.490 BB    0.8118 2120.72217   40.57563  20.0279
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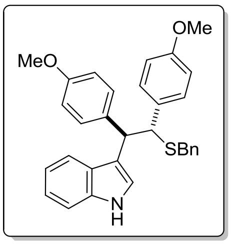
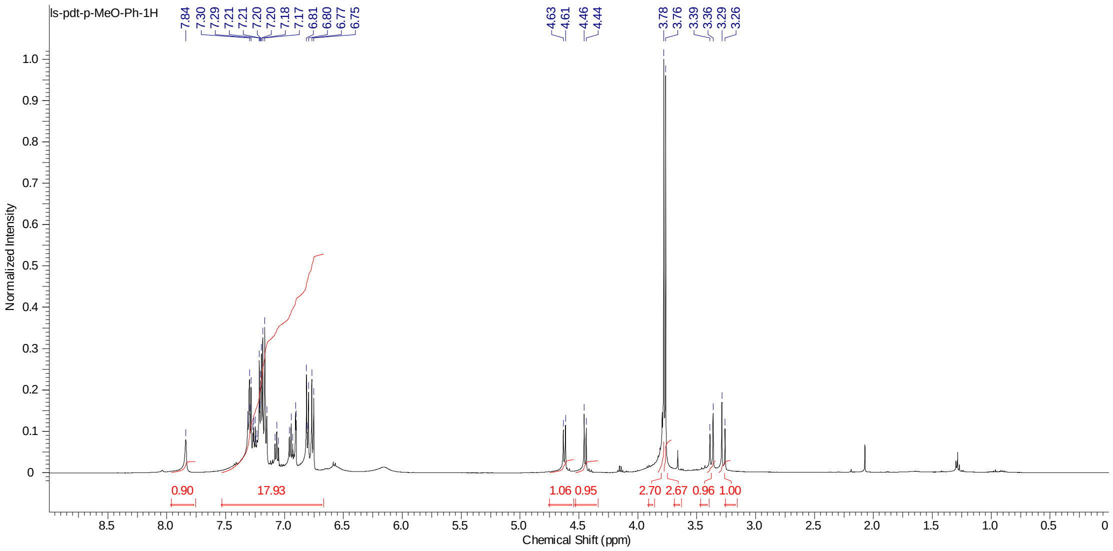
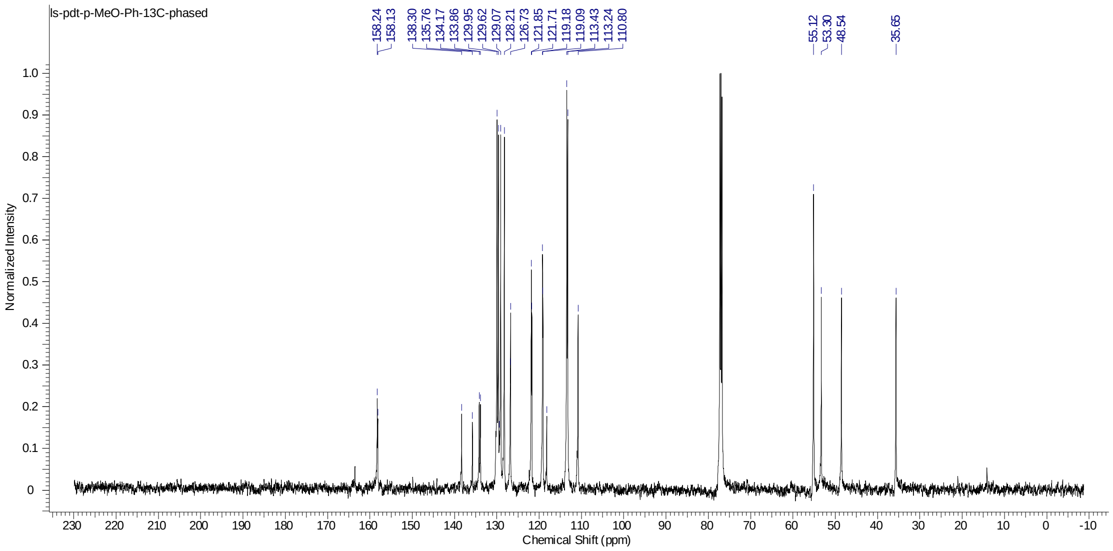
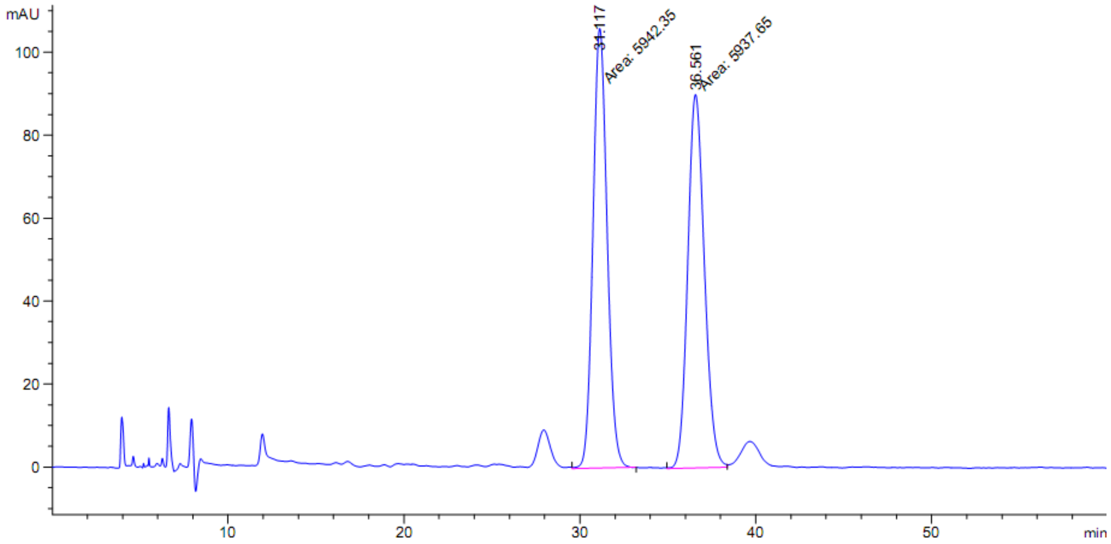


3-((1*R*,2*R*)-2-(benzylthio)-1,2-bis(4-methoxyphenyl)ethyl)-1*H*-indole (2x) Followed method B from **1x** (26.2 mg, 0.05 mmol), for 40 h, and yield of **2x** was determined by ^{1}H NMR to be 67%. The chromatographically isolated material usually contained a small amount of **3e** and/or trichloroacetamide. Analytically pure sample could be obtained through additional flash column chromatography purification at the expense of loss of yield. This material was determined to be 6% ee by chiral HPLC analysis (ChiralPak AD-H, 15% *i*-PrOH, 1 mL/min, 230 nm, t_r(major) = 36 min, t_r(minor) = 31 min). IR (Film): 3373, 3030, 2836, 1723, 1694, 1609, 1583, 1509 (s), 1455, 1247 (s), 1175, 1107, 1032, 908, 833,734 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.84 (br. s., 1H), 7.38 - 7.14 (m, 10H), 7.12 - 7.01 (m, 1H), 7.01 - 6.86 (m, 3H), 6.80 (d, *J*=8.8 Hz, 2H), 6.76 (d, *J*=8.3 Hz, 2H), 4.62 (d, *J*=9.3 Hz, 1H), 4.45 (d, *J*=8.8 Hz, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 3.37 (d, *J*=13.2 Hz, 1H), 3.27 (d, *J*=13.2 Hz, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 158.24, 158.13, 138.30, 135.76, 134.17, 133.86, 129.95, 129.62, 129.40, 129.07, 128.21, 126.82, 126.73, 121.85, 121.71, 119.18, 119.09, 118.20, 113.43, 113.24, 110.80, 55.12, 53.30, 48.54, 35.65; MS (ESI-APCI) exact mass calculated for [M-SBn] ($C_{24}H_{23}NO_2$) requires *m/z* 356.2, found *m/z* 356.1.





Racemic sample:



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Peak RetTime Type  Width     Area      Height     Area
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----|-------|----|-------|----------|----------|--------|
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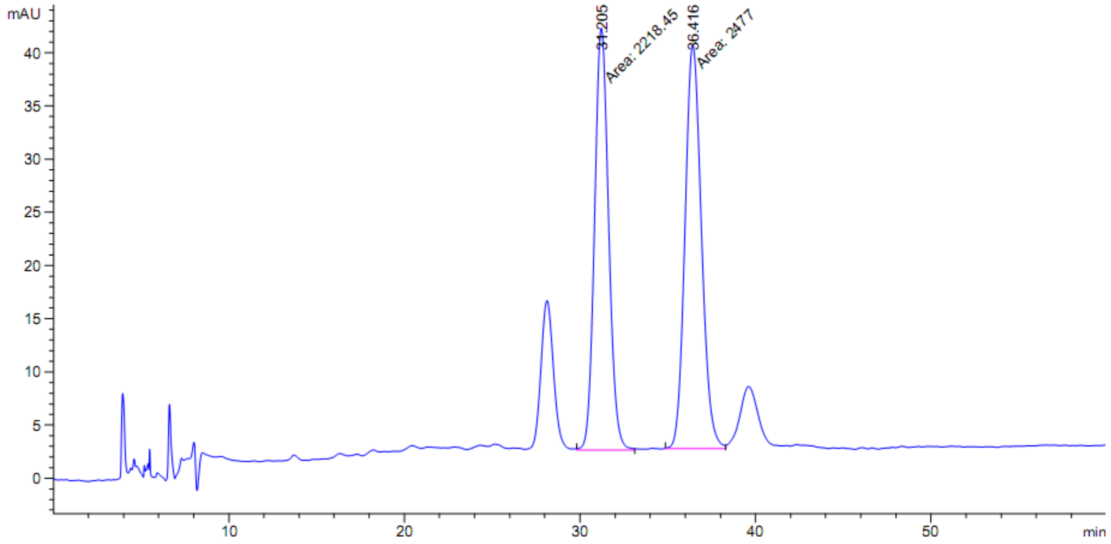
Enantioenriched sample:



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Peak RetTime Type  Width     Area      Height     Area
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----|-------|----|-------|----------|----------|--------|
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   2  36.416 MM    1.0865 2476.99536   37.99585  52.7531
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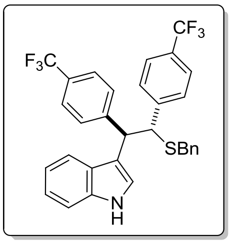
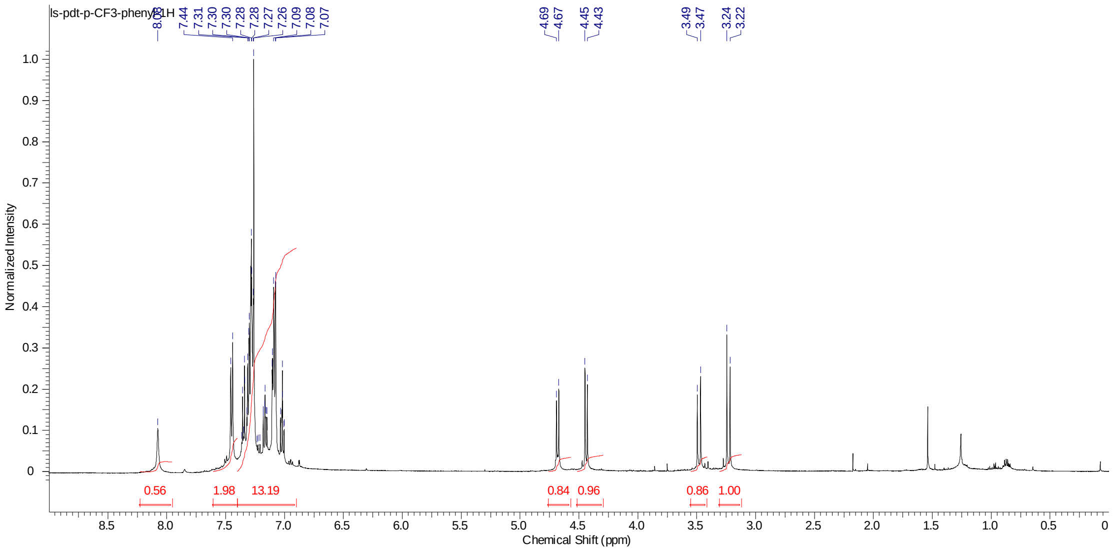
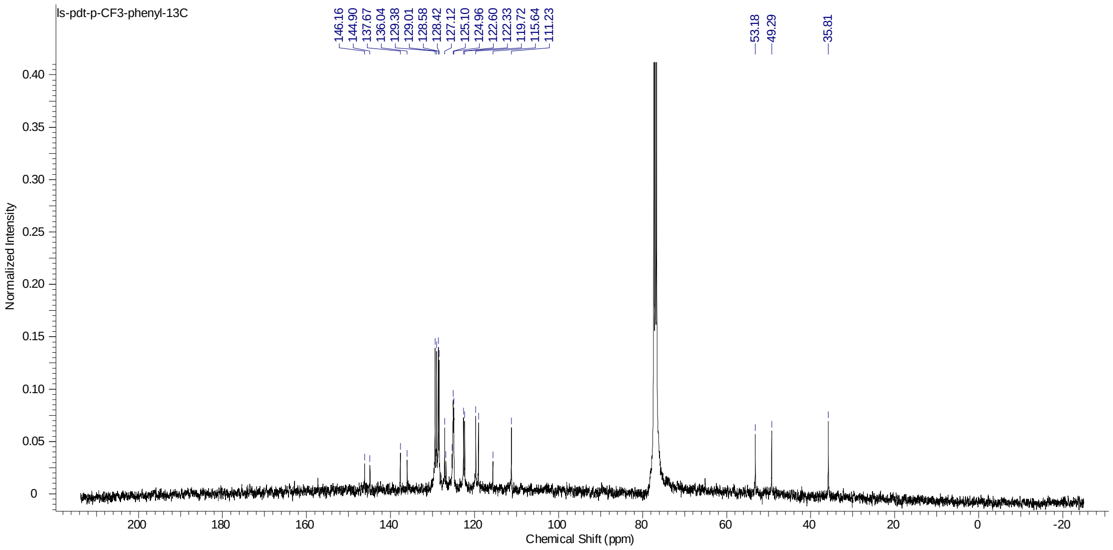


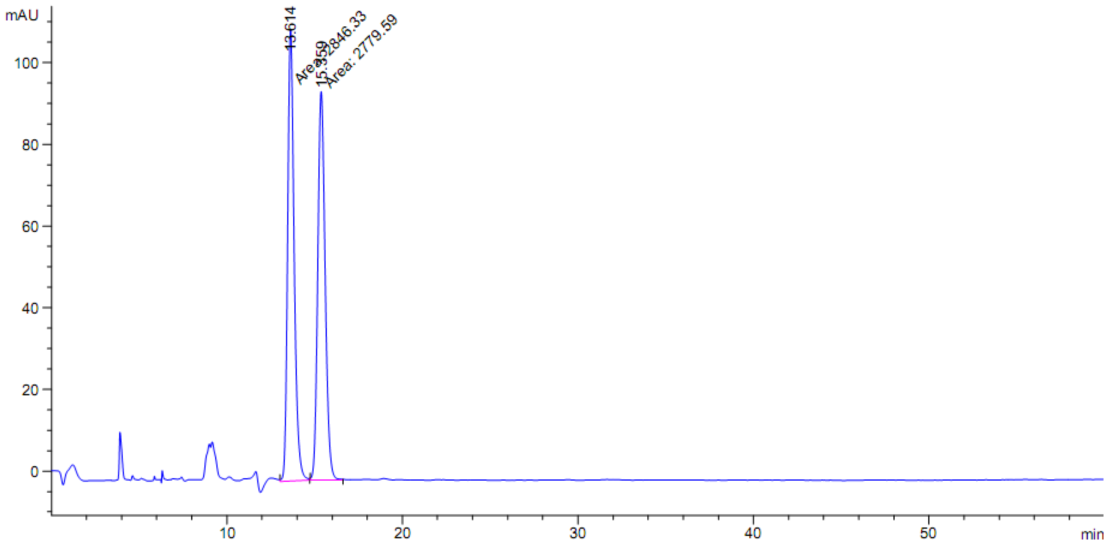
3-((1*R*,2*R*)-2-(benzylthio)-1,2-bis(4-(trifluoromethyl)phenyl)ethyl)-1*H*-indole (2y)

Followed method B from **1y** (30.0 mg, 0.05 mmol), for 42 h, and purified using silica gel chromatography to give 5.1 mg (18% yield) of **2y** as a colorless gel. This material was determined to be 5% ee by chiral HPLC analysis (ChiralPak AD-H, 10% *i*-PrOH, 1 mL/min, 230 nm, t_r(major) = 12 min, t_r(minor) = 14min). IR (Film): 3417, 2923, 1617, 1456, 1417, 1324 (s), 1164, 1120 (s), 1068, 1017, 742 cm^{-1}; ^{1}H NMR: (500 MHz, CDCl$_3$) δ 8.08 (br. s., 1H), 7.45 (d, *J*=8.3 Hz, 1H), 7.37 - 7.20 (m, 10H), 7.17 (ddd, *J*=1.0, 7.0, 8.2 Hz, 1H), 7.13 - 7.05 (m, 5H), 7.02 (ddd, *J*=1.0, 6.8, 7.8 Hz, 1H), 4.68 (d, *J*=9.8 Hz, 1H), 4.44 (d, *J*=9.8 Hz, 1H), 3.48 (d, *J*=13.7 Hz, 1H), 3.23 (d, *J*=13.7 Hz, 1H); ^{13}C NMR: (125 MHz, CDCl$_3$) δ 146.16, 144.90, 137.67, 136.04, 129.38, 129.01, 128.58, 128.42, 127.12, 126.82, 125.35, 125.10, 124.96, 122.60, 122.33, 119.72, 119.07, 115.64, 111.23, 53.18, 49.29, 35.81 (the two CF$_3$ groups not observed); MS (ESI-APCI) exact mass calculated for [M+H] ($C_{31}H_{23}F_6NS$) requires *m/z* 432.1, found *m/z* 432.1.





Racemic sample:



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Peak RetTime Type  Width     Area      Height     Area
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----|-------|----|-------|----------|----------|--------|
  1  13.614 MM    0.4290 2846.32935  110.58447  50.5931
  2  15.359 MM    0.4869 2779.59399   95.13863  49.4069
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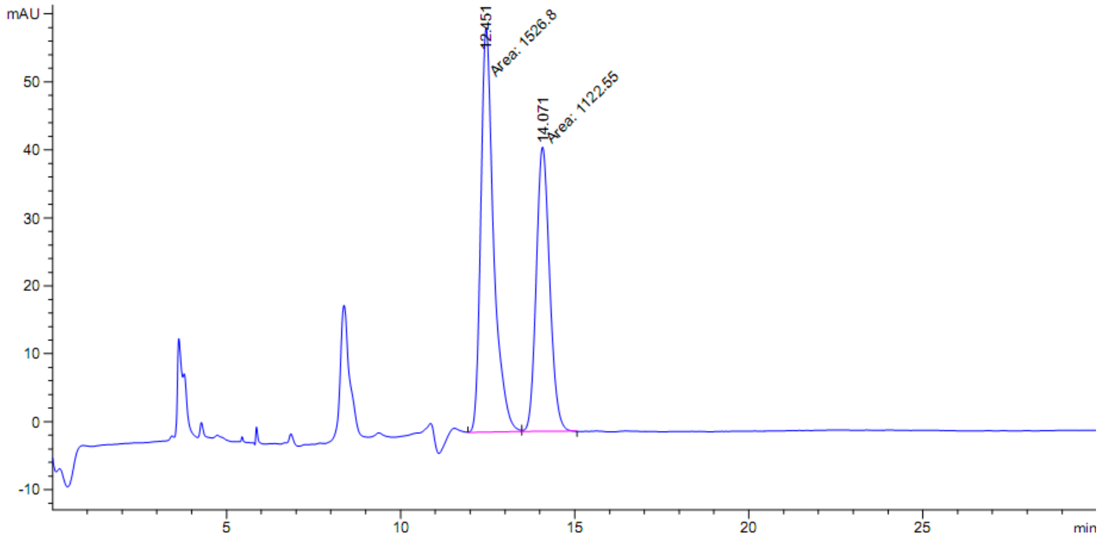
Enantioenriched sample:



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Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
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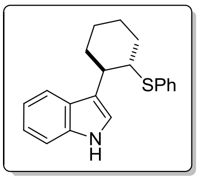
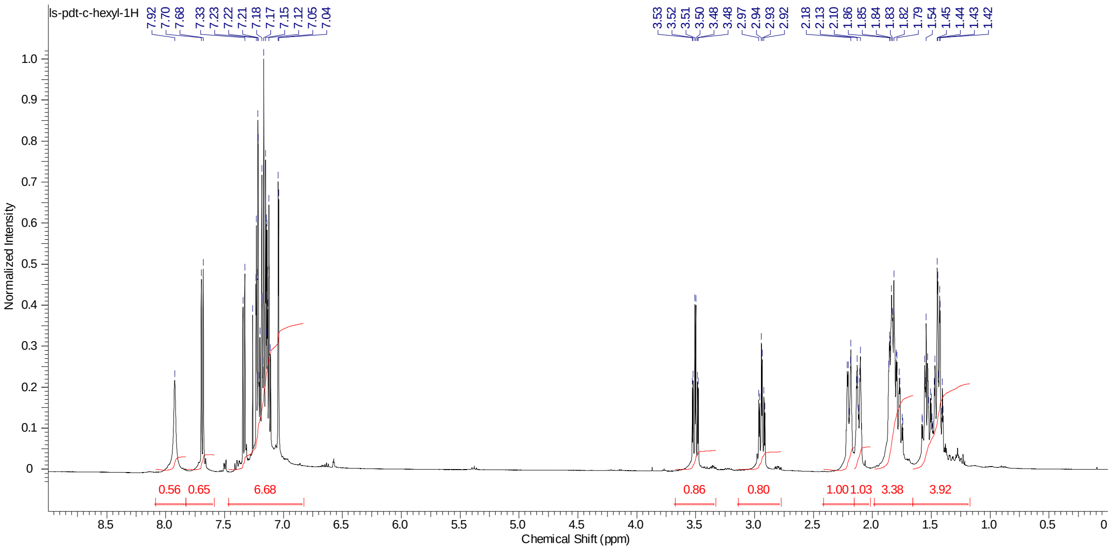
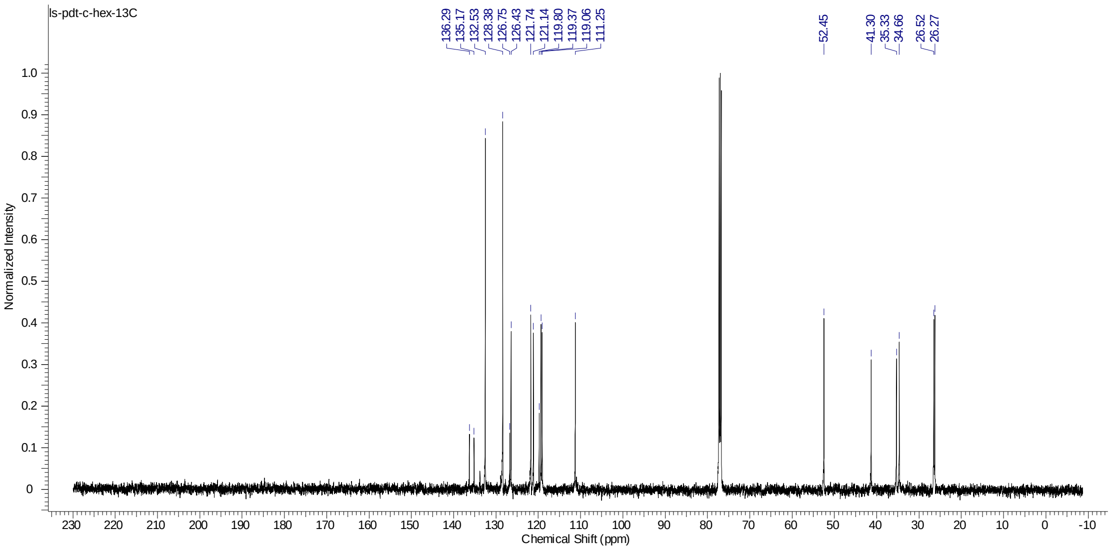


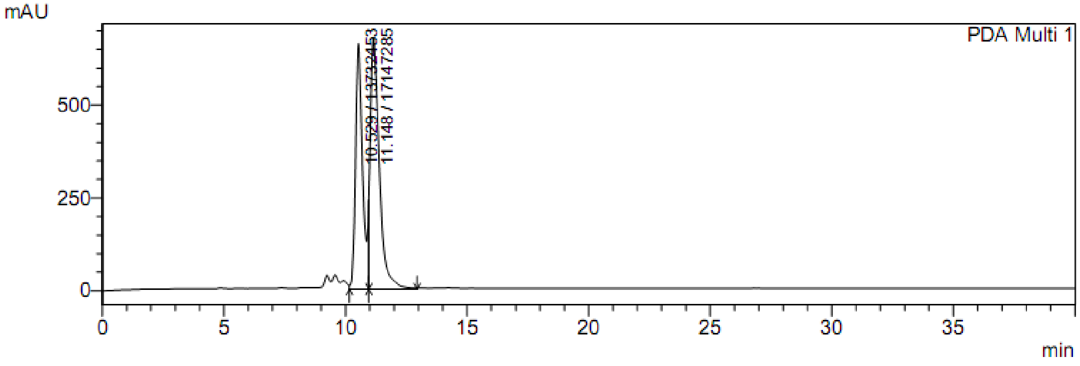
3-((1*R*,2*S*)-2-(benzylthio)cyclohexyl)-1*H*-indole (2z)

Followed method B from **1z** (17.6 mg, 0.05 mmol), for 26 h, and purified using silica gel chromatography to give 2.5 mg (16% yield) of **2z** as a white solid/gel. This material was determined to be 9% ee by chiral HPLC analysis (ChiralPak AS-H, 10% *i*-PrOH, 1 mL/min, 220 nm, t_r(major) = 10 min, t_r(minor) = 11 min). IR (Film): 3420 (br., s), 3056, 2928 (s), 2852, 1581, 1477, 1455, 1336, 1095, 910, 739 (s), 694 cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.92 (br. s., 1H), 7.69 (d, *J*=7.8 Hz, 1H), 7.34 (d, *J*=7.8 Hz, 1H), 7.25 - 7.09 (m, 6H), 7.04 (d, *J*=2.4 Hz, 2H), 3.50 (dt, *J*=3.4, 11.0 Hz, 1H), 2.94 (dt, *J*=3.9, 11.2 Hz, 1H), 2.38 - 2.16 (m, 1H), 2.16 - 2.02 (m, 1H), 1.92 - 1.68 (m, 3H), 1.60 - 1.36 (m, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 136.29, 135.17, 132.53, 128.38, 126.75, 126.43, 121.74, 121.14, 119.80, 119.37, 119.06, 111.25, 52.45, 41.30, 35.33, 34.66, 26.52, 26.27; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{20}H_{22}NS$) requires *m/z* 308.2, found *m/z* 308.1.





Racemic sample:



PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
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2	11.148	17147285	676018	55.529	50.551
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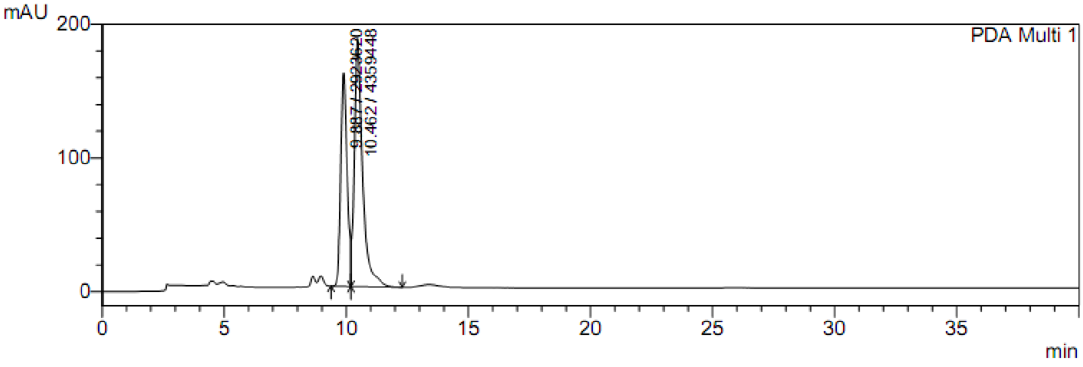
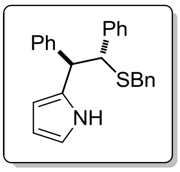
Enantioenriched sample:



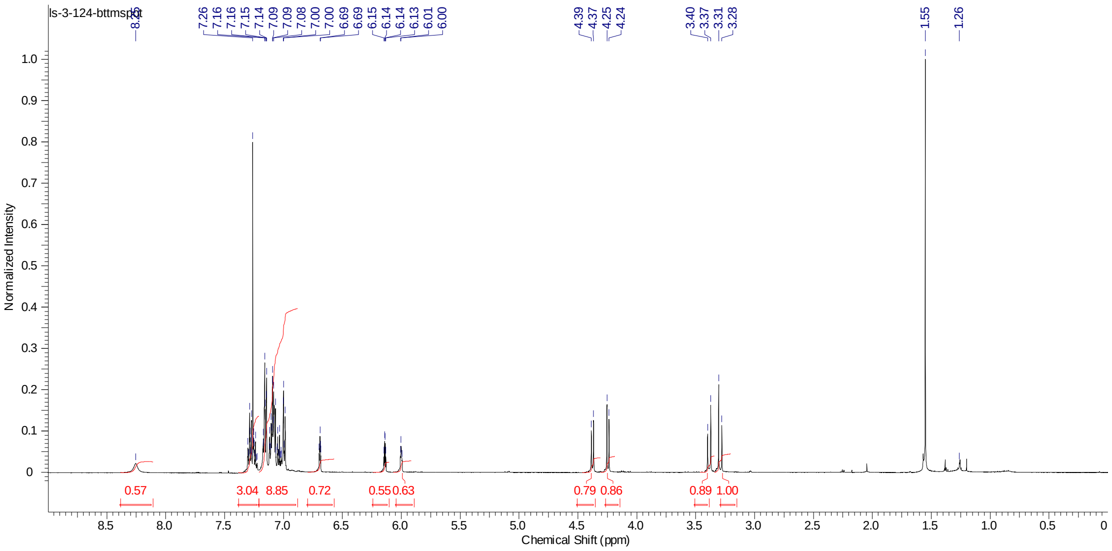
PDA Ch1 220nm 4nm

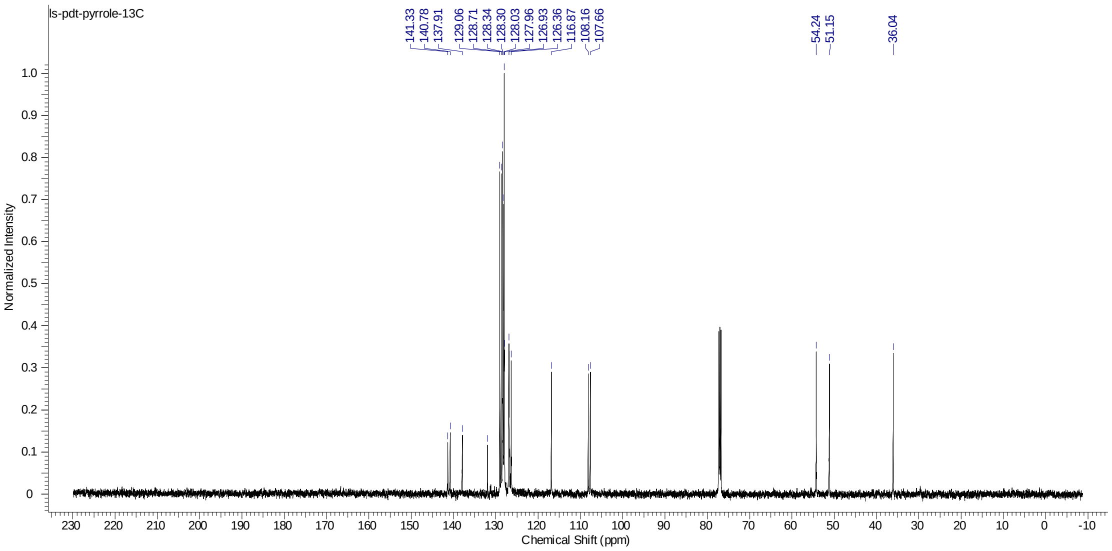
Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.887	2923620	159842	40.143	46.272
2	10.462	4359448	185595	59.857	53.728
Total		7283068	345436	100.000	100.000



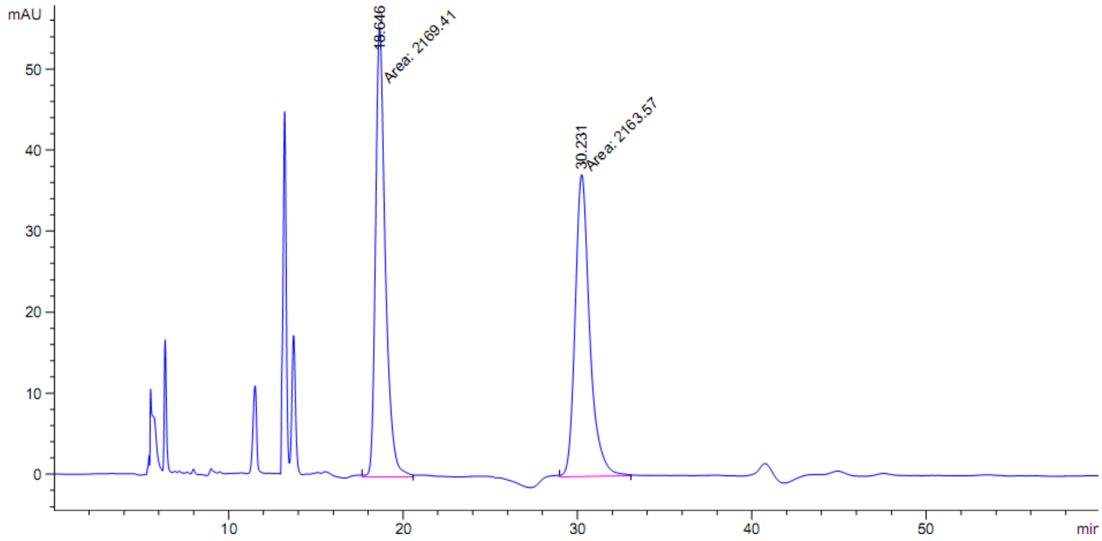
2-(benzylthio)-1,2-diphenylethyl)-1*H*-pyrrole

Followed method B from **1a** (22.3 mg, 0.05 mmol), for 46 h, and purified using silica gel chromatography to give 13.6 mg (67% yield) of the desired product and bis-alkylation products (7.6:1 favoring the desired product) as a colorless gel. The desired product was determined to be 9% ee by chiral HPLC analysis (ChiralPak AD-H, 5% *i*-PrOH, 1 mL/min, 230 nm, t_r(major) = 19 min, t_r(minor) = 30 min). The products resulting from bis-alkylation of pyrrole were a mixture of diastereomers and were not separable by HPLC. IR (Film): 3428 (br.), 3027, 2914, 1600, 1492, 1452 (s), 1174, 1095, 1072, 1029, 911, 696 (s) cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.25 (br. s., 1H), 7.38 - 7.21 (m, 4H), 7.20 - 6.97 (m, 11H), 6.69 (dd, *J*=2.9, 4.4 Hz, 1H), 6.14 (dd, *J*=2.9, 5.9 Hz, 1H), 6.00 (dd, *J*=2.9, 4.4 Hz, 1H), 4.38 (d, *J*=9.3 Hz, 1H), 4.24 (d, *J*=9.3 Hz, 1H), 3.42 - 3.35 (m, 1H), 3.33 - 3.25 (m, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 141.33, 140.78, 137.91, 131.94, 129.06, 128.71, 128.34, 128.30, 128.03, 127.96, 126.93, 126.86, 126.36, 116.87, 108.16, 107.66, 54.24, 51.15, 36.04; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{25}H_{24}NS$) requires *m/z* 370.2, found *m/z* 370.2.





Racemic sample:



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Peak RetTime Type  Width     Area      Height     Area
 #    [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
  1  18.646 MM    0.6532 2169.41284   55.35432  50.0674
  2  30.231 MM    0.9679 2163.57202   37.25562  49.9326
```
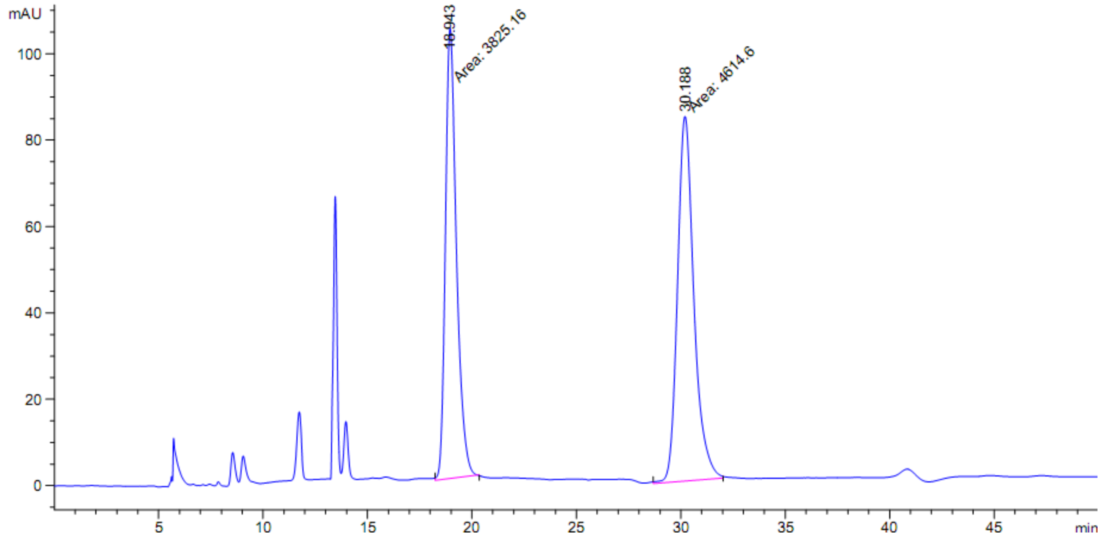
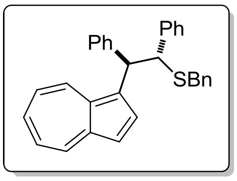

Enantioenriched sample:

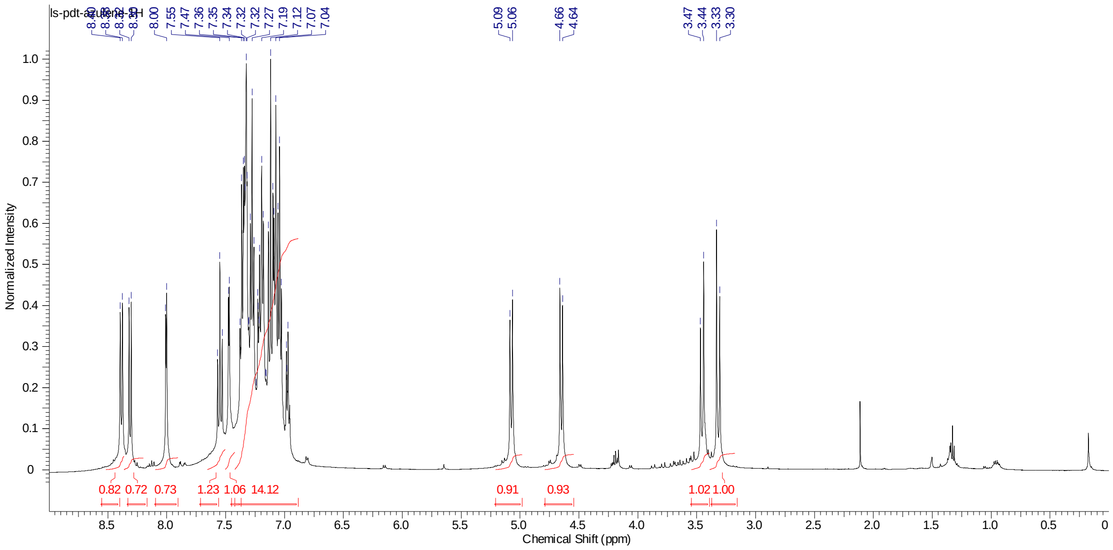


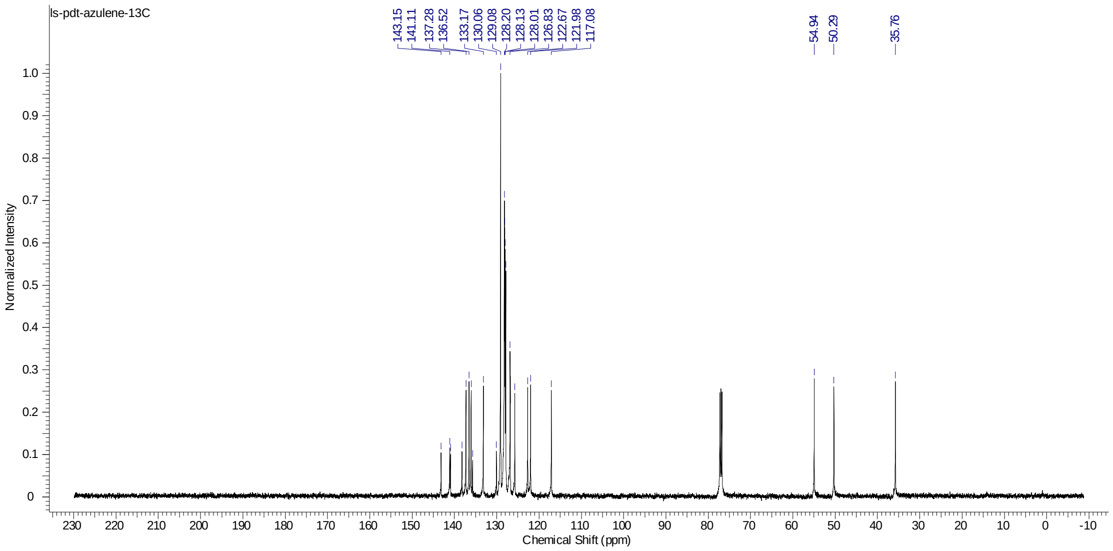
```
Peak RetTime Type  Width     Area      Height     Area
 #    [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
  1  18.943 MM    0.6106 3825.15503  104.40643  45.3231
  2  30.188 MM    0.9103 4614.59961   84.48951  54.6769
```



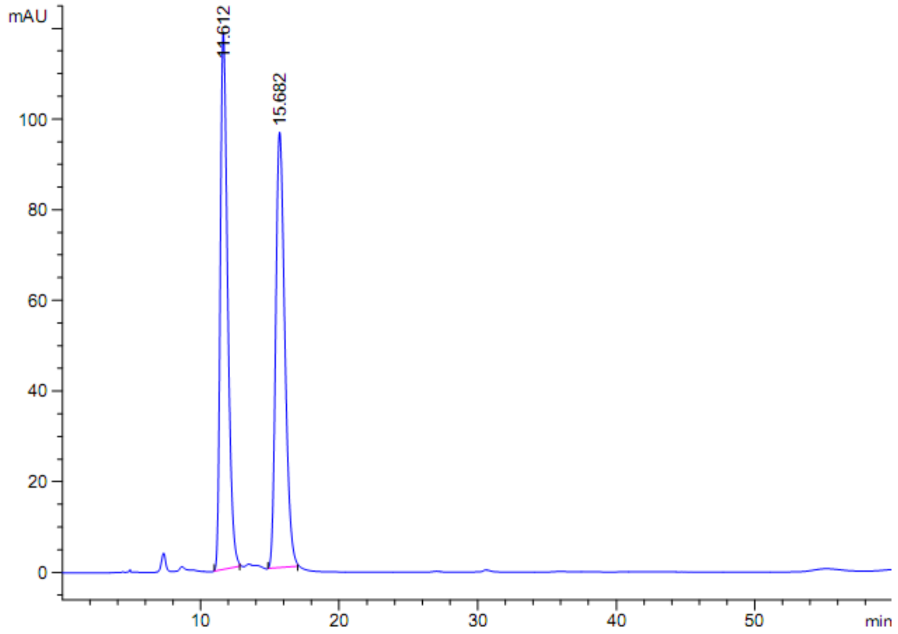
2-(azulen-1-yl)-1,2-diphenylethyl)(benzyl)sulfane

Followed method B from **1a** (23.2 mg, 0.05 mmol), for 72 h, and purified using silica gel chromatography to give 4.3 mg (20% yield) of desired product as a blue gel. This material was determined to be 32% ee by chiral HPLC analysis (ChiralPak OD-H, 2% MeOH, 3 mL/min, 300 nm, t_r(major) = 12 min, t_r(minor) = 17 min). IR (Film): 3026, 2913, 1574 (s), 1492 (s), 1452 (s), 1394 (s), 1238, 1072, 1028, 943, 736, 695 (s) cm^{-1}; ^{1}H NMR: (500 MHz, CDCl$_3$) δ 8.39 (d, *J*=9.8 Hz, 1H), 8.31 (d, *J*=9.3 Hz, 1H), 8.01 (d, *J*=3.9 Hz, 1H), 7.55 (t, *J*=9.8 Hz, 1H), 7.47 (d, *J*=3.4 Hz, 1H), 7.24 (m, 17H), 5.08 (d, *J*=11.2 Hz, 1H), 4.65 (d, *J*=11.2 Hz, 1H), 3.45 (d, *J*=13.7 Hz, 1H), 3.32 (d, *J*=13.7 Hz, 1H); ^{13}C NMR: (125 MHz, CDCl$_3$) δ 143.15, 141.11, 140.94, 138.19, 137.28, 136.52, 136.06, 135.70, 133.17, 130.06, 129.08, 128.20, 128.13, 128.01, 127.85, 126.83, 126.78, 125.71, 122.67, 121.98, 117.08, 54.94, 50.29, 35.76; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{31}H_{27}S$) requires *m/z* 431.2, found *m/z* 431.1.



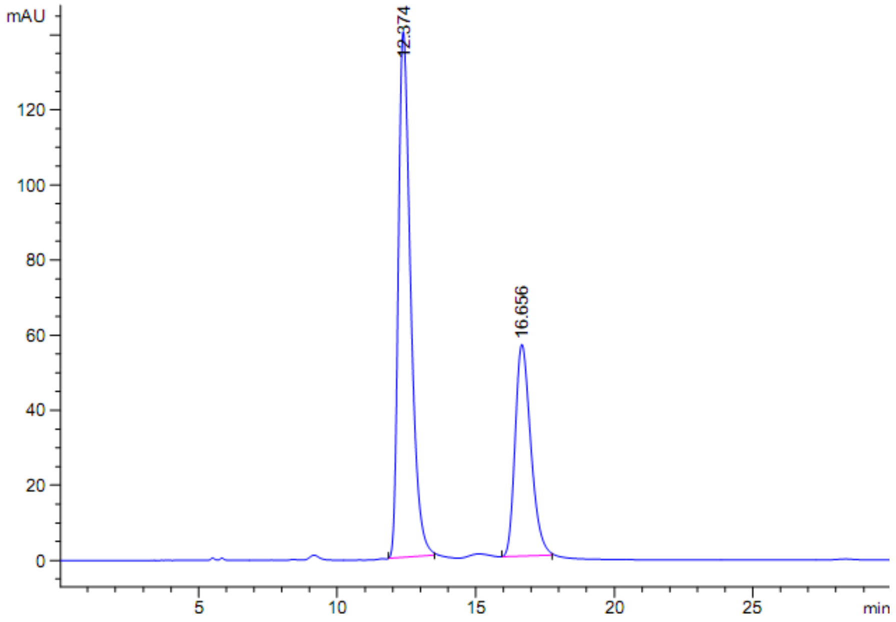


Racemic sample:



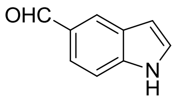
```
Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  11.612 BB    0.5678 4380.72754  118.36784  49.9424
   2  15.682 BB    0.7091 4390.83887   96.09332  50.0576
```

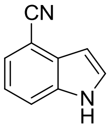
Enantioenriched sample:



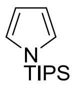
```
Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  12.374 BB    0.4699 4323.57275  140.14844  66.1099
   2  16.656 BB    0.6022 2216.40625   56.43709  33.8901
```

Nucleophiles that didn’t produce desired products in the thiourea-catalyzed episulfonium ion opening reaction:

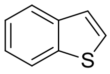




N ~ 2.83



N = 3.12

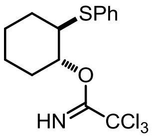


N ~ -1.01

Nucleophilicity parameters were obtained from Mayr’s database of reactivity parameter.

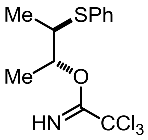
The *N* values of 4-cyanoindole and benzothiophene were estimated using data for 5-cyanoindole and thiophene, respectively.

Episulfonium precursors that didn’t produce high reactivity/selectivity:



with 20 mol% **5** and 10 mol% HOTf

16%, 9% ee



with 20 mol% **5** and 10 mol% HOTf

33%, 6% ee