Diastereo- and Enantioselective Copper-Catalyzed Intramolecular Carboamination of Alkenes for the Synthesis of Hexahydro-1*H*-benz[*f*]indoles

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Supporting Information 1

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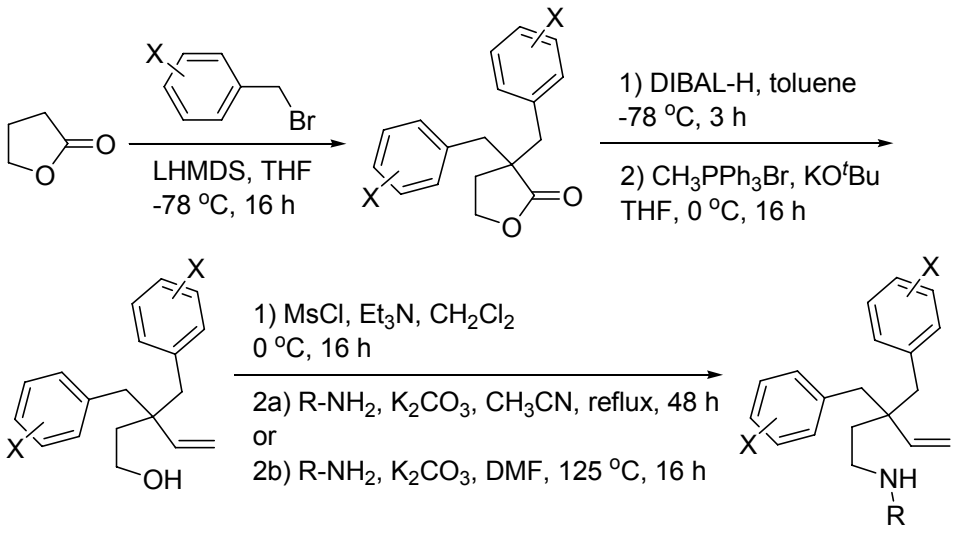
General information:

All reactions were performed under an argon atmosphere with stirring. (*R*,*R*)-2,2′-Isopropylidenebis(4-phenyl-2-oxazoline) [(*R*,*R*)-Ph-Box] was purchased from Aldrich. All other reagents were purchased from Aldrich, Acros or Strem. Solvents were purified using a solvent filtration system. $PhCF_3$ was purchased from Acros and was used without further purification. ^1H NMR spectra were recorded at 300, 400 or 500 MHz using Varian instruments. ^{13}C NMR data were recorded at 75 or 125 MHz. Coupling constants (*J*) are in hertz. Abbreviations used are s = singlet, d = doublet, t = triplet, m = multiplet, ABq = AB quartet and br = broad. IR spectra were taken neat using a Nicolet-Impact 420 FTIR. Wave numbers in cm^{-1} are reported for characteristic peaks. High resolution mass spectra were obtained at SUNY, Buffalo's mass spec. facility on a ThermoFinnigan MAT XL spectrometer. Optical rotations were obtained using a Rudolph Autopol I Polarimeter fitted with a micro cell with a 1 dm path length. Enantiomeric excess was determined by high performance liquid chromatography (HPLC) using CHIRALCEL OD-H or Chiralpak AD-RH, or Regis (*S*,*S*)-Whelk chiral analytical column (UV detection at 254 nm). Melting points were obtained on an electrothermal melting point apparatus and are reported uncorrected. X-ray structures were obtained at the x-ray crystallographic facilities at the University of Rochester and the University at Bufffalo.

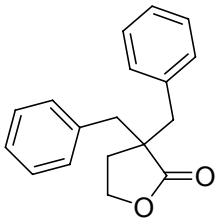
Synthesis of substrates

The disubstituted sulfonamide substrates **1a**-**h**, **5a**, and **1k** were synthesized from γ-butyrolactone in 5 steps via the following route:[1]



Representative procedure for dibenzylation of γ-butyrolactone:

3,3-Dibenzyl-dihydrofuran-2(3*H*)-one (12).[1]

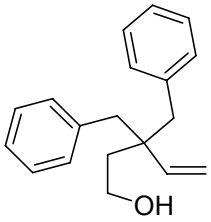


12

To a solution of hexamethyldisilazane (16.0 mL, 76.7 mmol, 2.2 equiv) in THF (60 mL) under argon, a 1.6 M solution of *n*-BuLi (48.0 mL, 76.7 mmol, 2.2 equiv) in hexanes was added at -78 °C and the resulting solution was allowed to stir for 20 min. γ-Butyrolactone (2.68 mL, 34.8 mmol) was then added dropwise. After 20 min benzyl bromide (9.11 mL, 76.7 mmol, 2.2 equiv) was added dropwise and the reaction was allowed to warm to rt and was stirred for 16 h. The reaction mixture was then quenched with water (40 mL) and extracted with EtOAc (150, 50 and 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 80:20 hexanes/EtOAc) to afford 6.54 g (70% yield) of **12** as a white solid, mp 128-130 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.18 (m, 10H), 3.36 (t, J = 7.5 Hz, 2H), 2.99 (ABq, J_{AB} = 14.0, $\Delta\nu$ = 207.1 Hz, 4H), 2.78 (d, J = 13.4 Hz, 2H), 2.15 (t, J = 7.4 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.1, 136.4, 130.1, 128.5, 127.1, 65.2, 49.8, 43.8, 29.0; IR (neat): 1752, 1455, 1448, 1377, 1222, 1168, 1082, 1027, 761, 714, 701, 676 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_{18}H_{18}O_2$: 266.1301, found: 266.1305.

Representative DIBAL-H reduction and Wittig olefination of dibenzylated lactone:

3,3-Dibenzylpent-4-en-1-ol (13).[1]



13

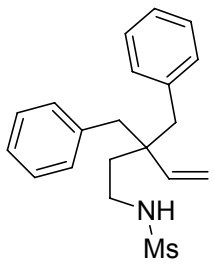
To a solution of the lactone **12** (3.60 g, 13.5 mmol) in toluene (90 mL) under argon at -78 °C, a 1.0 M solution of diisobutyl aluminum hydride in toluene (27.0 mL, 27.0 mmol, 2.0 equiv) was added dropwise. The reaction mixture was stirred for 3 h and the temperature was kept constant at -78 °C. The reaction was then quenched with an aqueous solution of sodium potassium tartrate (30 mL) and was stirred for 16 hours at rt. The aqueous phase was extracted with Et_2O (2 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to afford the crude lactol as a clear oil which was used in the next step without further purification.

To a solution of methyl triphenyl phosphonium bromide (14.5 g, 40.6 mmol, 3.0 equiv) in THF (60 mL) under argon at 0 °C, was added KO^{t}Bu (4.55 g, 40.6 mmol, 3.0 equiv) and the yellow mixture was stirred for 10 min. A solution of the crude lactol in THF (30 mL) was then added dropwise and the reaction was allowed to warm to rt and was stirred for 16 h. The reaction mixture was then quenched with water (50 mL) and extracted with Et_2O (150, 50 and 50 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column

chromatography (SiO_2, 80:20 hexanes/EtOAc) to afford 3.33 g (92% yield, 2 steps) of **13** as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 – 7.17 (m, 6H), 7.16 – 7.10 (m, 4H), 5.79 (dd, J = 11.1, 17.7 Hz, 1H), 5.10 (d, J = 11.1 Hz, 1H), 4.90 (d, J = 17.7 Hz, 1H), 3.81 (t, J = 7.5 Hz, 2H), 2.73 (ABq, J_{AB} = 13.5, $\Delta\nu$ = 24.5 Hz, 4H), 1.65 – 1.57 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.7, 137.7, 130.9, 127.7, 126.1, 113.1, 59.6, 44.4, 42.9, 36.8; IR (neat): 3344, 3083, 3061, 3027, 2936, 2855, 1635, 1601, 1495, 1453, 1415, 1089, 1032, 1005, 915, 757, 702 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_{19}H_{22}O$: 266.1665, found: 266.1677.

Representative sulfonamide syntheses via S_N2 displacement:

***N*-(3,3-Dibenzylpent-4-enyl)methanesulfonamide (1a).**[1]

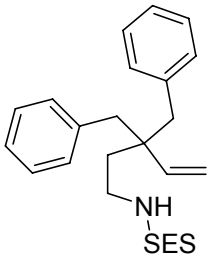


1a

To a solution of the alcohol **13** (0.786 g, 2.95 mmol) in CH_2Cl_2 (30 mL) under argon at 0 °C, was added triethylamine (1.23 mL, 8.85 mmol, 3.0 equiv) and methane sulfonyl chloride (0.274 mL, 3.54 mmol, 1.2 equiv) dropwise. The reaction was allowed to warm to rt and was stirred for 16 h. The reaction mixture was then quenched with water (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford the crude mesylate as a clear oil which was used in the next step without further purification.

To a solution of the crude mesylate in CH_3CN (50 mL) under argon, was added methanesulfonamide ($MsNH_2$, 1.12 g, 11.8 mmol, 4.0 equiv) and potassium carbonate (1.63 g, 11.8 mmol, 4.0 equiv) at rt. The resulting solution was refluxed at 90 °C and allowed to stir for 48 h. The reaction mixture was cooled to rt then quenched with water (30 mL) and extracted with Et_2O (60, 30 and 30 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 60:40 hexanes/EtOAc) to afford 443 mg (44% yield, 2 steps) of **1a** as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.19 (m, 6H), 7.16 – 7.10 (m, 4H), 5.76 (dd, J = 11.1, 17.7 Hz, 1H), 5.16 (d, J = 11.1 Hz, 1H), 4.91 (d, J = 17.8 Hz, 1H), 4.06 (t, J = 5.9 Hz, 1H), 3.29 – 3.21 (m, 2H), 2.87 (s, 3H), 2.74 (ABq, J_{AB} = 13.5, $\Delta\nu$ = 27.3 Hz, 4H), 1.56 – 1.50 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.9, 137.3, 130.8, 127.9, 126.40, 113.8, 44.1, 43.0, 40.4, 39.5, 34.5; IR (neat): 3305, 2933, 1601, 1494, 1452, 1412, 1321, 1150, 1072, 973, 916, 758, 703 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_{20}H_{25}NO_2S$: 343.1601, found: 343.1600.

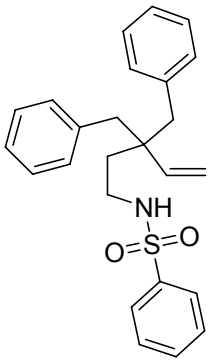
***N*-(3,3-Dibenzylpent-4-enyl)-2-(trimethylsilyl)ethanesulfonamide (1b).**



1b

Alcohol **13** was converted to sulfonamide **1b** using the same procedure as **13** to **1a** except $SESNH_2$ (1.2 equiv) was the sulfonamide nucleophile and displacement was carried out in DMF at 125 °C for 16 hours. Substrate **1b** was obtained as a clear oil (39% yield, 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.18 (m, 6H), 7.16 – 7.10 (m, 4H), 5.76 (dd, J = 11.1, 17.7 Hz, 1H), 5.15 (d, J = 11.1 Hz, 1H), 4.89 (d, J = 17.7 Hz, 1H), 4.00 (t, J = 6.1 Hz, 1H), 3.28 – 3.20 (m, 2H), 2.89 – 2.82 (m, 2H), 2.73 (ABq, J_{AB} = 13.5, $\Delta\nu$ = 26.1 Hz, 4H), 1.55 – 1.47 (m, 2H), 0.98 – 0.92 (m, 2H), 0.05 – 0.01 (m, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.9, 137.3, 130.8, 127.9, 126.4, 113.8, 48.8, 44.2, 43.1, 39.5, 34.7, 10.6, -2.0; IR (neat): 3280, 3028, 2951, 1602, 1495, 1454, 1417, 1322, 1263, 1251, 1168, 1142, 1077, 915, 858, 842, 757, 703 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{24}H_{36}NO_2SSi$: 430.2231, found: 430.224.

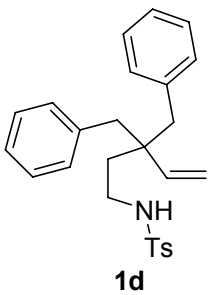
***N*-(3,3-Dibenzylpent-4-enyl)benzenesulfonamide (1c).**



1c

Alcohol **13** was converted to sulfonamide **1c** using the same procedure as **13** to **1a** except $BsNH_2$ (4.0 equiv) was the sulfonamide nucleophile and displacement was carried out in DMF at 125 °C for 16 h. Substrate **1c** was obtained as a white solid (89% yield, 2 steps), mp 79-81 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 – 7.79 (m, 2H), 7.60 – 7.54 (m, 1H), 7.53 – 7.46 (m, 2H), 7.23 – 7.16 (m, 6H), 7.03 – 6.97 (m, 4H), 5.65 (dd, J = 11.1, 17.7 Hz, 1H), 5.07 (d, J = 11.1 Hz, 1H), 4.77 (d, J = 17.7 Hz, 1H), 4.30 (t, J = 5.9 Hz, 1H), 3.14 – 3.06 (m, 2H), 2.63 (ABq, J_{AB} = 13.5, $\Delta\nu$ = 26.4 Hz, 4H), 1.42 – 1.34 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.8, 139.9, 137.2, 132.6, 130.7, 129.1, 127.8, 127.0, 126.3, 113.7, 44.05 43.0, 39.4, 33.7; IR (neat): 3289, 2928, 2363, 2341, 1601, 1495, 1447, 1416, 1326, 1161, 1094, 1072, 916, 755, 723, 704, 689, 583 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_{25}H_{27}NO_2S$: 405.1757, found: 405.1740.

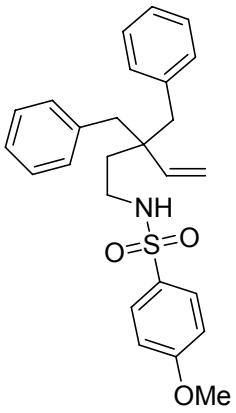
***N*-(3,3-Dibenzylpent-4-enyl)-4-methylbenzenesulfonamide (1d).**



1d

Alcohol **13** was converted to sulfonamide **1d** using the same procedure as **13** to **1a** except $TsNH_2$ (4.0 equiv) was the sulfonamide nucleophile. Substrate **1d** was obtained as a white solid (86% yield, 2 steps), mp 99-101 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.1 Hz, 2H), 7.24 – 7.15 (m, 6H), 7.03 – 6.96 (m, 4H), 5.65 (dd, J = 11.1, 17.7 Hz, 1H), 5.07 (d, J = 11.1 Hz, 1H), 4.78 (d, J = 17.7 Hz, 1H), 4.27 (t, J = 5.9 Hz, 1H), 3.12 – 3.04 (m, 2H), 2.63 (ABq, J_{AB} = 13.5, $\Delta\nu$ = 26.5 Hz, 4H), 2.43 (s, 3H), 1.42 – 1.34 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.8, 143.3, 137.2, 136.9, 130.7, 129.6, 127.8, 127.1, 126.3, 113.6, 44.0, 43.0, 39.3, 33.7, 21.5; IR (neat): 3286, 3028, 2926, 1636, 1599, 1495, 1453, 1416, 1327, 1290, 1161, 1094, 1073, 913, 815, 757, 704, 662, 552 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_{26}H_{29}NO_2S$: 419.1914, found: 419.1910.

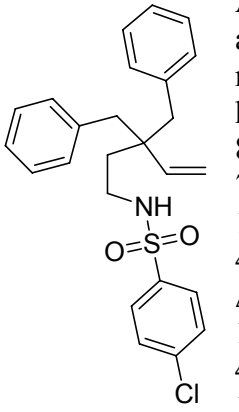
***N*-(3,3-Dibenzylpent-4-enyl)-4-methoxybenzenesulfonamide (1e).**



1e

Alcohol **13** was converted to sulfonamide **1e** using the same procedure as **13** to **1a** except $PMBSNH_2$ (4.0 equiv) was the sulfonamide nucleophile and displacement was carried out in DMF at 125 ^{o}C for 16 h. Substrate **1e** was obtained as a white solid (85% yield, 2 steps), mp 102-104 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 – 7.72 (m, 2H), 7.24 – 7.16 (m, 6H), 7.03 – 6.92 (m, 6H), 5.66 (dd, J = 11.0, 17.7 Hz, 1H), 5.08 (d, J = 11.1 Hz, 1H), 4.78 (d, J = 17.7 Hz, 1H), 4.12 (t, J = 5.9 Hz, 1H), 3.87 (s, 3H), 3.12 – 3.03 (m, 2H), 2.64 (ABq, J_{AB} = 13.0, $\Delta\nu$ = 26.1 Hz, 4H), 1.42 – 1.33 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.8, 143.8, 137.2, 131.4, 130.7, 129.2, 127.8, 126.2, 114.2, 113.6, 55.5, 44.0, 43.0, 39.3, 33.7; IR (neat): 3282, 3028, 2940, 1636, 1597, 1580, 1497, 1455, 1442, 1416, 1327, 1303, 1260, 1181, 1155, 1096, 1073, 1028, 914, 834, 802, 757, 704, 668, 563 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_{26}H_{29}NO_3S$: 435.1863, found: 435.1850.

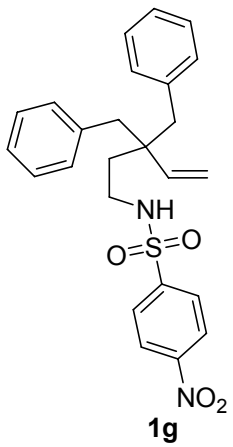
4-Chloro-*N*-(3,3-dibenzylpent-4-enyl)benzenesulfonamide (1f).



1f

Alcohol **13** was converted to sulfonamide **1f** using the same procedure as **13** to **1a** except $PCBSNH_2$ (4.0 equiv) was the sulfonamide nucleophile and displacement was carried out in DMF at 125 ^{o}C for 16 h. Substrate **1f** was obtained as a white solid (83% yield, 2 steps), mp 85-87 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 – 7.70 (m, 2H), 7.47 – 7.42 (m, 2H), 7.24 – 7.18 (m, 6H), 7.04 – 6.98 (m, 4H), 5.66 (dd, J = 11.1, 17.7 Hz, 1H), 5.09 (d, J = 11.1 Hz, 1H), 4.80 (d, J = 17.7 Hz, 1H), 4.29 (t, J = 6.0 Hz, 1H), 3.14 – 3.05 (m, 2H), 2.65 (ABq, J_{AB} = 13.0, $\Delta\nu$ = 28.7 Hz, 4H), 1.42 – 1.33 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7, 139.0, 138.5, 137.1, 130.7, 129.3, 128.4, 127.9, 126.3, 113.8, 44.1, 43.0, 39.4, 33.8; IR (neat): 3282, 3085, 3061, 3028, 2927, 2856, 1636, 1601, 1586, 1495, 1477, 1453, 1416, 1396, 1331, 1279, 1163, 1095, 1014, 914, 828, 754, 704, 619 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{25}H_{27}ClNO_2S$: 440.1446, found: 440.1433.

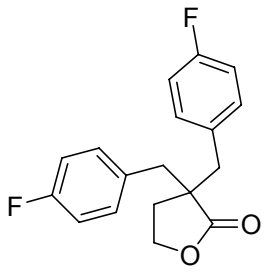
***N*-(3,3-Dibenzylpent-4-enyl)-4-nitrobenzenesulfonamide (1g).**



1g

Alcohol **13** was converted to sulfonamide **1g** using the same procedure as **13** to **1a** except $NsNH_2$ (4.0 equiv) was the sulfonamide nucleophile and displacement was carried out in DMF at 125 °C for 16 hours. Substrate **1g** was obtained as a pale yellow oil (77% yield, 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 – 8.26 (m, 2H), 7.96 – 7.91 (m, 2H), 7.24 – 7.17 (m, 6H), 7.06 – 6.99 (m, 4H), 5.65 (dd, J = 11.1, 17.7 Hz, 1H), 5.11 (d, J = 11.1 Hz, 1H), 4.82 (d, J = 17.7 Hz, 1H), 4.49 (t, J = 5.9 Hz, 1H), 3.20 – 3.11 (m, 2H), 2.66 (ABq, J_{AB} = 14.0, $\Delta\nu$ = 30.1 Hz, 4H), 1.40 – 1.33 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.9, 146.1, 143.6, 137.0, 130.7, 128.1, 127.9, 126.4, 124.3, 113.9, 44.1, 42.9, 39.6, 34.0; IR (neat): 3318, 2929, 1605, 1529, 1495, 1453, 1348, 1311, 1165, 1093, 916, 854, 736, 704, 685, 610 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_{25}H_{26}N_2O_4S$: 450.1608, found: 450.1605.

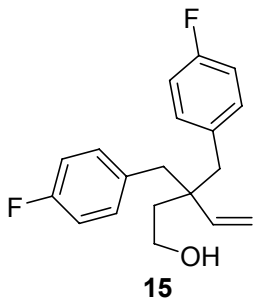
3,3-Bis(4-fluorobenzyl)-dihydrofuran-2(3*H*)-one (14).



14

Lactone **14** was synthesized using the same procedure as the syntheses of **12** but with 1-(bromomethyl)-4-fluorobenzene as electrophile. Lactone **14** was obtained as a white solid (70% yield), mp 82-84 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (dd, J = 5.4, 8.5 Hz, 4H), 7.00 (t, J = 8.6 Hz, 4H), 3.43 (t, J = 7.4 Hz, 2H), 2.95 (ABq, J_{AB} = 13.6, $\Delta\nu$ = 208.1 Hz, 4H), 2.13 (t, J = 7.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.6, 162.1 (d, J_{CF} = 244.2 Hz), 132.0 (d, J_{CF} = 3.37 Hz), 131.6 (d, J_{CF} = 7.95 Hz), 115.5 (d, J_{CF} = 21.1 Hz), 65.1, 49.8, 42.9, 28.9; IR (neat): 2922, 1757, 1603, 1510, 1448, 1379, 1226, 1169, 1096, 1028, 835, 735, 607, 539 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_{18}H_{16}F_2O_2$: 302.1113, found: 302.1119.

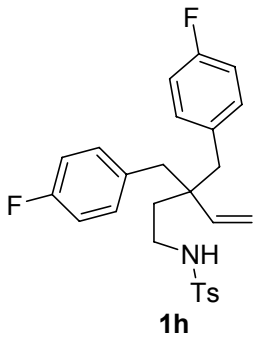
3,3-Bis(4-fluorobenzyl)pent-4-en-1-ol (15).



15

Lactone **14** was converted to alcohol **15** using same procedure as **12** to **13**. Alcohol **15** was obtained as a clear oil (90% yield, 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 – 7.05 (m, 4H), 6.97 – 6.91 (m, 4H), 5.74 (dd, J = 11.0, 17.7 Hz, 1H), 5.12 (d, J = 11.0 Hz, 1H), 4.88 (d, J = 17.7 Hz, 1H), 3.81 (td, J = 3.5, 7.4 Hz, 2H), 2.68 (ABq, J_{AB} = 13.0, $\Delta\nu$ = 20.3 Hz, 4H), 1.61 – 1.55 (m, 2H), 1.25 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.6 (d, J_{CF} = 243.0 Hz), 144.2, 133.2 (d, J_{CF} = 3.37 Hz), 132.2 (d, J_{CF} = 7.42 Hz), 114.6 (d, J_{CF} = 20.5 Hz), 113.6, 59.4, 43.5, 42.9, 36.6; IR (neat): 3348, 2936, 1603, 1509, 1417, 1223, 1159, 1038, 1016, 918, 838, 826, 776 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_{19}H_{20}F_2O$: 302.1477, found: 302.1480.

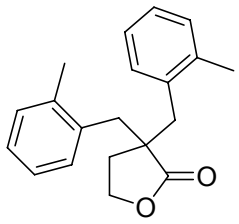
***N*-(3,3-Bis(4-fluorobenzyl)pent-4-enyl)-4-methylbenzenesulfonamide (1h).**



1h

Alcohol **15** was converted to sulfonamide **1h** using the same procedure as **13** to **1a** except $TsNH_2$ (4.0 equiv) was the sulfonamide nucleophile. Substrate **1h** was obtained as a clear oil (89% yield, 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, J = 8.3 Hz, 2H), 7.32 – 7.26 (m, 2H), 6.99 – 6.84 (m, 8H), 5.60 (dd, J = 11.1, 17.7 Hz, 1H), 5.08 (d, J = 11.1 Hz, 1H), 4.75 (d, J = 17.7 Hz, 1H), 4.51 (t, J = 5.9 Hz, 1H), 3.10 – 3.00 (m, 2H), 2.58 (ABq, J_{AB} = 14.0, $\Delta\nu$ = 22.8 Hz, 4H), 2.43 (s, 3H), 1.40 – 1.33 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.5 (d, J_{CF} = 243.3 Hz), 143.5, 143.3, 136.8, 132.7 (d, J_{CF} = 3.22 Hz), 132.0 (d, J_{CF} = 7.72 Hz), 129.7, 127.0, 114.6 (d, J_{CF} = 21.0 Hz), 114.1, 43.1, 42.9, 39.2, 33.7, 21.5; IR (neat): 3282, 3042, 2929, 2861, 1636, 1601, 1509, 1446, 1417, 1326, 1306, 1290, 1222, 1159, 1094, 1016, 914, 840, 826, 816, 776, 735, 662, 552 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{26}H_{28}F_2NO_2S$: 456.1803, found: 456.1808.

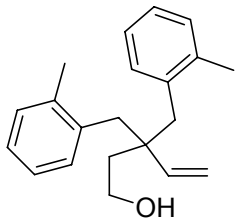
3,3-Bis(2-methylbenzyl)dihydrofuran-2(3*H*)-one (21).



21

Lactone **21** was synthesized using the same procedure as the syntheses of **12** but with 1-(bromomethyl)-2-methylbenzene as electrophile. Lactone **21** was obtained as a white solid (72% yield), mp 111-113 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 – 7.08 (m, 8H), 3.48 (t, J = 7.2 Hz, 2H), 3.09 (ABq, J_{AB} = 14.0, $\Delta\nu$ = 79.9 Hz, 4H), 2.28 (s, 6H), 2.06 (t, J = 7.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.6, 136.9, 135.1, 130.6, 130.4, 127.1, 126.2, 65.5, 50.1, 39.2, 28.7, 20.1; IR (neat): 1763, 1493, 1453, 1378, 1163, 1029, 775, 750, 734 cm^{-1}; HRMS (ESI) calcd for $[M + Na]^+$ $C_{20}H_{22}O_2N_a$: 317.1512, found: 317.1505.

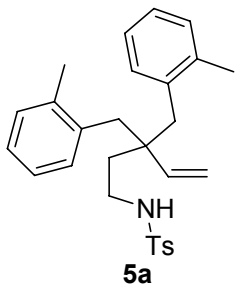
3,3-Bis(2-methylbenzyl)pent-4-en-1-ol (22).



22

Lactone **21** was converted to alcohol **22** using the same procedure as **12** to **13**. Alcohol **22** was obtained as a clear oil (43% yield, 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 – 7.07 (m, 8H), 5.81 (dd, J = 11.1, 17.8 Hz, 1H), 5.05 (d, J = 11.1 Hz, 1H), 4.93 (d, J = 17.8 Hz, 1H), 3.81 (t, J = 6.6 Hz, 2H), 2.81 (ABq, J_{AB} = 13.5, $\Delta\nu$ = 9.56 Hz, 4H), 2.25 (s, 6H), 1.83 (t, J = 7.4 Hz, 2H), 1.24 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.2, 137.5, 136.3, 131.4, 130.5, 126.2, 125.2, 112.7, 59.7, 44.6, 40.0, 37.4, 20.6; IR (neat): 3327, 3018, 2948, 1635, 1603, 1492, 1455, 1034, 914, 770, 745 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_{21}H_{26}O$: 294.1978, found: 294.1984.

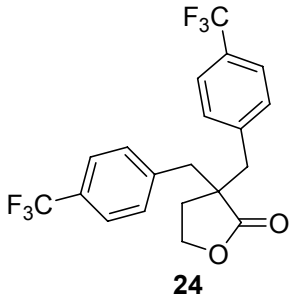
***N*-(3,3-Bis(2-methylbenzyl)pent-4-enyl)-4-methylbenzenesulfonamide (5a).**



5a

Alcohol **22** was converted to sulfonamide **5a** using the same procedure as **13** to **1a** except $TsNH_2$ (4.0 equiv) was the sulfonamide nucleophile. Substrate **5a** was obtained as a white solid (90% yield, 2 steps), mp 100-102 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.1 Hz, 2H), 7.11 (d, J = 4.0 Hz, 4H), 7.09 – 7.02 (m, 2H), 6.98 (d, J = 7.4 Hz, 2H), 5.66 (dd, J = 11.1, 17.8 Hz, 1H), 5.02 (d, J = 11.1 Hz, 1H), 4.81 (d, J = 17.8 Hz, 1H), 4.23 (t, J = 5.9 Hz, 1H), 3.17 – 2.93 (m, 2H), 2.72 (ABq, J_{AB} = 14.0, $\Delta\nu$ = 11.3 Hz, 4H), 2.43 (s, 3H), 2.17 (s, 6H), 1.62 (t, J = 8.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.4, 143.3, 137.40, 136.9, 135.8, 131.2, 130.6, 129.7, 127.1, 126.3, 125.3, 113.3, 44.6, 39.6, 39.5, 34.5, 21.5, 20.6; IR (neat): 3282, 3019, 2994, 2360, 2341, 1599, 1493, 1455, 1327, 1094, 915, 814, 746, 662, 552 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{28}H_{34}NO_2S$: 448.2305, found: 448.2302.

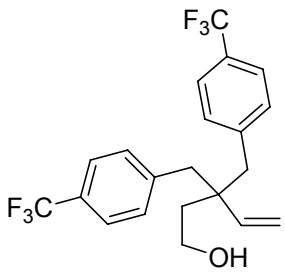
3,3-Bis(4-(trifluoromethyl)benzyl)-dihydrofuran-2(3*H*)-one (24).



24

Lactone **24** was synthesized using the same procedure as the syntheses of **12** but with 1-(bromomethyl)-4-(trifluoromethyl)benzene as electrophile. Lactone **24** was obtained as a white solid (92% yield), mp 142-144 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.1 Hz, 4H), 7.34 (d, J = 8.0 Hz, 4H), 3.46 (t, J = 7.4 Hz, 2H), 3.07 (ABq, J_{AB} = 13.2, $\Delta\nu$ = 162.0 Hz, 4H), 2.15 (t, J = 7.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.0, 140.1, 130.5, 129.8 (q, J_{CF} = 32.4 Hz), 125.6 (q, J_{CF} = 3.67 Hz), 122.2, 65.10, 49.55, 43.38, 28.92; IR (neat): 2360, 2340, 1759, 1618, 1421, 1324, 1164, 1132, 1121, 1109, 1068, 1028, 1020, 838 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_{20}H_{16}F_6O_2$: 402.1049, found: 402.1054.

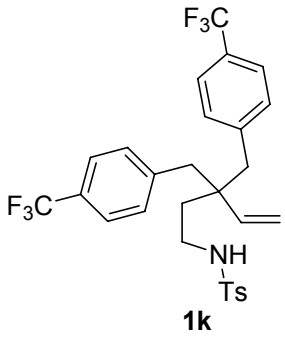
3,3-Bis(4-(trifluoromethyl)benzyl)pent-4-en-1-ol (25).



25

Lactone **24** was converted to alcohol **25** using the same procedure as **12** to **13**. Alcohol **25** was obtained as a clear oil (99% yield, 2 steps). ^1H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, J = 8.1 Hz, 4H), 7.27 (d, J = 7.6 Hz, 4H), 5.75 (dd, J = 11.1, 17.7 Hz, 1H), 5.17 (d, J = 11.1 Hz, 1H), 4.92 (d, J = 17.7 Hz, 1H), 3.86 (dd, J = 7.3, 12.4 Hz, 2H), 2.80 (ABq, J_{AB} = 13.5, $\Delta\nu$ = 19.8 Hz, 4H), 1.60 (t, J = 7.3 Hz, 2H), 1.25 (t, J = 5.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.6, 141.7, 131.1, 128.7 (q, J_{CF} = 32.2 Hz), 124.7 (q, J_{CF} = 3.75 Hz), 122.5, 114.2, 59.3, 44.3, 43.2, 36.6; IR (neat): 3340, 2936, 1618, 1419, 1326, 1164, 1119, 1069, 1019, 922, 854 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_{21}H_{20}F_6O_1$: 402.1413, found: 402.1413.

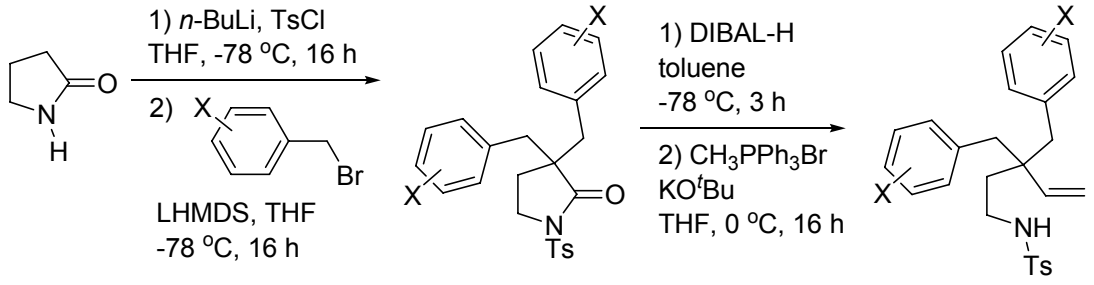
***N*-(3,3-Bis(4-(trifluoromethyl)benzyl)pent-4-enyl)-4-methylbenzenesulfonamide (1k).**



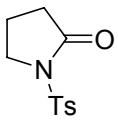
1k

Alcohol **25** was converted to sulfonamide **1k** using the same procedure as **13** to **1a** except $TsNH_2$ (4.0 equiv) was the sulfonamide nucleophile. Substrate **1k** was obtained as a white solid (92% yield, 2 steps), mp 116-118 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, J = 8.0 Hz, 2H), 7.47 (d, J = 8.0 Hz, 4H), 7.30 (d, J = 8.1 Hz, 2H), 7.13 (d, J = 8.0 Hz, 4H), 5.62 (dd, J = 11.1, 17.7 Hz, 1H), 5.13 (d, J = 11.0 Hz, 1H), 4.79 (d, J = 17.7 Hz, 1H), 4.42 (t, J = 5.9 Hz, 1H), 3.16 – 3.05 (m, 2H), 2.70 (ABq, J_{AB} = 13.5, $\Delta\nu$ = 23.8 Hz, 4H), 2.44 (s, 3H), 1.40 (t, J = 8.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.6, 142.7, 141.1, 136.9, 130.9, 129.7, 128.8 (q, J_{CF} = 32.3 Hz), 127.1, 124.8 (q, J_{CF} = 3.67 Hz), 122.4, 114.7, 43.9, 43.19, 4.11, 33.9, 21.4; IR (neat): 3279, 2935, 1618, 1419, 1326, 1161, 1120, 1068, 1019, 853, 816, 762, 662, 553 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{28}H_{28}F_6NO_2S$: 556.1739, found: 556.1736.

The disubstituted sulfonamide substrates **1i**, **1j**, **3a** and **5b** were synthesized from pyrrolidin-2-one in 4 steps via the following route:[2,3]



1-Tosylpyrrolidin-2-one (16).

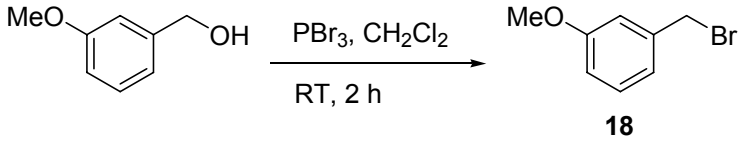


16

Ts-lactam **16** was synthesized following the procedure described by Dake and co-workers.[2] To a solution of pyrrolidin-2-one (0.910 mL, 11.7 mmol) in THF (50 mL) under argon, a 2.5 M solution of *n*-BuLi (5.16 mL, 12.9 mmol, 1.1 equiv) in hexanes was added at -78 °C and allowed to stir for 15 min. 4-Methylbenzene-1-sulfonyl chloride (TsCl, 2.46 g, 12.9 mmol, 1.1 equiv) in THF (50 mL) was then added dropwise and the reaction was allowed to warm to rt and was stirred for 16 h. The reaction mixture was then quenched with water (40 mL) and extracted with Et_2O (120, 40 and 40 mL). The combined organic layers was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 50:50 hexanes/EtOAc) to afford 2.50 g (89% yield) of **16** as a white solid, mp 135-137 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.2 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 3.89 (t, J = 7.0 Hz, 2H), 2.47 – 2.39 (m, 5H), 2.13 – 2.01 (m,

2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.2, 145.0, 135.0, 129.5, 127.9, 47.2, 32.1, 21.5, 18.1; IR (neat): 1728, 1594, 1352, 1297, 1198, 1170, 1117, 961, 814, 713, 665, 559 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{11}H_{14}NO_3S$: 240.0689, found: 240.0690. Data match those previously reported.[4]

Representative procedure for benzylbromide syntheses:



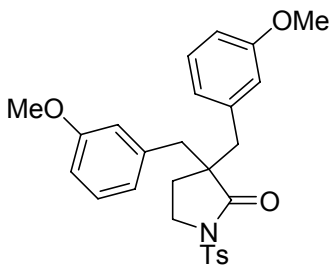
18

1-(Bromomethyl)-3-methoxybenzene (18).

Benzylbromide **18** was synthesized following the procedure described by Go and co-workers.[5] (3-Methoxyphenyl)methanol (1.24 mL, 10.0 mmol) was added to PBr_3 (0.564 mL, 6.00 mmol, 0.6 equiv) in dry CH_2Cl_2 (30 mL) under argon at rt for 2 h. The reaction was quenched with ice water (15 mL) and the aqueous phase was extracted twice with CH_2Cl_2 (15 and 15 mL). All combined organic layers were washed with saturated $NaHCO_3$ (10 mL), and brine (10 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was used in the next step without further purification. Data match those previously reported.[6]

Representative procedure for dibenzylation of 1-tosylpyrrolidin-2-one:

3,3-Bis(3-methoxybenzyl)-1-tosylpyrrolidin-2-one (20).



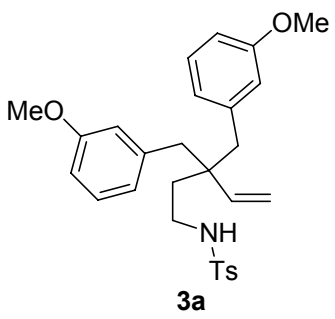
20

Lactam **20** was synthesized following the procedure described by Mendiola and co-workers.[3] To a solution of hexamethyldisilazane (2.09 mL, 10.0 mmol, 2.4 equiv) in THF (20 mL) under argon, a 1.6 M solution of *n*-BuLi (6.25 mL, 10.0 mmol, 2.4 equiv) in hexanes was added at -78 °C and allowed to stir for 20 min. 1-Tosylpyrrolidin-2-one (**16**) (1.00 g, 4.18 mmol) in THF (20 mL) was then added dropwise. After 20 min 1-(bromomethyl)-3-methoxybenzene (**18**) (10.0 mmol, 2.4 equiv) in THF (10 mL) was added dropwise and the reaction was allowed to warm to rt and was stirred for 16 h. The reaction mixture was then quenched with water (30 mL) and extracted with Et_2O (100, 50 and 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 80:20 hexanes/EtOAc) to afford 1.17 g (59% yield, 2 steps) of **20** as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.2 Hz, 2H), 6.98 (t, J =

7.9 Hz, 2H), 6.73 (dd, J = 2.4, 8.2 Hz, 2H), 6.61 (s, 2H), 6.51 (d, J = 7.5 Hz, 2H), 3.74 (s, 6H), 3.11 – 3.00 (m, 4H), 2.58 (d, J = 13.5 Hz, 2H), 2.49 (s, 3H), 1.99 (t, J = 7.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.5, 159.4, 144.7, 137.6, 135.2, 129.4, 129.3, 128.1, 122.1, 115.4, 112.5, 55.0, 51.9, 44.0, 43.8, 25.5, 21.6; IR (neat): 3025, 3001, 2917, 2837, 1728, 1599, 1584, 1489, 1467, 1455, 1438, 1363, 1264, 1170, 1131, 1091, 1042, 868, 776, 756, 699, 665, 600, 573, 573 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{27}H_{30}NO_5S$: 480.1839, found: 480.1830.

Representative DIBAL-H reduction and Wittig olefination of dibenzylated lactam:

***N*-(3,3-Bis(3-methoxybenzyl)pent-4-enyl)-4-methylbenzenesulfonamide (3a).**

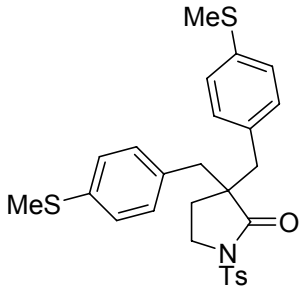


3a

Sulfonamide **3a** was synthesized following the procedure described by Mendiola and co-workers.[3] To a solution of the lactam **20** (1.05 g, 2.20 mmol) in toluene (50 mL) under argon at -78 °C, a 1.0 M solution of diisobutyl aluminum hydride in toluene (3.52 mL, 3.52 mmol, 1.6 equiv) was added dropwise. The reaction mixture was stirred for 3 h and the temperature was kept constant at -78 °C. The reaction was then quenched with an aqueous solution of sodium potassium tartrate (20 mL) and was stirred for 16 h at rt. The aqueous phase was extracted with Et_2O (2 × 30 mL). The combined organic layers was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to afford the crude lactol as a clear oil which was used in the next step without further purification.

To a solution of methyl triphenyl phosphonium bromide (2.36 g, 6.60 mmol, 3.0 equiv) in THF (15 mL) under argon at 0 °C, was added KO^{t}Bu (0.741 g, 6.60 mmol, 3.0 equiv) and the yellow mixture was allowed to stir for 10 min. A solution of the crude lactol in THF (20 mL) was then added dropwise and the reaction was allowed to warm to rt and was stirred for 16 h. The reaction mixture was then quenched with water (20 mL) and extracted with Et_2O (80, 30 and 30 mL). The combined organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 80:20 hexanes/EtOAc) to afford 0.921 g (87% yield, 2 steps) of **3a** as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.1 Hz, 2H), 7.13 (t, J = 8.0 Hz, 2H), 6.78 – 6.72 (m, 2H), 6.63 – 6.57 (m, 4H), 5.69 (dd, J = 11.1, 17.8 Hz, 1H), 5.09 (d, J = 11.2 Hz, 1H), 4.81 (d, J = 17.7 Hz, 1H), 4.26 (t, J = 6.0 Hz, 1H), 3.76 (s, 6H), 3.11 – 3.03 (m, 2H), 2.62 (ABq, J_{AB} = 13.5, $\Delta\nu$ = 23.4 Hz, 4H), 2.42 (s, 3H), 1.43 (t, J = 8.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 144.1, 143.3, 138.8, 136.9, 129.7, 128.7, 127.0, 123.1, 116.5, 113.6, 111.6, 55.1, 44.1, 43.0, 39.4, 34.0, 21.5; IR (neat): 3280, 2936, 1600, 1583, 1489, 1454, 1435, 1326, 1264, 1158, 1093, 1045, 752, 662, 552 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{28}H_{34}NO_4S$: 480.2203, found: 480.2202.

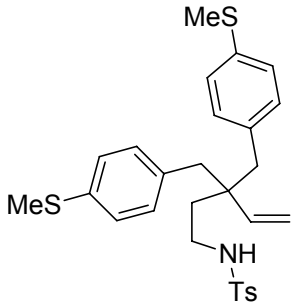
3,3-Bis(4-(methylthio)benzyl)-1-tosylpyrrolidin-2-one (17).



17

Lactam **17** was synthesized using the same procedure as the syntheses of **20** but with (4-(bromomethyl)phenyl)(methyl)sulfane as electrophile. Lactam **17** was obtained as a white solid (87% yield), mp 146-148 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, J = 8.3 Hz, 2H), 7.35 (d, J = 8.1 Hz, 2H), 6.94 (d, J = 8.4 Hz, 4H), 6.87 (d, J = 8.2 Hz, 4H), 3.06 – 2.94 (m, 4H), 2.54 (d, J = 12.9 Hz, 5H), 2.43 (d, J = 8.3 Hz, 6H), 1.94 (t, J = 7.2 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.5, 144.9, 136.9, 135.1, 132.8, 130.3, 129.5, 128.3, 126.4, 52.1, 43.9, 43.2, 25.4, 21.8, 15.7; IR (neat): 2919, 1727, 1597, 1494, 1440, 1364, 1231, 1187, 1170, 1115, 1092, 815, 733, 662, 547 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{27}H_{30}NO_3S_3$: 512.1382, found: 512.1369.

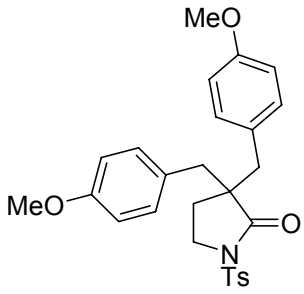
***N*-(3,3-Bis(4-(methylthio)benzyl)pent-4-enyl)-4-methylbenzenesulfonamide (1i)**.



1i

Lactam **17** was converted to sulfonamide **1i** using the same procedure as **20** to **3a**. Substrate **1i** was obtained as a yellow oil (82% yield, 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 – 7.67 (m, 2H), 7.31 – 7.27 (m, 2H), 7.12 – 7.06 (m, 4H), 6.91 (d, J = 8.2 Hz, 4H), 5.61 (dd, J = 11.0, 17.7 Hz, 1H), 5.05 (d, J = 11.1 Hz, 1H), 4.75 (d, J = 17.7 Hz, 1H), 4.40 (t, J = 5.9 Hz, 1H), 3.09 – 3.01 (m, 2H), 2.59 (ABq, J_{AB} = 13.5, Δv = 24.5 Hz, 4H), 2.48 – 2.41 (m, 9H), 1.40 – 1.33 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.6, 143.4, 136.8, 136.1, 134.0, 131.1, 129.6, 127.0, 126.1, 113.9, 43.4, 43.1, 39.2, 33.7, 21.5, 15.8; IR (neat): 1598, 1494, 1325, 1155, 1090, 908, 814, 662 cm^{-1}; HRMS (ESI) calcd for $[M + Na]^+$ $C_{28}H_{33}NO_2S_3Na$: 534.1566, found: 534.1567.

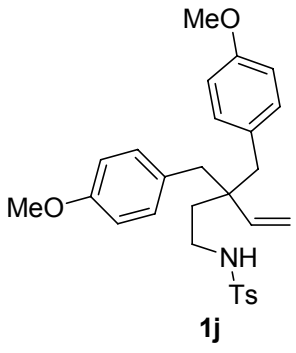
3,3-Bis(4-methoxybenzyl)-1-tosylpyrrolidin-2-one (19).



19

Lactam **19** was synthesized using the same procedure as the syntheses of **20** but with 1-(bromomethyl)-4-methoxybenzene[5] as electrophile. Lactam **19** was obtained as a clear oil (85% yield, 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 – 7.80 (m, 2H), 7.37 – 7.32 (m, 2H), 6.89 – 6.83 (m, 4H), 6.64 – 6.58 (m, 4H), 3.76 (s, 6H), 3.02 (d, J = 13.6 Hz, 2H), 2.99 – 2.93 (m, 2H), 2.52 (d, J = 13.3 Hz, 5H), 1.97 – 1.91 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.9, 158.4, 144.8, 135.2, 130.9, 129.4, 128.4, 128.2, 113.7, 55.1, 52.2, 43.9, 42.9, 25.4, 21.7; IR (neat): 1724, 1611, 1512, 1363, 1248, 1170, 1113, 1034, 814, 729, 662 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_{27}H_{29}NO_5S$: 479.1761, found: 479.1767.

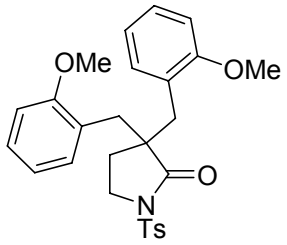
***N*-(3,3-Bis(4-methoxybenzyl)pent-4-enyl)-4-methylbenzenesulfonamide (1j).**



1j

Lactam **19** was converted to sulfonamide **1j** using the same procedure as **20** to **3a**. Substrate **1j** was obtained as a yellow oil (90% yield, 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, J = 8.0 Hz, 2H), 7.30 – 7.25 (m, 2H), 6.90 (d, J = 8.4 Hz, 4H), 6.73 (d, J = 8.1 Hz, 4H), 5.62 (dd, J = 11.1, 17.7 Hz, 1H), 5.04 (d, J = 11.0 Hz, 1H), 4.74 (d, J = 17.8 Hz, 1H), 4.40 (t, J = 5.9 Hz, 1H), 3.77 (d, J = 0.7 Hz, 6H), 3.09 – 3.00 (m, 2H), 2.55 (ABq, J_{AB} = 13.5, Δv = 23.5 Hz, 4H), 2.43 (s, 3H), 1.39 – 1.31 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.0, 144.0, 143.3, 136.9, 131.5, 129.6, 129.2, 127.1, 113.5, 113.2, 55.1, 43.0, 43.0, 39.3, 33.6, 21.5; IR (neat): 2924, 1610, 1511, 1441, 1325, 1257, 1178, 1159, 1094, 1035, 916, 815, 662 cm^{-1}; HRMS (ESI) calcd for $[M + Na]^+$ $C_{28}H_{33}NO_4SNa$: 502.2023, found: 502.2039.

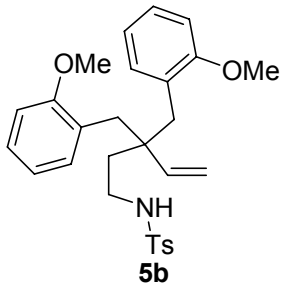
3,3-Bis(2-methoxybenzyl)-1-tosylpyrrolidin-2-one (23).



23

Lactam **23** was synthesized using the same procedure as the syntheses of **20** but with 1-(bromomethyl)-2-methoxybenzene[5,7] as electrophile. Lactam **23** was obtained as a white solid (91% yield, 2 steps), mp 94-96 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 8.2 Hz, 2H), 7.14 (t, J = 7.8 Hz, 2H), 6.88 (d, J = 7.4 Hz, 2H), 6.79 (d, J = 8.2 Hz, 2H), 6.60 (t, J = 7.4 Hz, 2H), 3.75 (s, 6H), 3.14 (t, J = 7.1 Hz, 2H), 2.93 (ABq, J_{AB} = 17.0, Δv = 81.4 Hz, 4H), 2.47 (s, 3H), 1.88 (t, J = 7.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.1, 157.7, 144.5, 135.5, 131.6, 129.3, 128.1, 127.9, 125.2, 120.4, 110.1, 55.1, 52.4, 44.4, 36.0, 25.6, 21.6; IR (neat): 3067, 3025, 2922, 2837, 1728, 1599, 1587, 1494, 1465, 1440, 1363, 1291, 1246, 1170, 1116, 1091, 1053, 1025, 814, 755, 732, 663, 588, 576, 547 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{27}H_{30}NO_5S$: 480.1839, found: 480.1830.

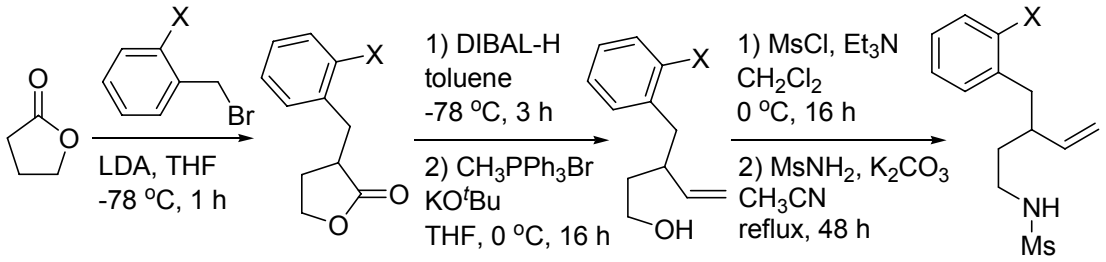
***N*-(3,3-Bis(2-methoxybenzyl)pent-4-enyl)-4-methylbenzenesulfonamide (5b).**



5b

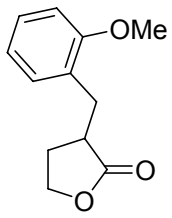
Lactam **23** was converted to sulfonamide **5b** using the same procedure as **20** to **3a**. Substrate **5b** was obtained as a white solid (84% yield, 2 steps), mp 65-67 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, J = 8.5 Hz, 2H), 7.23 (d, J = 8.5 Hz, 2H), 7.15 (td, J = 1.7, 7.9 Hz, 2H), 6.96 (dd, J = 1.7, 7.7 Hz, 2H), 6.81 – 6.75 (m, 4H), 5.64 (dd, J = 11.0, 17.7 Hz, 1H), 4.91(m, d, J = 11.0 Hz, 1H), 4.66 (d, J = 17.5 Hz, 1H), 4.49 (t, J = 5.9 Hz, 1H), 3.69 (s, 6H), 3.10 (dt, J = 6.0, 10.1 Hz, 2H), 2.71 (ABq, J_{AB} = 13.5, Δv = 18.1 Hz, 4H), 2.39 (s, 3H), 1.39 (t, J = 8.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.9, 144.5, 143.0, 137.0, 132.5, 129.5, 127.3, 127.0, 126.2, 119.7, 111.8, 110.4, 55.0, 43.9, 39.8, 36.7, 33.4, 21.4; IR (neat): 3273, 2933, 2836, 1599, 1585, 1493, 1463, 1439, 1327, 1290, 1245, 1160, 1128, 1094, 1052, 1030, 754, 662, 552 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_{28}H_{33}NO_4S$: 479.2125, found: 479.2124.

The monosubstituted sulfonamide substrates **9a** and **9b** were synthesized from γ-butyrolactone via the following route:[1]



Representative procedure for monobenzylation of γ-butyrolactone:

3-(2-Methoxybenzyl)-dihydrofuran-2(3*H*)-one (30).[1]

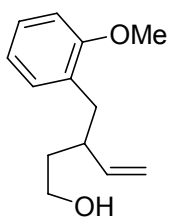


30

Lactone **30** was synthesized following the procedure described by Houpis and co-workers.[1] *n*-BuLi (1.6 M in hexanes, 24.0 mL, 38.0 mmol, 1.08 equiv) was added to diisopropylamine (5.40 mL, 38.0 mmol, 1.08 equiv) in THF (50 mL) under argon and allowed to stir for 15 min at –78 °C. γ-Butyrolactone (2.70 mL, 35.0 mmol) was added neat for 20 minutes at –78 °C. Then 1-(bromomethyl)-2-methoxybenzene[5,7] (35.0 mmol, 1.0 equiv) in THF (20 mL) was added dropwise via syringe over 20 min. The reaction was stirred for 1 h at –78 °C under argon. The reaction was quenched with aqueous NH_4Cl (50 mL) and extracted with Et_2O (150, 50 and 50 mL). All combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 80:20 hexanes/EtOAc) to afford 5.75 g (80% yield) of **30** as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (td, *J* = 1.7, 7.9 Hz, 1H), 7.13 (dd, *J* = 1.6, 7.4 Hz, 1H), 6.91 – 6.83 (m, 2H), 4.26 (td, *J* = 3.1, 8.6 Hz, 1H), 4.12 (td, *J* = 6.7, 9.2 Hz, 1H), 3.82 (s, 3H), 3.32 (dd, *J* = 4.6, 13.6 Hz, 1H), 2.94 (ddd, *J* = 4.6, 9.9, 18.6 Hz, 1H), 2.66 (dd, *J* = 9.9, 13.6 Hz, 1H), 2.16 (dddd, *J* = 3.2, 6.7, 8.7, 12.0 Hz, 1H), 1.97 (ddd, *J* = 9.7, 12.7, 18.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.2, 157.5, 130.5, 128.0, 126.9, 120.5, 110.2, 66.5, 55.1, 39.6, 30.8, 28.2; IR (neat): 3632, 3516, 3065, 2940, 2837, 1767, 1672, 1601, 1588, 1494, 1461, 1440, 1374, 1320, 1292, 1245, 1152, 1120, 1048, 1024, 958, 817, 756, 590 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_{12}H_{14}O_3$: 206.0937, found: 206.0944. Data match those previously reported.[8]

Representative DIBAL-H reduction and Wittig olefination of monobenzylated lactone:

3-(2-Methoxybenzyl)pent-4-en-1-ol (31).



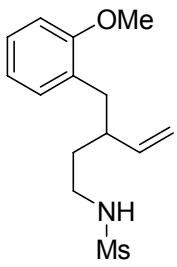
31

Alcohol **31** was synthesized following the procedure described by Houpis and co-workers.[1] To a solution of the lactone **30** (2.37 g, 11.5 mmol) in toluene (100 mL) under argon at -78 °C, a 1.2 M solution of diisobutyl aluminum hydride in toluene (14.4 mL, 17.2 mmol, 2.0 equiv) was added dropwise. The reaction mixture was stirred for 3 h and the temperature was kept constant at -78 °C. The reaction was then quenched with an aqueous solution of sodium potassium tartrate (30 mL) and was stirred for 16 hours at rt. The aqueous phase was extracted with Et_2O (2 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to afford the crude lactol as a clear oil which was used in the next step without further purification.

To a solution of methyl triphenyl phosphonium bromide (12.3 g, 34.5 mmol, 3.0 equiv) in THF (70 mL) under argon at 0 °C, was added KO^{t}Bu (3.87 g, 34.5 mmol, 3.0 equiv) and the yellow mixture was allowed to stir for 10 min. A solution of the crude lactol in THF (20 mL) was then added dropwise and the reaction was allowed to warm to rt and was stirred for 16 h. The reaction mixture was then quenched with water (50 mL) and extracted with Et_2O (150, 50 and 50 mL). The combined organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 80:20 hexanes/EtOAc) to afford 1.90 g (80% yield, 2 steps) of **31** as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 – 7.13 (m, 1H), 7.06 (dd, J = 1.5, 7.3 Hz, 1H), 6.84 (dd, J = 7.6, 14.9 Hz, 2H), 5.67 (ddd, J = 8.7, 10.2, 17.1 Hz, 1H), 4.97 – 4.86 (m, 2H), 3.81 (s, 3H), 3.70 (td, J = 6.2, 11.3 Hz, 1H), 3.62 (dq, J = 6.6, 13.1 Hz, 1H), 2.72 (dd, J = 6.6, 13.2 Hz, 1H), 2.59 (dd, J = 7.7, 13.2 Hz, 1H), 2.51 (m, 1H), 1.74 – 1.64 (m, 1H), 1.59 – 1.50 (m, 1H), 1.41 (t, J = 5.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.5, 142.5, 130.9, 128.6, 127.1, 120.1, 114.6, 110.2, 61.4, 55.2, 41.3, 37.0, 35.8; IR (neat): 3375, 2933, 1597, 1494, 1460, 1333, 1245, 1039, 915, 755 cm^{-1}; HRMS (ESI) calcd for $[M + Na]^+$ $C_{13}H_{18}O_2Na$: 229.1199, found: 229.1200.

Representative sulfonamide syntheses via S_N2 displacement:

***N*-(3-(2-Methoxybenzyl)pent-4-enyl)methanesulfonamide (9b).**

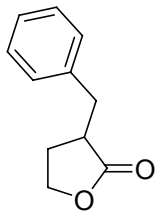


9b

Sulfonamide **9b** was synthesized following the procedure described by Houpis and co-workers.[1] To a solution of the alcohol **31** (2.00 g, 9.70 mmol) in CH_2Cl_2 (40 mL) under argon at 0 °C, was added triethylamine (4.06 mL, 29.1 mmol, 3.0 equiv) and methane sulfonyl chloride (0.90 mL, 11.6 mmol, 1.2 equiv) dropwise. The reaction was allowed to warm to rt and was stirred for 16 h. The reaction mixture was then quenched with water (30 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford the crude mesylate as a clear oil which was used in the next step without further purification.

To a solution of the crude mesylate in CH_3CN (40 mL) under argon, was added methanesulfonamide ($MsNH_2$, 1.85 g, 19.4 mmol, 2.0 equiv) and potassium carbonate (2.68 g, 19.4 mmol, 2.0 equiv) at rt. The resulting solution was refluxed at 90 °C and allowed to stir for 48 h. The reaction mixture was cooled to rt, quenched with water (30 mL) and extracted with Et_2O (80, 40 and 40 mL). The combined organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 60:40 hexanes/EtOAc) to afford 2.21 g (80% yield, 2 steps) of **9b** as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 – 7.14 (m, 1H), 7.04 (dd, *J* = 1.5, 7.3 Hz, 1H), 6.88 – 6.82 (m, 2H), 5.63 (ddd, *J* = 8.8, 10.1, 17.1 Hz, 1H), 5.02 – 4.86 (m, 2H), 4.29 (s, 1H), 3.82 (s, 3H), 3.19 (td, *J* = 5.9, 13.3 Hz, 1H), 3.08 (td, *J* = 7.1, 14.0 Hz, 1H), 2.88 (s, 3H), 2.70 (dd, *J* = 6.9, 13.2 Hz, 1H), 2.62 – 2.54 (m, 1H), 2.48 – 2.37 (m, 1H), 1.66 (ddd, *J* = 4.8, 7.3, 19.5 Hz, 1H), 1.57 – 1.49 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.5, 141.5, 131.0, 128.0, 127.4, 120.2, 115.4, 110.3, 55.3, 41.7, 41.5, 40.3, 35.7, 33.9; IR (neat): 3734, 3462, 3282, 1317, 1242, 1148, 755 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{14}H_{22}NO_3S$: 284.1315, found: 284.1318.

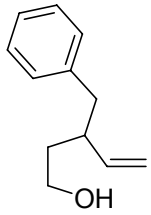
3-Benzyl-dihydrofuran-2(3*H*)-one (28).



28

Lactone **28** was synthesized using the same procedure as the syntheses of **30** but with benzyl bromide as electrophile. Lactone **28** was obtained as a clear oil (76% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.20 (m, 5H), 4.25 – 4.16 (m, 1H), 4.15 – 4.12 (m, 1H), 3.26 (dd, *J* = 4.0, 10.0 Hz, 1H), 2.88 – 2.81 (m, 1H), 2.77 – 2.73 (m, 1H), 2.27 – 2.21 (m, 1H), 2.03 – 1.95 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.7, 138.4, 128.9, 128.7, 126.7, 66.5, 41.1, 36.1, 28.0; IR (neat): 3529, 2985, 2358, 1767, 1452, 1150, 1022 cm^{-1}; HRMS (EI) calcd. for $[M]^+$ $C_{11}H_{12}O_2$: 176.0832, found: 176.0833. Data match those previously reported.[9]

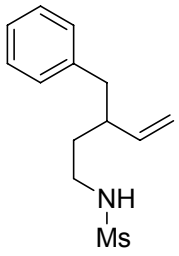
3-Benzylpent-4-en-1-ol (29).



29

Lactone **28** was converted to alcohol **29** using the same procedure as **30** to **31**. Alcohol **29** was obtained as a yellow oil (50% yield, 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.25 (m, 2H), 7.20 – 7.13 (m, 3H), 5.68 – 5.61 (m, 1H), 4.99 – 4.93 (m, 2H), 3.68 – 3.59 (m, 2H), 2.65 (d, J = 7.0 Hz, 2H), 2.47 (s, br, 1H), 1.73 – 1.68 (m, 1H), 1.53 – 1.49 (m, 1H), 1.25 (t, J = 5.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.9, 140.0, 129.3, 128.1, 125.9, 115.2, 61.2, 42.7, 42.0, 36.8; IR (neat): 3330, 3029, 2927, 2361, 1642, 1452, 1046 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_{12}H_{16}O$: 176.1196, found: 176.1198. Data match those previously reported.[10]

***N*-(3-Benzylpent-4-enyl)methanesulfonamide (9a).**

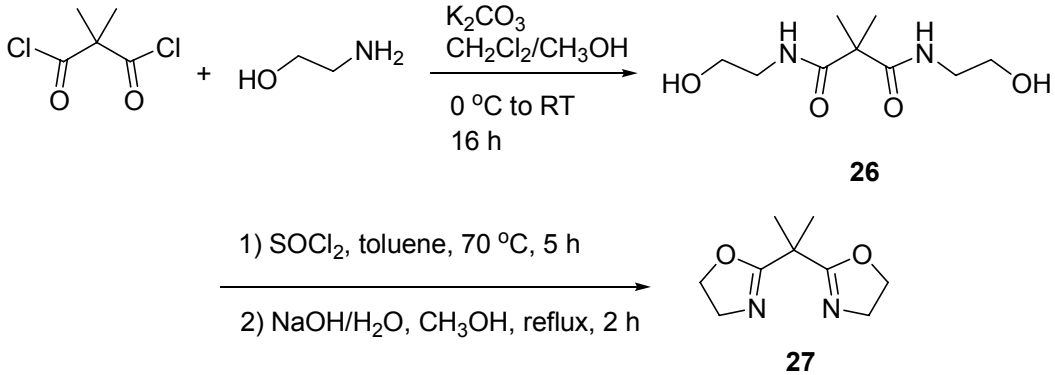


9a

Alcohol **29** was converted to sulfonamide **9a** using the same procedure as **31** to **9b**. Substrate **9a** was obtained as a clear oil (63% yield, 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 2H), 7.21 – 7.18 (m, 1H), 7.13 (d, J = 7.5 Hz, 2H), 5.65 – 5.58 (m, 1H), 5.05 – 4.96 (m, 2 H), 4.15 (s, br, 1H), 3.19 – 3.15 (m, 1H), 3.07 – 3.03 (m, 1H), 2.88 (s, 3H), 2.71 – 2.60 (m, 2H), 2.41 – 2.39 (m, 1H), 1.71 – 1.68 (m, 1H), 1.53 – 1.49 (m, 1H); ^{13}C NMR (75.5, $CDCl_3$) δ 141.0, 139.6, 129.2, 128.3, 126.2, 116.1, 43.4, 41.8, 41.5, 40.3, 34.0; IR (neat): 3286, 2930, 2360, 1419, 1318, 1150, 1078 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_{13}H_{19}NO_2S$: 253.1131, found: 253.1125.

Synthesis of achiral ligand:

2-(2-(4,5-Dihydrooxazol-2-yl)propan-2-yl)-4,5-dihydrooxazole (27).



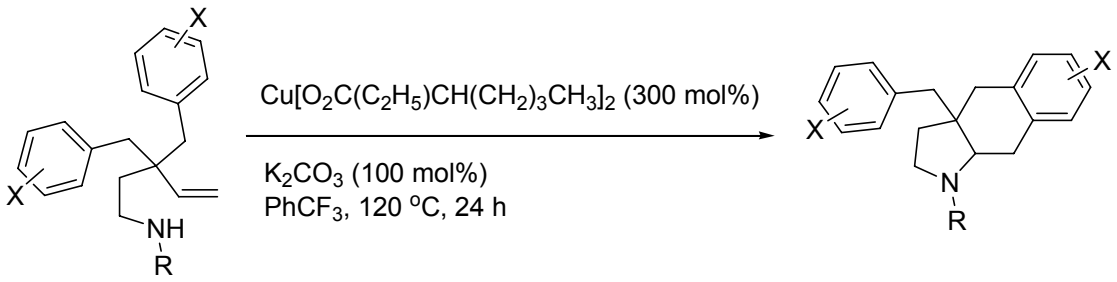
The achiral ligand **27** was synthesized with modifications to a route described by Denmark and co-workers[11]. K_2CO_3 (2.76 g, 20.0 mmol, 4.0 equiv) was suspended in CH_2Cl_2 (50 mL) at 0 °C under argon. Ethanolamine (0.640 mL, 10.5 mmol, 2.1 equiv) was added to the mixture. Dimethylmalonyl dichloride 0.660 mL, 5.00 mmol) in CH_2Cl_2

(10 mL) was added dropwise to the cold mixture. The mixture was stirred for 16 h and allowed to warm to rt. CH_3OH (50 mL) was added and the mixture was stirred for 2 h. The whole reaction mixture was filtered through Celite (5 g) and rinsed twice with CH_3OH (2 × 10 mL). The filtrate was concentrated *in vacuo*. The crude product was used directly into the next step without further purification.

Bisamide **26** was dissolved in toluene (30 mL) and heated to 70 ^oC under argon. Thionyl chloride (1.50 mL, 20.0 mmol, 4.0 equiv) was added in one portion to the mixture and the resulting mixture was heated and stirred at 70 ^oC for 5 h. The reaction was cooled to rt then to 0 ^oC. Saturated $NaHCO_3$ solution (15 mL) was added to the mixture. The mixture was extracted with CH_2Cl_2 (5 × 30 mL) and the combined organic extracts were dried over Na_2SO_4, filtered, concentrated *in vacuo* to provide a pale yellow oil.

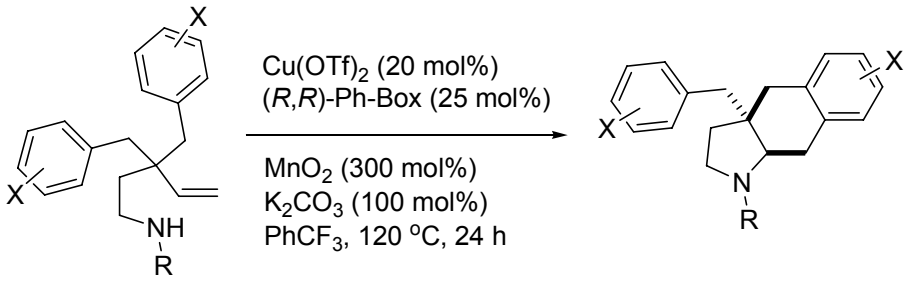
The crude amide was dissolved in 17.0 mL 5% methanolic NaOH solution (0.830 g NaOH was completely dissolved in 0.850 mL H_2O; then diluted with 16.1 mL CH_3OH) and heated to reflux for 2 h under argon. The reaction was cooled to rt and concentrated *in vacuo*. The resulting residue was partitioned between CH_2Cl_2 (10 mL) and H_2O (10 mL). The aqueous phase was extracted with CH_2Cl_2 (5 × 10 mL). All combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo* and air dry overnight to provide a pale yellow oil. The oil was refrigerated to afford 911 mg (40%, 3 steps) analytical pure bis(oxaozline) **27** as a slight yellow wax solid, mp 52-54 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 4.30 (t, J = 9.5 Hz, 4H), 3.88 (t, J = 9.5 Hz, 4H), 1.53 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 68.0, 54.4, 38.6, 24.2; IR (neat): 3356, 2984, 2943, 1737, 1656, 1536, 1471, 1390, 1359, 1255, 1198, 1147, 1121, 1073, 984, 960, 920 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_9H_{14}N_2O_2$: 182.1050, found: 182.1050.

General achiral carboamination procedure



The racemic benz[*f*]indoles, for chiral HPLC comparison, were obtained using the reported achiral carboamination reaction conditions with stoichiometric copper(II) 2-ethylhexanoate (3.0 equiv).[12,13]

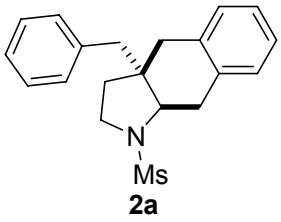
General catalytic enantioselective carboamination procedure:



$Cu(OTf)_2$ (20 mol%), (*R*,*R*)-Ph-Box (25 mol%) and $PhCF_3$ (0.1 M with respect to substrate) were combined in a pressure tube equipped with a magnetic stir bar under argon. The mixture was stirred at 60 °C for 2 h. The solution was treated with MnO_2 (3.0 equiv), K_2CO_3 (1.0 equiv) and sulfonamide substrate (1.0 equiv, 0.111 – 0.291 mmol scale). The tube was refreshed by argon for 2 min, sealed and heated at 120 °C in an oil bath for 24 h. Filtration of the cooled solution and removal of the solvent *in vacuo* afforded a crude residue. Chromatography on SiO_2 (15 – 25% EtOAc in hexanes) afforded purified product. The products were further purified by HPLC prior to enantiomeric excess analysis on analytical chiral HPLC columns.

Representative procedure for catalytic enantioselective carboamination:

(3a*R*,9a*R*)-3a-Benzyl-1-(methylsulfonyl)-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (2a).

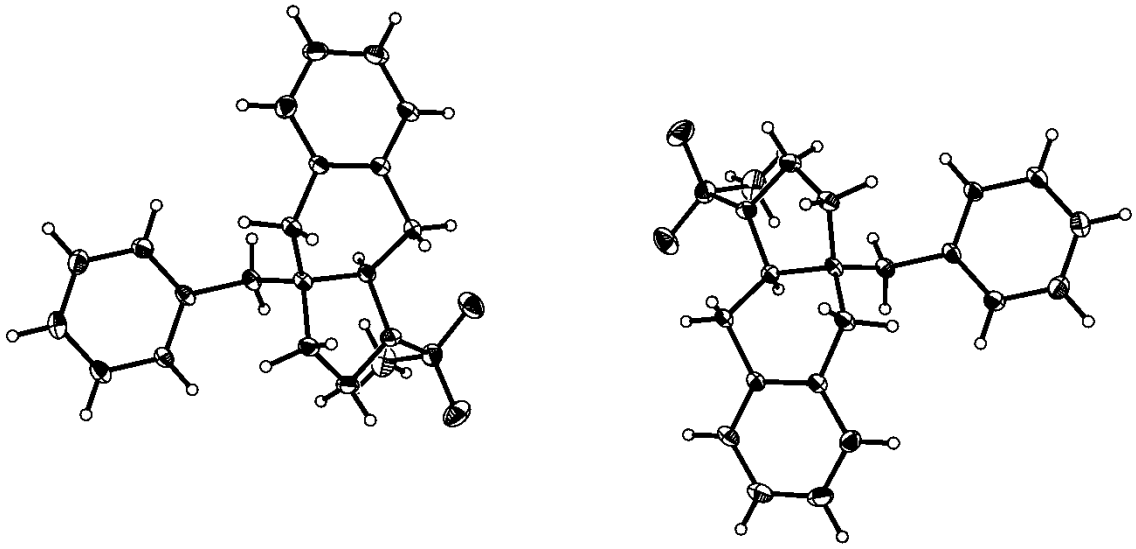


2a

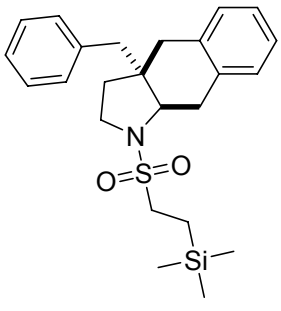
A stock solution of (*R*,*R*)-Ph-Box was prepared (15 mg/mL in $PhCF_3$, 0.45 M) and stored in the refrigerator. The solution was warmed to rt for 2 h prior to use. $Cu(OTf)_2$ (21.1 mg, 0.0582 mmol, 20 mol%) was weighed in a glove box and transferred to a 50 mL pressure tube with a stirring bar. The tube was sealed and removed from the glove box. The (*R*,*R*)-Ph-Box solution (1.62 mL, 0.0727 mmol, 25 mol%) was syringed into the tube, and the vessel was refreshed with argon for 2 min, sealed and stirred at 60 °C for 2 h. Upon cooling to rt, K_2CO_3 (40.2 mg, 0.291 mmol, 1.0 equiv) and MnO_2 (75.9 mg, 0.873 mmol, 3.0 equiv) were added. Sulfonamide **1a** (100 mg, 0.291 mmol) was dissolved in $PhCF_3$ (1.0 mL) in a 20 mL vial and the solution was tansferred into the reaction tube. The vial was rinsed with $PhCF_3$ (0.29 mL) and the rinse was added to the reaction. The tube was refreshed with argon for 2 min, sealed and stirred at 120 °C. After 24 h, the reaction mixture was cooled to rt, diluted with CH_2Cl_2 (10 mL) and vacuum filtered through a pad of silica gel (5 g). The silica gel was further rinsed with EtOAc (3 × 30 mL) and the combined filtrate was concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 80:20 hexanes/EtOAc) to afford 99 mg (99% yield) of **2a** as a white solid (99% yield), mp 88-90 °C; $[\alpha]_D^{23}$ = -44.1° (c = 1, $CHCl_3$), ee = 82%, determined by HPLC analysis [Chiralpak AD-RH, 10% H_2O/MeOH, 0.9 mL/min, λ =

254 nm, t(major) = 8.20 min, t(minor) = 9.68 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.08 (m, 9H), 3.75 (t, *J* = 5.5 Hz, 1H), 3.23 (dt, *J* = 7.5, 9.8 Hz, 1H), 3.15 (ddd, *J* = 5.1, 7.1, 10.0 Hz, 1H), 3.04 – 2.94 (m, 2H), 2.77 – 2.62 (m, 6H), 2.53 (d, *J* = 14.6 Hz, 1H), 2.08 – 1.99 (m, 1H), 1.66 – 1.56 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.2, 137.1, 136.0, 130.7, 128.4, 128.2, 127.7, 126.8, 126.7, 126.6, 64.8, 48.5, 47.5, 45.6, 39.2, 35.8, 35.6, 35.2; HRMS (ESI) calcd for $[M + Na]^+$ $C_{20}H_{23}NO_2SNa$: 364.1342, found: 364.1326. The white solid was recrystallized from CH_2Cl_2/hexanes and the absolute and relative configuration was assigned by X-ray structure.

X-ray crystal structure of 2a



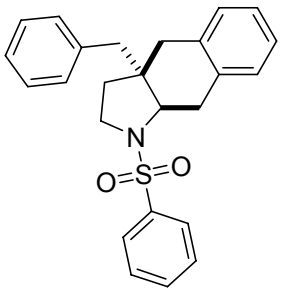
(3a*R*,9a*R*)-3a-Benzyl-1-(2-(trimethylsilyl)ethylsulfonyl)-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (2b).



2b

Benz[*f*]indole **2b** was obtained from catalytic enantioselective carboamination of **1b** as a clear oil (93% yield). $[\alpha]_D^{23}$ = -30.5° (c = 1, $CHCl_3$); ee = 83%, determined by HPLC analysis [Chiralpak AD-RH, 3% IPA/hexane, 1.0 mL/min, λ = 254 nm, t(major) = 6.85 min, t(minor) = 8.13 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.05 (m, 9H), 3.96 (t, *J* = 5.1 Hz, 1H), 3.38 (dt, *J* = 7.4, 9.7 Hz, 1H), 3.06 – 2.67 (m, 9H), 2.49 (d, *J* = 14.7 Hz, 1H), 2.00 (ddd, *J* = 5.4, 6.9, 12.5 Hz, 1H), 1.62 – 1.49 (m, 1H), 0.97 (m, 2H), 0.03 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.4, 137.3, 136.0, 130.6, 128.3, 128.1, 127.8, 126.7, 126.6, 126.6, 64.6, 48.0, 47.7, 47.4, 45.7, 38.6, 35.8, 35.2, 10.0, -2.0; IR (neat): 3025, 2952, 2918, 1602, 1493, 1455, 1329, 1250, 1140, 1043, 861, 841, 754, 704, 577 cm^{-1}; HRMS (ESI) calcd for $[M + Na]^+$ $C_{24}H_{33}NO_2SSiNa$: 450.1893, found: 450.1900. The absolute and relative stereochemistry was assigned by analogy to **2a**.

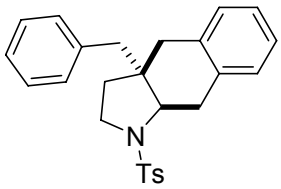
(3a*R*,9a*R*)-3a-Benzyl-1-(phenylsulfonyl)-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (2c).



2c

Benz[*f*]indole **2c** was obtained from catalytic enantioselective carboamination of **1c** as a clear oil (99% yield). $[\alpha]_D^{23}$ = -80.6° (c = 1, $CHCl_3$); ee = 94%, determined by HPLC analysis [Chiralpak AD-RH, 50% CH_3CN/H_2O, 0.7 mL/min, λ = 254 nm, t(minor) = 72.58 min, t(major) = 85.71 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 – 7.84 (m, 2H), 7.63 – 7.57 (m, 1H), 7.57 – 7.51 (m, 2H), 7.26 – 7.13 (m, 6H), 7.05 (d, *J* = 6.1 Hz, 1H), 6.87 (dt, *J* = 2.3, 4.2 Hz, 2H), 3.49 (t, *J* = 5.7 Hz, 1H), 3.29 (ddd, *J* = 3.9, 7.2, 10.0 Hz, 1H), 3.16 (td, *J* = 6.6, 9.5 Hz, 1H), 3.00 (ddd, *J* = 5.7, 14.8, 36.9 Hz, 2H), 2.52 (ABq, J_{AB} = 14.5, Δ*v* = 145.3 Hz, 2H), 2.10 (ABq, J_{AB} = 13.5, Δ*v* = 154.9 Hz, 2H), 1.68 (ddd, *J* = 3.9, 6.6, 12.8 Hz, 1H), 1.44 (ddd, *J* = 7.3, 9.2, 12.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.1, 136.7, 136.2, 132.8, 130.4, 129.0, 128.2, 128.1, 127.7, 127.6, 126.6, 126.6, 126.5, 65.8, 48.2, 47.7, 44.6, 38.01, 35.9, 34.2; IR (neat): 3026, 2915, 1493, 1455, 1446, 1343, 1165, 1093, 1038, 752, 708, 693, 597, 573 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{25}H_{26}NO_2S$: 404.1679, found: 404.1681. The absolute and relative stereochemistry was assigned by analogy to **2a**.

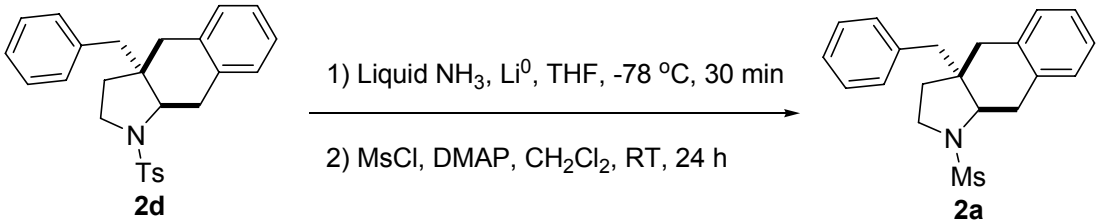
(3a*R*,9a*R*)-3a-Benzyl-1-tosyl-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (2d).



2d

Benz[*f*]indole **2d** was obtained from catalytic enantioselective carboamination of **1d** as a clear oil (96% yield). $[\alpha]_D^{23}$ = -73.3° (c = 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 – 7.73 (m, 2H), 7.32 (d, *J* = 7.9 Hz, 2H), 7.26 – 7.13 (m, 6H), 7.08 – 7.03 (m, 1H), 6.88 (dt, *J* = 2.3, 4.3 Hz, 2H), 3.46 (t, *J* = 5.7 Hz, 1H), 3.29 (ddd, *J* = 3.8, 7.2, 9.9 Hz, 1H), 3.14 (td, *J* = 6.6, 9.6 Hz, 1H), 3.00 (ddd, *J* = 5.7, 14.8, 38.6 Hz, 2H), 2.52 (ABq, J_{AB} = 14.5, Δ*v* = 145.8 Hz, 2H), 2.42 (s, 3H), 2.12 (ABq, J_{AB} = 13.5, Δ*v* = 135.9 Hz, 2H), 1.68 (ddd, *J* = 3.8, 6.5, 12.8 Hz, 1H), 1.43 (ddd, *J* = 7.3, 9.4, 12.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.6, 137.2, 137.1, 136.3, 133.8, 130.5, 129.6, 128.3, 128.1, 127.8, 127.6, 126.6, 126.5, 126.5, 65.7, 48.2, 47.6, 44.7, 38.0, 35.9, 34.1, 21.5; IR (neat): 1599, 1493, 1452, 1338, 1160, 1096, 1031, 915, 817, 729, 706, 657, 584, 551 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{26}H_{28}NO_2S$: 418.1835, found: 418.1839.

The compound **2d** was converted to the mesylate **2a** via desulfonylation reaction. The desulfonylation was performed by modification of the procedure reported in our previous copper catalyzed enantioselective carboamination studies.[14]



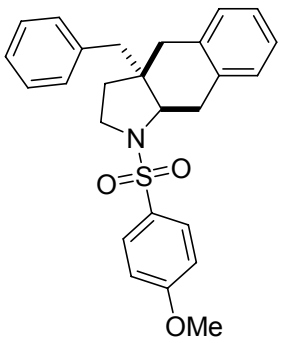
2d **2a**

(3a*R*,9a*R*)-3a-Benzyl-1-(methylsulfonyl)-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (2a).

Ammonia (50 mL) was condensed in a volume-marked three-neck flask containing benz[*f*]indole **2d** (100 mg, 0.24 mmol) and dry THF (5 mL) at -78 ^{o}C under argon. Lithium metal (15 mg, 2.16 mmol) was added over 15 minutes. After the mixture was stirred at -78 ^{o}C under argon for 30 min, solid NH_4Cl (5.0 g) was added, and the solution was warmed to room temperature, and allowed to evaporate overnight. EtOAc (30 mL) and aqueous KOH (20%, 20 mL) were added to the resulting residue. The aqueous phase was extracted with EtOAc (3 × 30 mL). All combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The resulted crude amine was used directly in next step without further purification.

The crude amine was dissolved in CH_2Cl_2 (10 mL) under argon at 0 ^{o}C. The solution was then treated with 1,1-dimethyl amino pyridine (47.6 mg, 0.39 mmol) and methane sulfonyl chloride (0.03 mL, 0.39 mmol) and allowed to warm to room temperature and was stirred overnight. The reaction was then quenched with water (10 mL) and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). All combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 80:20 hexanes/EtOAc) to afford 70 mg (86% yield, 2 steps) of **2a** (from **2d**) as a white solid. $[\alpha]_D^{23}$ = -46.9^{o} (c = 1, $CHCl_3$), ee = 96%, determined by HPLC analysis [Chiralpak AD-RH, 10% H_2O/MeOH, 0.9 mL/min, λ = 254 nm, t(major) = 8.13 min, t(minor) = 9.73 min]; NMR data matched compound **2a**.

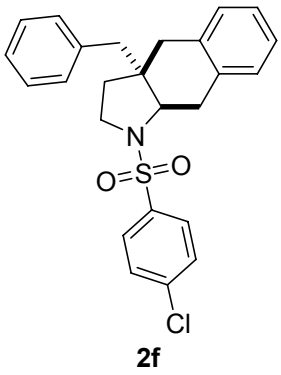
(3a*R*,9a*R*)-3a-Benzyl-1-(4-methoxyphenylsulfonyl)-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (2e).



2e

Benz[*f*]indole **2e** was obtained from catalytic enantioselective carboamination of **1e** as a white solid (99% yield), mp 139-141 ^{o}C; $[\alpha]_D^{23}$ = -79.7^{o} (c = 1, $CHCl_3$), ee = 93%, determined by HPLC analysis [Chiralpak AD-RH, 5% IPA/hexane, 1.0 mL/min, λ = 254 nm, t(major) = 17.16 min, t(minor) = 19.41 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 – 7.77 (m, 2H), 7.28 – 7.12 (m, 6H), 7.06 (d, *J* = 6.5 Hz, 1H), 7.03 – 6.96 (m, 2H), 6.95 – 6.88 (m, 2H), 3.85 (s, 3H), 3.44 (t, *J* = 5.7, 1H), 3.29 (ddd, *J* = 3.6, 7.2, 10.6 Hz, 1H), 3.12 (td, *J* = 6.5, 9.7 Hz, 1H), 3.01 (ddd, *J* = 5.7, 14.8, 36.4 Hz, 2H), 2.52 (ABq, J_{AB} = 14.5, Δ*v* = 147.8 Hz, 2H), 2.14 (ABq, J_{AB} = 14.0, Δ*v* = 131.5 Hz, 2H), 1.70 (ddd, *J* = 3.6, 6.5, 12.8 Hz, 1H), 1.44 (ddd, *J* = 7.3, 9.5, 12.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.0, 137.1, 137.1, 136.3, 130.5, 129.8, 128.4, 128.2, 128.1, 127.6, 126.6, 126.5, 126.5, 114.1, 65.7, 55.5, 48.2, 47.6, 44.6, 38.0, 35.9, 34.0; IR (neat): 3029, 2912, 1595, 1577, 1496, 1456, 1341, 1307, 1260, 1157, 1093, 1029, 837, 805, 754, 705, 669, 590, 559 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{26}H_{28}NO_3S$: 434.1784, found: 434.1783. The absolute and relative stereochemistry was assigned by analogy to **2a**.

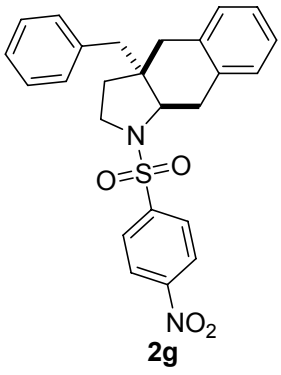
(3a*R*,9a*R*)-3a-Benzyl-1-(4-chlorophenylsulfonyl)-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (2f).



2f

Benz[*f*]indole **2f** was obtained from catalytic enantioselective carboamination of **1f** as a clear oil (99% yield) except the reaction was run at 110 °C since the chloro substituent is labile at high temperature under these conditions. $[\alpha]_D^{23}$ = -68.6° (c = 1, $CHCl_3$), ee = 96%, determined by HPLC analysis [Chiralpak AD-RH, 3% IPA/hexane, 1.0 mL/min, λ = 254 nm, t(major) = 12.57 min, t(minor) = 15.13 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 – 7.74 (m, 2H), 7.53 – 7.46 (m, 2H), 7.28 – 7.13 (m, 6H), 7.06 (dd, *J* = 2.9, 4.8 Hz, 1H), 6.95 – 6.88 (m, 2H), 3.50 (t, *J* = 5.5 Hz, 1H), 3.25 (ddd, *J* = 4.1, 7.2, 9.9 Hz, 1H), 3.08 (ddd, *J* = 6.2, 11.9, 20.5 Hz, 2H), 2.96 (dd, *J* = 5.3, 14.9 Hz, 1H), 2.55 (ABq, J_{AB} = 14.5, Δ*v* = 132.7 Hz, 2H), 2.23 (ABq, J_{AB} = 14.0, Δ*v* = 121.5 Hz, 2H), 1.73 (ddd, *J* = 4.1, 6.6, 12.8 Hz, 1H), 1.47 (ddd, *J* = 7.3, 9.0, 12.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.3, 137.0, 136.9, 135.9, 135.6, 130.4, 129.3, 129.0, 128.2, 128.2, 127.7, 126.7, 126.6, 126.6, 65.6, 48.2, 47.7, 44.9, 38.4, 35.6, 34.3; IR (neat): 3026, 2962, 2917,1585, 1493, 1476, 1455, 1394, 1347, 1261, 1165, 1094, 1040, 1013, 827, 800, 756, 705, 620, 581 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{25}H_{25}ClNO_2S$: 438.1289, found: 438.1287. The absolute and relative stereochemistry was assigned by analogy to **2a**.

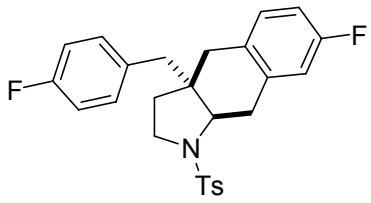
(3a*R*,9a*R*)-3a-Benzyl-1-(4-nitrophenylsulfonyl)-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (2g).



2g

Benz[*f*]indole **2g** was obtained from catalytic enantioselective carboamination of **1g** as a clear oil (99% yield). $[\alpha]_D^{23}$ = -70.5° (c = 1, $CHCl_3$), ee = 97%, determined by HPLC analysis [Chiralpak AD-RH, 5% IPA/hexane, 1.0 mL/min, λ = 254 nm, t(major) = 17.25 min, t(minor) = 20.69 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 – 8.30 (m, 2H), 7.98 – 7.94 (m, 2H), 7.23 – 7.19 (m, 3H), 7.19 – 7.11 (m, 3H), 7.09 – 7.04 (m, 1H), 6.94 – 6.89 (m, 2H), 3.60 (t, *J* = 5.4 Hz, 1H), 3.24 (ddd, *J* = 4.8, 7.1, 10.0, 1H), 3.17 – 2.95 (m, 3H), 2.57 (ABq, J_{AB} = 15.5, Δ*v* = 116.0 Hz, 2H), 2.28 (ABq, J_{AB} = 13.0, Δ*v* = 121.0 Hz, 2H), 1.82 – 1.74 (m, 1H), 1.56 – 1.48 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.0, 143.3, 136.8, 136.6, 135.5, 130.4, 128.6, 128.2, 128.2, 127.7, 126.8, 126.7, 124.2, 65.5, 48.2, 47.8, 44.9, 38.60, 35.4, 34.5; IR (neat): 3103, 3025, 2918, 1604, 1530, 1493, 1455, 1350, 1311, 1166, 1092, 1041, 1013, 856, 755, 705, 687, 613 cm^{-1}; HRMS (ESI) calcd for $[M + Na]^+$ $C_{25}H_{24}N_2O_4SNa$: 471.1349, found: 471.1345. The absolute and relative stereochemistry was assigned by analogy to **2a**.

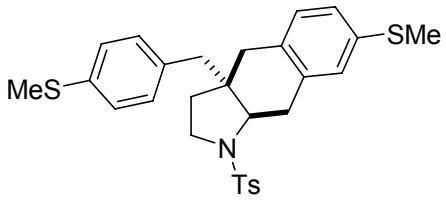
(3a*R*,9a*R*)-3a-(4-Fluorobenzyl)-7-fluoro-1-tosyl-2,3,3a,4,9,9a-hexahydro-1*H* benzo[*f*]indole (2h).



2h

Benz[*f*]indole **2h** was obtained from catalytic enantioselective carboamination of **1h** as a clear oil (89% yield). $[\alpha]_D^{23}$ = -60.5° (c = 1, $CHCl_3$), ee = 96%, determined by HPLC analysis [Chiralpak AD-RH, 5% IPA/hexane, 1.0 mL/min, λ = 254 nm, t(major) = 15.80 min, t(minor) = 14.62 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 – 7.69 (m, 2H), 7.33 (dd, *J* = 0.4, 8.4 Hz, 2H), 6.97 (dd, *J* = 5.5, 8.1 Hz, 1H), 6.94 – 6.79 (m, 6H), 3.47 (t, *J* = 5.4 Hz, 1H), 3.24 (ddd, *J* = 4.1, 7.2, 10.0 Hz, 1H), 3.09 (ddd, *J* = 6.1, 12.0, 20.4 Hz, 2H), 2.87 (dd, *J* = 5.3, 15.0 Hz, 1H), 2.46 (ABq, J_{AB} = 15.0, Δ*v* = 98.1 Hz, 2H), 2.44 (s, 3H), 2.18 (ABq, J_{AB} = 13.5, Δ*v* = 109.7 Hz, 2H), 1.63 (ddd, *J* = 4.1, 6.7, 12.8 Hz, 1H), 1.42 (ddd, *J* = 7.2, 9.0, 12.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.6, 160.7 (d, J_{CF} = 1.9 Hz), 143.7, 138.1 (d, J_{CF} = 7.7 Hz), 133.9, 132.6 (d, J_{CF} = 2.9 Hz), 132.4 (d, J_{CF} = 2.9 Hz), 131.8 (d, J_{CF} = 7.7 Hz), 129.6, 128.7 (d, J_{CF} = 7.7 Hz), 127.7, 115.4 (d, J_{CF} = 21.2 Hz), 115.0 (d, J_{CF} = 21.2 Hz), 113.1 (d, J_{CF} = 21.2 Hz), 64.7, 48.2, 47.6, 44.0, 37.5, 35.7, 34.2, 21.5; IR (neat): 1597, 1507, 1491, 1447, 1338, 1223, 1161, 1093, 1140, 564, 550 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{26}H_{26}F_2NO_2S$: 454.1647, found: 454.1650. The absolute and relative stereochemistry was assigned by analogy to **2a**.

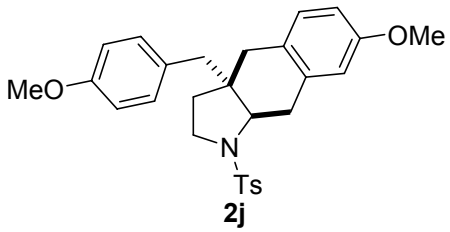
(3a*R*,9a*R*)-3a-(4-(Methylthio)benzyl)-7-(methylthio)-1-tosyl-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (2i).



2i

Benz[*f*]indole **2i** was obtained from catalytic enantioselective carboamination of **1i** as a clear oil (91% yield). $[\alpha]_D^{23}$ = -104.1° (c = 1, $CHCl_3$), ee = 97%, determined by HPLC analysis [Chiralpak AD-RH, 5% H_2O/MeOH, 0.3 mL/min, λ = 254 nm, t(minor) = 85.52 min, t(major) = 95.39 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 10.0 Hz, 2H), 7.13 – 6.80 (m, 7H), 3.46 (t, *J* = 6.0 Hz, 1H), 3.31 – 3.27 (m, 1H), 3.15 – 3.09 (m, 1H), 3.05 – 2.99 (m, 1H), 2.93 – 2.90 (m, 1H), 2.48 (ABq, J_{AB} = 15.0, Δ*v* = 122.1 Hz, 2H), 2.48 – 2.43 (m, 9H), 2.13 (ABq, J_{AB} = 13.5, Δ*v* = 130.0 Hz, 2H), 1.60 – 1.72 (m, 1H), 1.38 – 1.44 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.6, 137.2, 137.1, 136.3, 133.9, 130.5, 129.6, 129.5, 128.3, 128.1, 127.8, 127.7, 126.6, 126.5, 65.7, 48.2, 47.6, 38.1, 37.9, 35.9, 35.8, 34.2, 21.5; IR (neat): 2359, 1598, 1491, 1342, 1161, 910 cm^{-1}; HRMS (ESI) calcd for $[M + Na]^+$ $C_{28}H_{31}NO_2S_3Na$: 532.1409, found: 532.1429. The absolute and relative stereochemistry was assigned by analogy to **2a**.

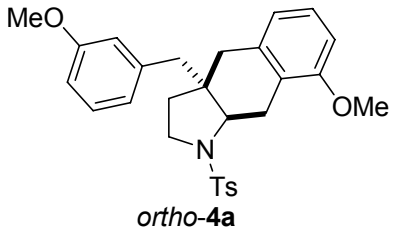
(3a*R*,9a*R*)-3a-(4-Methoxybenzyl)-7-methoxy-1-tosyl-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (2j).



2j

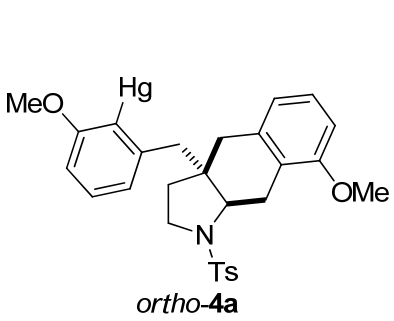
Benz[*f*]indole **2j** was obtained from catalytic enantioselective carboamination of **1j** as a clear oil (89% yield). $[\alpha]_D^{23}$ = -73.3° (c = 1, $CHCl_3$), ee = 96%, determined by HPLC analysis [Chiralpak AD-RH, 70-100% gradient MeOH/H_2O, 0.7-1.0 mL/min, λ = 254 nm, t(minor) = 51.93 min, t(major) = 54.81 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 10.0 Hz, 2H), 7.33 (d, *J* = 10.0 Hz, 2H), 6.96 (d, *J* = 10.0 Hz, 1H), 6.82 – 6.89 (m, 6H), 3.79 (d, *J* = 8.0 Hz, 6H), 3.43 (t, *J* = 7.0 Hz, 1H), 3.31 – 3.27 (m, 1H), 3.15 – 3.09 (m, 1H), 3.05 – 2.90 (m, 2H), 2.44 (ABq, J_{AB} = 18.5, Δ*v* = 135.8 Hz, 2H), 2.43 (s, 3H), 2.06 (ABq, J_{AB} = 17.0, Δ*v* = 140.0 Hz, 2H), 1.65 – 1.60 (m, 1H), 1.54 – 1.39 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5, 158.3, 143.6, 137.6, 133.9, 131.4, 129.6, 129.3, 129.1, 128.4, 127.8, 113.8, 113.5, 112.0, 65.6, 55.3, 55.2, 48.5, 47.7, 43.8, 37.2, 36.3, 34.0, 21.6; IR (neat): 2358, 1613, 1509, 1337, 1162, 1024, 913, 748, 513, 497 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_{28}H_{31}NO_4S$: 477.1968, found: 477.1974. The absolute and relative stereochemistry was assigned by analogy to **2a**.

(3a*R*,9a*R*)-3a-(3-Methoxybenzyl)-8-methoxy-1-tosyl-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (*ortho*-4a).

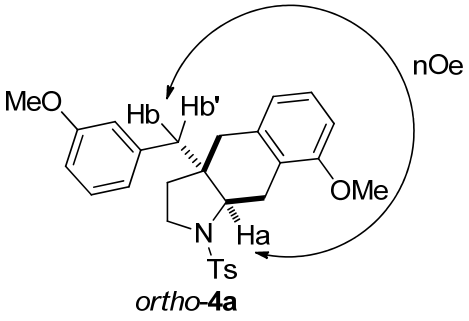


ortho-**4a**

Benz[*f*]indoles *ortho*-**4a** and *para*-**4a** were obtained from catalytic enantioselective carboamination of **3a** [97% yield, *ortho*-**4a** : *para*-**4a** (1.5 : 1)]. They were separated by prep HPLC using EtOAc/hexanes (*para*-**4a** eluted first). Benz[*f*]indole *ortho*-**4a** was obtained as a clear oil. $[\alpha]_D^{23}$ = 71.3° (c = 1, $CHCl_3$), ee = 96%, determined by HPLC analysis [Chiralpak AD-RH, 5% IPA/hexane, 1.0 mL/min, λ = 254 nm, t(minor) = 21.67 min, t(major) = 31.99 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 – 7.74 (m, 2H), 7.30 (dd, *J* = 0.4, 8.4 Hz, 2H), 7.18 – 7.07 (m, 2H), 6.78 – 6.73 (m, 2H), 6.69 (d, *J* = 7.4 Hz, 1H), 6.50 (d, *J* = 7.6 Hz, 1H), **6.48 – 6.45 (m, 1H)**, 3.83 (s, 3H), 3.78 (s, 3H), 3.48 (t, *J* = 5.8 Hz, 1H), 3.33 – 3.19 (m, 2H), 3.08 (dd, *J* = 1.8, 5.8 Hz, 2H), 2.63 (d, *J* = 14.7 Hz, 1H), 2.43 – 2.36 (m, 4H), 2.12 (ABq, J_{AB} = 13.5, Δ*v* = 147.9 Hz, 2H), 1.66 (ddd, *J* = 4.7, 6.8, 12.6 Hz, 1H), 1.43 (dt, *J* = 7.7, 12.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 156.9, 143.4, 138.9, 138.4, 134.4, 129.6, 129.04 127.8, 126.8, 124.0, 122.9, 120.3, 116.7, 111.3, 108.8, 65.4, 55.6, 55.1, 47.7, 47.4, 44.4, 37.6, 34.2, 27.8, 21.5; IR (neat): 2933, 1589, 1489, 1479, 1455, 1440, 1343, 1264, 1160, 1092, 1039, 782, 753, 665, 591, 550 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{28}H_{32}NO_4S$: 478.2047, found: 478.2050. The absolute stereochemistry was assigned by analogy to **2a**. The regiochemistry was assigned analysis of the ^{1}H NMR (only one aromatic proton with no vicinal coupling). The relative stereochemistry was assigned by NOE.

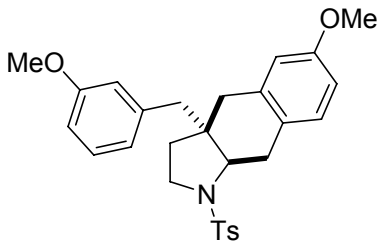


ortho-**4a**



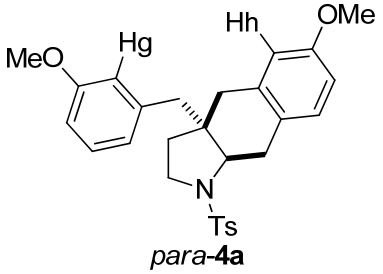
ortho-**4a**

(3a*R*,9a*R*)-3a-(3-Methoxybenzyl)-6-methoxy-1-tosyl-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (*para*-4a).

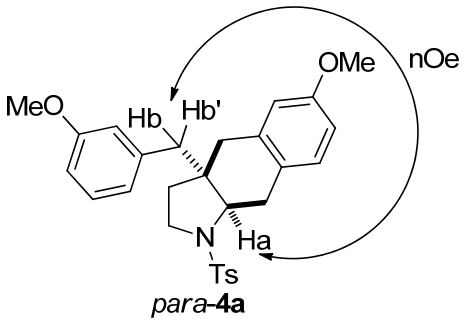


para-**4a**

Benz[*f*]indole *para*-**4a** was obtained as a clear oil. $[\alpha]_D^{23}$ = -68.8° (c = 1, $CHCl_3$), ee = 96%, determined by HPLC analysis [Chiralpak AD-RH, 70-100% gradient MeOH/H_2O, 0.7-1.0 mL/min, λ = 254 nm, t(major) = 43.41 min, t(minor) = 50.85 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.15 (t, *J* = 7.9 Hz, 1H), 7.09 (d, *J* = 8.2 Hz, 1H), 6.73 (ddd, *J* = 2.6, 8.2, 18.8 Hz, 2H), **6.64 (d, *J* = 2.5 Hz, 1H)**, 6.48 (d, *J* = 7.6 Hz, 1H), **6.45 (d, *J* = 2.0 Hz, 1H)**, 3.78 (d, *J* = 3.1 Hz, 6H), 3.43 (t, *J* = 5.7 Hz, 1H), 3.29 (ddd, *J* = 3.9, 7.2, 10.9 Hz, 1H), 3.15 (td, *J* = 6.6, 9.6 Hz, 1H), 2.94 (qd, *J* = 5.7, 14.8 Hz, 2H), 2.49 (ABq, J_{AB} = 15.0, Δ*v* = 146.5 Hz, 2H), 2.42 (s, 3H), 2.09 (ABq, J_{AB} = 14.0, Δ*v* = 142.6 Hz, 2H), 1.68 (ddd, *J* = 3.9, 6.5, 12.7 Hz, 1H), 1.44 (ddd, *J* = 7.3, 9.1, 12.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 158.4, 143.5, 138.7, 138.4, 133.9, 129.6, 129.0, 129.0, 128.3, 127.7, 122.9, 116.9, 113.9, 111.2, 66.1, 55.2, 55.1, 48.1, 47.6, 44.7, 38.3, 35.1, 34.3, 21.5; IR (neat): 3014, 2935, 2836, 1609, 1598, 1584, 1494, 1455, 1436, 1342, 1262, 1161, 1093, 1039, 816, 800, 754, 660, 593, 549; HRMS (ESI) calcd for $[M + H]^+$ $C_{28}H_{32}NO_4S$: 478.2047, found: 478.2053. The absolute stereochemistry was assigned by analogy to **2a**. The regiochemistry was assigned analysis of the ^{1}H NMR (two aromatic protons with no vicinal coupling). The relative stereochemistry was assigned by NOE.

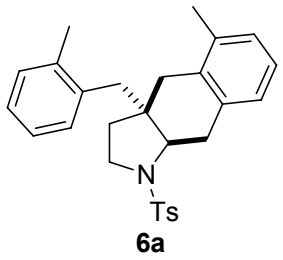


para-**4a**



para-**4a**

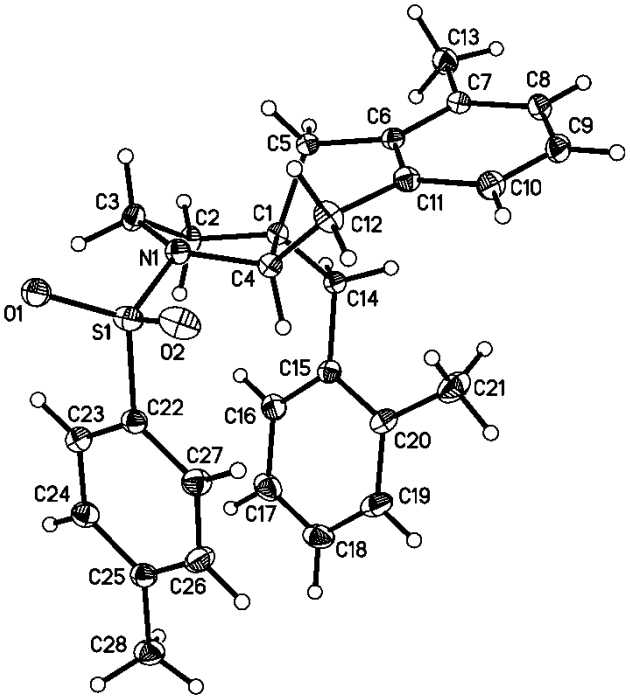
(3a*R*,9a*R*)-5-Methyl-3a-(2-methylbenzyl)-1-tosyl-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (6a).

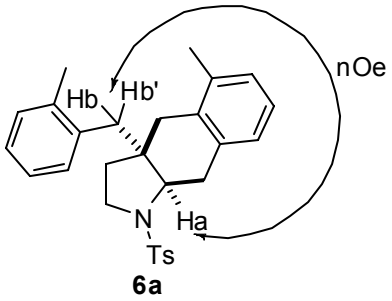


6a

Benz[*f*]indole **6a** and **7a** were obtained from catalytic enantioselective carboamination of **5a** [95% yield, **6a** : **7a** (2.5 : 1)]. They were separated by prep HPLC using EtOAc/hexanes (**7a** eluted first). Benz[*f*]indole **6a** was obtained as a white solid, mp 115-117 ^{o}C; $[\alpha]_D^{23}$ = -38.9^{o} (c = 1, $CHCl_3$), ee = 98%, determined by HPLC analysis [Chiralpak AD-RH, 70-100% gradient MeOH/H_2O, 0.7-0.9 mL/min, λ = 254 nm, t(major) = 40.05 min, t(minor) = 45.74 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.12 – 6.98 (m, 6H), 6.92 (d, *J* = 7.4 Hz, 1H), 3.65 (t, *J* = 4.8 Hz, 1H), 3.21 – 3.14 (m, 2H), 3.09 (ddd, *J* = 7.1, 8.2, 10.0 Hz, 1H), 2.90 (dd, *J* = 5.4, 15.2 Hz, 1H), 2.56 (ABq, J_{AB} = 14.5, Δν = 45.4 Hz, 2H), 2.46 – 2.38 (m, 4H), 2.26 (d, *J* = 14.1 Hz, 1H), 2.14 (s, 3H), 2.04 (s, 3H), 1.61 (ddd, *J* = 4.8, 7.0, 12.0 Hz, 1H), 1.44 (dt, *J* = 7.7, 12.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.3, 136.9, 135.8, 135.7, 135.2, 134.8, 134.2, 130.9, 130.8, 129.5, 128.1, 127.7, 126.5, 126.3, 126.0, 125.6, 64.6, 48.9, 47.5, 41.1, 35.7, 34.7, 34.3, 21.5, 20.2, 19.1; IR (neat): 3021, 2963, 2921, 1597, 1493, 1472, 1452, 1343, 1162, 1093, 1048, 1018, 815, 773, 748, 665, 589, 550 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{28}H_{32}NO_2S$: 446.2148, found: 446.2152. The white solid was recrystallized from isopropyl alcohol. The absolute and relative stereochemistry was assigned by X-ray structure. NOE between Ha and Hb also confirmed relative stereochemistry.

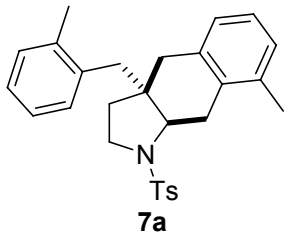
X-ray crystal structure of 6a





6a

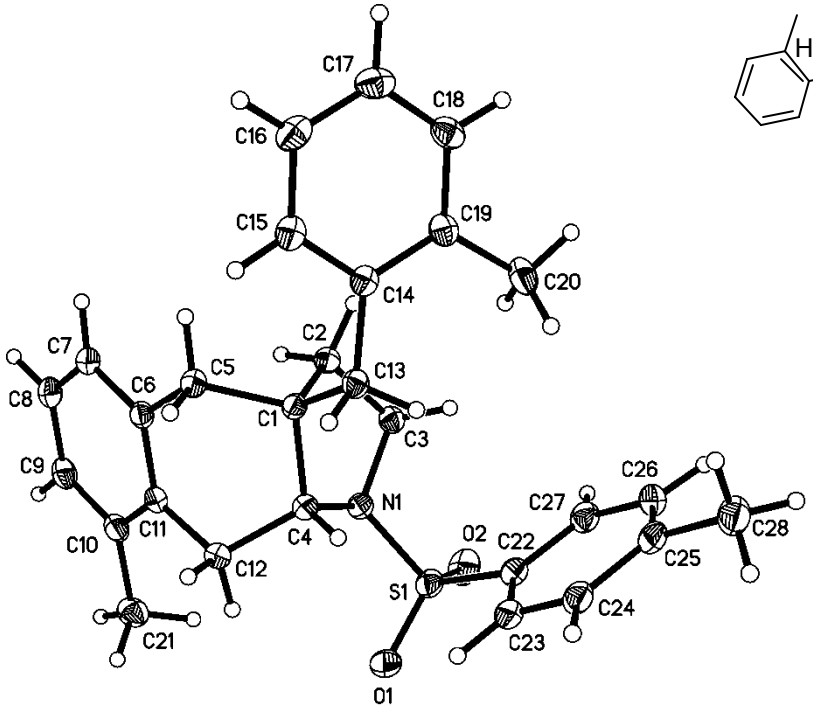
(3a*R*,9a*R*)-8-Methyl-3a-(2-methylbenzyl)-1-tosyl-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (7a).

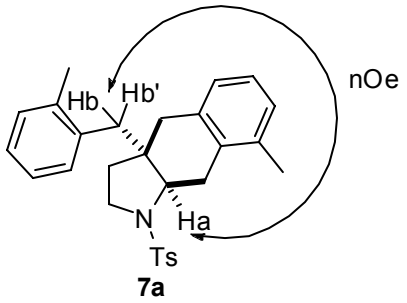


7a

Benz [*f*]indole **7a** was obtained as a clear oil. $[\alpha]_D^{23}$ = -49.4° (c = 1, $CHCl_3$), ee = 96%, determined by HPLC analysis [Regis (*S*,*S*)-Whelk, 5% IPA/Hexane, 1.0 mL/min, λ = 254 nm, t(minor) = 34.15 min, t(major) = 35.94 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.15 – 7.01 (m, 5H), 6.95 – 6.86 (m, 2H), 3.54 (t, *J* = 5.0 Hz, 1H), 3.33 – 3.19 (m, 2H), 3.09 (td, *J* = 6.8, 9.6 Hz, 1H), 2.84 (dd, *J* = 5.0, 15.3 Hz, 1H), 2.65 (d, *J* = 14.5 Hz, 1H), 2.49 – 2.33 (m, 8H), 2.16 – 2.06 (m, 4H), 1.60 (ddd, *J* = 3.7, 6.7, 12.7 Hz, 1H), 1.48 – 1.39 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.5, 137.0, 136.9, 136.1, 135.8, 134.5, 133.6, 131.4, 130.8, 129.6, 128.3, 127.8, 126.6, 125.9, 125.6, 125.5, 65.8, 48.8, 47.7, 40.7, 39.0, 33.8, 31.5, 21.5, 20.3, 19.4; IR (neat): 3021, 2962, 2922, 1597, 1493, 1472, 1452, 1343, 1162, 1092, 1030, 815, 802, 753, 665, 589, 549 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{28}H_{32}NO_2S$: 446.2148, found: 446.2148. The absolute stereochemistry was assigned by analogy to **6a**. The relative stereochemistry and regiochemistry were assigned by X-ray structure of (±) **7a**. NOE between Ha and Hb also confirmed relative stereochemistry.

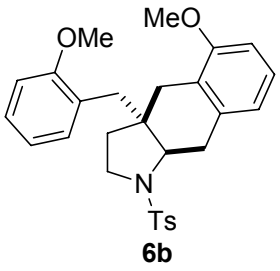
X-ray crystal structure of (±) 7a





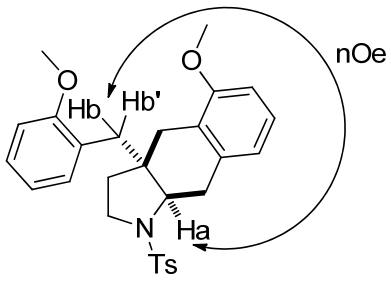
7a

(3a*R*,9a*R*)-3a-(2-Methoxybenzyl)-5-methoxy-1-tosyl-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (6b).

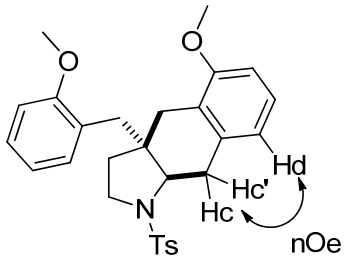


6b

Benz[*f*]indole **6b** and **7b** were obtained from catalytic enantioselective carboamination of **5b** [99% yield, **6b** : **7b** (1.5 : 1)]. They were separated by prep HPLC using EtOAc/hexanes (**6b** eluted first). Benz[*f*]indole **6b** was obtained as a clear oil. $[\alpha]_D^{23}$ = -42.2° (c = 1, $CHCl_3$), ee = 98%, determined by HPLC analysis [Chiralpak AD-RH, 5% IPA/hexane, 1.0 mL/min, λ = 254 nm, t(minor) = 14.41 min, t(major) = 17.44 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.3 Hz, 2H), 7.26 (d, *J* = 7.9 Hz, 2H), 7.20 – 7.10 (m, 2H), 7.02 (dd, *J* = 1.7, 7.4 Hz, 1H), 6.88 – 6.71 (m, 4H), 3.79 (s, 3H), 3.68 (s, 3H), 3.38 (t, *J* = 5.8 Hz, 1H), 3.32 (ddd, *J* = 3.0, 7.4, 10.3 Hz, 1H), 3.21 (td, *J* = 6.5, 9.6 Hz, 1H), 3.02 (qd, *J* = 5.9, 14.7 Hz, 2H), 2.85 (d, *J* = 15.2 Hz, 1H), 2.44 – 2.34 (m, 4H), 2.13 (ABq, J_{AB} = 13.0, Δ*v* = 44.6 Hz, 2H), 1.64 – 1.56 (m, 1H), 1.42 (ddd, *J* = 7.5, 9.8, 12.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.8, 156.3, 143.2, 138.3, 133.7, 132.7, 129.3, 127.8, 127.7, 126.7, 126.0, 125.4, 120.8, 120.1, 110.3, 108.4, 65.9, 55.4, 54.8, 48.3, 48.0, 37.6, 36.1, 34.1, 30.2, 21.5; IR (neat): 3023, 2958, 2938, 2836, 1588, 1493, 1477, 1440, 1341, 1265, 1245, 1161, 1112, 1092, 1072, 1030, 755, 665, 593, 551 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{28}H_{32}NO_4S$: 478.2047, found: 478.2055. The absolute stereochemistry was assigned by analogy to **6a**. The relative stereochemistry and regiochemistry were assigned by NOE.

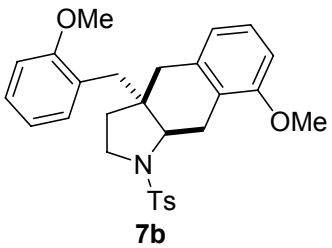


6b



6b

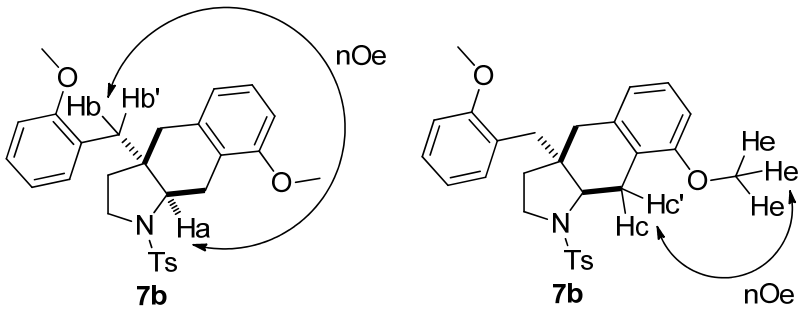
(3a*S*,9a*R*)-3a-(2-Methoxybenzyl)-8-methoxy-1-tosyl-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (7b).



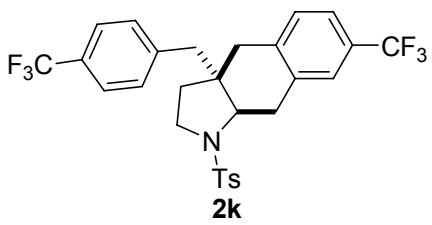
7b

Benz[*f*]indole **7b** was obtained as a clear oil. $[\alpha]_D^{23}$ = -37.0° (c = 1, $CHCl_3$), ee = 99%, determined by HPLC analysis [Chiralpak AD-RH, 10% IPA/hexane, 0.3 mL/min, λ = 254 nm, t(minor) = 48.83 min, t(major) = 54.72 min]; ^{1}H NMR (500 MHz,) δ 7.77 – 7.72 (m, 2H), 7.29 – 7.24 (m, 2H), 7.22 – 7.16 (m, 1H), 7.12 – 7.07 (m, 1H), 6.93 – 6.65 (m, 5H), 3.84 (s, 3H), 3.70 (s, 3H), 3.48 (t, *J* = 5.7 Hz, 1H), 3.31 – 3.19 (m, 2H), 3.10 (ddd, *J* = 5.7, 15.5, 39.1 Hz, 2H), 2.68 (d, *J* = 14.7 Hz, 1H), 2.42 – 2.33 (m, 4H), 2.19 (ABq, J_{AB} = 13.5, Δ*v* = 36.0 Hz, 2H), 1.65 – 1.57 (m, 1H), 1.39 (ddt, *J* = 5.6, 7.3, 11.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.8, 156.9, 143.2, 139.0, 134.1, 132.5, 129.3, 127.9, 127.8, 126.6, 126.1, 124.4, 120.3, 120.1,

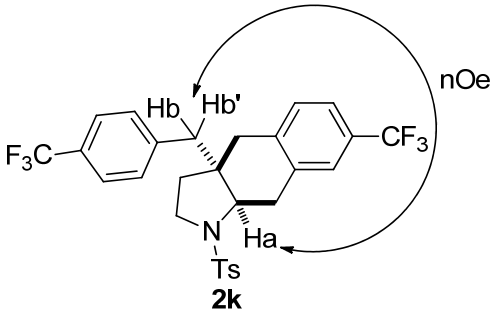
110.5, 108.7, 65.6, 55.6, 54.9, 48.2, 47.6, 38.1, 37.4, 33.7, 28.0, 21.5; IR (neat): 3023, 2942, 2836, 1588, 1493, 1472, 1440, 1342, 1265, 1245, 1161, 1091, 1033, 755, 665, 591, 550 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{28}H_{32}NO_4S$: 478.2047, found: 478.2050. The absolute stereochemistry were assigned by analogy to **7a**. The relative stereochemistry and regiochemistry were assigned by NOE.



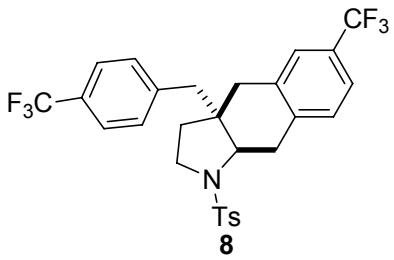
(3a*R*,9a*R*)-3a-(4-(Trifluoromethyl)benzyl)-1-tosyl-7-(trifluoromethyl)-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (2k).



Benz[*f*]indoles **2k** and **8** were obtained from catalytic enantioselective carboamination of **1k** [90% yield, **2k** : **8** (3 : 1)]. They were separated by prep HPLC using EtOAc/hexanes (**8** eluted first). Benz[*f*]indole **2k** was obtained as a white solid, mp 71-73 ^oC; $[\alpha]_D^{23}$ = -54.7^o (c = 1, $CHCl_3$), ee = 96%, determined by HPLC analysis [Chiralpak AD-RH, 5% IPA/Hexane, 1.0 mL/min, λ = 254 nm, t(major) = 11.36 min, t(minor) = 13.21 min]; ^1H NMR (500 MHz, CDCl3) δ 7.75 (d, *J* = 8.1 Hz, 2H), 7.50 (d, *J* = 7.9 Hz, 2H), 7.42 (d, *J* = 7.7 Hz, 1H), 7.39 – 7.33 (m, 3H), 7.14 (d, *J* = 7.7 Hz, 1H), 7.02 (d, *J* = 7.9 Hz, 2H), 3.59 (t, *J* = 5.2 Hz, 1H), 3.30 – 3.20 (m, 1H), 3.20 – 3.09 (m, 2H), 2.94 (dd, *J* = 5.2, 15.1 Hz, 1H), 2.65 (d, *J* = 14.7 Hz, 1H), 2.52 – 2.37 (m, 5H), 2.23 (d, *J* = 13.4 Hz, 1H), 1.74 – 1.65 (m, 1H), 1.45 (dt, *J* = 8.1, 12.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.9, 140.9, 140.8, 136.8, 134.1, 130.6, 129.7, 129.1 (q, J_{CF} = 32.4 Hz), 127.9, 127.7, 125.9 (d, J_{CF} = 10.8 Hz), 125.2 (q, J_{CF} = 3.7 Hz), 125.0 (q, J_{CF} = 3.7 Hz), 123.6 (q, J_{CF} = 3.8 Hz), 122.3 (d, J_{CF} = 10.9 Hz), 64.7, 48.01, 47.5, 44.8, 38.2, 35.3, 34.6, 21.5; IR (neat): 3027, 2961, 2929, 2873, 1619, 1598, 1442, 1419, 1326, 1162, 1120, 1068, 1038, 1019, 817, 757, 660, 599, 588, 551 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{28}H_{26}F_6NO_2S$: 554.1583, found: 554.1594. The absolute stereochemistry was assigned by analogy to **2a**. The relative stereochemistry was assigned by NOE.

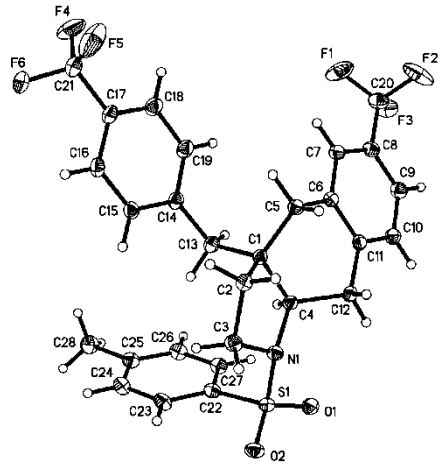


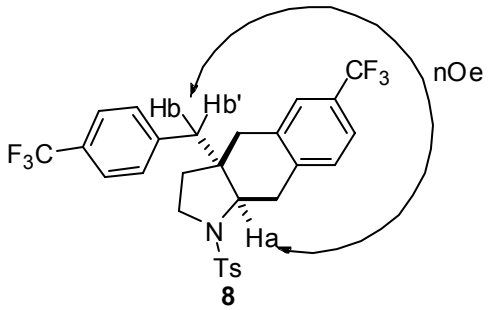
(3a*R*,9a*R*)-3a-(4-(Trifluoromethyl)benzyl)-1-tosyl-6-(trifluoromethyl)-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (8).



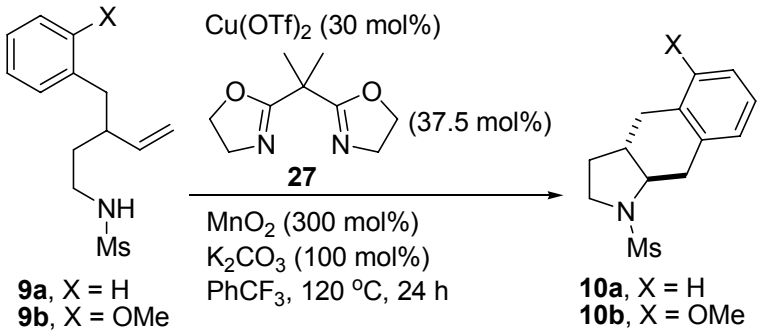
Benz[*f*]indole **8** was obtained as a clear oil. $[\alpha]_D^{23}$ = -55.3° (c = 1, $CHCl_3$), ee = 96%, determined by HPLC analysis [Chiralpak AD-RH, 5% IPA/Hexane, 1.0 mL/min, λ = 254 nm, t(major) = 9.75 min, t(minor) = 11.69 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.47 (dd, *J* = 8.0, 15.3 Hz, 3H), 7.40 – 7.24 (m, 4H), 6.99 (d, *J* = 7.9 Hz, 2H), 3.54 (t, *J* = 5.2 Hz, 1H), 3.32 – 3.15 (m, 2H), 3.07 (td, *J* = 6.7, 9.6 Hz, 1H), 2.95 (dd, *J* = 5.1, 15.1 Hz, 1H), 2.66 (d, *J* = 14.7 Hz, 1H), 2.54 – 2.35 (m, 5H), 2.20 (d, *J* = 13.4 Hz, 1H), 1.66 (ddd, *J* = 3.8, 6.5, 12.7 Hz, 1H), 1.51 – 1.40 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.9, 140.8, 140.2, 137.4, 133.7, 130.6, 129.7, 129.3 (q, J_{CF} = 14.8), 128.8, 128.7, 127.8, 125.9 (d, J_{CF} = 14.3 Hz), 125.2 (q, J_{CF} = 3.7 Hz), 124.3, (q, J_{CF} = 3.7 Hz), 123.8 (q, J_{CF} = 3.8 Hz), 122.3 (d, J_{CF} = 14.1 Hz), 64.6, 48.0, 47.5, 44.7, 38.3, 35.5, 34.4, 21.5; IR (neat): 3026, 2957, 2925, 2874, 1619, 1598, 1440, 1419, 1327, 1163, 1118, 1068, 818, 756, 661, 590, 546 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{28}H_{26}F_6NO_2S$: 554.1583, found: 554.1584. The absolute stereochemistry was assigned by analogy to **2a**. The relative stereochemistry and regiochemistry were assigned by X-ray structure of (±) **8**. NOE between Ha and Hb also confirmed relative stereochemistry.

X-ray crystal structure of (±) 8

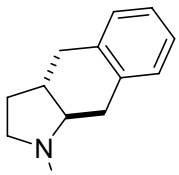




Catalytic carboamination of monosubstitued sulfonamides

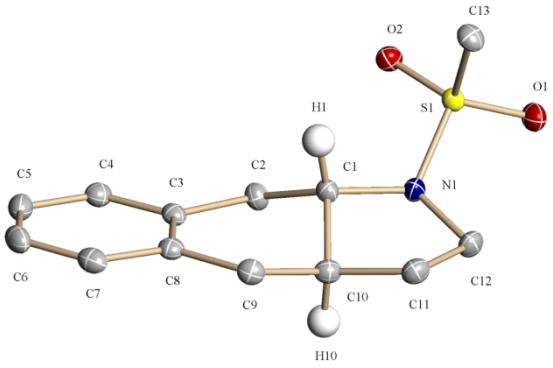


Representative catalytic carboamination of monosubstitued sulfonamides: (±)-*trans*-1-(Methylsulfonyl)-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (*trans*-10a).

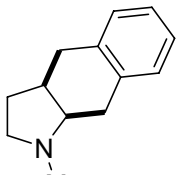


trans-**10a**

$Cu(OTf)_2$ (42.9 mg, 0.118 mmol, 30 mol%), bis(oxazoline) **27** (27.0 mg, 37.5 mol%) and $PhCF_3$ (2.0 mL) were combined in a pressure tube equipped with a magnetic stir bar under argon. The mixture was stirred at 60 °C for 2 hours. The solution was treated with MnO_2 (103 mg, 1.18 mmol, 3.0 equiv), K_2CO_3 (54.6 mg, 0.395 mmol, 1.0 equiv) and substrate **9a** (100 mg, 0.395 mmol) in $PhCF_3$ (1.95 mL). The tube was refreshed by argon for 2 minutes, sealed and heated at 120 °C in an oil bath for 24 hours. The cooled solution was diluted with CH_2Cl_2 (10 mL) and vacuum filtered under through silica gel (5 g). Then the silica gel was rinsed with EtOAc (3 × 30 mL). The filtrate was concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 60:40 hexanes/EtOAc) to afford 87 mg (87% yield, *trans* : *cis* 5 : 1) of *trans*-**10a** and *cis*-**10a**. The diastereomers were separated by prep HPLC using EtOAc/hexanes (*trans*-**10a** eluted first). Benz[*f*]indole *trans*-**10a** was obtained as a white solid, mp 166-168 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (t, J = 8.3 Hz, 4H), 3.66 – 3.47 (m, 3H), 3.24 – 3.05 (m, 2H), 2.97 – 2.79 (m, 4H), 2.76 – 2.63 (m, 1H), 2.23 – 2.06 (m, 2H), 1.71 – 1.53 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.9, 134.6, 130.1, 129.0, 126.2, 62.5, 49.2, 43.0, 37.0, 34.8, 34.3, 29.9; IR (neat): 2899, 2341, 1451, 1333, 1154, 1031, 965 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{13}H_{18}NO_2S$: 252.1053, found 252.1048. The relative stereochemistry was assigned by X-ray of *trans*-**10a**.



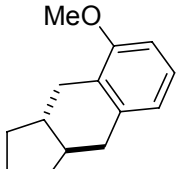
(±)-*cis*-1-(Methylsulfonyl)-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (*cis*-10a).



cis-**10a**

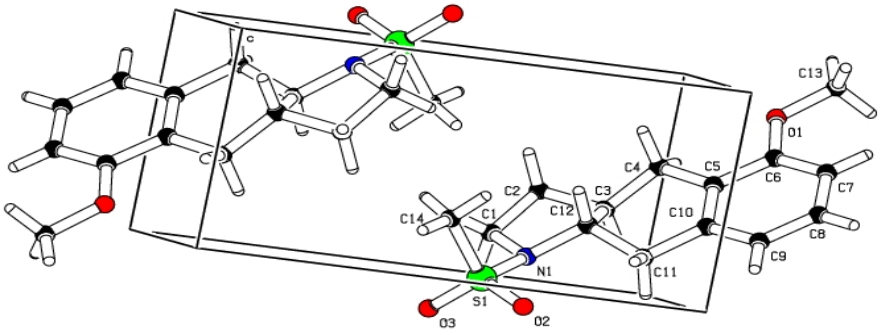
Benz[*f*]indole *cis*-**10a** was obtained as a white solid, mp 111-113 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 – 7.08 (m, 4H), 3.87 (ddd, *J* = 5.5, 7.5, 9.4 Hz, 1H), 3.40 – 3.30 (m, 1H), 3.27 – 3.17 (m, 1H), 3.08 (dd, *J* = 5.5, 14.6 Hz, 1H), 2.94 – 2.80 (m, 5H), 2.70 (dq, *J* = 7.7, 15.7 Hz, 1H), 2.58 (dd, *J* = 7.1, 14.6 Hz, 1H), 2.17 – 2.07 (m, 1H), 1.68 (ddd, *J* = 8.5, 12.6, 15.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.4, 136.3, 128.2, 127.2, 126.6, 126.5, 59.5, 48.5, 38.1, 35.3, 35.2, 33.6, 31.3; IR (neat): 2936, 2361, 1460, 1330, 1154, 1039, 752, 563, 522, 451 cm^{-1}; HRMS (ESI) calcd for $[M + Na]^+$ $C_{13}H_{17}NO_2SNa$: 274.0872, found: 274.0877.

(±)-*trans*-5-Methoxy-1-(methylsulfonyl)-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (*trans*-10b).

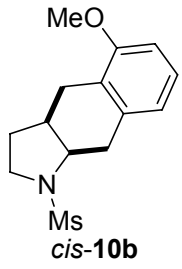


trans-**10b**

Benz[*f*]indole **10b** (81% yield, *trans* : *cis* 15 : 1) was synthesized from **9b** using the same procedure as **10a**. The diastereomers were separated by prep HPLC using EtOAc/hexanes (*trans*-**10b** eluted first). Benz[*f*]indole *trans*-**10b** was obtained as a white solid, mp 179-182 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (t, *J* = 7.9 Hz, 1H), 6.76 (d, *J* = 7.7 Hz, 1H), 6.69 (d, *J* = 8.1 Hz, 1H), 3.82 (s, 3H), 3.64 – 3.48 (m, 3H), 3.26 – 3.10 (m, 2H), 2.96 – 2.83 (m, 4H), 2.34 (dd, *J* = 12.4, 16.5 Hz, 1H), 2.19 (dt, *J* = 5.5, 12.0 Hz, 1H), 2.13 – 2.01 (m, 1H), 1.69 – 1.60 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.1, 136.0, 126.8, 124.0, 122.1, 107.4, 62.2, 55.2, 49.3, 42.7, 37.1, 34.5, 30.1, 28.5; IR (neat): 2955, 1581, 1467, 1331, 1255, 1154, 1080 cm^{-1}; HRMS (ESI) calcd for $[M + Na]^+$ $C_{14}H_{19}NO_3SNa$: 304.0978, found: 304.0971. The relative stereochemistry was assigned by X-ray of *trans*-**10b**.

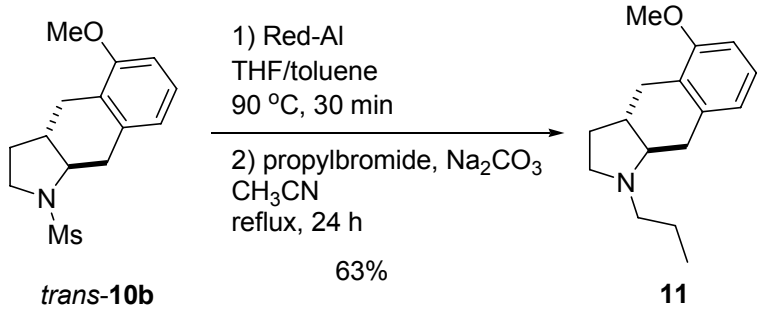


(±)-*cis*-5-Methoxy-1-(methylsulfonyl)-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (*cis*-10b).



cis-**10b**

Benzo[*f*]indole *cis*-**10b** was obtained as a white solid, mp 113-115 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (t, *J* = 7.9 Hz, 1H), 6.80 (d, *J* = 7.4 Hz, 1H), 6.75 (d, *J* = 8.2 Hz, 1H), 3.87 – 3.79 (m, 4H), 3.38 (ddd, *J* = 4.0, 7.2, 9.9 Hz, 1H), 3.25 – 3.19 (m, 1H), 3.06 (dd, *J* = 6.1, 15.0 Hz, 2H), 2.89 – 2.76 (m, 4H), 2.67 – 2.58 (m, 1H), 2.50 (dd, *J* = 6.8, 15.4 Hz, 1H), 2.16 – 2.08 (m, 1H), 1.69 (ddd, *J* = 8.8, 12.5, 16.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.1, 137.6, 126.8, 125.2, 120.8, 108.5, 59.2, 55.4, 48.3, 37.5, 35.2, 35.1, 31.4, 25.1; IR (neat): 2932, 2841, 1587, 1474, 1331, 1263, 1155, 1101,1055, 1039, 778 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ $C_{14}H_{20}NO_3S$: 282.1158, found: 282.1163.



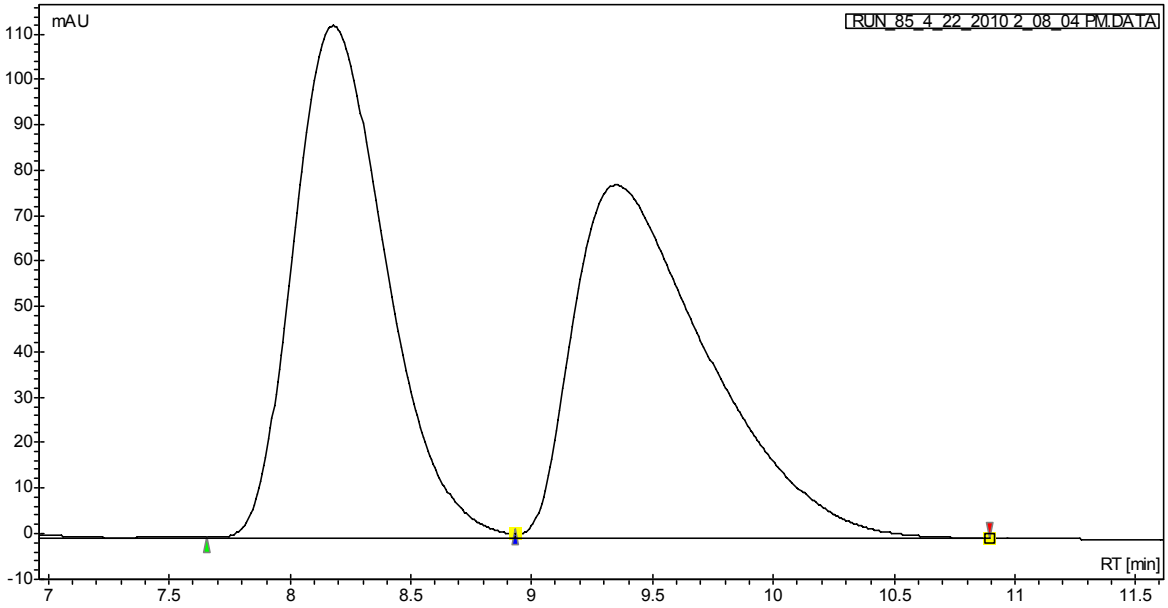
trans-**10b** **11**

(±)-*trans*-5-Methoxy-1-propyl-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]indole (11).

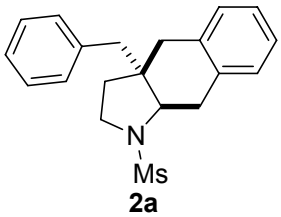
Benz[*f*]indole *trans*-**10b** (71mg, 0.252 mmol) was dissolved in THF (10 mL) under argon. Toluene (20 mL) was added to the mixture, then sodium bis(2-methoxyethoxy)aluminumhydride (Red-Al) in toluene (65 wt.%, 0.385 mL, 1.262 mmol) was added dropwise.[15] The resulting mixture was heated in 90 °C oil bath. The condenser (running water closed) was charged with argon flow on top and put into flask neck with space let the argon flow take away the THF for 15 minutes. Then the condenser (running water open) was charged with argon bloom on top and was closed with flask. The heating was allowed for additional 15 minutes. The reaction mixture was cooled to room temperature and quenched by adding a 1 M NaOH solution (20 mL) dropwise. The aqueous phase was extracted with Et_2O (3 × 50 mL). All combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was used without further purification in the next step.

The crude amine was dissolved in CH_3CN (20 mL) under argon.[16] The solution was then treated with Na_2CO_3 (107 mg, 1.01 mmol) and propylbromide (0.091 mL, 1.01 mmol) and was heated to reflux and stirred for 24 hours. The reaction was cooled to room temperature and quenched with 1 M NaOH (15 mL) added dropwise. The resulting mixture was extracted with Et_2O (3 × 60 mL). All combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash

column chromatography (SiO_2, 98:1:1 $CH_2Cl_2/CH_3OH/NH_3{\cdot}H_2O$) to afford 39 mg (63% yield, 2 steps) of **11** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (t, *J* = 7.9 Hz, 1H), 6.76 (d, *J* = 7.6 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 1H), 3.81 (s, 3H), 3.43 – 3.33 (m, 1H), 3.13 (ddd, *J* = 4.9, 16.1, 20.0 Hz, 2H), 2.86 (dt, *J* = 8.6, 17.2 Hz, 1H), 2.76 – 2.63 (m, 1H), 2.34 (dt, *J* = 7.9, 15.4 Hz, 1H), 2.29 – 2.20 (m, 1H), 2.19 – 2.03 (m, 3H), 2.00 – 1.86 (m, 1H), 1.66 – 1.46 (m, 3H), 0.94 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.4, 137.0, 126.3, 125.7, 122.1, 107.1, 66.6, 56.9, 55.2, 53.0, 40.8, 35.6, 29.8, 28.4, 21.7, 12.2; IR (neat): 2955, 2931, 2836, 2795, 1653, 1580, 1469, 1438, 1248, 1095, 1078, 1064, 768 cm^{-1}; HRMS (EI) calcd for $[M]^+$ $C_{16}H_{23}NO$: 245.1774, found: 245.1779. Data match those previously reported.[16]



#	Time [min]	Area [%]
1	8.18	49.97
2	9.35	50.03



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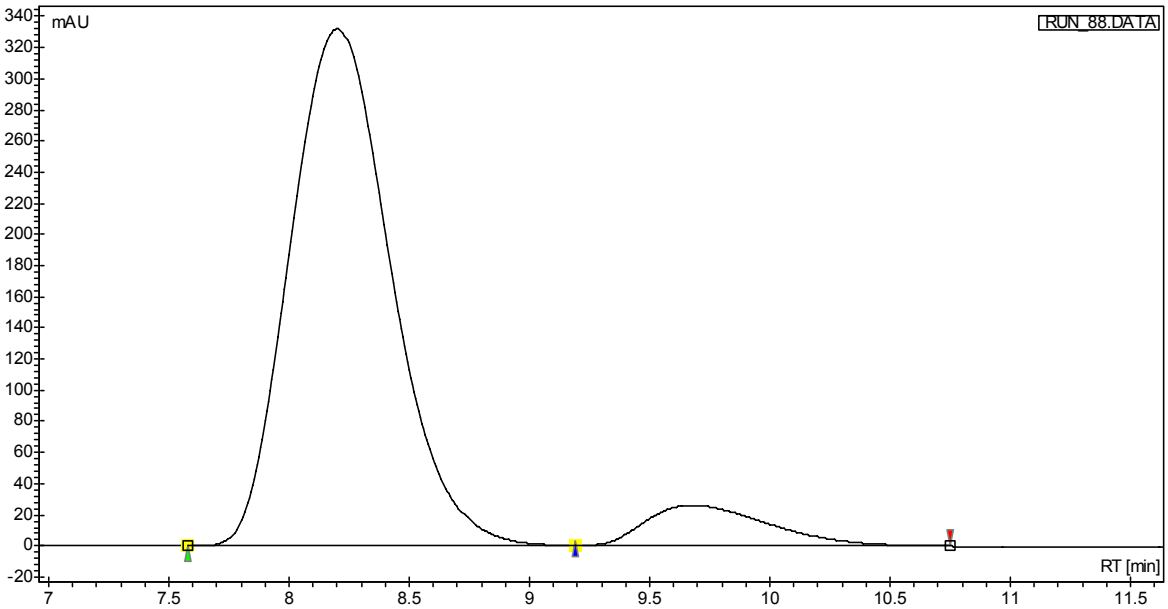
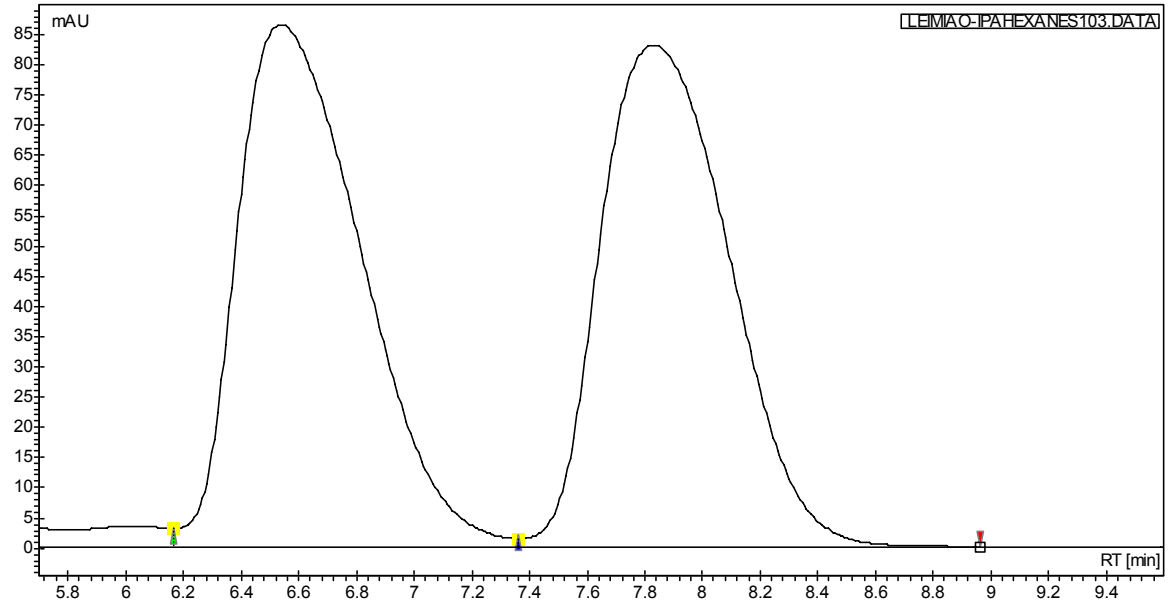
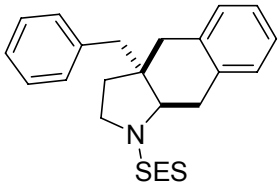


#	Time [min]	Area [%]
1	8.20	91.12
2	9.68	8.88



#	Time [min]	Area [%]
1	6.54	50.06
2	7.83	49.94



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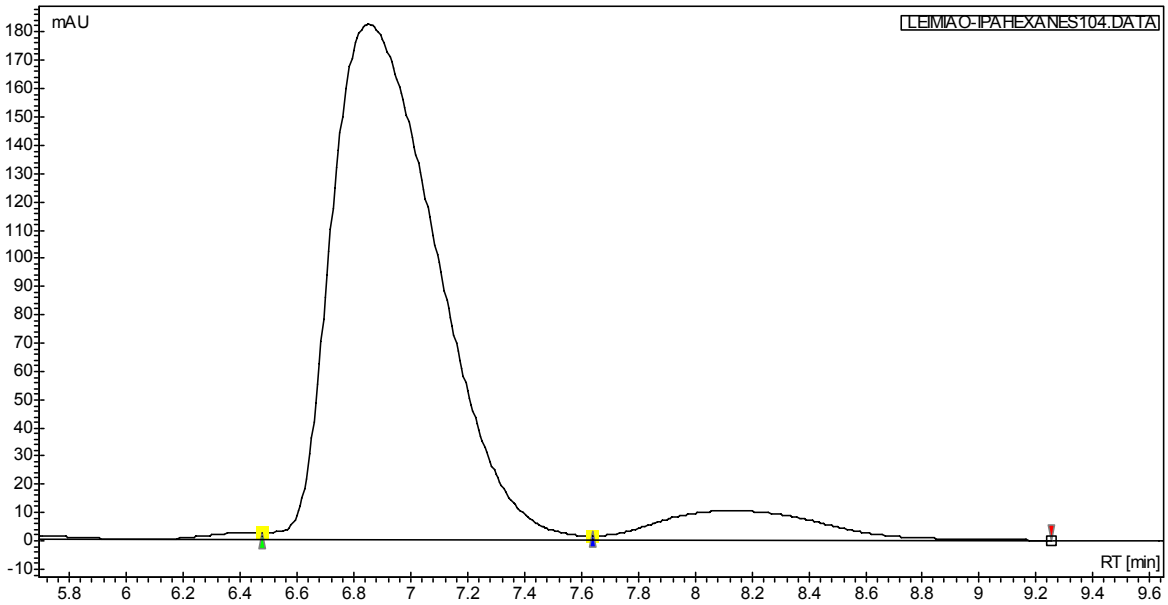
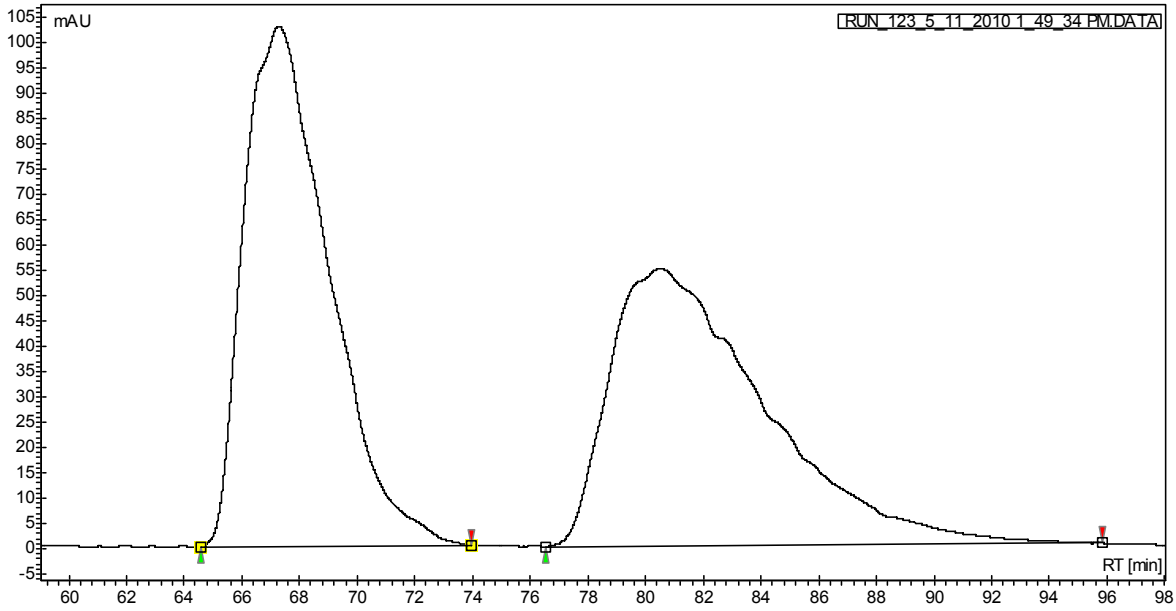
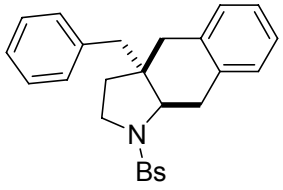


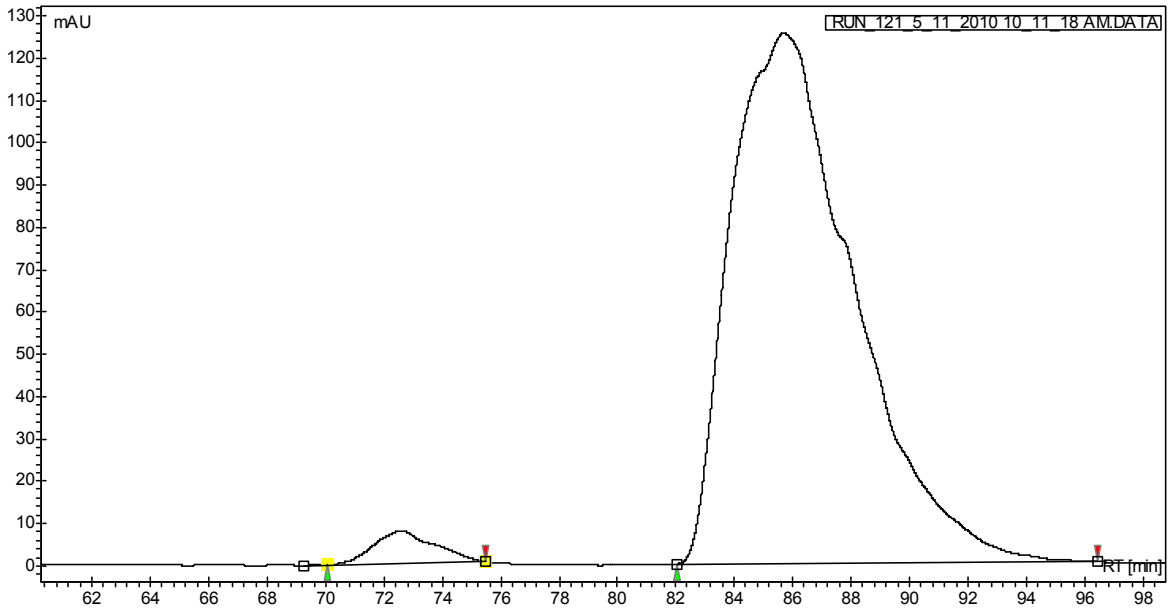
#	Time [min]	Area [%]
1	6.85	91.78
2	8.13	8.22



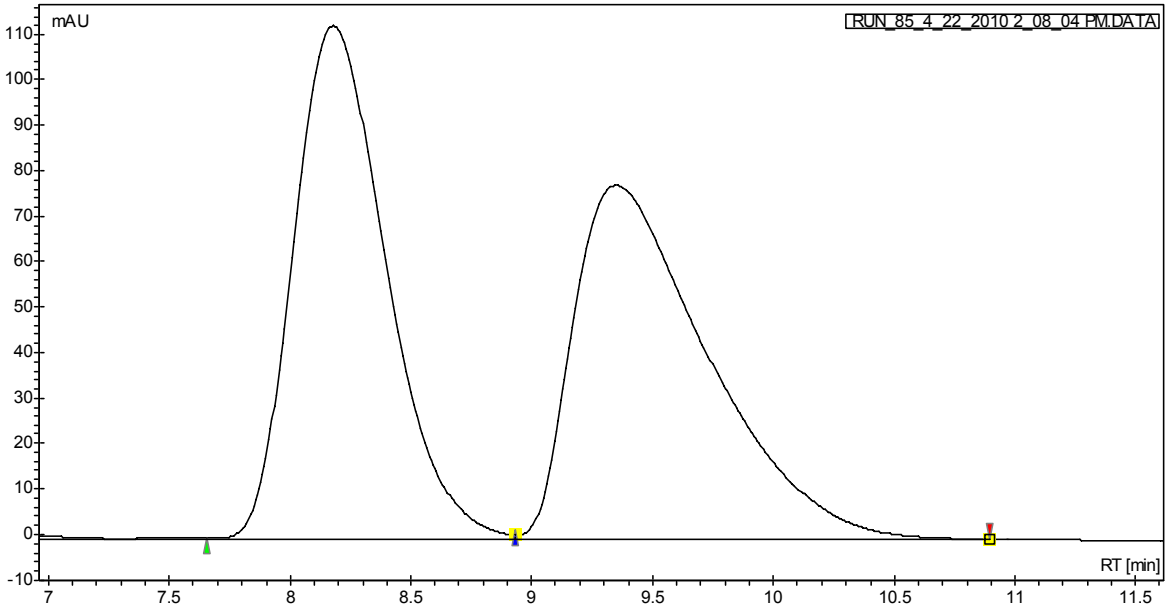
#	Time [min]	Area [%]
1	67.28	50.71
2	80.47	49.29



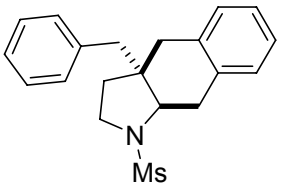
2c



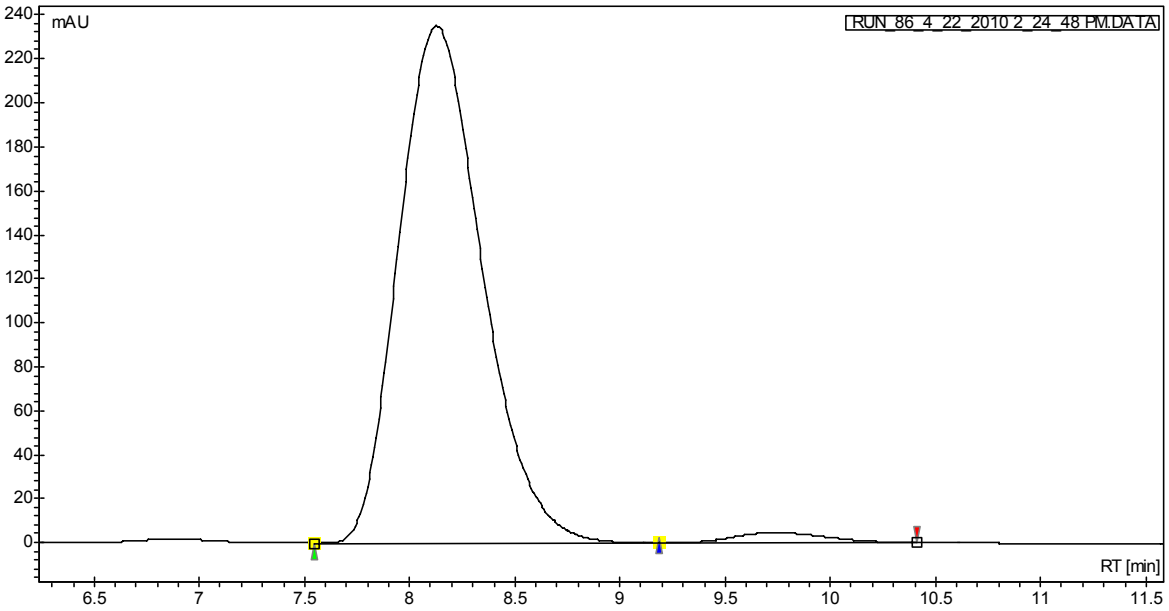
#	Time [min]	Area [%]
1	72.58	3.03
2	85.71	96.97



#	Time [min]	Area [%]
1	8.18	49.97
2	9.35	50.03



2a (from **2d**)



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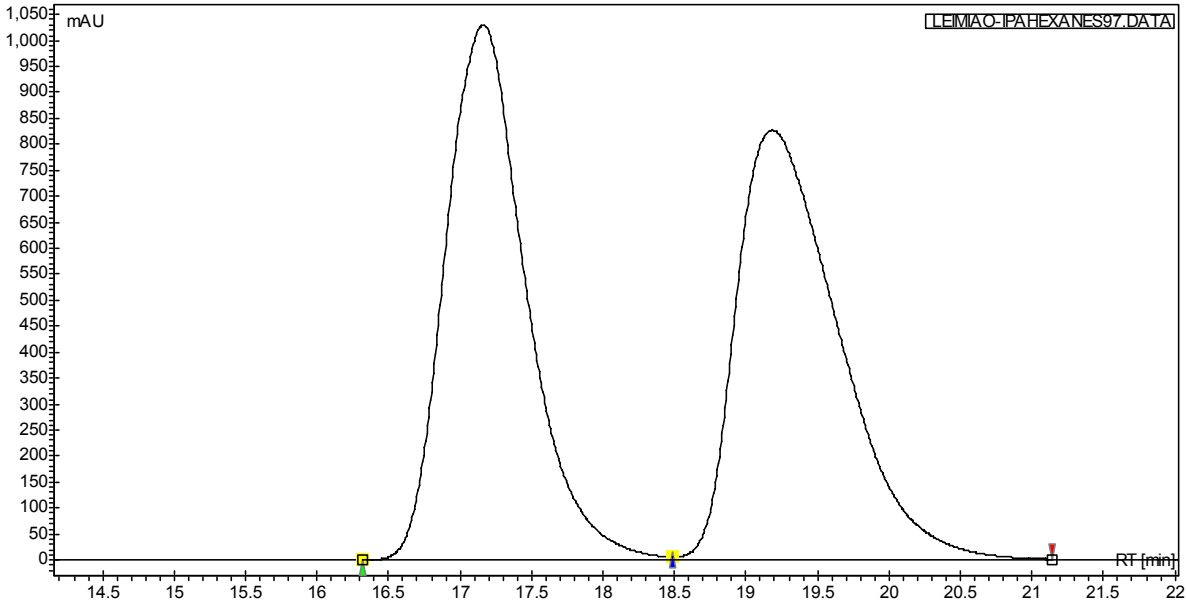
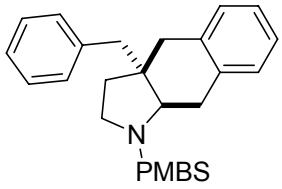
1	8.13	97.87
2	9.73	2.13



#	Time [min]	Area [%]
1	17.16	49.71
2	19.19	50.29



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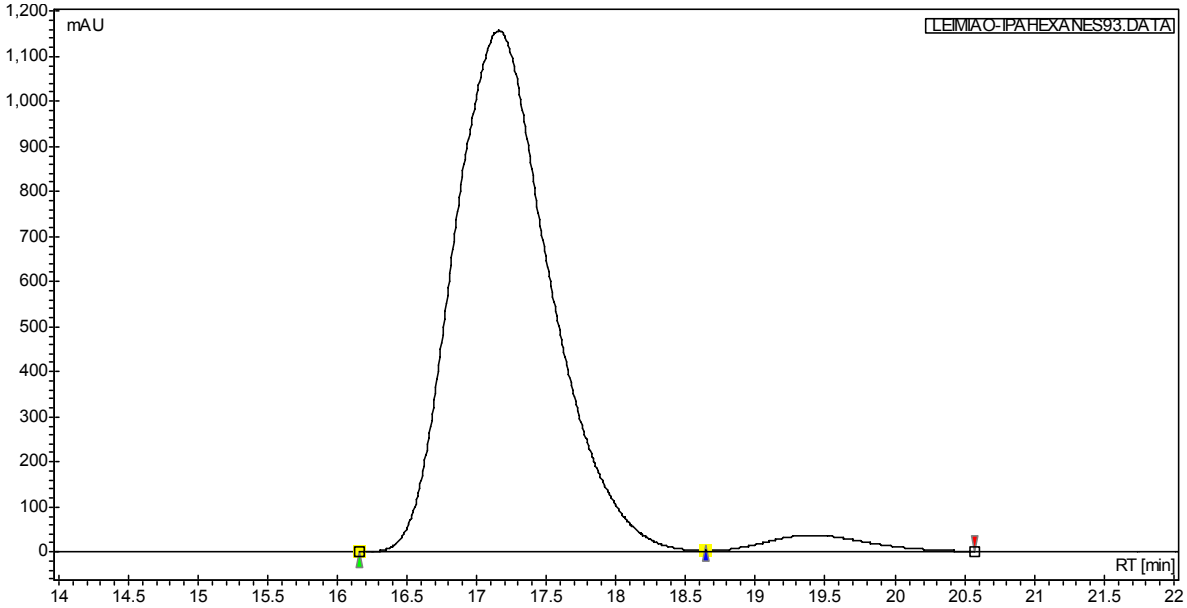

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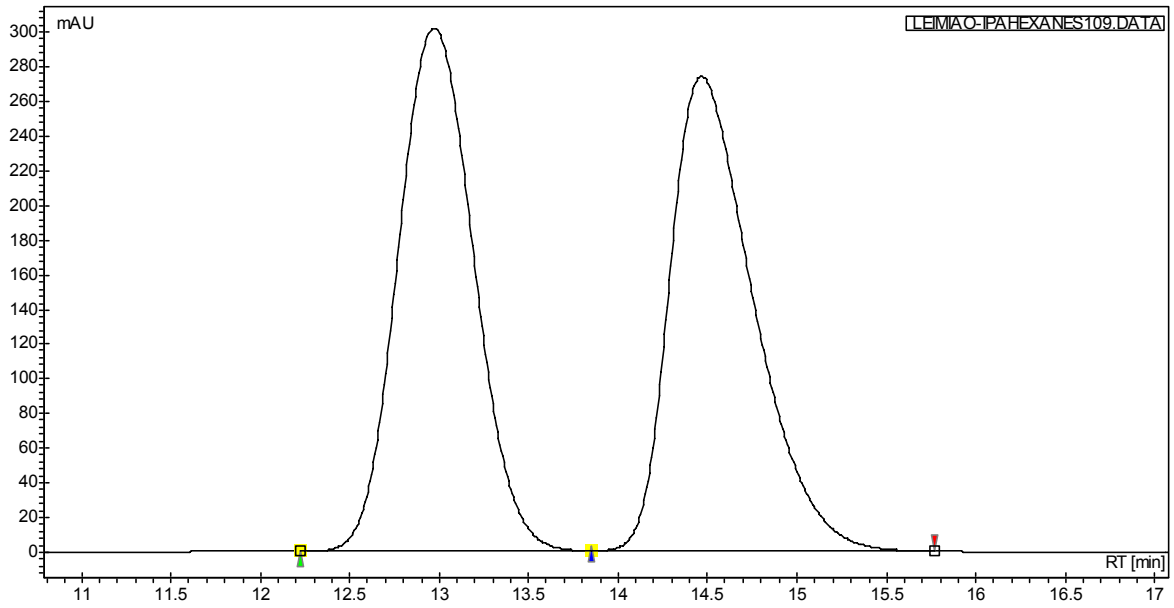
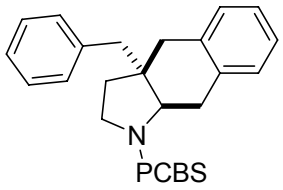
1	17.16	96.73
2	19.41	3.27



#	Time [min]	Area [%]
1	12.97	49.99
2	14.47	50.01



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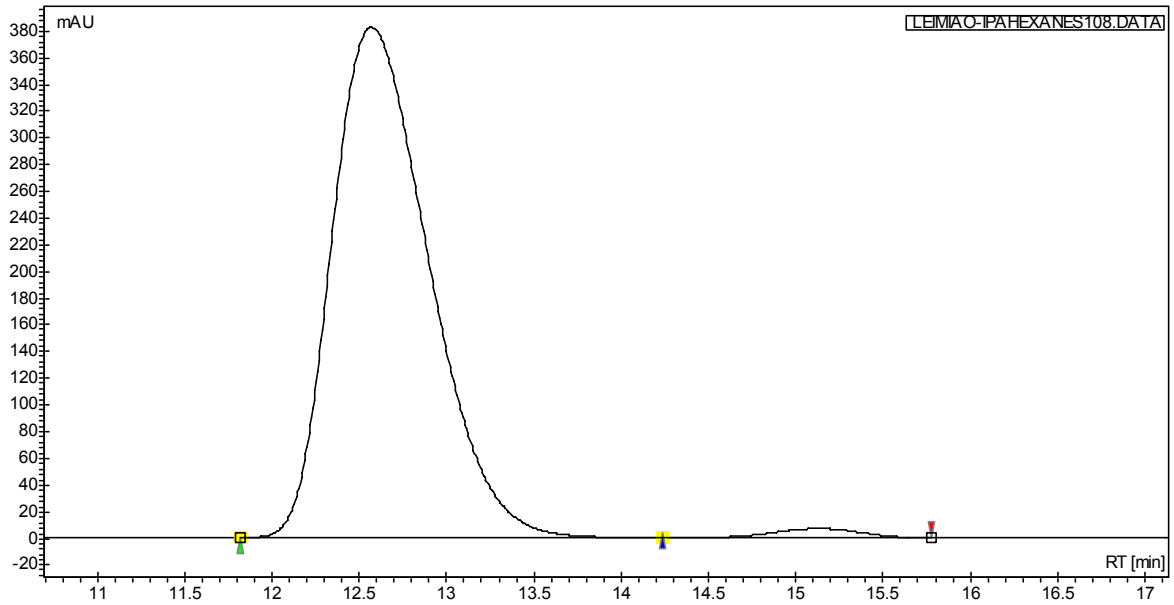

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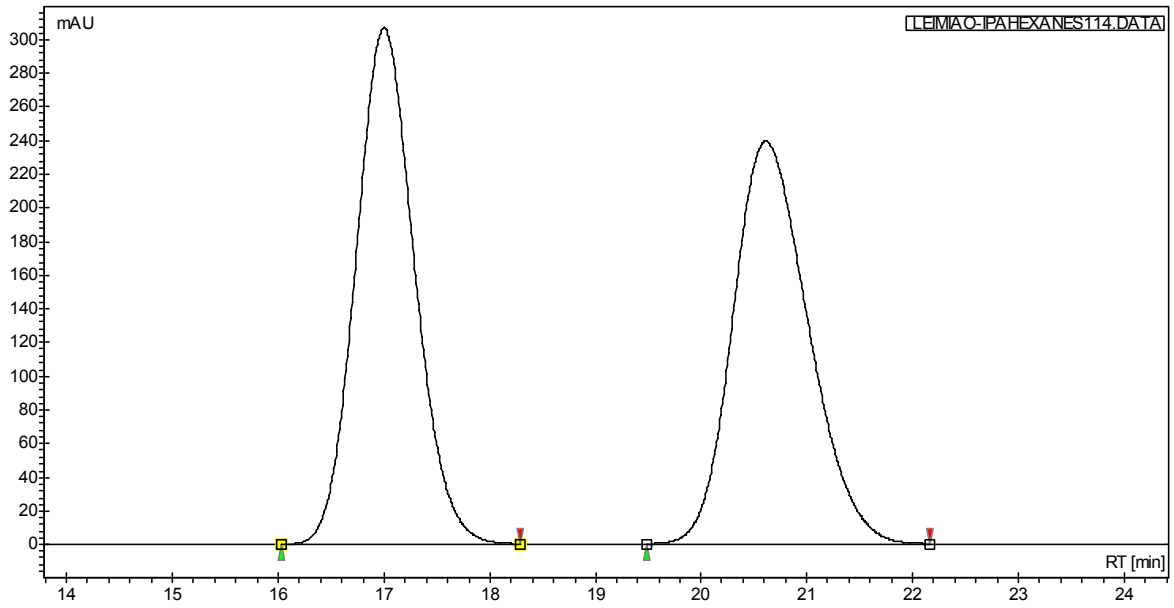
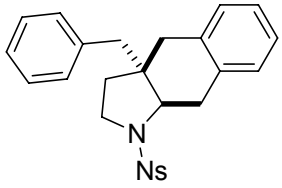
1	12.57	98.39
2	15.13	1.61



#	Time [min]	Area [%]
1	17.00	49.96
2	20.61	50.04



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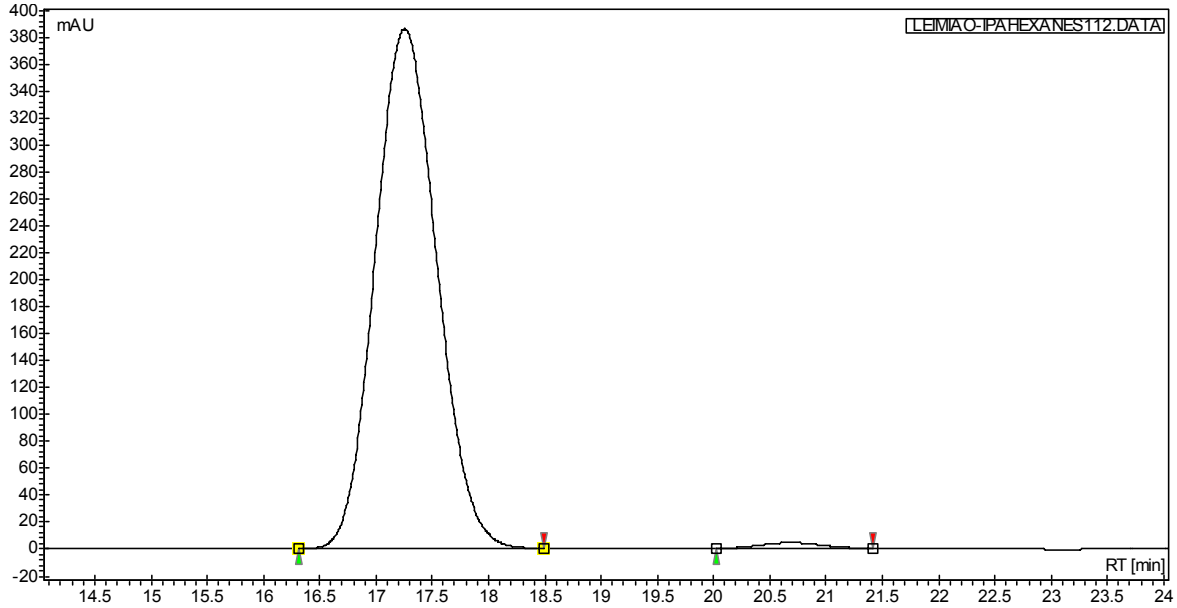

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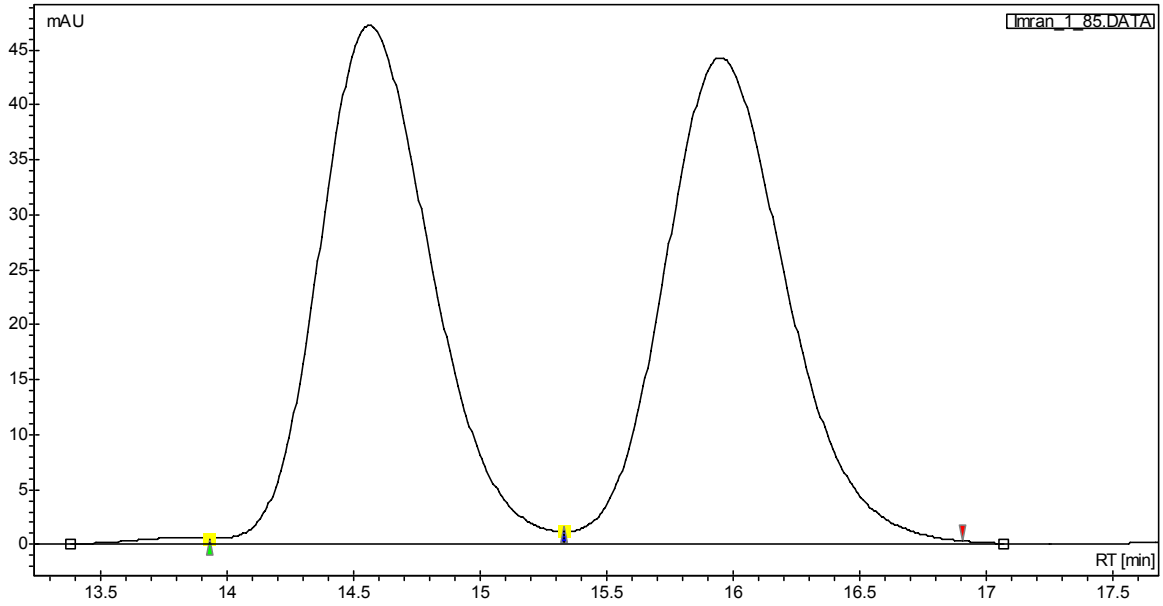
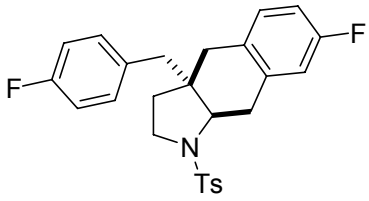
1	17.25	98.80
2	20.69	1.20



#	Time [min]	Area [%]
1	14.56	49.46
2	15.95	50.54



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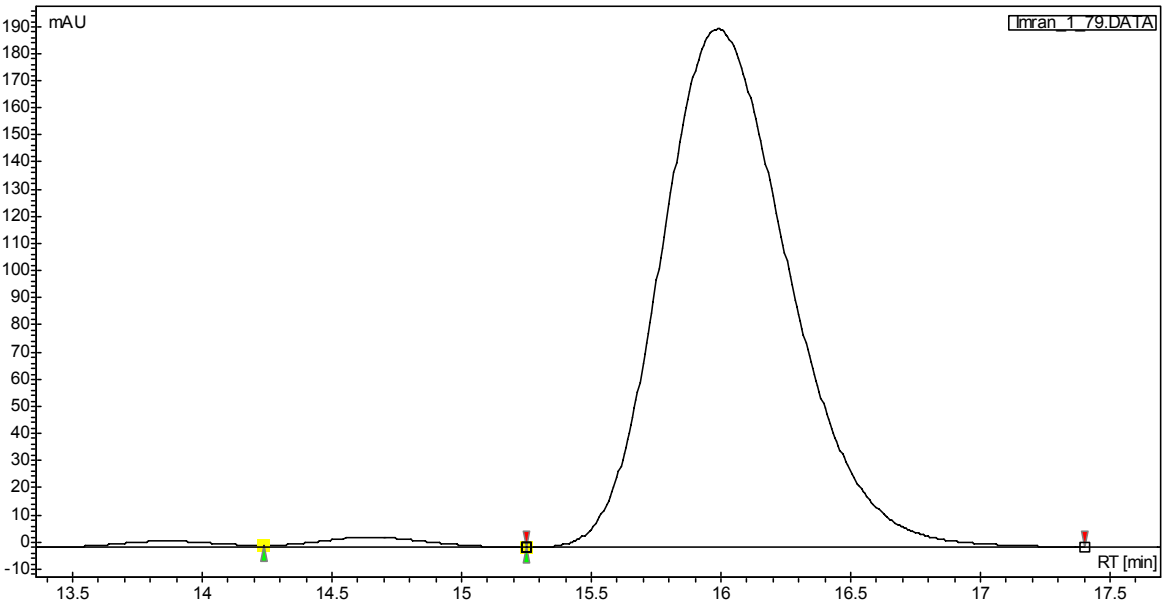

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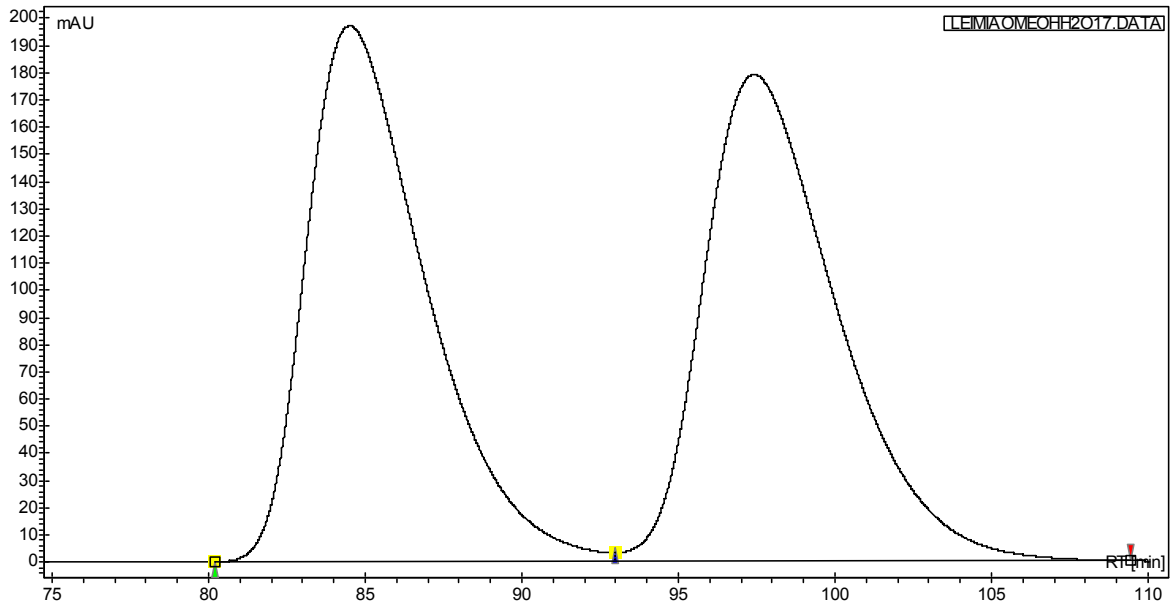
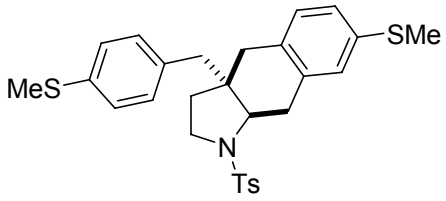
1	14.65	1.68
2	15.99	98.32



#	Time [min]	Area [%]
1	84.50	49.77
2	97.41	50.23



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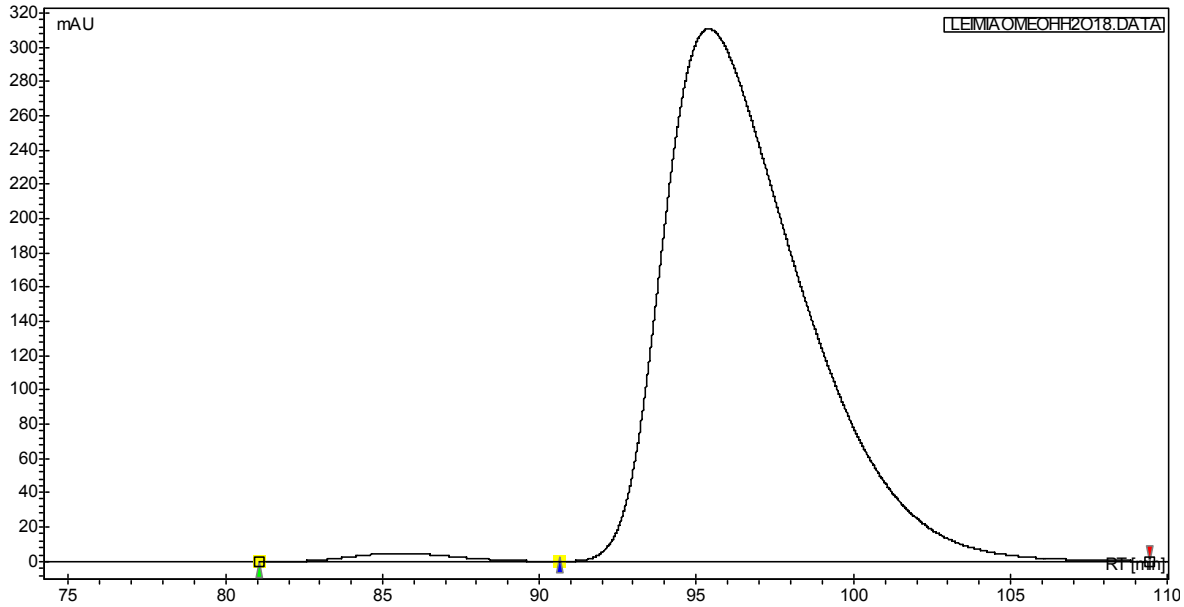
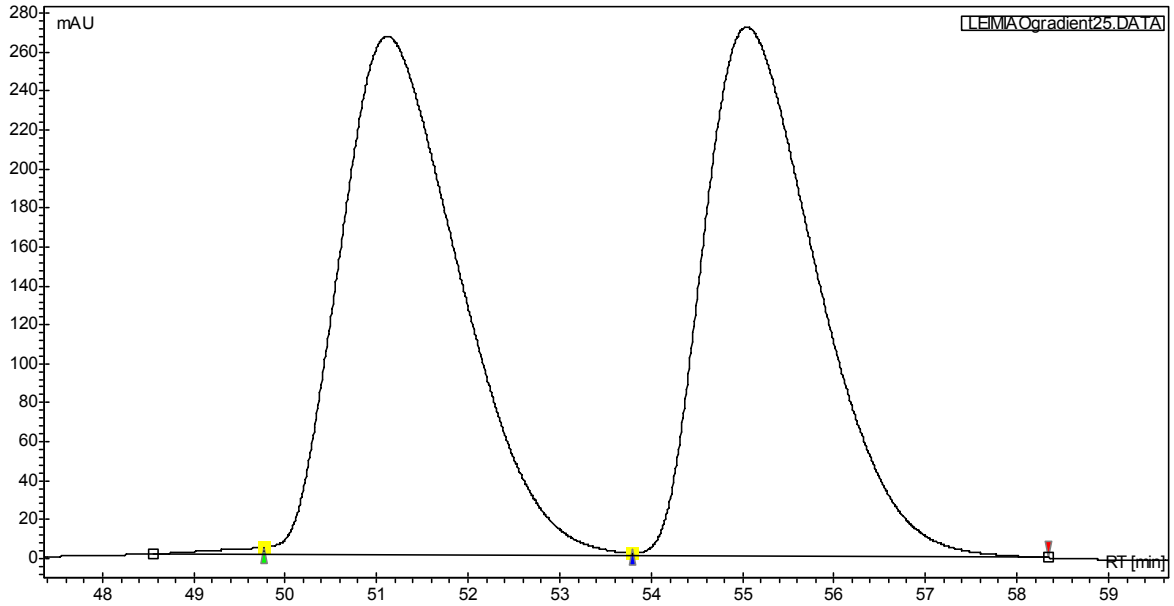


#	Time [min]	Area [%]
1	85.52	1.35
2	95.39	98.65



#	Time [min]	Area [%]
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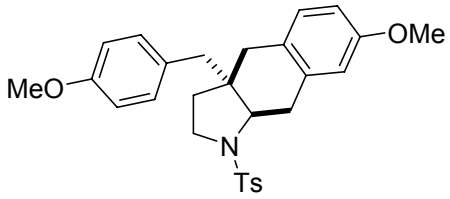
2	55.05	49.25



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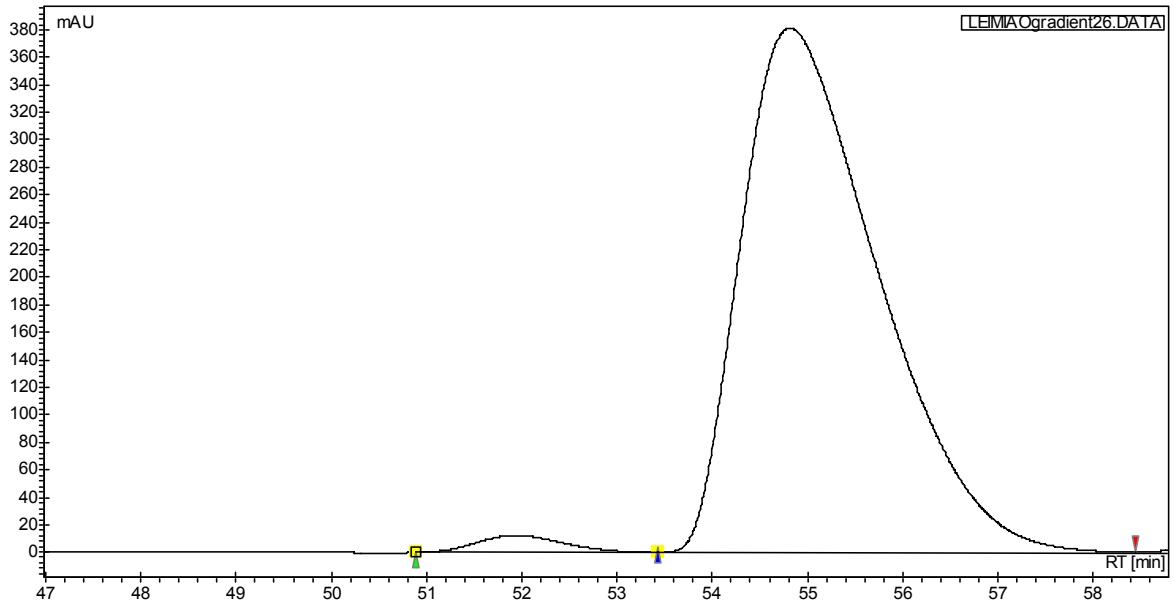
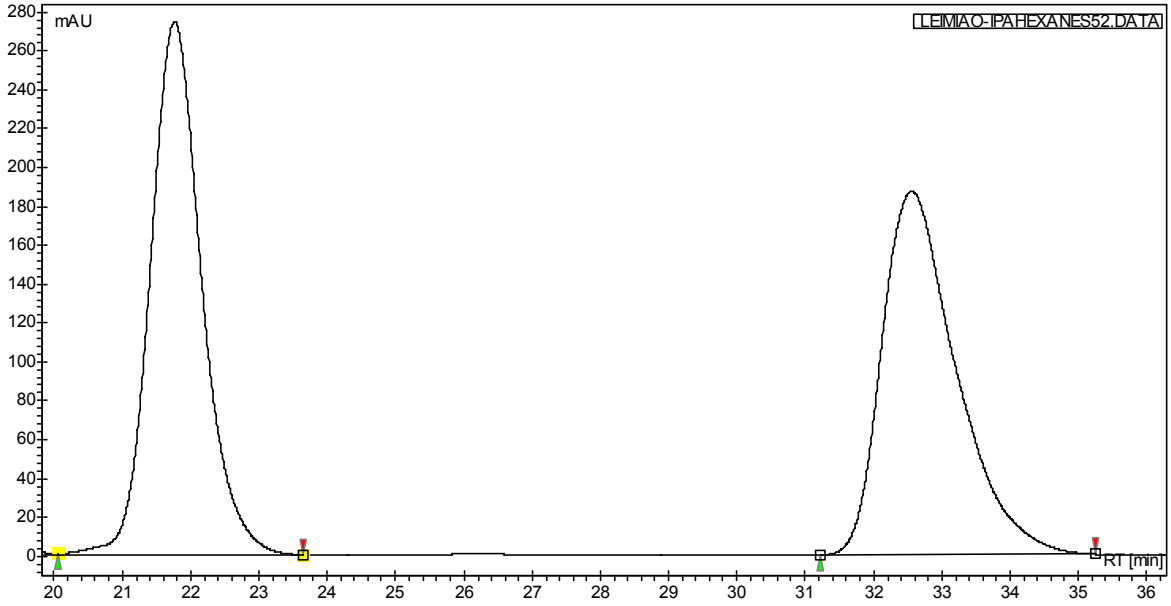
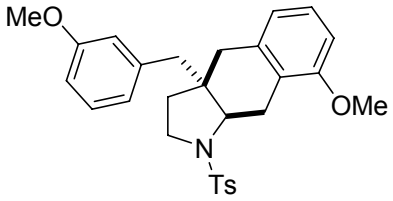


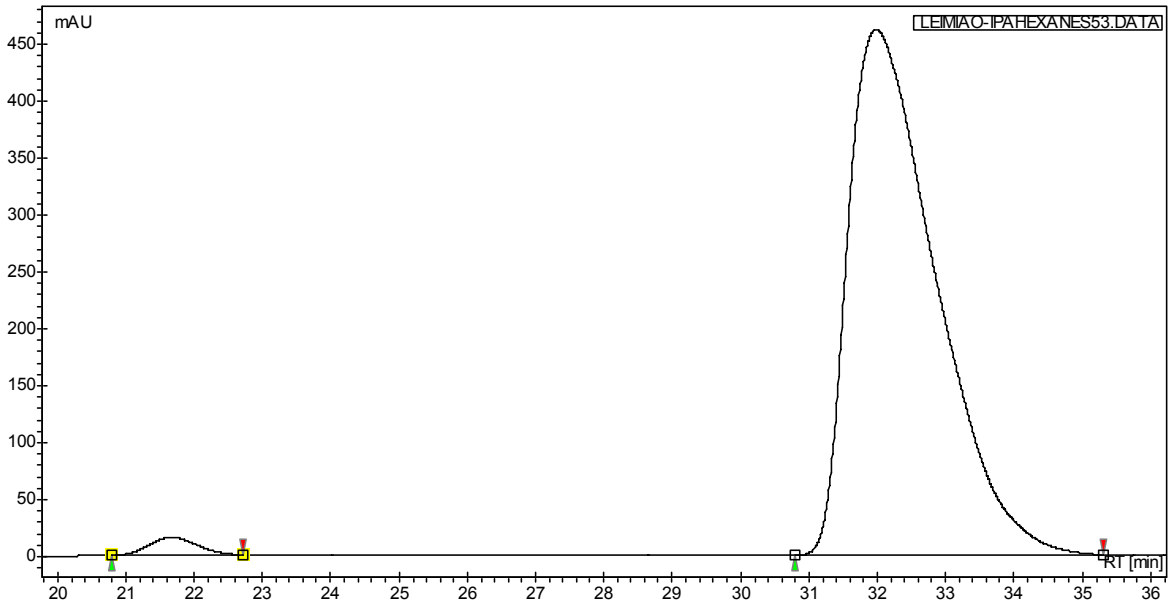
#	Time [min]	Area [%]
1	51.93	2.05
2	54.81	97.95



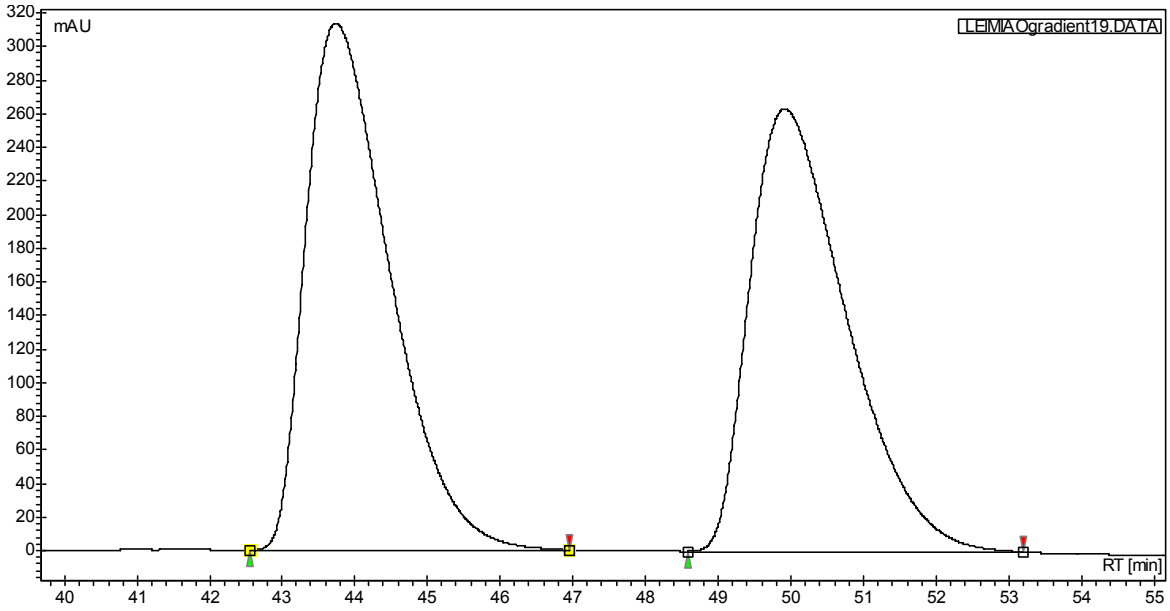
#	Time [min]	Area [%]
1	21.77	50.45
2	32.56	49.55



ortho-**4a**



#	Time [min]	Area [%]
1	21.67	1.85
2	31.99	98.15



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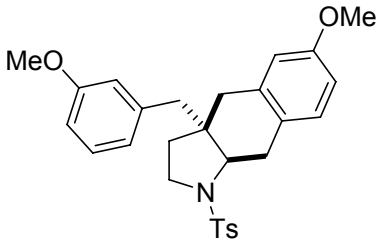
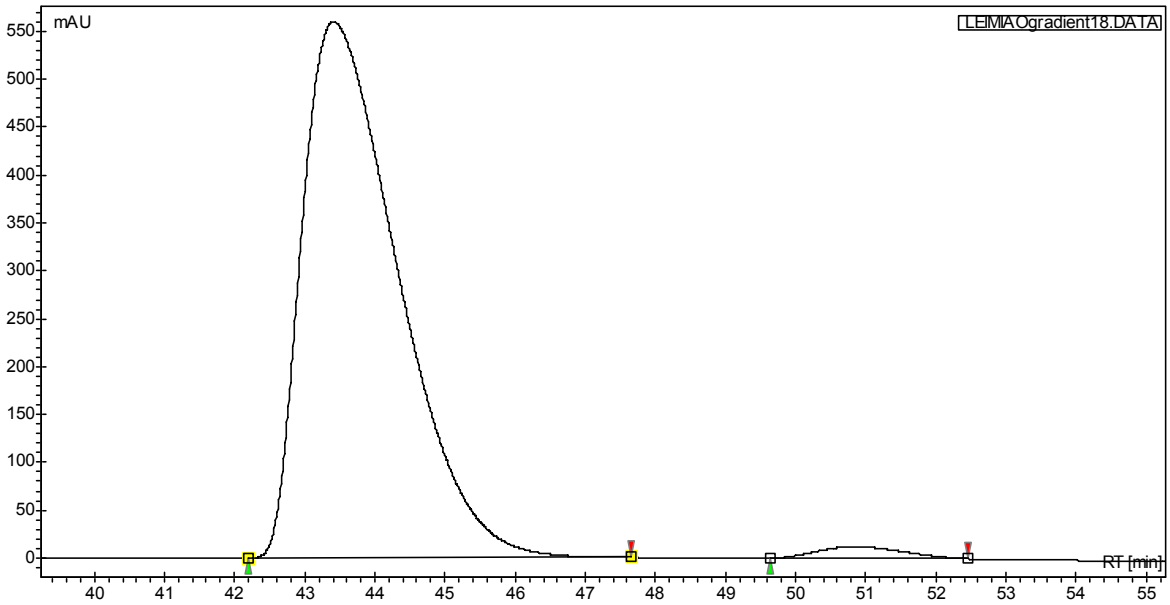
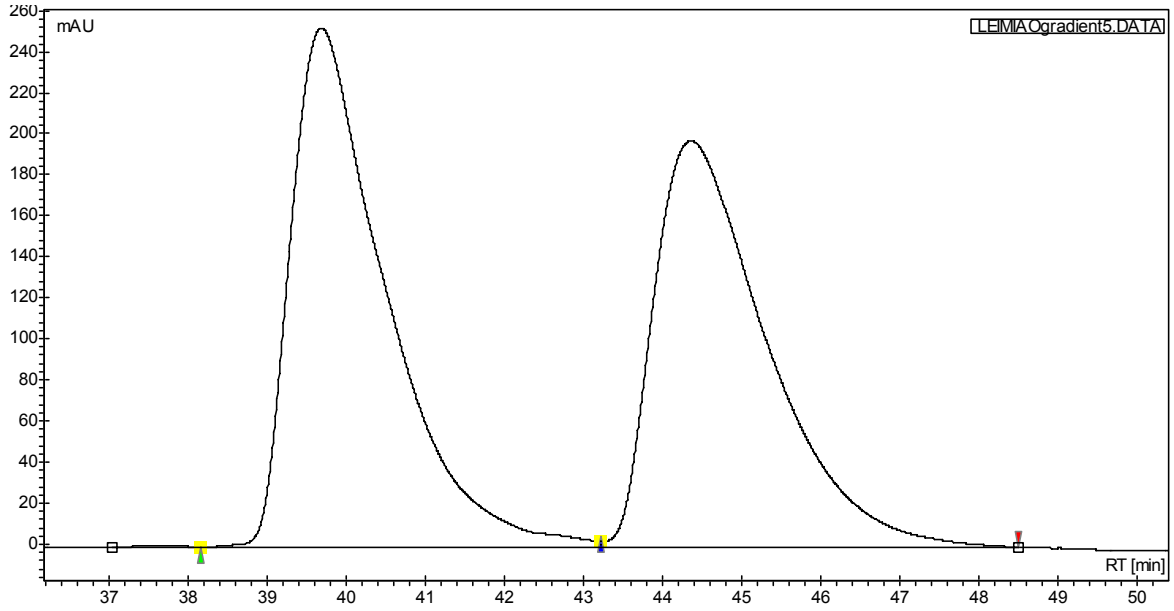
2	49.92	49.16



para-**4a**



#	Time [min]	Area [%]
1	43.41	98.03
2	50.85	1.97



#	Time [min]	Area [%]
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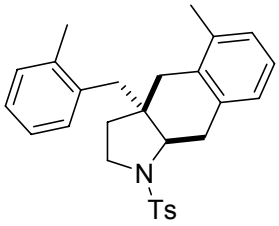
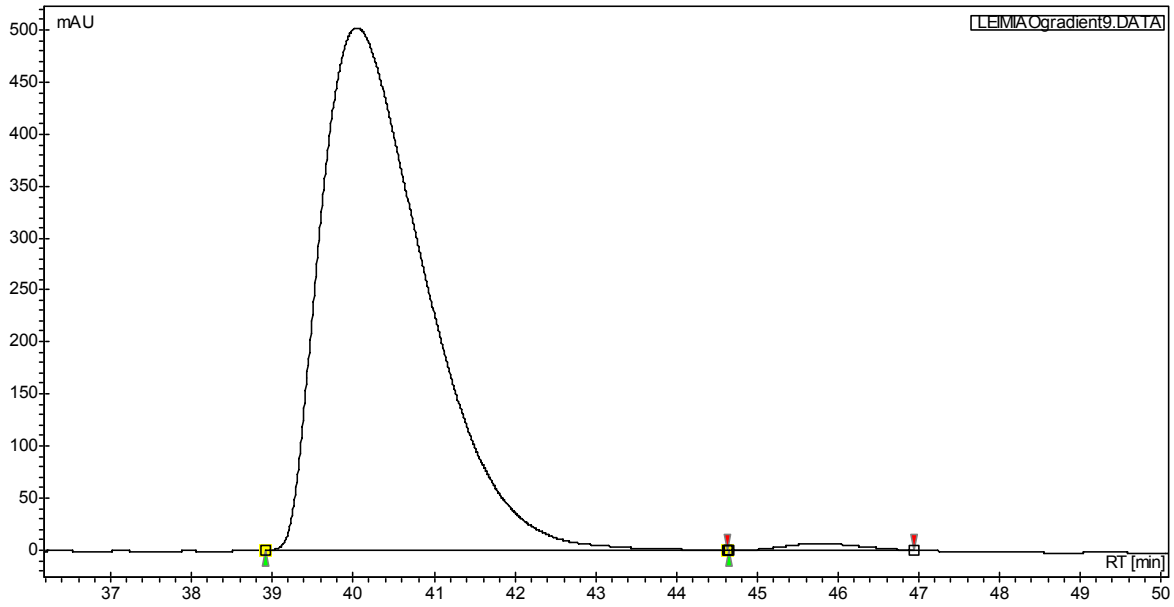


6a



#	Time [min]	Area [%]
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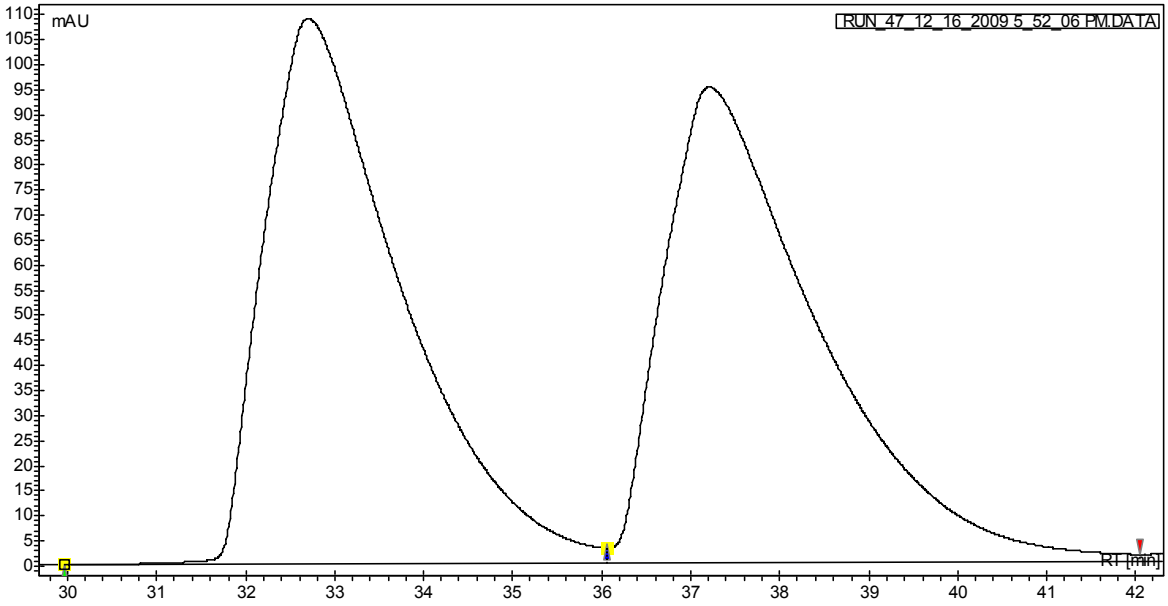

#	Time [min]	Area [%]
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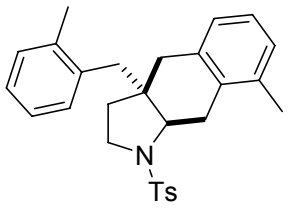
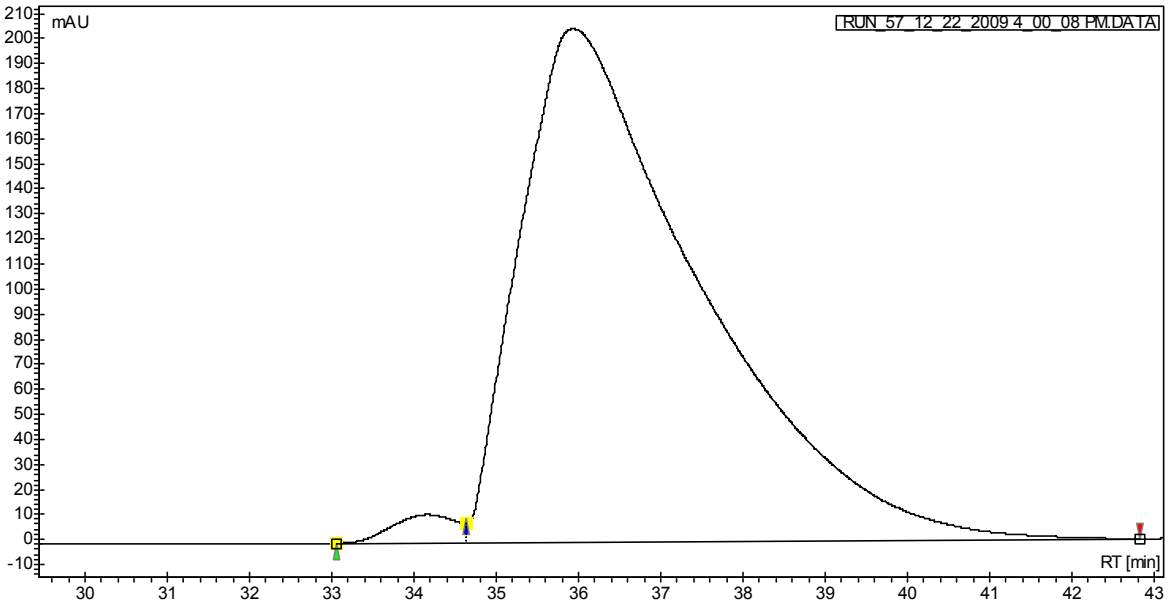
2	37.21	49.68



7a



#	Time [min]	Area [%]
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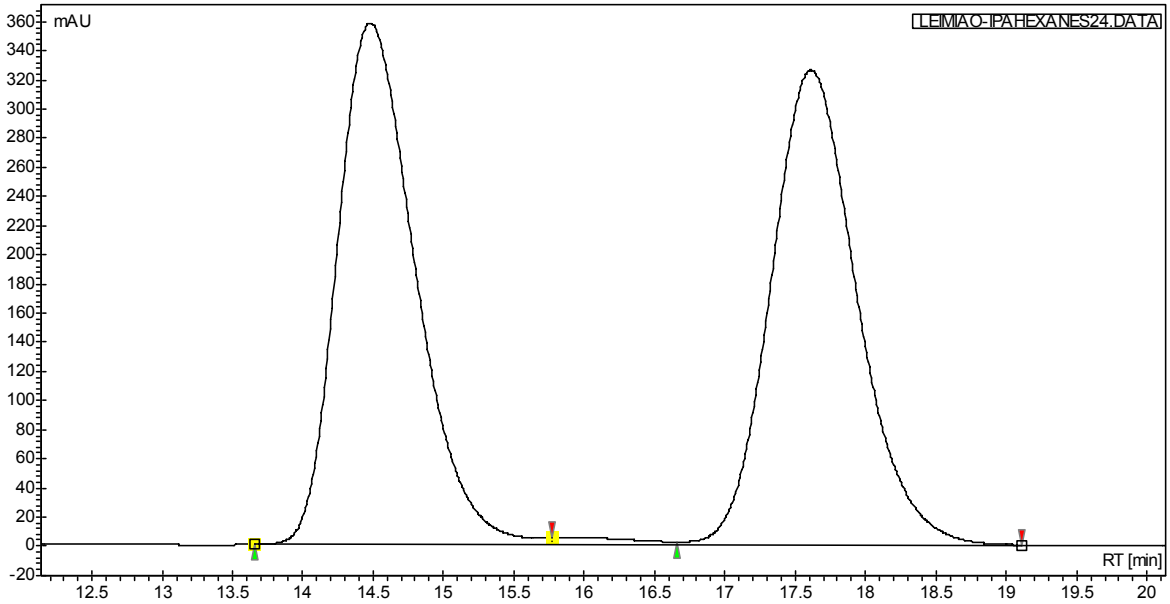

#	Time [min]	Area [%]
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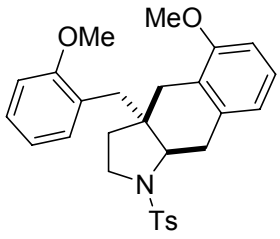
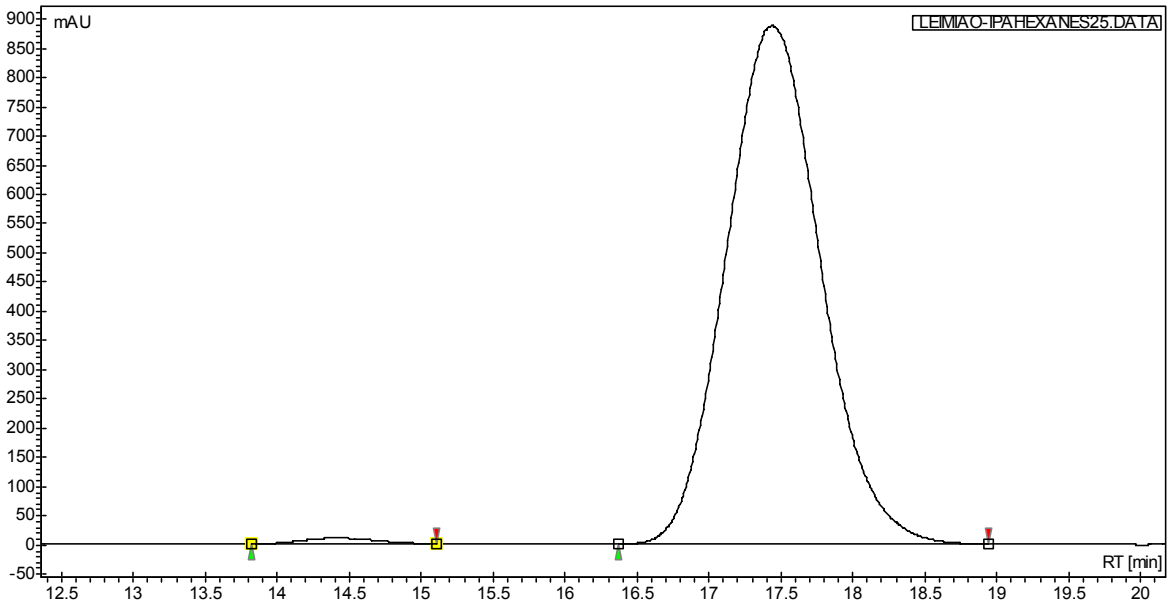
2	17.61	50.07



6b



#	Time [min]	Area [%]
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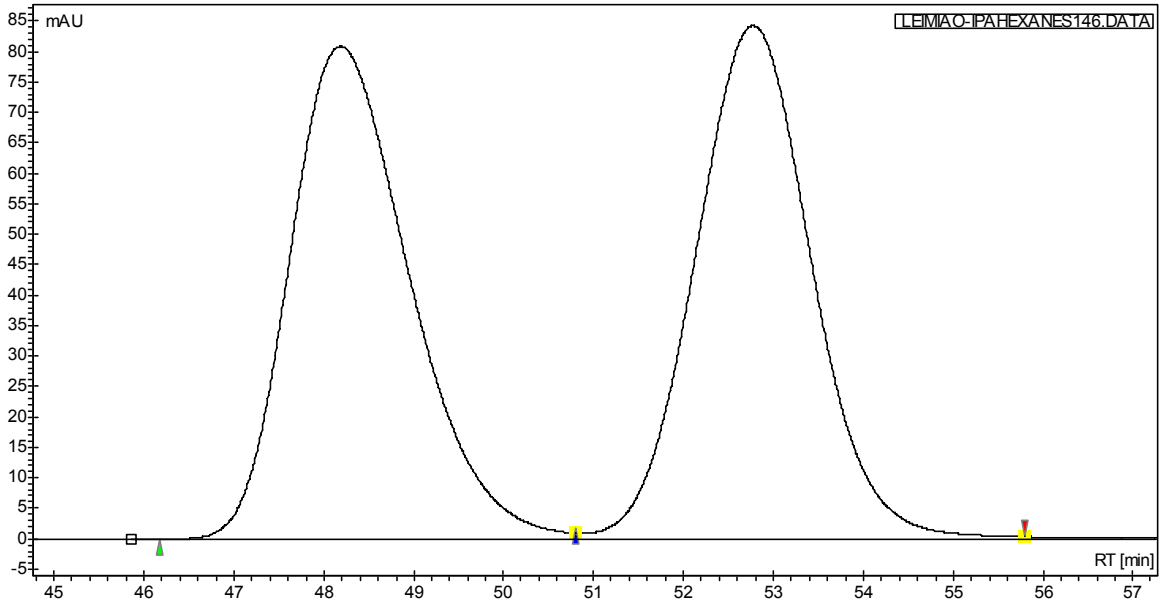
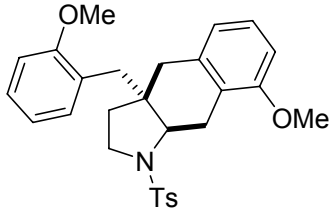
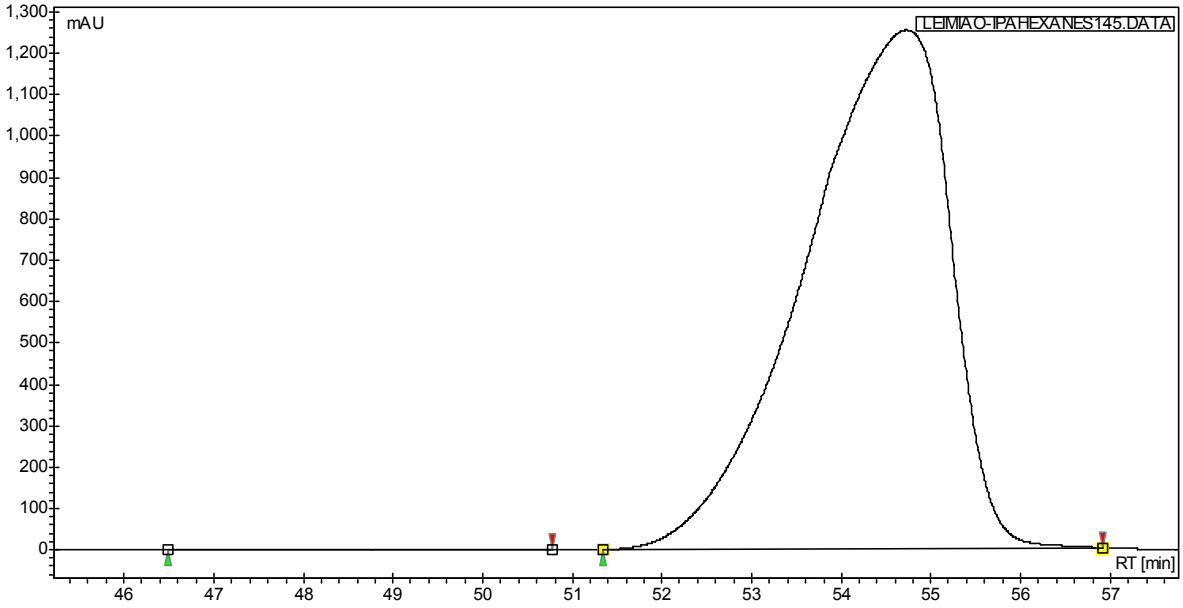


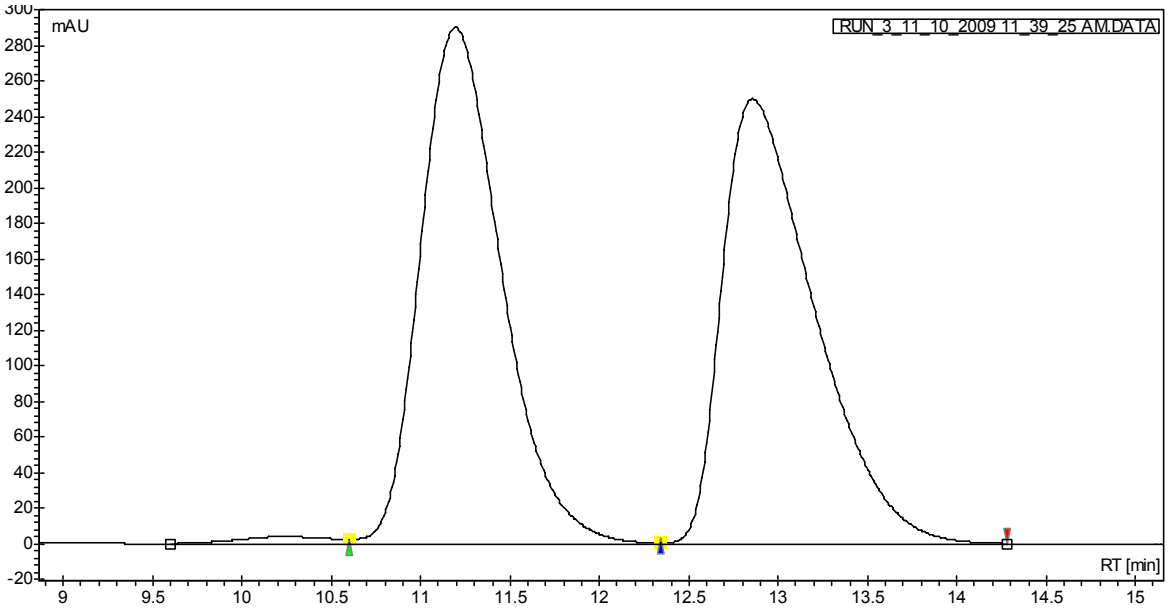
#	Time [min]	Area [%]
1	48.19	49.74
2	52.77	50.26



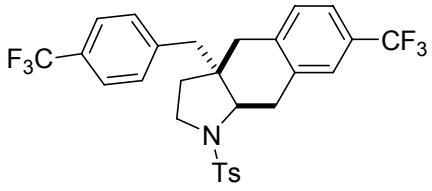
7b



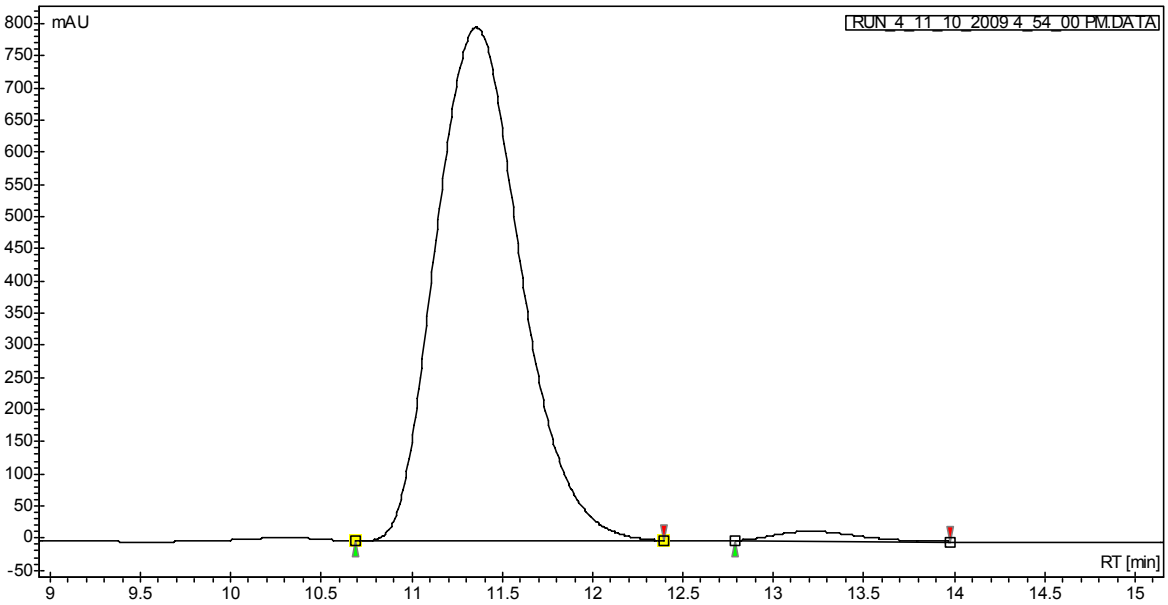
#	Time [min]	Area [%]
1	48.83	0.10
2	54.72	99.90



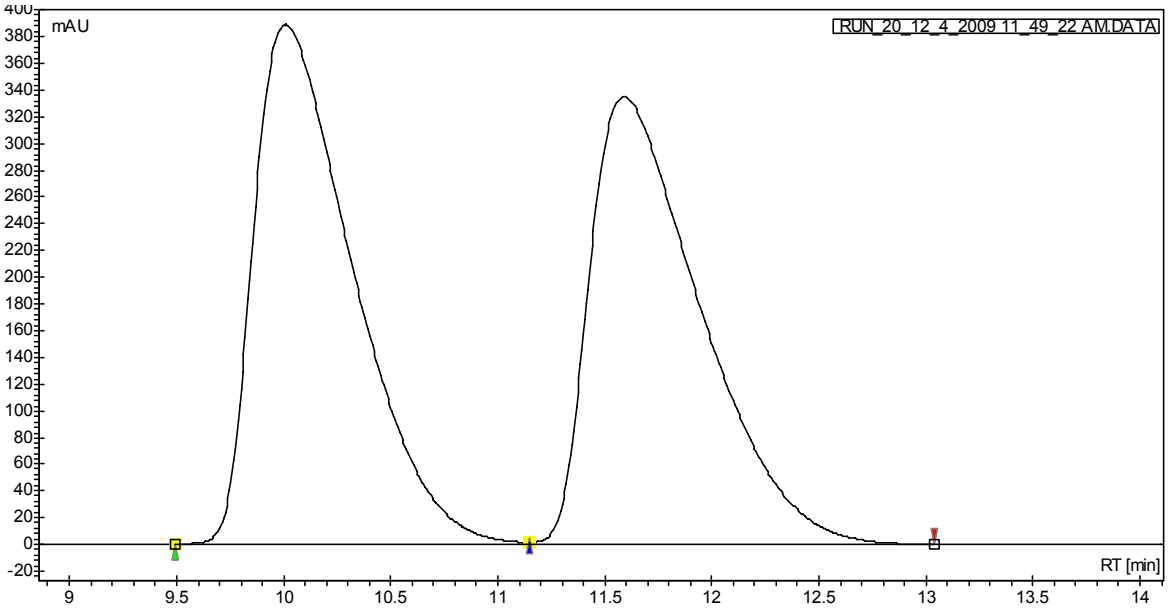
#	Time [min]	Area [%]
1	11.19	50.51
2	12.86	49.49



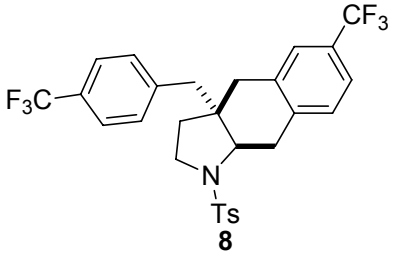
2k



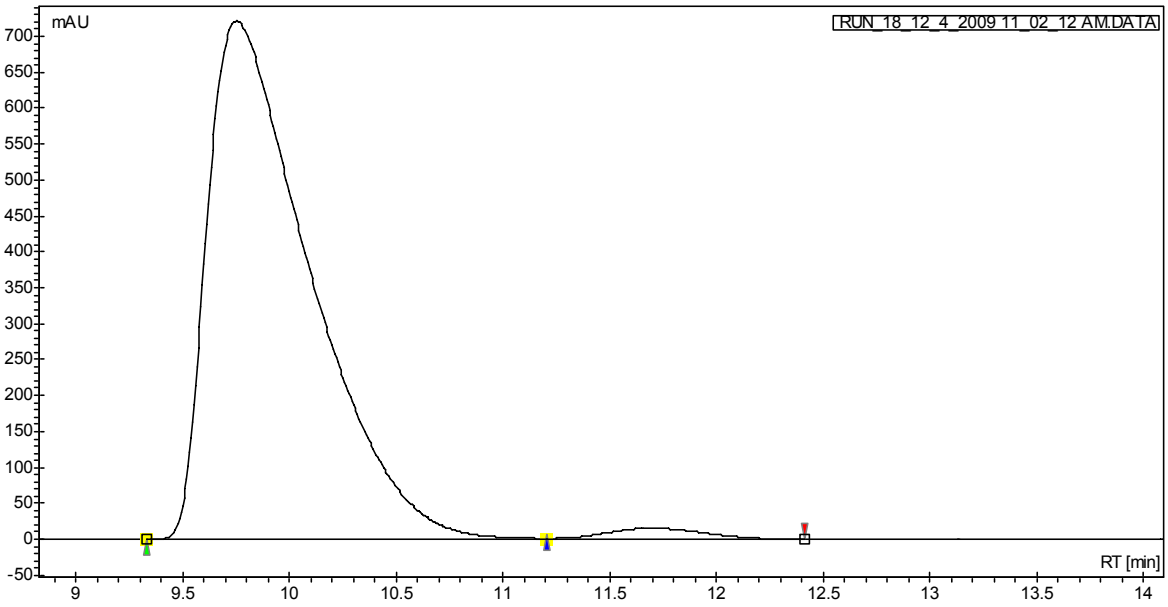
#	Time [min]	Area [%]
1	11.36	98.22
2	13.21	1.78



#	Time [min]	Area [%]
1	10.01	50.92
2	11.59	49.08



8



#	Time [min]	Area [%]
1	9.75	97.93
2	11.69	2.07

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