Chiral Indoline Synthesis Via Enantioselective Copper-Catalyzed Alkene Hydroamination/Cyclization

Benjamin W. Turnpenny,‡ Kiante L. Hyman‡ and Sherry R. Chemler*

Department of Chemistry, University at Buffalo,
The State University of New York, Buffalo, NY 14260, schemler@buffalo.edu

Supporting Information I

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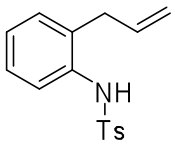
General Experimental Information: All reagents were used out of the bottle as purchased from the supplier without further purification unless otherwise noted. MnO_2 for the hydroamination experiments was purchased as activated, ca. 85%, <5 μm. Solvents for reactions were dried under Argon using a commercial solvent filtration system. ^{1}H NMR spectra were recorded in $CDCl_3$ (using 7.26 ppm for reference of residual $CHCl_3$) at 300, 400 or 500 MHz. ^{13}C NMR spectra were recorded in $CDCl_3$ (using 77.0 ppm as internal reference) at 75.5 or 125.7 MHz. 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 JASCO P-2000 Polarimeter fitted with a micro cell with a 100 mm path length. Melting points are reported as uncorrected.

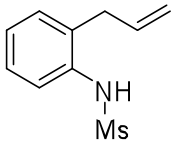
Substrates **1** were prepared from the corresponding anilines as previously reported.[1-3] Substrates **1a, 1b, 1e,** and **1k** are known compounds.



1a

N-(2-Allyl-phenyl)-4-methyl-benzenesulfonamide (1a)[4]

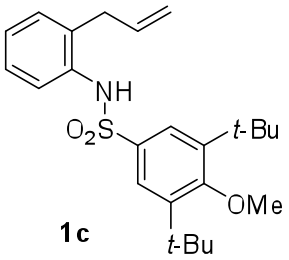
The known sulfonamide **1a** was obtained from sulfonylation of 2-allylaniline with tosyl chloride in 62% yield (1.33 g). The ^{1}H NMR spectrum matched the reported values.[4] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J=8.0 Hz, 2H), 7.41 (d, J=8.0 Hz, 1H), 7.26-7.18 (m, 3H), 7.14-7.06 (m, 2H), 6.53 (s, 1H), 5.83-5.73 (m, 1H), 5.11 (dd, J=8.4, 1.6 Hz, 1H), 4.93 (dd, J=15.6, 1.6 Hz, 1H), 3.01 (d, J=6.0 Hz, 2H), 2.40 (s, 3H).



1b

***N*-(2-Allyl-phenyl)-4-methyl-sulfonamide (1b)[4]**

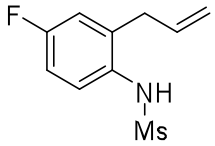
The known sulfonamide **1b** was obtained from sulfonylation of 2-allylaniline with methanesulfonyl chloride in 82% yield (3.46 g). The ^{1}H NMR spectrum matched the reported values.[4] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, J=8.0 Hz, 1H), 7.30-7.16 (m, 3H), 6.40 (s, 1H), 5.99-5.92 (m, 1H), 5.20 (dd, J=9.5, 1.0 Hz, 1H), 5.08 (dd, J=16.0, 1.0 Hz, 1H), 3.44 (d, J = 6.5 Hz, 2H), 3.01 (s, 3H).



1c

***N*-(2-Allylphenyl)-3,5-di-*tert*-butyl-4-methoxybenzenesulfonamide (1c)**

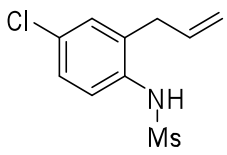
The sulfonamide **1c** was obtained from sulfonylation of 2-allylaniline with 3,5-bis(1,1-dimethylethyl)-4-methoxy-benzenesulfonyl chloride, which was synthesized as reported by Toru and coworkers.[5] 2-Allylaniline (0.847 g, 6.4 mmol) was dissolved in 40 mL of dry methylene chloride and cooled to 0 °C in an ice water bath. The solution was treated with pyridine (2.3 mL, 19.1 mmol, 3 equiv), 3,5-bis(1,1-dimethylethyl)-4-methoxy-benzenesulfonyl chloride (2.43 g, 7.6 mmol, 1.2 equiv), and 4-dimethylaminopyridine (78 mg, 0.64 mmol, (0.1 equiv). The mixture stirred overnight, warming up to rt. The mixture was diluted with 40 mL of water and extracted with CH_2Cl_2 (3 x 40 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography of the resulting crude product on SiO_2 (5-20% ether in hexanes gradient) afforded sulfonamide **1c** as a white solid in 67% yield (1.77 g). mp 173-175 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J=7.6 Hz, 1H), 7.49 (s, 2H), 7.28-7.23 (m, 1H), 7.13 (t, J=16.4 Hz, 1H), 7.04 (d, J=8 Hz, 1H), 6.40 (s, 1H), 5.70-5.64 (m, 1H), 5.08 (dd, J=8.4, 1.6 Hz, 1H), 4.90 (dd, J=15.6, 1.6 Hz, 1H), 3.66 (s, 3H), 2.80 (d, J=6 Hz, 2H), 1.31 (s, 18H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 163.5, 145.1, 135.5, 135.3, 133.0, 132.4, 130.3, 127.8, 126.5, 125.7, 125.5, 117.1, 64.7, 36.1, 35.9, 31.6; IR (neat, thin film) υ 3264, 2957, 1641, 1456, 1406, 1392, 1365, 1337, 1275, 1229, 1166, 1118, 1008, 910 cm^{-1}; HRMS (ESI) calcd for $[M]^+$ $C_{24}H_{33}O_3N_1S_1$: 415.2181, found 415.2183.



1d

***N*-(2-Allyl-4-fluorophenyl)methanesulfonamide (1d)**

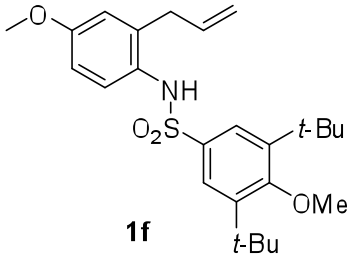
Sulfonamide **1d** was obtained as a white solid from sulfonylation of 2-allyl-4-fluoroaniline with methane sulfonyl chloride in 58% yield (220 mg). mp 81-83 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.44 (m, 1H), 7.01-6.96 (m, 2H), 6.23 (s, 1H), 5.97-5.88 (m, 1H), 5.22 (dd, J=8.4, 1.6 Hz, 1H), 5.08 (dd, J=15.6, 1.6 Hz, 1H), 3.44 (d, J=4.4 Hz, 2H), 3.00 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 161.0 (d, J_{CF}=246.2 Hz), 136.3 (d, J_{CF}=8.1 Hz), 134.9, 130.4 (d, J_{CF}=3.5 Hz), 126.7 (d, J_{CF}=8.1 Hz), 117.5, 117.3 (d, J_{CF}=23.0 Hz), 114.4 (d, J_{CF}=21.9 Hz), 39.8, 35.9; IR (neat, thin film) υ 3271, 2932, 1591, 1496, 1391, 1326, 1213, 1153, 966 cm^{-1}; HRMS (ESI) calcd for $[M]^+$ $C_{10}H_{12}O_2N_1F_1S_1$: 229.0573, found 229.0579.



1e

***N*-(2-Allyl-4-chlorophenyl)methanesulfonamide (1e)[6]**

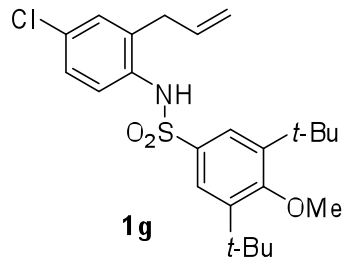
The known sulfonamide **1e** was obtained from sulfonylation of 2-allyl-4-chloroaniline with methanesulfonyl chloride in 64% yield (235 mg). The ^{1}H NMR spectrum matched the reported.[6] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (d, J=8.1 Hz, 1H), 7.27-7.22 (m, 2H), 6.35 (s, 1H), 5.97-5.88 (m, 1H), 5.23 (dd, J=8.7, 1.8 Hz, 1H), 5.09 (dd, J=16.0, 1.8 Hz, 1H), 3.40 (d, J=6.0 Hz, 2H), 3.00 (s, 3H).



1f

***N*-(2-Allyl-4-methoxyphenyl)-3,5-di-*tert*-butyl-4-methoxybenzenesulfonamide (1f)**

Sulfonamide **1f** was obtained as a white solid from sulfonylation of 2-allyl-4-methoxyaniline in 48% yield (397 mg) using the same procedure as described for **1c**. mp 144-146 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (s, 2H), 7.33 (d, J=9.0 Hz, 1H), 6.76 (d, J=9.0 Hz, 1H), 6.58 (s, 1H), 6.20 (s, 1H), 5.66-5.60 (m, 1H), 5.05 (dd, J=7.0, 1.5 Hz, 1H), 4.89 (dd, J=15.5, 1.5 Hz, 1H), 3.76 (s, 3H), 3.67 (s, 3H), 2.72 (d, J=6.5 Hz, 2H), 1.32 (s, 18H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 163.5, 158.5, 157.1, 145.1, 135.9, 135.4, 133.0, 128.7, 127.7, 125.7, 117.0, 115.6, 112.5, 64.7, 55.5, 36.1, 36.0, 31.7; IR (neat, thin film) υ 3235, 2964, 2360, 1614, 1579, 1495, 1403, 1331, 1290, 1256, 1227, 1167, 1128, 1043, 1004, 915 cm^{-1}; HRMS (ESI) calcd for $[M+H]^+$ $C_{25}H_{36}O_4N_1S_1$: 446.2360, found 446.2373.

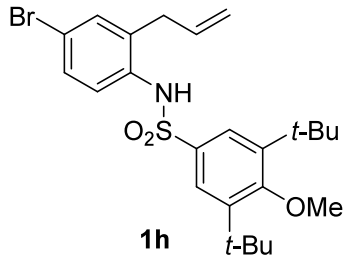


1g

***N*-(2-Allyl-4-chlorophenyl)-3,5-di-*tert*-butyl-4-methoxybenzenesulfonamide (1g)**

Sulfonamide **1g** (322 mg, 60% yield) was obtained from sulfonylation of 2-allyl-4-chloroaniline using the same procedure as described for **1c**. mp 148-150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ

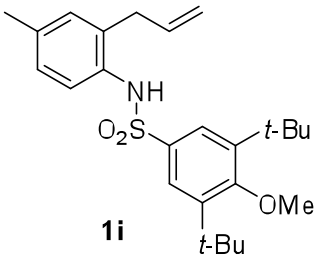
7.49 (s, 2H), 7.44 (d, J=8.8 Hz, 1H), 7.22 (d, J=8.8 Hz, 1H), 7.04 (s, 1H), 6.36 (s, 1H), 5.65-5.60 (m, 1H), 5.11 (dd, J=8.4, 1.2 Hz, 1H), 4.91 (dd, J=16.0, 1.2 Hz, 1H), 3.67 (s, 3H), 2.79 (d, J=5.6 Hz, 2H), 1.33 (s, 18H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 163.7, 145.3, 134.6, 134.5, 133.8, 132.8, 132.0, 130.0, 127.7, 127.0, 125.5, 117.8, 64.7, 36.1, 35.6, 31.6; IR (neat, thin film) υ 3259, 2963, 1700, 1650, 1481, 1392, 1333, 1256, 1227, 1167, 1115, 1005, 886 cm^{-1}; HRMS (ESI) calcd for $[M]^+$ $C_{24}H_{32}O_3N_1Cl_1S_1$: 449.1791, found 449.1788.



1h

***N*-(2-Allyl-4-bromophenyl)-3,5-di-*tert*-butyl-4-methoxybenzenesulfonamide (1h)**

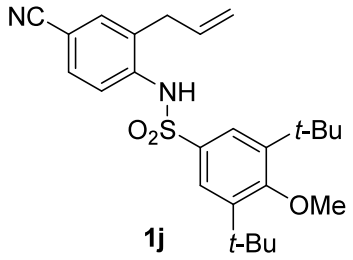
The sulfonamide **1h** (280 mg, 47% yield) was obtained using the same procedure as described for **1c**. mp 152-154°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 2H), 7.38-7.37 (m, 2H), 7.19 (s, 1H), 6.34 (s, 1H), 5.67-5.60 (m, 1H), 5.12 (dd, J=7.2, 1.6 Hz, 1H), 4.92 (dd, J=14.0, 1.6 Hz, 1H), 3.67 (s, 3H), 2.79 (d, J=6.0 Hz, 2H), 1.33 (s, 18H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 163.7, 145.3, 134.6, 134.5, 134.4, 133.0, 132.7, 130.7, 127.1, 125.5, 119.8, 117.8, 64.7, 36.1, 35.6, 31.6; IR (neat, thin film) υ 3264, 2962, 1481, 1392, 1329, 1256, 1227, 1166, 1116, 1005, 913 cm^{-1}; HRMS (ESI) calcd for $[M+H]^+$ $C_{24}H_{33}O_3N_1Br_1S_1$: 494.1359, found 494.1350.



1i

***N*-(2-Allyl-4-methylphenyl)-3,5-di-*tert*-butyl-4-methoxybenzenesulfonamide (1i)**

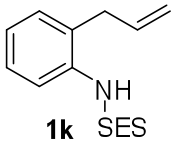
The sulfonamide **1i** (248 mg, 34% yield) was obtained using the same procedure as described for **1c**. mp 161-163°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (s, 2H), 7.36 (d, J=8.0 Hz, 1H), 7.05 (d, J=8.0 Hz, 1H), 6.84 (s, 1H), 6.29 (s, 1H), 5.70-5.60 (m, 1H), 5.06 (dd, J=8.8, 1.6 Hz, 1H), 4.89 (dd, J=15.6, 1.6 Hz, 1H), 3.66 (s, 3H), 2.73 (d, J=6.0 Hz, 2H), 2.27 (s, 3H), 1.31 (s, 18H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 163.5, 145.0, 136.6, 135.6, 133.0, 132.8, 132.5, 130.8, 128.3, 126.2, 125.6, 116.9, 64.7, 36.1, 35.9, 31.6, 20.8; IR (neat, thin film) υ 3252, 2958, 1394, 1335, 1228, 1166, 1116, 1006, 908 cm^{-1}; HRMS (ESI) calcd for $[M]^+$ $C_{25}H_{35}O_3N_1S_1$: 429.2332, found 429.2342.



1j

***N*-(2-Allyl-4-cyanophenyl)-3,5-di-*tert*-butyl-4-methoxybenzenesulfonamide (1j)**

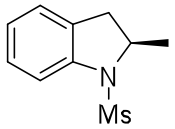
Sulfonamide **1j** (96 mg, 56% yield) was obtained from sulfonylation of 3-allyl-4-aminobenzonitrile using the same procedure as described for **1c**. mp 158-160°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J=8.0 Hz, 1H), 7.57 (s, 2H), 7.54 (d, J=10.8 Hz, 1H), 7.36 (s, 1H), 6.72 (s, 1H), 5.71-5.67 (m, 1H), 5.18 (dd, J=8.7, 1.2 Hz, 1H), 4.95 (dd, J=16.0, 1.2 Hz, 1H), 3.67 (s, 3H), 3.02 (d, J=5.6 Hz, 2H), 1.34 (s, 18H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 164.0, 145.6, 139.9, 134.1, 133.7, 132.5, 131.7, 131.0, 125.5, 122.7, 118.5, 118.3, 108.76, 64.7, 53.4, 36.1, 35.6, 31.6, 22.6, 14.1; IR (neat, thin film) υ 3279, 2965, 2230, 1607, 1575, 1494, 1396, 1339, 1254, 1228, 1168, 1117, 1003, 912 cm^{-1}; HRMS (ESI) calcd for $[M]^+$ $C_{25}H_{32}O_3N_2S_1$: 440.2128, found 440.2130.



1k

***N*-(2-Allylphenyl)-2-(trimethylsilyl)ethanesulfonamide (1k)[2]**

The known sulfonamide **1k** was obtained from sulfonylation of 2-allylaniline with 2-(trimethylsilyl)ethanesulfonyl chloride in 80% yield (1.05 g). The 1H NMR spectra matched the reported values.[2] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J=8.0 Hz, 1H), 7.28-7.13 (m, 3H), 6.32 (s, 1H), 6.00-5.92 (m, 1H), 5.19 (dd, J=8.4, 1.6 Hz, 1H), 5.08 (dd, J = 16.6, 1.6 Hz, 1H), 3.44 (d, J = 7.6 Hz, 2H), 3.07-3.03 (m, 2H), 1.07-1.03 (m, 2H), 0.0 (s, 9H).



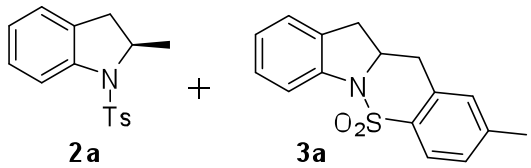
2b

Representative Procedure for the Catalytic Enantioselective Hydroamination

(*R*)-2-Methyl-1-(methylsulfonyl)indoline (2b)[7]

$Cu(OTf)_2$ (12.8 mg, 0.036 mmol, 15 mol%), in a nitrogen filled glove box, was placed in a glass pressure tube equipped with a magnetic stir bar. A solution of (*R,R*)-Ph-box (15.0 mg, 0.045 mmol, 19 mol%) in dry $PhCH_3$ (2.4 mL, 0.1 M) was added via syringe through a septum. The

tube was capped and the reaction mixture was placed in a 60 °C oil bath and stirred. After 2 h, the catalyst solution was cooled to 23 °C. The sulfonamide substrate **2b** (50 mg, 0.237 mmol, 1 equiv) was added to the glass pressure tube, under an argon atmosphere, and the resulting solution was treated with 2,6-di-*tert*-butyl-4-methylpyridine (48.7 mg, 0.237 mmol, 1 equiv), MnO_2 (61.8 mg, 0.711 mmol, 3 equiv), and 1,4-cyclohexadiene (0.068 mL, 57.0 mg, 0.711 mmol, 3 equiv). Flame-dried 4 Å mol. sieves (20 mg/mL) were stirred at rt for 20 min before being added to the reaction mixture. The tube was capped and the reaction mixture was placed in a 100 °C oil bath and stirred. After 8 h, the reaction mixture was cooled to 23 °C, diluted with EtOAc (10 mL), sonicated, filtered through Celite with EtOAc (140 mL), and concentrated *in vacuo*. Flash chromatography on SiO_2 (10-25% EtOAc/hexanes gradient) provided purified hydroamination adduct **2b** (36.5 mg, 73%). The product was further purified by HPLC and subsequently analyzed via chiral HPLC column [Regis (*S,S*)-Whelk, 5% IPA/hexanes, 1 mL/min, λ=254 nm, t(major) = 16.63 min, t(minor) = 14.93 min] revealing 77% enantiomeric excess. $[\alpha]_D^{19}$ = -14.9 (*c* 0.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J=8.8 Hz, 1H), 7.22-7.18 (m, 2H), 7.05 (t, J=16.0 Hz, 1H), 4.47-4.42 (m, 1H), 3.49-3.42 (m, 1H), 2.84 (s, 3H), 2.70 (dd, J=12.4, 4.0 Hz, 1H), 1.45 (d, J=6.8 Hz, 3H). This ^{1}H NMR matched the reported values.[7]



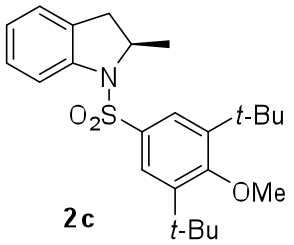
2a **3a**

(*R*)-2-Methyl-1-tosylindoline (2a)[7]

Hydroamination adduct **2a** (11.0 mg, 39%) was obtained using the general catalytic enantioselective hydroamination procedure, except 20 mol% of $Cu(OTf)_2$ and 25 mol% of (*R,R*)-Ph-box was used and the reaction was run at 110 °C. The hydroamination to carboamination ratio was determined to be 43:57 based on the integrations of the hydrogen peak at 4.34 ppm at the 2-position of the hydroamination product and the hydrogen peak at 4.90 ppm at the 11a-position of the carboamination product in the crude ^{1}H NMR spectrum. (The spectral data of carboamination product 3a has previously been reported by our group[8]). Hydroamination adduct **2a** was purified by flash chromatography on SiO_2 (10-25% EtOAc/hexanes gradient). The product was further purified by HPLC and subsequently analyzed via chiral HPLC column [Regis (*S,S*)-Whelk, 5% IPA/hexanes, 1 mL/min, λ=254 nm, t(major) = 12.80 min, t(minor) = 15.43 min] revealing 90% enantiomeric excess. $[\alpha]_D^{23}$ = +161.7 (*c* 0.22, $CHCl_3$, 90% ee). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, J=8.0 Hz, 1H), 7.55 (d, J=8.5 Hz, 2H), 7.21 (t, J=12.0 Hz, 1H), 7.16 (d, J=8.5 Hz, 2H), 7.05-6.99 (m, 2H), 4.36-4.32 (m, 1H), 2.92-2.87 (m, 1H), 2.43 (dd, J=12.5, 3.0 Hz, 1H), 2.35 (s, 3H), 1.43 (d, J=6.5 Hz, 3H).

11a,12-dihydro-2-methyl-5,5-dioxide-11*H*-Indolo[1,2-*b*][1,2]benzothiazine (3a)[8]

Carboamination adduct **3a** (13.0 mg, 46%) was obtained from the same reaction as **2a** as a colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) 7.74 (d, J=8.0 Hz, 1 H), 7.55 (d, J=8.0 Hz, 1 H), 7.18-6.96 (m, 5 H), 4.94-4.89 (m, 1 H), 3.49 (dd, J=10.5, 5.5 Hz, 1 H), 3.34 (dd, J=9.0, 7.0 Hz, 1 H), 3.07 (dd, J=9.5, 6.6 Hz, 1 H), 2.93 (dd, J=8.0, 7.5 Hz, 1 H), 2.37 (s, 3 H).

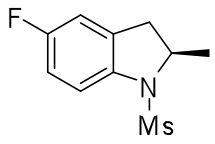


2c

(*R*)-1-(3,5-Di-*tert*-butyl-4-methoxyphenylsulfonyl)-2-methylindoline (2c)

Hydroamination adduct **2c** (35.9 mg, 72%) was obtained using the same procedure as for **2b** except 20 mol% of $Cu(OTf)_2$, 25 mol% of (*R,R*)-Ph-box, and 5 equiv of 1,4-cyclohexadiene were used and the reaction was run at 110 °C. Compound **2c** was obtained as a white solid. The hydroamination to carboamination ratio was determined to be 94:6 based on the relative integrations of the hydrogen peak at 4.27 ppm at the 2-position of the hydroamination product to the hydrogen peak at 4.87 ppm at the 11a-position of the carboamination product in the crude ^{1}H NMR. Data for **2c**: mp 147-150 °C; $[\alpha]_D^{18}$ = +117.8 (*c* 0.54, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J=8.4 Hz, 1H), 7.47 (s, 2H), 7.22 (t, J=11.6 Hz, 1H), 7.04-7.02 (m, 2H), 4.30-4.25 (m, 1H), 3.62 (s, 3H), 2.73-2.66 (m, 1H), 2.38 (dd, J=14.0, 1.6 Hz, 1H), 1.40 (d, J=6.4 Hz, 3H), 1.27 (s, 18H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 163.4, 157.1, 144.9, 141.5, 132.2, 131.8, 127.7, 125.4, 125.1, 124.8, 118.0, 64.6, 58.5, 36.1, 36.0, 31.6, 23.3; IR (neat, thin film) υ 2963, 1603, 1478, 1461, 1406, 1356, 1254, 1226, 1170, 1128, 1004, 883 cm^{-1}; HRMS (ESI) calcd for $[M]^+$ $C_{24}H_{34}O_3N_1S_1$: 416.2254, found 416.2244.

Hydroamination adduct **2c** was purified by flash chromatography on SiO_2 (2-20% EtOAc/hexanes gradient). The product was further purified by HPLC and subsequently analyzed via chiral HPLC column [Regis (*S,S*)-Whelk, 1% IPA/hexanes, 1 mL/min, λ=254 nm, t(major) = 12.59 min, t(minor) = 11.75 min] revealing 86% enantiomeric excess.



2d

(*R*)-5-Fluoro-2-methyl-1-(methylsulfonyl)indoline (2d)

Hydroamination adduct **2d** (34.5 mg, 69%) was obtained using the same procedure as for **2b**. Compound **2d** was obtained as a colorless oil. $[\alpha]_D^{22}$ = +12.3 (*c* 0.06, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.35 (m, 1H), 6.92-6.87 (m, 1H), 4.48-4.43 (m, 1H), 3.48-3.40 (m, 1H), 2.82 (s, 3H), 2.68 (dd, J=12.8, 2.7 Hz, 1H), 1.45 (d, J=6.4 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 116.5 (d, J_{CF}=8.1 Hz), 114.6 (d, J_{CF}=23.0 Hz), 112.7 (d, J_{CF}=24.2 Hz), 59.3, 36.5, 36.0, 23.4; IR (neat, thin film) υ 2932, 1706, 1605, 1507, 1484, 1462, 1418, 1380, 1345, 1215, 1162, 1096, 1066, 962 cm^{-1}; HRMS (ESI) calcd for $[M]^+$ $C_{10}H_{12}O_2N_1F_1S_1$: 229.0573, found 229.0563.

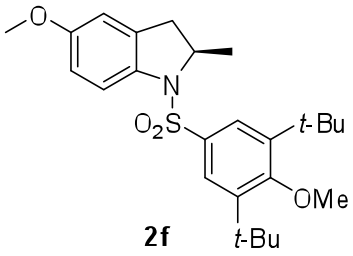
Hydroamination adduct **2d** was purified by flash chromatography on SiO_2 (10-25% EtOAc/hexanes gradient). The product was further purified by HPLC and subsequently analyzed via chiral HPLC column [Regis (*S,S*)-Whelk, 5% IPA/hexanes, 1 mL/min, λ=254 nm, t(major) = 18.56 min, t(minor) = 16.98 min] revealing 76% enantiomeric excess.

2e

(*R*)-5-Chloro-2-methyl-1-(methylsulfonyl)indoline (2e)

Hydroamination adduct **2e** (33 mg, 66%) was obtained using the same procedure as for **2b**. Compound **2e** was obtained as a colorless oil. $[\alpha]_D^{21}$ = -12.9 (*c* 0.13, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, J=5.0 Hz, 1H), 7.18-7.16 (m, 1H), 4.47-4.45 (m, 1H), 3.46-3.41 (m, 1H), 2.84 (s, 1H), 2.68 (dd, J=13.0, 3.0 Hz, 1H), 1.45 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 128.0, 125.7, 116.2, 59.2, 36.4, 36.3, 23.3; IR (neat, thin film) υ 2926, 1474, 1347, 1247, 1160, 1013, 961 cm^{-1}; HRMS (ESI) calcd for $[M]^+$ $C_{10}H_{12}O_2N_1Cl_1Na_1S_1$: 268.0169, found 268.0174.

Hydroamination adduct **2e** was purified by flash chromatography on SiO_2 (2-20% EtOAc/hexanes gradient). The product was further purified by HPLC and subsequently analyzed via chiral HPLC column [Regis (*S,S*)-Whelk, 5% IPA/hexanes, 1 mL/min, λ=254 nm, t(major) = 18.29 min, t(minor) = 16.14 min] revealing 73% enantiomeric excess.

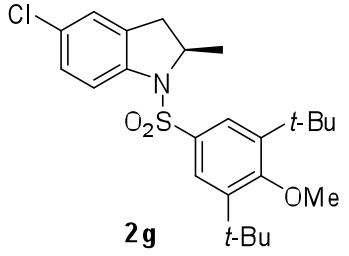


2f

(*R*)-1-(3,5-Di-*tert*-butyl-4-methoxyphenylsulfonyl)-5-methoxy-2-methylindoline (2f)

Hydroamination adduct **2f** (36.1 mg, 72%) was obtained using the same procedure as for **2b** except 20 mol% of $Cu(OTf)_2$, 25 mol% of (*R,R*)-Ph-box, and 5 equiv of 1,4-cyclohexadiene were used and the reaction was run at 110 °C for 24 h. Compound **2f** was obtained as a colorless oil. The hydroamination to carboamination ratio was determined to be 73:27 based on integration of the hydrogen peak at 4.25 ppm at the 2-position of the hydroamination product and the hydrogen peak at 4.88 ppm at the 11a-position of the carboamination product in the crude ^{1}H NMR.Data for **2f**: $[\alpha]_D^{23}$ = +145.8 (*c* 0.49, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J=8.4 Hz, 1H), 7.42 (s, 2H), 6.78 (d, J=8.8 Hz, 1H), 6.58 (s, 1H), 4.27-4.23 (m, 1H), 3.74 (s, 3H), 3.63 (s, 3H), 2.54-2.48 (m, 1H), 2.27 (dd, J=13.6, 1.6 Hz, 1H), 1.36 (d, J=6.8 Hz, 3H), 1.27 (s, 18H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 163.4, 157.7, 144.8, 134.7, 134.4, 131.3, 125.6, 119.4, 112.9, 110.9, 64.6, 58.8, 55.7, 36.2, 36.0, 31.6, 23.0; IR (neat, thin film) υ 2963, 1607, 1486, 1405, 1350, 1260, 1227, 1201, 1169, 1128, 1033, 1003, 886 cm^{-1}; HRMS (ESI) calcd for $[M]^+$ $C_{25}H_{35}O_4N_1S_1$: 445.2281, found 445.2282.

Hydroamination adduct **2f** was purified by flash chromatography on SiO_2 (10-25% EtOAc/hexanes gradient). The product was further purified by HPLC and subsequently analyzed via chiral HPLC column [Regis (*S,S*)-Whelk, 1% IPA/hexanes, 0.7 mL/min, λ=254 nm, t(major) = 31.10 min, t(minor) = 28.81 min] revealing 84% enantiomeric excess.



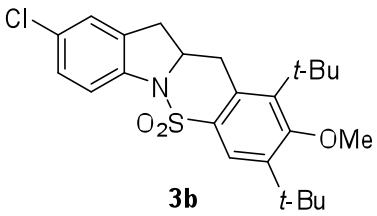
2g

(*R*)-5-Chloro-1-(3,5-di-*tert*-butyl-4-methoxyphenylsulfonyl)-2-methylindoline (2g)

Hydroamination adduct **2g** (33.8 mg, 68%) was obtained using the same procedure as for **2b** except 20 mol% of $Cu(OTf)_2$, 25 mol% of (*R,R*)-Ph-box, and the reaction was run at 110 °C for 24 h. Compound **2g** was obtained as a white solid. The hydroamination to carboamination ratio was determined to be 74:26 based on the integrations of the hydrogen peak at 4.29 ppm at the 2-position of the hydroamination product and the hydrogen peak at 4.90 ppm at the 11a-position of

the carboamination product in the crude ^{1}H NMR. Data for **2g**: mp 129-132 °C; $[\alpha]_D^{18}$ = +201.7 (*c* 0.05, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J=8.8 Hz, 1H), 7.46 (s, 2H), 7.20 (d, J=6.0 Hz, 1H), 7.02 (s, 1H), 4.32-4.27 (m, 1H), 3.64 (s, 3H), 2.70-2.64 (m, 1H), 2.37 (dd, J=13.6, 2.4 Hz, 1H), 1.4 (d, J=6.4 Hz, 3H), 1.29 (s, 18H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 163.6, 145.1, 140.2, 134.2, 131.5, 130.1, 127.7, 125.4, 125.2, 118.9, 64.6, 58.8, 36.0, 35.9, 31.6, 23.2; IR (neat, thin film) υ 2962, 1746, 1471, 1406, 1359, 1260, 1170, 1114, 881 cm^{-1}; HRMS (ESI) calcd for $[M]^+$ $C_{24}H_{32}O_3N_1Cl_1S_1$: 449.1786, found 449.1783.

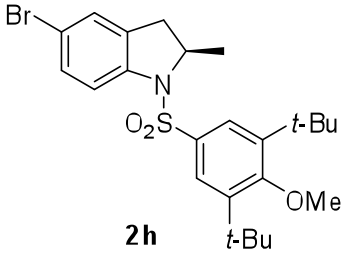
Hydroamination adduct **2g** was purified by flash chromatography on SiO_2 (10-25% EtOAc/hexanes gradient). The product was further purified by HPLC and subsequently analyzed via chiral HPLC column [Regis (*S,S*)-Whelk, 1% IPA/hexanes, 1 mL/min, λ=254 nm, t(major) = 12.91 min, t(minor) = 11.14 min] revealing 89% enantiomeric excess.



3b

1,3-Di-*tert*-butyl-9-chloro-11a,12-dihydro-2-methoxy-5,5-dioxide-11*H*-Indolo[1,2-*b*][1,2]benzothiazine 3b

Carboamination adduct **3b** (10.1 mg, 20%) was obtained as a colorless oil from the same reaction as **2g**. Data for **3b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.39 (d, J=8.0 Hz, 1H), 7.14 (d, J=8.5 Hz, 1H), 7.04 (s, 1H), 4.96-4.82 (m, 1H), 3.96-3.82 (m, 1H), 3.67 (d, J=12.8 Hz, 1H), 3.56 (s, 3H), 3.11-2.99 (m, 1H), 2.92-2.79 (m, 1H), 1.55 (s, 9H), 1.35 (s, 9H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 164.4, 143.3, 133.5, 129.9, 127.8, 124.6, 121.8, 64.9, 62.1, 37.3, 35.8, 32.7, 30.9, 22.7, 14.1; IR (neat, thin film) υ 2963, 1650, 1540, 1472, 1342, 1232, 1163, 1121, 1042, 910 cm^{-1}; HRMS (ESI) calcd for $[M]^+$ $C_{24}H_{30}O_3N_1Cl_1S_1$: 447.1629, found: 447.1630.



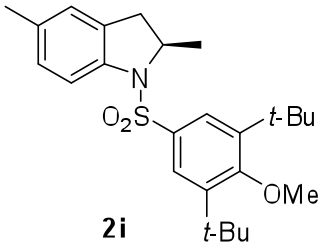
2h

(*R*)-5-Bromo-1-(3,5-di-*tert*-butyl-4-methoxyphenylsulfonyl)-2-methylindoline (2h)

Hydroamination adduct **2h** (31.1 mg, 62%) was obtained using the same procedure as for **2b** except 20 mol% of $Cu(OTf)_2$, 25 mol% of (*R,R*)-Ph-box, and 5 equiv of 1,4-cyclohexadiene were

used and the reaction was run at 110 °C. Compound **2h** was obtained as a white solid. The hydroamination to carboamination ratio was determined to be 74:26 based on the integrations of the hydrogen peak at 4.29 ppm at the 2-position of the hydroamination product and the hydrogen peak at 4.90 ppm at the 11a-position of the carboamination product in the crude ^{1}H NMR. Data for **2h**: mp 133-136 °C; $[\alpha]_D^{22}$ = +74.1 (*c* 0.13, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J=8.4 Hz, 1H), 7.47 (s, 2H), 7.35 (d, J=8.4 Hz, 1H), 7.17 (s, 1H), 4.30-4.27 (m, 1H), 3.64 (s, 3H), 2.72-2.66 (m, 1H), 2.37 (dd, J=14.0, 2.0 Hz, 3H), 1.40 (d, J=6.4 Hz, 3H), 1.29 (s, 18H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 163.6, 145.1, 140.7, 134.6, 131.5, 130.6, 128.2, 125.4, 119.3, 117.6, 110.0, 64.6, 58.8, 36.0, 35.8, 31.6, 23.2; IR (neat, thin film) υ 2962, 1471, 1396, 1355, 1227, 1169, 1114, 816 cm^{-1}; HRMS (ESI) calcd for $[M]^+$ $C_{24}H_{32}O_3N_1Br_1S_1$: 493.1281, found 493.1271.

Hydroamination adduct **2h** was purified by flash chromatography on SiO_2 (10-25% EtOAc/hexanes gradient). The product was further purified by HPLC and subsequently analyzed via chiral HPLC column [Regis (*S,S*)-Whelk, 1% IPA/hexanes, 1 mL/min, λ=254 nm, t(major) = 11.85 min, t(minor) = 10.47 min] revealing 86% enantiomeric excess.



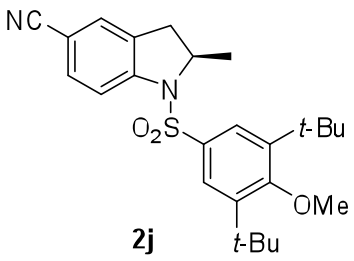
2i

(*R*)-1-(3,5-Di-*tert*-butyl-4-methoxyphenylsulfonyl)-2,5-dimethylindoline (2i)

Hydroamination adduct **2i** (35.1 mg, 70%) was obtained using the same procedure as for **2b** except 20 mol% of $Cu(OTf)_2$, 25 mol% of (*R,R*)-Ph-box, and 5 equiv of 1,4-cyclohexadiene were used and the reaction was run at 110 °C. Compound **2i** was obtained as a white solid. The hydroamination to carboamination ratio was determined to be 93:7 based on the integrations of the hydrogen peak at 4.25 ppm at the 2-position of the hydroamination product and the hydrogen peak at 4.87 ppm at the 11a-position of the carboamination product in the crude ^{1}H NMR. Data for **2i**: mp 122-125 °C; $[\alpha]_D^{21}$ = +142.1 (*c* 0.34, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, J=8.5 Hz, 1H), 7.44 (s, 2H), 7.03 (d, J=8.0 Hz, 1H), 6.84 (s, 1H), 4.27-4.24 (m, 1H), 3.62 (s, 3H), 2.60-2.55 (m, 1H), 2.29 (dd, J=14.5, 2.0 Hz, 3H), 2.26 (s, 3H), 1.37 (d, J=7.0 Hz, 3H), 1.27 (s, 18H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 163.4, 144.8, 139.1, 134.8, 132.7, 131.6, 128.3, 125.6, 125.5, 118.2, 118.1, 64.7, 64.6, 58.6, 36.0, 31.7, 31.6, 31.5, 23.2, 20.9; IR (neat, thin film) υ 2963, 1487, 1405, 1352, 1255, 1227, 1169, 1128, 1005, 886 cm^{-1}; HRMS (ESI) calcd for $[M]^+$ $C_{25}H_{35}O_3N_1S_1$: 429.2332, found 429.2335.

Hydroamination adduct **2i** was purified by flash chromatography on SiO_2 (10-25% EtOAc/hexanes gradient). The product was further purified by HPLC and subsequently analyzed

via chiral HPLC column [Regis (*S,S*)-Whelk, 3% IPA/hexanes, 0.5 mL/min, λ=254 nm, t(major) = 20.92 min, t(minor) = 19.52 min] revealing 88% enantiomeric excess.

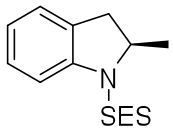


2j

(*R*)-1-(3,5-Di-*tert*-butyl-4-methoxyphenylsulfonyl)-2-methylindoline-5-carbonitrile (2j)

Hydroamination adduct **2j** (28.4 mg, 57%) was obtained using the same procedure as for **2b** except 20 mol% of $Cu(OTf)_2$, 25 mol% of (*R,R*)-Ph-box, and 5 equiv of 1,4-cyclohexadiene were used and the reaction was run at 110 °C. Compound **2j** was obtained as a white solid. The hydroamination to carboamination ratio was determined to be 65:35 based on the integration of the hydrogen peak at 4.37 ppm at the 2-position of the hydroamination product and the hydrogen peak at 4.93 ppm at the 11a-position of the carboamination product in the crude ^{1}H NMR. Data for **2j**: mp 142-145 °C; $[\alpha]_D^{19}$ = +90.2 (*c* 0.28, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, J=8.4 Hz, 1H), 7.54-7.52 (m, 3H), 7.34 (s, 1H), 4.39-4.34 (m, 1H), 3.66 (s, 3H), 2.97-2.91 (m, 1H), 2.54 (dd, J=13.2, 3.2 Hz, 1H), 1.46 (d, J=6.8 Hz, 3H), 1.31 (s, 18H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 163.9, 145.6, 145.4, 132.6, 132.5, 131.8, 128.9, 125.3, 116.9, 107.3, 64.6, 59.0, 36.1, 35.8, 31.6, 23.4; IR (neat, thin film) υ 2965, 2227, 1608, 1483, 1406, 1359, 1259, 1170, 1109, 886 cm^{-1}; HRMS (ESI) calcd for $[M]^+$ $C_{25}H_{32}O_3N_2S_1$: 440.2128, found 440.2133.

Hydroamination adduct **2j** was purified by flash chromatography on SiO_2 (10-25% EtOAc/hexanes gradient). The product was further purified by HPLC, however the enantiomers were not able to be separated on several chiral HPLC columns.



2k

(*R*)-2-Methyl-1-(2-(trimethylsilyl)ethylsulfonyl)indoline (2k)

Hydroamination adduct **2k** (32.2 mg, 64%) was obtained using the same procedure as for **2b** except 20 mol% of $Cu(OTf)_2$, 25 mol% of (*R,R*)-Ph-box, and the reaction was run at 110 °C. Compound **2k** was obtained as a colorless oil. $[\alpha]_D^{22}$ = +21.1 (*c* 0.10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, J=7.6 Hz, 1H), 7.20-7.16 (m, 2H), 7.01 (t, J=14.0 Hz, 1H), 4.55-4.51 (m, 1H), 3.48-3.42 (m, 1H), 2.98-2.91 (m, 2H), 2.69 (dd, J=13.2, 2.8 Hz, 1H), 1.43 (d, J=6.0 Hz, 3H), 1.06-1.02 (m, 1H), 0.96-0.92 (m, 1H), -0.03 (s, 9H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 141.2,

130.2, 127.9, 125.5, 123.5, 114.6, 59.0, 46.8, 36.5, 23.6, 9.9, -2.1; IR (neat, thin film) υ 2955, 1603, 1479, 1460, 1346, 1251, 1149, 1104, 1022, 938 cm^{-1}; HRMS (ESI) calcd for $[M + Na]^+$ $C_{14}H_{23}O_2N_1Na_1S_1Si_1$: 320.1111, found: 320.1102.

Hydroamination adduct **2k** was purified by flash chromatography on SiO_2 (10-25% EtOAc/hexanes gradient). The product was further purified by HPLC and subsequently analyzed via chiral HPLC column [Regis (*S,S*)-Whelk, 3% IPA/hexanes, 1 mL/min, λ=254 nm, t(major) = 11.07 min, t(minor) = 10.36 min] revealing 72% enantiomeric excess.

(R)-2-Methylindoline (4)

(*R*)-*N*-Mesyl-2-methylindoline **2b** (0.0335 g, 0.159 mmol, 77% ee) in xylenes (0.8 mL) was treated with a solution of Red-Al in toluene (0.16 mL of a 3.5 M solution, 3.6 equiv) under Ar.[9] The resulting solution was equipped with a condensor and heated at reflux under Ar (ca. 140 °C) for 1 h. The reaction was then cooled to 0 °C, diluted with Et_2O and quenched with a few drops of H_2O. The mixture was filtered through Celite with Et_2O and the filtrate was concentrated in vacuo. Purification by flash chromatography on SiO_2 (2-20% EtOAc in hexanes gradient) afforded 14.4 mg (68%) of (*R*)-2-methylindoline (**4**), whose ^1H NMR spectrum was identical to that of the commercially available racemate. $[\alpha]_D^{18}$ = +10 (*c* 0.08, PhH); lit. for (*S*)-2-methylindoline: $[\alpha]_D^{23}$ = -11 (*c* 0.11, PhH).[10]

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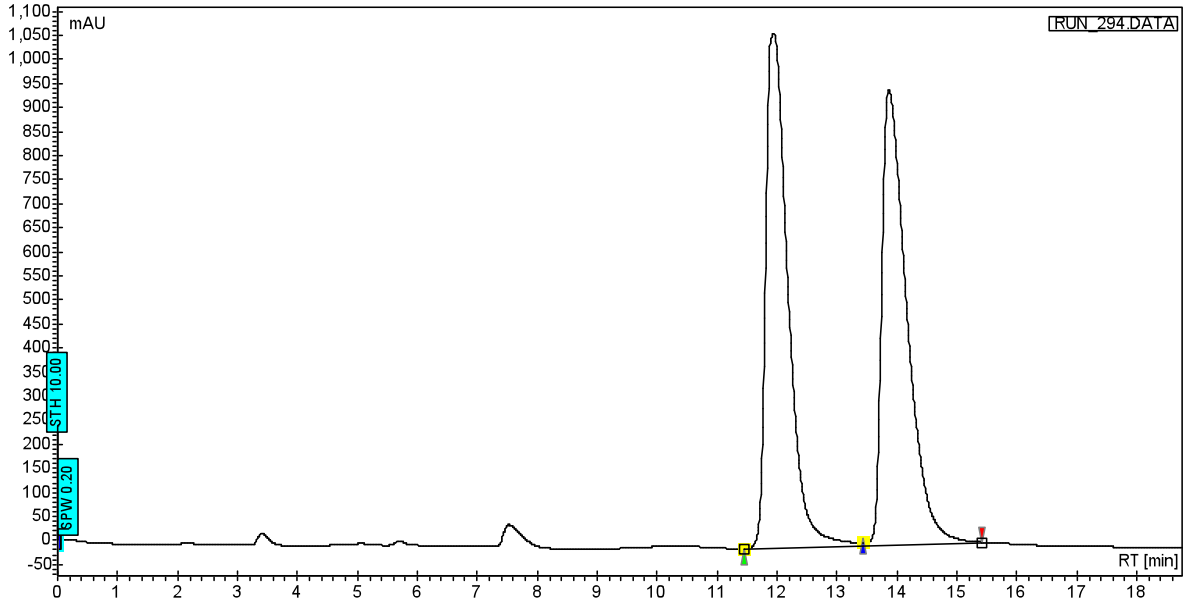
HPLC Traces:



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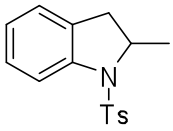

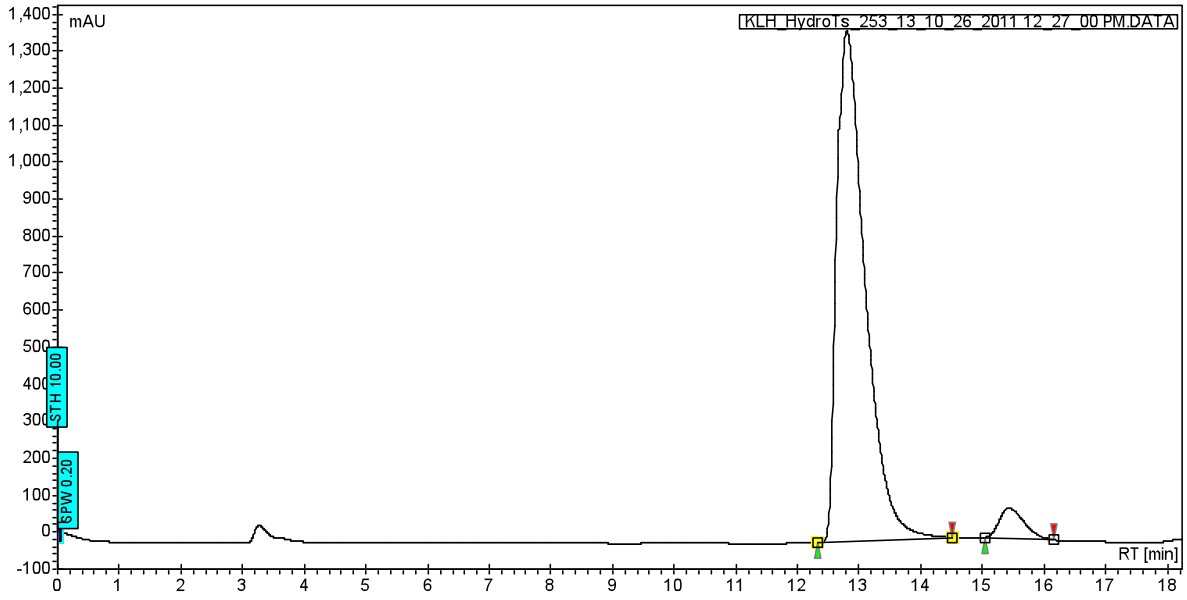

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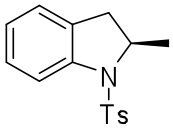
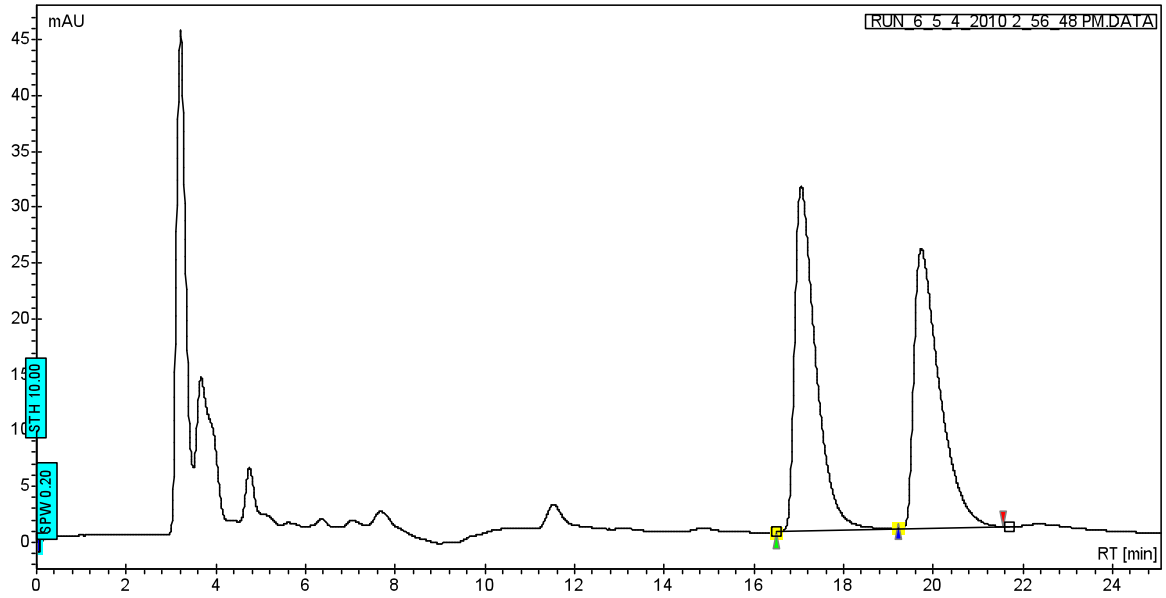
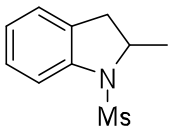
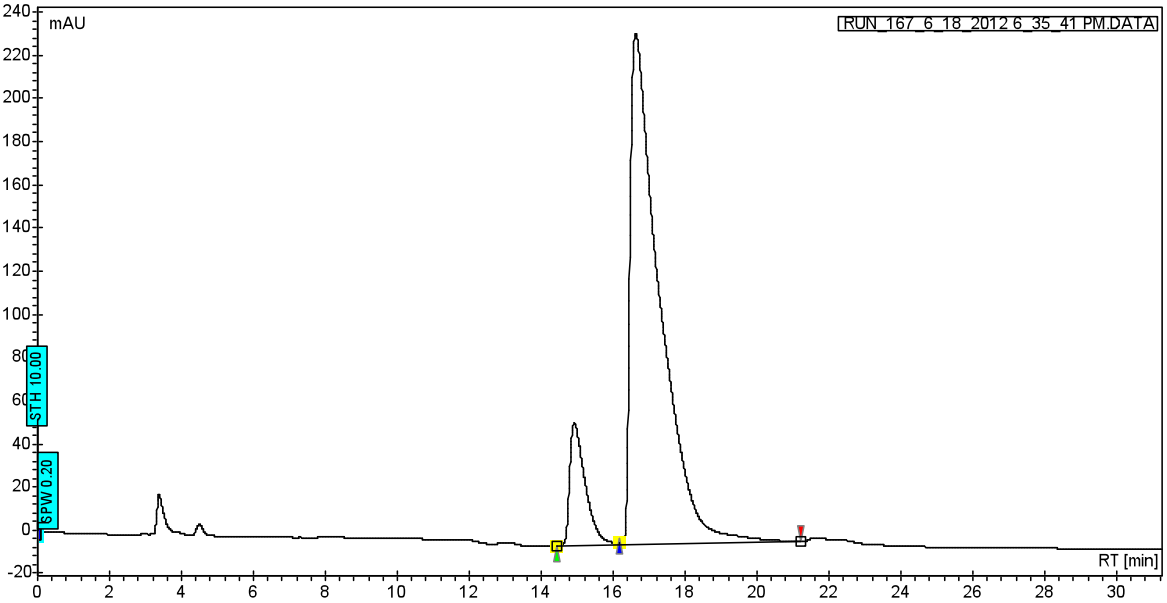


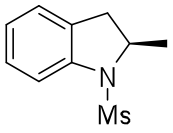


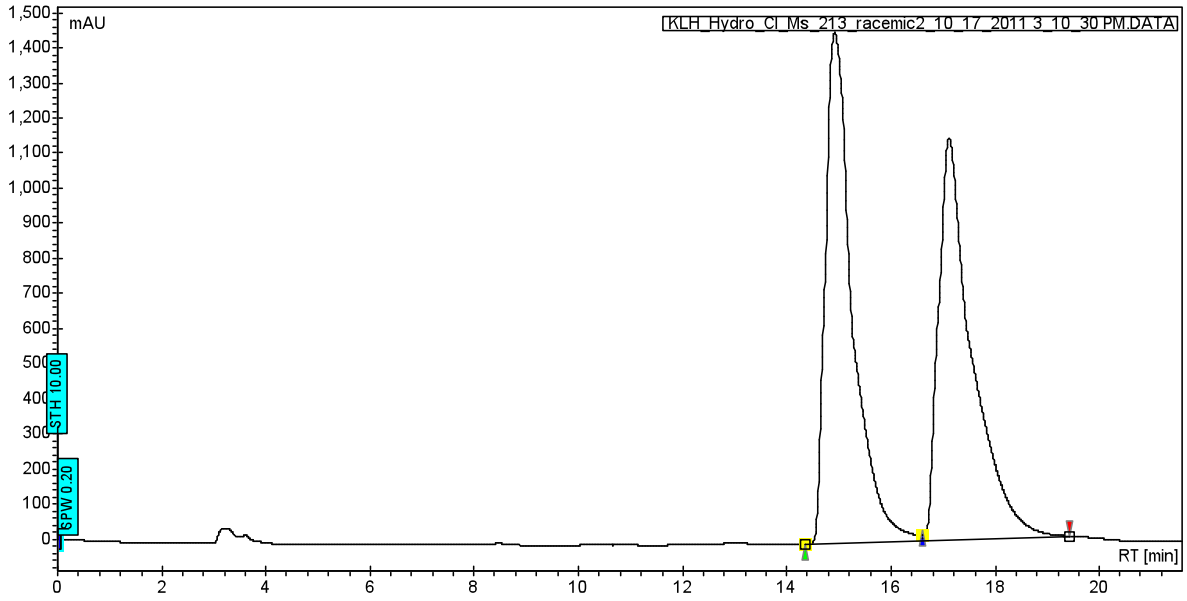
#	Time[min]	Area[%]
1	17.05	50.39
2	19.74	49.61



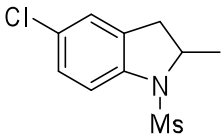


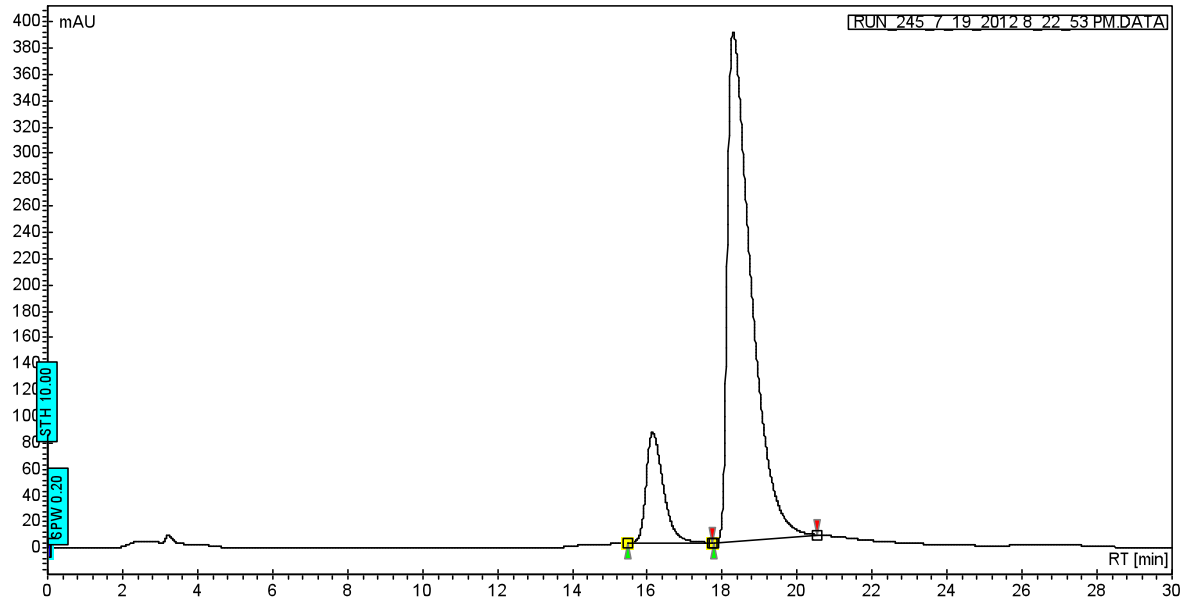
#	Time[min]	Area[%]
1	14.93	11.40
2	16.63	88.60



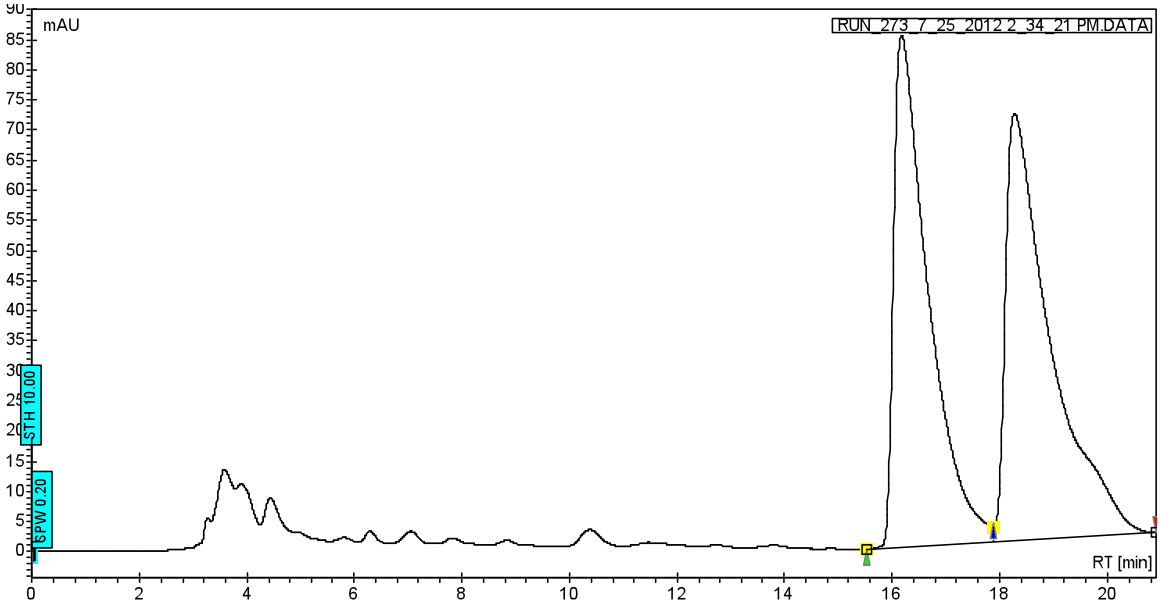


#	Time[min]	Area[%]
1	14.92	50.78
2	17.11	49.22

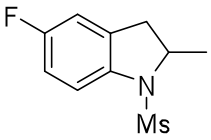


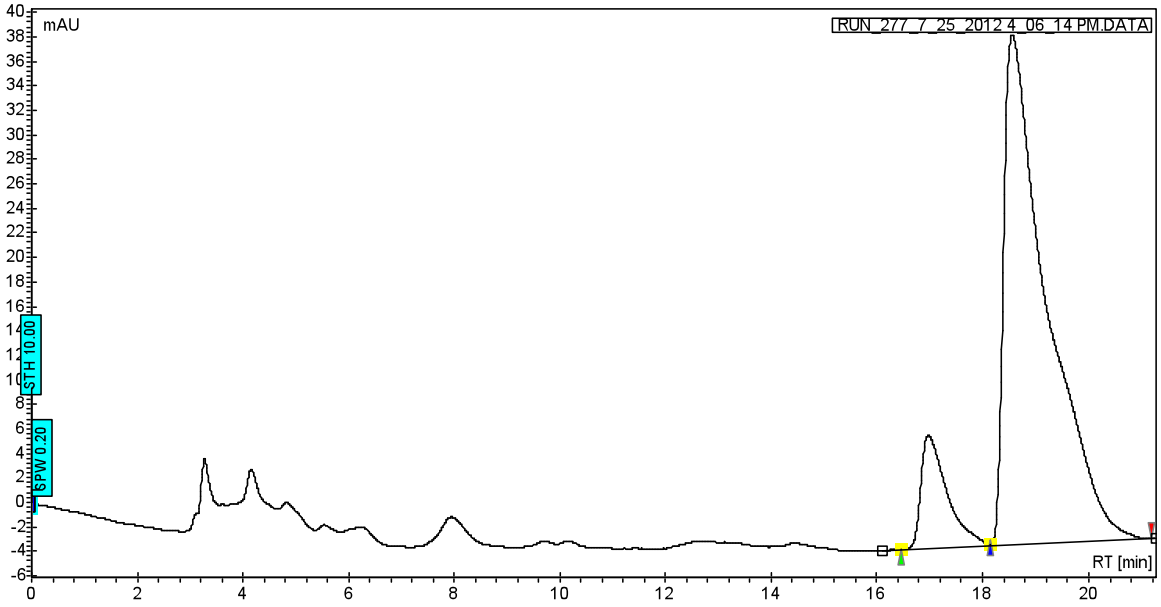


#	Time[min]	Area[%]
1	16.14	13.77
2	18.29	86.23

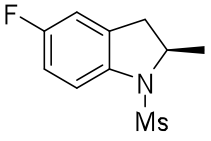


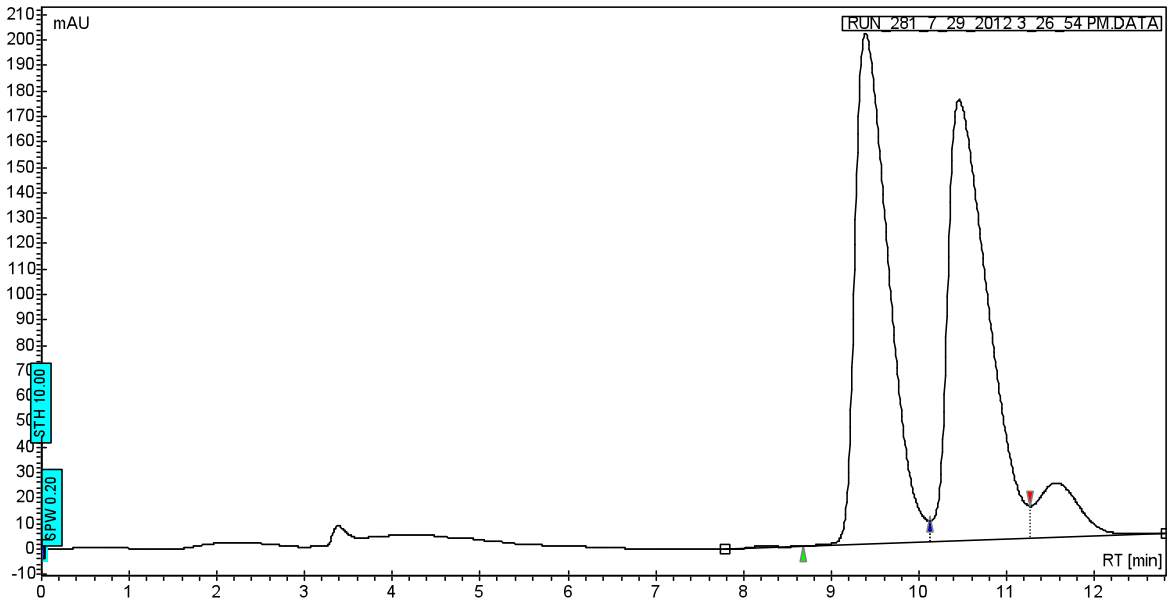
#	Time[min]	Area[%]
1	16.17	48.09
2	18.27	51.91



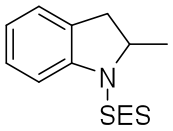


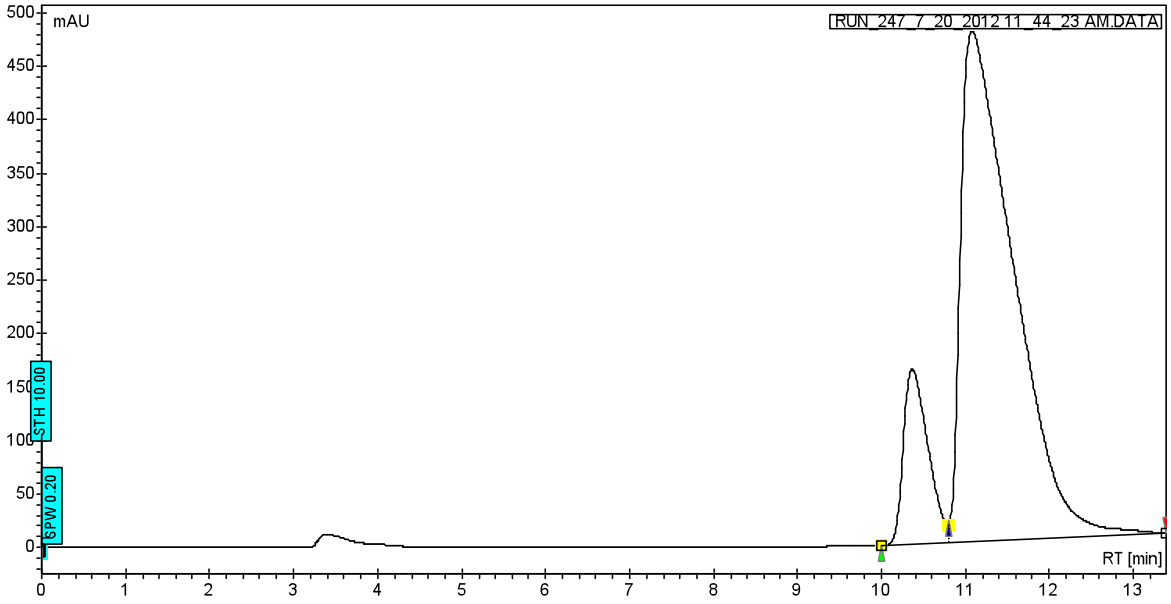
#	Time[min]	Area[%]
1	16.98	12.05
2	18.56	87.95



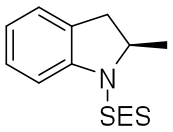


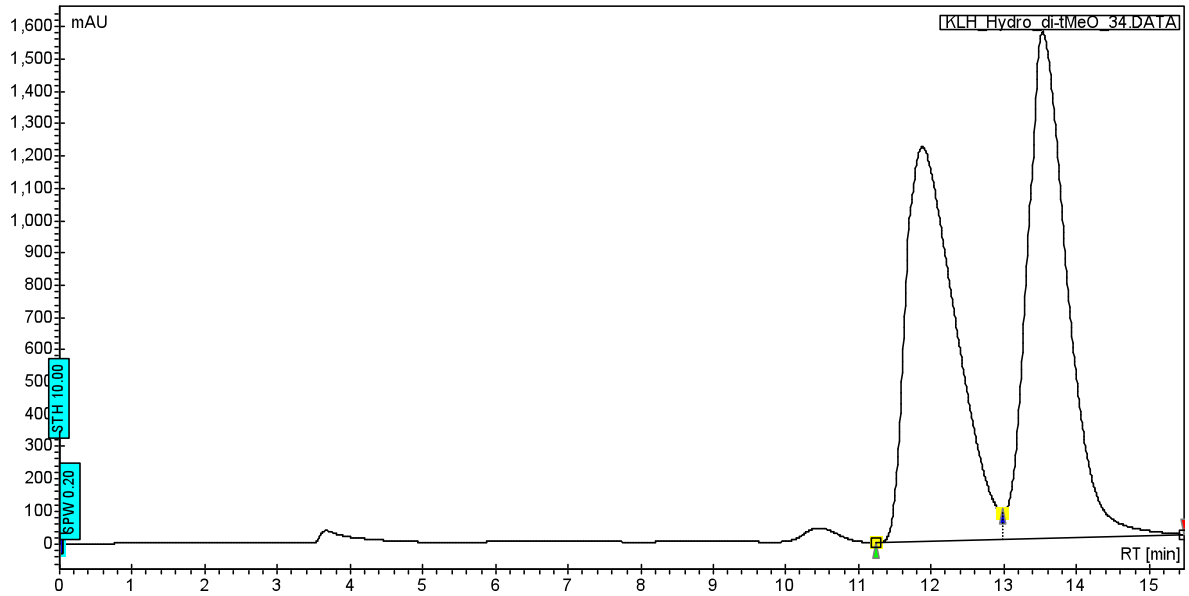
#	Time[min]	Area[%]
1	9.39	49.20
2	10.46	50.80



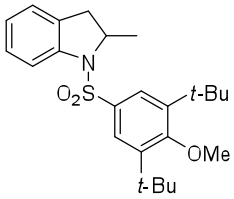


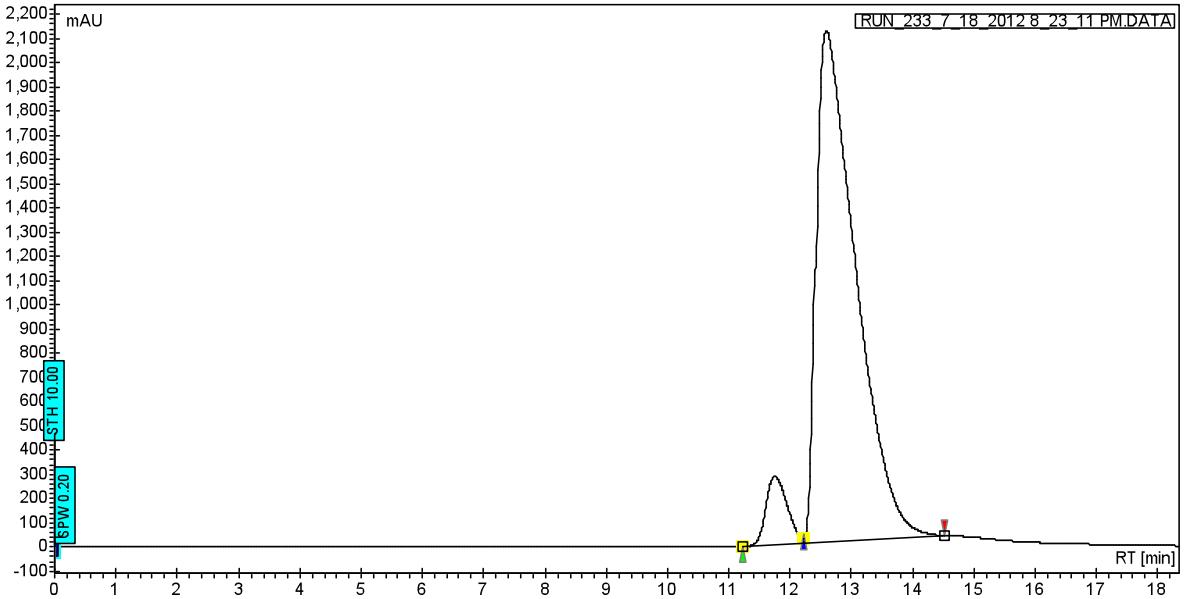
#	Time[min]	Area[%]
1	10.36	13.87
2	11.07	86.13



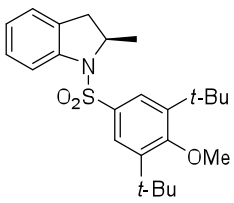


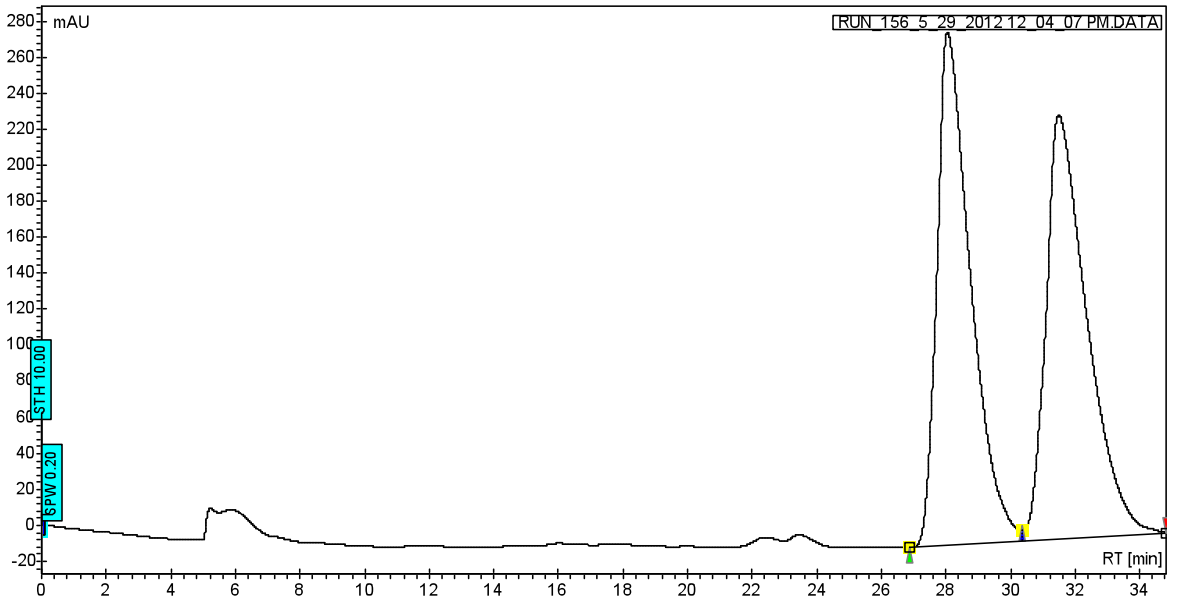
#	Time[min]	Area[%]
1	11.94	50.08
2	13.85	49.92



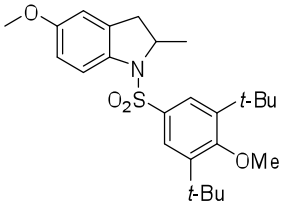


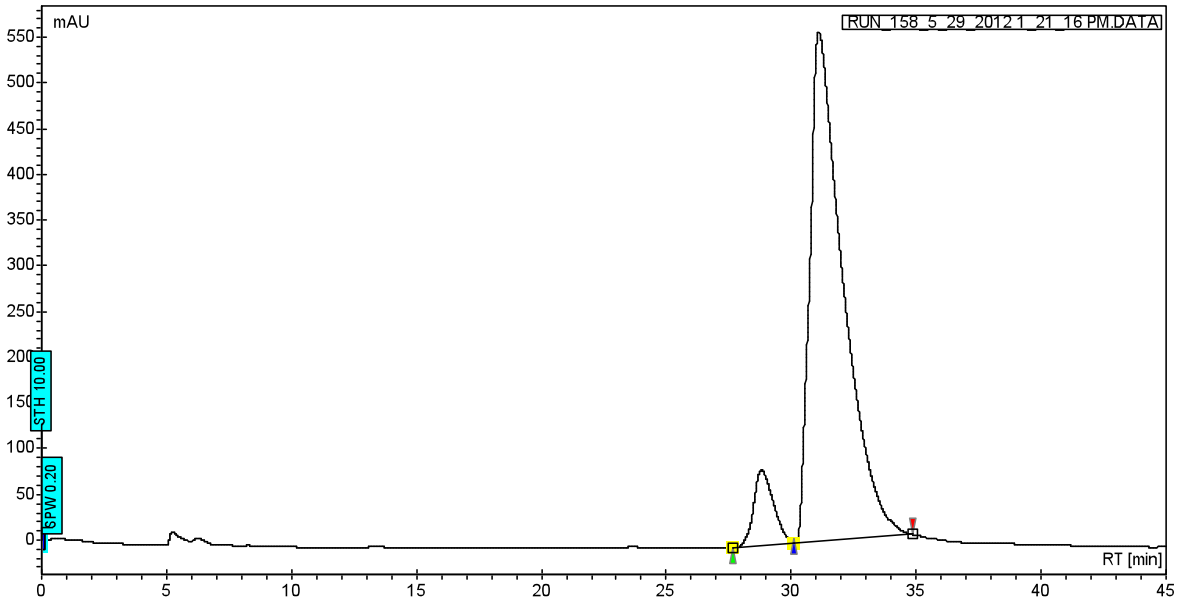
#	Time[min]	Area[%]
1	11.75	6.79
2	12.59	93.21



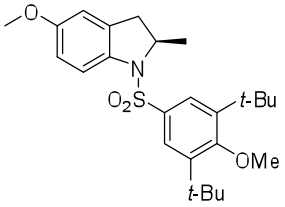


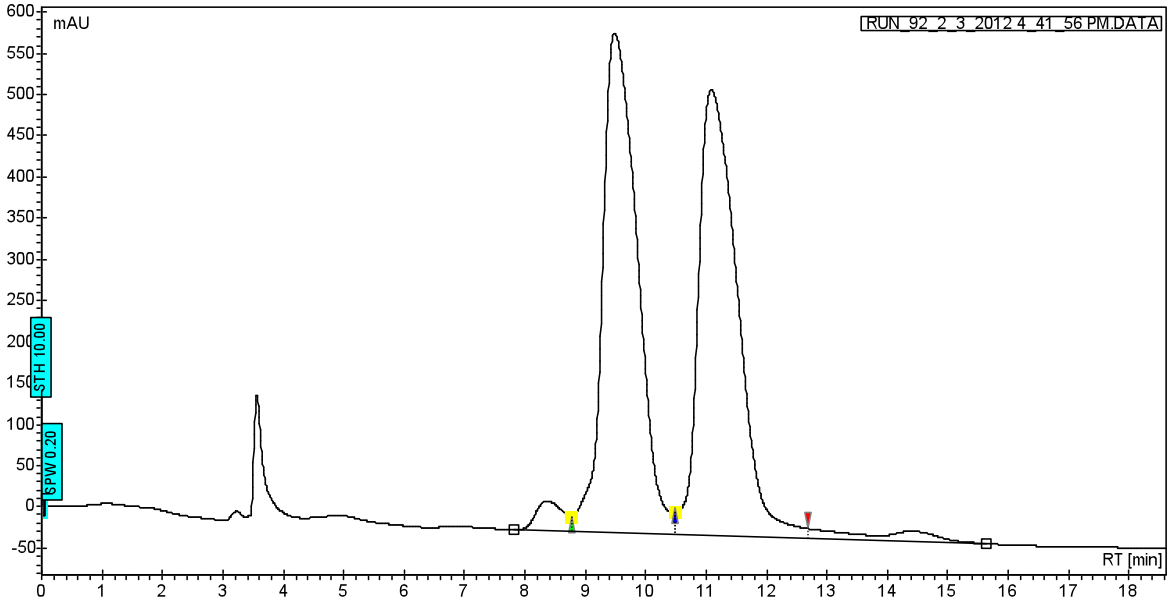
#	Time[min]	Area[%]
1	28.05	49.78
2	31.49	50.22



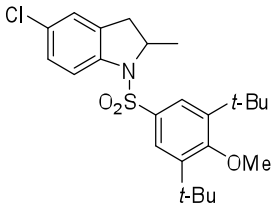


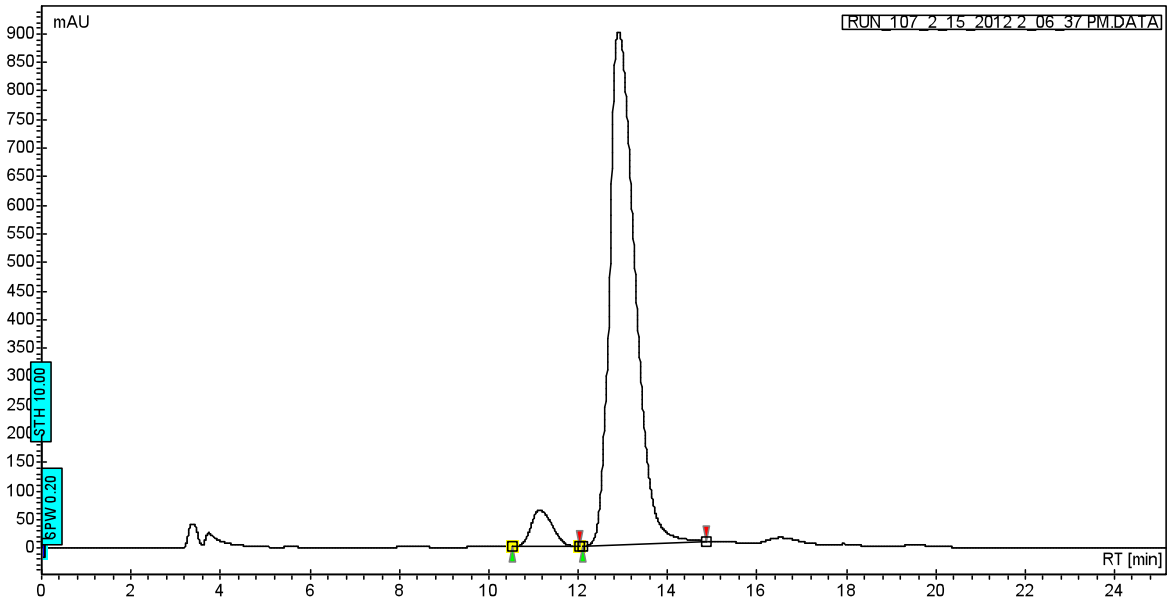
#	Time[min]	Area[%]
1	28.81	8.22
2	31.10	91.78



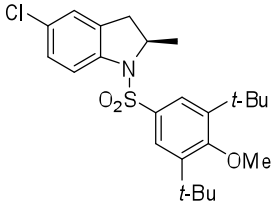


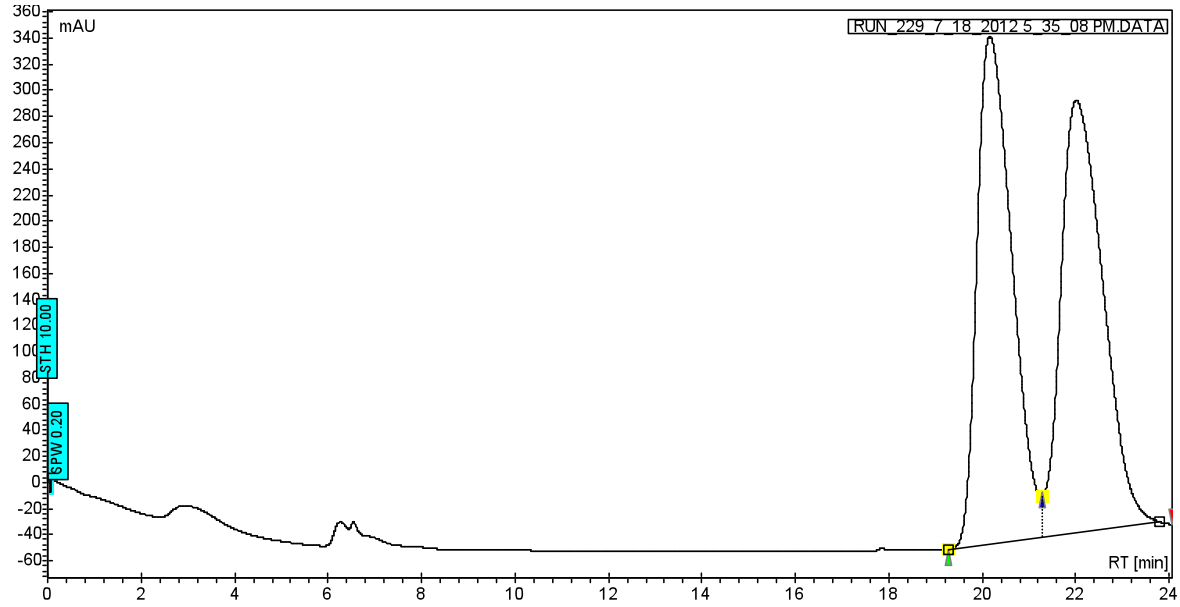
#	Time[min]	Area[%]
1	9.49	50.05
2	11.09	49.95



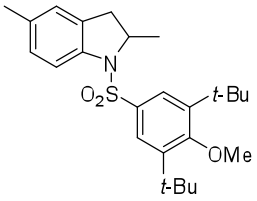


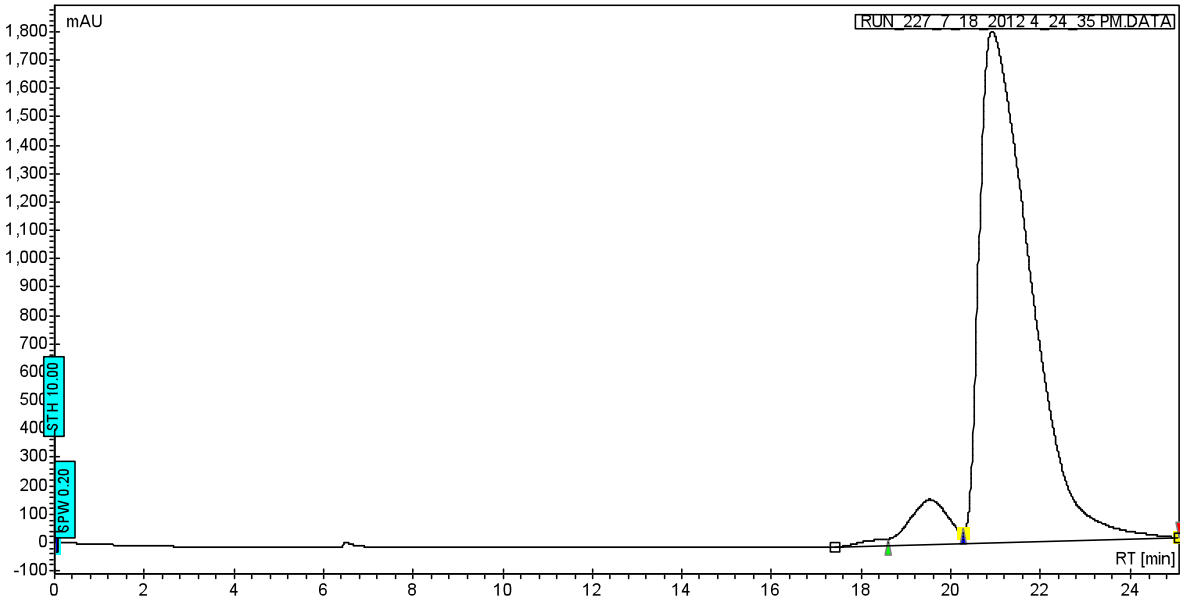
#	Time[min]	Area[%]
1	11.14	5.69
2	12.91	94.31



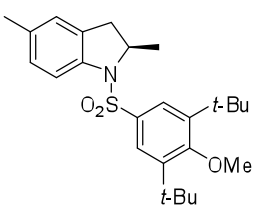


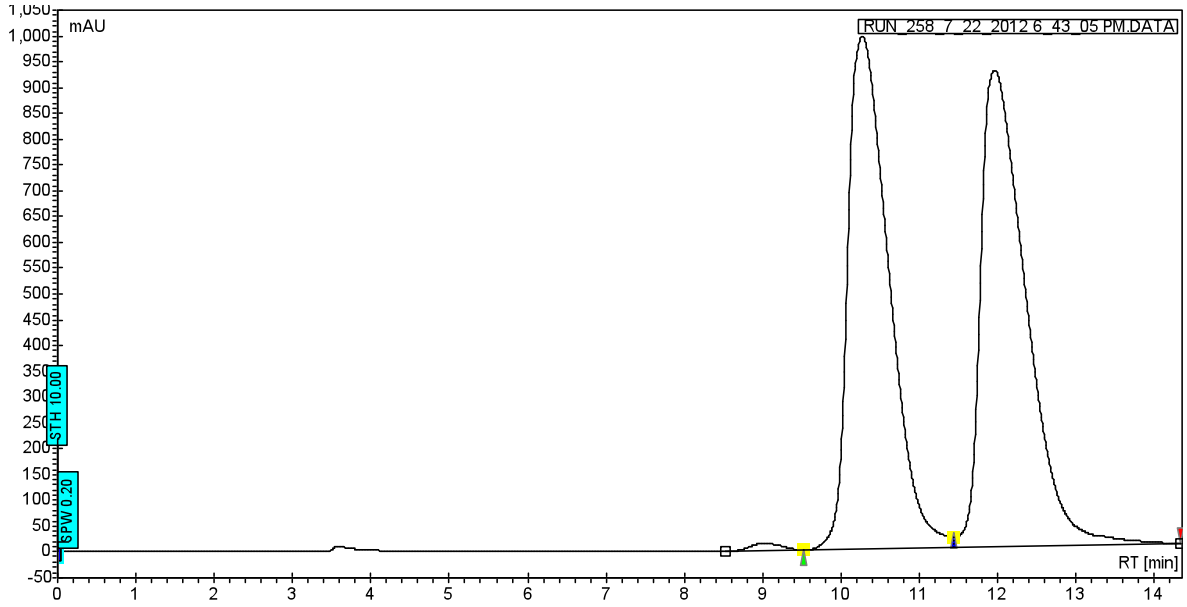
#	Time[min]	Area[%]
1	20.16	49.20
2	22.01	50.80



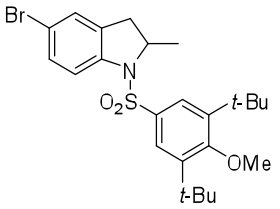


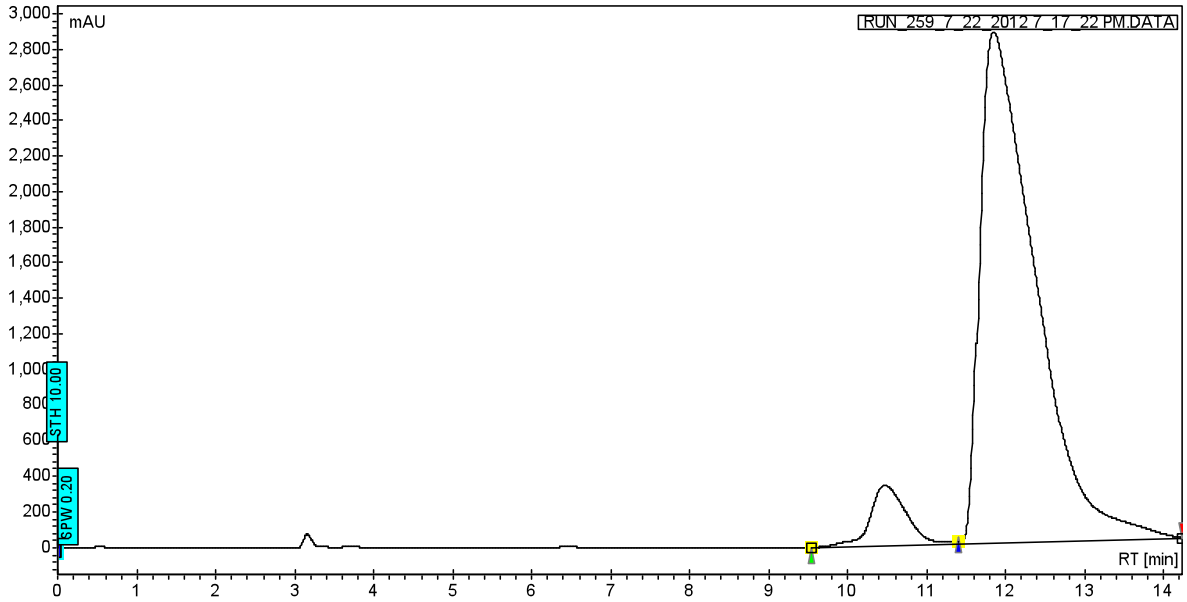
#	Time[min]	Area[%]
1	19.52	6.27
2	20.92	93.73





#	Time[min]	Area[%]
1	10.27	49.33
2	11.97	50.67





#	Time[min]	Area[%]
1	10.47	7.16
2	11.85	92.84