

Multigram Synthesis of A Chiral Substituted Indoline Via Copper-Catalyzed Alkene Aminooxygenation

Fatima C. Sequeira, Michael T. Bovino, Anthony J. Chipre, Sherry R. Chemler*

Supporting Information

General experimental information: All reagents were used out of the bottle as purchased from the supplier without further purification unless otherwise noted. ^1H NMR spectra were recorded in CDCl_3 (using 7.26 ppm for reference of residual CHCl_3) at 300, 400 or 500 MHz unless otherwise noted. ^{13}C NMR spectra were recorded in CDCl_3 (using 77.0 ppm as internal reference) at 75 MHz unless otherwise noted. 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 1 fitted with a micro cell with a 100 mm path length. Melting points are reported as uncorrected.

N-Allyl-4-fluoroaniline (**1**):

A 250-mL round-bottomed flask equipped with a magnetic stir bar was charged with K_2CO_3 (12.7 g, 91.6 mmol, 1.90 equiv), sealed with a rubber septum and purged with argon by means of a needle inlet and outlet. The flask was charged with anhydrous *N,N*-dimethylformamide (40.0 mL) and 4-fluoroaniline (11.6 mL, 121 mmol, 2.50 equiv) added via syringe, and the reaction mixture was stirred for 10 minutes. Allyl bromide (4.19 mL, 48.2 mmol, 1.0 equiv) is added via syringe over a period of 5 minutes. The reaction vessel was then equipped with a reflux condenser and sealed with a rubber septum, with a needle outlet exiting through a bubbler to relieve pressure. The reaction was then heated for 24 h at 70 °C. Potassium carbonate was a suspension in the reaction mixture. The reaction vessel was allowed to cool to room temperature before water (75 mL) was added and the mixture was stirred for 10 minutes. The mixture was then transferred to a 250 mL separatory funnel and extracted with EtOAc (3 × 50 mL). The resulting organic phases are combined and washed with brine (3 × 50 mL). The combined organic layers were dried over Na_2SO_4 (65 g), filtered, and concentrated by rotary evaporation to afford a dark red oil. ^1H NMR of the crude product shows 10-15% of *N,N*-diallyl-4-fluoroaniline. The separation of the title compound and *N,N*-diallyl-4-fluoroaniline was collected by fractional vacuum distillation. The crude mixture was transferred to a 100-mL round-bottom flask equipped with a magnetic stir bar and a 17-cm Vigreux column fitted with a short path distillation head and cow-type distillation receiver with three 25-mL round bottom receivers. The distillation bath was carefully increased from 25 °C to 119 °C. Two fractions are collected, distilling at 25-32 °C (0.5 mmHg), providing the *N,N*-dimethylformamide and 4-fluoroaniline. The second fraction was collected from distilled 50 to 58 °C (0.5 mmHg), this was collected providing the title compound **1** as a clear oil. (4.50 g, 75% yield)

^1H NMR (400 MHz, CDCl_3) δ : 6.92-6.87 (m, 2H), 6.58-6.54 (m, 2H), 5.92 (m, 1H), 5.31-5.16 (m, 2H), 3.74 (dt, $J = 1.6, 5.2$ Hz, 2H), 3.65 (bs, 1H).

^{13}C NMR (75 MHz, CDCl_3) 155.6 (d, $J = 234.9$ Hz), 144.0 (d, $J = 2.3$ Hz), 135.3, 116.0 (d, $J = 44.9$ Hz), 115.4, 113.7 (d, $J = 8.1$ Hz), 47.0.

IR (thin film): 3426, 1613, 1523, 1313, 1220 cm^{-1} .

HRMS (ESI) calcd for $\text{C}_9\text{H}_{11}\text{NF}$ $[\text{M}+\text{H}]^+$: 152.0870; found 152.0865.

2-Allyl-4-fluoroaniline:

An oven-dried 250 mL pressure tube was equipped with a stir bar, sealed with a rubber septum and flushed with argon, introduced via a needle inlet with another needle outlet. The tube was charged with *N*-allyl-4-fluoroaniline (4.50 g, 29.5 mmol, 1.0 equiv) and xylenes (70.0 mL), both added via syringe. The pressure tube was cooled to $-78\text{ }^\circ\text{C}$ in a dry ice/acetone bath and the solution was stirred for 10 minutes. Boron trifluoride etherate (4.08 mL, 35.4 mmol, 1.2 equiv) was then added via syringe and the solution was stirred for 10 min at $-78\text{ }^\circ\text{C}$ and then brought to room temperature. The reaction mixture was a peach color. At this point the reaction vessel was sealed with the pressure tube screw cap and was placed into an oil bath and heated at $180\text{ }^\circ\text{C}$ for 10 hours. Overheating the reaction or longer reaction time can result in formation of a hydroamination side product. The reaction vessel was then allowed to cool to room temperature and the reaction mixture was quenched with 2M NaOH (52 mL). The mixture was transferred to a 250-mL separatory funnel and extracted with EtOAc ($3 \times 60\text{ mL}$). The resulting organic phases were combined, washed with brine ($2 \times 60\text{ mL}$) and filtered. The combined organic layers were dried over Na_2SO_4 (65 g), filtered, and concentrated by rotary evaporation (20 mmHg, $50\text{ }^\circ\text{C}$) in a 250 mL round-bottomed flask to afford a dark red oil. Residual solvents were removed under vacuum. The crude title compound is obtained (4.53 g) in sufficient purity for use in the subsequent step.

^1H NMR (500 MHz, CDCl_3) δ : 6.80-6.75 (m, 2H), 6.61 (dd, $J = 5.0, 8.5\text{ Hz}$, 1H), 5.94 (m, 1H), 5.16-5.08 (m, 2H), 3.52 (bs, 2H), 3.27 (d, $J = 6.5\text{ Hz}$, 2H).

^{13}C NMR (75 MHz, CDCl_3) 156.5 (d, $J = 236.0\text{ Hz}$), 140.6 (d, $J = 2.3\text{ Hz}$), 135.0, 125.8 (d, $J = 6.9\text{ Hz}$), 116.7, 116.6 (d, $J = 5.4\text{ Hz}$), 116.4 (d, $J = 18.3\text{ Hz}$), 113.7 (d, $J = 21.8\text{ Hz}$), 36.2.

IR (thin film): 3439, 3381, 3048, 2889, 1627, 1489, 1424, 1237, 11475 cm^{-1} .

HRMS (ESI) calcd for $\text{C}_9\text{H}_{11}\text{NF}$ $[\text{M}+\text{H}]^+$: 152.0870; found 152.0868.

N-(2-Allyl-4-fluorophenyl)-4-methylbenzenesulfonamide (2)

The 250 mL round-bottomed flask containing the crude 2-allyl-4-fluoroaniline (**2**) (4.50 g, 29.5 mmol, 1.0 equiv) was equipped with a magnetic stir bar, sealed with a septum and purged with an argon atmosphere by means of an inlet and outlet. The oil was dissolved in dichloromethane (29.0 mL) and treated with pyridine (7.23 mL, 88.7 mmol, 3.0 equiv), both added via syringe. This solution was allowed to stir for 10 min and was then treated with 4-methylbenzene-1-sulfonyl chloride (6.67 g, 34.9 mmol, 1.2 equiv) and the solution was stirred for 16 h at room temperature. The reaction mixture was then transferred to a 250 mL separatory funnel and washed with 1M HCl ($3 \times 60\text{ mL}$). The combined aqueous layer washes were extracted with CH_2Cl_2 ($1 \times 30\text{ mL}$). The resulting organic phases are combined and washed with brine ($2 \times 60\text{ mL}$), and the combined organic layer was dried with Na_2SO_4 (50 g), filtered and concentrated by rotary evaporation (20 mmHg, $35\text{ }^\circ\text{C}$) to afford a dark red mixture. The product **2** was purified

by flash column chromatography using a 0-15% EtOAc/ hexanes gradient and the resulting solid was dried to constant weight under reduced pressure affords the title compound as a pale yellow solid (6.49 g, 75% yield over two steps).

Mp 78 °C.

^1H NMR (500 MHz, CDCl_3) δ : 7.50-7.48 (dd, $J = 8.0, 2.0$ Hz, 2H), 7.20-7.14 (m, 3H), 6.79 (m, 1H), 6.73 (dd, $J = 2.0, 9.0$ Hz, 1H), 6.56 (bs, 1H), 5.63 (m, 1H), 5.02 (dd, $J = 1.5, 8.5$ Hz, 1H), 5.85 (dd, 1.5, 17.0, 1H), 3.00 (d, $J = 6.0$ Hz, 2H), 2.93 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) 161.0 (d, $J = 246.0$ Hz), 143.9, 136.5 (d, $J = 6.9$ Hz), 134.8, 130.4 (d, $J = 3.4$ Hz), 129.6, 128.2, 127.8 (d, $J = 9.2$ Hz), 127.0, 117.4, 117.0 (d, $J = 23.0$ Hz), 114.1 (d, $J = 21.8$ Hz), 35.7, 21.5.

IR (thin film): 3263, 1590, 1497, 1167, 1093 cm^{-1} .

HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{16}\text{O}_2\text{NFSNa}$ $[\text{M}+\text{Na}]^+$: 328.0778; found 328.0772.

2,2-Bis{2-[4(*R*),5(*S*)-diphenyl-1-3-oxzolinyl]}propane (3)

This procedure is an adaptation of a similar ligand alkylation reported by Denmark.¹ An oven-dried 250 mL single neck round-bottomed flask equipped with a stir bar was charged with 2,2'-methylenebis[4(*R*),5(*S*)-4,5-diphenyl-2-oxazoline] (1.50 g, 3.27 mmol, 1 equiv) and the flask was sealed with a rubber septum and purged with argon via a needle inlet and outlet. The compound was dissolved in anhydrous tetrahydrofuran (100 mL) and treated with diisopropylamine (0.47 mL, 3.33 mmol, 1 equiv) and TMEDA (1.00 mL, 6.67 mmol, 2 equiv), added via syringe. The flask was then placed in a -75 °C bath (dry ice and isopropanol). The mixture was stirred at this temperature for 5 min and then treated with a 1.6 M solution of *n*-butyl lithium in hexanes (4.10 mL, 6.56 mmol, 2 equiv), added via syringe. Upon the addition of the *n*-butyl lithium the solution became a mustard yellow color. The reaction was then warmed to -20 °C over 15 min. Once at -20°C this temperature was maintained for 30 minutes after which the temperature was lowered to -75 °C and iodomethane (0.42 mL, 6.73 mmol, 2 equiv) was added via syringe. Upon completion of the addition, the cold bath was removed and the reaction mixture was stirred at 22 °C under argon for 16 h. The reaction turned to a white heterogeneous mixture upon completion. The reaction was quenched with saturated aqueous NH_4Cl solution (50 mL) and diluted with additional water (25 mL) to dissolve any salts that may form. The mixture was transferred to a 500 mL separatory funnel and extracted with Et_2O (3 X 100 mL). The combined organics were washed with saturated NaCl solution (100 mL) and dried over MgSO_4 (1 g), filtered, and concentrated by rotary evaporation (20 mmHg, 40 °C). The crude white solid was purified by flash chromatography using 50% dichloromethane/ hexanes gradient. All material was dried under reduced pressure to afford the title compound **3** as a fluffy white solid (1.37 g, 86% yield).

Mp: 160 °C.

$[\alpha]_{\text{D}}^{25}$ 362.0 ($c = 1.0, \text{CH}_2\text{Cl}_2$), Lit. $[\alpha]_{\text{D}}^{25}$ 367.0 ($c = 1.05, \text{CH}_2\text{Cl}_2$).²

^1H NMR (400 MHz, CDCl_3): δ 7.02 (s, 10 H), 6.96 (s, 10 H), 5.97 (d, $J = 10$ Hz, 2H), 5.59 (d, $J = 10.4$ Hz, 2H), 1.92 (s, 6 H).

^{13}C NMR (75 MHz, CDCl_3): δ 170.4, 137.5, 136.2, 127.9, 127.6, 127.4, 126.9, 126.6, 86.3, 73.8, 39.6, 24.8; IR: cm^{-1} 3030, 2931, 1656, 1454, 1143, 1114, 975.

HRMS (ESI) calc'd for $\text{C}_{33}\text{H}_{31}\text{O}_2\text{N}_2$ $[\text{M}+1]^+$: 487.2374; found 487.2380.

(S)-5-Fluoro-2-(2,2,6,6-tetramethyl-piperidin-1-yloxymethyl)-1-tosylindoline (4)

An oven-dried, 500 mL, 14/20 neck size, round-bottomed flask equipped with a magnetic stirring bar was brought into a glove box under an argon environment, where the flask was charged with $\text{Cu}(\text{OTf})_2$ (0.76 g, 2.1 mmol, 0.15 equiv) and (4*R*, 5*S*)-diphenylbis(oxazoline) **3** (1.22 g, 2.5 mmol, 0.18 equiv) then the flask was sealed with a rubber septum. The flask was removed from the glove box and placed under argon via a needle inlet and outlet. Freshly dried toluene (78 mL) is added by syringe and the mixture was heated at 70 °C for 2.5 hours. The solution turned an emerald green color. This catalyst solution was allowed to cool to room temperature then TEMPO (6.51 g, 41.7 mmol, 3.00 equiv) was added as a solid. Sulfonamide **2** (4.25 g, 13.9 mmol, 1 equiv) was added via syringe as a solution in 99.2 mL of toluene. Prior to use, the substrate was azeotroped with benzene to ensure any residual water is removed. Benzene was removed by rotary evaporation. The compound was allowed to dry under reduced pressure for 3 hours prior to use. The flask was back-filled with argon to ambient pressure. (The substrate should not be used unless it is a solid.) The solution was put under an oxygen atmosphere (1 atm, balloon, by introduction through a 14/20 glass adapter fitted with to a vacuum hose attached to the balloon) and was heated at 110 °C (oil bath) for 6 hours. The reaction temperature should not surpass 120 °C, otherwise side products have been observed.

The reaction mixture was cooled to room temperature, the stir bar was removed and the reaction was concentrated by rotary evaporation to afford a brown oil. The crude oil was purified by flash chromatography using a 0-10% EtOAc/hexanes. The product **4** was dried under reduced pressure to a constant mass of 5.47-5.69 g affording the title compound as an off-white solid (5.47-5.69 g, 86-89% yield) in 89% ee (enantiomeric excess determined by chiral HPLC on Chiralpak AD-RH). The optical purity of indoline **4** was further enriched to >98% ee by recrystallization from hexanes (4.28 g of pure **4** obtained).

Mp 87-89 °C; $[\alpha]_{\text{D}}^{22} = 92.6$ ($c = 1.0$, CHCl_3), ee = 89%, determined by Varian Prostar High Performance Liquid Chromatography, using the Chiralpak AD-RH, 10% IPA/hexane, 0.4 mL/min, $\lambda = 254$ nm, $t(\text{major}) = 9.32$ min, $t(\text{minor}) = 8.14$ min].

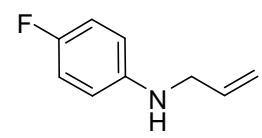
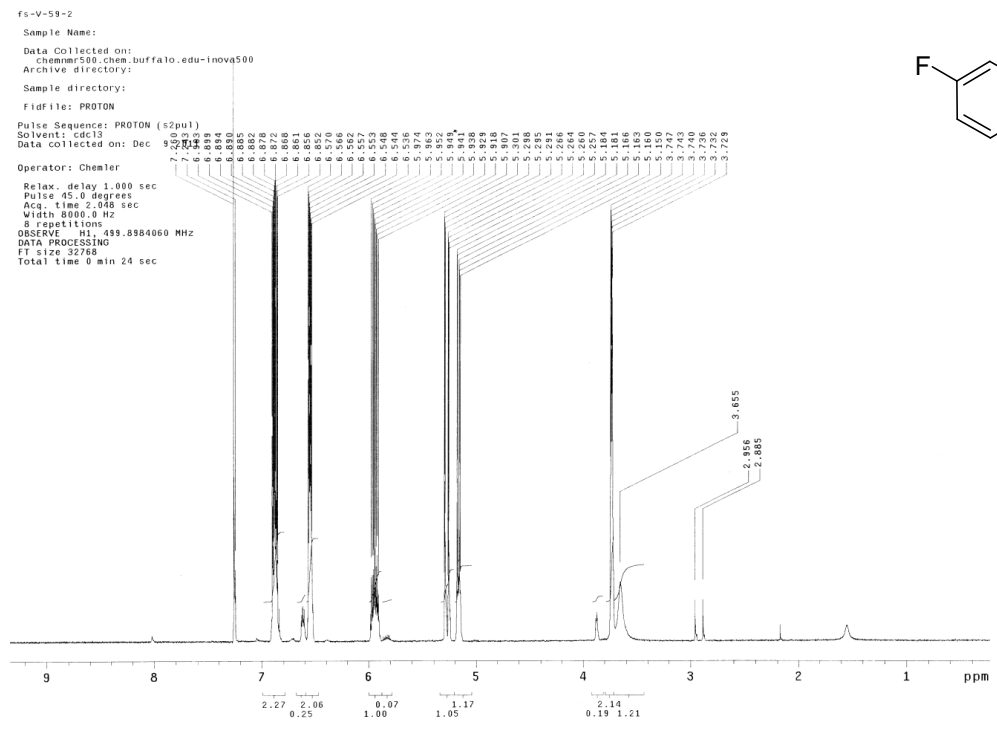
^1H NMR (500 MHz, CDCl_3) δ 7.58 (dd, $J = 5.0, 3.5$ Hz, 1H), 7.51-7.49 (d, $J = 8.0, 2.0$ Hz, 2H), 7.16 (d, $J = 8.0$ Hz, 2H), 6.87 (dt, $J = 9.0$ Hz, 1H), 6.74 (dd, $J = 2.5, 5.5$ Hz, 1H), 4.34 (m, 1H), 3.98-3.93 (m, 2H), 2.76 (d, $J = 16.5$ Hz, 1H), 2.66 (dd, $J = 9.5, 16.0$ Hz, 1H), 2.36 (s, 3H), 1.44-1.38 (m, 5 H), 1.23 (d, $J = 10.0$ Hz, 1H), 1.15 (d, $J = 7.5$ Hz, 6H), 0.95 (s, 3H), 0.83 (s, 3H).

^{13}C NMR (75 Hz, CDCl_3) δ 160.3 (d, $J = 243.0$ Hz), 143.9, 138.0 (d, $J = 2.6$ Hz), 135.1 (d, $J = 9.2$ Hz), 134.8, 129.6, 127.0, 118.2 (d, $J = 9.2$ Hz), 113.9 (d, $J = 23.1$ Hz), 111.8 (d, $J = 27.5$ Hz), 78.7, 61.4, 59.9, 39.5, 33.1, 31.7, 21.5, 20.0, 19.8, 16.9.

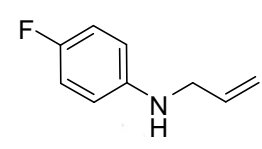
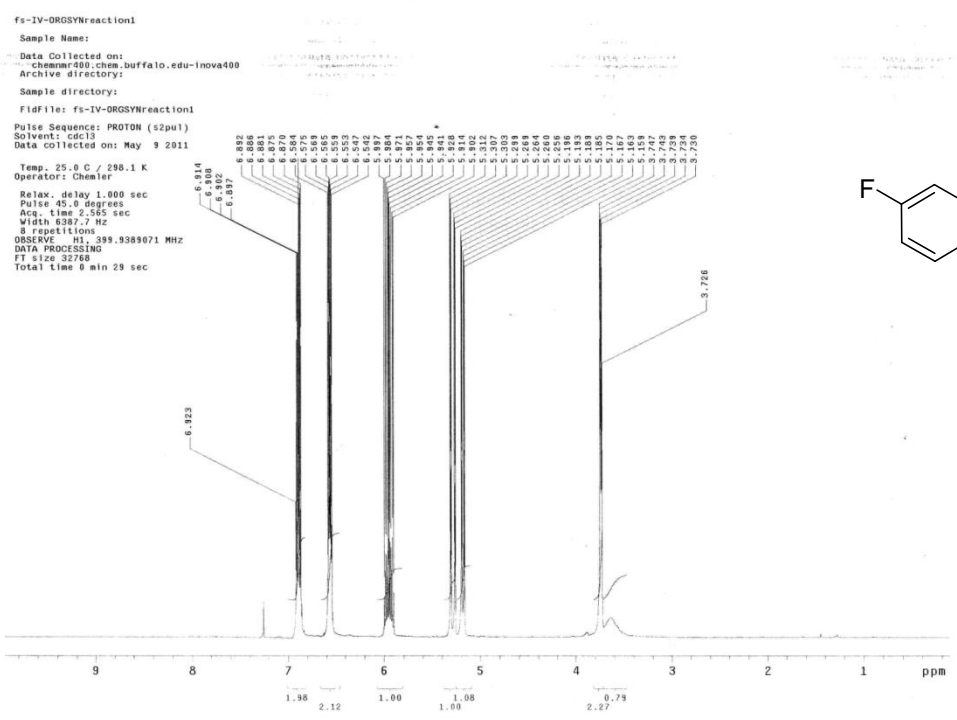
IR (neat): 2936, 1600, 1480, 1480, 1356, 1263, 1163 cm^{-1} .

HRMS (ESI) calcd for $[\text{M}+1]^+$ $\text{C}_{25}\text{H}_{34}\text{O}_3\text{N}_2\text{FS}$: 461.2275, found: 461.2274.

Anal calcd for $C_{25}H_{33}FN_2O_3S$: C, 65.19; H, 7.22; N, 6.09; Found: C, 65.28, H, 7.09; N, 6.09 (\pm 0.3%).

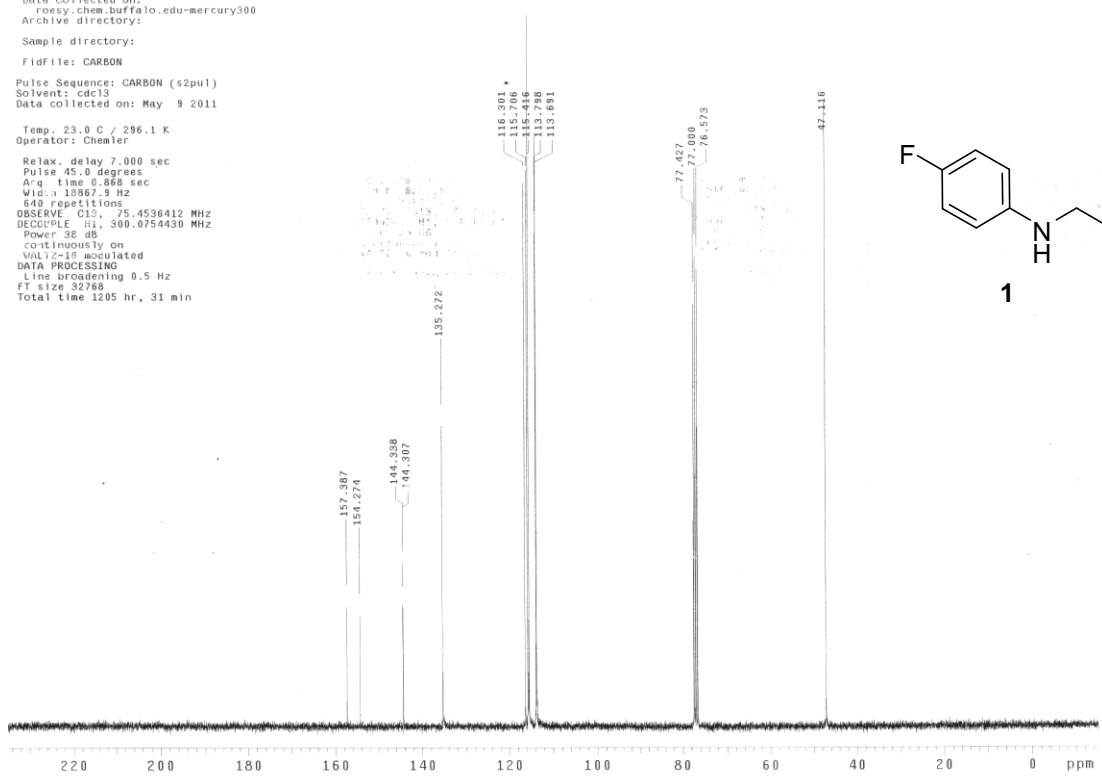


1, after distillation

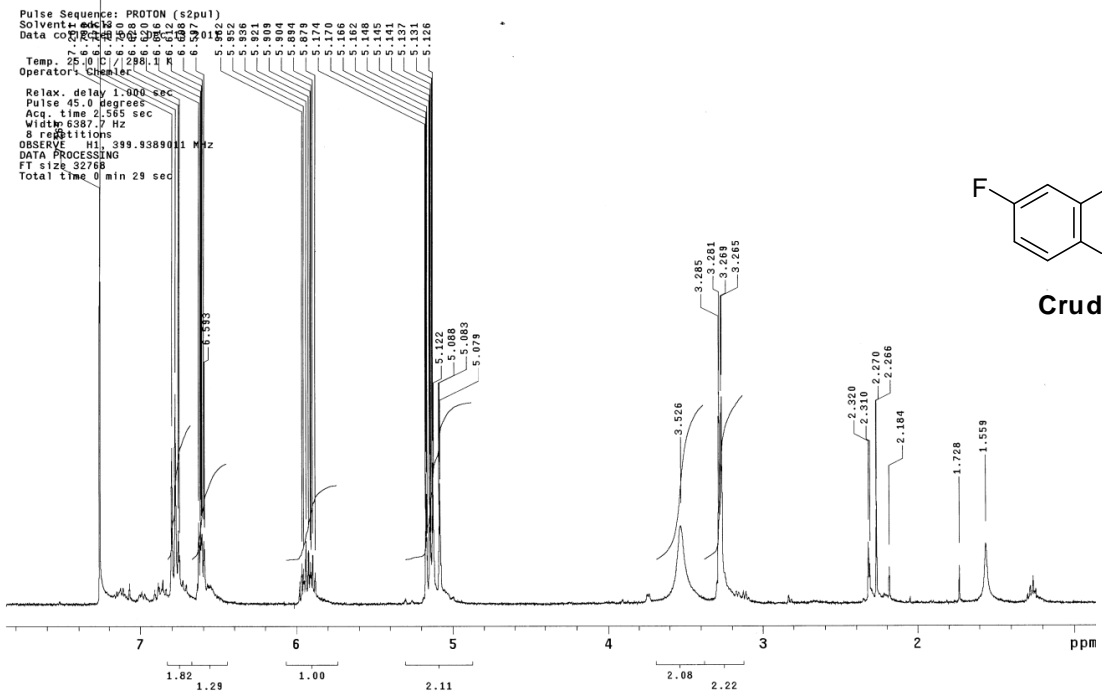


1

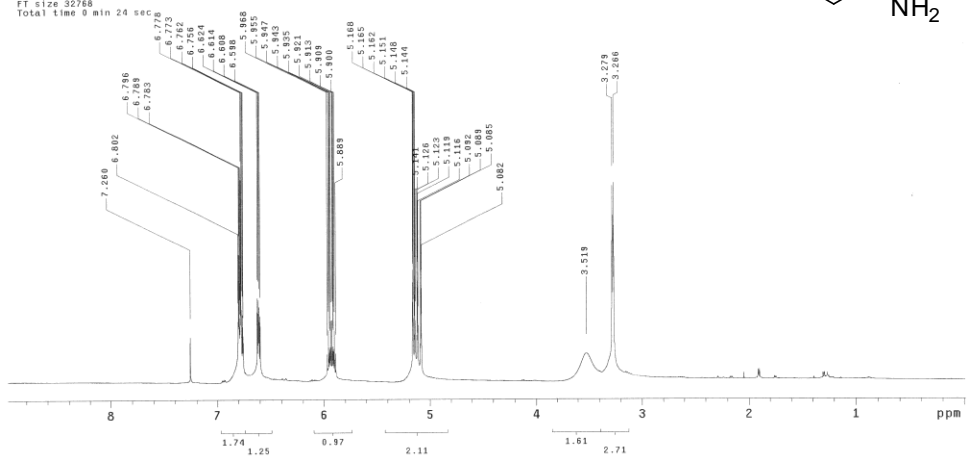
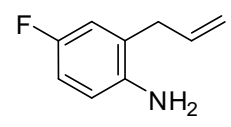
Reaction1
 Sample Name:
 Data Collected on:
 roesy.chem.buffalo.edu=mercury300
 Archive directory:
 Sample directory:
 FidFile: CARBON
 Pulse Sequence: CARBON (s2pul)
 Solvent: cdcl3
 Data collected on: May 9 2011
 Temp. 23.0 C / 296.1 K
 Operator: Chemler
 Relax. delay 7.000 sec
 Pulse 45.0 degrees
 Acq. time 0.868 sec
 Width 12967.9 Hz
 640 repetitions
 OBSERVE C13, 75.4536412 MHz
 DECOUPLE H1, 300.9754430 MHz
 Power 36 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 32788
 Total time 1205 hr, 31 min



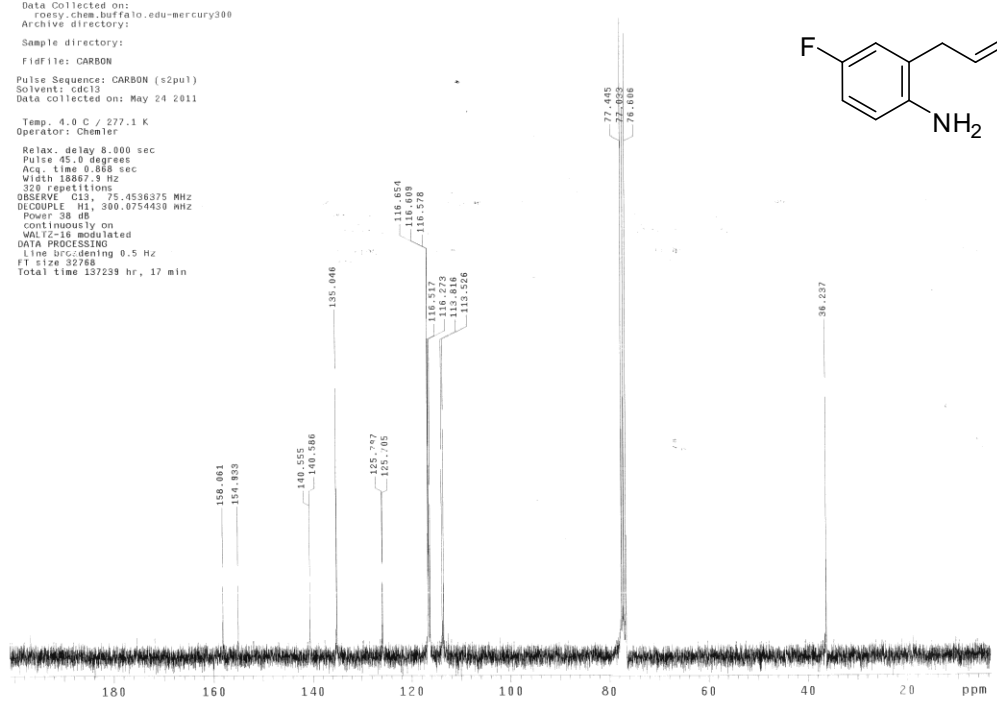
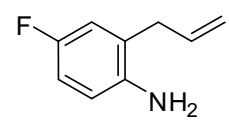
fs-V-60-retake
 Sample Name:
 Data Collected on:
 chemmr400.chem.buffalo.edu-inova400
 Archive directory:
 Sample directory:
 FidFile: PRDTON
 Pulse Sequence: PROTON (s2pul)
 Solvent: cdcl3
 Data collected on: May 9 2011
 Temp. 25.0 C / 298.1 K
 Operator: Chemler
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 2.565 sec
 Width 6367.7 Hz
 8 repetitions
 OBSERVE H1, 399.9389011 MHz
 DATA PROCESSING
 FT size 32768
 Total time 6 min 29 sec



fs-IV-reaction2-clean1
 Sample Name:
 Data Collected on:
 chemmp500.chem.buffalo.edu-inova500
 Archive directory:
 Sample directory:
 Fidfile: fs-IV-reaction2-clean2
 Pulse Sequence: PROTON (s2pul)
 Solvent: cdcl3
 Data collected on: May 17 2011
 Operator: Chemler
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 2.048 sec
 Width 8000.0 Hz
 8 repetitions
 OBSERVE HI, 499.8984050 MHz
 DATA PROCESSING
 FT size 32788
 Total time 0 min 24 sec



fs-IV-ORGrreaction2
 Sample Name:
 Data Collected on:
 roesy.chem.buffalo.edu-mercury300
 Archive directory:
 Sample directory:
 Fidfile: CARBON
 Pulse Sequence: CARBON (s2pul)
 Solvent: cdcl3
 Data collected on: May 24 2011
 Temp: 4.0 C / 277.1 K
 Operator: Chemler
 Relax. delay 8.000 sec
 Pulse 45.0 degrees
 Acq. time 0.868 sec
 Width 18867.5 Hz
 320 repetitions
 OBSERVE C13, 76.4536375 MHz
 DECOUPLE HI, 300.0754430 MHz
 Power 38 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 32788
 Total time 137239 hr, 17 min



fs-ORGSYN-Reaction3Cleanproton

Sample Name:

Data Collected on:
chemmr500.chem.buffalo.edu-inova500
Archive directory:

Sample directory:

Fidfile: PROTON

Pulse Sequence: PROTON (*2pul)

Solvent: cdc13

Data collected on: May 9 2011

Operator: Chemler

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 2.048 sec

Width 8000.0 Hz

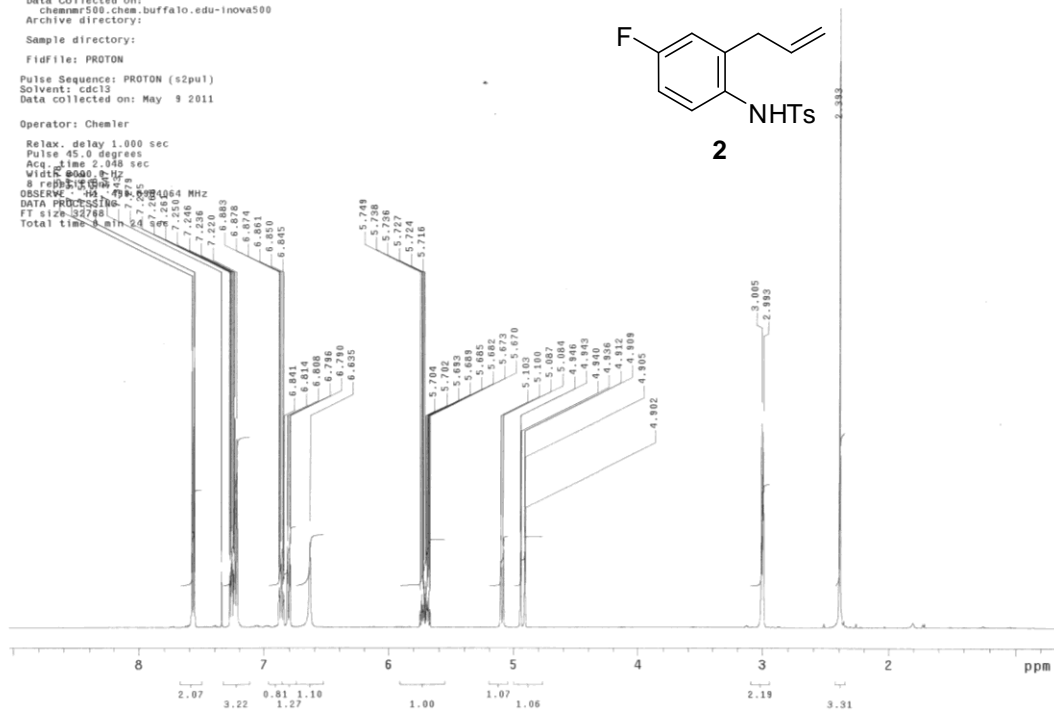
8 repetitions

OBSERVE F1 500.1364 MHz

DATA PROCESSING

FT size 32768

Total time 24.24



Reaction 3

Sample Name:

Data Collected on:
roesy.chem.buffalo.edu-mercury300
Archive directory:

Sample directory:

Fidfile: CARBON

Pulse Sequence: CARBON (*2pul)

Solvent: cdc13

Data collected on: May 7 2011

Temp. 23.0 C / 296.1 K

Operator: Chemler

Relax. delay 7.000 sec

Pulse 45.0 degrees

Acq. time 0.868 sec

Width 18887.5 Hz

320 repetitions

OBSERVE F1 125.4536435 MHz

PULSE F2 101.6254439 MHz

Power 38 dB

continuously on

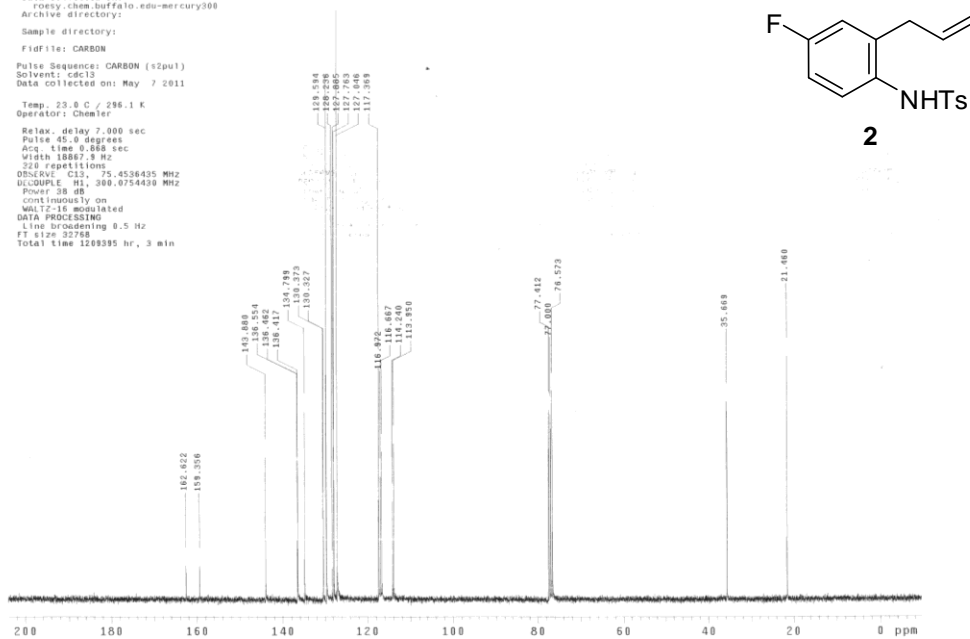
MULTI: 18 modulated

DATA PROCESSING

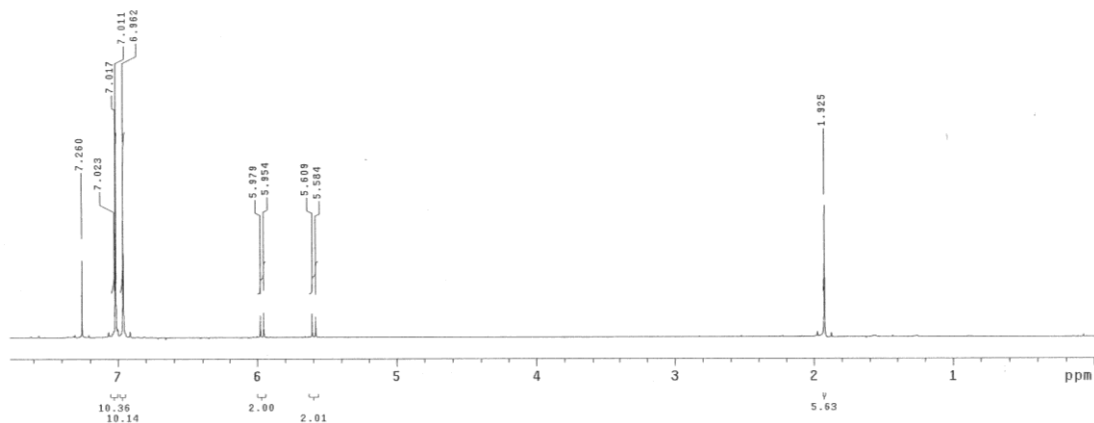
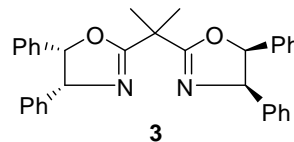
Line broadening 0.5 Hz

FT size 32768

Total time 1209395 hr, 3 min

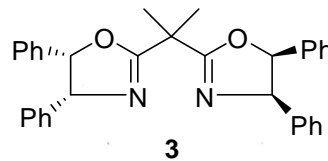
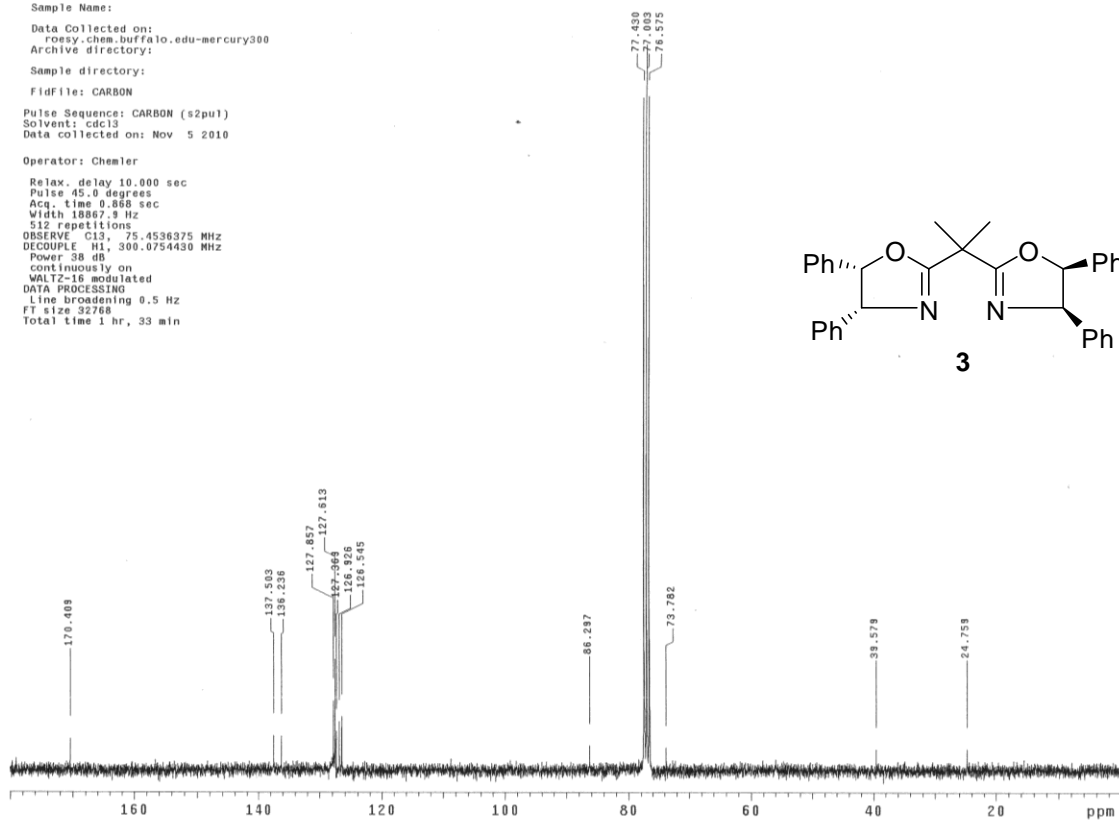


Sample Name:
 Data Collected on:
 chemar400.chem.buffalo.edu-inova400
 Archive directory:
 Sample directory:
 Fidfile: PROTON
 Pulse Sequence: PROTON (s2pul)
 Solvent: cdcl3
 Data collected on: Nov 5 2010
 Temp. 25.0 C / 298.1 K
 Operator: Chemler
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 2.565 sec
 Width 6387.7 Hz
 8 repetitions
 OBSERVE H1, 399.9389027 MHz
 DATA PROCESSING
 FT size 32768
 Total time 0 min 29 sec



STANDARD CARBON PARAMETERS

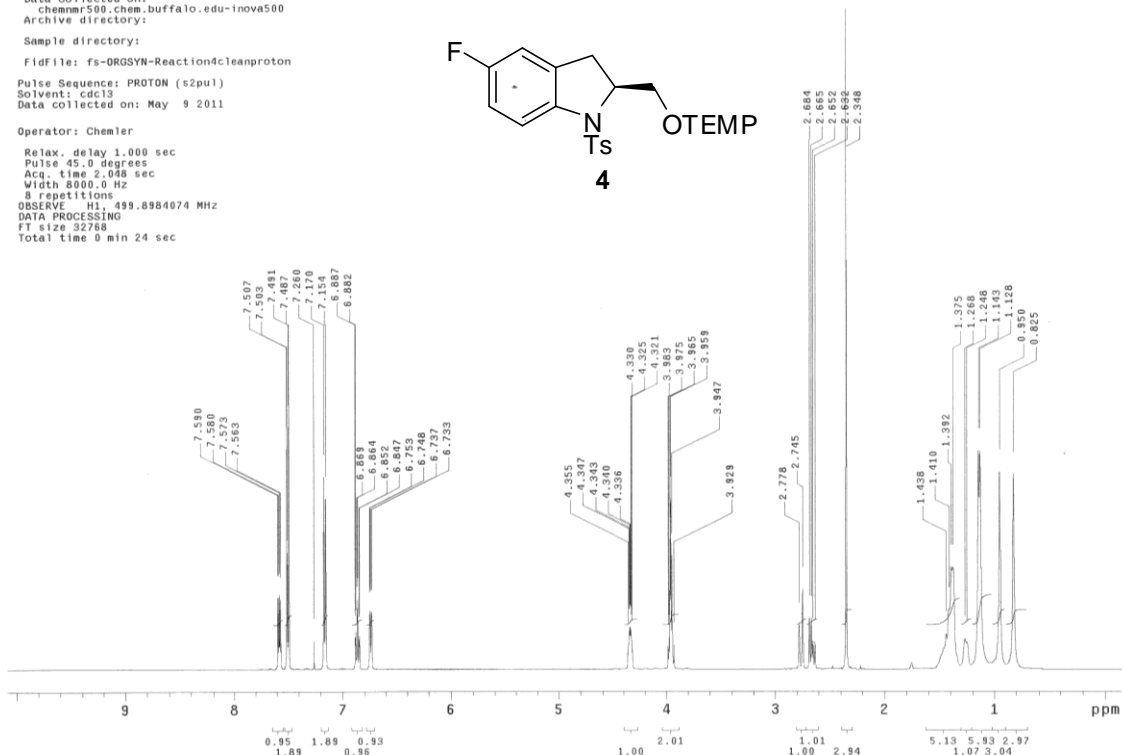
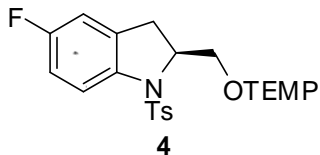
Sample Name:
 Data Collected on:
 roesy.chem.buffalo.edu-mercury300
 Archive directory:
 Sample directory:
 Fidfile: CARBON
 Pulse Sequence: CARBON (s2pul)
 Solvent: cdcl3
 Data collected on: Nov 5 2010
 Operator: Chemler
 Relax. delay 10.000 sec
 Pulse 45.0 degrees
 Acq. time 0.989 sec
 Width 18867.9 Hz
 512 repetitions
 OBSERVE C13, 75.4536375 MHz
 DECOUPLE H1, 300.0754430 MHz
 Power 38 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 32768
 Total time 1 hr, 33 min



fs-ORGSYN-Reaction4cleanproton

Sample Name:
 Data Collected on:
 chemmr500.chem.buffalo.edu-inova500
 Archive directory:
 Sample directory:
 FidFile: fs-ORGSYN-Reaction4cleanproton
 Pulse Sequence: PROTON (s2pul)
 Solvent: cdc13
 Data collected on: May 9 2011

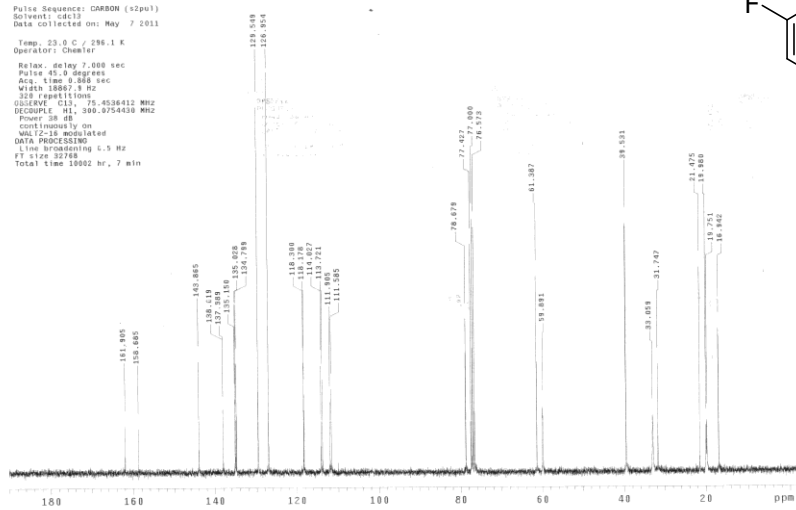
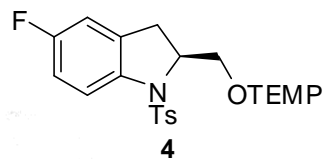
Operator: Chemler
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 2.048 sec
 Width 8000.0 Hz
 8 repetitions
 OBSERVE H1, 499.8984074 MHz
 DATA PROCESSING
 FT size 32768
 Total time 0 min 24 sec



fs-IV-reaction4

Sample Name:
 Data Collected on:
 rosey.chem.buffalo.edu-mercury380
 Archive directory:

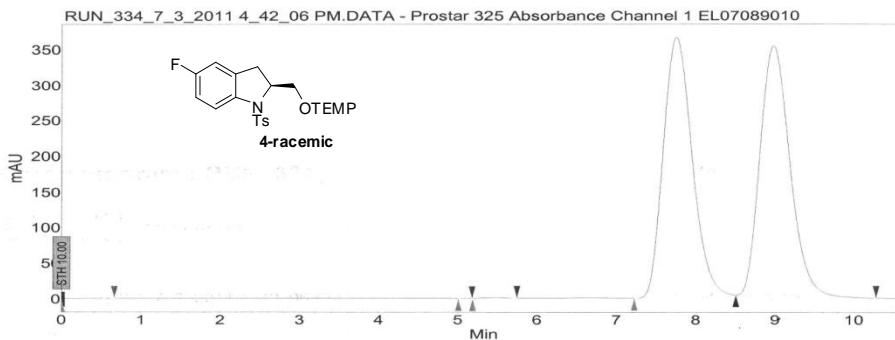
Sample directory:
 Fidfile: fs-IV-reaction4
 Pulse Sequence: CARBON (s2pul)
 Solvent: cdc13
 Data collected on: May 7 2011
 Temp. 23.0 C / 296.1 K
 Operator: Chemler
 Relax. delay 7.000 sec
 Pulse 45.0 degrees
 Acq. time 9.388 sec
 Width 18887.8 Hz
 100 repetitions
 OBSERVE C13, 75.4536412 MHz
 DECOUPLE H1, 399.8754039 MHz
 Power 28 dB
 continuous ly on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.5 Hz
 FT size 32768
 Total time 10002 hr, 7 min



Chromatogram : RUN_334_7_3_2011 4_42_06 PM_channel1

System : System_1
Method : FS-afterflush IPA for column
User : Administrator

Acquired : 7/3/2011 4:42:29 PM
Processed : 7/3/2011 4:53:20 PM
Printed : 7/3/2011 4:54:26 PM



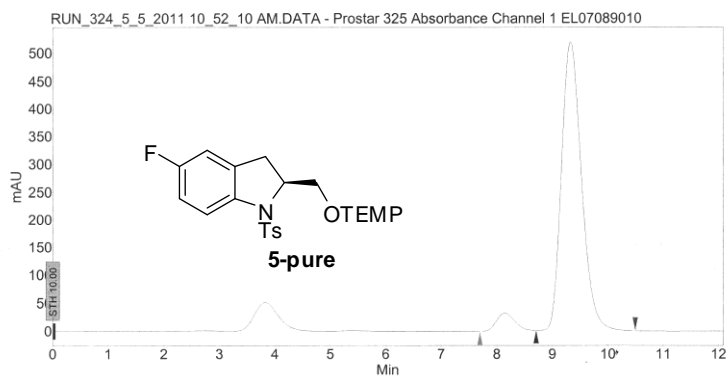
Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	0.27	0.08	0.6	0.3	0.083
2	UNKNOWN	5.09	0.01	0.5	0.0	0.015
3	UNKNOWN	5.44	0.12	1.1	0.4	0.123
4	UNKNOWN	7.75	49.55	365.9	155.1	49.546
5	UNKNOWN	8.97	50.23	353.8	157.2	50.234
Total			100.00	721.9	313.0	100.000

Chromatogram : RUN_324_5_5_2011 10_52_10 AM_channel1

System : System_1
Method : FS-afterflush IPA for column
User : Administrator

Acquired : 5/5/2011 10:52:33 AM
Processed : 5/5/2011 11:04:47 AM
Printed : 5/5/2011 11:11:24 AM



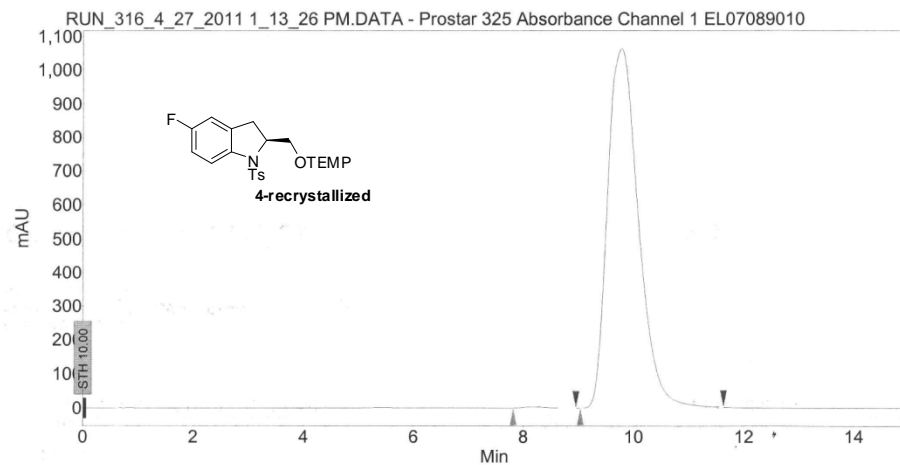
Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	8.14	5.61	32.8	13.0	5.614
2	UNKNOWN	9.32	94.39	520.1	218.5	94.386
Total			100.00	552.9	231.5	100.000

Chromatogram : RUN_316_4_27_2011 1_13_26 PM_channel1

System : System_1
 Method : FS-afterflush IPA for column
 User : Administrator

Acquired : 4/27/2011 1:13:55 PM
 Processed : 4/27/2011 1:29:00 PM
 Printed : 5/5/2011 10:28:53 AM



Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	8.17	0.23	3.5	1.6	0.231
2	UNKNOWN	9.77	99.77	1063.3	691.4	99.769
Total			100.00	1066.8	693.0	100.000

References:

- (1) Denmark, S. E.; Stiff, C. M. *The Journal of Organic Chemistry* **2000**, *65*, 5875-5878.
- (2) Masamune, S.; Lowenthal, R. E. U.S. (1994), US 5298623 A 19940329