ENANTIOSELECTIVE SILVER-CATALYZED PROPARGYLATION OF ALDIMINES

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SUPPORTING INFORMATION

I. GENERAL PROCEDURES

All reactions were set up under an atmosphere of N_2 in the absence of light. All glassware was either oven or flame-dried prior to use. Methanol (MeOH), tetrahydrofuran (THF) and dimethylformamide (DMF) were degassed with argon and then passed through two 4 x 36 inch columns of anhydrous neutral A-2 alumina (8 x 14 mesh; LaRoche Chemicals; activated under a flow of argon at 350 ºC for 12 h) to remove H_2O. All other solvents were purchased "anhydrous" commercially, or purified as described (vide infra). Flash chromatography was performed using Silica Gel 60A (170-400 mesh) from Fisher Scientific. Analytical thin-layer chromatography (TLC) was performed using Silica Gel 60 F254 precoated plates (0.25 mm thickness). Visualization was accomplished by irradiation with a UV lamp and/or staining with *p*-anisaldehyde (PAA) solutions. Melting points (m.p.) were obtained using a Mel-Temp melting point apparatus and are uncorrected. ^1H NMR spectra were recorded on Bruker GN-500 (500 MHz ^1H, 125.7 MHz ^{13}C), CRYO-500 (500 MHz ^1H, 125.7 MHz ^{13}C), DRX-400 (400 MHz ^1H, 100MHz ^{13}C, 376.5 MHz ^{19}F), or Avance-600 (600 MHz ^1H, 150 MHz ^{13}C) spectrometers. Proton chemical shifts are reported in ppm (δ) relative to internal tetramethylsilane (TMS, δ 0.00). Data is reported as follows: chemical shift, multiplicity [singlet (s), broad singlet (brs), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), doublet of triplets (dt), doublet of doublet of doublets (ddd), doublet of doublet of triplets (ddt), triplet of doublets (td), apparent quartet (aq), apparent pentet (ap), apparent doublet of triplets (adt), multiplet (m)], coupling constants [Hz], integration. Carbon chemical shifts are reported in ppm (δ) relative to the respective solvent resonance as the internal standard ($CDCl_3$, δ 77.23 ppm). Data is reported as follows: chemical shift, multiplicity [quartet (q)], coupling constants [Hz]. NMR data were collected at 25 ºC. Infrared spectra were obtained on a Mattson Instruments Galaxy 5000 spectrometer. High-resolution mass spectrometry was performed by the University of California, Irvine Mass Spectrometry Center. Optical rotations were measured with a Jasco P-1010 digital polarimeter. SFC determinations of enantiopurity were performed on a Berger Analytical instrument using a Daicel™ Chiralpak® column (AS-H or OJ-H; 120 bar, 50 °C).

Allenylboronic acid pinacol ester was prepared according to the procedure reported by Yoshida and co-workers.[1] Substrates **1a-h** and **4** were prepared according to procedures previously reported.[2] *tert*-Butyl alcohol was purchased from Fisher, distilled over CaH_2 and stored over activated 3Å Mol Sieves. All other chemicals were purchased commercially and used as received.

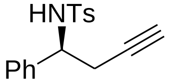
II. EXPERIMENTAL

A. REPRESENTATIVE PROCEDURE FOR PROPARGYLATION OF ALDIMINES

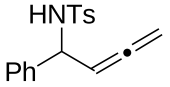
Preparation of Catalyst Stock Solution

In a glovebox, a dry 1 mL volumetric flask was charged with AgF (3.2 mg, 0.025 mmol, 1.0 equiv) and Walphos W001-1 (28 mg, 0.030 mmol, 1.2 equiv). The vial was capped with a 24/40 septum and removed from the glovebox. Anhydrous methanol was added to dilute up to the 1 mL mark. A stir bar was added and the orange solution was stirred for 25 min at RT. Stirring was discontinued and the solution allowed to settle for 5 min.

Representative Addition Procedure

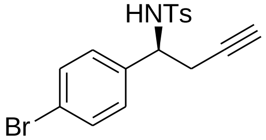


(*S*)-1-phenyl-*N*-tosyl-3-butynylamine 3a. Catalyst stock solution (400 μL, 25 mM, 10 mol % Ag) was transferred to a 1.0 mL conical vial sealed with a screw top cap fit with a septum and equipped with a triangular stir bar. The methanol was carefully removed under reduced pressure using a diaphragm pump (560 mmHg to 20 mmHg). The pressure was then further reduced (0.5 Torr) to remove any trace solvent. After 45 min, the vial was back-filled with N_2 and THF (400 μL) was added followed by *tert*-butanol (11 μL, 0.11 mmol, 1.1 equiv). Phenylaldimine **1a** (26 mg, 0.10 mmol, 1.0 equiv) and potassium *tert*-butoxide (2.2 mg, 0.020 mmol, 0.20 equiv) were added under a flow of N_2. The reaction was stirred at RT for 10 min to dissolve the imine and was then cooled to –20 ºC for 5 min. Allenylboronic acid pinacol ester (36 μL, 0.20 mmol, 2.0 equiv) was added via syringe. The N_2 line was removed and the reaction was stirred at –20 ºC for 8 h. The crude reaction mixture was filtered through a plug of silica gel (20 mL) with 100% Et_2O to remove the catalyst. Et_2O was removed in vacuo and the resulting crude residue was purified by silica gel chromatography (25-60% Et_2O in hexane, 1% TEA) to give the desired product **3a** as white solid (91%). Spectral data was consistent with literature values.[3] **TLC R_f** = 0.2 (4:1 hexane/EtOAc, stains pink with PAA); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.62 (d, *J* = 8.2, 2H), 7.24–7.10 (m, 7H), 5.26 (d, *J* = 6.9, 1H) 4.50 (aq, *J* = 6.4, 1H), 2.63 (dd, *J* = 6.0, 2.5, 2H), 2.38 (s, 3H), 1.97 (d, *J* = 2.5, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 143.6, 139.4, 137.4, 129.7, 128.7, 128.1, 127.4, 126.8, 79.3, 72.4, 55.9, 27.4, 21.7; **$[\alpha]^{23}_{D}$** –57.8 (*c* 0.79, $CHCl_3$); **SFC** analysis (AS-H, 20.0% IPA, 3 mL/min, 215 nm) indicated 96% ee: t_R (minor) = 4.42 min, t_R (major) = 5.33 min.

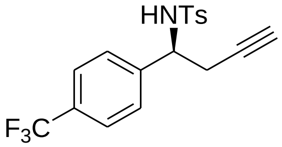


1-phenyl-*N*-tosyl-2,3-butadienylamine 2a was produced in small quantities as a side product in certain propargylation reactions during optimization of the reaction conditions A slow column is sufficient to separate the two products. **TLC R$_f$** = 0.2 (4:1 hexane/EtOAc, stains pink with PAA); **m.p.** 86–86 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.64 (d, *J* = 8.5, 2H), 7.23 (m, 7H), 5.25 (m, 1H), 4.98 (s, 2H), 4.82 (m, 1H), 4.74 (m, 1H), 2.40 (s, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 207.0, 143.4, 140.1, 137.9, 129.6, 128.8, 128.1, 127.5, 127.2, 92.9, 79.7, 55.8, 21.7; **IR** (film, cm^{-1}) 3417, 1957, 1637, 1326, 1159; **HRMS** (TOF MS ES+) *m*/*z* calculated for $[C_{17}H_{17}NO_2S + Na]^+$ 322.0878, found 322.0869.

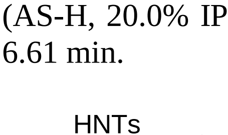
B. Characterization Data for Products



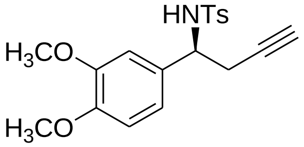
(*S*)-1-(4-bromophenyl)-*N*-tosyl-3-butynylamine 3b was isolated as an off-white solid (73%): **TLC R$_f$** = 0.2 (4:1 hexane/EtOAc, stains pink with PAA); **m.p.** 120–123 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.59 (d, *J* = 8.3, 2H), 7.33 (d, *J* = 8.4, 2H), 7.19 (d, *J* = 8.1, 2H), 7.03 (d, *J* = 8.3, 2H), 5.15 (d, *J* = 7.1, 1H), 4.47 (aq, *J* = 6.3, 1H), 2.62 (ddd, *J* = 16.9, 6.1, 2.6, 1H), 2.57 (ddd, *J* = 16.9, 5.8, 2.6, 1H), 2.41 (s, 3H), 2.01 (t, *J* = 2.6, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 143.9, 138.3, 137.2, 131.7, 129.7, 128.6, 127.4, 122.1, 78.7, 72.9, 55.2, 27.3, 21.7; **IR** (film, cm^{-1}) 3273, 3051, 2918, 1597, 1491, 1317, 1161, 1072; **HRMS** (TOF MS ES+) *m*/*z* calculated for $[C_{17}H_{16}BrNO_2S + Na]^+$ 399.9983, found 399.9997; **$[\alpha]^{17}_{D}$** –68.4 (*c* 0.46, $CHCl_3$); **SFC** analysis (AS-H, 20.0% IPA, 3 mL/min, 215 nm) indicated 98% ee: t_R (minor) = 6.34 min, t_R (major) = 8.47 min.



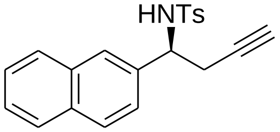
(*S*)-1-(4-(trifluoromethyl)phenyl)-*N*-tosyl-3-butynylamine 3c was isolated as an off-white solid (96%): **TLC R$_f$** = 0.2 (4:1 hexane/EtOAc, stains pink with PAA); **m.p.** 150–153 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.56 (d, *J* = 8.2, 2H), 7.43 (d, *J* = 8.2, 2H), 7.26 (d, *J* = 8.1, 2H), 7.14 (d, *J* = 8.1, 2H), 5.35 (d, *J* = 7.3, 1H), 4.58 (aq, *J* = 6.4, 1H), 2.66 (ddd, *J* = 17.0, 6.0, 2.6, 1H), 2.60 (ddd, *J* = 16.9, 5.7, 2.6, 1H), 2.37 (s, 3H), 2.03 (t, *J* = 2.6, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 143.9, 143.2, 137.1, 130.2 (q, *J* = 32.4, 1C), 129.7, 127.33, 127.32, 125.5 (q, *J* = 3.7, 1C), 124.1 (q, *J* = 272.1, 1C), 78.5, 73.1, 55.4, 27.3, 21.6; **IR** (film, cm^{-1}) 3286, 3248, 2926, 1427, 1327, 1161, 1113, 1068; **HRMS** (TOF MS ES+) *m*/*z* calculated for $[C_{18}H_{16}F_3NO_2S + Na]^+$ 390.0752, found 390.0745; **$[\alpha]^{17}_{D}$** –46.6 (*c* 0.76, $CHCl_3$); **SFC** analysis (AS-H, 20.0% IPA, 3 mL/min, 215 nm) indicated 96% ee: t_R (minor) = 4.46 min, t_R (major) = 6.61 min.



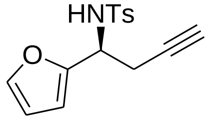
(*S*)-1-(2-bromophenyl)-*N*-tosyl-3-butynylamine 3d was isolated as an off-white solid (74%): **TLC R$_f$** = 0.1 (4:1 hexane/EtOAc, stains pink with PAA); **m.p.** 135–138 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.64 (d, *J* = 8.3, 2H), 7.44 (dd, *J* = 8.0, 1.0, 1H), 7.28 (dd, *J* = 7.8, 1.5, 1H), 7.20–7.14 (m, 3H), 7.06 (td, *J* = 7.6, 1.6, 1H), 5.37 (d, *J* = 7.3, 1H), 4.93 (dt, *J* = 7.2, 5.8, 1H), 2.69 (ddd, *J* = 17.0, 5.6, 2.7, 1H), 2.57 (ddd, *J* = 17.0, 5.9, 2.6, 1H), 2.36 (s, 3H), 2.00 (t, *J* = 2.6, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 143.7, 138.3, 136.9, 133.0, 129.7, 129.4, 128.8, 127.6, 127.4, 122.4, 78.5, 72.8, 54.7, 26.2, 21.7; **IR** (film, cm^{-1}) 3284, 3068, 2919, 1597, 1421, 1321, 1161, 1081; **HRMS** (TOF MS ES+) *m/z* calculated for $[C_{17}H_{16}BrNO_2S + Na]^+$ 399.9983, found 399.9985; **$[\alpha]^{23}_D$** –44.3 (*c* 0.53, $CHCl_3$); **SFC** analysis (OJ-H, 15.0% IPA, 3 mL/min, 215 nm) indicated 95% ee: t_R (major) = 3.69 min, t_R (minor) = 4.35 min.



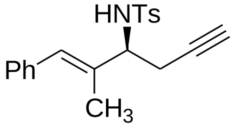
(*S*)-1-(3,4-dimethoxyphenyl)-*N*-tosyl-3-butynylamine 3e was synthesized with the general method substituting DMF for THF.[4] The title compound was isolated after 16 h as a white solid (99%): **TLC R$_f$** = 0.1 (4:1 hexane/EtOAc, stains purple with PAA); **m.p.** 131–134 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.61 (d, *J* = 8.2, 2H), 7.19 (d, *J* = 8.1, 2H), 6.74–6.69 (m, 2H), 6.60 (s, 1H), 5.14 (d, *J* = 6.7, 1H), 4.46 (q, *J* = 6.3, 1H), 3.84 (s, 3H), 3.73 (s, 3H), 2.64 (dd, *J* = 6.7, 2.6, 2H), 2.39 (s, 3H), 2.01 (t, *J* = 2.6, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 149.0, 148.9, 143.6, 137.6, 131.8, 129.6, 127.4, 119.1, 111.0, 109.9, 79.6, 72.4, 56.1, 55.8, 55.7, 27.4, 21.7; **IR** (film, cm^{-1}) 3423, 3288, 3937, 1639, 1517, 1454, 1326, 1265, 1159; **HRMS** (TOF MS ES+) *m/z* calculated for $[C_{19}H_{21}NO_4S + Na]^+$ 382.1089, found 382.1094; **$[\alpha]^{23}_D$** –52.7 (*c* 1.46, $CHCl_3$); **SFC** analysis (AS-H, 20.0% IPA, 3 mL/min, 215 nm) indicated 90% ee: t_R (minor) = 5.10 min, t_R (major) = 11.53 min.



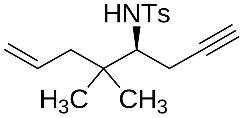
(*S*)-1-(2-naphthyl)-*N*-tosyl-3-butynylamine 3f was isolated as a white solid (81%): **TLC R$_f$** = 0.2 (4:1 hexane/EtOAc, stains purple with PAA); **m.p.** 140–142 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.78–7.73 (m, 1H) 7.70–7.65 (m, 2H), 7.58 (d, *J* = 8.2, 2H), 7.54 (s, 1H), 7.47–7.42 (m, 2H), 7.25 (dd, *J* = 8.5, 1.6, 1H), 7.04 (d, *J* = 8.1, 2H), 5.39 (d, *J* = 7.2, 1H), 4.67 (aq, *J* = 6.5, 1H), 2.73 (dd, *J* = 6.1, 2.6, 2H), 2.42 (s, 3H), 1.97 (t, *J* = 2.6, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 143.6, 137.4, 136.4, 133.1, 133.0, 129.5, 128.6, 128.1, 127.7, 127.3, 126.41, 126.35, 126.1, 124.4, 79.3, 72.5, 56.1, 27.4, 21.5; **IR** (film, cm^{-1}) 3286, 3052, 2920, 1599, 1423, 1329, 1159, 1070; **HRMS** (TOF MS ES+) *m/z* calculated for $[C_{21}H_{19}NO_2S + Na]^+$ 372.1034, found 372.1035; **$[\alpha]^{17}_D$** –82.5 (*c* 1.23, $CHCl_3$); **SFC** analysis (AS-H, 20.0% IPA, 3 mL/min, 215 nm) indicated 96% ee: t_R (minor) = 7.32 min, t_R (major) = 11.66 min.



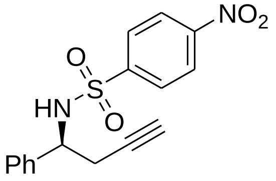
(*S*)-1-(2-furyl)-*N*-tosyl-3-butynylamine 3g was isolated as an off-white solid (93%): **TLC R$_f$** = 0.2 (4:1 hexane/EtOAc, stains purple with PAA); **m.p.** 86–89 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.70 (d, *J* = 8.2, 2H), 7.27–7.21 (m, 3H) 6.20 (dd, *J* = 3.1, 1.8, 1H), 6.13 (d, *J* = 3.2, 1H), 5.15 (d, *J* = 8.7, 1H), 4.61 (adt, *J* = 8.5, 6.0, 1H), 2.74 (ddd, *J* = 16.9, 4.9, 2.6, 1H), 2.66 (ddd, *J* = 16.8, 6.7, 2.6, 1H), 2.41 (s, 3H), 1.98 (t, *J* = 2.6, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 151.7, 143.7, 142.5, 137.6, 129.8, 127.3, 110.4, 107.9, 78.9, 72.1, 50.2, 25.3, 21.7; **IR** (film, cm^{-1}) 3294, 3255, 3045, 2985, 1597, 1454, 1329, 1161, 1072, 1011; **HRMS** (TOF MS ES+) *m/z* calculated for $[C_{15}H_{15}NO_3S + Na]^+$ 312.0670, found 312.0663; **$[\alpha]^{17}_D$** –57.1 (*c* 0.92, $CHCl_3$); **SFC** analysis (AS-H, 20.0% IPA, 3 mL/min, 215 nm) indicated 97% ee: t_R (minor) = 3.61 min, t_R (major) = 3.95 min.



(*S*,E)-2-methyl-1-phenyl-*N*-tosyl-1,5-hexenynyl-3-amine 3h was isolated as an off-white solid (47%): **TLC R$_f$** = 0.2 (4:1 hexane/EtOAc, stains pink with PAA); **m.p.** 86–89 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.76 (d, *J* = 8.2, 2H), 7.29 (t, *J* = 7.6, 2H), 7.24 (d, *J* = 8.1, 2H), 7.20 (t, *J* = 7.5, 1H), 7.05 (d, *J* = 7.5, 2H), 6.33 (s, 1H), 5.01 (d, *J* = 7.0, 1H), 4.02 (q, *J* = 6.6, 1H), 2.56 (ddd, *J* = 16.8, 6.1, 2.6, 1H), 2.49 (ddd, *J* = 16.9, 6.6, 2.6, 1H), 2.39 (s, 3H), 2.04 (t, *J* = 2.6, 1H); **^{13}C NMR** (CDCl$_3$, 125 MHz) δ 143.7, 137.6, 137.0, 134.7, 129.8, 129.1, 128.8, 128.2, 127.6, 126.9, 79.3, 72.3, 59.4, 24.7, 21.7, 14.1; **IR** (film, cm^{-1}) 3286, 3059, 2922, 1441, 1329, 1159, 1072; **HRMS** (TOF MS ES+) *m*/*z* calculated for [$C_{20}H_{21}NO_2S$ + Na]$^+$ 362.1192, found 362.1225; **[α]^{17}$_D$** –36.4 (*c* 0.78, CHCl$_3$); **SFC** analysis (AS-H 20.0% IPA, 3 mL/min, 215 nm) indicated 89% ee: t$_R$ (minor) = 3.88 min, t$_R$ (major) = 5.71 min.



(*S*)-5,5-dimethyl-*N*-tosyloct-7-en-1-yn-4-amine 3i was isolated as an off-white solid (40%): **TLC R$_f$** = 0.3 (4:1 hexane/EtOAc, stains purple with PAA); **m.p.** 69–70 °C; **^{1}H NMR** (CDCl$_3$, 500 MHz) δ 7.78 (d, *J* = 8.1, 2H), 7.19 (d, *J* = 7.9, 2H), 5.76 (ap, *J* = 7.4, 1H), 5.05 (d, *J* = 4.7, 1H), 5.00 (d, *J* = 16.9, 1H), 4.91 (d, *J* = 10.2, 1H), 3.17 (ddd, *J* = 9.9, 6.3, 3.1, 1H), 2.42 (s, 3H), 2.29 (dt, *J* = 17.4, 2.8, 1H), 2.09 (ddd, *J* = 17.4, 6.3, 2.8, 1H), 2.05 (d, *J* = 7.2, 2H), 1.96 (t, *J* = 2.6, 1H), 0.91 (s, 3H), 0.90 (s, 3H); **^{13}C NMR** (CDCl$_3$, 125 MHz) δ 143.6, 138.4, 134.4, 129.8, 127.3, 118.3, 80.5, 72.8, 58.1, 44.0, 38.6, 24.3, 24.0, 21.8, 20.2; **IR** (film, cm^{-1}) 3292, 3074, 2967, 1427, 1331, 1159, 1092; **HRMS** (TOF MS ES+) *m*/*z* calculated for [$C_{17}H_{23}NO_2S$ + Na]$^+$ 328.1347, found 328.1337; **[α]^{24}$_D$** 44.2 (*c* 0.24, CHCl$_3$); **SFC** analysis (OD-H 5.0% IPA, 2.5 mL/min, 215 nm) indicated 74% ee: t$_R$ (major) = 6.04 min, t$_R$ (minor) = 6.99 min.



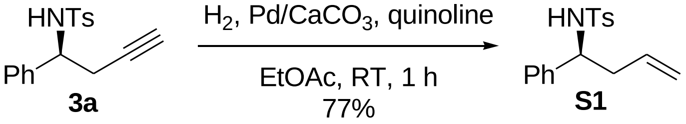
(*S*)-1-phenyl-*N*-nosyl-3-butynylamine 5 was synthesized using the general method with an additional 2.0 equivalents of allenylboronic acid pinacol ester added after 4 hours. The title compound was isolated after 16 h as a white solid (70%): **TLC R$_f$** = 0.1 (4:1 hexane/EtOAc, stains pink with PAA); **m.p.** 147–149 °C; **^{1}H NMR** (CDCl$_3$, 500 MHz) δ 8.14 (d, *J* = 8.8, 2H), 7.80 (d, *J* = 8.8, 2H), 7.22–7.14 (m, 3H), 7.10 (d, *J* = 7.0, 2H), 5.43 (d, *J* = 7.1, 1H), 4.65 (aq, *J* = 6.4, 1H), 2.74 (ddd, *J* = 17.0, 5.9, 2.6, 1H), 2.64 (ddd, *J* = 17.0, 6.2, 2.6, 1H), 2.06 (t, *J* = 2.6, 1H); **^{13}C NMR** (CDCl$_3$, 125 MHz) δ 149.9, 146.4. 138.5, 128.8, 128.55, 128.52, 126.8, 124.1, 78.8, 73.0, 56.3, 27.6; **IR** (film, cm^{-1}) 3284, 3247, 3099, 2926, 1525, 1350, 1306, 1165, 1086; **HRMS** (TOF MS ES-) *m*/*z* calculated for [$C_{16}H_{14}N_2O_4S$ – H]$^-$ 329.0596, found 329.0606; **[α]^{17}$_D$** –33.6 (*c* 0.43, CHCl$_3$); **SFC** analysis (AS-H 20.0% IPA, 3 mL/min, 215 nm) indicated 92% ee: t$_R$ (minor) = 3.18 min, t$_R$ (major) = 3.45 min.

C. METHOD FOR THE PREPARATION OF RACEMIC STANDARDS

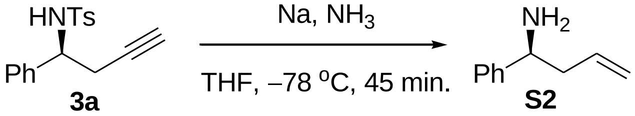
In a glovebox, an oven-dried vial was charged with AgBF$_4$ (3.2 mg, 0.025 mmol, 1.0 equiv), tri(*o*-tolyl)phosphine (28 mg, 0.030 mmol, 1.2 equiv) and a stir bar. The vial was capped with a screw top cap fitted with a septum and removed from the glovebox. Anhydrous CH$_2$Cl$_2$ (0.8 mL), *tert*-butanol (21 µL, 0.22 mmol, 1.1 equiv) and allenylboronic acid pinacol ester (72 µL, 0.40 mmol, 2.0 equiv) were added and the solution stirred. Benzaldimine (0.20 mmol, 1.0 equiv) and KO*t*-Bu (4.5 mg, 0.020 mmol, 0.20 equiv) were added under a flow of N$_2$ and the reaction was stirred at RT for 24 h upon which the crude reaction mixture was dry-loaded onto a silica gel column for purification (5-30% EtOAc in hexane, 1% TEA).

D. PROOF OF STEREOCHEMISTRY

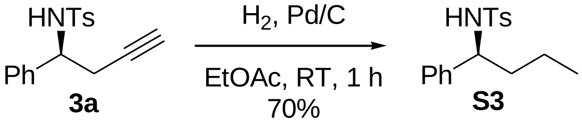
(*S*)-1-Phenyl-*N*-tosyl-3-butynylamine **3a** was derivatized for comparison of optical rotation to values reported in the literature. Three derivatives were prepared as there is inconsistency in the literature. Reduction to homoallylic sulfonamide **S1** and amine **S2** and comparison to literature values for optical rotations for those compounds were both consistent with formation of (*S*)-**3a** when the W001-1 enantiomer of Walphos-1 was employed. However, reduction to sulfonamide **S3** and comparison to the literature values was consistent with formation of (*R*)-**3a**. We hypothesize that the value reported for the optical rotation of (*S*)-**S3** is incorrect, and assign the absolute stereochemistry of **3a** using **S1** and **S2** as references.



(*S*)-1-Phenyl-*N*-tosyl-3-butynylamine **3a** was reduced to (*S*)-1-phenyl-*N*-tosyl-3-butenylamine **S1** using a modified procedure from Kozmin and co-workers.[5] A 25-mL round bottom flask equipped with a stir bar was charged with homopropargyl sulfonamide **3a** (60 mg, 0.20 mmol, 1.0 equiv) and EtOAc (2mL) followed by Lindlar's catalyst (22 mg, 0.010 mmol, 5 mol %, 5% wt) and quinoline (73 μL, 0.62 mmol, 3.11 equiv). The reaction was prestirred under N_2. After 30 min the, N_2 line was removed and a balloon filled with H_2 was added to the reaction. The flask was evacuated and back-filled with H_2 from the balloon three times to ensure saturation of the atmosphere with hydrogen. The reaction was stirred at RT until complete by TLC (1 h). The reaction was then filtered through a pad of celite with washing with EtOAc. The solvent was removed in vacuo and the residue was purified by column chromatography (5-30% EtOAc in hexane, 1% TEA) followed by a recrystallization from CH_2Cl_2/hexane to afford the desired product as an off-white solid (70%). Spectroscopic data for **S1** was consistent with literature values.[6] **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.55 (d, *J* = 8.3, 2H), 7.22–7.12 (m, 5H), 7.10–7.04 (m, 2H), 5.57–5.44 (m, 1H), 5.11–5.01 (m, 2H), 4.77 (d, *J* = 6.4, 1H), 4.38 (q, *J* = 6.6, 1H), 2.53–2.39 (m, 2H), 2.37 (s, 3H); **$[\alpha]^{24}_D$** –63.1 (*c* 0.43, $CHCl_3$); **SFC** analysis (AS-H 20.0% IPA, 3 mL/min, 215 nm) indicated 98% ee: t_R (minor) = 3.59 min, t_R (major) = 4.36 min. Absolute configuration was assigned by comparing data available for (*R*)-1-phenyl-*N*-tosyl-3-butenylamine: **$[\alpha]^{24}_D$** +62.4 (*c* 1.00, $CHCl_3$) corresponding to 97% ee.[7]



(*S*)-1-phenyl-*N*-tosyl-3-butynylamine **3a** was reduced to (*S*)-1-phenyl-3-butenylamine **S2** using a modified procedure from Szabó and co-workers.[8] A 25-mL 3-neck round bottom flask equipped with a stirbar and a condenser was charged with a solution of **3a** (76 mg, 0.25 mmol, 1.0 equiv). The reaction apparatus was cooled to –78 °C and ammonia (5 mL) was condensed after being passed through a tube packed with dri-rite. Sodium was added under a flow of nitrogen in small pieces until the blue color became persistent (100 mg). The reaction was stirred for 45 min. at which time methanol was added until the solution became clear and colorless. The reaction was allowed to warm to room temperature over 3 h at which time MeOH was removed in vacuo. The crude residue was partitioned between water and CH_2Cl_2. The layers were separated and the aqueous layer was washed twice with additional CH_2Cl_2. The organics were combined and dried over $MgSO_4$ and concentrated. The residue was purified by column chromatography (10-30% MeOH in CH_2Cl_2, stain with $KMnO_4$) to afford the desired product as a light yellow oil (10 mg, 26%). Spectroscopic data for the product was consistent with literature values.[8] **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.39–7.29 (m, 4H), 7.29–7.20 (m, 1H), 5.80–5.67 (m, 1H), 5.17–5.04 (m, 2H), 4.01 (at, *J* = 6.7, 1H), 2.55–2.29 (m, 2H), 2.35 (brs, 2H); **$[\alpha]^{23}_D$** –21.6 (*c* 0.35, $CHCl_3$); Absolute configuration was assigned by comparing data available for (*R*)-1-phenyl-3-butenylamine: **$[\alpha]^{23}_D$** +29 (*c* 0.99, $CHCl_3$).[8]



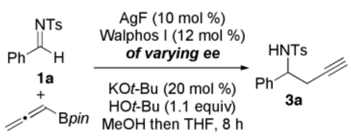
(*S*)-1-Phenyl-*N*-tosyl-3-butynylamine **3a** was reduced to (*S*)-1-phenyl-*N*-tosyl-butylamine **S3** using a modified procedure from Stoltz and co-workers.[9] A 10-mL round bottom flask equipped with a stir bar was charged with homopropargyl sulfonamide **3a** (20 mg, 0.067 mmol, 1.0 equiv) and EtOAc (1 mL) followed by Pd/C (14 mg, 0.0076 mmom, 0.010 equiv, 5% wt). The flask was evacuated and back-filled with H_2 from a balloon three times to ensure saturation of the atmosphere with hydrogen. The reaction was stirred at RT until complete by TLC (1hr). The reaction was then filtered through a pad of silica gel topped with celite with EtOAc. The solvent was removed in vacuo and the residue was purified by column chromatography (5-30% EtOAc in hexane, 1% TEA) to afford the desired product as an off-white solid (17 mg, 77%). Spectroscopic data for butanyl sulfonamide **S3** was consistent with literature values.[10] **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.52 (d, *J* = 8.3, 2H), 7.16–7.07 (m, 5H), 7.03–6.97 (m, 2H), 4.98 (d, *J* = 7.3, 1H), 4.27 (q, *J* = 7.3, 1H), 2.35 (s, 3H), 1.81–1.57 (m, 2H), 1.34–1.07 (m, 2H), 0.83 (t, *J* = 7.3, 3H); **$[\alpha]^{23}_D$** –21.7 (*c* 0.50, $CHCl_3$); **SFC** analysis (AS-H 20.0% IPA, 3 mL/min, 215 nm) indicated 96% ee: t_R (minor) = 3.45 min, t_R (major) = 4.27 min. Optical rotation data obtained to assign absolute configuration was not in agreement with literature value reported for (*S*)-1-phenyl-*N*-tosyl-butylamine: **$[\alpha]^{20}_D$** +37.0 (*c* 0.26, $CHCl_3$) corresponding to 66% ee.[11]

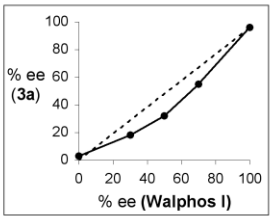
E. NON-LINEAR STUDY

Catalyst stock solutions were prepared following the procedure described in section II.A; one containing Walphos W001-1 and the other containing the enantiomer, Walphos W001-2. Different volumes of these stock solutions were mixed to provide catalyst of varying ee (Table 1). For example 200 μL of W001-1 stock solution and 200 μL of W001-2 were combined in order to provide catalyst of 0% ee. The mixture was allowed to stir at RT for 5 min and the reaction was carried out following the general procedure.

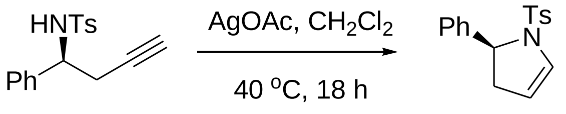
Table 1. Design of the Non-Linear Experiment.

W001-1		W001-2		ee of catalyst (%)	ee of product (%)
Vol (μL)	%	Vol (μL)	%		
200	50	200	50	0	3
260	65	140	35	30	18
300	75	100	25	50	32
60	15	340	85	70	54
400	100	0	0	100	97





F. CYCLIZATION OF PROPARGYL SULFONAMIDE 3A



3a 97% ee

6 97% ee

Homopropargyl sulfonamide **3a** was cyclized to 2-pyrroline **6** based on a reaction scheme reported by Knölker.[12] In a glovebox, an oven-dried vial was charged with AgOAc (33 mg, 0.020 mmol, 1.0 equiv) and a stir bar. The vial was capped with a screw top cap fitted with a septum and removed from the glovebox. Anhydrous CH_2Cl_2 (1.0 mL) was added via syringe and the slurry was stirred for 5 min. Homopropargyl sulfonamide **3a** was then added by under a flow of N_2. The N_2 line was removed and the reaction was stirred sealed at 40 ºC. After 18h, silica gel was added to the crude reaction mixture and the solvent was removed in vacuo. The crude was then purified by column chromatography (5-30% EtOAc in hexane, 1% TEA) to afford an off-white solid (99%): **TLC R$_f$** = 0.4 (4:1 hexane/EtOAc, stains yellow with PAA); **m.p.** 86–86 ºC; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.62 (d, *J* = 8.1, 2H), 7.34–7.22 (m, 5H) 6.52 (dt, *J* = 4.2, 2.1, 1H), 5.11 (dt, *J* = 4.2, 2.5, 1H), 4.73 (dd, *J* = 10.9, 6.3, 1H), 2.91 (ddt, *J* = 16.6, 10.9, 2.4, 1H), 2.47 (ddt, *J* = 16.6, 6.3, 2.2, 1H), 2.43 (s, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 143.9, 142.9, 134.2, 131.1, 129.8, 128.8, 127.9, 127.8, 126.6, 110.4, 63.2, 40.9, 21.4; **IR** (film, cm^{-1}) 3417, 1957, 1637, 1326, 1159; **HRMS** (TOF MS ES+) *m/z* calculated for $[C_{17}H_{17}NO_2S + Na]^+$ 322.0878, found 322.0870; **$[\alpha]^{17}_D$** –328.2 (*c* 0.53, $CHCl_3$); **SFC** analysis (AS-H, 20.0% IPA, 3 mL/min, 215 nm) indicated 97% ee: t_R (minor) = 4.00 min, t_R (major) = 4.71 min.

III. REFERENCES

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(2) (a) Imine **1a** was prepared according to the procedure reported by F. Chemla, V. Hebbe and J.-F. Normant, *Synthesis*, 2000, **1**, 75; (b) Imines **1b-1h** were prepared according to the procedure reported by W. B. Jennings and C. J. Lovely, *Tetrahedron*, 1991, **47**, 5561; (c) Imine **4** was prepared according to the procedure reported by K. M. Partridge, M. E. Anzovino and T. P. Yoon, *J. Am. Chem. Soc.*, 2008, **130**, 2920.
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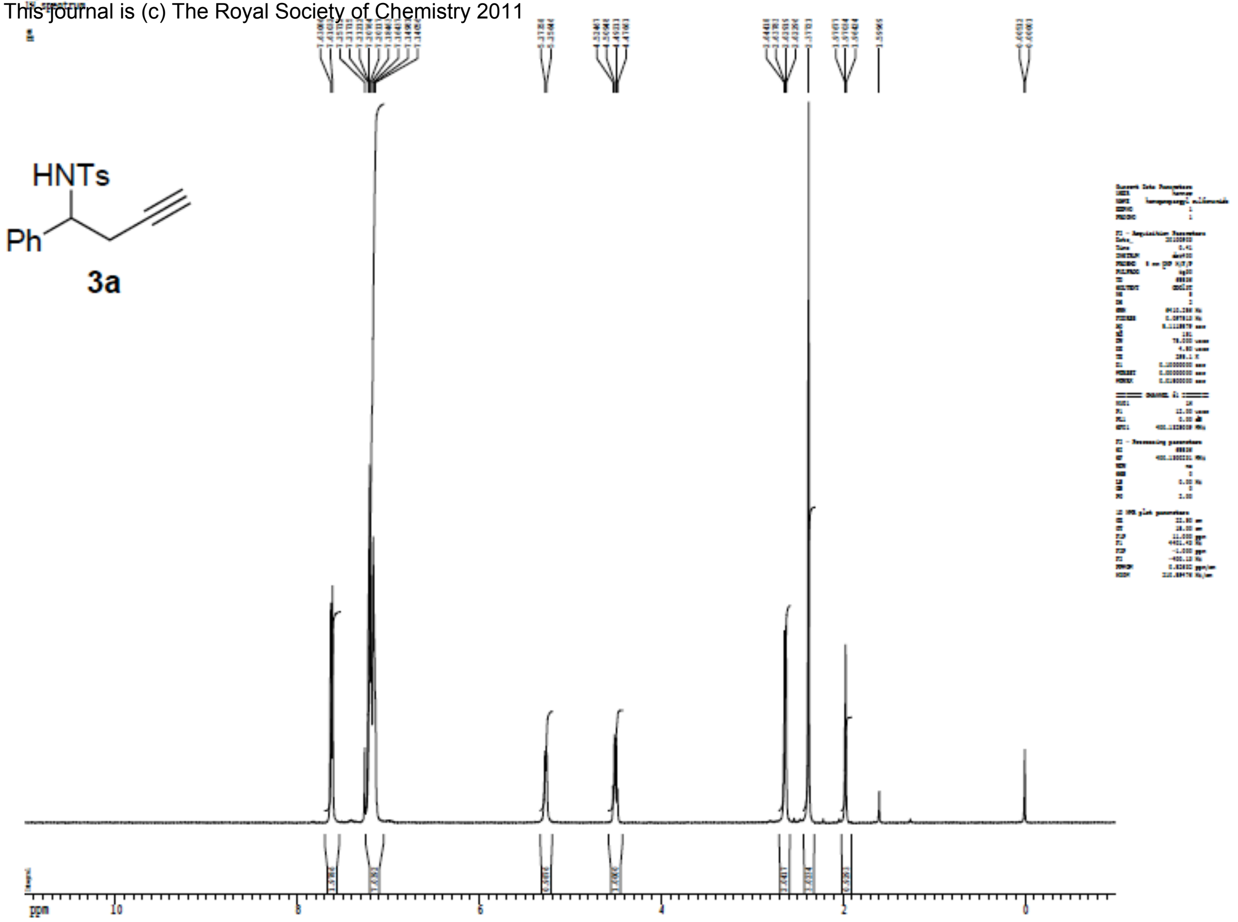
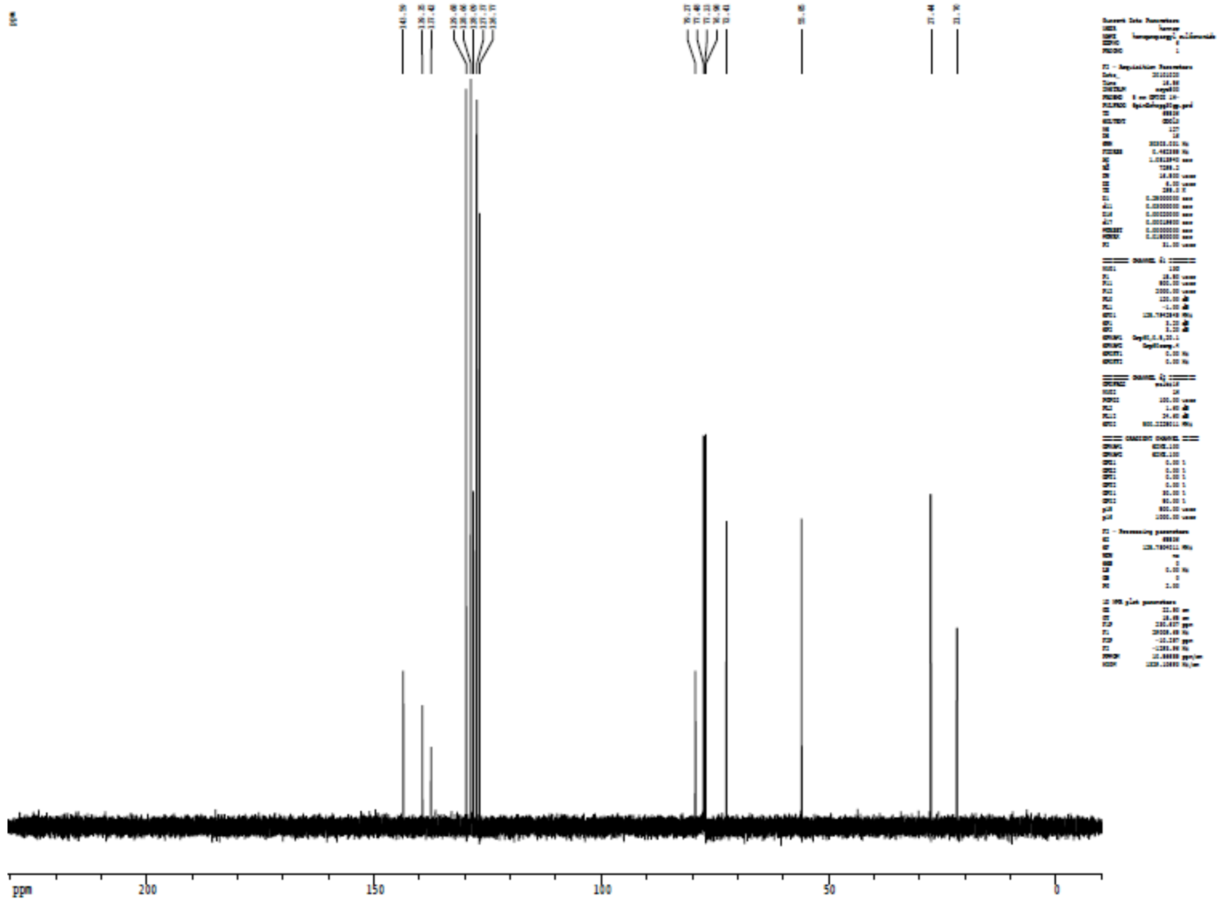
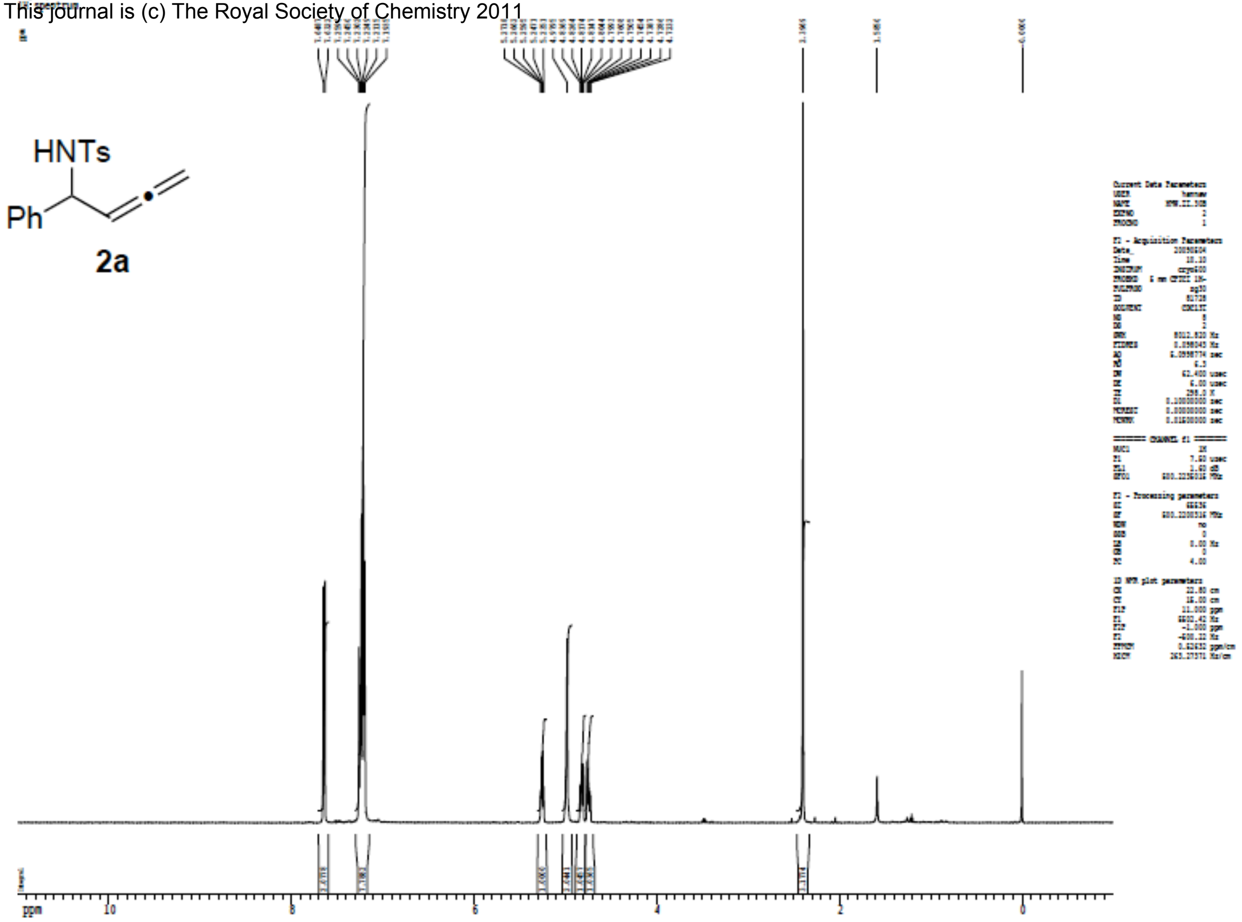
(11) G.-N. Ma, T. Zhang and M. Shi, *Org. Lett.*, 2009, **11**, 875.
(12) R. Martin, B. M. Jäger, S. Richter, R. Fedorov, D. J. Manstein, H. O. Gutzeit and H.-J. Knölker, *Angew. Chem. Int. Ed.*, 2009, **48**, 8042.



Z-restored spin-echo 13C spectrum with 1H decoupling





2a

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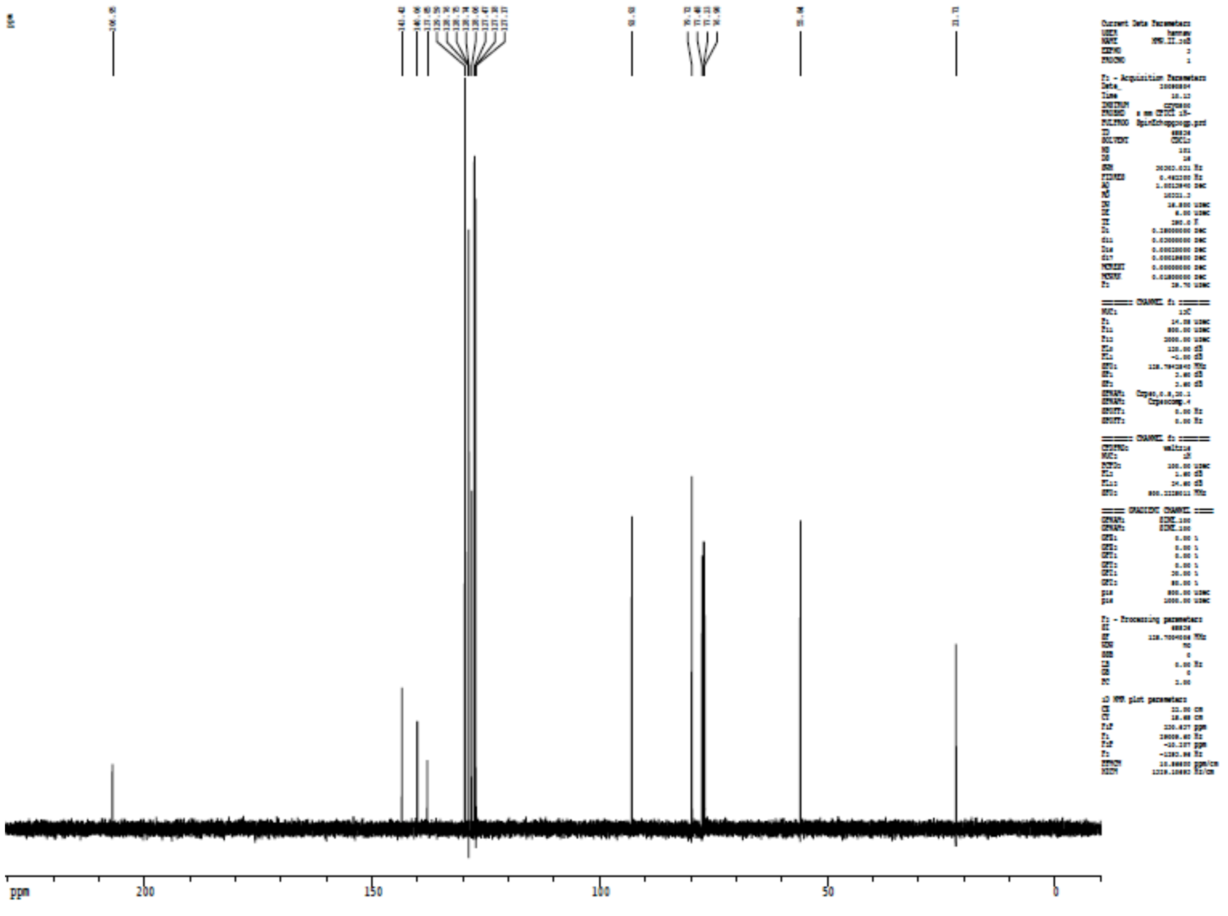

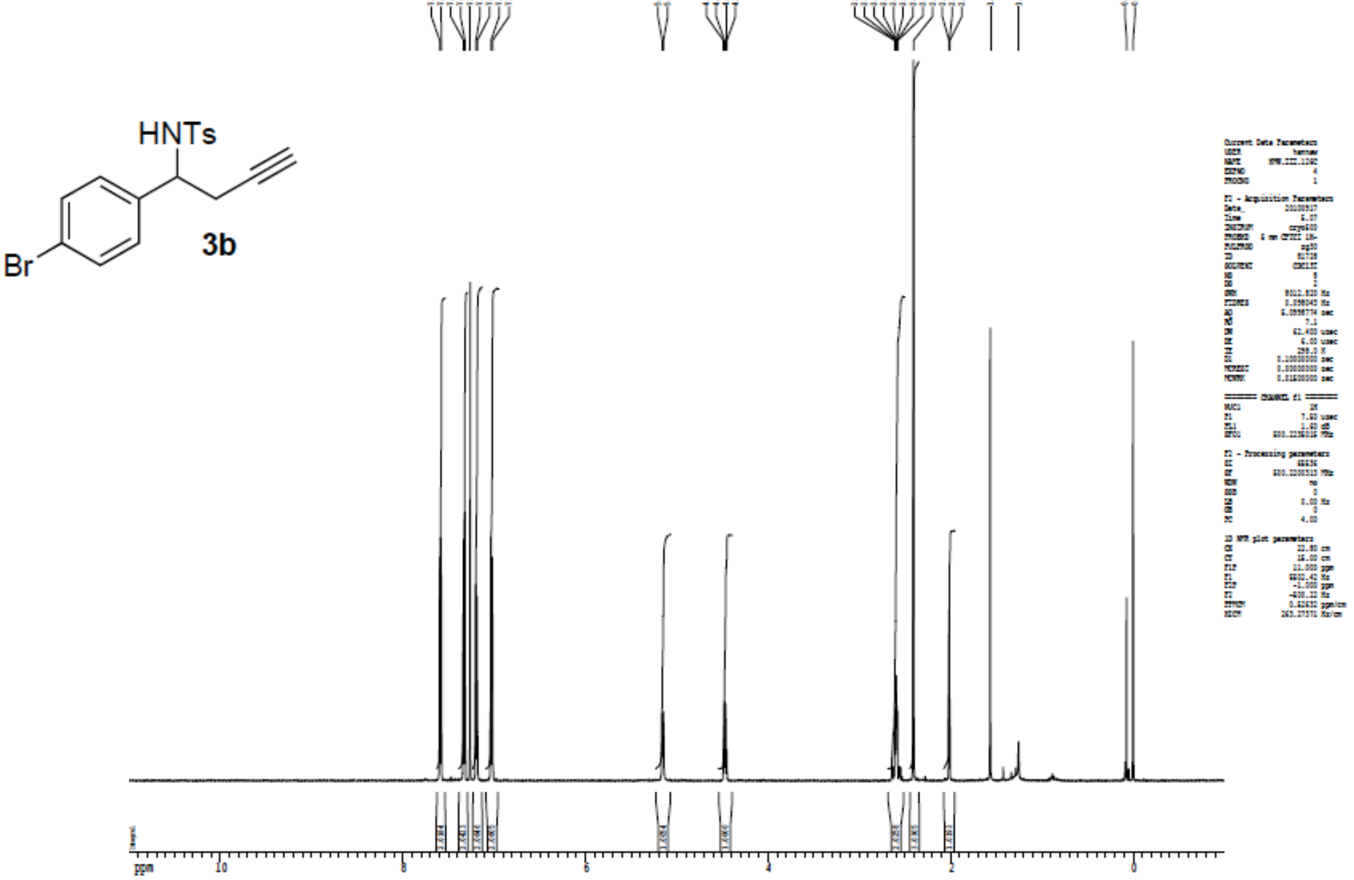

3b

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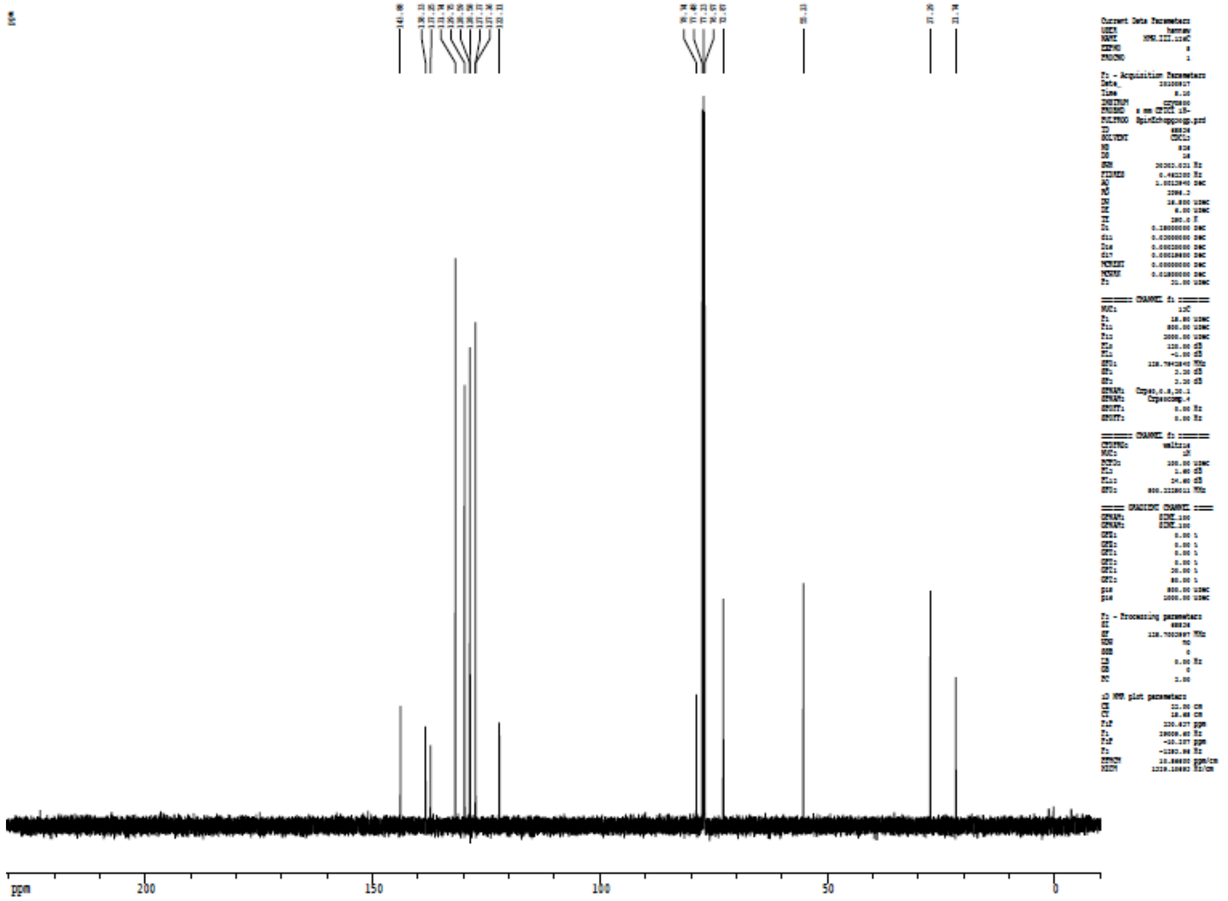

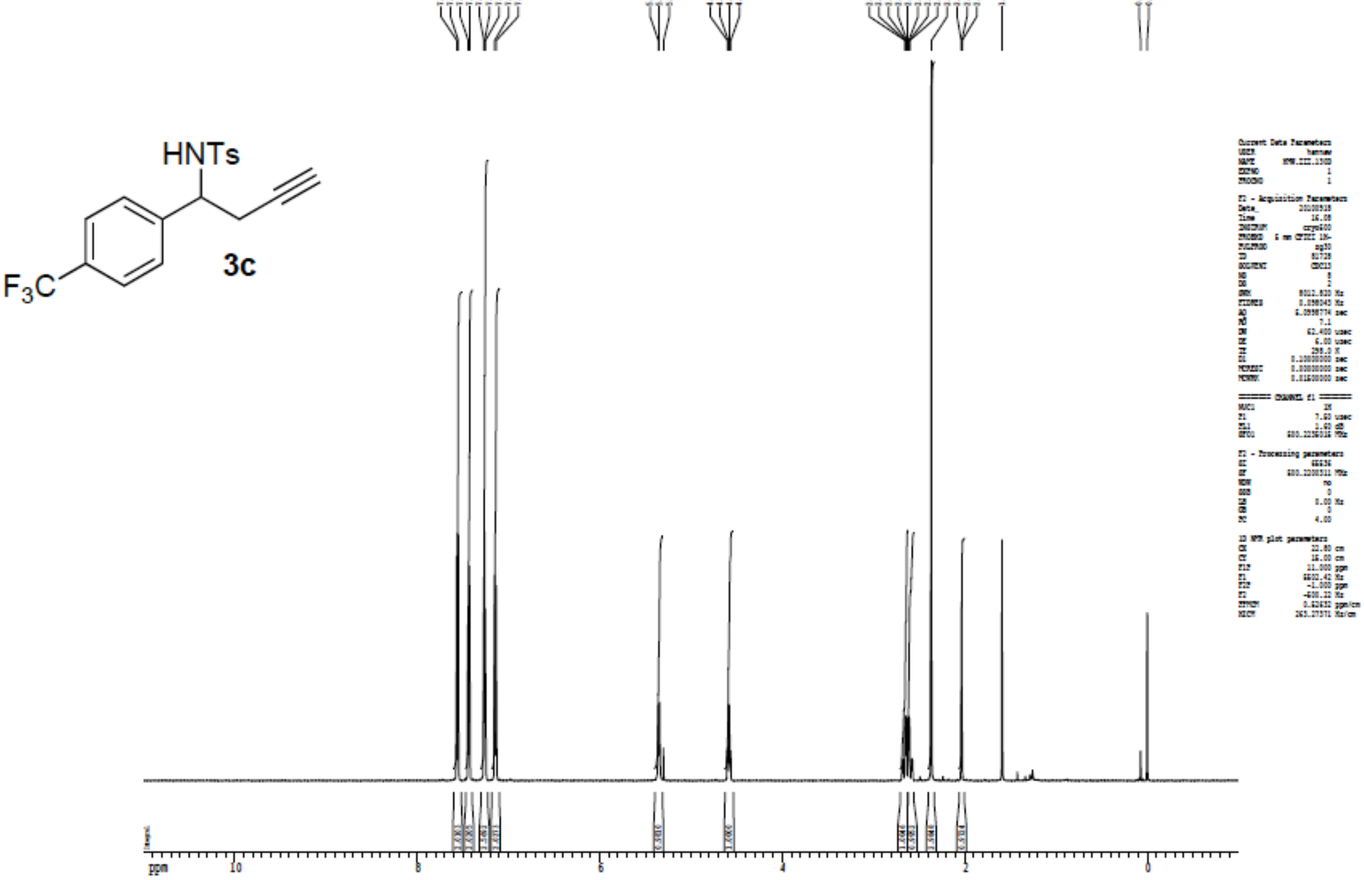

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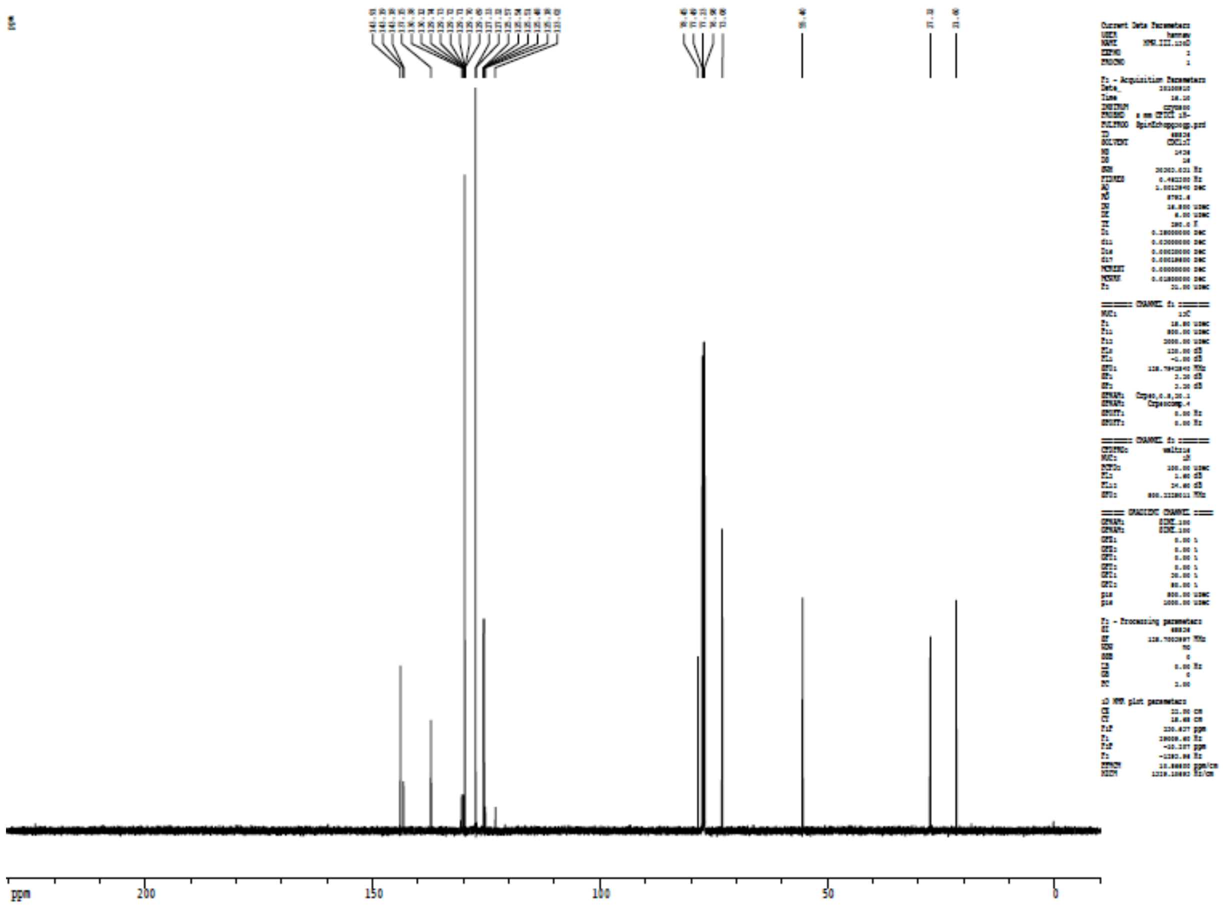

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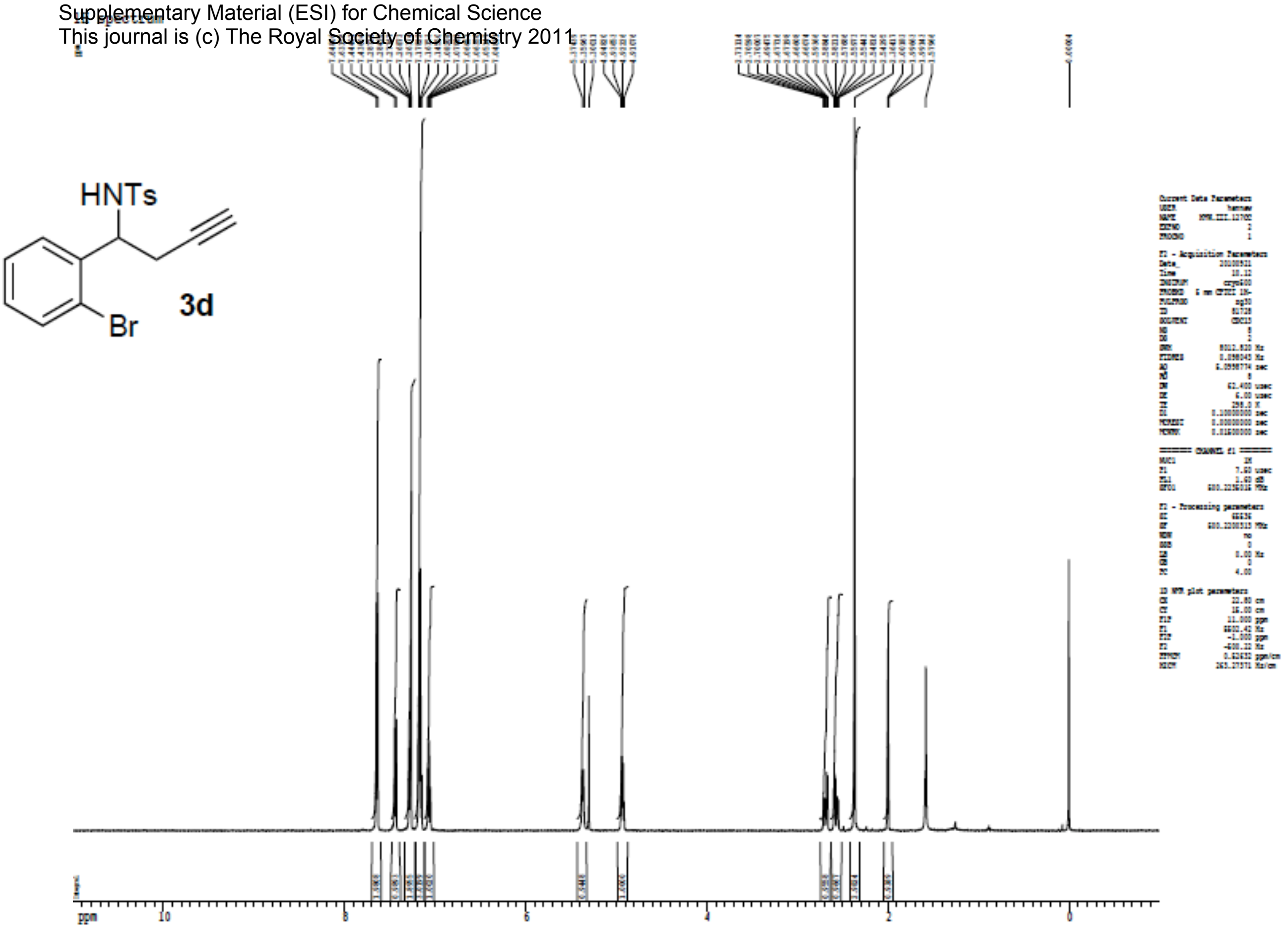

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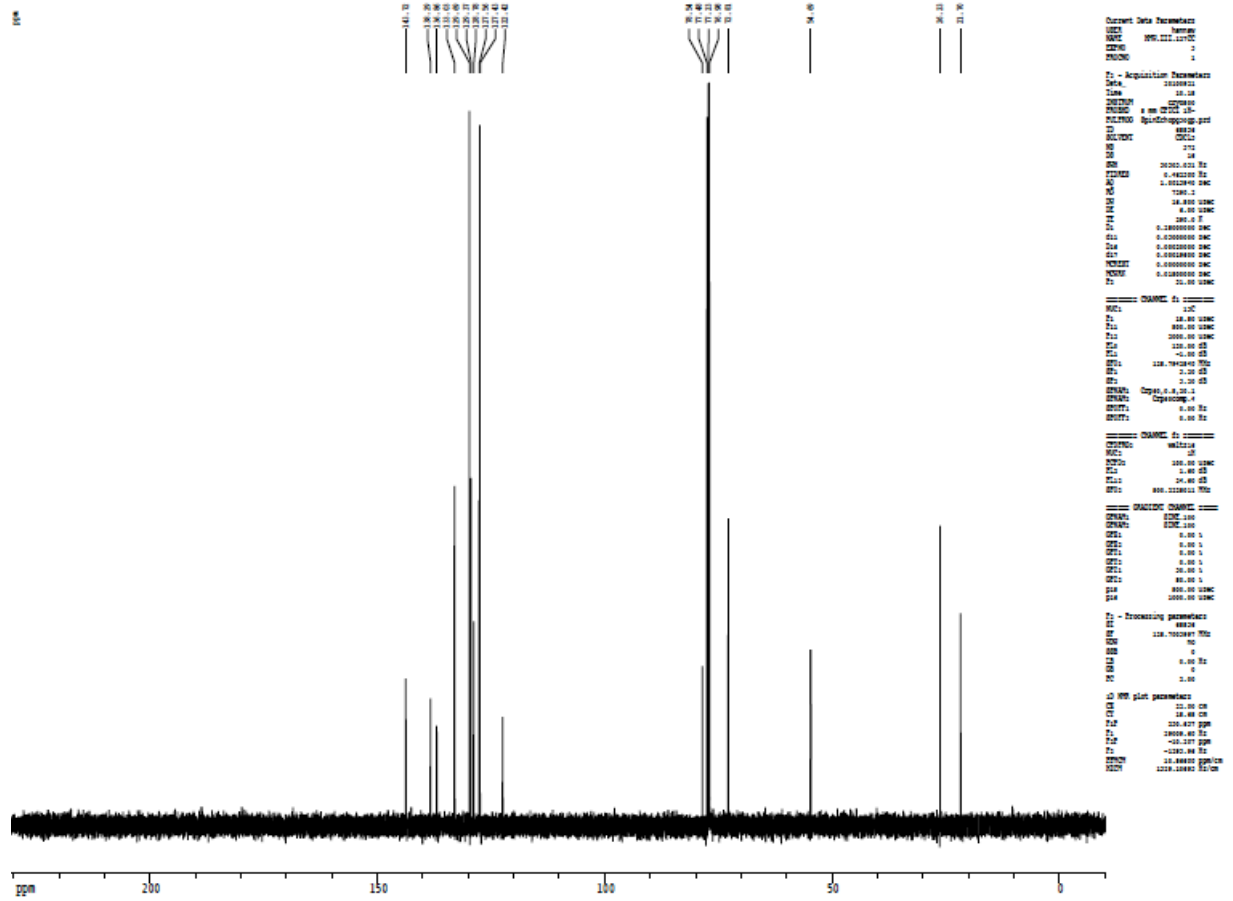

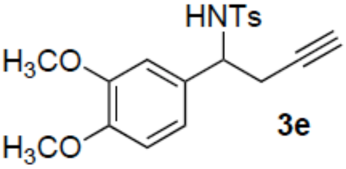

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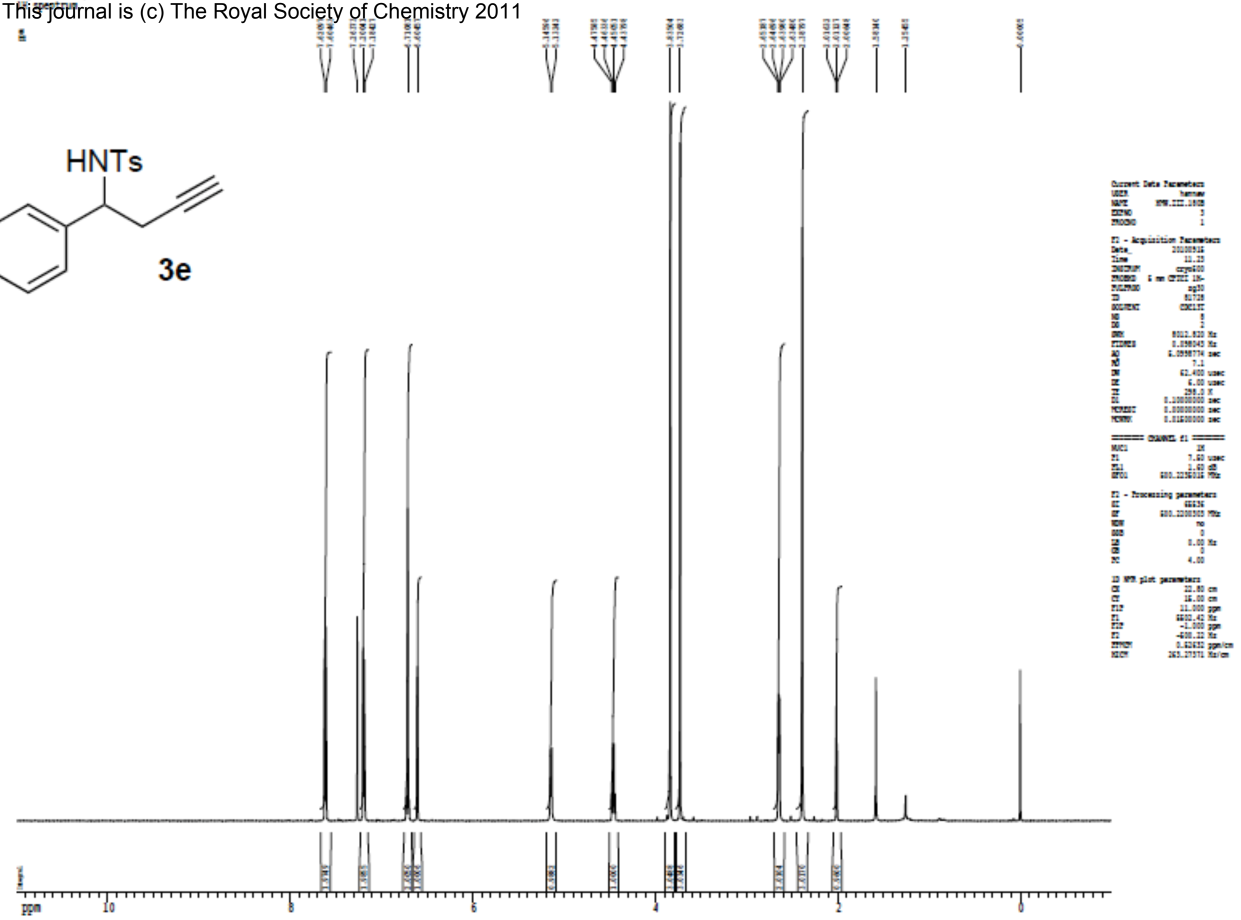

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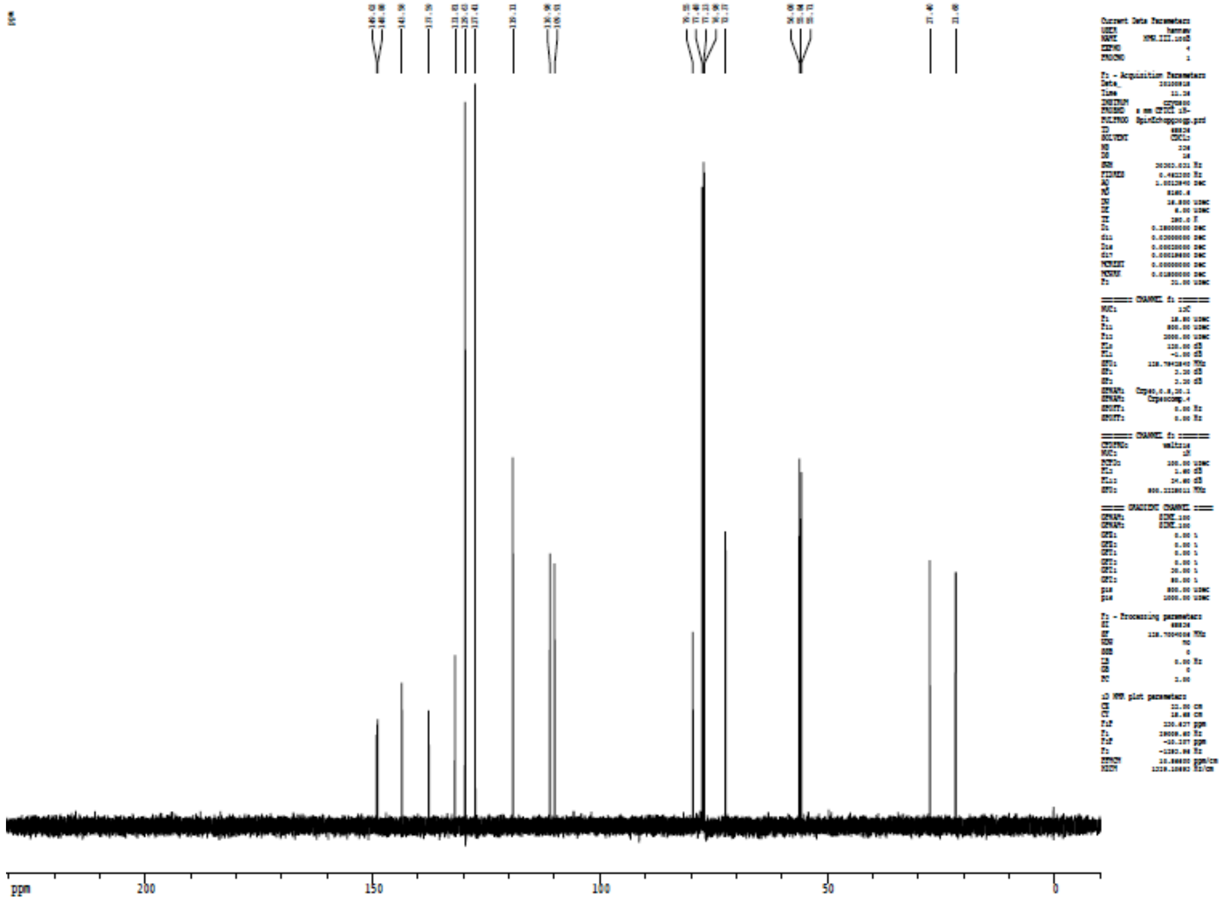
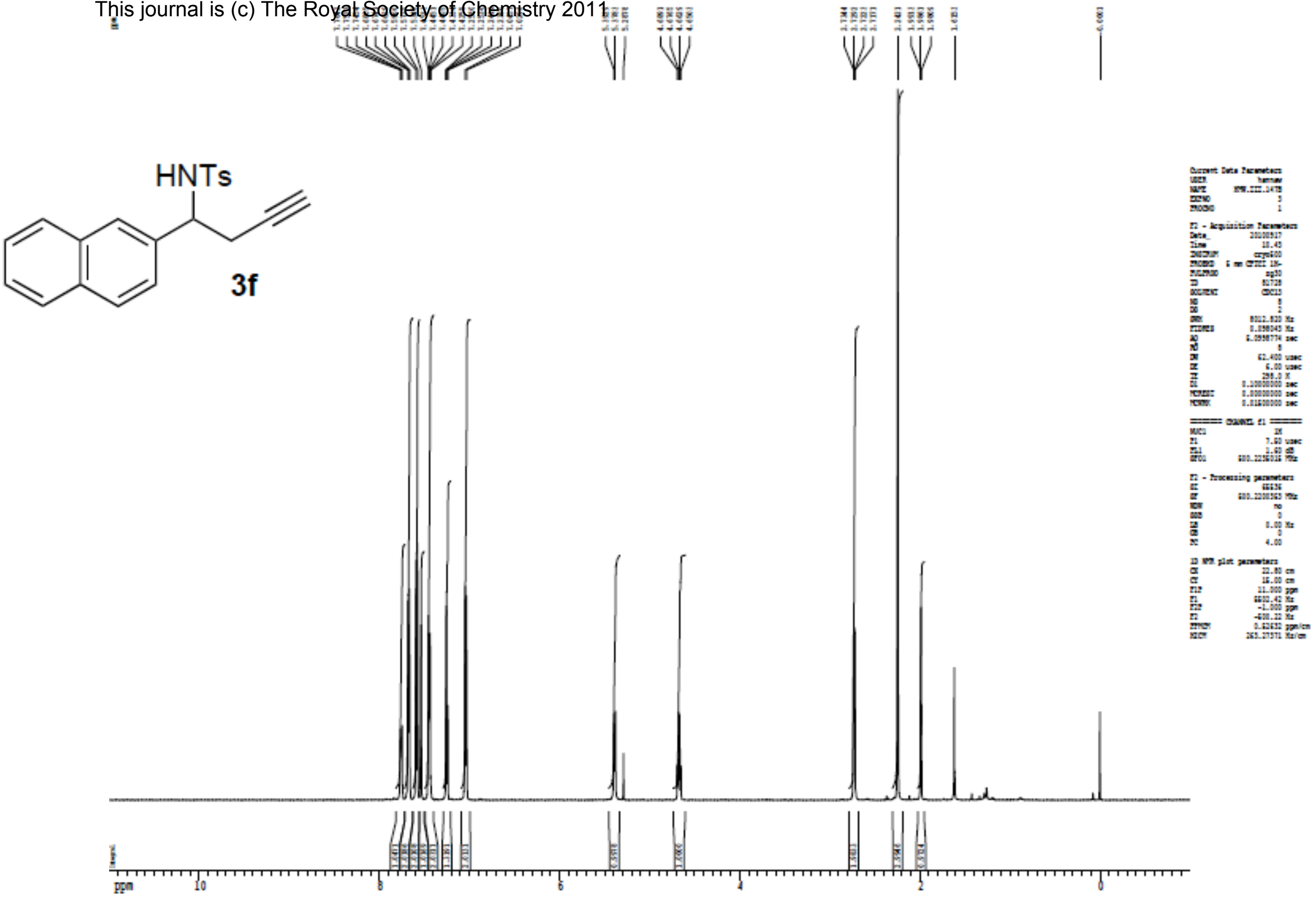
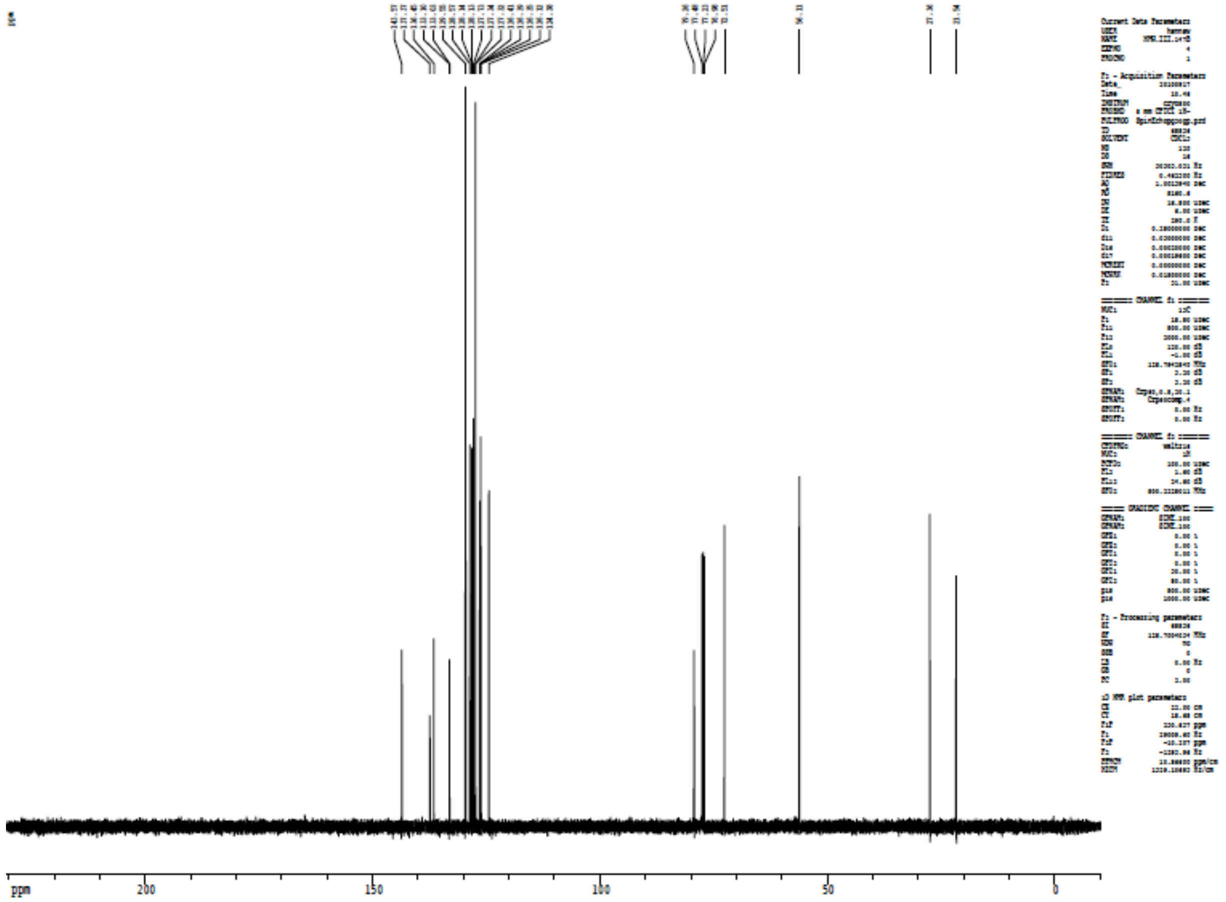
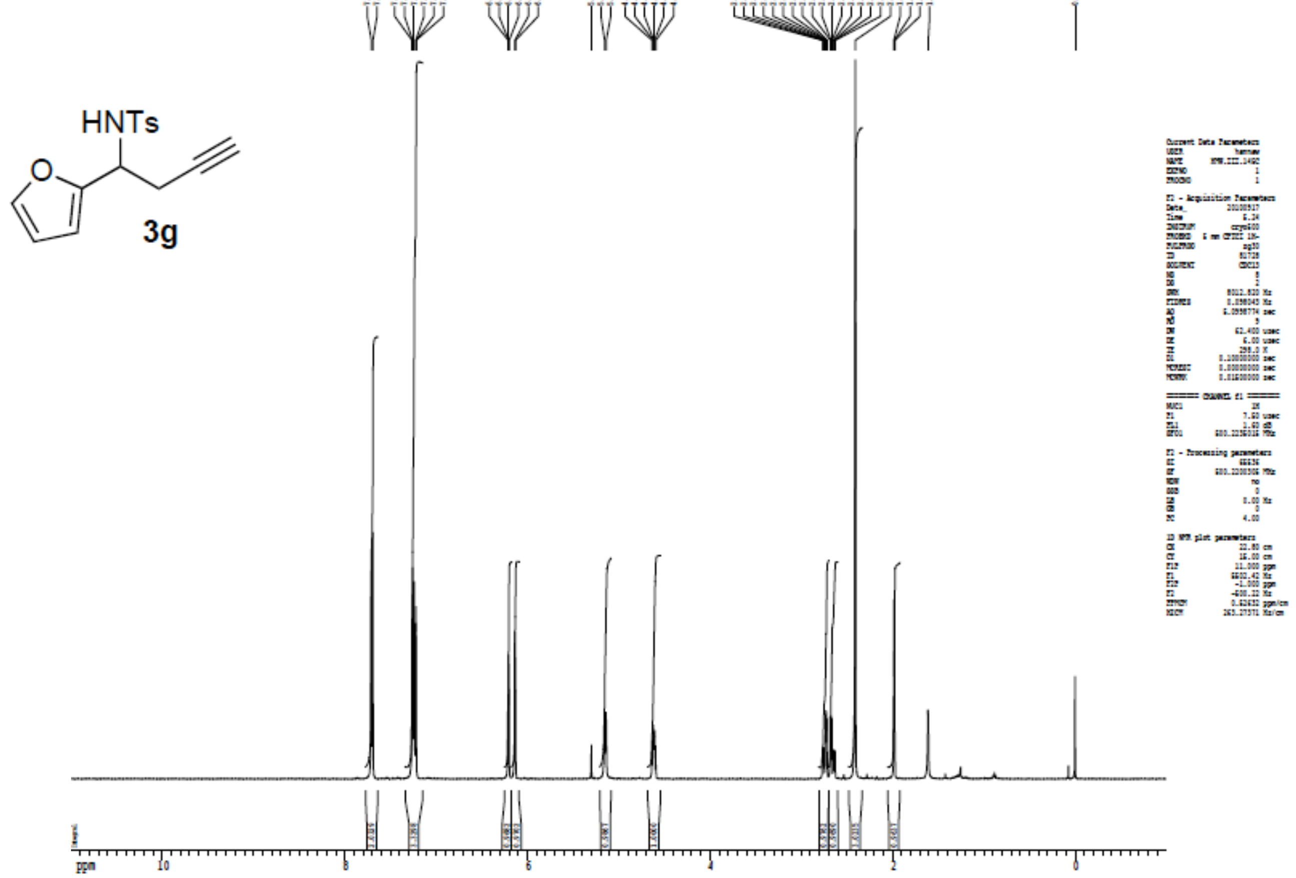




3f

Z-restored spin-echo 13C spectrum with 1H decoupling

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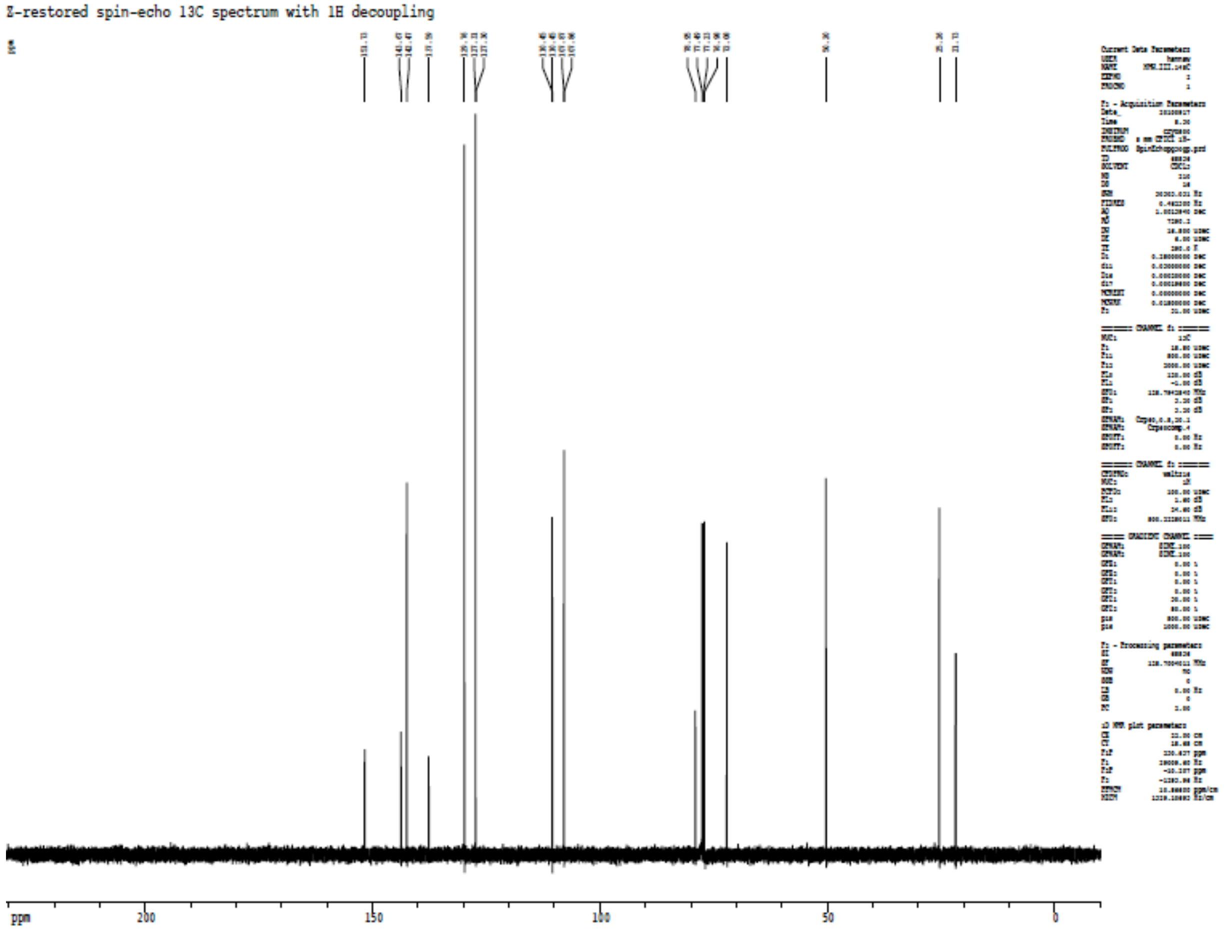
3g


Z-restored spin-echo 13C spectrum with 1H decoupling
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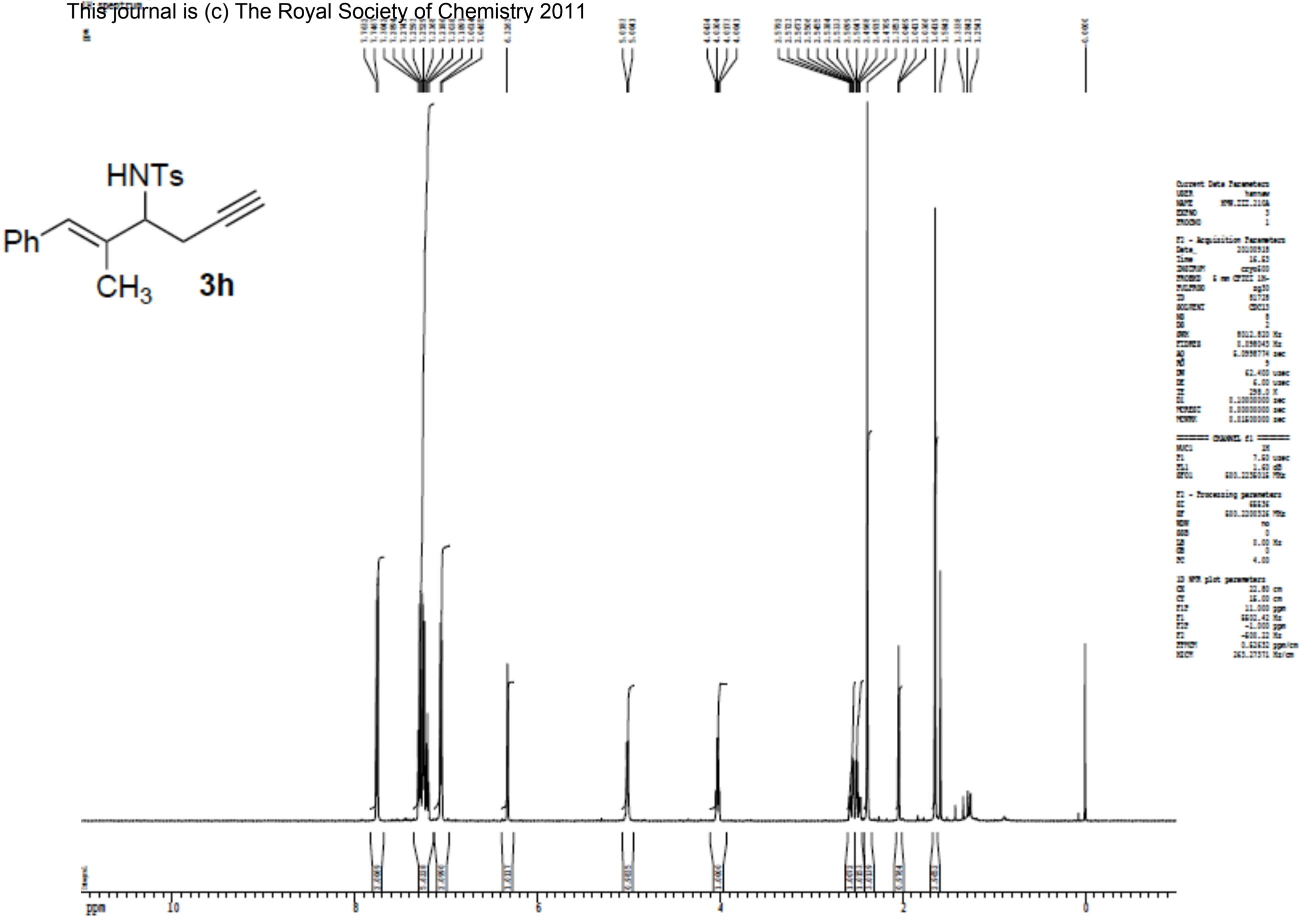
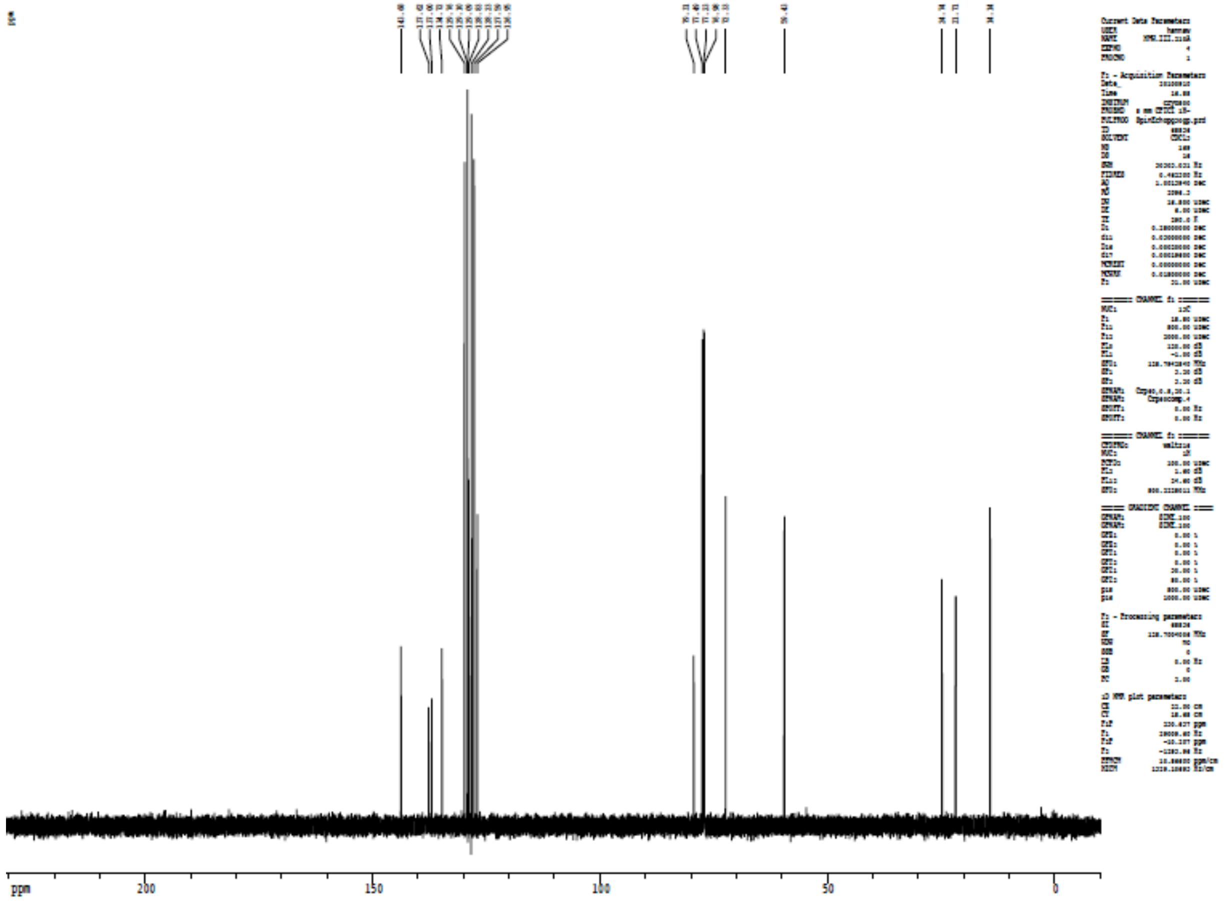
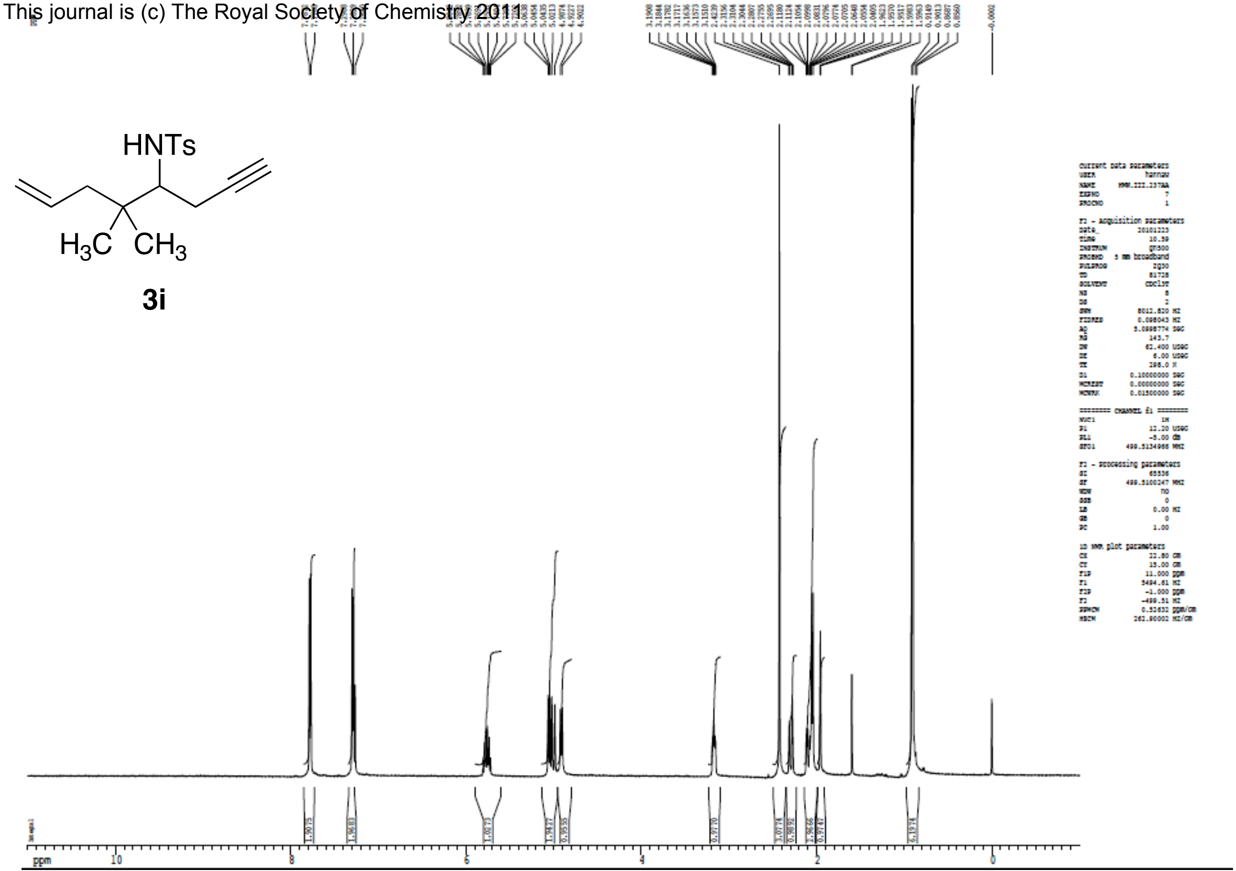


Z-restored spin-echo 13C spectrum with 1H decoupling





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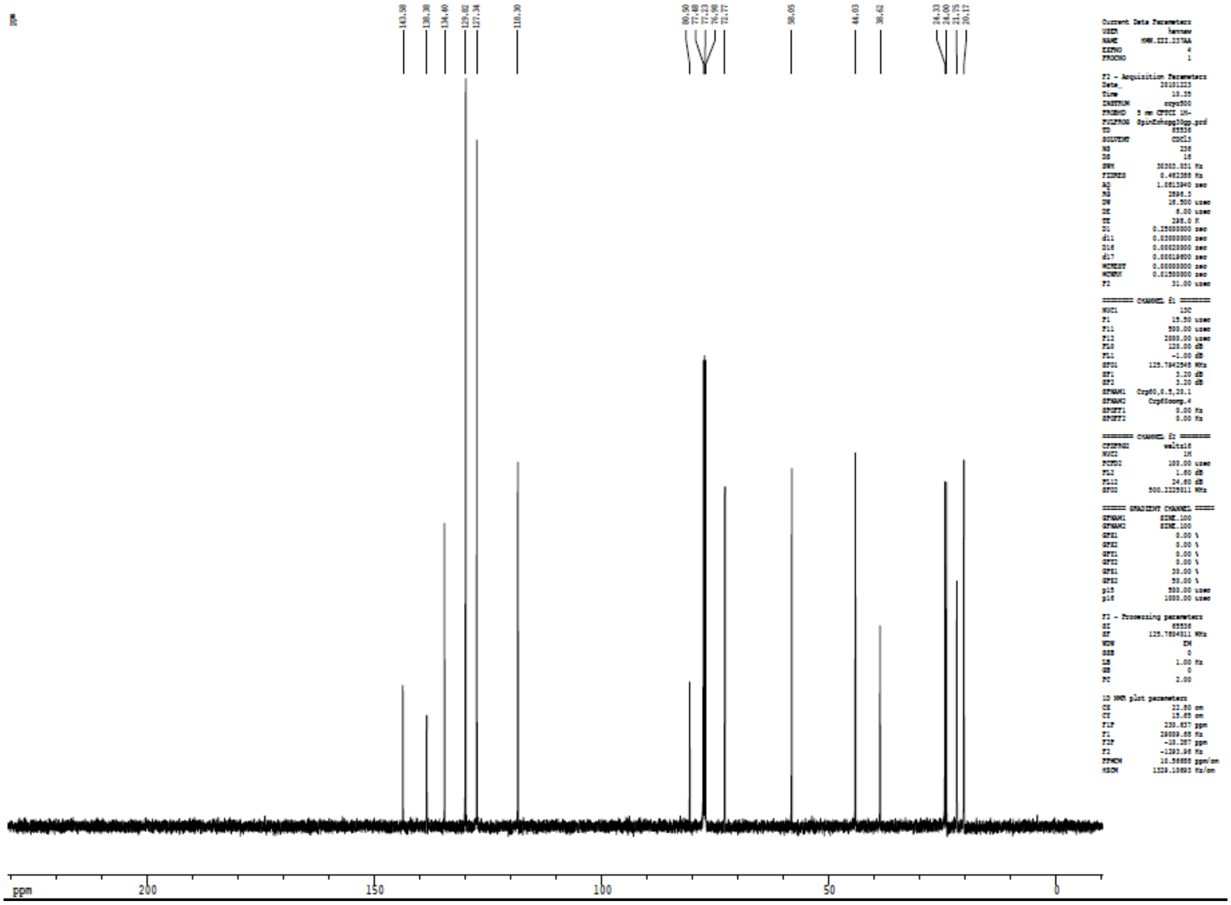
Z-restored spin-echo 13C spectrum with 1H decoupling



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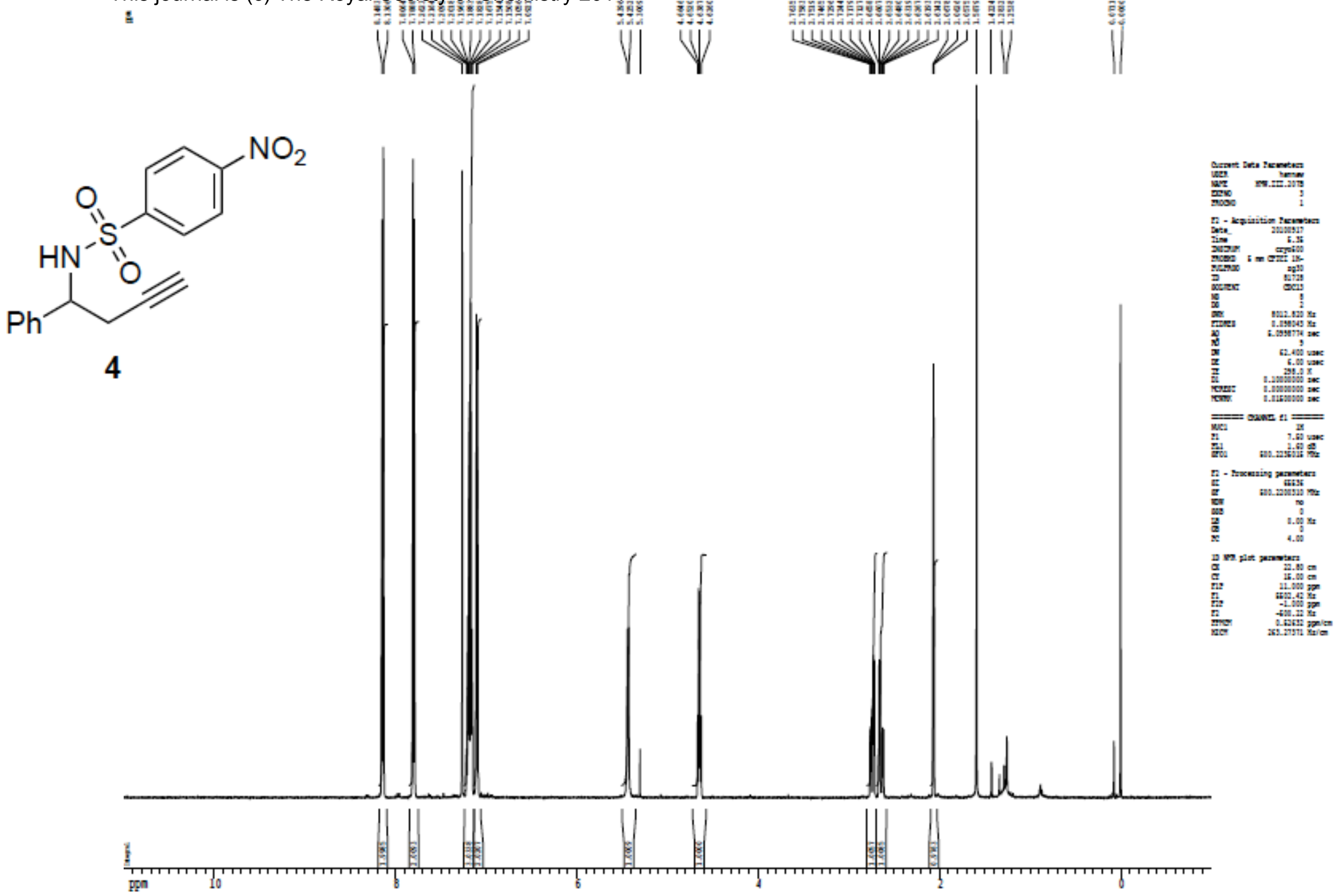
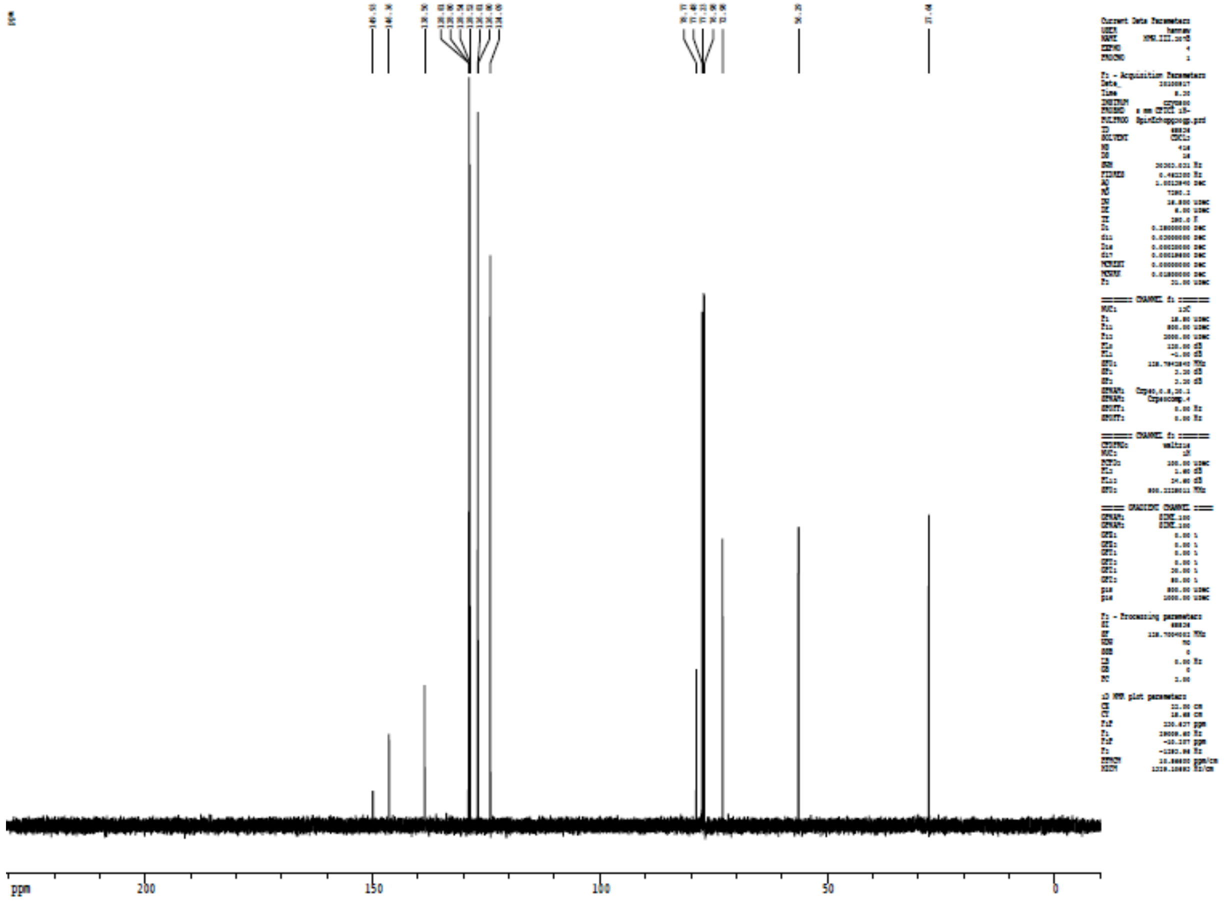
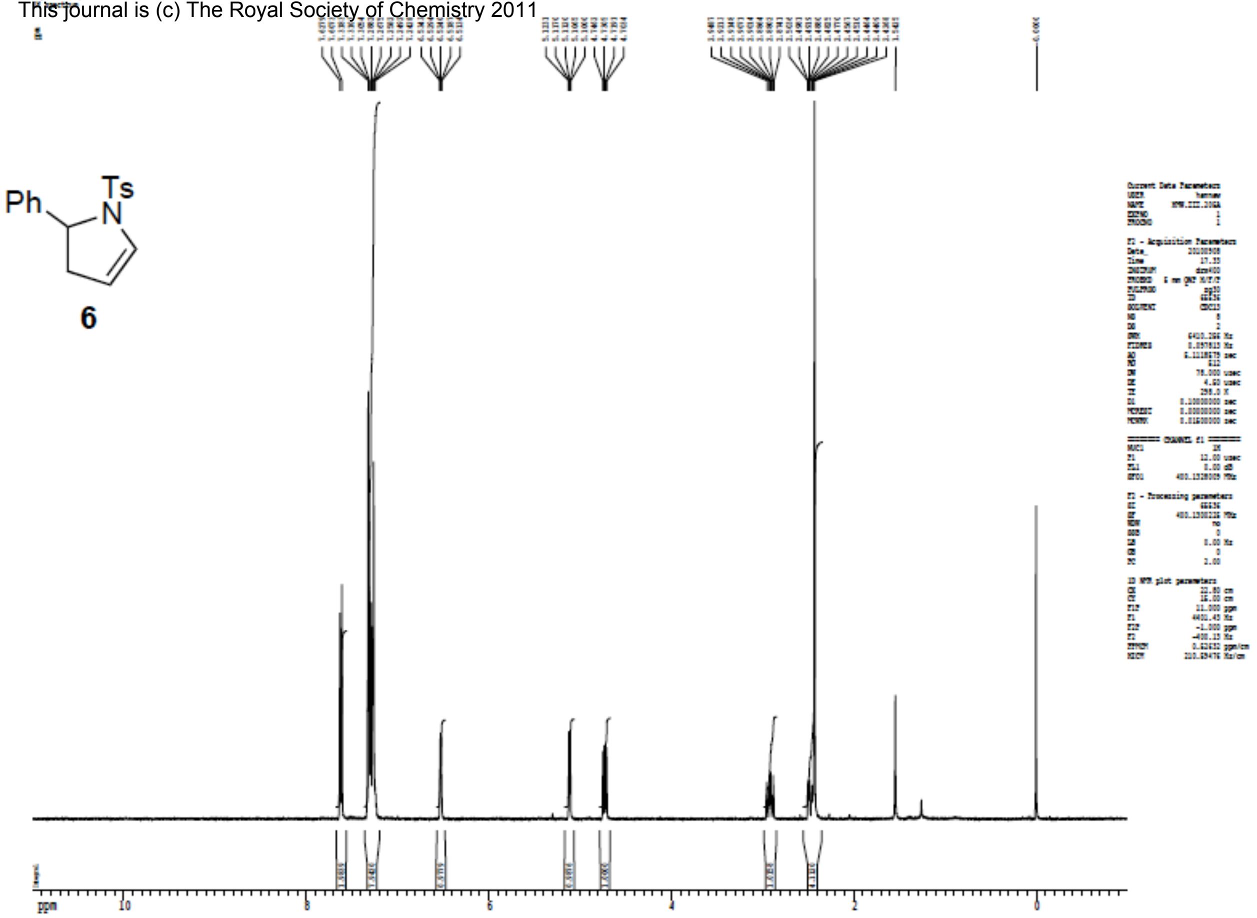


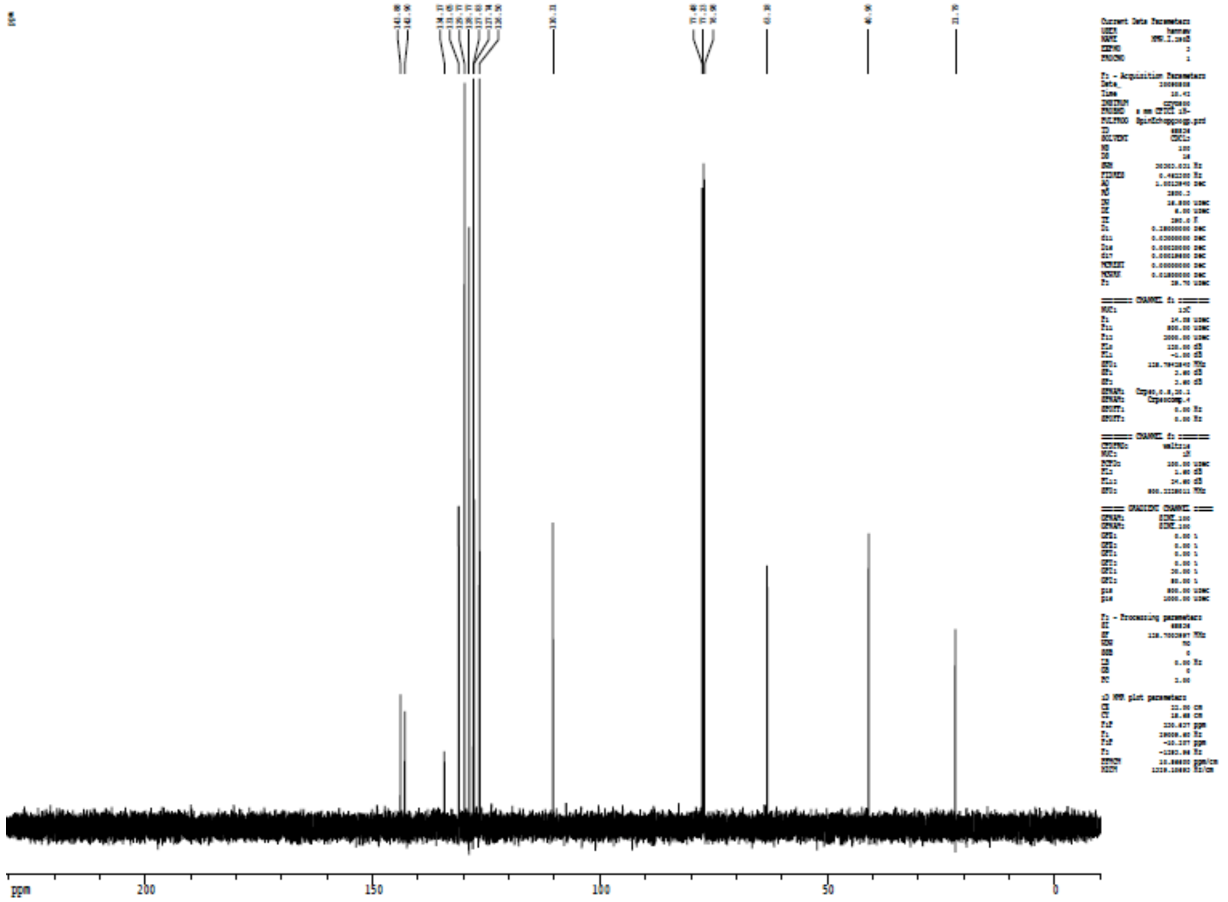
Z-restored spin-echo 13C spectrum with 1H decoupling

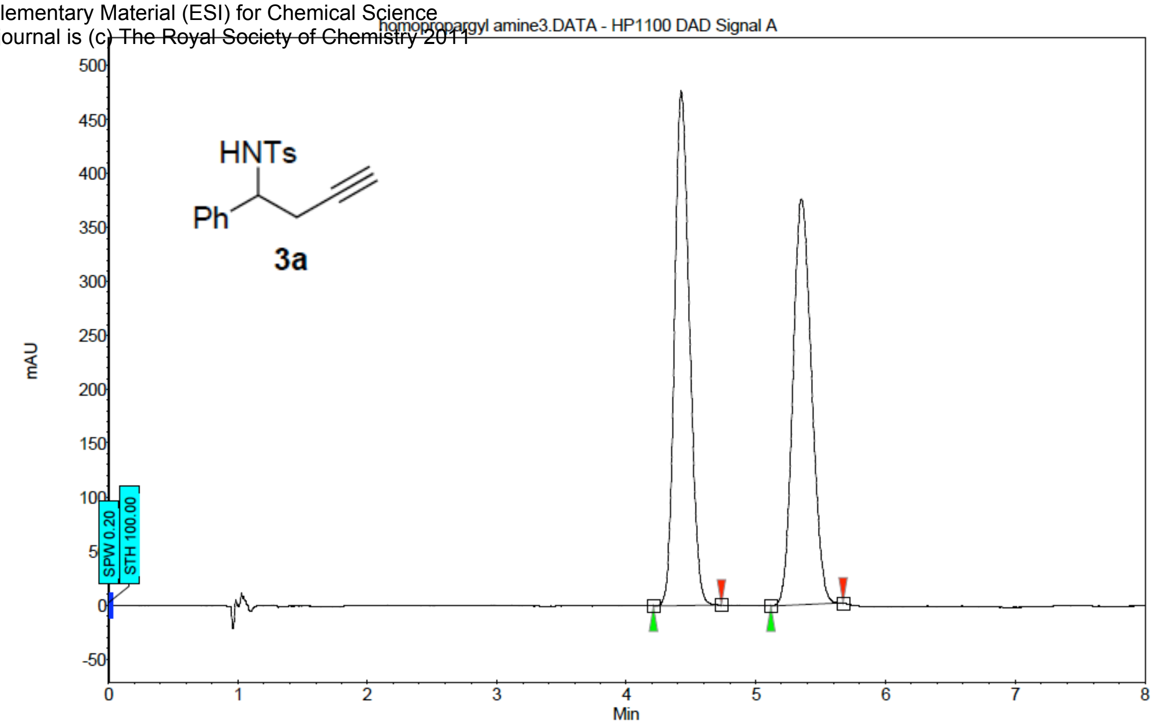




6

Z-restored spin-echo 13C spectrum with 1H decoupling





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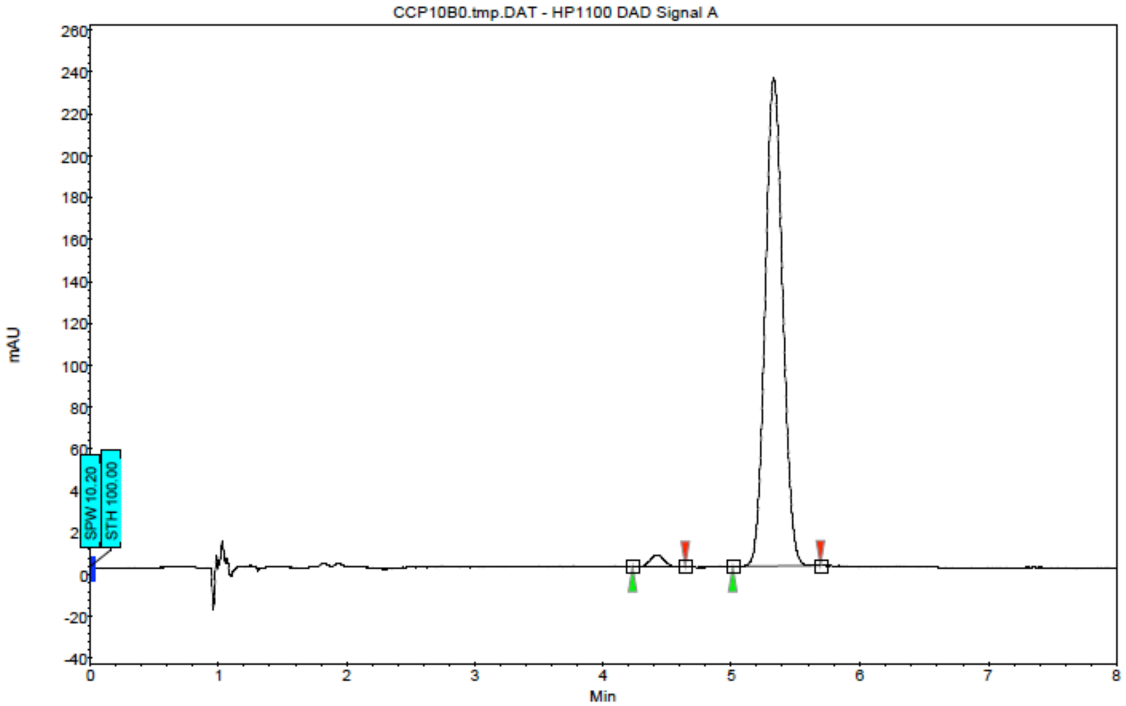
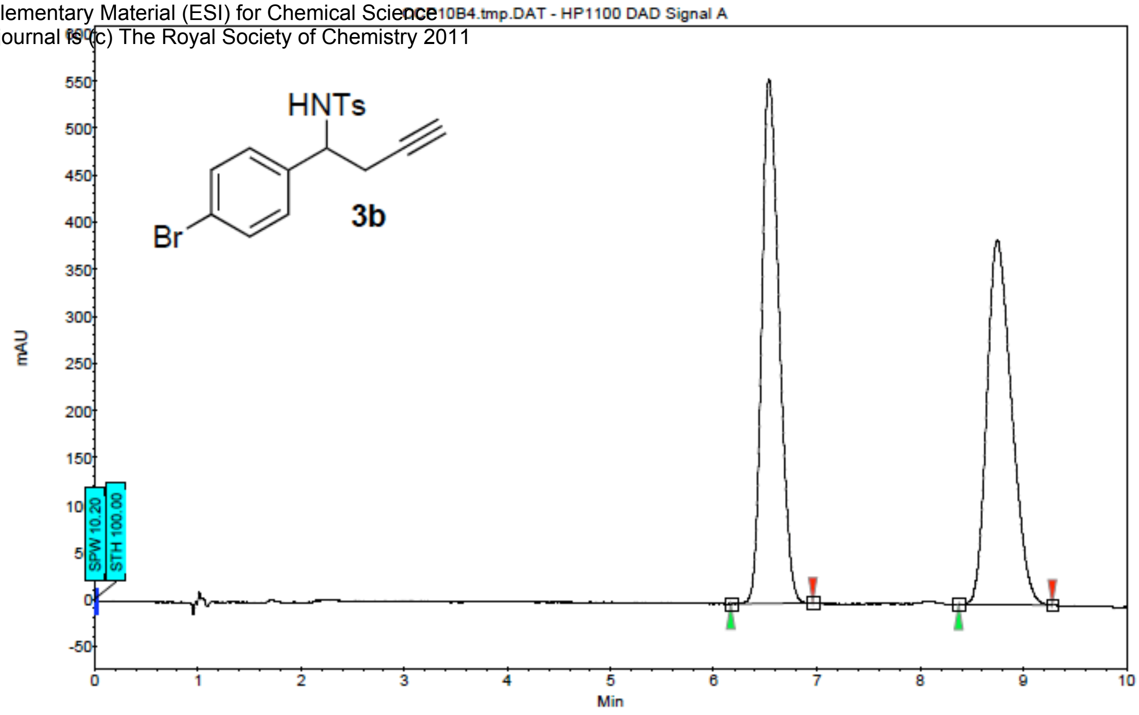
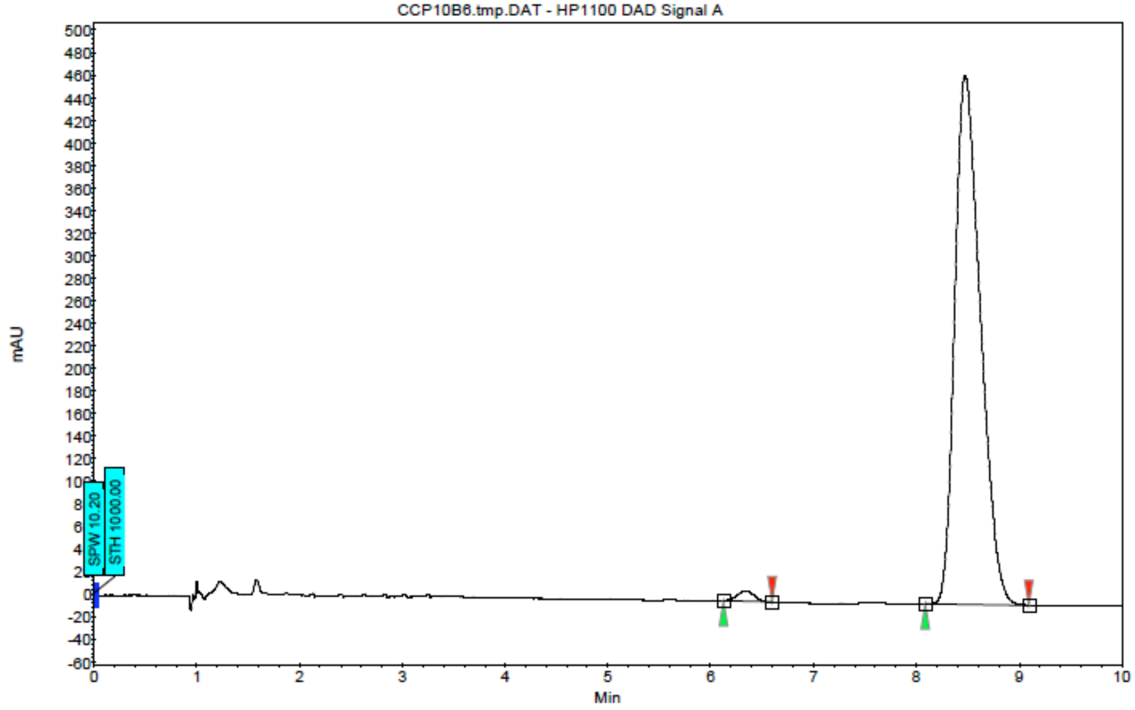


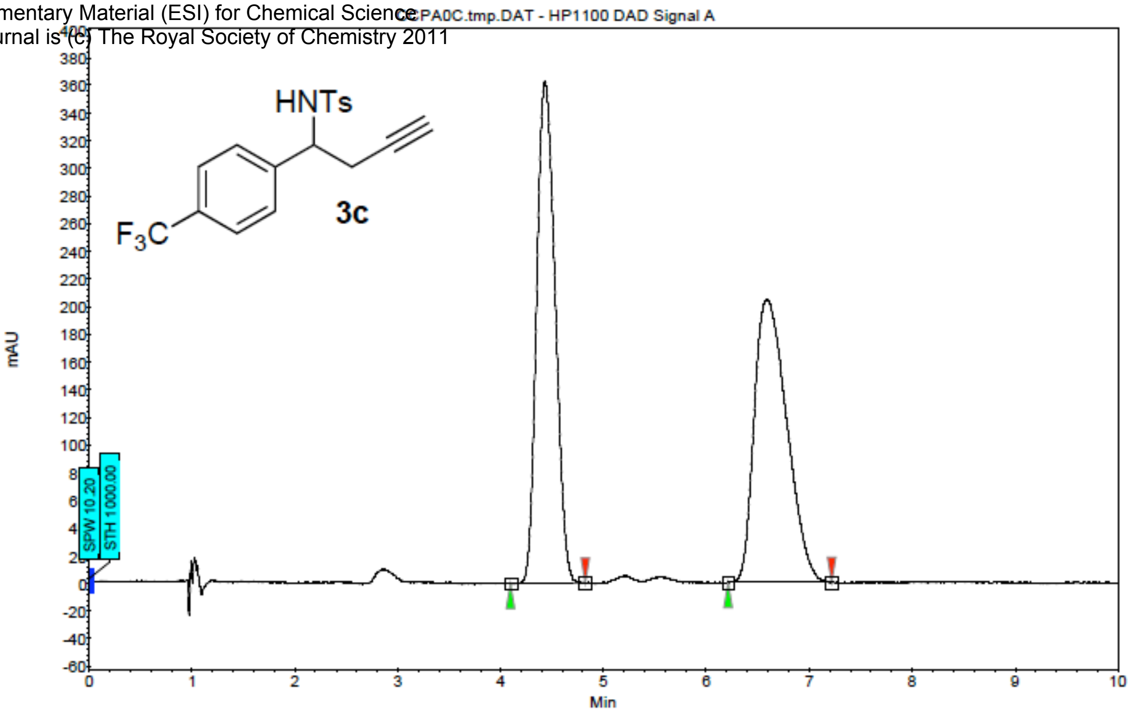
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.23	4.42	4.64	0.00	1.89	5.7	0.7	1.894
2	UNKNOWN	5.01	5.33	5.69	0.00	98.11	233.1	36.9	98.106
Total						100.00	238.8	37.6	100.000



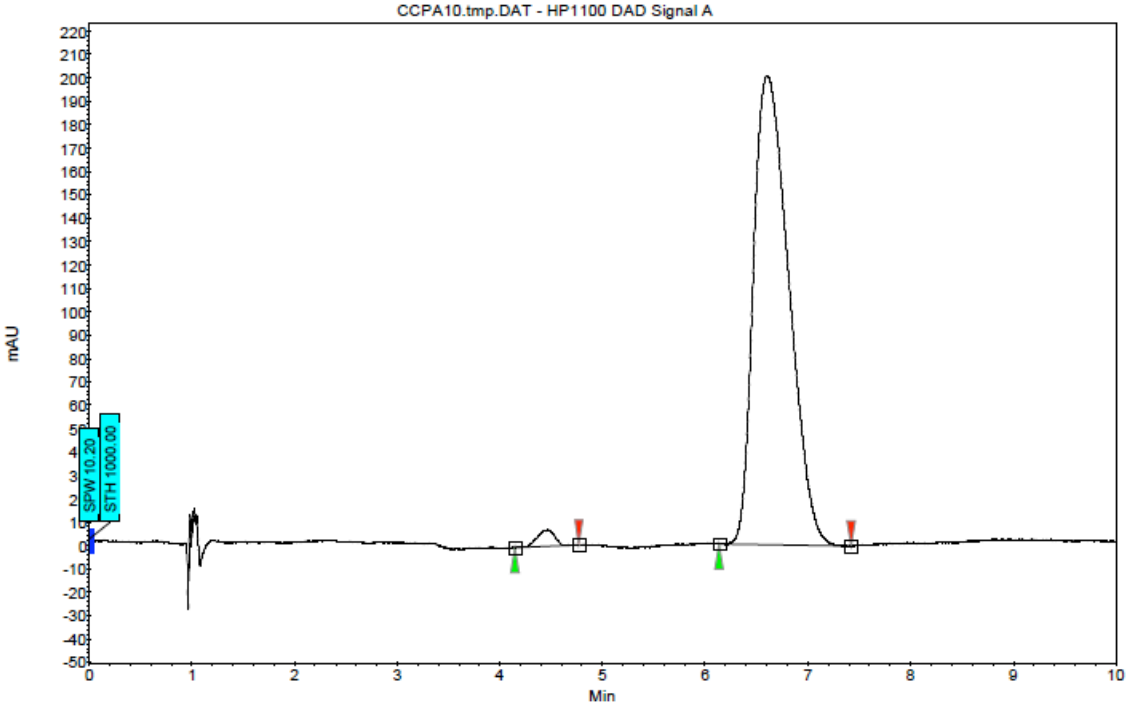
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.17	6.54	6.96	0.00	50.33	556.4	109.0	50.335
2	UNKNOWN	8.37	8.75	9.28	0.00	49.67	387.1	107.6	49.665
Total						100.00	943.5	216.6	100.000



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.13	6.34	6.60	0.00	1.24	9.1	1.7	1.239
2	UNKNOWN	8.08	8.47	9.09	0.00	98.76	468.9	135.5	98.761
Total						100.00	478.0	137.2	100.000

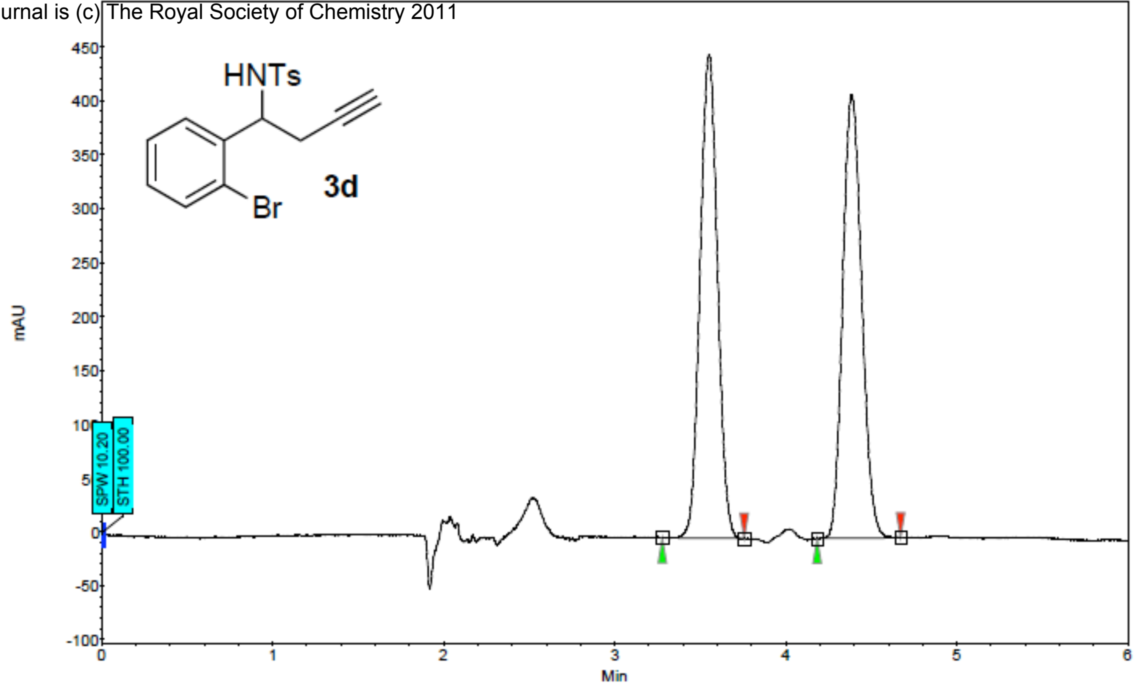


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.09	4.43	4.83	0.00	50.06	363.0	75.5	50.056
2	UNKNOWN	6.21	6.59	7.22	0.00	49.94	205.1	75.3	49.944
Total						100.00	568.1	150.8	100.000



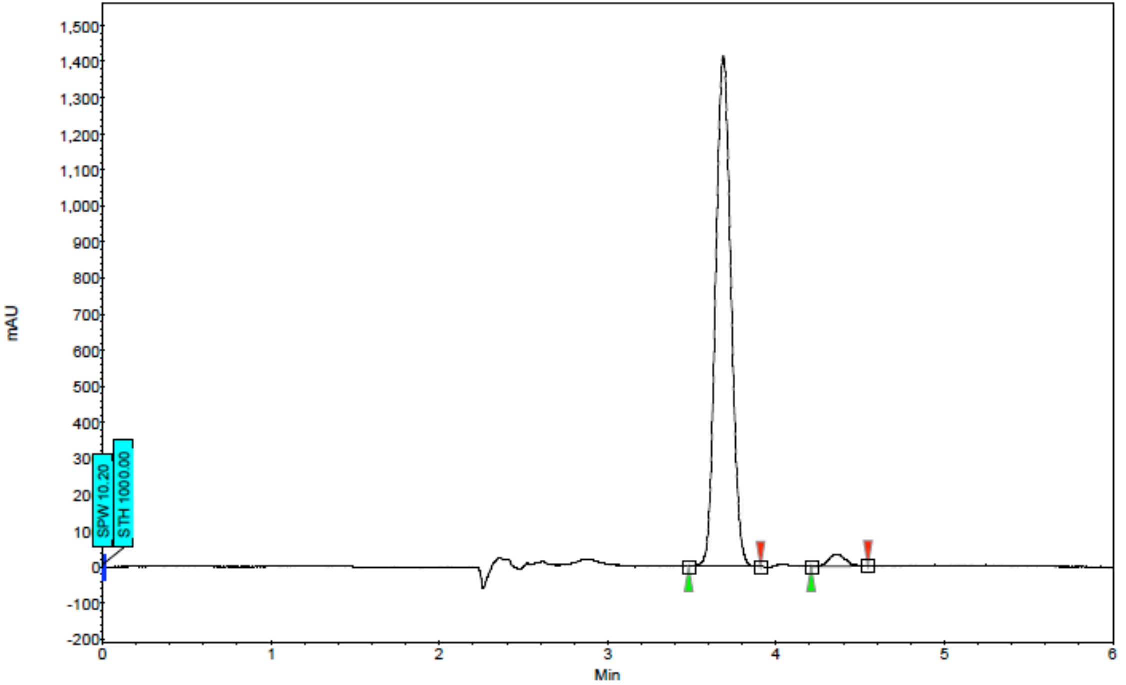
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.14	4.46	4.77	0.00	1.72	6.9	1.4	1.724
2	UNKNOWN	6.14	6.61	7.42	0.00	98.28	200.5	79.8	98.276
Total						100.00	207.4	81.2	100.000

CCP10B2.tmp.DAT - HP1100 DAD Signal A

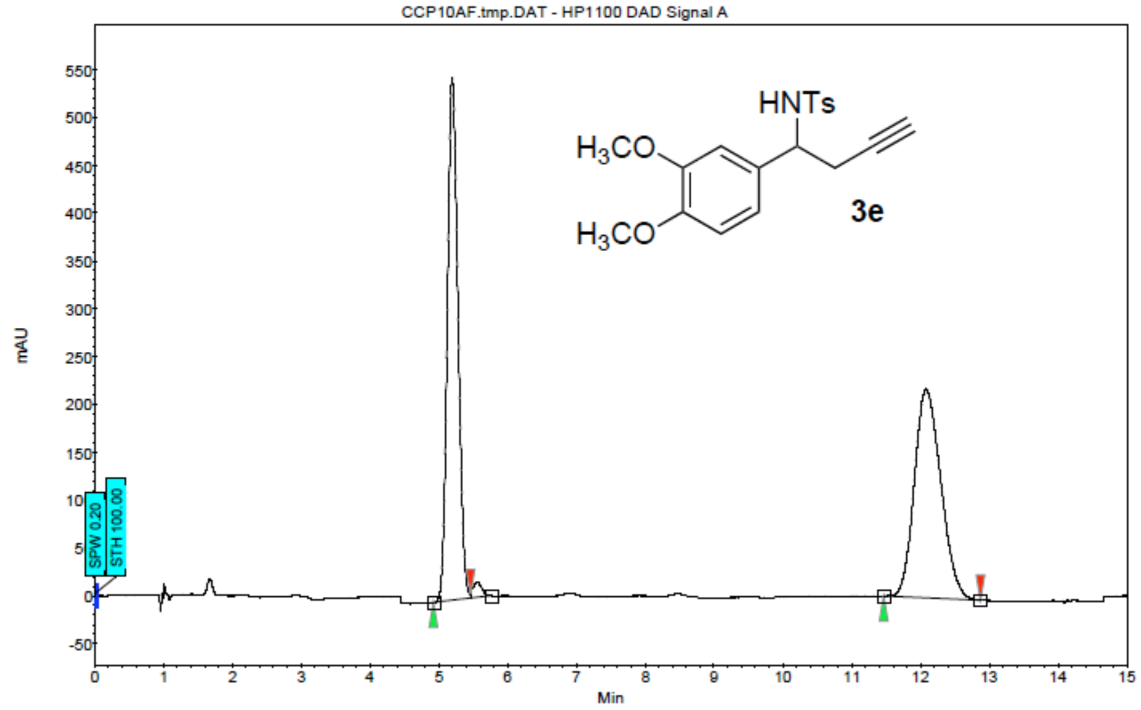


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.28	3.55	3.76	0.00	50.05	448.6	53.0	50.054
2	UNKNOWN	4.19	4.39	4.67	0.00	49.95	410.9	52.8	49.946
Total						100.00	859.5	105.8	100.000

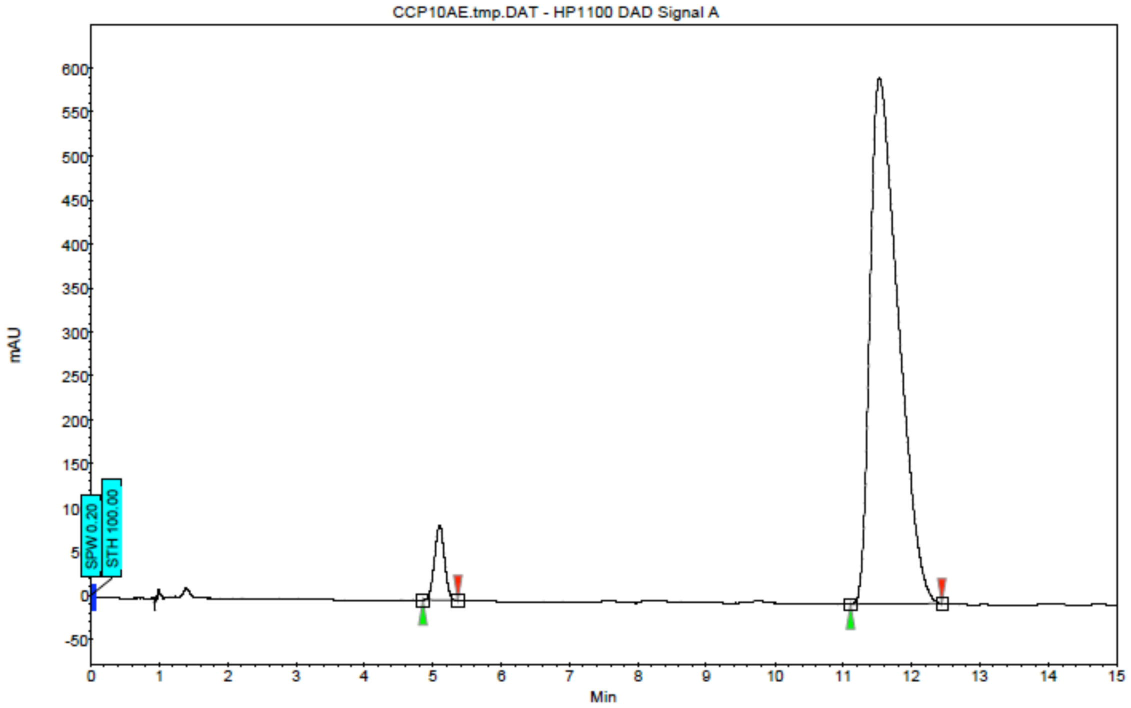
CCP10B1.tmp.DAT - HP1100 DAD Signal A



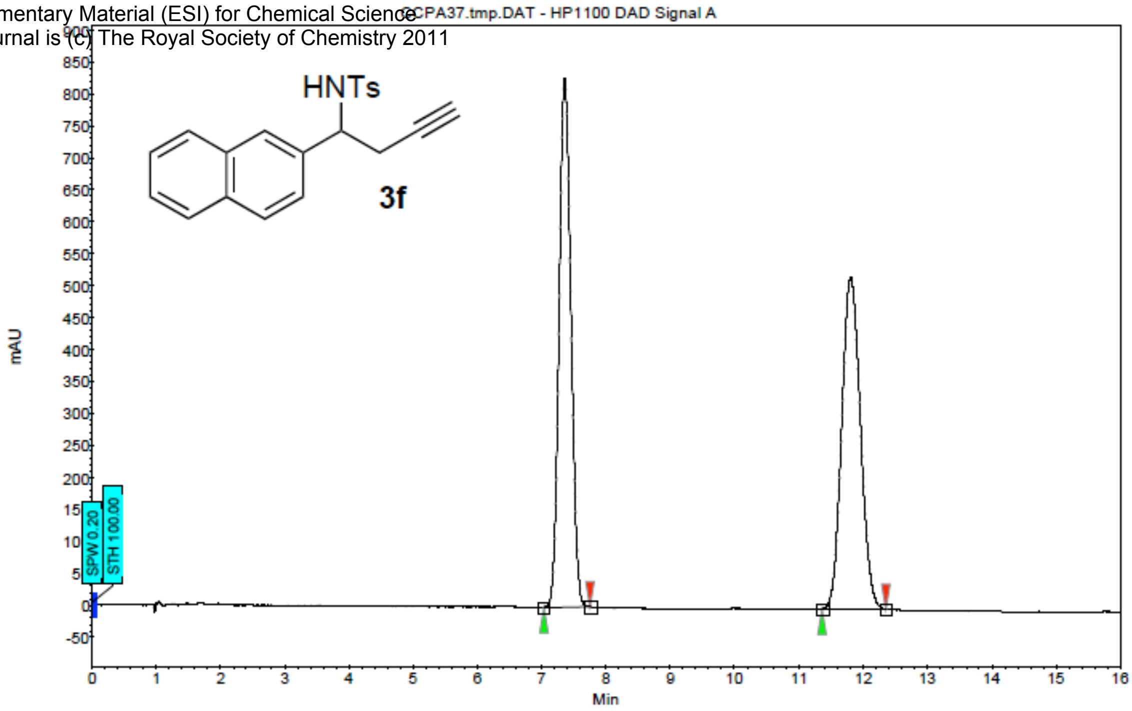
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.48	3.69	3.91	0.00	97.46	1415.2	149.8	97.463
2	UNKNOWN	4.21	4.35	4.55	0.00	2.54	33.6	3.9	2.537
Total						100.00	1448.8	153.7	100.000



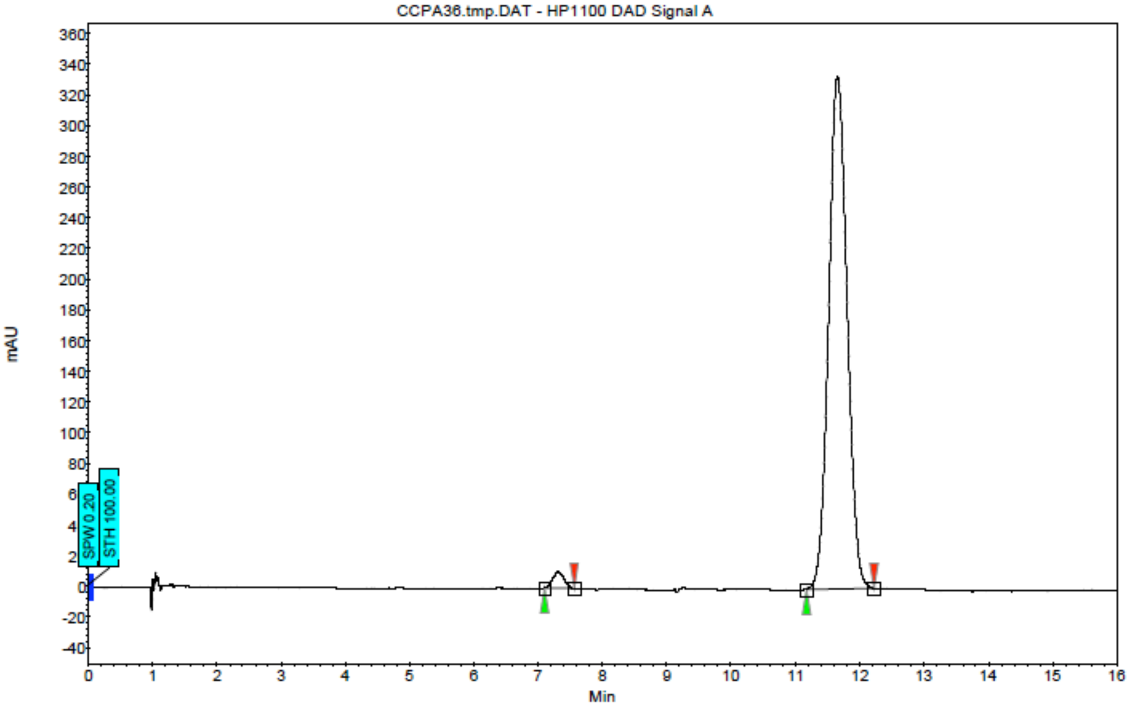
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.92	5.19	5.46	0.00	50.22	546.2	98.3	50.221
2	UNKNOWN	11.47	12.08	12.87	0.00	49.78	218.0	97.5	49.779
Total						100.00	764.3	195.8	100.000



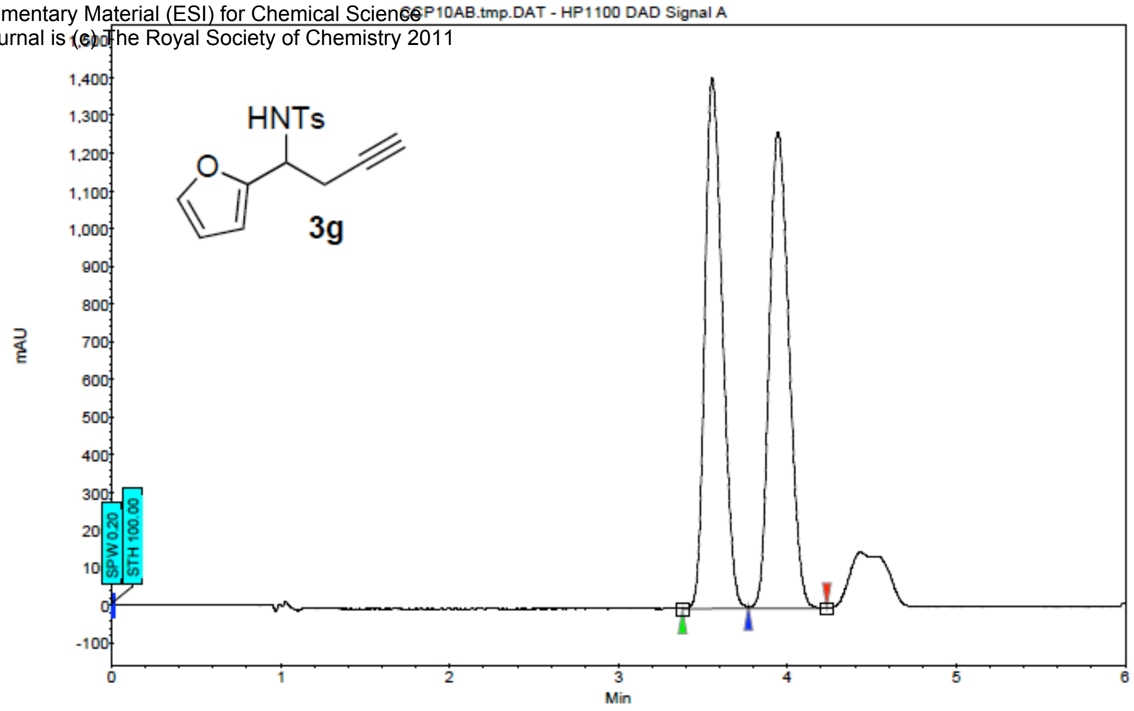
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.85	5.10	5.36	0.00	4.88	84.7	14.6	4.880
2	UNKNOWN	11.11	11.53	12.44	0.00	95.12	598.4	285.2	95.120
Total						100.00	683.1	299.8	100.000



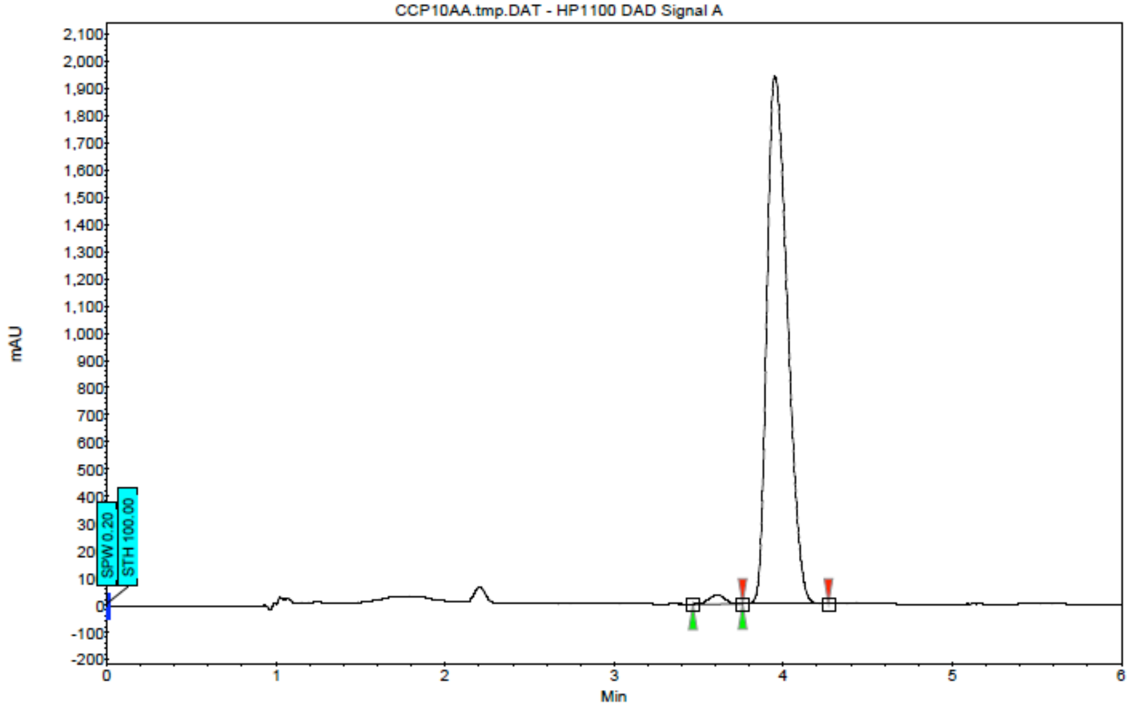
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	7.03	7.35	7.76	0.00	50.07	828.0	175.4	50.068
2	UNKNOWN	11.36	11.81	12.35	0.00	49.93	519.7	175.0	49.932
Total						100.00	1347.8	350.4	100.000



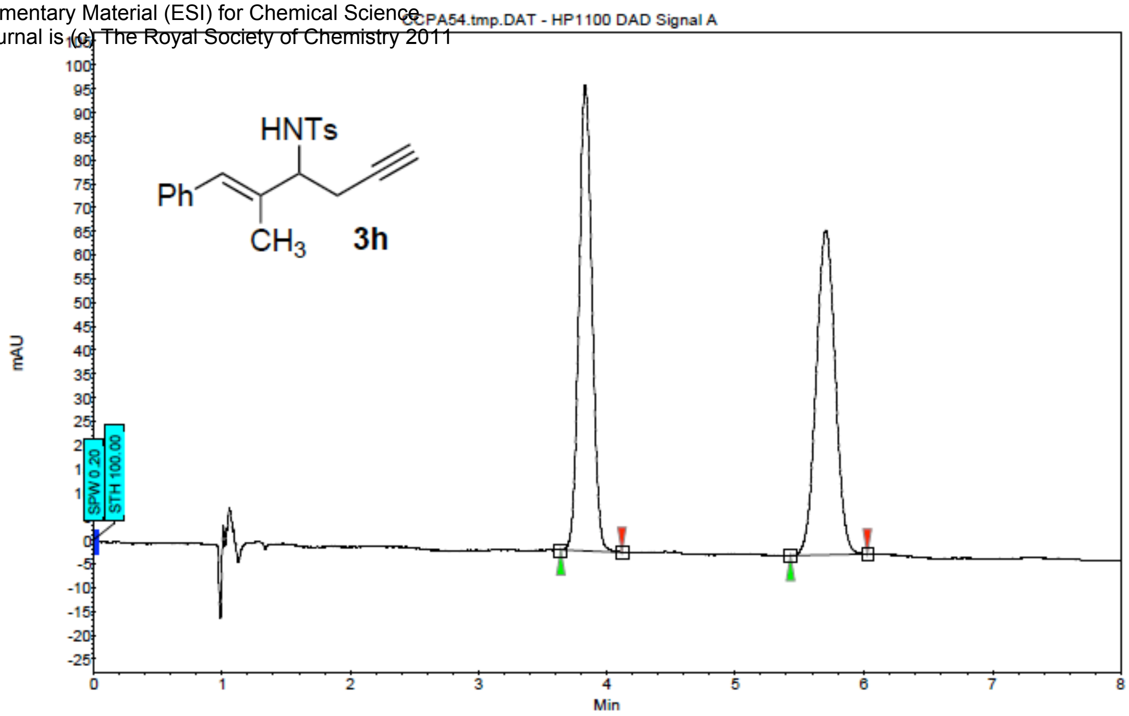
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	7.09	7.32	7.56	0.00	1.89	10.8	2.1	1.893
2	UNKNOWN	11.17	11.66	12.23	0.00	98.11	333.9	110.9	98.107
Total						100.00	344.7	113.1	100.000



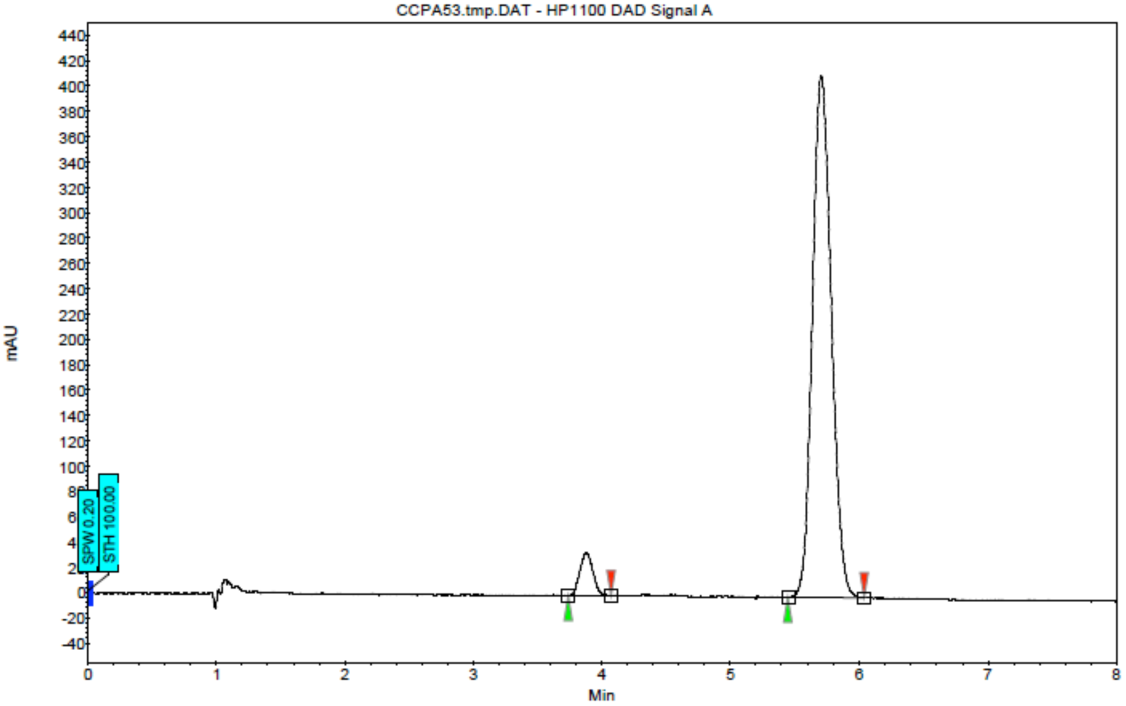
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.38	3.56	3.77	0.00	49.89	1407.3	168.9	49.887
2	UNKNOWN	3.77	3.95	4.24	0.00	50.11	1263.4	169.7	50.113
Total						100.00	2670.7	338.6	100.000



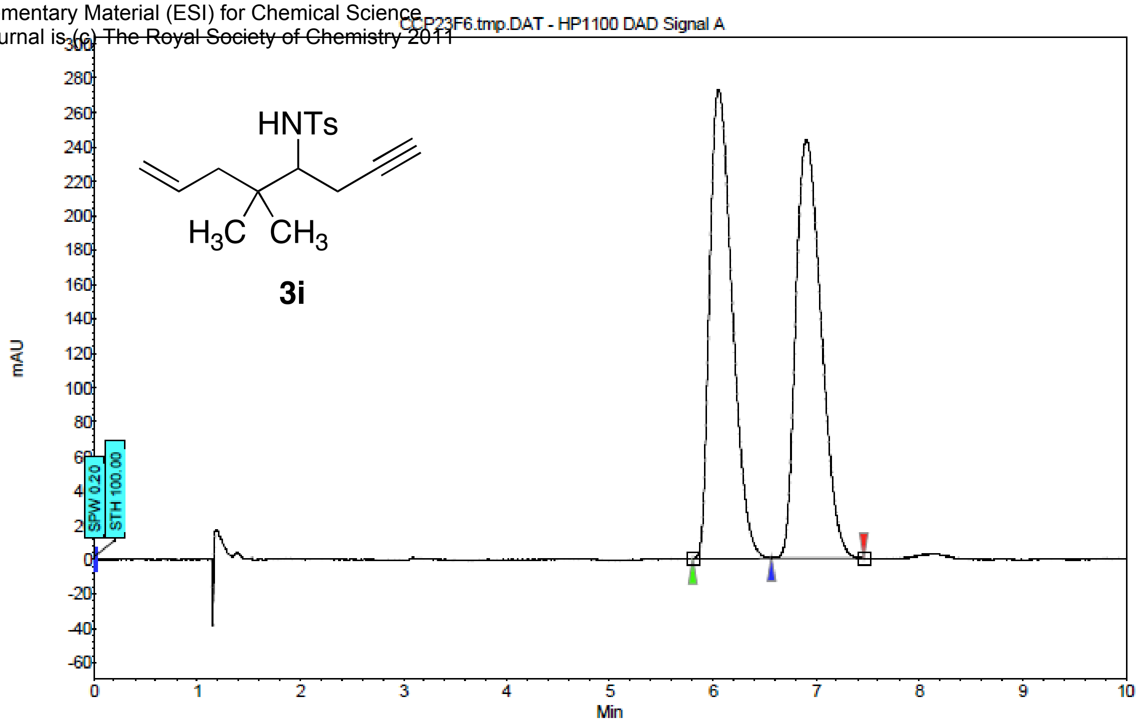
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.47	3.61	3.76	0.00	1.40	34.7	3.9	1.402
2	UNKNOWN	3.76	3.95	4.27	0.00	98.60	1944.0	271.6	98.598
Total						100.00	1978.7	275.4	100.000



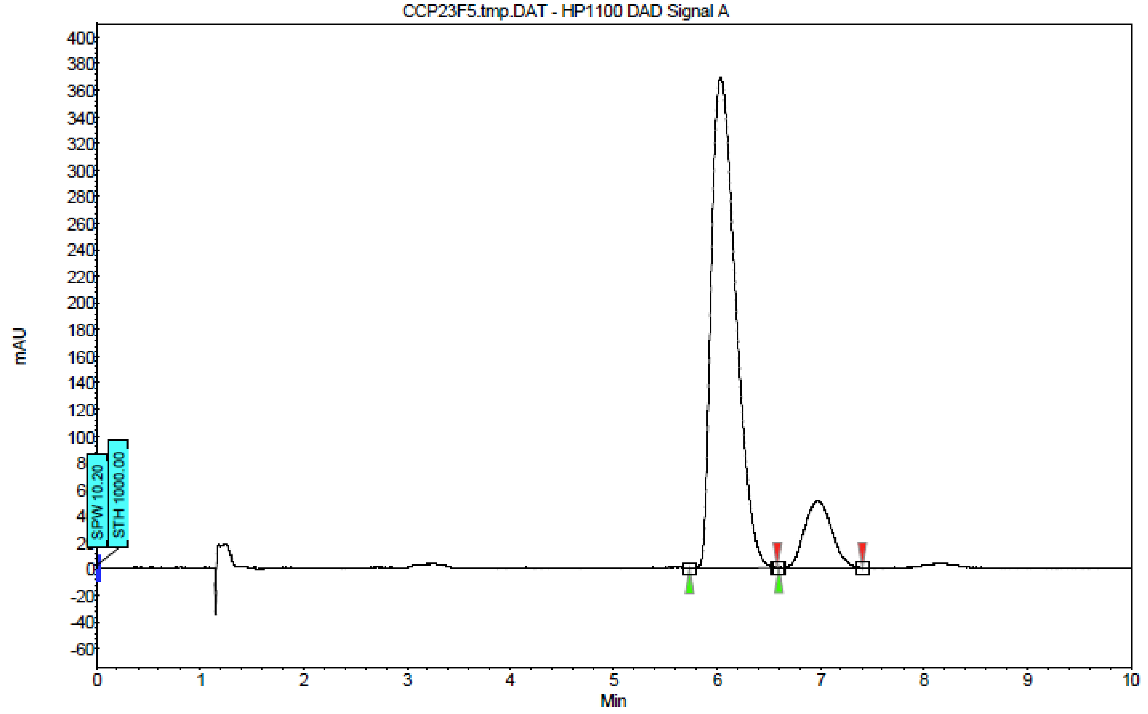
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.64	3.83	4.12	0.00	50.00	98.0	11.8	50.004
2	UNKNOWN	5.43	5.70	6.03	0.00	50.00	68.4	11.8	49.996
Total						100.00	166.4	23.5	100.000



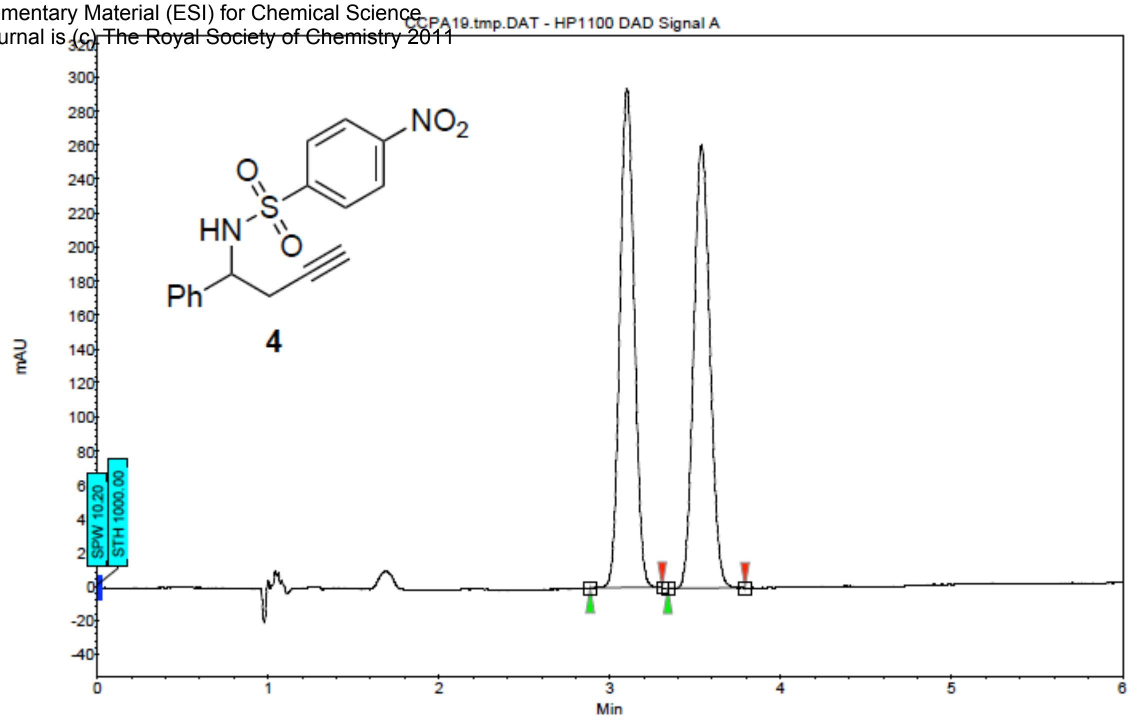
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.74	3.88	4.07	0.00	5.43	33.6	4.0	5.429
2	UNKNOWN	5.45	5.71	6.04	0.00	94.57	411.9	69.9	94.571
Total						100.00	445.5	73.9	100.000



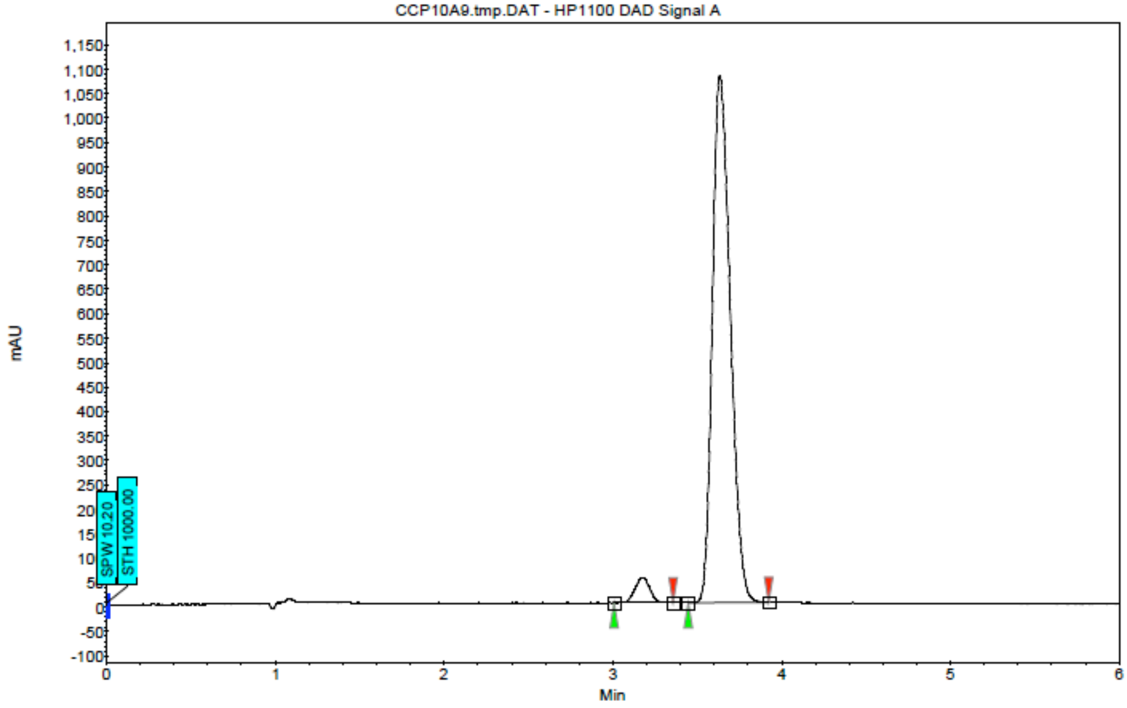
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.81	6.06	6.57	0.00	49.80	272.7	69.0	49.802
2	UNKNOWN	6.57	6.91	7.46	0.00	50.20	243.2	69.6	50.198
Total						100.00	515.9	138.6	100.000



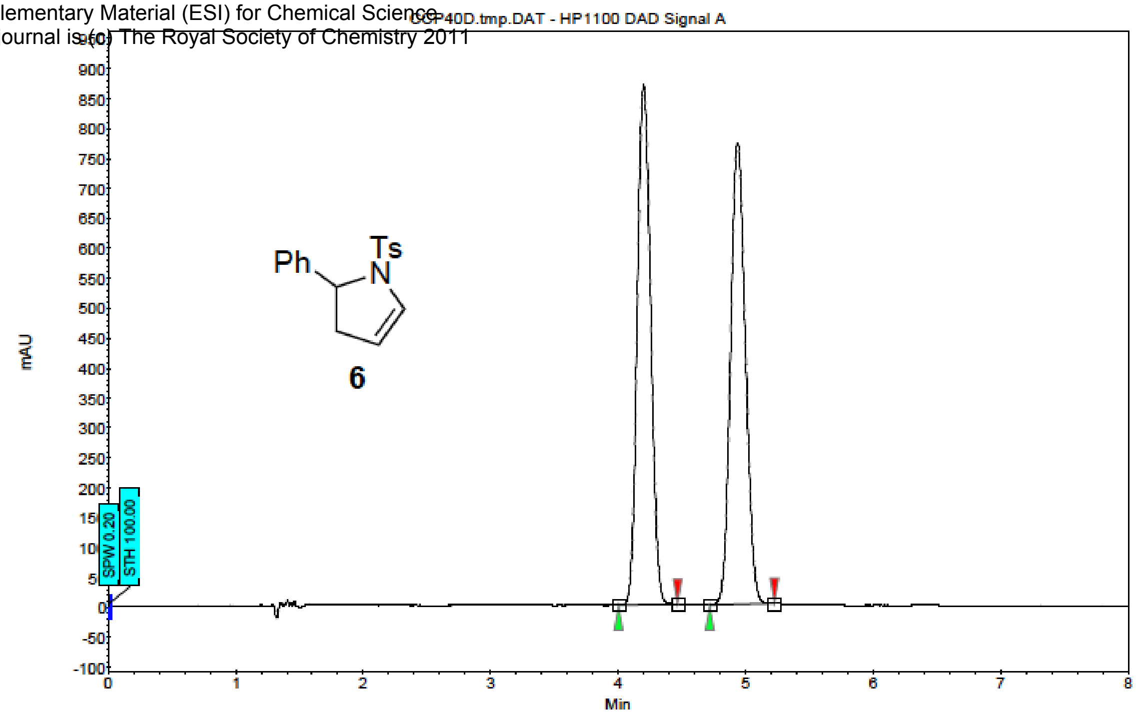
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.73	6.04	6.58	0.00	86.82	368.9	100.5	86.824
2	UNKNOWN	6.60	6.99	7.41	0.00	13.18	50.2	15.3	13.176
Total						100.00	419.1	115.8	100.000



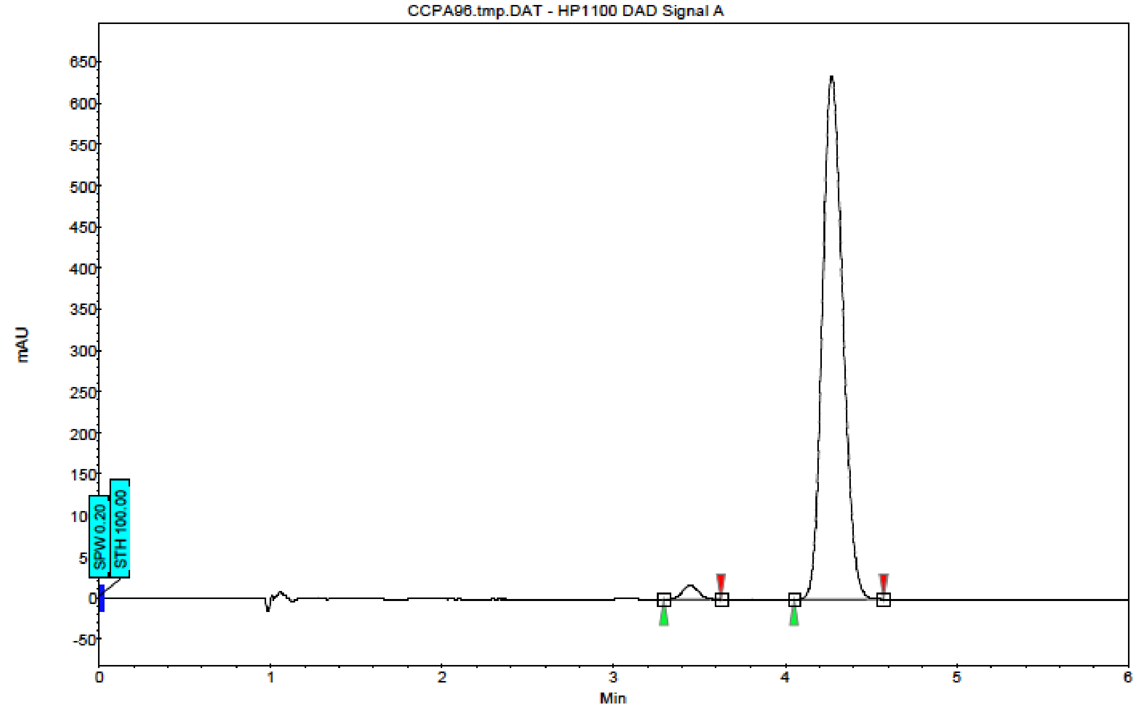
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	2.89	3.10	3.31	0.00	50.07	294.0	28.7	50.074
2	UNKNOWN	3.34	3.54	3.79	0.00	49.93	260.7	28.6	49.926
Total						100.00	554.8	57.3	100.000



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.01	3.18	3.36	0.00	3.76	51.0	5.2	3.761
2	UNKNOWN	3.45	3.64	3.92	0.00	96.24	1077.6	132.0	96.239
Total						100.00	1128.6	137.1	100.000



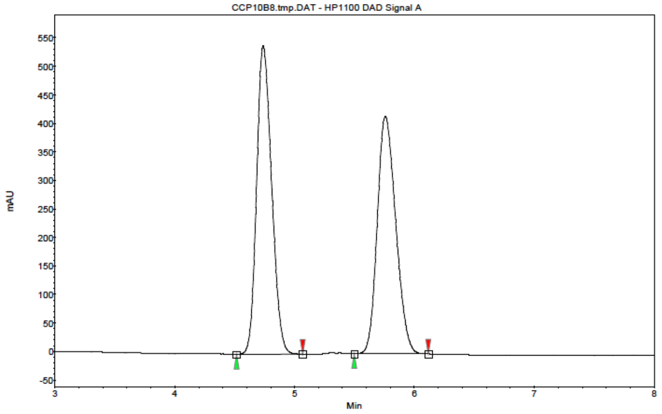
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.00	4.20	4.47	0.00	50.06	869.8	105.2	50.064
2	UNKNOWN	4.72	4.94	5.23	0.00	49.94	770.1	104.9	49.936
Total						100.00	1639.9	210.1	100.000



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.29	3.45	3.63	0.00	2.11	16.7	1.9	2.105
2	UNKNOWN	4.05	4.27	4.57	0.00	97.89	634.4	87.4	97.895
Total						100.00	651.1	89.3	100.000

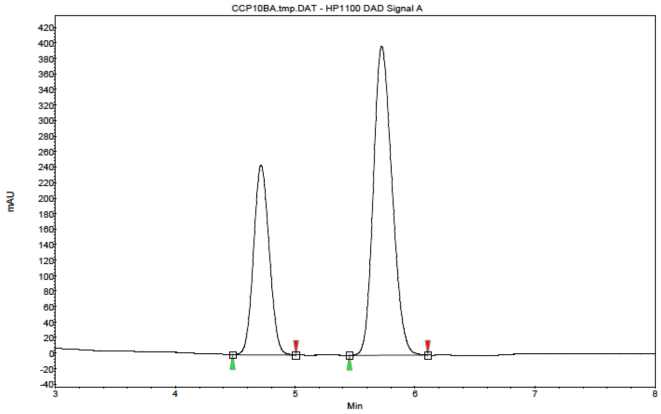
SFC Traces for the Non-Linear Experiment

Catalyst ee = 0%



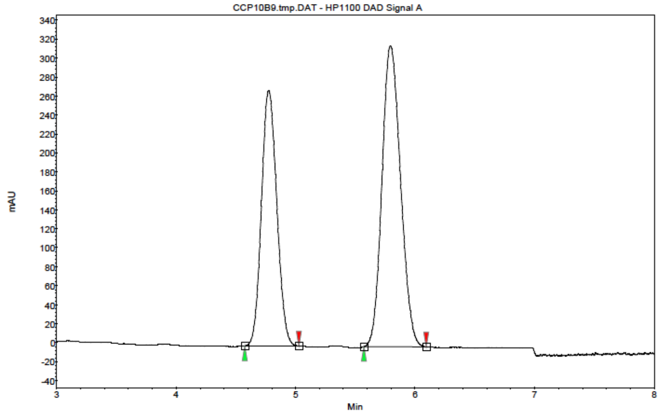
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	4.52	4.74	5.07	0.00	51.34	541.1	78.5	51.343
2	UNKNOWN	5.50	5.76	6.12	0.00	48.66	416.3	74.4	48.657
Total						100.00	957.4	153.0	100.000

Catalyst ee = 50%



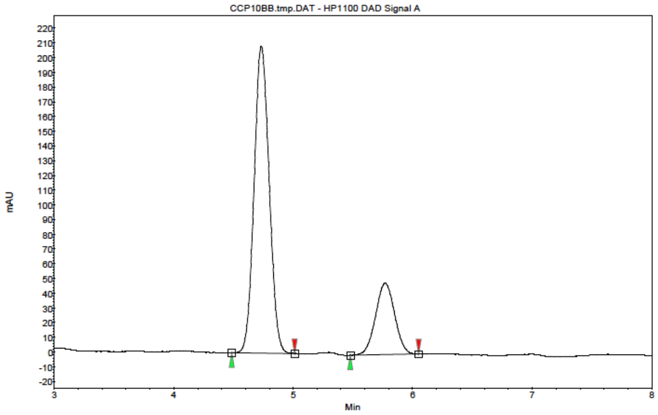
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	4.48	4.71	5.01	0.00	34.01	244.8	36.9	34.008
2	UNKNOWN	5.45	5.72	6.11	0.00	65.99	398.3	71.7	65.992
Total						100.00	643.2	108.6	100.000

Catalyst ee = 30%



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	4.57	4.78	5.03	0.00	41.20	269.4	40.0	41.201
2	UNKNOWN	5.57	5.79	6.09	0.00	58.80	317.2	57.1	58.799
Total						100.00	586.6	97.1	100.000

Catalyst ee = 70%



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	4.49	4.73	5.01	0.00	77.27	208.3	30.4	77.274
2	UNKNOWN	5.48	5.77	6.05	0.00	22.73	48.4	8.9	22.726
Total						100.00	256.7	39.4	100.000