Electronic Supplementary Material (ESI) for ChemComm.


# Selective oxidations of activated alcohols in water at room temperature

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# Supporting Information

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## I. General Experimental Information

Unless otherwise noted, all reactions were performed in microwave vials (Biotage), or 1 dram vials (VWR). A 2 wt. % TPGS-750-M/$H_2O$ solution was prepared by dissolving 4 g TPGS-750-M in 196 g water (HPLC grade). All chemicals were used as received. Analytical thin layer chromatography (TLC) was performed using Silica Gel 60 F254 plates (Merck, 0.25 mm thick). The developed chromatogram was analyzed by UV lamp (254 nm), aqueous potassium permanganate ($KMnO_4$), dinitrophenylhydrazine (DNP), or magic stain (PMA, phosphor-molybdic acid). Flash chromatography was performed in glass columns using Silica Flash® P60 (SiliCycle, 40-63 μm). GC/FID data was recorded on an Agilent 7890A. A HP-5 cross-linked 5% phenylmethylpolysiloxanediphenyl column (30 m x 0.250 mm, 0.25 micron, Agilent Technologies) was employed. $^1H$ and $^{13}C$ spectra were recorded at 22 °C on a Varian UNITY INOVA Avance 400 MHz, Varian UNITY INOVA 500 MHz, or Varian Unity Inova 600 MHz. Chemical shifts in $^1H$ NMR spectra are reported in parts per million (ppm) on the δ scale from an internal standard of residual chloroform (7.27 ppm). NMR processing was done using ACD/NMR processor academic edition v.12.01. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant in Hertz (Hz), and integration. Chemical shifts of $^{13}C$ NMR spectra are reported in ppm from the central peak of $CDCl_3$ (77.00 ppm) on the δ scale. High resolution mass analyses were obtained using a VG70 double-focusing magnetic sector instrument (VG Analytical) for EI, a PE Sciex Q-TOF2 quadrupole/TOF instrument (Waters Corp.) for ESI, and a GCT Premier orthogonal acceleration time-of-flight (Waters Corp.) for FI.

## II. General Method for Oxidations

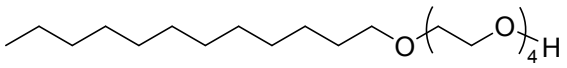
To a 5 mL microwave vial equipped with stir bar was added the alcohol (0.5 mmol), followed by CuBr (3.6 mg, 0.025 mmol, 0.05 equiv), BPy (3.9 mg, 0.025 mmol, 0.05 equiv), TEMPO (3.9 mg, 0.025 mmol, 0.05 equiv), NMI (4.0 μL, 4.1 mg, 0.05 mmol, 0.1 equiv) and 2% TPGS-750-M solution (0.5 mL)was added and vigorously stirred until complete by TLC. Then extracted with the minimal amount of EtOAc, passed through a silica plug and evaporated. Purified via flash column chromatography. NOTE: If an emulsion has formed centrifuge for ~3 min. to break emulsion.

## III. General Methods for Reduction Reactions

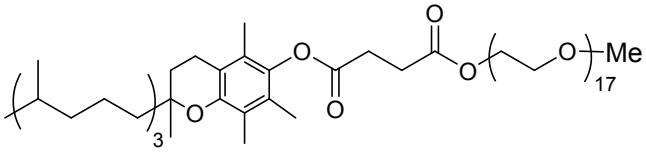
**Representative reduction of an aldehyde or ketone with $NaBH_4$.**
To 18 mmol of the starting aldehyde in MeOH (72 mL), $NaBH_4$ was added portion-wise over 3 h. The reaction proceeded until TLC indicated completion. The solvent was removed *in vacuo*. The slurry was transferred to a separatory funnel with the aid of water and EtOAc. The solution was extracted (3x) with EtOAc. The organics were washed with water, 1 M HCl, saturated $NaHCO_3$, brine, and dried over anhydrous $MgSO_4$.

**Representative reduction of a carboxylic acid with lithium aluminum hydride.**
To an oven dried round-bottom flask was added 5 mmol of the starting acid under an argon atmosphere. Dry THF was added (230 mL) and the solution was cooled to 0 °C. Lithium aluminum hydride was added as a solution (26 mmol, 1.3 M) over 1 h and the solution was allowed to warm to rt overnight. The solution was quenched with EtOAc and water. The solution was extracted with EtOAc (3x), washed with water, brine, and dried over anhydrous $MgSO_4$.

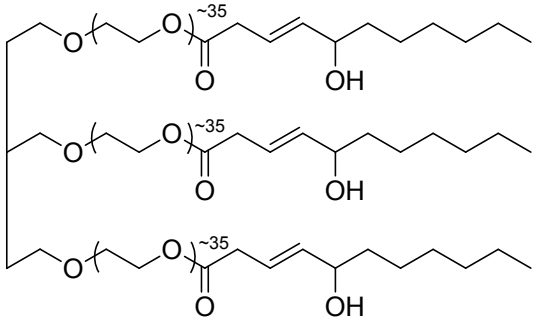
## IV. Figure 1: Monomer structures of ionic and nonionic surfactants screened



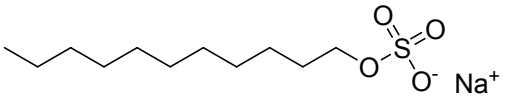
Brij 30



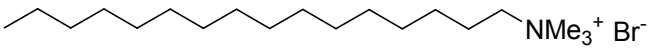
TPGS-750-M



(one component of) cremophor EL

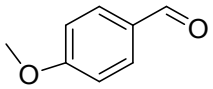


SDS (sodium dodecyl sulfate)



CTAB: cetyltrimethylammonium bromide

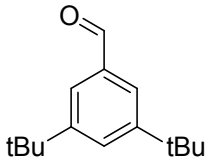
## V. Characterization of Oxidized Aldehyde Products



**[Table 2: Product]: 4-Methoxybenzaldehyde ($C_8H_8O_2$)** was obtained following the general method for oxidations using commercially available (4-methoxyphenyl)methanol (69 mg, 0.5 mmol), affording the title compound as a pale yellow oil (4 h, 66 mg, 98% yield), compound data matches those previously reported.[1]

**$R_f$:** 0.67, 1:2 (EtOAc:hexanes)

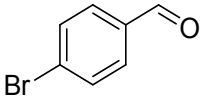
**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 9.92 (s, 1H), 7.87 (d, $J$ = 8.8 Hz, 2H), 7.04 (d, $J$ = 8.6 Hz, 2H), 3.92 (s, 3H).




**[5]: 3,5-Di-*t*-butylbenzaldehyde ($C_{15}H_{22}O$)** was obtained following the general method for oxidations using prepared (3,5-di-*t*-butylphenyl)methanol (110 mg, 0.5 mmol), to afford the title compound following purification by flash column chromatography, eluted with 1:19 EtOAc:hexanes, as a white crystalline solid (5 h, 97 mg, 89% yield). Compound data matches those previously reported.[2]

**$R_f$:** 0.55 1:9 (EtOAc:hexanes)

**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 10.02 (s, 1H), 7.74 (m, 3H), 1.38 (s, 18H).

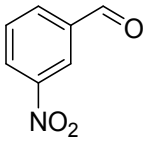



**[6]: 4-Bromobenzaldehyde ($C_7H_5BrO$)** was obtained following the general method for oxidations using commercially available (4-bromophenyl)methanol (93 mg. 0.50 mmol), affording the title compound as a white solid (10h, 92 mg, 97% yield). Compound data matches previously those reported.[3]

**$R_f$:** 0.76, 1:2 (EtOAc:hexanes)

**mp:** 57-59 C

**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 9.99 (s, 1H), 7.78-7.74 (m, 2H), 7.72-7.68 (m, 2H).

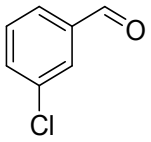



**[7]: 3-Nitrobenzaldehyde ($C_7H_5NO_3$)** was obtained following the general method for oxidations using commercially available (3-nitrophenyl)methanol (77 mg, 0.5 mmol), affording the title compound as an orange solid (16 h, 68 mg, 90% yield). Compound data matched those previously reported.[1]

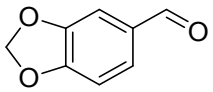
**$R_f$:** 0.63, 1:2 (EtOAc:hexanes)

**mp:** 54-56 C

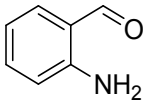
**$^1$H NMR (400 MHz, $CDCl_3$, δ):** 10.14 (s, 1H), 8.73 (t, $J$ = 1.8 Hz, 1H), 8.51 (dqt, $J$ = 8.04 Hz, 1.3 Hz, 1H), 8.25 (dt, $J$ = 7.8 Hz, 1.3 Hz, 1H), 7.78 (t, $J$ = 7.8 Hz, 1H).




**[8]: 3-Chlorobenzaldehyde ($C_7H_5ClO$)** was obtained following the general method for oxidations using (3-chlorophenyl)methanol (142.6 mg, 1.0 mmol), CuBr (7.2 mg, 0.05 mmol, 0.05 equiv), BPy (7.8 mg, 0.05 mmol, 0.05 equiv), TEMPO (7.8 mg, 0.05 mmol, 0.05 equiv), and NMI (8.0 µL, 8.2 mg, 0.10 mmol, 0.1 equiv). To this was added 1.5 mL of a 2 wt % solution of TPGS-750-M (0.66 M) in water and the mixture was vigorously stirred, affording the title compound as a white solid (18 h, 112 mg, 0.80 mmol, 80% yield). Compound data matches those previously reported.[4]
**$R_f$:** 0.39 1:9 (EtOAc:hexanes)
**mp:** 148-152 C
**$^1$H NMR (400 MHz, $CDCl_3$, δ):** 9.99 (s, 1H), 7.87 (t, *J* = 2.0 Hz, 1H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.62 (dd, *J* = 8.1 Hz, 1.7 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 1H).

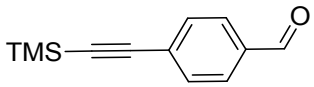



**[9]: Piperonal ($C_8H_6O_3$)** was obtained following the general method for oxidations using commercially available benzo[d][1,3]dioxol-5-ylmethanol (76 mg, 0.50 mmol), affording the title compound as a white solid, (7 h, 72 mg, 97% yield). Compound data matches that of previously reported material.[1]
**$R_f$:** 0.61, 1:2 (EtOAc:hexanes)
**mp:** 35-37 C
**$^1$H NMR (400 MHz, $CDCl_3$, δ):** 9.81 (s, 1H), 7.41 (dd, *J* = 7.8 Hz, 1.3 Hz), 7.34 (d, *J* = 1.3 Hz, 1H), 6.93 (d, *J* = 7.8 Hz, 2H), 6.08 (s, 2H).

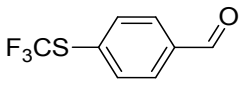



**[10]: 2-Aminobenzaldehyde ($C_7H_7NO$)** was obtained following the general method for oxidations using commercially available (2-aminophenyl)methanol (62 mg 0.50 mmol), affording the title compound as a red liquid (5 h, 57 mg, 95%). Compound data matches those previously reported.[5]
**$^1$H NMR (600 MHz, $CDCl_3$, δ):** 9.89 (s, 1H), 7.51 (dd, *J* = 7.9 Hz, 1.3 Hz, 1H), 7.35-7.31 (m, 1H), 6.77 (t, *J* = 7.6 Hz, 1H), 6.67 (d, *J* = 8.2 Hz, 1H), 6.13 (br, s, 2H).

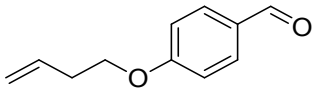
**Comparison oxidation at reduced temperatures**. The identical reaction was run at ice bath temperatures to test if an anticipated greater concentration of dissolved oxygen in the nanomicelles would lead to an enhanced rate of oxidation. While at RT the reaction is complete in 5 h, after 7 h at ca. 0 °C it was only 80% complete, with no further progress being observed after 8 h.



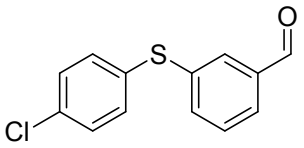

**[11]: 4-((Trimethylsilyl)ethynyl)benzaldehyde ($C_{12}H_{14}OSi$)** was obtained following the general method for oxidations using commercially available (4-((trimethylsilyl)ethynyl)phenyl)methanol (102 mg, 0.50 mmol), affording the title compound as a white solid (16 h, 88 mg, 87% yield). Compound data matches those previous reported.[6]
**$R_f$:** 0.47, 1:2 (EtOAc:hexanes)
**mp:** 69-71 C
**$^1$H NMR (600 MHz, $CDCl_3$, δ):** 10.0 (s, 1H), 7.83 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 2H), 0.28 (s, 3H).



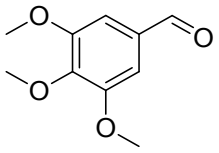

**[12]: 4-((Trifluoromethyl)thio)benzaldehyde ($C_8H_5F_3OS$)** was obtained following the general method for oxidations using prepared (4-((trifluoromethyl)thio)phenyl)methanol (104 mg, 0.5 mmol), affording the title compound as a white crystalline solid (21 h, 84 mg, 81% yield) following flash column chromatography of the crude product eluted with 1:9 EtOAc:hexanes. Compound data matches that of commercially available material CAS: 4021-50-5.
**$R_f$:** 0.45, 1:9 (EtOAc:hexanes)
**mp:** 90-91°C
**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 10.08 (s, 1H), 7.94 (d, *J* = 8.3 Hz, 2H), 7.82 (d, *J* = 8.3 Hz, 1H).



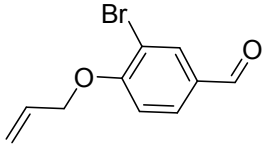

**[13]: 4-(But-3-en-1-yloxy)benzaldehyde ($C_{11}H_{12}O_2$)** was obtained following the general method for oxidations using prepared (4-(but-3-en-1-yloxy)phenyl)methanol (89 mg, 0.5 mmol) to afford the title compound following purification by flash column chromatography, eluted with 1:9 EtOAc:hexanes, as a colorless oil (16 h, 78 mg, 89% yield). Compound data matches that previously reported.[7]
**$R_f$:** 0.34, 1:9 (EtOAc:hexanes)
**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 9.89 (s, 1H), 7.84 (d, *J* = 8.8 Hz, 2H), 7.01 (d, *J* = 8.6 Hz, 2H), 5.91 (ddt, *J* = 17.1 Hz, 10.3 Hz, 6.6 Hz, 1H), 5.17 (m, 2H), 4.11 (t, *J* = 6.6 Hz, 2H), 2.59 (m, 2H)



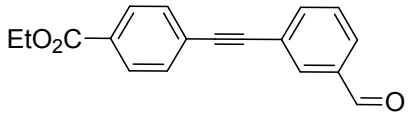

**[14]: 4-((4-Chlorophenyl)thio) benzaldehyde ($C_{13}H_9ClOS$)** was obtained following the general method for oxidations using prepared (3-((4-chlorophenyl)thio)phenyl)methanol (126 mg, 0.5 mmol), affording the title compound as a pale yellow solid (20 h, 113 mg, 91% yield).
**$R_f$:** 0.76, 1:2 (EtOAc:hexanes)
**mp:** 72-76 C
**$^1$H NMR (400 MHz, $CDCl_3$, δ):** 10.36 (s, 1H), 7.89 (dd, *J* = 7.8 Hz, 1.6 Hz, 1H), 7.4 (dt, *J* = 7.8 Hz, 1.8 Hz, 1H), 7.39-7.34 (m, 5H), 7.09 (dd, *J* = 8.0 Hz, 0.8 Hz, 1H);
**$^{13}$C NMR (126 MHz, $CDCl_3$, δ):** 191.37, 140.92, 134.75, 134.43, 134.13, 133.71, 132.24, 131.78, 130.15, 129.91, 126.49;
**IR (quartz crystal):** ν 3079, 2849, 2754, 1671, 759, 674 $cm^{-1}$.
**HRMS (EI) (*m/z*):** $[M]^+$ calc. for $C_{13}H_9ClOS$, 248.0063; found 248.0060.




**[15]: 3,4,5-Trimethoxy benzaldehyde ($C_{10}H_{12}O_4$)** was obtained following the general method for oxidations using commercially available (3,4,5-trimethoxyphenyl)methanol (102 mg, 0.5 mmol), affording the title compound as a pale yellow solid, (9 h, 89 mg, 0.46 mmol, 91%). Compound data matches that previously reported.[8]
**$R_f$:** 0.43, 1:2 (EtOAc:hexanes)
**mp:** 68-69 C.
**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 9.89 (s, 1H), 7.16 (s, 2H), 3.96 (s, 9H).




**[16]: 4-(Allyloxy)-3-bromobenzaldehyde ($C_{10}H_9BrO_2$)** was obtained following the general method for oxidations using prepared (4-(allyloxy)-3-bromophenyl)methanol (121.5 mg, 0.5 mmol) to afford the title compound, following purification by flash chromatography eluted with 1:2 (EtOAc:hexanes) as a yellow oil (15h, 107 mg, 89% yield).
**$R_f$:** 0.39 1:4 (EtOAc:hexanes)
**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 9.85 (s, 1H), 8.10 (m, 1H), 7.80 (m, 1H), 7.00 (d, J = 8.6Hz, 1H), 6.07 (m, 1H), 5.52 (m, 1H), 5.37 (m, 1H), 4.72 (dt, J = 4.9Hz, 1.5Hz, 2H);
**$^{13}$C NMR (126 MHz, $CDCl_3$, δ):** 189.48, 159.66, 134.70, 131.54, 130.88, 130.77, 118.46, 113.03, 112.74, 69.86;
**IR (quartz crystal):** ν 3364, 3081, 3019, 2988, 2935, 2835, 2728, 1688, 1261, 1238, 1145, 666 $cm^{-1}$
**HRMS (EI) (*m/z*):** $[M]^+$ calc. for $C_{10}H_9BrO_2$, 239.9786; found 239.9788.



**[17]: Ethyl 4-((3-formylphenyl)ethynyl)benzoate ($C_{18}H_{14}O_3$)** was obtained following the general method for oxidations using prepared ethyl 4-((3-(hydroxymethyl)phenyl)ethynyl)benzoate (140 mg, 0.5 mmol) to afford the title compound as a white crystalline solid following purification by flash column chromatography eluted with 2:98 MeOH:DCM (52 h, 125 mg, 91% yield).

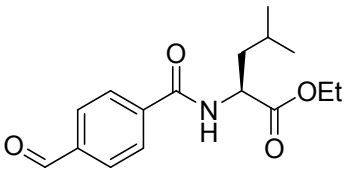
**$R_f$:** 0.85, 1:9 (MeOH:DCM)

**mp:** 90-91 °C

**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 10.03 (s, 1H), 8.05 (m, 3H), 7.87 (d, *J* = 7.7 Hz, 1H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.61 (d, *J* = 8.3 Hz, 2H), 7.55 (t, *J* = 7.8 Hz, 1H), 4.40 (q, *J* = 7.0 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H).

**$^{13}$C NMR (500 MHz, $CDCl_3$, δ):** 191.34, 165.92, 137.12, 136.53, 132.99, 131.54, 130.29, 129.52, 129.34, 129.18, 127.14, 123.97, 90.51, 90.09, 61.18, 14.29.

**HRMS (EI) (*m/z*):** $[M]^+$ calcd for $C_{18}H_{14}O_3$: 278.0943; found: $[M+Na]^+$: 301.0832



**[18]: Ethyl (4-formylbenzoyl)-*L*-leucinate** was obtained following the general method for oxidations, Ethyl (4-(hydroxymethyl)benzoyl)-*L*-leucinate (146.8 mg, 0.5 mmol), affording the title compound as yellow waxy solid, (Run 1: 24 h, 92 mg, 0.32 mmol, 63% yield) (Run 2: 24 h, 100.5 mg, 0.34 mmol, 69% yield), 0.33 mmol, 66% average yield of the two runs.

**$R_f$:** 0.55; 1:1 (EtOAc:hexanes)

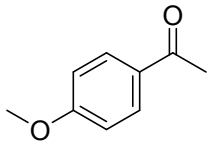
**$^1$H NMR (600 MHz, $CDCl_3$, δ):** 10.10 (s, 1H), 7.97 (s, 4H), 6.61 (d, *J* = 7.9 Hz, 1H), 4.86 (dt, J = 8.5 Hz, 5 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 1.74 (m, 3H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.01 (dd, *J* = 13, 6.3Hz, 6H).

**$^{13}$C NMR (126 MHz, $CDCl_3$, δ):** 191.46, 173.04, 165.94, 139.15, 138.35, 129.84, 127.76, 61.64, 51.39, 41.91, 25.03, 22.81, 22.12, 14.17.

**IR (quartz crystal):** ν 3332, 2957, 1742, 1638, 1611, 1573, 1521, 1499, 1372, 1348, 1293, 1224, 1198, 1157, 1027, 1016, 858, 840, 763, 562, 500, 479 $cm^{-1}$

**HRMS (EI) (*m/z*):** $[M]^+$ calc. for $C_{16}H_{21}NO_4$: 291.1471; found $[M+Na]^+$: 314.1374.

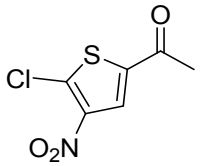
## VI. Characterization of Oxidized Ketone Products




**[19]: 1-(4-Methoxyphenyl)ethan-1-one ($C_9H_{10}O_2$)** was obtained following the general method for oxidations using commercially available 1-(4-methoxyphenyl)ethan-1-ol (76 mg, 0.50 mmol) stirred at 40 C to afford the title compound as slightly orange crystals (12 h, 71 mg, 95% yield). Compound data matches those previously reported.[9]

**mp:** 33-35 C

**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 7.95 (m, 2H), 6.95 (m, 2H), 3.88 (s, 3H), 2.57 (s, 3H).

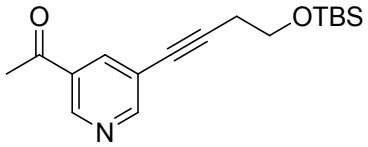



**[20]: 1-(5-Chloro-4-nitrothiophen-2-yl)ethan-1-one** was obtained following the general method for oxidations using prepared 1-(5-chloro-4-nitrothiophen-2-yl)ethan-1-ol (104 mg, 0.50 mmol) stirred at 40 C to afford the title compound as a off white solid (12 h, 99 mg, 96% yield). Compound data matches those previously reported.[10]

**$R_f$:** 0.40, 1:9 (EtOAc:hexanes)

**mp:** 82-84 C

**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 8.08 (s, 1H), 2.59 (s, 3H).

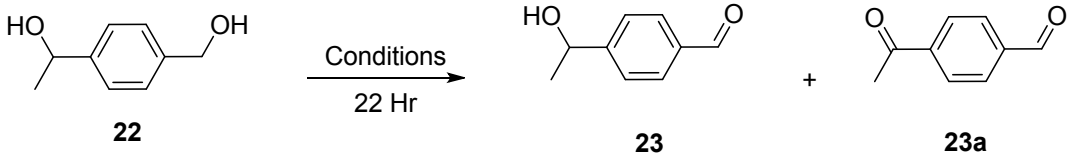



**[21]: 1-(5-(4-((*t*-Butyldimethylsilyl)oxy)but-1-yn-1-yl)pyridin-3-yl)ethanone ($C_{17}H_{25}NO_2Si$)** was obtained following the general method for oxidations. 1-(5-(4-((*t*-Butyldimethylsilyl)oxy)but-1-yn-1-yl)pyridin-3-yl)ethanol (64 mg, 0.21 mmol, 1 equiv) was added to a conical 5 mL microwave vial with CuBr (1.6 mg, 0.011 mmol, 0.05 equiv), bpy (1.8 mg, 0.011 mmol, 0.05 equiv), and TEMPO (1.8 mg, 0.011 mmol, 0.05 equiv). To this 0.4 mL of a 2 wt % solution of TPGS-750-M in water was syringed in. NMI (2 μL, 1.8 mg, 0.022 mmol, 0.1 equiv) was added to the vial. The reaction was stirred for 48 h at 45 °C before conversion stopped, by TLC analysis. The crude was extracted with ether and dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo and the crude was purified by flash column chromatography, eluted with 3:7 EtOAc:hexanes, affording the title compound (48 h, 53 mg, 84% yield) as a light yellow oil.

**$R_f$:** 0.3 (3:7, EtOAc:hexanes)

**$^1$H NMR (600 MHz, $CDCl_3$, δ):** 9.01 (s, 1H), 8.76 (s, 1H), 8.20 (d, *J* = 1.9 Hz, 1H), 3.82 (t, *J* = 6.9 Hz, 2H), 2.65 (t, *J* = 6.9 Hz, 1H), 2.62 (s, 1H), 0.91 (s, 9H), 0.09 (s, 6H).
**$^{13}$C NMR (126 MHz, $CDCl_3$, δ):** 196.04, 155.39, 147.64, 138.05, 92.76, 61.50, 29.69, 26.78, 25.86, 25.64, 23.87, 18.35, -5.26.
**IR (quartz crystal):** ν 2954, 2928, 2855, 1745, 1696, 1108, 836, 778 $cm^{-1}$
**HRMS (EI) (*m/z*):** $[M]^+$ calc. for $C_{17}H_{25}NO_2Si$, 303.1655; found $[M+H]^+$304.1724

## VII. Characterization of Oxidized 1° Benzylic versus 2° Benzylic Alcohols

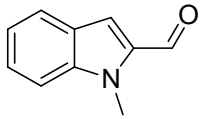


**22** **23** **23a**

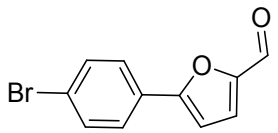
**[23]: 4-(1-Hydroxyethyl)benzaldehyde ($C_9H_{10}O_2$)**, was obtained following the general method for oxidations using prepared 1-(4-(hydroxymethyl)phenyl)ethanol (76.1 mg, 0.5 mmol), purification by flash chromatography to title compound as a clear liquid (71.7 mg, 0.47 mmol, 94% yield). Compound data matches those previously reported.[11]
**$R_f$:** 0.2 1:1 (EtOAc:hexanes)
**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 10.00 (d, *J* = 2.1 Hz, 1H), 7.87 (m, 2H), 7.55 (m, 2H), 5.03 (qt, *J* = 6.5 Hz, 1H), 2.06 (br, s, 1H), 1.52 (dd, *J* = 6.5 Hz, 2.6 Hz, 3H).

**[23a] 4-Acetylbenzaldehyde ($C_9H_8O_2$)** was purified by flash chromatography to afford title compound as a clear liquid (4.0 mg, 0.03 mmol, 6% yield). Compound data matches those previously reported.[11]
**$R_f$:** 0.52 1:1 (EtOAc:hexanes)
**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 10.13 (d, *J* = 2.1 Hz, 1H), 8.12 (m, 2H), 8.00 (m, 2H), 2.68 (m, 3H).

## VIII. Characterization of Heteroaromatic Benzylic-like Alcohols




**[24]: 1-Methyl-1*H*-indole-2-carbaldehyde** was obtained following the general method for oxidations using prepared (1-methyl-1*H*-indol-2-yl)methanol (80.6 mg, 0.5 mmol), purification by flash chromatography (1:9, EtOAc:hexanes) to afford 1-methyl-1*H*-indole-2-carbaldehyde as a pale yellow solid, (29 h, 66.5 mg, 84% yield) . Compound data matches previously reported.[12]
**$R_f$:** 0.36, 1:9 (EtOAc:hexanes)
**mp:** 84-86 C
**$^1$H NMR (400 MHz, $CDCl_3$, δ):** 9.90 (s, 1H), 7.75 (d, *J* = 8.3 Hz, 1H), 7.47-7.40 (m, 2H), 7.22-7.17 (m, 1H), 4.11 (s, 3H).

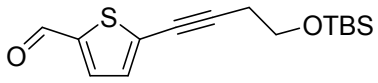



**[25]: 5-(4-Bromophenyl)furan-2-carbaldehyde** was obtained following the general method for oxidations using prepared (5-(4-bromophenyl)furan-2-yl)methanol (63.3 mg, 0.25 mmol), CuBr (1.7 mg, 0.0125 mmol, 0.05 equiv), BPy (2.0 mg, 0.0125 mmol, 0.05 equiv), and TEMPO (2.0 mg, 0.0125 mmol, 0.05 equiv), and NMI (2.0 μL, 2.1 mg, 0.025 mmol, 0.1 equiv). To this 0.5 mL of a 2 wt % solution of TPGS-750-M in water was added and stirred vigorously to afford the title compound as a pale red solid (6 h, 53 mg, 0.21 mmol, 85% yield). Compound data matches those previously reported.[13]

**$R_f$:** 0.54, 1:2 (EtOAc:hexanes)

**mp:** 156-158 C

**$^1$H NMR (400 MHz, $CDCl_3$, δ):** 9.67 (s, 1H), 7.70 (dt, *J* = 8.6 Hz, 1.8 Hz, 2H), 7.59 (dt *J* = 8.6 Hz, 1.8 Hz, 2H), 7.32 (d, *J* = 3.9 Hz, 1H), 6.85 (d, *J* = 3.6 Hz, 1H).




**[26]:5-(4-((*t*-Butyldimethylsilyl)oxy)but-1-yn-1-yl)thiophene-2-carbaldehyde ($C_{15}H_{22}O_2SSi$)** was obtained following the general method for oxidations using the synthesized (5-(4-((*t*-butyldimethylsilyl)oxy)but-1-yn-1-yl)thiophen-2-yl)methanol, (61 mg, 0.206 mmol, 1 equiv) was added to a 4 mL vial with CuBr (1.5 mg, 0.01 mmol, 0.05 equiv), bpy (1.6 mg, 0.01 mmol, 0.05 equiv), and TEMPO (1.6 mg, 0.01 mmol, 0.05 equiv). To this 0.4 mL of a 2 wt % solution of TPGS-750-M in water was added. NMI (1.7 μL, 1.7 mg, 0.021 mmol, 0.1 equiv) was then added to the vial and stirred at 45 °C before conversion stopped. The crude was then extracted with ether and dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo and the crude product was purified by flash column chromatography, affording the title compound (31 h, 46 mg, 72% yield), as a light orange oil.

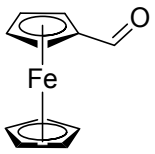
**$R_f$:** 0.3, 1:9 (EtOAc:hexanes)

**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 9.83 (s, 1H), 7.61 (d, *J* = 3.9 Hz, 1H), 7.16 (d, *J* = 3.9 Hz, 1H), 3.83 (t, *J* = 6.7 Hz, 2H), 2.68 (t, *J* = 6.7 Hz, 2H), 1.00 – 0.86 (m, 9H), 0.10 (s, 6H).

**$^{13}$C NMR (126 MHz, $CDCl_3$, δ):** 182.37, 143.07, 135.99, 133.72, 131.95, 97.35, 74.44, 61.27, 25.86, 24.26, 18.33, -5.26.

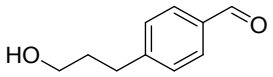
**IR (quartz crystal):** ν 2953, 2928, 2856, 2809, 2739, 2228, 1668, 1521, 1472, 1463, 1449, 1384, 1361, 1346, 1252, 1215, 1188, 1103, 1048, 1006, 990, 939, 910, 834, 807, 775, 753 $cm^{-1}$

**HRMS (EI) (*m/z*):** $[M]^+$ calc. for $C_{15}H_{22}O_2SSi$, 294.1111; found $[M+Na]^+$ 317.1007

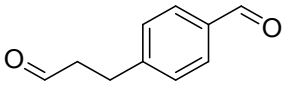



**[27]: Ferrocenecarboxaldehyde ($C_{11}H_{10}FeO$)** was obtained following the general method for oxidations using commercially available ferrocenemethanol (108 mg, 0.5 mmol), affording the title compound as a purple solid (24 h, 94 mg, 88% yield). Compound data matches those previously reported.[14]
**$^1$H NMR (600 MHz, $CDCl_3$, δ):** 9.99 (s, 1H), 4.81 (s, 2H), 4.62 (s, 2H), 4.29 (s, 5H).

**IX. Characterization of Benzylic versus Aliphatic Alcohol Oxidation Products**

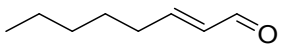



**[28]: 4-(3-Hydroxypropyl)benzaldehyde ($C_{10}H_{12}O_2$)** was obtained following the general method for oxidations using prepared 3-(4-(hydroxymethyl)phenyl)propan-1-ol (83.0 mg, 0.5 mmol), to afford title compound as a clear liquid following purification by flash chromatography (14 h, 72.4 mg, 88% yield). Compound data matches those previously reported.[15]
**$R_f$:** 0.32, 1:1 (EtOAc:hexanes)
**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 9.99 (s, 1H), 7.88 (m, 2H), 7.38 (d, $J$ = 8.06 Hz, 2H), 3.70 (t, $J$ = 6.35 Hz, 2H), 2.82 (t, $J$ = 7.8 Hz, 2H), 1.88-1.97 (m, 2H).




**[29]: 4-(3-Oxopropyl)benzaldehyde ($C_{10}H_{10}O_2$)** was purified by flash chromatography to afford title compound as a clear liquid (7.8 mg, 10% yield). Compound data matches those previously reported.[16]
**$R_f$:** 0.48, 1:1 (EtOAc:hexanes)
**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 9.99 (s, 1H), 9.84 (d, $J$ = 1 Hz, 1H), 7.82 (d, $J$ = 7.8 Hz, 2H), 7.38 (d, $J$ = 8 Hz, 2H), 3.05 (t, $J$ = 7.4 Hz, 2H), 2.85 (t, $J$ = 7.4 Hz, 2H).

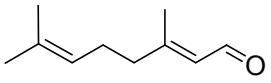
**X. Characterization of Primary Allylic Alcohols**




**[30]: (*E*)-Oct-2-enal ($C_8H_{14}O$)** was obtained following the general method for oxidations using commercially available (*E*)-oct-2-en-1-ol (64 mg, 0.5 mmol) to afford the title compound as a pale yellow oil (9 h, 60 mg, 93% yield). Compound data matches those previously reported.[17]

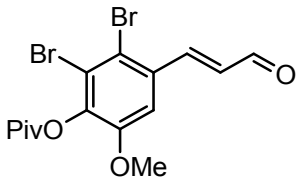
**$R_f$:** 0.30, 1:19 (EtOAc:hexanes)

**$^1$H NMR (400 MHz, $CDCl_3$, δ):** 9.52 (d, $J$ = 7.8 Hz, 1H), 6.87 (dt, $J$ = 15.5 Hz, 6.8 Hz., 1H), 6.14 (m, 1H), 2.35 (m, 2H), 1.53 (t, $J$ = 7.3 Hz, 2H), 1.31 – 1.36 (m, 4H), 0.91 (m, 3H).



**[31]: Geranial ($C_{10}H_{16}O$)** was obtained following the general method for oxidations using commercially available geraniol (77 mg, 0.5 mmol) to afford the title compound as a pale yellow oil (10 h, 73 mg, 97% yield). Compound data matches those previously reported.[18]

**$^1$H NMR (600 MHz, $CDCl_3$, δ):** 10.0 (d, *J* = 8.4 Hz, 1H), 5.89 (dd, *J* = 8.0 Hz, 1.0 Hz, 1H), 5.08 (t, *J* = 6.6 Hz, 1H), 2.19-2.27 (m, 4H), 2.17 (d, *J* = 1.0 Hz, 3H), 1.70 (s, 3H), 1.62 (s, 3H).




**[32]: (*E*)-2,3-Dibromo-6-methoxy-4-(3-oxoprop-1-en-1-yl)phenyl pivalate** was obtained following the general method for oxidations using prepared (*E*)-2,3-dibromo-4-(3-hydroxyprop-1-en-1-yl)-6-methoxyphenyl pivalate (211 mg, 0.5 mmol), followed by the addition of another equivalent of catalyst system: copper bromide (3.6 mg) 2,2'-bipyridine (3.9 mg), (2,2,6,6-tetramethylpiperidin-1-yl)oxy (3.9 mg), and *N*-methylimidazole (4 μL) after 12 h, affording the title compound after 24 h. (162 mg, 0.385 mmol, 77% yield)

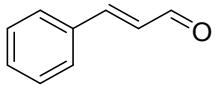
**$R_f$**: 0.73, $Et_2O$

**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 9.79 (d, *J* = 7.5 Hz, 1H), 7.92 (d, *J* = 16 Hz, 1H), 7.15 (s, 1H), 6.60 (dd, *J* = 16, 7.5 Hz, 1H), 3.86 (s, 3H), 1.42 (s, 9H).

**$^{13}$C NMR (126 MHz, $CDCl_3$, δ):** 192.98, 174.76, 151.57, 151.06, 141.32, 133.28, 131.39, 122.52, 119.09, 109.62, 56.40, 39.25, 27.03

**IR (quartz crystal):** ν 2974, 2933, 2851, 1753, 1677, 1455, 1263, 1087, 967, 826, 580 $cm^{-1}$

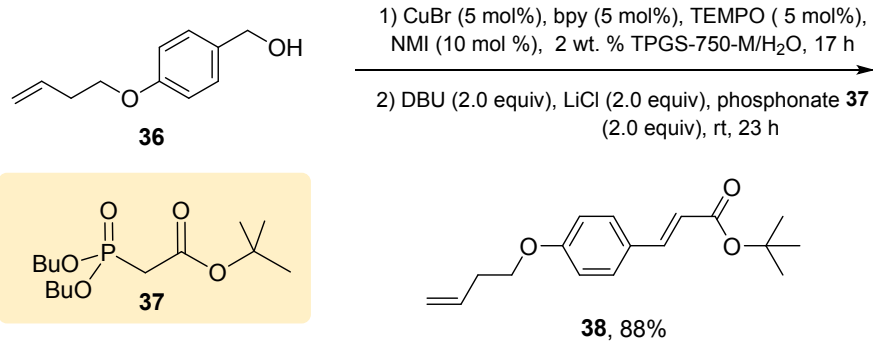
**HRMS (EI) (*m/z*):** $[M]^+$ calc. for $C_{15}H_{16}Br_2O_4$ [M+] : 417.9415; found $[M+Na]^+$: 440.9297



**[35]: Cinnamaldehyde ($C_9H_8O$)** was obtained following the general method for oxidations using commercially available cinnamyl alcohol (67 mg, 0.50 mmol), to afford the title compound as a yellow liquid (9 h, 53 mg, 80% yield). Compound data matches those previously reported.[19]

**$^1$H NMR (400 MHz, $CDCl_3$, δ):** 9.72 (d, *J* = 7.6 Hz, 1H), 7.44-7.59 (m, 6H), 6.73 (m, 1H).

## XI. Tandem Oxidation/ Horner- Emmons-Wadsworth Reaction




**[38]: (*E*)-*t*-Butyl 3-(4-(but-3-en-1-yloxy)phenyl)acrylate ($C_{17}H_{22}O_3$)** was obtained following the general method for oxidations Prepared (4-(but-3-en-1-yloxy)phenyl)methanol (**36**) (89 mg, 0.5 mmol), CuBr (3.6 mg, 5 mol %), bpy (4.0 mg, 5 mol %), TEMPO (4.0 mg, 5 mol %), NMI (0.004 mL, 10 mol %) and 1.0 mL TPGS-750-M (2 wt % solution) were added to a 5 mL microwave vial with a stir bar. The reaction was stirred vigorously while open to air at rt for 17 h. *t*-Butyl-2-(dibutoxyphosphoryl)acetate, **37**) (308 mg, 1.0 mmol), LiCl (42.4 mg, 1.0 mmol), and 1,8-diazabicyclo[5.4.0]undec-7-ene (152 mg, 1.0 mmol) were added to the reaction vial by weight and the reaction was stirred for 23 h. The reaction mixture was purified by flash chromatography, eluted with 1:99 (EtOAc:hexanes), affording the title compound (120.5 mg, 0.44 mmol, 88% yield)

**mp:** 69-72 °C

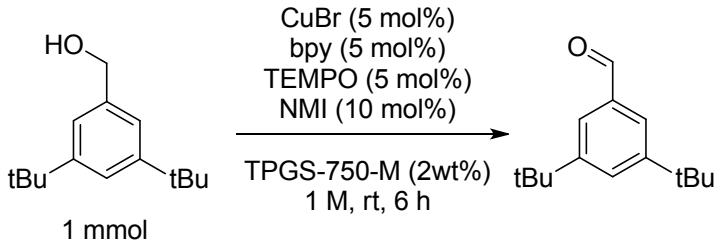
**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 7.55 (d, $J$ = 15.8 Hz, 1H), 7.46 (m, 2H), 6.89 (m, 2H), 6.25 (d, $J$ = 16.1 Hz, 1H), 5.91 (dd, $J$ = 17.1 Hz, 10.4 Hz, 1H), 5.18 (dd, $J$ = 17.1 Hz, 1.8 Hz, 1H), 5.13 (m, 1H), 4.05 (t, $J$ = 6.7 Hz, 2H), 2.56 (m, 2H), 1.54 (s, 9H);

**$^{13}$C NMR (126 MHz, $CDCl_3$, δ):** 166.67, 160.45, 143.19, 134.16, 129.52, 128.63, 127.38, 117.67, 117.20, 114.79, 103.74, 80.20, 67.27, 33.52, 28.23;

**IR (quartz crystal):** ν 3076, 3005, 2977, 2933, 1699, 1691, 1512, 1284, 1271, 1209, 1176, 1143, 1121 $cm^{-1}$

**HRMS (EI) (*m/z*):** $[M]^+$ calc. for $C_{17}H_{22}O_3$, 274.1569; found $[M+Na]^+$, 297.1473.

## XII: Recycle Study and E Factor Calculations




**4** **5**

Following the general method for oxidations using alcohol **4** (220mg, 1.0 mmol), CuBr (7.2 mg, 0.05 mmol, 0.05 equiv), BPy (7.8 mg, 0.05 mmol, 0.05 equiv), TEMPO (7.8 mg, 0.05 mmol, 0.05 equiv), and NMI (8.0 µL, 8.2 mg, 0.10 mmol, 0.1 equiv) were added to a 5 mL microwave vial with a stir bar. 1.0 mL of 2% TPGS-750-M solution was added and vigorously stirred until complete by TLC. 0.25ml EtOAc was added and stirred slowly (to prevent emulsion) for 5 minutes, then removed via pipette, passed through a silica gel plug. The solvent was evaporated

and analyzed by GC. Argon was then bubbled through the reaction mixture for 10 minutes to remove residual EtOAc. Then another equivalent of alcohol **4**, TEMPO, bpy, and NMI were added. This procedure was followed for a total of five reactions. NOTE: If an emulsion has formed centrifuge for ~3 min. to break emulsion.

| Run | Yield (%) |
|---|---|
| 1 | 92 |
| 2 | 89 |
| 3 | 83[a] |
| 4 | 93 |
| 5 | 87 |

[a] Added CuBr (5 mol%) for run number 3

**E Factor Calculations:**

**Calculations:**

Densities used: $H_2O$ = 1 g/mL, EtOAc = 0.897 g/mL

Product mass: 218.34 g/mol

$$\textbf{E Factor} = \frac{\text{Solvents (g)}}{\text{Pure product (g)}}$$

| Run | Mass(mg) |
|---|---|
| 1 | 200.1 |
| 2 | 194.3 |
| 3 | 181.2 |
| 4 | 203.1 |
| 5 | 190.0 |

$$\text{Single Run w/out Aq.} = \frac{0.224\ \text{g}}{0.200\ \text{g}} = 1.1$$

$$\text{Single Run w/ Aq.} = \frac{1.224\ \text{g}}{0.200\ \text{g}} = 6.1$$

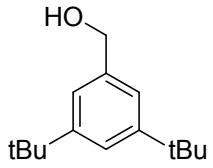
$$\text{Recycle w/out Aq.} = \frac{1.121\ \text{g}}{0.969\ \text{g}} = 1.2$$

$$\text{Recycle w/ Aq.} = \frac{2.121\ \text{g}}{0.969\ \text{g}} = 2.2$$

**E Factors**

| Single Run | Recycling |
|---|---|
| w/out Aq. = 1.1 | w/out Aq. = 1.2 |
| w/ Aq. = 6.1 | w/ Aq. = 2.2 |

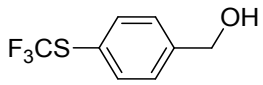
## XIII. Synthesis and Characterization of Prepared Alcohols




**[4]: (3,5-Di-*t*-butylphenyl)methanol ($C_{15}H_{24}O$)** was prepared following the general carboxylic acid reduction procedure. To a dry 100 mL round bottom flask charged with argon and stir bar was suspended $LiAlH_4$ (455 mg, 12 mmol) in THF (30 mL), after which the mixture was chilled to 0 °C. 3,5-Di-*t*-butylbenzoic acid (1.4 g, 6 mmol) in THF (30 mL) was added via syringe drop-wise at 0 °C and the reaction mixture allowed to warm to rt overnight. The reaction was complete after 14 h as judged by TLC. The reaction was quenched with deionized water and poured into a separatory funnel containing 1:1 $Et_2O$:sat. Rochelles salt (200 mL), then extracted with $Et_2O$ (3 x 50 mL), washed with brine (1 x 50 mL) and concentrated in vacuo. No purification of product was needed, yielding 1.27 g, 96% of a white crystalline solid. Compound data matches that of commercially available material CAS: 77387-57-6.

**$R_f$:** 0.48, 3:7 (EtOAc:hexanes)

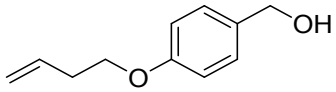
**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 7.38 (m, 1H), 7.23 (m, 2H), and 1.34 (s, 18H).



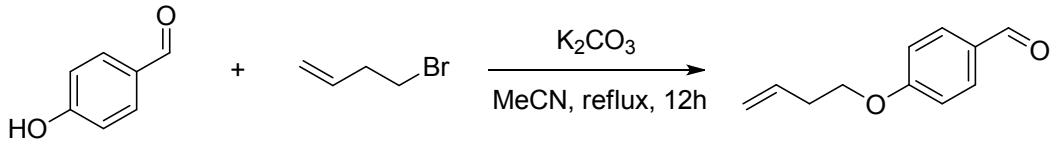

**Synthesis of (4-((trifluoromethyl)thio)phenyl)methanol ($C_8H_7F_3OS$).** Followed the general reduction procedure, using 4-((trifluoromethyl)thio)benzaldehyde (412 mg, 2.0 mmol), $NaBH_4$ (37.8 mg, 0.5 mmol), and EtOH (4 mL). The reaction was complete after 30 min as judged by TLC. The crude product was passed over a $SiO_2$ pad and eluted with $Et_2O$ to yield 403 mg, 97% of a white crystalline solid; compound data matches that of commercially available material CAS: 56456-52-1

**$R_f$:** 0.15, 1:9 (EtOAc:hexanes)

**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 7.65 (d, $J$ = 8.04 Hz, 2H), 7.43 (d, $J$ = 7.98 Hz, 2H), 4.76 (s, 1H).




**Synthesis of [36] (4-(But-3-en-1-yloxy)phenyl)methanol ($C_{11}H_{14}O_2$)**

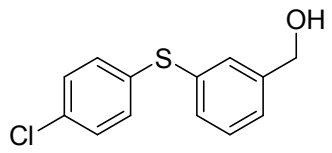



4-Hydroxybenzaldehyde (500 mg, 4.1 mmol) and potassium carbonate (1.41 g, 10.2 mmol) were added to a 50 mL flame dried round bottom with stir bar. Acetonitrile (8 mL) was added followed by 4-bromo-1-butene (0.83 mL, 8.2 mmol). The reaction was refluxed in an oil bath for 12 h. The solvent was removed in vacuo and the residue was transferred to a separatory funnel with 10 mL of DCM, and 10 mL of water. The solution was extracted with DCM (2 x 10 mL), the organic phase was washed with sat. $NaHCO_3$, water, brine, and dried over anhydrous $Na_2SO_4$, yielding 4-(but-3-en-1-yloxy)benzaldehyde as a light yellow oil (554 mg, 3.14 mmol, 77% yield).

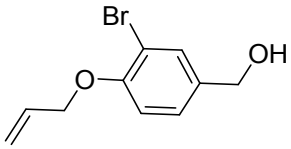
Following the standard procedure for the reduction of aldehydes, 4-(but-3-en-1-yloxy)benz-aldehyde (529 mg, 3 mmol) was added to a 50 mL round bottom flask containing a stir bar and 25 mL of MeOH and the mixture was stirred. Sodium borohydride (114 mg, 3 mmol) was added portion-wise to the reaction over 1 h until completion by TLC. The reaction was quenched with 10 mL of a 1 M HCl solution, then NaOH was added to bring the pH to ~10. The solution was poured into a separatory funnel and extracted with $Et_2O$ (3 x 20 mL). The organics were washed with water, brine, and dried over anhydrous $Na_2SO_4$, yielding the title compound (444 mg, 2.5 mmol, 83% yield) as a yellow oil. Compound data matches those previously reported.[7]

**$R_f$:** 0.45, 1:9 (EtOAc:hexanes)

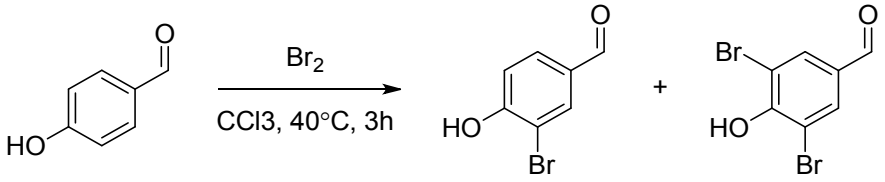
**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 7.28 (m, 2H), 6.9 (m, 2H), 5.92 (m, 1H), 5.15 (m, 2H), 4.63 (d, *J* = 5.7 Hz, 2H), 4.03 (t, *J* = 6.7 Hz, 2H), 2.55 (m, 2H), 1.56 (m, 1H);



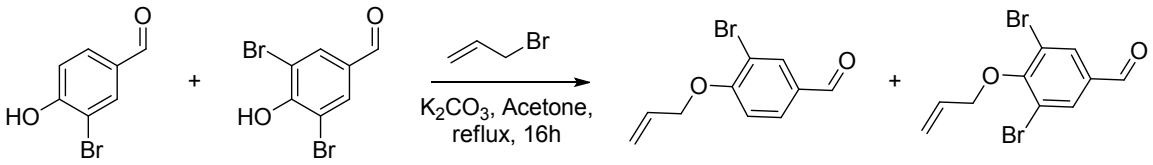

**(3-((4-Chlorophenyl)thio)phenyl)methanol ($C_{13}H_{11}ClOS$).** Following the general procedure for reduction of aldehydes, commercially available 4-((4-chlorophenyl)thio) benzaldehyde (595 mg, 2.4 mmol) was added to a round bottom flask along with 10 mL MeOH and stirred. $NaBH_4$ (0.6 equiv, 53 mg, 1.4 mmol), was added portion-wise over 1 h and monitored by TLC to determine completion. The solvent was removed in vacuo and the slurry transferred to a separatory funnel with water and EtOAc. The mixture was extracted with EtOAc (3 x 10 mL), the organics were washed with water, then 1 M HCl, saturated $NaHCO_3$, brine, and dried over anhydrous $Na_2SO_4$, affording the title compound (551 mg, 2.2 mmol, 92% yield).
**$R_f$:** 0.56, 1:2 (EtOAc:hexanes)
**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 7.54 (dt, *J* = 8.0 Hz, 0.7 Hz, 1H), 7.38 (d, *J* = 1.5 Hz, 2H), 7.27 (m, 3H), 7.13 (m, 2H), 4.78 (s, 2H), 2.05 (br, s, 1H);
**$^{13}$C NMR (126 MHz, $CDCl_3$, δ):** 142.48, 134.73, 134.14, 132.59, 131.92, 130.54, 129.36, 129.19, 128.83, 128.65, 63.56;
**IR (quartz crystal):** ν 3237, 3056, 3017, 2897, 2846, 2943, 1880, 1626, 1572 $cm^{-1}$
**HRMS (EI) (*m/z*):** $[M]^+$ calc. for $C_{13}H_{11}ClOS$, 250.0219; found $[M]^+$ 250.0214.




**Synthesis of (4-(allyloxy)-3-bromophenyl)methanol ($C_{10}H_{11}BrO_2$)**




4-Hydroxybenzaldehyde (3.660 g, 30 mmol) was added to a round bottom flask equipped with a stir bar and 100 mL of chloroform and placed into an oil bath set at 40 °C. Bromine (6.440 g, 2.12 mL, 40.5 mmol) was added to 60 mL of chloroform and placed into an addition funnel. The bromine solution was added to the benzaldehyde solution dropwise over 2 h, after which the reaction was quenched with $NaHSO_3$, the solvent was removed in vacuo, and the residue was dissolved in EtOAc, washed with water, brine, and dried over anhydrous $Na_2SO_4$ yielding 5.660 g (~27.8 mmol) of a mixture of mono-brominated and di-brominated products.




The crude mixture of brominated products (5.660 g, 27.8 mmol) and potassium carbonate (4.3 g, 30.6 mmol) was added to an argon-purged round bottom flask with 150 mL acetone and a stir bar. Allyl bromide (4.03 g, 2.93 mL, 33.4 mmol) was added and the flask was fitted with a water condenser, purged with argon and refluxed for 16 h. The solvent was removed in vacuo, and the residue was dissolved in EtOAc and transferred to a separatory funnel, washing in with water and EtOAc. The solution was extracted with EtOAc (2 x 75 mL) and the organic extracts were washed with water, brine, and dried over anhydrous $Na_2SO_4$. The crude product was purified by flash chromatography on $SiO_2$, eluting with a gradient of EtOAc:hexanes (3:97,1:19:1:9,3:17) to separate products, yielding 1.341 g (5.6 mmol, 20% yield) of 4-(allyloxy)-3-bromobenzaldehyde**.**

Following the general aldehyde reduction procedure, 4-(allyloxy)-3-bromobenzaldehyde (1.205 g, 5.0 mmol) was added to a round bottom flask equipped with a stir bar and 40 mL of MeOH. Sodium borohydride (360 mg, 9.4 mmol) was added portion-wise over 2 h. The reaction was monitored by TLC until complete. The reaction was quenched with 15 mL of a 1 M HCl solution, then NaOH until pH ~10. The solution was transferred to a separatory funnel and extracted with $Et_2O$ (3 x 30 mL). The organic was washed with water, brine, and dried over anhydrous $Na_2SO_4$. The product was purified by flash column chromatography to afford the title compound as a yellow oil (1.02 g, 4.2 mmol, 88% yield).

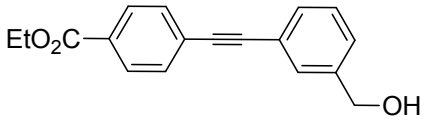
**$R_f$:** 0.43, 1:2 (EtOAc:hexanes)

**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 7.55 (d, *J* = 15.8 Hz, 1H), 7.46 (m, 2H), 6.89 (m, 2H), 6.25 (d, *J* = 16.1 Hz, 1H), 5.91 (dd, *J* = 17.1 Hz, 10.4Hz, 1H), 5.18 (dd, *J* = 17.1 Hz, 1.8 Hz, 1H), 5.13 (m, 1H), 4.05 (t, *J* = 6.7 Hz, 2H), 2.56 (m, 2H), 1.54 (s, 9H);

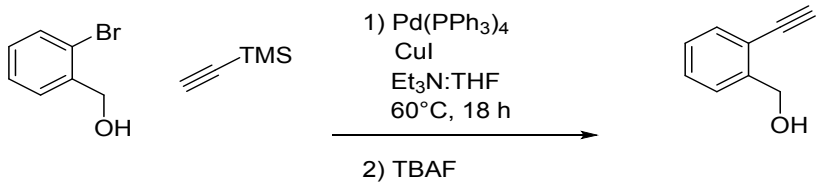
**$^{13}$C NMR (126 MHz, $CDCl_3$, δ):** 166.67, 160.45, 143.19, 134.16, 129.52, 128.63, 127.38, 117.67, 117.20, 114.79, 103.74, 80.20, 67.27, 33.52, 28.23;

**IR (quartz crystal):** ν 3327, 3092, 3020, 2930, 2870, 1493, 1252, 1233, 1046 $cm^{-1}$

**HRMS (EI) (*m/z*):** $[M]^+$ calc. for $C_{10}H_{11}BrO_2$, 241.9942; found 241.9947.




**Synthesis of ethyl 4-((3-(hydroxymethyl)phenyl)ethynyl)benzoate ($C_{18}H_{16}O_3$)**

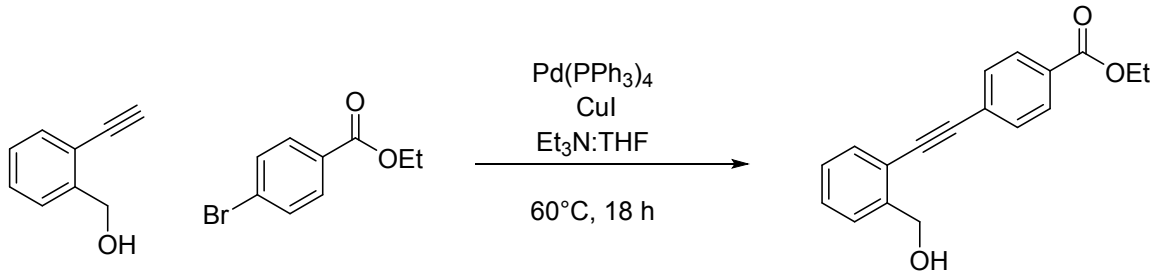



To a dry 150 mL bomb flask charged with argon and a stir bar was added $Pd(PPh_3)_4$ (173 mg, 0.15 mmol), CuI (14 mg, 0.08 mmol), aryl bromide (2.81g, 15 mmol), $Et_3N$:THF 4:1 (30 mL), followed by drop-wise addition of TMS-acetylene (1.92 g, 19.5 mmol). The flask was placed in a 60 °C oil bath and stirred for 18 h. It was then diluted with $Et_2O$ (100 mL), washed with 2 N HCl (3 x 10 mL), sat. $NaHCO_3$ (1 x 10 mL), brine (1 x 5 mL), and then dried over anhydrous $MgSO_4$ and concentrated in vacuo. The dissolved silyl acetylene intermediate and TBAF (4.31 g, 16.5 mmol) in THF were stirred at rt for 1 h, and then concentrated in vacuo. The crude product was purified by flash column chromatography, eluted with 2:8 EtOAc:hexanes, to yield (2-ethynylphenyl)methanol (1.81 g, 91% yield) as an off white solid. Compound data match those previously reported.[20]

**$R_f$:** 0.30, 3:7 (EtOAc:hexanes)

**$^1$H NMR (500 MHz, $CDCl_3$, δ)**: 7.46 (m, 1H), 7.40 (m, 1H), 7.30 (m, 2H), 4.60 (d, $J$ = 5.06 Hz, 2H), 3.08 (s, 1H), 2.47 (br s, 1H).

**Synthesis of ethyl 4-((3-(hydroxymethyl)phenyl)ethynyl)benzoate**



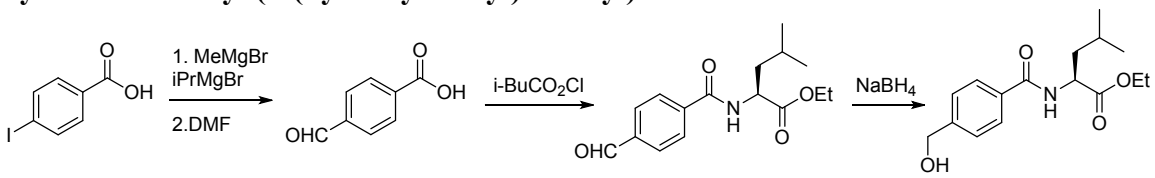

To a dry 15 mL bomb flask charged with argon and a stir bar was added $Pd(PPh_3)_4$ (11.6 mg, 0.01 mmol), CuI (1 mg, 0.005 mmol), ethyl 4-bromobenzoate (229 mg, 1 mmol), and $Et_3N$:THF 4:1 (2 mL), followed by prepared (2-ethynylphenyl)methanol (172 mg, 1.3 mmol). The reaction was placed in a 60 °C oil bath and stirred for 16 h. The reaction mixture was then diluted with $Et_2O$ (10 mL), washed with 2 N HCl (3 x 5 mL), sat. $NaHCO_3$ (1 x 25 mL), brine (1 x 25 mL) dried over anhydrous $MgSO_4$ and concentrated in vacuo. The crude product was purified by flash column chromatography, eluted with 1:9 MeOH:DCM, to yield the title product (262 mg, 94% yield) as a yellow solid.

**mp:** 59 – 60 °C

**$R_f$:** 0.55, 1:9 (MeOH:DCM)

**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 8.04 (d, *J* = 8.6 Hz, 2H), 7.59 (m, 3H), 7.49 (td, *J* = 4.4, 1.6 Hz, 3H), 7.38 (m, 2H), 4.73 (s, 2H), 4.4 (q, *J* = 7.3 Hz, 7.0, 2H), 1.69 (br, s, 1H), 1.42 (t, J = 7.1 Hz, 3H)
**$^{13}$C NMR (126 MHz, $CDCl_3$, δ):** 166.07, 141.21, 131.46, 130.88, 130.11, 129.88, 129.48, 128.66, 127.78, 127.23, 122.97, 92.05, 88.80, 64.82, 61.14, 14.31
**HRMS (EI) (m/z):** $[M]^+$ calc. for $C_{18}H_{16}O_3$: 280.1099; found: $[M+Na]^+$ 303.1004.

**Synthesis of Ethyl (4-(hydroxymethyl)benzoyl)-*L*-leucinate**

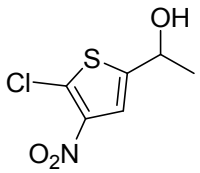



*p*-Iodobenzoic acid (2.482 g) was added to a flame-dried round bottom flask under argon, covered with a rubber septa, and 42 mL of a freshly prepared [0.5 M] solution of LiCl in THF was added and the slurry was stirred for 5 min. The flask was cooled to -20 ˚C whereupon 4.8 mL of MeMgBr (2.08 M) in THF was added drop-wise with periodic venting of the flask (methane gas evolution). Following the addition, the flask was stirred for 20 min at -20 ˚C. *i*-PrMgBr (7.1 mL, 1.55 M) in THF was added drop-wise and following the addition the cooling bath was removed and the mixture stirred while warming to rt over 45 min. The flask was then recooled to -20 ˚C whereupon 1.93 mL of dry DMF was added drop-wise and the cooling bath was removed and the mixture was left to stir while warming to rt over 4 h. The reaction was quenched by drop-wise addition of 1 N $NaHSO_4$ and the THF was removed from the flask *in vacuo.* The residue was then dissolved in 300 mL of DCM, transferred to a separatory funnel, and the flask rinsed in with water and DCM. The solution was then basified by addition of 1 N $NaHCO_3$ until the pH remained around 7-8. DCM was then removed in vacuo, and the aqueous layer was then acidified with aqueous HCl until the pH remained below 2. During re-acidification, the product aldehyde was observed to precipitate out. The aqueous layer and precipitated aldehyde were then extracted 5x with DCM, dried over anhydrous $Na_2SO_4$ and concentrated under vacuum to yield approximately 1 g of 4-formyl benzoic acid as a white solid.

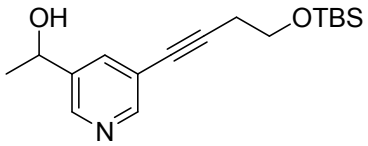
4-Formylbenzoic acid (750.6 mg, 5 mmol, 1 equiv) was added to a 100 mL flame dried round bottom flask under argon, followed by 25 mL dry THF, and 0.732 mL (1.1 equiv) of $Et_3N$, and the mixture cooled to 0 ˚C in an ice bath. Isobutylchloroformate (0.686 mL, 1.05 equiv) was then added drop-wise and the slurry was stirred for 1 h at 0 ˚C. In a separate 50 mL flame dried round bottom flask was added *L*-leucinate ethyl ester as the hydrochloride salt, followed by 25 mL of THF. The solution was cooled to 0 ˚C and $Et_3N$ (1.534 mL, 2.2 equiv) was added via syringe. Once 1 h had elapsed the solution containing leucine was transferred via cannula to the solution of mixed carbonic anhydride at 0 ˚C. The cooling bath was removed and the solution was left to stir overnight at rt. The reaction was quenched with sat. $NaHCO_3$ and the THF was removed from the flask under vacuum. The crude residue was dissolved in DCM and extracted twice, the combined organic extracts were washed with brine, dried over anhydrous $Na_2SO_4$ and then concentrated under vacuum. The crude material was purified via flash chromatography gradient elution with 20-50% EtOAc/hexanes to yield the product as a white solid in 68% yield.
**$^1$H NMR (600 MHz, $CDCl_3$, δ):** 10.09 (s, 1H), 7.96 (s, 4H), 6.60 (d, *J* = 7.8 Hz, 1H), 4.85 (t, *J* = 2.4 Hz, 1H), 4.24 (q, *J* = 6.6 Hz, 2H), 1.76 (m, 3H), 1.32 (t, *J* = 6.6 Hz, 3H), 1.00 (dd, *J* = 14.4, 5.4 Hz, 6H)

**$^{13}$C NMR (126 MHz, $CDCl_3$, δ):** 191.620, 173.195, 166.101, 193.321, 138.505, 129.997, 127.992, 61.802, 51.549, 42.071, 25.189, 22.970, 22.278, 14.324

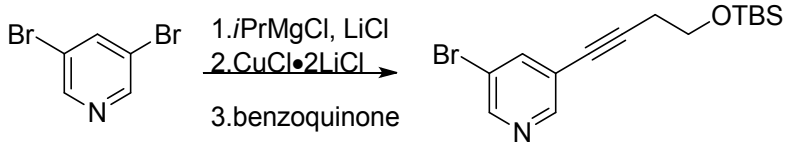
In a 25 mL round bottom flask, 420 mg (1.44 mmol, 1 equiv) of aldehyde was dissolved in 12 mL of a 1:1 mixture of EtOH/THF, and the reaction mixture was cooled in an ice bath. $NaBH_4$ (164 mg, 3 equiv) was added portion-wise, and the mixture was stirred until TLC staining with DNP showed no remaining aldehyde. Once complete, the volatiles were removed in vacuo and the crude residue was re-suspended in DCM (50 mL) and transferred to a separatory funnel, saturated aqueous $NaHCO_3$ was added, and the mixture extracted 3x with DCM. The combined organics were washed with a small quantity of water, brine, dried over anhydrous $Na_2SO_4$ and concentrated under vacuum. Flash chromatography eluting with 80% EtOAc/hexanes yielded 392 mg (92.8%) of title compound as a white wax.
**$R_f$:** 0.11, 1:1 (EtOAc:hexanes)
**$^1$H NMR (600 MHz, $CDCl_3$, δ):** 7.64 (d, *J* = 7.8 Hz, 2H), 7.26 (d, *J* = 7.8 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 1H), 4.78 (m, 1H), 4.63 (s, 2H), 4.18 (q, *J* = 7.2 Hz, 2H), 3.27 (br, s, 1H), 1.75-1.60 (m, 3H), 1.27 (t, *J* = 7.2 Hz, 3H), 0.94 (dd, *J* = 6.0, 6.0 Hz)
**$^{13}$C NMR (151 MHz, $CDCl_3$, δ):** 173.45, 167.14, 145.01, 132.58, 127.12, 126.54, 64.25, 61.44, 51.18, 41.60, 24.93, 22.79, 21.95, 14.09



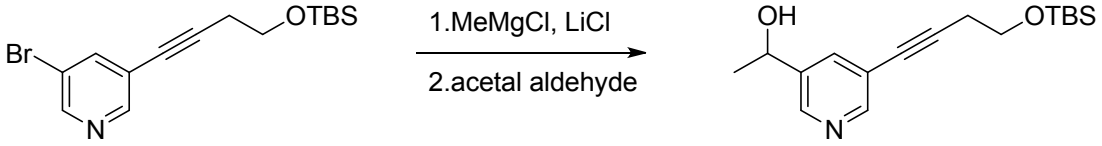

**1-(5-Chloro-4-nitrothiophen-2-yl)ethanol ($C_6H_6ClNO_3S$)** was prepared following the general ketone reduction procedure. Commercially available 1-(5-chloro-4-nitrothiophen-2-yl)ethan-1-one (210 mg, 1.0 mmol) was added to a round bottom flask with 10 mL MeOH and stirred. $NaBH_4$ (76 mg, 2.0 mmol, 2.0 equiv) was added and monitored by TLC to determine completion (20 min). The solvent was removed in vacuo and the slurry transferred to a separatory funnel with water and EtOAc. The solution was extracted with EtOAc (3 x 20 mL), the organics were washed with water, 1 M HCl, saturated $NaHCO_3$, brine, and dried over anhydrous $Na_2SO_4$, affording the title compound (164 mg, 0.78 mmol, 77% yield) as an orange oil.
**$R_f$:** 0.73, 1:1 (EtOAc:hexanes)
**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 7.38 (m, 1H), 5.05 (qt, *J* = 6.1Hz, 1H), 2.17 (br, s, 1H), 1.60 (d, *J* = 6.1Hz, 3H);
**$^{13}$C NMR (126 MHz, $CDCl_3$, δ):** 146.66, 131.50, 118.54, 117.72, 66.12, 24.86;
**IR (quartz crystal):** ν 3371, 3112, 2982, 2977, 2928, 1520, 1363 $cm^{-1}$.
**HRMS (EI) (*m/z*):** $[M]^+$ calc. for $C_6H_6ClNO_3S$, 206.9757; found $[M]^+$ 206.9755.




**Synthesis of 1-(5-(4-((*t*-Butyldimethylsilyl)oxy)but-1-yn-1-yl)pyridin-3-yl)ethanol ($C_{17}H_{27}NO_2Si$)**




3,5-Dibromopyridine (1 g, 4.24 mmol, 1 equiv) was added to an argon-purged round bottom flask with a stir bar under a flow of argon. THF (1 mL) was added and cooled to 0 °C. *i*-PrMgCl (1.2 M, 4.16 mL, 4.66 mmol) was then added drop-wise to the reaction. The reaction was stirred for 30 min at 0 °C. The solution was then canulated to a flask with CuCl (0.683 g, 5.08 mmol, 1.2 equiv), LiCl (0.197 g, 4.66 mmol, 1.1 equiv), and THF (5 mL, 1 M) cooled to –50 °C and stirred for 1 h at -50 °C. But-3-yn-1-yloxy)(*t*-butyl)dimethylsilane (1.56 g, 8.5 mmol, 2.0 equiv) was dissolved in THF. This solution was then cooled to -78 °C and 2.4 M *n*-BuLi (3.53 mL, 8.5 mmol, 2.0 equiv) was added to the flask and stirred for 1 h. The resulting solution of lithiated alkyne was transferred to the copper solution -50 °C and allowed to stir for 1 h. A solution 1,4-benzoquinone (865 mg, 8 mmol) in THF (12 mL) was then added to the reaction, which was subsequently cooled to -78 °C. The reaction stirred overnight as a black liquid. The crude mixture was then passed over a bed of Celite and eluted by $Et_2O$. The filtrate was washed with 2 M $NH_4OH$, extracted with ether, and the organics were washed with brine, and dried over anhydrous $MgSO_4$.




To a dry flask with a stir bar under a flow of argon, 3-bromo-5-(4-((*t*-butyldimethylsilyl)oxy)but-1-yn-1-yl)pyridine (0.126 g, 0.37 mmol, 1 equiv) was added. THF (2 mL) was added, and then MeMgCl (1.2 M, 0.31 mL, 0.37 mmol) was added drop-wise at rt. The reaction was stirred for 3 h at rt. The flask was then cooled to -78 °C and the acetal aldehyde was syringed in one portion. The reaction was stirred overnight coming to rt, and was then quenched with sat. $NH_4Cl$, extracted with EtOAc (2 x 10 mL). The organics were washed with brine, and then dried over anhydrous $MgSO_4$. The crude product was purified by flash column chromatography, eluting with 3:7 EtOAc:hexanes, affording the title compound (91 mg, 80% yield) as a light yellow oil.

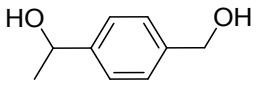
$R_f$: 0.15 (3:7, EtOAc:hexanes)

**$^1$H NMR (600 MHz, $CDCl_3$, δ):** 8.51 (s, 1H) 8.47 (s, 1H), 7.73 (s, 1H), 4.92 (q, *J* = 6.5 Hz, 1H), 3.81 (t, *J* = 7.0 Hz, 2H), 2.63 (t, *J* = 7.0 Hz, 2H), 1.50 (d, *J* = 6.5 Hz, 3H), 0.90 (s, 9H), 0.08 (s, 6H).

**$^{13}$C NMR (126 MHz, $CDCl_3$, δ):** 150.82, 145.46, 135.99, 91.31, 78.17, 67.76, 61.64, 25.87, 25.16, 23.85, 18.34, -5.26.

**IR (quartz crystal):** ν 3272, 2953, 2928, 2856, 2240, 1575, 1472 $cm^{-1}$

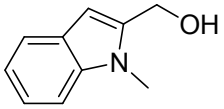
**HRMS (EI) (*m/z*):** $[M]^+$ calc. for $C_{17}H_{27}NO_2Si$, 305.1811; found $[M+H]^+$ 306.1877.




**[19]: 1-(4-(Hydroxymethyl)phenyl)ethanol ($C_9H_{12}O_2$)** was obtained following the general reduction with lithium aluminum hydride. Commercially available 4-acetylbenzoic acid (740 mg, 5.0 mmol) was added to 100 mL THF and then cooled to 0 C. Lithium aluminum hydride (1.20 g, 30 mmol) was added portion-wise over a 1 h period and the solution was allowed to warm to rt overnight. The mixture was quenched with 80 mL EtOAc and 100 mL of water, and transferred to a separatory funnel. The mixture was extracted with EtOAc (2 x 100 mL), the organics were washed with water, brine, and dried over anhydrous $Na_2SO_4$ furnishing the title compound as a pale yellow oil (563 mg, 3.7 mmol, 74% yield). Compound data matches those previously reported.[11]

**$R_f$:** 0.17, 1:1 (EtOAc:hexanes)

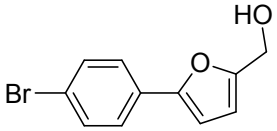
**$^1$H NMR (400 MHz, $CDCl_3$, δ):** 7.37 (m, 4H), 4.91 (qt, *J* = 6.4Hz, 1H), 4.7 (s, 2H), 1.72 (br, s, 2H), 1.5 (s, 3H).




**(1-Methyl-1H-indol-2-yl)methanol ($C_{10}H_{11}NO$).** To commercially available 1-methyl-1*H*-indole-2-carbaldehyde (795 mg, 5 mmol) in a round bottom flask was added 30 mL MeOH and the solution stirred. $NaBH_4$ (1.1 equiv, 214 mg, 5.6 mmol), was added portion-wise over 1 h and the reaction was monitored by TLC to determine completion. The solvent was removed in vacuo and the slurry transferred to a separatory funnel with water and EtOAc. The solution was extracted with EtOAc (3 x 30 mL), the organics were washed with water, 1 M HCl, saturated $NaHCO_3$, brine, and dried over anhydrous $Na_2SO_4$, affording the title compound (741 mg, 4.6 mmol, 92% yield). Compound data matches those previously reported.[21]

**$R_f$:** 0.26, 1:4 (EtOAc:hexanes)

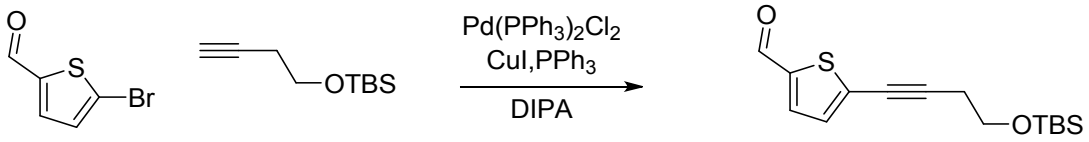
**$^1$H NMR (400 MHz, $CDCl_3$, δ):** 7.60 (d, *J* = 7.9Hz, 1H), 7.34 (m, 1H), 7.24 (m, 1H) 7.12 (m, 1H), 6.47 (s, 1H), 4.83 (s, 1H), 3.83 (m,3H).




**(5-(4-Bromophenyl)furan-2-yl)methanol ($C_{11}H_9BrO_2$).** To commercially available 5-(4-bromophenyl)furfural (423 mg, 1.7 mmol) in a round bottom flask was added 10 mL MeOH and the solution stirred. $NaBH_4$ (38 mg, 1.0 mmol, 0.6 equiv) was added portion-wise over 1 h and the reaction was monitored by TLC to determine completion. The solvent was removed in vacuo and the slurry transferred to a separatory funnel with water and EtOAc. The solution was extracted with EtOAc (3 x 20 mL), the organics were washed with water, 1 M HCl, saturated $NaHCO_3$, brine, and dried over anhydrous $Na_2SO_4$ affording the title compound (374 mg, 1.5 mmol, 88% yield). Compound data matches those previously reported.[22]

**$^1$H NMR (400 MHz, $CDCl_3$, δ):** 7.53 (m, 4H), 6.61 (d, J = 3.2Hz, 1H), 6.39 (d, J = 3.2Hz, 1H), 4.67 (s, 2H) 1.69 (br, s, 1H)


**Synthesis of (5-(4-((*t*-butyldimethylsilyl)oxy)but-1-yn-1-yl)thiophen-2-yl)methanol ($C_{15}H_{24}O_2SSi$)**

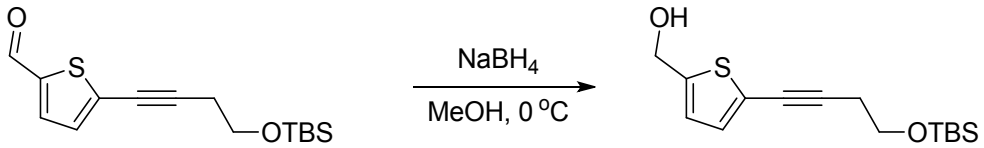



To an flame dried, argon purged flask, 5-bromothiophene-2-carbaldehyde (0.595 g, 3.14 mmol, 1 equiv), (but-3-yn-1-yloxy)(*t*-butyl)dimethylsilane (0.811 g, 4.41 mmol, 1.4 equiv), and $Pd(PPh)_3Cl_2$ (0.024 g, 0.0345 mmol, 0.011 equiv) were added. The flask was then vacuum purged with argon twice. Then, DIPA (13 mL) was added to the flask. The reaction was stirred in a 40 $^oC$ oil bath for 20 min after which $PPh_3$ (0.016 g, 0.0628 mmol, 0.02 equiv) was added to the flask and the reaction was heated to 80 $^oC$ for 12 h. The reaction was then cooled to rt and washed with water and extracted with EtOAc. The organics were then washed with brine, and dried over anhydrous $MgSO_4$. The solvent was removed in vacuo and the crude oil was purified by a flash column chromatography using a gradient from 100% hexanes to 6:94 $Et_2O$:hexanes, affording 5-(4-((*t*-butyldimethylsilyl)oxy)but-1-yn-1-yl)thiophene-2-carbaldehyde (0.66 g, 2.24 mmol, 71% yield) as a light yellow oil.

**$R_f$ :** 0.30, 1:9 (EtOAc:hexanes)

**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 9.83 (s, 1H), 7.61 (d, *J* = 3.9 Hz, 1H), 7.16 (d, *J* = 3.9 Hz, 1H), 3.83 (t, *J* = 6.7 Hz, 2H), 2.68 (t, *J* = 6.7 Hz, 2H), 1.00 – 0.86 (m, 9H), 0.10 (s, 6H).

**$^{13}$C NMR (126 MHz, $CDCl_3$, δ):** 182.37, 143.07, 135.99, 133.72, 131.95, 97.35, 74.44, 61.27, 25.86, 24.26, 18.33, -5.26.



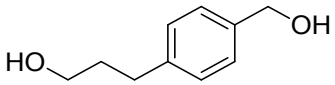

To a microwave vial, 5-(4-((*t*-butyldimethylsilyl)oxy)but-1-yn-1-yl)thiophene-2-carbaldehyde (**26**) (0.07 g, 0.238 mmol, 1 equiv) was added, followed with MeOH (1 mL) and the resulting solution was cooled to 0 $^oC$. $NaBH_4$ (0.018 g, 0.476 mmol, 2 equiv) was then added slowly to this mixture, with stirring over 1 h. The MeOH was the removed in vacuo and the crude product was washed with water and extracted with $Et_2O$. The organics were washed with brine, dried over anhydrous $MgSO_4$ and the solvent removed in vacuo. The crude product was then purified by flash column chromatography, eluted with 1:9 (EtOAc:hexanes) yielding 61 mg, 87% yield, of the title product as a light orange oil.

**$R_f$:** 0.10, 1:9 (EtOAc:hexanes)

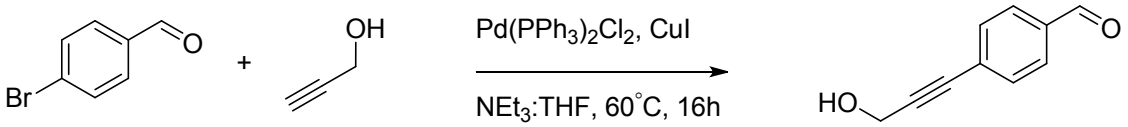
**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 6.99 (d, *J* = 3.6 Hz, 1H), 6.83 (dt, *J* = 3.6, 0.8 Hz, 1H), 4.76 (s, 2H), 3.81 (t, *J* = 6.9 Hz, 2H), 2.64 (t, *J* = 6.9 Hz, 2H), 0.96 – 0.90 (m, 9H), 0.15 – 0.07 (m, 6H).

**$^{13}$C NMR (126 MHz, $CDCl_3$, δ):** 144.56, 131.06, 125.00, 124.05, 103.72, 91.64, 74.74, 61.67, 60.07, 25.88, 24.07, 18.34, -5.25.

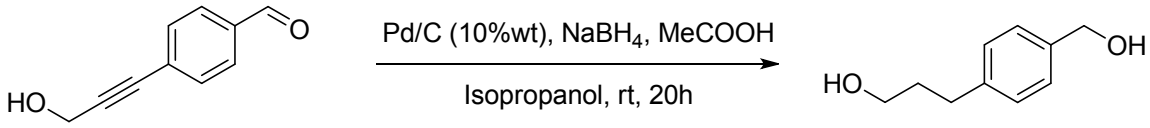
**IR (quartz crystal):** ν 3341, 2953, 2928, 2856, 1471, 1463, 1384, 1361, 1252, 1217, 1188, 1161, 1102, 1056, 1005, 938, 909, 834, 804, 775 $cm^{-1}$
**HRMS (EI) (*m/z*):** $[M]^+$ calc. for $C_{15}H_{24}O_2SSi$, 296.1266; found $[M+Na]^+$319.1159.




**Synthesis of 3-(4-(hydroxymethyl)phenyl)propan-1-ol [Scheme 5:SM] ($C_{10}H_{14}O_2$)**

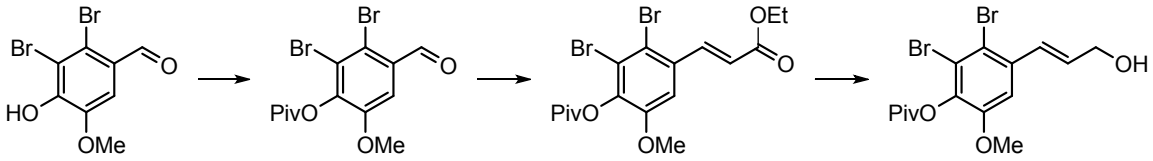



4-Bromobenzaldehye (1202 mg, 6.5 mmol) was added to a round bottom flask containing 2 mL THF, to which propargyl alcohol (280.3 mg, 0.3 mL, 5.0 mmol) was added via syringe, followed by 8 mL of $NEt_3$. $Pd(PPh_3)_2Cl_2$ (70.2 mg, 0.05 mmol) and copper iodide (19.2 mg, 0.05 mmol) were added to the mixture, which was then placed into an oil bath set at 60 C, for 16 h. Water was added to the solution which was transferred to a separatory funnel with water and $Et_2O$. The solution was extracted with $Et_2O$ (3 x 50 mL), the organics were washed with water, 2 M HCl, brine, and dried over anhydrous $Na_2SO_4$. The crude material was purified by flash column chromatography on $SiO_2$, eluting with 1:2 (EtOAc:hexanes) to provide 4-(3-hydroxyprop-1-yn-1-yl)benzaldehyde (634 mg, 3.95 mmol, 79% yield).




4-(3-Hydroxyprop-1-yn-1-yl)benzaldehyde (634 mg, 3.95 mmol), and Pd/C (63.4 mg, 10% by weight) was added to an argon purged 100 mL round bottom flask charged with isopropanol (25 mL) and a stir bar. With stirring, acetic acid (1.0 mL, 16 mmol) was added followed by sodium borohydride (950 mg, 24 mmol) in one portion, and the reaction stirred for 3 h. Another portion of sodium borohydride (620 mg, 16 mmol) was then added and the mixture stirred overnight to reach completion. The reaction was quenched with 2 M HCl (6 mL) until evolution of $H_2$ was complete, and the pH was adjusted to ~10 using NaOH, and the solution was then filtered over $SiO_2$ and Celite. The filtrate was transferred to a separatory funnel and extracted with EtOAc (2 x 50 mL). The organics were washed with water, brine and dried over anhydrous $Na_2SO_4$. The solvent was removed in vacuo to afford the title compound 3-(4-(hydroxymethyl)phenyl)propan-1-ol (464 mg, 2.8 mmol, 71% yield) as a yellow waxy solid. Compound data matched those previously reported.[23]
**$R_f$:** 0.17, 1:1 (EtOAc:hexanes)
**$^1$H NMR (500 MHz, $CDCl_3$, δ):** 7.30 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 4.67 (s, 2H), 3.68 (t, *J* = 6.4 Hz, 2H), 2.72 (m, 2H), 1.9 (m, 2H), 1.57 (br, s, 2H)

**(*E*)-2,3-dibromo-4-(3-hydroxyprop-1-en-1-yl)-6-methoxyphenyl pivalate ($C_{15}H_{18}Br_2O_4$)**

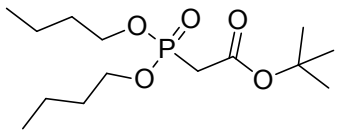



2,3-Dibromo-4-hydroxy-5-methoxybenzaldehyde (1.859 g, 6.0 mmol) was dissolved in 15 mL of dry DCM under an argon atmosphere. Once the solid was completely dissolved, the flask was placed in an ice bath and stirred for 5 min, whereupon 0.531 mL of dry pyridine was added. The solution was stirred for an additional 15 min at which point pivaloyl chloride (0.808 mL) was added dropwise. The solution was stirred for 30 min at 0 ˚C, and then the cooling bath was removed and the solution stirred for 4 h while warming to rt. The reaction was then diluted 3x with DCM, transferred to a separatory funnel, and shaken with 1 N aqueous HCl. The aqueous layer was removed and the organic layer was then shaken 2x with sat. $CuSO_4$, 1x with a small quantity of water, 1x with sat. $NaHCO_3$, brine, and dried over anhydrous $Na_2SO_4$ and concentrated in vacuo. The crude material was passed through a short silica column eluting with 15% $Et_2O$/hexanes to give 1.471 g (62%) of 2,3-dibromo-4-formyl-6-methoxyphenyl pivalate as a flaky white solid.
**$^1$H NMR (400 MHz, $CDCl_3$, δ):** 10.307 (s, 1H), 7.500 (s, 1H), 3.873 (s, 3H), 1.409 (s, 9H).

NaH (132 mg, 3.3 mmol; 60 wt. %) in mineral oil was dissolved in 10 mL anhydrous THF and 0.654 mL (3.3 mmol) of triethyl phosphonoacetate was added cautiously drop-wise and the solution was stirred for 1 h at rt. 2,3-Dibromo-4-formyl-6-methoxyphenyl pivalate (1.182 g, 3 mmol) was added in one portion, the flask sealed with a glass stopcock, and the mixture let stir overnight. The reaction was diluted with 50 mL DCM, transferred to a separatory funnel and shaken with 10 mL sat. aq. $NH_4Cl$. The aqueous layer was removed, and the organic layer was then shaken with sat. aq. $NaHCO_3$, a small quantity of water, brine, and dried over anhydrous $Na_2SO_4$. The organic extract was then passed through a pad of basic alumina eluting with EtOAc, and concentrated in vacuo to give 1.215 g (87%) of ethyl (*E*)-3-(2,3-dibromo-5-methoxy-4-(pivaloyloxy)phenyl)acrylate as a white solid which was immediately carried on to the next step.

The flask containing the enoate was fitted with a stir bar, septa, purged with argon, whereupon 20 mL of anhydrous DCM was added via syringe. The flask was cooled to 0 ˚C in an ice bath and stirred for 5-10 min. Neat DIBAL-H (1 mL) was added slowly, drop-wise, and the reaction was stirred overnight with melting of the ice bath. The reaction was quenched with cautious addition of a sat. solution of Rochelle's salt, diluted 5x with DCM, and the solution was shaken vigorously in a separatory funnel. The aqueous layer was removed and the organic layer was dried with brine, anhydrous $Na_2SO_4$, and concentrated in vacuo. Flash chromatography eluting with 50-100% EtOAc/hexanes yielded 260 mg (*E*)-2,3-dibromo-4-(3-hydroxyprop-1-en-1-yl)-6-methoxyphenyl pivalate as a white solid.
**$R_f$:** 0.55, 1:1 (EtOAc:hexanes)
**$^1$H NMR (400 MHz, $CDCl_3$, δ):** 7.06 (s, 1H), 6.97 (d, $J$ = 16 Hz, 1H), 6.23 (dt, $J$ = 15.6, 5.6 Hz, 1H), 4.39 (t, $J$ = 5.6 Hz, 2H), 3.84 (s, 3H), 1.41 (s, 9H)

**Synthesis of [37]: *t*-butyl 2-(dibutoxyphosphoryl)acetate ($C_{14}H_{29}O_5P$)**



To an argon-purged round bottom flask equipped with a stir bar was added commercially available tributyl phosphate (94%; 750 mg, 0.90 mL) and commercially available *t*-butyl bromoacetate (585 mg, 0.48 mL). The reaction was heated in an oil bath set at 90 °C for 24 h with stirring, yielding the title compound as a clear oil (907 mg, 2.94 mmol, 98% yield). Compound data matches those previously reported.[24]

**$^1$H NMR (400 MHz, $CDCl_3$, δ):** 4.09 (m, 4H), 2.91 (d, $J$ = 1 Hz, 1H), 2.86 (d, $J$ = 1 Hz, 1H), 1.67 (m, 4H), 1.50-1.37 (m, 13H), 0.94 (m, 6H).

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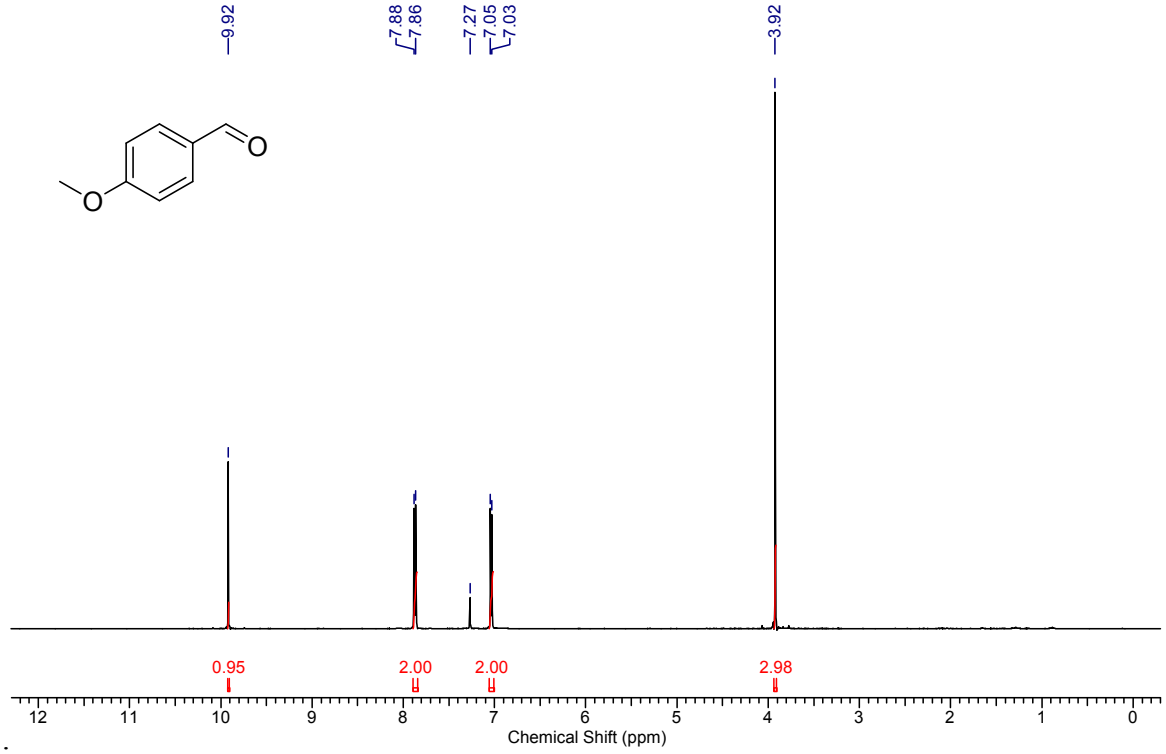
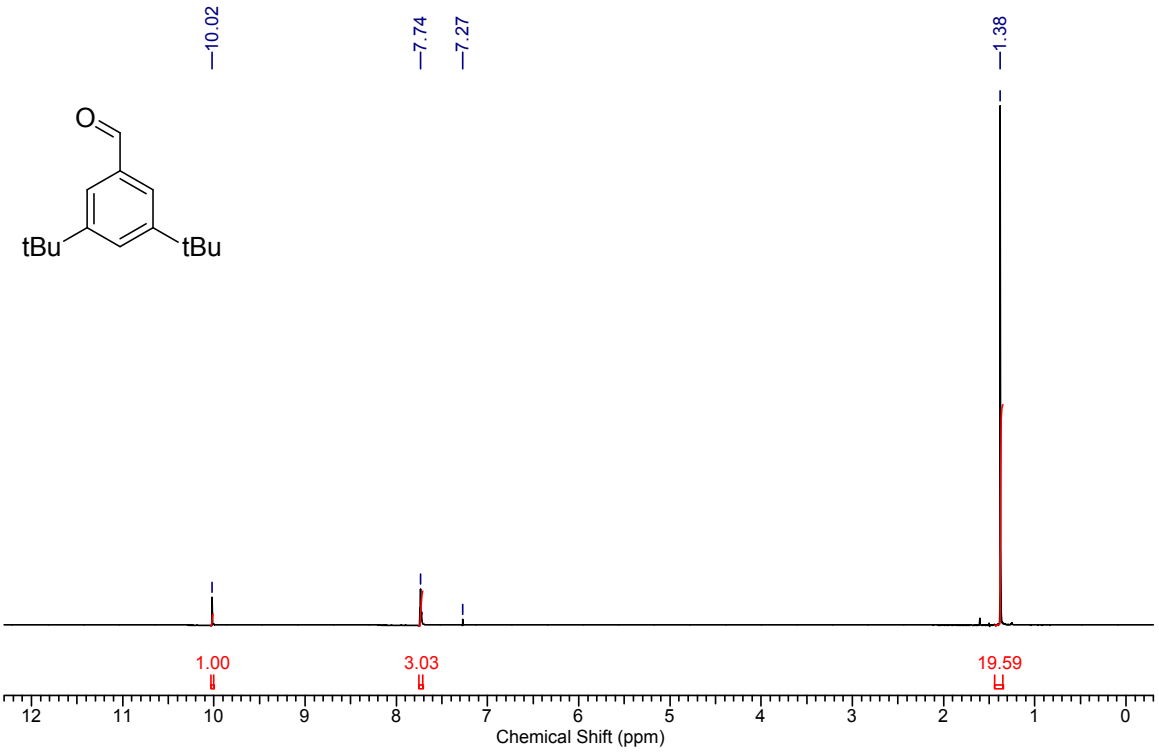
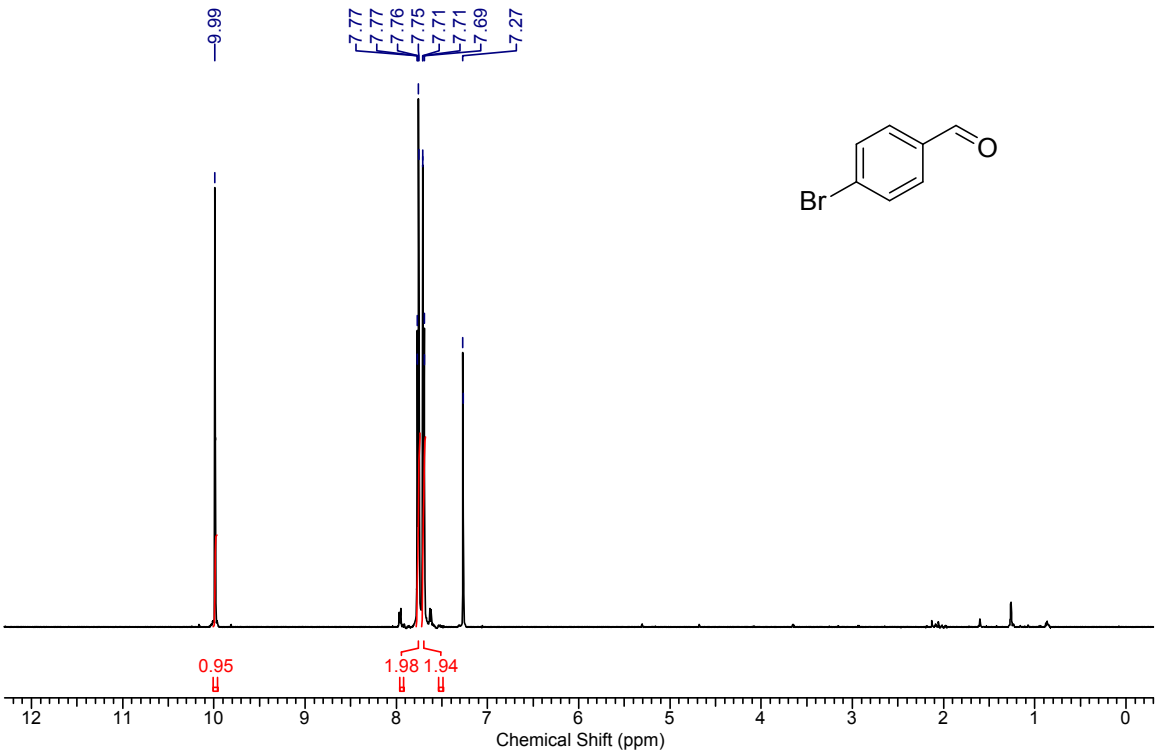
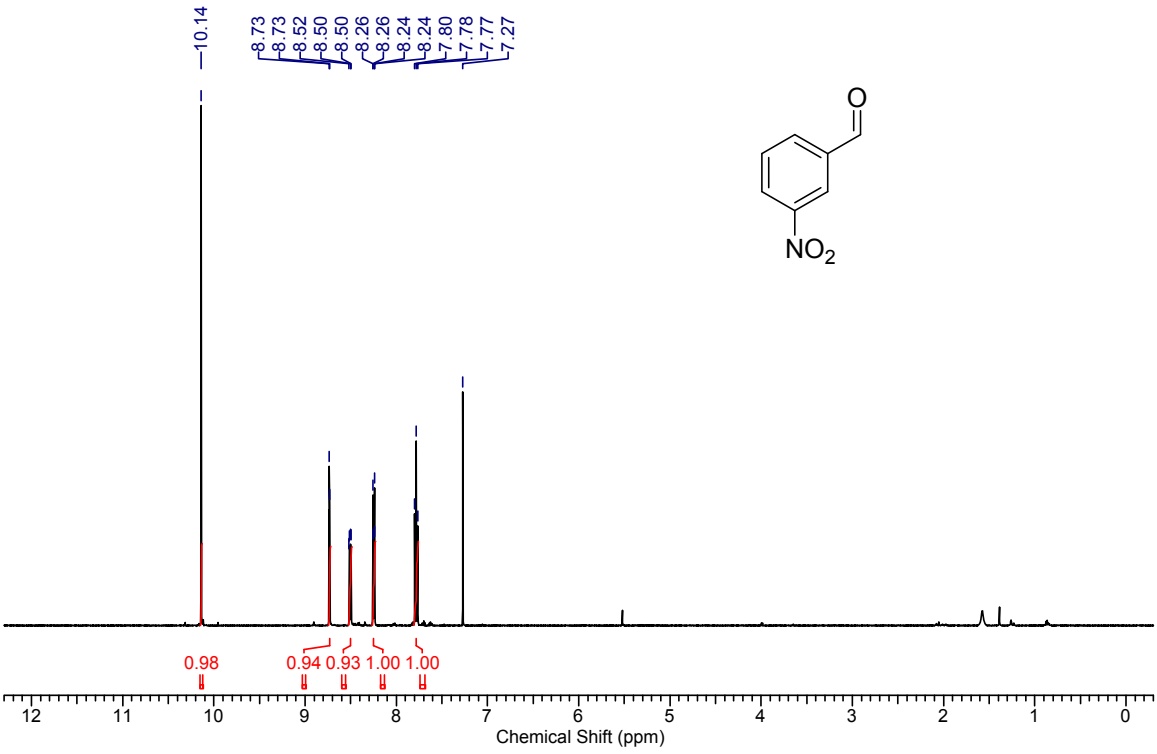
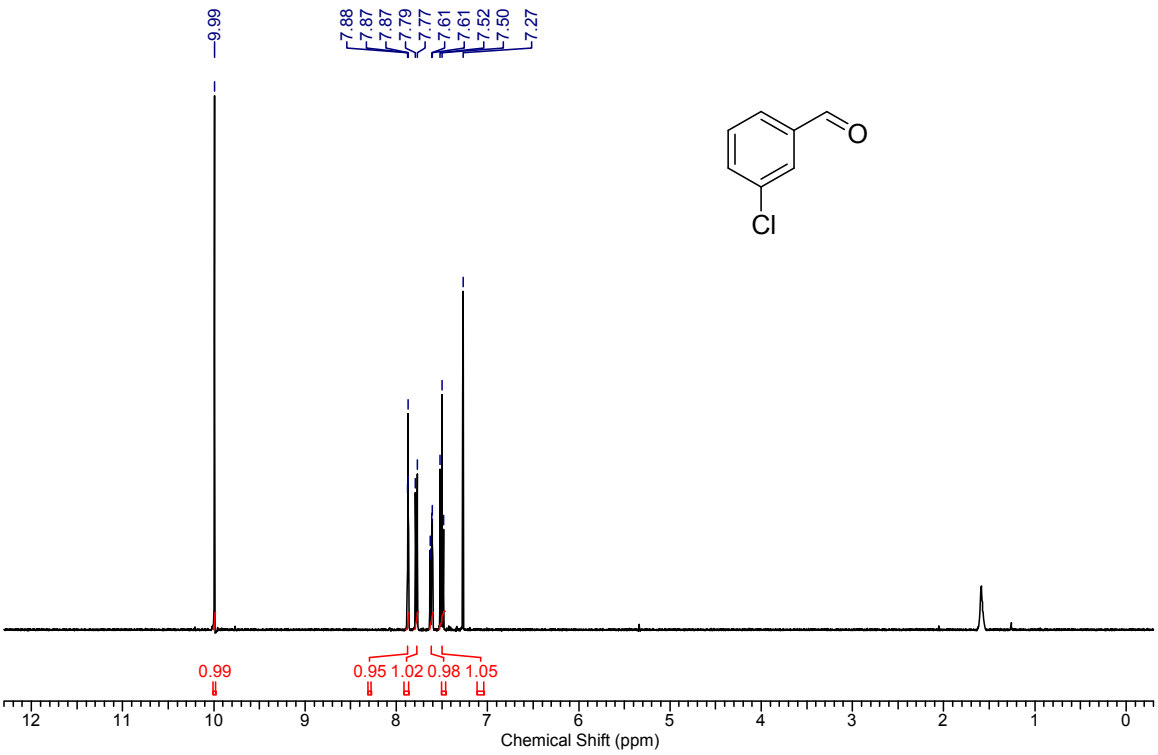
## XIV. $^{1}H$ and $^{13}C$ NMR Spectra of Oxidized Products:

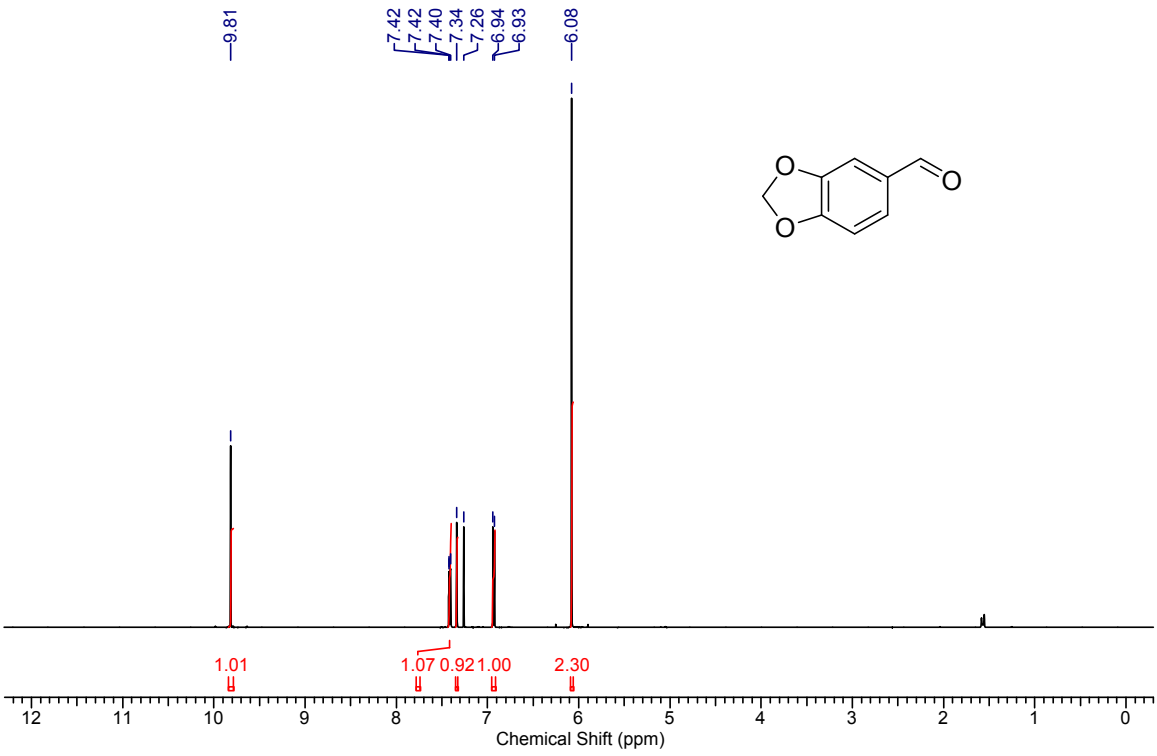


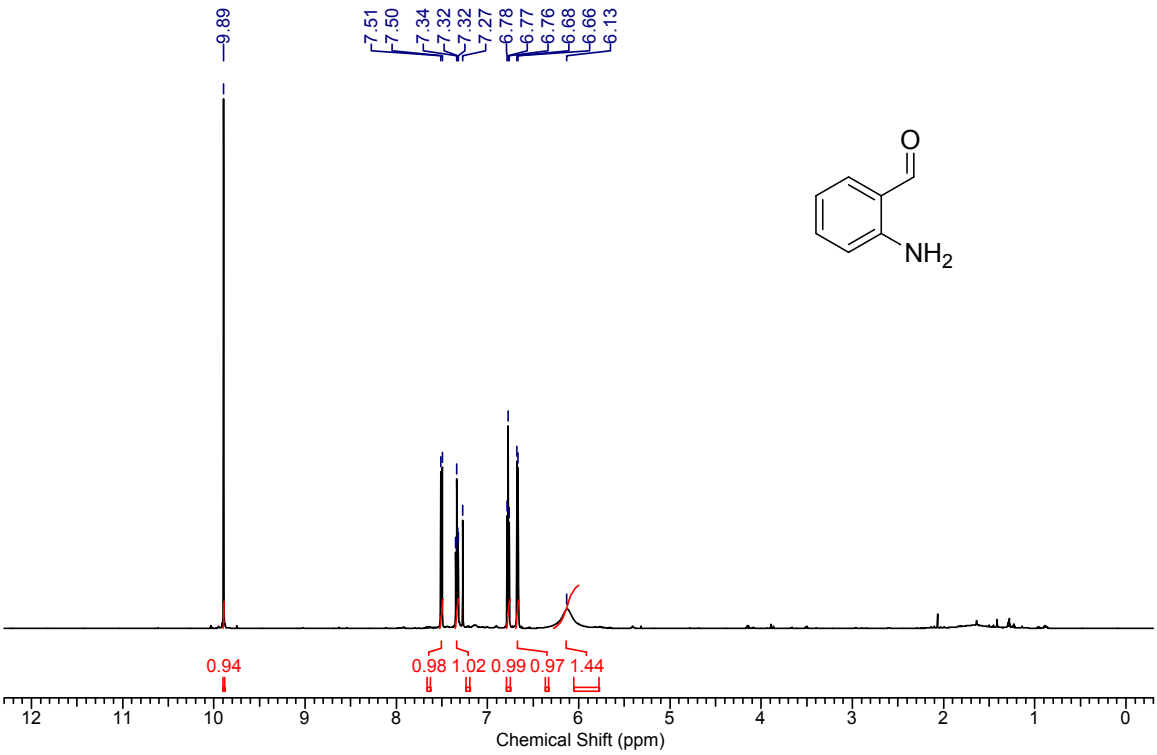



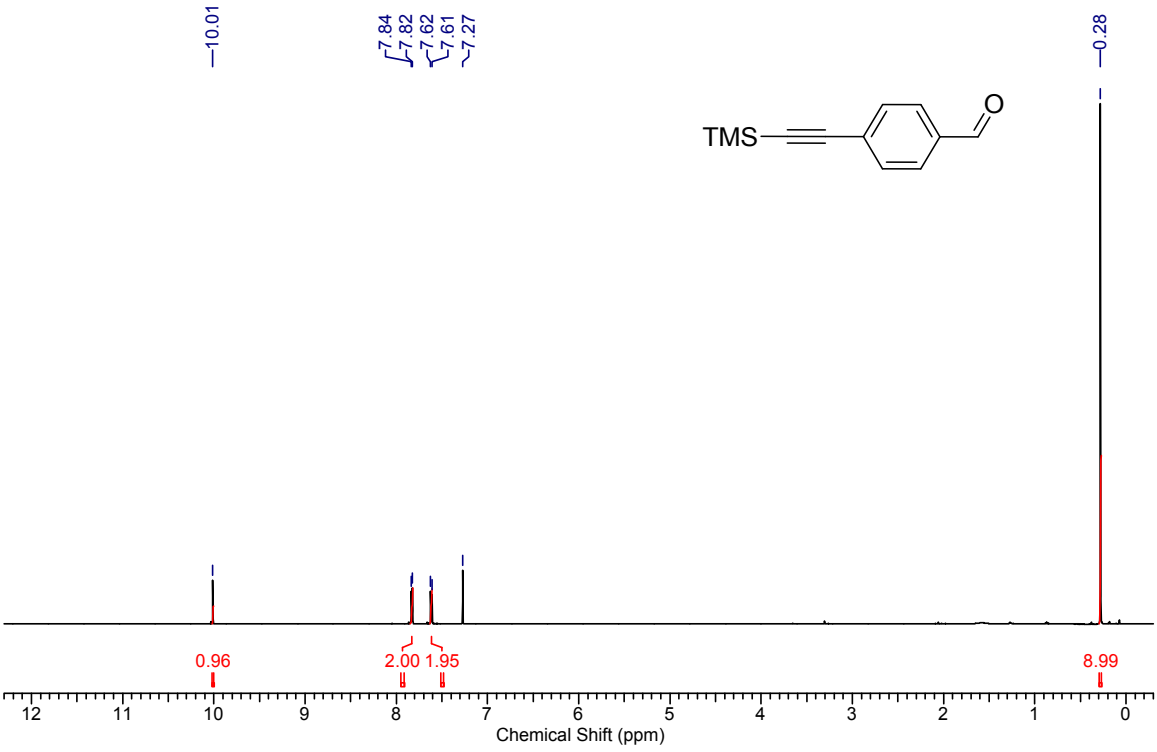

9.99
7.77
7.77
7.76
7.75
7.71
7.71
7.69
7.27
O
Br
0.95
1.98
1.94
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

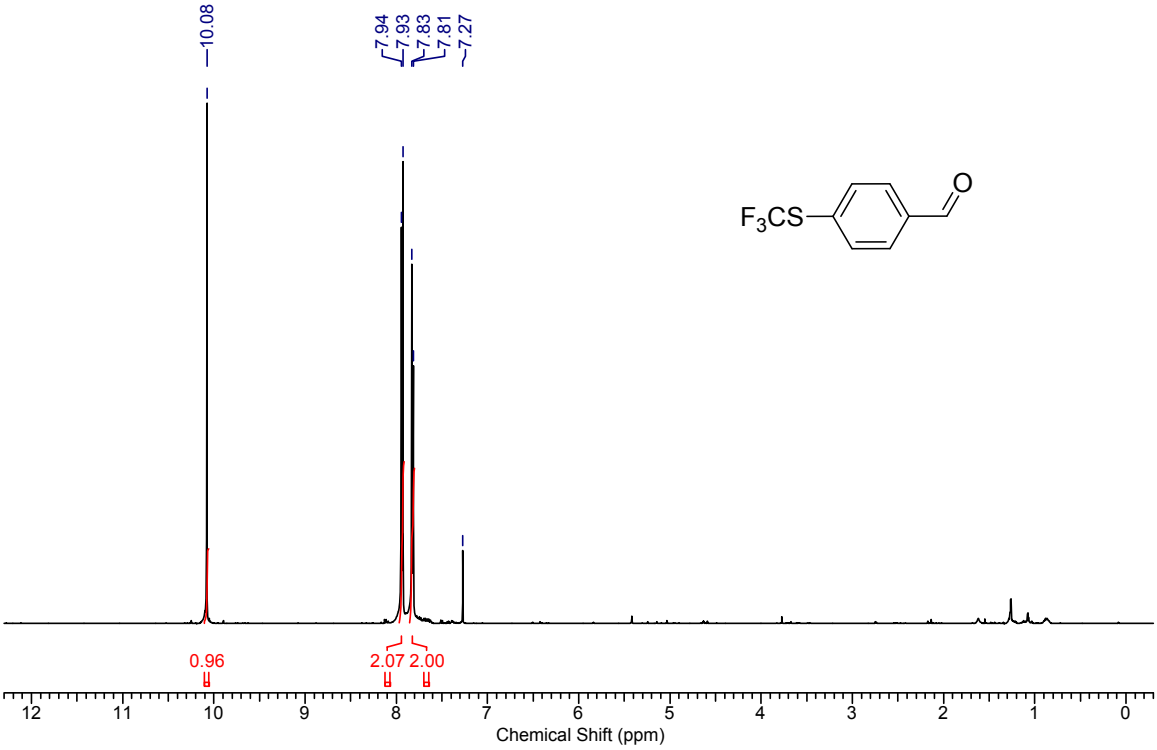

10.14
8.73
8.73
8.52
8.50
8.50
8.26
8.26
8.24
8.24
7.80
7.78
7.77
7.27
O
NO2
0.98
0.94
0.93
1.00
1.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

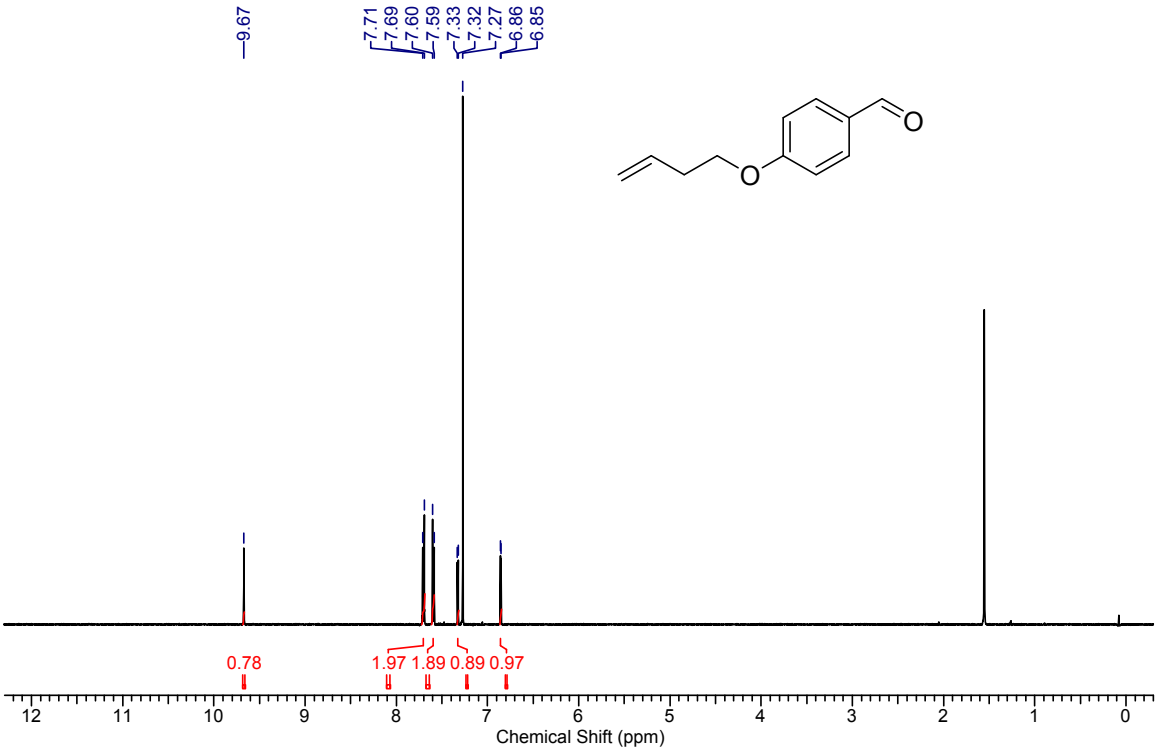

9.99
7.88
7.87
7.87
7.79
7.77
7.61
7.61
7.52
7.50
7.27
O
Cl
0.99
0.95
1.02
0.98
1.05
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

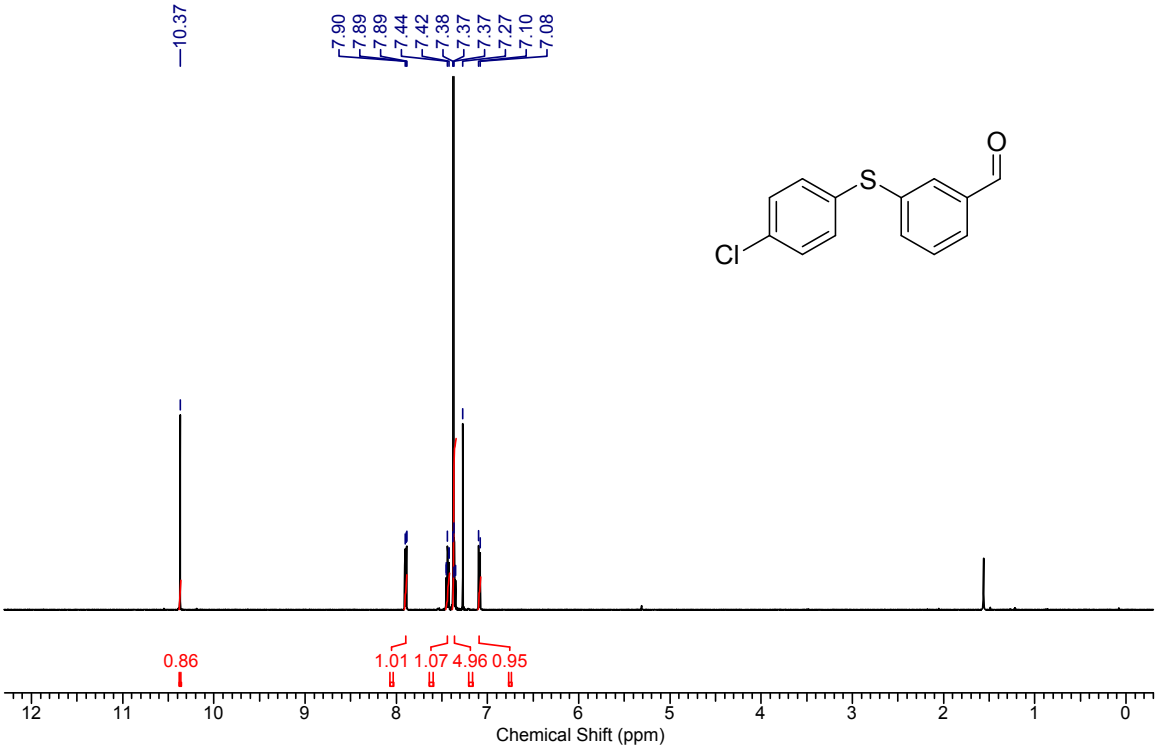

9.81
7.42
7.42
7.40
7.34
7.26
6.94
6.93
6.08
O
O
O
1.01
1.07
0.92
1.00
2.30
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

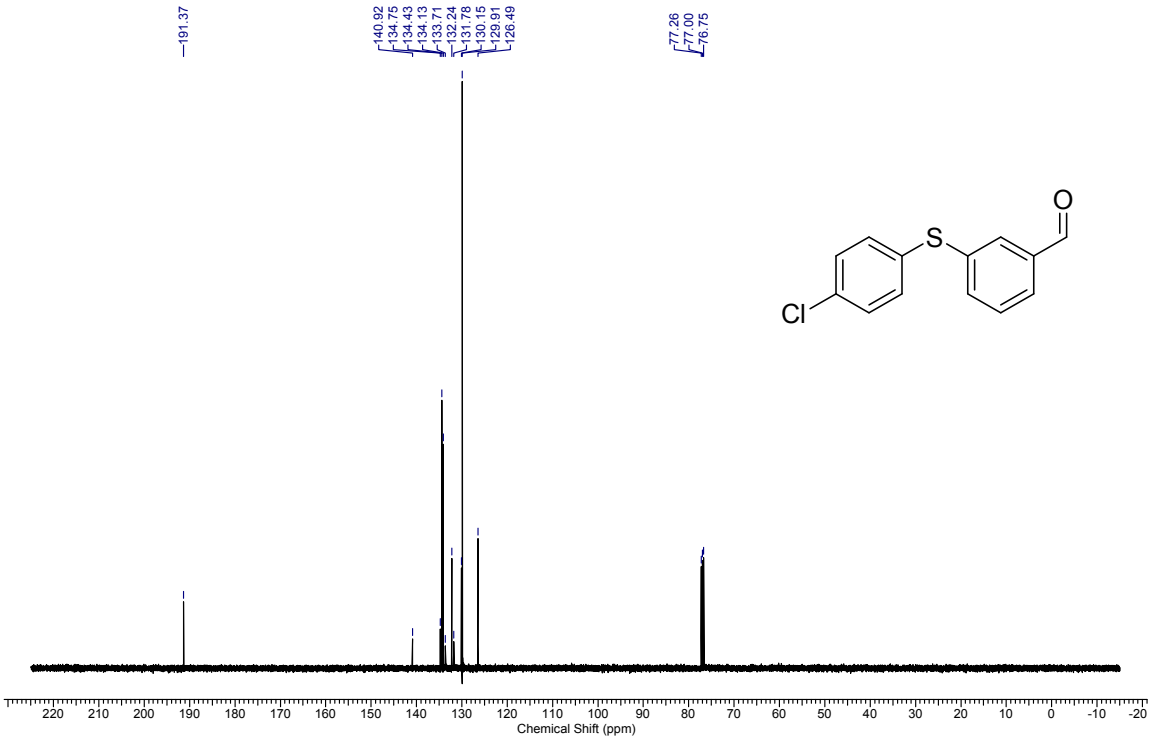

9.89
7.51
7.50
7.34
7.32
7.32
7.27
6.78
6.77
6.76
6.68
6.66
6.13
O
NH2
0.94
0.98
1.02
0.99
0.97
1.44
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

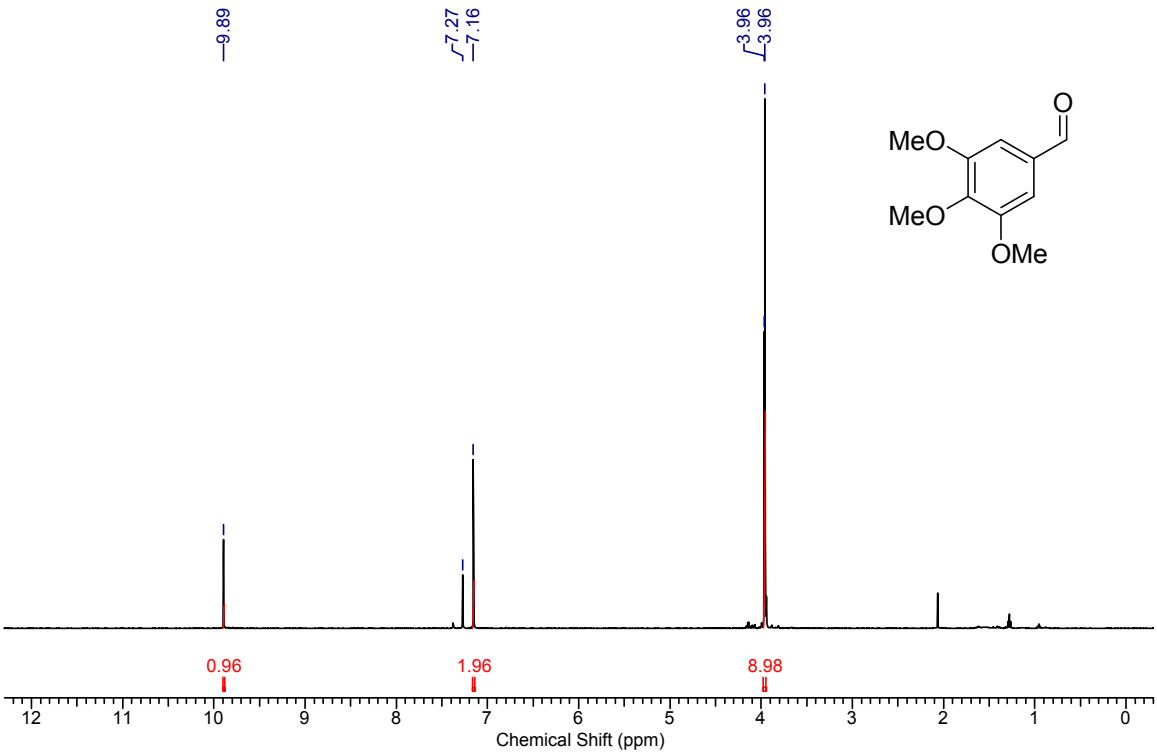

10.01
7.84
7.82
7.62
7.61
7.27
0.28
TMS
O
0.96
2.00
1.95
8.99
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

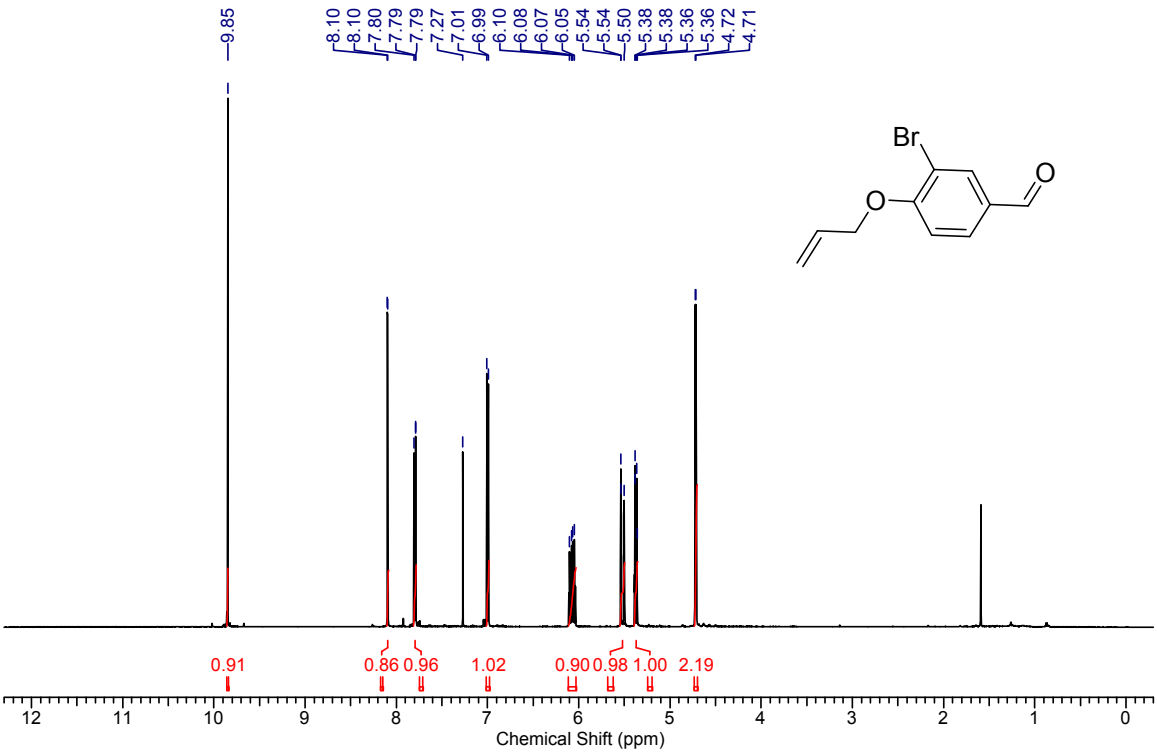

10.08
7.94
7.93
7.83
7.81
7.27
F3CS
O
0.96
2.07
2.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

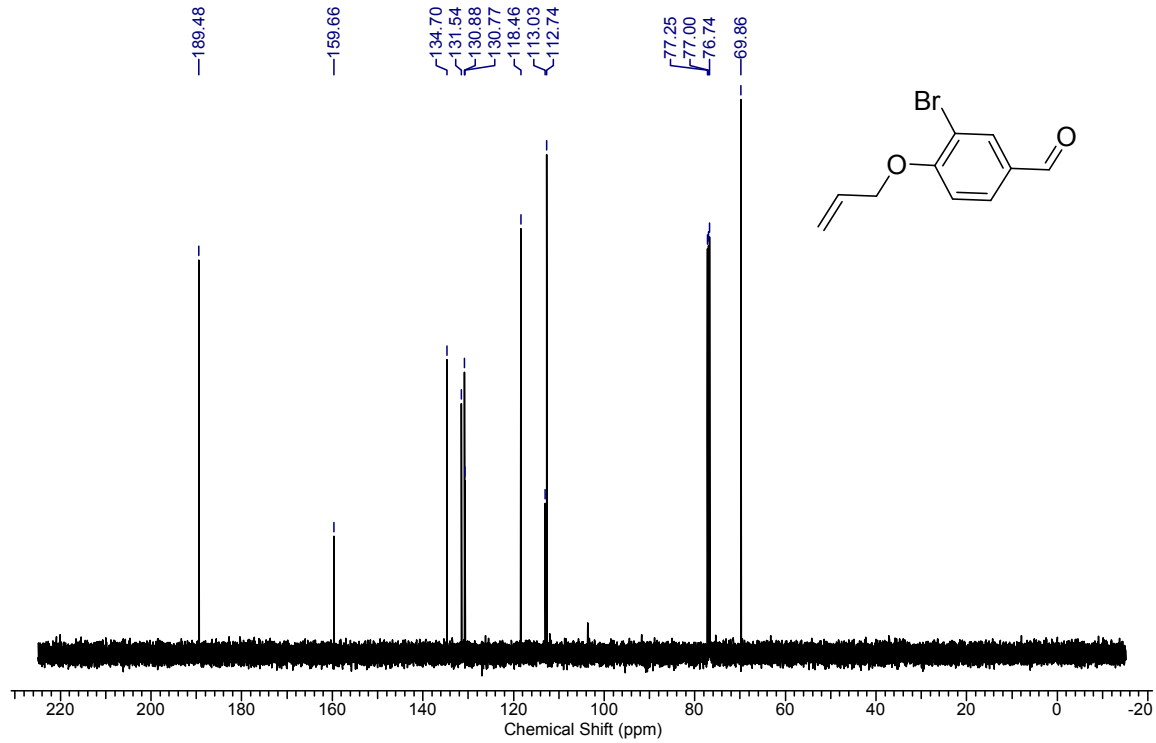

9.67
7.71
7.69
7.60
7.59
7.33
7.32
7.27
6.86
6.85
O
O
0.78
1.97
1.89
0.89
0.97
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


10.37
7.90
7.89
7.89
7.44
7.42
7.38
7.37
7.37
7.27
7.10
7.08
O
S
Cl
0.86
1.01
1.07
4.96
0.95
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

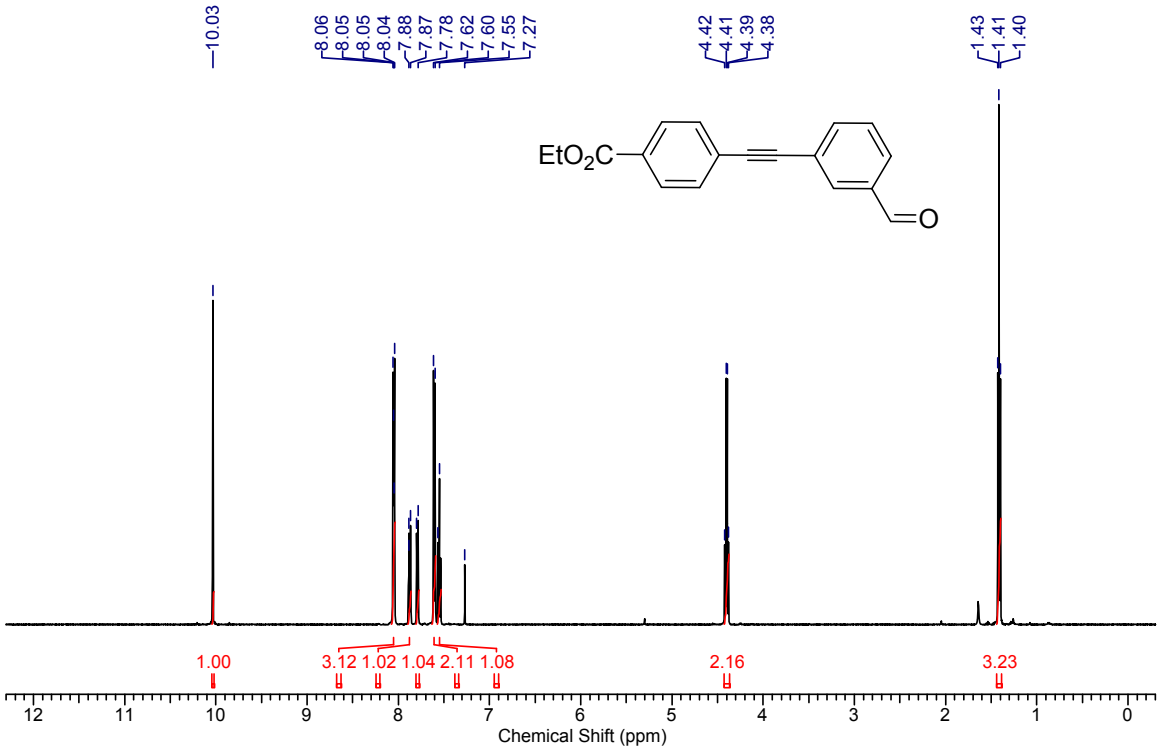

191.37
140.92
134.75
134.43
134.13
133.71
132.24
131.78
130.15
129.91
126.49
77.26
77.00
76.75
O
S
Cl
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
Chemical Shift (ppm)

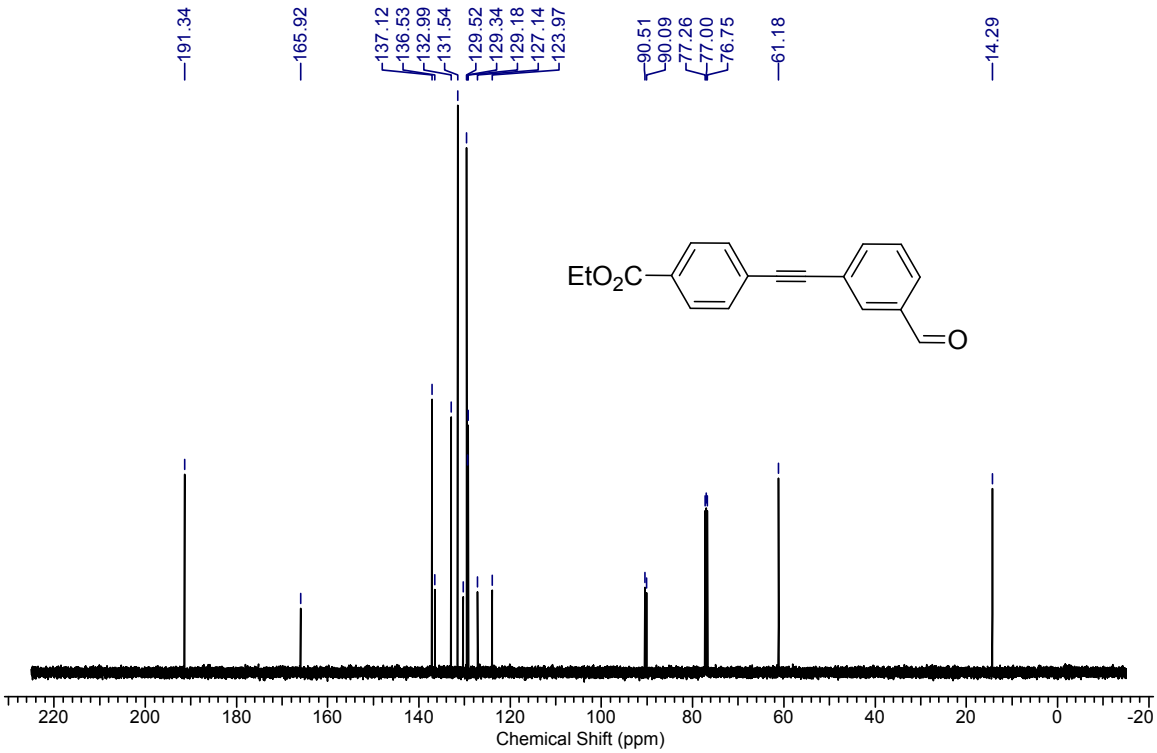

9.89
7.27
7.16
3.96
3.96
O
MeO
MeO
OMe
0.96
1.96
8.98
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

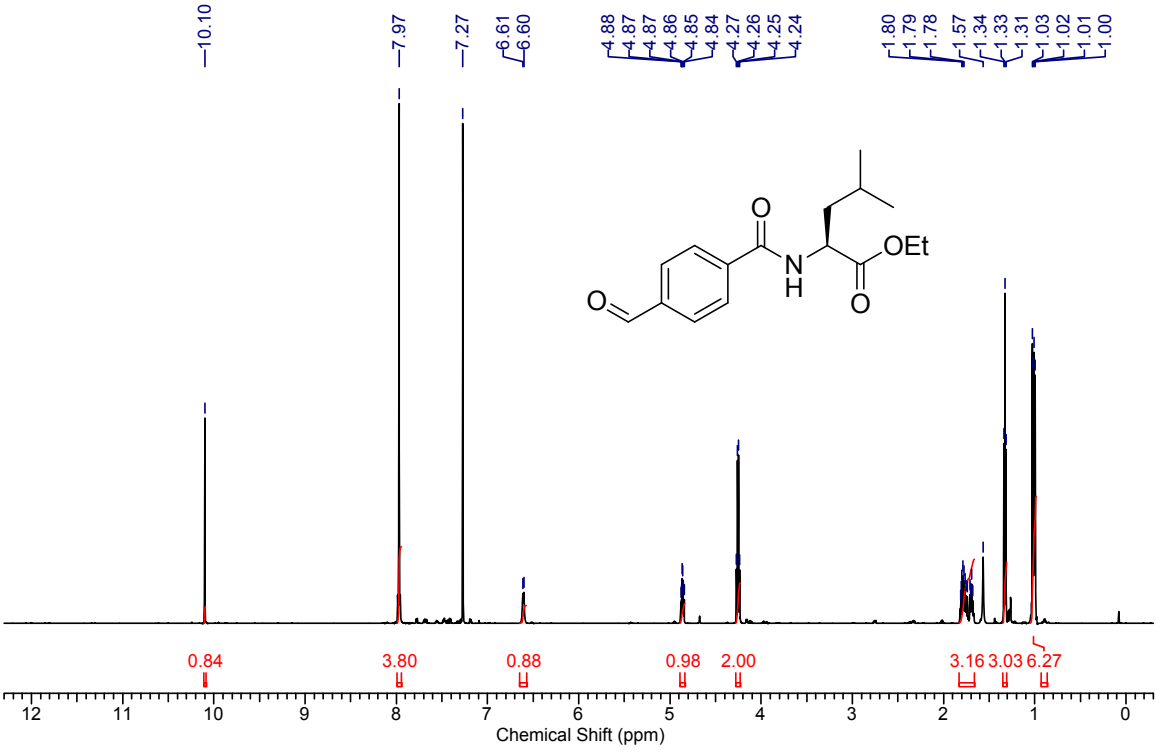

9.85
8.10
8.10
7.80
7.79
7.79
7.27
7.01
6.99
6.10
6.08
6.07
6.05
5.54
5.54
5.50
5.38
5.38
5.36
5.36
4.72
4.71
Br
O
O
0.91
0.86
0.96
1.02
0.90
0.98
1.00
2.19
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

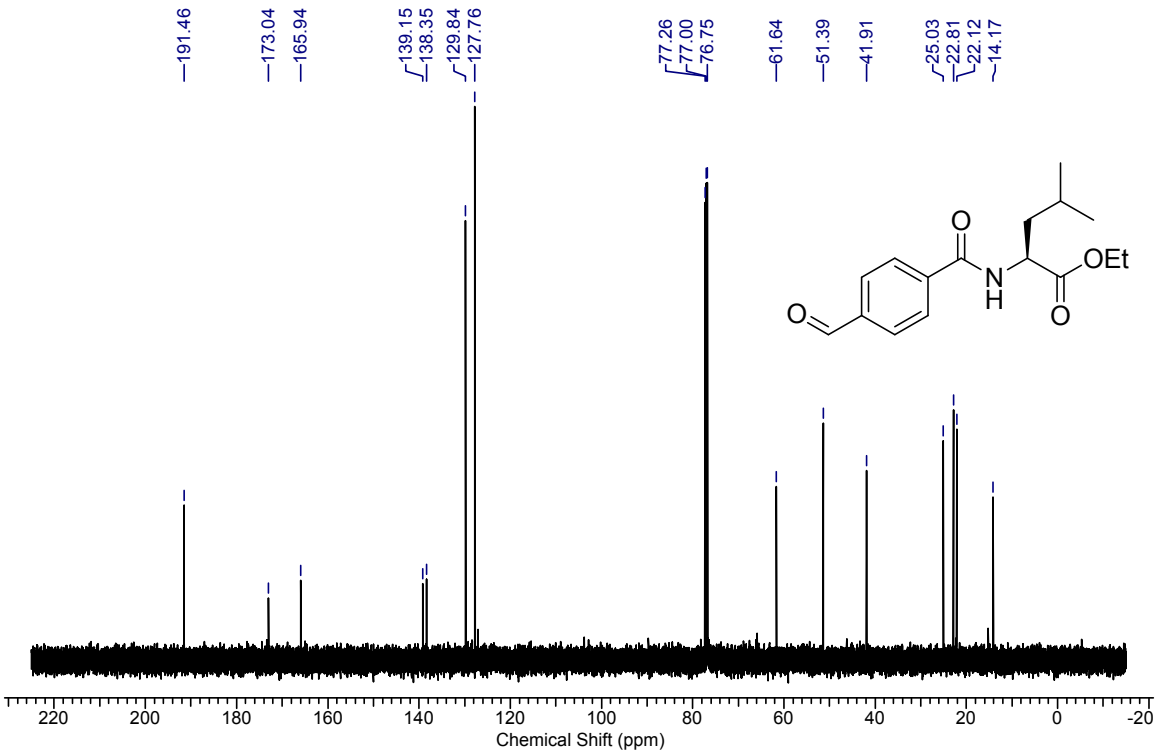


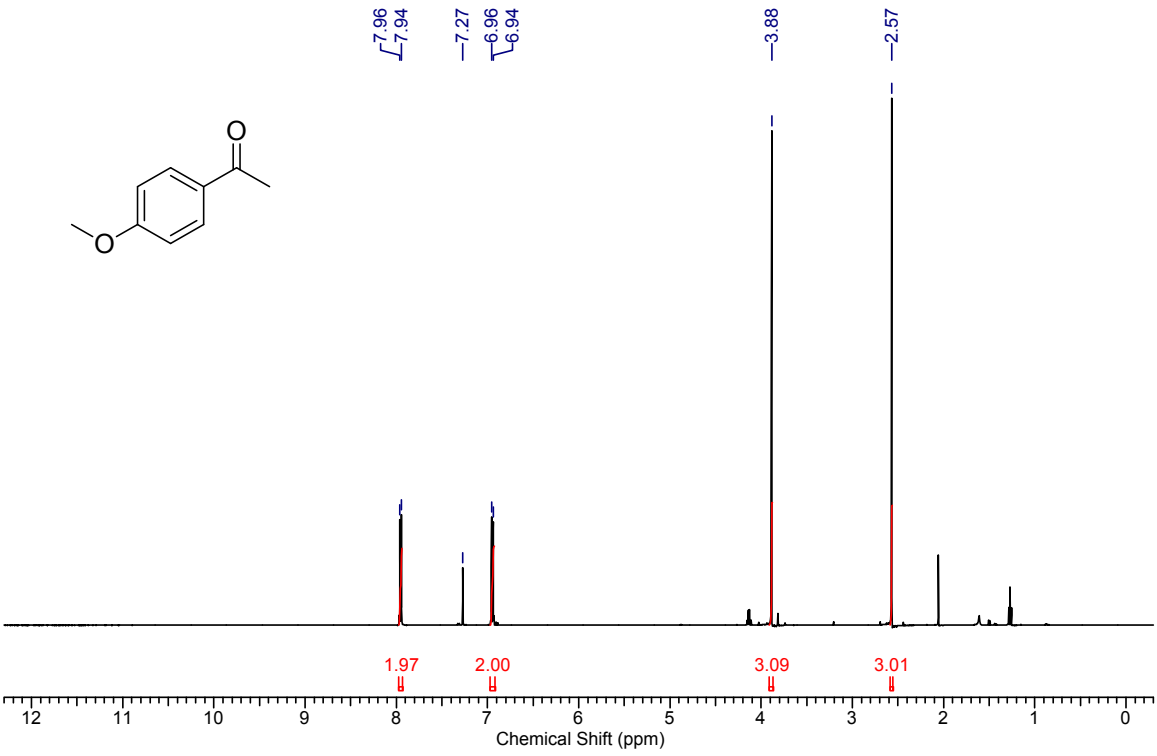

**$^{13}$C-NMR** of **4-(allyloxy)-3-bromobenzaldehyde** in $CDCl_3$

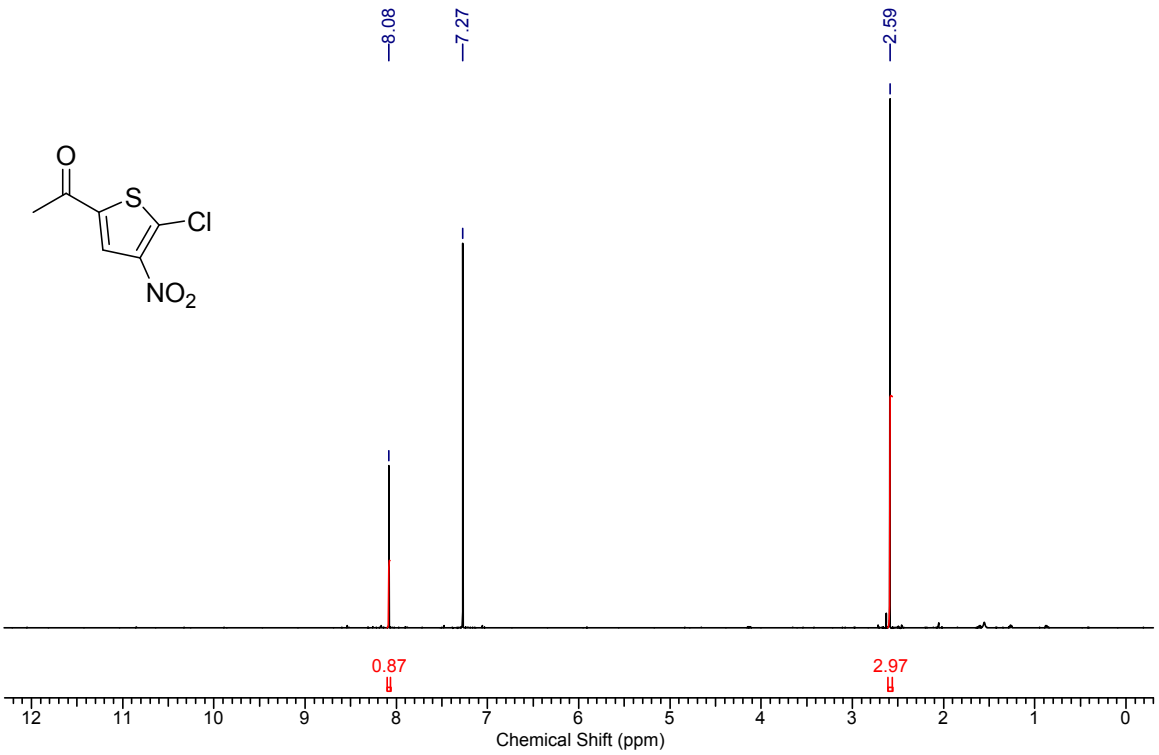


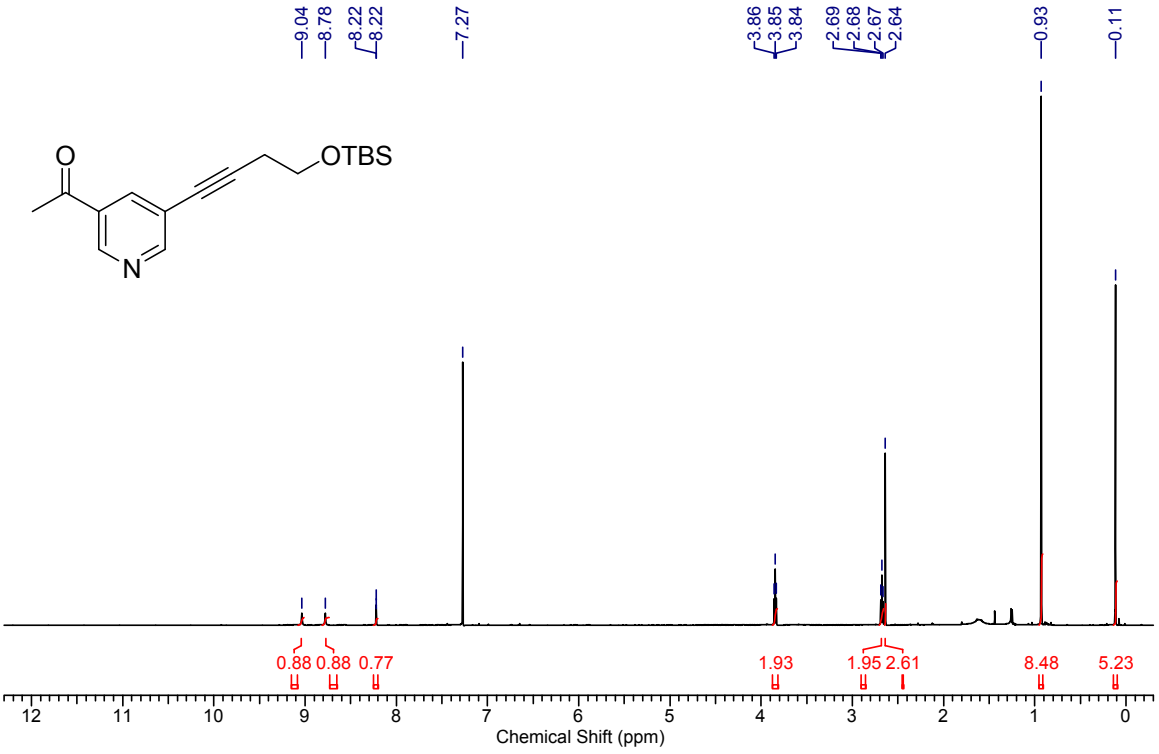

191.34
165.92
137.12
136.53
132.99
131.54
129.52
129.34
129.18
127.14
123.97
90.51
90.09
77.26
77.00
76.75
61.18
14.29
EtO2C
O
220
200
180
160
140
120
100
80
60
40
20
0
-20
Chemical Shift (ppm)

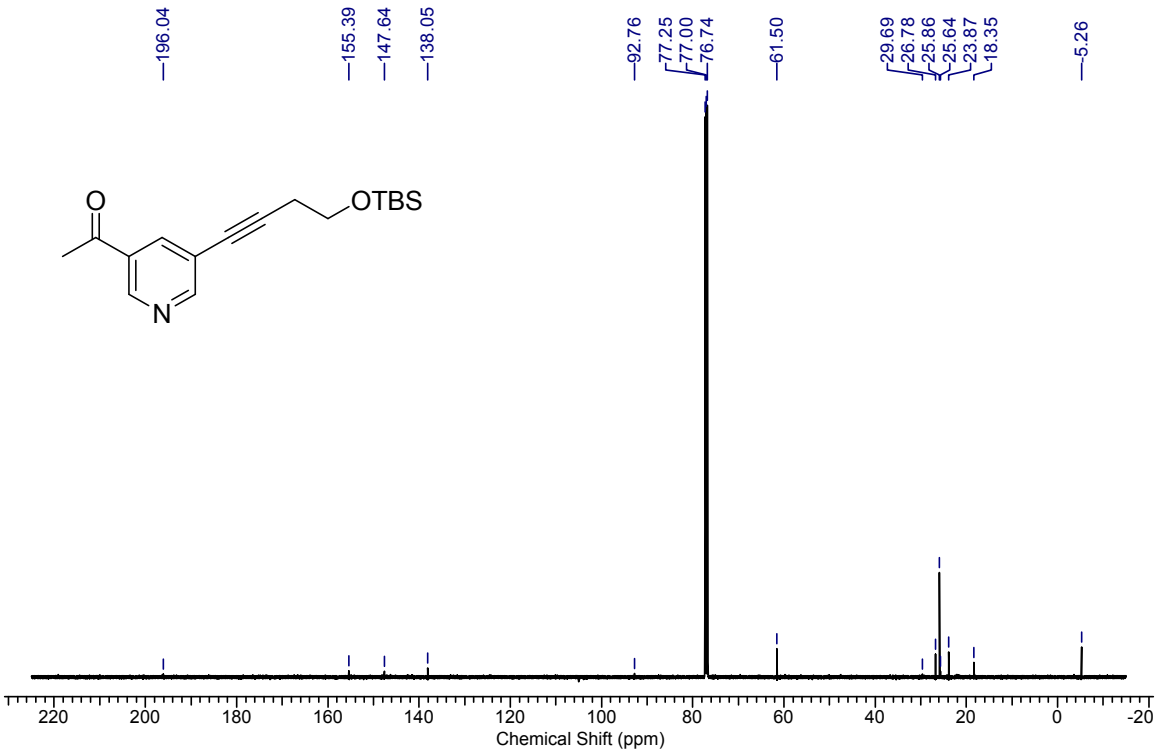

10.10
7.97
7.27
6.61
6.60
4.88
4.87
4.87
4.86
4.85
4.84
4.27
4.26
4.25
4.24
1.80
1.79
1.78
1.57
1.34
1.33
1.31
1.03
1.02
1.01
1.00
O
N
H
OEt
O
O
0.84
3.80
0.88
0.98
2.00
3.16
3.03
6.27
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

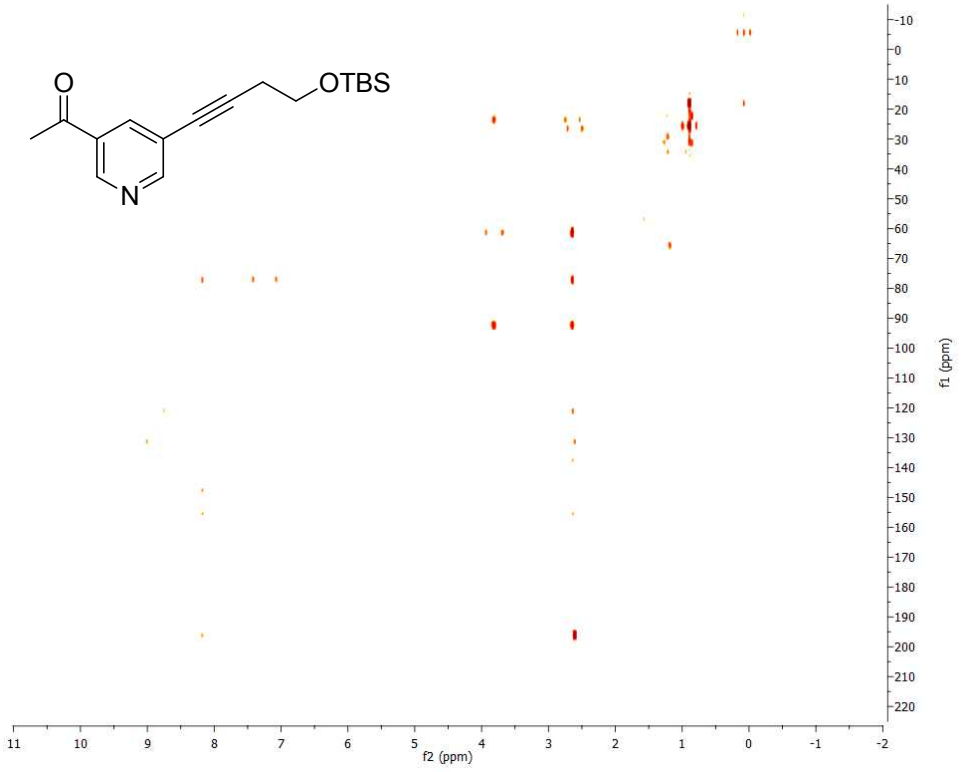

191.46
173.04
165.94
139.15
138.35
129.84
127.76
77.26
77.00
76.75
61.64
51.39
41.91
25.03
22.81
22.12
14.17
O
N
H
OEt
O
O
220
200
180
160
140
120
100
80
60
40
20
0
-20
Chemical Shift (ppm)

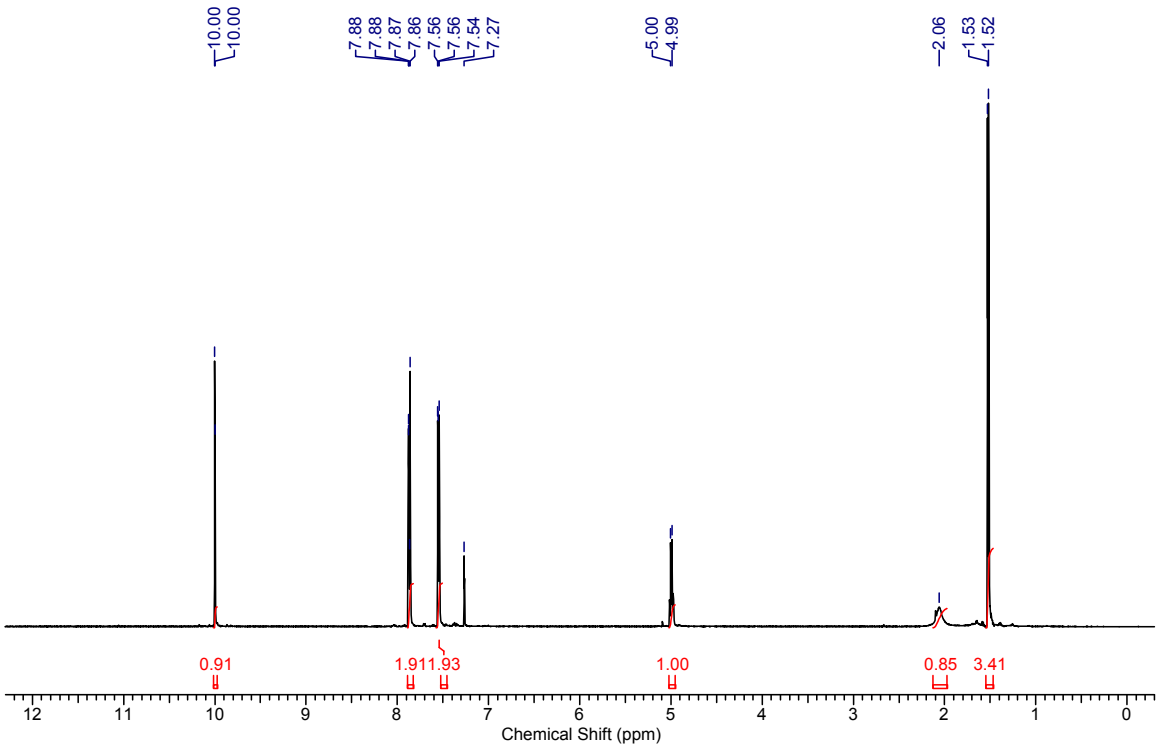

7.96
7.94
7.27
6.96
6.94
3.88
2.57
O
O
1.97
2.00
3.09
3.01
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

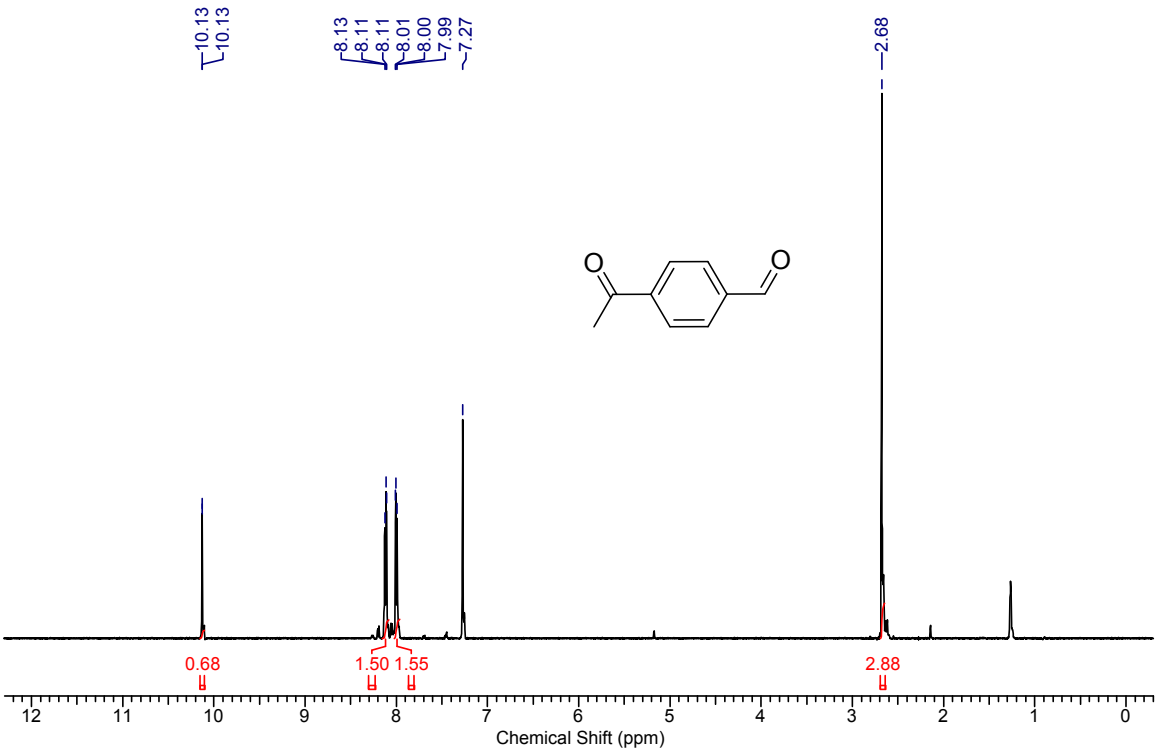

8.08
7.27
2.59
O
S
Cl
NO2
0.87
2.97
12 11 10 9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)

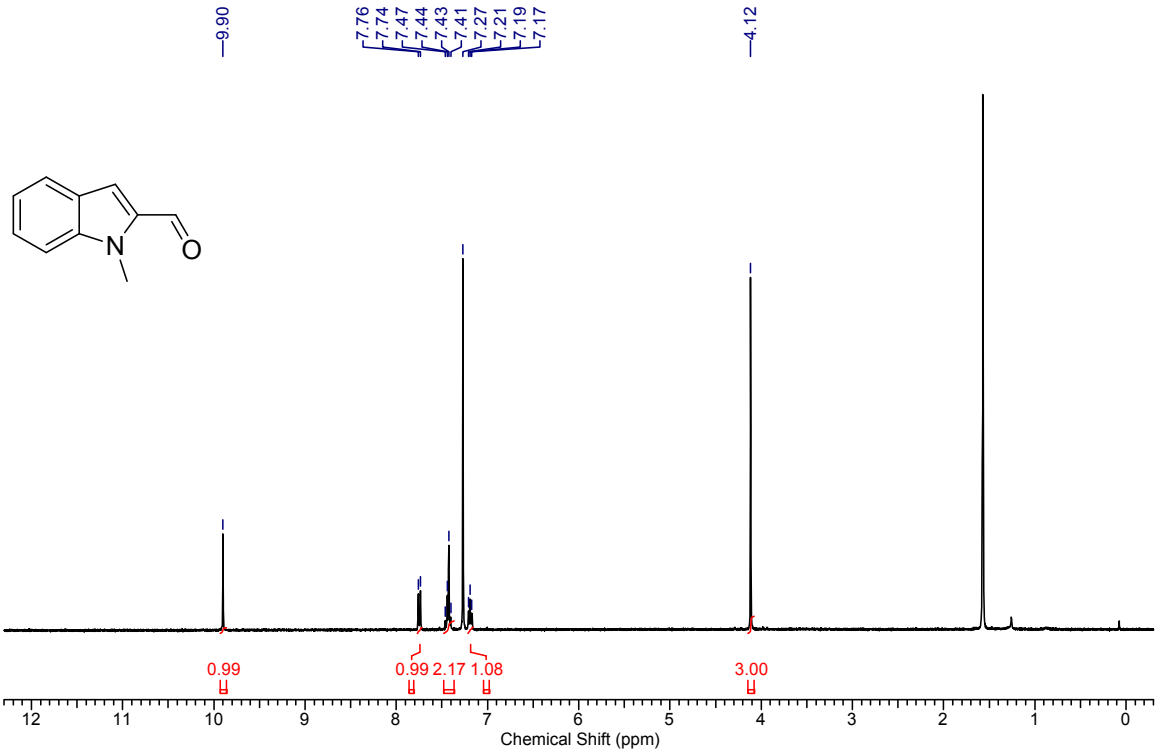

9.04
8.78
8.22
8.22
7.27
3.86
3.85
3.84
2.69
2.68
2.67
2.64
0.93
0.11
O
OTBS
N
0.88 0.88 0.77
1.93
1.95 2.61
8.48
5.23
12 11 10 9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)

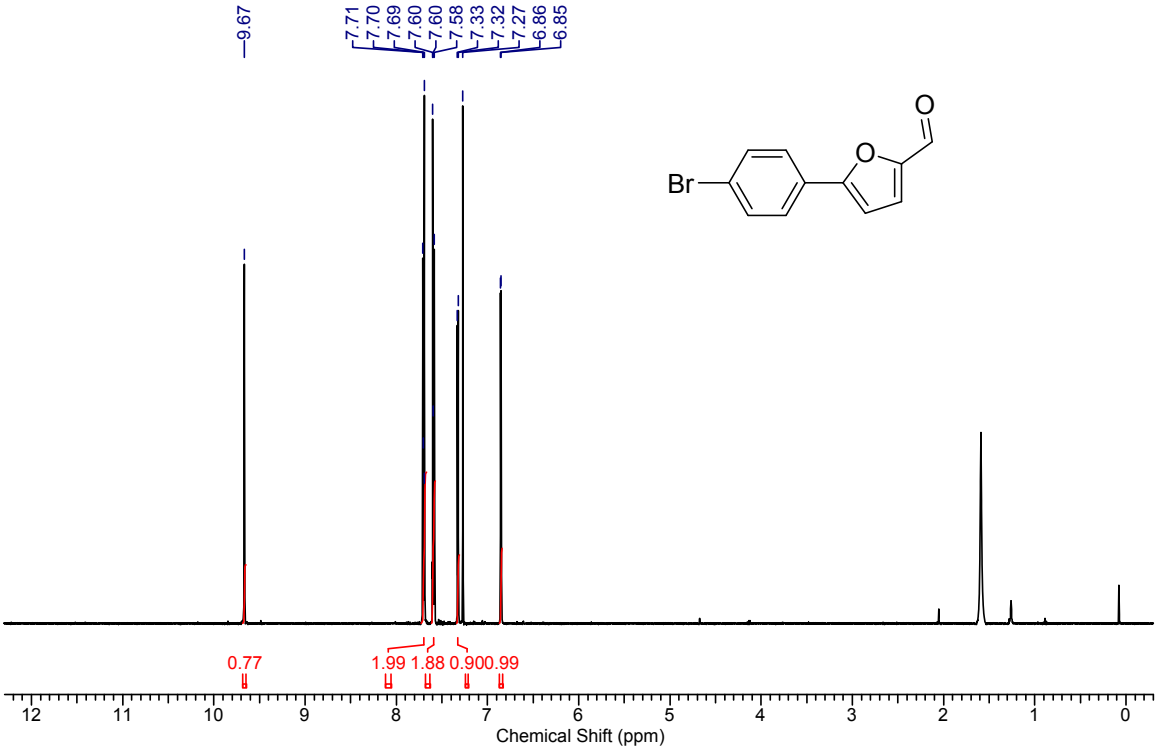

196.04
155.39
147.64
138.05
92.76
77.25
77.00
76.74
61.50
29.69
26.78
25.86
25.64
23.87
18.35
5.26
O
OTBS
N
220
200
180
160
140
120
100
80
60
40
20
0
-20
Chemical Shift (ppm)

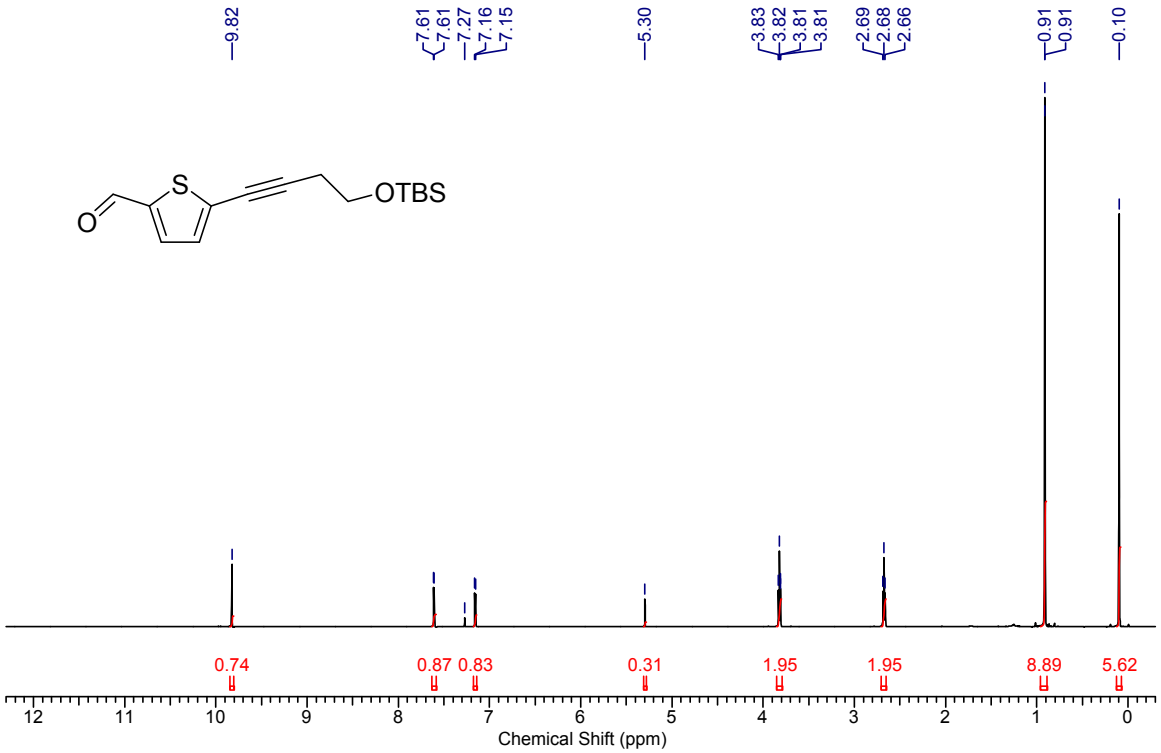

O
OTBS
N
f2 (ppm)
f1 (ppm)

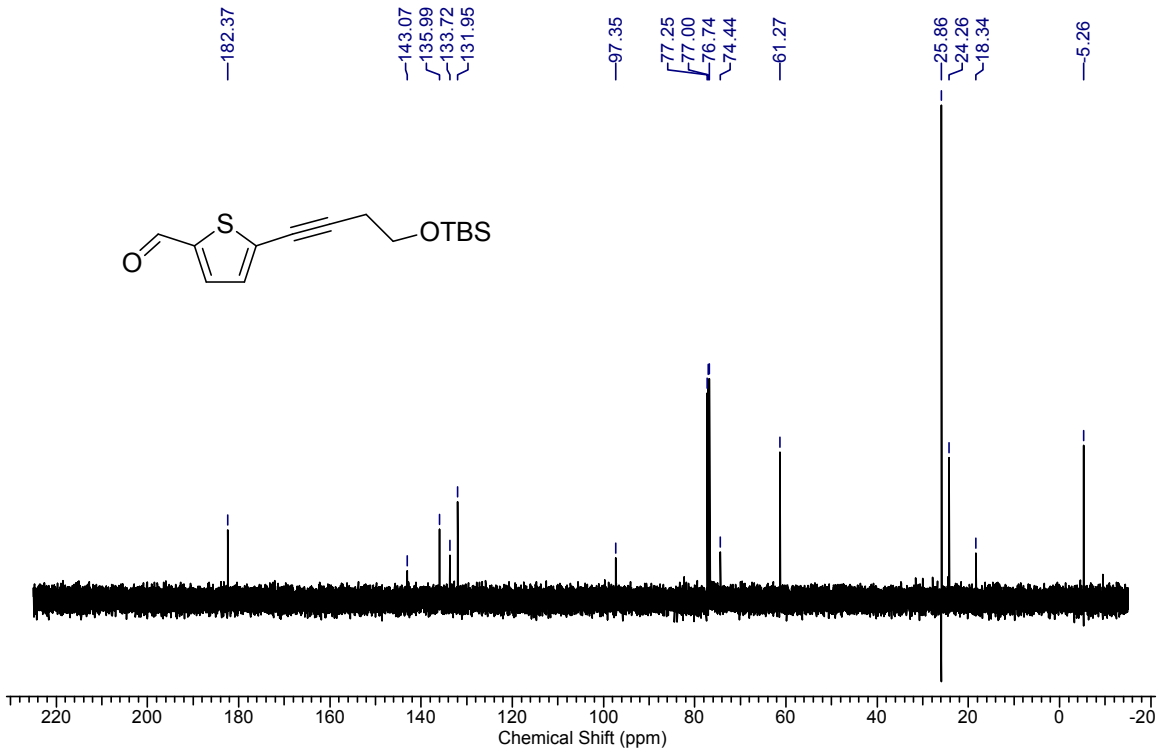

10.00
10.00
7.88
7.88
7.87
7.86
7.56
7.56
7.54
7.27
5.00
4.99
2.06
1.53
1.52
0.91
1.91
1.93
1.00
0.85
3.41
Chemical Shift (ppm)

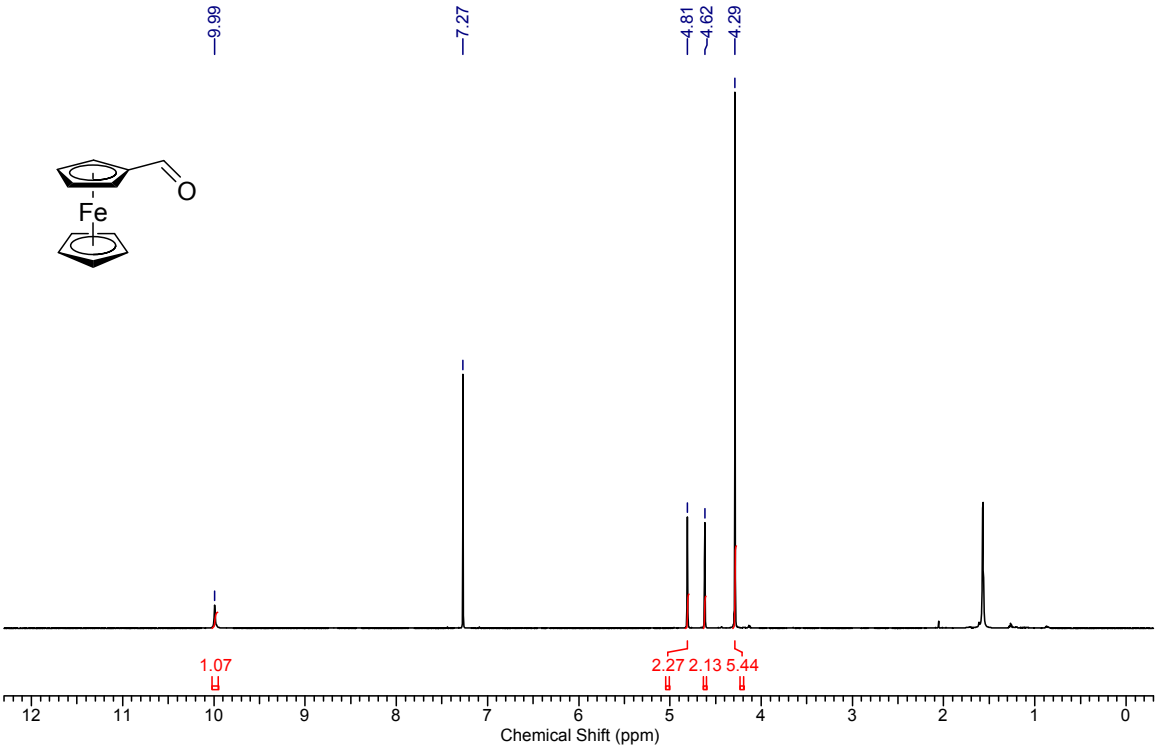

10.13
10.13
8.13
8.11
8.11
8.01
8.00
7.99
7.27
2.68
O
O
0.68
1.50
1.55
2.88
Chemical Shift (ppm)

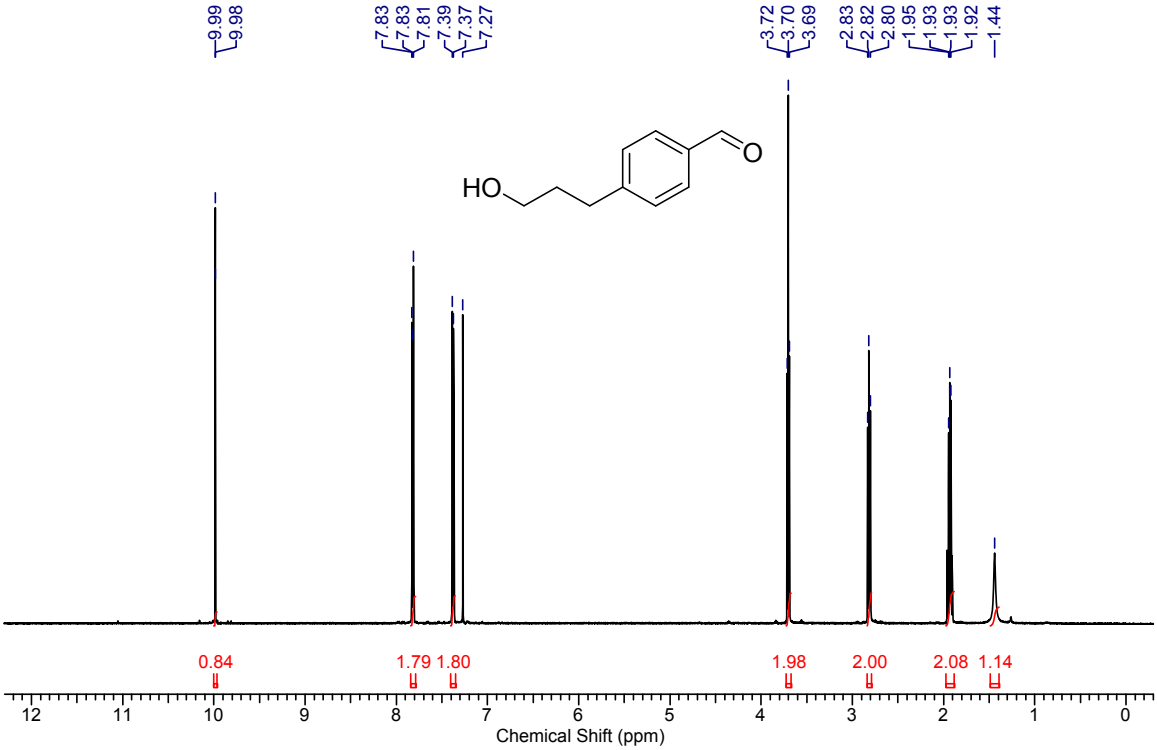

9.90
7.76
7.74
7.47
7.44
7.43
7.41
7.27
7.21
7.19
7.17
4.12
N
O
0.99
0.99
2.17
1.08
3.00
Chemical Shift (ppm)

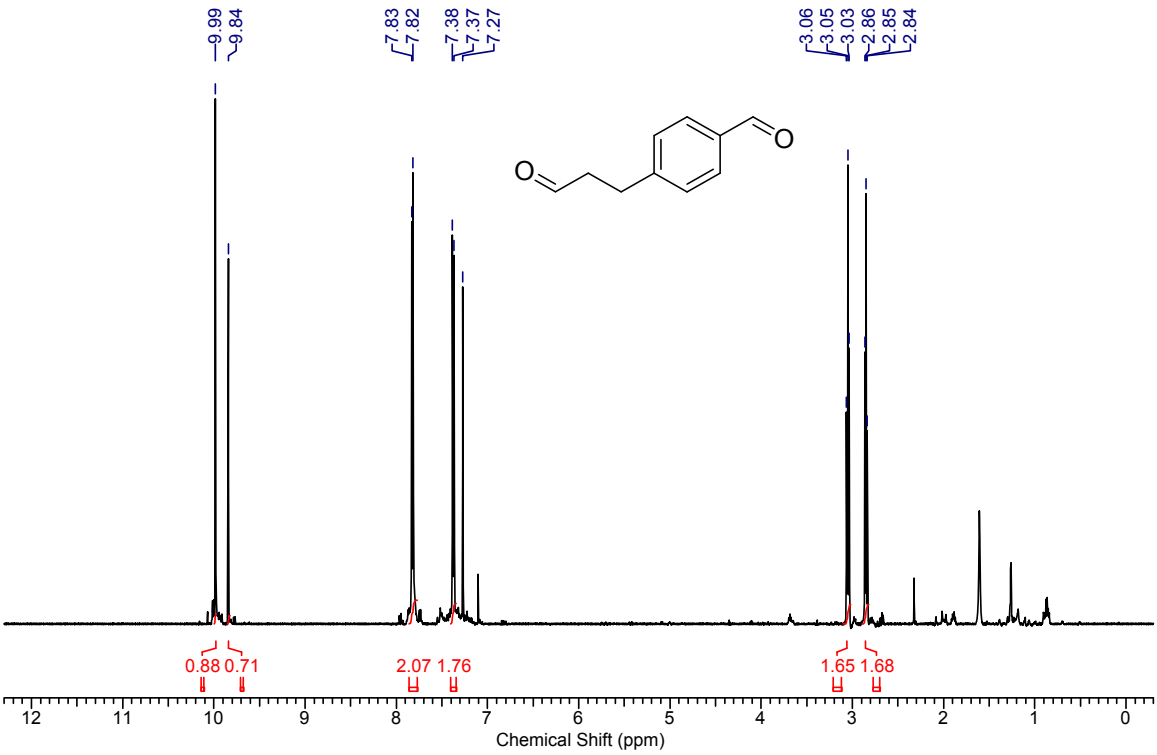

9.67
7.71
7.70
7.69
7.60
7.60
7.58
7.33
7.32
7.27
6.86
6.85
Br
O
O
0.77
1.99
1.88
0.90
0.99
Chemical Shift (ppm)

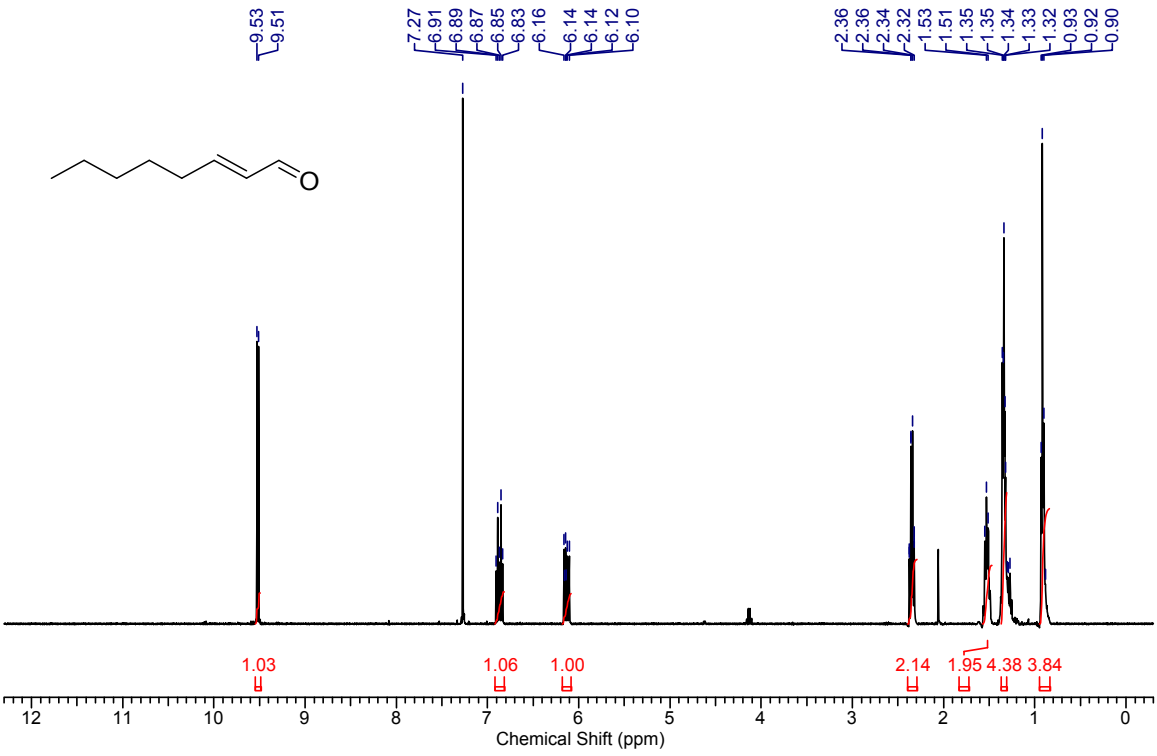

9.82
7.61
7.61
7.27
7.16
7.15
5.30
3.83
3.82
3.81
3.81
2.69
2.68
2.66
0.91
0.91
0.10
S
O
OTBS
0.74
0.87
0.83
0.31
1.95
1.95
8.89
5.62
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

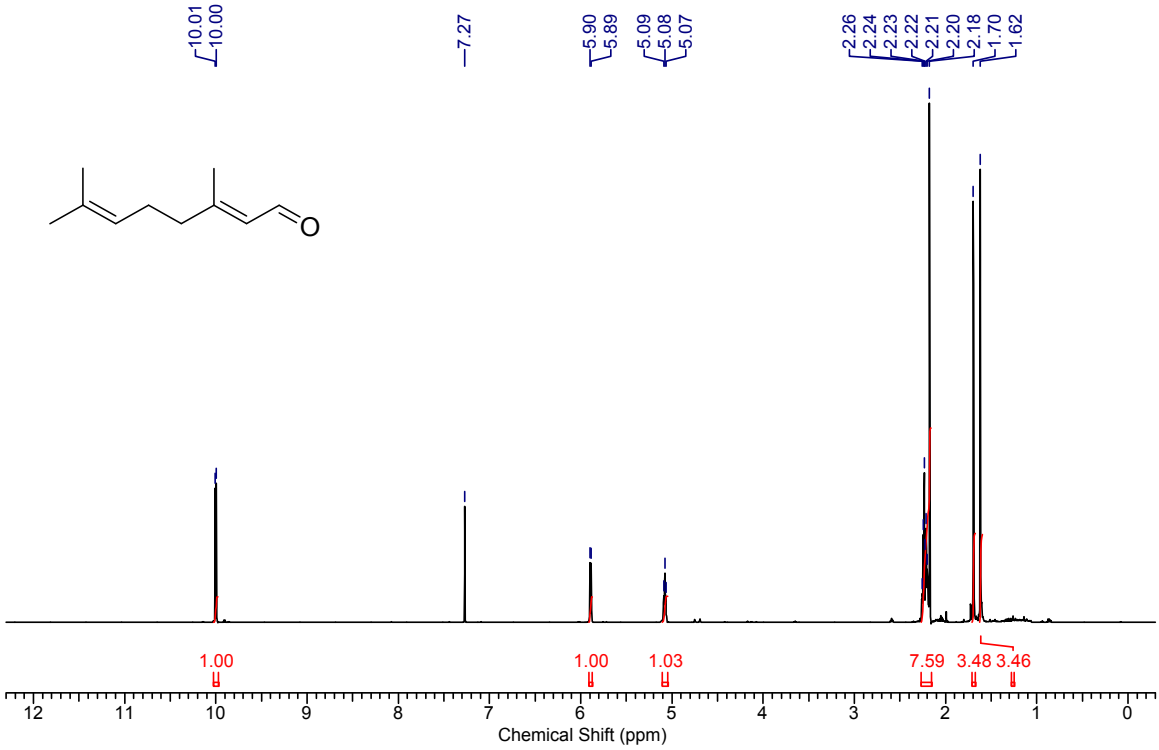

182.37
143.07
135.99
133.72
131.95
97.35
77.25
77.00
76.74
74.44
61.27
25.86
24.26
18.34
5.26
S
O
OTBS
220
200
180
160
140
120
100
80
60
40
20
0
-20
Chemical Shift (ppm)

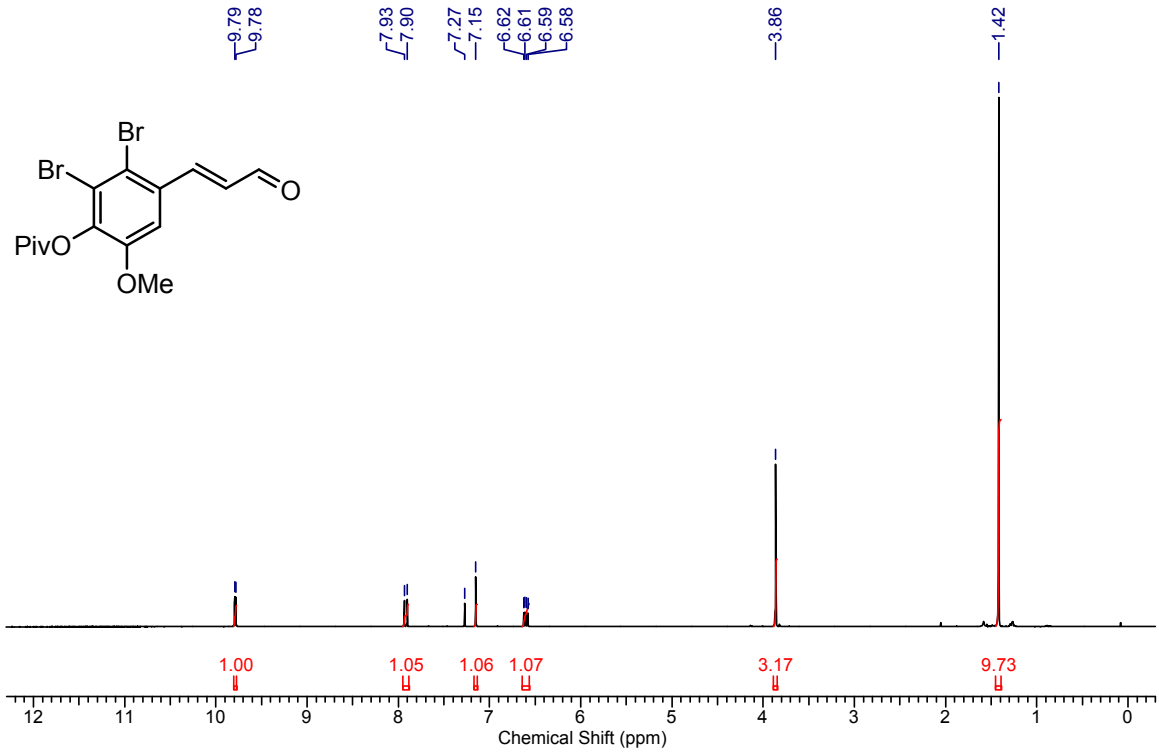

9.99
7.27
4.81
4.62
4.29
Fe
O
1.07
2.27
2.13
5.44
Chemical Shift (ppm)

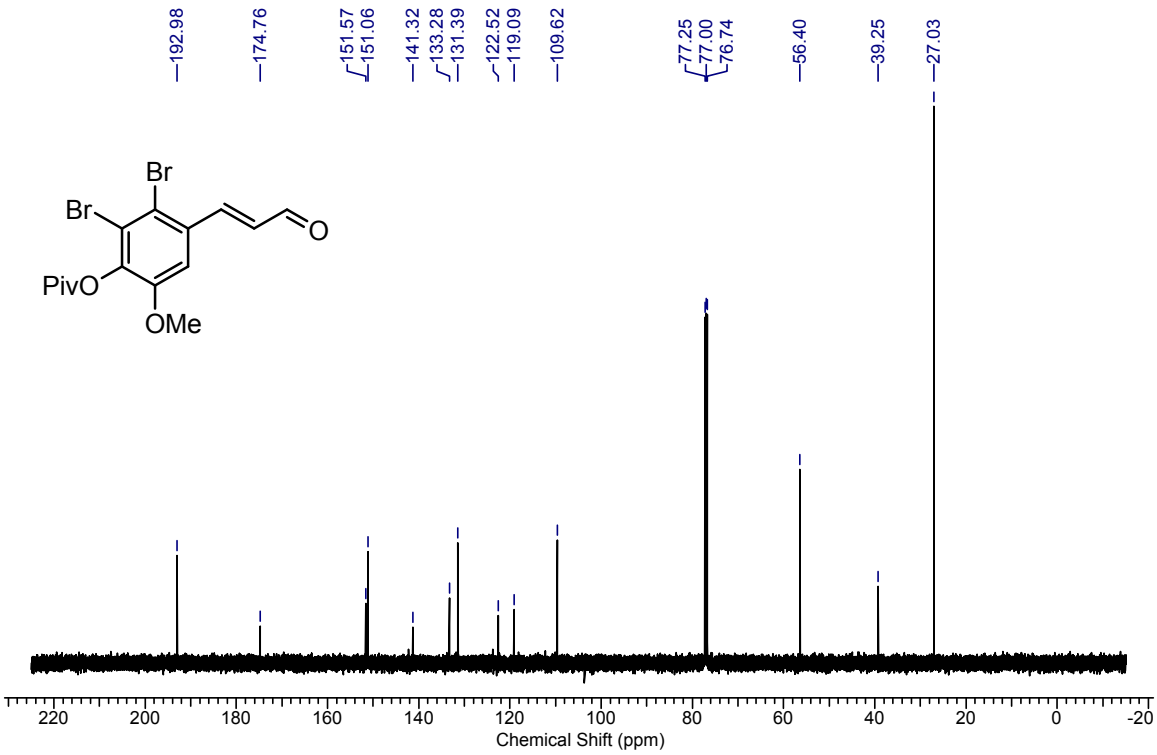

9.99
9.98
7.83
7.83
7.81
7.39
7.37
7.27
3.72
3.70
3.69
2.83
2.82
2.80
1.95
1.93
1.93
1.92
1.44
HO
O
0.84
1.79
1.80
1.98
2.00
2.08
1.14
Chemical Shift (ppm)

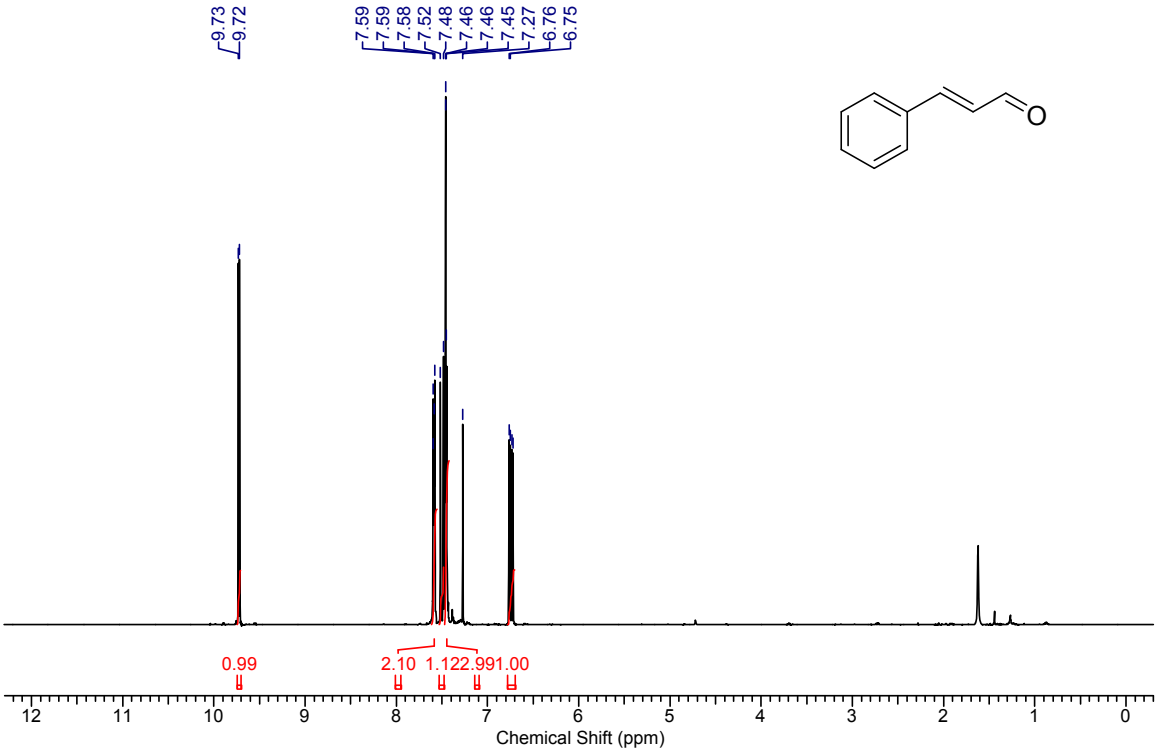

9.99
9.84
7.83
7.82
7.38
7.37
7.27
3.06
3.05
3.03
2.86
2.85
2.84
O
O
0.88 0.71
2.07 1.76
1.65 1.68
12 11 10 9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)

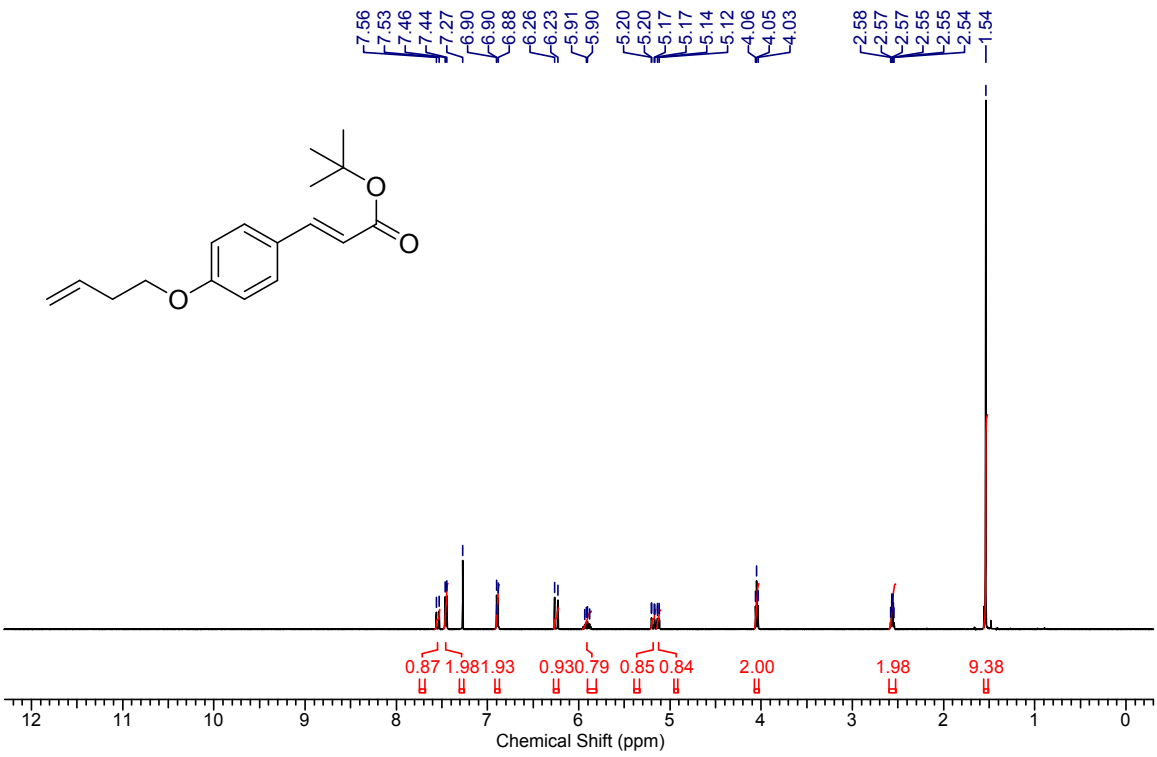

9.53
9.51
7.27
6.91
6.89
6.87
6.85
6.83
6.16
6.14
6.14
6.12
6.10
2.36
2.36
2.34
2.32
1.53
1.51
1.35
1.35
1.34
1.33
1.32
0.93
0.92
0.90
O
1.03
1.06
1.00
2.14
1.95
4.38
3.84
12 11 10 9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)

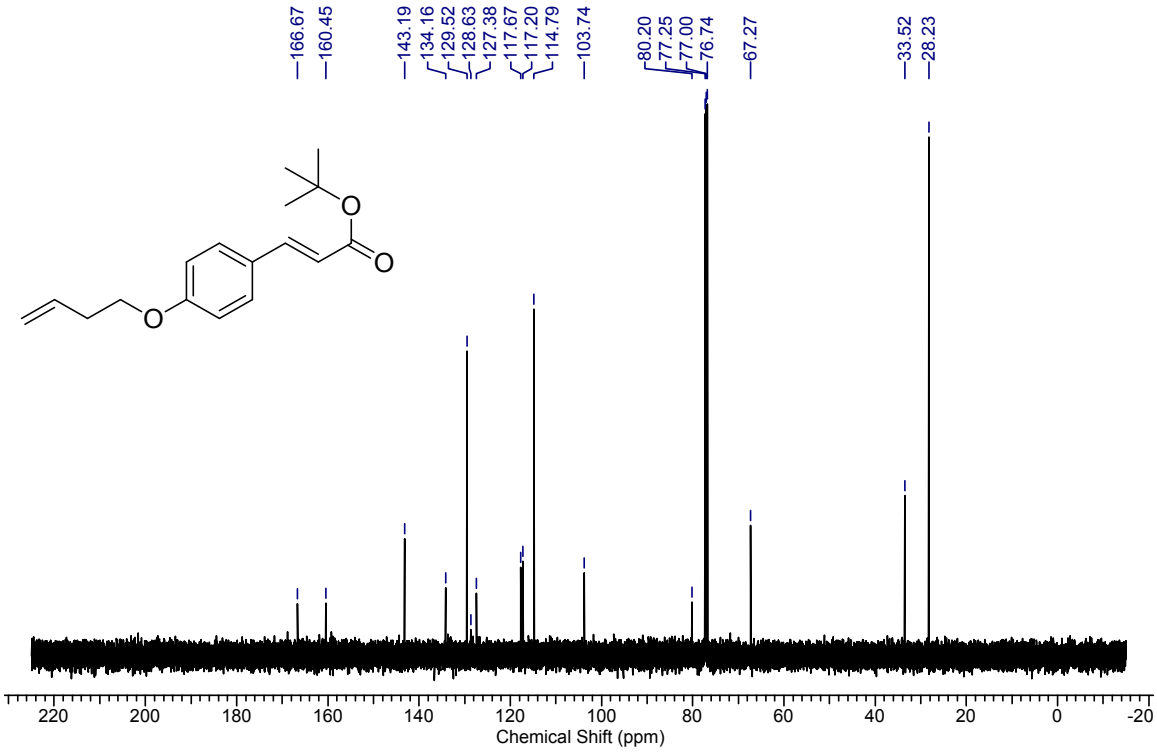

10.01
10.00
7.27
5.90
5.89
5.09
5.08
5.07
2.26
2.24
2.23
2.22
2.21
2.20
2.18
1.70
1.62
O
1.00
1.00
1.03
7.59
3.48
3.46
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


9.79
9.78
7.93
7.90
7.27
7.15
6.62
6.61
6.59
6.58
3.86
1.42
Br
Br
PivO
OMe
O
1.00
1.05
1.06
1.07
3.17
9.73
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

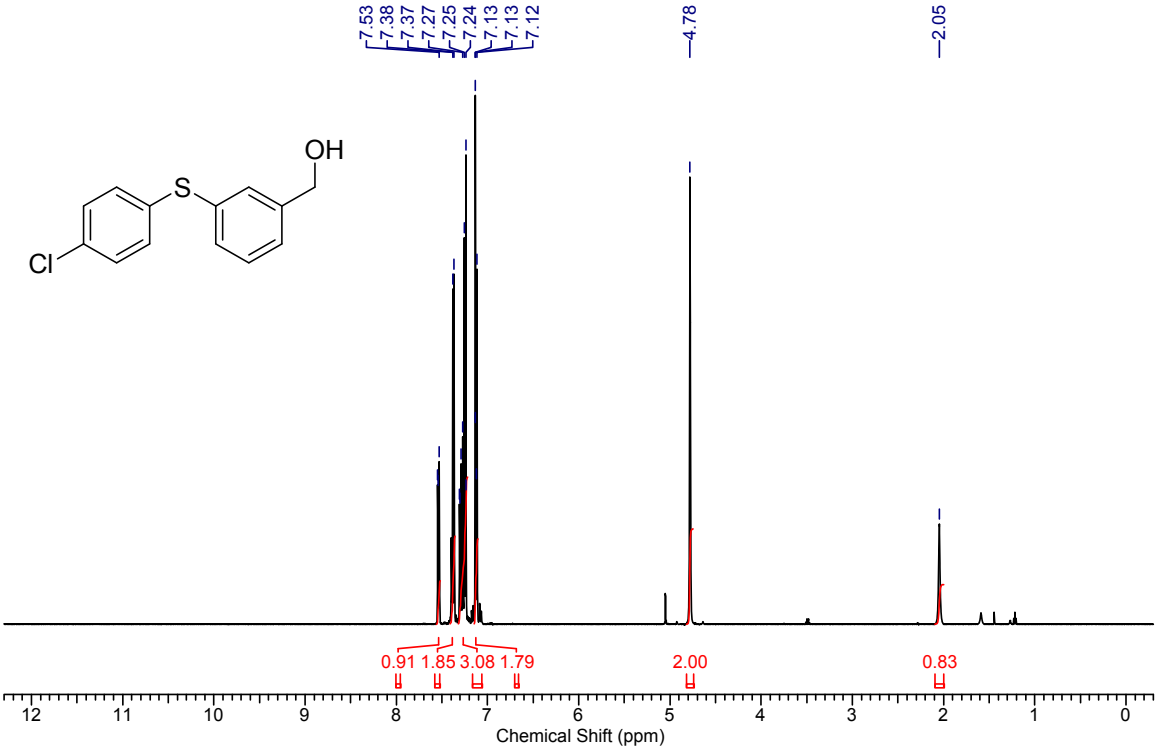

192.98
174.76
151.57
151.06
141.32
133.28
131.39
122.52
119.09
109.62
77.25
77.00
76.74
56.40
39.25
27.03
Br
Br
PivO
OMe
O
220
200
180
160
140
120
100
80
60
40
20
0
-20
Chemical Shift (ppm)

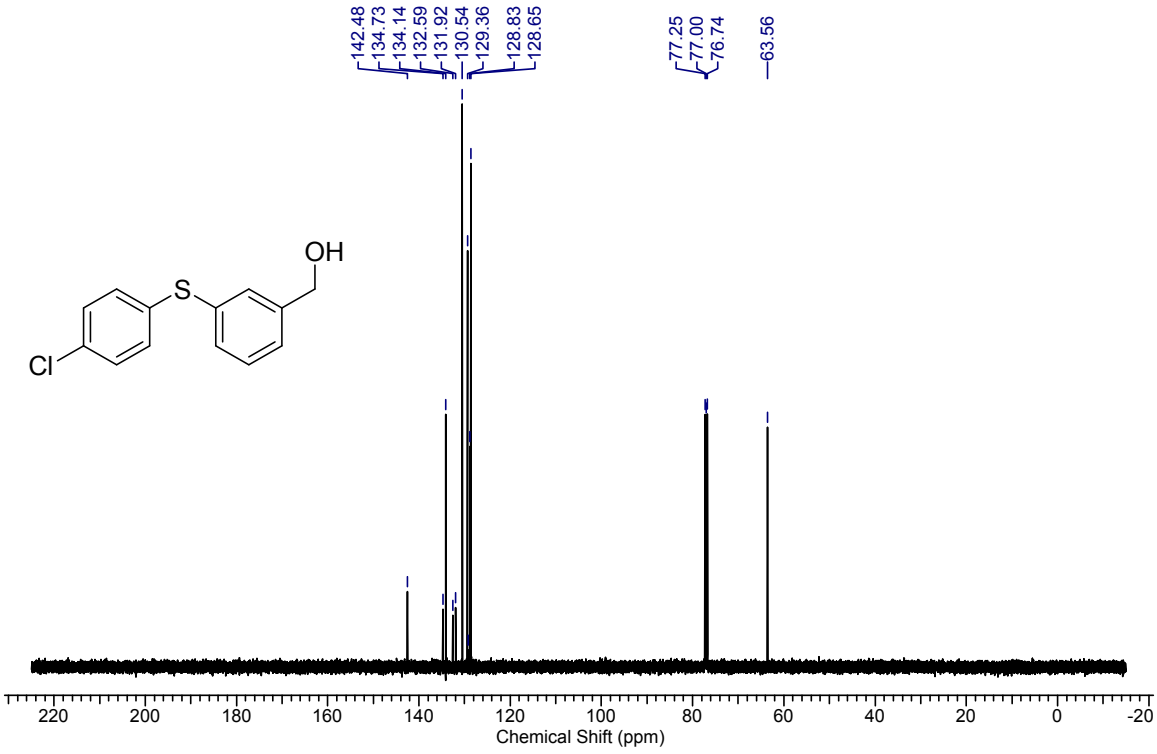

9.73
9.72
7.59
7.59
7.58
7.52
7.48
7.46
7.46
7.45
7.27
6.76
6.75
O
0.99
2.10
1.12
2.99
1.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

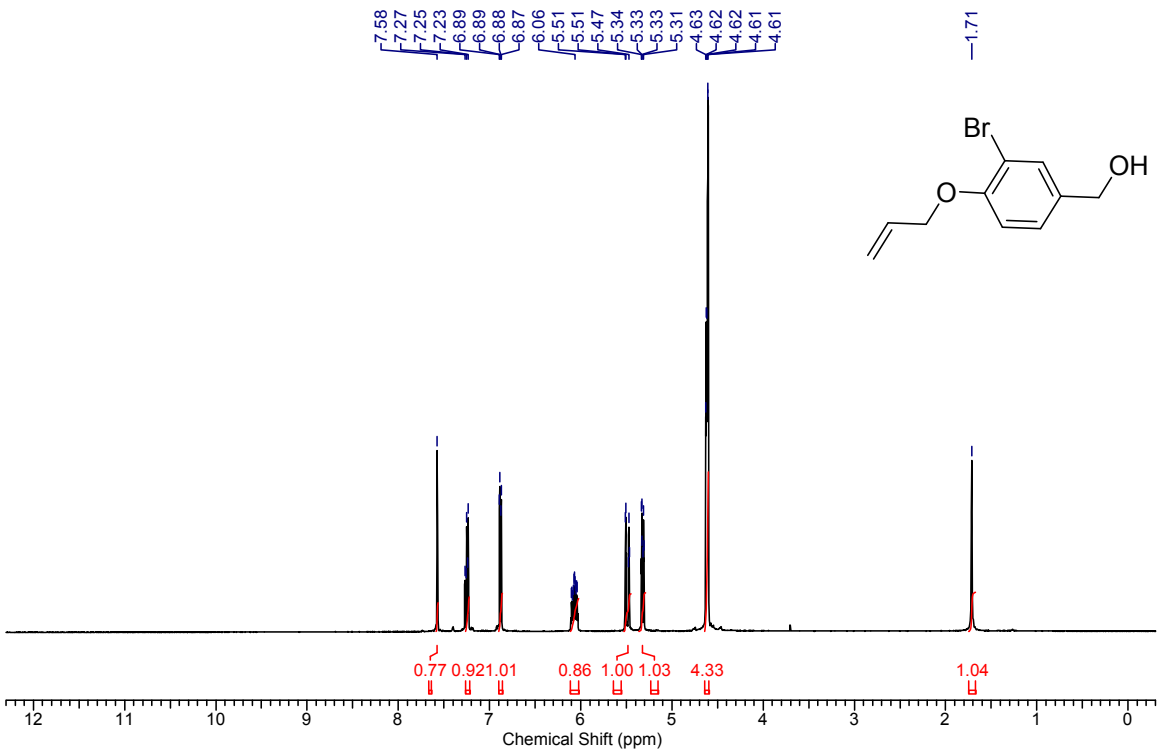

7.56
7.53
7.46
7.44
7.27
6.90
6.88
6.26
6.23
5.91
5.90
5.20
5.20
5.17
5.14
5.12
4.06
4.05
4.03
2.58
2.57
2.57
2.55
2.55
2.54
1.54
0.87
1.98
1.93
0.93
0.79
0.85
0.84
2.00
1.98
9.38
Chemical Shift (ppm)

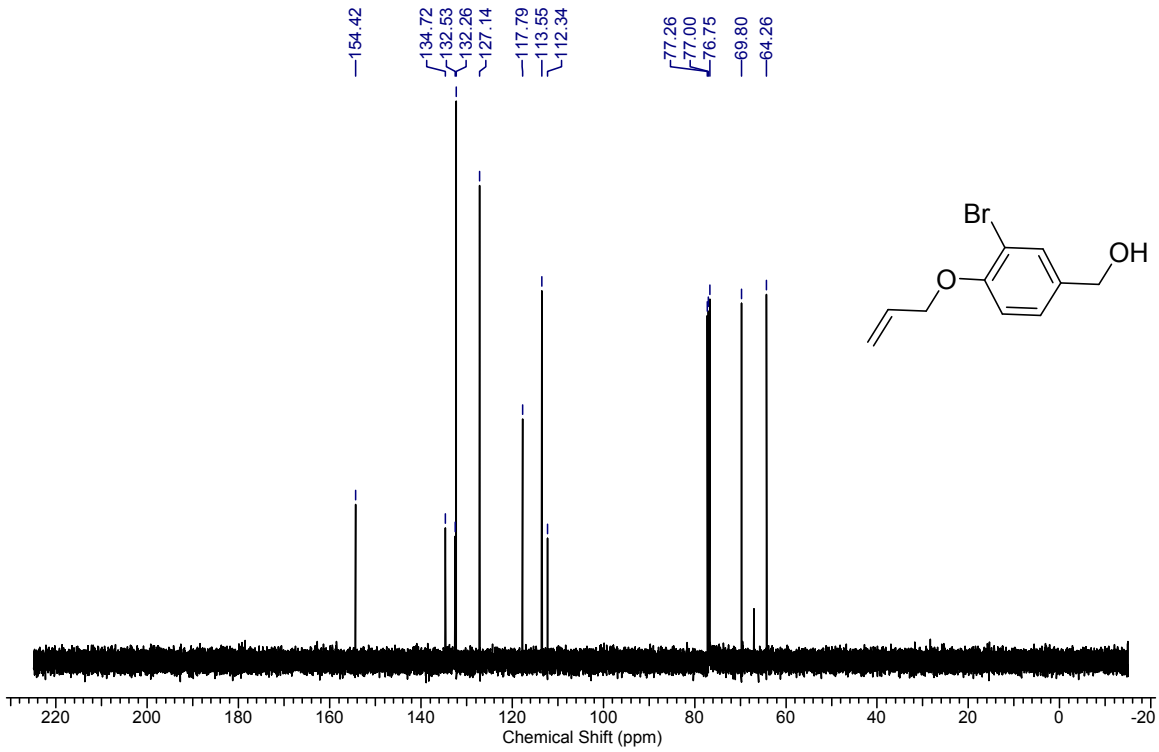

166.67
160.45
143.19
134.16
129.52
128.63
127.38
117.67
117.20
114.79
103.74
80.20
77.25
77.00
76.74
67.27
33.52
28.23
Chemical Shift (ppm)

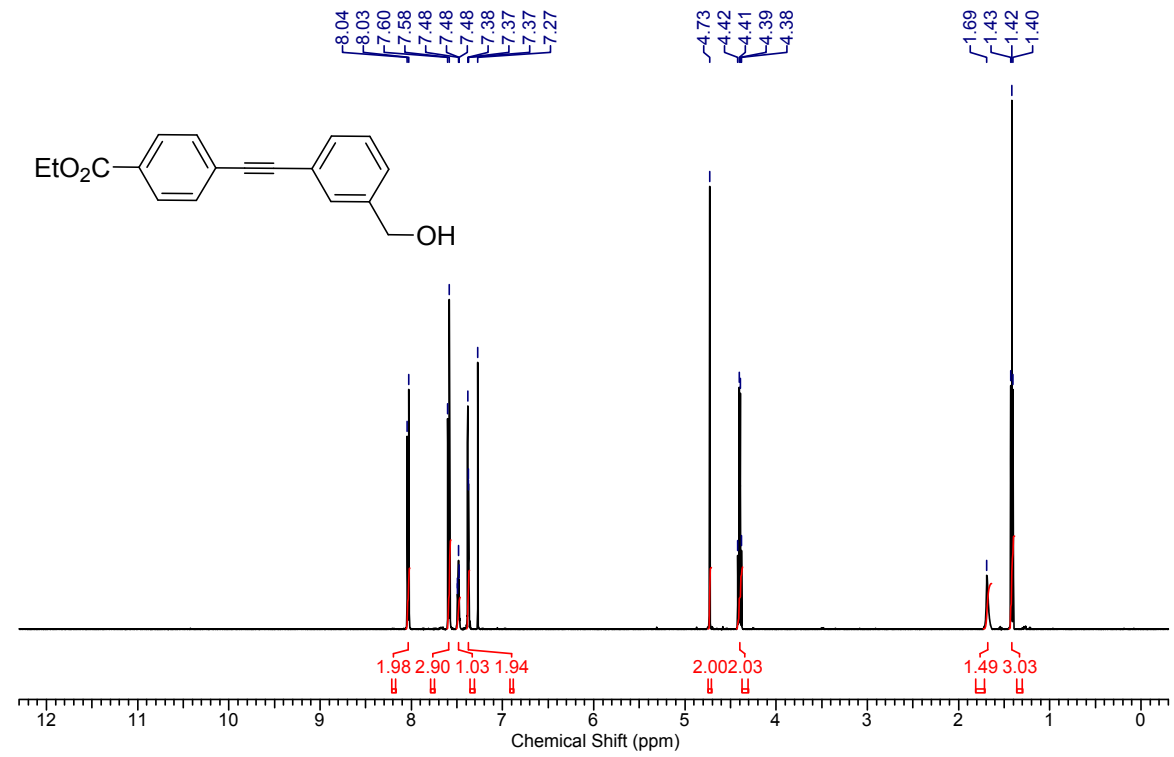
## XV. $^{1}H$ and $^{13}C$ NMR Spectra of Prepared Starting Materials

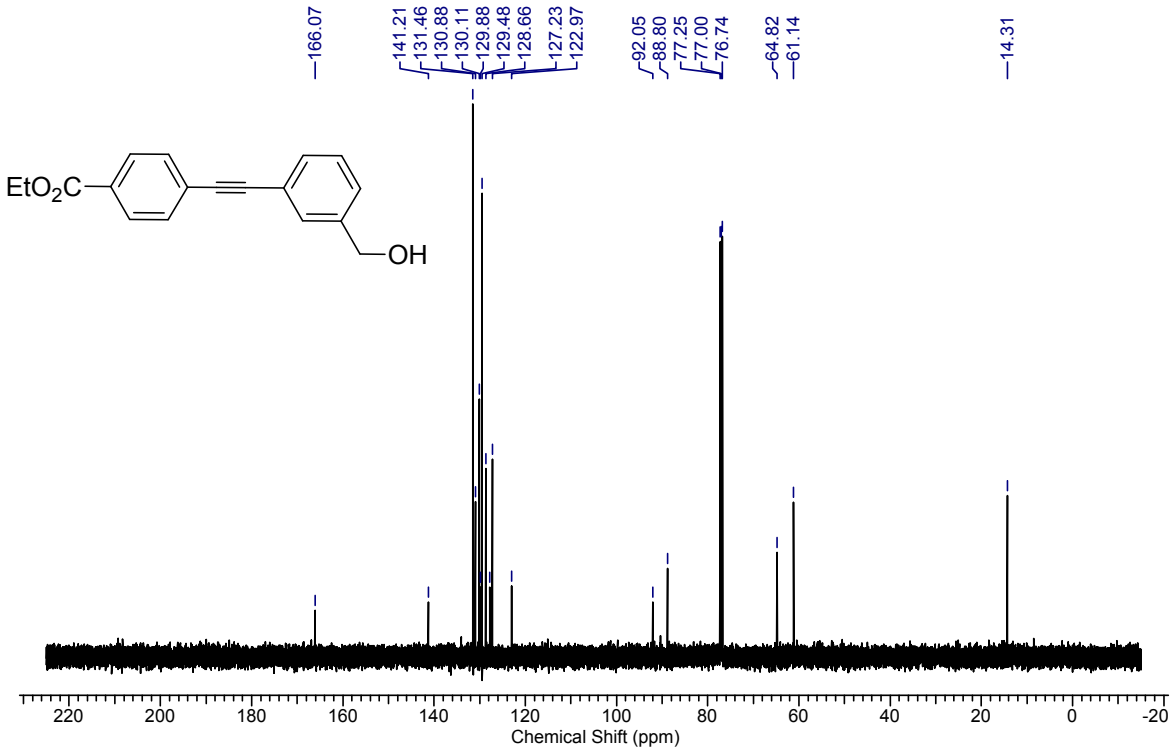


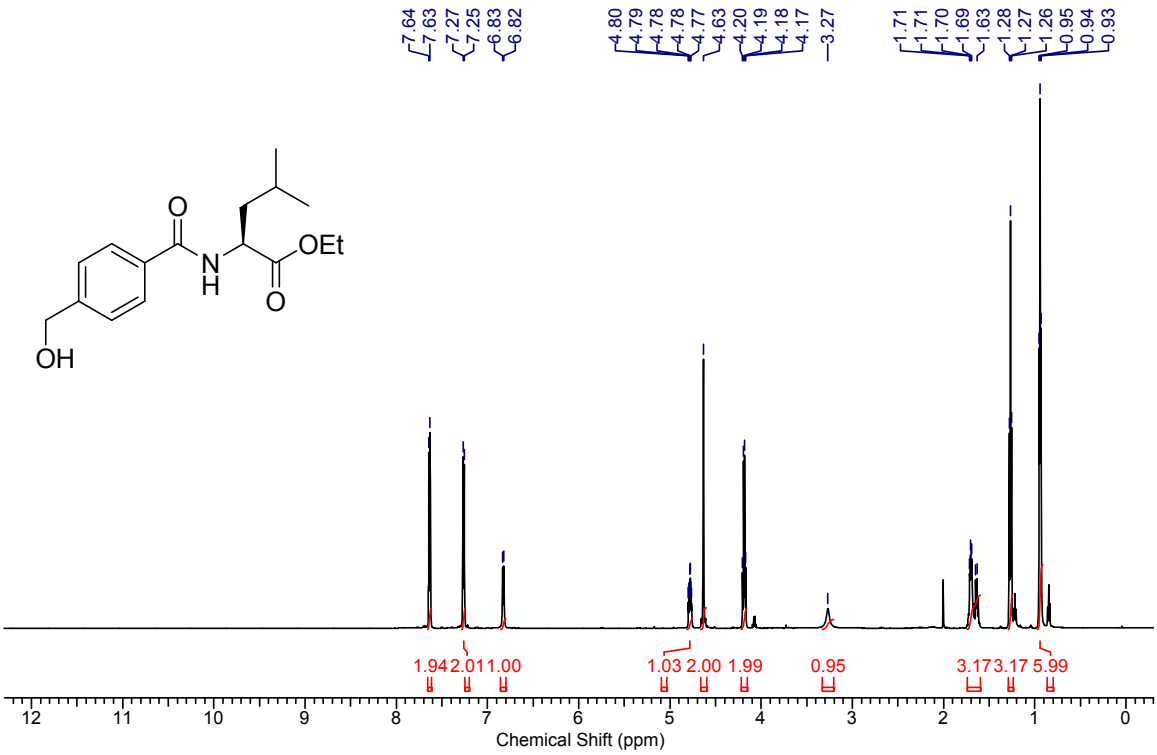



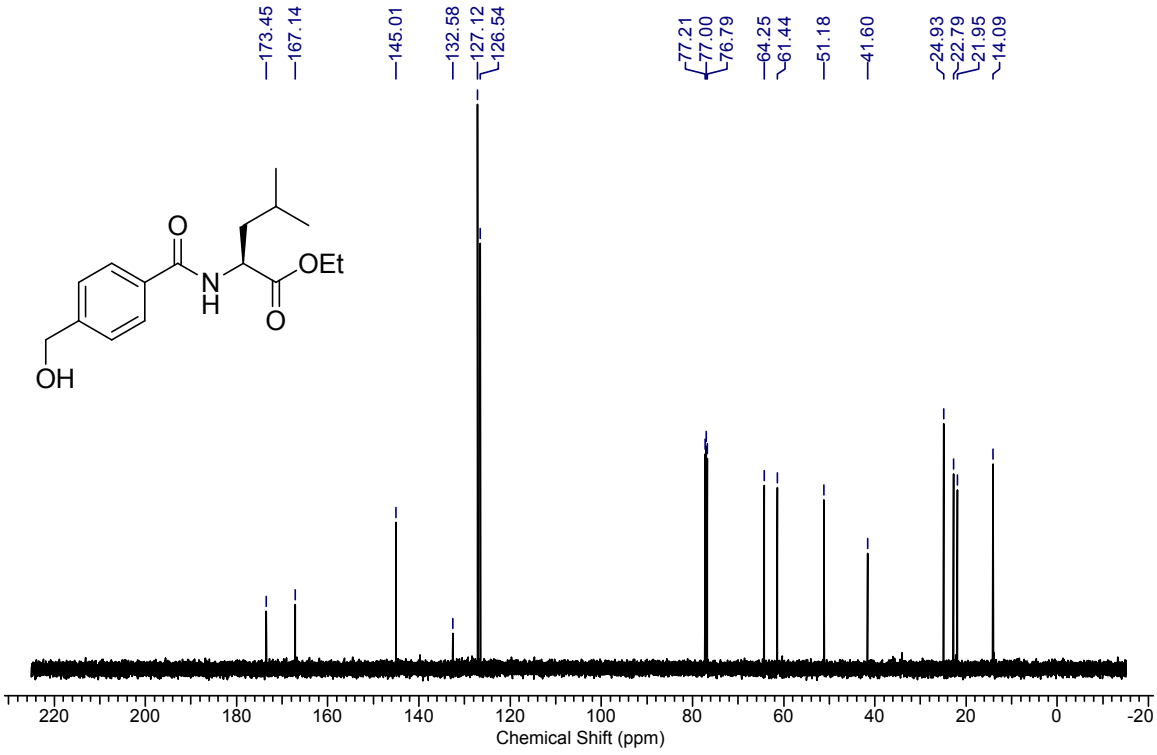

7.58
7.27
7.25
7.23
6.89
6.89
6.88
6.87
6.06
5.51
5.51
5.47
5.34
5.33
5.33
5.31
4.63
4.62
4.62
4.61
4.61
1.71
Br
OH
O
0.77
0.92
1.01
0.86
1.00
1.03
4.33
1.04
Chemical Shift (ppm)

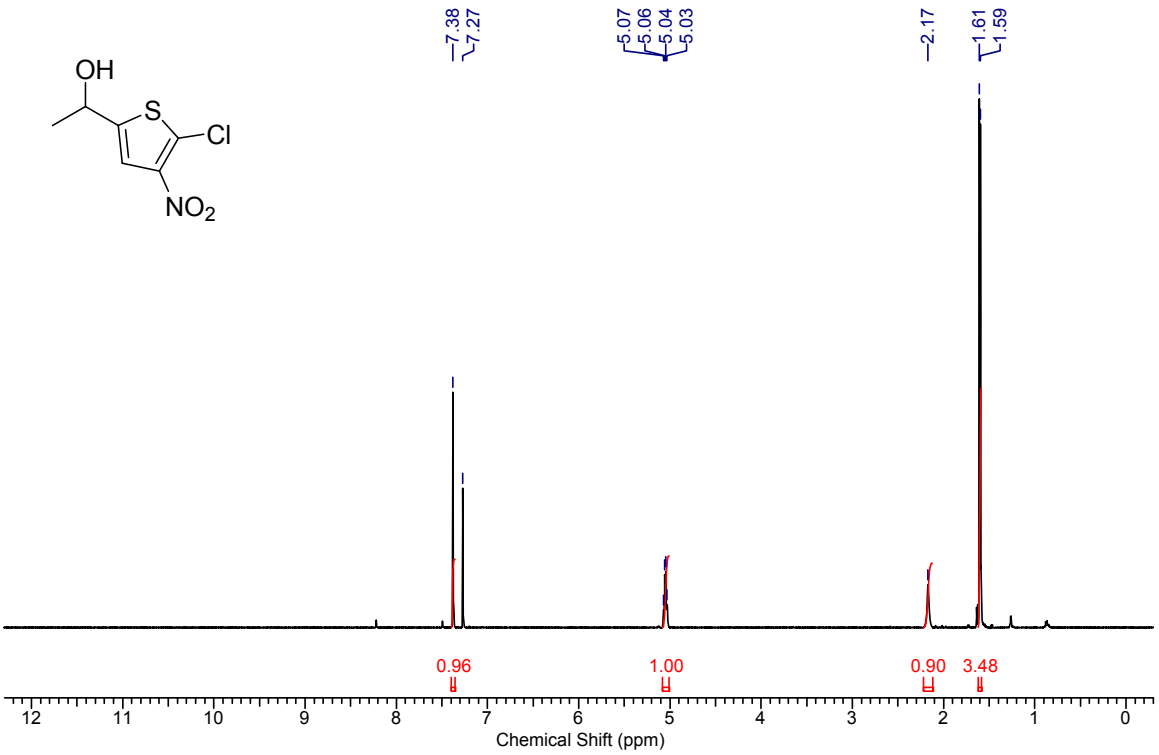

154.42
134.72
132.53
132.26
127.14
117.79
113.55
112.34
77.26
77.00
76.75
69.80
64.26
Br
OH
O
Chemical Shift (ppm)

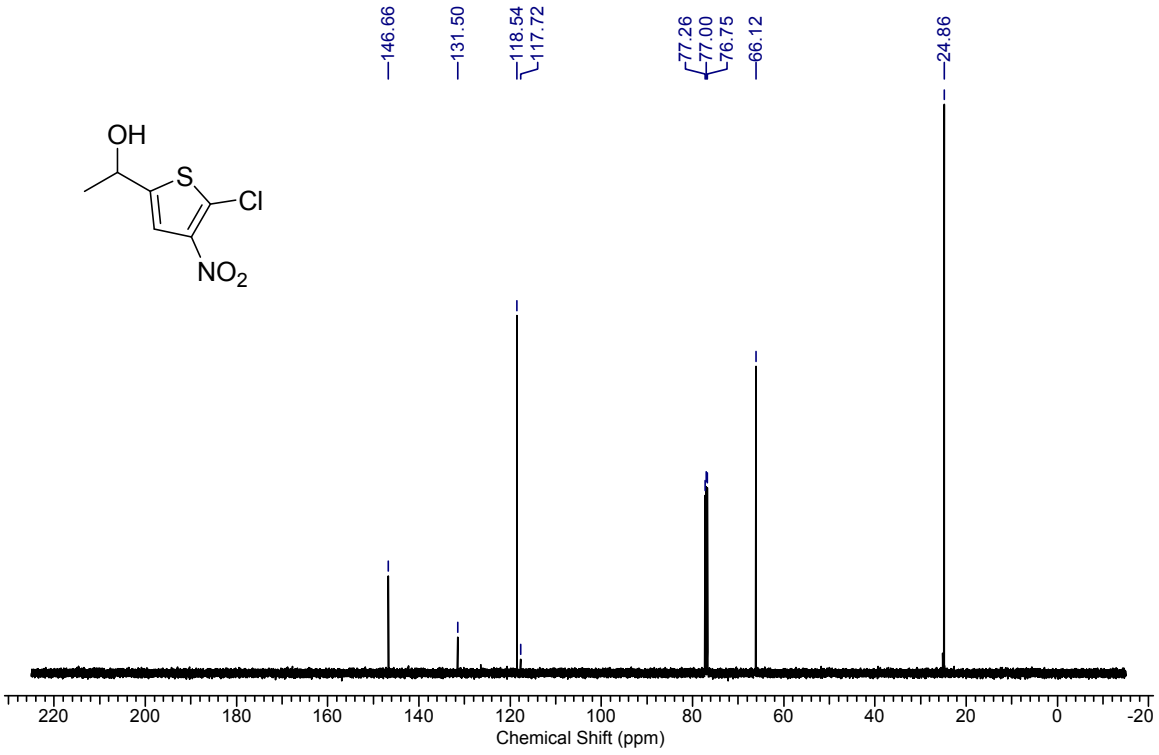

8.04
8.03
7.60
7.58
7.48
7.48
7.48
7.38
7.37
7.37
7.27
4.73
4.42
4.41
4.39
4.38
1.69
1.43
1.42
1.40
EtO2C
OH
1.98 2.90 1.03 1.94
2.00 2.03
1.49 3.03
Chemical Shift (ppm)

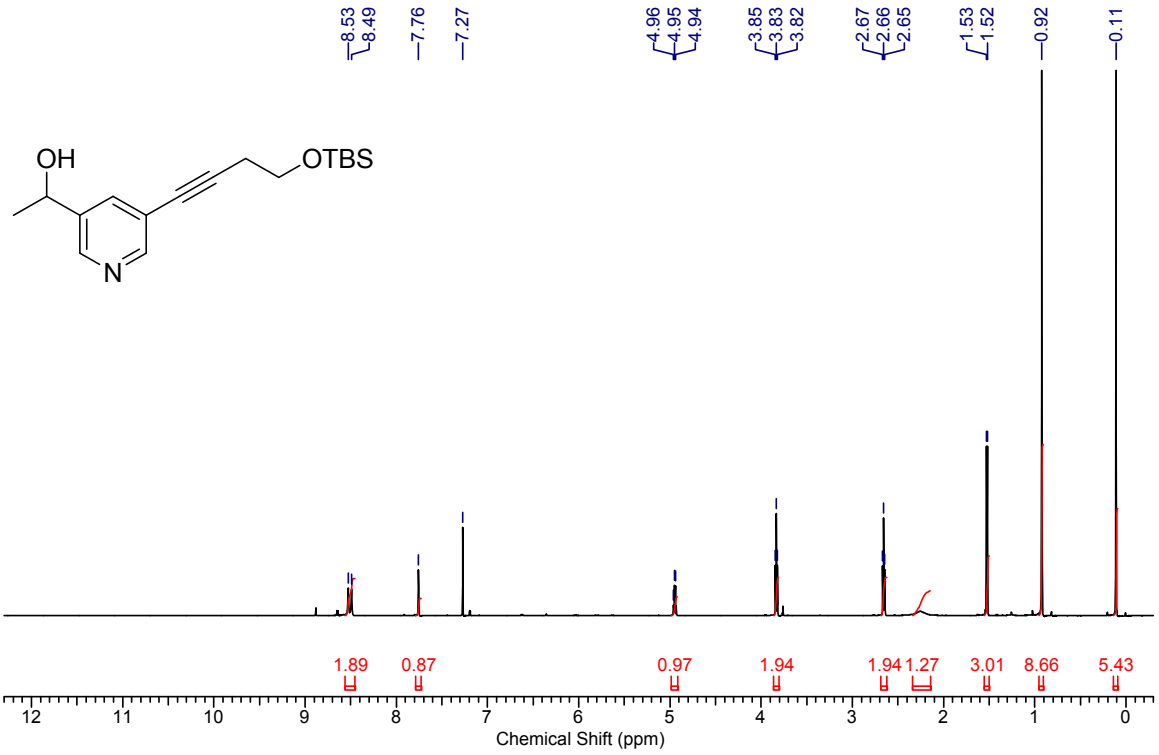

166.07
141.21
131.46
130.88
130.11
129.88
129.48
128.66
127.23
122.97
92.05
88.80
77.25
77.00
76.74
64.82
61.14
14.31
EtO2C
OH
Chemical Shift (ppm)

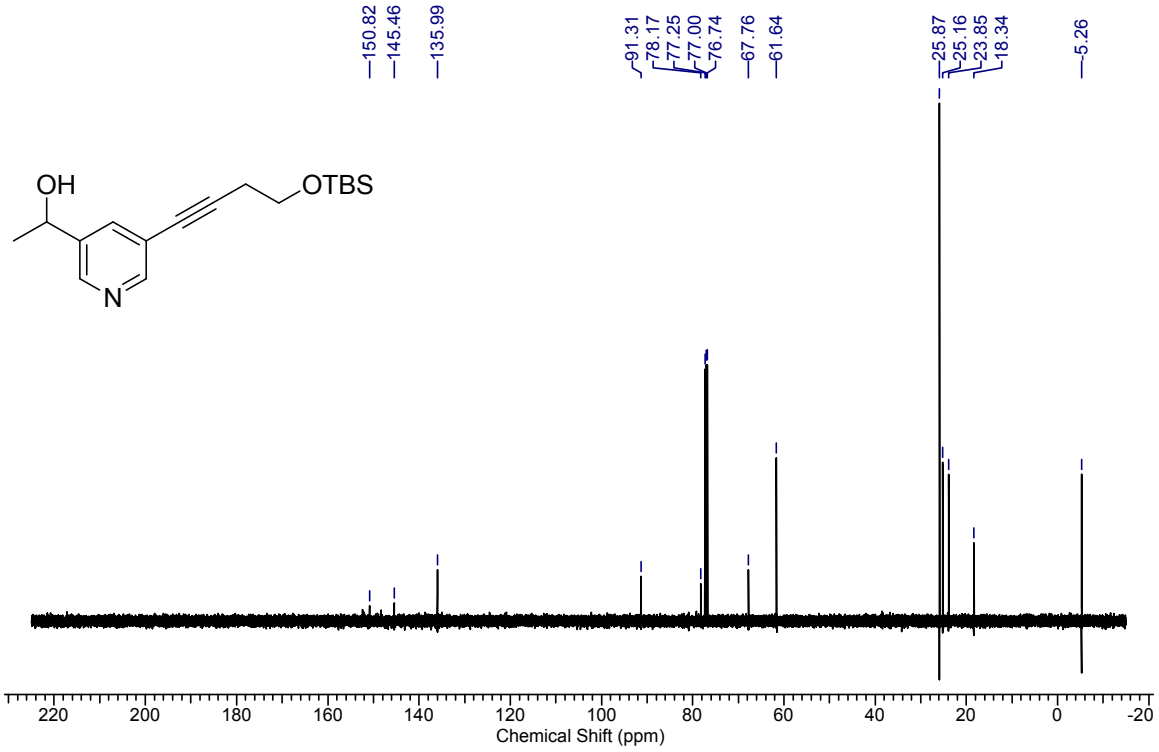

7.64
7.63
7.27
7.25
6.83
6.82
4.80
4.79
4.78
4.78
4.77
4.63
4.20
4.19
4.18
4.17
3.27
1.71
1.71
1.70
1.69
1.63
1.28
1.27
1.26
0.95
0.94
0.93
O
N
H
OEt
O
OH
1.94
2.01
1.00
1.03
2.00
1.99
0.95
3.17
3.17
5.99
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

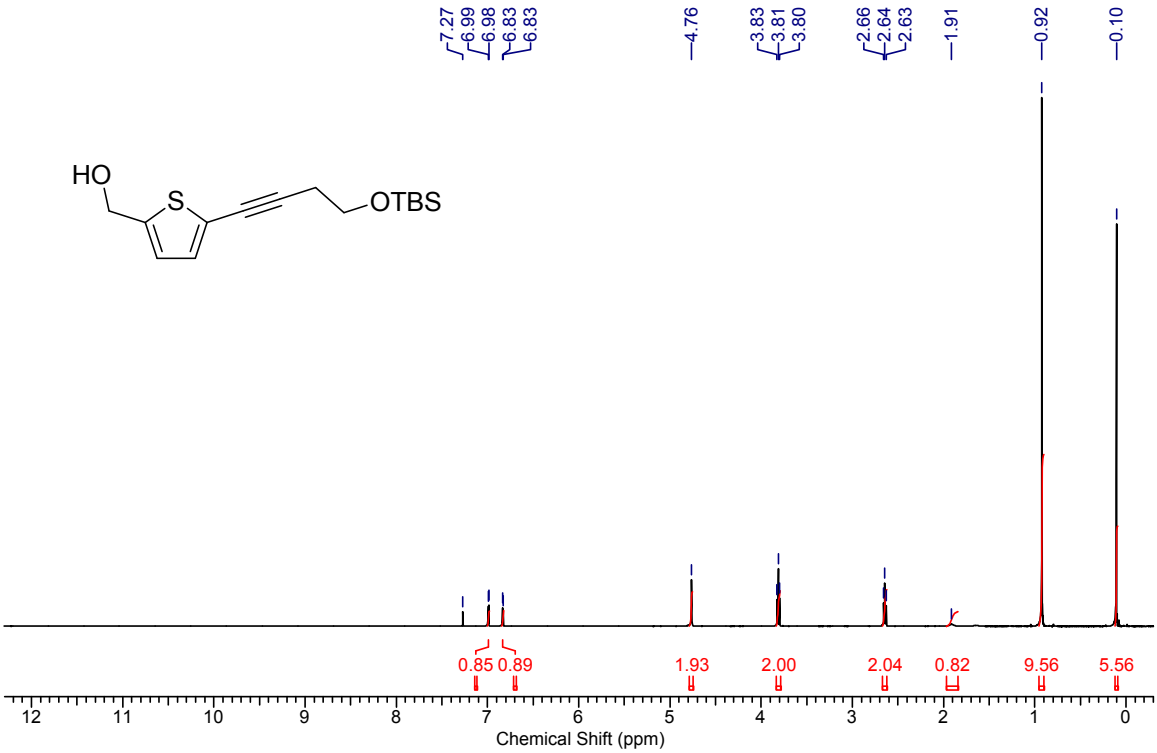

173.45
167.14
145.01
132.58
127.12
126.54
77.21
77.00
76.79
64.25
61.44
51.18
41.60
24.93
22.79
21.95
14.09
O
N
H
OEt
O
OH
220
200
180
160
140
120
100
80
60
40
20
0
-20
Chemical Shift (ppm)

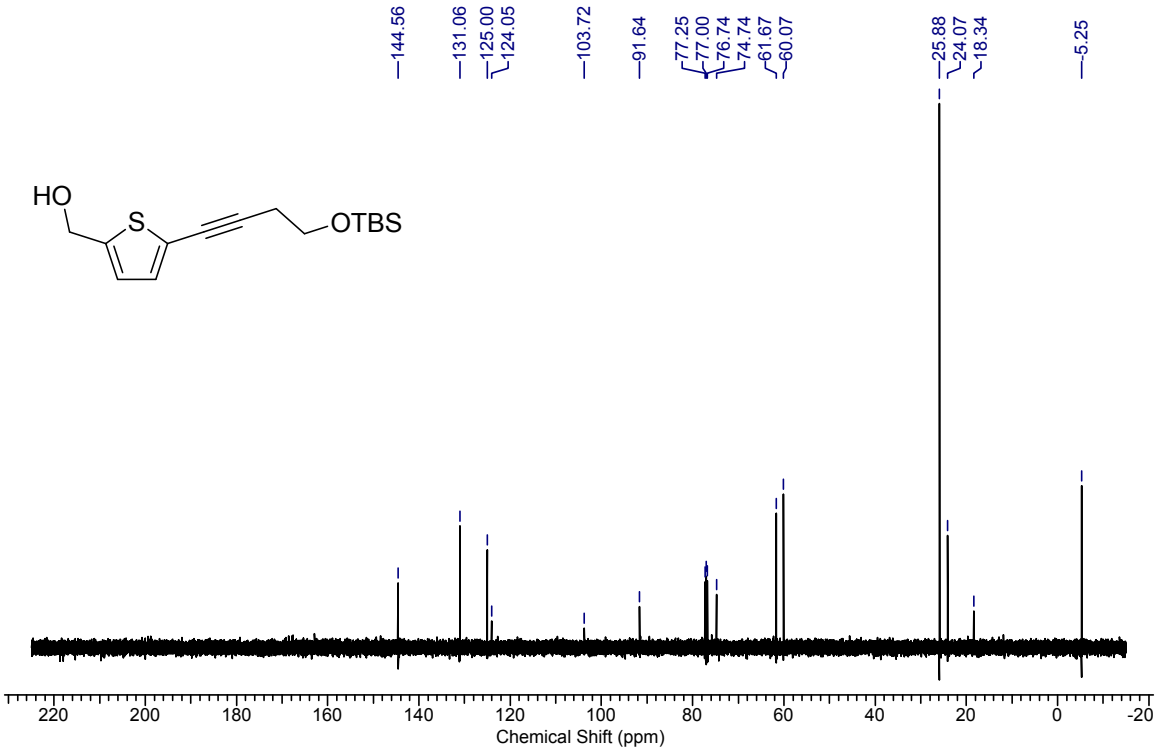

OH
S
Cl
NO2
7.38
7.27
5.07
5.06
5.04
5.03
2.17
1.61
1.59
0.96
1.00
0.90
3.48
Chemical Shift (ppm)

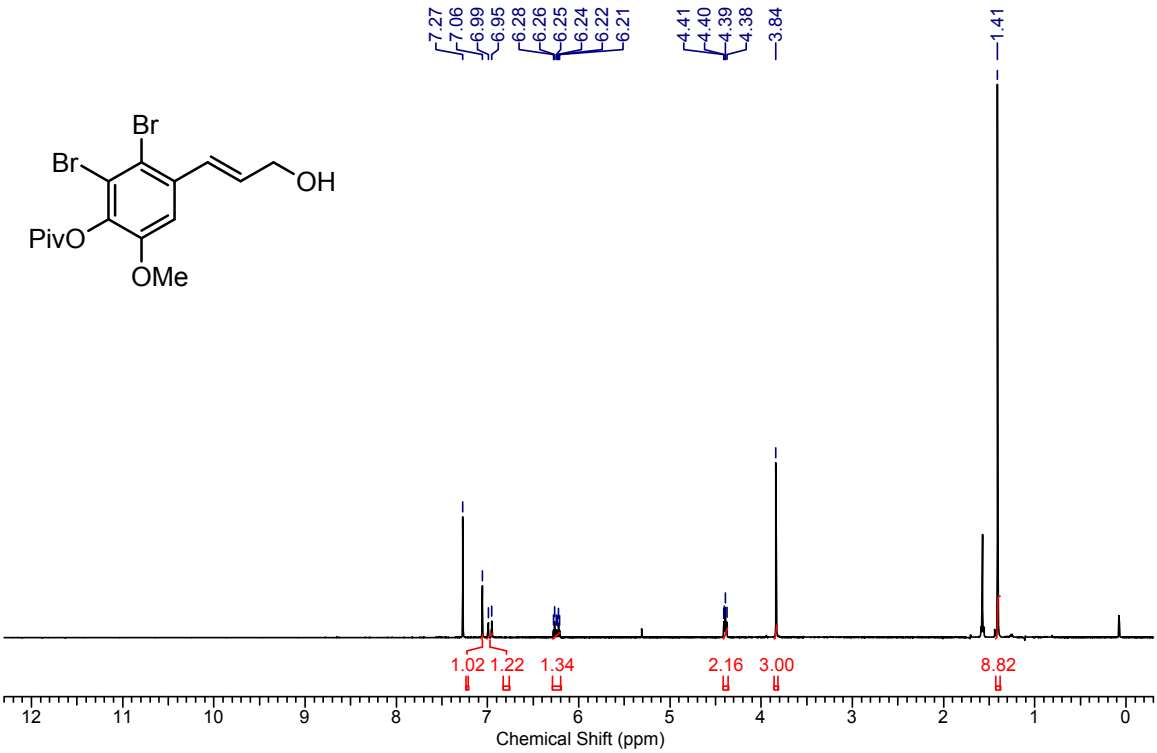

OH
S
Cl
NO2
146.66
131.50
118.54
117.72
77.26
77.00
76.75
66.12
24.86
Chemical Shift (ppm)


8.53
8.49
7.76
7.27
4.96
4.95
4.94
3.85
3.83
3.82
2.67
2.66
2.65
1.53
1.52
0.92
0.11
OH
OTBS
N
1.89
0.87
0.97
1.94
1.94
1.27
3.01
8.66
5.43
Chemical Shift (ppm)


150.82
145.46
135.99
91.31
78.17
77.25
77.00
76.74
67.76
61.64
25.87
25.16
23.85
18.34
5.26
OH
OTBS
N
Chemical Shift (ppm)


7.27
6.99
6.98
6.83
6.83
4.76
3.83
3.81
3.80
2.66
2.64
2.63
1.91
0.92
0.10
HO
S
OTBS
0.85
0.89
1.93
2.00
2.04
0.82
9.56
5.56
Chemical Shift (ppm)


144.56
131.06
125.00
124.05
103.72
91.64
77.25
77.00
76.74
74.74
61.67
60.07
25.88
24.07
18.34
5.25
HO
S
OTBS
Chemical Shift (ppm)


Br
Br
OH
PivO
OMe
7.27
7.06
6.99
6.95
6.28
6.26
6.25
6.24
6.22
6.21
4.41
4.40
4.39
4.38
3.84
1.41
1.02
1.22
1.34
2.16
3.00
8.82
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)