Electronic Supplementary Material (ESI) for Chemical Science.

Supporting Information

Flow Chemistry as a Discovery Tool to Access sp^2-sp^3 Cross-Coupling Reactions *via* Diazo Compounds

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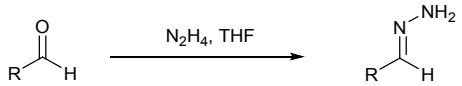
General experimental section. ^{1}H-NMR spectra were recorded on a Bruker Avance DPX-400 DRX-500 Cryo or DRX-600 spectrometer with the residual solvent peak as the internal reference ($CDCl_3$ = 7.26 ppm). ^{1}H resonances are reported to the nearest 0.01 ppm. ^{13}C-NMR spectra were recorded on the same spectrometers with the central resonance of the solvent peak as the internal reference ($CDCl_3$ = 77.16 ppm). All ^{13}C resonances are reported to the nearest 0.1 ppm. DEPT 135, COSY, HMQC, and HMBC experiments were used to aid structural determination and spectral assignment. The multiplicity of ^{1}H signals are indicated as: s = singlet, d = doublet, t = triplet, m = multiplet, br. = broad, or combinations of thereof. Coupling constants (*J*) are quoted in Hz and reported to the nearest 0.1 Hz. Where appropriate, averages of the signals from peaks displaying multiplicity were used to calculate the value of the coupling constant. Infrared spectra were recorded neat on a PerkinElmer Spectrum One FT-IR spectrometer using Universal ATR sampling accessories. Unless stated otherwise, reagents were obtained from commercial sources and used without purification. The removal of solvent under reduced pressure was carried out on a standard rotary evaporator. Data regarding high resolution mass spectrometry (HRMS) could not be collected due to the molecular structure; low resolution mass data are reported. Unless otherwise stated, all boronic acids are commercially available and were used as purchased without further purification. Unless otherwise stated, all the flow reactions were performed using a Uniqsis FlowSyn platform.[1] In-line IR spectroscopy was performed using the Mettler Toledo FlowIR® device.[2]

Preparation of hydrazones:



In a round-bottom flash containing 12 mL of N_2H_4 (1M in THF, 12 mmol), a solution of aldehyde (1M in THF, 10 mmol) was slowly added. The mixture was stirred for 30 min at room temperature. The mixture was evaporated under reduced pressure to give the desired hydrazone compound. Hydrazones were used without further purification for the generation of diazo compound.

General procedure for the generation of diazo compounds:

Conditioning phase: A solution of hydrazone (1 mmol, 0.1 M) and Hünig's base (2 equiv.) in CH_2Cl_2 (10 mL) was passed through the column reactor (Omnifit® column[3], 6.6 mm i.d. × 50 mm length), packed with activated MnO_2 (0.86 g),[4] at a flow rate of 0.5 mL min^{-1} for 20 min (*phase 1*) and the reactor output was monitored using a Flow-IR® device.[2] The flow was switched to solvent (Hünig base, 0.2 M in CH_2Cl_2) for 10 min (*phase 2*). The column was then ready for the generation of the diazo compound.

Generation phase: A solution of hydrazone (2 mmol, 0.1 M) and Hünig's base (2 equiv.) in CH_2Cl_2 (20 mL) was passed through a conditioned column reactor (Omnifit® column[3], 6.6 mm i.d. × 50 mm length)(*phase 3*). When the FlowIR® showed that the intensity of the diazo peak (region 2050-2100 $cm^{-1,}$ **Figure S1**) was stable (0.2 A.U.),[2] the reactor output was collected every 6 min (0.3 mmol) or 9 min (0.45 mmol, excess of diazo compound) in a vial containing the appropriate reagent (0.6 mmol of carboxylic acid or 0.3 mmol of boronic acid) equipped with a stirring bar. The mixture was stirred until the gas evolution ceased and the colour of diazo compound disappeared. The reaction mixture was diluted with EtOAc and washed with water. After evaporation of dried organic layer, the desired product was obtained. In few cases, purification over silica gel was necessary for analytically pure products.

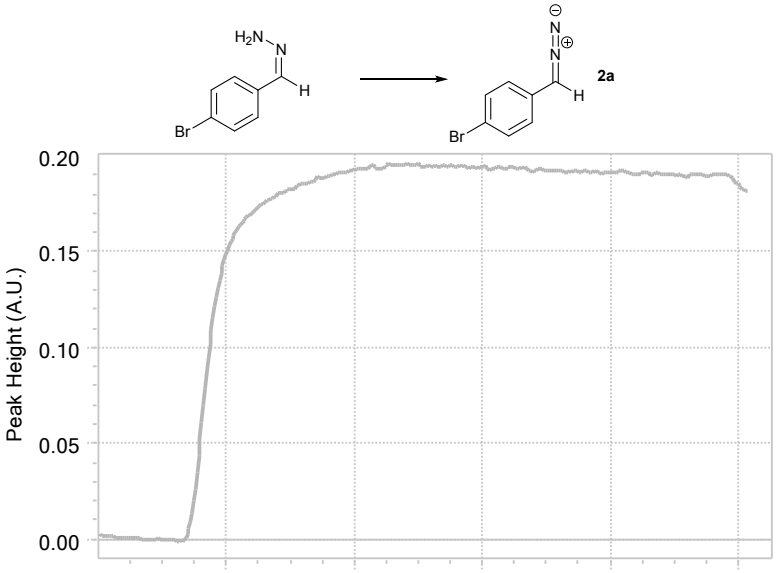


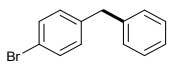
Figure S1. FlowIR® data (peak at 2069 cm^{-1}) for the generation of **2a**.

General procedure for the regeneration of spent MnO_2:

A solution of TBHP (12 mmol, 0.6 M) and Hünig base (2 equiv.) in CH_2Cl_2 (20 mL) was passed through a column reactor (Omnifit® column[3], 6.6 mm i.d. × 50 mm length) packed with the spent MnO_2 (0.86 g) at a flow rate of 0.5 mL min^{-1}. The column was then flushed with CH_2Cl_2 (10 mL) at a flow rate of 1.00 mL min^{-1}, before using it for the oxidation of the hydrazone. After each recycle stage, no conditioning phase was needed. *CAUTION: the oxidation process is highly exothermic!*

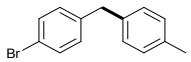
Characterisation data for compounds

1-benzyl-4-bromobenzene (8a)



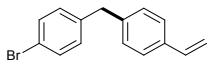
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.4 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.25 (d, *J* = 7.3 Hz, 1H), 7.19 (d, *J* = 7.3 Hz, 2H), 7.08 (d, *J* = 8.2 Hz, 2H), 3.95 (s, 2H) ppm; **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 140.6, 140.2, 131.6, 130.8, 129.0, 128.7, 126.4, 120.1, 41.4 ppm; spectra in agreement with reported literature: R. B. Bedford, M. A. Hall, G. R. Hodges, M. Huwe and M. C. Wilkinson *Chem. Commun.*, 2009, 6430–6432

1-bromo-4-(4-methylbenzyl)benzene (8b)



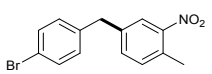
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.3 Hz, 2H), 7.11 (d, *J* = 8.1 Hz, 2H), 7.07 (d, *J* = 7.9 Hz, 2H), 3.90 (s, 2H), 2.33 (s, 3H) ppm; **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 140.5, 137.5, 136.0, 131.6, 130.7, 129.4, 128.9, 120.0, 41.0, 21.2 ppm; **MS:** (EI+) $C_{14}H_{13}Br^+$ (M^+) calc.: 260.0, det.: 260.1; **FT-IR:** film, $\tilde{\nu}$ (cm^{-1}) = 3022, 2919, 1513, 1486, 1433, 1403, 1110, 1069, 1010, 847.

1-bromo-4-(4-vinylbenzyl)benzene (8c)



^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 8.3 Hz, 2H), 6.71 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.73 (d, *J* = 17.6 Hz, 1H), 5.24 (d, *J* = 10.9 Hz, 1H), 3.93 (s, 2H) ppm; **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 140.2, 140.1, 136.6, 135.9, 131.7, 131.6, 130.7, 129.2, 126.5, 113.6, 41.1 ppm; **MS:** (EI+) $C_{15}H_{13}Br^+$ (M^+) calc.: 274.0, det.: 274.0; **FT-IR:** film, $\tilde{\nu}$ (cm^{-1}) = 2978, 2916, 1627, 1509, 1484, 1438, 1402, 1114, 1069, 1010, 992, 91, 864.

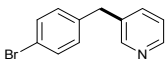
4-(4-bromobenzyl)-1-methyl-2-nitrobenzene (8d)



^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 1.7 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.28 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.25 (d, *J* = 8.1 Hz, 1H), 7.05 (d, *J* = 8.2 Hz, 2H), 3.96 (s, 2H), 2.56 (s, 3H) ppm; **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 149.4, 139.9, 138.7, 133.5, 133.1, 132.0, 131.7, 130.7, 124.8, 120.7, 40.5, 20.2 ppm; **MS:** (EI+) $C_{14}H_{12}BrNO_2^+$ (M^+) calc.:

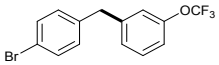
305.0, det.: 305.0. **FT-IR:** film, $\tilde{\nu}$ (cm^{-1}) = 2987, 2930, 1519, 1485, 1345, 1311, 1299, 1207, 1156, 1069, 1010, 904, 850.

3-(4-bromobenzyl)pyridine (8e)



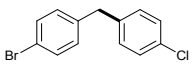
^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 2H, H_o), 7.44 – 7.41 (m, 3H, *H*), 7.21 (dd, 1H, , ^3J = 7.9, 4.8 Hz, $H_{m\text{-}pyr}$), 7.05 (d, 2H, , ^3J = 8.6 Hz, $H_{Ar\text{-}Br}$), 3.93 (s, 2H, CH_2) ppm; **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 150.0, 147.8, 138.7, 136.3, 135.9, 131.8, 128.6, 123.5, 120.4, 38.4. **HR-MS:** (ESI+) $C_{12}H_{11}NBr^+$ $(M+H)^+$ calc.: 248.0069, det.: 248.0061. **FT-IR:** film, $\tilde{\nu}$ (cm^{-1}) = 3028, 2927, 1734, 1575, 1487, 1423, 1404, 1239, 1070, 1044, 1011, 912, 845.

1-(4-bromobenzyl)-3-(trifluoromethoxy)benzene (8f)



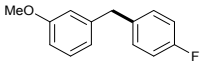
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.3 Hz, 2H), 7.31 (t, *J* = 7.9 Hz, 1H), 7.13 – 7.00 (m, 5H), 3.95 (s, 2H) ppm; **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 149.6, 142.9, 139.1, 131.9, 130.8, 130.0, 127.3, 121.5, 120.6 (q, *J* = 257 Hz), 120.5, 118.9, 41.1 ppm; **MS:** (EI+) $C_{14}H_{10}BrF_3O^+$ (M^+) calc.: 330.0, det.: 330.1; **FT-IR:** film, $\tilde{\nu}$ (cm^{-1}) = 2910, 1612, 1589, 1487, 1447, 1404, 1251, 1211, 1155, 1071, 1011, 973, 865.

1-bromo-4-(4-chlorobenzyl)benzene (8g)



^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.41 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.3 Hz, 2H), 7.09 (d, *J* = 8.3 Hz, 2H), 7.03 (d, *J* = 8.2 Hz, 2H), 3.90 (s, 2H) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 139.7, 139.0, 132.3, 131.8, 130.7, 130.3, 128.8, 120.3, 40.8 ppm; spectra in agreement with reported literature: G. Schfer and J. W. Bode, *Angew. Chem. Int. Ed.* 2011, **50**, 10913 –10916.

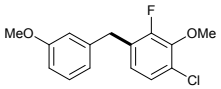
1-(4-fluorobenzyl)-3-methoxybenzene (8h)



^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.20 (t, 1H, ^3J = 7.7 Hz, H_{Ar}), 7.14 (m, 2H, H_{Ar}), 6.96 (t, 1H, ^3J = 8.4 Hz, H_{Ar}), 6.74 (m, 3H, H_{Ar}), 3.92 (s, 2H, CH_2), 3.77 (s, 3H, OCH_3) ppm; **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 178.0 (d, *J* = 26.4 Hz), 159.7,

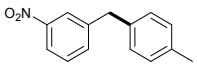
141.7 (d, *J* = 257 Hz), 136.6, 130.2 (d, *J* = 7.9 Hz), 129.5, 121.2, 115.2 (d, *J* = 21.5 Hz), 114.7, 111.3, 55.1, 41.1 ppm. **MS:** (EI+) $C_{14}H_{13}FO^+$ (M^+) calc.: 216.1, det.: 216.2. **FT-IR:** film, $\tilde{\nu}$ (cm^{-1}) = 2918, 1600, 1508, 1488, 1258, 1221, 1157, 1050.

1-chloro-3-fluoro-2-methoxy-4-(3-methoxybenzyl)benzene (8i)



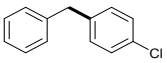
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.24 (t, 1H, ^3J = 7.9, H_o), 7.07 (dd, 1H, ^3J = 8.2, 1.7 Hz, H_p), 6.82 – 6.75 (m, 4H, H_{Ar}), 3.98 (d, 3H, ^5J = 1.2 Hz, OCH_3), 3.96 (s, 2H, CH_2), 3.80 (s, 3H, OCH_3) ppm; **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 159.8, 154.5 (d, *J* = 249 Hz), 144.3 (d, *J* = 13.7 Hz), 140.7, 129.6, 128.4 (d, *J* = 15.0 Hz), 126.2 (d, *J* = 3.4 Hz), 125.0 (d, *J* = 4.9 Hz), 124.8 (d, *J* = 4.0 Hz), 121.1, 114.7, 111.6, 61.5 (d, *J* = 4.5 Hz), 55.2, 34.5 (d, *J* = 3.1 Hz) ppm; **MS:** (EI+) $C_{15}H_{14}ClFO_2^+$ (M^+) calc.: 280.1, det.: 280.1. **FT-IR:** film, $\tilde{\nu}$ (cm^{-1}) = 2937, 2834, 1737, 1599, 1584, 1489, 1463, 1421, 1256, 1232, 1149, 1039, 891. The boronic acid ***4-chloro-2-fluoro-3-methoxyphenyl)boronic acid*** was obtained using a reported protocol.[5]

1-(4-methylbenzyl)-3-nitrobenzene (8j)



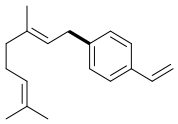
^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 8.05 (d, *J* = 3.1 Hz, 1H), 7.52 (dt, *J* = 7.6, 1.4 Hz, 1H), 7.48 – 7.40 (m, 1H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 4.05 (s, 2H), 2.34 (s, 3H) ppm; **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 148.5, 143.6, 136.4, 136.4, 135.1, 129.6, 129.4, 128.9, 123.7, 121.4, 41.2, 21.1 ppm; **MS:** (EI+) $C_{14}H_{13}NO_2^+$ $(M+H)^+$ calc.: 227.1, det.: 227.1; **FT-IR:** film, $\tilde{\nu}$ (cm^{-1}) = 3070, 2918, 1525, 1514, 1438, 1347, 1315, 1111, 1096, 1078, 909, 895.

1-benzyl-4-chlorobenzene (8k)



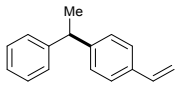
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.30-7.42 (m, 5H), 7.26 (d, 2H), 7.20 (d, *J* = 8.5 Hz, 2H), 4.03 (s, 2H) ppm. **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 140.7, 139.7, 132.0, 130.4, 129.0, 128.7, 126.4, 41.3 ppm; spectra in agreement with reported literature:: M. Amatorea and C. Gosmini *Chem. Commun.,* **2008**, 5019-5021.

(E)-1-(3,7-dimethylocta-2,6-dien-1-yl)-4-vinylbenzene (8l)



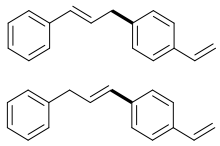
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.34 (d, 2H, ^{3}J = 7.9 Hz, H_o), 7.16 (d, 2H, ^{3}J = 7.9 Hz, H_o), 6.71 (dd, 1H, ^{3}J = 17.6, 10.8 Hz, $H_{vinylic}$), 5.71 (d, 1H, ^{3}J = 17.6 Hz, $H_{vinylic}$), 5.35 (m, 1H, $H_{vinylic\ geranyl}$), 5.20 (d, 1H, ^{3}J = 10.8 Hz, $H_{vinylic}$), 5.12 (m, 1H, $H_{vinylic\ geranyl}$), 3.76 (d, 2H, J = 7.3 Hz, $CH_{2\ benzylic}$),2.13 (m, 2H, $H_{allylic}$), 2.07 (m, 2H, H $_{allylic}$), 1.72 (s, 3H, CH_3), 1.71 (s, 3H, CH_3), 1.61 (s, 3H, CH_3) ppm; **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 141.5, 136.7, 136.3, 135.1, 131.5, 128.5, 128.5, 126.2, 126.2, 124.2, 122.8, 112.9, 39.7, 33.9, 26.6, 25.7, 17.7, 16.1 ppm; **MS:** (EI+) $C_{18}H_{24}^{+}$ (M^{+}) calc.: 240.2, unable to measure; **FT-IR:** film, $\tilde{\nu}$ (cm^{-1}) = 2974, 1698, 1380, 1290, 1073.

1-(1-phenylethyl)-4-vinylbenzene (8m)



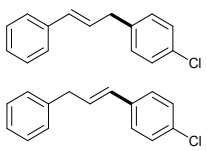
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.36 (d, 2H, ^{3}J = 8.0 Hz, H_o), 7.31 (t, 2H, ^{3}J = 8.1 Hz, H_m), 7.23 (d, 2H, ^{3}J = 8.0 Hz, H_m), 7.23 – 7.20 (m, 3H, H_{Ph}), 6.72 (dd, 1H, ^{3}J = 17.4, 10.8 Hz, $H_{vinylic}$), 5.72 (dd, 1H, J = 17.6, 0.75 Hz, $H_{vinylic}$), 5.23 (dd, 1H, ^{3}J = 10.8, 0.75 Hz, $H_{vinylic}$), 4.17 (q, 1H, ^{3}J = 7.2 Hz, CH_{sp3}), 1.67 (d, 3H, ^{3}J = 7.2 Hz, CH_3) ppm**^{13}C-NMR** (100 MHz, $CDCl_3$) δ 146.2, 146.1, 136.6, 135.5, 128.4, 127.8, 127.6, 126.2, 126.1, 113.2, 44.5, 21.8 ppm; **MS:** (EI+) $C_{16}H_{16}^{+}$ (M^{+}) calc.: 208.1, det.: 208.1; **FT-IR:** film, $\tilde{\nu}$ (cm^{-1}) = 3083, 3025, 2966, 2930, 1629, 1509, 1492, 1450, 1372, 1028, 1015, 988, 903, 840.

Mixture of ***1-cinnamyl-4-vinylbenzene*** and ***(E)-1-(3-phenylprop-1-en-1-yl)-4-vinylbenzene (8n, 8n')***



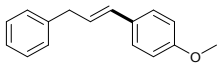
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.15 (m, 9H, H_{Ar}), 6.80 – 6.65 (m, 1H, CH_{vinyl}), 6.50 – 6.30 (m, 2H, $CH_{2\ vinyl}$), 5.75 (d, 1H, J = 17.7 Hz, H_{vinyl}), 5.24 (d, 1H, J = 10.8 Hz, H_{vinyl}) 3.58 (d, J = 6.4 Hz, $CH_{2\ maj}$), 3.52 (d, J = 6.3 Hz, $CH_{2\ min}$) ppm; **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 140.1, 139.8, 137.5, 137.1, 136.6, 136.5, 136.4, 135.7, 131.2, 130.7, 129.3, 129.1, 128.9, 128.7, 128.5, 127.1, 126.4, 126.4, 126.3, 126.2, 126.1, 39.4 (maj), 39.1 (min) ppm; **MS:** (EI+) $C_{17}H_{16}^{+}$ $(M^{+})^{+}$ calc.: 220.1, det.: 220.2. **FT-IR:** film, $\tilde{\nu}$ (cm^{-1}) = 3025, 2918, 2850, 1698, 1602, 1495, 1452, 1269, 1207, 1167, 1072, 1015, 966.

Mixture of ***1-chloro-4-cinnamylbenzene*** and ***(E)-1-chloro-4-(3-phenylprop-1-en-1-yl)benzene(8o, 8o')***



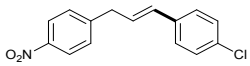
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.15 (m, 9H, H_{Ar}), 6.50 – 6.25 (m, 2H, H_{vinyl}), 3.55 (d, J = 6.1 Hz, $CH_{2\ maj}$), 3.52 (d, J = 6.8 Hz, $CH_{2\ min}$) ppm;. **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 139.9, 138.6, 137.3, 136.0, 132.7, 131.5, 130.0, 130.0, 129.9, 128.7, 128.6, 128.6, 128.5, 127.3, 127.3, 126.3, 126.1, 39.3 (maj), 38.6 (min) ppm; **MS:** (EI+) $C_{15}H_{13}Cl^{+}$ (M^{+}) calc.: 228.1, det.: 228.1. **FT-IR:** film, $\tilde{\nu}$ (cm^{-1}) = 3026, 2923, 1490, 1451, 1429, 1404, 1091, 1012, 964, 824.

(E)-1-methoxy-4-(3-phenylprop-1-en-1-yl)benzene (8p')



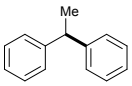
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.3 – 7.15 (m, 7H, H_{Ar}), 6.87 (d, 2H,z ^{3}J = 8.9 Hz, H_o), 6.43 (d, 1H, ^{3}J = 15.2 Hz, CH_{sp2}), 6.24 (dt, 1H, ^{3}J = 15.7, 6.9 Hz, CH_{sp2}), 3.82 (s, 3H, OCH_3), 3.55 (d, 2H, ^{3}J = 6.9 Hz, CH_2) ppm; **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 158.9, 140.5, 130.5, 130.3, 128.7, 128.5, 127.2, 127.1, 126.1, 113.9, 55.3, 39.3 ppm; spectra in agreement with reported literature: J. Barluenga, L. Florentino , F. Aznar and C. Valdés *Org. Lett*., 2011, **13** (3), 510–513.

(E)-1-chloro-4-(3-(4-nitrophenyl)prop-1-en-1-yl)benzene (8q')



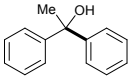
^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.17 (d, 2H, ^{3}J = 8.6 Hz, H_{ArNO2}), 7.39 (d, 2H, ^{3}J = 8.6 Hz, H_{ArNO2}), 7.28 (s, 4H, H_{ArCl}), 6.44 (d, 1H, ^{3}J = 15.6 Hz, H_{sp2}), 6.29 (dt, 1H, ^{3}J = 15.6, 6.8 Hz, H_{sp2}), 3.65 (d, 2H, ^{3}J = 6.8 Hz, CH_2) ppm; **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 147.6, 146.7, 135.4, 133.2, 131.3, 129.4, 128.8, 127.7, 127.4, 123.8, 39.0 ppm; **MS:** (EI+) $C_{15}H_{12}ClNO_2^{+}$ $(M+H)^{+}$ calc.: 273.1, det.: 273.1. **FT-IR:** film, $\tilde{\nu}$ (cm^{-1}) = 2916, 2853, 1594, 1513, 1489, 1341, 1108, 1086, 1010, 970, 848, 833, 822.

ethane-1,1-diyldibenzene (8s)



^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.30 (t, 4H, ^{3}J = 7.3 Hz, H_m), 7.24 (d, 4H, ^{3}J = 7.1 Hz, H_o), 7.20 (t, 2H, ^{3}J = 7.4 Hz, H_p), 4.17 (q, 1H, ^{3}J = 7.3 Hz, CH_{sp3}), 1.66 (d, 3H, ^{3}J = 7.3 Hz, CH_3) ppm; **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 146.4, 128.3, 127.6, 126.0, 44.8, 21.9 ppm; spectra in agreement with reported literature: S. Sawadjoon, A. Lundstedt, and J. S. M. Samec, *ACS Catal.* **2013**, 3, 635−642.

1,1-diphenylethan-1-ol (11)

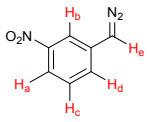


^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.44 (d, 4H, ^{3}J = 7.1 Hz, H_o), 7.34 (t, 4H, ^{3}J = 7.5 Hz, H_m), 7.26 (m, 2H, H_p), 2.20 (s, 1H, OH), 1.98 (s, 3H, CH_3) ppm; **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 148.0, 128.2, 127.0, 125.8, 76.2, 30.9 ppm; spectra in agreement with reported literature: H. Zong, H. Huang, J. Liu, G. Bian, and L. Song, *J. Org. Chem.* **2012**, 77, 4645−4652.

NMR studies

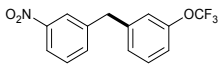
The diazo compound **2b** was prepared using a solution of the corresponding hydrazone in CD_2Cl_2 (0.1 M) with in the presence of Hünig's (2 equiv). A sample of the solution was analysed in an NMR tube (0.7 mL), after addition of a solution of boronic acid (0.35 mL, 0.2 M in CD_2Cl_2). The analysis was carried out for 13 h and data were collected every 10 minutes.

1-(diazomethyl)-3-nitrobenzene (2b)



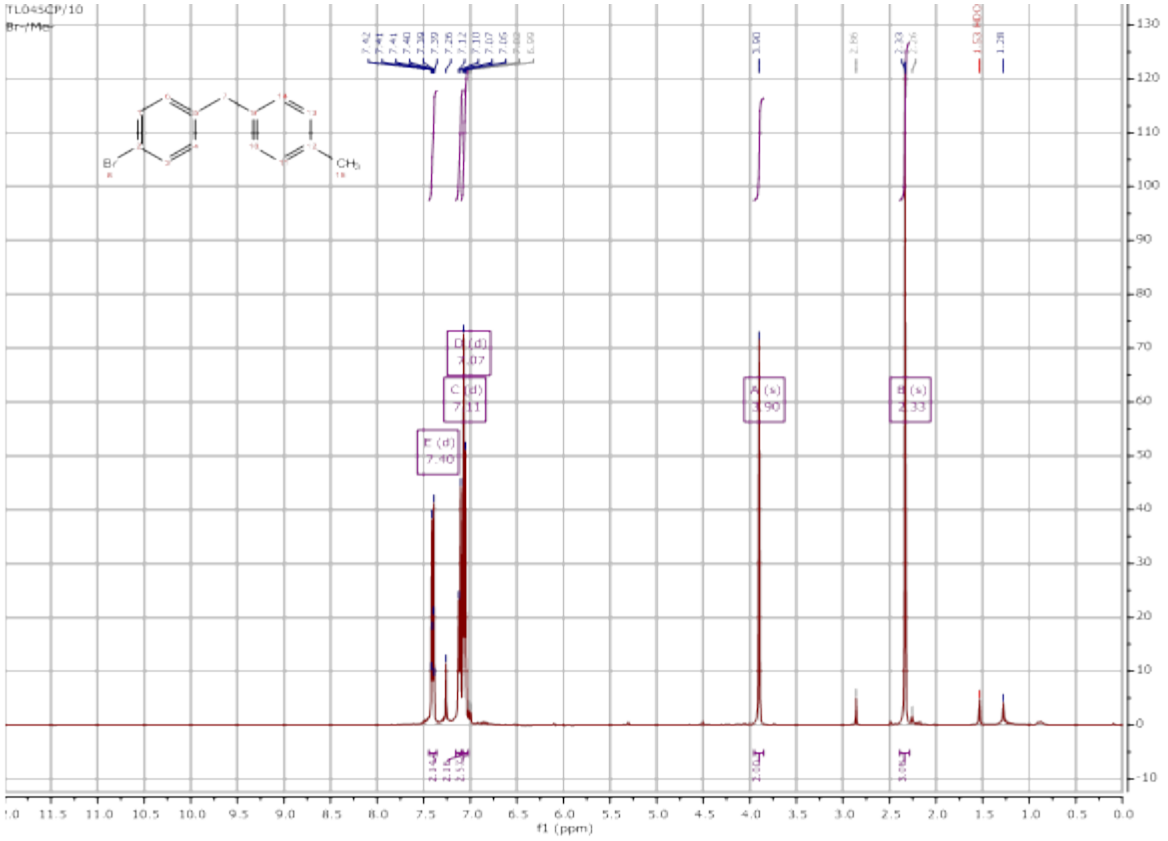
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, J = 8.4, 1.8 Hz, H_a), 7.76 (t, J = 2.3 Hz, H_b), 7.46 (t, J = 8.0 Hz, H_c), 7.23 (d, J = 8.4 Hz, H_d), 5.16 (s, H_e) ppm; **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 149.1, 133.1, 129.8, 126.5, 118.2, 115.4, 63.4 ppm.

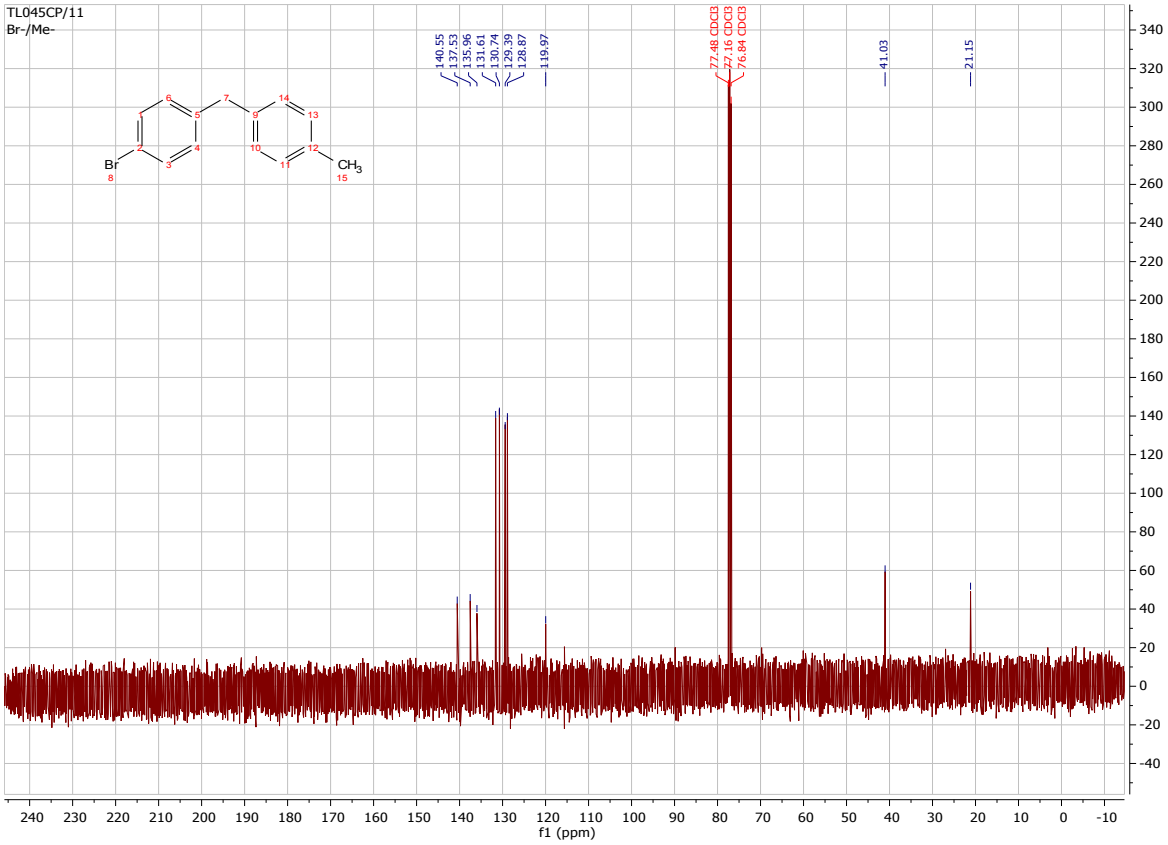
1-nitro-3-(3-(trifluoromethoxy)benzyl)benzene (8r)

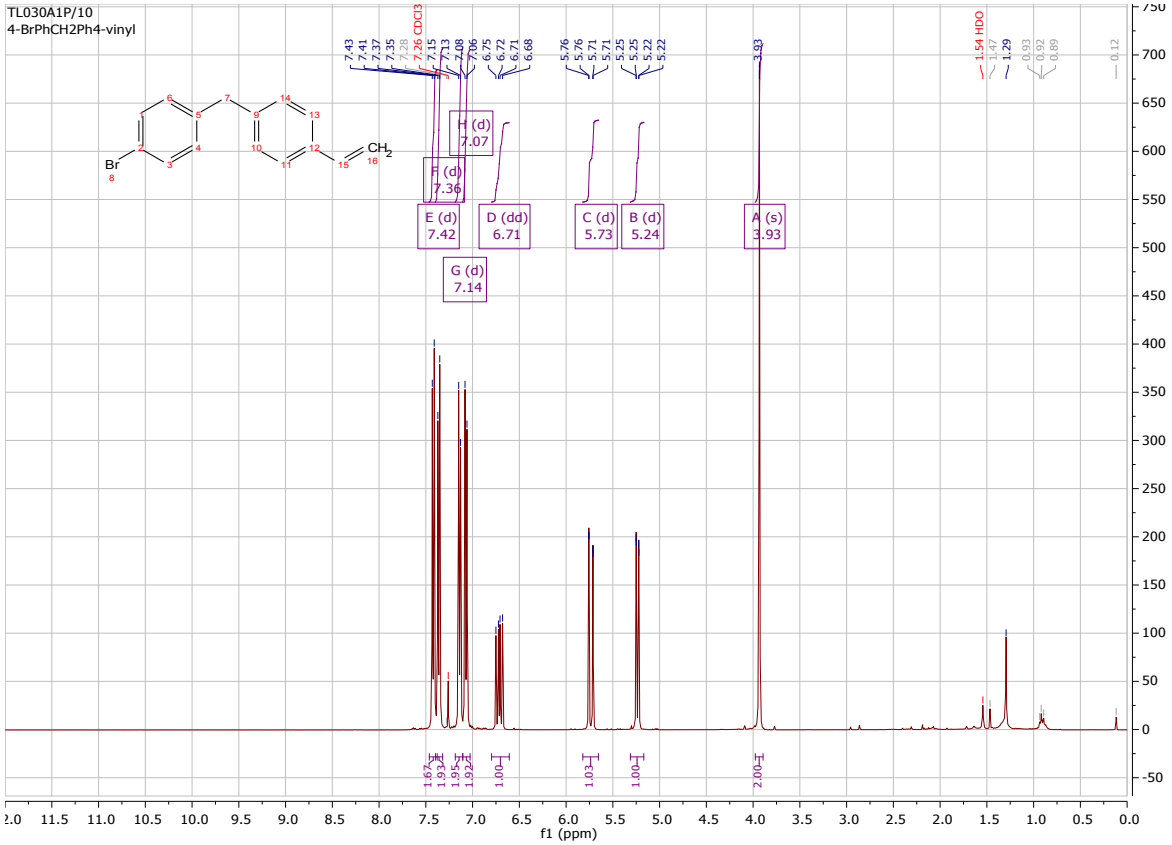


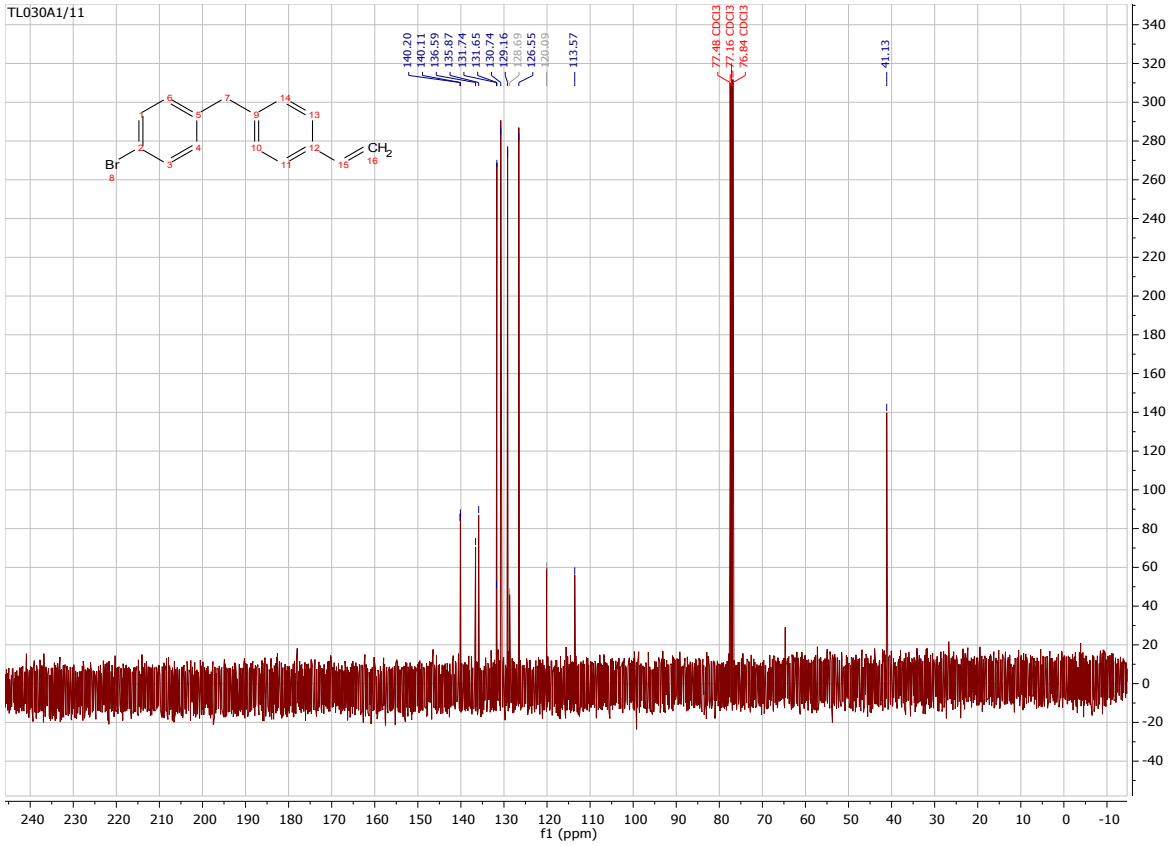
^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.12 (dt, 1H, J = 7.8, 1.8 Hz, H_{ArNO2}), 8.08 (s, 1H, H_{ArNO2}), 7.53 – 7.48 (m, 2H, H_{Ar}), 7.36 (t, 1H, J = 8.5 Hz, H_{ArOCF3}), 7.13 (d, 1H, J = 7.7 Hz, H_{Ar}), 7.05 (s, 1H, H_{ArOCF3}), 4.12 (s, 2H, CH_2) ppm; **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 149.6 (q, J = 1.95 Hz), 148.5, 142.1, 141.6, 135.0, 130.1, 129.6, 127.2, 123.7, 121.7, 121.4, 120.5 (q, J = 257 Hz), 119.1, 41.1 ppm; **MS:** (EI+) $C_{14}H_{10}F_3NO_3^+$ (M^+) calc.: 297.1, det.: 297.1. **IR:** film, $\tilde{\nu}$ (cm^{-1}) = 3068, 1610, 1589, 1529, 1489, 1448, 1349, 1252, 1213, 1159, 1097, 1003, 862, 804.

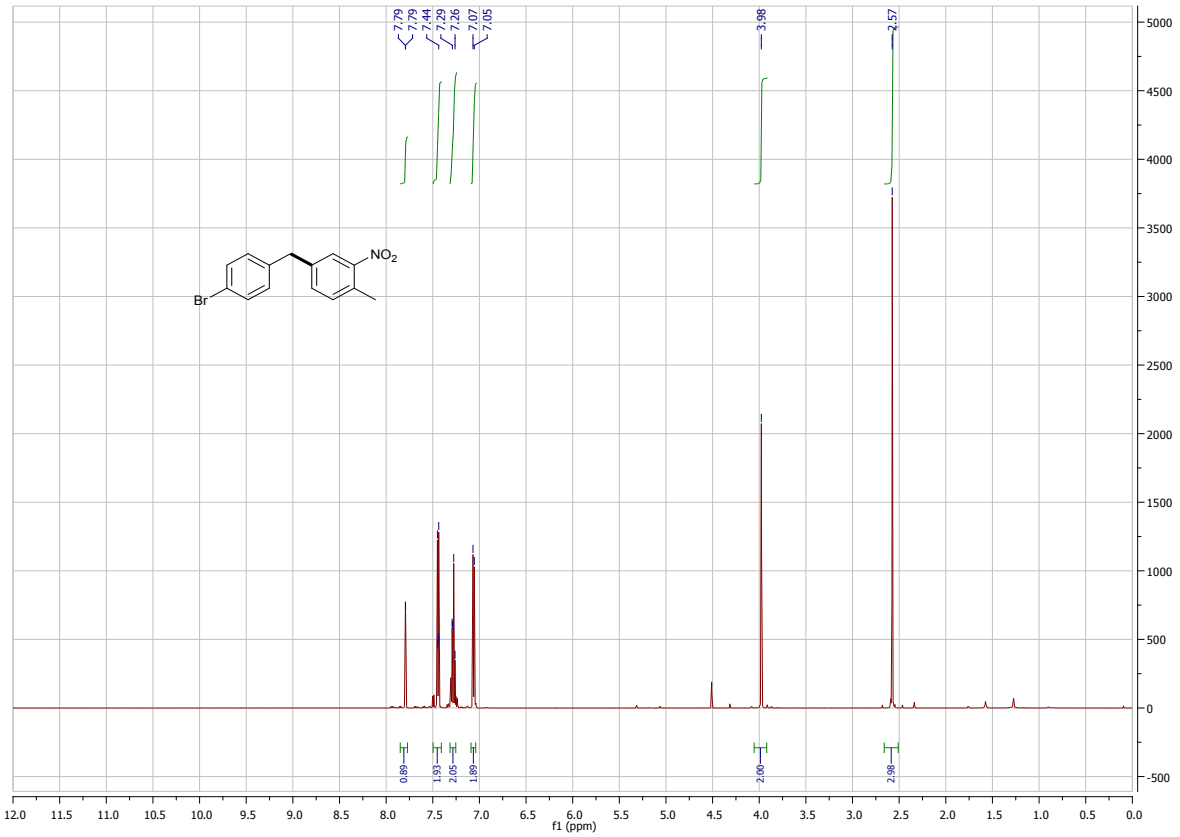
^{1}H-NMR and ^{13}C-NMR spectra

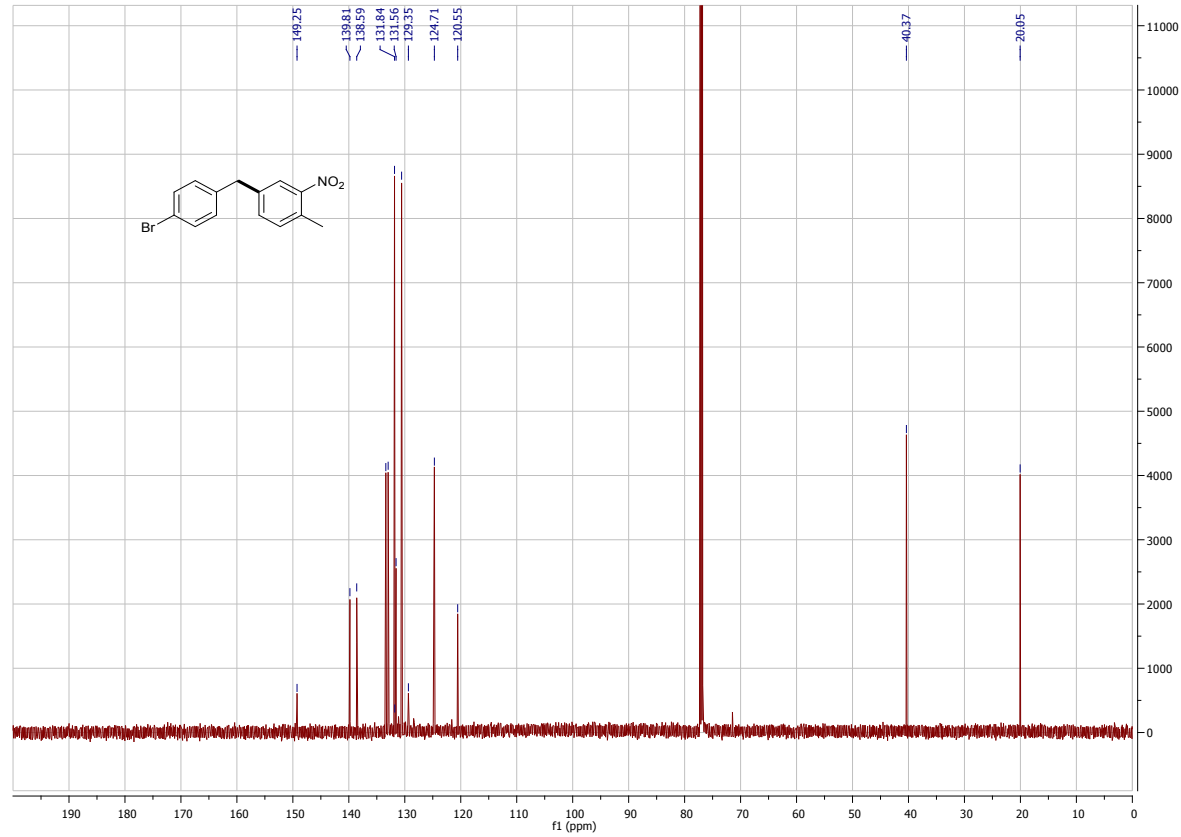


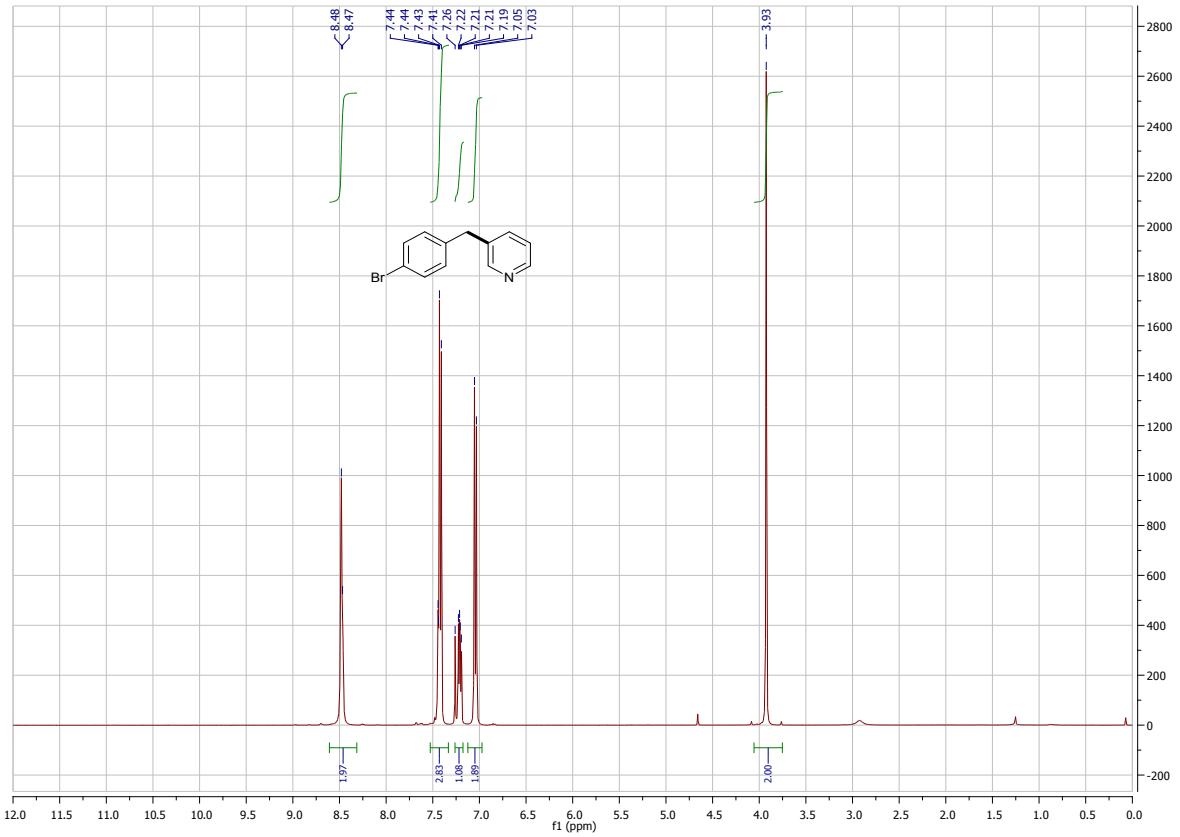


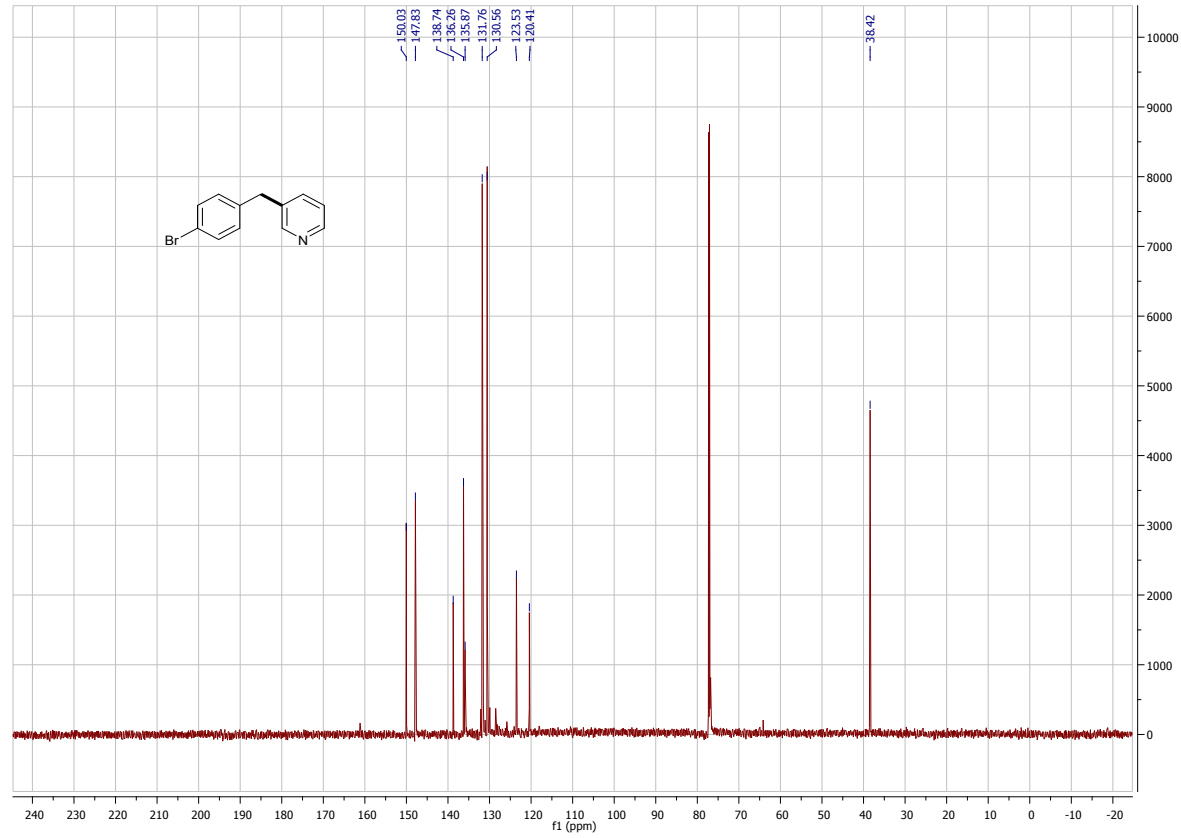

TL030A1P/10
4-BrPhCH2Ph4-vinyl
H (d) 7.07
F (d) 7.36
E (d) 7.42
D (dd) 6.71
C (d) 5.73
B (d) 5.24
G (d) 7.14
A (s) 3.93
f1 (ppm)

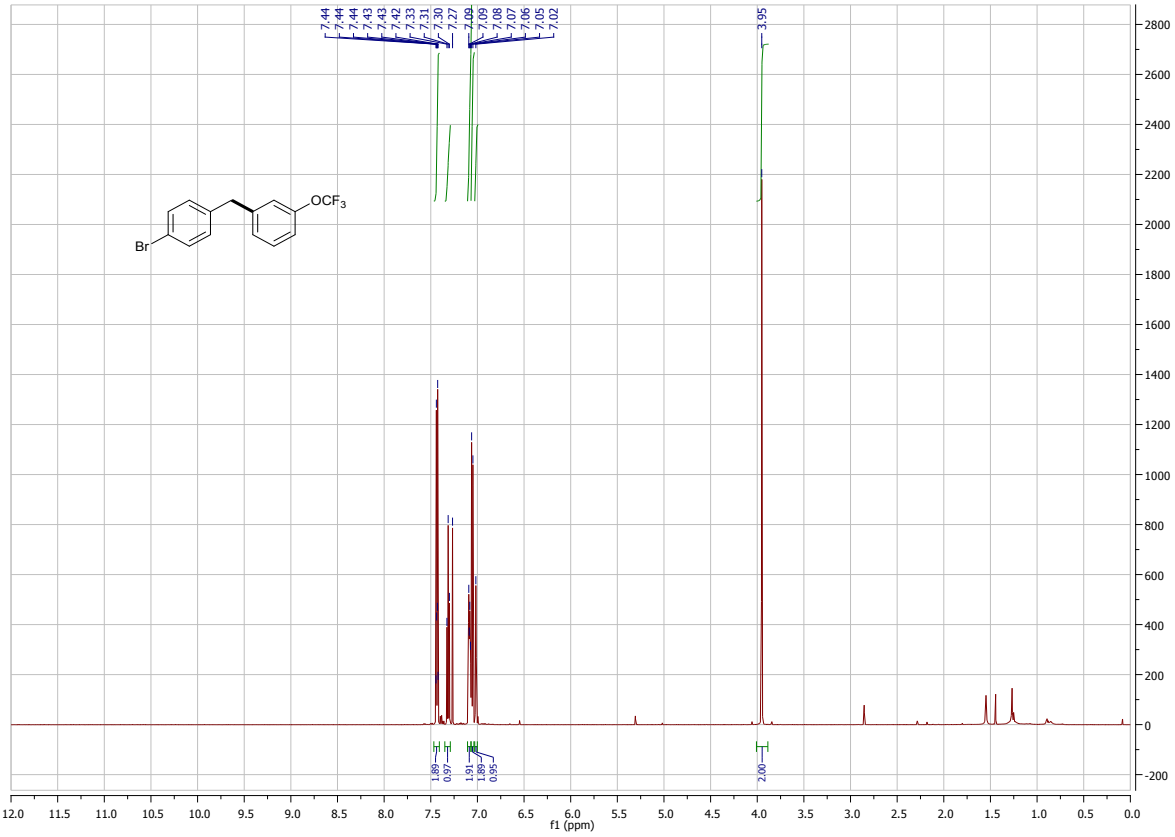

TL030A1/11
f1 (ppm)

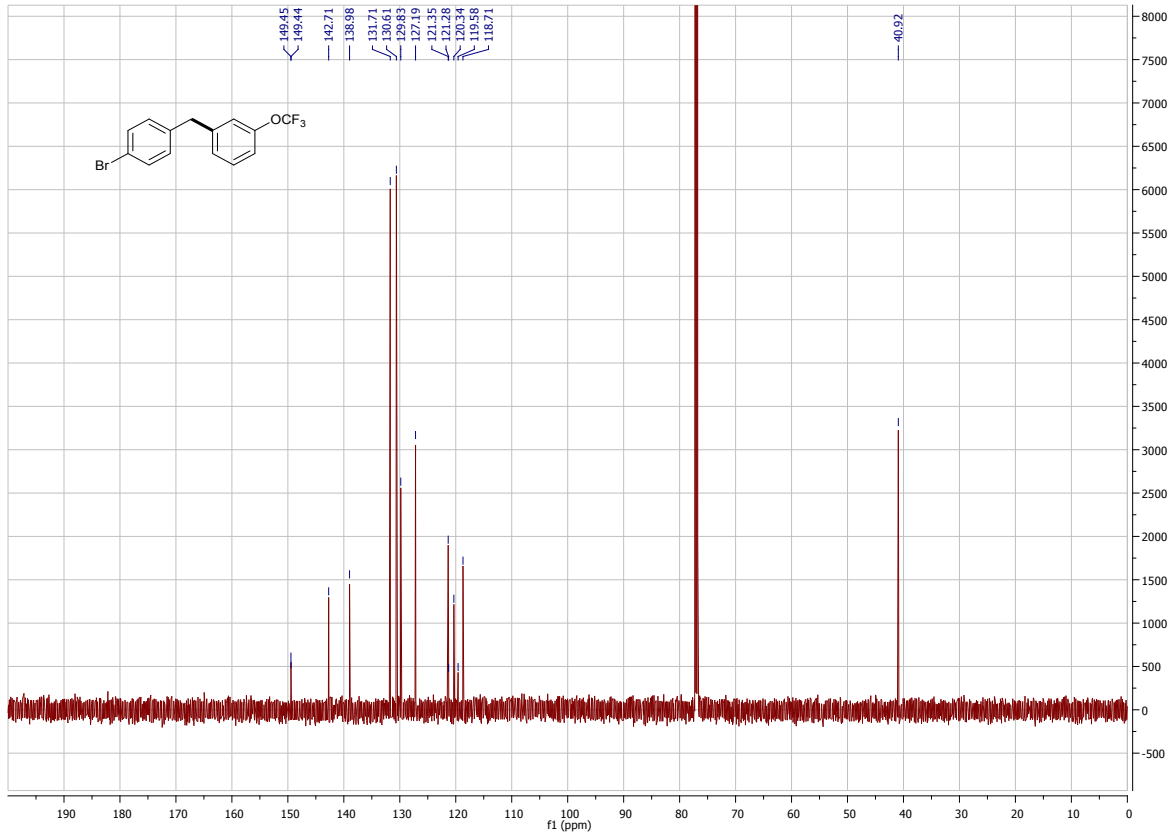

7.79
7.79
7.44
7.29
7.26
7.07
7.05
3.98
2.57
NO2
Br
0.89
1.93
2.05
1.89
2.00
2.98
f1 (ppm)

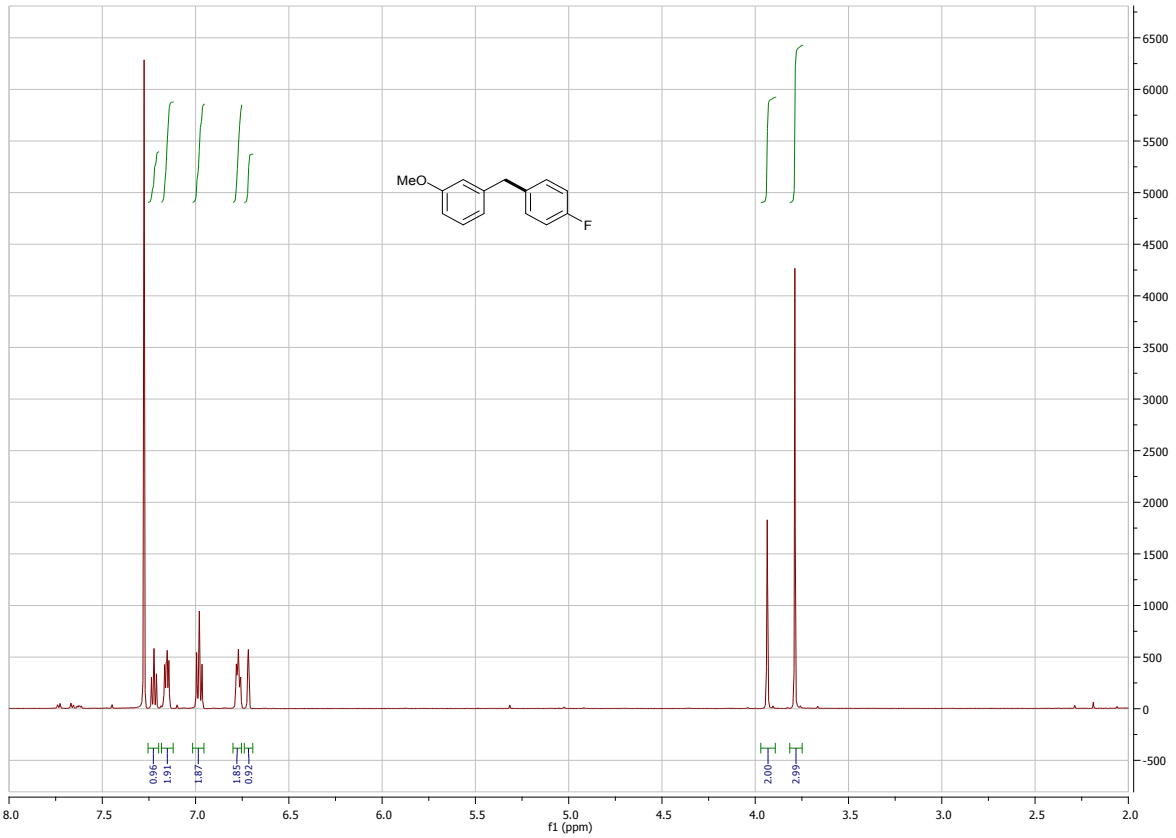

149.25
139.81
138.59
131.84
131.56
129.35
124.71
120.55
40.37
20.05
NO2
Br
f1 (ppm)

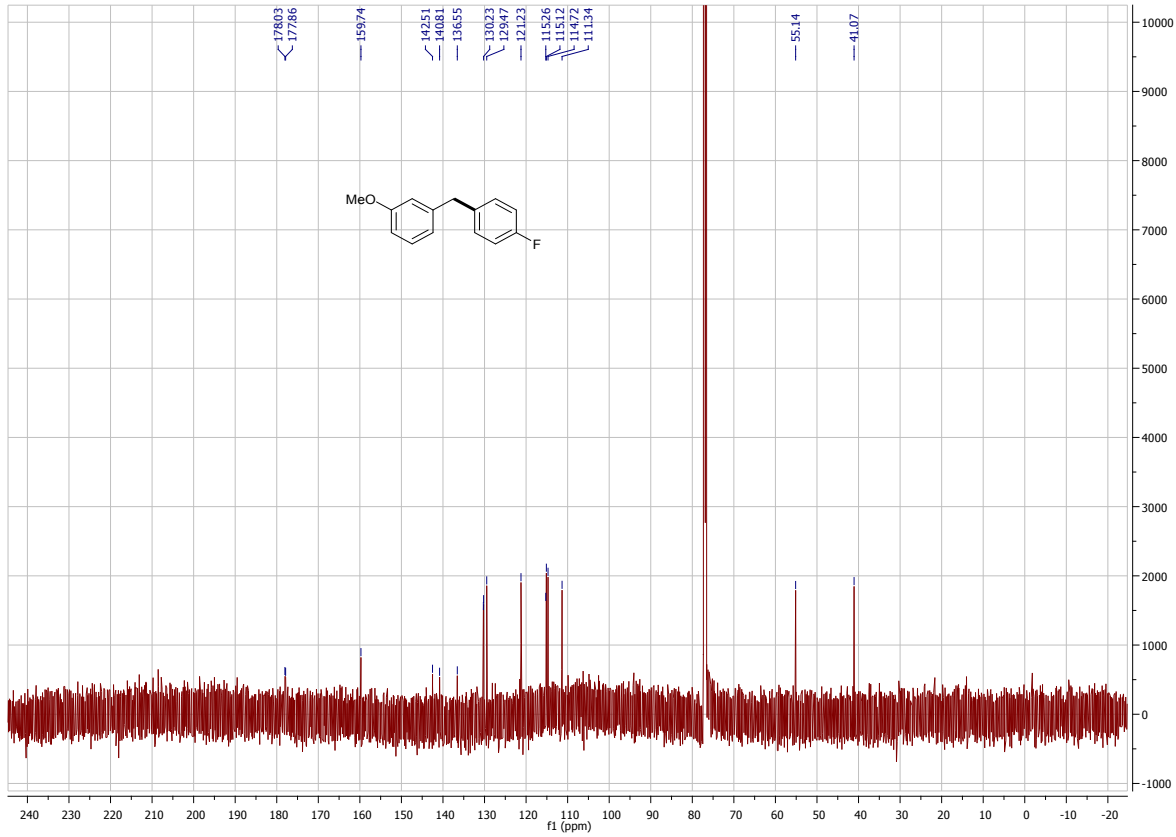

8.48
8.47
7.44
7.44
7.43
7.41
7.26
7.22
7.21
7.21
7.19
7.05
7.03
3.93
Br
N
1.97
2.83
1.08
1.89
2.00
f1 (ppm)

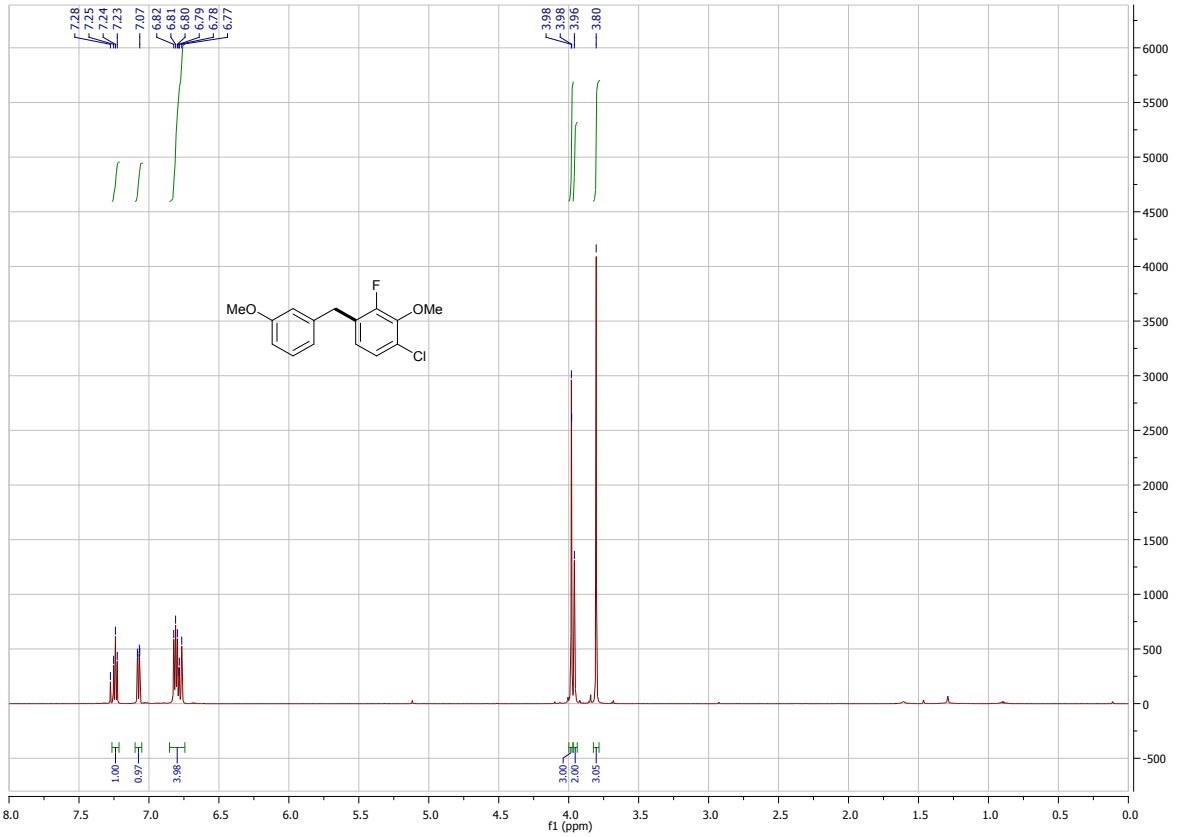

150.03
147.83
138.74
136.26
135.87
131.76
130.56
123.53
120.41
38.42
Br
N
f1 (ppm)

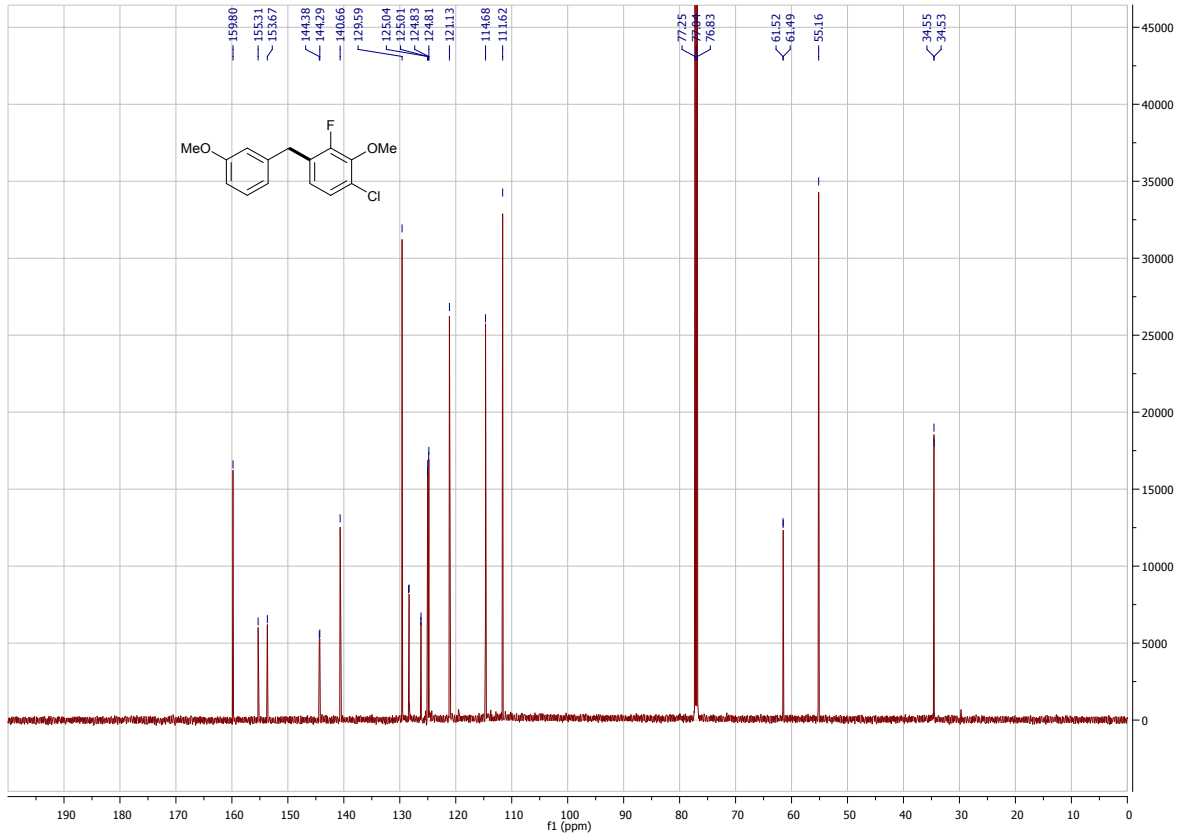

7.44
7.44
7.44
7.43
7.43
7.42
7.42
7.33
7.31
7.30
7.27
7.09
7.09
7.08
7.07
7.06
7.05
7.02
3.95
OCF3
Br
1.89
0.97
1.91
1.88
0.95
2.00
f1 (ppm)


149.45
149.44
142.71
138.98
131.71
130.61
129.83
127.19
121.35
121.28
120.34
119.58
118.71
40.92
OCF3
Br
f1 (ppm)

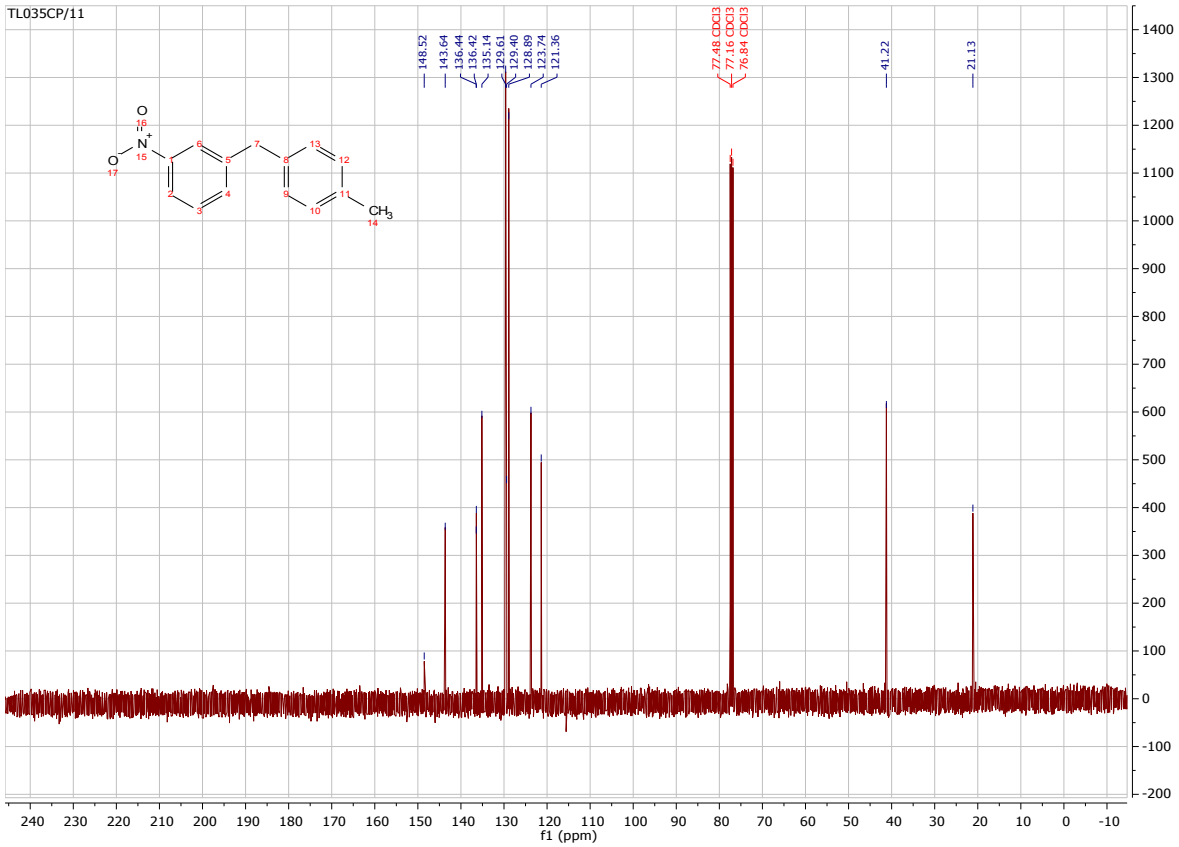

MeO
F
0.96
1.91
1.87
1.85
0.92
2.00
2.99
f1 (ppm)

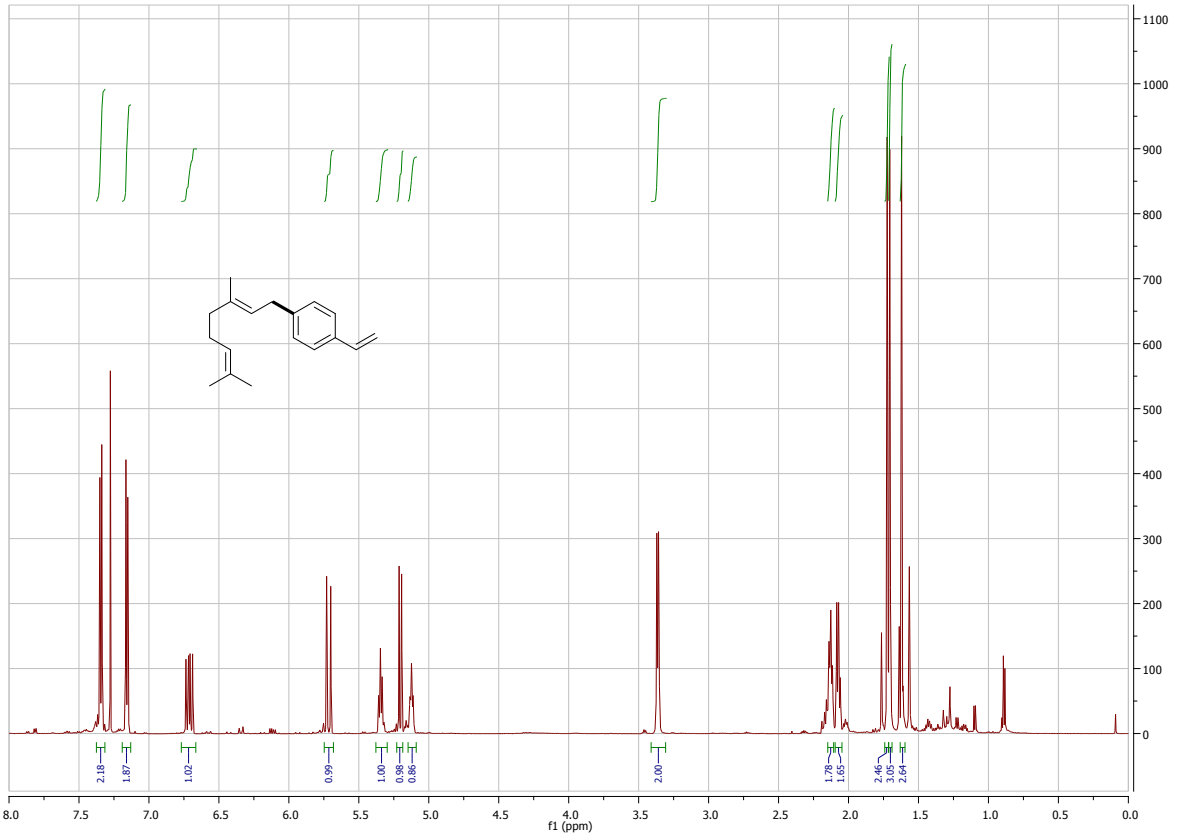

17803
17786
15974
14251
14081
13655
13023
12947
12123
11526
11512
11472
11134
55.14
41.07
MeO
F
f1 (ppm)

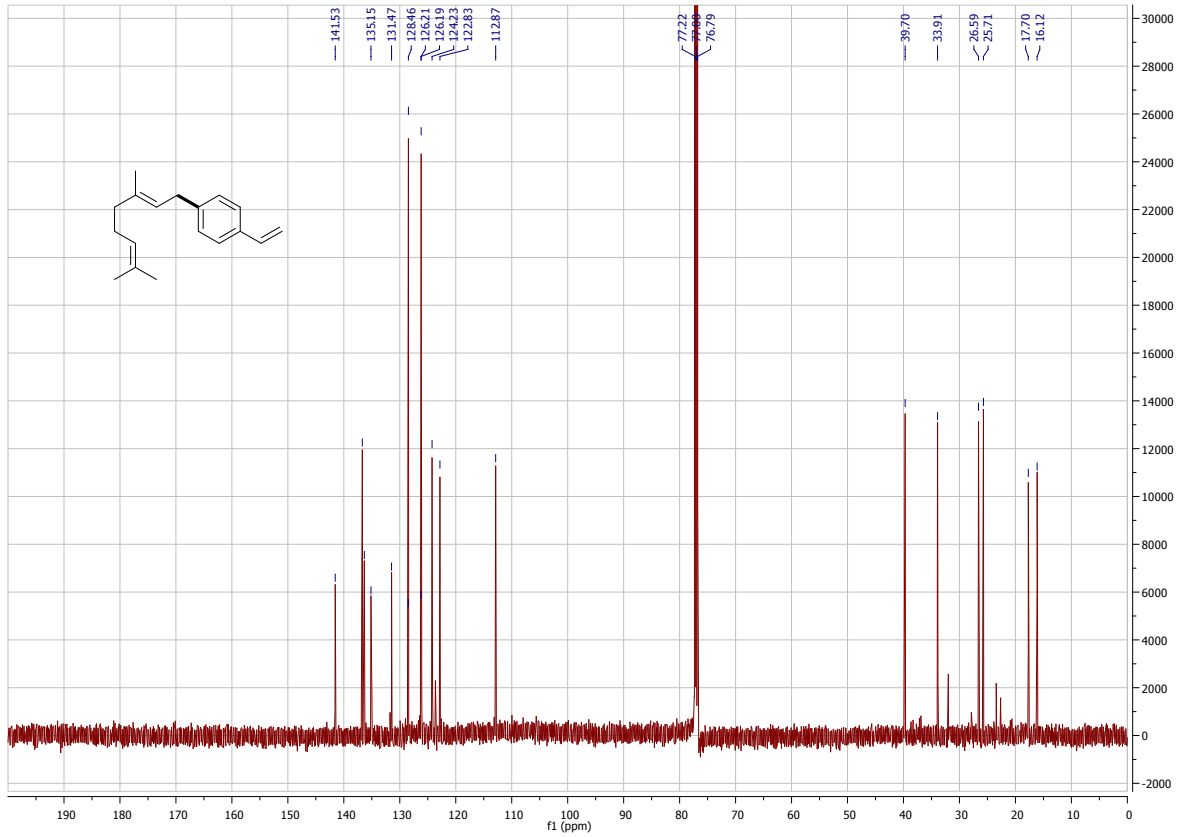

7.28
7.25
7.24
7.23
7.07
6.82
6.81
6.80
6.79
6.78
6.77
3.98
3.98
3.96
3.80
F
MeO
OMe
Cl
1.00
0.97
3.98
3.00
2.00
3.05
f1 (ppm)

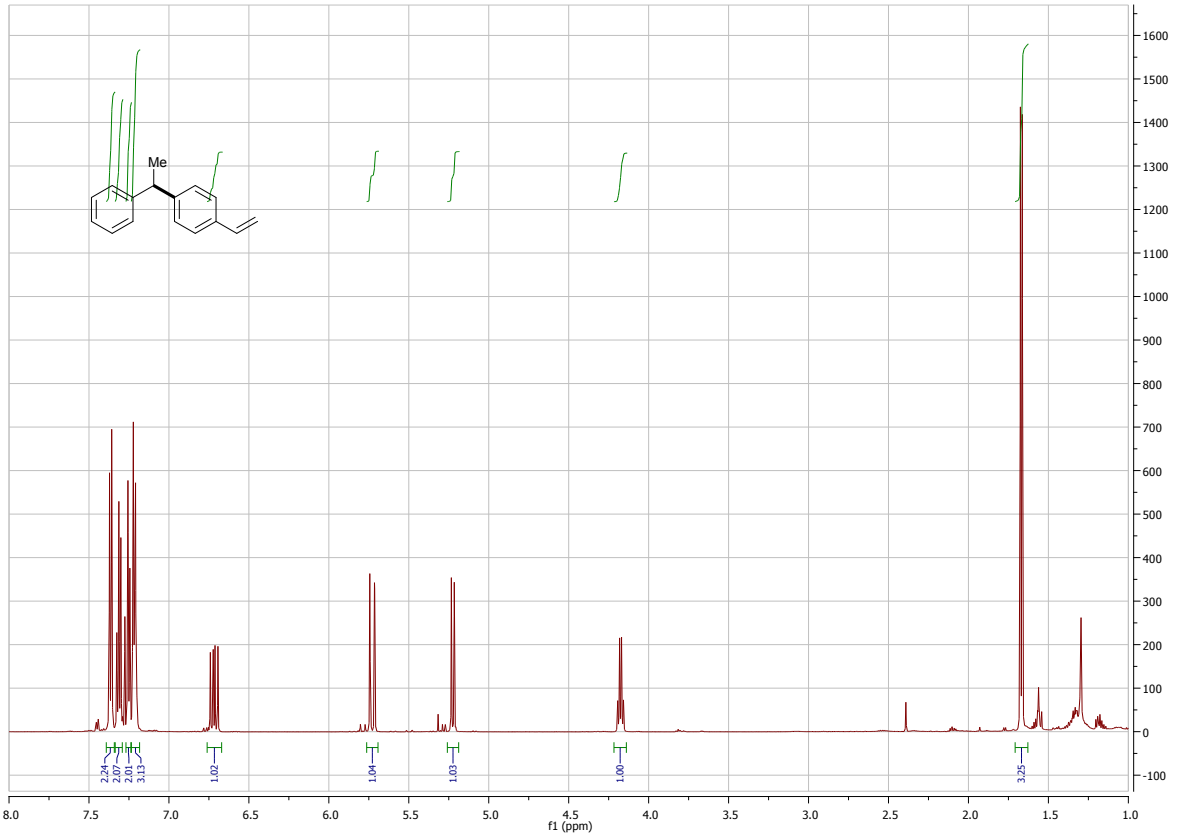

159.80
155.31
153.67
144.38
144.29
140.66
129.59
125.04
125.01
124.83
124.81
121.13
114.68
111.62
77.25
77.04
76.83
61.52
61.49
55.16
34.55
34.53
F
MeO
OMe
Cl
f1 (ppm)

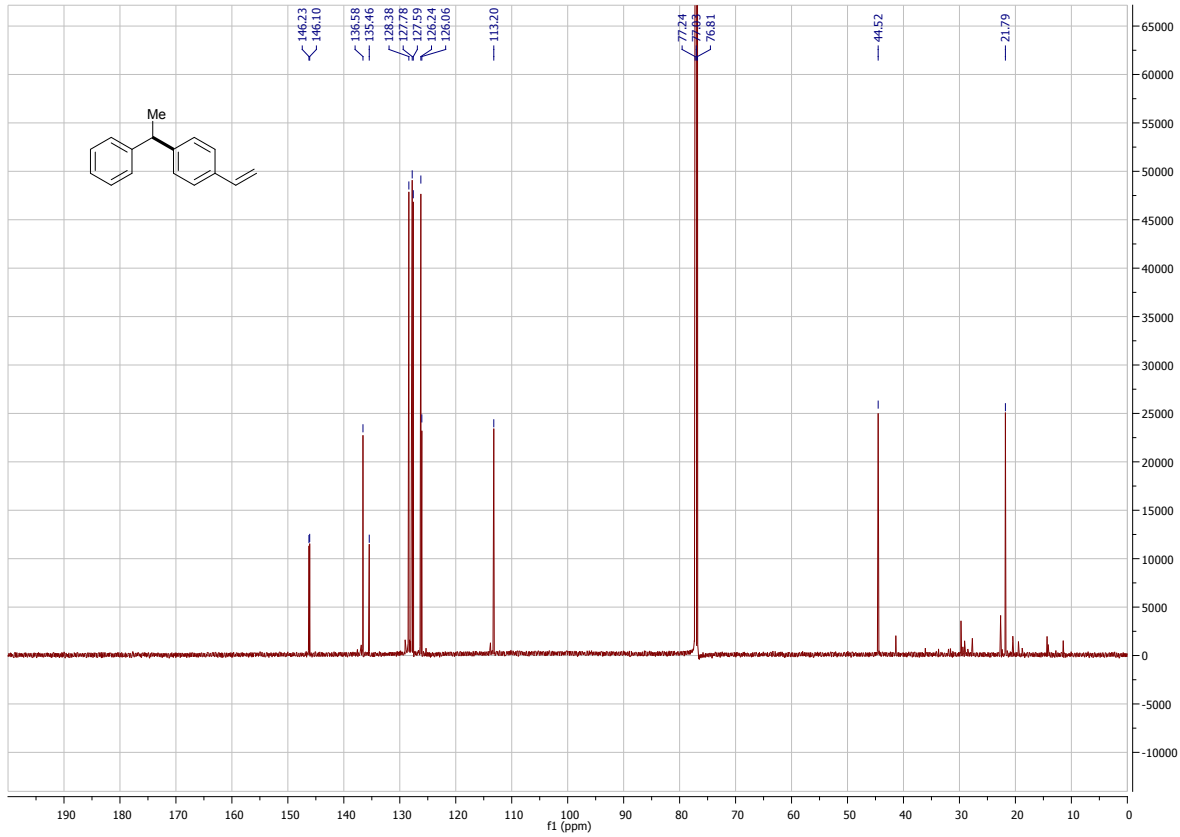

TL035CP/10
8.07
8.06
8.06
8.05
8.05
8.04
7.53
7.53
7.51
7.51
7.51
7.49
7.47
7.46
7.46
7.45
7.44
7.44
7.43
7.42
7.15
7.13
7.10
7.08
4.05
2.34
F (d)
7.09
H (s)
8.07
D (m)
7.44
G (d)
8.05
C (dt)
7.52
E (d)
7.14
B (s)
4.05
A (s)
2.34
1.29
0.72
0.96
0.98
1.91
1.95
2.00
3.12
f1 (ppm)

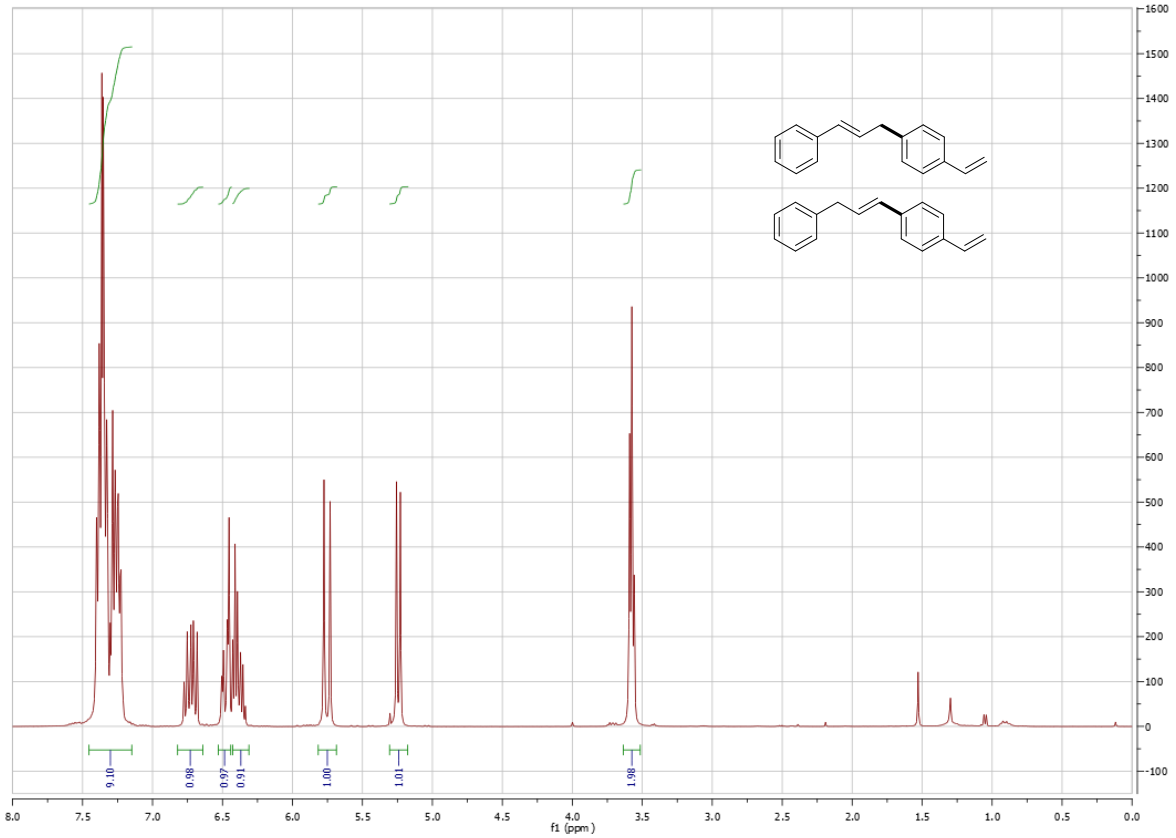

TL035CP/11
148.52
143.64
136.44
136.42
135.14
129.61
129.40
128.89
123.74
121.36
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
41.22
21.13
f1 (ppm)

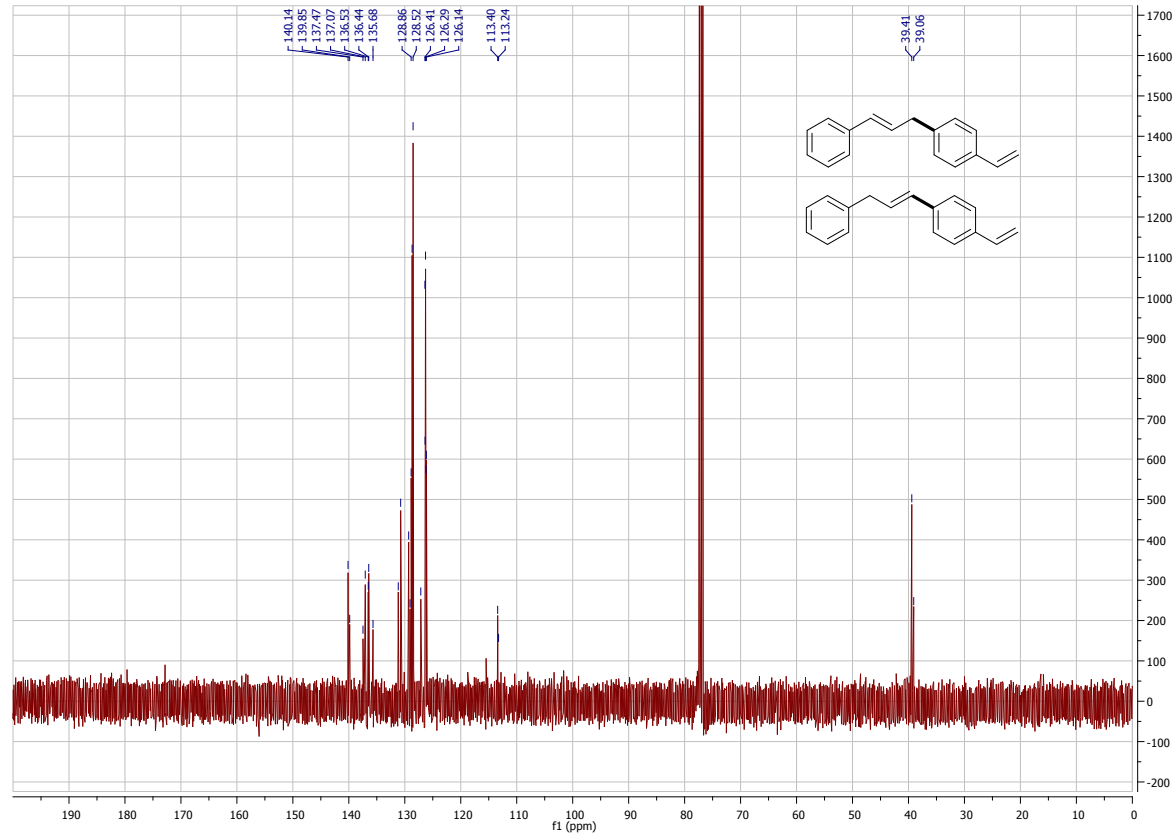

2.18
1.87
1.02
0.99
1.00
0.98
0.86
2.00
1.78
1.65
2.46
3.05
2.64
f1 (ppm)

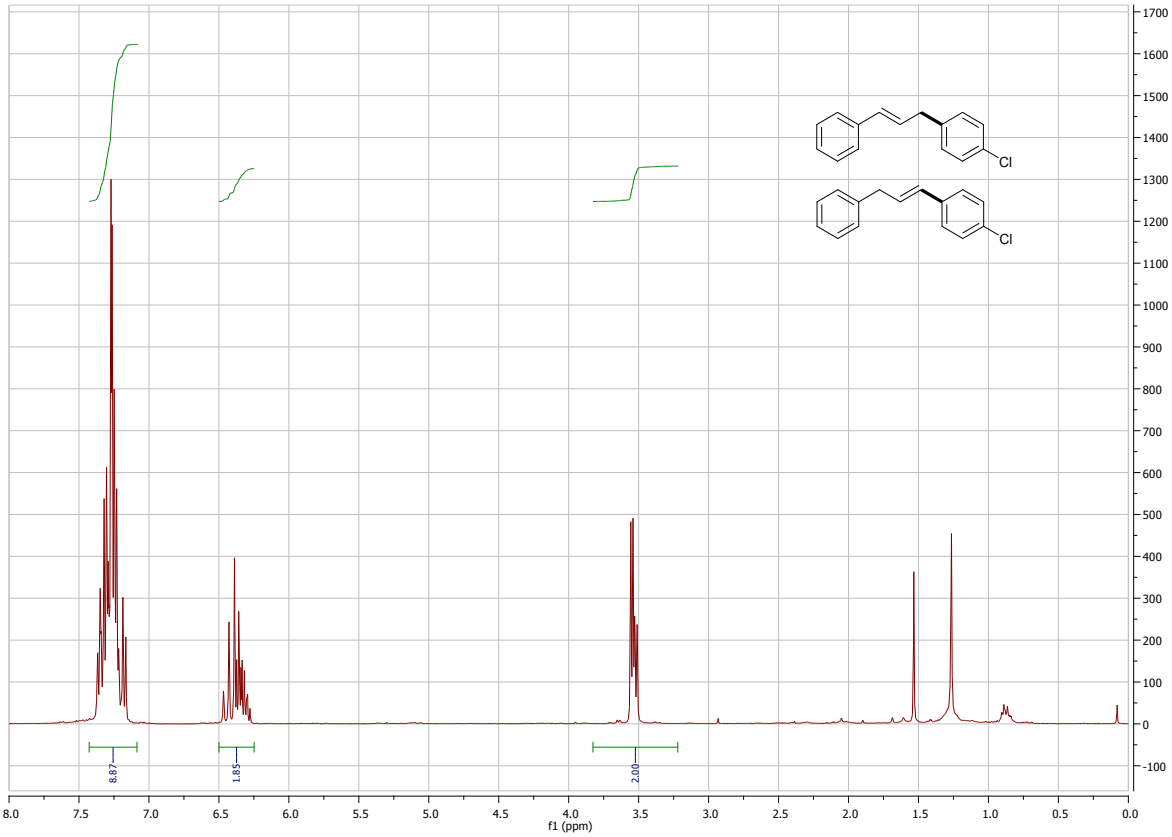

141.53
135.15
131.47
128.46
126.21
126.19
124.23
122.83
112.87
77.22
77.00
76.79
39.70
33.91
26.59
25.71
17.70
16.12
f1 (ppm)

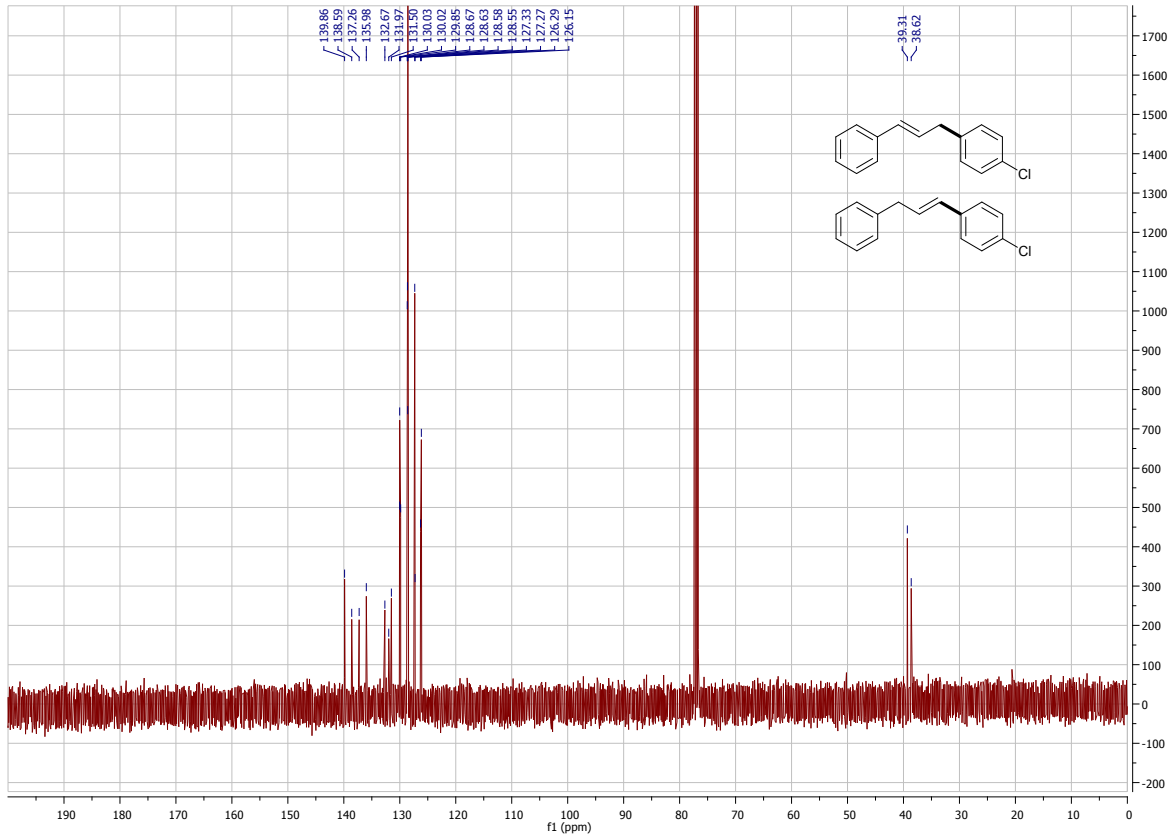

Me
2.24
2.07
2.01
3.13
1.02
1.04
1.03
1.00
3.25
f1 (ppm)

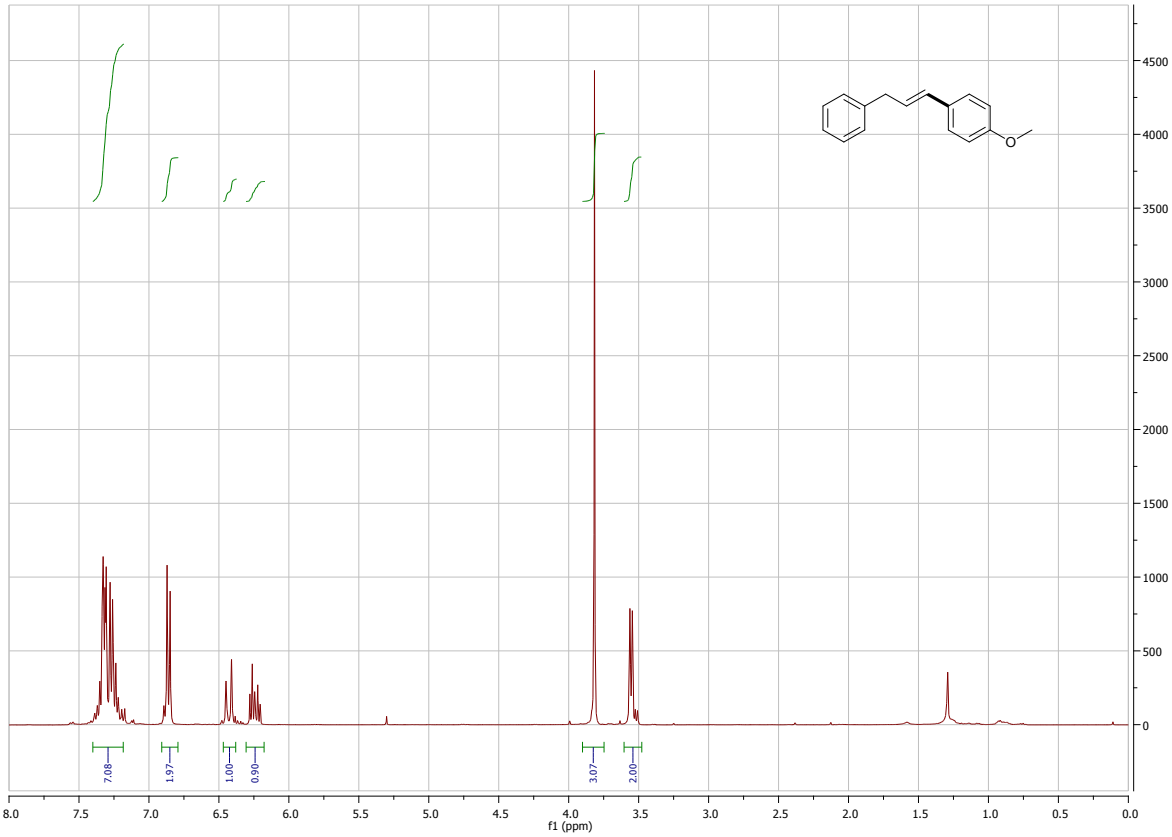

Me
146.23
146.10
136.58
135.46
128.38
127.78
127.59
126.24
126.06
113.20
77.24
77.03
76.81
44.52
21.79
f1 (ppm)

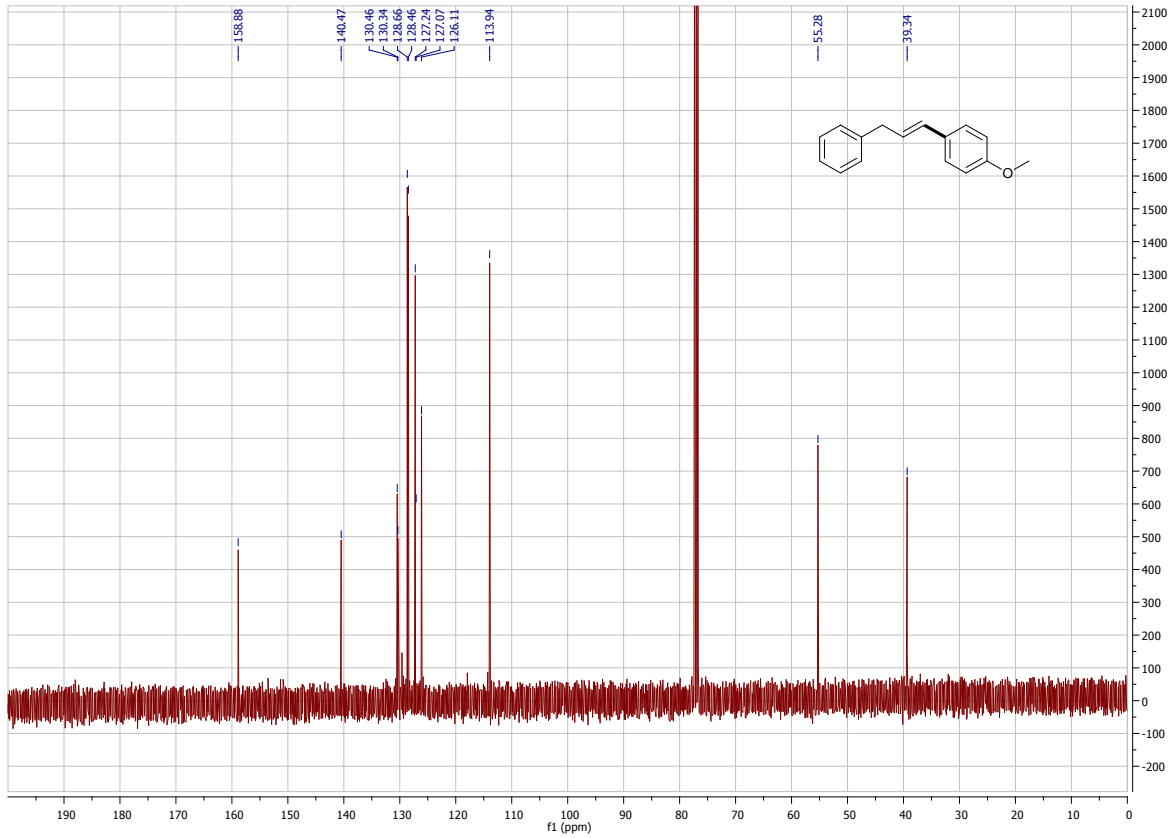

9.10
0.98
0.97
0.91
1.00
1.01
1.98
f1 (ppm)

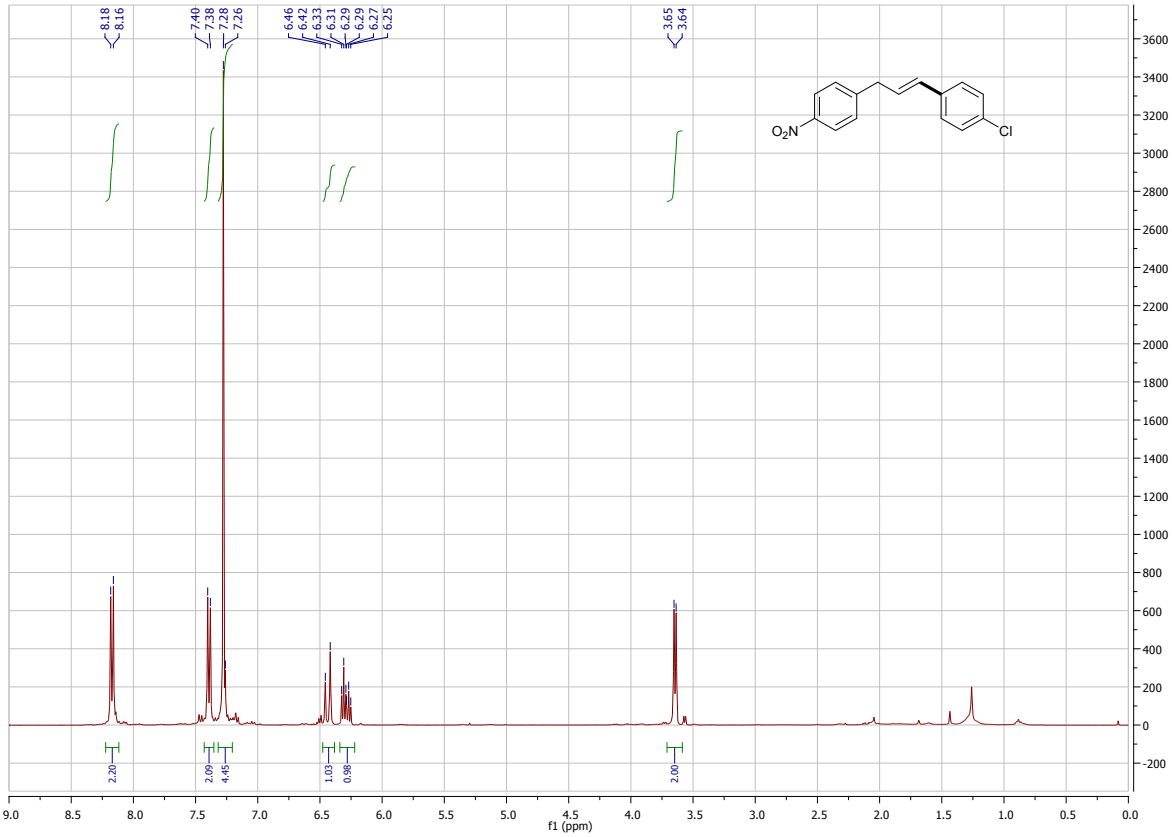

140.14
139.85
137.47
137.07
136.53
136.44
135.68
128.86
128.52
126.41
126.29
126.14
113.40
113.24
39.41
39.06
f1 (ppm)

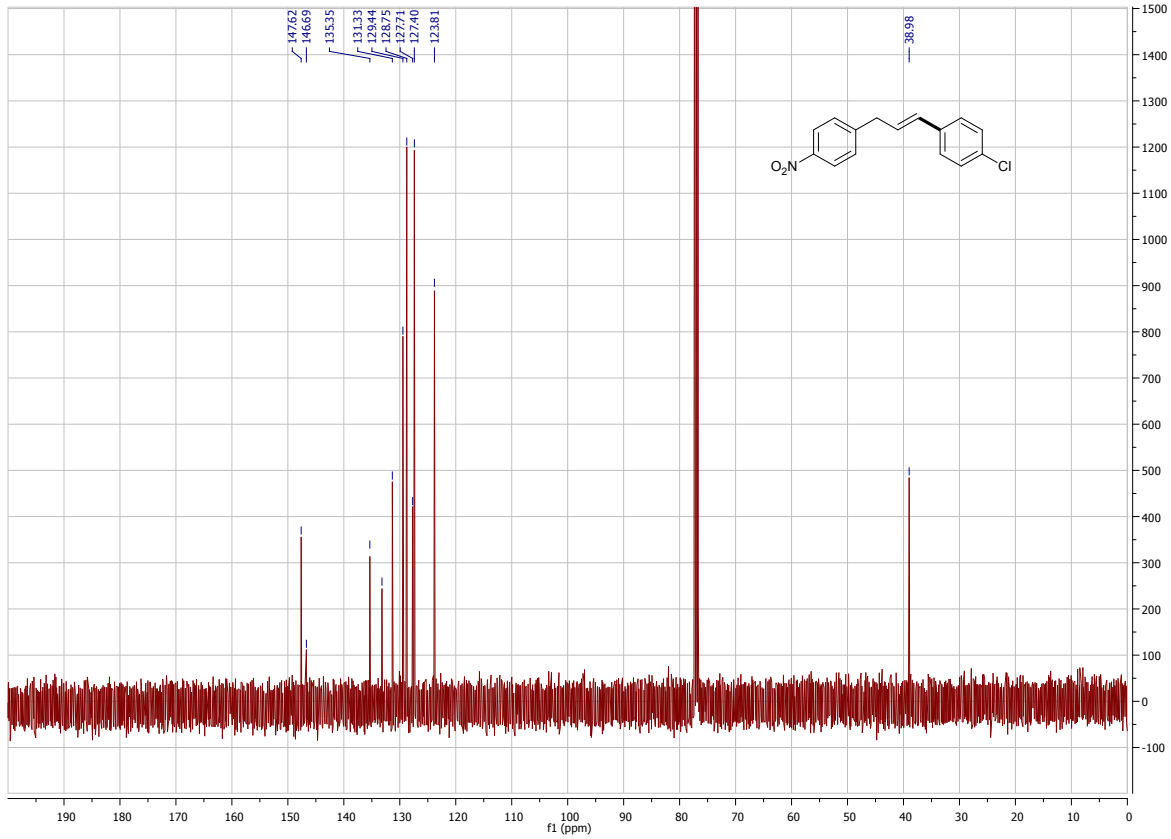

Cl
Cl
8.87
1.85
2.00
f1 (ppm)

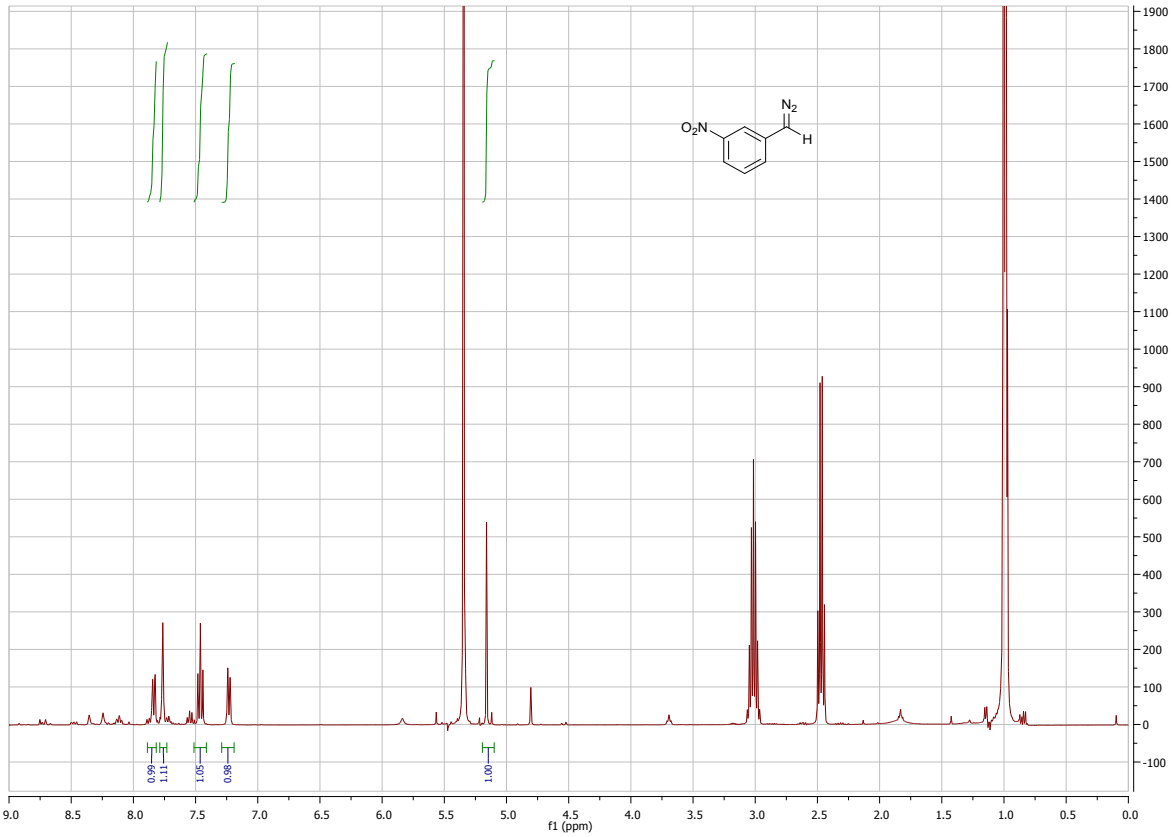

139.86
138.99
137.26
135.98
132.67
131.97
131.50
130.03
130.02
129.85
128.67
128.63
128.58
128.55
127.33
127.27
126.29
126.15
39.31
38.62
Cl
Cl
f1 (ppm)

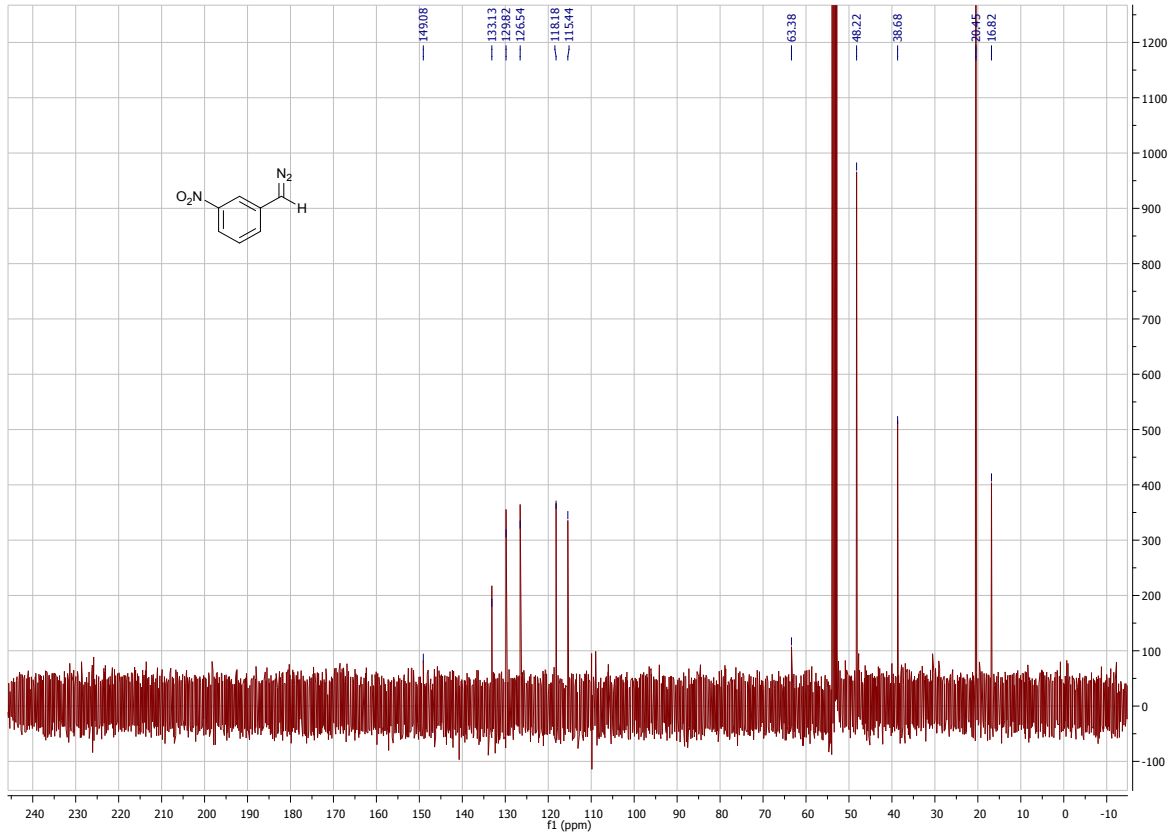

7.08
1.97
1.00
0.90
3.07
2.00
f1 (ppm)
O

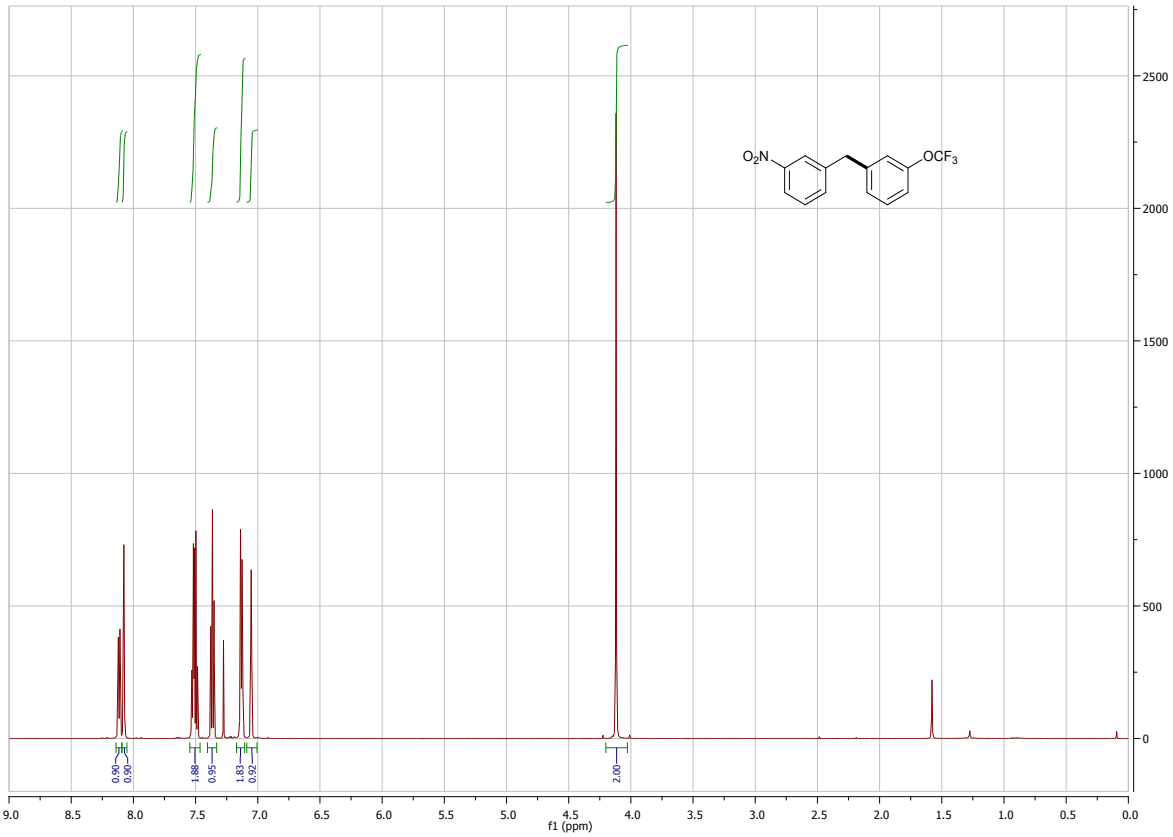

158.88
140.47
130.46
130.34
128.66
128.46
127.24
127.07
126.11
113.94
55.28
39.34
f1 (ppm)
O

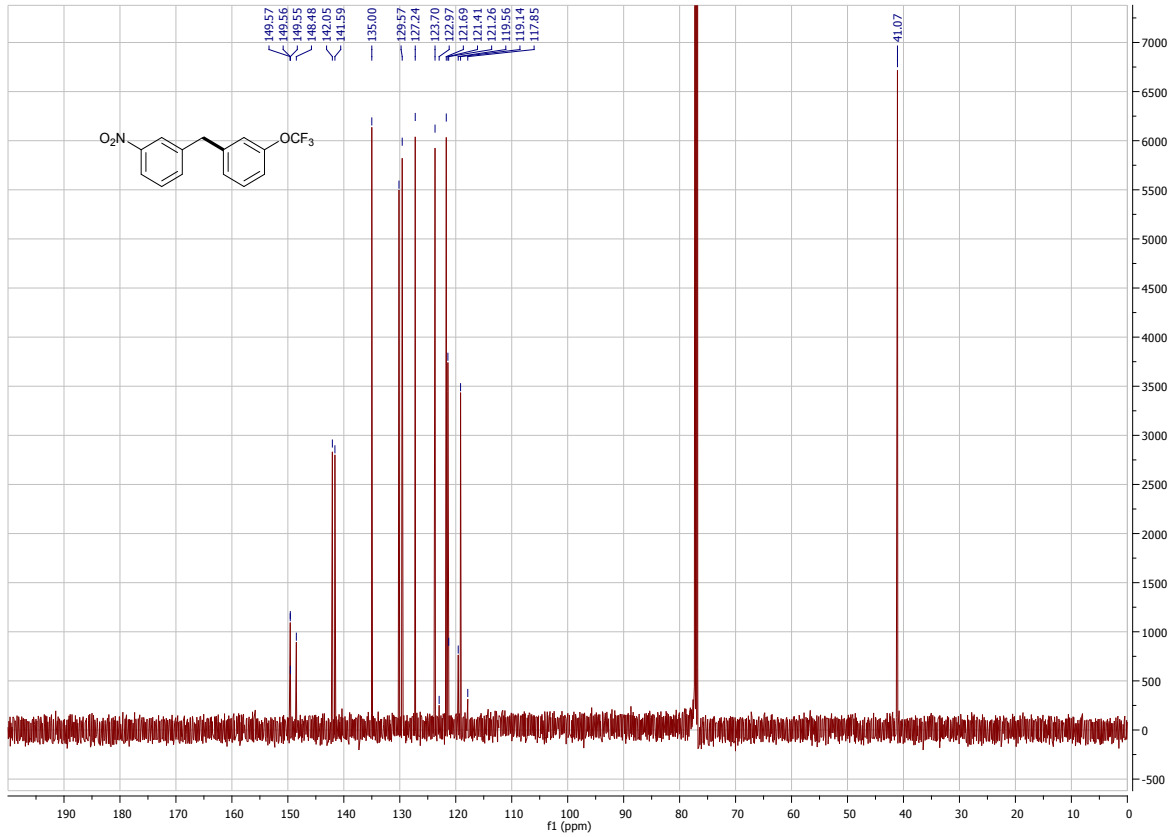

8.18
8.16
7.40
7.38
7.28
7.26
6.46
6.42
6.33
6.31
6.29
6.29
6.27
6.25
3.65
3.64
O2N
Cl
2.20
2.09
4.45
1.03
0.98
2.00
f1 (ppm)


147.62
146.69
135.35
131.33
129.44
128.75
127.71
127.40
123.81
38.98
O2N
Cl
f1 (ppm)


N2
O2N
H
0.99
1.11
1.05
0.98
1.00
f1 (ppm)


149.08
133.13
129.82
126.54
118.18
115.44
63.38
48.22
38.68
26.45
16.82
N2
O2N
H
f1 (ppm)


O2N
OCF3
0.90
0.99
1.88
0.95
1.83
0.92
2.00
f1 (ppm)


149.57
149.56
149.55
148.48
142.05
141.59
135.00
129.57
127.24
123.70
122.97
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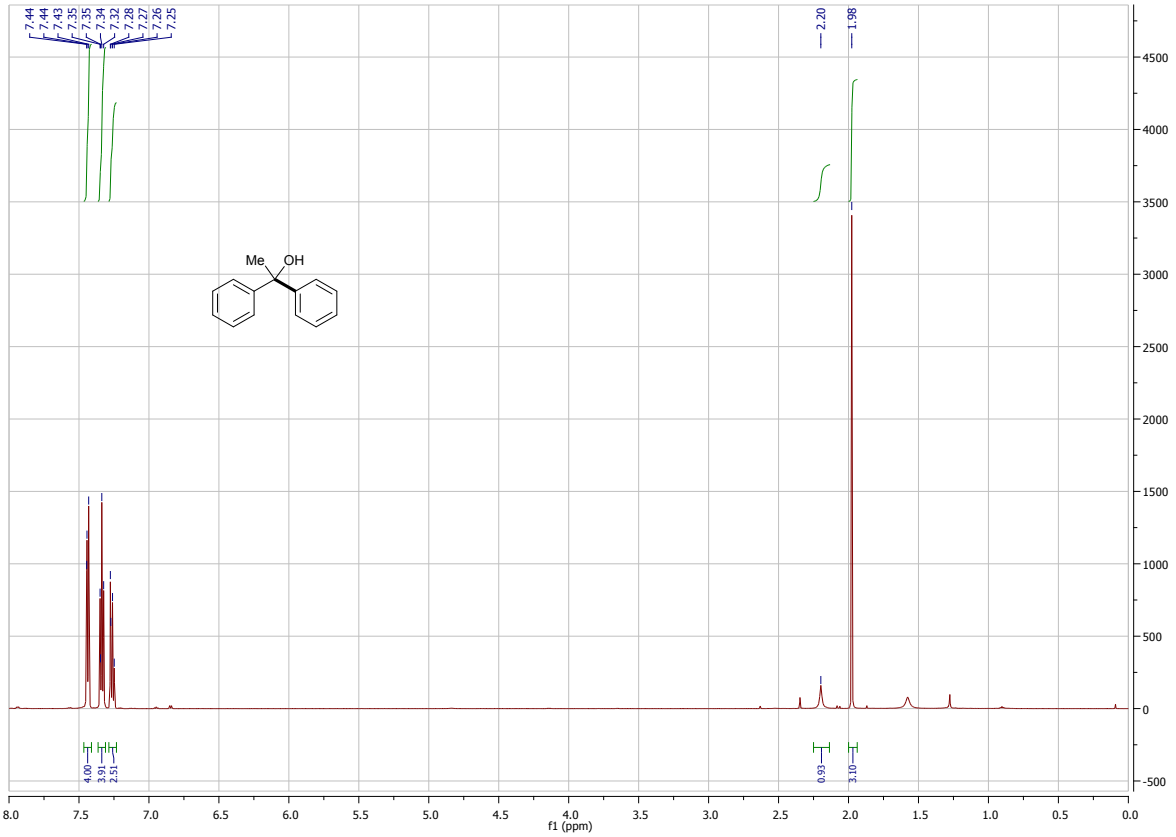
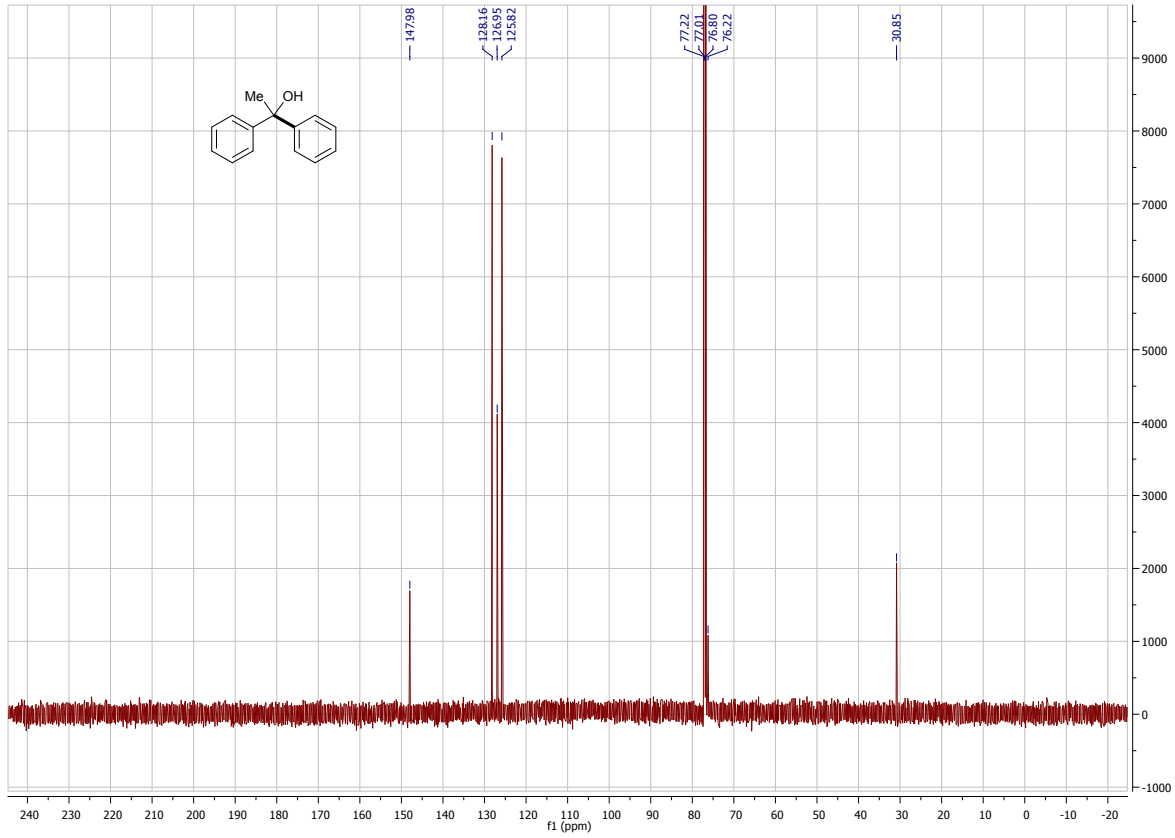
121.41
121.26
119.56
119.14
117.85
41.07
O2N
OCF3
f1 (ppm)


7.44
7.44
7.43
7.35
7.35
7.34
7.32
7.28
7.27
7.26
7.25
2.20
1.98
Me
OH
4.00
3.91
2.51
0.93
3.10
f1 (ppm)


147.98
128.16
126.95
125.82
77.22
77.01
76.80
76.22
30.85
Me
OH
f1 (ppm)

References

1. For information about the Uniqsis FlowSyn system, see: http://www.uniqsis.com/

2. For information about the Mettler Toledo FlowIR®, see: http://uk.mt.com/gb/en/home/products/L1_AutochemProducts/ReactIR/flow-ir-chemis.html

3. For information about Omnifit® glass columns, see: http://www.omnifit.com/

4. Activated MnO_2 was purchased from Sigma Aldrich (cod. 63548).

5. J. A. Newby, D. W. Blaylock, P. M. Witt, R. M. Turner, P. L. Heider, B. H. Harji, D. L. Browne and S. V. Ley, *Org. Process Res. Dev*., (DOI: 10.1021/op500221s).