Supporting Information

for

Chemoselective Efficient Synthesis of Functionalized β-oxonitriles through Cyanomethylation of Weinreb Amides

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Material and Methods

Melting points were determined on a Reichert–Kofler hot-stage microscope and are uncorrected. Mass spectra were obtained on a Shimadzu QP 1000 instrument (EI, 70 eV) and on a Bruker maXis 4G instrument (ESI-TOF, HRMS). IR spectra were recorded on a Perkin-Elmer FTIR 1605 spectrophotometer. ^{1}H, ^{13}C, ^{15}N, ^{19}F and ^{17}O NMR spectra were recorded with a Bruker Avance III 400 spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C, 40 MHz for ^{15}N, 376 MHz for ^{19}F, 54 MHz for ^{17}O) or a Bruker Avance 500 spectrometer (500 MHz for ^{1}H, 125 MHz for ^{13}C, 50 MHz for ^{15}N, 470 MHz for ^{19}F) at 297 K using a "directly" detecting broadband observe (BBFO) probe. The center of the solvent signal was used as an internal standard which was related to TMS with δ 7.26 ppm (^{1}H in $CDCl_3$) and δ 77.0 ppm (^{13}C in $CDCl_3$). ^{15}N NMR spectra (gs-HMBC, gs-HSQC) were referenced against neat, external nitromethane, ^{19}F NMR spectra by absolute referencing via Ξ ratio. ^{17}O NMR spectra were taken from approximately 1M solutions and are referenced against external H_2O (0 ppm). For the latter 10 000 to 300 000 scans were accumulated (pulse width 90°, acquisition time 0.15 s, relaxation delay 0.2 s, spectral width 500-600 ppm) and Fourier transformed after a 200-250 Hz line broadening by exponential multiplication. To decrease acoustic ringing a pre-scan delay DE = 100 μs was used in the pulse sequence. Spin-spin coupling constants (*J*) are given in Hz. In some cases, full and unambiguous assignment of all resonances was performed by combined application of standard NMR techniques, such as APT, HSQC, HMBC, COSY and NOESY experiments. Light petroleum refers to the fraction with boiling point 40–65 °C.

All the reactions were carried out under inert atmosphere of nitrogen. Acetonitrile derivatives were purified immediately before their use by distillation. THF was distilled over Na / benzophenone. Chemicals were purchased from Sigma-Aldrich, Acros, Alfa Aesar and TCI Europe. Starting Weinreb amides were prepared according to our previously reported method.[1]

General Procedures for the Cyanomethylation of Weinreb amides

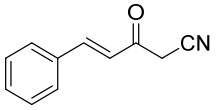
- **Cyanomethylation of α,β-unsaturated Weinreb amides (General Procedure 1)**

To a solution of dry acetonitrile derivative (2.0 equiv) in anhydrous THF cooled at -78 °C, MeLi-LiBr (1.5 M in Et_2O, 1.5 equiv) was added dropwise during 5 min and the resulting mixture was stirred for 30 min. Then, a solution of Weinreb amide (1.0 equiv) in THF was added and the stirring was continued for additional 1.5 h at – 78 °C. A solution of saturated aqueous NH_4Cl was added and after removing of the cooling-bath the system was allowed to reach rt. After extracting the organic phase with diethyl ether, two additional washings with brine followed. Finally, the organic phase was dried over Na_2SO_4 and, the pure cyanoketones were recovered upon removal of the solvent under vacuum.

- **Cyanomethylation of non α,β-unsaturated Weinreb amides (General Procedure 2)**

To a solution of dry acetonitrile derivative (4.5 equiv) in anhydrous THF cooled at -78 °C, MeLi-LiBr (1.5 M in Et_2O, 4.0 equiv) was added dropwise during 5 min and the resulting mixture was stirred for 30 min. Then, a solution of Weinreb amide (1.0 equiv) in THF was added and, the stirring was continued for additional 1.5 h at – 78 °C. A solution of saturated aqueous NH_4Cl was added and after, removing of the cooling-bath, the system was allowed to reach rt. The organic phase was extracted with diethyl ether and two additional washings with brine followed. Finally, the organic phase was dried over Na_2SO_4 and the pure cyanoketones were recovered upon removal of the solvent under vacuum.

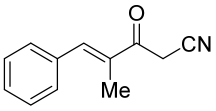
(4*E*)-3-oxo-5-phenyl-4-pentenenitrile (2)



By following the general procedure 1, starting from (2*E*)-*N*-methoxy-*N*-methyl-3-phenylacrylamide **1a** (0.191 g, 1.0 mmol, 1.0 equiv), CH_3CN (0.08 g, 0.1 mL, 2.0 mmol, 2.0 equiv) and MeLi-LiBr (1.0 mL, 1.5 mmol, 1.5 equiv) in THF, β-oxonitrile **2** was obtained in 86% yield (0.147 g) as a yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.68 (d, ^3J = 16.0 Hz, 1H, PhC<u>H</u>=CH) 7.58 (m, 2H, Ph H-2, 6), 7.45 (m, 1H, Ph H-4), 7.44 (m, 2H, Ph H-3,5), 6.86 (d, ^3J = 16.0 Hz, 1H, PhCH=C<u>H</u>), 3.73 (s, 2H, CH_2CN). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 186.3 (C=O), 146.5 (Ph<u>C</u>H=CH), 133.3 (Ph C-1), 131.6 (Ph C-4), 129.1 (Ph C-3,5), 128.8 (Ph C-2,6), 122.4 (PhCH=<u>C</u>H), 114.0 (CN), 30.8 (<u>C</u>H_2CN). **^{15}N NMR** (40 MHz, $CDCl_3$) δ: -126.6 (CN). **IR** (NaCl, ν_{max}, cm^{-1}): 2253, 1792, 1683, 1608, 1470, 1379. **Mp:** 97 °C (lit.,[2] 97-98 °C). **Elemental Analysis (%)** for $C_{11}H_9NO$. Calcd: C, 77.17; H, 5.30; N, 8.18. Found: C, 77.31; H, 6.99; N, 8.29.

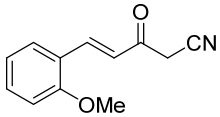
(4*E*)-4-methyl-3-oxo-5-phenyl-4-pentenenitrile (4a)



By following the general procedure 1, starting from (2*E*)-*N*-methoxy-*N*,2-dimethyl-3-phenylacrylamide (0.205 g, 1.0 mmol, 1.0 equiv), CH_3CN (0.08 g, 0.1 mL, 2.0 mmol, 2.0 equiv) and MeLi-LiBr (1.0 mL, 1.5 mmol, 1.5 equiv) in THF, β-oxonitrile **4a** was obtained in 87% yield (0.161 g) as a yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.44 (s, 1H, C<u>H</u>=CCO), 7.43 (m, 4H, Ph H-2,3,5,6), 7.40 (m, 1H, Ph H-4), 3.97 (s, 2H, CH_2CN), 2.10 (s, 3H, CH=CC<u>H</u>$_3$). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 189.1 (C=O), 141.8 (<u>C</u>H=CCO), 135.4 (CH=<u>C</u>CO), 134.6 (Ph C-1), 129.9 (Ph C-2,6), 129.4 (Ph C-4), 128.6 (Ph C-3,5), 114.3 (CN, ^2J(CN,CH_2) = 10.3 Hz), 28.6 (<u>C</u>H_2CN, ^1J(CH_2) = 134.6 Hz), 13.1 (CH=C<u>C</u>H_3, ^1J(CH_3) = 129.0 Hz, ^3J(CH_3,=CH) = 8.0 Hz). **^{15}N NMR** (40 MHz, $CDCl_3$) δ: -127.4 (CN). **IR** (NaCl, ν_{max}, cm^{-1}): 2253, 1793, 1684, 1469, 1382. **Mp:** 80°C. **Elemental Analysis (%)** for $C_{12}H_{11}NO$. Calcd.: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.97; H, 6.11; N, 7.70.

(4*E*)-5-(2-methoxyphenyl)-3-oxo-4-pentenenitrile (4b)

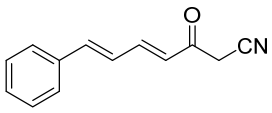


By following the general procedure 1, starting from (2*E*)-*N*-methoxy-3-(2-methoxyphenyl)-*N*-methylacrylamide (0.221 g, 1.0 mmol, 1.0 equiv), CH_3CN (0.08 g, 0.1 mL, 2.0 mmol, 2.0 equiv) and

MeLi-LiBr (1.0 mL, 1.5 mmol, 1.5 equiv) in THF, β-oxonitrile **4b** was obtained in 85% yield (0.173 g) as a yellow semi-solid mass.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.97 (d, *J* = 16.2Hz, 1H, Ph-C<u>H</u>=CH), 7.54 (m, 1H, Ph H-6), 7.42 (m, 1H, Ph H-4), 6.99 (m, 1H, Ph H-5), 6.94 (m, 1H, Ph H-3), 6.94 (d, *J* = 16.2Hz, 1H, Ph-CH=C<u>H</u>), 3.91 (s, 3H, OCH_3), 3.74 (s, 2H, CH_2CN). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 186.9 (C=O), 158.9 (Ph C-2), 141.9 (Ph-<u>C</u>H=CH), 133.0 (Ph C-4), 129.4 (Ph C-6), 123.2 (Ph-CH=<u>C</u>H), 122.3 (Ph C-1), 120.9 (Ph C-5), 114.2 (CN), 111.1 (Ph C-3), 55.6 (OCH3), 30.5 (<u>C</u>H_2CN). **IR** (NaCl, ν_{max}, cm^{-1}): 3076, 2258, 1691. **Elemental Analysis (%)** for $C_{12}H_{11}NO_2$. Calcd.: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.77; H, 5.62; N, 7.10.

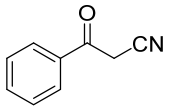
(4*E*,6*E*)-3-oxo-7-phenyl-4,6-heptadienenitrile (4c)



By following the general procedure 1, starting from (2*E*,4*E*)-*N*-methoxy-*N*-methyl-5-phenyl-2,4-pentadienamide (0.217 g, 1.0 mmol, 1.0 equiv), CH_3CN (0.08 g, 0.1 mL, 2.0 mmol, 2.0 equiv) and MeLi-LiBr (1.0 mL, 1.5 mmol, 1.5 equiv) in THF, β-oxonitrile **4c** was obtained in 90% yield (0.184 g) as a brown solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.46 (dd, *J* = 15.2, 10.9 Hz, 1H, H-5), 7.49 (m, 2H, Ph H-2,6), 7.37 (m, 3H, Ph H-3,4,5), 7.06 (d, *J* = 15.6 Hz, 1H, H-7), 6.91 (dd, *J* = 15.6, 10.9 Hz, 1H, H-6), 6.41 (d, *J* = 15.2 Hz, 1H, H-4), 3.64 (s, 2H, CH_2CN). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 186.2 (C=O), 146.4 (C-5), 144.5 (C-7), 135.4 (Ph C-1), 129.9 (Ph C-4), 128.9 (Ph C-3,5), 127.6 (Ph C-2,6), 125.7 (C-6), 125.4 (C-4), 114.1 (CN), 30.6 (<u>C</u>H_2CN). **IR** (NaCl, ν_{max}, cm^{-1}): 2253, 1792, 1467, 1379. **Mp:** 69-70 °C. **Elemental Analysis (%)** for $C_{13}H_{11}NO$. Calcd: C, 79.16; H, 5.62; N, 7.10. Found: C, 79.29; H, 5.71; N, 7.19.

2-oxo-3-phenylpropanenitrile (4d)

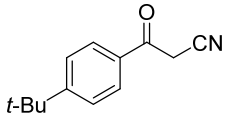


By following the general procedure 2, starting from *N*-methoxy-*N*-methylbenzamide (0.165 g, 1.0 mmol, 1.0 equiv), CH_3CN (0.18 g, 0.24 mL, 4.5 mmol, 4.5 equiv) and MeLi-LiBr (2.7 mL, 4.0 mmol, 4.0 equiv) in THF, β-oxonitrile **4d** was obtained in 90% yield (0.130 g) as a light yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.91 (m, 2H, Ph H-2,6), 7.66 (m, 1H, Ph H-4), 7.52 (m, 2H, Ph H-3,5), 4.10 (s, 2H, CH_2CN). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 187.1 (C=O), 134.7 (Ph C-4), 134.2 (Ph C-1), 129.1 (Ph C-3,5), 128.4 (Ph C-2,6), 113.8 (CN), 29.4 (<u>C</u>H_2CN). **^{15}N NMR** (40 MHz, $CDCl_3$) δ: -126.0 (CN). **^{17}O NMR** (54 MHz, $CDCl_3$) δ: 542 (C=O). **IR** (NaCl, ν_{max}, cm^{-1}): 3070, 2253, 1696, 1605,

1002. **Mp:** 80-82 °C (lit.,[3] 81 °C). **Elemental Analysis (%)** for C_9H_7NO. Calcd: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.61; H, 4.99; N, 9.80.

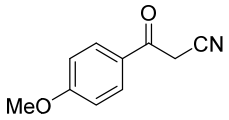
3-[4-(2-methyl-2-propanyl)phenyl]-3-oxopropanenitrile (4e)



By following the general procedure 2, starting from 4-*tert*-butyl-*N*-methoxy-*N*-methylbenzamide (0.221 g, 1.0 mmol, 1.0 equiv), CH_3CN (0.18 g, 0.24 mL, 4.5 mmol, 4.5 equiv) and MeLi-LiBr (2.7 mL, 4.0 mmol, 4.0 equiv) in THF, β-oxonitrile **4e** was obtained in 92% yield (0.185 g) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.85 (m, 2H, Ph H-2,6), 7.53 (m, 2H, Ph H-3,5), 4.06 (s, 2H, CH_2CN) 1.34 (s, 9H, $C(CH_3)_3$). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 186.6 (C=O), 158.8 (Ph C-4), 131.7 (Ph C-1), 128.5 (Ph C-2,6), 126.1 (Ph C-3,5), 113.9 (CN), 35.3 ($\underline{C}(CH_3)_3$), 30.9 ($C(\underline{C}H_3)_3$), 29.2 ($\underline{C}H_2CN$, $^1J(CH_2)$ = 134.3 Hz, $^2J(CN,CH_2)$ = 10.2 Hz). **^{15}N NMR** (40 MHz, $CDCl_3$) δ: -126.5 (CN). **IR** (NaCl, ν_{max}, cm^{-1}): 3076, 2258, 1700. **Mp:** 75°C (lit.,[4] 74-77°C). **Elemental Analysis (%)** for $C_{13}H_{15}NO$. Calcd.: C, 77.58; H, 7.51; N, 6.96. Found: C, 77.72; H, 7.65; N, 7.06.

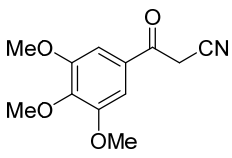
3-(4-methoxyphenyl)-3-oxopropanenitrile (4f)



By following the general procedure 2, starting from *N*,4-dimethoxy-*N*-methylbenzamide (0.195 g, 1.0 mmol, 1.0 equiv), CH_3CN (0.18 g, 0.24 mL, 4.5 mmol, 4.5 equiv) and MeLi-LiBr (2.7 mL, 4.0 mmol, 4.0 equiv) in THF, β-oxonitrile **4f** was obtained in 83% yield (0.141 g) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.89 (m, 2H, Ph H-2,6), 6.97 (m, 2H, Ph H-3,5), 4.02 (s, 2H, CH_2CN), 3.89 (s, 3H, OCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 185.4 (C=O), 164.7 (Ph C-4), 130.9 (Ph C-2,6), 127.2 (Ph C-1), 114.3 (Ph C-3,5), 114.1 (CN), 55.6 (OCH3, $^1J(OCH_3)$ = 144.9 Hz), 29.0 ($\underline{C}H_2CN$, $^1J(CH_2)$ = 134.2 Hz, $^2J(CN,CH_2)$ = 10.2 Hz). **^{15}N NMR** (40 MHz, $CDCl_3$) δ: -126.7 (CN). **^{17}O NMR** (54 MHz, CD_3CN) δ: 521 (C=O), 65 (OCH_3). **IR** (NaCl, ν_{max}, cm^{-1}): 3081, 2250, 1701, 1602, 1524,999. **Mp:** 119-120°C (lit.,[3] 123-126 °C). **Elemental Analysis (%)** for $C_{10}H_9NO_2$. Calcd.: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.69; H, 5.26; N, 8.12.

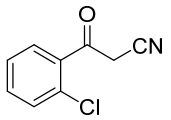
3-oxo-3-(3,4,5- trimethoxyphenyl)propanenitrile (4g)



By following the general procedure 2, starting from *N*,3,4,5-tetramethoxy-*N*-methylbenzamide (0.225 g, 1.0 mmol, 1.0 equiv), CH_3CN (0.18 g, 0.24 mL, 4.5 mmol, 4.5 equiv) and MeLi-LiBr (2.7 mL, 4.0 mmol, 4.0 equiv) in THF, β-oxonitrile **4g** was obtained in 79% yield (0.190 g) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.15 (s, 2H, Ph H-2,6), 4.05 (s, 2H, CH_2CN), 3.94 (s, 3H, Ph 4-OCH_3), 3.92 (s, 6H, Ph 3,5-OCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 185.8 (C=O), 153.3 (Ph C-3,5) 144.1 (Ph C-4), 129.2 (Ph C-1), 113.8 (CN), 106.1 (Ph C-2,6), 61.0 (Ph C-4-O<u>C</u>H_3), 56.4 (Ph C-3,5-O<u>C</u>H_3), 29.2 (<u>C</u>H_2CN). **^{15}N NMR** (40 MHz, $CDCl_3$) δ: -126.0 (CN). **IR** (NaCl, ν_{max}, cm^{-1}): 3077, 2253, 1706, 1598, 1520. **Mp:** 129-130°C. **Elemental Analysis (%)** for $C_{12}H_{13}NO_4$. Calcd.: C, 61.27; H, 5.57; N, 5.95. Found: C, 61.40; H, 5.69; N, 6.09.

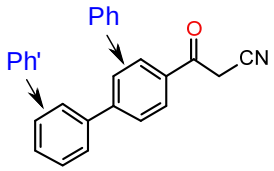
3-(2-chlorophenyl)-3-oxopropanenitrile (4h)



By following the general procedure 2, starting from 2-chloro-*N*-methoxy-*N*-methylbenzamide (0.200 g, 1.0 mmol, 1.0 equiv), CH_3CN (0.18 g, 0.24 mL, 4.5 mmol, 4.5 equiv) and MeLi-LiBr (2.7 mL, 4.0 mmol, 4.0 equiv) in THF, β-oxonitrile **4h** was obtained in 89% yield (0.162 g) as a yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.63 (m, 1H, Ph H-6), 7.51 (m, 1H, Ph H-4), 7.47 (m, 1H, Ph H-3), 7.40 (m, 1H, Ph H-5), 4.15 (s, 2H, CH_2CN). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 189.4 (C=O), 135.6 (Ph C-1), 133.7 (Ph C-4), 131.7 (Ph C-2), 131.0 (Ph C-3), 130.4 (Ph C-6), 127.5 (Ph C-5), 113.3 (CN), 32.9 (<u>C</u>H_2CN). **^{15}N NMR** (40 MHz, $CDCl_3$) δ: -126.5 (CN). **IR** (NaCl, ν_{max}, cm^{-1}): 3082, 2256, 1698, 1002. **Mp:** 51-54 °C (lit.,[5] 50-54°C). **Elemental Analysis (%)** for C_9H_6ClNO. Calcd.: C, 60.19; H, 3.37; N, 7.80. Found: C, 60.30; H, 3.48; N, 7.89.

3-(4-biphenylyl)-3-oxopropanenitrile (4i)

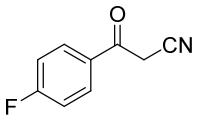


By following the general procedure 2, starting from *N*-methoxy-*N*-methyl-4-phenylbenzamide (0.241 g, 1.0 mmol, 1.0 equiv), CH_3CN (0.18 g, 0.24 mL, 4.5 mmol, 4.5 equiv) and MeLi-LiBr (2.7 mL, 4.0 mmol, 4.0 equiv) in THF, β-oxonitrile **4i** was obtained in 91% yield (0.203g) as a yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00 (m, 2H, Ph H-2,6), 7.74 (m, 2H, Ph H-3,5), 7.63 (m, 2H, Ph´ H-2,6), 7.49 (m, 2H, Ph´ H-3,5), 7.43 (m, 1H, Ph´ H-4), 4.11 (s, 2H, CH_2CN). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 186.6 (C=O), 147.5 (Ph C-4), 139.2 (Ph´ C-1), 132.9 (Ph C-1), 129.1 (Ph C-2,6, Ph´ C-3,5), 128.7 (Ph´ C-4), 127.7 (Ph C-3,5), 127.3 (Ph´ C-2,6), 113.8 (CN), 29.4 (<u>C</u>H_2CN). **IR** (NaCl, ν_{max}, cm^{-}

[1]): 3078, 2252, 1703, 1595, 996. **Mp:** 112 °C (lit.,[6] 112-113 °C). **Elemental Analysis (%)** for $C_{15}H_{11}NO$. Calcd.: C, 81.43; H, 5.01; N, 6.33. Found: C, 81.52; H, 5.12; N, 6.48.

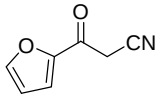
3-(4-fluorophenyl)-3-oxopropanenitrile (4j)



By following the general procedure 2, starting from 4-fluoro-*N*-methoxy-*N*-methylbenzamide (0.183 g, 1.0 mmol, 1.0 equiv), CH_3CN (0.18 g, 0.24 mL, 4.5 mmol, 4.5 equiv) and MeLi-LiBr (2.7 mL, 4.0 mmol, 4.0 equiv) in THF, β-oxonitrile **4j** was obtained in 93% yield (0.151 g) as a light yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (m, 2H, Ph H-2,6), 7.20 (m, 2H, Ph H-3,5), 4.08 (s, 2H, CH_2CN). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 185.6 (C=O), 166.6 (Ph C-4, $^1J_{C,F}$ = 258.1 Hz), 131.3 (Ph C-2,6, $^3J_{C,F}$ = 9.7 Hz), 130.7 (Ph C-1, $^4J_{C,F}$ = 3.0 Hz), 116.4 (Ph C-3,5 $^2J_{C,F}$ = 22.2 Hz), 113.6 (CN), 29.4 ($\underline{C}H_2CN$). **^{15}N NMR** (40 MHz, $CDCl_3$) δ: -125.6 (CN). **^{17}O NMR** (54 MHz, $CDCl_3$) δ: 536. **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -101.6 (m). **IR** (NaCl, ν_{max}, cm^{-1}): 3078, 2252, 1703, 1595, 996. **Mp:** 85-86°C (lit.,[3] 84-86 °C). **Elemental Analysis (%)** for C_9H_6FNO. Calcd.: C, 66.26; H, 3.71; N, 8.59. Found: C, 66.38; H, 3.79; N, 8.71.

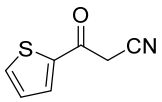
3-(2-furyl)-3-oxopropanenitrile (4k)



By following the general procedure 2, starting from *N*-methoxy-*N*-methyl-2-furancarboxamide (0.155 g, 1.0 mmol, 1.0 equiv), CH_3CN (0.18 g, 0.24 mL, 4.5 mmol, 4.5 equiv) and MeLi-LiBr (2.7 mL, 4.0 mmol, 4.0 equiv) in THF, β-oxonitrile **4k** was obtained in 82% yield (0.114 g) as a light yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.65 (d, *J* = 1.6 Hz, 1H, Furyl H-5), 7.36 (d, *J* = 3.6 Hz, 1H, Furyl H-3), 6.62 (dd, *J* = 3.6, 1.6 Hz, 1H, Furyl H-4), 3.98 (s, 2H, CH_2CN). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 175.8 (C=O), 150.3 (Furyl C-2), 147.8 (Furyl C-5), 119.3 (Furyl C-3), 113.4 (CN), 113.3 (Furyl C-4), 28.8 ($\underline{C}H_2CN$, $^1J(CH_2)$=135.6 Hz). **^{15}N NMR** (40 MHz, $CDCl_3$) δ: -126.9 (CN). **^{17}O NMR** (54 MHz, $CDCl_3$) δ: 510 (C=O), 239 (Furan-O). **IR** (NaCl, ν_{max}, cm^{-1}): 2247, 1699, 998. **Mp:** 69 °C (lit.,[7] 66-68 °C). **Elemental Analysis (%)** for $C_7H_5NO_2$. Calcd.: C, 62.22; H, 3.73; N, 10.37. Found: C, 62.35; H, 3.81; N, 10.46.

3-oxo-3-(2-thienyl)propanenitrile (4l)

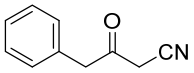


By following the general procedure 2, starting from *N*-methoxy-*N*-methyl-2-thiophenecarboxamide (0.171 g, 1.0 mmol, 1.0 equiv), CH_3CN (0.18 g, 0.24 mL, 4.5 mmol, 4.5 equiv) and MeLi-LiBr (2.7

mL, 4.0 mmol, 4.0 equiv) in THF, β-oxonitrile **4l** was obtained in 80% yield (0.123 g) as a yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.79 (dd, *J* = 4.9, 1.1 Hz, 1H, Th H-5), 7.78 (dd, *J* = 3.9, 1.1 Hz, 1H, Th H-3), 7.20 (dd, *J* = 4.9, 3.9 Hz, 1H, Th H-4), 4.01 (s, 2H, CH_2CN). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 179.5 (C=O), 140.8 (Th C-2, ^2J(C-2,H-3) = 7.0 Hz, ^3J(C-2,H-4) = 9.0 Hz, ^3J(C-2,H-5) = 5.9 Hz), 136.3 (Th C-5, ^1J(C-5,H-5) = 186.4 Hz, ^2J(C-5,H-4) = 7.2 Hz, ^3J(C-5,H-3) = 10.9 Hz), 133.7 (Th C-3, ^1J(C-3,H-3) = 167.8 Hz, ^2J(C-3,H-4) = 5.5 Hz, ^3J(C-3,H-5) = 9.3 Hz), 128.7 (Th C-4, ^1J(C-4,H-4) = 171.6 Hz, ^2J(C-4,H-3) = 4.1 Hz, ^3J(C-4,H-5) = 4.1 Hz), 113.4 (CN, ^2J(CN,CH_2) = 10.3 Hz), 29.5 ($\underline{C}H_2CN$, ^1J(CH_2) = 135.0 Hz). **IR** (NaCl, ν_{max}, cm^{-1}): 3079, 2254, 1691. **Mp:** 133 °C (lit.,[3] 131-135 °C). **Elemental Analysis (%)** for C_7H_5NOS. Calcd.: C, 55.61; H, 3.33; N, 9.26; S, 21.21. Found: C, 55.71; H, 3.41; N, 9.40; S, 21.12.

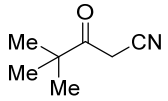
3-oxo-4-phenylbutanenitrile (4m)



By following the general procedure 2, starting from *N*-methoxy-*N*-methyl-2-phenylacetamide (0.179 g, 1.0 mmol, 1.0 equiv), CH_3CN (0.18 g, 0.24 mL, 4.5 mmol, 4.5 equiv) and MeLi-LiBr (2.7 mL, 4.0 mmol, 4.0 equiv) in THF, β-oxonitrile **4m** was obtained in 84% yield (0.132 g) as a yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35 (m, 2H, Ph H-3,5), 7.31 (m, 1H, Ph H-4), 7.20 (m, 2H, Ph H-2,6), 3.82 (s, 2H, Ph-$C\underline{H}_2$), 3.48 (s, 2H, CH_2CN). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 195.6 (C=O), 131.9 (Ph C-1), 129.3 (Ph C-2,6), 129.0 (Ph C-3,5), 127.7 (Ph C-4), 113.7 (CN), 48.9 (Ph-$\underline{C}$H), 31.2 ($\underline{C}H_2CN$). **^{15}N NMR** (40 MHz, $CDCl_3$) δ: -126.8 (CN) **^{17}O NMR** (54 MHz, $CDCl_3$) δ: 574 (C=O). **IR** (NaCl, ν_{max}, cm^{-1}): 2248, 1702. **Mp:** 30 °C (lit.,[8] 29 °C). **Elemental Analysis (%)** for $C_{10}H_9NO$. Calcd.: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.55; H, 5.82; N, 8.94.

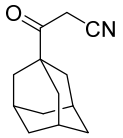
4,4-dimethyl-3-oxopentanenitrile (4n)



By following the general procedure 2, starting from *N*-methoxy-*N*,2,2-trimethylpropanamide (0.145 g, 1.0 mmol, 1.0 equiv), CH_3CN (0.18 g, 0.24 mL, 4.5 mmol, 4.5 equiv) and MeLi-LiBr (2.7 mL, 4.0 mmol, 4.0 equiv) in THF, β-oxonitrile **4n** was obtained in 74% yield (0.092 g) as a light brown solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.64 (s, 2H, CH_2CN), 1.18 (s, 9H, $C(CH_3)_3$). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 202.8 (C=O), 114.1 (CN), 44.5 ($\underline{C}(CH_3)_3$), 27.4 ($\underline{C}H_2CN$, ^1J(CH_2) = 134.1 Hz), 26.0 ($C(\underline{C}H_3)_3$, ^1J(CH_3) = 127.6 Hz). **^{15}N NMR** (40 MHz, $CDCl_3$) δ: -127.8 (CN). **^{17}O NMR** (54 MHz, $CDCl_3$) δ: 560 (C=O). **IR** (NaCl, ν_{max}, cm^{-1}): 2252, 1699. **Mp**: 70 °C (lit.,[2] 70 °C). **Elemental Analysis (%)** for $C_7H_{11}NO$. Calcd.: C, 67.17; H, 8.86; N, 11.19. Found: C, 67.29; H, 8.97; N, 11.31.

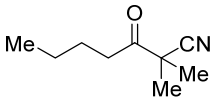
3-(adamantan-1-yl)-3-oxopropenenitrile (4o)



By following the general procedure 2, starting from *N*-methoxy-*N*-methyl-1-adamantanecarboxamide (0.223 g, 1.0 mmol, 1.0 equiv), CH_3CN (0.18 g, 0.24 mL, 4.5 mmol, 4.5 equiv) and MeLi-LiBr (2.7 mL, 4.0 mmol, 4.0 equiv) in THF, β-oxonitrile **4o** was obtained in 68% yield (0.145 g) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.58 (s, 2H, CH_2CN), 2.08 (m, 3H, Adamant H-3,5,7), 1.82 (d, J = 2.8 Hz, 6H, Adamant H-2,8,9), 1.76 (m, 3H, Adamant H-4,6,10) 1.68 (m, 3H, Adamant H-4, 6, 10). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 202.2 (C=O), 114.1 (CN), 46.8 (Adamant C-1), 37.9 (Adamant C-2,8,9), 36.1 (Adamant C-4,6,10), 27.6 (Adamant C-3,5,7), 27.0 ($\underline{C}H_2CN$). **^{15}N NMR** (40 MHz, $CDCl_3$) δ: -127.5 (CN). **^{17}O NMR** (54 MHz, $CDCl_3$) δ: 561 (C=O). **IR** (NaCl, ν_{max}, cm^{-1}): 2249, 1703, 998. **Mp**: 112 °C. **Elemental Analysis (%)** for $C_{13}H_{17}NO$. Calcd.: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.92; H, 8.52; N, 6.99.

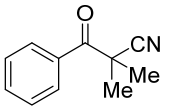
2,2-dimethyl-3-oxoheptanenitrile (6a)



By following the general procedure 2, starting from *N*-methoxy-*N*-methylpentanamide (0.145 g, 1.0 mmol, 1.0 equiv), $(CH_3)_2CCN$ (0.31 g, 0.4 mL, 4.5 mmol, 4.5 equiv) and MeLi-LiBr (2.7 mL, 4.0 mmol, 4.0 equiv) in THF, β-oxonitrile **6a** was obtained in 82% yield (0.121 g) as a light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.77 (t, J = 7.3 Hz, 2H, CH_2CO), 1.59 (m, 2H, $C\underline{H}_2CH_2CO$), 1.47 (s, 6H, $C(C\underline{H}_3)_2$), 1.32 (m, 2H, $C\underline{H}_2CH_3$), 0.91 (t, J = 7.4 Hz, 3H, $CH_2C\underline{H}_3$). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 204.3 (C=O), 122.0 (CN), 43.5 ($\underline{C}(CH_3)_2$), 38.3 ($\underline{C}H_2CO$), 25.6 ($\underline{C}H_2CH_2CO$), 23.8 ($C(\underline{C}H_3)_2$), 22.0 ($\underline{C}H_2CH_3$), 13.7 ($CH_2\underline{C}H_3$). **IR** (NaCl, ν_{max}, cm^{-1}): 2253, 1709. **Elemental Analysis (%)** for $C_9H_{15}NO$. Calcd.: C, 70.55; H, 9.87; N, 9.14. Found: C, 70.77; H, 10.01; N, 9.28.

2, dimethyl-3-oxo-3-phenylpropanenitrile (6b)

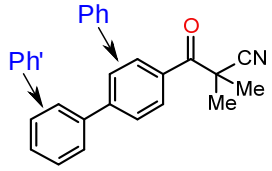


By following the general procedure 2, starting from *N*-methoxy-*N*-methylbenzamide (0.165 g, 1.0 mmol, 1.0 equiv), $(CH_3)_2CCN$ (0.31 g, 0.4 mL, 4.5 mmol, 4.5 equiv) and MeLi-LiBr (2.7 mL, 4.0 mmol, 4.0 equiv) in THF, β-oxonitrile **6b** was obtained in 86% yield (0.149 g) as a light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.14 (m, 2H, Ph H-2,6), 7.58 (m, 1H, Ph H-4), 7.47 (m, 2H, Ph H-3,5), 1.69 (s, 6H, $C(C\underline{H}_3)_2$). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 193.7 (C=O), 133.6 (Ph C-4), 133.4 (Ph C-1), 129.2 (Ph C-2,6), 128.5 (Ph C-3,5), 122.4 (CN), 40.6 ($\underline{C}CN$), 25.4 ($C(\underline{C}H_3)_2$). **^{15}N NMR** (40 MHz,

$CDCl_3$) δ: -129.0 (CN). **IR** (NaCl, ν_{max}, cm^{-1}): 3081, 2260, 1713, 1523, 1491, 1001. **Elemental Analysis (%)** for $C_{11}H_{11}NO$. Calcd.: C, 76.28; H, 6.40; N, 8.09. Found: C, 76.39; H, 6.54; N, 8.22.

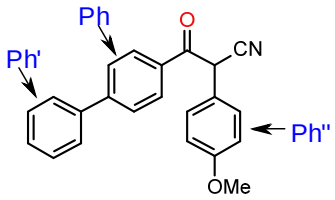
3-(4-biphenylyl)-2,2-dimethyl-3-oxopropanenitrile (6c)



By following the general procedure 2, starting from *N*-methoxy-*N*-methyl-4-phenylbenzamide (0.241 g, 1.0 mmol, 1.0 equiv), $(CH_3)_2CCN$ (0.31 g, 0.4 mL, 4.5 mmol, 4.5 equiv) and MeLi-LiBr (2.7 mL, 4.0 mmol, 4.0 equiv) in THF, β-oxonitrile **6c** was obtained in 87% yield (0.217 g) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.26 (m, 2H, Ph H-2,6), 7.73 (m, 2H, Ph H-3,5), 7.64 (m, 2H, Ph´ H-2,6), 7.49 (m, 2H, Ph´ H-3,5), 7.42 (m, 1H, Ph´ H-4), 1.76 (s, 6H, $(C\underline{H}_3)_2C$). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 193.3 (C=O), 146.5 (Ph C-4), 139.4 (Ph´ C-1), 132.1 (Ph C-1), 130.1 (Ph C-2,6), 129.0 (Ph´ C-3,5), 128.5 (Ph´ C-4), 127.3 (Ph C-3,5, Ph´ C-2,6), 122.7 (CN), 40.7 ($\underline{C}CN$), 25.6 ($C(\underline{C}H_3)_2$). **^{15}N NMR** (40 MHz, $CDCl_3$) δ: -130.3 (CN). **IR** (NaCl, ν_{max}, cm^{-1}): 3081, 2260, 1713, 1523, 1491, 1001. **Mp**: 96-97 °C. **Elemental Analysis (%)** for $C_{17}H_{15}NO$. Calcd.: C, 81.90; H, 6.06; N, 5.62. Found: C, 82.12; H, 6.18; N, 5.77.

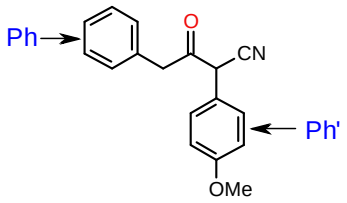
3-(4-biphenylyl)-2-(4-methoxyphenyl)-3-oxopropanenitrile (6d)



By following the general procedure 2, starting from *N*-methoxy-*N*-methyl-4-phenylbenzamide (0.241 g, 1.0 mmol, 1.0 equiv), 4-Methoxyphenylacetonitrile (0.66 g, 0.36 mL, 4.5 mmol, 4.5 equiv) and MeLi-LiBr (2.7 mL, 4.0 mmol, 4.0 equiv) in THF, β-oxonitrile **6d** was obtained in 80% yield (0.261 g) as a pink solid

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.01 (m, 2H, Ph H-2,6), 7.67 (m, 2H, Ph H-3,5), 7.59 (m, 2H, Ph´ H-2,6), 7.47 (m, 2H, Ph´ H-3,5), 7.41 (m, 1H, Ph´ H-4), 7.38 (m, 2H, Ph´´ H-2, 6), 6.92 (m, 2H, Ph´´ H-3, 5), 5.59 (s, 1H, -HCCN), 3.79 (s, 3H, OCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 188.6 (C=O), 160.1 (Ph´´ C-4), 147.0 (Ph C-4), 139.2 (Ph´ C-1), 132.2 (Ph C-1), 129.8 (Ph C-2,6), 129.5 (Ph´´ C-2,6), 129.0 (Ph´ C-3,5), 128.6 (Ph´ C-4), 127.5 (Ph C-3,5), 127.2 (Ph´ C-2,6), 122.2 (Ph´´ C-1), 116.8 (CN), 115.1 (Ph ´´ C-3,5), 55.3 (OCH_3) 46.0 (-$\underline{C}$HCN). **^{15}N NMR** (40 MHz, $CDCl_3$) δ: -127.1 (CN). **IR** (NaCl, ν_{max}, cm^{-1}): 3083, 2256, 1708, 997. **Mp**: 108 °C. **Elemental Analysis (%)** for $C_{22}H_{17}NO_2$. Calcd.: C, 80.71; H, 5.23; N, 4.28. Found: C, 80.84; H, 5.32; N, 4.36.

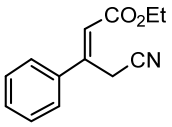
2-(4-methoxyphenyl)-3-oxo-4-phenylbutanenitrile (6e)



By following the general procedure 2, starting from *N*-methoxy-*N*-methyl-2-phenylacetamide (0.179 g, 1.0 mmol, 1.0 equiv), 4-methoxyphenylacetonitrile (0.66 g, 0.36 mL, 4.5 mmol, 4.5 equiv) and MeLi-LiBr (2.7 mL, 4.0 mmol, 4.0 equiv) in THF, β-oxonitrile **6e** was obtained in 77% yield (0.204 g) as a viscous yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.31 (m, 3H, Ph H-3,4,5), 7.24 (m, 2H, Ph´ H-2,6), 7.07 (m, 2H, Ph H-2,6), 6.94 (m, 2H, Ph´ H-3,5), 4.73 (s, 1H, CHCN), 3.83 and 3.76, (AB-System, ^{2}J = 15.9 Hz, 2H, $COC\underline{H}_2$), 3.82 (s, 3H, OCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 196.6 (C=O), 160.2 (Ph´ C-4), 132.1 (Ph C-1), 129.5 (Ph´ C-2,6), 129.4 (Ph C-2,6), 128.8 (Ph C-3,5), 127.5 (Ph C-4), 121.3 (Ph´ C-1), 116.3 (CN), 115.0 (Ph´ C-3,5), 55.3 (OCH_3), 49.0 ($\underline{C}HCN$), 46.3 (CH_2). **^{15}N NMR** (40 MHz, $CDCl_3$) δ: -126.3 (CN). **IR** (NaCl, ν_{max}, cm^{-1}): 2261, 1702. **Elemental Analysis (%)** for $C_{17}H_{15}NO_2$. Calcd.: C, 76.96; H, 5.70; N, 5.28. Found: C, 77.10; H, 5.81; N, 5.40.

Synthesis of ethyl (2*E*)-4-cyano-3-phenyl-2-butenoate (7)



To a solution of cyanoketone **4d** (145 mg, 1.0 mmol, 1.0 equiv) dissolved in dry 2-MeTHF (2 mL) was added (carbethoxymethylene)triphenylphosphorane (383 mg, 1.1 mmol, 1.1 equiv) and the resulting mixture was stirred for 16 h at rt. Then, a saturated solution of NH_4Cl (aq) was added and the organic phase directly extracted in 2-MeTHF, dried over Na_2SO_4 and filtered. After removal of the solvent under reduced pressure and purification of the crude through silica gel chromatography (petroleum ether – ethyl acetate, 95:5), compound **7** was obtained as a yellowish oil (187 mg, 87% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.50 – 7.33 (m, 5H, Ph-H), 5.78 (s, 1H, alkene-H), 4.13 (q, J = 7.1 Hz, 2H, OCH_2), 3.89 (s, 2H, $C\underline{H}_2CN$), 1.19 (t, J = 7.1 Hz, 3H, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 168.6, 155.9, 136.9, 129.0, 126.10, 116.8, 99.1, 61.5, 39.3, 13.9. **IR** (NaCl, ν_{max}, cm^{-1}): 2250, 1711, 1490, 998. **Elemental Analysis (%)** for $C_{13}H_{13}NO_2$. Calcd: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.74; H, 6.26; N, 6.31.

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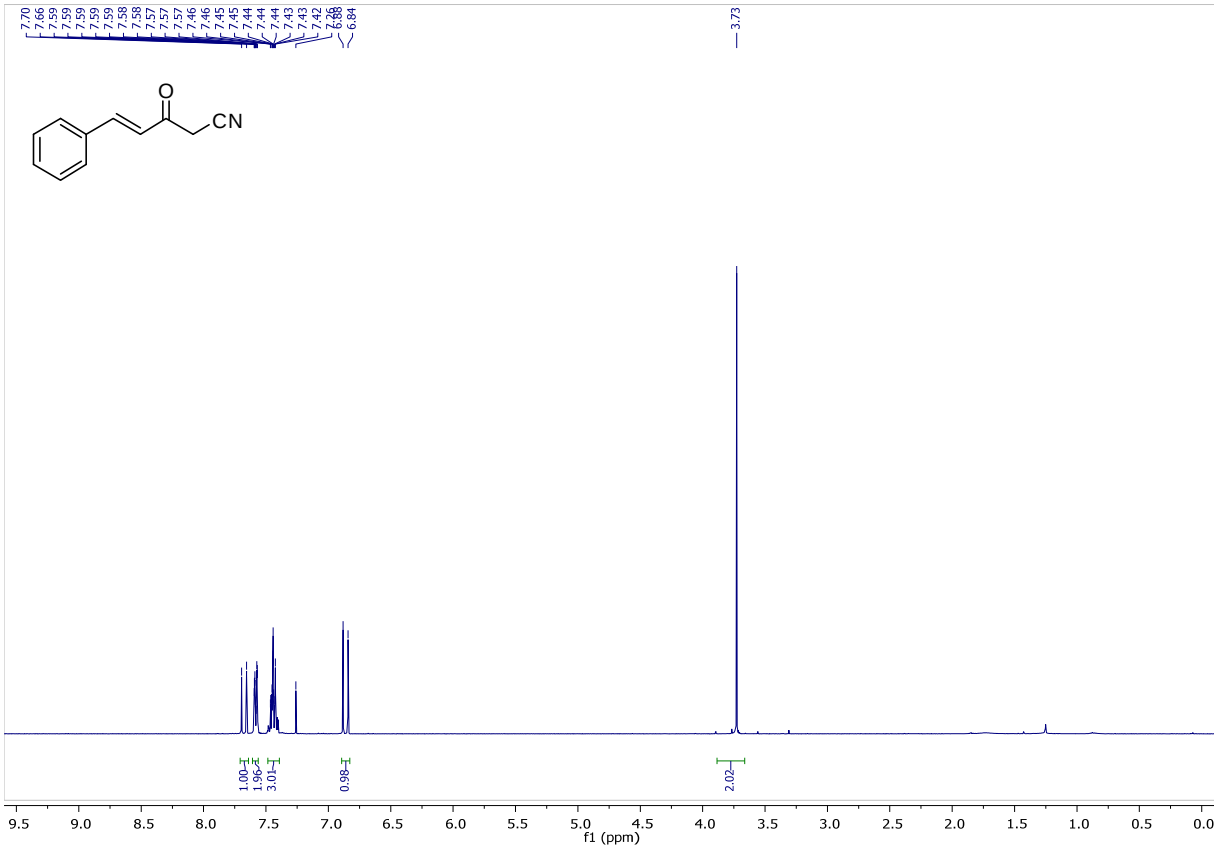
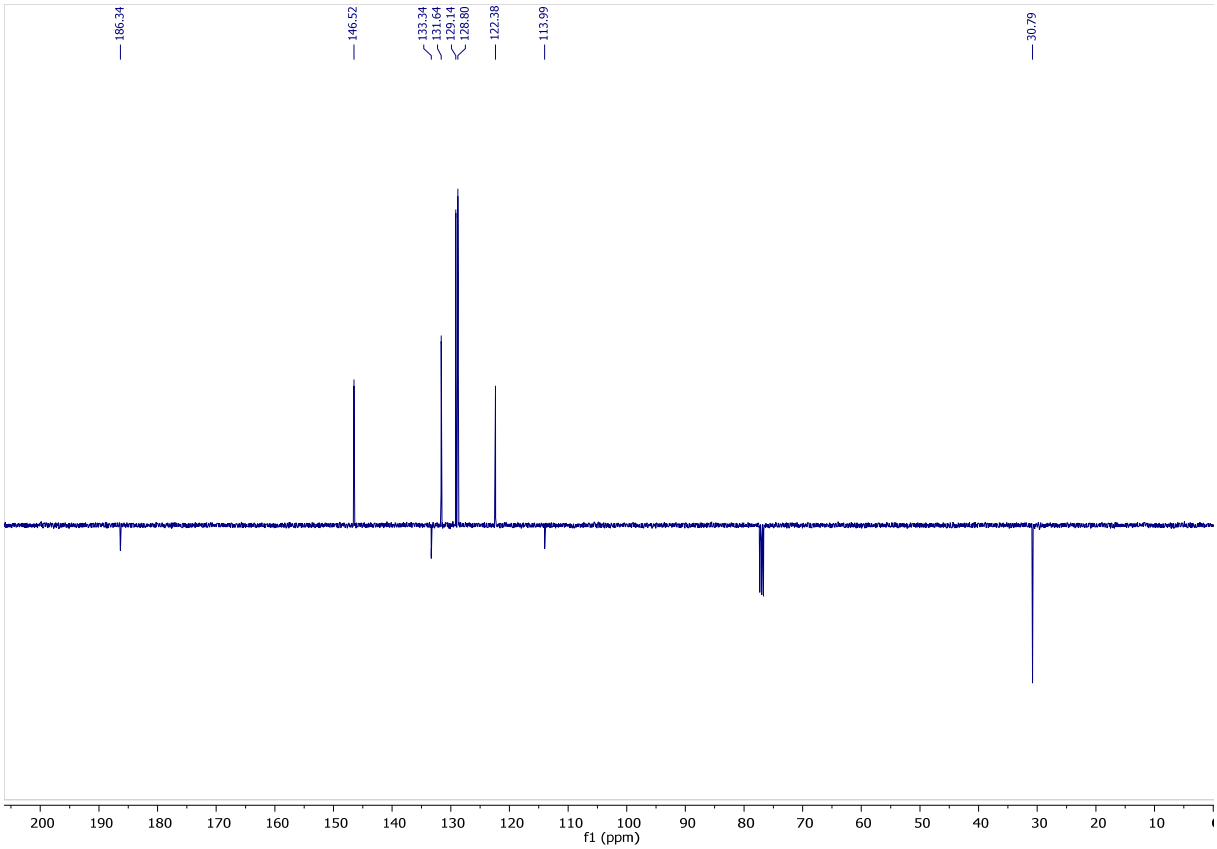
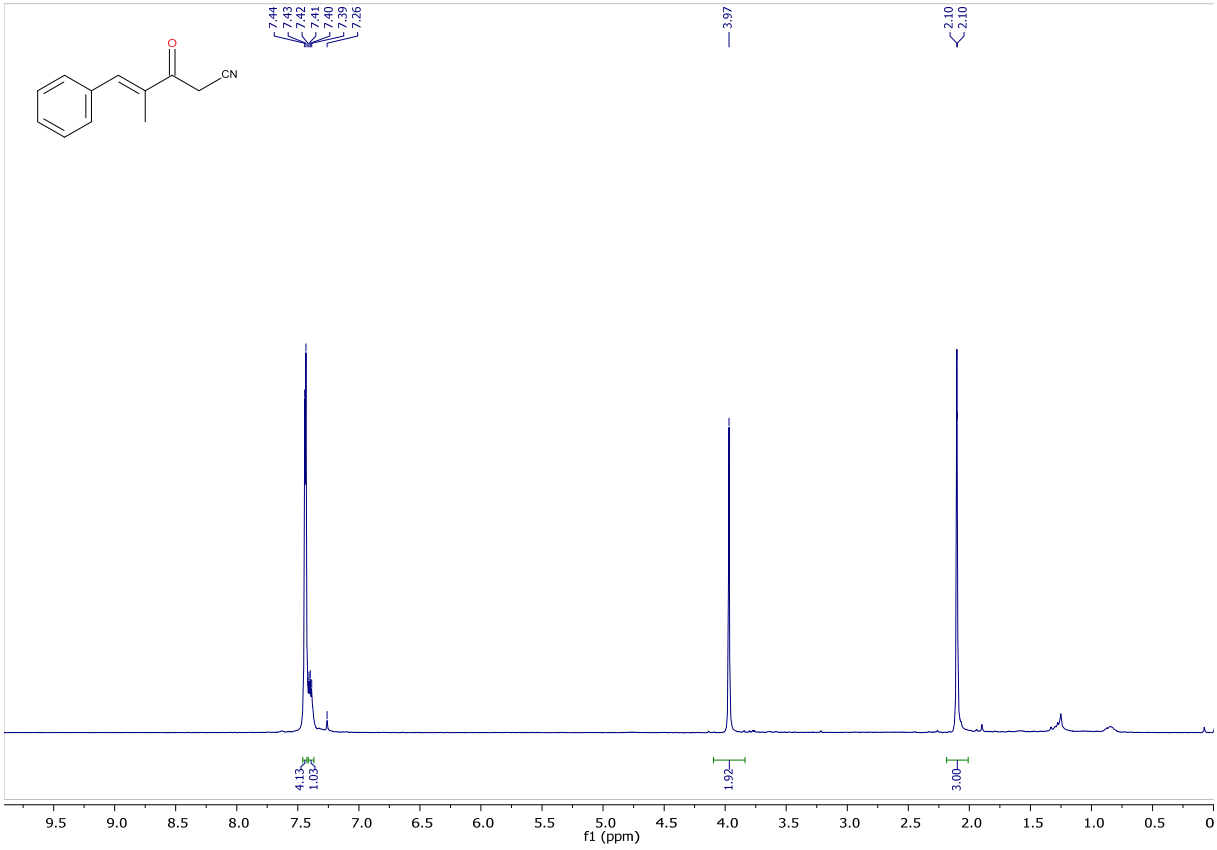
Copies of ^{1}H and ^{13}C spectra for all the compounds.

2





4a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3.97
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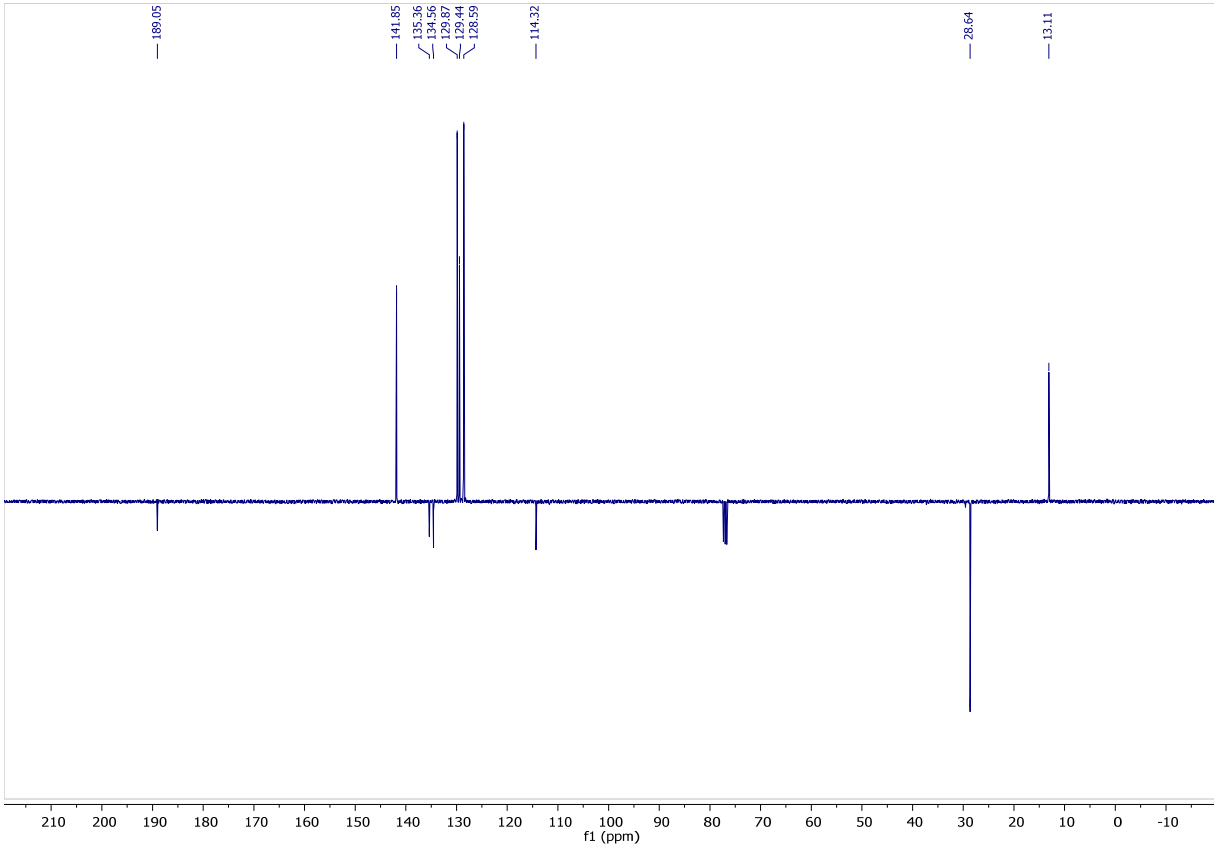
2.10
O
CN
4.13
1.03
1.92
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)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141.85
135.36
134.56
129.87
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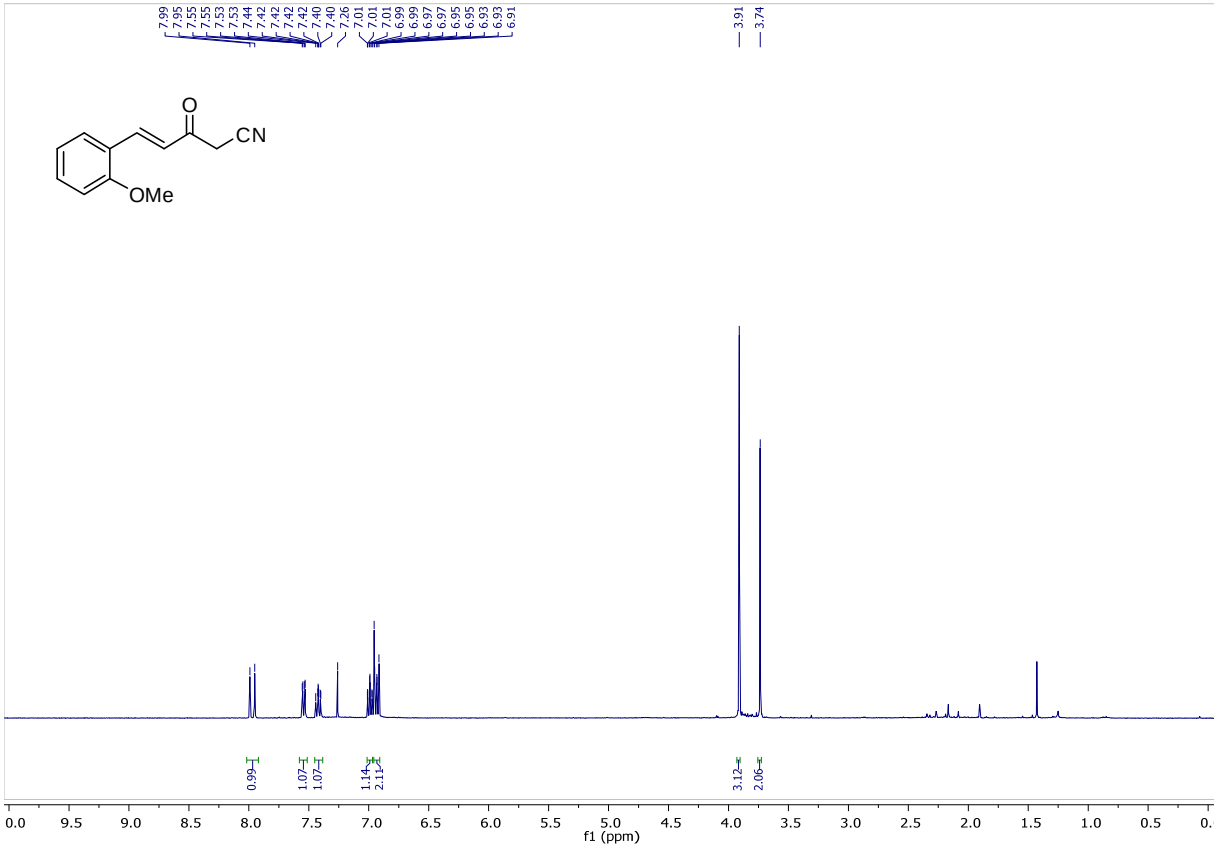
114.32
28.64
13.11
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

4b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7.42
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7.42
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7.40
7.40
7.26
7.01
7.01
7.01
6.99
6.99
6.97
6.97
6.95
6.95
6.93
6.93
6.91
3.91
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O
CN
OMe
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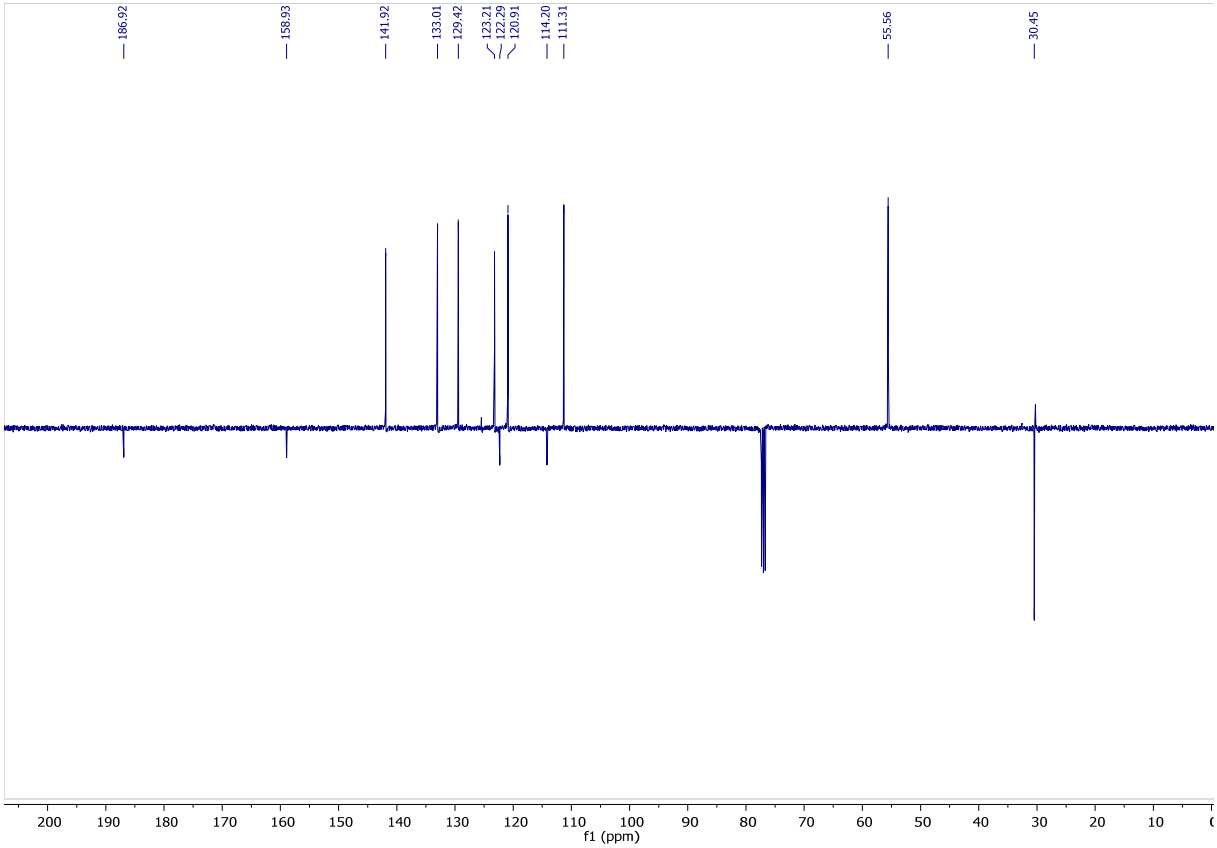
1.07
1.07
1.14
2.13
3.12
2.06
f1 (ppm)


186.92
158.93
141.92
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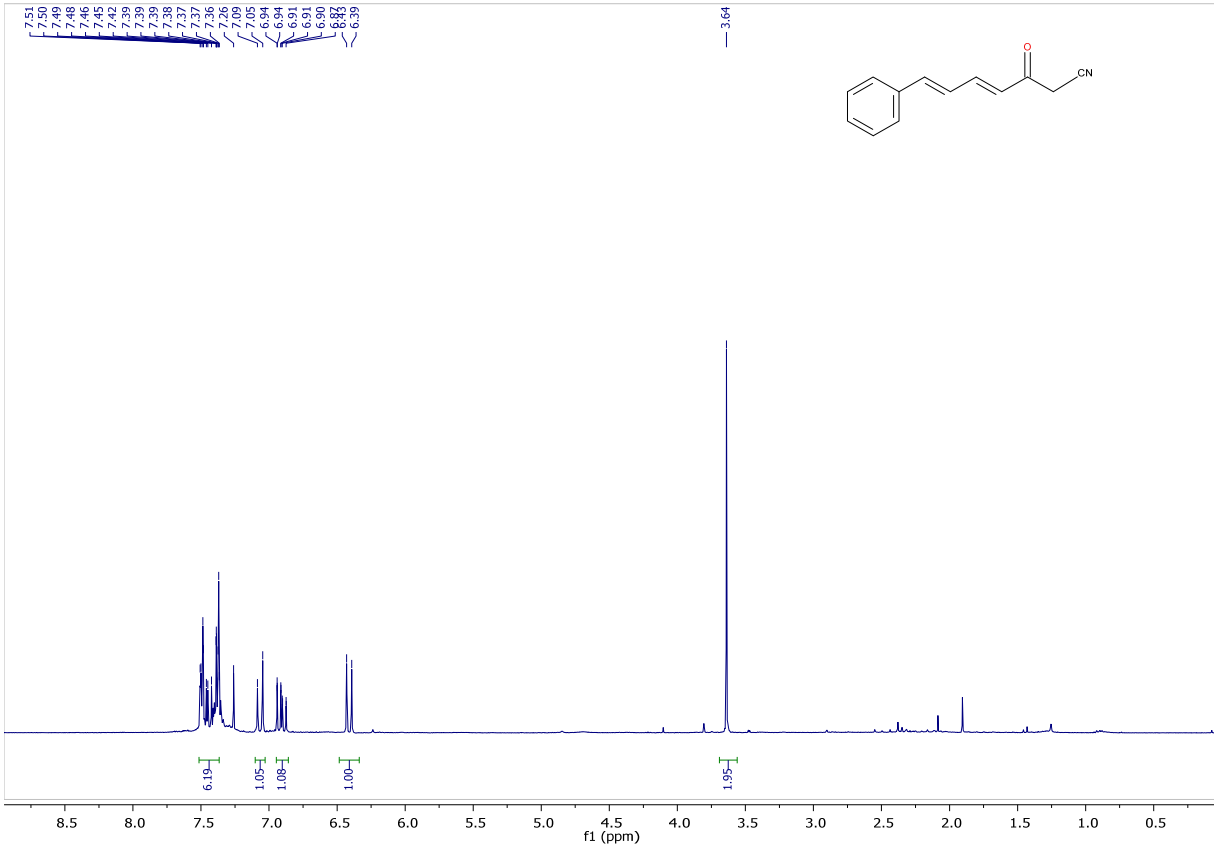
123.21
122.29
120.91
114.20
111.31
55.56
30.45
f1 (ppm)

4c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7.37
7.36
7.26
7.09
7.05
6.94
6.94
6.91
6.91
6.90
6.43
6.43
6.39
3.64
O
CN
6.19
1.05
1.08
1.00
1.95
8.5
8.0
7.5
7.0
6.5
6.0
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3.0
2.5
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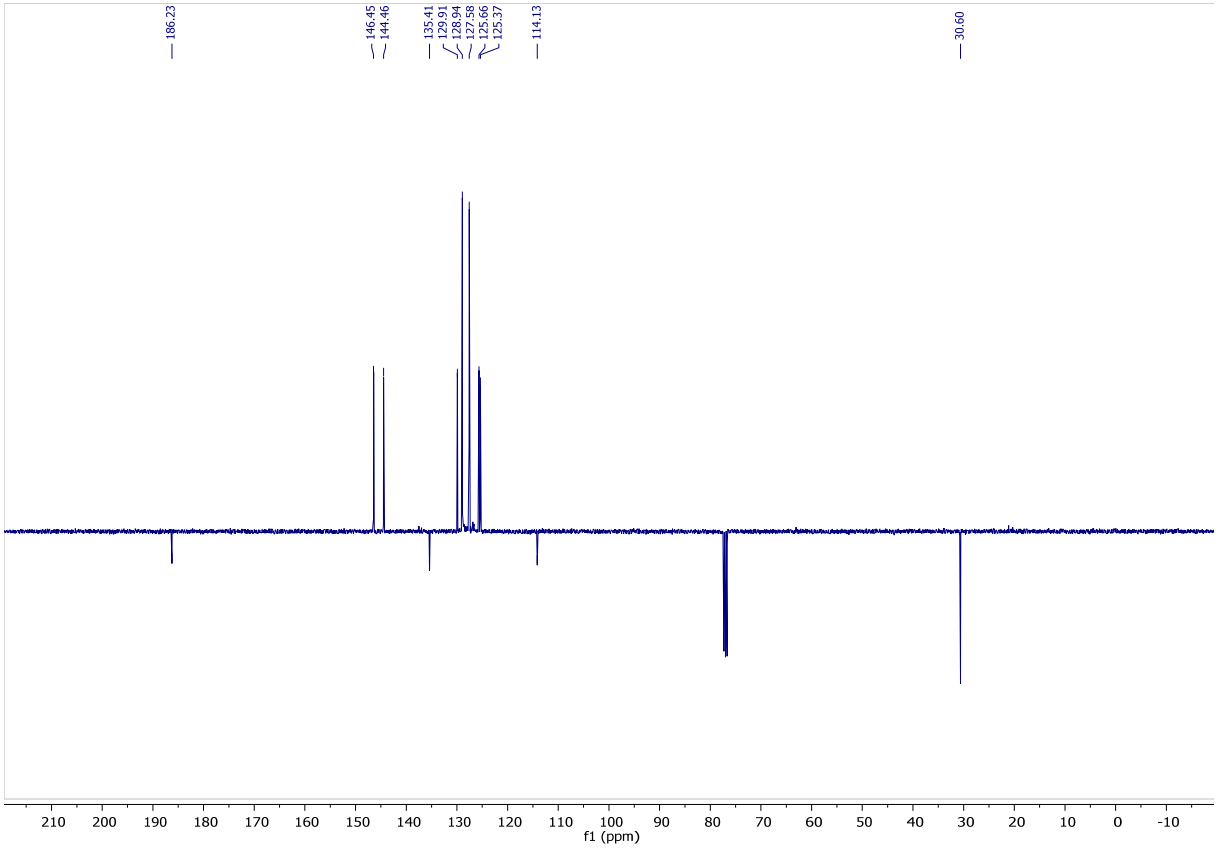
1.5
1.0
0.5
f1 (ppm)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144.46
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129.91
128.94
127.58
125.66
125.37
114.13
30.60
210
200
190
180
170
160
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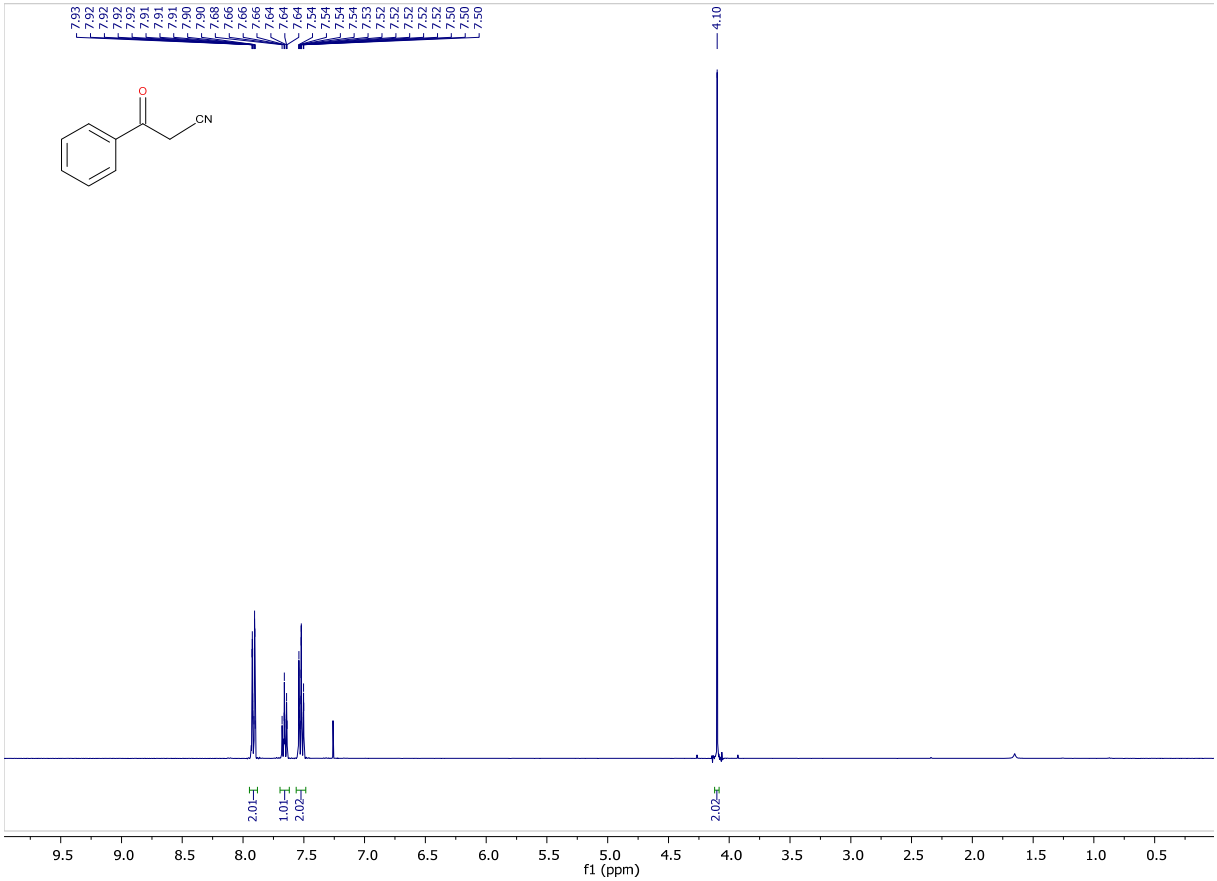
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

4d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7.64
7.64
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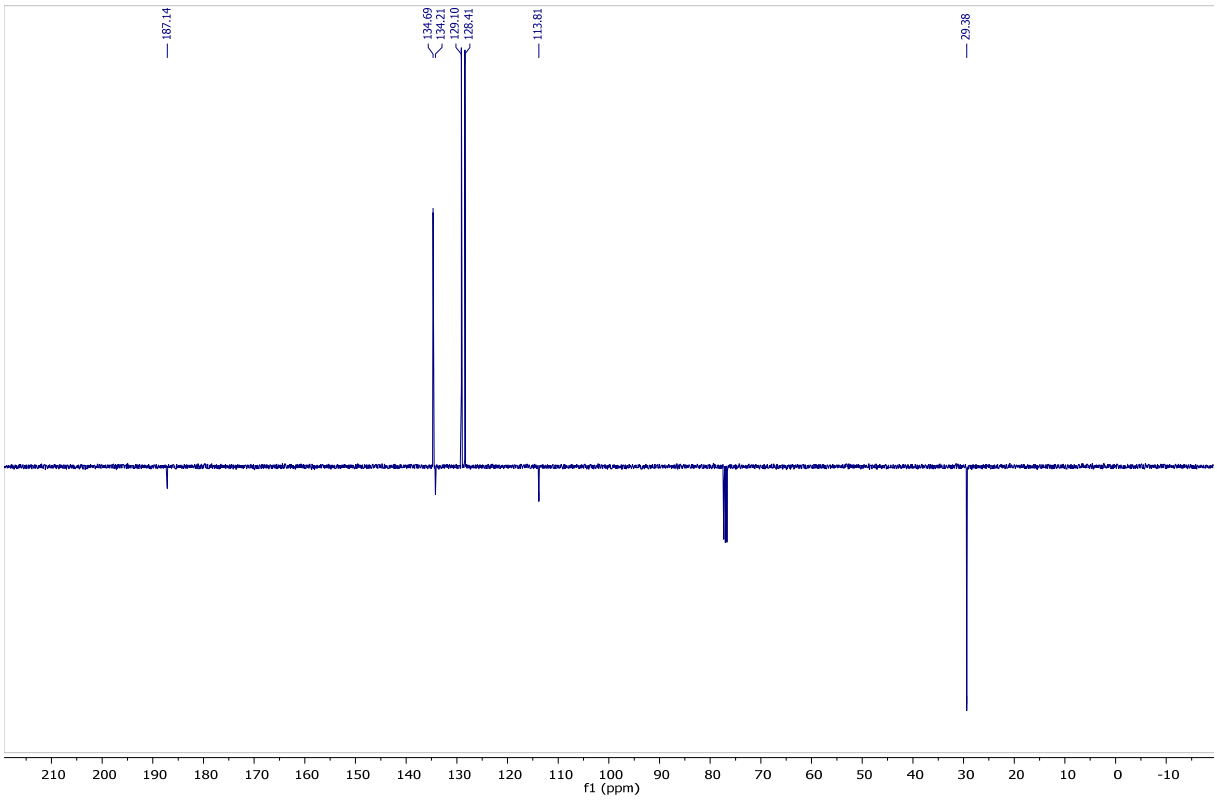
7.54
7.54
7.53
7.52
7.52
7.52
7.52
7.52
7.50
7.50
7.50
4.10
O
CN
2.01
1.01
2.02
2.02
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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134.69
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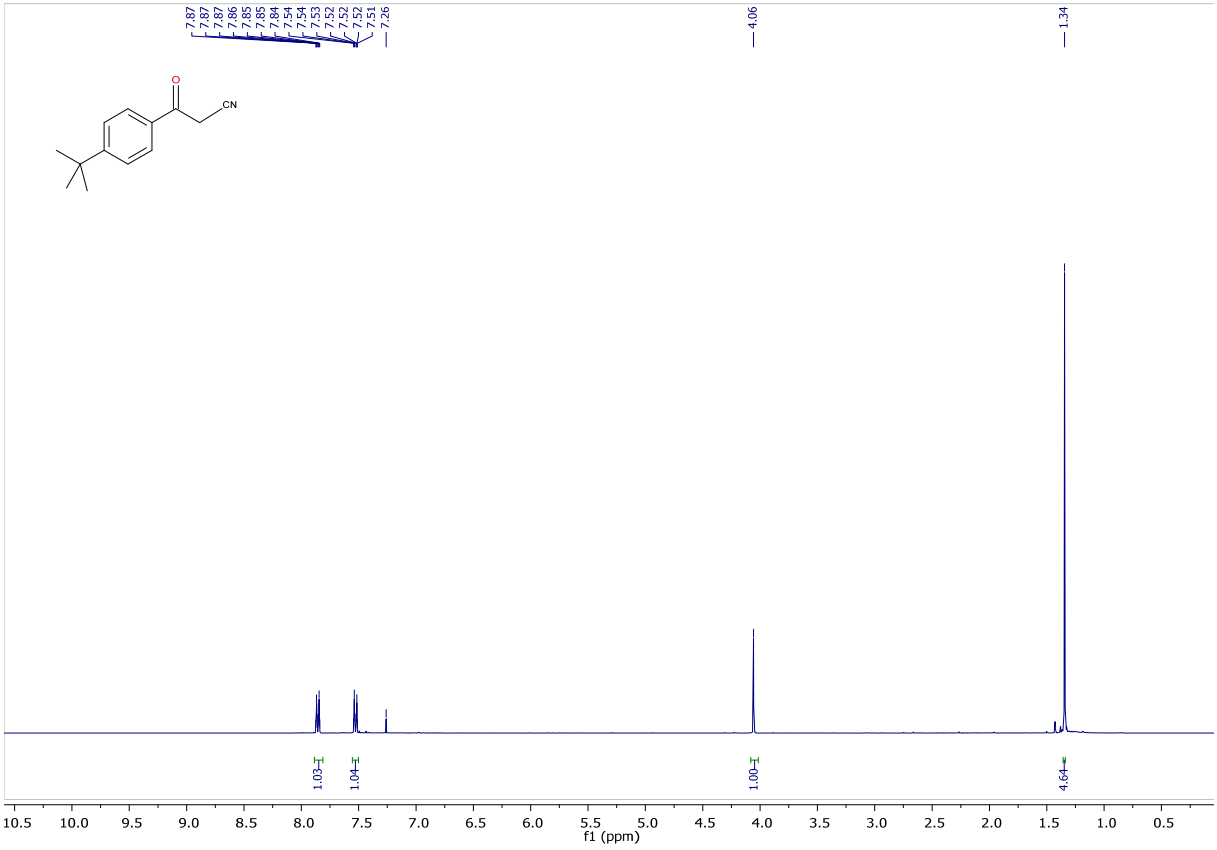
29.38
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

4e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7.54
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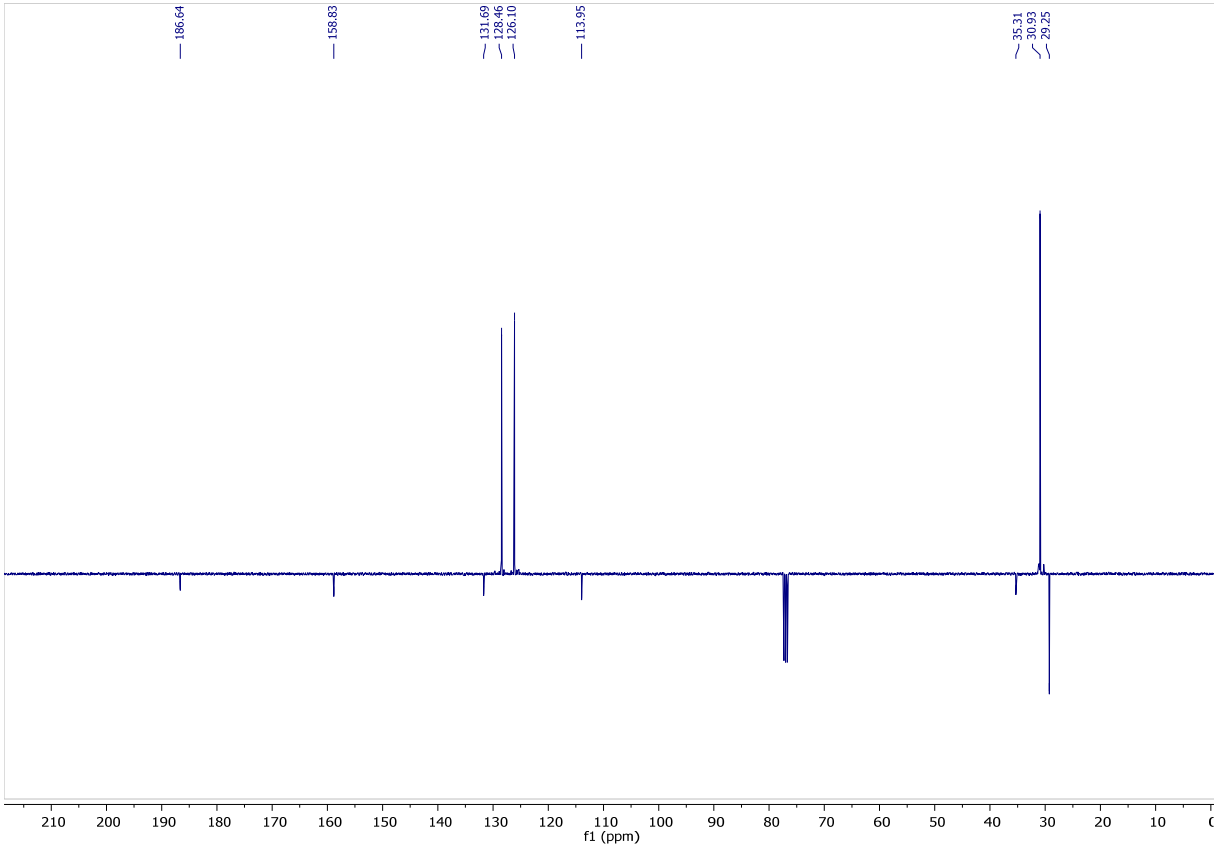
7.53
7.52
7.52
7.52
7.51
7.26
4.06
1.34
O
CN
1.03
1.04
1.00
4.64
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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128.46
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113.95
35.31
30.93
29.25
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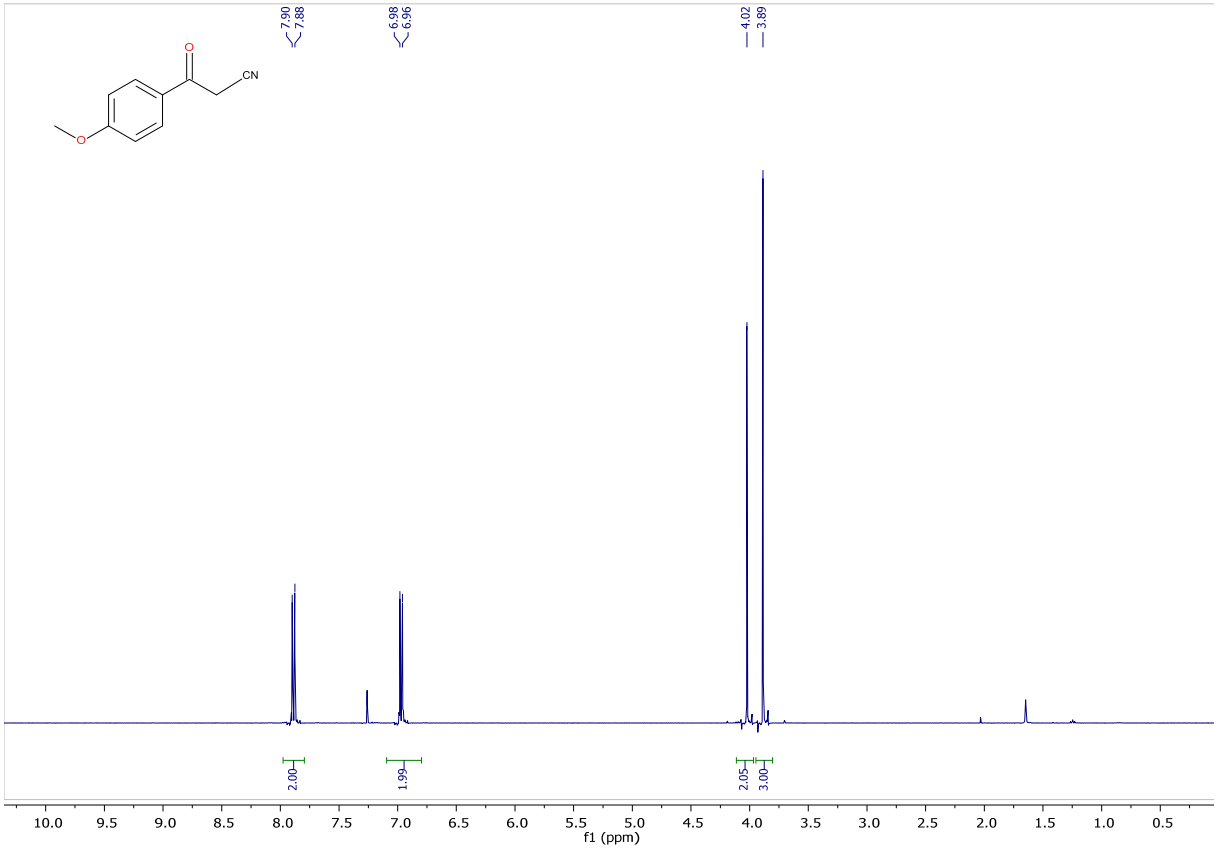
f1 (ppm)

4f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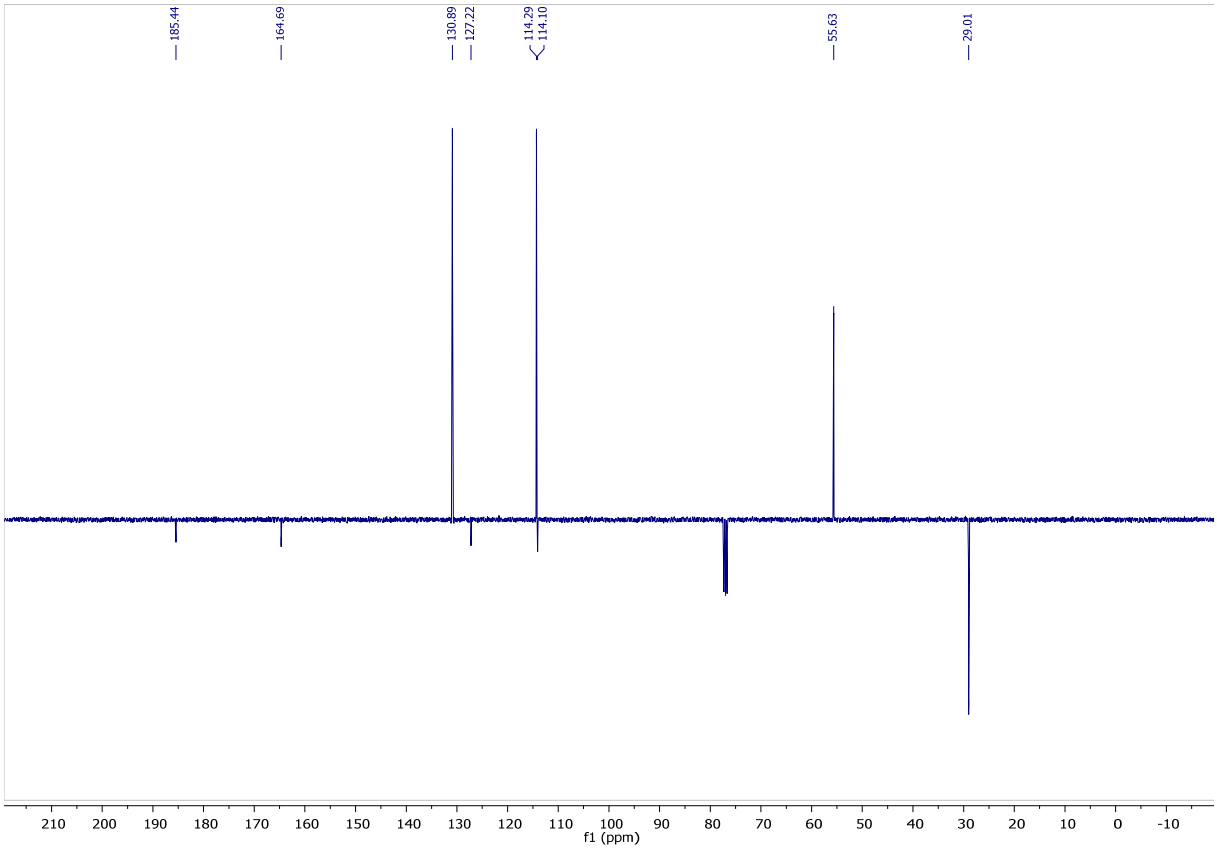
7.88
6.98
6.96
4.02
3.89
O
CN
O
2.00
1.99
2.05
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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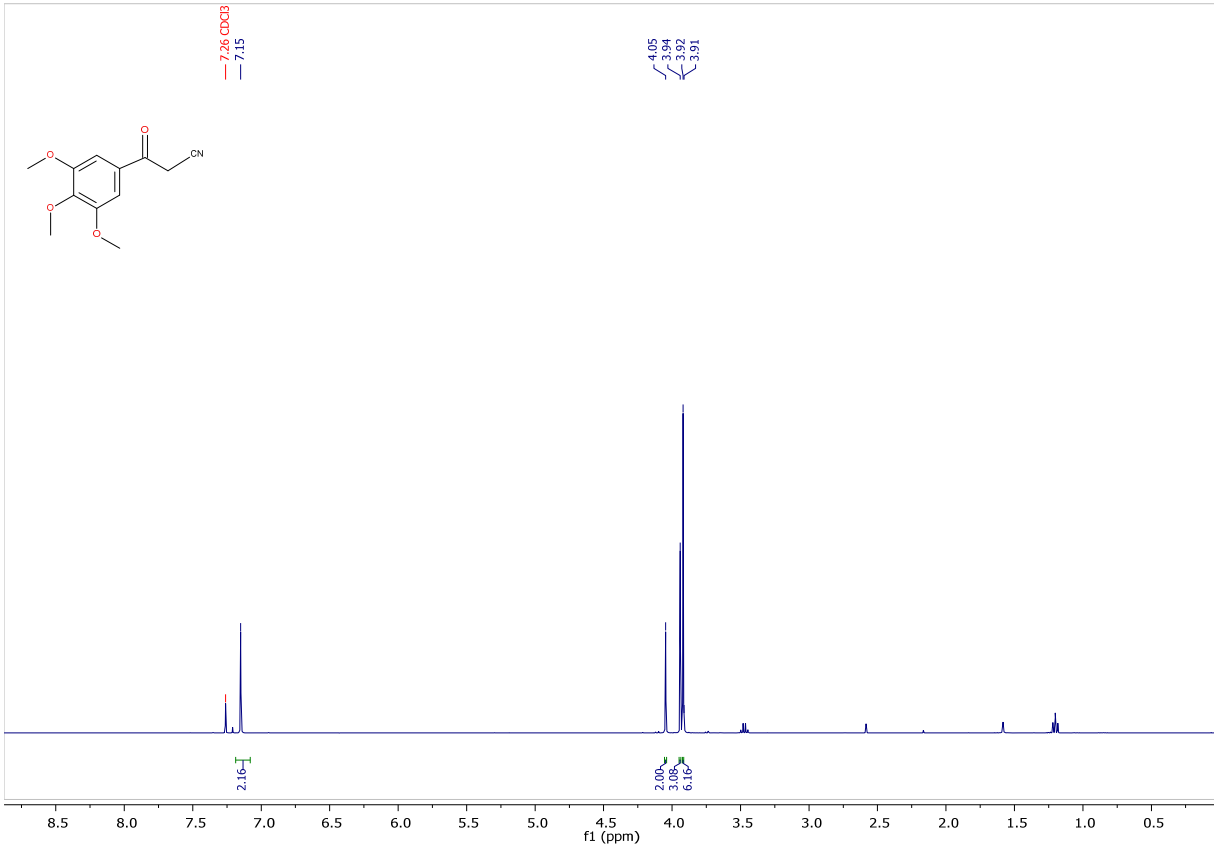
164.69
130.89
127.22
114.29
114.10
55.63
29.01
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

4g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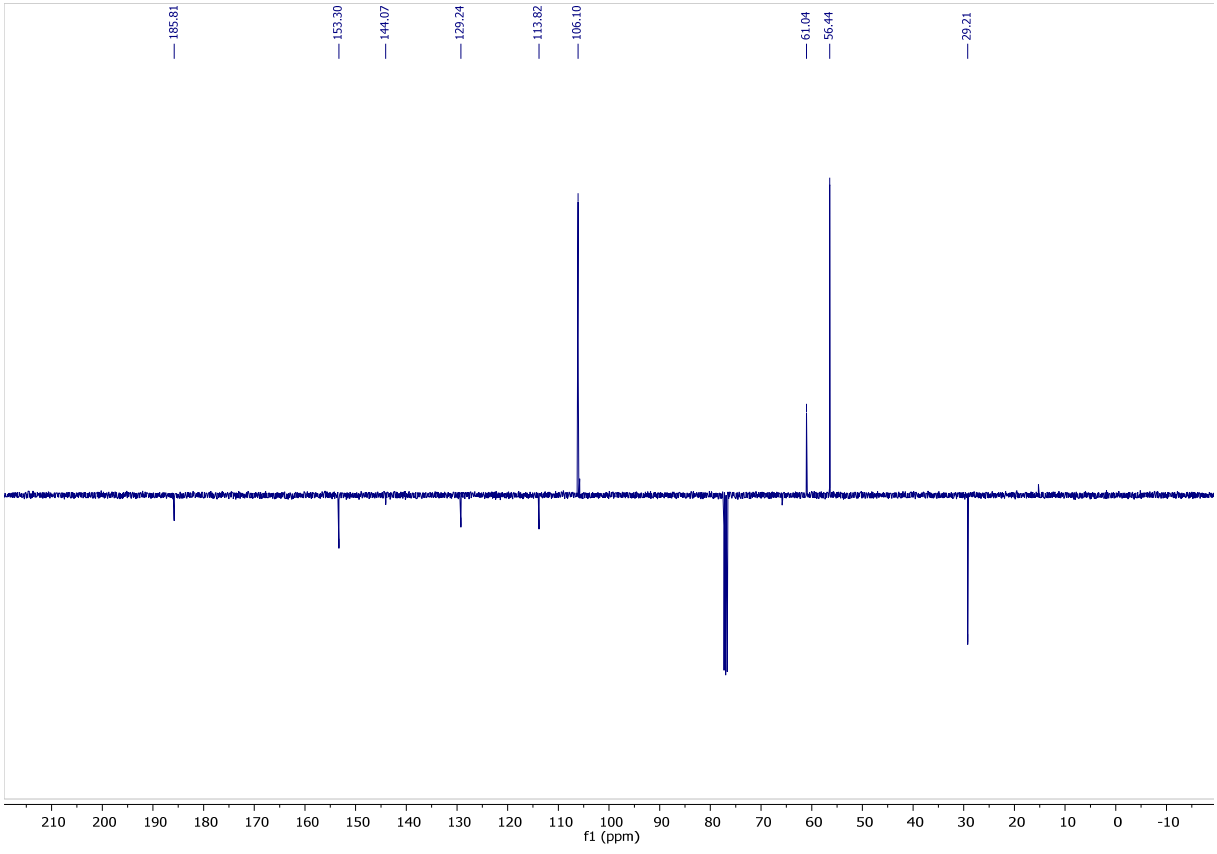
4.05
3.94
3.92
3.91
O
CN
O
O
O
2.16
2.00
3.08
6.16
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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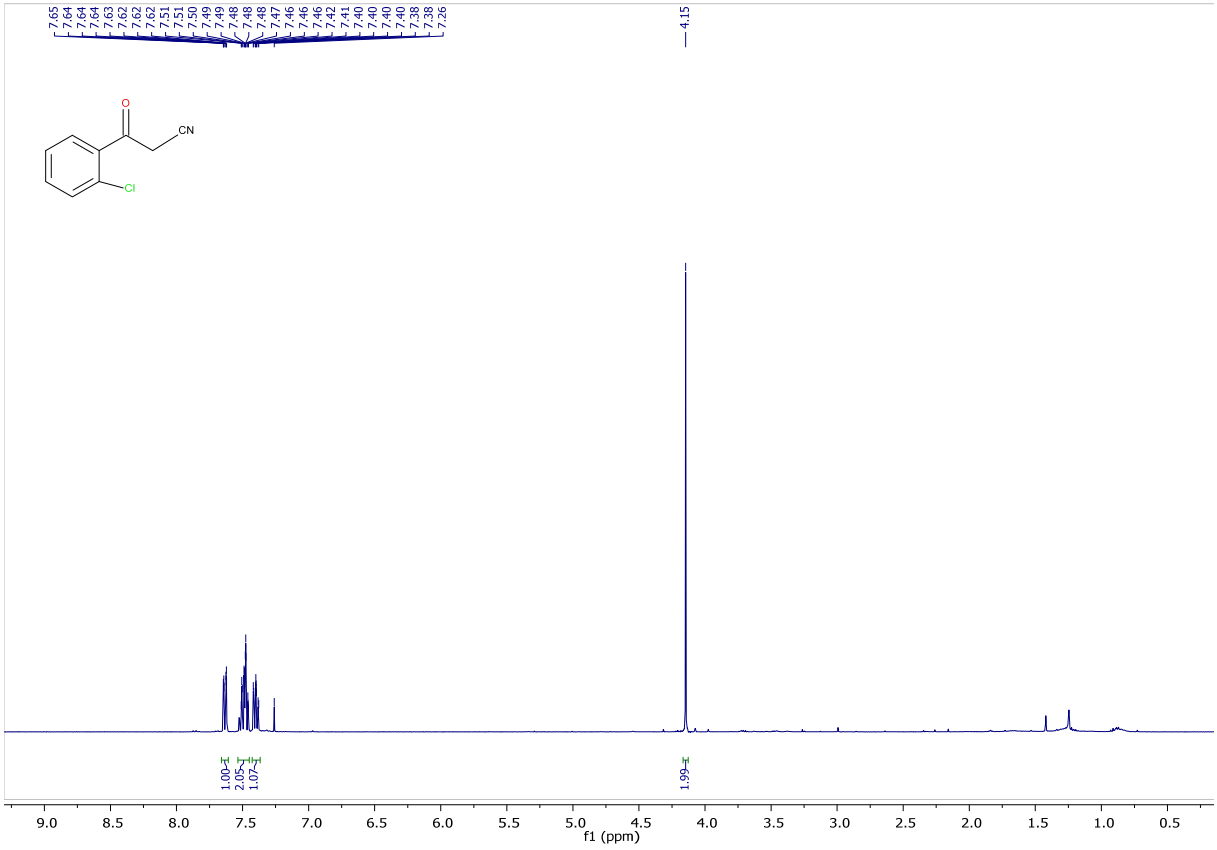
153.30
144.07
129.24
113.82
106.10
61.04
56.44
29.21
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

4h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7.63
7.62
7.62
7.62
7.51
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7.50
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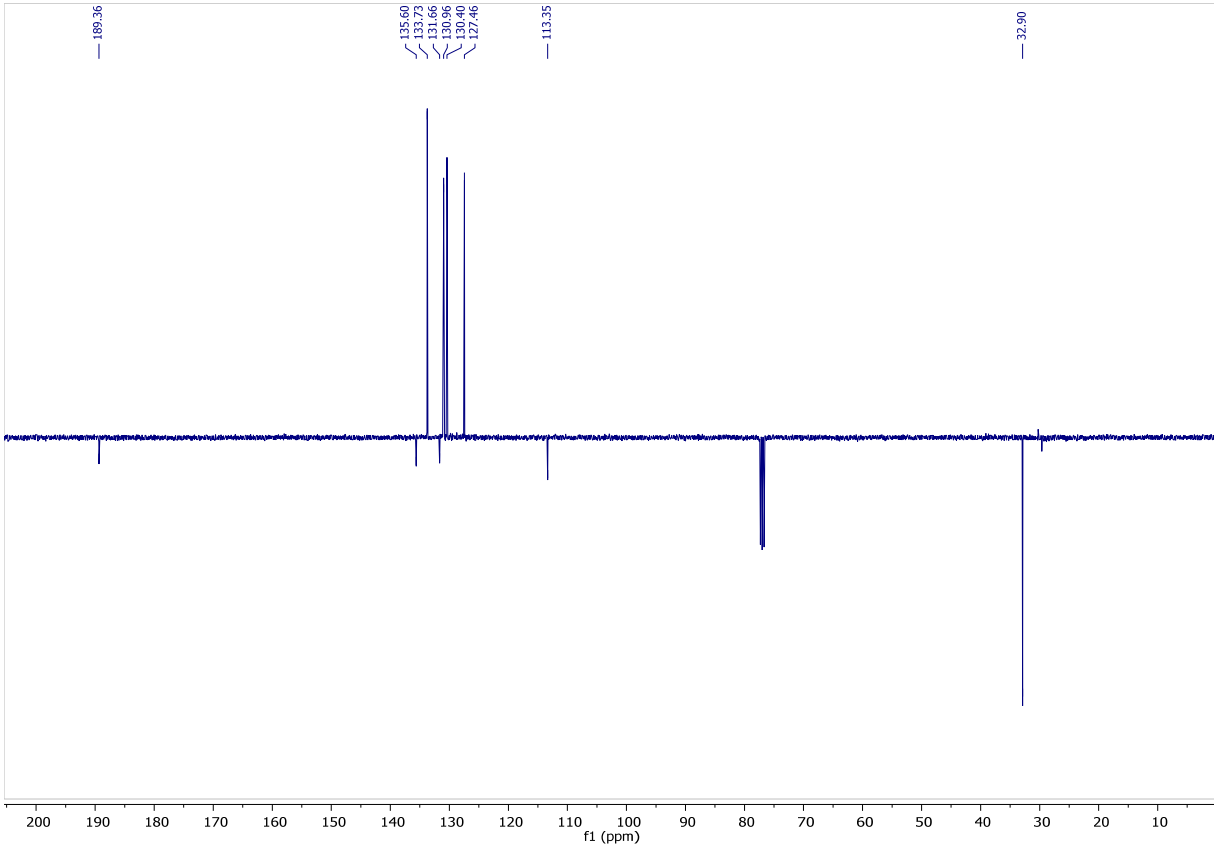
7.46
7.46
7.46
7.42
7.41
7.40
7.40
7.40
7.40
7.38
7.38
7.26
4.15
O
CN
Cl
1.00
2.05
1.07
1.99
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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133.73
131.66
130.96
130.40
127.46
113.35
32.90
200
190
180
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150
140
130
120
110
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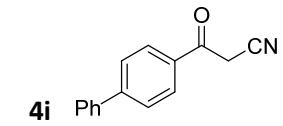
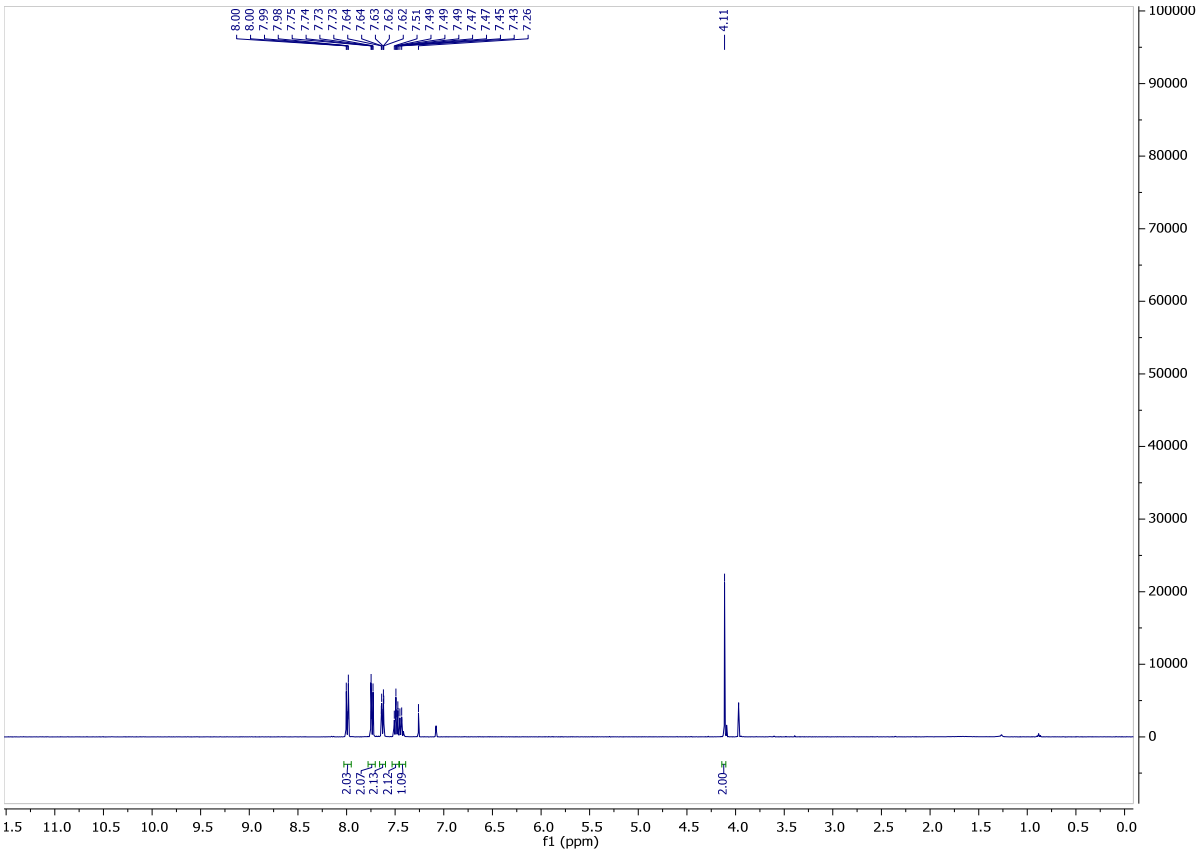
90
80
70
60
50
40
30
20
10
f1 (ppm)

4i


O
CN
Ph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7.73
7.64
7.64
7.63
7.62
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7.51
7.49
7.49
7.49
7.47
7.47
7.45
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7.26
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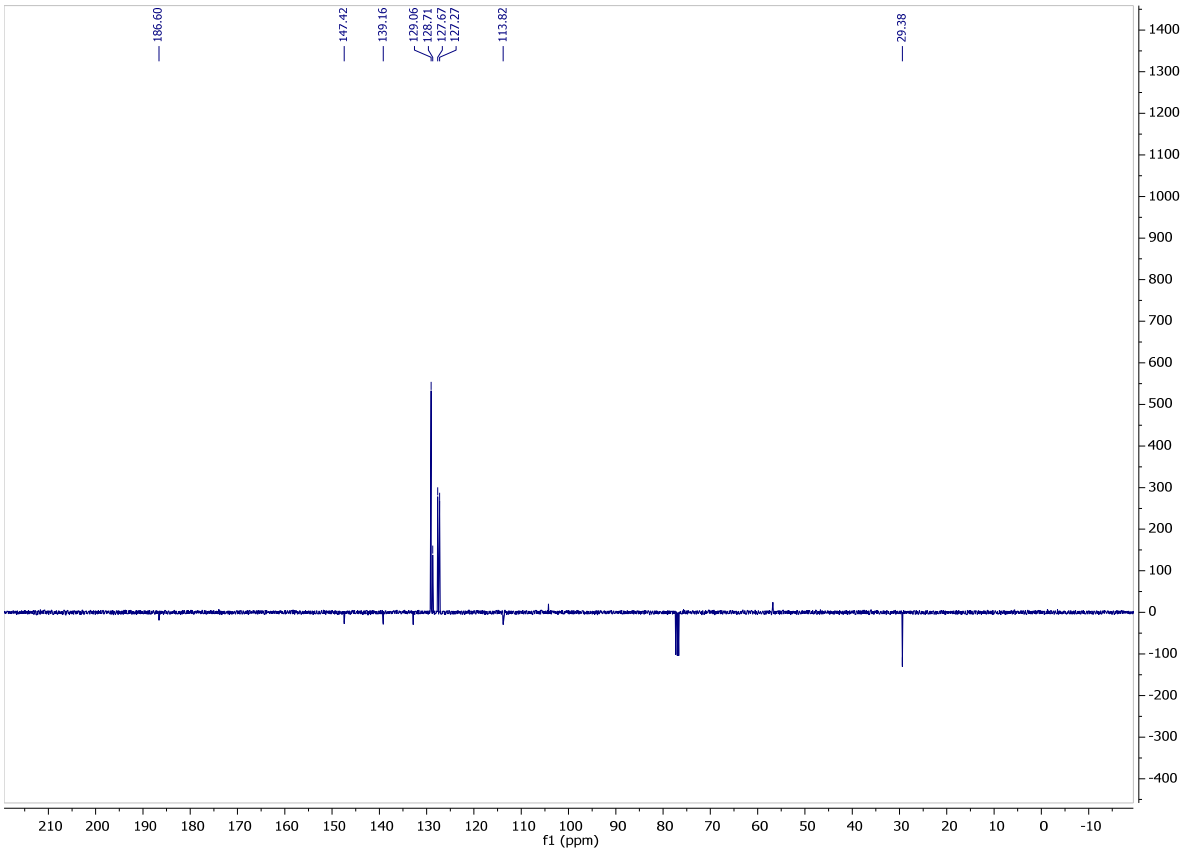
2.07
2.13
2.13
1.09
2.00
f1 (ppm)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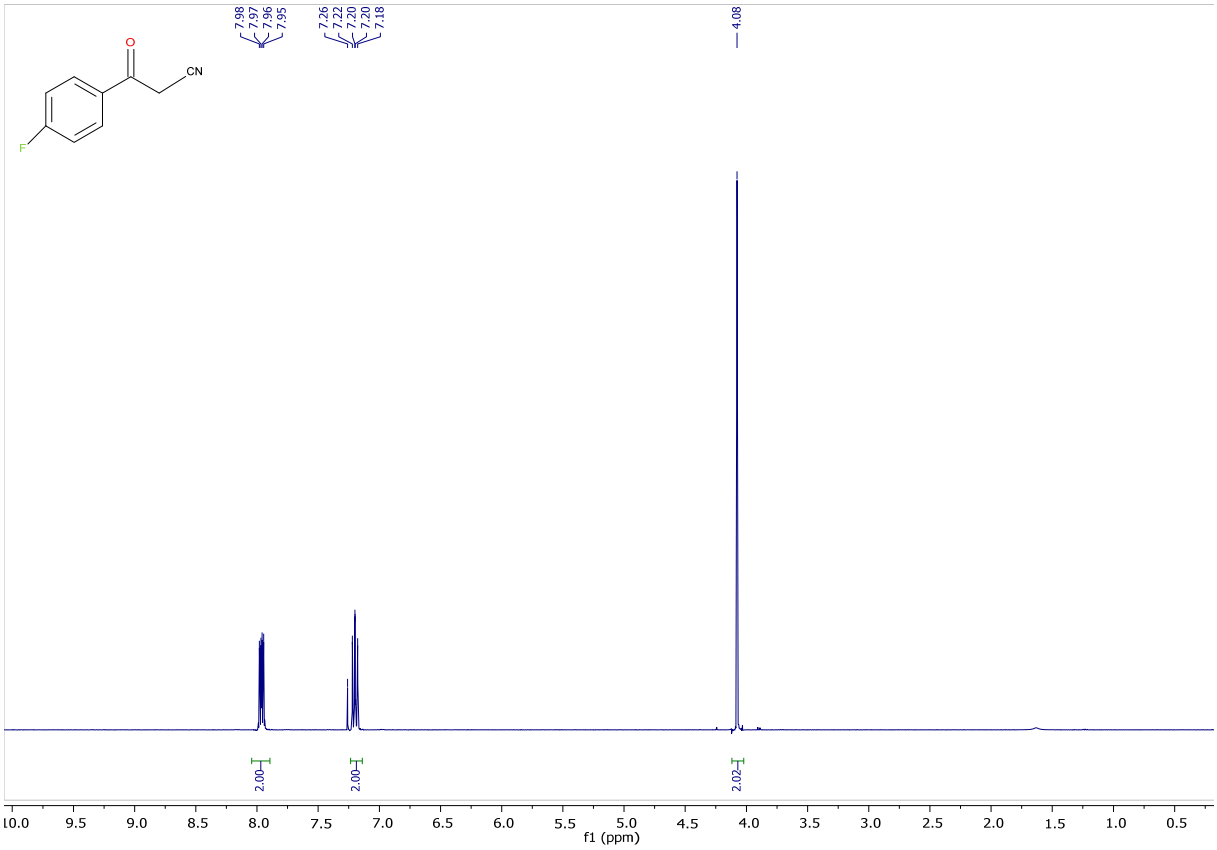
29.38
f1 (ppm)

4j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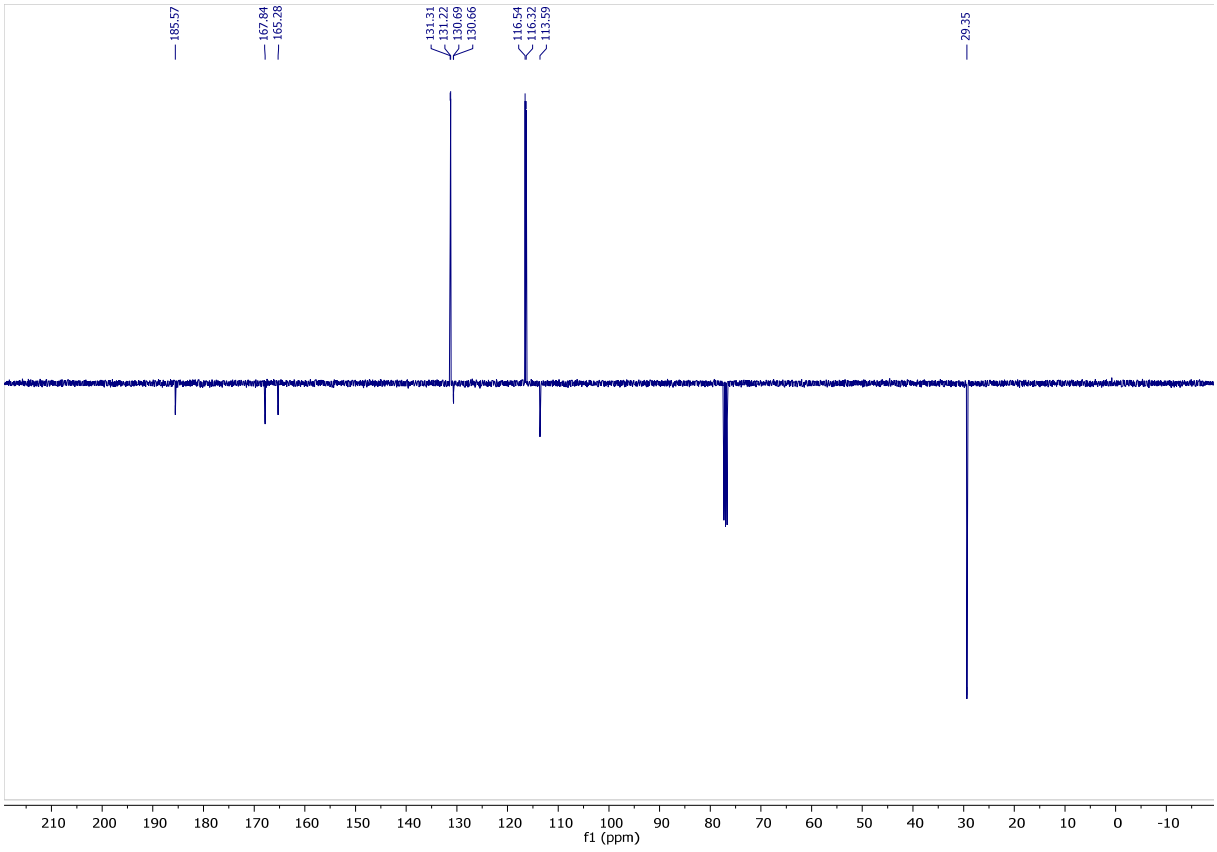
7.26
7.22
7.20
7.20
7.18
4.08
O
CN
F
2.00
2.00
2.02
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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113.59
29.35
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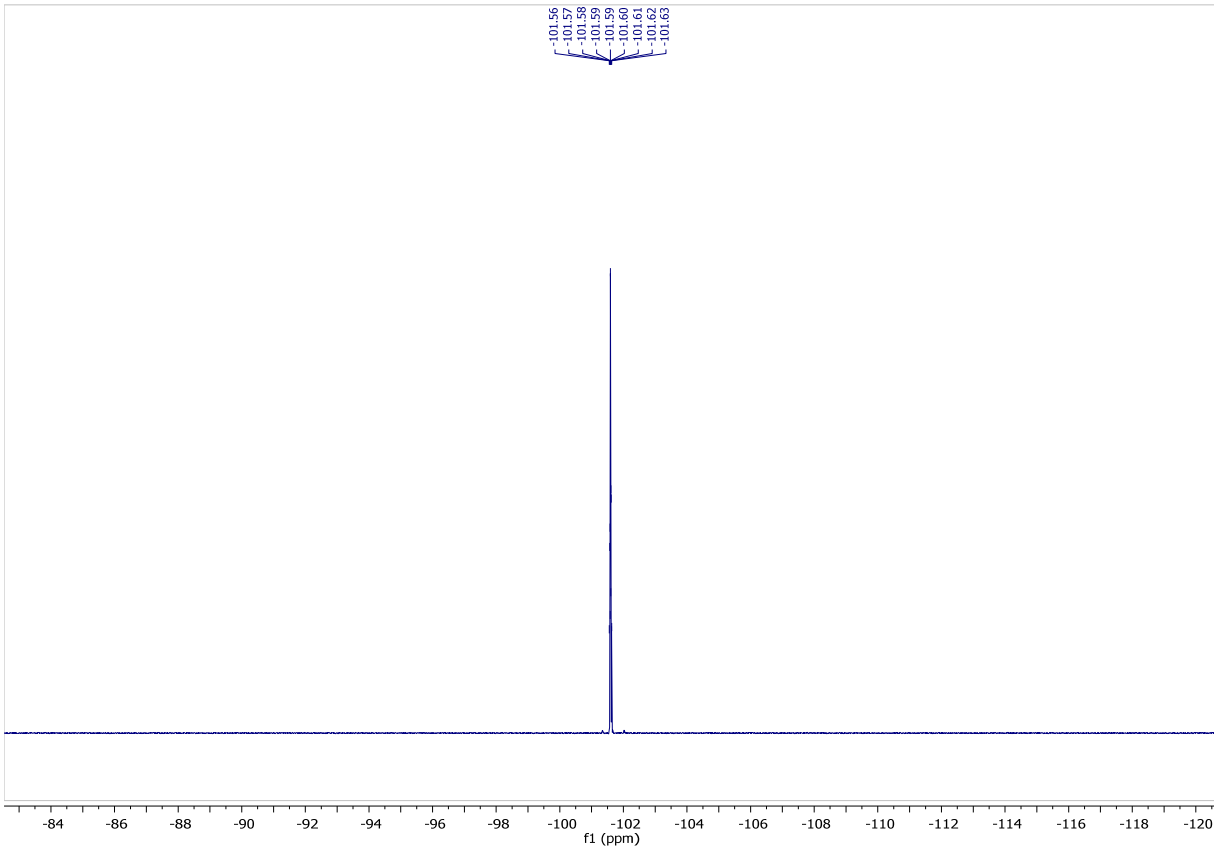
f1 (ppm)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-101.59
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-88
-90
-92
-94
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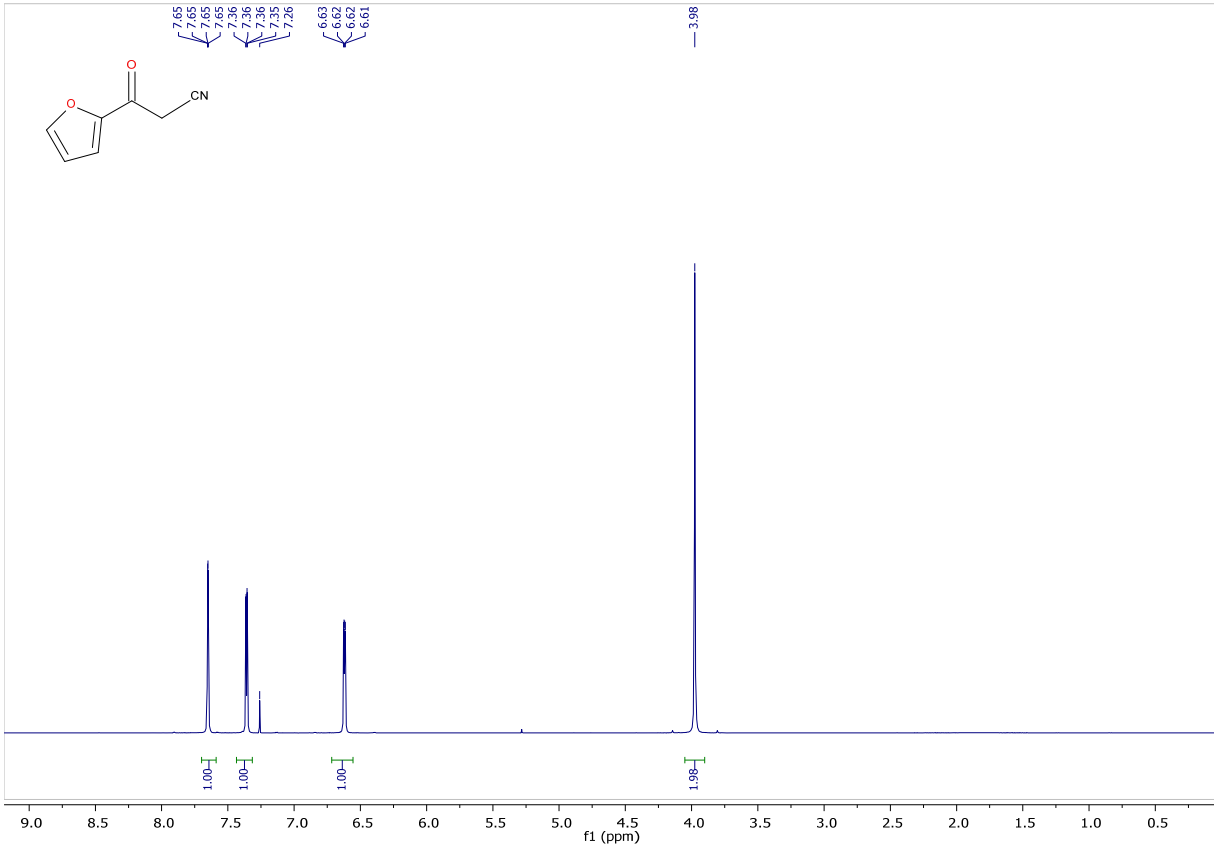
-116
-118
-120
f1 (ppm)

4k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7.36
7.36
7.36
7.35
7.26
6.63
6.62
6.62
6.61
3.98
O
O
CN
1.00
1.00
1.00
1.98
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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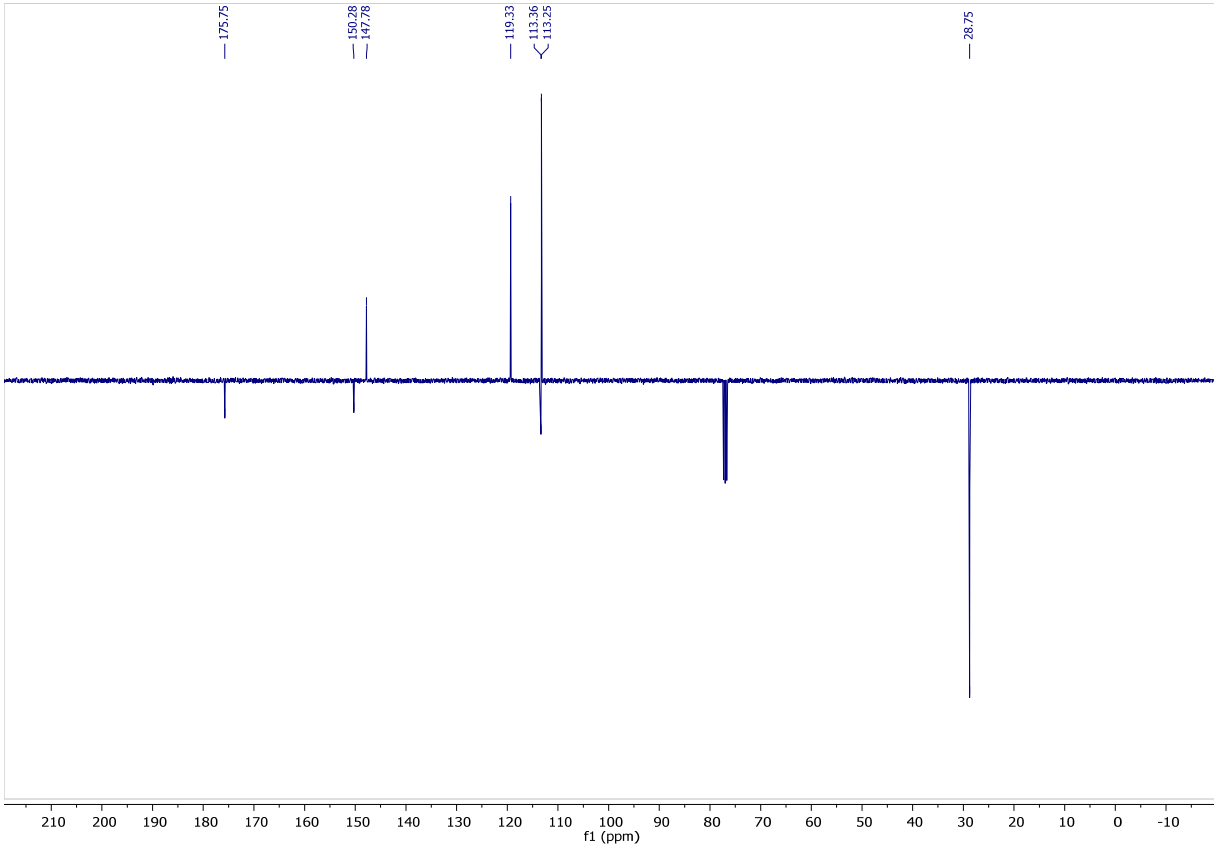
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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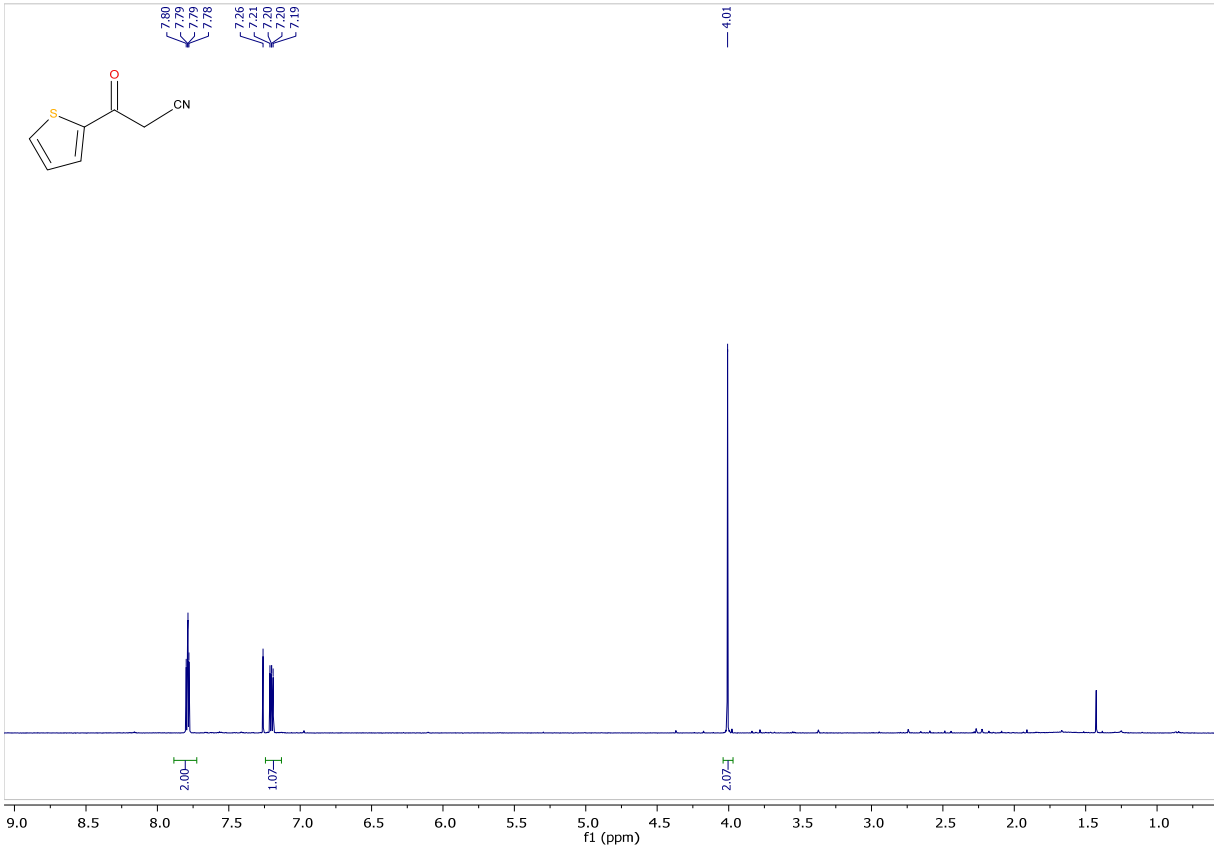
28.75
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

4l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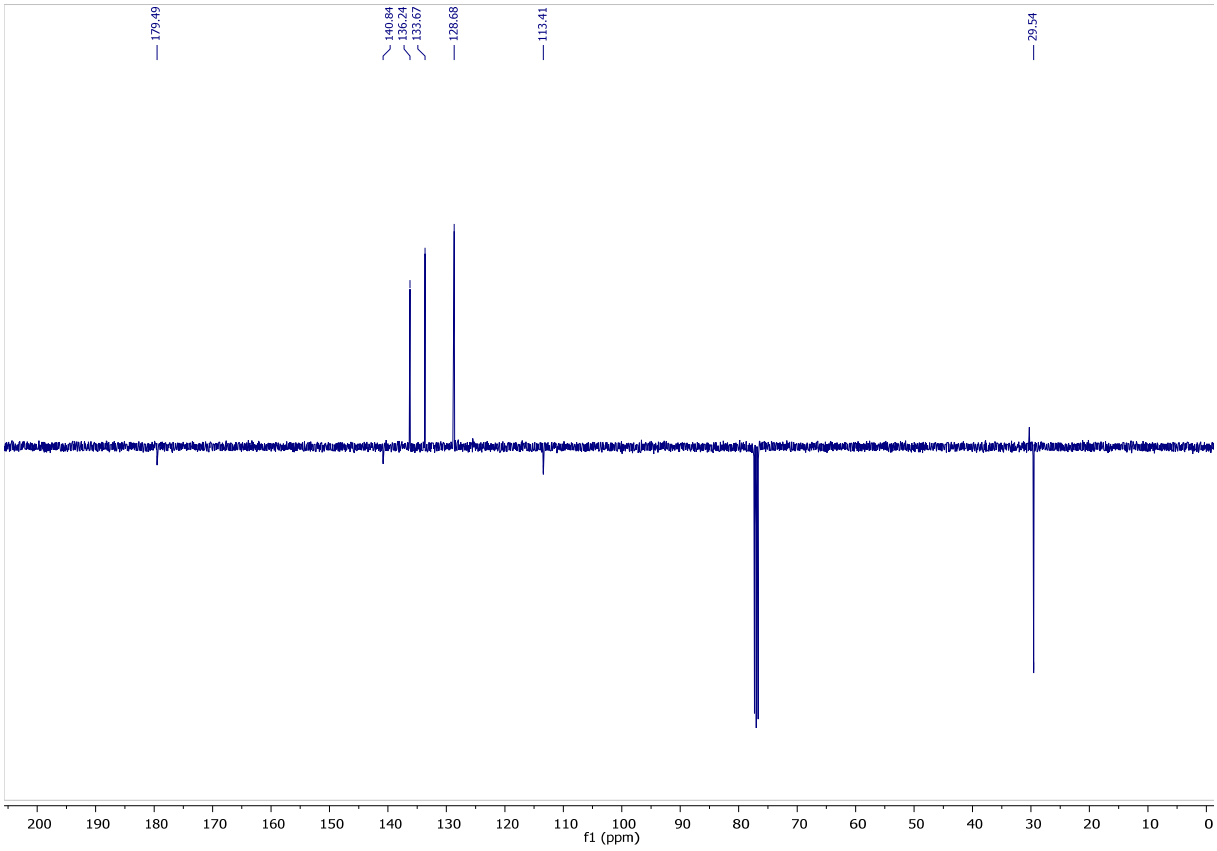
7.20
7.20
7.19
4.01
O
S
CN
2.00
1.07
2.07
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)


179.49
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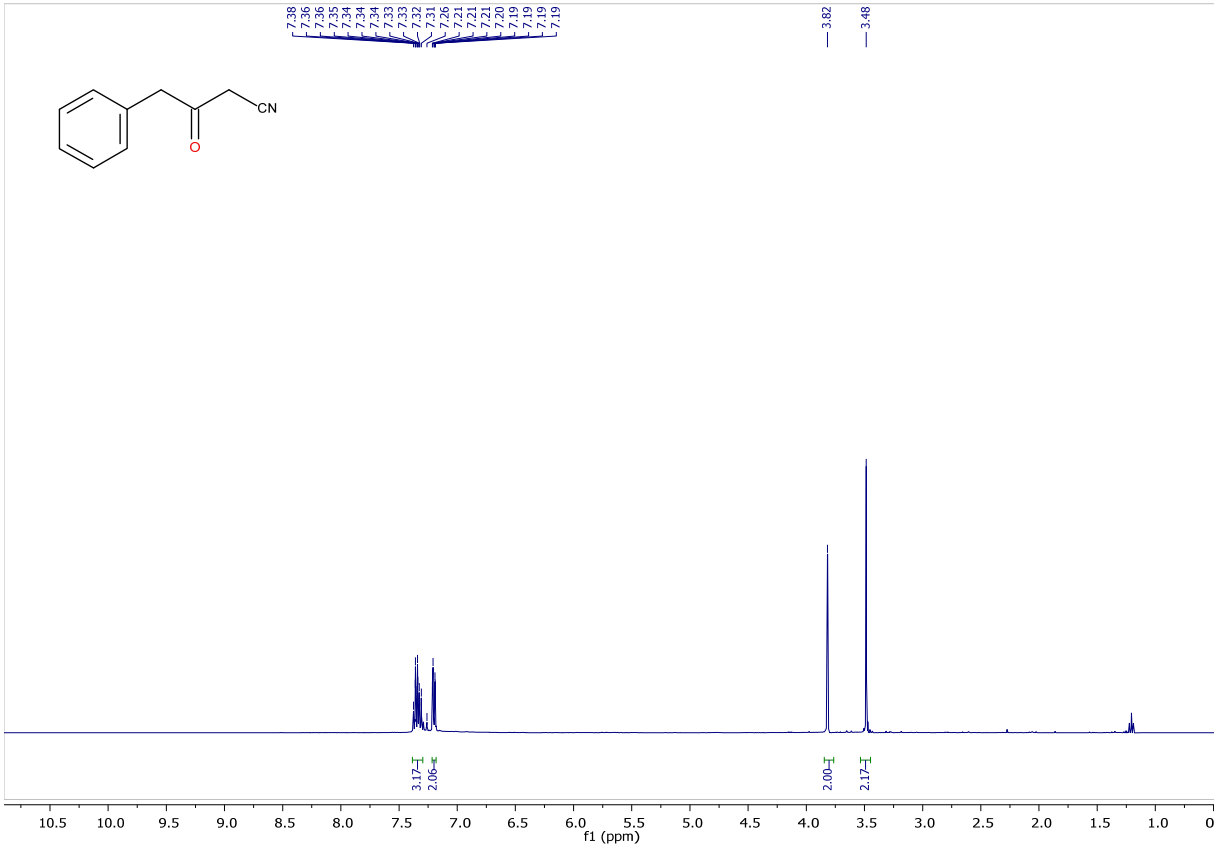
133.67
128.68
113.41
29.54
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

4m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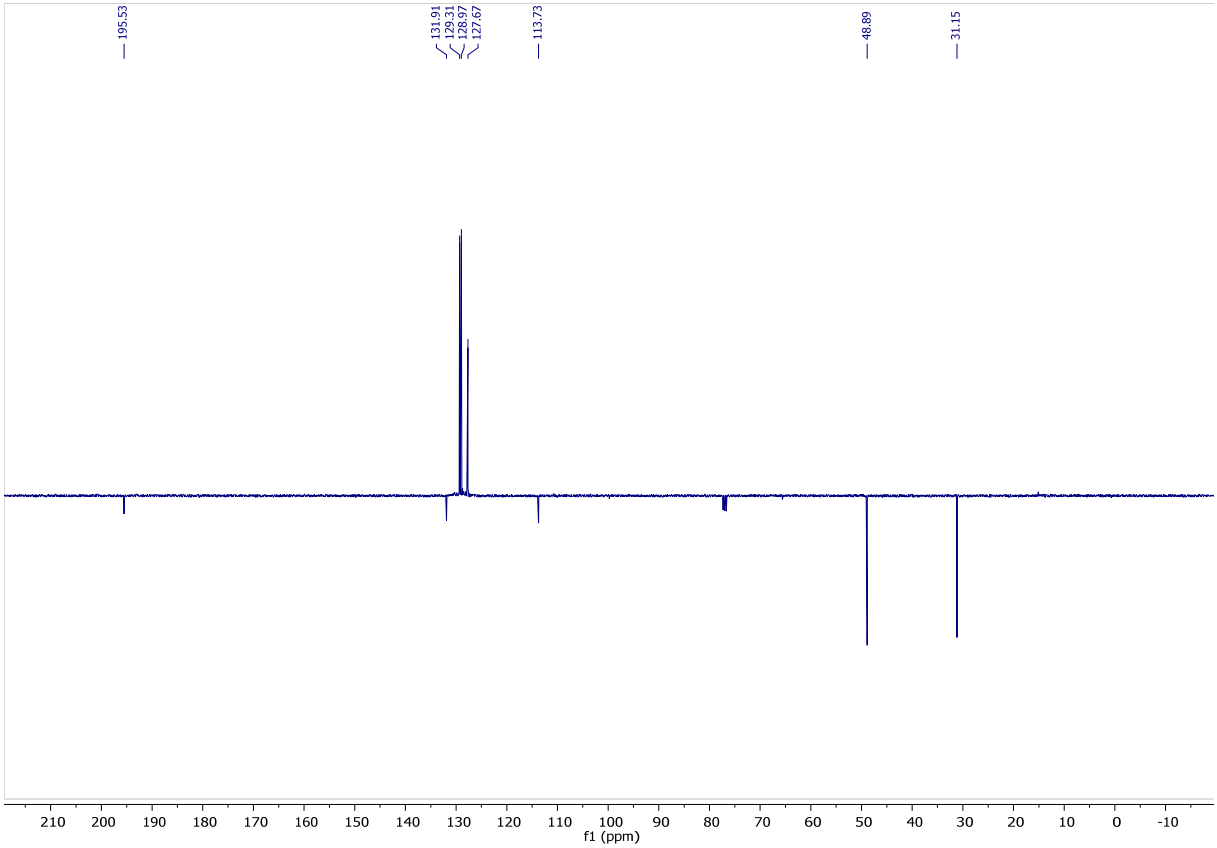
7.34
7.33
7.33
7.32
7.31
7.26
7.21
7.21
7.20
7.19
7.19
7.19
7.19
3.82
3.48
CN
O
3.17
2.06
2.00
2.17
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0
f1 (ppm)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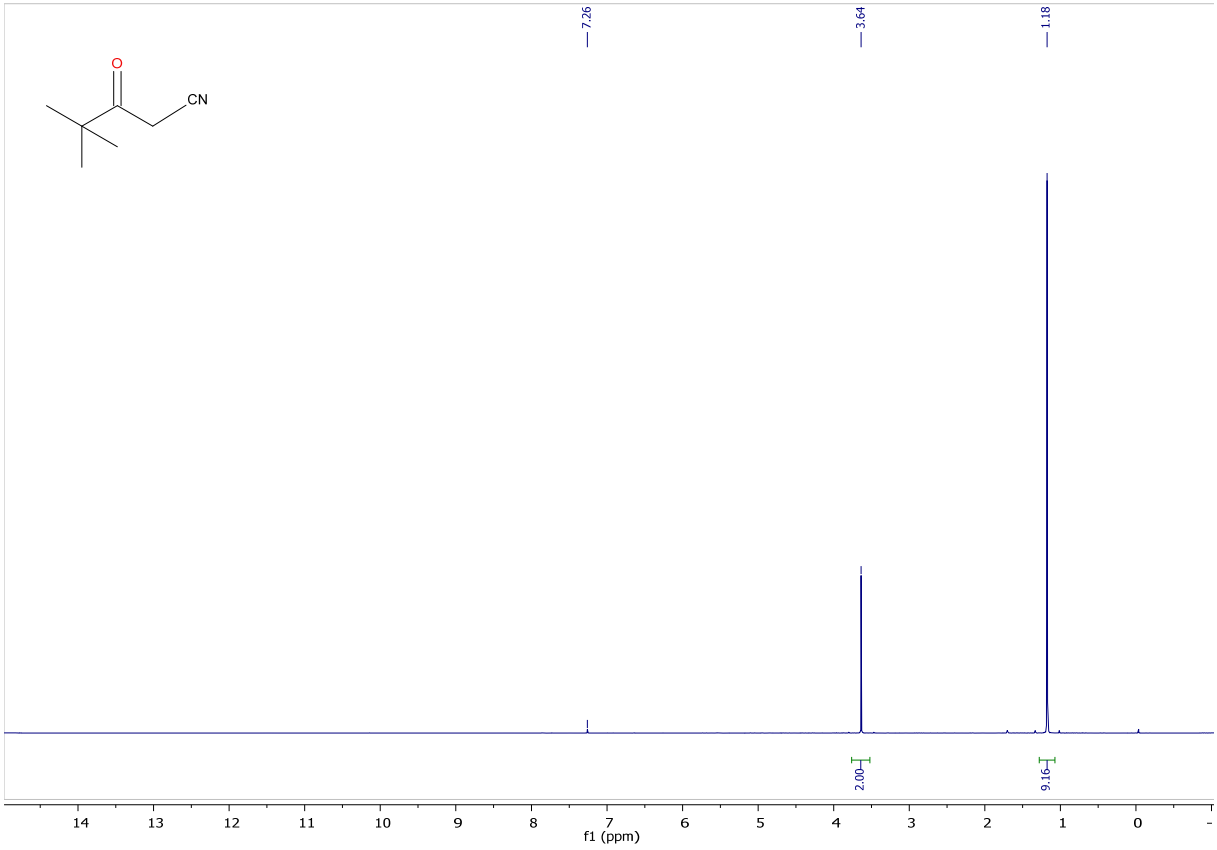
131.91
129.31
128.97
127.67
113.73
48.89
31.15
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

4n


7.26
3.64
1.18
O
CN
2.00
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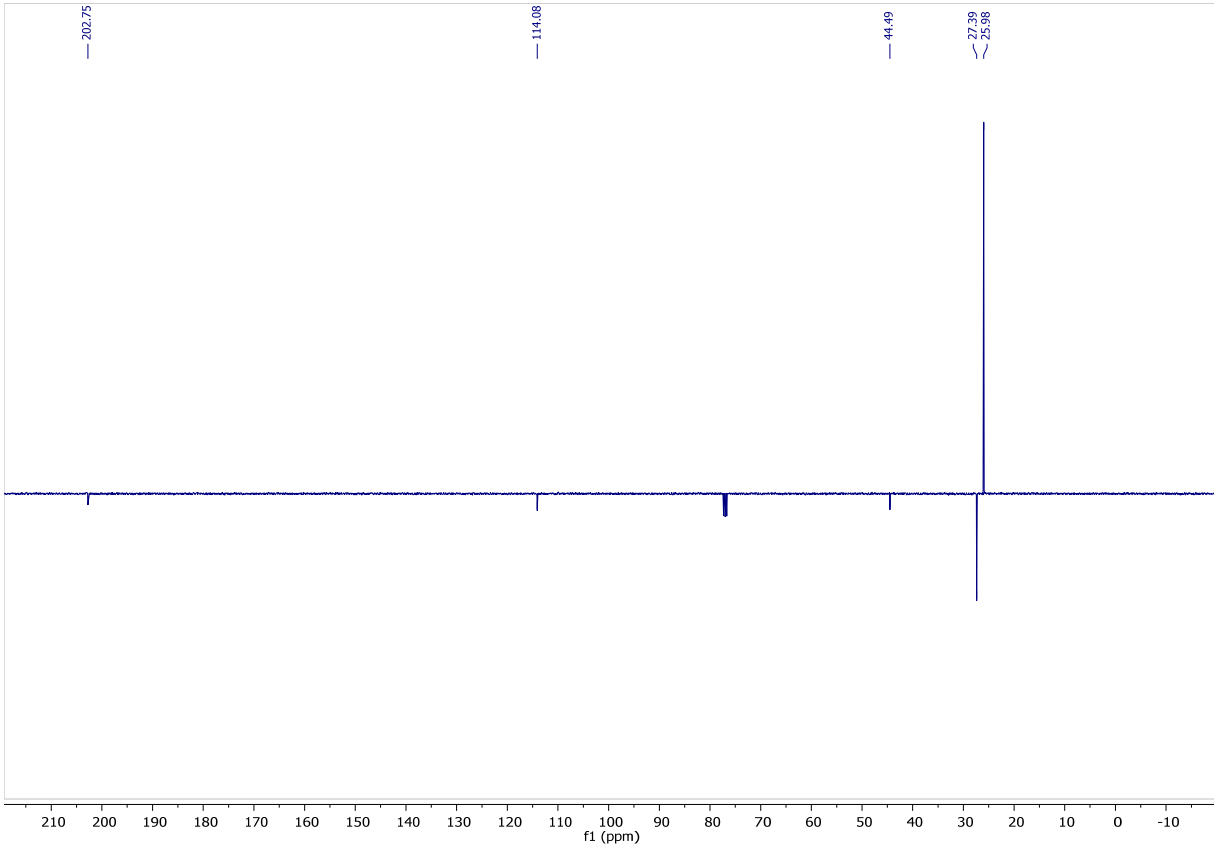
f1 (ppm)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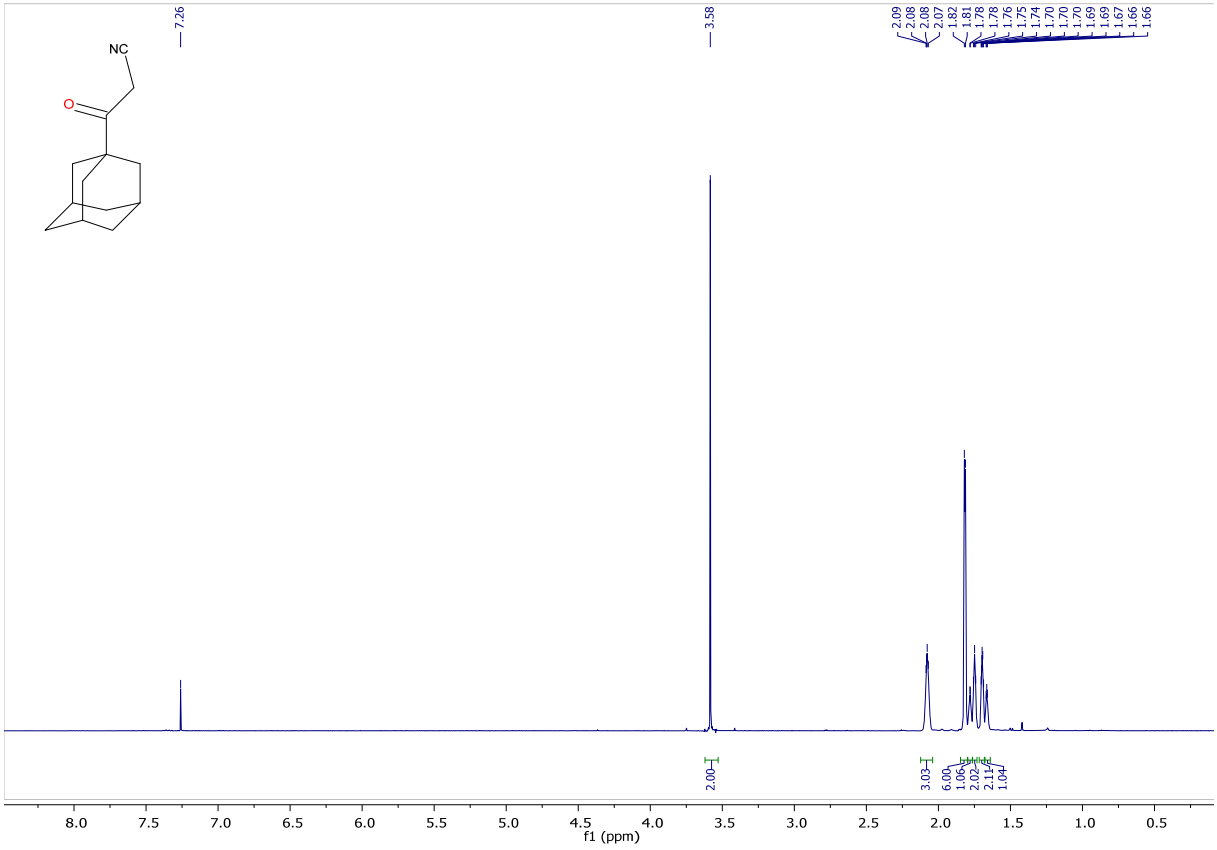
27.39
25.98
f1 (ppm)

4o


NC
O
7.26
3.58
2.09
2.08
2.08
2.07
1.82
1.81
1.78
1.78
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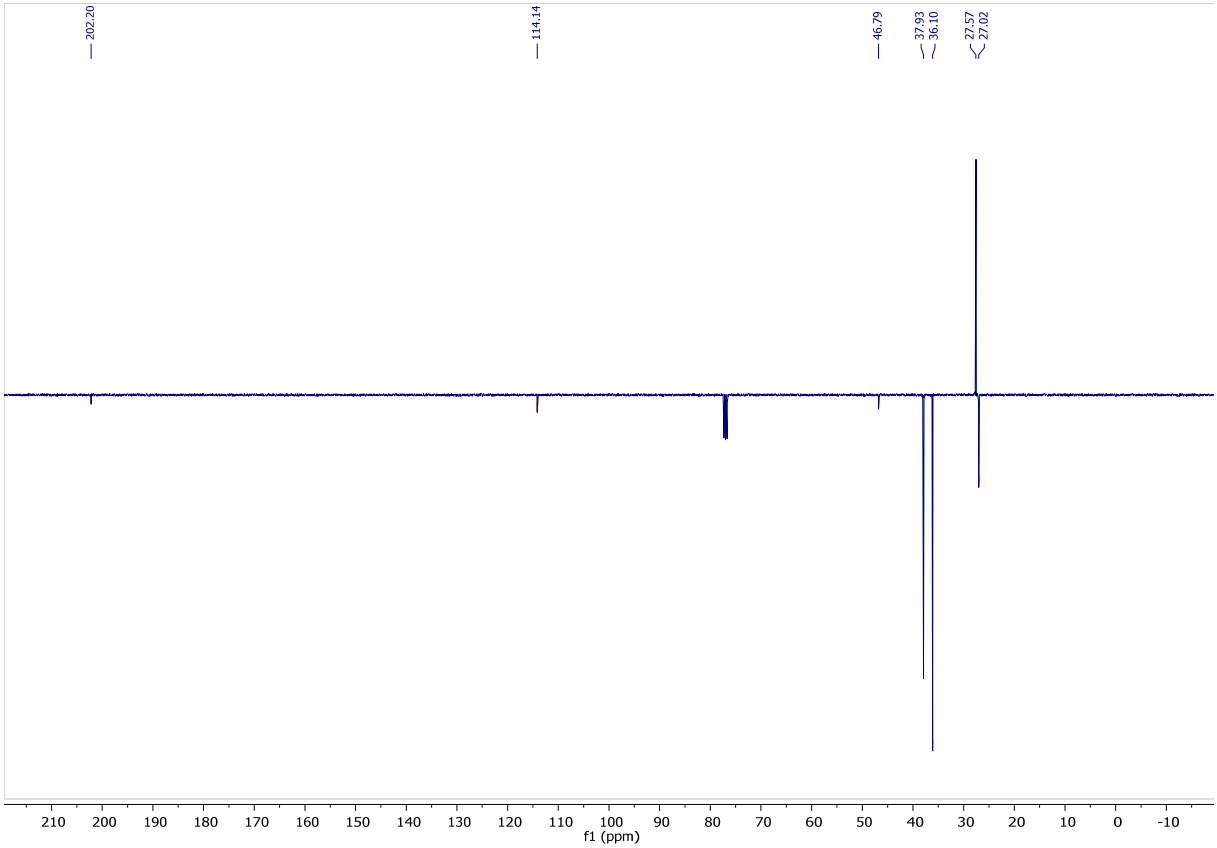
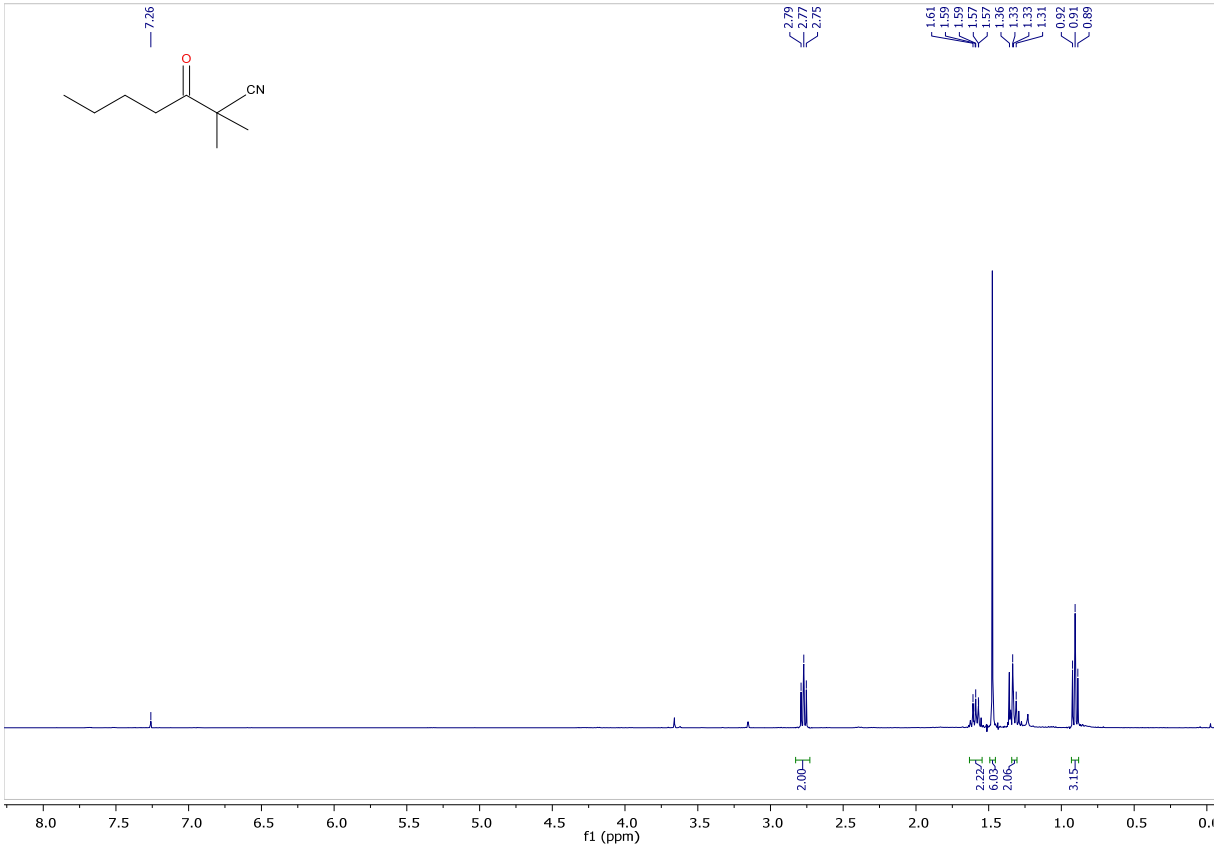
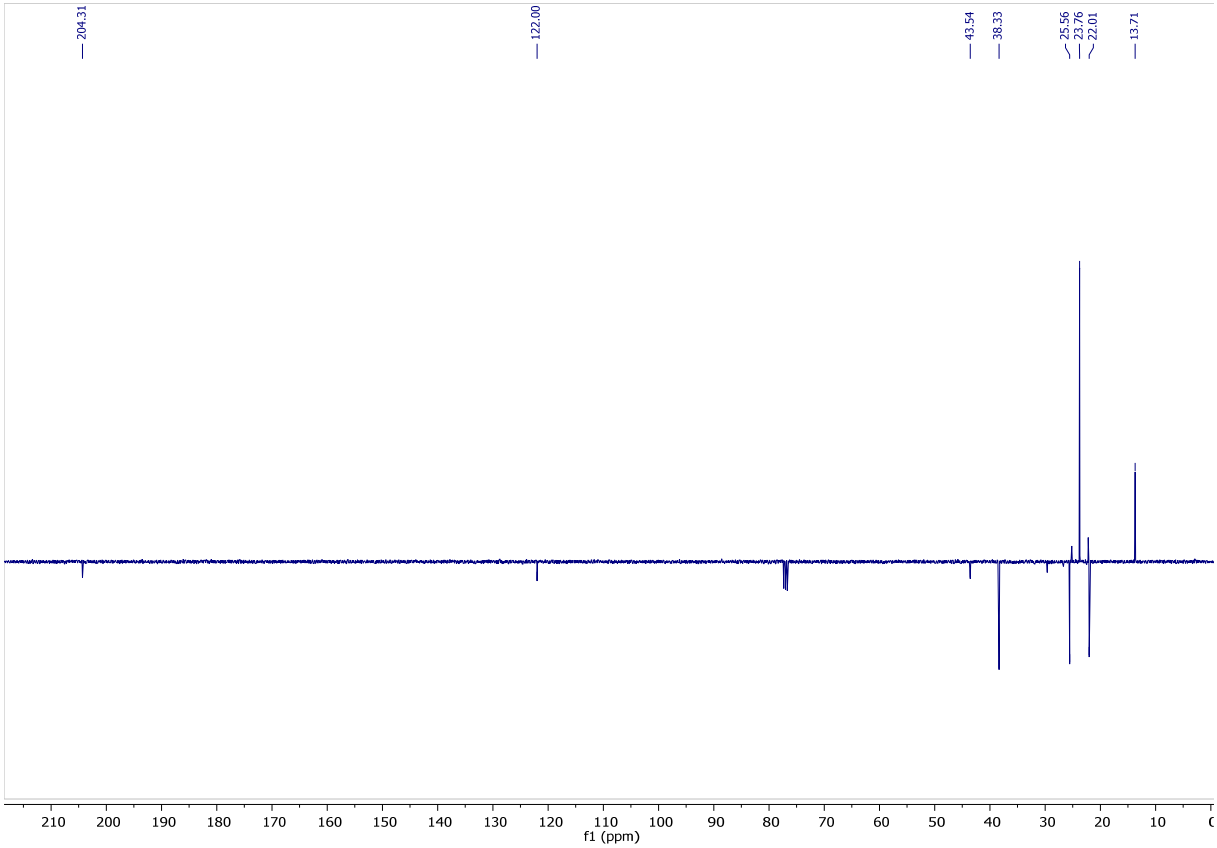
1.75
1.74
1.70
1.70
1.70
1.69
1.69
1.67
1.66
1.66
2.00
3.03
6.00
1.06
2.02
2.11
1.04
f1 (ppm)

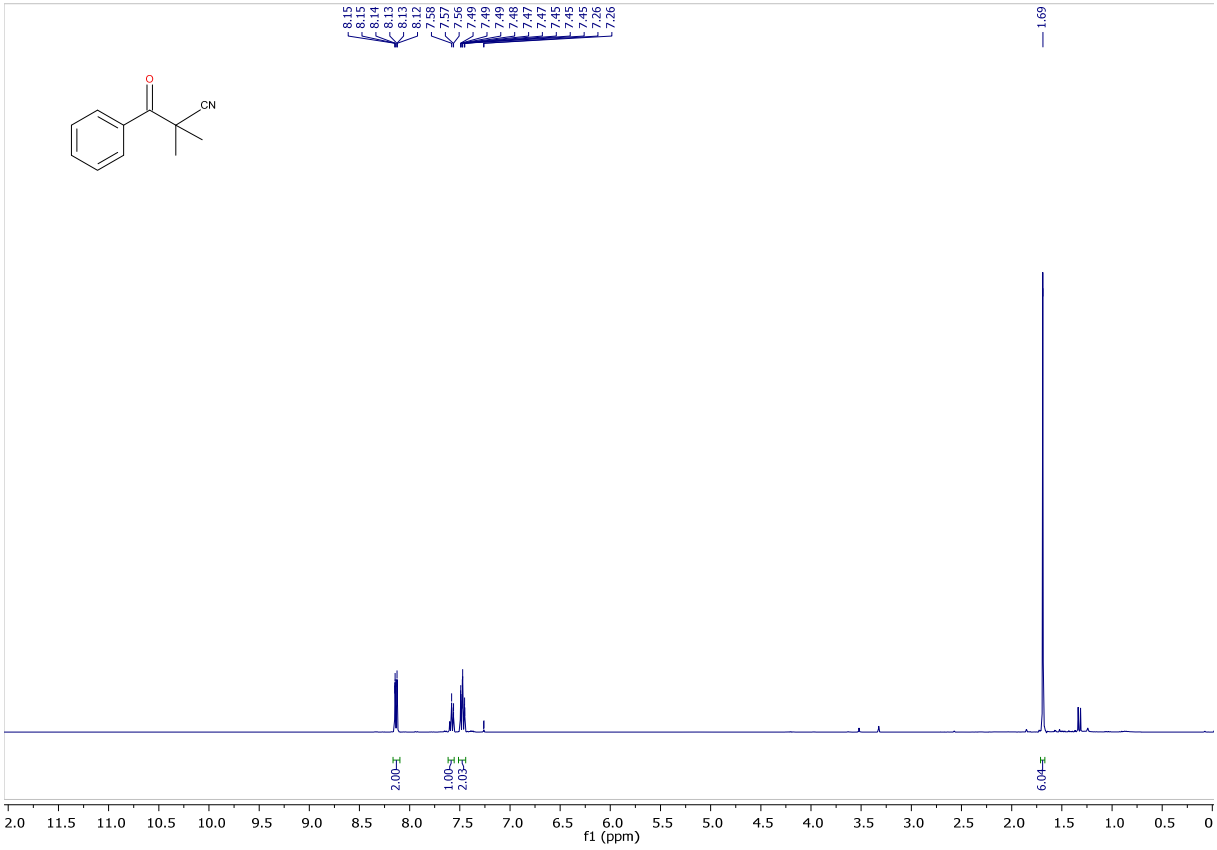

202.20
114.14
46.79
37.93
36.10
27.57
27.02
f1 (ppm)

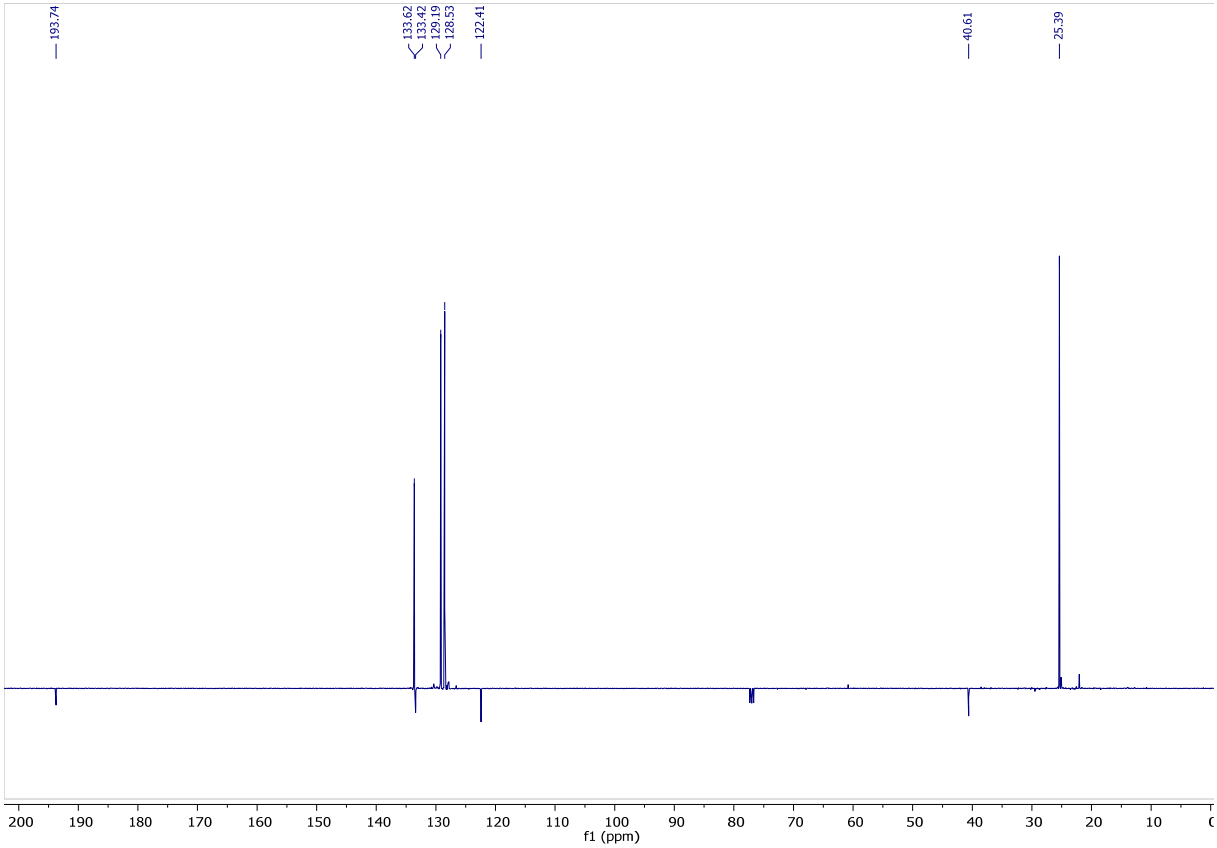
6a


7.26
2.79
2.77
2.75
1.61
1.59
1.59
1.57
1.57
1.36
1.33
1.33
1.31
0.92
0.91
0.89
O
CN
2.00
2.22
6.03
2.06
3.15
f1 (ppm)

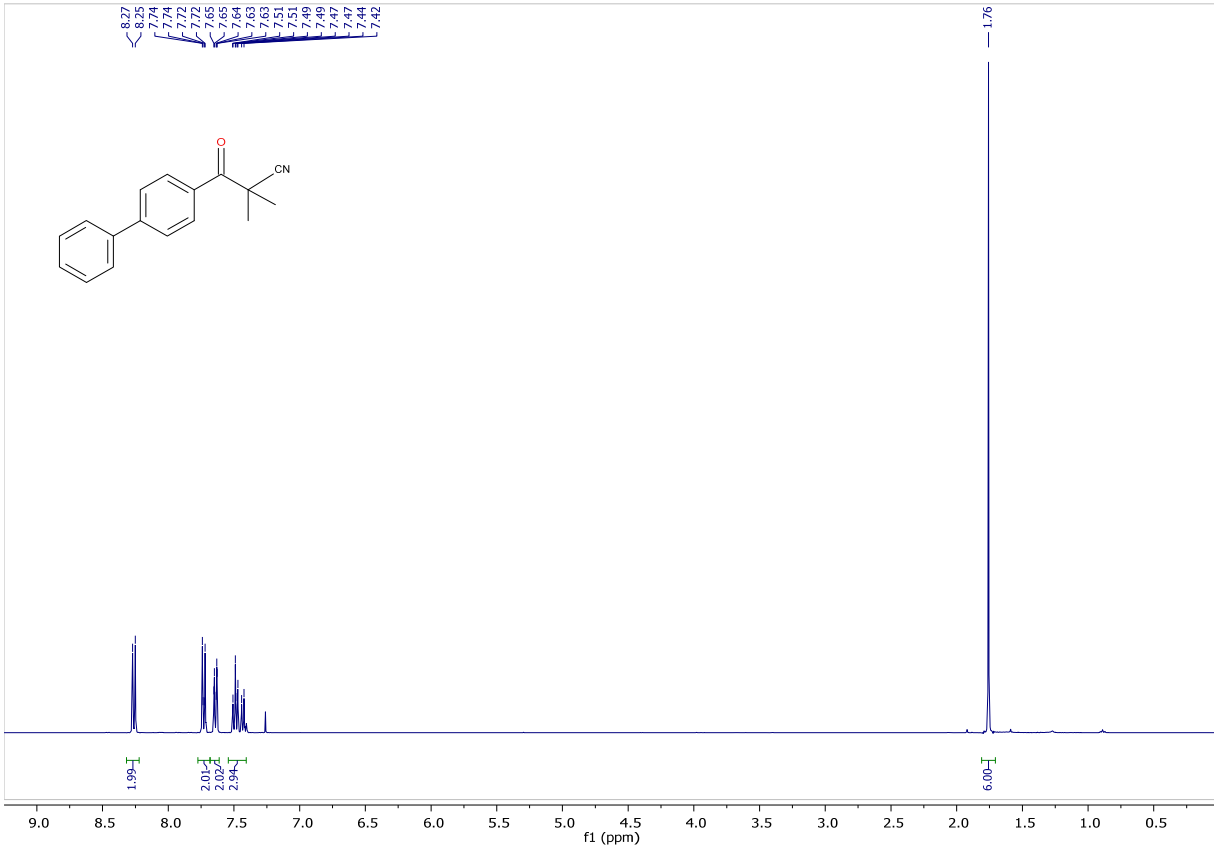

204.31
122.00
43.54
38.33
25.56
23.76
22.01
13.71
f1 (ppm)

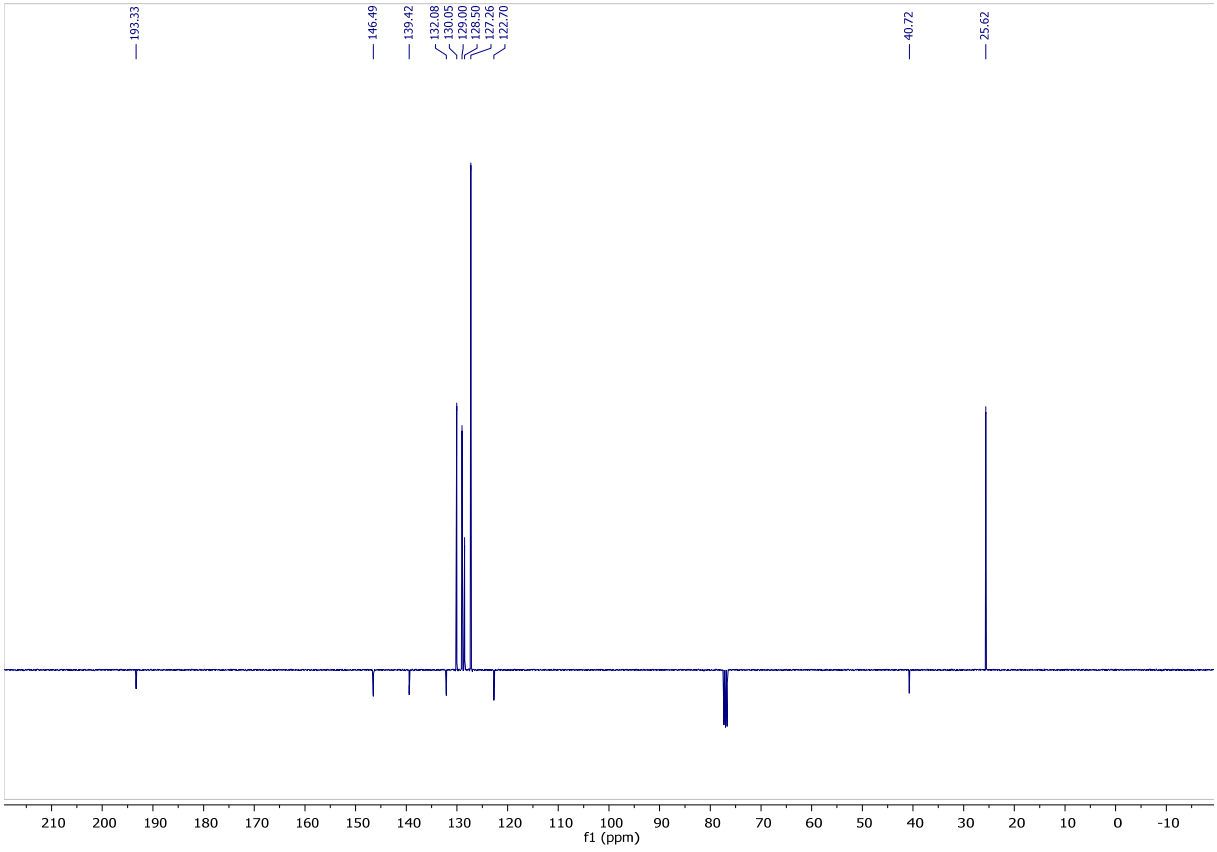
6b


8.15
8.15
8.14
8.13
8.13
8.12
7.58
7.57
7.55
7.49
7.49
7.49
7.48
7.47
7.47
7.45
7.45
7.45
7.26
7.26
1.69
O
CN
2.00
1.00
2.03
6.04
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

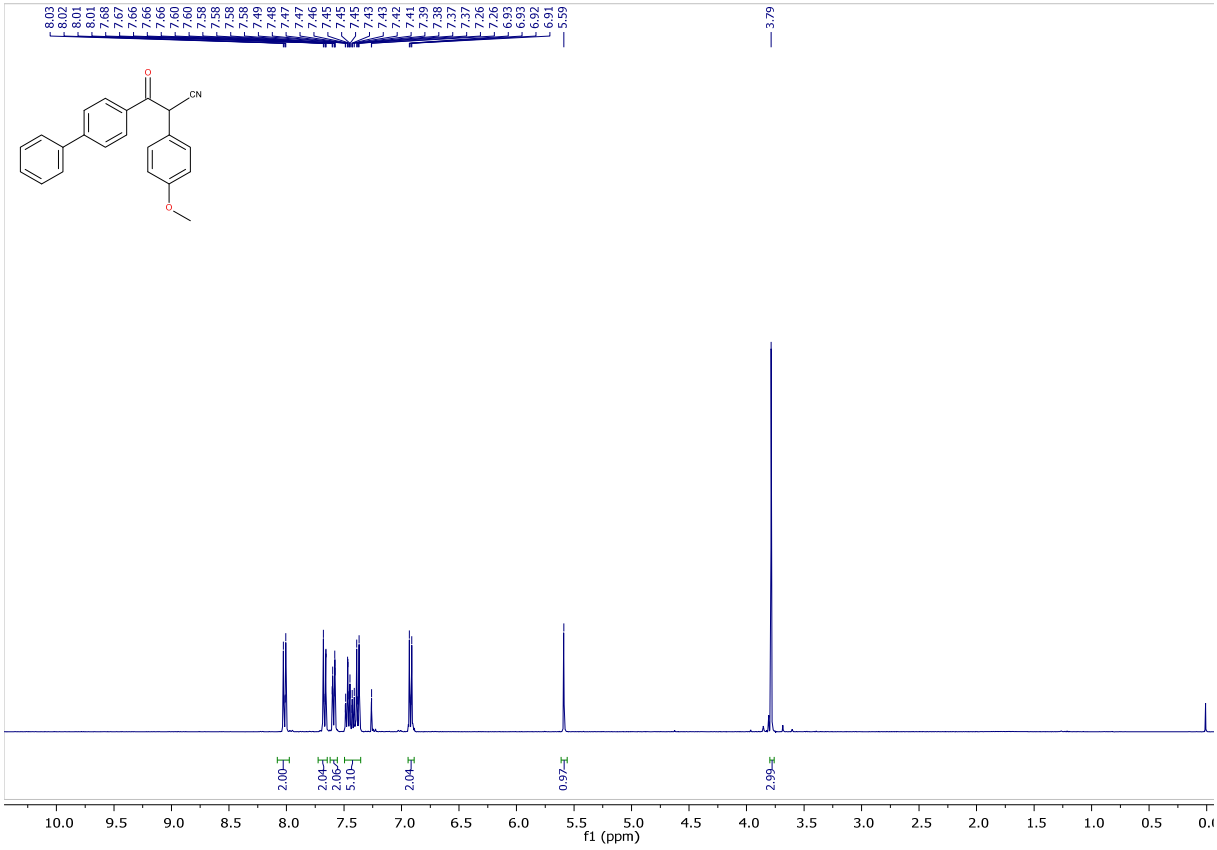

193.74
133.62
133.42
129.19
128.53
122.41
40.61
25.39
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

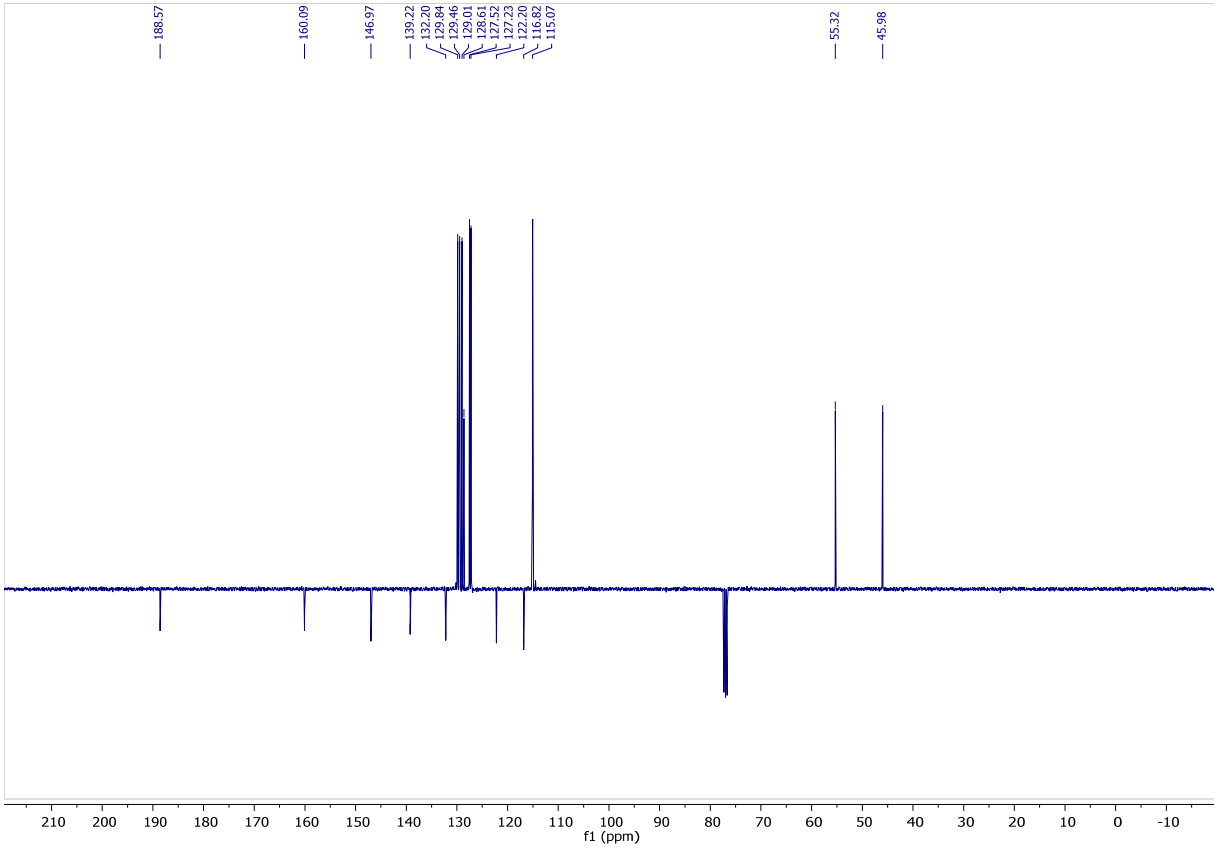
6c

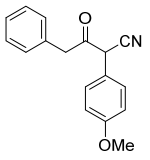

8.27
8.25
7.74
7.74
7.72
7.72
7.65
7.65
7.64
7.63
7.63
7.51
7.51
7.49
7.49
7.47
7.47
7.44
7.42
1.76
O
CN
1.99
2.01
2.02
2.94
6.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


193.33
146.49
139.42
132.08
130.05
129.00
128.50
127.26
122.70
40.72
25.62
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

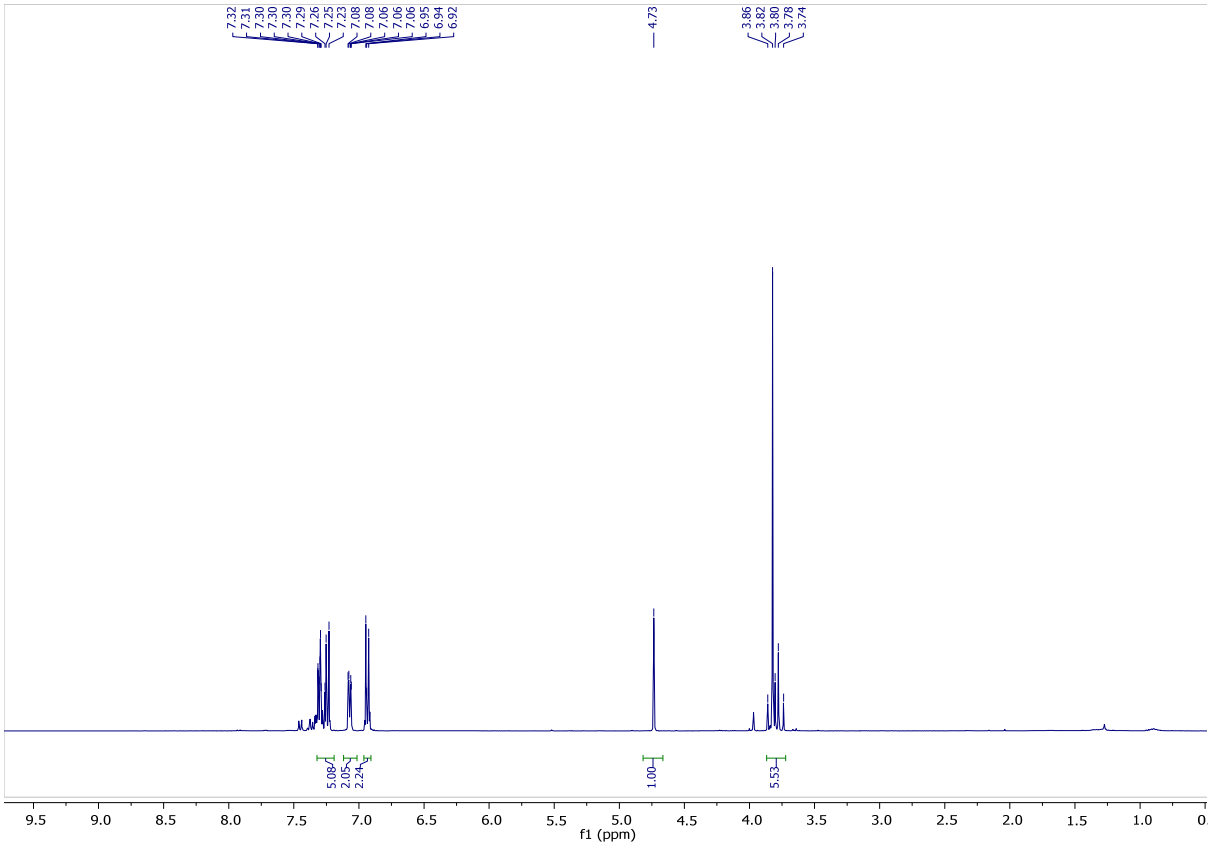
6d


8.03
8.02
8.01
8.01
7.68
7.67
7.66
7.66
7.66
7.60
7.60
7.58
7.58
7.58
7.58
7.49
7.48
7.47
7.47
7.46
7.45
7.45
7.45
7.43
7.43
7.42
7.41
7.39
7.38
7.37
7.37
7.26
7.26
6.93
6.93
6.92
6.91
5.59
3.79
O
CN
O
2.00
2.04
2.06
5.10
2.04
0.97
2.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


188.57
160.09
146.97
139.22
132.20
129.84
129.46
129.01
128.61
127.52
127.23
122.20
116.82
115.07
55.32
45.98
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


O
CN
OMe

6e


7.32
7.31
7.30
7.30
7.30
7.29
7.26
7.25
7.23
7.08
7.08
7.06
7.06
7.06
6.95
6.94
6.92
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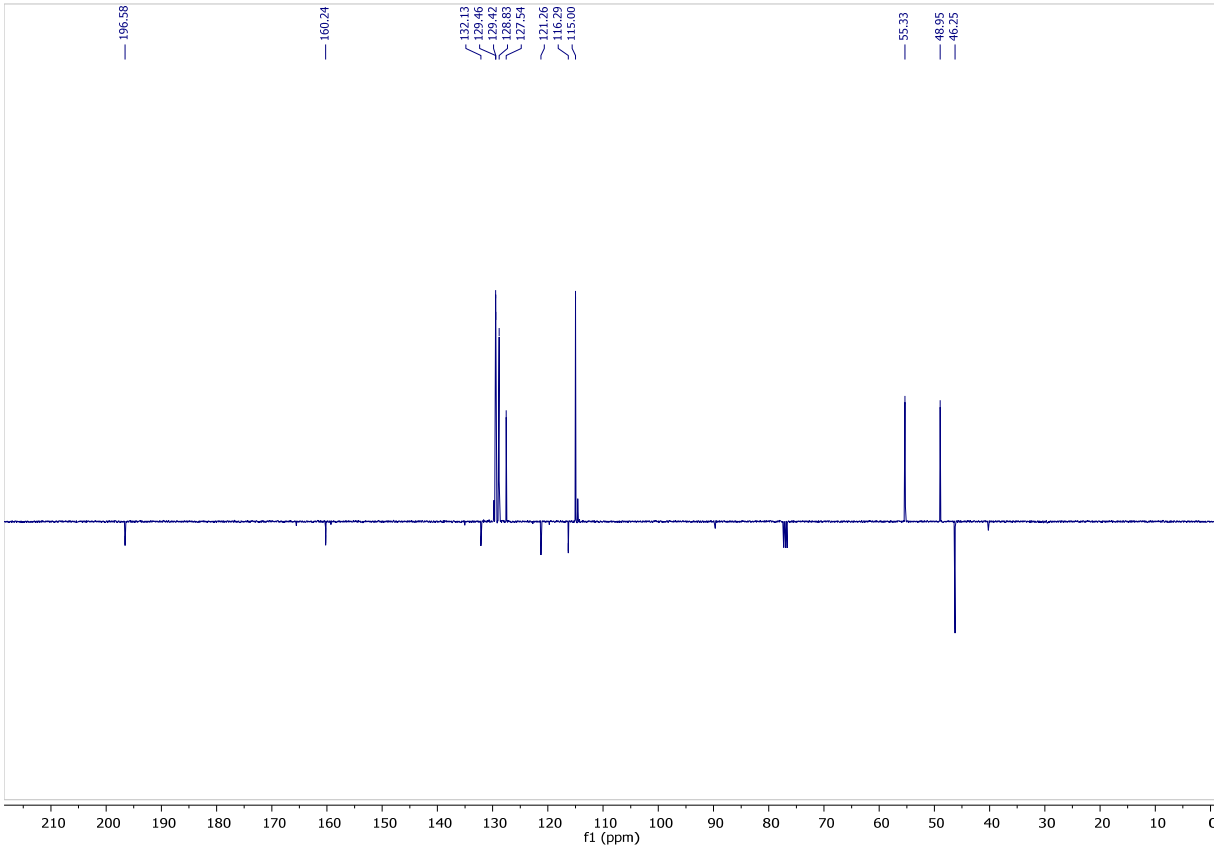
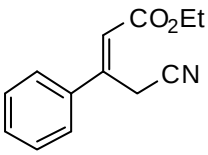
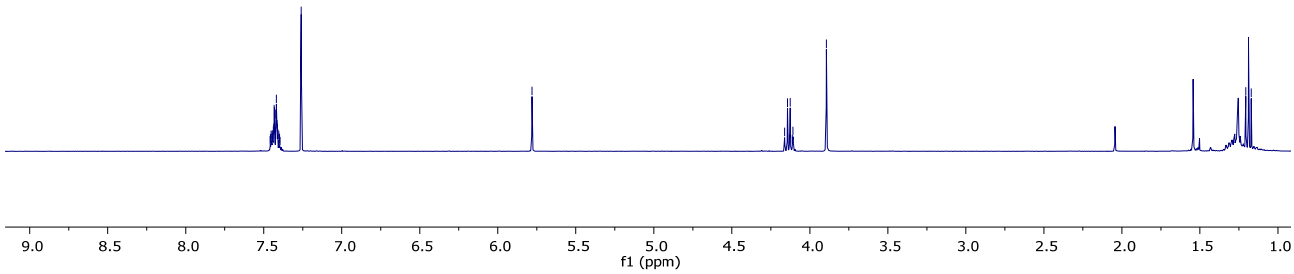
5.08
2.05
2.24
1.00
5.53
f1 (ppm)

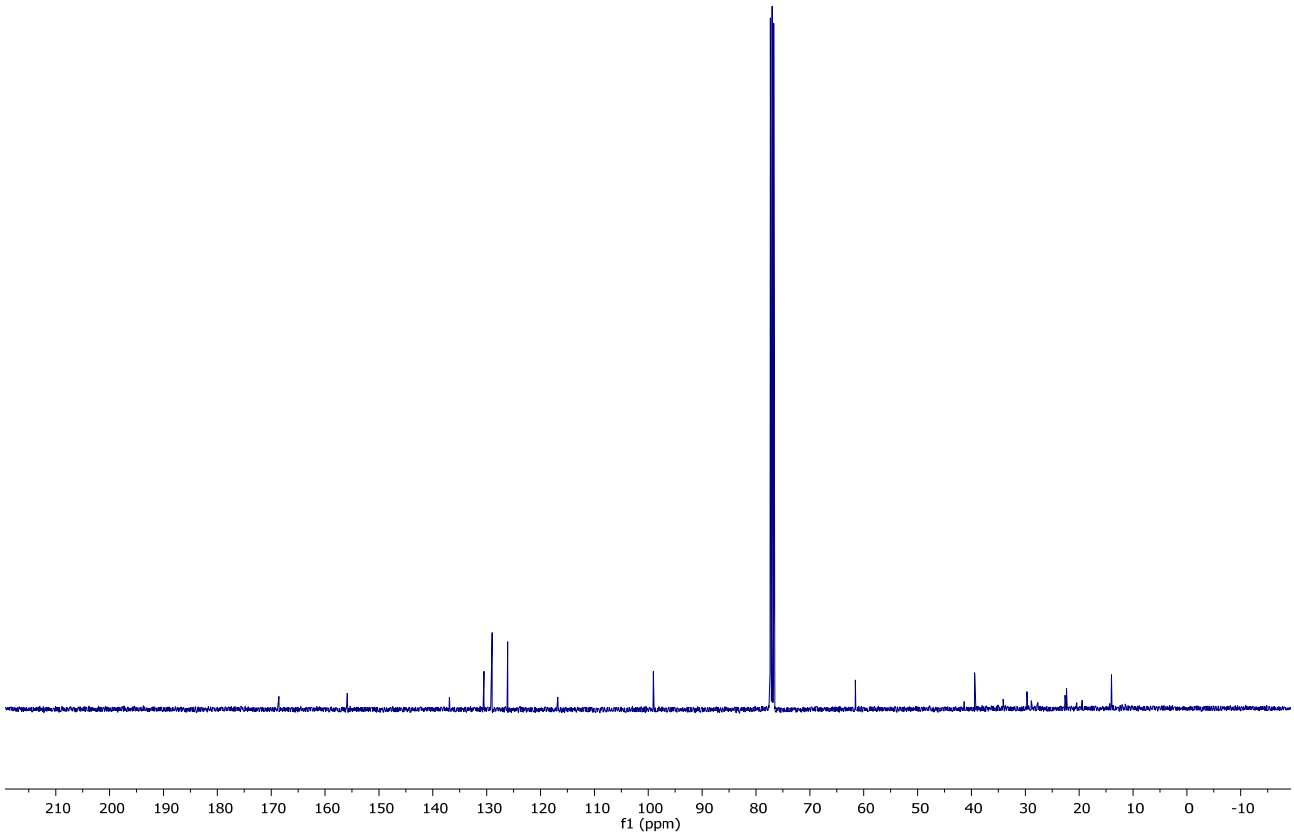

196.58
160.24
132.13
129.46
129.42
128.83
127.54
121.26
116.29
115.60
55.33
48.95
46.25
f1 (ppm)


7.46
7.46
7.45
7.45
7.45
7.44
7.44
7.44
7.44
7.43
7.43
7.43
7.42
7.42
7.41
7.41
7.41
7.40
7.40
7.40
7.40
7.26
5.78
4.16
4.14
4.13
4.13
4.11
4.11
3.89
1.21
1.19
1.17


CO2Et
CN

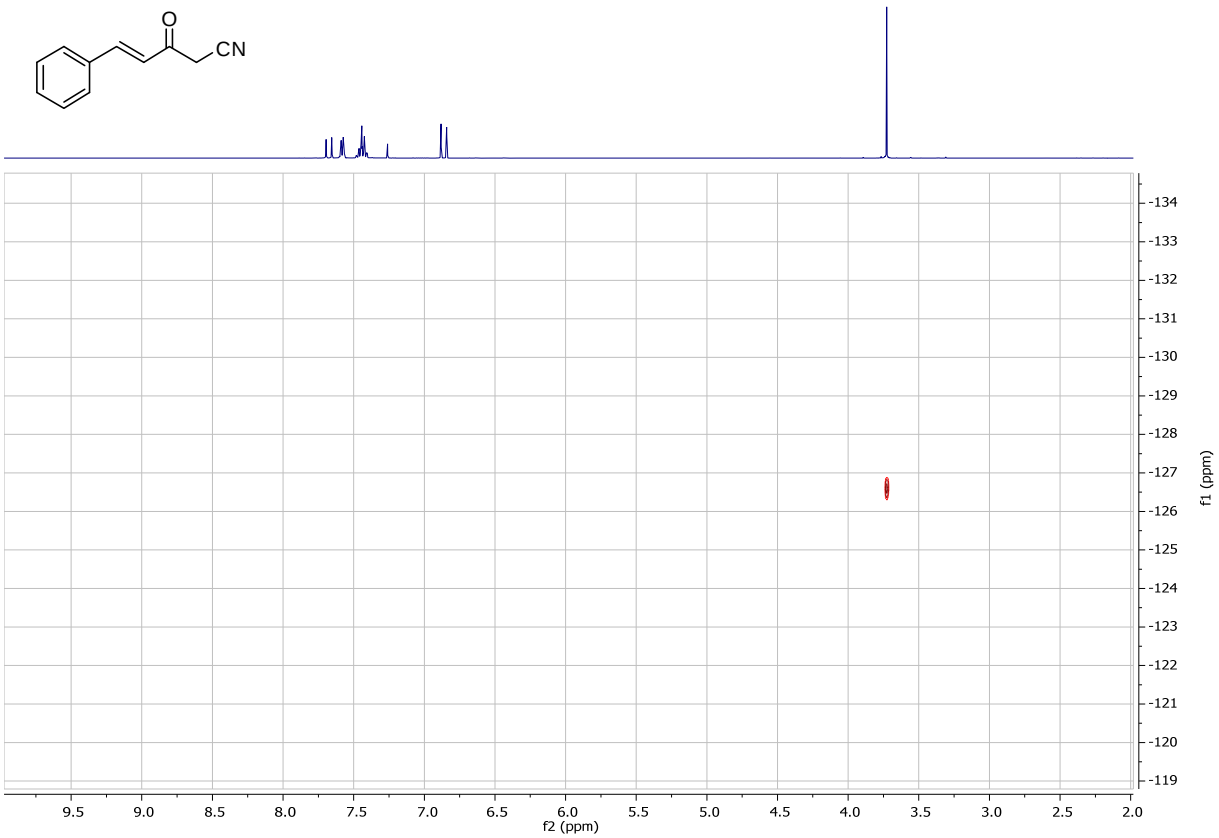
7


9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

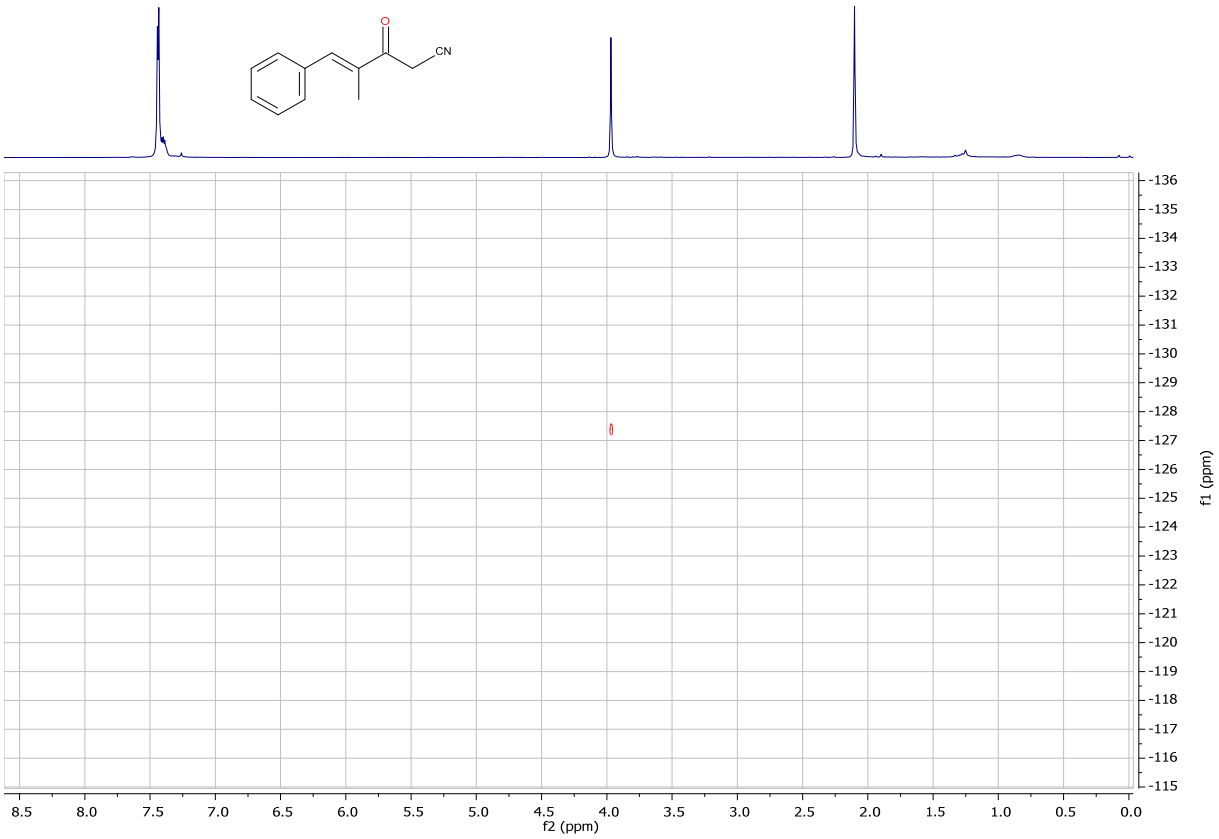

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

Copies of ^{15}N NMR spectra for selected compounds

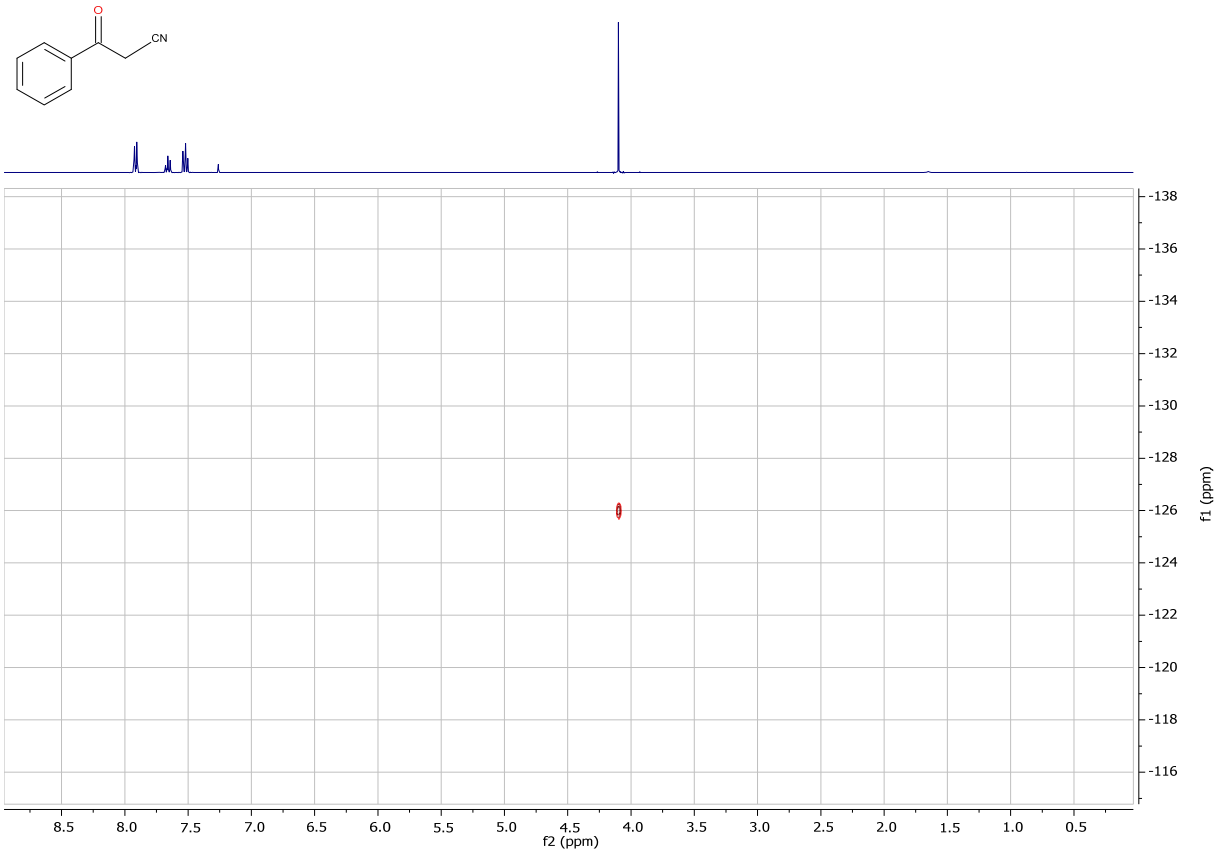
2 (^{1}H,^{15}N - HMBC)



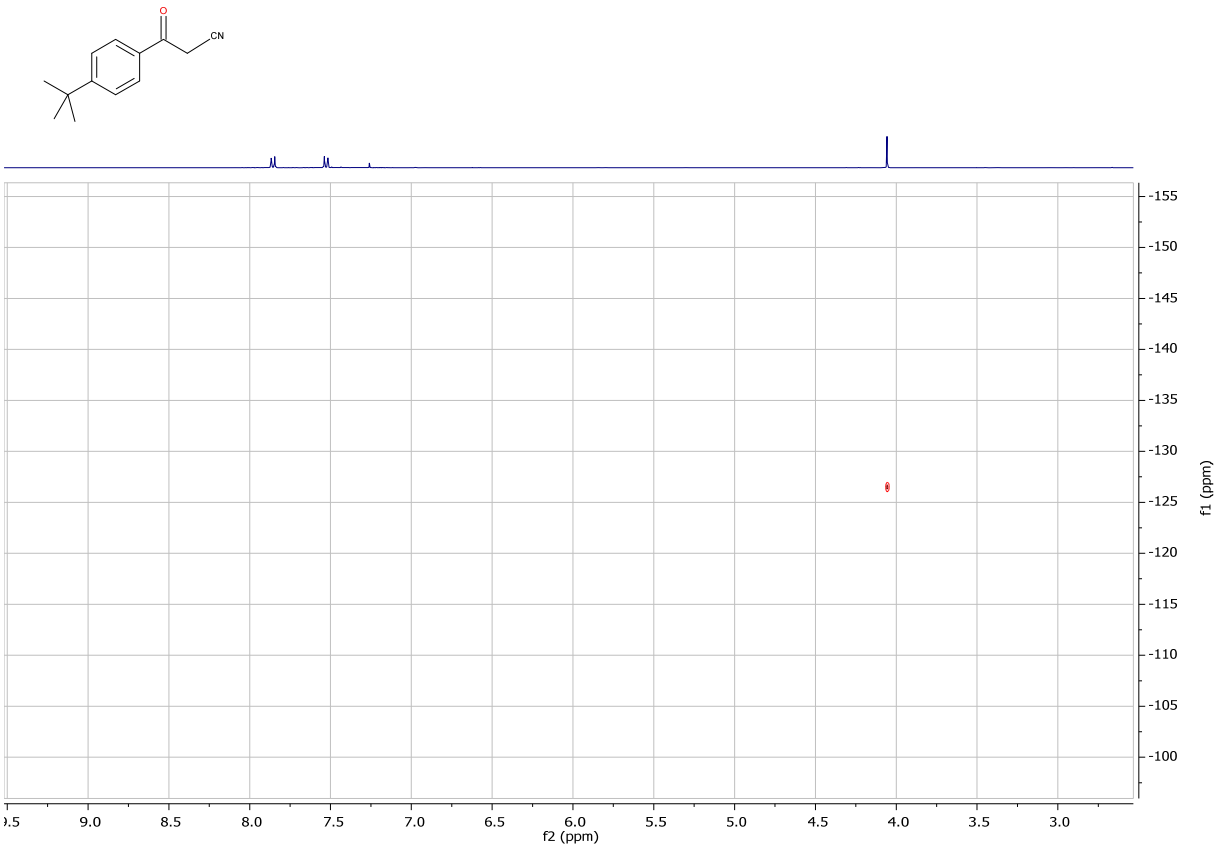
4a (^{1}H,^{15}N - HMBC)



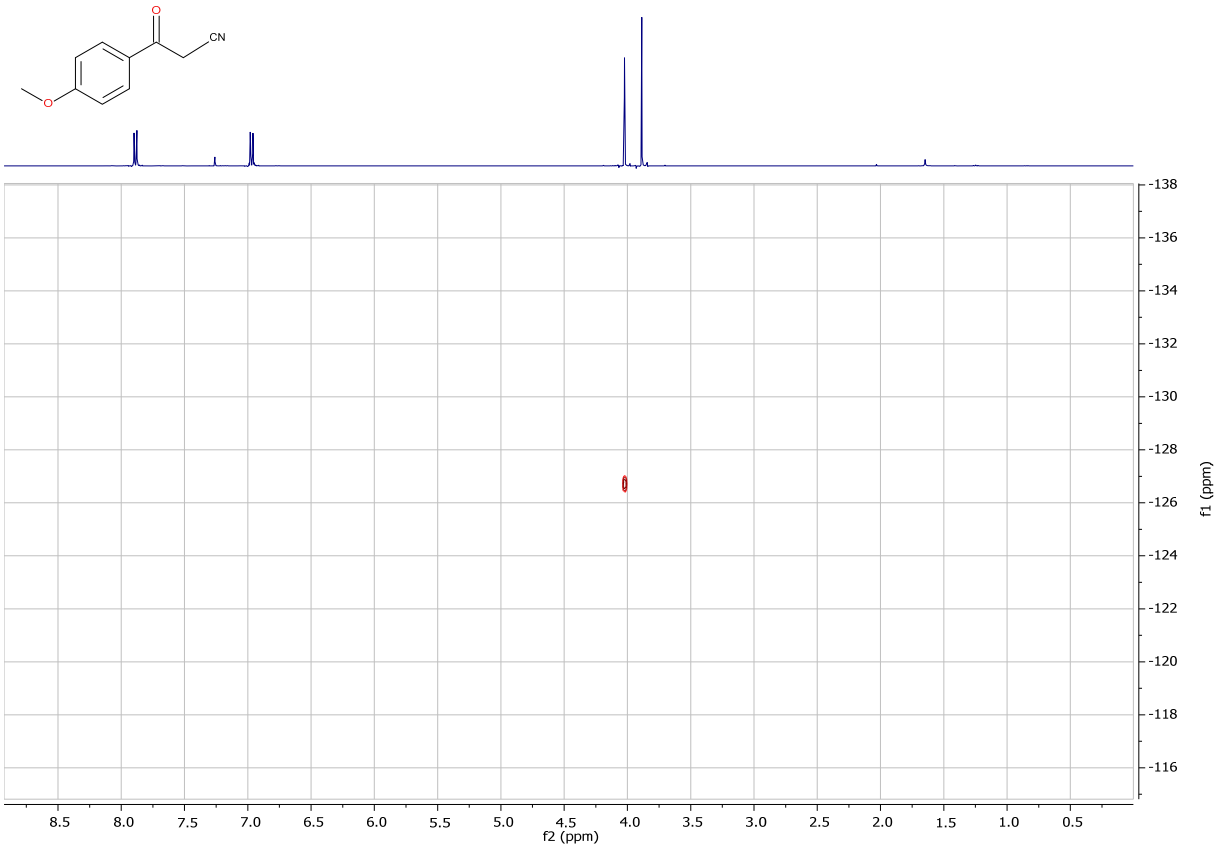
4d (^{1}H,^{15}N - HMBC)



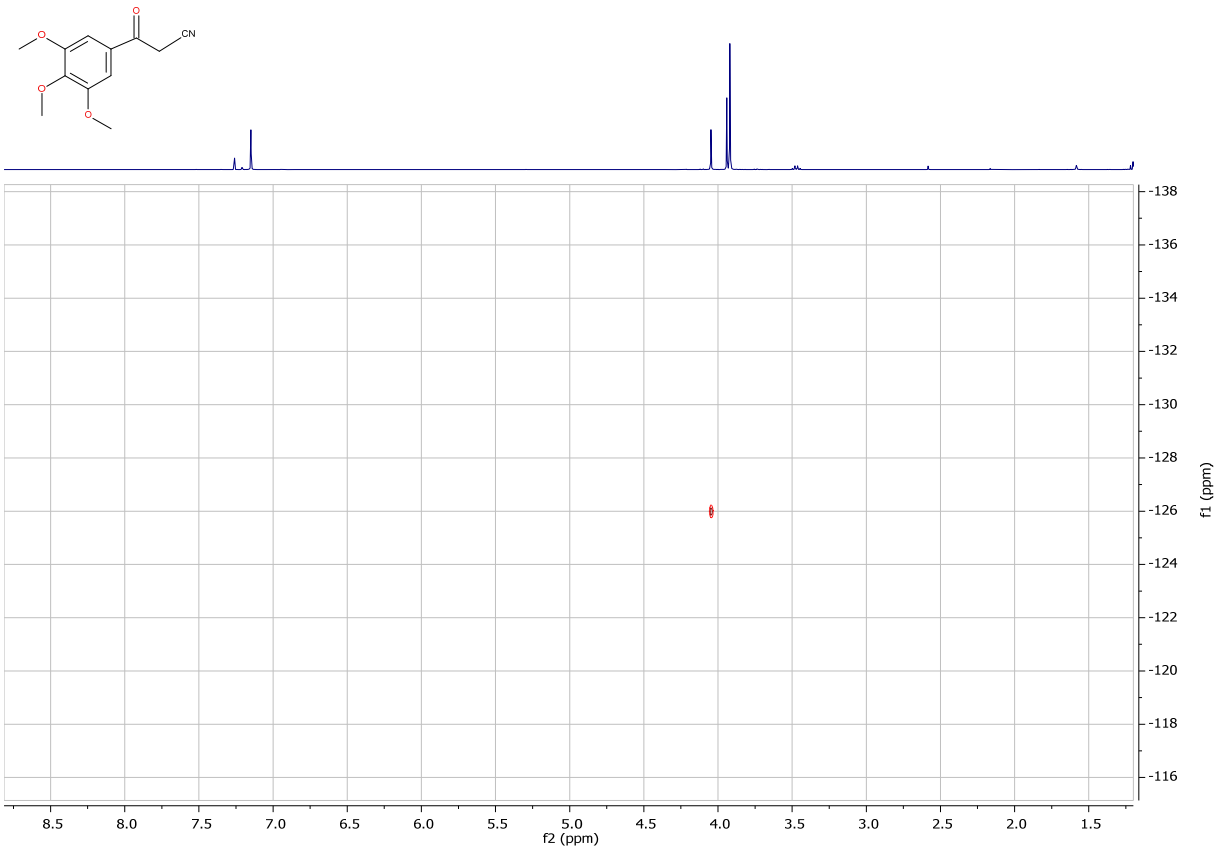
4e (^{1}H,^{15}N - HMBC)



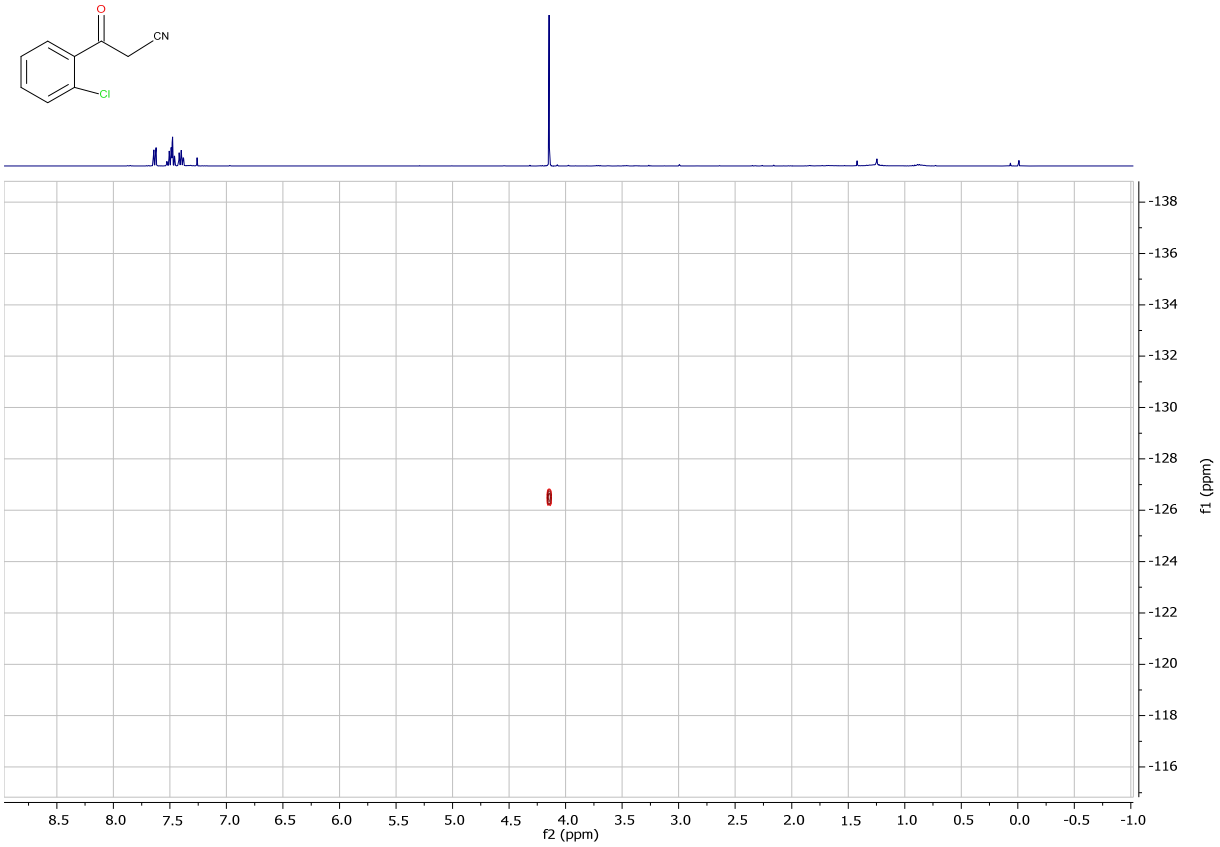
4f (^{1}H,^{15}N - HMBC)



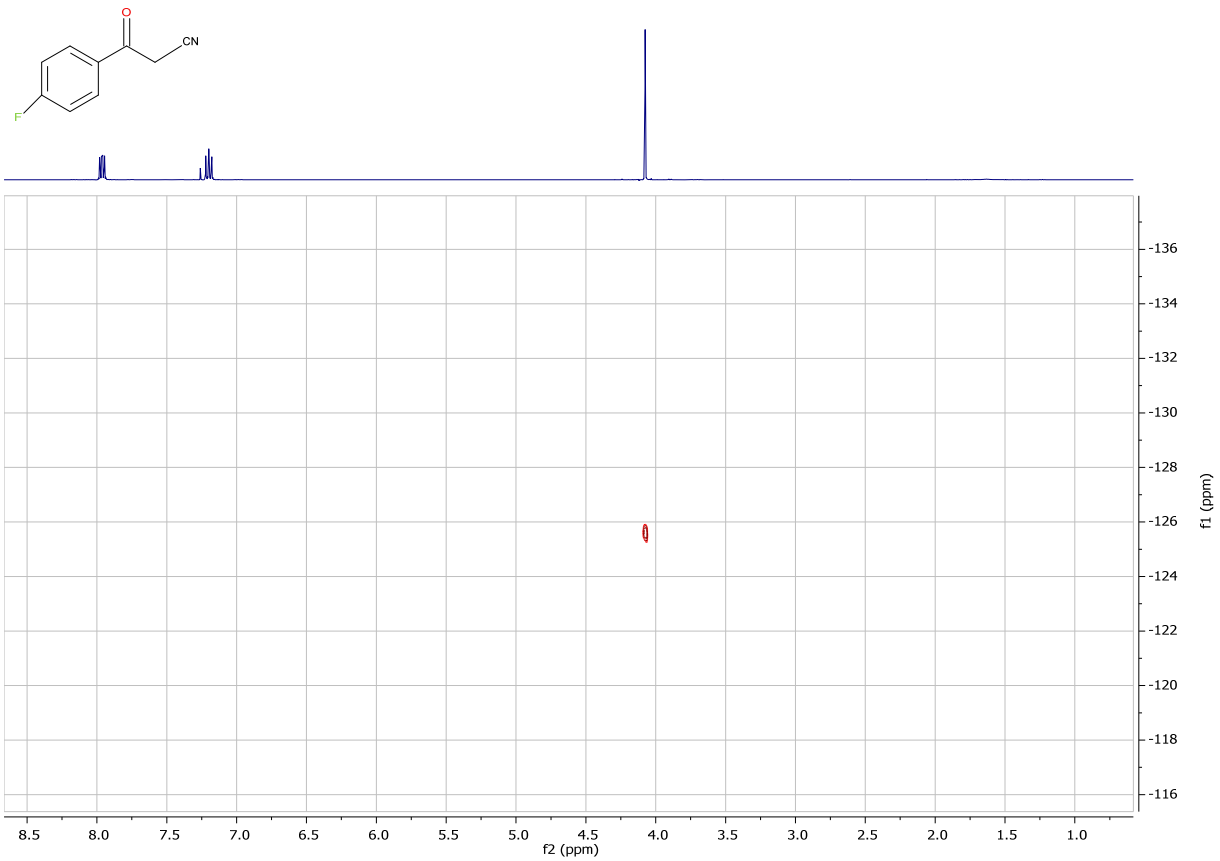
4g (^{1}H,^{15}N - HMBC)



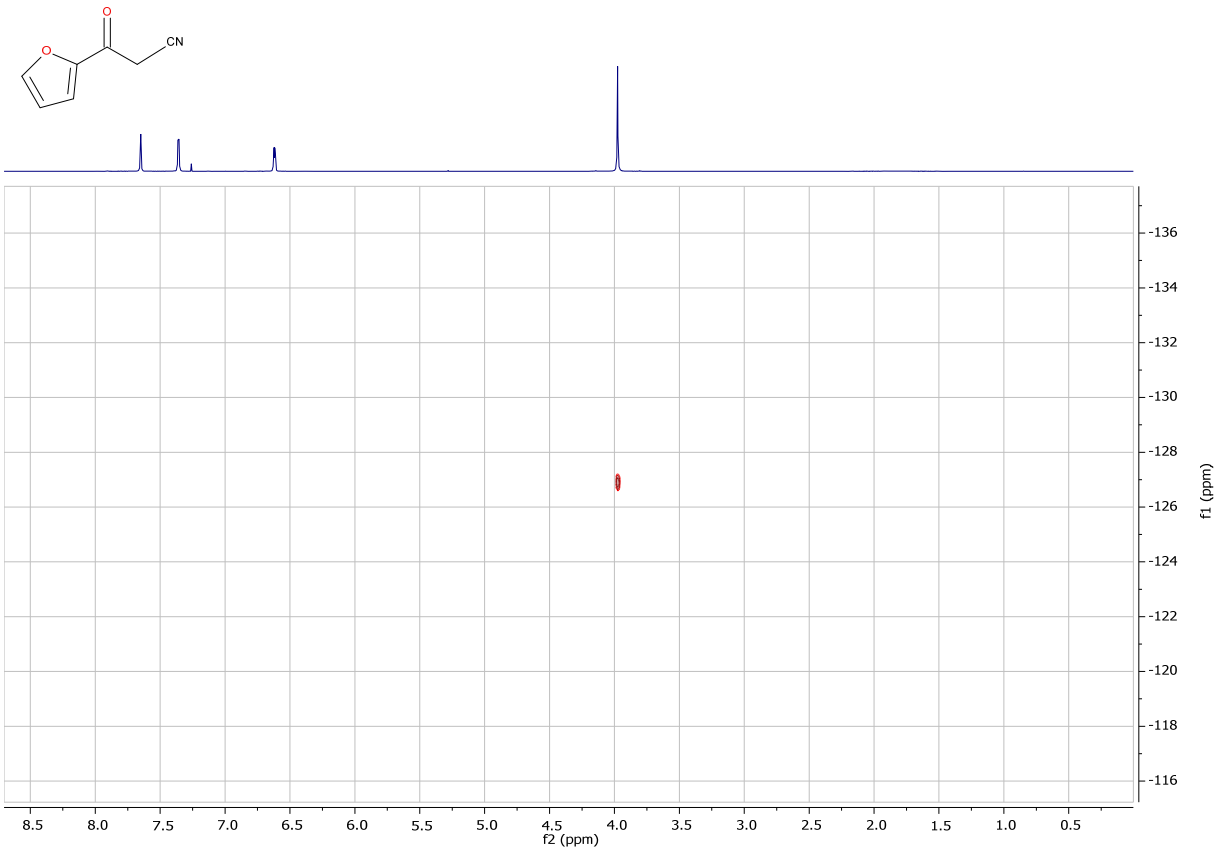
4h (^{1}H,^{15}N - HMBC)



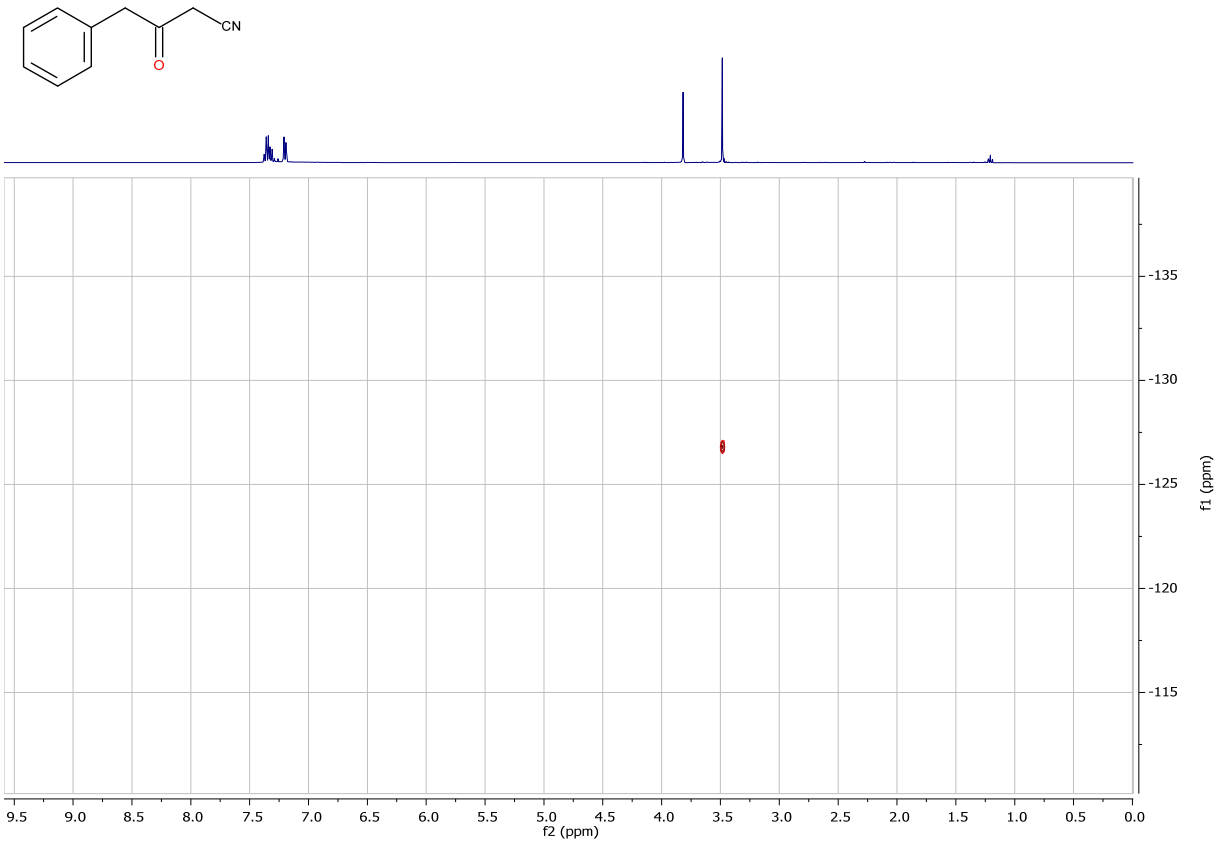
4j (^{1}H,^{15}N - HMBC)



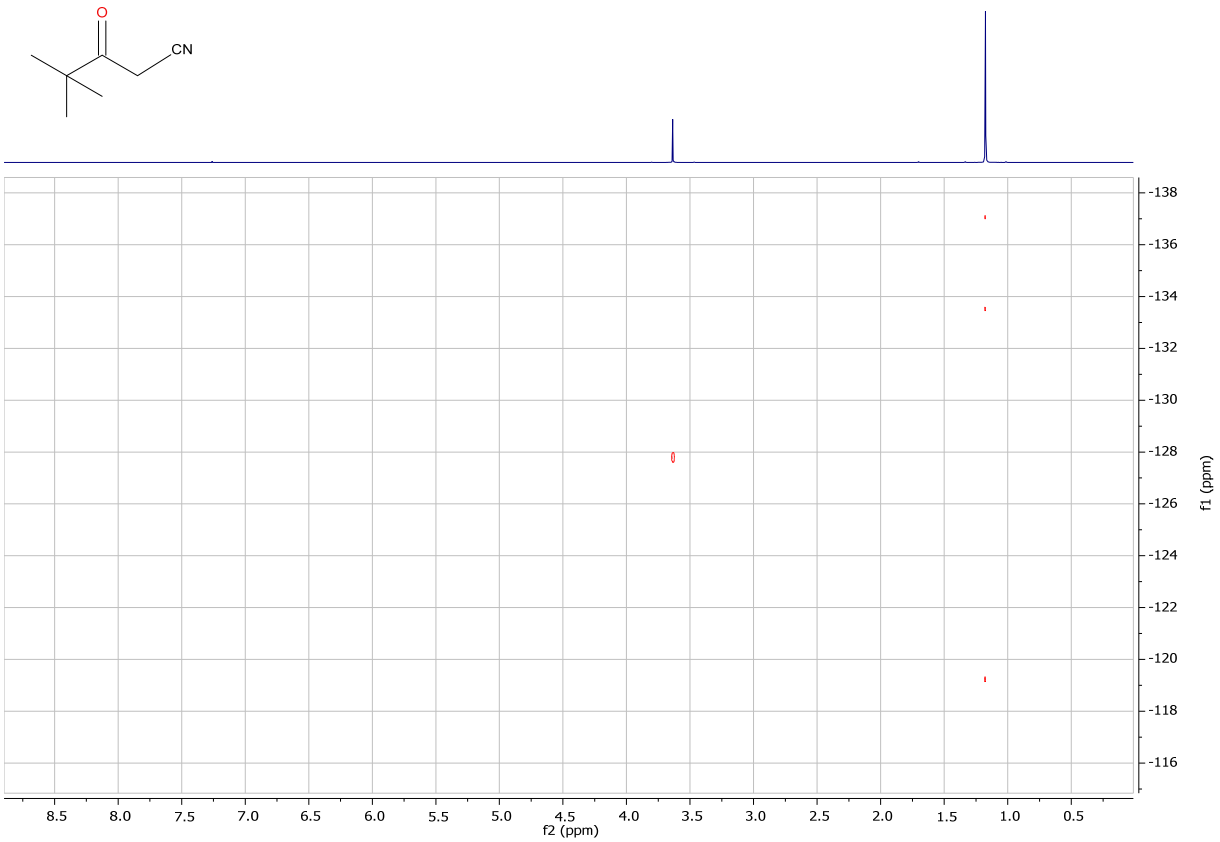
4k (^{1}H,^{15}N - HMBC)



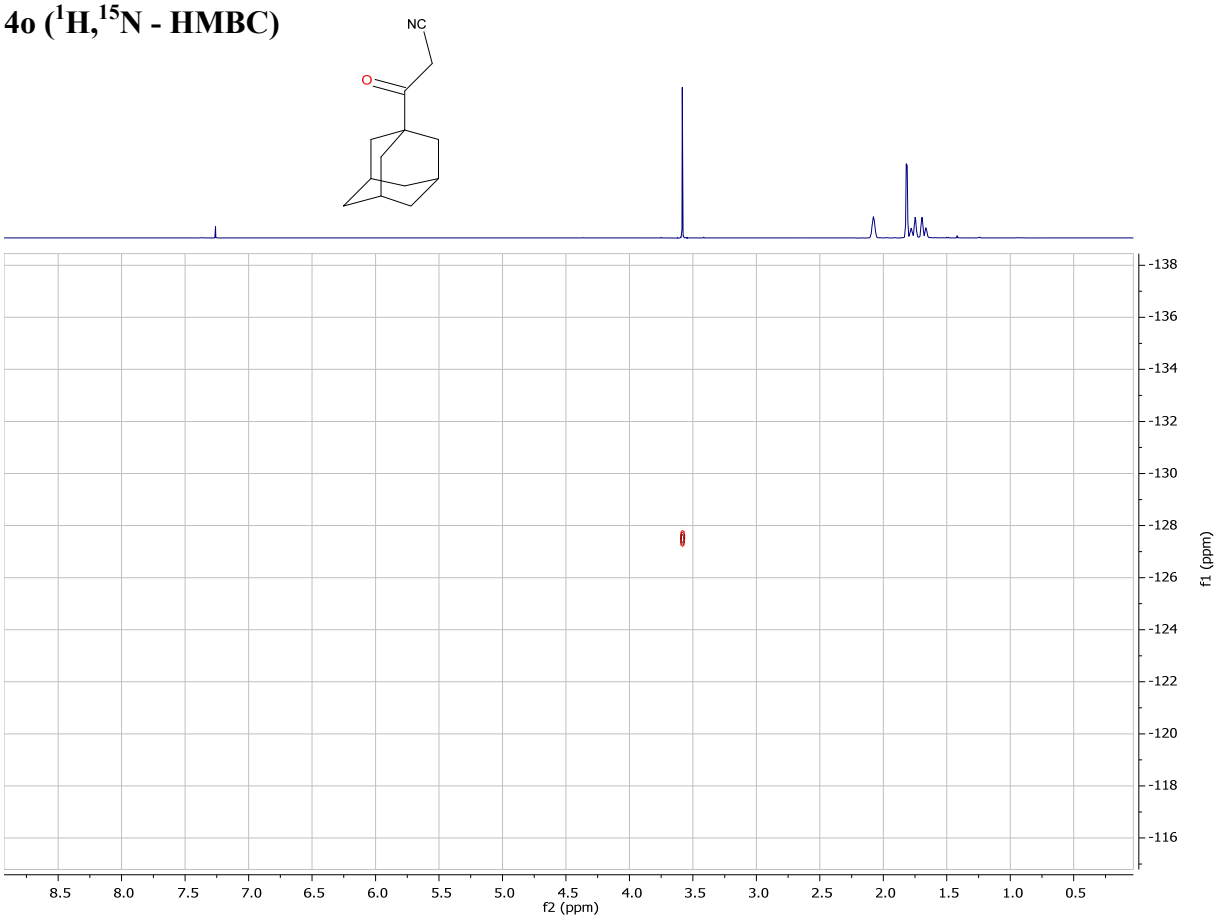
4m (^{1}H,^{15}N - HMBC)



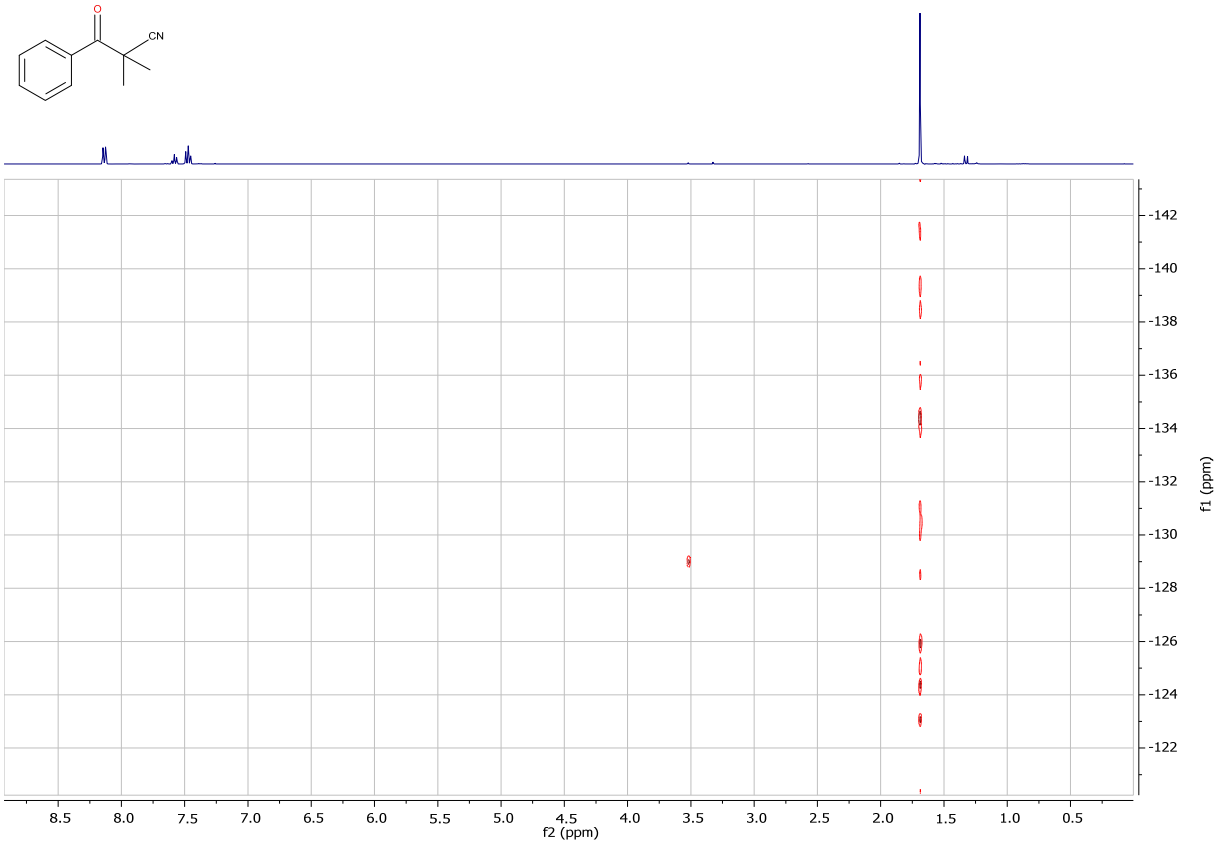
4n (^{1}H,^{15}N - HMBC)



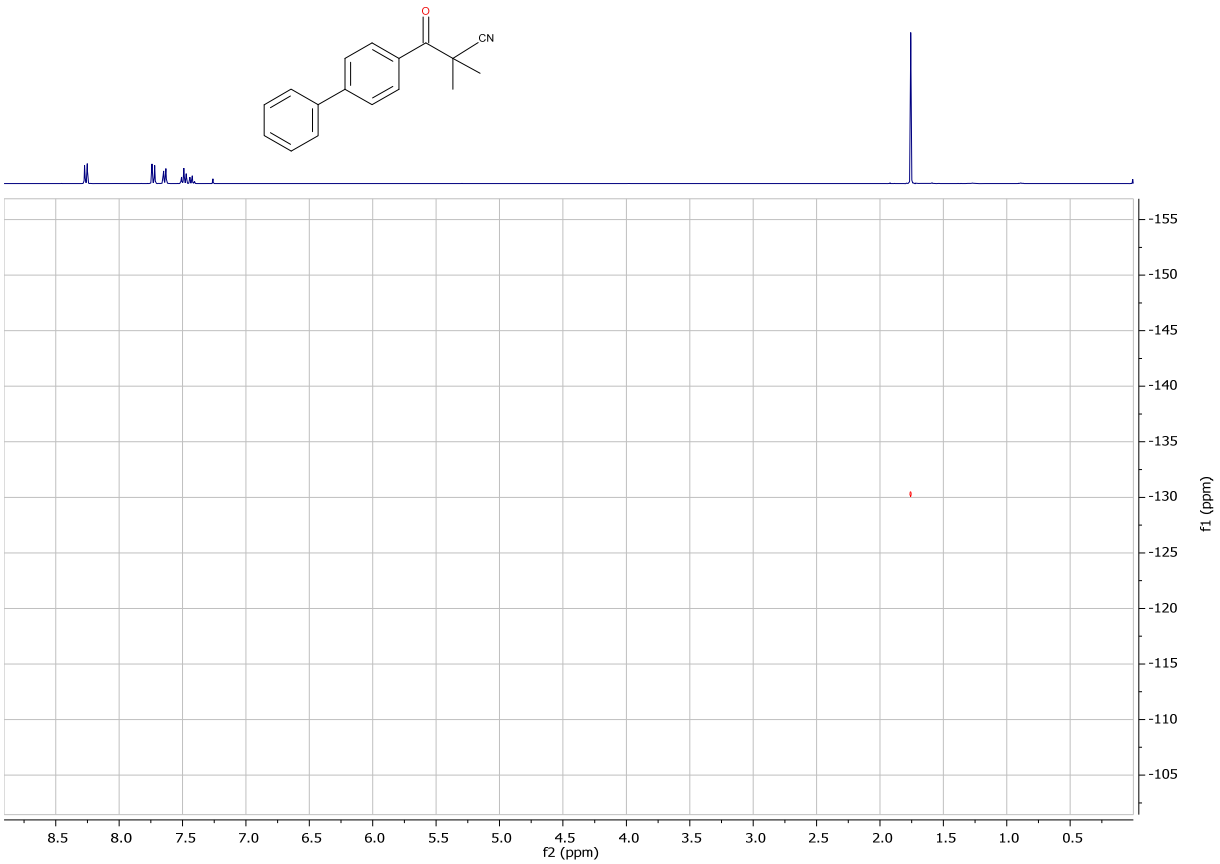
4o (^{1}H,^{15}N - HMBC)



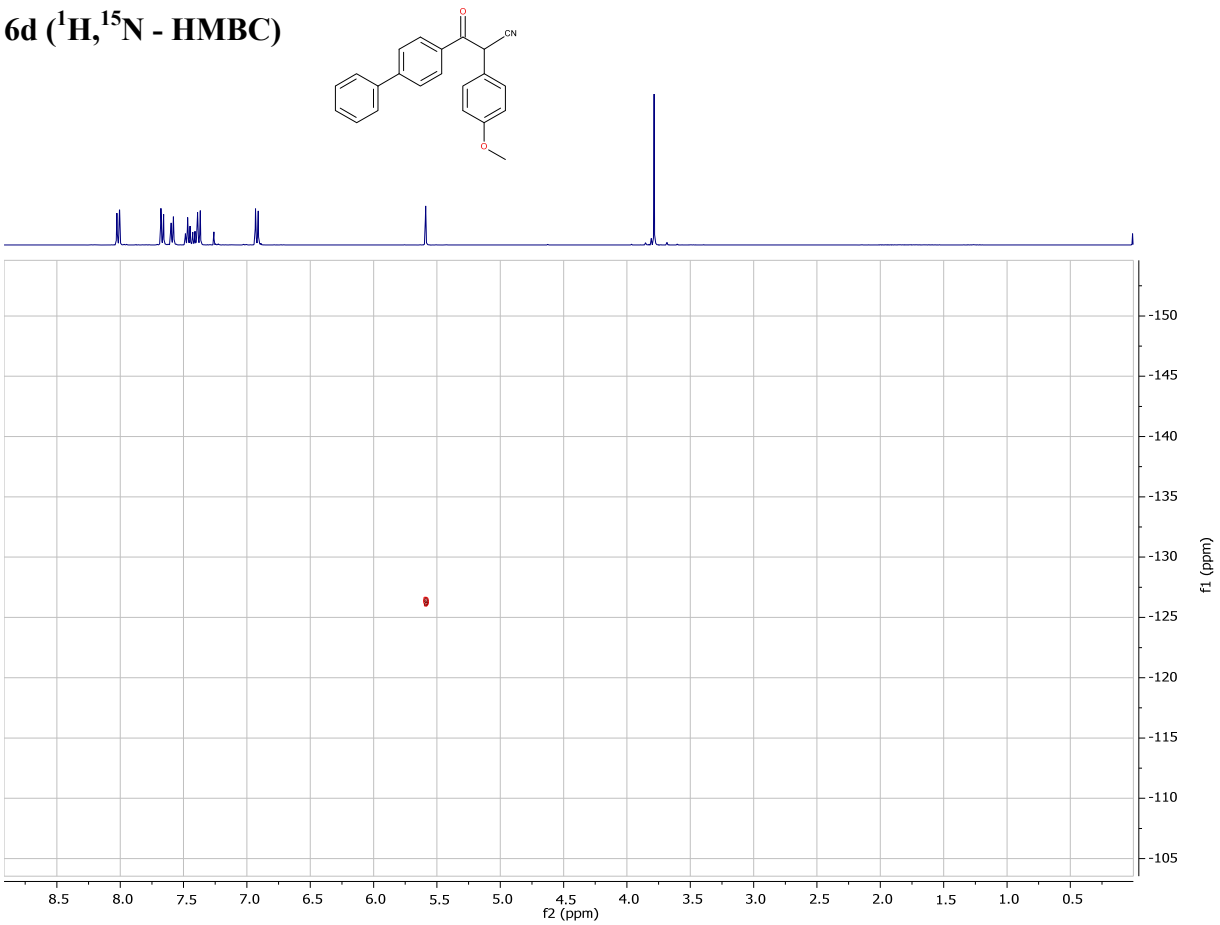
6b (^{1}H,^{15}N - HMBC)



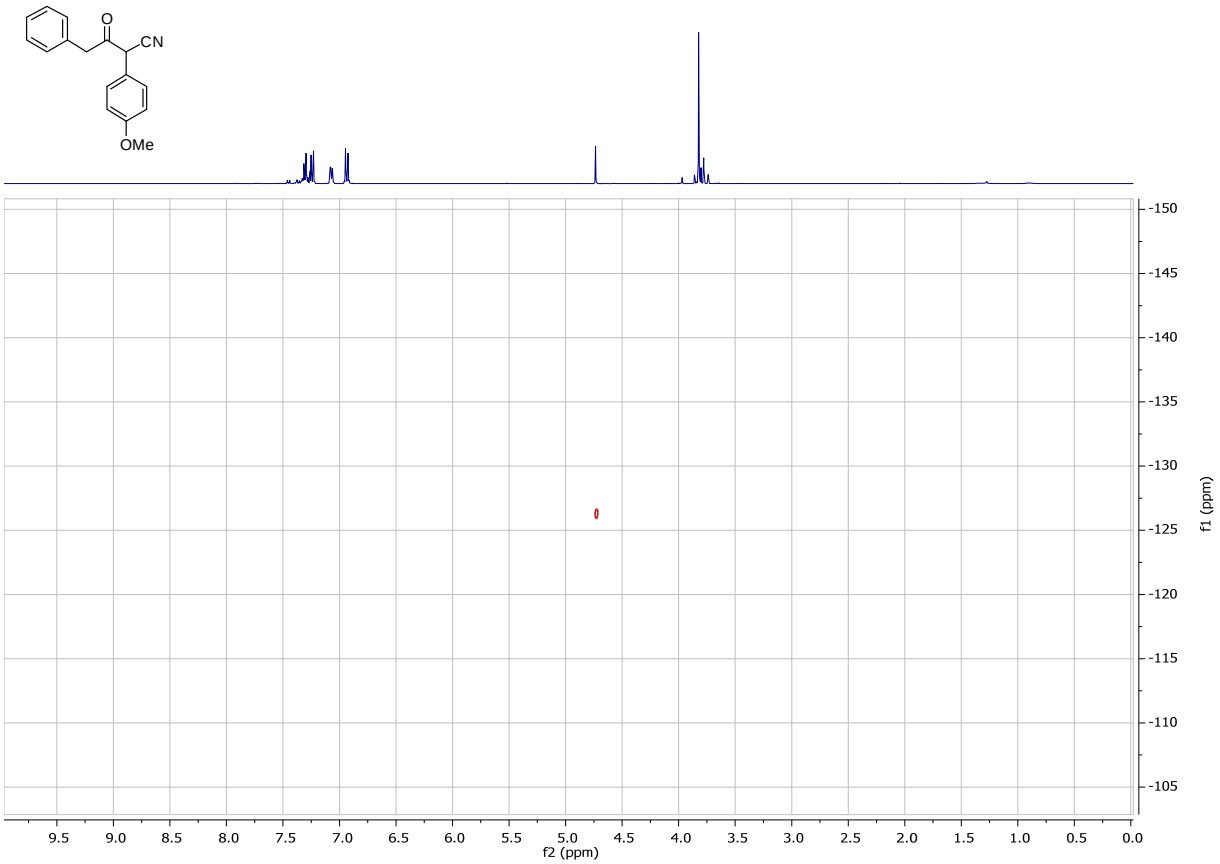
6c (^{1}H,^{15}N - HMBC)



6d (^{1}H,^{15}N - HMBC)

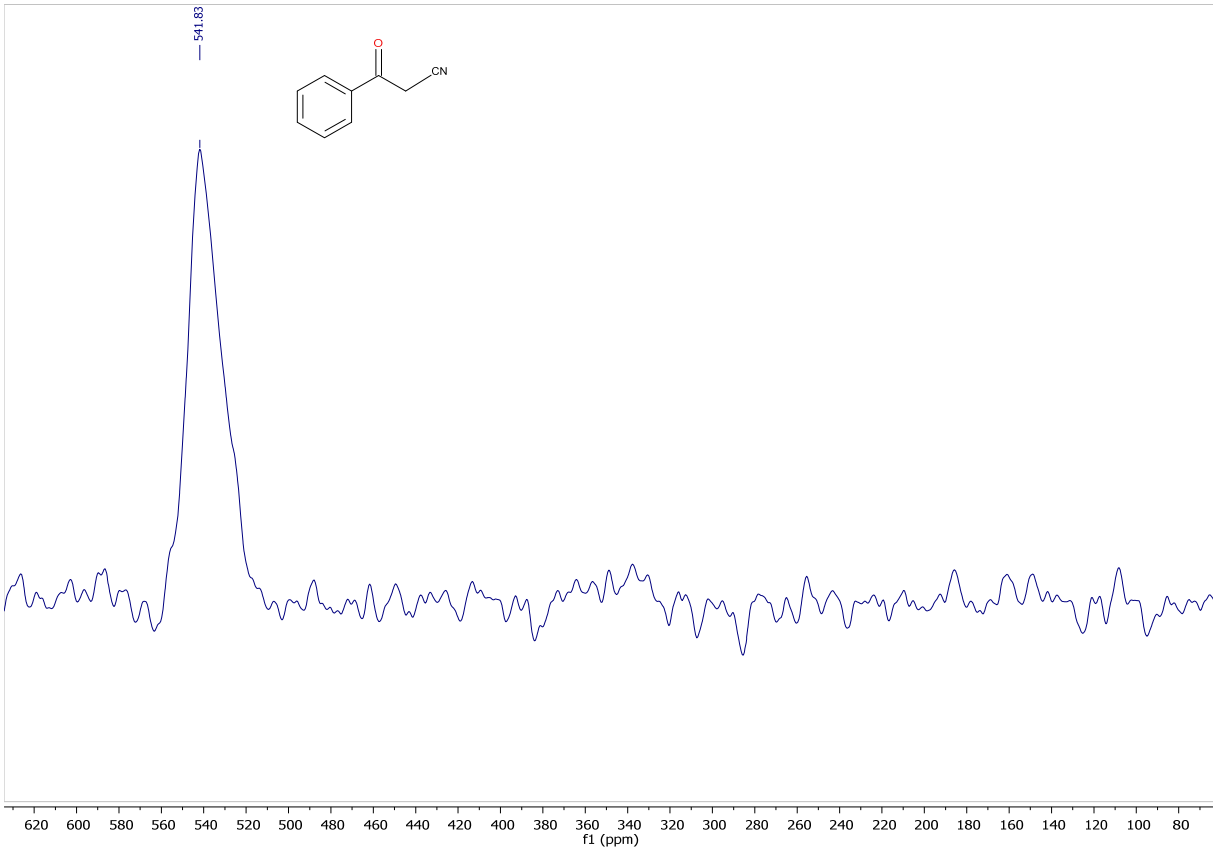


6e (^{1}H,^{15}N - HMBC)

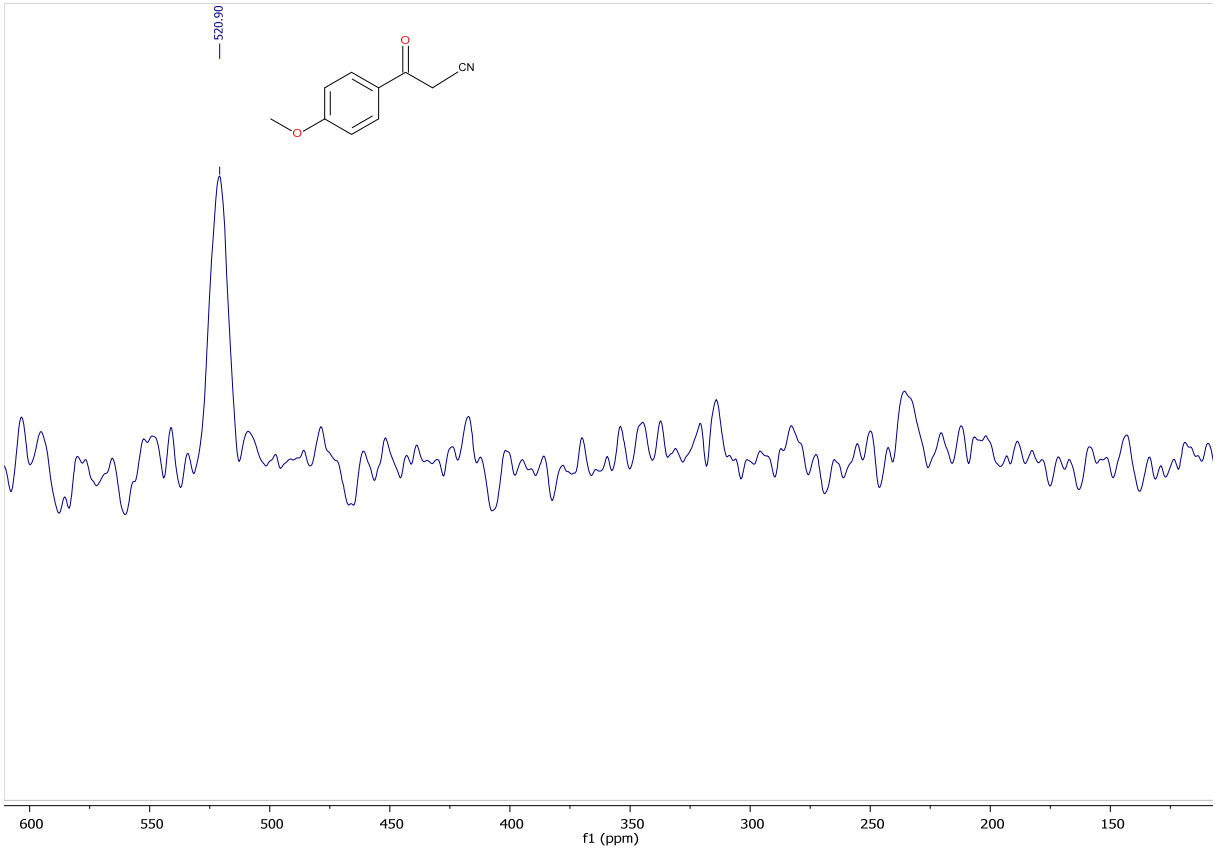


Copies of ^{17}O NMR spectra for selected compounds

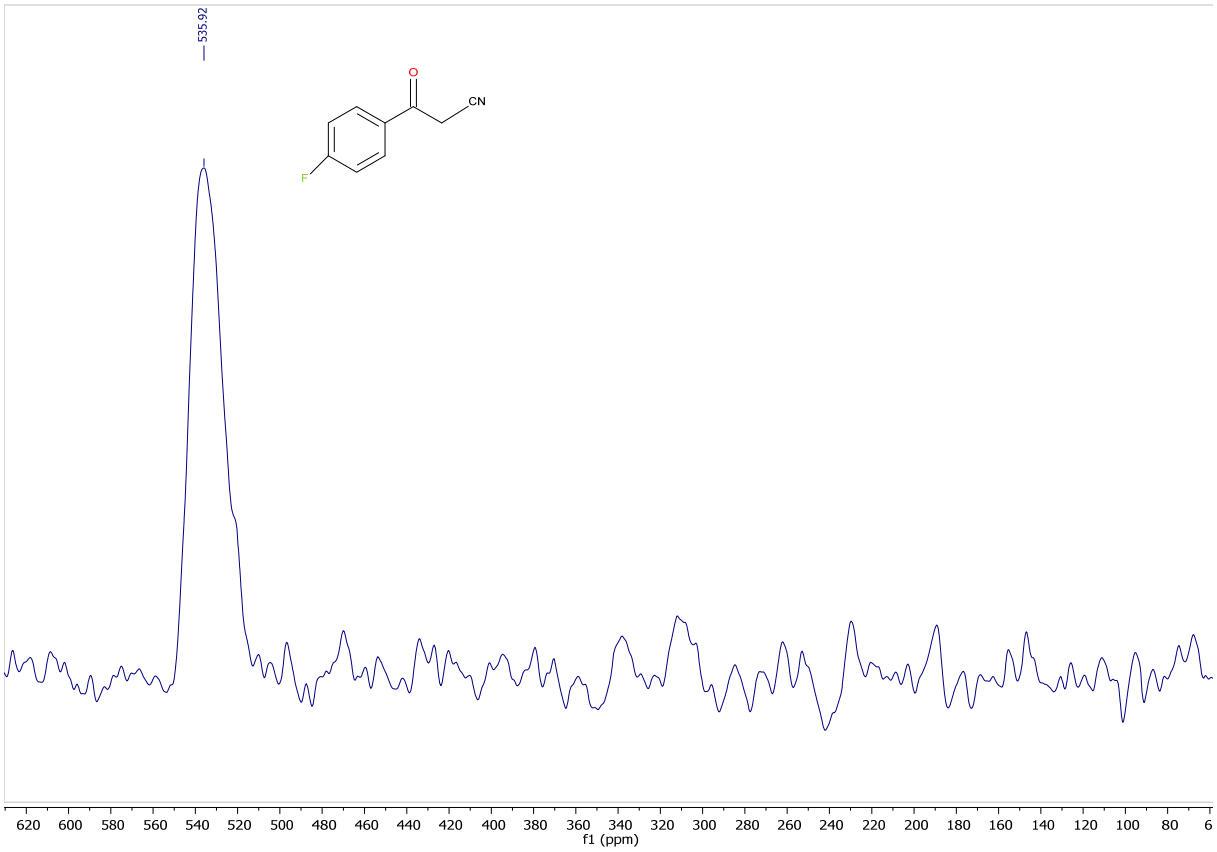
4d (^{17}O NMR)



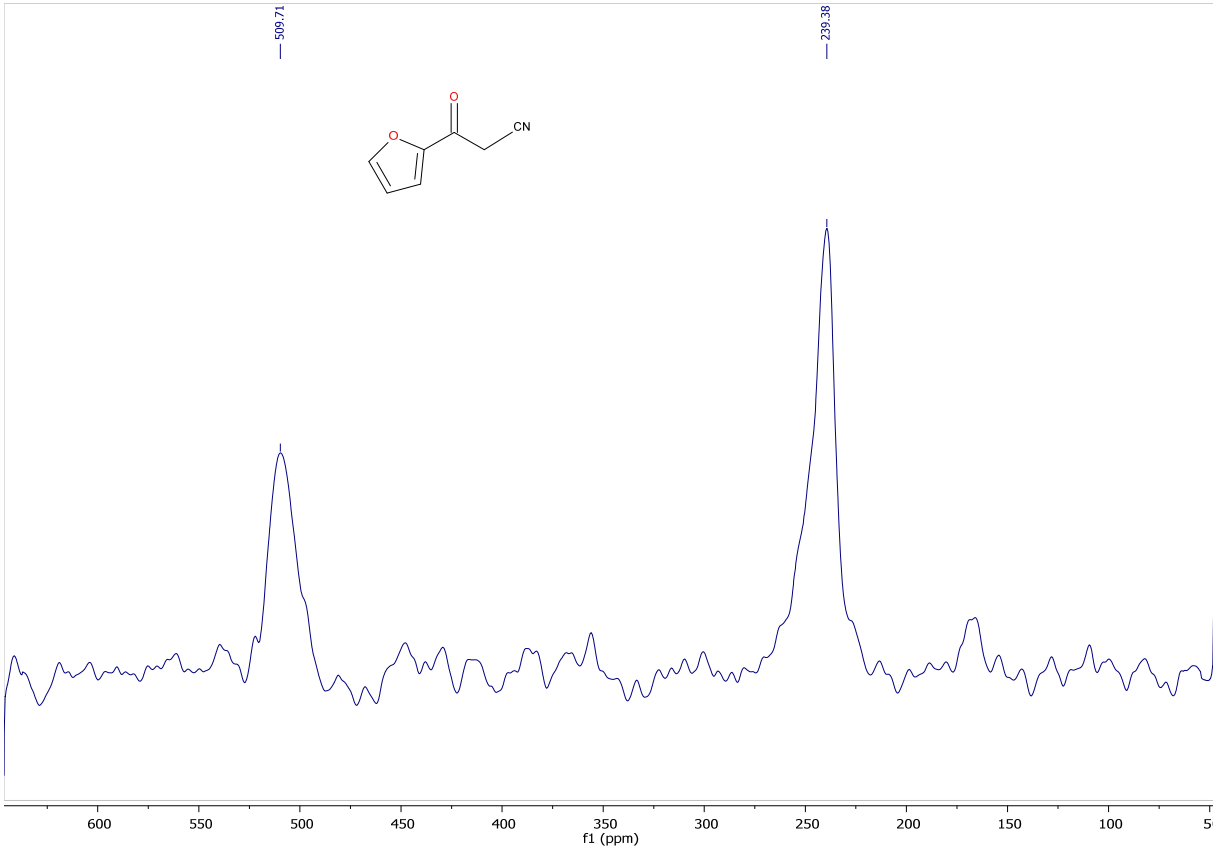
4f (^{17}O NMR)



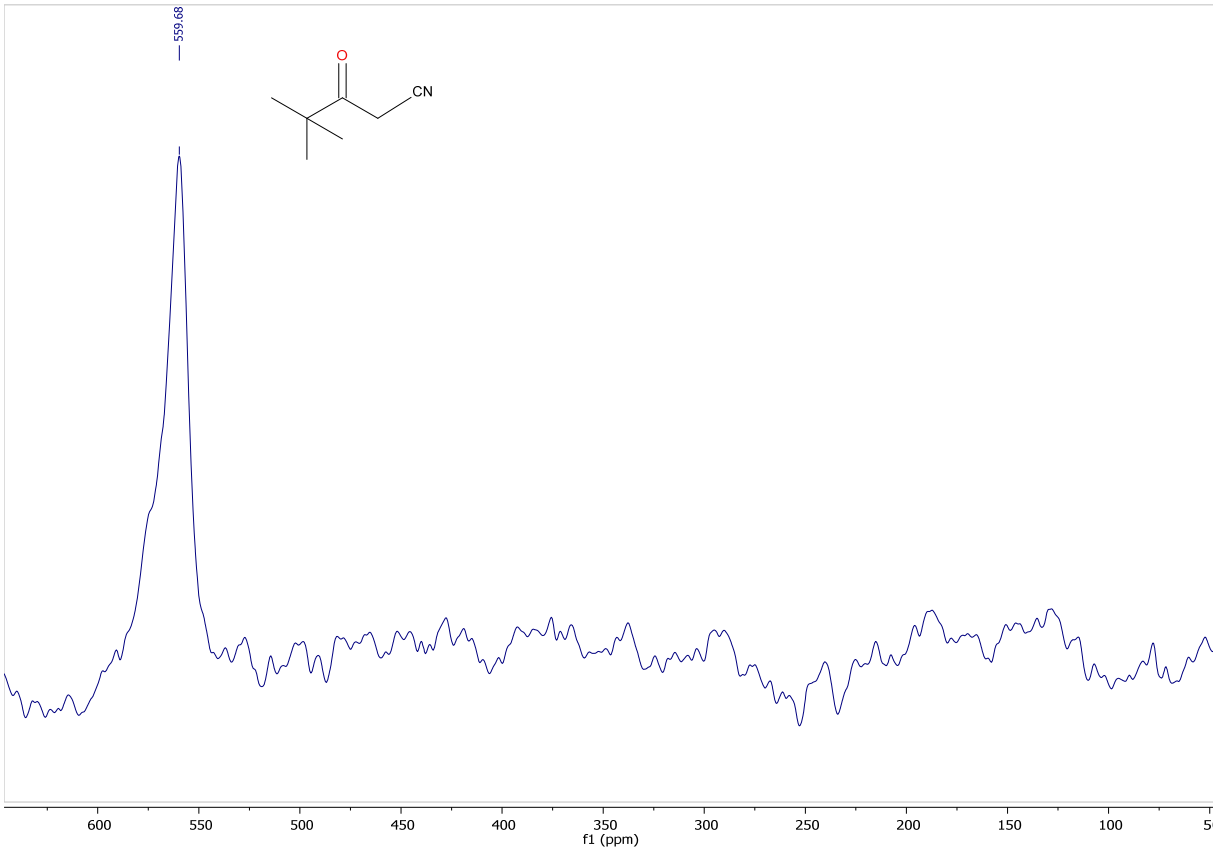
4j (^{17}O)


535.92
O
CN
F
620 600 580 560 540 520 500 480 460 440 420 400 380 360 340 320 300 280 260 240 220 200 180 160 140 120 100 80 6
f1 (ppm)

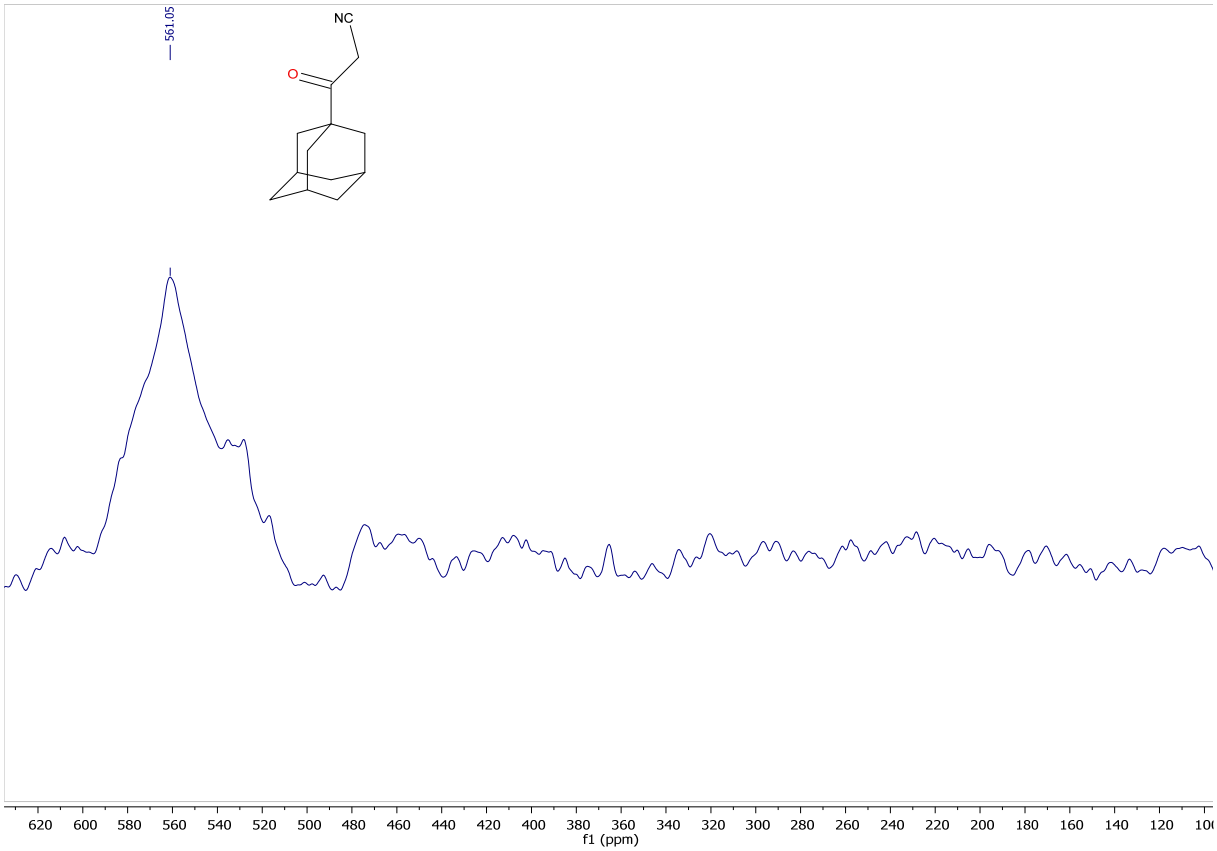
4k (^{17}O)


509.71
239.38
O
O
CN
600 550 500 450 400 350 300 250 200 150 100 5
f1 (ppm)

4n (^{17}O)


559.68
O
CN
600
550
500
450
400
350
300
250
200
150
100
f1 (ppm)

4o (^{17}O)


561.05
NC
O
620
600
580
560
540
520
500
480
460
440
420
400
380
360
340
320
300
280
260
240
220
200
180
160
140
120
f1 (ppm)