Supporting information

HCl·DMPU-Assisted One-pot and Metal-free Conversion Of Aldehydes to Nitriles

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General Methods

^{1}H and ^{13}C decoupled NMR spectra were recorded either at 400 or 500 MHz and 101 MHz using $CDCl_3$, CD_2Cl_2 or DMSO as a solvent. The chemical shifts are reported in δ (ppm) values (^{1}H and ^{13}C NMR relative to $CHCl_3$, δ 7.26 ppm for ^{1}H NMR and δ 77.16 ppm for ^{13}C NMR and for DMSO δ 2.50 ppm for ^{1}H NMR and δ 39.52 ppm for ^{13}C NMR, multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), m (multiplet), and br (broad). Coupling constants (J) are reported in hertz (Hz). Data for ^{1}H, ^{13}C and ^{19}F NMR were recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz), and integration. All reagents and solvents were employed without further purification. The products were purified using a commercial flash chromatography system. TLC was developed on silica gel 60 F254 aluminum sheets.

General Procedures.

Procedure for Generation of HCl/ DMPU: The reagent HCl·DMPU was prepared as reported in the literature.[1, 2]

General procedure for the synthesis of nitriles (3) and (5).

General procedure A: To a stirred solution of aldehyde (0.5 mmol) and hydroxylamine hydrochloride (0.7 mmol) in acetonitrile (1 ml) was added HCl·DMPU (0.5 mmol). The reaction mixture was vigorously stirred for 3-4 hours at 60 °C. The progress of the reaction was monitored by TLC. After heating, the reaction mixture was cooled at rt and then diluted with EtOAc (10 ml) and water (10 ml). The layers were then separated, and the organic layer was washed successively with brine (2 x 8 ml). The aqueous layer was extracted with EtOAc (3 x 10 ml). The combined extract was dried over anhydrous Na_2SO_4. The filtrate was concentrated under reduced pressure and the crude product was purified by flash column chromatography on silica gel or preparative TLC to give the corresponding nitrile analog both with a mixture of ethyl acetate and hexane as an eluent.

Synthesis of 3,4-bis(2-methoxyethoxy)benzaldehyde (8).[3]

General procedure B : 3,4-Bis(2-methoxyethoxy)benzaldehyde (**8**) was synthesized according to a modified procedure. Under a N_2 atmosphere, 3,4-dihydroxybenzaldehyde 6 (2.0 g, 14.5 mmol), K_2CO_3 (8.0 g, 58 mmol), and DMF (13.2 mL, 1.1 M) were added to a 100 mL round-bottomed flask equipped with a stir bar, and then the reaction mixture was subjected to stir at room temperature for 1 h before 1-bromo-2-methoxyethane 7 (4.84 g, 34.8 mmol) was introduced through the syringe. Then, the reaction was allowed

to react at 100 °C for an additional 5 h. After completion, the reaction was diluted with water and extracted with dichloromethane (3 × 30 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated to dryness. The residue was purified through silica gel chromatography using a mixture of ethyl acetate and hexane (v/v = 1:3 to 1:2) as the gradient eluent to afford the desired product as a yellow oil (2.6 g, 71% yield).

Synthesis of 3-bromo-4-isobutoxybenzonitrile (16).[4]

General procedure C: 3-bromo-4-isobutoxybenzonitrile (**16**) was synthesized according to a modified procedure. Under a N_2 atmosphere, 3-bromo-4-hydroxybenzonitrile (**15**) (2.0 g, 10.0 mmol), K_2CO_3 (3.0 g, 22 mmol), and DMF (4 mL) were added to a 50-mL round-bottomed flask equipped with a stirring bar, and then the mixture was subjected to stir at room temperature for 1 h before 1-bromo-2-methylpropane (1.64 g, 12 mmol) was introduced through the syringe. Then, the reaction was allowed to react at 95 °C for an additional 3 h. After completion, the reaction was diluted with water and extracted with dichloromethane (3 × 30 mL). Then, the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated to dryness. The residue was purified through silica gel chromatography using a mixture of ethyl acetate and hexane (v/v = 1:3 to 1:2) as the gradient eluent to afford the desired product as a yellow oil (2.9 g, 91% yield).

General procedure for the synthesis of nitriles (9), (12) and (15).

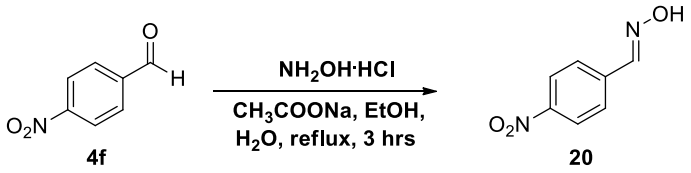
General procedure D: To a stirred solution of aldehyde (10 mmol) and hydroxylamine hydrochloride (12 mmol) in acetonitrile (5 ml) was added HCl·DMPU (10 mmol). The reaction mixture was vigorously stirred for 3-4 hours at 60 ^{O}C. The progress of the reaction was monitored by TLC. After heating, the reaction mixture was cooled at rt and then diluted by EtOAc (2 x 10ml) and water (2 x 10 ml). The layers were then separated, and the organic layer was washed successively with brine (2 x 10ml). The aqueous layer was extracted with EtOAc (3 x 10 ml). The combined extract was dried over anhydrous Na_2SO_4. The filtrate was concentrated under reduced pressure and the crude product was purified by flash column chromatography on silica gel or preparative TLC to give the corresponding nitrile analog both with a mixture of ethyl acetate and hexane as eluent.

General procedure for the synthesis of nitrile (19).

General procedure E: To a stirred solution of aldehyde (3.2g, 10 mmol) and hydroxylamine hydrochloride (2.07g, 30 mmol) in acetonitrile (5 ml) was added HCl·DMPU (3.6g, 10 mmol). The reaction mixture was vigorously stirred for 3-4 hours at 60 ^{O}C. The progress of the reaction was monitored by TLC. After heating,

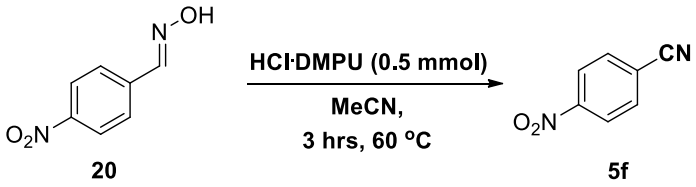
the reaction mixture was cooled to room temperature and then diluted by EtOAc (2 x 10ml) and water (2 x 10 ml). The layers were then separated, and the organic layer was washed successively with brine (2 x 10ml). The aqueous layer was extracted with EtOAc (3 x 10 ml). The combined extract was dried over anhydrous Na_2SO_4. The filtrate was concentrated under reduced pressure and the crude product was purified by flash column chromatography on silica gel or preparative TLC to give the corresponding nitrile analog both with a mixture of ethyl acetate and hexane as eluent.

General procedure for the synthesis of oxime (20).[5]



General procedure F: A mixture of aldehyde (2 mmol), $NH_2OH{\cdot}HCl$ (4.5 mmol), CH_3COONa (7.5 mmol), ethyl alcohol (0.5 mL) and water (2 mL) were placed in a 50 mL round-bottomed flask with a reflux condenser. Then the mixture was stirred under reflux, the progress was monitored by TLC. After the reaction, the contents were poured into a 100 mL beaker. After cooling, the precipitate was filtered with suction, thoroughly washed with water and dried under vacuum, then recrystallization with ethyl alcohol to obtain a pure solid.

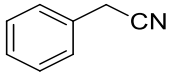
General procedure for the synthesis of nitrile (5f) from oxime (20).



General procedure G: To a stirred solution of oxime (0.5 mmol) in acetonitrile (1 ml) was added $HCl{\cdot}DMPU$ (0.5 mmol). The reaction mixture was vigorously stirred for 3 hours at 60 °C. The progress of the reaction was monitored by TLC. After heating, the reaction mixture was cooled at rt and then diluted with EtOAc (10 ml) and water (10 ml). The layers were then separated, and the organic layer was washed successively with brine (2 x 8 ml). The aqueous layer was extracted with EtOAc (3 x 10 ml). The combined extract was dried over anhydrous Na_2SO_4. The filtrate was concentrated under reduced pressure and the crude product was purified by flash column chromatography on silica gel or preparative TLC to give the corresponding nitrile analog both with a mixture of ethyl acetate and hexane as an eluent.

Physical and spectroscopic data of compounds

2-phenylacetonitrile (3a)[6]

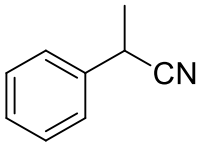


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a colorless oil (72.4 mg, 85 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.32 (m, 2H), 7.32 – 7.26 (m, 3H), 3.72 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 129.8, 129.0, 127.9, 117.7, 30.8, 23.5.

2-phenylpropanenitrile (3b)[7]

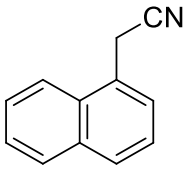


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a colorless oil (51.2 mg, 84 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.32 (m, 5H), 3.92 (q, *J* = 7.3 Hz, 1H), 1.66 (d, *J* = 7.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 137.0, 129.1, 128.0, 126.7, 121.6, 31.2, 21.4.

2-(napthalen-1-yl)acetonitrile (3c)[8]

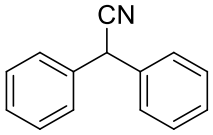


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a yellow oil (75.6 mg, 88 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 – 7.82 (m, 3H), 7.64 – 7.53 (m, 3H), 7.47 (t, *J* = 7.7 Hz, 1H), 4.11 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 133.4, 130.5, 128.9, 128.8, 126.8, 126.2, 126.1, 125.5, 125.2, 122.1, 117.4, 21.4.

2,2-diphenylacetonitrile (3d)[9]

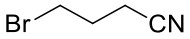


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a pale yellow solid (90.1 mg, 92 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.31 (m, 10H), 5.15 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$)) δ 136.0, 129.3, 128.3, 127.8, 119.7, 42.7.

4-bromobutanenitrile (3e)[10]

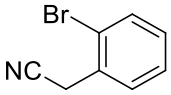


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a colorless oil (56.2 mg, 76 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.60 – 3.39 (m, 2H), 2.67 – 2.42 (m, 2H), 2.32 – 2.10 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 118.3, 30.6, 28.1, 15.9.

2-(2-bromophenyl)acetonitrile (3f)[11]

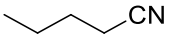


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a colorless oil (79.2 mg, 80 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.55 (m, 1H), 7.51 (d, *J* = 7.4 Hz, 1H), 7.35 (dd, *J* = 10.8, 4.2 Hz, 1H), 7.21 (dd, *J* = 14.7, 7.2 Hz, 1H), 3.82 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 133.0, 129.8, 129.6, 128.1, 123.6, 116.8, 109.9, 24.8.

Pentanenitrile (3g)[12]

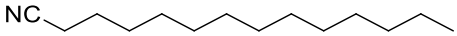


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a colorless oil (32.7 mg, 76 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (t, *J* = 7.1 Hz, 2H), 1.79 – 1.66 (m, 2H), 1.57 (dq, *J* = 14.6, 7.3 Hz, 2H), 1.04 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 119.8, 27.3, 21.8, 16.8, 13.2.

Tetradecanenitrile (3h)[13]

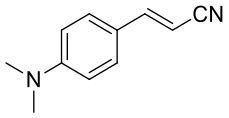


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a colorless oil (86.0 mg, 81 % yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.34 (t, *J* = 7.2 Hz, 2H), 1.72 – 1.62 (m, 2H), 1.45 (dd, *J* = 14.8, 7.1 Hz, 2H), 1.29 (d, *J* = 15.1 Hz, 18H), 0.89 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 119.8, 31.8, 29.6, 29.4, 29.3, 29.2, 28.7, 28.6, 25.3, 22.6, 17.1, 14.0.

E-3-(4-(dimethylamino)phenyl)acrylonitrile (3i)[14]

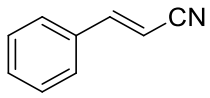


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a colorless oil (67.9 mg, 79 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.36 (m, 2H), 7.32 (d, *J* = 1.1 Hz, 1H), 6.72 (d, *J* = 8.8 Hz, 2H), 5.63 (d, *J*= 16.4 Hz, 1H), 3.09 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 150.5, 130.9, 129.0, 121.5, 119.7, 111.7, 89.5, 40.1.

3-Phenylacrylonitrile (3j)[13]

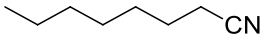


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a colorless oil (51.6 mg, 80 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.59 (m, 5H), 7.58-7.46 (s, 1H), 6.08 (d, *J* = 16.7 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 150.7, 133.7, 131.4, 129.3, 127.5, 118.3, 96.5.

Octanenitrile (3k) [15]

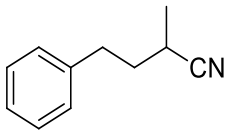


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a colorless oil (45.6 mg, 83 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (t, *J* = 7.1 Hz, 2H), 1.70 – 1.59 (m, 2H), 1.43 (dd, *J* = 14.4, 6.6 Hz, 2H), 1.30 (d, *J* = 8.5 Hz, 6H), 0.88 (t, *J* = 6.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 119., 31.3, 28.4, 28.2, 25.2, 22.3, 16.9, 13.8.

2-methyl-4-phenylbutanenitrile (3l)[16]

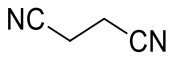


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a colorless oil (60.0 mg, 75 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (t, *J* = 7.3 Hz, 2H), 7.33 (dd, *J* = 19.1, 7.4 Hz, 3H), 3.05 – 2.93 (m, 1H), 2.87 (dd, *J* = 14.9, 7.1 Hz, 1H), 2.69 (dd, *J* = 15.0, 7.0 Hz, 1H), 2.06 (dt, *J* = 17.8, 6.8 Hz, 1H), 1.96 (dt, *J* = 13.6, 6.9 Hz, 1H), 1.44 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8, 128.3, 128.1, 126.1, 122.5, 35.4, 32.9, 24.6, 17.7.

Butanedinitrile(3m)[17]

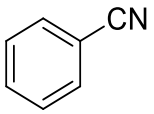


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a colorless oil (32.7 mg, 84 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.78 (s, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 116.1, 14.6.

Benzonitrile (5a)[18]

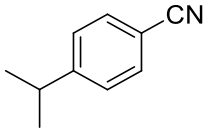


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a colorless oil (50.4 mg, 98 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.53 (m, 3H), 7.43 (t, *J* = 7.3 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 132.7, 132.0, 129.0, 118.8, 112.3.

4-isopropylbenzonitrile (5b)[19]

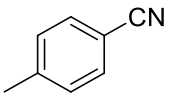


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a colorless oil (69.0 mg, 95 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.52 (d, 2H), 7.34 – 7.29 (d, 2H), 2.95 (dt, *J* = 13.8, 6.9 Hz, 1H), 1.25 (d, *J* = 6.9 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 132.3, 127.4, 119.2, 109.7, 34.5, 23.6.

4-methylbenzonitrile (5c)[20]

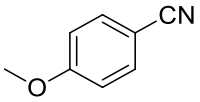


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a pale yellow solid (54.4 mg, 93 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.1 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 2.37 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 131.9, 129.7, 119.0, 109.2, 21.7.

4-methoxybenzonitrile (5d)[20]

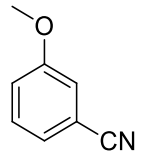


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a white solid (63.3 mg, 96 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.7 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 3.86 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 133.9, 119.1, 114.7, 103.9, 55.5.

3-methoxybenzonitrile (5e) [7]

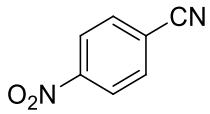


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a clear yellow oil (59.6 mg, 89 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 1H), 7.20 – 7.15 (m, 1H), 7.08 – 7.03 (m, 2H), 3.76 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 130.2, 124.3, 119.2, 118.6, 116.7, 113.1, 55.4.

4-nitrobenzonitrile (5f)[20]

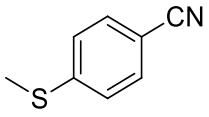


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a yellow solid (70.0 mg, 94 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 7.6 Hz, 2H), 7.89 (d, *J* = 7.5 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 150.1, 133.6, 124.4, 118.4, 116.9.

4-(methylthio)benzonitrile (5g)[20]

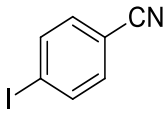


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a colorless oil (69.0 mg, 92 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.5 Hz, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 2.41 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 132.0, 125.3, 118.8, 107.5, 14.5.

4-iodobenzonitrile (5h) [21]

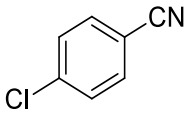


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a colorless oil (106.4 mg, 93 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.3 Hz, 2H), 6.93 (d, *J* = 8.4 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 138.0, 132.7, 117.7, 111.2, 99.8.

4-chlorobenzonitrile (5i)[22]

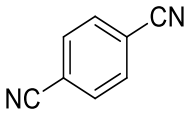


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a white solid (64.5 mg, 94 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.6 Hz, 2H), 7.45 (d, *J* = 8.2 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 139.5, 133.3, 129.6, 117.9, 110.7.

1,4-benzenedicarbonitrile (5j)[23]

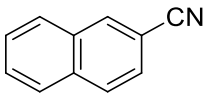


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a colorless oil (58.8 mg, 92 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.85 (s, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 132.7, 116.9, 116.7.

2-naphthonitrile (5k)[24]

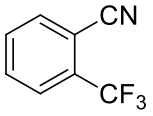


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a white solid (74.2 mg, 97 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.86 (t, *J* = 8.5 Hz, 3H), 7.63 – 7.54 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 134.5, 134.0, 132.1, 129.1, 128.9, 128.3, 128.0, 127.6, 126.2, 119.2, 109.3.

2-(trifluoromethyl)benzonitrile (5l)[25]



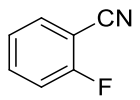
Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a colorless oil (78.6 mg, 92 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 18.1, 7.6 Hz,2H), 7.73 (dt, *J* = 21.0, 7.5 Hz, 2H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.02.

^{13}C NMR (100 MHz, $CDCl_3$) δ 134.6, 132.7, 132.6 (q, *J*= 3.2 Hz), 126.6 (q, *J* = 4.6 Hz) , 122.2 (q, *J*= 273.2 Hz) 115.3, 110.1.

2-fluorobenzonitrile (5m)[26]



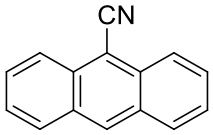
Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a colorless oil (56.8 mg, 94 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.70 (m, 2H), 7.58 – 7.14 (m, 2H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -106.1

^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2 (d, *J*=259 Hz), 135.2, 135.1, 133.6, 124.9, 116.7, 116.5, 114.0, 101.7, 101.6.

Anthracene-9-carbonitrile (5n)[27]

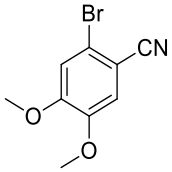


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a white solid (96.4 mg,95 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.37 (d, *J* = 8.7 Hz, 2H), 8.03 (d, *J* = 8.5 Hz, 2H), 7.68 (dd, *J* = 8.2, 7.1 Hz, 2H), 7.59 – 7.52 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 133.1, 132.6, 130.4, 128.8, 126.2, 125.1, 117.1, 105.2.

2-bromo-4,5-dimethoxybenzonitrile (5o)[28]

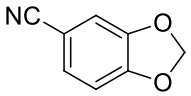


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a white solid (115.6 mg,96 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (s, 1H), 7.00 (s, 1H), 3.89 (s, 3H), 3.84 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 153.1, 148.4, 117.5, 117.5, 115.4, 115.1, 106.8, 56.4, 56.3.

Benzo[d][1,3]dioxole-5-carbonitrile (5p)[29]

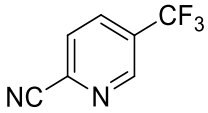


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as an off-white color solid (71.5 mg, 98 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.04 (d, *J* = 1.5 Hz, 1H), 6.86 (d, *J* = 8.1 Hz, 1H), 6.07 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 147.9, 128.1, 118.8, 111.3, 109.0, 104.9, 102.1.

5-(trifluoromethyl)picolinonitrile (5q)[30]



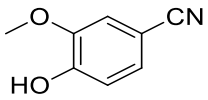
Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 2:8 ratio, provided the title compound as a colorless oil (61.5 mg, 72 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (s, 1H), 8.12 (d, *J* = 10.2 Hz, 1H), 7.87 (d, *J* = 8.1 Hz, 1H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.17.

^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 137.2, 134.7, 128.4 (q J= 118 Hz), 123.4, 121.2, 116.3,

4-hydroxy-3-methoxybenzonitrile (5r)[31]

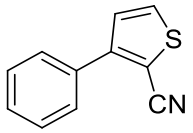


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 2:8 ratio, provided the title compound as a white solid (68.5 mg, 92 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.06 (d, *J* = 1.5 Hz, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 6.00 (s, 1H), 3.91 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.8, 146.5, 126.9, 119.2, 115.1, 113.6, 103.2, 56.1.

3-phenylthiophene-2-carbonitrile (5s)[32]

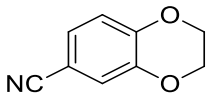


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a white solid (82.8 mg, 90 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.66 (s, 1H), 7.54 (d, *J* = 7.3 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 2H), 7.37 (t, *J* = 7.2 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.98, 136.09, 133.5, 129.0, 128.2, 126.6, 126.3, 114.0, 110.5.

2,3-dihydrobenzo[b][1,4]dioxine-6-carbonitrile (5t)[19]

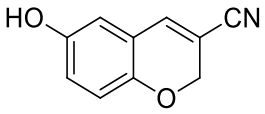


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a white solid (78.4 mg, 98 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.17 (m, 2H), 6.97 (d, *J* = 8.5 Hz, 1H), 4.37 (dd, *J* = 3.5, 1.5 Hz, 2H), 4.35 – 4.33 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.7, 143.8, 125.9, 121.2, 118.9, 118.2, 104.5, 64.6, 64.14.

6-hydroxy-2H-chromene-3-carbonitrile (5u)

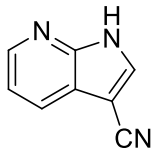


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 2:8 ratio, provided the title compound as a colorless oil (81.3 mg, 94 % yield).

^{1}H NMR (400 MHz, DMSO) δ 9.40 (s, 1H), 7.58 (s, 1H), 6.78 (d, *J* = 21.1 Hz, 3H), 4.82 (s, 2H).

^{13}C NMR (100 MHz, DMSO) δ 152.6, 147.0, 139.8, 121.2, 119.7, 117.3, 114.6, 104.0, 64.0.

1H-pyrrolo[2,3-b]pyridine-3-carbonitrile (5v)[33]

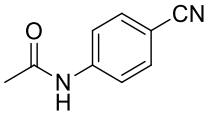


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 3:7 ratio, provided the title compound as a colorless oil (67.6 mg, 95 % yield).

^{1}H NMR (500 MHz, DMSO) δ 8.30 (d, *J* = 1.6 Hz, 1H), 8.29 (d, *J* = 1.6 Hz, 1H), 8.26 (dd, *J* = 4.7, 1.6 Hz, 1H), 8.24 (s,1H), 7.75 (s, 1H), 7.14 (dd, *J* = 7.9, 4.7 Hz, 1H).

^{13}C NMR (100 MHz, DMSO) δ 148.0, 143.8, 138.3, 131.1, 127.7, 118.6, 116.7, 105.9.

N-(4-cyanophenyl)acetamide (5w)[34]

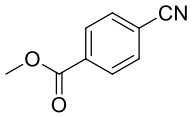


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 4:6 ratio, provided the title compound as a colorless oil (64.3mg, 92 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (q, *J* = 8.8 Hz, 4H), 7.08 (s, 1H), 2.04 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.13, 141.51, 132.92, 119.05, 118.42, 106.80, 24.43.

Methyl 4-cyanobenzoate (5x)[34]

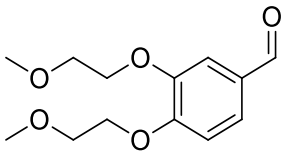


Prepared following *general procedure A* in 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 4:6 ratio, provided the title compound as a colorless oil (76.3 mg, 95 % yield).

^{1}H NMR (399 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.2 Hz, 2H), 7.55 (d, *J* = 8.2 Hz, 2H), 3.77 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.08, 133.59, 131.88, 129.75, 117.62, 116.07, 77.10, 77.02, 76.71, 76.43, 52.39.

3,4bis(2-methoxyethoxy)benzaldehyde (8)[4]

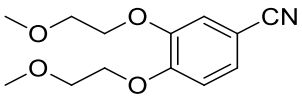


Prepared following *general procedure B* in 10 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 2:8 ratio, provided the title compound as a yellow oil (2.30g, 96 % yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.84 (s, 1H), 7.52 – 7.39 (m, 2H), 7.01 (d, *J* = 8.1 Hz, 1H), 4.27 – 4.17 (m, 5H), 3.85 – 3.78 (m, 5H), 3.47 (d, *J* = 0.9 Hz, 7H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 190.85, 154.36, 149.22, 130.29, 126.73, 112.50, 111.80, 59.32, 59.24.

3,4-bis(4-methoxybutoxy)benzonitrile (9)[4]

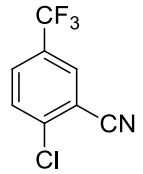


Prepared following *general procedure D* in 10 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a white solid (2.48 g, 98 % yield).

^{1}H NMR (399 MHz, $CDCl_3$) δ 7.24 (dd, *J* = 5.7, 1.9 Hz, 1H), 7.14 – 7.08 (m, 1H), 6.93 – 6.85 (m, 1H), 4.24 – 4.05 (m, 4H), 3.81 – 3.68 (m, 4H), 3.46 – 3.27 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$)δ 152.88, 148.87, 126.77, 119.09, 117.05, 113.49, 104.16, 70.76, 70.65, 69.02, 68.59, 59.22.

2-chloro-5-(trifluoromethyl)benzonitrile (12)[35]



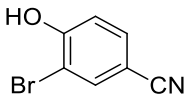
Prepared following *general procedure D* in 10 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a white solid (2.08 g, 98 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.95 (d, *J* = 8.5 Hz, 1H), 7.84 (d, *J* = 8.5 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.90, 131.11 (q, *J*= 3.1 Hz), 131.01, 130.67 (q, *J*=3.6 Hz), 129.96(q, *J*=34.3), 122.70 (q, *J*= 272.7 Hz), 114.77, 114.53.

^{19}F NMR (376 MHz, $CDCl_3$) δ 63.7.

3-bromo-4-hydroxybenzonitrile (15)[36]

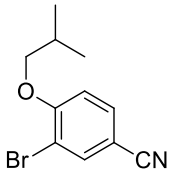


Prepared following *general procedure D* in 10 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 2:8 ratio, provided the title compound as a brown solid (1.86 g, 95 % yield).

^{1}H NMR (400 MHz, DMSO) δ 11.35 (s, 1H), 7.86 (d, *J* = 2.0 Hz, 1H), 7.48 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.89 (d, *J* = 8.5 Hz, 1H).

^{13}C NMR (100 MHz, DMSO) δ 158.84, 137.07, 133.64, 118.38, 117.06, 110.11, 102.80.

3-bromo-4-isobutoxybenzonitrile (16) [4]

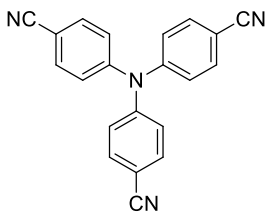


Prepared following *general procedure C* in 10 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a white solid (2.98 g, 91 % yield).

^{1}H NMR (399 MHz, $CDCl_3$) δ 7.77 (d, *J* = 2.0 Hz, 1H), 7.51 (d, *J* = 8.6 Hz, 1H), 6.85 (d, *J* = 8.6 Hz, 1H), 3.80 – 3.78 (m, 2H), 2.13 (dt, *J* = 13.2, 6.6 Hz, 1H), 1.03 (d, *J* = 6.7 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.03, 136.55, 132.92, 117.78, 112.59, 104.79, 75.61, 28.14, 18.99.

4,4',4''-nitrilotribenzonitrile (19)[37]

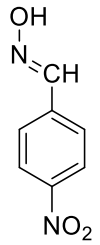


Prepared following *general procedure D* in 10 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 2:8 ratio, provided the title compound as a white solid (2.85 g, 91 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.1 Hz, 6H), 7.17 (d, *J* = 8.2 Hz,6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.19, 133.95, 124.59, 118.26, 108.01.

(E)-4-nitrobenzaldehyde oxime (20)[5]

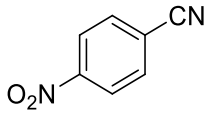


Prepared following *general procedure F in* 2 mmol scale. Purification by recrystallization, using ethyl alcohol, provided the title compound as a yellow solid (302 mg, 91 % yield).

^{1}H NMR (400 MHz, CDCl3)δ 8.26 (d, *J* = 7.1 Hz,2H), 8.21 (s, 1H), 7.86 (s, 1H), 7.76 (d, *J* = 7.1 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 148.51, 138.24, 127.79, 124.18.

4-nitrobenzonitrile (5f)[20]



Prepared following *general procedure G in* 0.5 mmol scale. Purification by flash column chromatography, using ethyl acetate and hexane as eluent on a 1:9 ratio, provided the title compound as a yellow solid (71.0 mg, 95 % yield).

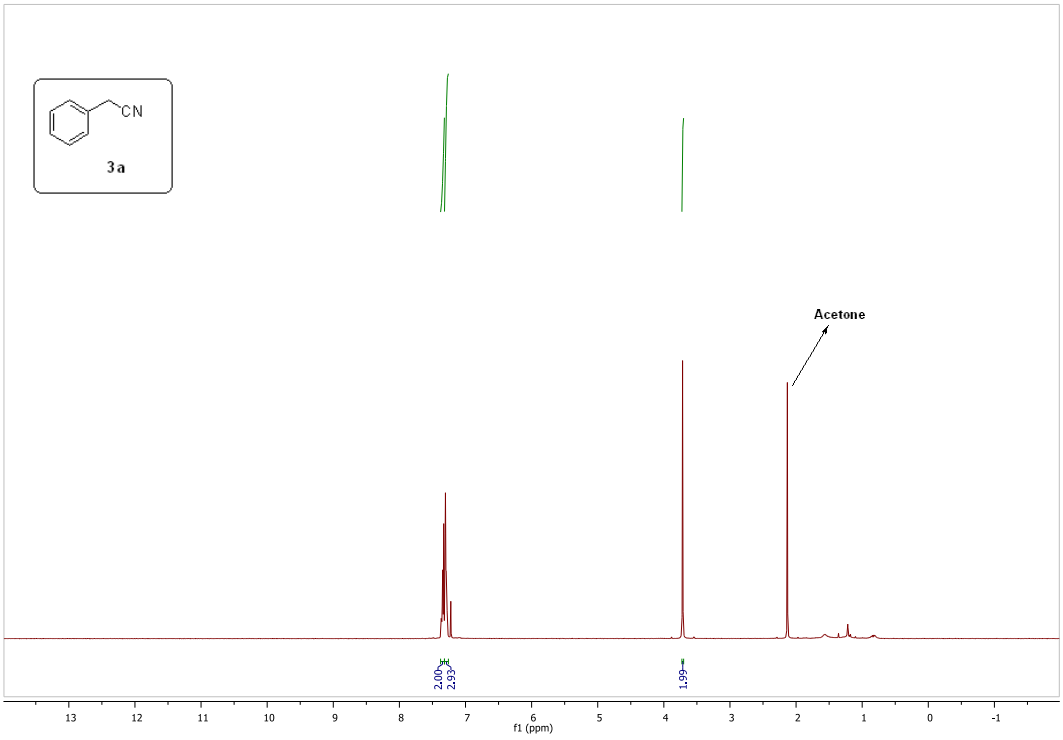
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 7.6 Hz, 2H), 7.89 (d, *J* = 7.5 Hz, 2H).

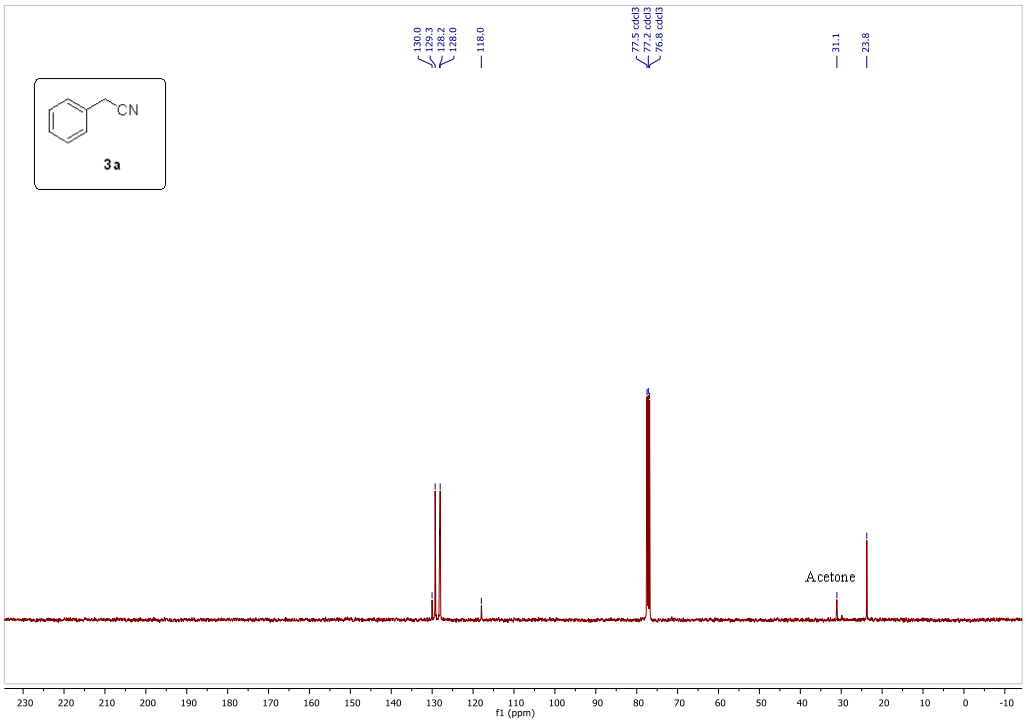
^{13}C NMR (100 MHz, $CDCl_3$) δ 150.1, 133.6, 124.4, 118.4, 116.9.

^{1}H NMR and ^{13}C NMR spectra of compounds

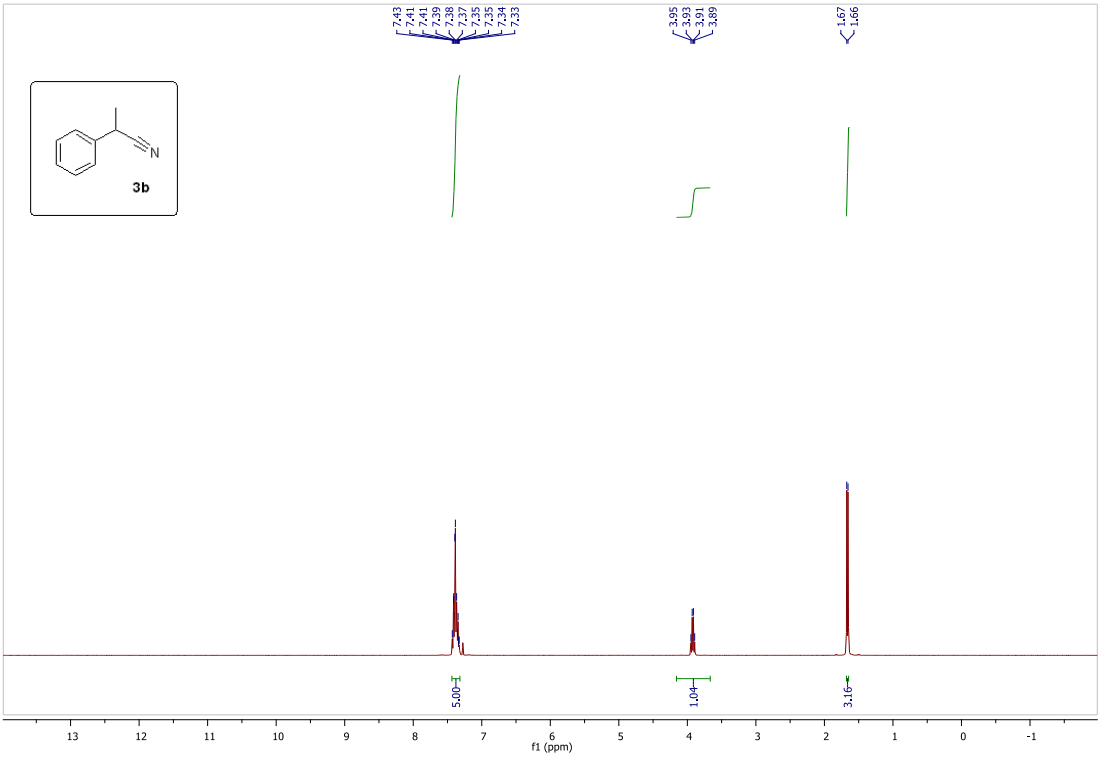
NMR spectral data for 3a-3o.

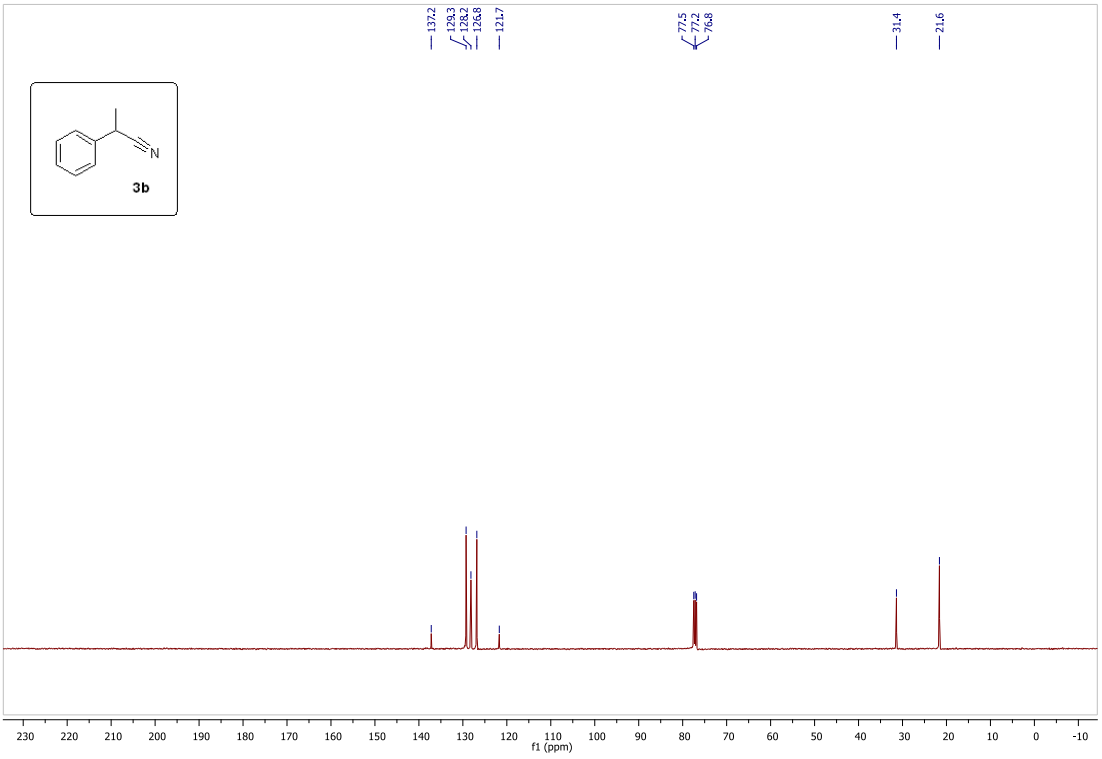
3a



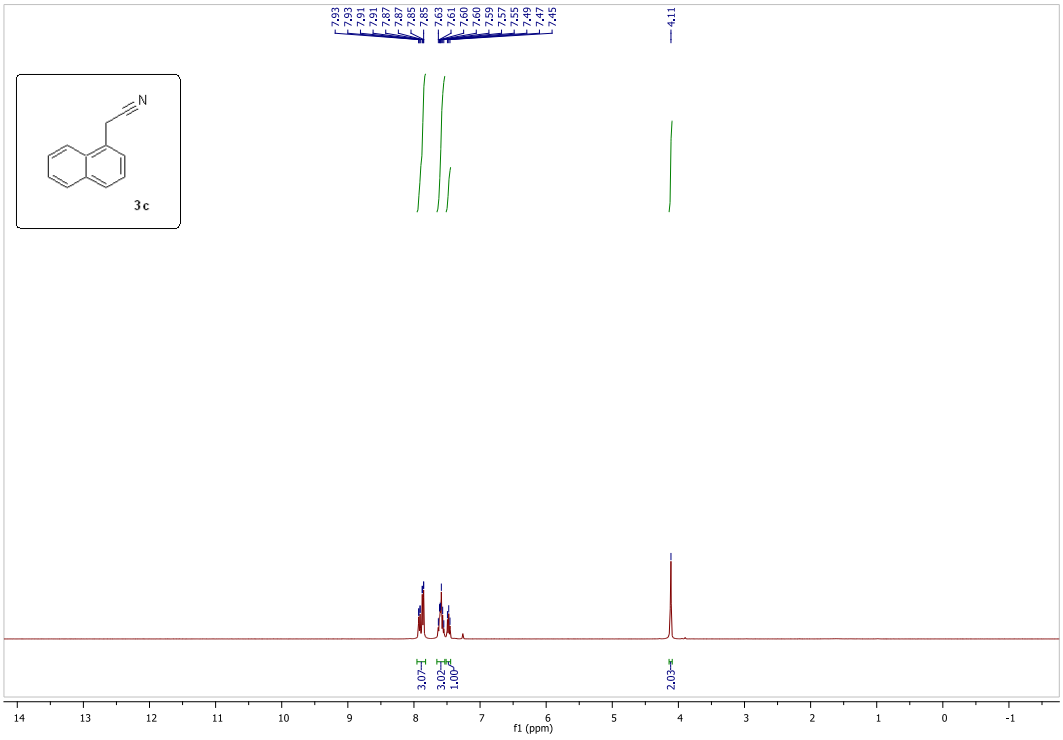

130.0
129.3
128.2
128.0
118.0
77.5 cdcl3
77.2 cdcl3
76.8 cdcl3
31.1
23.8
CN
3a
Acetone
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

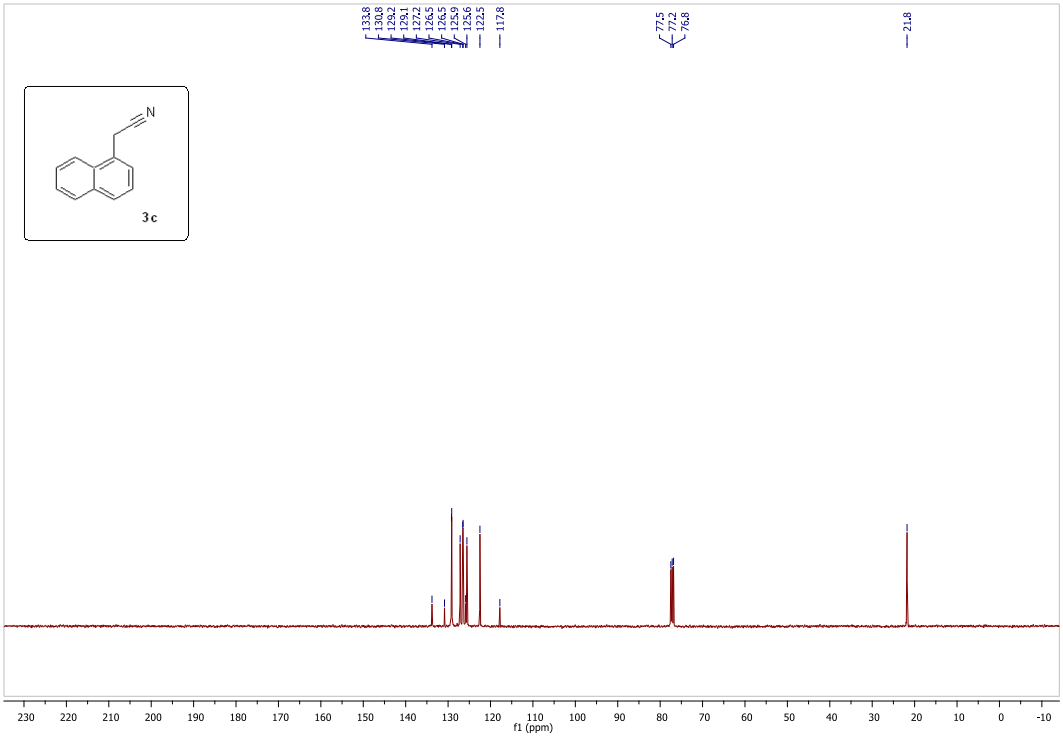
3b


7.43
7.41
7.41
7.39
7.38
7.37
7.35
7.35
7.34
7.34
7.33
3.95
3.93
3.91
3.89
1.67
1.66
3b
5.00
1.04
3.16
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

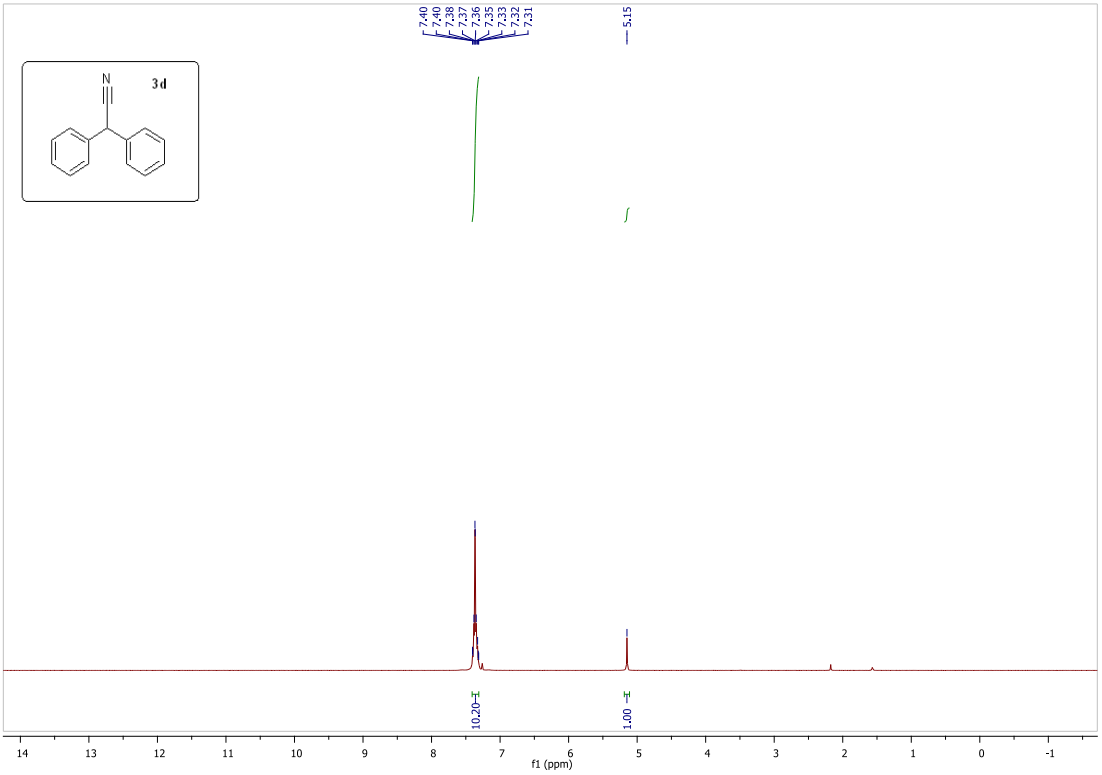

137.2
129.3
128.2
126.8
121.7
77.5
77.2
76.8
31.4
21.6
3b
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

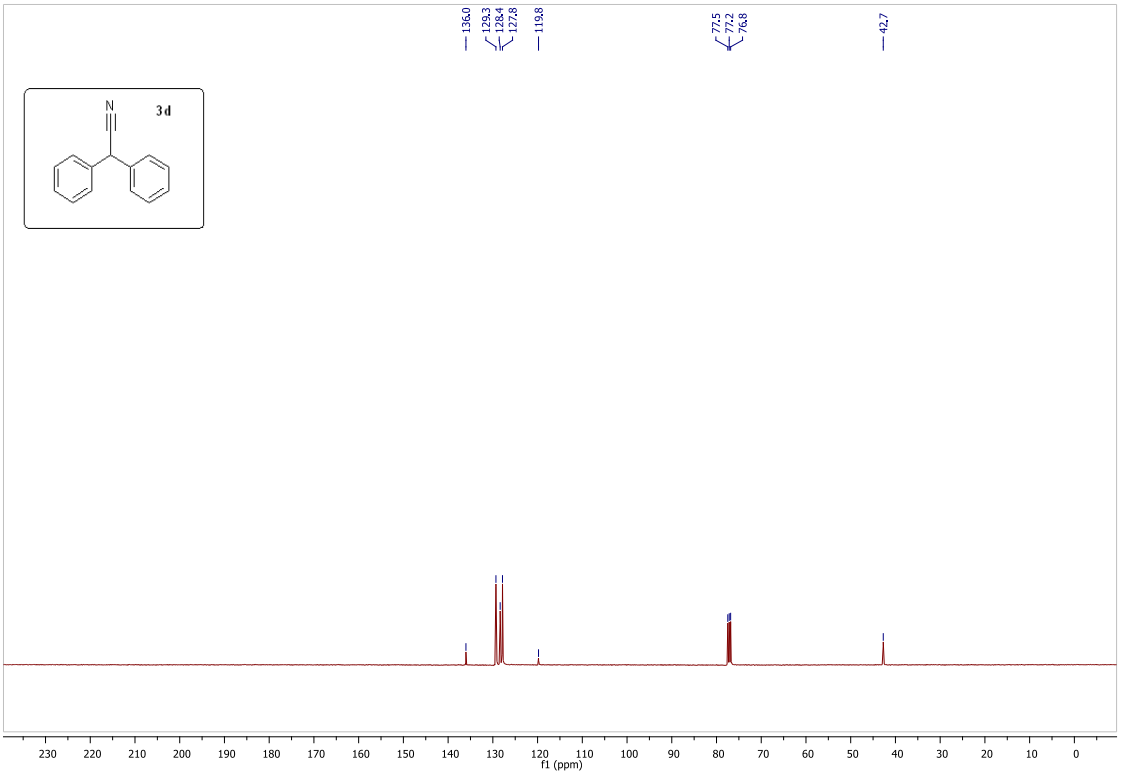
3c


7.93
7.93
7.91
7.91
7.87
7.87
7.85
7.85
7.63
7.61
7.60
7.60
7.59
7.57
7.55
7.49
7.47
7.45
4.11
3c
3.07
3.02
1.00
2.03
f1 (ppm)

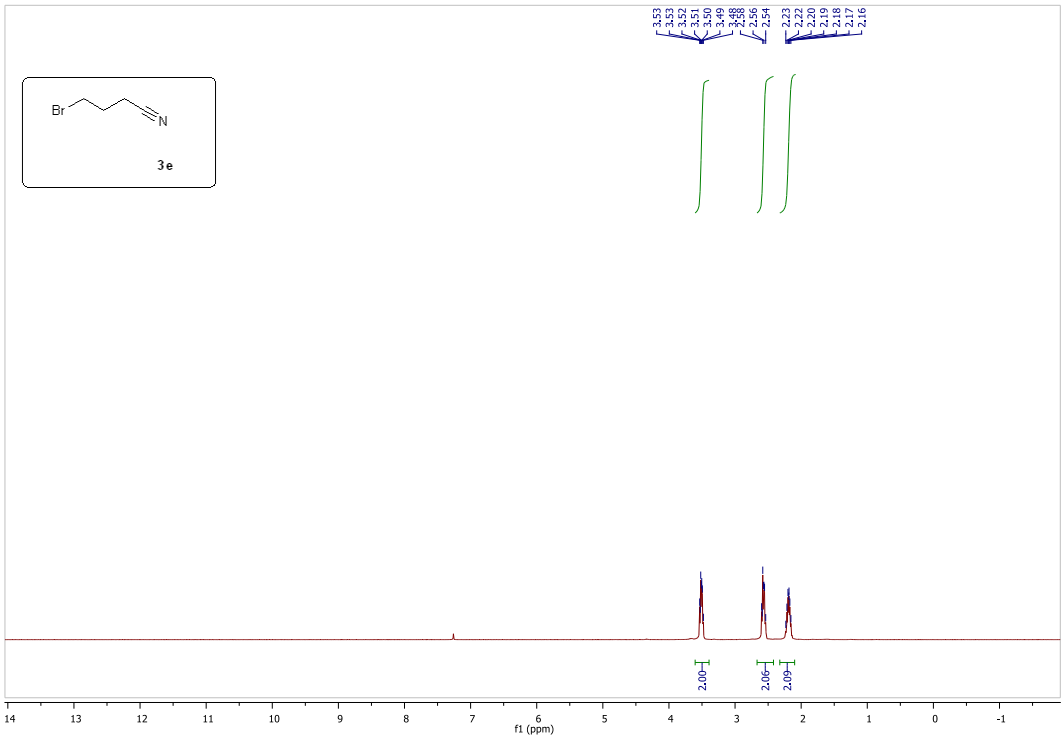

133.8
130.8
129.2
129.1
127.2
126.5
126.5
125.9
125.6
122.5
117.8
77.5
77.2
76.8
21.8
3c
f1 (ppm)

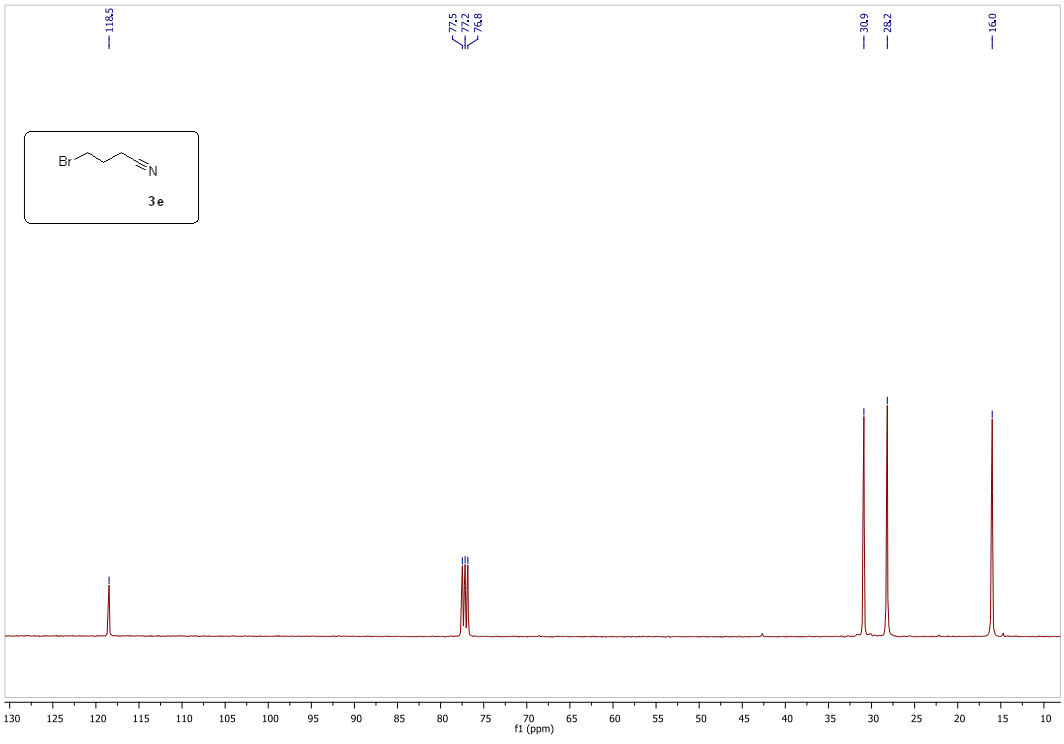
3d


7.40
7.40
7.38
7.37
7.36
7.35
7.33
7.32
7.31
5.15
3d
10.20
1.00
f1 (ppm)

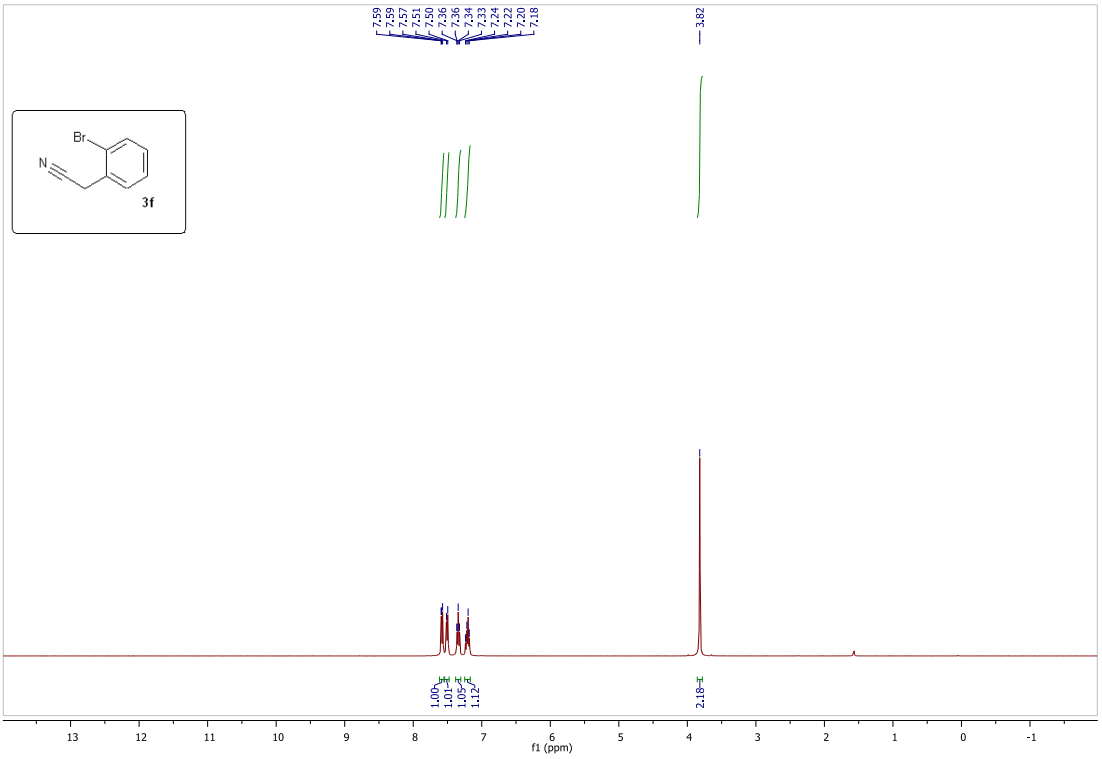

136.0
129.3
128.4
127.8
119.8
77.5
77.2
76.8
42.7
3d
f1 (ppm)

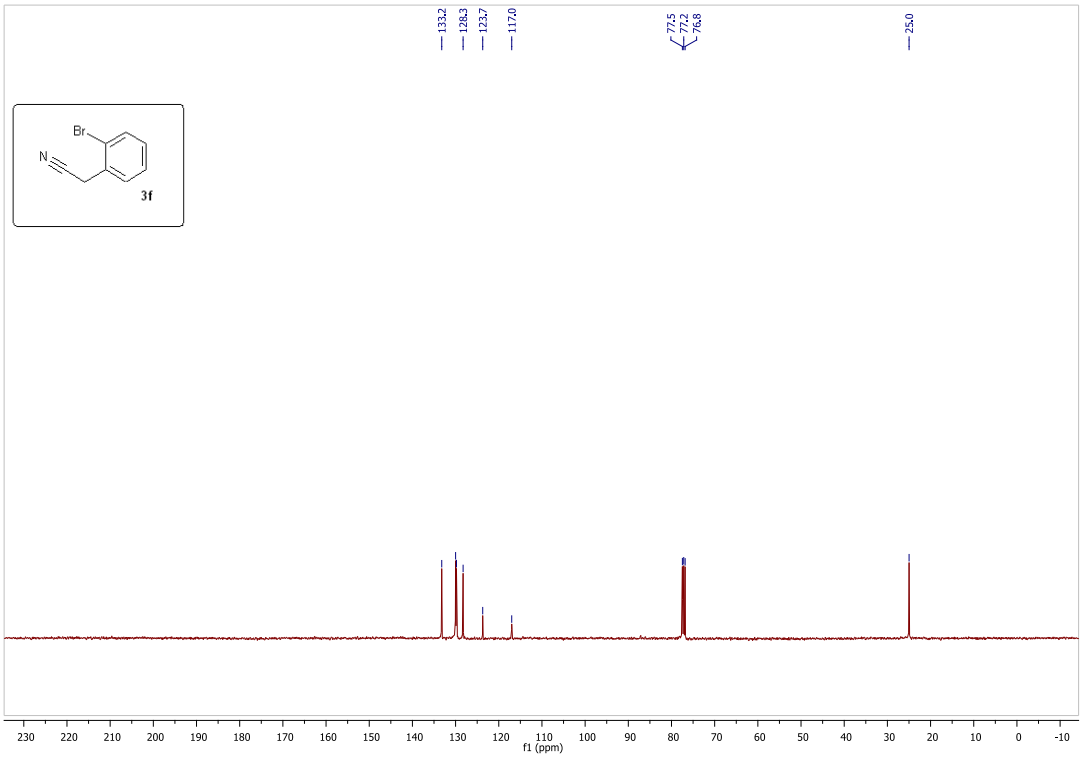
3e


3.53
3.53
3.52
3.51
3.50
3.49
3.48
3.48
2.56
2.54
2.23
2.22
2.20
2.19
2.18
2.17
2.16
Br
N
3e
2.00
2.06
2.09
f1 (ppm)

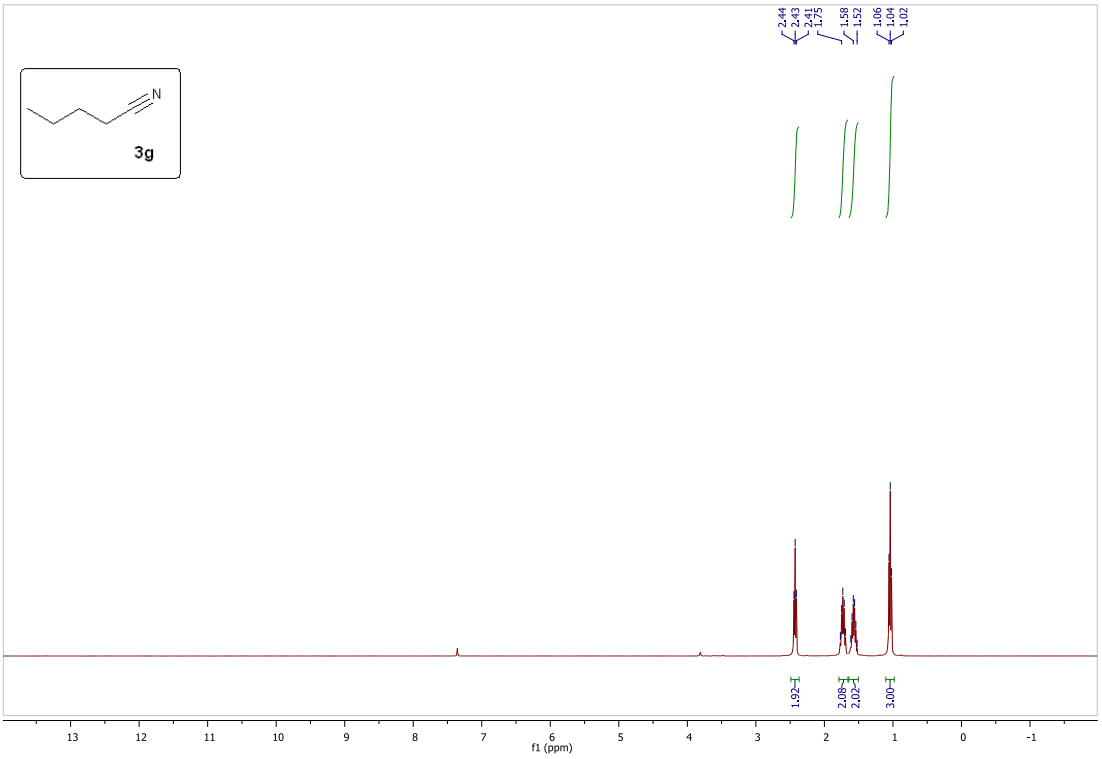

118.5
77.5
77.2
76.8
30.9
28.2
16.0
Br
N
3e
f1 (ppm)

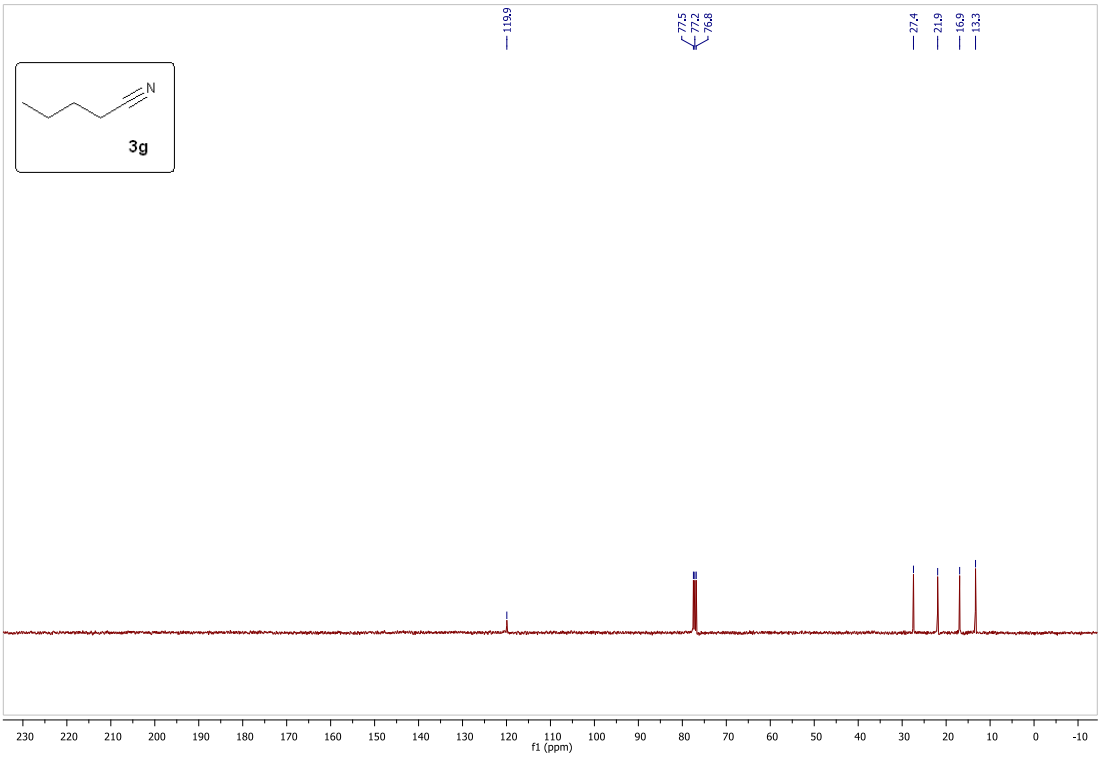
3f


7.59
7.59
7.57
7.51
7.50
7.36
7.34
7.33
7.24
7.22
7.20
7.18
3.82
Br
N
3f
1.00
1.01
1.05
1.12
2.18
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

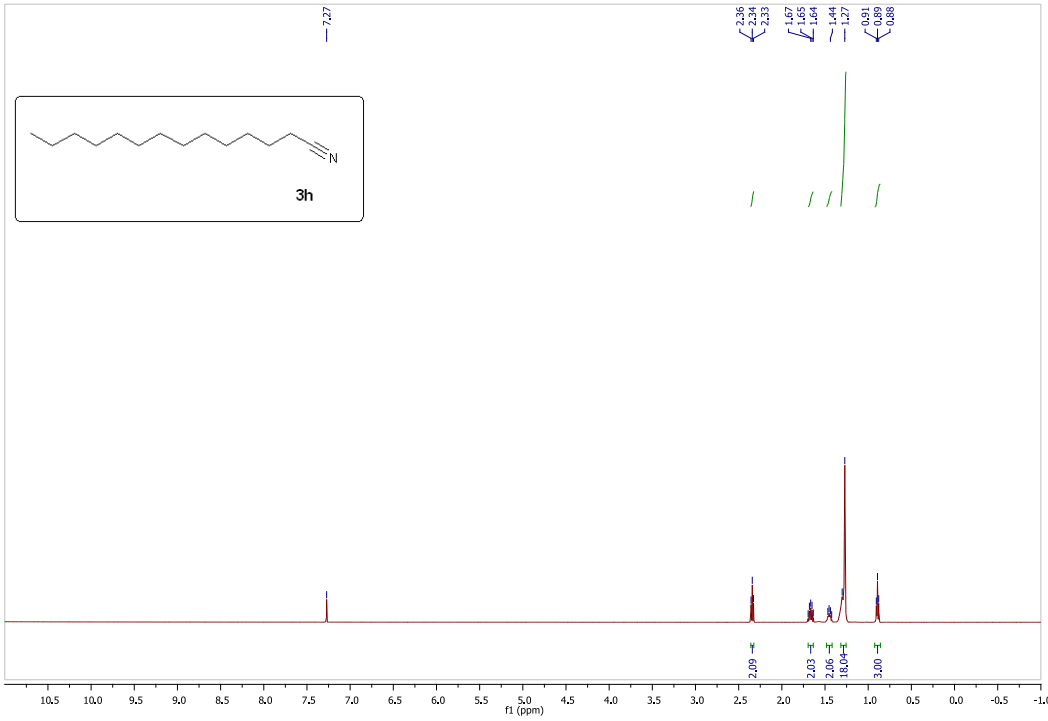

133.2
128.3
123.7
117.0
77.5
77.2
76.8
25.0
Br
N
3f
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

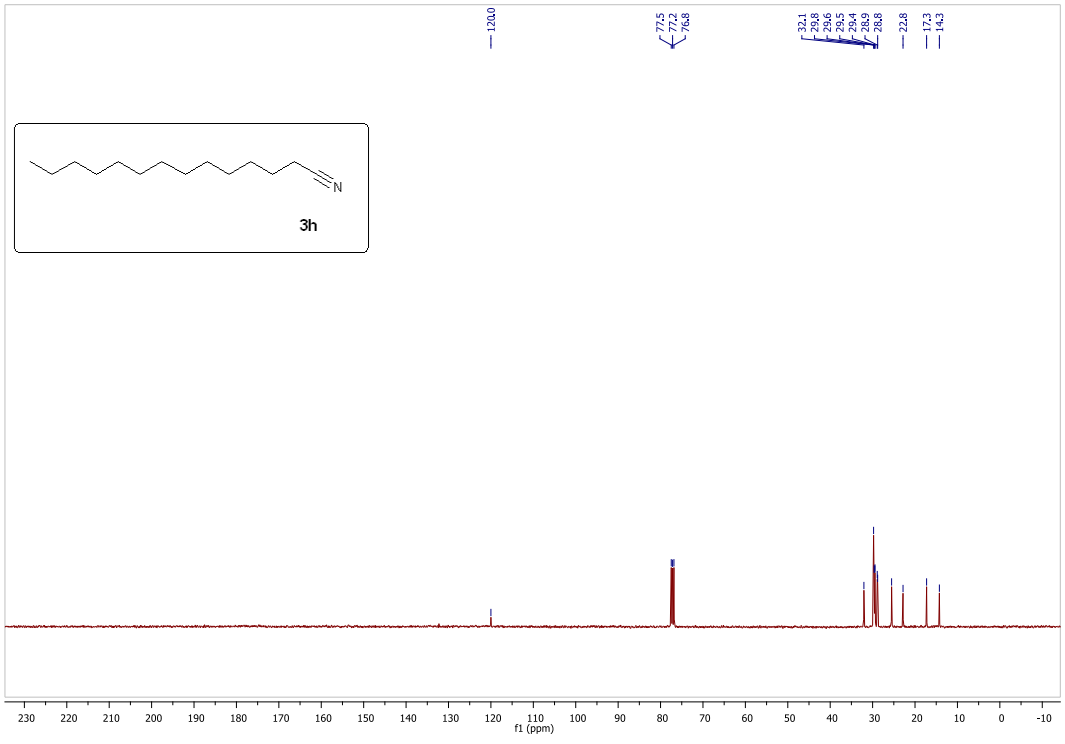
3g


2.44
2.43
2.41
1.75
1.58
1.52
1.06
1.04
1.02
N
3g
1.92
2.08
2.02
3.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

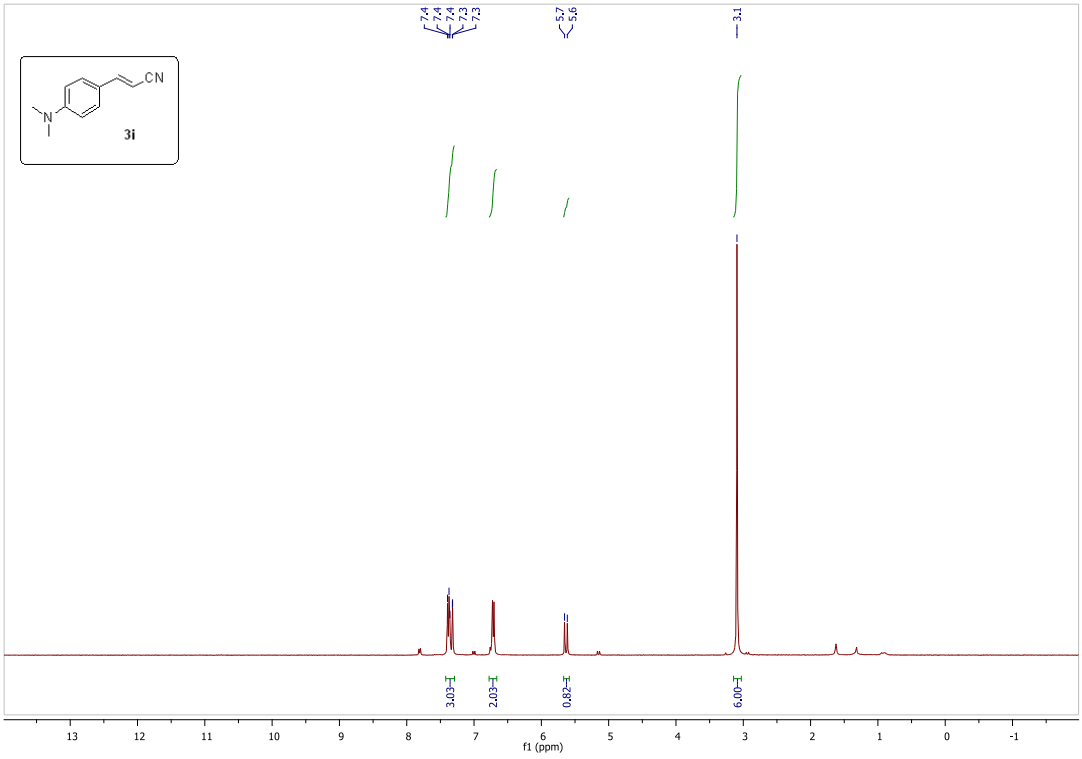

119.9
77.5
77.2
76.8
27.4
21.9
16.9
13.3
N
3g
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

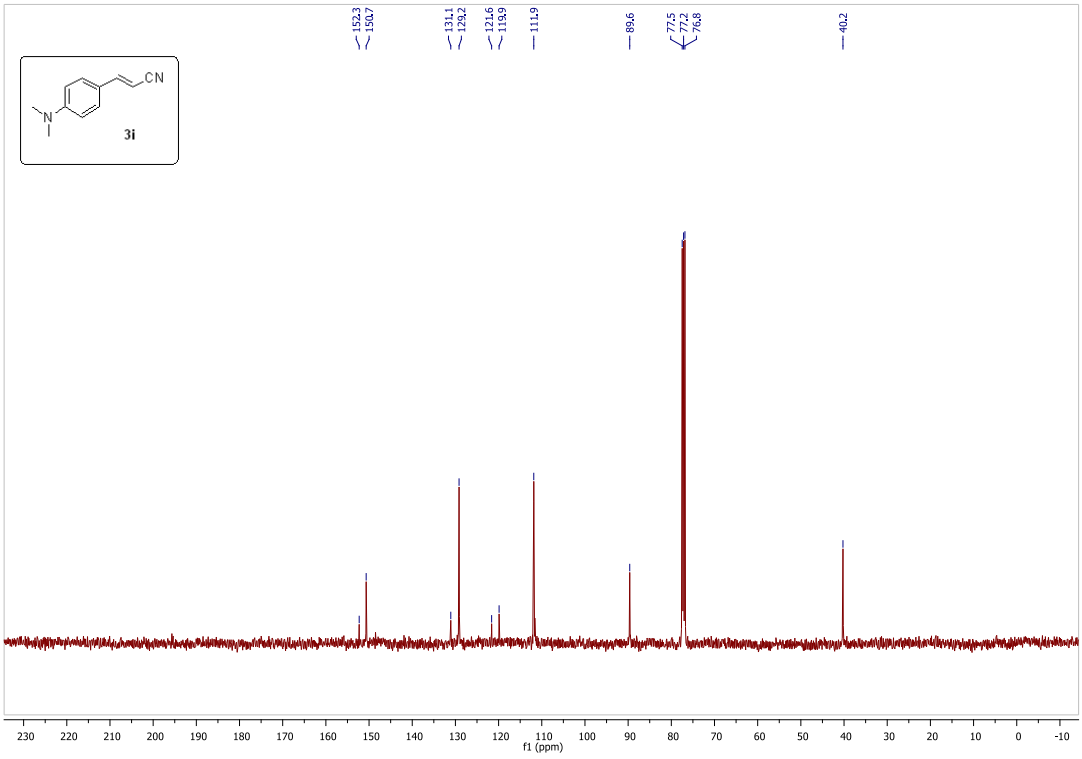
3h


7.27
2.36
2.34
2.33
1.67
1.65
1.64
1.44
1.27
0.91
0.89
0.88
N
3h
2.09
2.03
2.06
18.04
3.00
f1 (ppm)

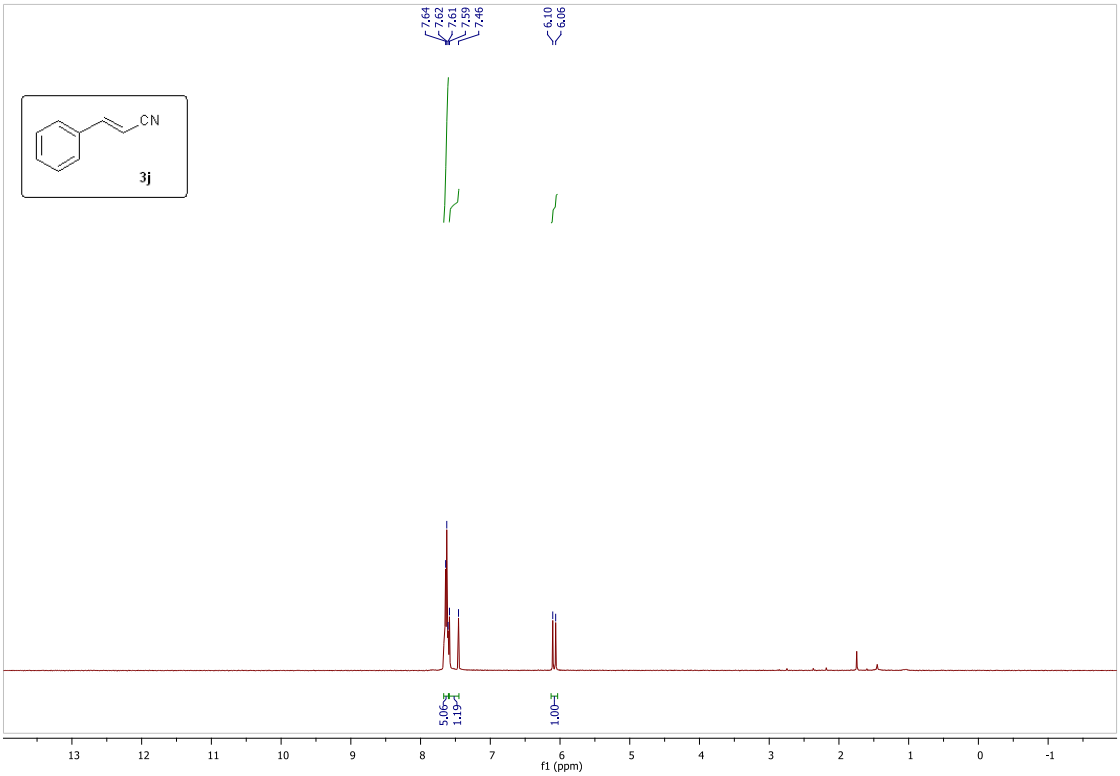

120.0
77.5
77.2
76.8
32.1
29.8
29.6
29.5
29.4
28.9
28.8
22.8
17.3
14.3
N
3h
f1 (ppm)

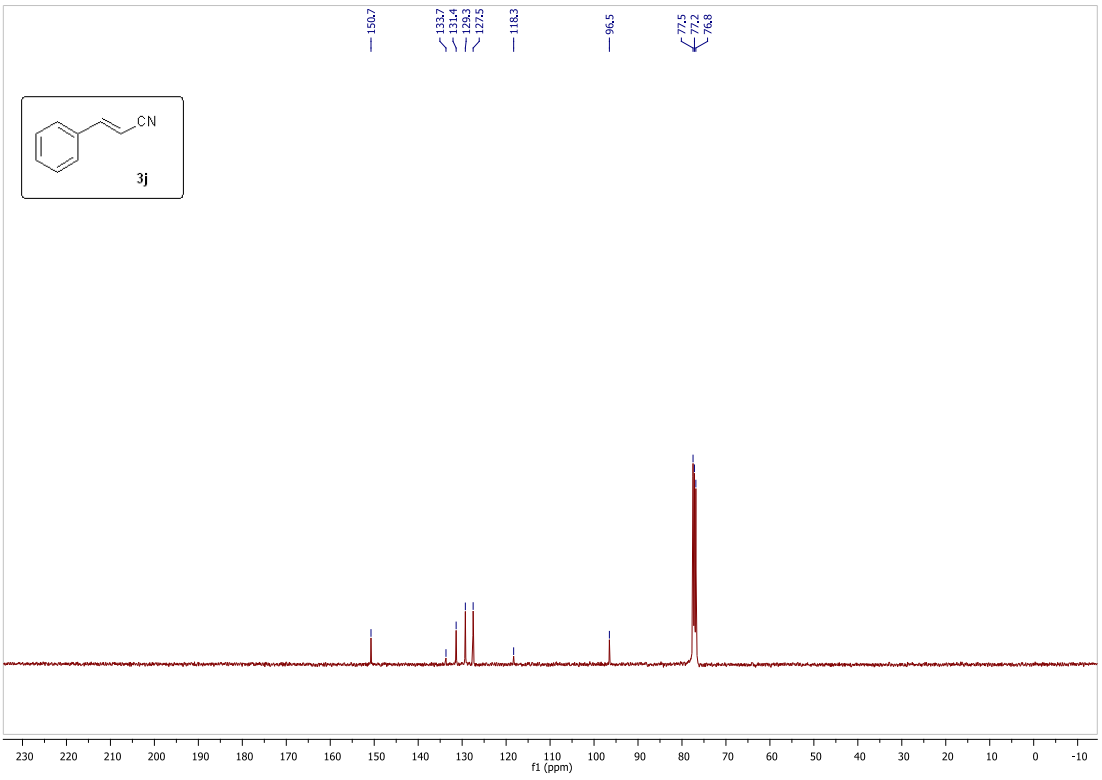
3i


7.4
7.4
7.4
7.3
7.3
5.7
5.6
3.1
CN
N
3i
3.03
2.03
0.82
6.00
f1 (ppm)

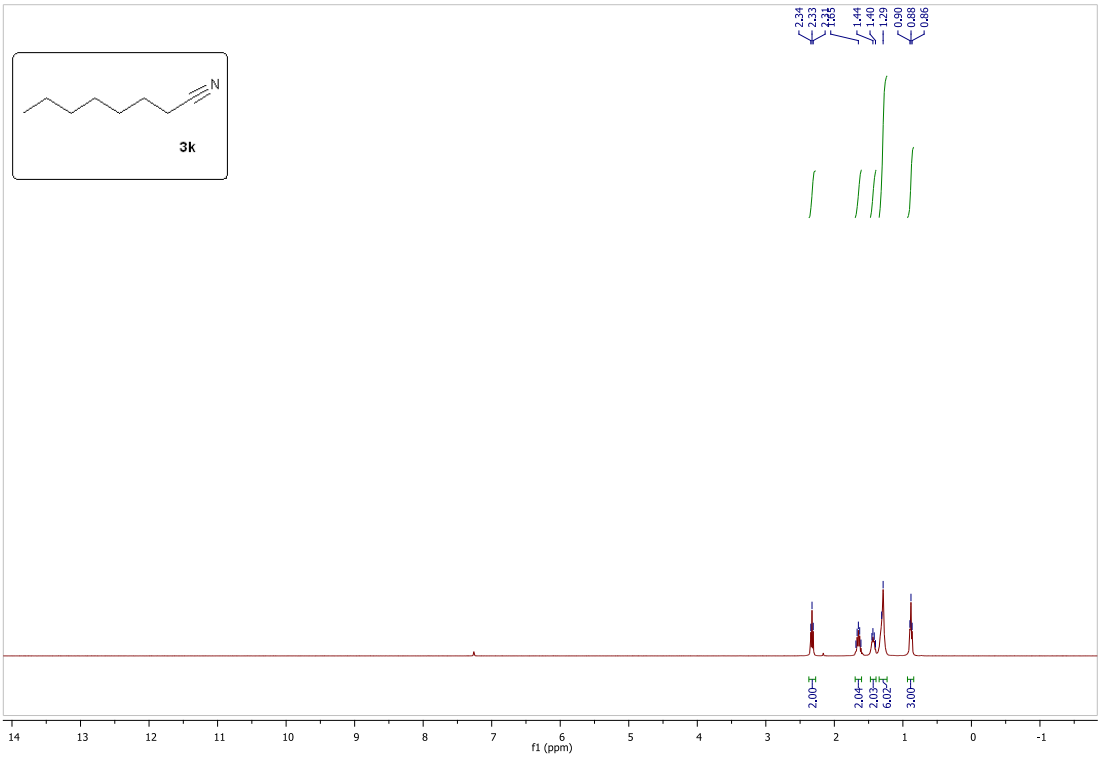

152.3
150.7
131.1
129.2
121.6
115.9
111.9
89.6
77.5
77.2
76.8
40.2
CN
N
3i
f1 (ppm)

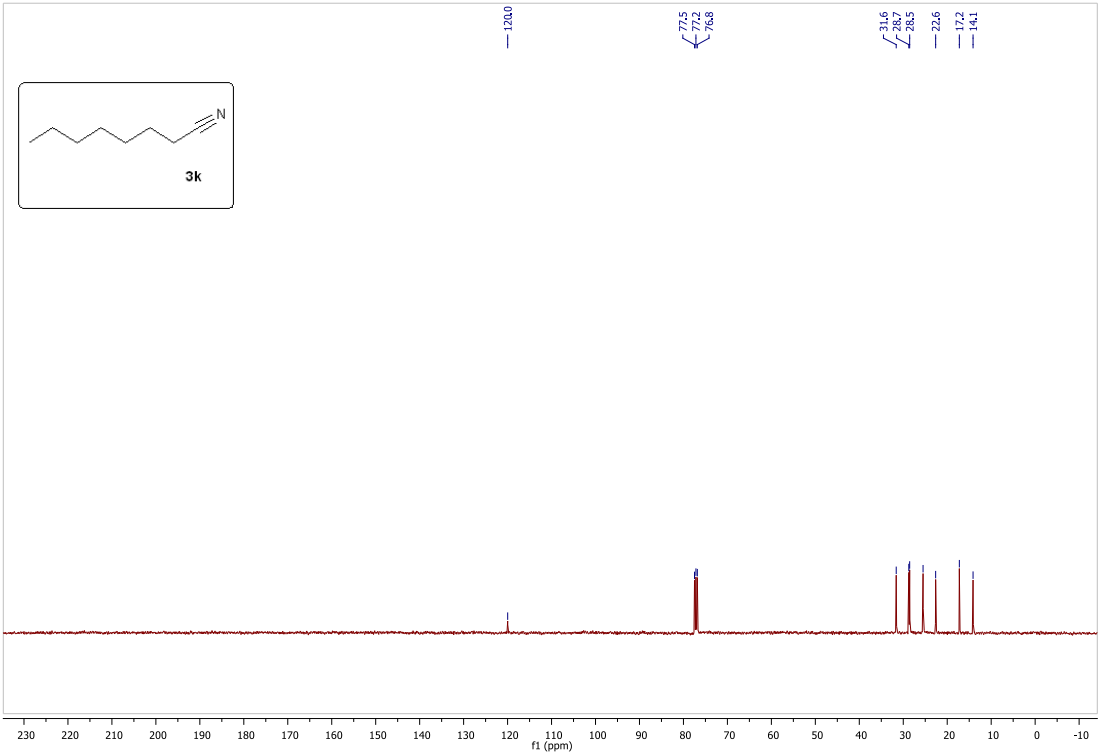
3j


7.64
7.62
7.61
7.59
7.46
6.10
6.06
CN
3j
5.06
1.19
1.00
f1 (ppm)

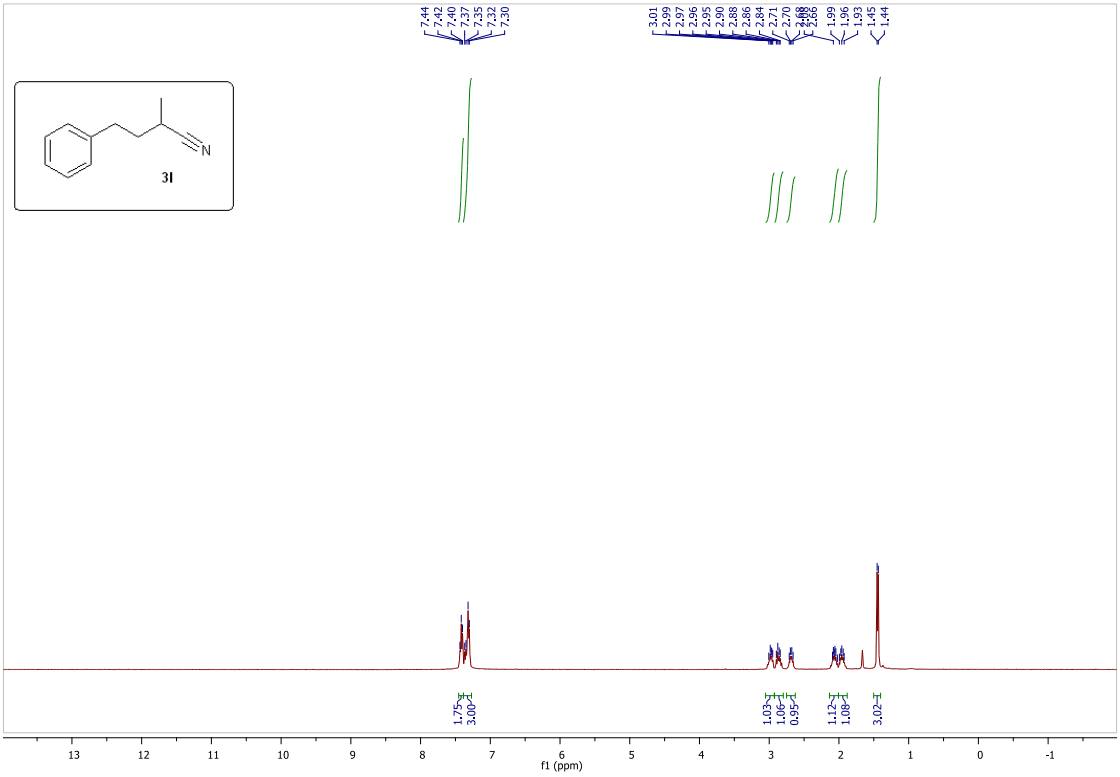

150.7
133.7
131.4
129.3
127.5
118.3
96.5
77.5
77.2
76.8
CN
3j
f1 (ppm)

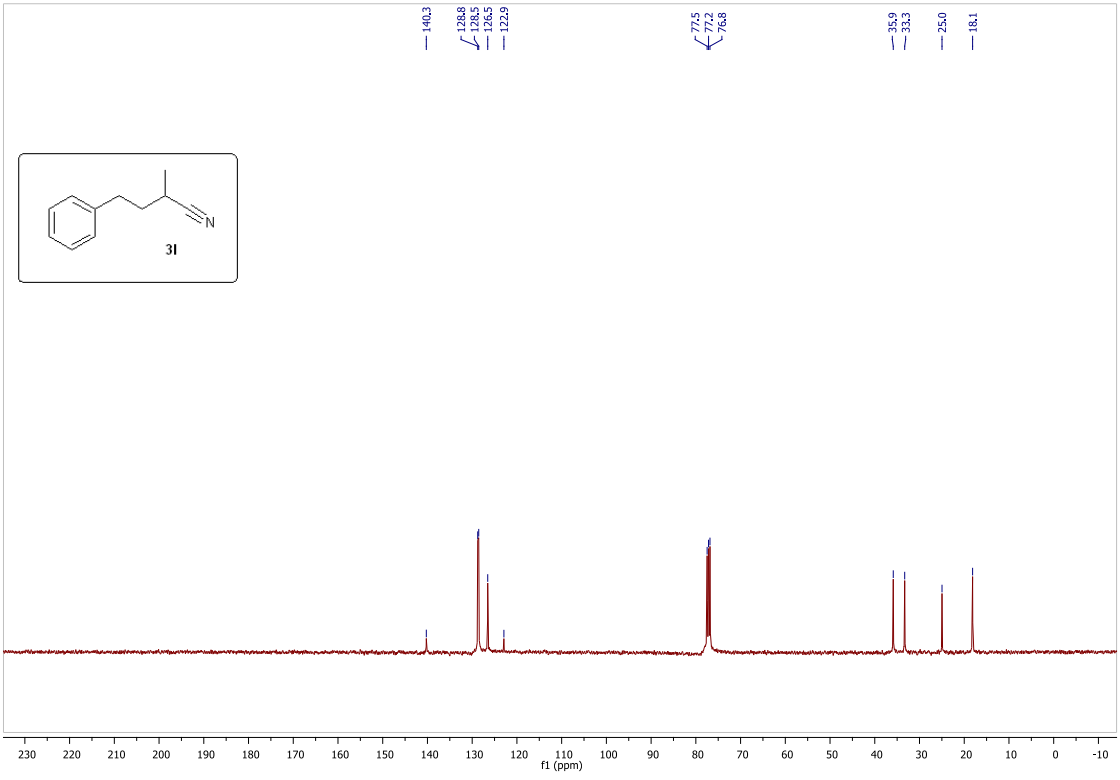
3k


2.34
2.33
2.33
1.44
1.40
1.29
0.90
0.88
0.86
N
3k
2.00
2.04
2.03
6.02
3.00
f1 (ppm)

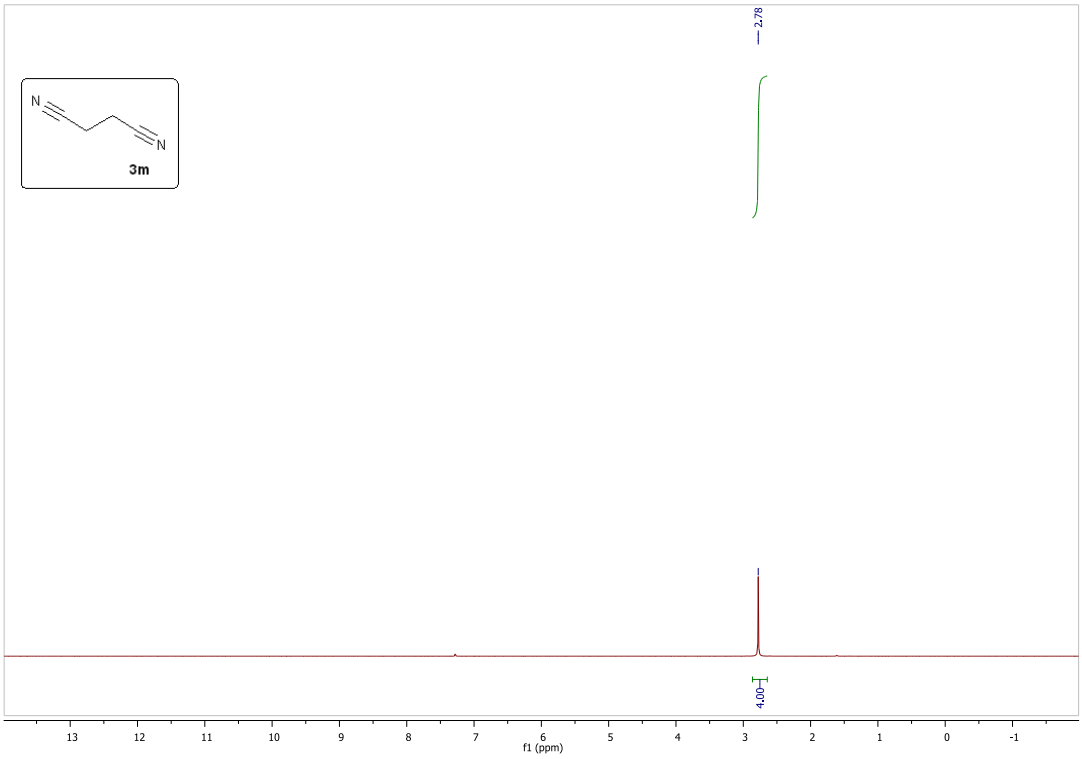

120.0
77.5
77.2
76.8
31.6
28.7
28.5
22.6
17.2
14.1
N
3k
f1 (ppm)

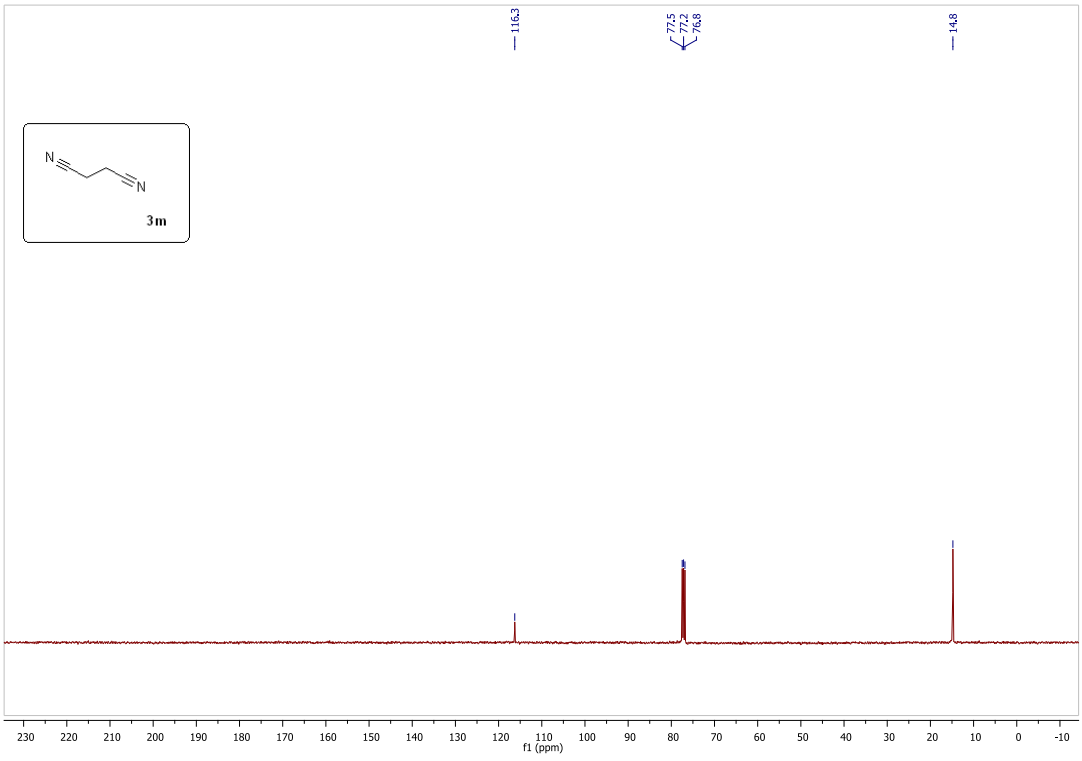
3l


7.44
7.42
7.40
7.37
7.35
7.32
7.30
3.01
2.99
2.97
2.96
2.95
2.90
2.88
2.86
2.84
2.71
2.70
1.99
1.96
1.93
1.45
1.44
N
3l
1.75
3.00
1.03
1.06
0.99
1.12
1.08
3.02
f1 (ppm)


140.3
128.8
128.5
126.5
122.9
77.5
77.2
76.8
35.9
33.3
25.0
18.1
N
3l
f1 (ppm)

3m

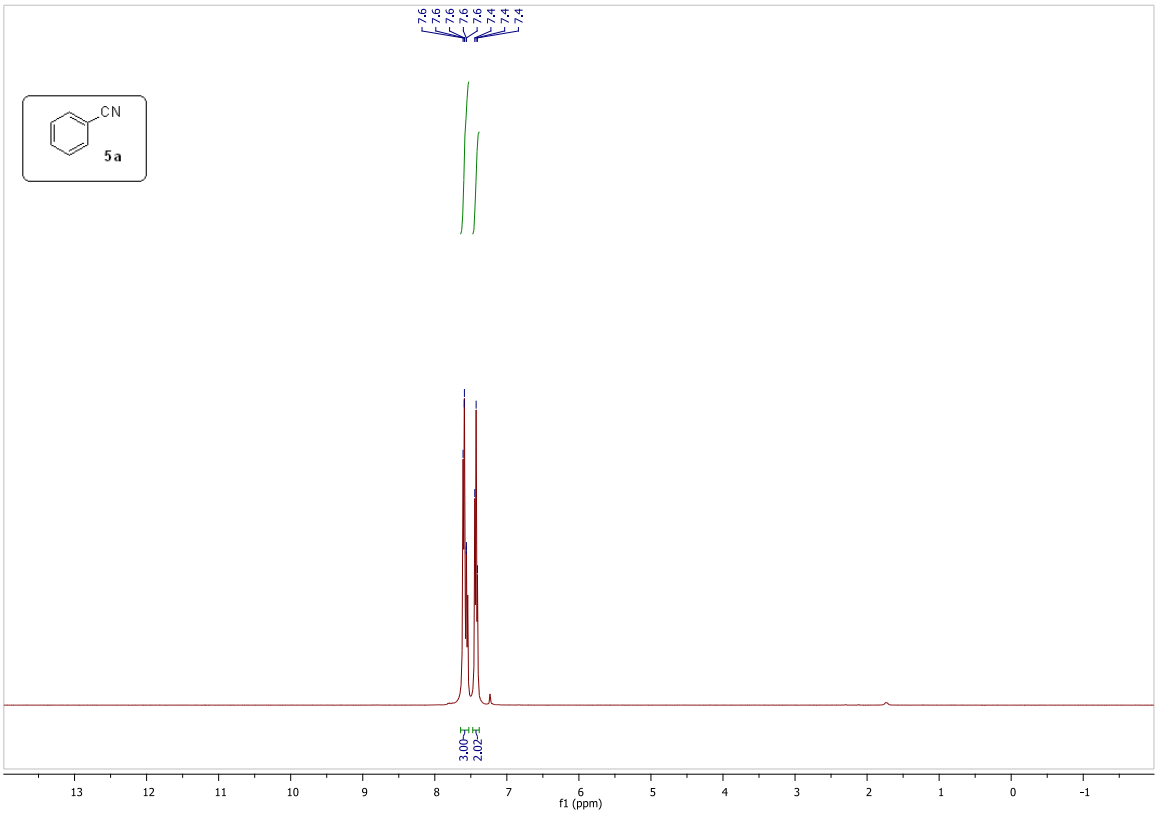

2.78
N
N
3m
4.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

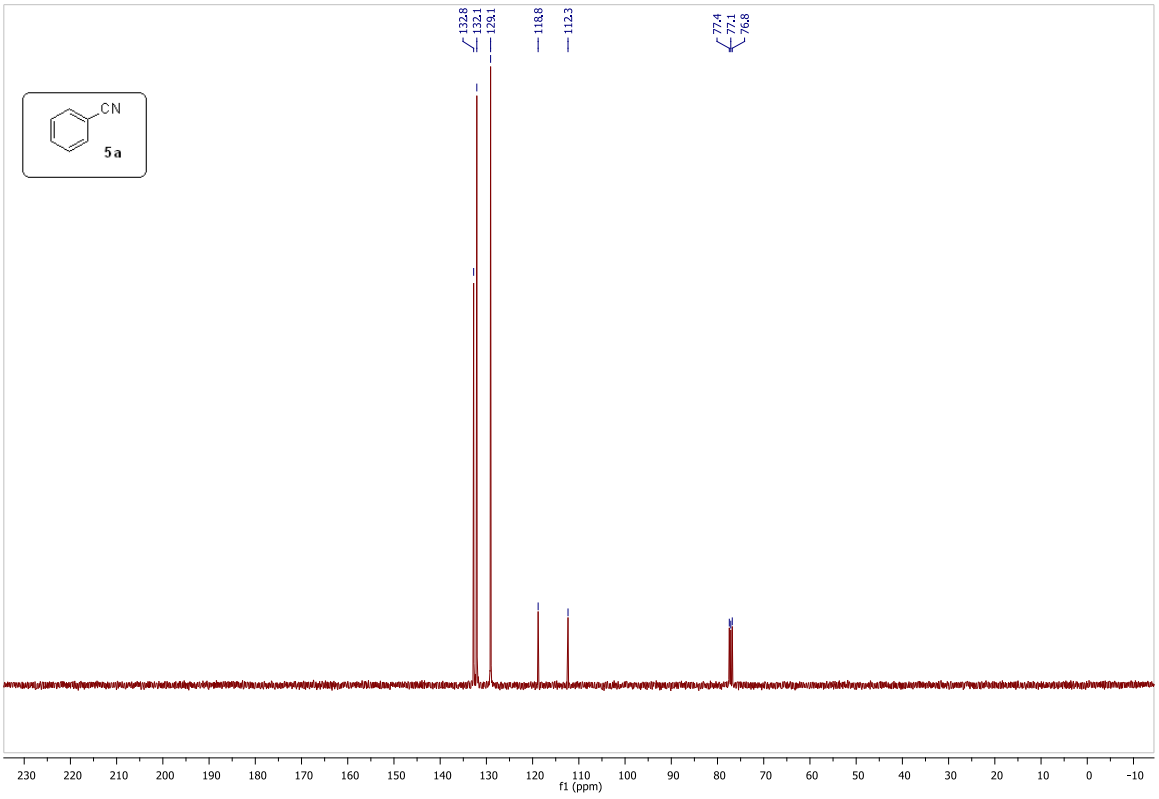

116.3
77.5
77.2
76.8
14.8
N
N
3m
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

^{1}H NMR AND ^{13}C NMR SPECTRA OF COMPUNDS

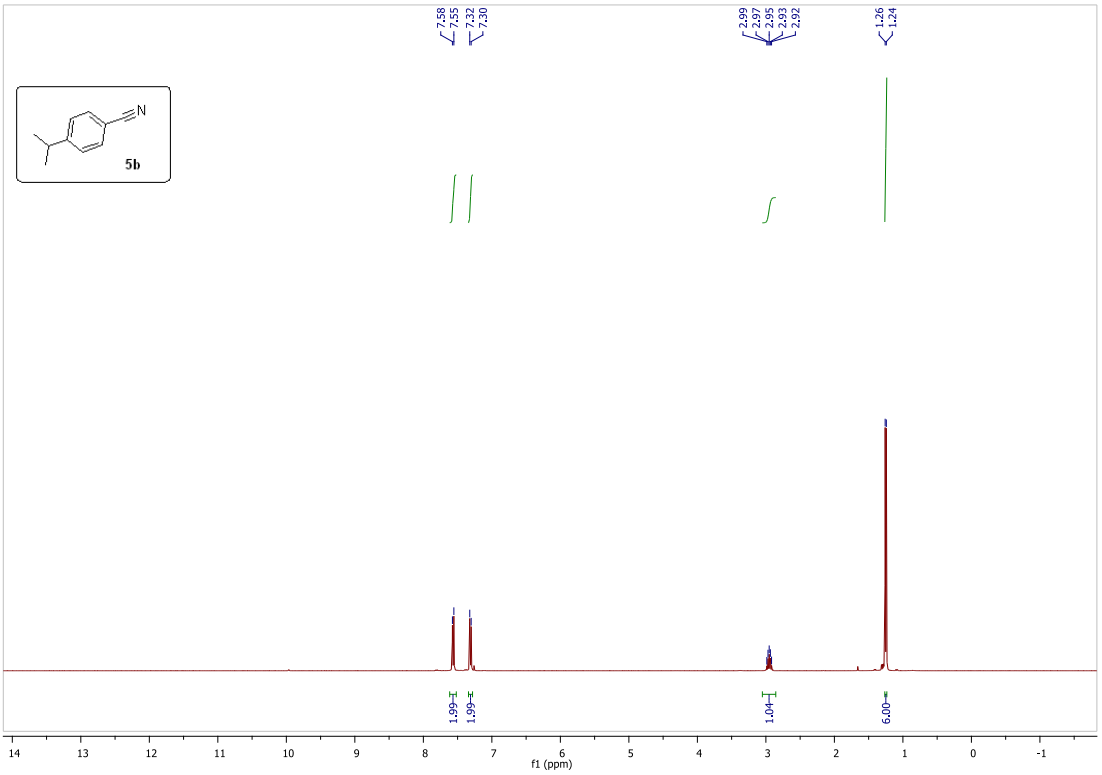
NMR spectral data for 5a-5v.

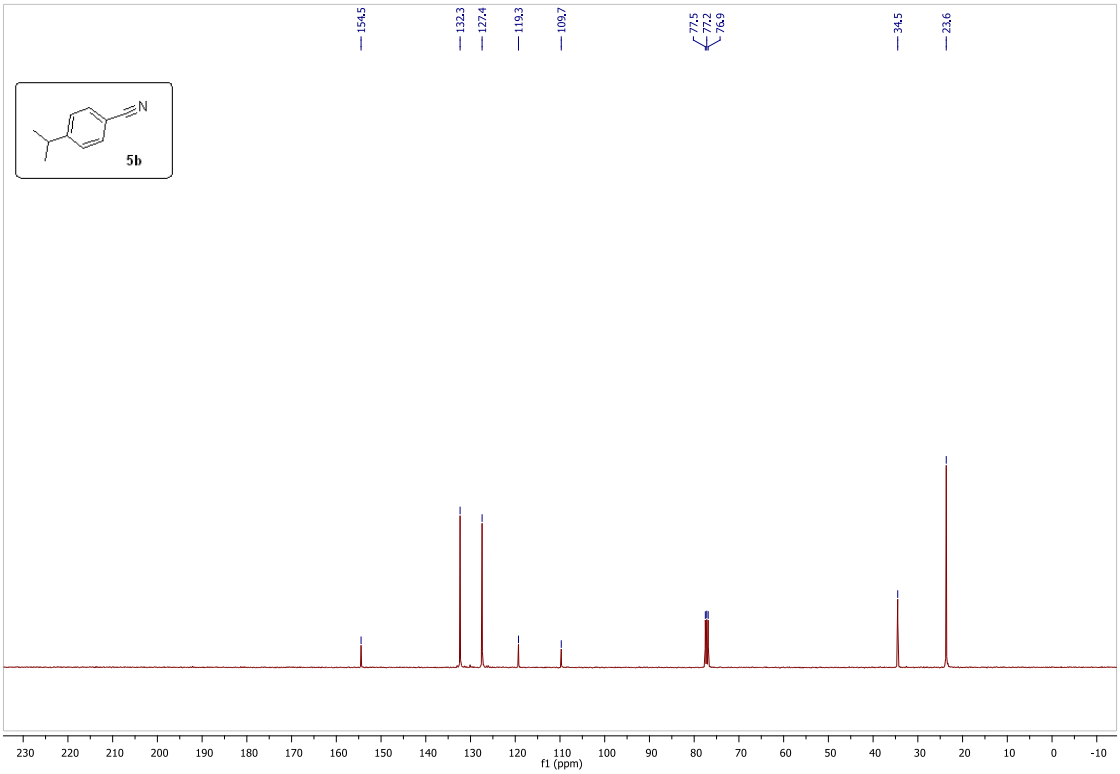
5a



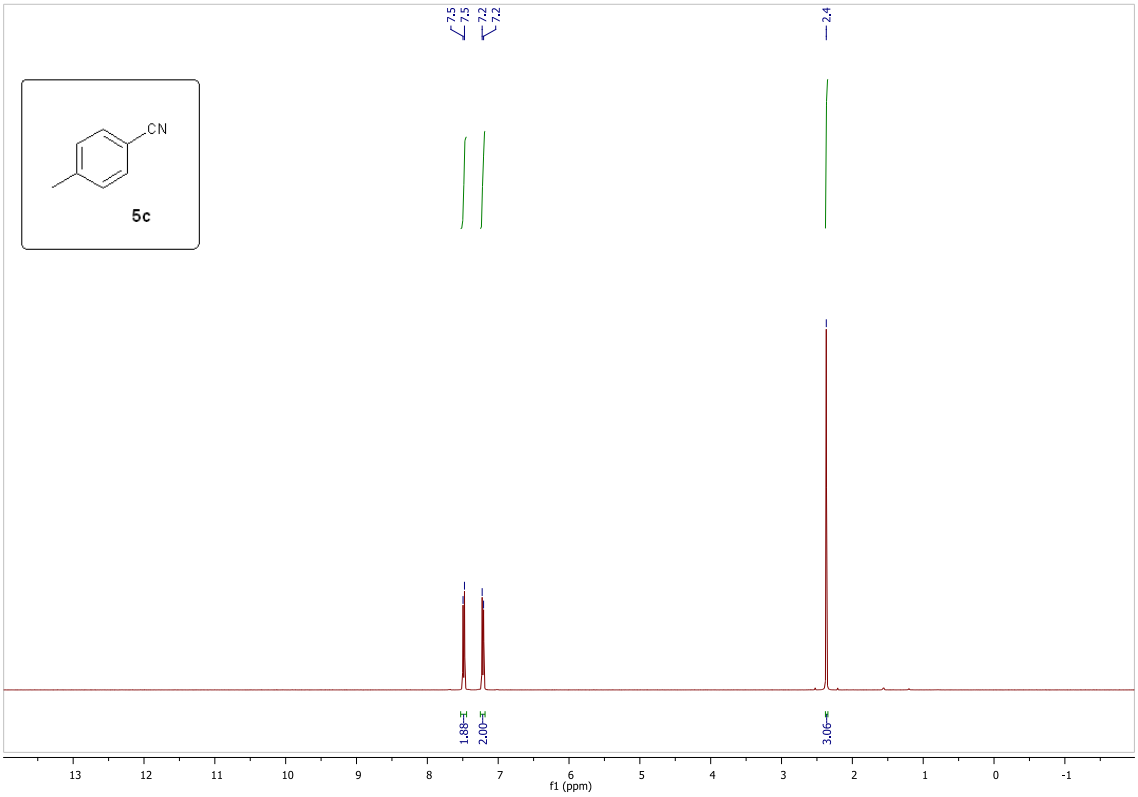

132.8
132.1
129.1
118.8
112.3
77.4
77.1
76.8
CN
5a
f1 (ppm)

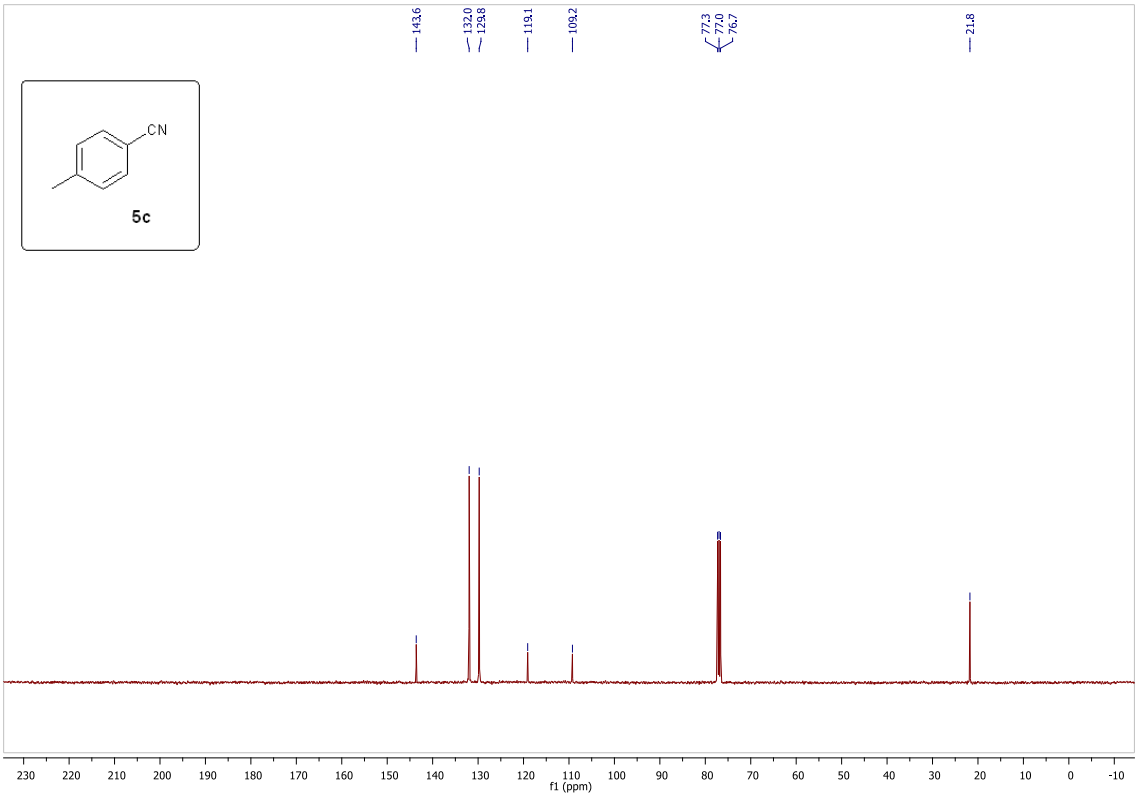
5b


7.58
7.55
7.32
7.30
2.99
2.97
2.95
2.93
2.92
1.26
1.24
N
5b
1.99
1.99
1.04
6.00
f1 (ppm)

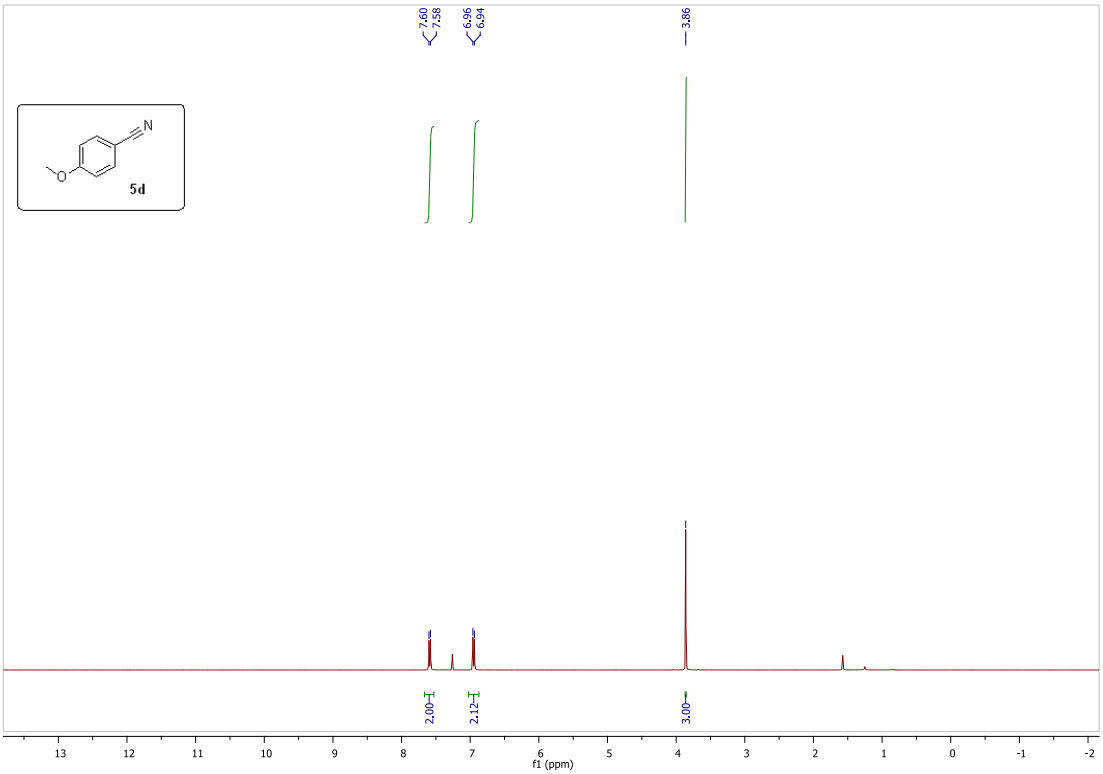

154.5
132.3
127.4
119.3
109.7
77.5
77.2
76.9
34.5
23.6
N
5b
f1 (ppm)

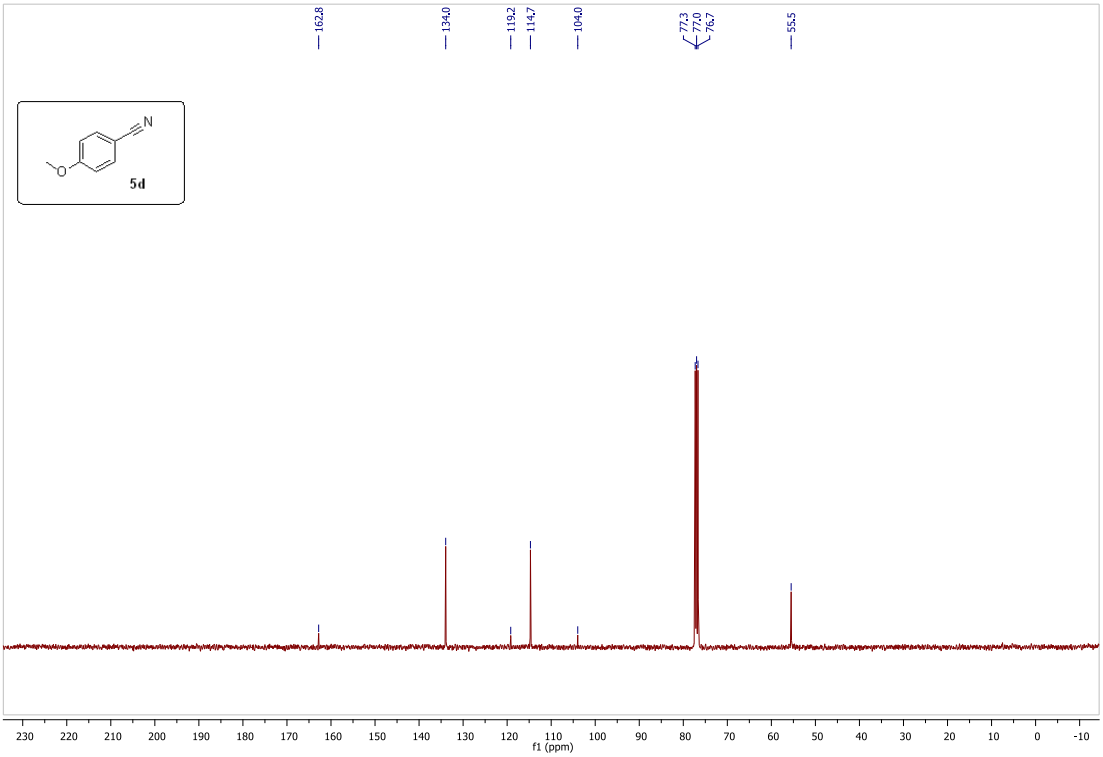
5c


7.5
7.5
7.2
7.2
2.4
CN
5c
1.88
2.00
3.06
f1 (ppm)

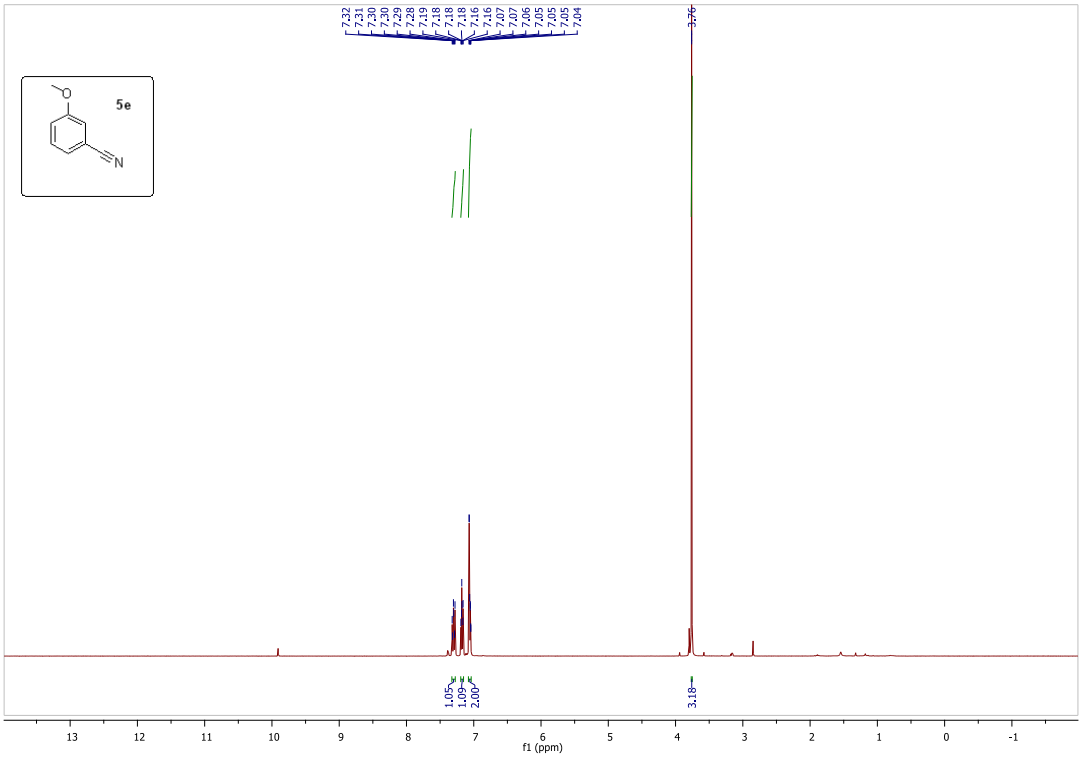

143.6
132.0
129.8
119.1
109.2
77.3
77.0
76.7
21.8
CN
5c
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

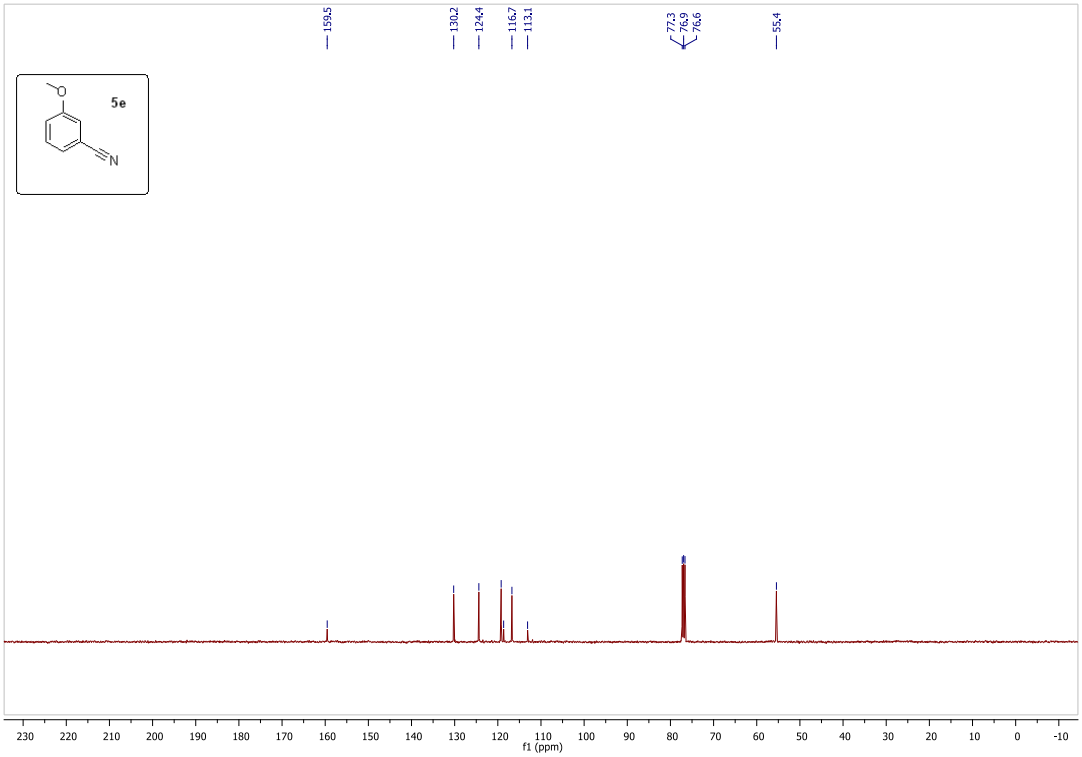
5d


7.60
7.58
6.96
6.94
3.86
N
O
5d
2.00
2.12
3.00
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)

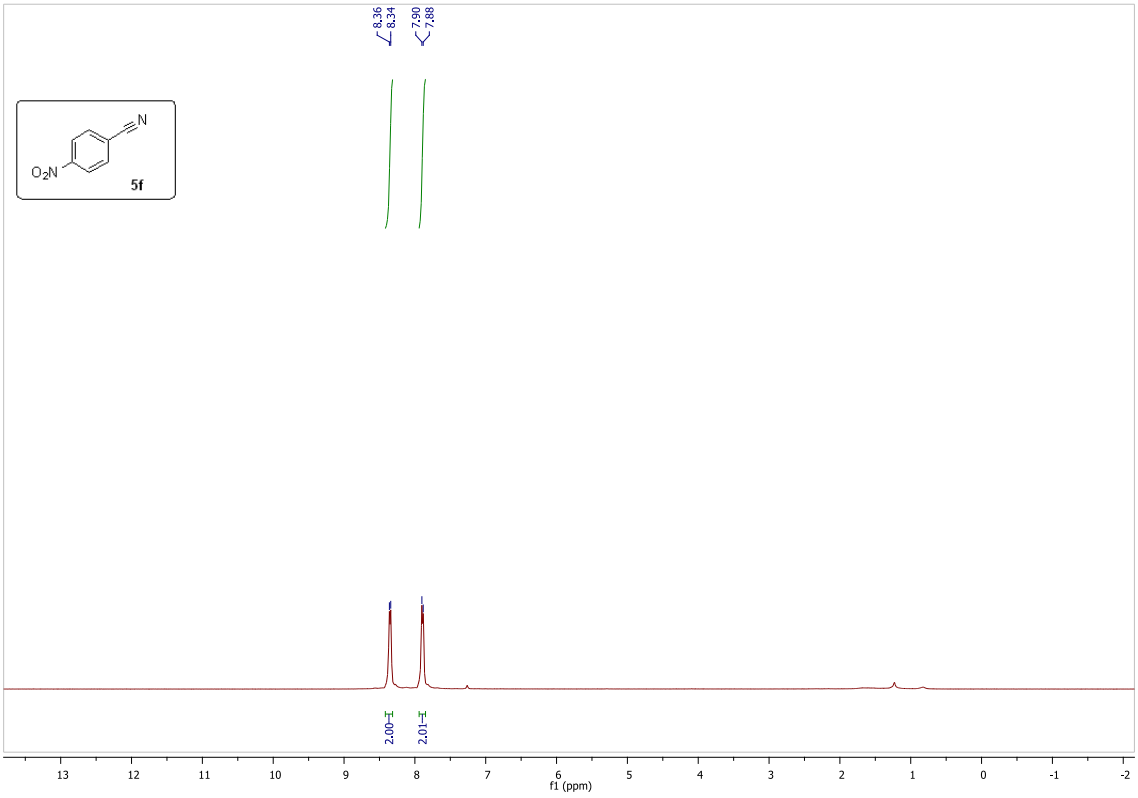

162.8
134.0
119.2
114.7
104.0
77.3
77.0
76.7
55.5
N
O
5d
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

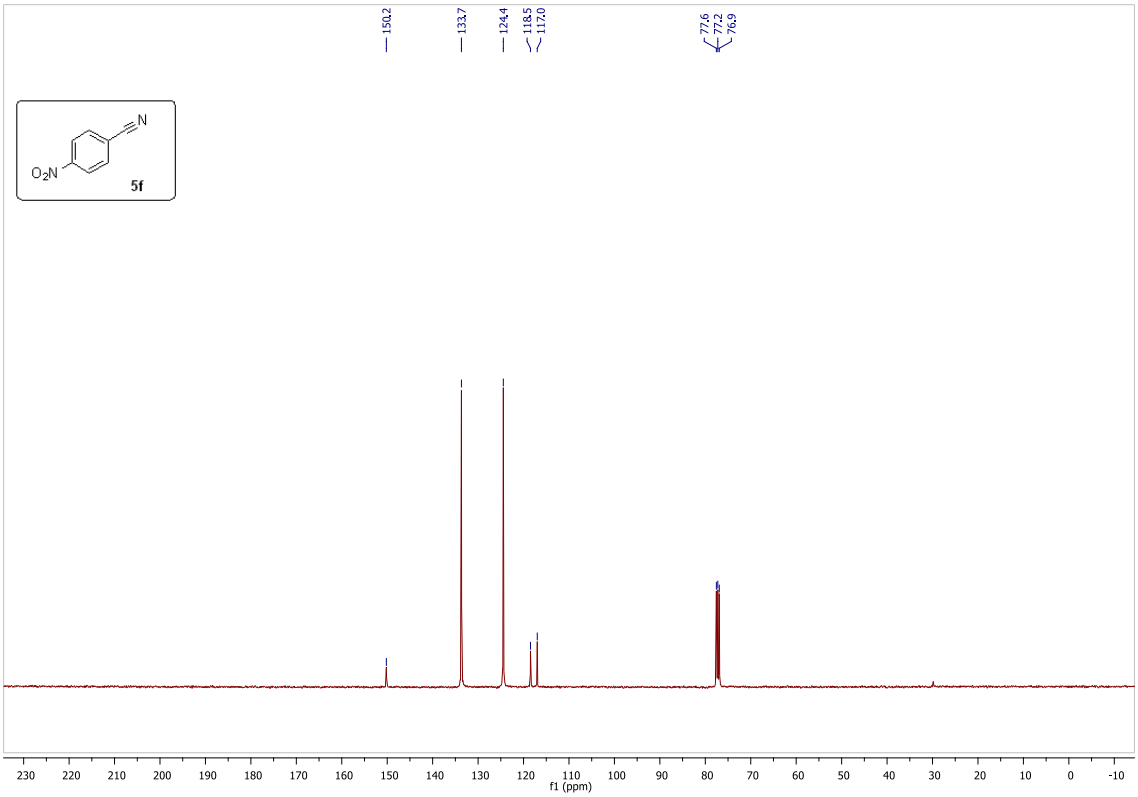
5e


7.32
7.31
7.30
7.30
7.29
7.28
7.19
7.18
7.18
7.16
7.16
7.07
7.07
7.06
7.05
7.05
7.05
7.04
3.76
O
5e
N
1.05
1.09
2.00
3.18
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)

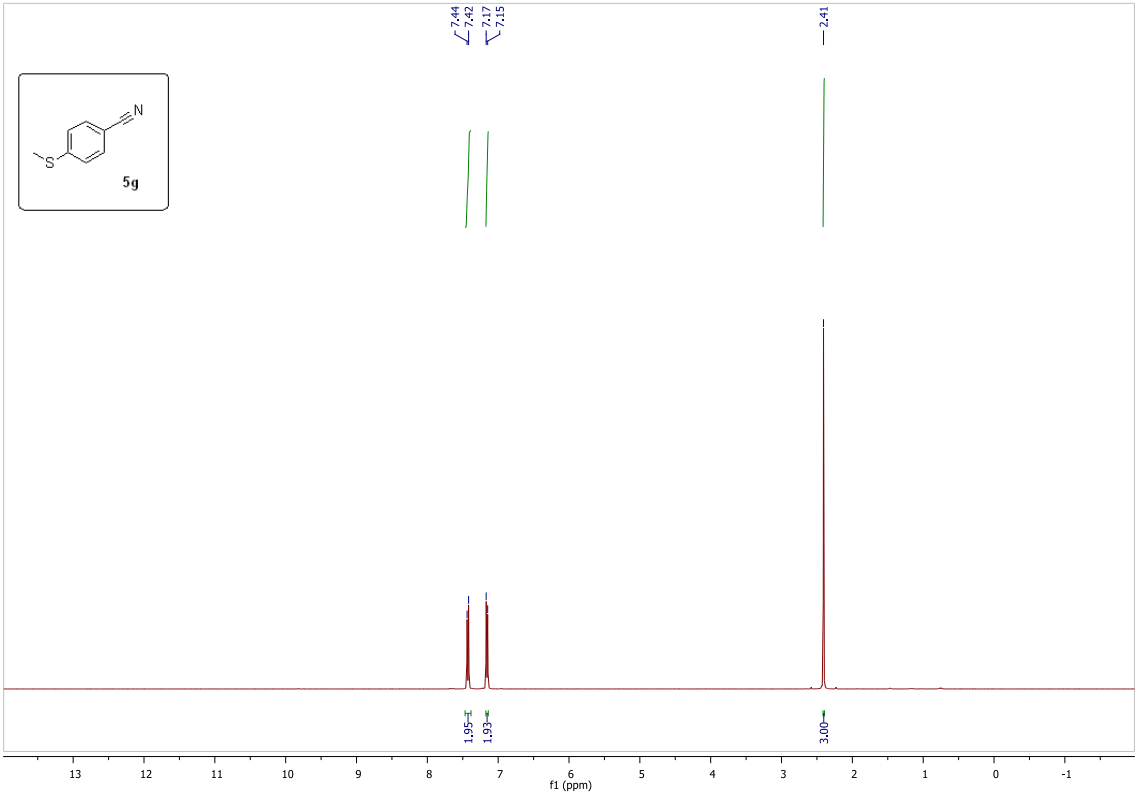

159.5
130.2
124.4
116.7
113.1
77.3
76.9
76.6
55.4
5e
f1 (ppm)

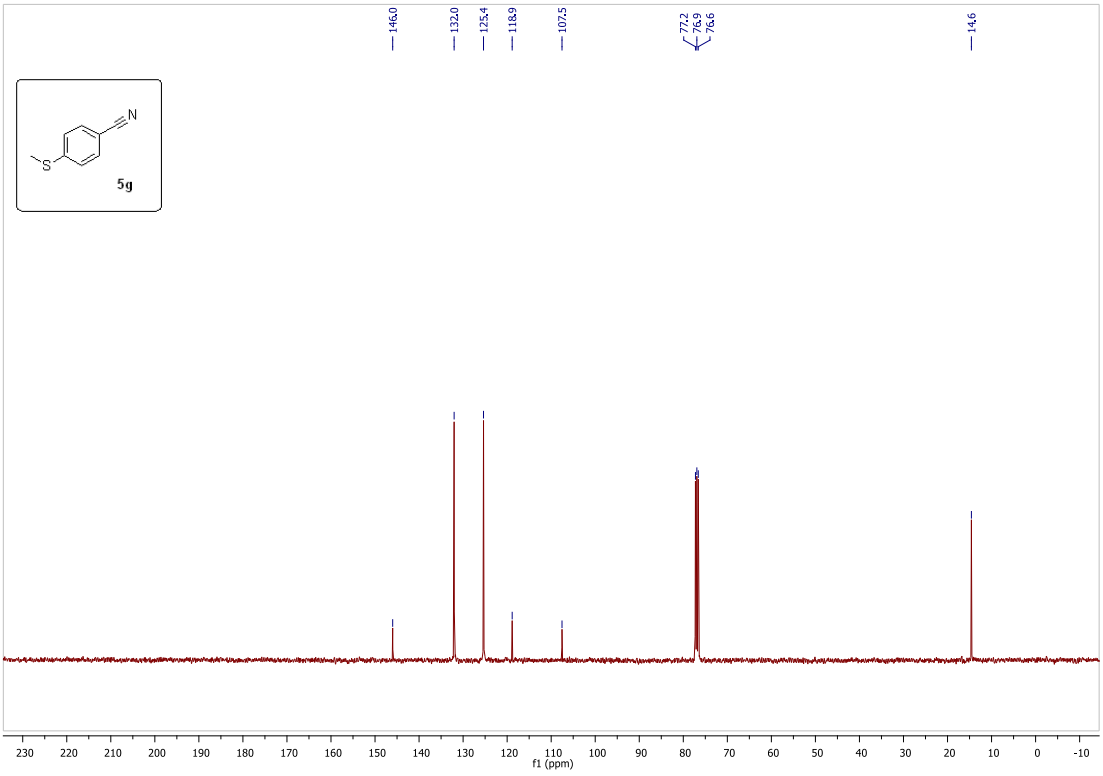
5f


8.36
8.34
7.90
7.88
5f
2.00
2.01
f1 (ppm)

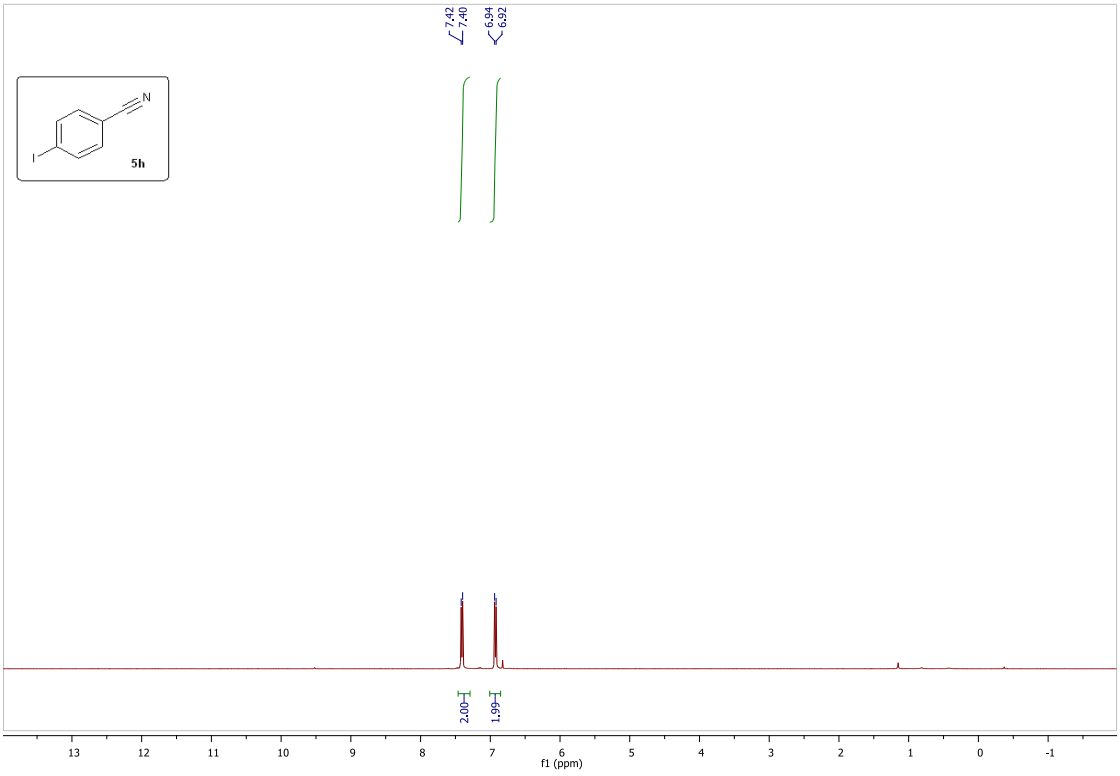

150.2
133.7
124.4
118.5
117.0
77.6
77.2
76.9
N
O2N
5f
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

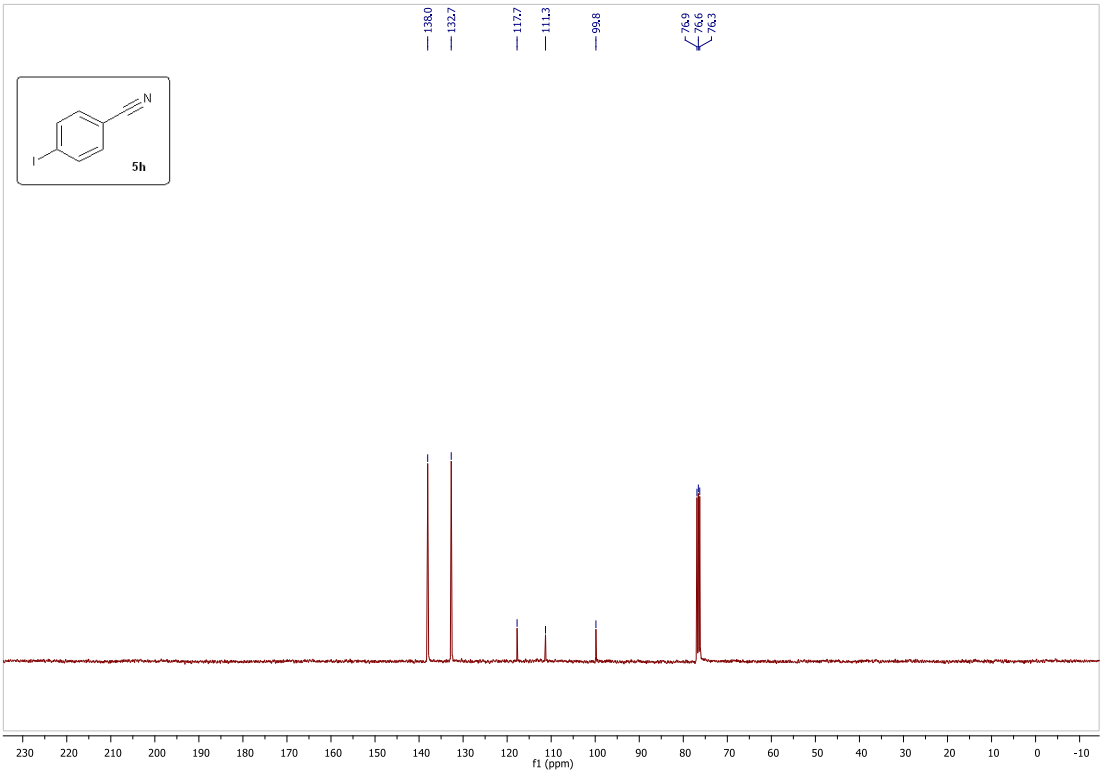
5g


7.44
7.42
7.17
7.15
2.41
N
S
5g
1.95
1.93
3.00
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)

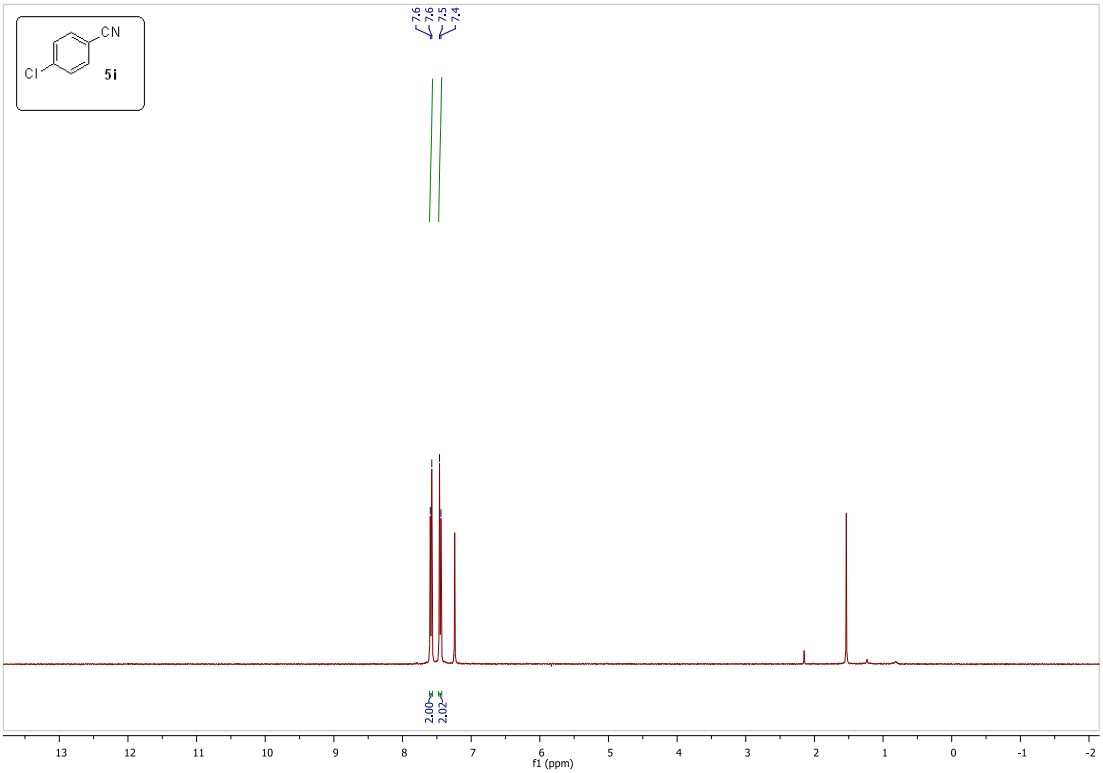

146.0
132.0
125.4
118.9
107.5
77.2
76.9
76.6
14.6
N
S
5g
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

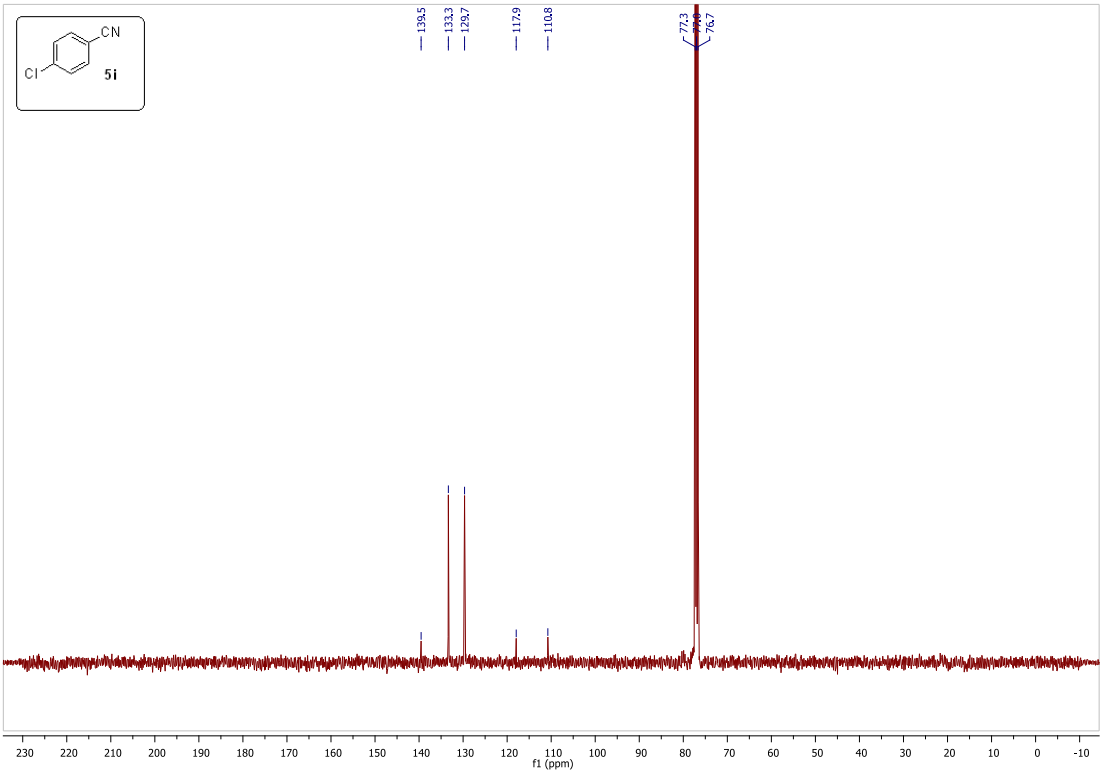
5h


7.42
7.40
6.94
6.92
N
I
5h
2.00
1.99
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)

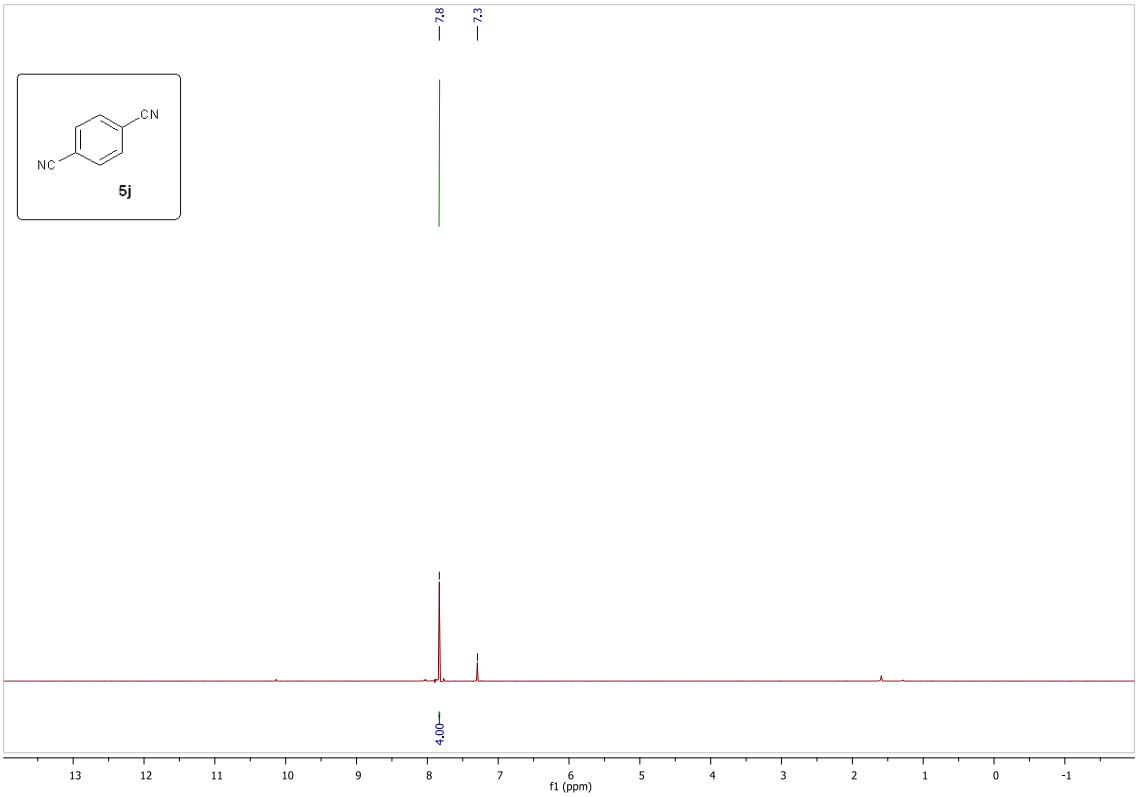

138.0
132.7
117.7
111.3
99.8
76.9
76.6
76.3
N
I
5h
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

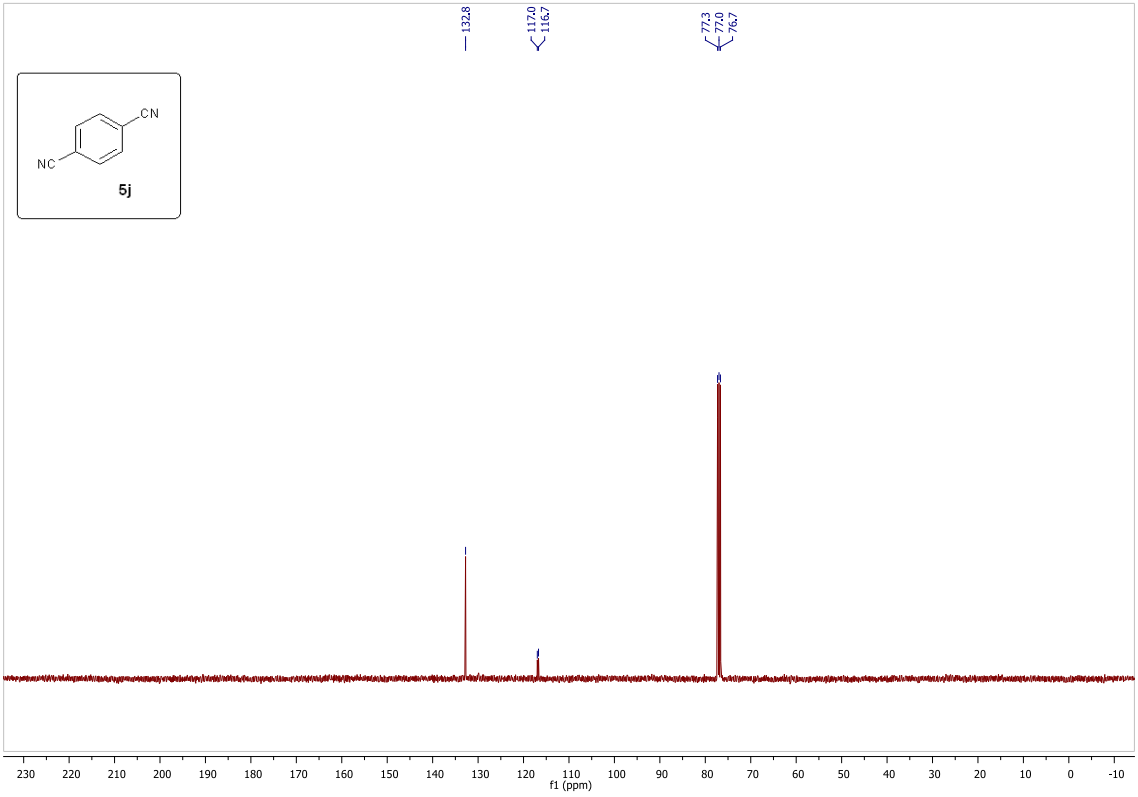
5i


7.6
7.6
7.5
7.4
CN
Cl
5i
2.00
2.02
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)

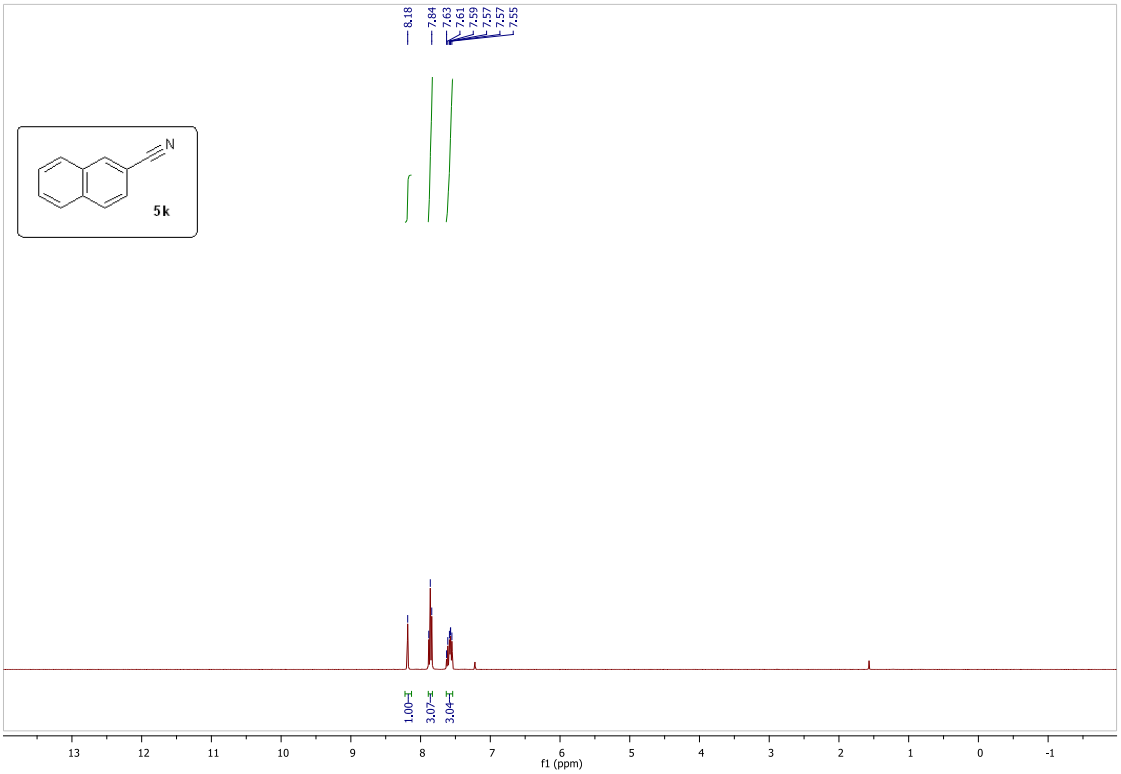

CN
Cl
5i
139.5
133.3
129.7
117.9
110.8
77.3
77.0
76.7
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

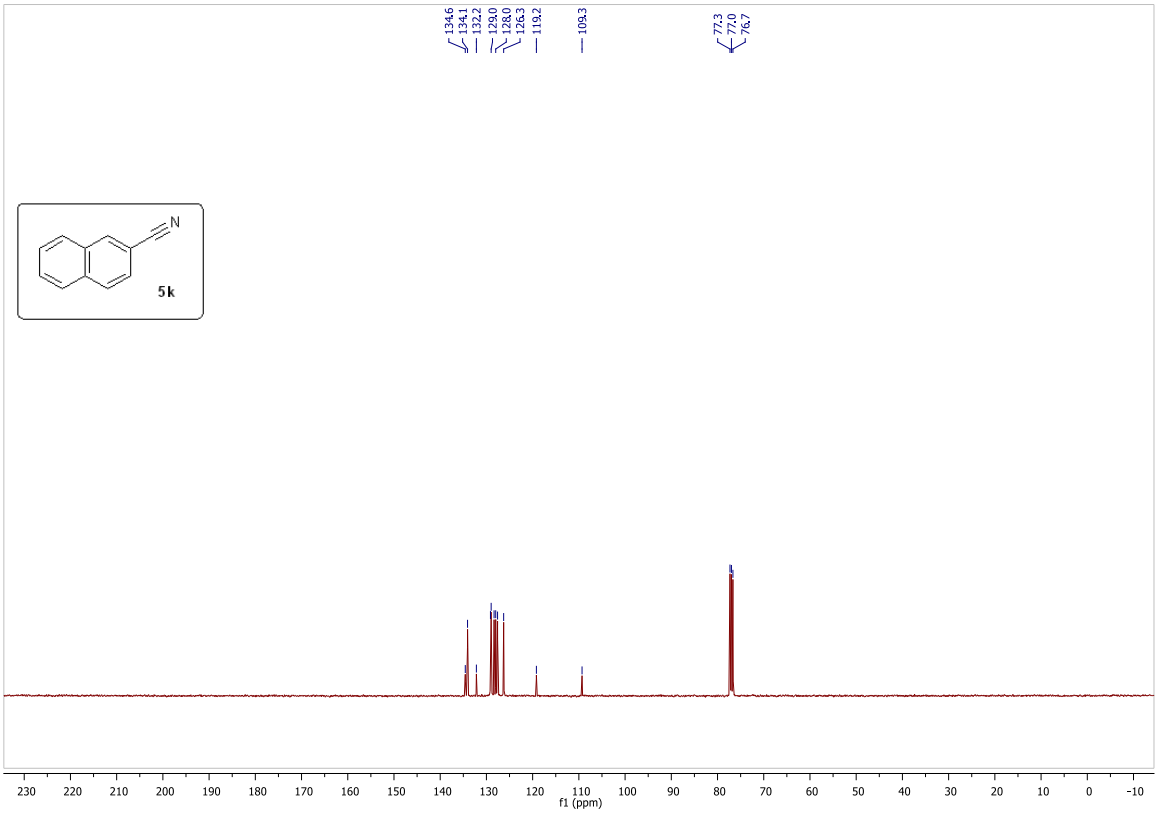
5j


7.8
7.3
CN
NC
5j
4.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

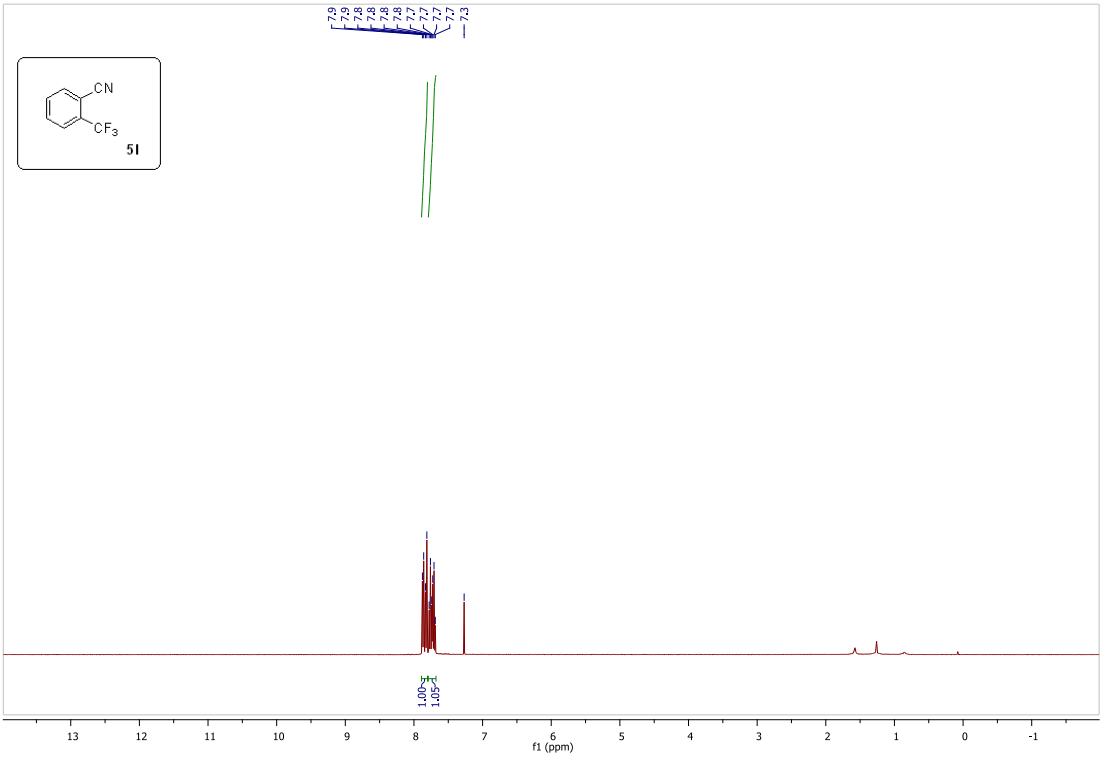

132.8
117.0
116.7
77.3
77.0
76.7
CN
NC
5j
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

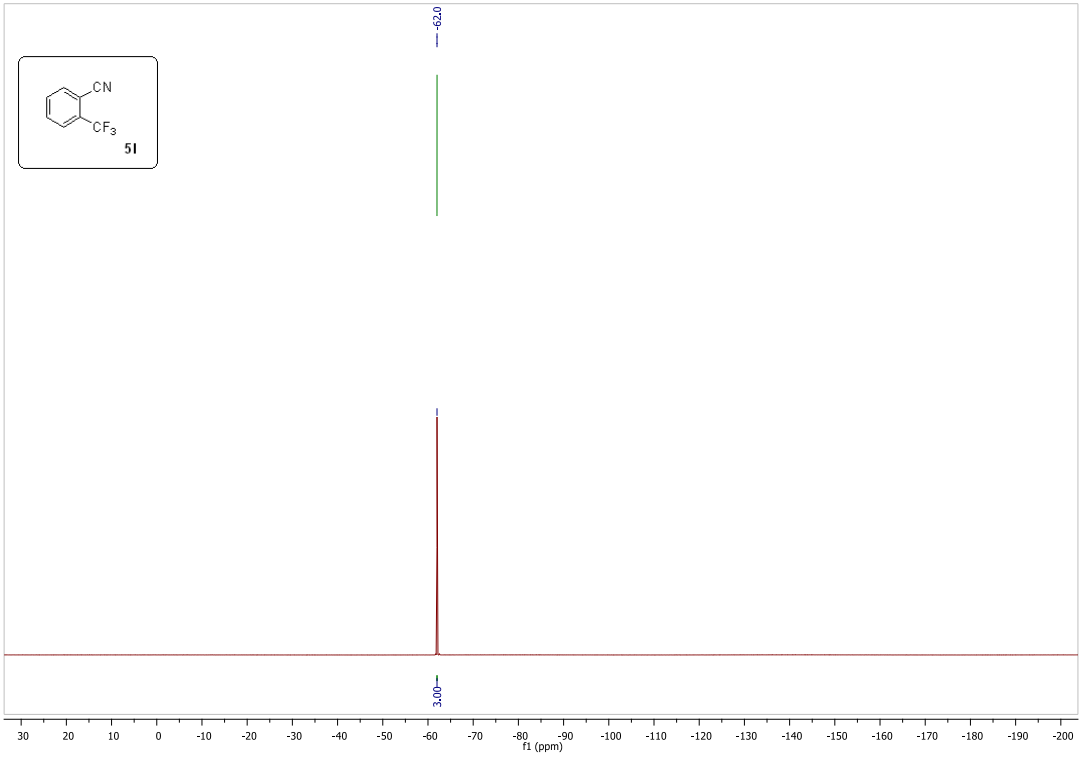
5k

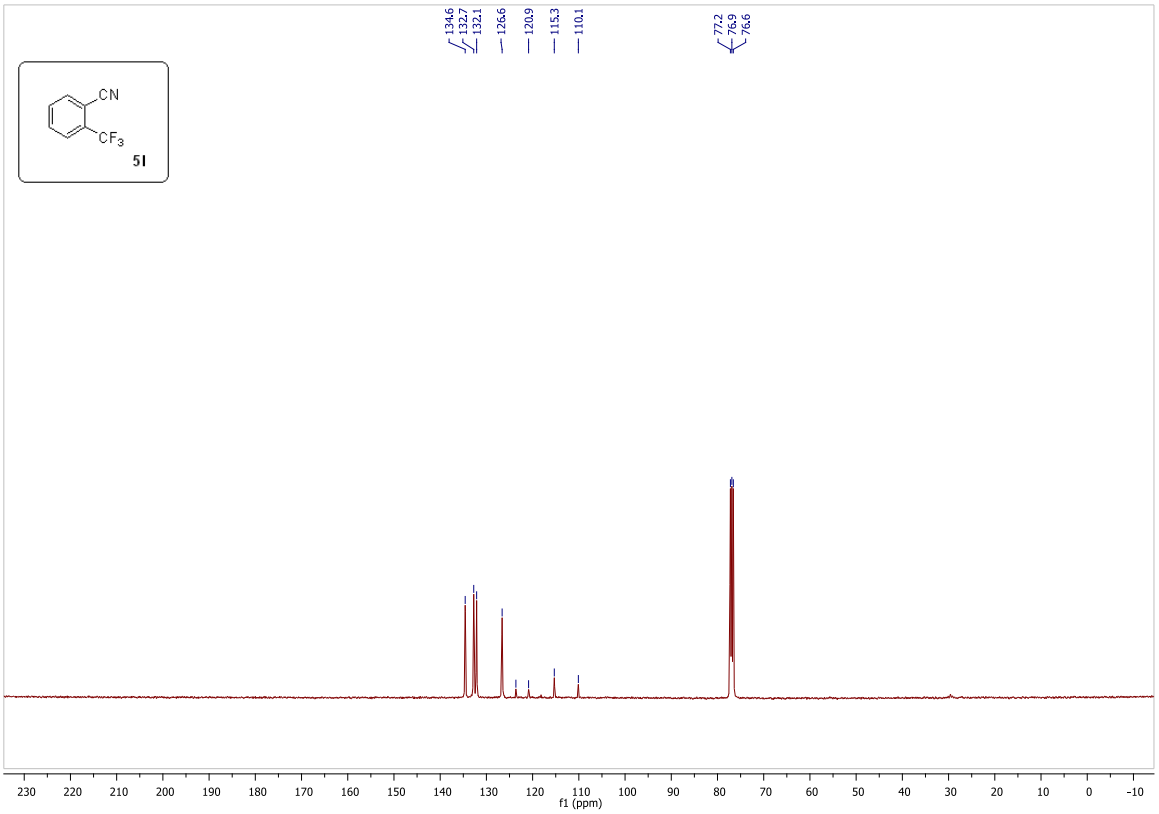

8.18
7.84
7.63
7.61
7.59
7.57
7.57
7.55
N
5k
1.00
3.07
3.04
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


134.6
134.1
132.2
129.0
128.0
126.3
119.2
109.3
77.3
77.0
76.7
N
5k
230
220
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)

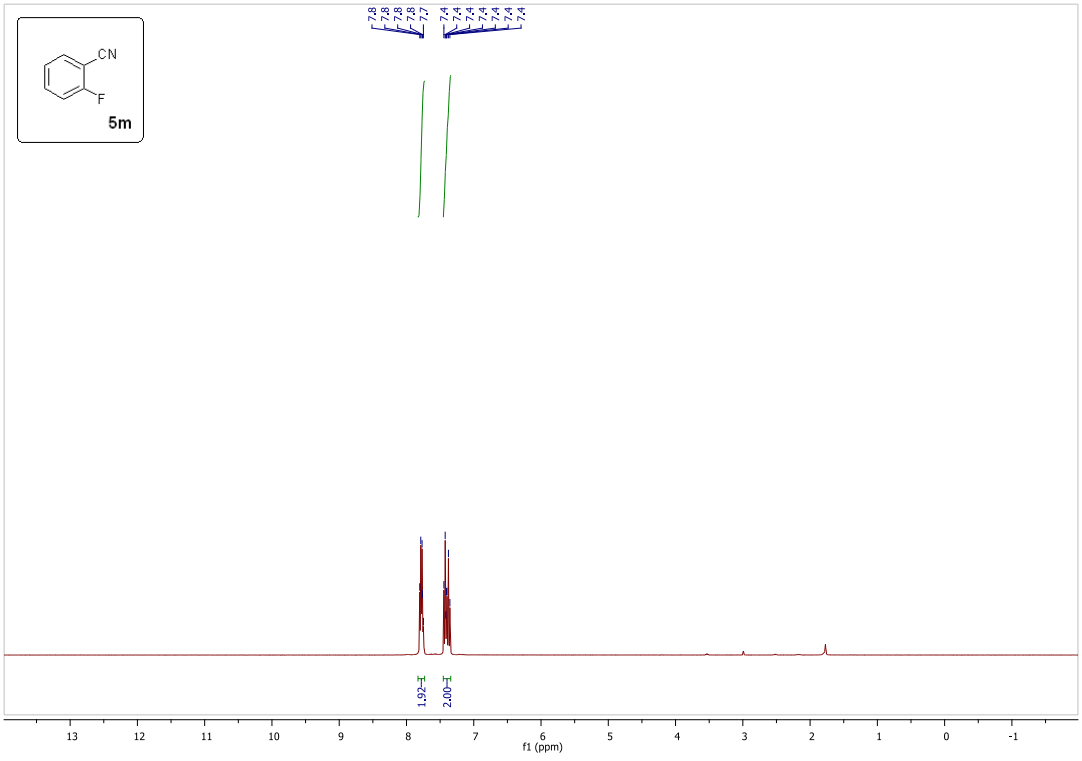
5l

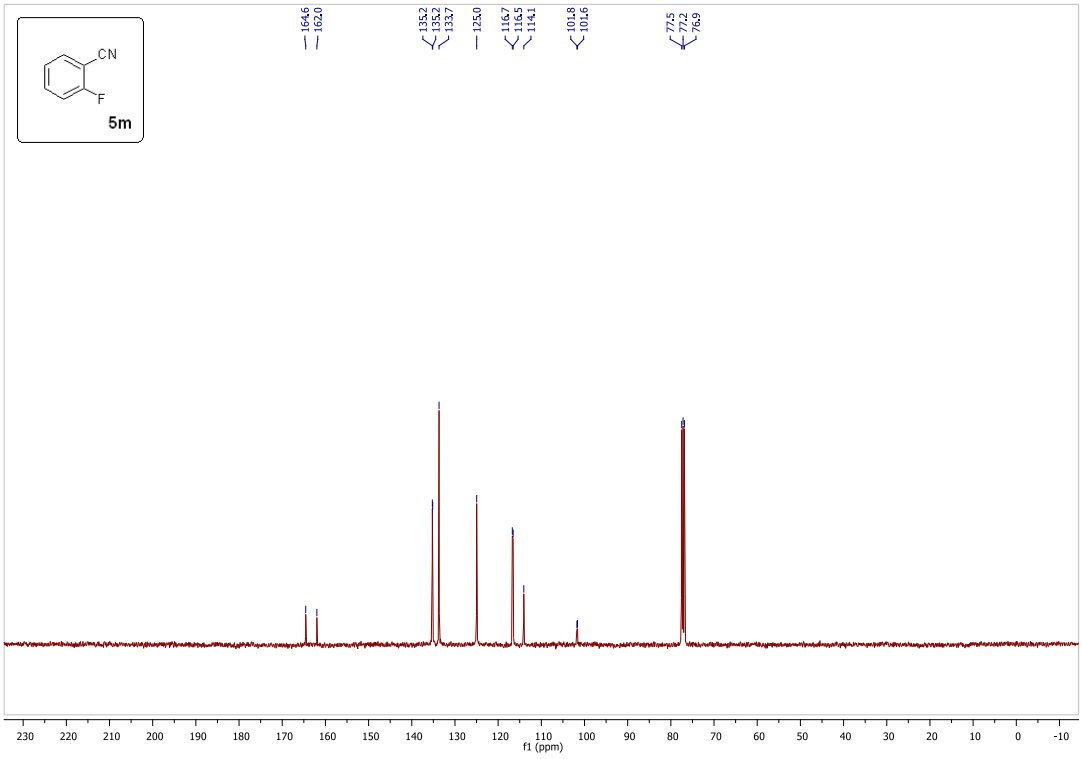

7.9
7.9
7.8
7.8
7.8
7.8
7.7
7.7
7.7
7.7
7.3
CN
CF3
5l
1.00
1.05
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

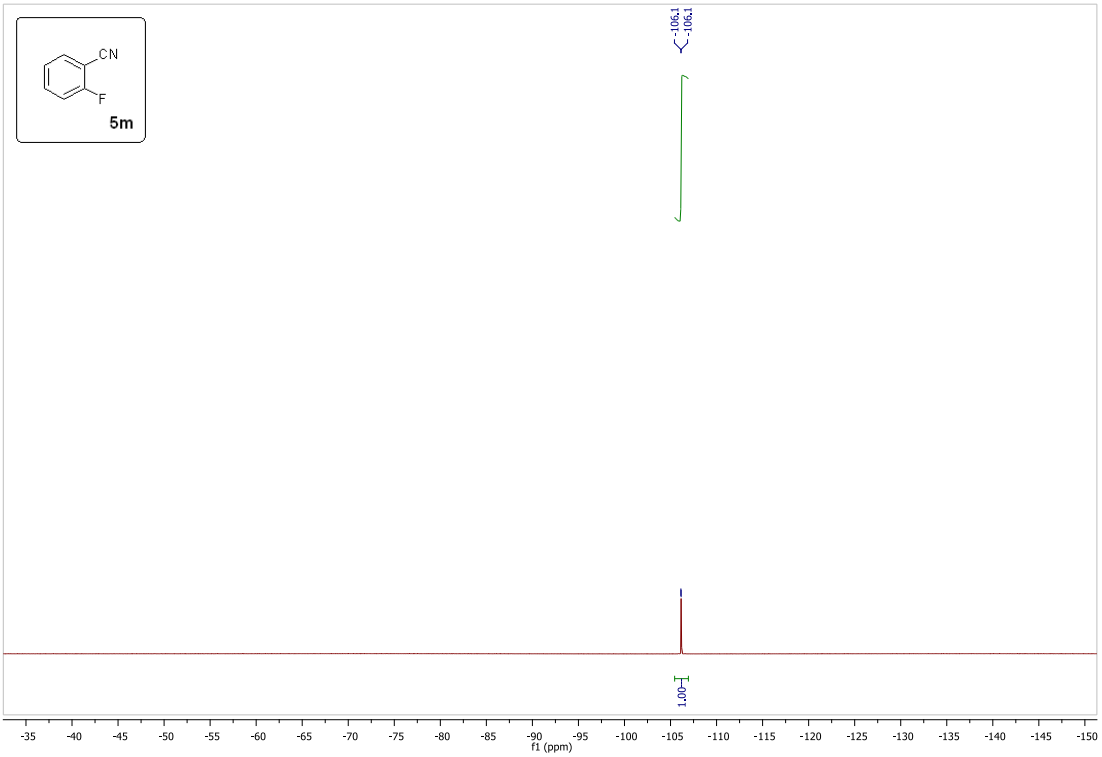

-62.0
CN
CF3
5l
3.00
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)


134.6
132.7
132.1
126.6
120.9
115.3
110.1
77.2
76.9
76.6
CN
CF3
5l
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

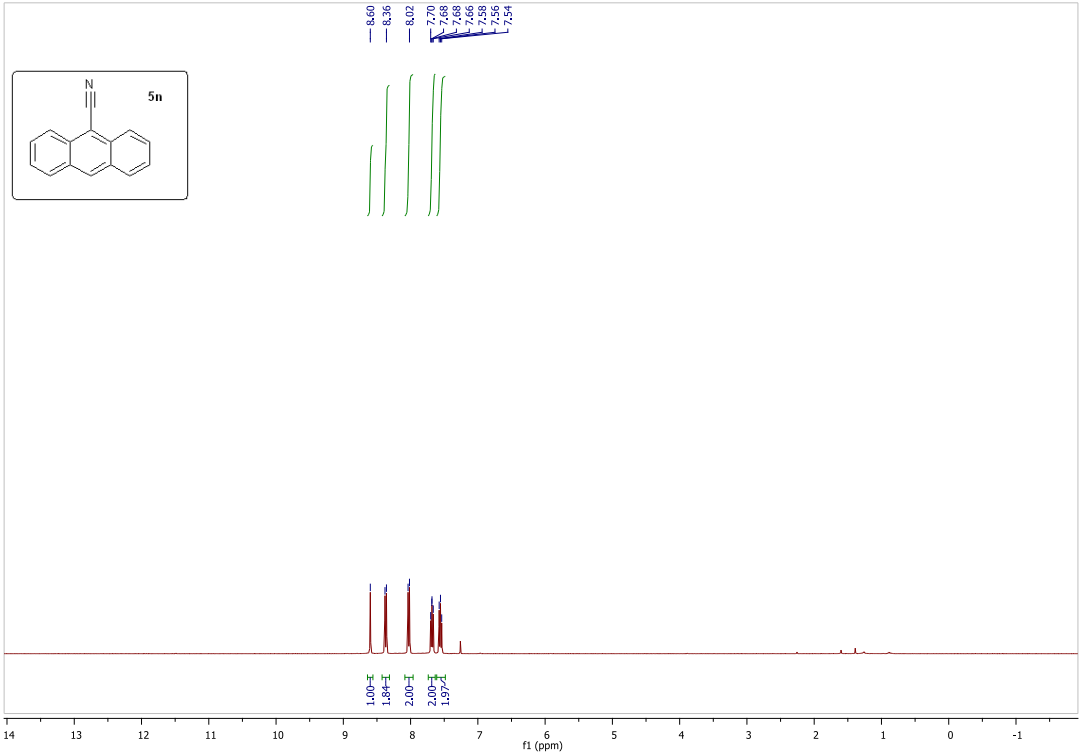
5m

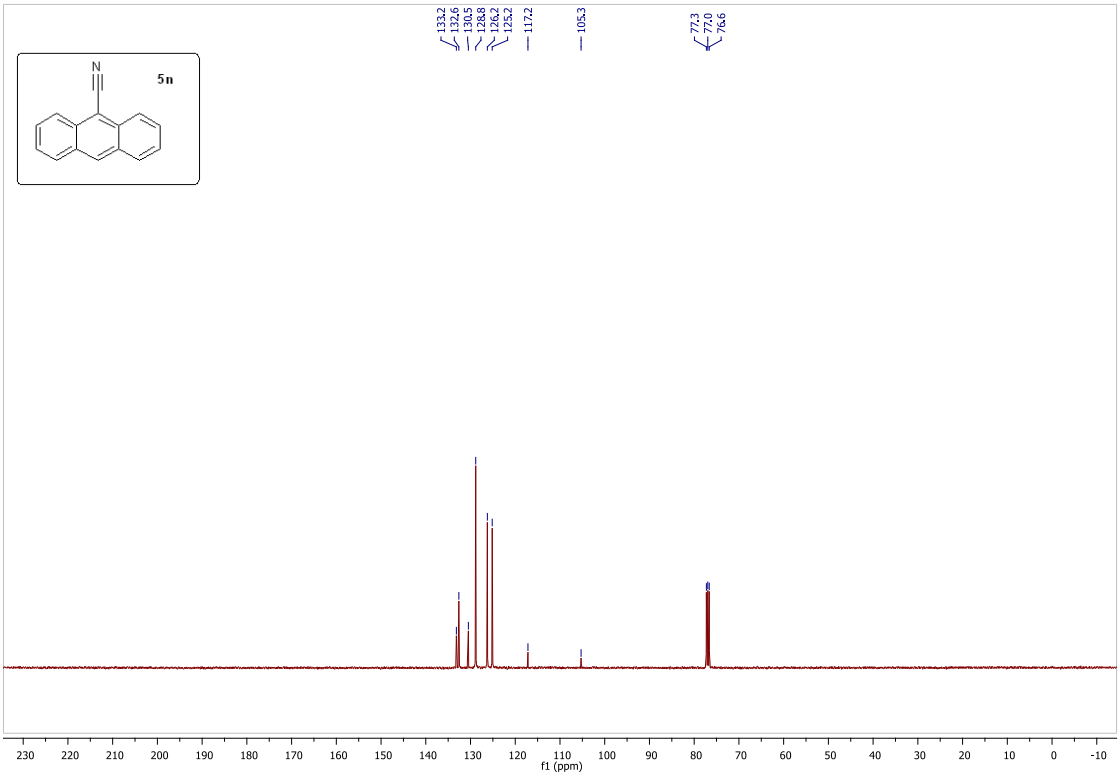

CN
F
5m
7.8
7.8
7.8
7.8
7.7
7.4
7.4
7.4
7.4
7.4
7.4
7.4
1.92
2.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


CN
F
5m
164.6
162.0
135.2
135.2
133.7
125.0
116.7
116.5
114.1
101.8
101.6
77.5
77.2
76.9
230
220
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)

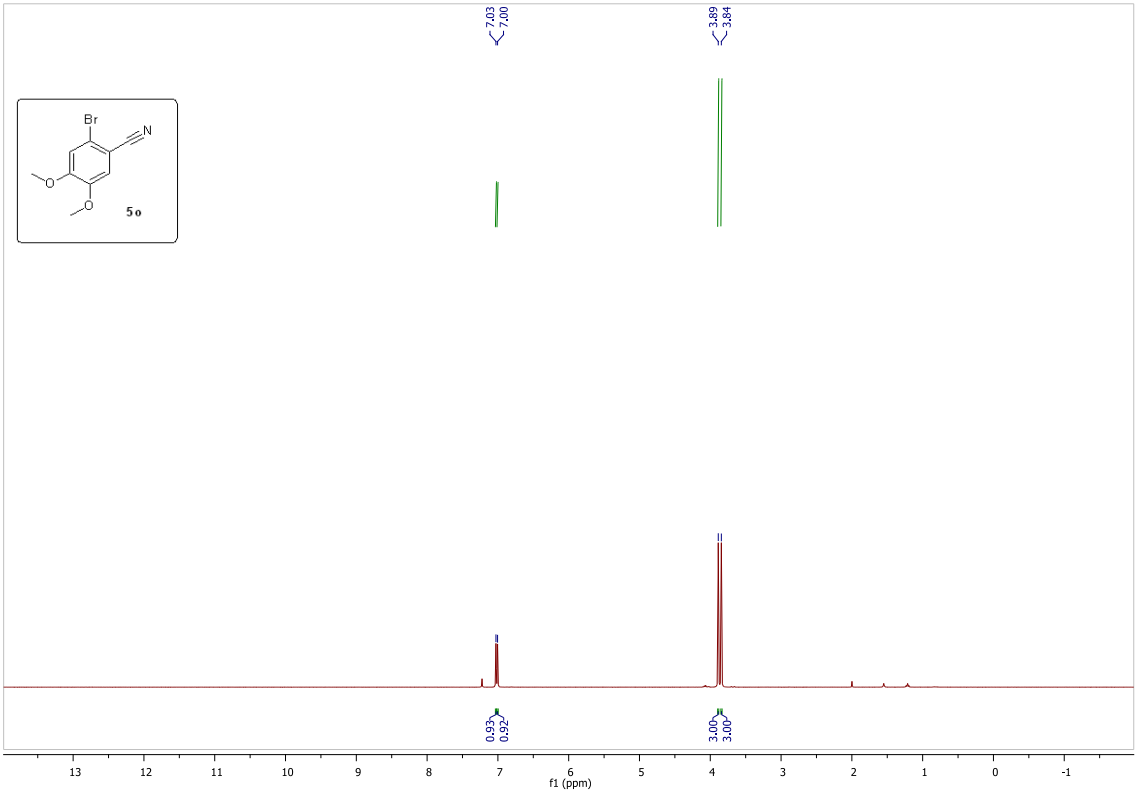

CN
F
5m
-106.1
-106.1
1.00
-35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150
f1 (ppm)

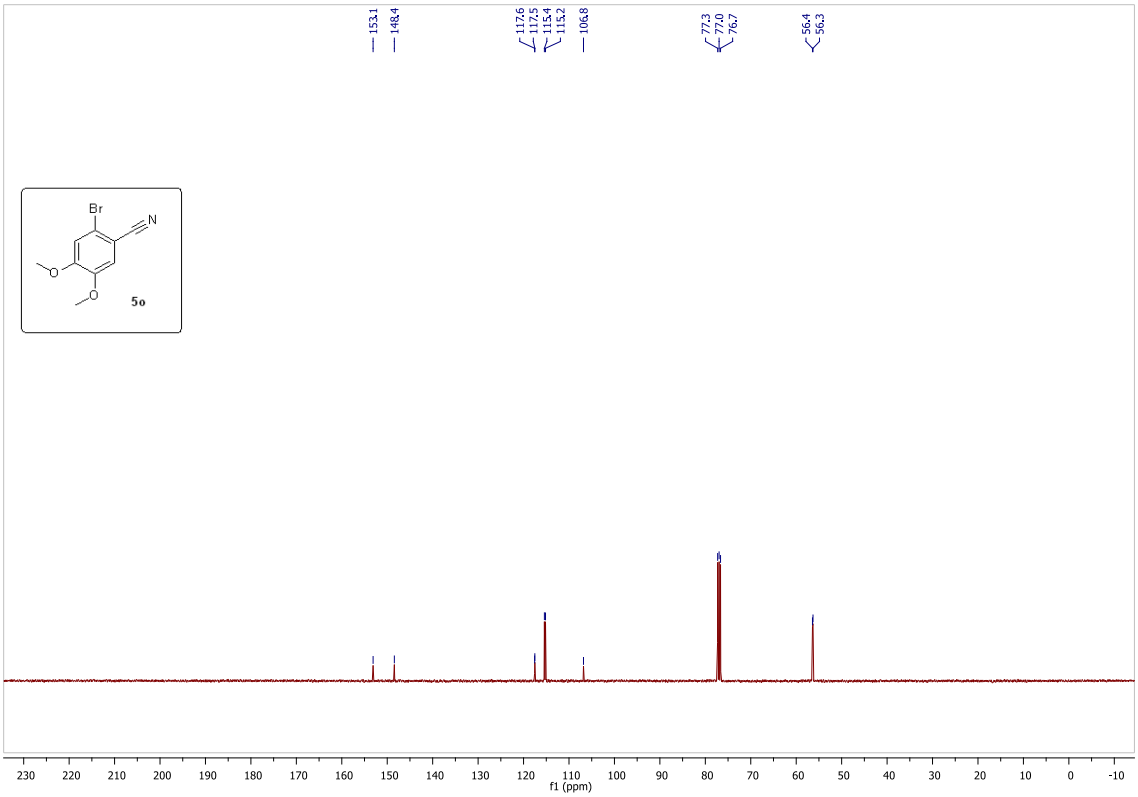
5n


8.60
8.36
8.02
7.70
7.68
7.68
7.66
7.58
7.56
7.54
N
5n
1.00
1.84
2.00
2.00
1.97
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)

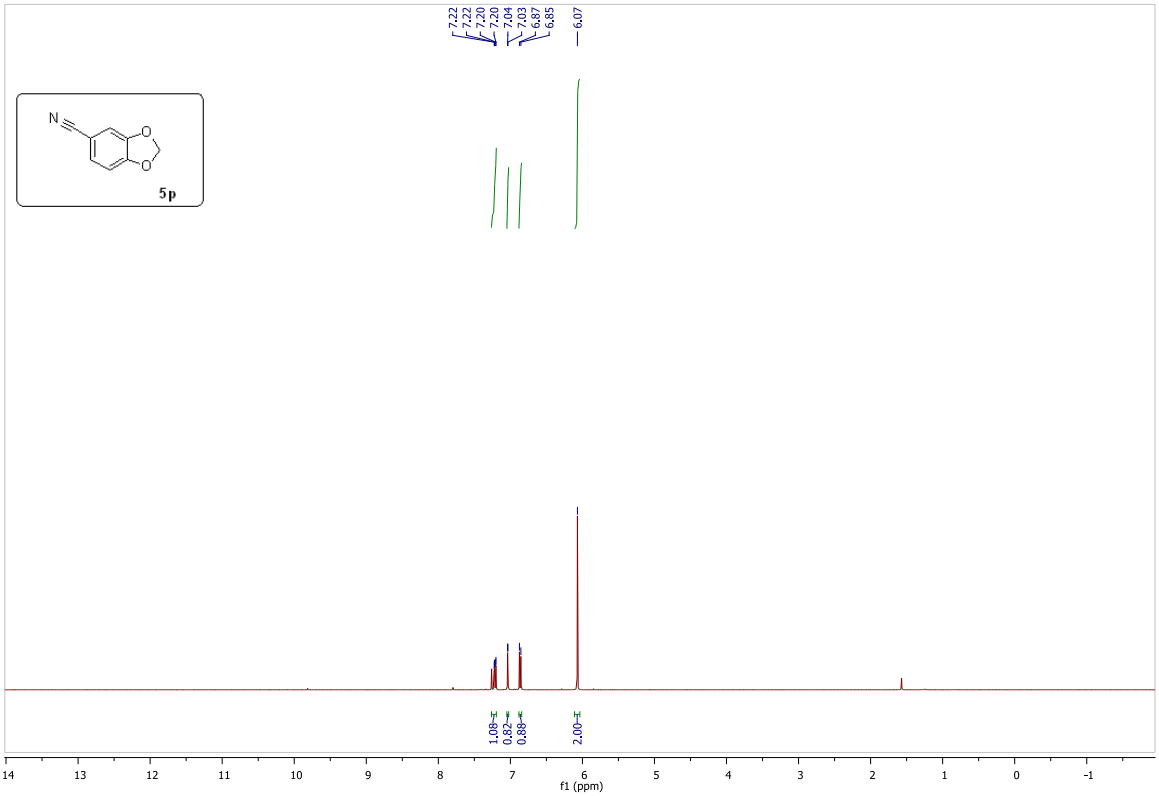

133.2
132.6
130.5
128.8
126.2
125.2
117.2
105.3
77.3
77.0
76.6
N
5n
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

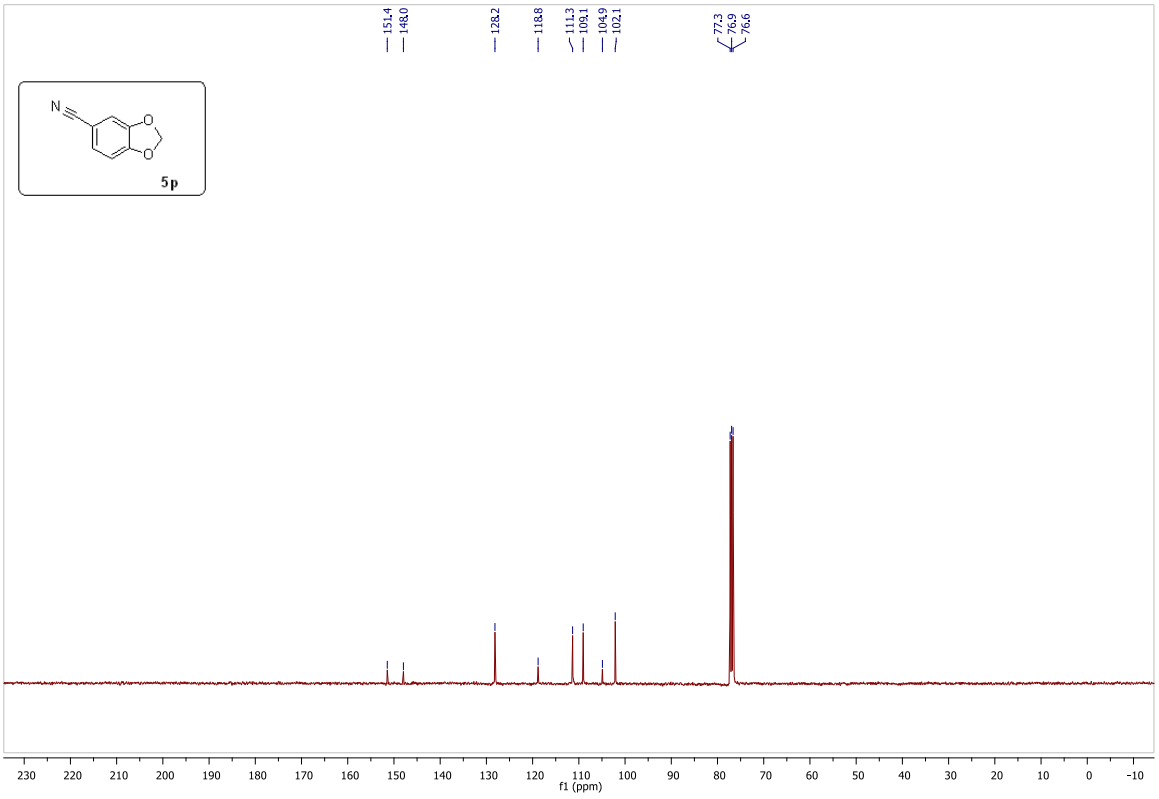
5o


7.03
7.00
3.89
3.84
Br
N
O
O
5o
0.93
0.92
3.00
3.00
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)

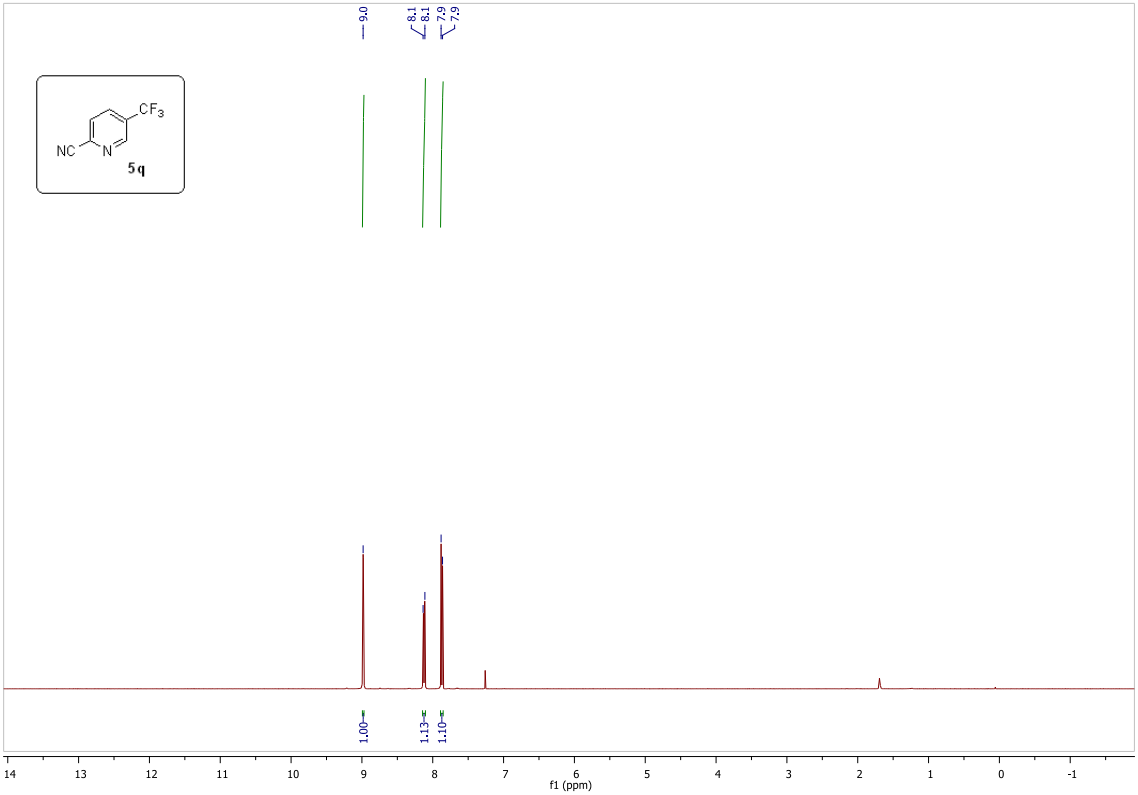

153.1
148.4
117.6
117.5
115.4
115.2
106.8
77.3
77.0
76.7
56.4
56.3
Br
N
O
O
5o
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

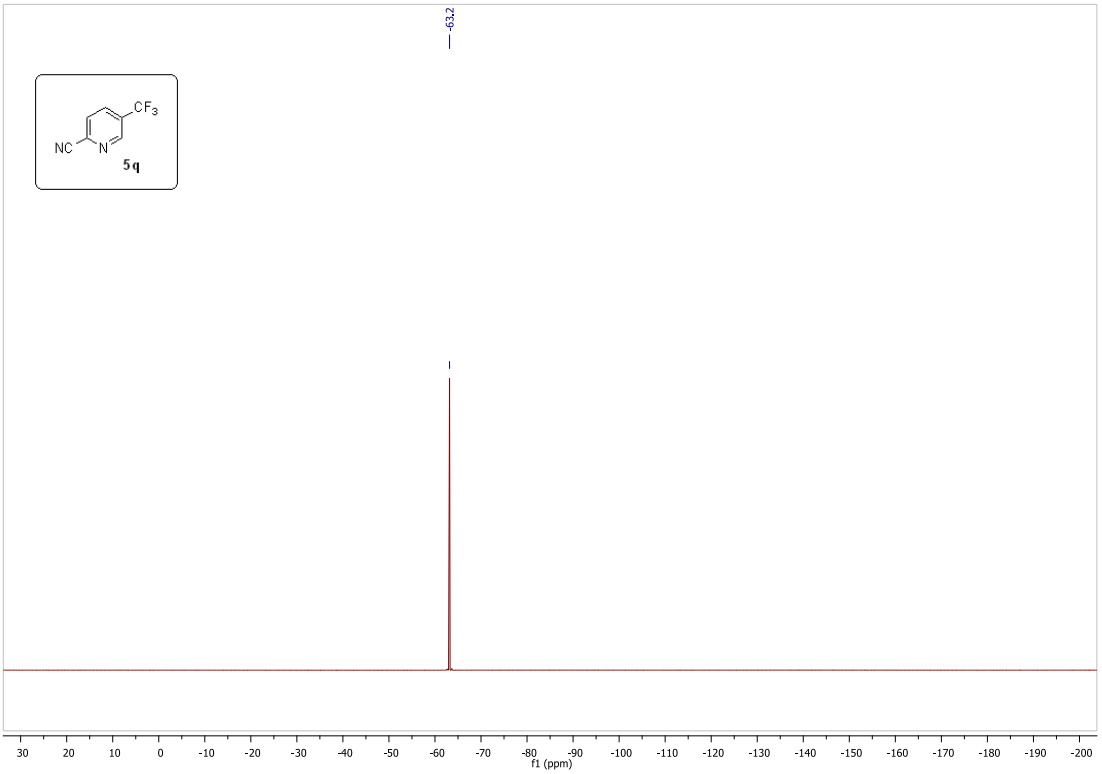
5p

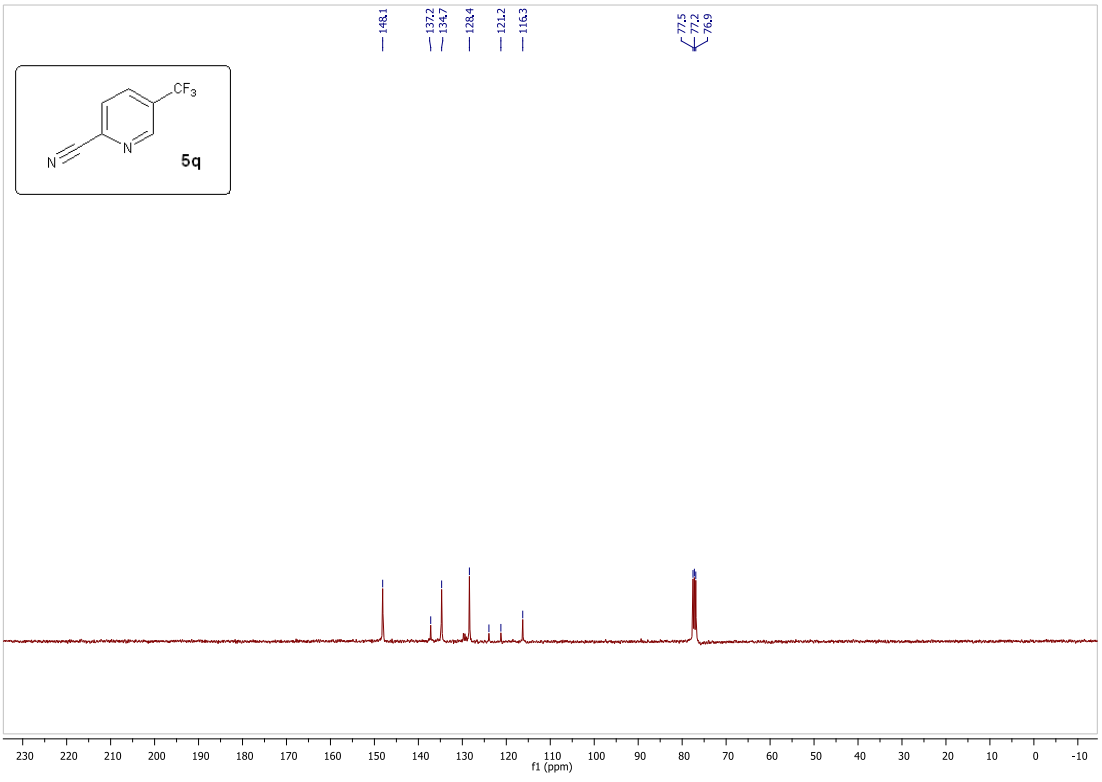

7.22
7.22
7.20
7.20
7.04
7.03
6.87
6.85
6.07
N
O
O
5p
1.08
0.82
0.89
2.00
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)


151.4
148.0
128.2
118.8
111.3
109.1
104.9
102.1
77.3
76.9
76.6
N
O
O
5p
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

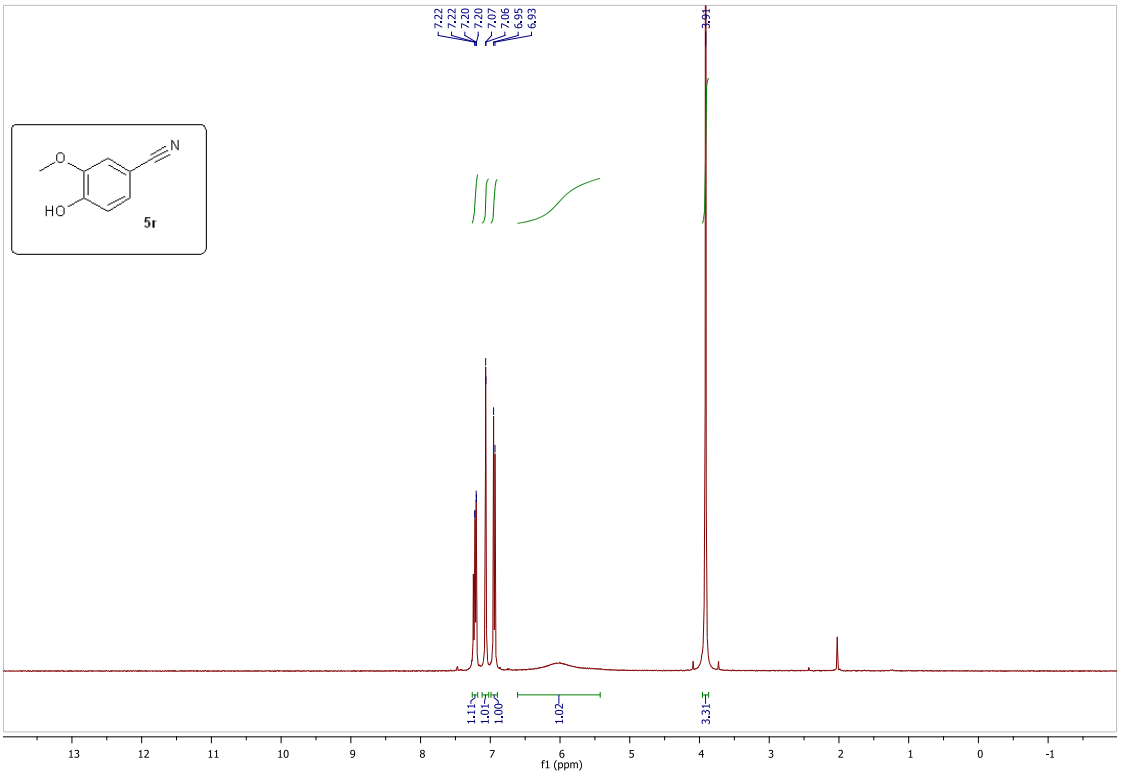
5q

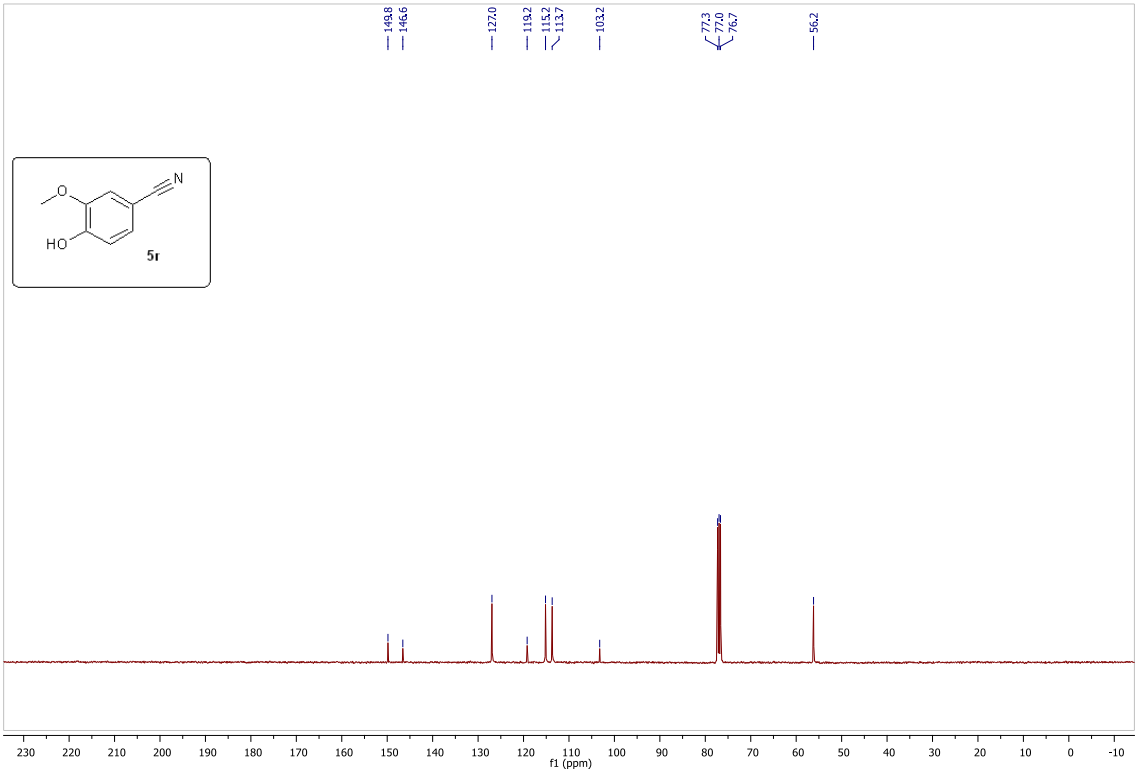

9.0
8.1
8.1
7.9
7.9
CF3
NC
N
5q
1.00
1.13
1.10
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)


63.2
CF3
NC
N
5q
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

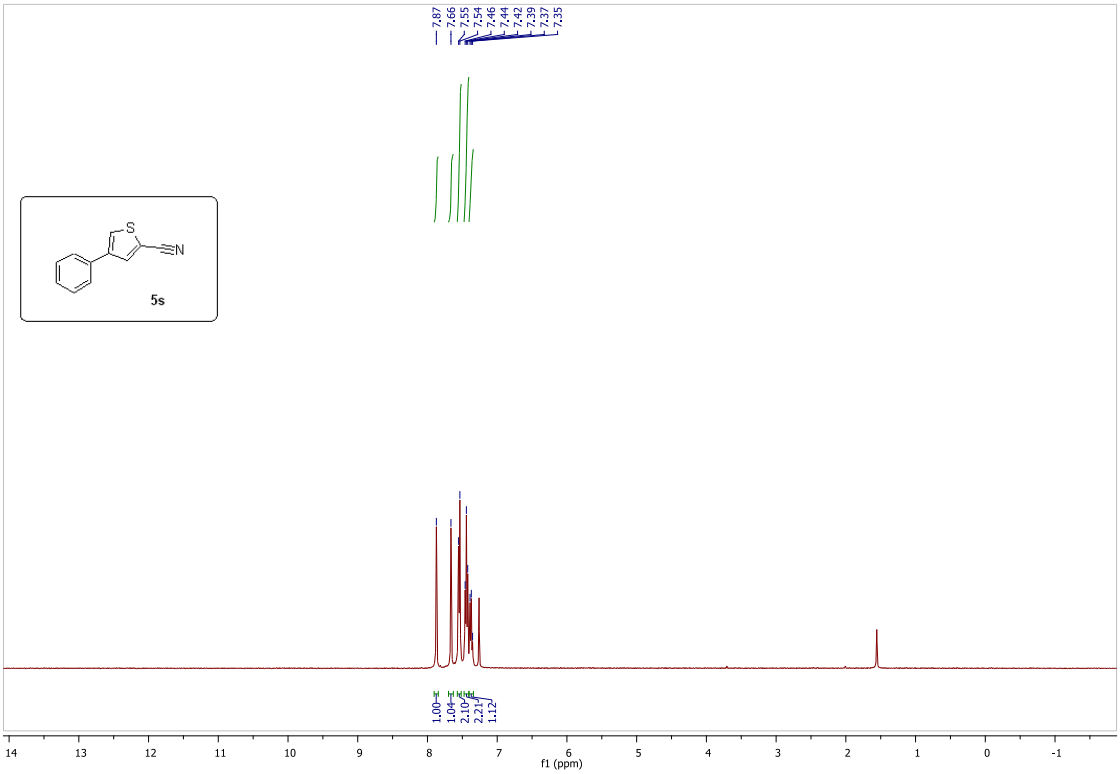

148.1
137.2
134.7
128.4
121.2
116.3
77.5
77.2
76.9
CF3
N
N
5q
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

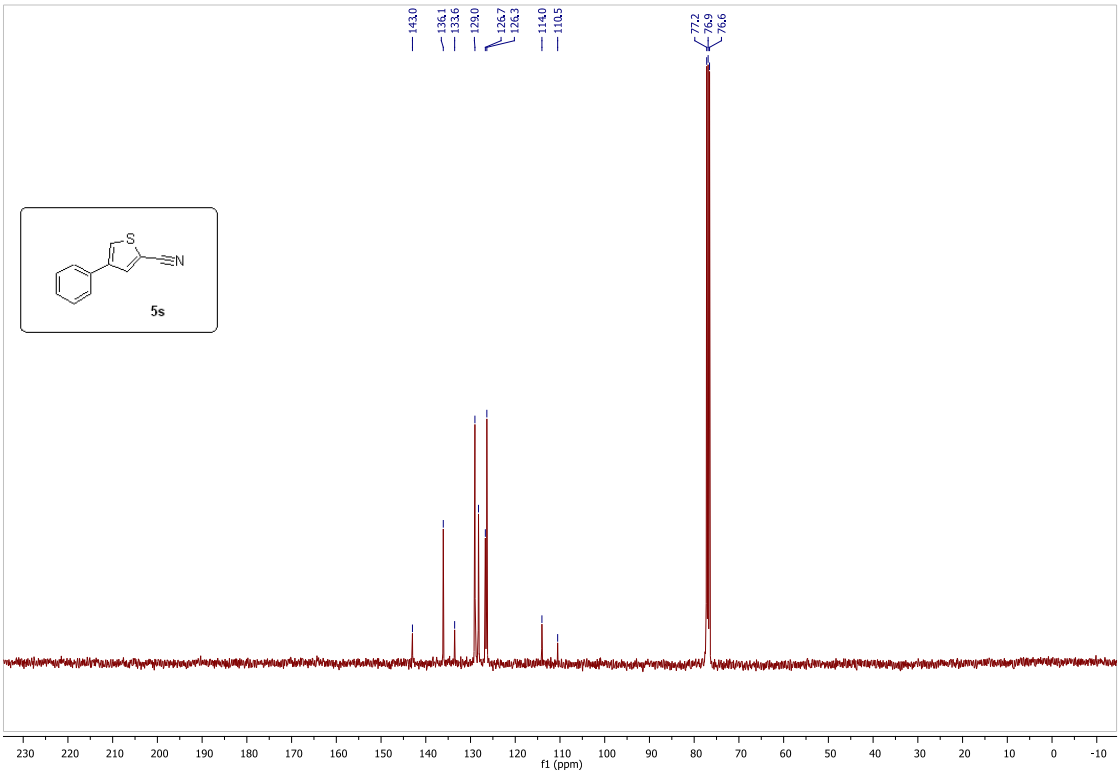
5r


7.22
7.22
7.20
7.20
7.07
7.06
6.95
6.93
3.91
HO
5r
1.11
1.01
1.00
1.02
3.31
f1 (ppm)

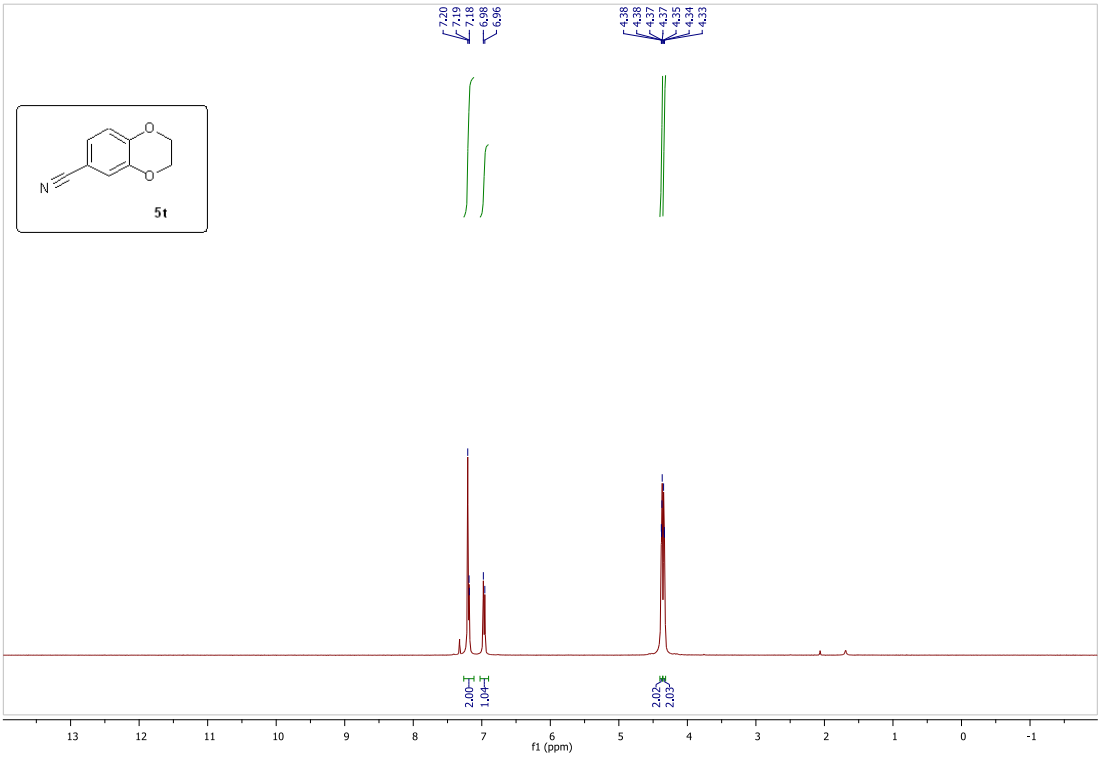

149.8
146.6
127.0
119.2
115.2
113.7
103.2
77.3
77.0
76.7
56.2
HO
5r
f1 (ppm)

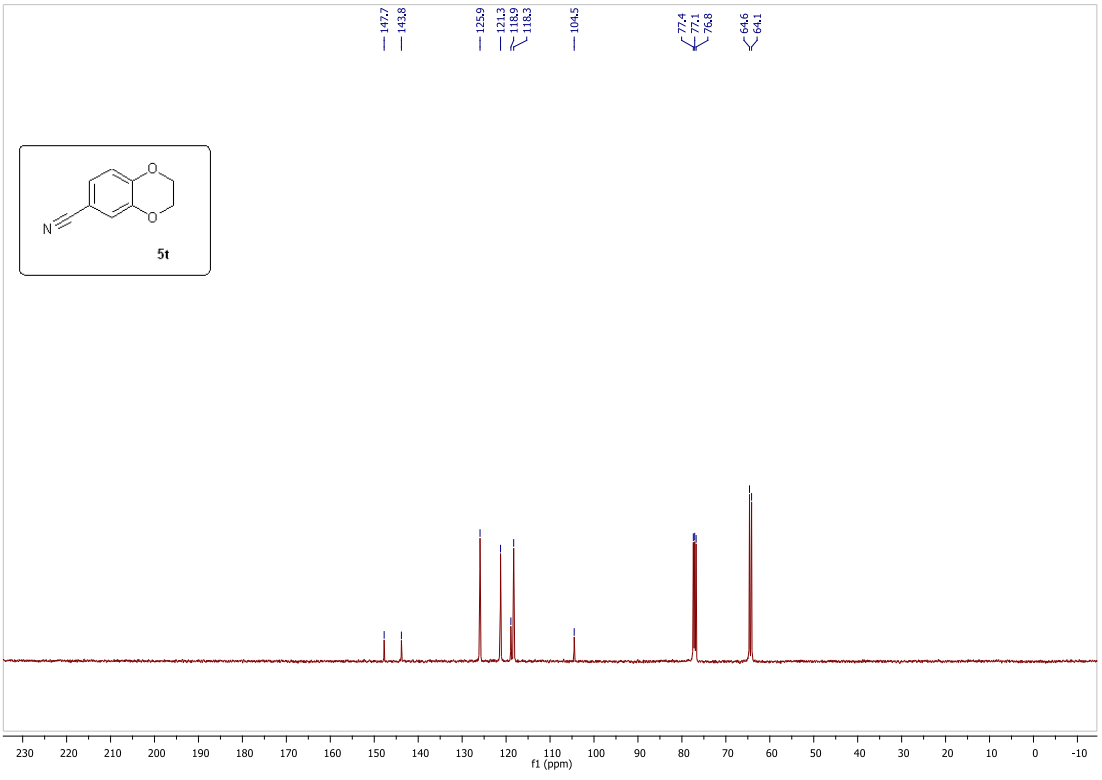
5s


7.87
7.66
7.55
7.54
7.46
7.44
7.42
7.39
7.37
7.35
S
N
5s
1.00
1.04
2.10
2.21
1.12
f1 (ppm)

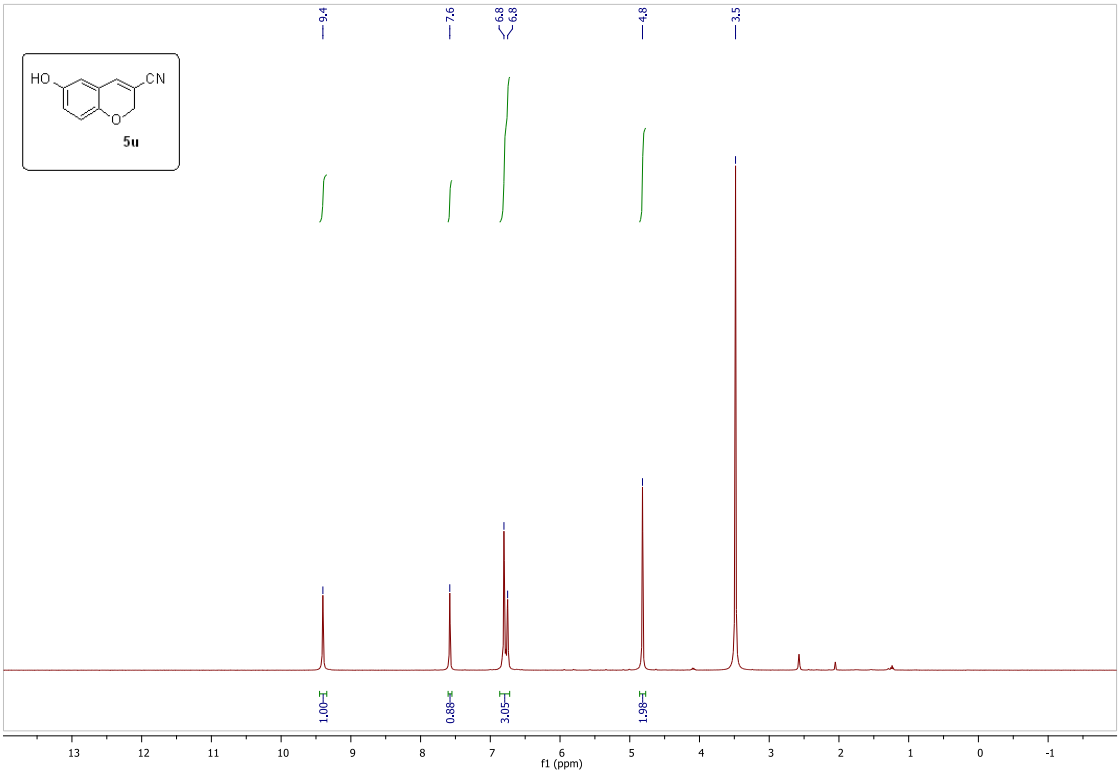

143.0
136.1
133.6
129.0
126.7
126.3
114.0
110.5
77.2
76.9
76.6
S
N
5s
f1 (ppm)

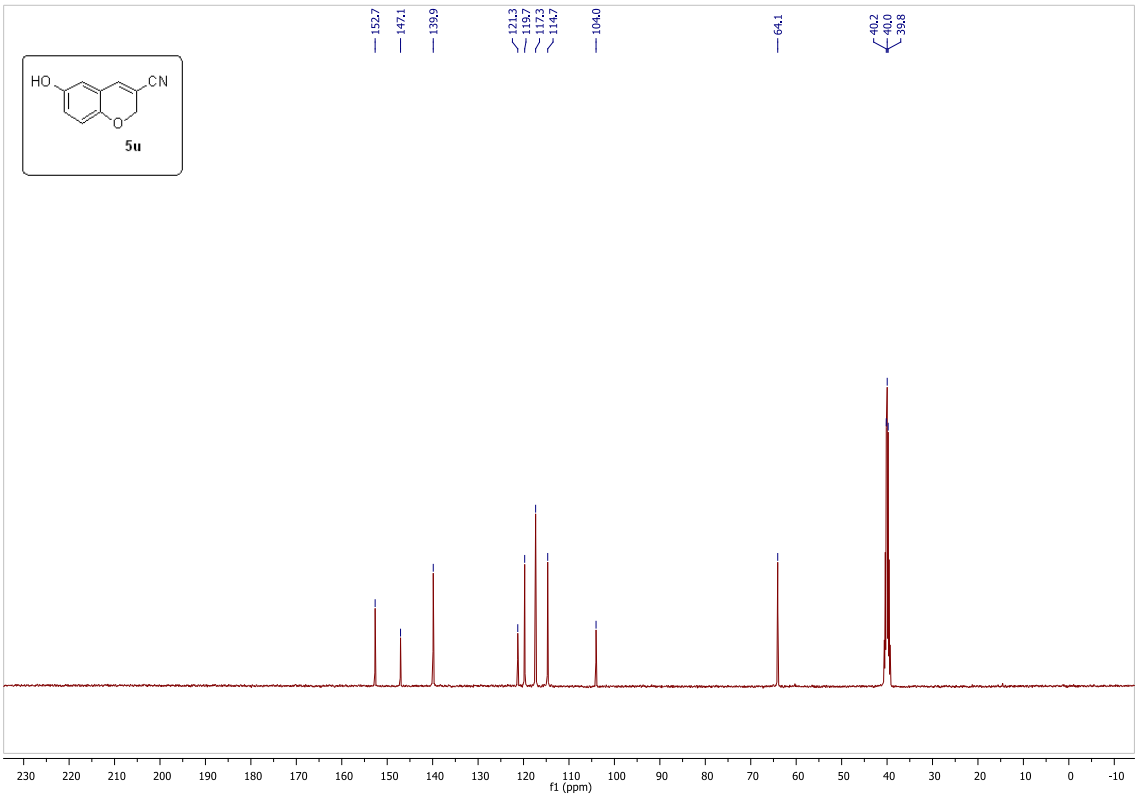
5t


7.20
7.19
7.18
6.98
6.96
4.38
4.38
4.37
4.37
4.35
4.34
4.33
5t
2.00
1.04
2.02
2.03
f1 (ppm)

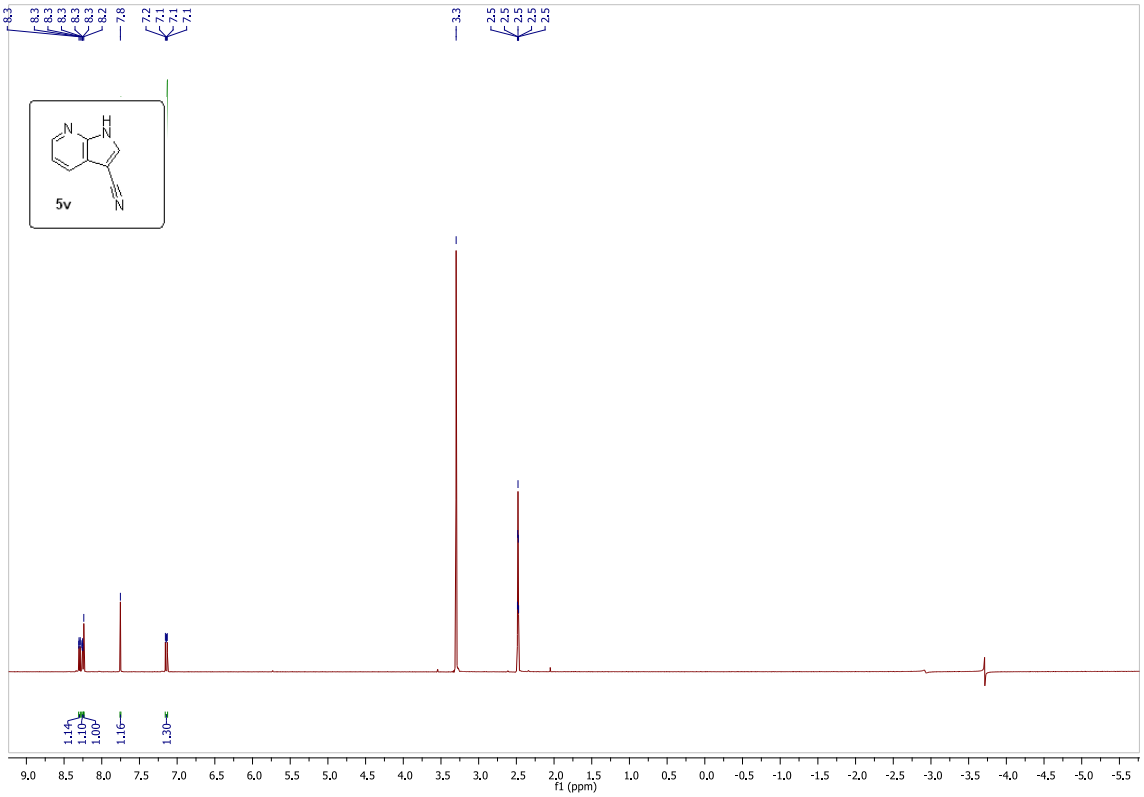

147.7
143.8
125.9
121.3
118.9
118.3
104.5
77.4
77.1
76.8
64.6
64.1
5t
f1 (ppm)

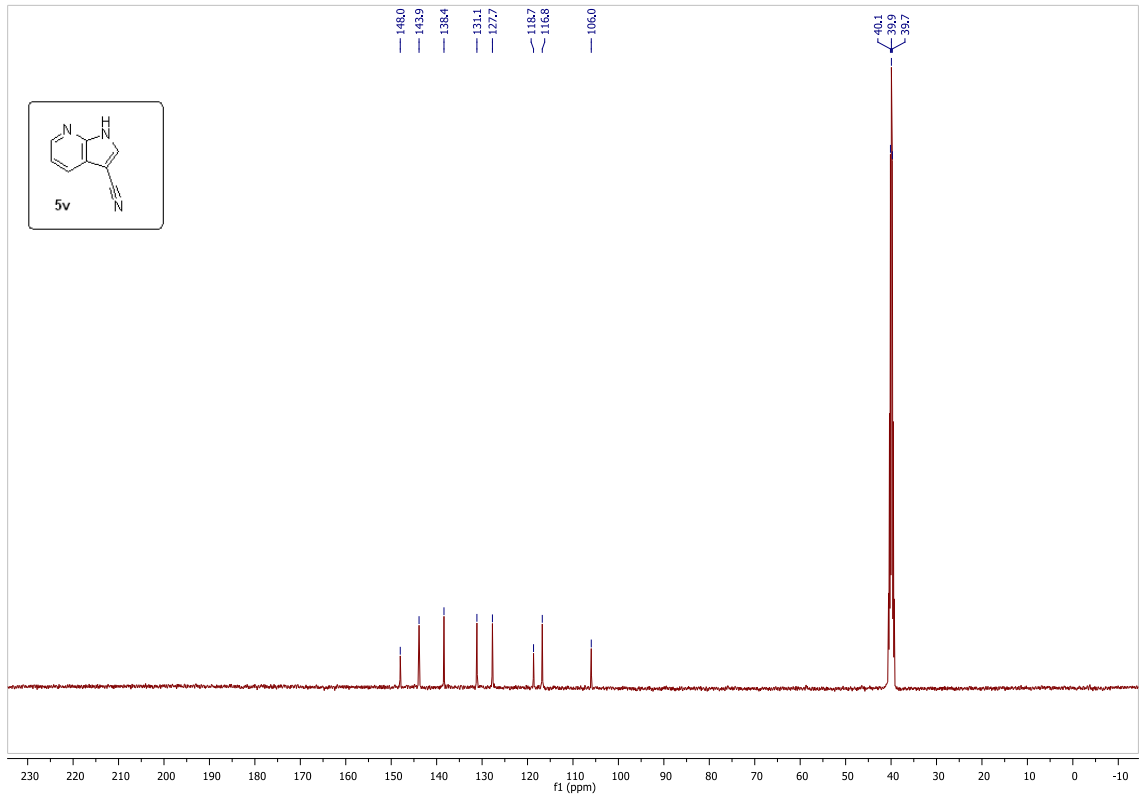
5u


9.4
7.6
6.8
6.8
4.8
3.5
HO
CN
O
5u
1.00
0.88
3.05
1.98
f1 (ppm)

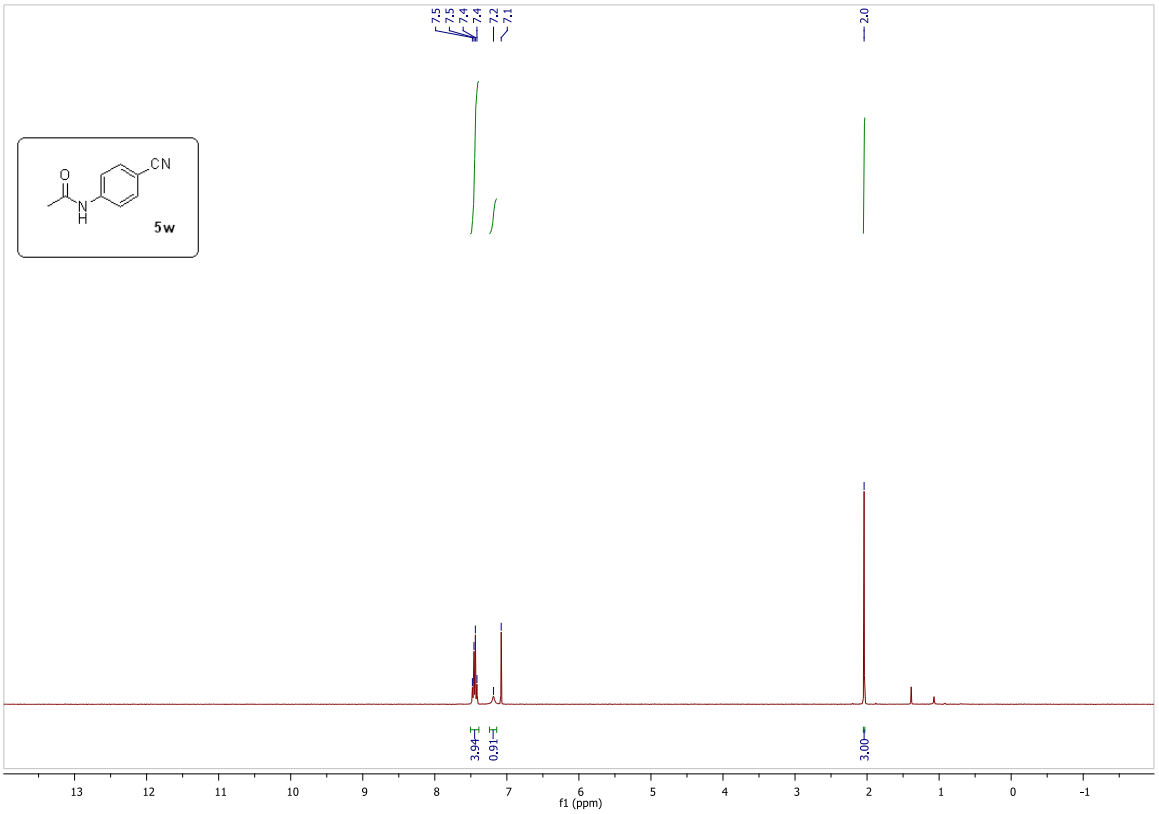

152.7
147.1
139.9
121.3
119.7
117.3
114.7
104.0
64.1
40.2
40.0
39.8
HO
CN
O
5u
f1 (ppm)

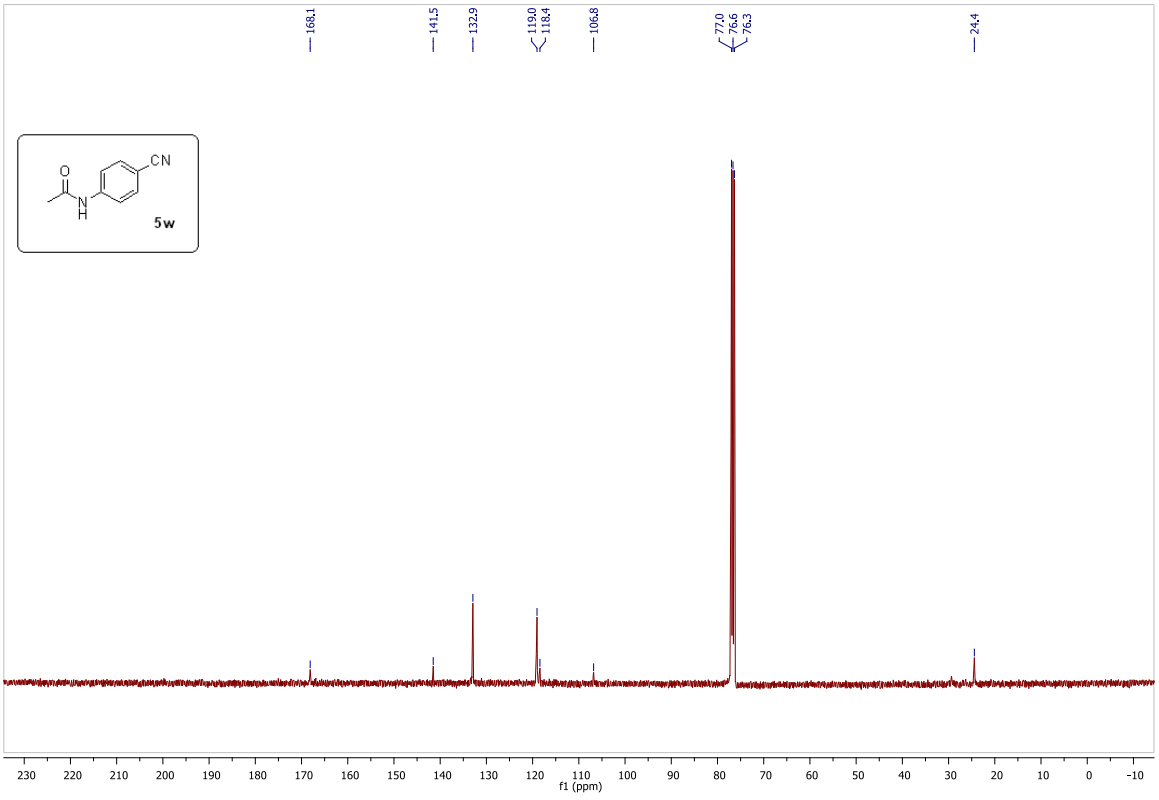
5v


8.3
8.3
8.3
8.3
8.3
8.2
7.8
7.2
7.1
7.1
7.1
3.3
2.5
2.5
2.5
2.5
2.5
5v
1.14
1.10
1.00
1.16
1.30
f1 (ppm)

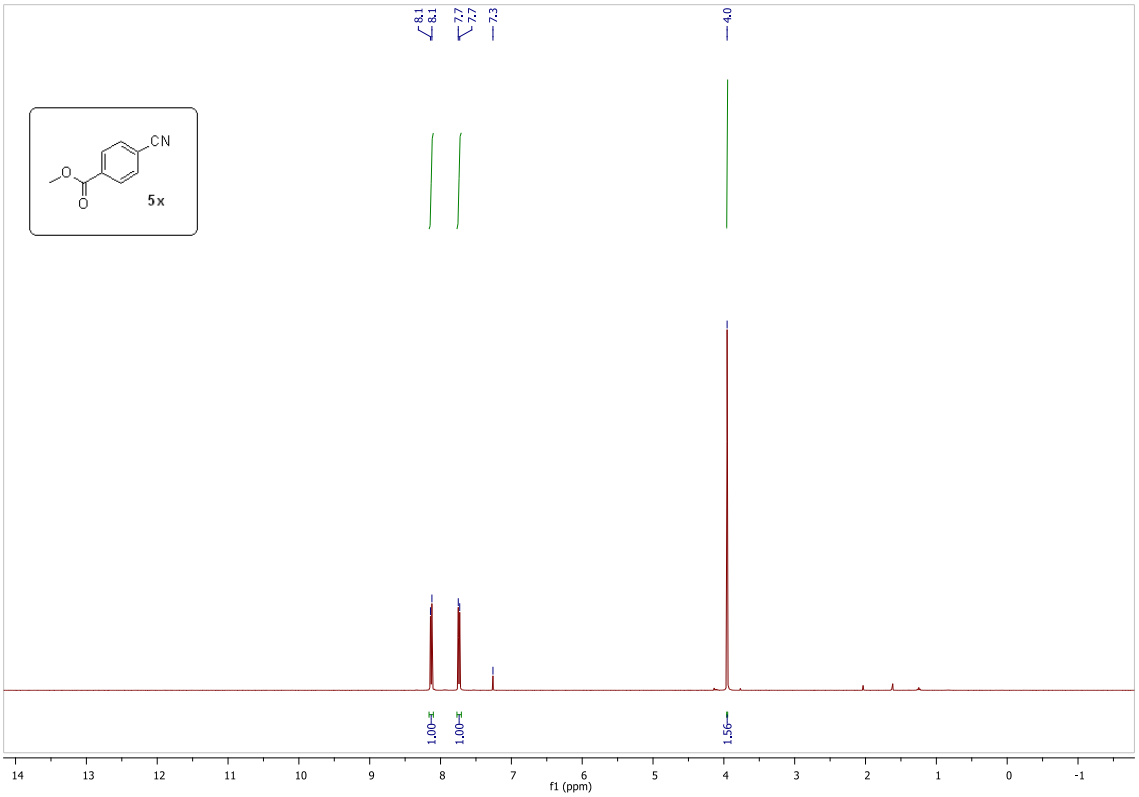

148.0
143.9
138.4
131.1
127.7
118.7
116.8
106.0
40.1
39.9
39.7
5v
f1 (ppm)

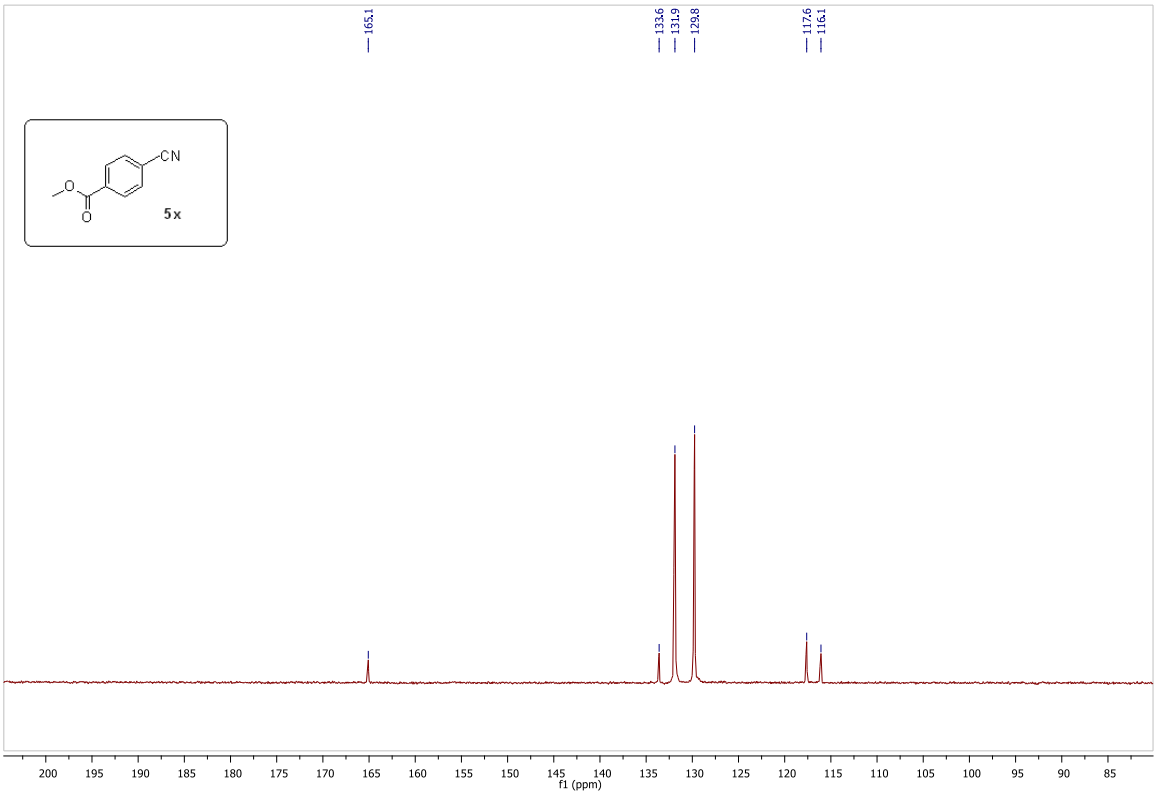
5w


7.5
7.5
7.4
7.4
7.2
7.1
2.0
CN
O
N
H
5w
3.94
0.91
3.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


168.1
141.5
132.9
119.0
118.4
106.8
77.0
76.6
76.3
24.4
CN
O
N
H
5w
230
220
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)

5x

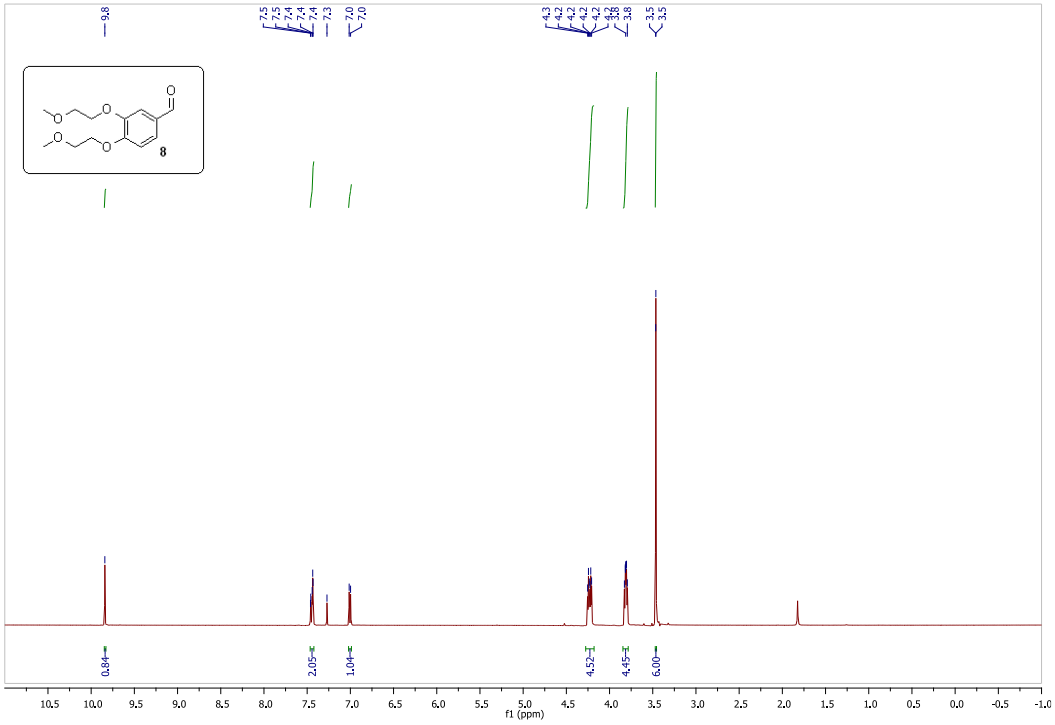

8.1
8.1
7.7
7.7
7.3
4.0
CN
O
O
5x
1.00
1.00
1.56
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)

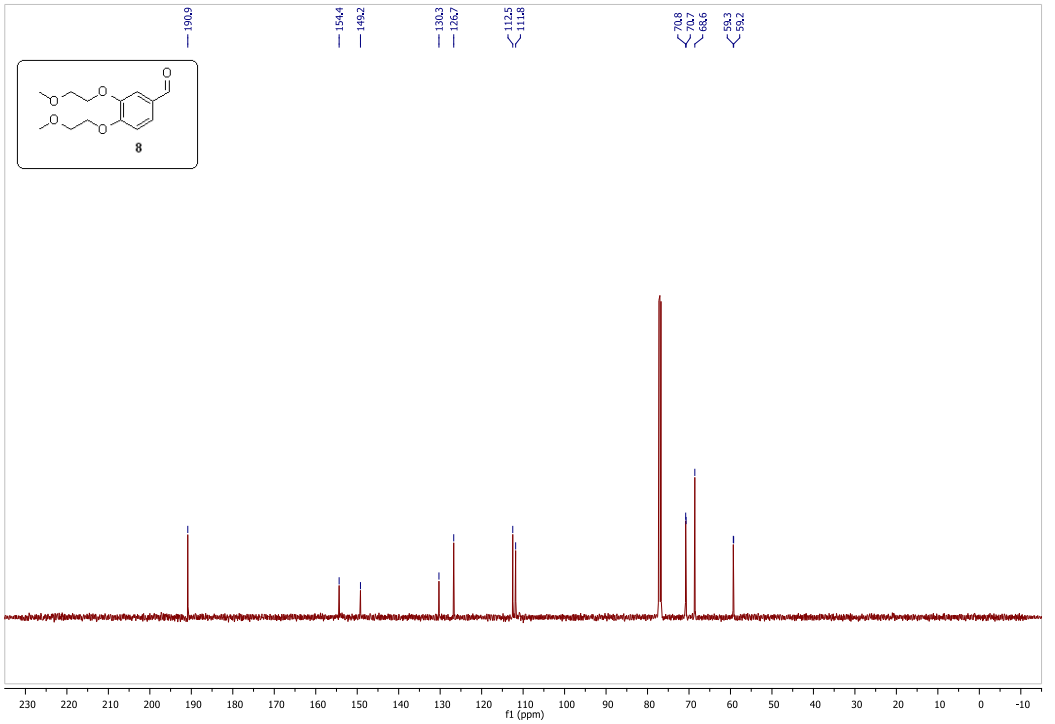

165.1
133.6
131.9
129.8
117.6
116.1
CN
O
O
5x
200 195 190 185 180 175 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85
f1 (ppm)

^{1}H NMR AND ^{13}C NMR SPECTRA OF COMPOUNDS

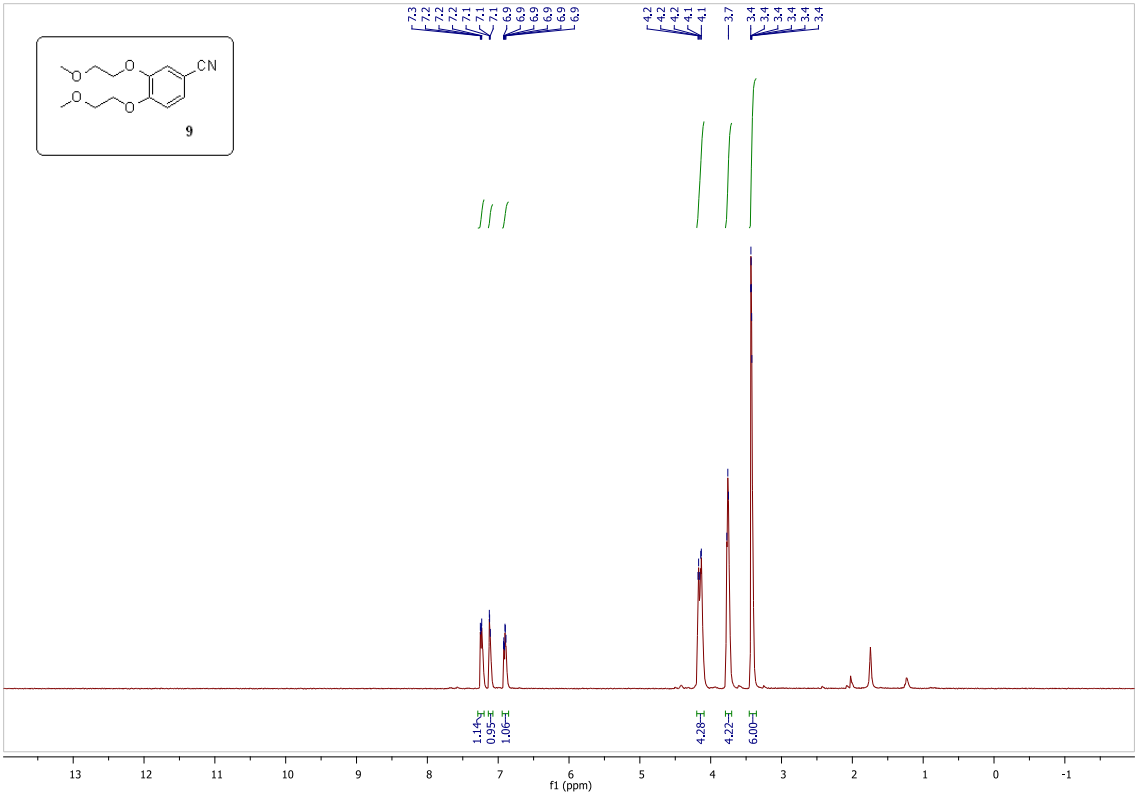
NMR spectral data for 8, 9, 12, 15, 16, 19

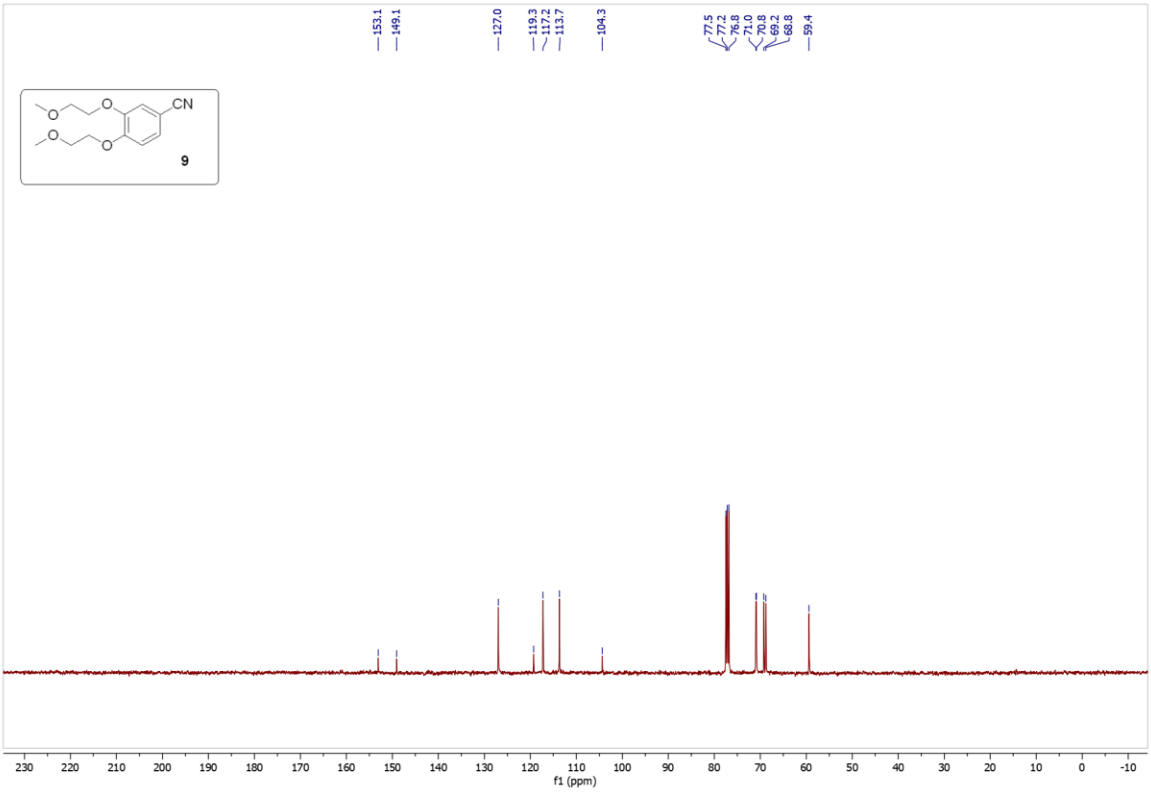
8



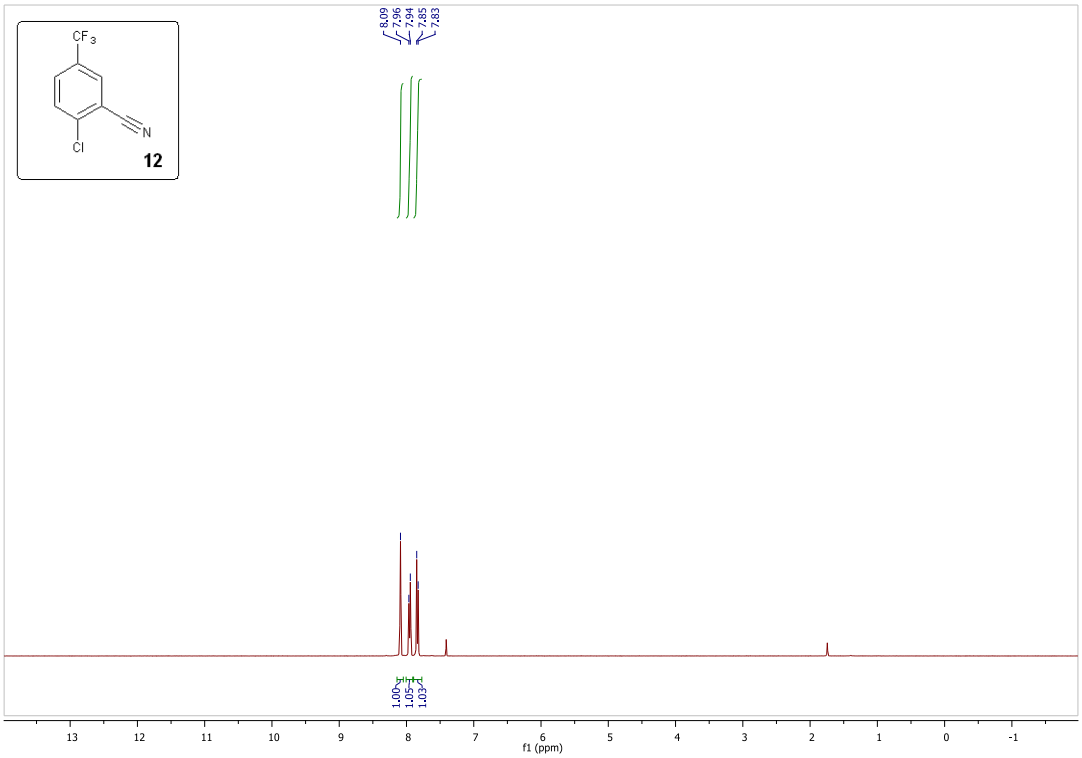


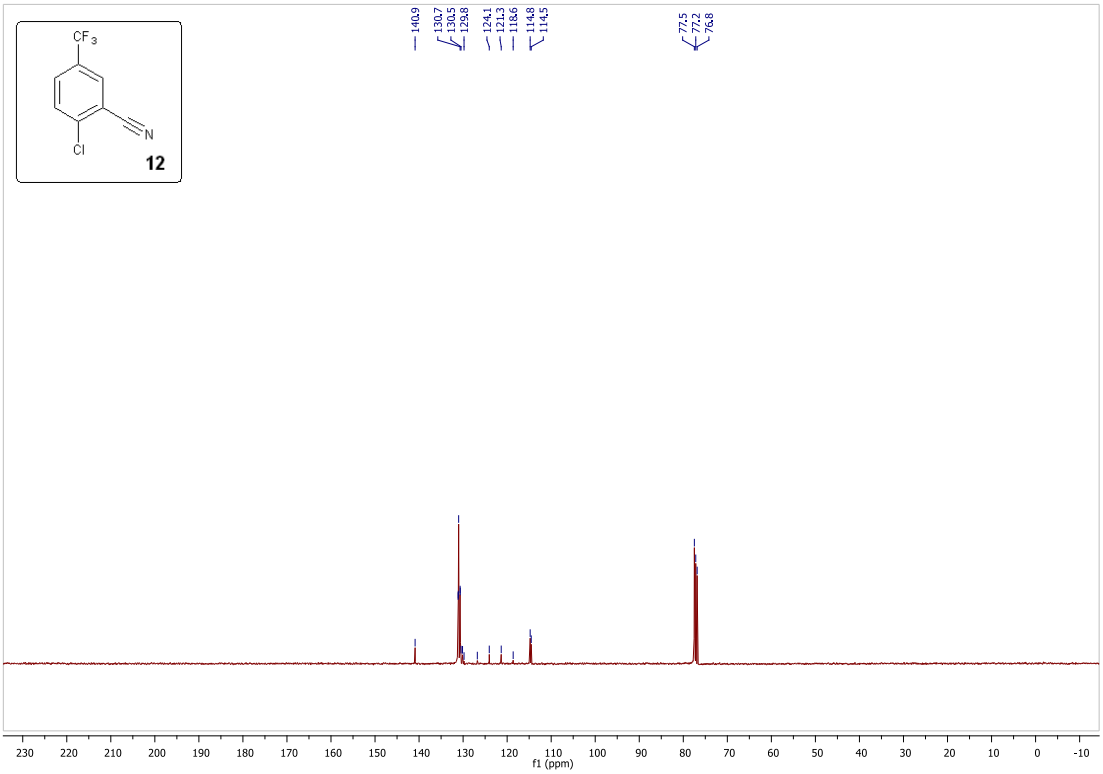
9

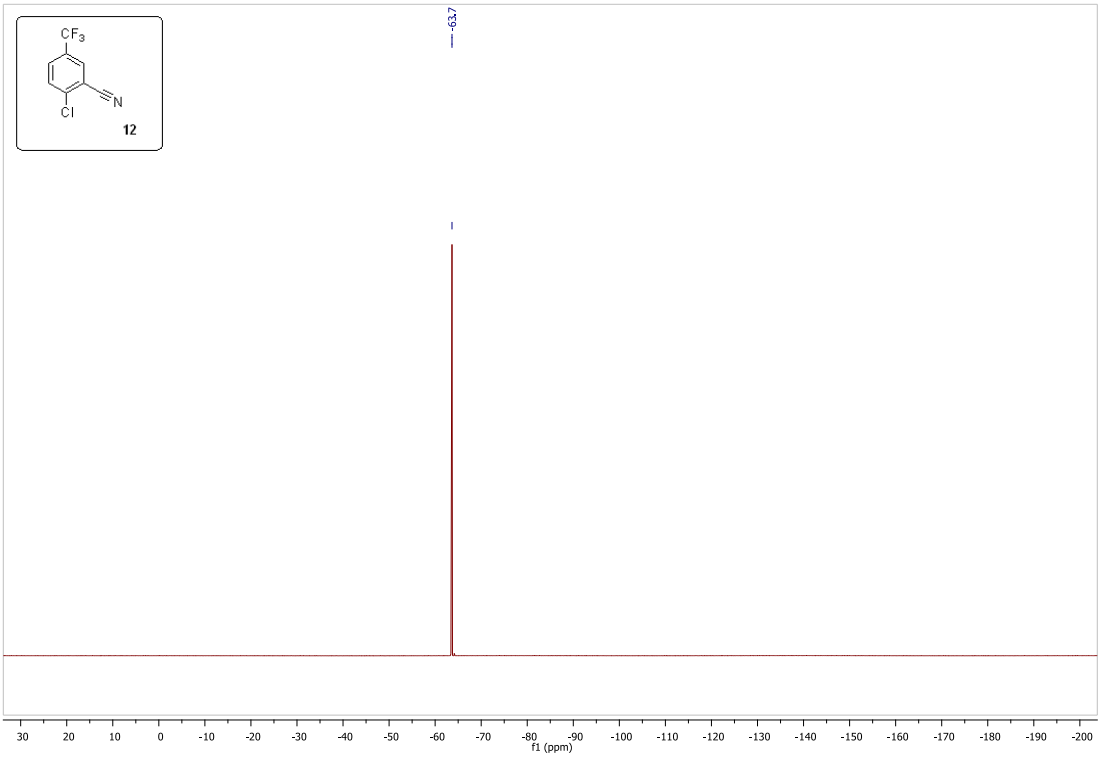

CN
9
7.3
7.2
7.2
7.2
7.1
7.1
7.1
6.9
6.9
6.9
6.9
6.9
4.2
4.2
4.2
4.1
4.1
3.7
3.4
3.4
3.4
3.4
3.4
3.4
1.14
0.95
1.06
4.28
4.22
6.00
f1 (ppm)


CN
9
153.1
149.1
127.0
119.3
117.2
113.7
104.3
77.5
77.2
76.8
71.0
70.8
69.2
68.8
59.4
f1 (ppm)

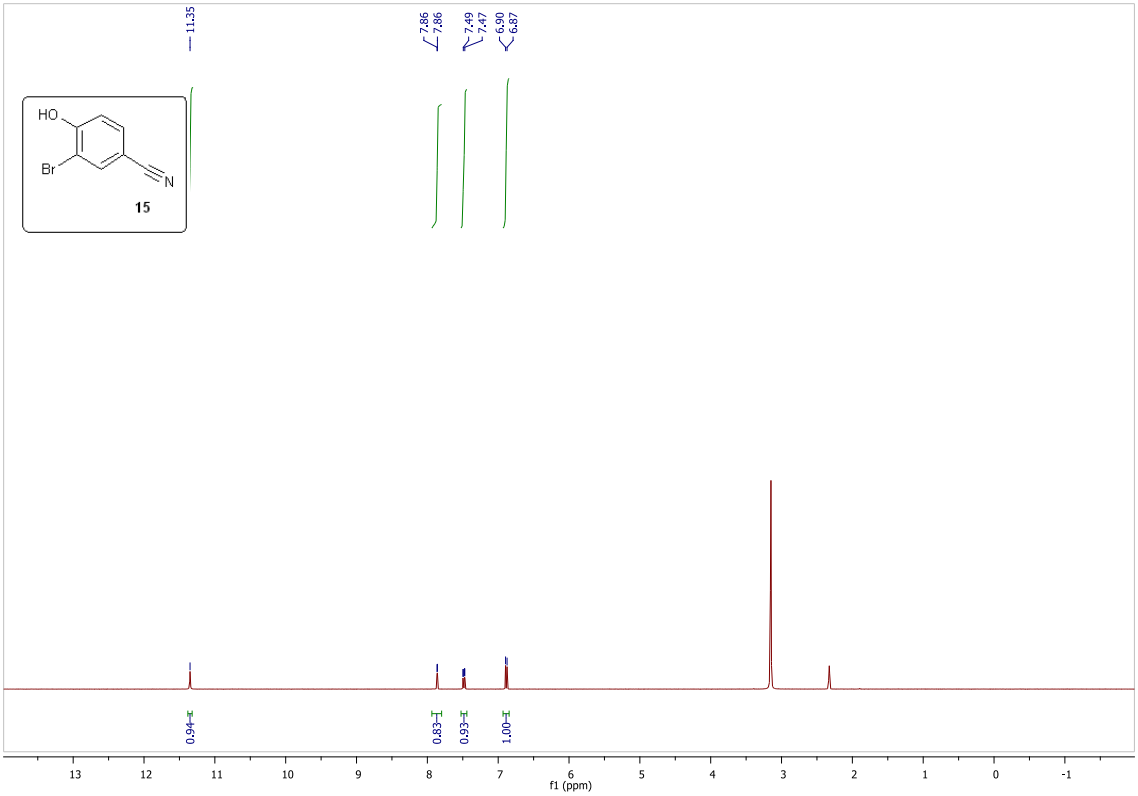
12

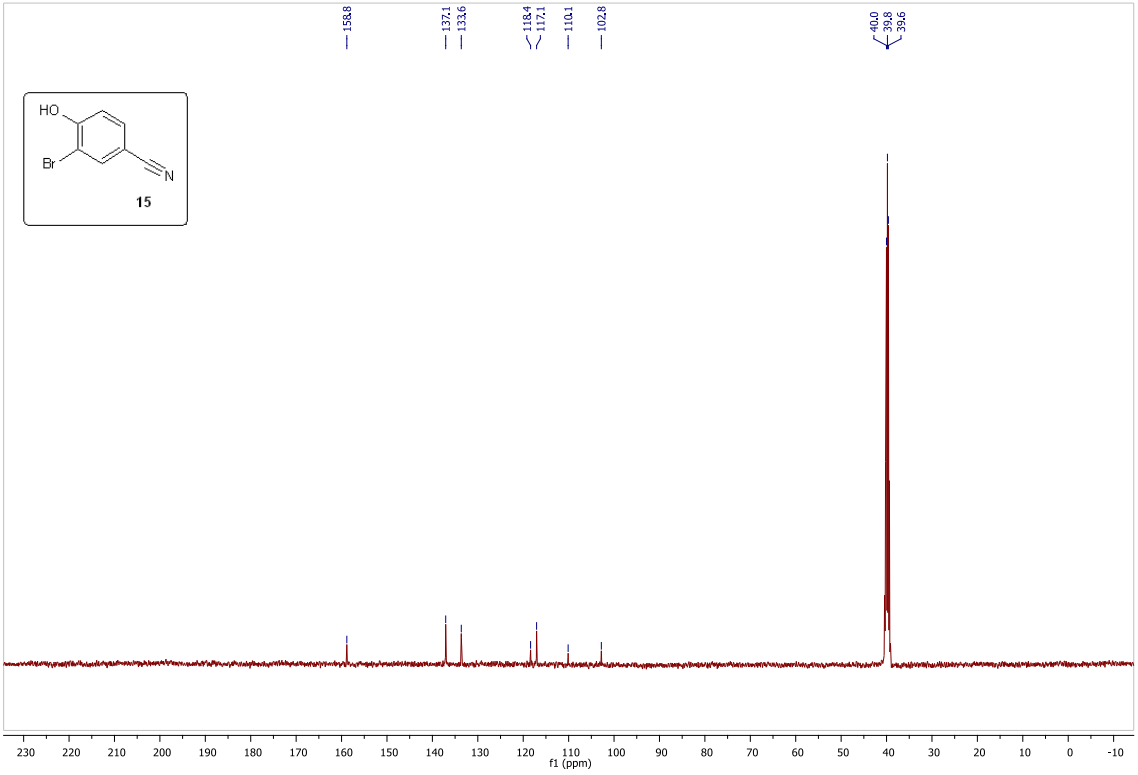

CF3
Cl
N
12
8.09
7.96
7.94
7.85
7.83
1.00
1.05
1.03
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


CF3
Cl
N
12
140.9
130.7
130.5
129.8
124.1
121.3
118.6
114.8
114.5
77.5
77.2
76.8
f1 (ppm)

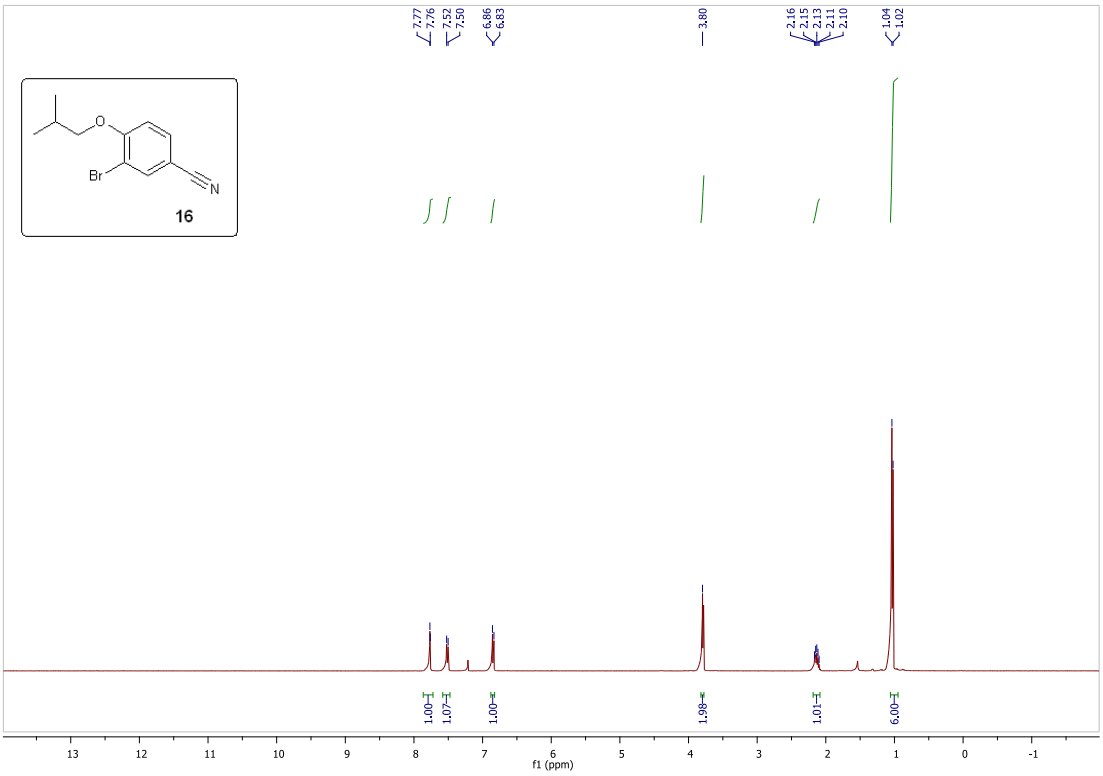

CF3
Cl
N
12
-63.7
f1 (ppm)

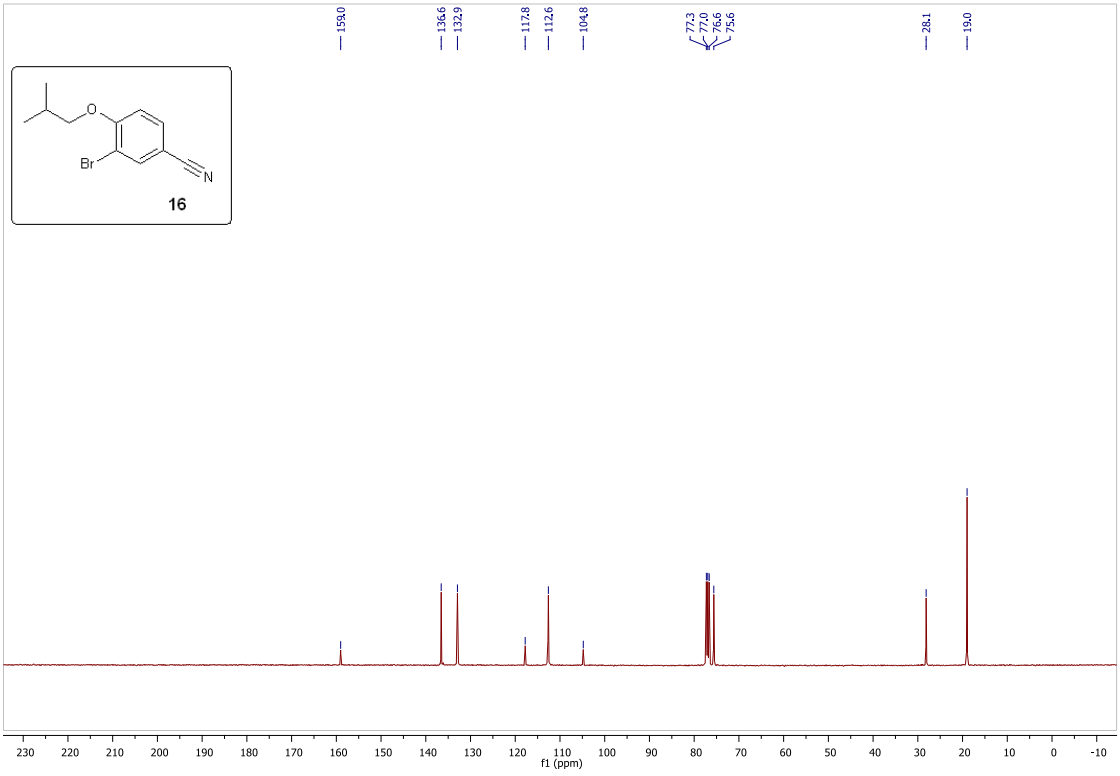
15


11.35
7.86
7.86
7.49
7.47
6.90
6.87
HO
Br
N
15
0.94
0.83
0.93
1.00
f1 (ppm)

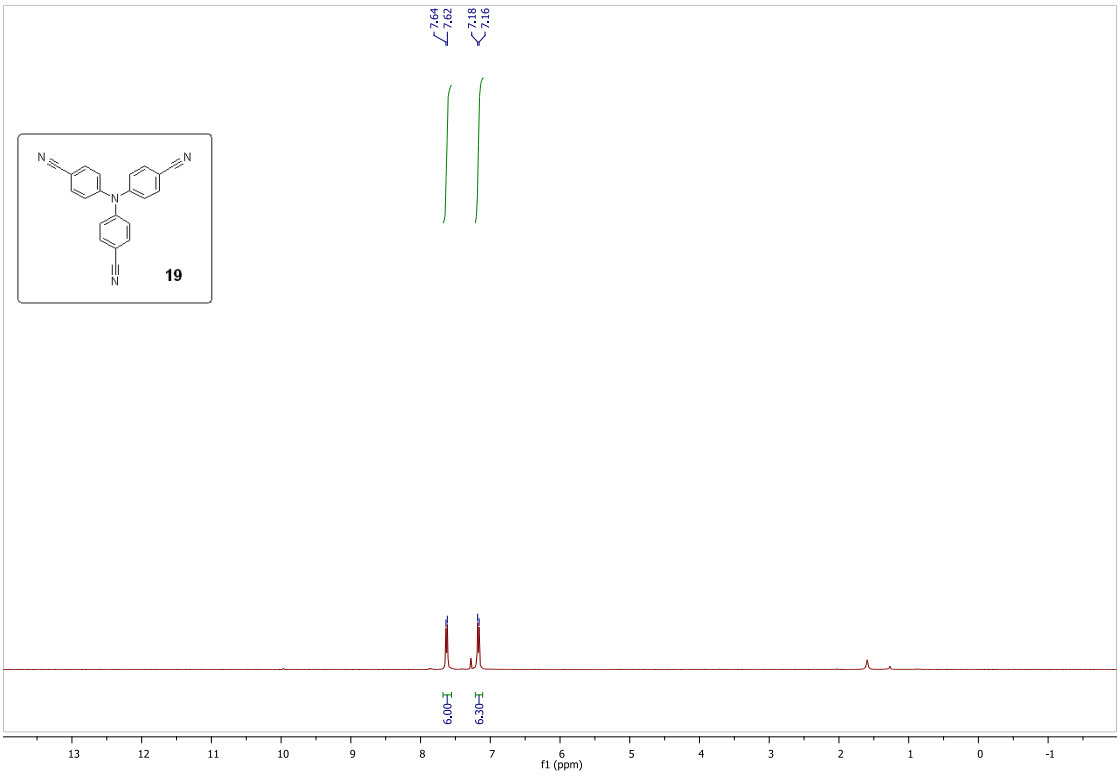

158.8
137.1
133.6
118.4
117.1
110.1
102.8
40.0
39.8
39.6
HO
Br
N
15
f1 (ppm)

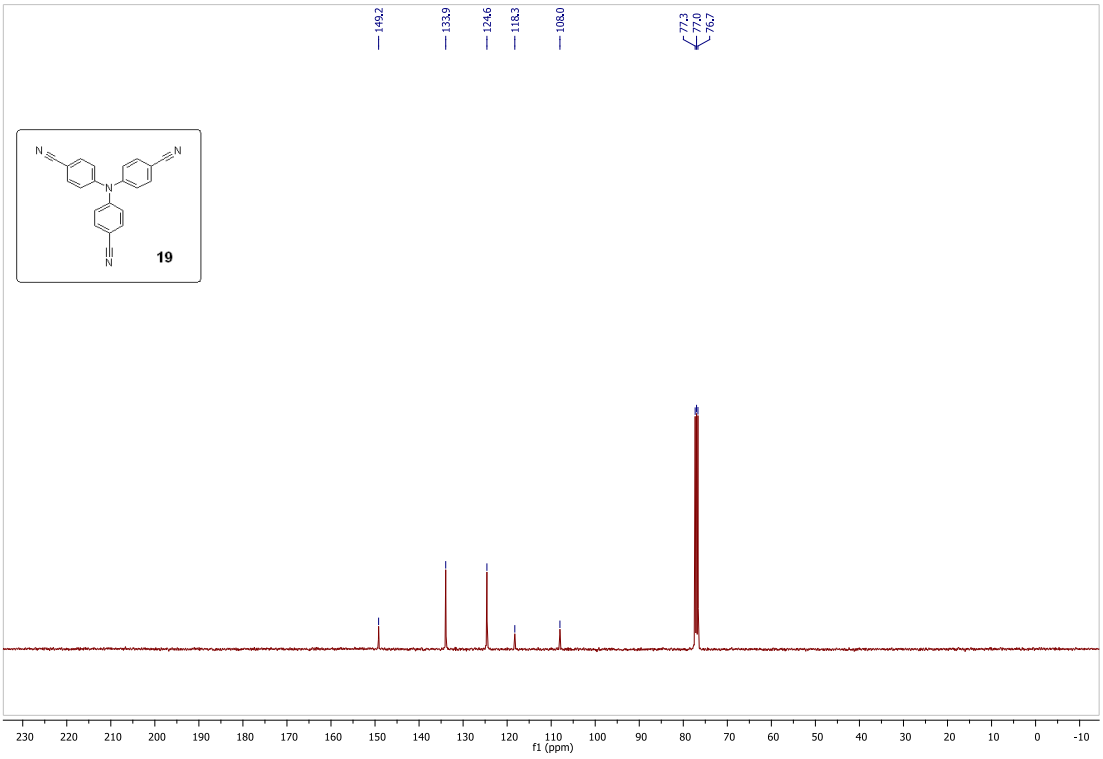
16


7.77
7.76
7.52
7.50
6.86
6.83
3.80
2.16
2.15
2.13
2.11
2.10
1.04
1.02
Br
O
N
16
1.00
1.07
1.00
1.98
1.01
6.00
f1 (ppm)


159.0
136.6
132.9
117.8
112.6
104.8
77.3
77.0
76.6
75.6
28.1
19.0
Br
O
N
16
f1 (ppm)

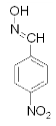
19


7.64
7.62
7.18
7.16
19
6.00
6.30
f1 (ppm)

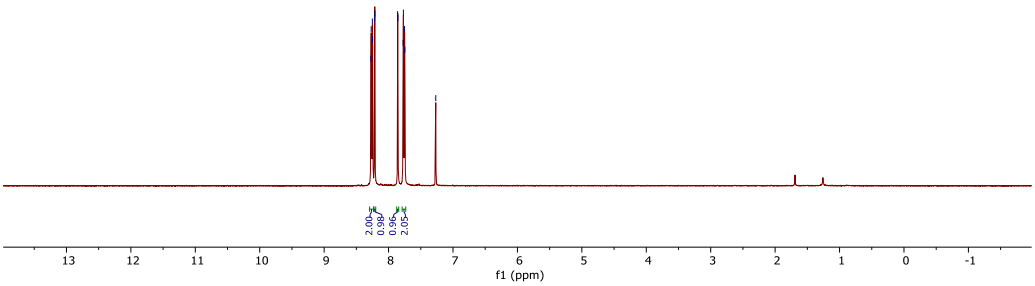

149.2
133.9
124.6
118.3
108.0
77.3
77.0
76.7
19
f1 (ppm)

NMR spectral data for (20)

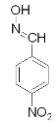
C:/Users/78662/Desktop/CHINMAY/11.fid/fid



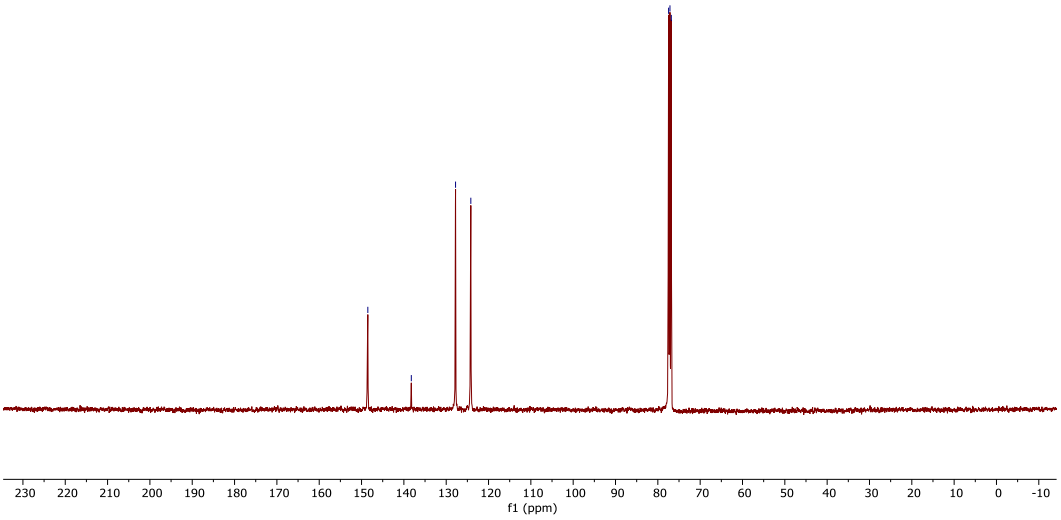
20



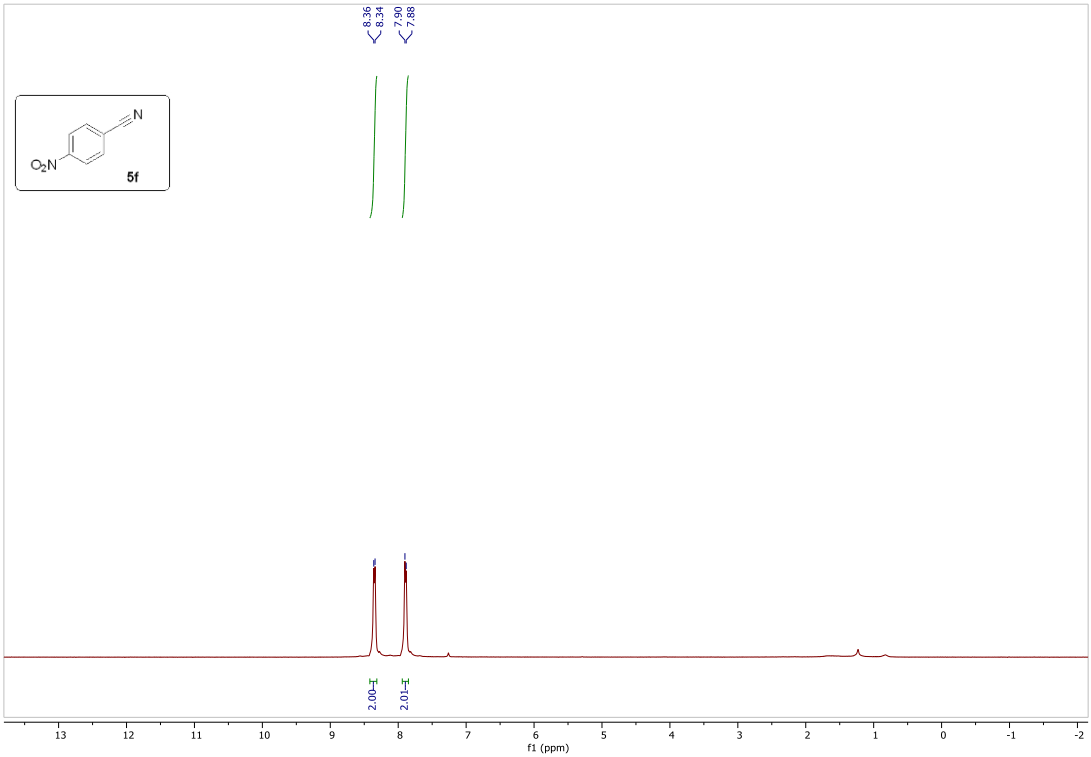
C:/Users/78662/Desktop/CHINMAY/CARBON_0111.fid%20/fid

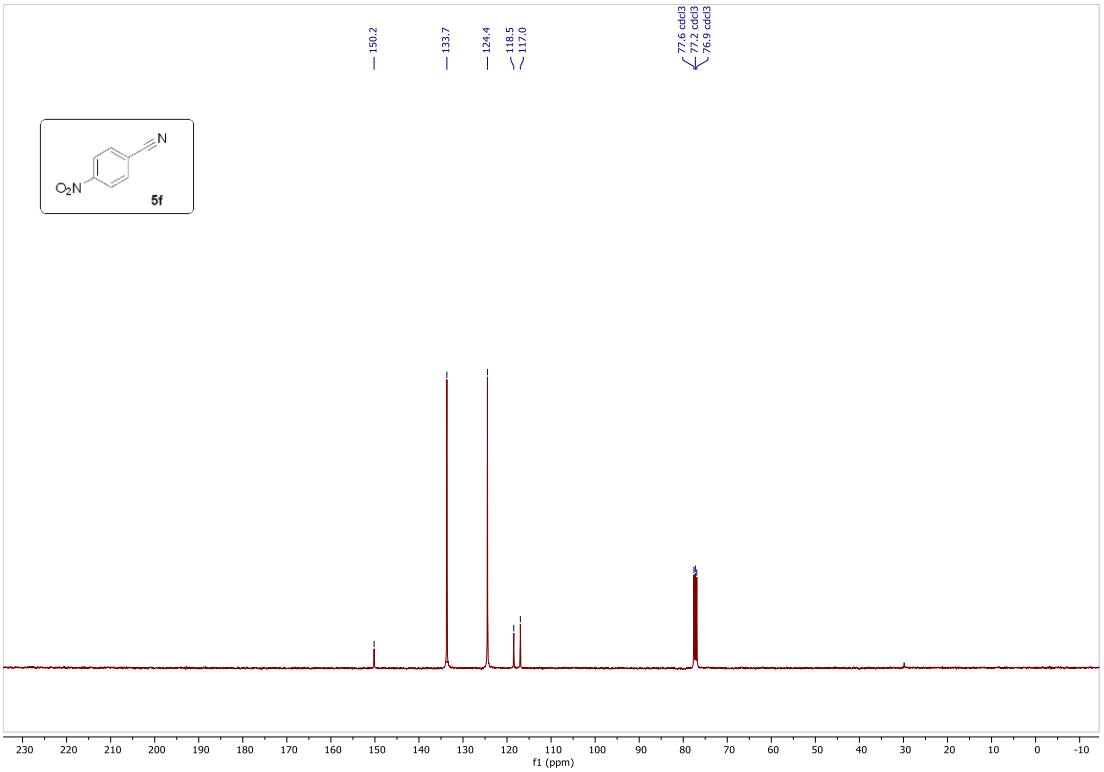


20



NMR spectral data for (5f)





References

1. S. Liang, R. Ebule, G. B. Hammond and B. Xu, *Org. Lett.*, 2017, **19**, 4524-4527.

2. R. Ebule, S. Liang, G. B. Hammond and B. Xu, *ACS Catal.*, 2017, **7**, 6798-6801.
3. K. Hyodo, K. Togashi, N. Oishi, G. Hasegawa and K. Uchida, *Org. Lett.*, 2017, **19**, 3005-3008.
4. Viana, H. *Chemistryselect* 2018**, *3*** (40), 11333.
5. G. Zhang, X. Wen, Y. Wang, X. Han, Y. Luan, L. Zheng, C. Ding and X. Cao, *RSC Advances*, 2013, **3**, 22918-22921.
6. V. N. Telvekar, K. N. Patel, H. S. Kundaikar and H. K. Chaudhari, *Tetrahedron Lett.*, 2008, **49**, 2213-2215.
7. K. Hyodo, K. Togashi, N. Oishi, G. Hasegawa and K. Uchida, *Org.Lett.*, 2017, **19**, 3005-3008.
8. R. Shang, D.-S. Ji, L. Chu, Y. Fu and L. Liu, *Angew. Chem. Int. Ed.*, 2011, **50**, 4470-4474.
9. C. O. Kangani, B. W. Day and D. E. Kelley, *Tetrahedron Lett.*, 2008, **49**, 914-918.
10. X. Li, S. M. Singh and F. Labrie, *Synth. Commun.*, 1994, **24**, 733-743.
11. N. Hisano, Y. Kamei, Y. Kansaku, M. Yamanaka and K. Mori, *Org. Lett.*, 2018, **20**, 4223-4226.
12. L. Claes, R. Matthessen, I. Rombouts, I. Stassen, T. De Baerdemaeker, D. Depla, J. A. Delcour, B. Lagrain and D. E. De Vos, *ChemSusChem*, 2015, **8**, 345-352.
13. S. Laulhé, S. S. Gori and M. H. Nantz, *J. Org. Chem.*, 2012, **77**, 9334-9337.
14. J.-S. Zhang, T. Chen, Y. Zhou, S.-F. Yin and L.-B. Han, *Org. Lett.*, 2018, **20**, 6746-6749.
15. K. Murugesan, T. Senthamarai, M. Sohail, M. Sharif, N. V. Kalevaru and R. V. Jagadeesh, *Green. Chem.*, 2018, **20**, 266-273.
16. B. Gaspar and E. M. Carreira, *Angew. Chem. Int. Ed.*, 2007, **46**, 4519-4522.
17. K. Kiyokawa, T. Nagata, J. Hayakawa and S. Minakata, *Chem. Eur. J*, 2015, **21**, 1280-1285.
18. V. Ajdačić, A. Nikolić, S. Simić, D. Manojlović, Z. Stojanović, J. Nikodinovic-Runic and I. M. Opsenica, *Synthesis*, 2018, **50**, 119-126.
19. R. V. Jagadeesh, H. Junge and M. Beller, *ChemSusChem*, 2015, **8**, 92-96.
20. Y. Zhao, G. Mei, H. Wang, G. Zhang and C. Ding, *Synlett*, 2019, **30**, 1484-1488.
21. P. Zhang, R. Zhuang, Z. Guo, X. Su, X. Chen and X. Zhang, *Chem. Eur. J.*, 2016, **22**, 16783-16786.
22. F. Verma, P. Shukla, S. R. Bhardiya, M. Singh, A. Rai and V. K. Rai, *Catal. Commun.*, 2019, **119**, 76-81.
23. H. Chen, S. Sun, H. Xi, K. Hu, N. Zhang, J. Qu and Y. Zhou, *Tetrahedron Lett.*, 2019, **60**, 1434-1436.
24. W.-Y. Fang and H.-L. Qin, *J.Org. Chem.*, 2019, **84**, 5803-5812.
25. J. Zheng, J.-H. Lin, X.-Y. Deng and J.-C. Xiao, *Org. Lett.*, 2015, **17**, 532-535.
26. S. D. Schimler, S. J. Ryan, D. C. Bland, J. E. Anderson and M. S. Sanford, *J. Org. Chem.*, 2015, **80**, 12137-12145.
27. Z. Shu, Y. Ye, Y. Deng, Y. Zhang and J. Wang, *Angew. Chem. Int. Ed.*, 2013, **52**, 10573-10576.
28. U. Dutta, S. Maiti, S. Pimparkar, S. Maiti, L. R. Gahan, E. H. Krenske, D. W. Lupton and D. Maiti, *Chem. Sci.*, 2019, **10**, 7426-7432.
29. G. Zhang, G. Zhang, J. Lei, S. Li, S. Xu, C. Ding and S. Shan, *Chemical Research in Chinese Universities*, 2016, **32**, 586-593.
30. W. Kemnitzer, J. Kuemmerle, H.-Z. Zhang, S. Kasibhatla, B. Tseng, J. Drewe and S. X. Cai, *Bioorg. Med. Chem. Lett.*, 2009, **19**, 4410-4415.
31. P. Ghosh, G. C. Pariyar, B. Saha and R. Subba, *Synth. Commun.*, 2016, **46**, 685-691.
32. T. Dohi, K. Morimoto, N. Takenaga, A. Maruyama and Y. Kita, *Chem. Pharm. Bull.*, 2006, **54**, 1608-1610.
33. M. Allegretti, R. Anacardio, M. C. Cesta, R. Curti, M. Mantovanini, G. Nano, A. Topai and G. Zampella, *Organic Process Research & Development*, 2003, **7**, 209-213.
34. J. Gurjar, J. Bater and V. V. Fokin, *Chem. Eur. J.*, 2019, **25**, 1906-1909.
35. K. Natte, R. V. Jagadeesh, M. Sharif, H. Neumann and M. Beller, *Org. Biomol. Chem.*, 2016, **14**, 3356-3359.
36. J. K. Augustine, A. Bombrun and R. N. Atta, *Synlett*, 2011, **2011**, 2223-2227.

37. A. Patra, S. P. Anthony and T. P. Radhakrishnan, *Adv. Funct. Mater.*, 2007, **17**, 2077-2084.