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A Practical Cobalt-Catalyzed Cross-Coupling of Benzylic Zinc Reagents with Aryl and Heteroaryl Bromides or Chlorides

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General Considerations: All reactions were carried out under an argon atmosphere in flame-dried glassware. Syringes which were used to transfer anhydrous solvents or reagents were purged with argon prior to use. THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen. Methyl *tert*-butyl ether (MTBE) was freshly distilled from sodium benzophenone ketyl under nitrogen. Yields refer to isolated yields of compounds estimated to be >95 % pure as determined by ^{1}H-NMR (25 °C) and GC-analysis. Chemical shifts are reported as δ-values in ppm relative to the solvent peak. NMR spectra were recorded on solutions in $CDCl_3$ (residual chloroform: δ = 7.25 ppm for ^{1}H-NMR and δ = 77.0 ppm for ^{13}C-NMR). For the characterization of the observed signal multiplicities the following abbreviations were used: s (singulet), d (doublet), t (triplet), dd (doublet of doublet), ddd (doublet of doublet of doublet), dt (doublet of triplet), dq (doublet of quartet), q (quartet), qn (quintet), m (multiplet) as well as br (broad). All reagents obtained from commercial sources were used without any further purification unless otherwise stated.

Typical Procedure for the Preparation of Benzylzinc(II) Chlorides (1a-i) (TP 1)

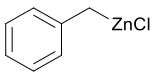
A dry and argon-flushed *Schlenk*-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with LiCl (0.53 g, 12.5 mmol, 1.25 equiv) and heated up to 450 °C for 5 min under high vacuum. After cooling to room temperature under vigorous stirring, $ZnCl_2$ (1.51 g, 11.0 mmol, 1.10 equiv) was added under argon, the *Schlenk*-tube was heated to 320 °C for 5 min, cooled to room temperature and charged with magnesium turnings (0.58 g, 24.0 mmol, 2.40 equiv). Freshly distilled THF (10-15 mL) was added and the reaction mixture was stirred at room temperature for a given time until full conversion of the starting material was observed. The completion of the metalation was monitored by GC-analysis of hydrolysed and iodolysed aliquots. When the oxidative insertion was complete, the solution of the corresponding benzylzinc(II) chloride was separated from the resulting salts via a syringe equipped with a filter and transferred to another pre-dried and argon-flushed *Schlenk*-tube, before being titrated against iodine.

Typical Procedure for the Cobalt-Catalyzed Cross-Coupling of Benzylzinc((II) Chlorides (1a-i) with Electrophiles (TP 2)

A dry and argon-flushed Schlenk-flask, equipped with a magnetic stirring bar and a rubber septum, was charged with $CoCl_2$ (5 mol%, ≥ 97% pure) and heated up to 450 °C for 5 min under high vacuum. After cooling to room temperature, the corresponding electrophile (1.0 equiv), freshly distilled MTBE (methyl *tert*-butyl ether) and isoquinoline (10 mol%) were added. Thereupon, the benzylzinc(II) chloride solution (1.30-1.50 equiv) was dropwise added at room temperature and the reaction mixture was stirred for a given time at 50 °C. The reaction mixture was monitored by GC-analysis of quenched aliquots. A saturated aqueous solution of NH_4Cl was added and the aqueous layer was extracted three times with EtOAc (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduce pressure. Purification of the crude products by flash column chromatography afforded the desired products.

Preparation of the Benzylzinc(II) chlorides (1a-i)

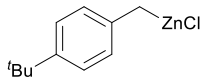
Preparation of benzylzinc(II) chloride (1a)



According to **TP1**, LiCl (0.53 g, 12.5 mmol, 1.25 equiv), $ZnCl_2$ (1.51 g, 11.0 mmol, 1.10 equiv), Mg turnings (0.58 g, 24.0 mmol, 2.40 equiv) and freshly distilled THF (15 mL) were used. The

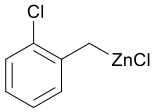
benzyl chloride (**2a**, 1.27 g, 1.16 mL, 10.0 mmol, 1.00 equiv) was dropwise added and the reaction mixture was stirred for 2 h at room temperature. The concentration of benzylzinc(II) chloride (**1a**) was determined by titration with iodine in THF (0.43 M, 69%).

Preparation of 4-*tert*-butylbenzylzinc(II) chloride (1b)



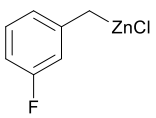
According to **TP1**, LiCl (0.53 g, 12.5 mmol, 1.25 equiv), $ZnCl_2$ (1.51 g, 11.0 mmol, 1.10 equiv), Mg turnings (0.58 g, 24.0 mmol, 2.40 equiv) and freshly distilled THF (15 mL) were used. The 4-*tert*-butylbenzyl chloride (**2b**, 1.83 g, 1.94 mL, 10.0 mmol, 1.00 equiv) was dropwise added and the reaction mixture was stirred for 5 h at room temperature. The concentration of 4-(*tert*-butyl)benzylzinc(II) chloride (**1b**) was determined by titration with iodine in THF (0.44 M, 70%).

Preparation of 2-chlorobenzylzinc(II) chloride (1c)



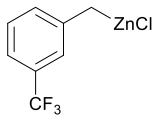
According to **TP1**, LiCl (0.53 g, 12.5 mmol, 1.25 equiv), $ZnCl_2$ (1.51 g, 11.0 mmol, 1.10 equiv), Mg turnings (0.58 g, 24.0 mmol, 2.40 equiv) and freshly distilled THF (15 mL) were used. The 2-chlorobenzyl chloride (**2c**, 1.61 g, 1.26 mL, 10.0 mmol, 1.00 equiv) was dropwise added and the reaction mixture was stirred for 1 h at room temperature. The concentration of 2-chlorobenzylzinc(II) chloride (**1c**) was determined by titration with iodine in THF (0.54 M, 81%).

Preparation of 3-fluorobenzylzinc(II) chloride (1d)



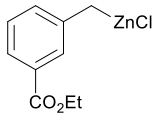
According to **TP1**, LiCl (0.53 g, 12.5 mmol, 1.25 equiv), $ZnCl_2$ (1.51 g, 11.0 mmol, 1.10 equiv), Mg turnings (0.58 g, 24.0 mmol, 2.40 equiv) and freshly distilled THF (10 mL) were used. The 3-fluorobenzyl chloride (**2d**, 1.45 g, 1.21 mL, 10.0 mmol, 1.00 equiv) was dropwise added and the reaction mixture was stirred for 2 h at room temperature. The concentration of 3-fluorobenzylzinc(II) chloride (**1d**) was determined by titration with iodine in THF (0.66 M, 66%).

Preparation of 3-(trifluoromethyl)benzylzinc(II) chloride (1e)



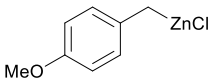
According to **TP1**, LiCl (0.53 g, 12.5 mmol, 1.25 equiv), $ZnCl_2$ (1.51 g, 11.0 mmol, 1.10 equiv), Mg turnings (0.58 g, 24.0 mmol, 2.40 equiv) and freshly distilled THF (10 mL) were used. The 3-(trifluoromethyl)benzyl chloride (**2e**, 1.95 g, 1.56 mL, 10.0 mmol, 1.00 equiv) was dropwise added and the reaction mixture was stirred for 1.5 h at room temperature. The concentration of 3-(trifluoromethyl)benzylzinc(II) chloride (**1e**) was determined by titration with iodine in THF (0.72 M, 72%).

Preparation of 3-(ethoxycarbonyl)benzylzinc(II) chloride (1f)



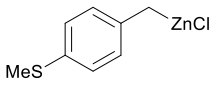
According to **TP1**, LiCl (0.53 g, 12.5 mmol, 1.25 equiv), $ZnCl_2$ (1.51 g, 11.0 mmol, 1.10 equiv), Mg turnings (0.58 g, 24.0 mmol, 2.40 equiv) and freshly distilled THF (15 mL) were used. The ethyl 3-(chloromethyl)benzoate (**2f**, 1.99 g, 1.70 mL, 10.0 mmol, 1.00 equiv) was dropwise added and the reaction mixture was stirred for 1.5 h at room temperature. The concentration of 3-(ethoxycarbonyl)benzylzinc(II) chloride (**1f**) was determined by titration with iodine in THF (0.38 M, 61%).

Preparation of 4-methoxybenzylzinc(II) chloride (1g)



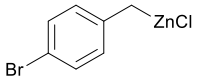
According to **TP1**, LiCl (0.53 g, 12.5 mmol, 1.25 equiv), $ZnCl_2$ (1.51 g, 11.0 mmol, 1.10 equiv), Mg turnings (0.58 g, 24.0 mmol, 2.40 equiv) and freshly distilled THF (10 mL) were used. The 4-methoxybenzyl chloride (**2g**, 1.57 g, 1.36 mL, 10.0 mmol, 1.00 equiv) was dropwise added and the reaction mixture was stirred for 1 h at room temperature. The concentration of 4-methoxy-benzylzinc(II) chloride (**1g**) was determined by titration with iodine in THF (0.56 M, 56%).

Preparation of 4-(methylthio)benzylzinc(II) chloride (1h)



According to **TP1**, LiCl (0.53 g, 12.5 mmol, 1.25 equiv), $ZnCl_2$ (1.51 g, 11.0 mmol, 1.10 equiv), Mg turnings (0.58 g, 24.0 mmol, 2.40 equiv) and freshly distilled THF (15 mL) were used. The 4-(methylthio)benzyl chloride (**2h**, 1.73 g, 1.48 mL, 10.0 mmol, 1.00 equiv) was dropwise added and the reaction mixture was stirred for 1 h at room temperature. The concentration of 4-(methylthio)benzylzinc(II) chloride (**1h**) was determined by titration with iodine in THF (0.35 M, 53%).

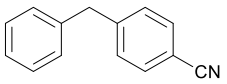
Preparation of 4-bromobenzylzinc(II) chloride (1i)



A dry and argon-flushed Schlenk-tube, equipped with a magnetic stirring bar and a rubber septum, was charged with LiCl (0.636 g, 15.0 mmol, 1.50 equiv) and heated up to 450 °C for 5 min under high vacuum. After cooling to room temperature under vigorous stirring, zinc dust (1.96 g, 30.0 mmol, 3.00 equiv) was added under argon, the *Schlenk*-tube was heated to 450 °C for 5 min, cooled to room temperature and charged with freshly distilled THF (15 mL). Then, trimethylsilyl chloride (0.05 g, 0.06 mL, 0.45 mmol) and 1,2-dibromoethane (0.08 g, 0.04 mL, 0.45 mmol) were added dropwise. The reaction mixture was shortly heated to reflux, 4-bromobenzyl chloride (2.05 g, 10.0 mmol, 1.00 equiv) was added at once at room temperature and the reaction mixture was stirred for 2.5 h. After the zinc dust set down, the metalated species was transferred into another pre-dried and argon-flushed Schlenk-tube. The concentration of 4-bromobenzylzinc(II) chloride (**1i**) was determined by titration with iodine in THF (0.44 M, 66%).

Cobalt-Catalyzed Cross-Coupling of Benzylzinc(II) Chlorides (1a-h) with 4-Bromobenzonitrile (3a) as Electrophile

Synthesis of 4-benzylbenzonitrile (4a)



Based on **TP2**, 4-bromobenzonitrile (**3a**, 182 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.50 mL). The benzylzinc(II) chloride solution (**1a**, 3.05 mL, 0.43 M, 1.30 mmol, 1.30 equiv) was dropwise added to this solution and the reaction mixture was stirred for 2 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : Et_2O = 19 : 1, R_f = 0.20) leading to the desired product **4a** (158 mg, 0.82 mmol, 82%) as a colourless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.50 (d, *J* = 8.4 Hz, 2H), 7.28-7.16 (m, 5H), 7.11 (d, *J* = 7.4 Hz, 2H), 3.98 (s, 2H).

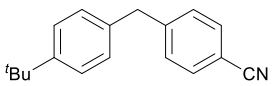
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 146.8, 139.4, 132.3, 129.7, 129.0, 128.8, 126.7, 119.0, 110.1, 42.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3064, 3029, 2926, 2228, 1734, 1507, 1496, 1454, 1414, 1373, 1242, 1178, 1113, 1074, 1046, 912, 854, 797, 761, 725, 698.

MS (EI, 70 eV, %) m/z = 194 (15), 193 (100), 192 (32), 190 (14), 165 (17), 91 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{11}N$**: 193.0891; found 193.0885.

Synthesis of 4-(4-*tert*-butyl)benzyl)benzonitrile (4b)



According to **TP2**, 4-bromobenzonitrile (**3a**, 182 mg, 1.0 mmol, 1.0 euqiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.50 mL). The 4-(*tert*-butyl)benzylzinc(II) chloride solution (**1b**, 3.00 mL,

0.44 M, 1.30 mmol, 1.30 equiv) was dropwise added to this solution and the reaction mixture was stirred for 4 h at 50 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.48) afforded the product **4b** (193 mg, 0.77 mmol, 77%) as an almost colourless liquid.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 7.57 (d, *J* = 8.5 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.6 Hz, 2H), 4.01 (s, 2H), 1.32 (s, 9H).

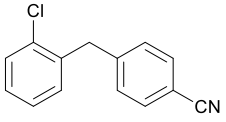
^{13}C-NMR (150 MHz, $CDCl_3$, ppm) δ = 149.4, 146.8, 136.2, 132.1, 129.6, 128.5, 125.5, 118.9, 109.8, 41.4, 34.3, 31.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2961, 2868, 2223, 1691, 1605, 1510, 1502, 1478, 1407, 1362, 1270, 1108, 1019, 864, 819, 794, 754, 719, 669.

MS (EI, 70 eV, %) m/z = 249 (19), 235 (18), 234 (100), 116 (38), 102 (10), 57 (19), 43 (21), 42 (11), 41 (14).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{19}N$**: 249.1517; found 249.1511.

Synthesis of 4-(2-chlorobenzyl)benzonitrile (4c)



According to **TP2**, 4-bromobenzonitrile (**3a**, 182 mg, 1.0 mmol, 1.0 euqiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.40 mL). The 2-chlorobenzylzinc(II) chloride solution (**1c**, 2.80 mL, 0.54 M , 1.50 mmol, 1.50 equiv) was dropwise added to this solution and the reaction mixture was stirred for 18 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.30) yielding the product **4c** (168 mg, 0.74 mmol, 74%) as a pale yellow solid.

M.p.: 54.6 °C

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.50 (d, *J* = 8.4 Hz, 2H), 7.35-7.30 (m, 1H), 7.21 (d, *J* = 8.6 Hz, 2H), 7.18-7.13 (m, 2H), 7.12-7.08 (m, 1H), 4.09 (s, 2H).

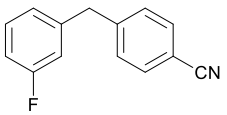
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 145.3, 137.1, 134.5, 132.4, 131.3, 130.0, 129.7, 128.5, 127.3, 119.1, 110.4, 39.5.

IR (ATR, cm^{-1}) ṽ = 2924, 2853, 2225, 1741, 1607, 1470, 1443, 1413, 1115, 1102, 1049, 1033, 1020, 915, 843, 805, 758, 741, 673.

MS (EI, 70 eV, %) m/z = 229 (17), 227 (46), 192 (100), 191 (21), 190 (42), 165 (29), 82 (13), 71 (14), 57 (22), 56 (12), 44 (11), 43 (34), 42 (21), 41 (18).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{10}ClN$**: 227.0502; found 227.0498.

Synthesis of 4-(3-fluorobenzyl)benzonitrile (4d)



Based on **TP2**, 4-bromobenzonitrile (**3a**, 182 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.00 mL). The 3-fluorobenzylzinc(II) chloride solution (**1d**, 1.97 mL, 0.66 M, 1.30 mmol, 1.30 equiv) was dropwise added to this solution and the reaction mixture was stirred for 1 h at 50 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.22) furnished the product **4d** (167 mg, 0.79 mmol, 79%) as a slightly yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.60 (d, *J* = 8.2 Hz, 2H), 7.33-7.27 (m, 3H), 6.99-6.81 (m, 3H), 4.04 (s, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 163.1 (d, ^{1}J(C,F) = 246 Hz), 145.9, 141.9 (d, ^{3}J(C,F) = 7.2 Hz), 132.5, 130.3 (d, ^{3}J(C,F) = 8.3 Hz), 129.7, 124.7 (d, ^{4}J(C,F) = 3.0 Hz), 118.9, 116.0 (d, ^{2}J(C,F) = 21 Hz), 113.8 (d, ^{2}J(C,F) = 21 Hz), 110.5, 41.7.

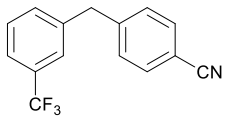
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −112.8.

IR (ATR, cm^{-1}) ṽ = 3060, 2927, 2227, 1606, 1588, 1504, 1485, 1448, 1414, 1246, 1177, 1136, 1114, 1073, 1021, 947, 877, 842, 818, 783, 753, 731, 696, 682.

MS (EI, 70 eV, %) m/z = 212 (14), 211 (100), 210 (24), 208 (10), 183 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{10}FN$**: 211.0797; found 211.0798.

Synthesis of 4-(3-(trifluoromethyl)benzyl)benzonitrile (4e)



With reference to **TP2**, 4-bromobenzonitrile (**3a**, 182 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (0.90 mL). The 3-(trifluoromethyl)benzylzinc(II) chloride solution (**1e**, 1.80 mL, 0.72 M, 1.30 mmol, 1.30 equiv) was dropwise added to this solution and the reaction mixture was stirred for 2 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.22) obtaining the product **4e** (184 mg, 0.70 mmol, 70%) as a pale yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.59 (d, *J* = 8.4 Hz, 2H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.47-7.41 (m, 2H), 7.34 (d, *J* = 7.0 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 2H), 4.10 (s, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 145.9, 140.7, 132.9, 132.7 (q, ^3J(C,F) = 3.8 Hz), 131.6 (q, ^2J(C,F) = 32 Hz), 130.1, 129.7, 126.0 (q, ^3J(C,F) = 3.8 Hz), 124.1 (q, ^3J(C,F) = 3.8 Hz), 124.4 (q, ^1J(C,F) = 271 Hz), 119.2, 111.0, 42.1.

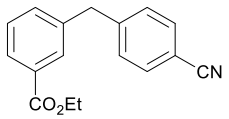
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −62.6.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2928, 2228, 1607, 1508, 1449, 1414, 1326, 1160, 1117, 1093, 1072, 1021, 919, 877, 847, 795, 753, 739, 700, 659.

MS (EI, 70 eV, %) m/z = 263 (10), 262 (17), 261 (100), 260 (16), 242 (15), 241 (34), 240 (18), 221 (10), 193 (11), 192 (66), 191 (16), 190 (28), 165 (17), 159 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{10}F_3N$**: 261.0765; found 261.0763.

Synthesis of ethyl 3-(4-cyanobenzyl)benzoate (4f)



According to **TP2**, 4-bromobenzonitrile (**3a**, 182 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (2.00 mL). The 3-(ethoxycarbonyl)benzylzinc(II) chloride solution (**1f**, 4.00 mL, 0.38 M, 1.50 mmol, 1.50 equiv) was dropwise added to this solution and the reaction mixture was stirred for 18 h at 50 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.12) gave the product **4f** (164 mg, 0.62 mmol, 62%) as a pale yellow liquid.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 7.92 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.89-7.85 (m, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.33 (dt, *J* = 7.6, 1.8 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 4.07 (s, 2H), 1.38 (t, *J* = 7.1 Hz, 3H).

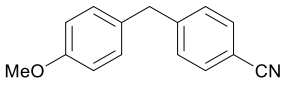
^{13}C-NMR (150 MHz, $CDCl_3$, ppm) δ = 166.3, 145.9, 139.5, 133.3, 132.3, 130.9, 130.0, 129.5, 128.7, 127.8, 118.7, 110.2, 61.0, 41.6, 14.2.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2983, 2254, 2229, 1712, 1606, 1588, 1444, 1367, 1280, 1187, 1105, 1081, 1021, 906, 851, 812, 758, 725, 670.

MS (EI, 70 eV, %) m/z = 266 (14), 265 (61), 238 (10), 237 (54), 236 (11), 221 (22), 220 (100), 192 (29), 191 (15), 190 (31), 165 (19).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{15}NO_2$**: 265.1103; found 265.1090.

Synthesis of 4-(4-methoxybenzyl)benzonitrile (4g)



Based on **TP2**, 4-bromobenzonitrile (**3a**, 182 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.16 mL). The 4-methoxybenzylzinc(II) chloride solution (**1g**, 2.30 mL, 0.56 M,

1.30 mmol, 1.30 equiv) was dropwise added to this solution and the reaction mixture was stirred for 2 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.26) affording the product **4g** (182 mg, 0.82 mmol, 82%) as a pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.49 (d, *J* = 8.3 Hz, 2H), 7.20 (d, *J* = 8.5 Hz, 2H), 7.01 (d, *J* = 8.7 Hz, 2H), 6.79 (d, *J* = 8.7 Hz, 2H), 3.91 (s, 2H), 3.72 (s, 3H).

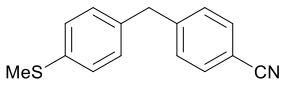
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 158.1, 147.0, 132.1, 131.2, 129.7, 129.3, 118.8, 113.9, 109.7, 55.0, 40.9.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3033, 3000, 2955, 2931, 2836, 2359, 2225, 1608, 1583, 1509, 1462, 1440, 1413, 1301, 1243, 1176, 1109, 1032, 917, 808, 761, 732.

MS (EI, 70 eV, %) m/z = 224 (15), 223 (100), 222 (27), 208 (20), 192 (14), 190 (13), 180 (13), 121 (37).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{13}NO$**: 223.0997; found 223.0993.

Synthesis of 4-(4-(methylthio)benzyl)benzonitrile (4h)



According to **TP2**, 4-bromobenzonitrile (**3a**, 182 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.85 mL). The 4-(methylthio)benzylzinc(II) chloride solution (**1h**, 3.70 mL, 0.35 M, 1.30 mmol, 1.30 equiv) was dropwise added to this solution and the reaction mixture was stirred for 18 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.27) leading to the product **4h** (156 mg, 0.65 mmol, 65%) as a white solid.

M.p.: 73.4 °C

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.49 (d, *J* = 8.3 Hz, 2H), 7.20 (d, *J* = 8.5 Hz, 2H), 7.14 (d, *J* = 8.3 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 3.92 (s, 2H), 2.40 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 146.7, 136.8, 136.3, 132.4, 129.7, 129.5, 127.2, 119.0, 110.2, 41.5, 16.1.

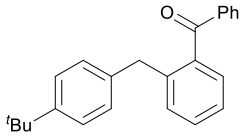
IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2915, 2227, 1693, 1604, 1493, 1435, 1404, 1321, 1207, 1091, 1015, 968, 959, 917, 860, 848, 812, 791, 744, 654.

MS (EI, 70 eV, %) m/z = 240 (17), 239 (100), 192 (72), 191 (20), 190 (32), 165 (19), 137 (17), 57 (13), 43 (22), 42 (13), 41 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{15}H_{13}NS$**: 265.1103; found 239.0766.

Cobalt-Catalyzed Cross-Coupling of Benzylzinc(II) Chlorides (1b-i) with Several Aryl and Heteroaryl Halides

Preparation of (2-(4-(*tert*-butyl)benzyl)phenyl)(phenyl)methanone (5a)



According to **TP2**, 2-bromo-benzophenone (**3b**, 261 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.50 mL). The 4-(*tert*-butyl)benzylzinc(II) chloride solution (**1b**, 3.00 mL, 0.44 M, 1.30 mmol, 1.30 equiv) was dropwise added to this solution and the reaction mixture was stirred for 4 h at 50 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.13) gave the desired product **5a** (210 mg, 0.64 mmol, 64%) as an almost colourless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.63 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.48-7.44 (m, 1H), 7.37-7.29 (m, 3H), 7.24-7.18 (m, 3H), 7.14-7.08 (m, 2H), 6.94 (d, *J* = 8.5 Hz, 2H), 3.87 (s, 2H), 1.17 (s, 9H).

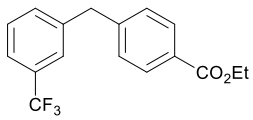
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 198.7, 148.8, 140.5, 139.1, 137.8, 137.5, 133.1, 130.9, 130.3 (2C), 129.0, 128.5, 128.3, 125.6, 125.2, 38.5, 34.4, 31.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3060, 3026, 2961, 2904, 2867, 2246, 1663, 1597, 1580, 1514, 1448, 1412, 1363, 1314, 1268, 1202, 1179, 1152, 1109, 1020, 1001, 936, 908, 842, 795, 763, 730, 709, 700, 668.

MS (EI, 70 eV, %) m/z = 329 (12), 328 (31), 327 (30), 313 (15), 272 (24), 271 (100), 255 (17), 254 (38), 195 (32), 194 (37), 193 (14), 165 (22), 147 (13), 105 (16), 91 (11), 77 (11), 57 (29), 43 (18), 42 (10), 41 (17).

HRMS (EI, 70 eV) m/z: calc. for **$C_{24}H_{24}O$**: 328.1827; found 328.1821.

Preparation of ethyl 4-(3-(trifluoromethyl)benzyl)benzoate (5b)



With reference to **TP2**, ethyl 4-bromobenzoate (**3c**, 229 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (0.90 mL). The 3-(trifluoromethyl)benzylzinc(II) chloride solution (**1e**, 1.80 mL, 0.72 M, 1.30 mmol, 1.30 equiv) was dropwise added to this solution and the reaction mixture was stirred for 18 h at 50 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 99 : 1, R_f = 0.13) gave the desired product **5b** (166 mg, 0.54 mmol, 54%) as a pale yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.92 (d, *J* = 8.3 Hz, 2H), 7.42-7.26 (m, 4H), 7.17 (d, *J* = 9.2 Hz, 2H), 4.30 (q, *J* = 7.1 Hz, 2H), 4.01 (s, 2H), 1.31 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 166.6, 145.3, 141.2, 132.4 (q, ^4J(C,F) = 1.0 Hz), 131.1 (q, ^2J(C,F) = 32 Hz), 130.1, 129.2, 129.0, 125.7 (q, ^3J(C,F) = 3.7 Hz), 124.2 (q, ^1J(C,F) = 271 Hz), 123.5 (q, ^3J(C,F) = 3.8 Hz), 61.0, 41.8, 14.5.

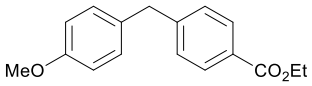
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) $\delta = -62.6$.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2983, 1713, 1610, 1449, 1415, 1367, 1329, 1273, 1161, 1119, 1101, 1073, 1021, 918, 905, 877, 851, 790, 769, 743, 699, 659.

MS (EI, 70 eV, %) m/z = 308 (22), 280 (20), 264 (19), 263 (100), 235 (39), 215 (12), 185 (20), 183 (20), 166 (20), 165 (37), 159 (29), 57 (10), 44 (10), 43 (13).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{15}F_3O_2$**: 308.1024; found 328.1017.

Preparation of ethyl 4-(4-methoxybenzyl)benzoate (5c)



According to **TP2**, ethyl 4-bromobenzoate (**3c**, 229 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.15 mL). The 4-methoxybenzylzinc(II) chloride solution (**1g**, 2.30 mL, 0.56 M, 1.30 mmol, 1.30 equiv) was dropwise added to this solution and the reaction mixture was stirred for 1 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.32) leading to the product **5c** (189 mg, 0.70 mmol, 70%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.90 (d, *J* = 8.1 Hz, 2H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.02 (d, *J* = 8.5 Hz, 2H), 6.77 (d, *J* = 8.5 Hz, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.90 (s, 2H), 3.71 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H).

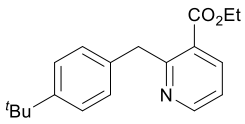
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 166.7, 158.3, 147.0, 132.4, 130.0, 129.9, 128.9, 128.5, 114.1, 60.9, 55.4, 41.2, 14.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2981, 2835, 1711, 1610, 1584, 1510, 1463, 1441, 1414, 1391, 1366, 1301, 1271, 1243, 1175, 1104, 1033, 1020, 920, 869, 854, 831, 798, 772, 740, 698.

MS (EI, 70 eV, %) m/z = 271 (18), 270 (100), 241 (12), 225 (37), 197 (62), 165 (14), 153 (10), 121 (25), 113 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{17}H_{18}O_3$**: 270.1256; found 270.1240.

Preparation of ethyl 2-(4-(*tert*-butyl)benzyl)nicotinate (5d)



According to **TP2**, ethyl 2-chloronicotinate (**3d**, 186 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.50 mL). The 4-(*tert*-butyl)benzylzinc(II) chloride solution (**1b**, 3.00 mL, 0.44 M, 1.30 mmol, 1.30 equiv) was dropwise added to this solution and the reaction mixture was stirred for 4 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.15) affording the product **5d** (284 mg, 0.95 mmol, 95%) as a pale yellow oil.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 8.68 (dd, *J* = 4.8, 1.9 Hz, 1H), 8.15 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.28 (d, *J* = 8.6 Hz, 2H), 7.24-7.18 (m, 3H), 4.56 (s, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.32 t, *J* = 7.1 Hz, 3H), 1.28 (s, 9H).

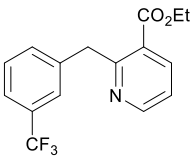
^{13}C-NMR (150 MHz, $CDCl_3$, ppm) δ = 166.5, 161.3, 151.7, 148.6, 138.3, 136.5, 128.5, 126.1, 125.0, 121.0, 61.3, 41.7, 34.2, 31.3, 14.1.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2961, 2868, 1721, 1582, 1567, 1514, 1437, 1364, 1255, 1130, 1111, 1078, 1056, 1019, 860, 806, 762, 743, 663.

MS (EI, 70 eV, %) m/z = 298 (21), 297 (100), 296 (45), 283 (16), 282 (75), 254 (12), 236 (20), 224 (14), 196 (20), 195 (24), 167 (11), 57 (28), 43 (29), 42 (20), 41 (18).

HRMS (EI, 70 eV) m/z: calc. for **$C_{19}H_{23}NO_2$**: 297.1729; found 297.1724.

Preparation of ethyl 2-(3-(trifluoromethyl)benzyl)nicotinate (5e)



With reference to **TP2**, ethyl 2-chloronicotinate (**3d**, 186 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in

freshly distilled MTBE (0.90 mL). The 3-(trifluoromethyl)benzylzinc(II) chloride solution (**1e**, 1.80 mL, 0.72 M, 1.30 mmol, 1.30 equiv) was dropwise added to this solution and the reaction mixture was stirred for 2 h at 50 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 9 : 1, R_f = 0.21) led to the product **5e** (186 mg, 0.60 mmol, 60%) as a pale yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.62 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.13 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.49 (s, 1H), 7.40-7.17 (m, 4H), 4.56 (s, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 166.4, 160.4, 152.2, 140.7, 138.9, 132.6 (q, ^4J(C,F) = 2.4 Hz), 130.6 (q, ^2J(C,F)= 32 Hz), 128.7, 126.2, 125.9 (q, ^3J(C,F) = 3.8 Hz), 124.4 (q, ^1J(C,F) = 271 Hz), 123.1 (q, ^3J(C,F) = 3.9 Hz), 121.7, 61.7, 42.2, 14.2.

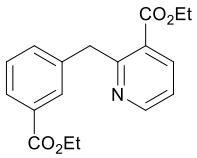
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −62.5.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3049, 2985, 2363, 1720, 1583, 1570, 1448, 1438, 1368, 1328, 1300, 1259, 1190, 1161, 1118, 1094, 1073, 1057, 1017, 917, 862, 822, 793, 782, 747, 734, 701, 676, 660.

MS (EI, 70 eV, %) m/z = 310 (18), 309 (83), 308 (92), 290 (12), 281 (11), 280 (54), 264 (52), 263 (59), 262 (13), 237 (16), 236 (100), 235 (59), 234 (65), 216 (18), 167 (31), 166 (23), 139 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{16}H_{14}F_3NO_2$**: 309.0977; found 309.0966.

Preparation of ethyl 2-(3-(ethoxycarbonyl)benzyl)nicotinate (5f)



According to **TP2**, ethyl 2-chloronicotinate (**3d**, 186 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (2.00 mL). The 3-(ethoxycarbonyl)benzylzinc(II) chloride solution (**1f**, 4.00 mL, 0.38 M, 1.50 mmol, 1.50 equiv) was dropwise added to this solution and the reaction mixture was stirred for 18 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.15) yielding the product **5f** (212 mg, 0.68 mmol, 68%) as a pale yellow oil.

^{1}H-NMR (600 MHz, $CDCl_3$, ppm) δ = 8.67 (dd, *J* = 4.8, 1.9 Hz, 1H), 8.17 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.94 (t, *J* = 1.8 Hz, 1H), 7.87-7.83 (m, 1H), 7.42 (ddd, *J* = 7.1, 1.8, 1.2 Hz, 1H), 7.30 (t, *J* = 7.7 Hz, 1H), 7.23 (dd, *J* = 7.9, 4.8 Hz, 1H), 4.62 (s, 2H), 4.33 (qd, *J* = 7.1, 0.8 Hz, 4H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H).

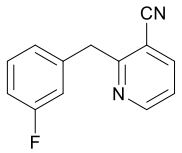
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 166.8, 166.5, 152.1, 140.1, 138.8, 133.6, 130.6, 130.2, 128.3, 127.5, 126.2, 121.5, 61.6, 60.9, 42.3, 14.4, 14.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2983, 2255, 1713, 1583, 1569, 1438, 1391, 1367, 1278, 1188, 1131, 1106, 1081, 1058, 1020, 906, 725, 694.

MS (EI, 70 eV, %) m/z = 314 (21), 313 (100), 312 (17), 268 (22), 256 (12), 240 (30), 239 (16), 238 (11), 221 (17), 212 (15), 211 (28), 194 (13), 167 (23), 166 (23).

HRMS (EI, 70 eV) m/z: calc. for **$C_{18}H_{19}NO_4$**: 313.1314; found 313.1322.

Preparation of 2-(3-fluorobenzyl)nicotinonitrile (5g)



With reference to **TP2**, 2-chloronicotinonitrile (**3e**, 139 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.00 mL). The 3-fluorobenzylzinc(II) chloride solution (**1d**, 2.00 mL, 0.66 M, 1.30 mmol, 1.30 equiv) was dropwise added to this solution and the reaction mixture was stirred for 3 h at 50 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.20) led to the product **5g** (142 mg, 0.67 mmol, 67%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.75 (dd, *J* = 4.9, 1.8 Hz, 1H), 7.93 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.32-7.22 (m, 2H), 7.16 (d, *J* = 7.7 Hz, 1H), 7.07 (dt, *J* = 9.8, 1.9 Hz, 1H), 6.92 (td, *J* = 8.9, 3.5 Hz, 1H), 4.38 (s, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 163.0 (d, ^1J(C,F) = 245 Hz), 162.9, 152.8, 140.8, 139.8 (d, 3J(C,F) = 7.5 Hz), 130.3 (d, ^3J(C,F) = 8.3 Hz), 124.9 (d, ^4J(C,F) = 2.9 Hz), 121.7, 116.8, 116.1 (d, ^2J(C,F) = 21 Hz), 114.1 (d, ^2J(C,F) = 22 Hz), 109.4, 42.8.

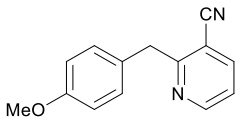
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −112.8.

IR (ATR, cm^{-1}) ṽ = 3062, 2961, 2930, 2856, 2228, 1614, 1589, 1580, 1564, 1486, 1447, 1431, 1247, 1160, 1137, 1093, 946, 880, 852, 800, 770, 735, 710, 685.

MS (EI, 70 eV, %) m/z = 212 (39), 211 (100), 210 (17), 190 (14), 129 (19), 109 (11).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_9FN_2$**: 212.0750; found 212.0750.

Preparation of 2-(4-methoxybenzyl)nicotinonitrile (5h)



According to **TP2**, 2-chloronicotinonitrile (**3e**, 139 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.15 mL). The 4-methoxybenzylzinc(II) chloride solution (**1g**, 2.30 mL, 0.56 M, 1.30 mmol, 1.30 equiv) was dropwise added to this solution and the reaction mixture was stirred for 2 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.17) obtaining the product **5h** (173 mg, 0.77 mmol, 77%) as an orange oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.65 (dd, *J* = 4.9, 1.8 Hz, 1H), 7.82 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.23 (d, *J* = 8.8 Hz, 2H), 7.16 (dd, *J* = 7.8, 4.9 Hz, 1H), 6.77 (d, *J* = 8.7 Hz, 2H), 4.24 (s, 2H), 3.69 (s, 3H).

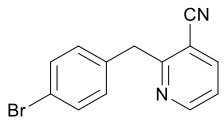
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 164.5, 158.9, 153.0, 141.0, 130.5, 130.0, 121.6, 117.4, 114.5, 109.3, 55.6, 42.7.

IR (ATR, cm^{-1}) ṽ = 3051, 2999, 2956, 2932, 2836, 2227, 1610, 1581, 1563, 1509, 1431, 1301, 1276, 1245, 1176, 1109, 1088, 1031, 943, 806, 788, 742, 720, 696.

MS (EI, 70 eV, %) m/z = 225 (16), 224 (100), 223 (55), 209 (53), 192 (12), 179 (13), 121 (50), 43 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{12}N_2O$**: 224.0950; found 224.0940.

Preparation of 2-(4-bromobenzyl)nicotinonitrile (5i)



With reference to **TP2**, 2-chloronicotinonitrile (**3e**, 139 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.50 mL). The 4-bromobenzylzinc(II) chloride solution (**1i**, 3.00 mL, 0.44 M, 1.30 mmol, 1.30 equiv) was dropwise added to this solution and the reaction mixture was stirred for 18 h at 50 °C. Purification of the crude product by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.24) furnished the product **5i** (186 mg, 0.68 mmol, 68%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.73 (dd, *J* = 4.9, 1.6 Hz, 1H), 7.92 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.41 (d, *J* = 8.5 Hz, 2H), 7.30-7.27 (m, 1H), 7.25 (d, *J* = 7.8 Hz, 2H), 4.33 (s, 2H).

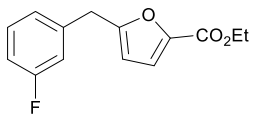
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 162.8, 152.4, 140.8, 136.2, 131.7, 130.8, 121.5, 121.0, 116.6, 109.1, 42.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3048, 2922, 2851, 2228, 1580, 1565, 1486, 1430, 1405, 1179, 1102, 1070, 1011, 842, 800, 767, 716, 701.

MS (EI, 70 eV, %) m/z = 274 (52), 273 (100), 272 (56), 271 (94), 248 (13), 246 (13), 192 (86), 171 (13), 167 (11), 166 (12).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_9BrN_2$**: 271.9949; found 271.9949.

Preparation of ethyl 5-(3-fluorobenzyl)furan-2-carboxylate (5j)



According to **TP2**, ethyl 5-bromofuran-2-carboxylate (**3f**, 220 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.00 mL). The 3-fluorobenzylzinc(II) chloride solution (**1d**, 2.00 mL, 0.66 M, 1.30 mmol, 1.30 equiv) was dropwise added to this solution and the reaction mixture was stirred for 3 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.26) obtaining the product **5j** (149 mg, 0.60 mmol, 60%) as pale yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.24-7.20 (m, 1H), 7.05 (d, *J* = 3.4 Hz, 1H), 6.98 (dd, *J* = 8.0, 1.3 Hz, 1H), 6.90 (m, 2H), 6.06 (dt, *J* = 3.4, 0.8 Hz, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 3.99 (s, 2H), 1.32 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 163.0 (d, ^1J(C,F) = 245 Hz), 158.9, 158.6, 144.1, 139.3 (d, ^3J(C,F) = 7.0 Hz), 130.2 (d, ^3J(C,F) = 8.0 Hz), 124.6 (d, ^4J(C,F) = 3.0 Hz), 119.0, 115.9 (d, ^2J(C,F) = 22 Hz), 113.9 (d, ^2J(C,F) = 20 Hz), 109.2, 60.9, 34.5, 14.5.

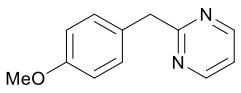
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −113.0.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3128, 2983, 2361, 1713, 1616, 1591, 1519, 1488, 1448, 1383, 1368, 1297, 1251, 1205, 1173, 1126, 1075, 1016, 970, 944, 912, 866, 789, 760, 731, 681.

MS (EI, 70 eV, %) m/z = 249 (10), 248 (67), 220 (10), 219 (23), 203 (42), 176 (17), 175 (100), 147 (16), 146 (40), 127 (10).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{13}FO_3$**: 248.0849; found 248.0845.

Preparation of 2-(4-methoxybenzyl)pyrimidine (6a)



With reference to **TP2**, 2-bromopyrimidine (**3g**, 159 g, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.15 mL). The 4-methoxybenzylzinc(II) chloride solution (**1g**, 2.30 mL, 0.56 M, 1.30 mmol, 1.30 equiv) was dropwise added to this solution and the reaction mixture was stirred for 2 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.10) leading to the desired product **6a** (142 mg, 0.71 mmol, 71%) as pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.58 (d, *J* = 4.9 Hz, 2H), 7.20 (d, 8.7 Hz, 2H), 7.01 (t, *J* = 4.9 Hz, 1H), 6.77 (d, *J* = 8.7 Hz, 2H), 4.16 (s, 2H), 3.68 (s, 3H).

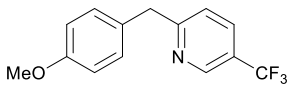
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 170.1, 158.1, 157.0 (2C), 130.1, 129.9, 118.3, 113.7, 54.9, 44.9.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 3036, 2998, 2955, 2932, 2835, 2360, 2341, 1734, 1610, 1570, 1559, 1509, 1462, 1414, 1373, 1300, 1281, 1239, 1176, 1108, 1032, 993, 867, 847, 806, 732, 713, 668.

MS (EI, 70 eV, %) m/z = 200 (19), 199 (10), 185 (11), 70 (12), 61 (17), 45 (14), 43 (100).

HRMS (EI, 70 eV) m/z: calc. for **$C_{12}H_{12}N_2O$**: 200.0950; found 200.0944.

Preparation of 2-(4-methoxybenzyl)-5-(trifluoromethyl)pyridine (6b)



According to **TP2**, 2-chloro-5-(trifluoromethyl)pyridine (**3h**, 182 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.15 mL). The 4-methoxybenzylzinc(II) chloride solution (**1g**, 2.30 mL, 0.56 M , 1.30 mmol, 1.30 equiv) was dropwise added to this solution and the reaction mixture was stirred for 2 h at 50 °C. Purification of the crude product by flash column

chromatography (SiO_2, *i*-hexane : EtOAc = 19 : 1, R_f = 0.24) afforded the product **6b** (222 mg, 0.83 mmol, 83%) as a pale yellow liquid.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 8.81 (s, 1H), 7.79 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.23-7.17 (m, 3H), 6.87 (d, *J* = 8.7 Hz, 2H), 4.17 (s, 2H), 3.79 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 165.3, 158.3, 146.1 (q, ^3J(C,F) = 4.1 Hz), 133.4 (q, ^3J(C,F) = 3.5 Hz), 130.3, 129.9, 124.1 (q, ^2J(C,F) = 33 Hz), 123.5 (q, ^1J(C,F) = 270 Hz), 122.4, 114.0, 55.1, 43.6.

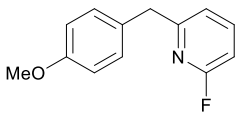
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −62.3.

IR (ATR, cm^{-1}) $\tilde{\nu}$ = 2935, 2837, 1606, 1573, 1511, 1492, 1464, 1441, 1391, 1325, 1301, 1245, 1163, 1120, 1077, 1034, 1015, 941, 867, 829, 810, 785, 755, 727, 710.

MS (EI, 70 eV, %) m/z = 268 (15), 267 (100), 266 (78), 253 (10), 252 (64), 235 (13), 224 (27), 222 (14), 121 (45).

HRMS (EI, 70 eV) m/z: calc. for **$C_{14}H_{12}F_3NO$**: 267.0871; found 267.0867.

Preparation of 2-fluoro-6-(4-methoxybenzyl)pyridine (6c)



With reference to **TP2**, 2-chloro-6-fluoropyridine (3i, 132 mg, 1.0 mmol, 1.0 equiv), $CoCl_2$ (7.0 mg, 0.05 mmol, 0.05 equiv), isoquinoline (13.0 mg, 0.10 mmol, 0.10 equiv) were used and dissolved in freshly distilled MTBE (1.15 mL). The 4-methoxybenzylzinc(II) chloride solution (**1g**, 2.30 mL, 0.56 M , 1.30 mmol, 1.30 equiv) was dropwise added to this solution and the reaction mixture was stirred for 2 h at 50 °C. The crude product was purified by flash column chromatography (SiO_2, *i*-hexane : EtOAc = 8 : 2, R_f = 0.20) leading to the desired product **6c** (113 mg, 0.52 mmol, 52%) as pale yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ = 7.69-7.59 (m, 1H), 7.19 (d, *J* = 8.7 Hz, 2H), 6.95 (dd, *J* = 7.3, 2.3 Hz, 1H), 6.85 (d, *J* = 8.7 Hz, 2H), 6.73 (dd, *J* = 8.1, 2.3 Hz, 1H), 4.02 (s, 2H), 3.78 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ = 163.5 (d, ^1J(C,F) = 238 Hz), 161.1 (d, ^2J(C,F)= 13 Hz), 158.8, 141.8 (d, ^3J(C,F) = 7.7 Hz), 131.2, 130.6, 120.5 (d, ^4J(C,F) = 4.2 Hz), 114.5, 107.0 (d, ^2J(C,F) = 37 Hz), 55.7, 43.5.

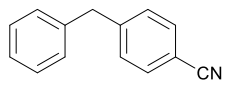
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ = −67.5.

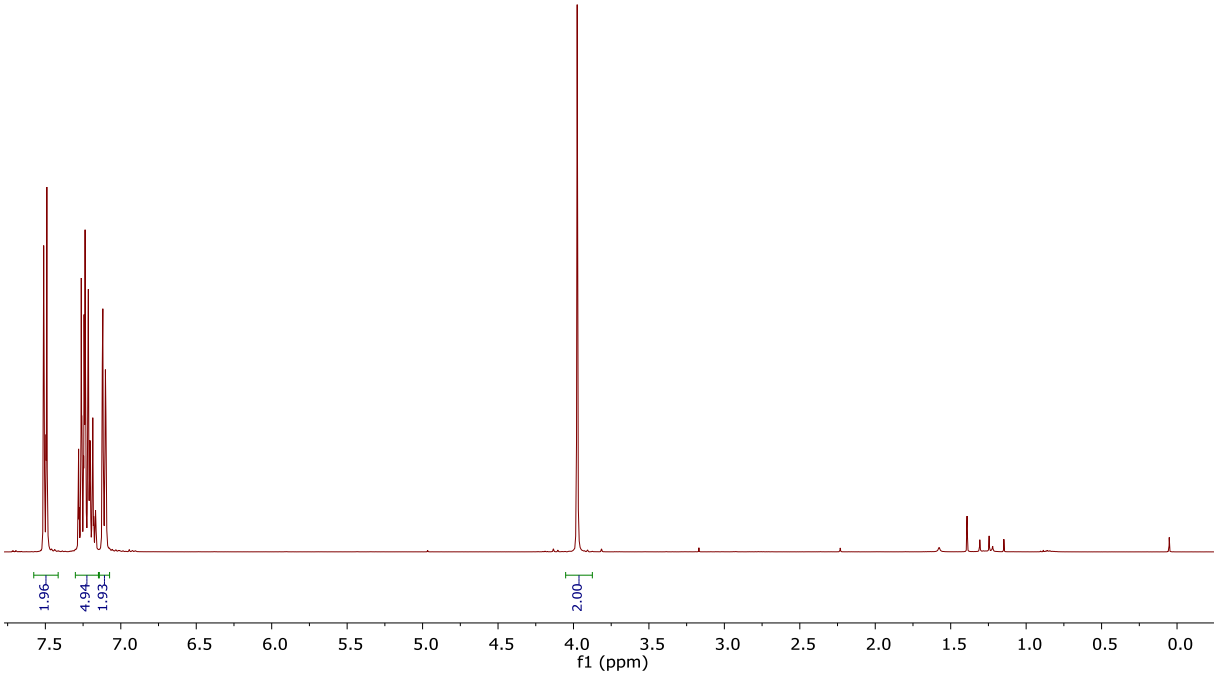
IR (ATR, cm^{-1}) ṽ = 3001, 2934, 2836, 1603, 1574, 1510, 1449, 1436, 1300, 1243, 1222, 1176, 1145, 1106, 1075, 1033, 995, 971, 848, 819, 797, 764, 746, 725, 704.

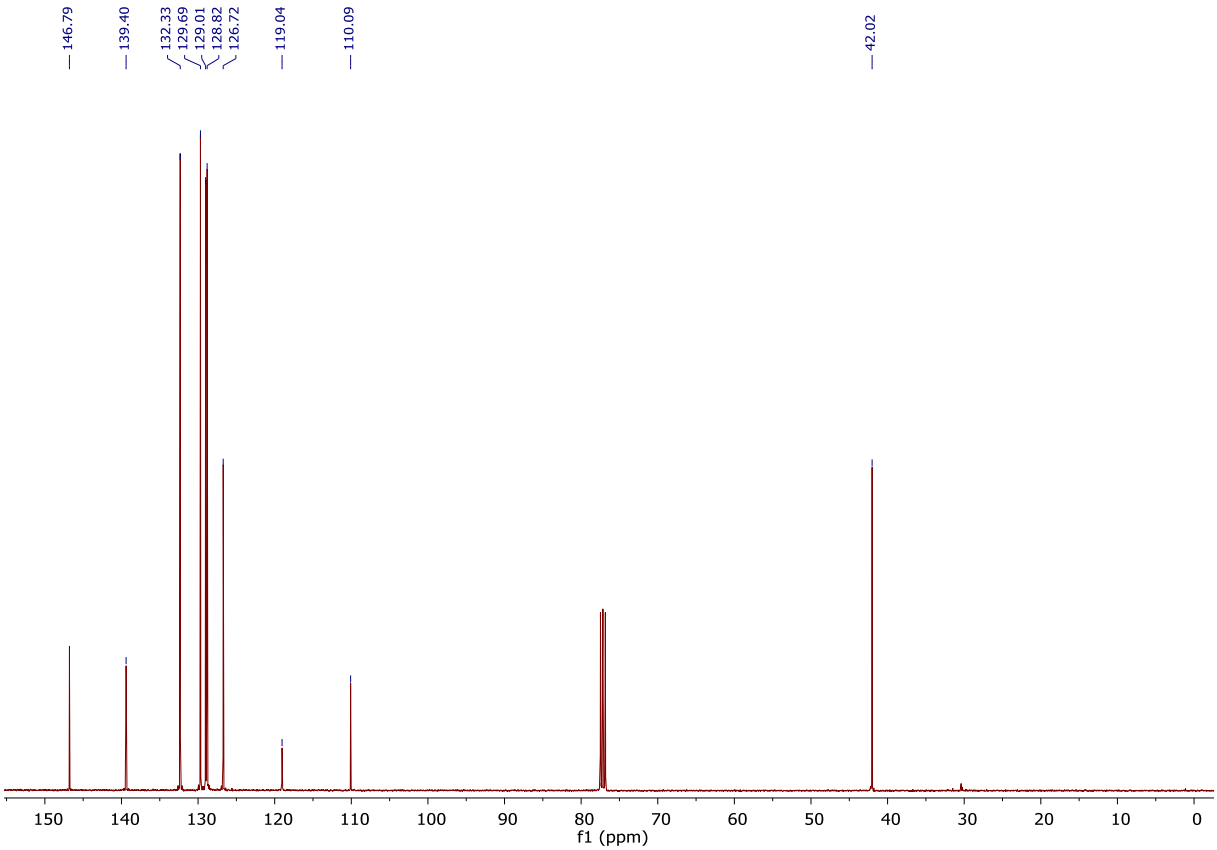
MS (EI, 70 eV, %) m/z = 218 (15), 217 (100), 216 (25), 202 (65), 185 (14), 174 (43), 172 (11), 121 (46).

HRMS (EI, 70 eV) m/z: calc. for **$C_{13}H_{12}FNO$**: 217.0903; found 217.0895.

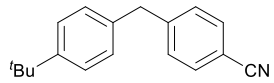
NMR-Spectra of 4-benzylbenzonitrile (4a)

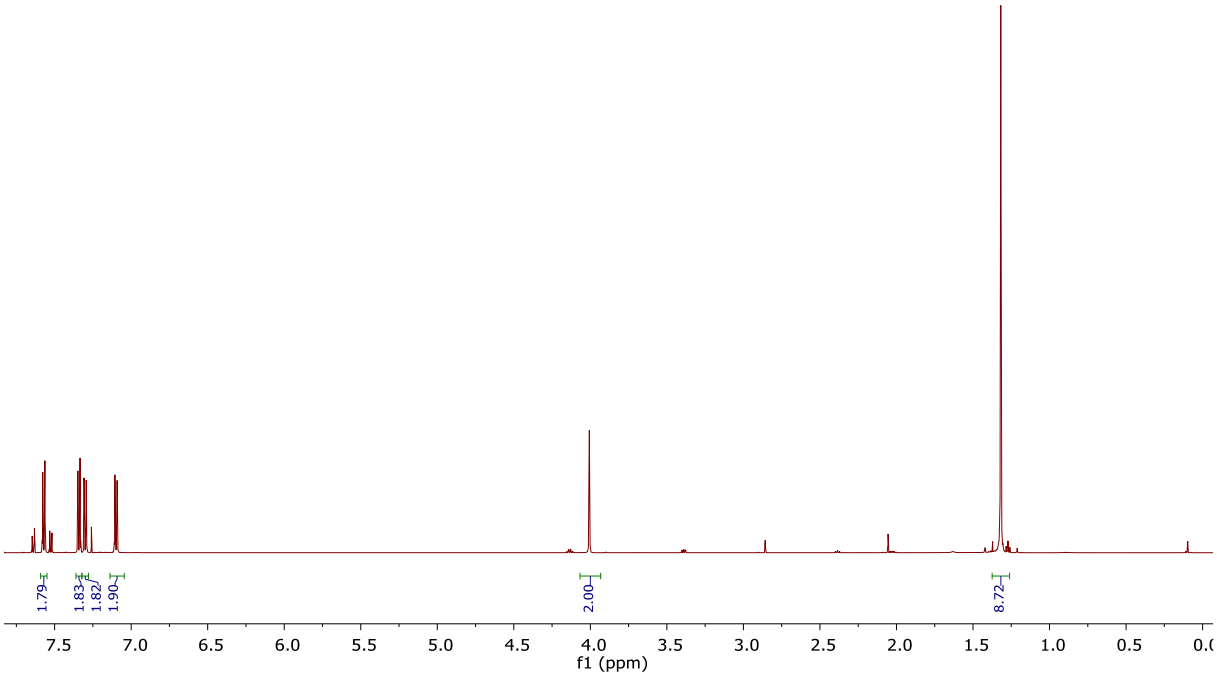


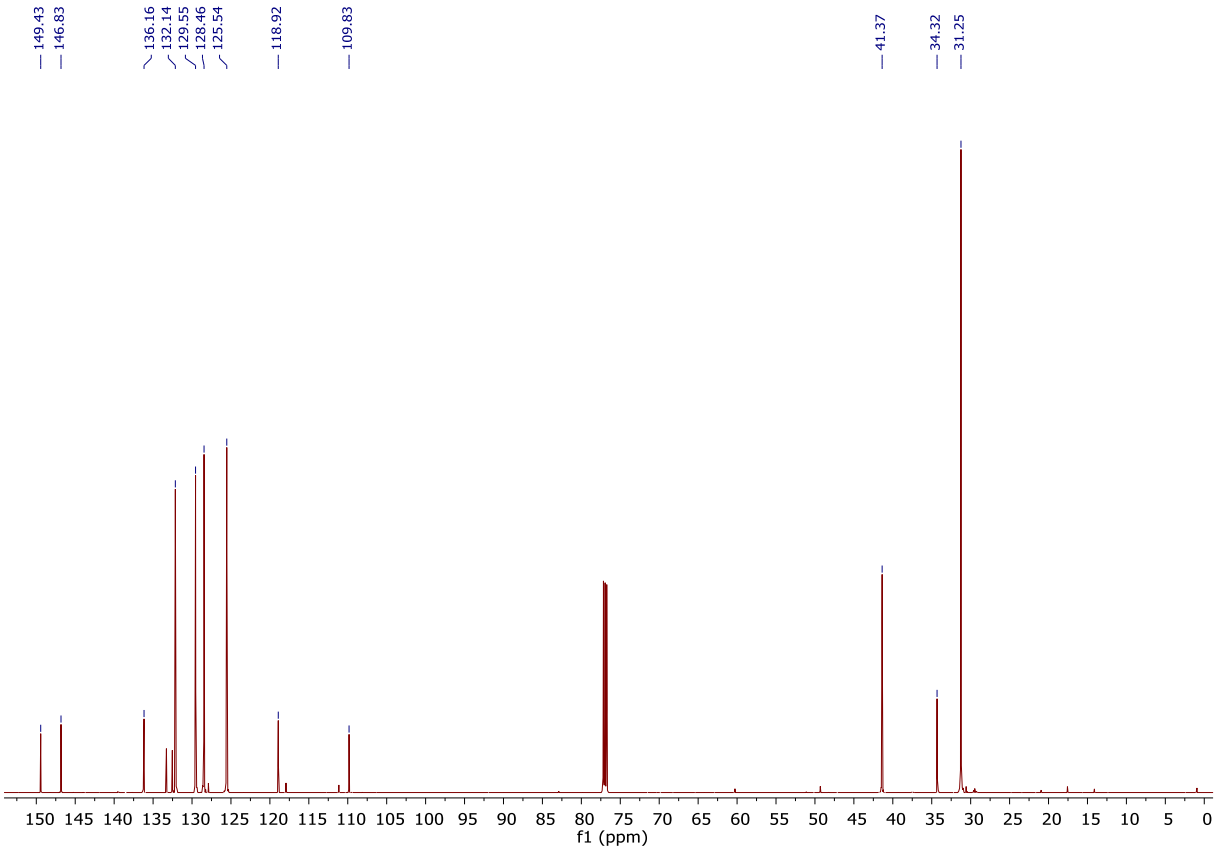




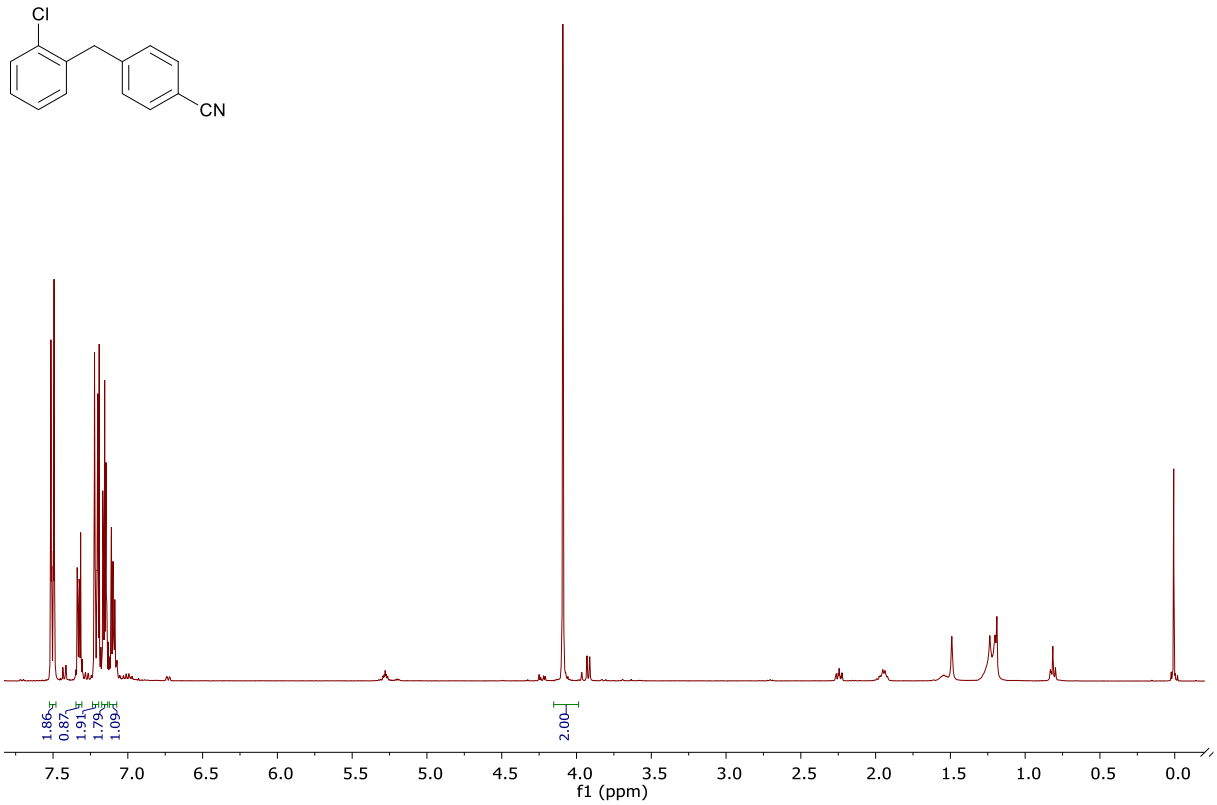
NMR-Spectra of 4-(4-*tert*-butyl)benzyl)benzonitrile (4b)

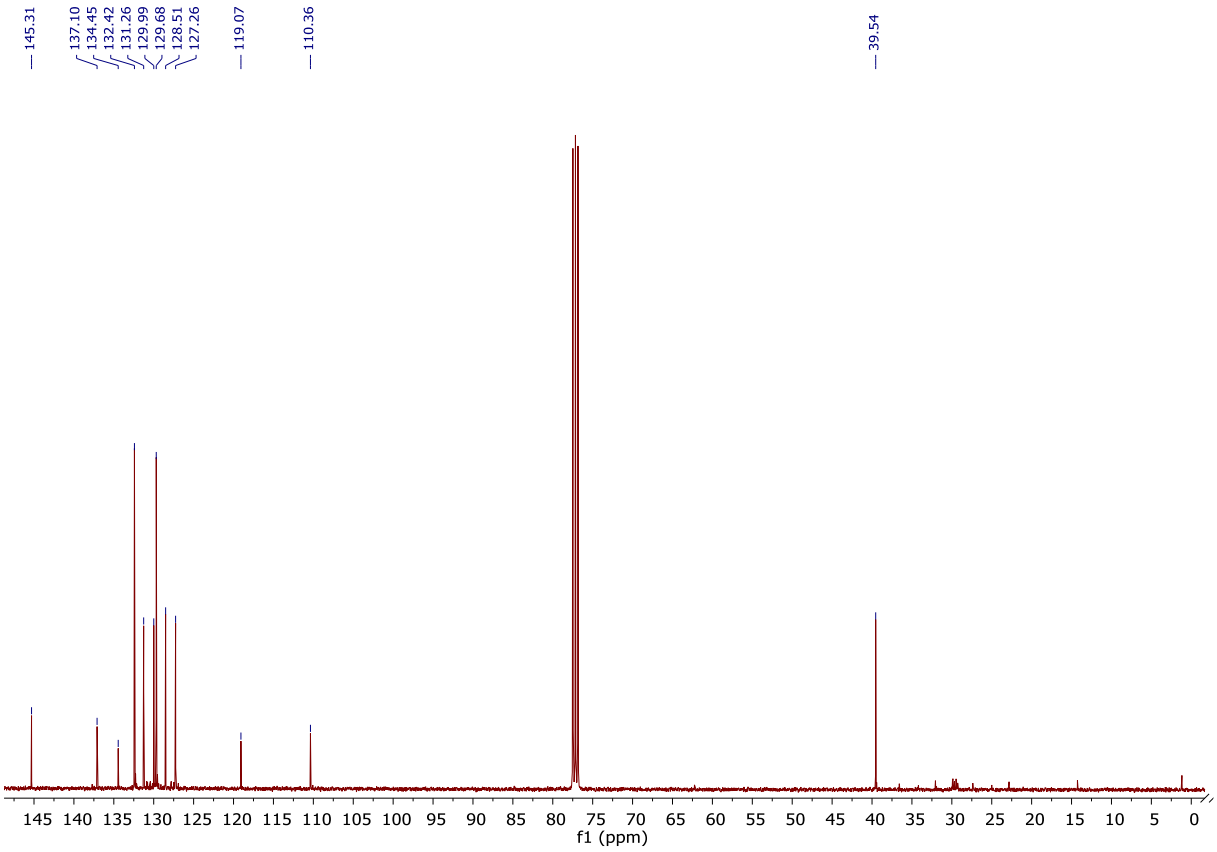




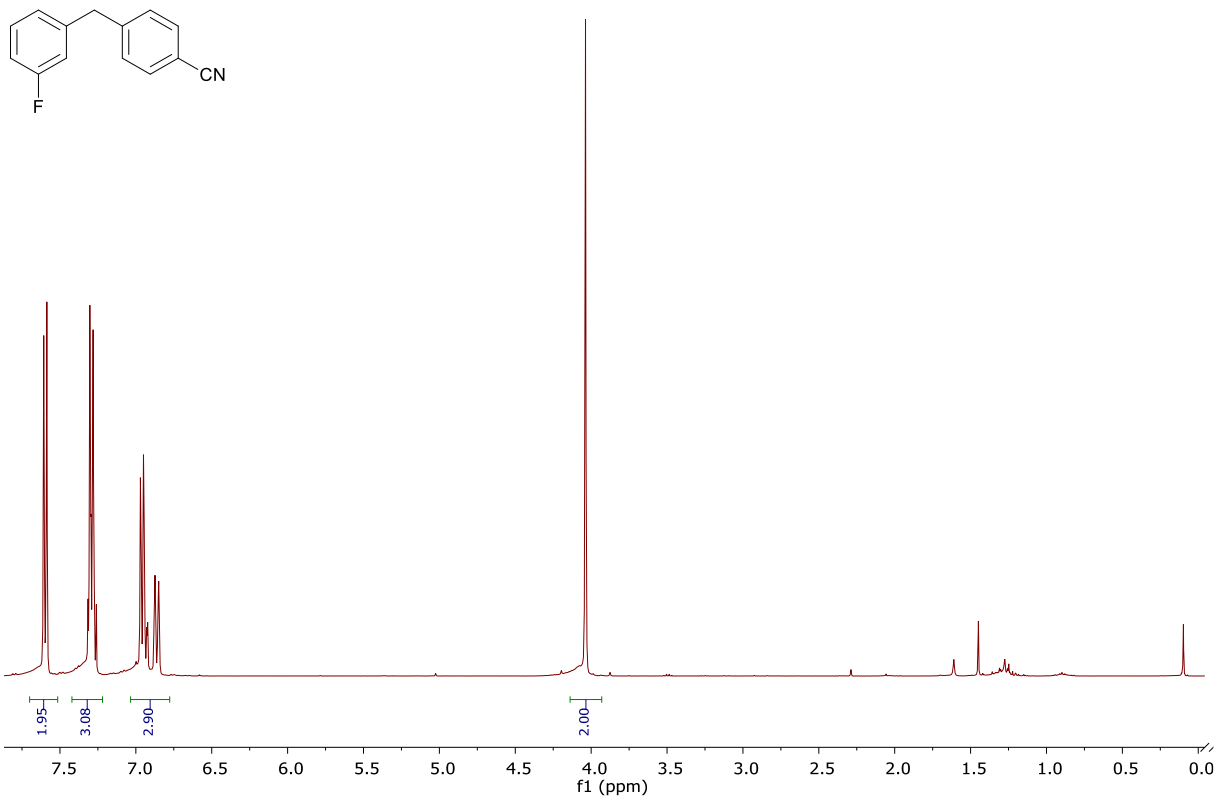


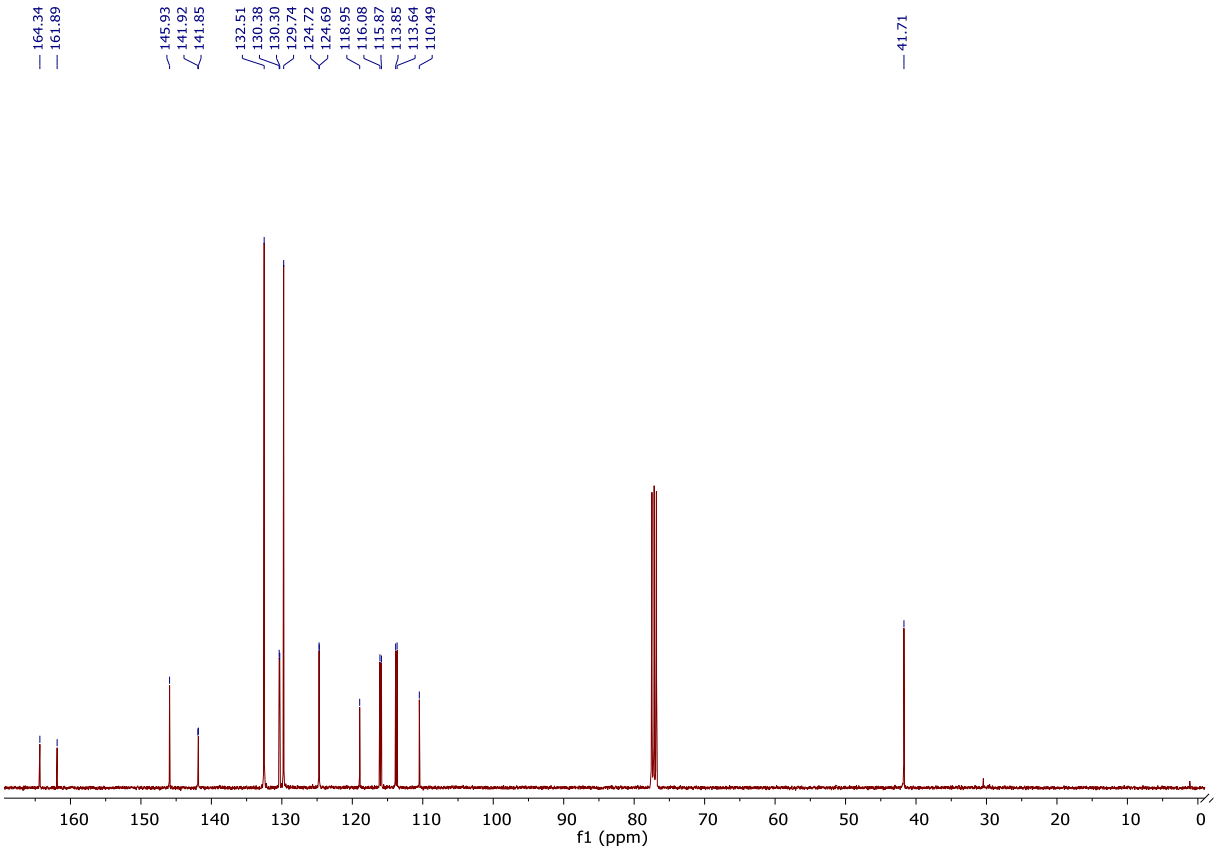
NMR-Spectra of 4-(2-chlorobenzyl)benzonitrile (4c)

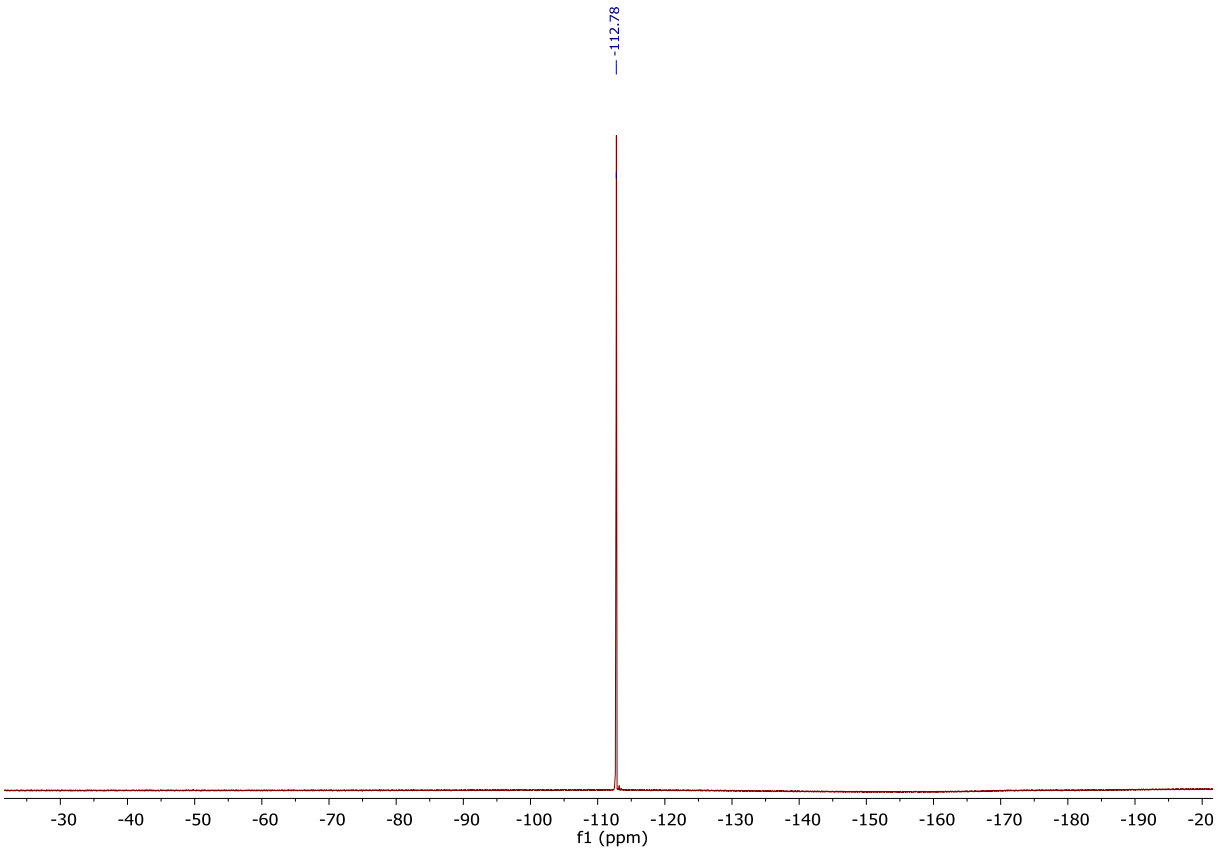




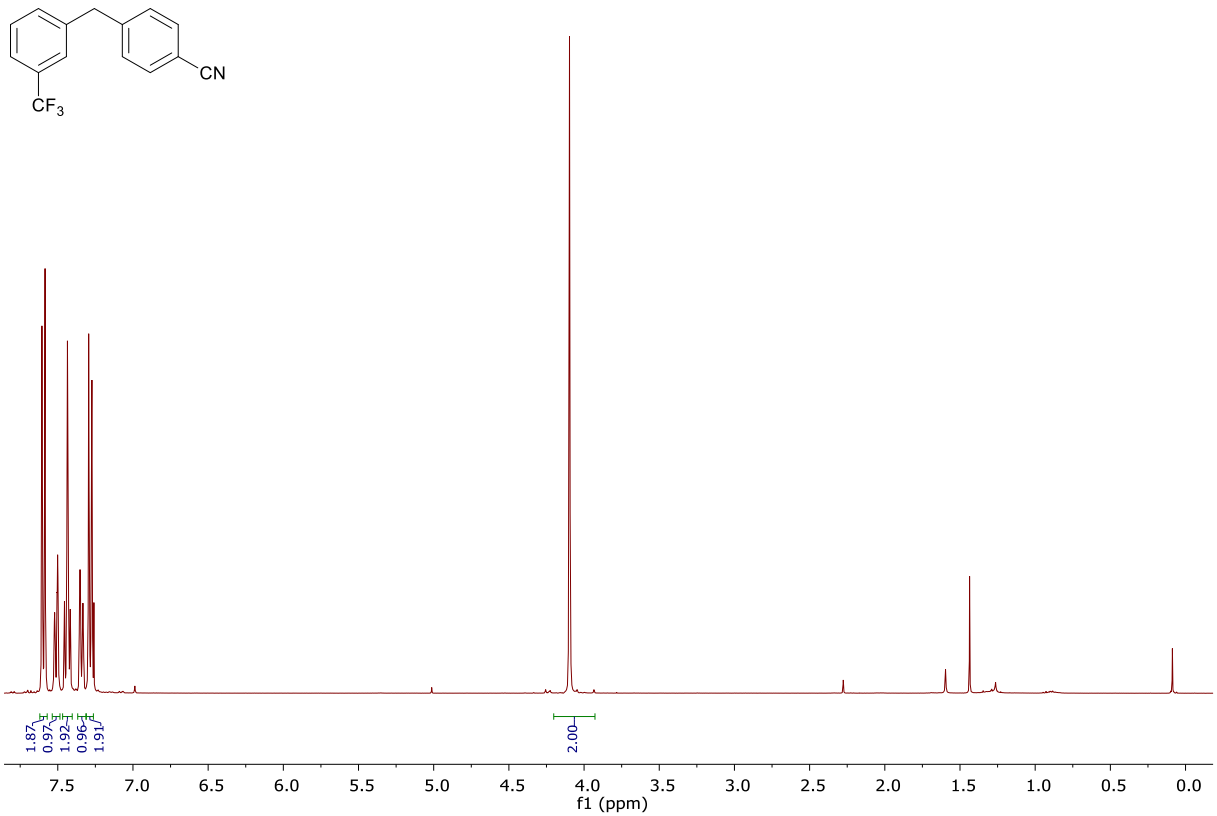
NMR-Spectra of 4-(3-fluorobenzyl)benzonitrile (4d)

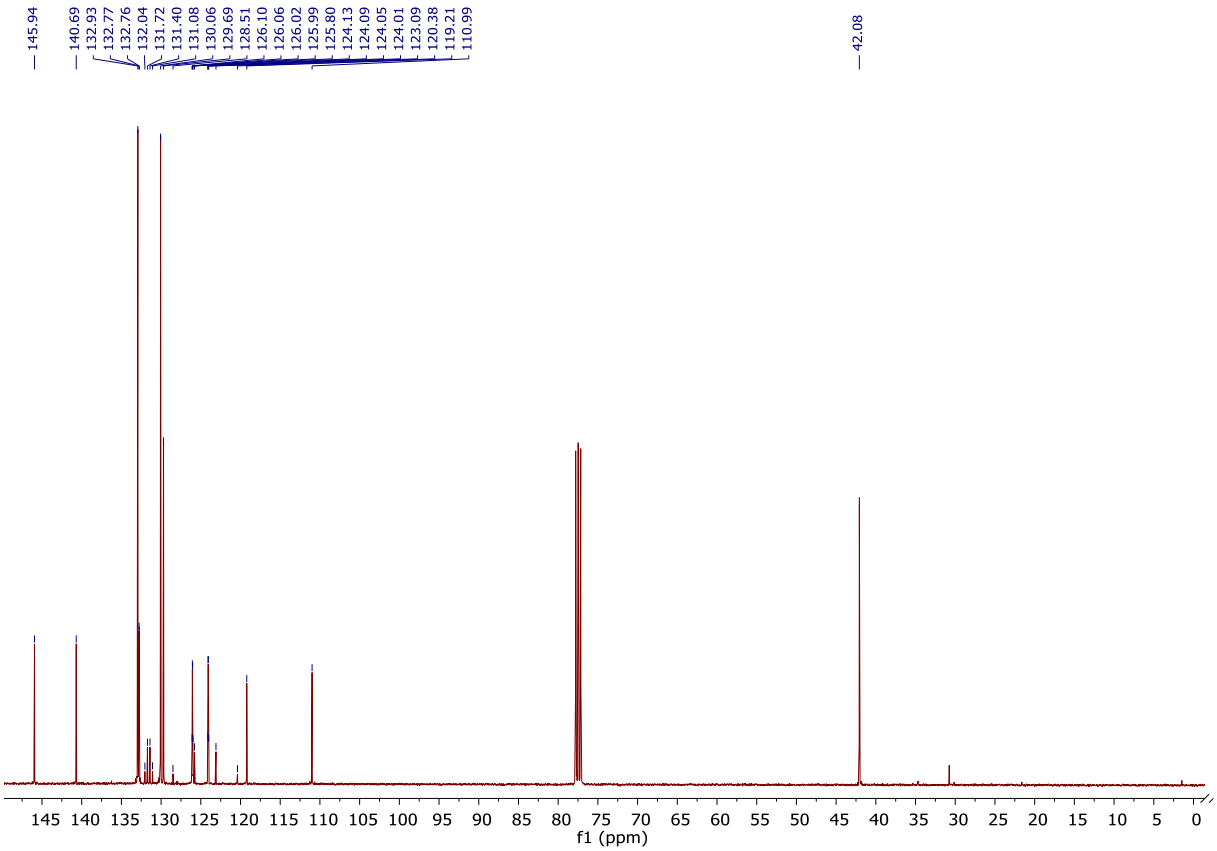






NMR-Spectra of 4-(3-(trifluoromethyl)benzyl)benzonitrile (4e)




145.94
140.69
132.93
132.77
132.76
132.04
131.72
131.40
131.08
130.06
129.69
128.51
126.10
126.06
126.02
125.99
125.80
124.13
124.09
124.05
124.01
123.09
120.38
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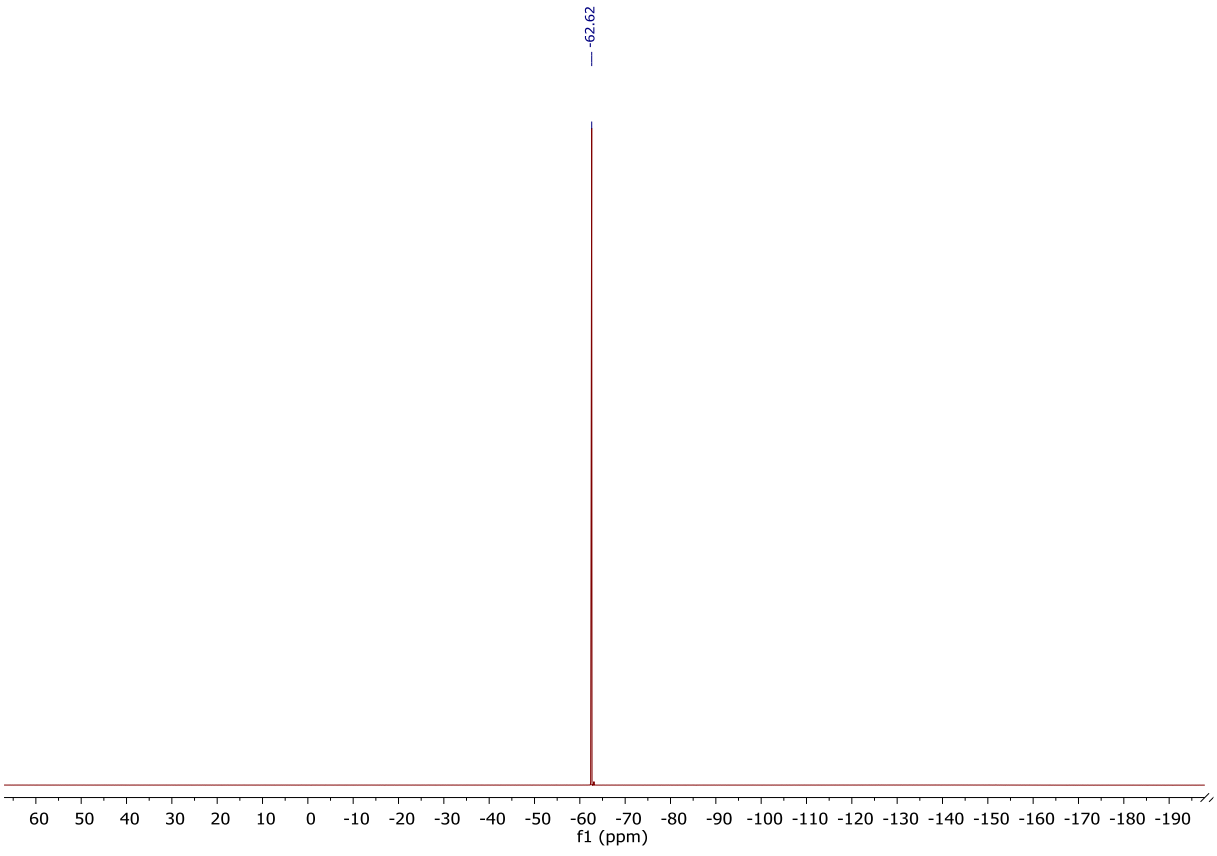
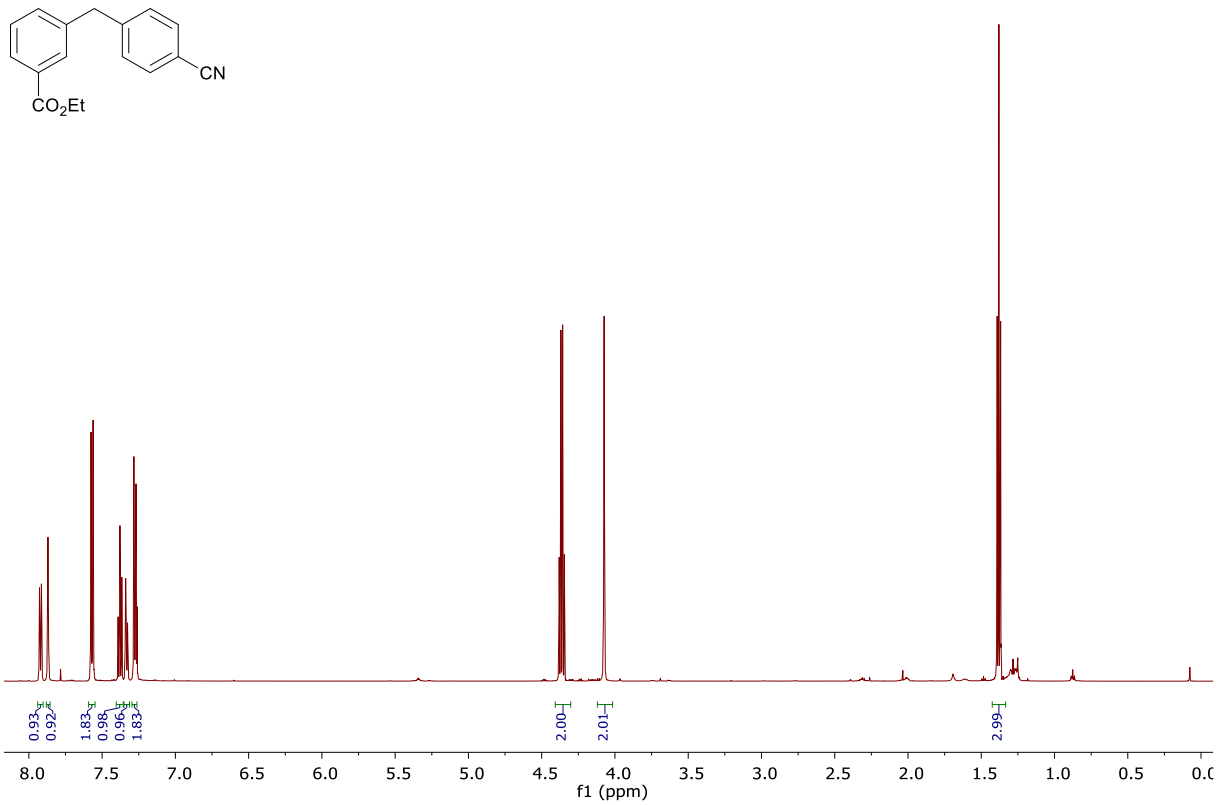
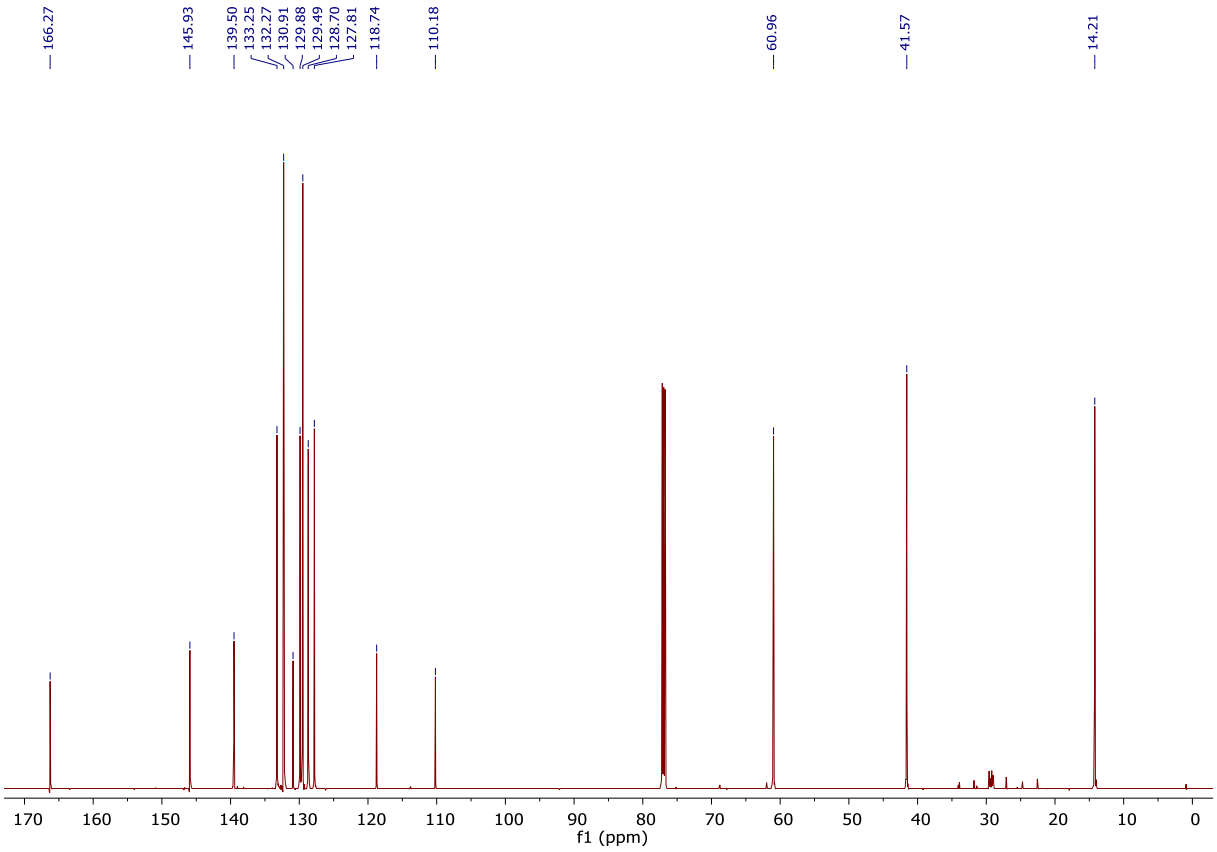
110.99
42.08
145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0
f1 (ppm)

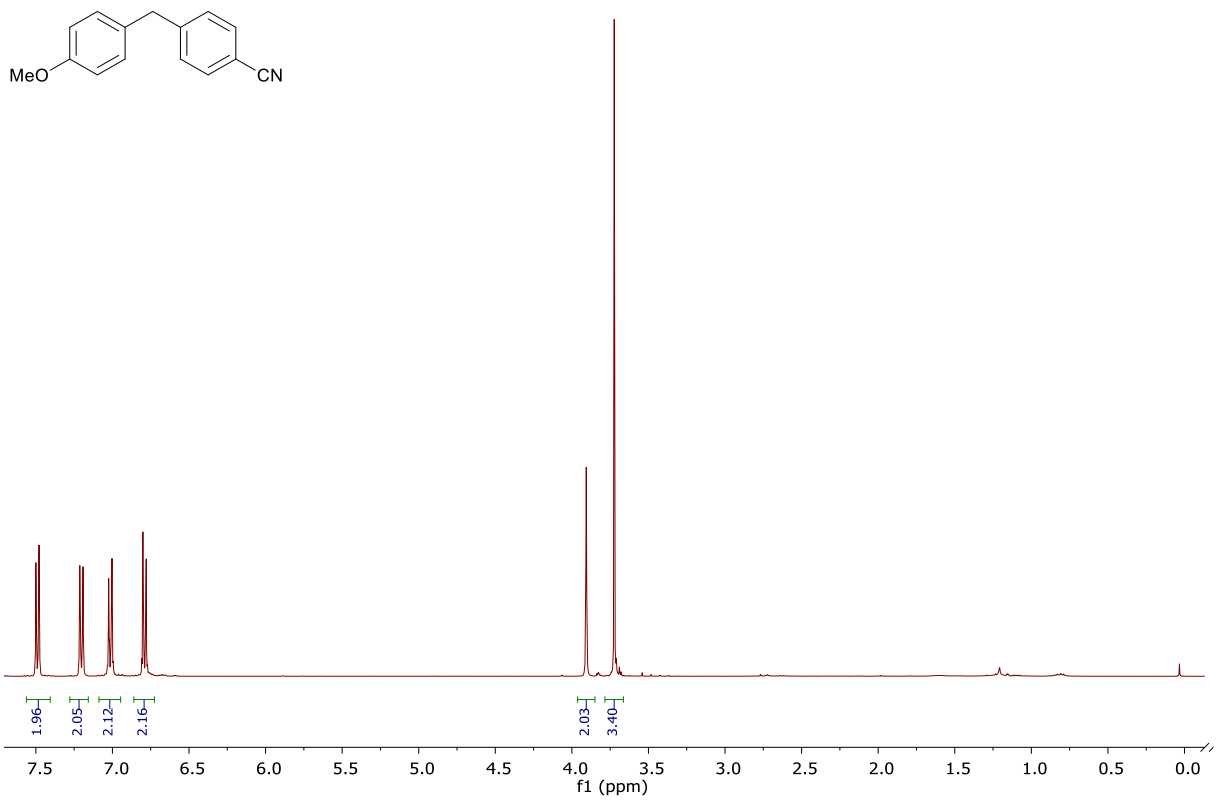

-62.62
60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

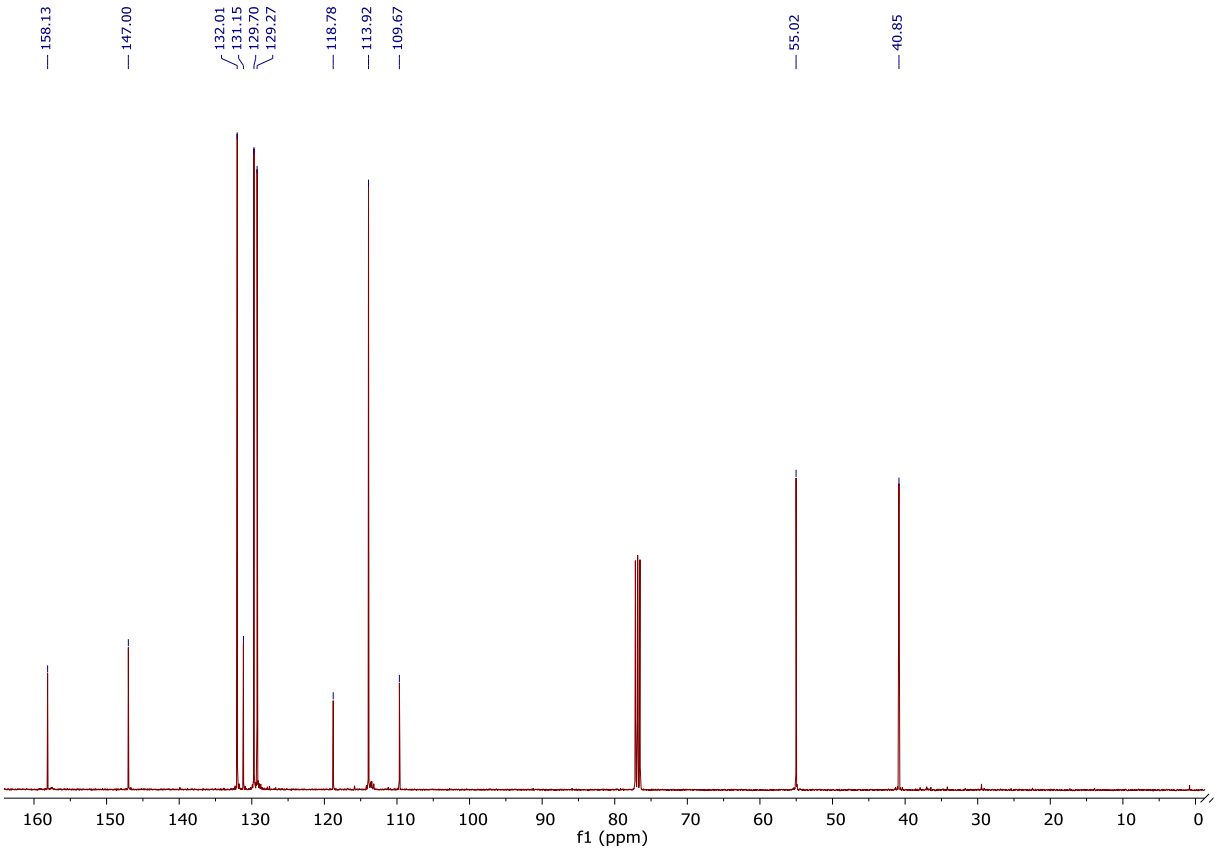
NMR-Spectra of ethyl 3-(4-cyanobenzyl)benzoate (4f)



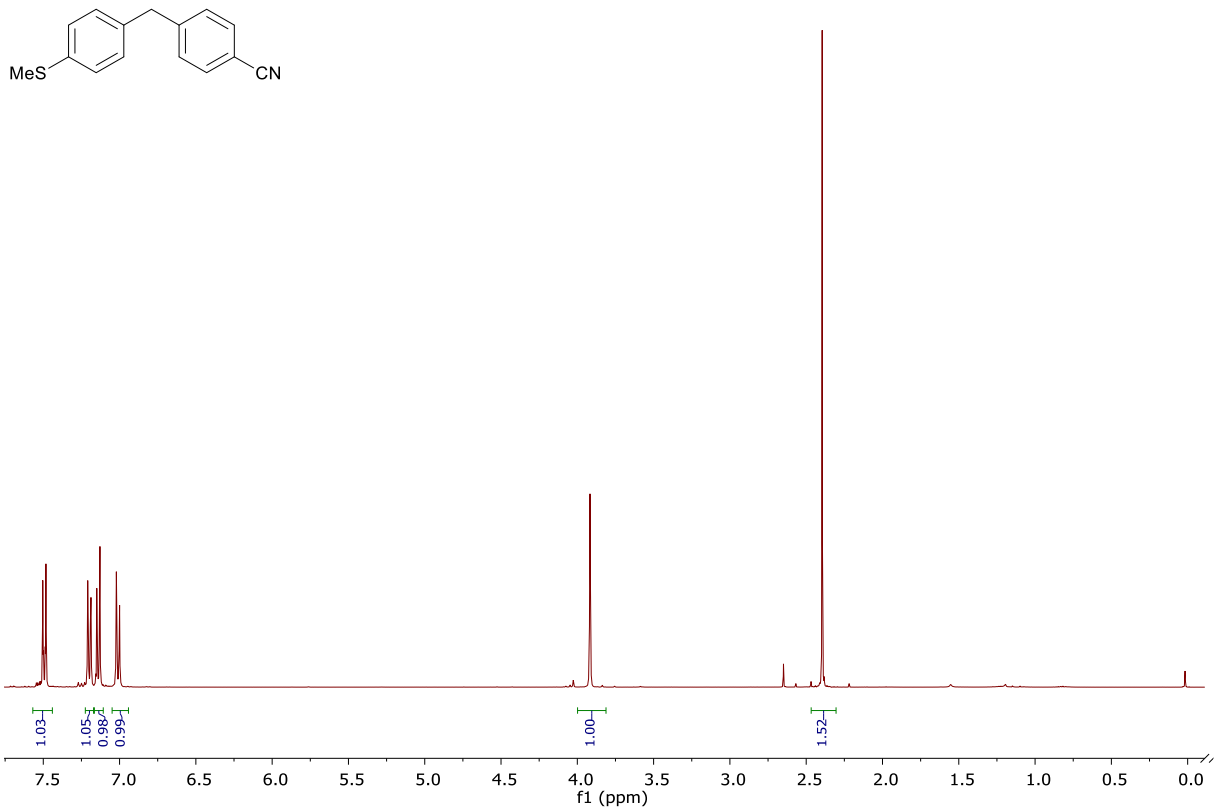


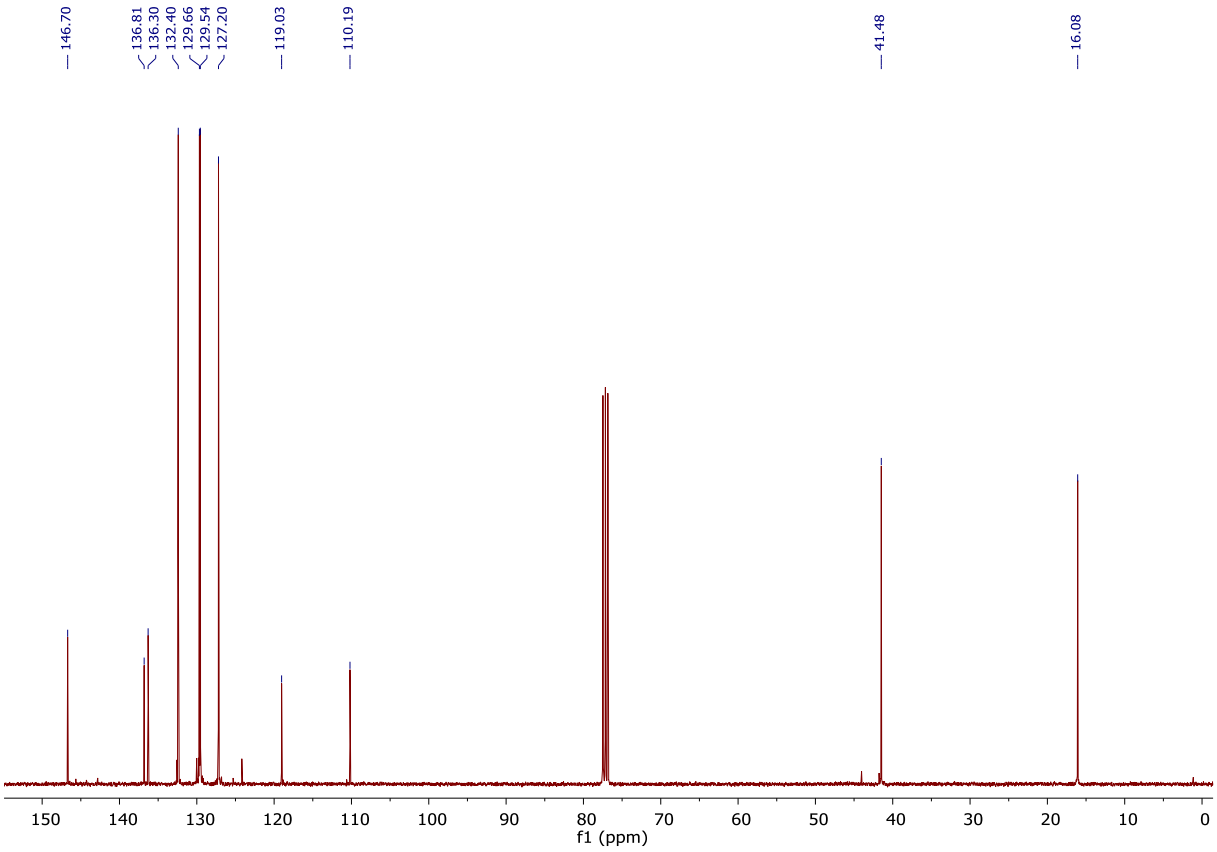
NMR-Spectra of 4-(4-methoxybenzyl)benzonitrile (4g)



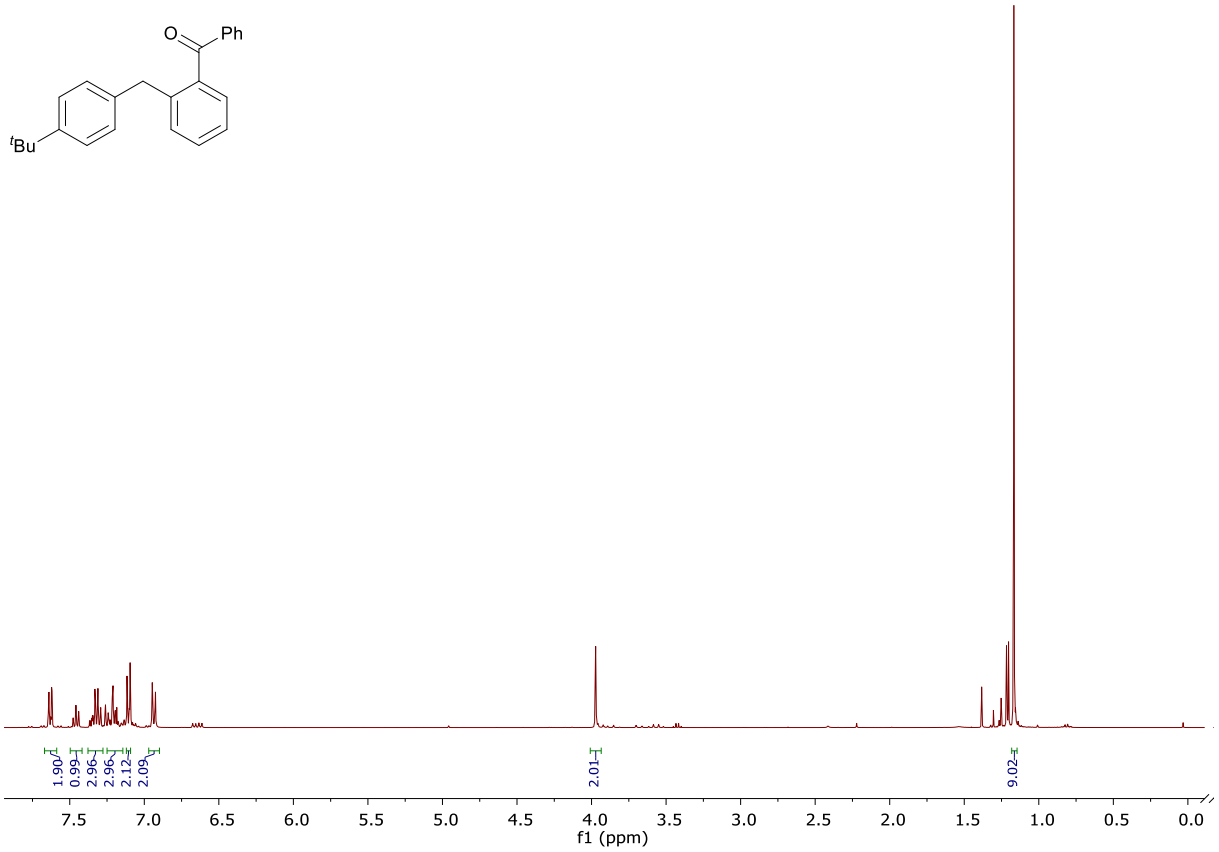


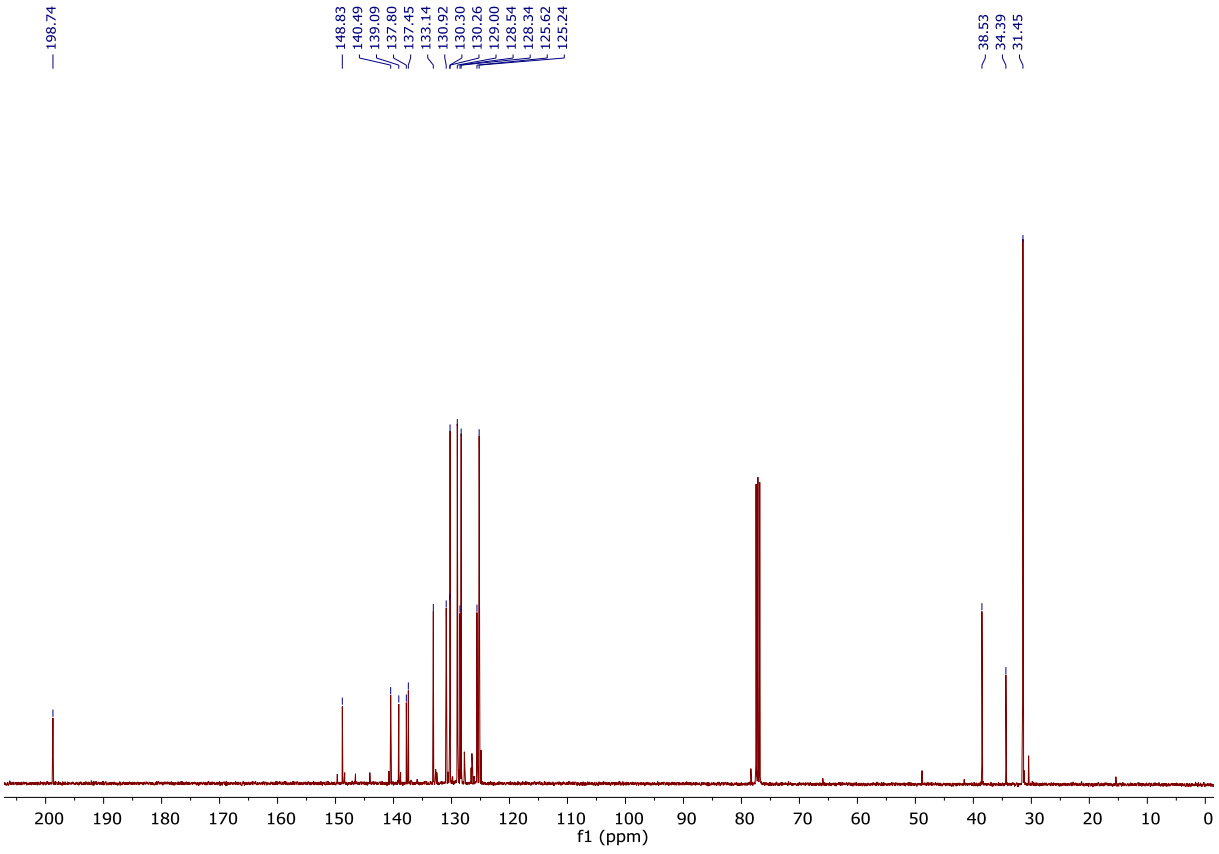
NMR-Spectra of 4-(4-(methylthio)benzyl)benzonitrile (4h)



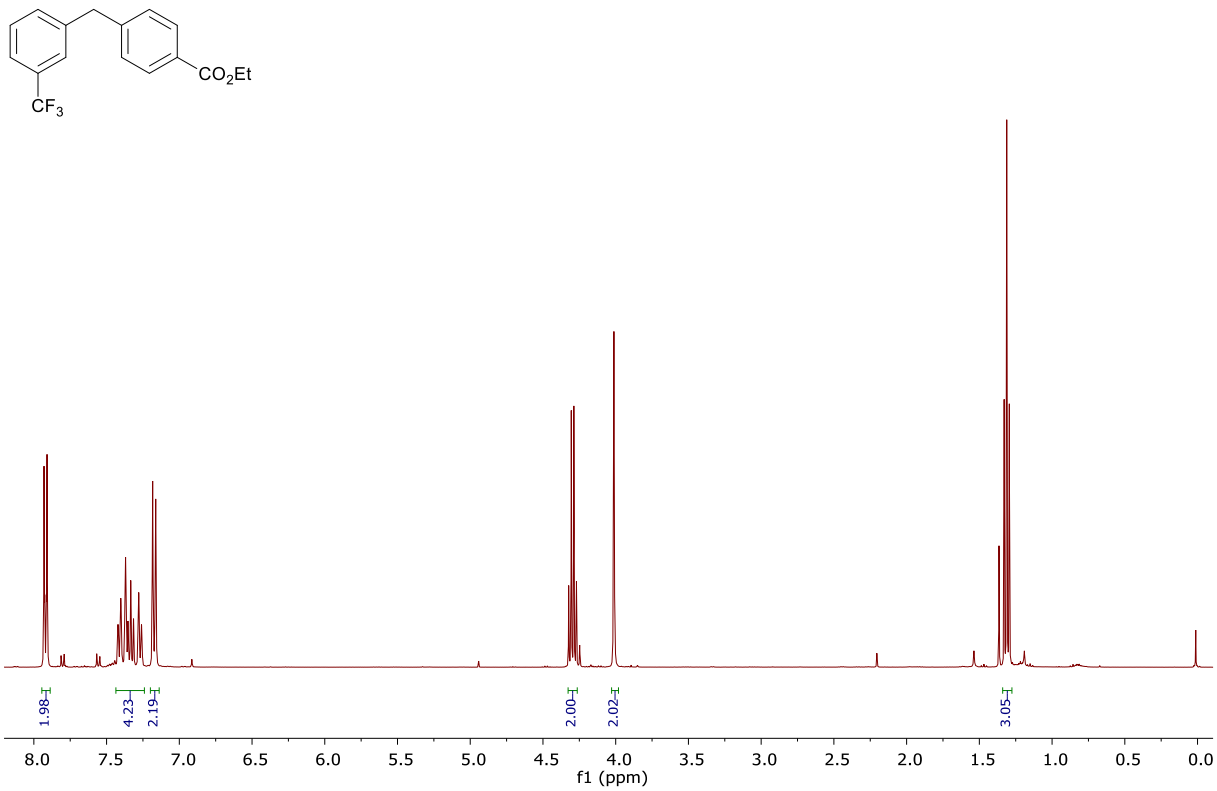


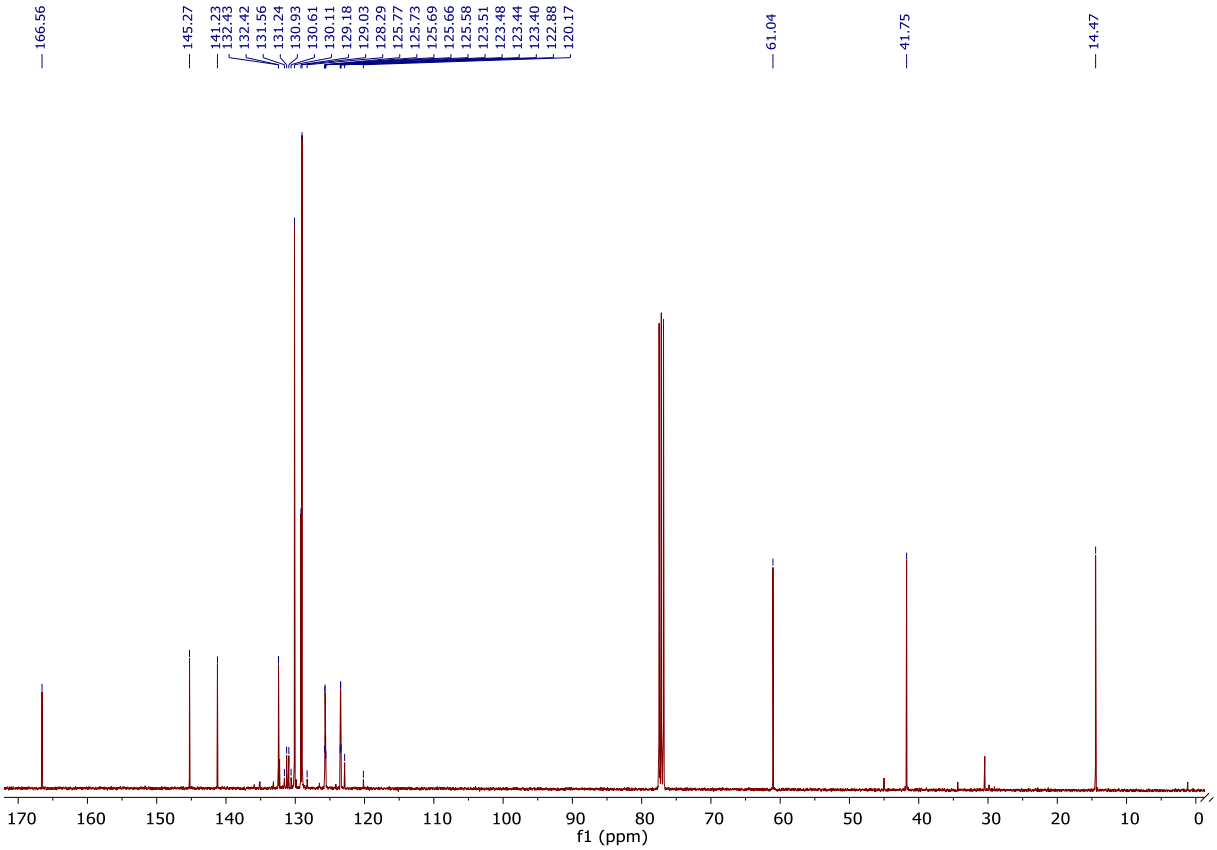
NMR-Spectra of (2-(4-(*tert*-butyl)benzyl)phenyl)(phenyl)methanone (5a)

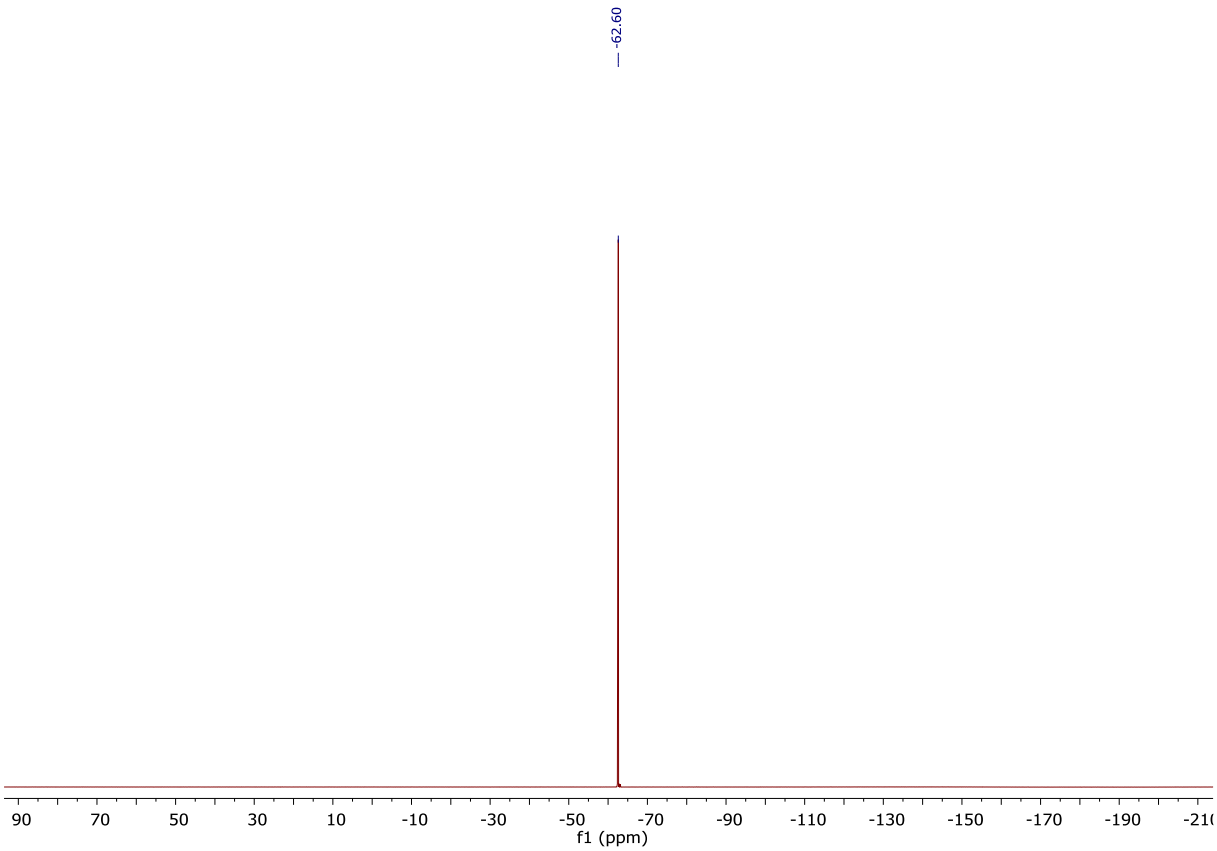




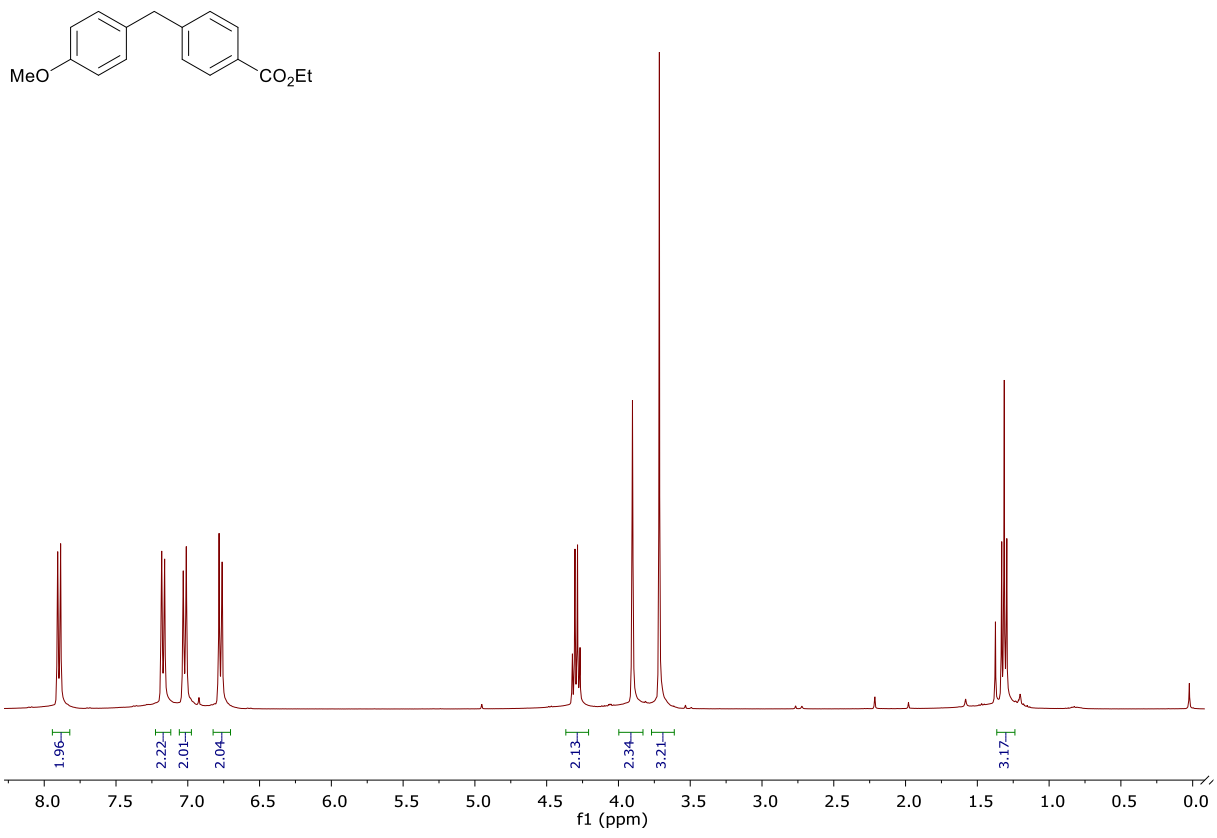
NMR-Spectra of ethyl 4-(3-(trifluoromethyl)benzyl)benzoate (5b)

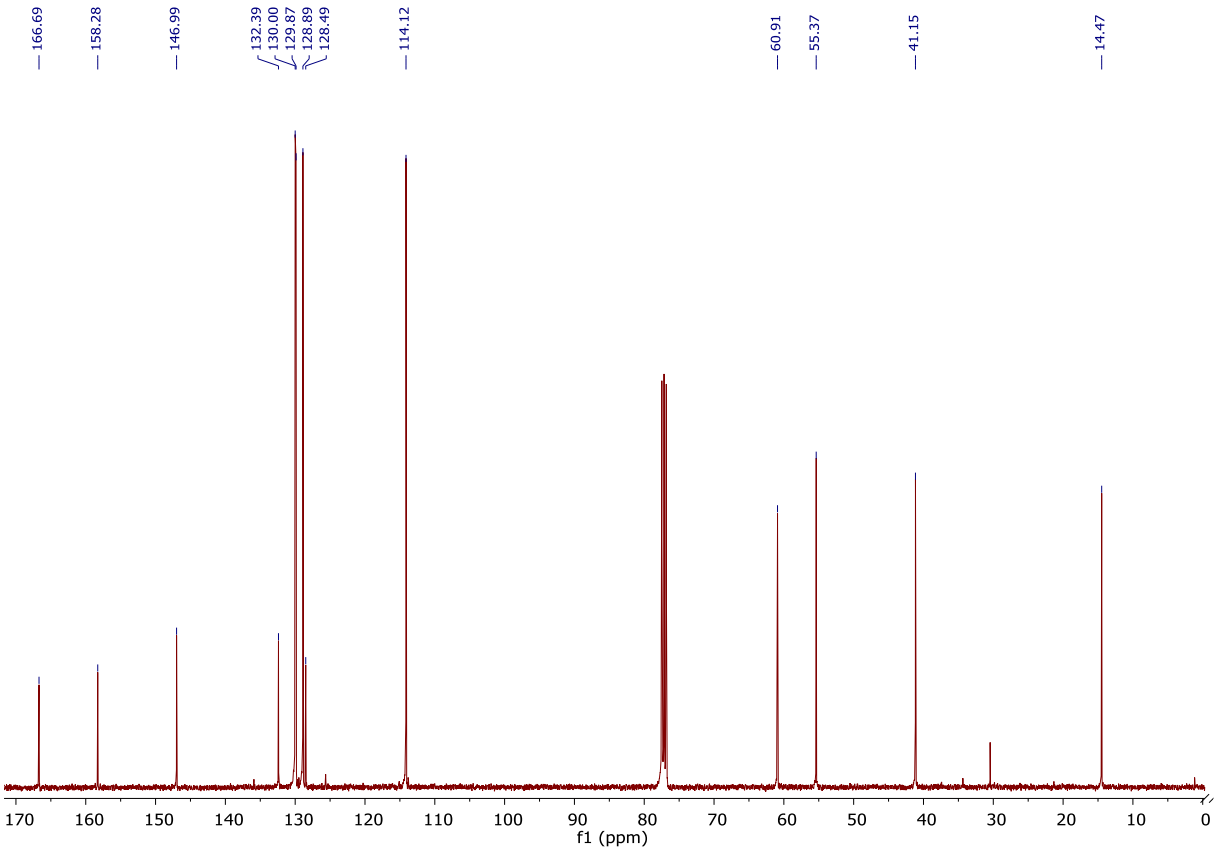




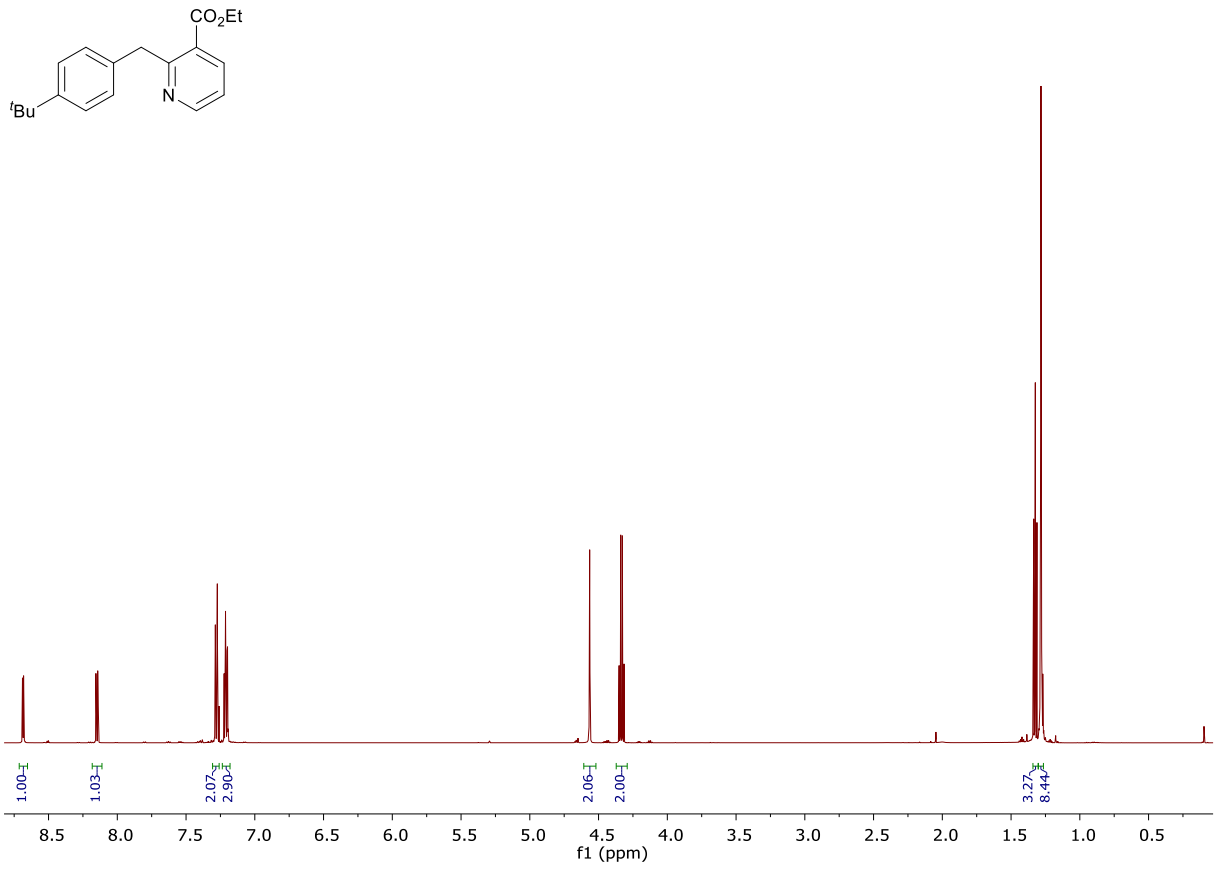


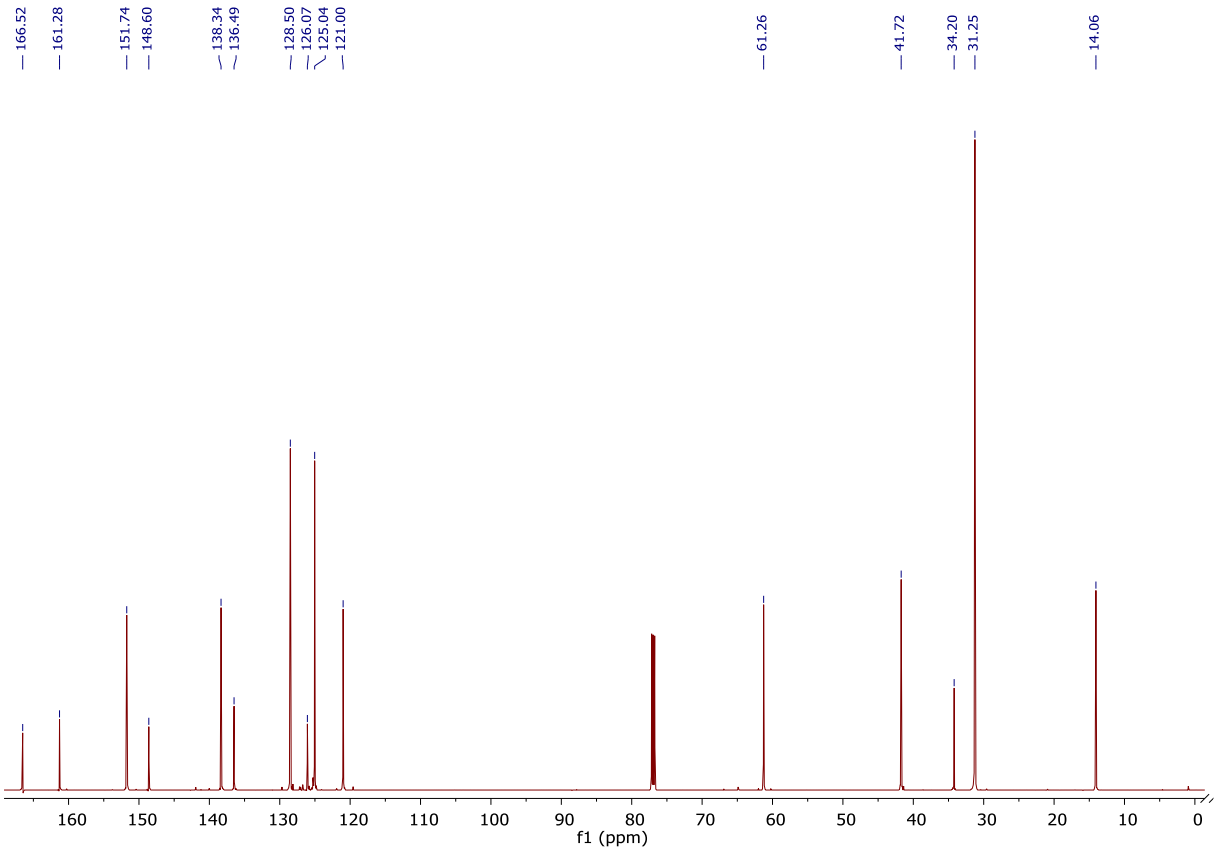
NMR-Spectra of ethyl 4-(4-methoxybenzyl)benzoate (5c)



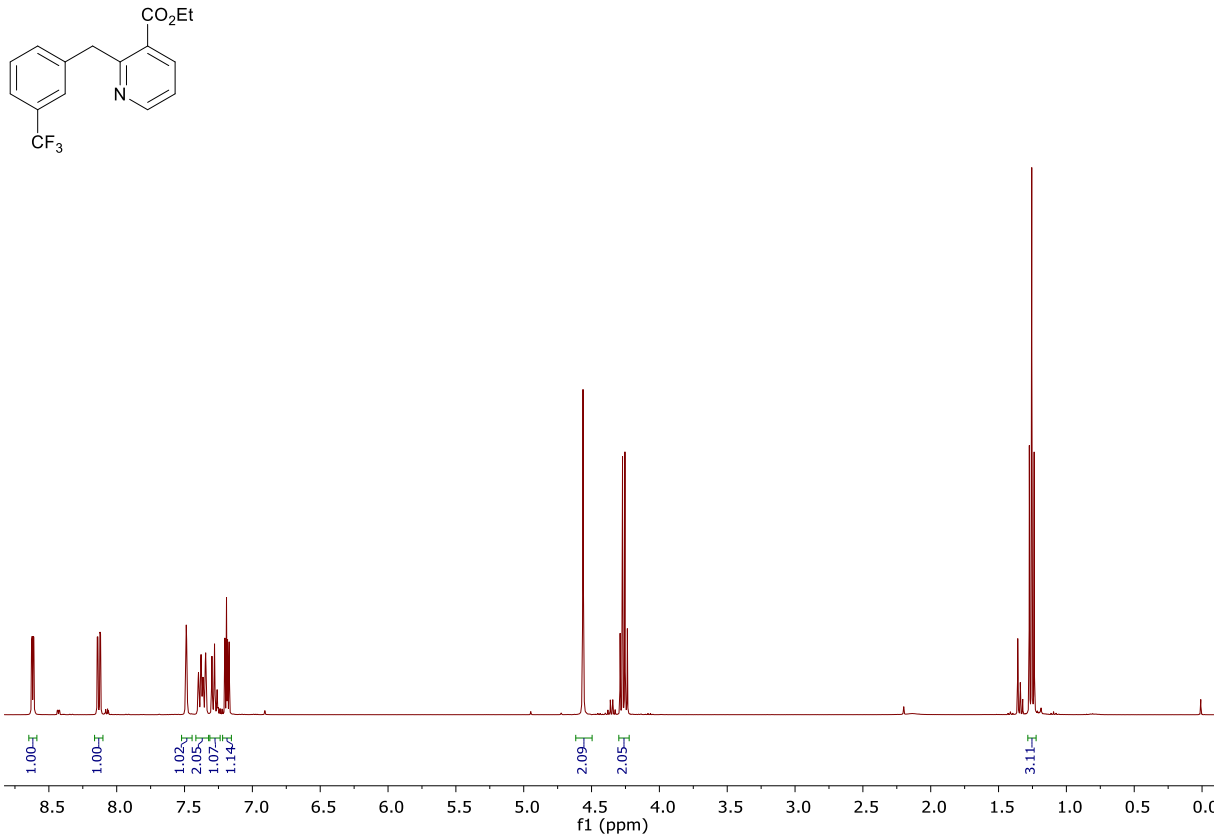


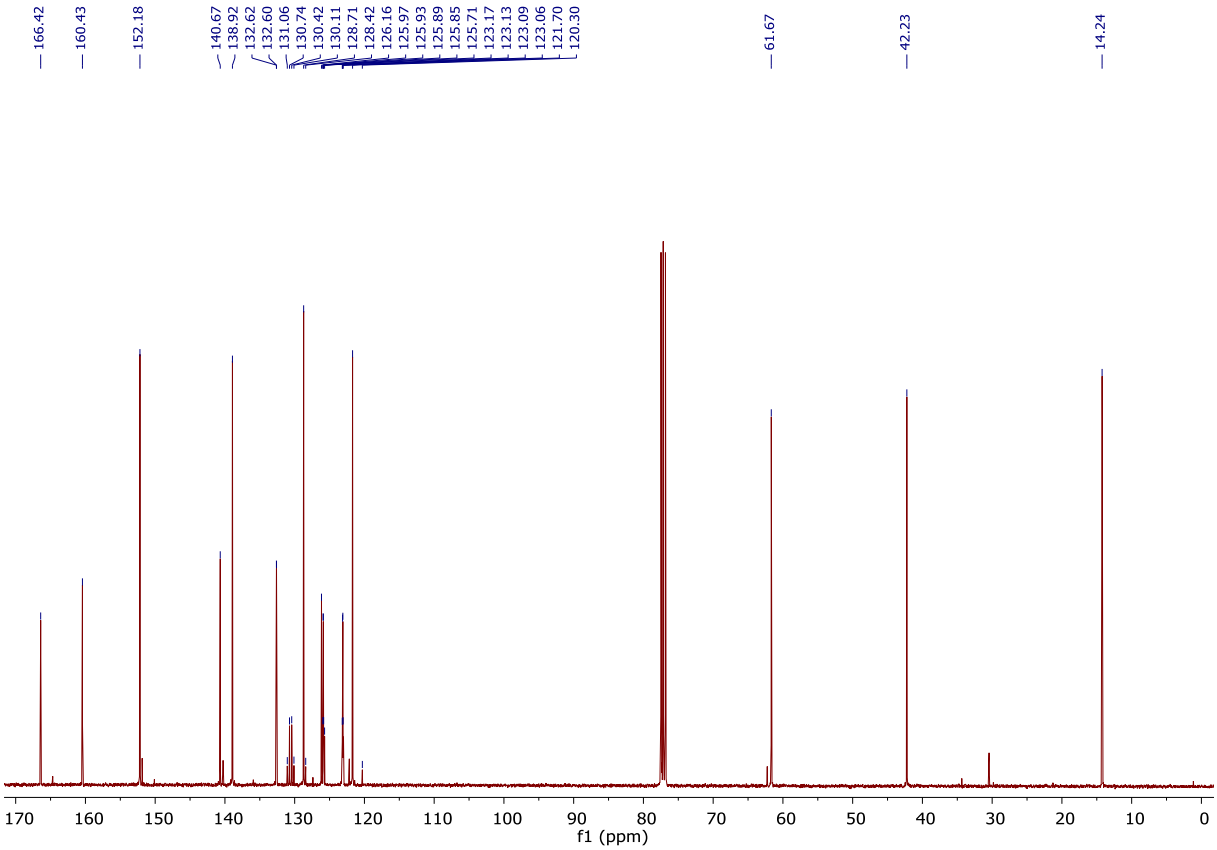
NMR-Spectra of ethyl 2-(4-(*tert*-butyl)benzyl)nicotinate (5d)

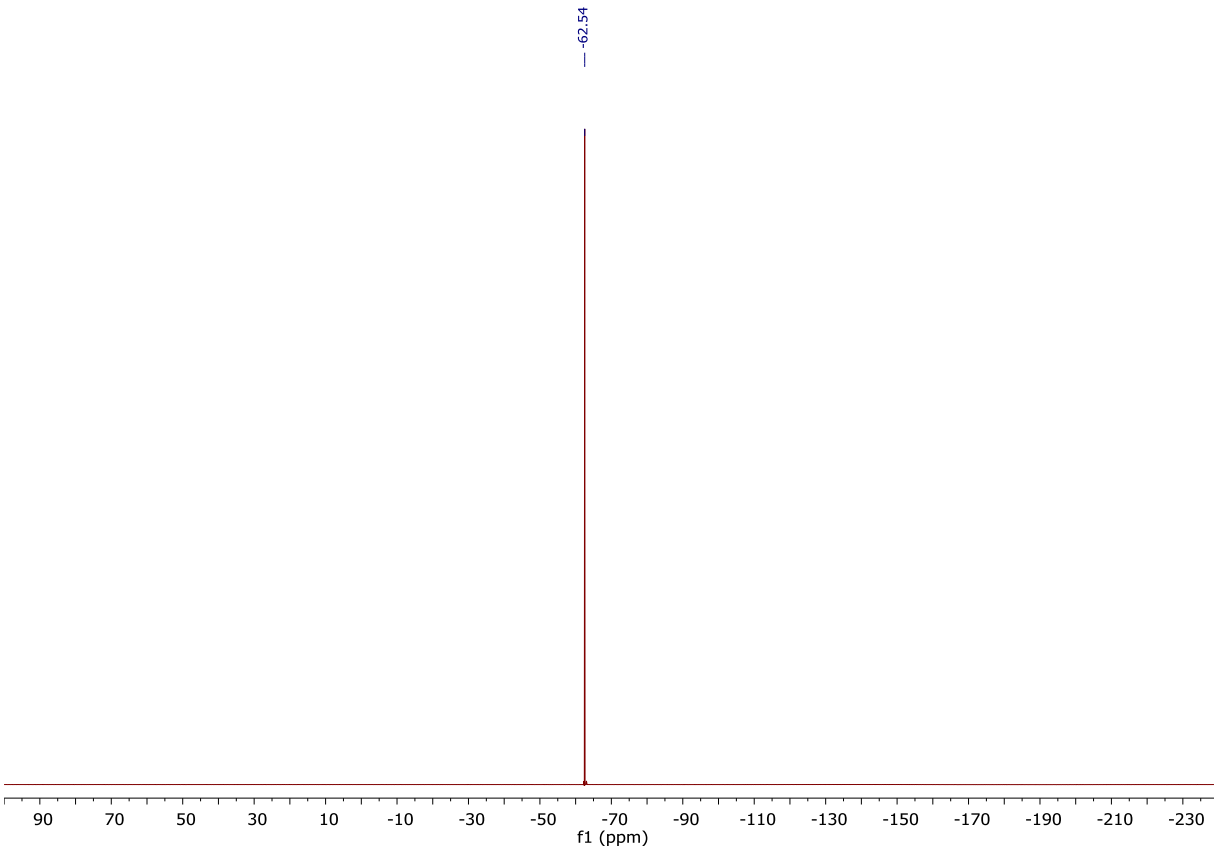




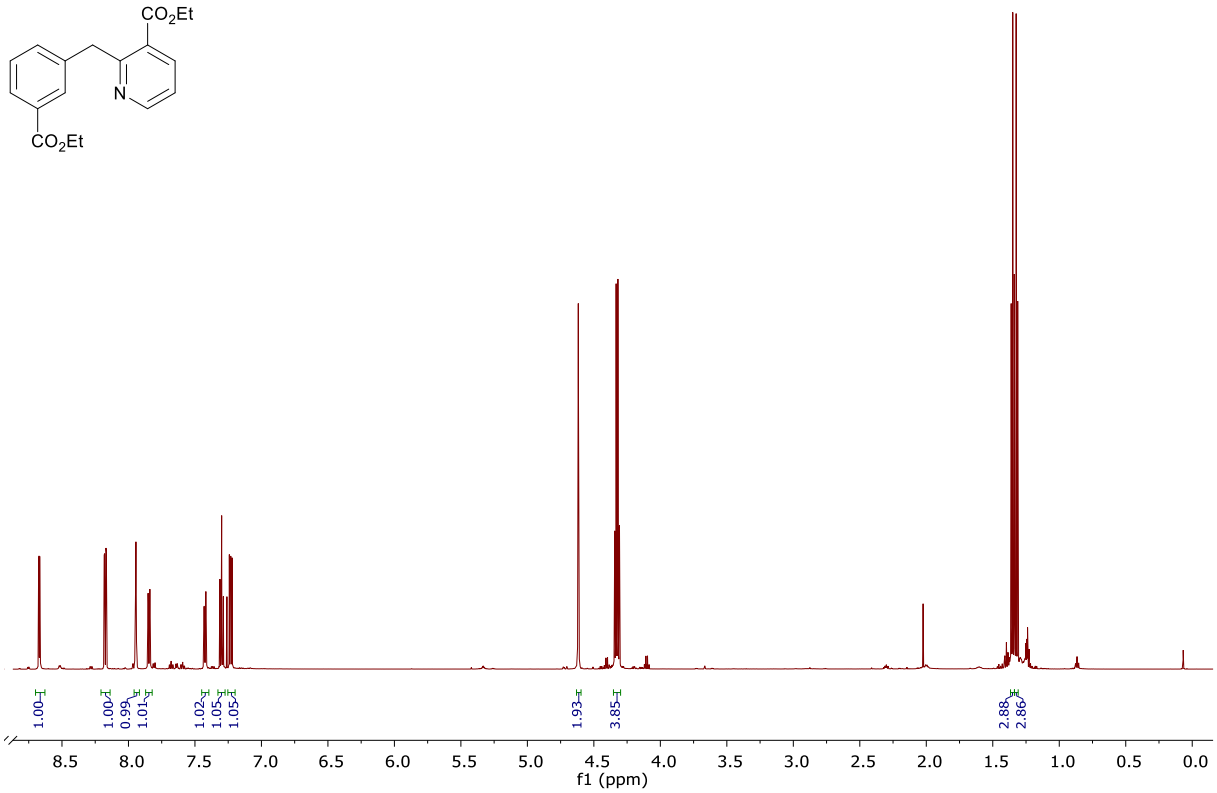
NMR-Spectra of ethyl 2-(3-(trifluoromethyl)benzyl)nicotinate (5e)

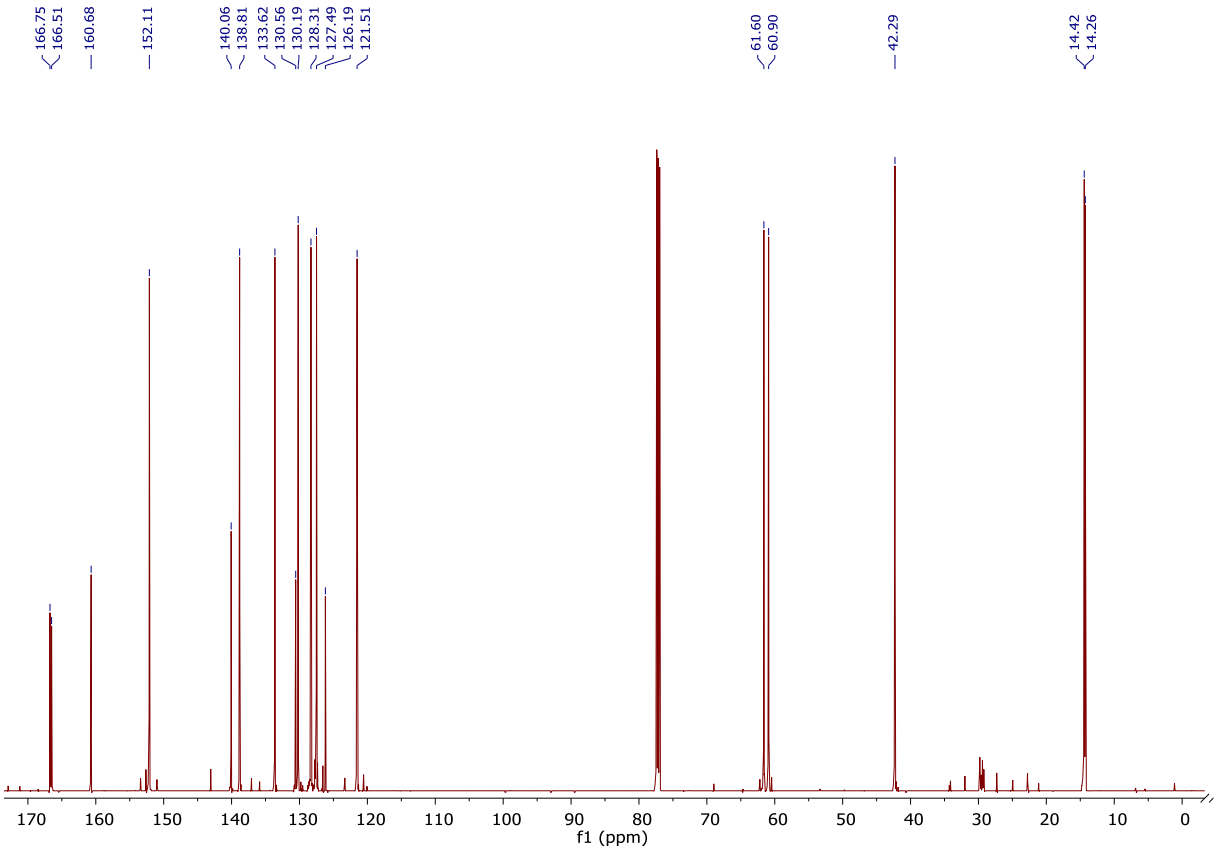



166.42
160.43
152.18
140.67
138.92
132.62
132.60
131.06
130.74
130.42
130.11
128.71
128.42
126.16
125.97
125.93
125.89
125.85
125.71
123.17
123.13
123.09
123.06
121.70
120.30
61.67
42.23
14.24
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

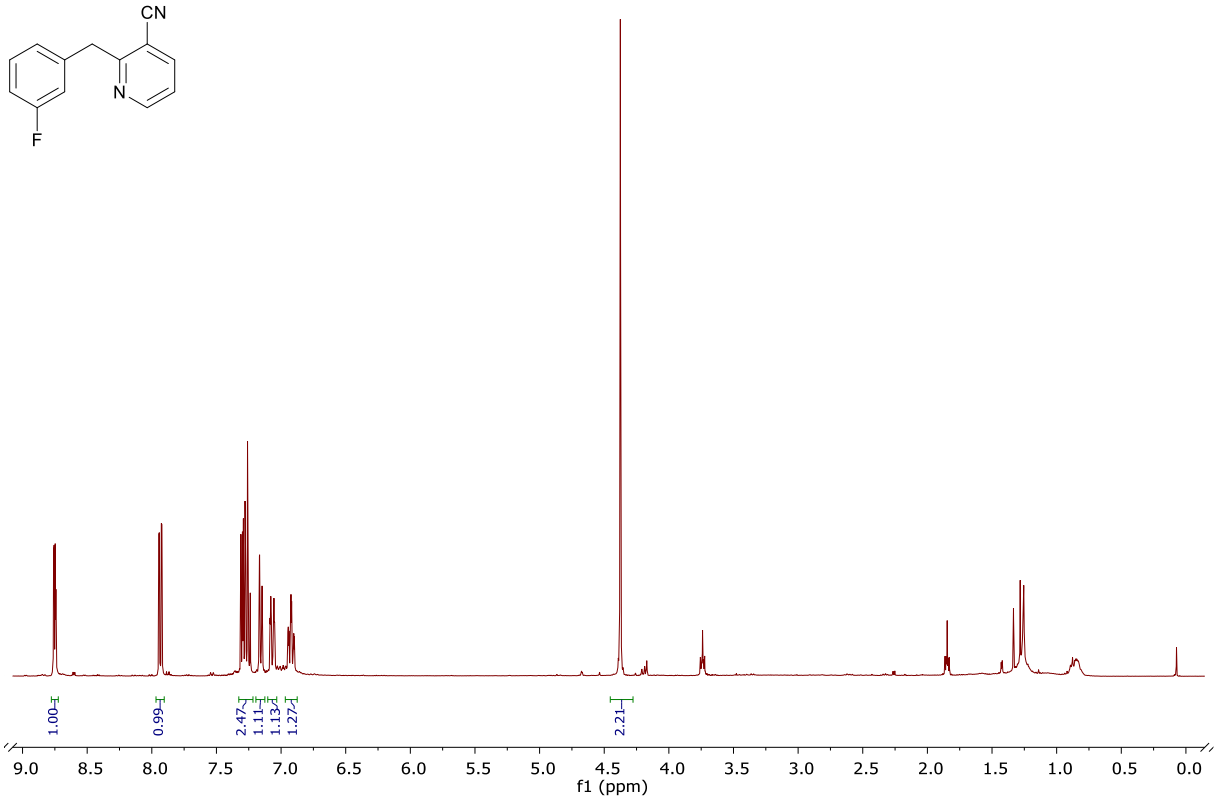

-62.54
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
-230
f1 (ppm)

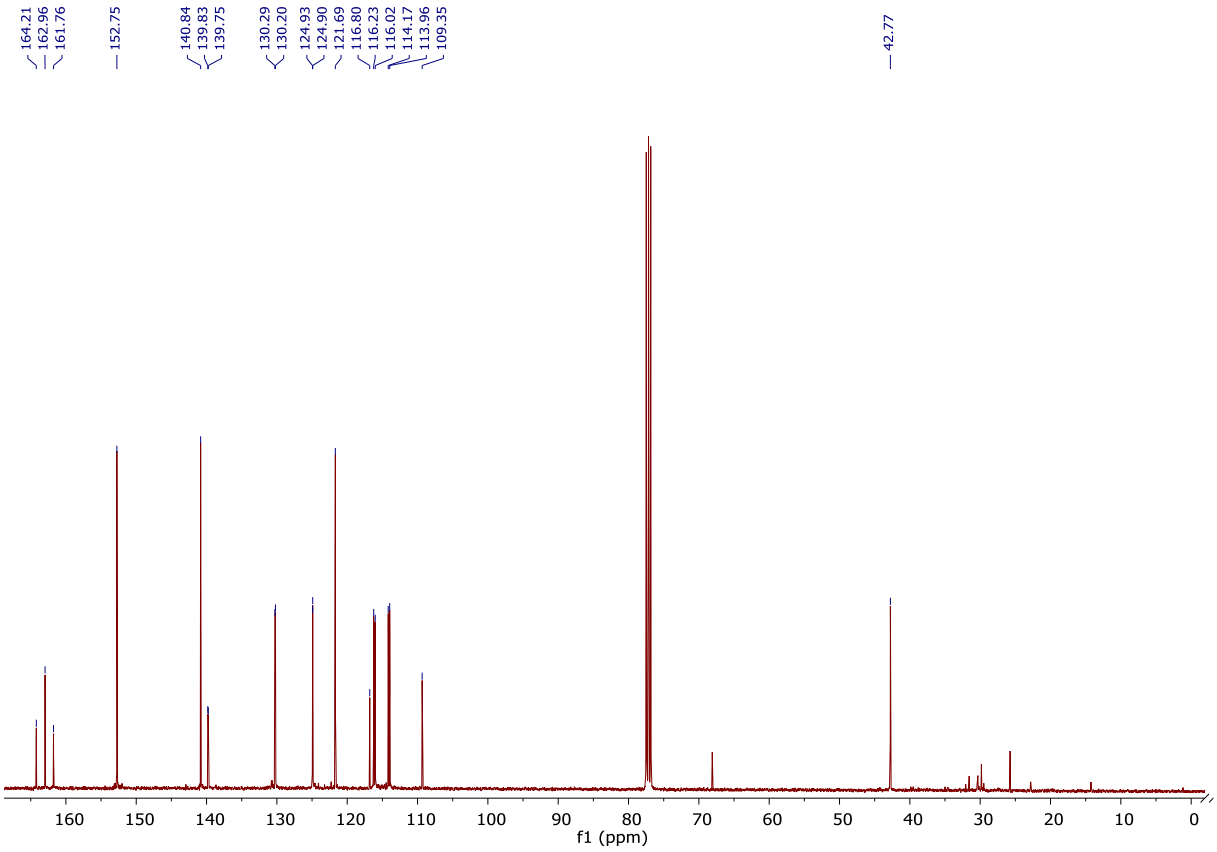
NMR-Spectra of ethyl 2-(3-(ethoxycarbonyl)benzyl)nicotinate (5f)

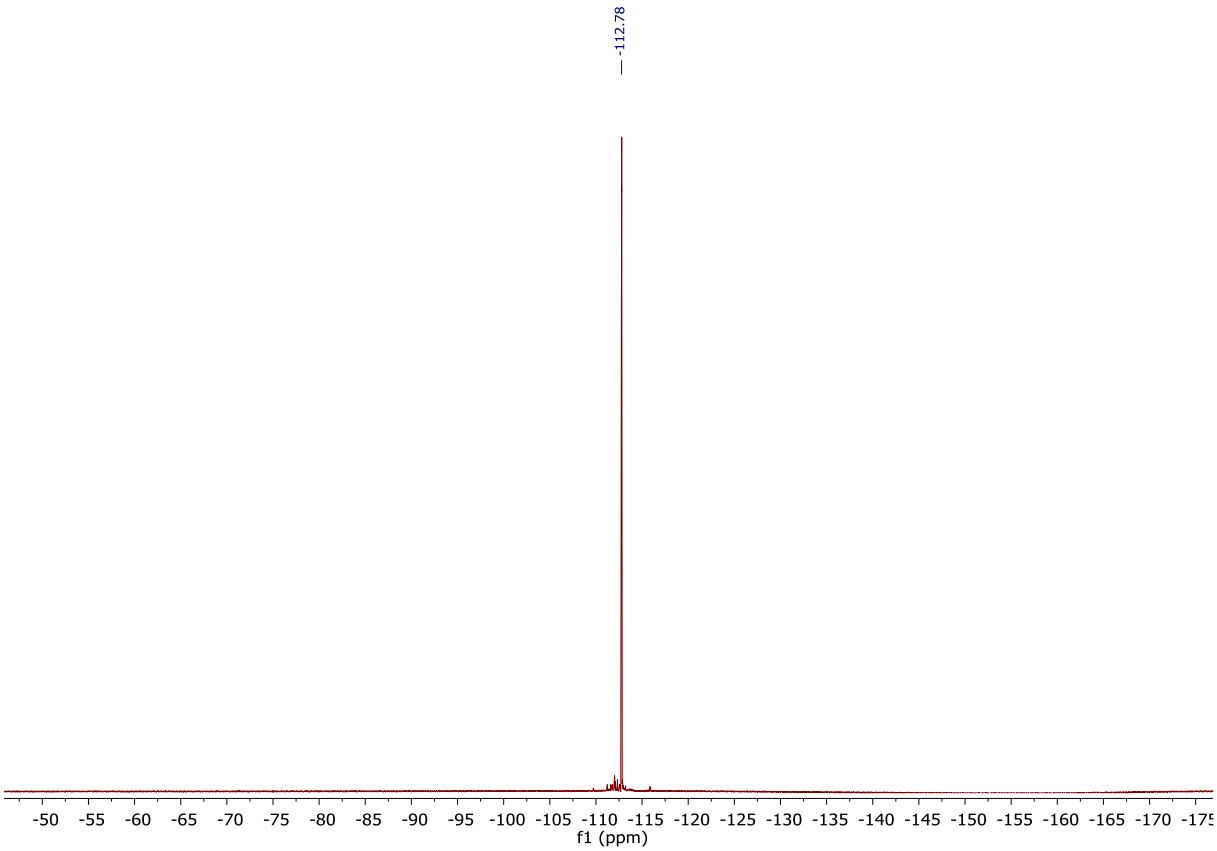




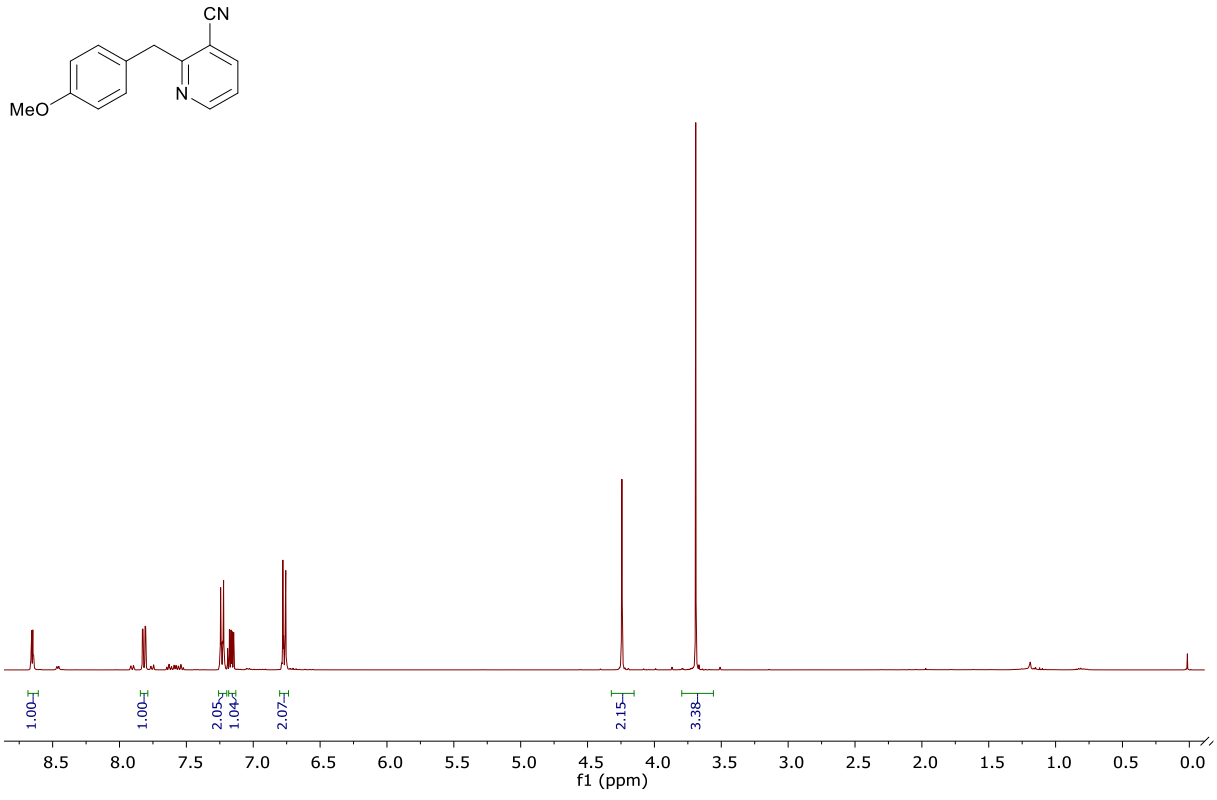
NMR-Spectra of 2-(3-fluorobenzyl)nicotinonitrile (5g)

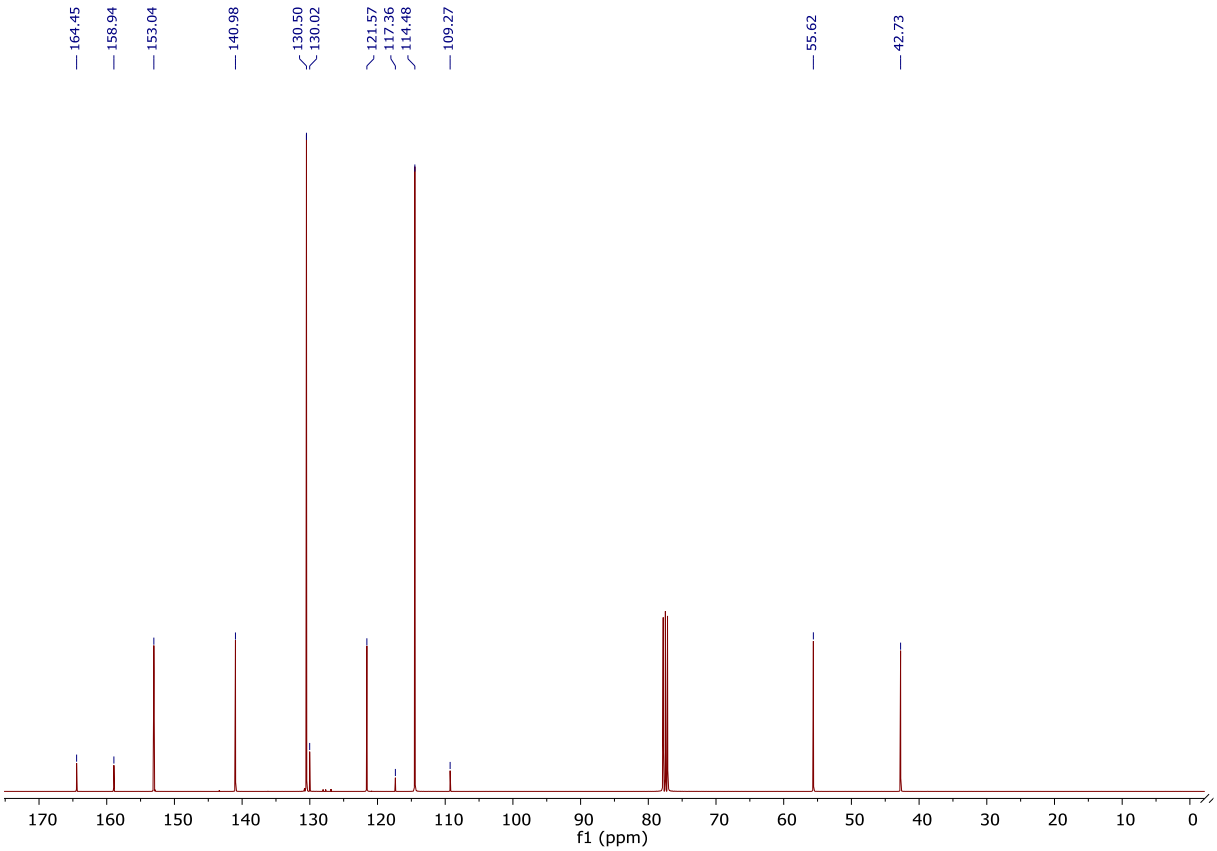




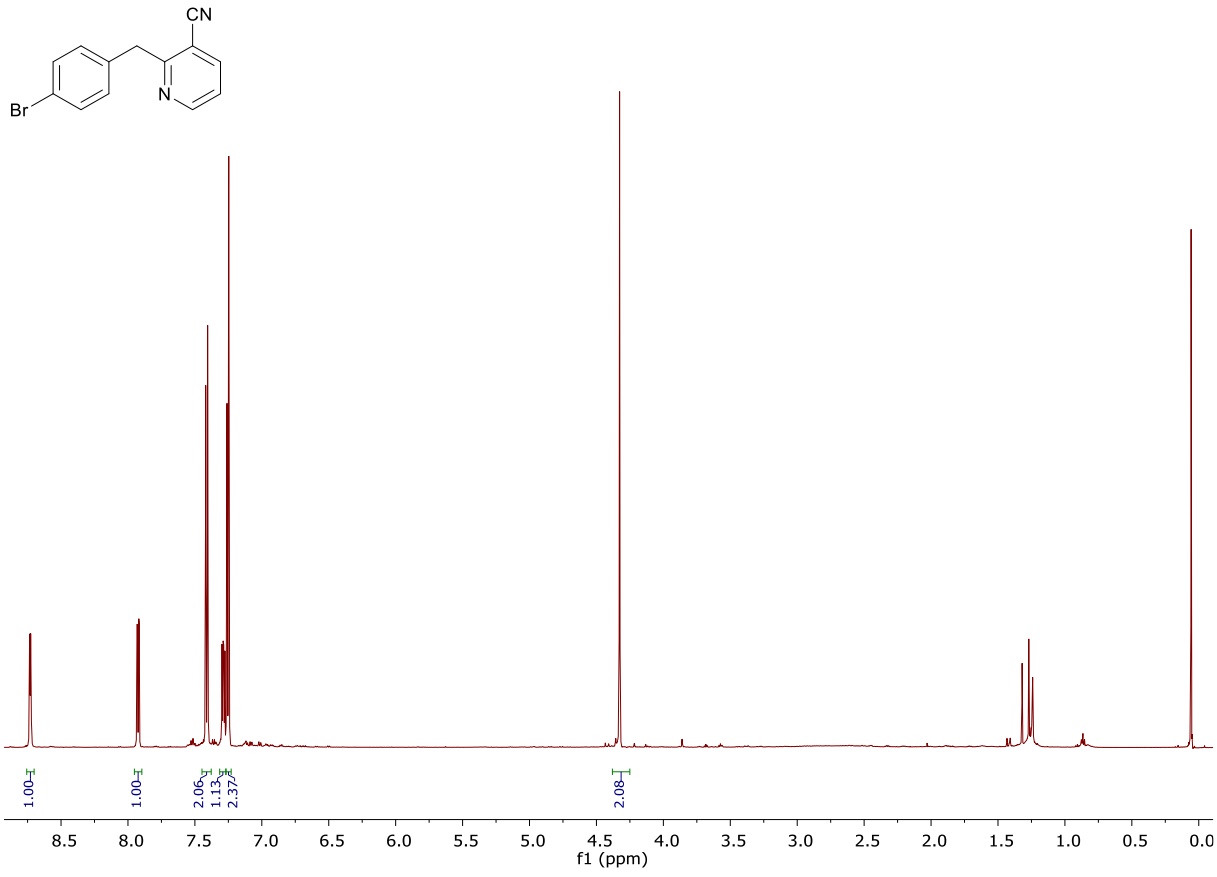


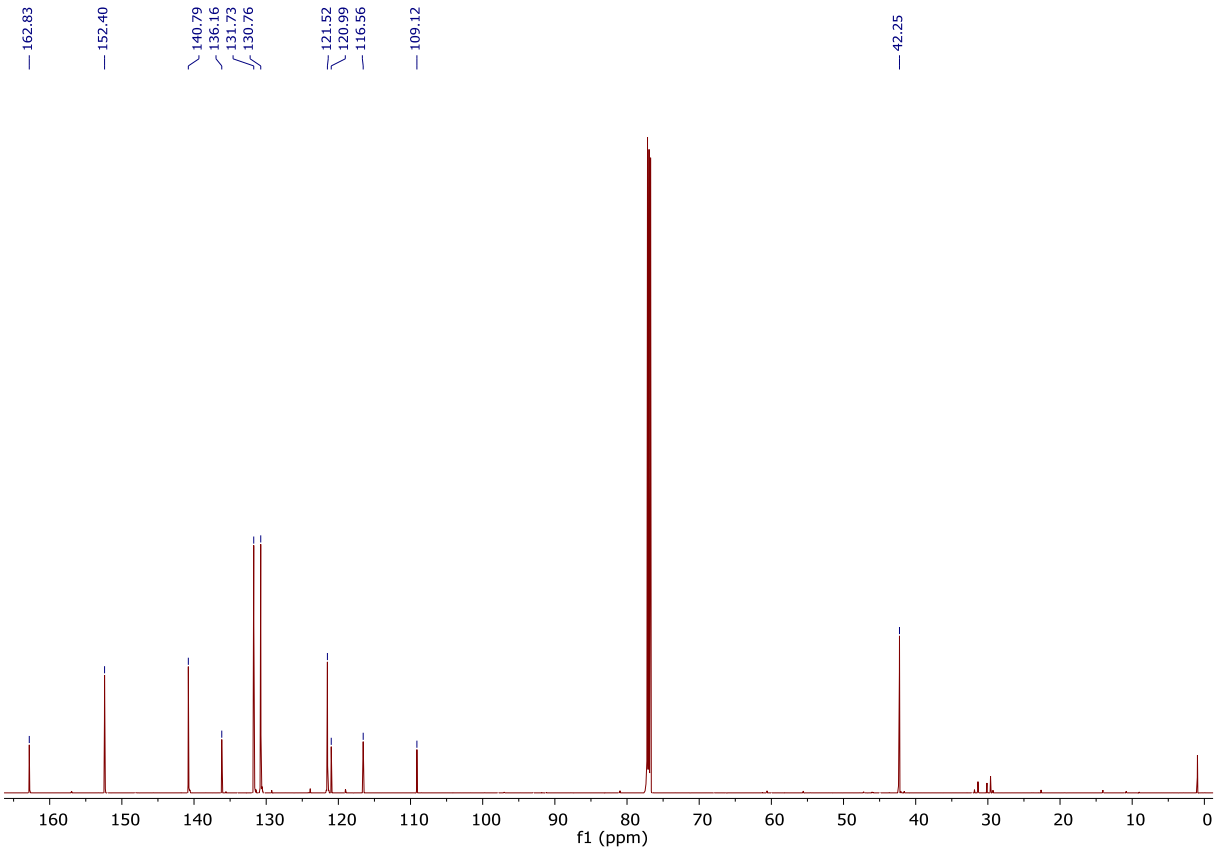
NMR-Spectra of 2-(4-methoxybenzyl)nicotinonitrile (5h)



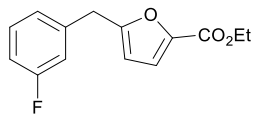


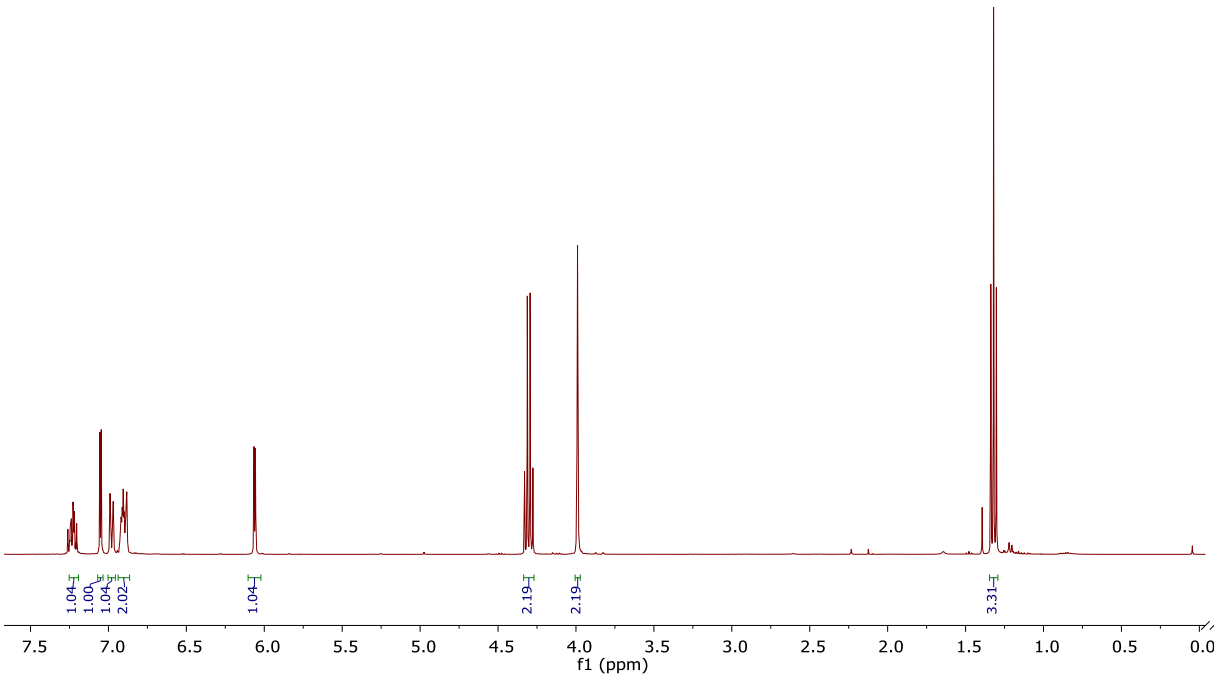
NMR-Spectra of 2-(4-bromobenzyl)nicotinonitrile (5i)

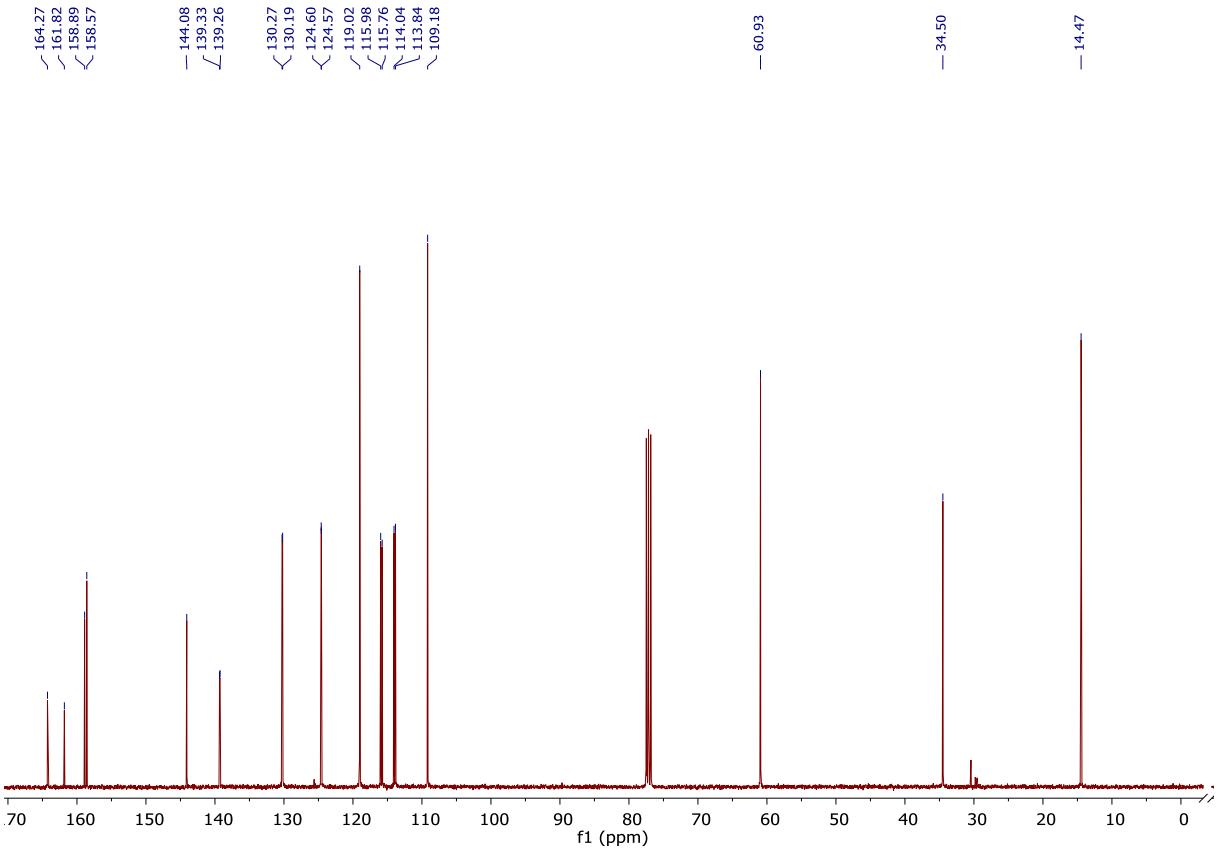


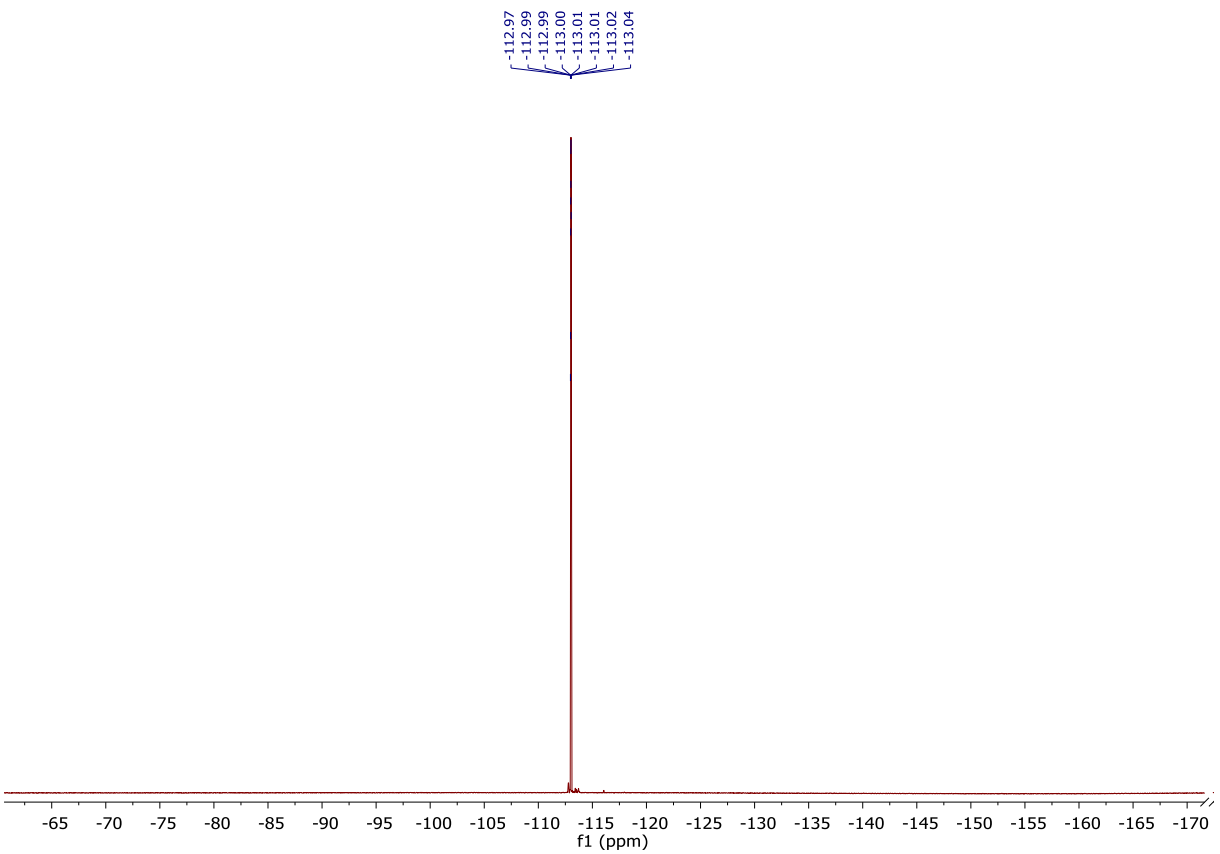


NMR-Spectra of ethyl 5-(3-fluorobenzyl)furan-2-carboxylate (5j)

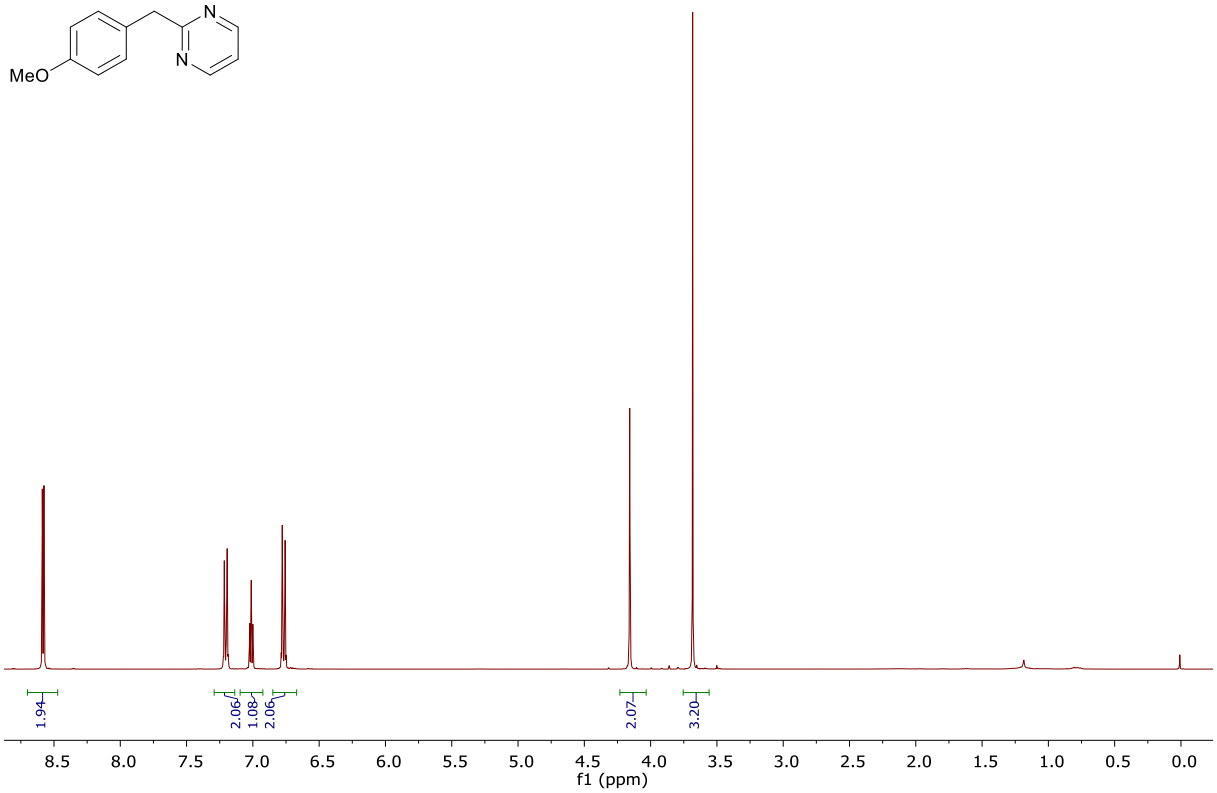


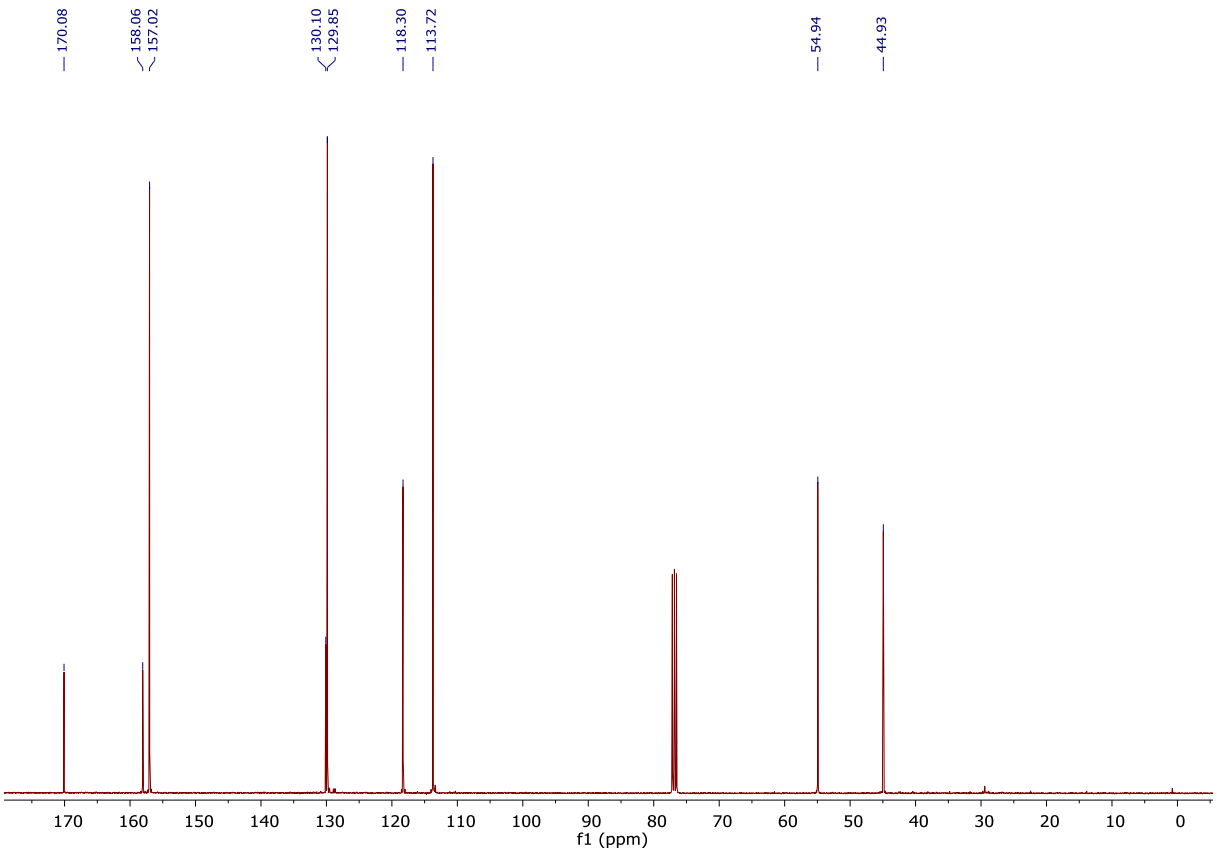



164.27
161.82
158.89
158.57
144.08
139.33
139.26
130.27
130.19
124.60
124.57
119.02
115.98
115.76
114.04
113.84
109.18
60.93
34.50
14.47
f1 (ppm)

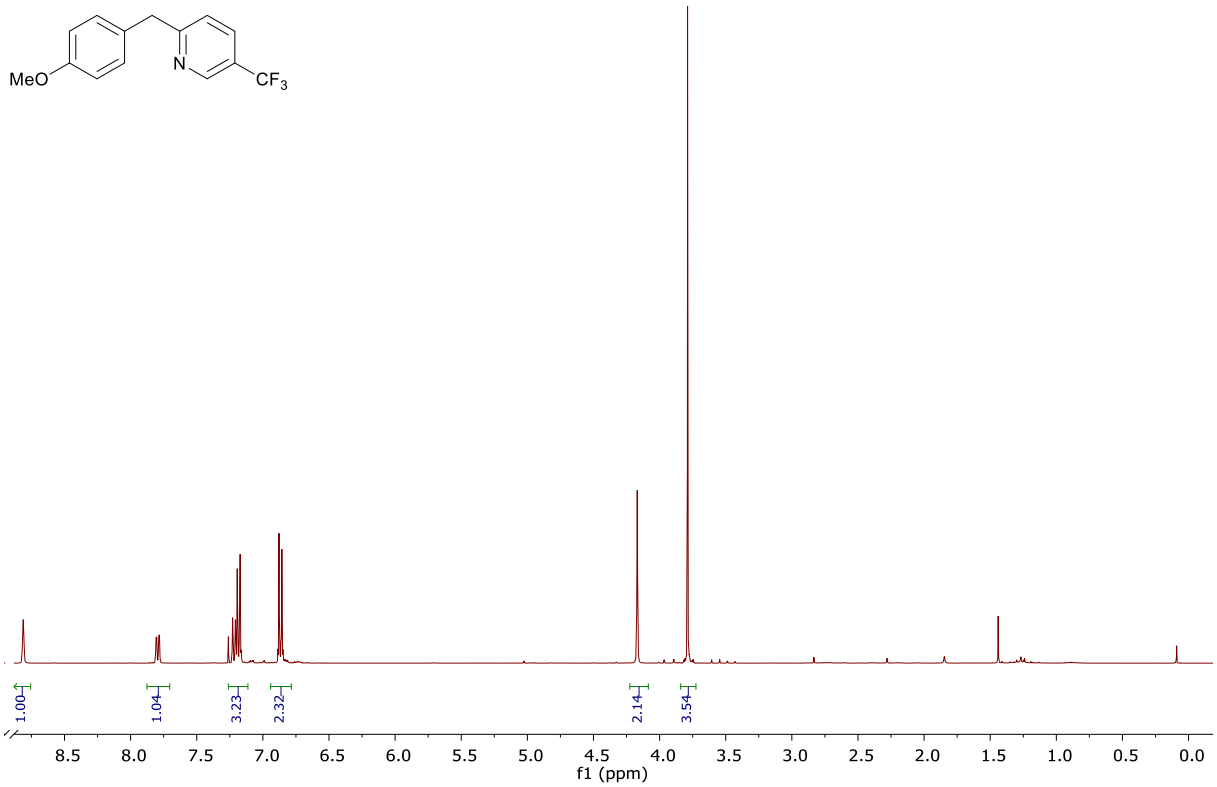

-112.97
-112.99
-112.99
-113.00
-113.01
-113.01
-113.02
-113.04
f1 (ppm)

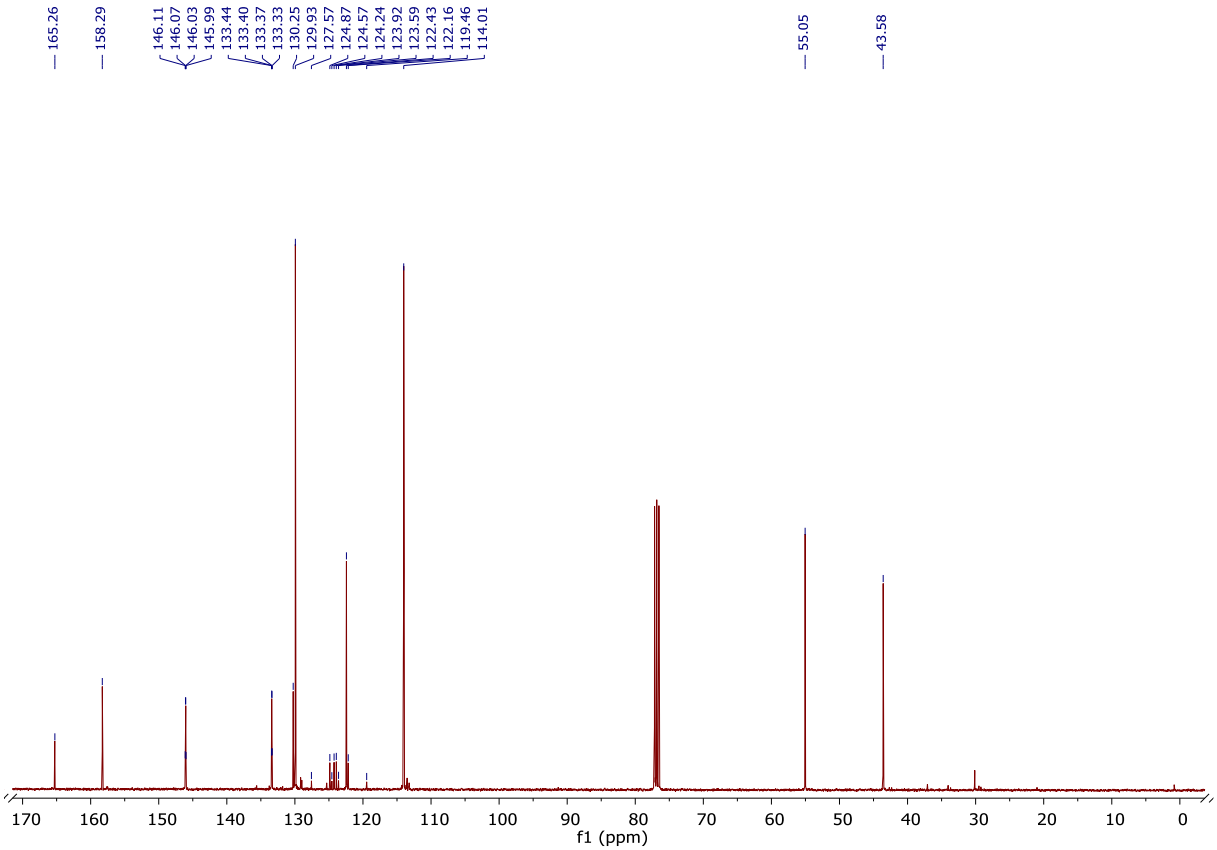
NMR-Spectra of 2-(4-methoxybenzyl)pyrimidine (6a)

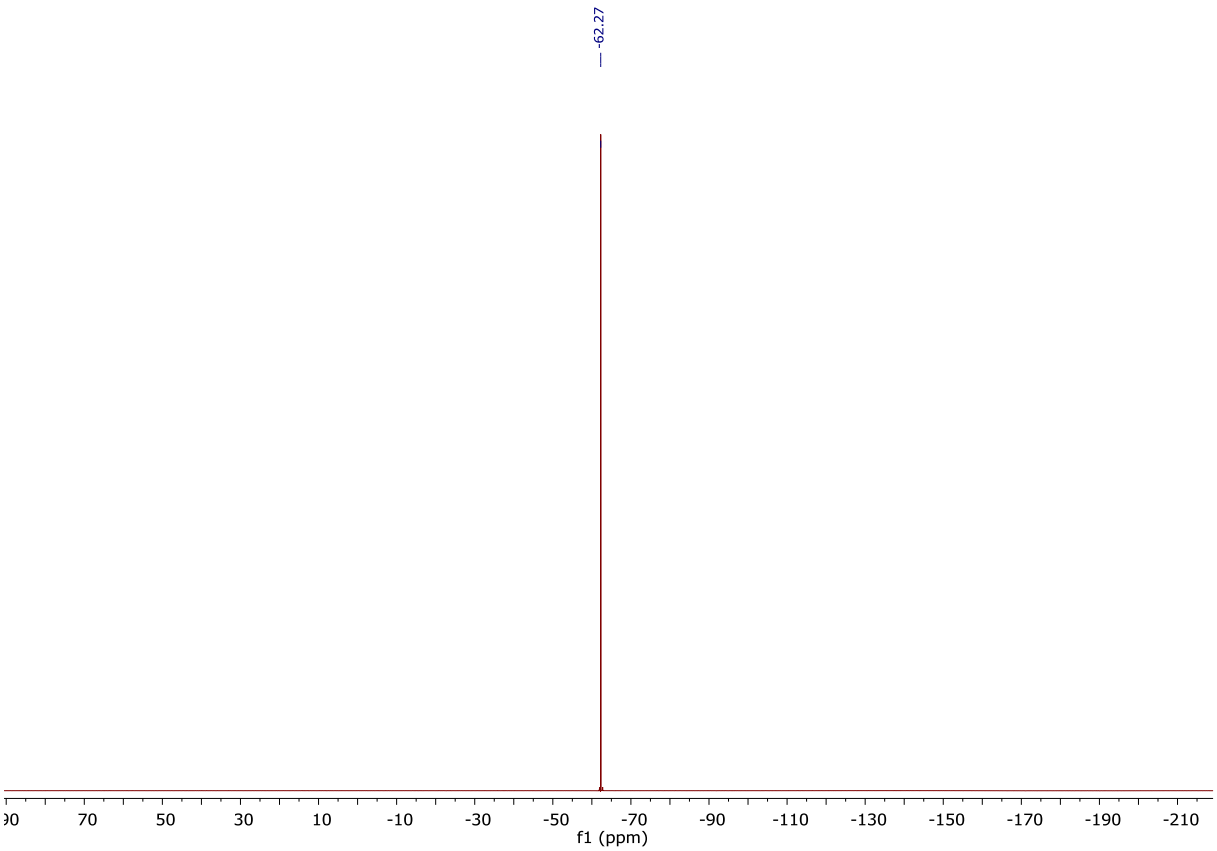




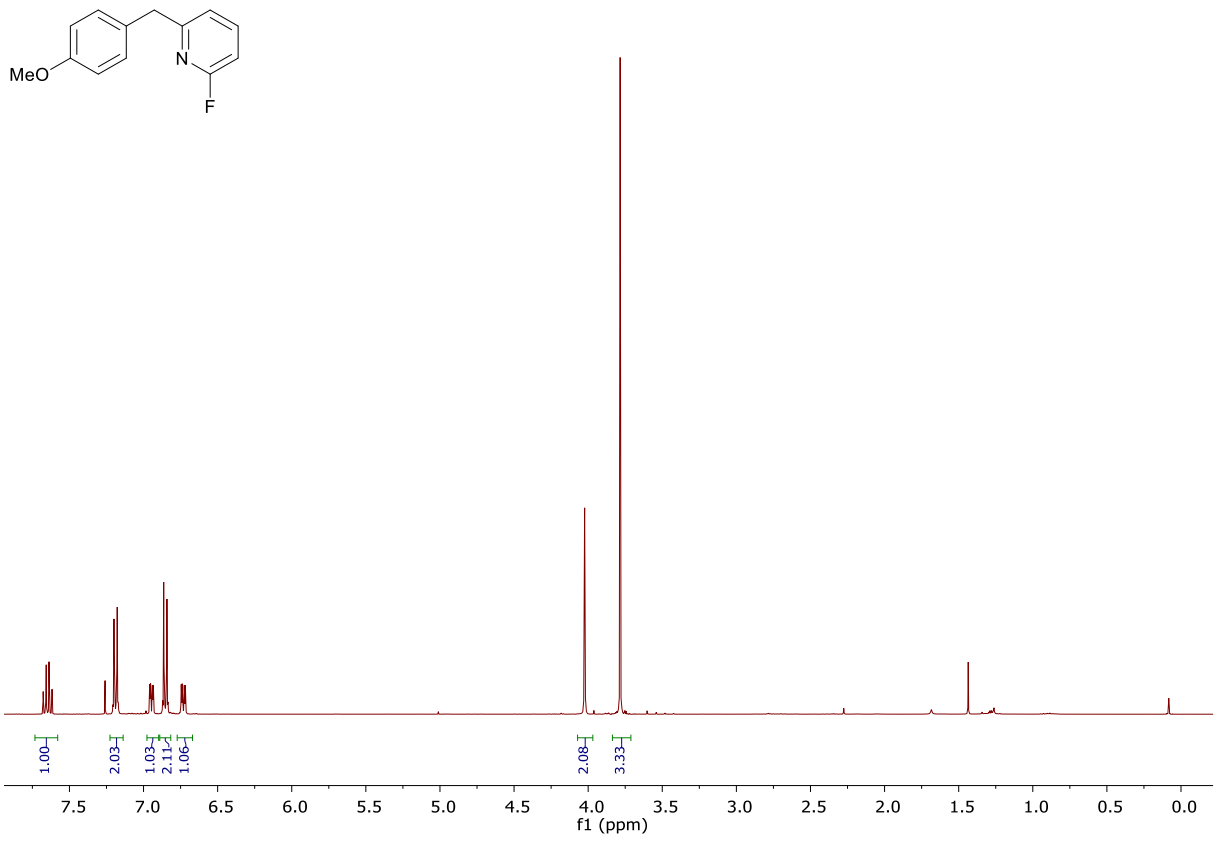
NMR-Spectra of 2-(4-methoxybenzyl)-5-(trifluoromethyl)pyridine (6b)

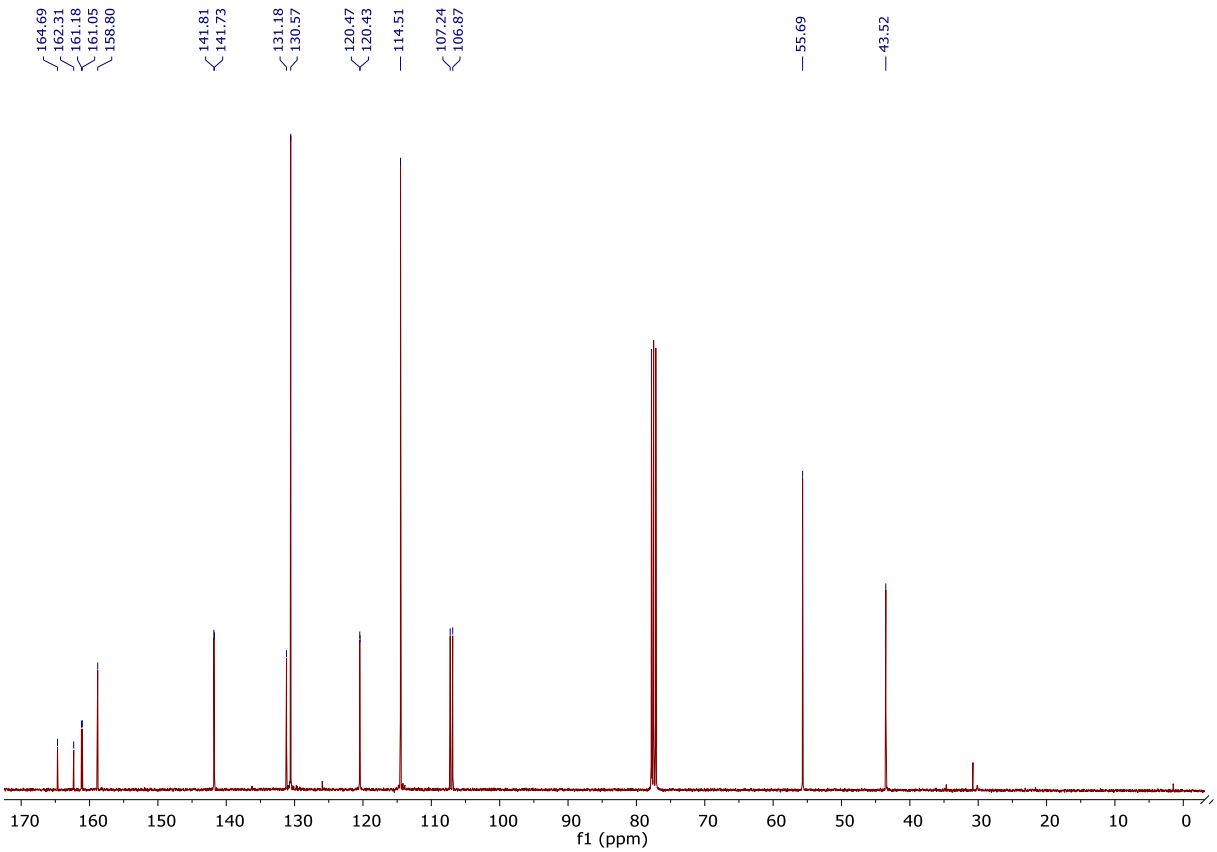






NMR-Spectra of 2-fluoro-6-(4-methoxybenzyl)pyridine (6c)




164.69
162.31
161.18
161.05
158.80
141.81
141.73
131.18
130.57
120.47
120.43
114.51
107.24
106.87
55.69
43.52
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

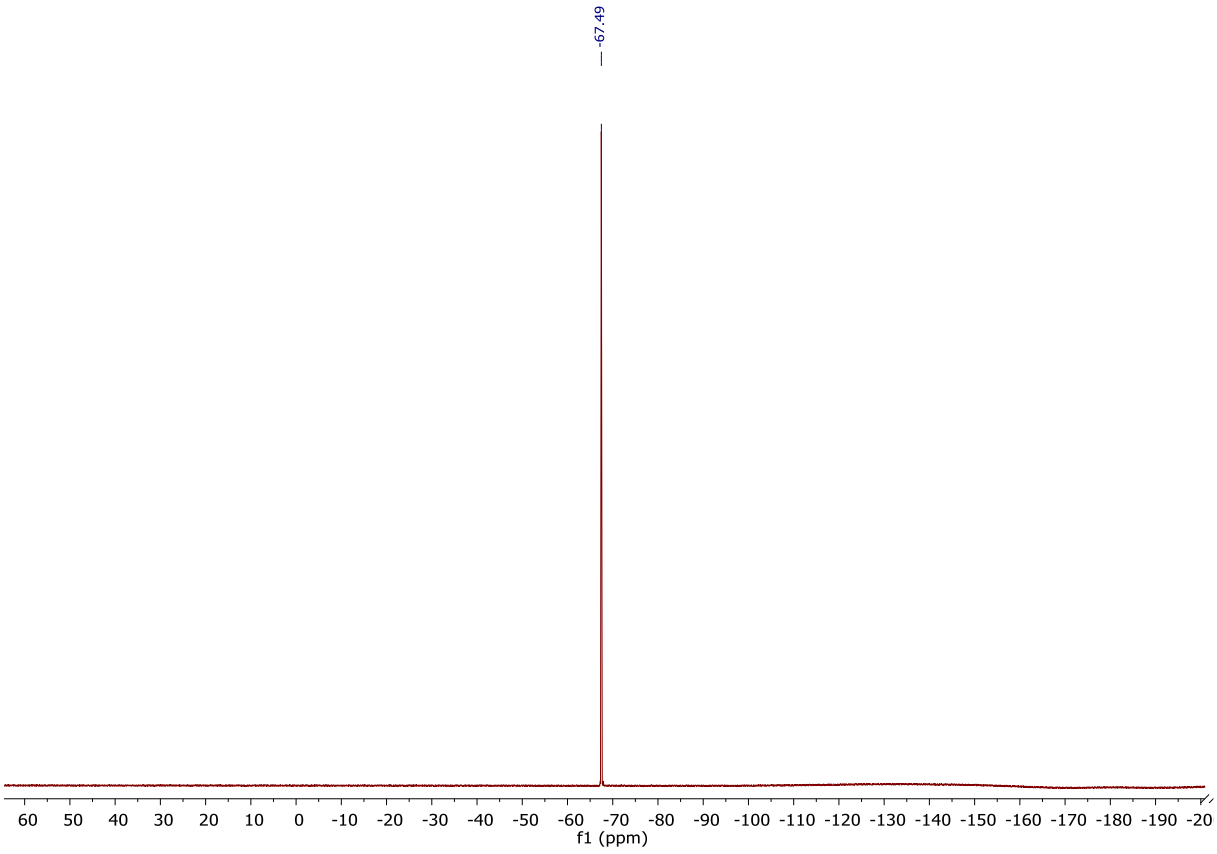
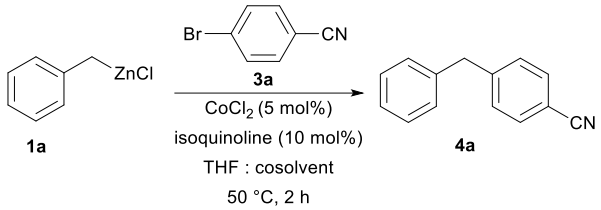

-67.49
60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20
f1 (ppm)

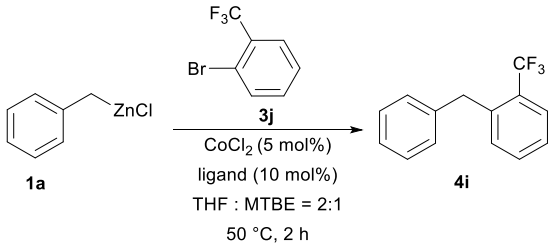
Table 1: Additional Solvent Screening for the Cross-Coupling of Benzylzinc Chloride (**1a**) with 4-Bromobenzonitrile (**3a**).



Entry	THF : Cosolvent	Solvent Ratio	Yield[a,b]
1	THF	-	77
2	THF : MTBE	1:1	60
3	THF : MTBE	1:2	57
4	THF : MTBE	2:1	82
5	THF : DMAc	2:1	72
6	THF : NMP	2:1	69
7	THF : MeCN	2:1	68
8	THF : DMPU	2:1	66
9	THF : DMF	2:1	56

[a] 1.3 equiv of benzylzinc chloride (**1a**) was used. [b] Isolated yields of pure product.

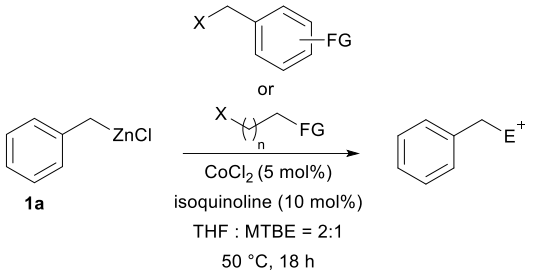
Table 2: Screening of appropriate Ligands for the Cross-Coupling of Benzylzinc Chloride (**1a**) with 2-Bromobenzotrifluoride (**3j**).

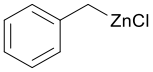
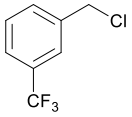
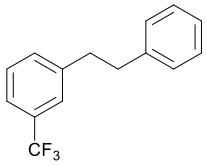
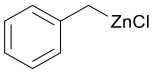
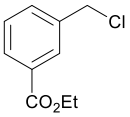
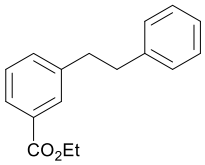
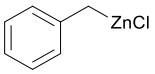
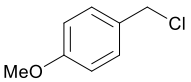
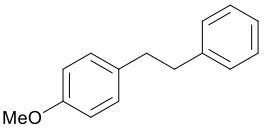
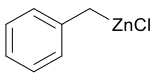
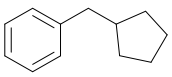
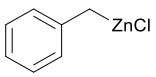
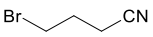
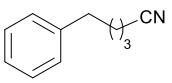
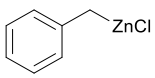
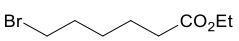
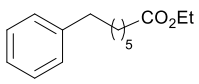


Entry	ligand	Yield[a,b]
1	PPh_3	0
2	dppe	0
3	SPhos	0
4	XPhos	15
5	XantPhos	28
6	pyridine	30
7	pyrimidine	18
8	pyrazine	traces
9	pyridazine	0
10	*N*,*N*-dimethylpyridin-4-amine	traces
11	2,2'-bipyridine	31
12	isoquinoline	31
13	6,7,8-trimethoxyisoquinoline	traces
14	*N*,*N*-dimethylquinolin-8-amine	traces

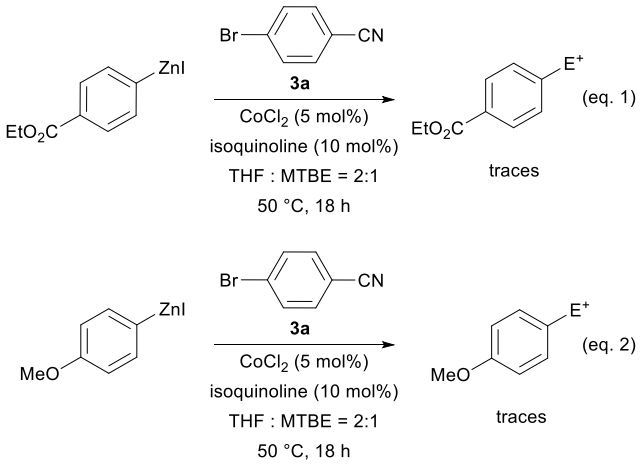
[a] 1.3 equiv of benzylzinc chloride (**1a**) was used. [b] Determined by GC-analysis with tetradecane as an internal standard.

Table 3: Attempts to extend the Reaction Scope. Co-Catalyzed Cross-Couplings of Benzylzinc Chloride (**1a**) with Selected Benzylic or Alkyl Halides.



Entry	Benzylic Zinc Reagent	Electrophile	Product, Yield[a,b]
			
1	**1a**		-
			
2	**1a**		-
			
3	**1a**		-
			
4	**1a**		-
			
5	**1a**		-
			
6	**1a**		-

[a] 1.3 equiv of benzylzinc chloride (**1a**) was used. [b] Determined by GC-analysis with tetradecane as an internal standard.



Scheme 1: Preliminary Experiments towards a Co-Catalyzed Cross-Coupling between Aryl Zinc Reagents and 4-Bromobenzonitrile (**3a**).