Polyfunctional Benzylic Zinc Chlorides by the Direct Insertion of Magnesium Into Benzylic Chlorides in the Presence of LiCl and $ZnCl_2$

Albrecht Metzger, Fabian M. Piller and Paul Knochel*

Ludwig-Maximilians-Universität München,

Department Chemie und Biochemie

Butenandtstrasse 5-13, Haus F, 81377 München (Germany)

Fax: (+49) 089 2180 77680

e-mail: paul.knochel@cup.uni-muenchen.de

General 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. Yields refer to isolated yields of compounds estimated to be >95% pure as determined by ^{1}H-NMR (25 °C) and capillary GC. Column chromatography was performed using SiO_2 (0.040 – 0.063 mm, 230 – 400 mesh ASTM) from Merck. All reagents were obtained from commercial sources. Liquid aldehydes and acid chlorides were distilled prior to use. Magnesium turnings (> 99.5%) were obtained from Riedel-de Haën. CuCN, $ZnCl_2$ and LiCl were obtained from Fluka.

Preparation of LiCl solution:

LiCl solution (0.5 M in THF) was prepared by drying LiCl (5.25 g, 125 mmol) in a *Schlenk*-flask under vacuum at 140 °C for 5 h. After cooling, 250 mL dry THF was added and stirring was continued until all salts were dissolved.

Preparation of $ZnCl_2$ solution:

$ZnCl_2$ solution (1.0 M in THF) was prepared by drying $ZnCl_2$ (136.3 g, 100 mmol) in a *Schlenk*-flask under vacuum at 140 °C for 5 h. After cooling, 100 mL dry THF was added and stirring was continued until all salts were dissolved.

Preparation of CuCN·2LiCl solution:

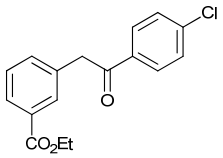
CuCN·2LiCl solution (1.0 M in THF) was prepared by drying CuCN (7.17 g, 80 mmol) and LiCl (6.77 g, 160 mmol) in a *Schlenk*-flask under vacuum at 140 °C for 5 h. After cooling, 80 mL dry THF was added and stirring was continued until all salts were dissolved.

Typical Procedure for the insertion reaction (TP1):

A dry and argon-flushed *Schlenk*-flask, equipped with a magnetic stirrer and a septum, was charged with magnesium turnings (122 mg, 5.0 mmol). LiCl (5.0 mL, 0.5 M in THF, 2.5 mmol) and $ZnCl_2$ (2.2 mL, 1.0 M in THF, 2.2 mmol) were added. The benzylic chloride (2.0 mmol) was added in one portion at the given temperature. The reaction mixture was

stirred for the given time and then canulated to a new *Schlenk*-flask for the reaction with an electrophile.

Ethyl 3-[2-(4-chlorophenyl)-2-oxoethyl]benzoate (4a):



The zinc reagent **1a** was prepared according to **TP1** from 3-ethoxycarbonylbenzyl chloride (397 mg, 2.0 mmol) in 2 h at 25 °C. The freshly prepared zinc reagent **1a** was added to CuCN·2LiCl (2.0 mL, 1.0 M in THF, 2.0 mmol) at -20 °C. After stirring for 15 min, 4-chlorobenzoyl chloride (**3a**) (245 mg, 1.4 mmol) was added and the mixture was stirred for 1.5 h at 0 °C followed by 30 min at 25 °C. The reaction mixture was quenched with sat. aq. NH_4Cl solution (40 mL) followed by 25% aq. NH_3 solution (20 mL) and extracted with Et_2O (3x 50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Flash column chromatography (pentane/Et_2O = 9:1) furnished **4a** as a colourless solid (347 mg, 81 %).

m.p.: 76-78 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ(ppm): 7.97-7.90 (m, 4H), 7.46-7.35 (m, 4H), 4.35 (q, *J* = 7.1 Hz, 2H), 4.30 (s, 2H), 1.37 (t, *J* = 7.2 Hz, 3H).

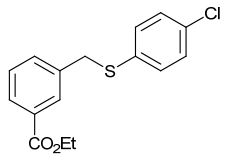
^{13}C-NMR (75 MHz, $CDCl_3$) δ(ppm): 195.8, 166.3, 139.8, 134.7, 134.4, 133.9, 130.9, 130.6, 129.9, 129.0, 128.7, 128.3, 61.0, 45.0, 14.3.

MS (70 eV, EI) *m/z* (%): 302 (1) [M^+], 259 (6), 257 (20), 141 (100), 139 (13), 113 (12), 111 (40).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2984 (w), 2914 (w), 1694 (vs), 1588 (m), 1394 (m), 1332 (s), 1280 (s), 1208 (vs), 1170 (s), 1108 (s), 1088 (s), 1030 (s), 1000 (s), 990 (s), 944 (m), 832 (s), 814 (vs), 796 (m), 752 (vs), 722 (s), 710 (m), 584 (m), 562 (s).

HRMS (EI) for $C_{17}H_{15}ClO_3$ (302.0710): 302.0702.

Ethyl 3-{[(4-chlorophenyl)thio]methyl}benzoate (4b):



The zinc reagent **1a** was prepared according to **TP1** from 3-ethoxycarbonylbenzyl chloride (397 mg, 2.0 mmol) in 2 h at 25 °C. The freshly prepared zinc reagent **1a** was added to *S*-(4-chlorophenyl) benzenesulfonothioate (**3b**) (399 mg, 1.4 mmol) in 1 mL THF at 0 °C. The mixture was stirred for 2 h at 25 °C. The reaction mixture was quenched with sat. aq. NH_4Cl solution (50 mL) and extracted with Et_2O (3x 50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Flash column chromatography (pentane → pentane/Et_2O = 98:2) furnished **4b** as a yellow solid (288 mg, 67 %).

m.p.: 41-43 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ(ppm): 7.94-7.88 (m, 2H), 7.45-7.39 (m, 1H), 7.37-7.30 (m, 1H), 7.20 (s, 4H), 4.36 (q, *J* = 7.2 Hz, 2H), 4.09 (s, 2H), 1.38 (t, *J* = 7.2 Hz, 3H).

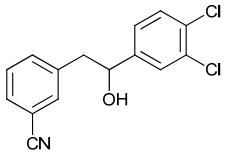
^{13}C-NMR (75 MHz, $CDCl_3$) δ(ppm): 166.2, 137.6, 134.0, 133.1, 132.8, 131.9, 130.8, 129.9, 129.0, 128.5, 128.5, 61.0, 39.1, 14.3.

MS (70 eV, EI) *m/z* (%): 306 (23) [M^+], 163 (100), 135 (12), 119(18) 89 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3052 (w), 2992 (w), 2934 (w), 1708 (s), 1584 (w), 1470 (s), 1444 (m), 1390 (m), 1282 (s), 1264 (m), 1234 (s), 1194 (s), 1176 (m), 1108 (s), 1090 (s), 1022 (m), 1006 (m), 944 (m), 934 (m), 806 (s), 778 (s), 730 (vs), 688 (s), 674 (m), 586 (m).

HRMS (EI) for $C_{16}H_{15}ClO_2S$ (306.0481): 306.0481.

3-[2-(3,4-Dichlorophenyl)-2-hydroxyethyl]benzonitrile (4c):



The zinc reagent **1b** was prepared according to **TP1** from 3-cyanobenzyl chloride[1] (303 mg, 2.0 mmol) in 2 h at 25 °C. The freshly prepared zinc reagent **1b** was added to 3,4-dichlorobenzaldehyde (**3c**) (245 mg, 1.4 mmol) in 1 mL THF at 0 °C. The mixture was stirred for 2 h at 25 °C. The reaction mixture was quenched with sat. aq. NH_4Cl solution (50 mL) and extracted with CH_2Cl_2 (3x 50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Flash column chromatography (pentane/Et_2O = 7:3) furnished **4c** as a colourless solid (341 mg, 83 %).

m.p.: 96-97 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ(ppm): 7.55-7.47 (m, 2H), 7.44-7.33 (m, 4H), 7.11 (dd, *J* = 8.2 Hz, 2.0 Hz, 1H), 4.86 (q, *J* = 6.4 Hz, 1H), 2.99 (d, *J* = 6.4 Hz, 2H), 2.02-1.89 (s, 1H).

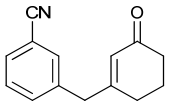
^{13}C-NMR (75 MHz, $CDCl_3$) δ(ppm): 143.5, 138.9, 134.1, 133.1, 132.7, 131.8, 130.5, 130.5, 129.2, 127.8, 125.1, 118.7, 112.5, 73.6, 45.1.

MS (70 eV, EI) *m/z* (%): 291 (2) [M^+], 179 (13), 177 (100), 175 (61), 147 (29), 117 (71), 111 (19), 90 (13), 75 (12).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3328 (m), 3260 (m), 2232 (m), 1484 (m), 1470 (s), 1426 (m), 1398 (m), 1202 (m), 1142 (m), 1058 (s), 1028 (s), 1014 (m), 904 (m), 818 (s), 798 (vs), 690 (s), 650 (s), 602 (m).

HRMS (EI) for $C_{15}H_{11}Cl_2NO$ (291.0218): 291.0214.

3-[(3-Oxocyclohex-1-en-1-yl)methyl]benzonitrile (4d):



The zinc reagent **1b** was prepared according to **TP1** from 3-cyanobenzyl chloride[1] (303 mg, 2.0 mmol) in 2 h at 25 °C. The freshly prepared zinc reagent **1b** was added to CuCN·2LiCl (2.0 mL, 1.0 M in THF, 2.0 mmol) at -20 °C. After stirring for 15 min, 3-iodocyclohex-2-enone (**3d**) (311 mg, 1.4 mmol) was added at –60 °C and the mixture was slowly warmed to 0°C over 18 h. The reaction mixture was quenched with sat. aq. NH_4Cl solution (100 mL) followed by 25% aq. NH_3 solution (50 mL) and extracted with Et_2O (3x 150 mL). The combined organic layers

were dried over $MgSO_4$ and concentrated *in vacuo*. Flash column chromatography (pentane/Et_2O = 1:2) furnished **4d** as a yellow liquid (227 mg, 77%).

^{1}H-NMR (300 MHz, $CDCl_3$) δ(ppm): 7.58-7.52 (m, 1H), 7.47-7.36 (m, 3H), 5.80-5.76 (m, 1H), 3.53 (s, 2H), 2.40-2.32 (m, 2H), 2.27-2.20 (m, 2H), 2.03-1.91 (m, 2H).

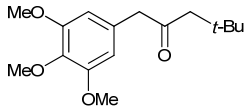
^{13}C-NMR (75 MHz, $CDCl_3$) δ(ppm): 199.3, 162.6, 138.4, 133.6, 132.5, 130.7, 129.5, 127.4, 118.5, 112.9, 43.7, 37.2, 29.3, 22.5.

MS (70 eV, EI) *m/z* (%): 211 (62) [M^+], 183 (100), 154 (48), 140 (16), 67 (23).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2926 (w), 2228 (m), 1660 (vs), 1626 (m), 1600 (w), 1582 (w), 1484 (w), 1428 (m), 1372 (m), 1348 (m), 1324 (m), 1250 (m), 1192 (m), 1128 (w), 968 (m), 906 (m), 884 (m), 796 (s), 758 (m), 724 (m), 694 (s), 672 (m), 556 (m).

HRMS (EI) for $C_{14}H_{13}NO$ (211.0997): 211.0994.

4,4-Dimethyl-1-(3,4,5-trimethoxyphenyl)pentan-2-one (4e):



The zinc reagent **1c** was prepared according to **TP1** from 3,4,5-trimethoxybenzyl chloride (433 mg, 2.0 mmol) in 1 h at 25 °C. The freshly prepared zinc reagent **1c** was cooled to -20 °C and CuCN·2LiCl (2.0 mL, 1.0 M in THF, 2.0 mmol) was added. After stirring for 15 min, 3,3-dimethylbutanoyl chloride (**3e**) (188 mg, 1.4 mmol) was added, the mixture warmed to 25 °C and was

stirred for 1 h. The reaction mixture was quenched with sat. aq. NH_4Cl solution (10 mL) followed by 25% aq. NH_3 solution (2 mL) and extracted with Et_2O (3x 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Flash column chromatography (CH_2Cl_2) furnished **4e** as a colourless solid (323 mg, 82 %).

m.p.: 65–66 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ(ppm): 6.37 (s, 2H), 3.83 (s, 6H), 3.82 (s, 3H), 2.35 (s, 2H), 1.00 (s, 9H).

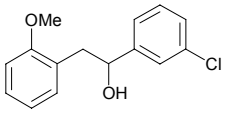
^{13}C-NMR (75 MHz, $CDCl_3$) δ(ppm): 207.9, 153.3, 137.0, 129.8, 106.5, 60.8, 56.1, 53.9, 52.2, 31.0, 29.7.

MS (70 eV, EI) *m/z* (%): 280 (15) [M^+], 181 (100), 99 (4), 57 (12).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2984 (w), 2954 (m), 2902 (w), 2868 (w), 1708 (m), 1586 (s), 1508 (m), 1464 (m), 1454 (m), 1438 (m), 1422 (s), 1384 (w), 1360 (m), 1350 (m), 1328 (m), 1268 (w), 1240 (s), 1188 (m), 1148 (m), 1124 (vs), 1072 (m), 1030 (w), 994 (s), 970 (m), 922 (w), 834 (w), 822 (m), 780 (m), 678 (m), 618 (m).

HRMS (EI) for $C_{16}H_{24}O_4$ (280.1675): 280.1675.

1-(3-Chlorophenyl)-2-(2-methoxyphenyl)ethanol (4f):



The zinc reagent **1d** was prepared according to **TP1** from 2-methoxybenzyl chloride (313 mg, 2.0 mmol) in 1 h at 25 °C. The

freshly prepared zinc reagent **1d** was added to 3-chlorobenzaldehyde (**3f**) (197 mg, 1.4 mmol) in 1 mL THF at 0 °C. The mixture was stirred for 4 h at 25 °C. The reaction mixture was quenched with sat. aq. NH_4Cl solution (50 mL) and extracted with Et_2O (3x 50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Flash column chromatography (pentane/Et_2O = 4:1) furnished **4f** as a colourless solid (338 mg, 92 %).

m.p.: 60-61 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ(ppm): 7.42-7.39 (m, 1H), 7.30-7.21 (m, 4H), 7.10-7.05 (m, 1H), 6.95-6.87 (m, 2H), 4.98-4.91 (m, 1H), 3.87 (s, 3H), 3.12 (m, 1H), 2.95 (dd, J = 13.6 Hz, 8.8 Hz, 1H), 2.64 (d, J = 2.9 Hz, 1H).

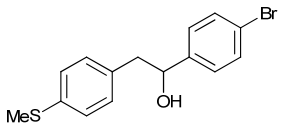
^{13}C-NMR (75 MHz, $CDCl_3$) δ(ppm): 157.5, 146.6, 134.1, 131.5, 129.4, 128.2, 127.3, 126.1, 126.0, 123.9, 120.8, 110.5, 73.7, 55.4, 41.2.

MS (70 eV, EI) *m/z* (%): 262 (<1) [M^+], 165 (2), 122 (100), 91 (25), 77 (13).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3322 (w), 3252 (w), 2946 (w), 2922 (w), 2838 (w), 1600 (m), 1492 (s), 1468 (s), 1438 (m), 1420 (m), 1292 (m), 1238 (vs), 1200 (m), 1182 (m), 1114 (s), 1080 (m), 1062 (s), 1050 (s), 1032 (s), 1008 (m), 872 (m), 786 (s), 764 (s), 750 (vs), 728 (m), 708 (s), 692 (s), 642 (m), 604 (s), 558 (s).

HRMS (EI) for $C_{15}H_{15}ClO_2$ (262.0761): 262.0747.

1-(4-Bromophenyl)-2-[4-(methylthio)phenyl]ethanol (4g):



The zinc reagent **1e** was prepared according to **TP1** from 4-(methylthio)benzyl chloride (345 mg, 2.0 mmol) in 1.5 h at 25 °C. The freshly prepared zinc reagent **1e** was added to 4-bromobenzaldehyde (**3g**) (259 mg, 1.4 mmol) in 1 mL THF at 25 °C. The mixture was stirred for 2 h. The reaction mixture was quenched with sat. aq. NH_4Cl solution (50 mL) and extracted with CH_2Cl_2 (3x 50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Flash column chromatography (pentane/Et_2O = 3:1) furnished **4g** as a colourless solid (372 mg, 82 %).

m.p.: 117-119 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ(ppm): 7.48-7.42 (m, 2H), 7.22-7.16 (m, 4H), 7.09-7.03 (m, 2H), 4.81 (dd, *J* = 7.6 Hz, 5.5 Hz, 1H), 2.98-2.88 (m, 2H), 2.46 (s, 3H), 1.86 (s, 1H).

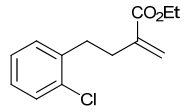
^{13}C-NMR (75 MHz, $CDCl_3$) δ(ppm): 142.6, 136.7, 134.3, 131.5, 130.0, 127.6, 126.9, 121.4, 74.6, 45.4, 16.0.

MS (70 eV, EI) *m/z* (%): 322 (3) [M^+], 187 (14), 185 (16), 138 (100), 123 (30), 91 (7), 77 (14).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3310 (w), 2914 (w), 1494 (m), 1488 (m), 1434 (m), 1424 (m), 1404 (m), 1092 (m), 1058 (s), 1008 (m), 1000 (m), 882 (w), 822 (vs), 792 (s), 716 (w).

HRMS (EI) for $C_{15}H_{15}BrOS$ (322.0027): 322.0018.

Ethyl 2-[2-(2-chlorophenyl)ethyl]acrylate (4h):



The zinc reagent **1f** was prepared according to **TP1** from 2-chlorobenzyl chloride (322 mg, 2.0 mmol) in 45 min at 25 °C. The freshly prepared zinc reagent **1f** was added to ethyl (2-bromomethyl)acrylate (**3h**) (309 mg, 1.6 mmol) in 0.5 mL THF at 25 °C. CuCN·2LiCl (0.01 mL, 1.0 M in THF, 0.01 mmol) was added and the mixture was stirred for 45 min. The reaction mixture was quenched with sat. aq. NH_4Cl solution (45 mL) followed by 25% aq. NH_3 solution (5 mL) and extracted with Et_2O (3x 50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Flash column chromatography (pentane/Et_2O = 98:2) furnished **4h** as a colourless liquid (295 mg, 77 %).

^{1}H-NMR (600 MHz, $CDCl_3$) δ(ppm): 7.33 (dd, *J* = 7.6 Hz, 1.3 Hz, 1H), 7.321-7.10 (m, 3H), 6.15 (d, *J* = 1.3 Hz, 1H), 5.49 (d, *J* = 1.3 Hz, 1H), 4.21 (q, *J* = 7.3 Hz, 2H), 2.94-2.89 (m, 2H), 2.64-2.59 (m, 2H), 1.31 (t, *J* = 7.1 Hz, 3H).

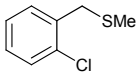
^{13}C-NMR (150 MHz, $CDCl_3$) δ(ppm): 167.0, 139.8, 138.9, 134.0, 130.5, 129.4, 127.5, 126.7, 125.4, 60.7, 32.7, 32.1, 14.2.

MS (70 eV, EI) *m/z* (%): 238 (11) [M^+], 193 (12), 164 (10), 157 (39), 129 (13), 127 (31), 125 (100), 89 (8).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2982 (w), 2936 (w), 1713 (vs), 1631 (w), 1475 (m), 1443 (m), 1303 (m), 1182 (s), 1139 (s), 1113 (m), 1052 (m), 1035 (s), 944 (m), 816 (m), 749 (vs), 673 (m).

HRMS (EI) for $C_{13}H_{15}O_2Cl$ (238.0761): 238.0762.

2-Chlorobenzyl methyl sulphide (4i):



The zinc reagent **1f** was prepared according to **TP1** from 2-chlorobenzyl chloride (322 mg, 2.0 mmol) in 45 min at 25 °C. $MeSO_2SMe$ (**3i**) (177 mg, 1.4 mmol) was added to the freshly prepared zinc reagent **1f** and the mixture was stirred for 16 h. The reaction mixture was quenched with sat. aq. NH_4Cl solution (10 mL) and extracted with Et_2O (3x 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Flash column chromatography (pentane) furnished **4i** as a colourless oil (214 mg, 89 %).

^{1}H-NMR (300 MHz, $CDCl_3$) δ(ppm): 7.38-7.32 (m, 2H), 7.24-7.15 (m, 2H), 3.80 (s, 2H), 2.05 (s, 3H).

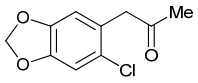
^{13}C-NMR (75 MHz, $CDCl_3$) δ(ppm): 136.0, 134.1, 130.7, 129.8, 128.3, 126.7, 35.7, 15.1.

MS (70 eV, EI) *m/z* (%): 172 (100) [M^+], 127 (94), 89 (24), 63 (10).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2914 (w), 1572 (w), 1472 (m), 1442 (m), 1424 (m), 1240 (w), 1120 (w), 1050 (m), 1036 (m), 978 (w), 958 (w), 944 (w), 850 (w), 822 (w), 762 (s), 738 (vs), 718 (w), 686 (m), 668 (m), 626 (w), 618 (vw), 598 (w), 578 (m).

HRMS (EI) for C_8H_9ClS (172.0113): 172.0109.

1-(6-Chloro-1,3-benzodioxol-5-yl)acetone (4j):



The zinc reagent **1g** was prepared according to **TP1** from 5-chloro-6-(chloromethyl)-1,3-benzodioxole (410 mg, 2.0 mmol) in 15 min at 25 °C. The freshly prepared zinc reagent **1g** was cooled to -20 °C and CuCN·2LiCl (2.0 mL, 1.0 M in THF, 2.0 mmol) was added. After stirring for 15 min, acetyl chloride (**3j**) (110 mg, 1.4 mmol) was added, the mixture warmed to 25 °C and was stirred for 3 h. The reaction mixture was quenched with sat. aq. NH_4Cl solution (10 mL) followed by 25% aq. NH_3 solution (2 mL) and extracted with Et_2O (3x 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Flash column chromatography (pentane/CH_2Cl_2 = 1:1) furnished **4j** as a colourless solid (227 mg, 76 %).

m.p.: 79–80 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ(ppm): 6.85 (s, 1H), 6.65 (s, 1H), 5.96 (s, 2H), 3.72 (s, 2H), 2.18 (s, 3H).

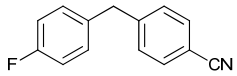
^{13}C-NMR (75 MHz, $CDCl_3$) δ(ppm): 205.1, 147.5, 146.8, 126.0, 125.6, 110.8, 109.9, 101.8, 48.1, 29.5.

MS (70 eV, EI) *m/z* (%): 212 (23) [M^+], 169 (100), 111 (6), 75 (9).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2912 (w), 1718 (vs), 1504 (s), 1488 (s), 1422 (m), 1406 (m), 1394 (m), 1356 (m), 1320 (m), 1256 (s), 1236 (m), 1202 (m), 1192 (m), 1160 (s), 1122 (s), 1034 (s), 990 (m), 968 (m), 924 (vs), 874 (s), 858 (m), 846 (s), 784 (w), 696 (m), 654 (m), 596 (w).

HRMS (EI) for $C_{10}H_9O_3Cl$ (212.0240): 212.0225.

4-(4-Fluorobenzyl)benzonitrile (4k):



The zinc reagent **1h** was prepared according to **TP1** from 4-fluorobenzyl chloride (289 mg, 2.0 mmol) in 45 min at 25 °C. A dry and argon-fushed *Schlenk*-flask was charged with 4-bromobenzonitrile (**3k**) (255 mg, 1.4 mmol), $Pd(OAc)_2$ (5 mg, 1 mol%) and S-Phos (16 mg, 2 mol%). THF (2.0 mL) was added. The mixture was stirred for 15 min and cooled to 0 °C. The freshly prepared zinc reagent **1h** was added, the reaction mixture warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched with sat. aq. NH_4Cl solution (10 mL) and extracted with Et_2O (3x 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. Flash column chromatography (pentane/CH_2Cl_2 = 4:1) furnished **4k** as a colourless solid (222 mg, 75 %).

m.p.: 67–69 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ(ppm): 7.57 (d, *J* = 8.2 Hz, 2H), 7.26 (d, *J* = 8.2 Hz, 2H), 7.13-7.08 (m, 2H), 7.02-6.96 (m, 2H), 4.00 (s, 2H).

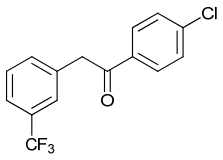
^{13}C-NMR (75 MHz, $CDCl_3$) δ(ppm): 163.3, 160.1, 146.5, 135.0 (d, *J* = 3.4 Hz), 132.3, 130.3 (d, *J* = 7.7 Hz), 118.9, 115.5 (d, *J* = 21.4 Hz), 110.2, 41.1.

MS (70 eV, EI) *m/z* (%): 211 (100) [M^+], 183 (15), 109 (16).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3040 (vw), 2934 (w), 2222 (m), 1920 (vw), 1884 (w), 1606 (m), 1500 (s), 1470 (w), 1446 (w), 1428 (w), 1412 (w), 1310 (w), 1302 (w), 1290 (w), 1258 (vw), 1214 (s), 1178 (m), 1154 (m), 1116 (m), 1104 (w), 1088 (w), 1016 (w), 984 (w), 968 (w), 954 (w), 938 (w), 922 (w), 868 (m), 844 (m), 814 (vs), 796 (m), 764 (s), 734 (m), 708 (w), 682 (m), 648 (w), 624 (w), 564 (vs).

HRMS (EI) for $C_{14}H_{10}NF$ (211.0797): 211.0771.

1-(4-Chlorophenyl)-2-[3-(trifluoromethyl)phenyl]ethanone (4l):



The zinc reagent **1i** was prepared according to **TP1** from 3-(trifluoromethyl)benzyl chloride (389 mg, 2.0 mmol) in 30 min at 25 °C. The freshly prepared zinc reagent **1i** was cooled to -20 °C and CuCN·2LiCl (2.0 mL, 1.0 M in THF, 2.0 mmol) was added. After stirring for 15 min, 4-chlorobenzoyl chloride (**3a**) (245 mg, 1.4 mmol) was added, the mixture warmed to 25 °C and was stirred for 1 h. The reaction mixture was quenched with sat. aq. NH_4Cl solution (10 mL) followed by 25% aq. NH_3 solution (2 mL) and extracted with Et_2O (3x 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Flash column chromatography (pentane/CH_2Cl_2 = 3:1) furnished **4l** as a colourless solid (382 mg, 91 %).

m.p.: 54–56 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ(ppm): 7.96-7.92 (m, 2H), 7.55-7.41 (m, 6H), 4.32 (s, 2H).

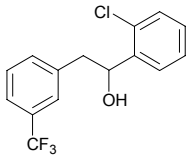
^{13}C-NMR (75 MHz, $CDCl_3$) δ(ppm): 195.4, 140.0, 135.0, 134.6, 133.0, 131.0 (q, J = 32.2 Hz), 129.8, 129.1, 129.1, 126.3 (q, J = 3.9 Hz) 124.0 (q, J = 3.9 Hz), 124.0 (q, J = 272.2 Hz), 44.9.

MS (70 eV, EI) *m/z* (%): 279 (2), 139 (100), 111 (18), 75 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 1694 (m), 1682 (s), 1588 (m), 1572 (m), 1488 (w), 1454 (m), 1400 (m), 1334 (s), 1302 (m), 1284 (w), 1210 (s), 1186 (m), 1176 (m), 1156 (s), 1118 (vs), 1106 (s), 1092 (vs), 1074 (vs), 1014 (m), 1004 (s), 990 (s), 960 (m), 942 (m), 922 (m), 904 (m), 878 (m), 852 (w), 832 (m), 818 (s), 812 (s), 792 (s), 784 (s), 762 (m), 754 (m), 720 (s), 700 (s), 656 (s), 628 (m), 620 (m), 598 (w), 584 (m), 562 (s).

HRMS (EI) for $C_{15}H_{10}OClF_3$ (298.0372): 298.0352.

1-(2-Chlorophenyl)-2-[3-(trifluoromethyl)phenyl]ethanol (4m):



The zinc reagent **1i** was prepared according to **TP1** from 3-(trifluoromethyl)benzyl chloride (389 mg, 2.0 mmol) in 30 min at 25 °C. The freshly prepared zinc reagent **1i** was added to 2-chlorobenzaldehyde (**3l**) (197 mg, 1.4 mmol) and the mixture was stirred for 1 h at 25 °C. The reaction mixture was quenched with sat. aq. NH_4Cl solution (50 mL) and extracted with CH_2Cl_2 (3x 50 mL). The combined organic layers were dried over $MgSO_4$

and concentrated *in vacuo*. Flash column chromatography (pentane/Et_2O = 7:1) furnished **4m** as a colourless solid (357 mg, 85 %).

m.p.: 44-45 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ(ppm): 7.62-7.15 (m, 8H), 5.33 (dd, *J* = 8.8 Hz, 3.3 Hz, 1H), 3.18 (dd, *J* = 13.8 Hz, 3.3 Hz, 1H), 2.89 (dd, *J* = 13.8 Hz, 8.8 Hz, 1H), 1.99 (s, 1H).

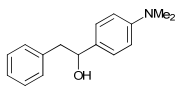
^{13}C-NMR (150 MHz, $CDCl_3$) δ(ppm): 140.9, 139.1, 133.0 (q, *J* = 1.5 Hz), 131.5, 130.7 (q, *J* = 32.1 Hz), 129.4, 128.8, 128.7, 127.2, 127.0, 126.3 (q, *J* = 4.0 Hz), 124.2 (q, *J* = 272.3 Hz), 123.5 (q, *J* = 4.0 Hz), 71.5, 43.7.

MS (70 eV, EI) *m/z* (%): 300 (<1) [M^+], 283 (4), 281 (10), 159 (15), 143 (100), 141 (32), 139 (12), 113 (22), 77 (46).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3332 (w), 3254 (w), 2932 (w), 1476 (w), 1448 (m), 1332 (s), 1322 (s), 1254 (w), 1198 (m), 1172 (s), 1160 (s), 1114 (vs), 1098 (s), 1072 (s), 1048 (s), 1034 (s), 1004 (m), 910 (m), 854 (m), 794 (s), 758 (s), 722 (m), 708 (s), 698 (s), 660 (m), 650 (m), 622 (m), 586 (s).

HRMS (EI) for $C_{15}H_{12}ClF_3O$ (300.0529): 300.0535.

1-[4-(Dimethylamino)phenyl]-2-phenylethanol(4n):



The zinc reagent **1j** was prepared according to **TP1** from benzyl chloride (253 mg, 2.0 mmol) in 2 h at 25 °C. The freshly prepared zinc reagent **1j** was added to 4-(dimethylamino) benzaldehyde (**3m**) (209 mg, 1.4 mmol) at 25 °C. The mixture was

stirred for 1 h. The reaction mixture was quenched with sat. aq. NH_4Cl solution (50 mL) and extracted with CH_2Cl_2 (3x 50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Flash column chromatography (pentane/Et_2O = 1:1) furnished **4n** as a yellow solid (331 mg, 98 %).

m.p.: 57-59 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ(ppm): 7.34-7.18 (m, 7H), 6.78-6.70 (m, 2H), 4.81 (t, *J* = 6.7 Hz, 1H), 3.02 (d, *J* = 6.7 Hz, 2H), 2.95 (s, 6H), 1.94 (s, 1H).

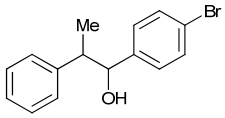
^{13}C-NMR (75 MHz, $CDCl_3$) δ(ppm): 150.1, 138.5, 131.9, 129.4, 128.4, 126.9, 126.3, 112.5, 75.1, 45.7, 40.7.

MS (70 eV, EI) *m/z* (%): 242 (100) [$(M+H)^+$], 222 (4), 136 (68), 115 (2), 63 (10).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3312 (m), 3054 (w), 3026 (w), 2922 (m), 2856 (m), 2812 (w), 1618 (s), 1526 (s), 1448 (m), 1358 (s), 1336 (m), 1324 (m), 1232 (m), 1188 (m), 1170 (m), 1068 (m), 1020 (s), 1002 (m), 946 (m), 814 (s), 794 (m), 746 (s), 732 (s), 696 (vs), 638 (m), 620 (m), 608 (s).

HRMS (ESI) for $C_{16}H_{20}NO$ (242.1545): 242.1540.

1-(4-Bromophenyl)-2-phenylpropan-1-ol (4o):



The zinc reagent **1k** was prepared according to **TP1** from 1-phenylethyl chloride (281 mg, 2.0 mmol) in 1 h at 25 °C. The freshly prepared zinc reagent **1k** was added to 4-bromobenzaldehyde (**3g**) (259 mg, 1.4 mmol) in THF (1 mL) at 25 °C. The mixture was stirred for 2 h. The reaction mixture was quenched with sat. aq. NH_4Cl solution (50 mL) and extracted with CH_2Cl_2 (3x 50 mL). The combined organic layers were dried

over $MgSO_4$ and concentrated *in vacuo*. Flash column chromatography (pentane/Et_2O = 9:1) furnished **4o** as a colourless solid (285 mg, 70 %). Two diastereomers were observed with a ratio of 1:2. Analtical data for the main diastereomer is given.

m.p.: 63-65 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ(ppm): 7.56-7.07 (m, 9H), 4.66 (d, *J* = 8.5 Hz, 1H), 3.06-2.94 (m, 1H), 2.00-1.83 (m, 1H), 1.13 (d, *J* = 7.1 Hz, 1H).

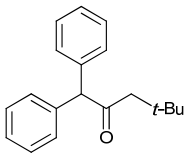
^{13}C-NMR (75 MHz, $CDCl_3$) δ(ppm): 142.8, 141.4, 131.3, 128.7, 128.7, 128.0, 127.1, 121.5, 79.0, 48.1, 18.0.

MS (70 eV, EI) *m/z* (%): 290 (2) [M^+], 211 (8), 185 (22), 91 (100), 78 (66), 51 (20).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3378 (w), 3028 (w), 2968 (w), 2896 (w), 2878 (w), 2360 (vw), 1602 (w), 1488 (m), 1450 (m), 1406 (m), 1378 (w), 1198 (w), 1092 (m), 1070 (m), 1036 (m), 1026 (m), 1004 (s), 992 (m), 906 (m), 834 (m), 820 (s), 774 (m), 756 (s), 698 (vs), 658 (m), 628 (m), 620 (m), 608 (m), 580 (s), 568 (m), 556 (m).

HRMS (EI) for $C_{15}H_{15}BrO$ (290.0306): 290.0302.

4,4-Dimethyl-1,1-diphenylpentan-2-one (4p):



The zinc reagent **1l** was prepared according to **TP1** from 1,1'-(chloromethylene)dibenzene (405 mg, 2.0 mmol) in 30 min at

0 °C. The freshly prepared zinc reagent **1l** was cooled to -20 °C and CuCN·2LiCl (2.0 mL, 1.0 M in THF, 2.0 mmol) was added. After stirring for 15 min, 3,3-dimethylbutanoyl chloride (**3e**) (188 mg, 1.4 mmol) was added, the mixture warmed to 25 °C and was stirred for 1 h. The reaction mixture was quenched with sat. aq. NH_4Cl solution (10 mL) followed by 25% aq. NH_3 solution (2 mL) and extracted with Et_2O (3x 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Flash column chromatography (pentane → pentane/CH_2Cl_2 = 3:2) furnished **4p** as a colourless solid (302 mg, 81 %).

m.p.: 45–47 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ(ppm): 7.35-7.20 (m, 10H), 5.09 (s, 1H), 2.44 (s, 2H), 1.01 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ(ppm): 207.8, 138.4, 129.0, 128.6, 127.1, 65.7, 54.9, 31.3, 29.6.

MS (70 eV, EI) *m/z* (%): 183 (1), 167 (100), 152 (10), 99 (18).

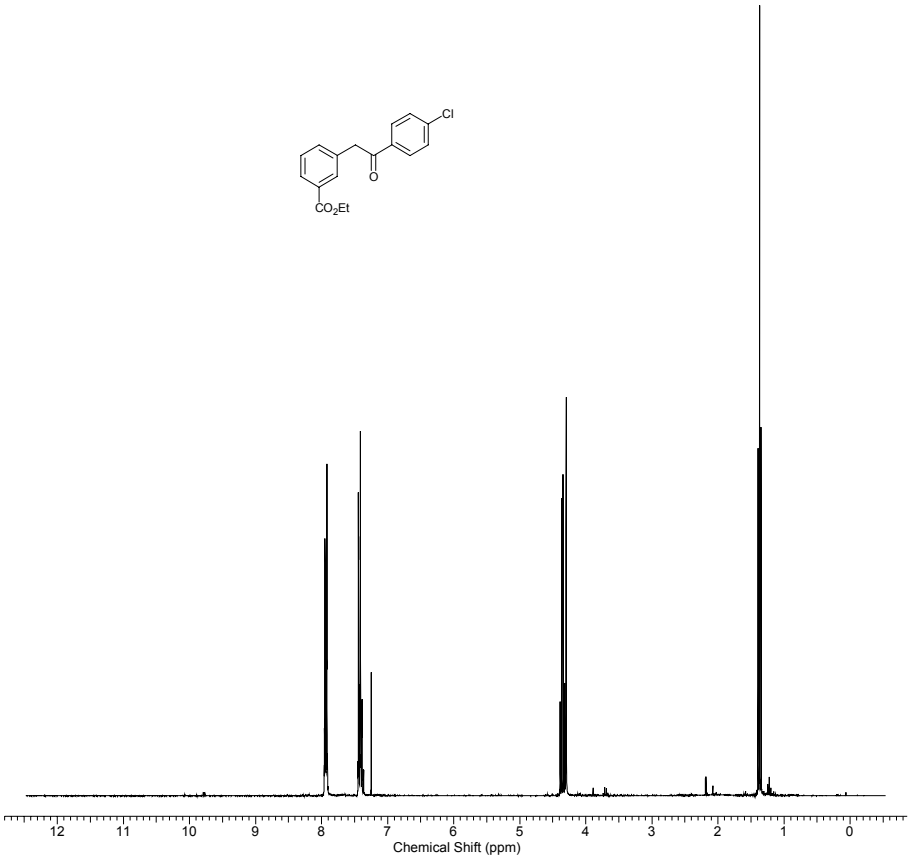
IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3060 (w), 3028 (w), 2980 (w), 2956 (m), 2904 (w), 2868 (w), 1714 (s), 1596 (w), 1582 (w), 1492 (m), 1464 (w), 1452 (m), 1398 (w), 1388 (w), 1360 (m), 1348 (m), 1306 (w), 1294 (w), 1272 (w), 1252 (w), 1230 (w), 1190 (w), 1154 (w), 1126 (w), 1084 (m), 1060 (m), 1032 (m), 1004 (w), 990 (w), 948 (w), 916 (w), 902 (w), 758 (m), 746 (s), 720 (s), 702 (vs), 692 (vs), 628 (m), 616 (m), 604 (s).

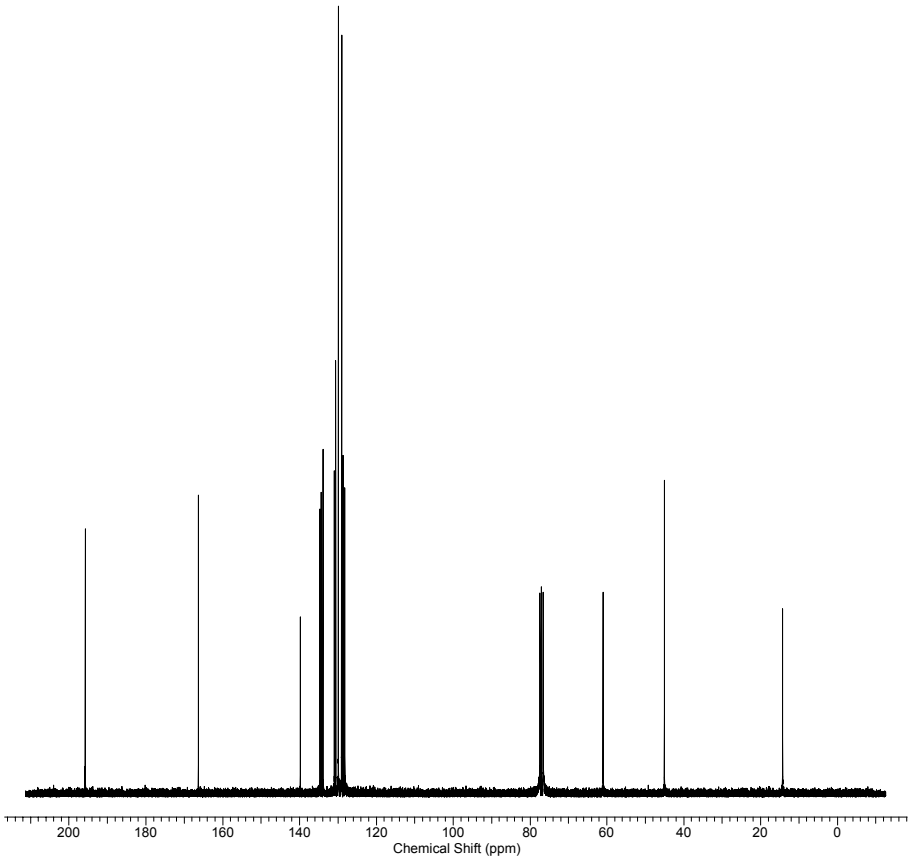
HRMS (EI) for $C_{19}H_{22}O$ (266.1671): 266.1659.

References

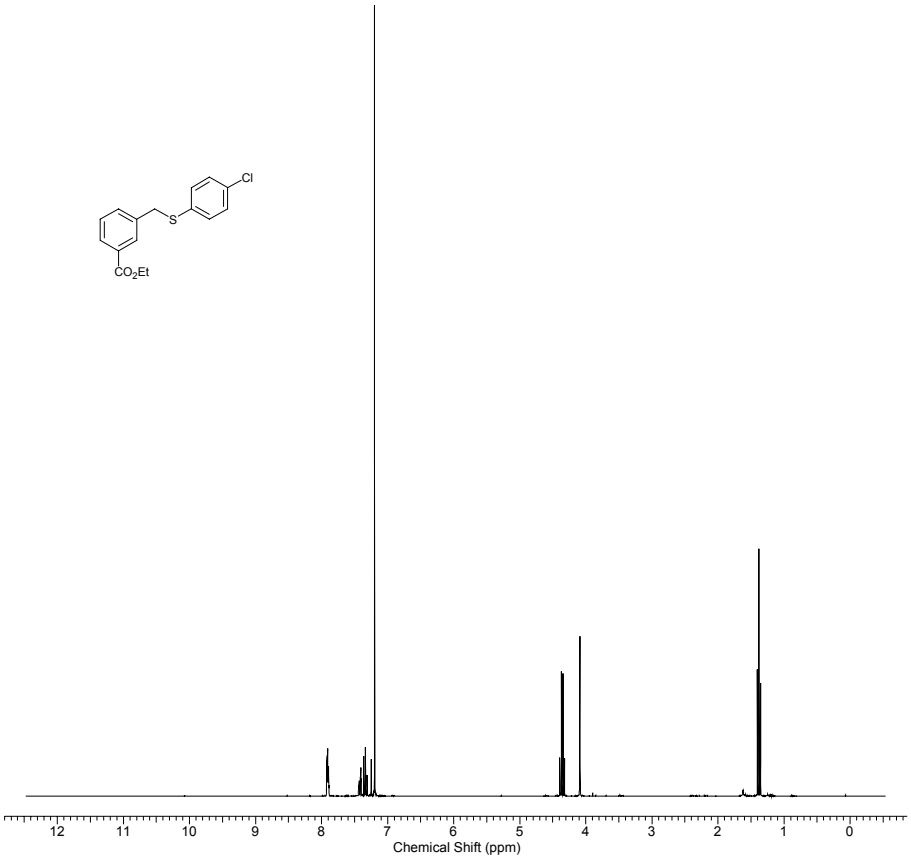
1 For the preparation of 3-cyanobenzyl chloride see: A. Metzger, M. A. Schade, P. Knochel, *Org. Lett.*, 2008, **10**, 1107.

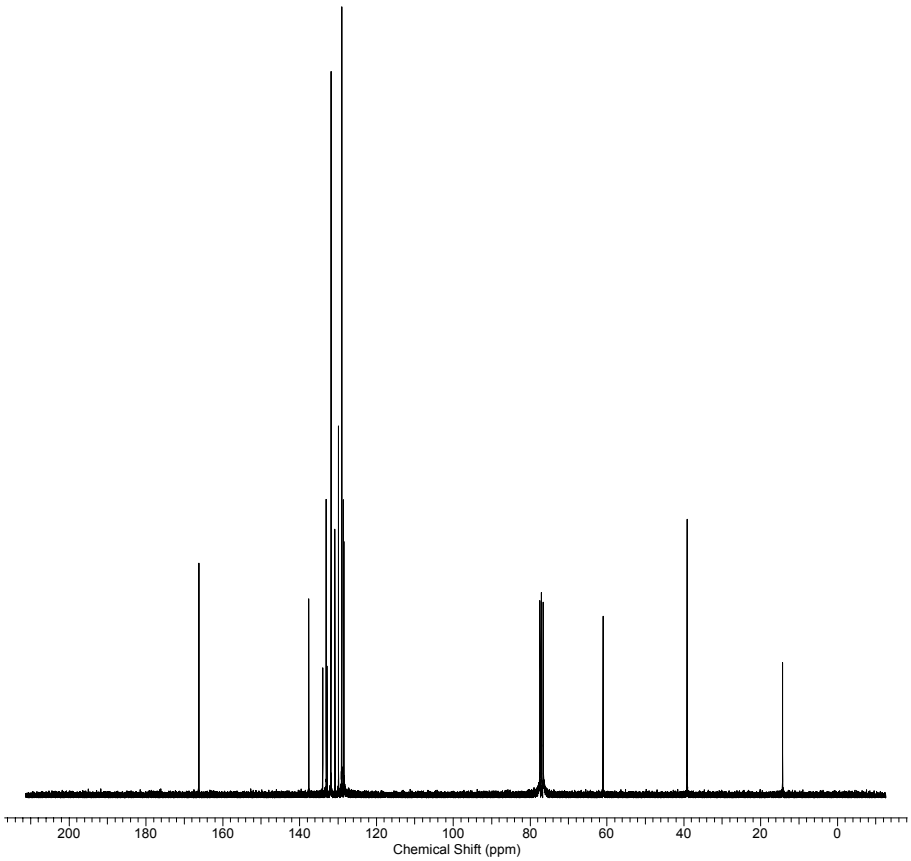
Ethyl 3-[2-(4-chlorophenyl)-2-oxoethyl]benzoate (4a)



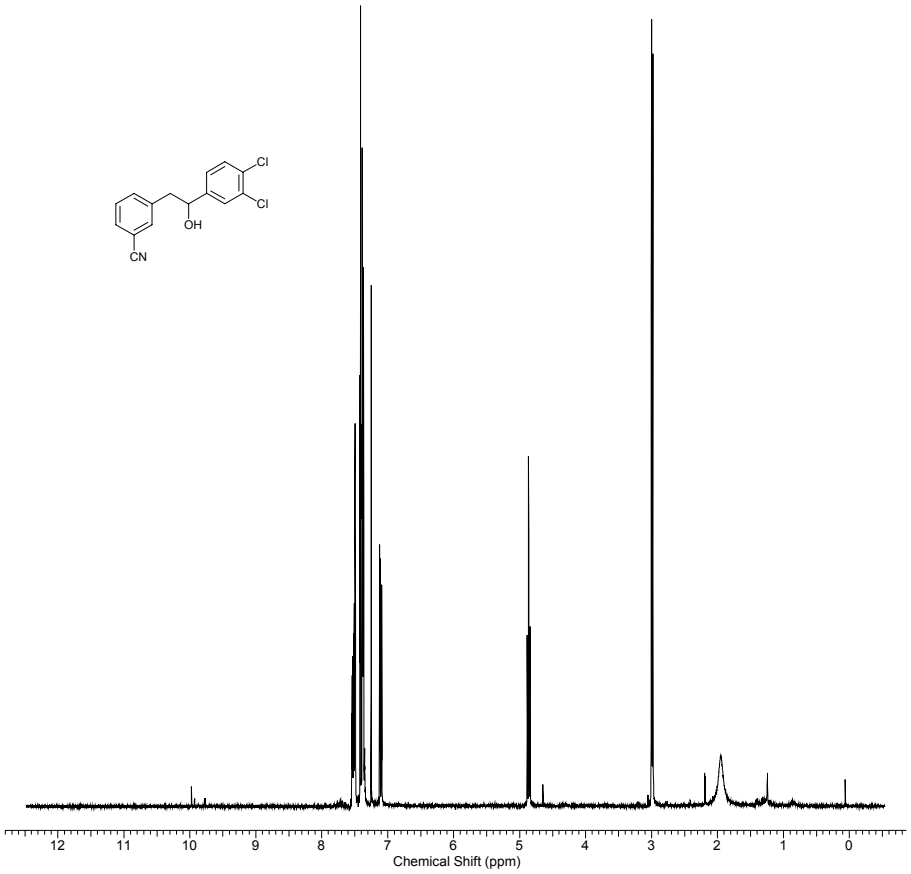


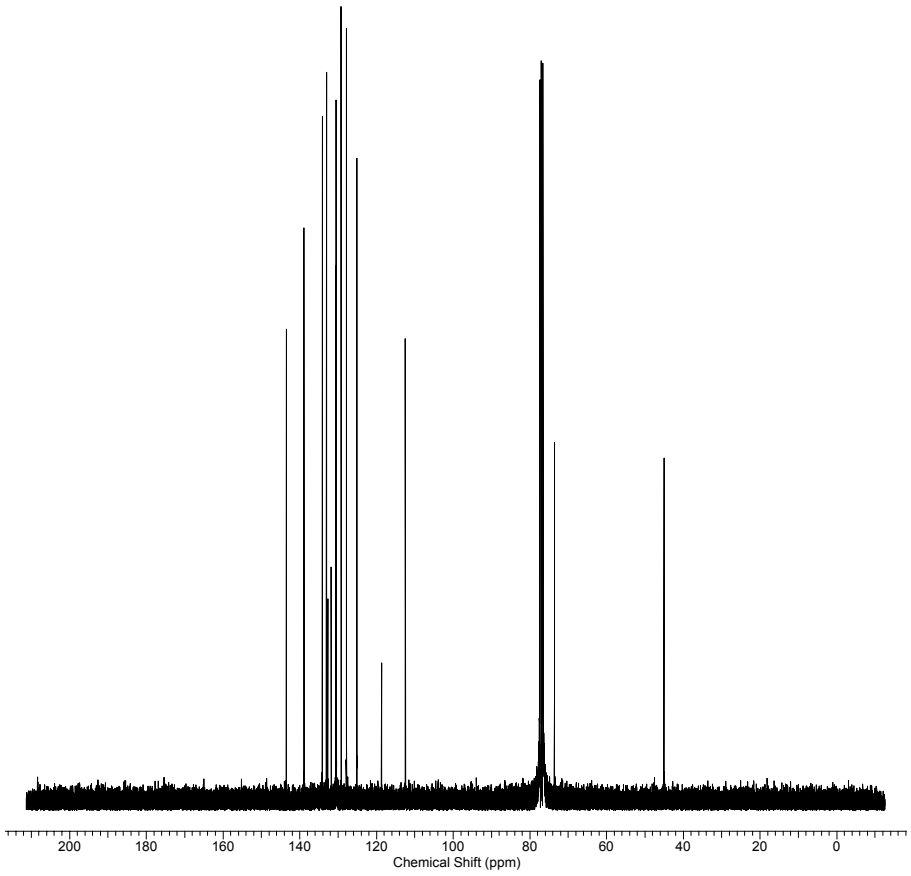
Ethyl 3-{[(4-chlorophenyl)thio]methyl}benzoate (4b)



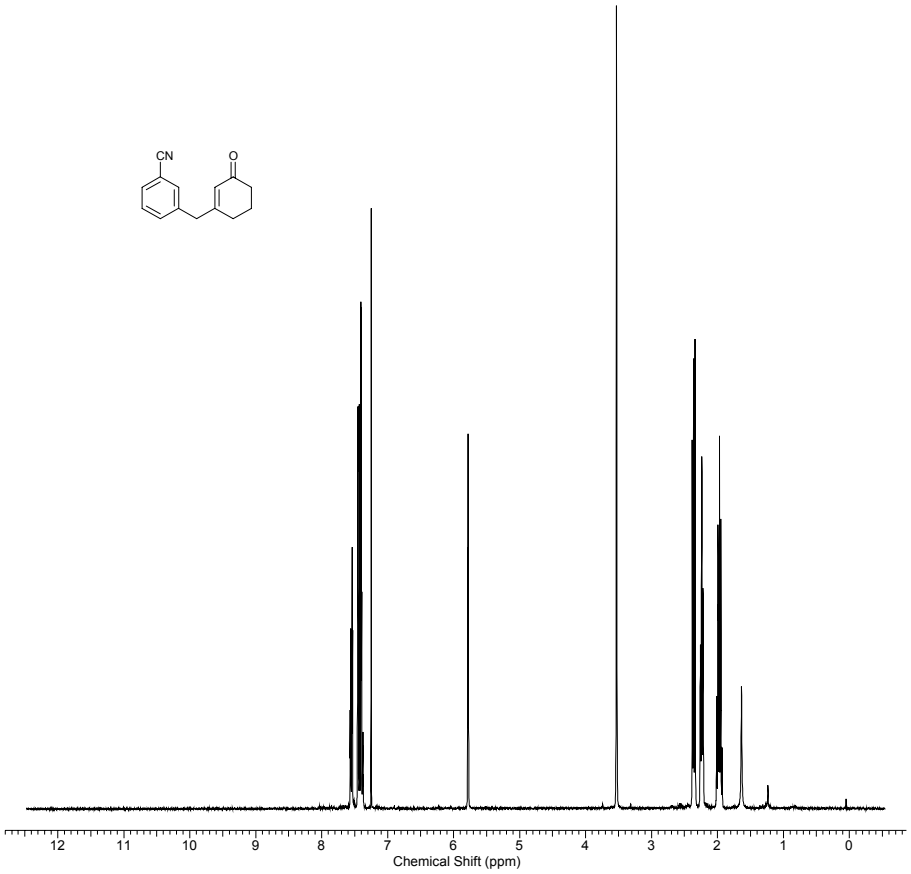


3-[2-(3,4-Dichlorophenyl)-2-hydroxyethyl]benzonitrile (4c)





3-[(3-Oxocyclohex-1-en-1-yl)methyl]benzonitrile (4d)


CN
O
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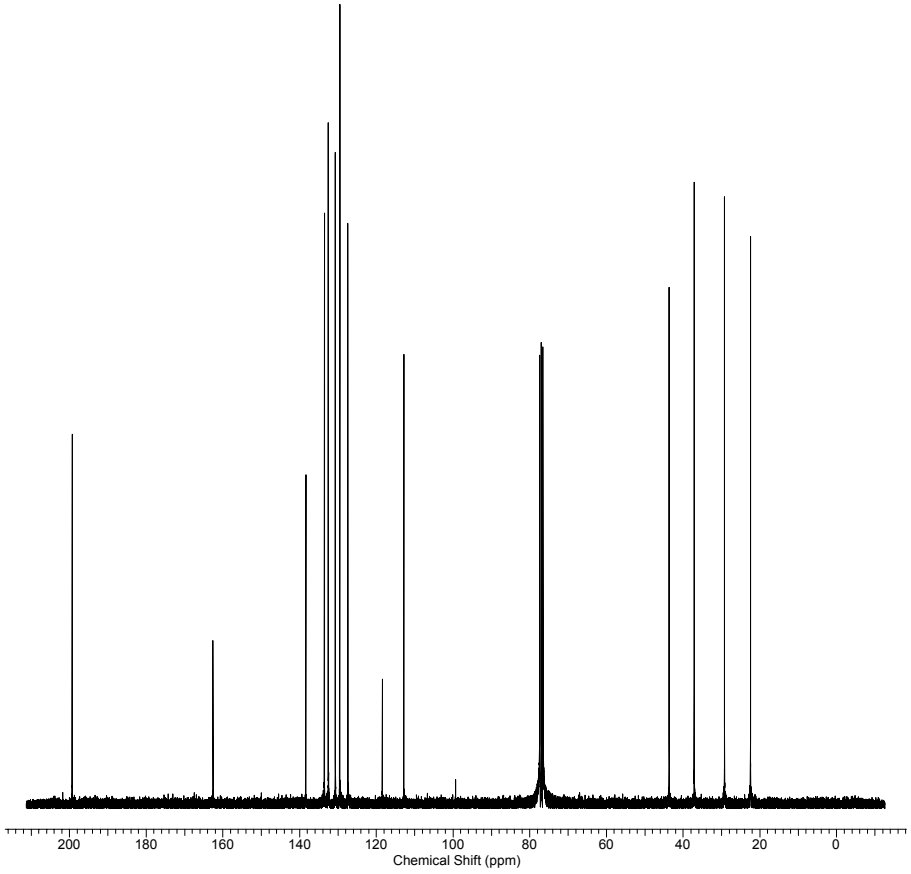
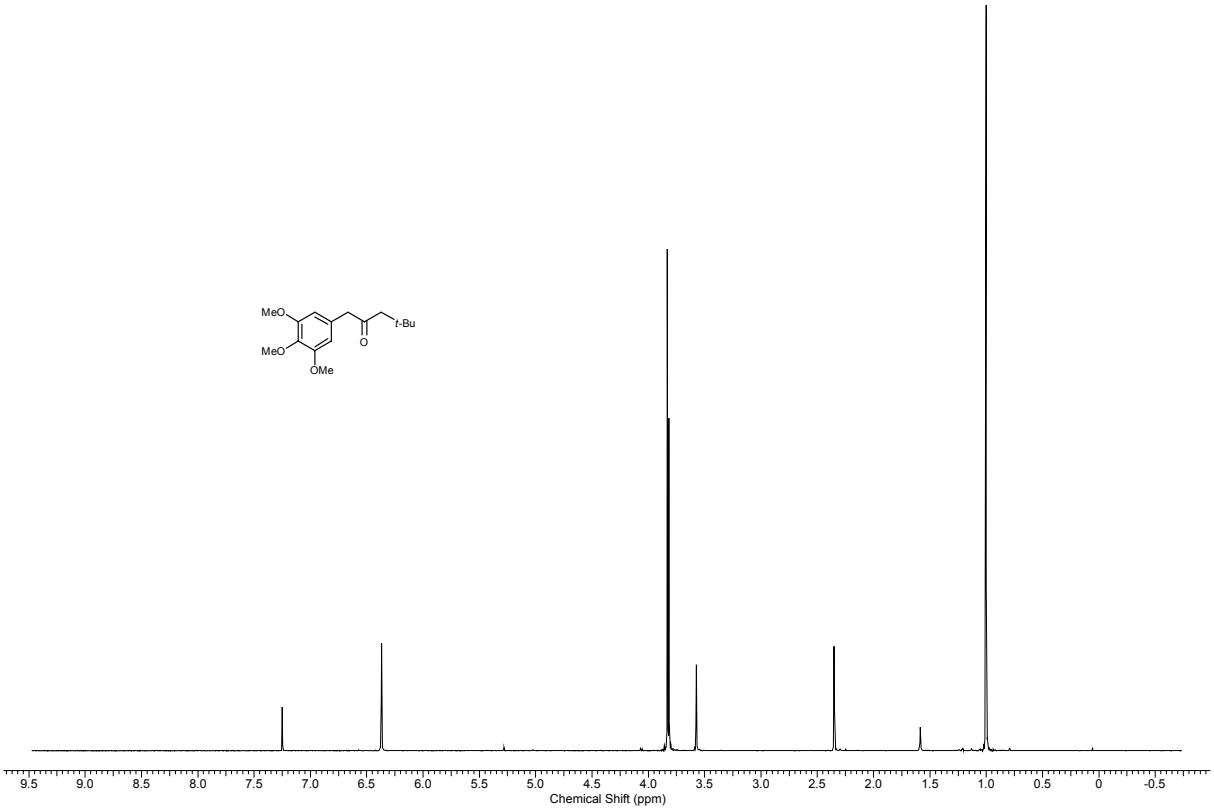
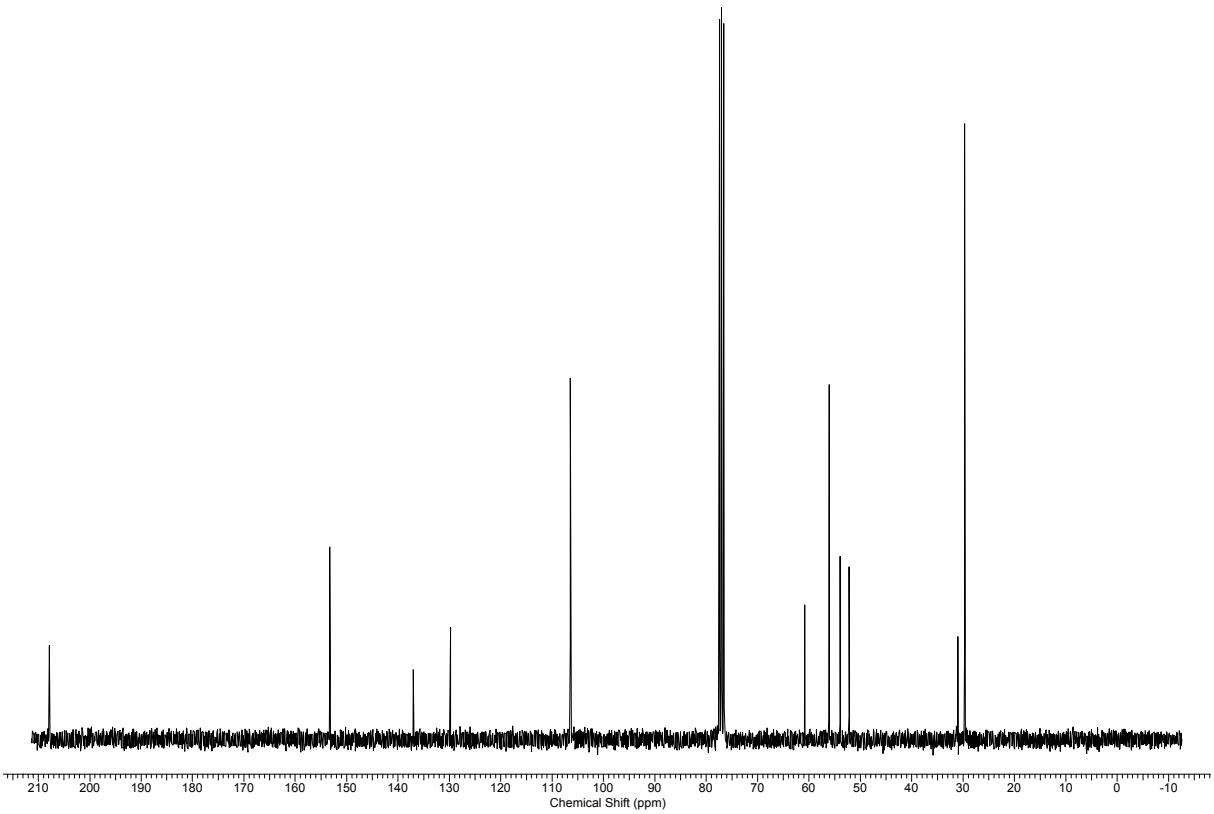
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

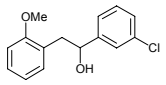

200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

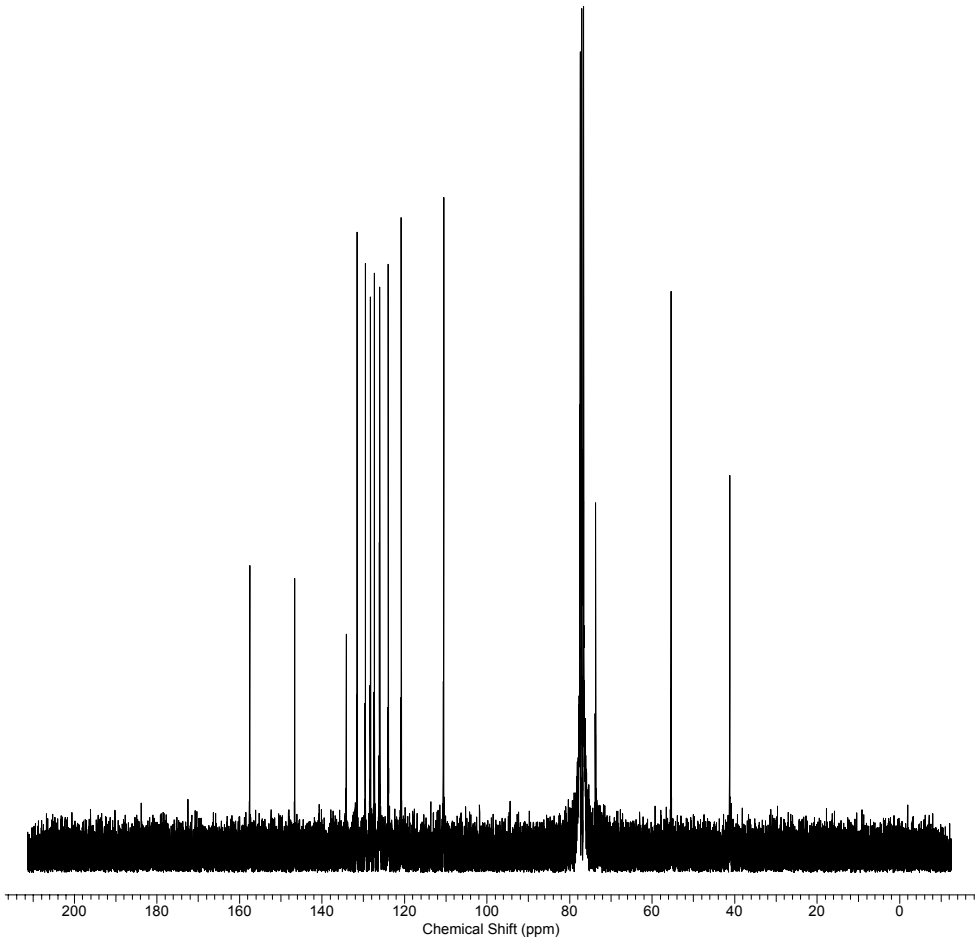
4,4-Dimethyl-1-(3,4,5-trimethoxyphenyl)pentan-2-one (4e):



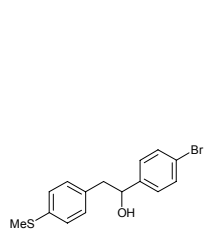


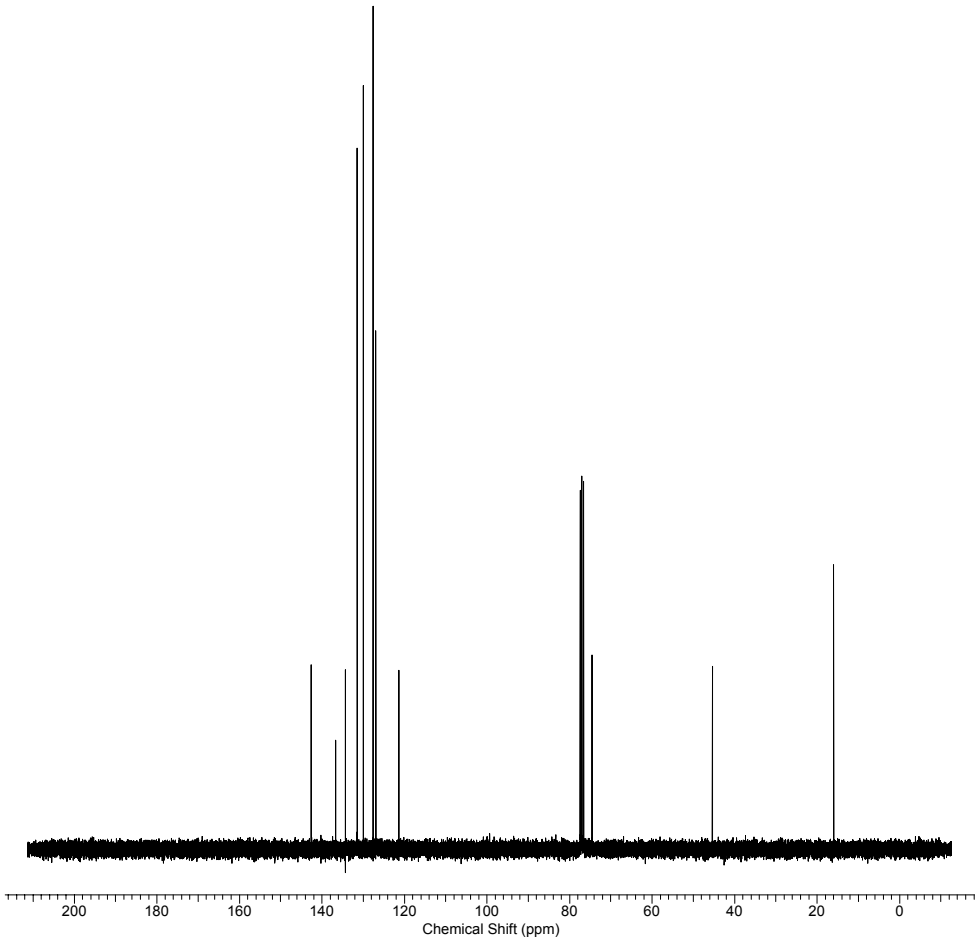
1-(3-Chlorophenyl)-2-(2-methoxyphenyl)ethanol (4f)



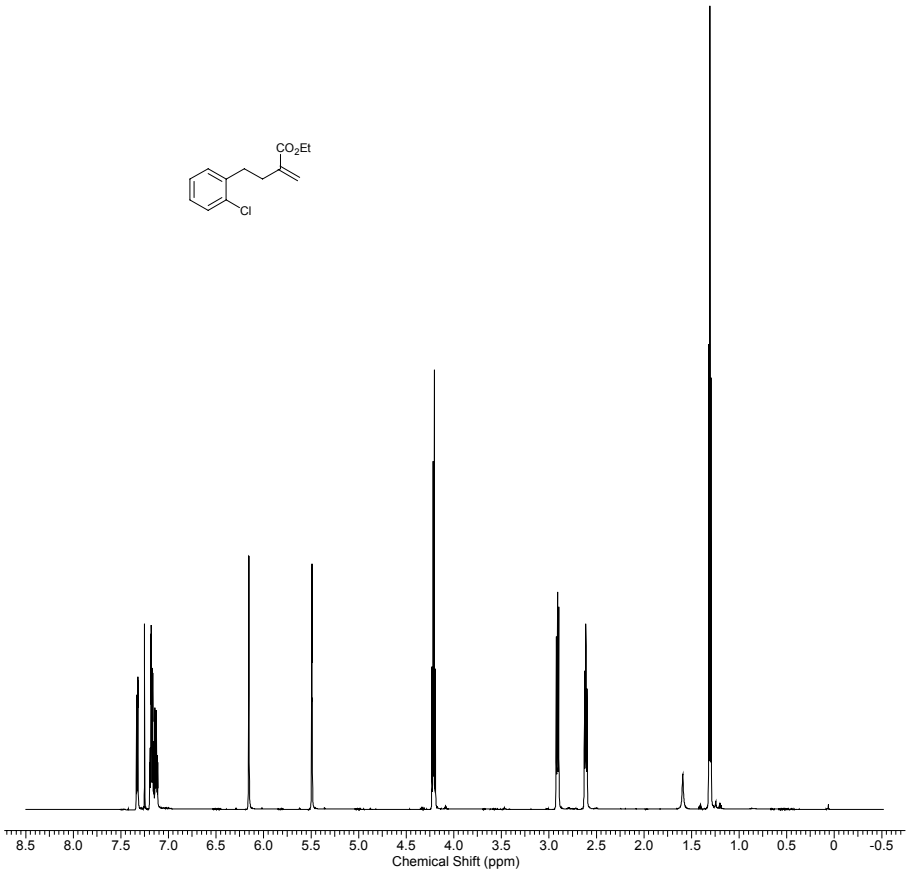


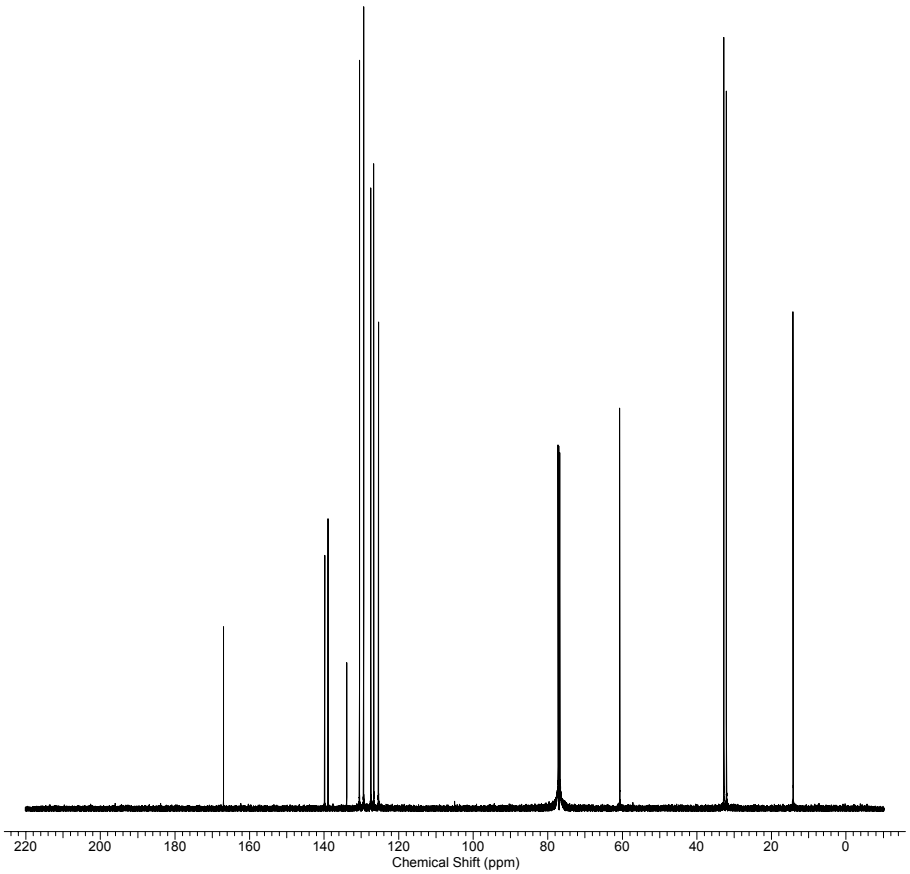
1-(4-Bromophenyl)-2-[4-(methylthio)phenyl]ethanol (4g)



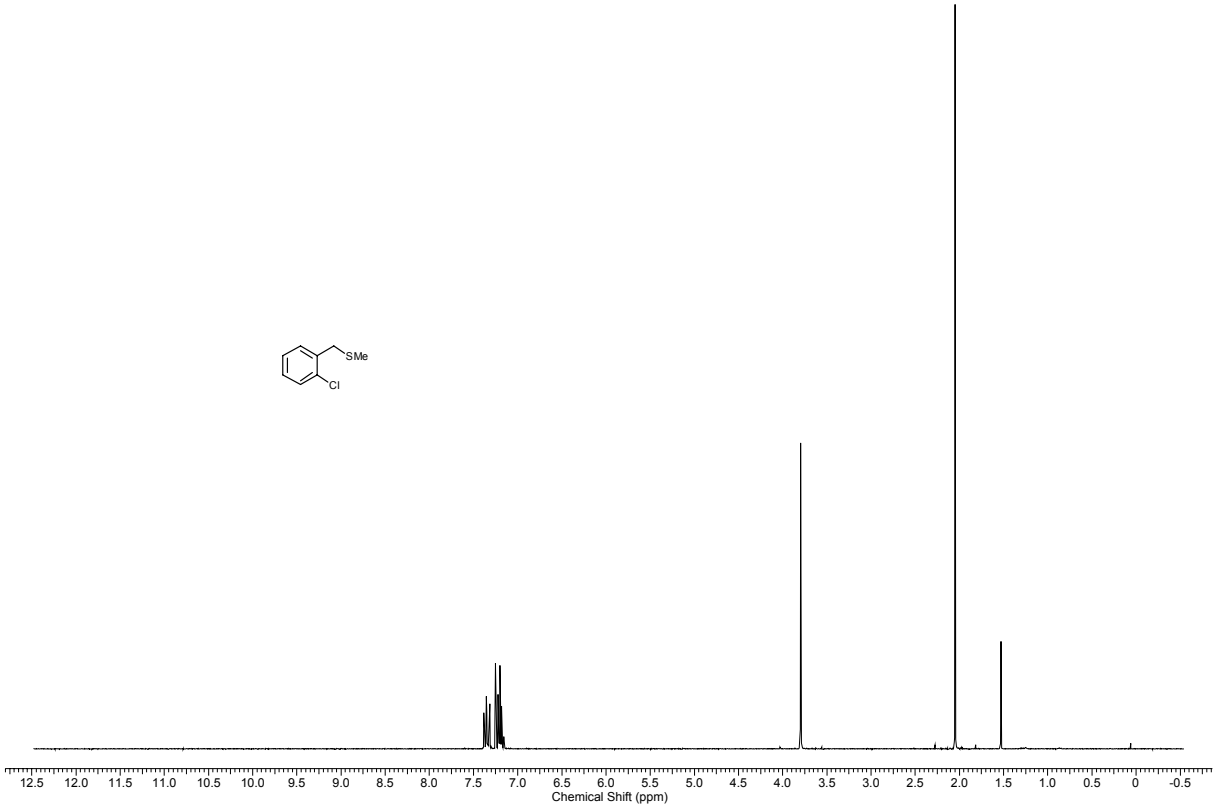


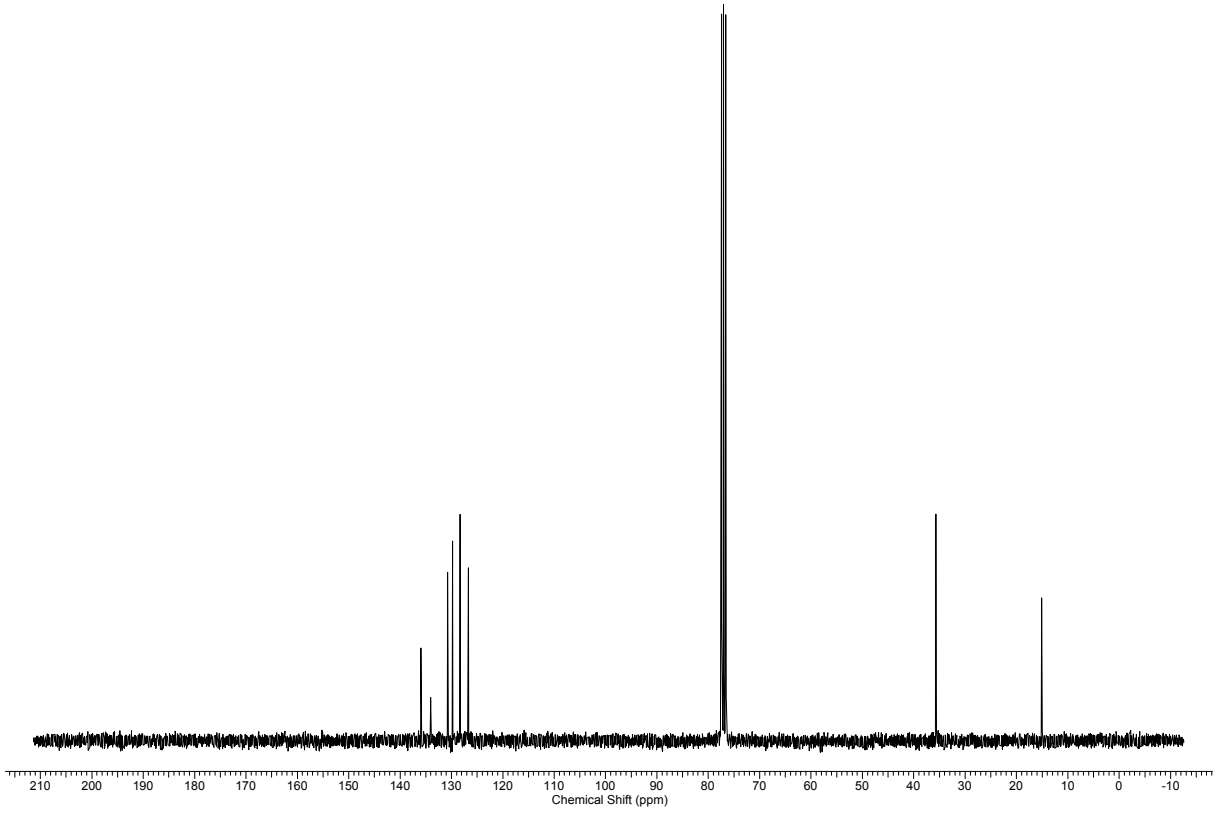
Ethyl 2-[2-(2-chlorophenyl)ethyl]acrylate (4h)



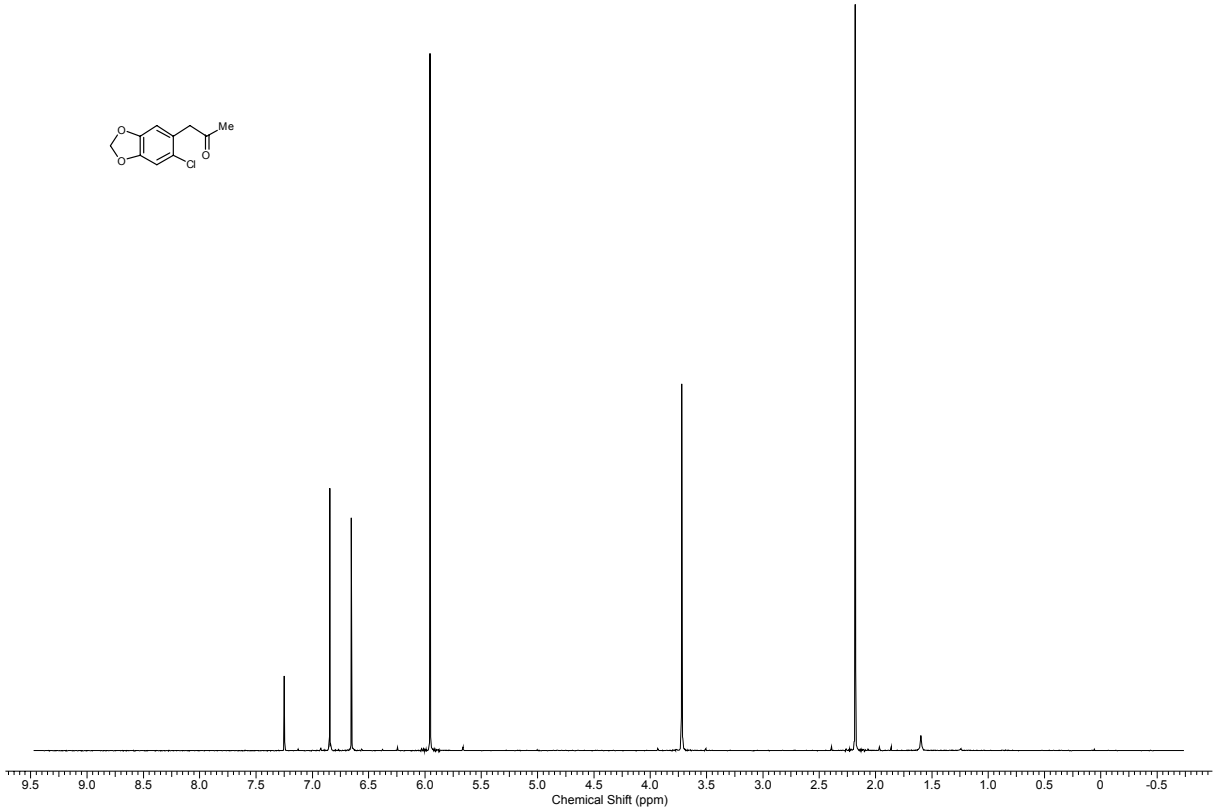


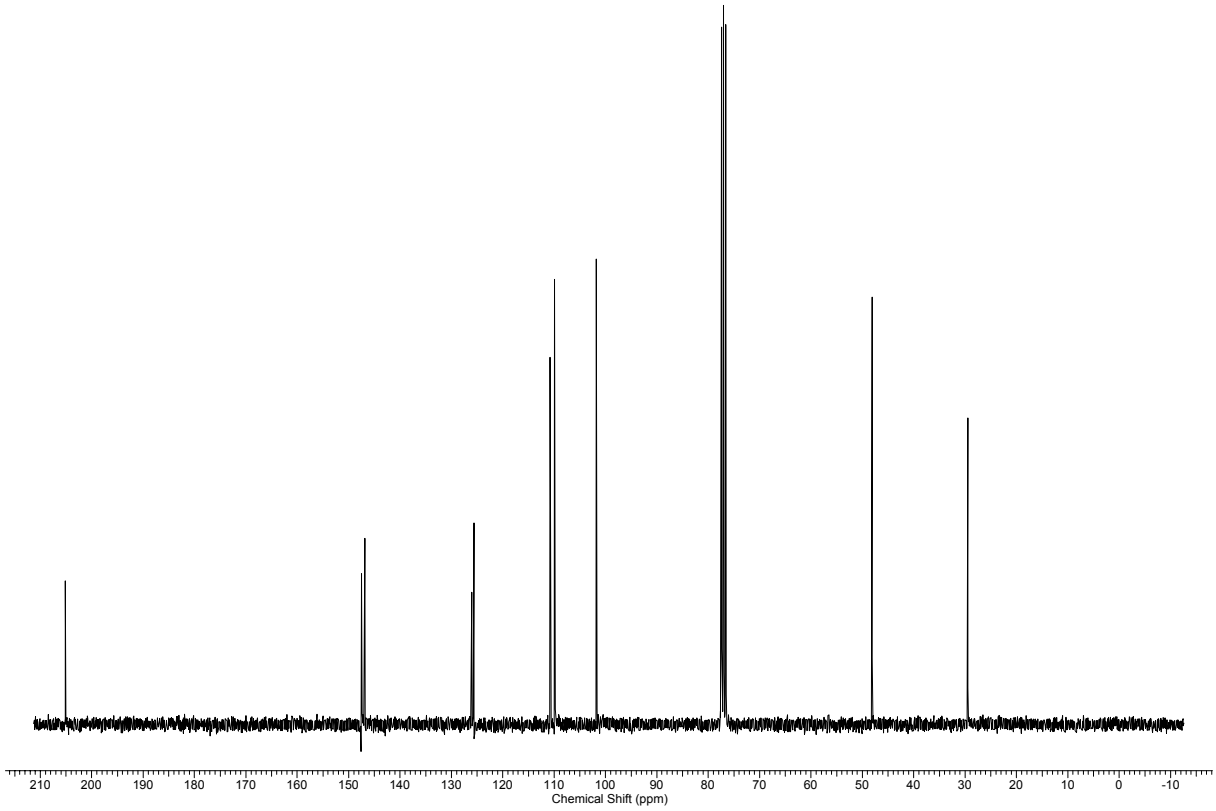
2-Chlorobenzyl methyl sulphide (4i):



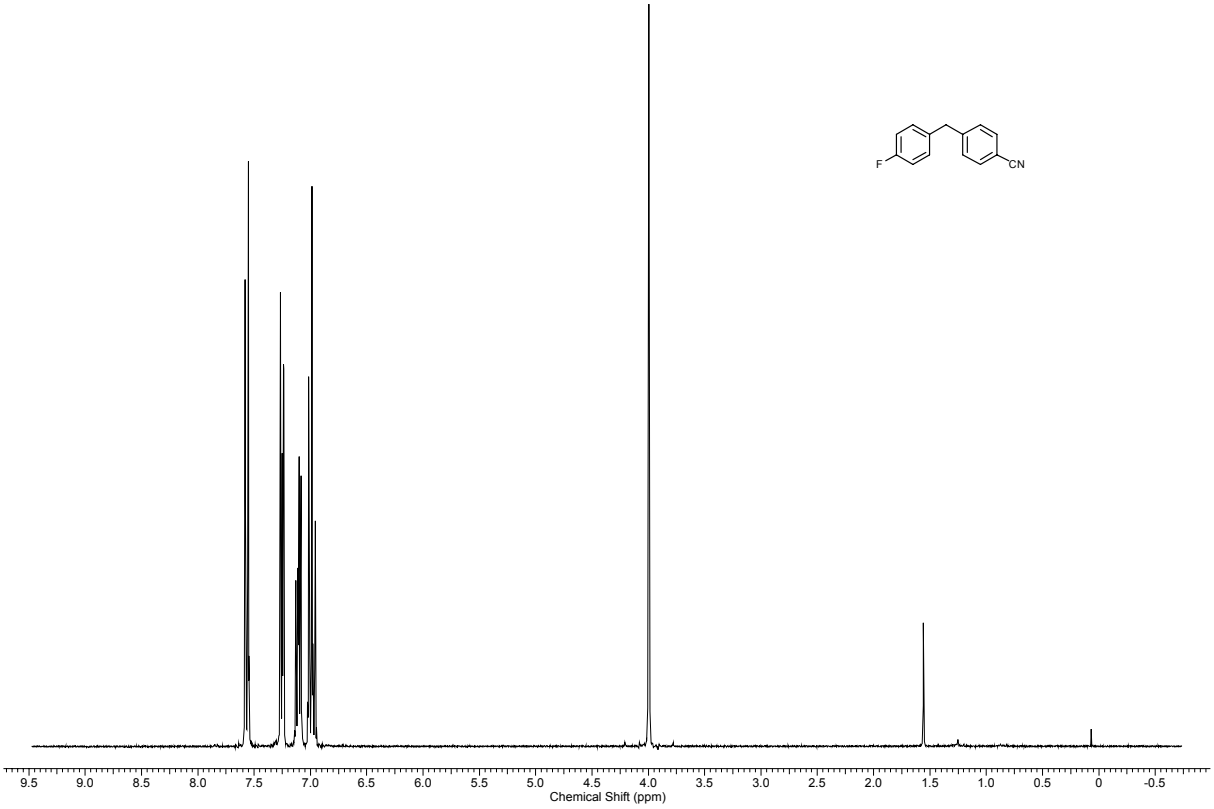


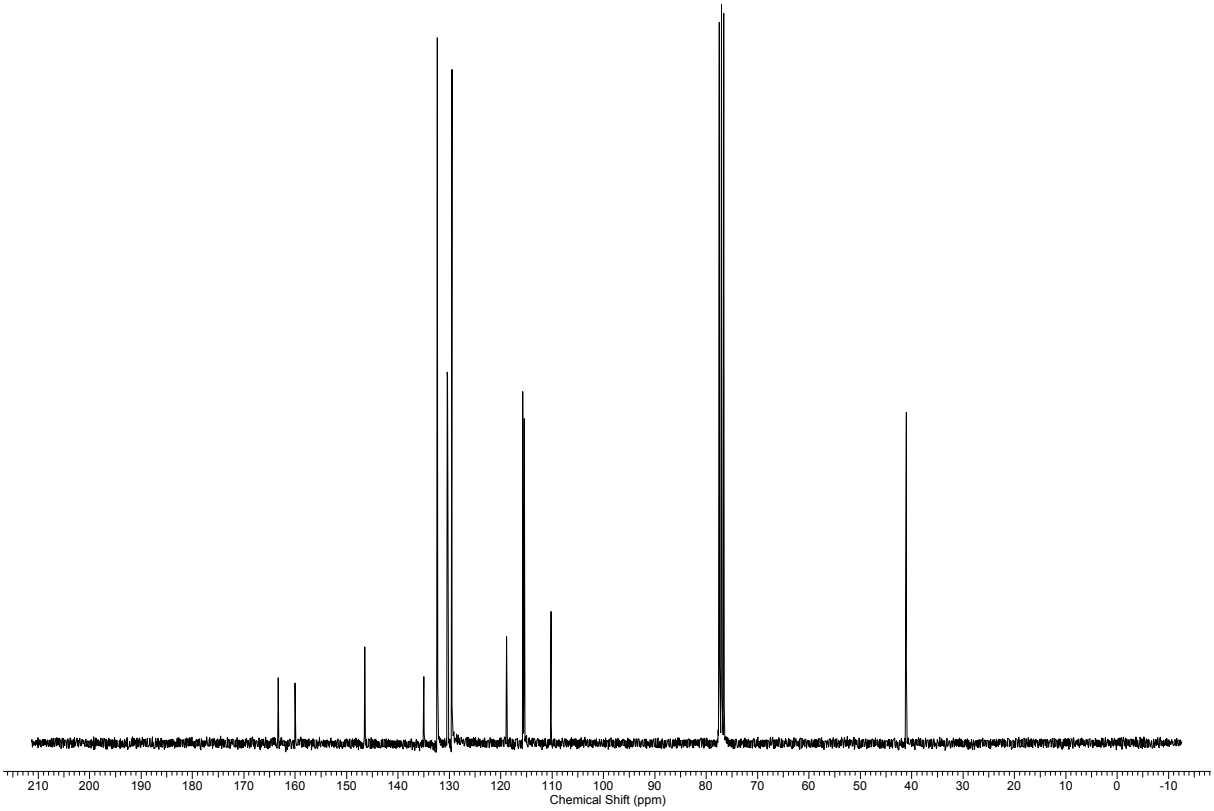
1-(6-Chloro-1,3-benzodioxol-5-yl)acetone (4j):



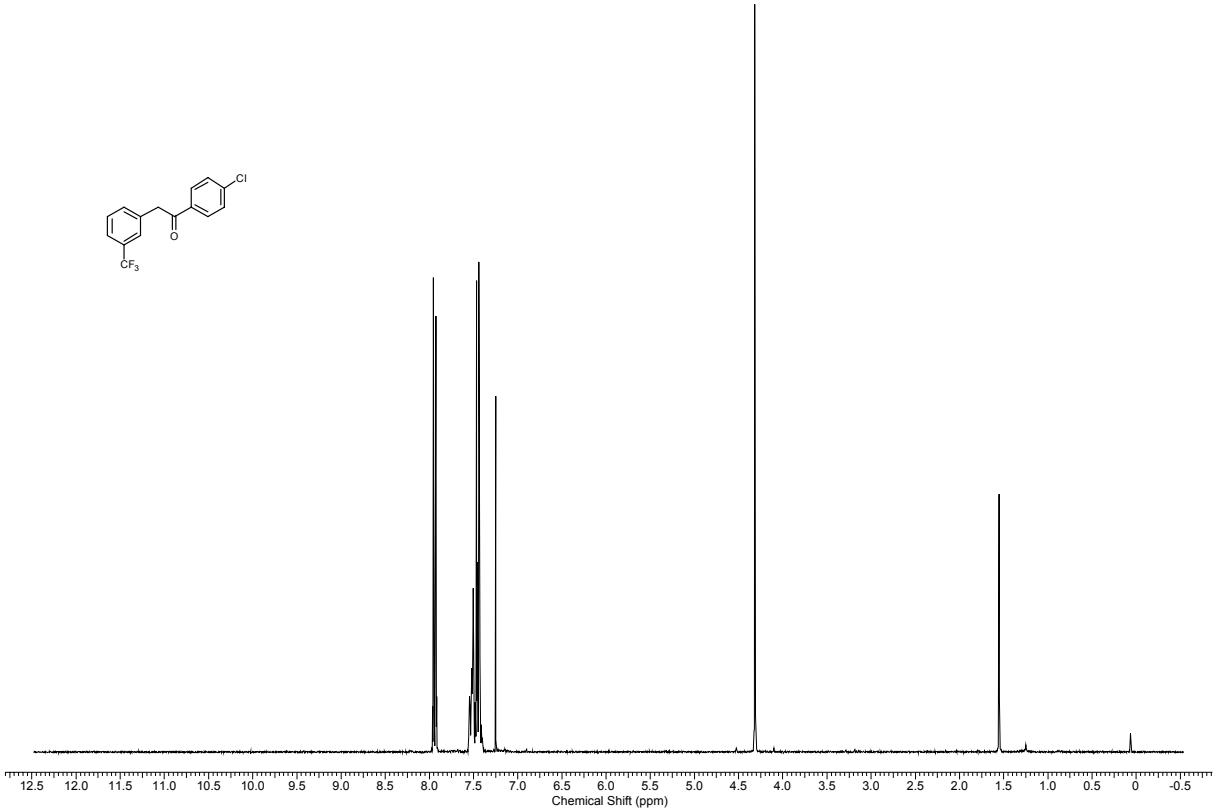


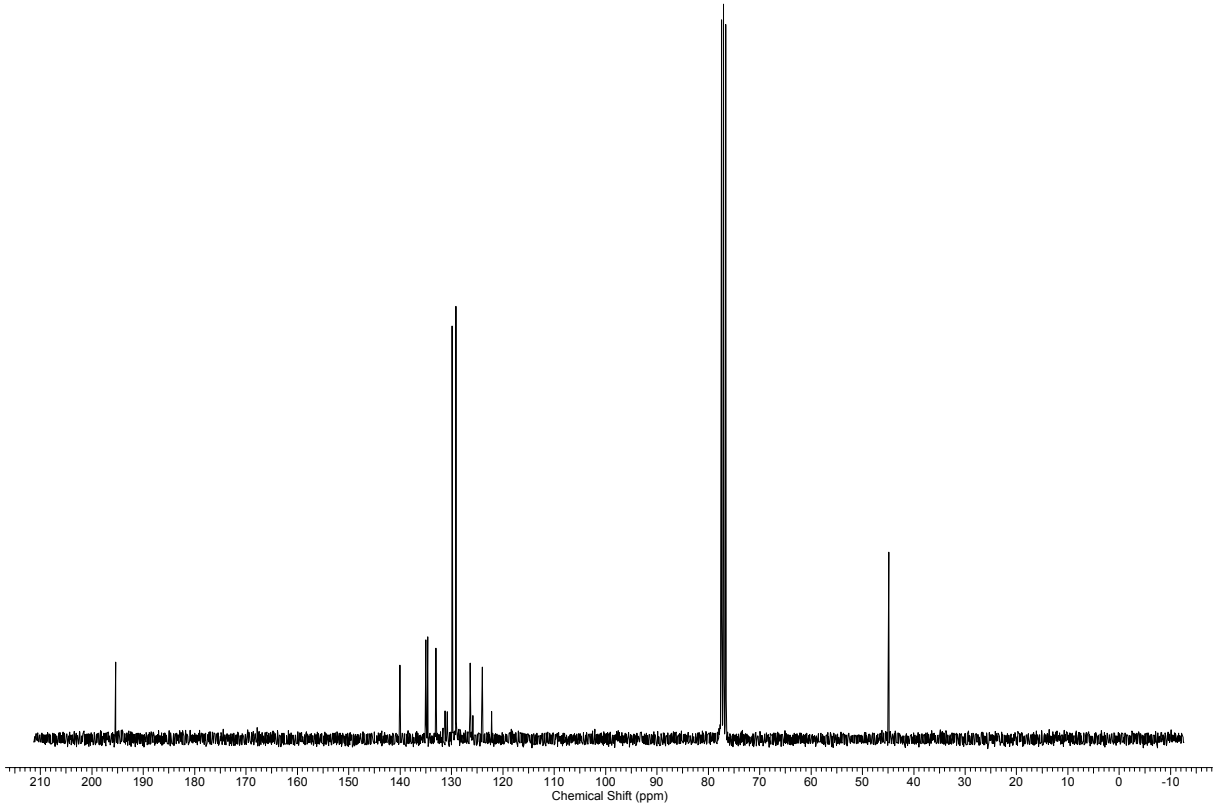
4-(4-Fluorobenzyl)benzonitrile (4k):



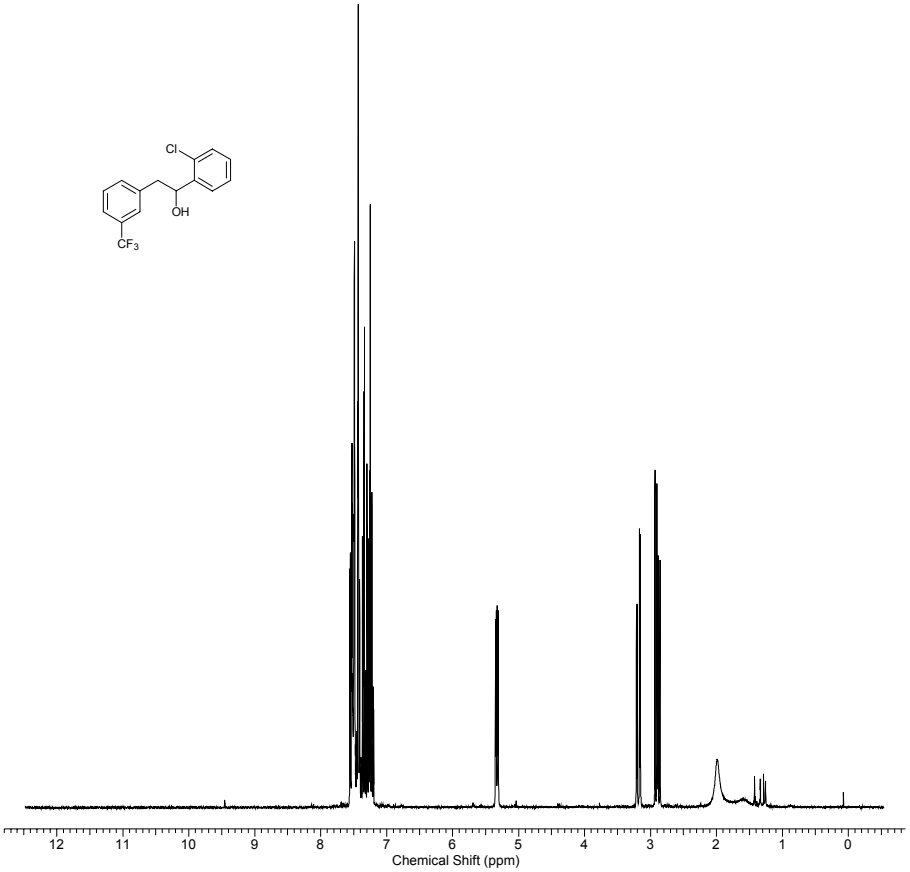


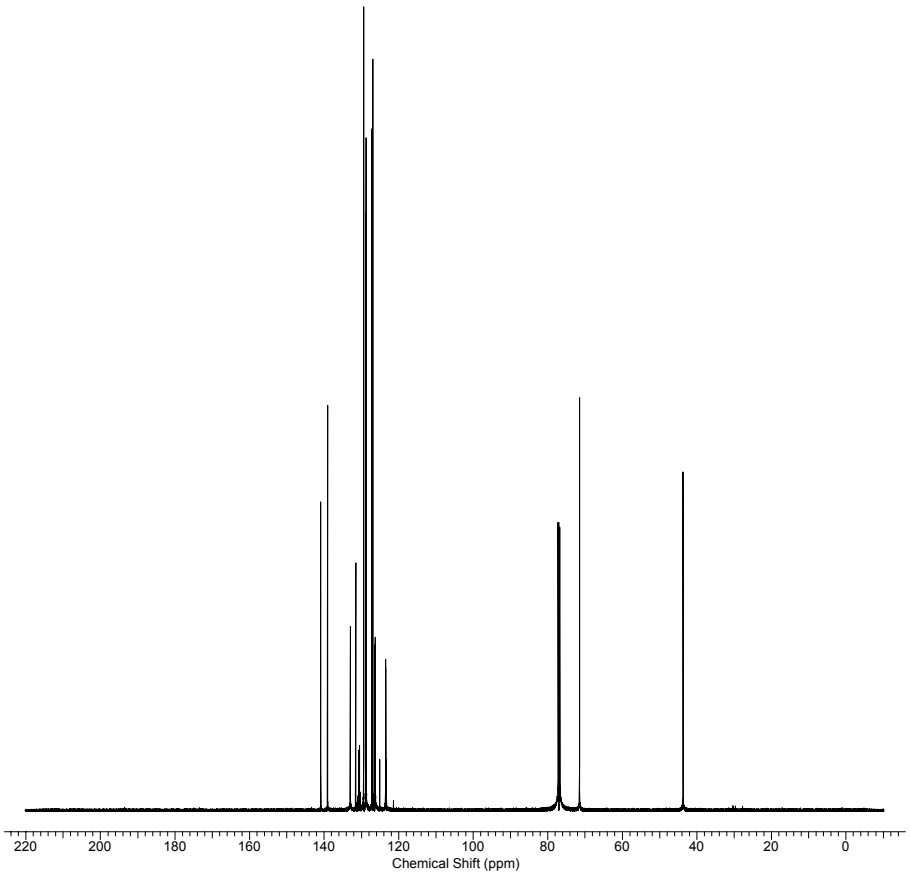
1-(4-Chlorophenyl)-2-[3-(trifluoromethyl)phenyl]ethanone (4l):



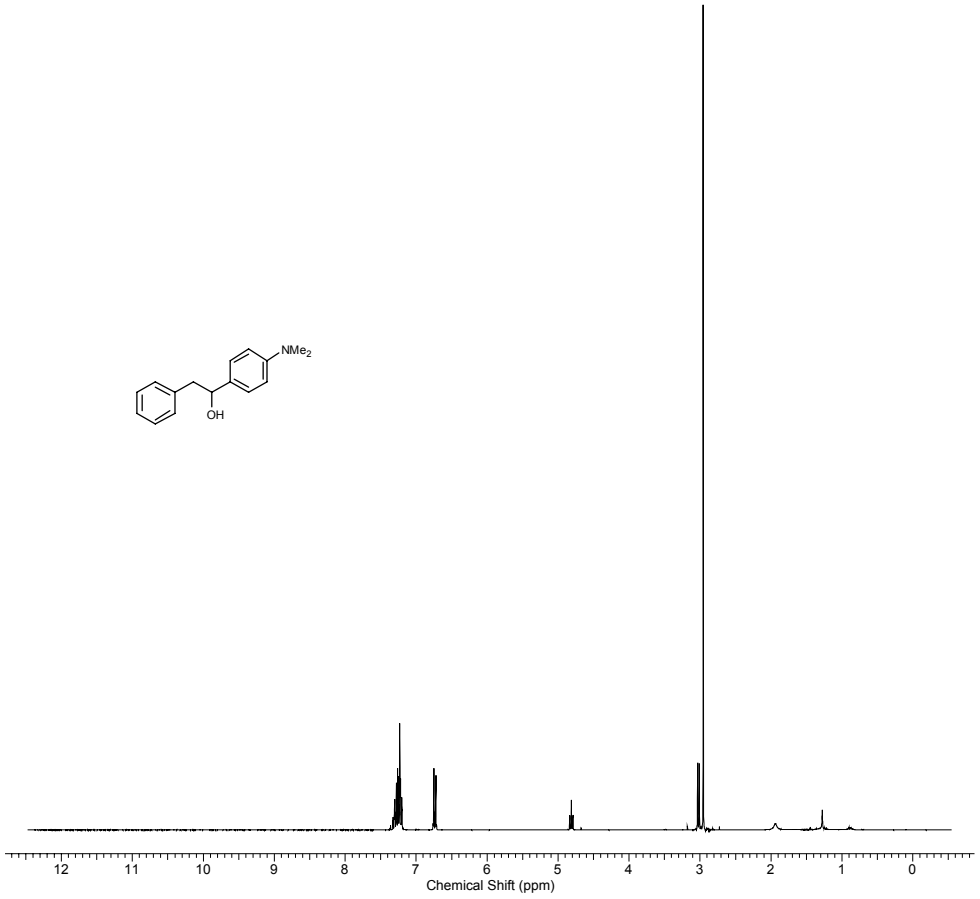


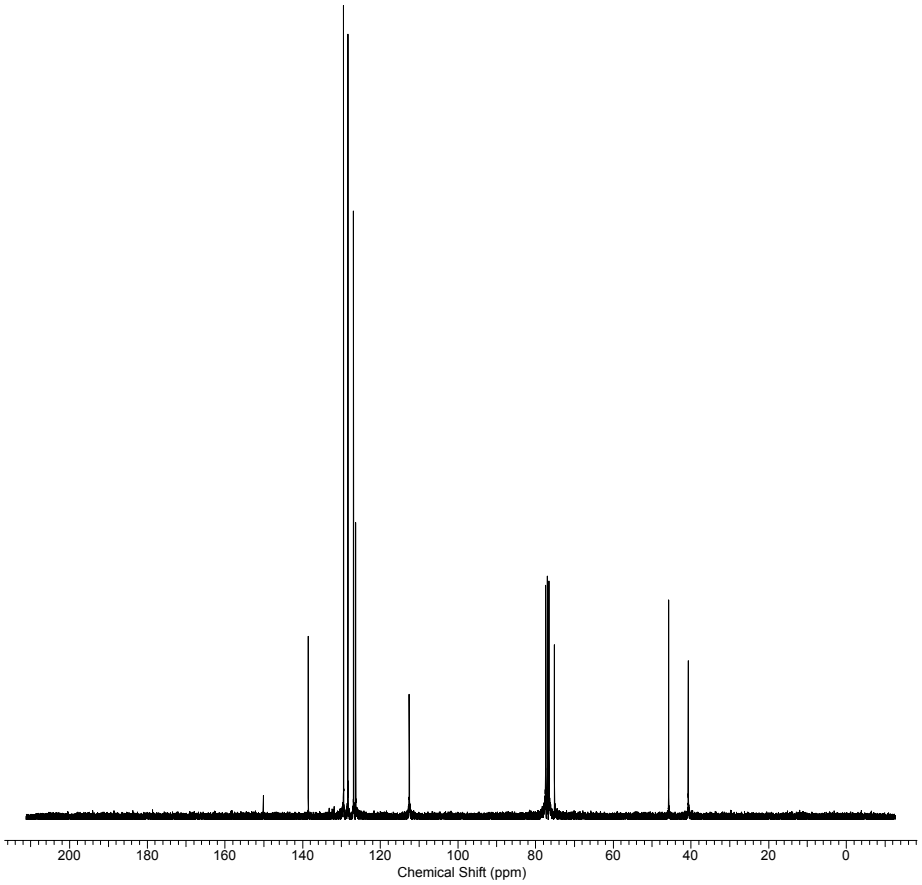
1-(2-Chlorophenyl)-2-[3-(trifluoromethyl)phenyl]ethanol (4m)



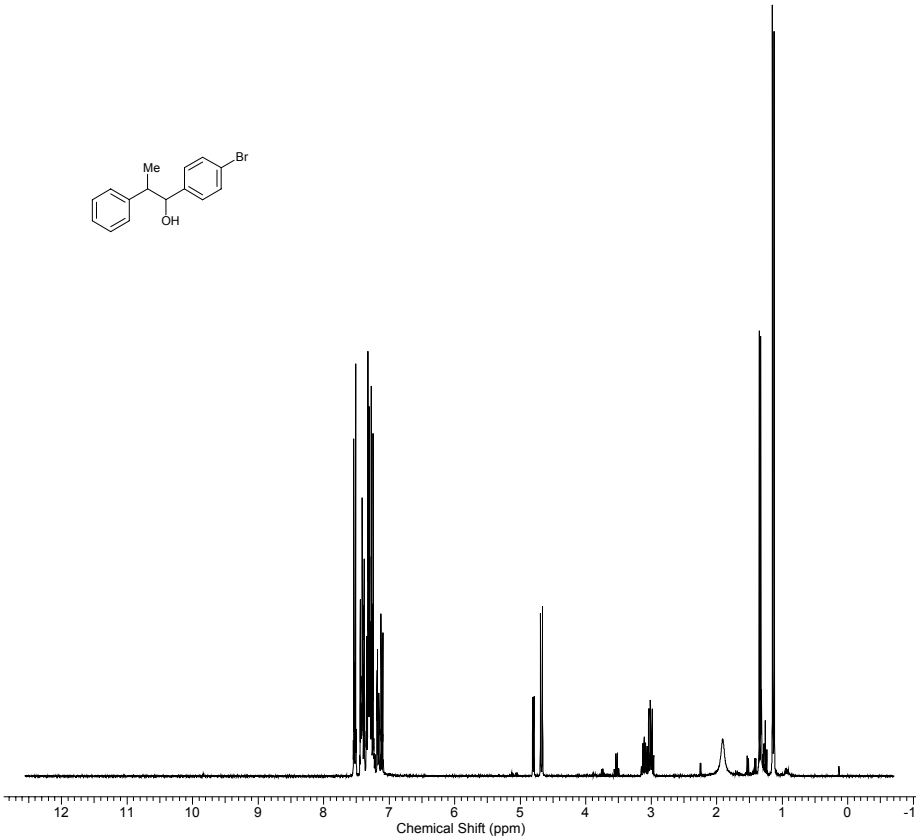


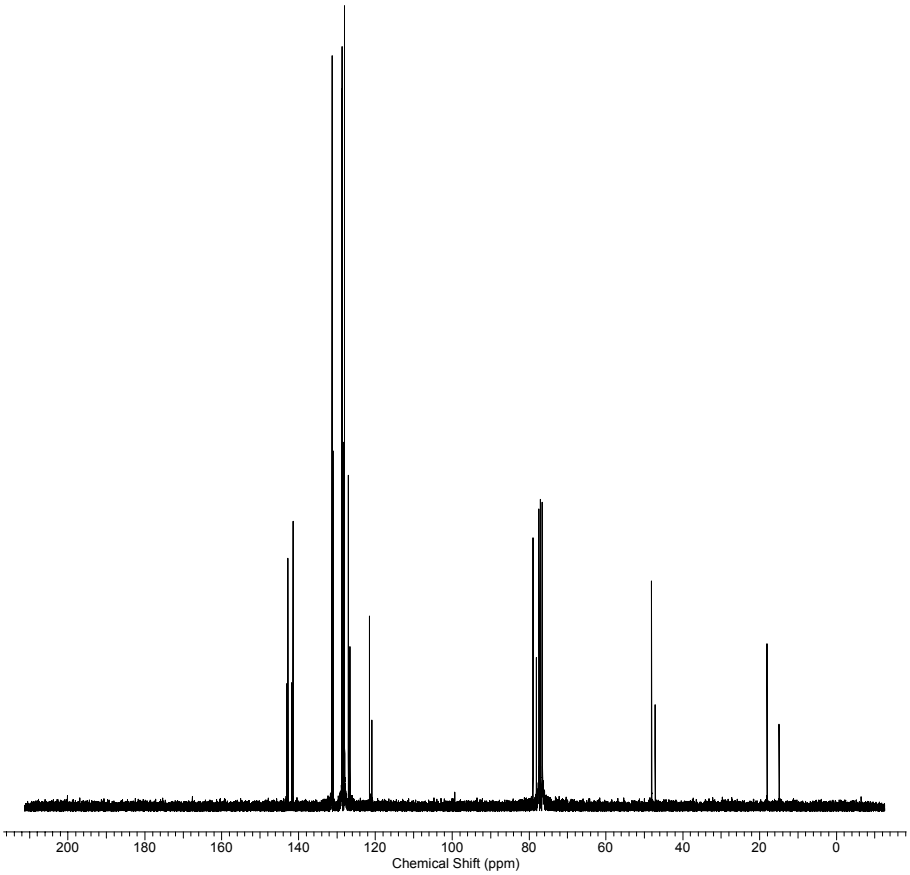
1-[4-(Dimethylamino)phenyl]-2-phenylethanol(4n)



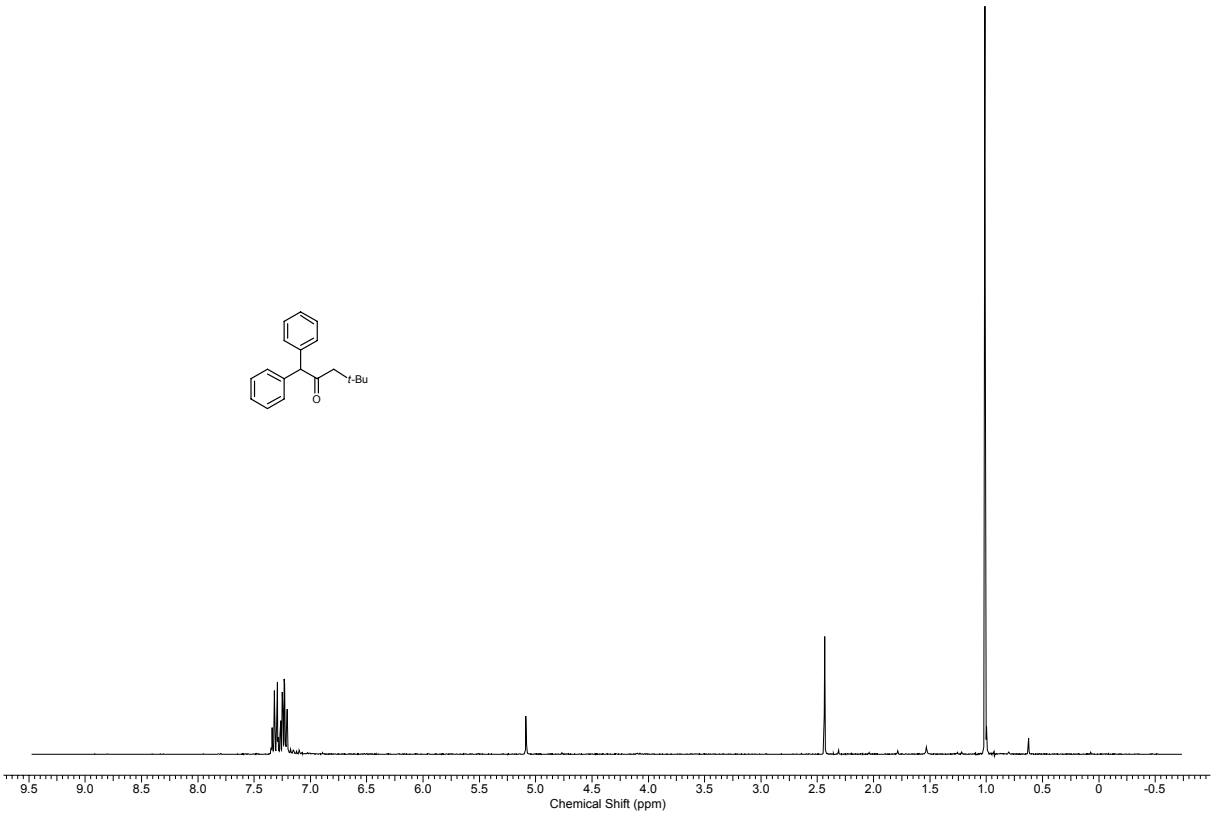


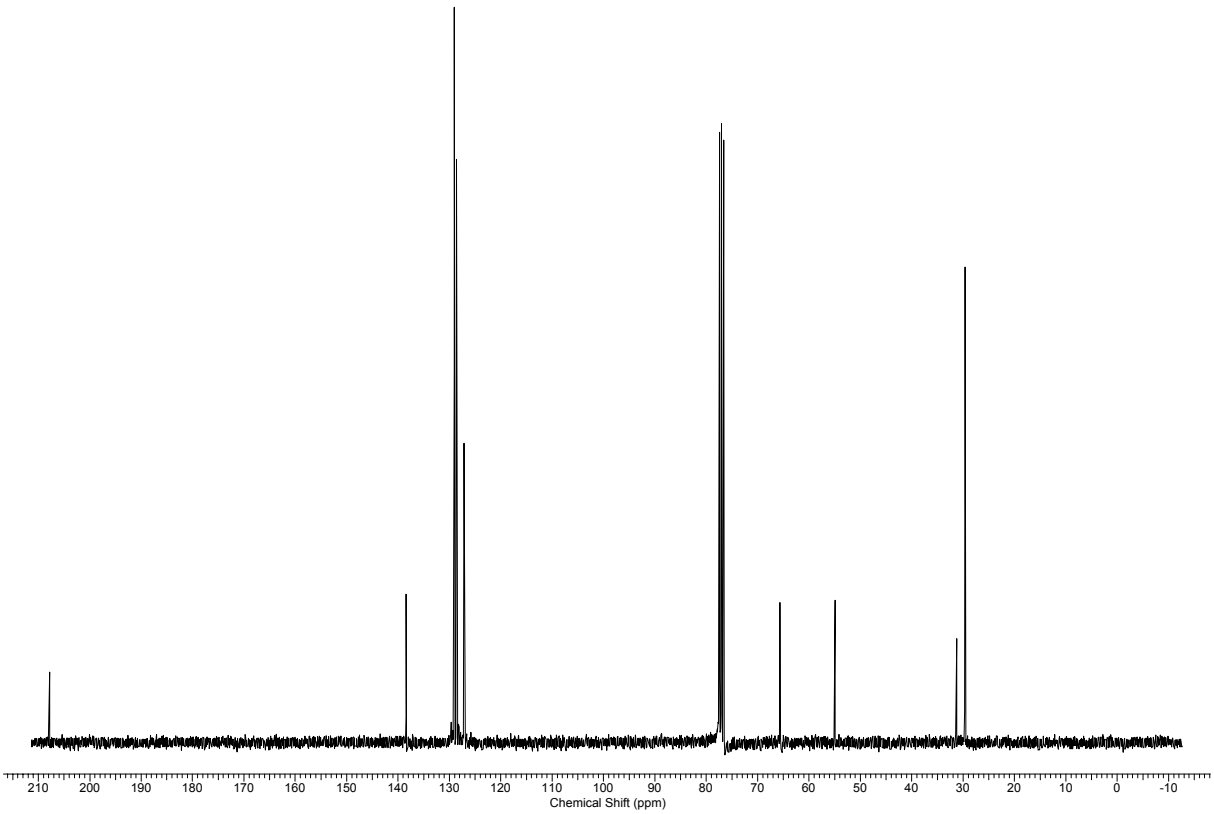
1-(4-Bromophenyl)-2-phenylpropan-1-ol (4o):





4,4-Dimethyl-1,1-diphenylpentan-2-one (4p):


t-Bu
O
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0 -0.5
Chemical Shift (ppm)


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