A facile, one-pot procedure for the conversion of aromatic aldehydes to esters, as well as thioesters and amides, *via* acyl hydrazide intermediates

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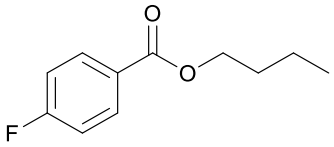
General Experimental

All reagents were purchased from Aldrich or AlfaAesar and were used as received without further purification unless otherwise stated. All reactions were carried out in carousel tubes (15 cm × 2 cm) equipped with an octagon-shaped magnetic stirrer bar (12.7 mm × 3 mm) unless otherwise stated. Where described below, Petrol refers to petroleum ether (b.p. 40-60 °C). All reactions were monitored by thin-layer chromatography (TLC) on pre-coated silica gel plates (254 μm). Flash column chromatography was carried out with Kieselgel 60M 0.04/0.063 mm (200-400 mesh) silica gel. ^{1}H NMR spectra were recorded at 300 MHz, 400 MHz, 500 MHz and 600 MHz and ^{13}C NMR at 75 MHz, 100 MHz, 125 MHz and 150 MHz on Bruker AMX300, AMX400, AMX500 and AMX600 spectrometers. ^{19}F NMR spectra were recorded at 376 MHz on Bruker AMX400 at ambient temperature unless otherwise stated, in $CDCl_3$ or d_6-DMSO (see below). The chemical shifts (δ) for ^{1}H and ^{13}C are quoted relative to residual signals of the solvent on the ppm scale. Coupling constants (*J* values) are reported in Hertz (Hz) and are H-H coupling constants unless otherwise stated. Signal multiplicities in ^{13}C NMR were determined using the distortionless enhancement by phase transfer (DEPT) spectral editing technique. Where applicable, only the peaks for the major rotamers of acyl hydrazides are assigned in the ^{1}H and spectra. Mass spectra were obtained on a VG70-SE mass spectrometer. Infrared spectra were obtained on a Perkin Elmer Spectrum 100 FTIR Spectrometer operating in ATR mode. Melting points were measured with a Gallenkamp apparatus and are uncorrected.

General procedure for one-pot ester synthesis

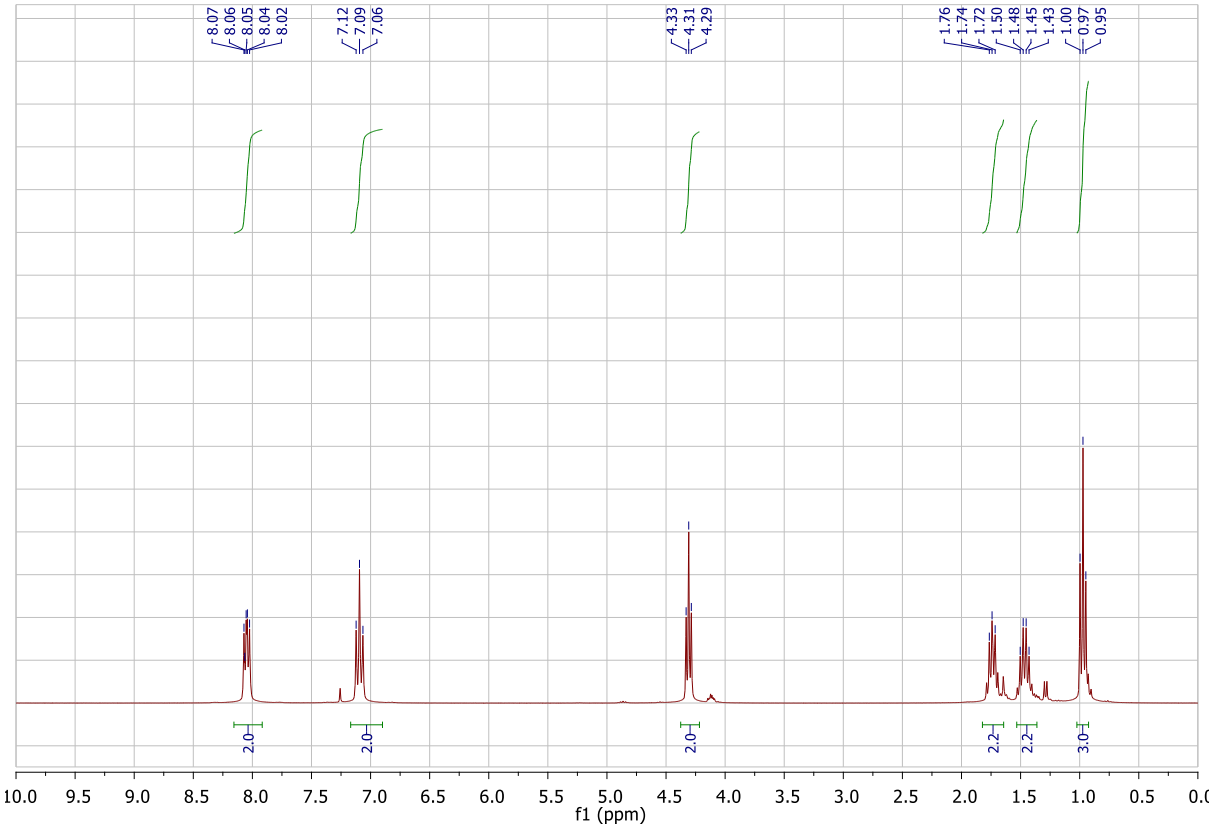
Aldehyde (0.5 mmol) was added to a solution of azodicarboxylate (0.6 mmol, 1.2 eq.) in DMF (500 μL) and the reaction mixture stirred at 300 rpm at 21 °C in a carousel tube for 24 h. After this time, Cs_2CO_3 (163 mg, 0.50 mmol, 1.0 eq.) and alcohol (0.55 mmol, 1.1 eq.) in dimethylformamide (1 mL) was added to the reaction mixture. After 16 h, the reaction mixture was diluted with diethyl ether (25 mL) and extracted with aq. sat. LiCl (2 × 25 mL). The organic layer was then dried ($MgSO_4$), filtered and the solvent was removed *in vacuo*. The resultant crude residue was purified as described below.

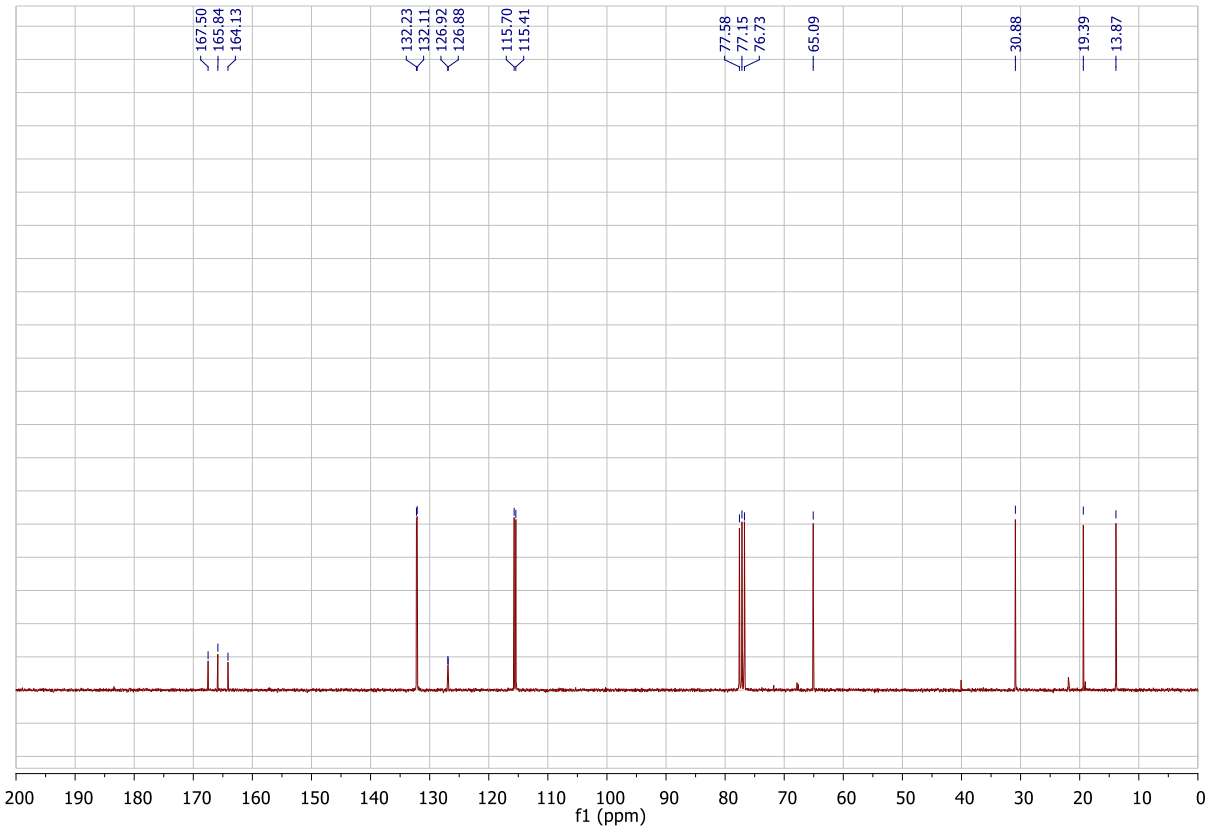
_n_-Butyl 4-fluorobenzoate



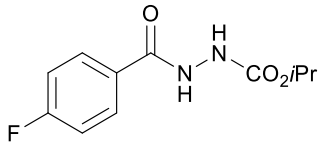
Purification by column chromatography (1%-5% EtOAc/Petrol) yielded *n*-butyl 4-fluorobenzoate as a clear oil (73 mg, 0.37 mmol, 74%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07-8.04 (m, 2H), 7.12-7.08 (m, 2H), 4.32 (t, J = 6.6 Hz, 2H), 1.75 (pent., J = 7.1 Hz, 2H), 1.47 (sxt., J = 7.5 Hz, 2H), 0.98 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9 (C), 165.8 (d, $J_{C\text{-}F}$ = 210.1 Hz, C), 132.2 (d, $J_{C\text{-}F}$ = 7.65 Hz, CH), 126.8 (d, $J_{C\text{-}F}$ = 4.4 Hz, C), 115.5 (d, $J_{C\text{-}F}$ = 18.2 Hz, CH), 65.1 (CH_2), 30.9 (CH_2), 19.4 (CH_2), 13.9 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ -106.5 (s, 1F); IR (thin film) 2960, 2875, 1726, 1601, 1509 cm^{-1}; LRMS (ESI) 197 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_{11}H_{14}O_2F$ $[M+H]^+$ 197.0908; observed 197.0914.

This reaction has also been carried out on a 5 mmol scale of aldehyde in a stoppered round bottom flask (100 mL). A yield of 665 mg (3.39 mmol, 68%) was obtained. ^{1}H NMR identical to that observed below.

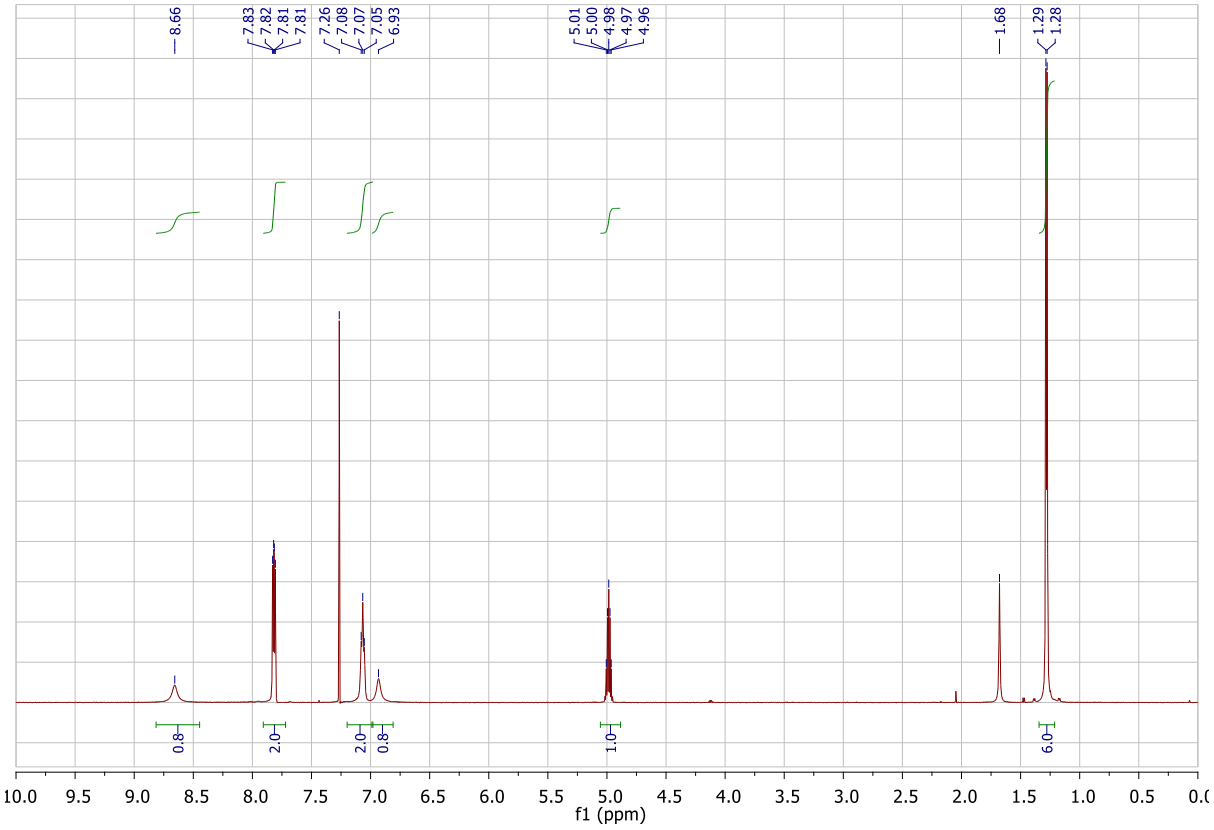


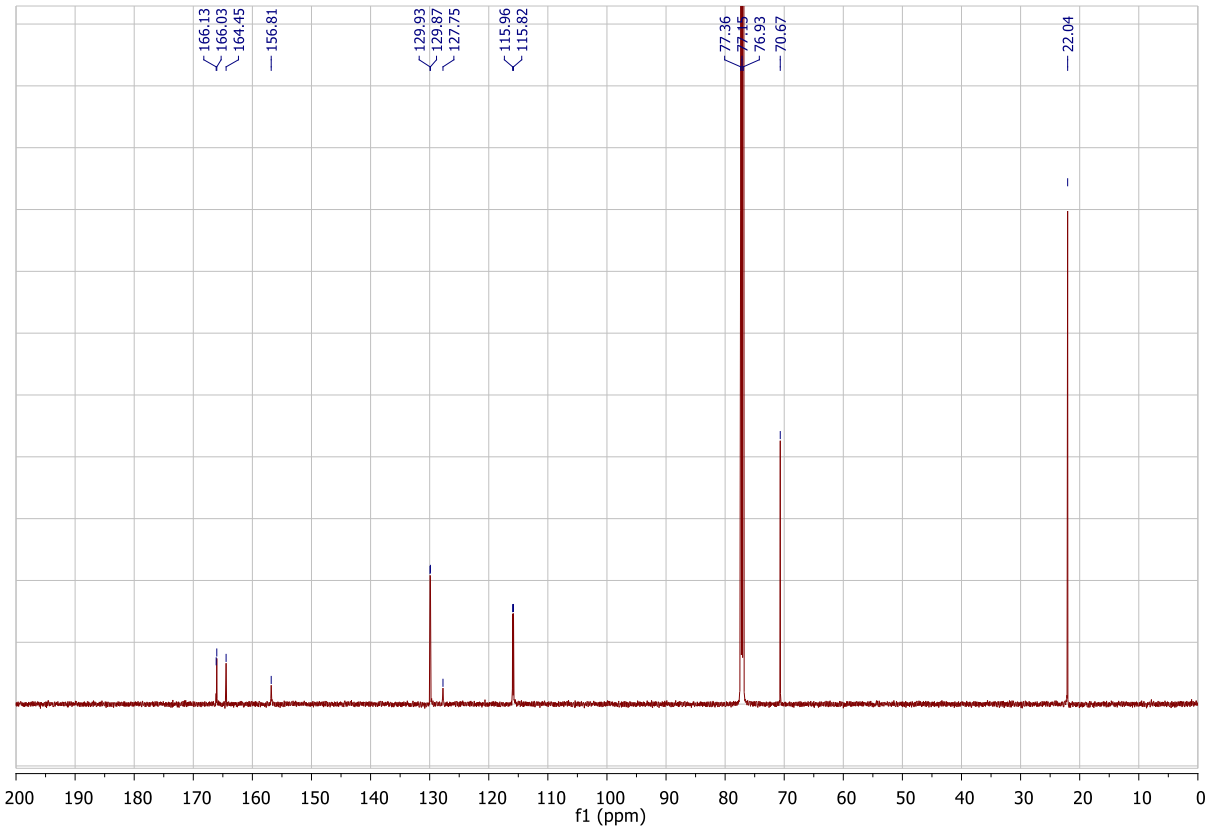

167.50
165.84
164.13
132.23
132.11
126.92
126.88
115.70
115.41
77.58
77.15
76.73
65.09
30.88
19.39
13.87
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Propan-2-yl 2-(4-fluorobenzoyl)hydrazinecarboxylate

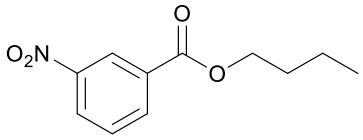


Purification by column chromatography (1%-5% EtOAc/Petrol) propan-2-yl 2-(4-fluorobenzoyl)hydrazinecarboxylate as a clear oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.66 (br s, 1H), 7.82 (m, 2H), 7.07 (t, J = 7.8 Hz, 2H), 6.93 (br s, 1H), 4.98 (septet, J = 6.3 Hz, 1H), 1.28 (d, J = 6.3 Hz, 6H); ^{13}C NMR (600 MHz, $CDCl_3$) δ 166.0 (C), 165.3 (d, $J_{C\text{-}F}$ = 250.1 Hz, C), 156.8 (C), 129.9 (d, $J_{C\text{-}F}$ = 9.0 Hz, CH_2), 127.8 (C), 115.9 (d, $J_{C\text{-}F}$ = 22.0 Hz, CH_2), 70.7 (CH), 22.0 (CH_3); IR (thin film) 3304, 2978, 2885, 1701, 1697, 1672, 1602 cm^{-1}; LRMS (ESI) 241 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_{11}H_{14}N_2O_3F$ $[M+H]^+$ 241.0918; observed 241.0915.

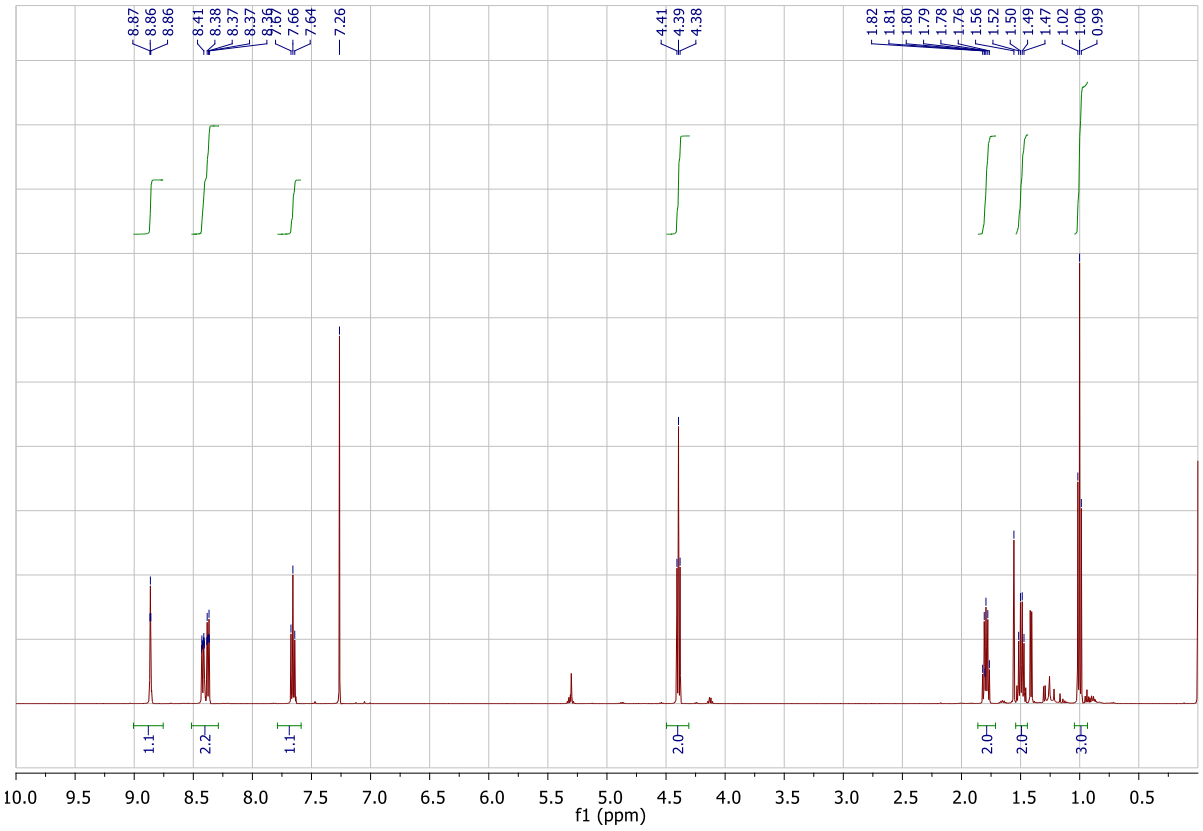


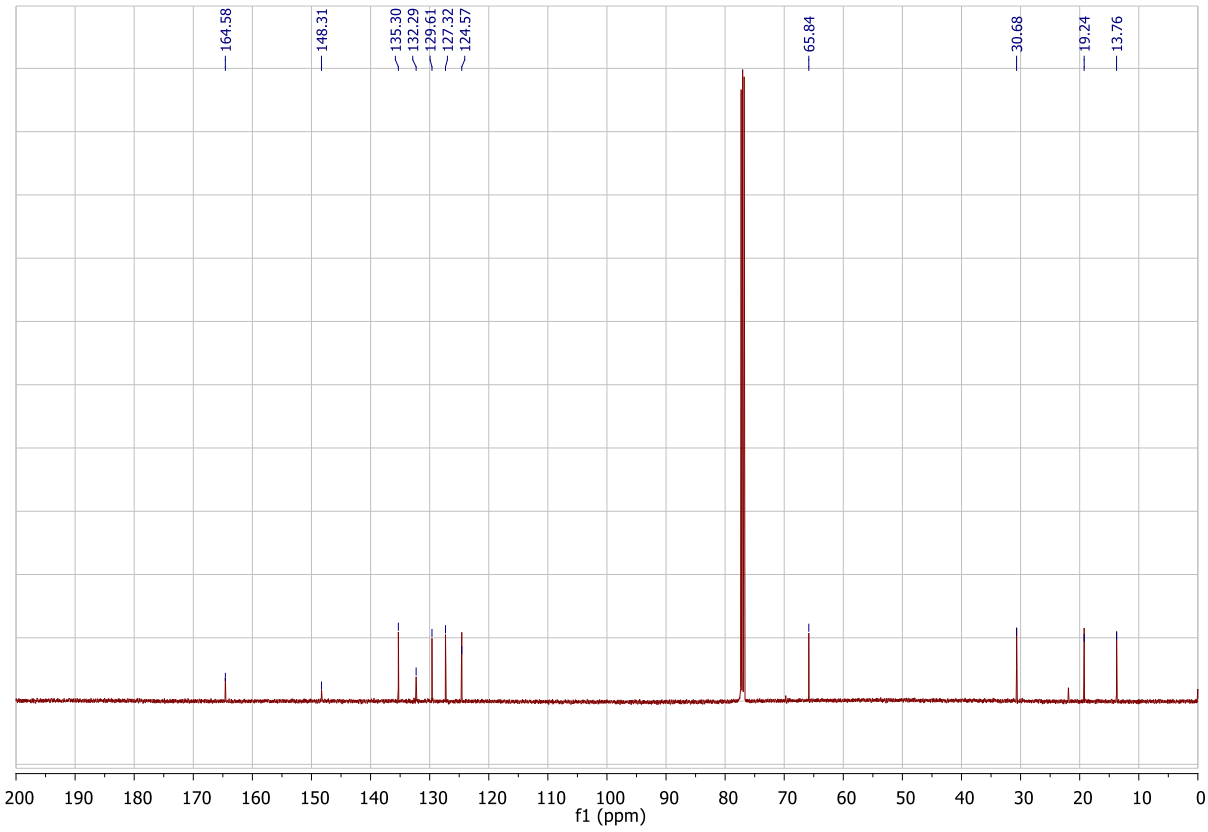

166.13
166.03
164.45
156.81
129.93
129.87
127.75
115.96
115.82
77.36
77.15
76.93
70.67
22.04
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

_n_-Butyl 3-nitrobenzoate

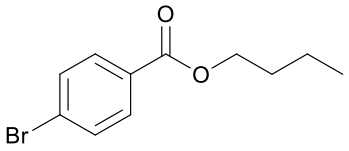


Purification by column chromatography (1%-5% EtOAc/Petrol) yielded *n*-butyl 3-nitrobenzoate as a clear oil (80 mg, 0.36 mmol, 72%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.86 (t, *J* = 2.3 Hz, 1H), 8.42 (ddd, *J* = 8.2, 2.3, 1.1 Hz, 1H), 8.38-8.35 (m, 1H), 7.66 (t, *J* = 8.2 Hz, 1H), 4.39 (t, *J* = 6.7 Hz, 2H), 1.82-1.74 (m, 2H), 1.48 (sxt., *J* = 6.7 Hz, 2H), 1.00 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.6 (C), 148.3 (C), 135.3 (CH), 132.3 (C), 129.6 (CH), 127.3 (CH), 124.6 (CH), 65.8 (CH_2), 30.7 (CH_2), 19.2 (CH_2), 13.8 (CH_3); IR (thin film) 2964, 2875, 2231, 1714 cm^{-1}; LRMS (ESI) 224 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_{11}H_{14}NO_4$ $[M+H]^+$ 224.0923; observed 224.0927.

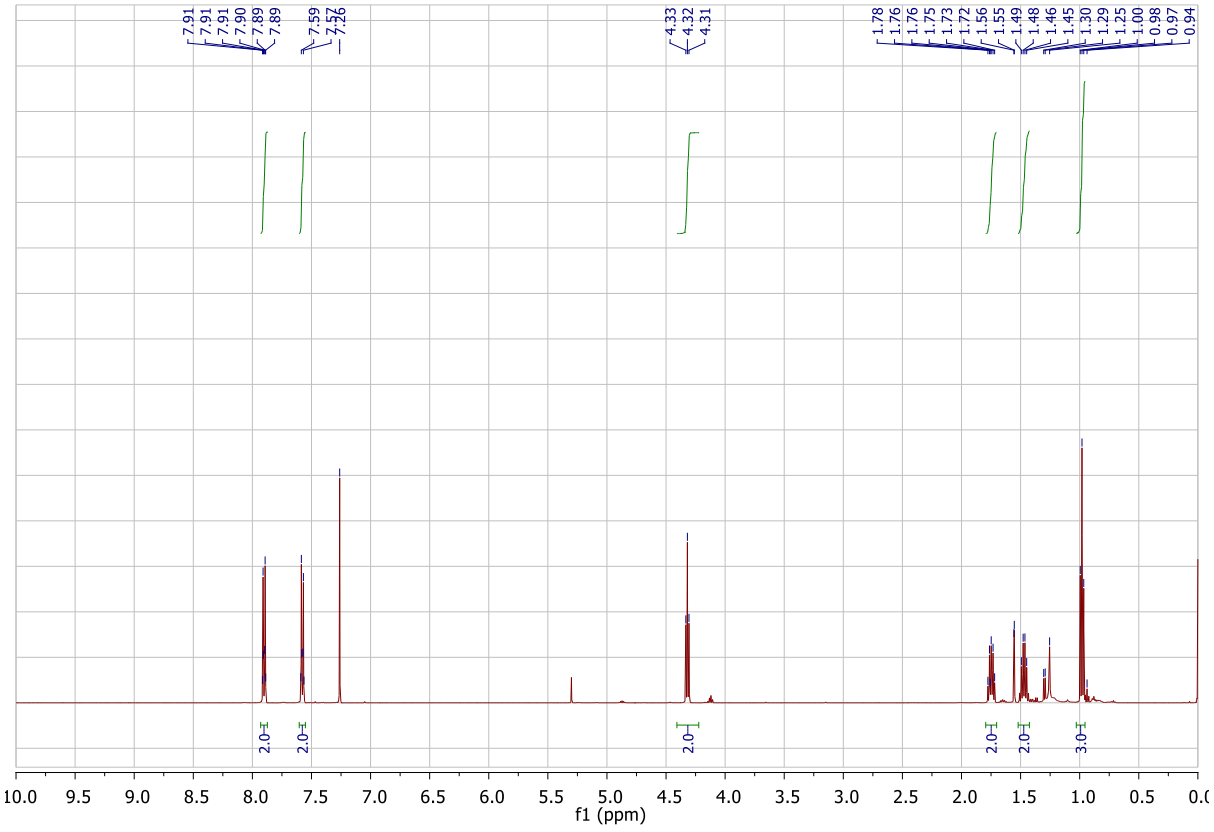


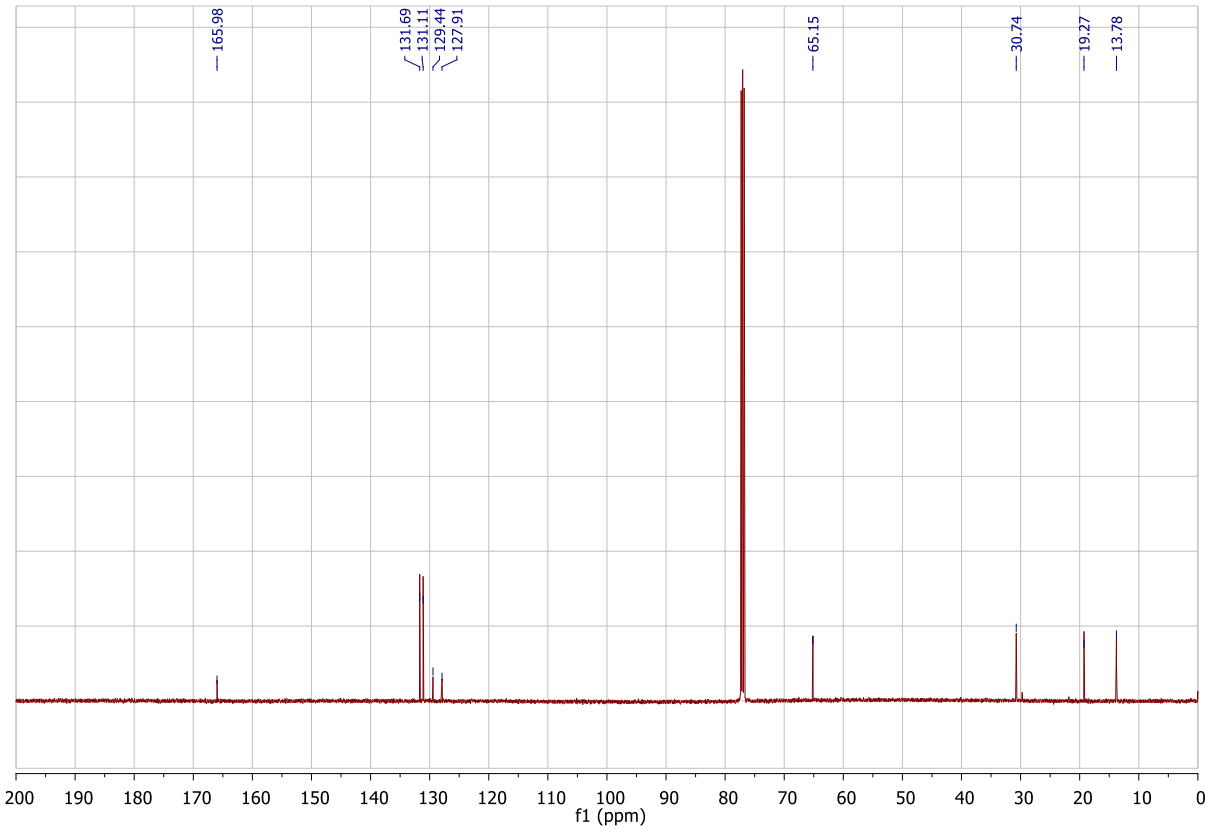

164.58
148.31
135.30
132.29
129.61
127.32
124.57
65.84
30.68
19.24
13.76
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

_n_-Butyl 4-bromobenzoate[1]

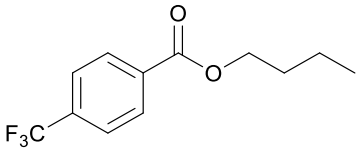


Purification by column chromatography (1%-5% EtOAc/Petrol) yielded *n*-butyl 4-bromobenzoate as a clear oil (91 mg, 0.35 mmol, 71%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91-7.89 (m, 2H), 7.59-7.57 (m, 2H), 4.32 (t, *J* = 6.6 Hz, 2H), 1.78-1.72 (m, 2H), 1.47 (sxt., *J* = 7.5 Hz, 2H), 0.98 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.0 (C), 131.7 (CH), 131.1 (CH), 129.4 (C), 127.9 (C), 65.2 (CH_2), 30.7 (CH_2), 19.3 (CH_2), 13.8 (CH_3); IR (thin film) 2960, 2873, 1720, 1590, 1485, 1397 cm^{-1}.

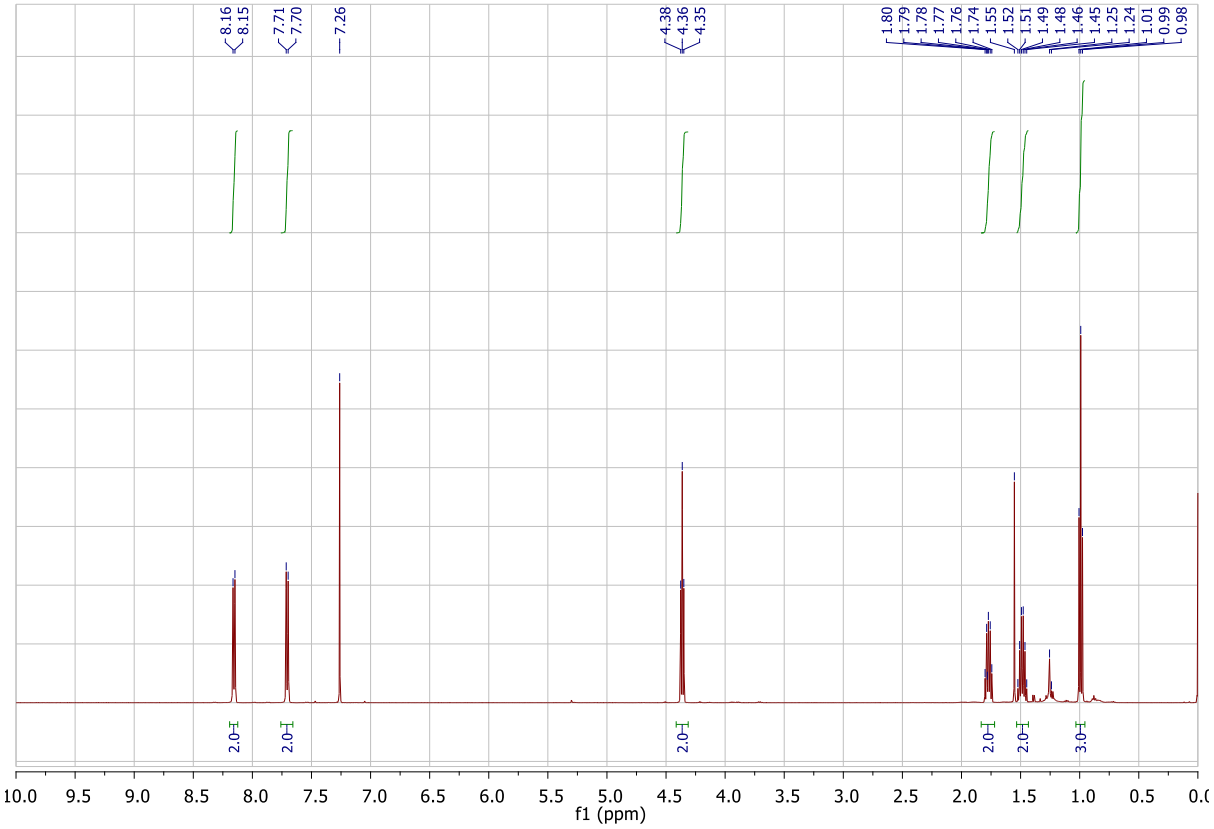


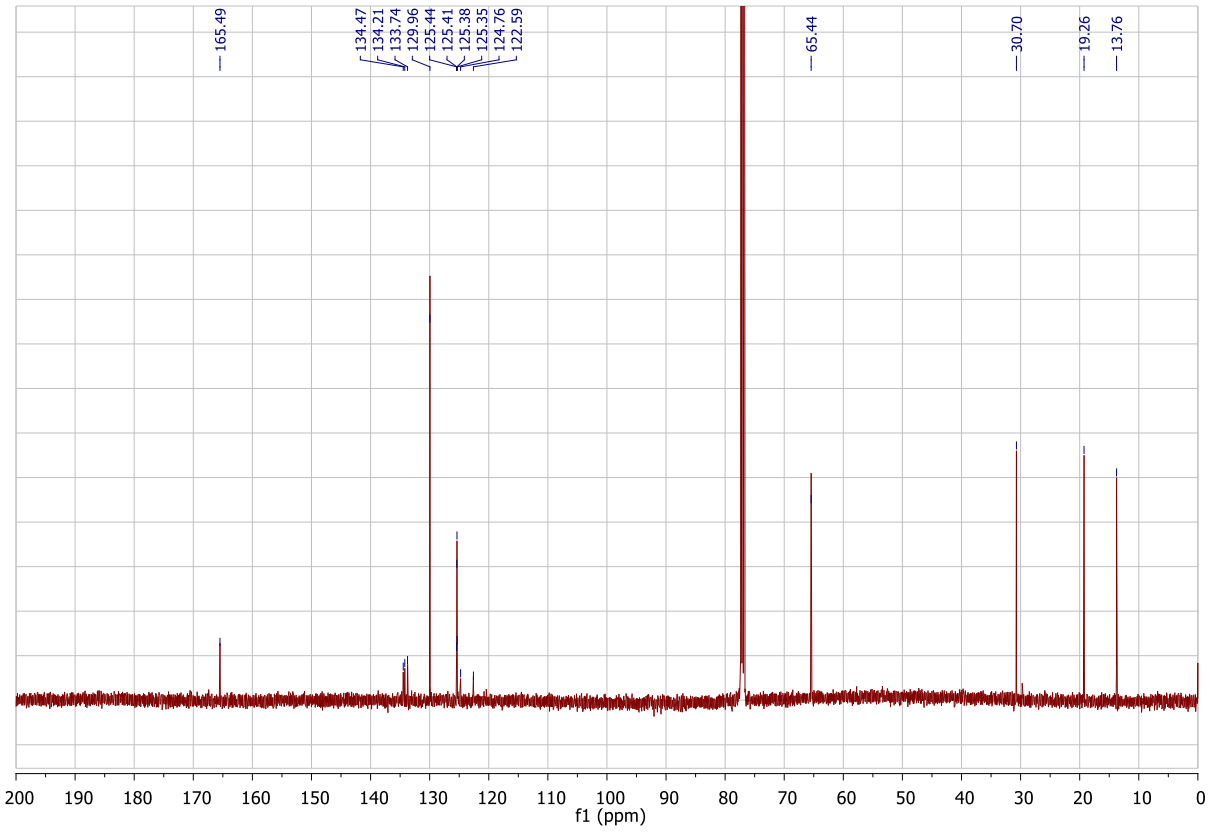

165.98
131.69
131.11
129.44
127.91
65.15
30.74
19.27
13.78
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

_n_-Butyl 4-(trifluoromethyl)benzoate[2]

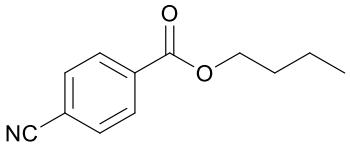


Purification by column chromatography (1%-5% EtOAc/Petrol) yielded *n*-butyl 4-(trifluoromethyl)benzoate as a clear oil (89 mg, 0.36 mmol, 72%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.1 Hz, 2H), 7.70 (d, *J* = 8.1 Hz, 2H), 4.36 (t, *J* = 6.7 Hz, 2H), 1.77 (m, 2H), 1.48 (sxt., *J* = 7.5 Hz, 2H), 0.99 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.5 (C), 134.3 (d, $J_{C\text{-}F}$ = 32.4 Hz, C), 133.7 (d, $J_{C\text{-}F}$ = 1.3 Hz, C), 129.9 (CH), 125.4 (q, $J_{C\text{-}F}$ = 4.0 Hz, CH), 123.5 (d, $J_{C\text{-}F}$ = 271.1 Hz, C), 65.4 (CH_2), 30.7 (CH_2), 19.3 (CH_2), 13.8 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ -64.1 (s, 1F); IR (thin film) 2980, 1720 cm^{-1}.

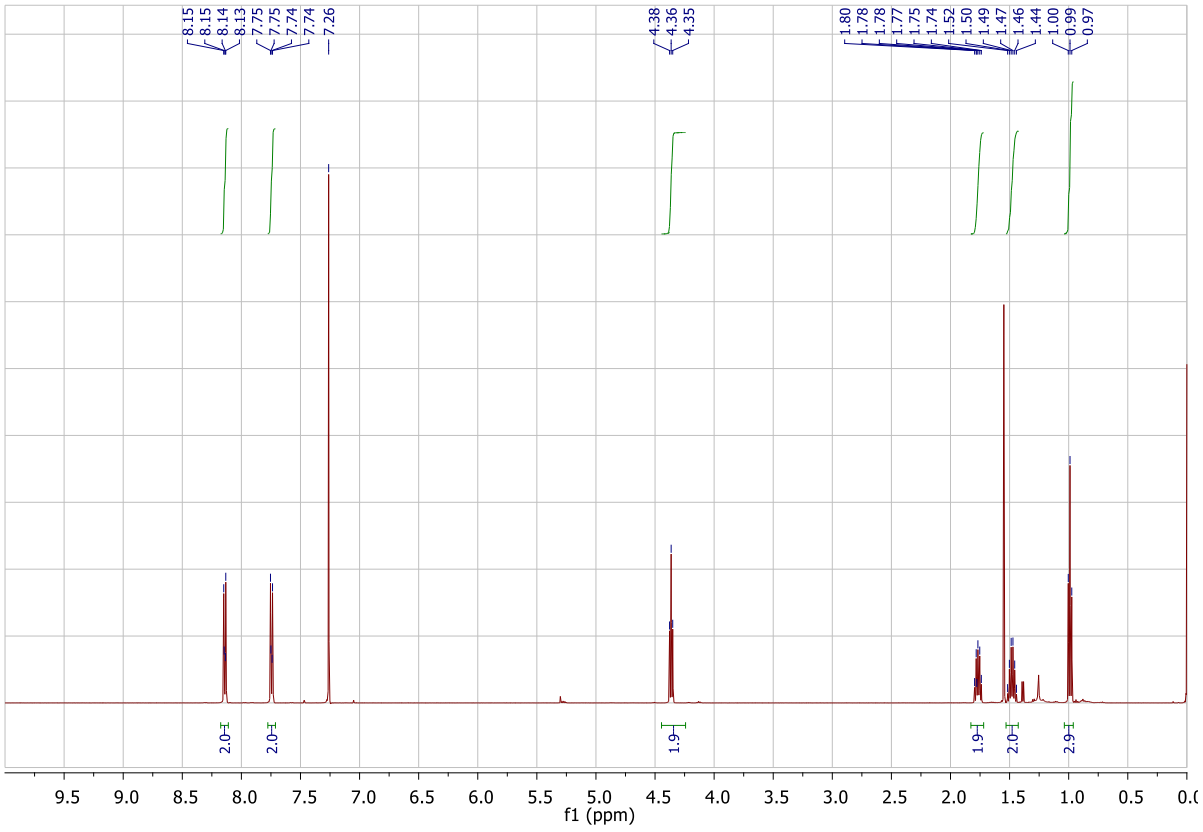


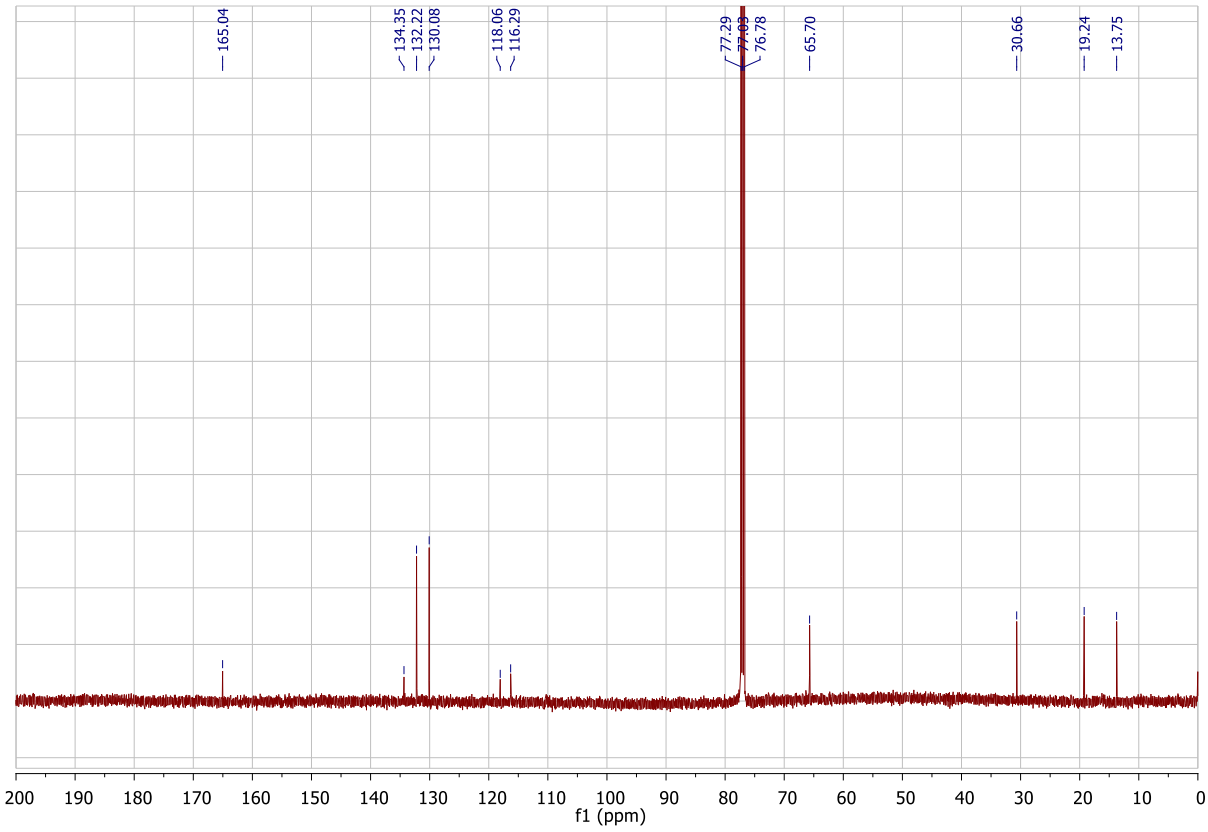

165.49
134.47
134.21
133.74
129.96
125.44
125.41
125.38
125.35
124.76
122.59
65.44
30.70
19.26
13.76
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

***n*-Butyl 4-cyanobenzoate**[1]

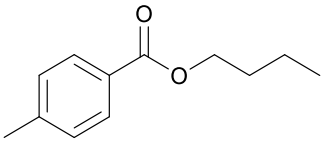


Purification by column chromatography (1%-5% EtOAc/Petrol) yielded *n*-butyl 4-cyanobenzoate as a clear oil (68 mg, 0.33 mmol, 67%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.6 Hz, 2H), 7.74 (d, *J* = 8.6 Hz, 2H), 4.36 (t, *J* = 6.7 Hz, 2H), 1.80-1.74 (m, 2H), 1.48 (sxt., *J* = 7.5 Hz, 2H), 0.99 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0 (C), 134.4 (C), 132.2 (CH), 130.1 (CH), 118.1 (C), 116.3 (C), 65.7 (CH_2), 30.7 (CH_2), 19.3 (CH_2), 13.8 (CH_3); IR (thin film) 2961, 2870, 2234, 1710 cm^{-1}.

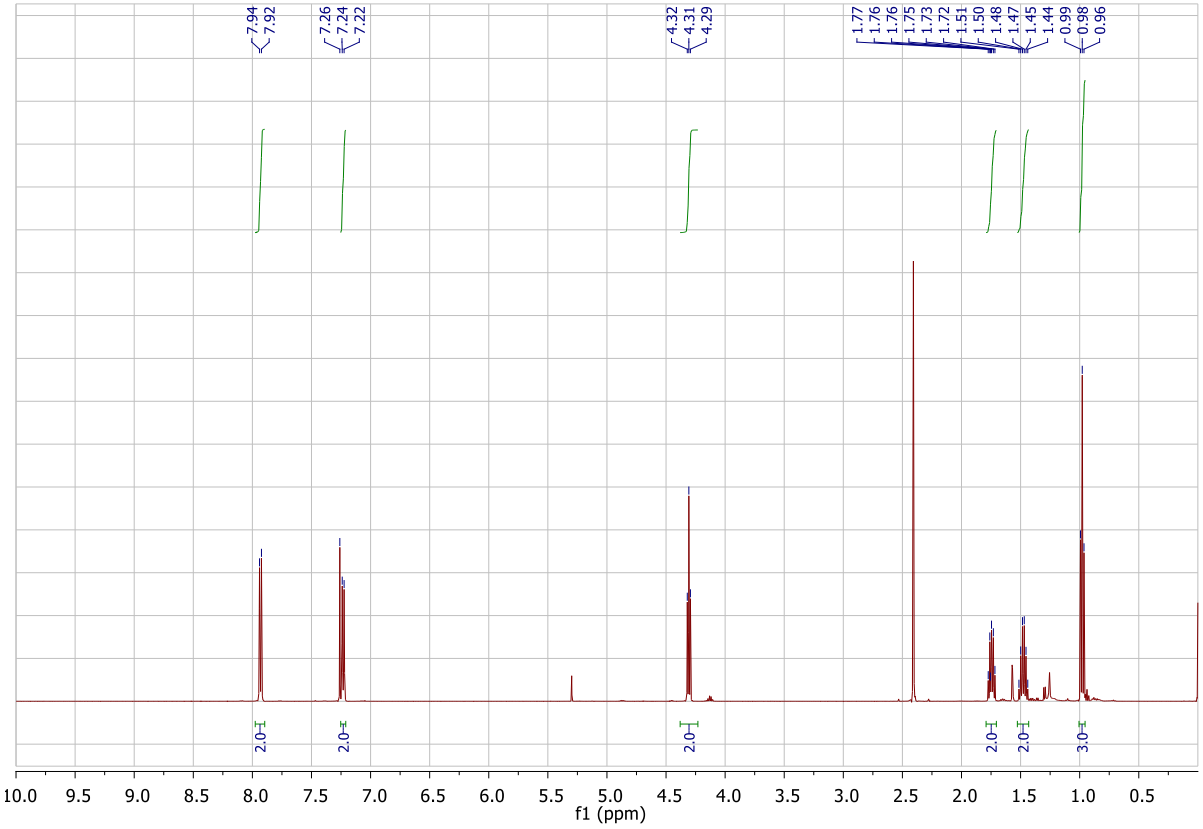


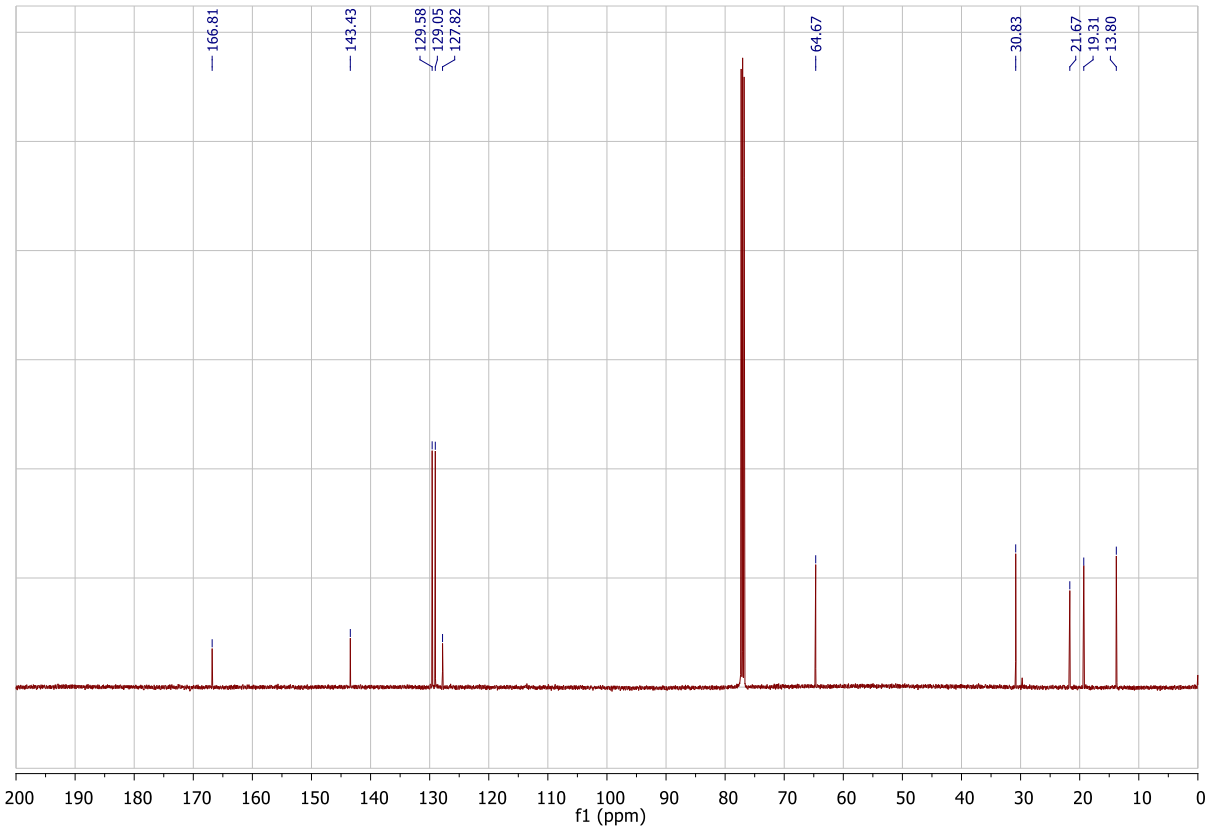

165.04
134.35
132.22
130.08
118.06
116.29
77.29
77.03
76.78
65.70
30.66
19.24
13.75
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

_n_-Butyl 4-methylbenzoate[2]

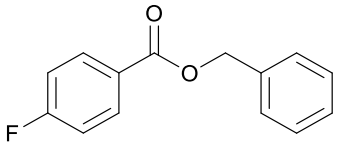


Purification by column chromatography (1%-5% EtOAc/Petrol) yielded *n*-butyl 4-methylbenzoate as a clear oil (69 mg, 0.36 mmol, 72%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 4.31 (t, *J* = 7.0 Hz, 2H), 1.78-1.71 (m, 2H), 1.46 (sxt., *J* = 7.5 Hz, 2H), 0.98 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.8 (C), 143.4 (C), 129.6 (CH), 129.1 (CH), 127.8 (C), 64.7 (CH_2), 30.8 (CH_2), 21.7 (CH_2), 19.3 (CH_3), 13.8 (CH_3); IR (thin film) 2950, 2871, 1718, 1598, 1489 cm^{-1}.

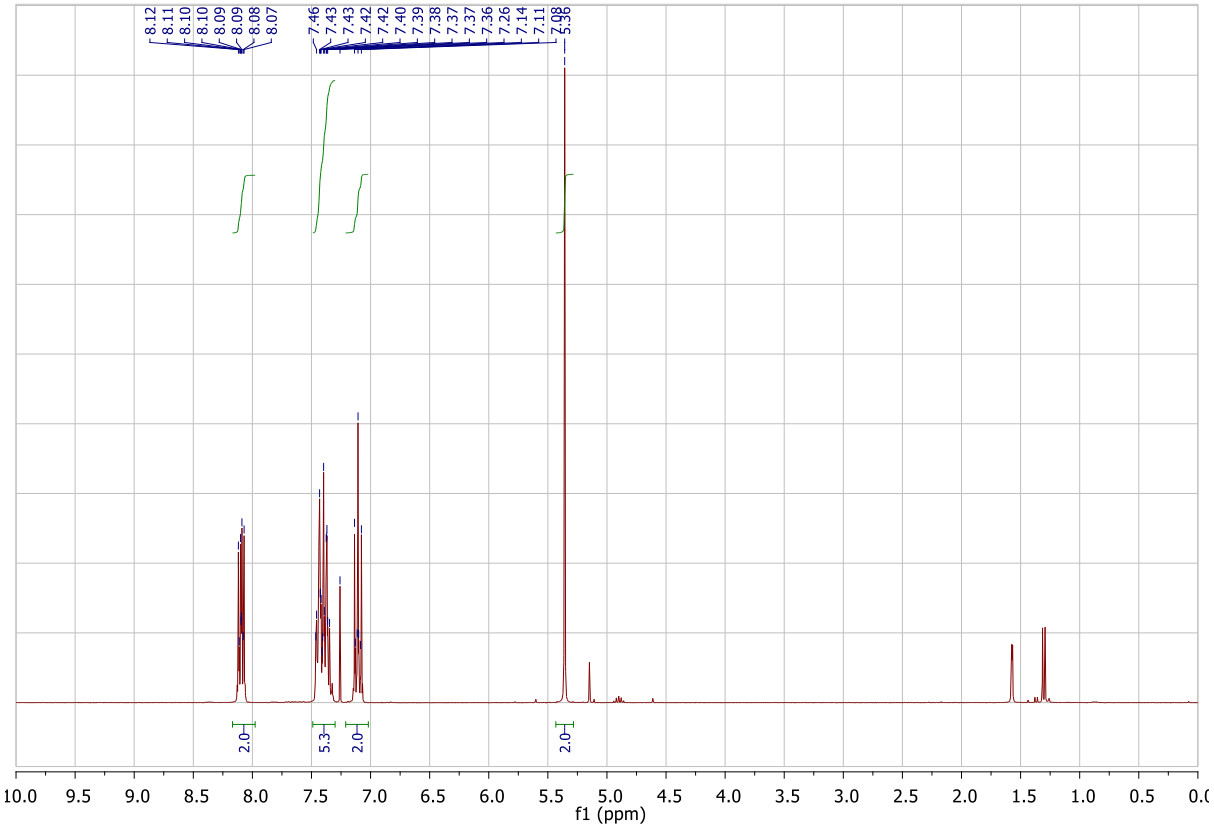


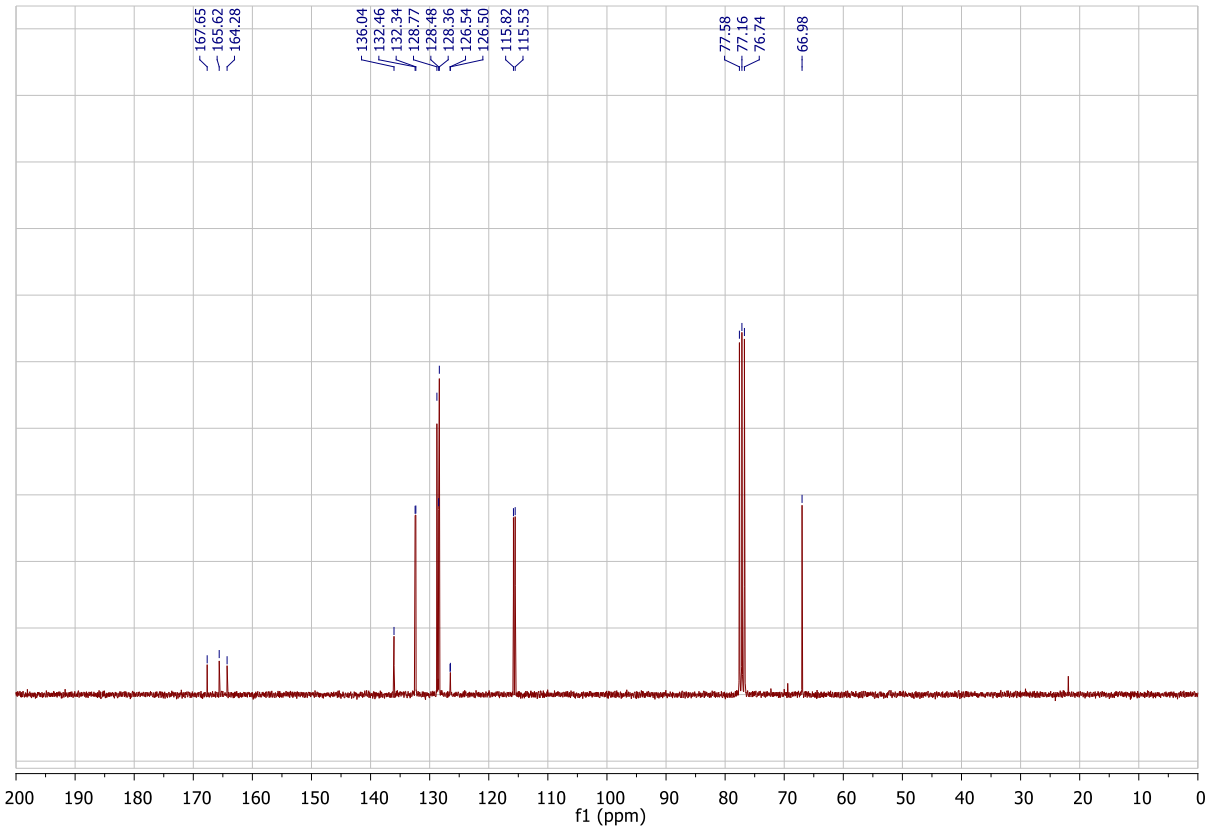

166.81
143.43
129.58
129.05
127.82
64.67
30.83
21.67
19.31
13.80
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Benzyl 4-fluorobenzoate

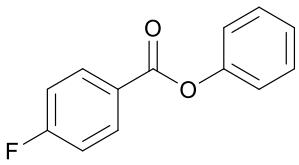


Purification by column chromatography (1%-5% EtOAc/Petrol) yielded benzyl 4-fluorobenzoate as a clear oil (87 mg, 0.38 mmol, 76%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12-8.06 (m, 2H), 7.46-7.34 (m, 5H), 7.17-7.05 (m, 2H), 5.36 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0 (d, $J_{C\text{-}F}$ = 258.5 Hz, C), 165.6 (C), 136.0 (C), 132.4 (d, $J_{C\text{-}F}$ = 9.3 Hz, CH), 128.8 (CH), 128.4 (CH), 128.4 (CH), 126.5 (d, $J_{C\text{-}F}$ = 3.3 Hz, C), 115.7 (d, $J_{C\text{-}F}$ = 22.0 Hz, CH), 67.0 (s, CH_2); IR (thin film) 3068, 3035, 2955, 1716, 1603, 1507 cm^{-1}; LRMS (EI) 230 (100, $[M]^+$); HRMS (EI) calcd for $C_{14}H_{11}O_2F$ $[M]^+$ 230.0738; observed 230.0739.

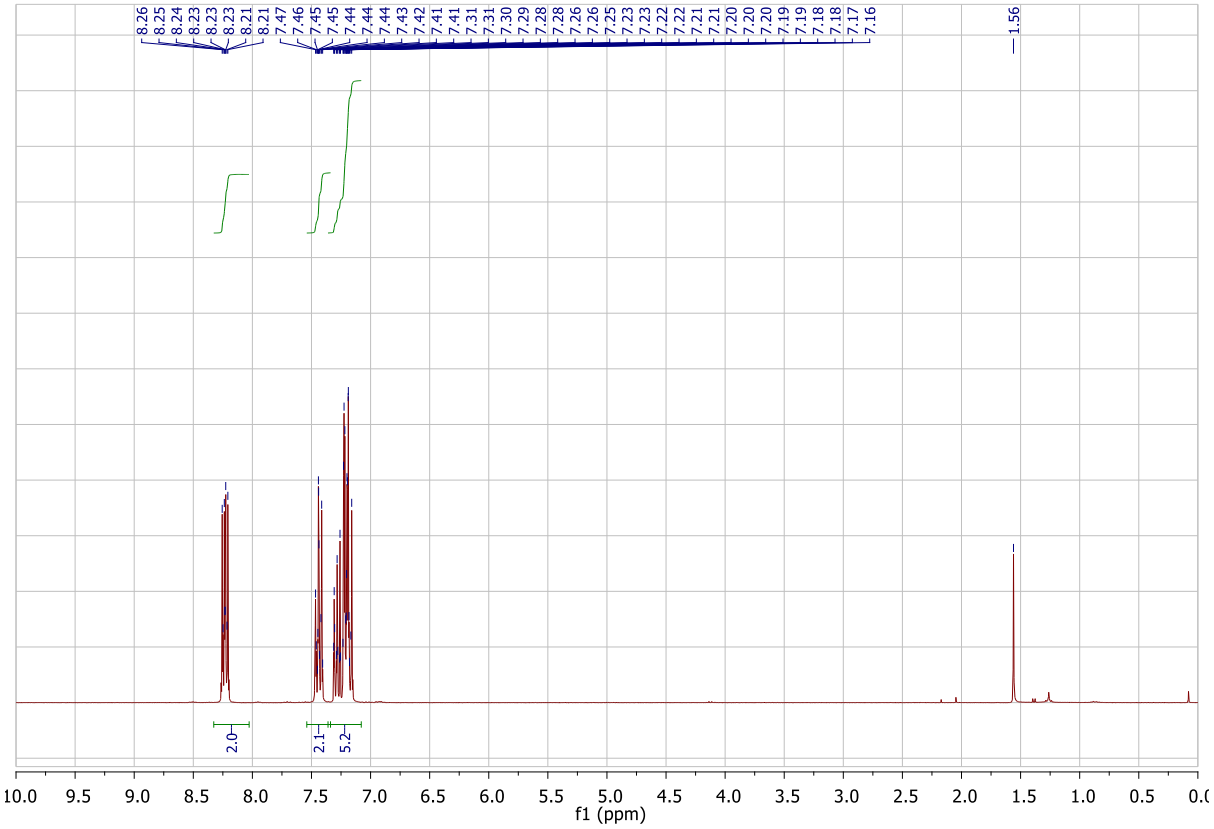


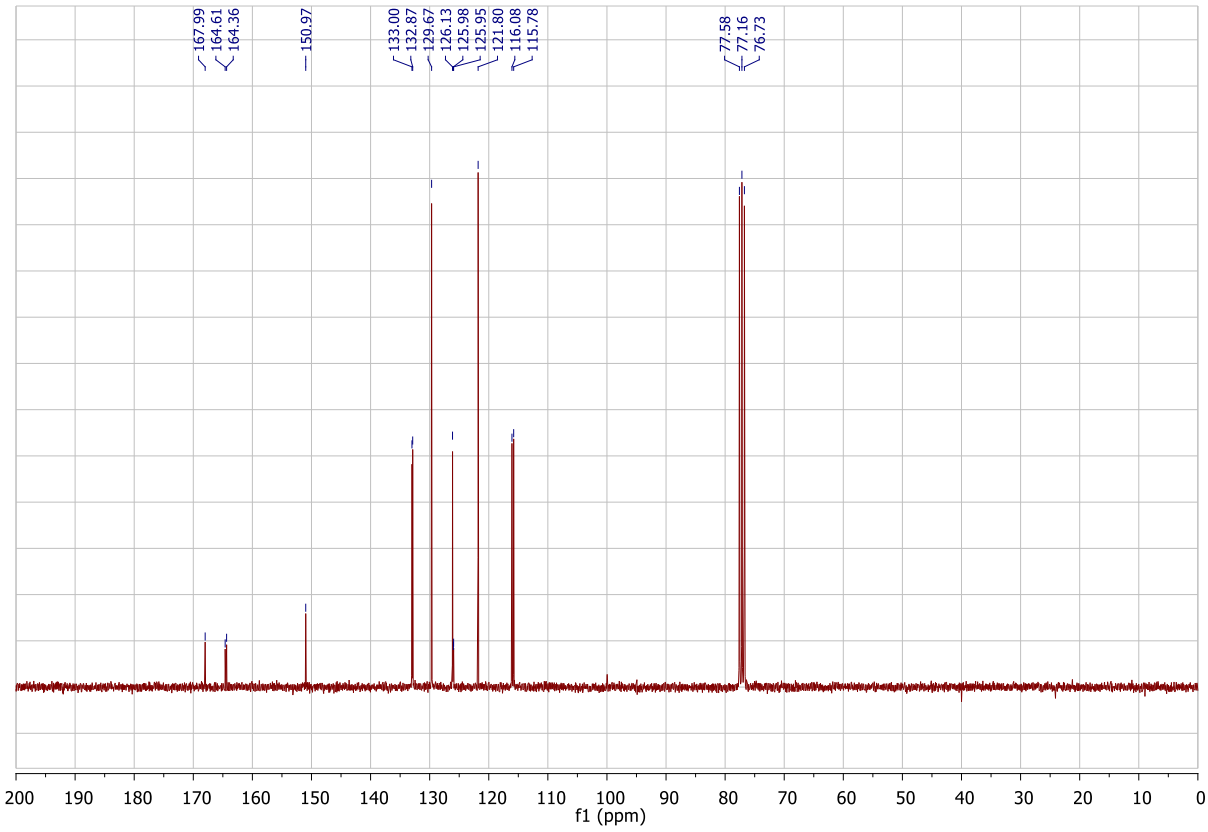

167.65
165.62
164.28
136.04
132.46
132.34
128.77
128.48
128.36
126.54
126.50
115.82
115.53
77.58
77.16
76.74
66.98
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Phenyl 4-fluorobenzoate

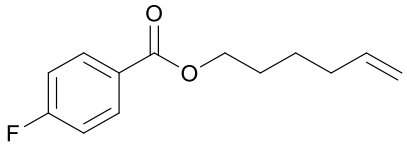


Purification by column chromatography (1%-5% EtOAc/Petrol) yielded phenyl 4-fluorobenzoate as a clear oil (56 mg, 0.26 mmol, 52%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28-8.21 (m, 2H), 7.49-7.39 (m, 2H), 7.32-7.13 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2 (d, $J_{C\text{-}F}$ = 273.3 Hz, C), 164.6 (C), 151.0 (C), 132.9 (d, $J_{C\text{-}F}$ = 9.9 Hz, CH), 129.7 (s, CH), 126.1 (CH), 126.0 (d, $J_{C\text{-}F}$ = 2.7 Hz, C), 121.8 (CH), 115.9 (d, $J_{C\text{-}F}$ = 22.0 Hz, CH); IR (thin film) 3075, 1734, 1605, 1596, 1505 cm^{-1}; LRMS (EI) 216 (100, $[M]^+$); HRMS (EI) calcd for $C_{13}H_9O_2F$ $[M]^+$ 216.0587; observed 216.0580.

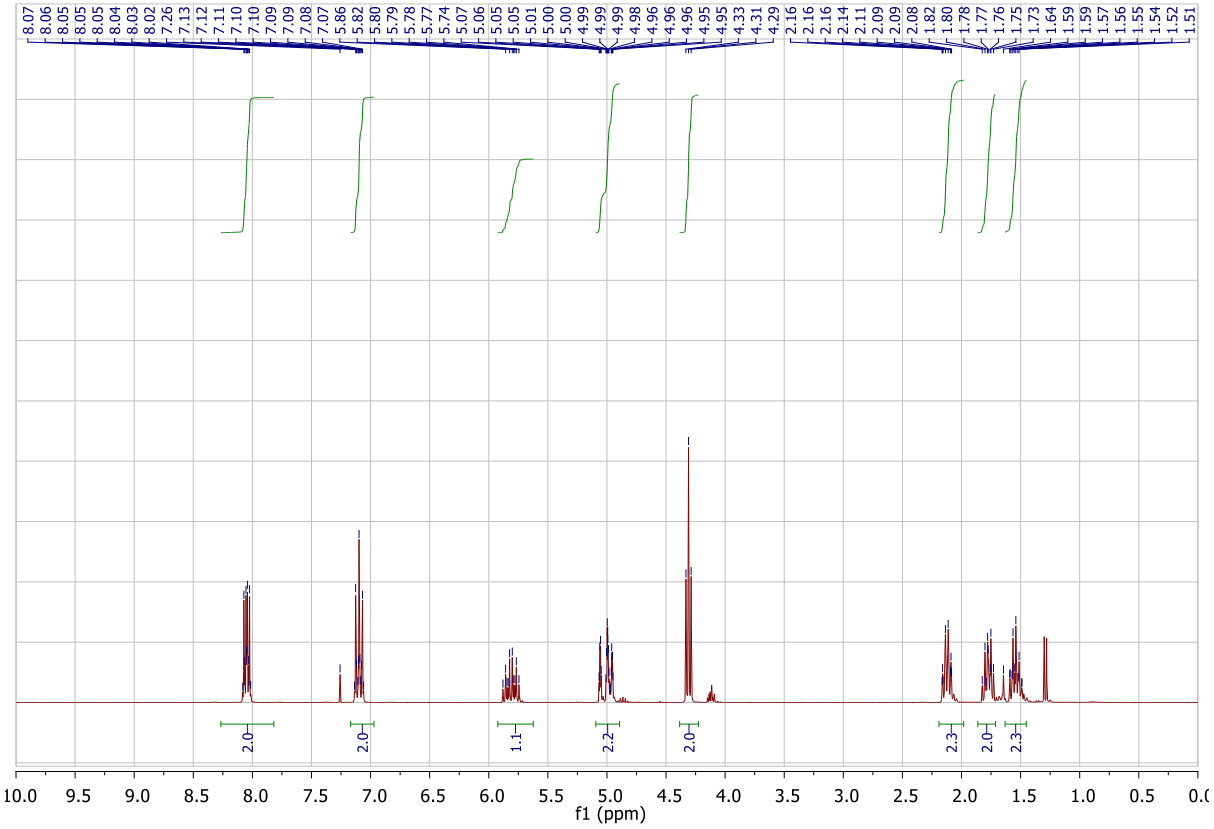


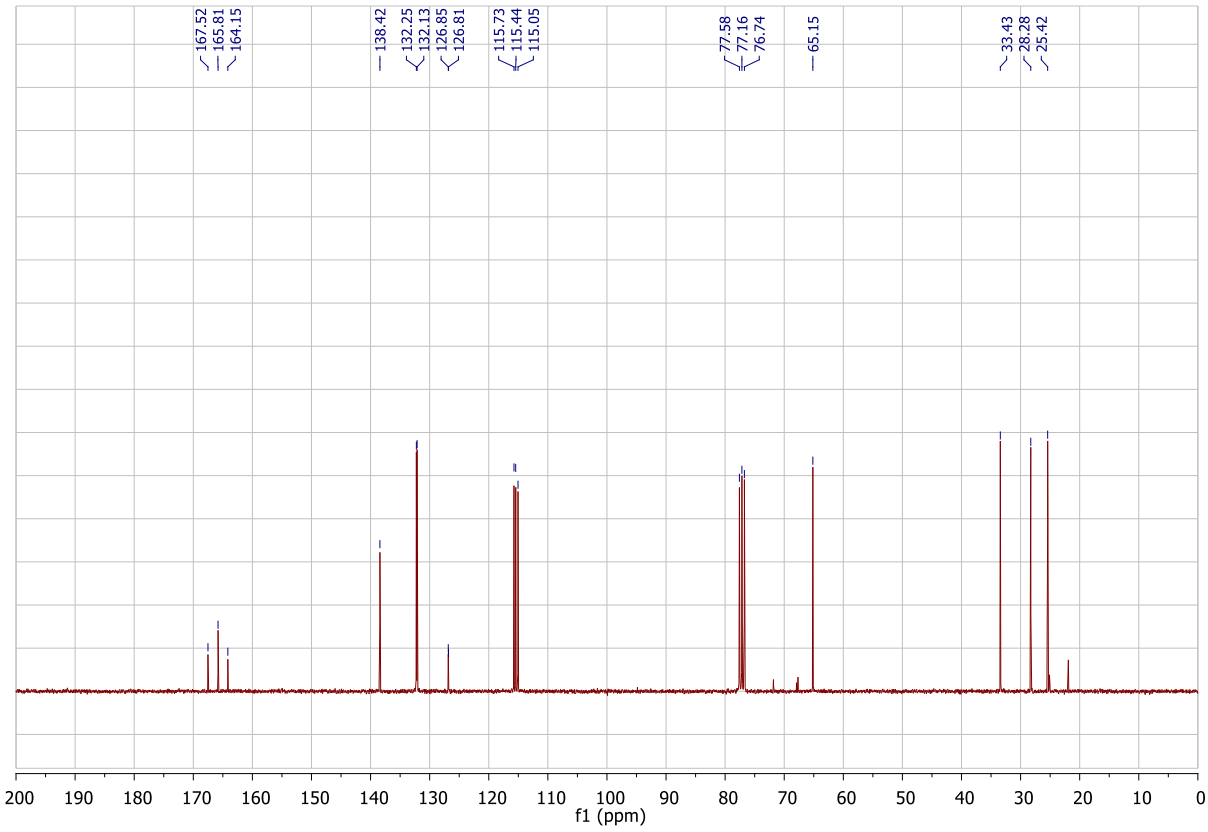

167.99
164.61
164.36
150.97
133.00
132.87
129.67
126.13
125.98
125.95
121.80
116.08
115.78
77.58
77.16
76.73
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

5-Hexenyl 4-fluorobenzoate

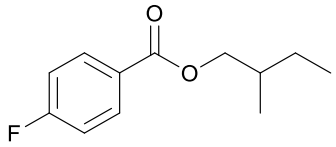


Purification by column chromatography (1%-10% EtOAc/Petrol) yielded 5-hexenyl 4-fluorobenzoate as a clear oil (78 mg, 0.35 mmol, 70%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.11-8.01 (m, 2H), 7.15-7.05 (m, 2H), 5.82 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H), 5.10-4.93 (m, 2H), 4.31 (t, *J* = 6.6 Hz, 2H), 2.13 (q, *J* = 7.2 Hz, 2H), 1.85-1.70 (m, 2H), 1.61-1.48 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9 (s, C), 165.8 (d, $J_{C\text{-}F}$ = 253.6 Hz, C), 138.4 (s, CH), 132.2 (d, $J_{C\text{-}F}$ = 9.3 Hz, CH), 126.8 (s, C), 115.6 (d, $J_{C\text{-}F}$ = 22.0 Hz, CH), 115.1 (s, CH_2), 65.2 (s, CH_2), 33.4 (s, CH_2), 28.3 (s, CH_2), 25.4 (s, CH_2); IR (thin film) 3079, 2928, 2858, 1721, 1604 cm^{-1}; LRMS (EI) 222 (100, $[M]^+$); HRMS (EI) calcd for $C_{13}H_{15}O_2F$ $[M]^+$ 222.1056; observed 222.1051.

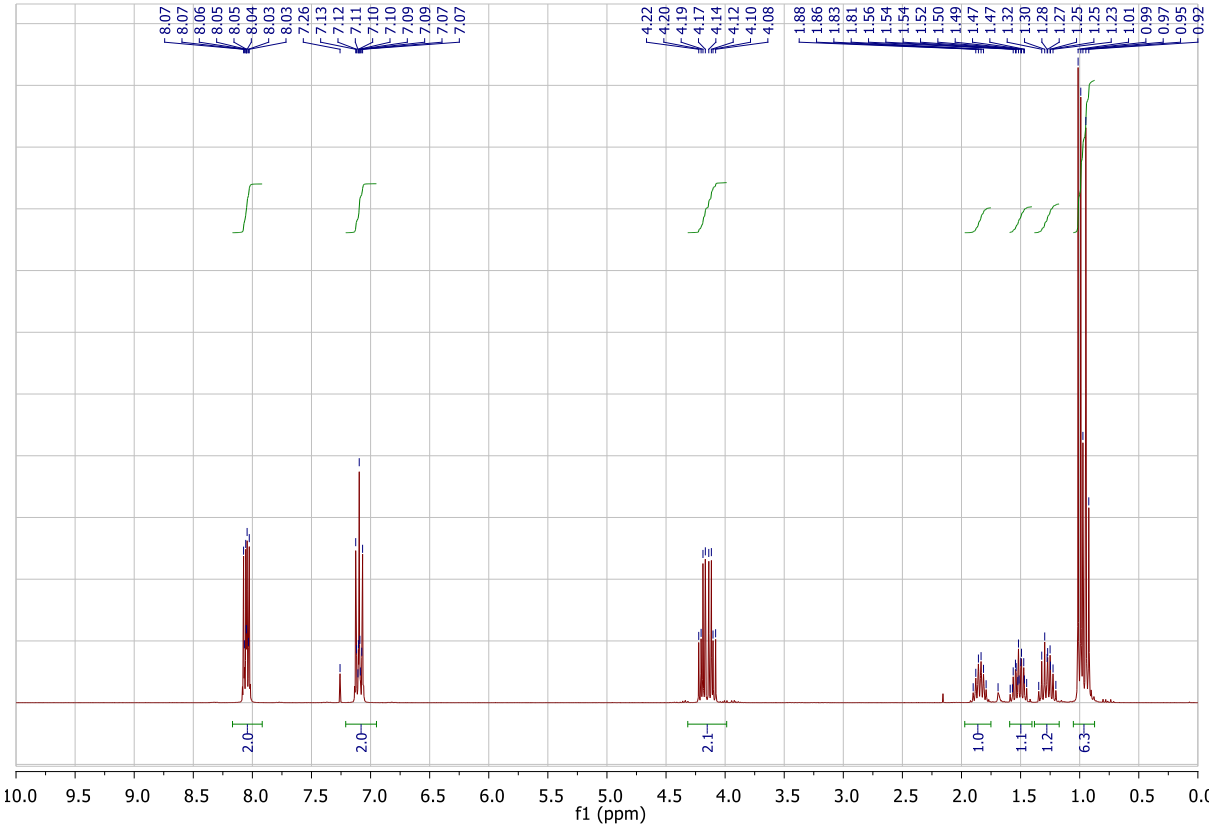


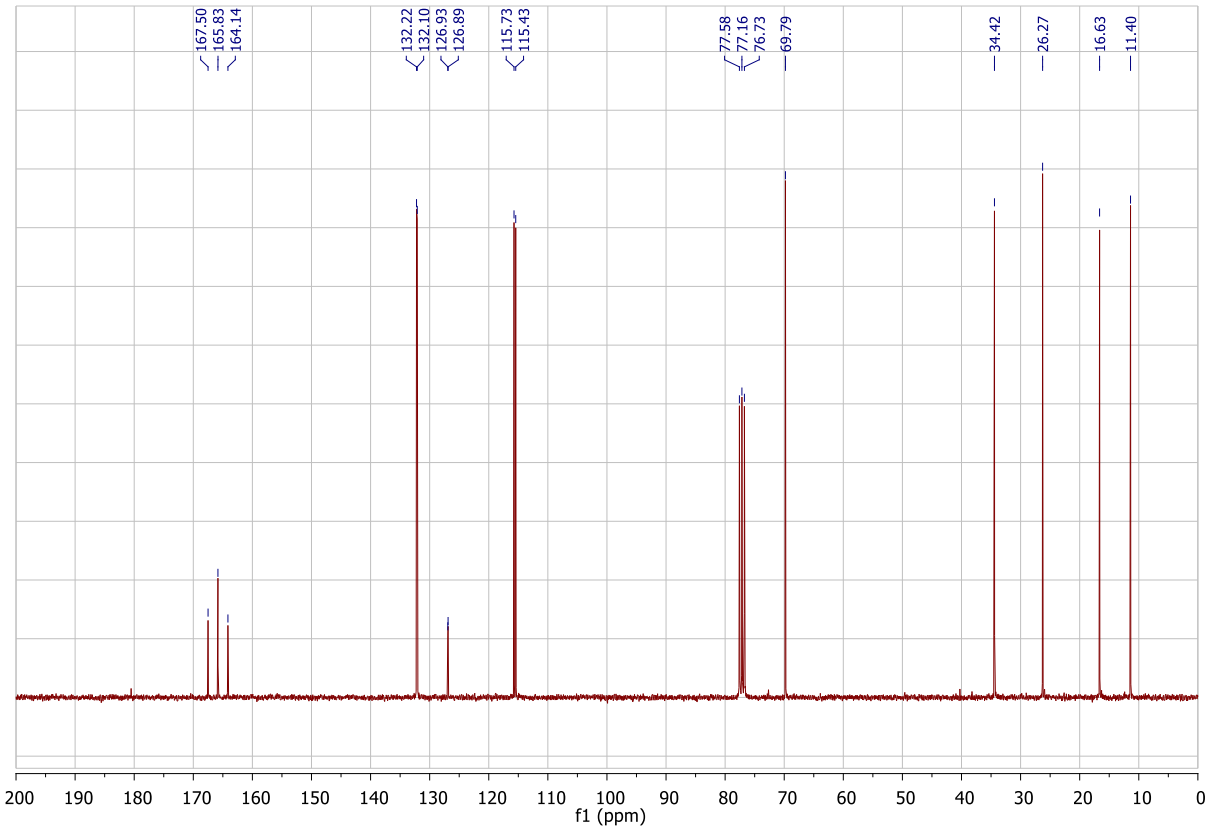

167.52
165.81
164.15
138.42
132.25
132.13
126.85
126.81
115.73
115.44
115.05
77.58
77.16
76.74
65.15
33.43
28.28
25.42
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

2-Methylbutyl 4-fluorobenzoate

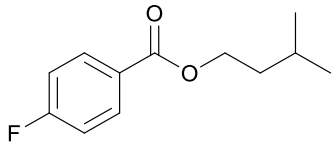


Purification by column chromatography (1%-5% EtOAc/Petrol) yielded 2-methylbutyl 4-fluorobenzoate as a clear oil (80 mg, 0.38 mmol, 76%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09-8.02 (m, 2H), 7.15-7.05 (m, 2H), 4.19 (dd, *J* = 13.6, 6.2 Hz, 1H), 4.11 (dd, *J* = 13.6, 6.4 Hz, 1H), 1.88-1.81 (m, 1H), 1.56-1.49 (m, 1H), 1.33-1.23 (m, 1H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.95 (t, *J* = 7.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 165.9 (C), 165.8 (d, $J_{C\text{-}F}$ = 253.6 Hz, C), 132.2 (d, $J_{C\text{-}F}$ = 2.0 Hz, CH), 126.9 (d, $J_{C\text{-}F}$ = 3.3 Hz, C), 115.6 (d, $J_{C\text{-}F}$ = 1.0 Hz, CH), 69.8 (CH_2), 34.4 (CH), 26.3 (CH_2), 16.6 (CH_3), 11.4 (CH_3); IR (thin film) 2964, 2936, 2878, 1719, 1603), 1508 cm^{-1}; LRMS (EI) 210 (100, $[M]^+$); HRMS (EI) calcd for $C_{12}H_{15}O_2F$ $[M]^+$ 210.1056; observed 210.1060.

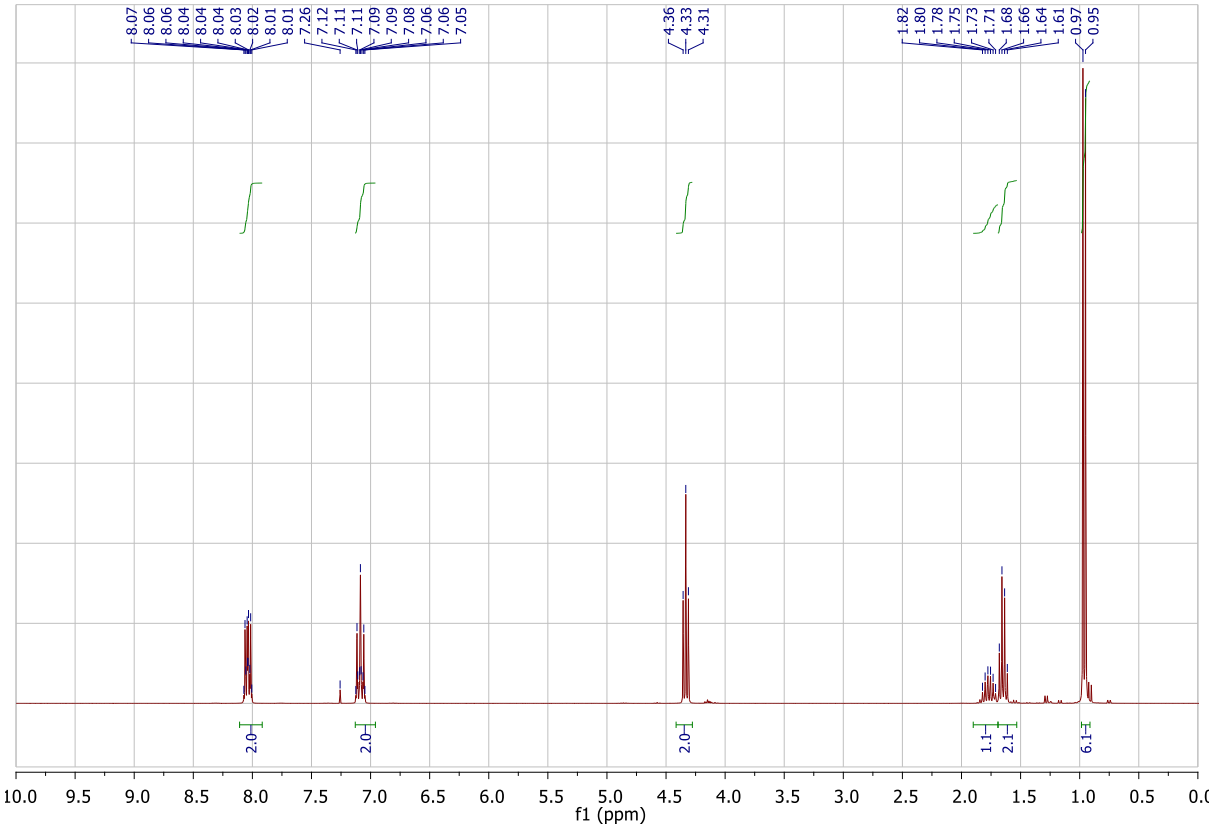


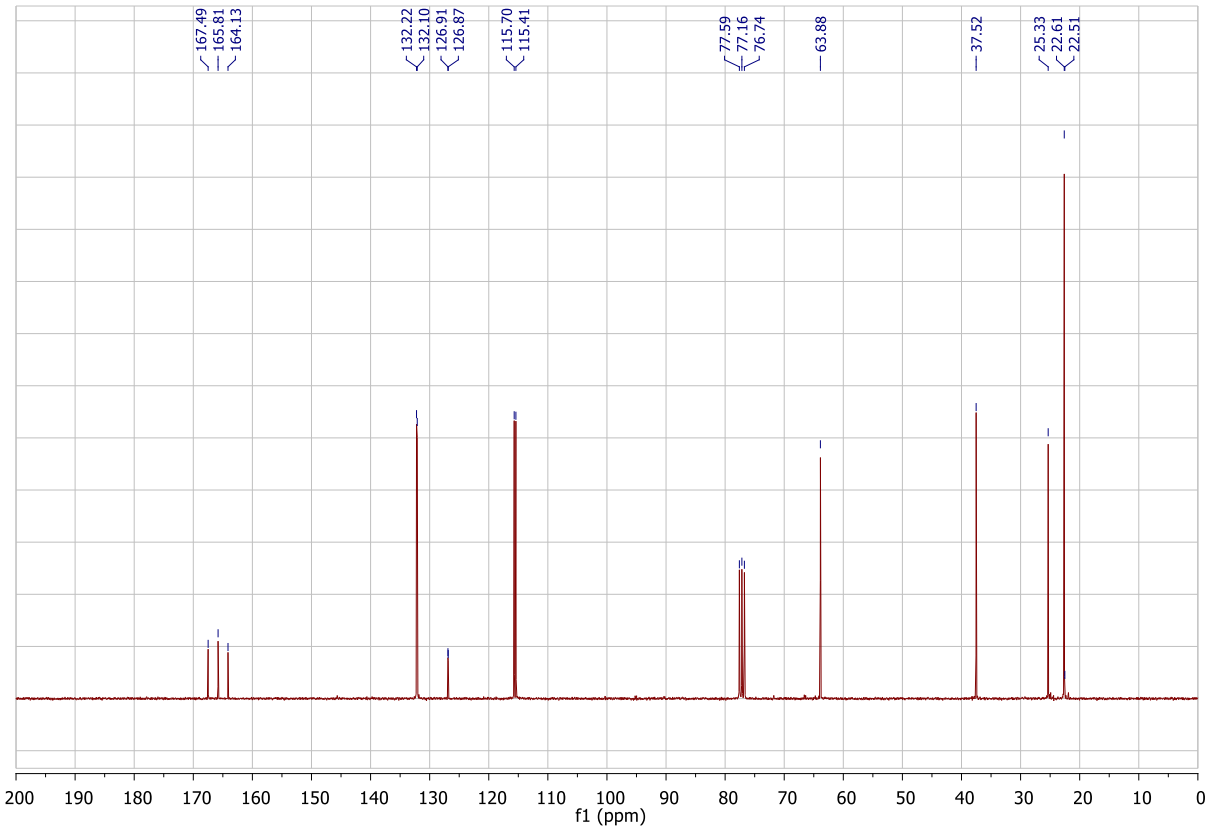

167.50
165.83
164.14
132.22
132.10
126.93
126.89
115.73
115.43
77.58
77.16
76.73
69.79
34.42
26.27
16.63
11.40
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

3-Methylbutyl 4-fluorobenzoate

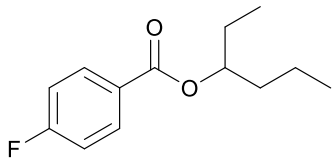


Purification by column chromatography (1%-5% EtOAc/Petrol) yielded 3-methylbutyl 4-fluorobenzoate as a clear oil (76 mg, 0.36 mmol, 72%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08-8.00 (m, 2H), 7.13-7.04 (m, 2H), 4.33 (t, J = 6.8 Hz, 2H), 1.73-1.60 (m, 2H), 1.78 (nonet, J = 6.6 Hz, 1H), 0.96 (d, J = 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8 (C), 165.8 (d, $J_{C\text{-}F}$ = 253.0, C), 132.2 (d, $J_{C\text{-}F}$ = 9.3 Hz, CH), 126.9 (d, $J_{C\text{-}F}$ = 3.3 Hz, C), 115.6 (d, $J_{C\text{-}F}$ = 22.0 Hz, CH), 63.9 (s, CH_2), 37.5 (s, CH_2), 25.3 (s, CH), 22.6 (s, CH_3); IR (thin film) 2959, 2872, 1716, 1604, 1508 cm^{-1}; LRMS (EI) 210 (100, [M]+); HRMS (EI) calcd for $C_{12}H_{15}O_2F$ [M]+ 210.1056; observed 210.1052.

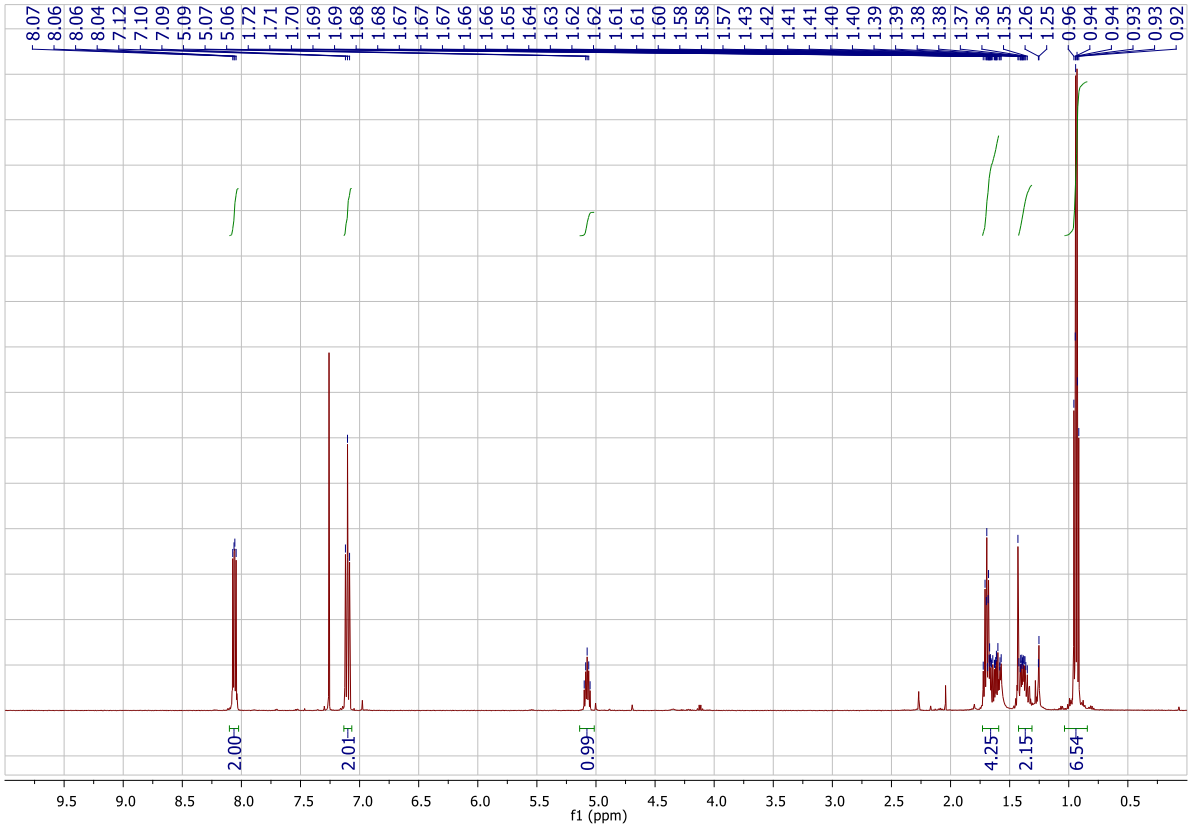


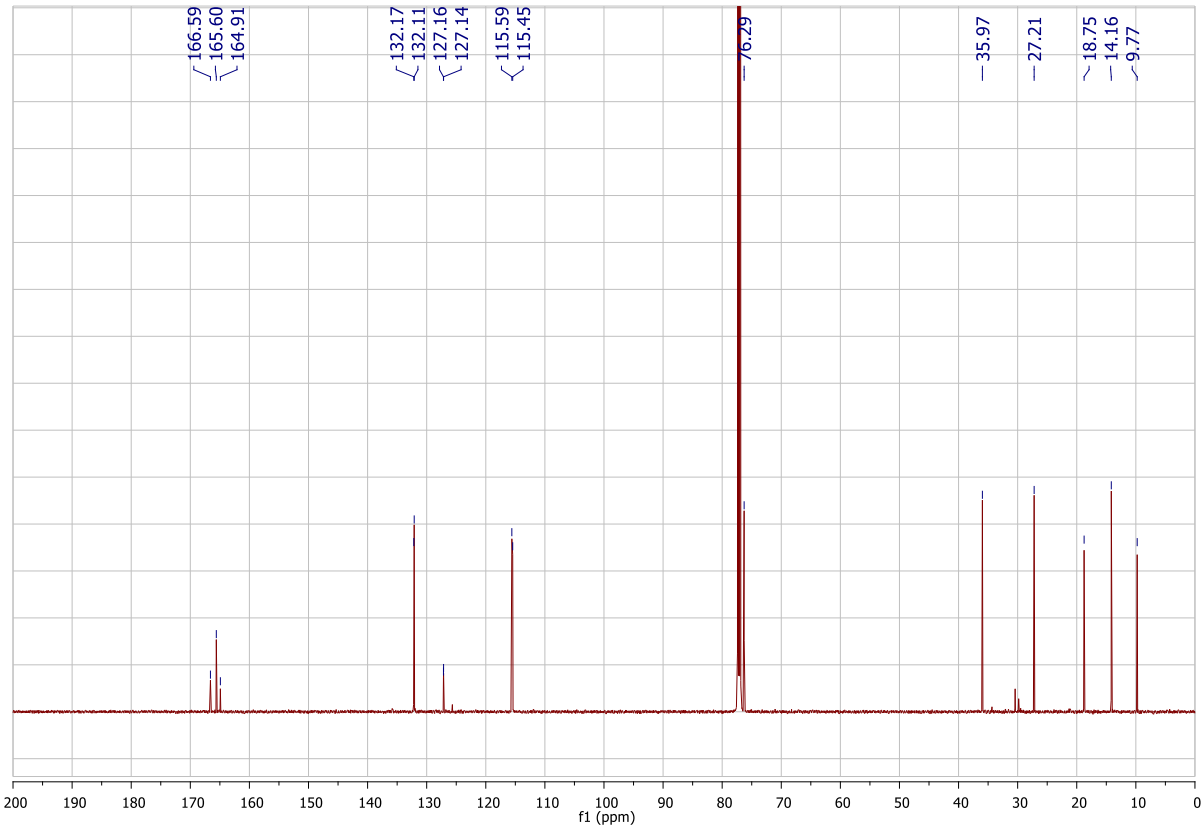

167.49
165.81
164.13
132.22
132.10
126.91
126.87
115.70
115.41
77.59
77.16
76.74
63.88
37.52
25.33
22.61
22.51
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Hexan-3-yl 4-fluorobenzoate

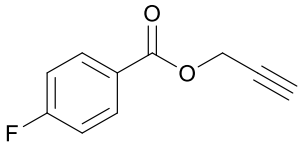


Purification by column chromatography (1%-5% EtOAc/Petrol) yielded hexan-3-yl 4-fluorobenzoate as a clear oil (76 mg, 0.34 mmol, 68%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08-8.03 (m, 2H), 7.13-7.08 (m, 2H), 5.11-5.04 (quintet, J = 7.0 Hz, 1H), 1.75-1.66 (m, 4H), 1.43-1.23 (m, 2H), 0.97-0.92 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.6 (C), 165.8 (d, $J_{C\text{-}F}$ = 252.0, C), 132.1 (d, $J_{C\text{-}F}$ = 9.0 Hz, CH), 127.2 (d, $J_{C\text{-}F}$ = 3.0 Hz, C), 115.5 (d, $J_{C\text{-}F}$ = 21.0 Hz, CH), 76.3 (s, CH), 36.0 (s, CH_2), 27.2 (s, CH_2), 18.8 (s, CH_2), 14.2 (s, CH_3), 9.8 (s, CH_3); IR (thin film) 2963, 2875, 1717, 1605, 1507 cm^{-1}; LRMS (CI) 242 (100, $[M+NH_4]^+$); HRMS (CI) calcd for $C_{13}H_{21}O_2NF$ $[M+NH_4]^+$ 242.1551; observed 242.1551.

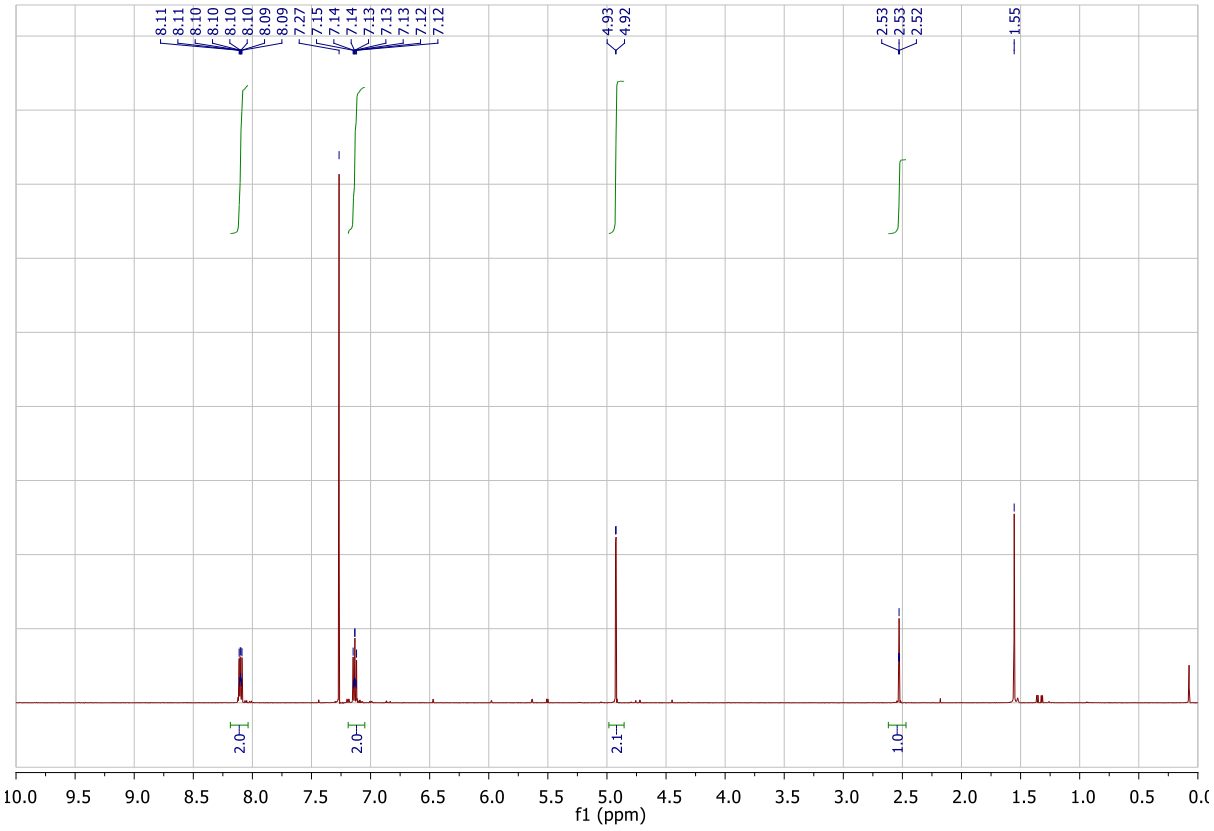


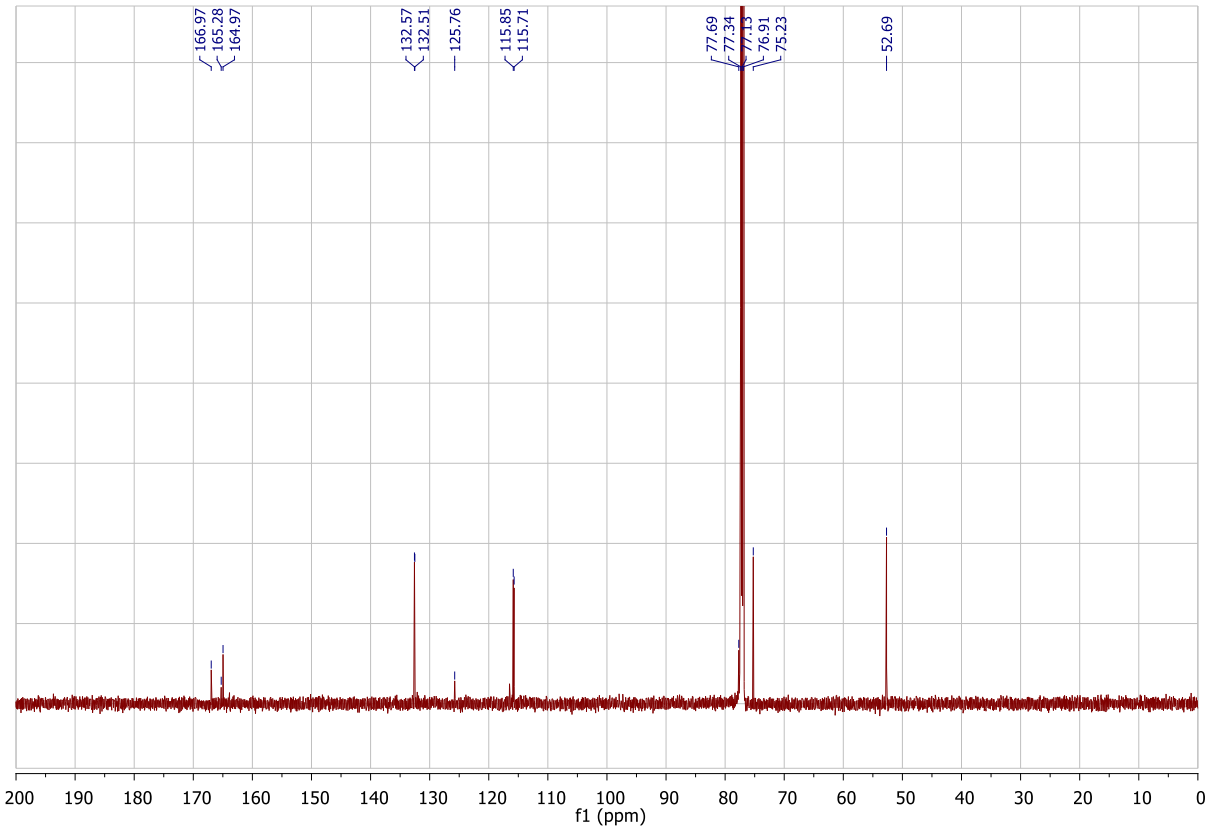

166.59
165.60
164.91
132.17
132.11
127.16
127.14
115.59
115.45
76.29
35.97
27.21
18.75
14.16
9.77
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Propanyl 4-fluorobenzoate



Purification by column chromatography (1%-5% EtOAc/Petrol) yielded propanyl 4-fluorobenzoate as a clear oil (68 mg, 0.38 mmol, 76%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13-8.08 (m, 2H), 7.16-7.11 (m, 2H), 4.92 (d, J = 2.7 Hz, 2H), 2.53 (t, J = 2.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0 (d, $J_{C\text{-}F}$ = 253.2 Hz, C), 165.3 (C), 132.5 (d, $J_{C\text{-}F}$ = 9.1 Hz, CH), 125.8 (d, $J_{C\text{-}F}$ = 2.9 Hz, C), 115.8 (d, $J_{C\text{-}F}$ = 22.1 Hz, CH), 77.7 (s, C), 75.2 (s, CH), 52.7 (s, CH_2); IR (thin film) 2962, 2859, 2210, 1712, 1600, 1502 cm^{-1}.

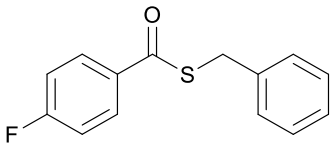



166.97
165.28
164.97
132.57
132.51
125.76
115.85
115.71
77.69
77.34
77.13
76.91
75.23
52.69
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

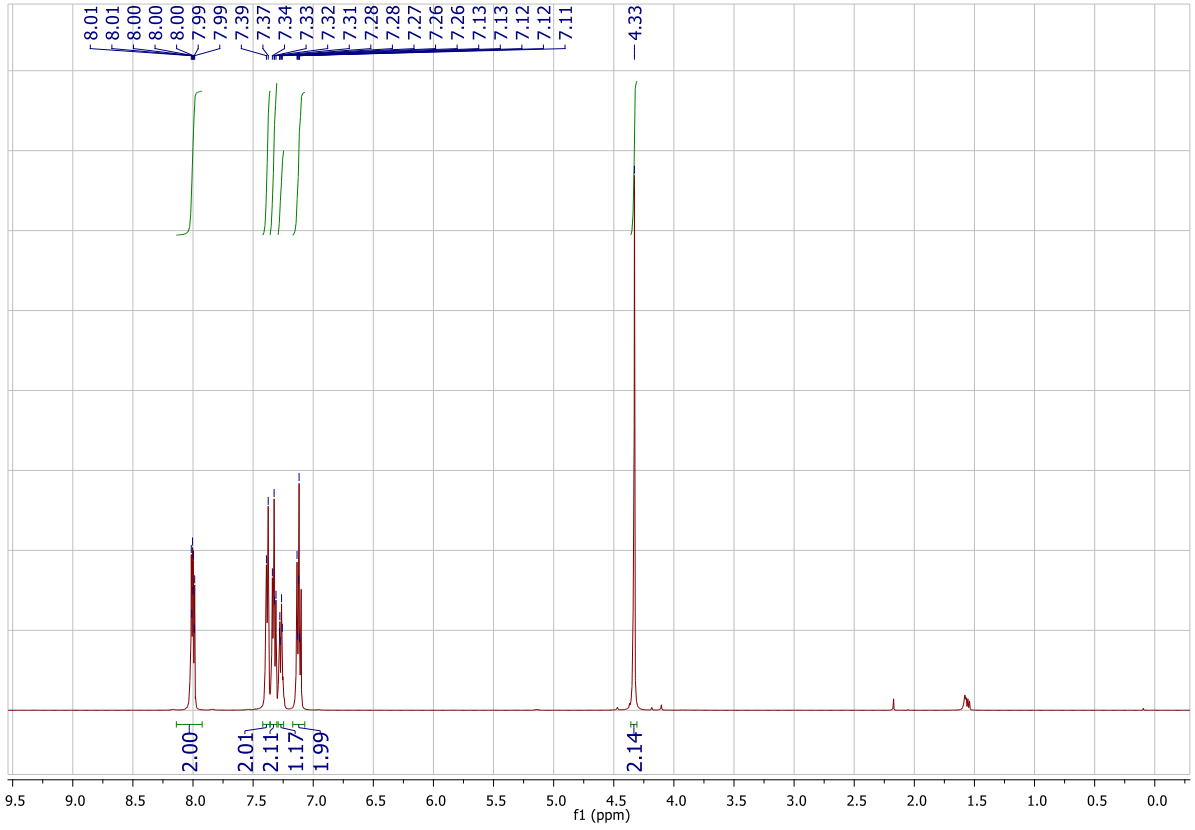
General procedure for one-pot thioester synthesis

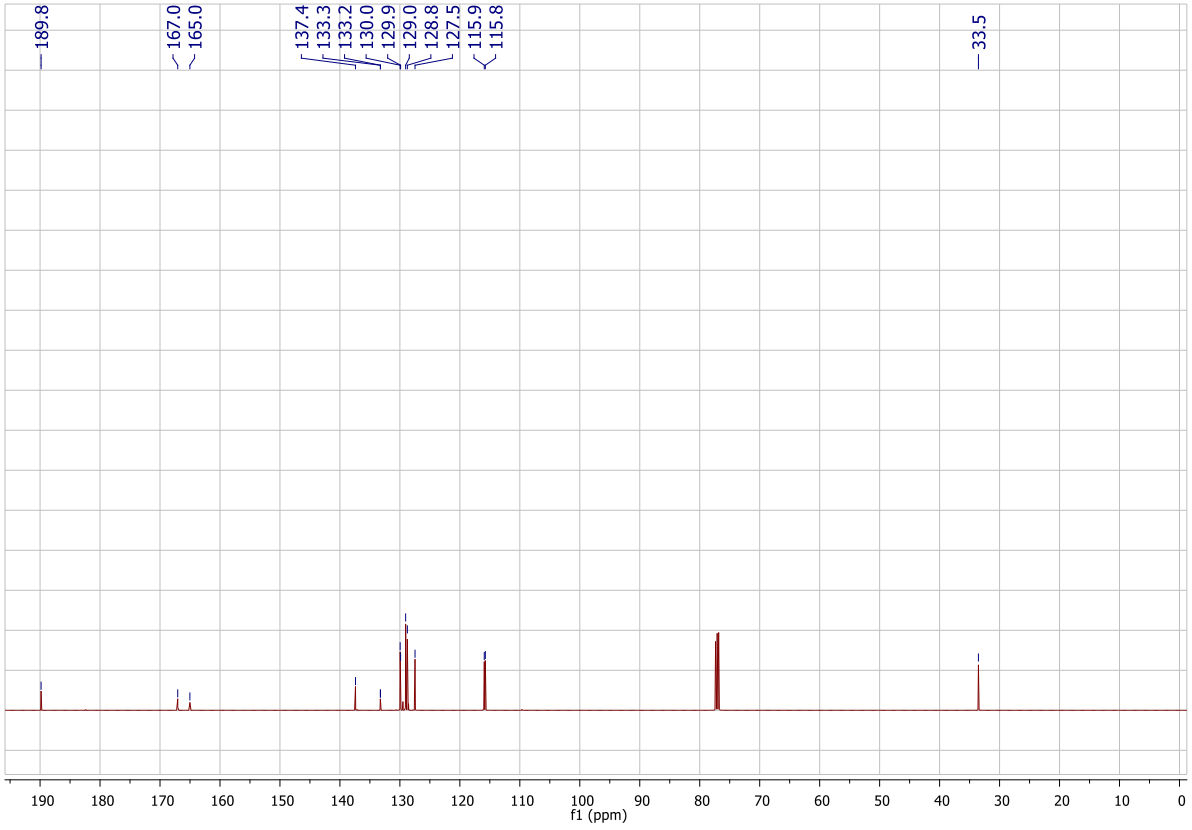
Aldehyde (0.5 mmol) was added to a solution of azodicarboxylate (0.6 mmol, 1.2 eq.) in DMF (500 µL) and the reaction mixture stirred at 300 rpm at 21 °C in a carousel tube for 24 h. After this time, Cs_2CO_3 (163 mg, 0.50 mmol, 1.0 eq.) and thiol (0.55 mmol, 1.1 eq.) in dimethylformamide (1 mL) was added to the reaction mixture. After 16 h, the reaction mixture was diluted with diethyl ether (25 mL) and washed with aq. sat. LiCl (2 × 25 mL). The organic layer was then dried ($MgSO_4$), filtered and the solvent was removed *in vacuo*. The resultant crude residue was purified as described below.

***S*-Benzyl 4-fluorobenzothioate**

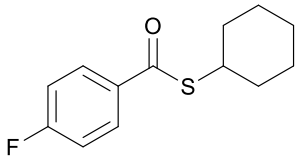


Purification by column chromatography (1–5% EtOAc/Petrol) yielded *S*-benzyl 4-fluorobenzothioate as a yellowish oil (86 mg, 0.35 mmol, 70%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07-7.97 (m, 2H), 7.43-7.37 (m, 2H), 7.37-7.30 (m, 2H), 7.30-7.23 (m, 1H), 7.17-7.08 (m, 2H), 4.33 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.8 (C), 166.0 (d, *J* = 254.9 Hz, C), 137.4 (C), 133.3 (d, *J* = 2.9 Hz, C), 129.9 (d, *J* = 9.3 Hz, CH), 129.0 (CH), 128.8 (CH), 127.5 (CH), 115.8 (d, *J* = 22.1 Hz, CH), 33.5 (CH_2); IR (thin film) 3030, 2926, 1657, 1597, 1503; LRMS (ESI) 247 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_{14}H_{12}FOS$ $[M+H]^+$ 247.0587; observed 247.0588.

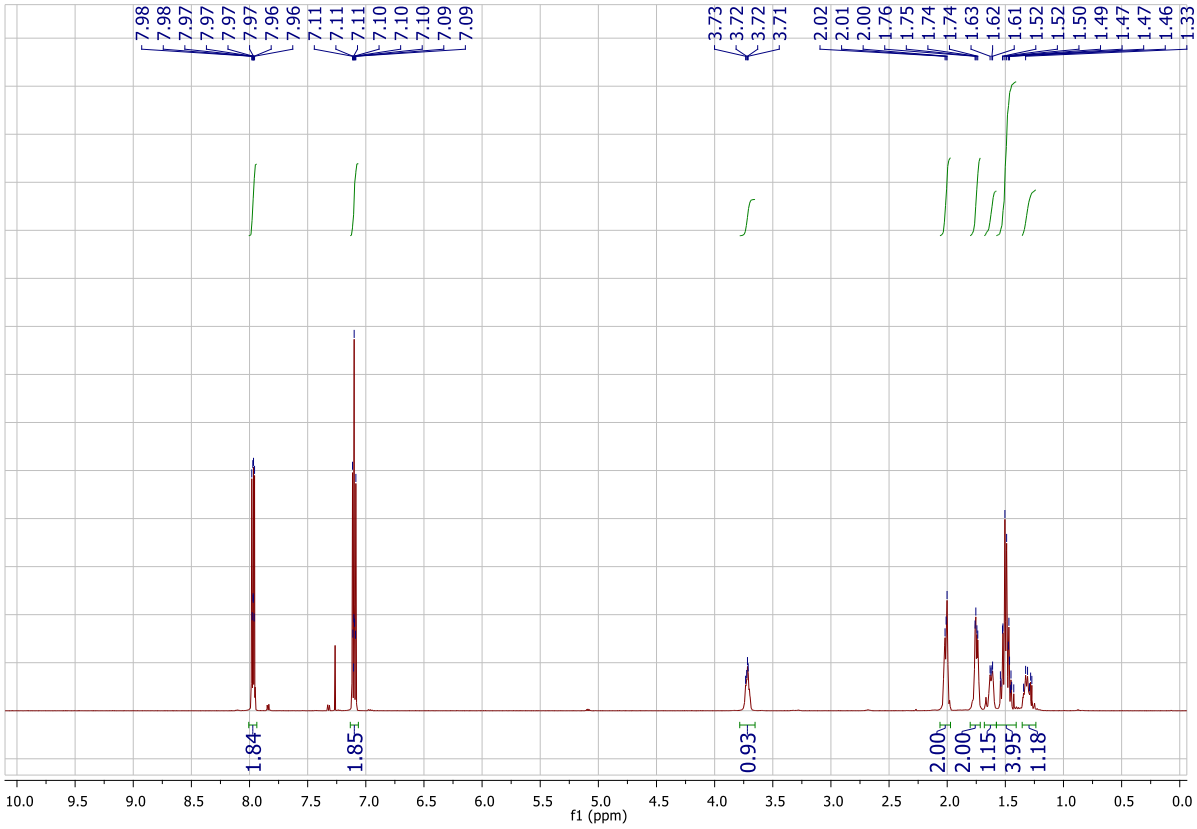


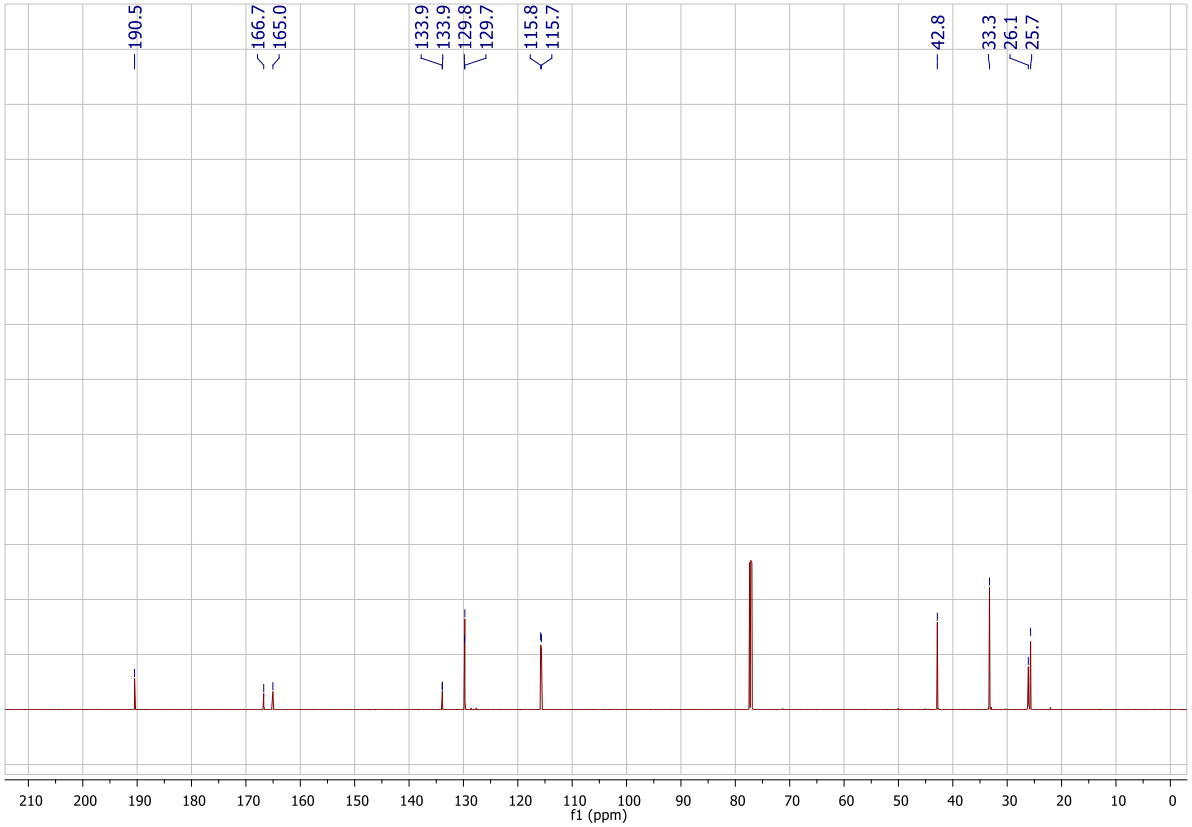

189.8
167.0
165.0
137.4
133.3
133.2
130.0
129.9
129.0
128.8
127.5
115.9
115.8
33.5
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

_S_-Cyclohexyl 4-fluorobenzothioate

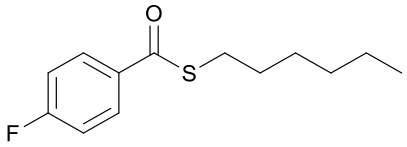


Purification by column chromatography (1–5% EtOAc/Petrol) yielded *S*-cyclohexyl 4-fluorobenzothioate as a clear oil (74 mg, 0.31 mmol, 62%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00-7.94 (m, 2H), 7.14-7.06 (m, 2H), 3.81-3.65 (m, 1H), 2.07-1.93 (m, 2H), 1.82-1.65 (m, 2H), 1.65-1.54 (m, 1H), 1.54-1.39 (m, 4H), 1.38-1.24 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 190.5 (s, C), 165.9 (d, $J_{C\text{-}F}$ = 254.3 Hz, C), 133.9 (d, $J_{C\text{-}F}$ = 3.2 Hz, C), 129.8 (d, $J_{C\text{-}F}$ = 9.4 Hz, CH), 115.7 (d, $J_{C\text{-}F}$ = 22.1 Hz, CH), 42.9 (CH), 33.3 (CH_2), 26.1 (CH_2), 25.7 (CH_2); IR (thin film) 2929, 2852, 1656, 1597, 1504 cm^{-1}; LRMS (ESI) 239 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_{13}H_{16}FOS$ $[M+H]^+$ 239.0900; observed 239.0899.

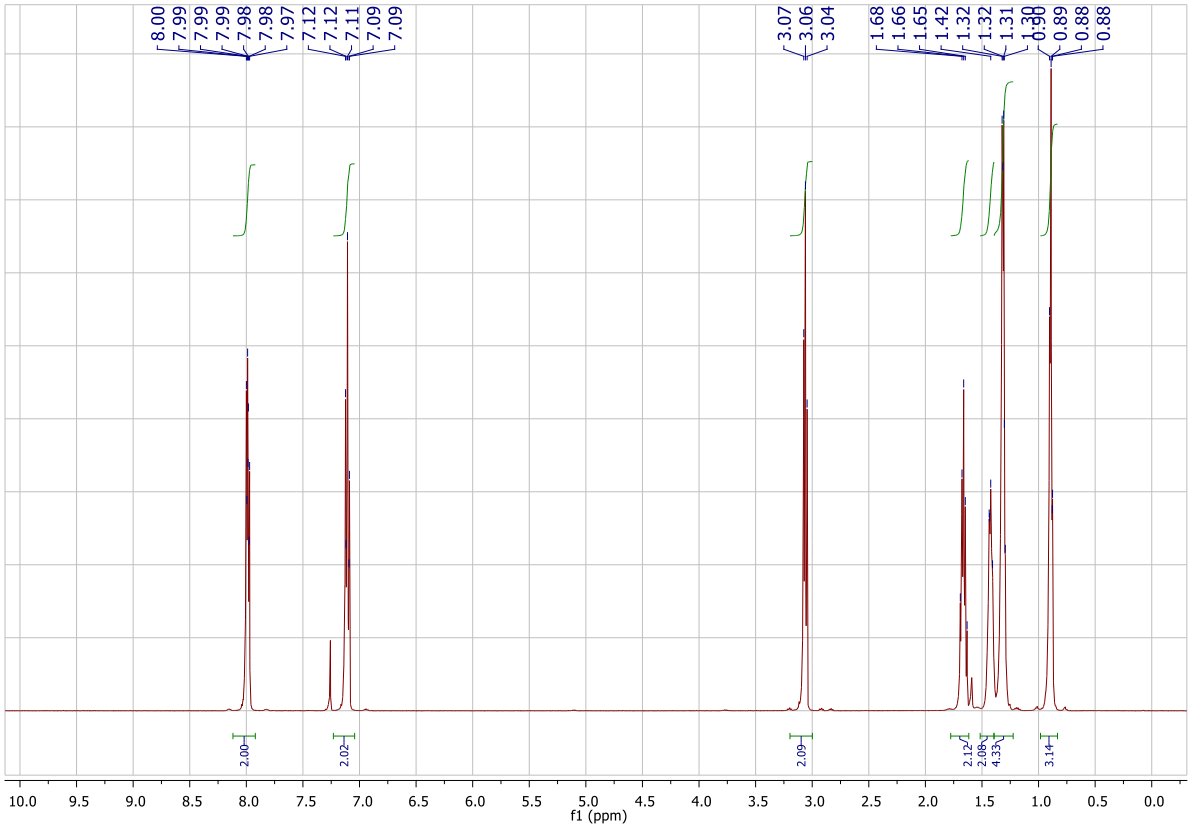


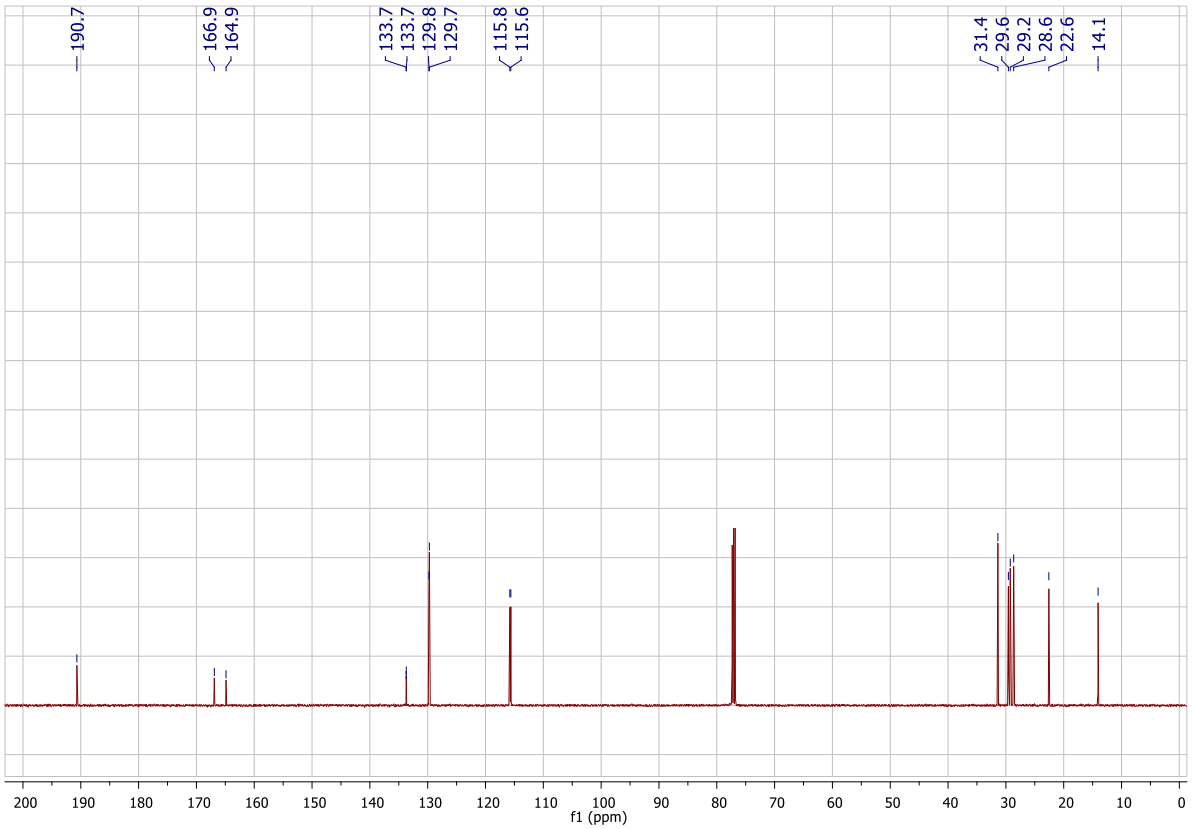

190.5
166.7
165.0
133.9
133.9
129.8
129.7
115.8
115.7
42.8
33.3
26.1
25.7
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

_S_-Hexyl 4-fluorobenzothioate

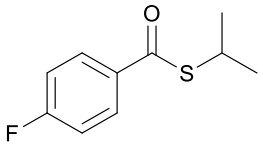


Purification by column chromatography (1–5% EtOAc/Petrol) yielded *S*-hexyl 4-fluorobenzothioate as a yellowish oil (86 mg, 0.36 mmol, 72%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20-7.91 (m, 2H), 7.18-7.06 (m, 2H), 3.06 (t, *J* = 7.5 Hz, 2H), 1.66 (quintet, *J* = 7.5 Hz, 2H), 1.56-1.36 (m, 2H), 1.36-1.02 (m, 4H), 0.89 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.7 (C), 165.9 (d, *J* = 254.9 Hz, C), 133.7 (d, *J* = 2.9 Hz, C), 129.8 (d, *J* = 9.2 Hz, CH), 115.7 (d, *J* = 22.1 Hz, CH), 31.4 (CH_2), 29.6 (CH_2), 29.2 (CH_2), 28.7 (CH_2), 22.6 (CH_2), 14.1 (CH_3); IR (thin film) 2956, 2928, 2857, 1659, 1599, 1504 cm^{-1}; LRMS (ESI) 241 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_{13}H_{18}FOS$ $[M+H]^+$ 241.1057; observed 241.1057.

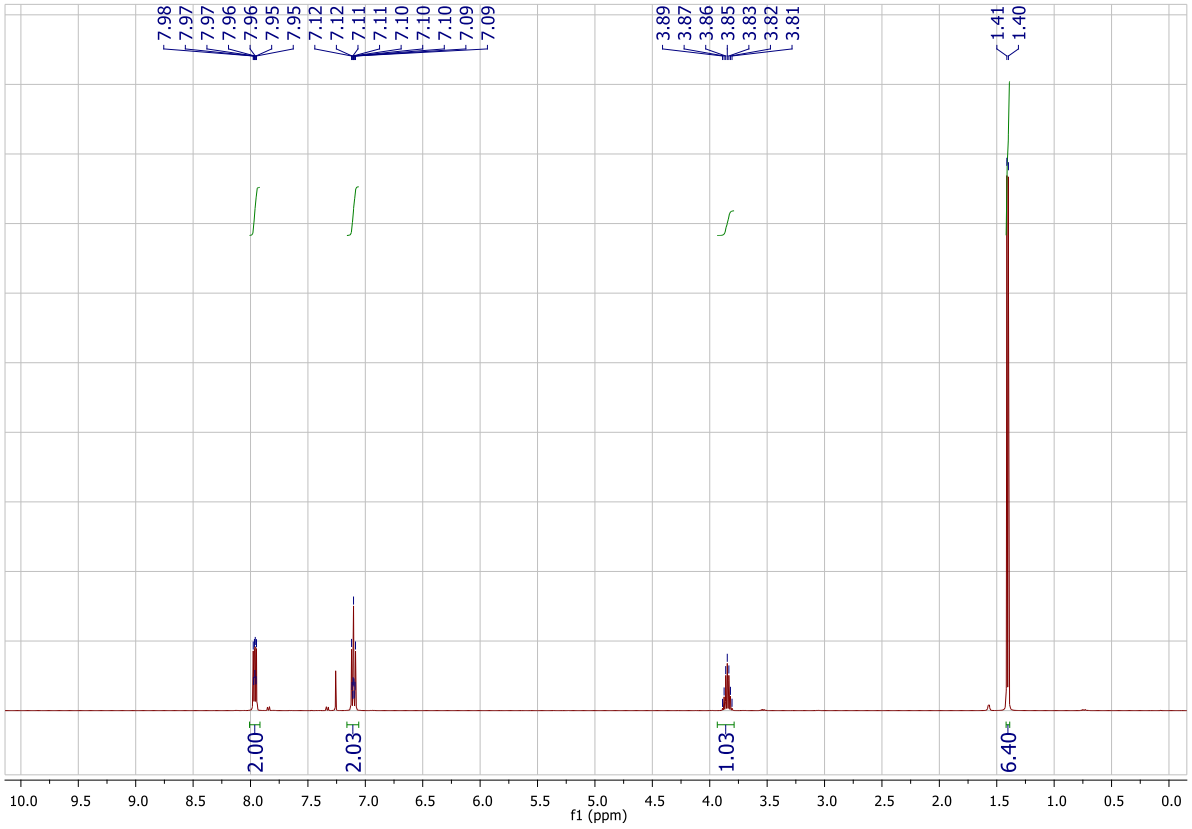


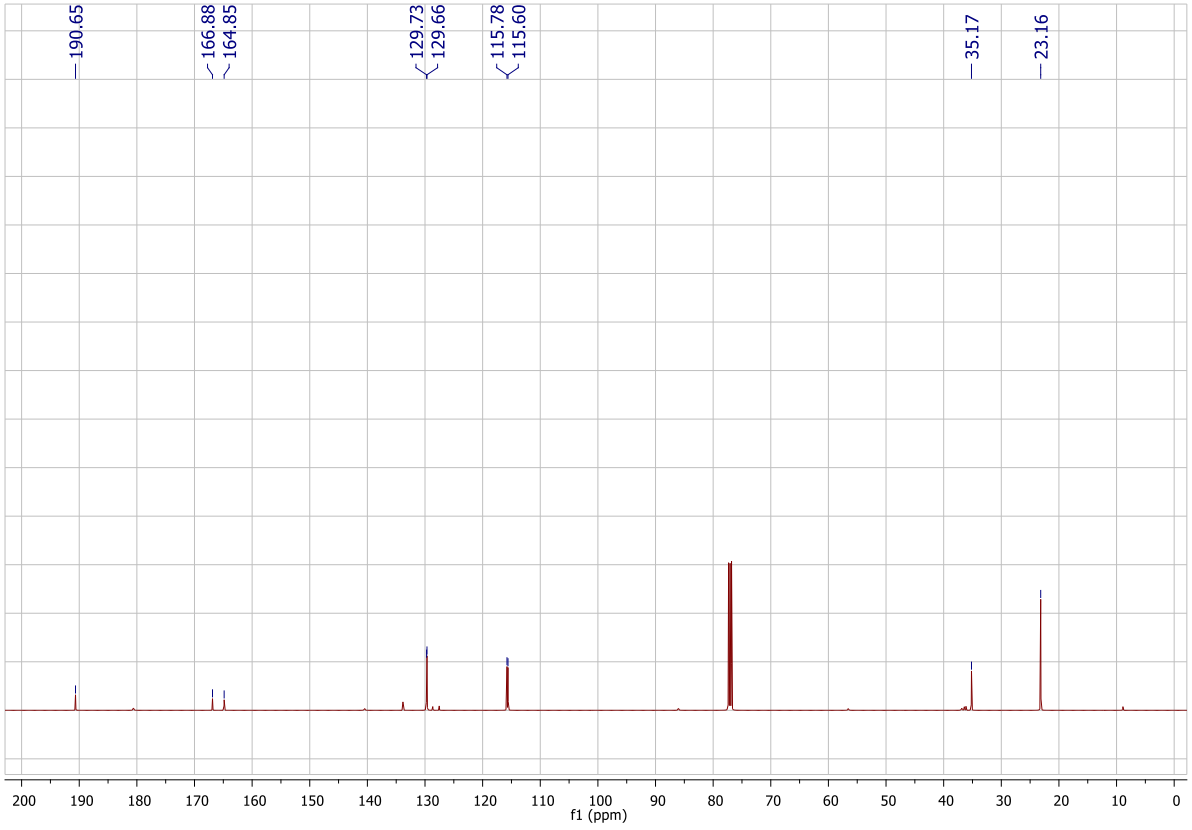

190.7
166.9
164.9
133.7
133.7
129.8
129.7
115.8
115.6
31.4
29.6
29.2
28.6
22.6
14.1
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

_S_-Isopropyl 4-fluorobenzothioate



Purification by column chromatography (1–5% EtOAc/Petrol) yielded *S*-isopropyl 4-fluorobenzothioate as a yellowish oil (57 mg, 0.29 mmol, 58%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 – 7.92 (m, 2H), 7.24 – 6.98 (m, 2H), 3.85 (hept, *J* = 6.9 Hz, 1H), 1.41 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.7 (C), 165.9 (d, *J* = 254.5 Hz, C), 133.8 (d, *J* = 2.9 Hz, C), 129.7 (d, *J* = 9.1 Hz, CH), 115.7 (d, *J* = 22.0 Hz, CH), 35.2 (CH), 23.2 (CH_3); IR (thin film) 2966, 2929, 2868, 1656, 1598, 1504 cm^{-1}; LRMS (ESI) 199 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_{10}H_{12}FOS$ $[M+H]^+$ 199.0587; observed 199.0585.

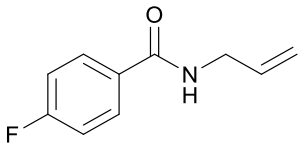



190.65
166.88
164.85
129.73
129.66
115.78
115.60
35.17
23.16
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

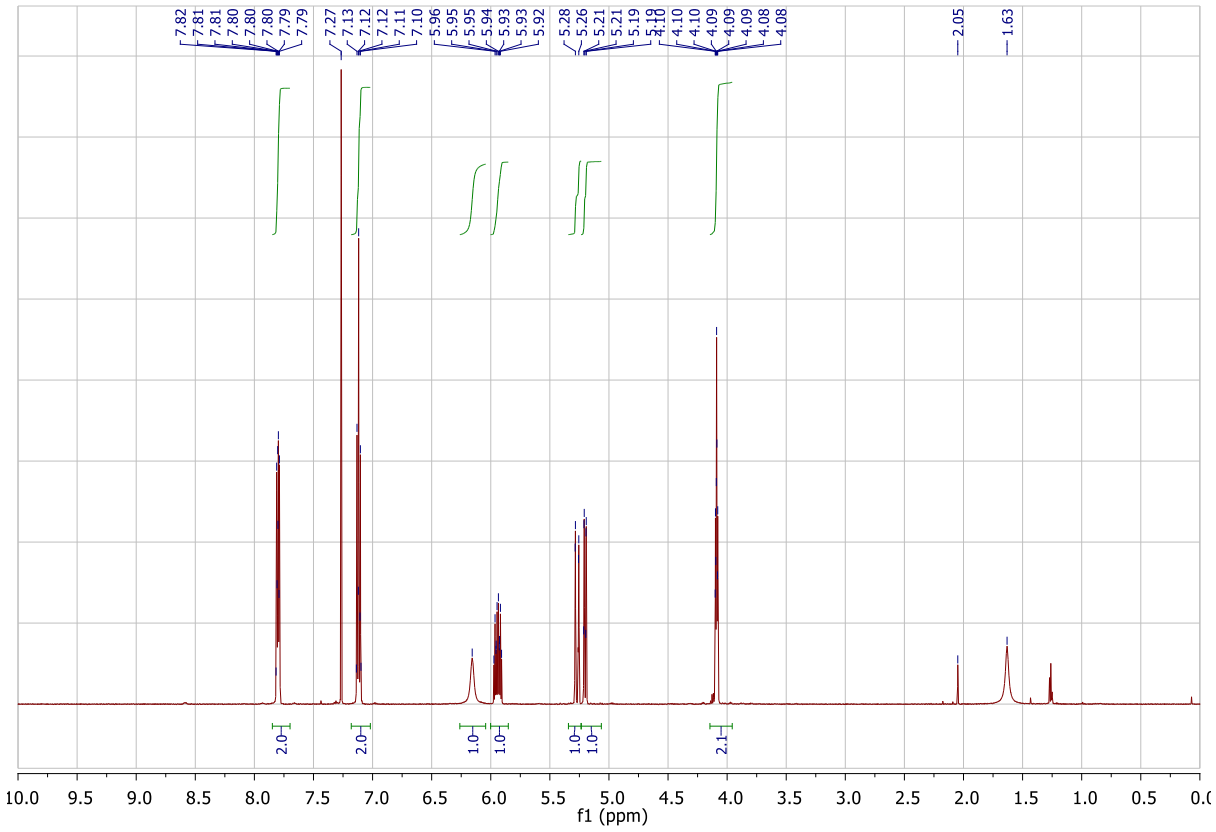
General procedure for one-pot amide synthesis

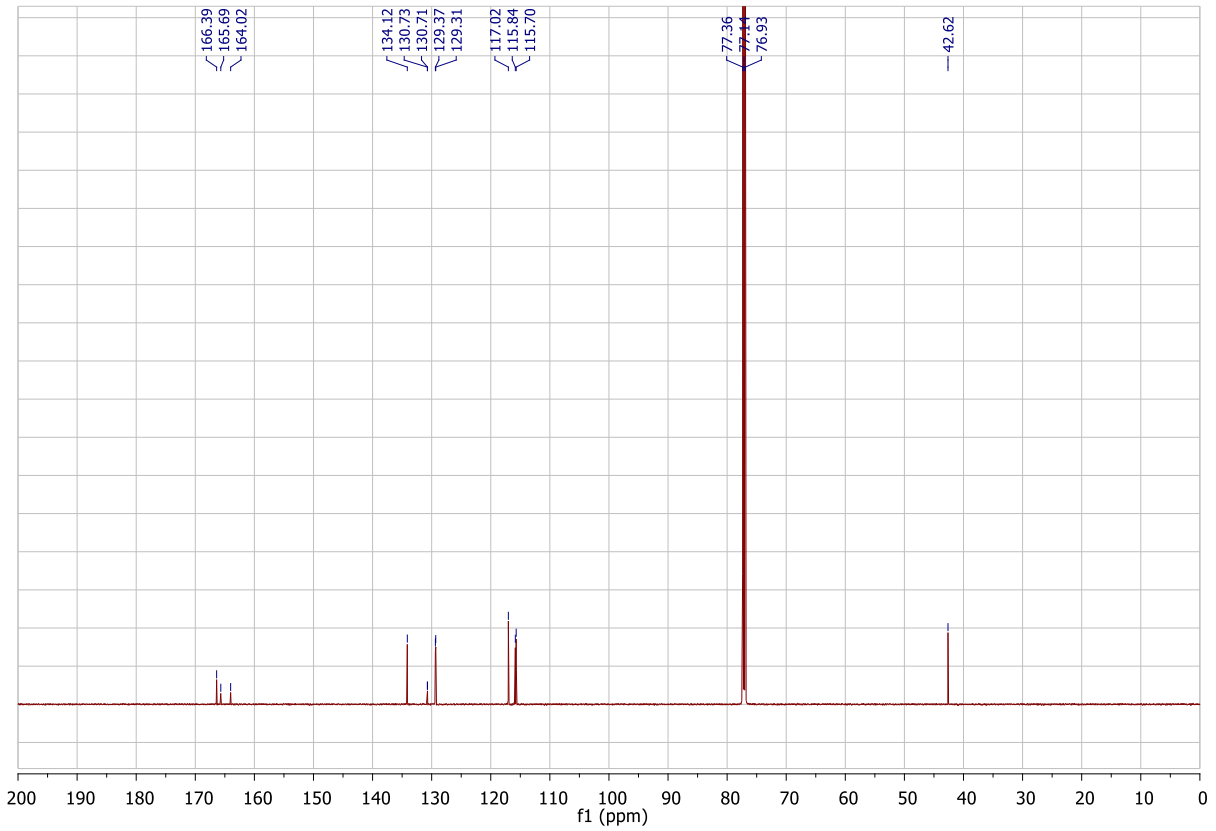
Aldehyde (0.5 mmol) was added to a solution of azodicarboxylate (0.6 mmol, 1.2 eq.) in DMF (500 μL) and the reaction mixture stirred at 300 rpm at 21 °C in a carousel tube for 24 h. After this time, amine (0.55 mmol, 1.1 eq.) in dimethylformamide (1 mL) was added to the reaction mixture. After 16 h, the reaction mixture was diluted with diethyl ether (25 mL) and extracted with aq. sat. LiCl (2 × 25 mL). The organic layer was then dried ($MgSO_4$), filtered and the solvent was removed *in vacuo*. The resultant crude residue was purified as described below.

4-Fluoro-*N*-(prop-2-en-1-yl)benzamide

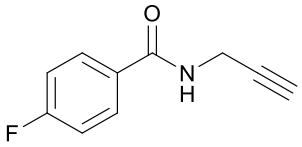


Purification by column chromatography (30%-95% Et_2O/Petrol) yielded 4-fluoro-*N*-(prop-2-en-1-yl)benzamide as a clear oil (64 mg, 0.35 mmol, 71%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84-7.75 (m, 2H), 7.10-7.14 (m, 2H), 6.16 (br s, 1H), 5.94 (ddt, J = 17.0, 10.0, 5.5 Hz, 1H), 5.27 (dd, J = 17.0, 1.5 Hz, 1H), 5.20 (dd, J = 10.0, 1.5 Hz, 1H), 4.09 (app. tt, J = 7.4, 1.5 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.4 (C), 164.9 (d, $J_{C\text{-}F}$ = 250.5 Hz, C), 134.1 (CH), 130.7 (d, $J_{C\text{-}F}$ = 3.1 Hz, C), 129.3 (d, $J_{C\text{-}F}$ = 8.8 Hz, CH), 117.0 (CH_2), 115.8 (d, $J_{C\text{-}F}$ = 22.9 Hz, CH), 42.6 (CH_2); IR (thin film) 3306, 3081, 1639, 1604, 1502 cm^{-1}; LRMS (ESI) 180 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_{10}H_{11}NOF$ $[M+H]^+$ 180.0819; observed 180.0817.

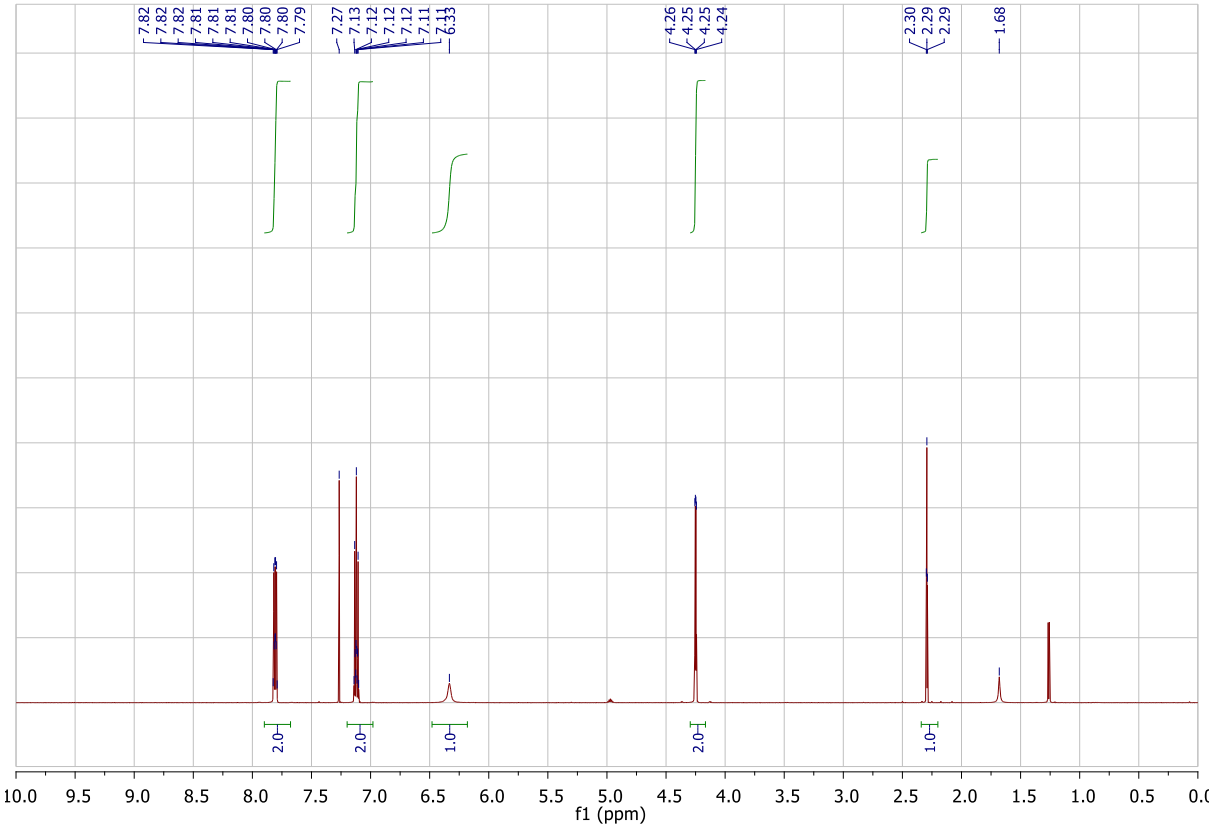

7.82
7.81
7.81
7.80
7.80
7.80
7.79
7.79
7.27
7.13
7.12
7.12
7.11
7.10
5.96
5.95
5.95
5.94
5.93
5.93
5.92
5.28
5.26
5.21
5.21
5.19
4.10
4.10
4.09
4.09
4.09
4.08
4.08
2.05
1.63
2.0
2.0
1.0
1.0
1.0
1.0
2.1
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

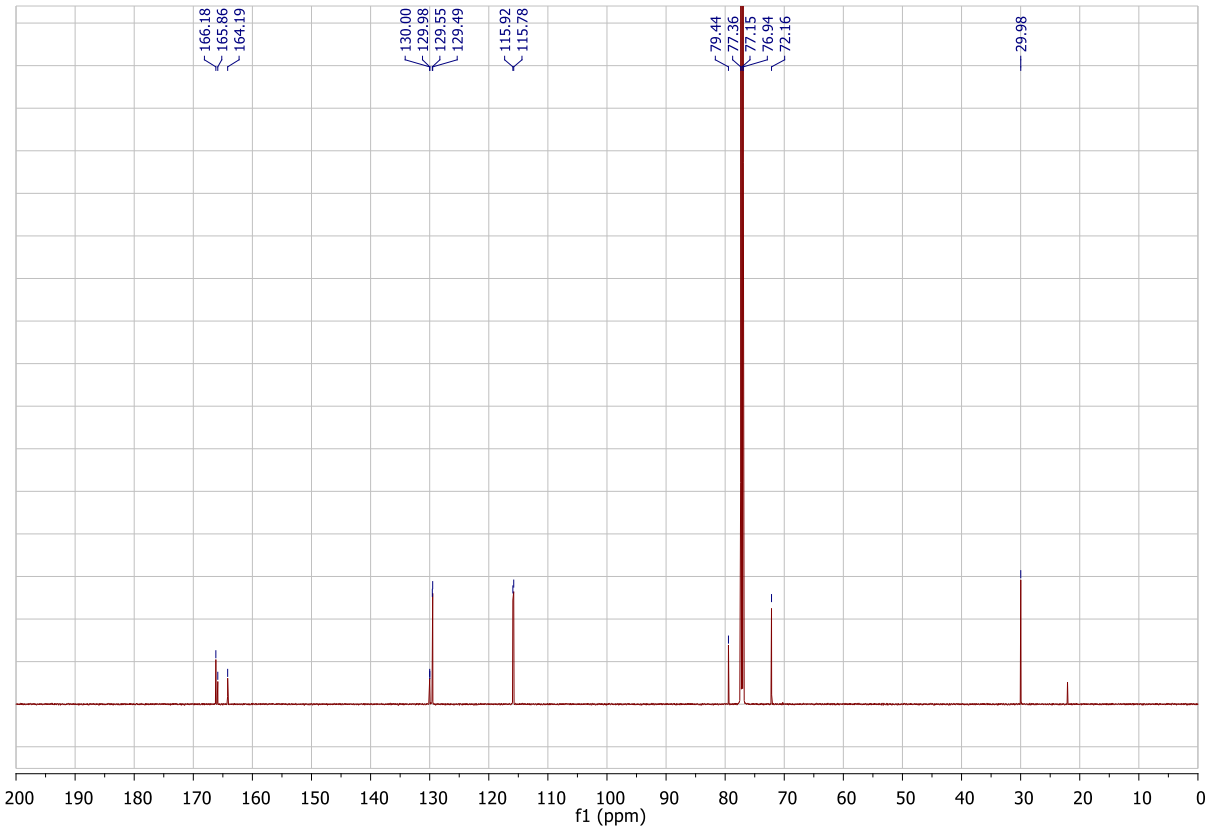

166.39
165.69
164.02
134.12
130.73
130.71
129.37
129.31
117.02
115.84
115.70
77.36
77.14
76.93
42.62
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

4-Fluoro-*N*-(prop-2-yn-1-yl)benzamide

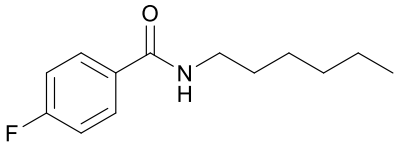


Purification by column chromatography (30%-95% Et_2O/Petrol) yielded 4-fluoro-*N*-(prop-2-yn-1-yl)benzamide as a clear oil (59 mg, 0.33 mmol, 67%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82-7.78 (m, 2H), 7.14-7.09 (m, 2H), 6.33 (br s, 1H), 4.16 (dd, J = 5.2, 2.6 Hz, 2H), 2.29 (t, J = 2.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.2 (C), 165.0 (d, $J_{C\text{-}F}$ = 250.5 Hz, C), 130.0 (d, $J_{C\text{-}F}$ = 3.1 Hz, C), 129.5 (d, $J_{C\text{-}F}$ = 8.7 Hz, CH), 115.8 (d, $J_{C\text{-}F}$ = 22.0 Hz, CH), 79.4 (CH), 30.0 (CH_2); IR (thin film) 3300, 2121, 1719, 1639, 1604, 1501 cm^{-1}; LRMS (ESI) 178 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_{10}H_9NOF$ $[M+H]^+$ 178.0663; observed 178.0663.

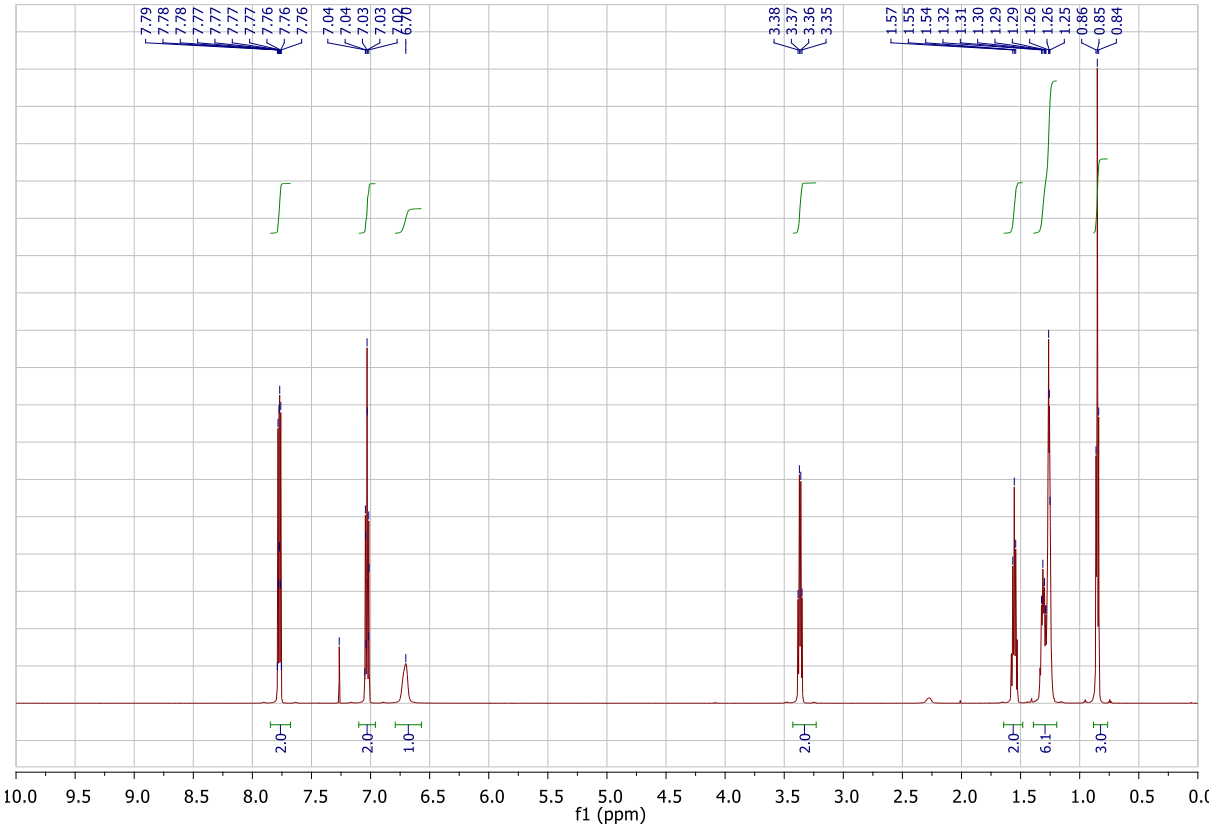


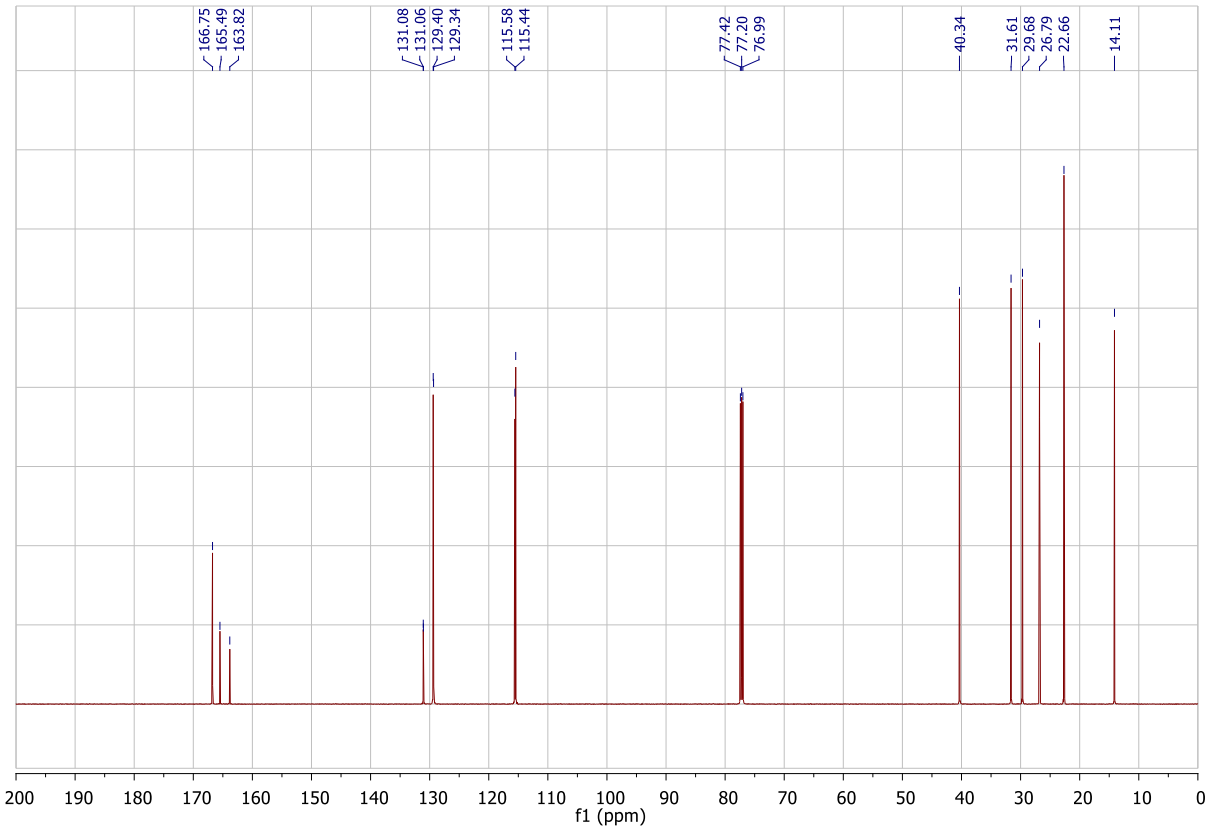

166.18
165.86
164.19
130.00
129.98
129.55
129.49
115.92
115.78
79.44
77.36
77.15
76.94
72.16
29.98
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

4-Fluoro-*N*-hexylbenzamide

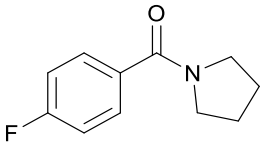


Purification by column chromatography (30%-90% Et_2O/Petrol) yielded 4-fluoro-*N*-hexylbenzamide as a clear oil (77 mg, 0.34 mmol, 69%). ^{1}H NMR (600 MHz, $CDCl_3$) 7.81-7.74 (m, 2H), 7.06-7.00 (m, 2H), 6.71 (br s, 1H), 3.37 (q, J = 7.0 Hz, 2H), 1.55 (quintet, J = 7.0 Hz, 2H), 1.31-1.25 (m, 6H), 0.85 (t, J = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) 166.8 (C), 164.7 (d, $J_{C\text{-}F}$ = 250.5 Hz, C), 131.1 (d, $J_{C\text{-}F}$ = 2.8 Hz, C), 129.4 (d, $J_{C\text{-}F}$ = 8.7 Hz, CH), 115.5 (d, $J_{C\text{-}F}$ = 22.0 Hz, CH), 40.3 (CH_2), 31.6 (CH_2), 29.7 (CH_2), 26.8 (CH_2), 22.7 (CH_2), 14.1 (CH_3); IR (thin film) 3304, 3076, 2928, 1635, 1604, 1501 cm^{-1}; LRMS (ESI) 224 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_{13}H_{19}NOF$ $[M+H]^+$ 224.1445; observed 224.1447.

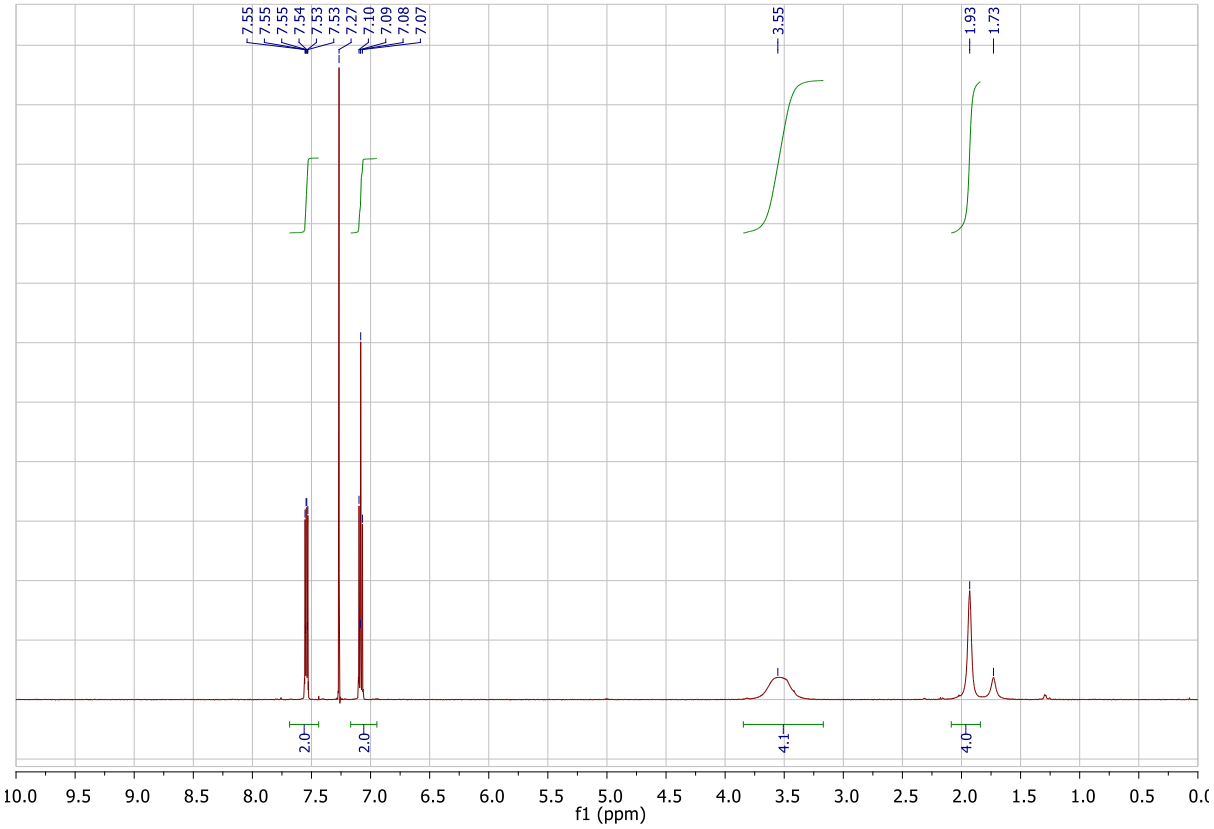


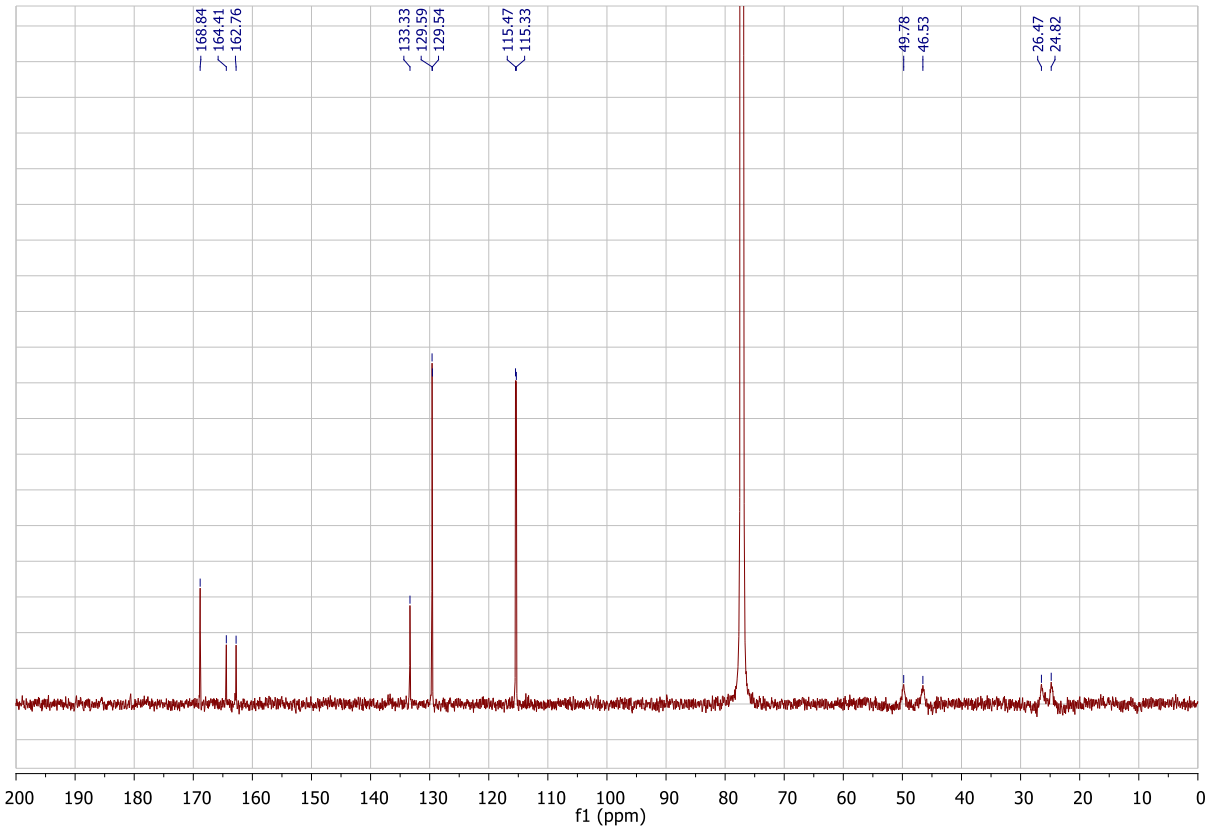

166.75
165.49
163.82
131.08
131.06
129.40
129.34
115.58
115.44
77.42
77.20
76.99
40.34
31.61
29.68
26.79
22.66
14.11
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

(4-Fluorophenyl)(pyrrolidin-1-yl)methanone

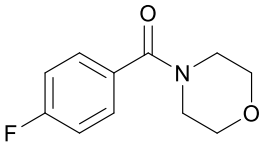


Purification by column chromatography (30%-95% Et_2O/Petrol) yielded (4-fluorophenyl)(pyrrolidin-1-yl)methanone as a white solid (58 mg, 0.30 mmol, 60%). m.p. 87-89 °C. ^{1}H NMR (600 MHz, $CDCl_3$) 7.57-7.50 (m, 2H), 7.14-7.05 (m, 2H), 3.54 (m, 4H), 1.93 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) 168.9 (C), 163.6 (d, $J_{C\text{-}F}$ = 249.2 Hz, C), 133.3 (C), 129.6 (d, $J_{C\text{-}F}$ = 8.1 Hz, CH), 115.4 (d, $J_{C\text{-}F}$ = 22.0 Hz, CH), 49.8 (CH_2), 46.5 (CH_2), 26.5 (CH_2), 24.8 (CH_2); IR (thin film) 3470, 2975, 2874, 1710, 1624, 1572 cm^{-1}; LRMS (ESI) 194 (100, $[M+H]^+$); HRMS (ESI) calcd for $C_{11}H_{13}NOF$ $[M+H]^+$ 194.0911; observed 194.0914.

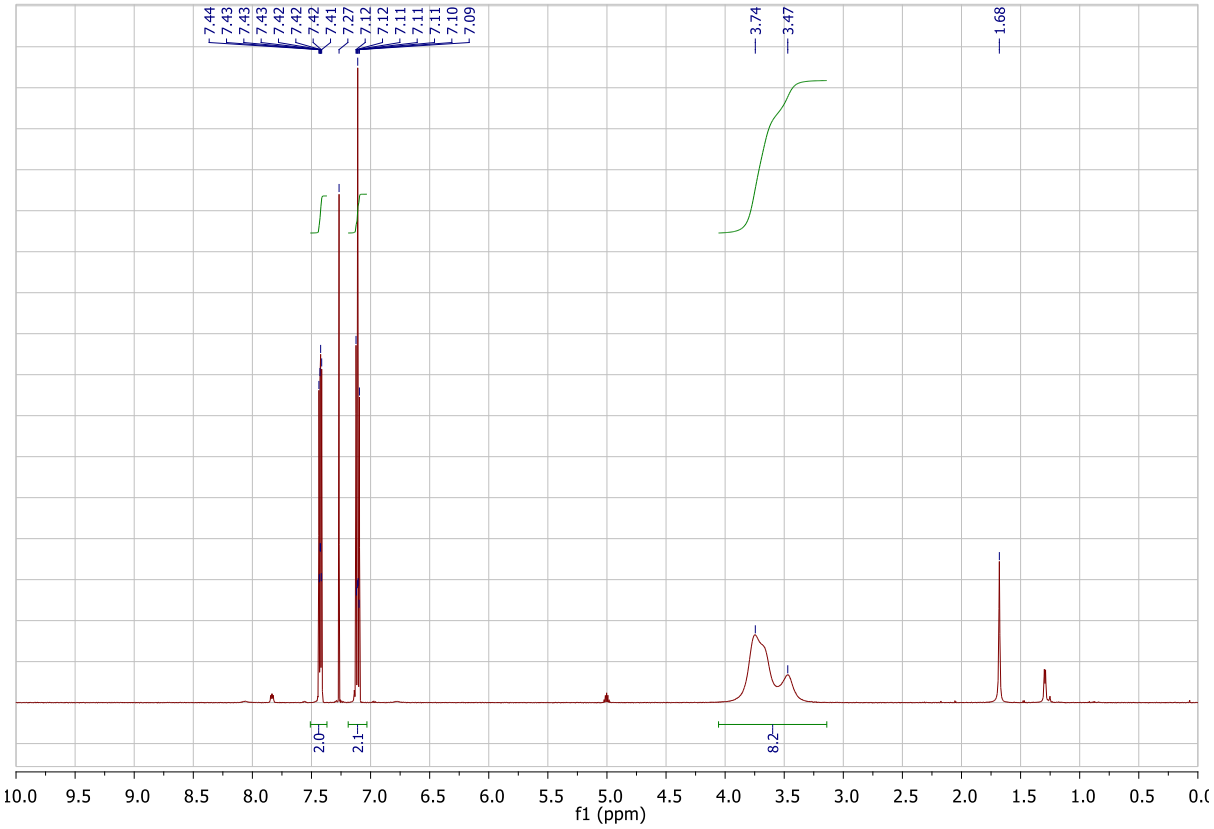


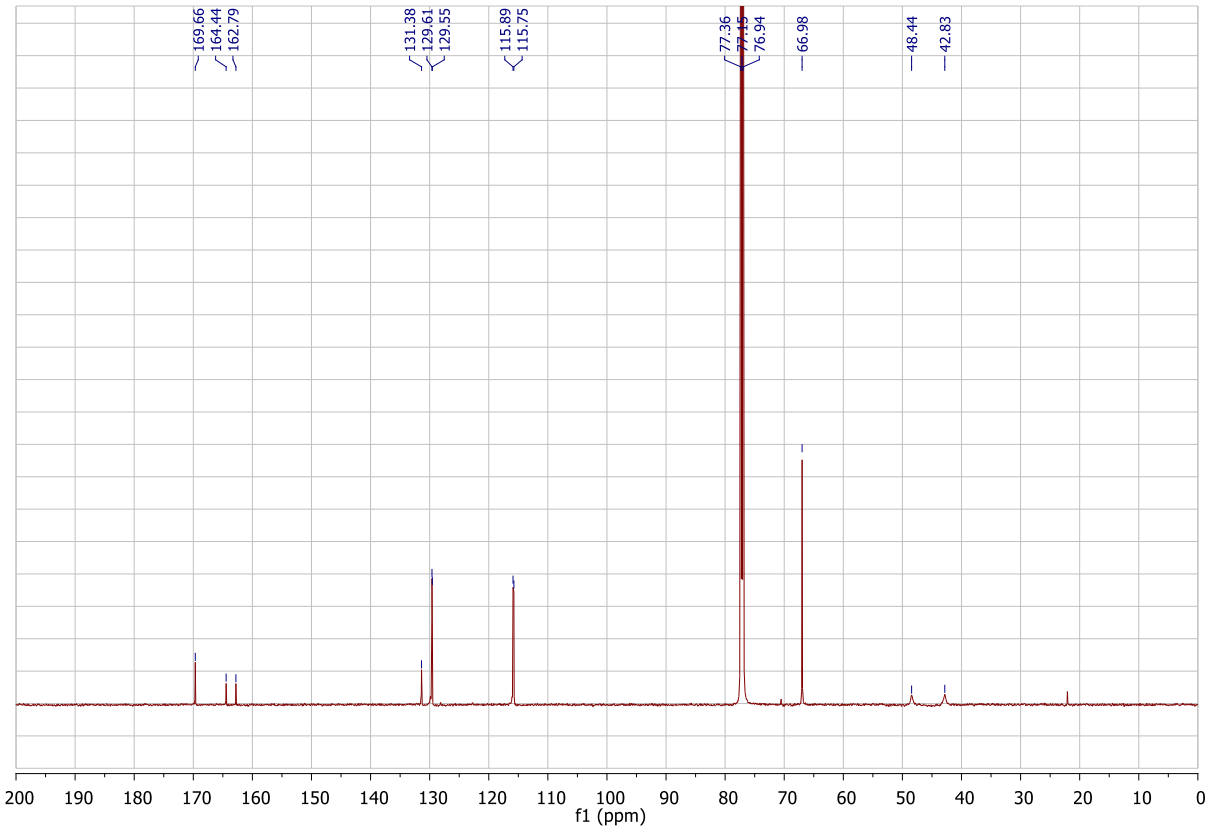

168.84
164.41
162.76
133.33
129.59
129.54
115.47
115.33
49.78
46.53
26.47
24.82
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

(4-Fluorophenyl)(morpholin-4-yl)methanone



Purification by column chromatography (30%-95% Et_2O/Petrol) yielded (4-fluorophenyl)(morpholin-4-yl)methanone as a clear oil (65 mg, 0.31 mmol, 62%). ^{1}H NMR (600 MHz, $CDCl_3$) 7.46-7.40 (m, 2H), 7.14-7.08 (m, 2H), 3.87-3.35 (m, 8H); ^{13}C NMR (150 MHz, $CDCl_3$) 169.7 (C), 163.6 (d, $J_{C\text{-}F}$ = 250.7 Hz, C), 131.4 (C), 129.6 (d, $J_{C\text{-}F}$ = 8.3 Hz, CH), 115.8 (d, $J_{C\text{-}F}$ = 22.1 Hz, CH), 70.0 (CH_2), 48.4 (CH_2), 42.8 (CH_2); IR (thin film) 3475, 2970, 2878, 1711, 1623, 1572 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{11}NOF$ $[M+H]^+$ 210.0860; observed 210.0865.




169.66
164.44
162.79
131.38
129.61
129.55
115.89
115.75
77.36
77.15
76.94
66.98
48.44
42.83
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

References

1. T. Iwasaki, Y. Maegawa, Y. Hayashi, T. Ohshima and K. Mashima, *J. Org. Chem.*, 2008, **73**, 5147–5150.

2. Y. Kita, Y. Nishii, A. Onoue and K. Mashima, *Adv. Synth. Catal.*, 2013, **355**, 3391–3395.