Electronic Supplementary Material (ESI) for ChemComm.

Selective Ruthenium-catalyzed Methylation of 2-Arylethanols using Methanol as C1 feedstock

Yang Li, Haoquan Li, Henrik Junge, and Matthias Beller*

Leibniz-Institut für Katalyse e.V. an der Universität Rostock, Albert Einstein Str. 29a, 18059 Rostock, Germany

Supporting Information

General information: ^{1}H NMR spectra were recorded on Bruker 300 MHz, ^{13}C NMR spectra were recorded on 75 MHz in the solvents indicated; chemical shifts are reported in units (ppm) by assigning $CDCl_3$ resonance in the ^{1}H spectrum as 7.26 ppm and $CDCl_3$ resonance in the ^{13}C spectrum as 77.0 ppm. All coupling constants (*J* values) were reported in Hertz (Hz). Column chromatography was performed on silica gel 200-300 mesh. HRMS were performed on Agilent ESI-TOF/MS. 2-(benzothiophen-3-yl)ethanol was prepared according to the reference.[1] If no special indicated, reagents were used as commercial sources and without further purification.

Table S1: Experiments with model substrate using cat. **1**, cat. **2**, the mixture of cat. **1** and cat. **2** under optimized conditions

Reaction time (h)	Yields with cat. **1** (%)	Yields with cat. **2** (%)	Yields with cat. **1** and **2** (%)
4	5	0	12
7	10	3	18
10	15	3	26
13	21	3	33
17	23	3	36
28[a]	36	4	58
45[b]	58	5	75

[a] The gas pressure was released at 17 h. [b]The gas pressure was released at 17 h, 28 h, respectively.

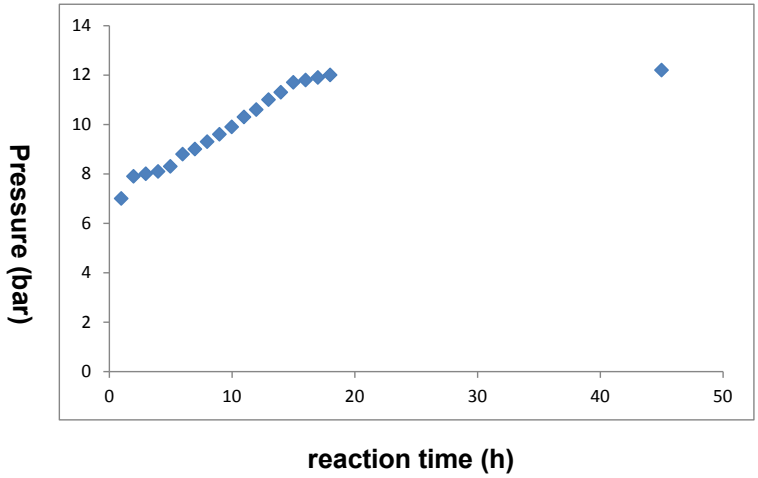


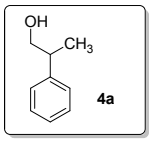
Figure S1. The reaction pressure versus reaction time
The reaction with model substrate was performed in optimized reaction conditions without pressure release.

General Procedure for synthesis of 2-(benzothiophen-3-yl)ethanol (3l):

To a suspension of $LiAlH_4$ (395 mg, 10.39 mmol) in anhydrous THF (50 mL) was added a solution of 2-(benzothiophen-3-yl)acetic acid (1.00 g, 5.20 mmol) in anhydrous THF (10 mL) dropwise in ice water bath. After addition, the reaction temperature was allowed to room temperature and then increased to 60 °C. The stirring was continued for 1 h. After cooling to room temperature, the reaction was quenched with water (0.4 mL), NaOH solution (30%, 0.4 mL). After stirring for a while, anhydrous $MgSO_4$ (4.0 g) was added. Then the mixture was filtered on celite, washed with EtOAc. The filtrate was evaporated in vacuo, the residue was purified by column chromatography on silica gel with eluting of hexane and ethyl acetate (3 :1) to afford 2-(benzothiophen-3-yl)ethanol (836.4 mg, 90% yield) as a pale yellow oil.

^{1}H NMR ($CDCl_3$, 300 M Hz): δ 7.87-7.84 (m, 1H), 7.77-7.74 (m, 1H), 7.41-7.31 (m, 2 H), 7.19 (s, 1H), 3.95-3.90 (m, 2 H), 3.12-3.07 (m, 2H), 1.24 (br, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 140.57, 138.90, 132.97, 124.37, 124.04, 122.98, 122.86, 121.65, 61.91, 31.94. MS (EI): m/z, 178.

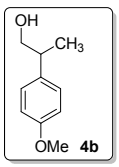
General Procedure for synthesis of compounds 4: To a stainless steel sealed tube (40 mL) was added base (0.25 mmol). Derivatives of 2-phenylethanol (2.5 mmol), anhydrous MeOH (2 mL), Ru-MACHO (0.0025 mmol) and Shvo catalyst (0.00125 mmol) were added in argon atmosphere in sequence. The reaction mixture was stirred at 140 °C for 17 h. After that the sealed tube was cooled to room temperature by water immediately and the pressure of reaction system was released. Then heating and stirring were continued for another 11 h. Another operation of release pressure was repeated. After stirring at 140 °C for 17 h again, the reaction mixture was cooled to room temperature and transferred to a flask. Solvents were evaporated in vacuo and the residue was purified by column chromatography on silica gel with eluting of hexane and ethyl acetate (the ratio is about 4 : 1) to afford compounds **4**



4a

According to the general procedure, compound **4a** was obtained in 87% yield (296.2 mg).

^{1}H NMR (300 M Hz, $CDCl_3$): δ = 7.34-7.28 (m, 2H), 7.24-7.19 (m, 3H), 3.66-3.64 (m, 2H), 2.95-2.88 (m, 1H), 1.73 (br, 1H), 1.26 (d, *J* = 9.0, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 143.67, 128.51 (2C), 127.41(2C), 126.55, 68.55, 42.33, 17.51. MS (EI): m/z, 136.

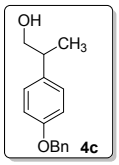


4b

According to the general procedure, compound **4b** was obtained in 76% yield (315.8 mg).

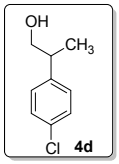
^{1}H NMR (300 M Hz, $CDCl_3$): δ = 7.15 (d, *J* = 9.0, 2H), 6.87 (d, *J* = 9.0, 2H), 3.79 (s, 3H), 3.65-3.63 (m, 2H), 2.89 (q, *J* = 6.9, 1H), 1.55 (s, 1H), 1.24 (d, *J* = 6.0, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 158.26, 135.58, 128.33 (2C), 113.97 (2C), 68.73, 55.20, 41.51, 17.68.

HRMS (EI), *m/z*: $[M]^+$ calculated for $C_{10}H_{14}O_2$:166.0988, found 166.0993.



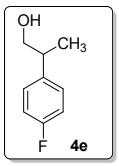
According to the general procedure, compound **4c** was obtained in 73% yield (440.5 mg).

^{1}H NMR (300 M Hz, $CDCl_3$): δ = 7.44-7.29 (m, 5H), 7.15 (d, *J* = 9.0, 2H), 6.94 (d, *J* = 9.0, 2H), 5.03 (s, 2H), 3.64-3.62 (m, 2H), 2.94-2.82 (m, 1H), 1.48 (br, 1H), 1.24 (d, *J* = 9.0, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 157.52, 137.02, 135.86, 128.52 (2C), 128.36 (2C), 127.89, 127.41(2C), 114.91(2C), 69.97, 68.71, 41.52, 17.67. HRMS (EI), *m/z*: $[M+H]^+$ calculated for $C_{16}H_{18}O_2$:242.1301, found 242.1298.



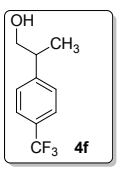
According to the general procedure, compound **4d** was obtained in 78% yield (332.7 mg).

^{1}H NMR (300 M Hz, $CDCl_3$): δ = 7.29 (d, *J* = 9.0, 2H), 7.16 (d, *J* = 9.0, 2H), 3.66 - 3.64 (m, 2H), 2.94-2.87 (m, 1H), 1.64 (br, 1H), 1.24 (d, *J* = 9.0, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 142.22, 132.22, 128.78(2C), 128.63(2C), 68.38, 41.77, 17.49. HRMS (EI), *m/z*: $[M]^+$ calculated for $C_9H_{11}Cl^{35}O$:170.0493, found 170.0495; $[M]^+$ calculated for $C_9H_{11}Cl^{37}O$:172.0463, found 172.0467.



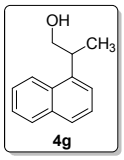
According to the general procedure, compound **4e** was obtained in 76% yield (292.9 mg).

^{1}H NMR (300 M Hz, $CDCl_3$): δ = 7.19-7.14 (m, 2H), 7.01-6.96 (m, 2H), 3.61-3.58 (m, 2H), 2.94-2.82 (m, 1H), 2.14 (br, 1H), 1.22 (d, *J* = 6.0, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 161.48 (d, *J* = 243.0), 139.41 (d, *J* = 3.0), 128.73 (d, *J* = 7.5, 2C), 115.16 (d, *J* = 21.0, 2C), 68.38 , 41.53 , 17.61. HRMS (EI), *m/z*: $[M]^+$ calculated for $C_9H_{11}OF$:154.0788, found 154.0785.



According to the general procedure, compound **4f** was obtained in 59% yield (302.7 mg).

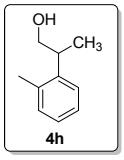
^{1}H NMR (300 M Hz, $CDCl_3$): δ = 7.59-7.56 (m, 2H), 7.37-7.33 (m, 2H), 3.73-3.69 (m, 2H), 3.04-2.97 (m, 1H), 1.55 (br, 1H), 1.29 (d, *J* = 6.0, 3H);^{13}C NMR (75 MHz, $CDCl_3$) δ = 148.03, 128.91 (q, *J* = 32.4), 127.81 (2C), 125.45 (q, *J* = 3.8, 2C), 124.22 (q, *J* = 270.0), 68.24, 42.29, 17.39. HRMS (EI), *m/z*: $[M]^+$ calculated for $C_{10}H_{11}OF_3$:204,0757, found 204,0755.



4g

According to the general procedure, the reaction was continued for another 17 h after 45 h heating and pressure release, compound **4g** was obtained in 84% yield (392.3 mg).

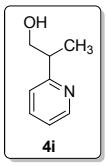
^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.14-8.10 (m, 1H), 7.86-7.83 (m, 1H), 7.73-7.70 (m, 1H), 7.53-7.36 (m, 4H), 3.91-3.73 (m, 3H), 1.72 (br, 1H), 1.40 (d, *J* = 6.0, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 139.51, 133.93, 131.88, 128.92, 126.98, 125.96, 125.47 (2C), 123.00, 122.97, 67.99, 36.29, 17.77. HRMS (EI), *m/z*: $[M]^+$ calculated for $C_{13}H_{14}O$:186.1039, found 186.1040.



4h

According to the general procedure, the reaction was continued for another 17 h after 45 h heating and pressure release, compound **4h** was obtained in 76% yield (285.3 mg).

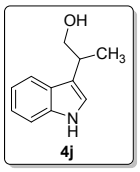
^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.20-7.08 (m, 4H), 3.75-3.62 (m, 2H), 3.29-2.18 (m, 1H), 2.35 (s, 3H), 1.64 (br, 1H), 1.23 (d, *J* = 6.0, 3H);^{13}C NMR (75 MHz, $CDCl_3$) δ = 141.75, 136.33, 130.46, 126.27, 126.17, 125.37, 67.91, 37.12, 19.56, 17.46. HRMS (EI), *m/z*: $[M]^+$ calculated for $C_{10}H_{14}O$:150.1039, found 150.1040.



4i

According to the general procedure, compound **4i** was obtained in 73% yield (252.1 mg).

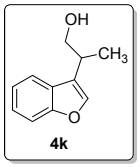
^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.47-8.45 (m, 1H), 7.64-7.59 (m, 1H), 7.19-7.10 (m, 2H); 4.23 (br, 1H), 3.89-3.82 (m, 2H), 3.10-3.00 (m, 1H), 1.30 (d, *J* = 9.0, 3H);^{13}C NMR (75 MHz, $CDCl_3$) δ = 164.79, 148.51, 136.74, 122.13, 121.44, 67.04, 41.99, 17.07. HRMS (EI), *m/z*: $[M-H]^+$ calculated for $C_8H_{10}ON$:136.0757, found 136.0760.



4j

According to the general procedure, compound **4j** was obtained in 66% yield (289.1 mg).

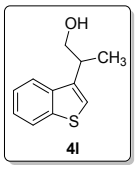
^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.16 (br, 1H), 7.63 (d, *J* = 9.0, 1H), 7.28 (d, *J* = 9.0, 1H), 7.20-7.07(m, 2H), 6.89 (d, *J* = 3.0, 1H), 3.82-3.70 (m, 2H), 3.28-3.19 (m, 1H), 1.79 (br, 1H), 1.35 (d, *J* = 6.0, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 136.42, 126.55, 121.85, 121.30, 119.08, 119.00, 117.48, 111.29, 67.63, 33.66, 17.19. HRMS (EI), *m/z*: $[M+H]^+$ calculated for $C_{11}H_{13}ON$:175.0992, found 175.0992.



4k

According to the general procedure, the reaction was performed on 1.17 mmol scale, compound **4k** was obtained in 65% yield (133.7 mg).

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.60-7.57 (m, 1H), 7.48-7.44 (m, 2H), 7.31- 7.19 (m, 2H), 3.85-3.71 (m, 2H), 3.18-3.11 (m, 1H), 1.75 (br, 1H), 1.37 (d, *J* = 6.0, 3H);^{13}C NMR (75 MHz, $CDCl_3$) δ = 155.49, 141.33, 127.21, 124.28, 122.31, 122.22, 119.96, 111.60, 66.97, 32.84, 16.50. HRMS (EI), *m/z*: $[M]^+$ calculated for $C_{11}H_{12}O_2$:176.0832, found 176.0829.

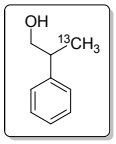


4l

According to the general procedure, compound **4l** was obtained in 84% yield (403.8 mg).

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.89-7.80 (m, 2H), 7.40-7.35 (m, 2H), 7.20 (s, 1H), 3.90-3.77 (m, 2H), 3.50-3.41 (m, 1H), 1.47 (br, 1H), 1.43 (d, *J* = 6.0, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 140.67, 138.58, 138.48, 124.40, 123.96, 122.97, 121.72, 121.15, 67.39, 35.85, 17.10. HRMS (EI), *m/z*: $[M]^+$ calculated for $C_{11}H_{12}OS$:192.0603, found 192.0606.

General Procedure for synthesis of compounds 4a using $^{13}CH_3OH$

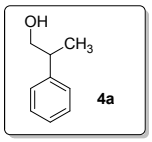


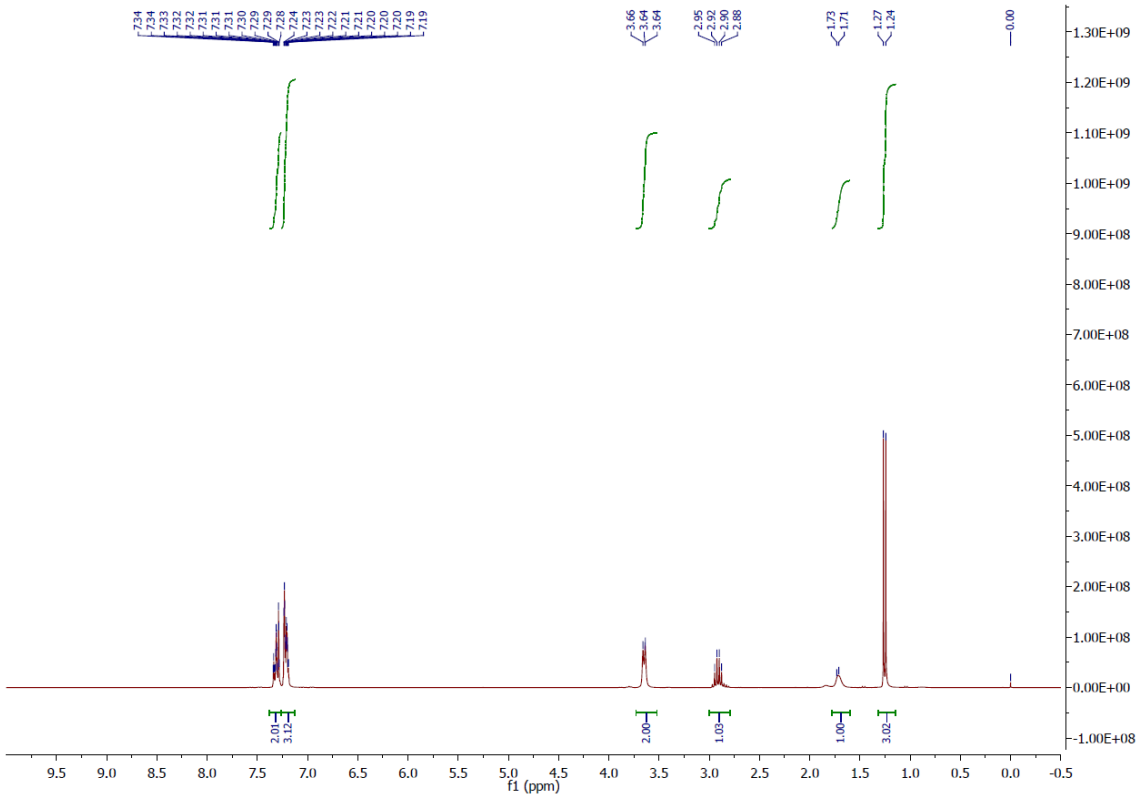
According to the general procedure using $^{13}CH_3OH$ instead of anhydrous CH_3OH, the desired compound was obtained in 70% yield (239.9 mg). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 143.72, 128.46 (2C), 127.39, 127.36, 126.48, 68.49, 42.29 (d, *J* = 34.5), 17.50.

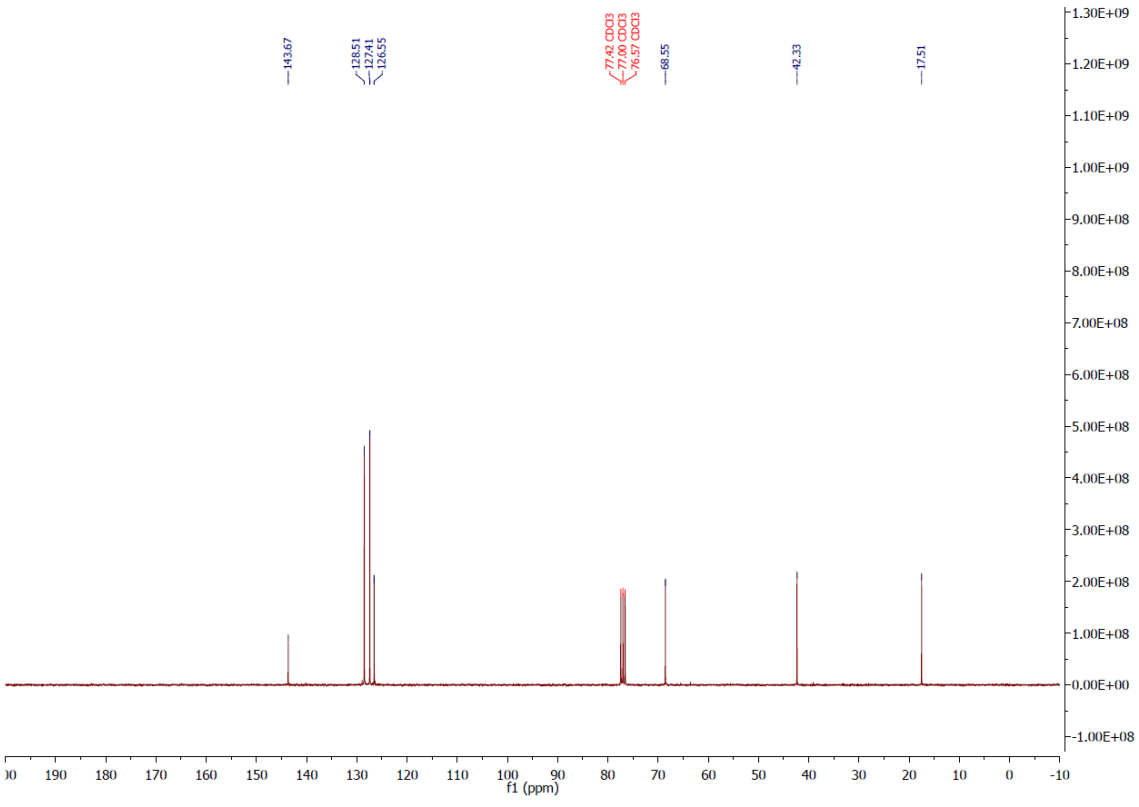
General Procedure for methylation of 1-butanol

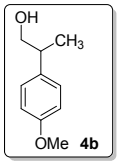
According to optimized conditions using 1-butanol as substrate, the reaction affords 2-methylbutan-1-ol in 11% and 20% GC yield at 140 °C and 160 °C, respectively.

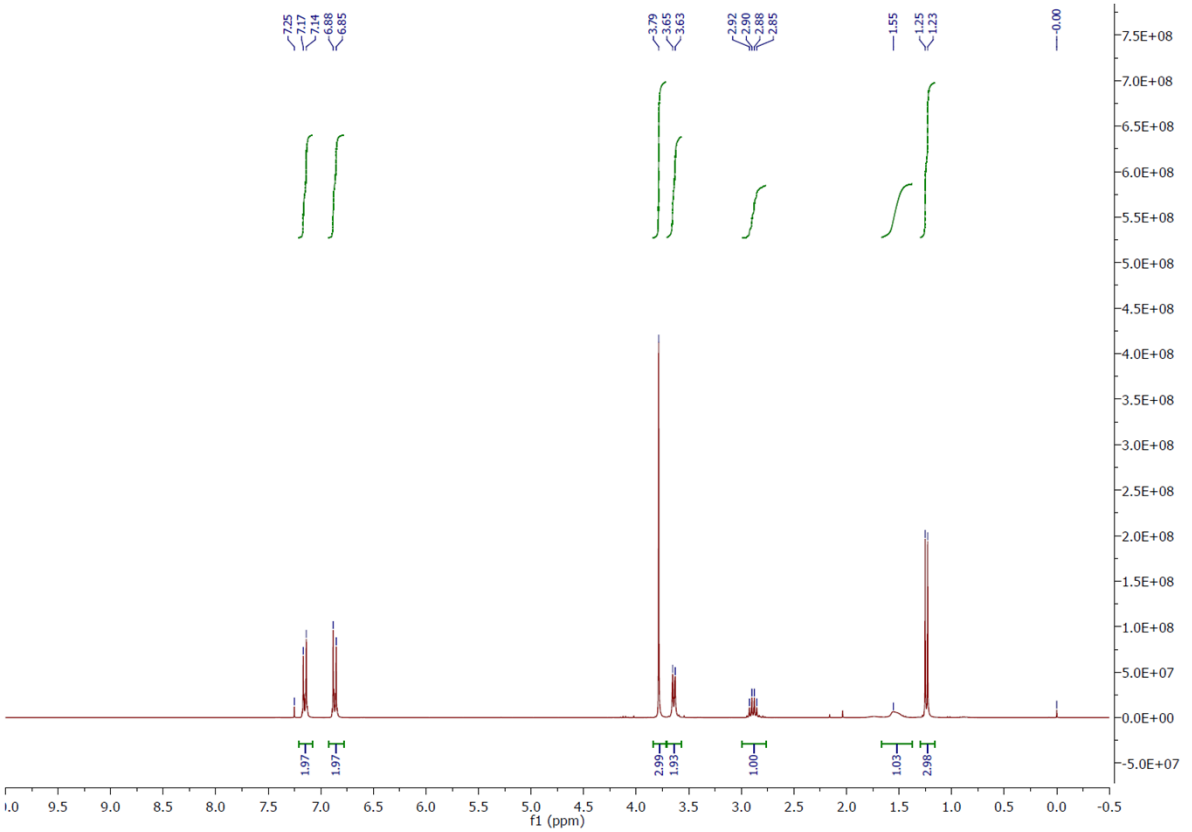
NMR spectrum

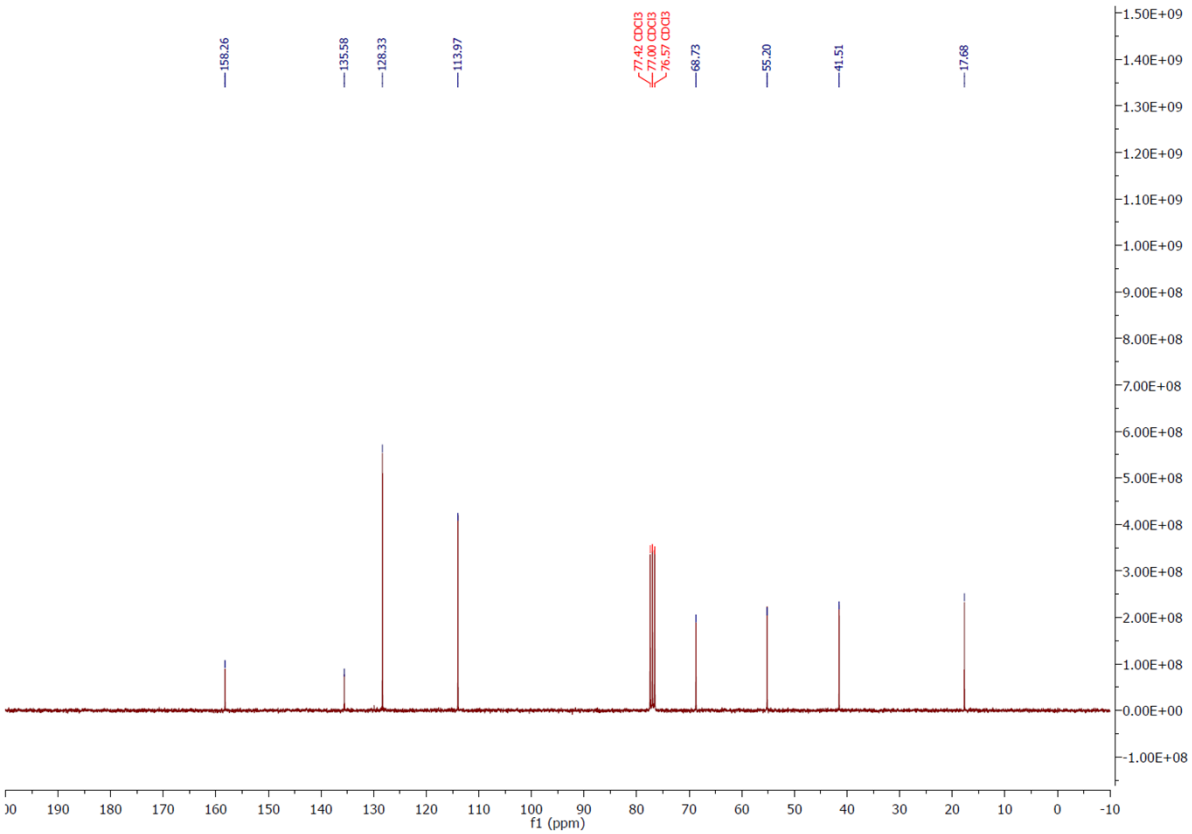







OH
CH3
OMe
4b


7.25
7.17
7.14
6.88
6.85
3.79
3.65
3.63
2.92
2.90
2.88
2.85
1.55
1.25
1.23
0.00
1.97
1.97
2.99
1.93
1.00
1.03
2.98
f1 (ppm)


158.26
135.58
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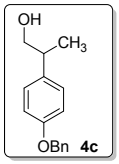
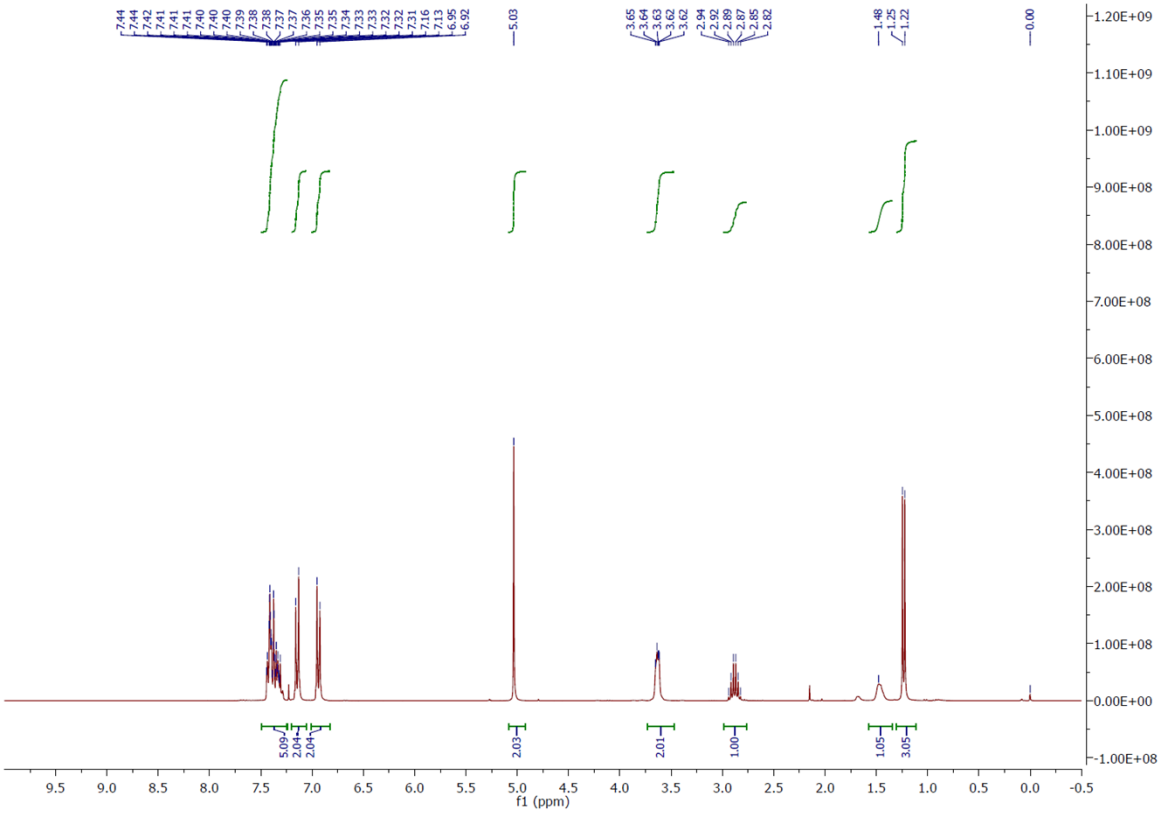
113.97
77.42 CDCl3
77.00 CDCl3
76.57 CDCl3
68.73
55.20
41.51
17.68
f1 (ppm)


OH
CH3
OBn 4c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7.41
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7.34
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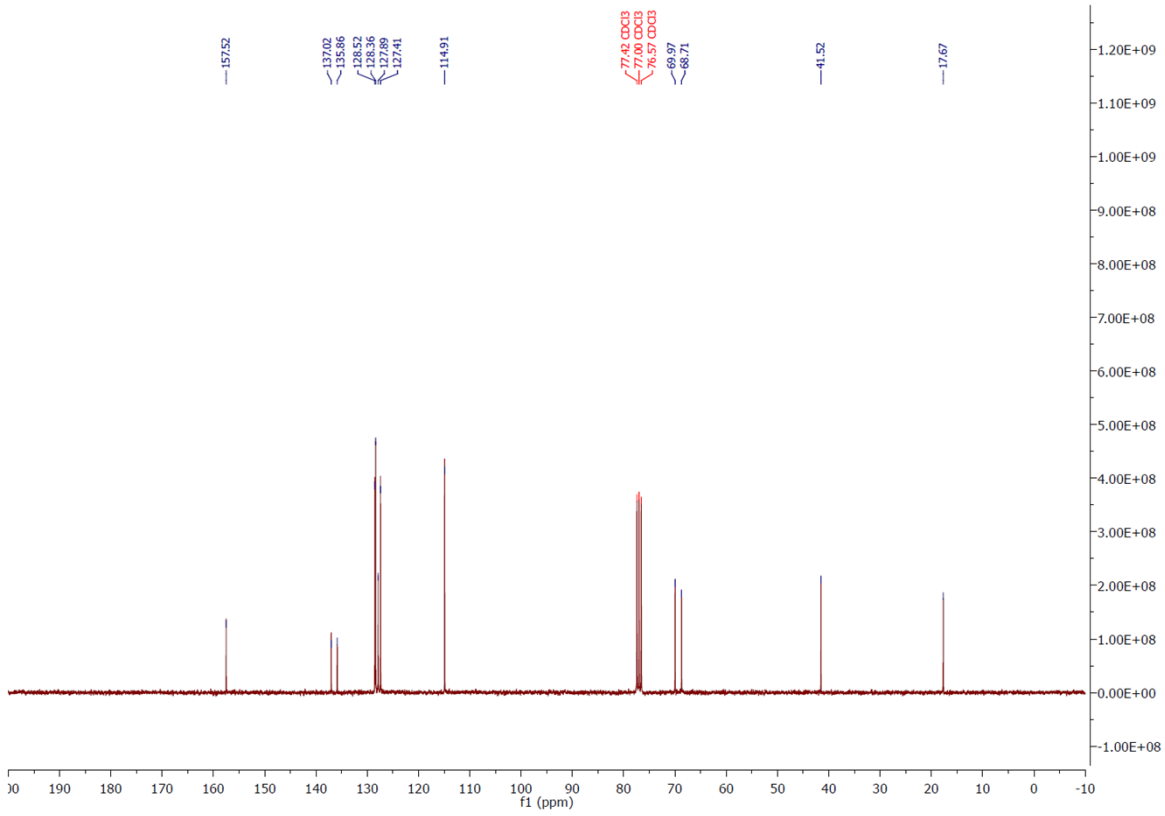
3.63
3.62
3.62
2.94
2.92
2.89
2.87
2.85
2.82
1.48
1.25
1.22
0.00
5.09
2.04
2.04
2.03
2.01
1.00
1.05
3.05
f1 (ppm)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135.86
128.52
128.36
127.89
127.41
114.91
77.42 CDCl3
77.00 CDCl3
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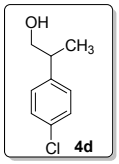
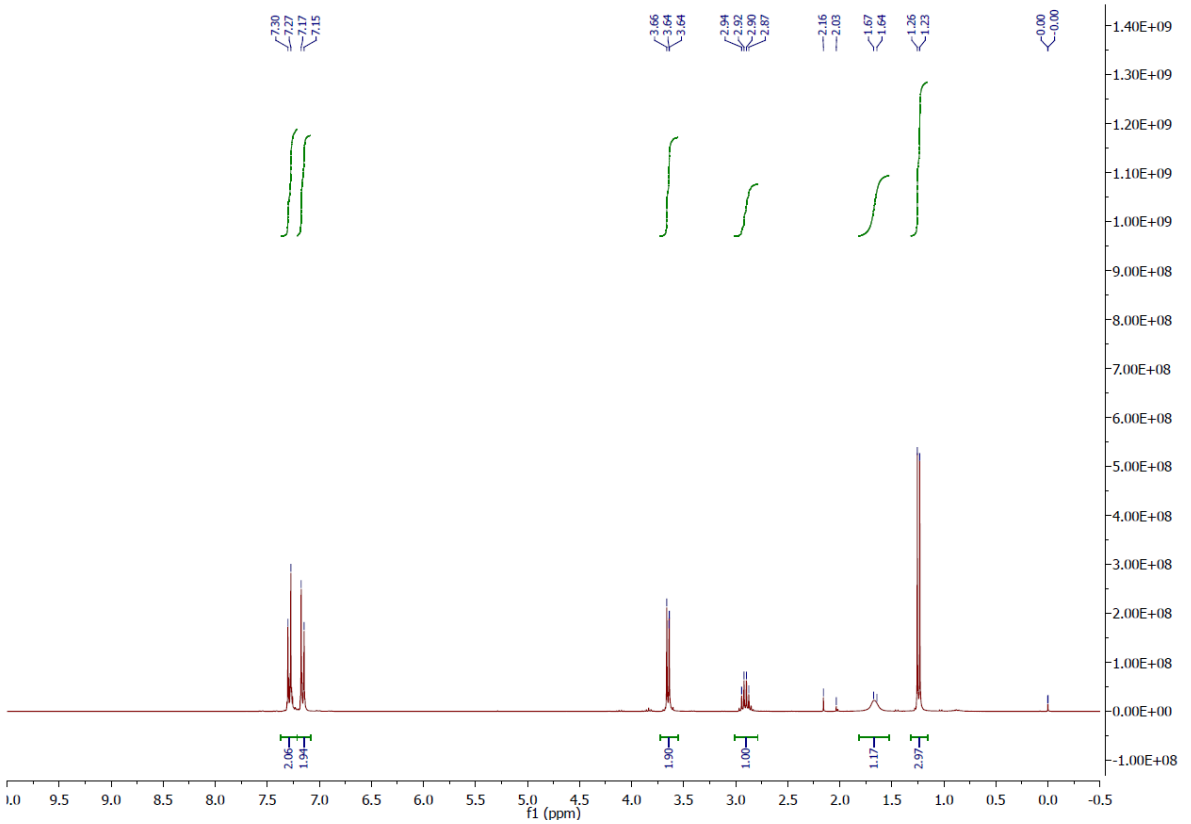
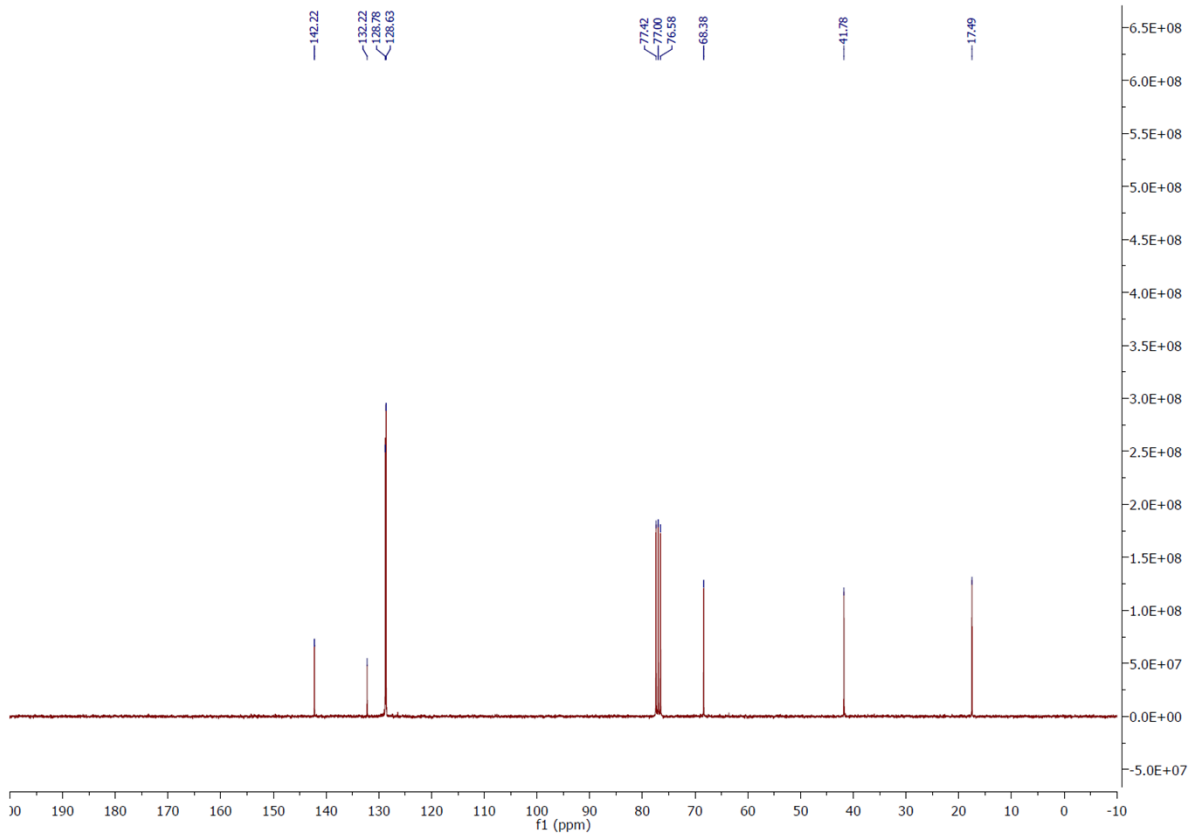
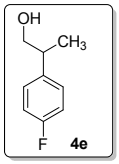
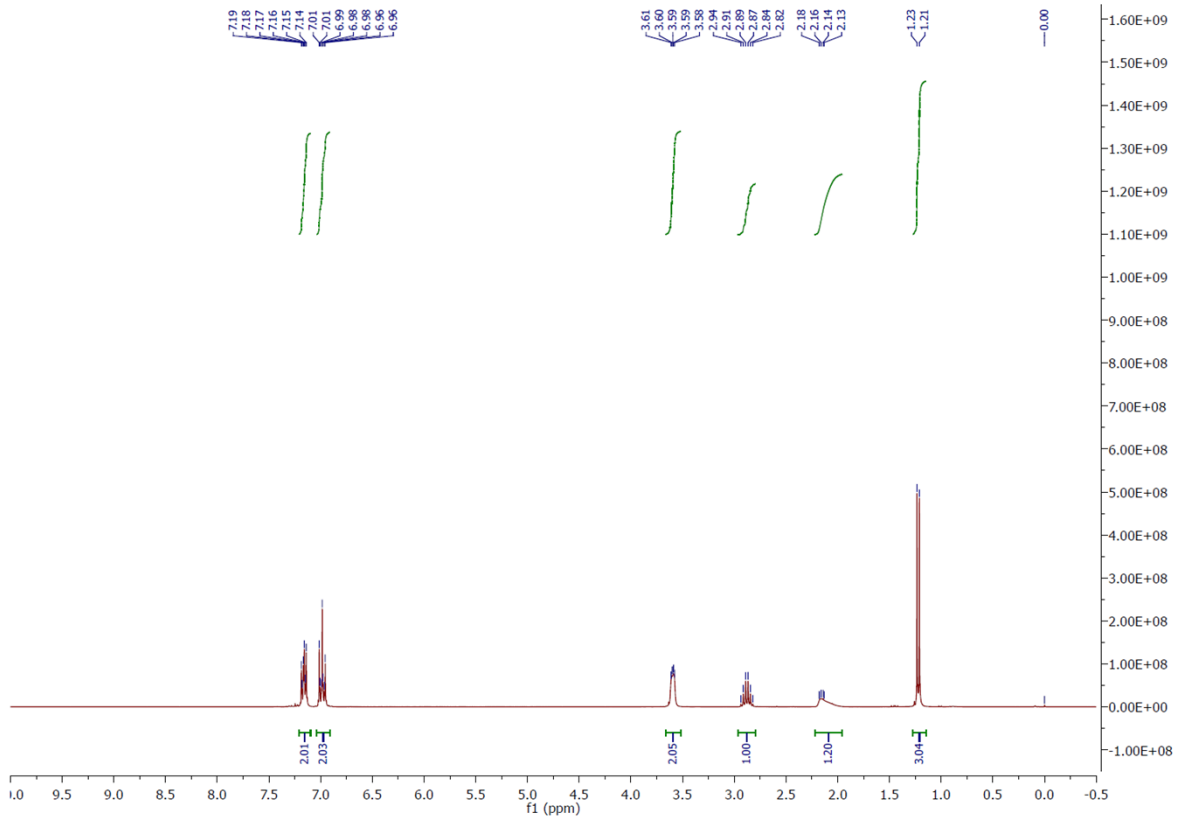
69.97
68.71
41.52
17.67
f1 (ppm)


OH
CH3
Cl
4d


7.30
7.27
7.17
7.15
3.66
3.64
3.64
2.94
2.92
2.90
2.87
2.16
2.03
1.67
1.64
1.26
1.23
0.00
0.00
2.06
1.94
1.90
1.00
1.17
2.97
f1 (ppm)


142.22
132.22
128.78
128.63
77.42
77.00
76.58
68.38
41.78
17.49
f1 (ppm)


OH
CH3
F
4e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7.17
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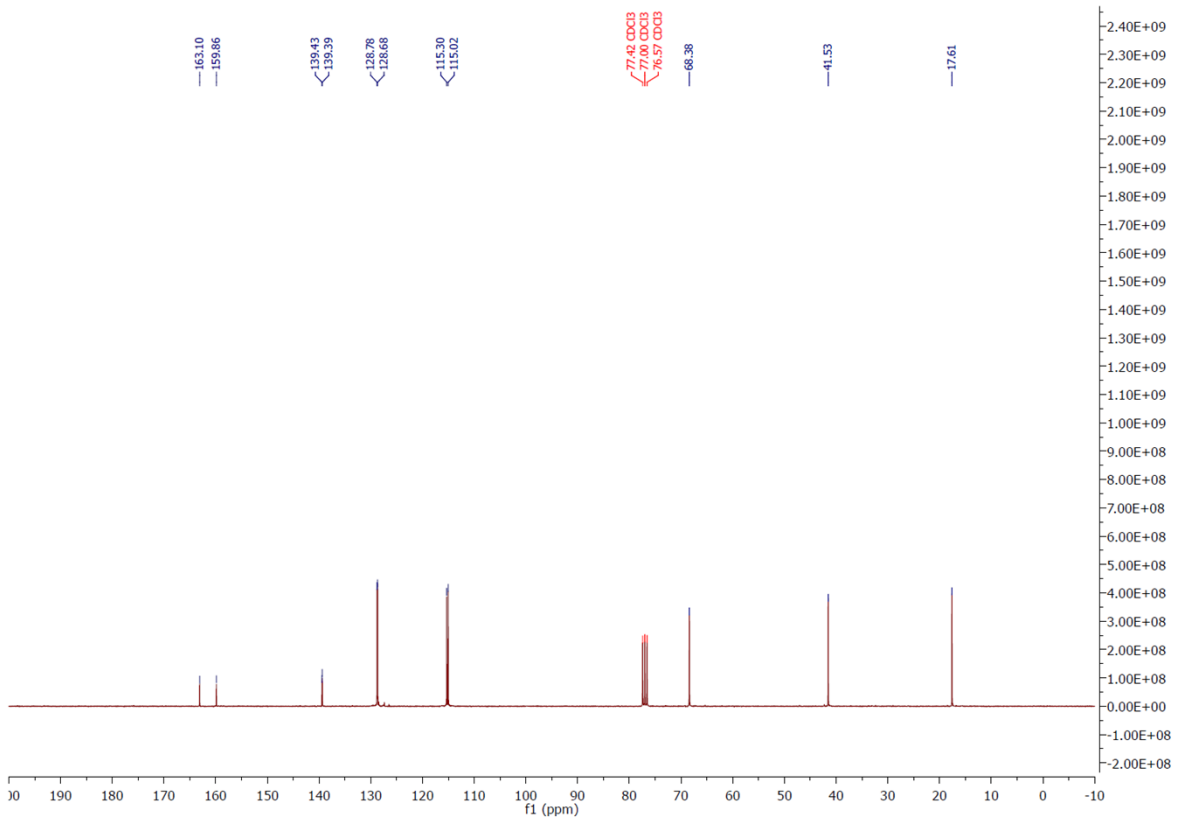
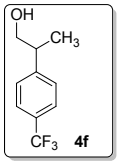
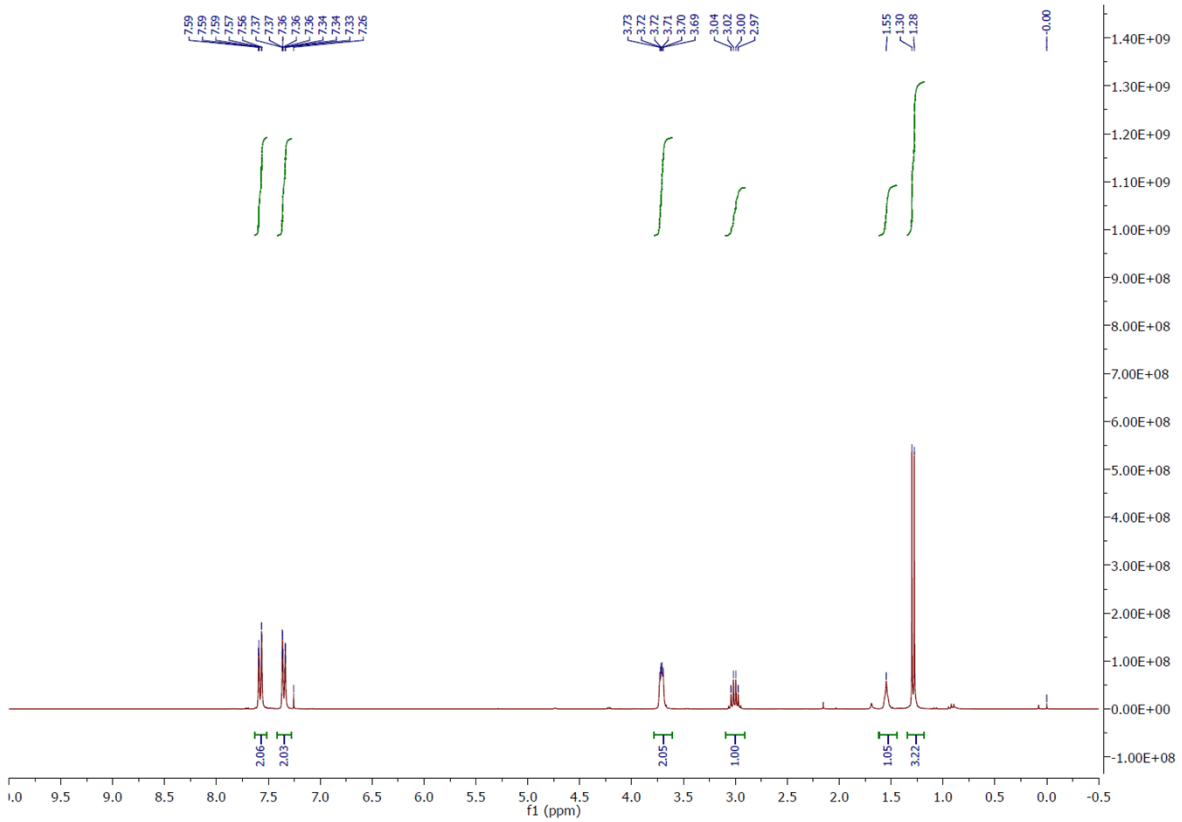
7.14
7.01
7.01
6.99
6.98
6.98
6.96
6.96
6.96
3.61
3.60
3.59
3.59
3.59
3.58
2.94
2.91
2.89
2.87
2.84
2.82
2.18
2.16
2.14
2.13
1.23
1.21
0.00
2.01
2.03
2.05
1.00
1.20
3.04
f1 (ppm)


163.10
159.86
139.43
139.39
128.78
128.68
115.30
115.02
77.42 CDCl3
77.00 CDCl3
76.57 CDCl3
68.38
41.53
17.61
f1 (ppm)


OH
CH3
CF3
4f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7.59
7.57
7.56
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7.36
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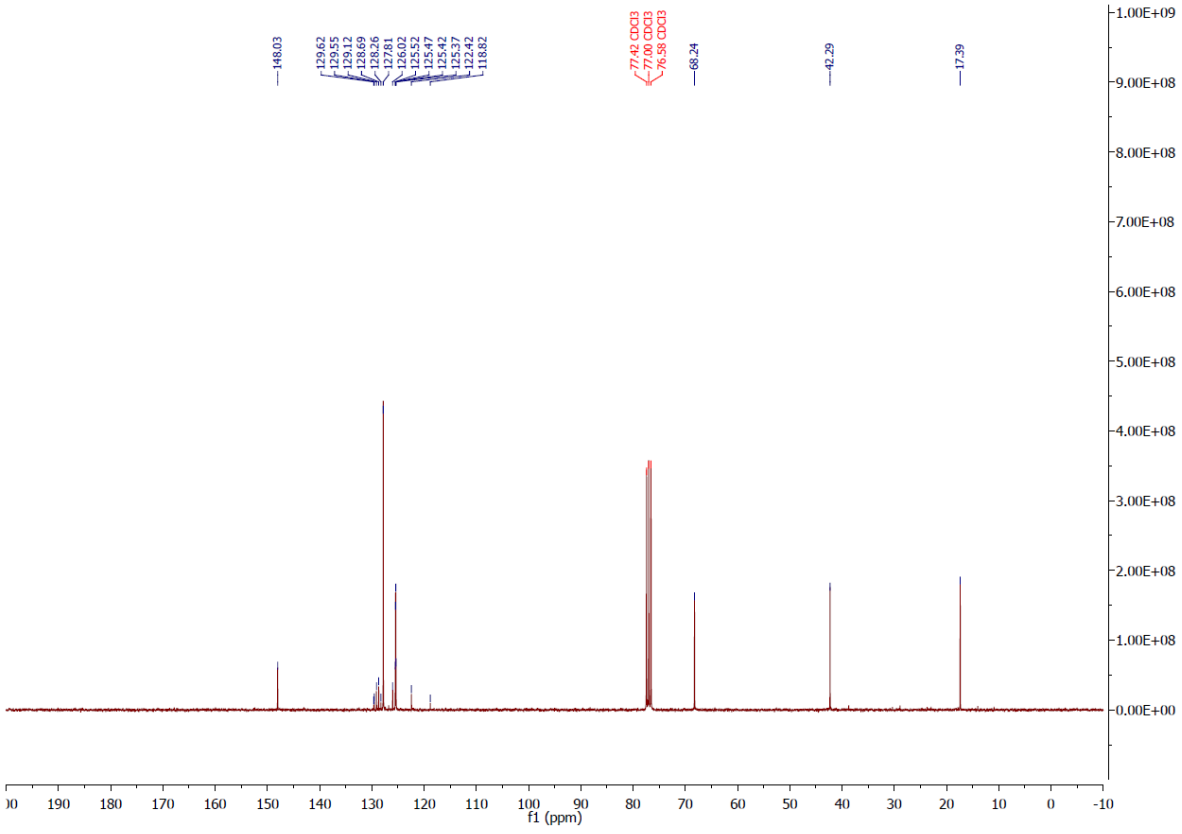
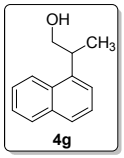
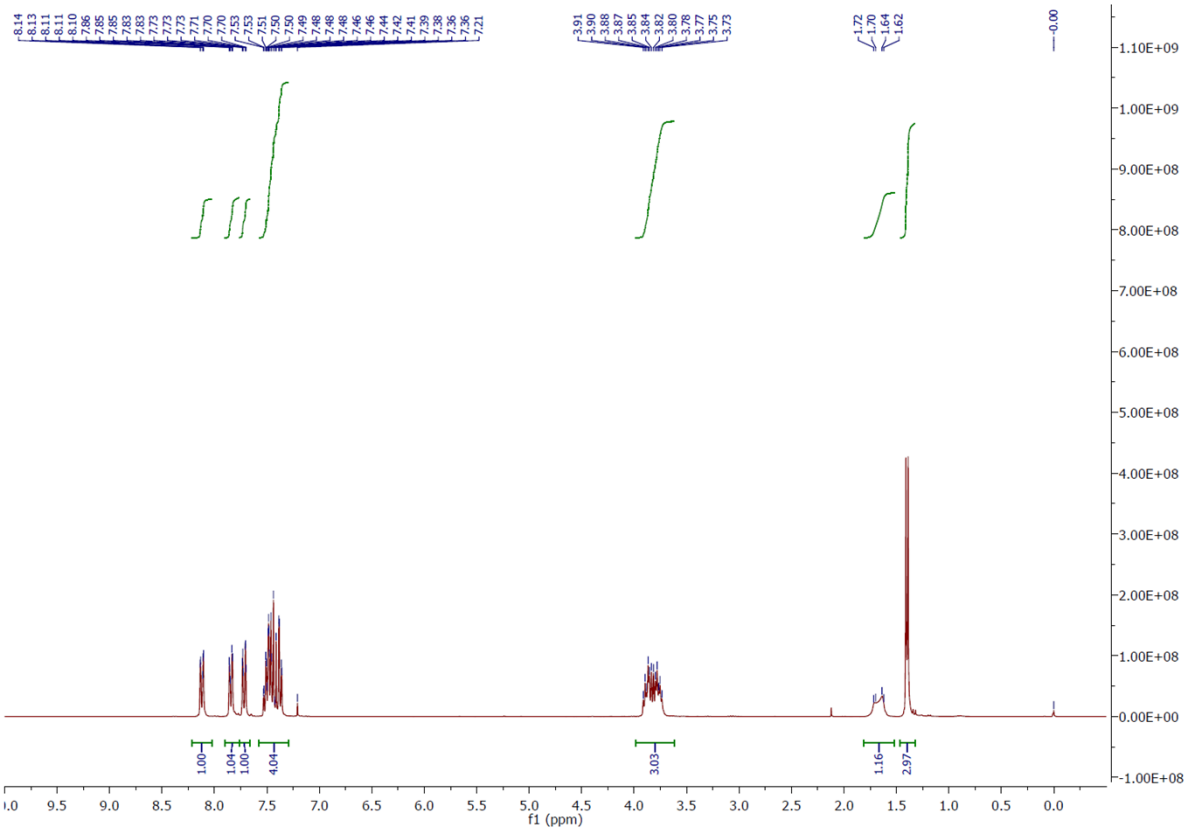
7.34
7.34
7.33
7.26
3.73
3.72
3.72
3.71
3.70
3.69
3.04
3.02
3.00
2.97
1.55
1.30
1.28
0.00
2.06
2.03
2.05
1.00
1.05
3.22
f1 (ppm)


148.03
129.62
129.55
129.12
128.69
128.26
127.81
126.02
125.52
125.47
125.42
125.37
122.42
118.82
77.42 CDCl3
77.00 CDCl3
76.58 CDCl3
68.24
42.29
17.39
f1 (ppm)


OH
CH3

4g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8.10
7.86
7.85
7.85
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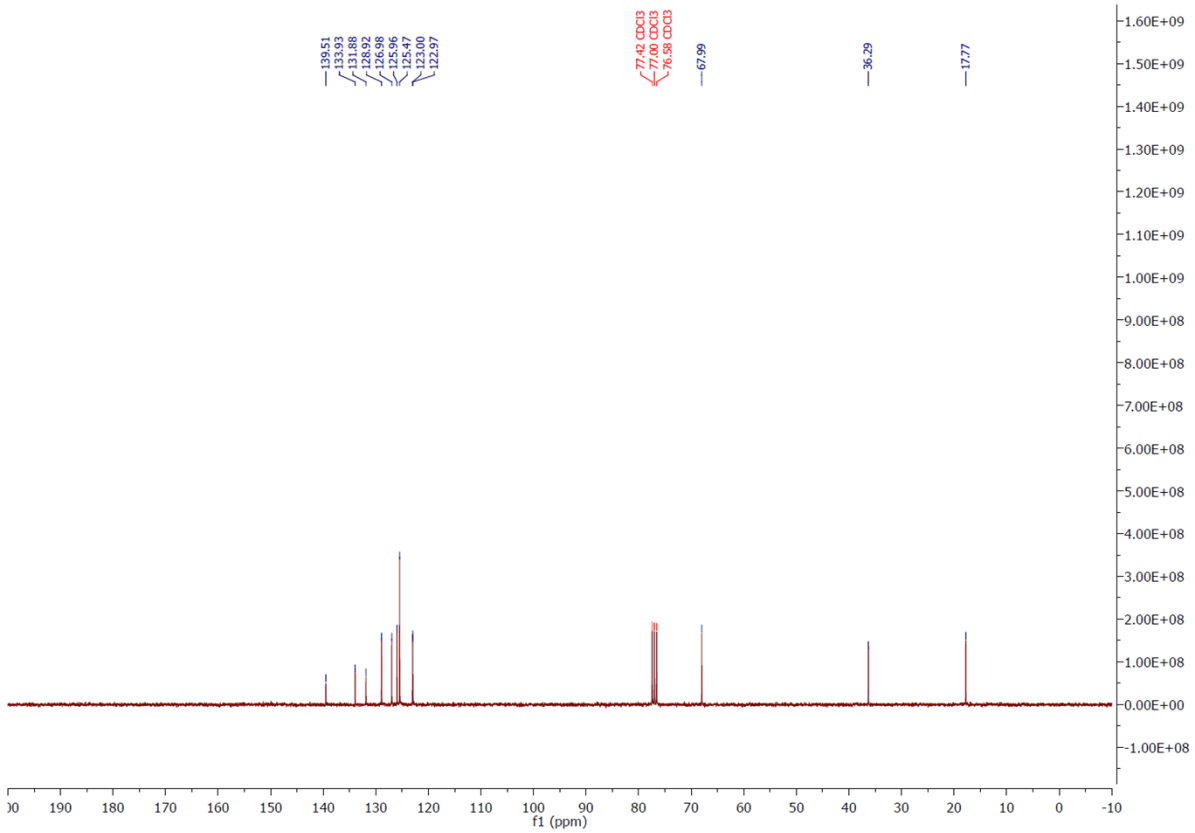
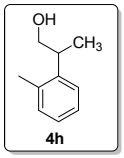
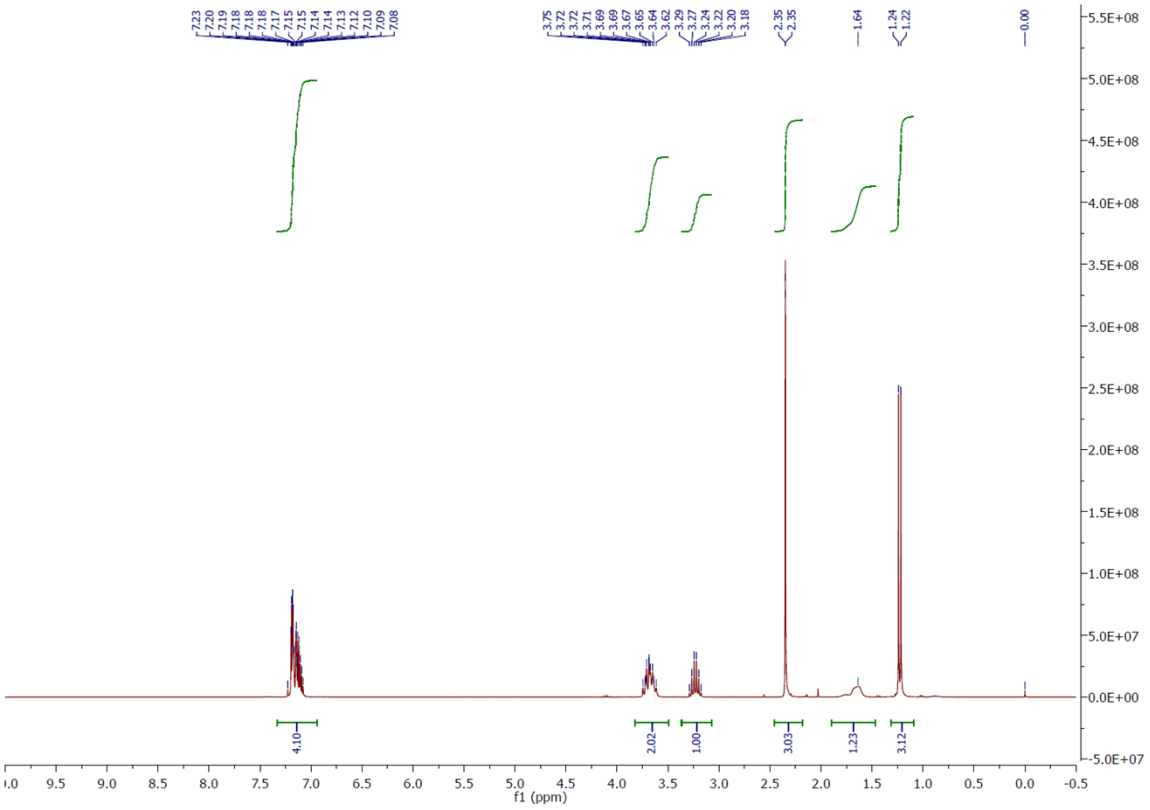
7.83
7.73
7.73
7.73
7.71
7.70
7.70
7.53
7.53
7.51
7.50
7.50
7.49
7.48
7.48
7.48
7.46
7.46
7.44
7.42
7.41
7.39
7.38
7.36
7.36
7.21
3.91
3.90
3.88
3.87
3.85
3.84
3.82
3.80
3.78
3.77
3.75
3.73
1.72
1.70
1.64
1.62
0.00
1.00
1.04
1.00
4.04
3.03
1.16
2.97
f1 (ppm)


139.51
133.93
131.88
128.92
126.98
125.96
125.47
123.00
122.97
77.42 CDCl3
77.00 CDCl3
76.58 CDCl3
67.99
36.29
17.77
f1 (ppm)


OH
CH3

4h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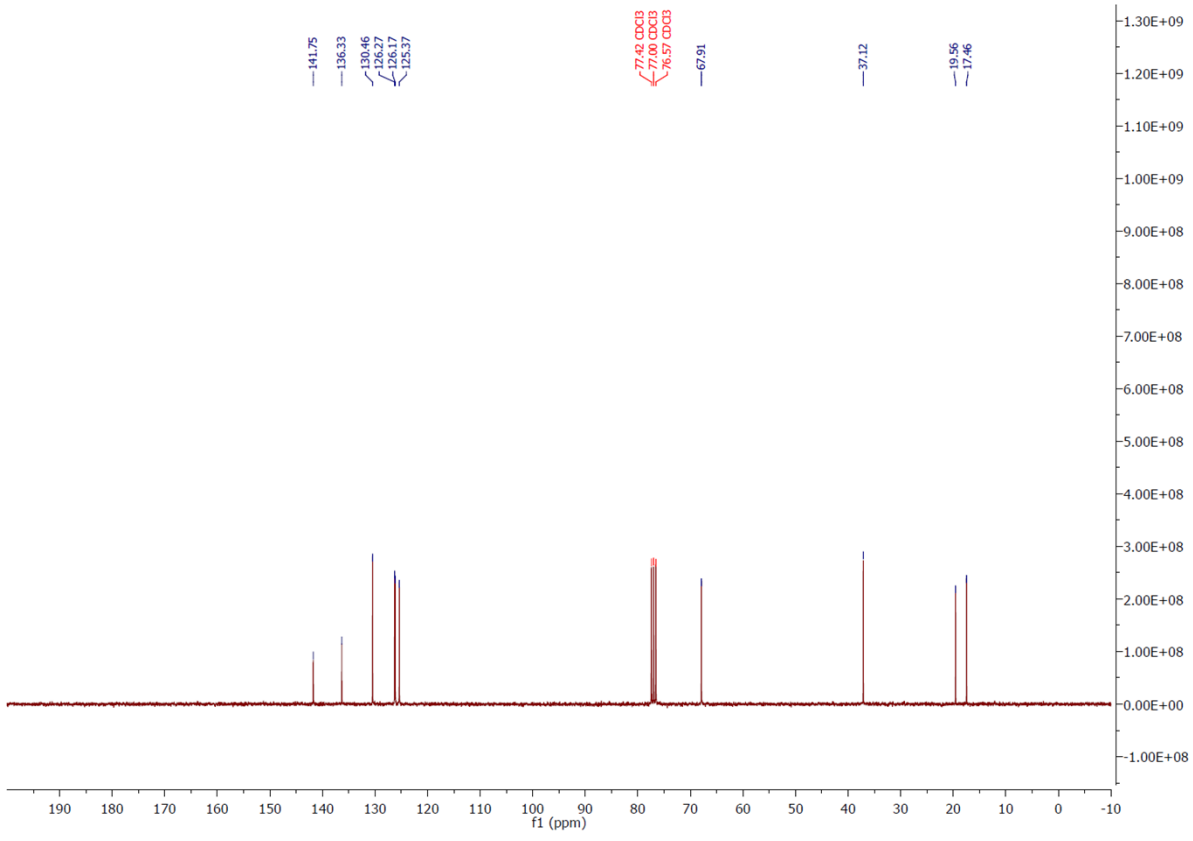
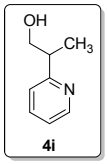
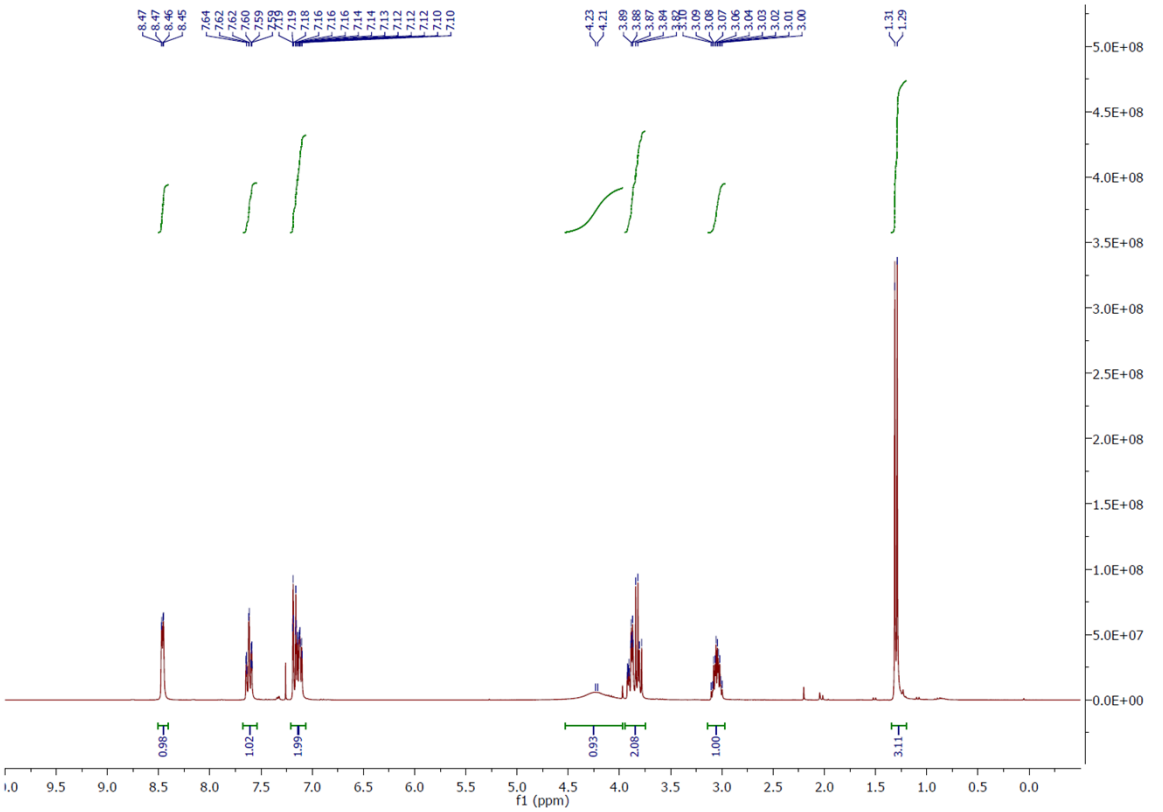
7.19
7.18
7.18
7.18
7.17
7.15
7.15
7.14
7.14
7.13
7.12
7.10
7.09
7.08
3.75
3.72
3.72
3.71
3.69
3.69
3.67
3.65
3.64
3.62
3.29
3.27
3.24
3.22
3.20
3.18
2.35
2.35
1.64
1.24
1.22
0.00
4.10
2.02
1.00
3.03
1.23
3.12
f1 (ppm)


141.75
136.33
130.46
126.27
126.17
125.37
77.42 CDCl3
77.00 CDCl3
76.57 CDCl3
67.91
37.12
19.56
17.46
f1 (ppm)


OH
CH3
N

4i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8.47
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7.60
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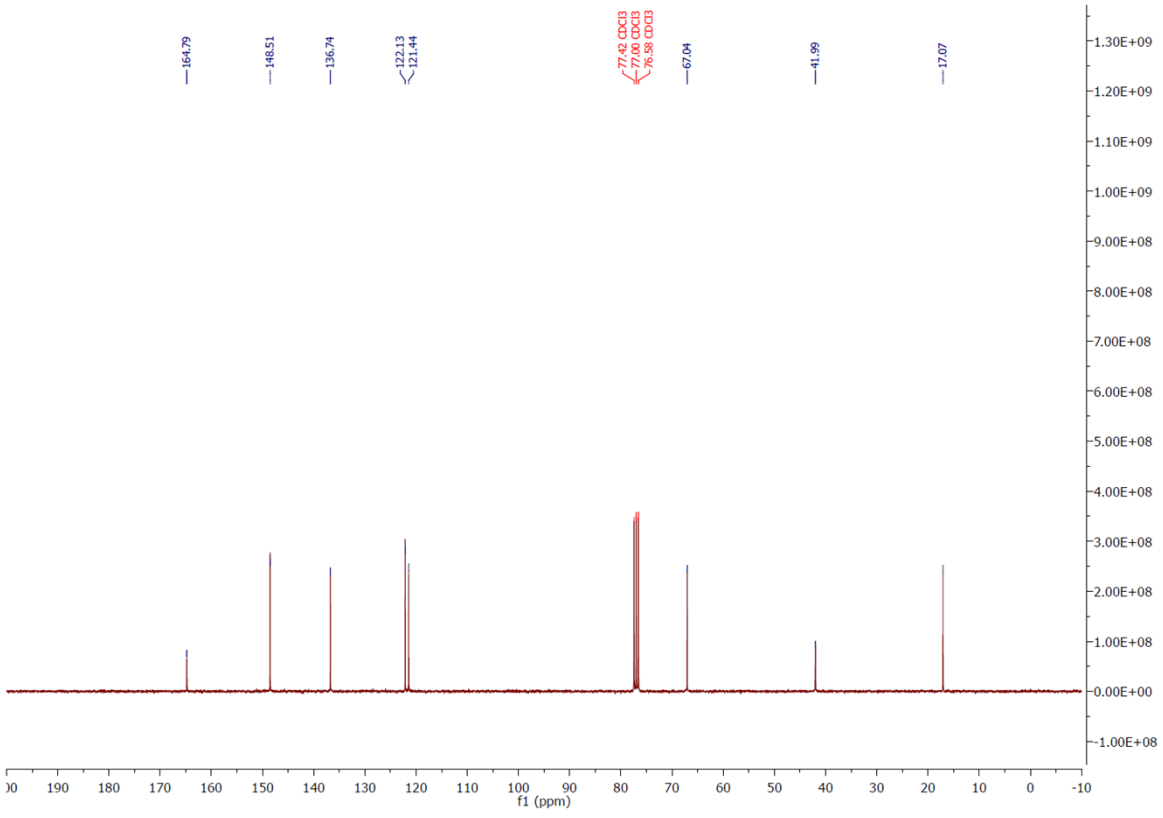
7.19
7.18
7.16
7.16
7.15
7.14
7.13
7.12
7.12
7.12
7.10
7.10
4.23
4.21
3.89
3.88
3.87
3.84
3.10
3.09
3.08
3.07
3.06
3.04
3.03
3.02
3.01
3.00
1.31
1.29
0.98
1.02
1.99
0.93
2.08
1.00
3.11
f1 (ppm)


164.79
148.51
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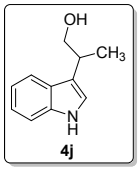
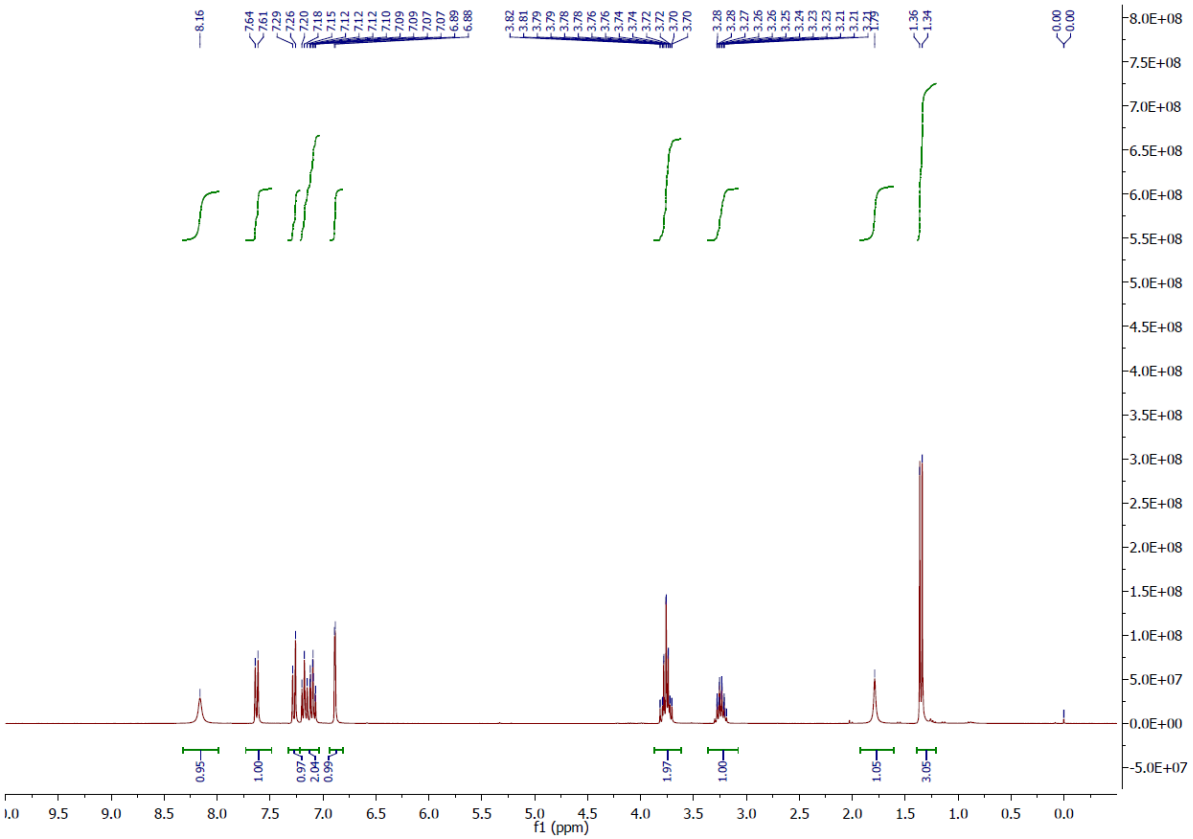
77.00 CDCl3
76.58 CDCl3
67.04
41.99
17.07
f1 (ppm)


OH
CH3
N
H

4j


8.16
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7.15
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7.12
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7.10
7.09
7.09
7.07
7.07
6.89
6.88
3.82
3.81
3.79
3.79
3.78
3.78
3.76
3.76
3.74
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3.23
3.23
3.21
3.21
1.36
1.34
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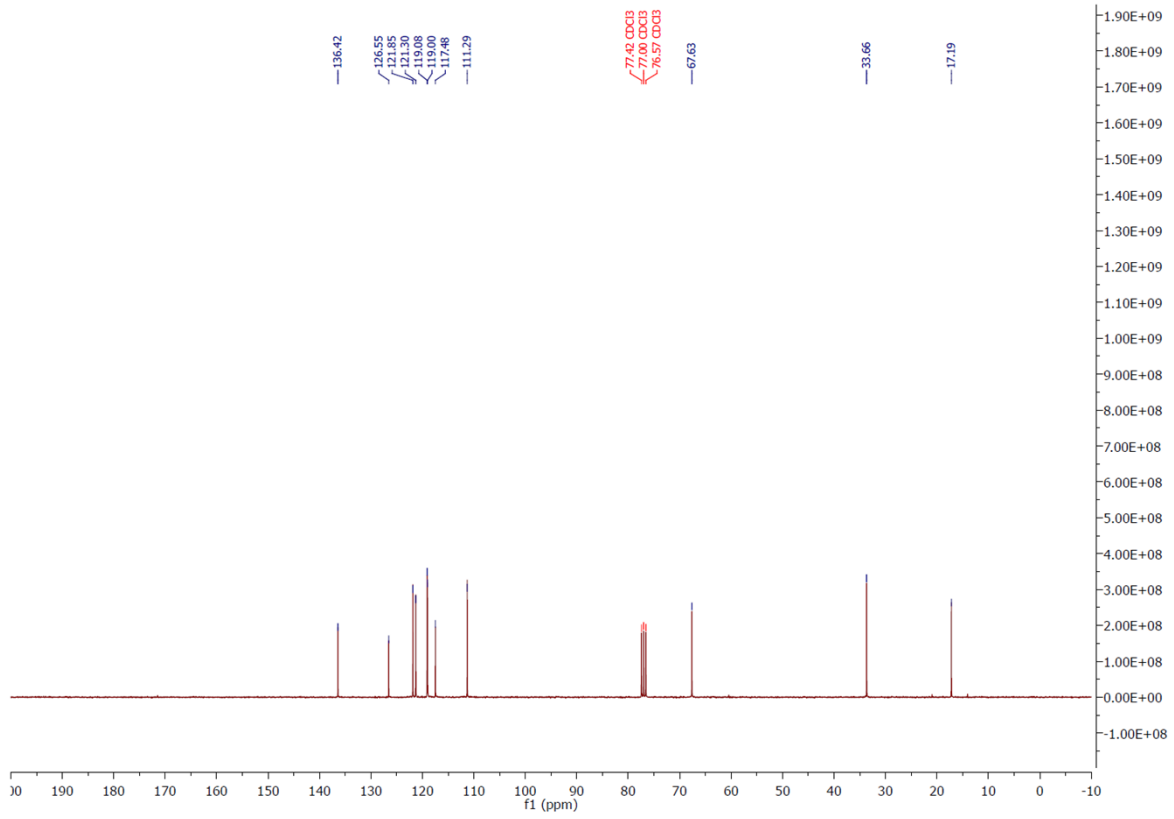
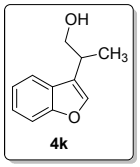
0.00
0.95
1.00
0.97
2.04
0.99
1.97
1.00
1.05
3.05
f1 (ppm)


136.42
126.55
121.95
121.30
119.08
119.00
117.48
111.29
77.42 CDCl3
77.00 CDCl3
76.57 CDCl3
67.63
33.66
17.19
f1 (ppm)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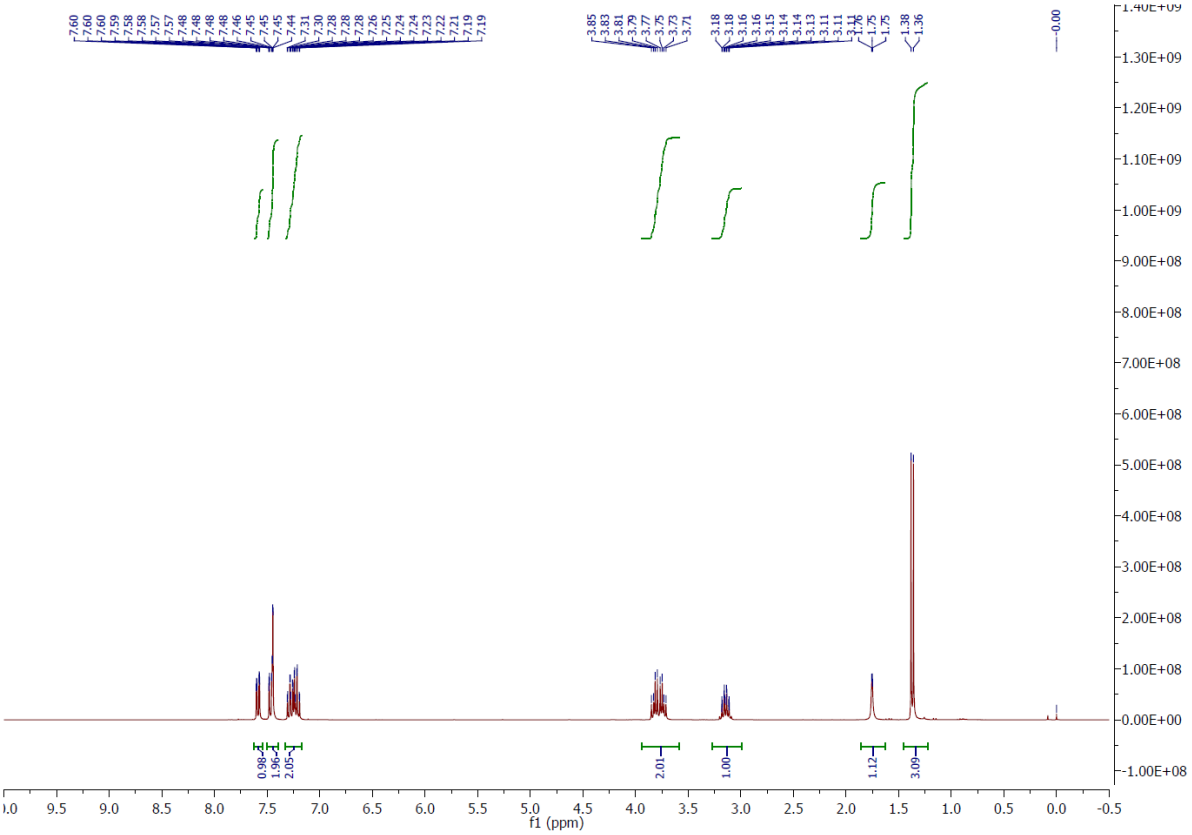
CH3
O
4k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7.48
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7.45
7.45
7.44
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7.28
7.28
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3.81
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3.77
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3.71
3.18
3.18
3.16
3.16
3.15
3.14
3.14
3.13
3.11
3.11
1.76
1.75
1.75
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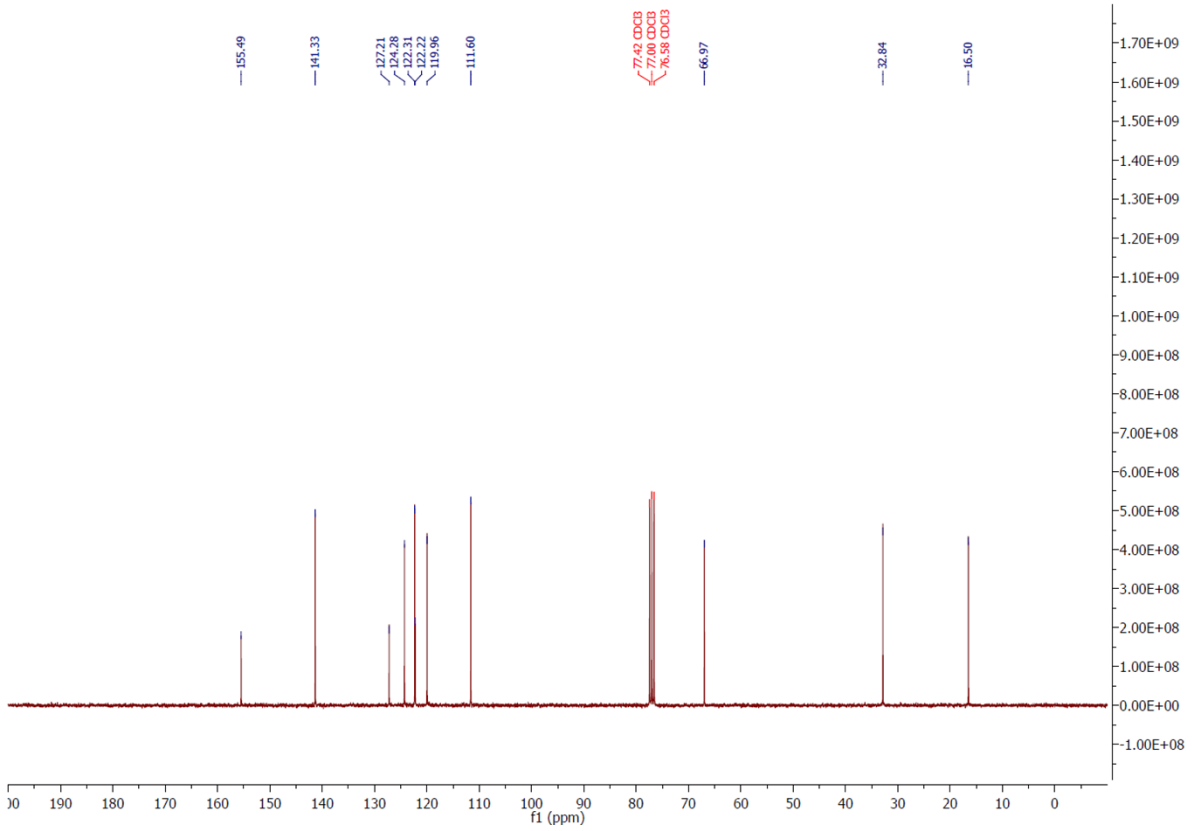
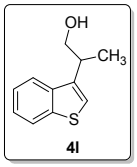
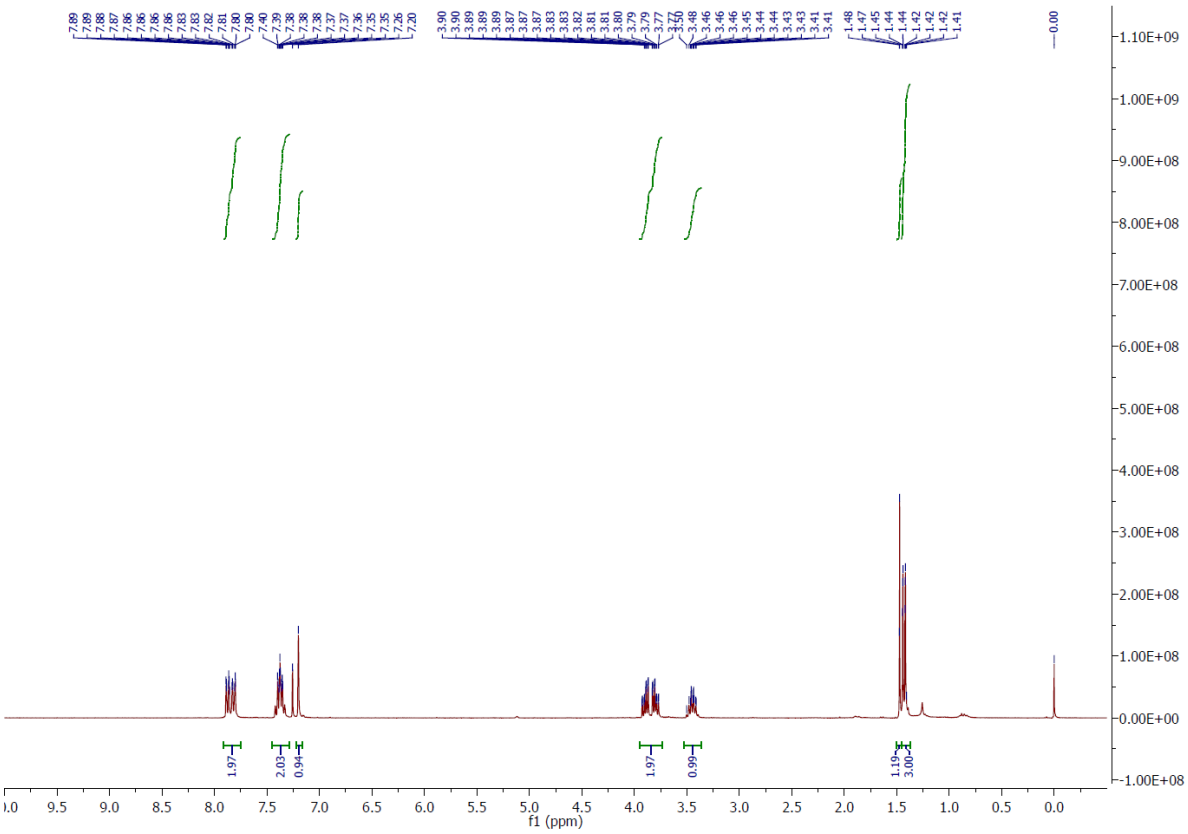
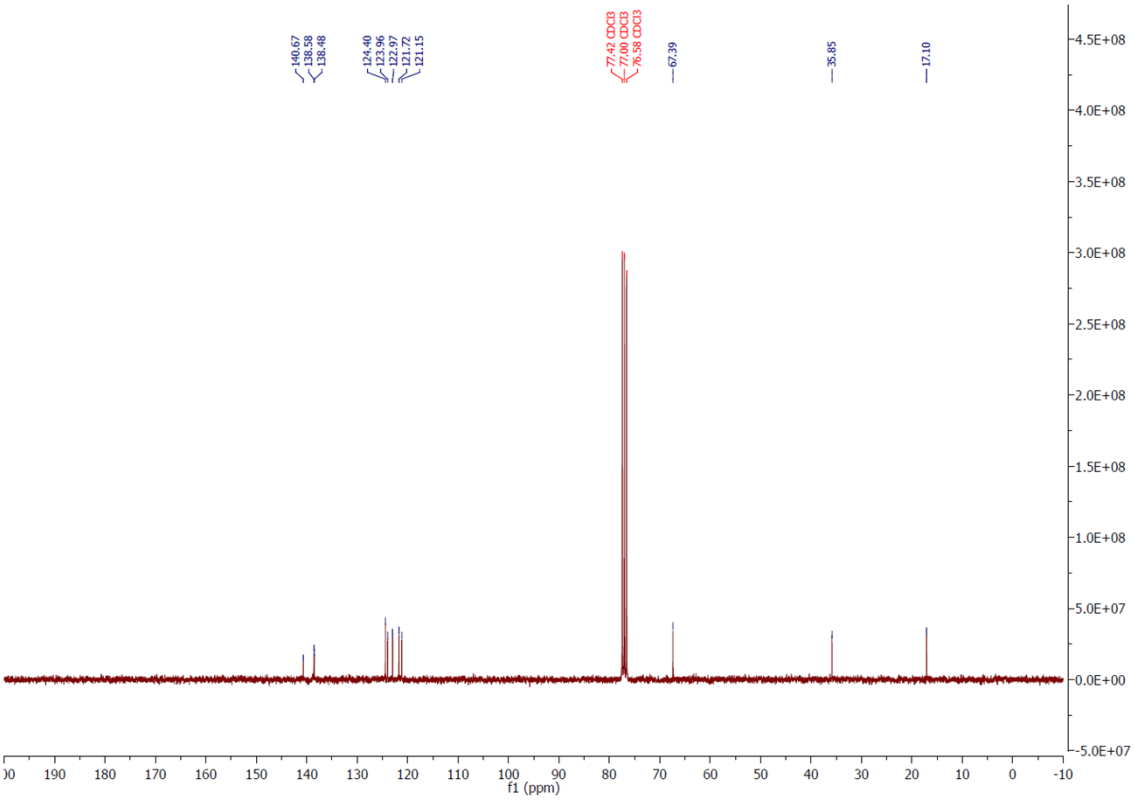
0.98
1.96
2.05
2.01
1.00
1.12
3.09
f1 (ppm)

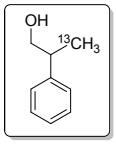

155.49
141.33
127.21
124.28
122.31
122.22
119.96
111.60
77.42 CDCl3
77.00 CDCl3
76.58 CDCl3
66.97
32.84
16.50
f1 (ppm)

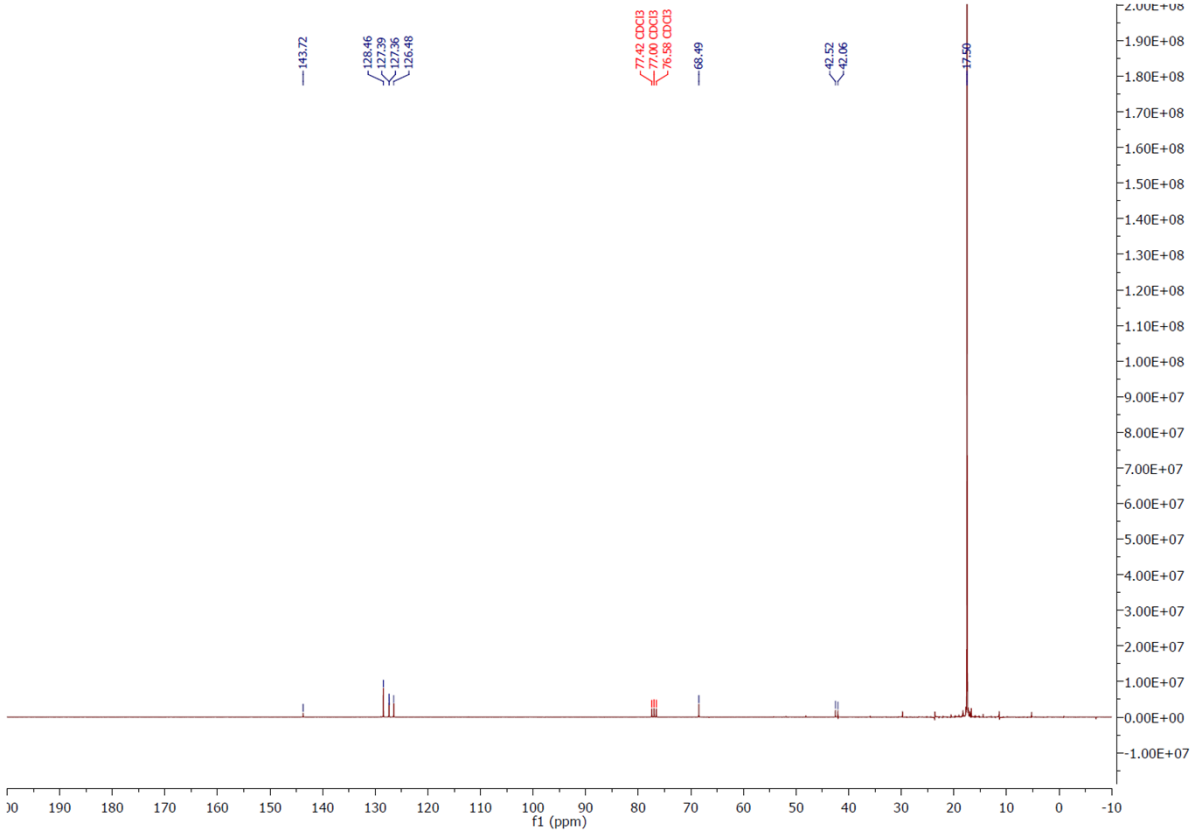


4l









Ref:

(1) B. Plouvier, G. N. Beatch, G. L. Jung, A. Zolotoy, T. Sheng, L. Clohs, T. D. Barrett, D. Fedida, W. Q. Wang, J. J. Zhu, Y. Liu, S. Abraham, L. Lynn, Y. Dong, R. A. Wall and M. J. A. Walker, *J. Med. Chem.* **2007**, *50*, 2818-2841.