Protodecarboxylation of benzoic acids under radical conditions

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Supporting Information

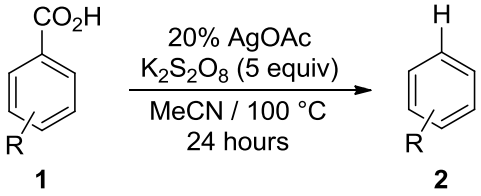
Contents

I. Experimental Procedures

General Methods:

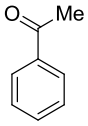
^{1}H and ^{13}C NMR spectra were recorded on a Brüker Ava400 (400 MHz) instrument and calibrated to residual solvent peaks: proton ($CDCl_3$: 7.26 ppm) and carbon ($CDCl_3$: 77.0 ppm). The ^{1}H data is presented as follows: chemical shift (in ppm on the δ scale), multiplicity (bs=broad singlet, s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet), the coupling constant (J, in Hertz) and integration. The ^{13}C data is reported as the ppm on the δ scale followed by the interpretation. TLC was performed on Merck $60F_{254}$ silica plates and visualised by UV light and potassium permanganate stains. The compounds were purified by flash chromatography using Merck Kieselgel 60 (particle size 40-63 μm) silica under a positive pressure. The eluent is quoted as a percentage. Anhydrous MeCN used for the proto-decarboxylation reaction was bought from Sigma-Aldrich and used as received. All other chemicals were purchased from a chemical supplier and used as received.

Protodecarboxylation of Benzoic Acids:



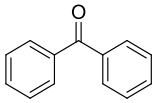
Scheme S1. Protodecarboxylation.

General procedure: A carousel tube (30 mL) was charged with compound **1** (0.3 mmol), AgOAc (10.0 mg, 0.06 mmol) and $K_2S_2O_8$ (405.5 mg, 1.5 mmol) in MeCN (3 mL), sealed and heated at 100 °C for 24 hr. The reaction mixture was allowed to cool down, diluted with Et_2O (10 mL) and poured into saturated aqueous $NaHCO_3$ (10 mL). The resulting mixture was extracted with Et_2O (2 × 10 mL) and the combined organic layers were dried over $MgSO_4$, filtered, and carefully concentrated under reduced pressure. In the case of volatile arenes (**2e**, **2f**, **2g**, **2h**, **2i**, **2k**, **2l** and **2m**) the reaction was quantified at this point using ^{1}H NMR. For less volatile arenes, the crude product was loaded onto a short column of silica and eluted with Et_2O/Pentane 0 – 10 %. The product-containing fractions were combined and concentrated under reduced pressure to yield product **2**.[1]

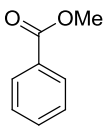


Acetophenone (**2a**). Compound **2a** was prepared following the general procedure with 4-acetylbenzoic acid (**1a**) (49.2 mg, 0.3 mmol). Colourless oil, Yield = 78%; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.97 – 7.95 (m, 2H), 7.59 – 7.55 (m, 1H), 7.49 – 7.45 (m, 2H), 2.61 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 198.2 (CO), 137.1 (quat), 133.1 (CH), 128.5 (2CH), 128.3 (2CH), 26.6 (CH_3).

3-Acetylbenzoic acid (**1b**) (49.2 mg, 0.3 mmol) was also protodecarboxylated following the same procedure to yield **2a** in 63% yield.

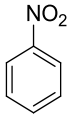


Benzophenone (**2b**). Compound **2b** was prepared following the general procedure with 4-benzoylbenzoic acid (**1c**) (54.7 mg, 0.3 mmol). White soli, Yield = 75%; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.83 – 7.79 (m, 4H), 7.62 – 7.57 (m, 2H), 7.51 – 7.47 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 196.7 (CO), 137.5 (2quat), 132.4 (2CH), 130.0 (4CH), 128.2 (4CH).



Methyl benzoate (**2c**). Compound **2c** was prepared following the general procedure with 4-(methoxycarbonyl)benzoic acid (**1d**) (54.0 mg, 0.3 mmol). Colourless oil, Yield = 82%; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.05 – 8.03 (m, 2H), 7.57 – 7.53 (m, 1H), 7.45 – 7.41 (m, 2H), 3.91 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 167.1 (CO), 132.8 (CH), 130.1 (quat), 129.5 (2CH), 128.3 (2CH), 52.0 (CH_3).

3-(Methoxycarbonyl)benzoic acid (**1e**) (54.0 mg, 0.3 mmol) was also protodecarboxylated following the same procedure to yield **2d** in 81% yield.

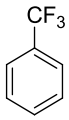


Nitrobenzene (**2d**). Compound **2d** was prepared from 3-nitrobenzoic acid (**1f**) (50.1 mg, 0.3 mmol), following the modified procedure using AgOAc (20.0 mg, 0.12 mmol) and $K_2S_2O_8$ (405.5 mg, 1.5 mmol). Yellow liquid, Yield = 54%; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.22 – 8.19 (m, 2H), 7.71 – 7.67 (m, 1H), 7.56 – 7.52 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 148.1 (quat), 134.5 (CH), 129.2 (2CH), 123.4 (2CH).

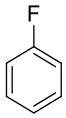
[1] CAS registry numbers for protodecarboxylated products **2**: Acetophenone **2a** [98-86-2], benzophenone **2b** [119-61-9], methyl benzoate **2c** [93-58-3], nitrobenzene **2d** [98-95-3], (trifluoromethyl)benzene **2e** [98-08-8], fluorobenzene **2f** [462-06-6], bromobenzene **2g** [108-86-1], iodobenzene **2h** [591-50-4], benzene **2i** [71-43-2], 1-bromo-2-nitrobenzene **2j** [577-19-5], 1-chloro-2-fluorobenzene **2k** [348-51-6], 1-bromo-2-fluorobenzene **2l** [1072-81-5], anisole **2m** [100-66-3], 1-methoxy-3-nitrobenzene **2n** [555-03-3], phenyl acetate [122-79-2].

4-Nitrobenzoic acid (**1g**) (50.1 mg, 0.3 mmol) and was also protodecarboxylated following the same procedure to yield **2d** in 61% yield.

2-Nitrobenzoic acid (**1n**) (50.1 mg, 0.3 mmol) was protodecarboxylated following the general procedure to yield **2d** in 84% yield.

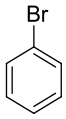


(Trifluoromethyl)benzene (**2e**). Compound **2e** was prepared following the general procedure with 3-(trifluoromethyl)benzoic acid (**1h**) (36.6 mg, 0.3 mmol). The yield of compound **2e** was determined to be 68% by ^{1}H NMR using nitromethane as the internal standard.

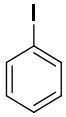


Fluorobenzene (**2f**). Compound **2f** was prepared following the general procedure with 4-fluorobenzoic acid (**1i**) (42.0 mg, 0.3 mmol). The yield of compound **2f** was determined to be 64% by ^{1}H NMR using nitromethane as the internal standard.

3-Fluorobenzoic acid (**1j**) (42.0 mg, 0.3 mmol) was also protodecarboxylated following the same procedure to yield **2f** in 57% yield, determined by ^{1}H NMR using nitromethane as the internal standard.

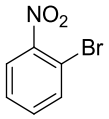


Bromobenzene (**2g**). Compound **2g** was prepared following the general procedure with 4-bromobenzoic acid (**1k**) (60.3 mg, 0.3 mmol). The yield of compound **2g** was determined to be 67% by ^{1}H NMR using nitromethane as the internal standard.



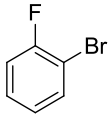
Iodobenzene (**2h**). Compound **2h** was prepared following the general procedure with 4-iodobenzoic acid (**1l**) (74.4 mg, 0.3 mmol). The yield of compound **2h** was determined to be 40% by ^{1}H NMR using nitromethane as the internal standard.

Benzene (**2i**). Compound **2i** was prepared following the general procedure with benzoic acid (**1m**) (36.6 mg, 0.3 mmol). The yield of compound **2i** was determined to be 52% by ^{1}H NMR using nitromethane as the internal standard.

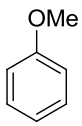


1-Bromo-2-nitrobenzene (**2j**). Compound **2j** was prepared following the general procedure with 3-bromo-4-nitrobenzoic acid (**1o**) (73.8 mg, 0.3 mmol). Yellow solid, Yield = 43%; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.87 – 7.82 (m, 1H), 7.77 – 7.72 (m, 1H), 7.49 – 7.41 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 135.1 (CH), 133.2 (CH), 128.2 (CH), 125.6 (CH), 114.4 (quat).

1-Chloro-2-fluorobenzene (**2k**). Compound **2k** was prepared following the general procedure with 3-chloro-4-fluorobenzoic acid (**1p**) (52.4 mg, 0.3 mmol). The yield of compound **2k** was determined to be 74% by ^{1}H NMR using nitromethane as the internal standard.

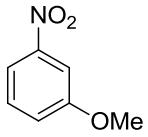


1-Bromo-2-fluorobenzene (**2l**). Compound **2l** was prepared following the general procedure with 3-bromo-4-fluorobenzoic acid (**1q**) (65.7 mg, 0.3 mmol). The yield of compound **2l** was determined to be 75% by ^{1}H NMR using nitromethane as the internal standard.

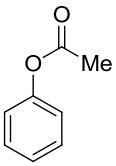


Anisole (**2m**). Compound **2m** was prepared following the general procedure with 4-methoxybenzoic acid (**1r**) (45.6 mg, 0.3 mmol). The yield of compound **2m** was determined to be 34% by ^{1}H NMR using nitromethane as the internal standard.

3-Methoxybenzoic acid (**1s**) (45.6 mg, 0.3 mmol) was also protodecarboxylated following the same procedure to yield **2m** in 45% yield, determined by ^{1}H NMR using nitromethane as the internal standard.



1-Methoxy-3-nitrobenzene (2n) Compound **2n** was prepared following the general procedure with 2-nitro-4-methoxybenzoic acid (**1t**) (59.1 mg, 0.3 mmol). Pale yellow solid, Yield = 58%; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.84 – 7.81 (ddd, J = 8.1, 2.1, 0.9 Hz, 1H), 7.73 – 7.72 (t, J = 2.3 Hz, 1H), 7.45 – 7.41 (t, J = 8.2 Hz, 1H), 7.24 – 7.21 (ddd, J = 8.3, 2.5, 0.9 Hz, 1H), 3.89 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 160.1 (quat), 149.2 (quat), 129.9 (CH), 121.3 (CH), 115.7 (CH), 108.1 (CH), 55.8 (CH_3).

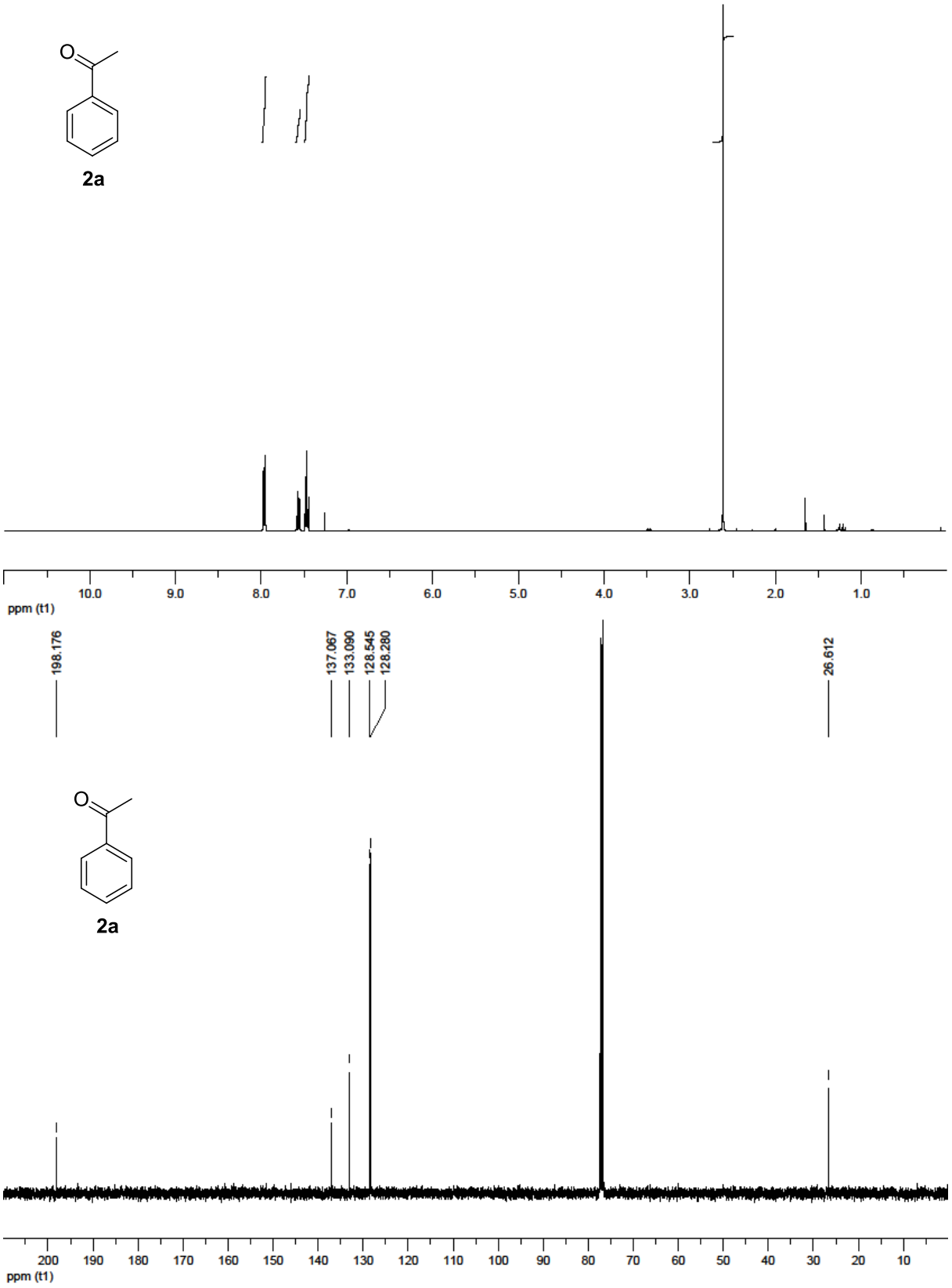


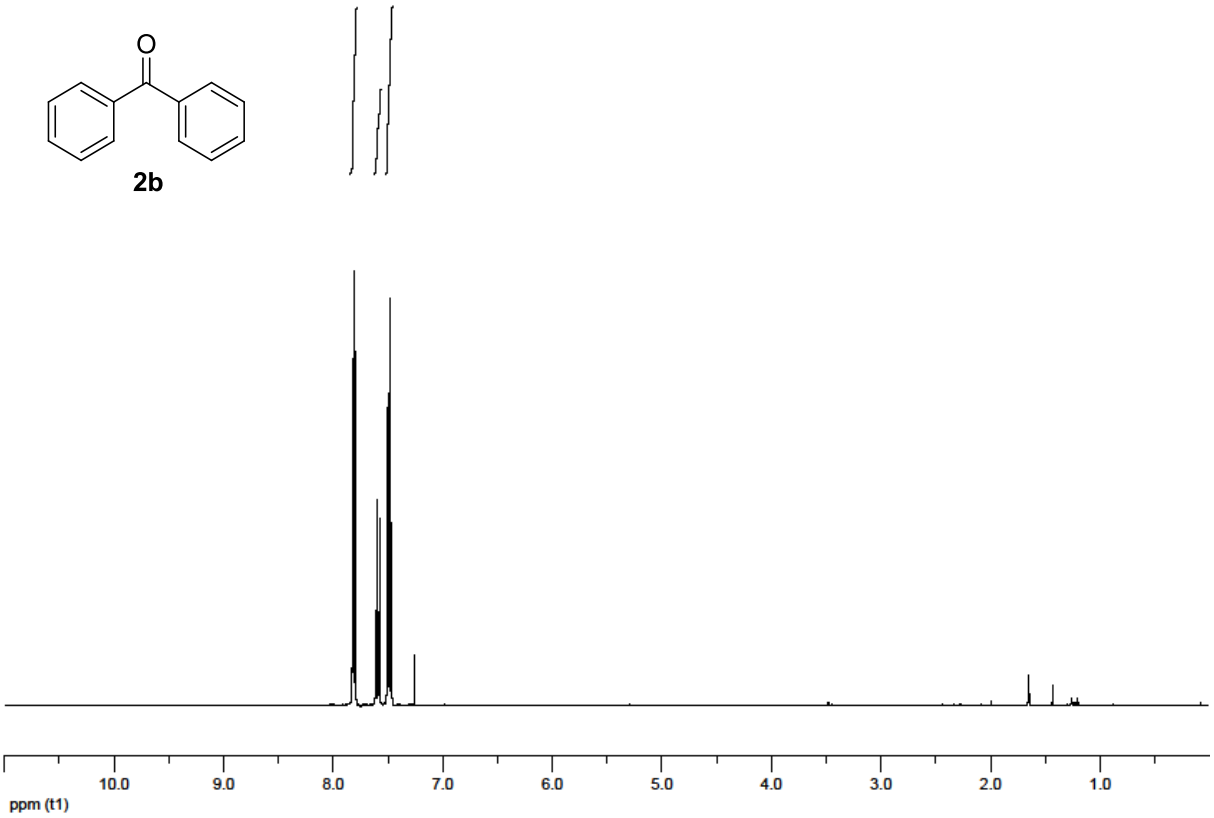
Phenyl acetate (**not in table**). Phenyl acetate was prepared following the general procedure with 2-acetoxybenzoic acid (54.0 mg, 0.3 mmol). Colourless oil, Yield = 31%; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.41 – 7.35 (m, 2H), 7.25 – 7.21 (m, 1H), 7.10 – 7.07 (m, 2H), 2.31 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 169.5 (CO), 150.6 (quat), 129.4 (2CH), 125.8 (CH), 121.6 (2CH), 21.1 (CH_3).

4-Acetoxybenzoic acid (54.0 mg, 0.3 mmol) was also protodecarboxylated following the same procedure to yield phenyl acetate in 25% yield.

2. NMR Spectra

NMR Spectra of Isolated Products




O
2b
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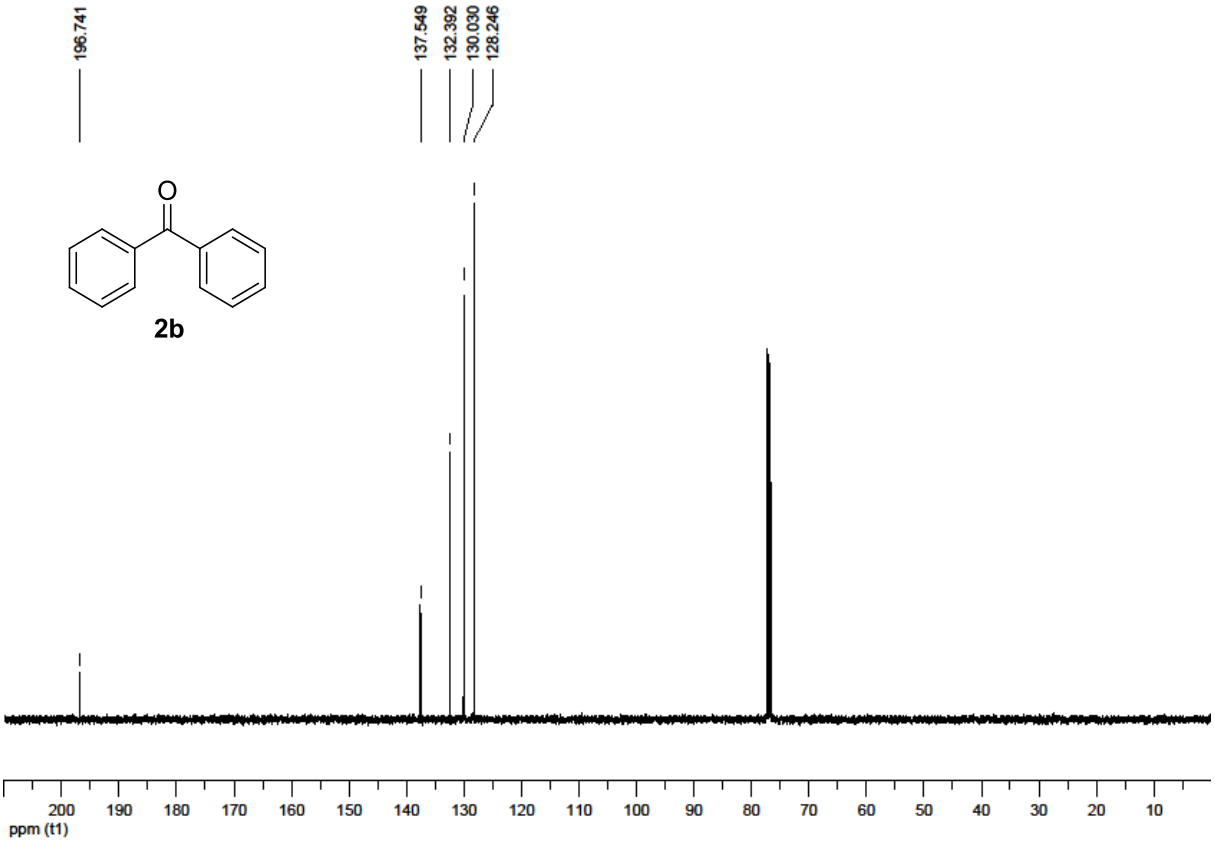
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


196.741
137.549
132.392
130.030
128.246
O
2b
200
190
180
170
160
150
140
130
120
110
100
90
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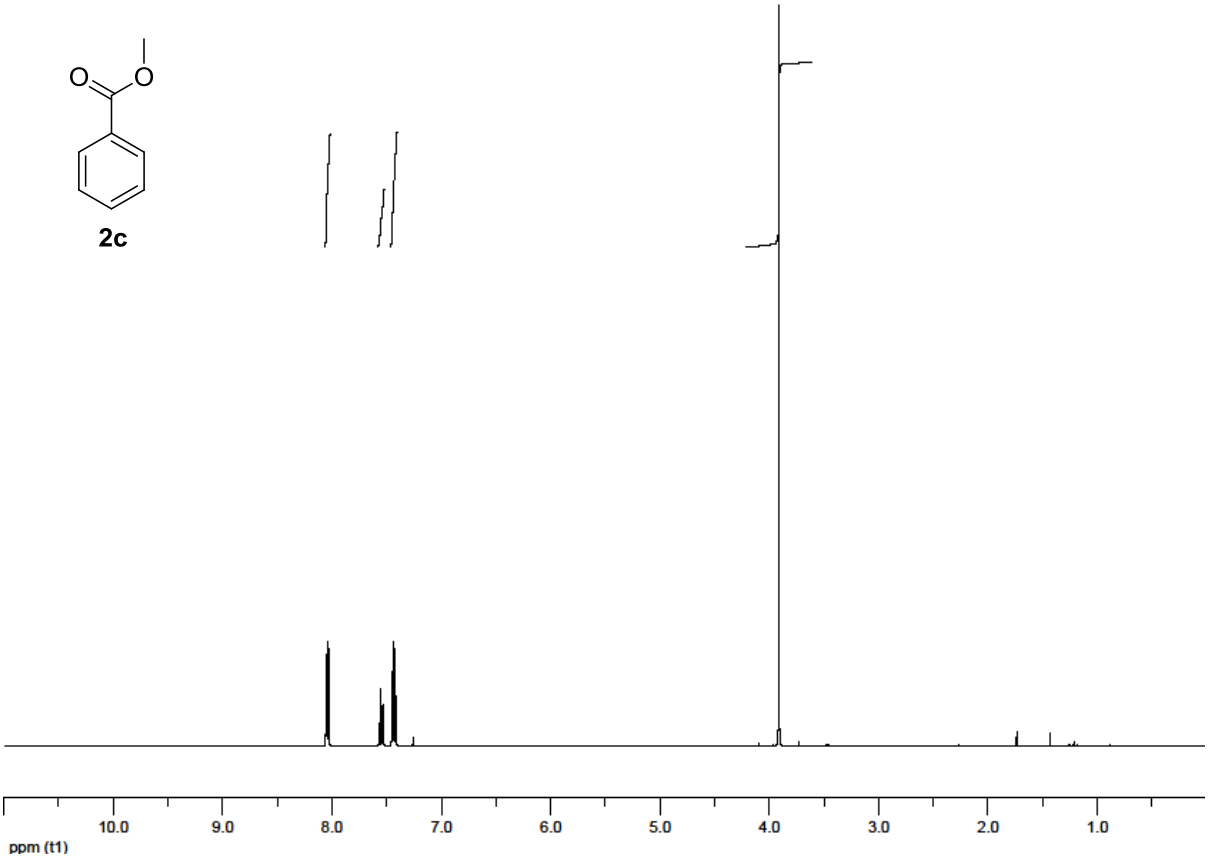
70
60
50
40
30
20
10
ppm (t1)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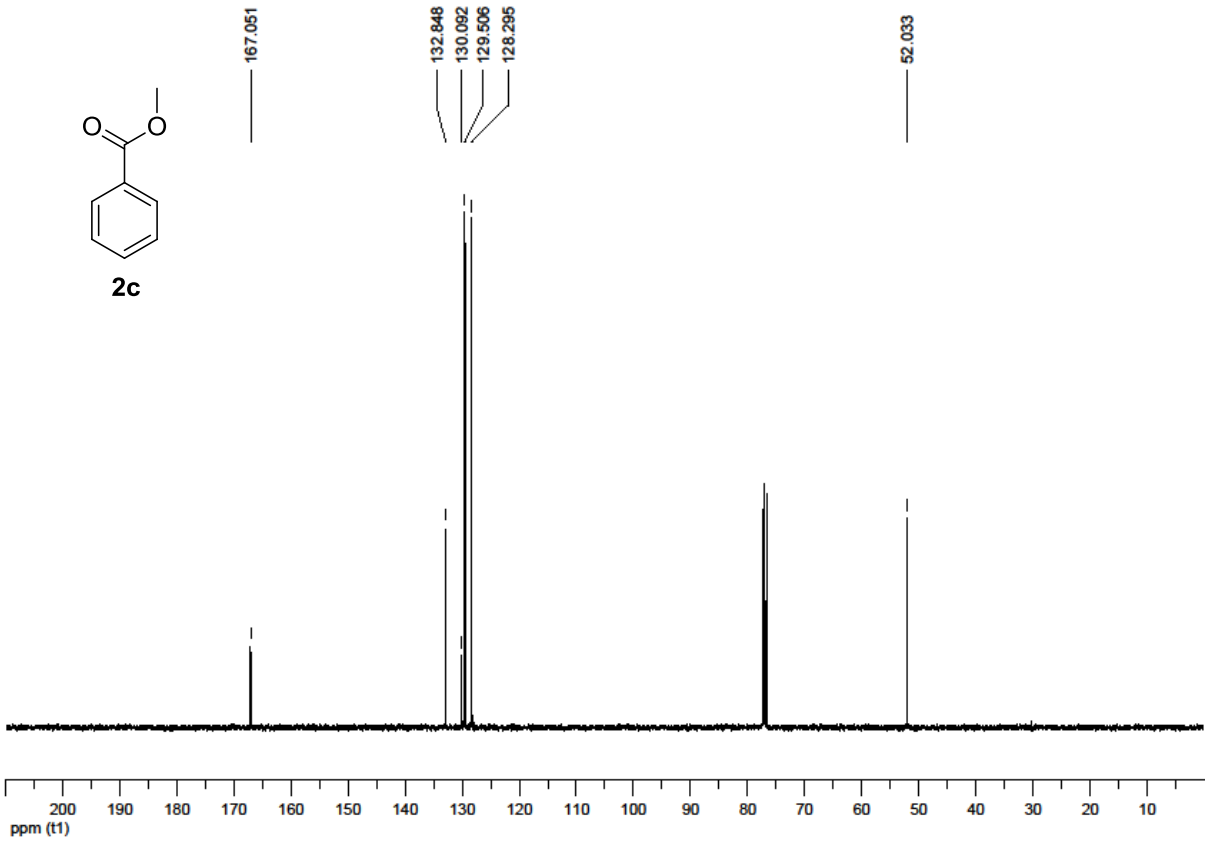
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)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132.848
130.092
129.506
128.295
52.033
2c
200
190
180
170
160
150
140
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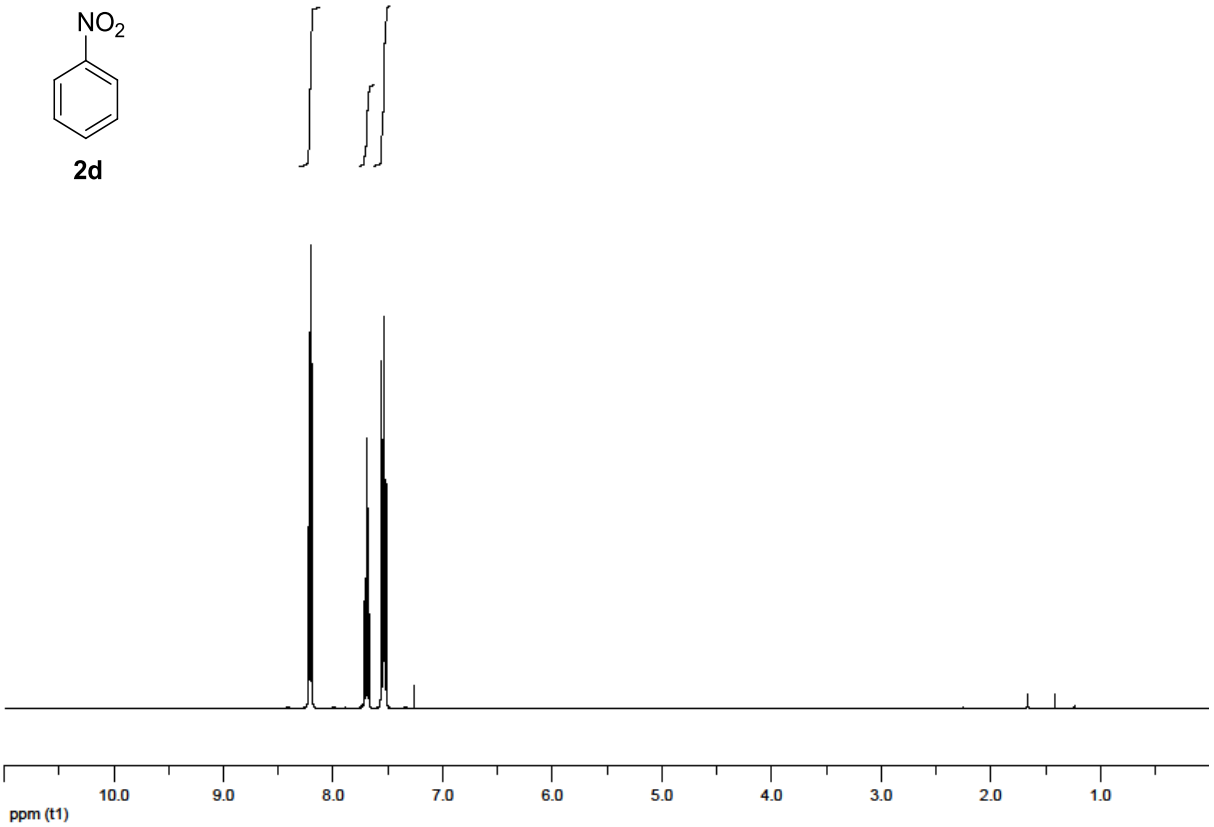
70
60
50
40
30
20
10
ppm (t1)


NO2
2d
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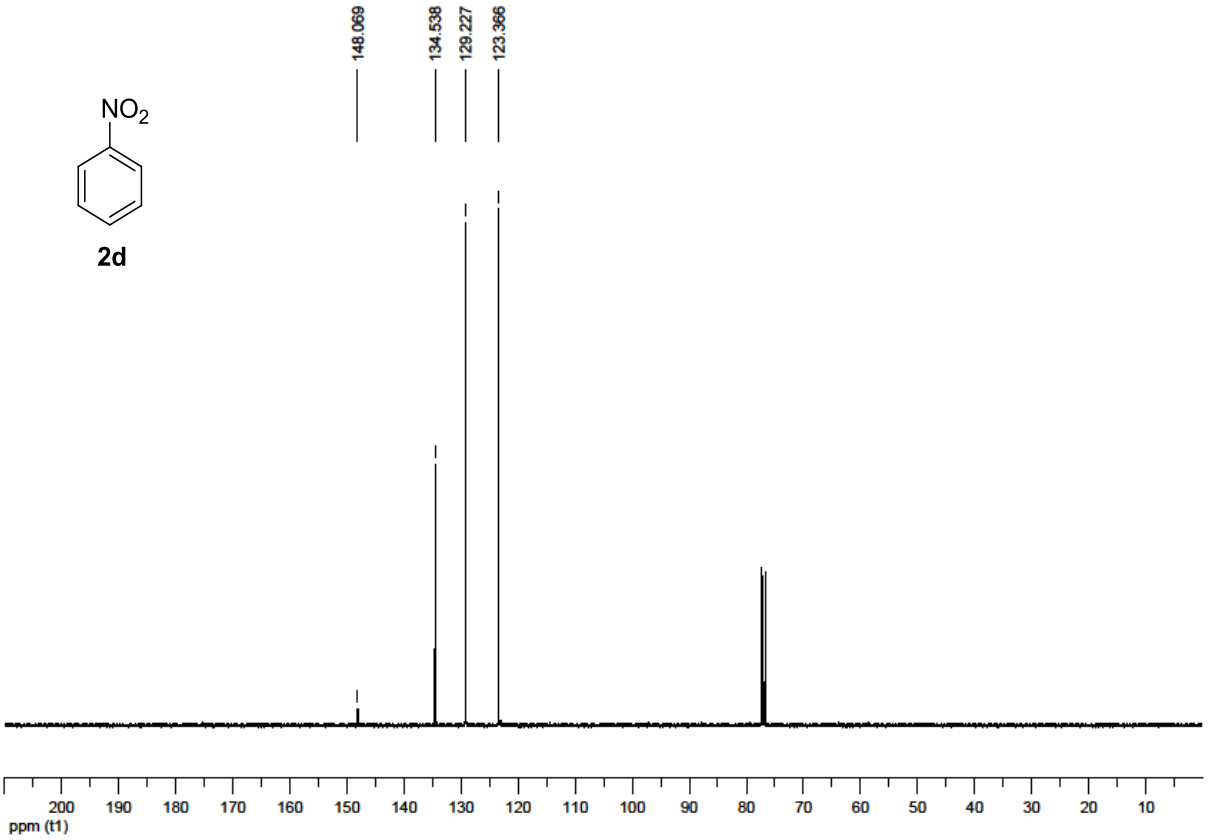
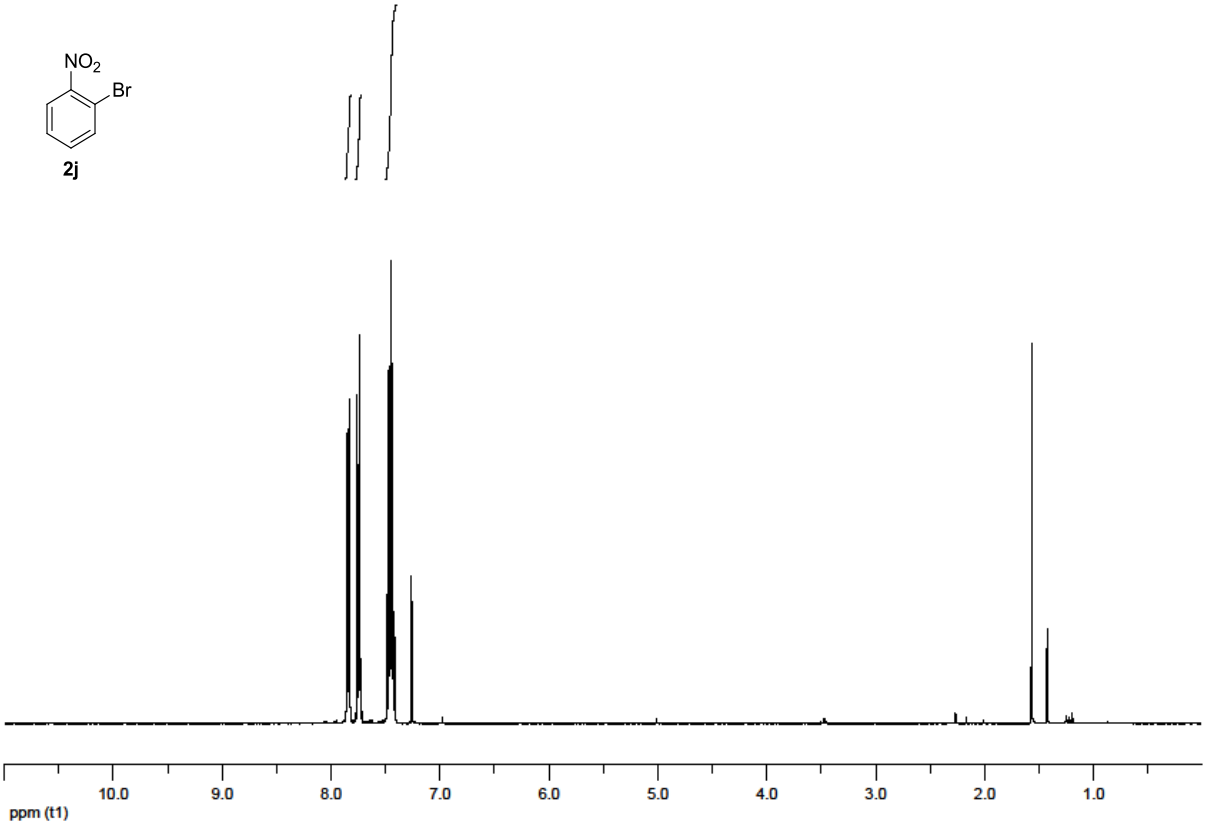
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


148.069
134.538
129.227
123.366
NO2
2d
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)


NO2
Br
2j
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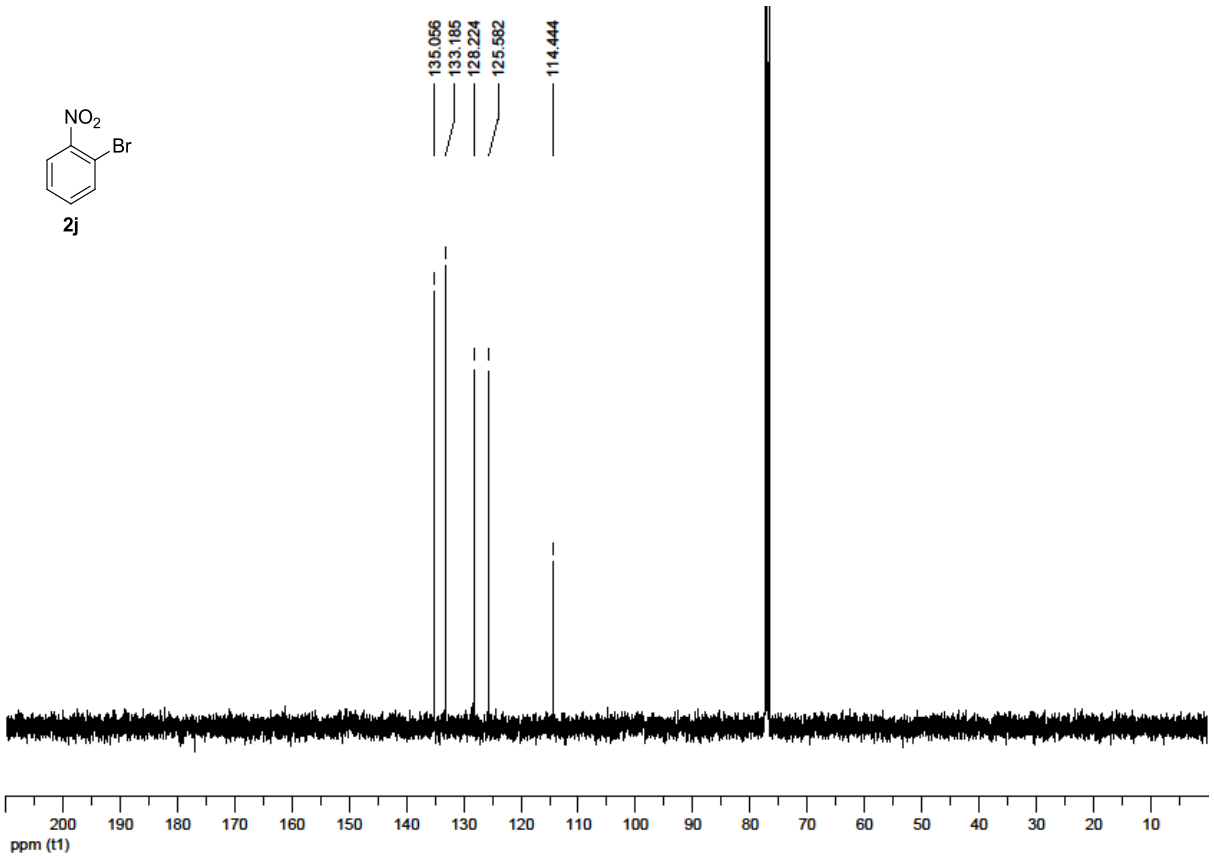
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


135.056
133.185
128.224
125.582
114.444
NO2
Br
2j
200
190
180
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160
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140
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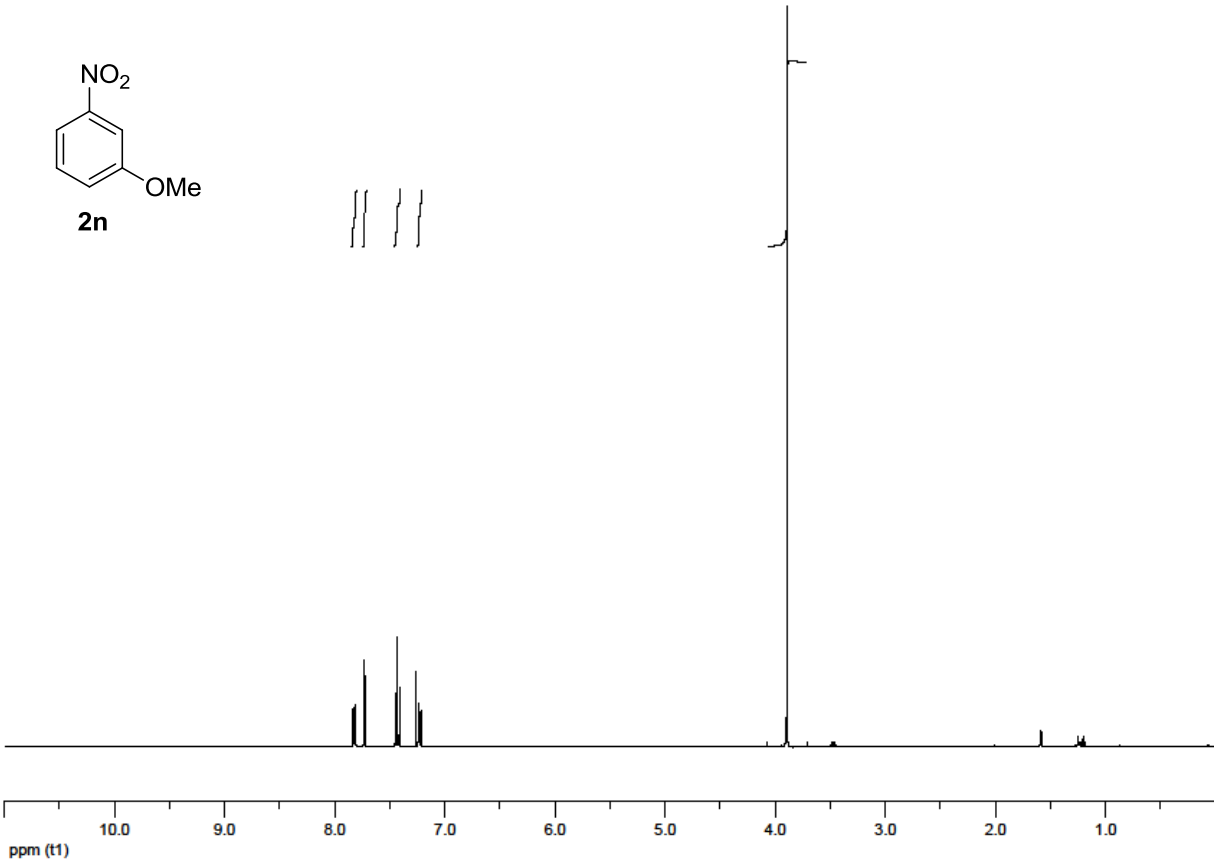
70
60
50
40
30
20
10
ppm (t1)


NO2
OMe
2n
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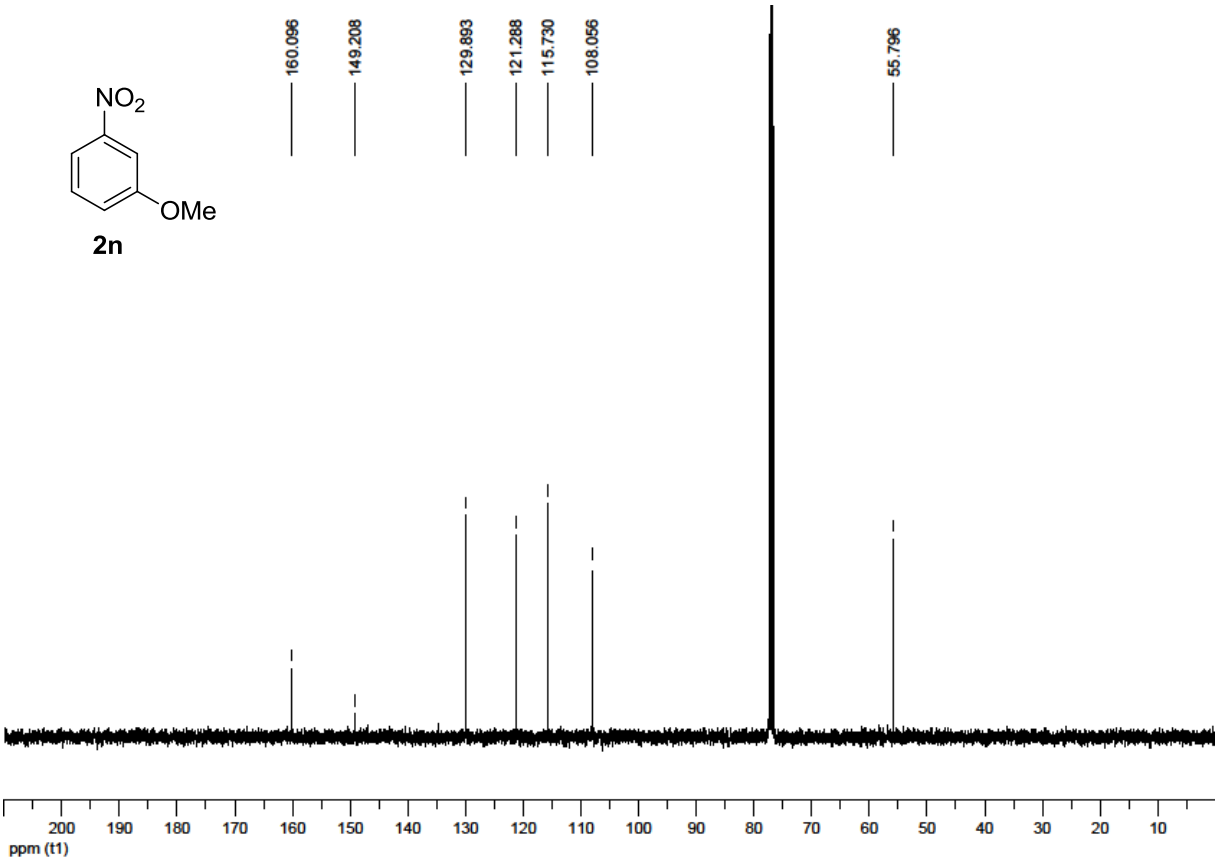
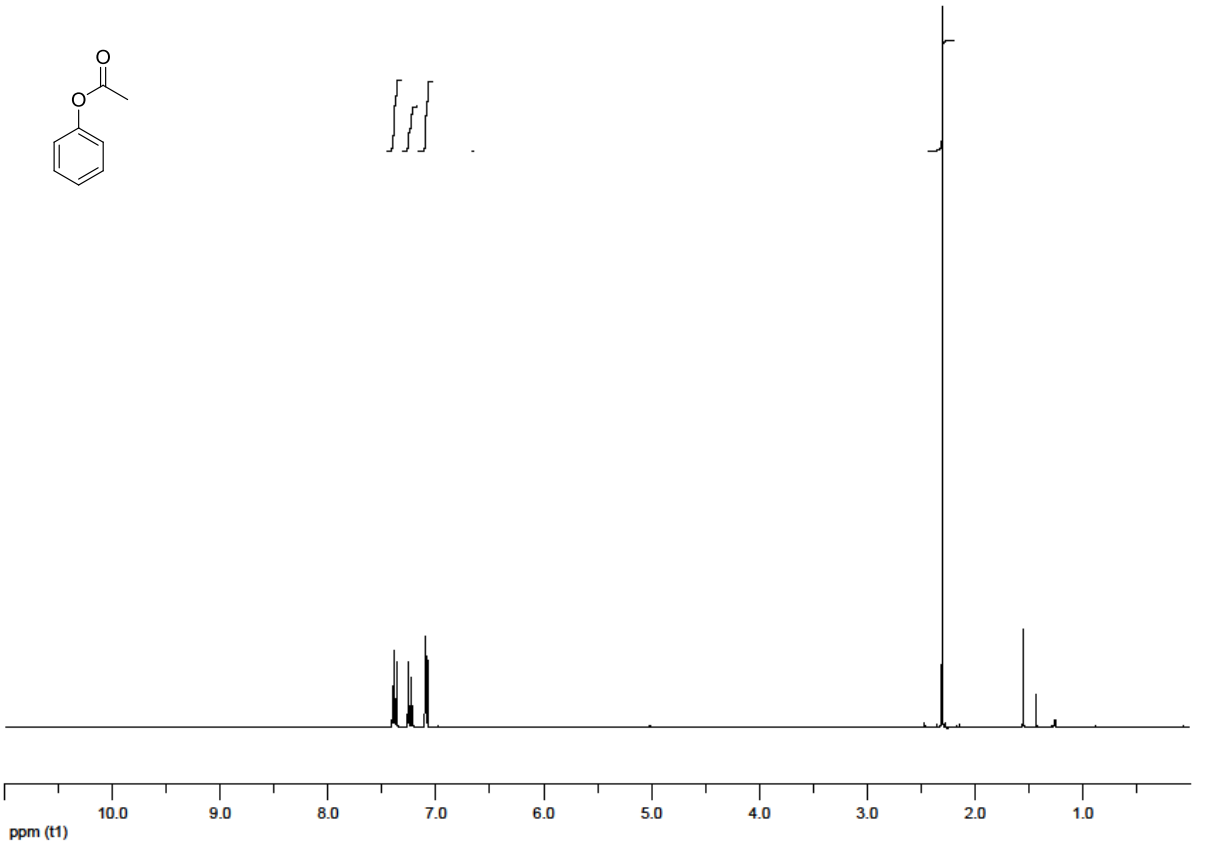
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


160.096
149.208
129.893
121.288
115.730
108.056
55.796
NO2
OMe
2n
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)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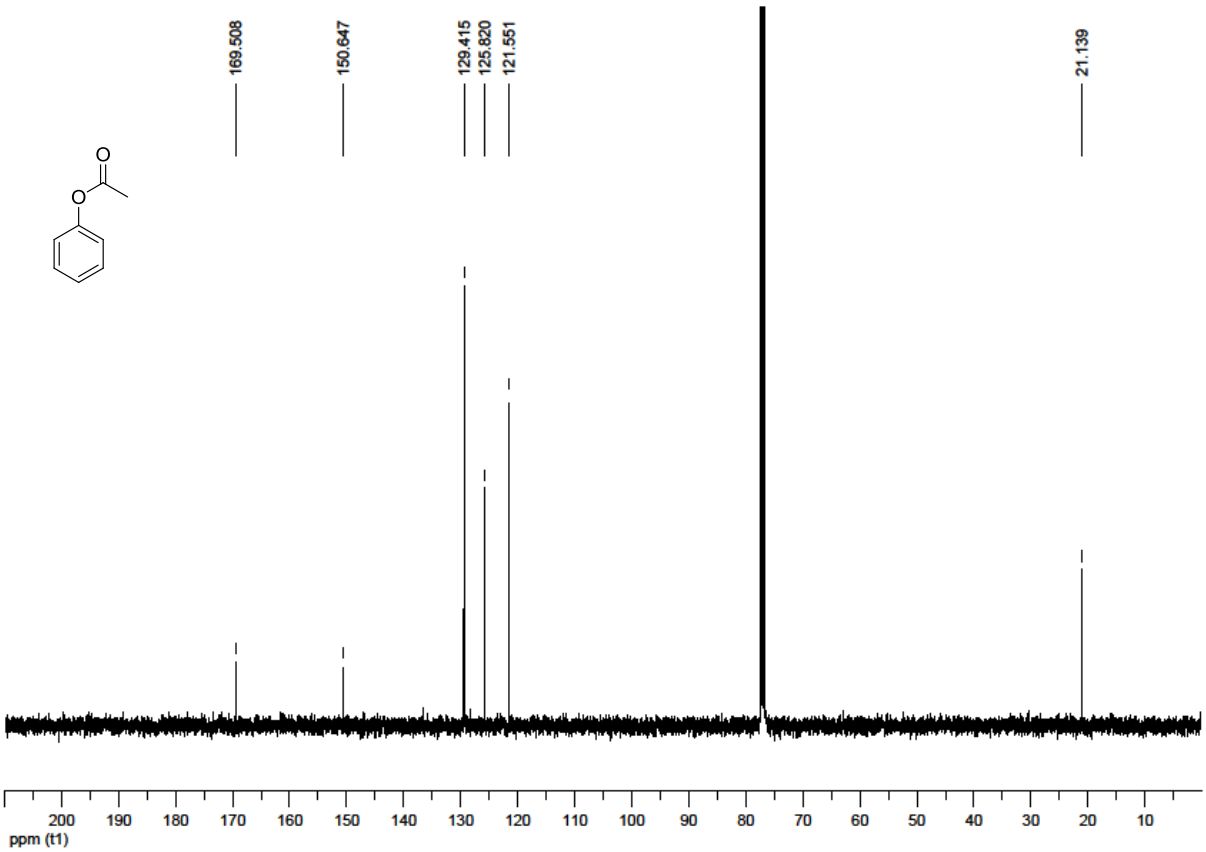
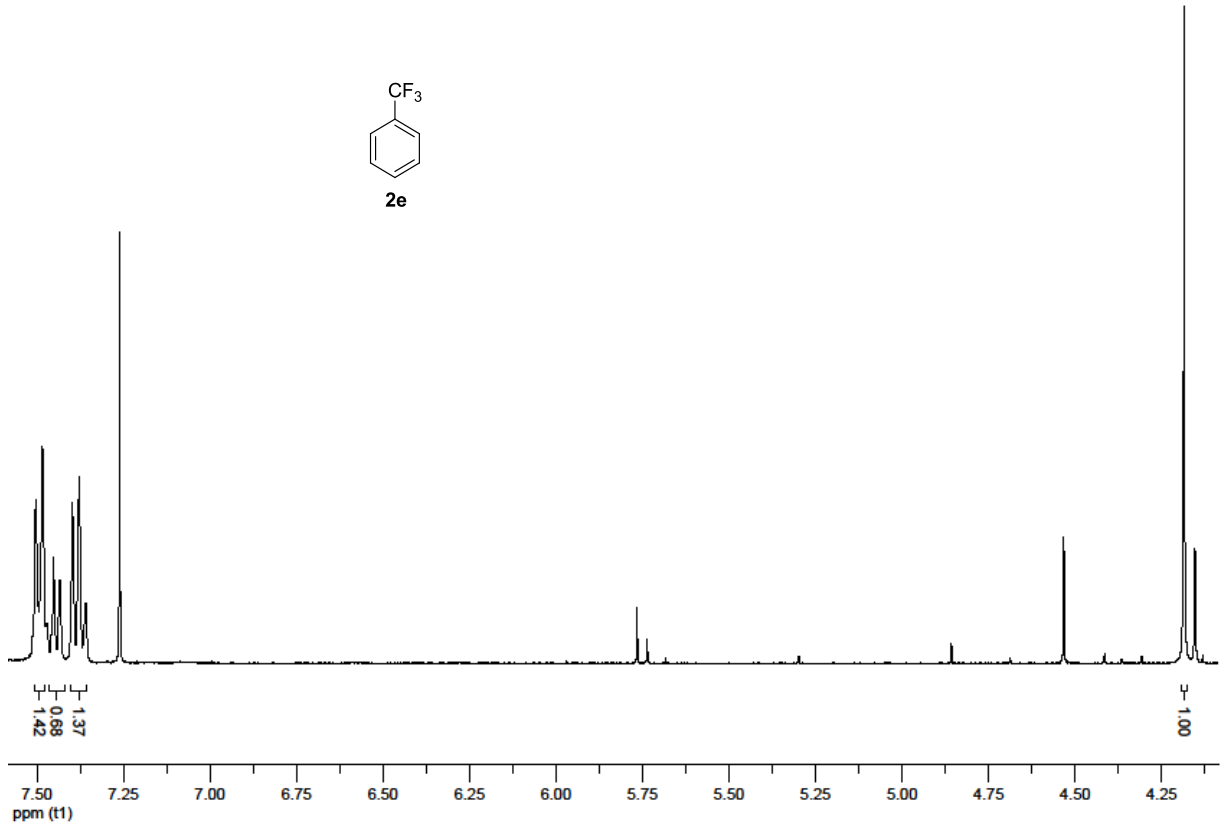
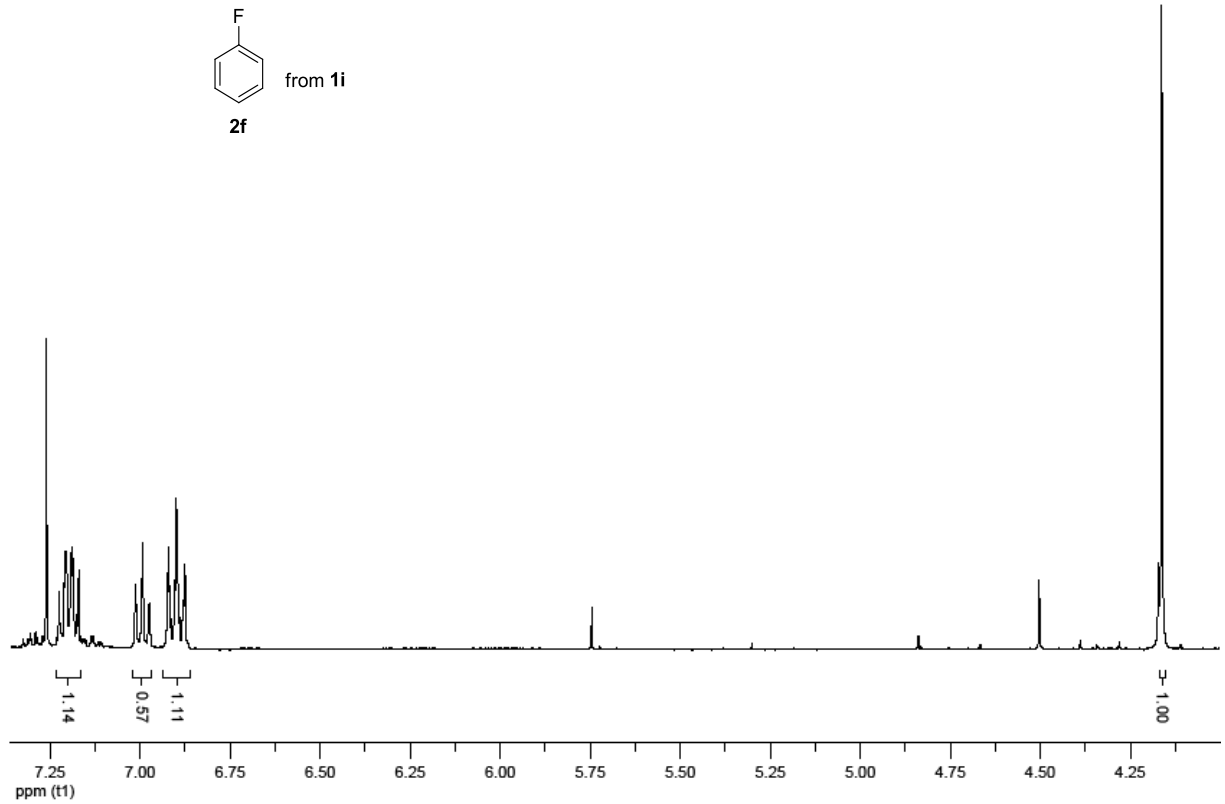
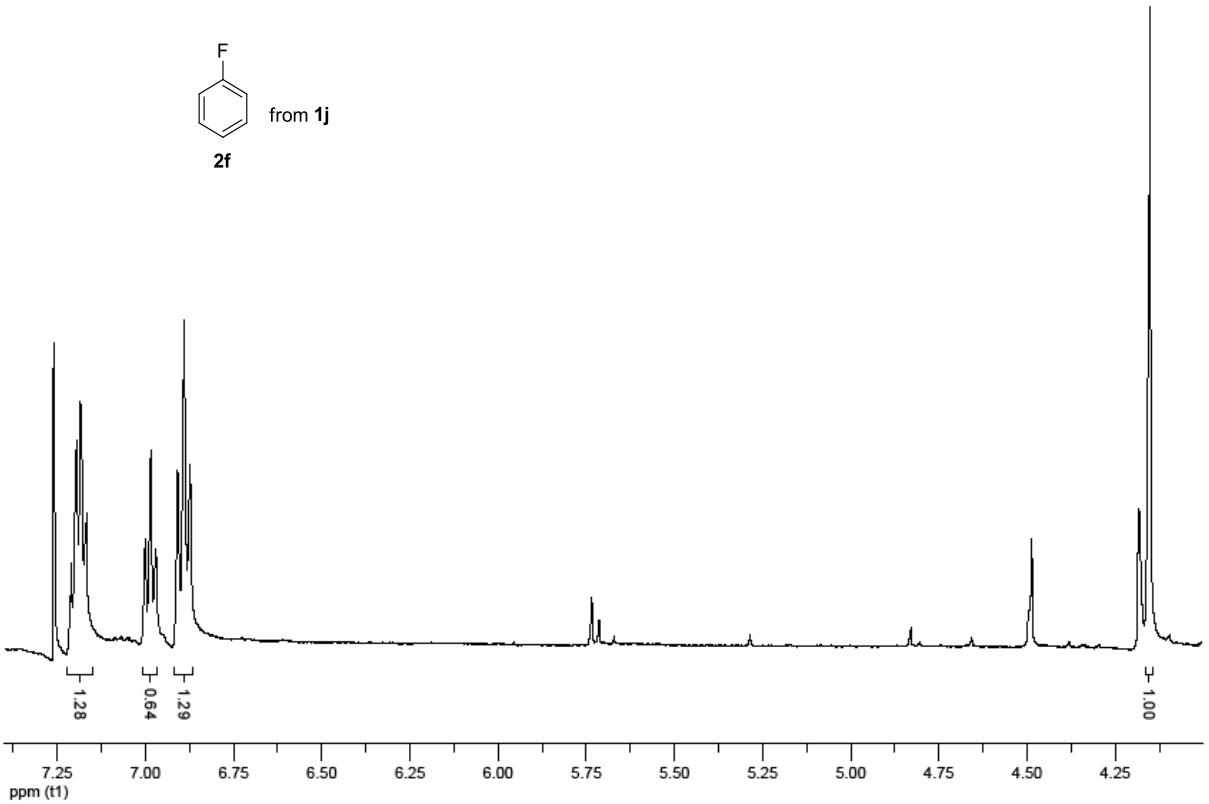
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

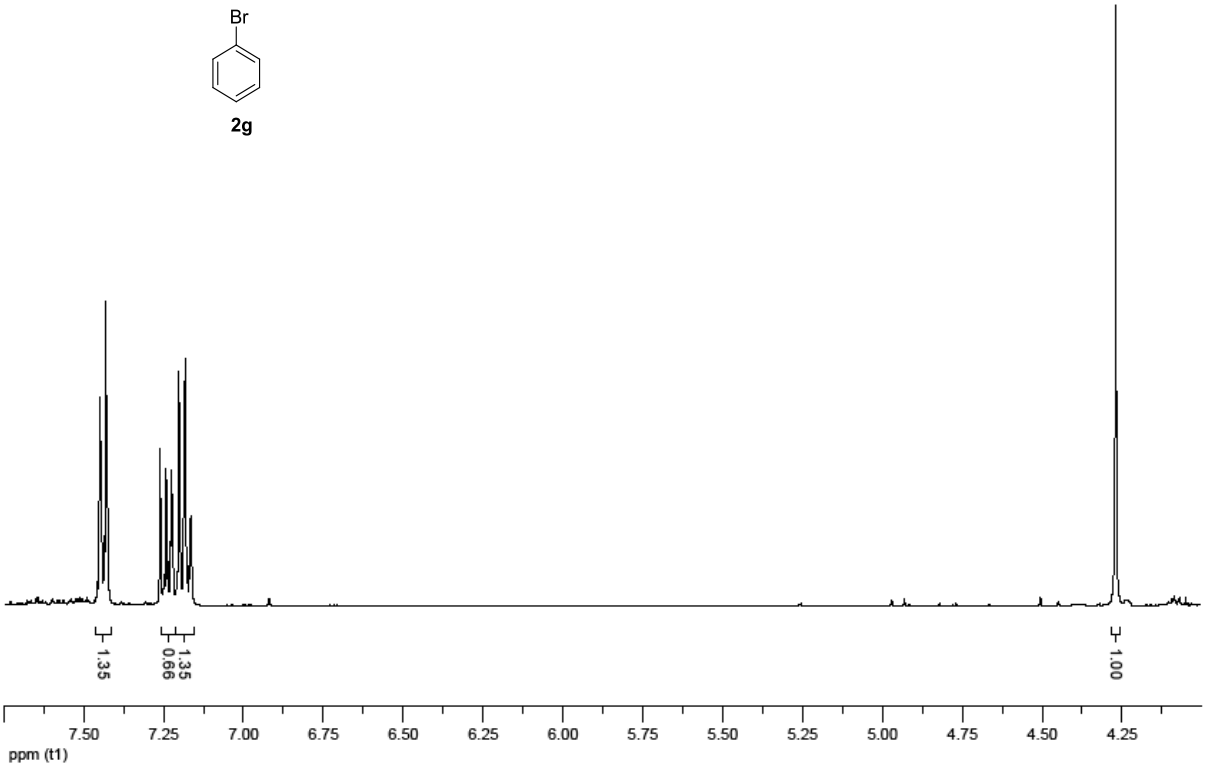

169.508
150.647
129.415
125.820
121.551
21.139
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)

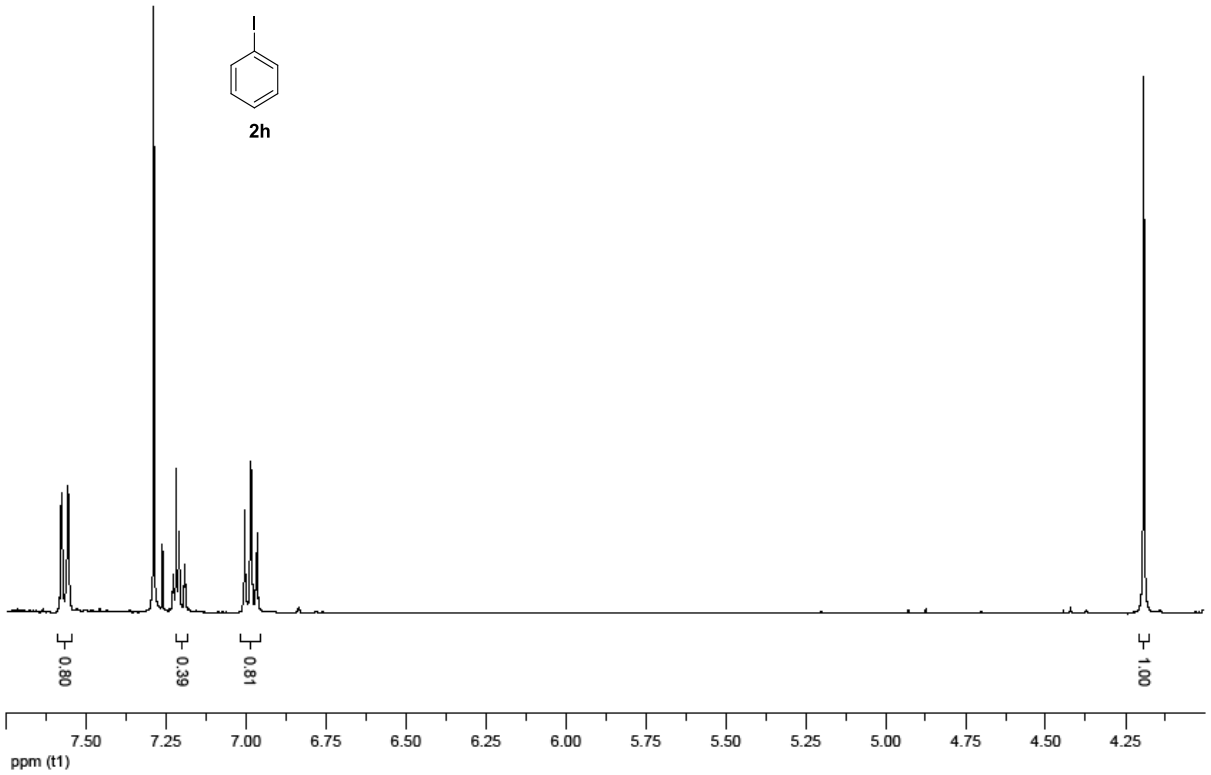
Crude ^{1}H NMR Spectra of Volatile Products (Nitromethane as the Standard)

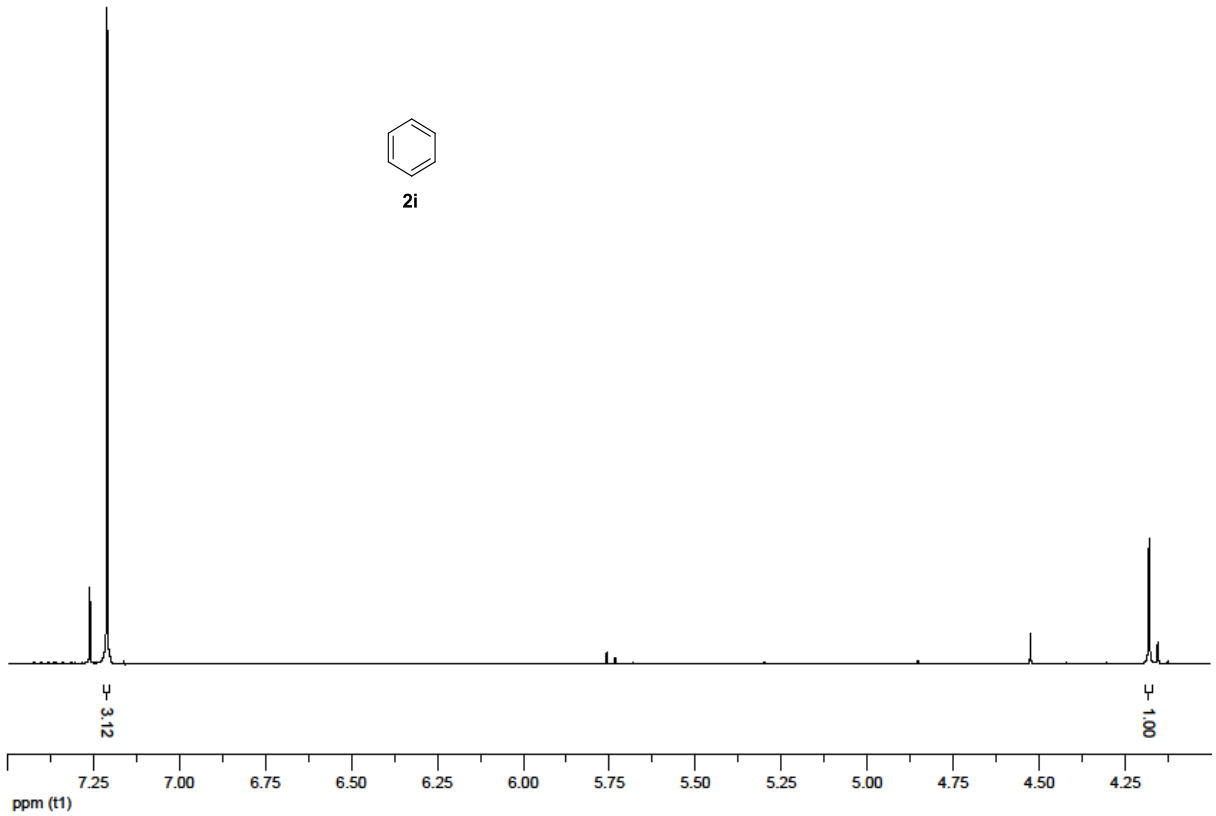


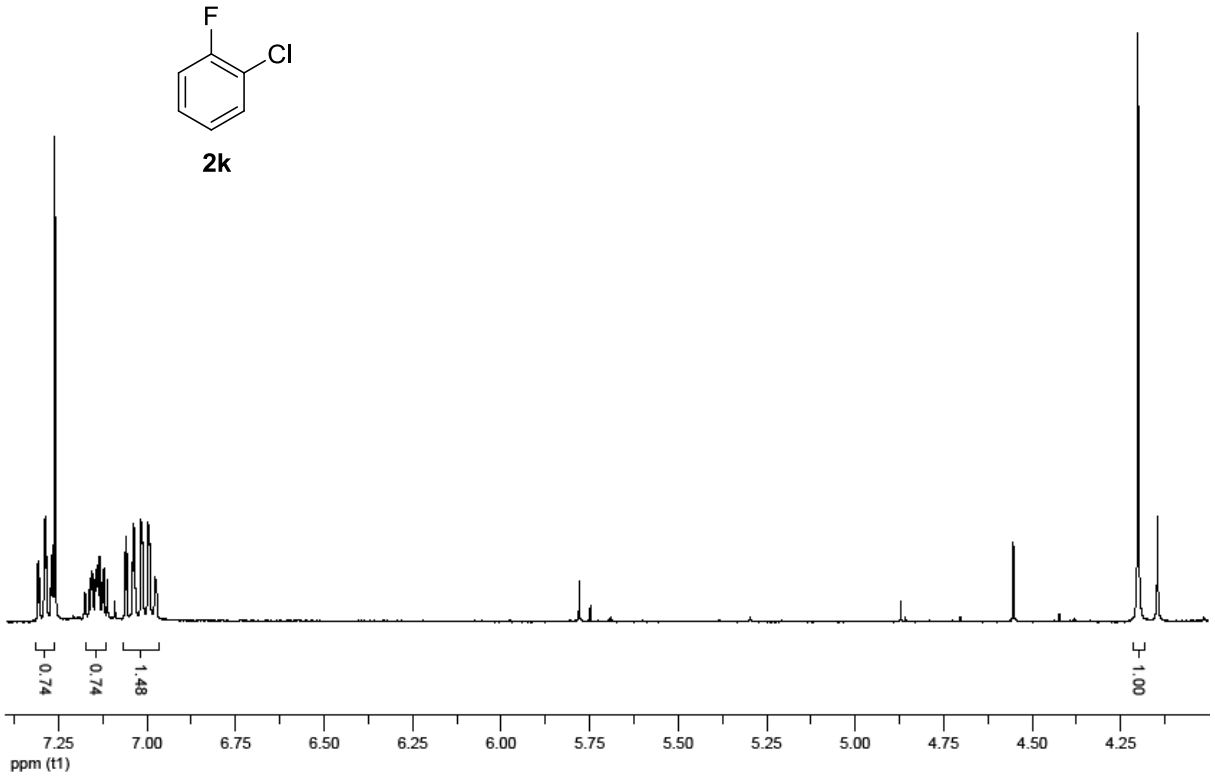


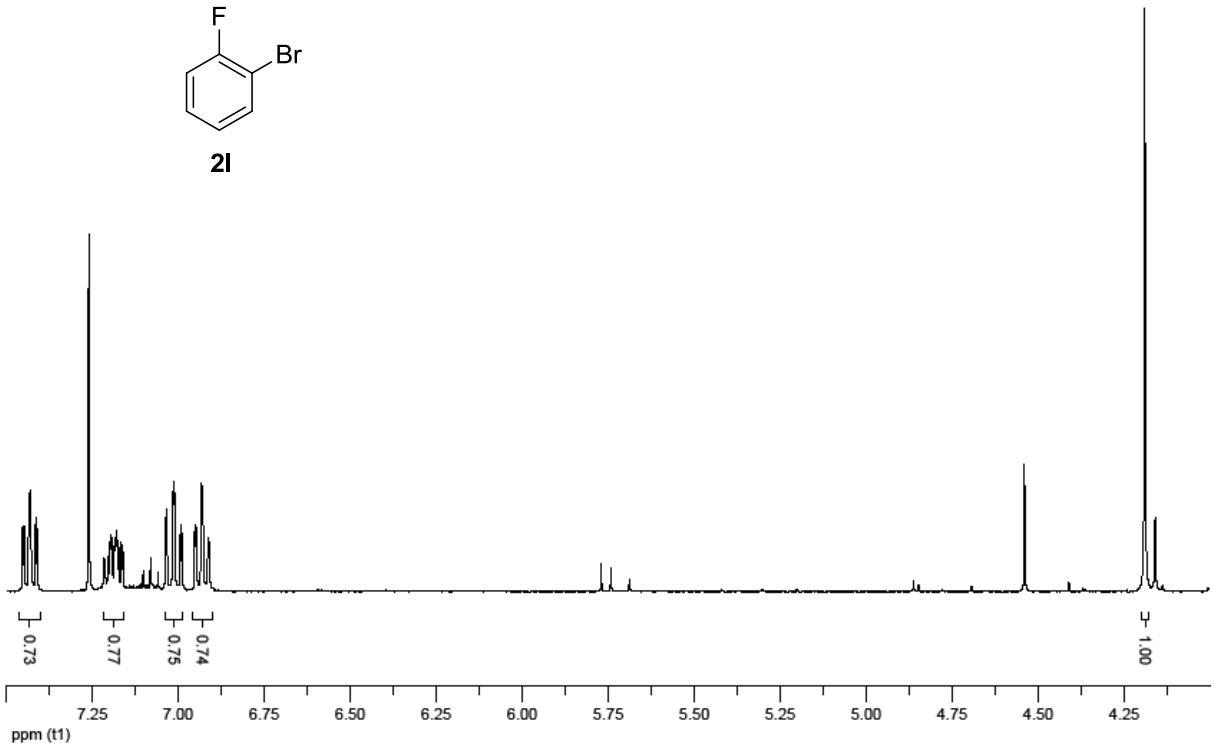


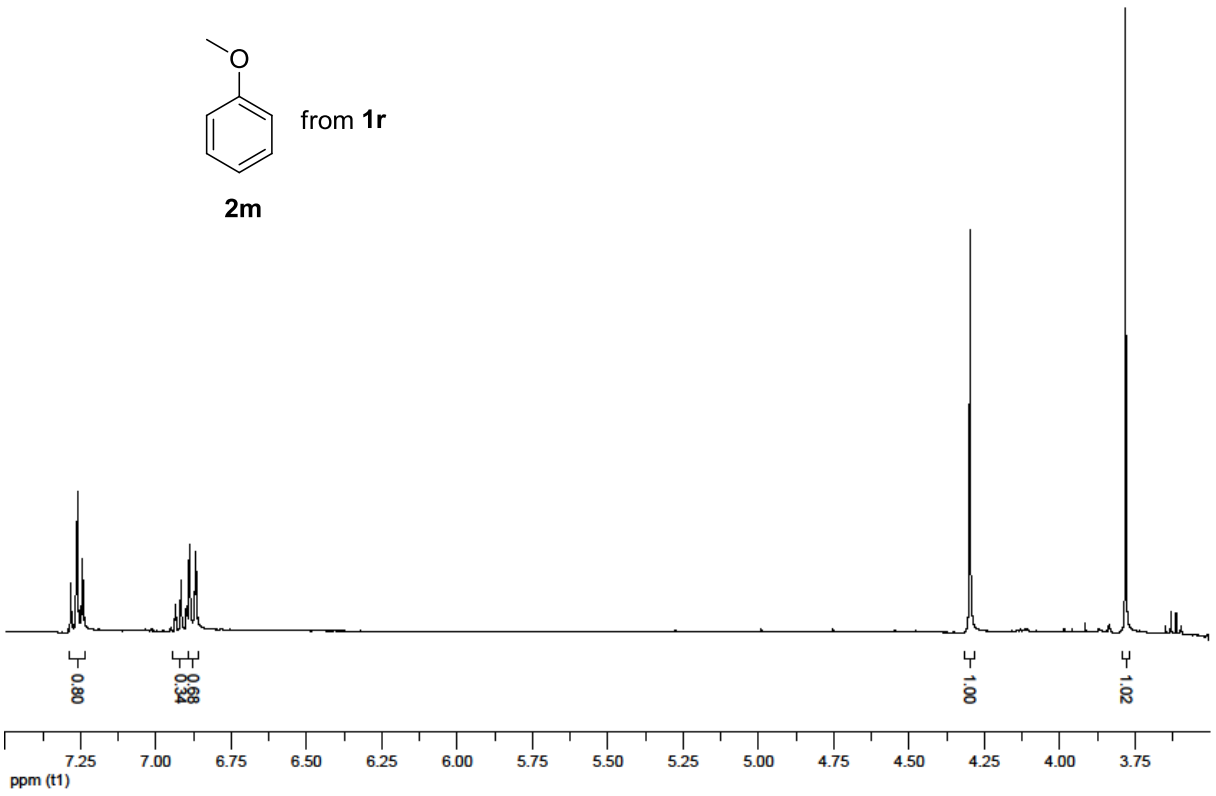


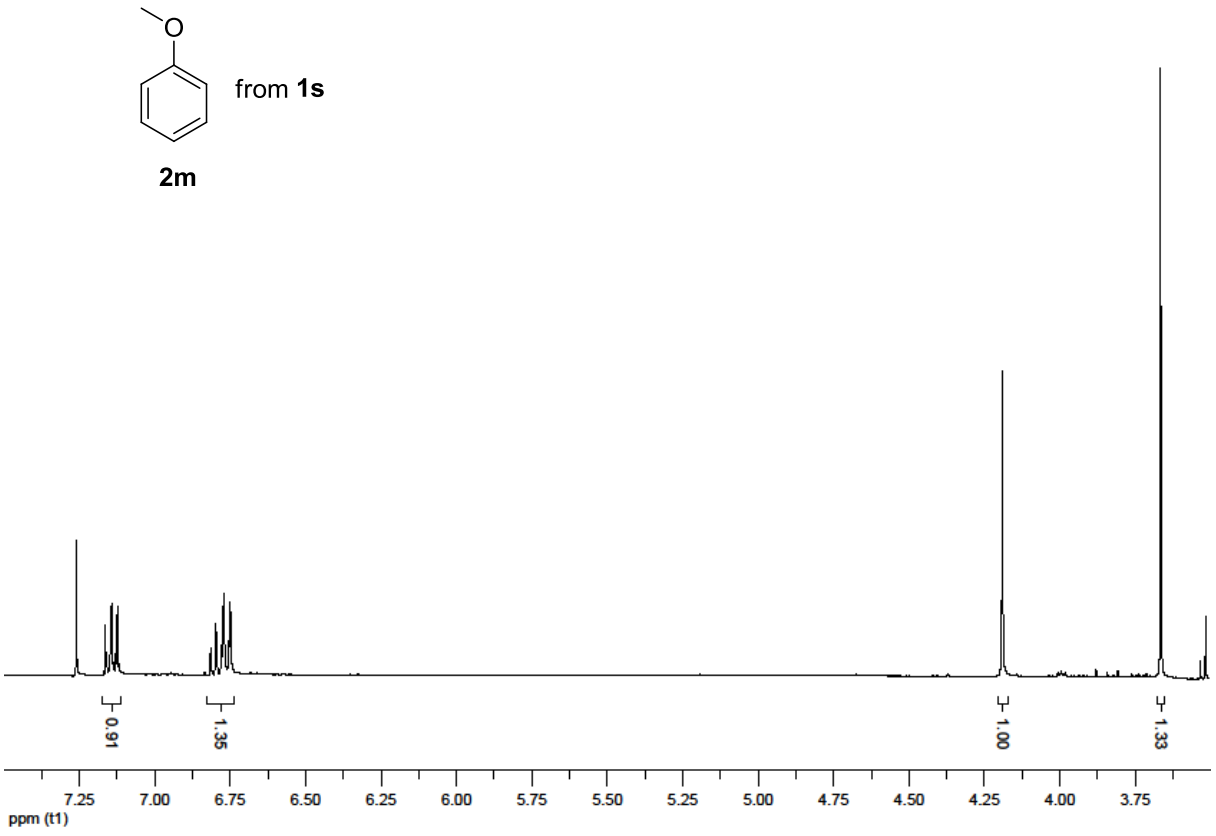

2h
0.80
0.39
0.81
1.00
7.50
7.25
7.00
6.75
6.50
6.25
6.00
5.75
5.50
5.25
5.00
4.75
4.50
4.25
ppm (t1)


2i
3.12
1.00
7.25
7.00
6.75
6.50
6.25
6.00
5.75
5.50
5.25
5.00
4.75
4.50
4.25
ppm (t1)


F
Cl
2k
0.74
0.74
1.48
1.00
7.25
7.00
6.75
6.50
6.25
6.00
5.75
5.50
5.25
5.00
4.75
4.50
4.25
ppm (t1)


F
Br
2l
0.73
0.77
0.75
0.74
1.00
7.25
7.00
6.75
6.50
6.25
6.00
5.75
5.50
5.25
5.00
4.75
4.50
4.25
ppm (t1)


from **1r**
2m
0.80
0.68
0.34
1.00
1.02
7.25
7.00
6.75
6.50
6.25
6.00
5.75
5.50
5.25
5.00
4.75
4.50
4.25
4.00
3.75
ppm (t1)


from **1s**
2m
0.91
1.35
1.00
1.33
7.25
7.00
6.75
6.50
6.25
6.00
5.75
5.50
5.25
5.00
4.75
4.50
4.25
4.00
3.75
ppm (t1)