Supplementary Information

P_2O_5-mediated Friedel-Crafts acylation of *activated* arenes with carboxylic acid as acylating agent

Rupali G Kalshetti, Ram D Mandle, Sanjay P Kamble & Arumugam Sudalai*
Chemical Engineering and Process Development Division
CSIR-National Chemical Laboratory, Dr. Homi Bhabha Road, Pune 411 008, India
E-mail: a.sudalai@ncl.res.in
Received 6 November 2019; accepted (revised) 11 November 2020

1. General information:

All reactions were carried out under an atmosphere of nitrogen unless otherwise noted. Solvents were purified and dried by standard procedures before use. Column chromatography was performed using silica gel (200-300 mesh). ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker-AV (400, 500 and 200 MHz, respectively) instrument internally referenced to tetramethylsilane (TMS) or chloroform signals. The structures of known compounds were further corroborated by comparing their ^{1}H NMR, ^{13}C NMR data and MS data with those of literature values. HR-MS were recorded on a Thermo Finnigan LCQ Advantage Spectrometer in ESI mode with a spray voltage of 4.8 kV. All chemicals are purchased from Sigma-Aldrich and used without further purification.

2.Typical procedure for the synthesis of 4-methoxy acetophenone [3a]

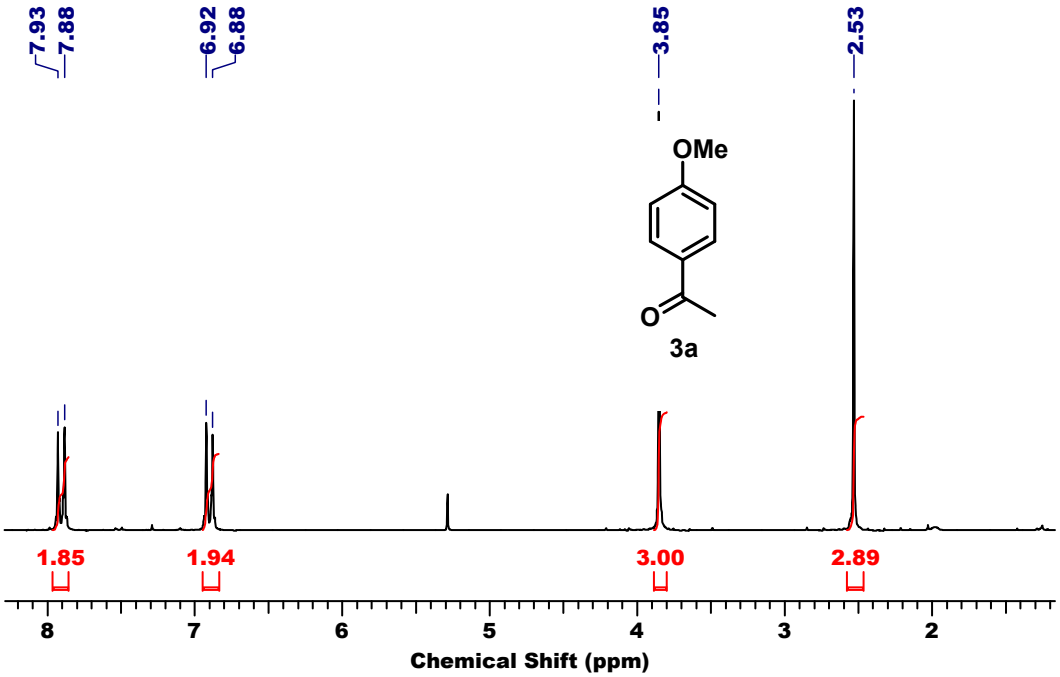
A round-bottomed flask was charged with anisole (500 mg, 4.62 mmol, 1 equiv.), glacial acetic acid (556 mg, 9.26 mmol, 2 equiv.), and P_2O_5 (328 mg, 2.314 mmol), under nitrogen atmosphere and the whole mixture stirred for 8 h at 80^oC**.** The reaction was then monitored by TLC and after the completion of reaction; it was quenched with sodium bicarbonate solution. The work-up of reaction mixture was done CH_2Cl_2 (50 mL) and water (15 mL) to remove traces of phosphoric acid if any. Organic layer was dried on sodium sulfate; Solvent was removed under vacuum distillation to furnish 645 mg of 4-methoxyacetophenone.

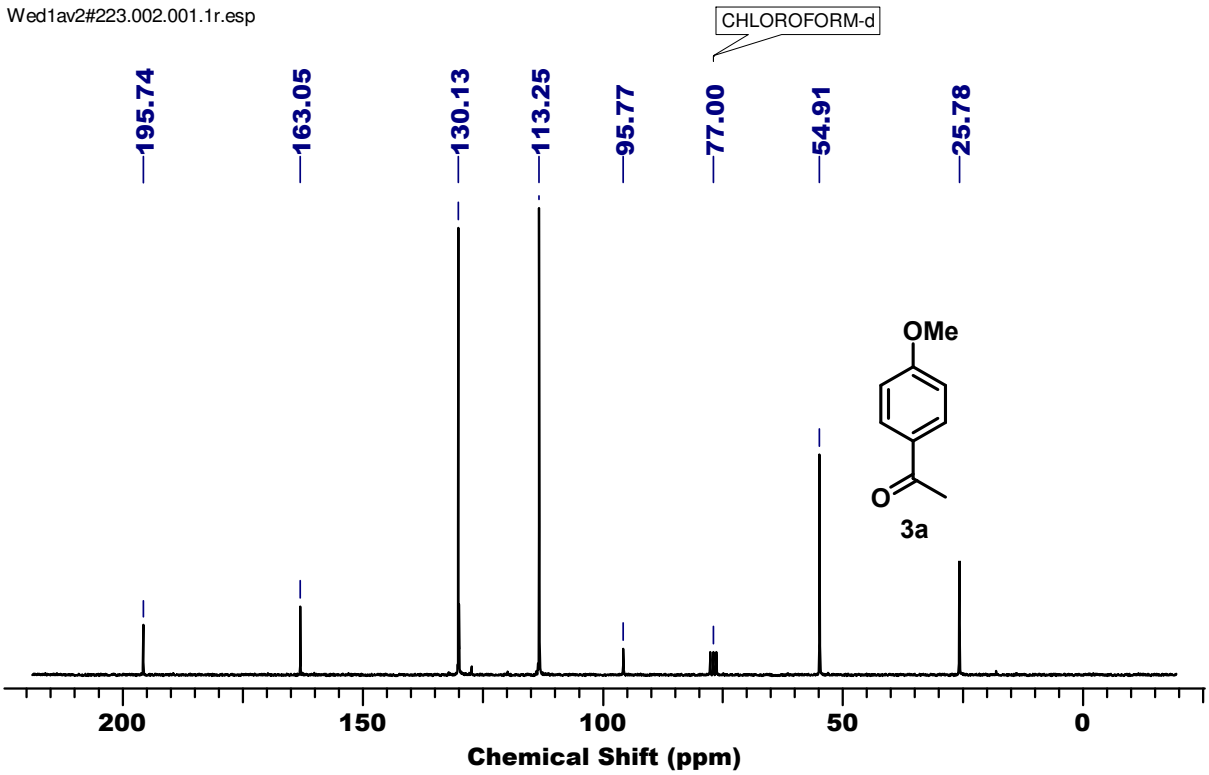
3. Typical procedure for the synthesis of 4-hydroxyacetophenone [6a]

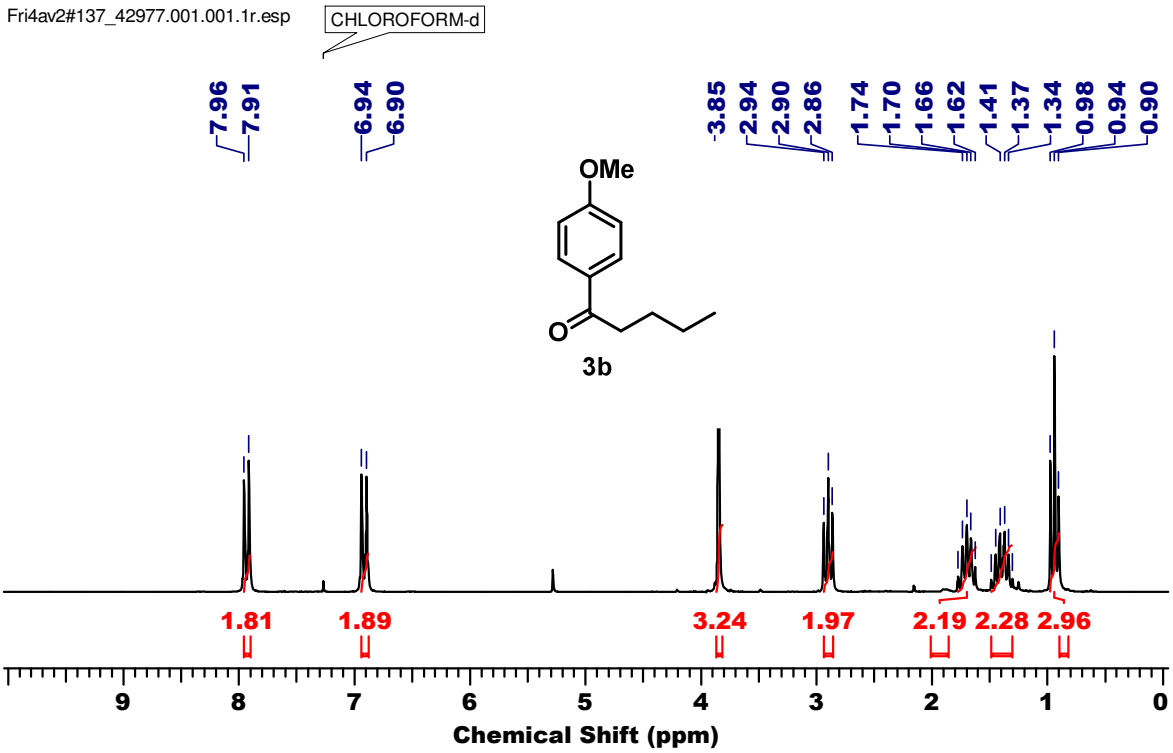
A round-bottomed flask was charged with phenol (500 mg, 5.319 mmol), glacial acetic acid (638 mg, 10.638 mmol), and P_2O_5 (372 mg, 2.659 mmol), and the whole mixture was stirred for 8 h at 120 ^oC**.** The reaction was then monitored by TLC and after the completion of reaction, it was quenched with sodium bicarbonate solution. The usual work-up of reaction mixture was done with CH_2Cl_2 (50 mL) and water (15 mL) to remove traces of phosphoric acid if any. Organic layer was dried on sodium sulfate; the volatiles were removed under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 20:1) to yield the desired product **6a** as off-white solid, 506 mg, yield 70%.

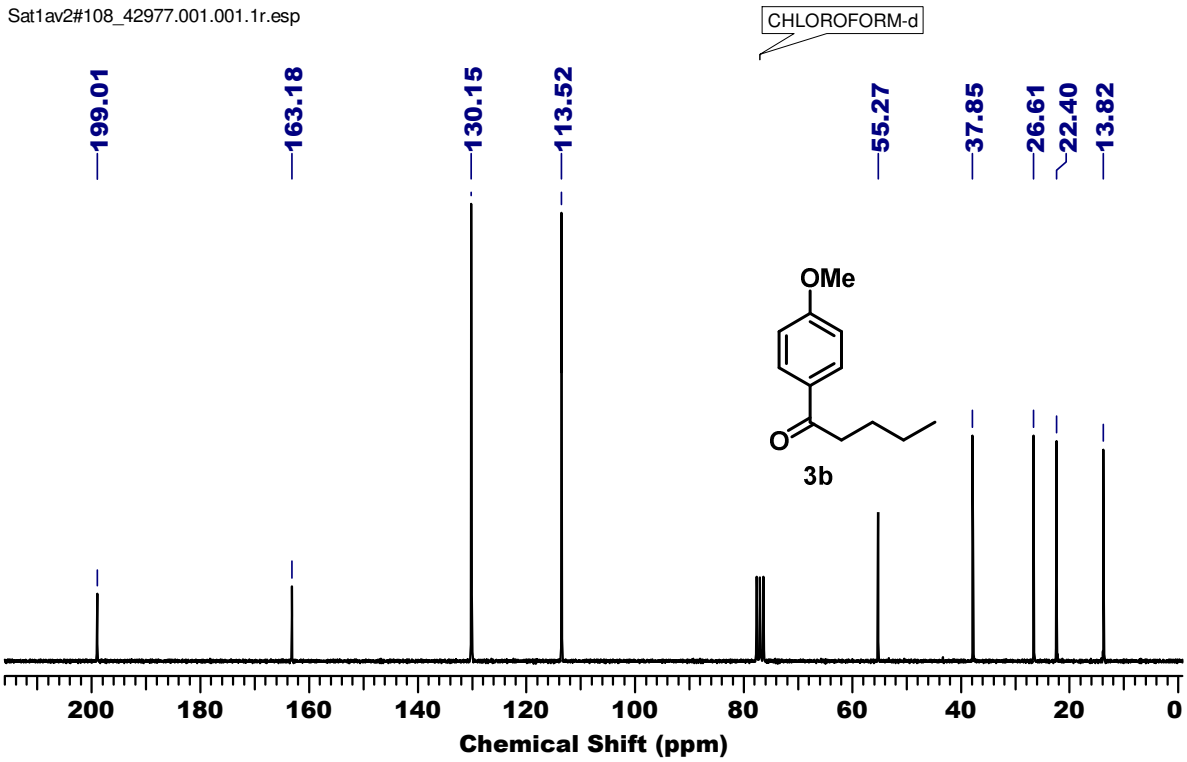
4. Characterization data of products:

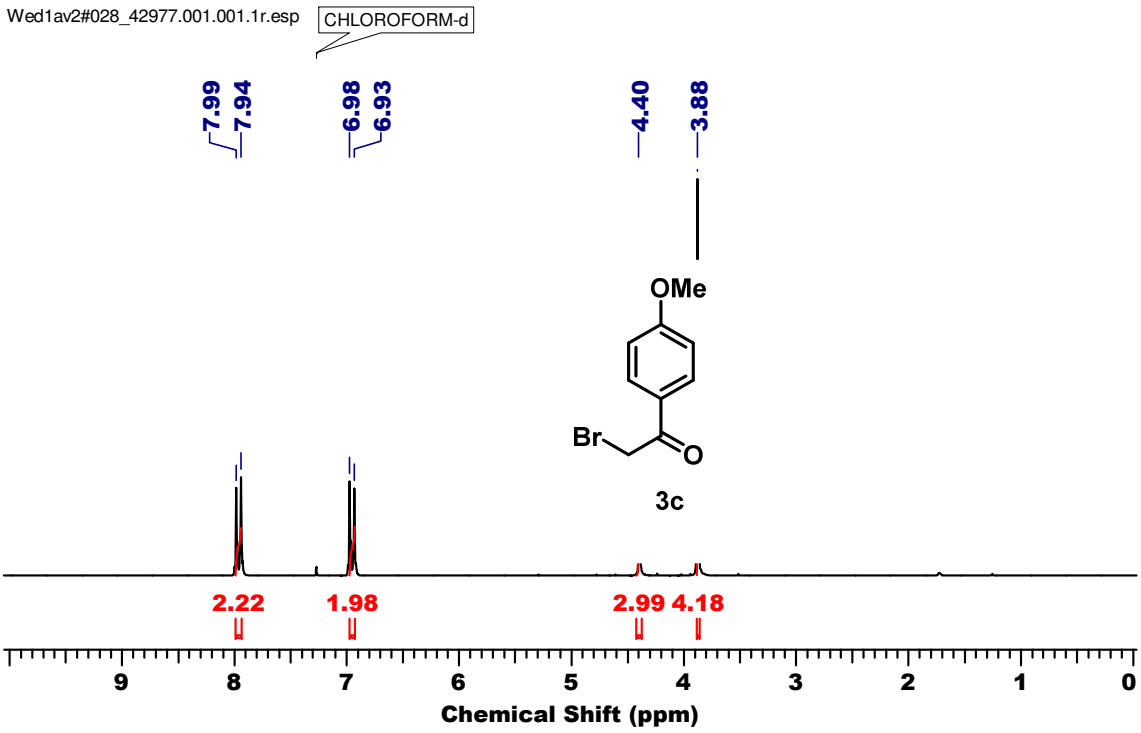
^{1}H and ^{13}C NMR spectra of products

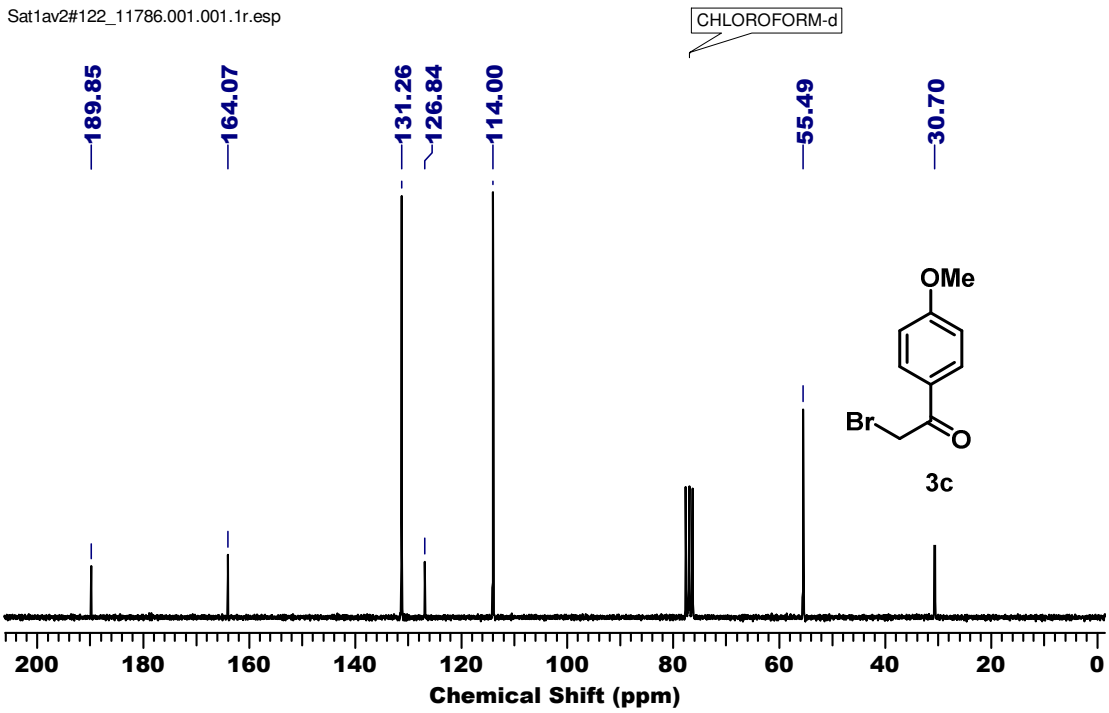


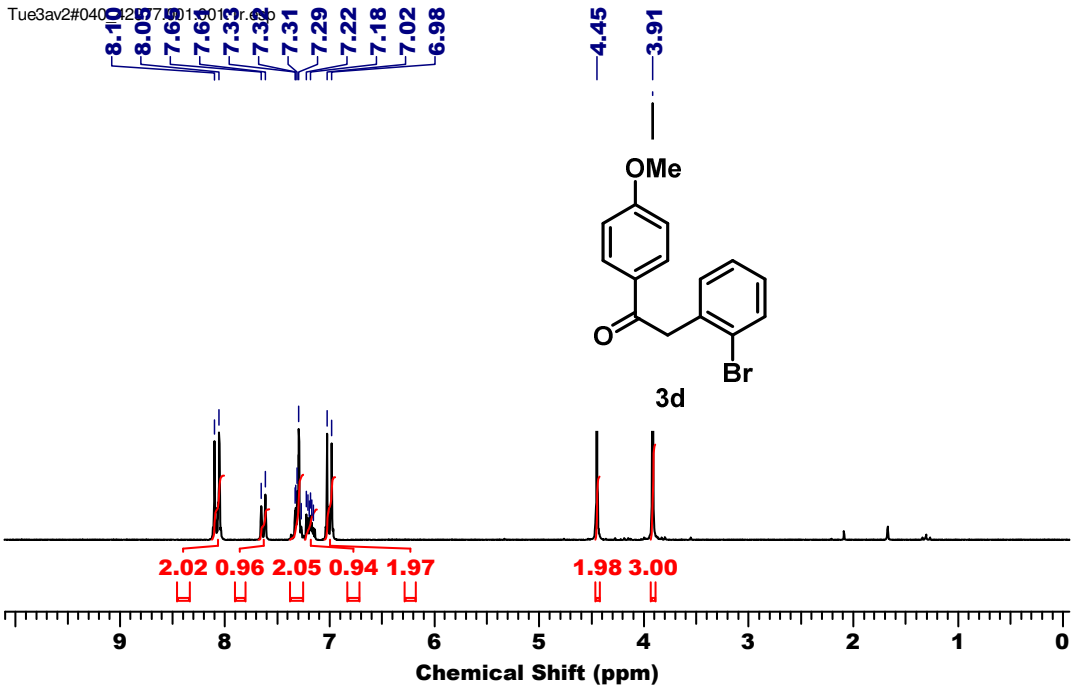

Wed1av2#223.002.001.1r.esp
CHLOROFORM-d
195.74
163.05
130.13
113.25
95.77
77.00
54.91
25.78
OMe
O
3a
200
150
100
50
0
Chemical Shift (ppm)

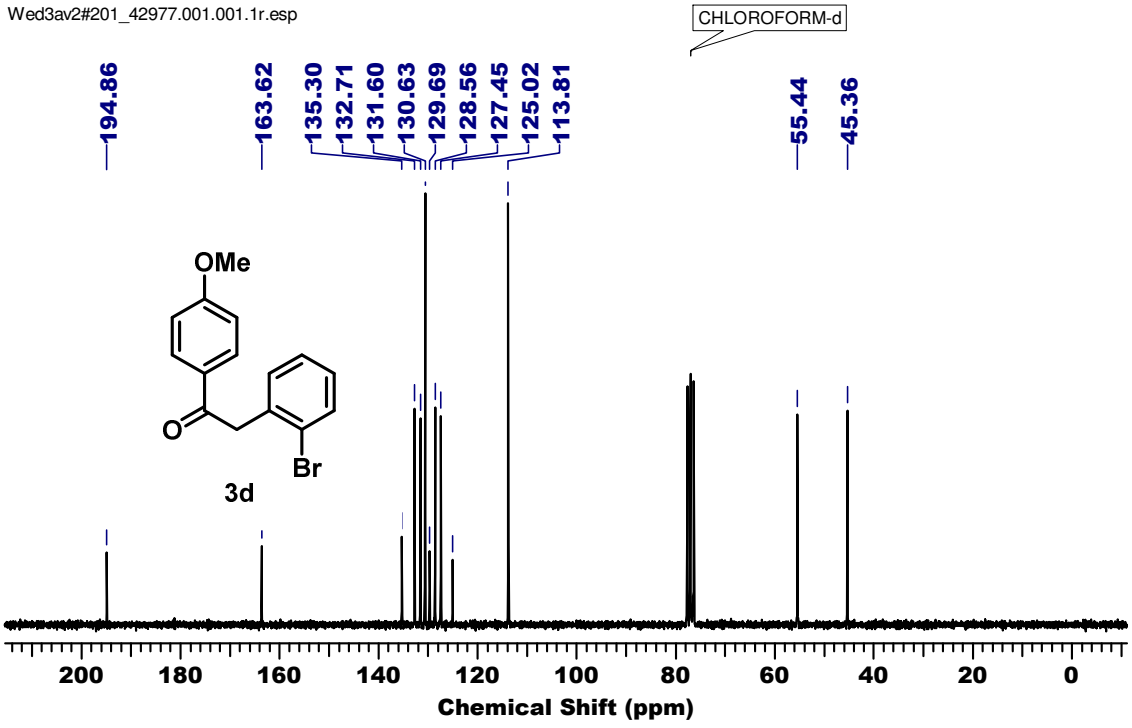

Fri4av2#137_42977.001.001.1r.esp
CHLOROFORM-d
7.96
7.91
6.94
6.90
3.85
2.94
2.90
2.86
1.74
1.70
1.66
1.62
1.41
1.37
1.34
0.98
0.94
0.90
OMe
O
3b
1.81
1.89
3.24
1.97
2.19
2.28
2.96
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

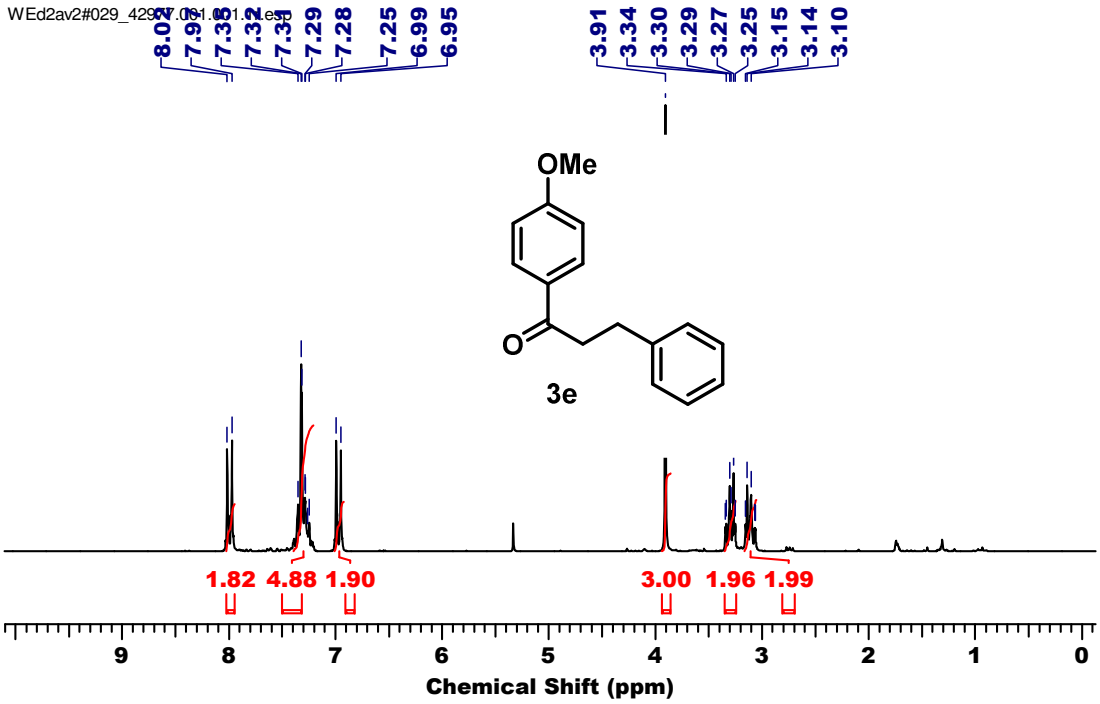

Sat1av2#108_42977.001.001.1r.esp
CHLOROFORM-d
199.01
163.18
130.15
113.52
55.27
37.85
26.61
22.40
13.82
OMe
O
3b
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

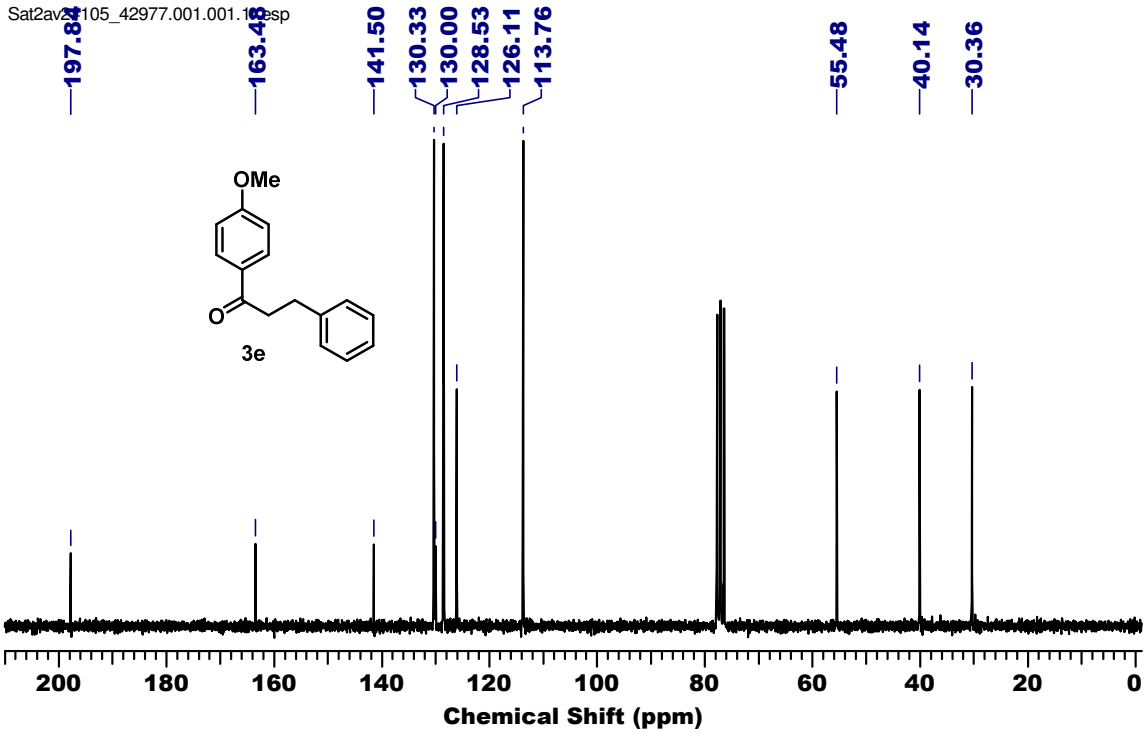

Wed1av2#028_42977.001.001.1r.esp
CHLOROFORM-d
7.99
7.94
6.98
6.93
4.40
3.88
OMe
Br
O
3c
2.22
1.98
2.99
4.18
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

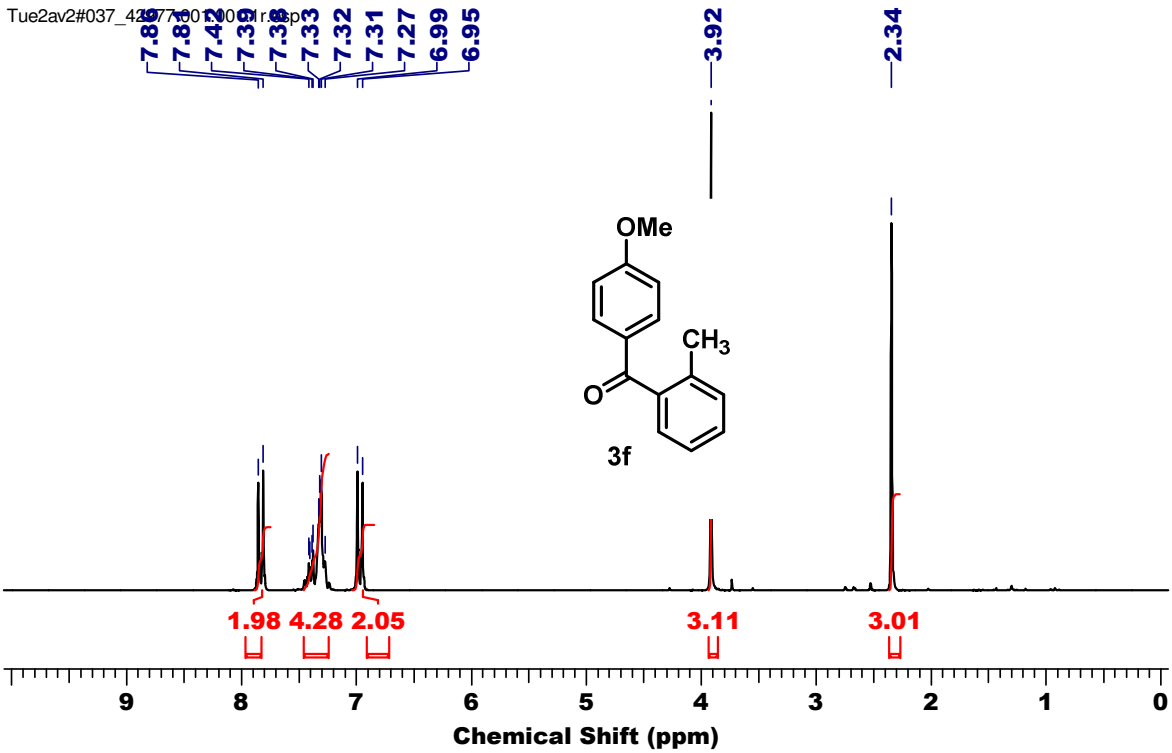

Sat1av2#122_11786.001.001.1r.esp
CHLOROFORM-d
189.85
164.07
131.26
126.84
114.00
55.49
30.70
OMe
Br
O
3c
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

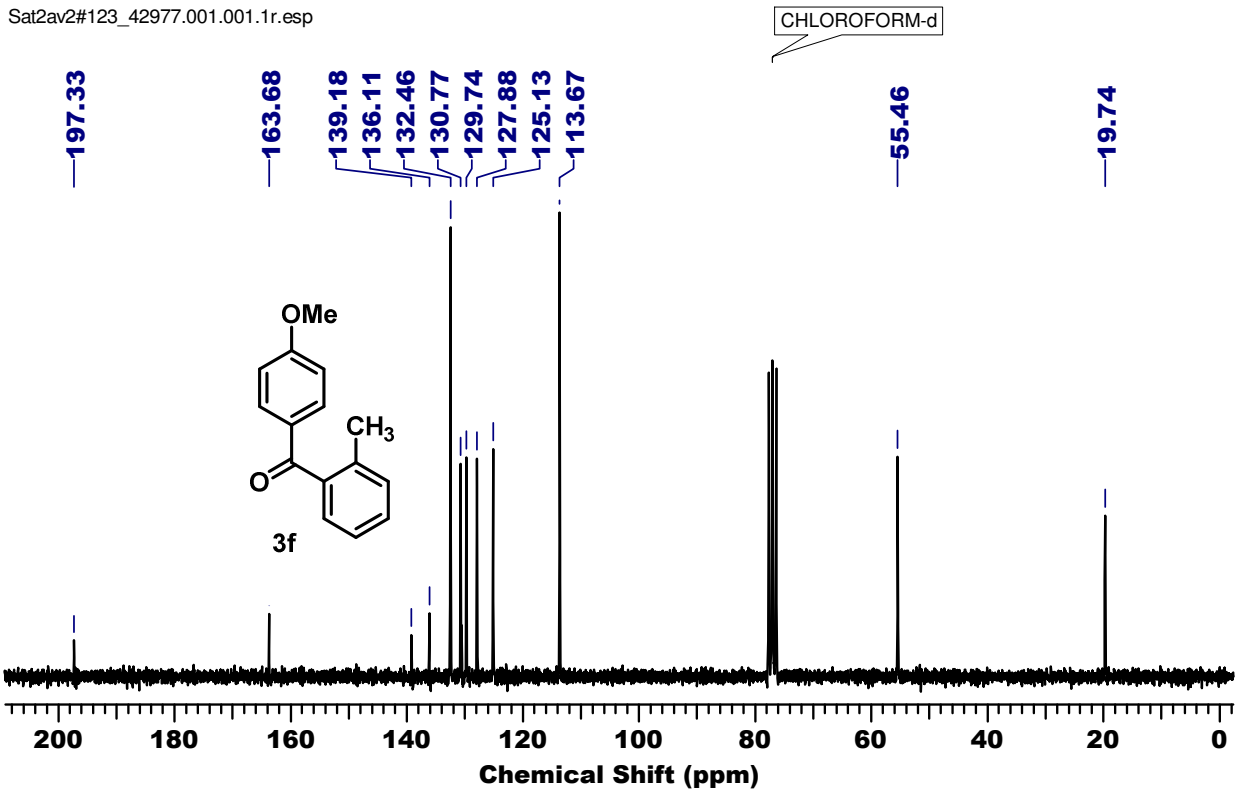

8.10
8.05
7.65
7.61
7.33
7.32
7.31
7.29
7.22
7.18
7.02
6.98
4.45
3.91
OMe
O
Br
3d
2.02 0.96 2.05 0.94 1.97
1.98 3.00
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

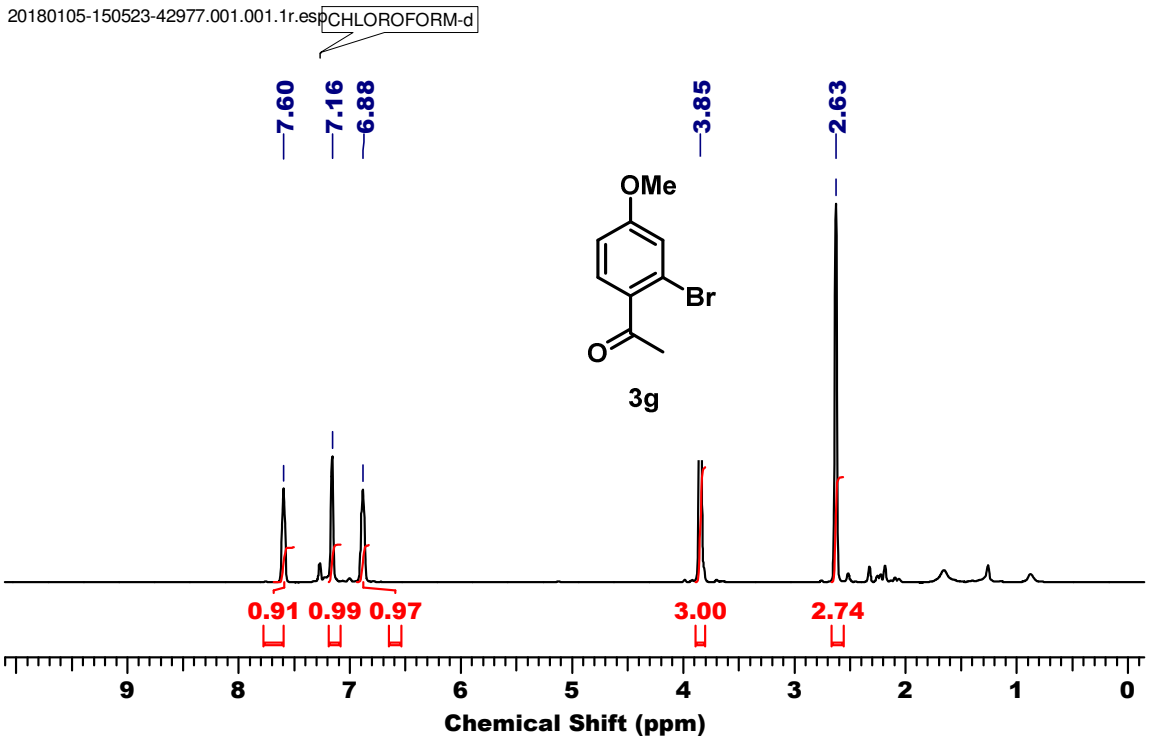

Wed3av2#201_42977.001.001.1r.esp
CHLOROFORM-d
194.86
163.62
135.30
132.71
131.60
130.63
129.69
128.56
127.45
125.02
113.81
55.44
45.36
OMe
O
Br
3d
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

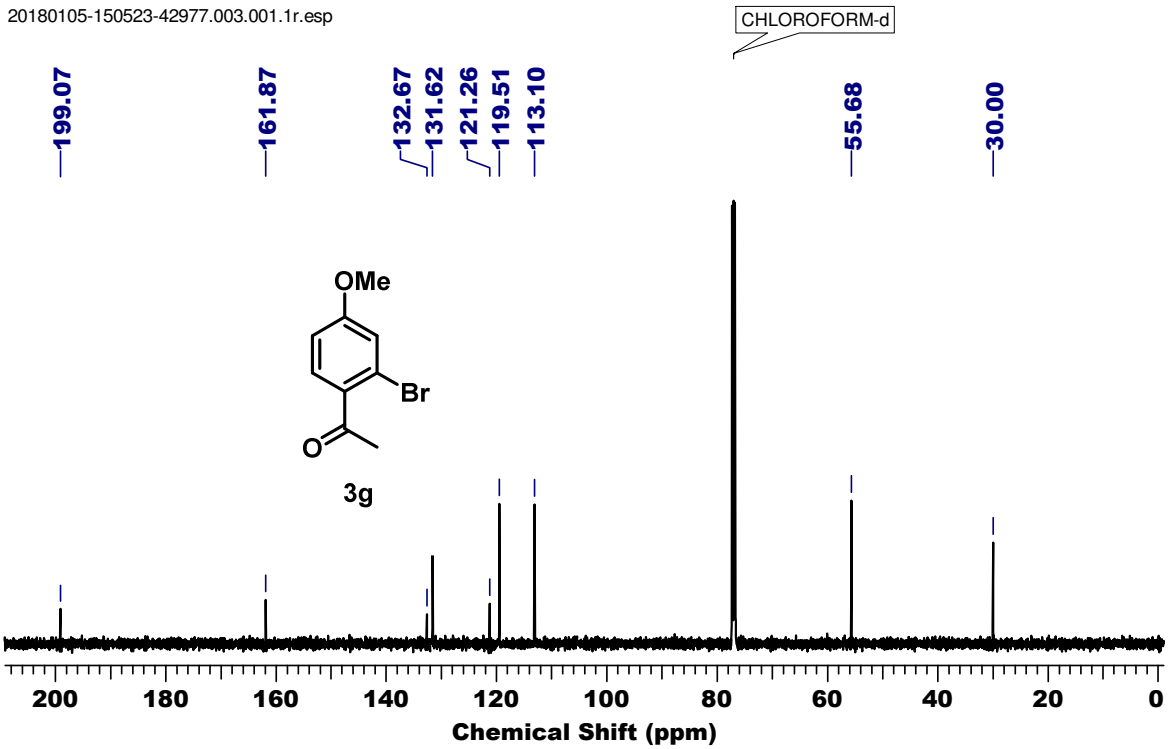

WEd2av2#029_42977.001.001.1.esp
8.01
7.95
7.35
7.32
7.31
7.29
7.28
7.25
6.99
6.95
3.91
3.34
3.30
3.29
3.27
3.25
3.15
3.14
3.10
OMe
O
3e
1.82
4.88
1.90
3.00
1.96
1.99
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

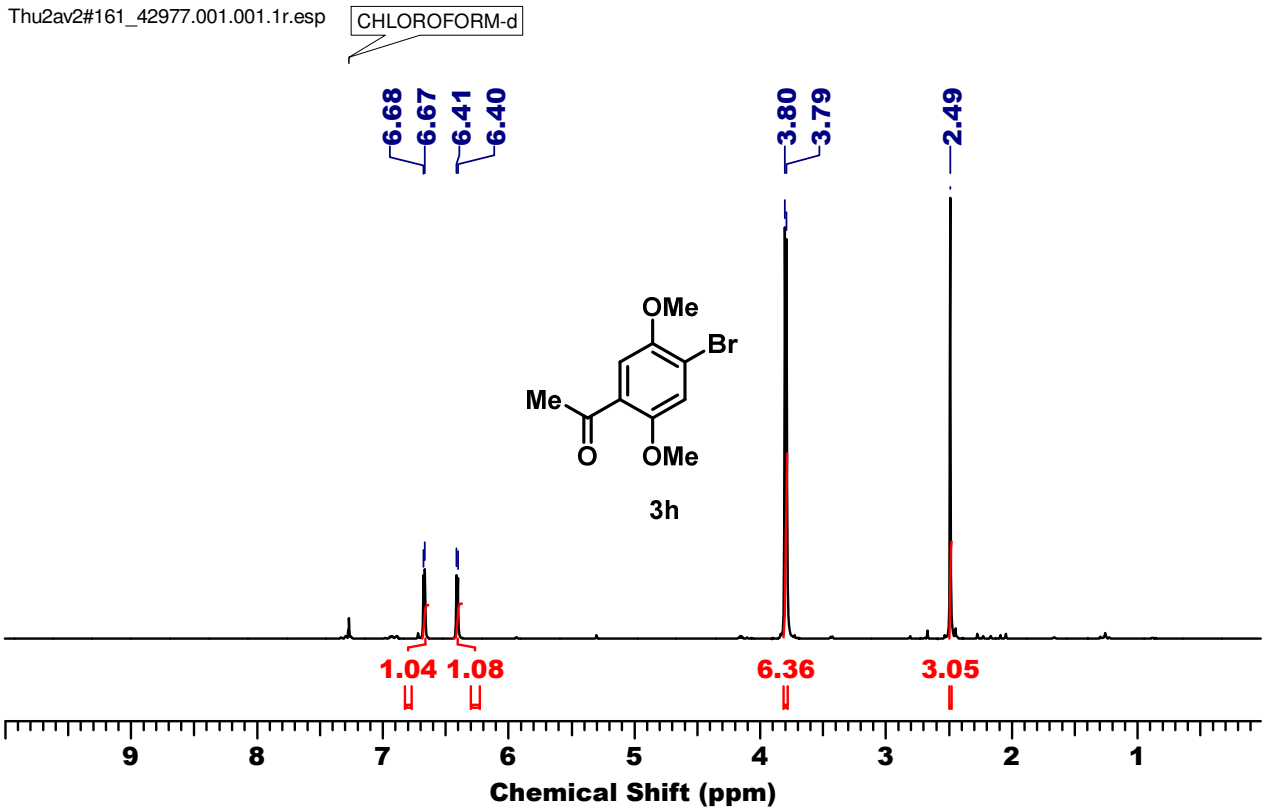

Sat2av2#105_42977.001.001.1.esp
197.84
163.48
141.50
130.33
130.00
128.53
126.11
113.76
55.48
40.14
30.36
OMe
O
3e
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

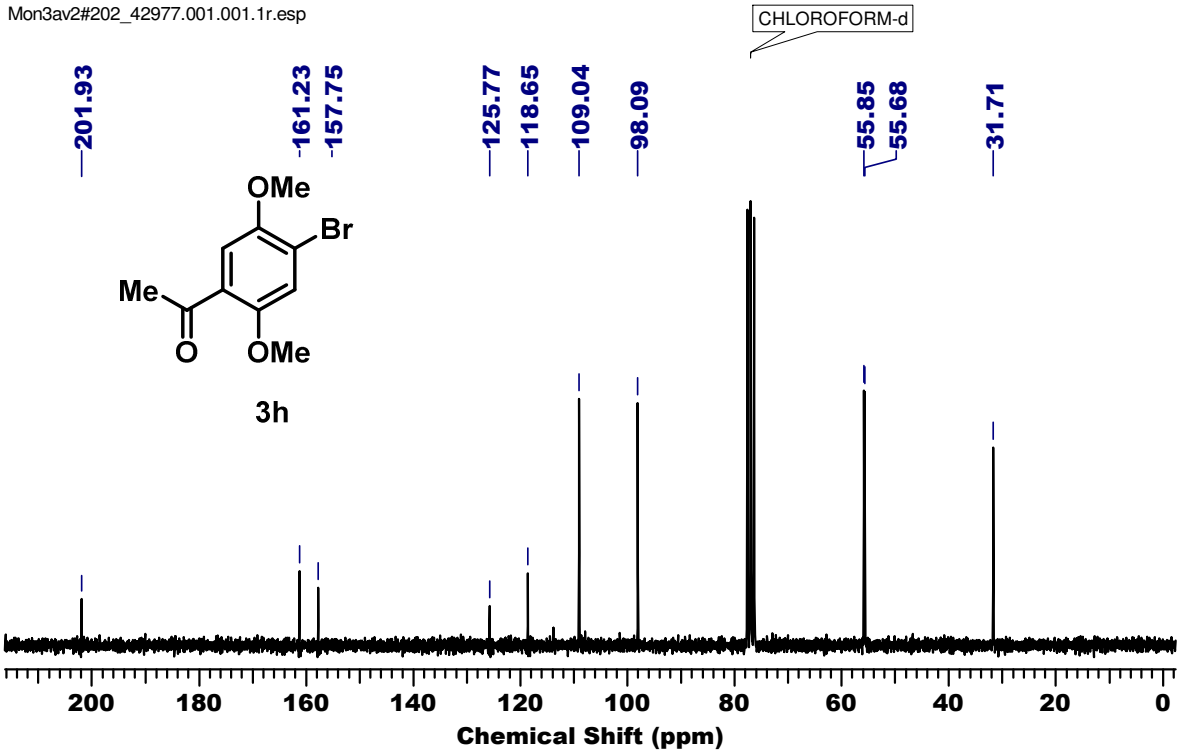

7.80
7.81
7.42
7.39
7.38
7.33
7.32
7.31
7.27
6.99
6.95
3.92
2.34
OMe
CH3
O
3f
1.98 4.28 2.05
3.11
3.01
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

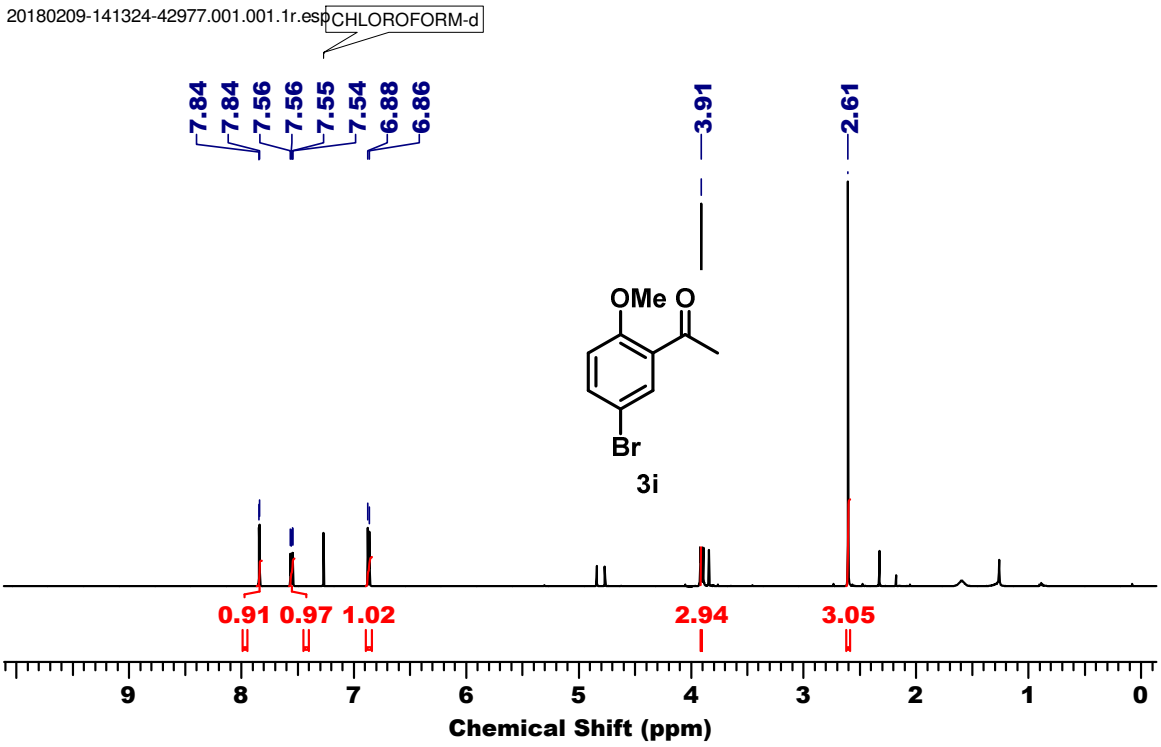

Sat2av2#123_42977.001.001.1r.esp
CHLOROFORM-d
197.33
163.68
139.18
136.11
132.46
130.77
129.74
127.88
125.13
113.67
55.46
19.74
OMe
CH3
O
3f
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

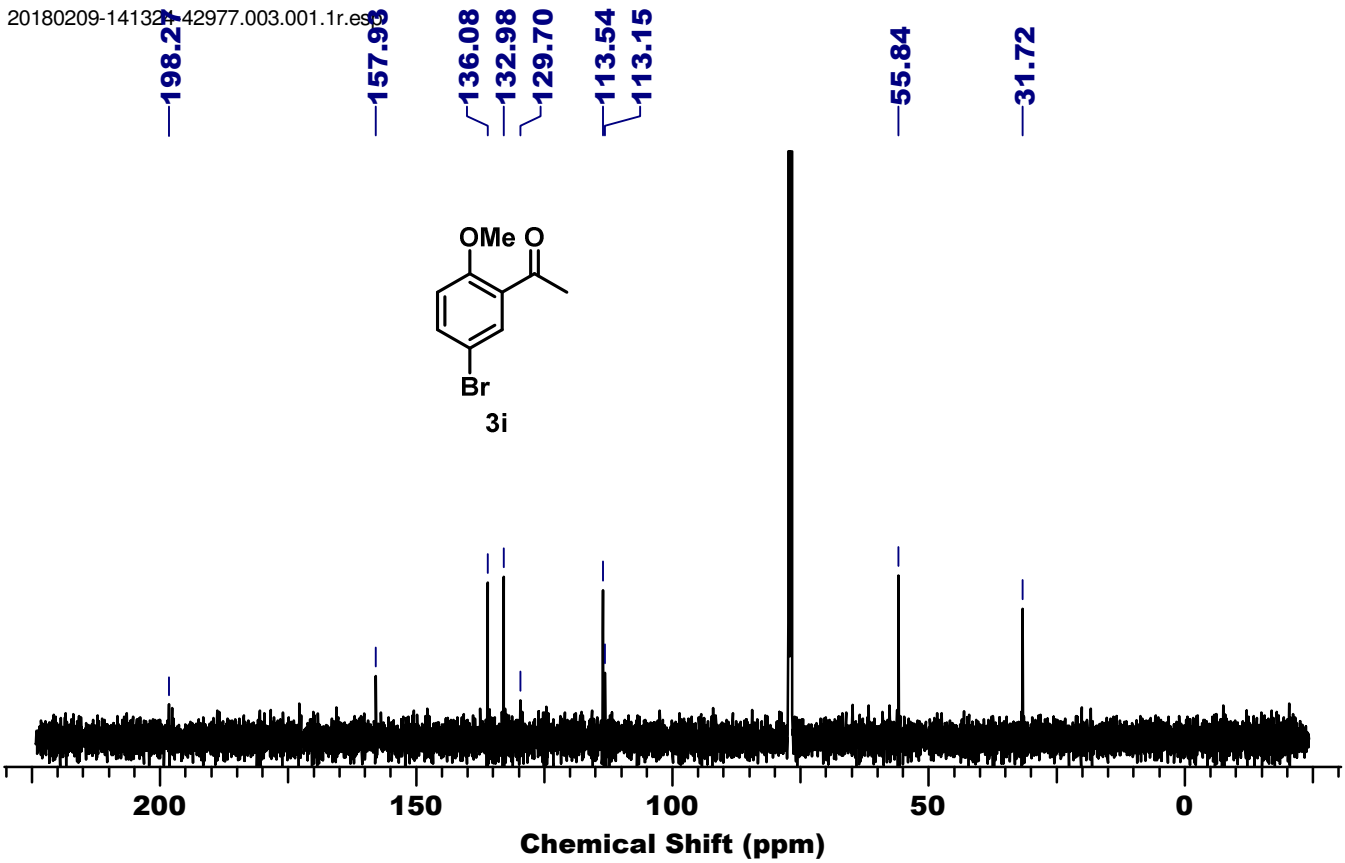

20180105-150523-42977.001.001.1r.esp
CHLOROFORM-d
7.60
7.16
6.88
3.85
2.63
OMe
Br
O
3g
0.91
0.99
0.97
3.00
2.74
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

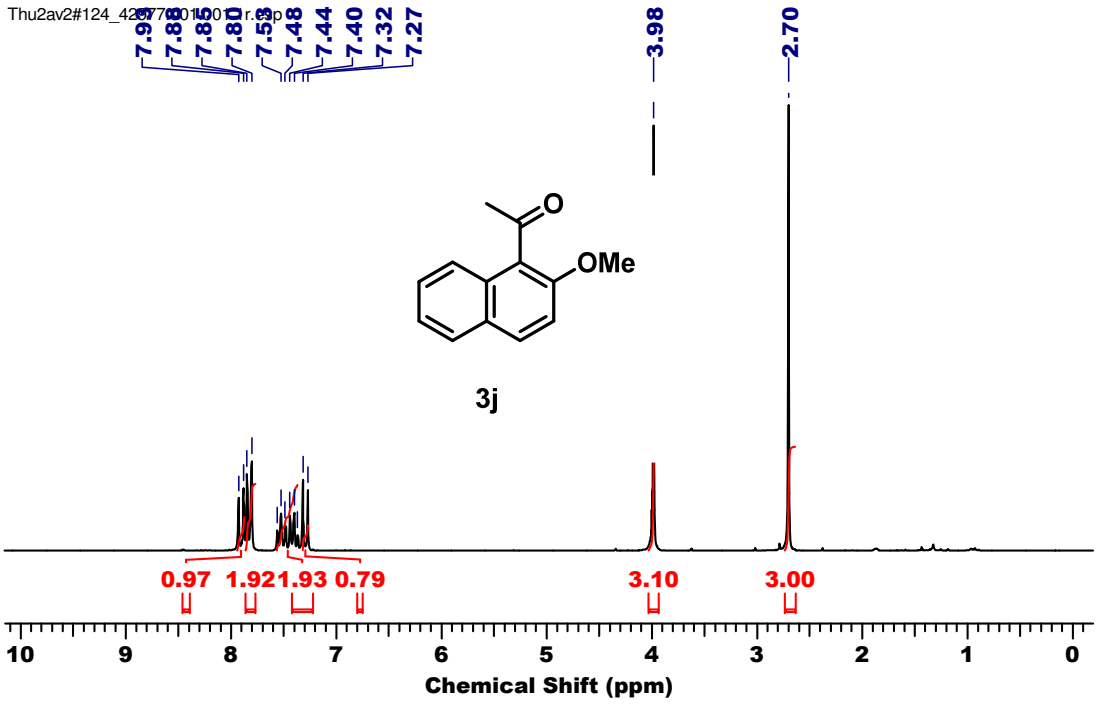

20180105-150523-42977.003.001.1r.esp
CHLOROFORM-d
199.07
161.87
132.67
131.62
121.26
119.51
113.10
55.68
30.00
OMe
Br
O
3g
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

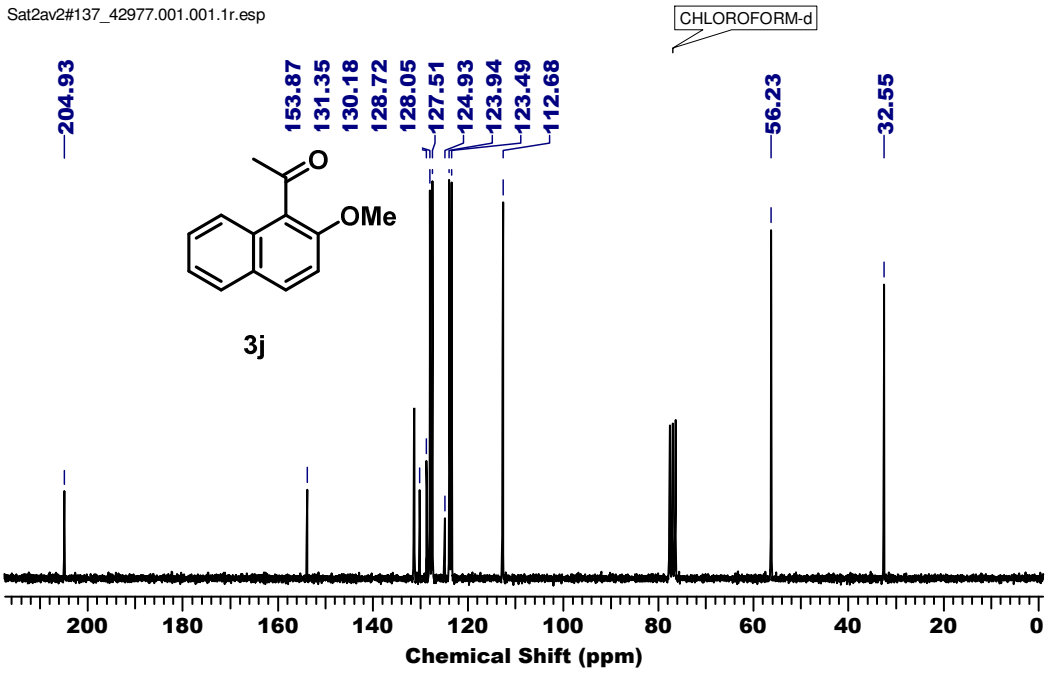

Thu2av2#161_42977.001.001.1r.esp
CHLOROFORM-d
6.68
6.67
6.41
6.40
3.80
3.79
2.49
OMe
Br
Me
O
OMe
3h
1.04
1.08
6.36
3.05
9
8
7
6
5
4
3
2
1
Chemical Shift (ppm)

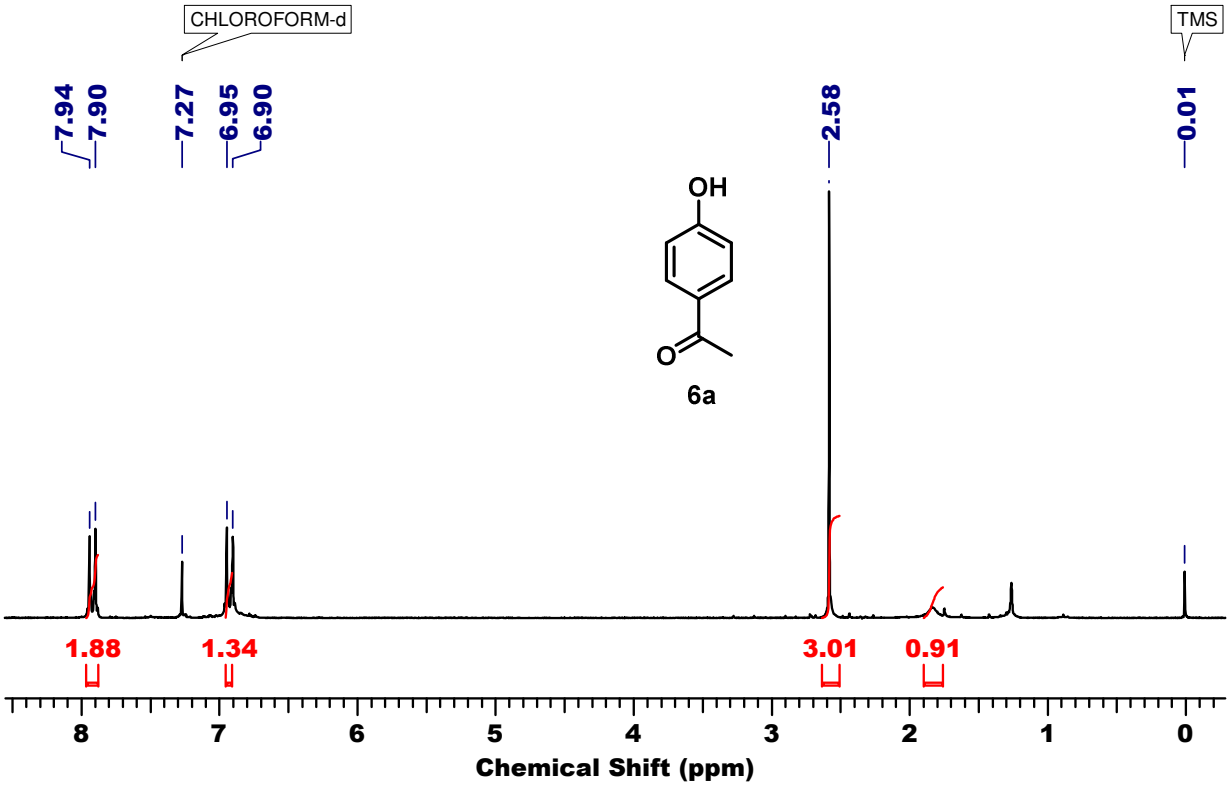

Mon3av2#202_42977.001.001.1r.esp
CHLOROFORM-d
201.93
161.23
157.75
125.77
118.65
109.04
98.09
55.85
55.68
31.71
OMe
Br
Me
O
OMe
3h
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

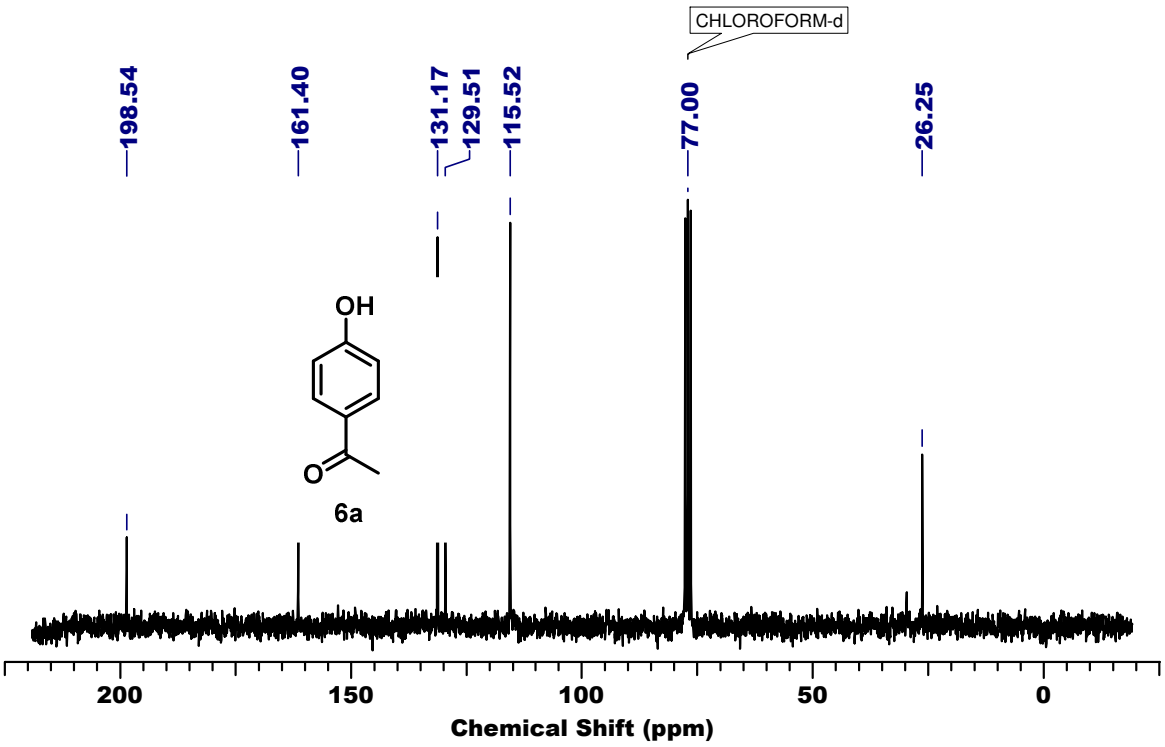

20180209-141324-42977.001.001.1r.esp
CHLOROFORM-d
7.84
7.84
7.56
7.56
7.55
7.54
6.88
6.86
3.91
2.61
OMe O
Br
3i
0.91 0.97 1.02
2.94
3.05
9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)

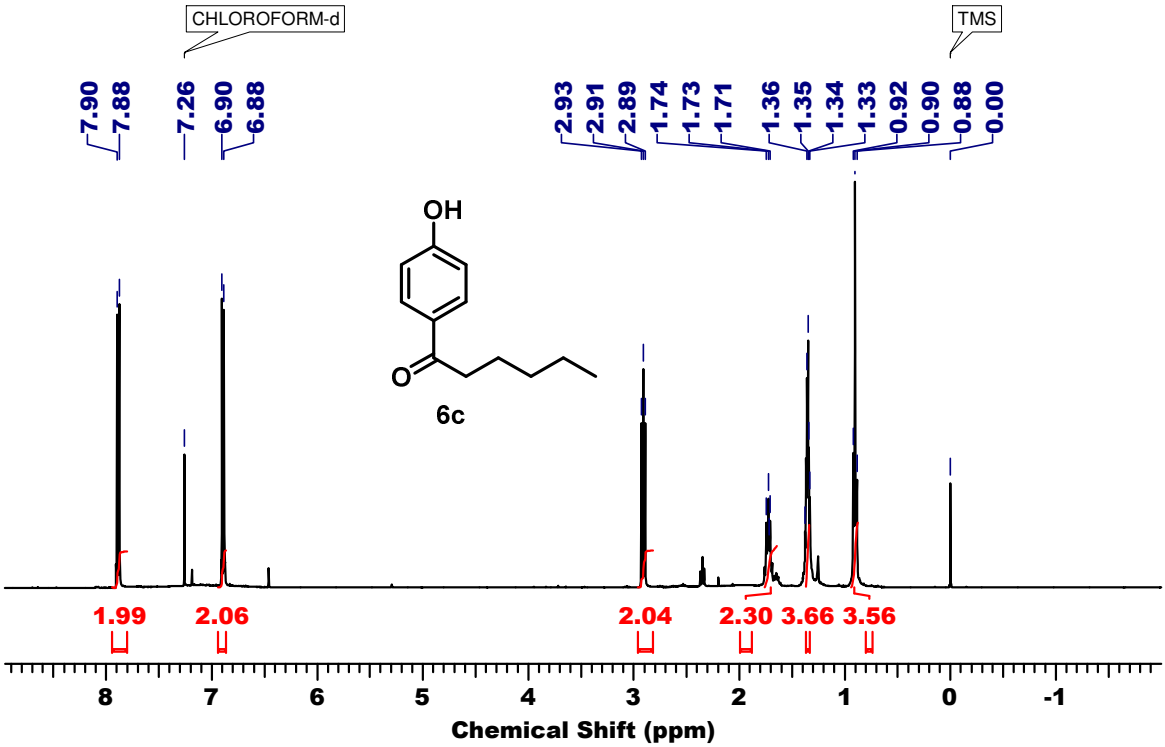

20180209-141324-42977.003.001.1r.esp
198.24
157.93
136.08
132.98
129.70
113.54
113.15
55.84
31.72
OMe O
Br
3i
200
150
100
50
0
Chemical Shift (ppm)

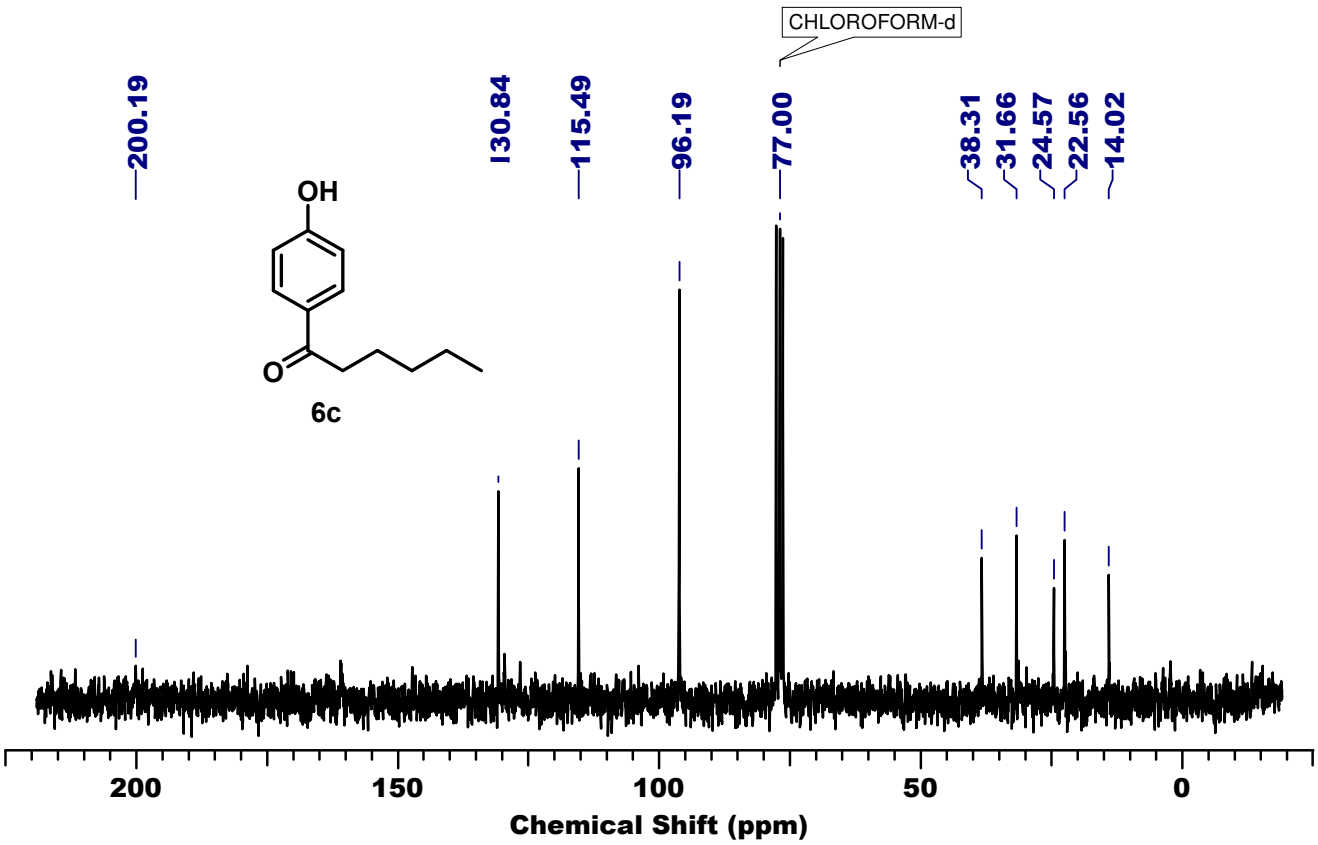

7.90
7.88
7.85
7.81
7.53
7.48
7.44
7.40
7.32
7.27
3.98
2.70
O
OMe
3j
0.97
1.92
1.93
0.79
3.10
3.00
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

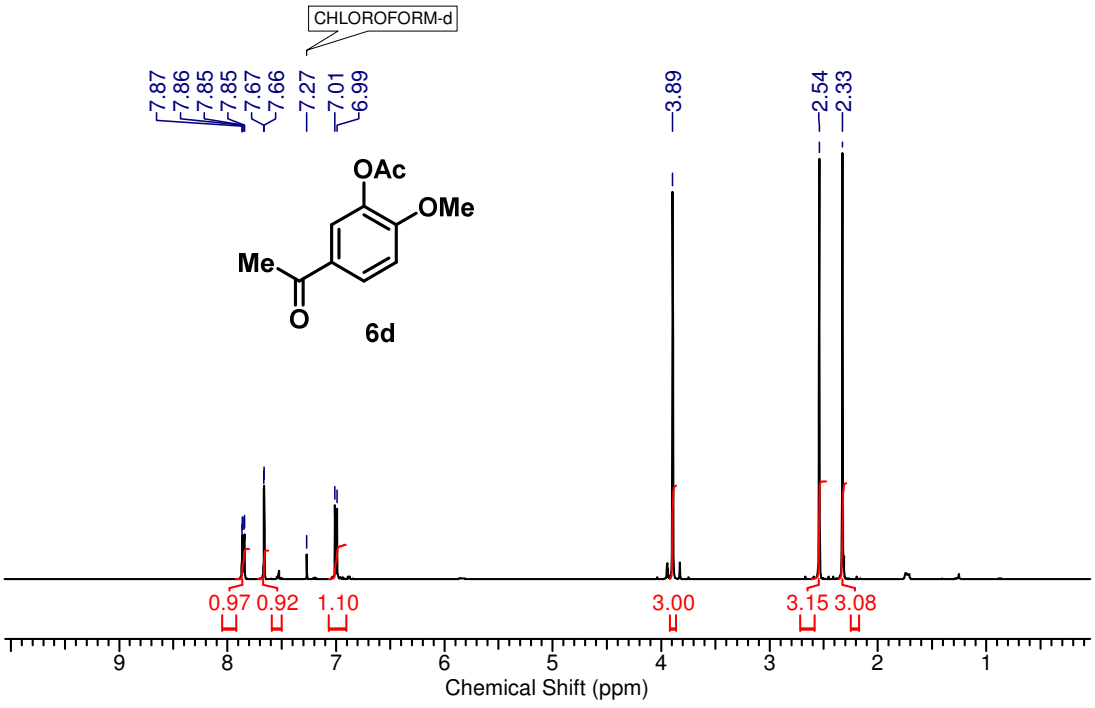

Sat2av2#137_42977.001.001.1r.esp
CHLOROFORM-d
204.93
153.87
131.35
130.18
128.72
128.05
127.51
124.93
123.94
123.49
112.68
56.23
32.55
O
OMe
3j
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

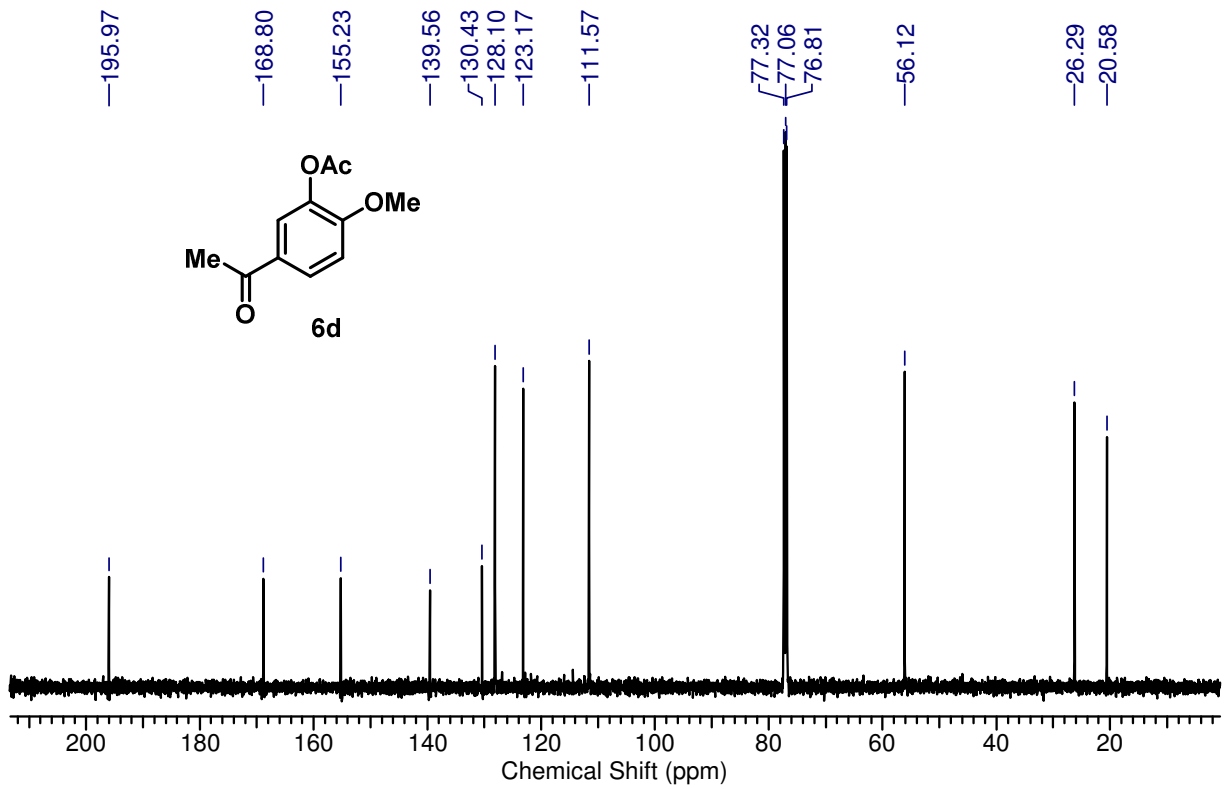

CHLOROFORM-d
TMS
7.94
7.90
7.27
6.95
6.90
2.58
0.01
OH
O
6a
1.88
1.34
3.01
0.91
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

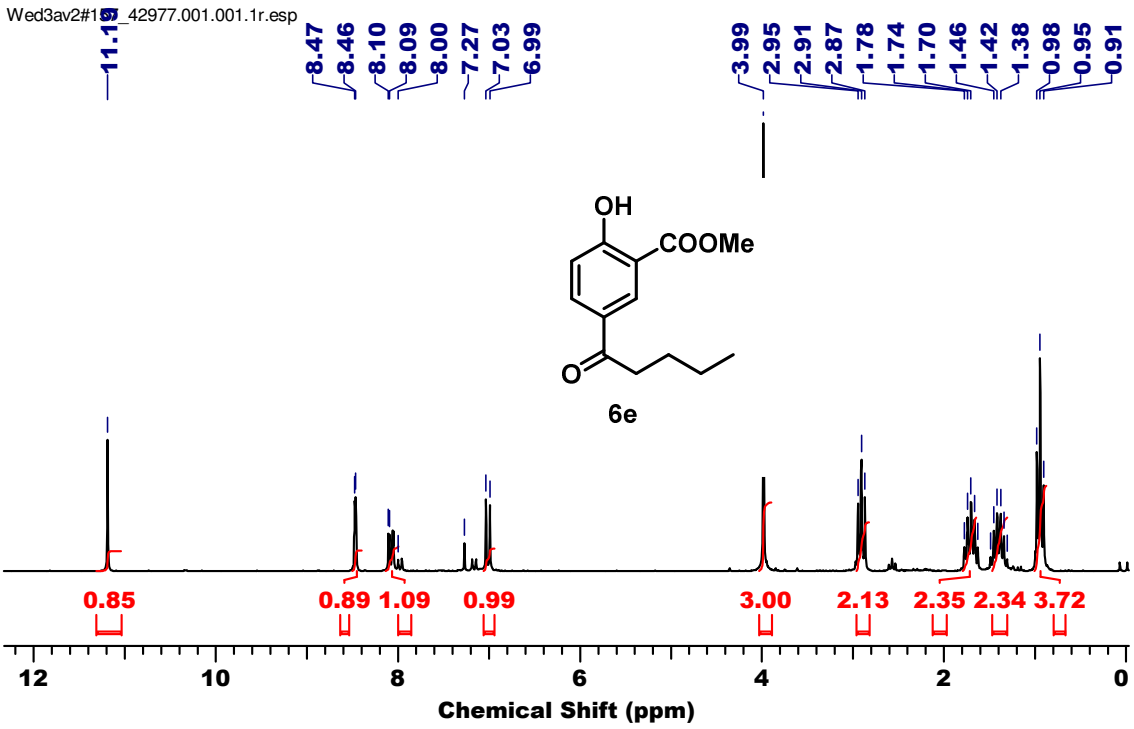

CHLOROFORM-d
198.54
161.40
131.17
129.51
115.52
77.00
26.25
OH
O
6a
200
150
100
50
0
Chemical Shift (ppm)

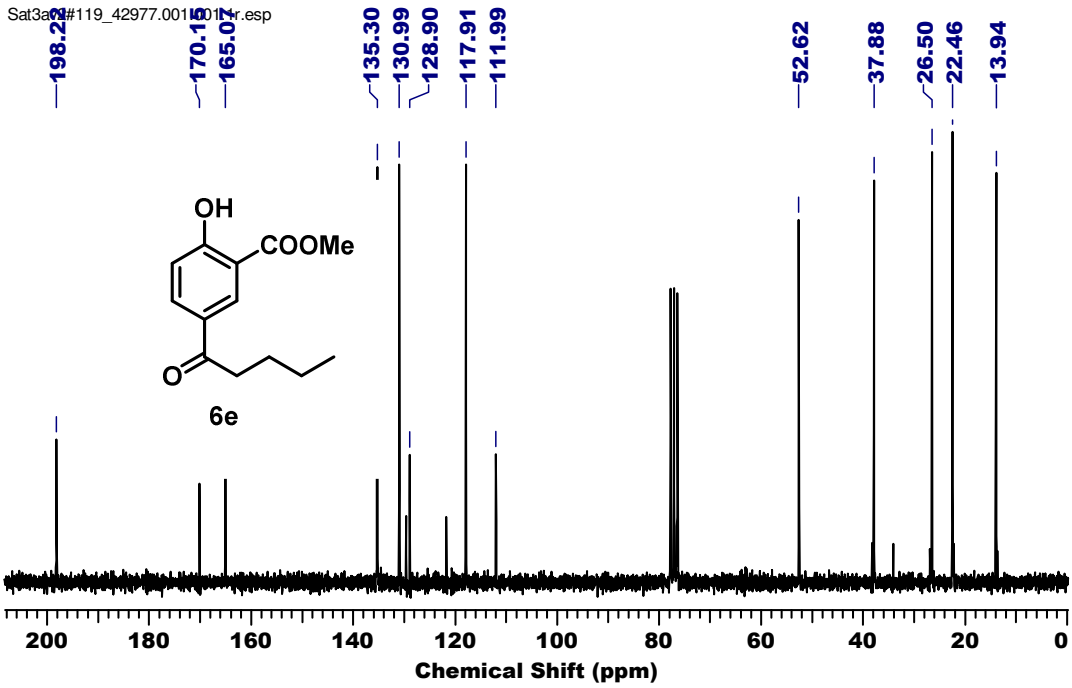

CHLOROFORM-d
TMS
7.90
7.88
7.26
6.90
6.88
2.93
2.91
2.89
1.74
1.73
1.71
1.36
1.35
1.34
1.33
0.92
0.90
0.88
0.00
OH
O
6c
1.99
2.06
2.04
2.30
3.66
3.56
8
7
6
5
4
3
2
1
0
-1
Chemical Shift (ppm)


CHLOROFORM-d
200.19
130.84
115.49
96.19
77.00
38.31
31.66
24.57
22.56
14.02
OH
O
6c
200
150
100
50
0
Chemical Shift (ppm)


CHLOROFORM-d
7.87
7.86
7.85
7.85
7.67
7.66
7.27
7.01
6.99
3.89
2.54
2.33
OAc
OMe
Me
O
6d
0.97
0.92
1.10
3.00
3.15
3.08
9
8
7
6
5
4
3
2
1
Chemical Shift (ppm)


195.97
168.80
155.23
139.56
130.43
128.10
123.17
111.57
77.32
77.06
76.81
56.12
26.29
20.58
OAc
OMe
Me
O
6d
200
180
160
140
120
100
80
60
40
20
Chemical Shift (ppm)


Wed3av2#157_42977.001.001.1r.esp
11.15
8.47
8.46
8.10
8.09
8.00
7.27
7.03
6.99
3.99
2.95
2.91
2.87
1.78
1.74
1.70
1.46
1.42
1.38
0.98
0.95
0.91
OH
COOMe
O
6e
0.85
0.89
1.09
0.99
3.00
2.13
2.35
2.34
3.72
12
10
8
6
4
2
0
Chemical Shift (ppm)


198.22
170.15
165.01
135.30
130.99
128.90
117.91
111.99
52.62
37.88
26.50
22.46
13.94
OH
COOMe
O
6e
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)