Supplementary Information

Organocatalytic regiospecific synthesis of 1*H*-indene-2-carbaldehyde derivatives: Suppression of cycloolefin isomerisation by employing sterically demanding catalyst

Hui Mao,[a§] Dong Wan Kim,[a§] Hun Yi Shin,[a§] Choong Eui Song*[b] and Jung Woon Yang*[a]

[a] Department of Energy Science, Sungkyunkwan University, Suwon 440-746, Republic of Korea
[b] Department of Chemistry, Sungkyunkwan University, Suwon 440-746, Republic of Korea

E-mail: s1673@skku.edu (C. E. Song); jwyang@skku.edu (J. W. Yang), Tel: +82-31-299-4276

§ These authors contributed equally to this work

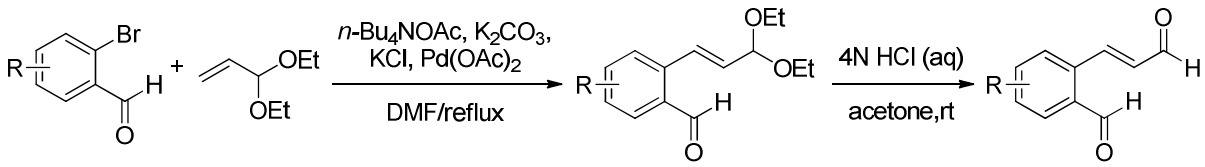
Contents

General Remarks

Thin-layer chromatography (TLC) was performed on Merck silica gel 60 F254. ^{1}H NMR spectra were recorded on a Varian at 500 MHz in $CDCl_3$ (δ 7.26 ppm) or DMSO-d_6 (δ 2.50 ppm), ^{13}C NMR spectral measurements were performed at 125 MHz using $CDCl_3$ (δ 77.16 ppm) or DMSO-d_6 (δ 39.52 ppm), ^{19}F NMR spectral measurements were performed at 470 MHz using $CDCl_3$. The terms m, s, d, t, and q. represent multiplet, singlet, doublet, triplet, and quadruplet, respectively. Commercial grade reagents and solvents were used without further purification. Mass analysis was performed using on an EI/DFS-Magnetic Sector mass spectrometer. Melting points were determined using a melting point apparatus.

General Procedure for the Synthesis of *ortho*-formyl *trans*-cinnamaldehydes (1a-1f and 1h-1i, Procedure A)

The following procedure was modified from a previously reported protocol [1]:



To a stirred solution of 2-bromobenzaldehyde (5 mmol) in 10 mL of DMF, acrolein diethyl ether acetal (1.302 g, 10 mmol), *n*-Bu_4NOAc (3.015 g, 10 mmol), K_2CO_3 (1.04 g, 7.5 mmol), KCl (372.8 mg, 5 mmol), and $Pd(OAc)_2$ (33.7 mg, 0.15 mmol) were added. The mixture was stirred at 90 °C for *ca*. 2 hours. After cooling, the reaction mixture was quenched with brine and extracted with diethyl ether. The combined organic layers were dried using sodium sulphate, filtered, and concentrated in *vacuo* to afford the crude mixture. Subsequently, to the solution of the mixture in acetone was added aqueous 4N HCl solution slowly at room temperature. After 30 min, the reaction mixture was quenched using brine and extracted with diethyl ether. The combined organic layers were dried using sodium sulphate, filtered, and concentrated in *vacuo*. The residue was purified by flash chromatography on silica gel (ethyl acetate/hexane) to afford the corresponding *o*-formyl *trans*-cinnamaldehydes (**1a-1f** and **1h-1i**).

General Procedure for the Synthesis of 1*H*-Indene-2-Carbaldehydes (4a-4j and 4'd-4'i, Procedure B)

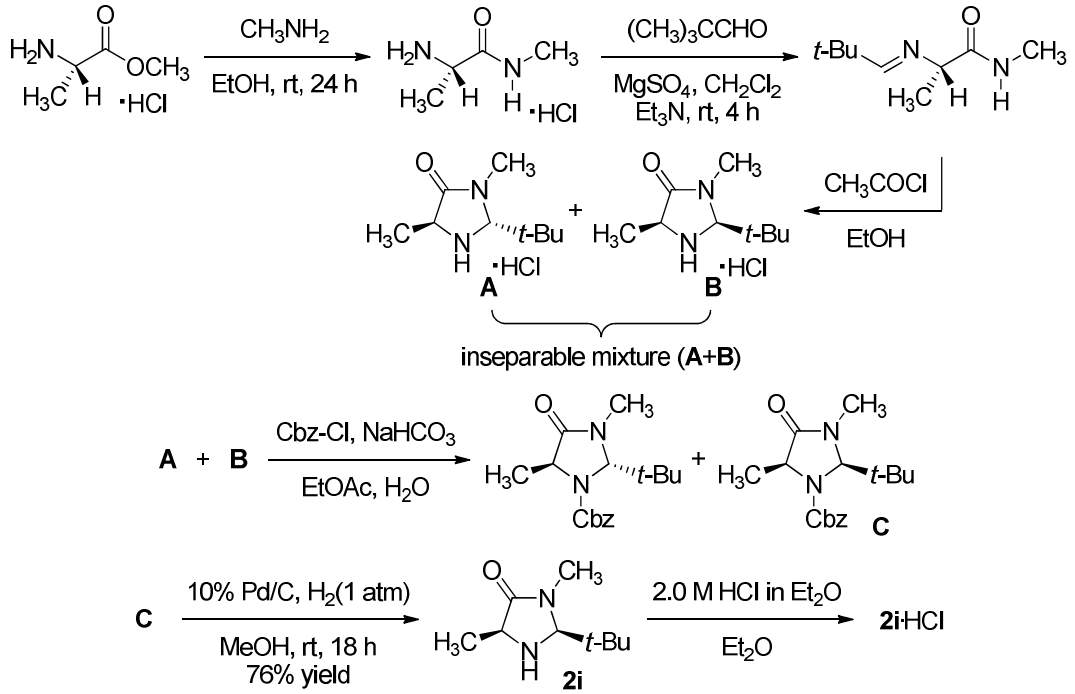
To a stirred solution of *o*-formyl (or acetyl) *trans*-cinnamaldehydes (0.5 mmol) in 5 mL of THF, Hantzsch ester **3a** (1.2 equiv, 0.6 mmol) in combination with either catalyst **2c** or **2h** (20 mol%, 0.1 mmol) were added. The mixture was stirred at room temperature for 1-20 h and monitored using thin layer chromatography. The reaction mixture was quenched with water and extracted with diethyl ether. The combined organic layers were dried over sodium sulphate, filtered, and concentrated in *vacuo*. The residue was purified by flash chromatography on silica

gel (diethyl ether/pentane) to afford the corresponding 1*H*-indene-2-carbaldehydes (**4a-4j** and **4'd-4'i**).

Synthesis of (2S,5S)-2-(*tert*-Butyl)-3,5-Dimethylimidazolidin-4-One (2i)

Catalyst **2i** was synthesized according to known procedure (with a slight modification) through the synthesis of compound **C**.[2]

- **Procedure for the hydrogenation of (2*R*,5*S*)-benzyl 2-(*tert*-butyl)-3,5-dimethyl-4-oxoimidazolidine-1-carboxylate (C):** To a solution of (2*R*,5*S*)-benzyl 2-(*tert*-butyl)-3,5-dimethyl-4-oxoimidazolidine-1-carboxylate (240.0 mg, 0.788 mmol) in EtOH/EtOAc (v/v=1:1, 7.8 mL) was added 10% Pd/C (8.4 mg, 0.078 mmol). The mixture was stirred under a static H_2 atmosphere (balloon) for 18 h. The reaction mixture was filtered through a pad of Celite, rinsing with EtOAc, and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (ethyl acetate/hexanes = 1:1) to give the corresponding product **2i** (102.4 mg, 76%).

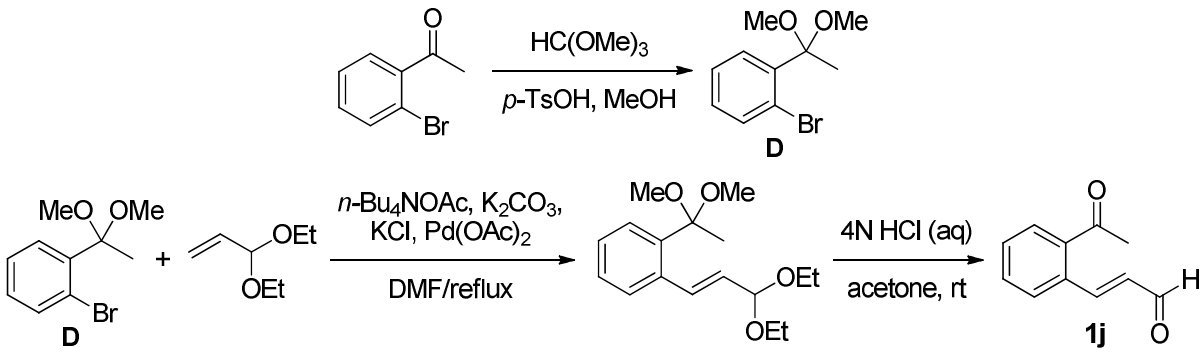


(2*R*,5*S*)-Benzyl 2-(*tert*-butyl)-3,5-dimethyl-4-oxoimidazolidine-1-carboxylate (C): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38–7.32 (m, 5H), 5.20–5.14 (m, 2H), 5.00 (brs, 1H), 4.24 (brs, 1H), 2.97 (s, 3H), 1.50 (d, J = 7.0 Hz, 2H), 0.99 (s, 9H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 172.25, 156.73, 136.21, 128.76, 128.46, 127.97, 82.48, 67.74, 56.30, 37.73, 31.66, 26.65, 18.00 ppm.

(2*S*,5*S*)-2-(*tert*-Butyl)-3,5-dimethylimidazolidin-4-one (2i)·HCl: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.59 (brs, 1H), 4.06 (brs, 1H), 3.03 (s, 3H), 1.81 (d, J = 6.4 Hz, 3H), 1.27 (s, 9H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 170.00, 81.13, 53.36, 35.54, 31.62, 25.57, 15.67 ppm.

Synthesis of (*E*)-3-(2-acetylphenyl)acrylaldehyde (1j)

Compound **1j** was synthesized according to general procedure A (with a slight modification) through the synthesis of compound **D** as starting material.



1-Bromo-2-(1,1-dimethoxyethyl)benzene (D): The physical and spectral data were identical to those previously reported for this compound.[3] Colorless oil; yield 90%; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.80 (dd, J = 7.9 Hz, 1.7 Hz, 1H), 7.59 (dd, J = 7.9 Hz, 1.1 Hz, 1H), 7.30–7.27 (m, 1H), 7.12–7.09 (m, 1H), 3.19 (s, 6H), 1.67 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 140.53, 134.89, 129.94, 129.24, 127.23, 120.53, 101.53, 48.73, 22.95 ppm.

2-Acetyl *trans*-cinnamaldehyde (1j): Yellow solid; yield 40%; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 9.74 (d, J = 7.8 Hz, 1H), 8.14 (d, J = 15.9 Hz, 1H), 7.84 (dd, J = 7.7 Hz, 1.3 Hz, 1H), 7.68–7.61 (m, 1H), 7.58 (td, J = 7.5 Hz, 1.2 Hz, 1H), 7.53 (td, J = 7.5 Hz, 1.4 Hz, 1H), 6.57 (dd, J = 15.9 Hz, 7.8 Hz, 1H), 2.66 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 200.83, 194.20, 152.25, 137.61, 134.65, 132.49, 131.03, 130.38, 129.96, 128.63, 29.18 ppm; IR (neat) 1683, 1621, 1596, 1565, 1479, 1358, 1257, 1133, 1111, 971, 764 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{11}H_{10}O_2Na$ $[M+Na]^+$ 197.0573, found 197.0578.

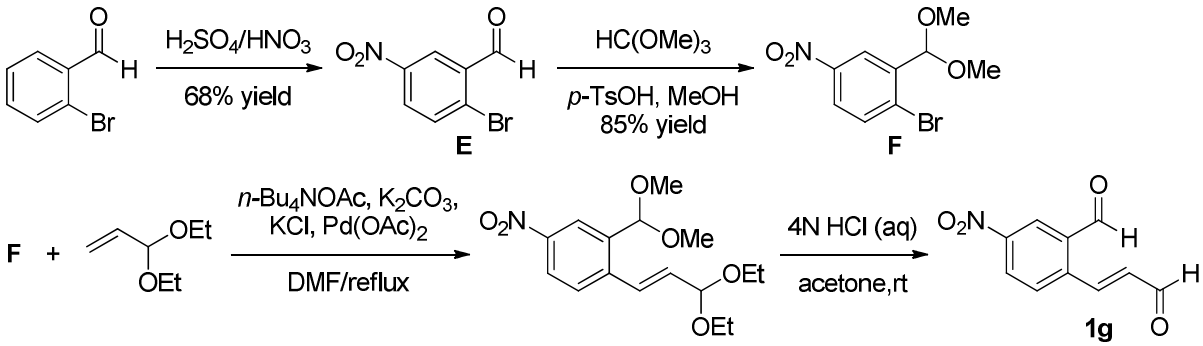
Synthesis of 4-nitro-2-formyl *trans*-cinnamaldehyde (1g)

Compound **1g** was synthesized according to general procedure A (with a slight modification) through the synthesis of compounds **E** and **F** as starting materials.

- **Procedure for the synthesis of 2-bromo-5-nitrobenzaldehyde (E):** To a mixture of 65% nitric acid (2 mL) and concentrated sulfuric acid (15 mL) was added dropwise 2-bromobenzaldehyde (4.0 g, 21.6 mmol) at 0 °C. The mixture was stirred at room temperature for 12 h and then dumped onto 100 mL ice. The aqueous solution was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried over Na_2SO_4. Upon filtration and solvent removal, the resulting residue was purified by recrystallization from a mixture of hexanes and ethyl acetate (1:4) to give pure 2-bromo-5-nitrobenzaldehyde (3.36 g, 68% yield) as a white crystal.

- **Procedure for the synthesis of 1-bromo-2-(dimethoxymethyl)-4-nitrobenzene (F):** To a

stirred solution of 2-bromo-5-nitrobenzaldehyde (1.14 g, 5.00 mmol) and trimethyl orthoformate (2.19 mL, 20.00 mmol) in MeOH (20 mL) were added catalytic amount of *p*-TsOH·H_2O (47.56 mg, 0.25 mmol). The mixture was stirred under reflux conditions for 3 hrs. After cooling, the reaction mixture was quenched with sat. $NaHCO_3$ and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (ethyl acetate/hexanes) to give the corresponding dimethyl acetal compound **F** (1.17 g, 85%).



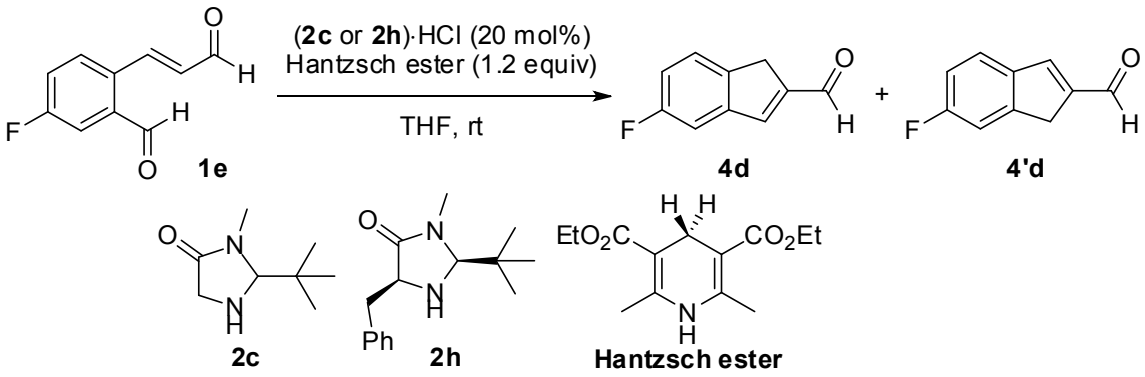
(i) 2-Bromo-5-nitrobenzaldehyde (E): The physical and spectral data were identical to those previously reported for this compound.[4] White crystal; yield 68%; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 10.39 (s, 1H), 8.73 (d, J = 2.8 Hz, 1H), 8.29 (dd, J = 8.7 Hz, 2.8 Hz, 1H), 7.89 (d, J = 8.7 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 189.37, 147.69, 135.30, 134.39, 133.00, 128.80, 124.74 ppm.

(ii) 1-Bromo-2-(dimethoxymethyl)-4-nitrobenzene (F): White solid; yield 85%; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.48 (d, J = 2.8 Hz, 1H), 8.06 (dd, J = 8.7 Hz, 2.8 Hz, 1H), 7.75 (d, J = 8.7 Hz, 1H), 5.58 (s, 1H), 3.40 (s, 1H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 147.30, 139.23, 134.16, 130.05, 124.65, 123.84, 101.75, 54.00 ppm; **HRMS** (ESI) *m*/*z* calcd for $C_9H_{10}BrNO_4$ $[M+H]^+$ 275.9866, found 275.9867.

(iii) 4-Nitro-2-formyl *trans*-cinnamaldehyde (1g): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.30 (s, 1H), 9.86 (d, J = 7.5 Hz, 1H), 8.75 (d, J = 2.4 Hz, 1H), 8.53 (s, 1H), 8.51–8.48 (m, 2H), 7.89 (d, J = 8.5 Hz, 1H), 6.74 (dd, J = 16.1 Hz, 7.5 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 192.97, 190.46, 148.98, 146.25, 141.32, 135.01, 134.36, 129.71, 128.88, 128.31 ppm; IR (neat) 1687, 1524, 1349, 1209, 1116, 977, 833, 742, 650, 640 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{10}H_7NO_4Na$ $[M+Na]^+$ 228.0267, found 228.0265.

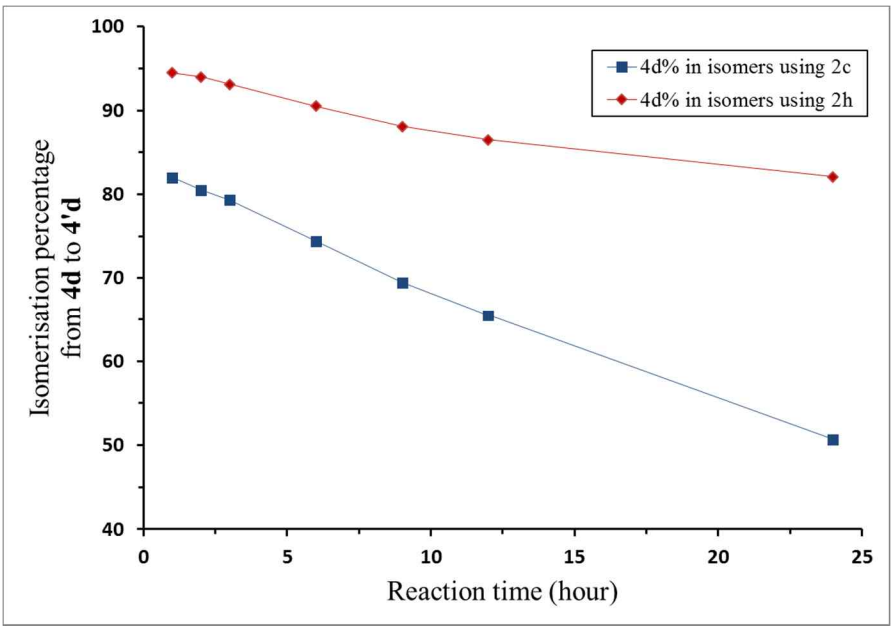
Phenomenon for Time-Dependent Cycloolefin Isomerisation

Controlled experiments are investigated by using either catalyst **2c** or **2h**.



The reaction of *o*-formyl *trans*-cinnamaldehyde **1e** with Hantzsch ester in the presence of either **2c** or **2h** as catalyst gave the corresponding indene-aldehyde **4d** as major product at initial stage. However, different regioisomer **4'd** was gradually formed with decreasing portion of **4d** at specified time point (1 h, 2 h, 3 h, 6 h, 9 h, 12 h and 24 h), which was determined by NMR analysis. These results indicate the time-dependent cycloolefin isomerisation phenomenon exists during the reaction course. The use of catalyst **2h** the isomerisation rate is much slower than that of catalyst **2c**.

Reaction time/hour	1	2	3	6	9	12	24
4d% in isomers using catalyst **2c**	82	80.5	79.3	74.4	69.5	65.5	50.7
4d% in isomers using catalyst **2h**	94.5	94	93.1	90.5	88.1	86.5	82.1



References

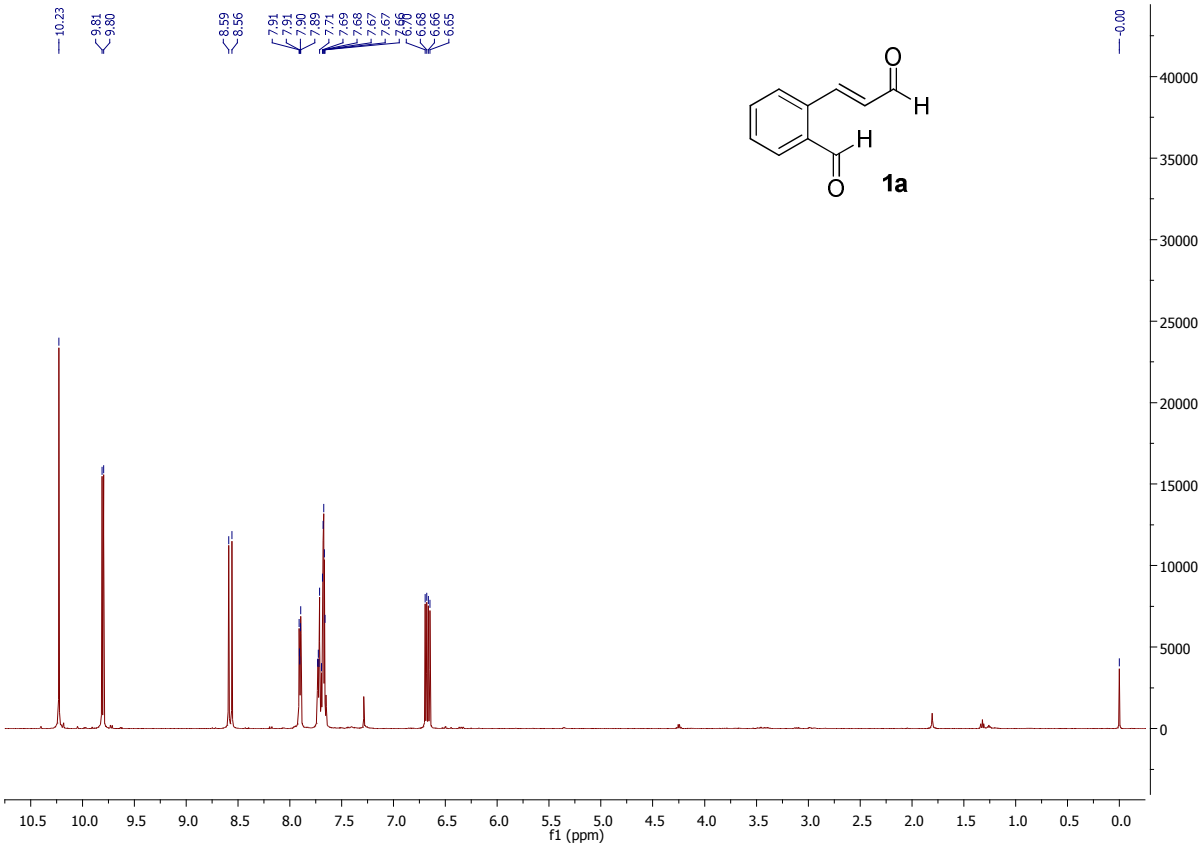
[1] J. W. Yang, M. T. Hechavarria Fonseca and B. List, *J. Am. Chem. Soc.,* 2005, **127**, 15036-15037.

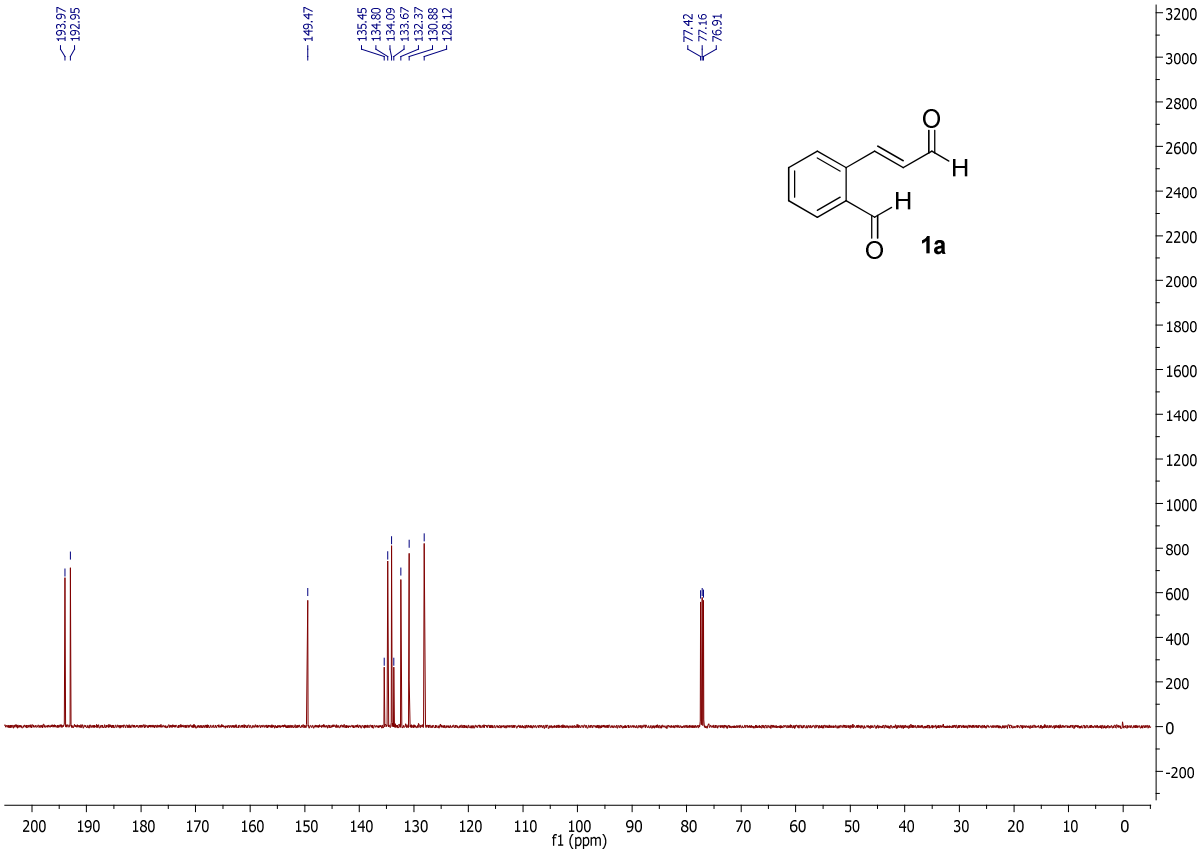
[2] T. H. Graham, B. D. Horning and D. W. C. MacMillan, *Org. Synth.,* 2011, **88**, 42-53.

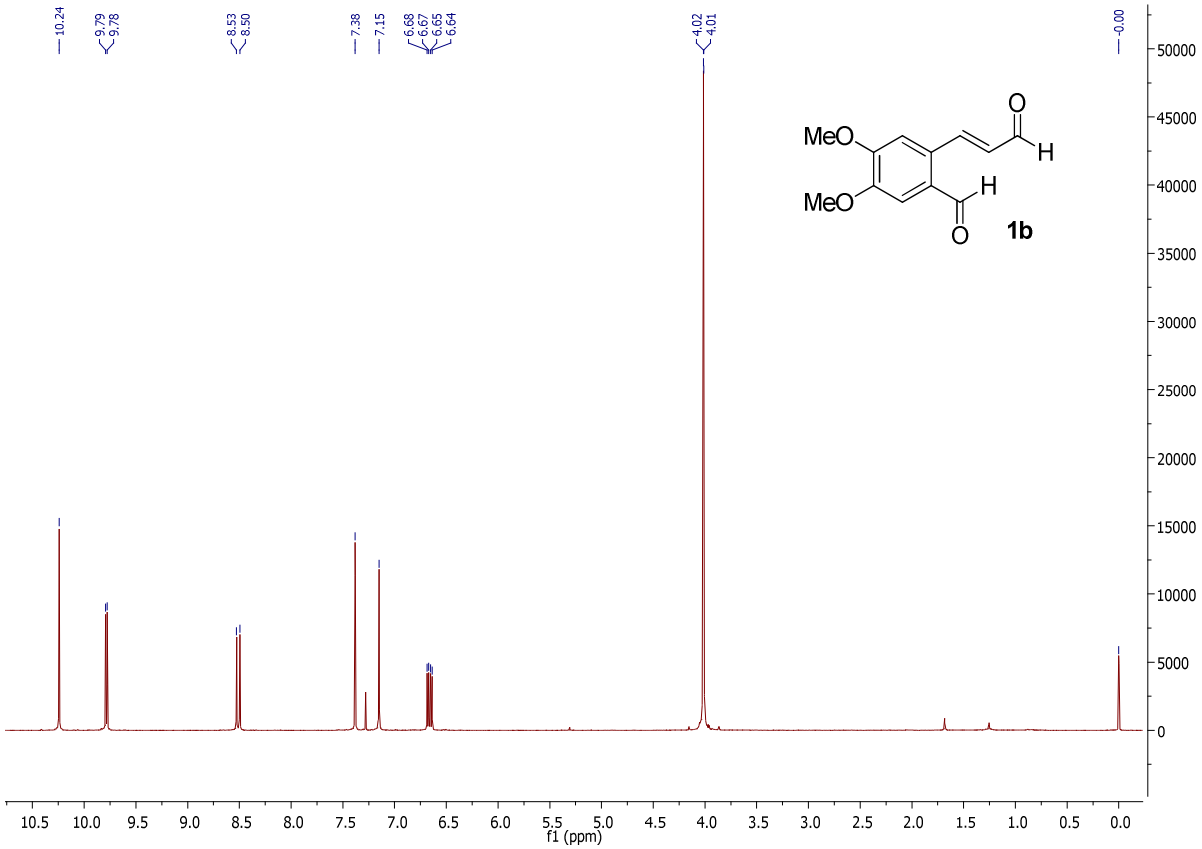
[3] Y. Fan, P. Feng, M. Liu, H. Pan and Y. Shi, *Org. Lett*., 2011, **13**, 4494-4497.

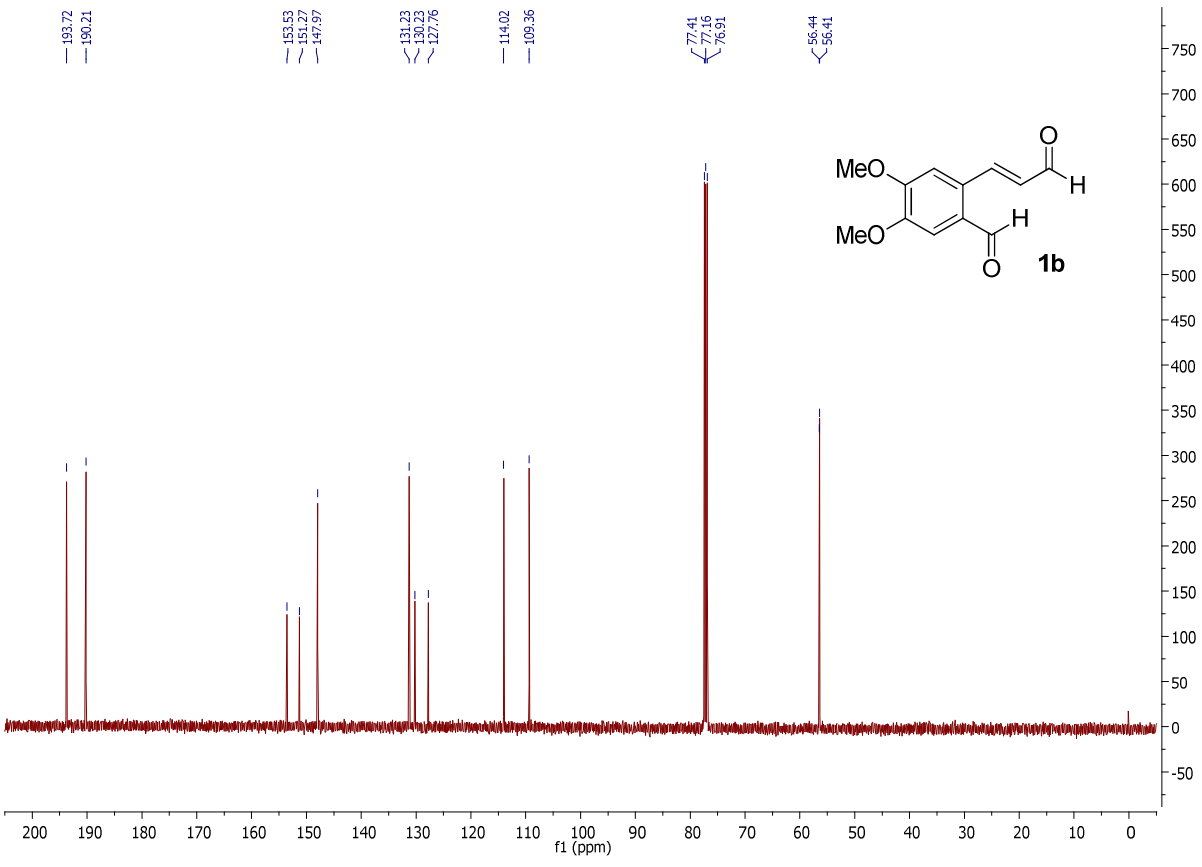
[4] E. Dubost, C. Fossey, T. Cailly, S. Rault and F. Fabis, *J. Org. Chem*., 2011, **76**, 6414-6420.

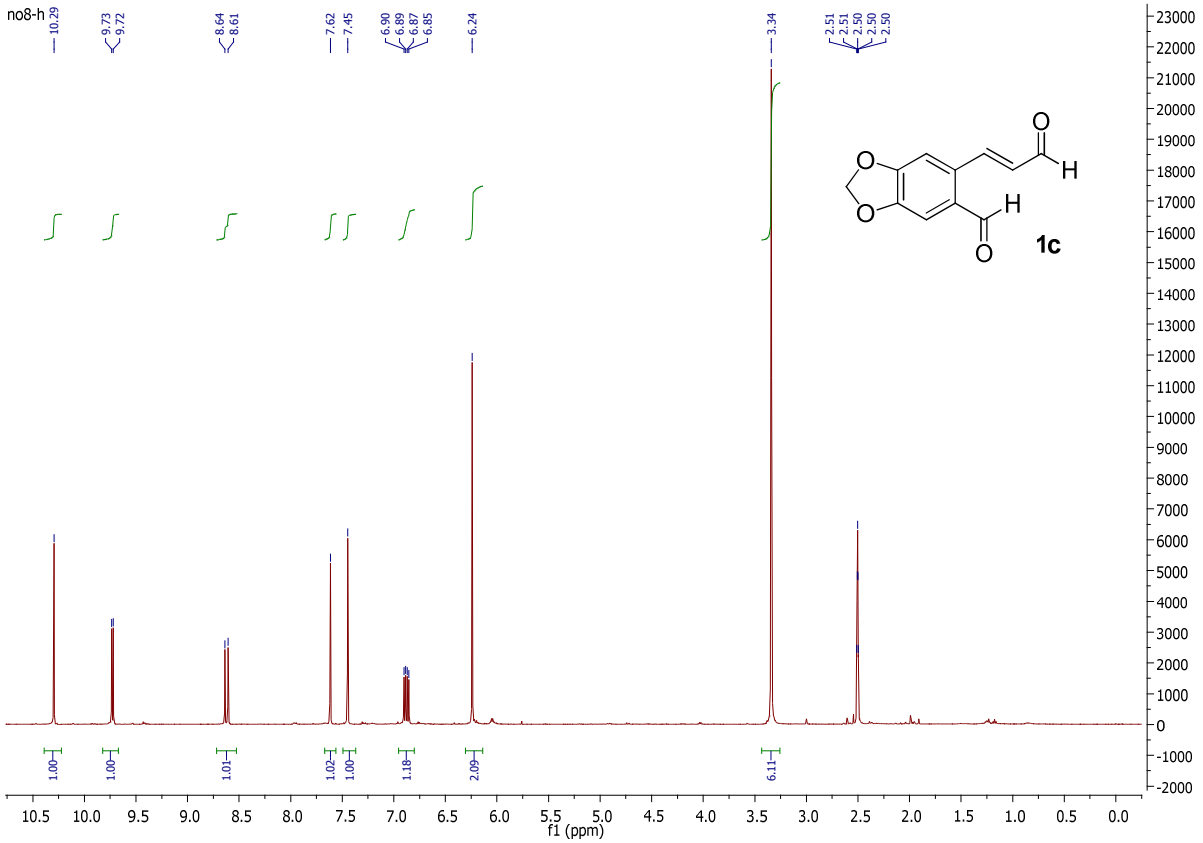
^{1}H NMR, ^{13}C NMR, and ^{19}F NMR Spectra of Products

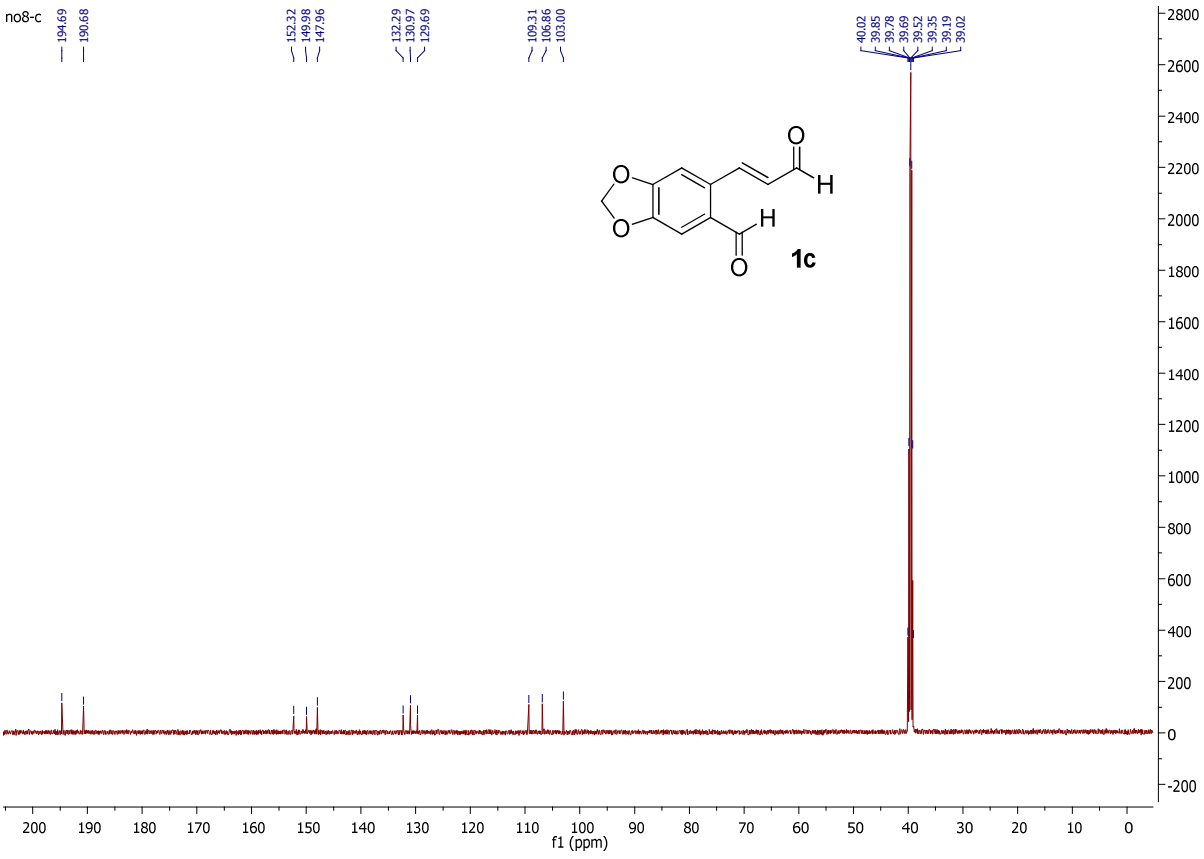


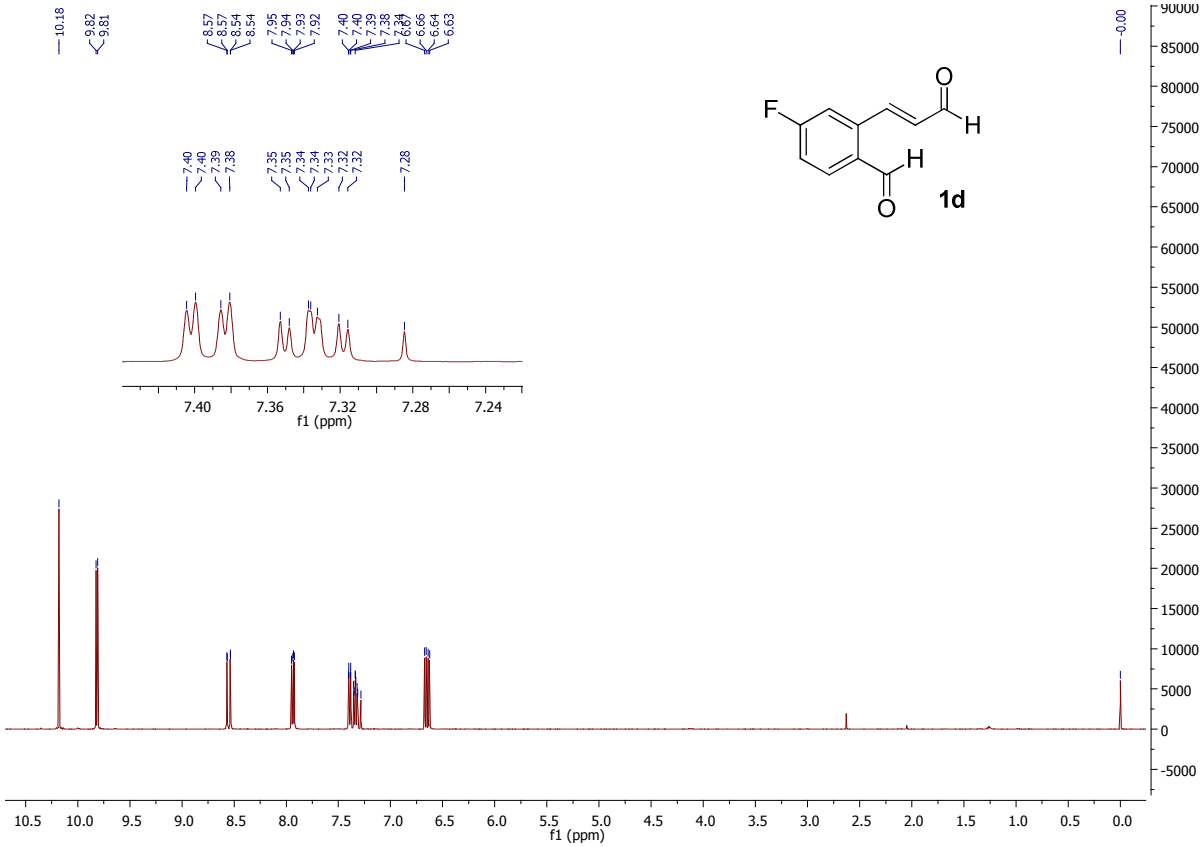


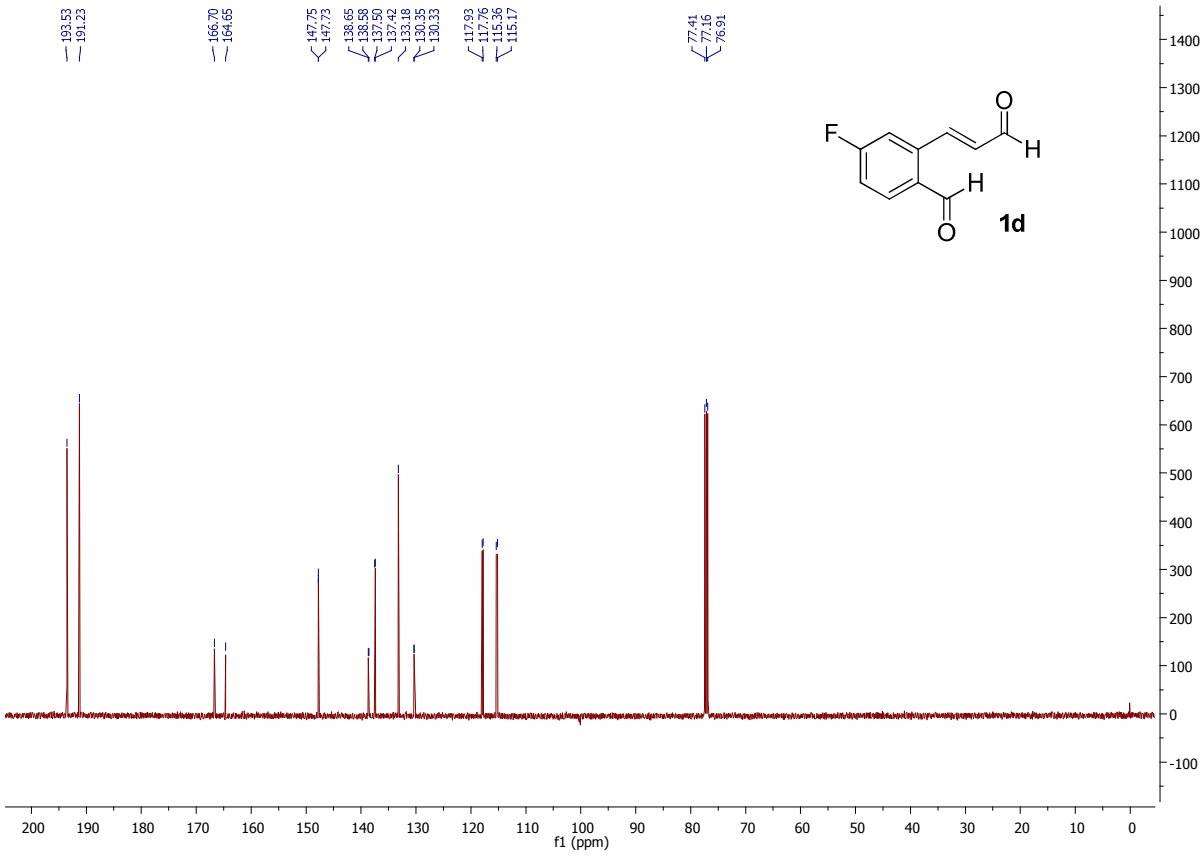

10.24
9.79
9.78
8.53
8.50
7.38
7.15
6.68
6.67
6.65
6.64
4.02
4.01
0.00
MeO
MeO
O
H
H
O
1b
f1 (ppm)

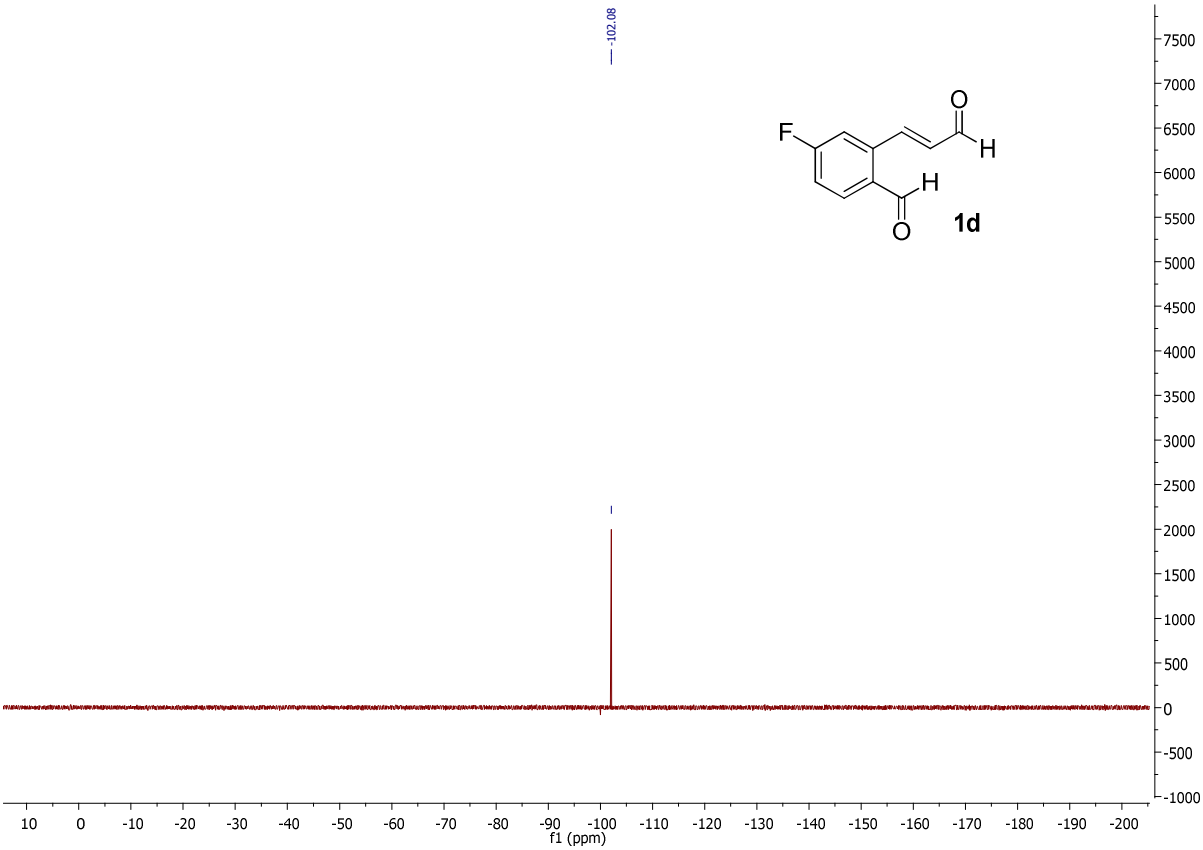

193.72
190.21
153.53
151.27
147.97
131.23
130.23
127.76
114.02
109.36
77.41
77.16
76.91
56.44
56.41
MeO
MeO
O
H
H
O
1b
f1 (ppm)

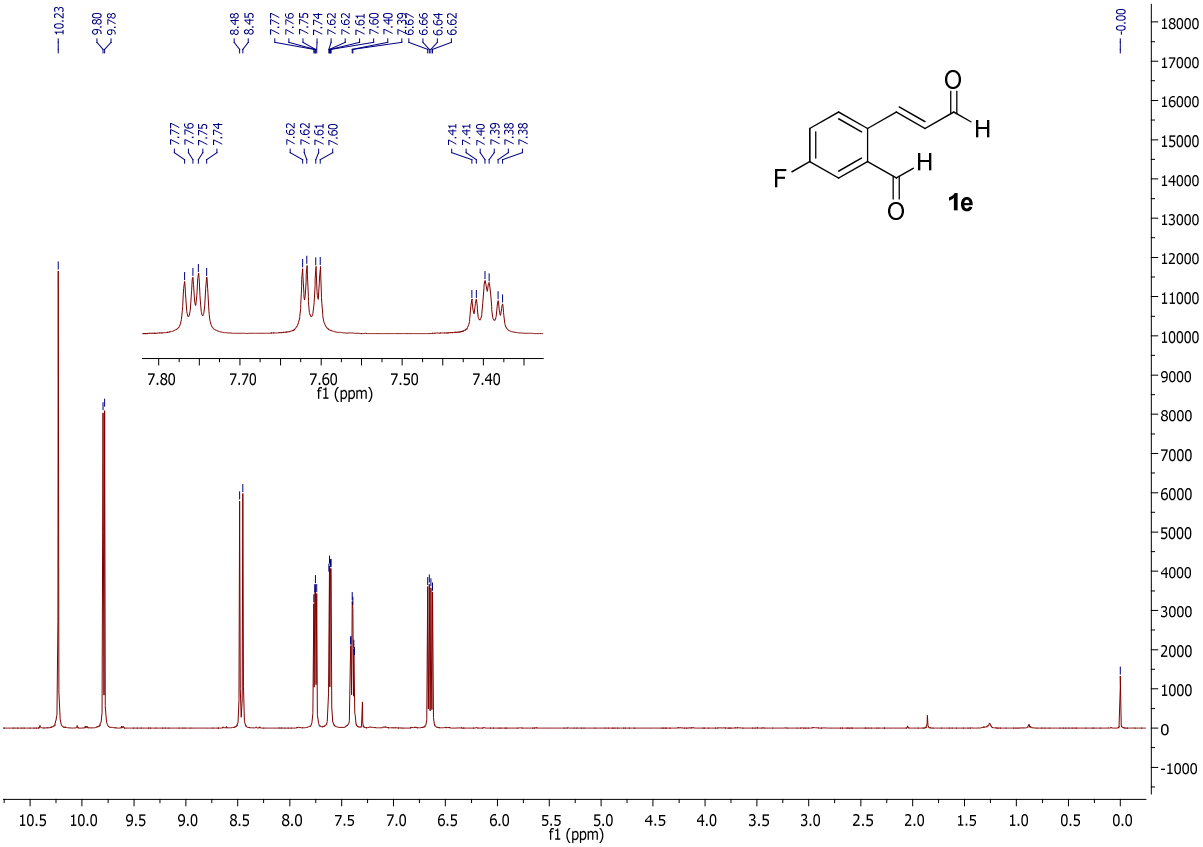

no8-h
10.29
9.73
9.72
8.64
8.61
7.62
7.45
6.90
6.89
6.87
6.85
6.24
3.34
2.51
2.51
2.50
2.50
2.50
1.00
1.00
1.01
1.02
1.00
1.18
2.09
6.11
f1 (ppm)
1c

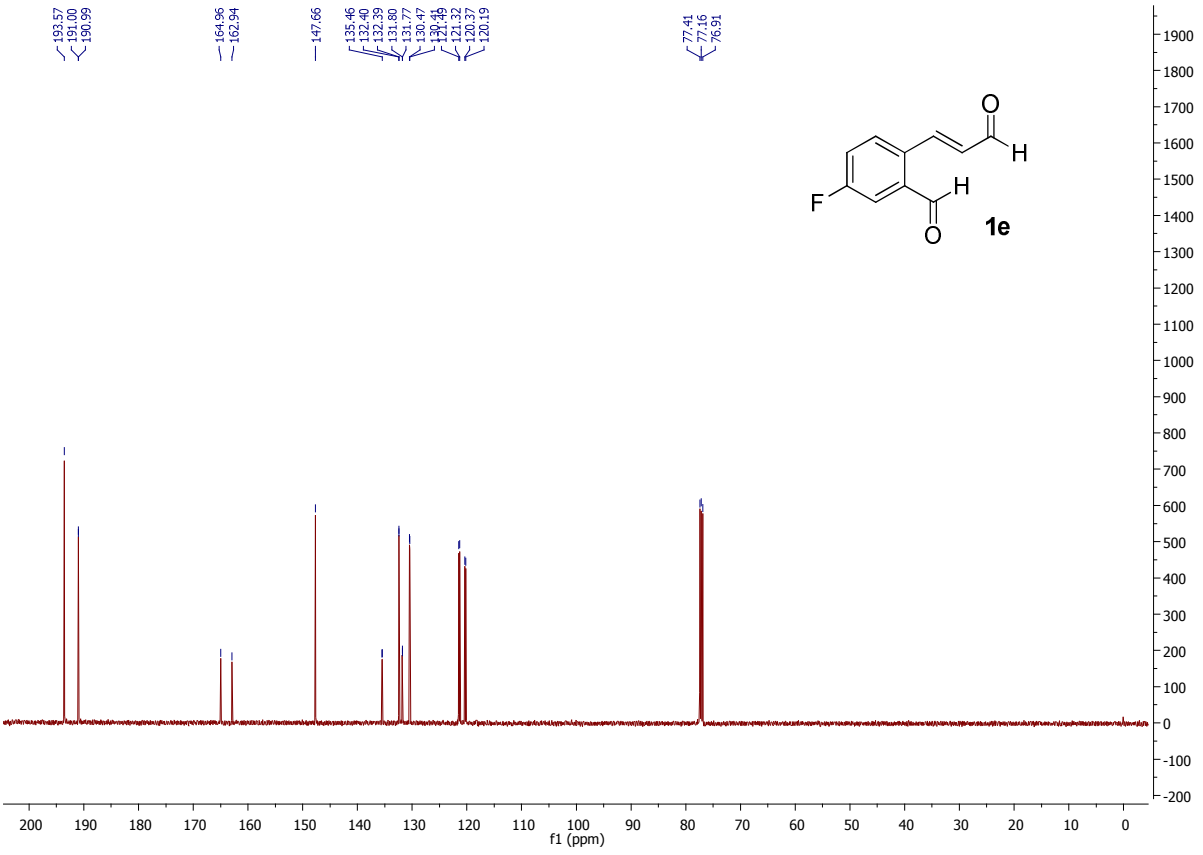

no8-c
194.69
190.68
152.32
149.98
147.96
132.29
130.97
129.69
109.31
106.86
103.00
40.02
39.85
39.78
39.69
39.52
39.35
39.19
39.02
f1 (ppm)
1c

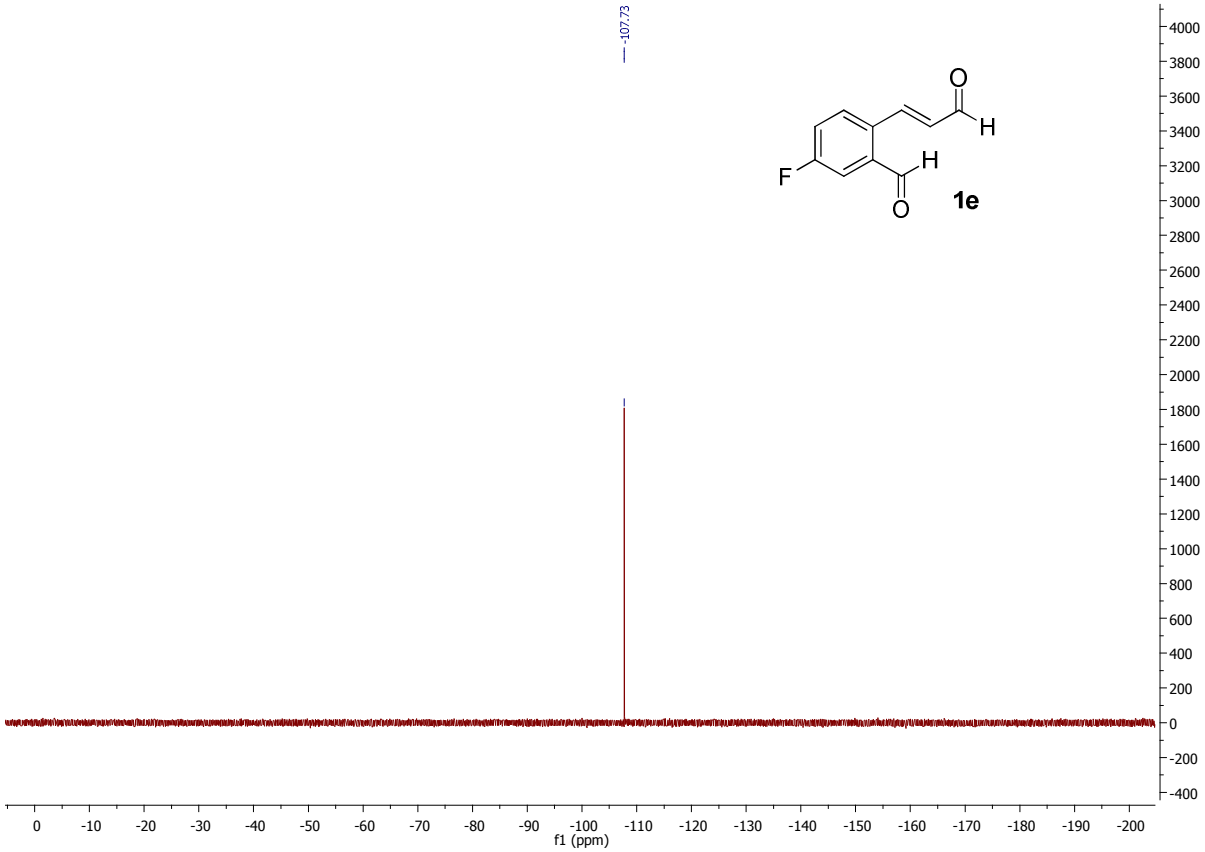

10.18
9.82
9.81
8.57
8.57
8.54
8.54
7.95
7.94
7.93
7.92
7.40
7.40
7.39
7.38
7.34
6.67
6.66
6.64
6.63
7.40
7.40
7.39
7.38
7.35
7.35
7.34
7.34
7.33
7.32
7.32
7.28
0.00
F
O
H
H
O
1d
7.40
7.36
7.32
7.28
7.24
f1 (ppm)
f1 (ppm)

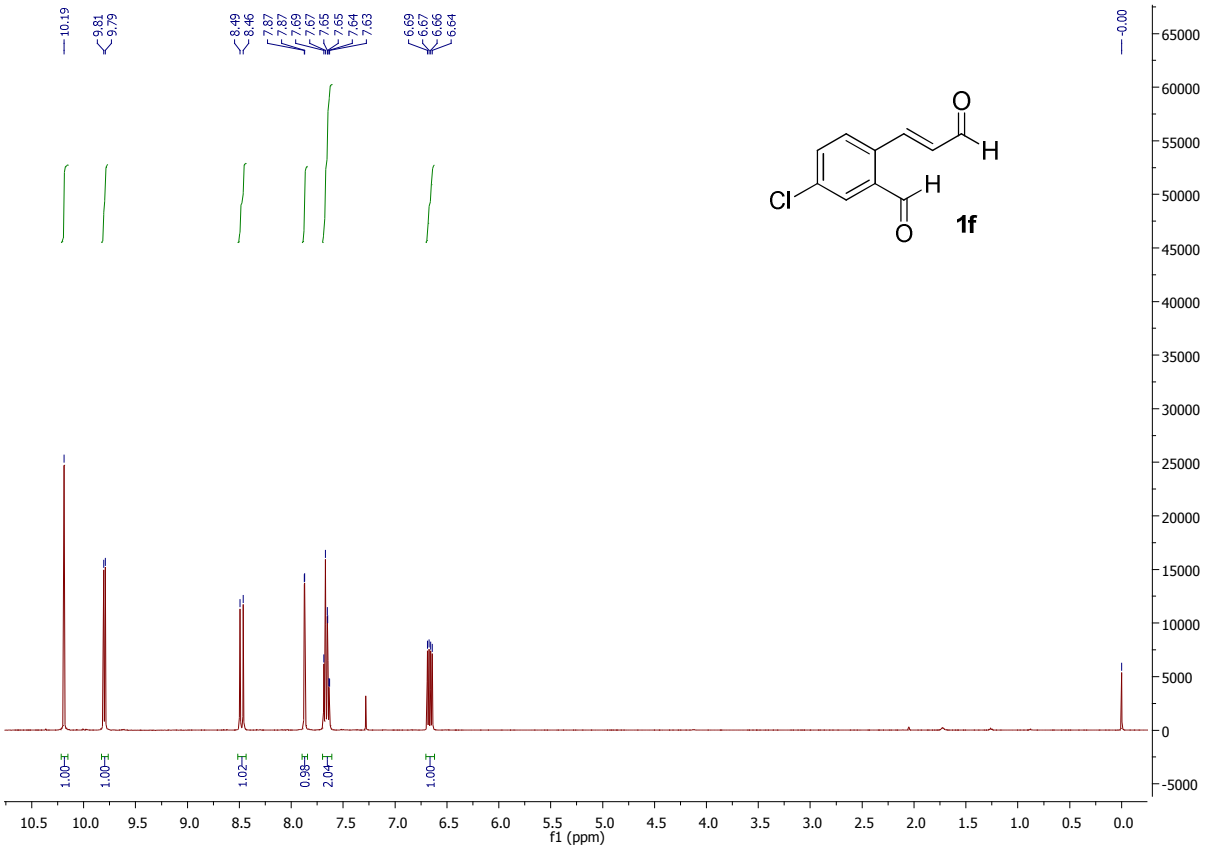

193.53
191.23
166.70
164.65
147.75
147.73
138.65
138.58
137.50
137.42
133.18
130.35
130.33
117.93
117.76
115.36
115.17
77.41
77.16
76.91
F
O
H
H
O
1d
f1 (ppm)

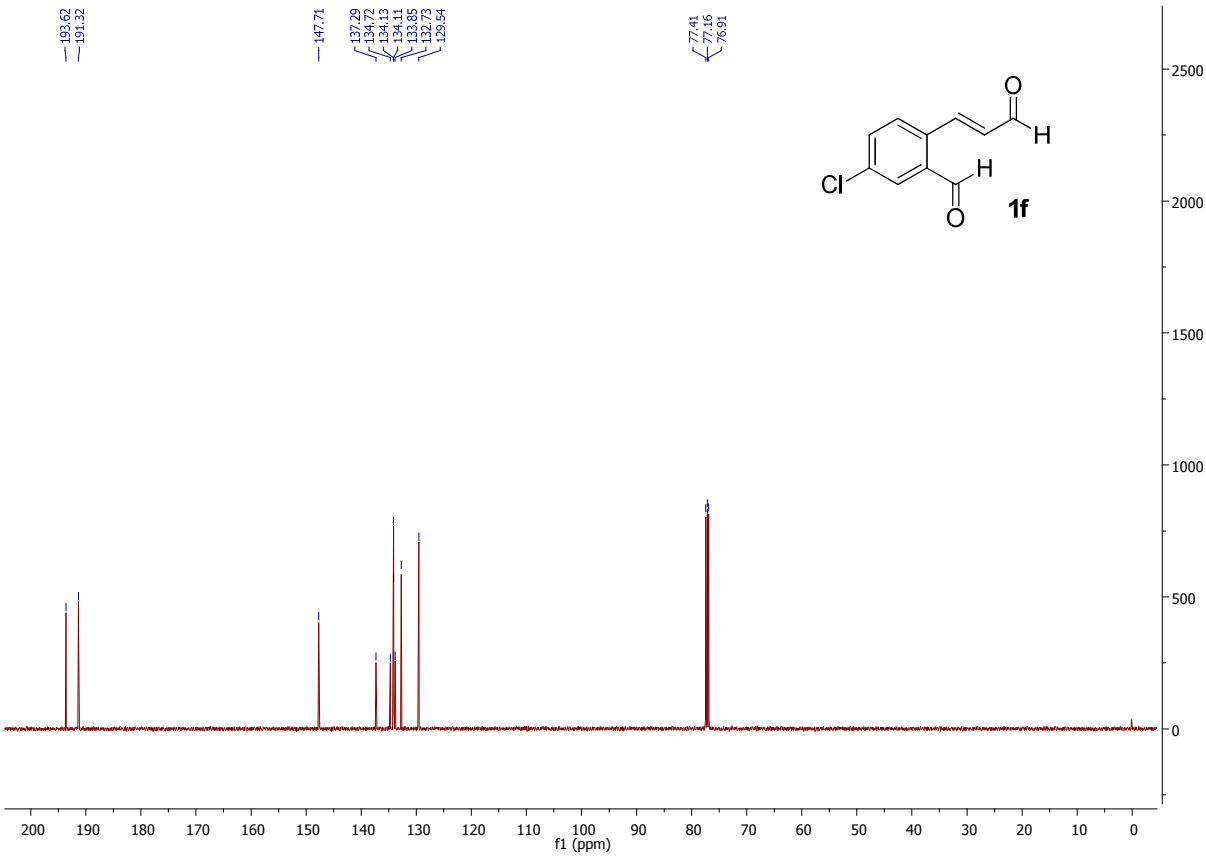

-102.08
F
O
H
H
O
1d
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
-1000
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

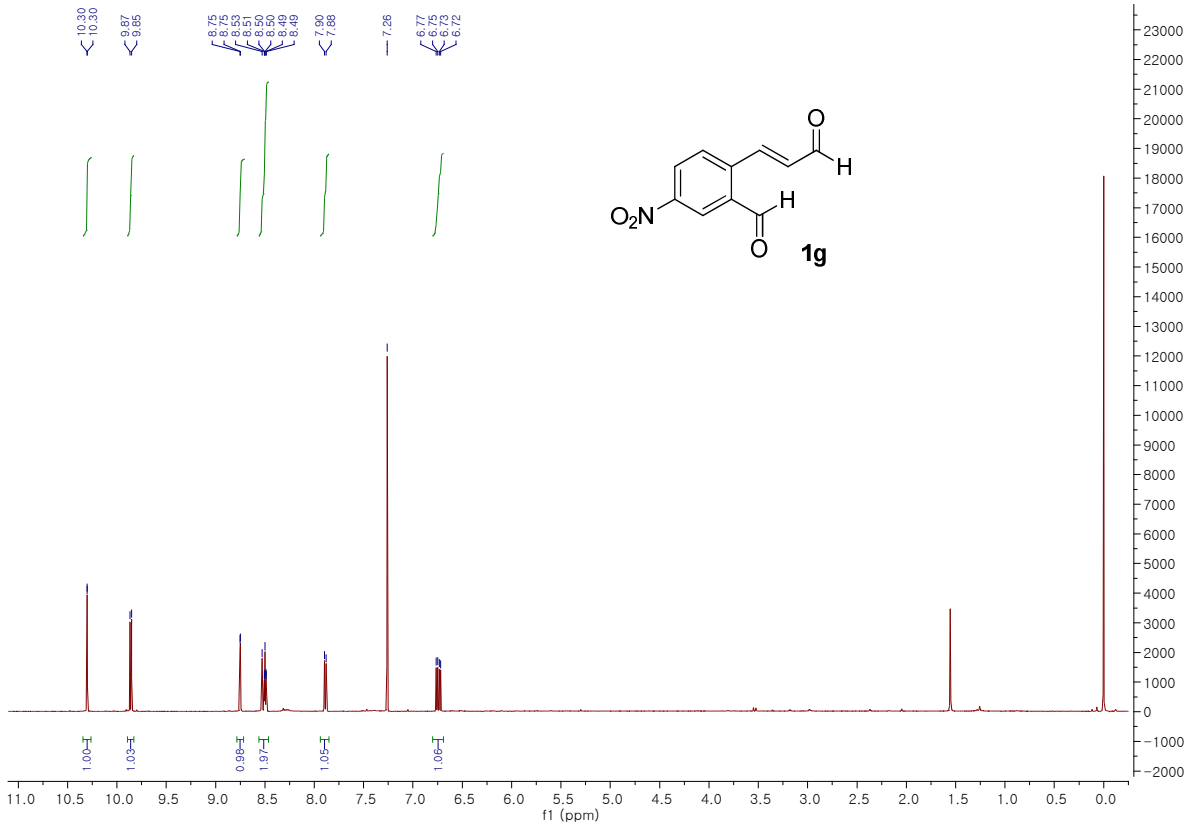

10.23
9.80
9.78
8.48
8.45
7.77
7.76
7.75
7.74
7.62
7.61
7.60
7.40
6.66
6.64
6.62
7.41
7.40
7.39
7.38
0.00
O
H
H
F
O
1e
7.80
7.70
7.60
7.50
7.40
f1 (ppm)
f1 (ppm)

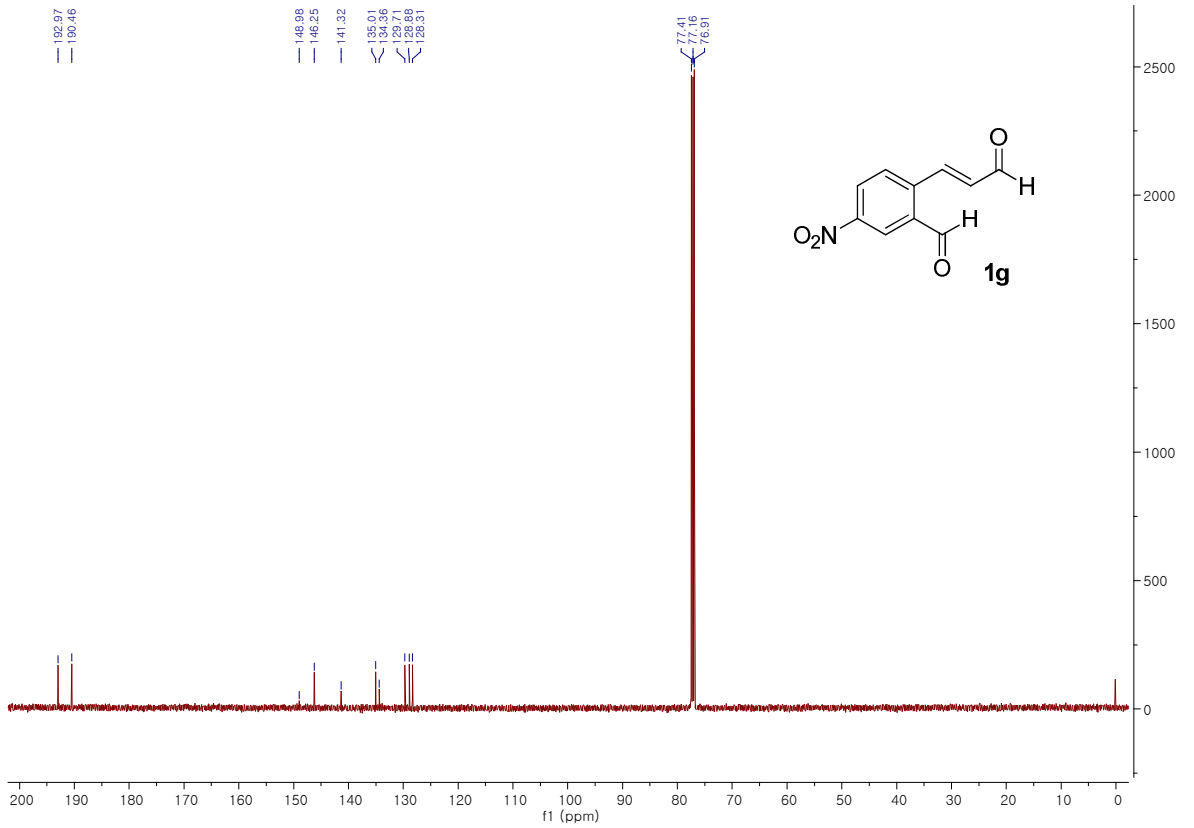

193.57
191.00
190.99
164.96
162.94
147.66
135.46
132.40
132.39
131.80
131.77
130.47
121.32
120.37
120.19
77.41
77.16
76.91
O
H
H
F
O
1e
f1 (ppm)

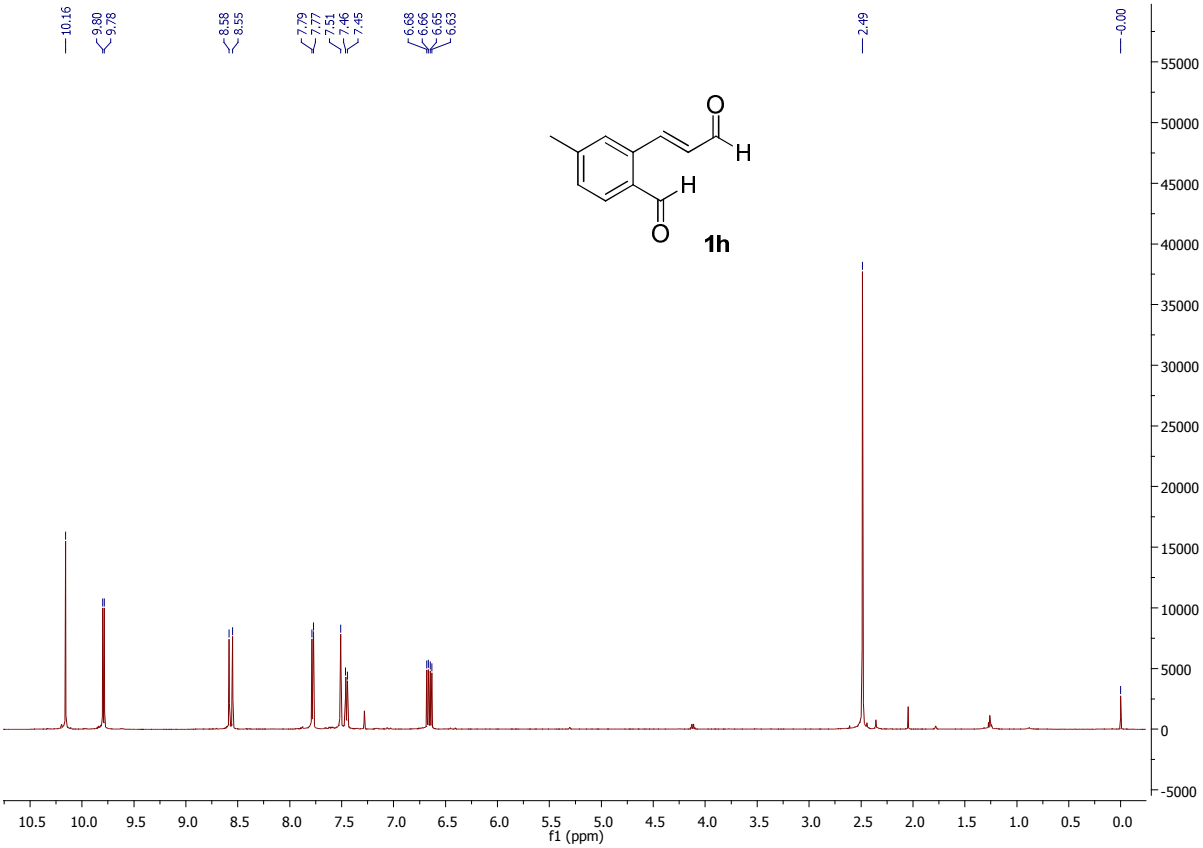

-107.73
O
H
F
H
O
1e
4000
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
-400
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

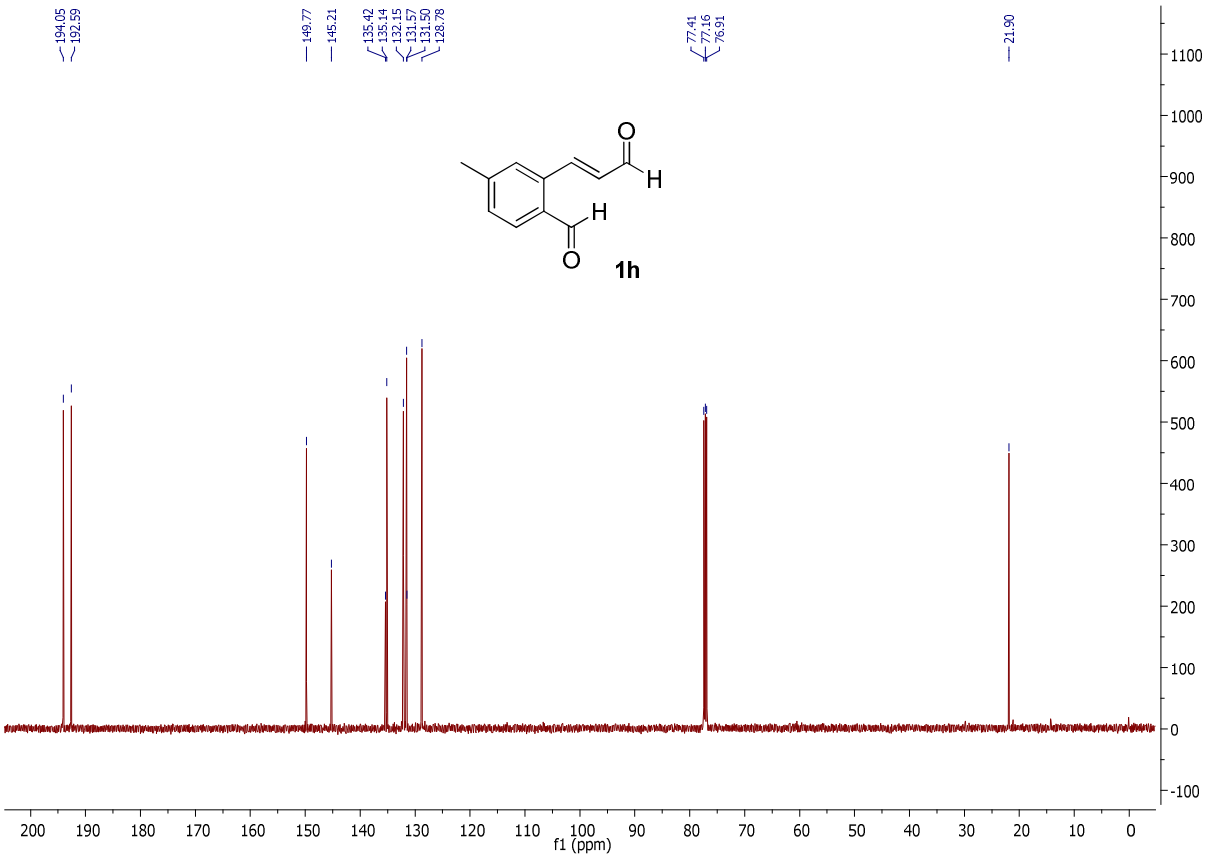

10.19
9.81
9.79
8.49
8.46
7.87
7.87
7.69
7.67
7.65
7.65
7.64
7.63
6.69
6.67
6.66
6.64
0.00
1.00
1.00
1.02
0.98
2.04
1.00
f1 (ppm)
Cl
O
H
H
O
1f

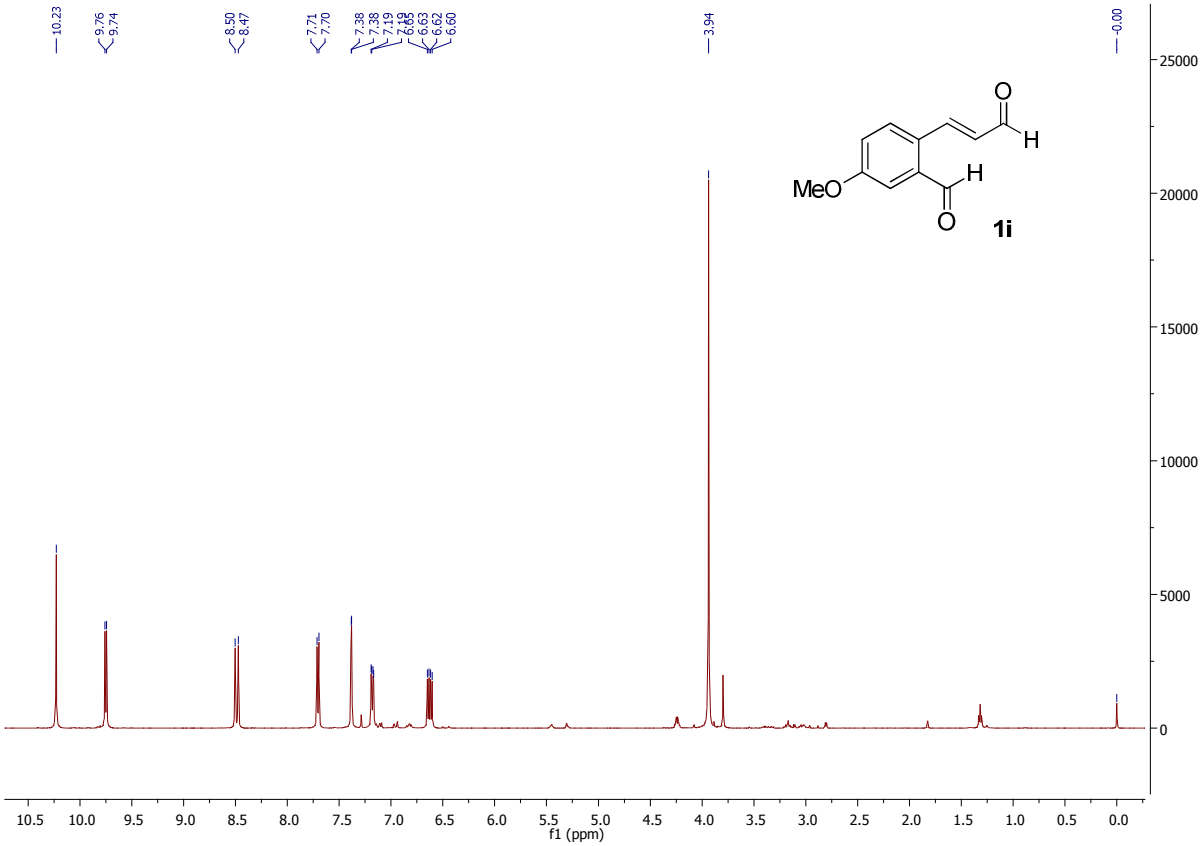

193.62
191.32
147.71
137.29
134.72
134.13
134.11
133.85
132.73
129.54
77.41
77.16
76.91
f1 (ppm)
Cl
O
H
H
O
1f

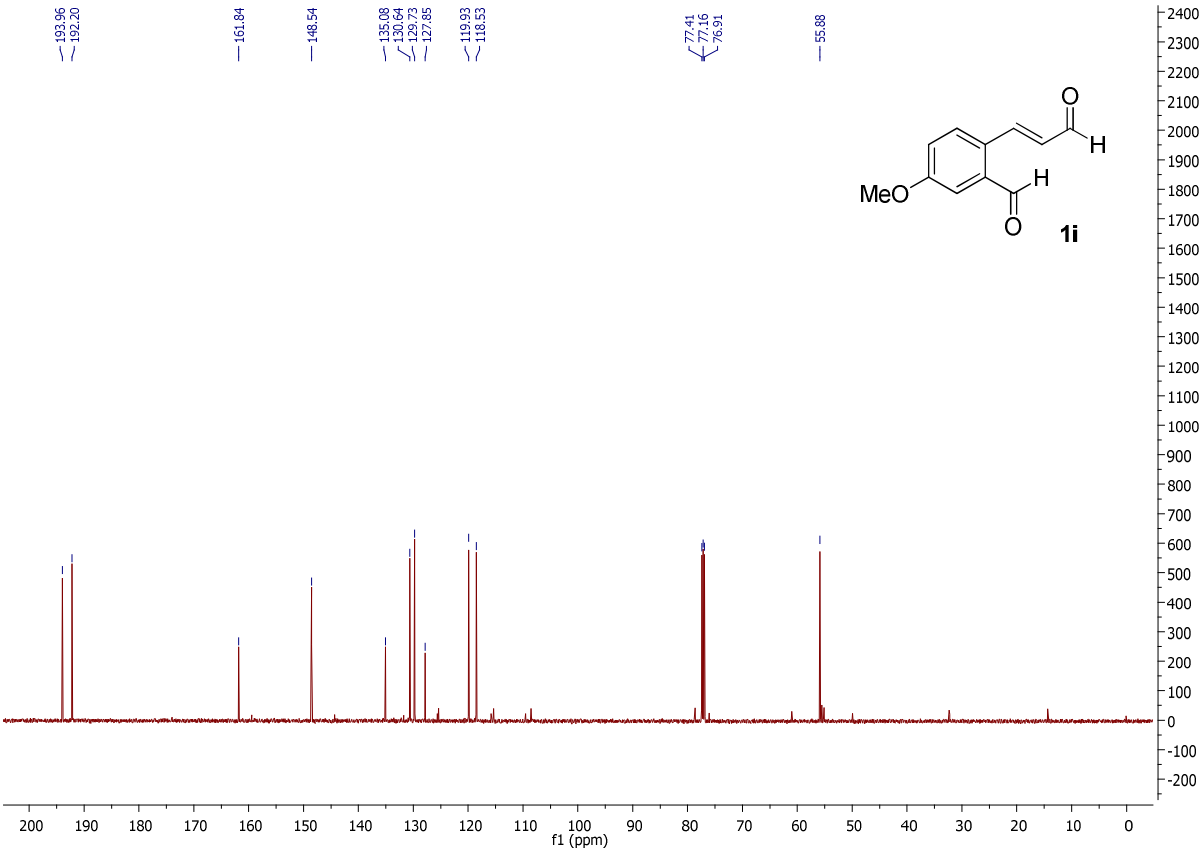

10.30
10.30
9.87
9.85
8.75
8.75
8.53
8.51
8.50
8.50
8.49
8.49
7.90
7.88
7.26
6.77
6.75
6.73
6.72
O
H
O2N
H
O
1g
1.00
1.03
0.99
1.97
1.05
1.06
f1 (ppm)

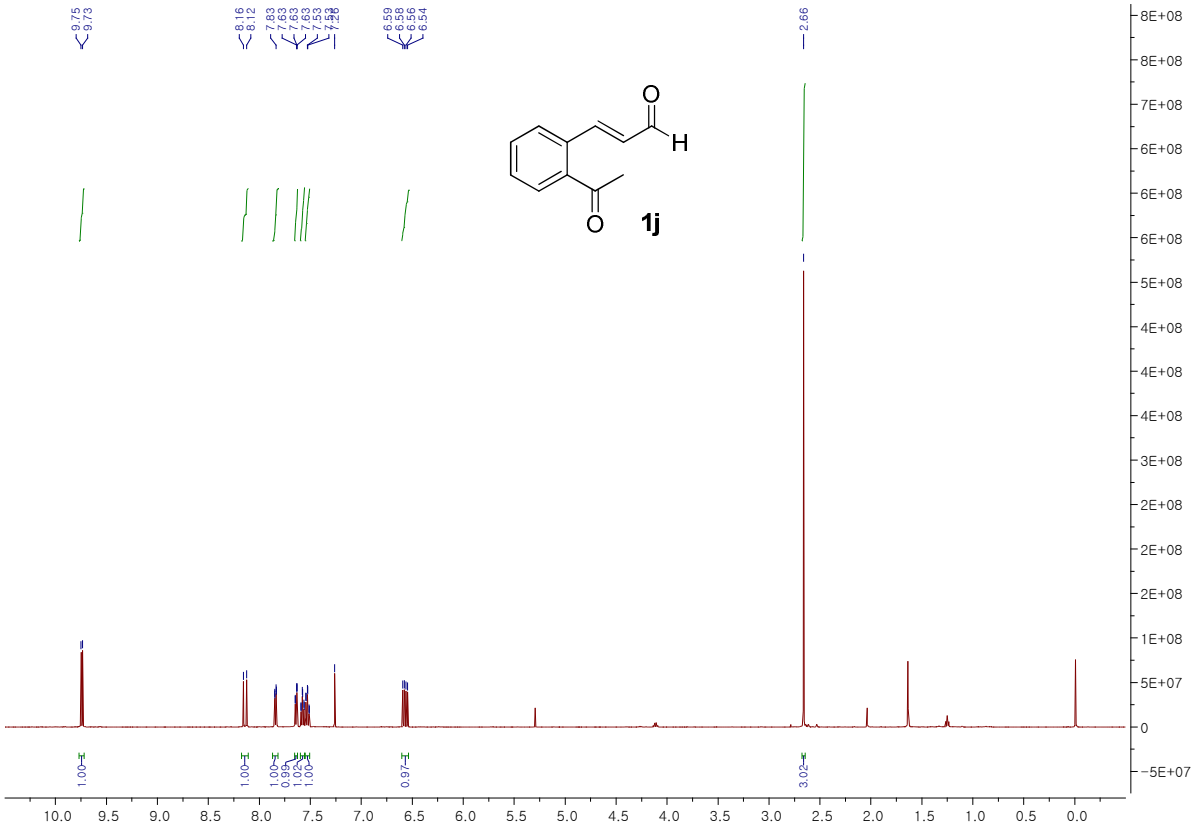

192.97
190.46
148.98
146.25
141.32
135.01
134.36
129.71
128.88
128.31
77.41
77.16
76.91
O
H
O2N
H
O
1g
f1 (ppm)

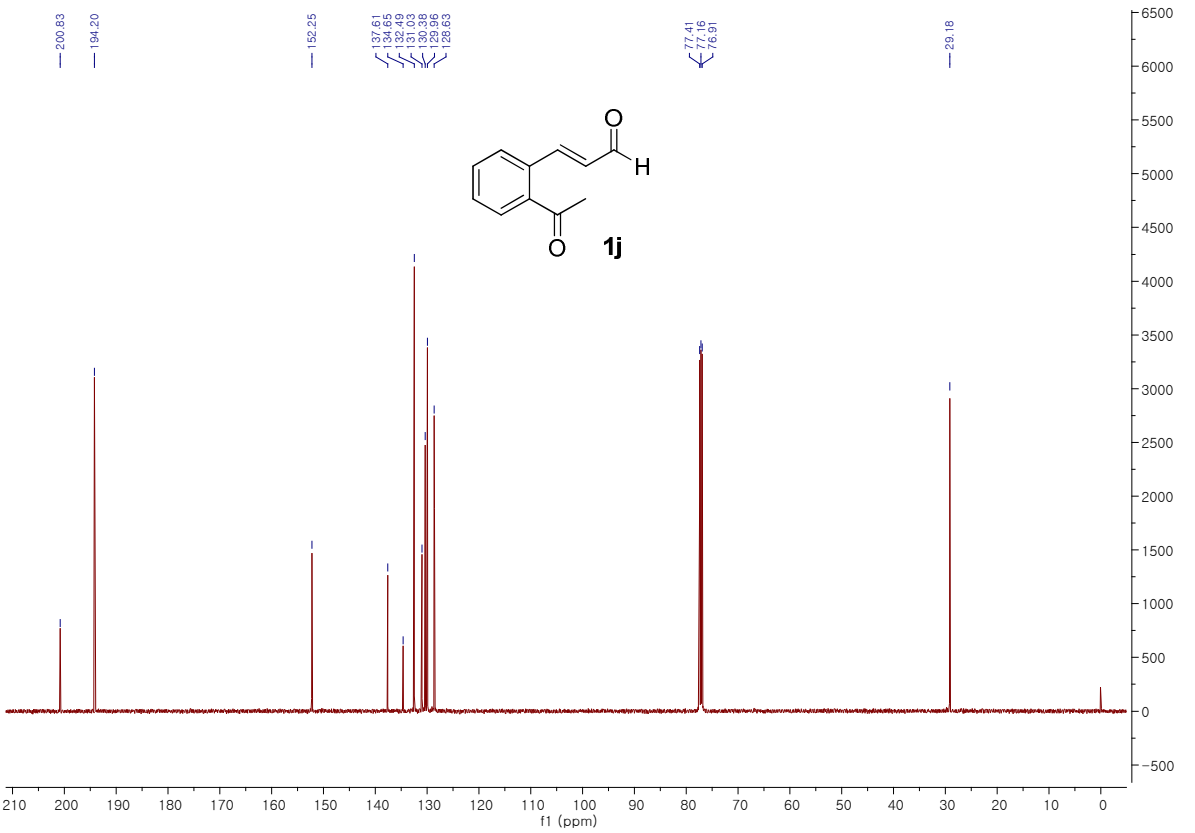

10.16
9.80
9.78
8.58
8.55
7.79
7.77
7.51
7.46
7.45
6.68
6.66
6.65
6.63
2.49
0.00
O
H
H
O
1h
f1 (ppm)

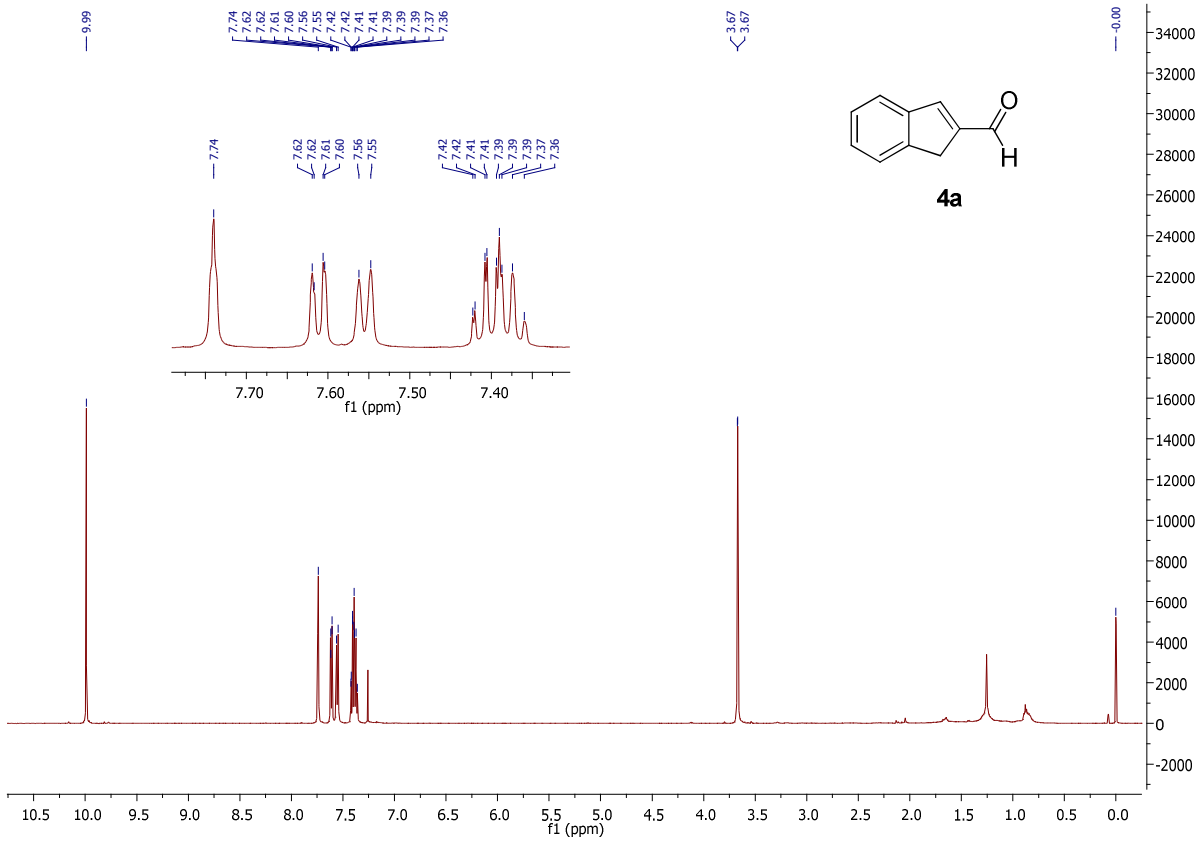

194.05
192.59
149.77
145.21
135.42
135.14
132.15
131.57
131.50
128.78
77.41
77.16
76.91
21.90
O
H
H
O
1h
f1 (ppm)

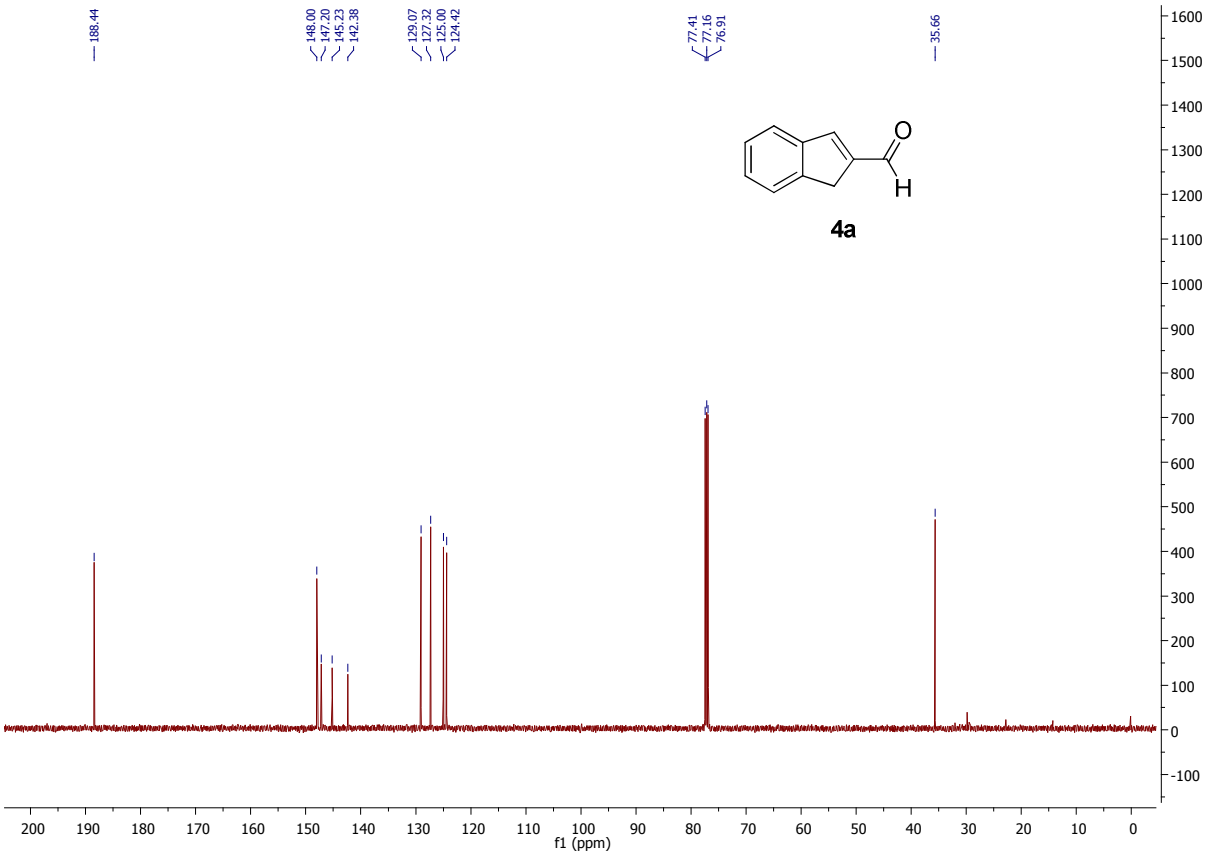

10.23
9.76
9.74
8.50
8.47
7.71
7.70
7.38
7.38
7.19
6.65
6.63
6.62
6.60
3.94
0.00
MeO
1i
f1 (ppm)

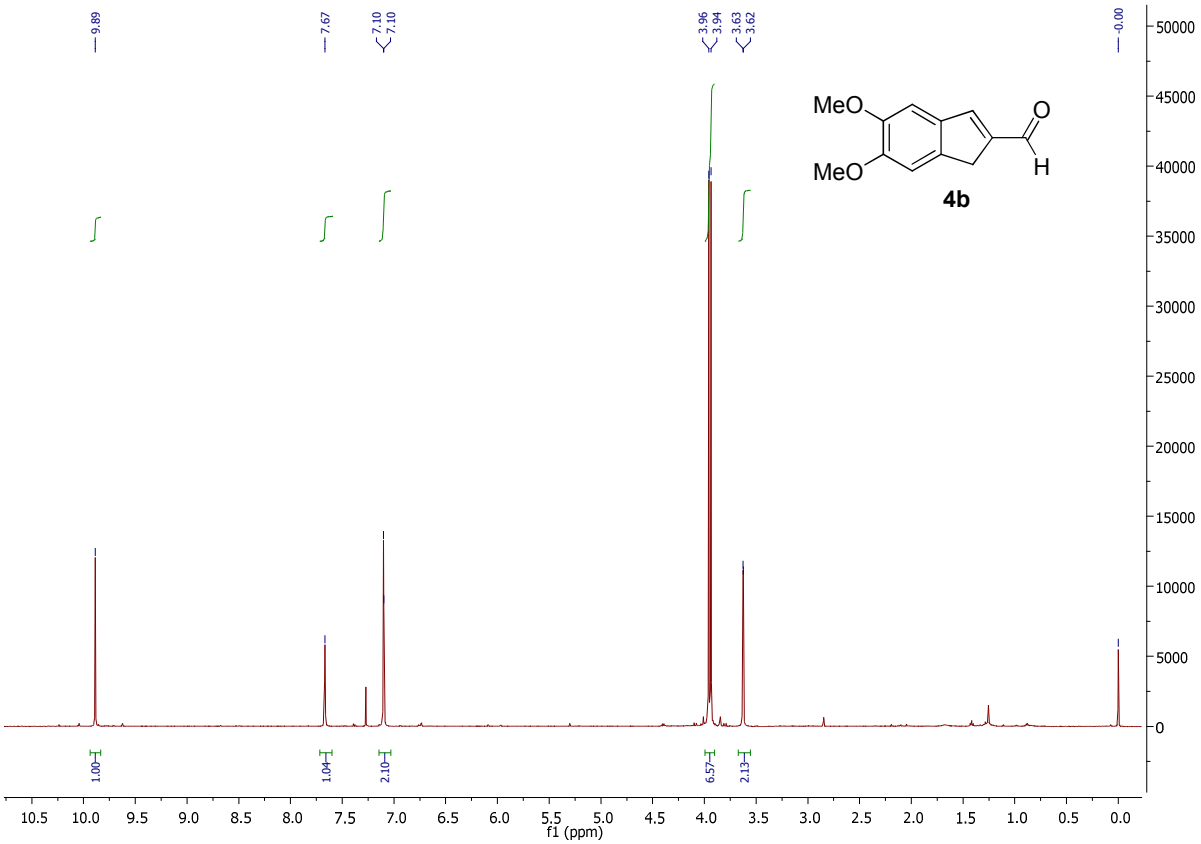

193.96
192.20
161.84
148.54
135.08
130.64
129.73
127.85
119.93
118.53
77.41
77.16
76.91
55.88
MeO
1i
f1 (ppm)

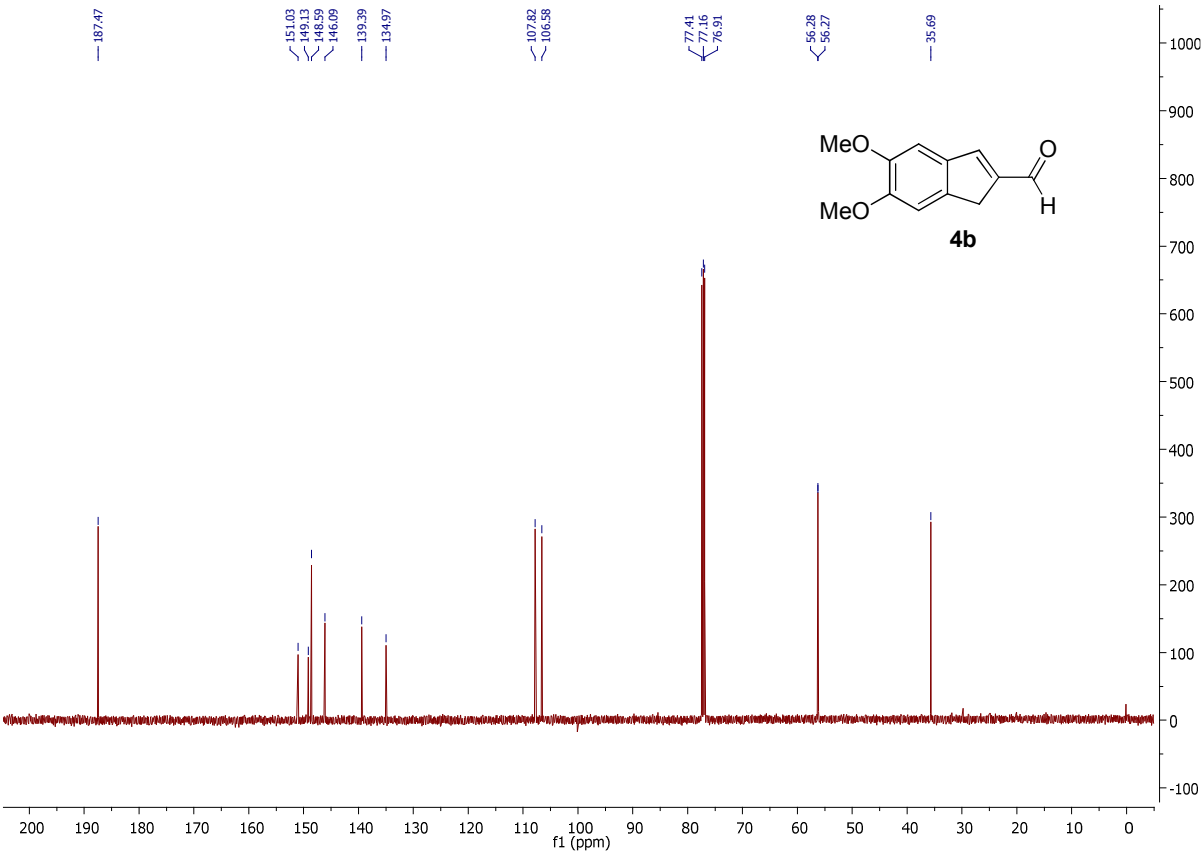

9.75
9.73
8.16
8.12
7.83
7.63
7.63
7.63
7.53
7.53
7.28
6.59
6.58
6.56
6.54
2.66
O
H
O
1j
1.00
1.00
0.99
1.02
1.00
0.97
3.02
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

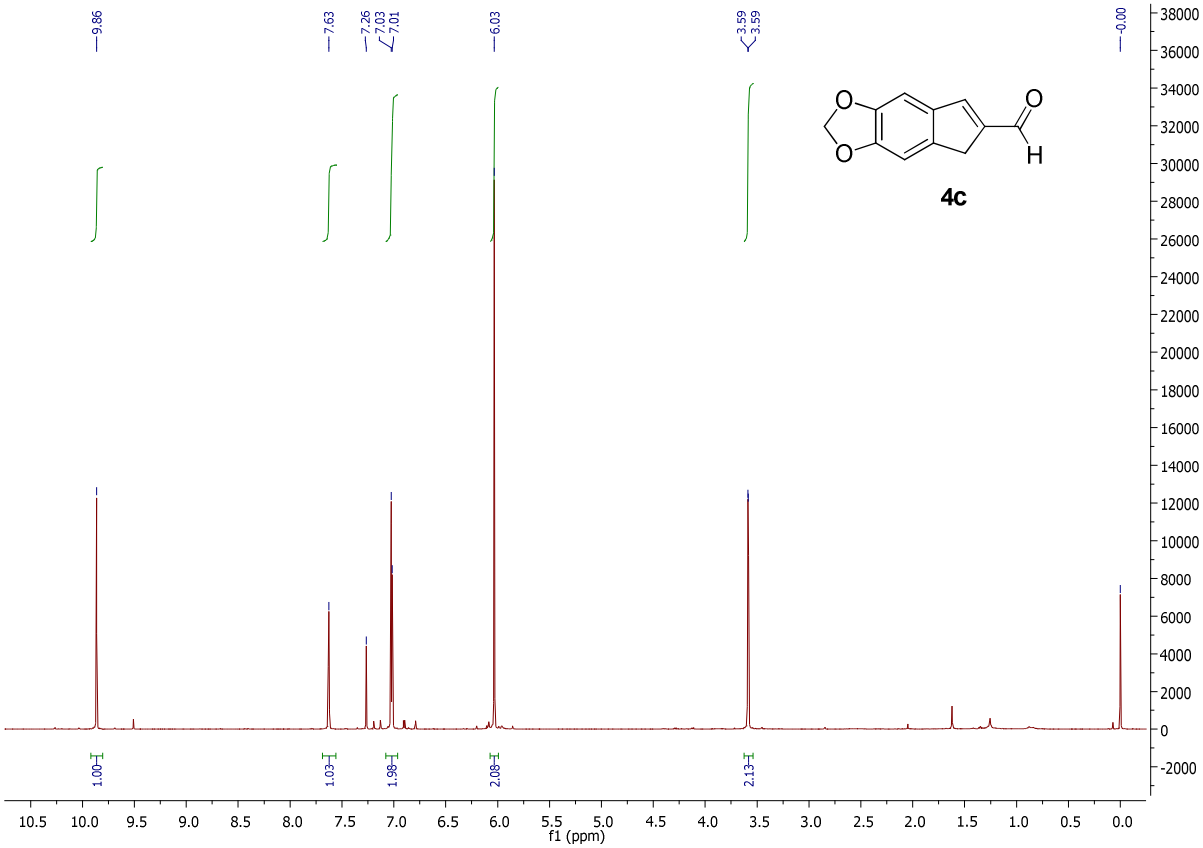

200.83
194.20
152.25
137.61
134.65
132.49
131.03
130.38
129.96
128.63
77.41
77.16
76.91
29.18
O
H
O
1j
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

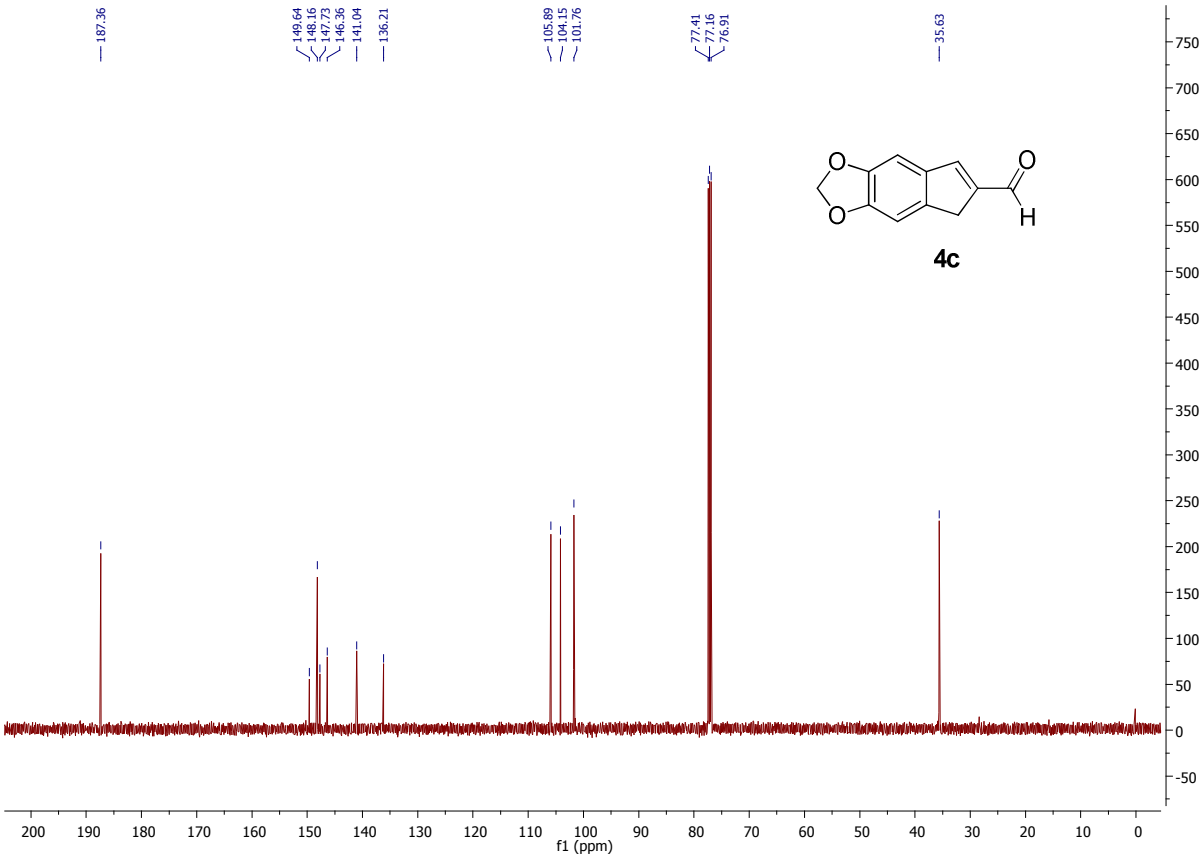

9.99
7.74
7.62
7.62
7.61
7.60
7.56
7.55
7.42
7.42
7.41
7.41
7.39
7.39
7.39
7.37
7.36
3.67
3.67
0.00
O
H
4a
f1 (ppm)
f1 (ppm)

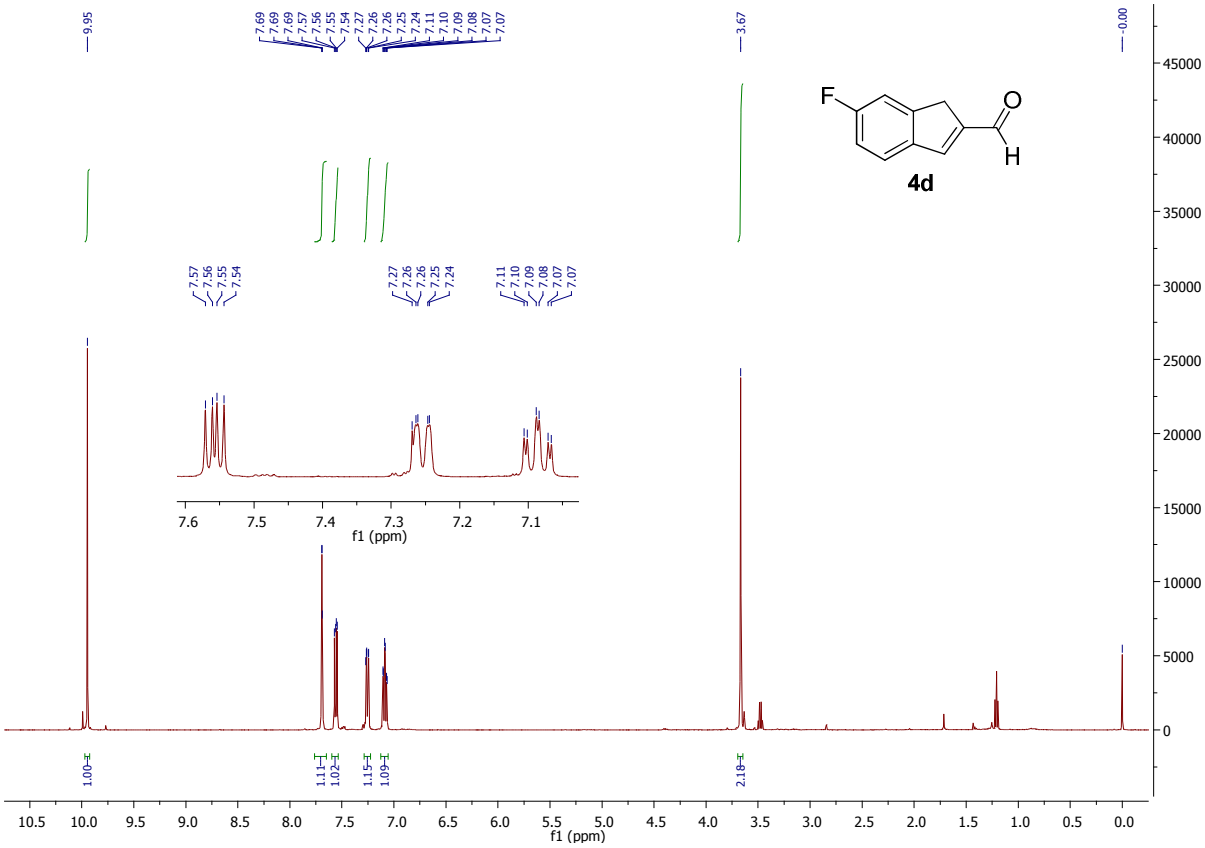

188.44
148.00
147.20
145.23
142.38
129.07
127.32
125.00
124.42
77.41
77.16
76.91
35.66
O
H
4a
f1 (ppm)

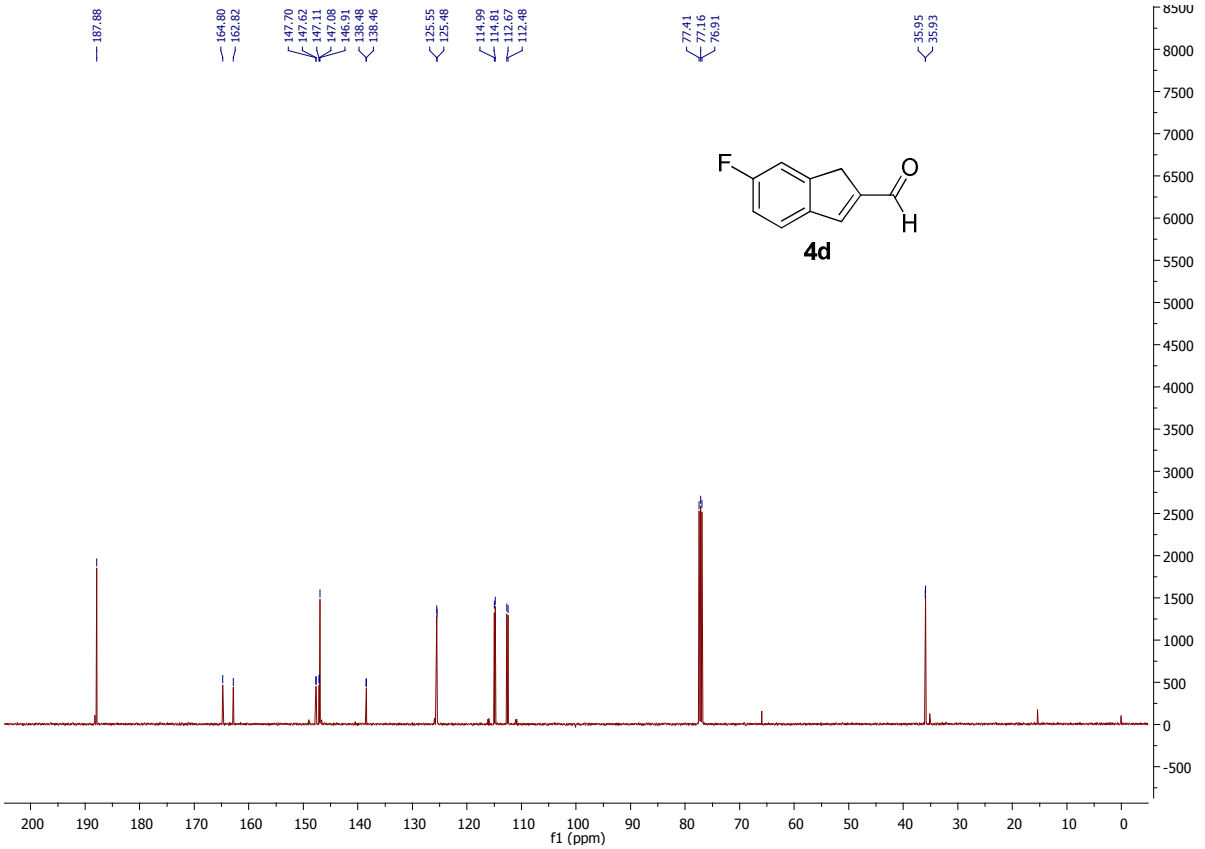

9.89
7.67
7.10
7.10
3.96
3.94
3.63
3.62
0.00
MeO
MeO
O
H
4b
1.00
1.04
2.10
6.57
2.13
f1 (ppm)

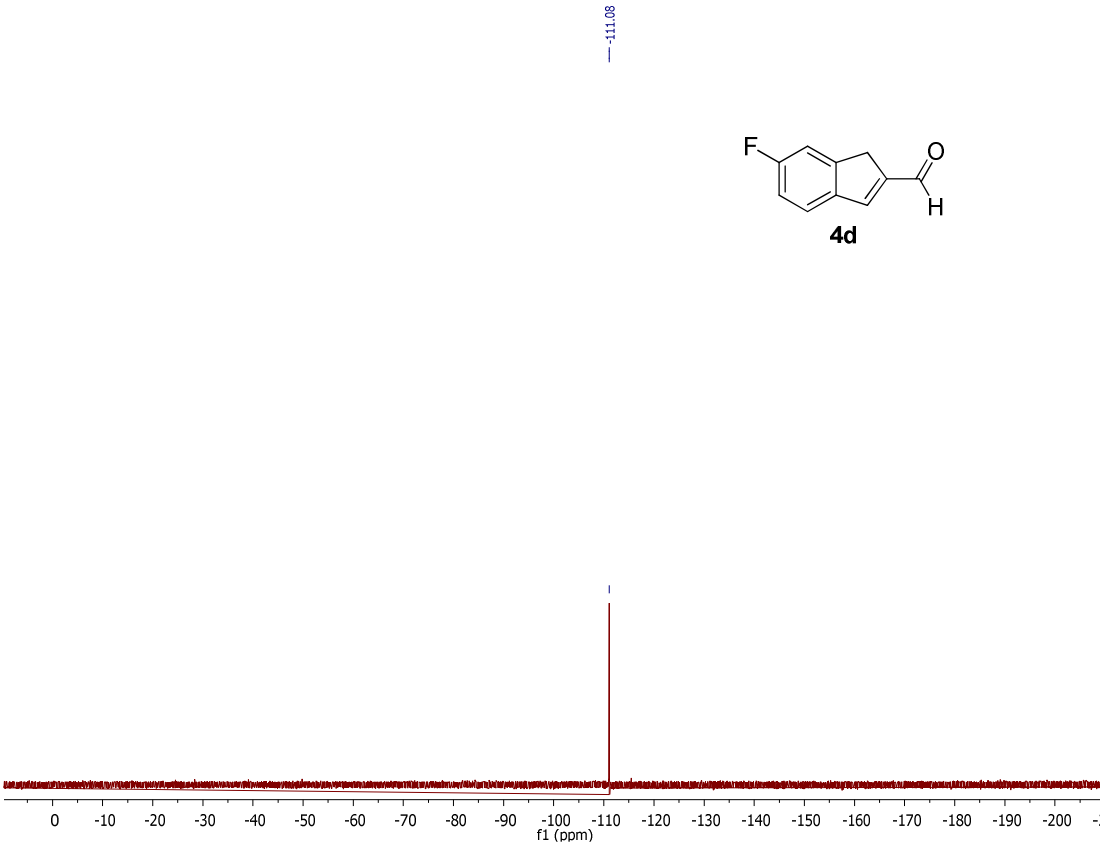

187.47
151.03
149.13
148.59
146.09
139.39
134.97
107.82
106.58
77.41
77.16
76.91
56.28
56.27
35.69
MeO
MeO
O
H
4b
f1 (ppm)


9.86
7.63
7.26
7.03
7.01
6.03
3.59
3.59
0.00
1.00
1.03
1.98
2.08
2.13
f1 (ppm)
4c

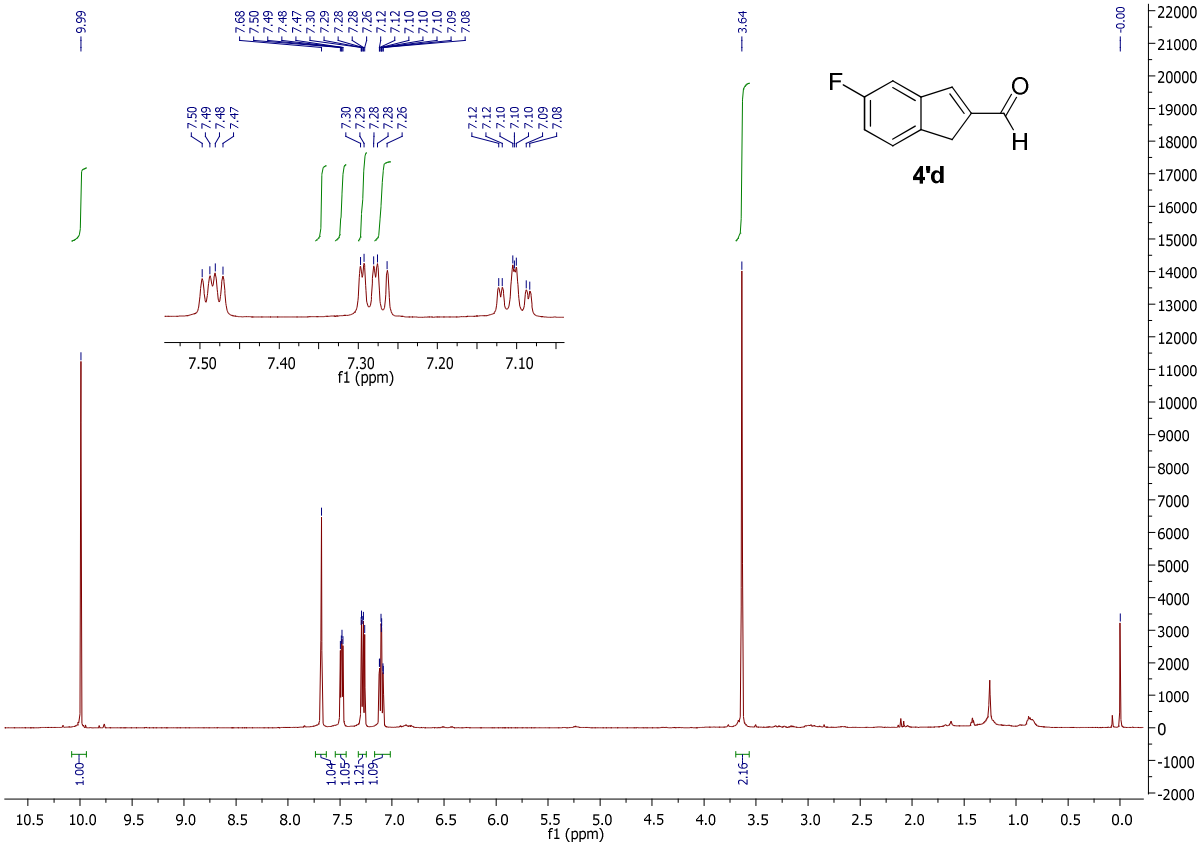

187.36
149.64
148.16
147.73
146.36
141.04
136.21
105.89
104.15
101.76
77.41
77.16
76.91
35.63
f1 (ppm)
4c

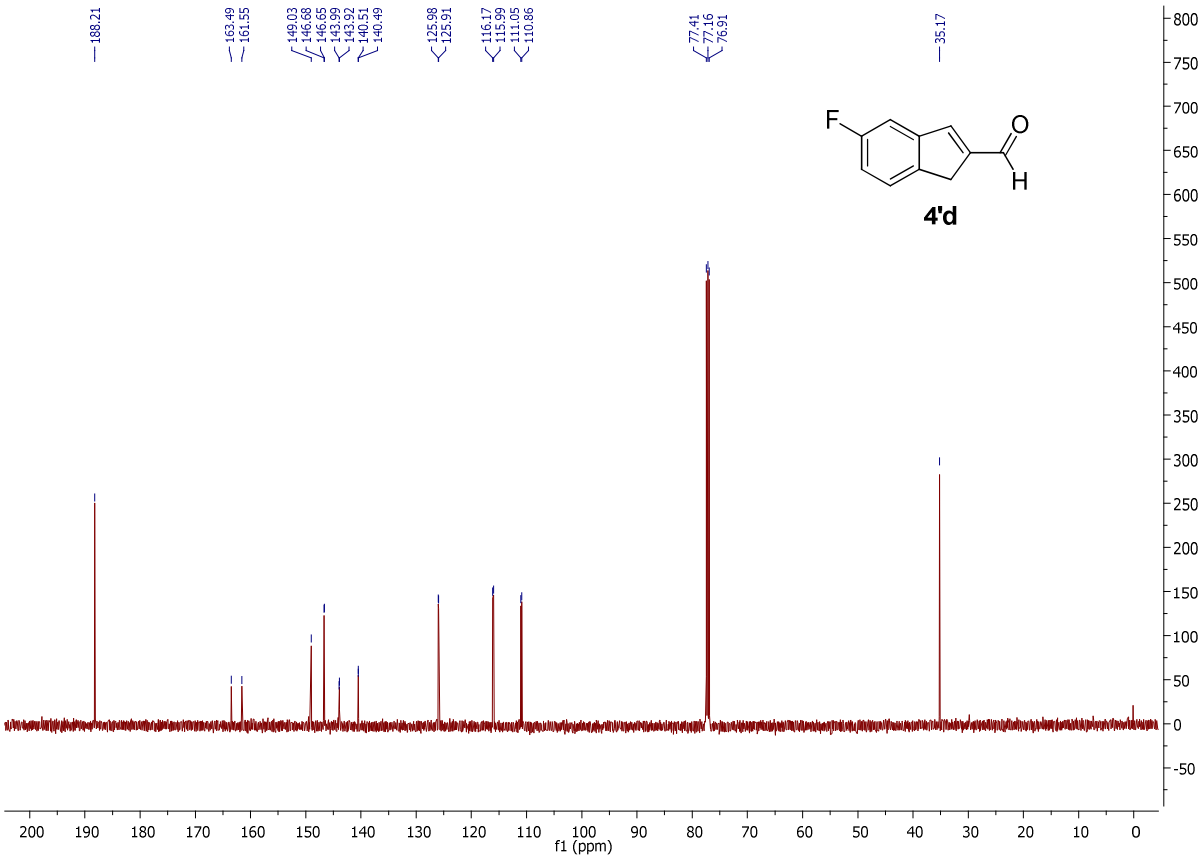

9.95
7.69
7.69
7.69
7.57
7.56
7.55
7.54
7.27
7.26
7.26
7.25
7.24
7.11
7.10
7.09
7.08
7.07
7.07
3.67
-0.00
F
O
H
4d
7.57
7.56
7.55
7.54
7.27
7.26
7.26
7.25
7.24
7.11
7.10
7.09
7.08
7.07
7.07
7.6
7.5
7.4
7.3
7.2
7.1
f1 (ppm)
1.00
1.11
1.02
1.15
1.09
2.18
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

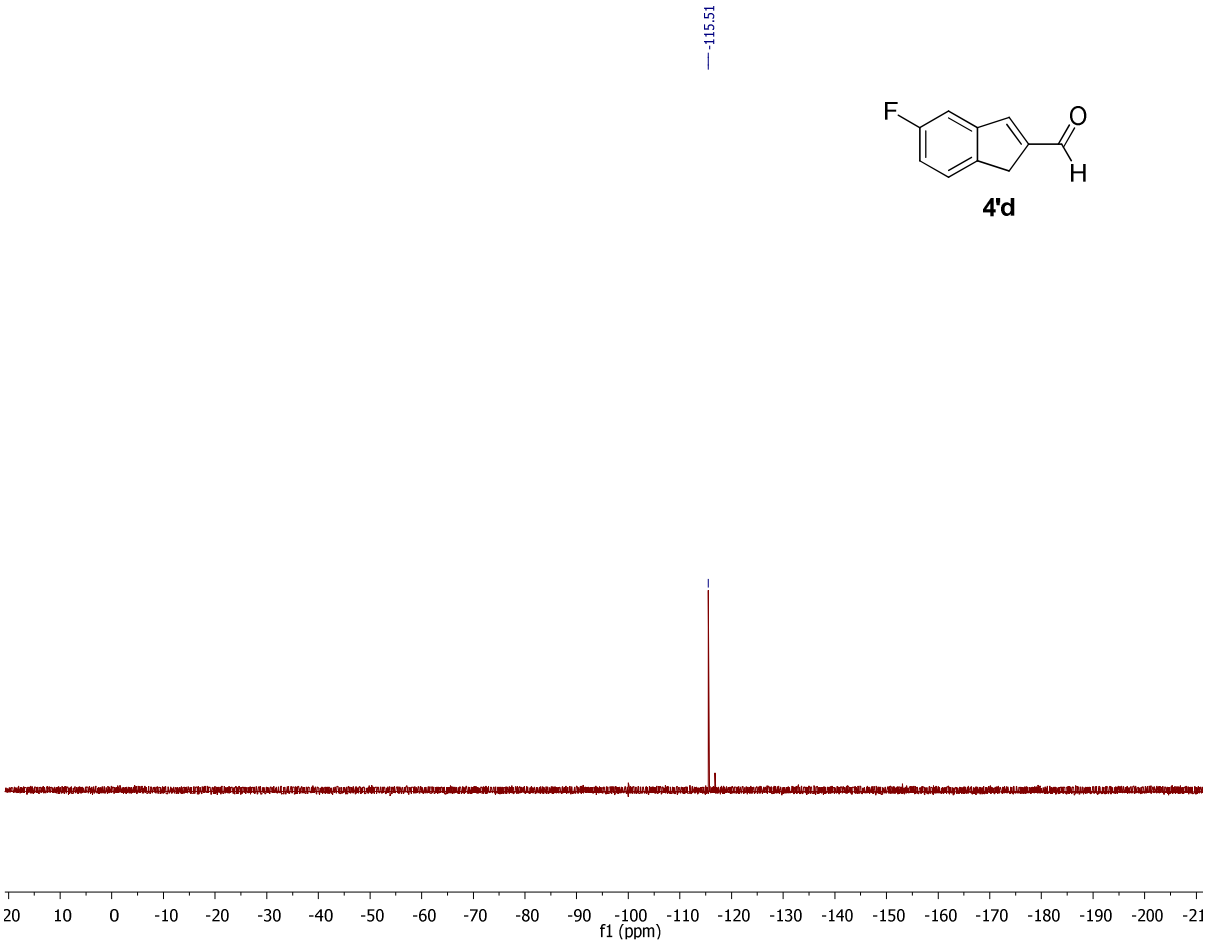

187.88
164.80
162.82
147.70
147.62
147.11
147.08
146.91
138.48
138.46
125.55
125.48
114.99
114.81
112.67
112.48
77.41
77.16
76.91
35.95
35.93
F
O
H
4d
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

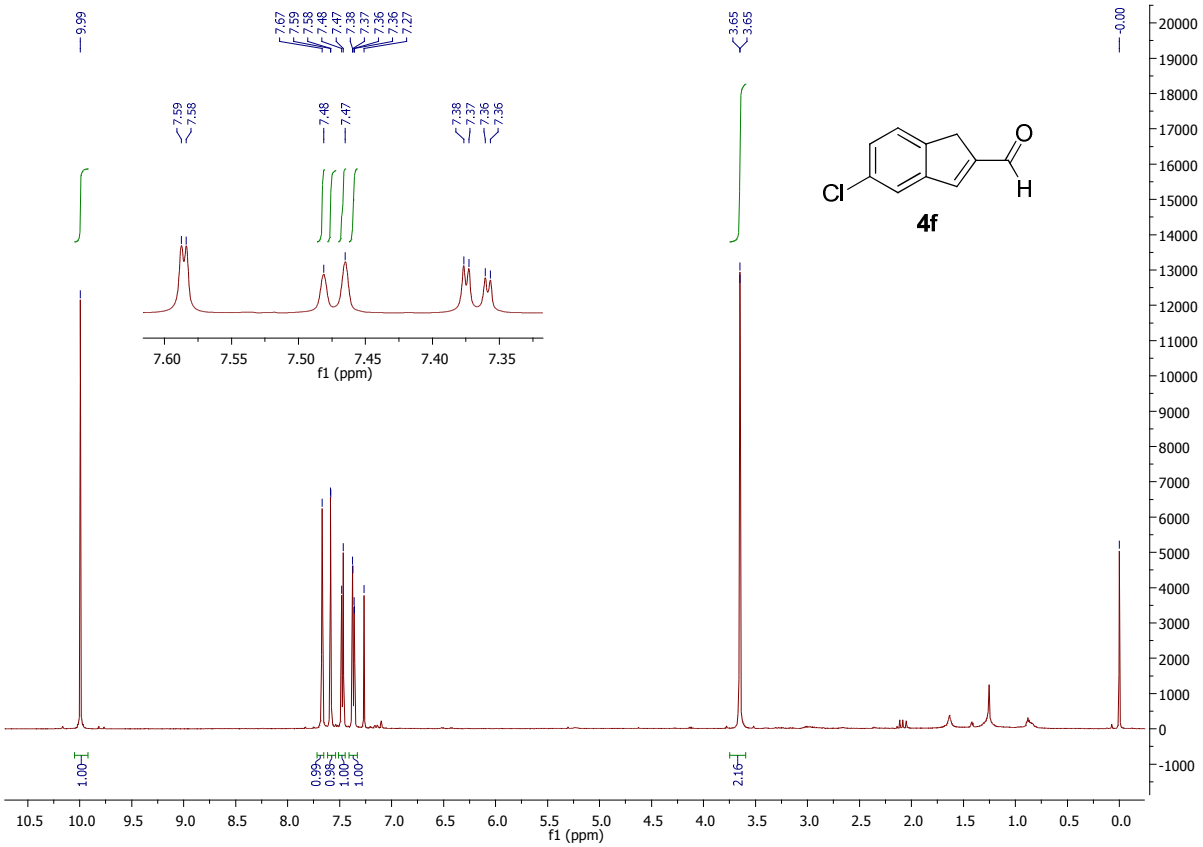

-111.08
F
O
H
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

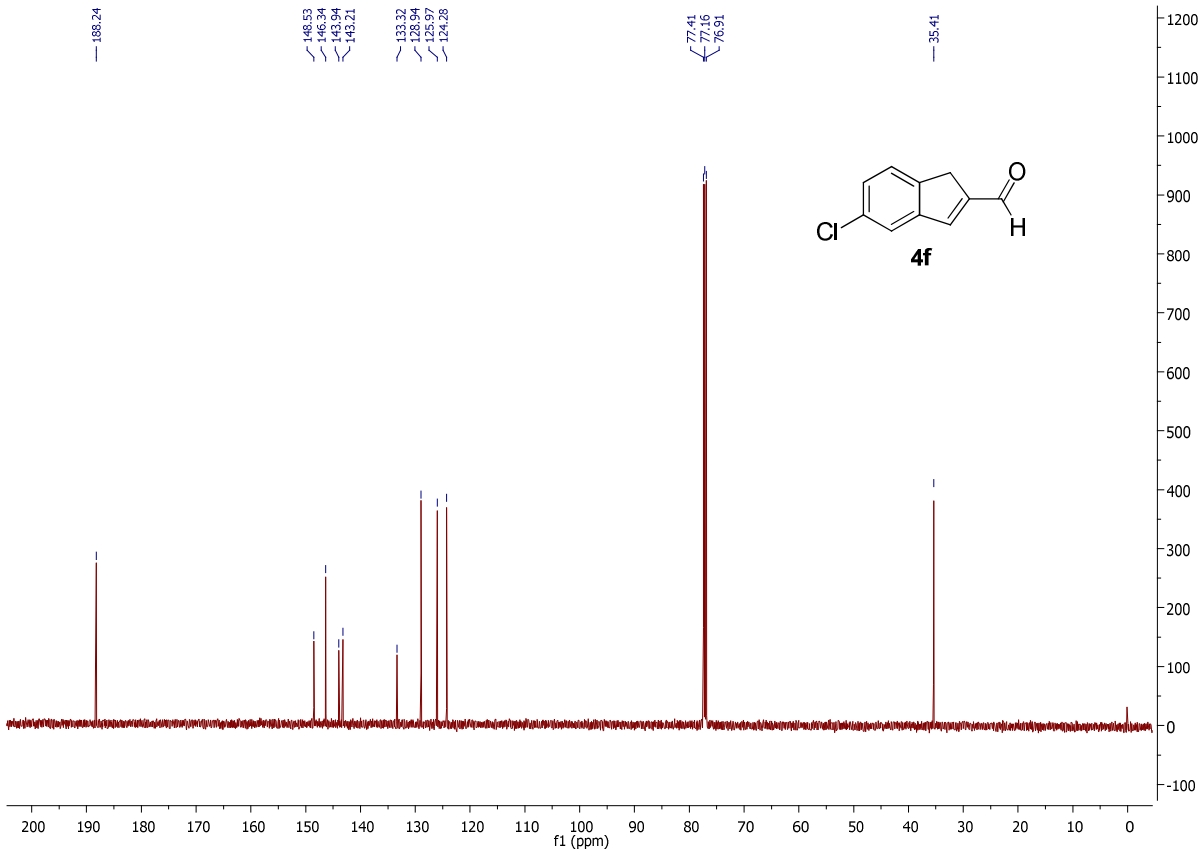
4d

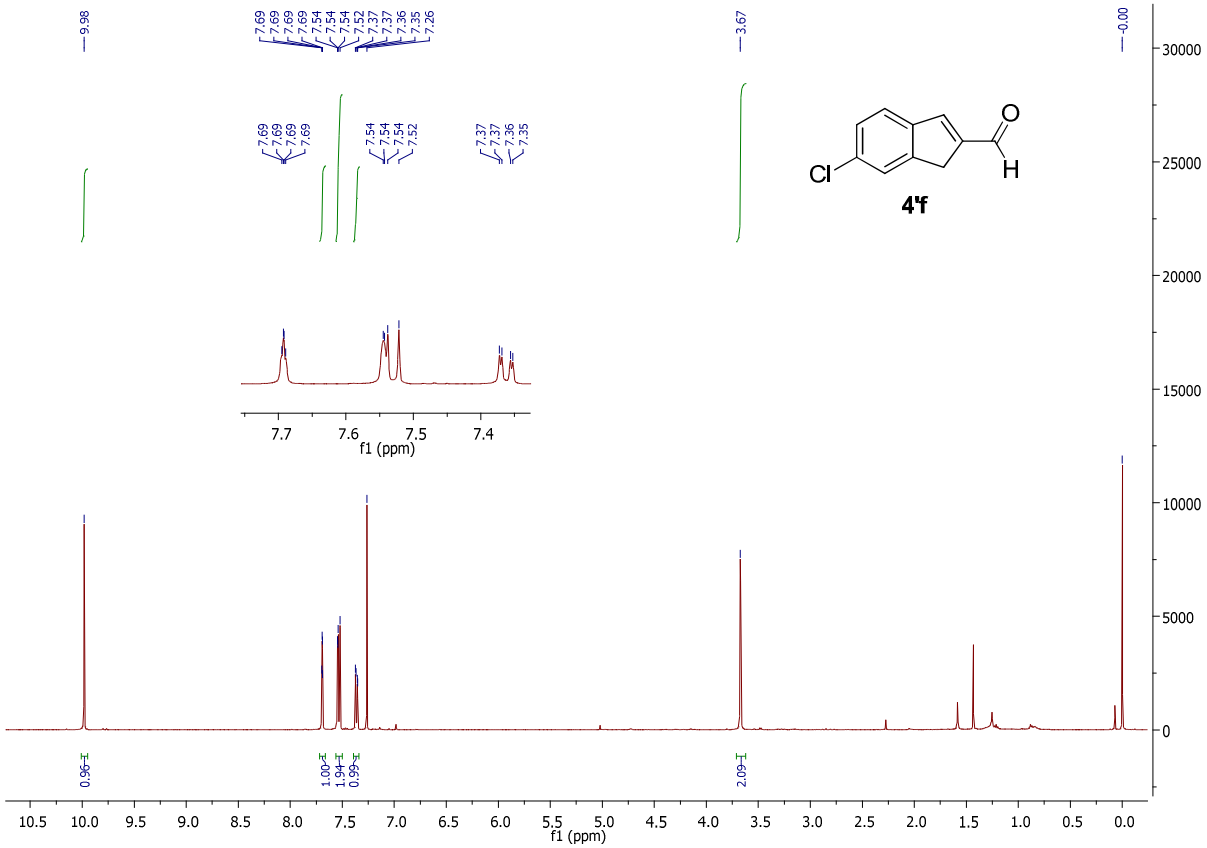

9.99
7.68
7.50
7.49
7.48
7.47
7.30
7.29
7.28
7.28
7.26
7.12
7.12
7.10
7.10
7.10
7.09
7.08
3.64
0.00
F
O
H
4'd
1.00
1.04
1.05
1.21
1.09
2.16
f1 (ppm)

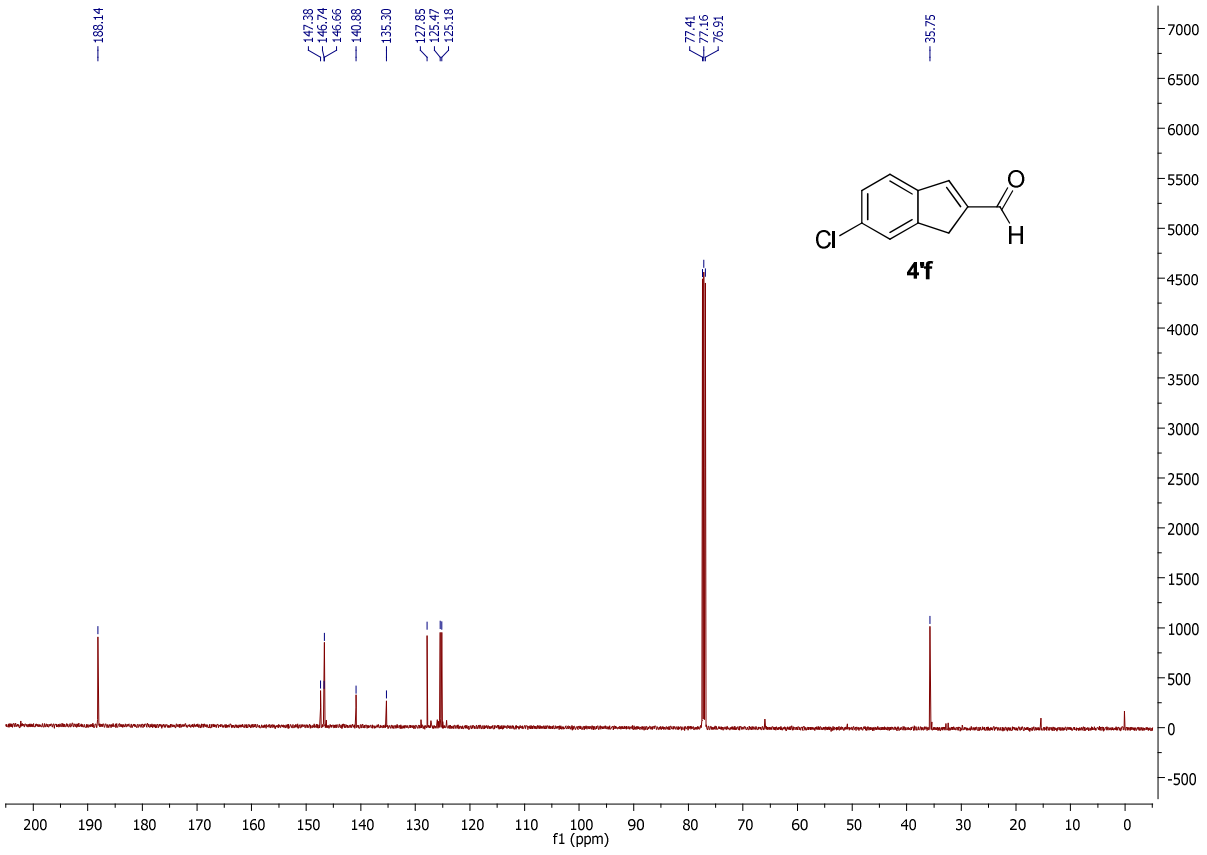

188.21
163.49
161.55
149.03
146.68
146.65
143.99
143.92
140.51
140.49
125.98
125.91
116.17
115.99
111.05
110.86
77.41
77.16
76.91
35.17
F
O
H
4'd
f1 (ppm)

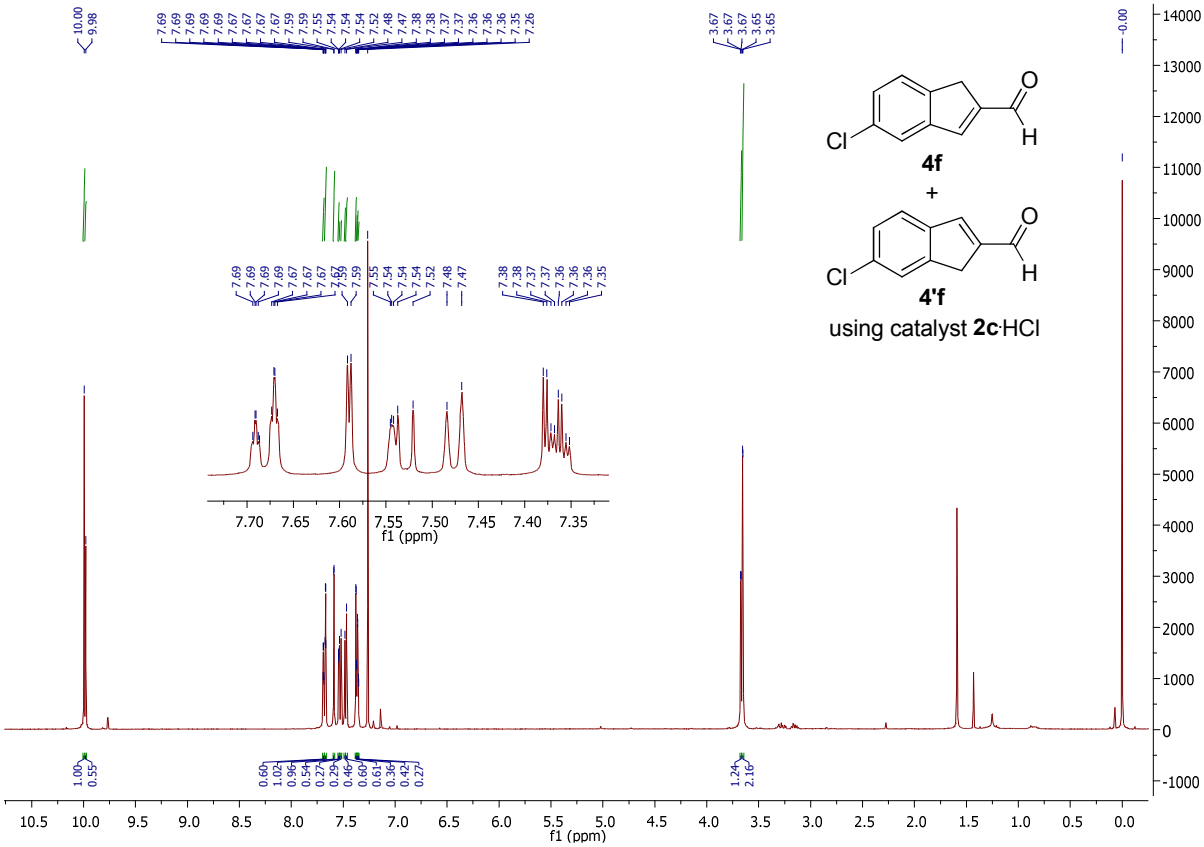

-115.51
F
O
H
4'd
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-21
f1 (ppm)

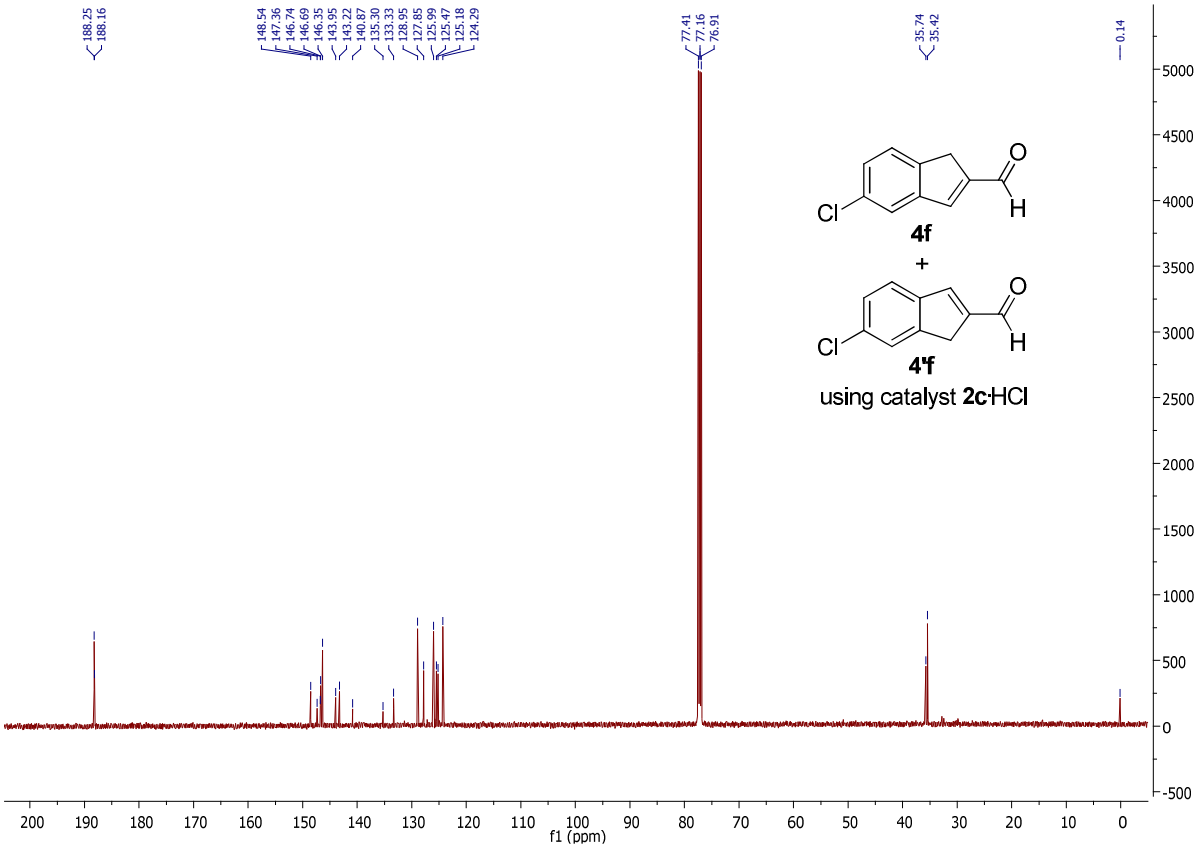

9.99
7.67
7.59
7.58
7.48
7.47
7.38
7.37
7.36
7.36
7.27
3.65
3.65
0.00
7.59
7.58
7.48
7.47
7.38
7.37
7.36
7.36
7.60
7.55
7.50
7.45
7.40
7.35
f1 (ppm)
Cl
O
H
4f
1.00
0.99
0.98
1.00
1.00
2.16
f1 (ppm)

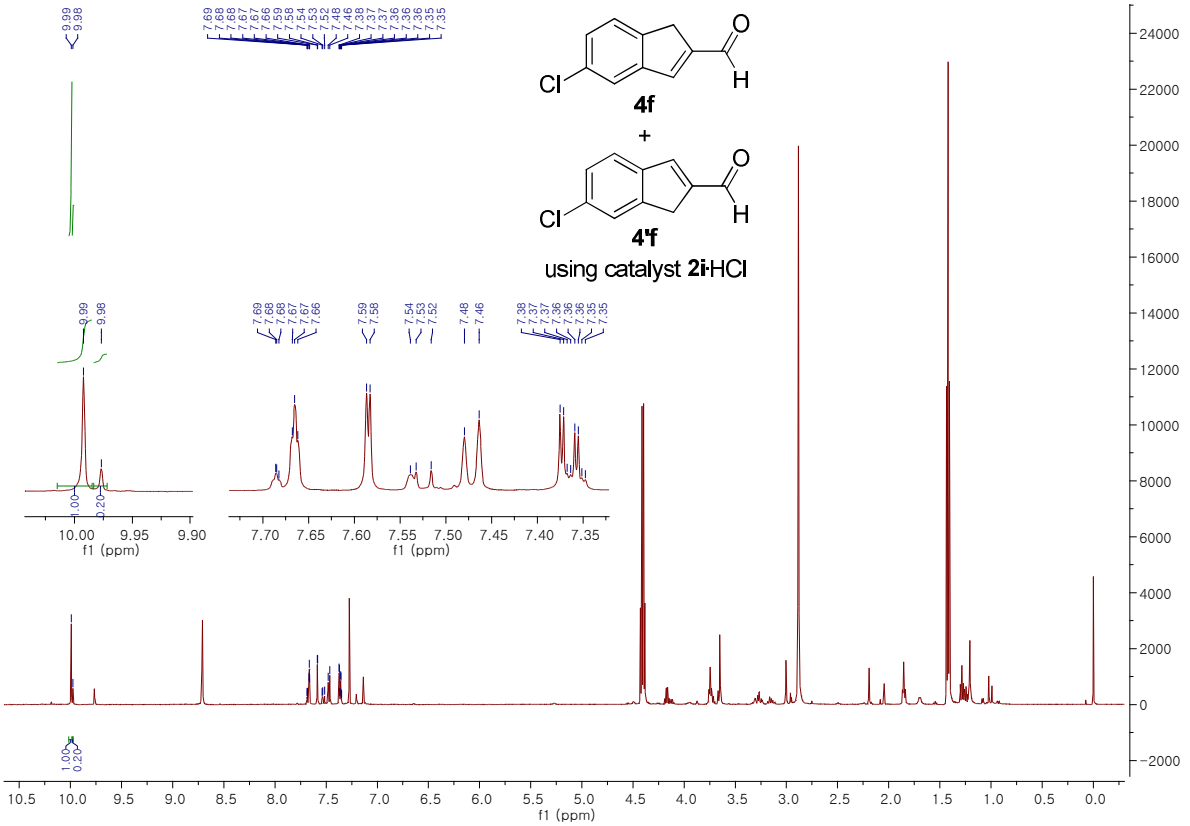

188.24
148.53
146.34
143.94
143.21
133.32
128.94
125.97
124.28
77.41
77.16
76.91
35.41
Cl
O
H
4f
f1 (ppm)

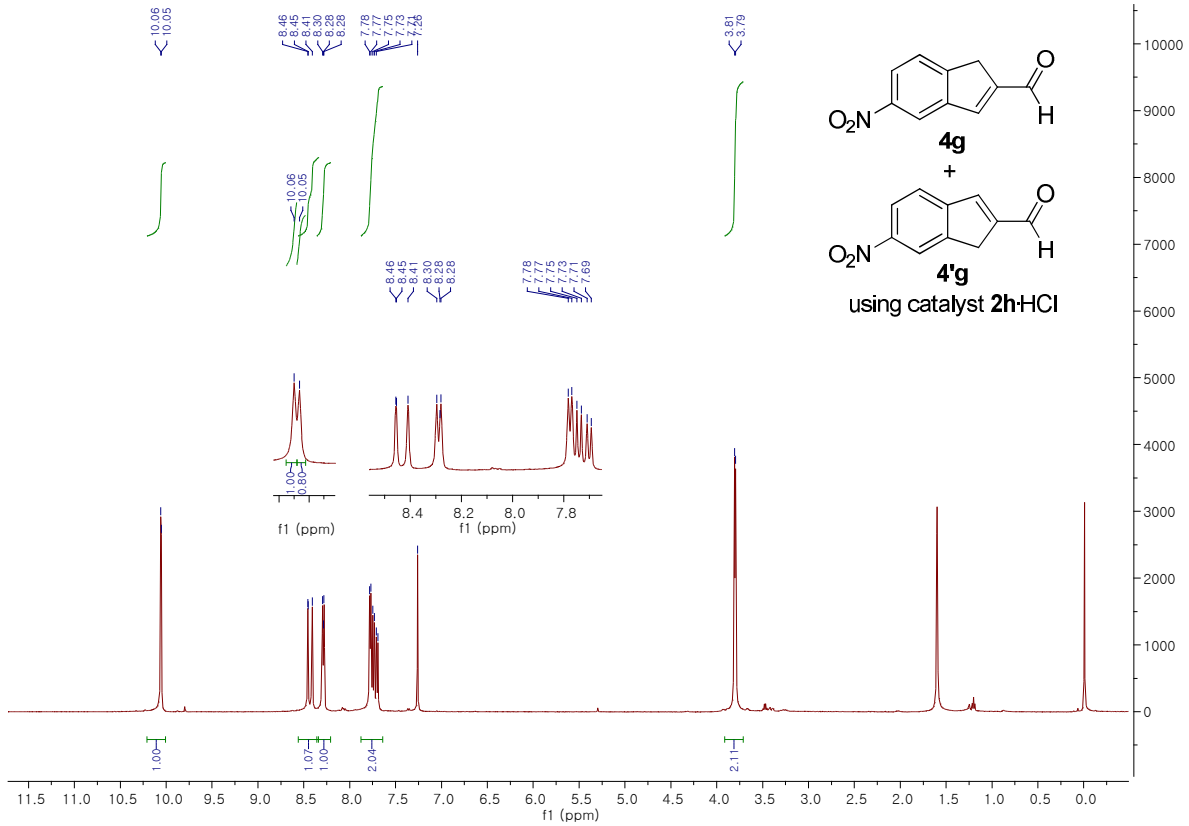

9.98
7.69
7.69
7.69
7.69
7.54
7.54
7.52
7.37
7.37
7.36
7.35
7.26
3.67
0.00
Cl
O
H
4'f
f1 (ppm)
0.96
1.00
1.94
0.99
2.09

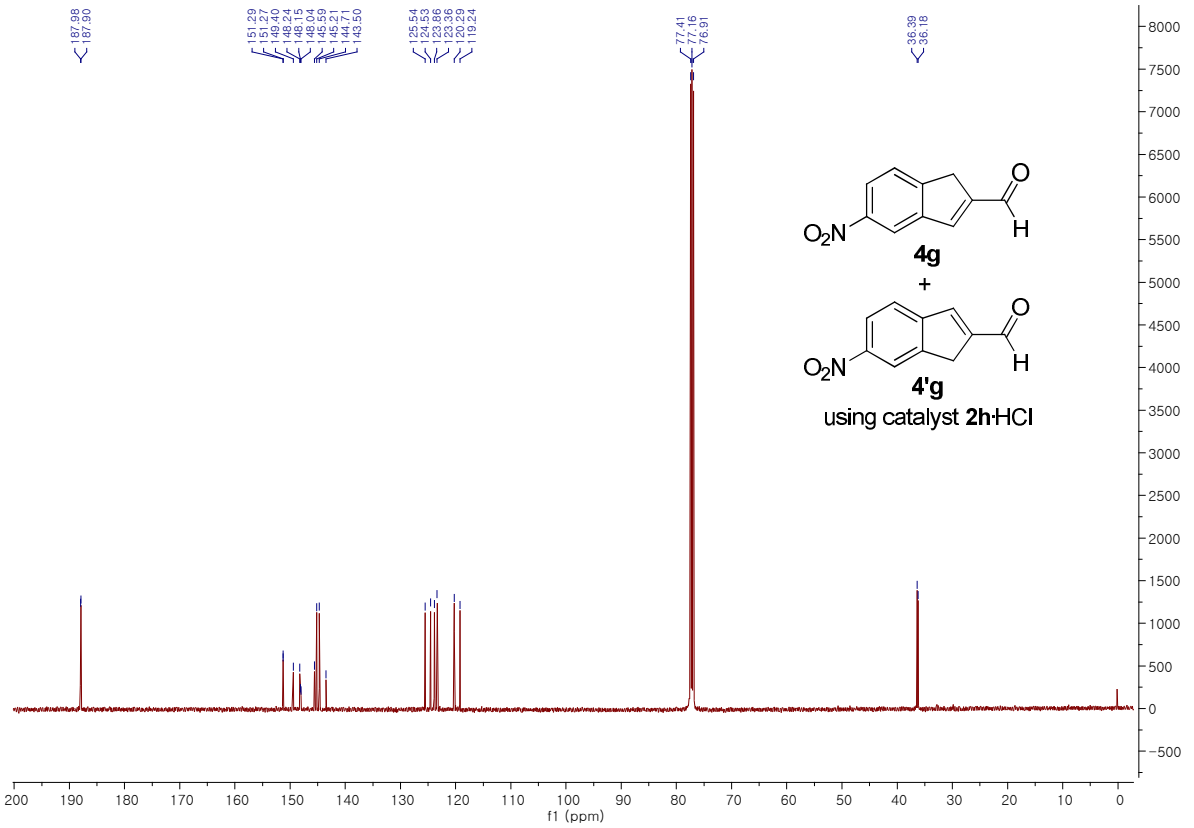

188.14
147.38
146.74
146.66
140.88
135.30
127.85
125.47
125.18
77.41
77.16
76.91
35.75
Cl
O
H
4'f
f1 (ppm)

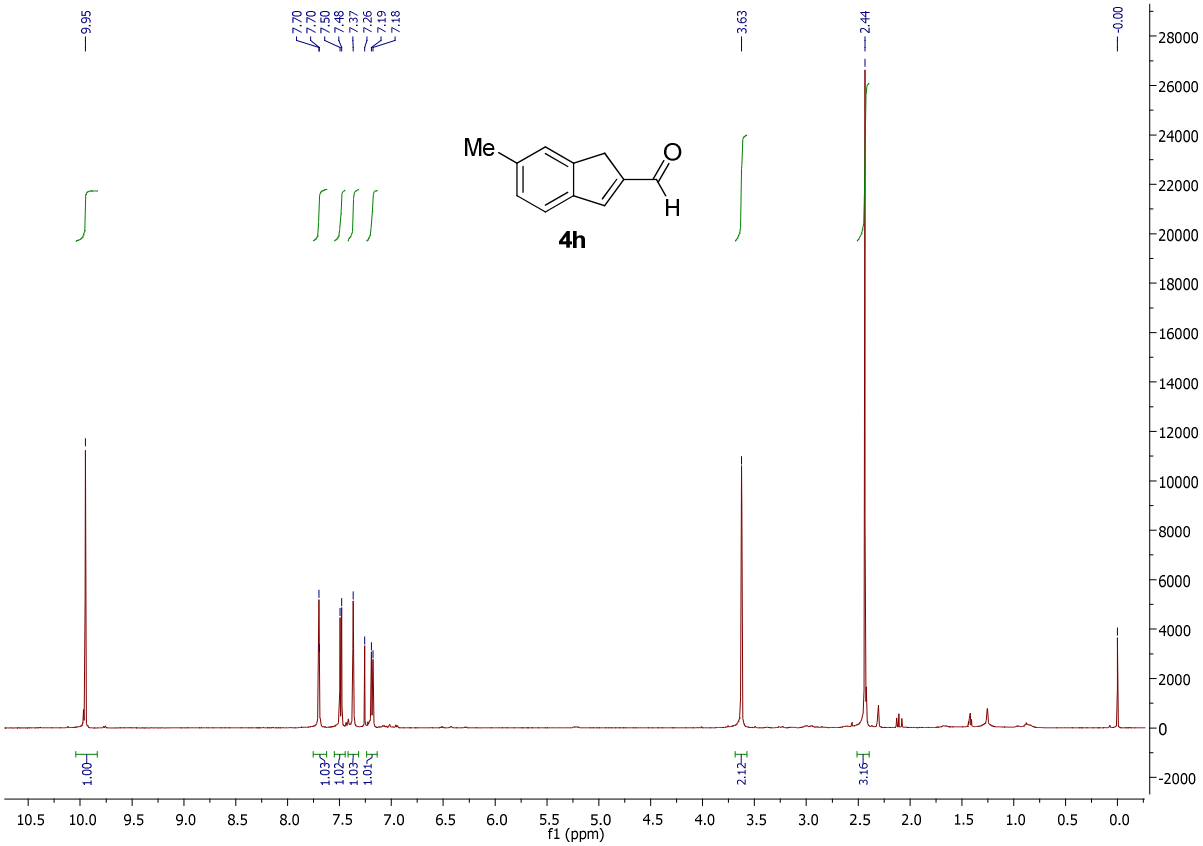

4f
+
4'f
using catalyst 2c·HCl
f1 (ppm)

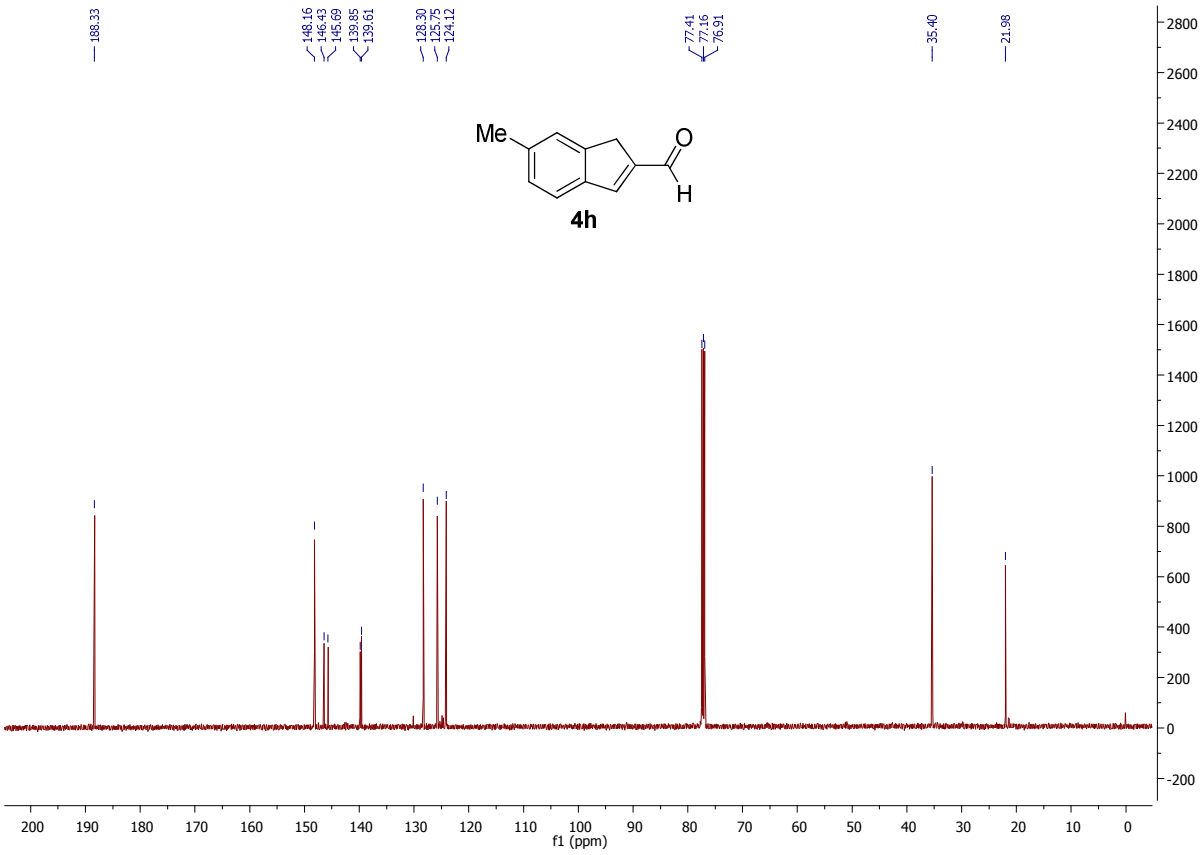

4f
+
4'f
using catalyst 2c·HCl
f1 (ppm)

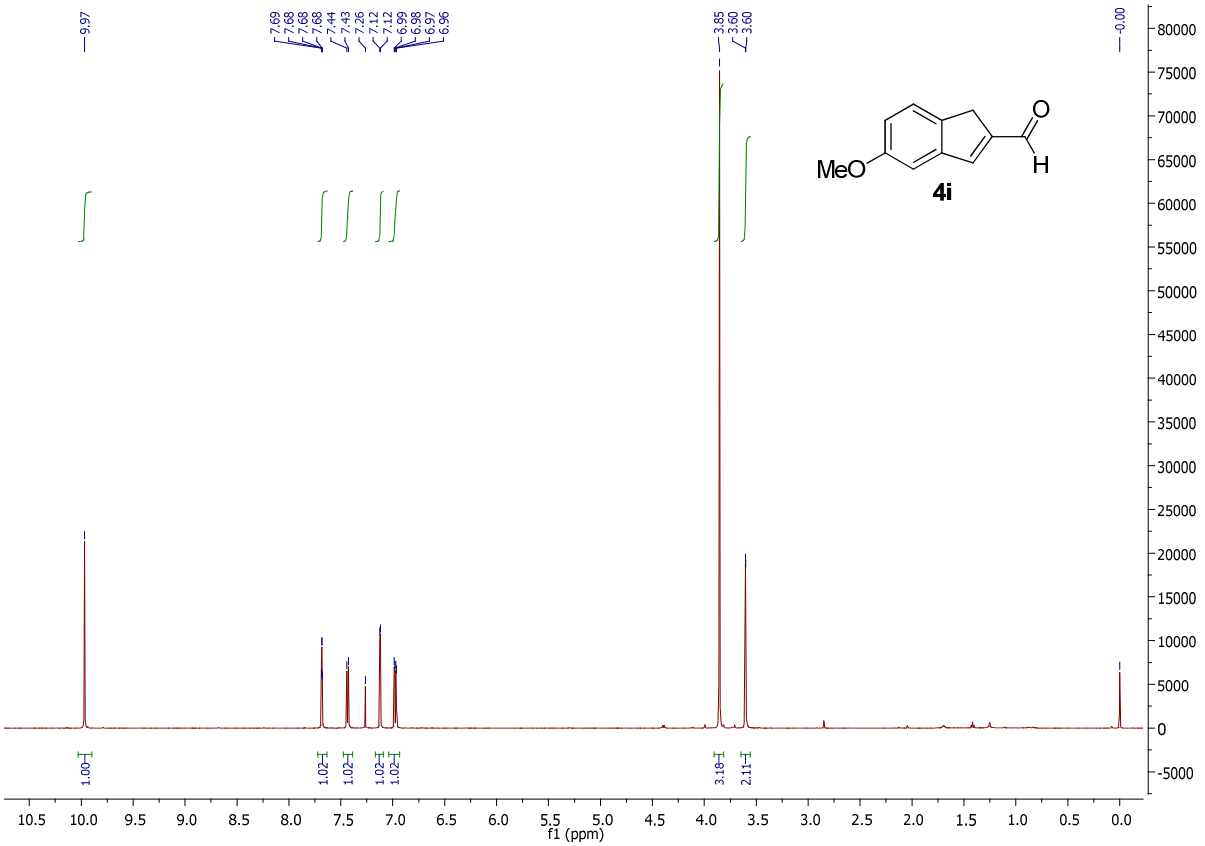

4f
+
4'f
using catalyst 2i·HCl
f1 (ppm)

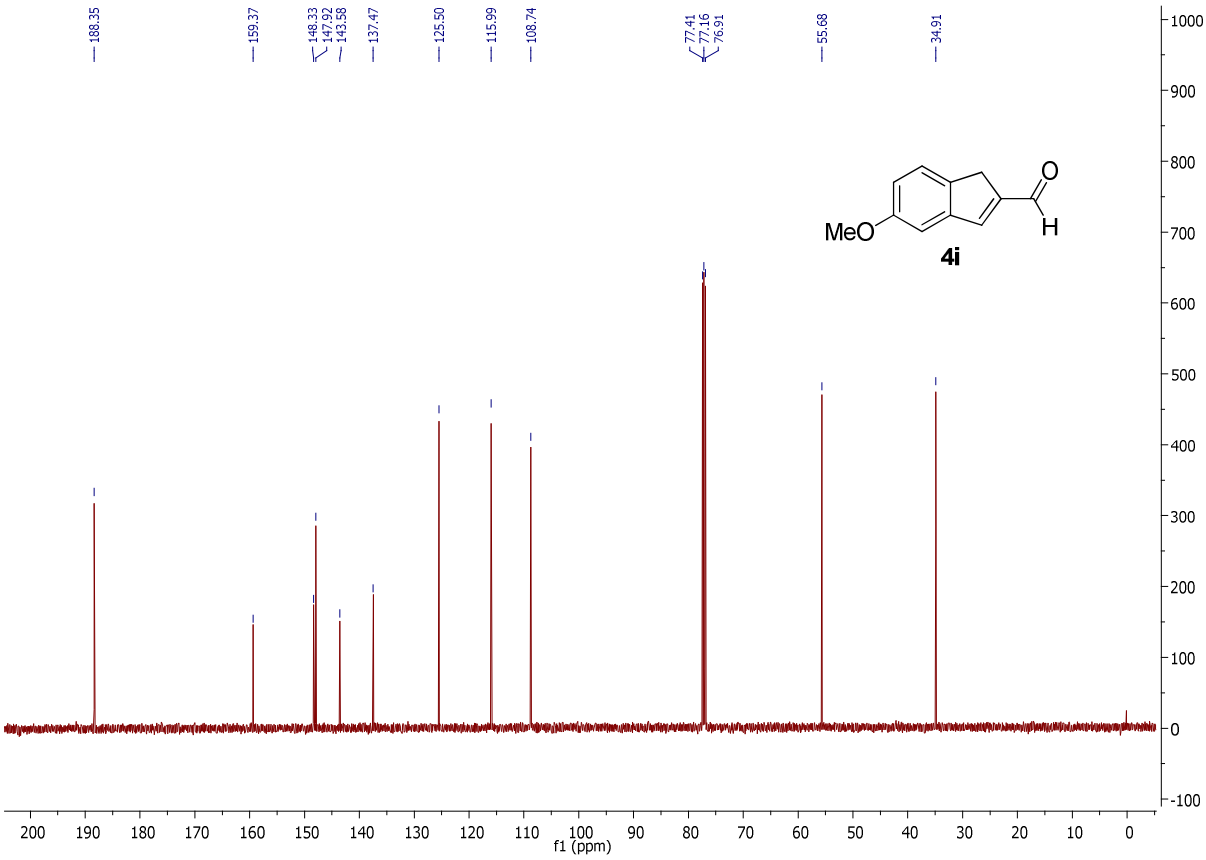

10.06
10.05
8.46
8.45
8.41
8.30
8.28
8.28
7.78
7.77
7.75
7.73
7.71
7.69
3.81
3.79
O2N
O
H
4g
+
4'g
using catalyst 2h·HCl
f1 (ppm)

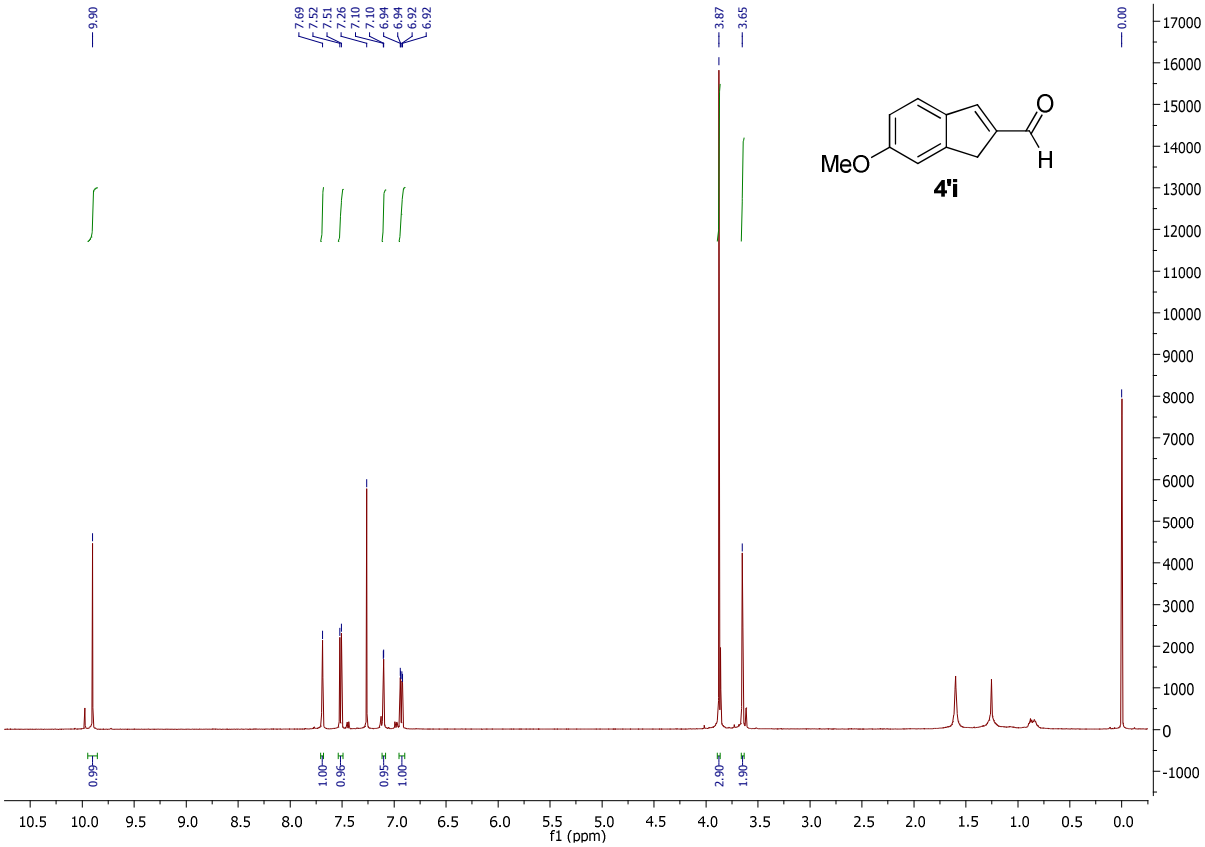

187.98
187.90
151.29
151.27
149.40
148.24
148.15
148.04
145.59
145.21
144.71
143.50
125.54
124.55
123.86
123.36
120.29
119.24
77.41
77.16
76.91
36.39
36.18
O2N
O
H
4g
+
4'g
using catalyst 2h·HCl
f1 (ppm)

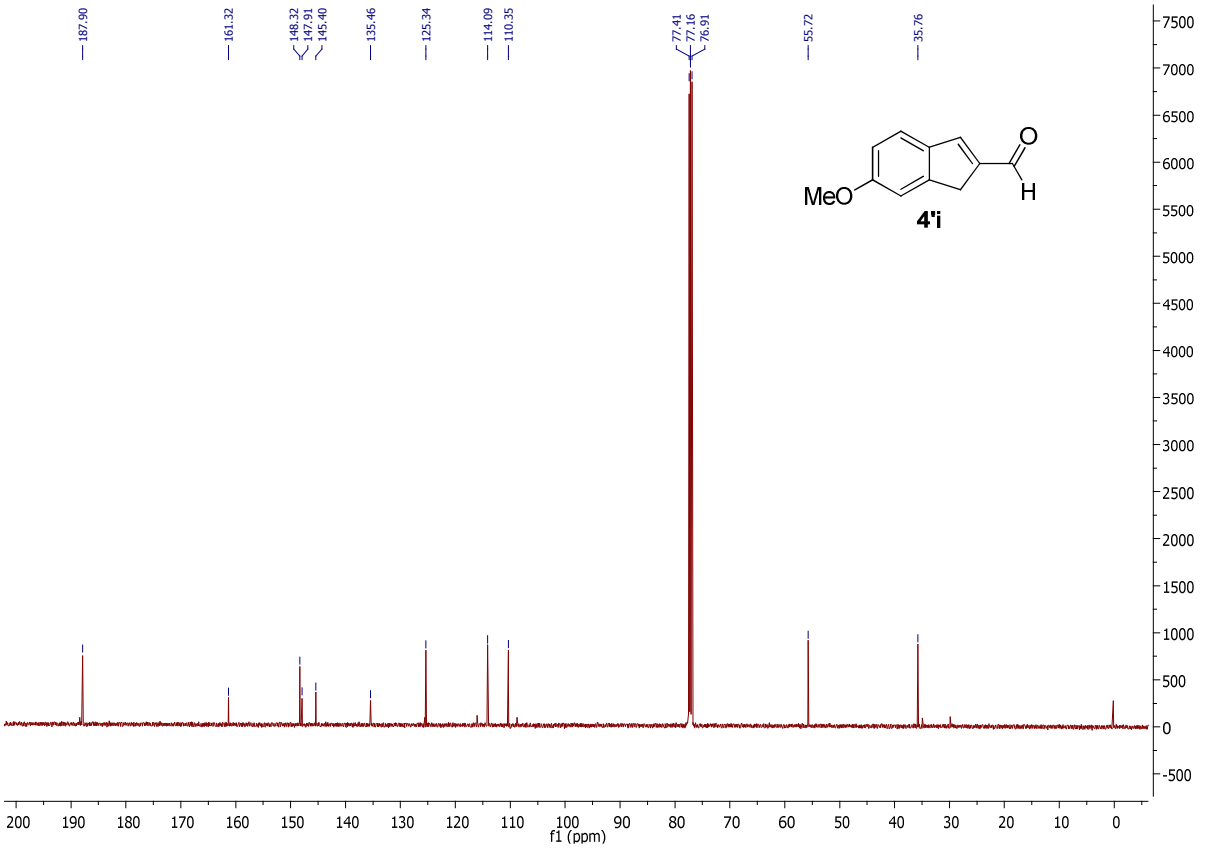

9.95
7.70
7.70
7.50
7.48
7.37
7.26
7.19
7.18
3.63
2.44
0.00
Me
O
H
4h
1.00
1.03
1.02
1.03
1.01
2.12
3.16
f1 (ppm)

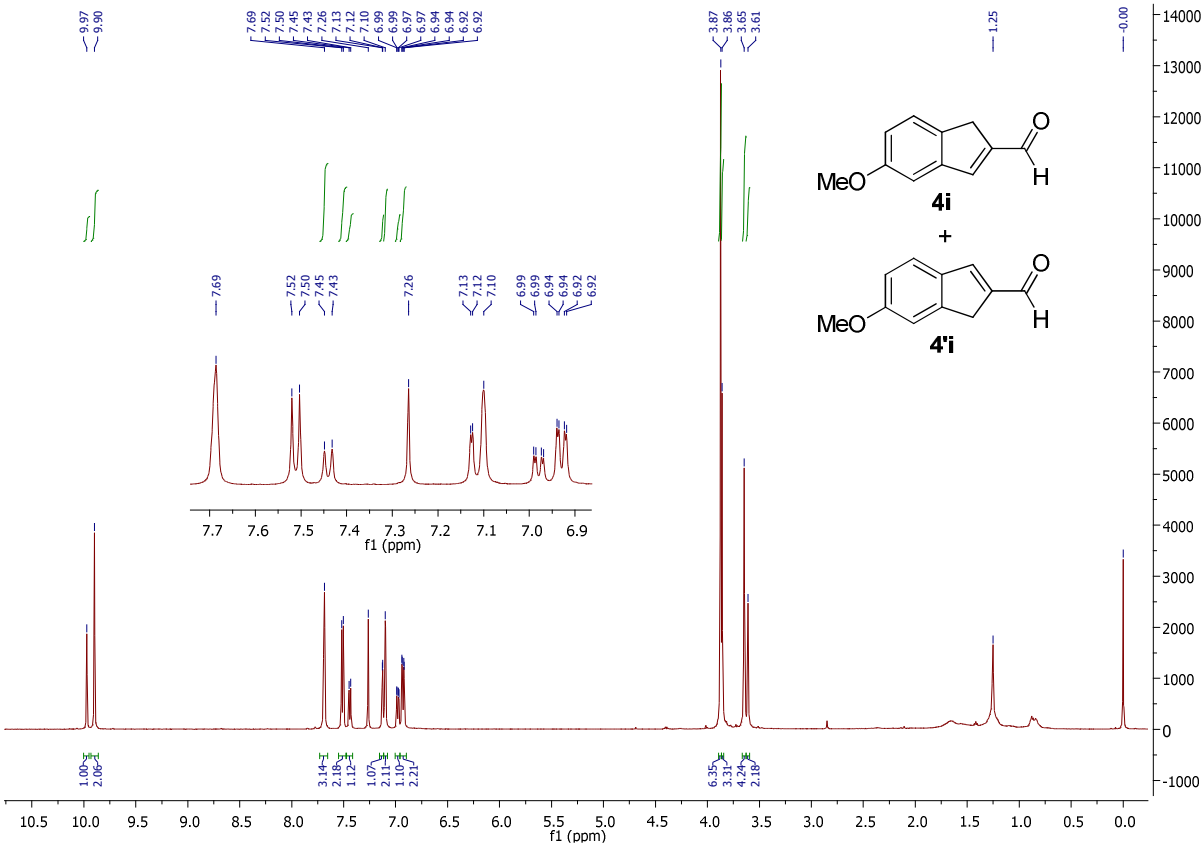

188.33
148.16
146.43
145.69
139.85
139.61
128.30
125.75
124.12
77.41
77.16
76.91
35.40
21.98
Me
O
H
4h
f1 (ppm)

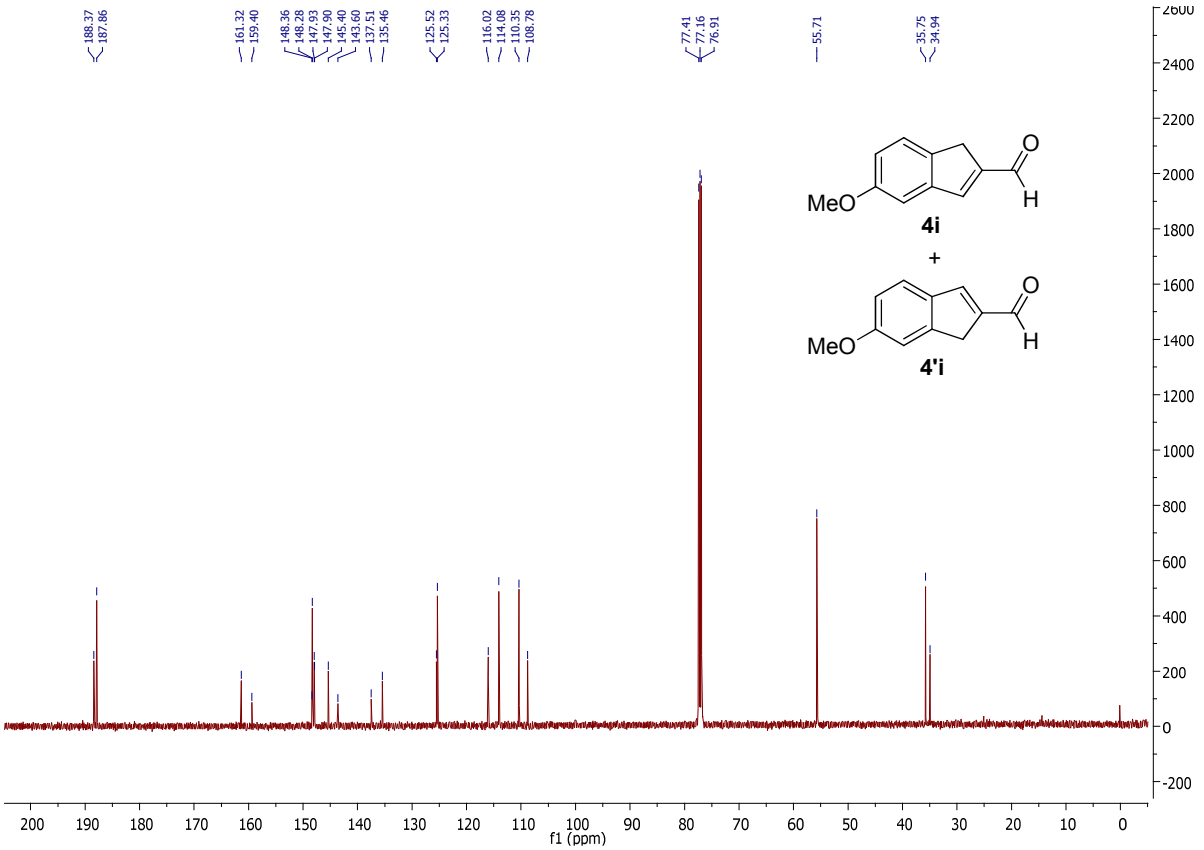

9.97
7.69
7.68
7.68
7.68
7.44
7.43
7.26
7.12
7.12
6.99
6.98
6.97
6.96
3.85
3.60
3.60
-0.00
1.00
1.02
1.02
1.02
1.02
3.18
2.11
MeO
O
H
4i
f1 (ppm)

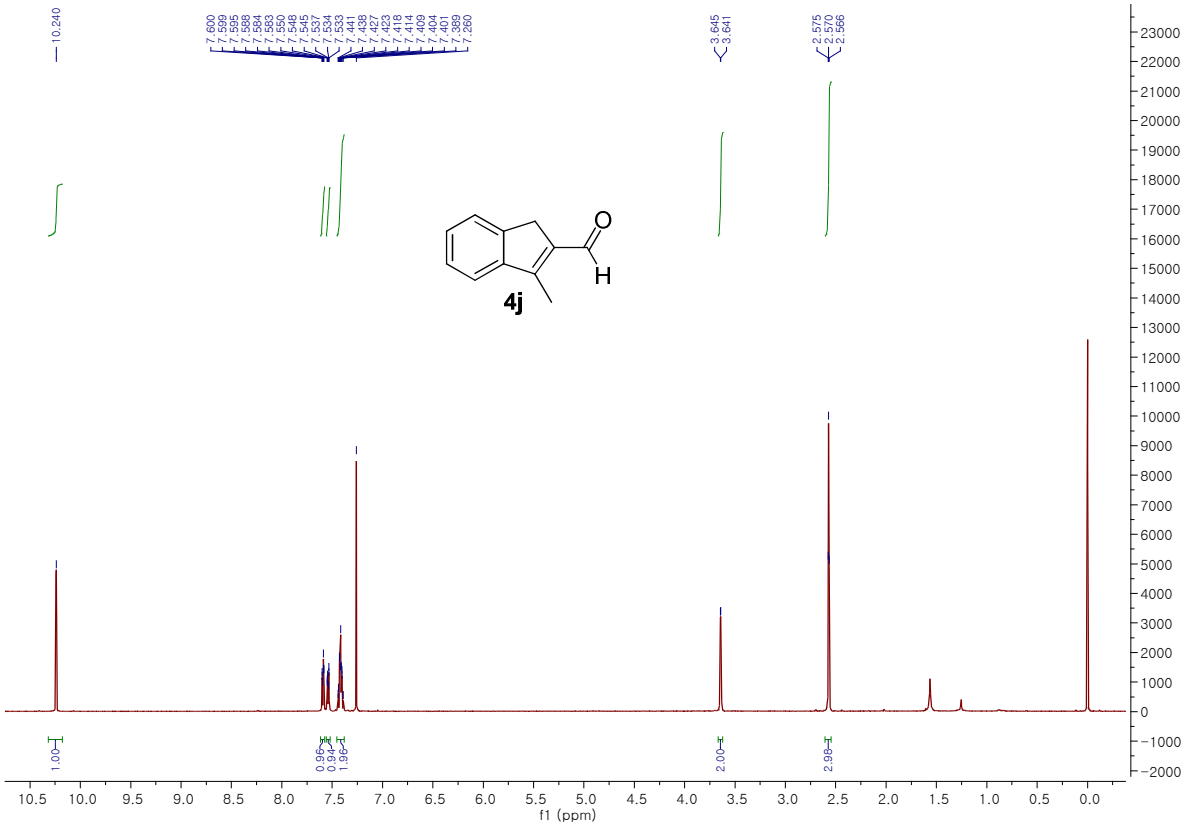

188.35
159.37
148.33
147.92
143.58
137.47
125.50
115.99
108.74
77.41
77.16
76.91
55.68
34.91
MeO
O
H
4i
f1 (ppm)

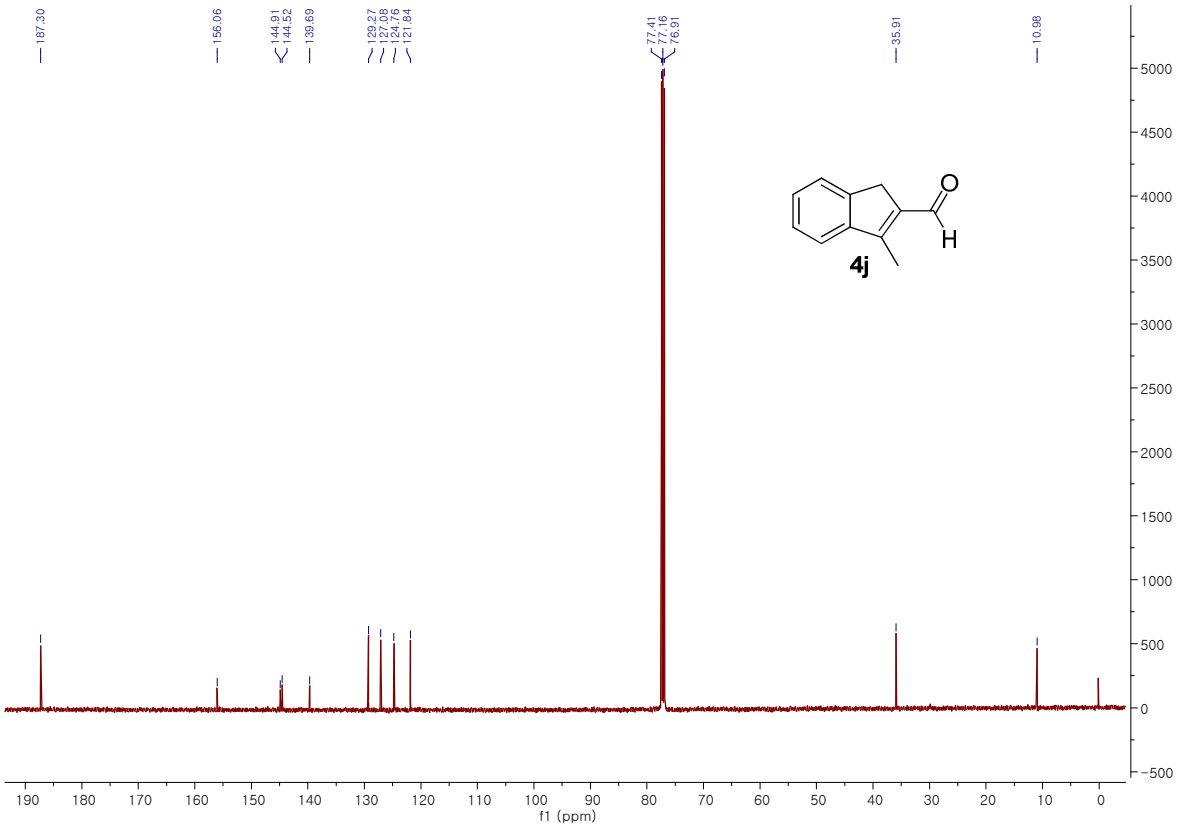

9.90
7.69
7.52
7.51
7.26
7.10
7.10
6.94
6.94
6.92
6.92
3.87
3.65
0.00
MeO
O
H
4'i
0.99
1.00
0.96
0.95
1.00
2.90
1.90
f1 (ppm)

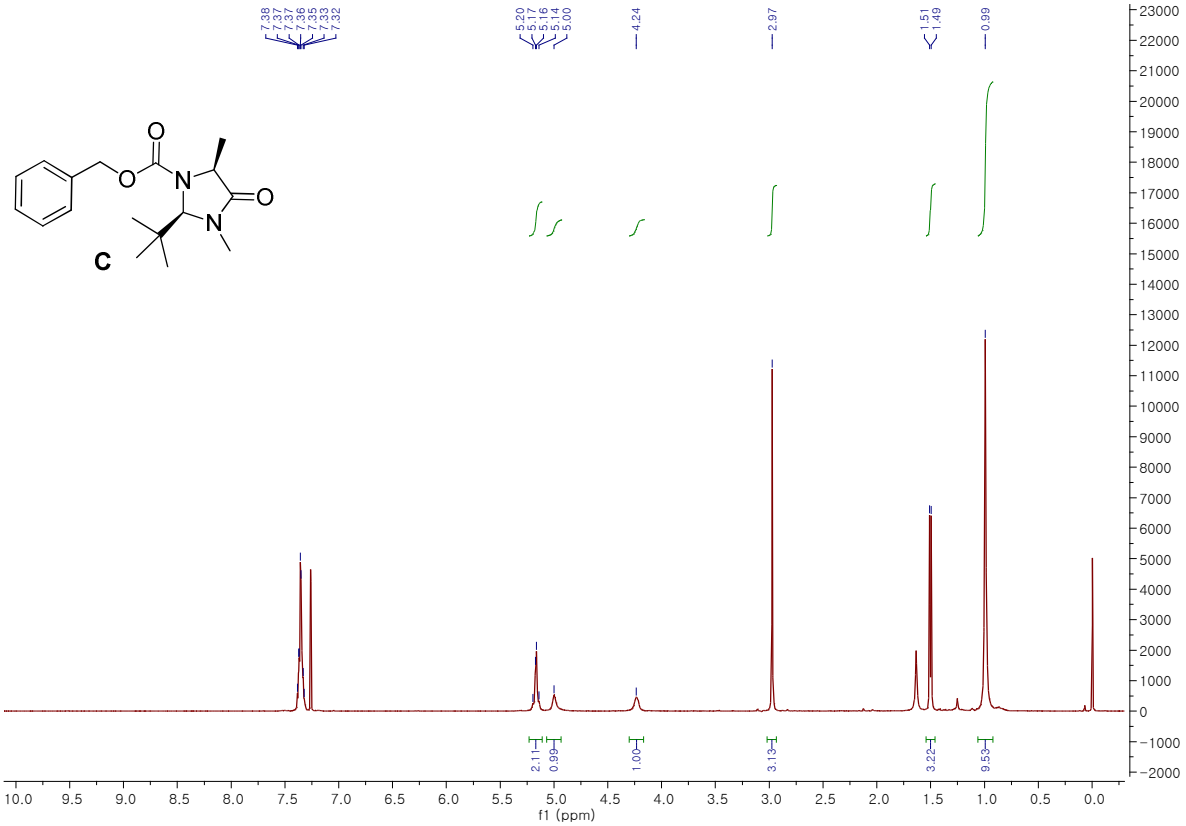

187.90
161.32
148.32
147.91
145.40
135.46
125.34
114.09
110.35
77.41
77.16
76.91
55.72
35.76
MeO
O
H
4'i
f1 (ppm)

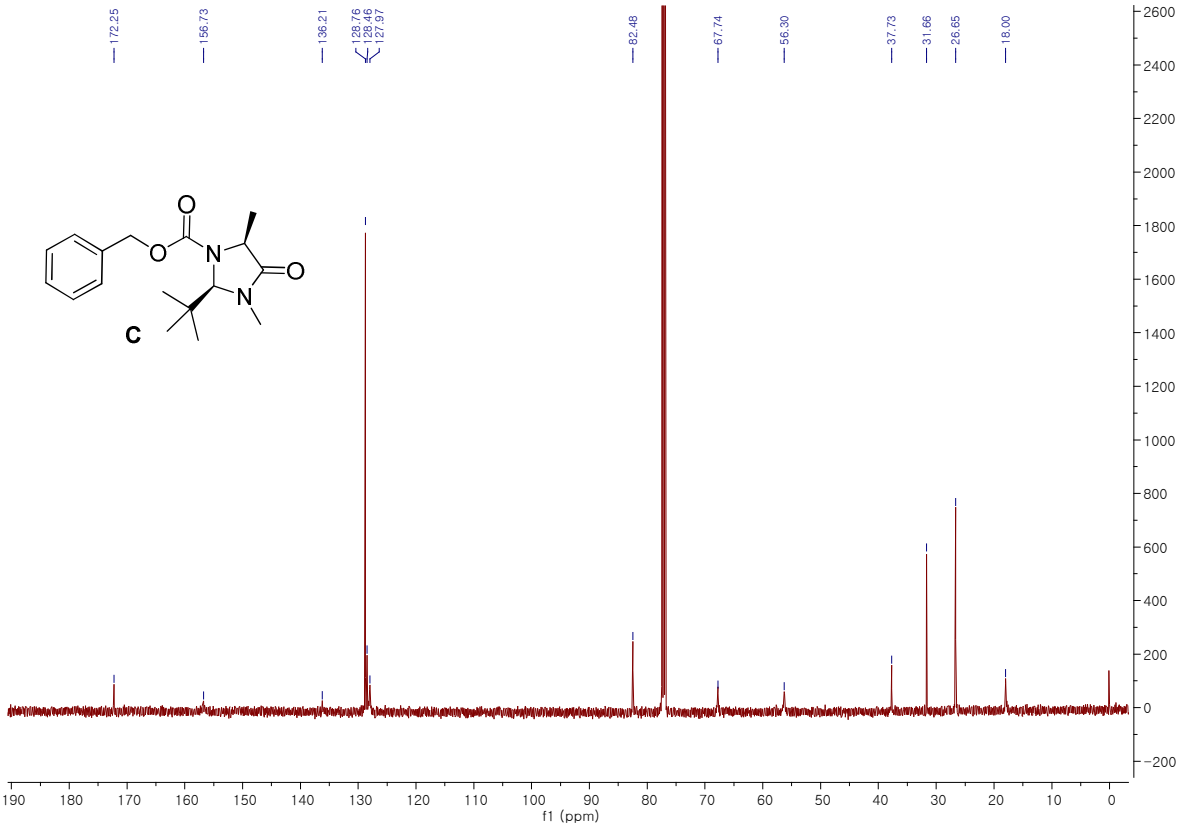

MeO
O
H
4i
+
MeO
O
H
4'i
f1 (ppm)

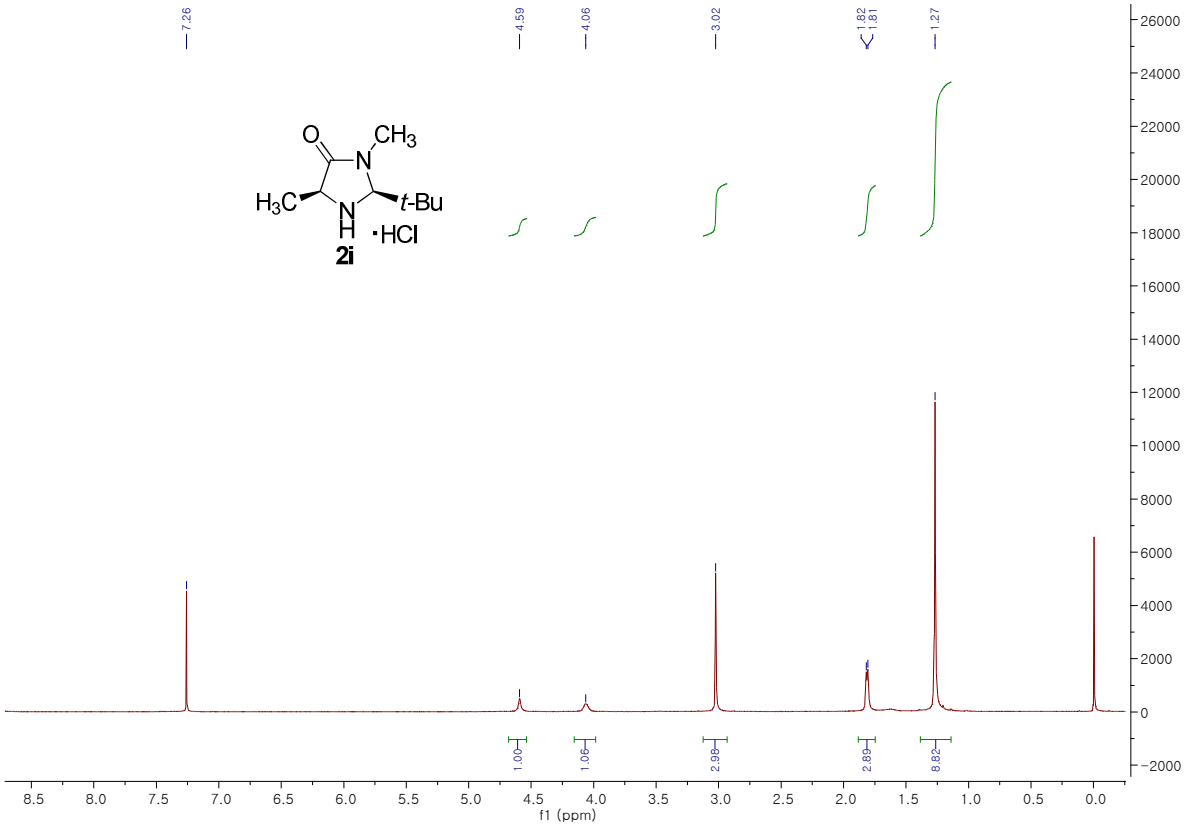

MeO
O
H
4i
+
MeO
O
H
4'i
f1 (ppm)

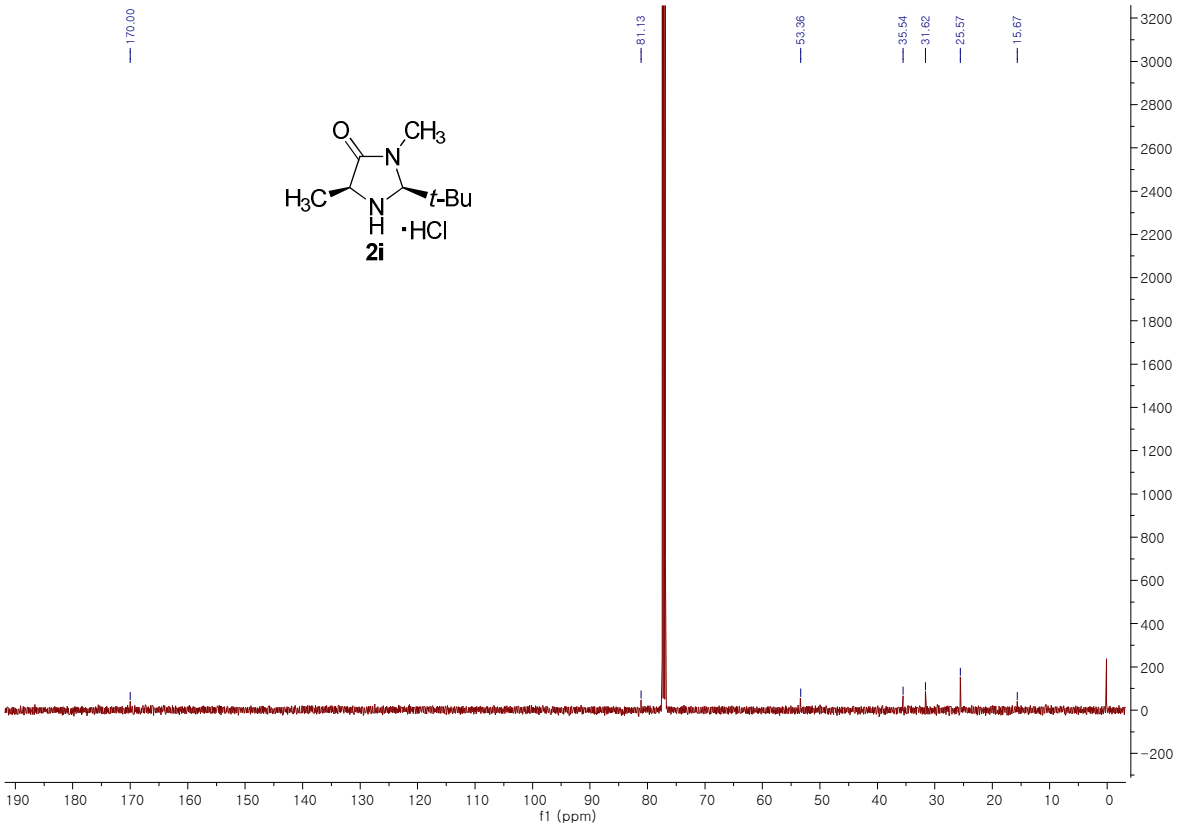

10.240
7.600
7.595
7.592
7.588
7.584
7.583
7.550
7.548
7.545
7.537
7.534
7.533
7.441
7.438
7.427
7.423
7.418
7.414
7.409
7.404
7.401
7.389
7.260
3.645
3.641
2.575
2.570
2.566
O
H
4j
1.00
0.96
0.94
1.96
2.00
2.98
f1 (ppm)

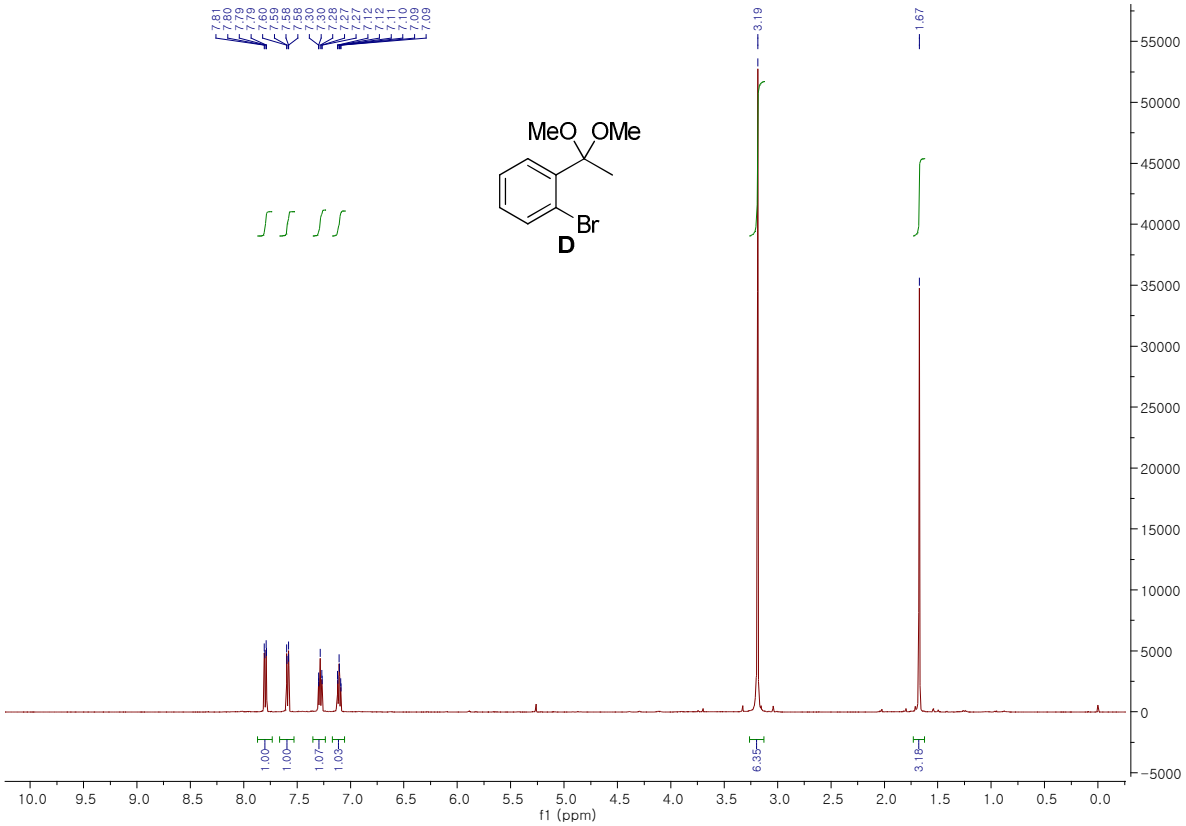

187.30
156.06
144.91
144.52
139.69
129.27
127.08
124.76
121.84
77.41
77.16
76.91
35.91
10.98
O
H
4j
f1 (ppm)

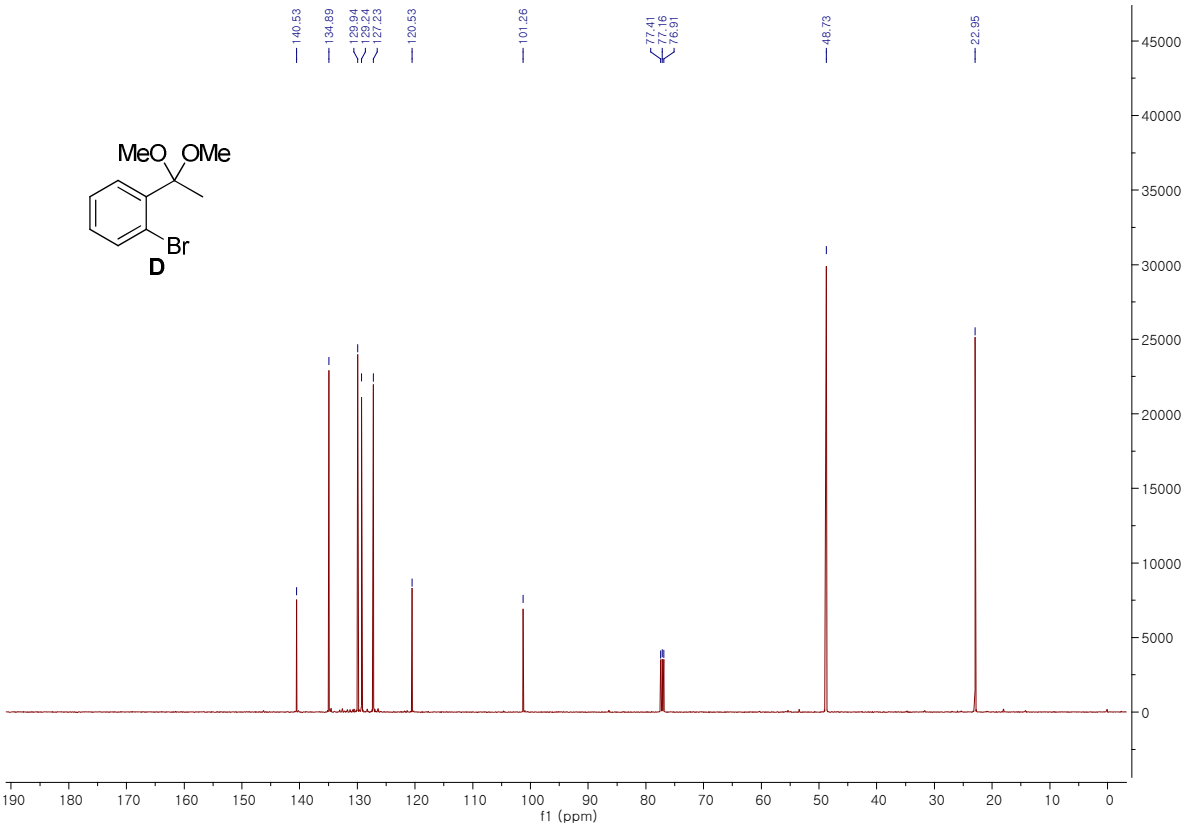

7.38
7.37
7.37
7.36
7.35
7.33
7.32
5.20
5.17
5.16
5.14
5.00
4.24
2.97
1.51
1.49
0.99
2.11
0.99
1.00
3.13
3.22
9.53
f1 (ppm)

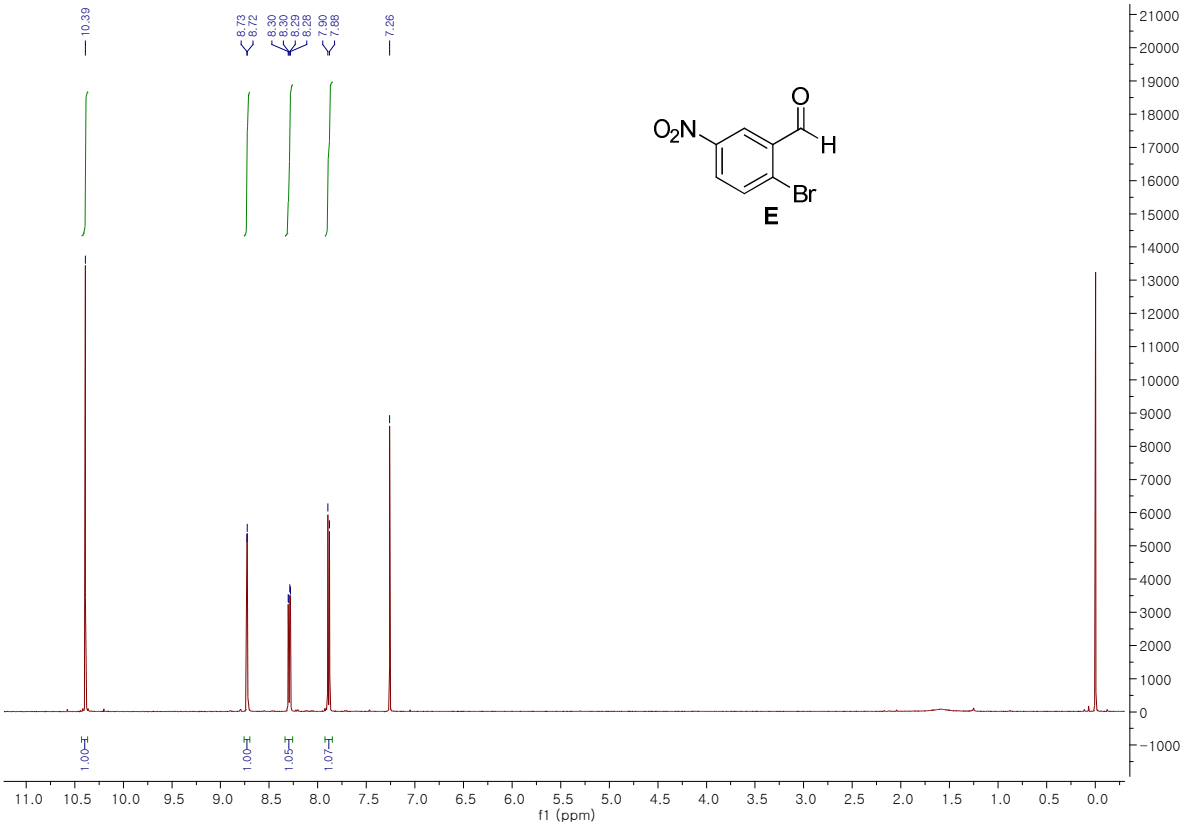

172.25
156.73
136.21
128.76
128.46
127.97
82.48
67.74
56.30
37.73
31.66
26.65
18.00
f1 (ppm)

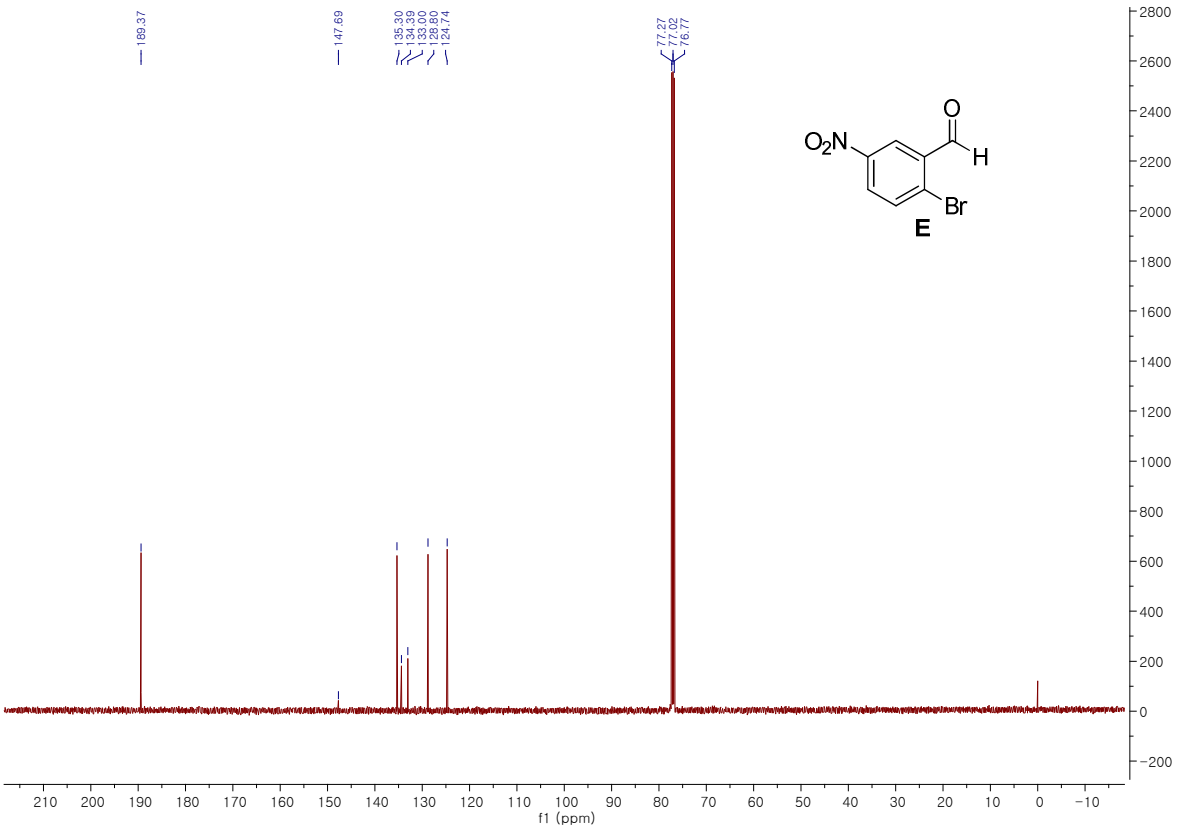

7.26
4.59
4.06
3.02
1.82
1.81
1.27
O
N
CH3
H3C
N
H
t-Bu
·HCl
2i
1.00
1.06
2.98
2.89
8.82
f1 (ppm)

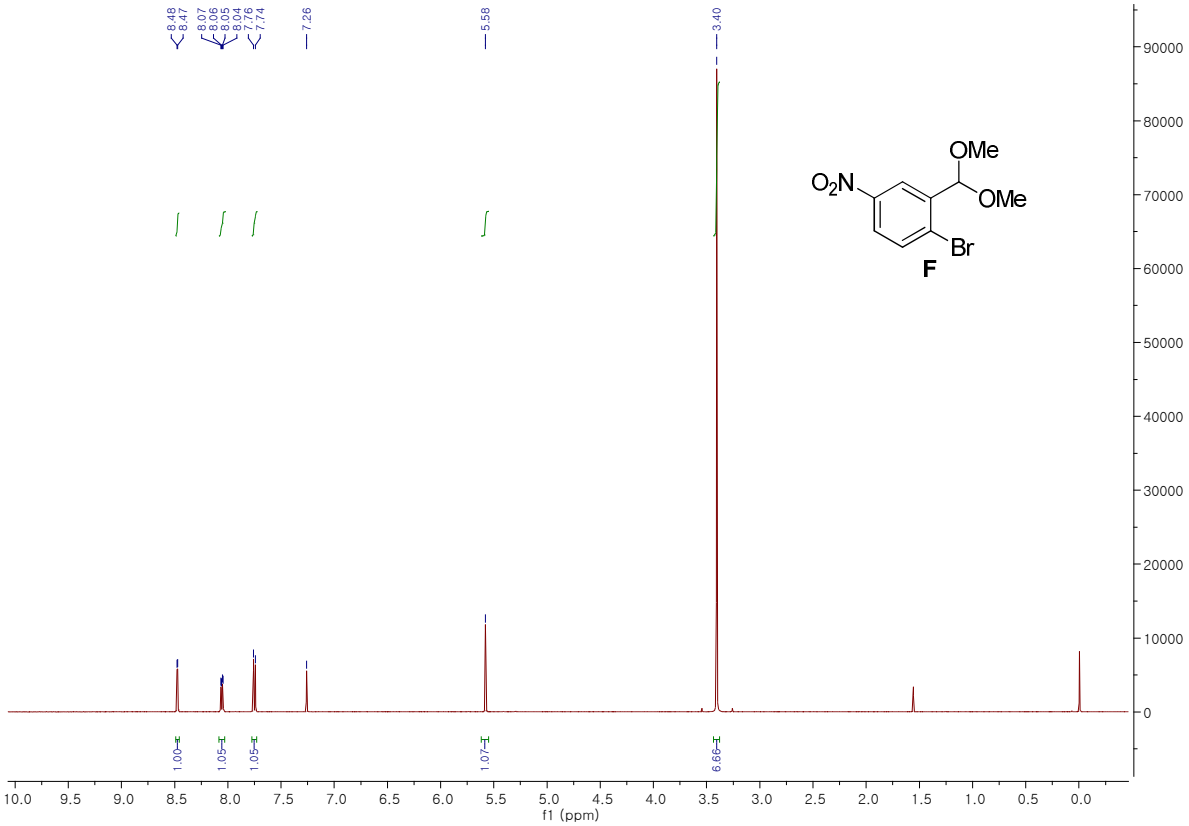

170.00
81.13
53.36
35.54
31.62
25.57
15.67
O
N
CH3
H3C
N
H
t-Bu
·HCl
2i
f1 (ppm)

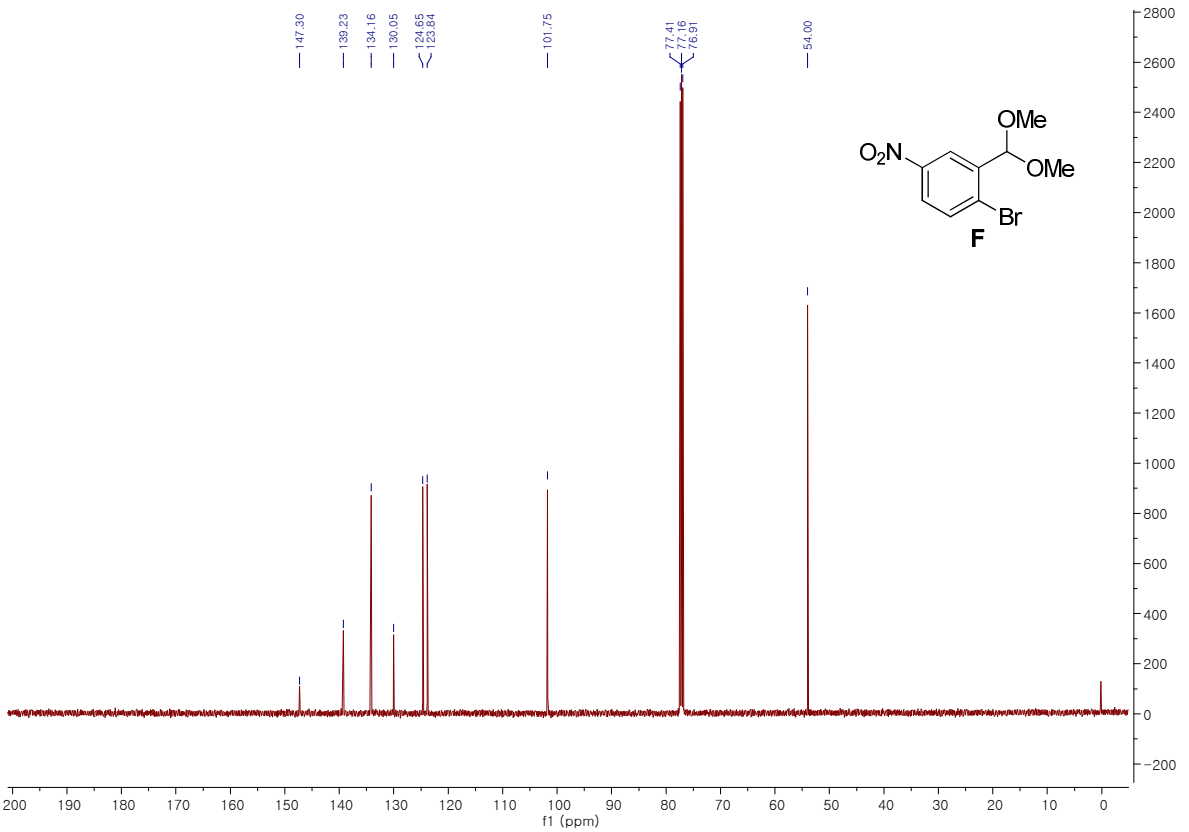

7.81
7.80
7.79
7.79
7.60
7.59
7.58
7.58
7.30
7.29
7.28
7.27
7.27
7.12
7.11
7.10
7.09
7.09
3.19
1.67
MeO
OMe
Br
D
1.00
1.00
1.07
1.03
6.35
3.18
f1 (ppm)


140.53
134.89
129.94
129.24
127.23
120.53
101.26
77.41
77.16
76.91
48.73
22.95
MeO
OMe
Br
D
f1 (ppm)


10.39
8.73
8.72
8.30
8.30
8.29
8.28
7.90
7.88
7.26
1.00
1.00
1.05
1.07
O2N
O
H
Br
E
f1 (ppm)


189.37
147.69
135.30
134.39
133.00
128.80
124.74
77.27
77.02
76.77
O2N
O
H
Br
E
f1 (ppm)


8.48
8.47
8.07
8.06
8.05
8.04
7.76
7.74
7.26
5.58
3.40
OMe
OMe
O_2N
Br
F
1.00
1.05
1.05
1.07
6.66
f1 (ppm)


147.30
139.23
134.16
130.05
124.65
123.84
101.75
77.41
77.16
76.91
54.00
OMe
OMe
O_2N
Br
F
f1 (ppm)