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Electronic Supplemental Information (ESI)

P-Trifluoromethyl ligands derived from *Josiphos* in the Ir-catalysed hydrogenation of 3,4-dihydroisoquinoline hydrochlorides

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Content

General procedures

Amides

All amides were synthesized following a general procedure, adding the corresponding acid chloride to a solution of the corresponding 2-phenylethanamine and triethylamine in DCM at 0 °C. The amides could all be precipitated as pure compounds by dropwise addition of an alkane (hexane, pentane) or ether (diethyl ether, tert. butylmethyl ether) to a solution of the crude amide in DCM or chloroform under stirring.

DHIQ*HCl / HI / HPF_6

All DHIQs investigated in this work were isolated starting from the amides, applying either a mixture of $POCl_3$ and P_2O_5 or following Movassaghis procedure applying Tf_2O in presence of 2-chloropyridine.[1] The crude reaction products were immediately protonated by hydrogen chloride in diethyl ether, hydrogen iodide or hexafluorophosphoric acid in water and purified by crystallization, precipitation or chromatography.

Racemic THIQ*HCl

To establish analytics for the screening samples, all racemic THIQ chlorides were prepared. The direct reduction of the DHIQ chlorides was achieved in a few cases by palladium on charcoal under hydrogen atmosphere. The pure product was conveniently obtained by filtration and evaporation of the solvent. Unfortunately, in several cases a sluggish conversion was observed even at 100 bar hydrogen pressure overnight. Hence, most samples were reduced by sodium borohydride, requiring subsequent reprotonation.

Standard screening experiment

A standard screening experiment for the enantioselective hydrogenation of 1-substituted 3,4-dihydroisoquinolinium chlorides was conducted as follows:

A 3 mL flat bottomed glas tube with a magnetic stirring bar was charged with 500 μmol of the substrate and 2.5 μmol (0.5 mol-%) of the precatalyst as [Ir(L)(cod)X]. The tube was purged with argon by means of three vacuum/argon cycles. 1 mL crown-capped solvent was added and the suspension (calculated to result a ~0.5 M solution) stirred for ten minutes under an argon atmosphere.

For the hydrogenation, the tube was closed by a screw cap with a hole for gas exchange. After tightly closing the autoclaves, the atmosphere was first inertized by three cycles of five bar nitrogen and subsequent pressure release. To change the atmosphere to hydrogen, ten bar hydrogen were applied and pressure released before the autoclaves were set to target reaction pressure. Then, stirring was switched on and the autoclaves heated to target temperature by external jacket heater.

After the reaction, heating was switched off and the autoclaves were kept under pressure for at least 30 minutes to cool below 30 °C. Thereafter, pressure was released and the autoclaves set under nitrogen again.

Analysis of the screening samples

To the samples was added 1,3,5-trimethoxybenzene (150 µmol) as internal standard and methanol until a clear homogeneous solution was obtained. Around 0.2 mL of this solution was directly evaporated to dryness in NMR tubes for determination of conversion and yield by integration of well separated signals (one scan, zero dummy scans).

Around 0.1 mL of the same solution was partitioned between NaOH (2 M in water, 1 mL) and hexane (1 mL). The hexane phase was separated, dried over Na_2SO_4 and filtered over a syringe filter. The clear colorless solutions were directly injected in HPLC for determination of *ee*.

Acetamidation of reaction products

If the enantiomers of the free tetrahydroisoquinoline were not separable or potentially overlapping with side products, internal standard or starting material, the reaction products were derivatized to their acetamide.

After determining conversion and yield by NMR spectroscopy, the remaining sample solution was evaporated to dryness. Acetic anhydride (0.5 mL) and triethylamine (1 mL) were added and the dark samples stirred overnight. After removing all volatiles under HV, the residue was filtered over silica before a sample was prepared for HPLC analysis.

Derivatization of 1-methyl-THIQ **13b** for GC analysis

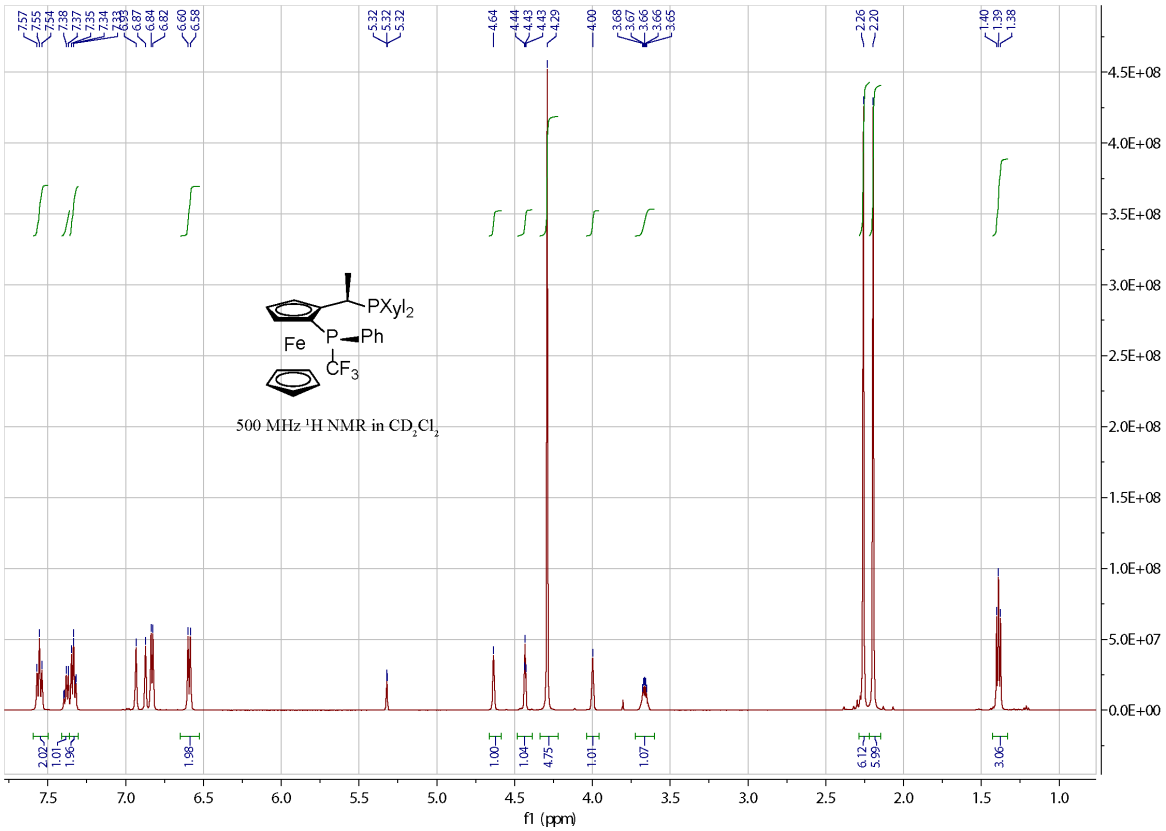
Derivatization for GC analysis: 1-Methyl-1,2,3,4-tetrahydroisoquinolin-2-ium chloride **13b***HCl (3.0 mg, 16.33 µmol, 1.0 eq.) was dissolved in acetonitrile (1 mL), triethylamine (30 µL, 21.78 mg, 215.24 µmol, 13.2 eq.) and (-)-(*R*)-menthyl chloroformate (20 µL, 20.4 mg, 93.27 µmol, 5.7 eq.) were added and the solution shaken for some minutes. This solution was directly injected into GC.[2]

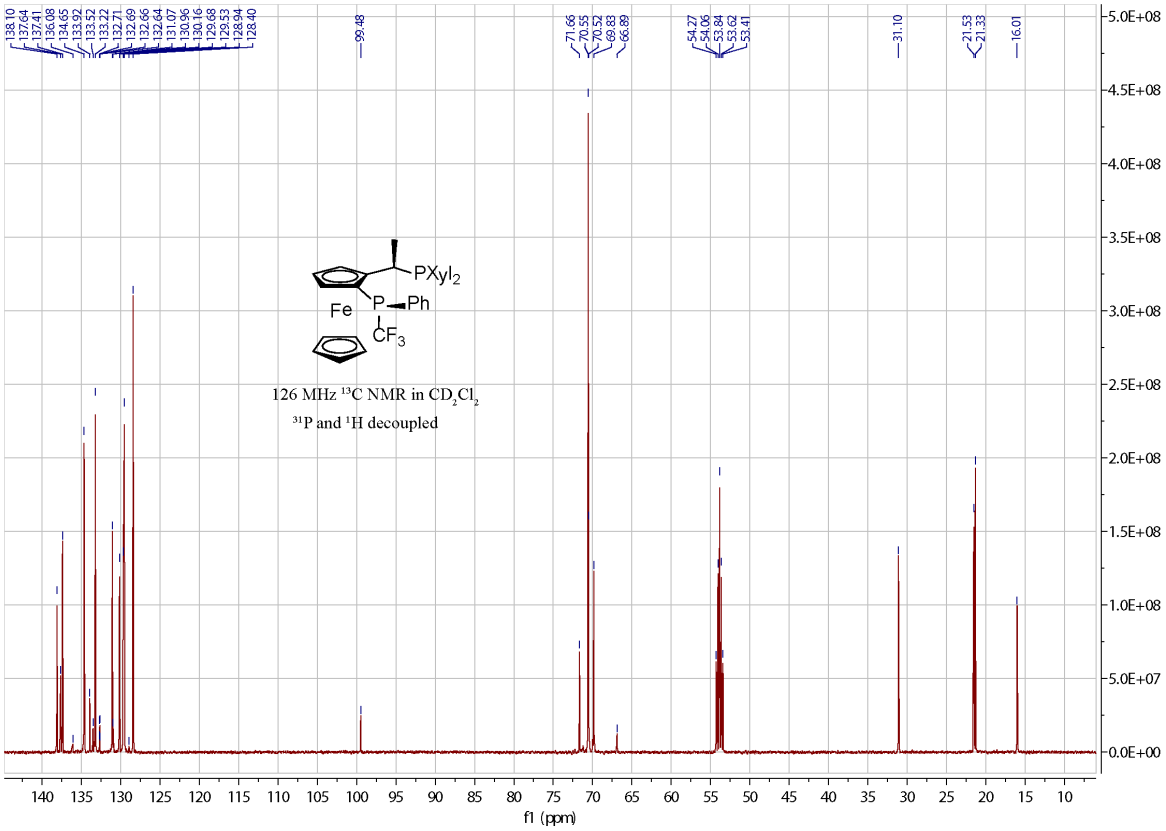
Determination of optical rotation sign

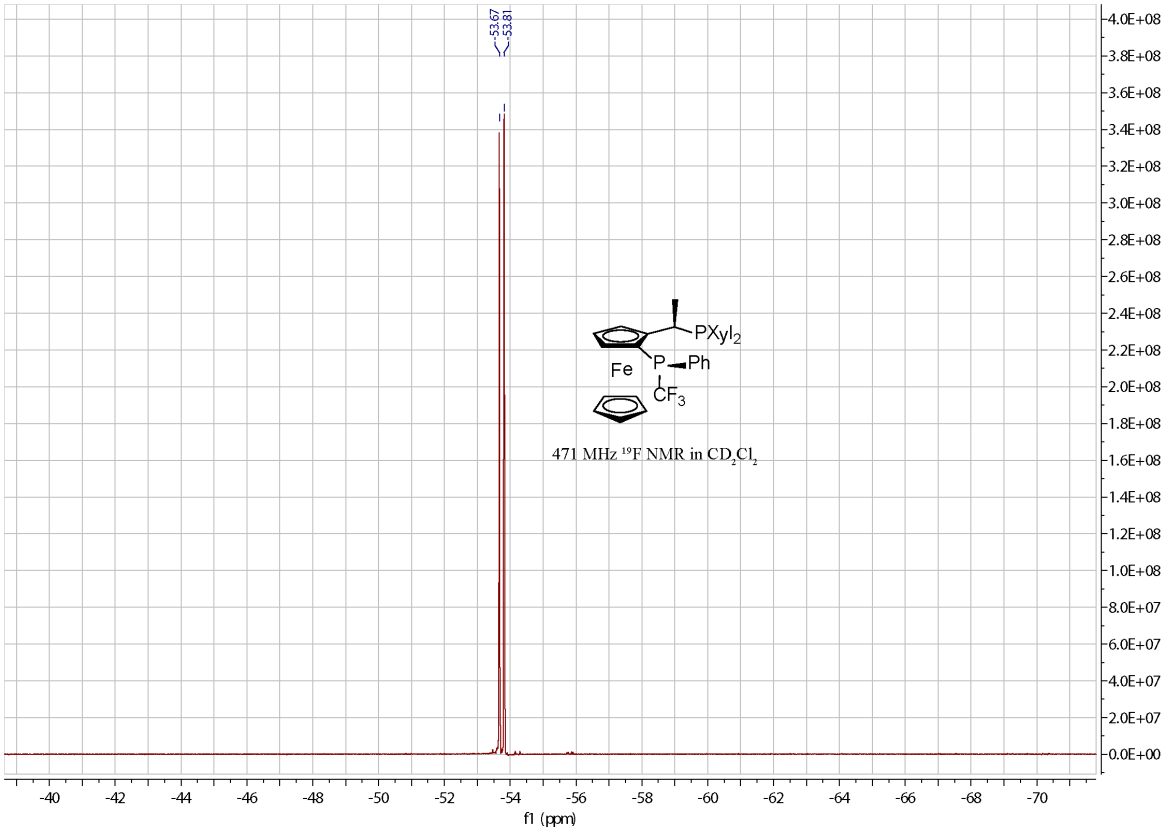
To assign the HPLC peaks to the corresponding enantiomers, the hydrogenation sample with the highest observed *ee* was purified and dissolved as hydrochloride in chloroform with a concentration of around 0.5 g/100 mL. The derivatized sample (acetamide) was used for determination of optical rotation where applicable. The optical rotations of these samples were recorded at 589 nm, in a 10 cm measuring cell at 20 °C. The assignment of the major peak in HPLC with the observed sign was possible in all the cases, although some of the observed optical rotation angles were rather small.

Ligands

(S_P)-(CF_3)Ph-Xyliphos (S_P)-**5**



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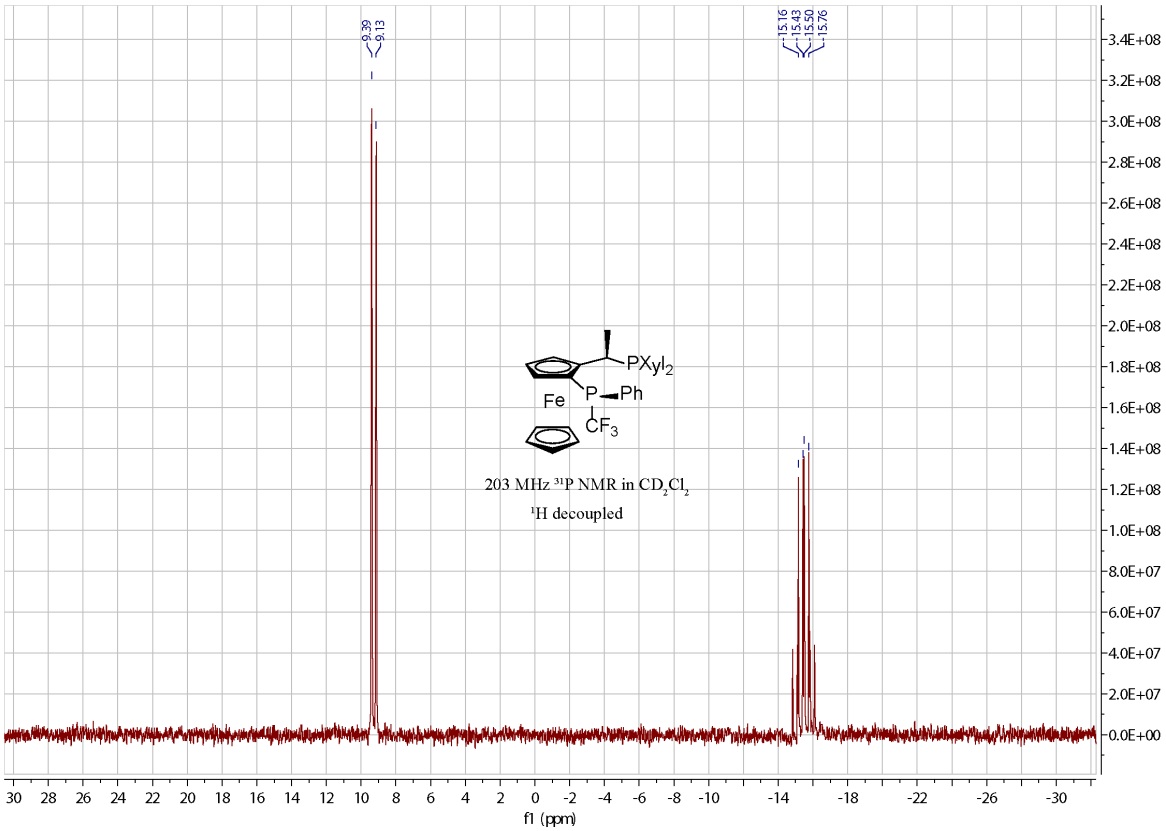
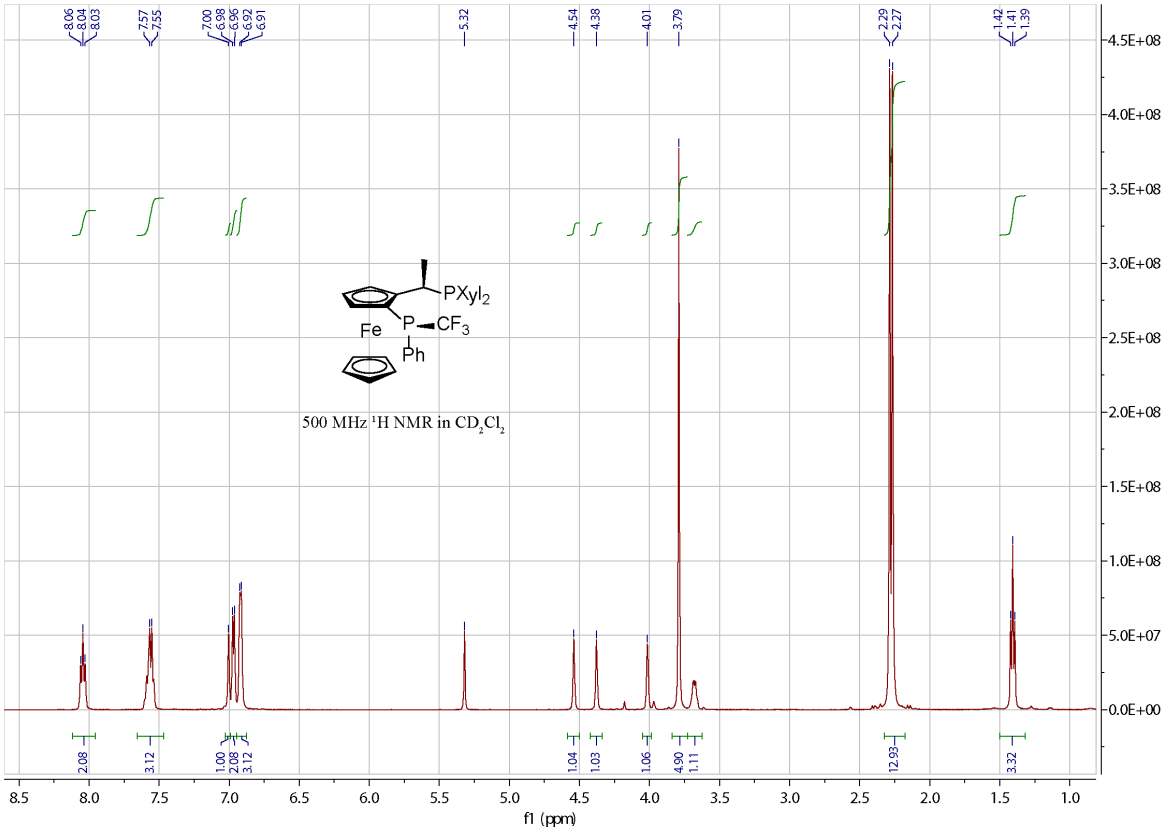
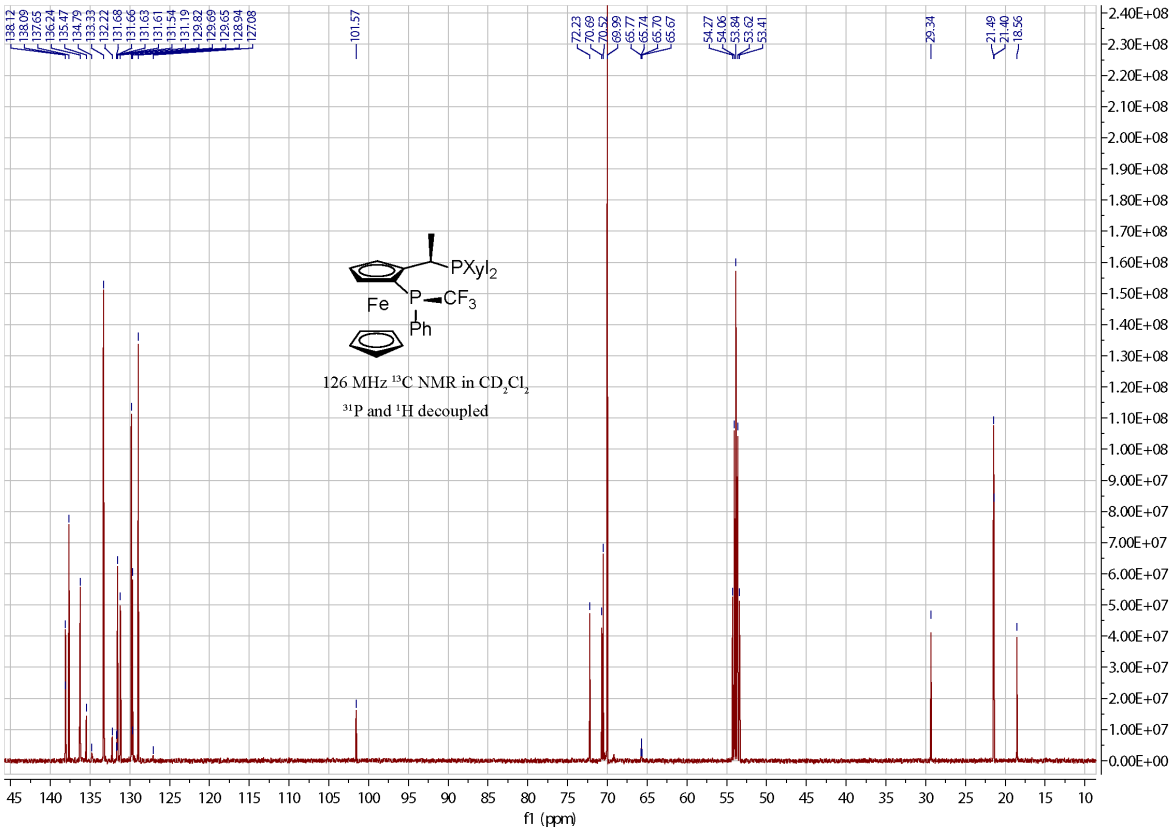
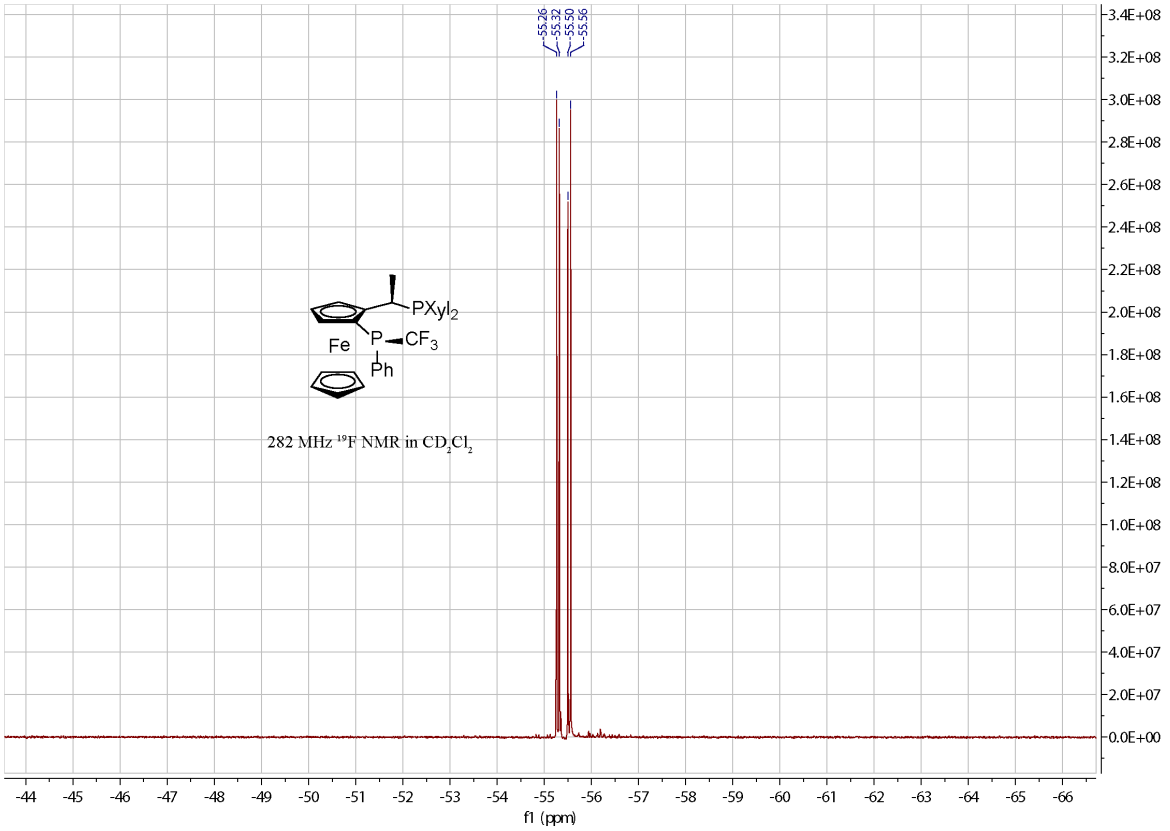
Fe
P
Ph
CF3
471 MHz 19F NMR in CD2Cl2
f1 (ppm)


9.39
9.13
15.16
15.43
15.50
15.76
PXyl2
Fe
P
Ph
CF3
203 MHz 31P NMR in CD2Cl2
1H decoupled
f1 (ppm)

(R_P)-(CF_3)Ph-Xyliphos (R_P)-**5**



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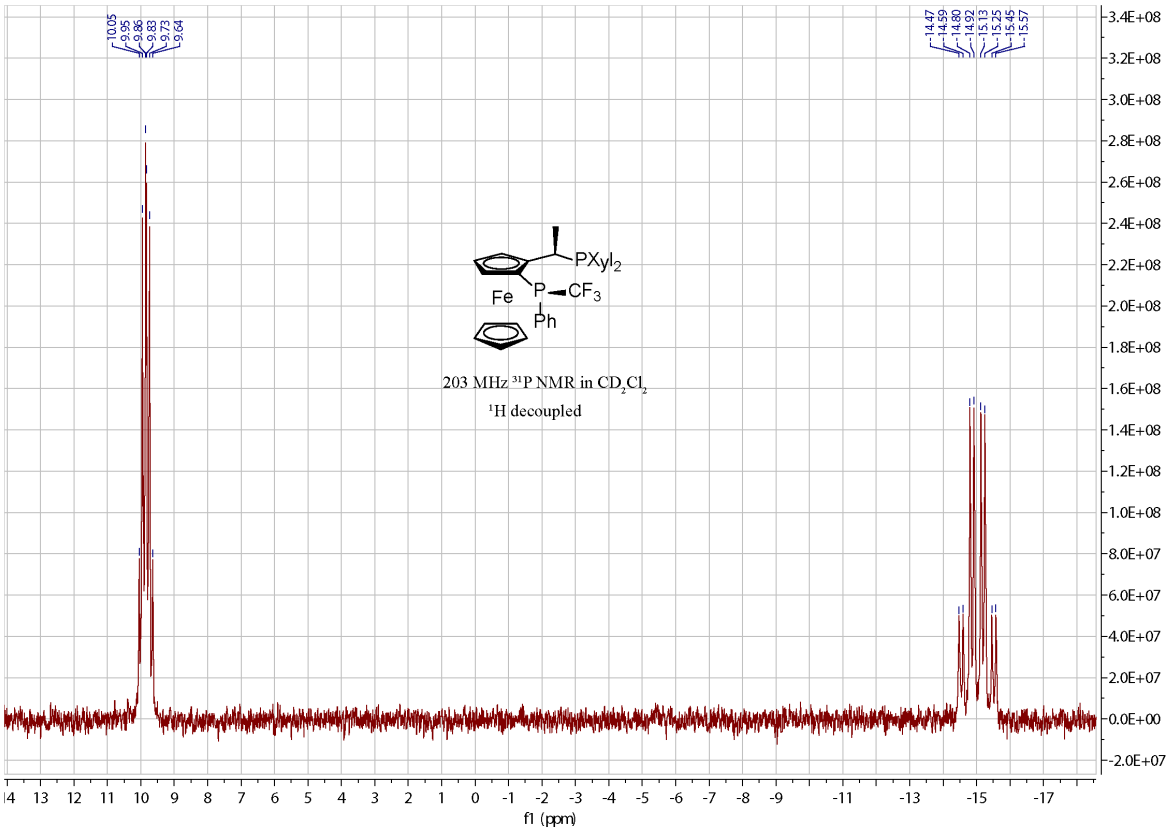
P
CF3
Ph
282 MHz 19F NMR in CD2Cl2
f1 (ppm)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9.73
9.64
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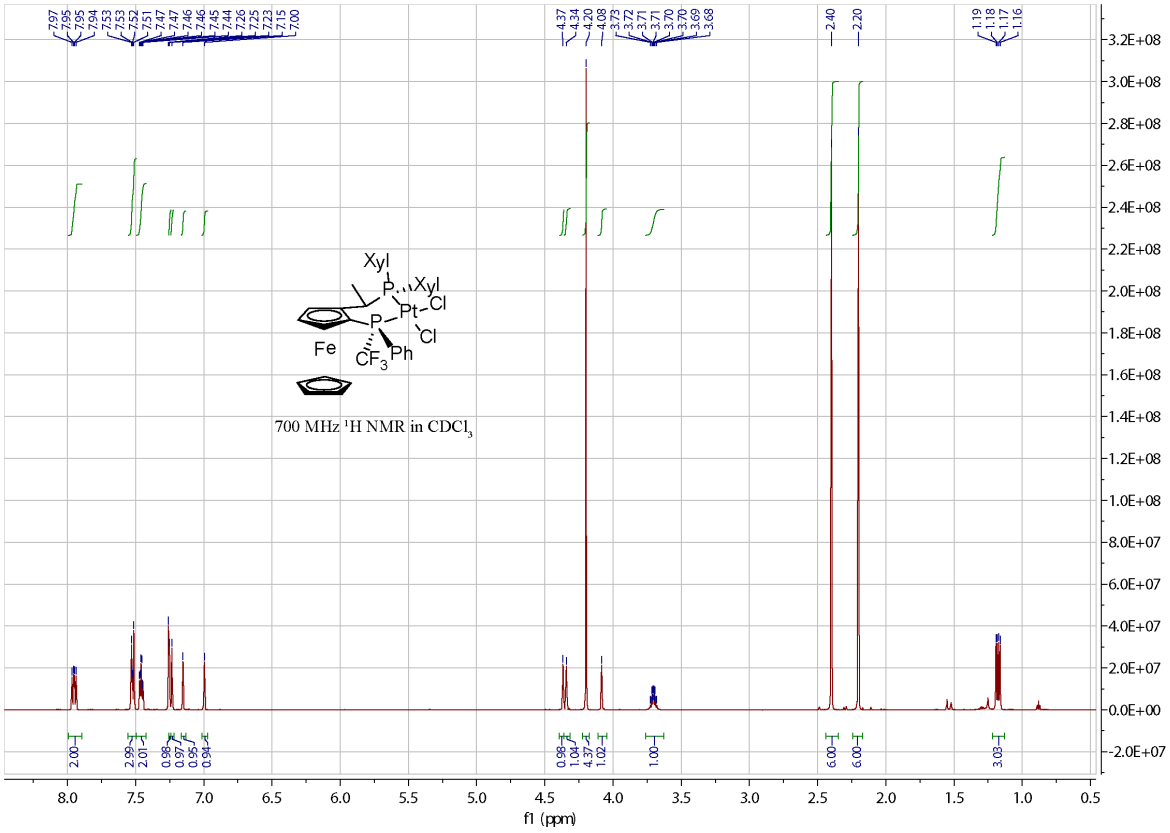
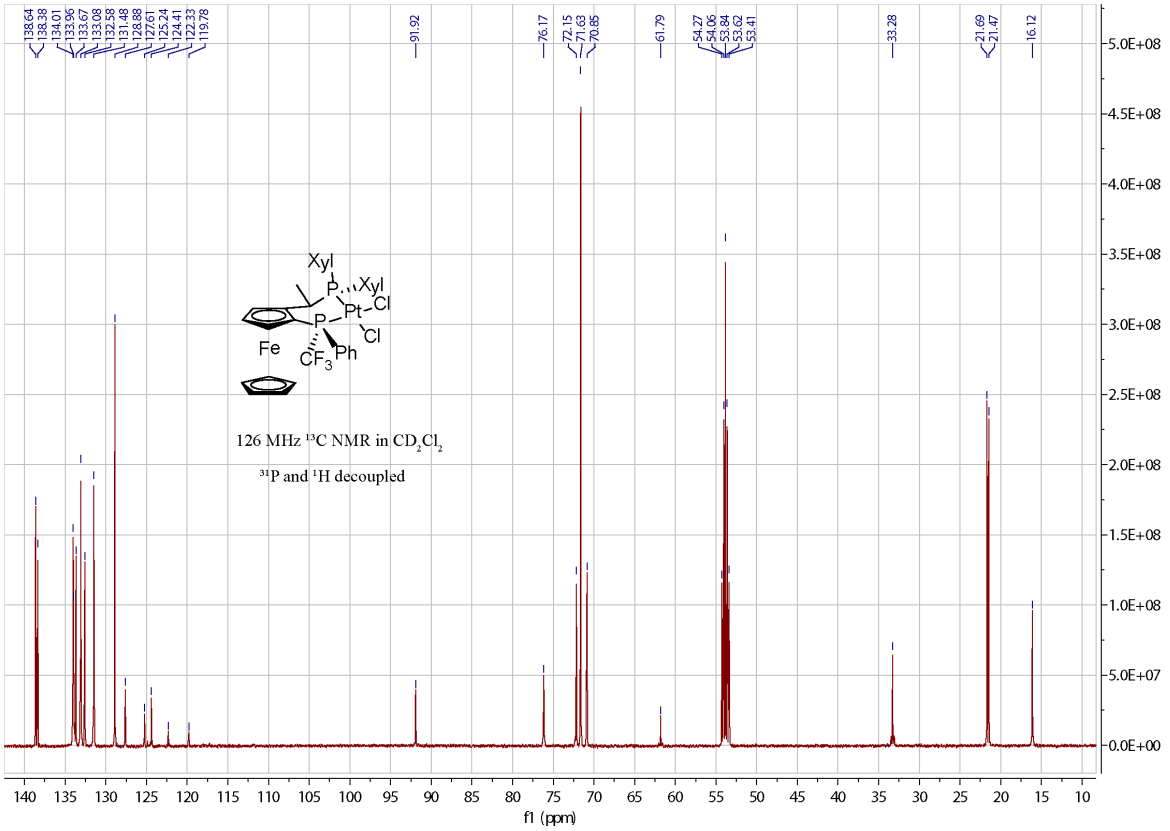
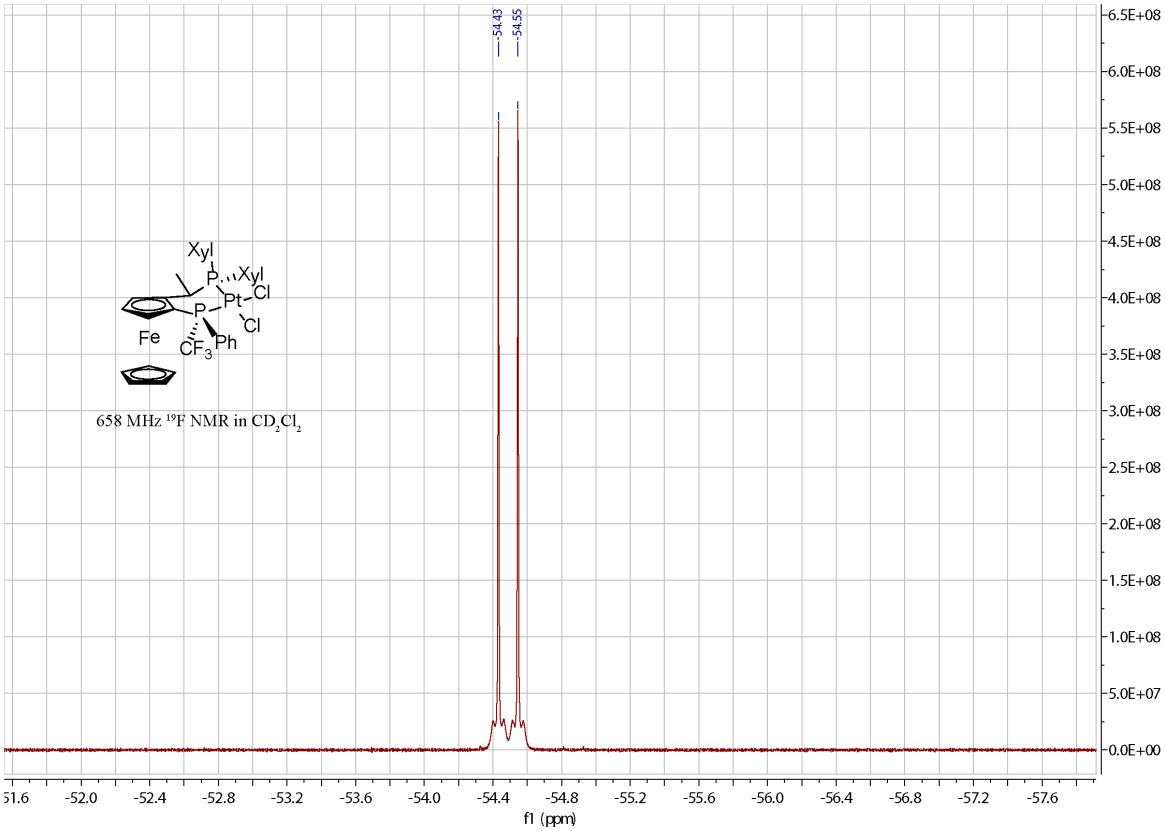
14.80
14.92
15.13
15.25
15.45
15.57
PXyl2
Fe
P
CF3
Ph
203 MHz 31P NMR in CD2Cl2
1H decoupled
f1 (ppm)

Complexes

[Pt((S_P)-(CF_3)Ph-Xyliphos)Cl_2] (S_P)-**11**






-54.43
-54.55
Xyl
P
Xyl
Pt
Cl
P
Cl
Fe
CF3
Ph
658 MHz 19F NMR in CD2Cl2
6.5E+08
6.0E+08
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
51.6
-52.0
-52.4
-52.8
-53.2
-53.6
-54.0
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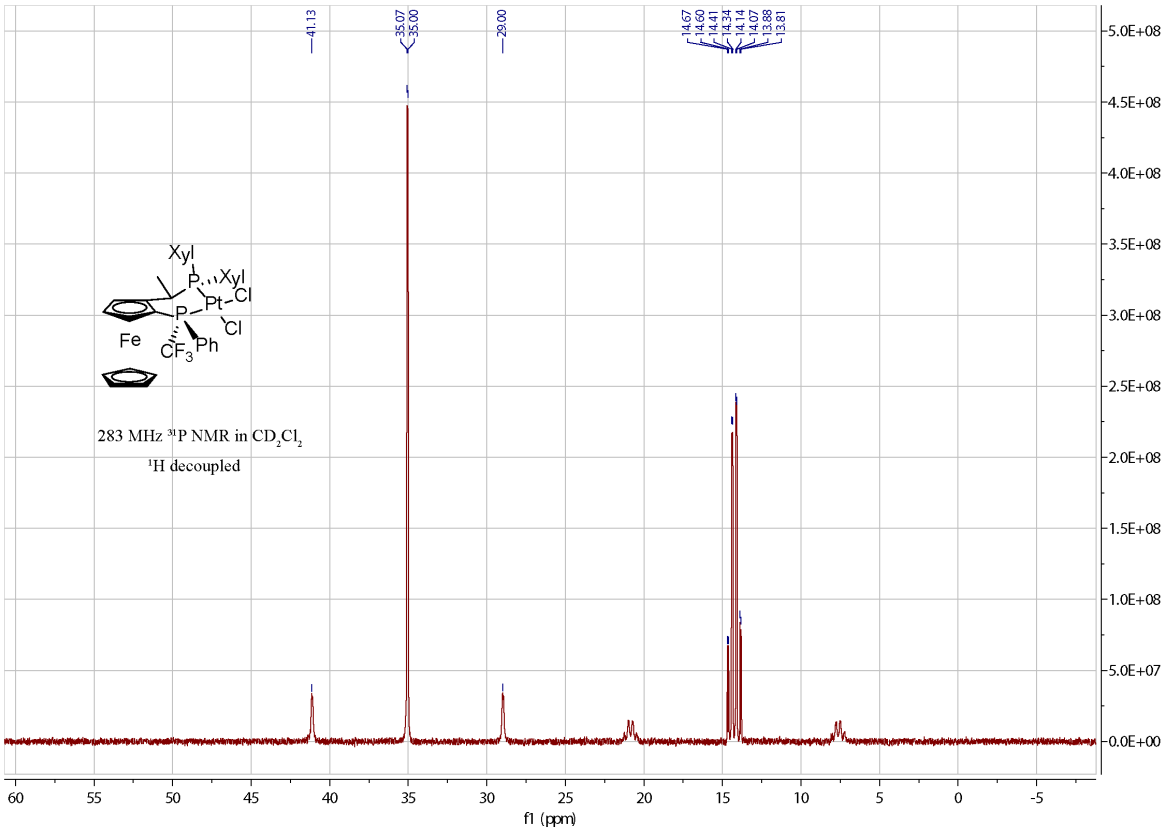
f1 (ppm)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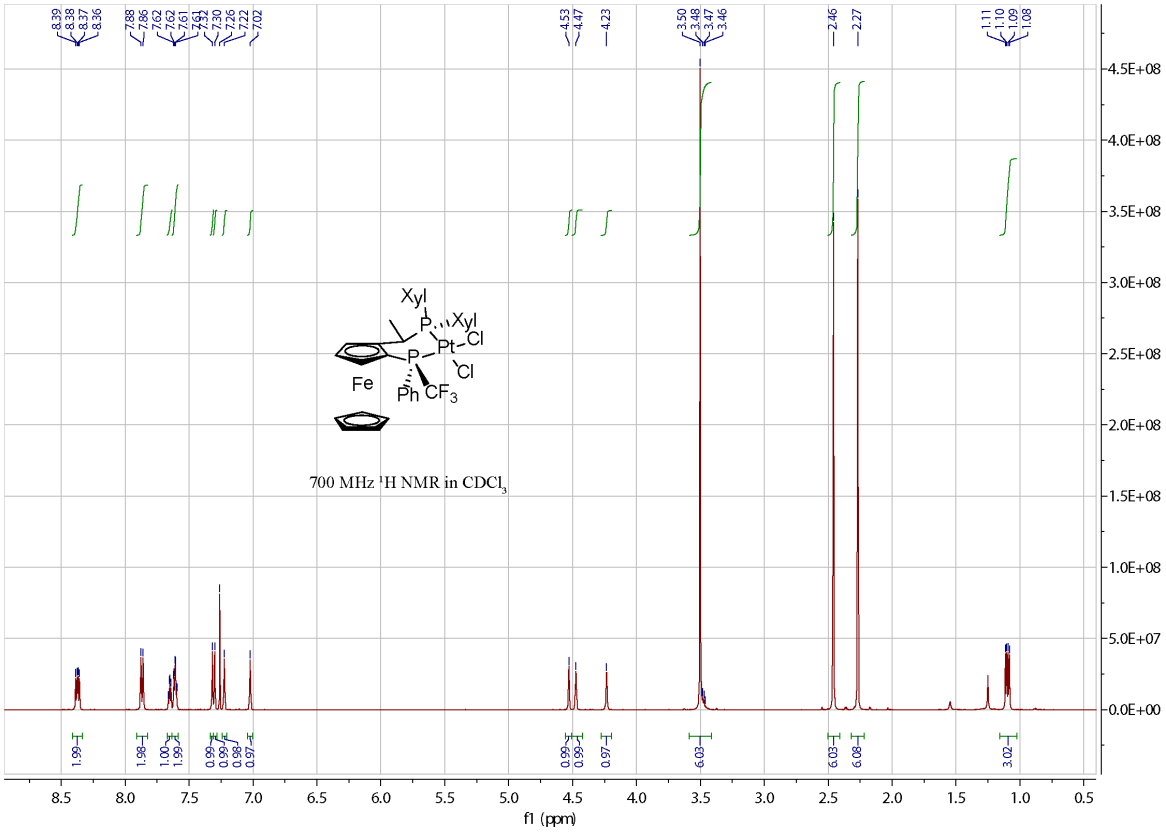
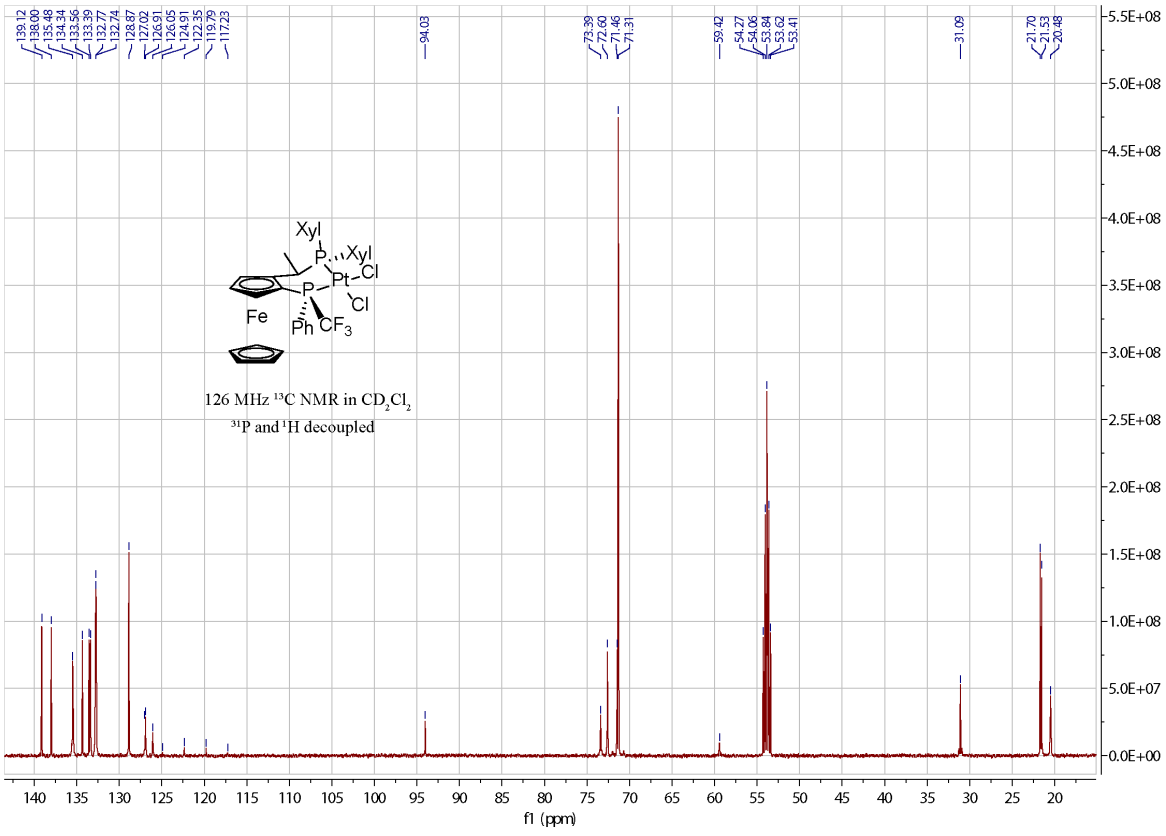
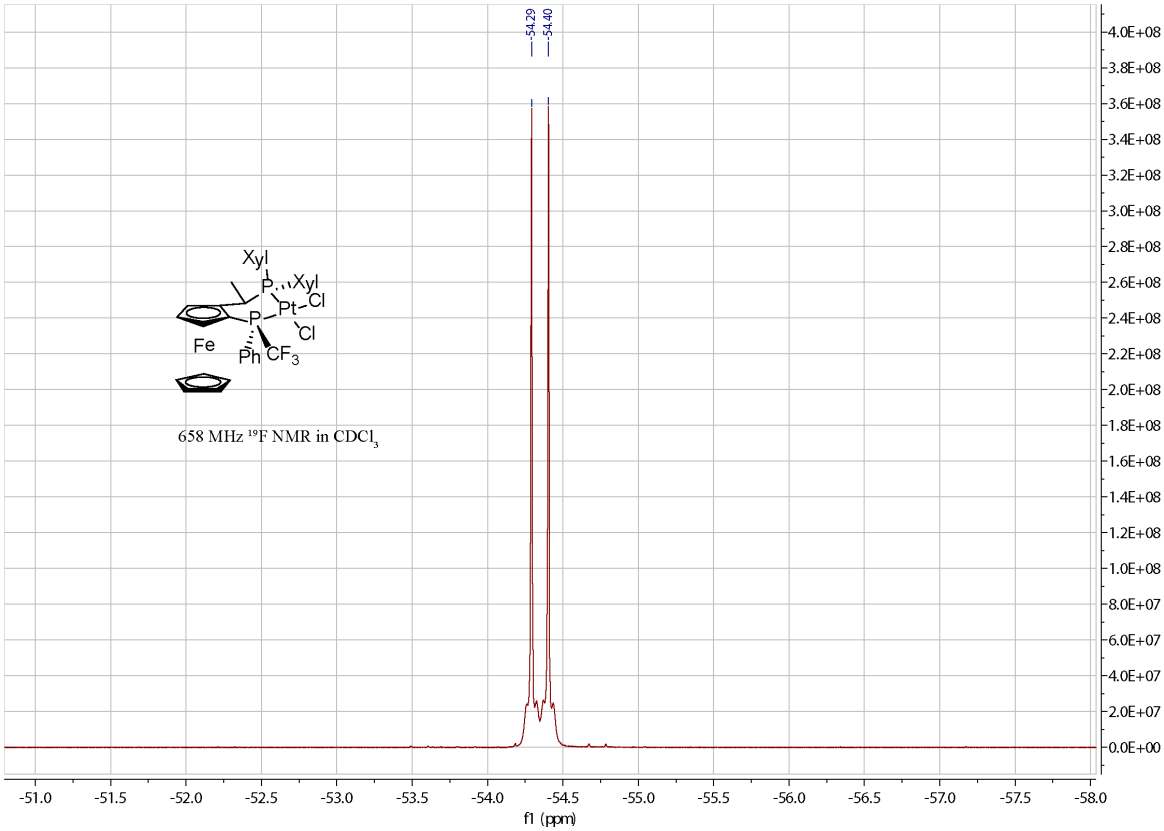
14.34
14.14
14.07
13.88
13.81
Xyl
P
Xyl
Pt
Cl
P
Cl
Fe
CF3
Ph
283 MHz 31P NMR in CD2Cl2
1H decoupled
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
f1 (ppm)

[Pt((*R*P)-(CF$_3$)Ph-Xyliphos)Cl$_2$] (*R*P)-**11**



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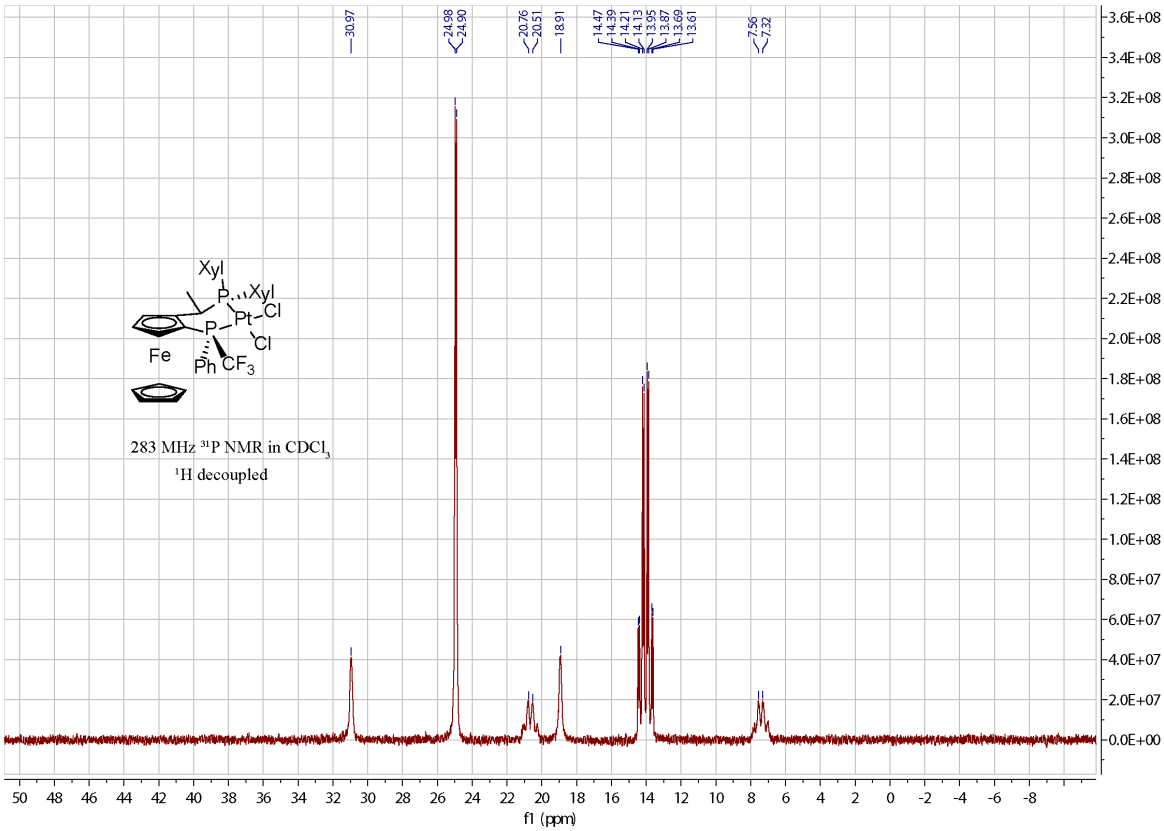
-54.40
Xyl
P
Xyl
Pt
Cl
P
Cl
Fe
Ph
CF3
658 MHz 19F NMR in CDCl3
4.0E+08
3.8E+08
3.6E+08
3.4E+08
3.2E+08
3.0E+08
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-51.0 -51.5 -52.0 -52.5 -53.0 -53.5 -54.0 -54.5 -55.0 -55.5 -56.0 -56.5 -57.0 -57.5 -58.0
f1 (ppm)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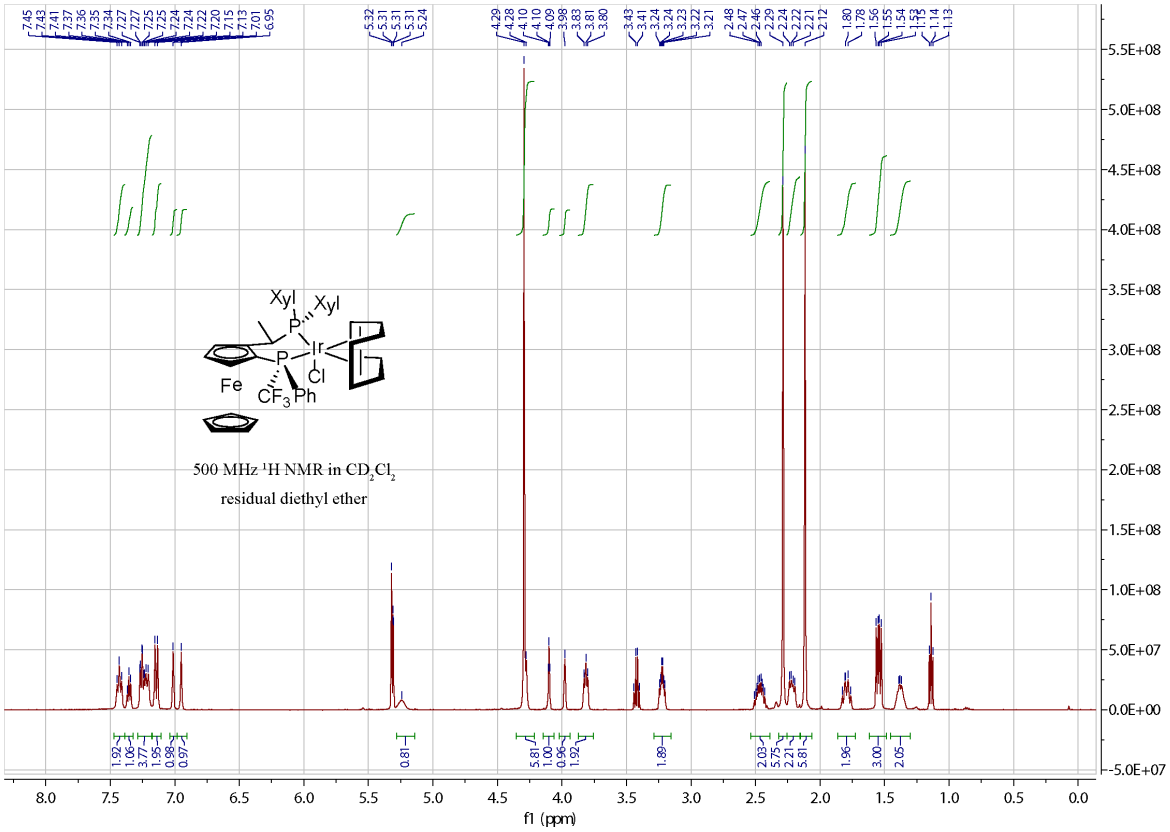
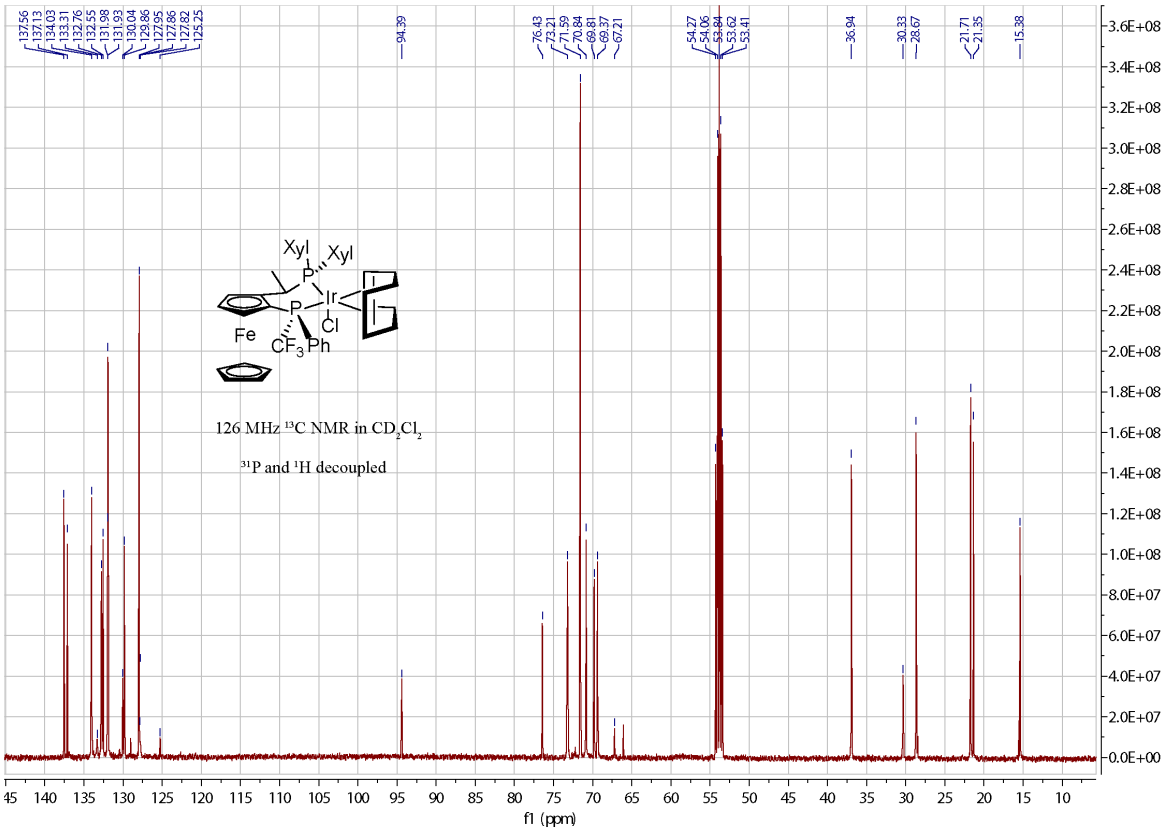
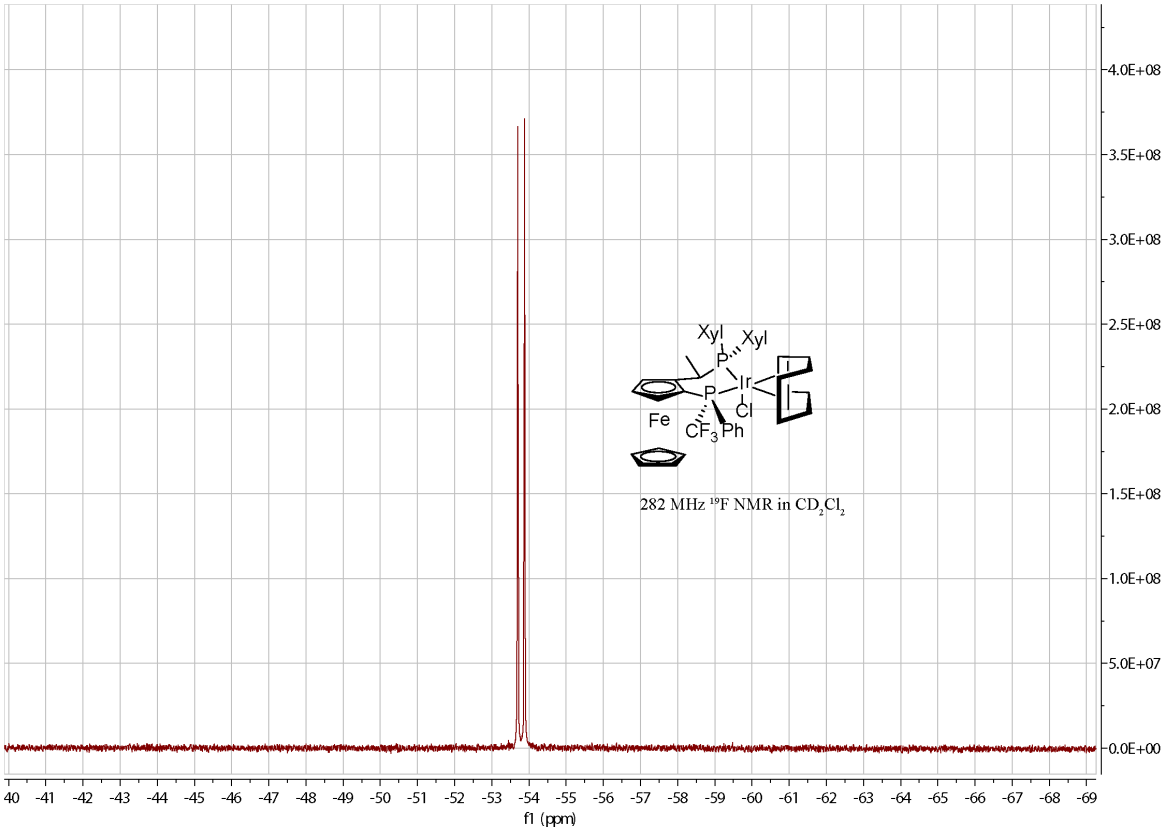
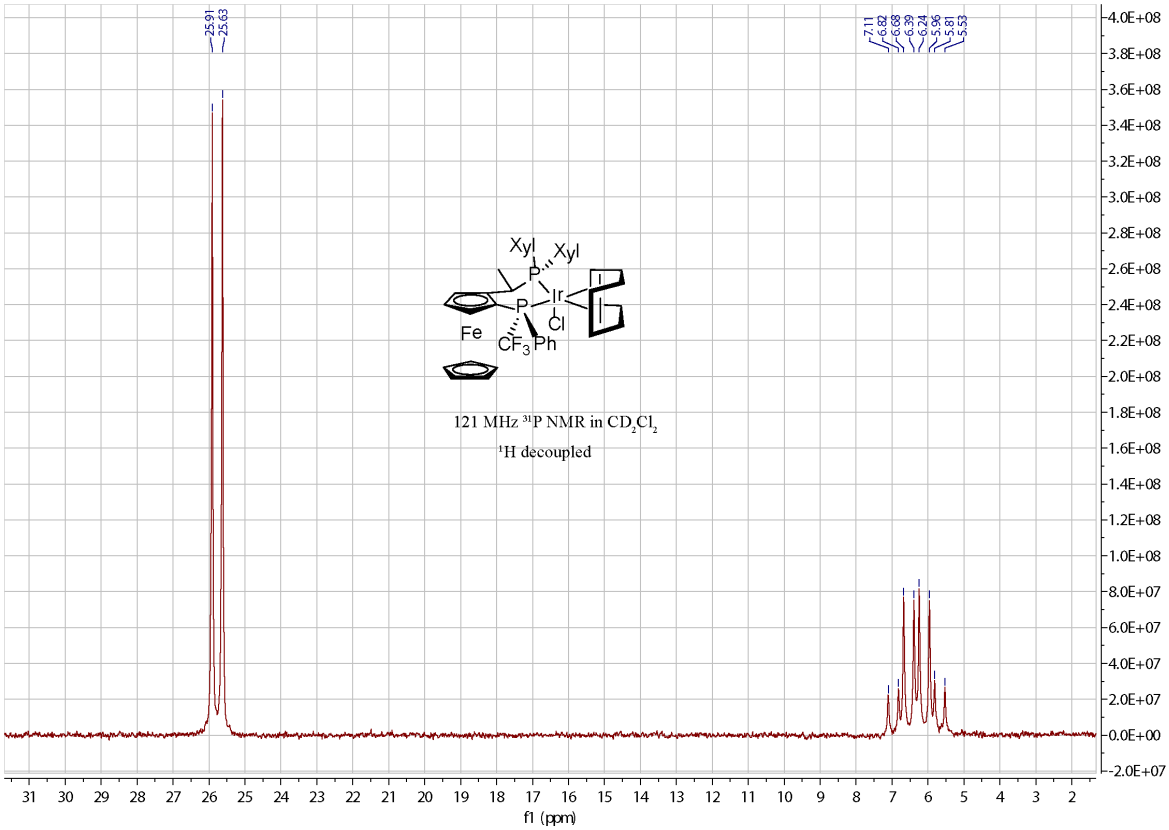
20.51
18.91
14.47
14.39
14.21
14.13
13.95
13.87
13.69
13.61
7.56
7.32
Xyl
P
Xyl
Pt
Cl
P
Cl
Fe
Ph
CF3
283 MHz 31P NMR in CDCl3
1H decoupled
3.6E+08
3.4E+08
3.2E+08
3.0E+08
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
50 48 46 44 42 40 38 36 34 32 30 28 26 24 22 20 18 16 14 12 10 8 6 4 2 0 -2 -4 -6 -8
f1 (ppm)

[Ir((*S*P)-(CF$_3$)Ph-Xyliphos)(cod)Cl] (*S*P)-**9**Cl






Xyl
Xyl
P
Ir
P
Cl
Fe
CF3
Ph
282 MHz 19F NMR in CD2Cl2
f1 (ppm)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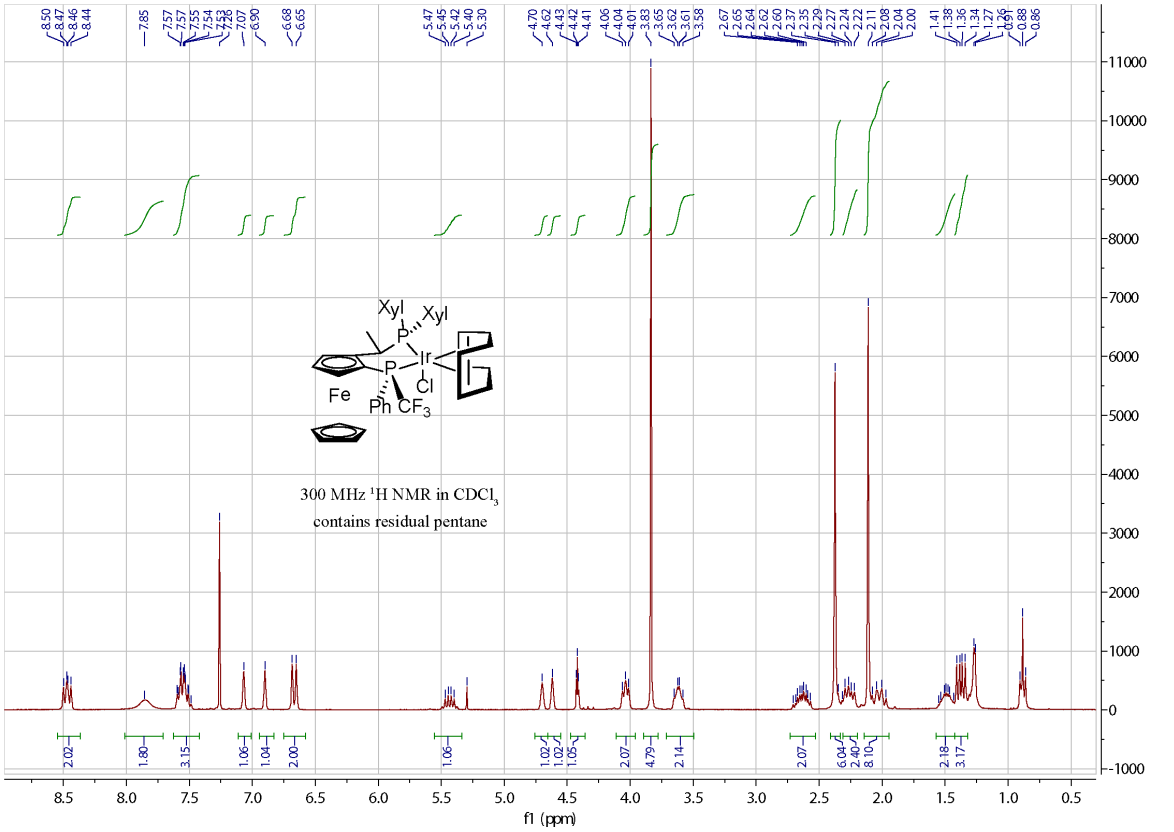
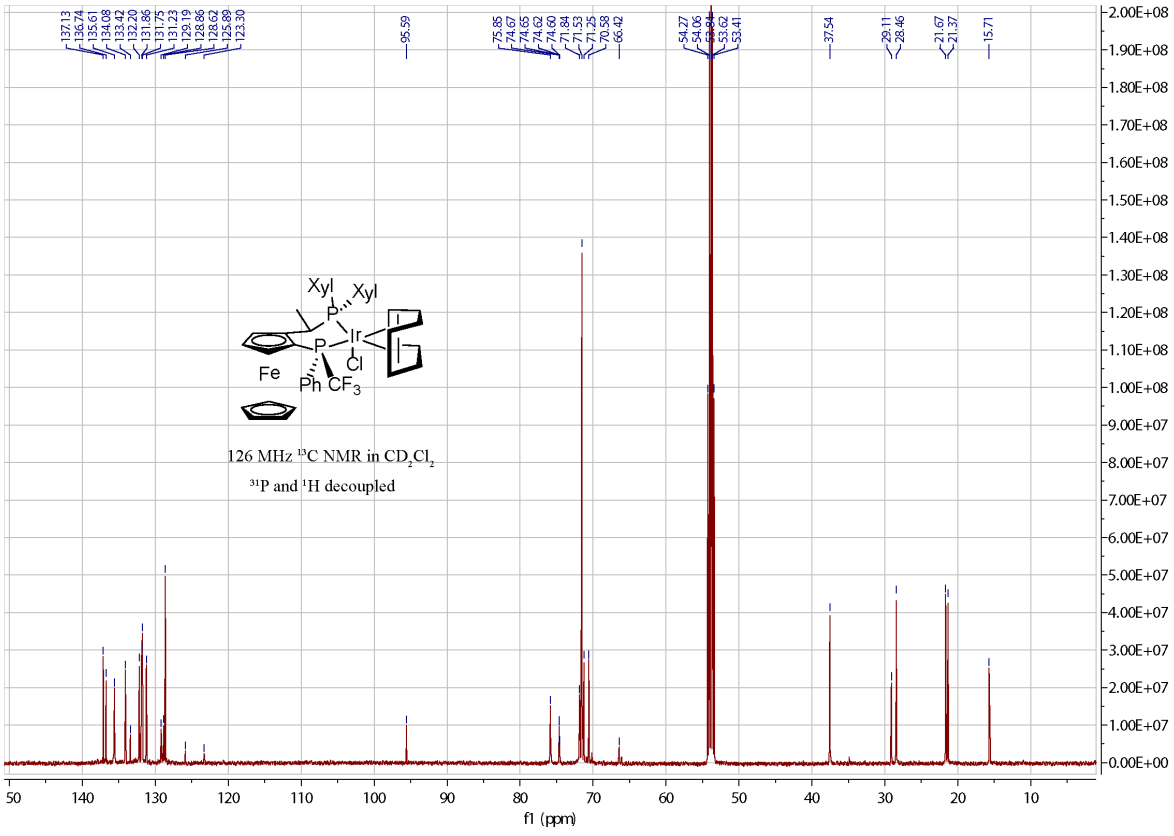
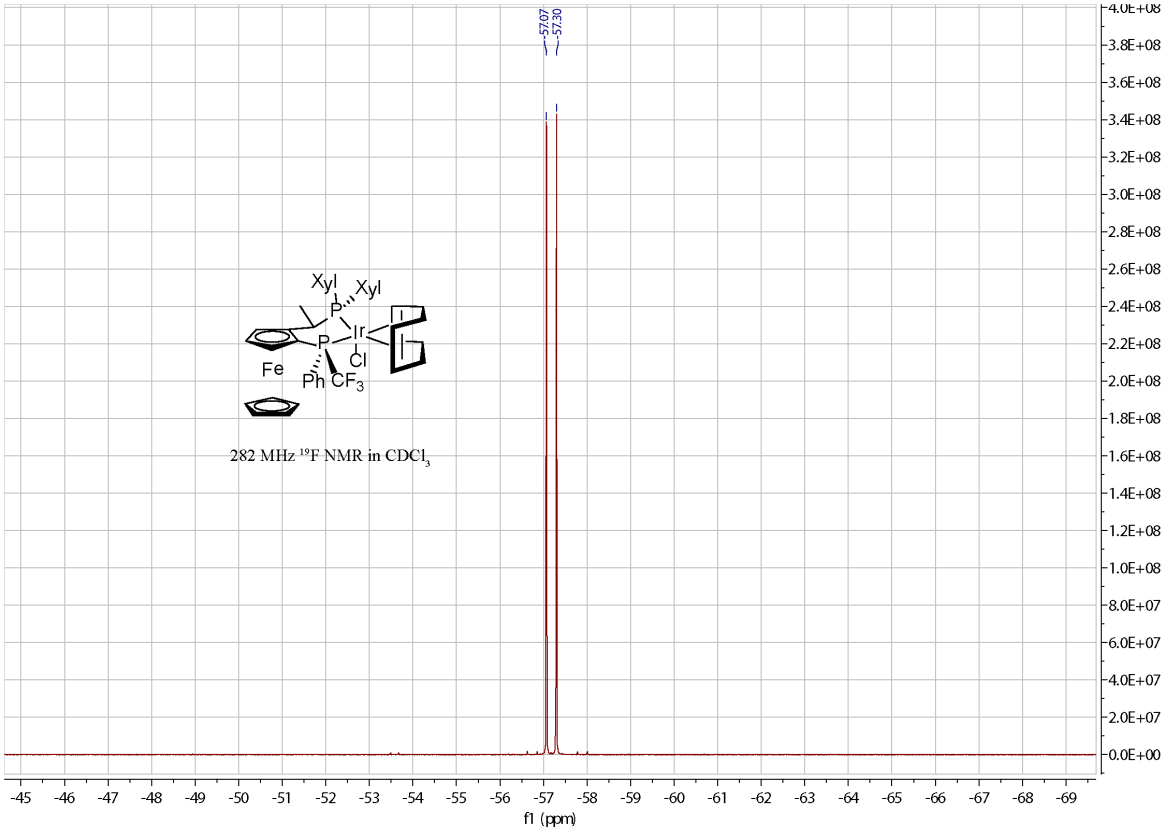
6.82
6.68
6.39
6.24
5.96
5.81
5.53
Xyl
Xyl
P
Ir
P
Cl
Fe
CF3
Ph
121 MHz 31P NMR in CD2Cl2
1H decoupled
f1 (ppm)

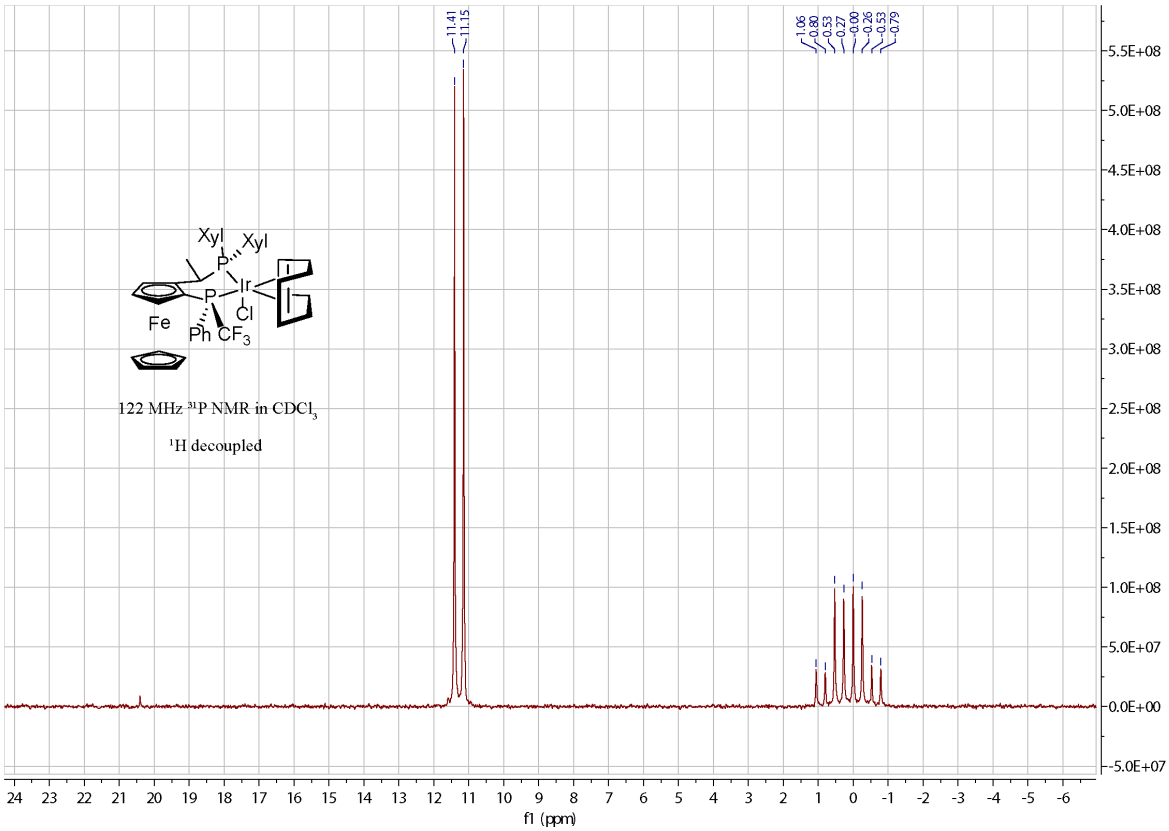
[Ir((R_P)-(CF_3)Ph-Xyliphos)(cod)Cl] (R_P)-**9**Cl







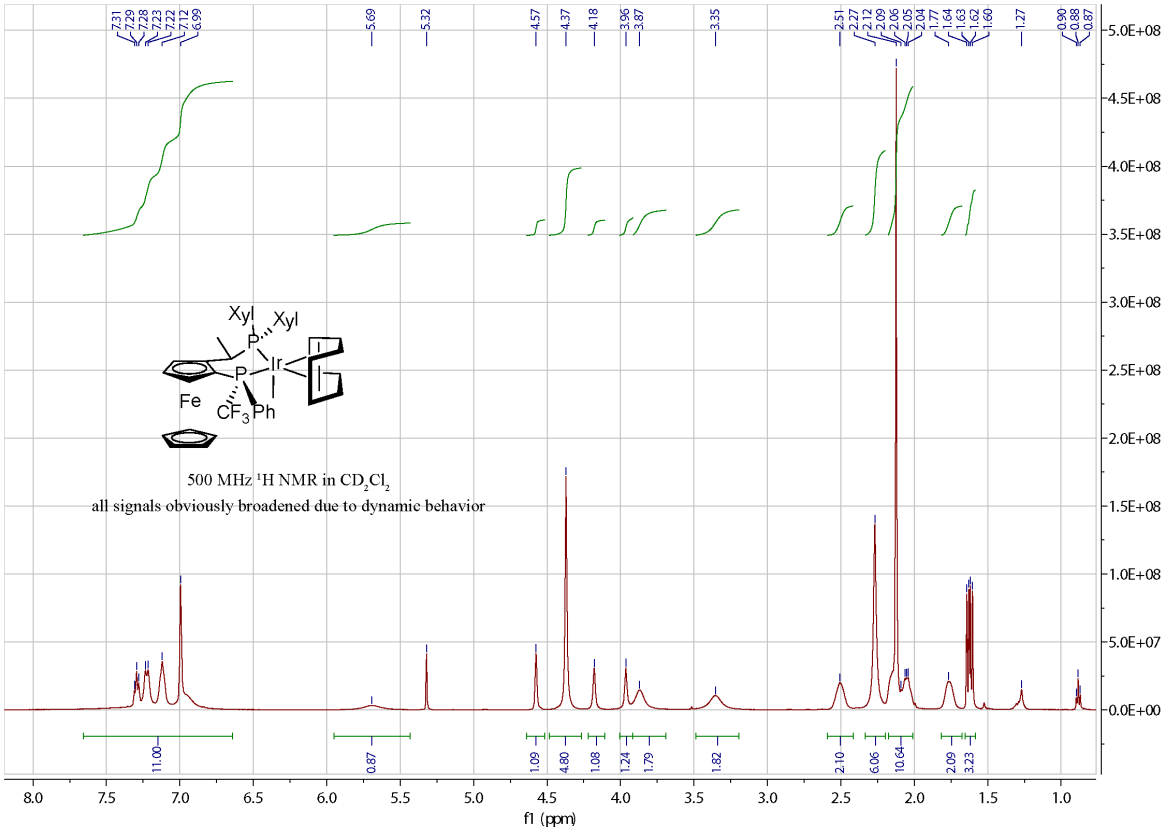
282 MHz ^{19}F NMR in $CDCl_3$

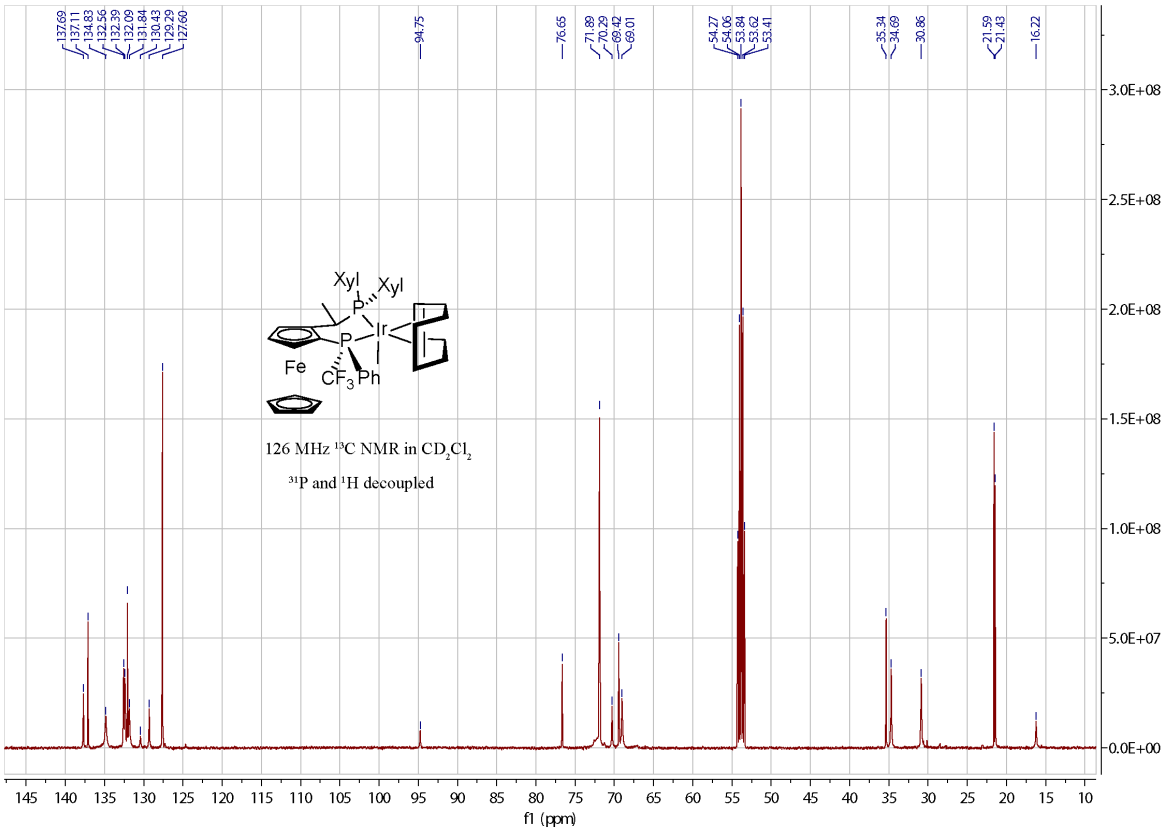


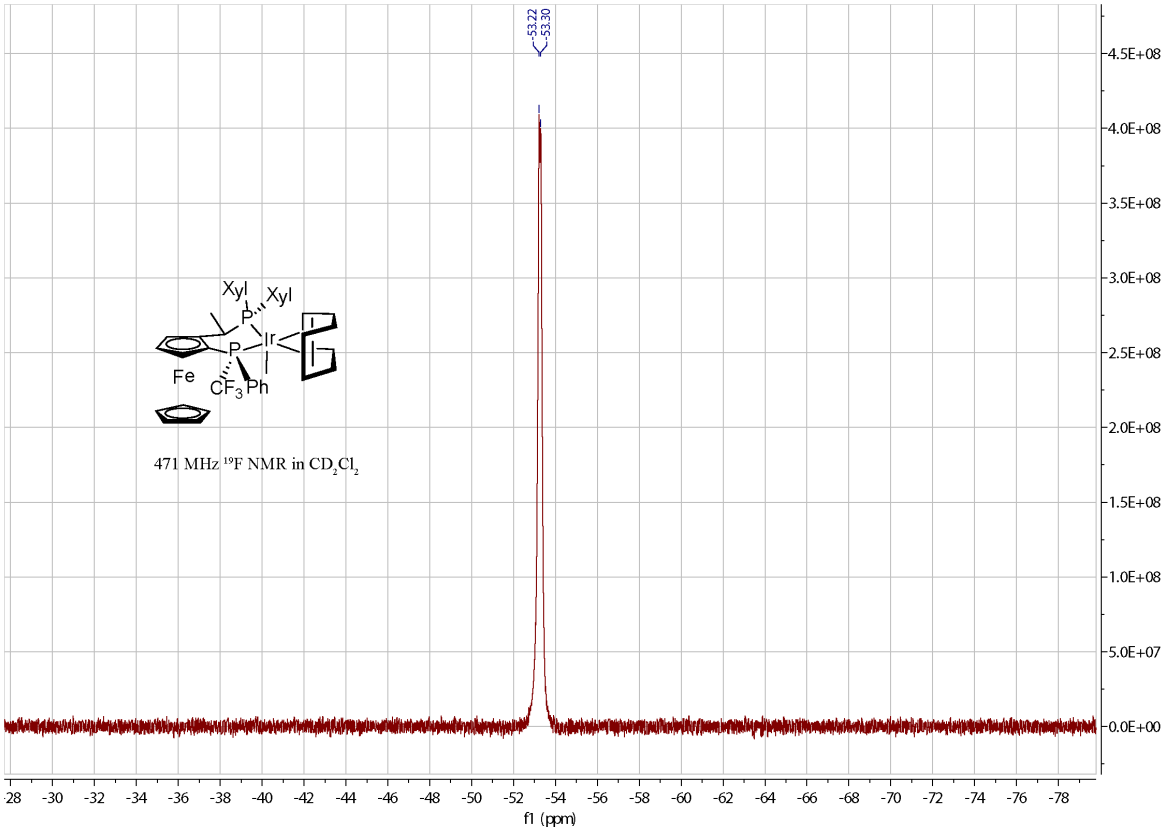
122 MHz ^{31}P NMR in $CDCl_3$

^{1}H decoupled

[Ir((*S*P)-(CF$_3$)Ph-Xyliphos)(cod)I] (*S*P)-**9I**



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Fe
CF3Ph
471 MHz 19F NMR in CD2Cl2
4.5E+08
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3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
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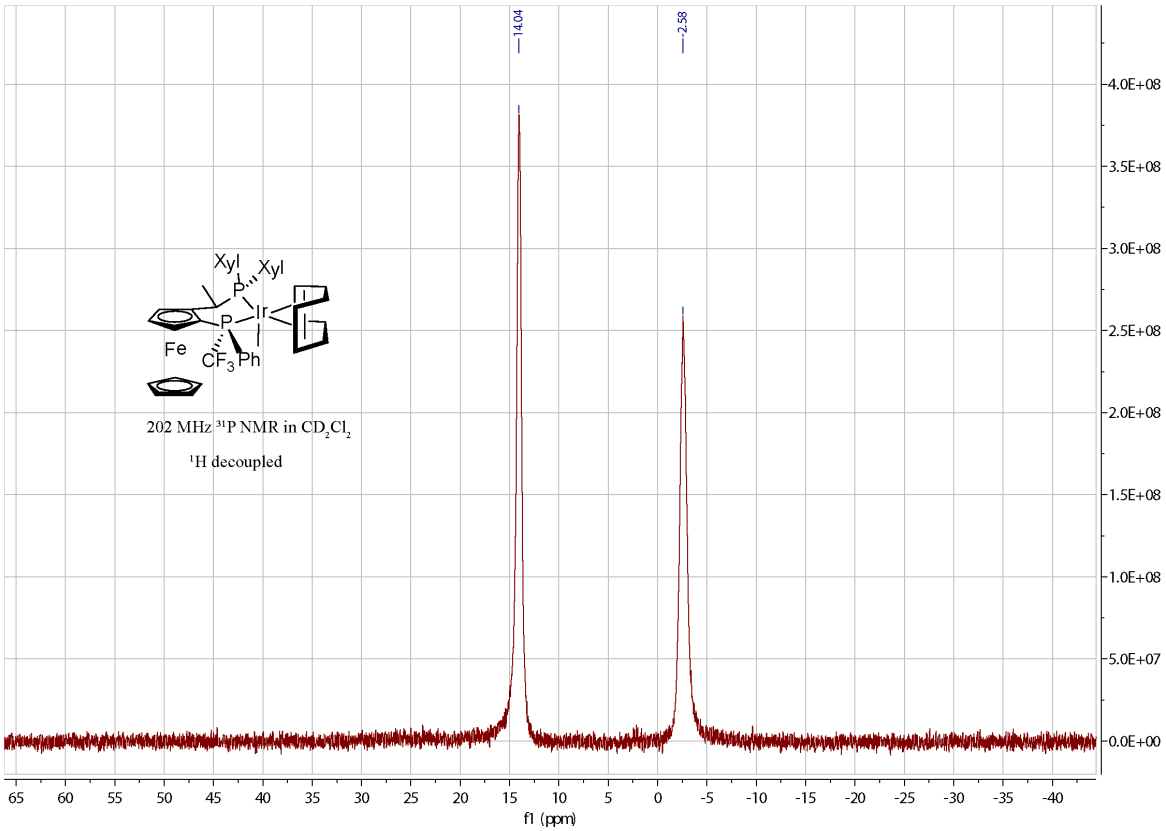
f1 (ppm)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2.58
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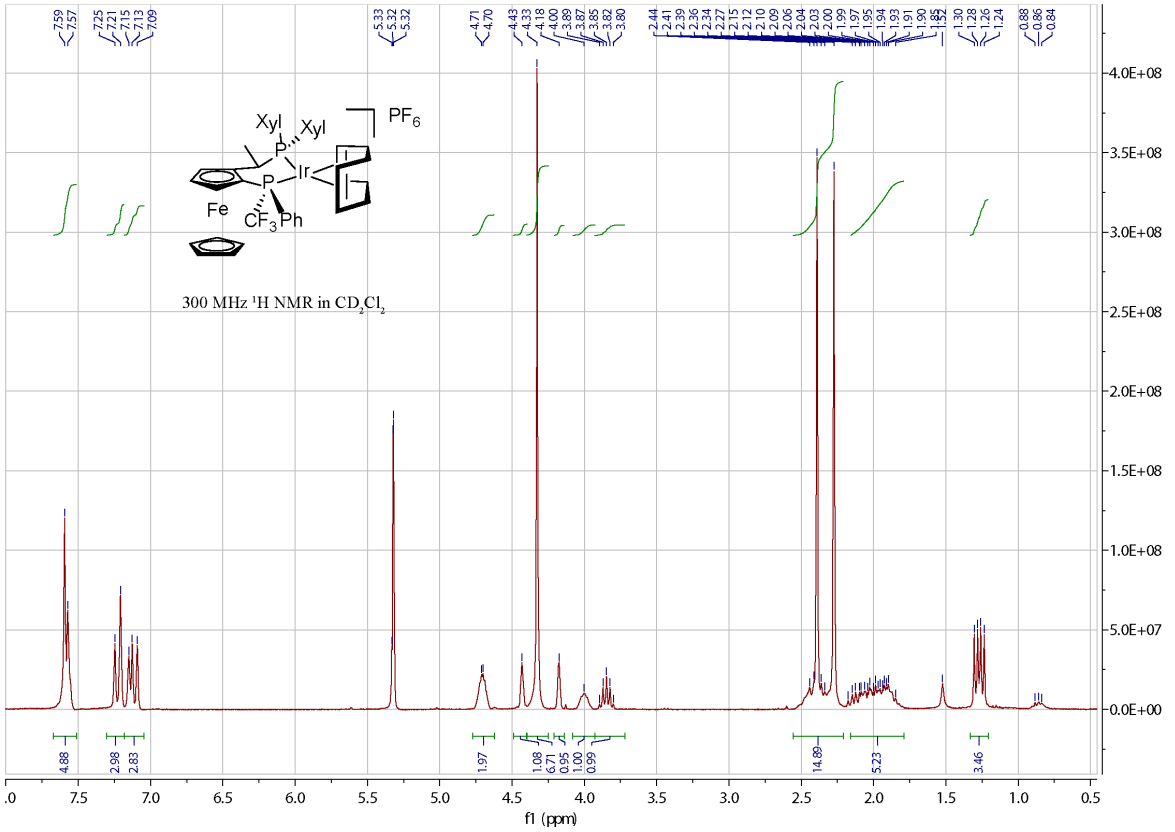
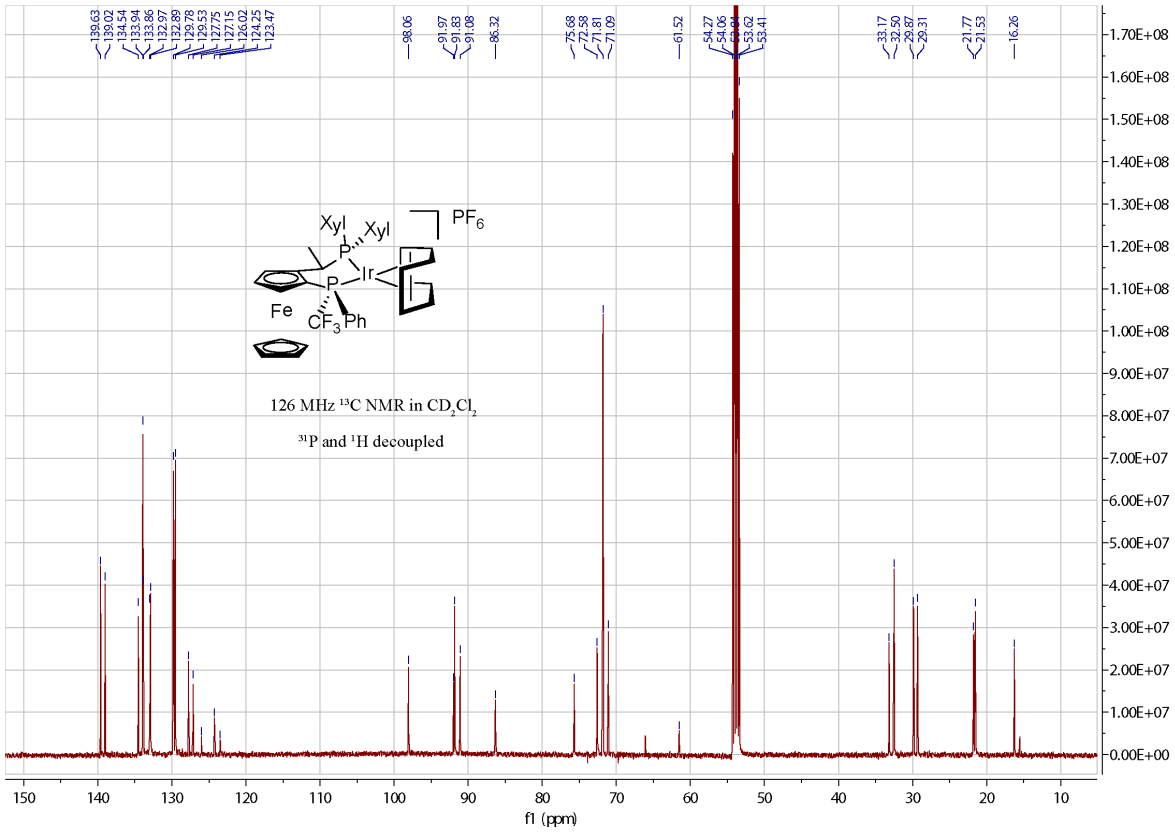
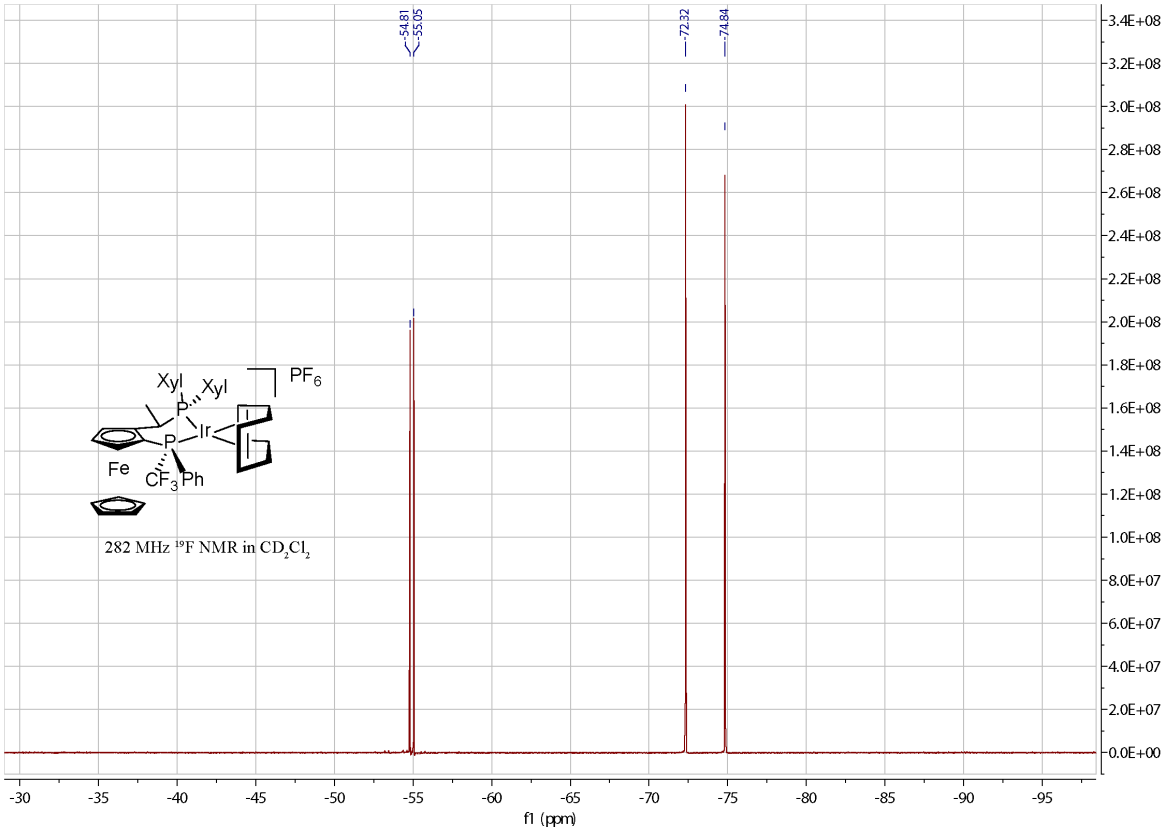
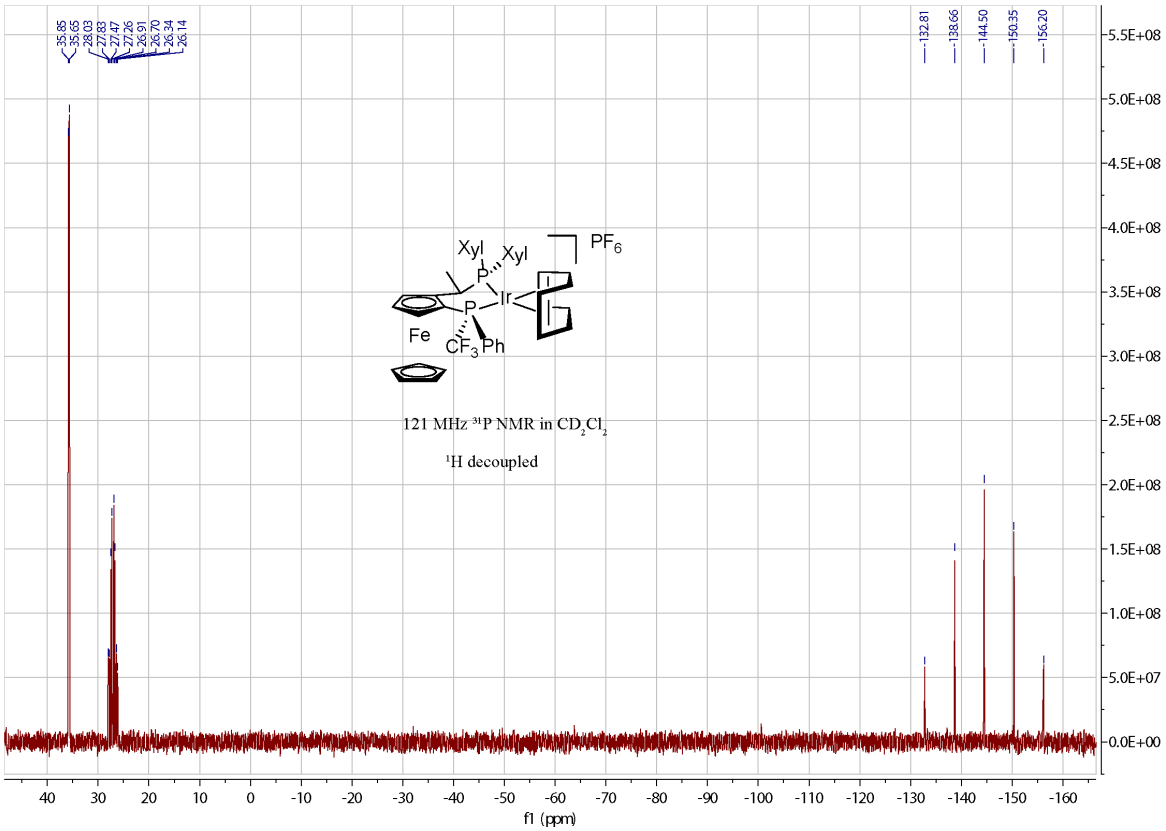
Xyl
P
P
Ir
Fe
CF3Ph
202 MHz 31P NMR in CD2Cl2
1H decoupled
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
65 60 55 50 45 40 35 30 25 20 15 10 5 0 -5 -10 -15 -20 -25 -30 -35 -40
f1 (ppm)

[Ir((*S*P)-(CF$_3$)Ph-Xyliphos)(cod)]PF$_6$ (*S*P)-**9**PF$_6$

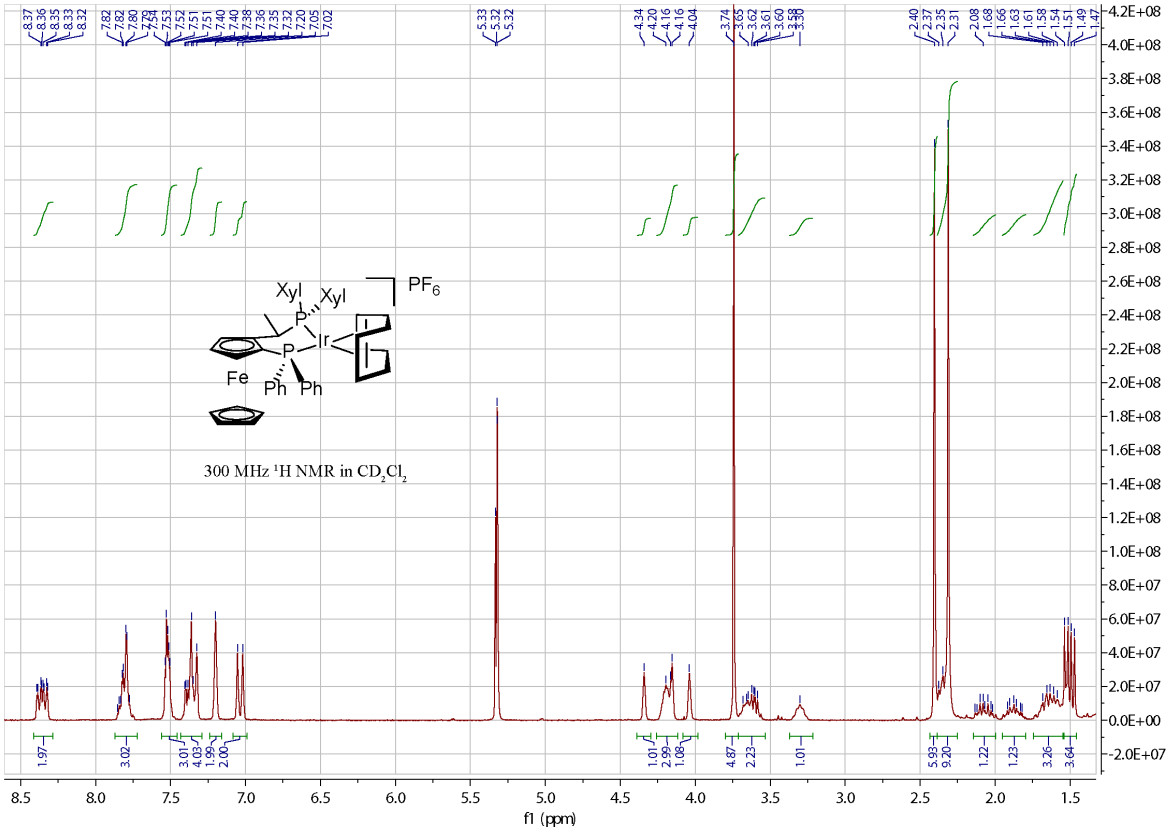


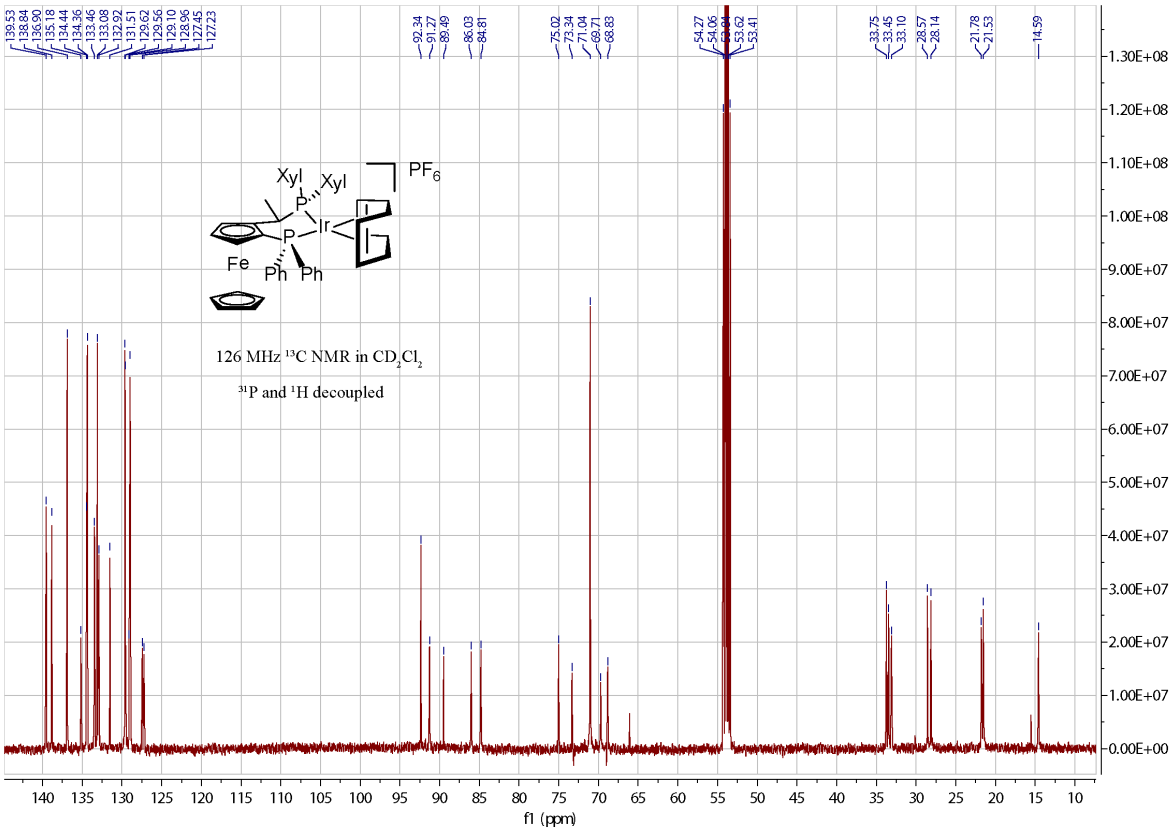


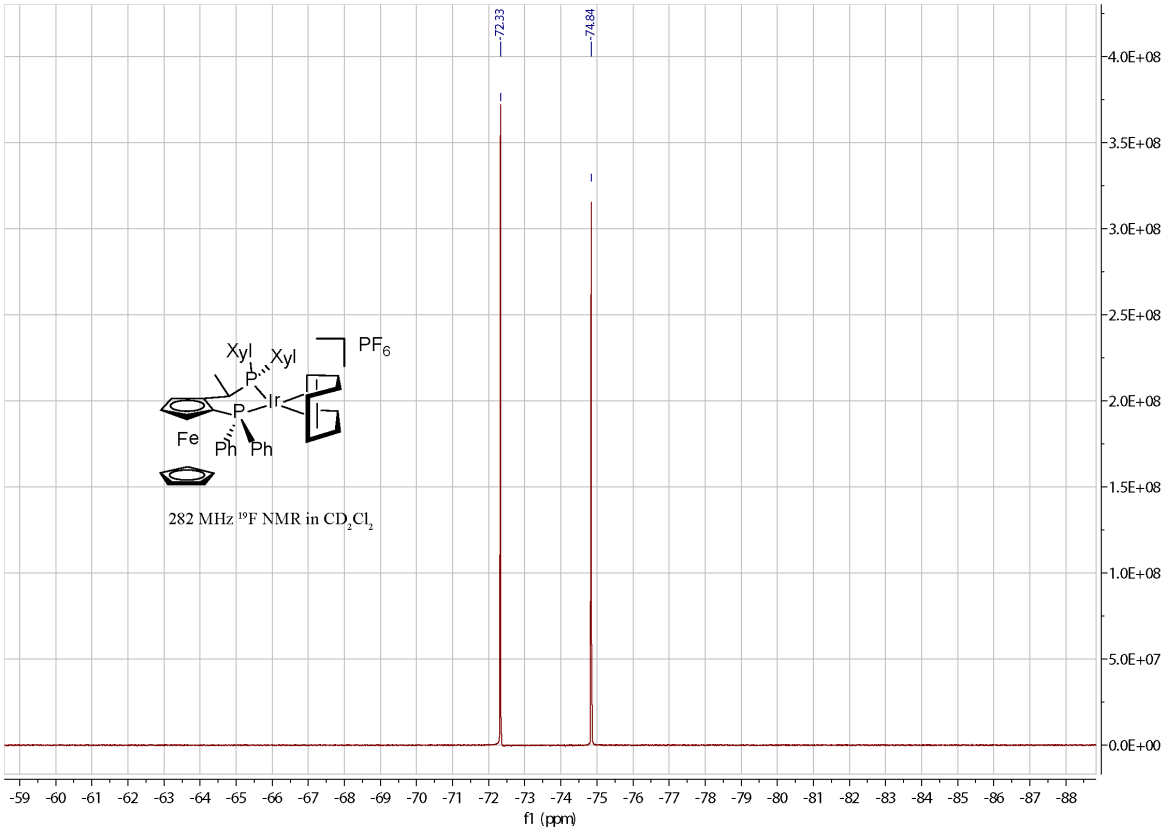

-54.81
-55.05
-72.32
-74.84
Xyl
Xyl
PF6
P
Ir
P
Fe
CF3Ph
282 MHz 19F NMR in CD2Cl2
f1 (ppm)

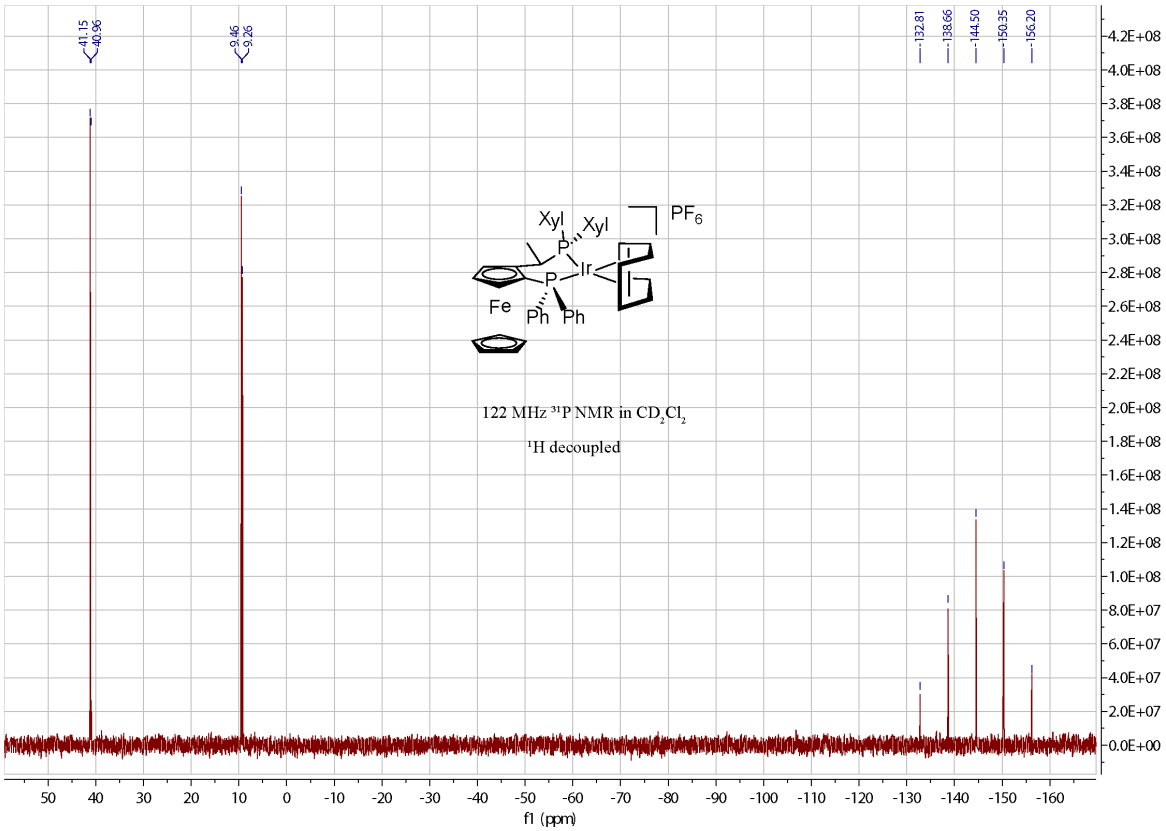

35.85
35.65
28.03
27.83
27.47
27.26
26.91
26.70
26.34
26.14
132.81
138.66
144.50
150.35
156.20
Xyl
Xyl
PF6
P
Ir
P
Fe
CF3Ph
121 MHz 31P NMR in CD2Cl2
1H decoupled
f1 (ppm)

[Ir((*R*,*S*)-Xyliphos)(cod)]PF_6 **10**PF_6

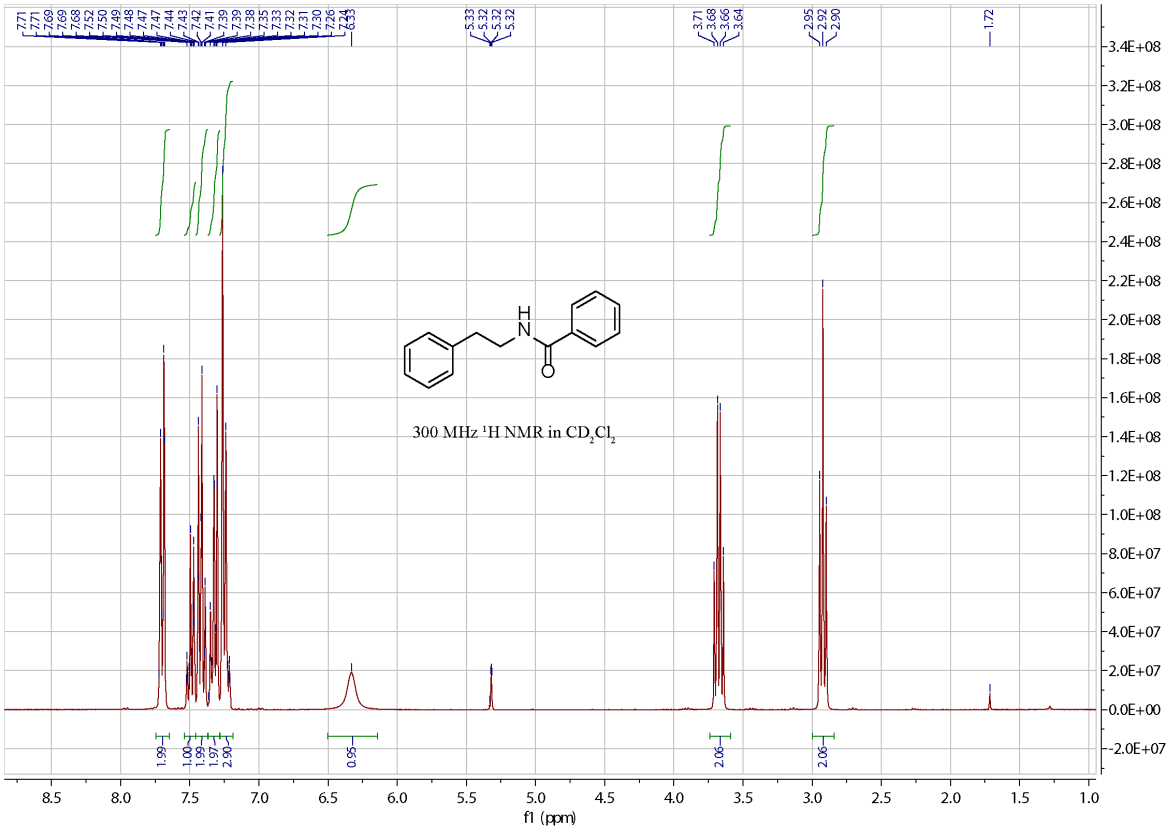


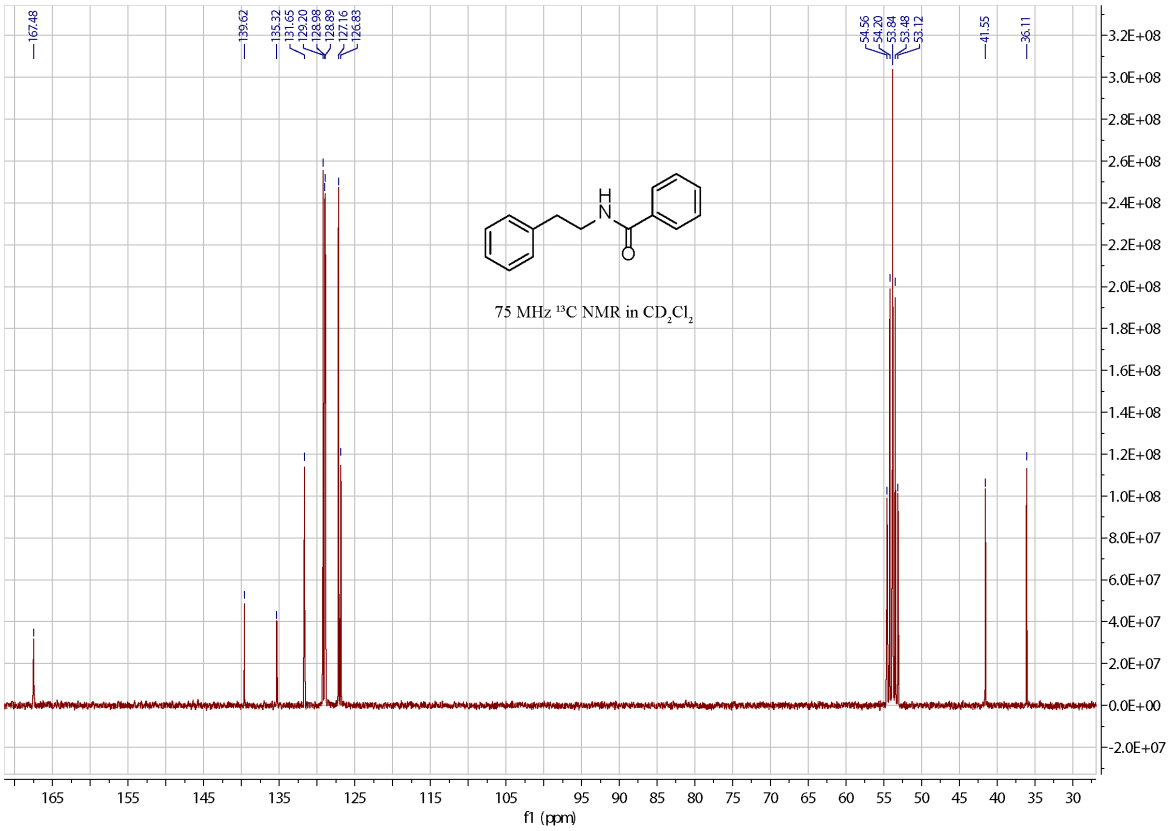



-72.33
-74.84
Xyl
Xyl
P
Ir
P
Fe
Ph
Ph
PF6
282 MHz 19F NMR in CD2Cl2
f1 (ppm)

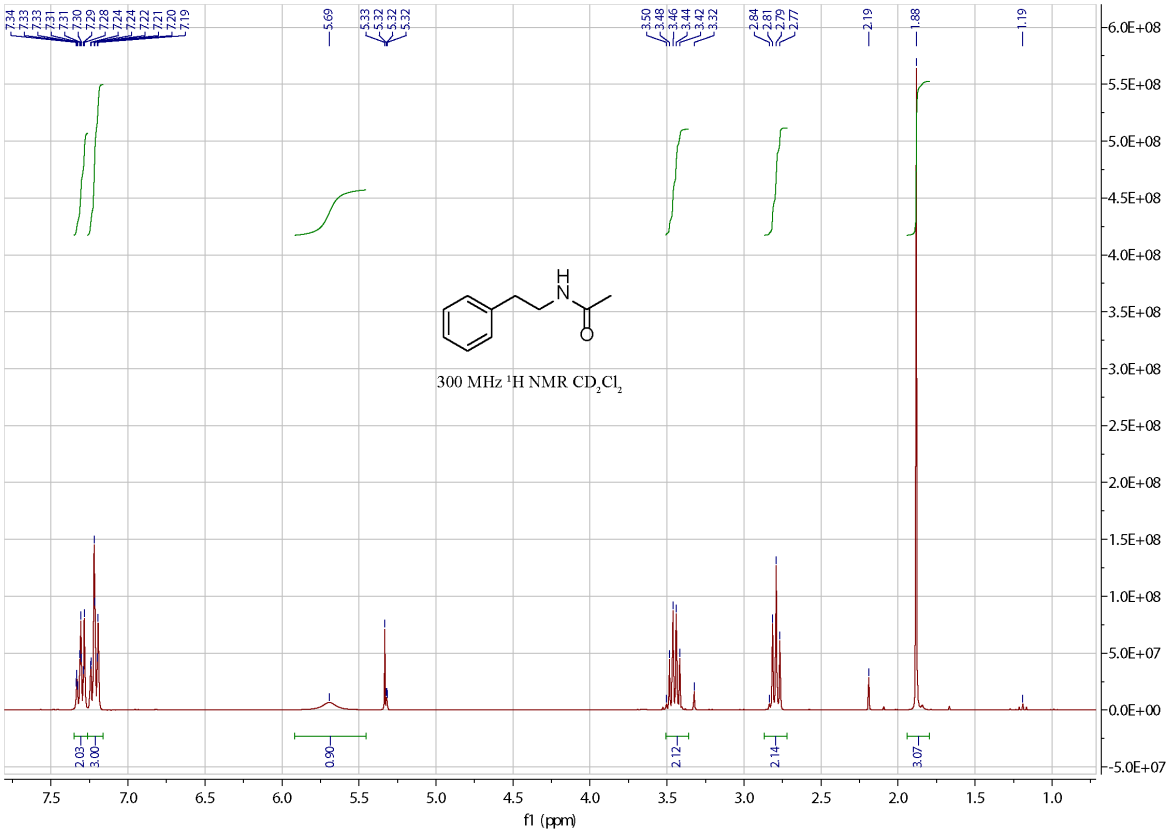

41.15
40.96
9.46
9.26
132.81
138.66
144.50
150.35
156.20
Xyl
Xyl
P
Ir
P
Fe
Ph
Ph
PF6
122 MHz 31P NMR in CD2Cl2
1H decoupled
f1 (ppm)

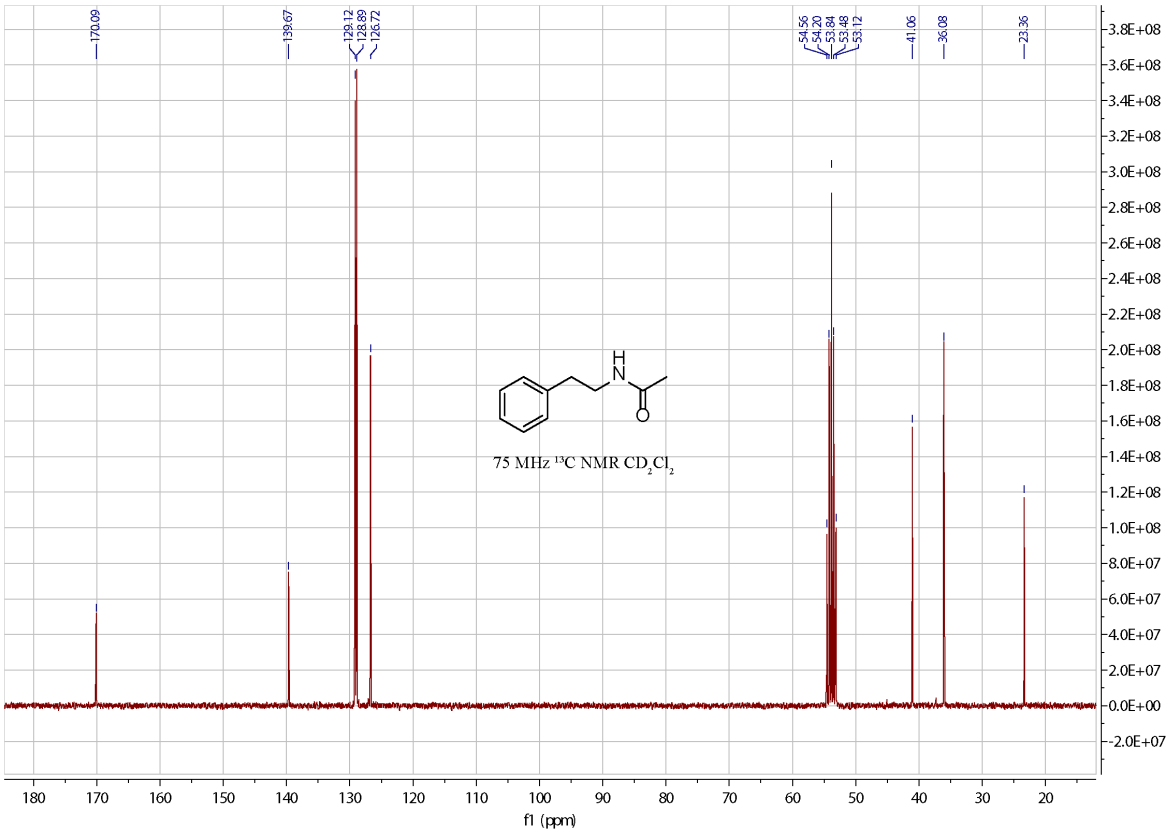
Ph-Amide


7.71
7.71
7.69
7.69
7.68
7.68
7.51
7.50
7.49
7.48
7.47
7.47
7.44
7.43
7.42
7.41
7.39
7.39
7.38
7.35
7.33
7.32
7.31
7.30
7.26
7.24
6.33
5.33
5.32
5.32
5.32
3.71
3.68
3.66
3.64
2.95
2.92
2.90
1.72
H
N
O
300 MHz ¹H NMR in CD2Cl2
1.99
1.00
1.99
1.97
2.90
0.95
2.06
2.06
f1 (ppm)

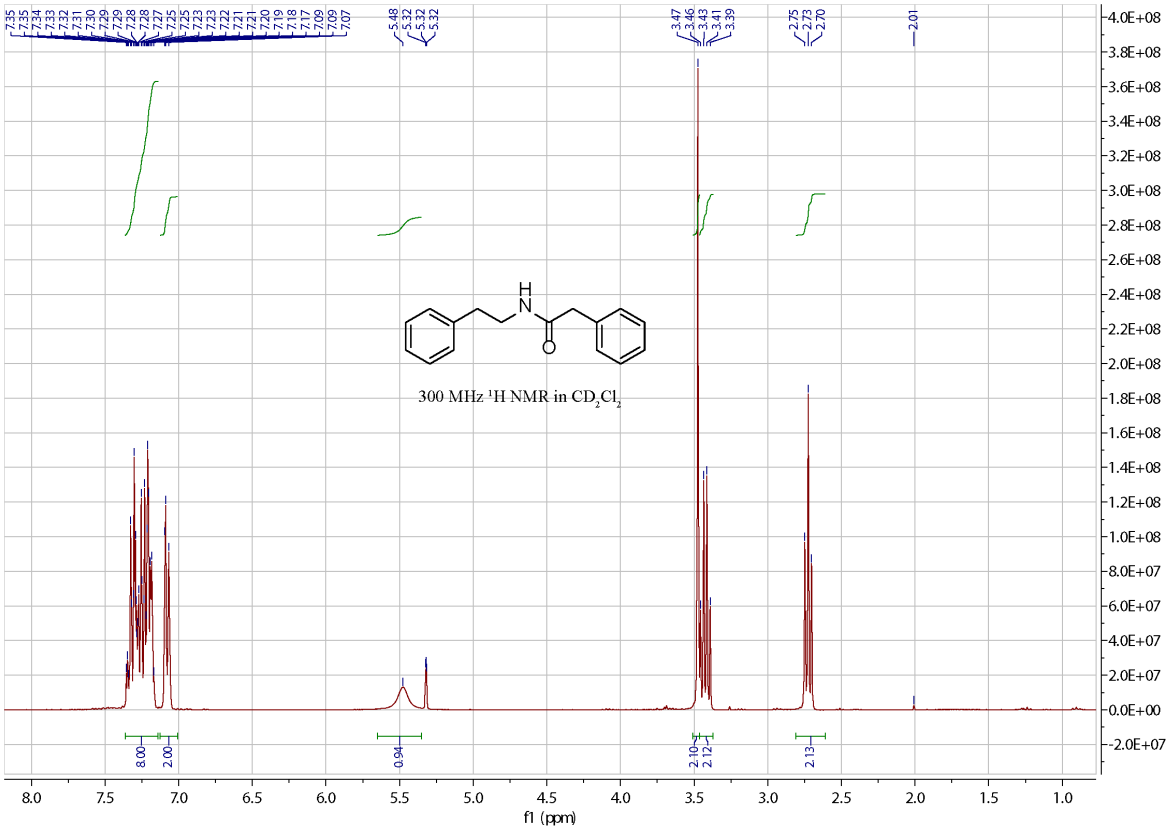

167.48
139.62
135.32
131.65
129.20
128.98
128.89
127.16
126.83
54.56
54.20
53.84
53.48
53.12
41.55
36.11
H
N
O
75 MHz ¹³C NMR in CD2Cl2
f1 (ppm)

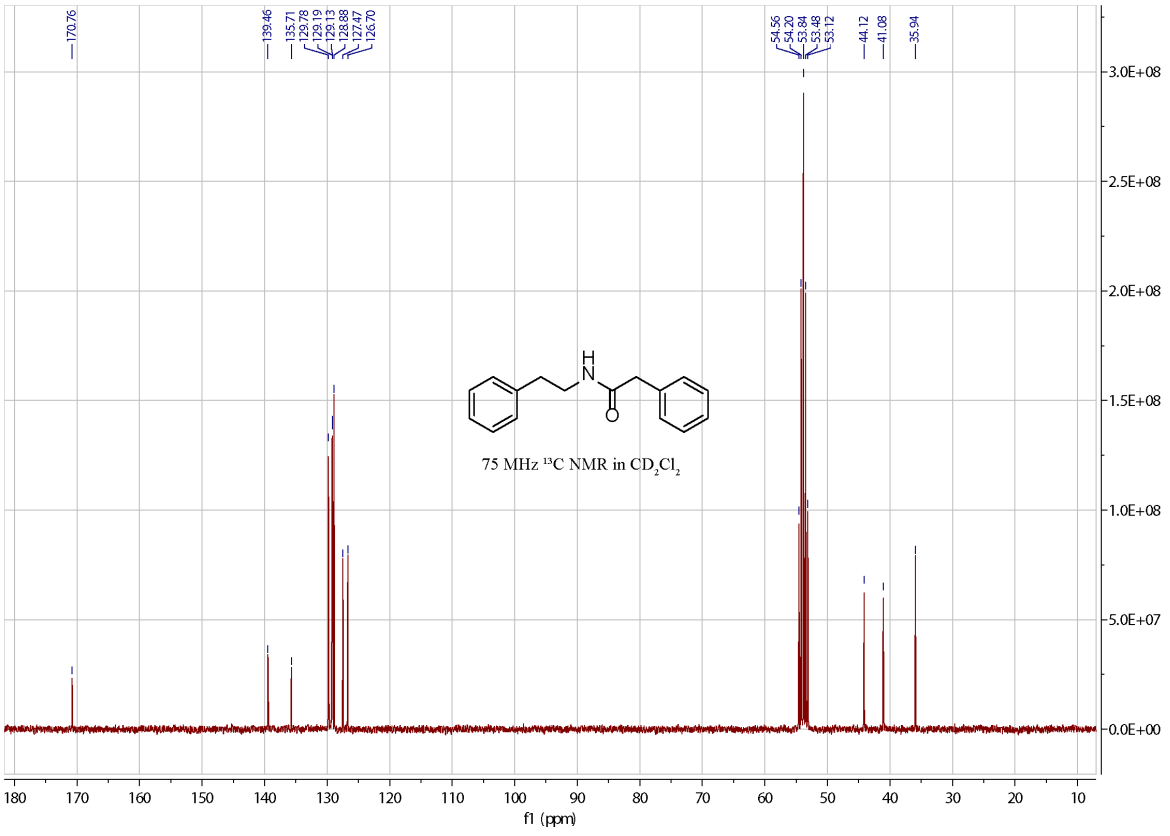
Me-Amide


7.34
7.33
7.33
7.33
7.31
7.31
7.30
7.29
7.28
7.24
7.24
7.22
7.21
7.20
7.19
5.69
5.33
5.32
5.32
5.32
3.50
3.48
3.46
3.44
3.42
3.32
2.84
2.81
2.79
2.77
2.19
1.88
1.19
H
N
O
300 MHz ¹H NMR CD2Cl2
2.03
3.00
0.90
2.12
2.14
3.07
6.0E+08
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
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
f1 (ppm)

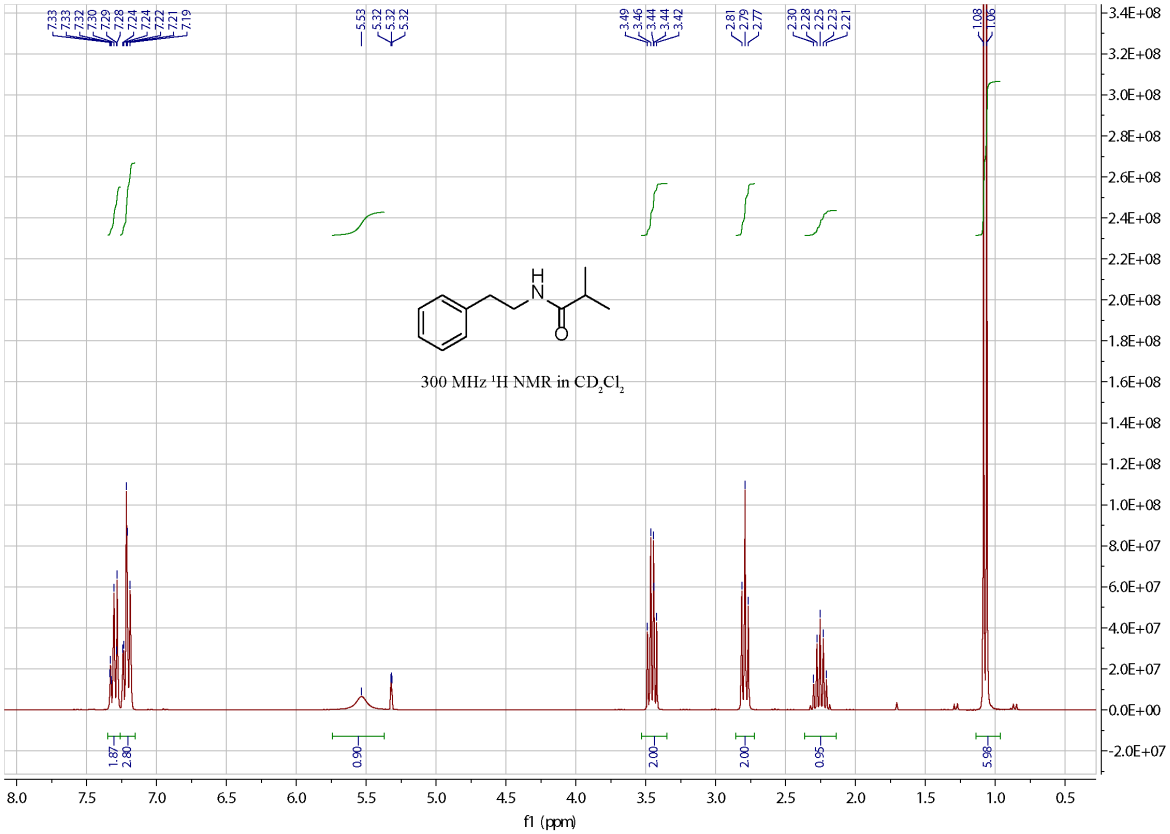

170.09
139.67
129.12
128.89
126.72
54.56
54.20
53.84
53.48
53.12
41.06
36.08
23.36
H
N
O
75 MHz ¹³C NMR CD2Cl2
3.8E+08
3.6E+08
3.4E+08
3.2E+08
3.0E+08
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

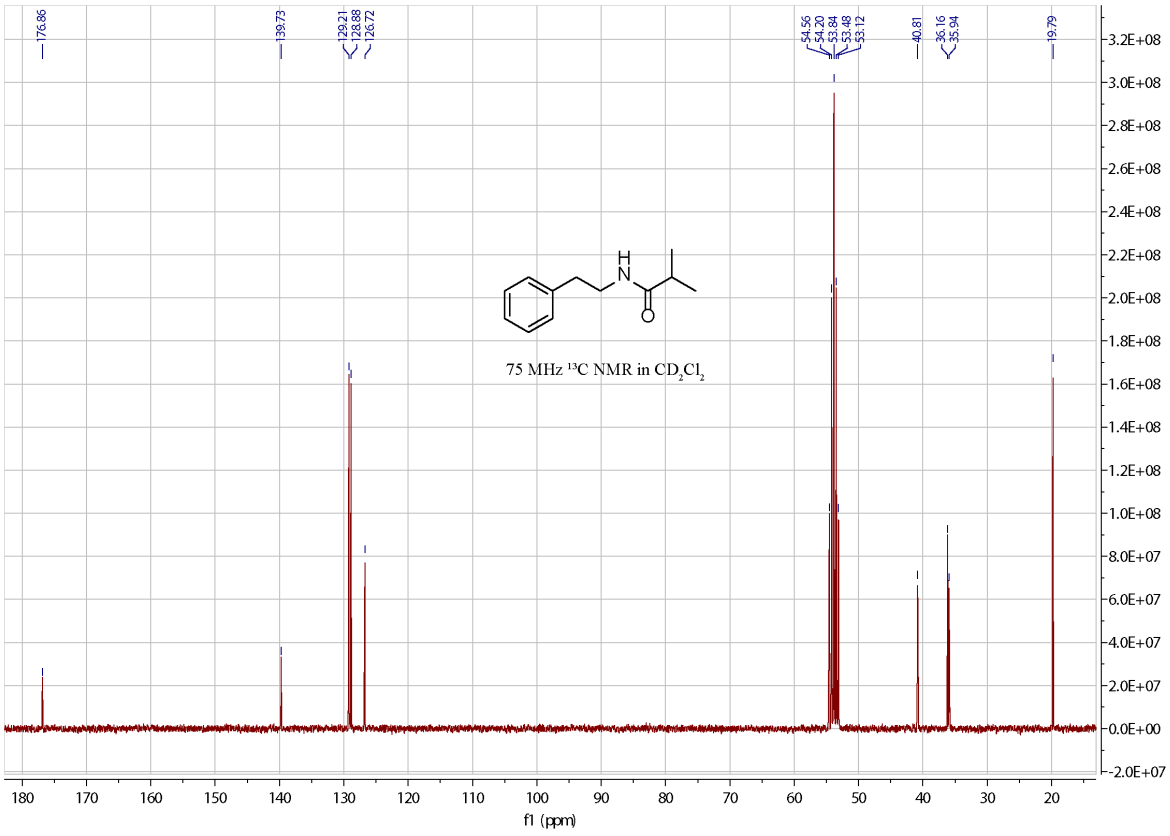
Bn-Amide


7.35
7.35
7.34
7.33
7.32
7.31
7.30
7.29
7.29
7.28
7.28
7.27
7.25
7.25
7.23
7.23
7.22
7.21
7.21
7.20
7.19
7.18
7.17
7.09
7.09
7.07
5.48
5.32
5.32
5.32
3.47
3.46
3.43
3.41
3.39
2.75
2.73
2.70
2.01
8.00
2.00
0.94
2.10
2.12
2.13
300 MHz ¹H NMR in CD2Cl2
f1 (ppm)

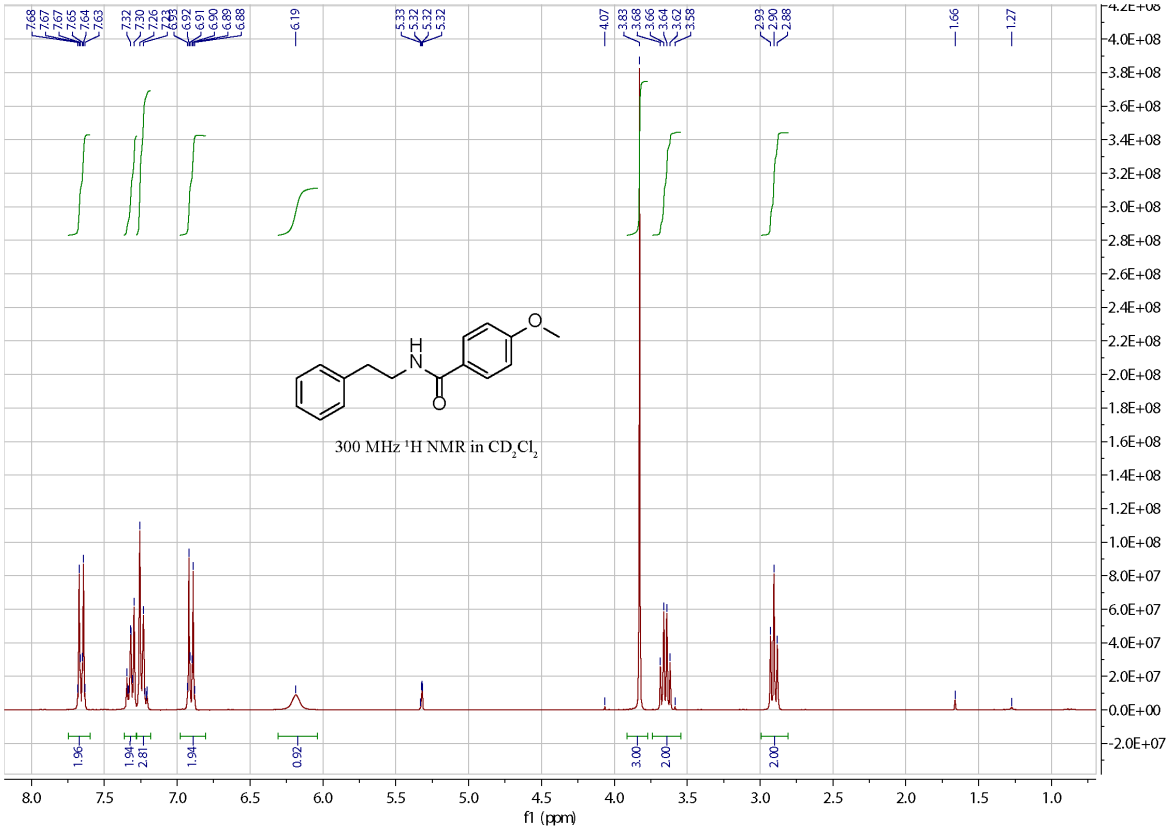

170.76
139.46
135.71
129.78
129.19
129.13
128.88
127.47
126.70
54.56
54.20
53.84
53.48
53.12
44.12
41.08
35.94
75 MHz ¹³C NMR in CD2Cl2
f1 (ppm)

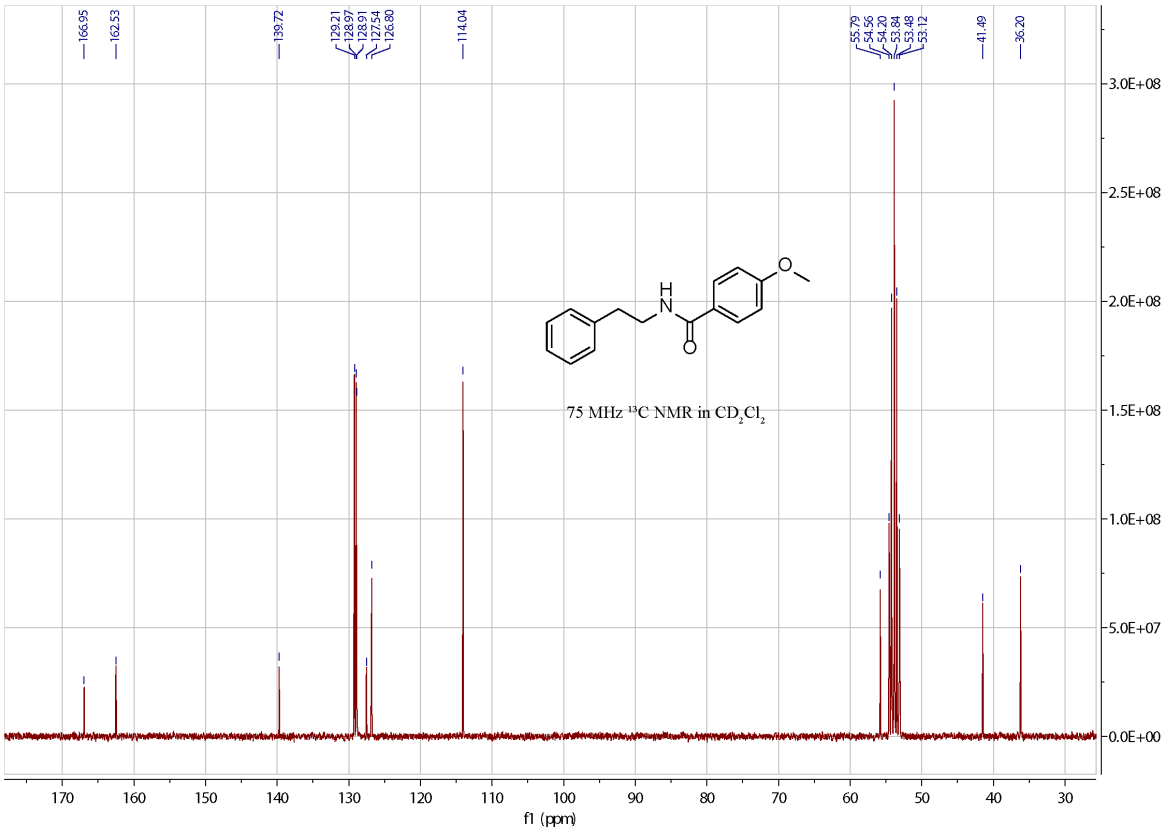
*i*Pr-Amide


7.33
7.33
7.32
7.30
7.29
7.28
7.24
7.24
7.22
7.21
7.19
5.53
5.32
5.32
5.32
3.49
3.46
3.44
3.44
3.42
2.81
2.79
2.77
2.30
2.28
2.25
2.23
2.21
1.08
1.06
H
N
O
300 MHz ¹H NMR in CD2Cl2
1.87
2.80
0.90
2.00
2.00
0.95
5.98
f1 (ppm)

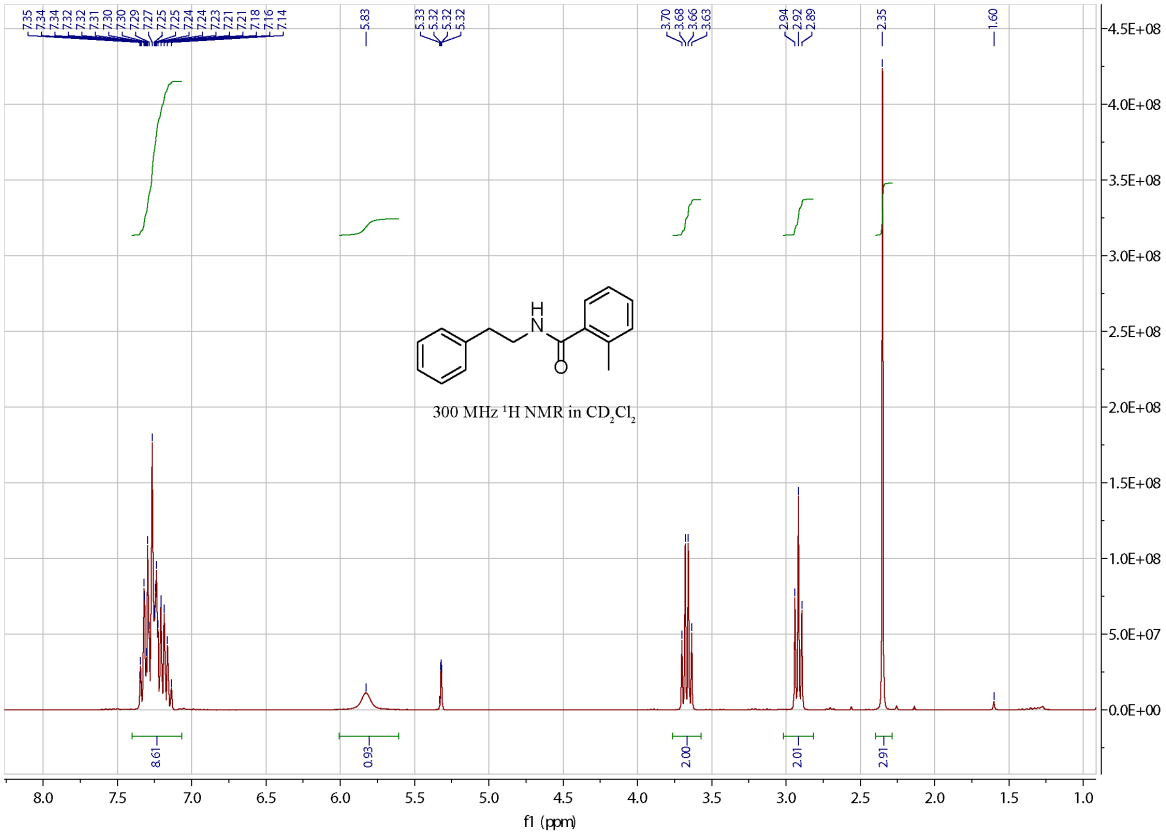

176.86
139.73
129.21
128.88
126.72
54.56
54.20
53.84
53.48
53.12
40.81
36.16
35.94
19.79
H
N
O
75 MHz ¹³C NMR in CD2Cl2
f1 (ppm)

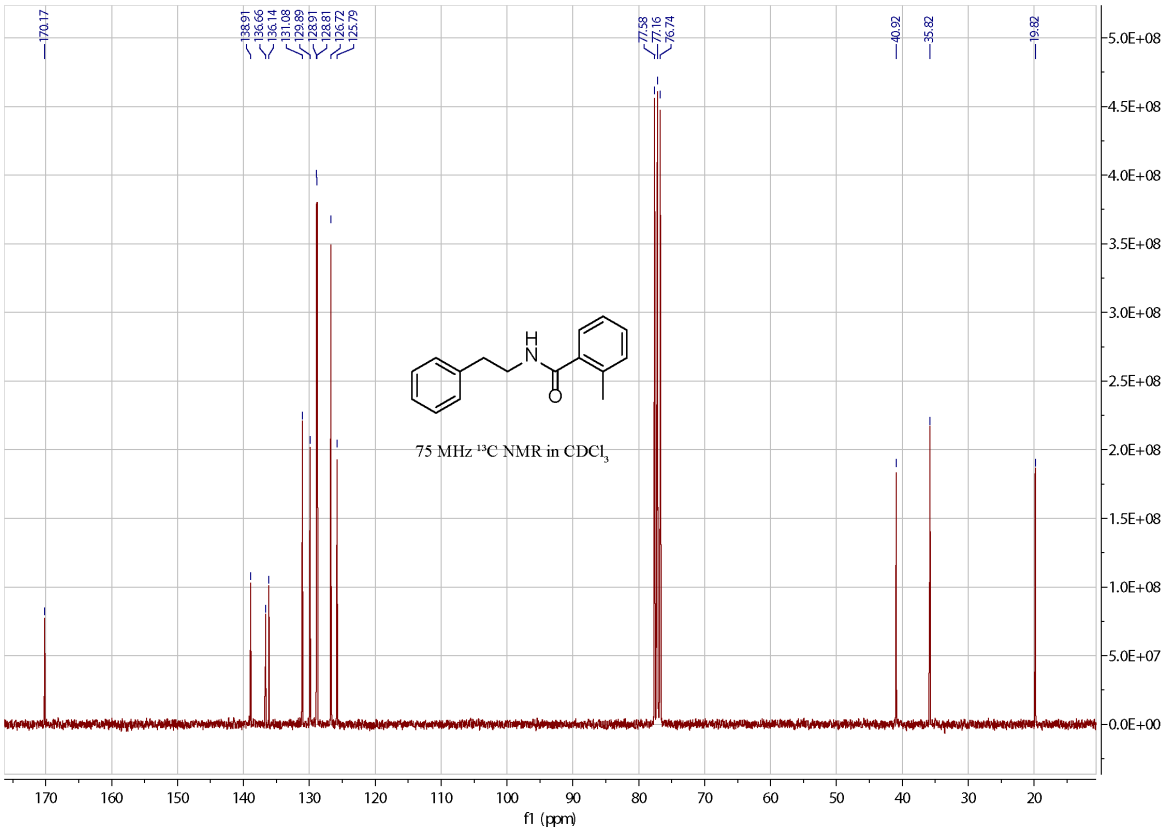
*p*OMePh-Amide



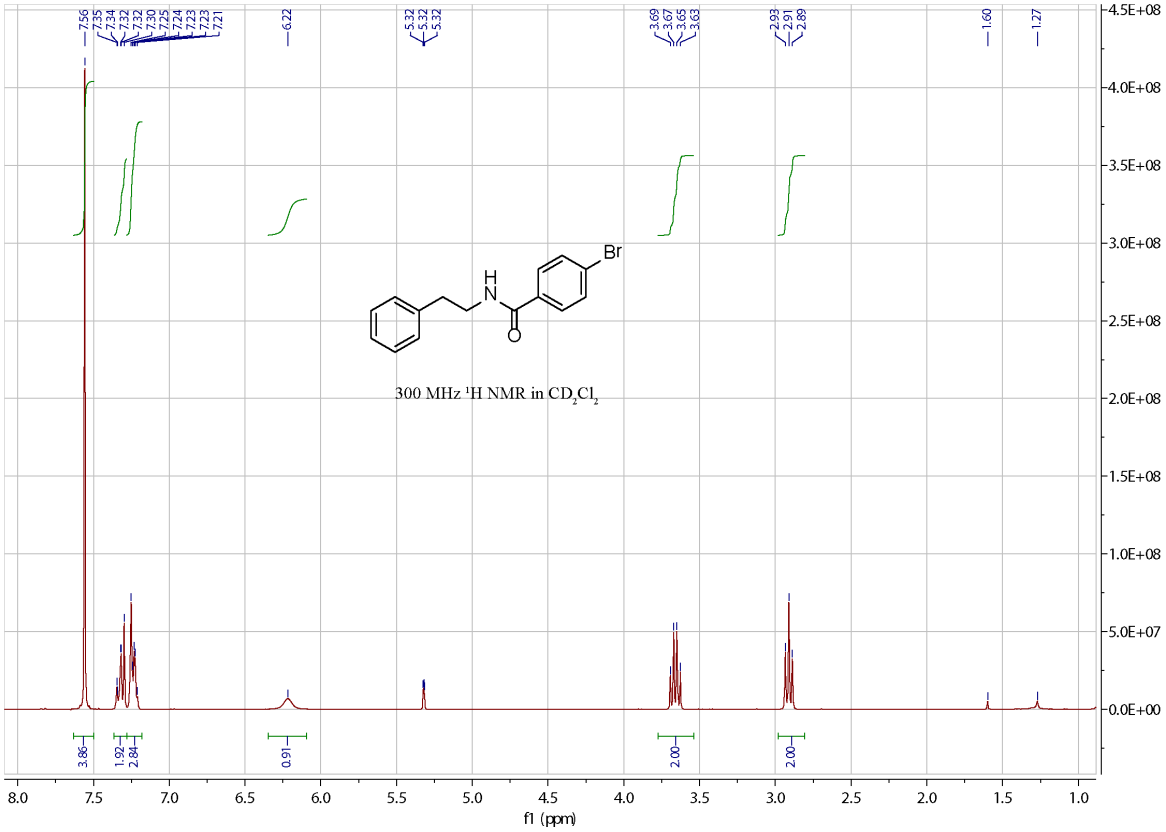


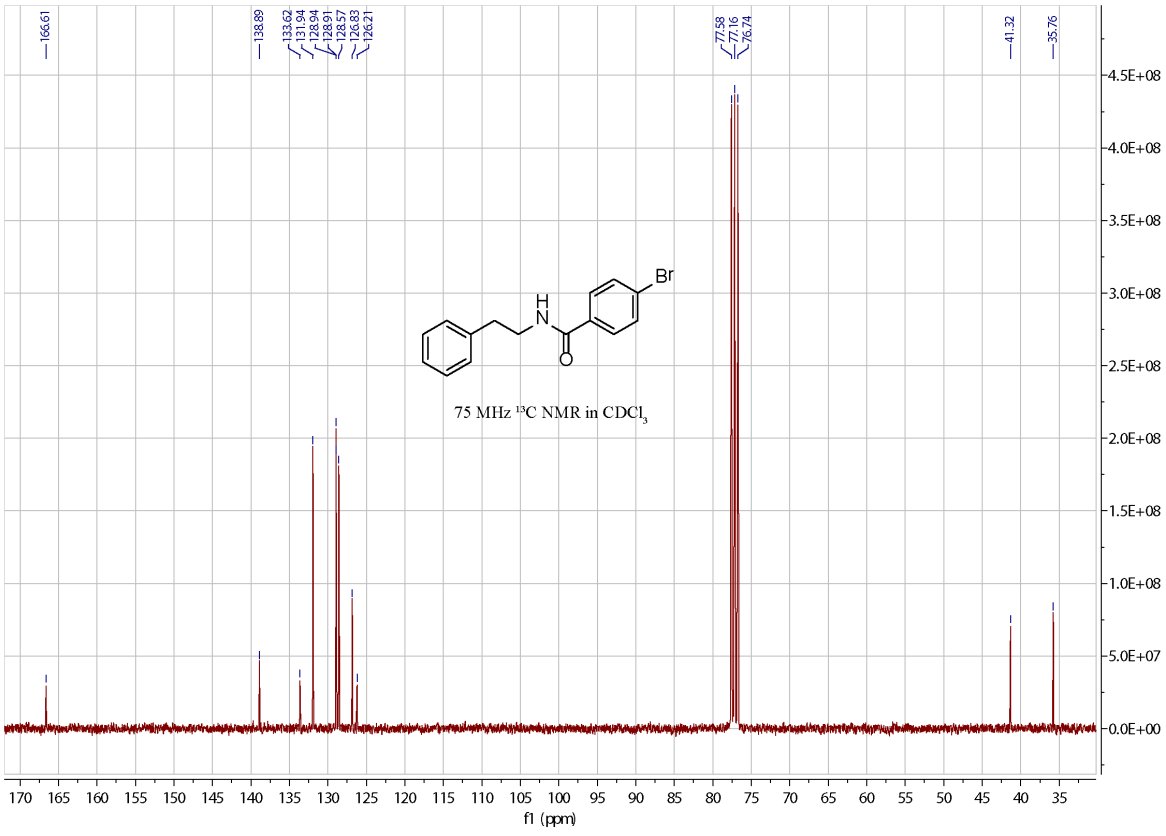
*o*Tol-Amide


7.35
7.34
7.34
7.32
7.32
7.31
7.30
7.30
7.29
7.27
7.25
7.25
7.24
7.24
7.23
7.21
7.21
7.18
7.16
7.14
5.83
5.33
5.32
5.32
5.32
3.70
3.68
3.66
3.63
2.94
2.92
2.89
2.35
1.60
H
N
O
300 MHz ¹H NMR in CD2Cl2
8.61
0.93
2.00
2.01
2.91
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
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
f1 (ppm)

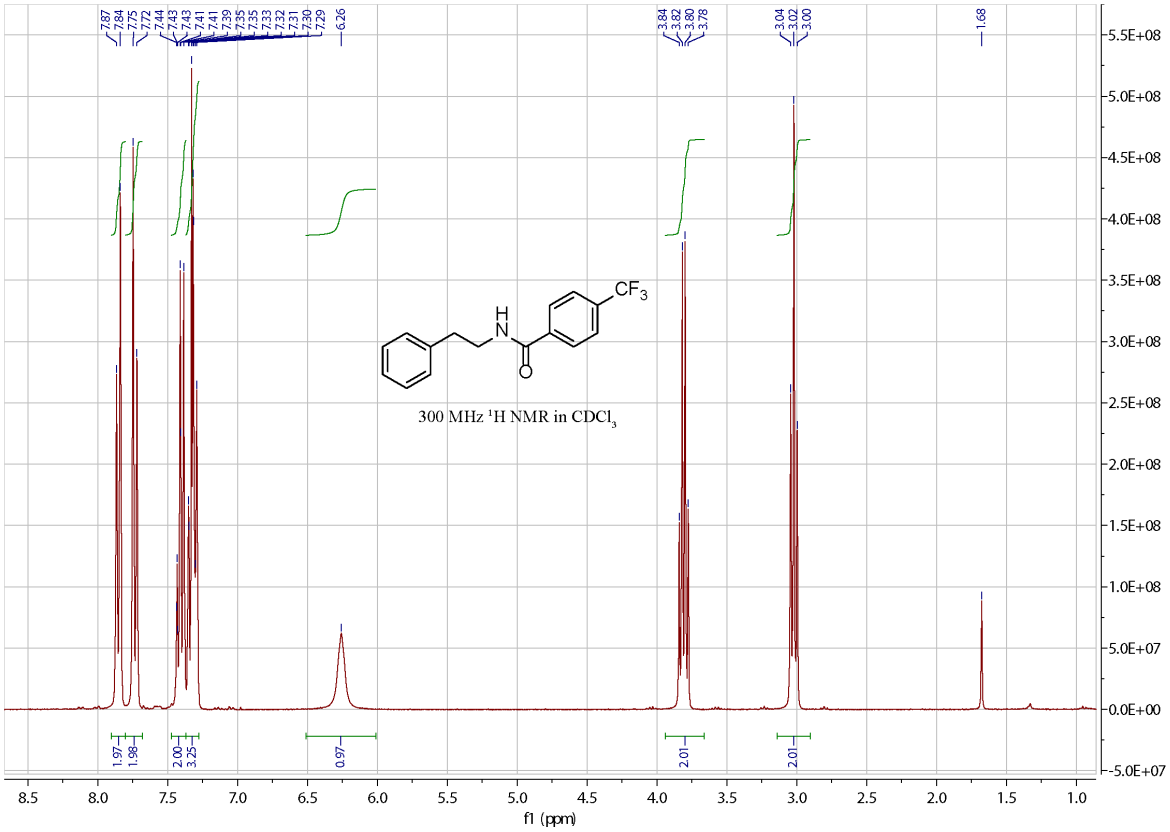

170.17
138.91
136.66
136.14
131.88
129.88
128.91
128.81
126.72
125.79
77.58
77.16
76.74
40.92
35.82
19.82
H
N
O
75 MHz ¹³C NMR in CDCl3
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

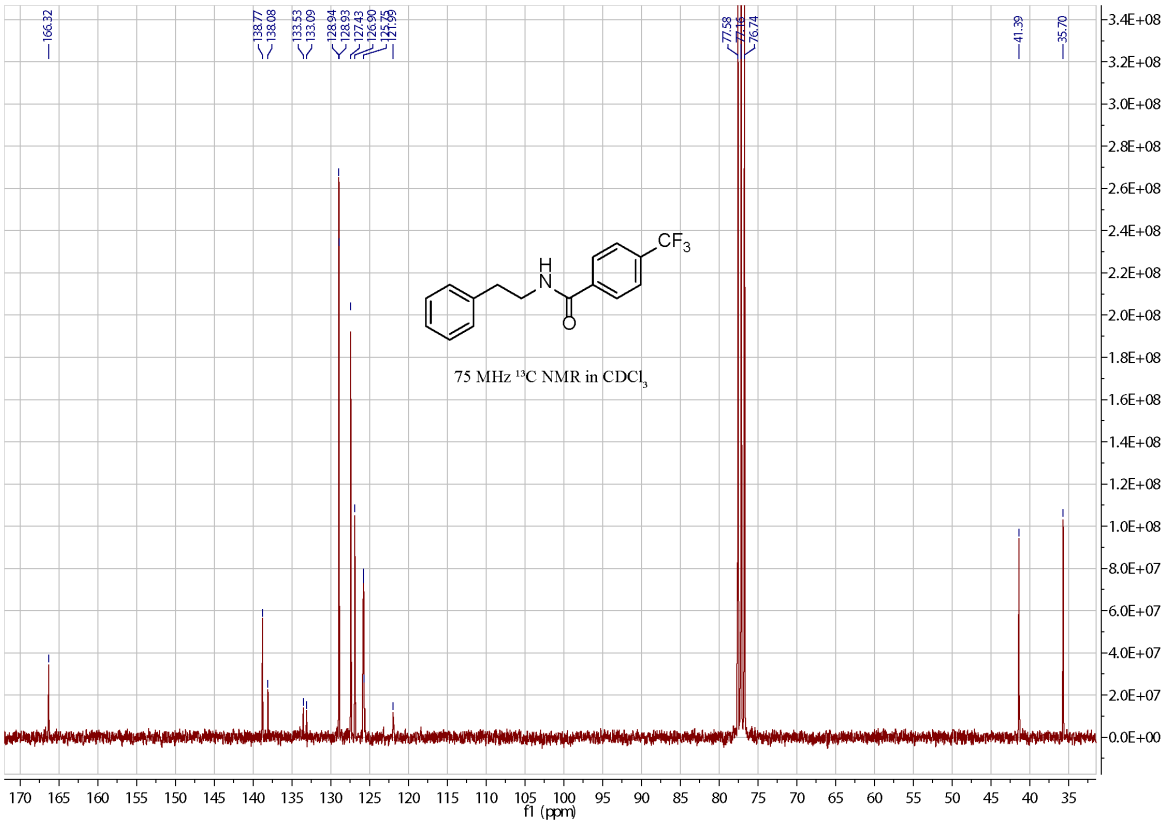
*p*BrPh-Amide

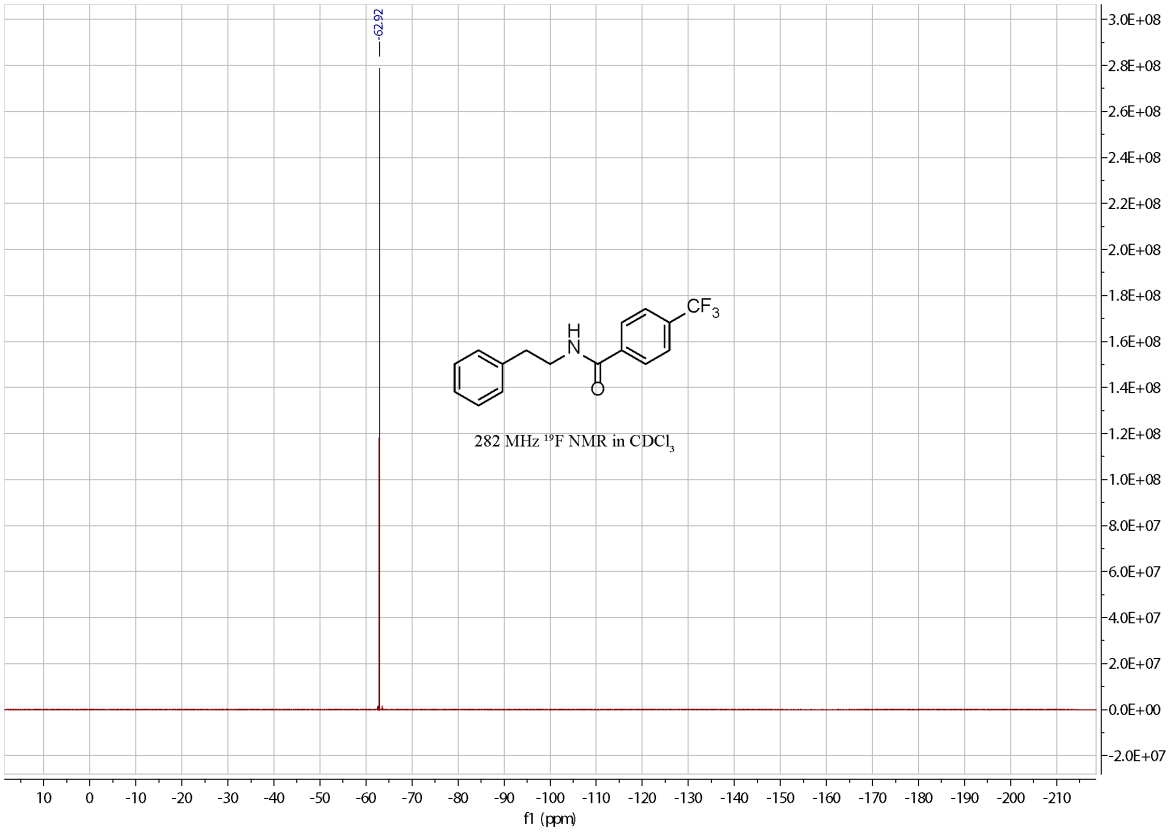

7.56
7.35
7.34
7.32
7.32
7.30
7.25
7.24
7.23
7.23
7.21
6.22
5.32
5.32
5.32
3.69
3.67
3.65
3.63
2.93
2.91
2.89
1.60
1.27
Br
H
N
O
300 MHz ¹H NMR in CD₂Cl₂
3.86
1.92
2.84
0.91
2.00
2.00
f1 (ppm)


166.61
138.89
133.62
131.94
128.94
128.57
126.83
126.21
77.58
77.16
76.74
41.32
35.76
Br
H
N
O
75 MHz ¹³C NMR in CDCl₃
f1 (ppm)

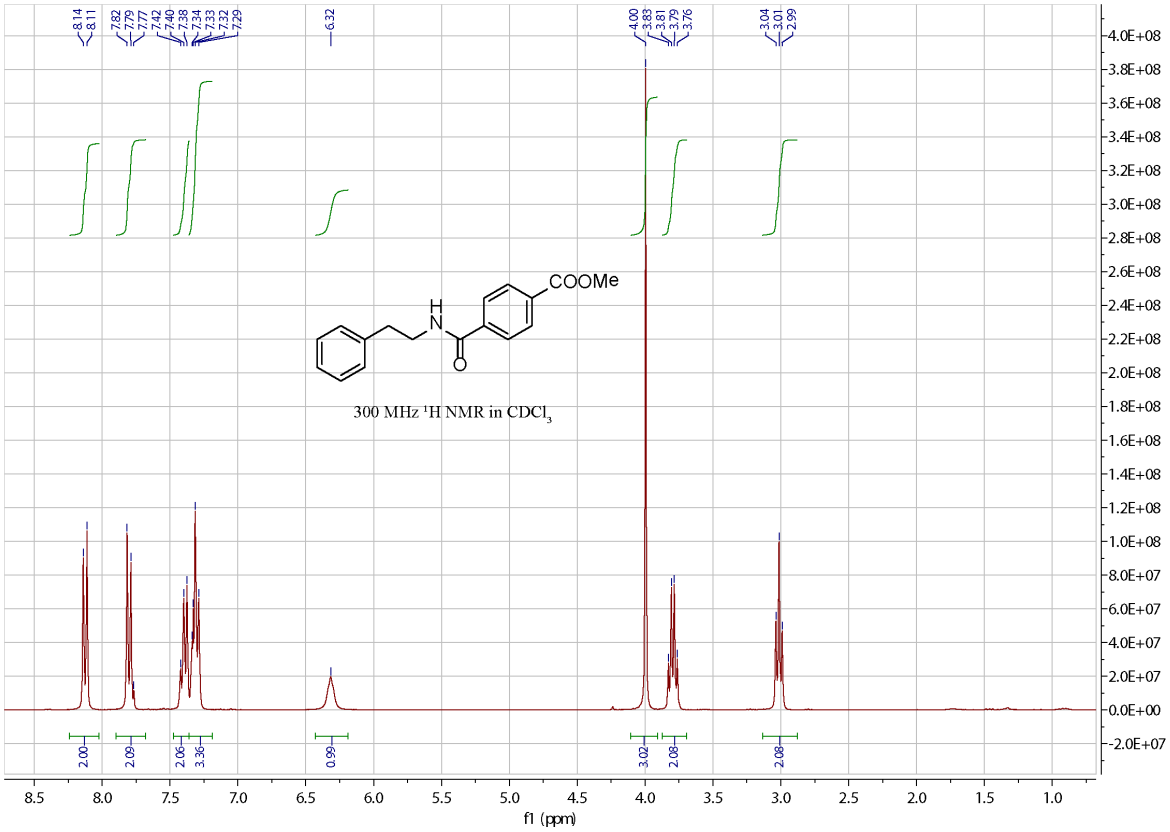
pCF_3Ph-Amide

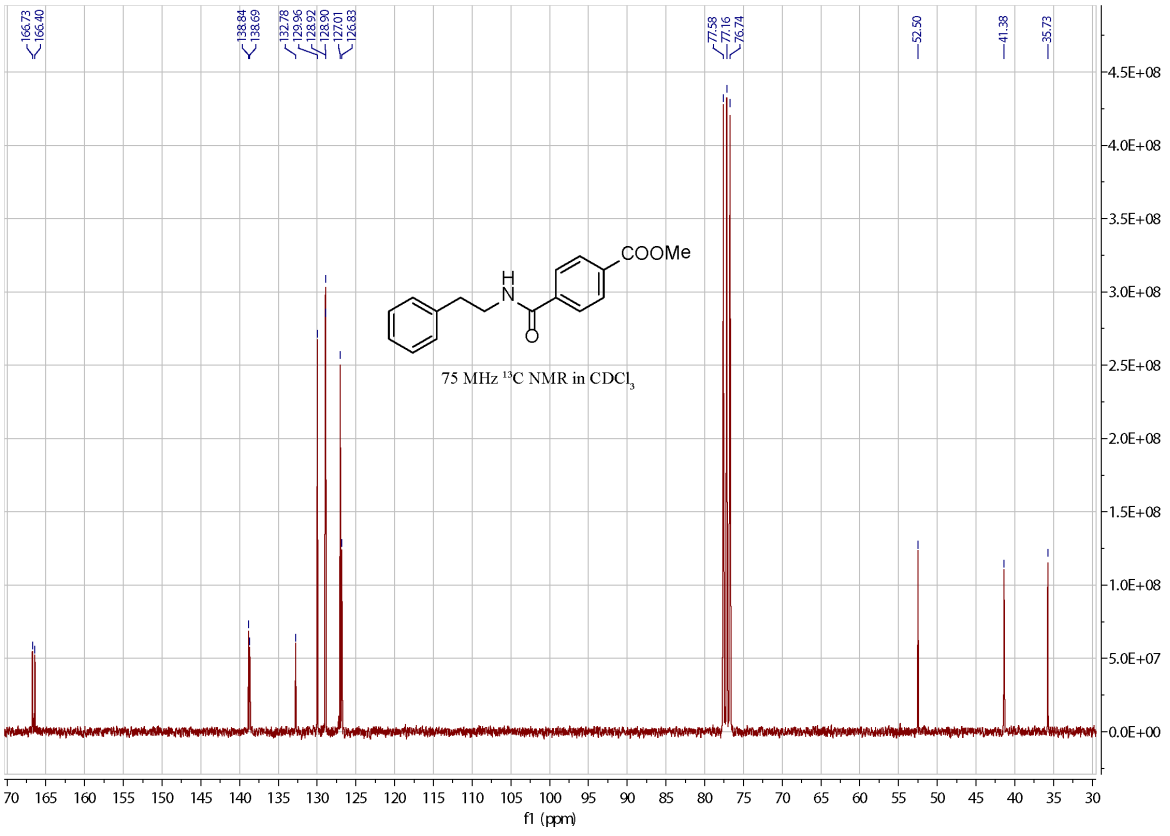




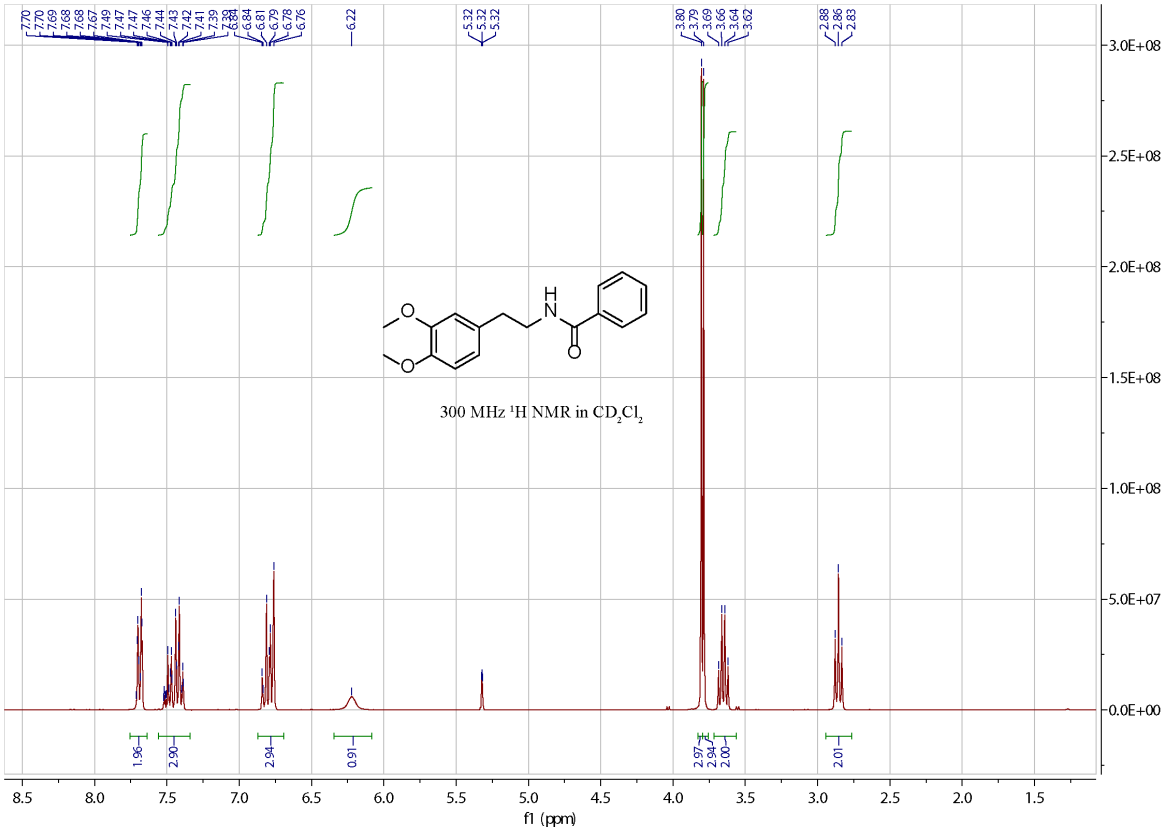

-62.92
CF3
H
N
O
282 MHz 19F NMR in CDCl3
3.0E+08
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

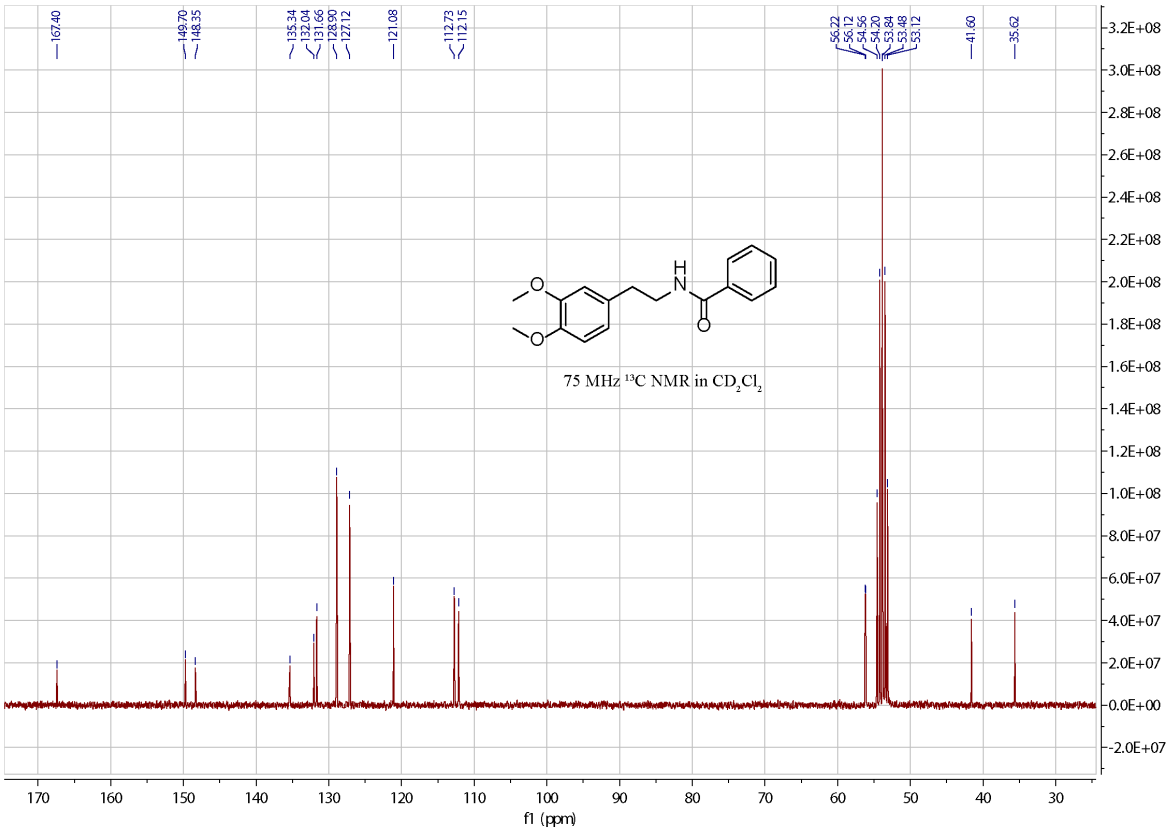
*p*COOMePh-Amide



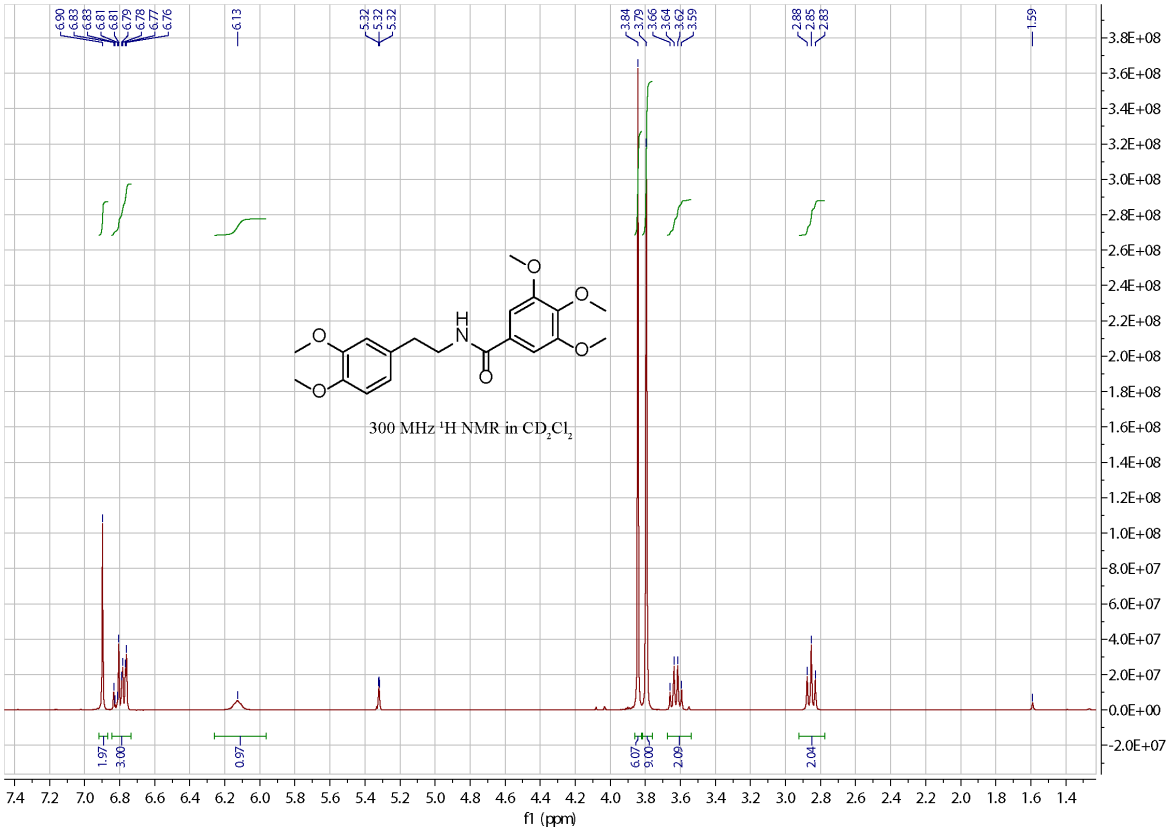


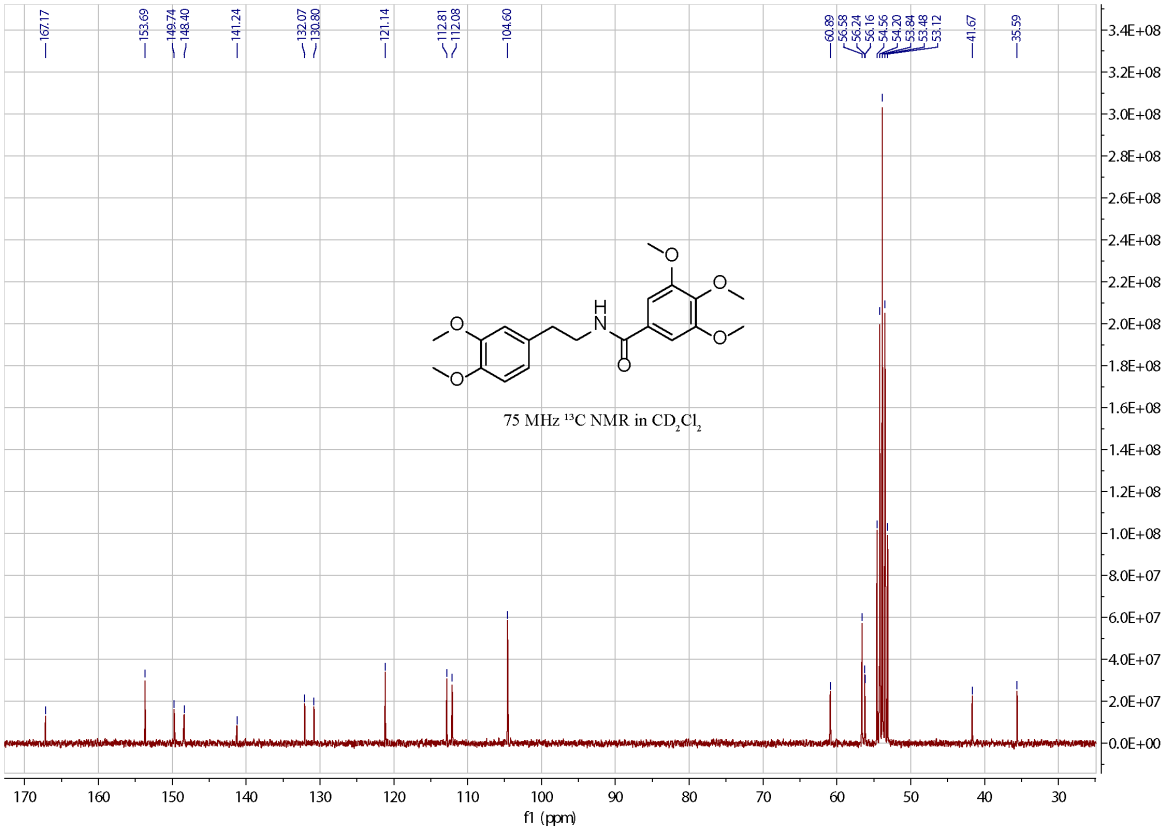
6,7-OMe-Amide


7.70
7.70
7.69
7.68
7.68
7.67
7.49
7.47
7.47
7.46
7.44
7.43
7.42
7.41
7.39
7.38
6.84
6.81
6.79
6.78
6.76
6.22
5.32
5.32
5.32
3.80
3.79
3.69
3.66
3.64
3.62
2.88
2.86
2.83
1.96
2.90
2.94
0.91
2.97
2.94
2.00
2.01
300 MHz ¹H NMR in CD2Cl2
f1 (ppm)

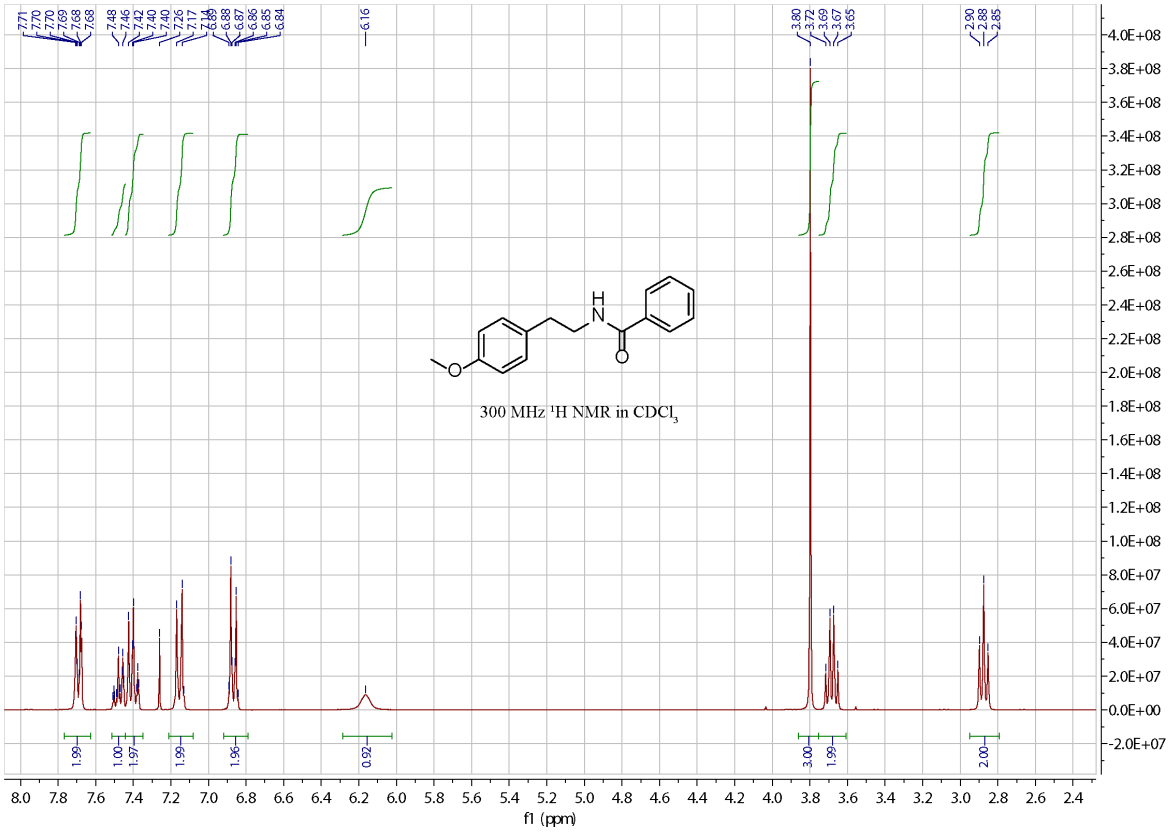

167.40
149.70
148.35
135.34
132.04
131.66
128.90
127.12
121.08
112.73
112.15
56.22
56.12
54.56
54.20
53.84
53.48
53.12
41.60
35.62
75 MHz ¹³C NMR in CD2Cl2
f1 (ppm)

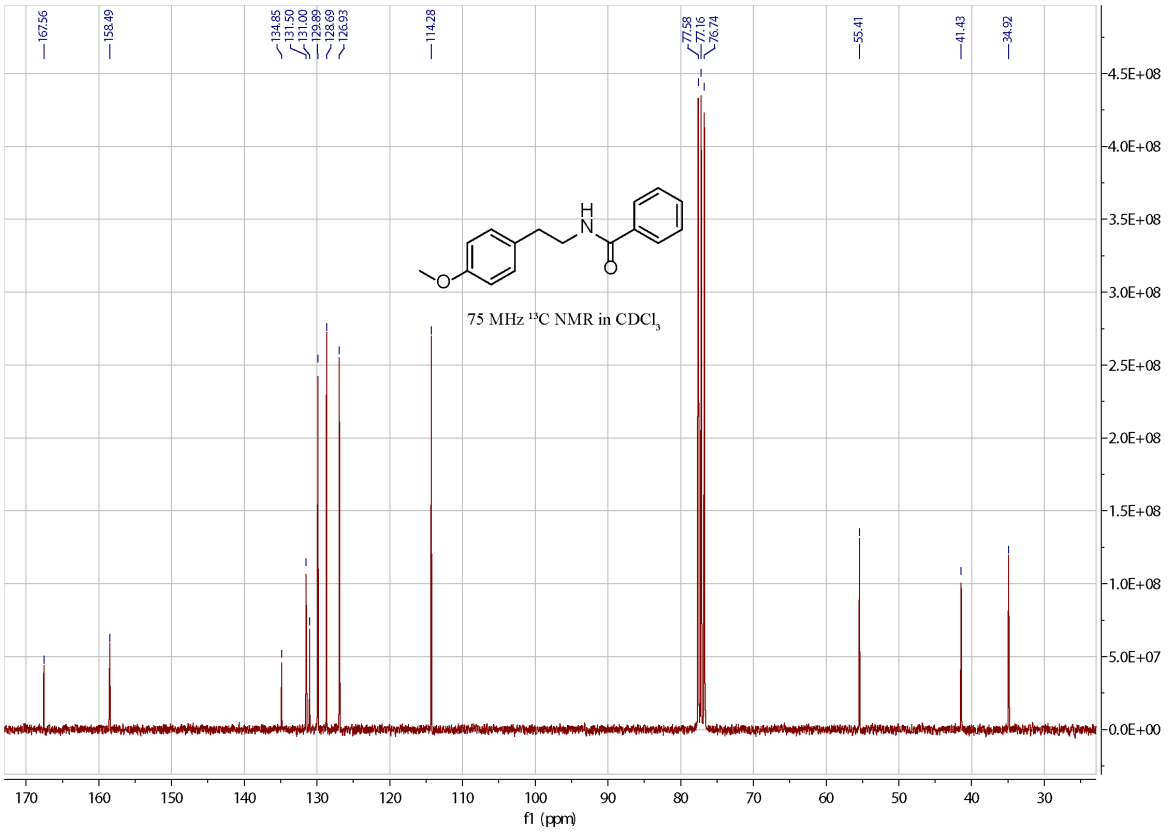
Penta-OMe-Amide



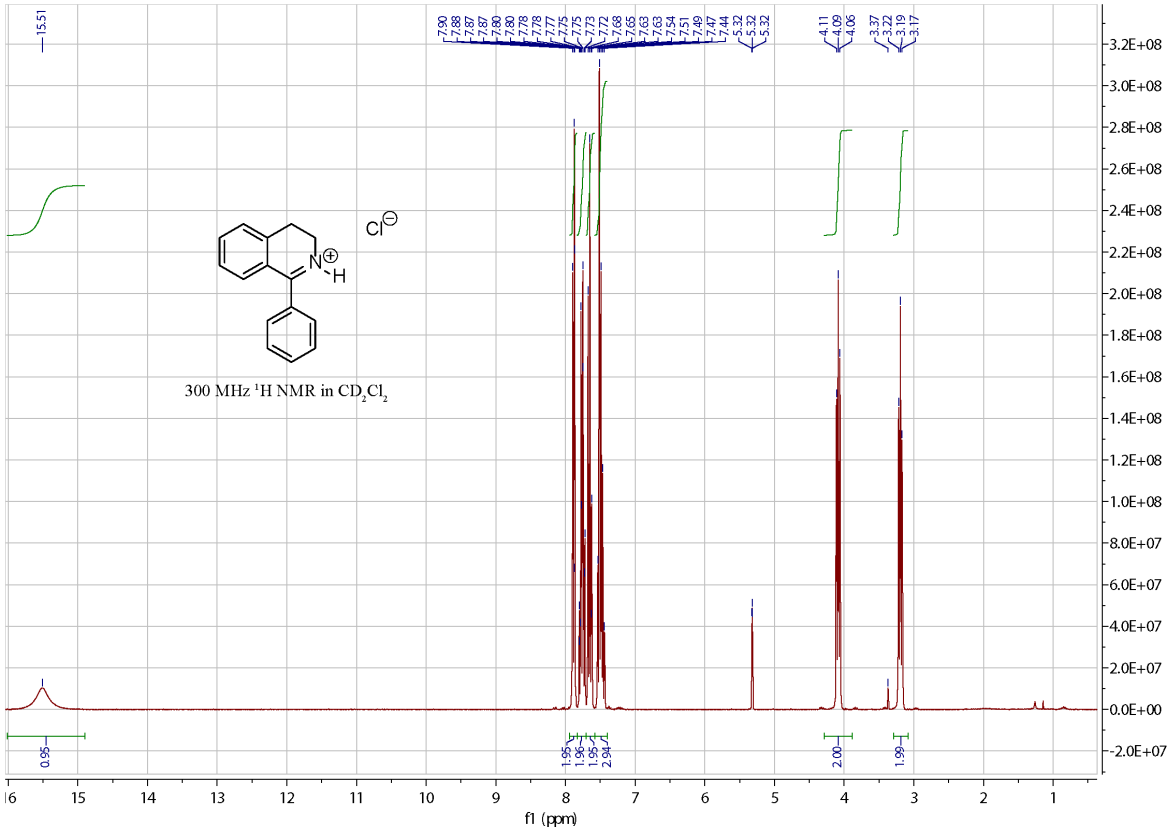


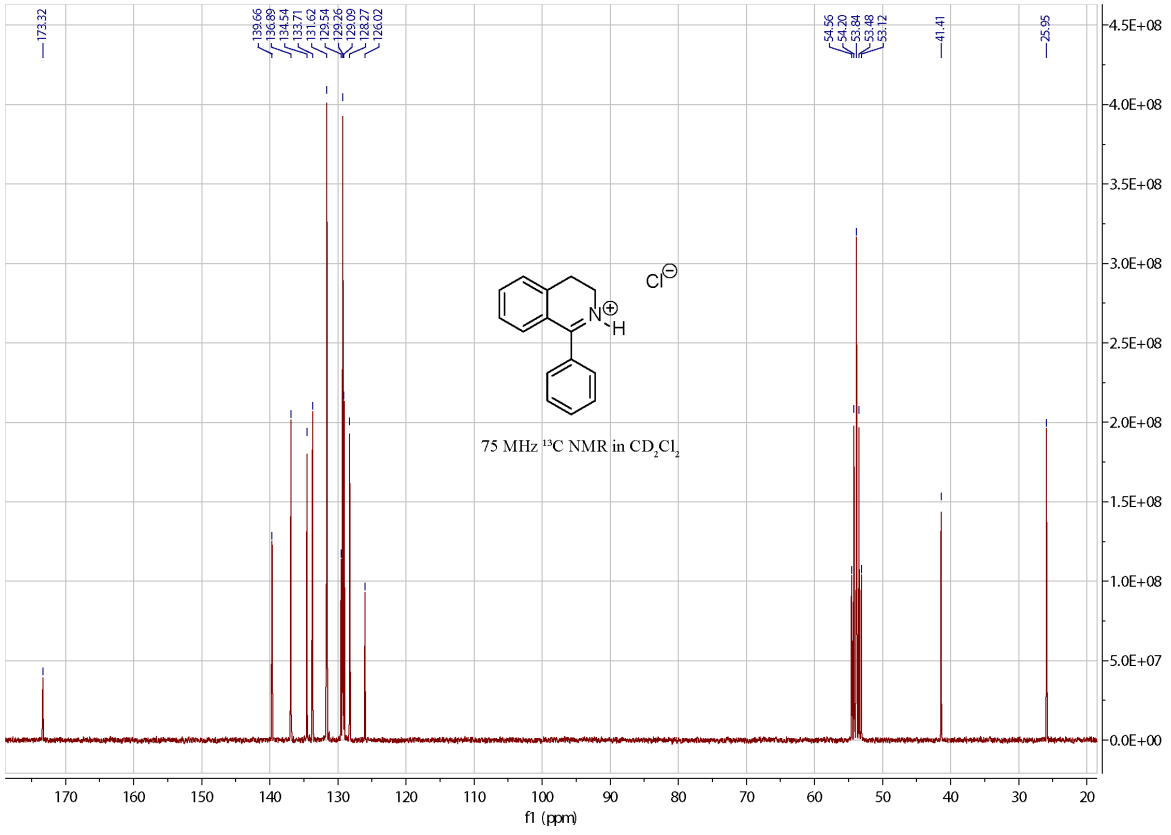
7-OMe-Amide


7.71
7.70
7.70
7.69
7.68
7.68
7.48
7.46
7.42
7.40
7.40
7.26
7.17
6.89
6.88
6.87
6.86
6.85
6.84
6.16
3.80
3.72
3.69
3.67
3.65
2.90
2.88
2.85
H
N
O
O
300 MHz ¹H NMR in CDCl3
1.99
1.00
1.97
1.99
1.96
0.92
3.00
1.99
2.00
f1 (ppm)

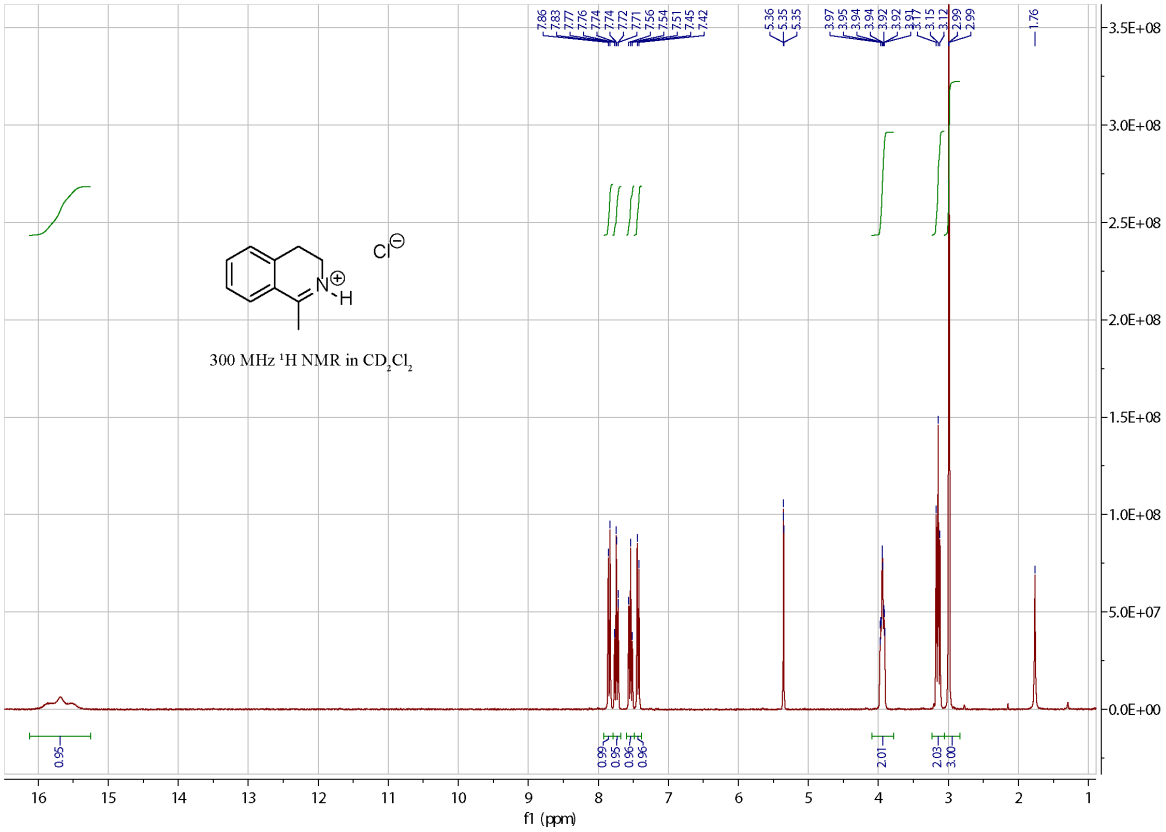

167.56
158.49
134.85
131.50
131.00
129.89
128.69
126.93
114.28
77.58
77.16
76.74
55.41
41.43
34.92
H
N
O
O
75 MHz ¹³C NMR in CDCl3
f1 (ppm)

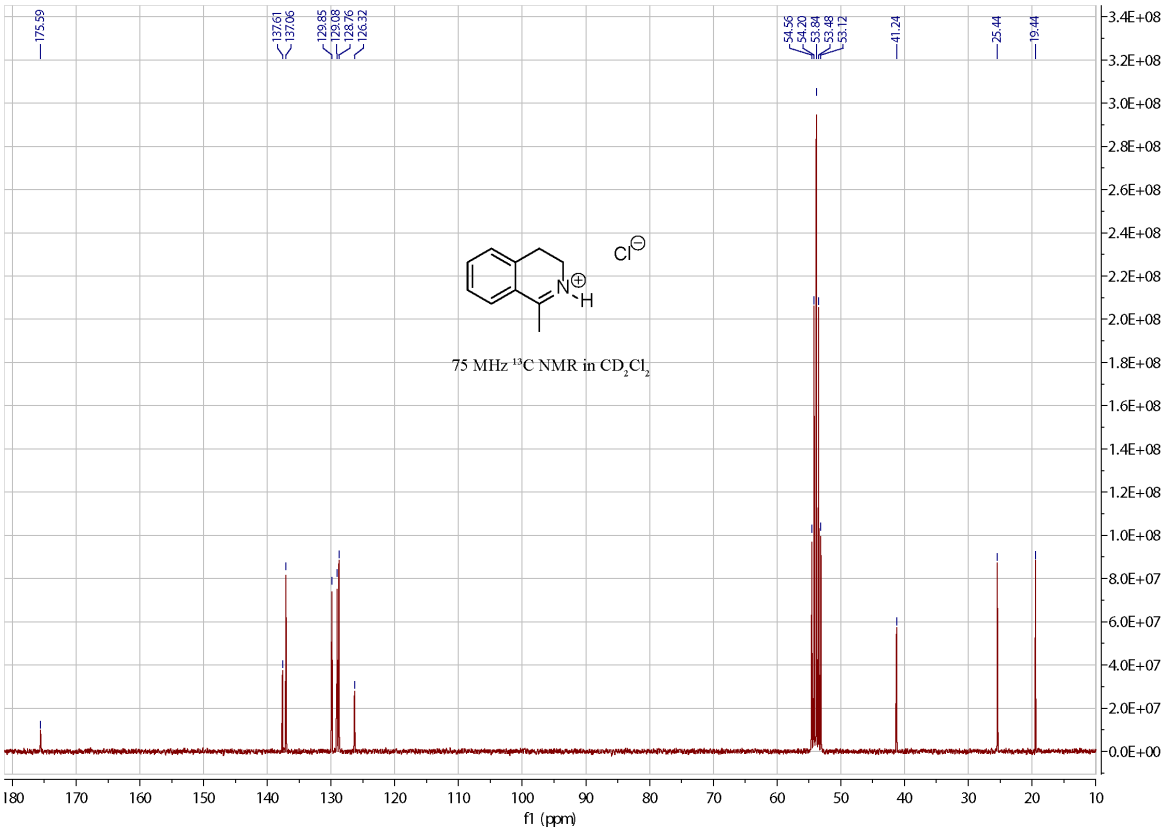
1-Ph-DHIQ*HCl **12a***HCl



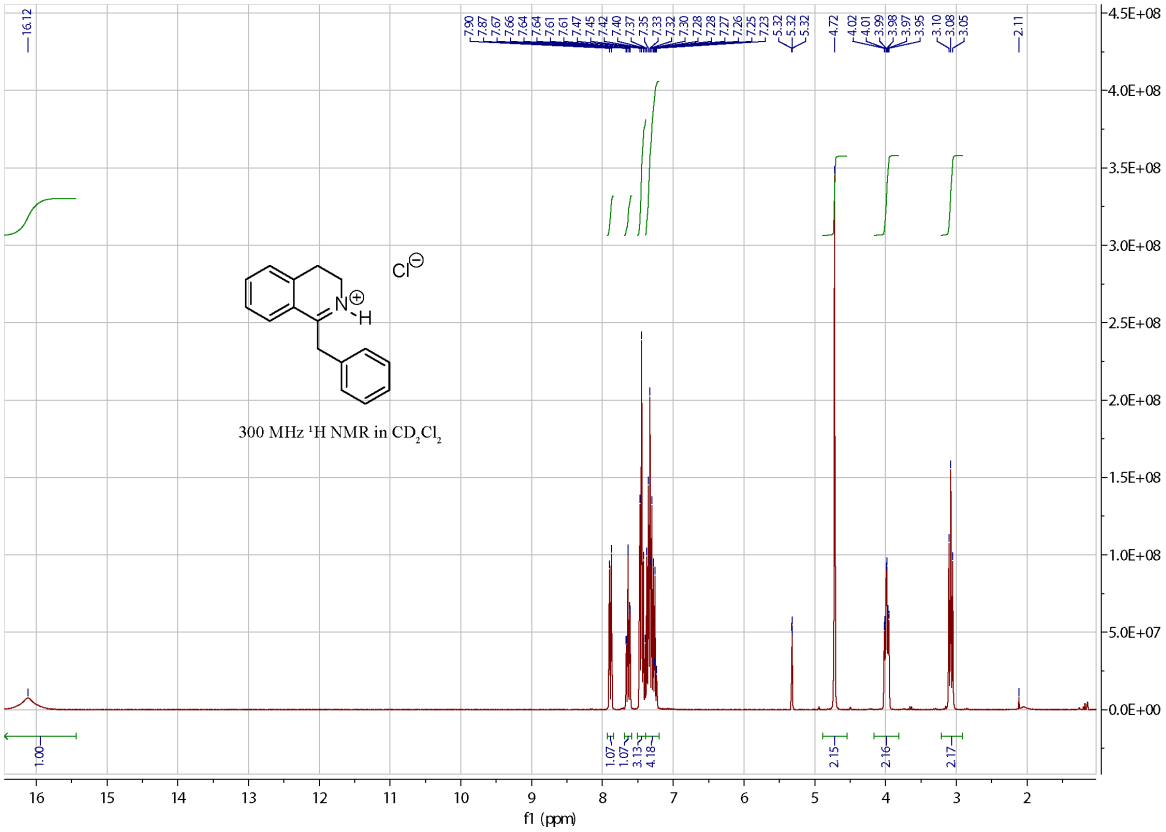


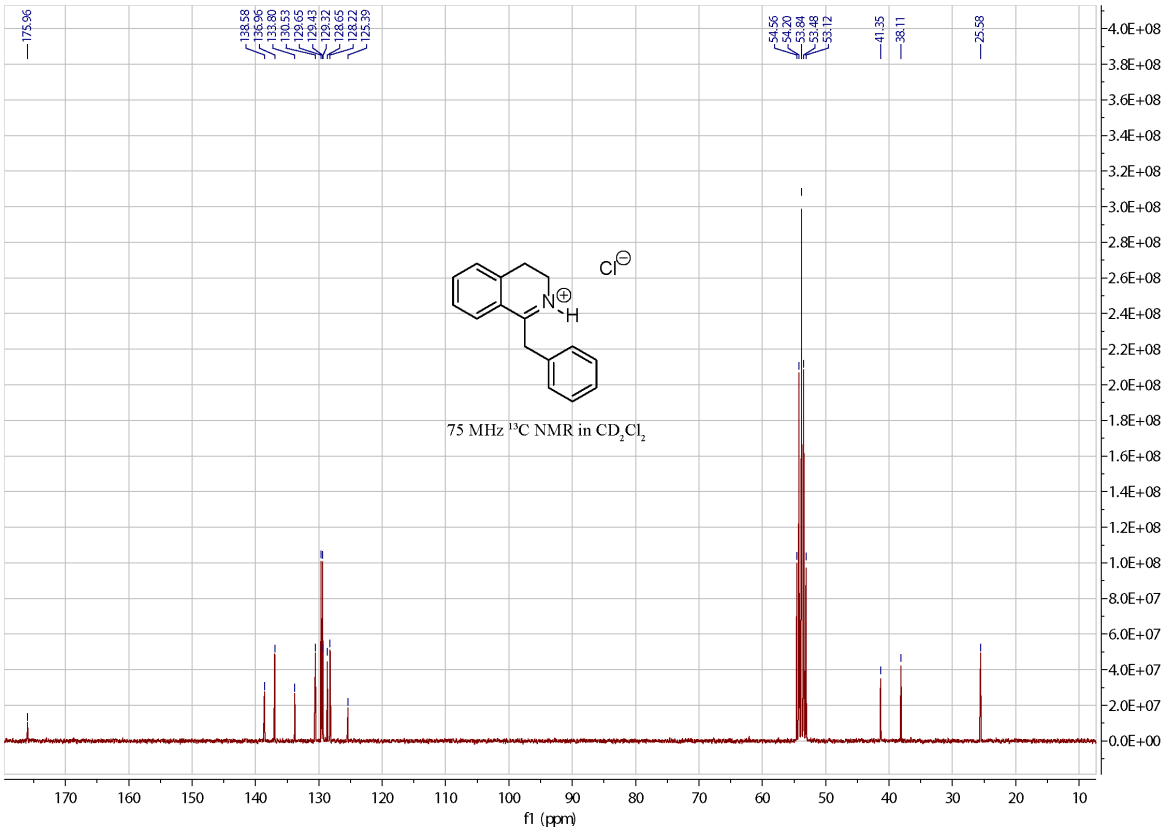
1-Me-DHIQ*HCl **12b***HCl



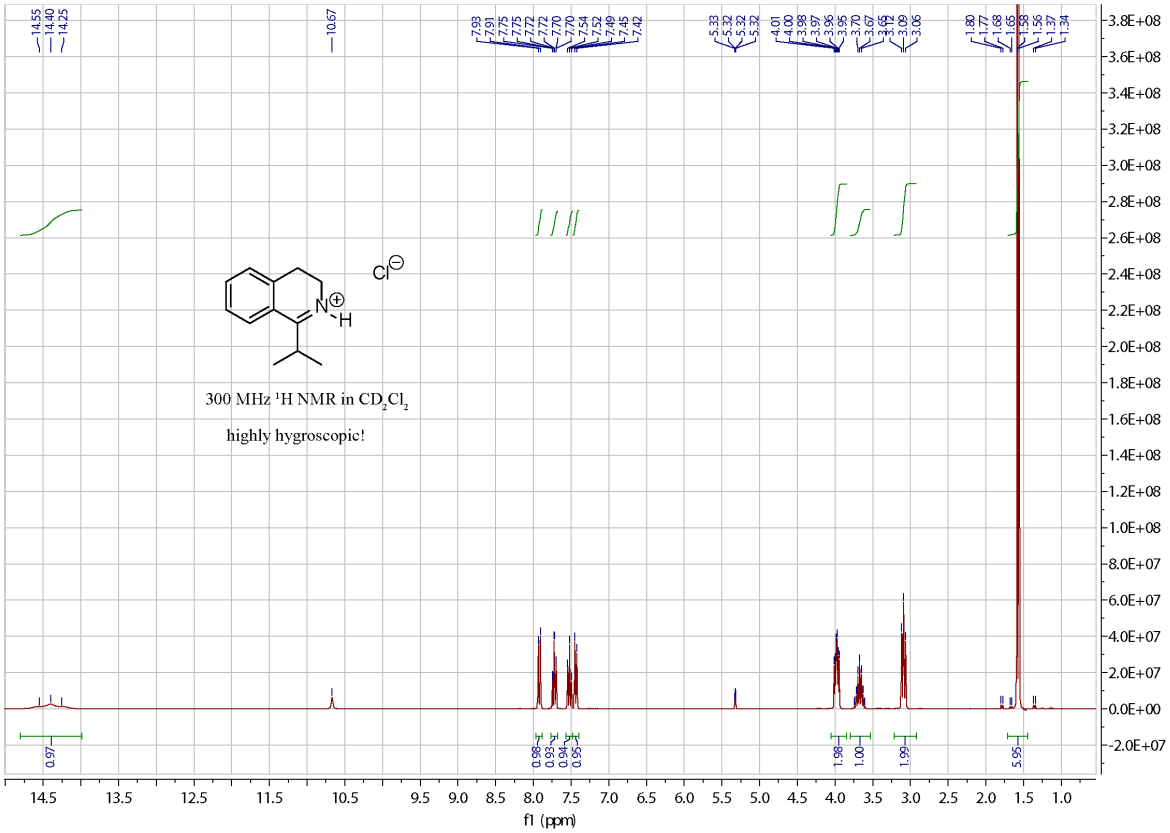


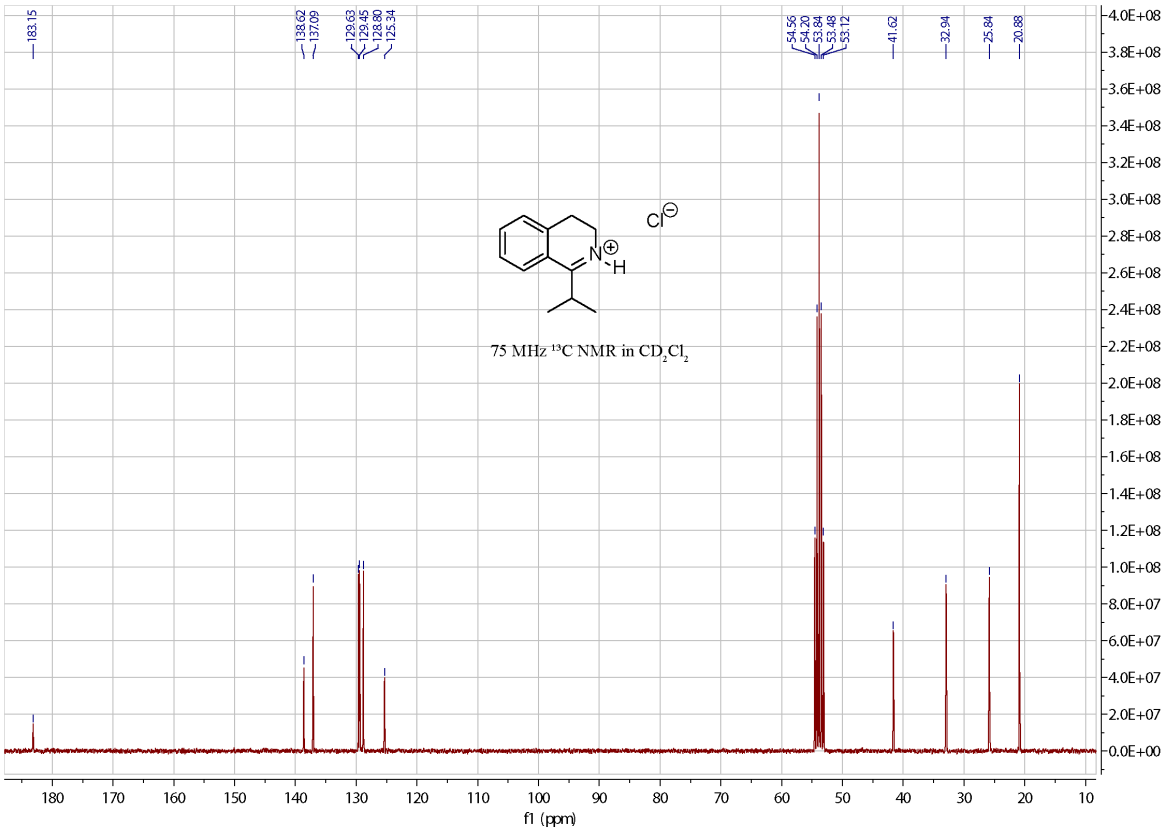
1-Bn-DHIQ*HCl **12c***HCl



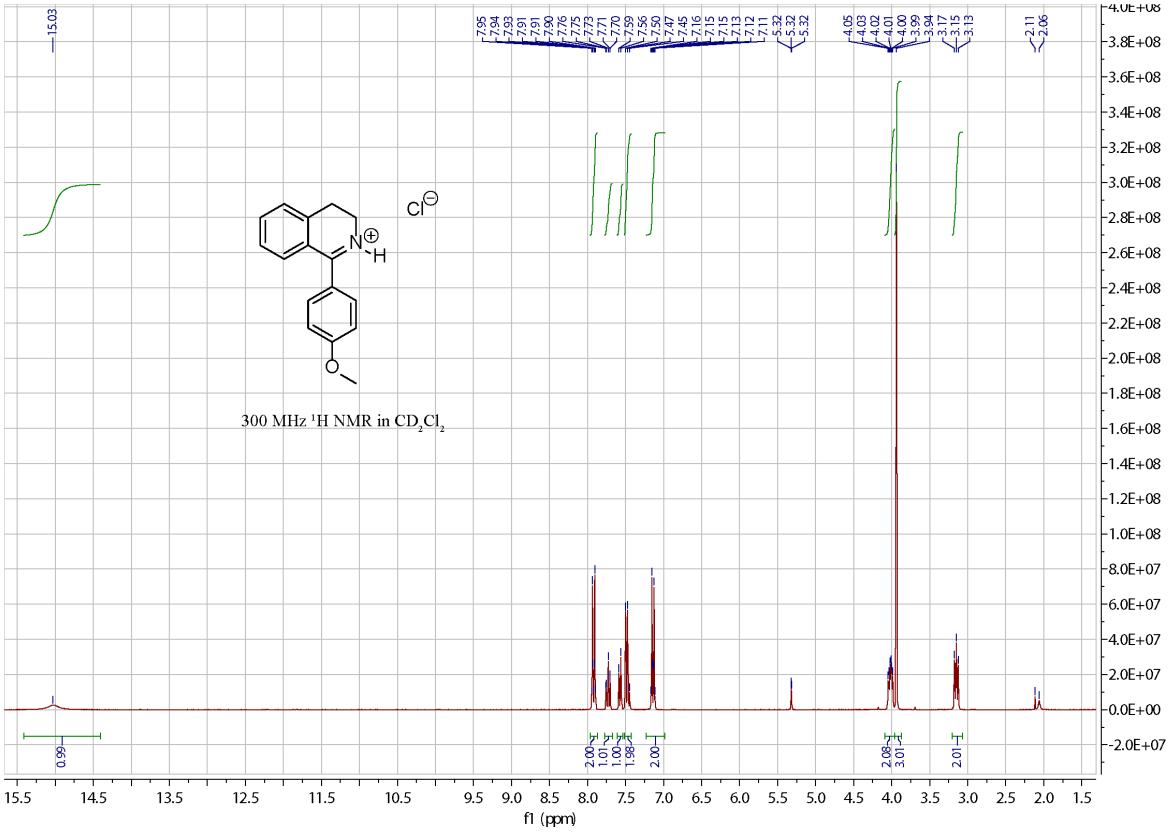


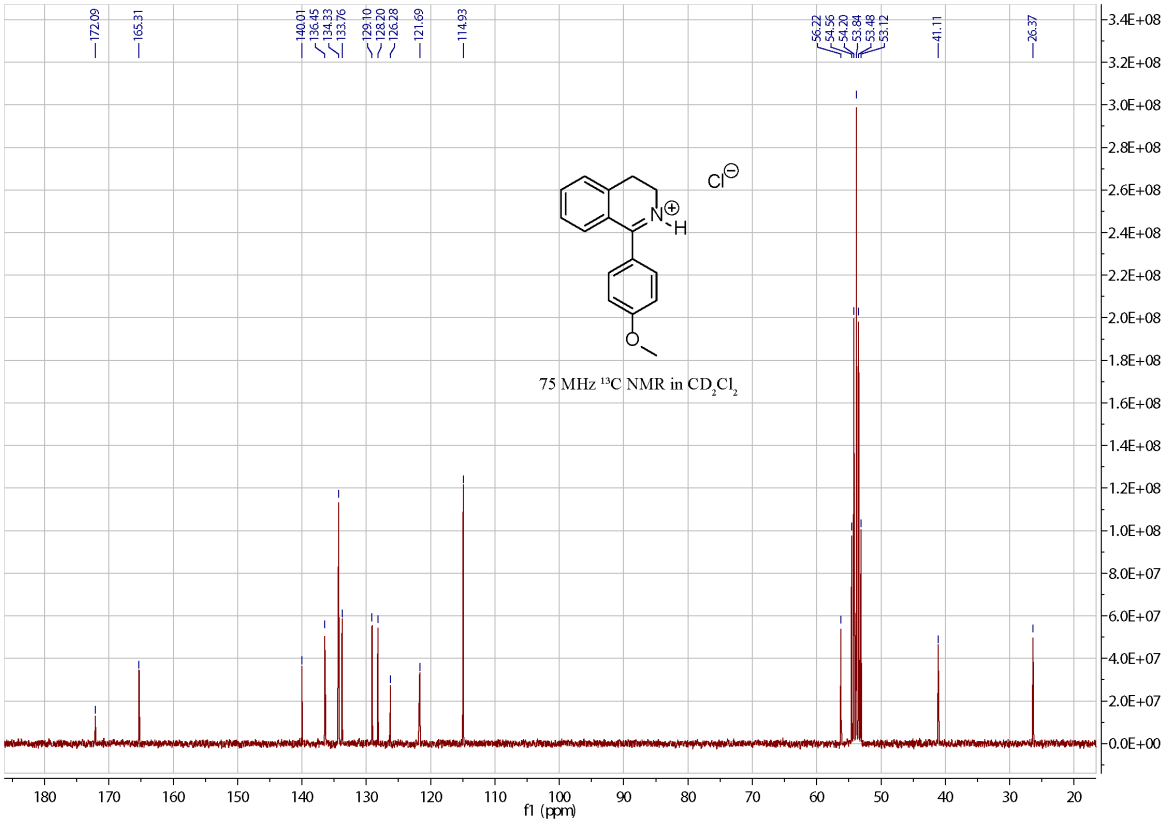
1-*i*Pr-DHIQ*HCl **12d***HCl



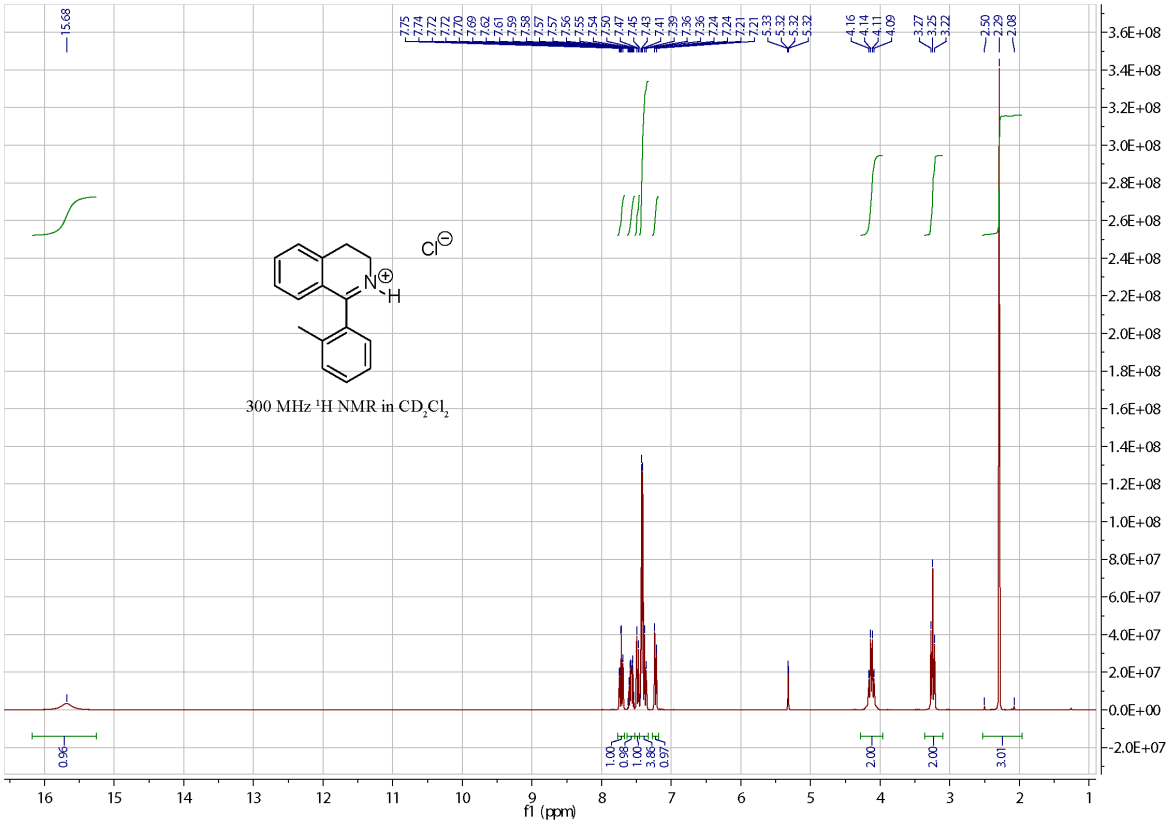


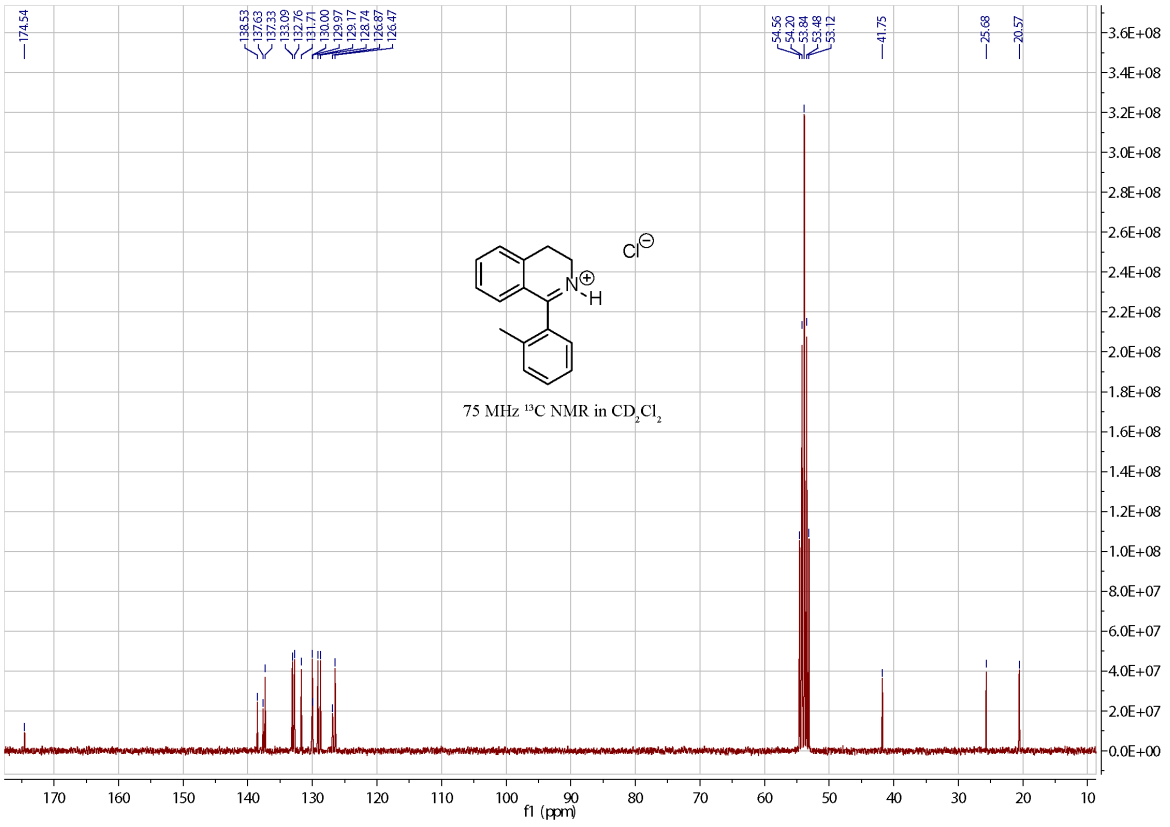
1-*p*OMePh-DHIQ*HCl **12e***HCl



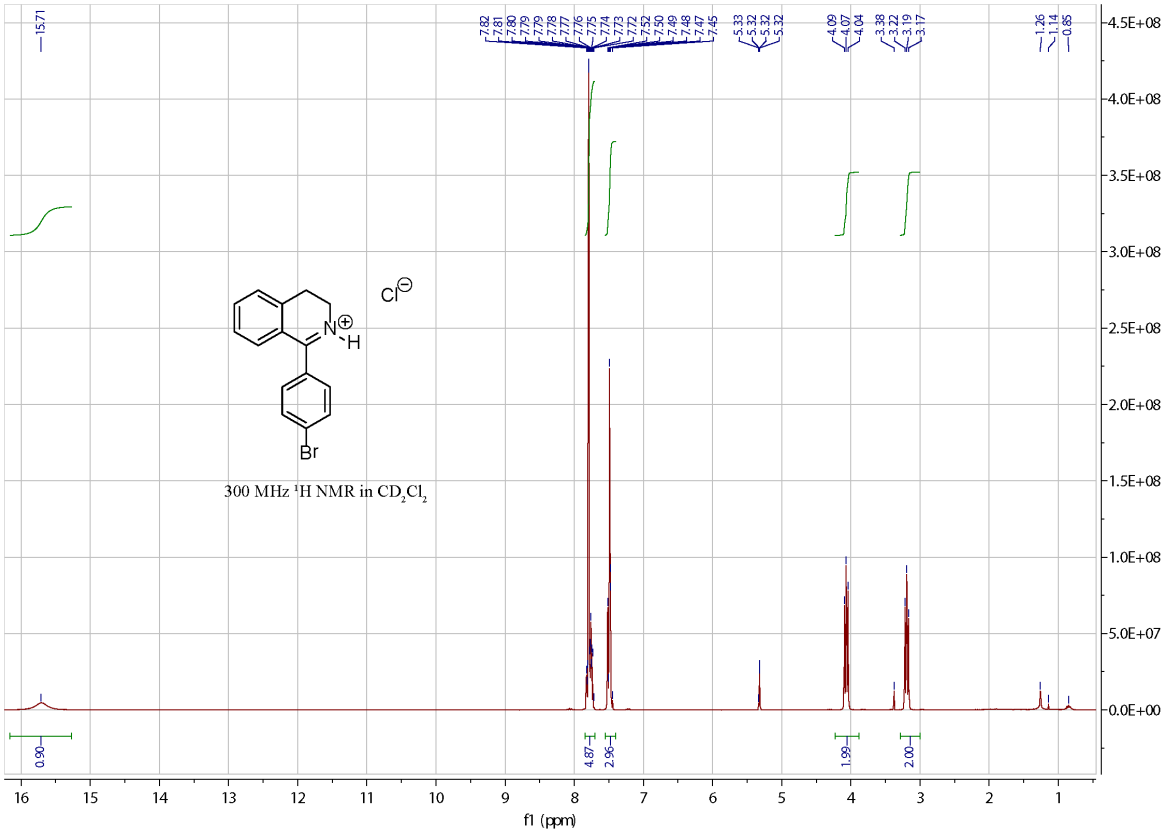


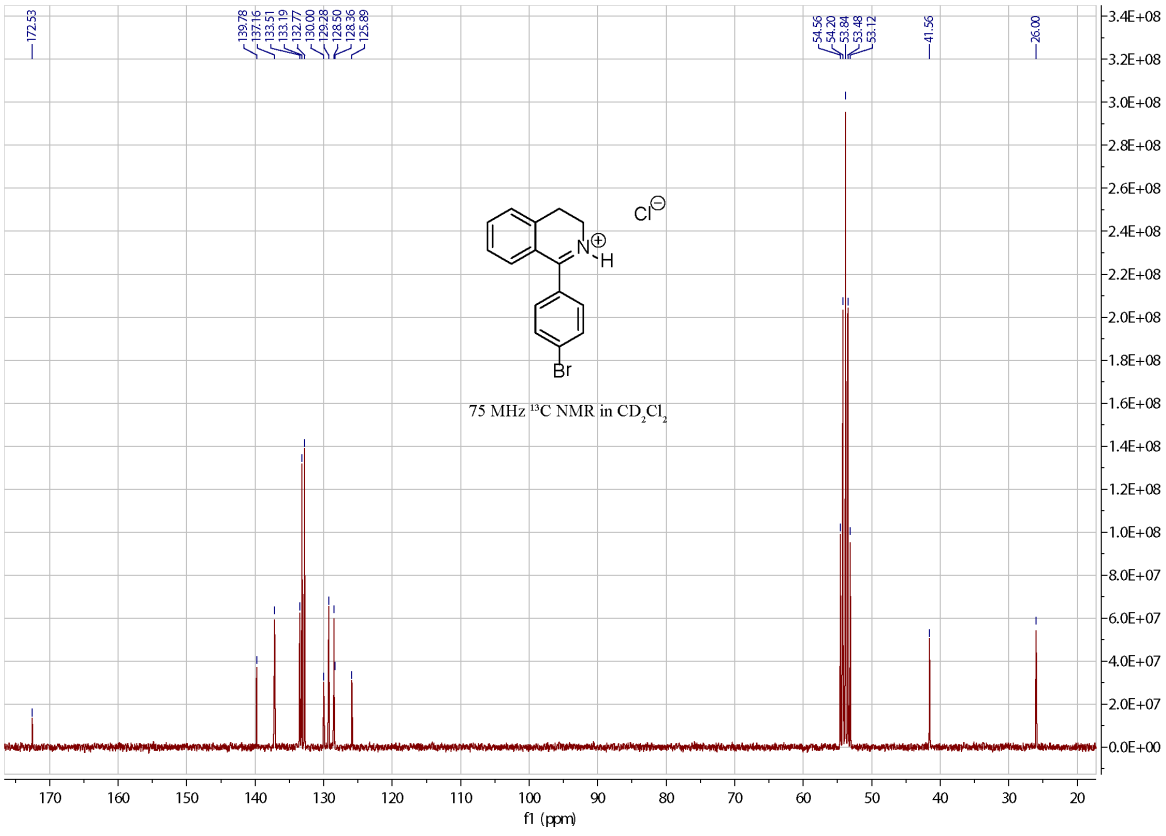
1-*o*Tol-DHIQ*HCl **12f***HCl



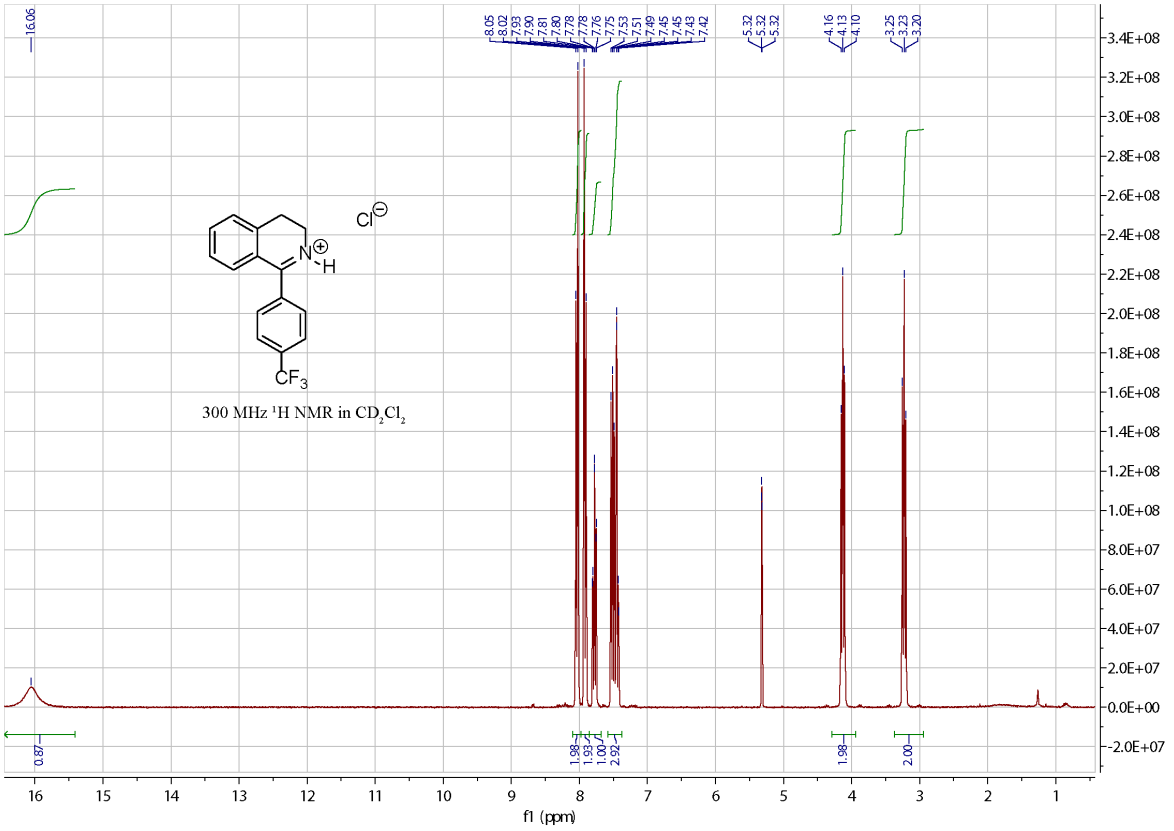


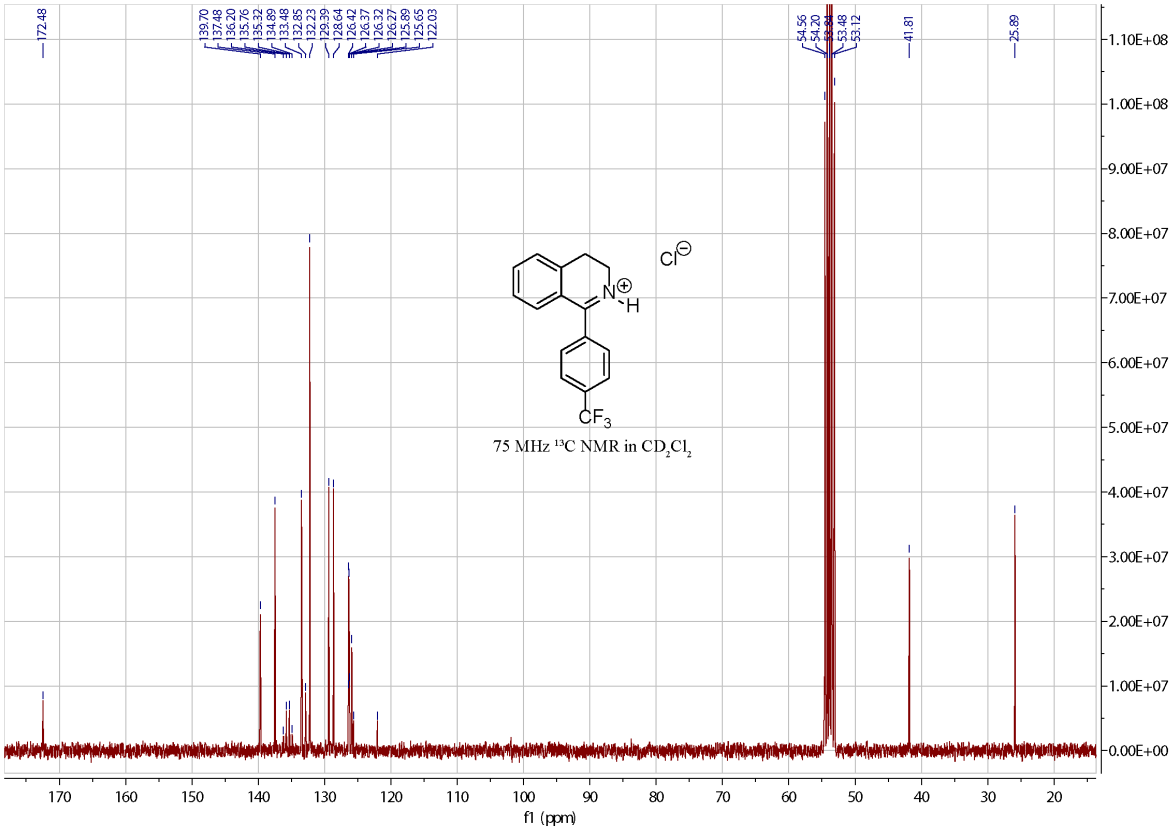
1-*p*BrPh-DHIQ*HCl **12g***HCl

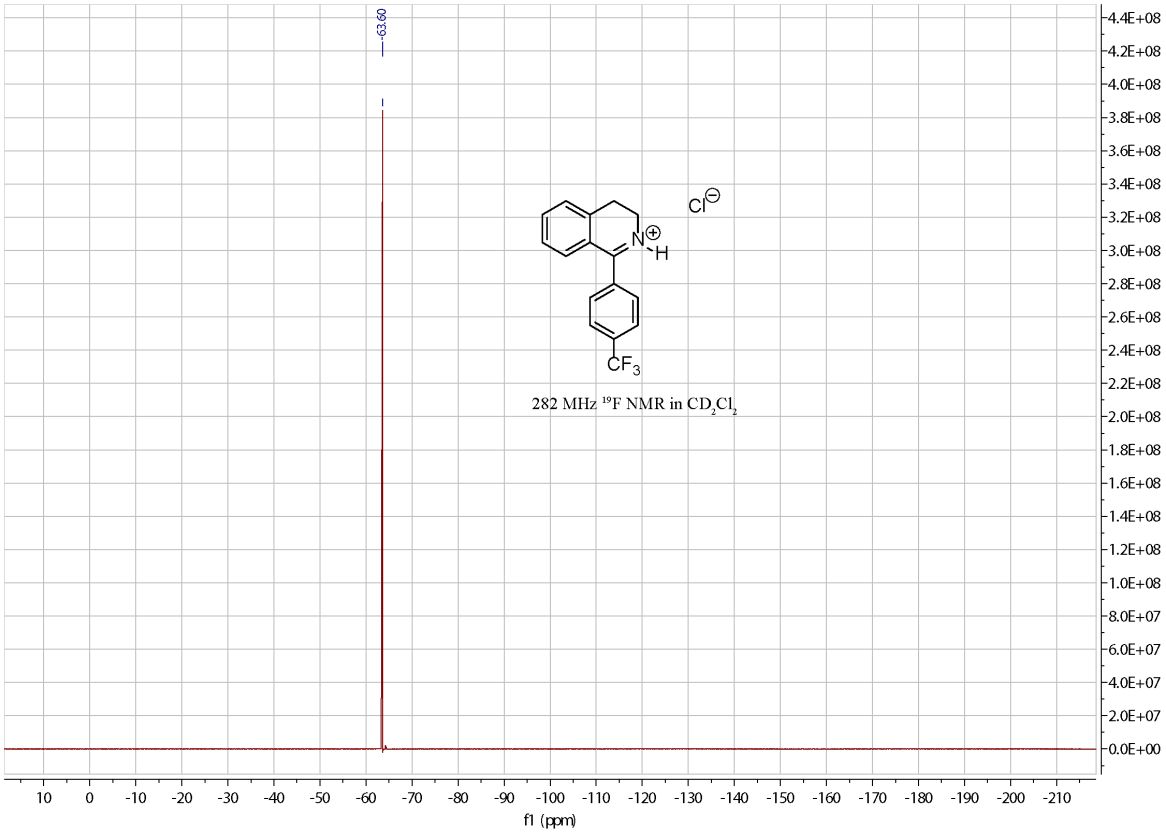




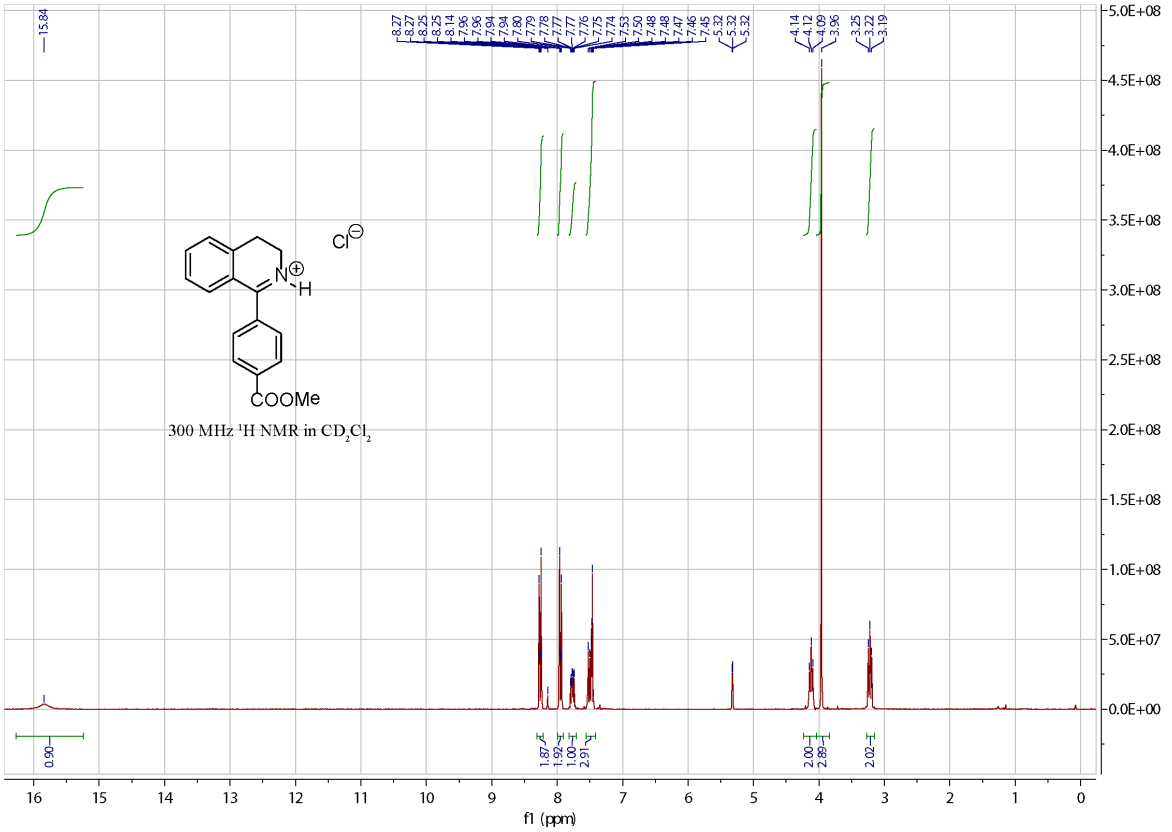
1-*p*CF_3Ph-DHIQ*HCl **12h***HCl

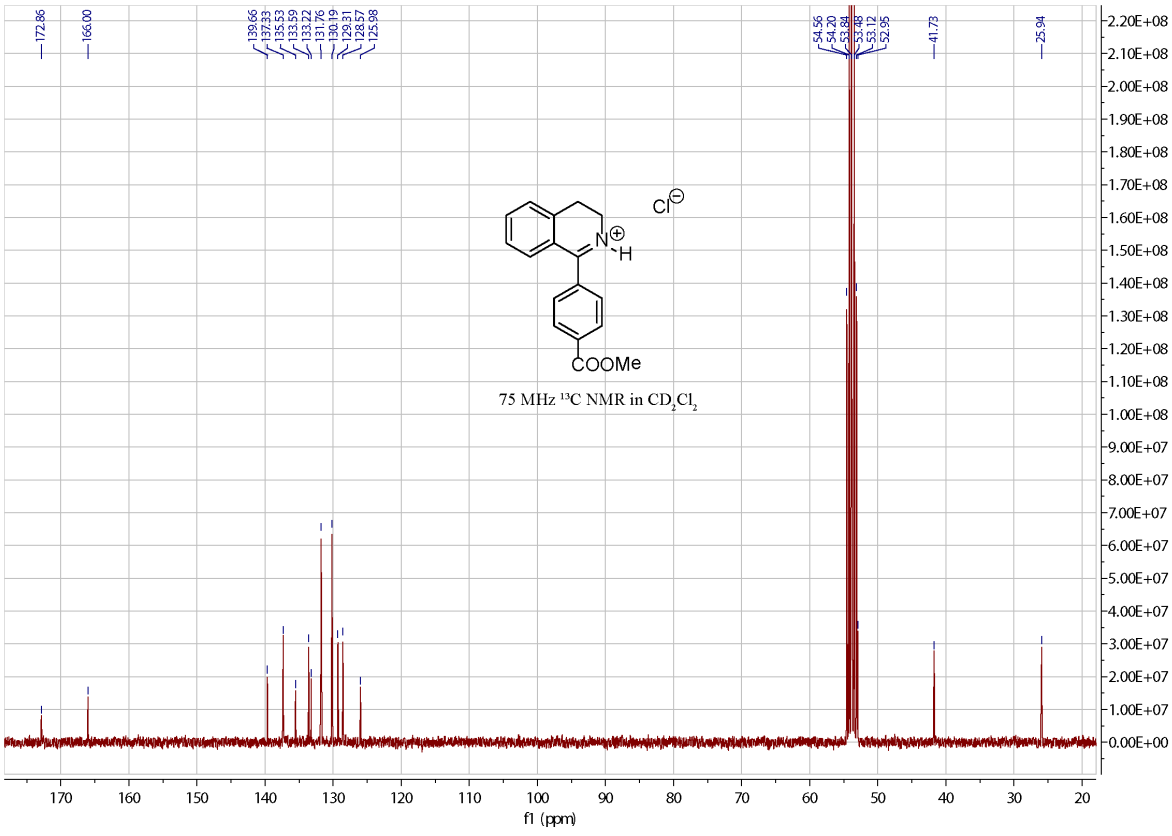




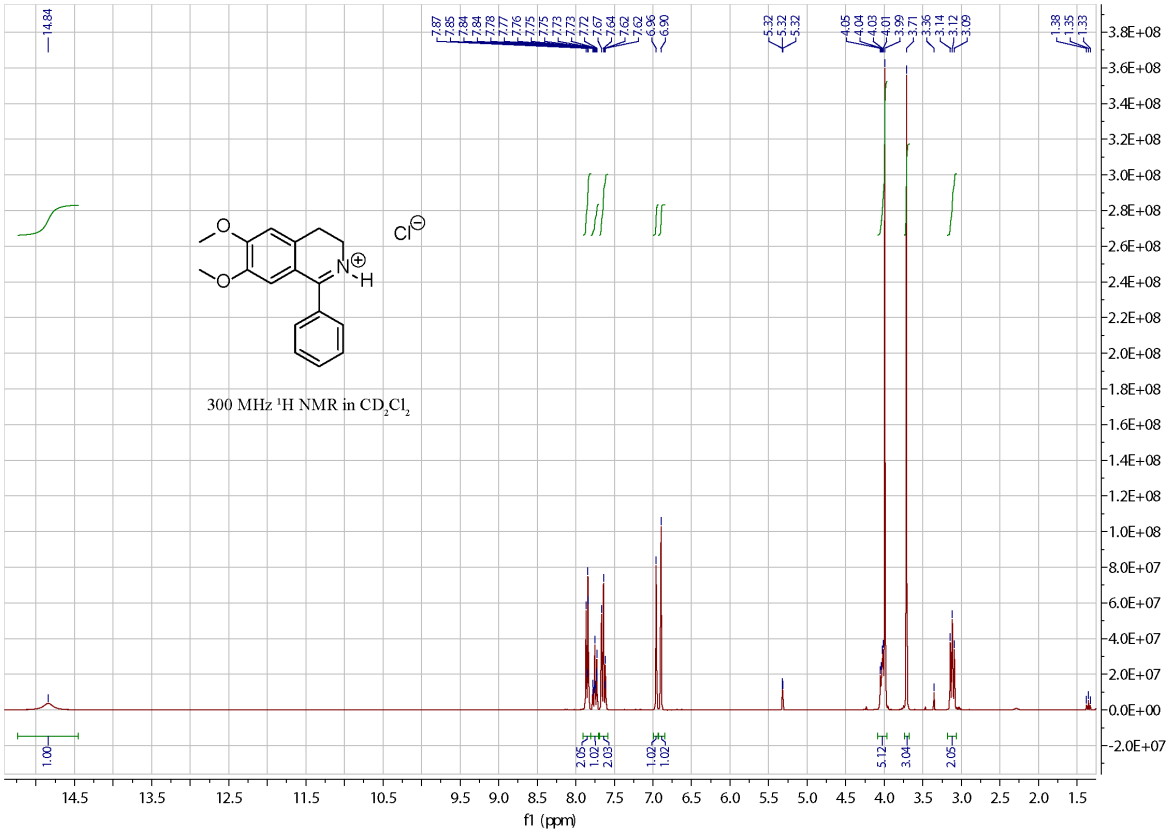

-63.60
Cl
N
H
CF3
282 MHz 19F NMR in CD2Cl2
4.4E+08
4.2E+08
4.0E+08
3.8E+08
3.6E+08
3.4E+08
3.2E+08
3.0E+08
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

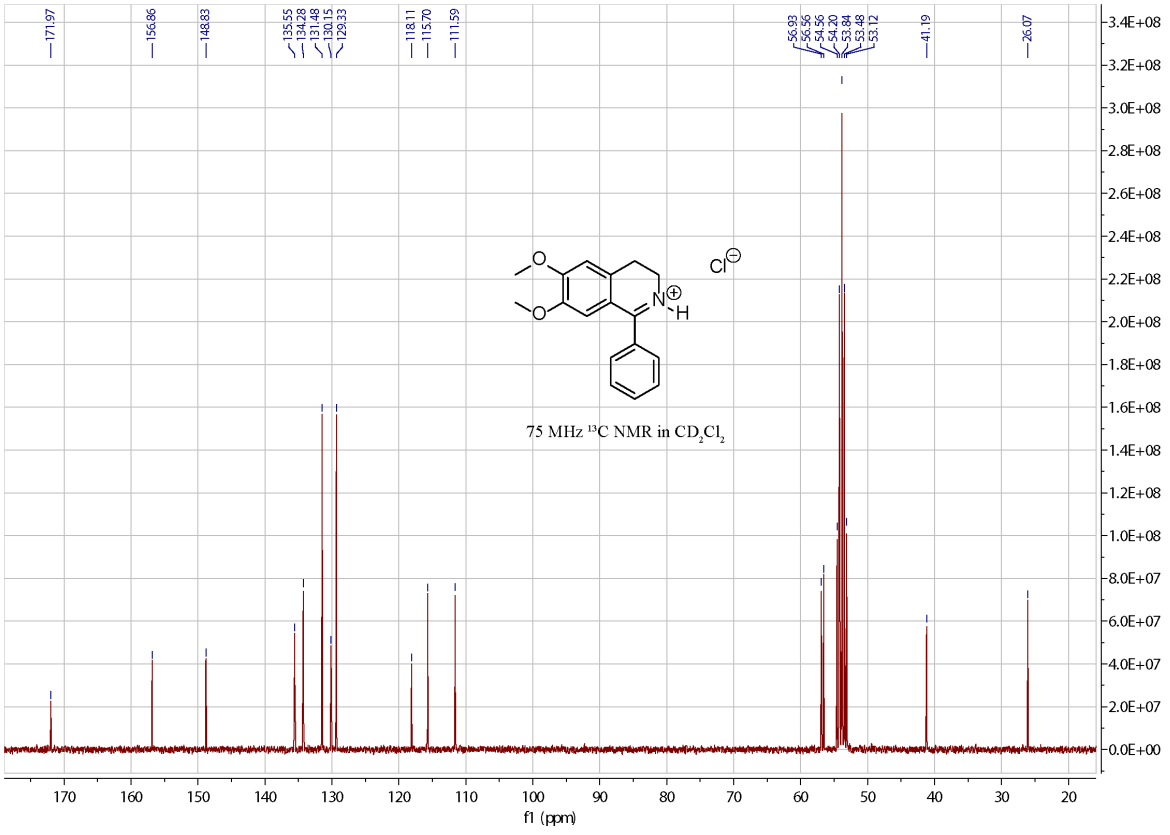
1-*p*COOMePh-DHIQ*HCl **12i***HCl



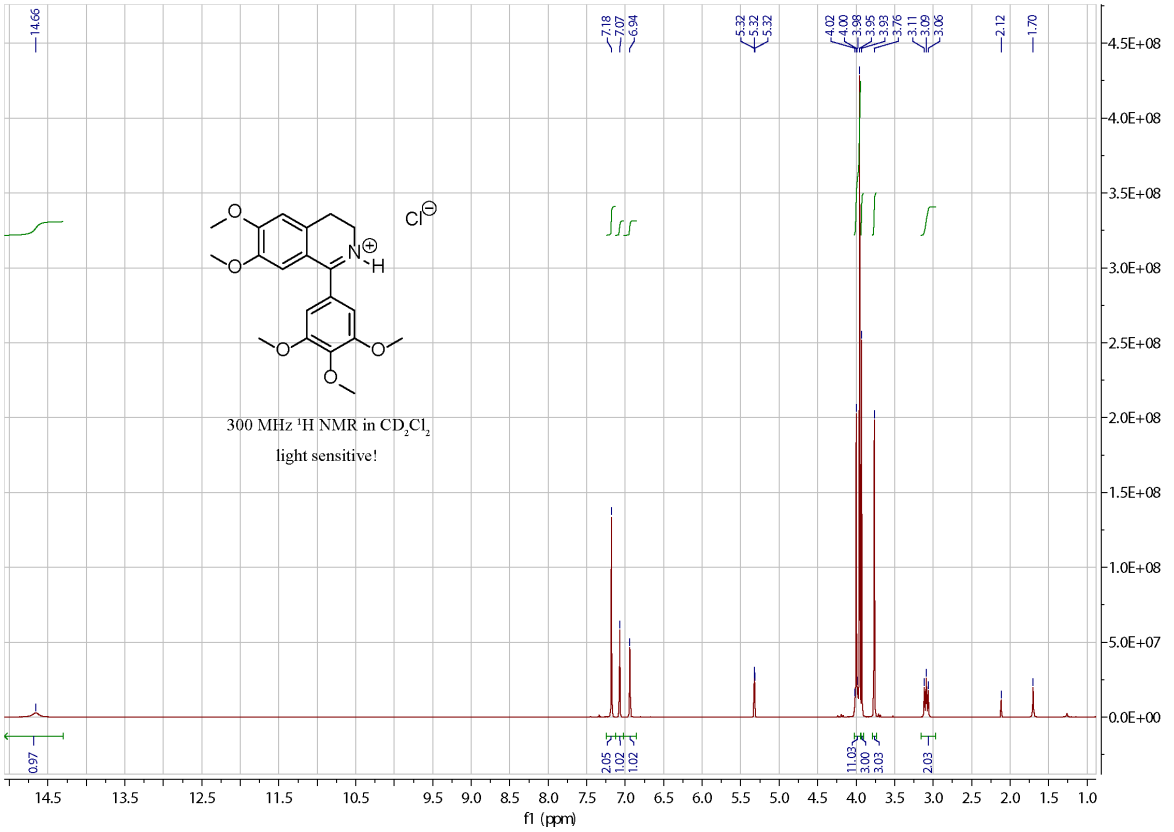


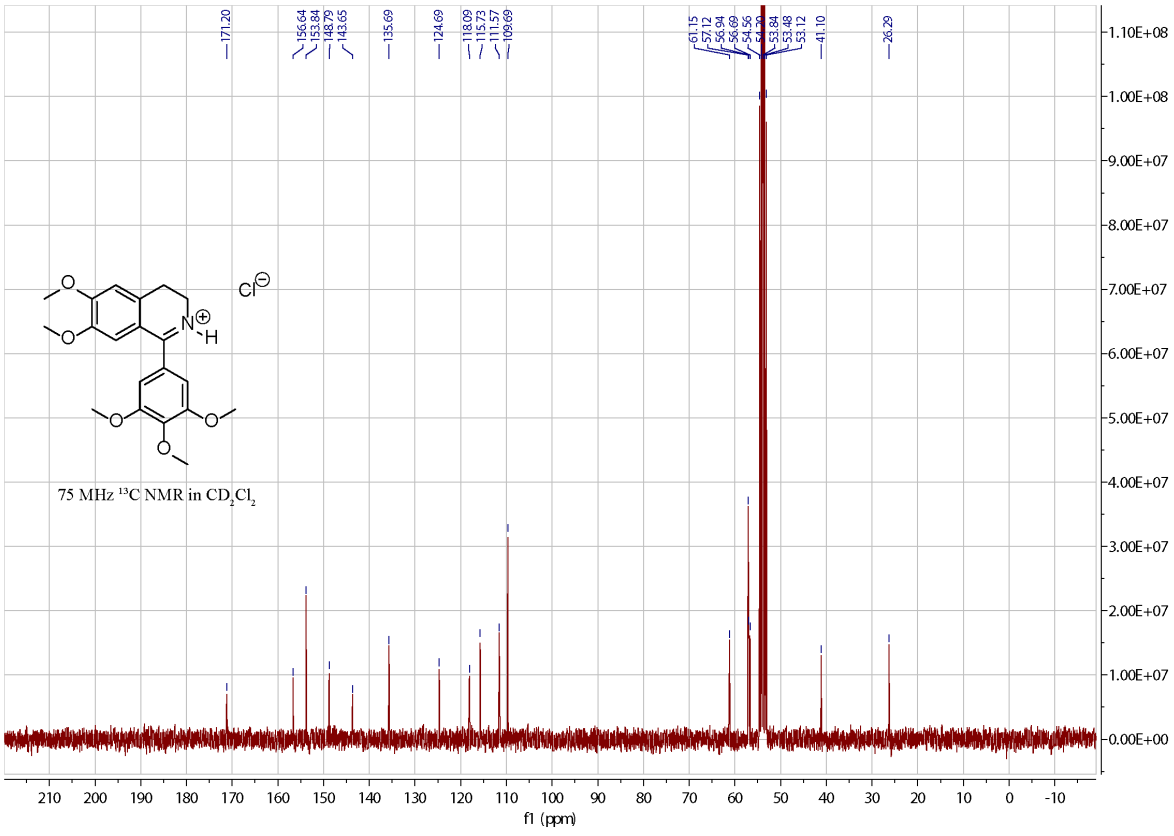
1-Ph-6,7-OMe-DHIQ*HCl **12j***HCl



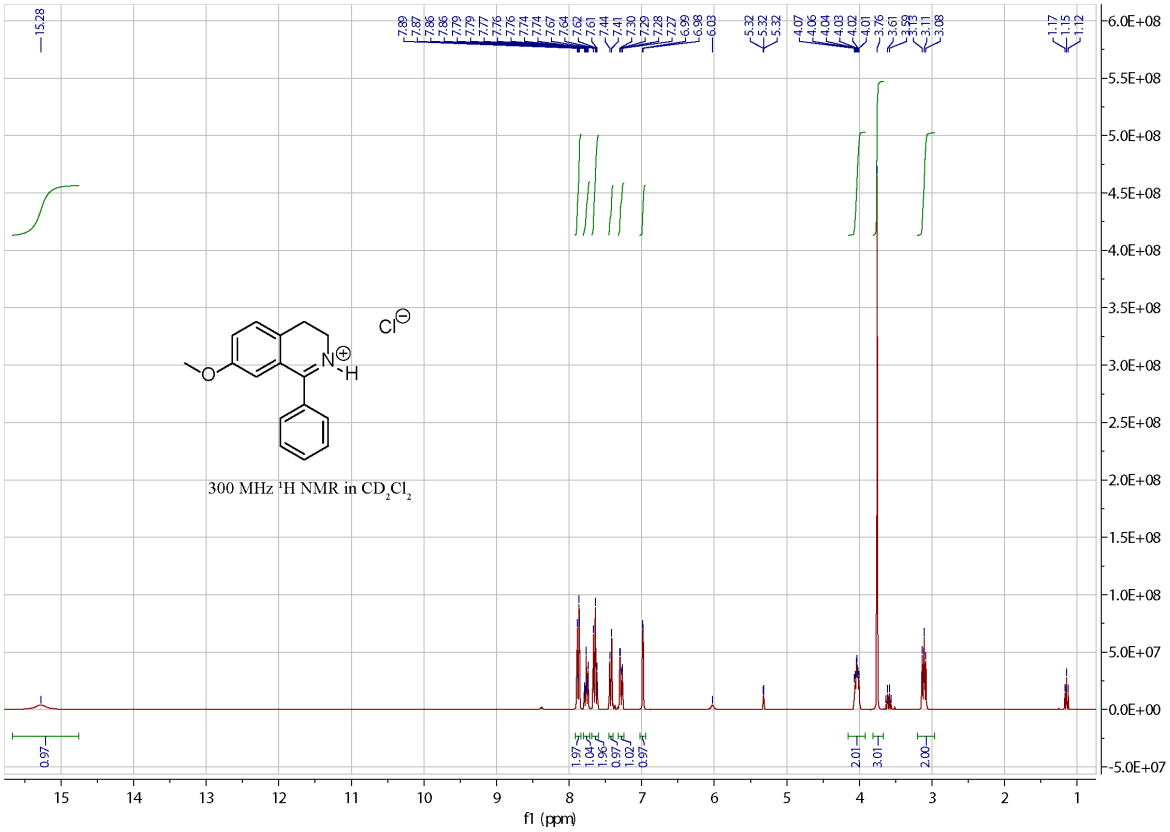


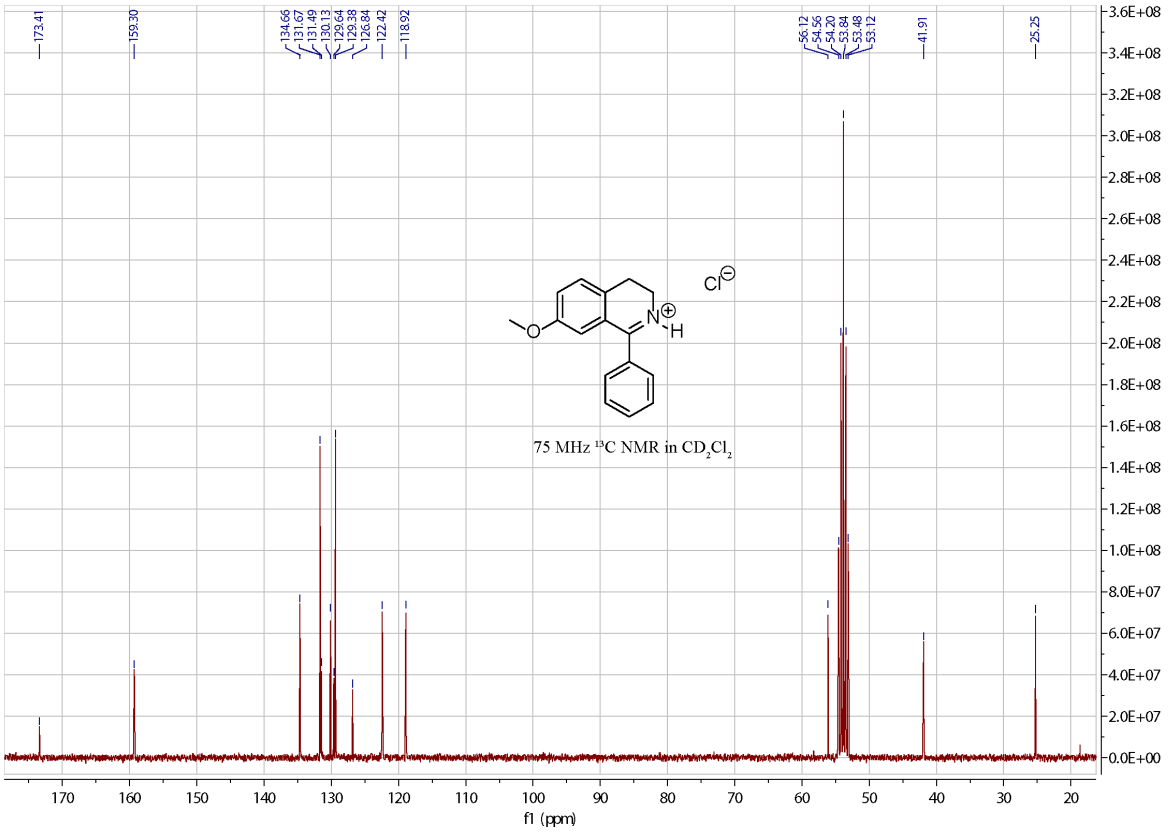
Penta-OMe-DHIQ*HCl **12k***HCl



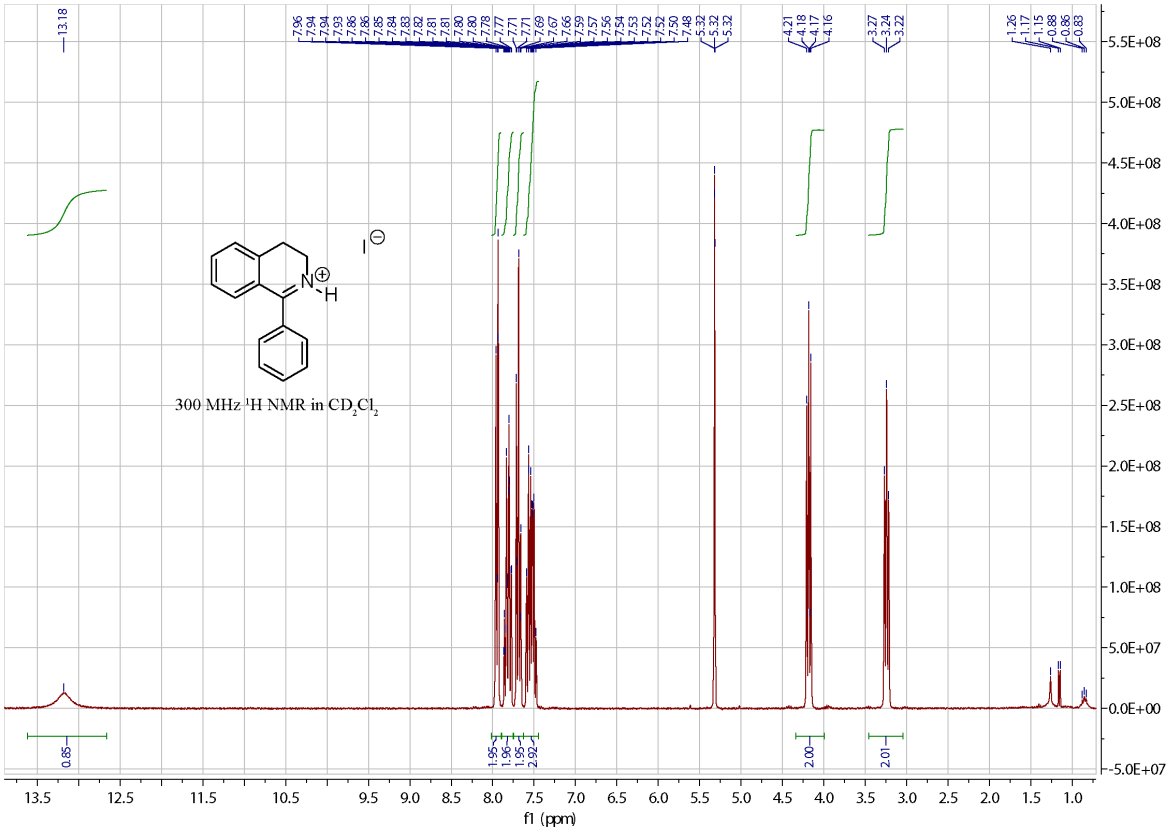


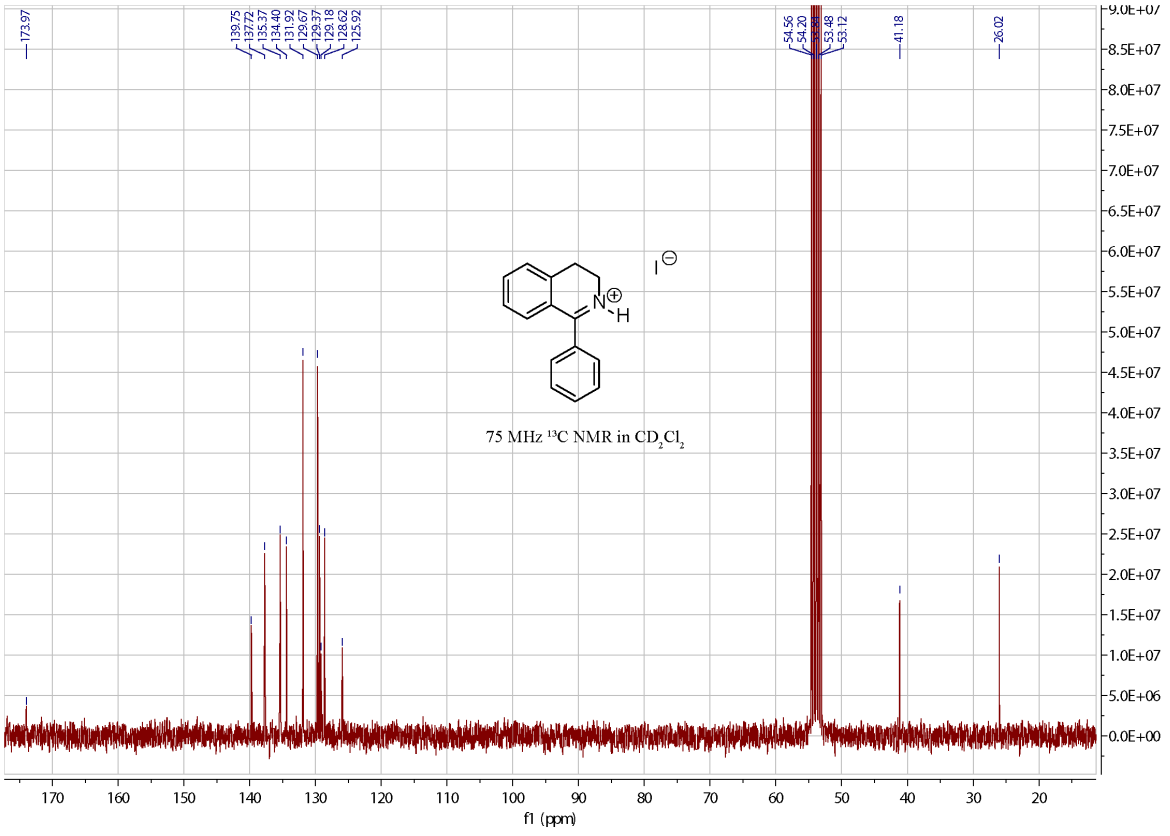
1-Ph-7-OMePh-DHIQ*HCl **12l***HCl



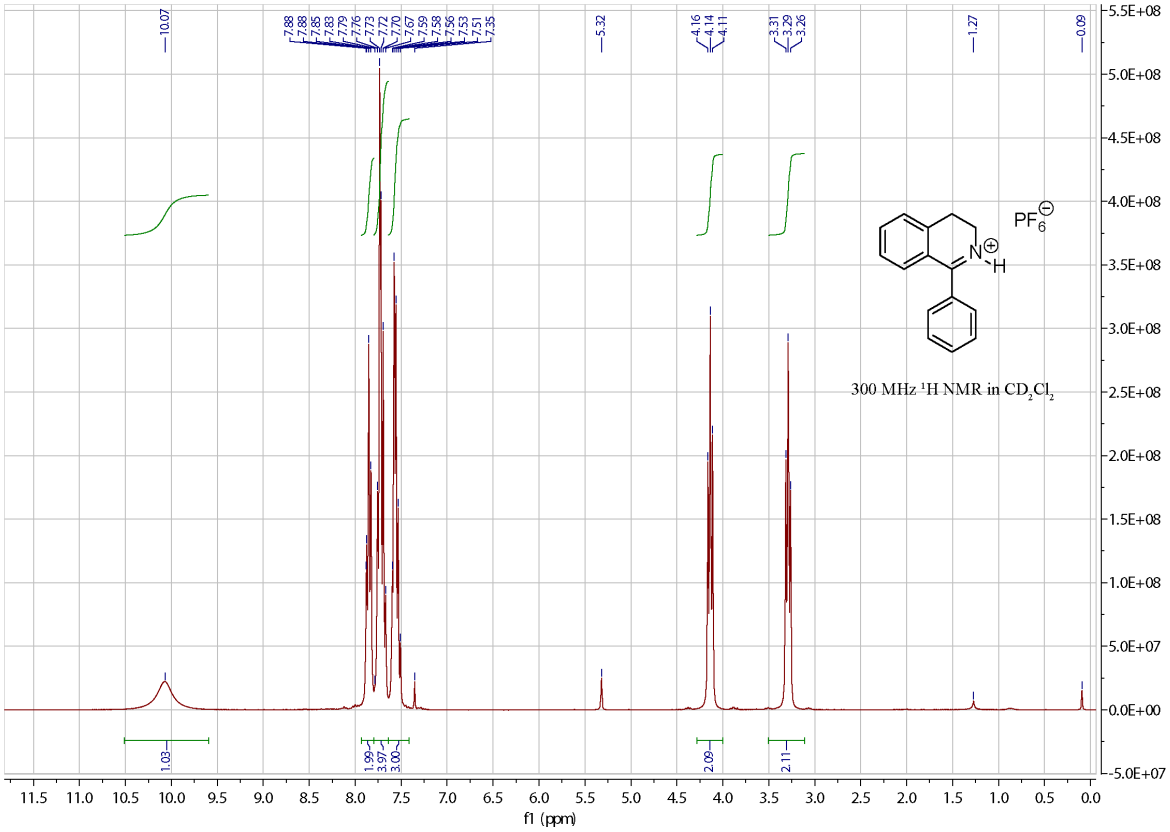


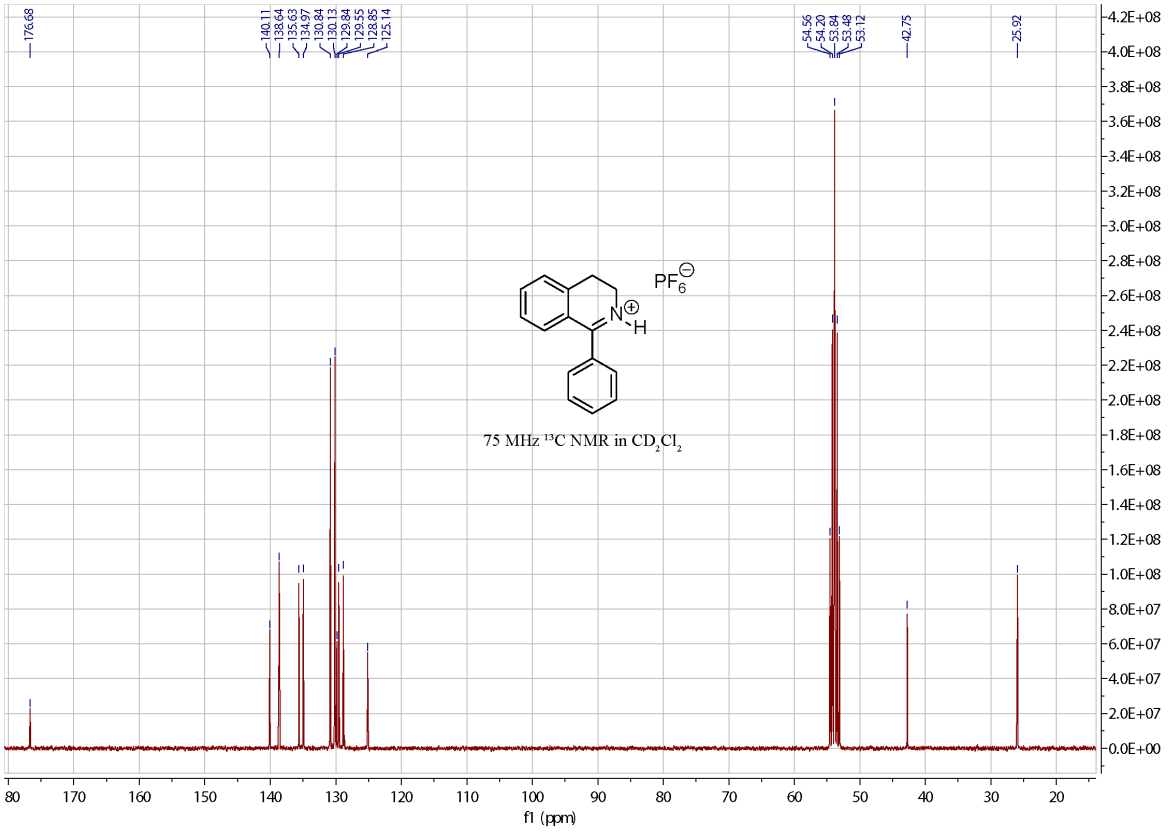
1-Ph-DHIQ*HI **12a***HI

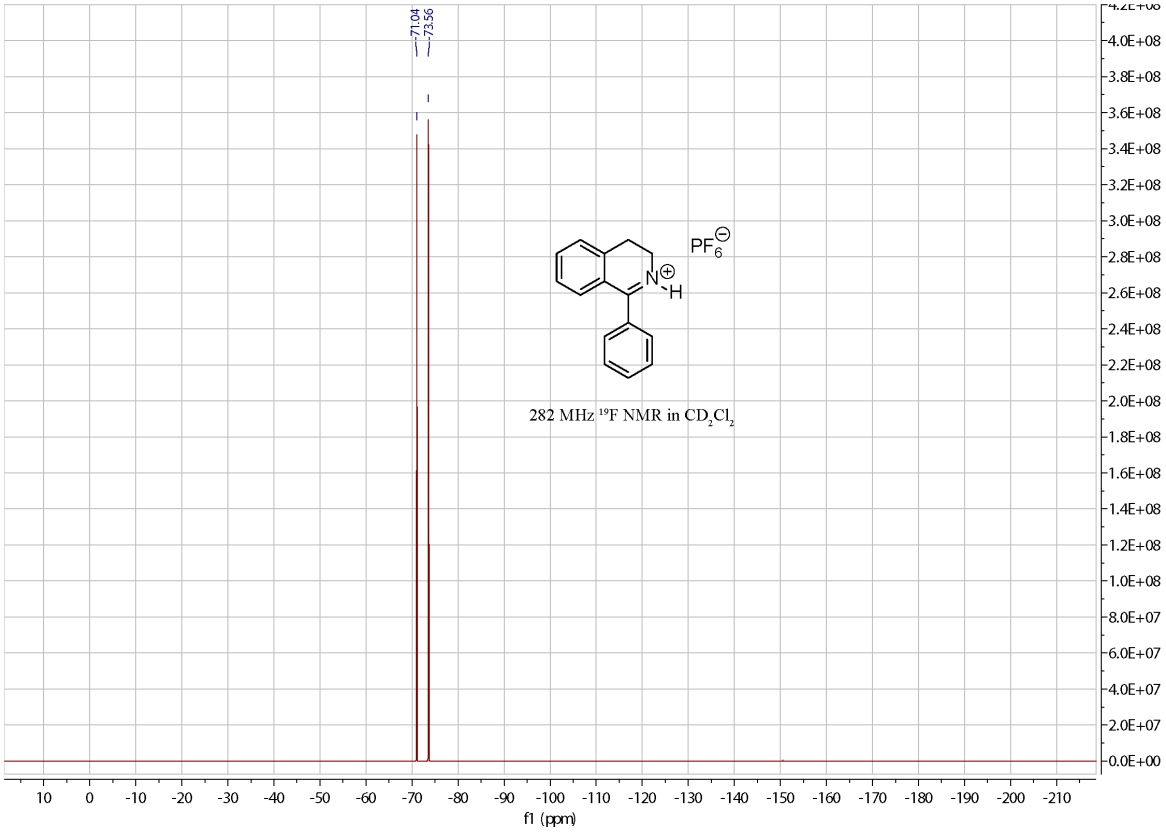


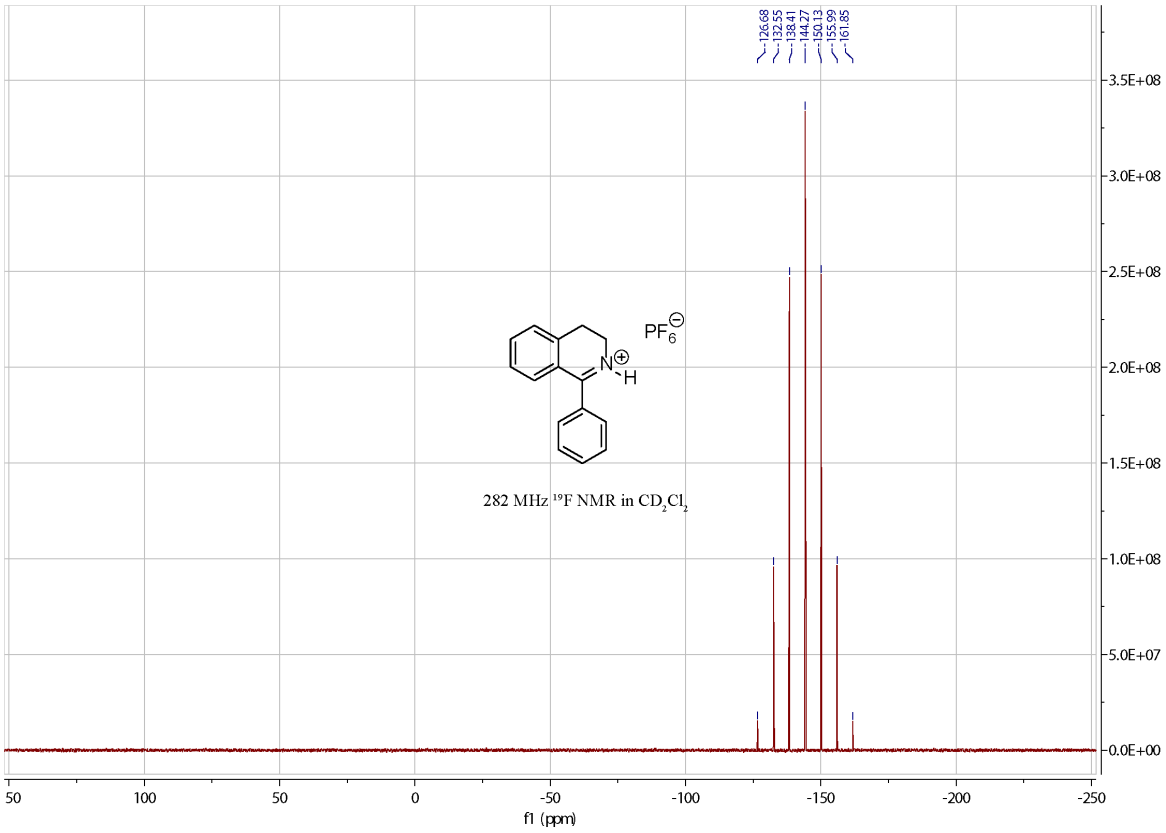


1-Ph-DHIQ*HPF_6 **12a***HPF_6

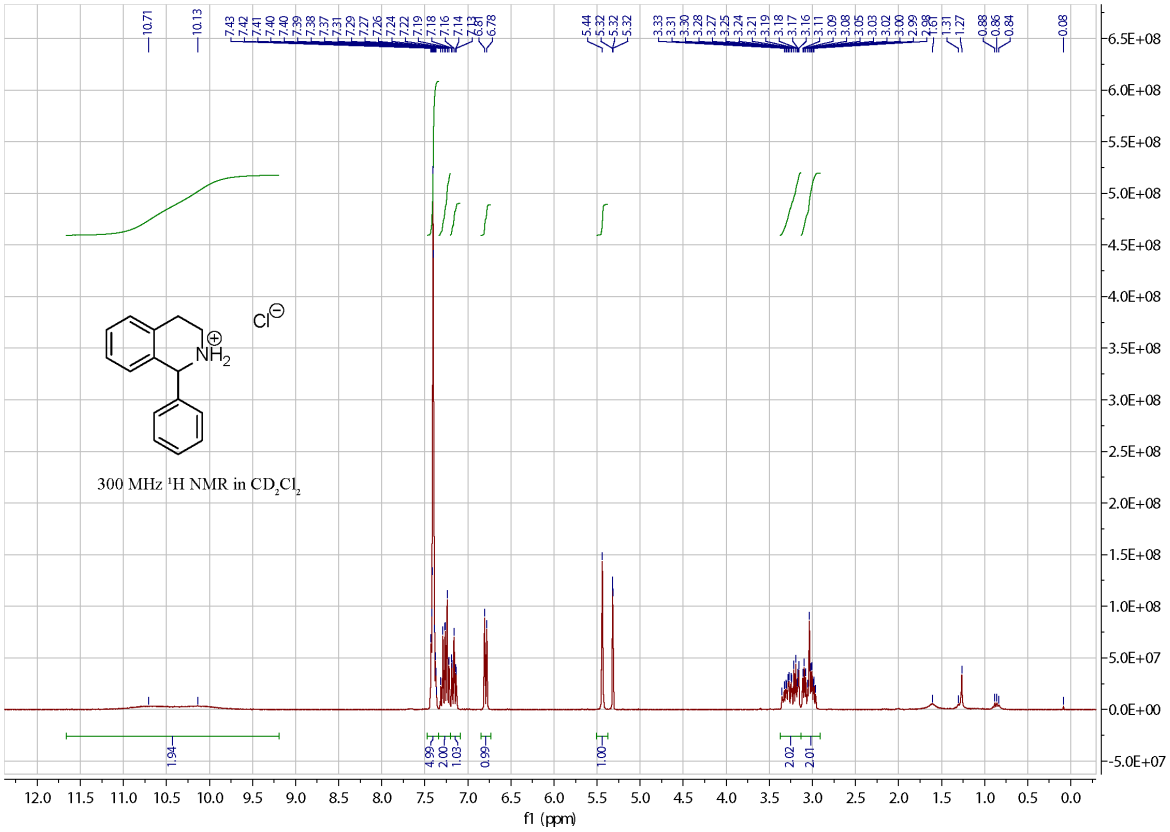


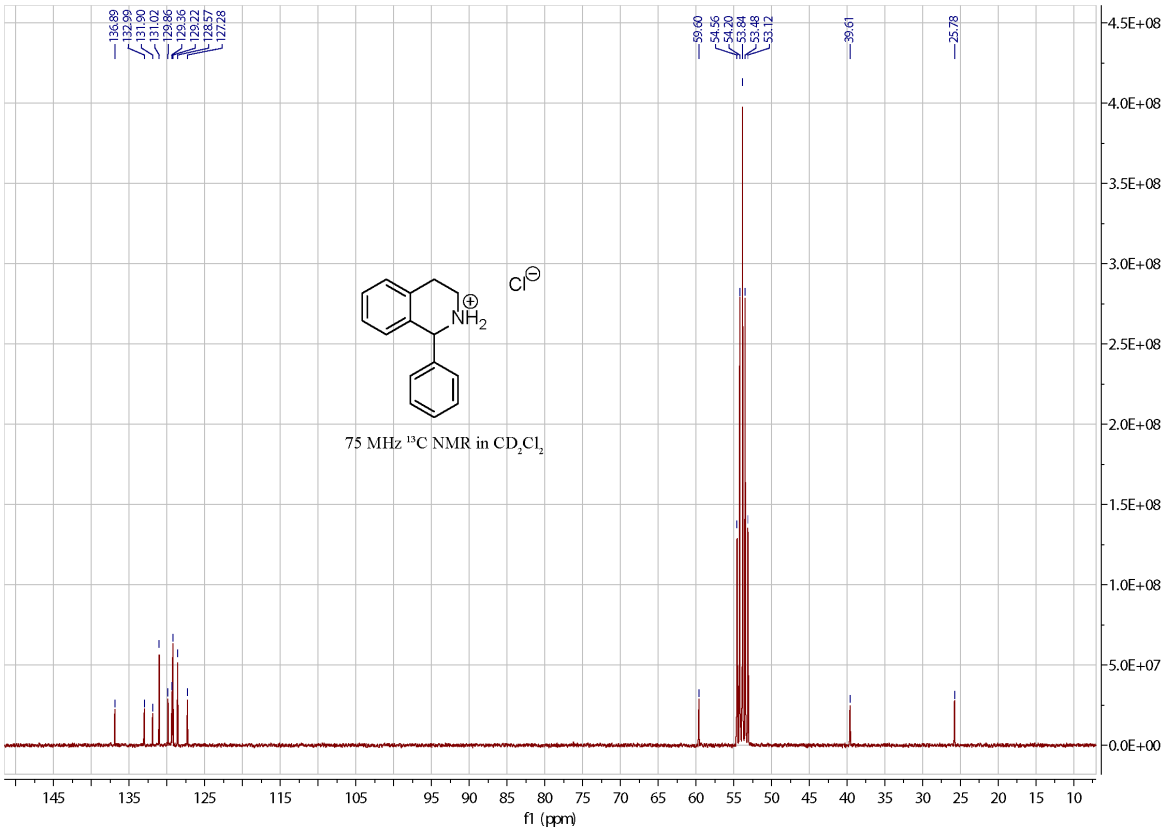



71.04
73.56
PF6
N
H
282 MHz 19F NMR in CD2Cl2
f1 (ppm)

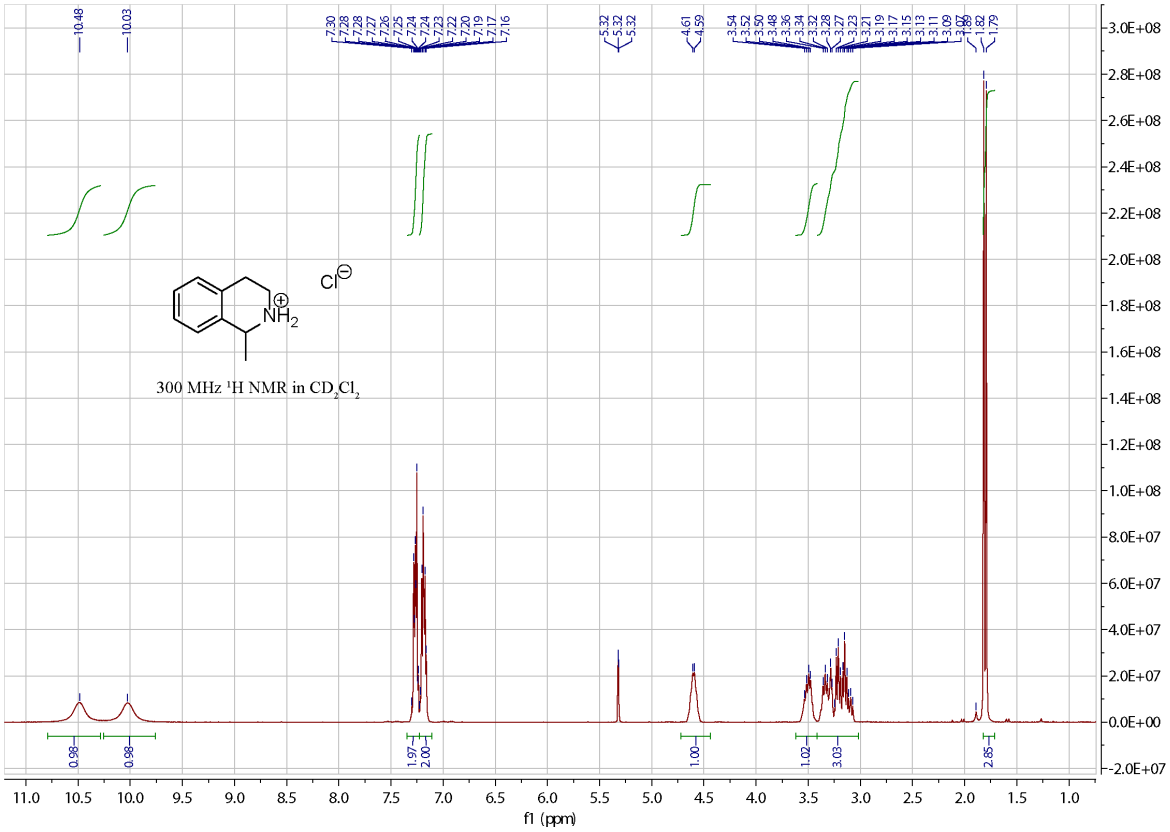

126.68
132.55
138.41
144.27
151.03
155.98
161.85
PF6
N
H
282 MHz 19F NMR in CD2Cl2
f1 (ppm)

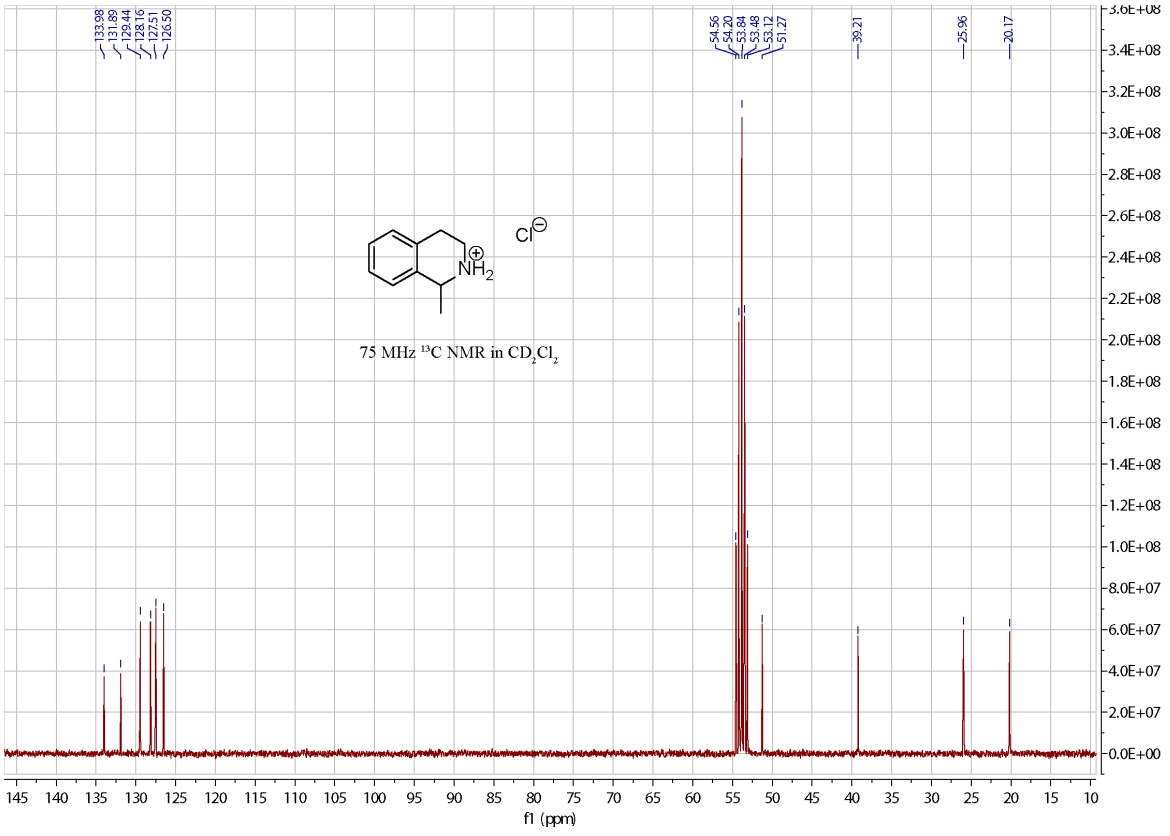
1-Ph-THIQ*HCl **13a***HCl



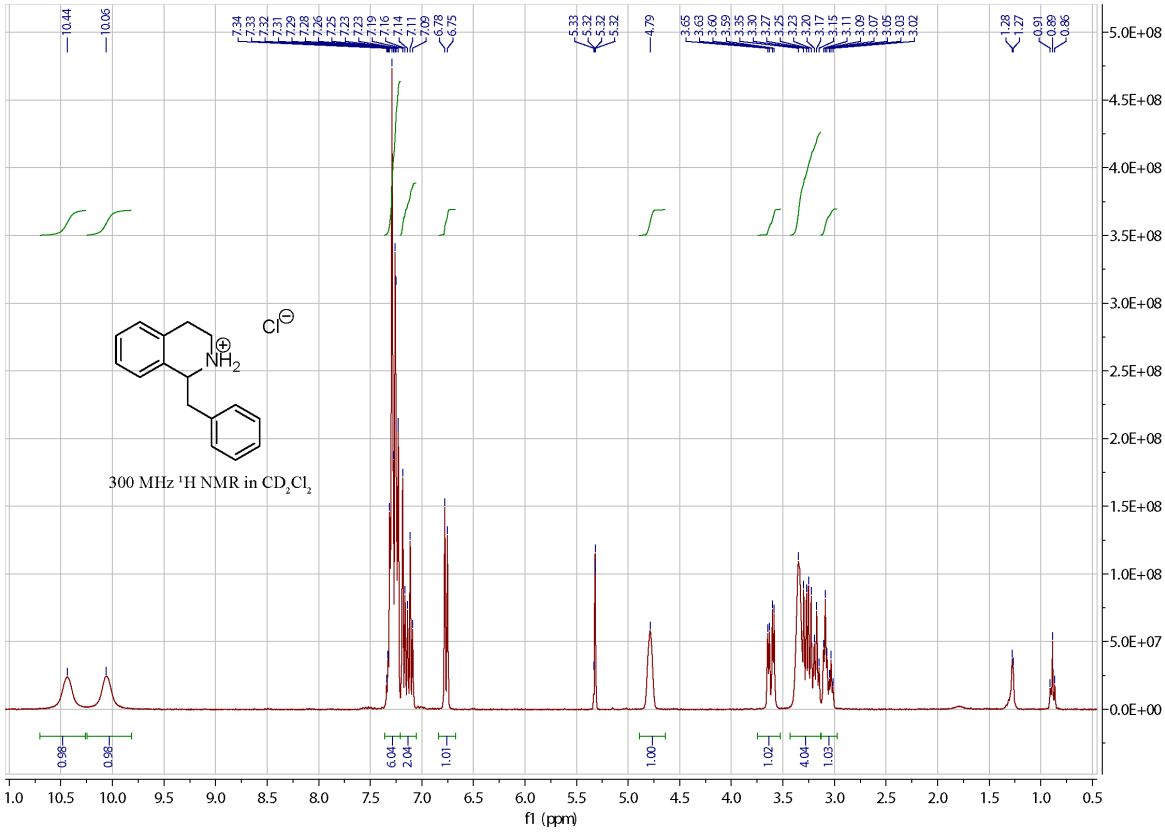


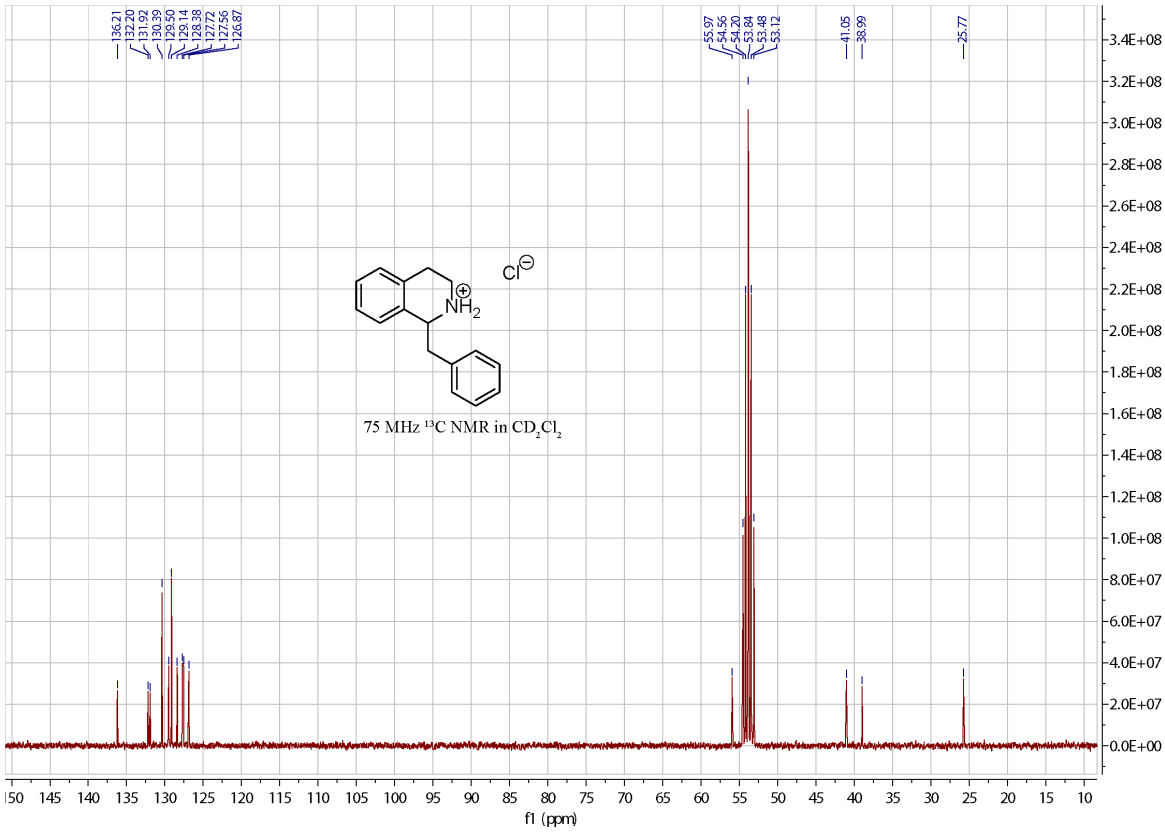
1-Me-THIQ*HCl **13b***HCl



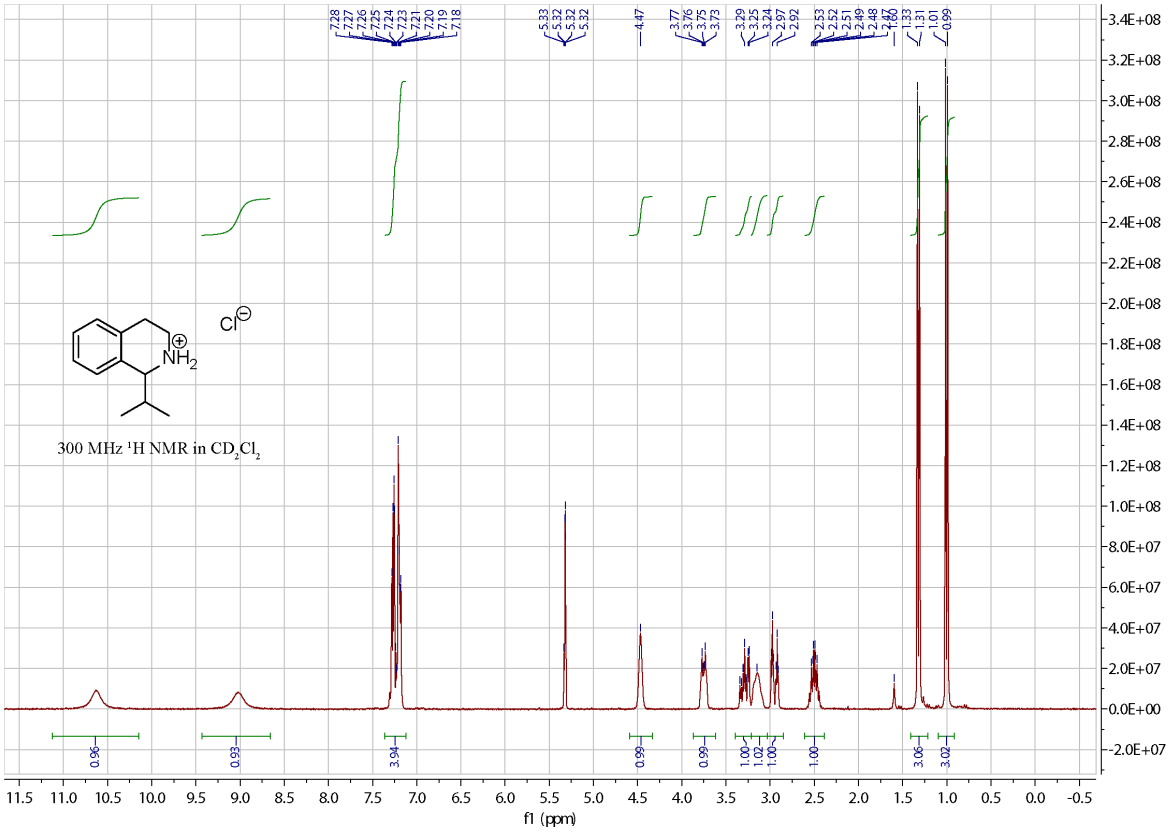


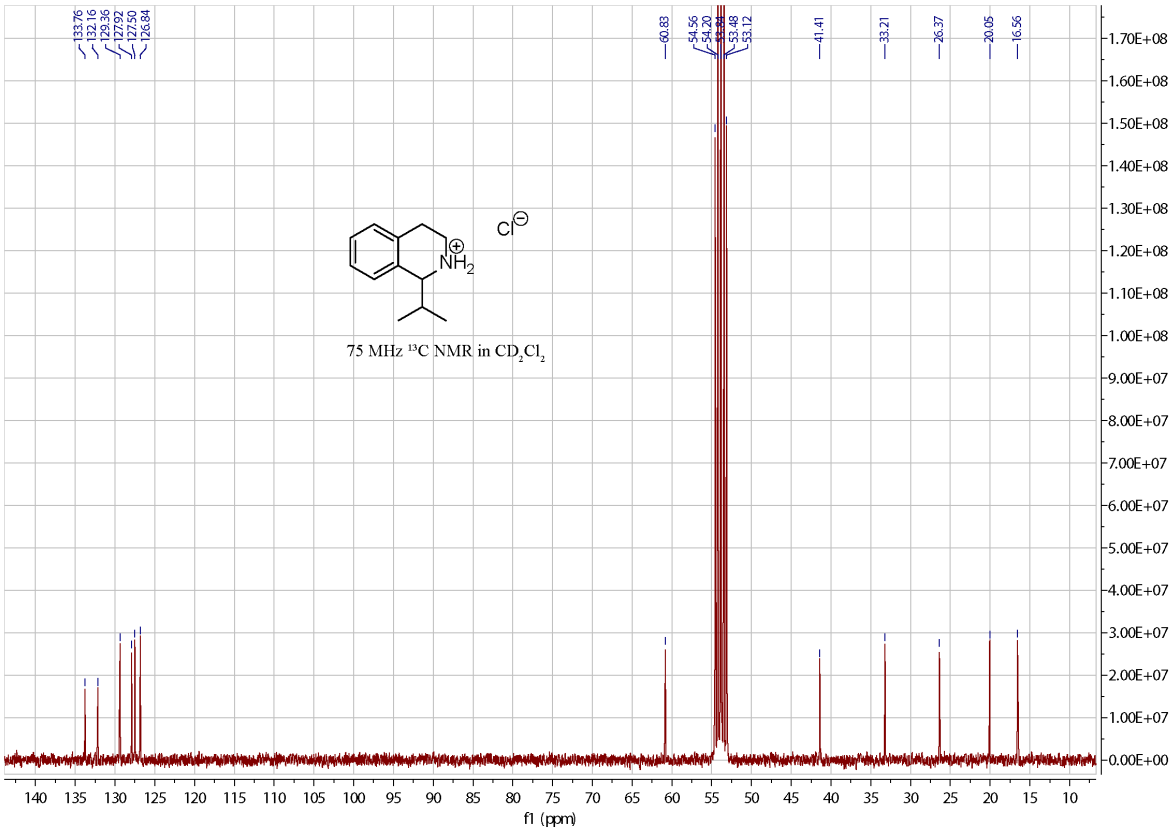
1-Bn-THIQ*HCl **13c***HCl



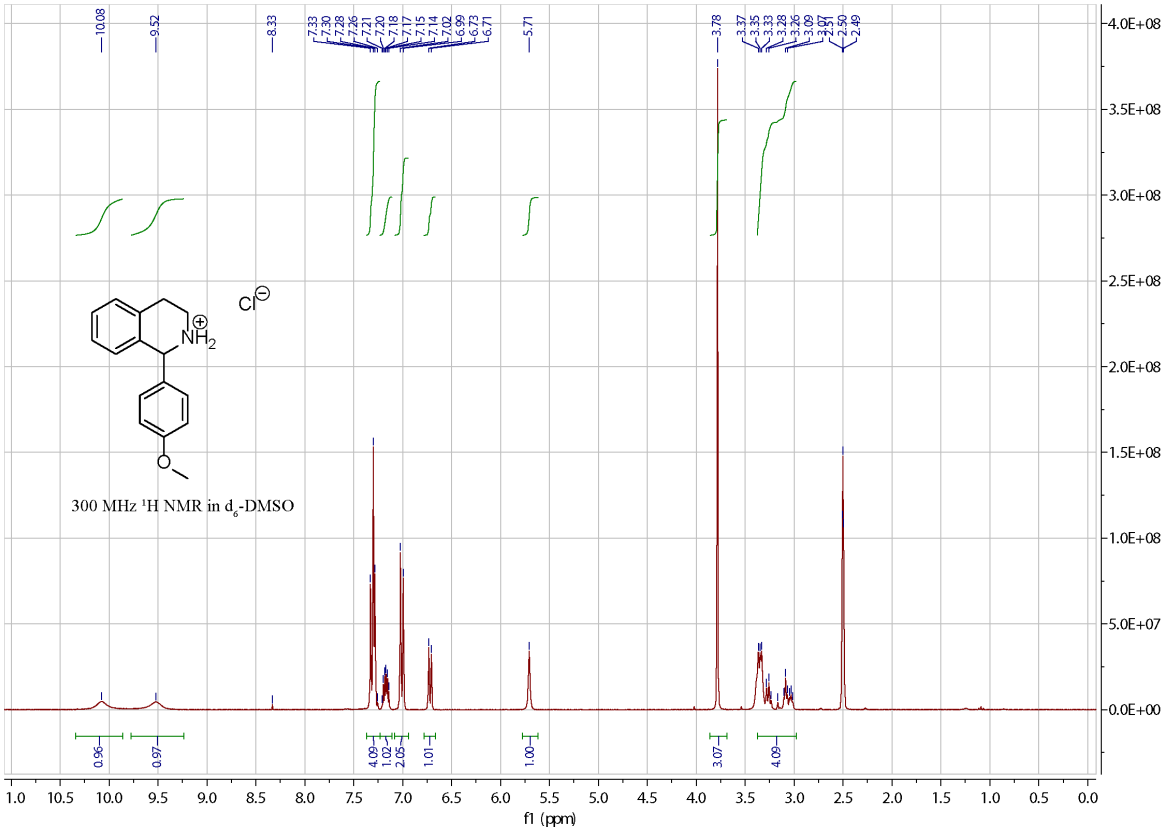


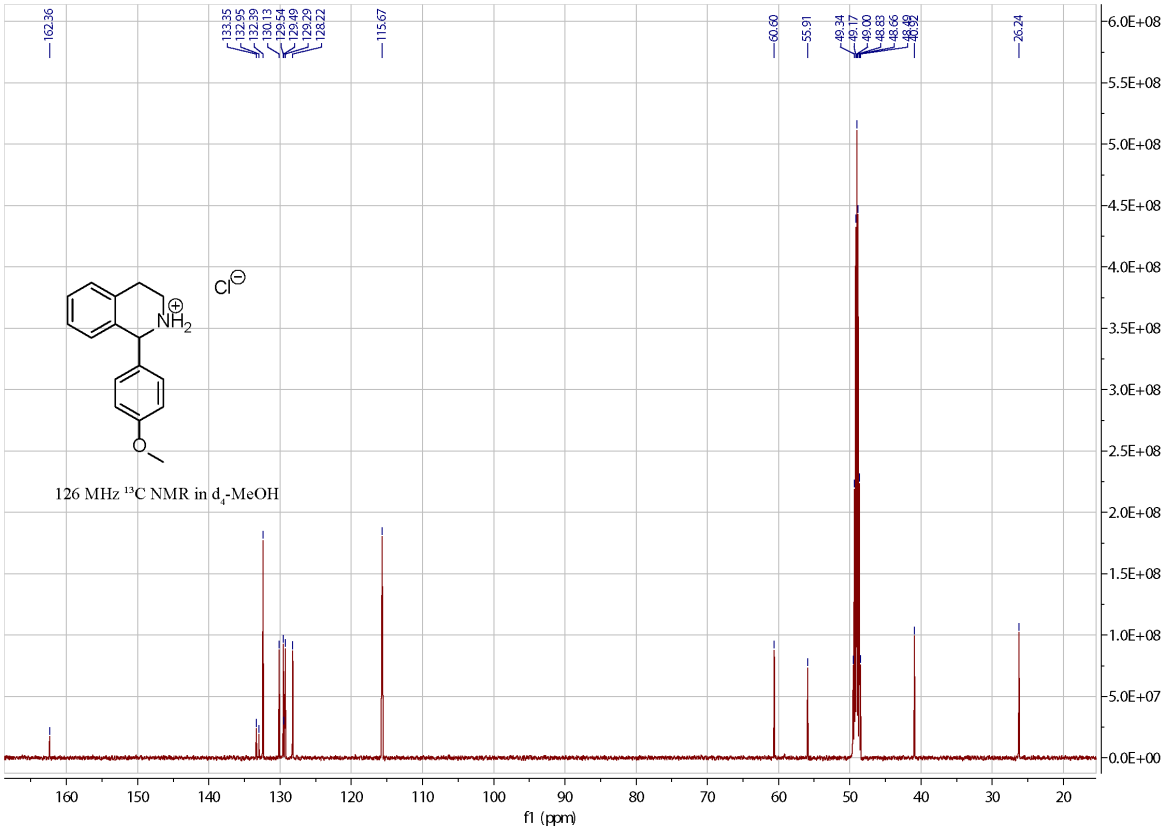
1-*i*Pr-THIQ*HCl **13d***HCl



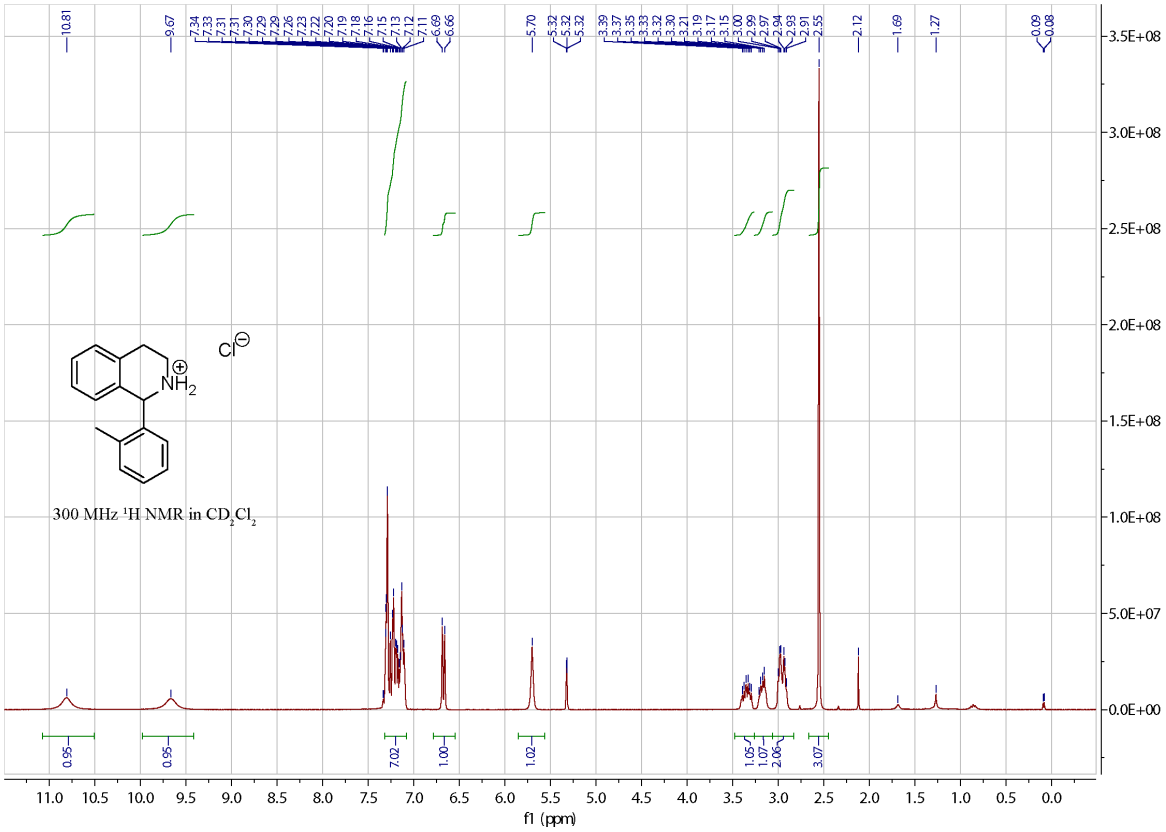


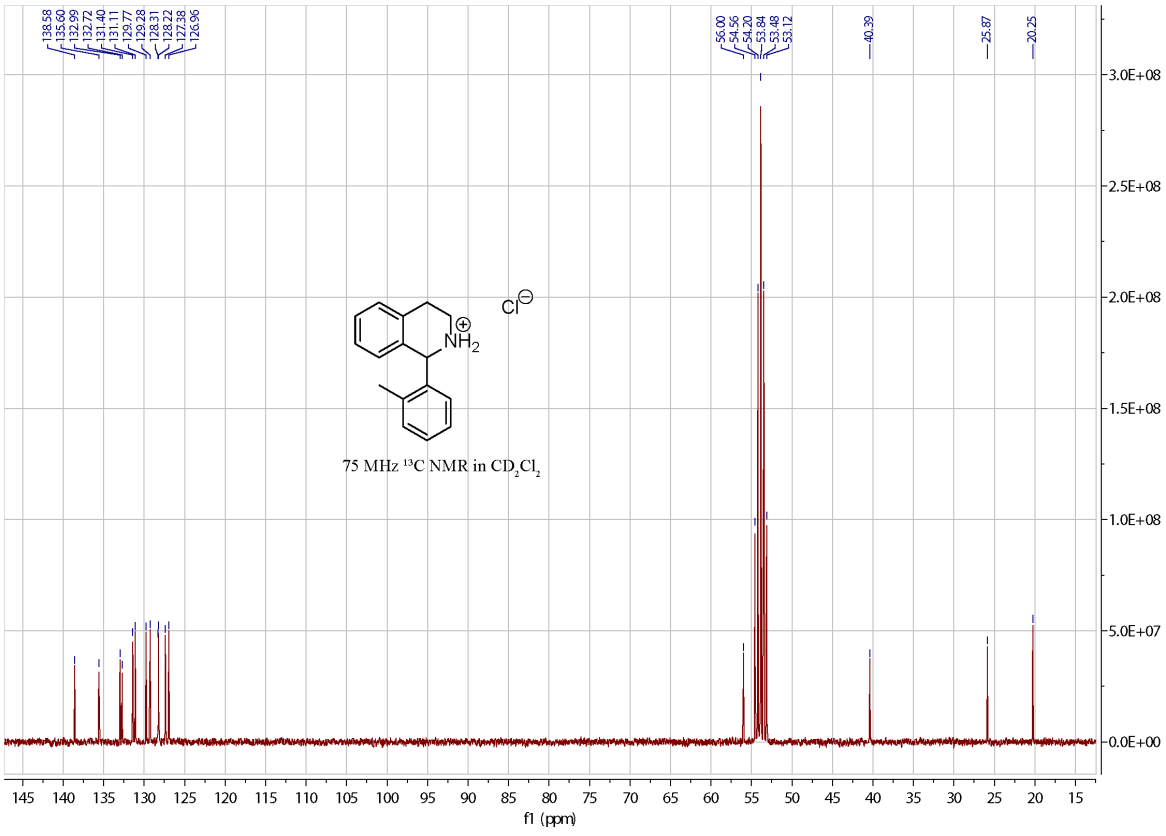
1-*p*OMePh-THIQ*HCl **13e***HCl



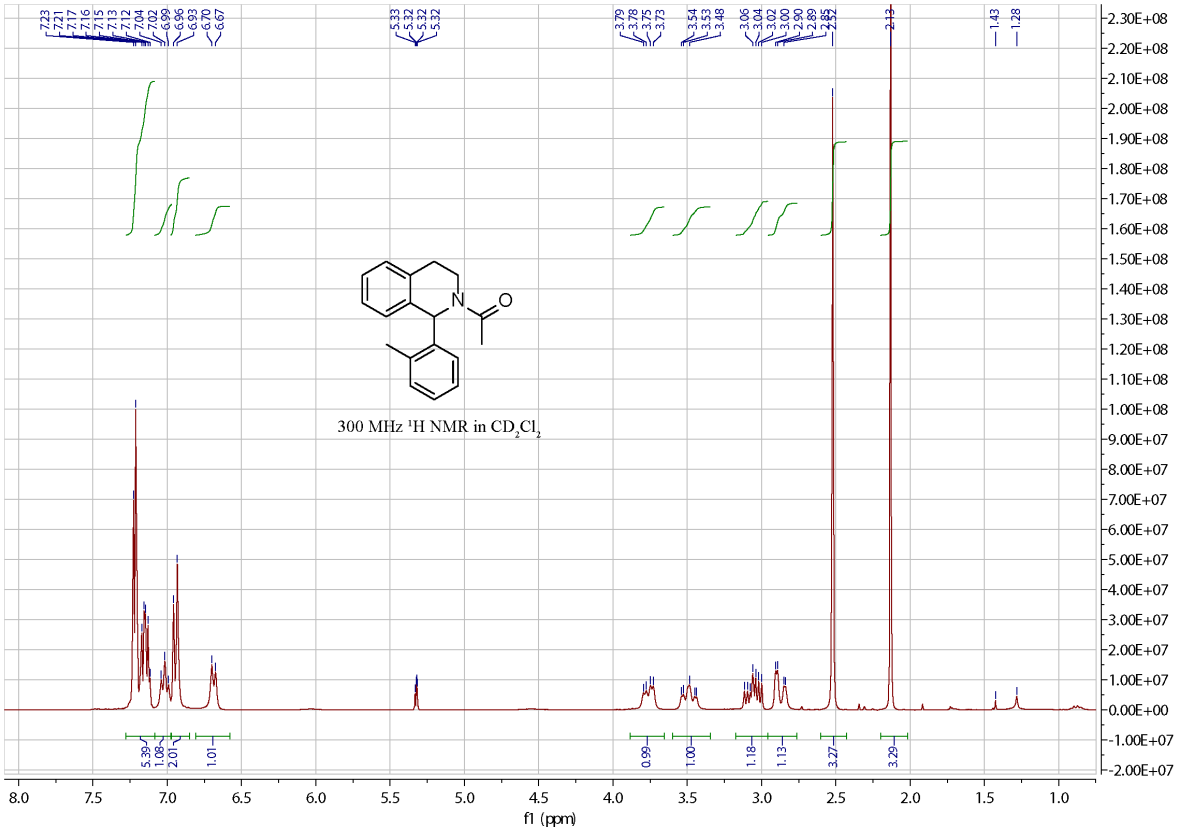


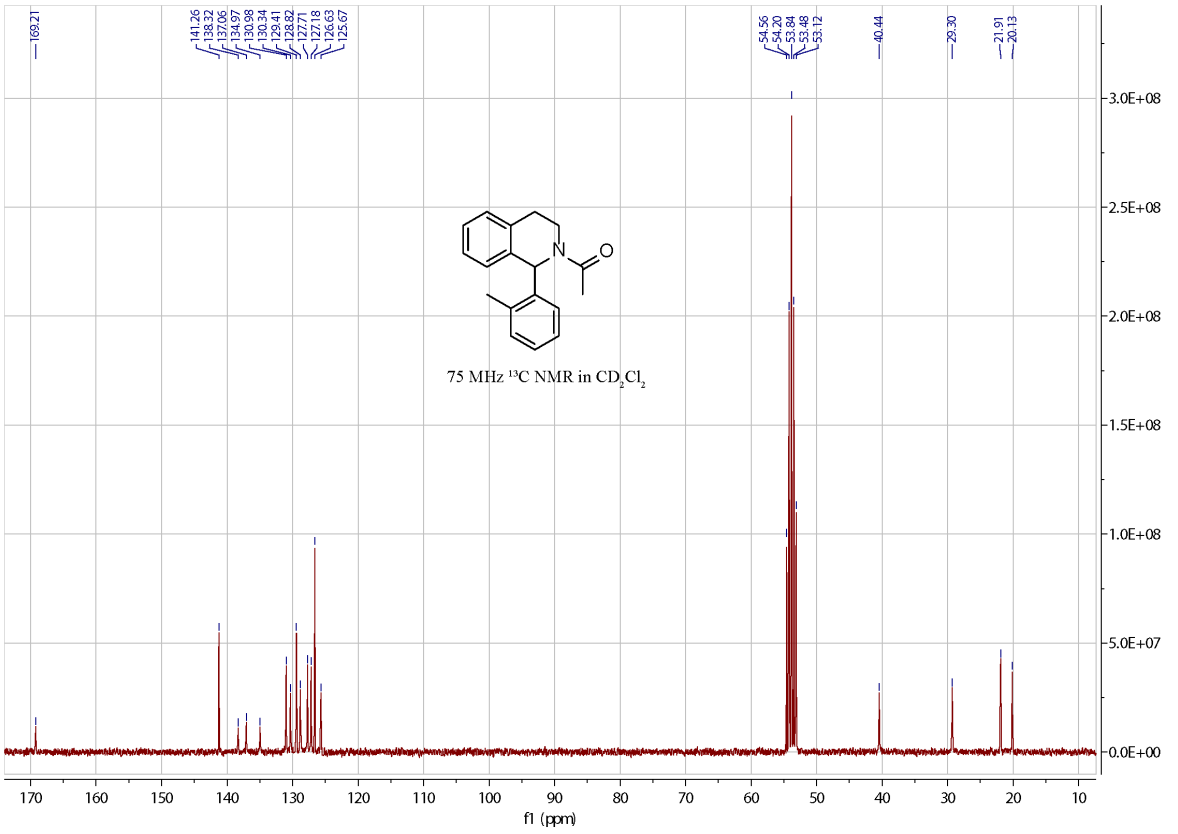
1-*o*Tol-THIQ*HCl **13f***HCl



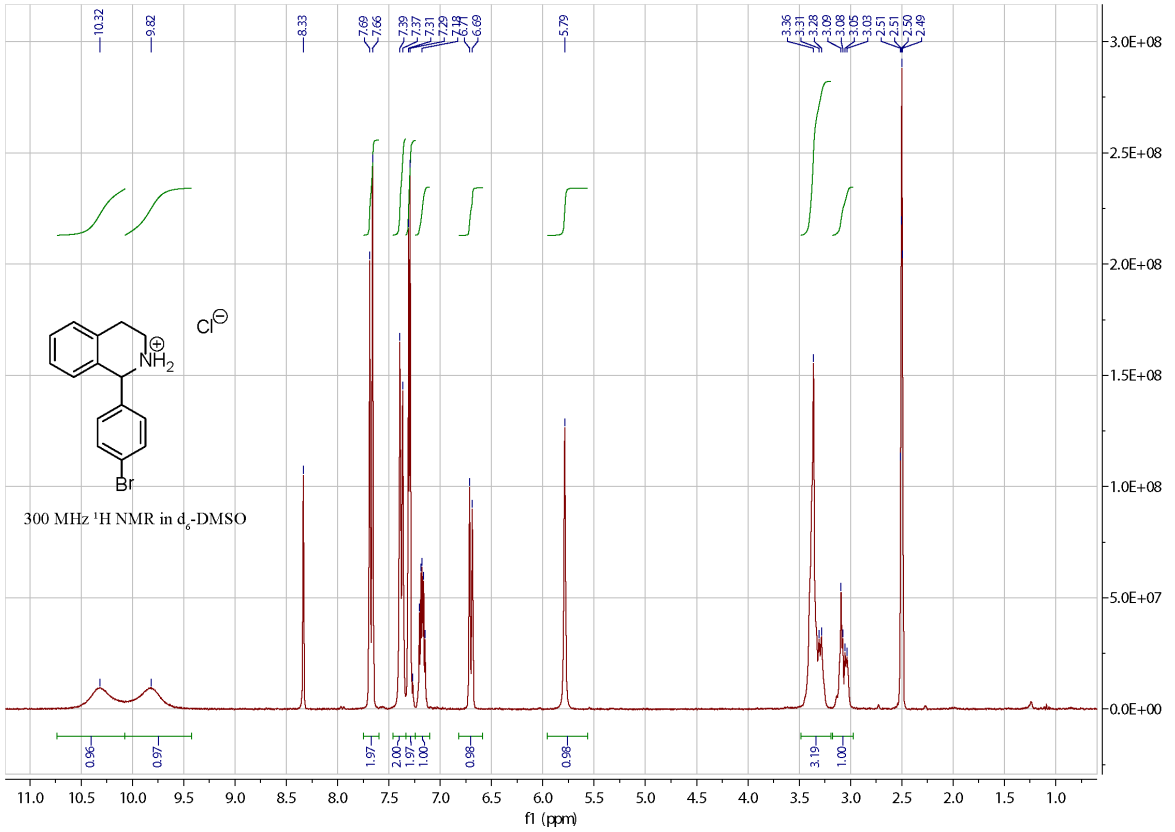


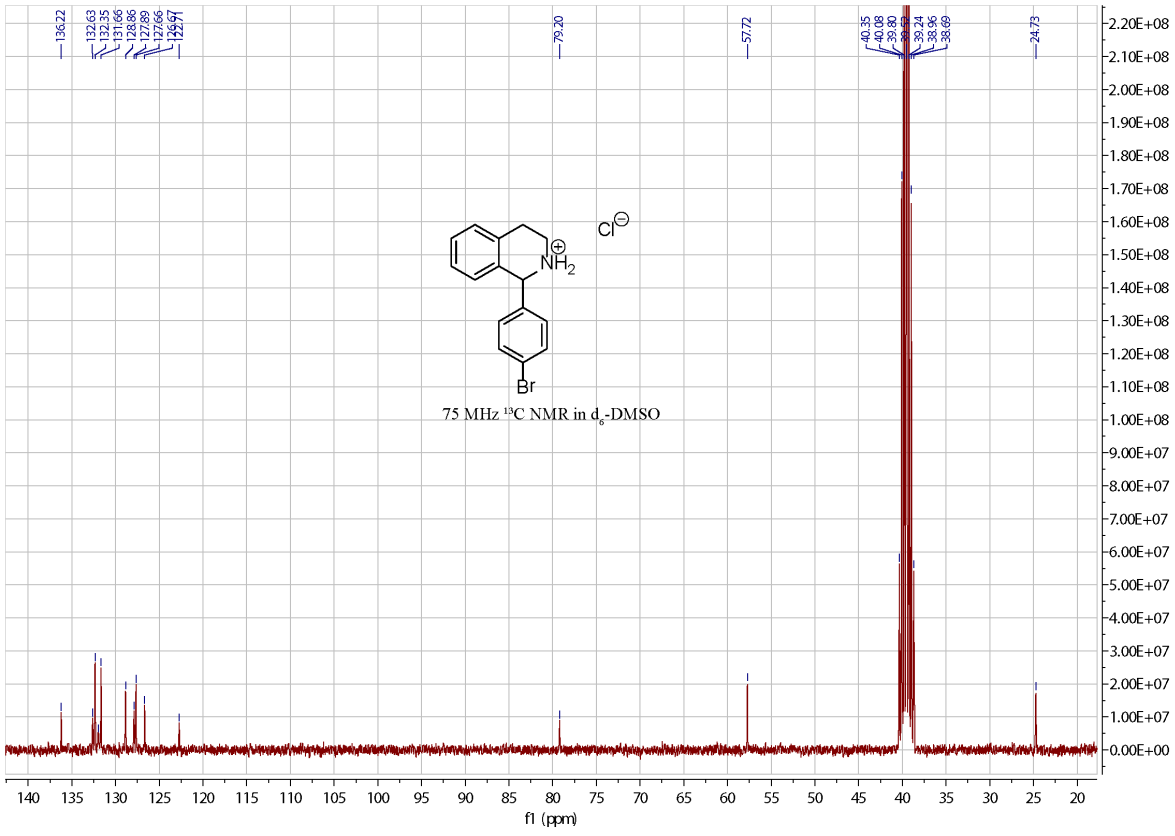
1-*o*Tol-THIQ acetamide **13f** acetamide



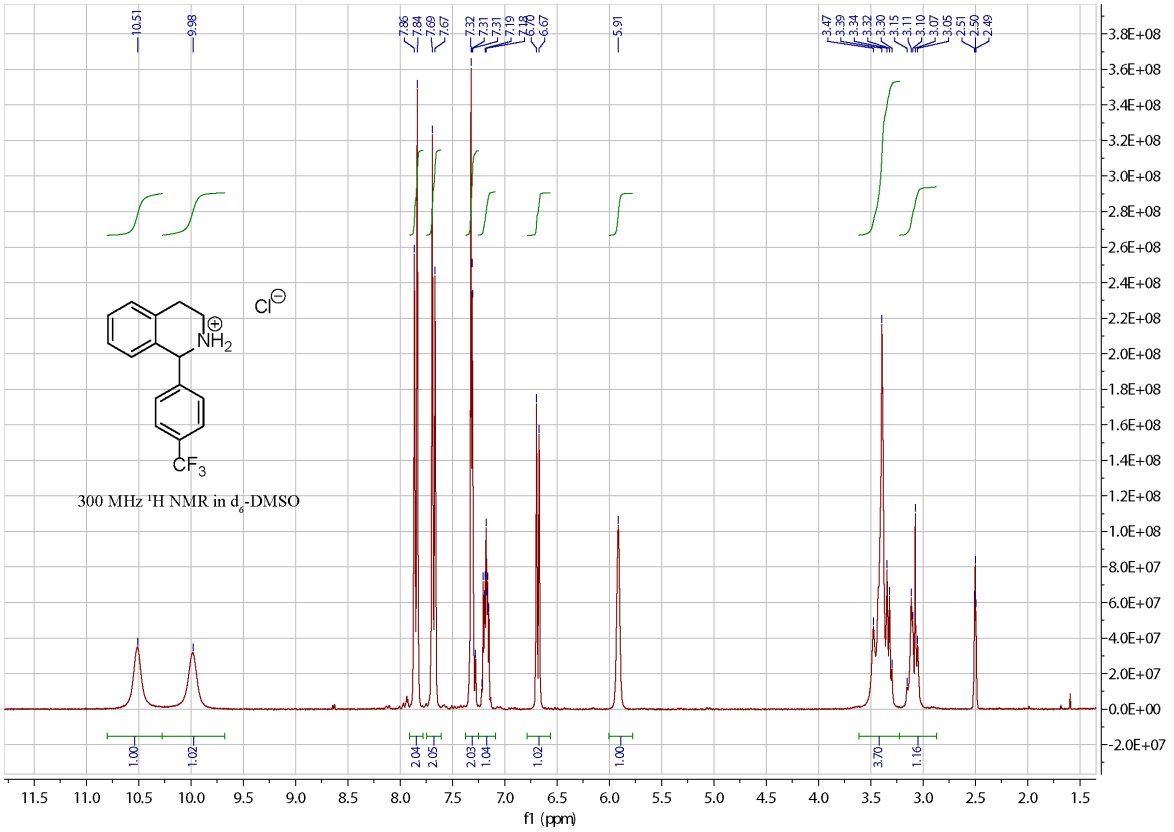


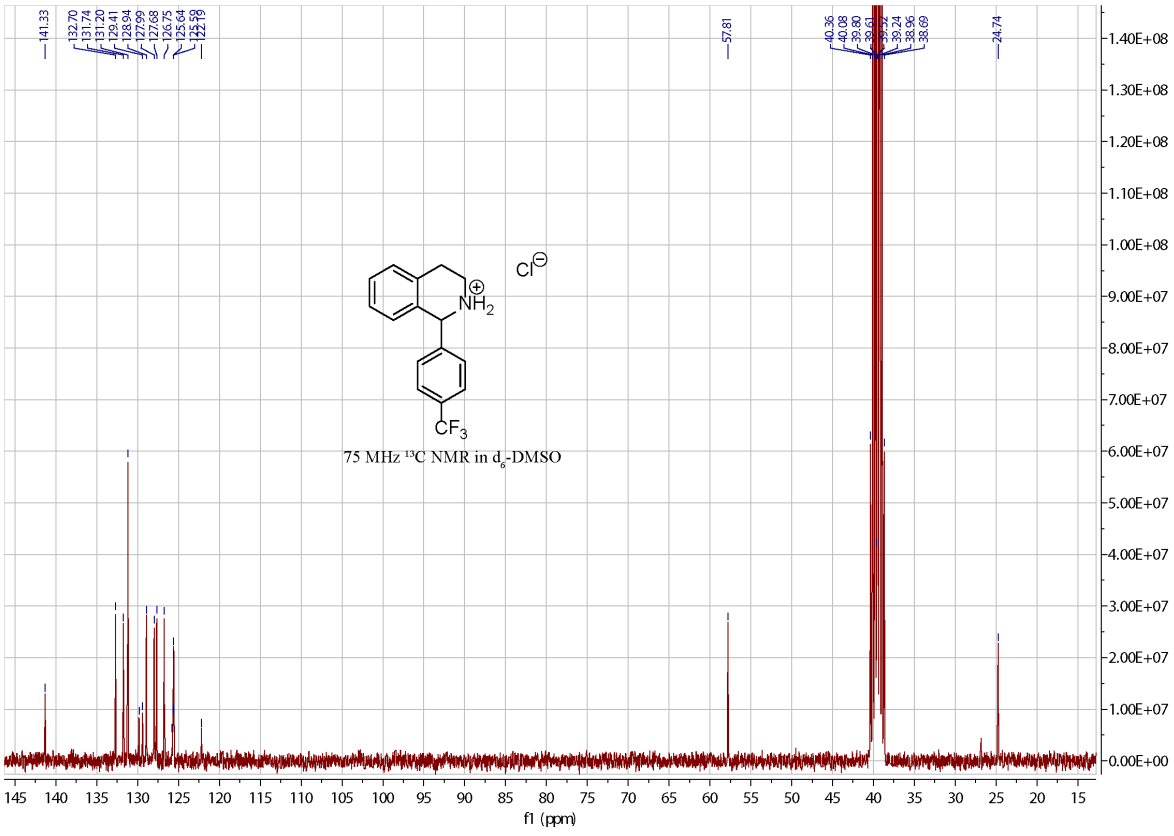
1-*p*BrPh-THIQ*HCl **13g***HCl

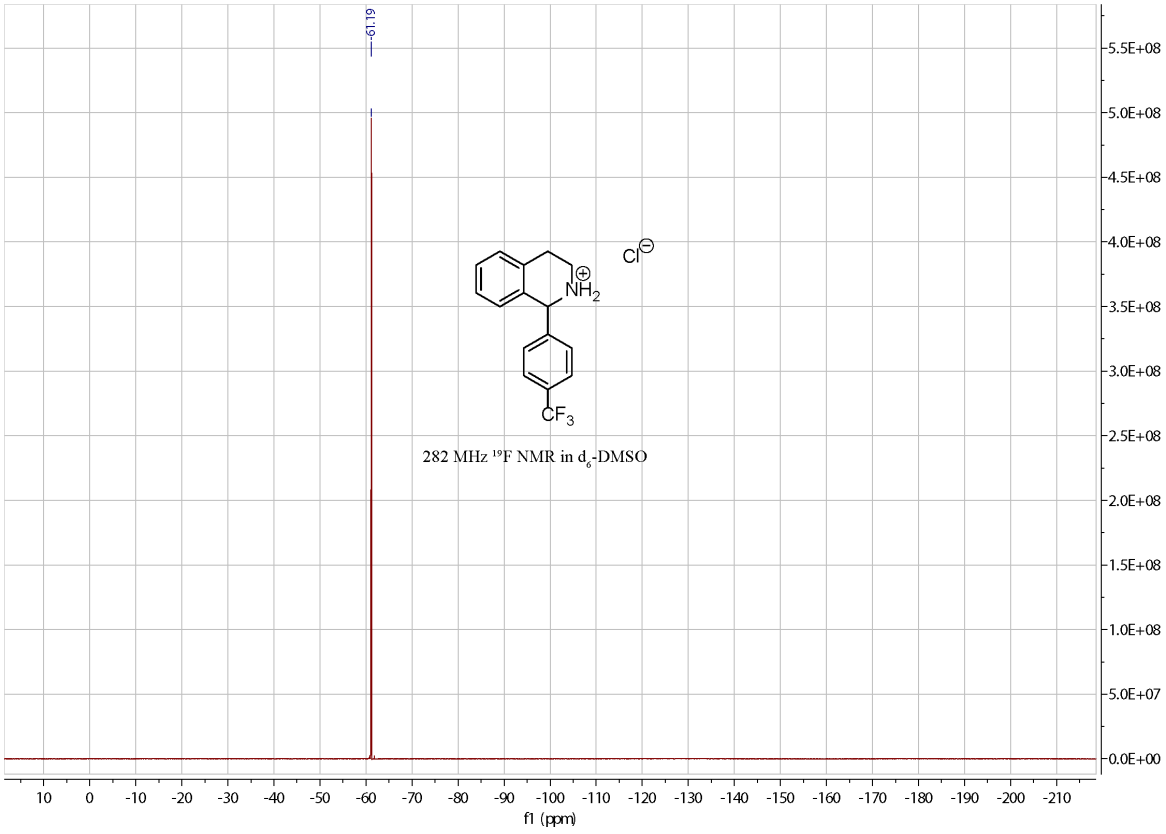




1-*p*CF_3Ph-THIQ*HCl **13h***HCl

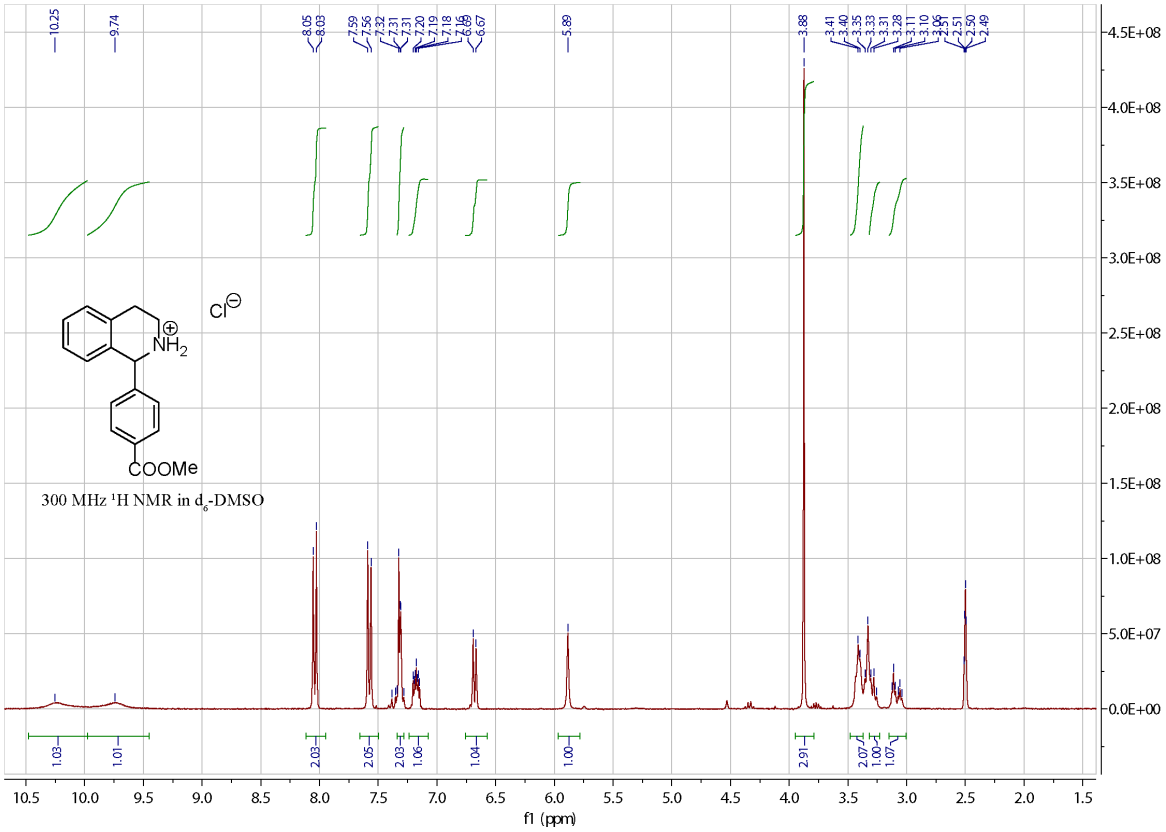


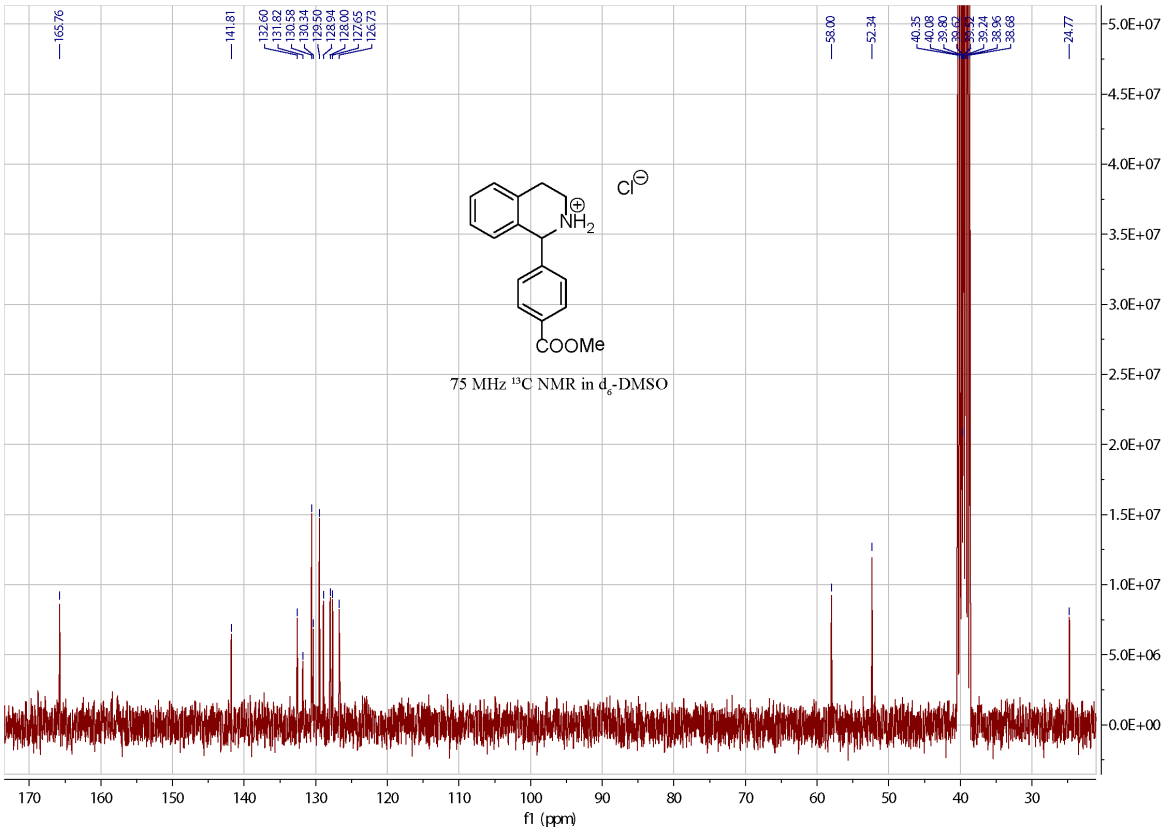




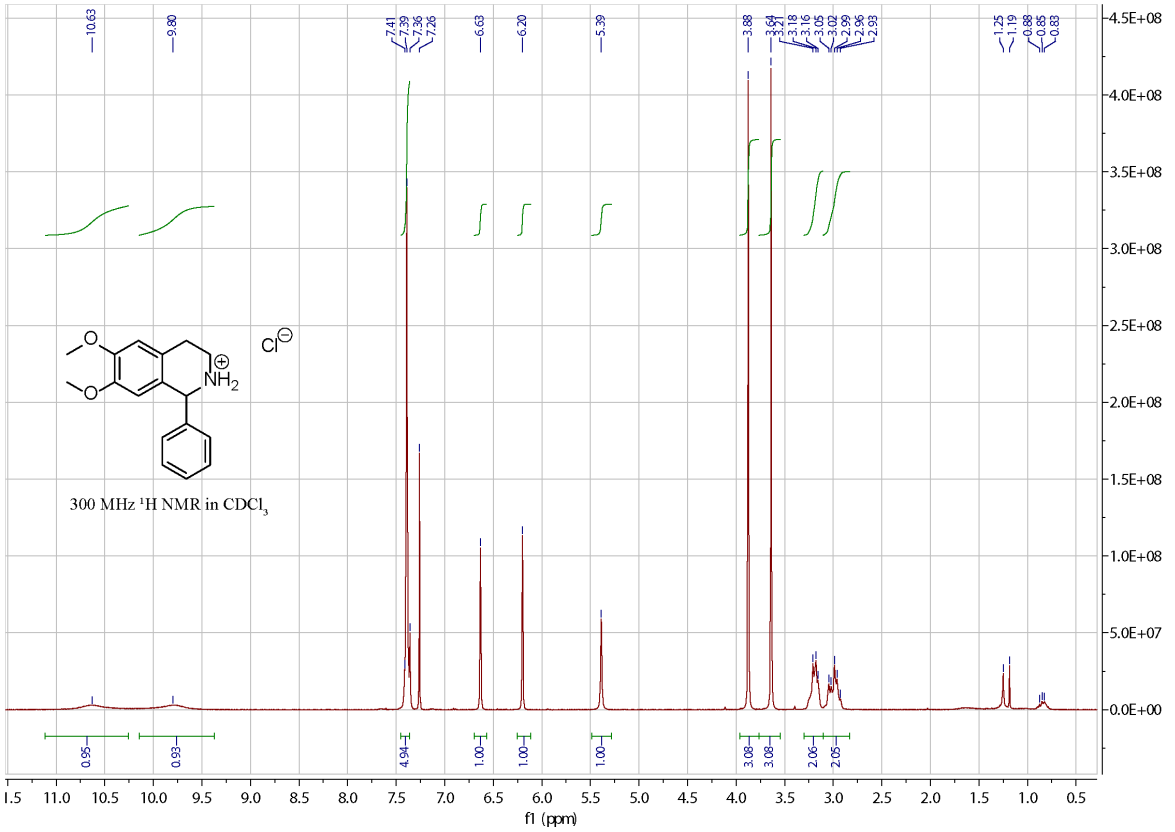
282 MHz ^{19}F NMR in d_6-DMSO

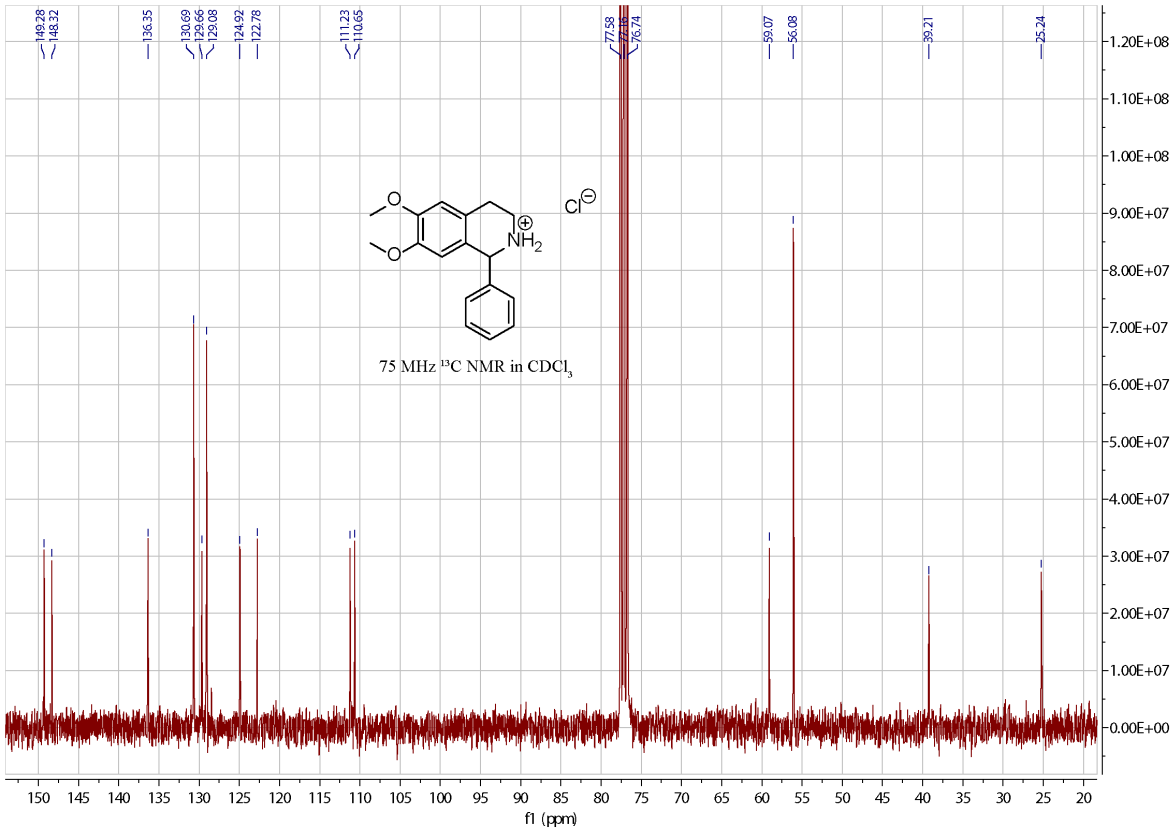
1-*p*COOMePh-THIQ*HCl **13i***HCl



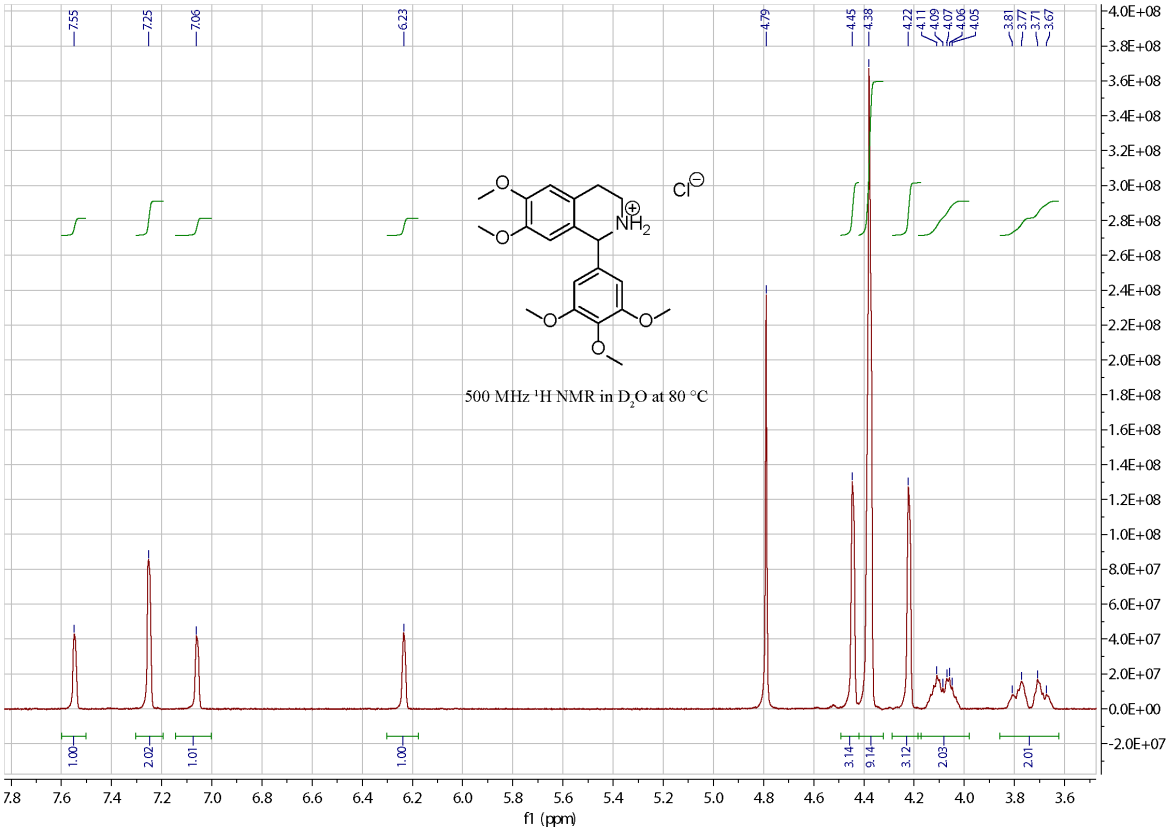


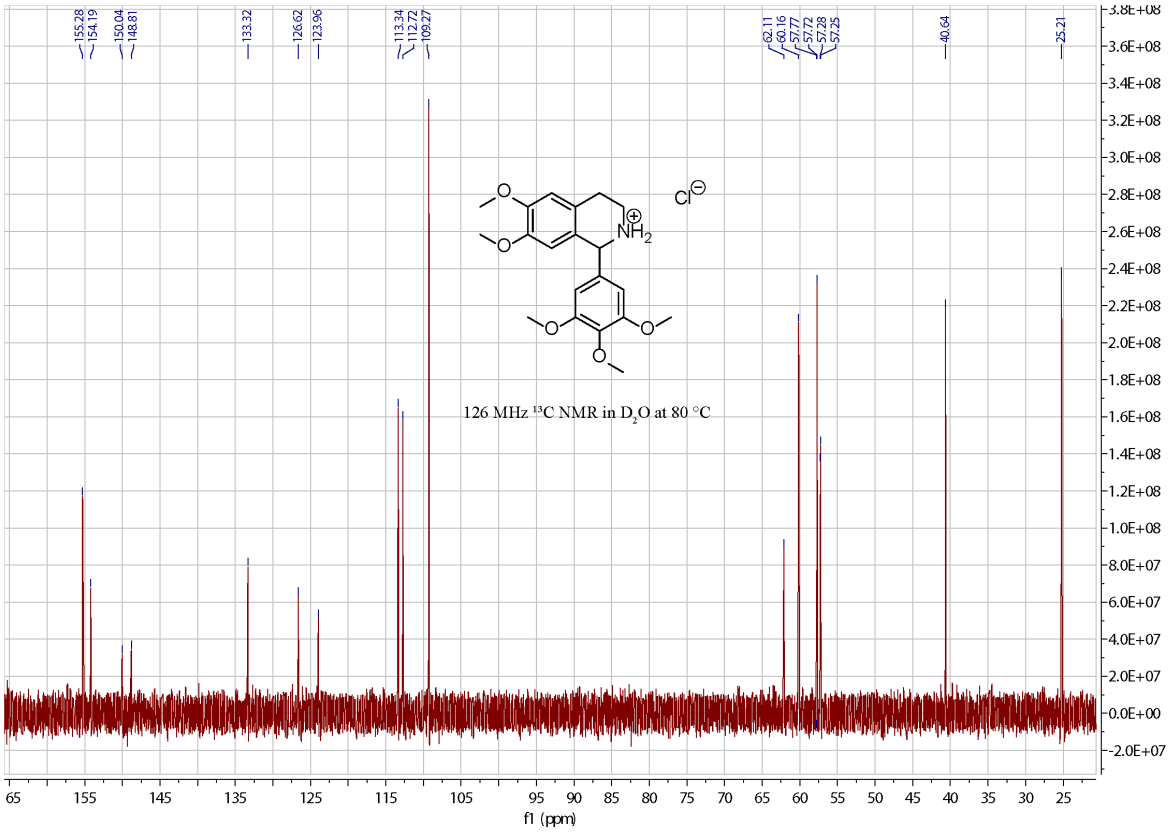
1-Ph-6,7-OMe-THIQ*HCl **13j***HCl



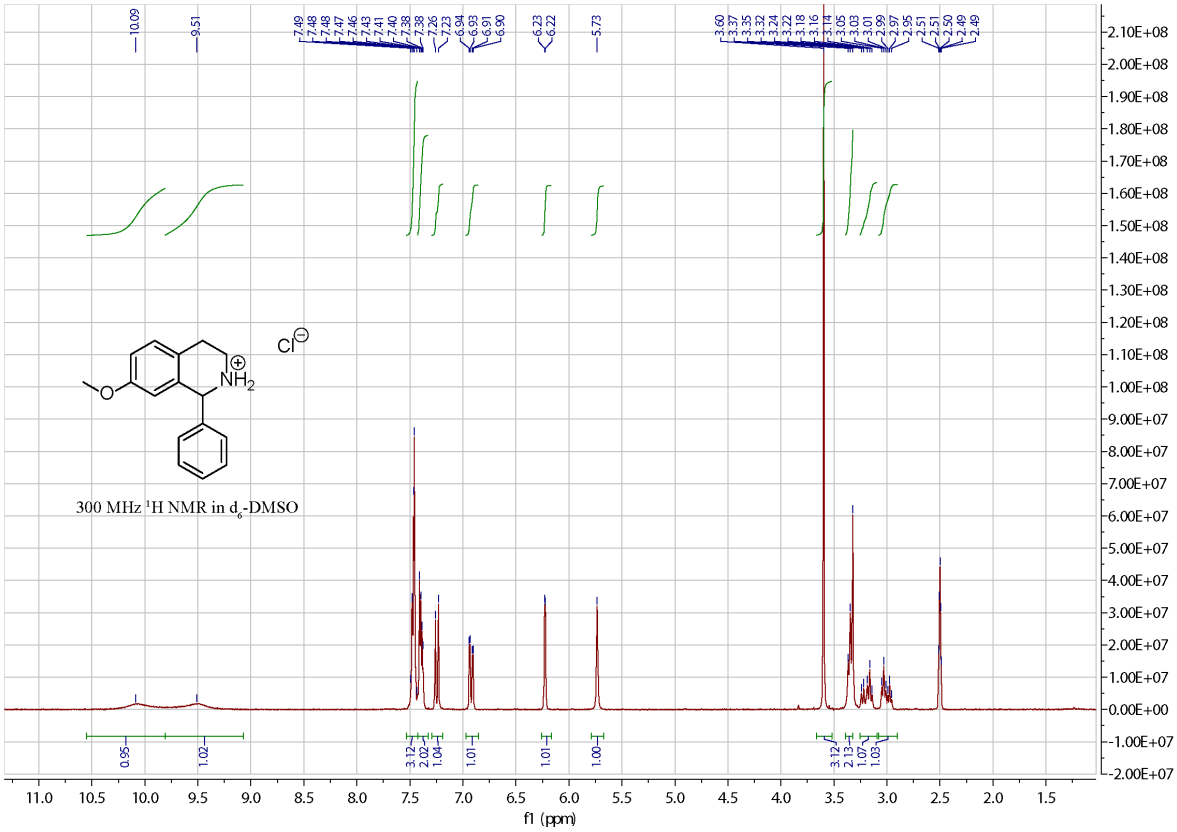


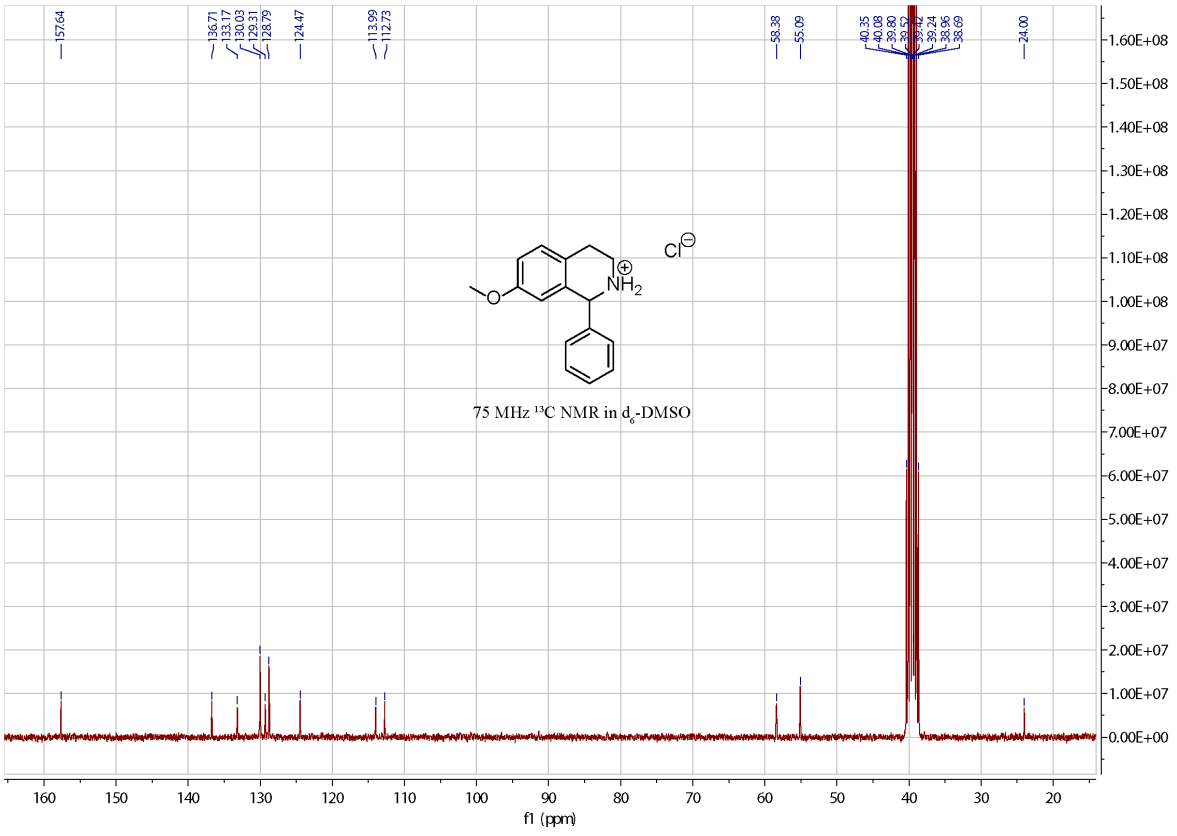
Penta-OMe-THIQ*HCl **13k***HCl





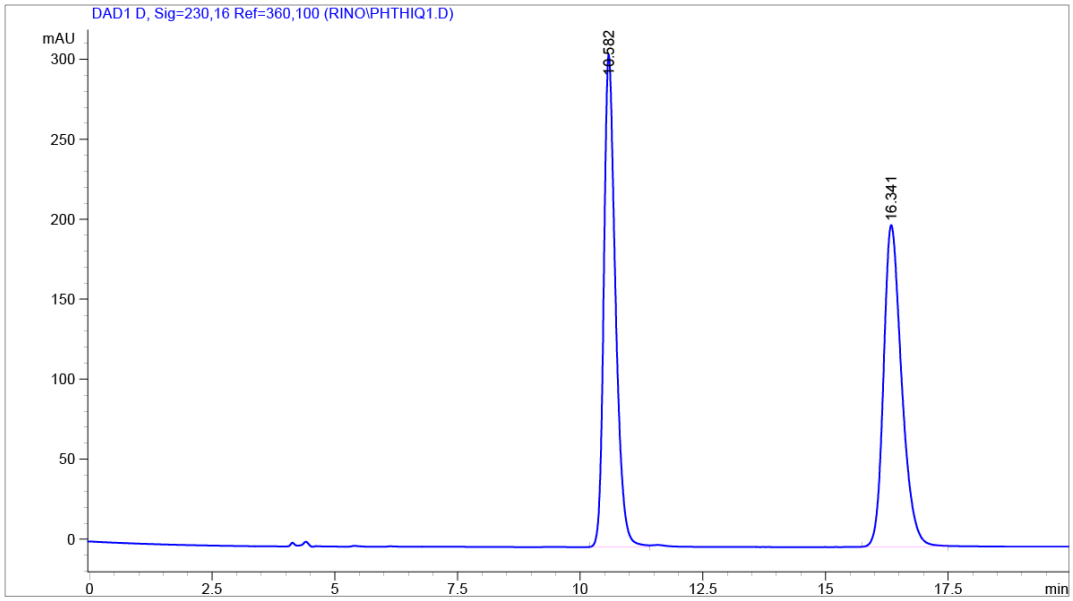
1-Ph-7-OMe-THIQ*HCl **13l***HCl



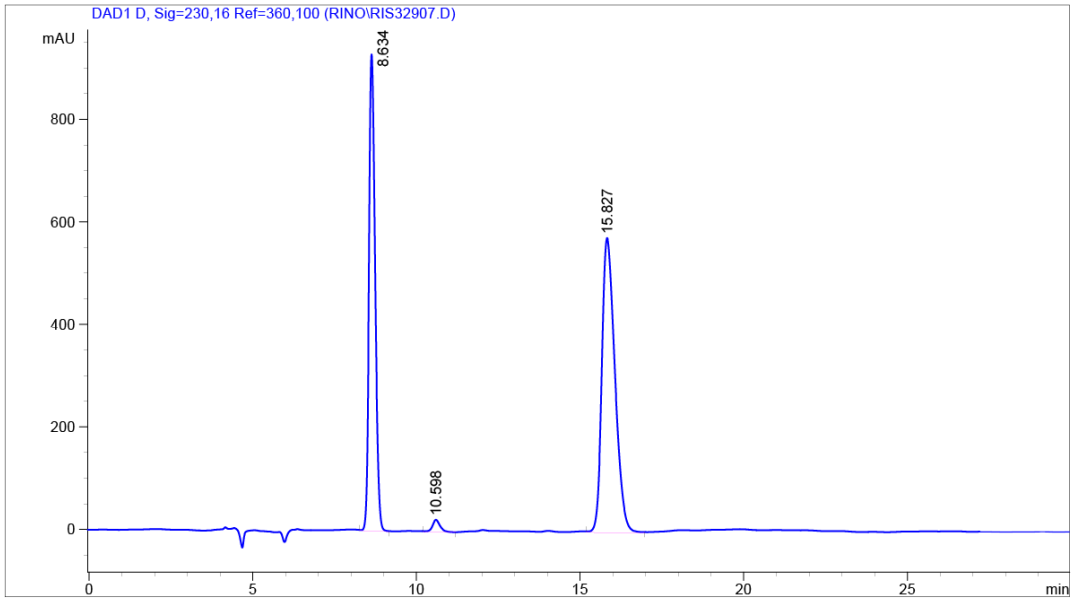


HPLC traces

1-Ph-THIQ **13a**



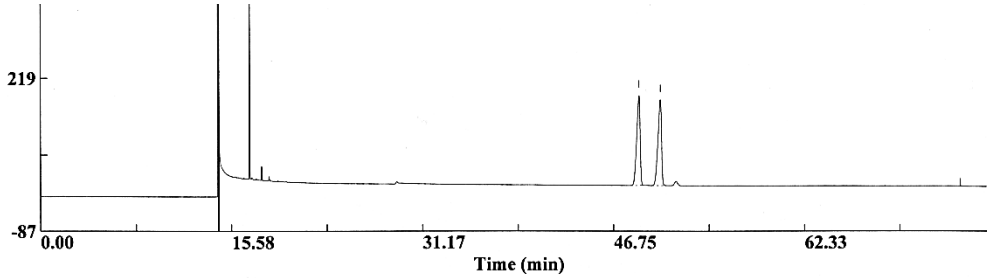
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.582	BV	0.2494	5102.32373	307.74002	49.6937
2	16.341	BB	0.3916	5165.21924	201.17023	50.3063



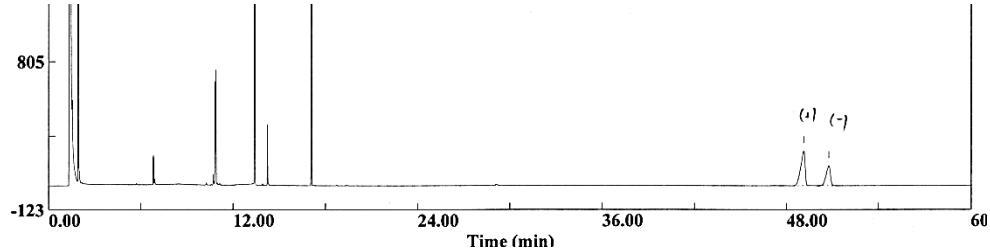
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.634	MM	0.2160	1.20658e4	931.02069	42.4386
2	10.598	MM	0.2598	361.23907	23.17511	1.2706
3	15.827	MM	0.4639	1.60041e4	574.93817	56.2908

HPLC (OD-H, hexane:2-propanol 95:5, 0.7 mL/min, 30 °C): $t_R(+)$ = 10.4 min and $t_R(-)$ = 15.8 min, t_{DHIQ} = 11.4 min.

1-Me-THIQ **13b** (*R*)-menthyl carbamate



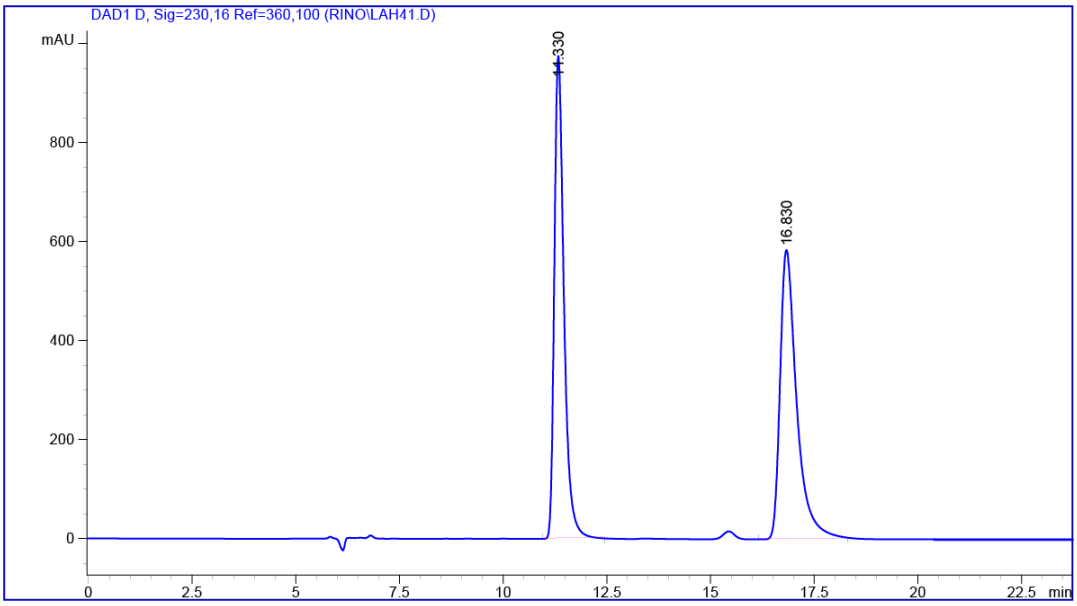
Component Name	Area (.1*uV*sec)	Area % (%)	Width at 50% (sec)	Asymm. at 10%
	4290338000	97.934	0.4	
	21623030	0.494	1.5	0.750
	34385450	0.785	18.2	0.442
	34480010	0.787	18.8	0.455
	4380827000			



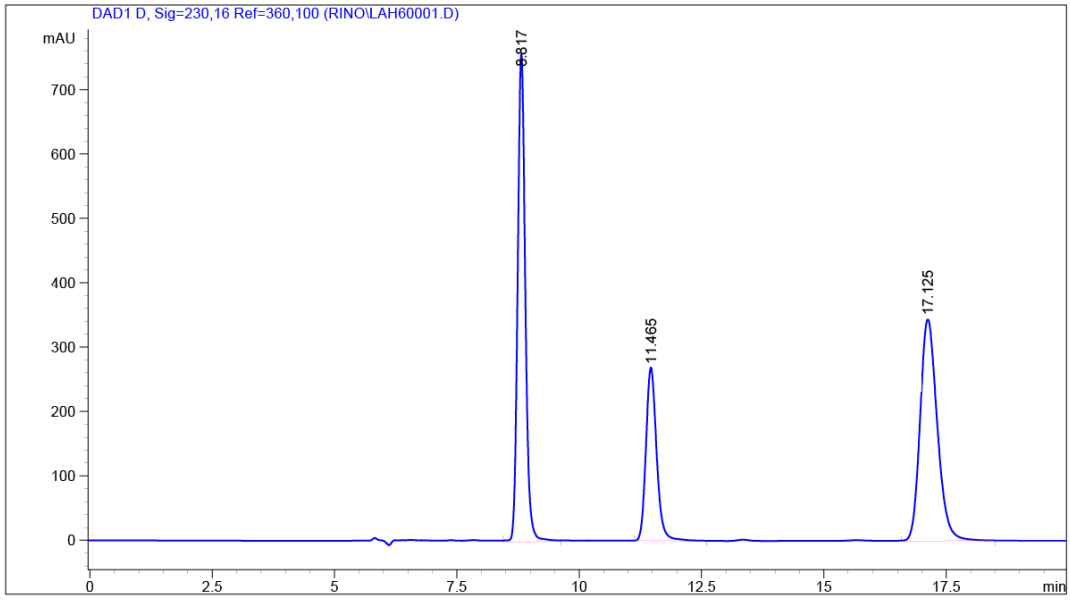
Component Name	Area (.1*uV*sec)	Area % (%)	Width at 50% (sec)	Asymm. at 10%
	43362620 (+)	63.993	18.6	0.373
	24399020 (-)	36.007	18.3	0.568
	67761640			

GC (OPTIMA-5, 30 m x 0.25 mm, 0.5 µm coating, 80 °C, 5 min, 10 °C/min, 200 °C, 43 min): $t_R(+) = 48.6$ min and $t_R(-) = 50.4$ min, $t_{DHIQ} = 13$ min, the stated sign for optical rotation corresponds to the underivatized 1-methyl-1,2,3,4-tetrahydroisoquinolin-2-ium chloride.

1-Bn-THIQ **13c**



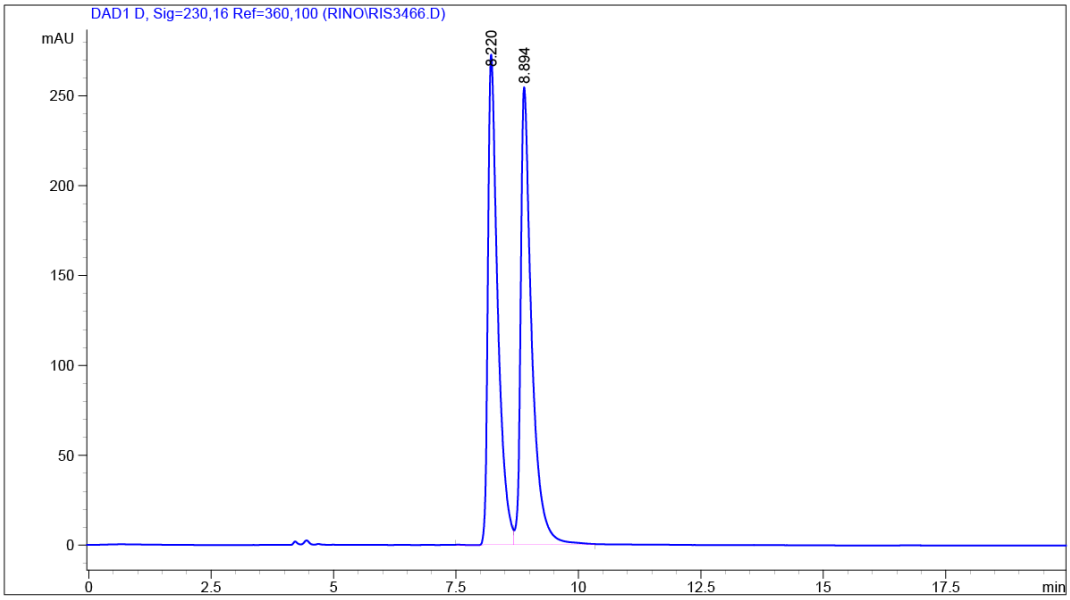
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.330	MM	0.2672	1.56346e4	975.04480	49.2857
2	16.830	MM	0.4601	1.60878e4	582.72498	50.7143



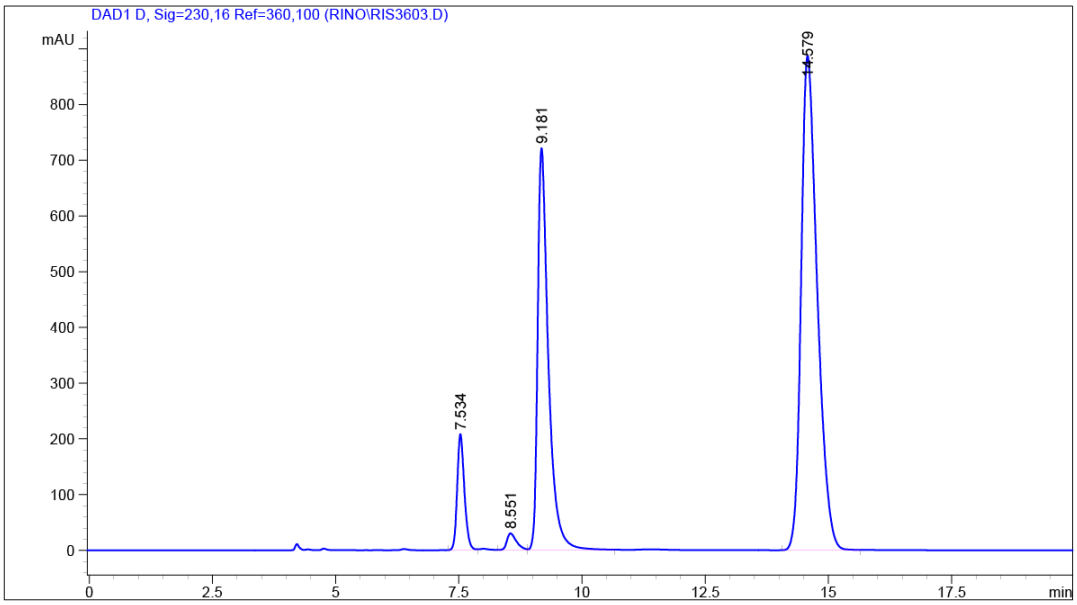
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.817	BB	0.1669	8234.69336	757.21106	39.7308
2	11.465	BB	0.2370	4082.46338	269.05750	19.6971
3	17.125	BB	0.3766	8409.05176	344.72250	40.5721

HPLC (AD-H, hexane:2-propanol 90:10, 0.5 mL/min, 25 °C): $t_R(+)$ = 11.3 min and $t_R(-)$ = 16.9 min, t_{DHIQ} = 13.8 min.

*i*Pr-THIQ **13d**



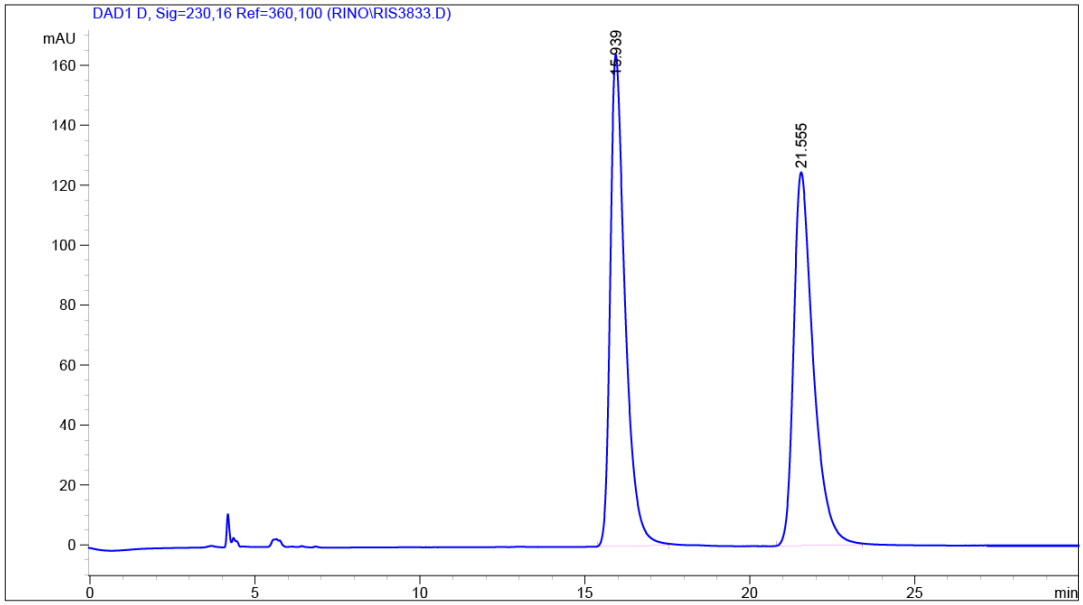
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.220	BV	0.2032	3817.06274	272.80191	48.9886
2	8.894	VB	0.2263	3974.67163	254.30919	51.0114



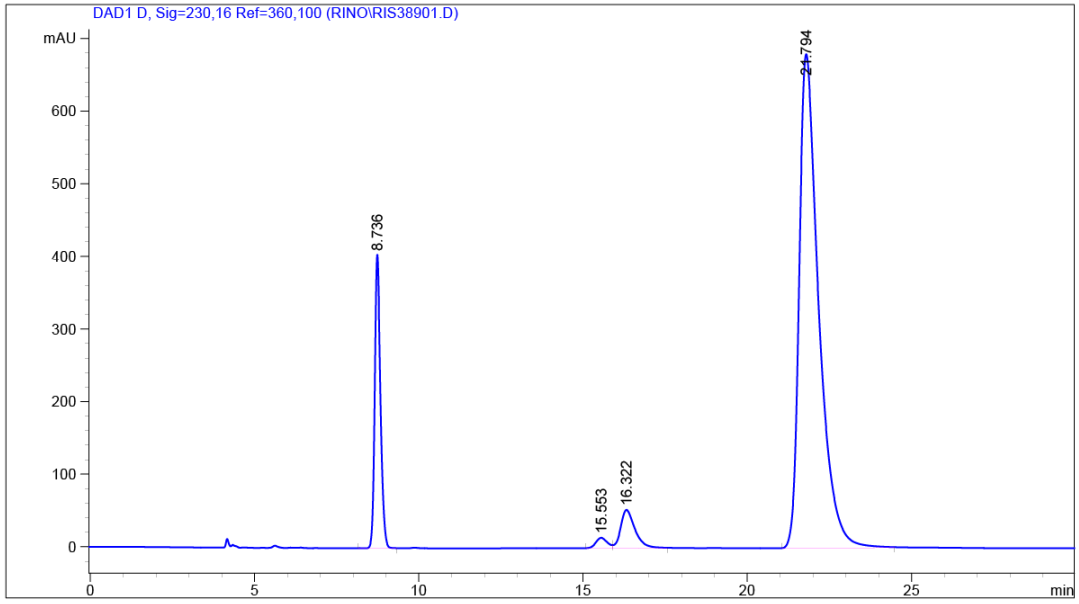
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.534	BV	0.1548	2121.21118	208.25243	6.2917
2	8.551	VV	0.2060	420.80875	30.30055	1.2482
3	9.181	VB	0.2252	1.09581e4	721.59015	32.5026
4	14.579	BB	0.3458	2.02143e4	887.38934	59.9576

HPLC (OD-H, hexane:2-propanol 99.5:0.5, 0.7 mL/min, 30 °C): t_R(-) = 8.2 min and t_R(+) = 8.9 min, t_{DHIQ} = 7.5 min.

1-*p*OMePh-THIQ **13e**



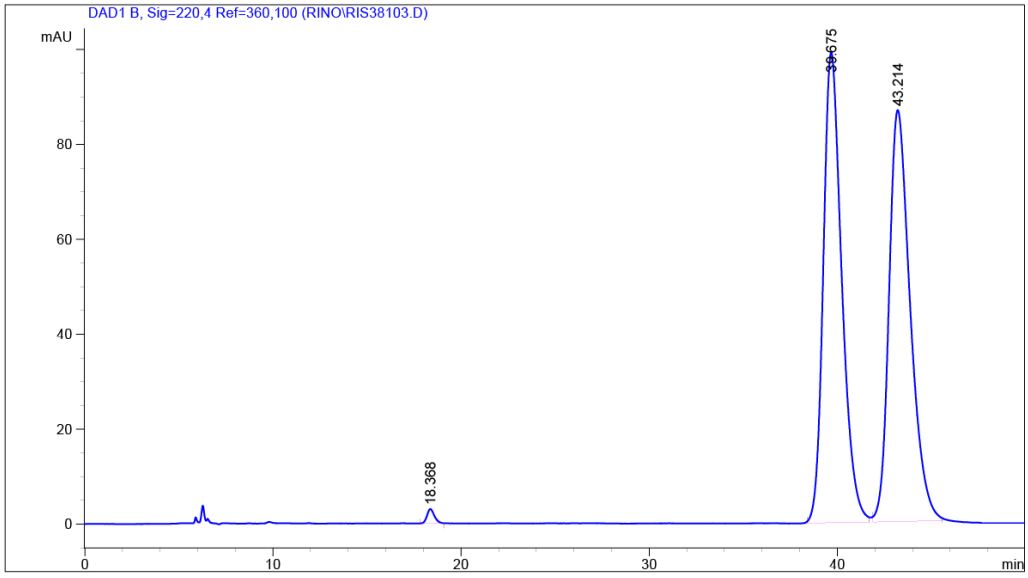
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.939	BB	0.4692	5132.87354	163.96968	49.9434
2	21.555	BB	0.6179	5144.51123	124.53471	50.0566



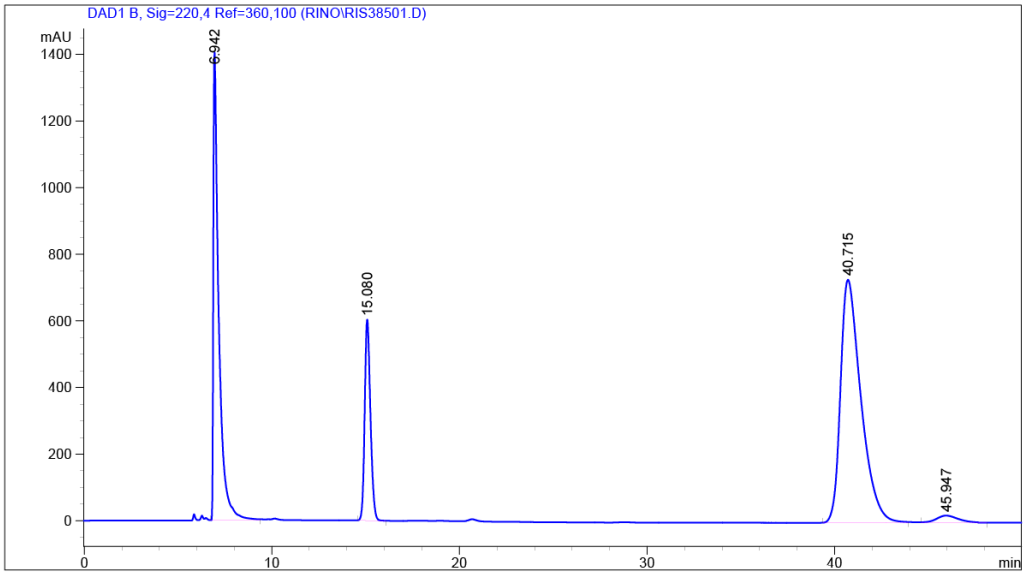
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.736	BB	0.1850	4887.26172	404.27197	14.0350
2	15.553	BV	0.3748	349.47086	14.41701	1.0036
3	16.322	VB	0.4536	1598.84680	52.75779	4.5915
4	21.794	BB	0.6120	2.79865e4	680.21521	80.3700

HPLC (OD-H, hexane:2-propanol 95:5, 0.7 mL/min, 25 °C): $t_R(+)$ = 15.9 min and $t_R(-)$ = 21.6 min, t_{DHIQ} = 14.8 min.

1-*o*Tol-THIQ **13f** acetamide



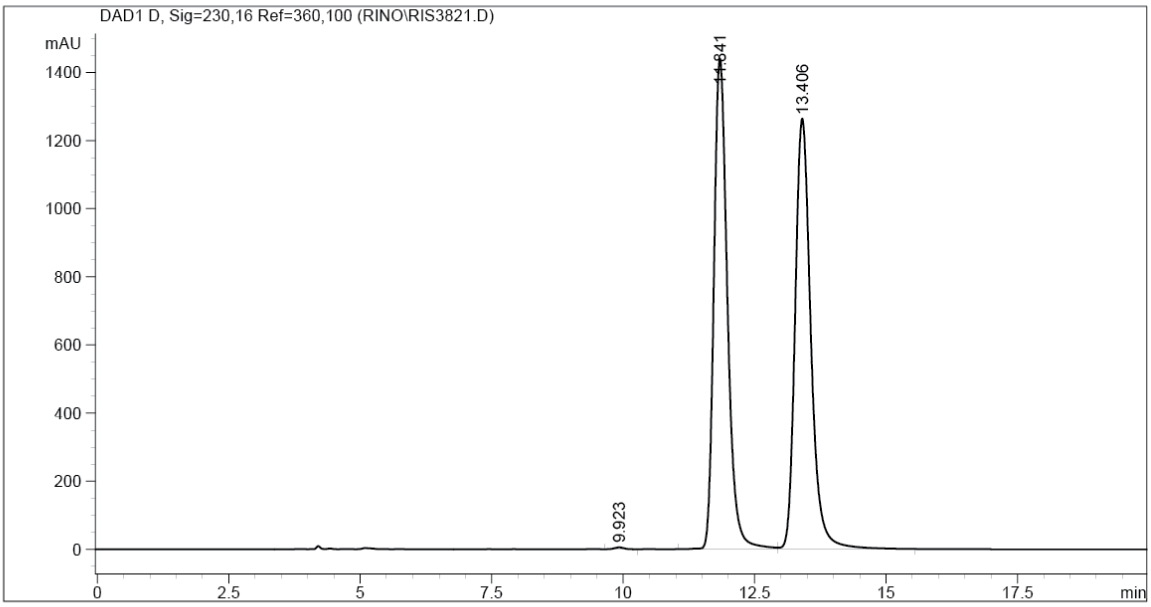
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.368	PB	0.4304	84.08421	3.04289	0.6180
2	39.675	BB	1.0305	6751.67334	99.14903	49.6230
3	43.214	BB	1.1712	6770.16553	86.68668	49.7590



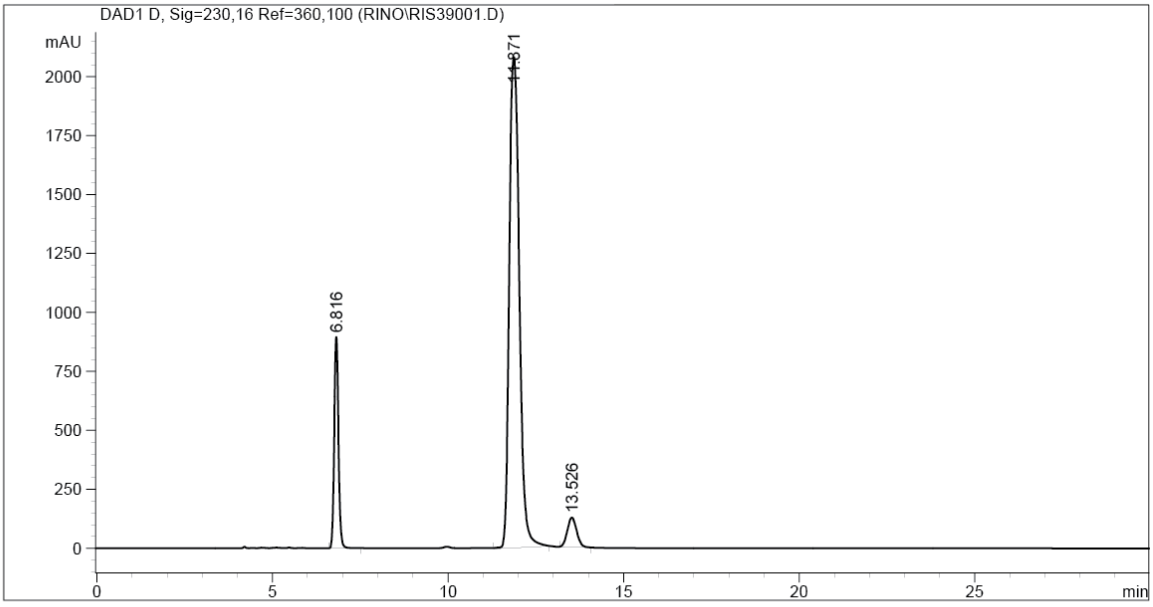
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.942	VB	0.2850	2.85234e4	1403.81982	29.0827
2	15.080	BB	0.3243	1.28473e4	603.60034	13.0991
3	40.715	BB	1.1299	5.50986e4	728.93311	56.1789
4	45.947	PB	1.1919	1607.77673	20.39009	1.6393

HPLC (OD-H, hexane:2-propanol 98:2, 0.5 mL/min, 25 °C): $t_R(-) = 39.7$ min and $t_R(+) = 43.2$ min, $t_{DHIQ} = 18.4$ min, signs were determined for the acetamide.

1-*p*BrPh-THIQ **13g**



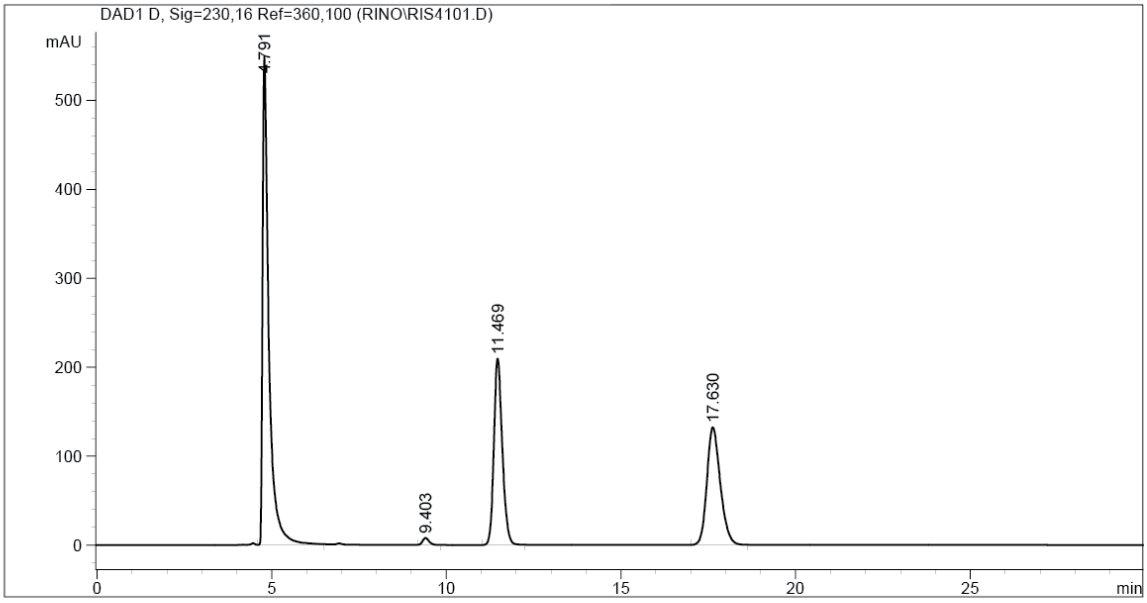
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.923	VP	0.2011	70.21542	5.49482	0.1343
2	11.841	BV	0.2774	2.58591e4	1440.44592	49.4758
3	13.406	VB	0.3231	2.63368e4	1263.74170	50.3898



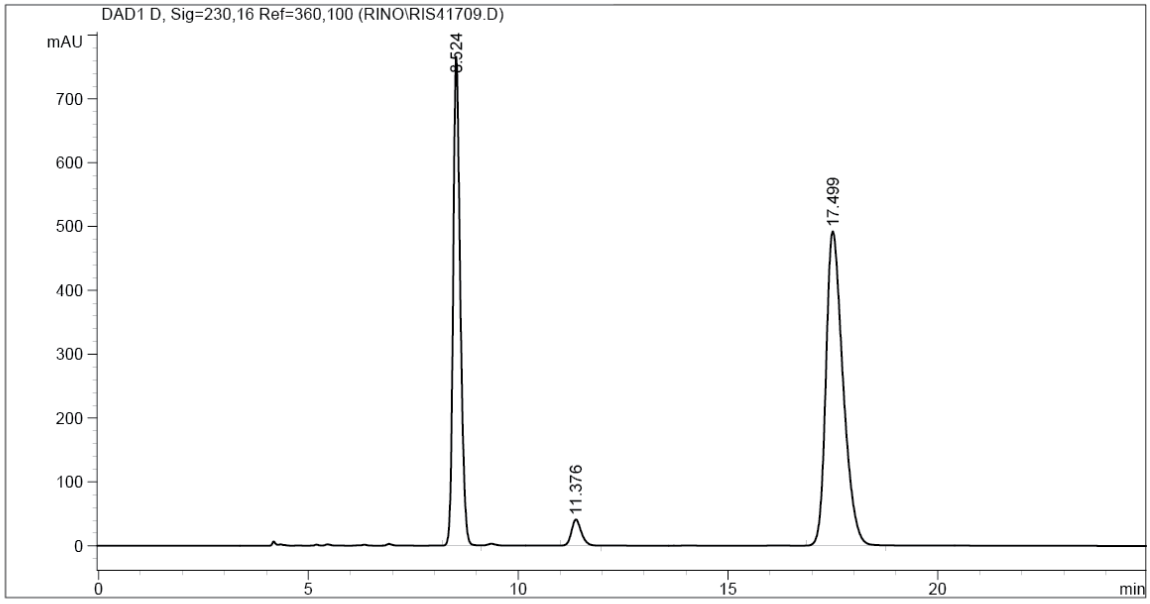
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.816	BB	0.1338	7503.02295	894.99512	14.6377
2	11.871	MM	0.3317	4.14360e4	2081.80518	80.8378
3	13.526	MM	0.3095	2319.18359	124.88968	4.5245

HPLC (AD-H, hexane:2-propanol 98:2, 0.7 mL/min, 25 °C): $t_R(-) = 11.8$ min and $t_R(+) = 13.4$ min, $t_{DHIQ} = 9.8$ min.

1-*p*CF_3Ph-THIQ **13h**



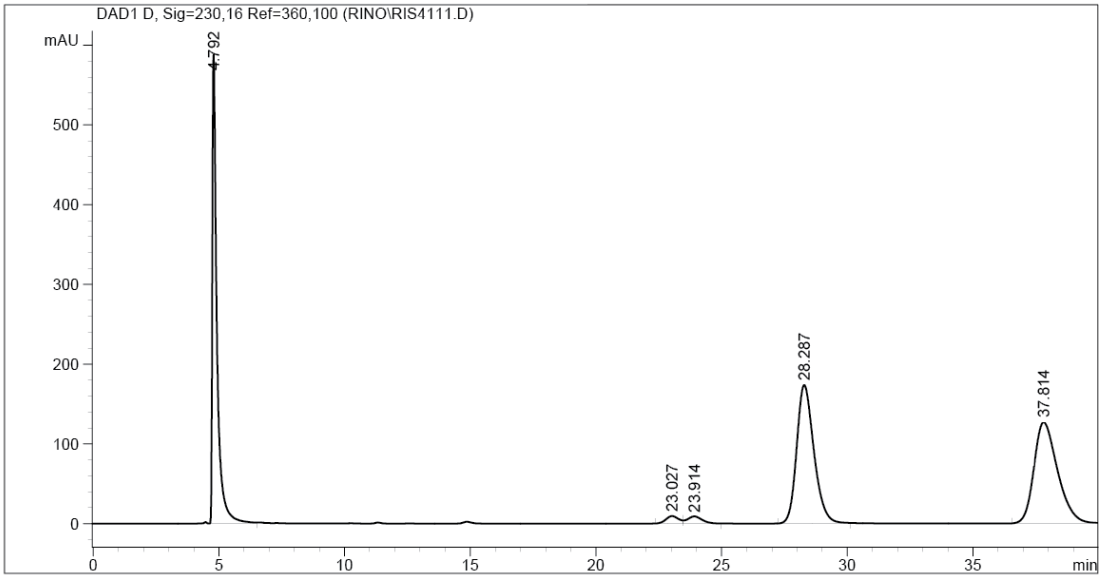
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.791	VB	0.1825	6901.15723	549.41272	49.0981
2	9.403	BB	0.1975	105.02669	7.97999	0.7472
3	11.469	BB	0.2558	3516.05640	209.55266	25.0149
4	17.630	BB	0.4077	3533.61816	132.27235	25.1398



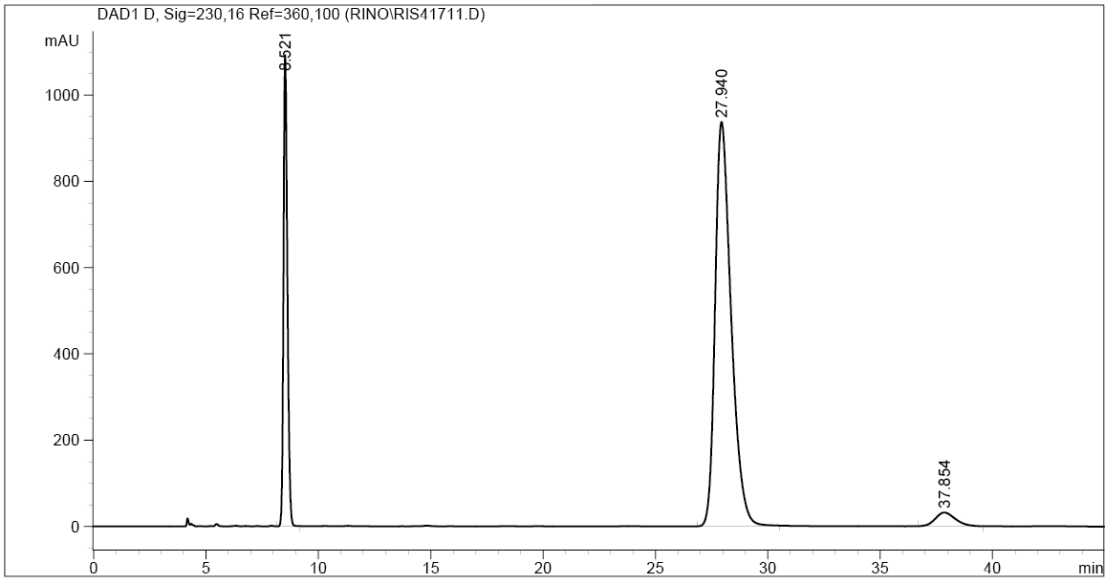
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.524	BB	0.1783	9066.36621	765.03467	38.3289
2	11.376	BB	0.2482	675.18726	40.99360	2.8544
3	17.499	PB	0.4298	1.39126e4	492.09189	58.8167

HPLC (OD-H, hexane:2-propanol 95:5, 0.7 mL/min, 30 °C): $t_R(+)$ = 11.5 min and $t_R(-)$ = 17.6 min, t_{DHIQ} = 6.9 min.

1-*p*COOMePh-THIQ **13i**



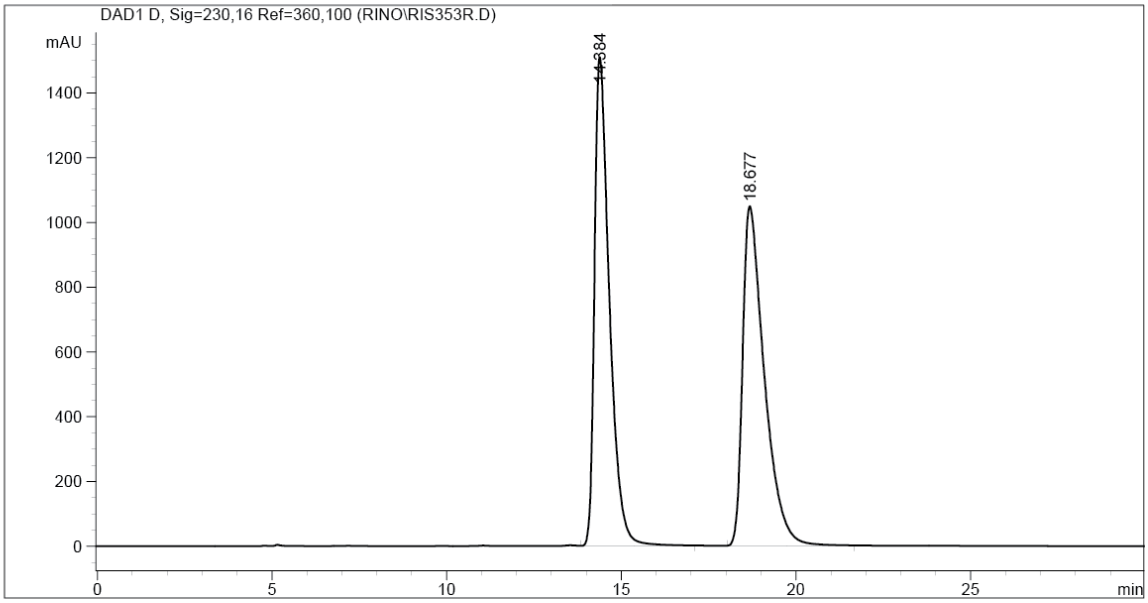
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.792	VB	0.1844	7485.39502	588.34662	30.1229
2	23.027	BV	0.5506	343.36667	9.47859	1.3818
3	23.914	VB	0.6145	372.28046	9.07747	1.4981
4	28.287	BB	0.7297	8302.72656	173.68613	33.4121
5	37.814	BBA	1.0013	8345.72266	127.23322	33.5851



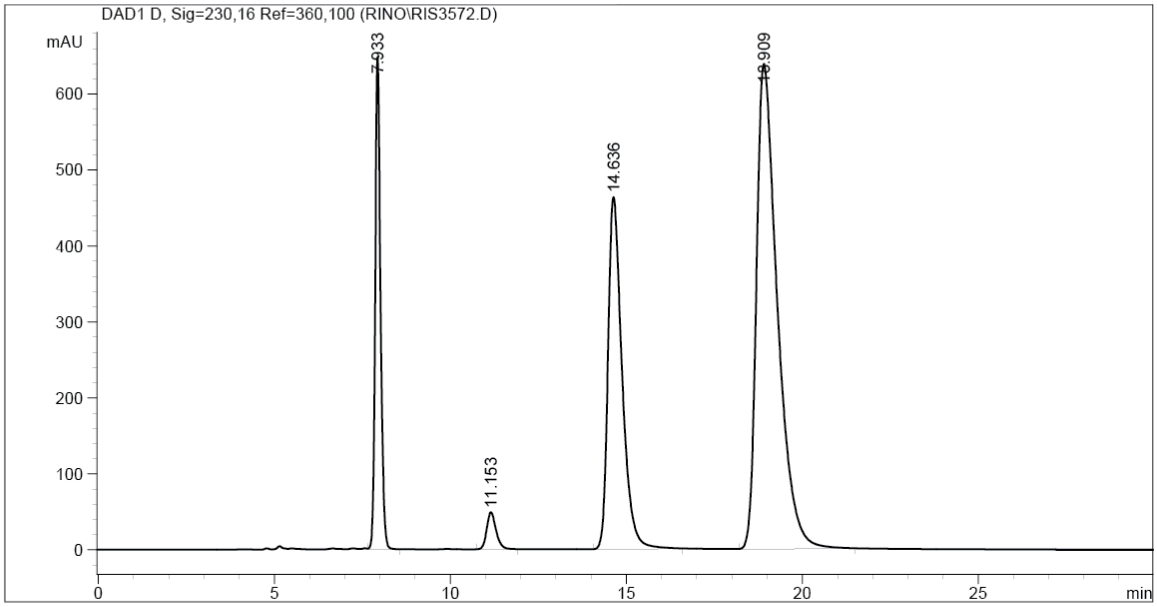
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.521	VB	0.1841	1.31129e4	1092.12122	21.2813
2	27.940	BB	0.7504	4.64853e4	937.55829	75.4424
3	37.854	BB	0.9671	2018.76587	32.04020	3.2763

HPLC (OD-H, hexane:2-propanol 95:5, 0.7 mL/min, 30 °C): $t_R(-) = 28.3$ min and $t_R(+) = 37.8$ min, $t_{DHIQ} = 11.3$ min.

1-Ph-6,7-OMe-THIQ **13j**



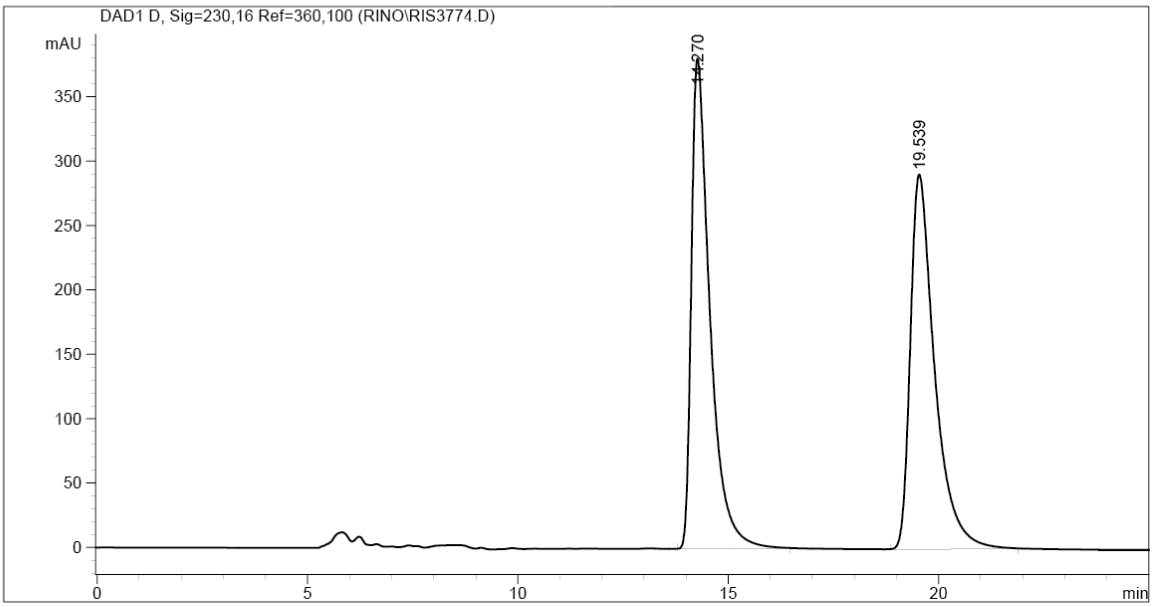
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.384	VB	0.4421	4.47800e4	1509.45996	49.7694
2	18.677	PB	0.6390	4.51949e4	1048.21423	50.2306



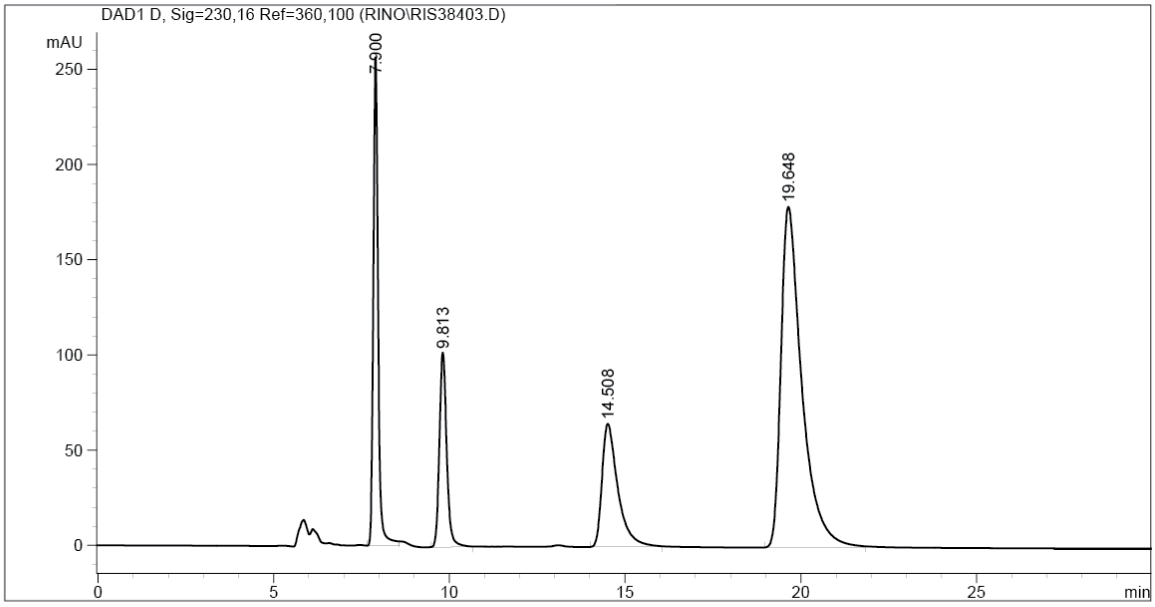
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.933	VB	0.1586	6802.47266	647.48718	14.4950
2	11.153	BB	0.2807	906.19275	48.77863	1.9310
3	14.636	BB	0.4203	1.28812e4	463.37177	27.4479
4	18.909	BB	0.6171	2.63398e4	638.72723	56.1261

HPLC (OD-H, hexane:2-propanol 80:20, 0.6 mL/min, 30 °C): $t_R(+)$ = 14.4 min and $t_R(-)$ = 18.7 min, t_{DHIQ} = 11.0 min.

Pent-OMe-THIQ **13k**



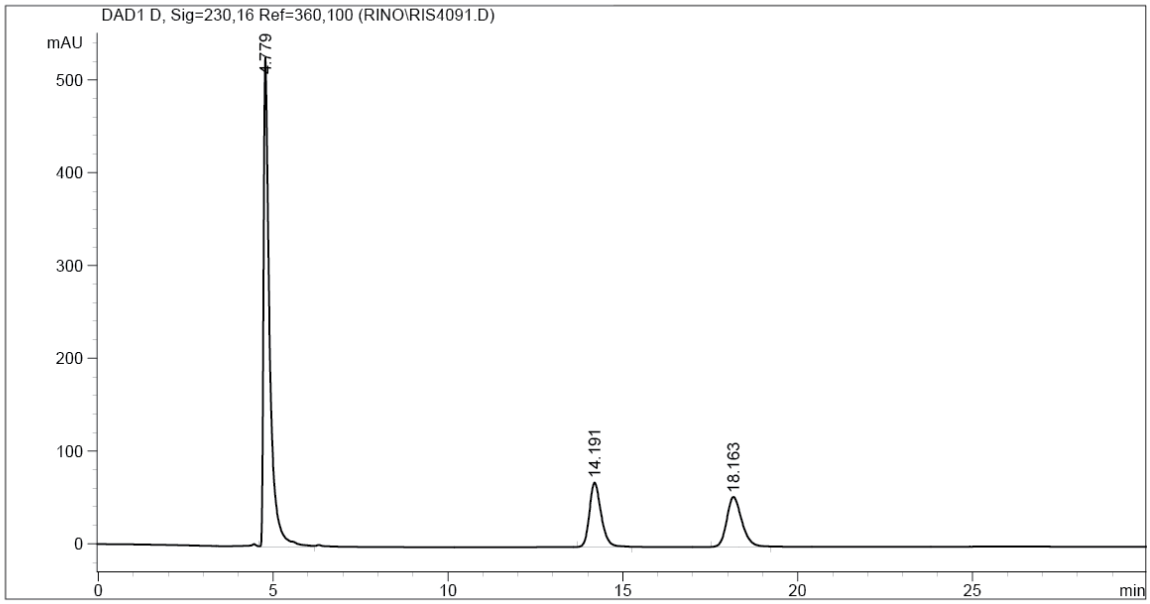
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.270	BB	0.4509	1.17079e4	380.57837	50.0287
2	19.539	BB	0.5930	1.16945e4	290.92090	49.9713



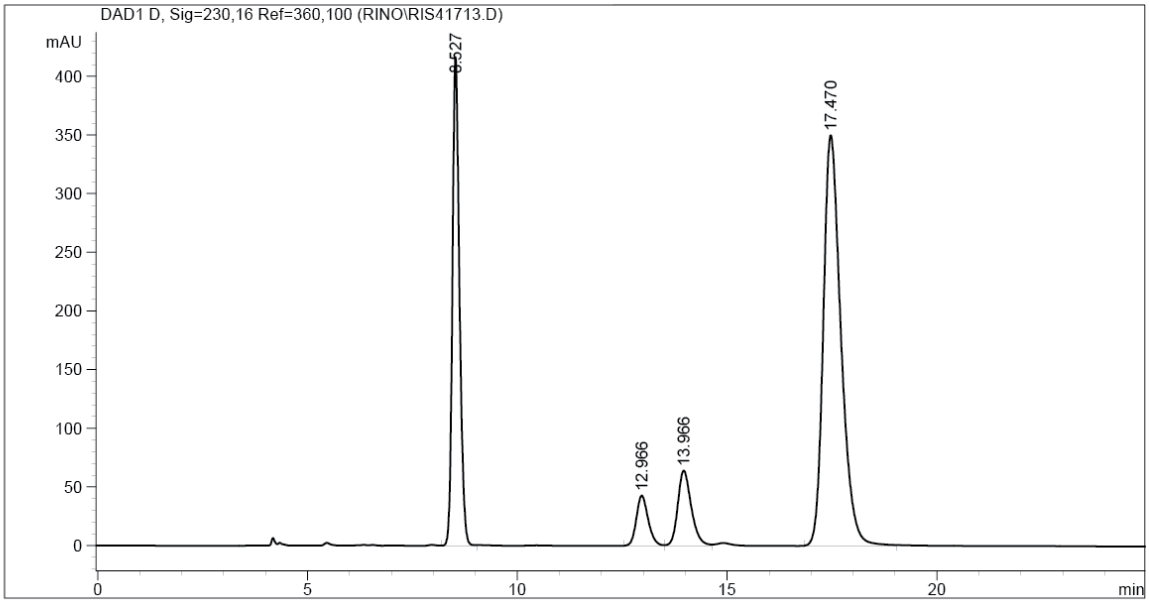
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.900	VB	0.1433	2446.06177	256.39951	18.3411
2	9.813	PB	0.2200	1469.66028	102.07909	11.0198
3	14.508	BB	0.4717	2037.96106	64.66176	15.2811
4	19.648	BB	0.6096	7382.82959	178.86273	55.3580

HPLC (AD-H, hexane:2-propanol 60:40, 0.5 mL/min, 25 °C): $t_R(-)$ = 14.3 min and $t_R(+)$ = 19.5 min, t_{DHIQ} = 9.8 min.

1-Ph-7-OMe-THIQ **13l**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.779	VV	0.1771	6380.02490	527.69714	66.3223
2	14.191	BB	0.3526	1622.54517	69.44540	16.8668
3	18.163	BB	0.4587	1617.16296	53.80482	16.8109



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.527	VB	0.1763	4861.37549	416.11179	28.0119
2	12.966	BV	0.3014	841.97705	42.82686	4.8516
3	13.966	VV	0.3429	1444.98083	64.13174	8.3262
4	17.470	BB	0.4444	1.02063e4	349.82849	58.8103

HPLC (OD-H, hexane:2-propanol 95:5, 0.7 mL/min, 30 °C): $t_R(-)$ = 14.2 min and $t_R(+)$ = 18.2 min, t_{DHIQ} = 12.9 min.

Literature

(1) M. Movassaghi, M. D. Hill, Org. Lett. 2008, 10, 3485-3488.

(2) J. Přech, V. Matoušek, J. Václavík, J. Pecháček, K. Syslová, P. Šot, J. Januščák, B. Vilhanová, M. Kuzma, J. Toman, P. Kačer, Am. J. Anal. Chem. 2013, 04, 125-133.