Synthesis

Reviews and Full Papers in Chemical Synthesis

Supporting Information

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Thieme

Supplementary Information

Isocyanoalkene Addition-Cyclization-Decarboxylation Cascades

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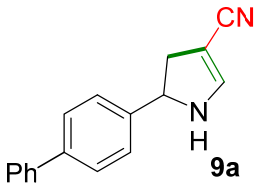
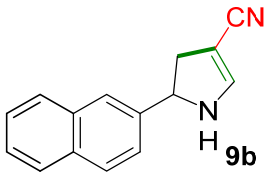
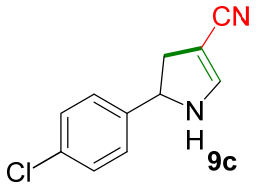
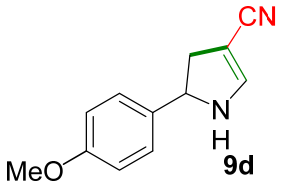
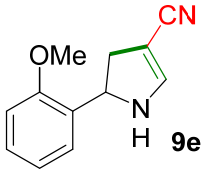
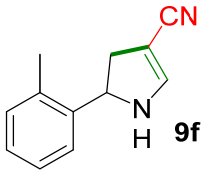
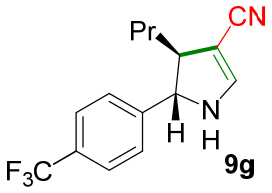
Department of Chemistry, Drexel University, 3400 Chestnut St., Philadelphia, PA 19104, United States.

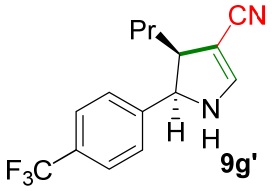
Compound	Procedure	^{1}H- and ^{13}C NMR	Other
 **9a**	-	S4	-
 **9b**	-	S5	-
 **9c**	-	S6	-
 **9d**	-	S7	-
 **9e**	-	S8	-



	-	S9	-



	-	S10	^{19}F NMR – S11



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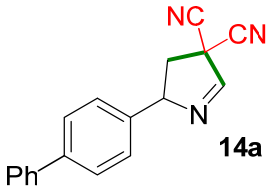

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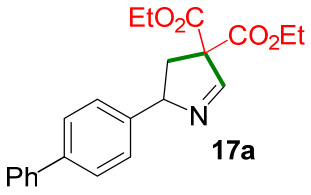

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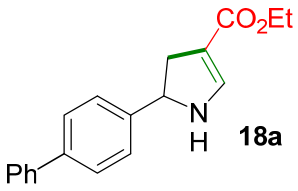

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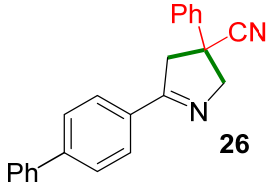

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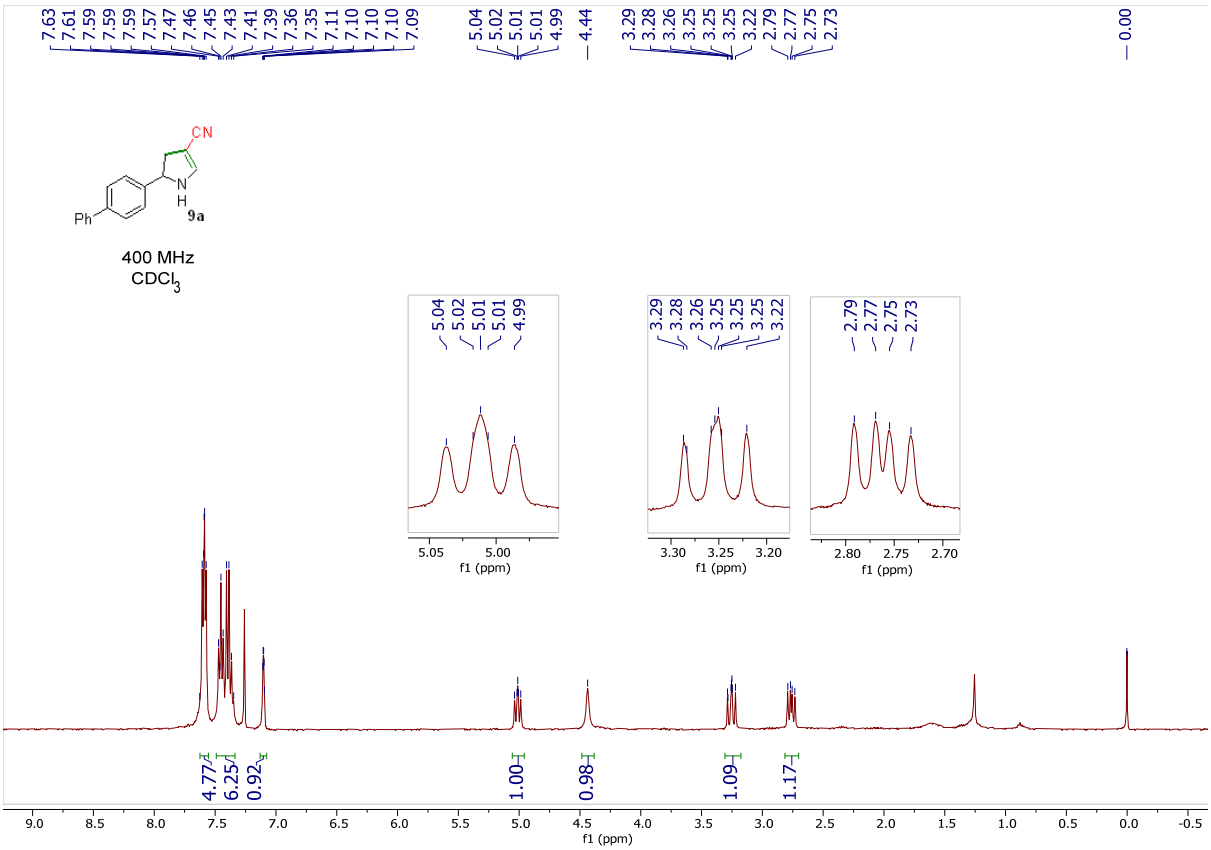
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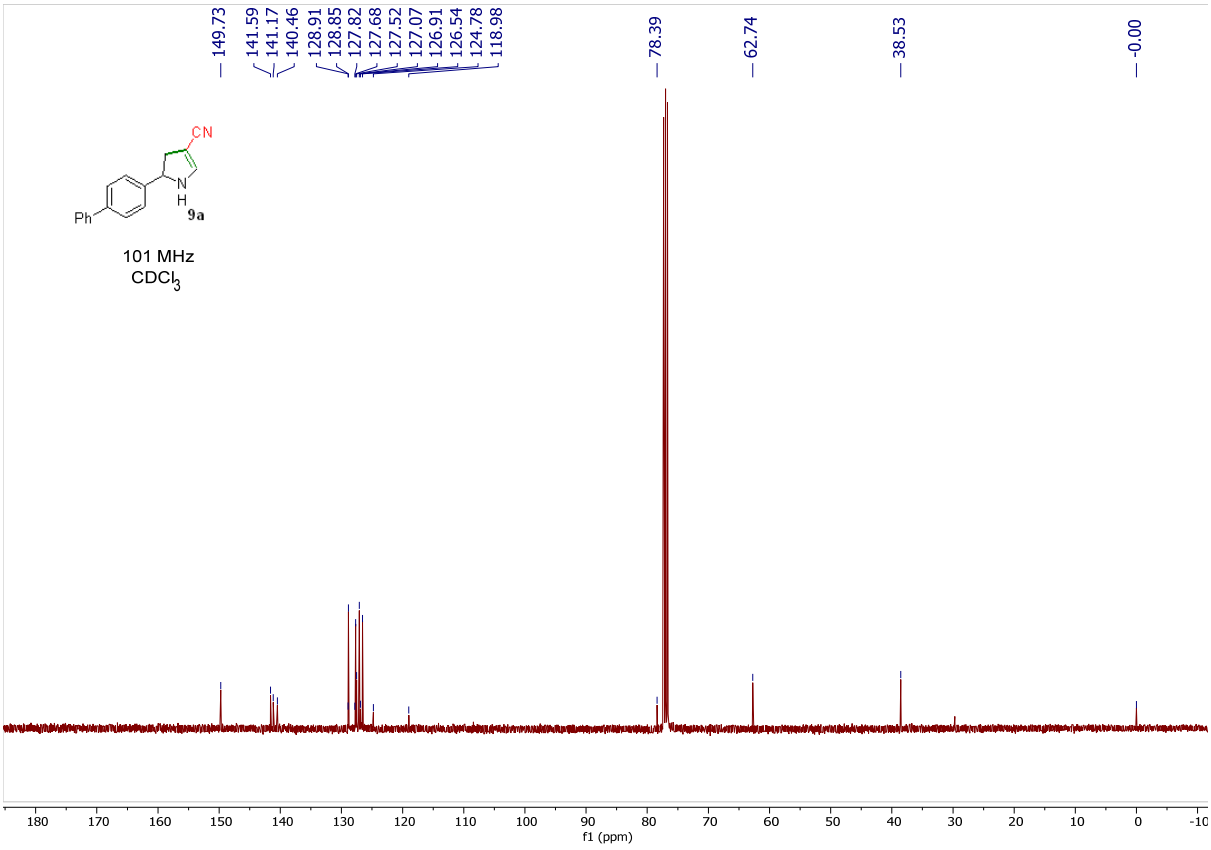
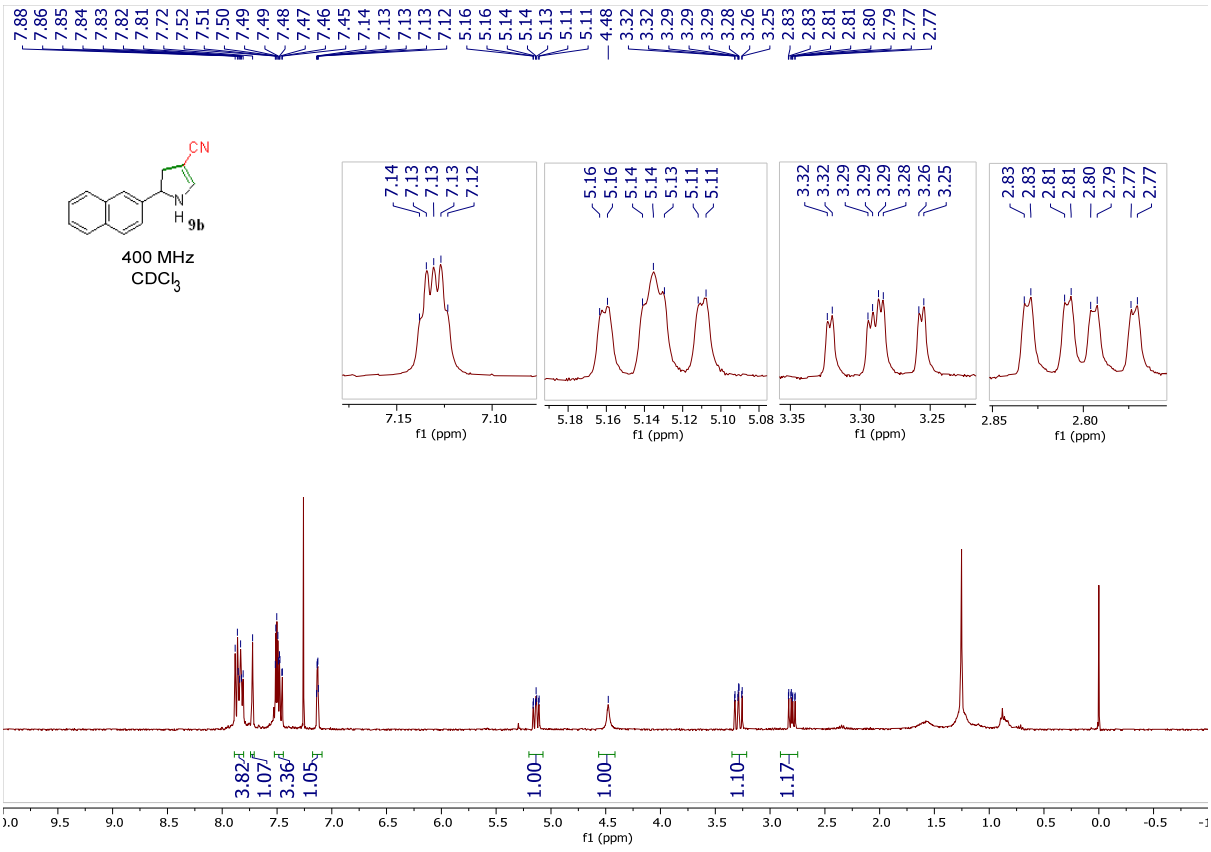
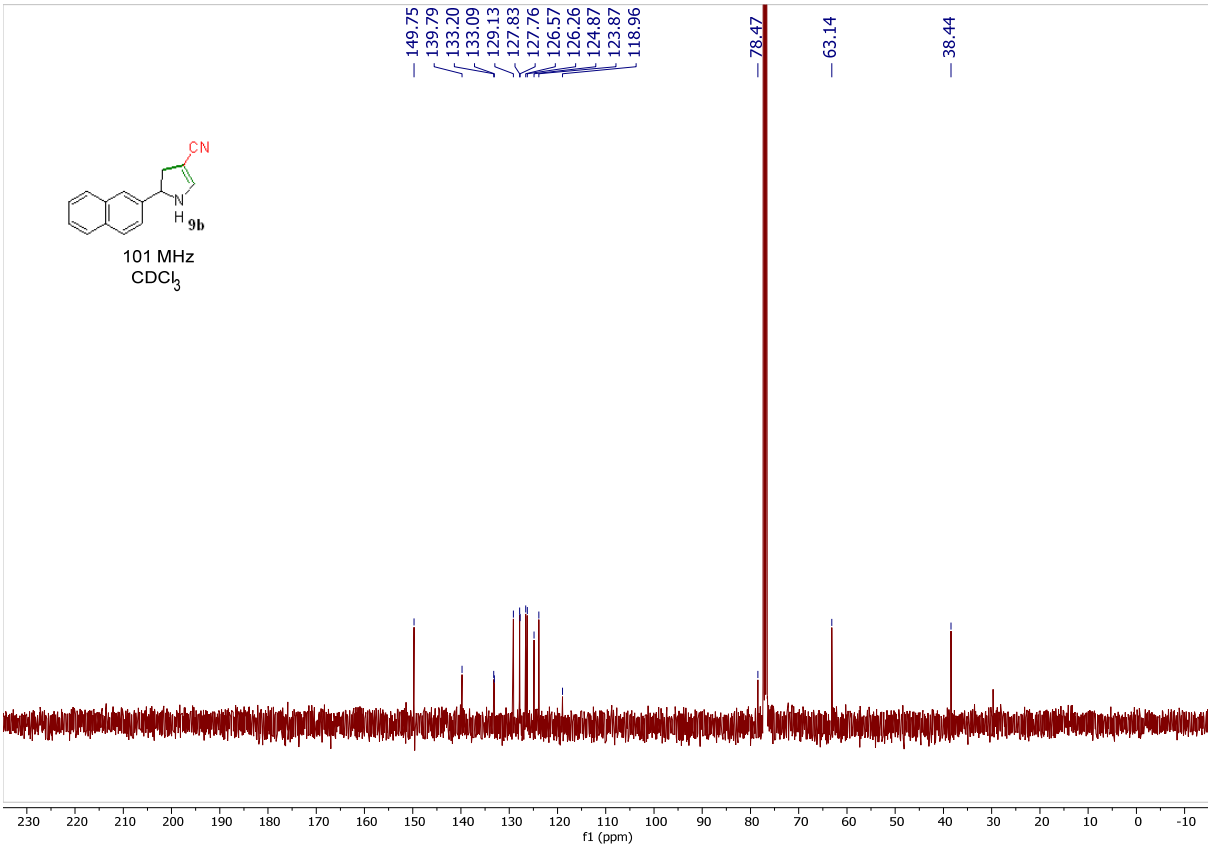
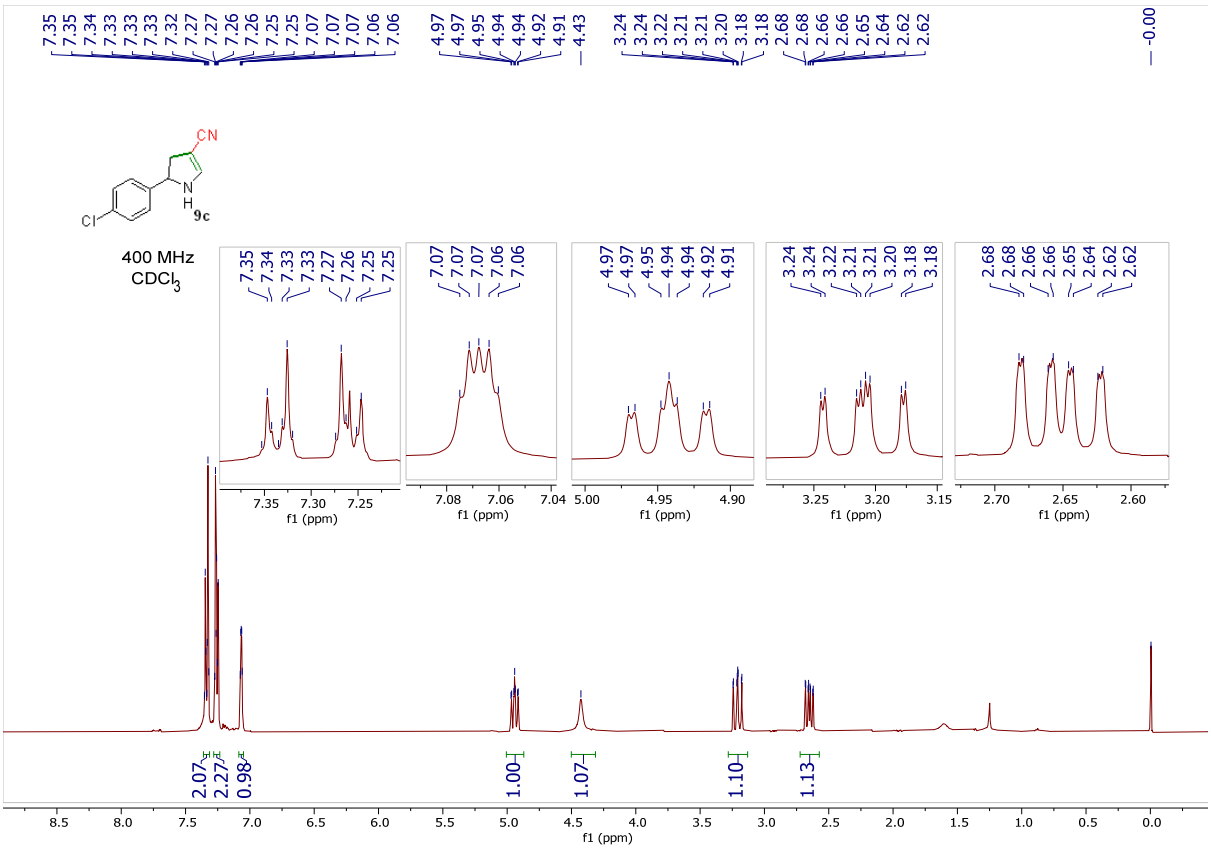
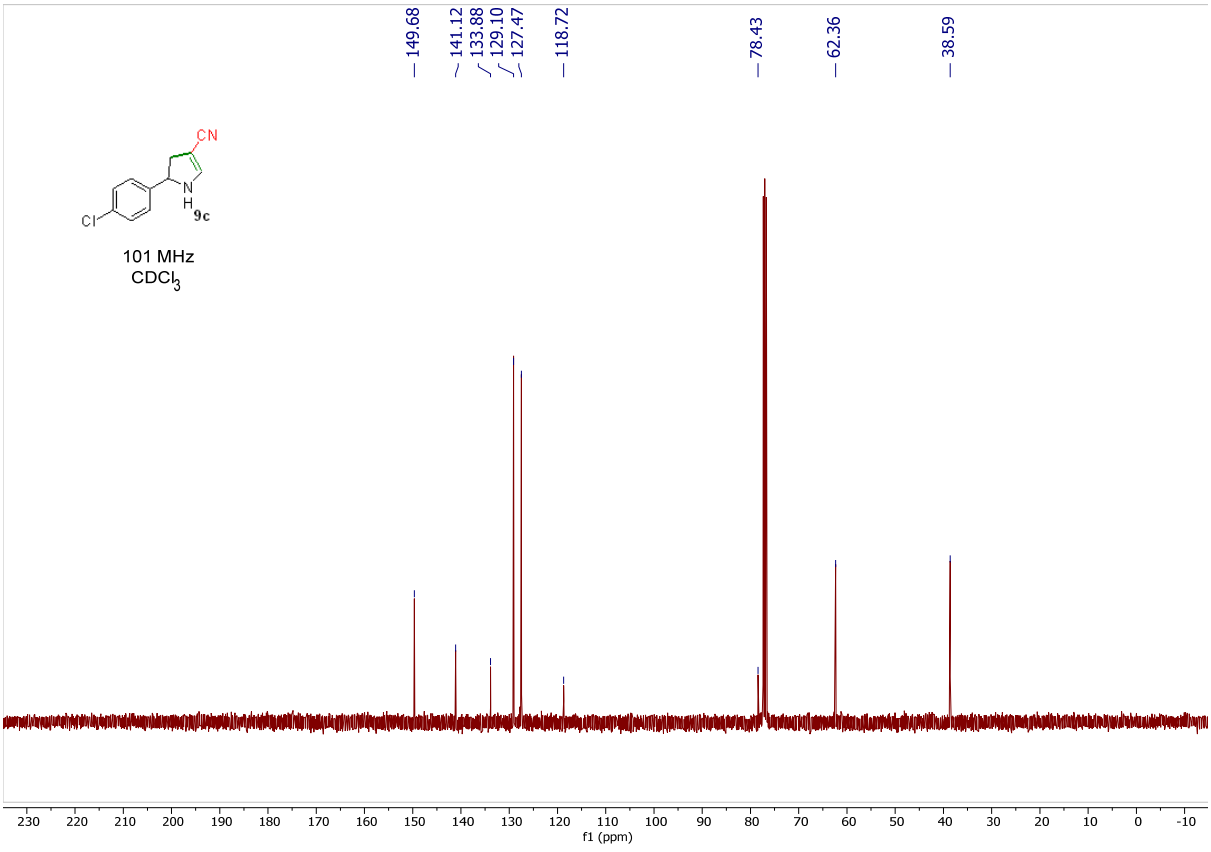
7.61
7.59
7.59
7.59
7.57
7.47
7.46
7.45
7.43
7.41
7.39
7.36
7.35
7.11
7.10
7.10
7.10
7.09
5.04
5.02
5.01
5.01
4.99
4.44
3.29
3.28
3.26
3.25
3.25
3.25
3.22
2.79
2.77
2.75
2.73
0.00
CN
N
H
Ph
9a
400 MHz
CDCl3
f1 (ppm)
4.77
6.25
0.92
1.00
0.98
1.09
1.17


149.73
141.59
141.17
140.46
128.91
128.85
127.82
127.68
127.52
127.07
126.91
126.54
124.78
118.98
78.39
62.74
38.53
-0.00
CN
N
H
Ph
9a
101 MHz
CDCl3
f1 (ppm)


7.88 7.86 7.85 7.84 7.83 7.82 7.81 7.72 7.52 7.51 7.50 7.49 7.49 7.48 7.47 7.46 7.45 7.14 7.13 7.13 7.13 7.12 5.16 5.14 5.14 5.13 5.11 5.11 4.48 3.32 3.32 3.29 3.29 3.29 3.28 3.26 3.25 2.83 2.83 2.81 2.81 2.80 2.79 2.77 2.77
CN
N
H
9b
400 MHz
CDCl3
7.14 7.13 7.13 7.13 7.12
5.16 5.16 5.14 5.14 5.13 5.11 5.11
3.32 3.32 3.29 3.29 3.29 3.28 3.26 3.25
2.83 2.83 2.81 2.81 2.80 2.79 2.77 2.77
f1 (ppm)
3.82 1.07 3.36 1.05 1.00 1.00 1.10 1.17
f1 (ppm)


149.75 139.79 133.20 133.09 129.13 127.83 127.76 126.57 126.26 124.87 123.87 118.96
78.47
63.14
38.44
CN
N
H
9b
101 MHz
CDCl3
f1 (ppm)


7.35 7.35 7.34 7.33 7.33 7.33 7.32 7.27 7.27 7.26 7.26 7.25 7.25 7.07 7.07 7.07 7.06 7.06
4.97 4.97 4.95 4.94 4.94 4.92 4.91 4.43
3.24 3.24 3.22 3.21 3.21 3.20 3.18 3.18
2.68 2.68 2.66 2.66 2.65 2.64 2.62 2.62
-0.00
CN
N
H
Cl
9c
400 MHz
CDCl3
f1 (ppm)
2.07
2.27
0.98
1.00
1.07
1.10
1.13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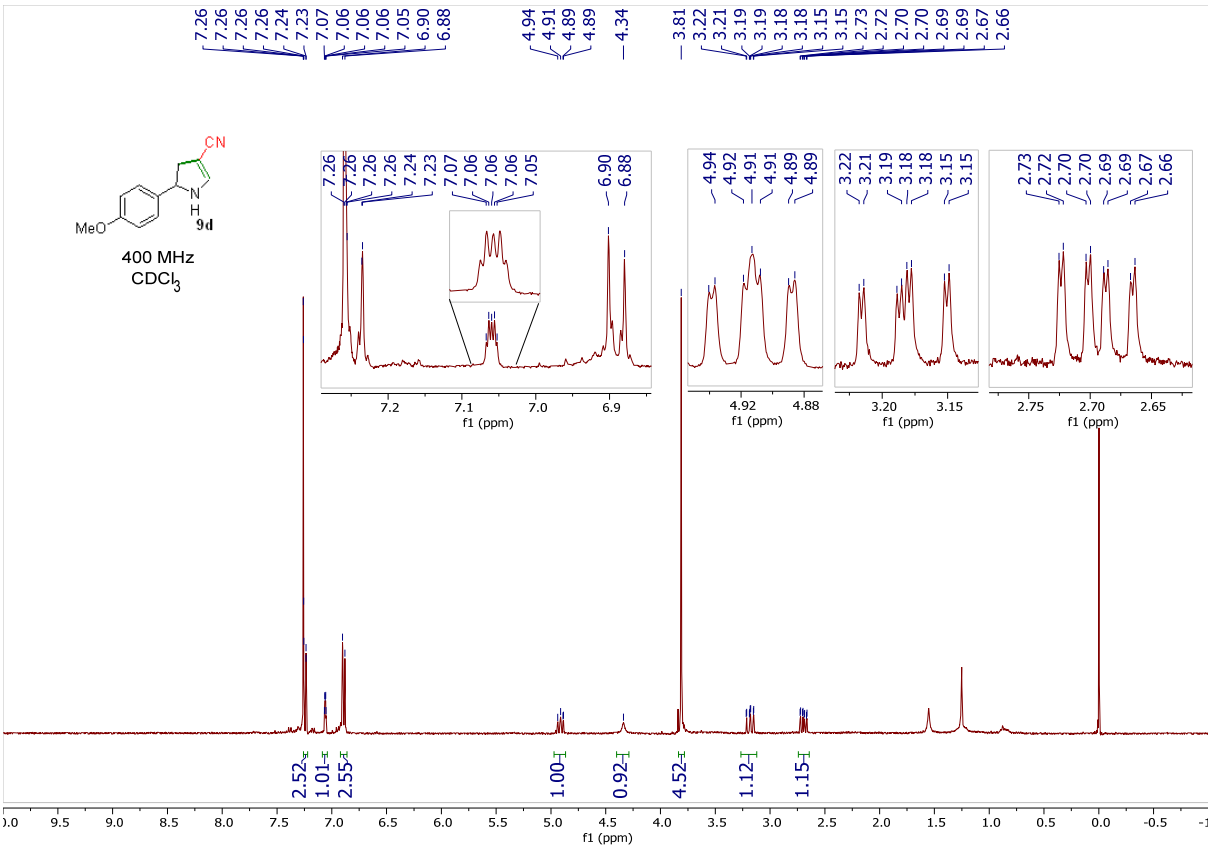
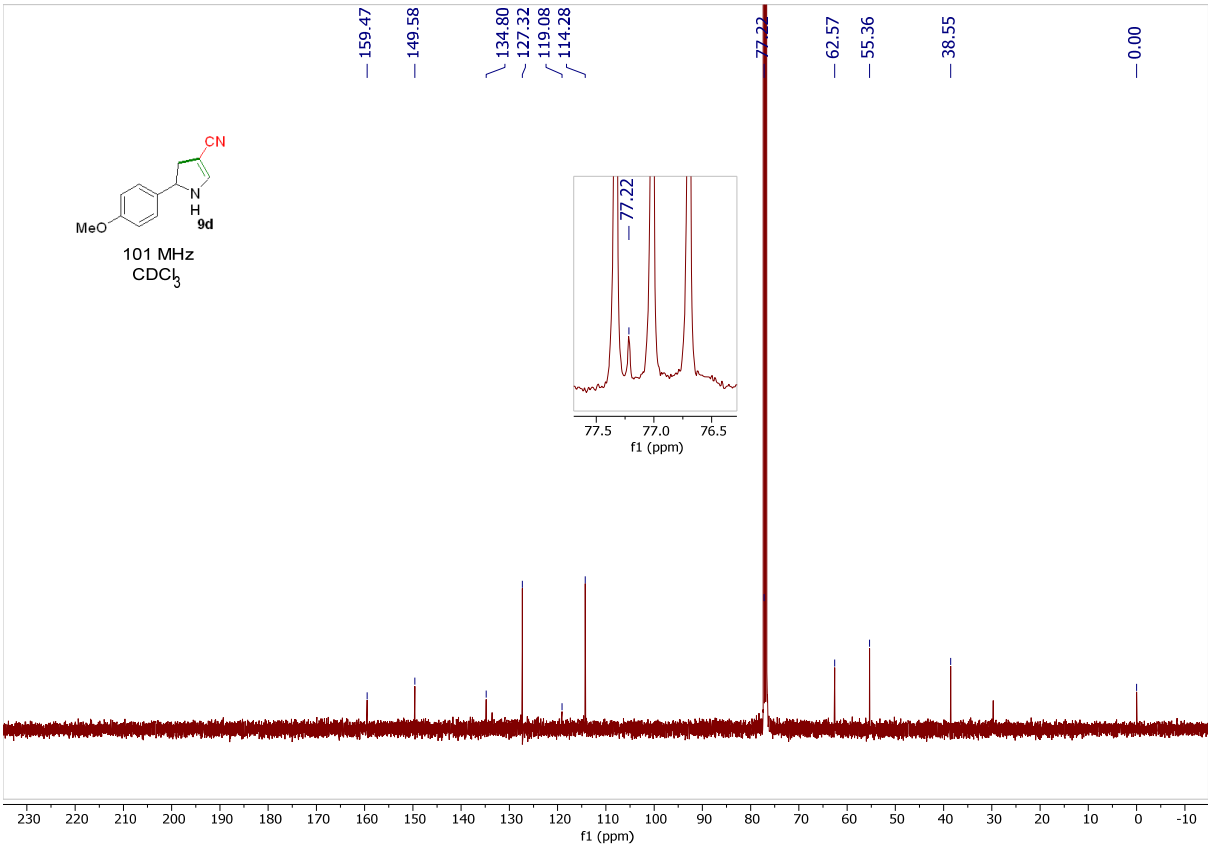
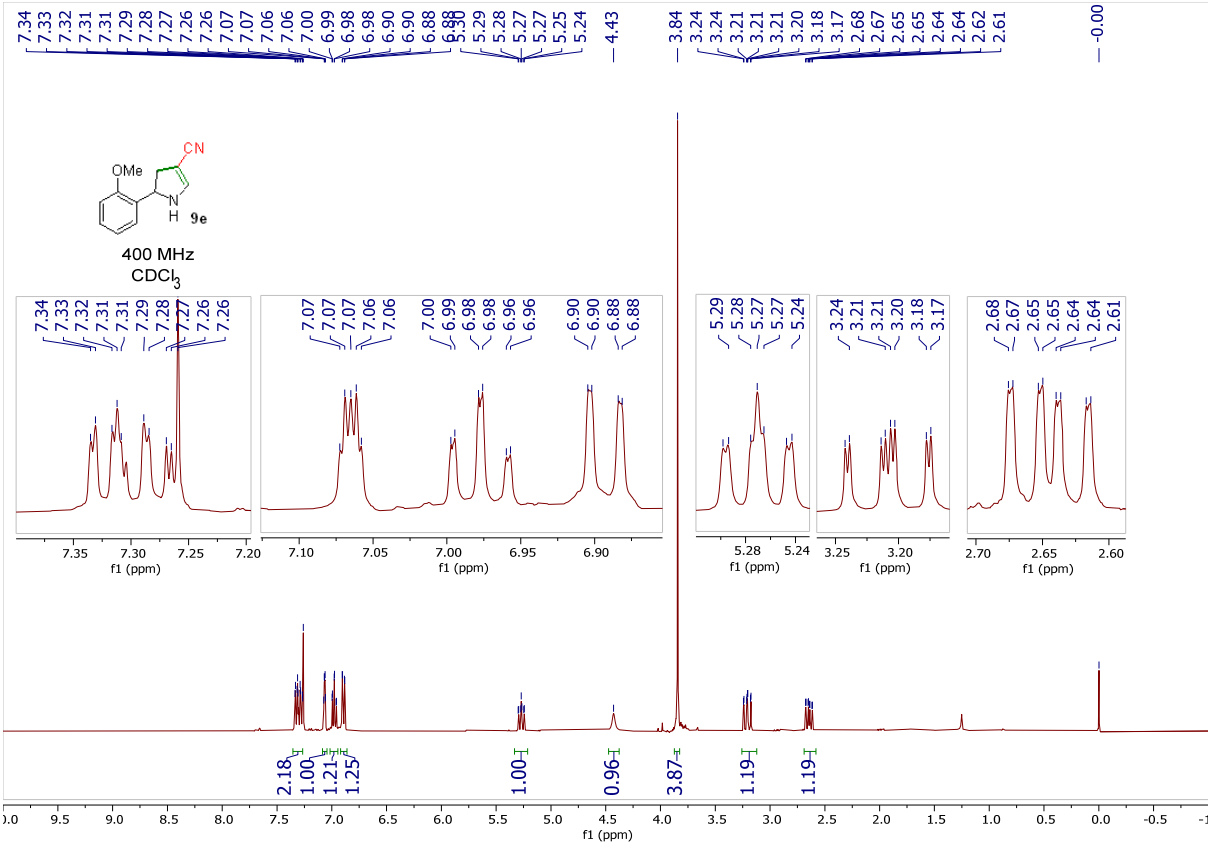
141.12
133.88
129.10
127.47
118.72
78.43
62.36
38.59
CN
N
H
Cl
9c
101 MHz
CDCl3
f1 (ppm)


7.26 7.26 7.26 7.26 7.24 7.23 7.07 7.06 7.06 7.06 7.05 6.90 6.88
4.94 4.91 4.89 4.89 4.34
3.81 3.22 3.21 3.19 3.19 3.18 3.18 3.15 3.15 2.73 2.72 2.70 2.70 2.69 2.67 2.66
CN
N
H
MeO
9d
400 MHz
CDCl3
f1 (ppm)
2.52 1.01 2.55 1.00 0.92 4.52 1.12 1.15


159.47 149.58 134.80 127.32 119.08 114.28
77.22
62.57 55.36 38.55 0.00
CN
N
H
MeO
9d
101 MHz
CDCl3
f1 (ppm)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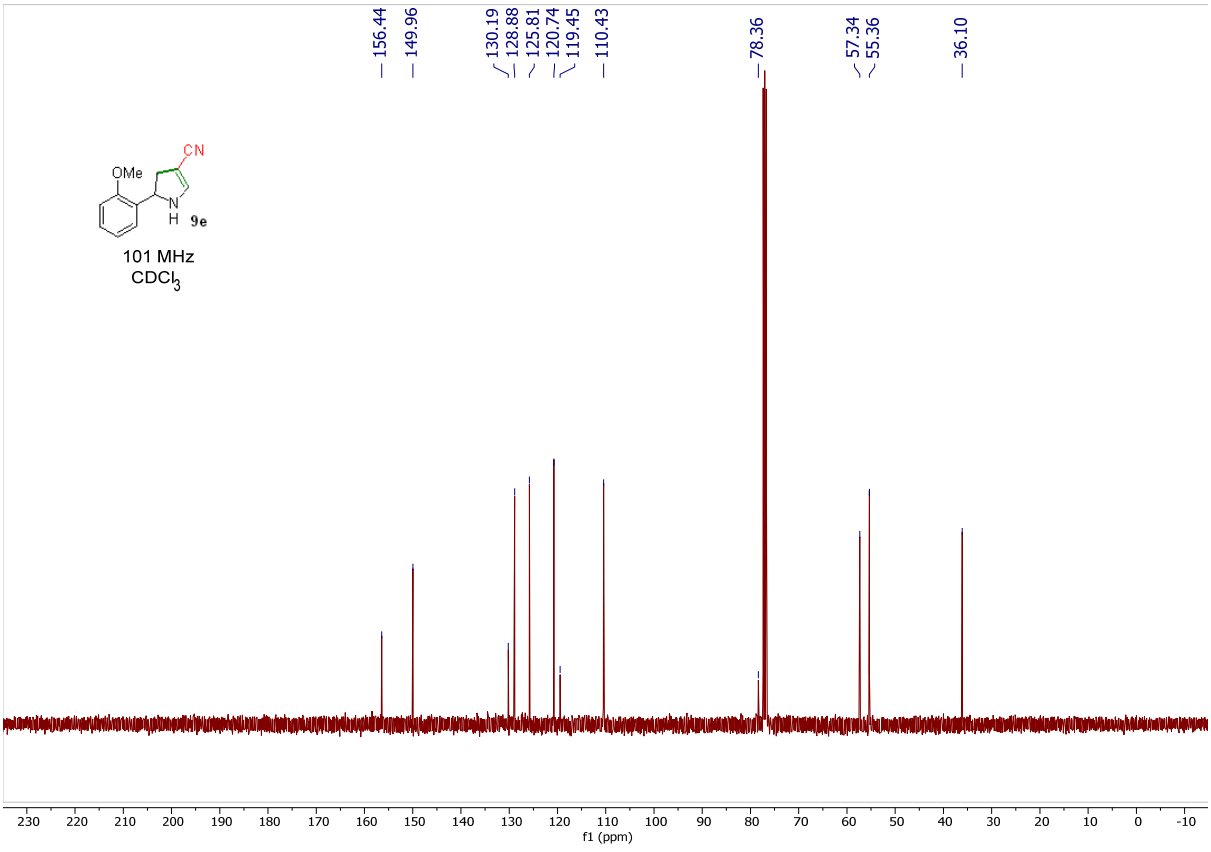
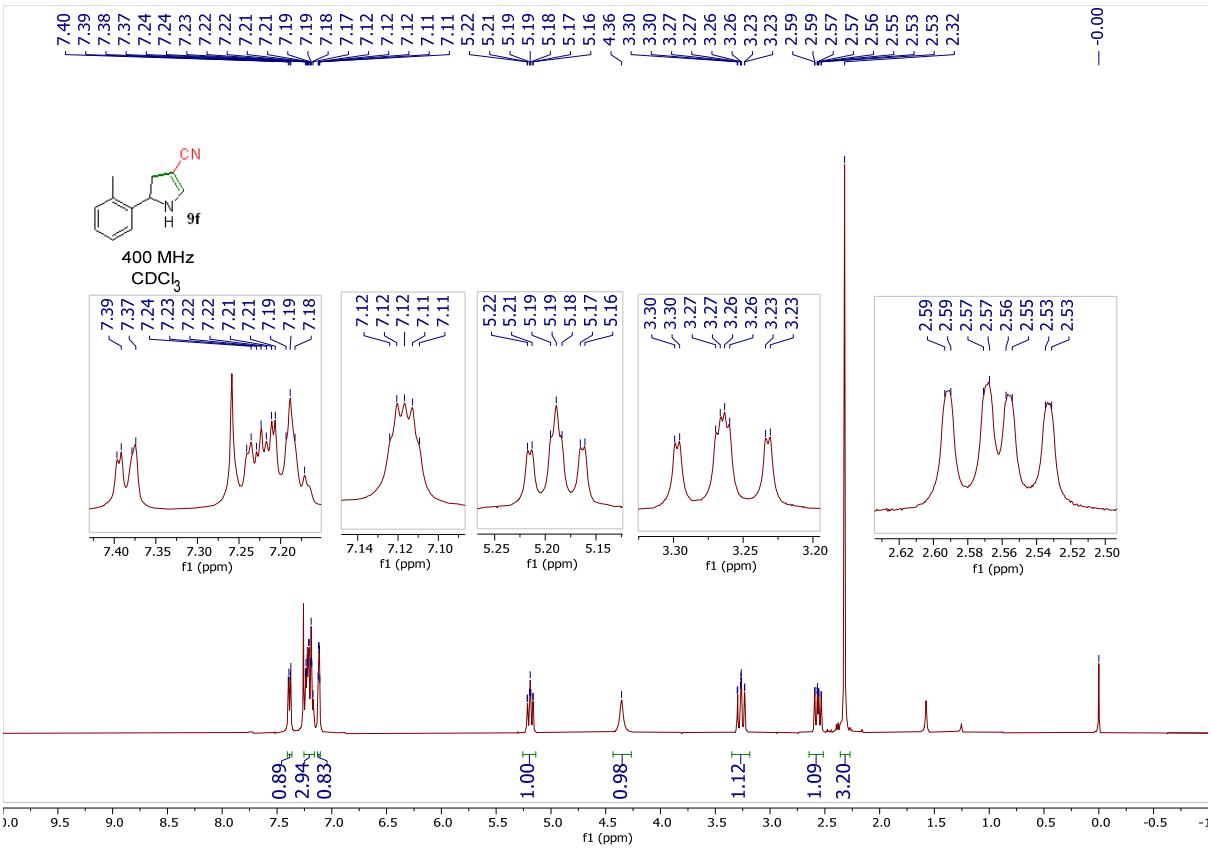
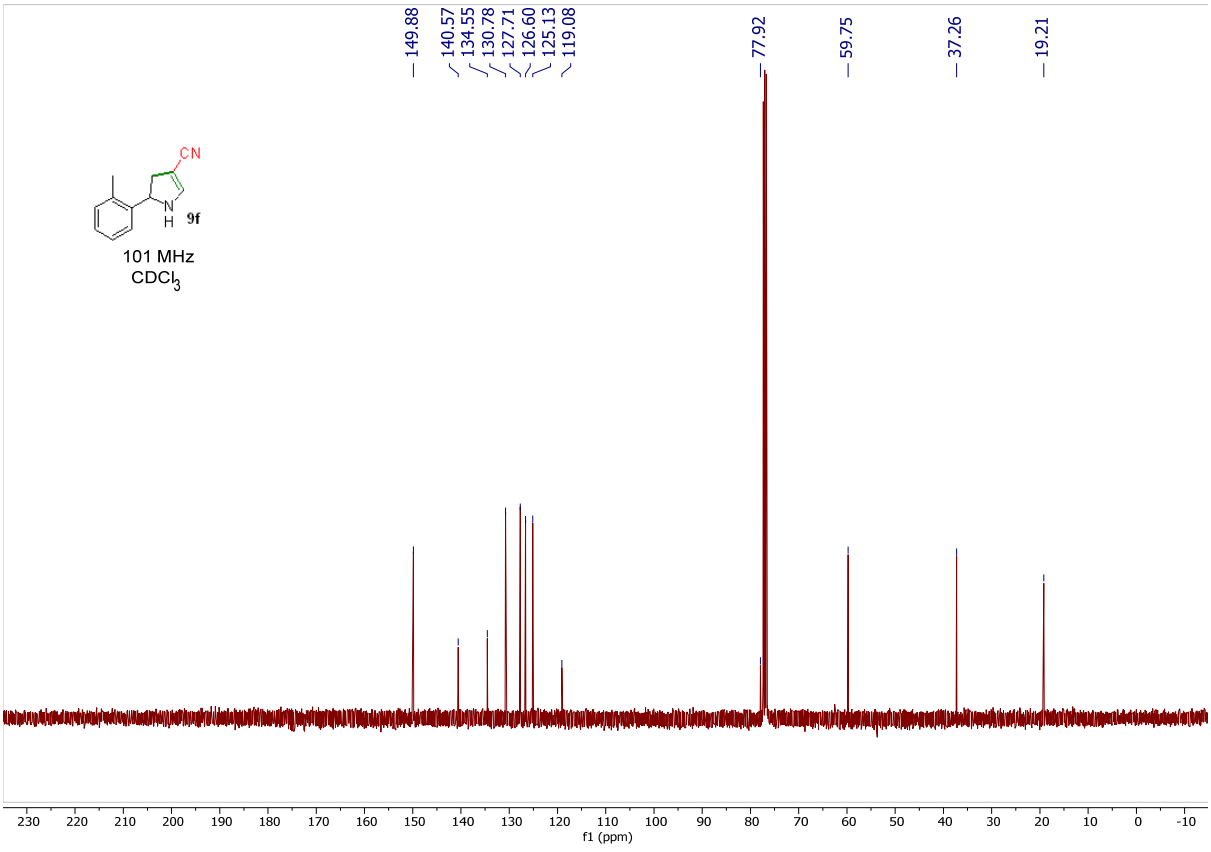
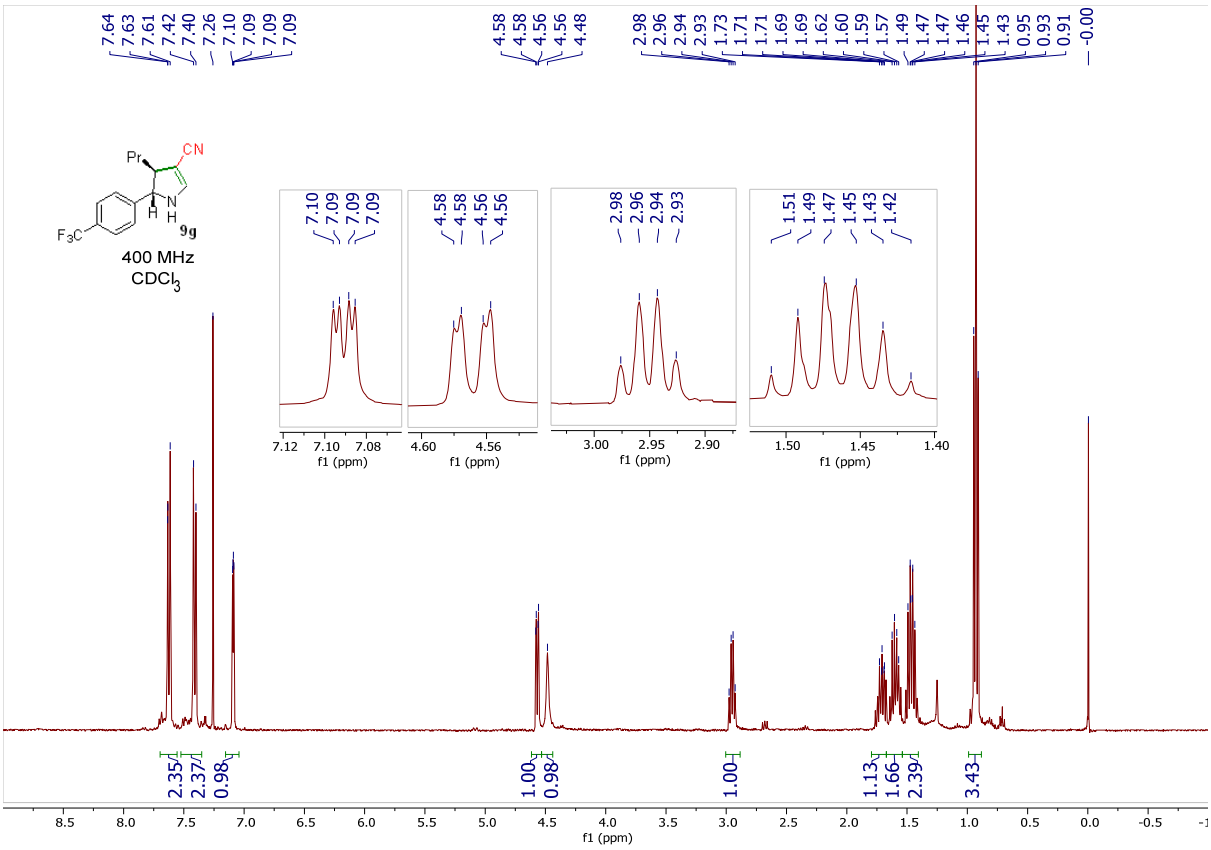
CN
H
9e
400 MHz
CDCl3
f1 (ppm)


OMe
CN
H
9e
101 MHz
CDCl3
f1 (ppm)


9f
400 MHz
CDCl3
f1 (ppm)


9f
101 MHz
CDCl3
f1 (ppm)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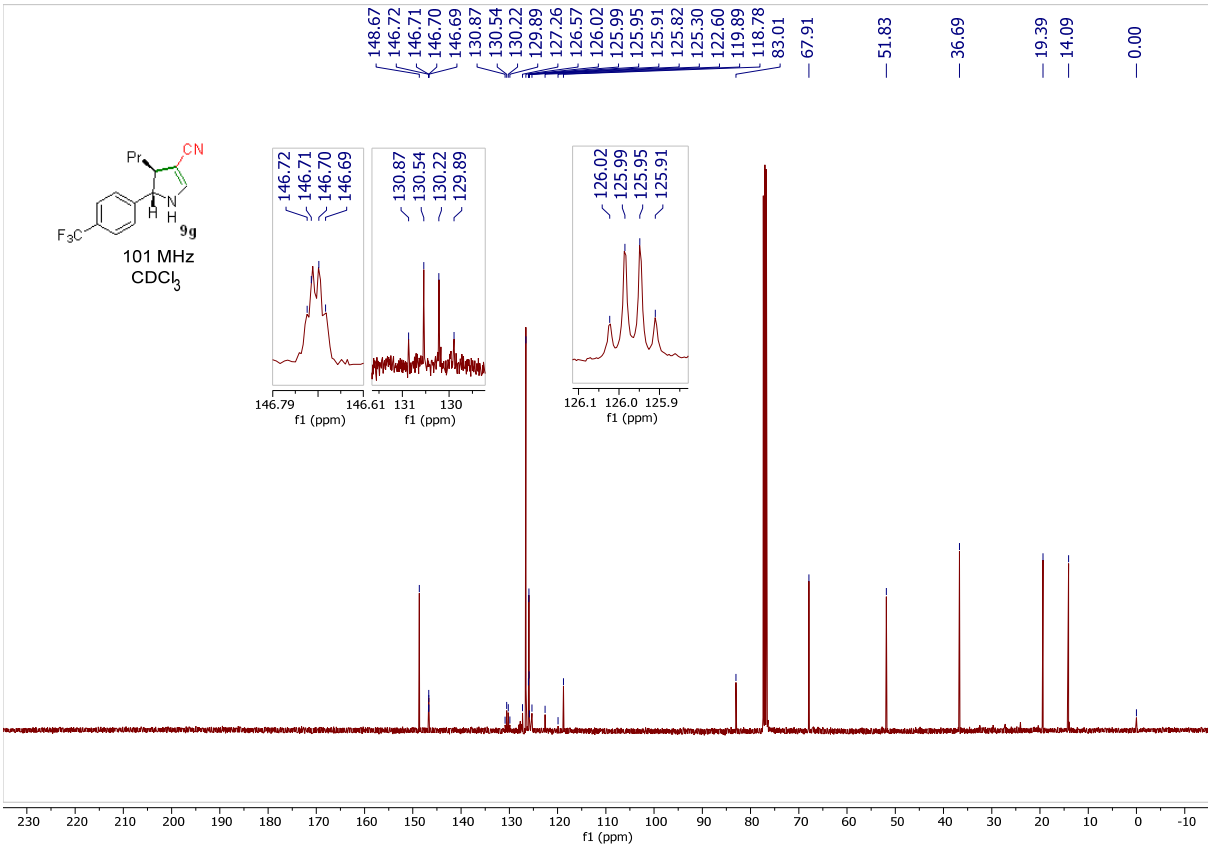
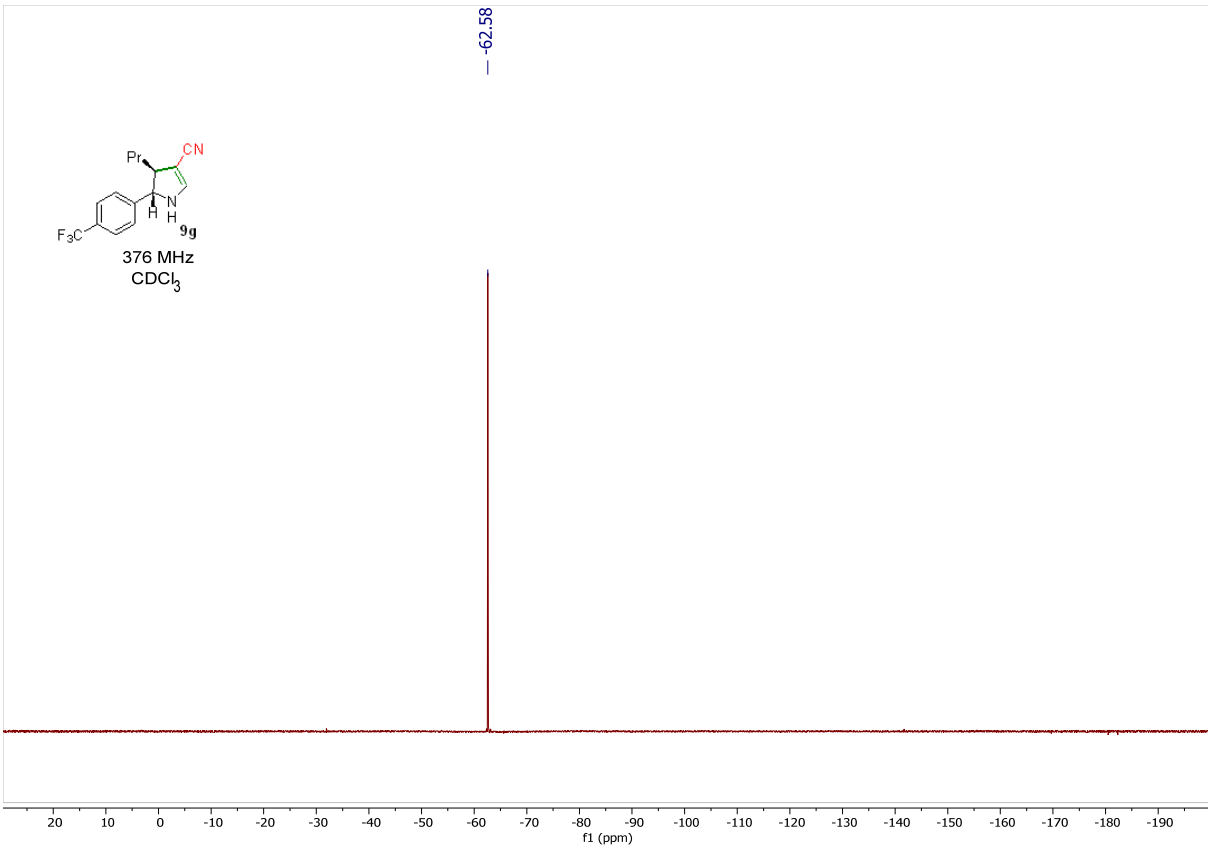
9g
f1 (ppm)


101 MHz
CDCl3
9g
f1 (ppm)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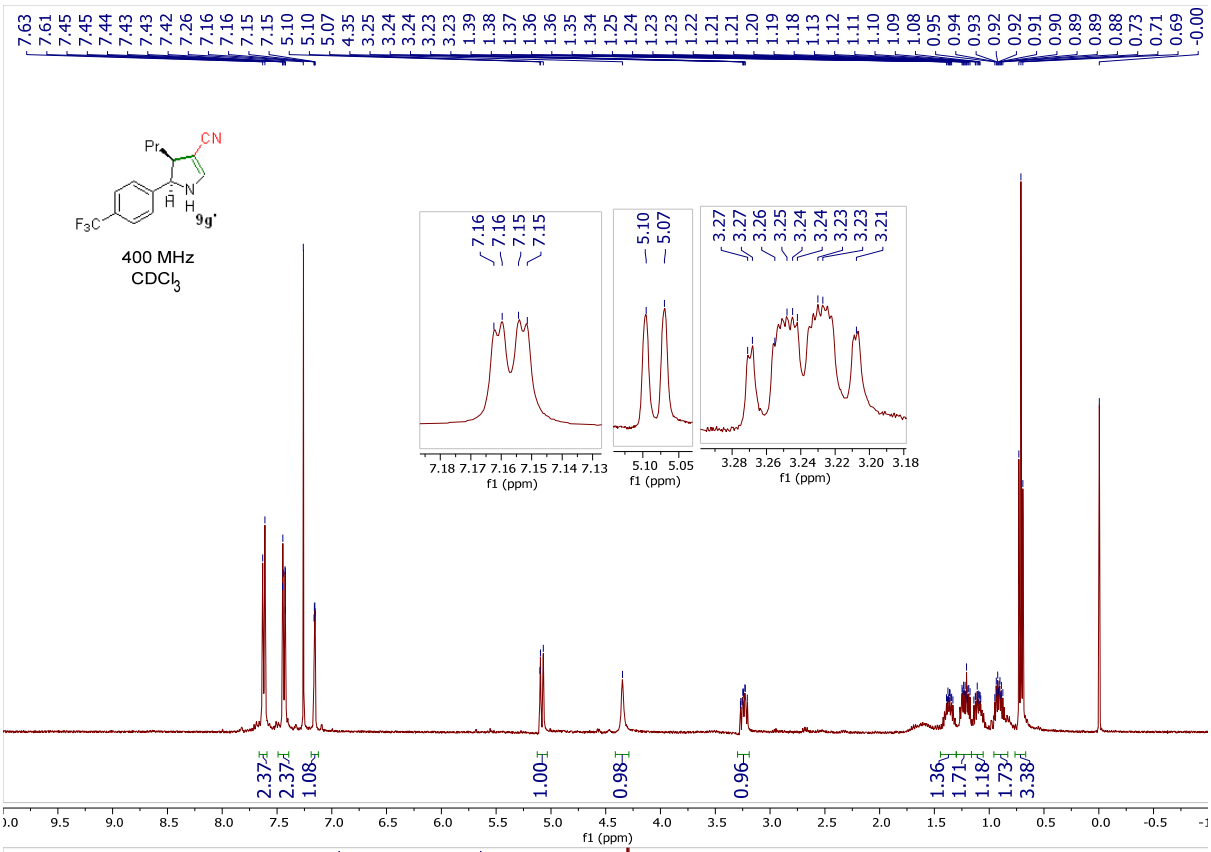
Pr
CN
N
H
H
F3C
9g
376 MHz
CDCl3
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)


9g'
400 MHz
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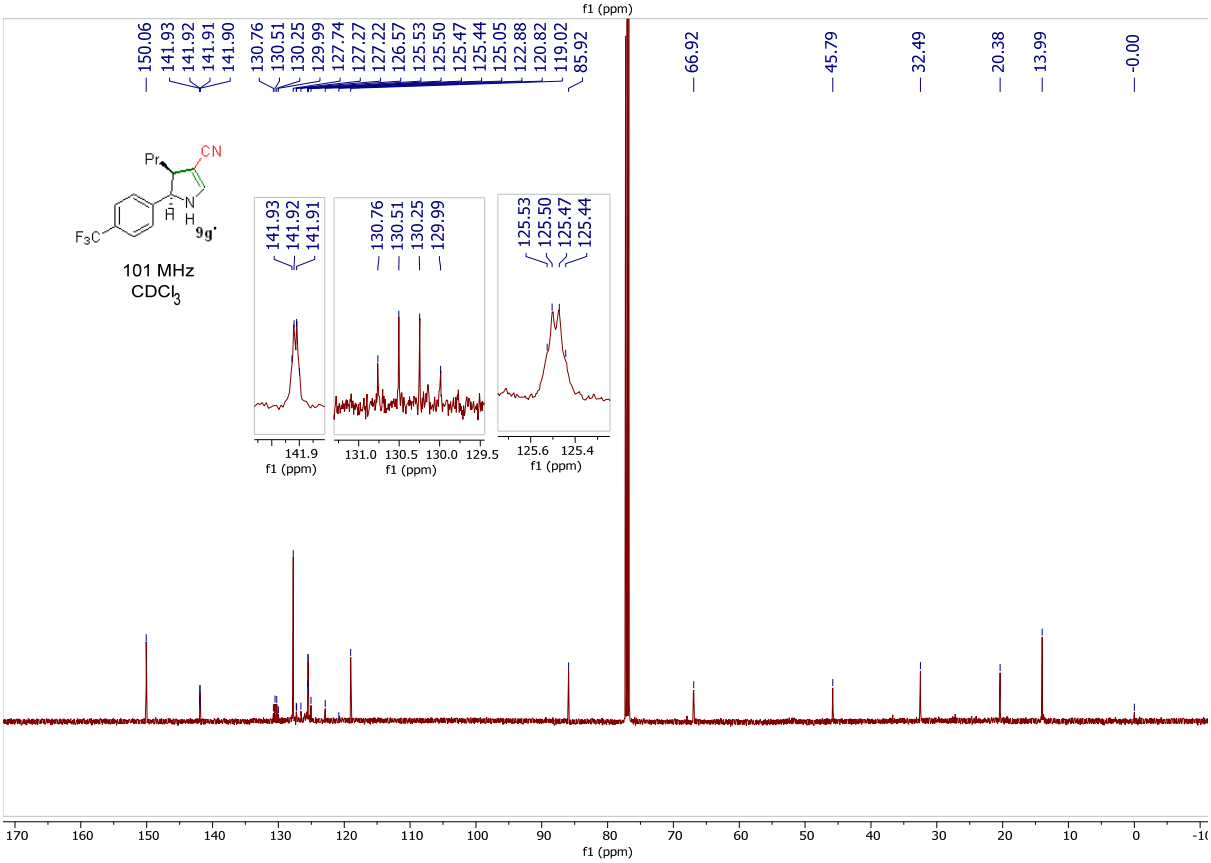
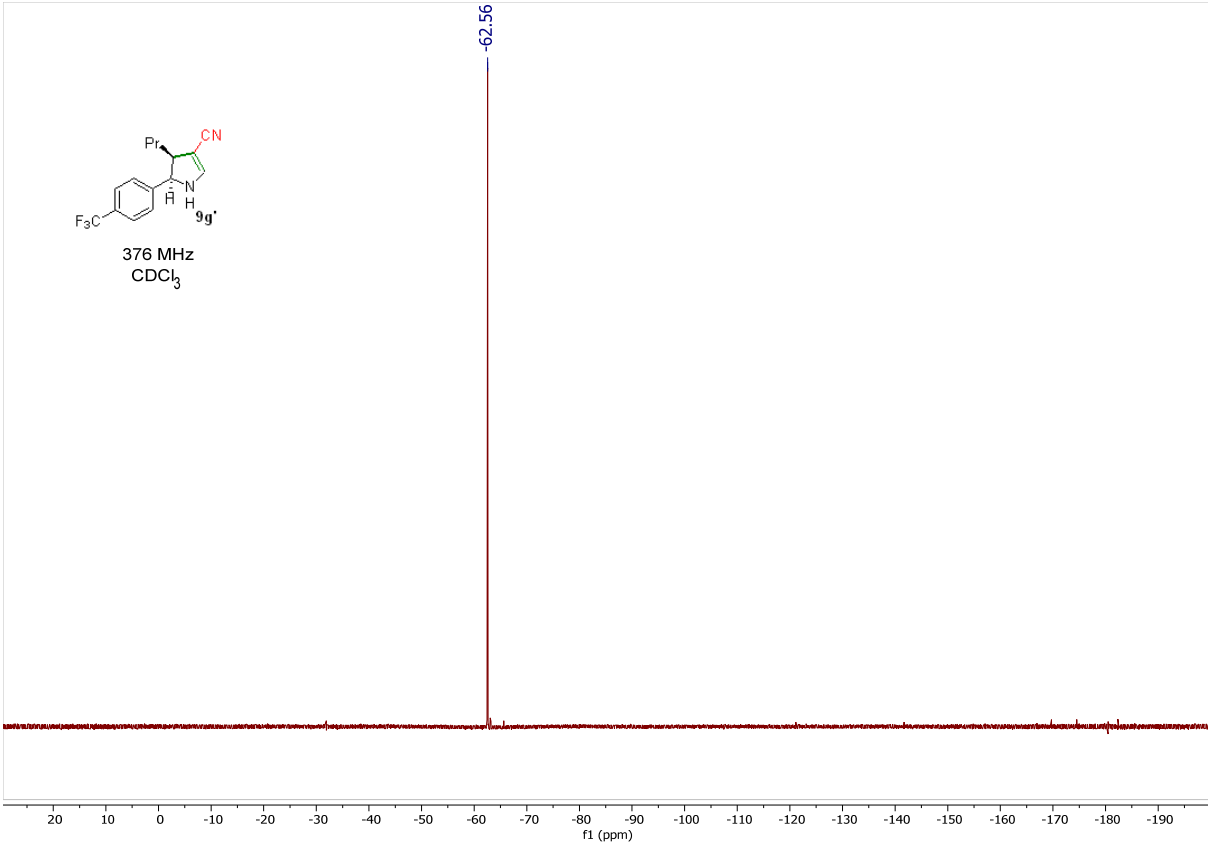
f1 (ppm)


9g'
101 MHz
CDCl3
f1 (ppm)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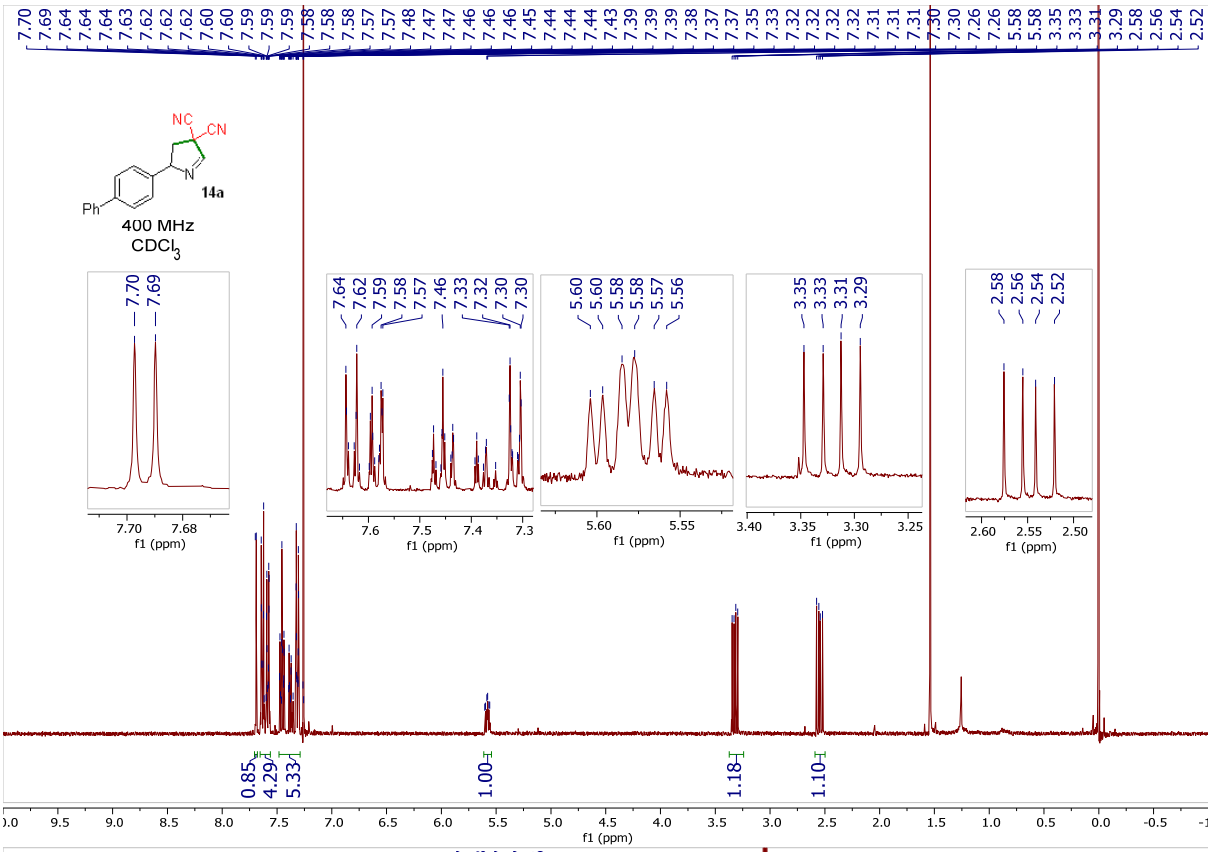
Pr
CN
H
N
H
F3C
9g'
376 MHz
CDCl3
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)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400 MHz
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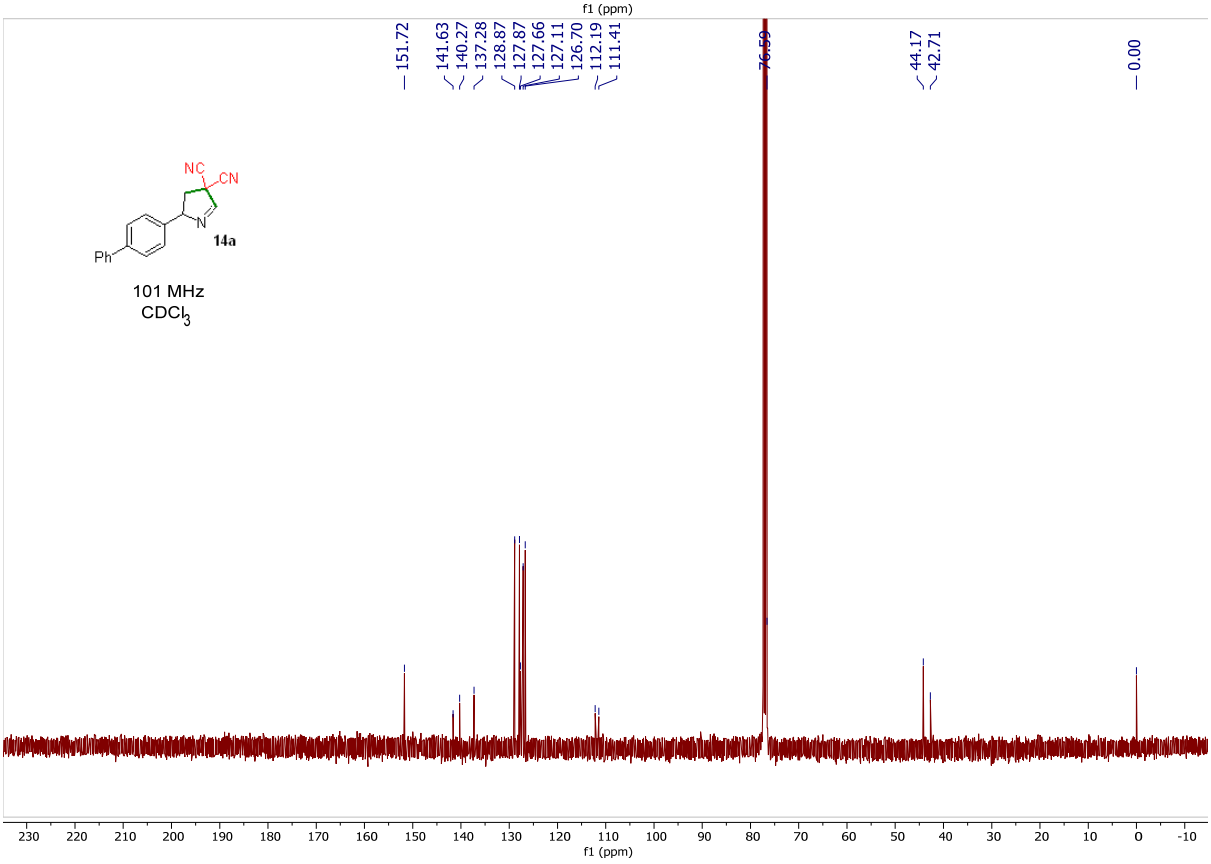
f1 (ppm)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101 MHz
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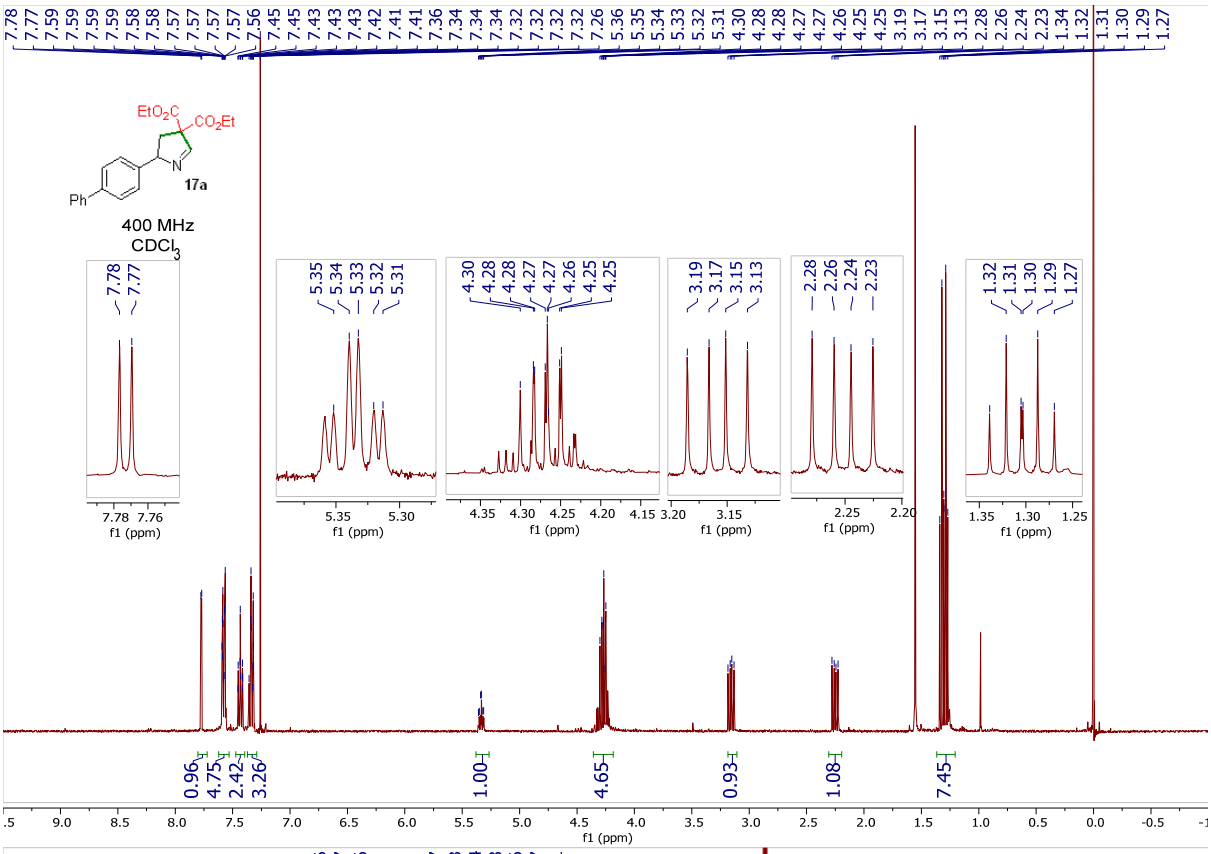
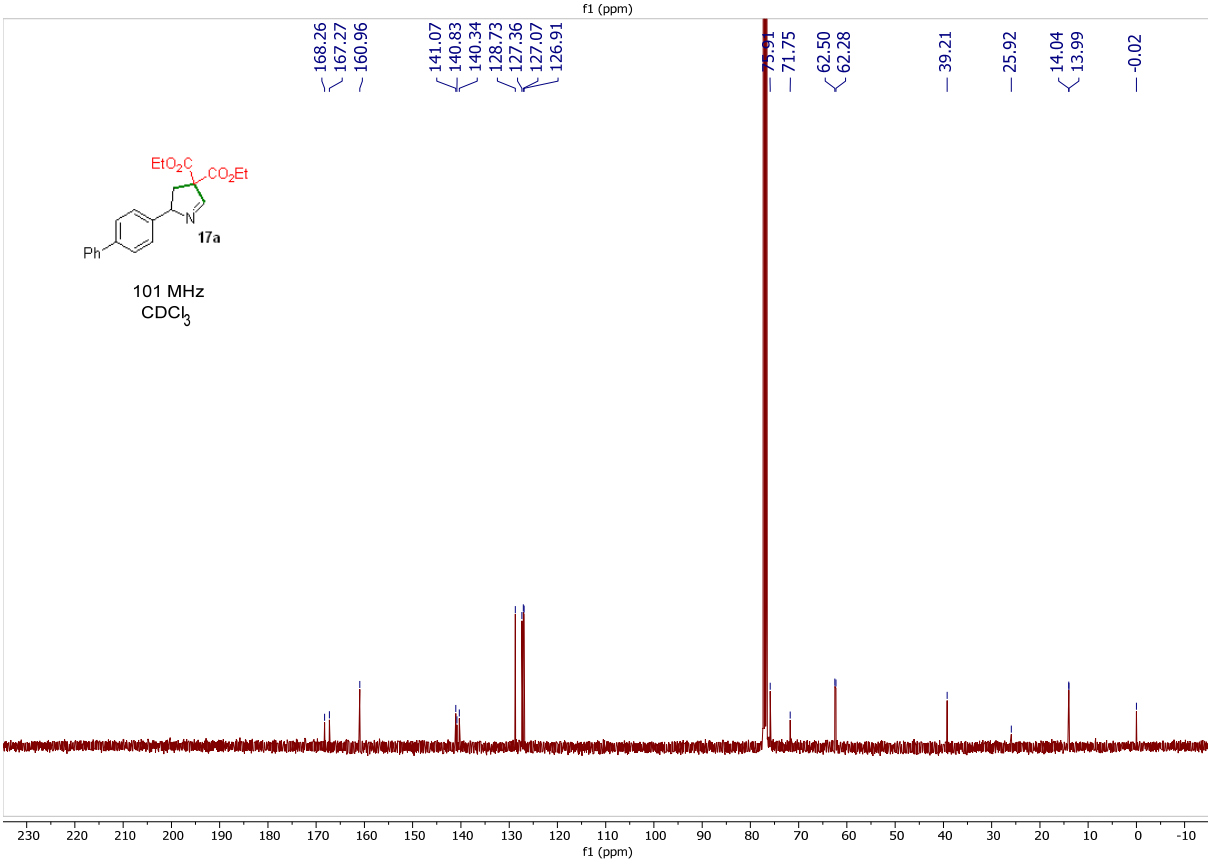
f1 (ppm)


EtO2C
CO2Et
N
Ph
17a
400 MHz
CDCl3
f1 (ppm)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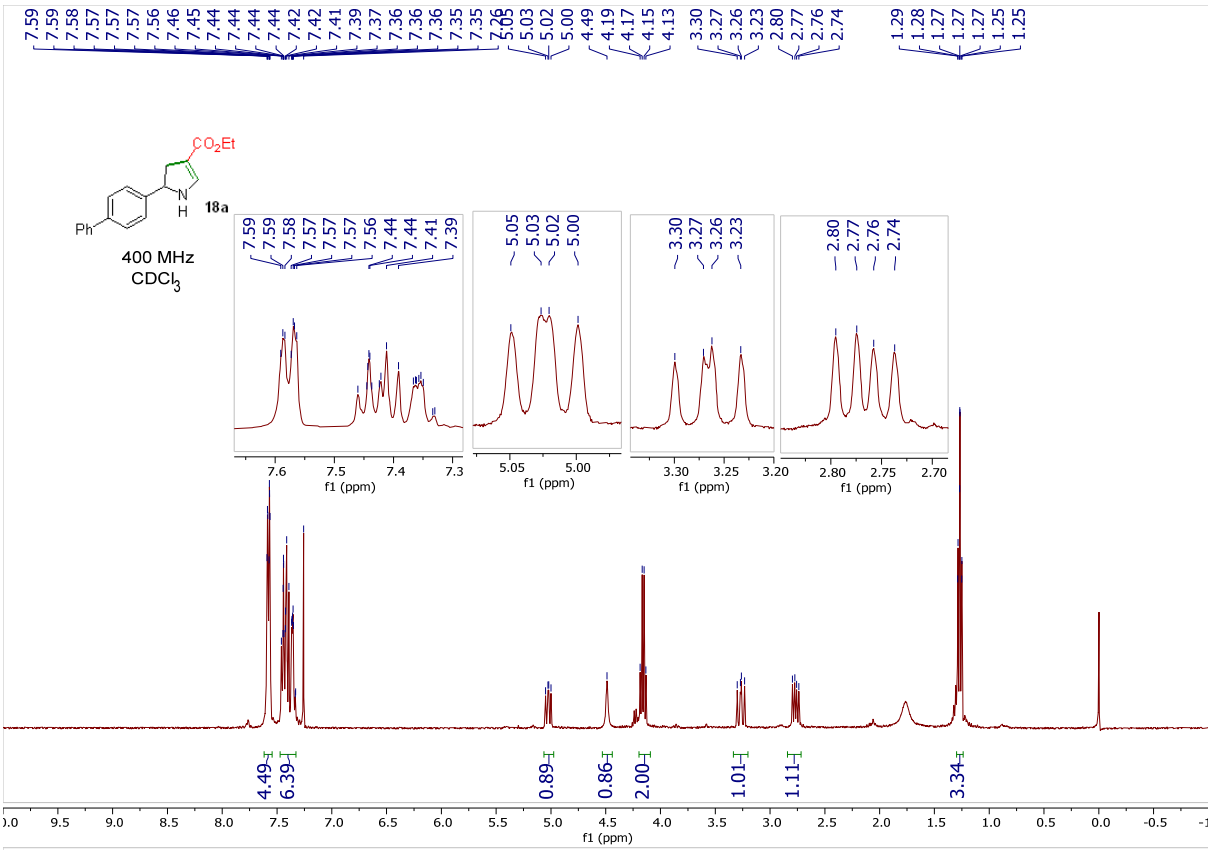
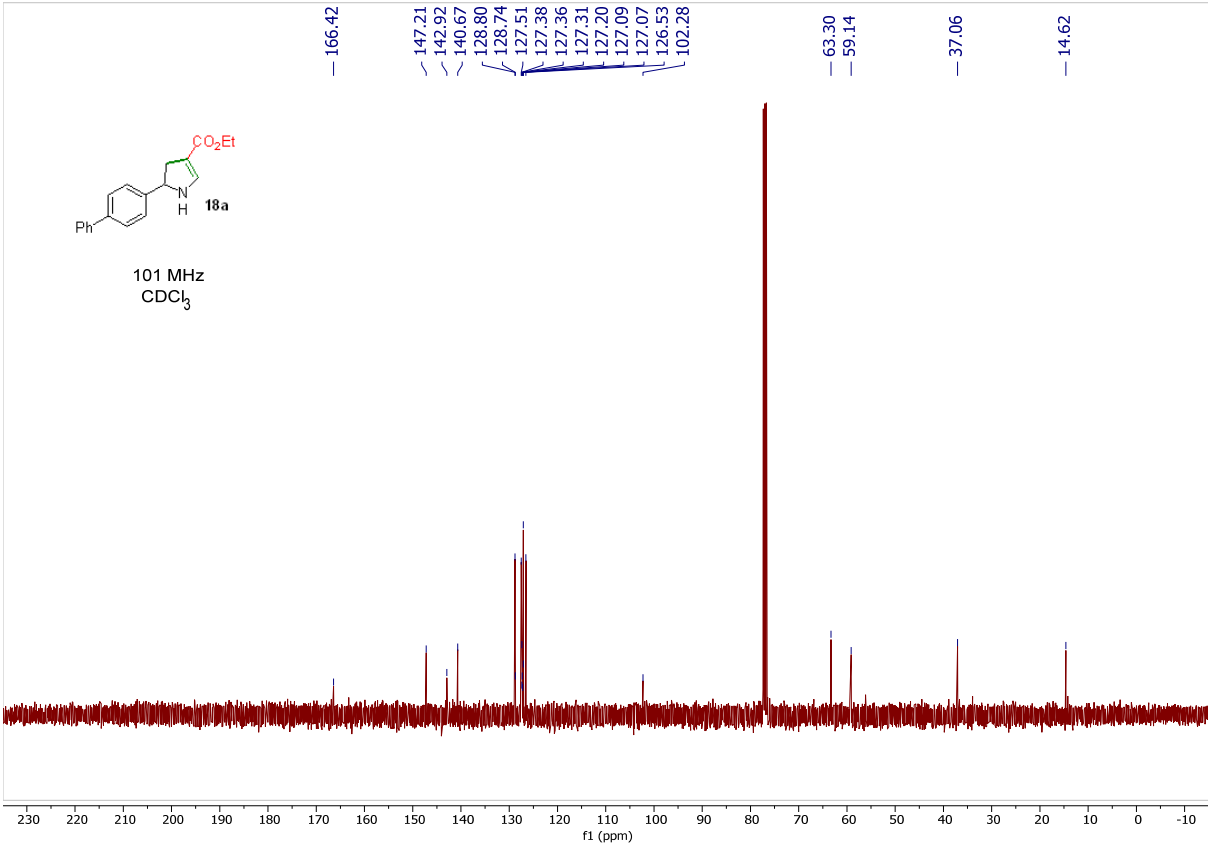
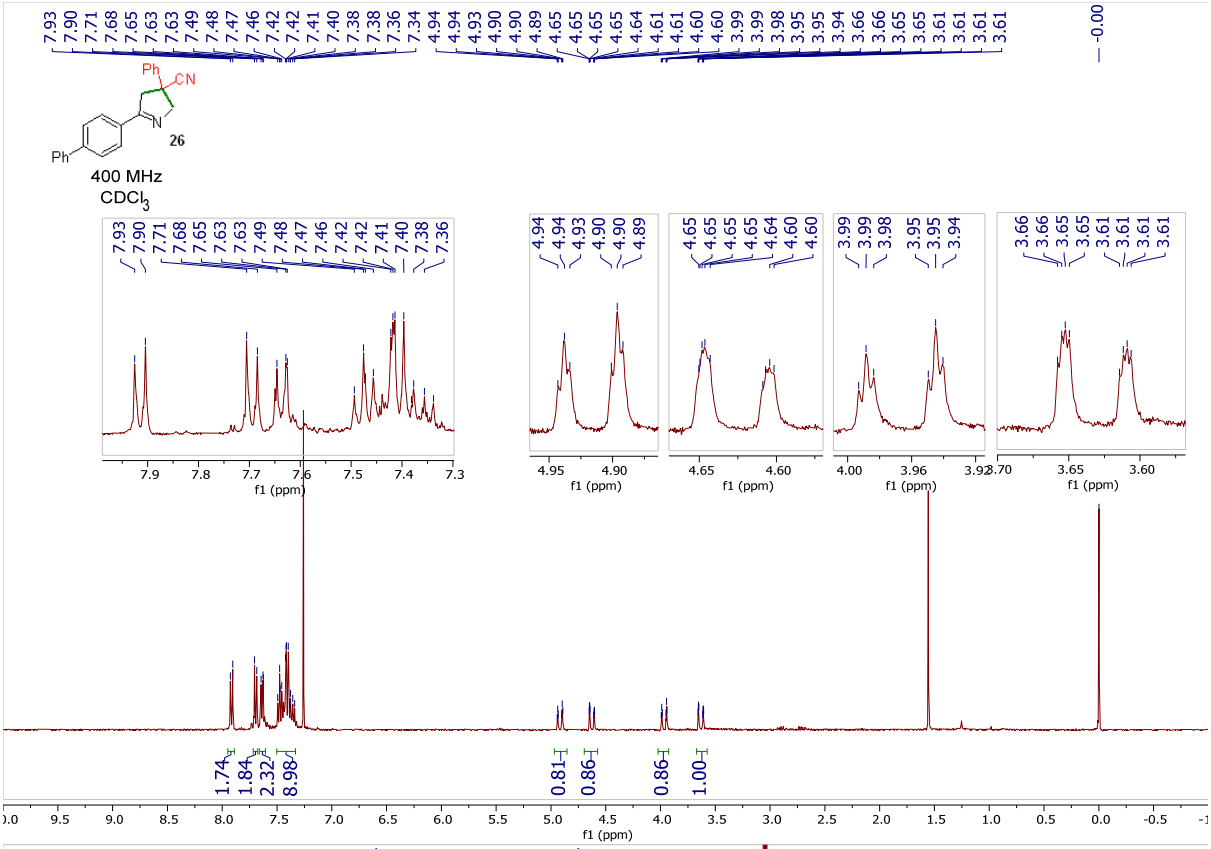
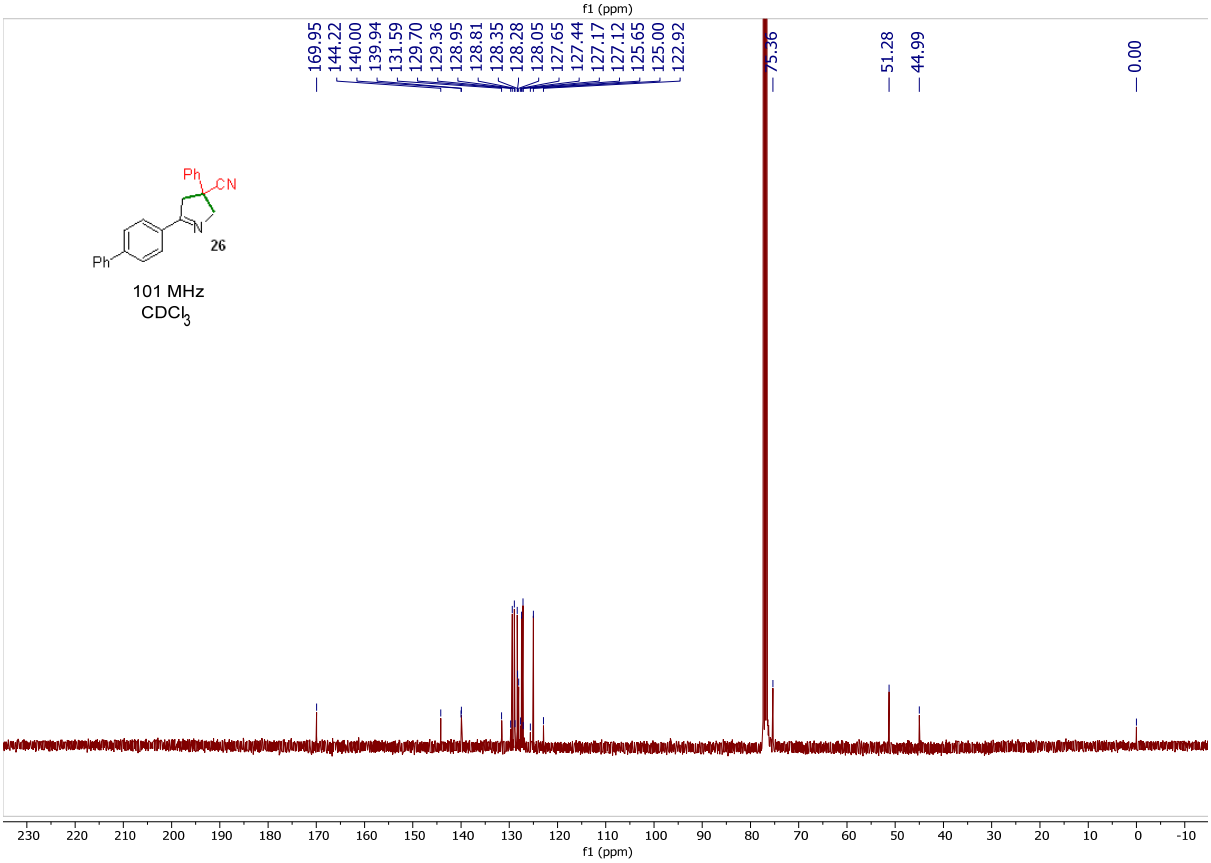
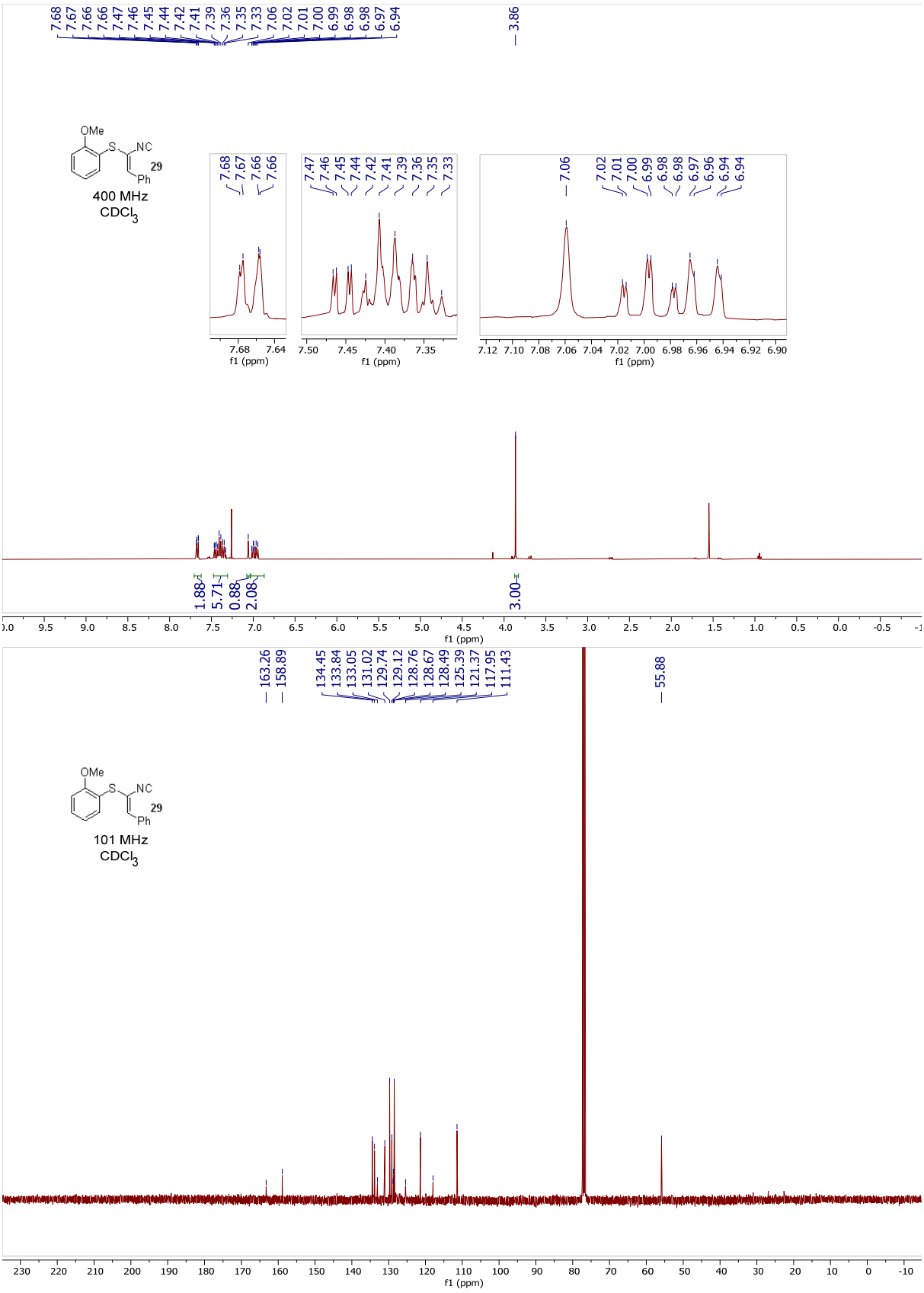
CO2Et
N
Ph
17a
101 MHz
CDCl3
f1 (ppm)

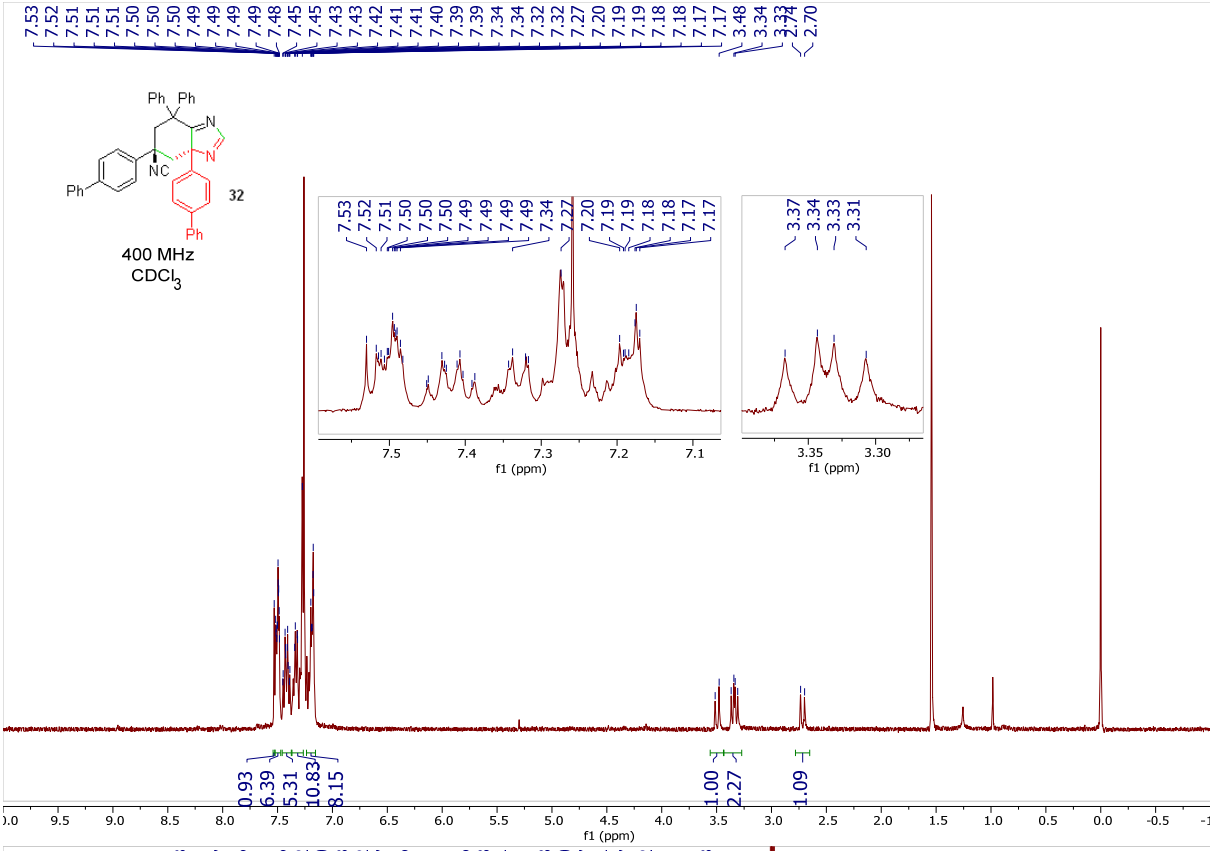

7.59 7.59 7.58 7.57 7.57 7.57 7.56 7.46 7.45 7.44 7.44 7.44 7.44 7.42 7.42 7.41 7.39 7.37 7.36 7.36 7.36 7.35 7.35 5.05 5.03 5.02 5.00 4.49 4.19 4.17 4.15 4.13 3.30 3.27 3.26 3.23 2.80 2.77 2.76 2.74 1.29 1.28 1.27 1.27 1.27 1.25 1.25
CO2Et
N
H
Ph
18a
400 MHz
CDCl3
f1 (ppm)
4.49 6.39 0.89 0.86 2.00 1.01 1.11 3.34

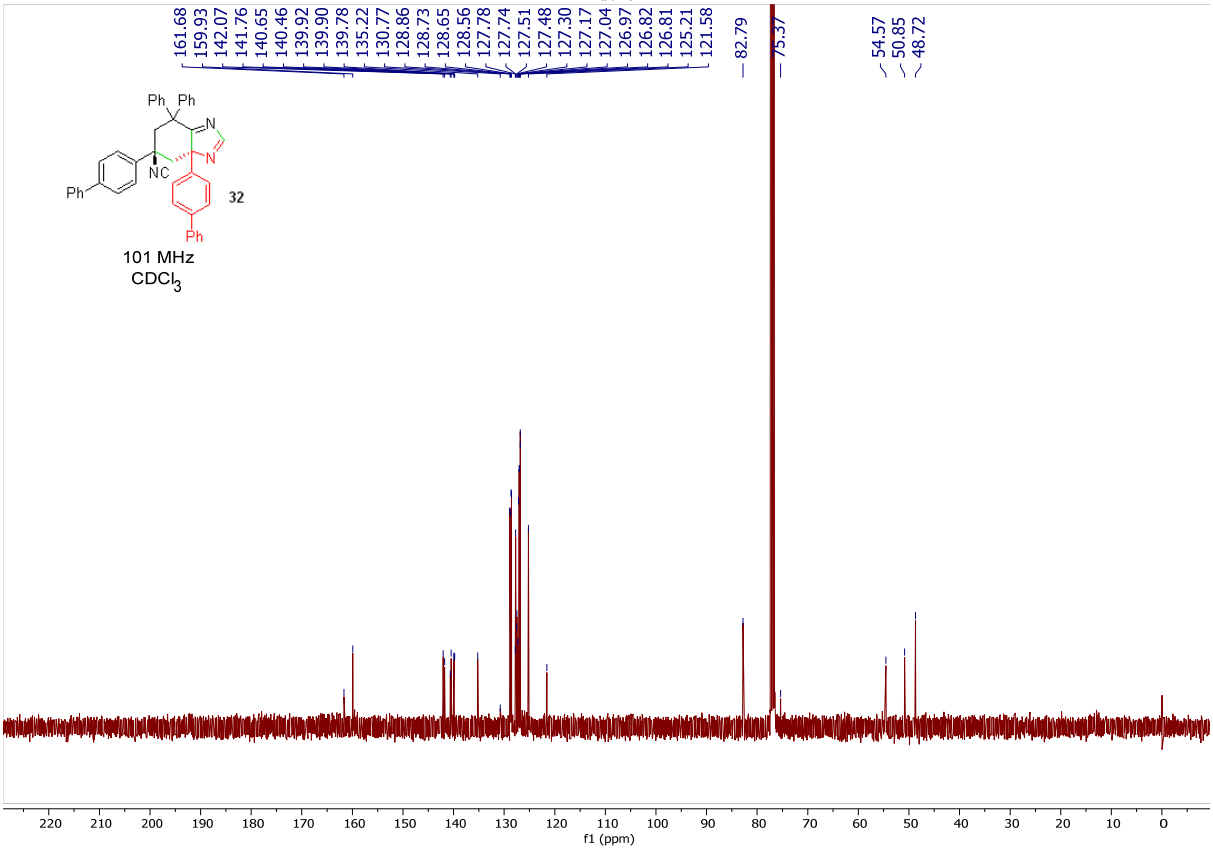

166.42 147.21 142.92 140.67 128.80 128.74 127.51 127.38 127.36 127.31 127.20 127.09 127.07 126.53 102.28 63.30 59.14 37.06 14.62
CO2Et
N
H
Ph
18a
101 MHz
CDCl3
f1 (ppm)

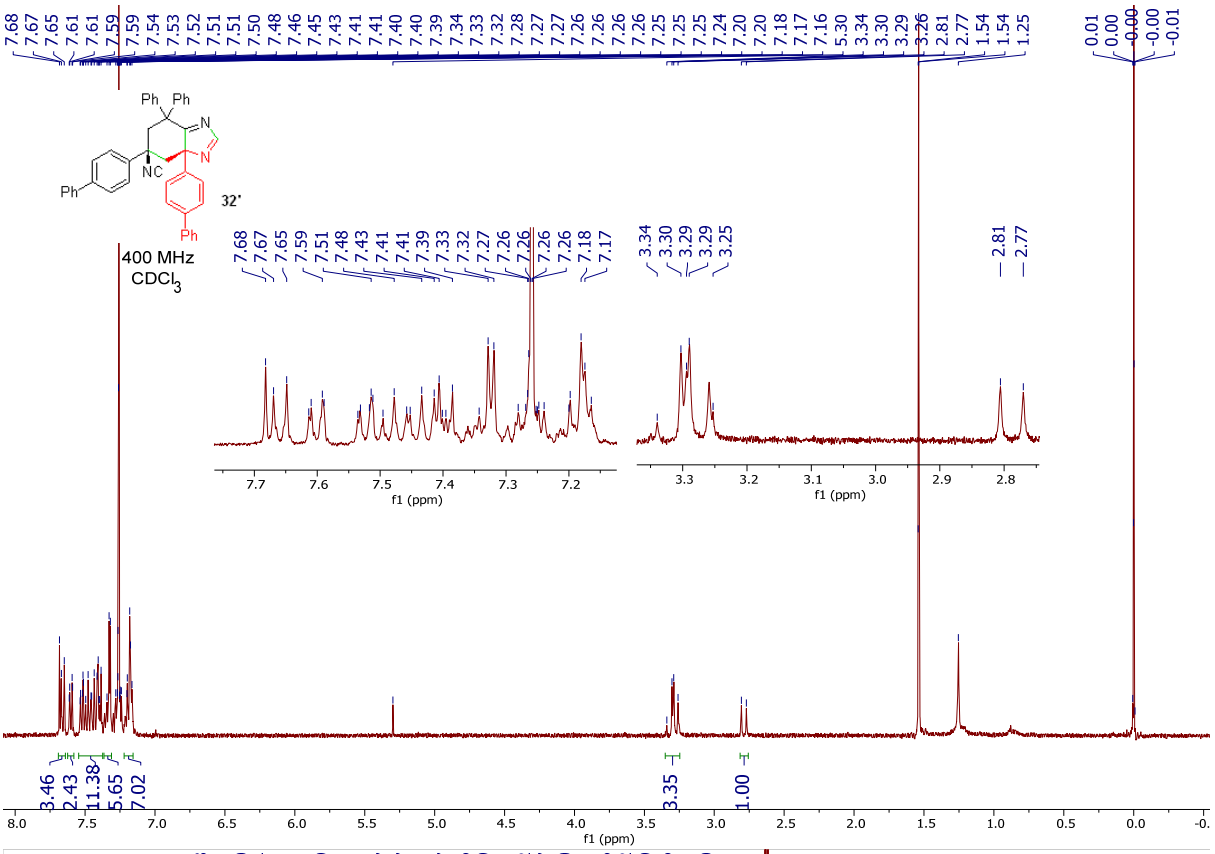

26
400 MHz
CDCl3
f1 (ppm)

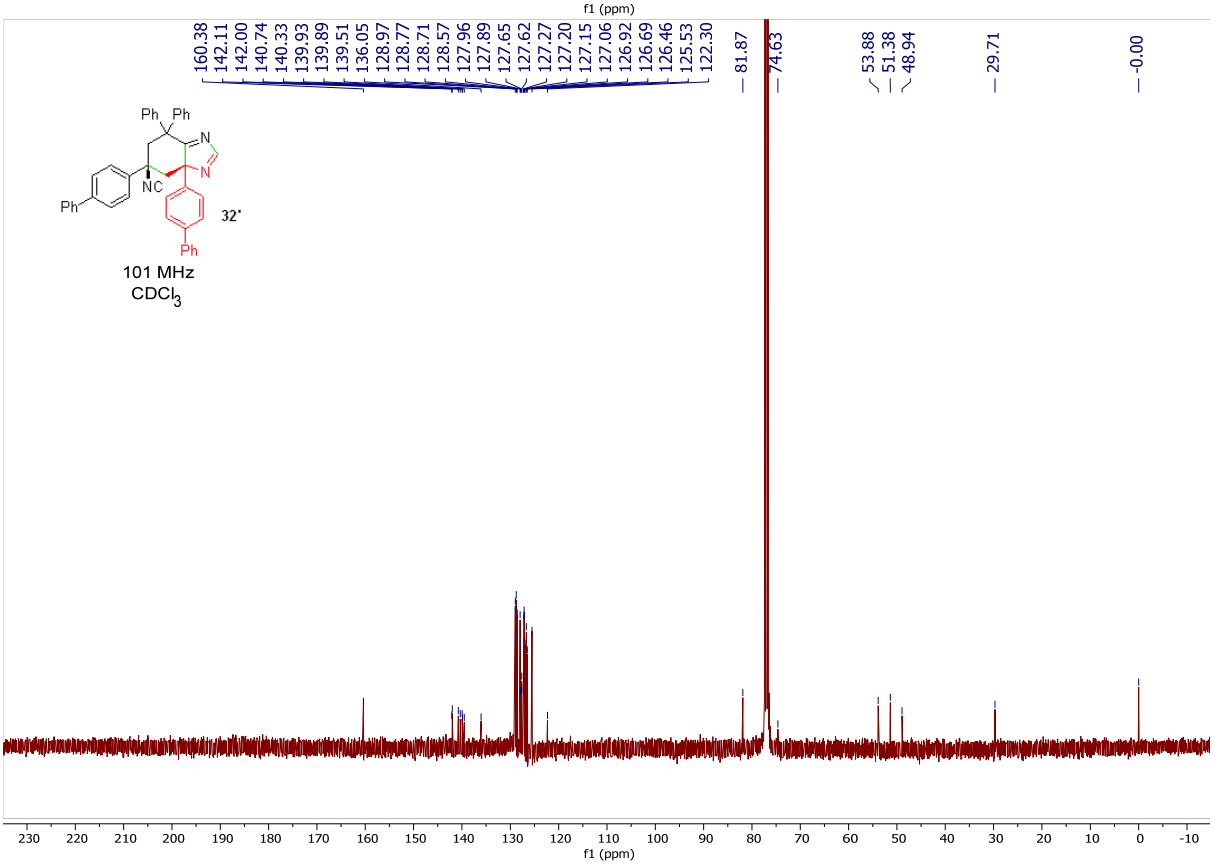

26
101 MHz
CDCl3
f1 (ppm)


OMe
S
NC
29
Ph
400 MHz
CDCl3
7.68
7.67
7.66
7.66
7.47
7.46
7.45
7.44
7.42
7.41
7.39
7.36
7.35
7.33
7.06
7.02
7.01
7.00
6.99
6.98
6.98
6.97
6.94
3.86
f1 (ppm)
1.88
5.71
0.88
2.08
3.00
163.26
158.89
134.45
133.84
133.05
131.02
129.74
129.12
128.76
128.67
128.49
125.39
121.37
117.95
111.43
55.88
101 MHz
CDCl3

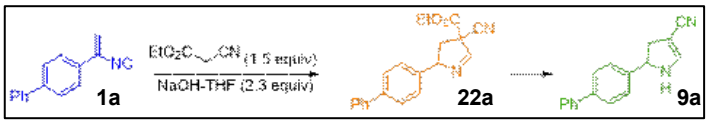

Ph Ph
N
NC
N
Ph
Ph
32
400 MHz
CDCl3
f1 (ppm)
f1 (ppm)
f1 (ppm)


Ph Ph
N
NC
N
Ph
Ph
32
101 MHz
CDCl3
f1 (ppm)


400 MHz
CDCl3
32'
f1 (ppm)


101 MHz
CDCl3
32'
f1 (ppm)

^{1}H NMR Reaction Monitoring



Ethyl cyanoacetate (24 µL, 0.2 mmol) was rapidly added, at t = 0, to a rt NaOH-THF stock solution (4.9 mL, 0.04 M, 0.2 mmol) of 4-(1-isocyanovinyl)-1,1'-biphenyl (30 mg, 0.15 mmol). Aliquots were removed at 5, 15, 30, 60, 130, and 370 min to which was added sat. aqueous NH_4Cl (1 mL). The samples were extracted with CH_2Cl_2 (3 x 1 mL), the combined organic phase was washed with water (1 x 3 mL) and then with brine (1 x 3 mL), and then the organic phase was dried over Na_2SO_4, filtered, and concentrated. The crude residue was then dissolved in 0.7 mL $CDCl_3$ and the ^{1}H NMR was collected for each of the time points.

Integration ratios of diagnostic ^{1}H NMR signals were compared to determine the mol fraction of each component using diagnostic signals as follows:

4-(1-isocyanovinyl)-1,1'-biphenyl: 5.85 (s, 1H).

ethyl 2-([1,1'-biphenyl]-4-yl)-4-cyano-3,4-dihydro-2H-pyrrole-4-carboxylate: 5.49 (ddd, J = 7.9, 7.3, 2.8 Hz, 1H)

5-([1,1'-Biphenyl]-4-yl)-4,5-dihydro-1H-pyrrole-3-carbonitrile: 5.01 (dd, *J* = 11.7, 9.0 Hz, 1H).

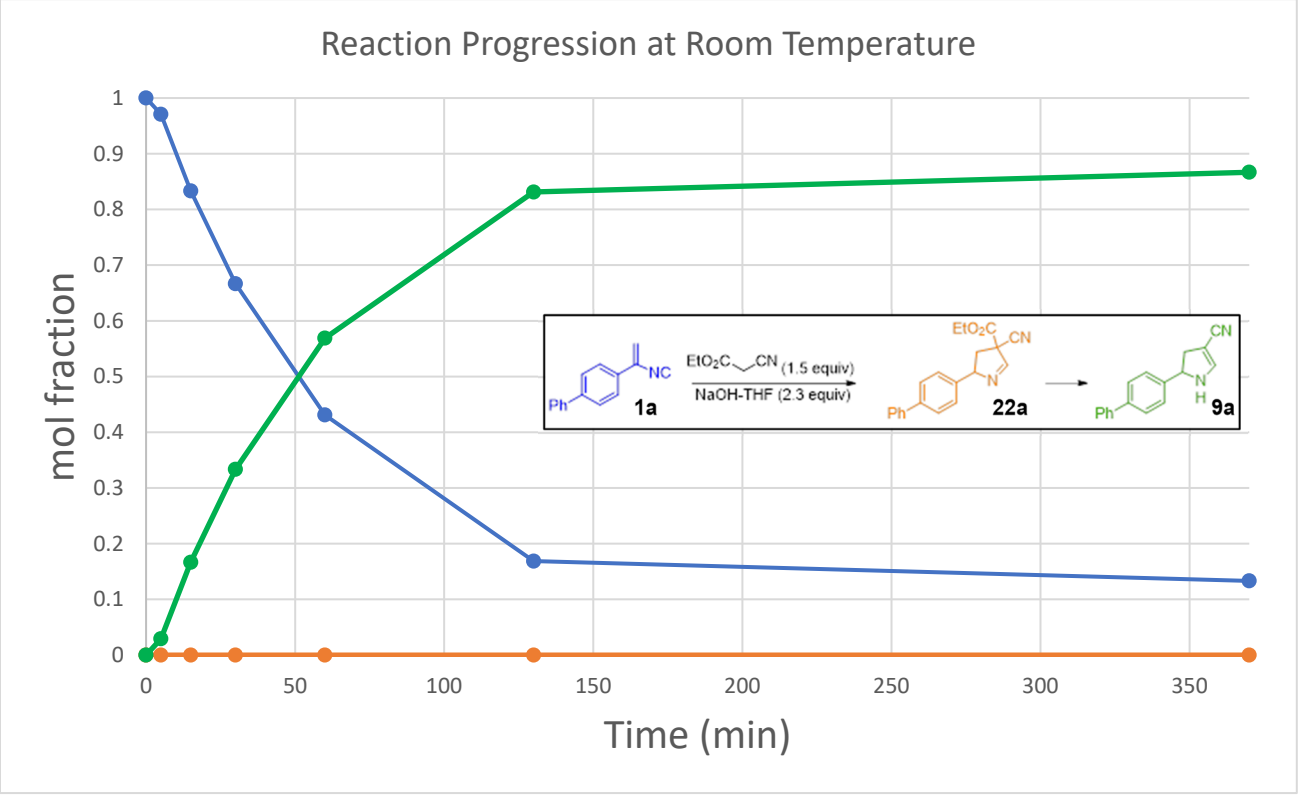
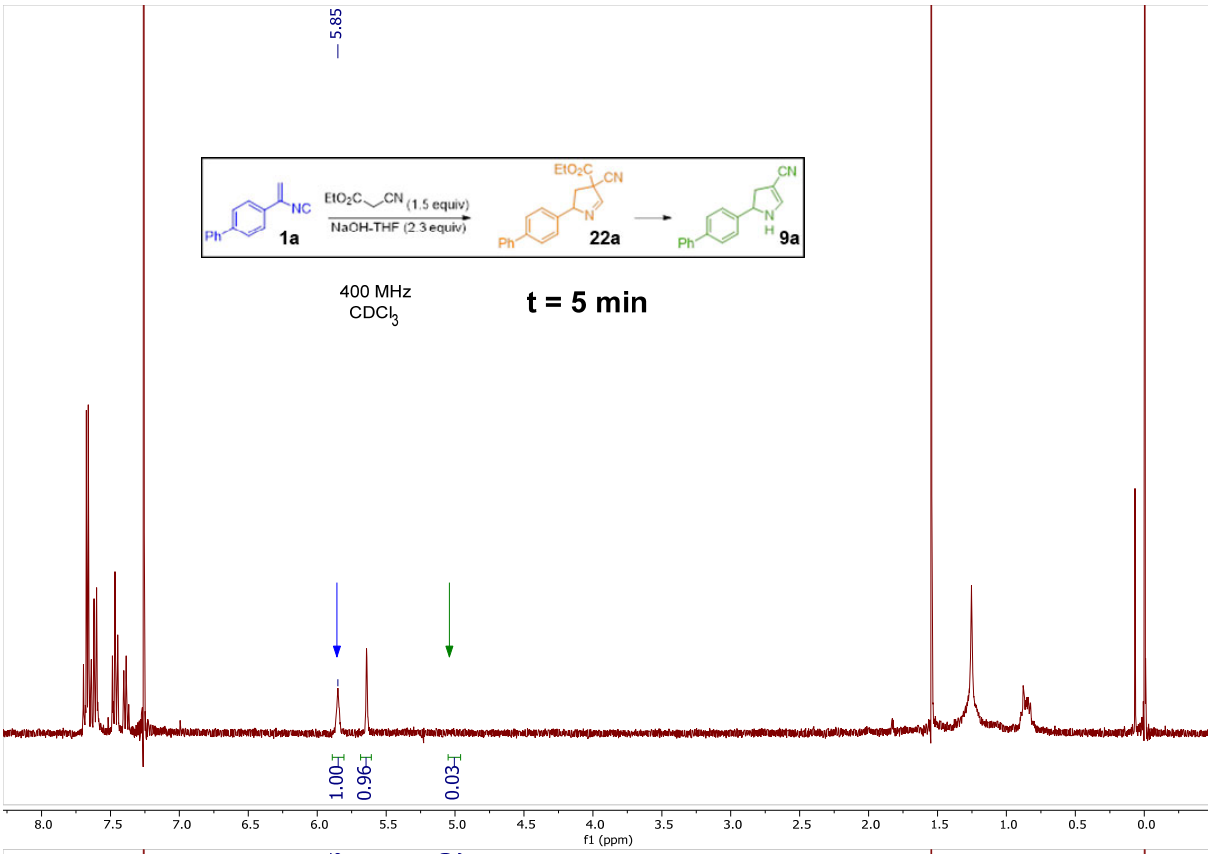
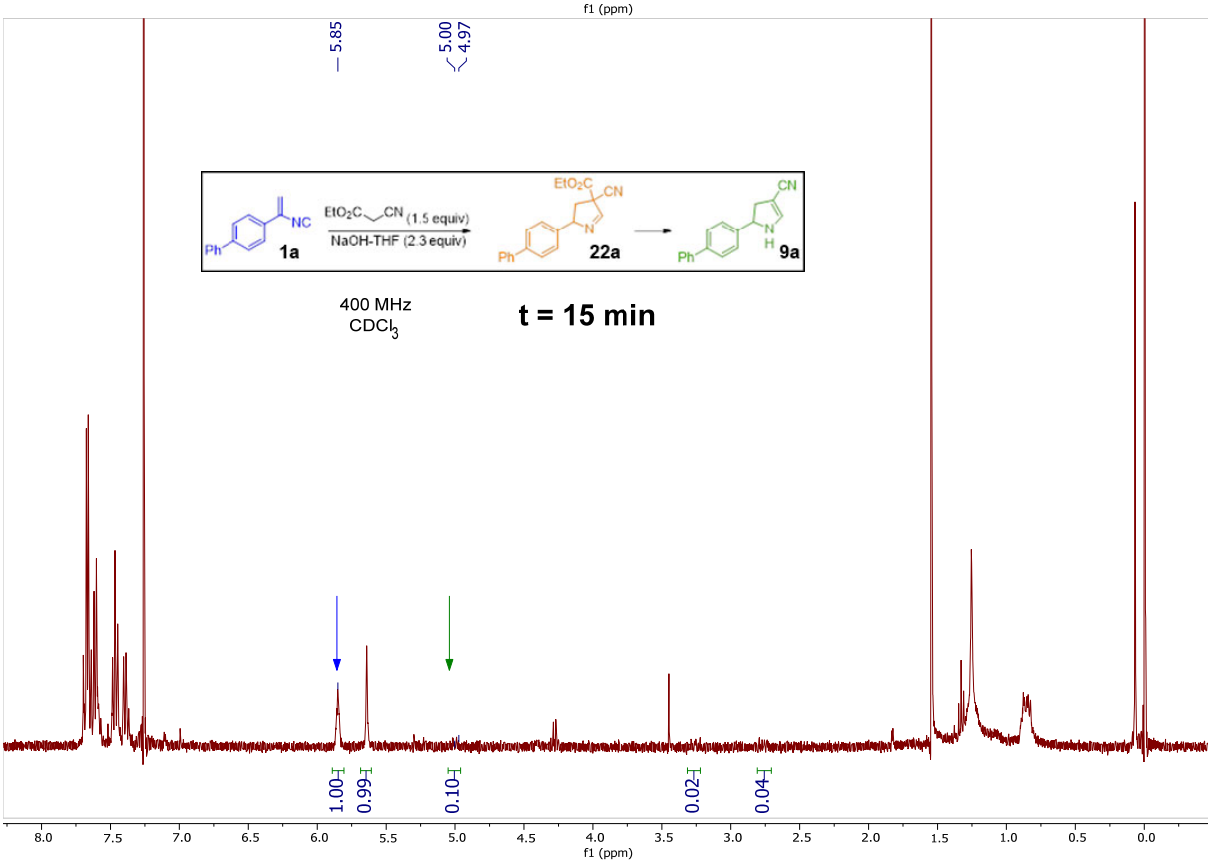
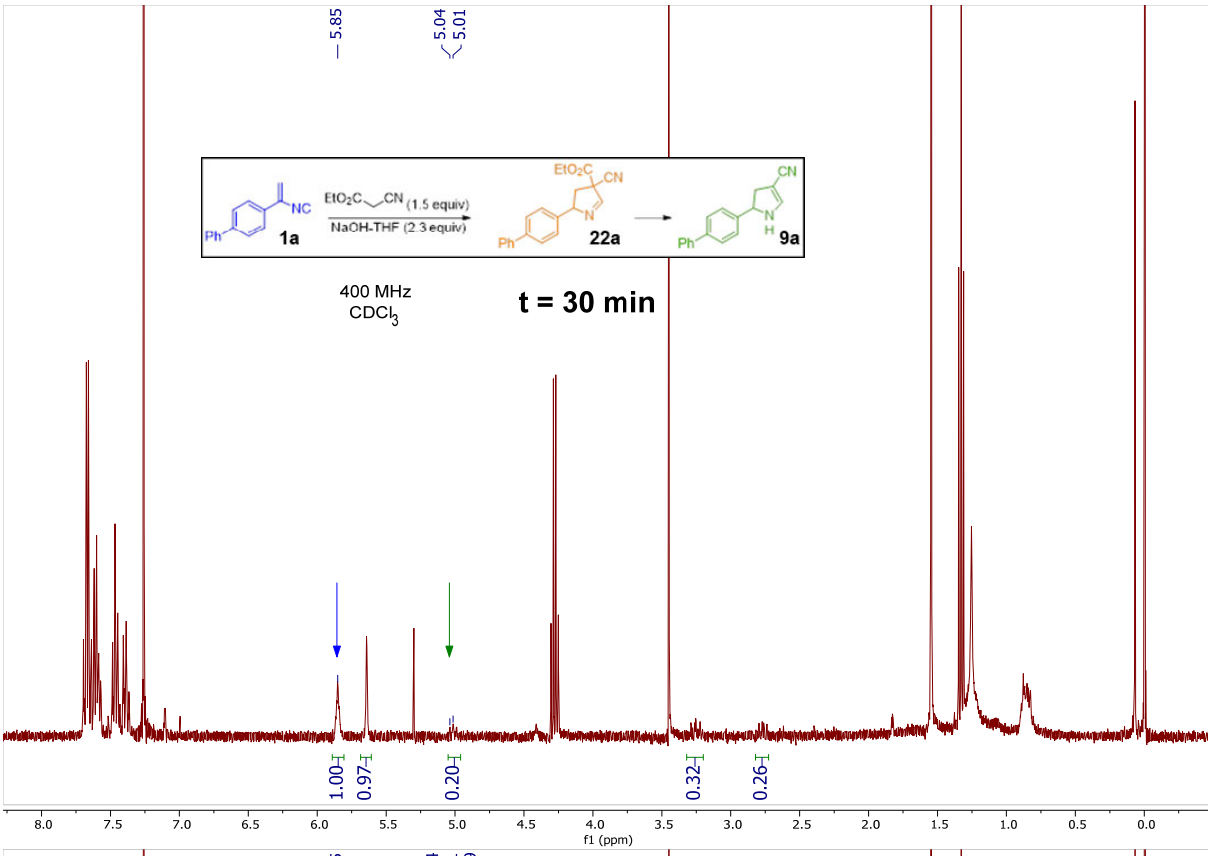


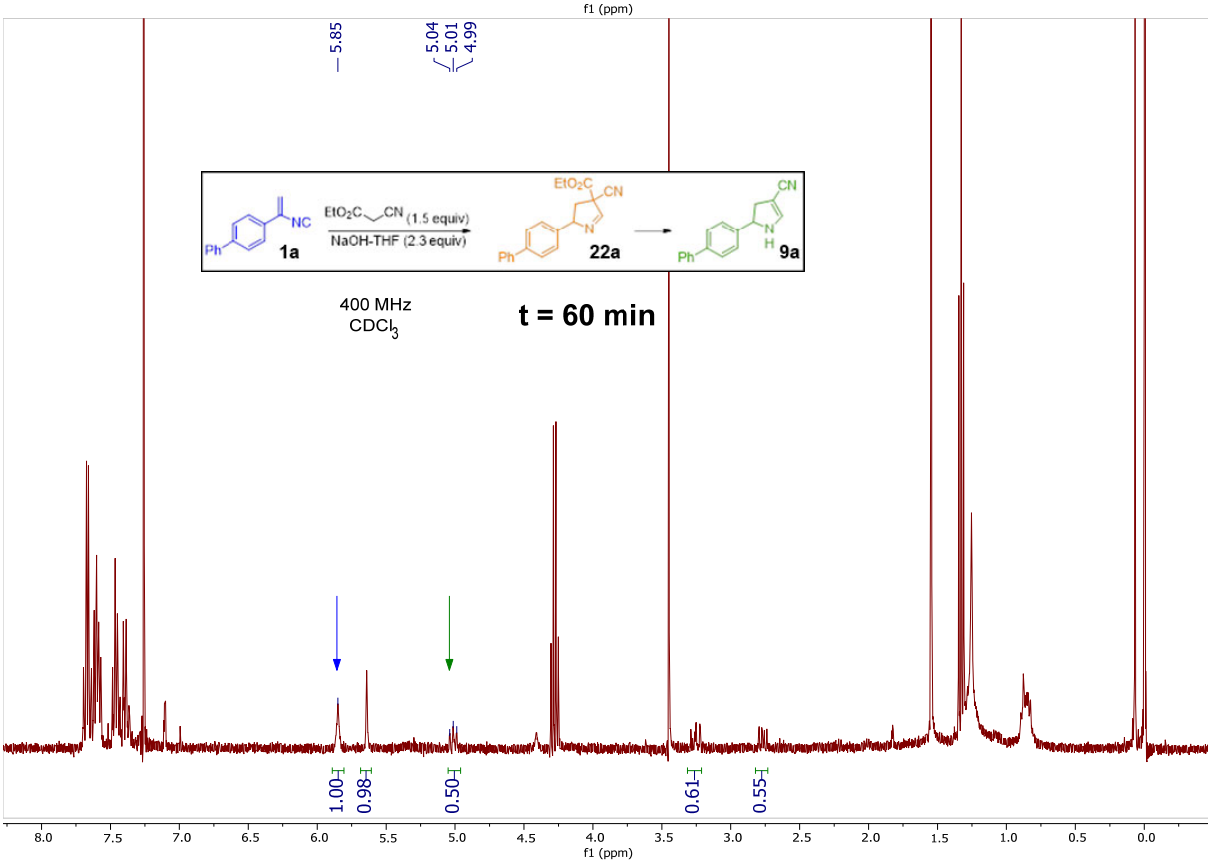
Table 1. Tabulated Data for ^{1}H NMR Reaction Monitoring.

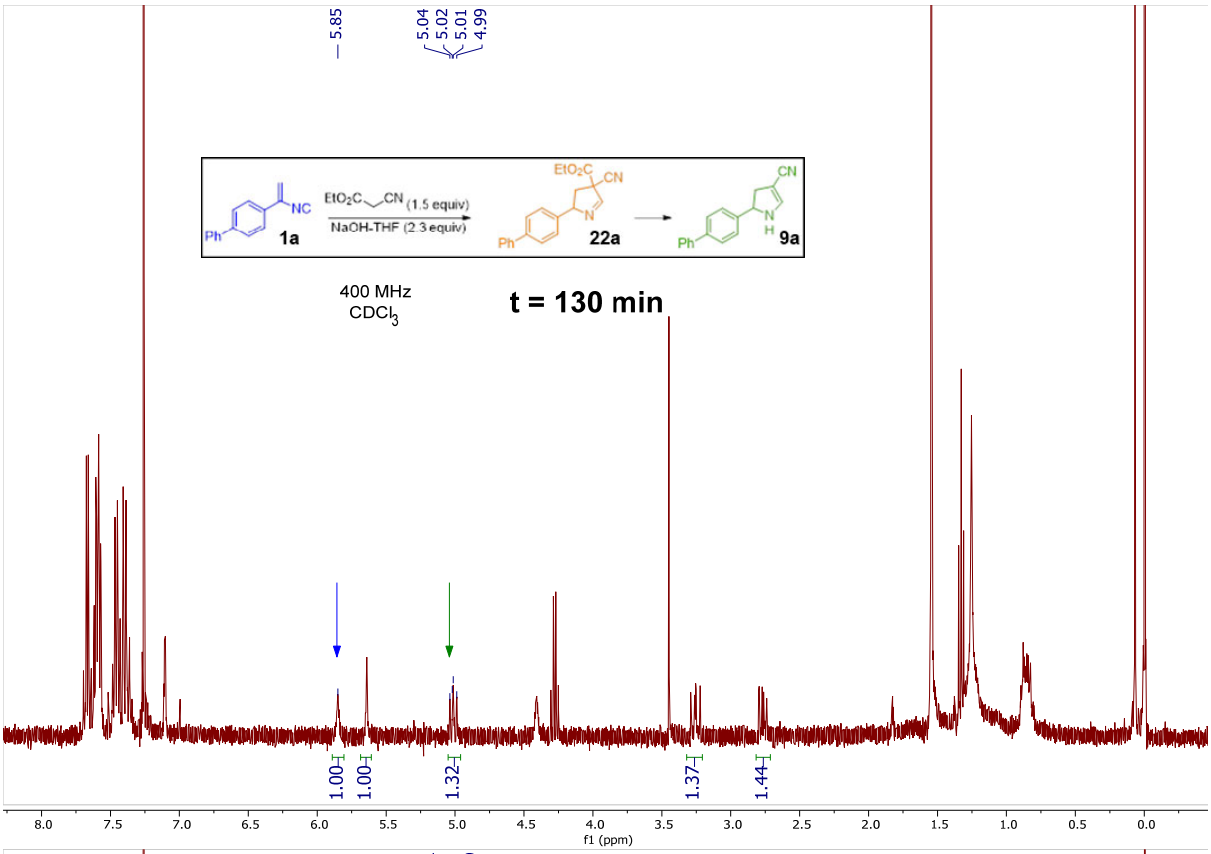
Aliquot Number	Time (min)	integration SM	integration pyrroline	integration enaminonitrile	% Conversion	mol fraction SM	mol fraction pyrroline	mol fraction enaminonitrile
0	0	1	0	0		1	0	0
1136-1	5	1	0	0.03	2.912621359	0.970873786	0	0.029126214
1136-2	15	1	0	0.2	16.66666667	0.833333333	0	0.166666667
1136-3	30	1	0	0.5	33.33333333	0.666666667	0	0.333333333
1136-4	60	1	0	1.32	56.89655172	0.431034483	0	0.568965517
1136-5	130	1	0	4.93	83.13659359	0.168634064	0	0.831365936
1136-6	370	1	0	6.51	86.68442077	0.133155792	0	0.866844208

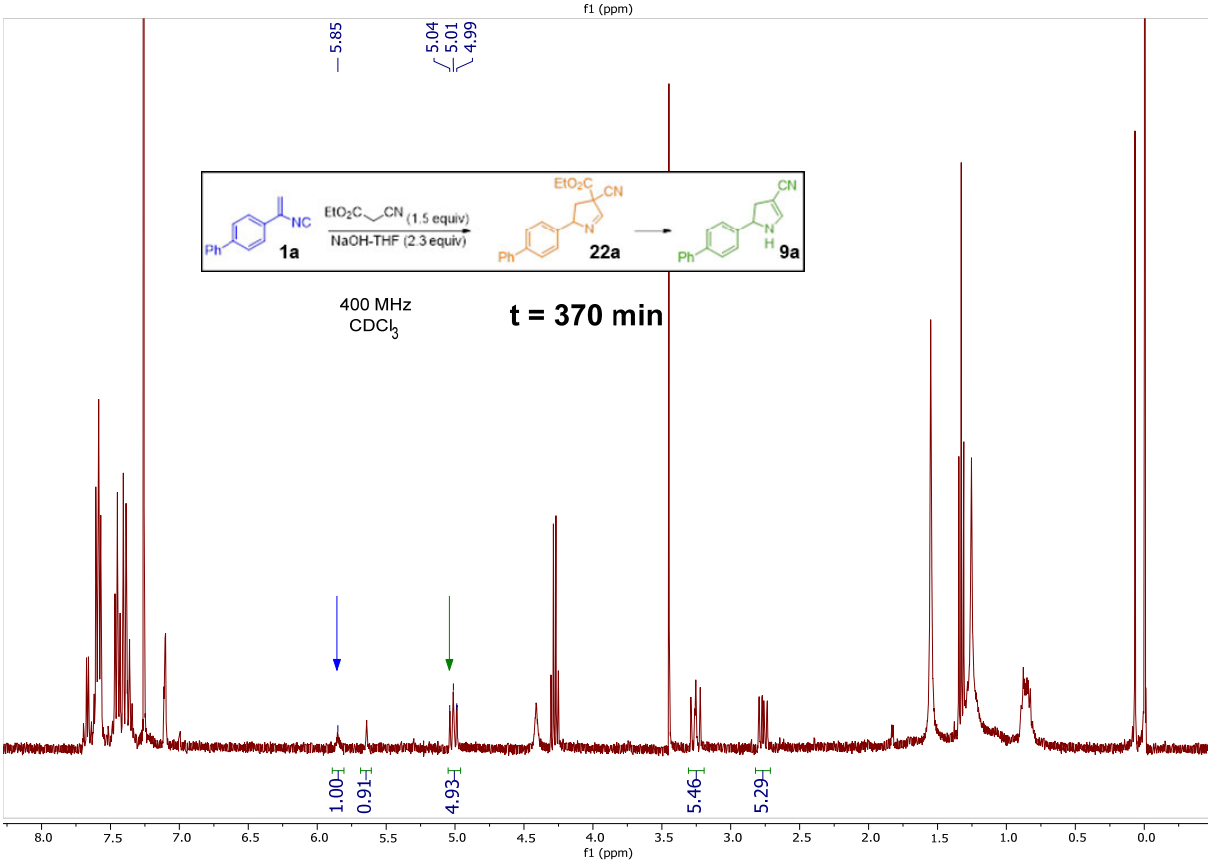

5.85
1a
1.5 equiv
NaOH-THF (2.3 equiv)
22a
9a
400 MHz
CDCl3
t = 5 min
1.00
0.96
0.03
f1 (ppm)


5.85
5.00
4.97
1a
1.5 equiv
NaOH-THF (2.3 equiv)
22a
9a
400 MHz
CDCl3
t = 15 min
1.00
0.99
0.10
0.02
0.04
f1 (ppm)


5.85
5.04
5.01
EtO2C CN (1.5 equiv)
NaOH-THF (2.3 equiv)
1a
22a
9a
400 MHz
CDCl3
t = 30 min
1.00
0.97
0.20
0.32
0.26
f1 (ppm)


5.85
5.04
5.01
4.99
EtO2C CN (1.5 equiv)
NaOH-THF (2.3 equiv)
1a
22a
9a
400 MHz
CDCl3
t = 60 min
1.00
0.98
0.50
0.61
0.55
f1 (ppm)


5.85
5.04
5.02
5.01
4.99
1a
1.5 equiv
NaOH-THF (2.3 equiv)
22a
9a
400 MHz
CDCl3
t = 130 min
1.00
1.00
1.32
1.37
1.44
f1 (ppm)


5.85
5.04
5.01
4.99
1a
1.5 equiv
NaOH-THF (2.3 equiv)
22a
9a
400 MHz
CDCl3
t = 370 min
1.00
0.91
4.93
5.46
5.29
f1 (ppm)