Copper-Catalyzed Chan–Lam Cyclopropylation of Phenols and Azaheterocycles

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SUPPORTING INFORMATION

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EXPERIMENTAL PROCEDURES

Photographic Depiction of Reaction Setup

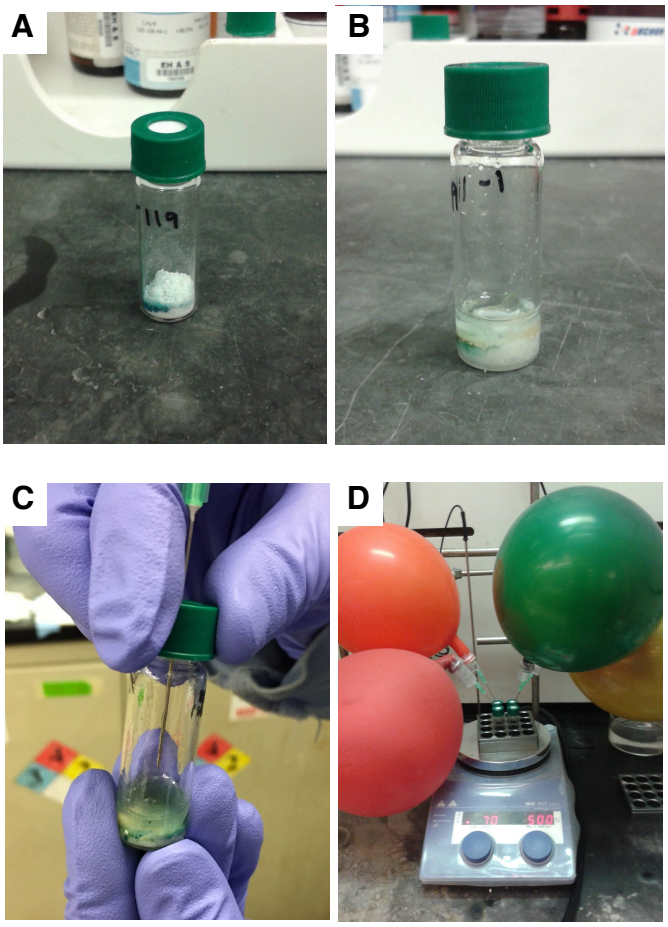
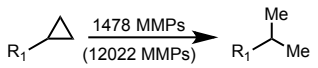
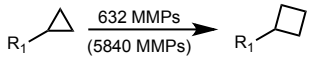
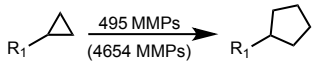
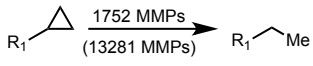
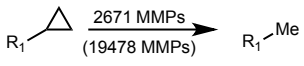
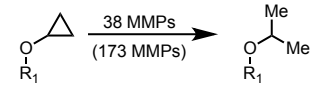
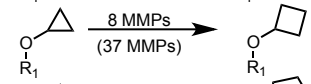
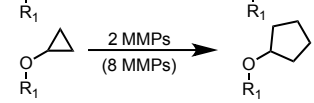
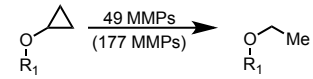
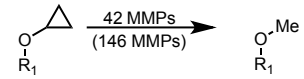
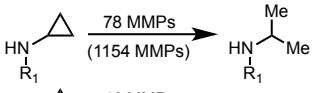
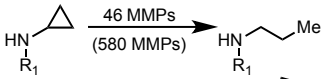
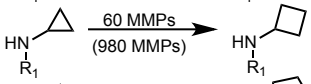
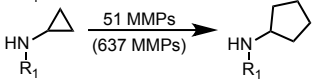
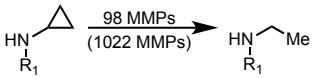
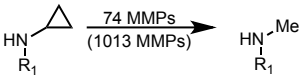


Figure S1. Photographic depiction of reaction setup detailed in general procedure. (A) Addition of stir bar and solid reagents. (B) Addition of solvents. (C) Purging with O_2 by loosening septum cap. (D) Reactions running on stir plate.

MMP DATA

Table S1. Matched molecular pair (MMP) data from Pfizer database.

Entry	Transforms	HLM $CL_{int,u}$ μ[a] [mL/min/kg]	HLM $CL_{int,u}$ s[b] [mL/min/kg]	HLM $CL_{int,u}$ %D/S/I[c]
(1)		12.8	53.2	18/76/6
(2)		17.4	47.9	23/74/3
(3)		33.5	63.2	42/55/3
(4)		42.4	77.0	48/46/6
(5)		0.61	46.2	10/82/8
(6)		–20.2	60.0	5/65/30
(7)		25.8	71.3	32/63/5
(8)		23.9	28.6	57/43/0
(9)		11.2	43.6	38/50/12
(10)		5.1	7.2	50/50/0
(11)		0.24	52.7	12/76/12
(12)		–4.49	64.5	14/55/31
(13)		16.3	59.3	26/64/10
(14)		32.4	62.4	35/61/4
(15)		38.9	68.0	35/63/2
(16)		31.9	62.5	45/51/4
(17)		25.6	65.7	25/66/9
(18)		–17.0	65.7	11/49/40

[a] Number above arrow correspods to matched molecular pairs (MMPs) with HLM data. Number in parentheses corresponds to total MMPs for that transform. [b] μ = mean change. [c] s = standard deviation. [d] %D/S/I = %decrease/%same/%increase (±20) in microsomal stability.

X-RAY CRYSTALLOGRAPHY

Experimental Summary

The single crystal X-ray diffraction studies were carried out on a Bruker APEX II Ultra CCD diffractometer equipped with Mo K_a radiation (l = 0.71073). Crystals of the subject compound were used as received (grown from $CDCl_3$) . A 0250x 0.240 x 0.200 mm colorless block was mounted on a Cryoloop with Paratone oil.

Data were collected in a nitrogen gas stream at 100(2) K using f and v scans. Crystal-to-detector distance was 40 mm using exposure time 1s with a scan width of 0.80°. Data collection was 99.9% complete to 25.242° in *q*. A total of 10049 reflections were collected covering the indices, -10<=h<=10, -10<=k<=10, -15<=l<=15. 1913 reflections were found to be symmetry independent, with a R_{int} of 0.0479. Indexing and unit cell refinement indicated a **P**rimitive, **Monoclinic** lattice. The space group was found to be ***P*2$_1$/n**. The data were integrated using the Bruker SAINT Software program and scaled using the SADABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure.

All nonhydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All carbon bonded hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014.

Position of the N-H hydrogen atoms have been refined using Uiso 1.2 of the parent atom and NO constrained DFIX.

Crystallographic data are summarized in Table S2.

Notes: Excellent data and model.
NH group forms hydrogen bond, Table S7

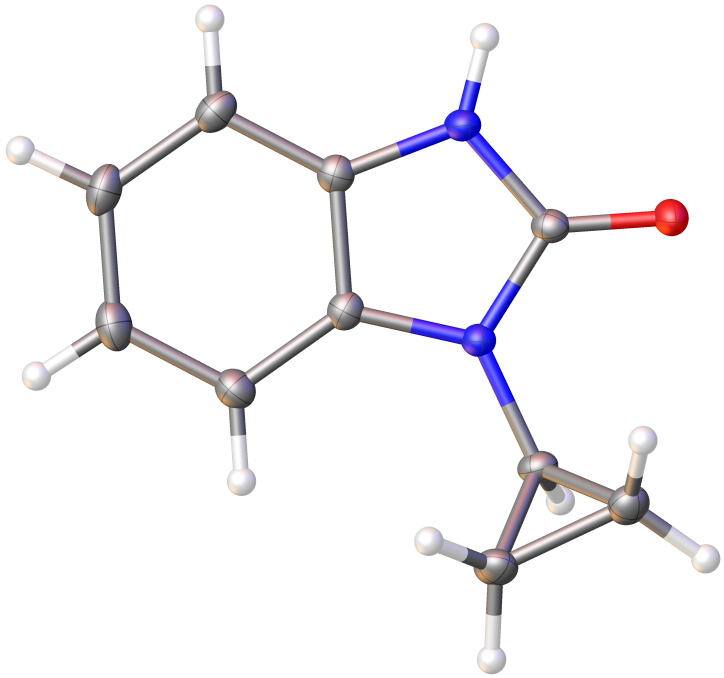


Table S2. Crystal data and structure refinement for Engle61 (**8a'**).

Report date	2017-11-07	
Identification code	engle61	
Empirical formula	C10 H10 N2 O	
Molecular formula	C10 H10 N2 O	
Formula weight	174.20	
Temperature	100.0 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 1 21/n 1	
Unit cell dimensions	a = 8.3909(2) Å	α= 90°.
	b = 8.3286(2) Å	β= 93.482(2)°.
	c = 12.4602(3) Å	γ = 90°.
Volume	869.17(4) $Å^3$	
Z	4	
Density (calculated)	1.331 Mg/m^3	
Absorption coefficient	0.089 mm^{-1}	
F(000)	368	
Crystal size	0.25 x 0.24 x 0.2 mm^3	
Crystal color, habit	colorless block	
Theta range for data collection	2.848 to 27.085°.	
Index ranges	-10<=h<=10, -10<=k<=10, -15<=l<=15	
Reflections collected	10049	
Independent reflections	1913 [R(int) = 0.0479]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.4917 and 0.4556	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1913 / 0 / 121	
Goodness-of-fit on F^2	1.062	
Final R indices [I>2sigma(I)]	R1 = 0.0347, wR2 = 0.0932	
R indices (all data)	R1 = 0.0387, wR2 = 0.0970	
Largest diff. peak and hole	0.217 and -0.243 $e.Å^{-3}$	

Table S3. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for Engle61 (**8a'**). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	7009(1)	5264(1)	2410(1)	18(1)
N(1)	7427(1)	5621(1)	4266(1)	14(1)
N(2)	7759(1)	3194(1)	3599(1)	16(1)
C(1)	7364(1)	4743(1)	3323(1)	15(1)
C(2)	8123(1)	3094(1)	4700(1)	15(1)
C(3)	8582(1)	1803(1)	5348(1)	18(1)
C(4)	8874(1)	2104(1)	6445(1)	21(1)
C(5)	8717(1)	3642(2)	6863(1)	22(1)
C(6)	8244(1)	4946(1)	6211(1)	18(1)
C(7)	7936(1)	4637(1)	5126(1)	15(1)
C(8)	7106(1)	7312(1)	4294(1)	15(1)
C(9)	5924(1)	7908(1)	5066(1)	20(1)
C(10)	5479(1)	7872(1)	3879(1)	20(1)

Table S4. Bond lengths [Å] and angles [°] for Engle61 (**8a'**).

O(1)-C(1)	1.2370(12)	C(3)-C(2)-C(7)	121.65(10)
N(1)-C(1)	1.3824(13)	C(2)-C(3)-H(3)	121.4
N(1)-C(7)	1.3945(13)	C(2)-C(3)-C(4)	117.21(10)
N(1)-C(8)	1.4346(13)	C(4)-C(3)-H(3)	121.4
N(2)-C(1)	1.3700(13)	C(3)-C(4)-H(4)	119.5
N(2)-C(2)	1.3905(13)	C(5)-C(4)-C(3)	121.06(10)
N(2)-H(2)	0.925(15)	C(5)-C(4)-H(4)	119.5
C(2)-C(3)	1.3844(14)	C(4)-C(5)-H(5)	119.1
C(2)-C(7)	1.4032(14)	C(4)-C(5)-C(6)	121.80(10)
C(3)-H(3)	0.9500	C(6)-C(5)-H(5)	119.1
C(3)-C(4)	1.3972(16)	C(5)-C(6)-H(6)	121.5
C(4)-H(4)	0.9500	C(7)-C(6)-C(5)	116.90(10)
C(4)-C(5)	1.3924(17)	C(7)-C(6)-H(6)	121.5
C(5)-H(5)	0.9500	N(1)-C(7)-C(2)	106.54(9)
C(5)-C(6)	1.3993(16)	C(6)-C(7)-N(1)	132.11(10)
C(6)-H(6)	0.9500	C(6)-C(7)-C(2)	121.36(10)
C(6)-C(7)	1.3852(14)	N(1)-C(8)-H(8)	116.4
C(8)-H(8)	1.0000	N(1)-C(8)-C(9)	118.04(9)
C(8)-C(9)	1.5076(15)	N(1)-C(8)-C(10)	117.67(9)
C(8)-C(10)	1.5042(15)	C(9)-C(8)-H(8)	116.4
C(9)-H(9A)	0.9900	C(10)-C(8)-H(8)	116.4
C(9)-H(9B)	0.9900	C(10)-C(8)-C(9)	59.92(7)
C(9)-C(10)	1.5040(15)	C(8)-C(9)-H(9A)	117.8
C(10)-H(10A)	0.9900	C(8)-C(9)-H(9B)	117.8
C(10)-H(10B)	0.9900	H(9A)-C(9)-H(9B)	114.9
		C(10)-C(9)-C(8)	59.93(7)
C(1)-N(1)-C(7)	109.60(9)	C(10)-C(9)-H(9A)	117.8
C(1)-N(1)-C(8)	122.83(9)	C(10)-C(9)-H(9B)	117.8
C(7)-N(1)-C(8)	127.45(9)	C(8)-C(10)-H(10A)	117.8
C(1)-N(2)-C(2)	109.83(8)	C(8)-C(10)-H(10B)	117.8
C(1)-N(2)-H(2)	124.8(9)	C(9)-C(10)-C(8)	60.15(7)
C(2)-N(2)-H(2)	125.3(9)	C(9)-C(10)-H(10A)	117.8
O(1)-C(1)-N(1)	126.18(10)	C(9)-C(10)-H(10B)	117.8
O(1)-C(1)-N(2)	127.00(10)	H(10A)-C(10)-H(10B)	114.9
N(2)-C(1)-N(1)	106.82(9)		
N(2)-C(2)-C(7)	107.14(9)		
C(3)-C(2)-N(2)	131.21(10)		

Table S5. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for Engle61 (**8a'**). The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	26(1)	15(1)	14(1)	1(1)	1(1)	-1(1)
N(1)	18(1)	12(1)	13(1)	-1(1)	1(1)	0(1)
N(2)	22(1)	12(1)	14(1)	-1(1)	2(1)	1(1)
C(1)	16(1)	13(1)	16(1)	-1(1)	3(1)	-2(1)
C(2)	12(1)	17(1)	16(1)	1(1)	2(1)	-1(1)
C(3)	15(1)	16(1)	24(1)	4(1)	2(1)	1(1)
C(4)	16(1)	24(1)	22(1)	9(1)	-1(1)	1(1)
C(5)	20(1)	29(1)	16(1)	3(1)	-2(1)	-3(1)
C(6)	18(1)	20(1)	17(1)	-2(1)	1(1)	-2(1)
C(7)	12(1)	16(1)	16(1)	2(1)	2(1)	-1(1)
C(8)	17(1)	11(1)	18(1)	-1(1)	3(1)	0(1)
C(9)	23(1)	18(1)	20(1)	-2(1)	6(1)	3(1)
C(10)	20(1)	19(1)	21(1)	1(1)	2(1)	4(1)

Table S6. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for Engle61 (**8a'**).

	x	y	z	U(eq)
H(3)	8693	757	5058	22
H(4)	9185	1245	6914	25
H(5)	8937	3812	7611	26
H(6)	8138	5994	6499	22
H(8)	8020	8042	4163	18
H(9A)	5422	7105	5525	24
H(9B)	6125	8968	5408	24
H(10A)	5406	8911	3492	24
H(10B)	4703	7049	3610	24
H(2)	7815(16)	2354(18)	3117(11)	24

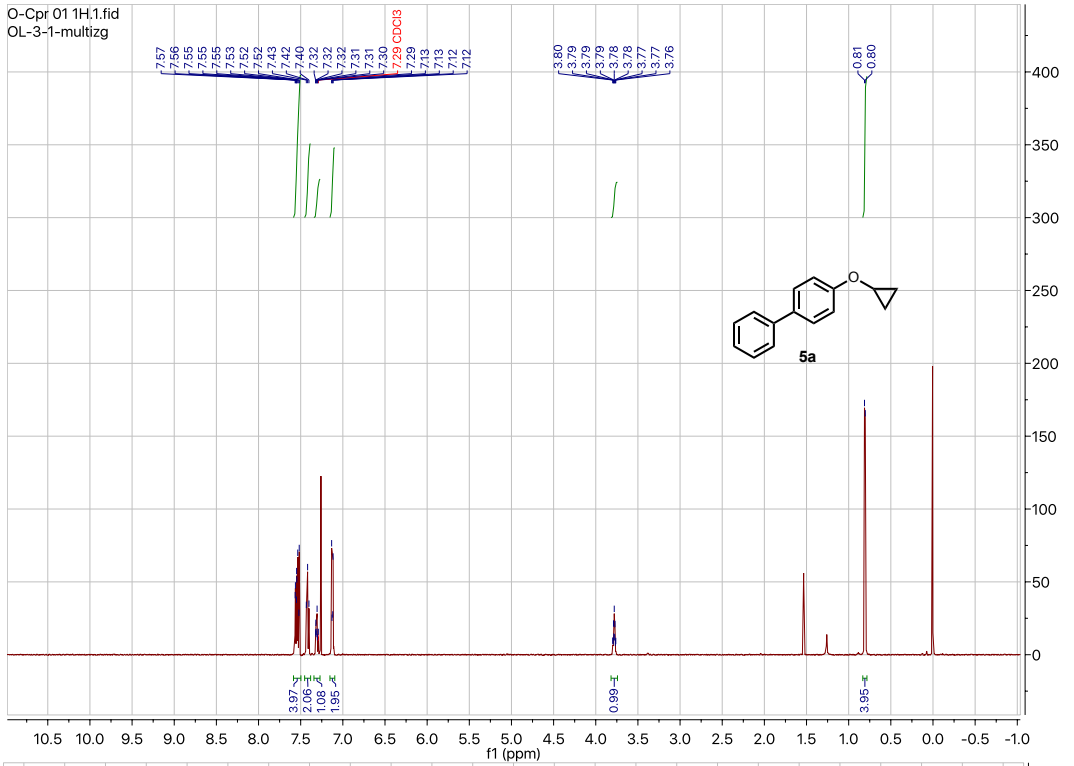
Table S7. Hydrogen bonds for Engle61 (**8a'**) [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(2)-H(2)...O(1)#1	0.925(15)	1.869(15)	2.7574(12)	160.2(13)

Symmetry transformations used to generate equivalent atoms:

#1 -x+3/2,y-1/2,-z+1/2

NMR SPECTRA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7.55
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7.55
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7.42
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7.32
7.32
7.31
7.31
7.30
7.29 CDCl3
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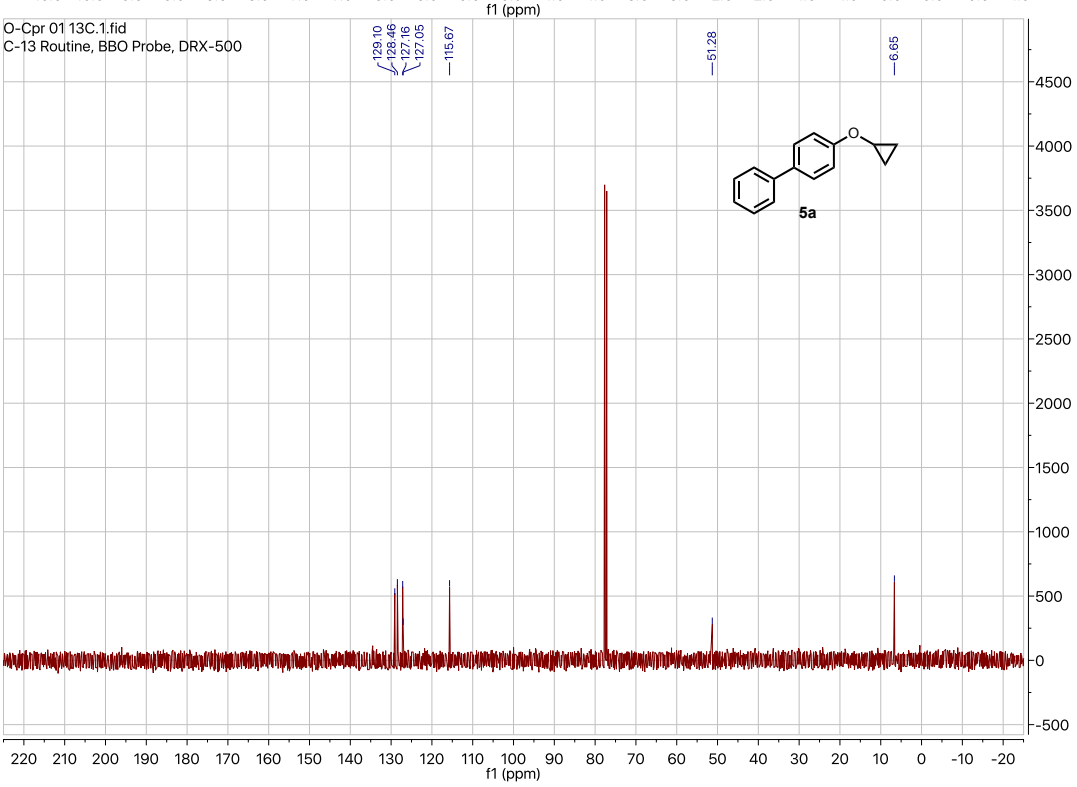
7.13
7.12
7.12
3.80
3.79
3.79
3.79
3.78
3.78
3.77
3.77
3.76
0.81
0.80
5a
3.97
2.06
1.08
1.95
0.99
3.95
f1 (ppm)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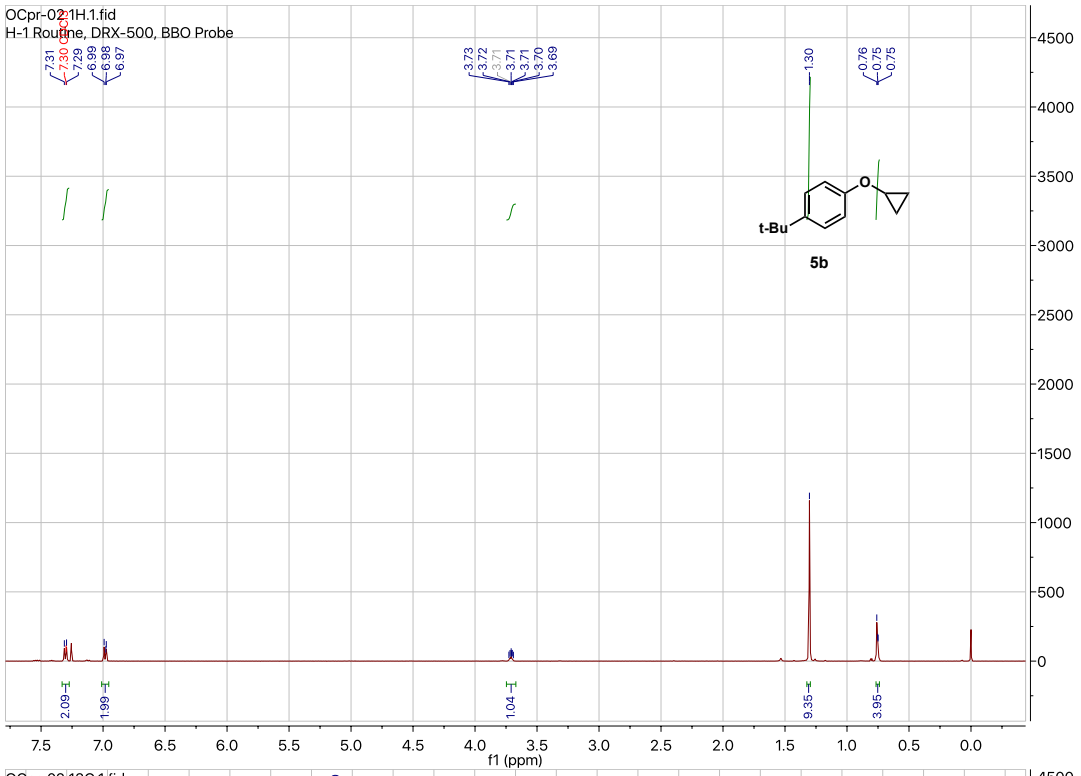
6.65
5a
f1 (ppm)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3.72
3.71
3.71
3.71
3.70
3.69
1.30
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t-Bu
O
5b
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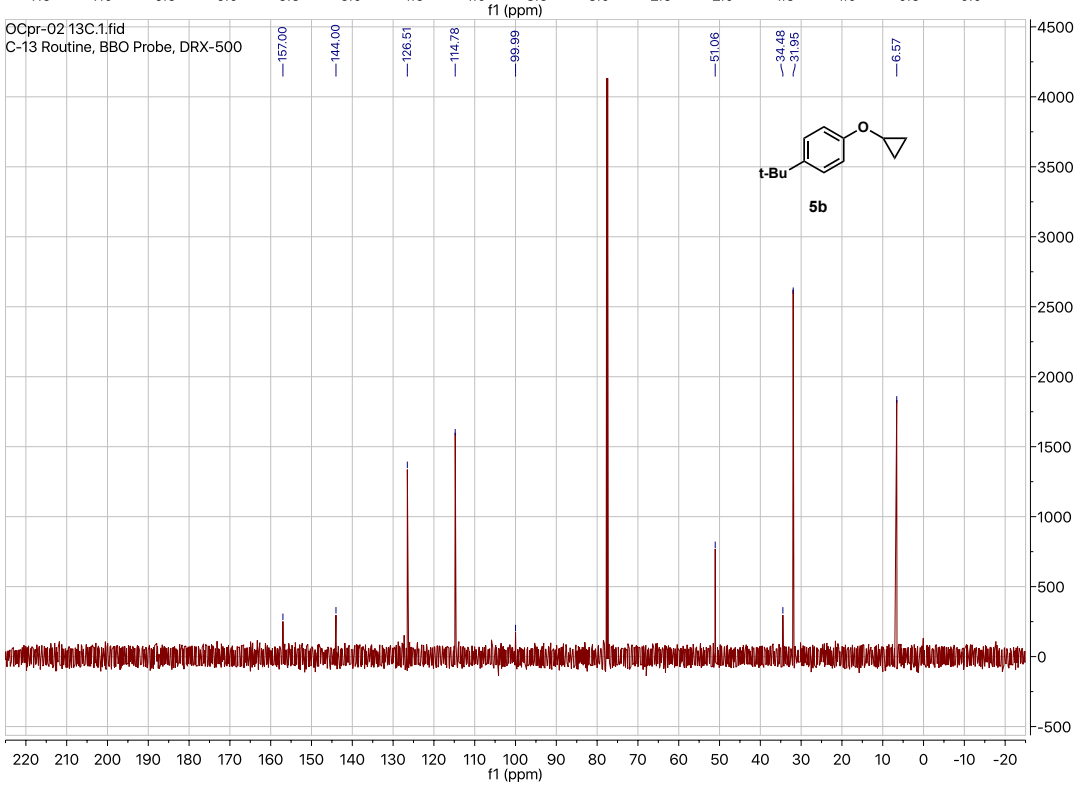
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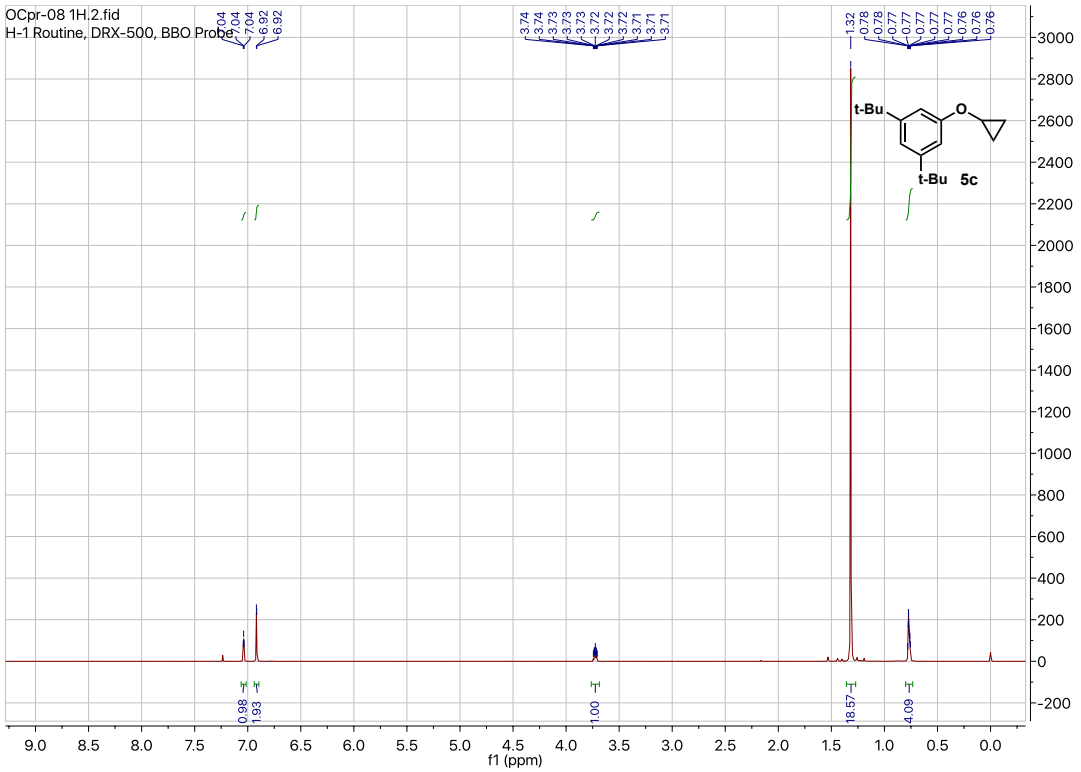
126.51
114.78
99.99
51.06
34.48
31.95
6.57
t-Bu
O
5b
f1 (ppm)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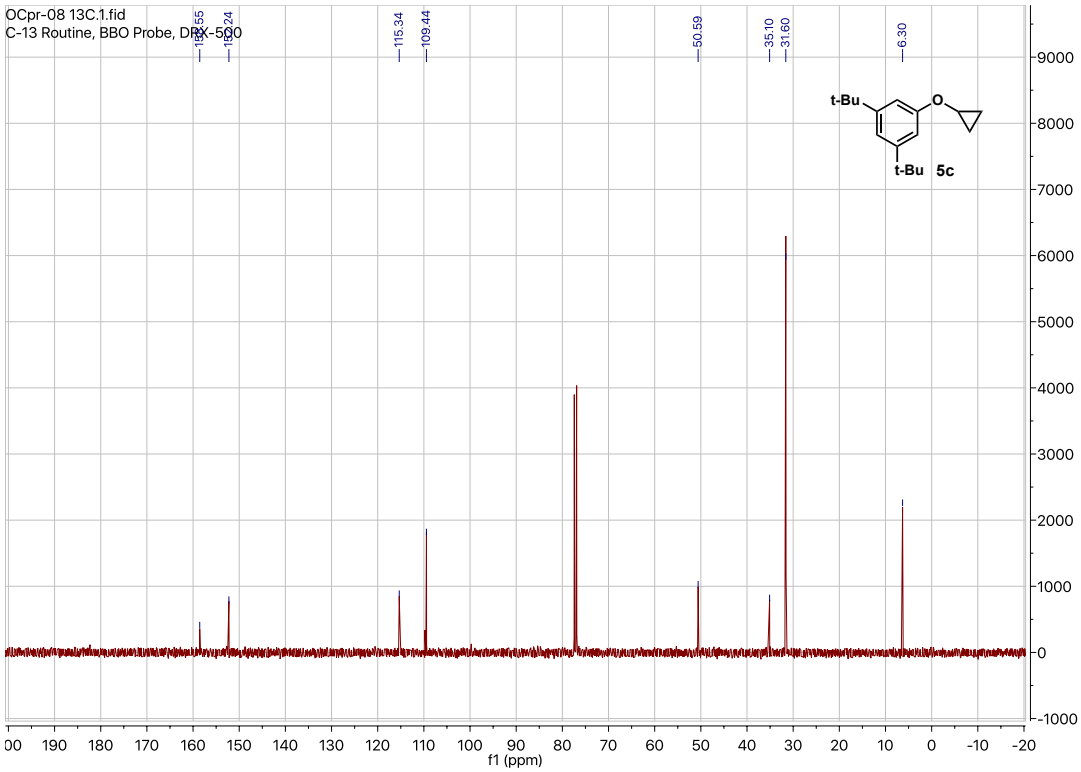
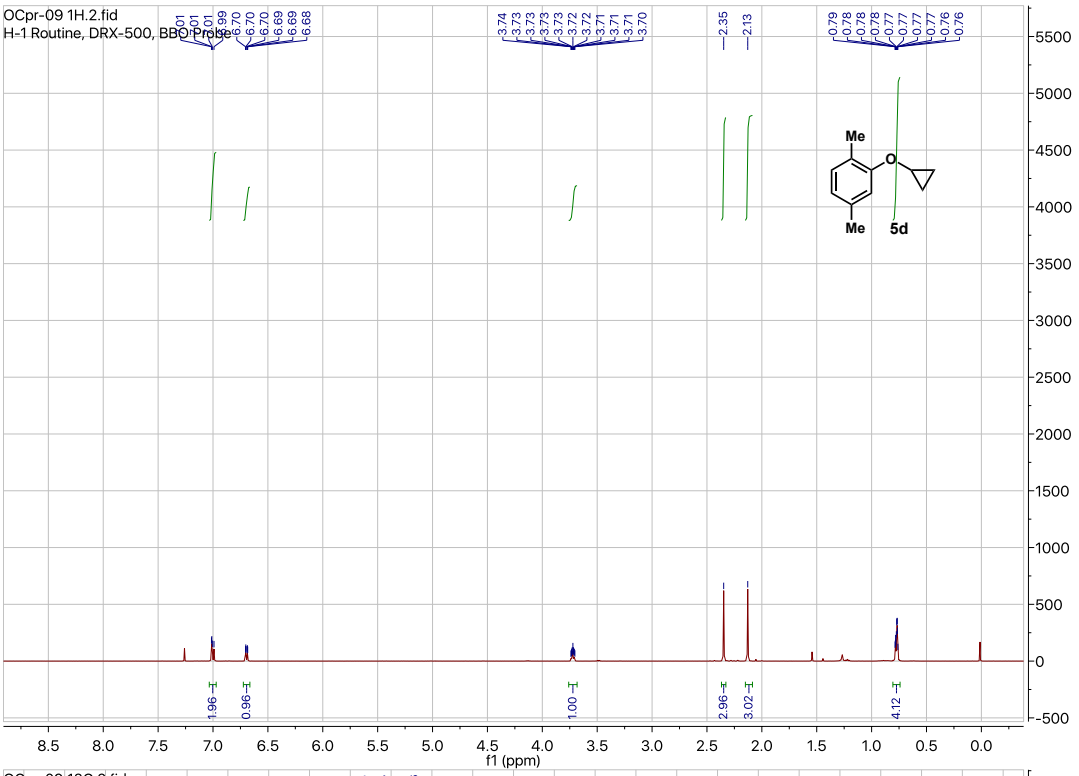
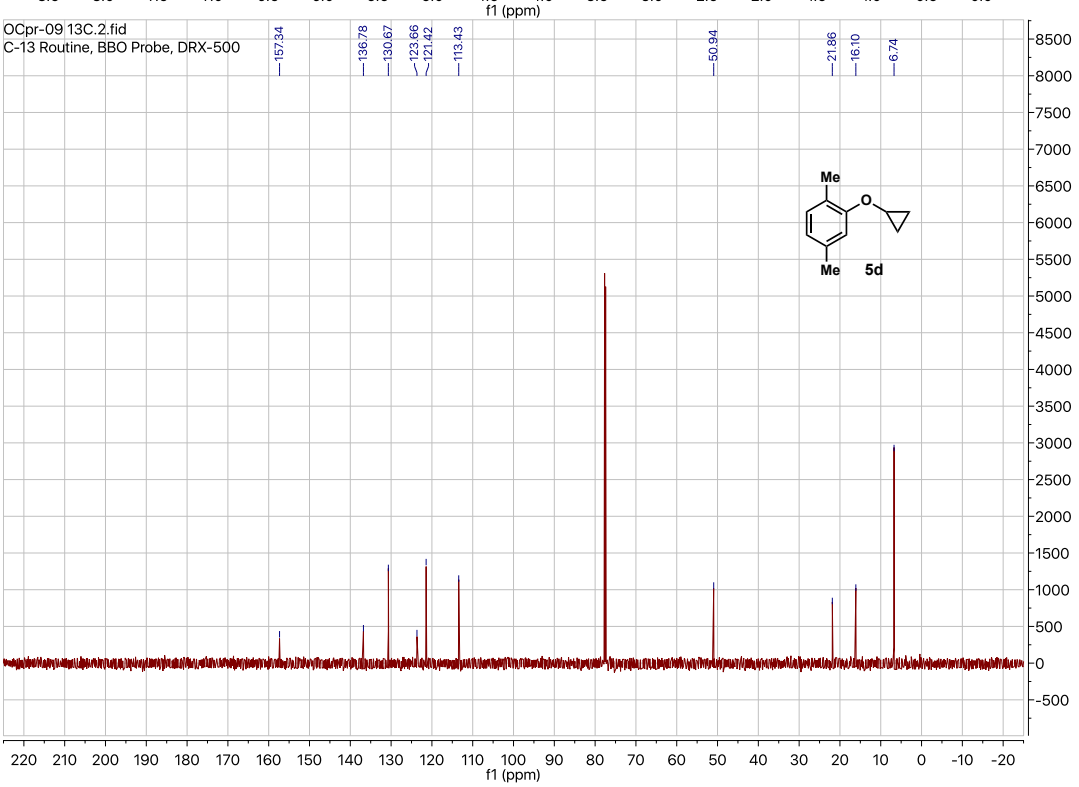
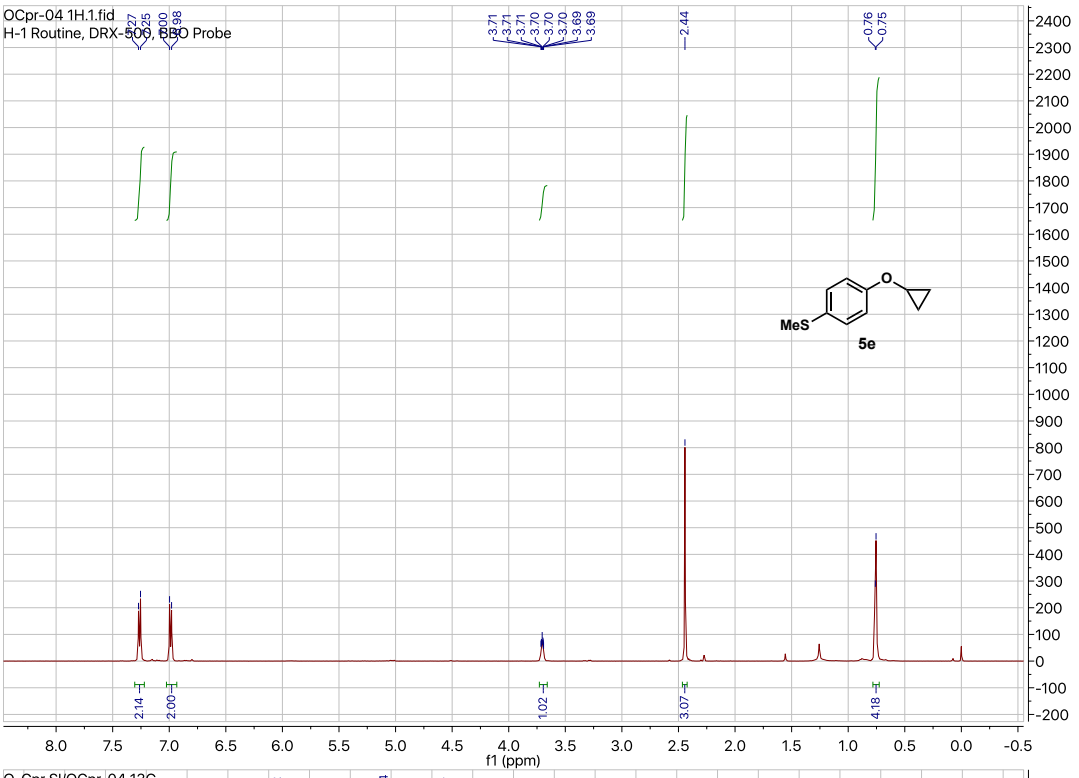
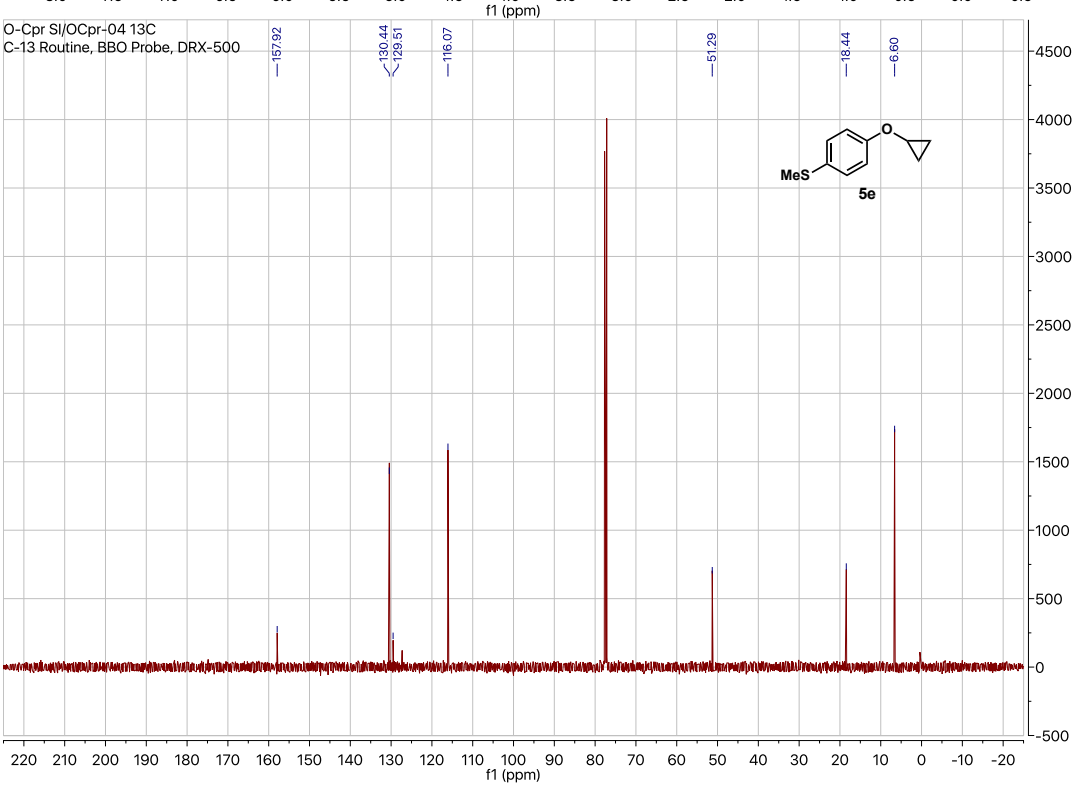
H-1 Routine, DRX-500, BBO Probe
t-Bu
t-Bu 5c
f1 (ppm)

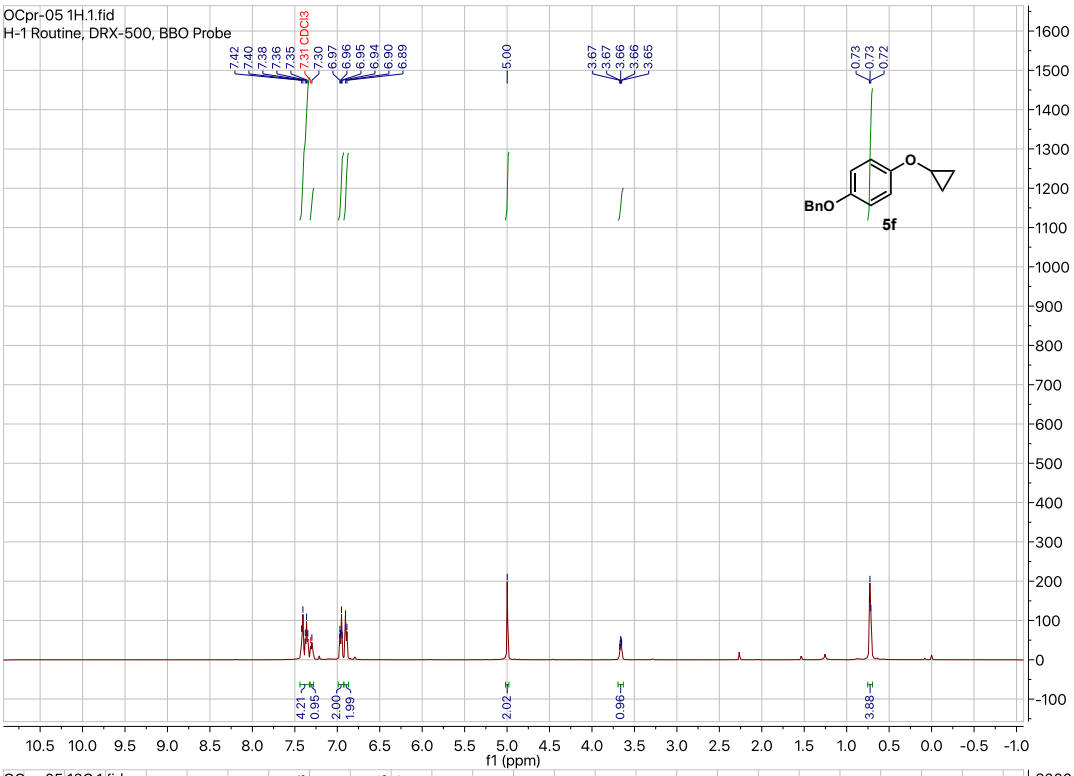

OCpr-08 13C.1.fid
C-13 Routine, BBO Probe, DRX-500
t-Bu
t-Bu 5c
f1 (ppm)

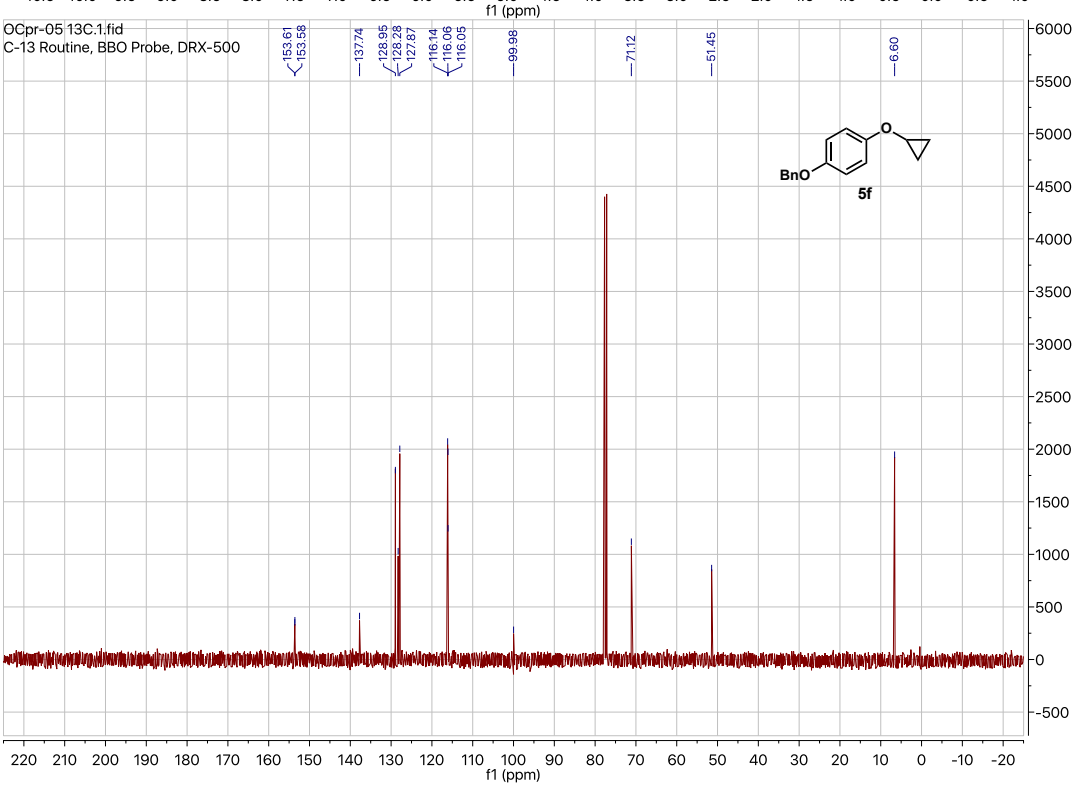

OCpr-09 1H.2.fid
H-1 Routine, DRX-500, BBO Probe
7.01
7.01
7.01
6.99
6.70
6.70
6.70
6.69
6.69
6.68
3.74
3.73
3.73
3.73
3.73
3.72
3.72
3.71
3.71
3.71
3.70
2.35
2.13
0.79
0.78
0.78
0.78
0.77
0.77
0.77
0.77
0.76
0.76
Me
O
Me
5d
1.96
0.96
1.00
2.96
3.02
4.12
f1 (ppm)

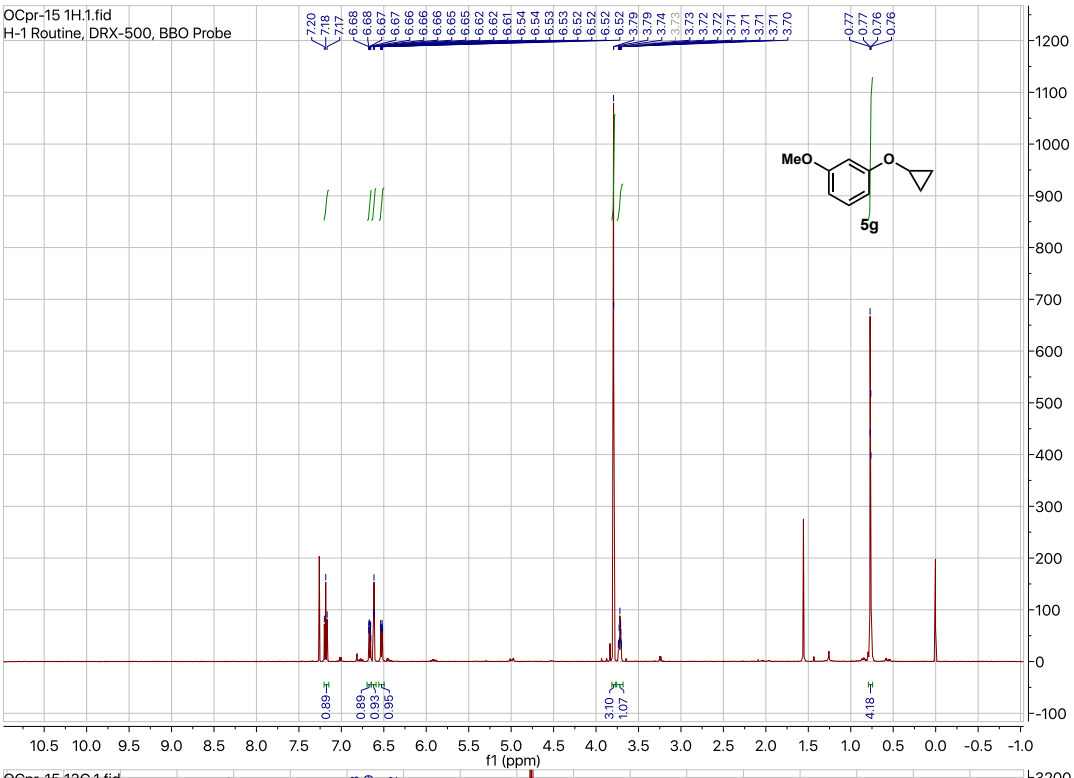

OCpr-09 13C.2.fid
C-13 Routine, BBO Probe, DRX-500
157.34
136.78
130.67
123.66
121.42
113.43
50.94
21.86
16.10
6.74
Me
O
Me
5d
f1 (ppm)

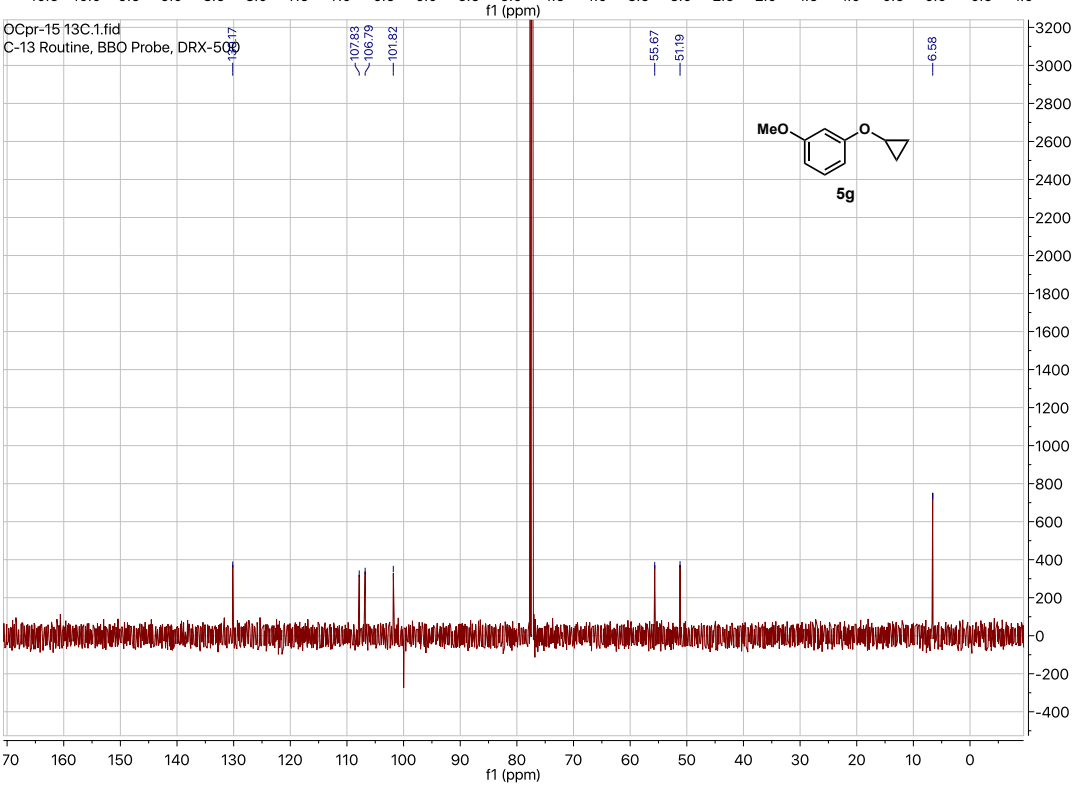

OCpr-04 1H.1.fid
H-1 Routine, DRX-500, BBO Probe
MeS
5e
f1 (ppm)

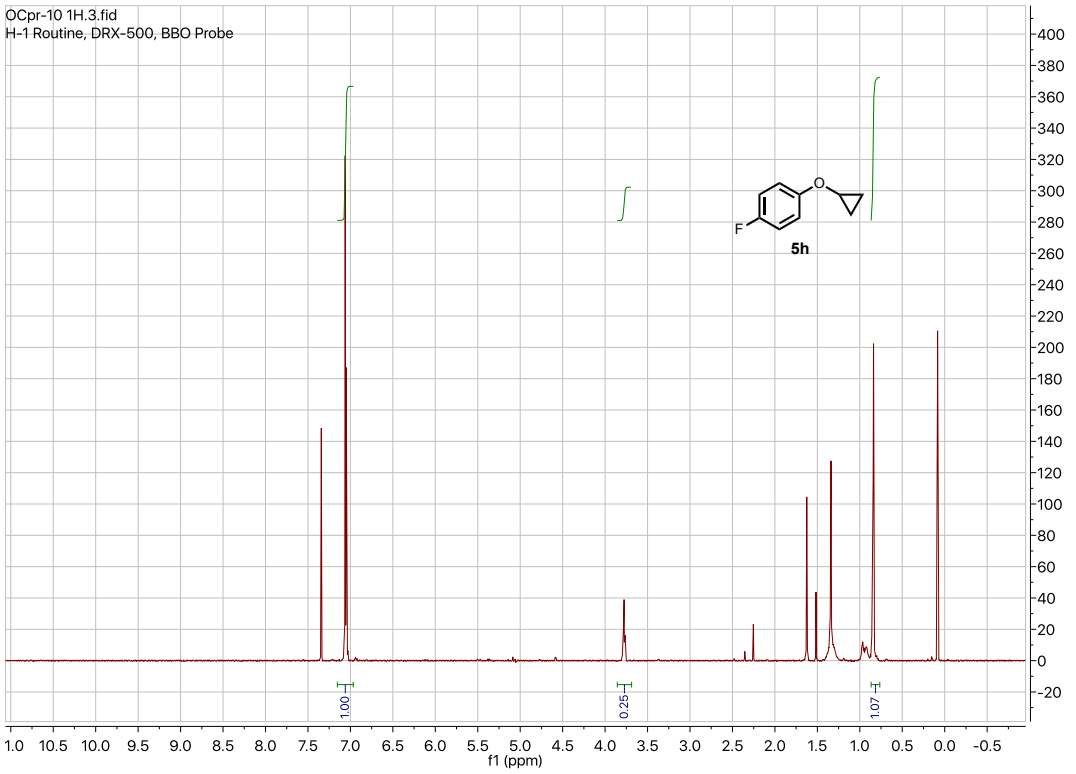

O-Cpr SI/OCpr-04 13C
C-13 Routine, BBO Probe, DRX-500
MeS
5e
f1 (ppm)

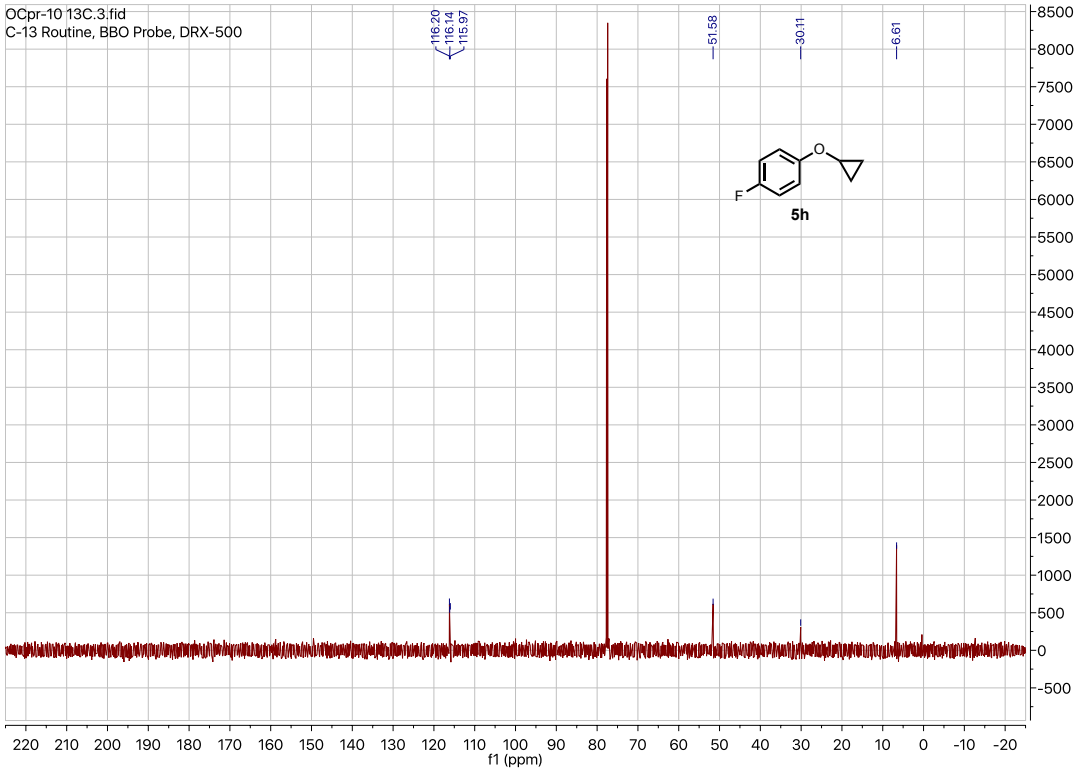

OCpr-05 1H.1.fid
H-1 Routine, DRX-500, BBO Probe
7.42
7.40
7.38
7.36
7.35
7.31 CDCl3
7.30
6.97
6.96
6.95
6.94
6.90
6.89
5.00
3.67
3.67
3.66
3.66
3.65
0.73
0.73
0.72
BnO
O
5f
4.21
0.95
2.00
1.99
2.02
0.96
3.88
f1 (ppm)

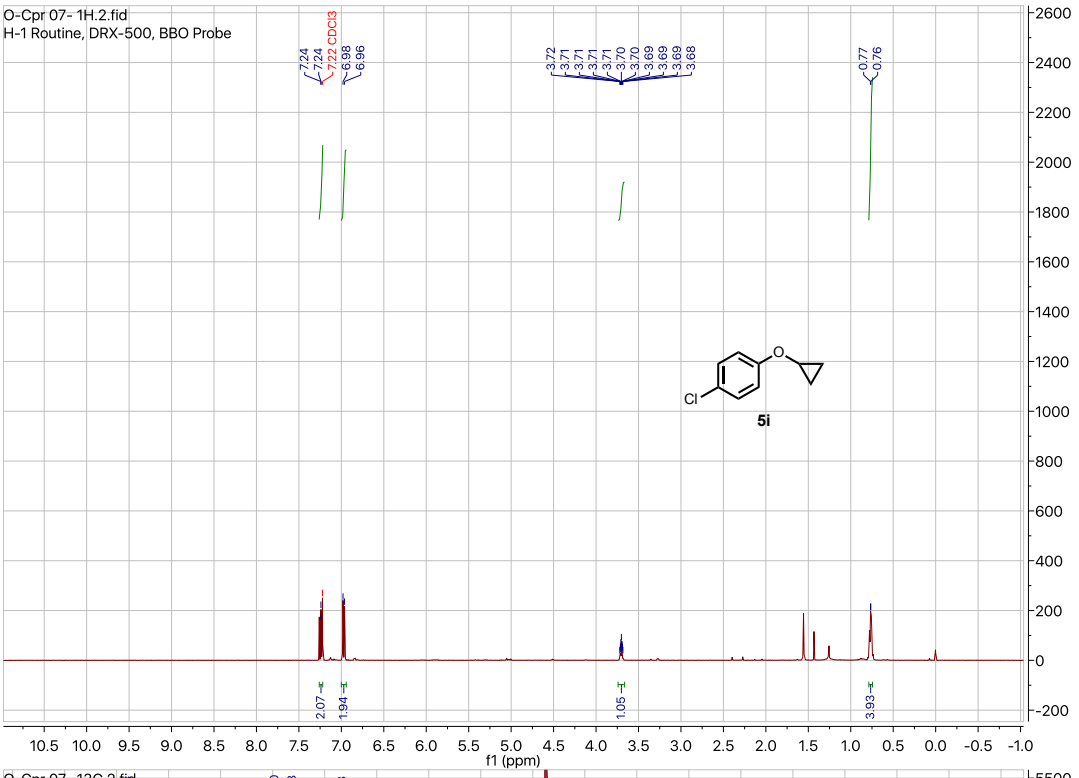

OCpr-05 13C.1.fid
C-13 Routine, BBO Probe, DRX-500
153.61
153.58
137.74
128.95
128.28
127.87
116.14
116.06
116.05
99.98
71.12
51.45
6.60
BnO
O
5f
f1 (ppm)

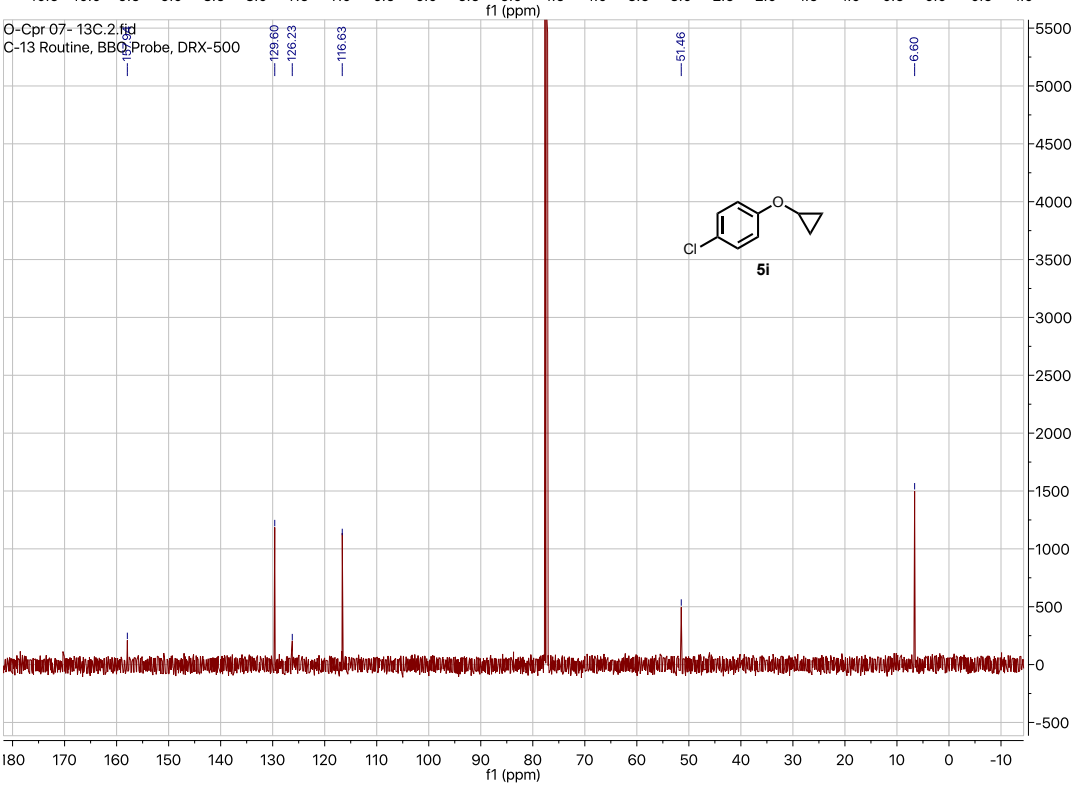

OCpr-15 1H.1.fid
H-1 Routine, DRX-500, BBO Probe
MeO
O
5g
f1 (ppm)

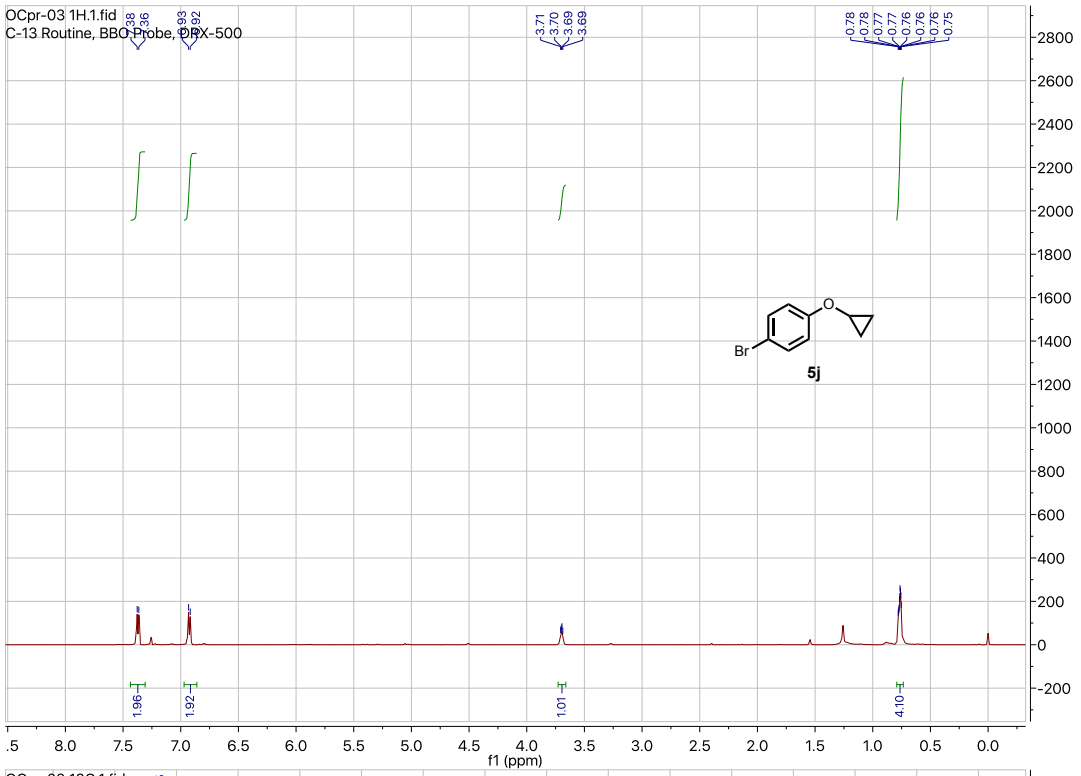

OCpr-15 13C.1.fid
C-13 Routine, BBO Probe, DRX-500
MeO
O
5g
f1 (ppm)

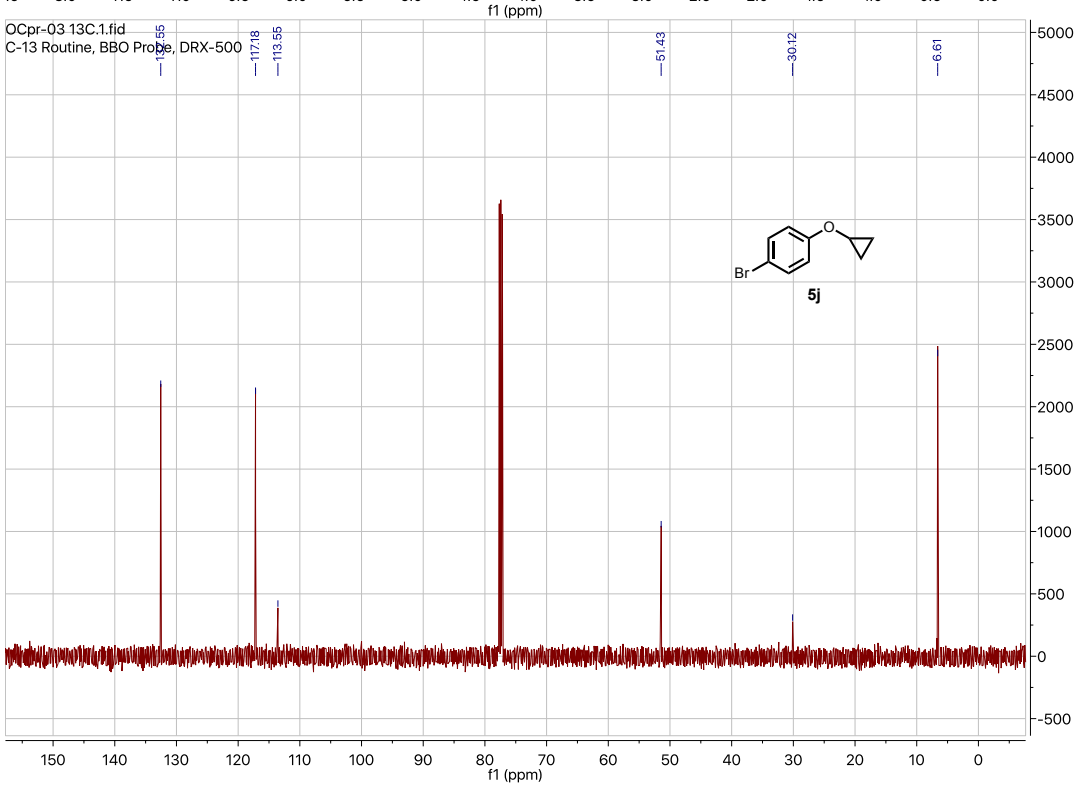

OCpr-10 1H.3.fid
H-1 Routine, DRX-500, BBO Probe
5h
1.00
0.25
1.07
f1 (ppm)

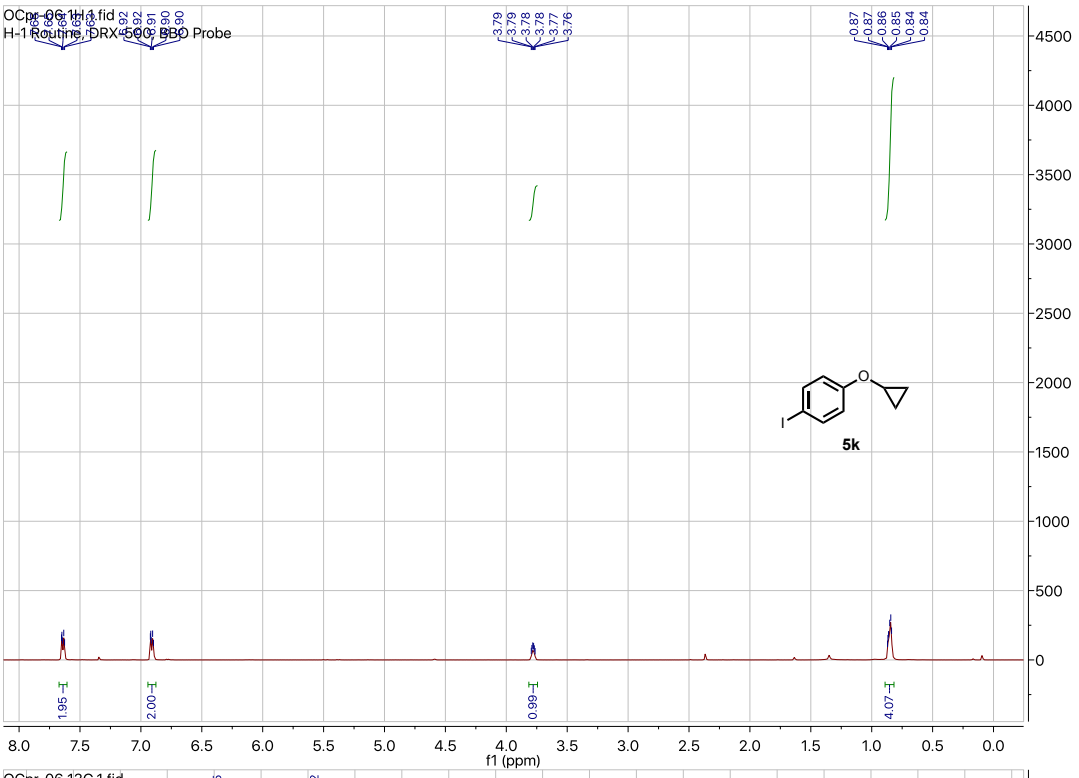

OCpr-10 13C.3.fid
C-13 Routine, BBO Probe, DRX-500
116.20
116.14
115.97
51.58
30.11
6.61
5h
f1 (ppm)

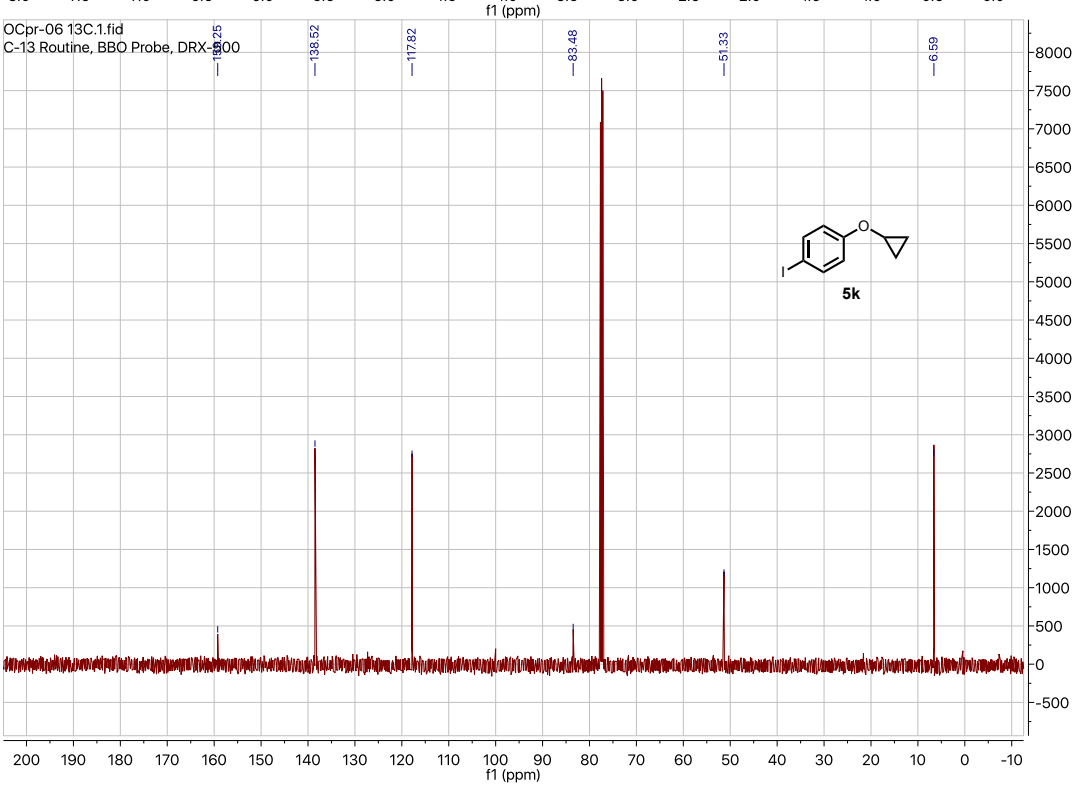

O-Cpr 07- 1H.2.fid
H-1 Routine, DRX-500, BBO Probe
7.24
7.24
7.22 CDCl3
6.98
6.96
3.72
3.71
3.71
3.71
3.71
3.70
3.70
3.69
3.69
3.69
3.68
0.77
0.76
2.07
1.94
1.05
3.93
f1 (ppm)
Cl
O
5i

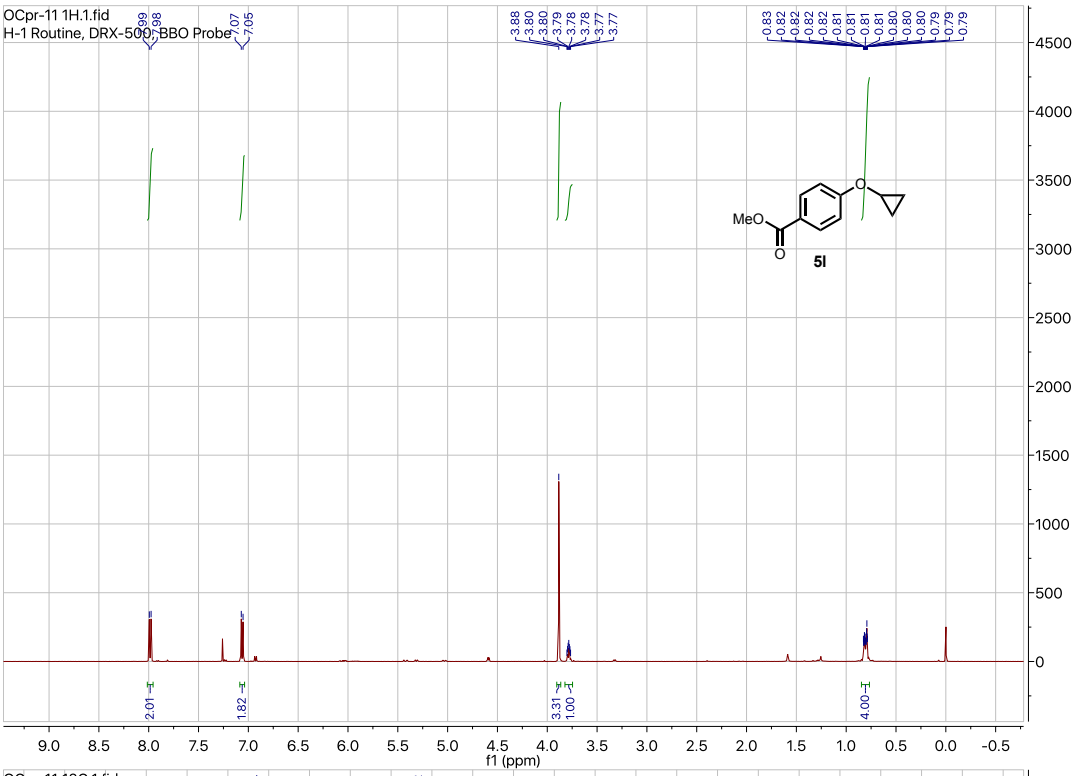

O-Cpr 07- 13C.2.fid
C-13 Routine, BBO Probe, DRX-500
129.60
126.23
116.63
51.46
6.60
f1 (ppm)
Cl
O
5i

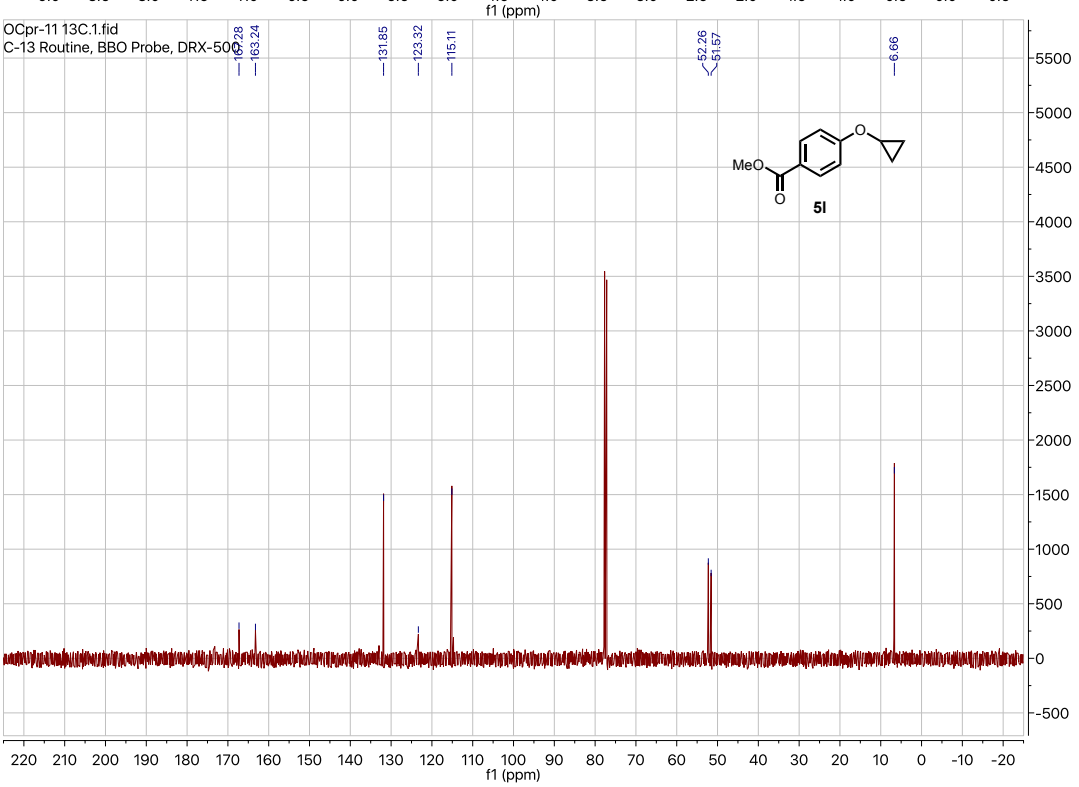

OCpr-03 1H.1.fid
C-13 Routine, BBO Probe, DRX-500
7.38
7.36
7.93
7.92
3.71
3.70
3.69
3.69
0.78
0.78
0.77
0.77
0.76
0.76
0.76
0.75
Br
O
5j
1.96
1.92
1.01
4.10
f1 (ppm)

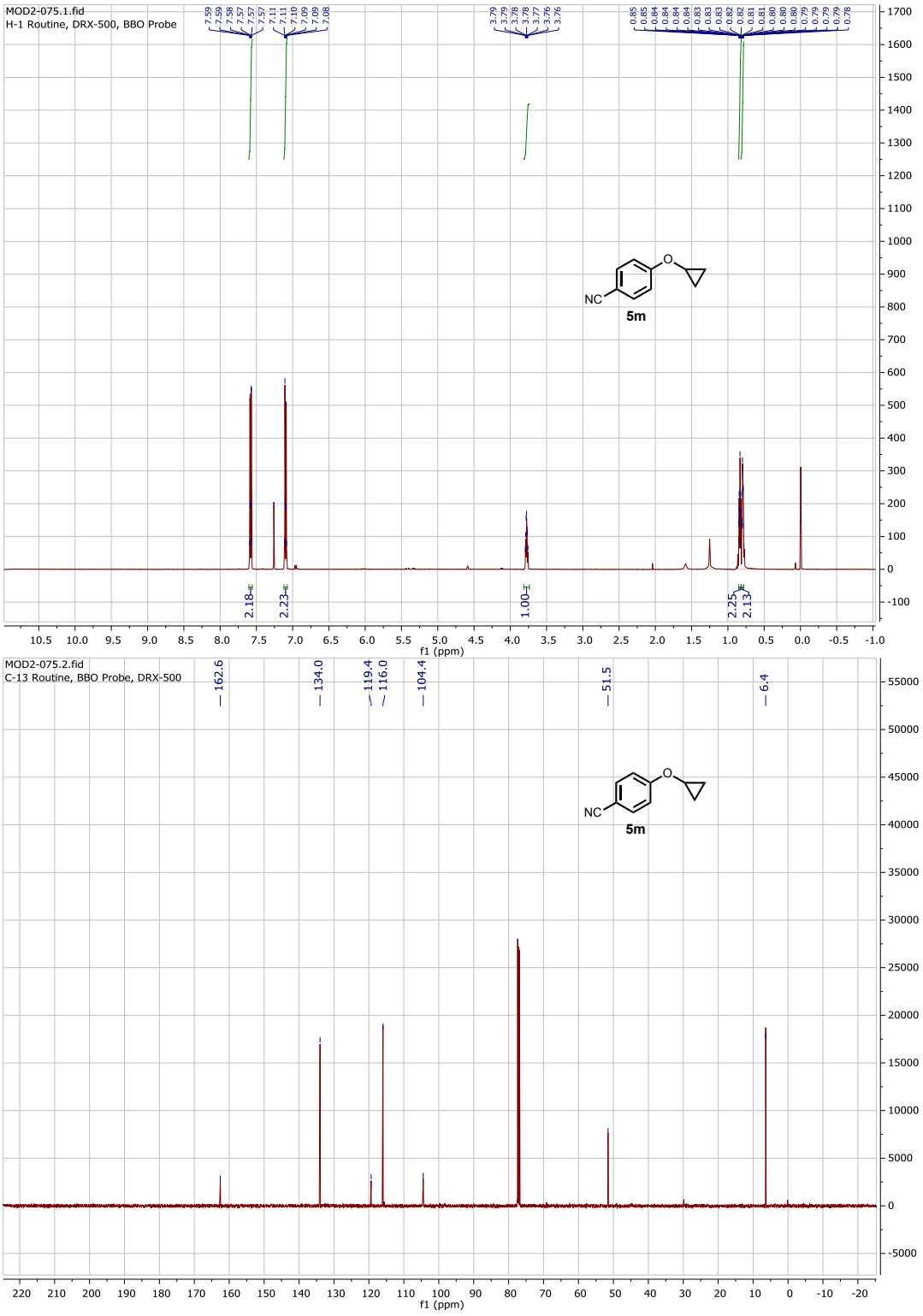

OCpr-03 13C.1.fid
C-13 Routine, BBO Probe, DRX-500
158.55
117.18
113.55
51.43
30.12
6.61
Br
O
5j
f1 (ppm)

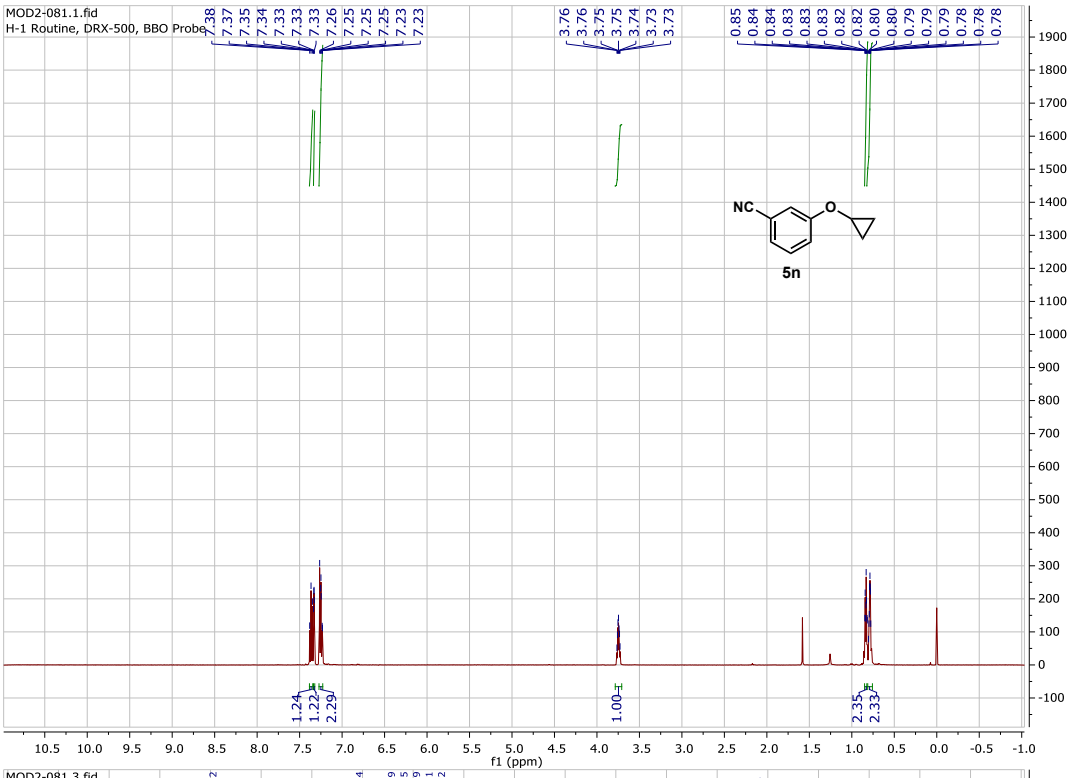

OCpr-06 1H.1.fid
H-1 Routine, DRX-500, BBO Probe
7.38
7.38
7.37
7.37
7.36
7.36
7.35
7.35
7.34
7.34
7.33
7.33
7.32
7.32
7.31
7.31
7.30
7.30
7.29
7.29
3.79
3.79
3.78
3.78
3.78
3.77
3.76
0.87
0.87
0.86
0.86
0.85
0.84
0.84
1.95
2.00
0.99
4.07
f1 (ppm)
5k

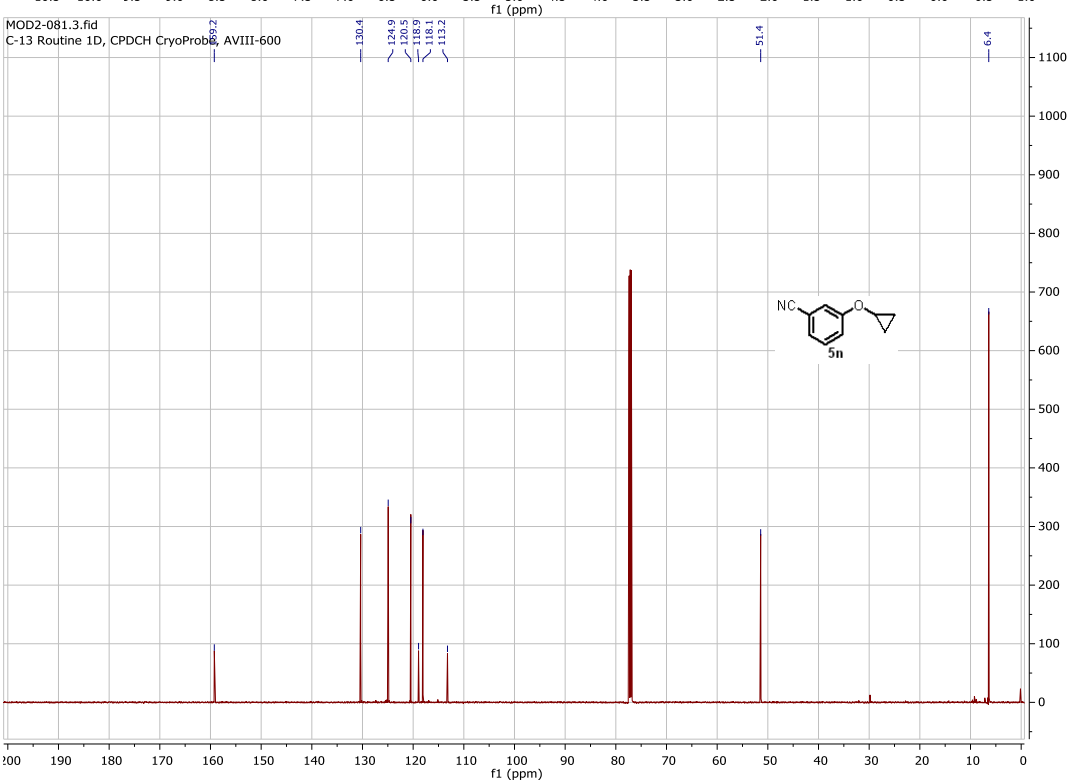

OCpr-06 13C.1.fid
C-13 Routine, BBO Probe, DRX-500
159.25
138.52
117.82
83.48
51.33
6.59
f1 (ppm)
5k

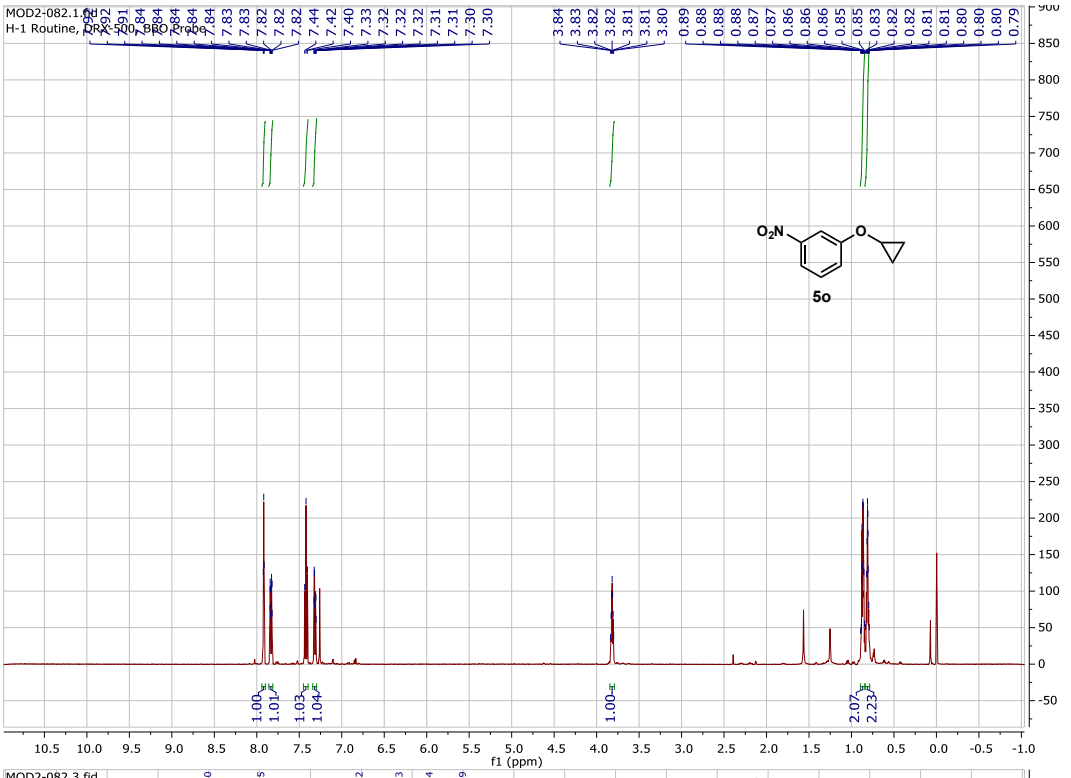

OCpr-11 1H.1.fid
H-1 Routine, DRX-500, BBO Probe
7.99
7.98
7.07
7.05
3.88
3.80
3.80
3.79
3.78
3.78
3.77
3.77
0.83
0.82
0.82
0.82
0.82
0.81
0.81
0.81
0.80
0.80
0.80
0.79
0.79
MeO
O
O
5l
2.01
1.82
3.31
1.00
4.00
f1 (ppm)

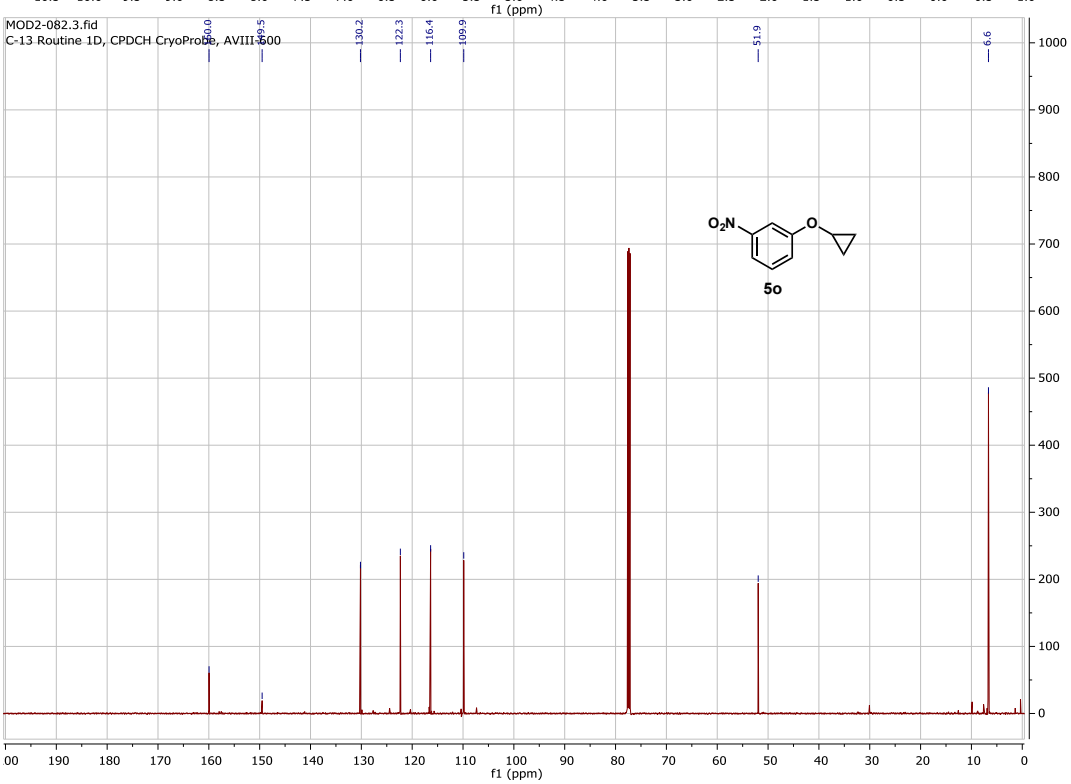

OCpr-11 13C.1.fid
C-13 Routine, BBO Probe, DRX-500
167.28
163.24
131.85
123.32
115.11
52.26
51.67
6.66
MeO
O
O
5l
f1 (ppm)

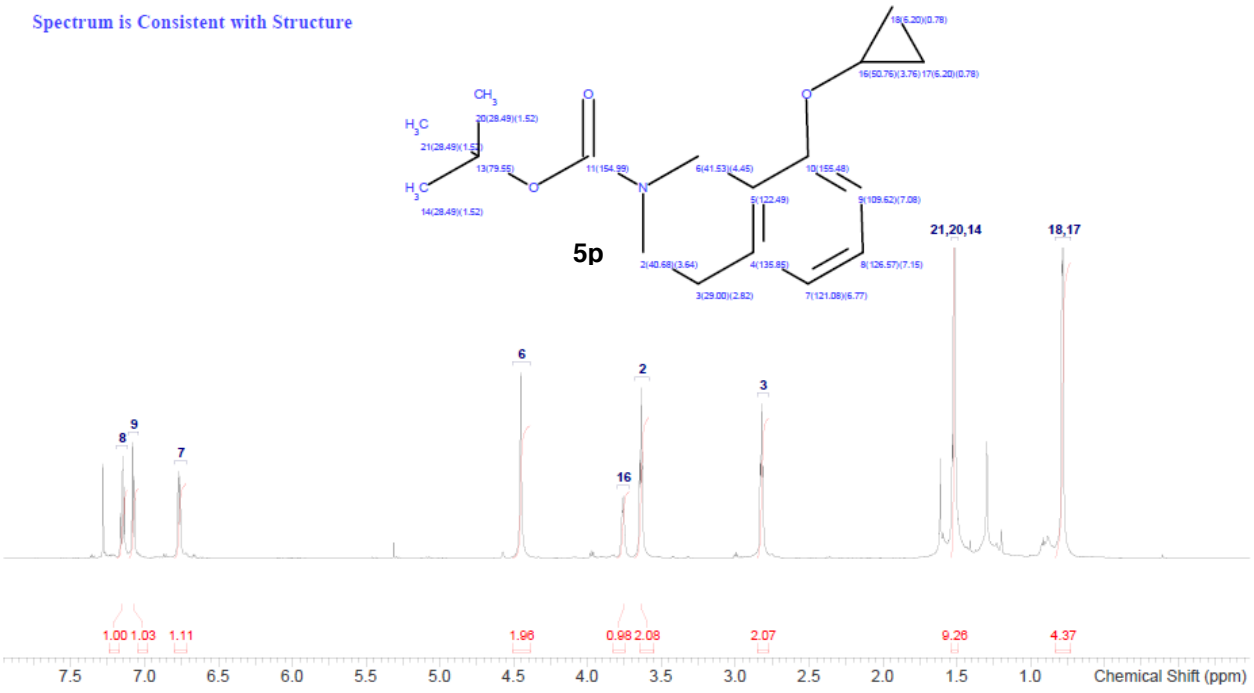

MOD2-075.1.fid
H-1 Routine, DRX-500, BBO Probe
7.59
7.59
7.58
7.57
7.57
7.57
7.11
7.10
7.09
7.09
7.08
3.79
3.79
3.78
3.78
3.77
3.76
3.76
0.85
0.85
0.84
0.84
0.84
0.84
0.83
0.83
0.83
0.82
0.81
0.81
0.80
0.80
0.80
0.79
0.79
0.79
0.78
NC
O
5m
2.18
2.23
1.00
2.25
2.13
f1 (ppm)
MOD2-075.2.fid
C-13 Routine, BBO Probe, DRX-500
162.6
134.0
119.4
116.0
104.4
51.5
6.4
NC
O
5m
f1 (ppm)

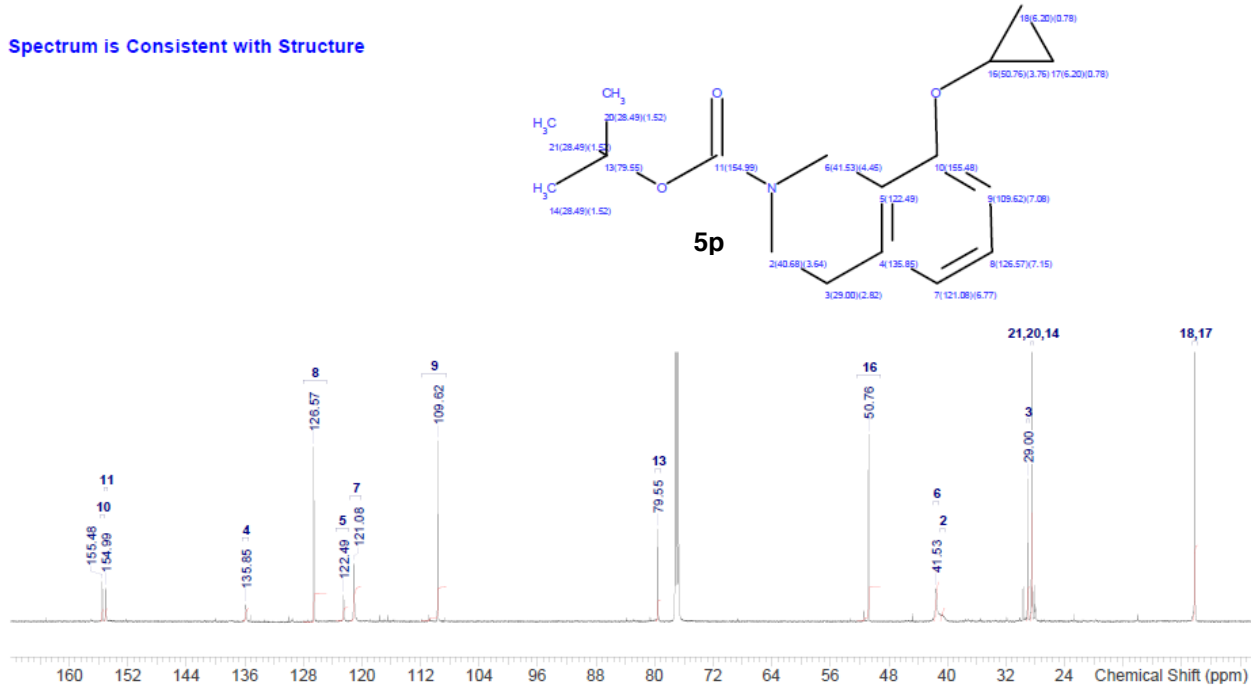

MOD2-081.1.fid
H-1 Routine, DRX-500, BBO Probe
7.38 7.37 7.35 7.34 7.33 7.33 7.33 7.26 7.25 7.25 7.25 7.23 7.23
3.76 3.76 3.75 3.75 3.74 3.73 3.73
0.85 0.84 0.84 0.83 0.83 0.83 0.82 0.82 0.80 0.80 0.79 0.79 0.78 0.78 0.78
NC
O
5n
1.24
1.22
2.29
1.00
2.35
2.33
f1 (ppm)

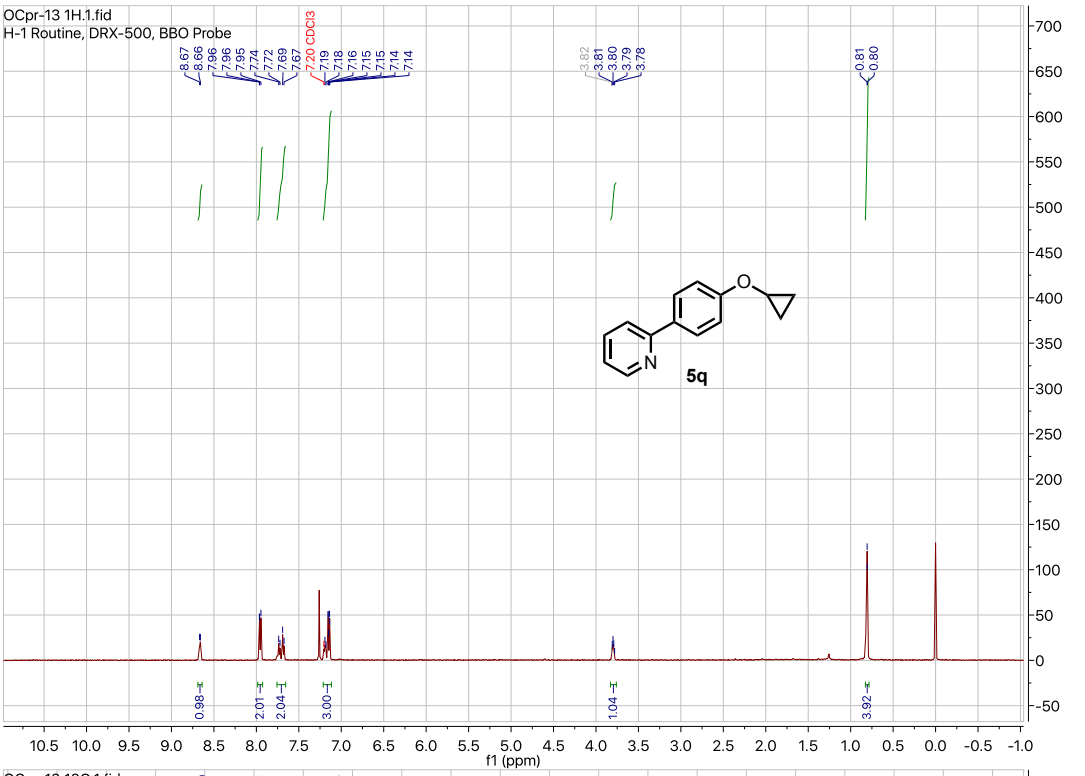

MOD2-081.3.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
159.2
130.4
124.9
120.5
118.9
118.1
113.2
51.4
6.4
NC
O
5n
f1 (ppm)

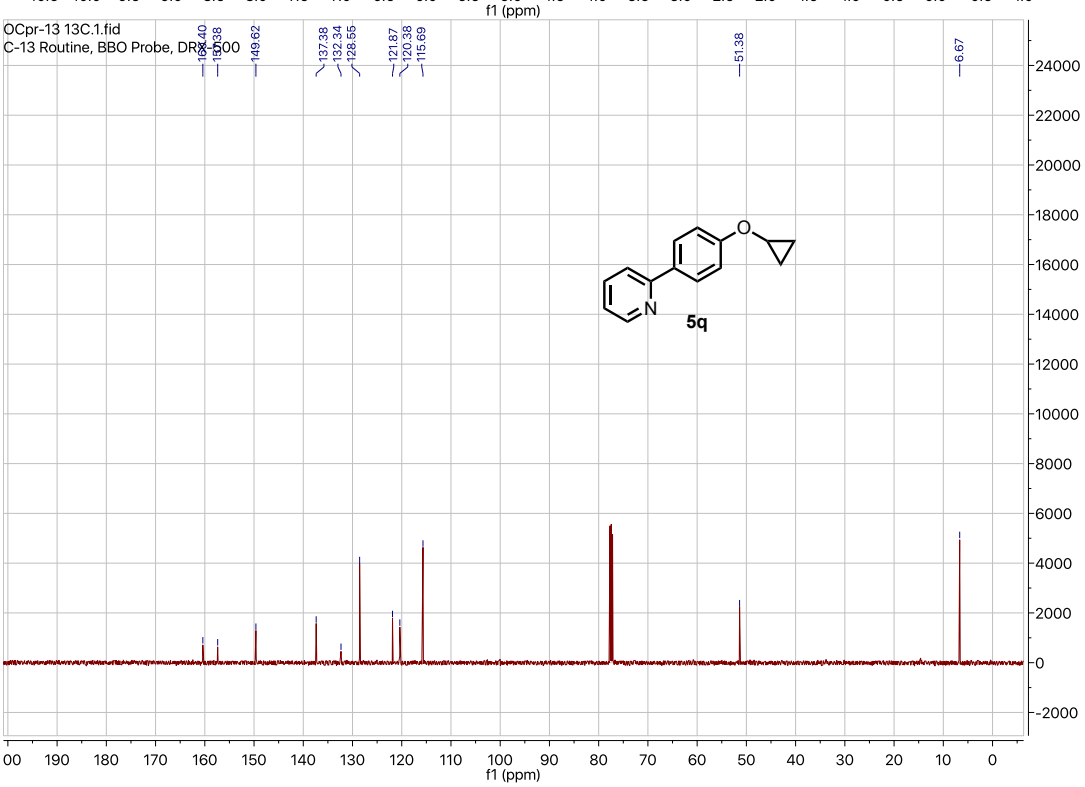

MOD2-082.1.fid
H-1 Routine, DRX-500, BBO Probe
f1 (ppm)
5o

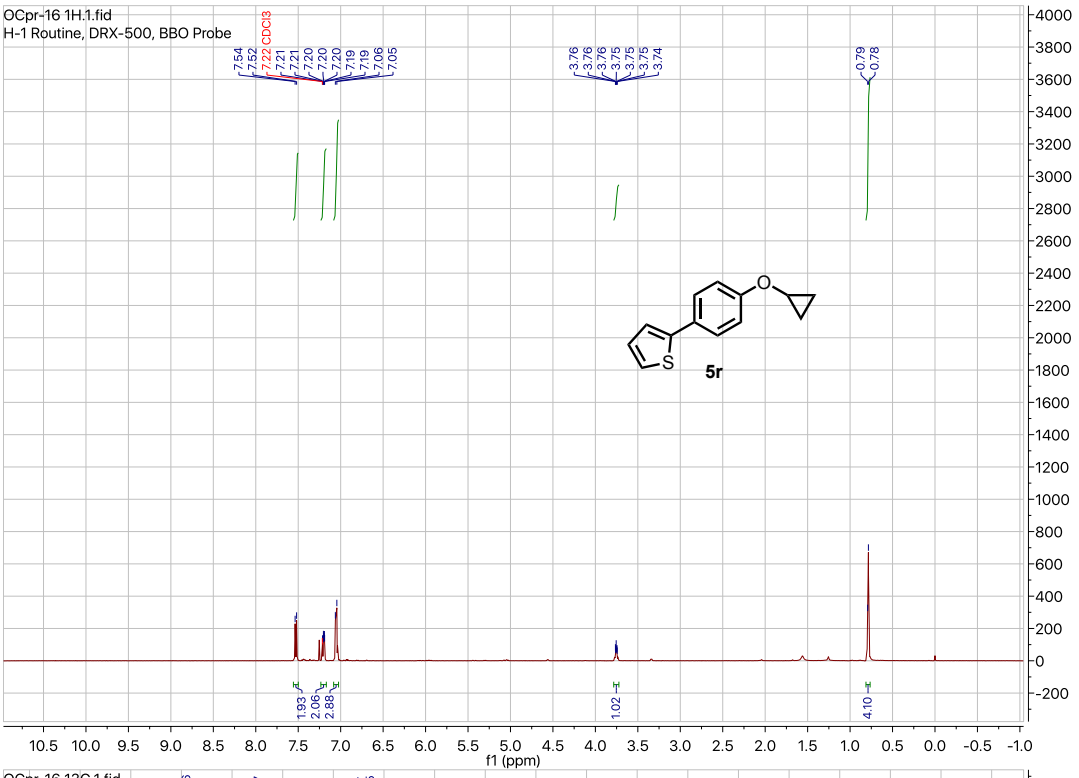

MOD2-082.3.fid
C-13 Routine 1D, CPDCH CryoProbe, AVIII-600
160.0
149.5
130.2
122.3
116.4
109.9
51.9
6.6
f1 (ppm)
5o

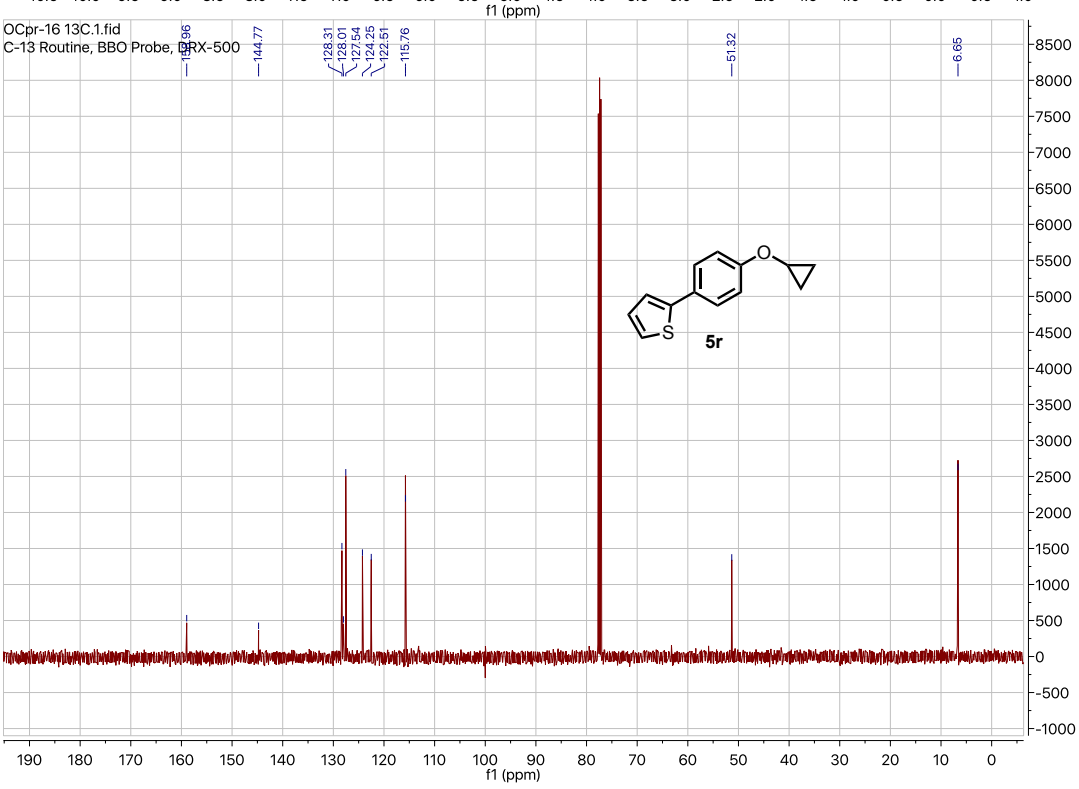

Spectrum is Consistent with Structure
5p
21,20,14
18,17
6
2
3
9
8
7
16
1.00 1.03 1.11
1.96
0.98 2.08
2.07
9.26
4.37
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
Chemical Shift (ppm)

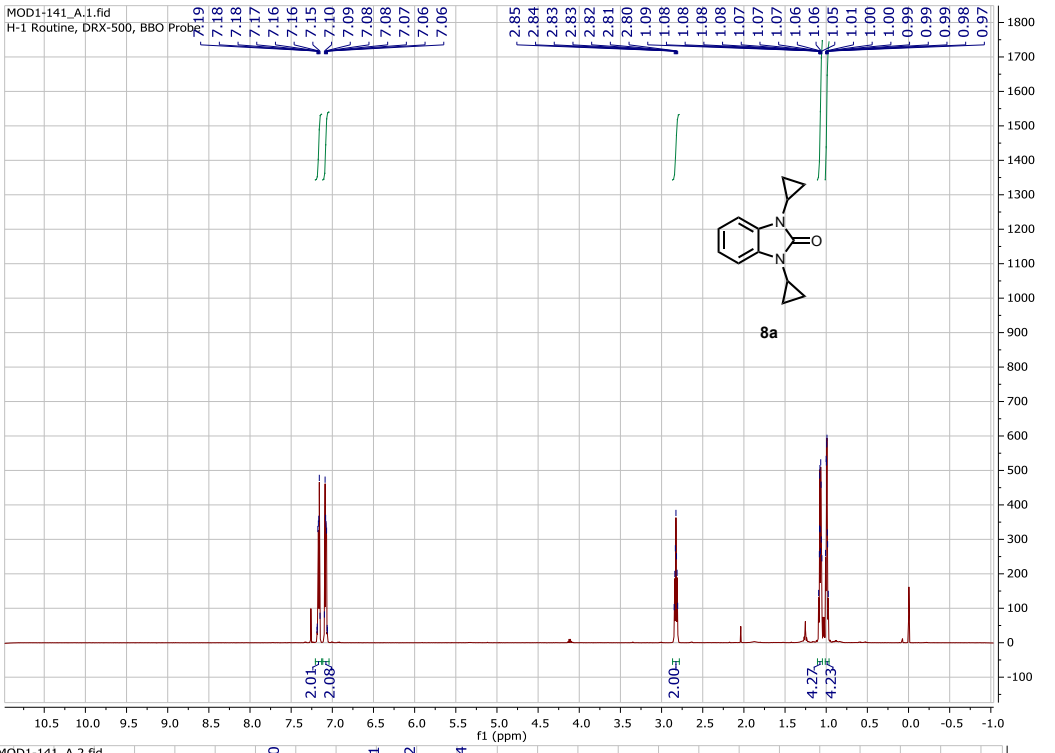

Spectrum is Consistent with Structure
5p
21,20,14
18,17
11
10
8
126.57
9
109.62
7
121.08
5
122.49
4
135.85
13
79.55
16
50.76
6
2
41.53
3
29.00
155.48
154.99
160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24
Chemical Shift (ppm)

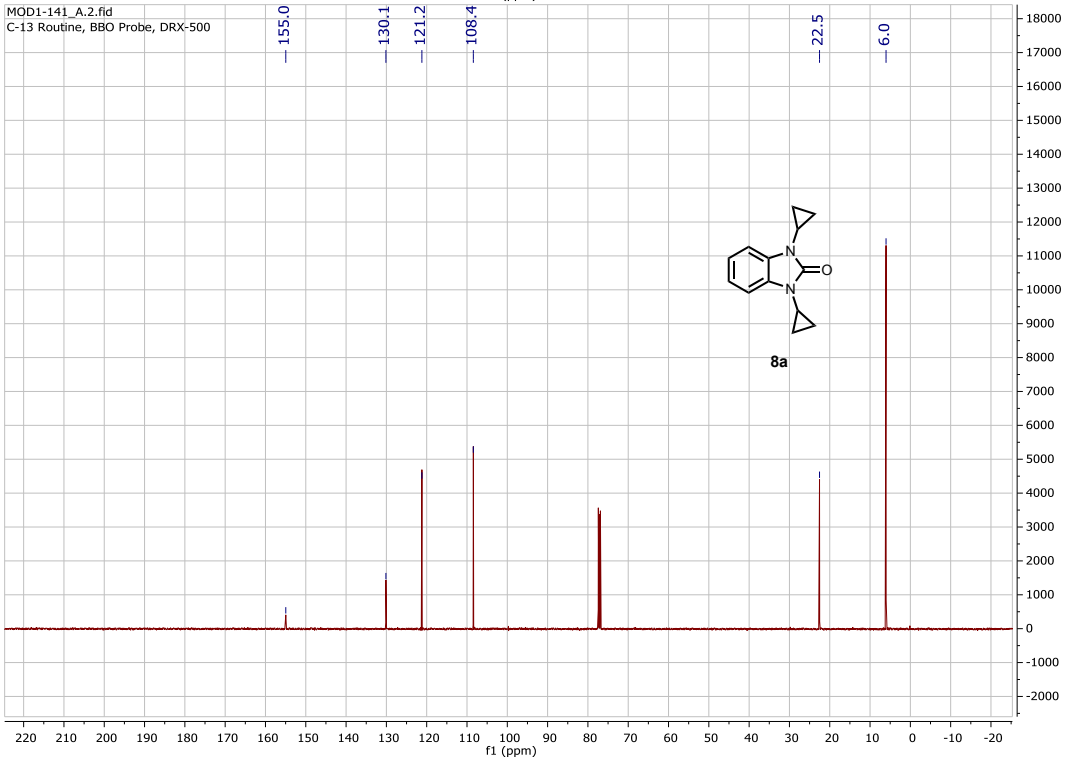

OCpr-13 1H.1.fid
H-1 Routine, DRX-500, BBO Probe
8.67
8.66
7.96
7.96
7.95
7.74
7.72
7.69
7.67
7.20 CDCl3
7.19
7.18
7.16
7.15
7.15
7.14
7.14
3.82
3.81
3.80
3.79
3.78
0.81
0.80
O
N
5q
0.98
2.01
2.04
3.00
1.04
3.92
f1 (ppm)

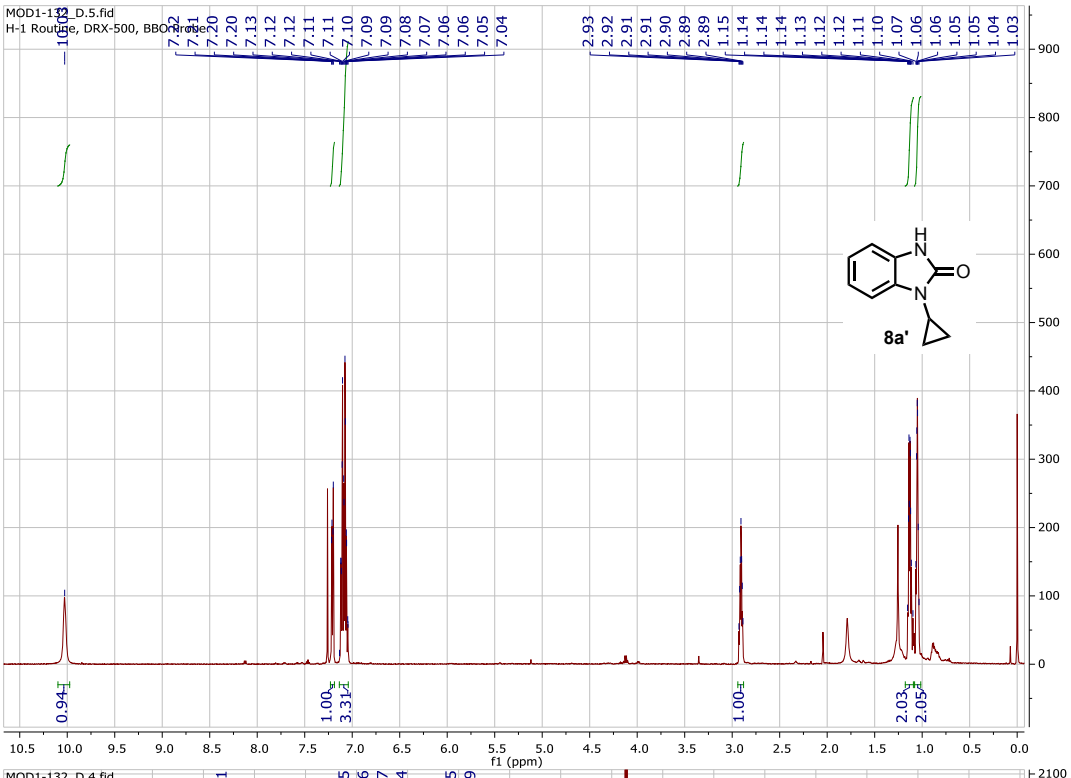

OCpr-13 13C.1.fid
C-13 Routine, BBO Probe, DRX-500
159.40
138.38
149.62
137.38
132.34
128.65
121.67
120.38
115.69
51.38
6.67
O
N
5q
f1 (ppm)

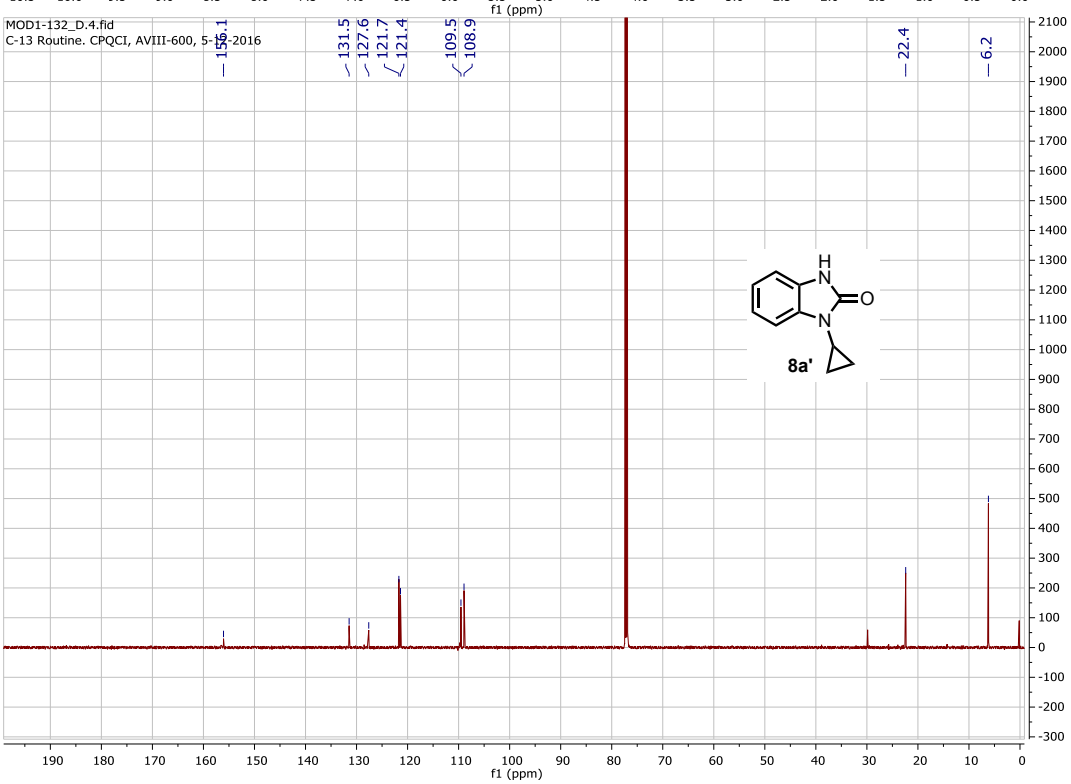

OCpr-16 1H.1.fid
H-1 Routine, DRX-500, BBO Probe
7.54
7.52
7.22 CDCl3
7.21
7.21
7.20
7.20
7.20
7.19
7.19
7.06
7.05
3.76
3.76
3.76
3.75
3.75
3.75
3.75
3.74
0.79
0.78
1.93
2.06
2.88
1.02
4.10
f1 (ppm)
5r

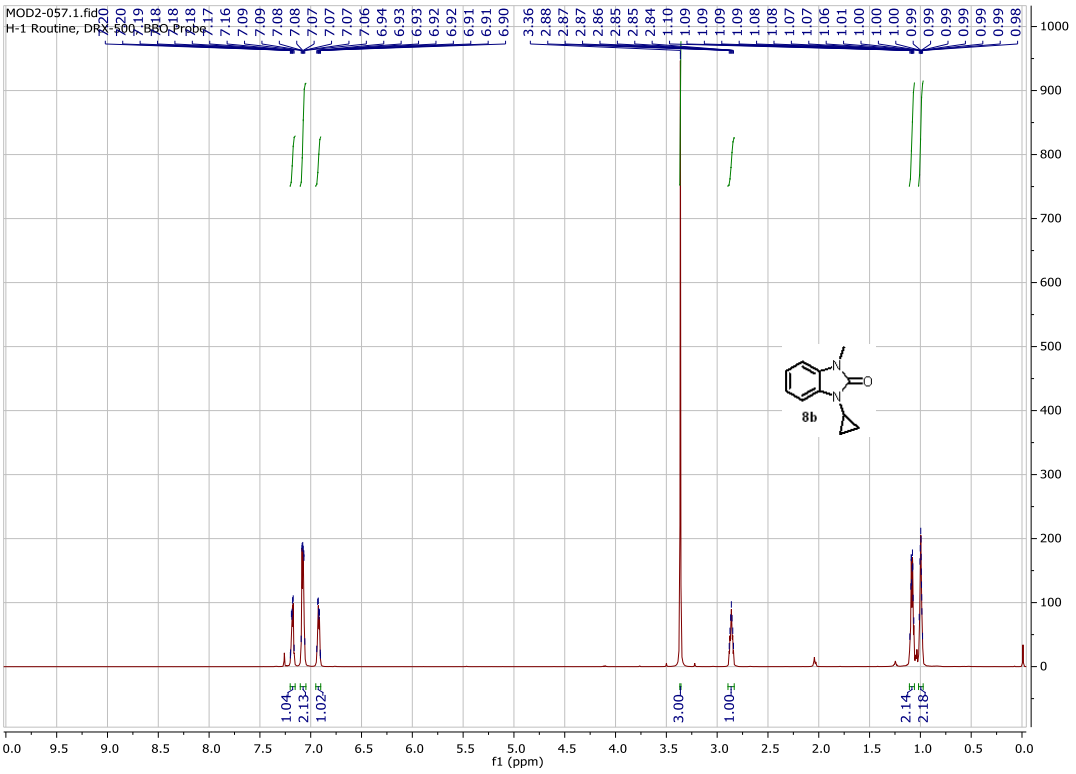

OCpr-16 13C.1.fid
C-13 Routine, BBO Probe, DRX-500
159.96
144.77
128.31
128.01
127.54
124.25
122.51
115.76
51.32
6.65
f1 (ppm)
5r

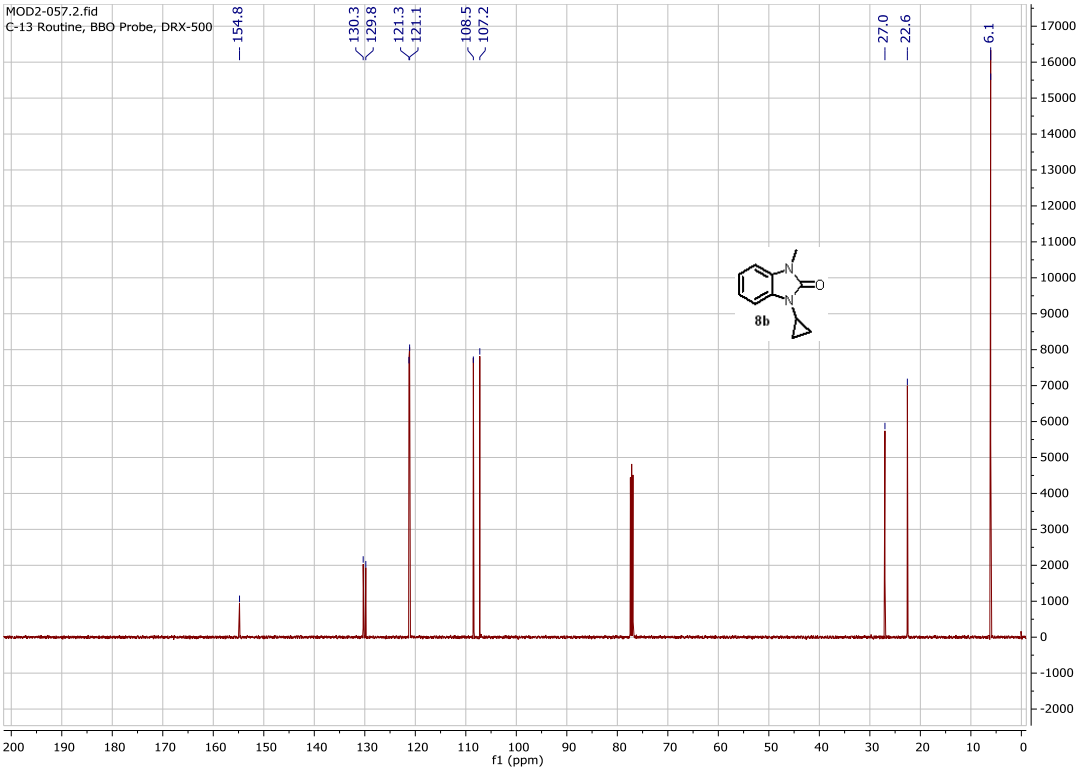

MOD1-141_A.1.fid
H-1 Routine, DRX-500, BBO Probe
7.19 7.18 7.18 7.17 7.16 7.16 7.15 7.10 7.09 7.08 7.08 7.07 7.06 7.06
2.85 2.84 2.83 2.83 2.82 2.81 2.80 1.09 1.08 1.08 1.08 1.07 1.07 1.07 1.06 1.06 1.05 1.01 1.00 1.00 0.99 0.99 0.99 0.98 0.97
2.01 2.08 2.00 4.27 4.23
f1 (ppm)

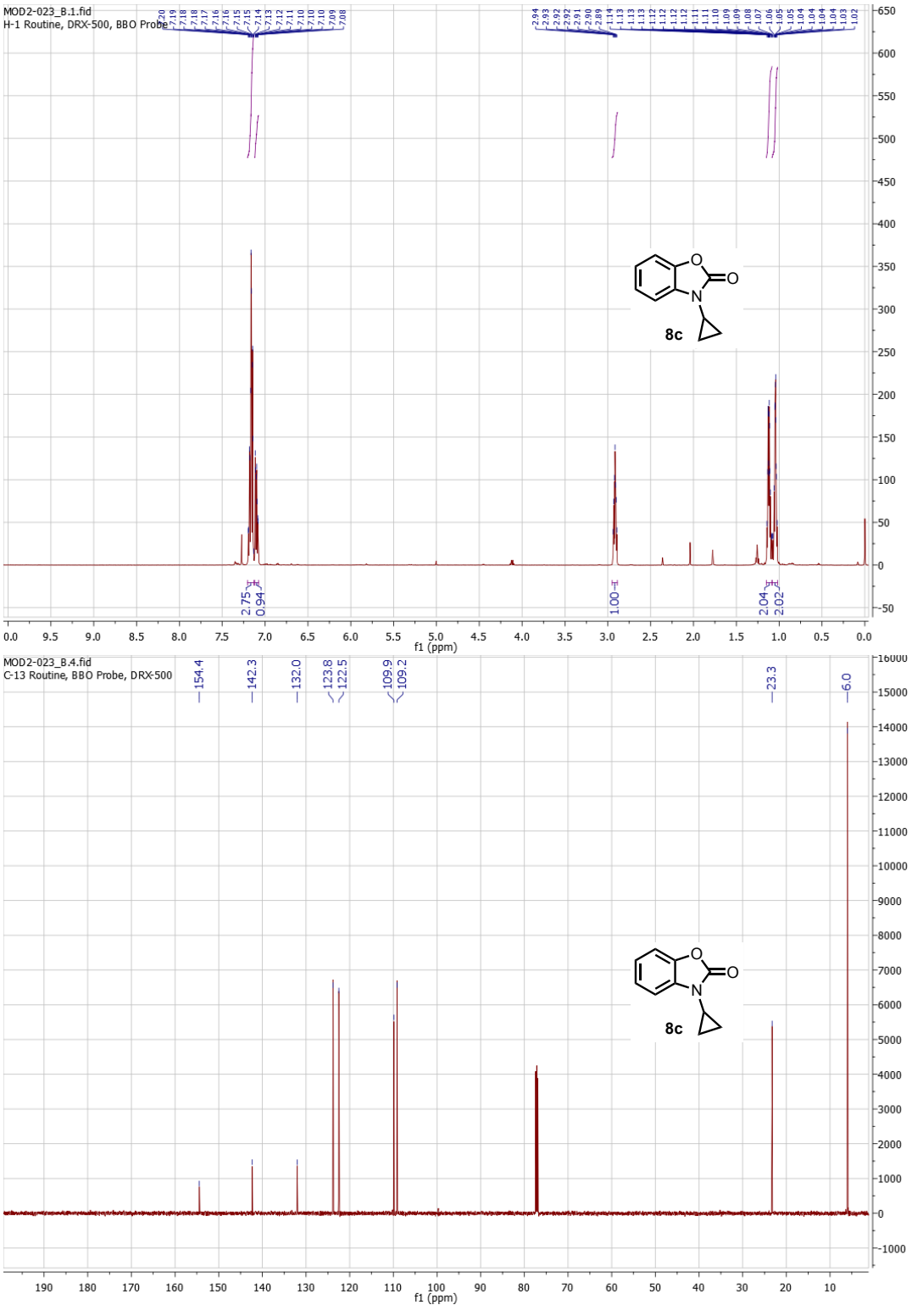

MOD1-141_A.2.fid
C-13 Routine, BBO Probe, DRX-500
155.0 130.1 121.2 108.4 22.5 6.0
f1 (ppm)

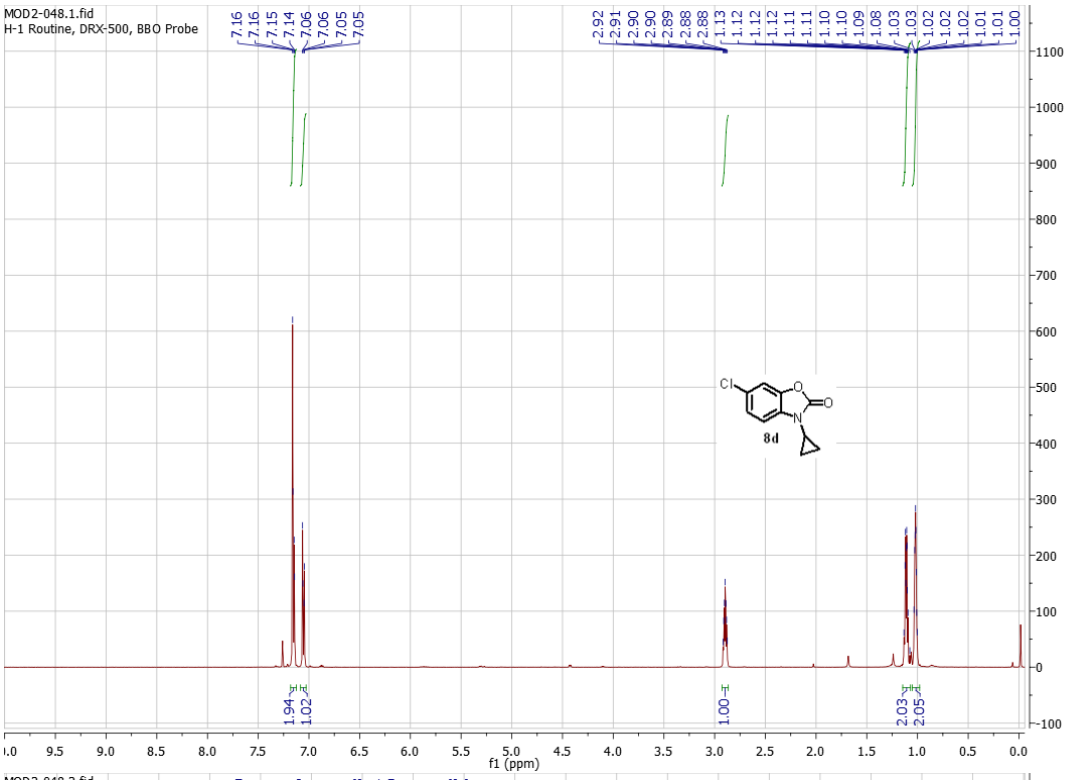

MOD1-132_D.5.fid
H-1 Routine, DRX-500, BBOnProbe
8a'

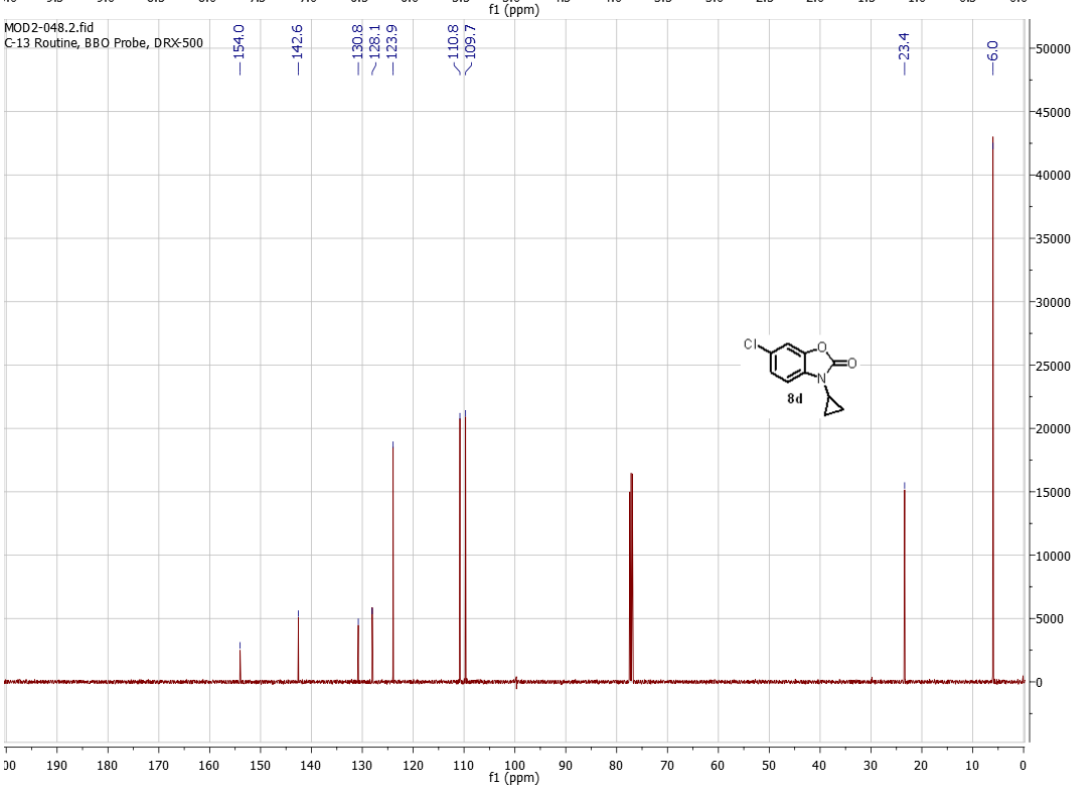

MOD1-132_D.4.fid
C-13 Routine. CPQCI, AVIII-600, 5-15-2016
8a'

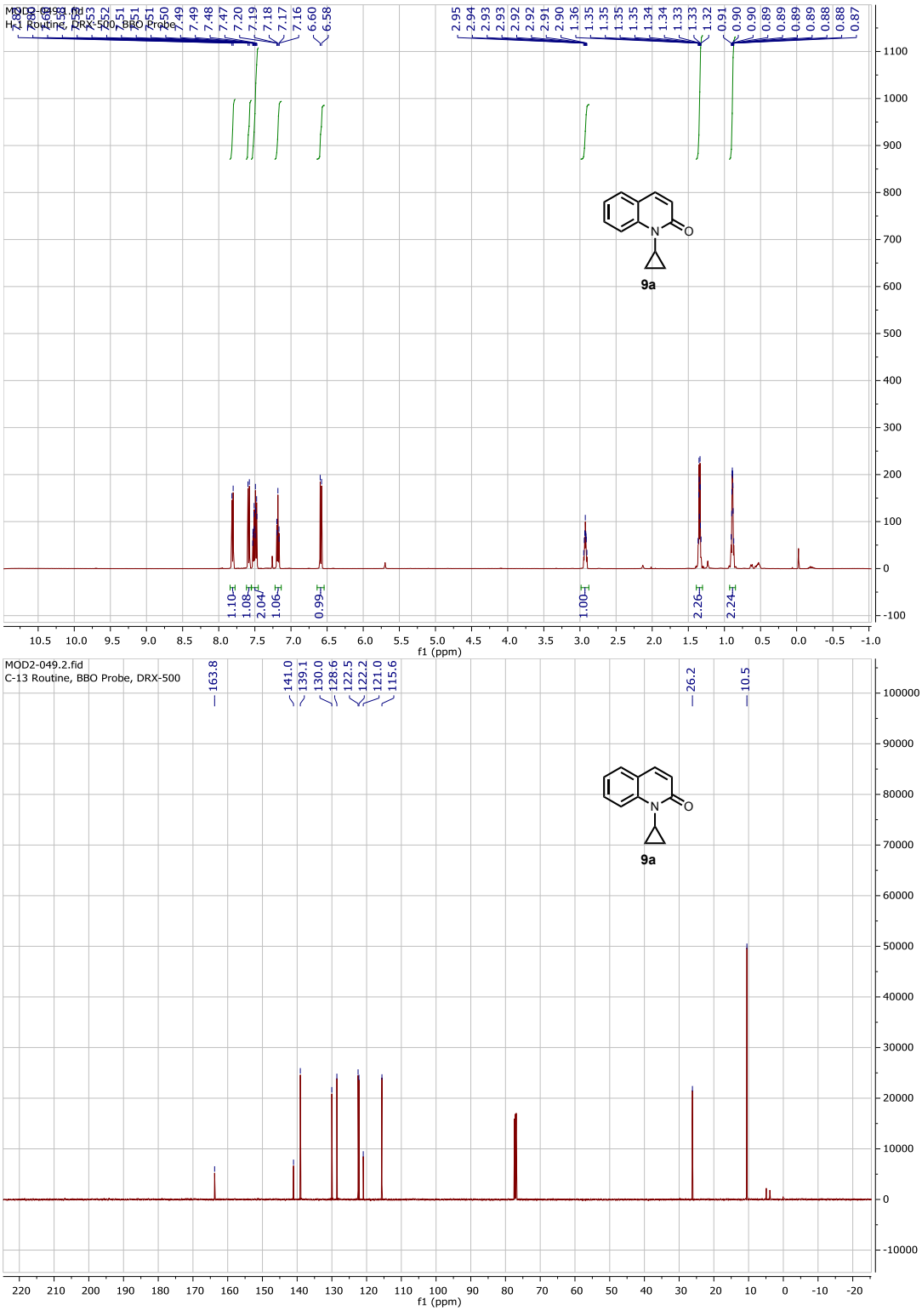

MOD2-057.1.fid
H-1 Routine, DRX-500, BBO Probe
8b
1.04
2.13
1.02
3.00
1.00
2.14
2.18
f1 (ppm)

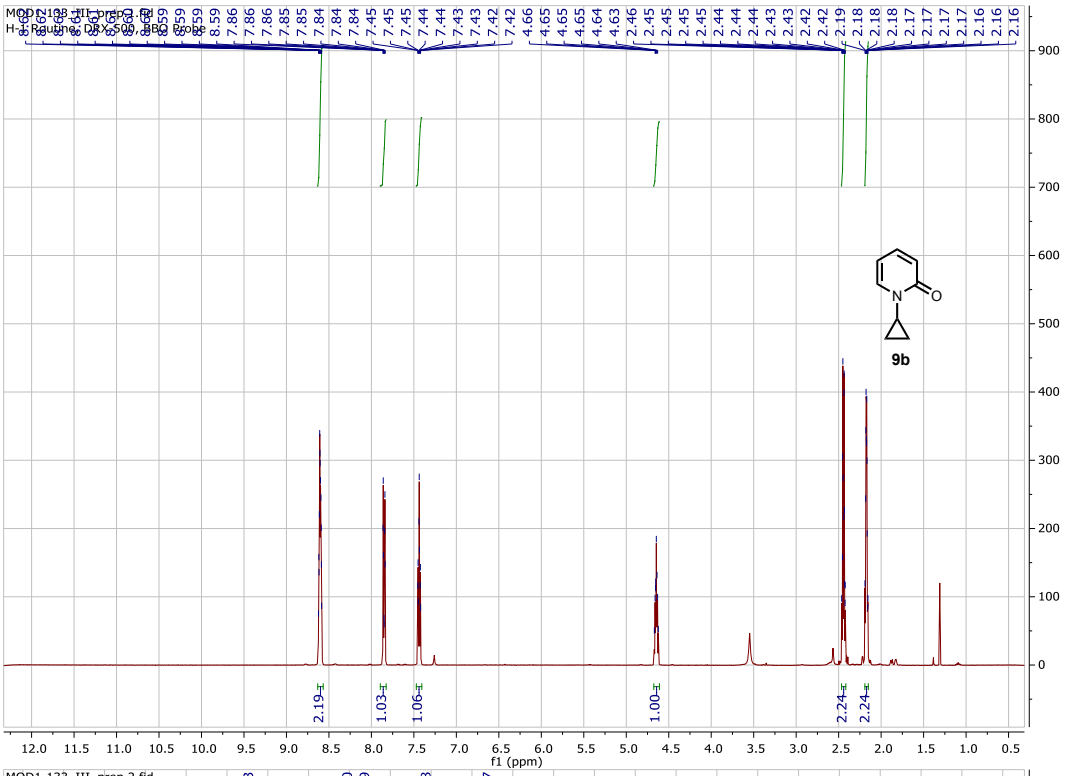

MOD2-057.2.fid
C-13 Routine, BBO Probe, DRX-500
154.8
130.3
129.8
121.3
121.1
108.5
107.2
27.0
22.6
6.1
8b
f1 (ppm)

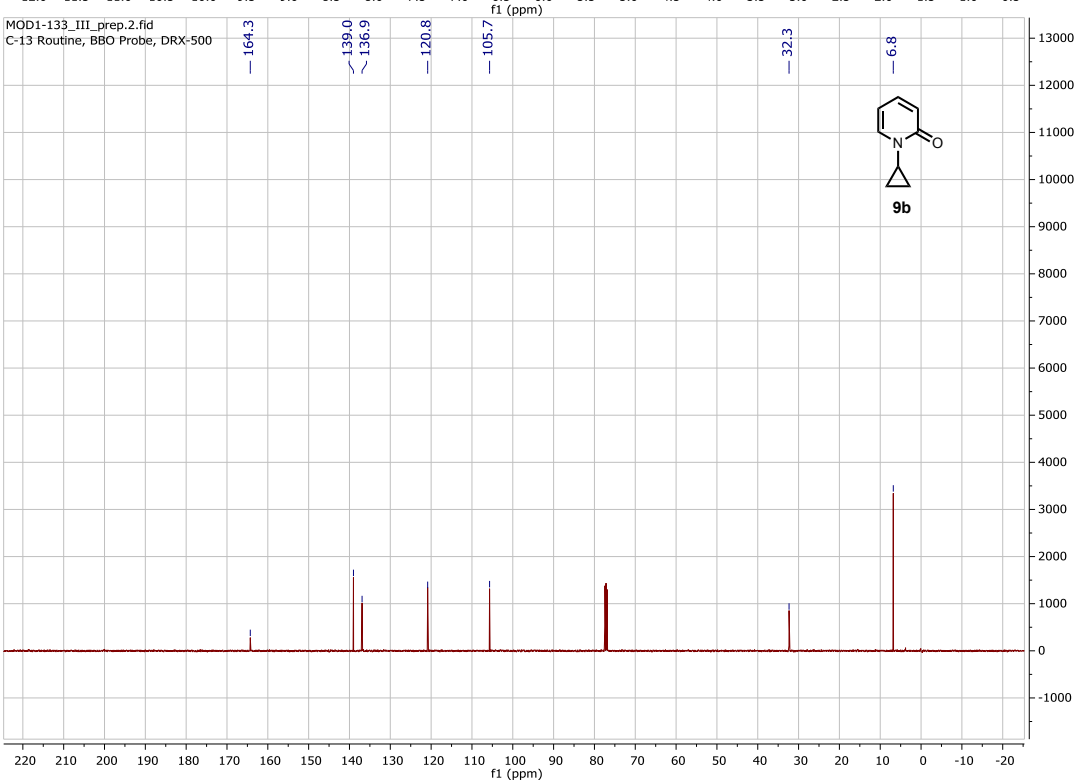

MOD2-023_B.1.fid
H-1 Routine, DRX-500, BBO Probe
8c
2.75
0.94
1.00
2.04
2.02
f1 (ppm)
MOD2-023_B.4.fid
C-13 Routine, BBO Probe, DRX-500
154.4
142.3
132.0
123.8
122.5
109.9
109.2
23.3
6.0
8c
f1 (ppm)

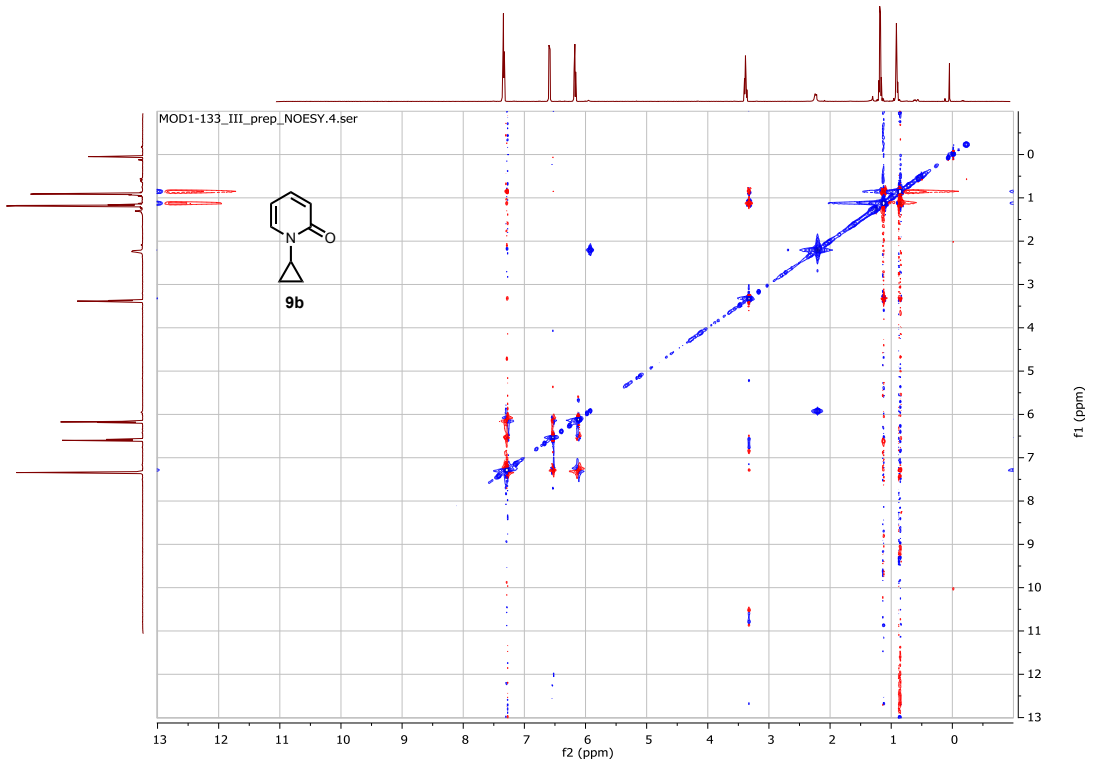

MOD2-048.1.fid
H-1 Routine, DRX-500, BBO Probe
7.16
7.16
7.15
7.14
7.06
7.06
7.05
7.05
2.92
2.91
2.90
2.90
2.89
2.88
2.88
1.13
1.12
1.12
1.12
1.11
1.11
1.10
1.10
1.09
1.08
1.03
1.03
1.02
1.02
1.02
1.01
1.01
1.00
Cl
O
O
N
8d
1.94
1.02
1.00
2.03
2.05
f1 (ppm)

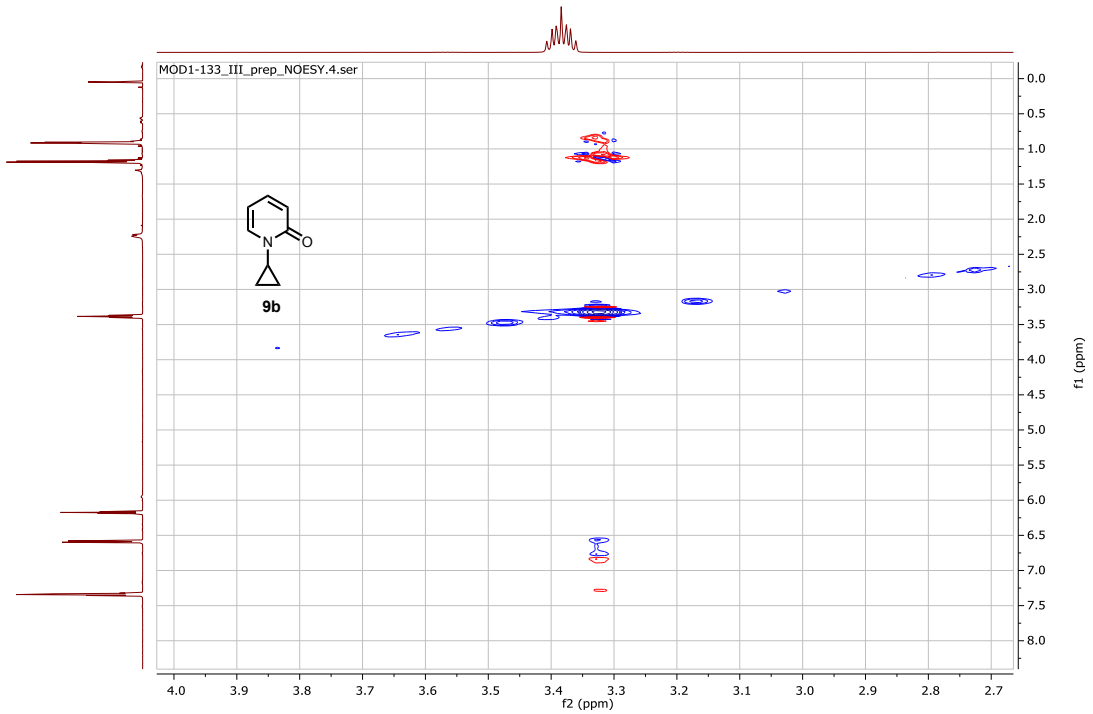

MOD2-048.2.fid
C-13 Routine, BBO Probe, DRX-500
154.0
142.6
130.8
128.1
123.9
110.8
109.7
23.4
6.0
Cl
O
O
N
8d
f1 (ppm)

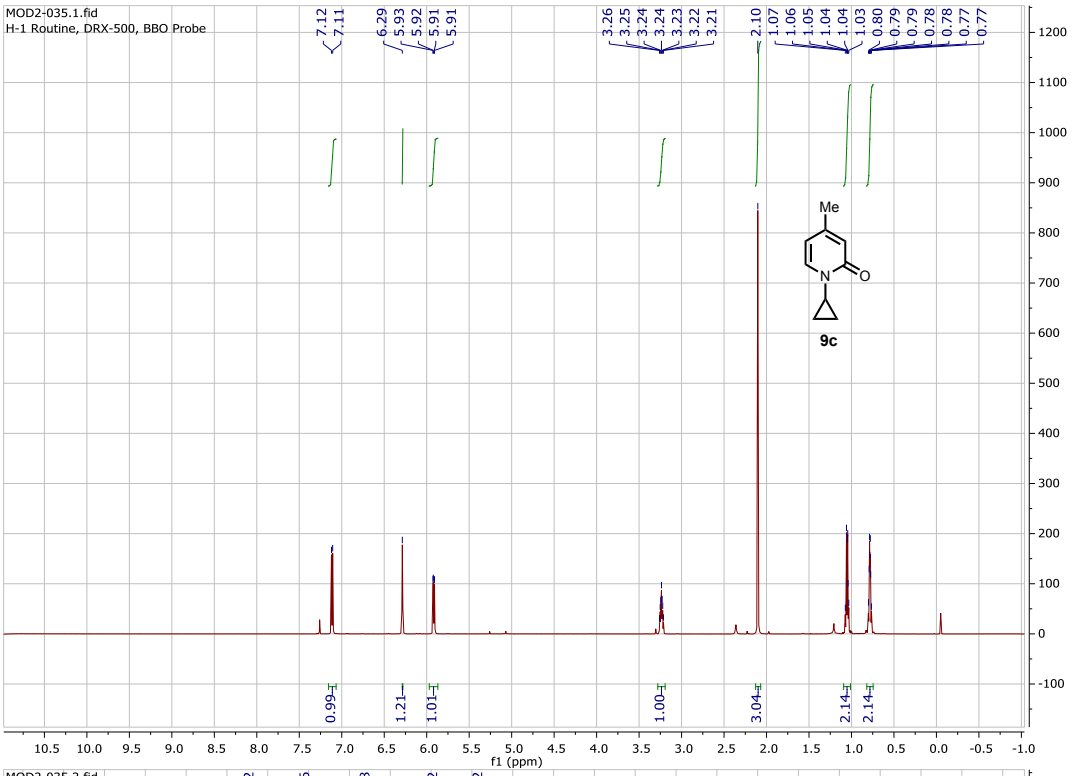

MOD2-049.1.fid
H-1 Routine, DRX-500, BBO Probe
9a
f1 (ppm)
MOD2-049.2.fid
C-13 Routine, BBO Probe, DRX-500
9a
f1 (ppm)

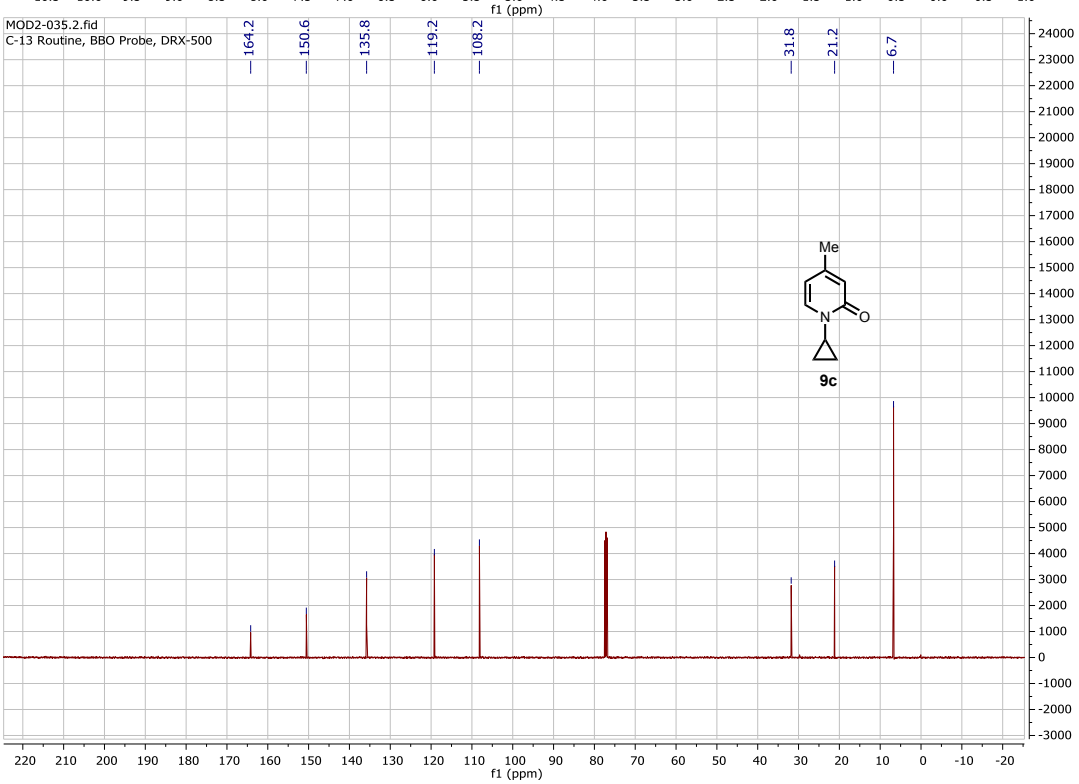

9b
2.19
1.03
1.06
1.00
2.24
2.24
f1 (ppm)

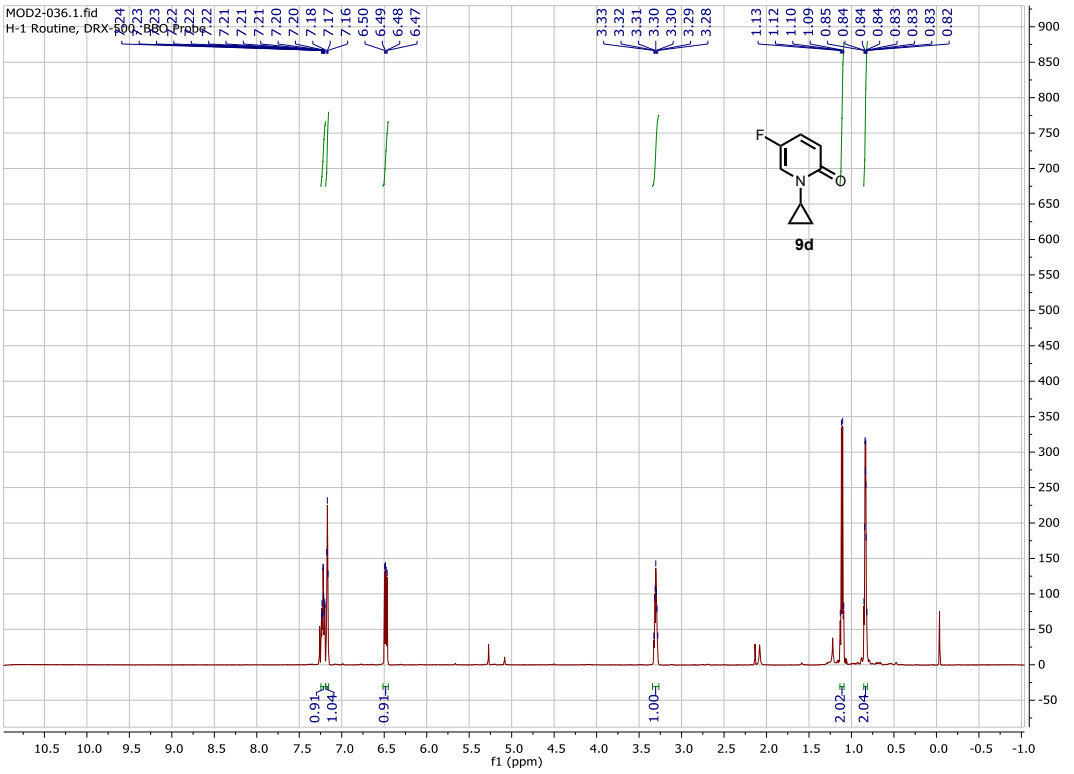

MOD1-133_III_prep.2.fid
C-13 Routine, BBO Probe, DRX-500
164.3
139.0
136.9
120.8
105.7
32.3
6.8
9b
f1 (ppm)

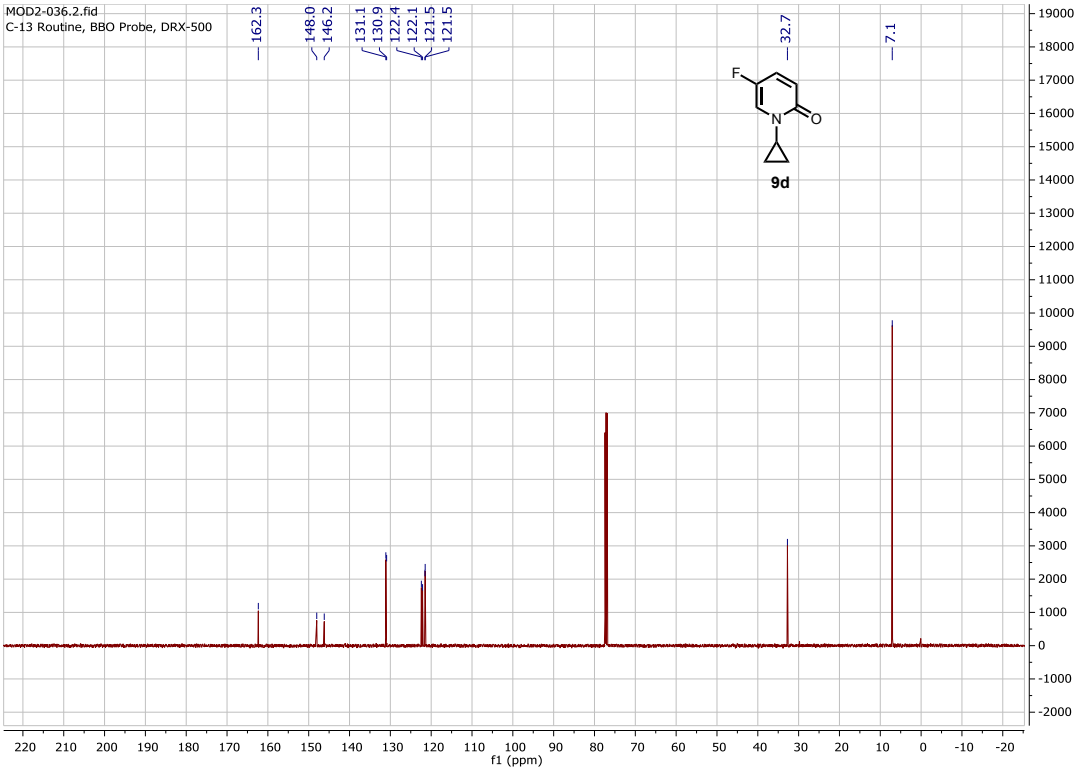

MOD1-133_III_prep_NOESY.4.ser
9b
f2 (ppm)
f1 (ppm)

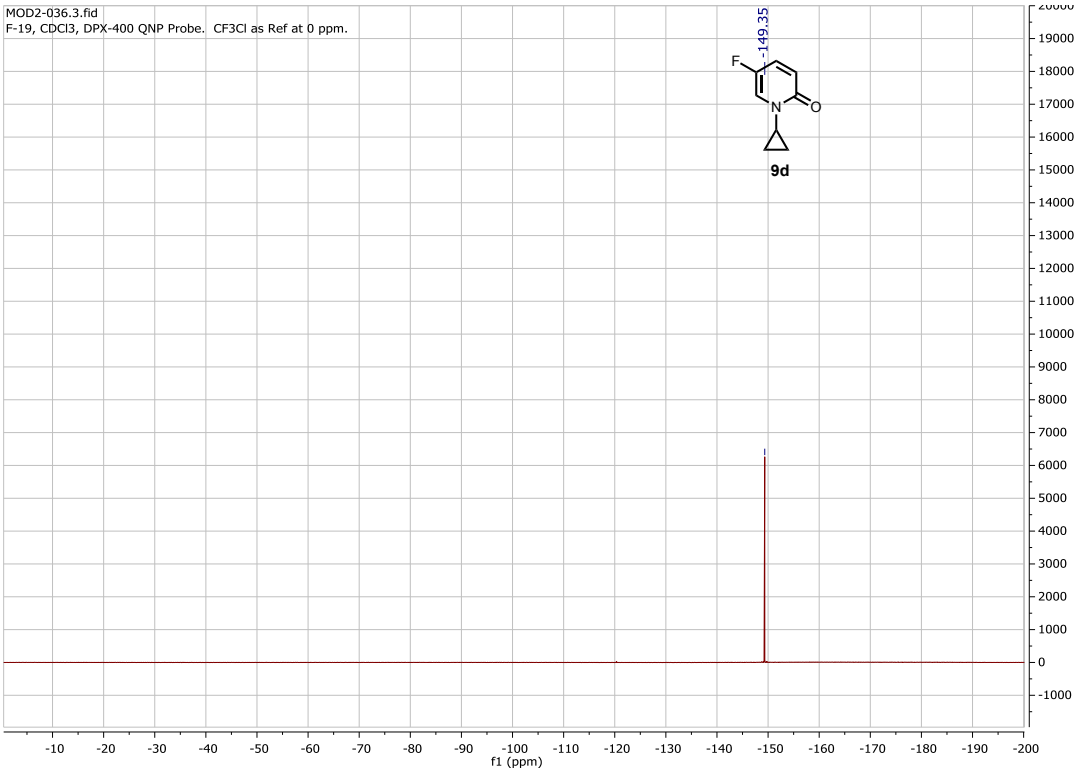

MOD1-133_III_prep_NOESY.4.ser
9b
f2 (ppm)
f1 (ppm)

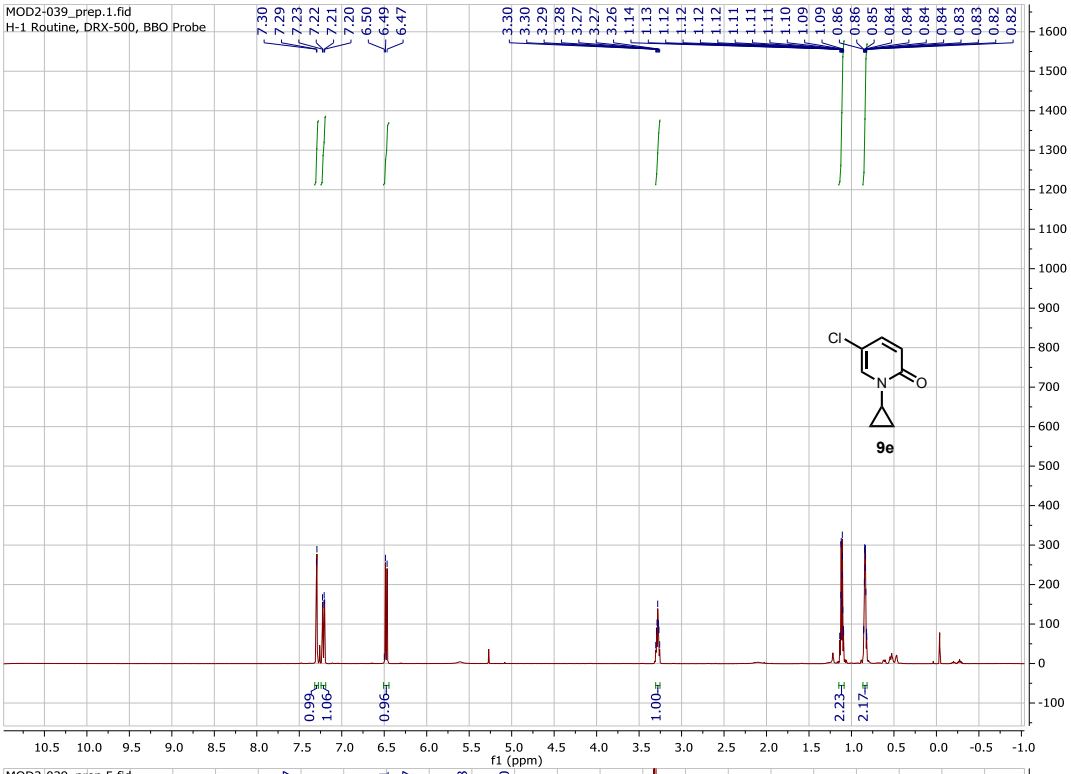

MOD2-035.1.fid
H-1 Routine, DRX-500, BBO Probe
7.12
7.11
6.29
5.93
5.92
5.91
5.91
3.26
3.25
3.24
3.24
3.23
3.22
3.21
2.10
1.07
1.06
1.05
1.04
1.04
1.03
0.80
0.79
0.79
0.78
0.78
0.77
0.77
0.99
1.21
1.01
1.00
3.04
2.14
2.14
Me
N
O
9c
f1 (ppm)

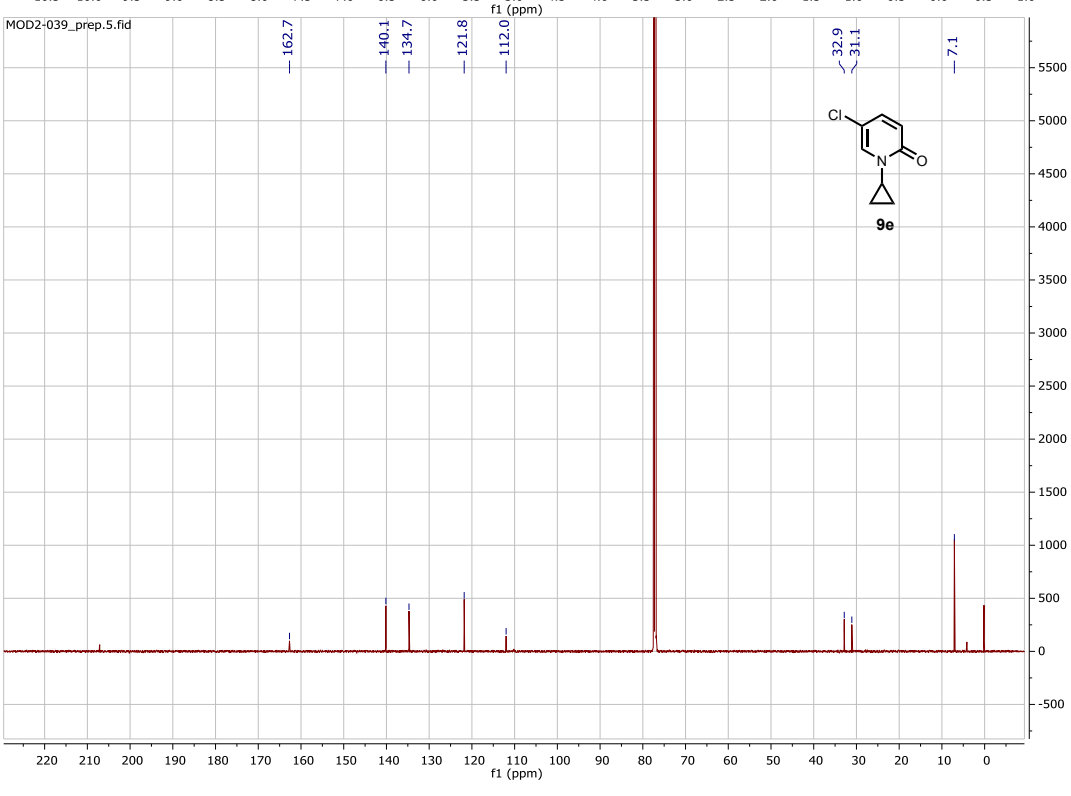

MOD2-035.2.fid
C-13 Routine, BBO Probe, DRX-500
164.2
150.6
135.8
119.2
108.2
31.8
21.2
6.7
Me
N
O
9c
f1 (ppm)

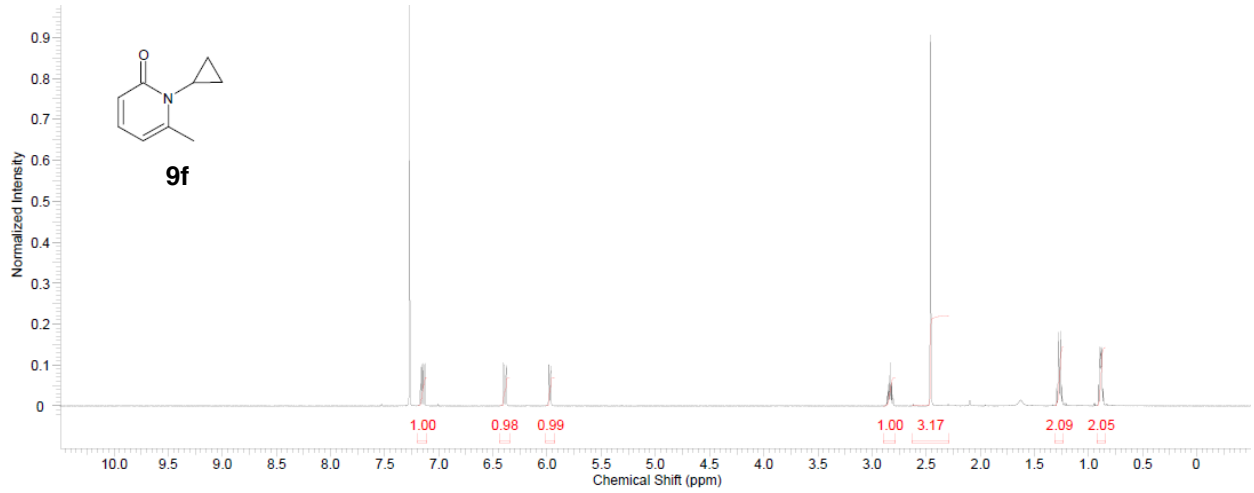

MOD2-036.1.fid
H-1 Routine, DRX-500, BBO Probe
7.24 7.23 7.23 7.22 7.22 7.22 7.21 7.21 7.21 7.20 7.20 7.18 7.17 7.16 6.50 6.49 6.48 6.47
3.33 3.32 3.31 3.30 3.30 3.30 3.29 3.28
1.13 1.12 1.10 1.09 0.85 0.84 0.84 0.84 0.83 0.83 0.83 0.82
F
N
O
9d
0.91 1.04 0.91 1.00 2.02 2.04
f1 (ppm)

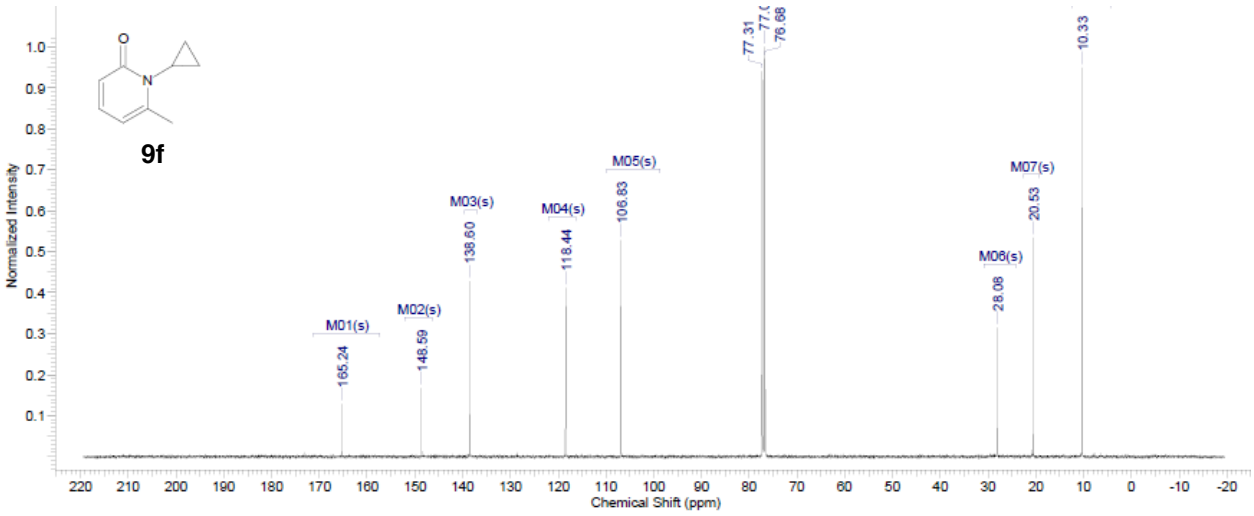

MOD2-036.2.fid
C-13 Routine, BBO Probe, DRX-500
162.3 148.0 146.2 131.1 130.9 122.4 122.1 121.5 121.5
32.7 7.1
F
N
O
9d
f1 (ppm)

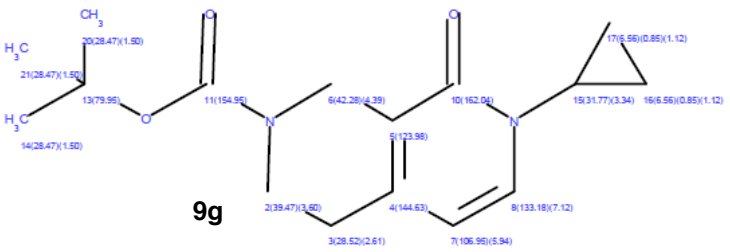

MOD2-036.3.fid
F-19, CDCl3, DPX-400 QNP Probe. CF3Cl as Ref at 0 ppm.
-149.35
F
N
O
9d
f1 (ppm)


MOD2-039_prep.1.fid
H-1 Routine, DRX-500, BBO Probe
7.30
7.29
7.23
7.22
7.21
7.20
6.50
6.49
6.47
3.30
3.30
3.29
3.28
3.27
3.27
3.26
1.14
1.13
1.12
1.12
1.12
1.12
1.11
1.11
1.11
1.10
1.09
1.09
0.86
0.86
0.85
0.84
0.84
0.84
0.84
0.83
0.83
0.82
0.82
Cl
N
O
9e
0.99
1.06
0.96
1.00
2.23
2.17
f1 (ppm)

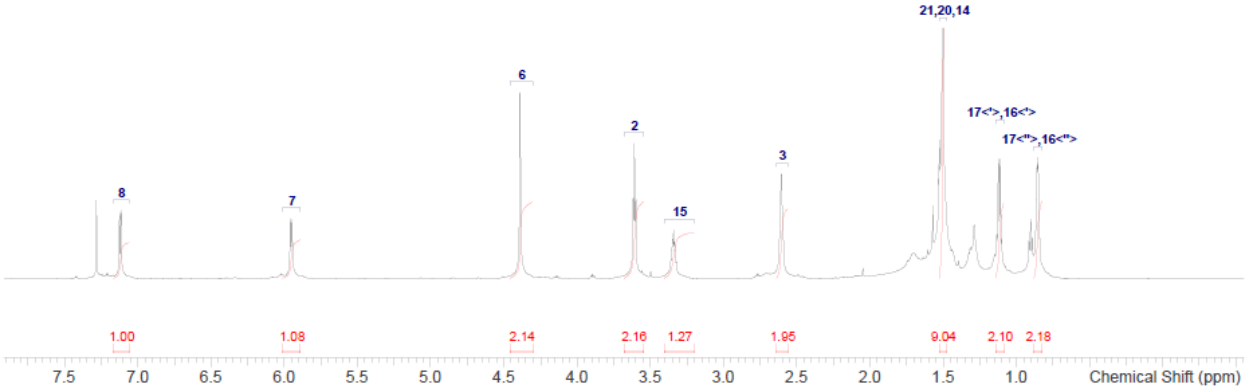

MOD2-039_prep.5.fid
162.7
140.1
134.7
121.8
112.0
32.9
31.1
7.1
Cl
N
O
9e
f1 (ppm)

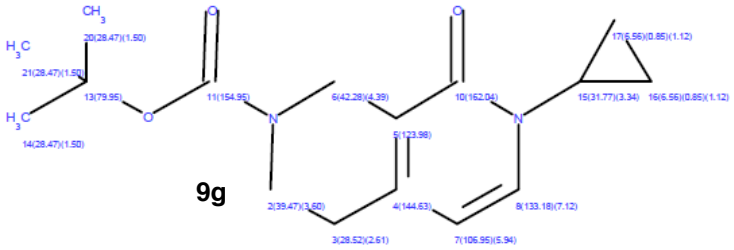

9f
Normalized Intensity
1.00
0.98
0.99
1.00
3.17
2.09
2.05
Chemical Shift (ppm)


9f
Normalized Intensity
M01(s)
165.24
M02(s)
148.59
M03(s)
138.60
M04(s)
118.44
M05(s)
106.83
77.31
76.66
M06(s)
28.08
M07(s)
20.53
10.33
Chemical Shift (ppm)

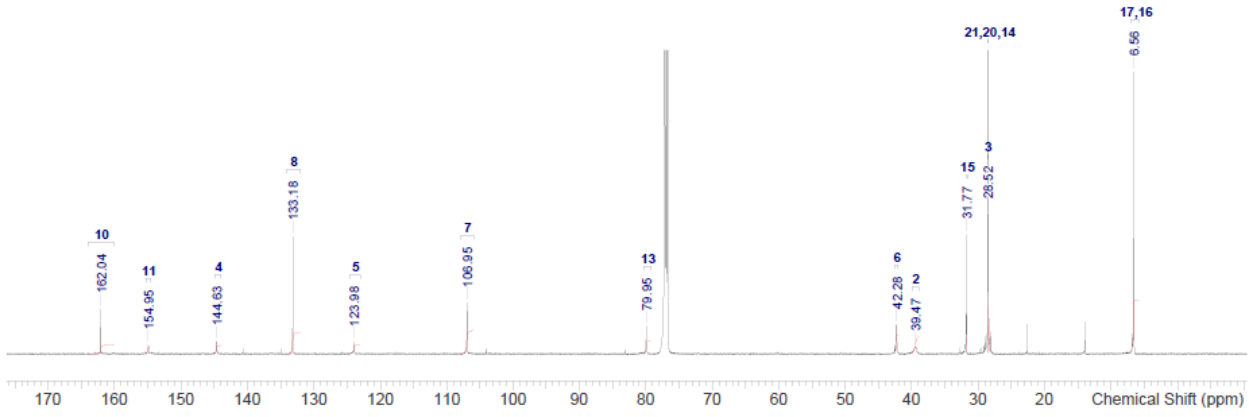


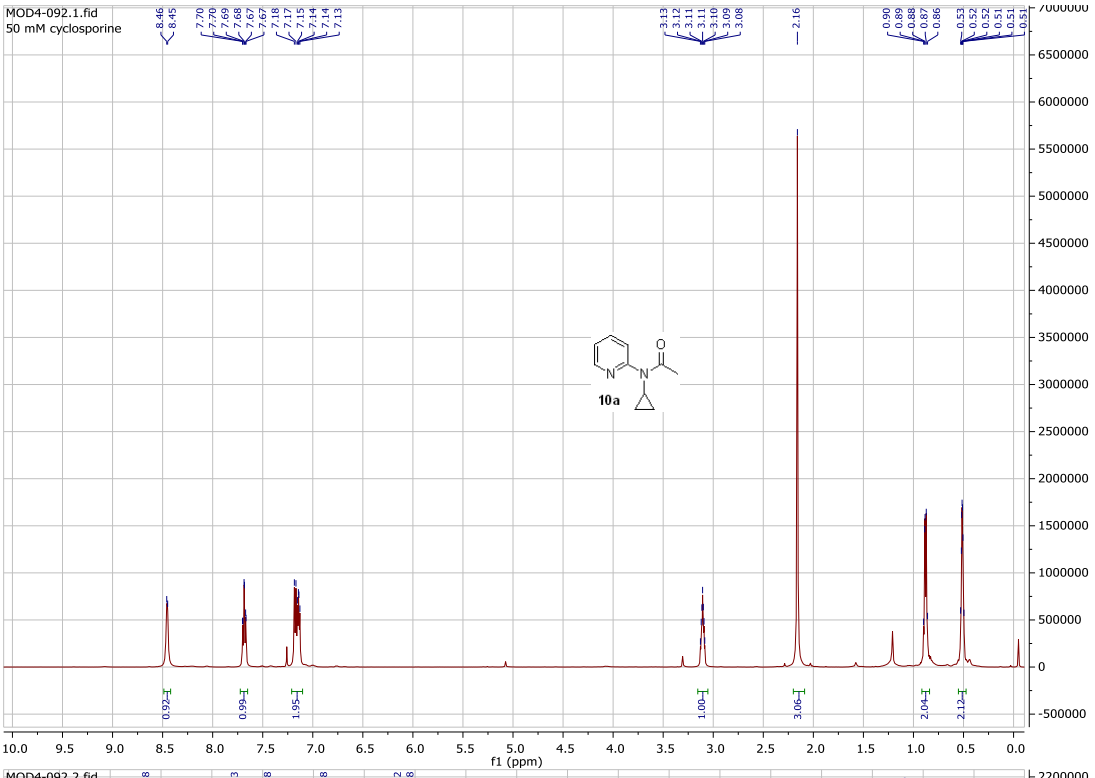
9g

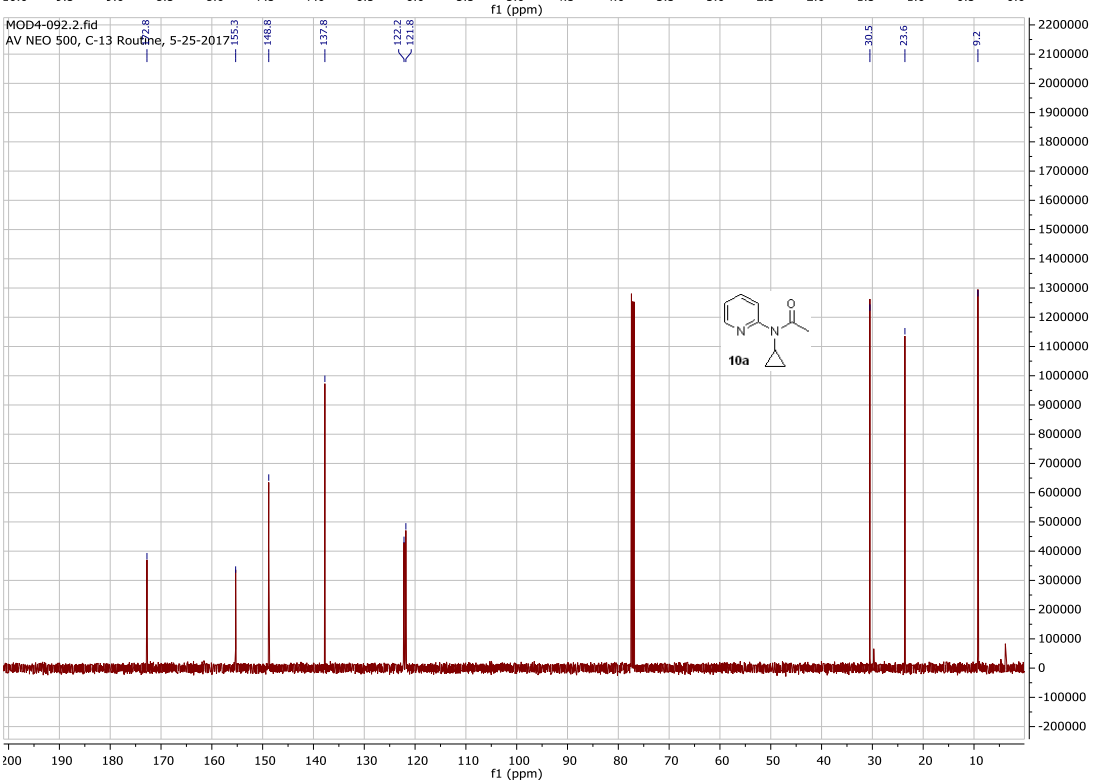

21,20,14
6
2
3
17<*>,16<*>
17<*'>,16<*'>
8
7
15
1.00
1.08
2.14
2.16
1.27
1.95
9.04
2.10
2.18
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)

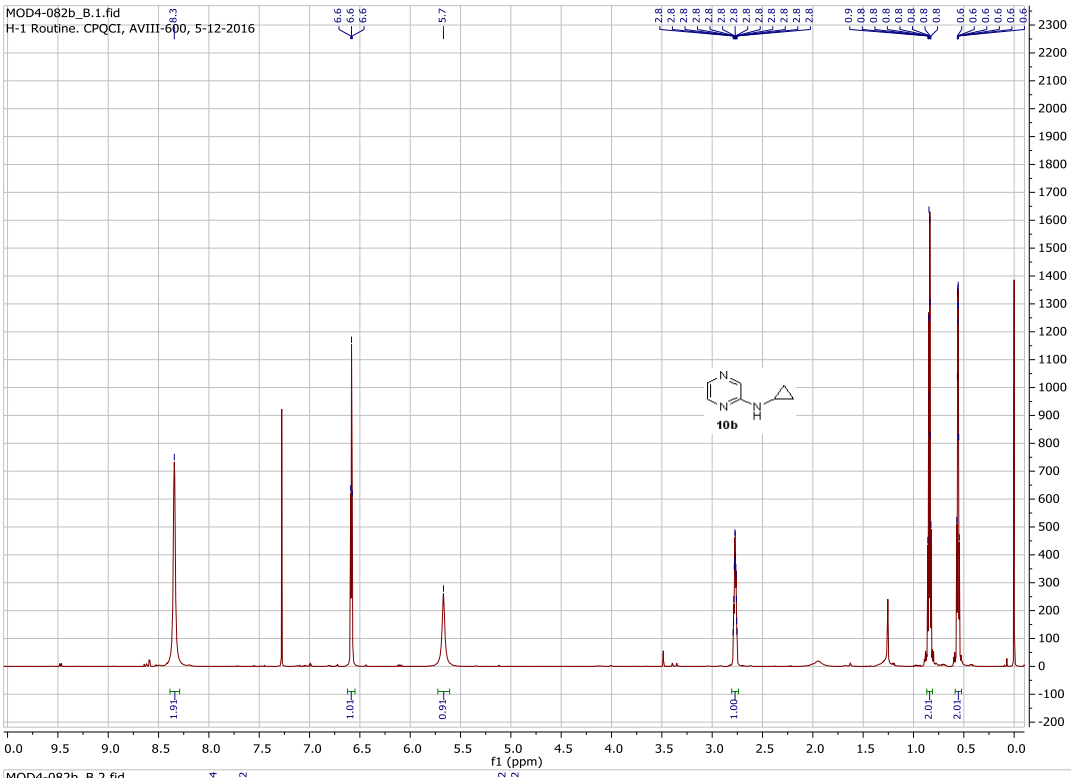


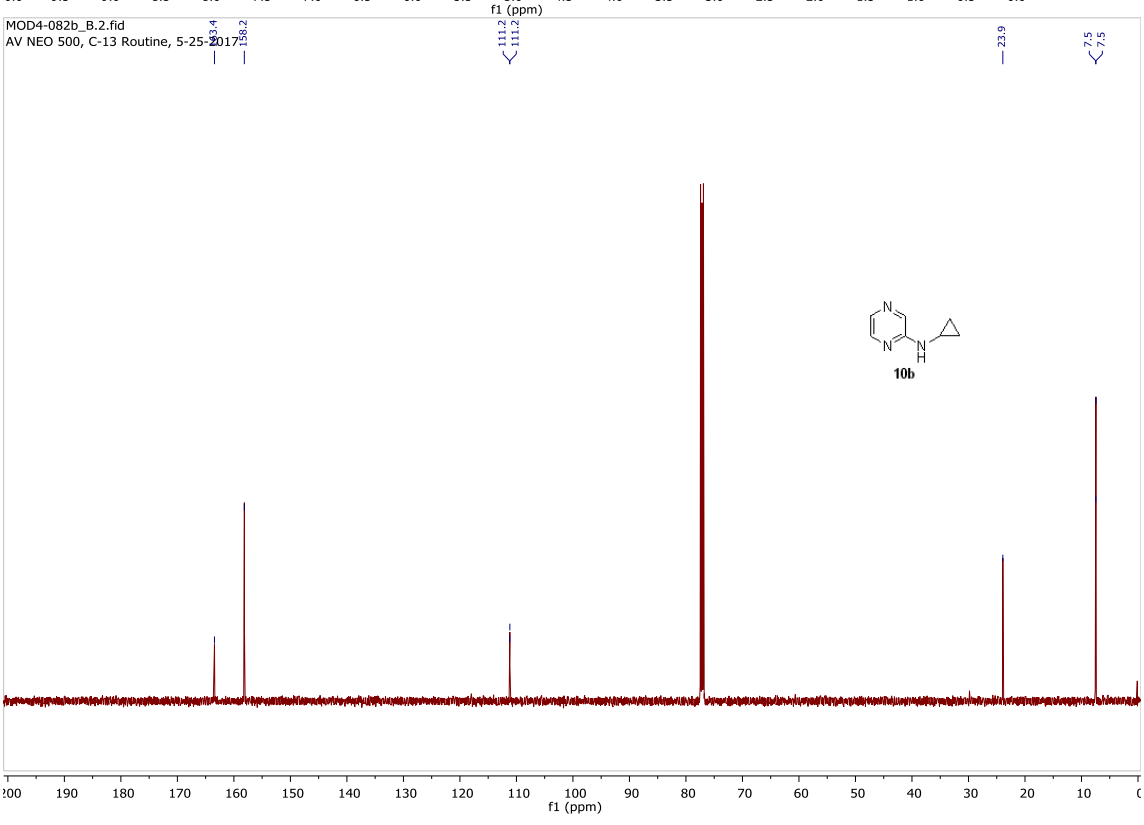
9g

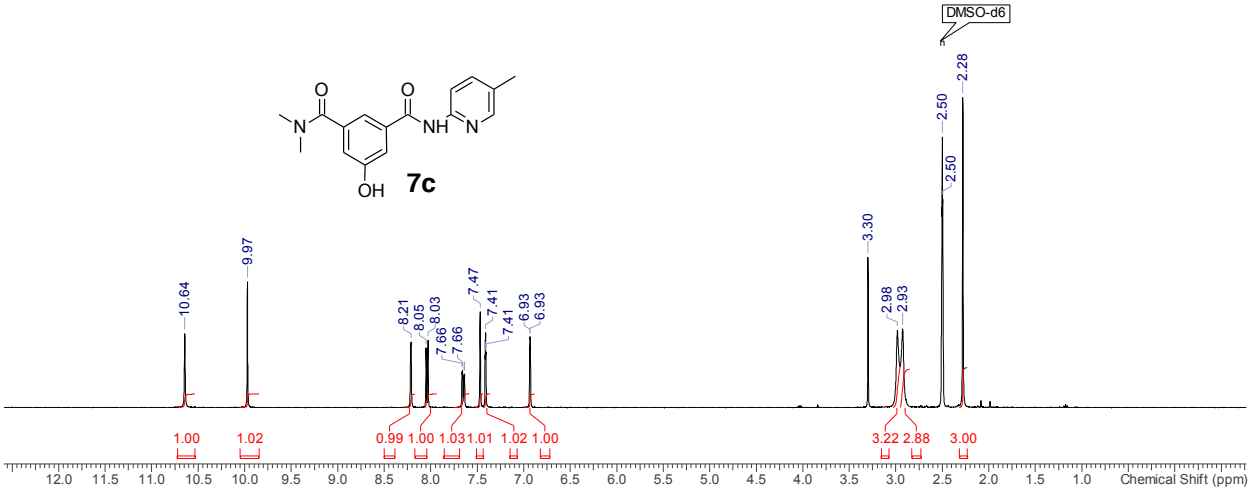

17,16
6.56
21,20,14
3
28.52
15
31.77
6
42.28
2
39.47
13
79.95
7
106.95
4
144.63
5
123.98
11
154.95
10
162.04
8
133.18
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
Chemical Shift (ppm)

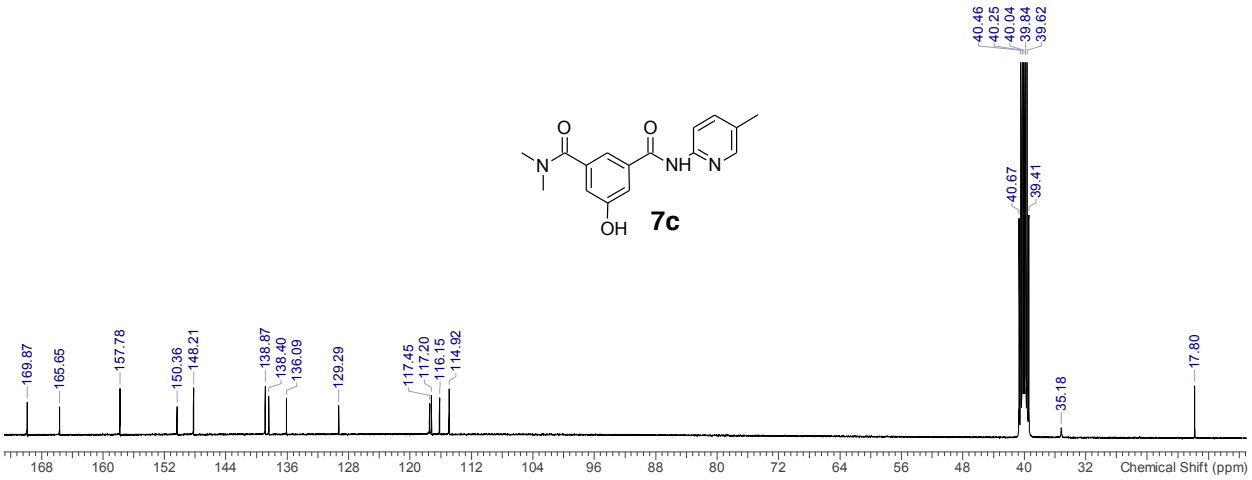

MOD4-092.1.fid
50 mM cyclosporine
8.46
8.45
7.70
7.70
7.69
7.68
7.67
7.67
7.18
7.17
7.15
7.14
7.14
7.13
3.13
3.12
3.11
3.11
3.10
3.09
3.08
2.16
0.90
0.89
0.88
0.87
0.86
0.53
0.52
0.52
0.51
0.51
0.51
10a
0.92
0.99
1.95
1.00
3.06
2.04
2.12
f1 (ppm)

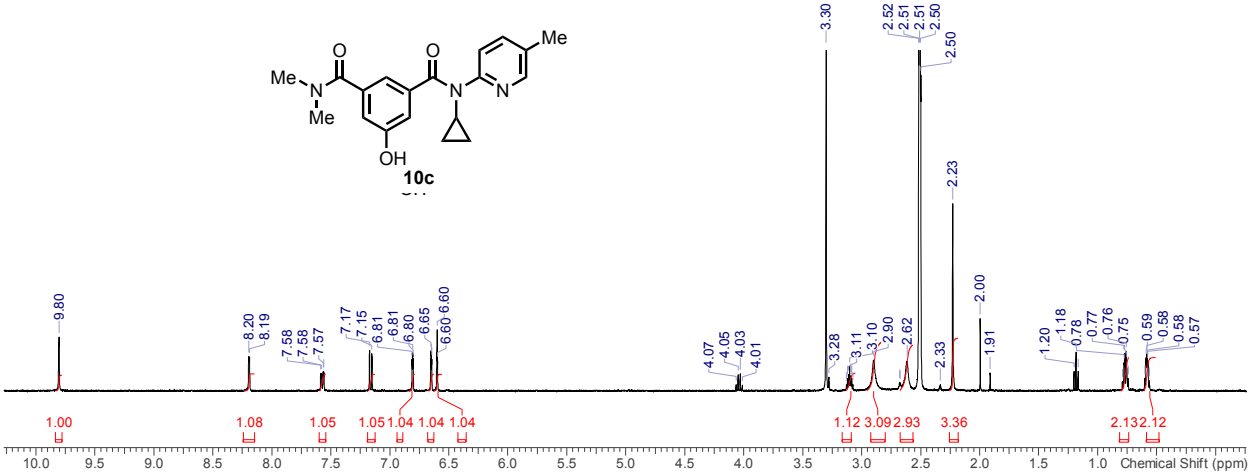

MOD4-092.2.fid
AV NEO 500, C-13 Routine, 5-25-2017
172.8
155.3
148.8
137.8
122.2
121.8
30.5
23.6
9.2
10a
f1 (ppm)

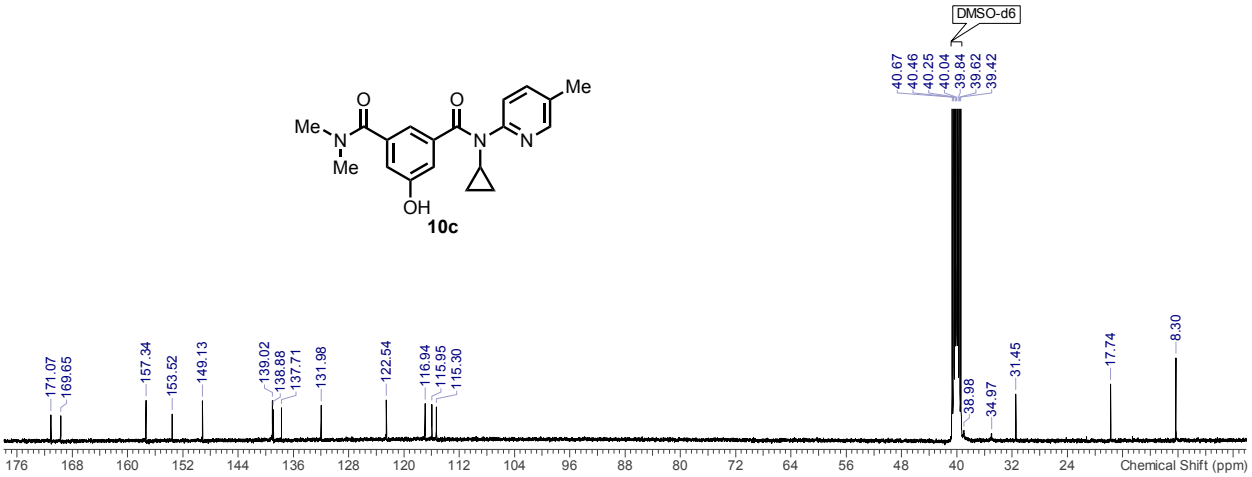

MOD4-082b_B.1.fid
H-1 Routine. CPQCI, AVIII-600, 5-12-2016
f1 (ppm)
10b

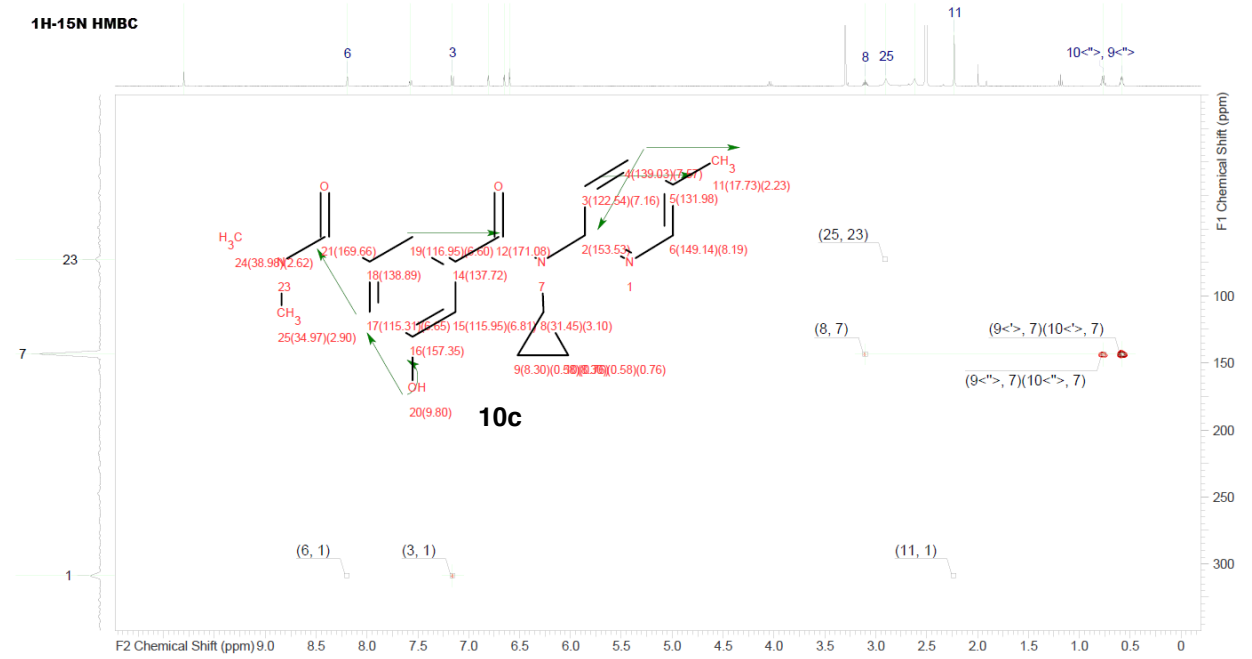

MOD4-082b_B.2.fid
AV NEO 500, C-13 Routine, 5-25-2017
f1 (ppm)
10b


DMSO-d6
7c
10.64
9.97
8.21
8.05
8.03
7.66
7.66
7.47
7.41
7.41
6.93
6.93
3.30
2.98
2.93
2.50
2.50
2.28
1.00
1.02
0.99
1.00
1.03
1.01
1.02
1.00
3.22
2.88
3.00
Chemical Shift (ppm)


7c
40.46
40.25
40.04
39.84
39.62
40.67
39.41
169.87
165.65
157.78
150.36
148.21
138.87
138.40
136.09
129.29
117.45
117.20
116.15
114.92
35.18
17.80
Chemical Shift (ppm)


10c
Chemical Shift (ppm)


DMSO-d6
10c
Chemical Shift (ppm)


1H-15N HMBC
10c
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)