Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Bismuth(III)-catalyzed cycloisomerization and (hetero)arylation of alkynols: a simple access to 2-(hetero)aryl tetrahydrofurans and tetrahydropyrans

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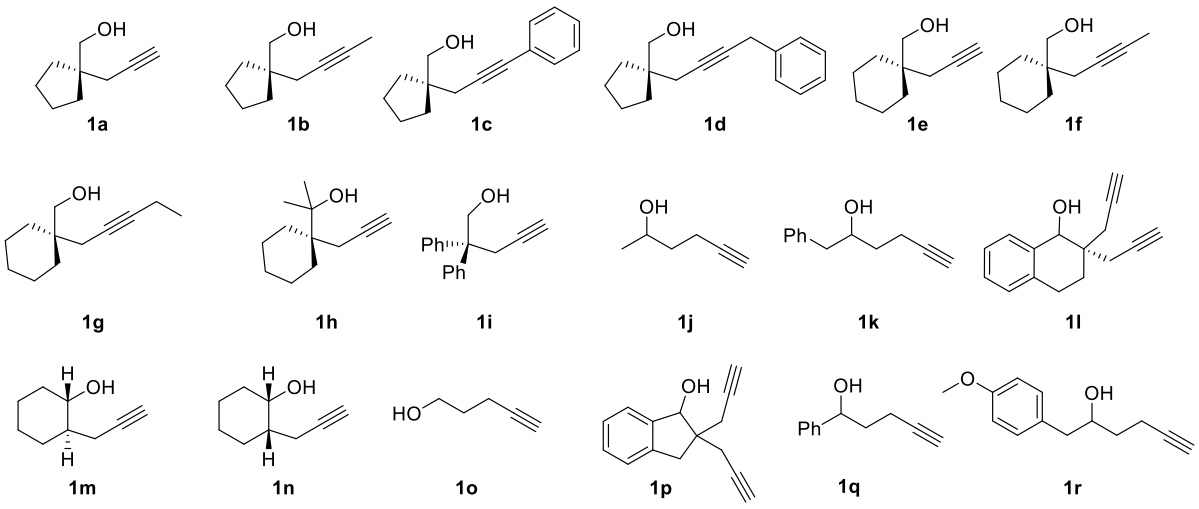
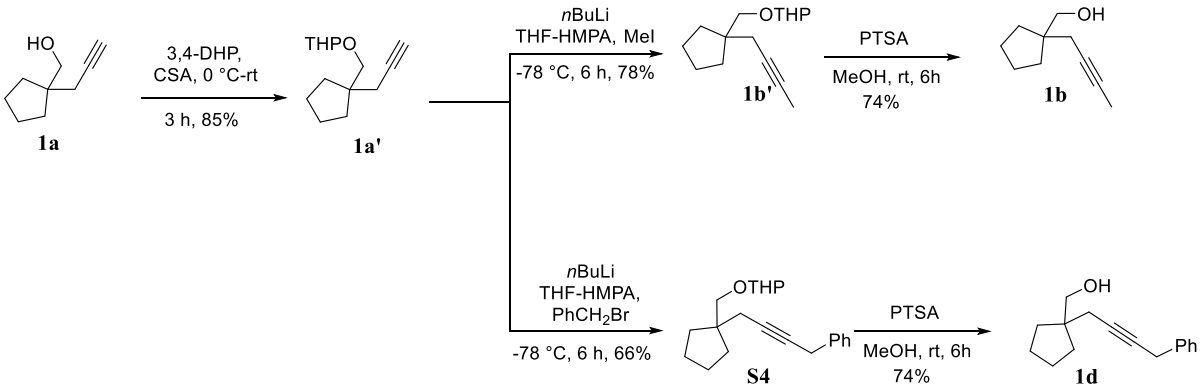
Electronic Supplementary Information

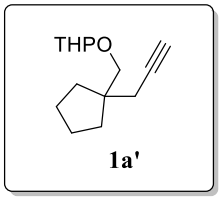
1. Synthesis of Alkynols (4-Pentyn-1-ols):



Compound **1a-j, 1l**&**1q** were prepared using known literature procedures.[1] **1k** and **1r** was prepared using reported procedure.[2] **1o** was purchased from commercial sources.



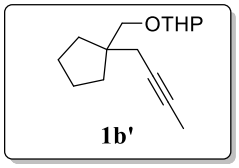
((1-(Prop-2-yn-1-yl) cyclopentyl) methoxy) tetrahydro-2H-pyran (1a'):



[1] Kambale, D. A.; Thorat, S. S.; Pratapure, M. S.; Gonnade, R. G.; Kontham, R.*Chem. Commun.,* **2017**, *53*, 6641−6644.
[2]Fananas, F. J.; Fernandez, A.; Cevic, D.; Rodrıguez, F. *J. Org. Chem*. **2009**, *74*, 932-934.

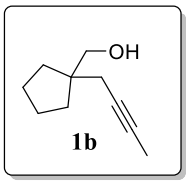
((1-(Prop-2-yn-1-yl) cyclopentyl) methoxy) tetrahydro-2H-pyran (**1a'**) was prepared using reported procedure[1]. ^{1}H NMR ($CDCl_3$, 200MHz) δ 4.61 (m, 1H) 3.97-3.79 (m, 1H), 3.62 (d, *J* = 9.35 Hz, 1H), 3.57-3.35 (m, 1H), 3.19 (d, *J* = 9.35 Hz, 1H), 2.31 (t, *J* = 2.40 Hz, 2H), 1.91 (t, *J* = 2.65 Hz, 1H), 1.67-1.56 (m, 14H).

2-((1-(But-2-yn-1-yl) cyclopentyl) methoxy) tetrahydro-2H-pyran (1b'):



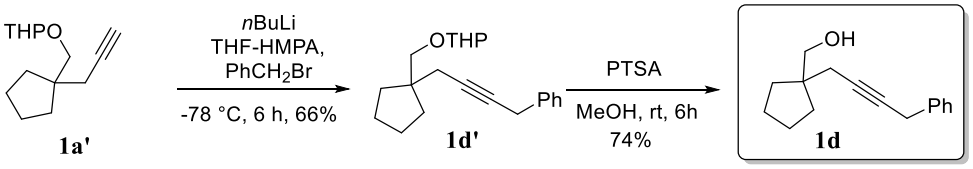
2-((1-(But-2-yn-1-yl)cyclopentyl) methoxy) tetrahydro-2H-pyran (**1b'**) was prepared using reported procedure[1.] ^{1}H NMR ($CDCl_3$, 200 MHz) δ 4.66-4.55 (m, 1 H), 3.97-3.79 (m, 1 H), 3.61 (d, *J* = 9.09 Hz, 1 H), 3.56-3.44 (m, 1 H), 3.17 (d, *J* = 9.09 Hz, 1 H), 2.27-2.19 (m, 2H), 1.78 (t, *J* = 2.53 Hz, 3 H), 1.67-1.42 (m, 14 H).

(1-(But-2-yn-1-yl) cyclopentyl) methanol (1b):



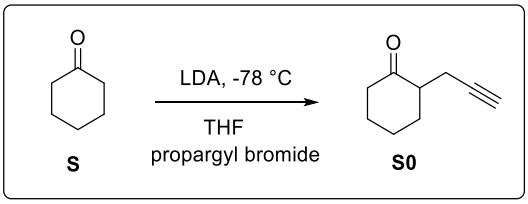
(1-(But-2-yn-1-yl) cyclopentyl) methanol (**1b**) was prepared using reported procedure[1.] ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.50 (s, 2H), 2.18-2.12 (m, 2H), 2.08 (m, 1H), 1.78 (t, *J* = 2.59 Hz, 3H), 1.68-1.53 (m, 4H), 1.53-1.40 (m, 4H).

2-((1-(but-2-yn-1-yl)cyclopentyl)methoxy)tetrahydro-2H-pyran (1d):



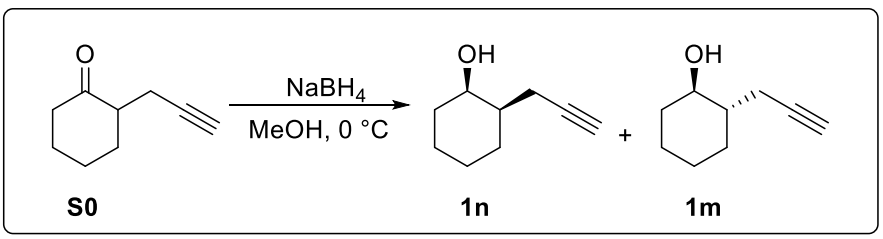
2-((1-(but-2-yn-1-yl)cyclopentyl)methoxy)tetrahydro-2H-pyran (**1d**) was prepared using reported procedure[1], by using crude (**1d'**). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.39-7.15 (m, 5 H), 3.61-3.55 (m, 2 H), 3.53-3.50 (m, 2 H), 2.37-2.23 (m, 2 H), 1.95 (d, *J* = 2.65 Hz, 1 H), 1.66-1.57 (m, 4 H), 1.54-1.46 (m, 4 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 131.6, 128.2, 127.6, 123.8, 87.6, 82.8, 68.7, 38.2, 32.0, 26.2, 26.1, 21.6, 14.2.

2-(prop-2-yn-1-yl)cyclohexan-1-one (S0):



To a flame dried (100 mL) two neck round bottom flask, anhydrous THF (30 mL) was added under argon atmosphere and cooled it to -78 °C, to this diisopropylamine (4.35 mL, 3.05 mmol) followed by *n*-butyllithium (1.6 M in hexanes, 19 mL,) was added drop wise at -78 °C and stirred for 45 min at 0 °C to generate LDA solution. To this LDA solution was added cyclohexanone (**S**) (3.75 mL,3.05 mmol) in THF (20 mL) and stirred the reaction mixture at -78 °C for 30 min, then warmed to 0 °C and stirred for another 30 min. Reaction mixture was cooled back to -78 °C and propargyl bromide (80% in toluene, 2.31 mL, 3.05 mmol) was added drop wise. The resulting mixture was stirred at -78 °C for 1 h and warmed to 25 °C and stirred for overnight. The reaction was quenched with saturated aqueous NH_4Cl solution and extracted with EtOAc (3x25 mL), combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to afford 2-(prop-2-yn-1-yl)cyclohexan-1-one (**S0**) crude which was subjected to the next step without further purification. (1.5 g) TLC: R_f = 0.6.

2-(Prop-2-yn-1-yl)cyclohexan-1-ol(1n) &2-(prop-2-yn-1-yl)cyclohexan-1-ol (1m);

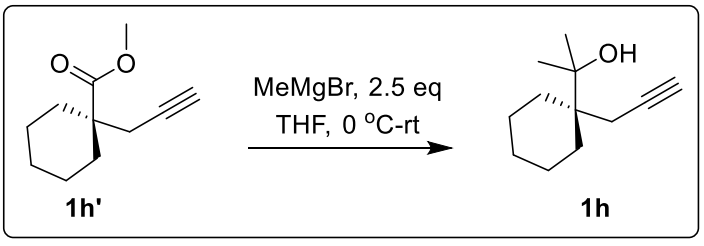


To a solution of 2-(prop-2-yn-1-yl)cyclohexan-1-one (**S0**)(1.5 g 11.01 mmol) in methanol (10 mL), sodium borohydride (0.25 g, 6.61 mmol) was slowly added at 0 °C. The reaction mixture was stirred at 0 °C for 30 min and then for 2.5 h at room temperature, after which the solvent was evaporated under reduced pressure. Aqueous NH_4Cl solution (10 mL) was added to the resulting suspension, and then extracted with EtOAc (3×5 mL). Organic phases were combined and dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated under reduced pressure, and the resulting crude product was purified by silica gel column chromatography (SiO_2, 2% EtOAc/hexanes) to afford a mixture of alcohols **1n** (1,2-*cis*) (614 mg, 50%, colourless liquid) and **1m**, (1,2-*trans* fused) (694 mg, 57%, colourless liquid). TLC: R_f = 0.4 & 0.1 (SiO_2, 2% EtOAc/hexanes);

Data for **1n**: ^{1}H NMR ($CDCl_3$, 500 MHz) (*cis*): δ 4.07 (s, 1H), 2.31 (ddd, *J* = 16.78, 7.82, 2.67 Hz, 1H), 2.18 (ddd, *J* = 16.78, 6.87, 2.67 Hz, 1H), 2.0 (t, *J* = 2.67 Hz, 1H), 1.86-1.77 (m, 1H), 1.71-1.59 (m, 3H), 1.59-1.40 (m, 5H), 1.34-1.23 (m, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 83.5, 69.2, 68.3, 40.8, 32.9, 26.2, 25.1, 21.5, 20.1.

Data for **1m**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.39-3.37 (m, 1H), 2.49-2.43 (m, 1H), 2.32 (ddd, *J* = 16.78, 6.87, 2.67 Hz, 1H), 2.02-1.95 (m, 3H), 1.84-1.89 (m, 1H), 1.79-1.73 (m, 1H),1.71-1.65 (m, 2H) , 1.49-1.40 (m, 1H), 1.31-1.15 (m, 4H),); ^{13}C NMR ($CDCl_3$, 126 MHz): δ82.9, 73.5, 69.7, 43.9, 35.5, 30.2, 25.4, 24.8, 21.7.

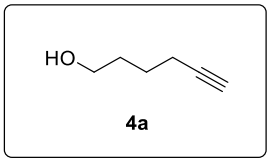
2-(1-(prop-2-yn-1-yl)cyclohexyl)propan-2-ol (1h)



To a flame dried (100 mL) two neck round bottom flask, methyl 1-(prop-2-yn-1-yl)cyclohexane-1-carboxylate (**1h'**) (2 g,1.10 mmol)in anhydrous THF (30 mL) and cooled it to 0 °C followed by methyl magnesium bromide (1.0 M THF) (22 ml, 2.77 mmol) was added drop wise under argon atmosphere after completion of addition gradually increased temperature to rt. Reaction monitored by TLC, after completion of reaction quenched with Aqueous NH_4Cl solution (10 mL), extracted with EtOAc (3×5 mL). Organic phases were

combined and dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated under reduced pressure, and the resulting crude product was purified by silica gel column chromatography (SiO_2, 4% EtOAc/hexanes) to afford a mixture of alcohols **1h** (2-(1-(prop-2-yn-1-yl)cyclohexyl)propan-2-ol) (1.43 g, 71%) as a colourless liquid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.43 (d, *J* = 2.78, 2H), 2.33 (br. s, 1H), 2.8 (t, *J* = 2.78, 1H), 1.71-1.32 (m, 10H), 1.25 (s, 6H).

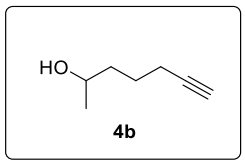
Synthesis of Alkynols (5-Hexyn-1-ols):



4a

Alkynol **4a** was purchased from commercial sources.

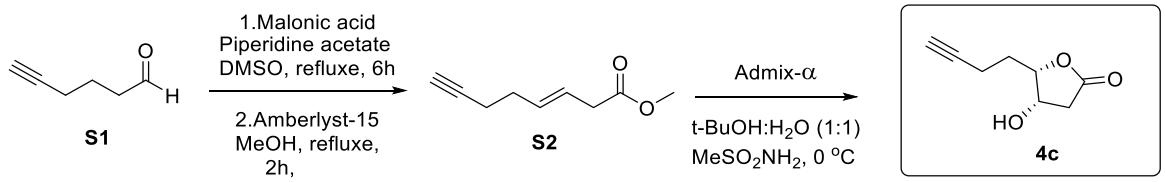
Hept-6-yn-2-ol (4b):



4b

Hept-6-yn-2-ol (**4b**) was prepared using reported procedure.[3] ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.87-3.78 (m, 1H), 2.24-2.19 (m, 2H), 1.97 (t, *J* = 2.6 Hz, 1H), 1.70-1.50 (m, 4H), 1.20 (d, *J* = 6.1 Hz, 3H);^{13}C NMR ($CDCl_3$, 126 MHz): δ 84.3, 68.5, 67.6, 38.2, 24.7, 23.6, 18.4.

5-(But-3-yn-1-yl)-4-hydroxydihydrofuran-2(3*H*)-one (4c):

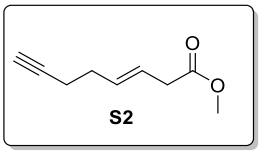


S1 **S2** **4c**

[3] Shibata, N.; Tsuchiya, T.; Hashimoto, Y.; Morita, N.; Ban, S.; Tamura, O. *Org. Biomol. Chem.,* **2017**, *15*, 3025–3034.

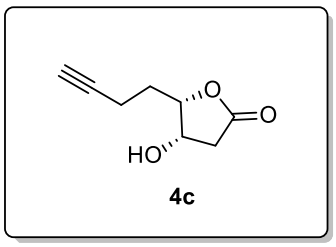
(See below experimental procedures and data)

Methyl-(*E*)-oct-3-en-7-ynoate (S2):



A freshly prepared solution of piperidinium acetate (by mixing piperidine (35 μL, 0.41 mmol) and acetic acid (20 μL, 0.37 mmol)) in DMSO (1 mL) was injected in to a stirred solution of the readily available hept-5-ynal (**S1**) (1.5 g, 15.61 mmol) and malonic acid (3.24 g, 31.2 mmol), in DMSO (40 mL), the resulting reaction mixture was stirred for 6 h at 160 ^{o}C. Then it was quenched by adding water and extracted with diethyl ether (3x50 mL) and dried over anhydrous sodium sulphate, concentrated under reduced pressure to afford crude (*E*)-oct-3-en-7-ynoic acid, which was subjected to the next step without further purification. The (*E*)-oct-3-en-7-ynoic acid (0.9 g, 6.51 mmol) was dissolved in methanol (5 mL), then amberlyst-15 (2.05 g, 6.5 mmol) was added to the reaction mixture and refluxed for 1 h. The reaction mixture was cooled to room temperature and filtered through sintered funnel and washed with diethyl ether (20 mL) and dried over anhydrous sodium sulphate. Then, filtered using sintered funnel and concentrated under reduced pressure. Purification of the crude product by column chromatography (SiO_2, 2% EtOAc/hexanes) afforded the pure methyl-(*E*)-oct-3-en-7-ynoate (**S2**) (1.6 g, 78%) as a yellow oil. TLC: R_f = 0.8 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.69-5.59 (m, 2H), 3.69 (s, 3H), 3.11-3.03 (m, 2H), 2.34-2.21 (m, 4H), 1.97 (s, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 172.3, 132.3, 123.1, 83.7, 68.7, 51.7, 37.7, 31.4, 18.5.

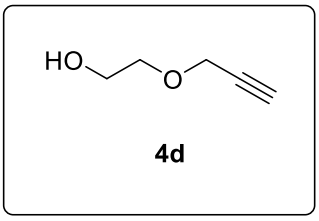
5-(But-3-yn-1-yl)-4-hydroxydihydrofuran-2(3*H*)-one (4c):



To a solution of methyl (*E*)-oct-3-en-7-ynoate (**S2**) (0.1g, 0.66mmol) in 2 mL of t-BuOH:H_2O (1:1) in a single neck round bottom flask, was added AD-mix-α (0.92 g, 0.66

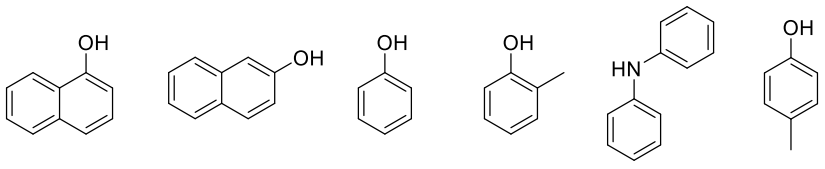
mmol)and methane sulfonamide (0.062 g, 0.66) at 0 ^{o}C. The resulting reaction mixture was stirred for 36 h at 0 ^{o}C under argon atmosphere. Then it was quenched with saturated aqueous solution of sodium sulphite (Na_2SO_3), then extracted with *t*-BuOMe (2x10 mL), dried over anhydrous sodium sulphate. Filtered and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography (SiO_2, 40% EtOAc/hexanes) to afford 5-(but-3-yn-1-yl)-4-hydroxydihydrofuran-2(3*H*)-one (**4c**) (0.080 g, 79%) as a colourless oil. TLC: R_f = 0.12 (SiO_2, 40% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 4.66-4.5 (m, 2H), 2.83 (dd, *J* = 17.8, 5.05 Hz, 1H), 2.64-2.5 (m, 1H), 2.49-2.26 (m, 2H), 2.23-1.86 (m, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 176.1, 83.7, 83.1, 69.6, 68.6, 39.3, 27.1, 14.7.

2-(Prop-2-yn-1-yloxy)ethan-1-ol (4d):



4d

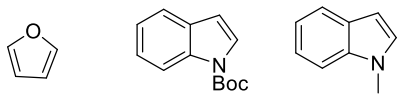
2-(prop-2-yn-1-yloxy)ethan-1-ol (**4d**) was prepared using reported procedure.[4] ^{1}H NMR ($CDCl_3$, 200 MHz): δ 4.23-4.11 (m, 2H), 3.75-3.71 (m, 2H), 3.67-3.57 (m, 2H), 2.64 (br.s, 1H), 2.45 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 79.5, 74.8, 71.3, 61.6, 58.4.



2a **2b** **2c** **2d** **2e** **2f**

2a, 2b, 2c, 2d, 2e and **2f** were purchased from commercial sources.

[4] Harada, T.; Muramatsu, K.; Mizunashi, K.; Kitano, C.; Imaoka, D.; Fujiwara, T.; Kataoka, H. *J. Org. Chem.*, **2008**, *73*, 249–258.



6a **6b** **6c**

Compounds **6a** and **6c** are purchased from commercial sources.

Compound **6b** was prepared using known procedure.[5]

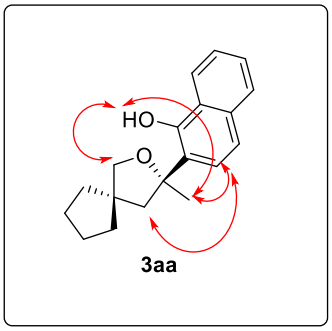


Figure 1. Key NOE interactions in compound **3aa**.

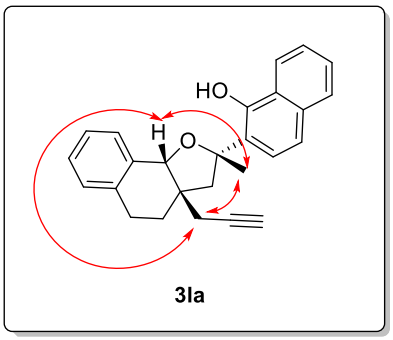


Figure 2. Key NOE interactions in compound **3la**.

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[5]Jeanese, C. B.; Jason, A. J.; Gordon, W. G.; *Tetrahedron Letters*, **2013**, *54*, 2759–2762.

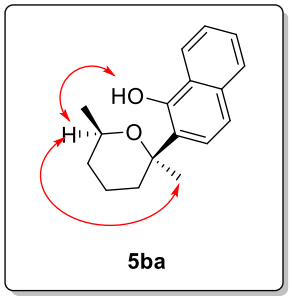


Figure 3. Key NOE interactions in compound **5ba**.

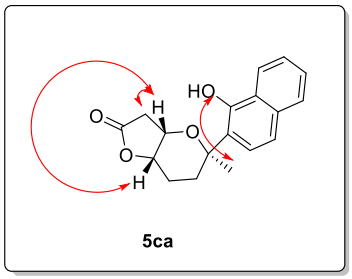
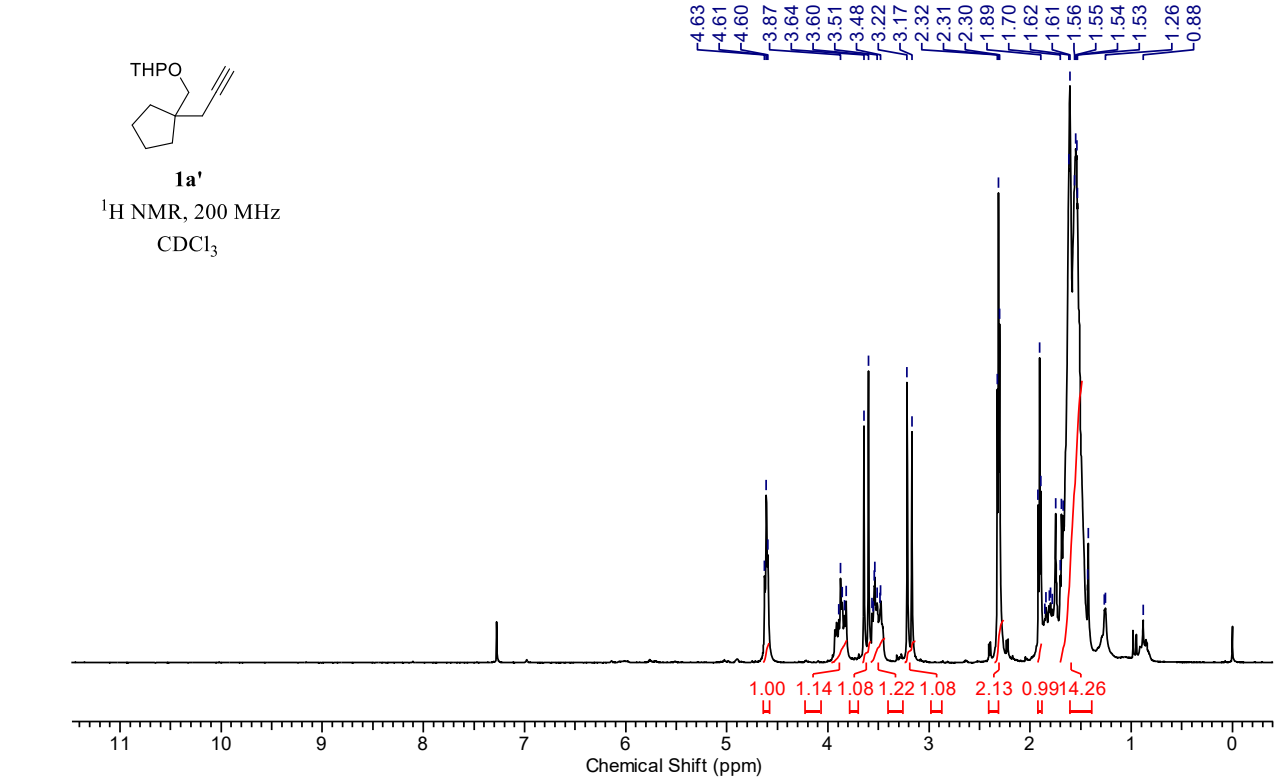


Figure 4. Key NOE interactions in compound **5ca**.

^{1}H ,^{13}C and 2D NMR Spectra

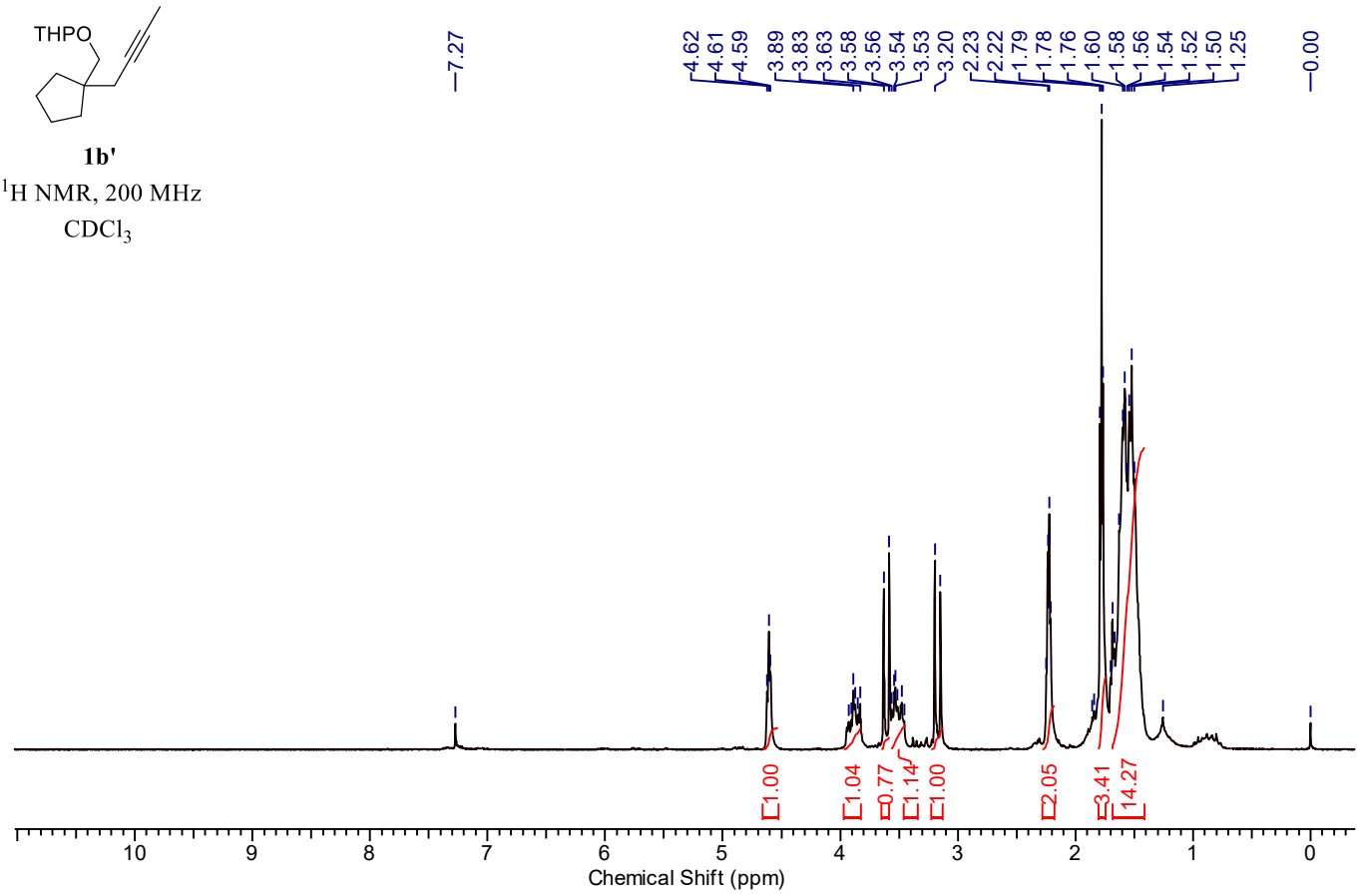
/HPLC Reports



1a'

^{1}H NMR, 200 MHz

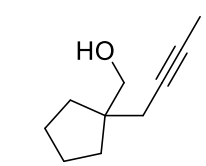
$CDCl_3$



1b'

^{1}H NMR, 200 MHz

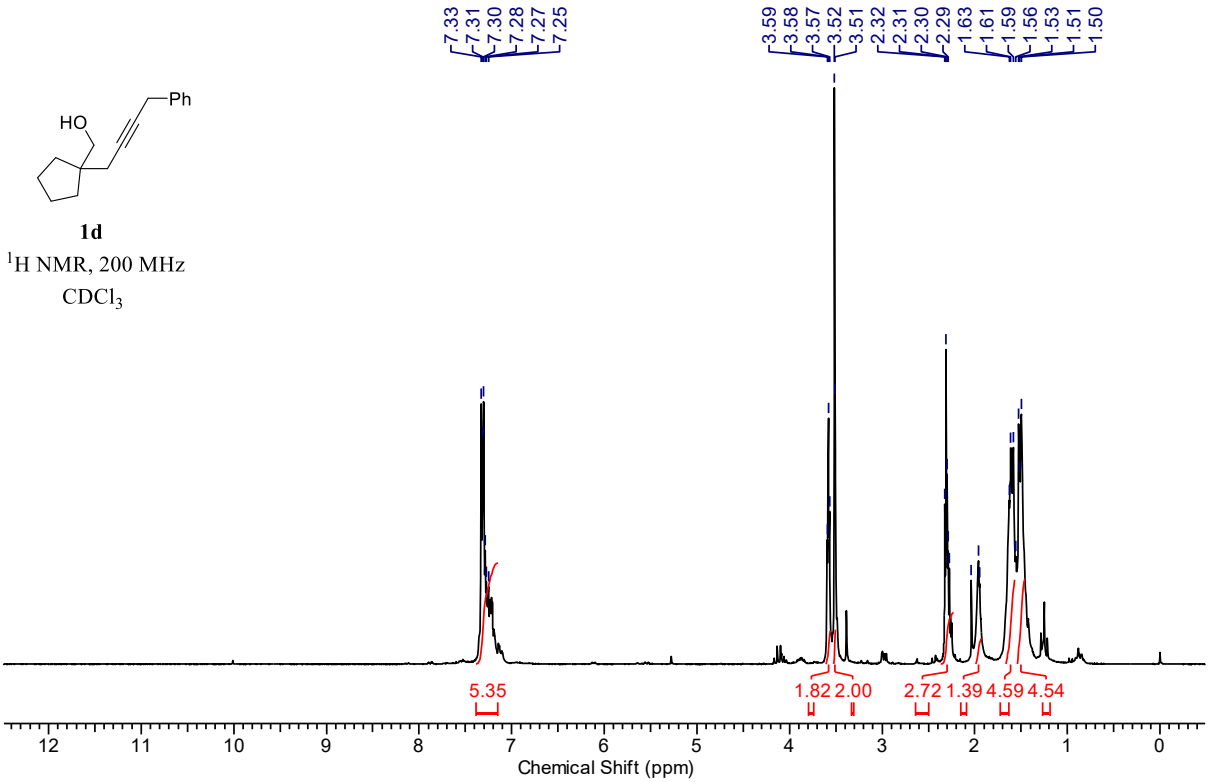
$CDCl_3$



1b

^{1}H NMR, 200 MHz

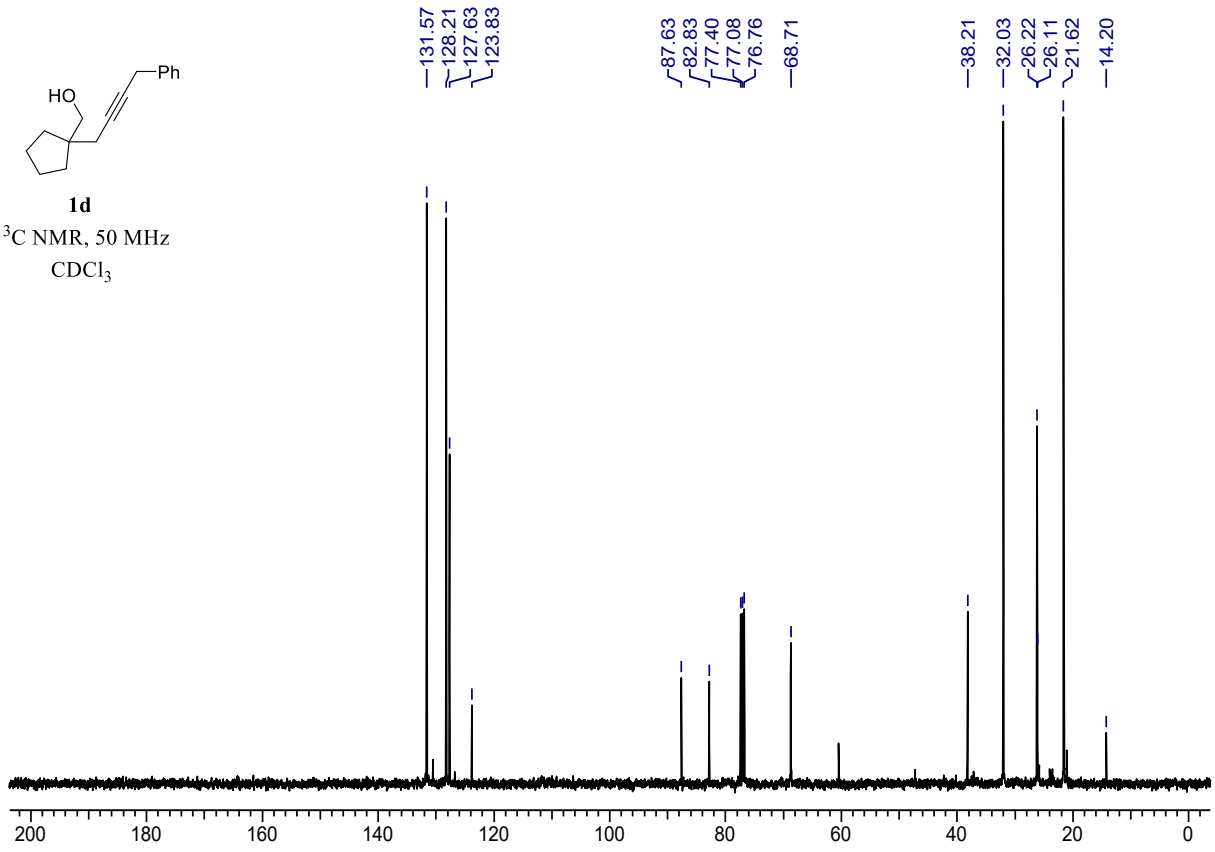
$CDCl_3$



1d

^{1}H NMR, 200 MHz

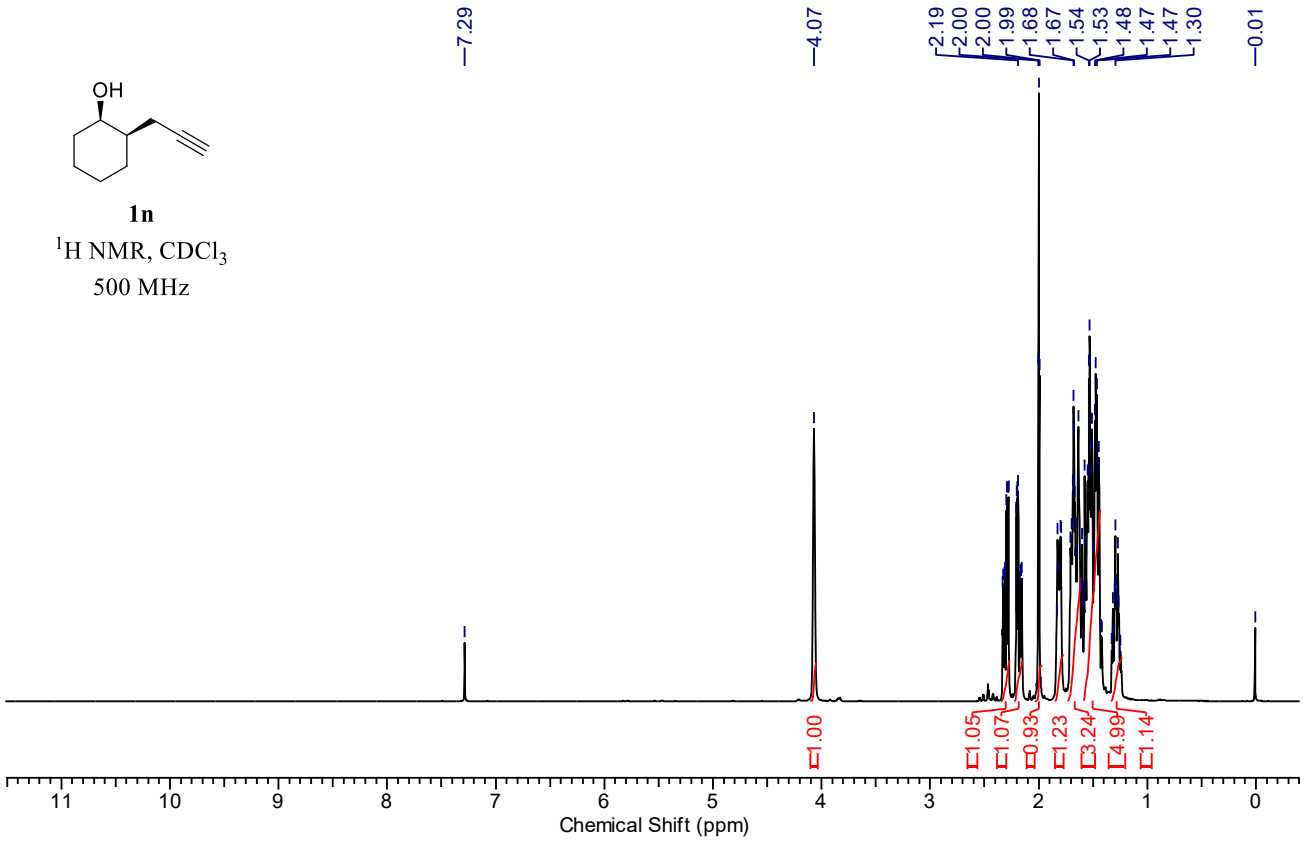
$CDCl_3$



1d

^{13}C NMR, 50 MHz

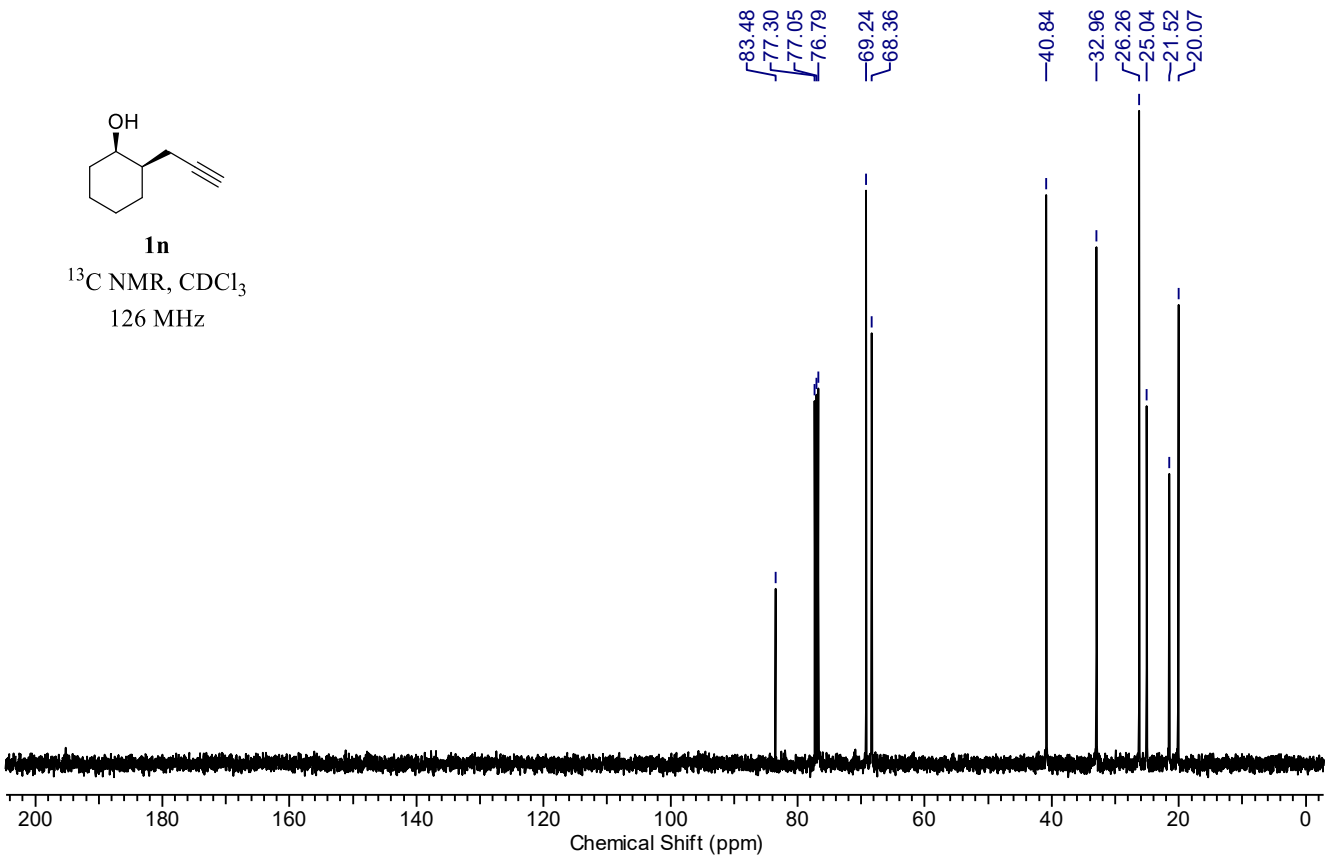
$CDCl_3$



1n

^{1}H NMR, $CDCl_3$

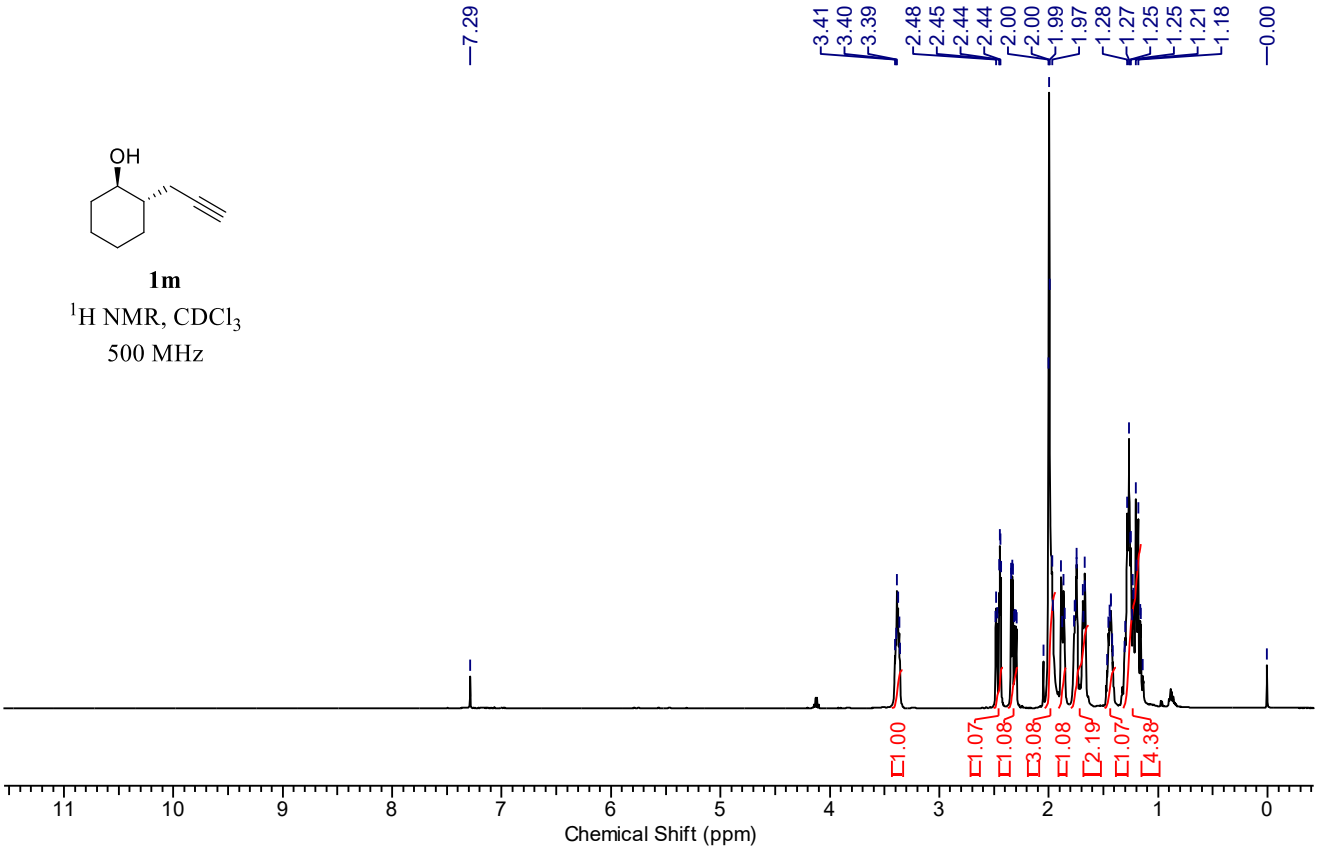
500 MHz

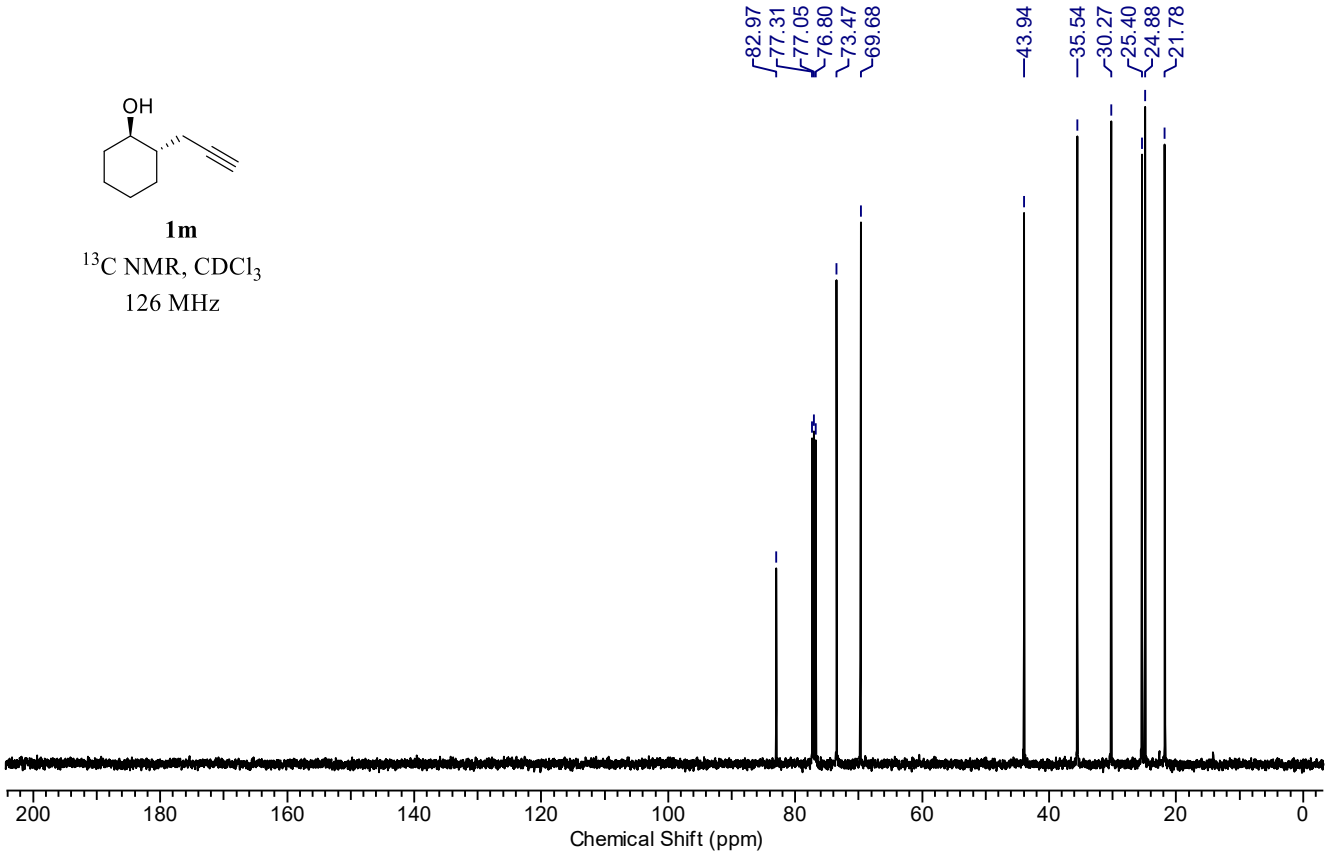


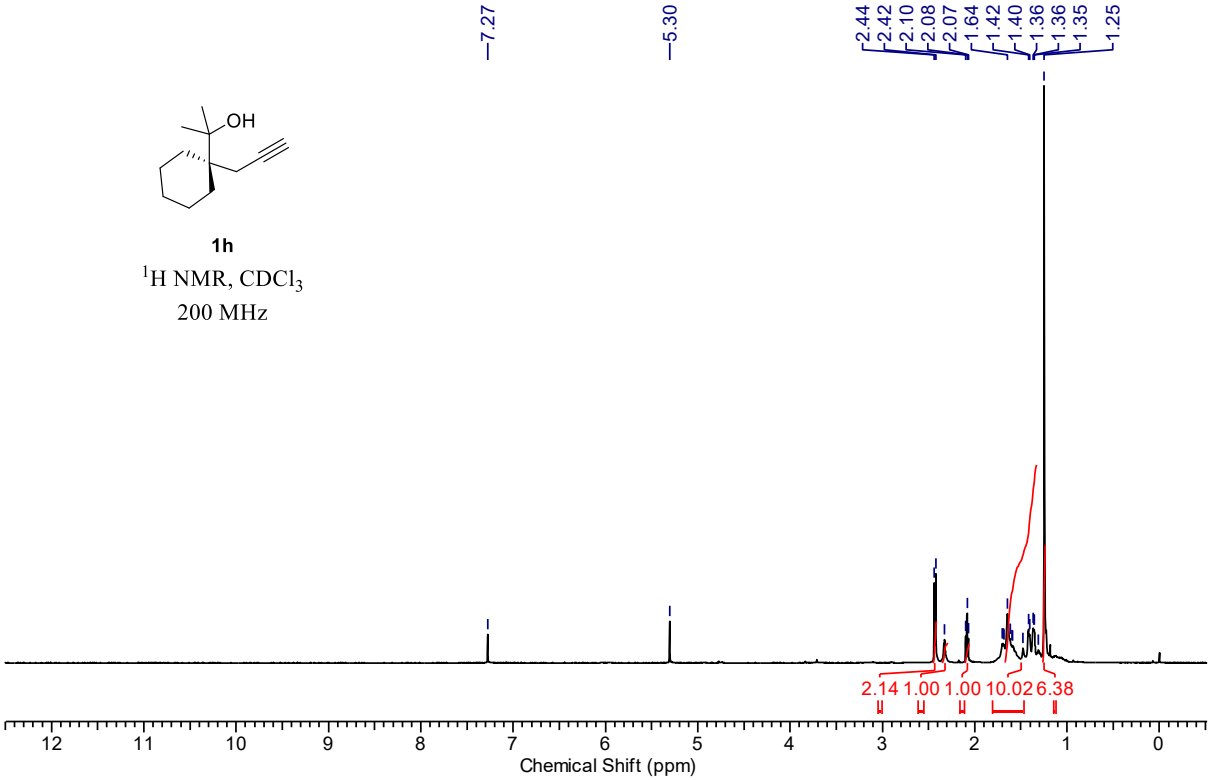
1n

^{13}C NMR, $CDCl_3$

126 MHz


OH
1m
1H NMR, CDCl3
500 MHz
7.29
3.41
3.40
3.39
2.48
2.45
2.44
2.44
2.00
2.00
1.99
1.97
1.28
1.27
1.25
1.25
1.21
1.18
0.00
1.00
1.07
1.08
3.08
1.08
2.19
1.07
4.38
Chemical Shift (ppm)

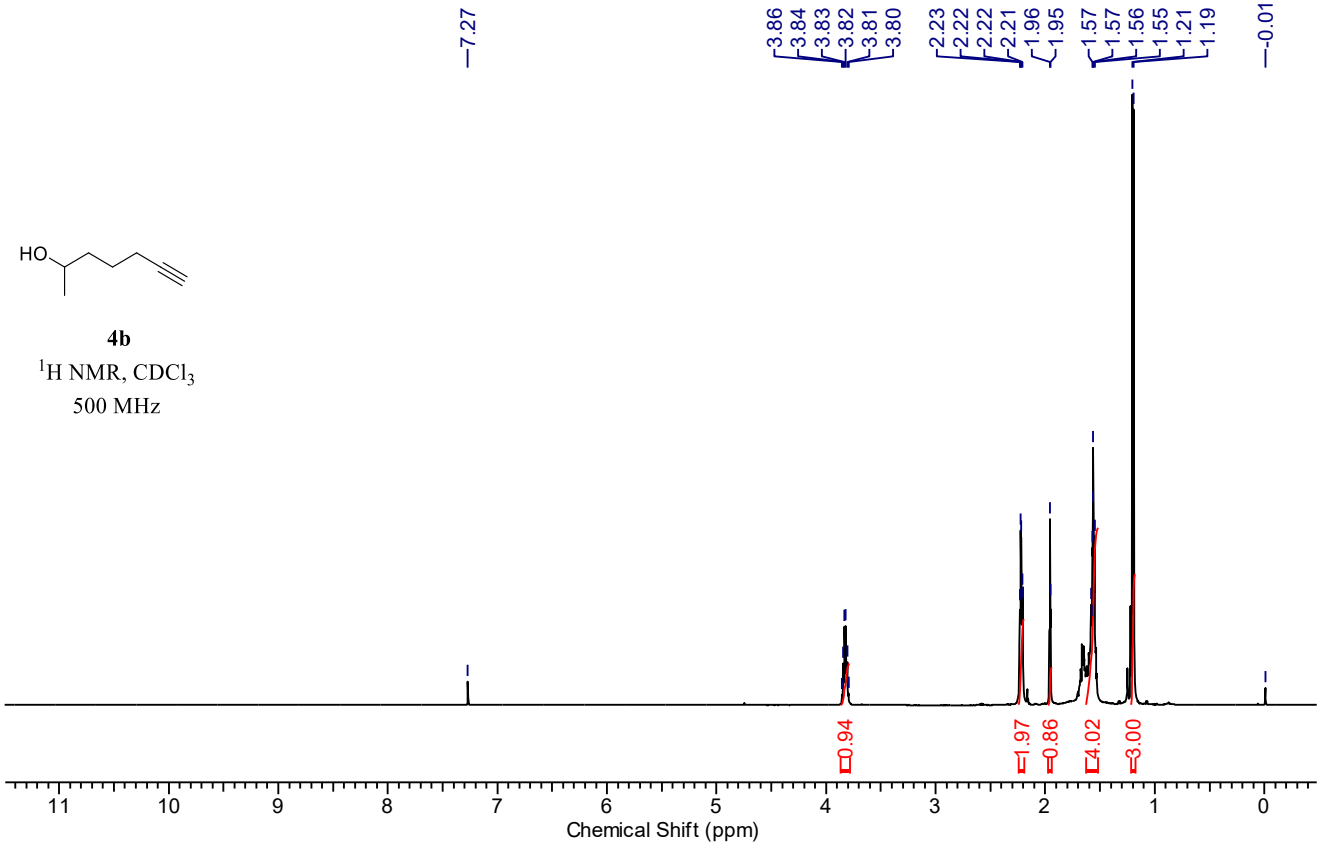

OH
1m
13C NMR, CDCl3
126 MHz
82.97
77.31
77.05
76.80
73.47
69.68
43.94
35.54
30.27
25.40
24.88
21.78
Chemical Shift (ppm)



1h

^{1}H NMR, $CDCl_3$

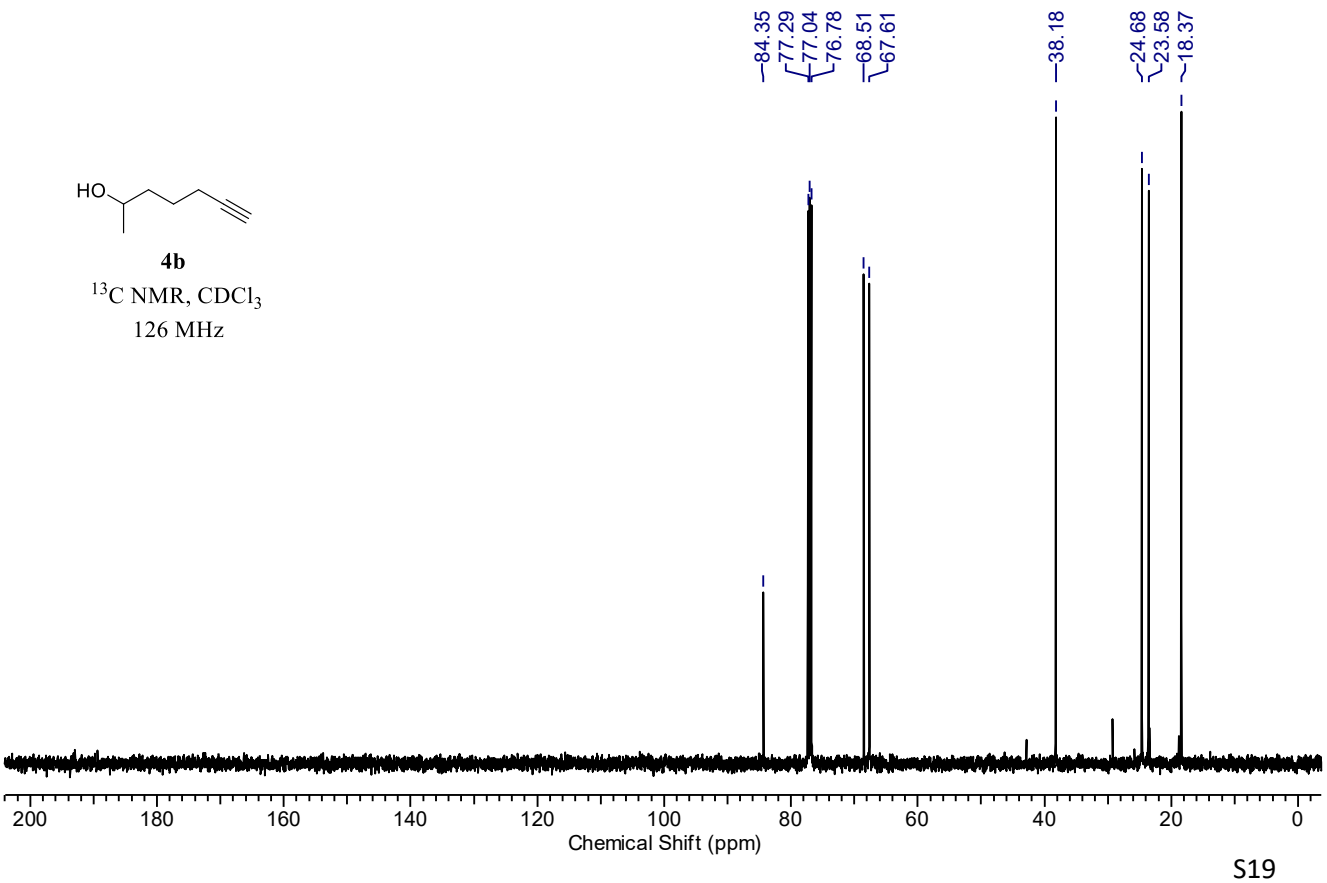
200 MHz



4b

^{1}H NMR, $CDCl_3$

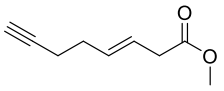
500 MHz



4b

^{13}C NMR, $CDCl_3$

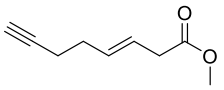
126 MHz



S2

^{1}H NMR, $CDCl_3$

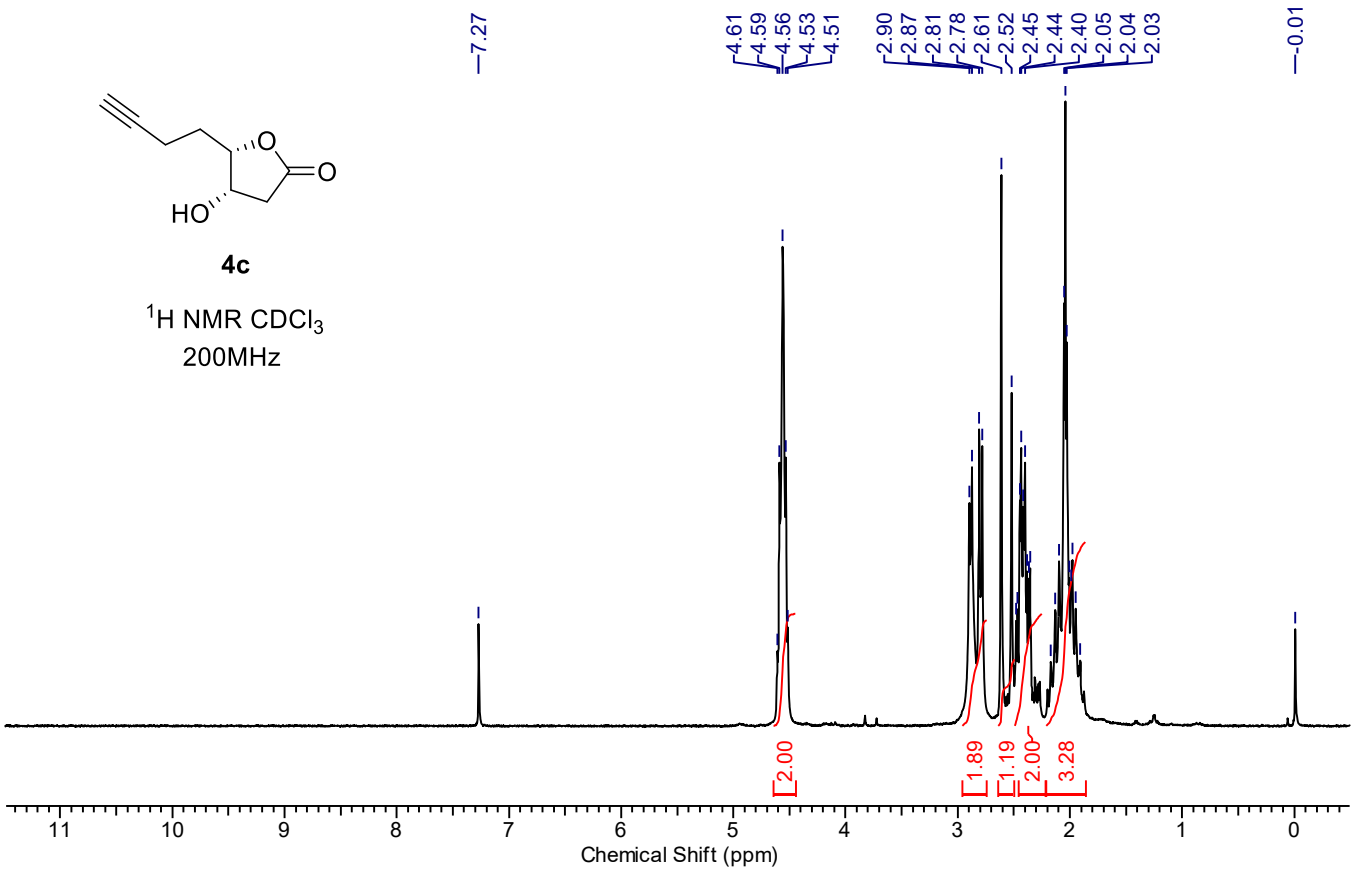
500 MHz



S2

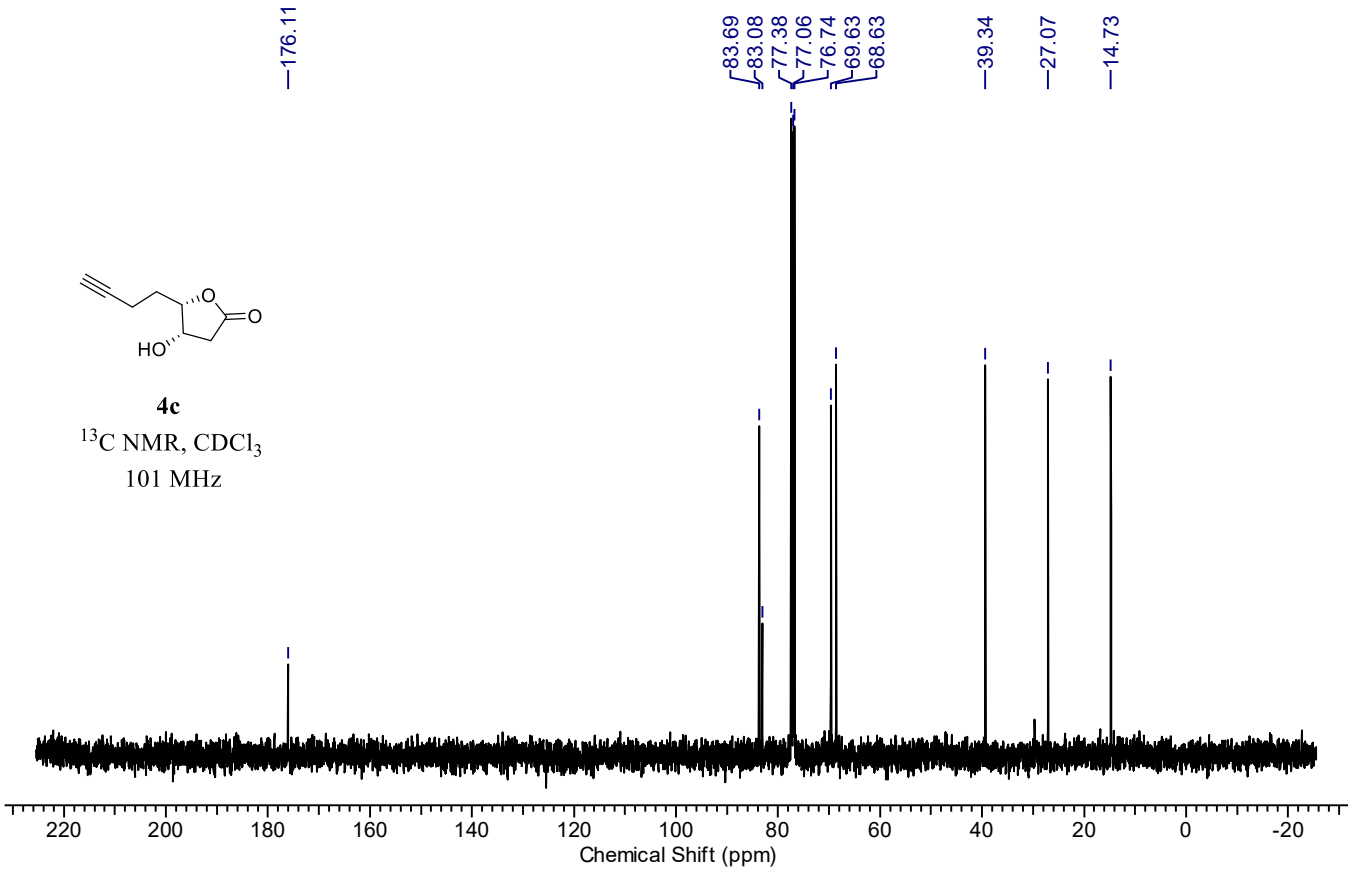
^{13}C NMR, $CDCl_3$

126 MHz



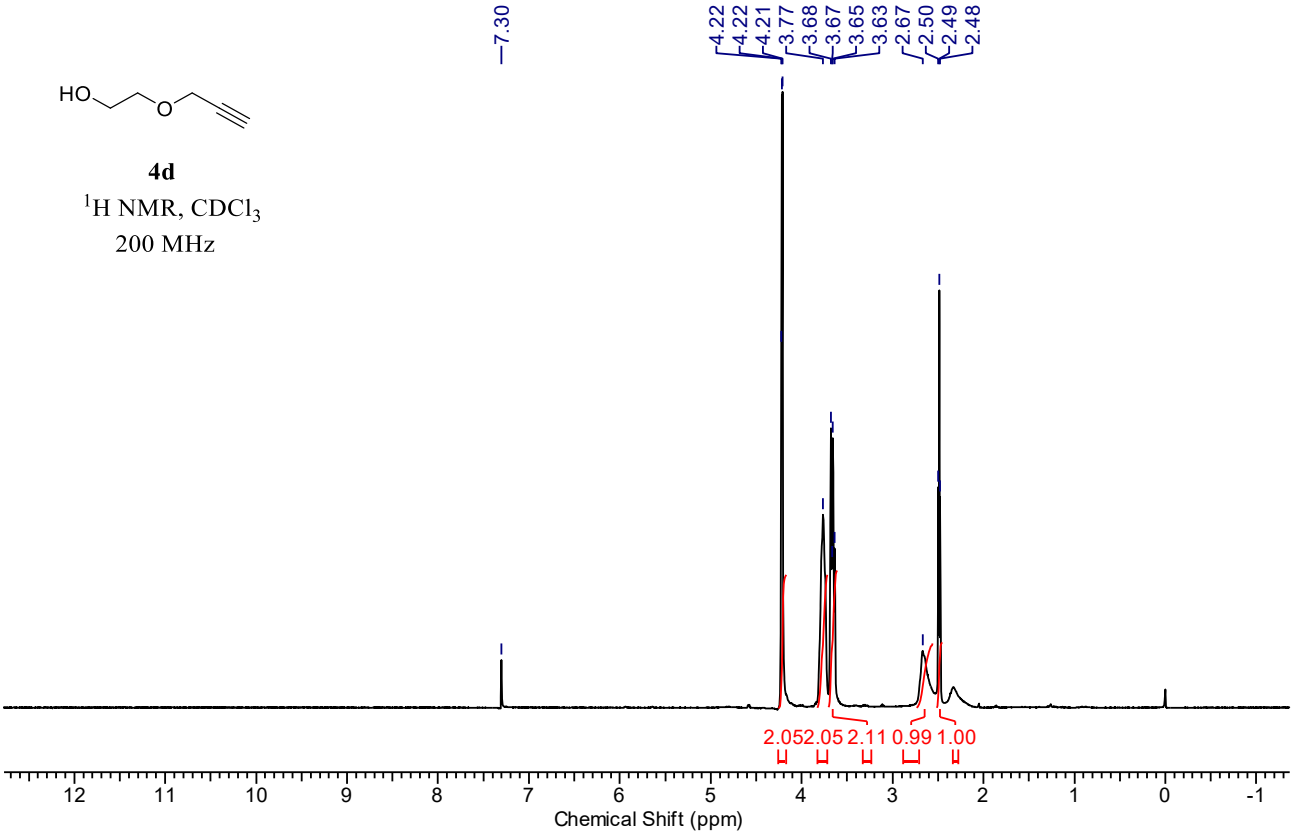
4c

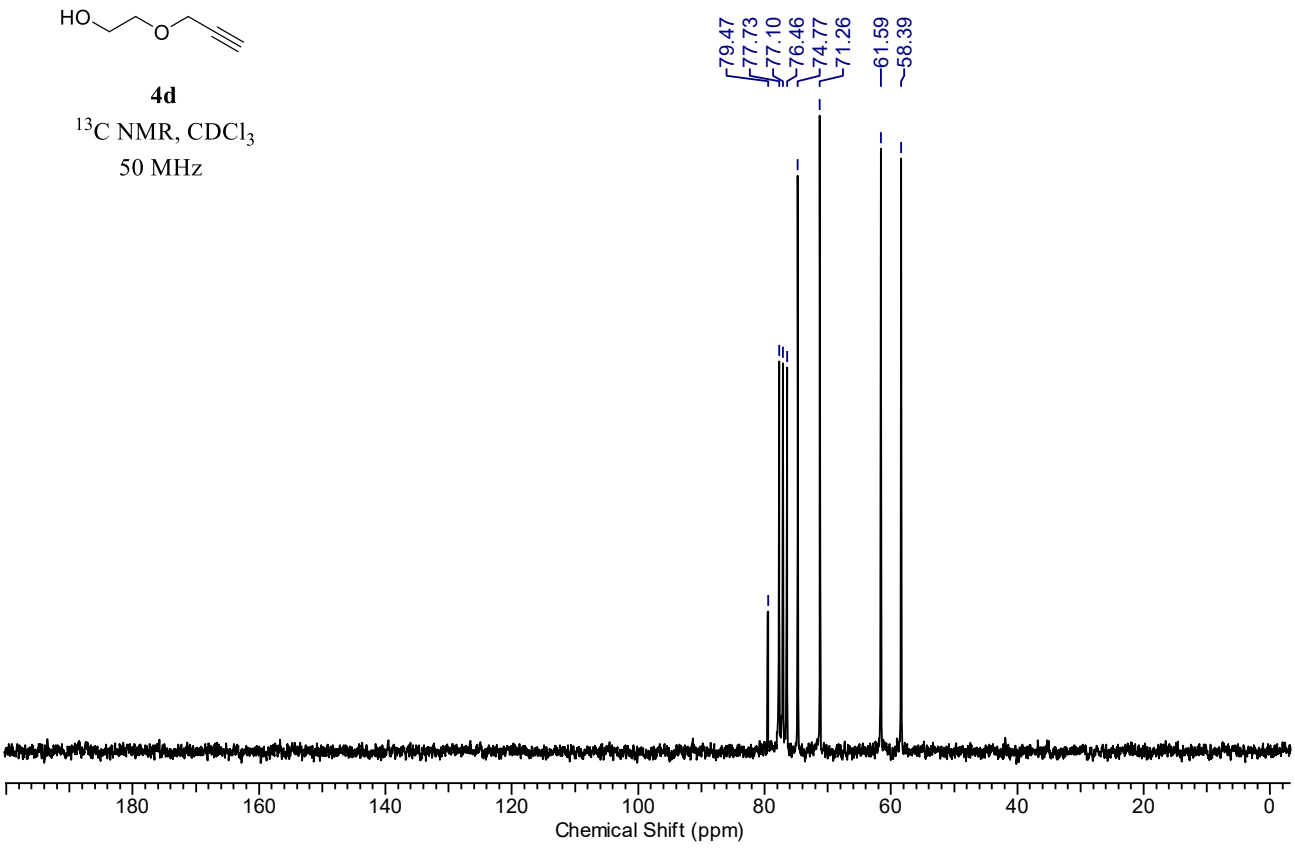
^{1}H NMR $CDCl_3$
200MHz

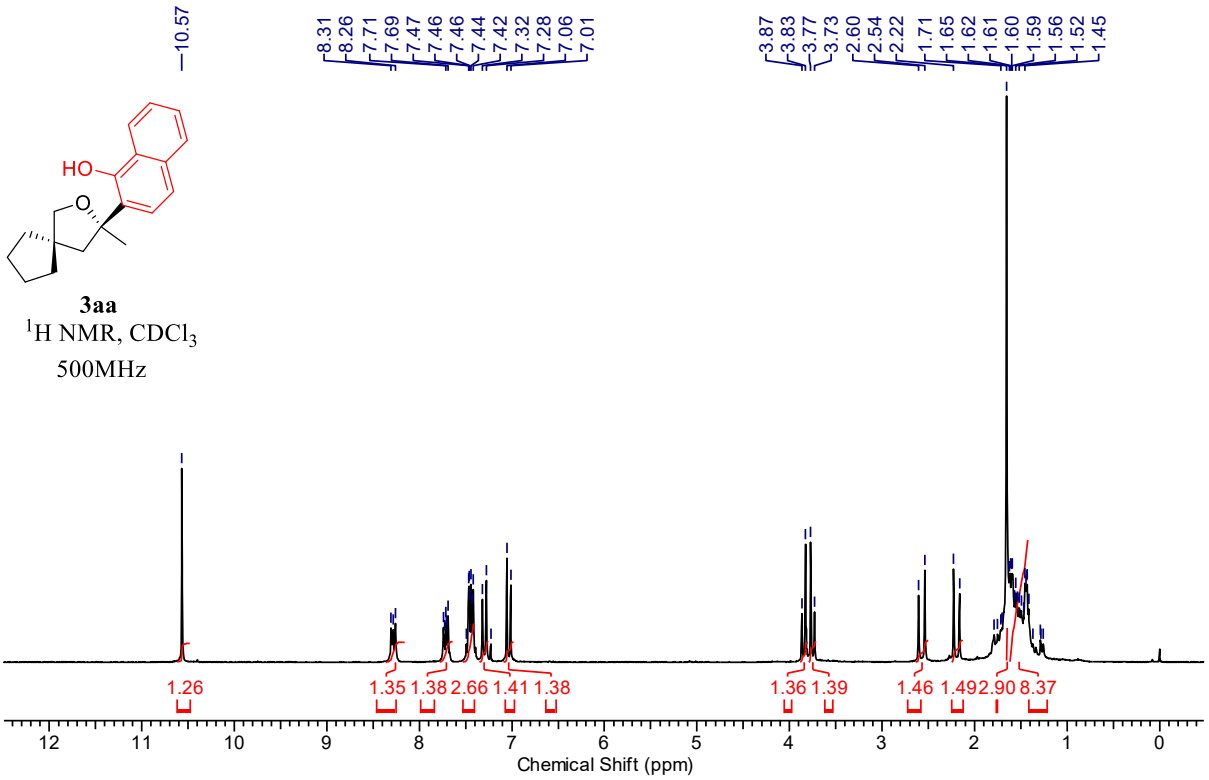


4c

^{13}C NMR, $CDCl_3$
101 MHz


HO
O
4d
^{1}H NMR, CDCl$_3$
200 MHz
7.30
4.22
4.22
4.21
3.77
3.68
3.67
3.65
3.63
2.67
2.50
2.49
2.48
2.05
2.05
2.11
0.99
1.00
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical Shift (ppm)

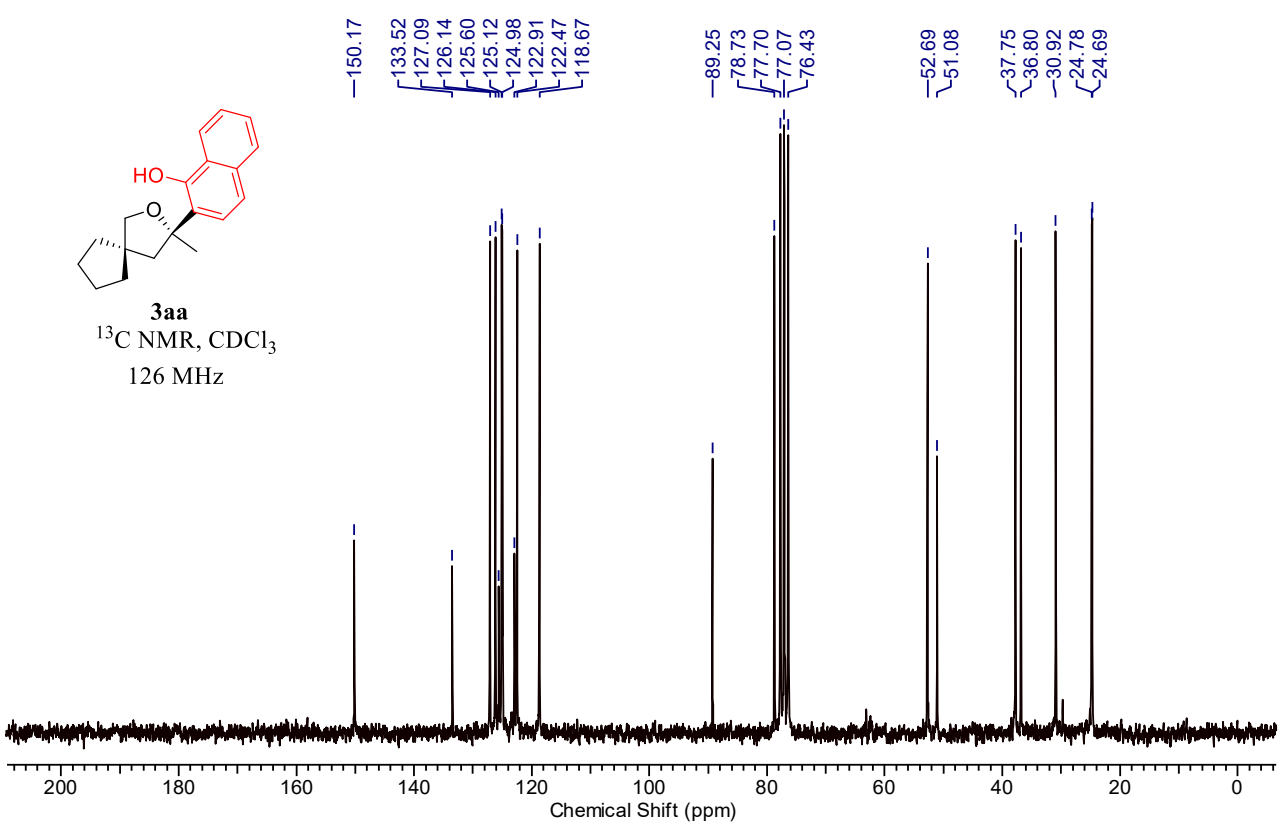

HO
O
4d
^{13}C NMR, CDCl$_3$
50 MHz
79.47
77.73
77.10
76.46
74.77
71.26
61.59
58.39
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)



3aa

^{1}H NMR, $CDCl_3$

500MHz

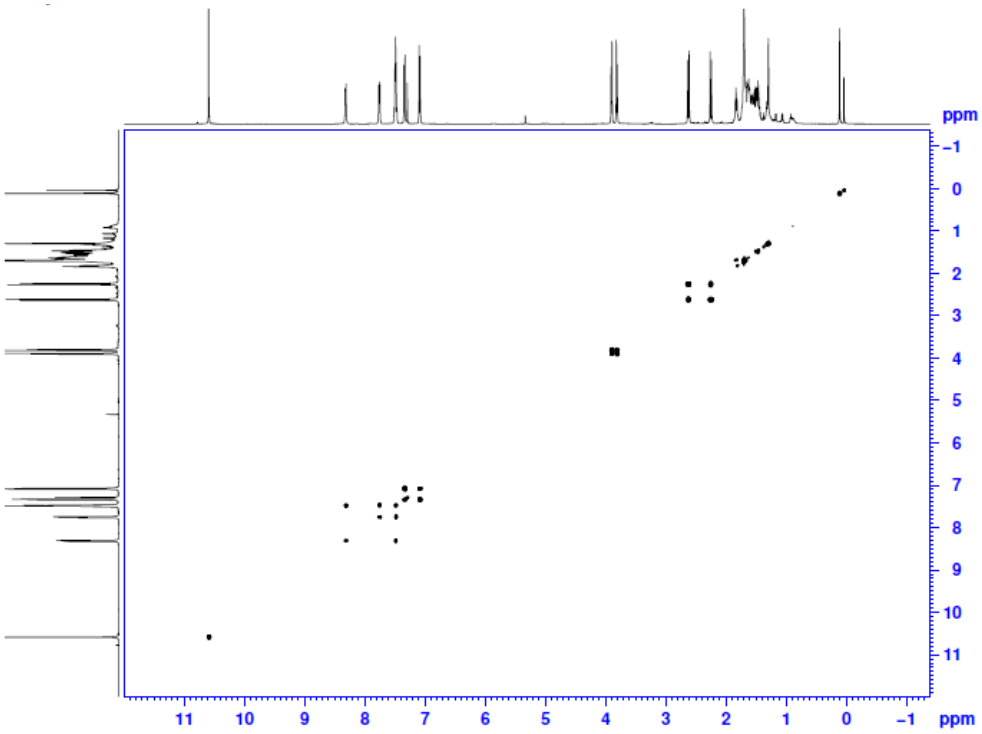


3aa

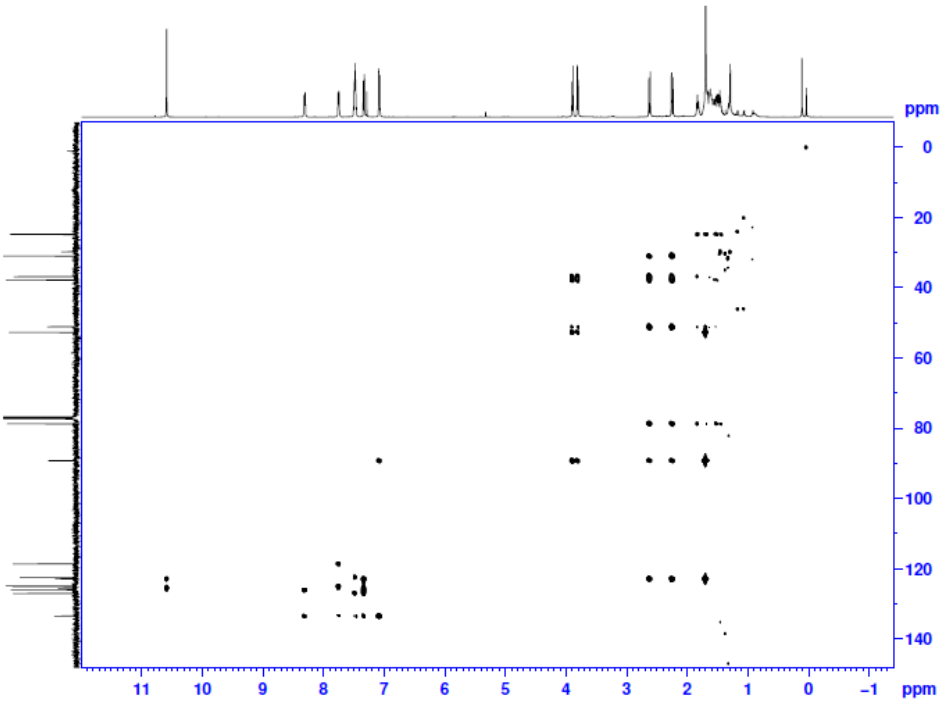
^{13}C NMR, $CDCl_3$

126 MHz

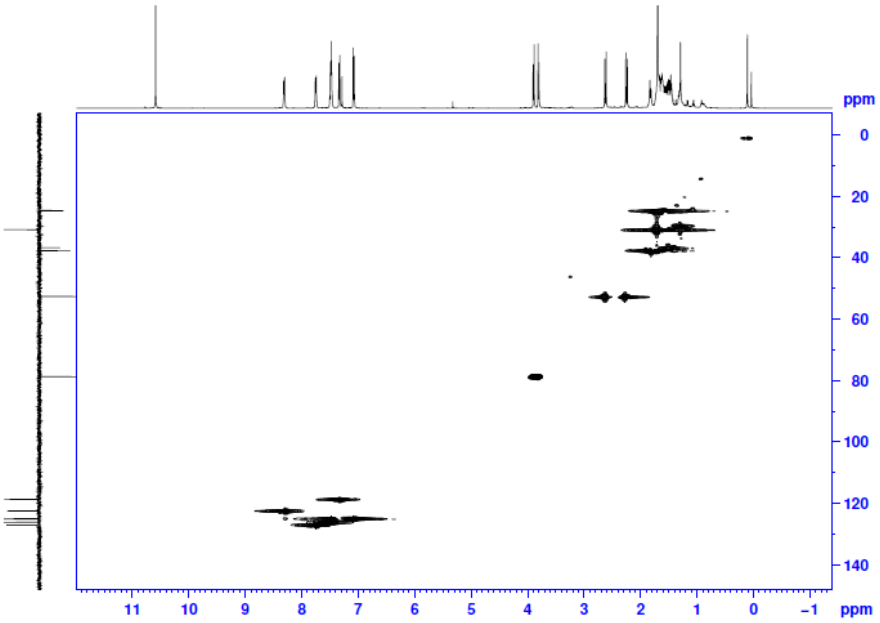
(3aa):


ppm
-1
0
1
2
3
4
5
6
7
8
9
10
11
11 10 9 8 7 6 5 4 3 2 1 0 -1 ppm

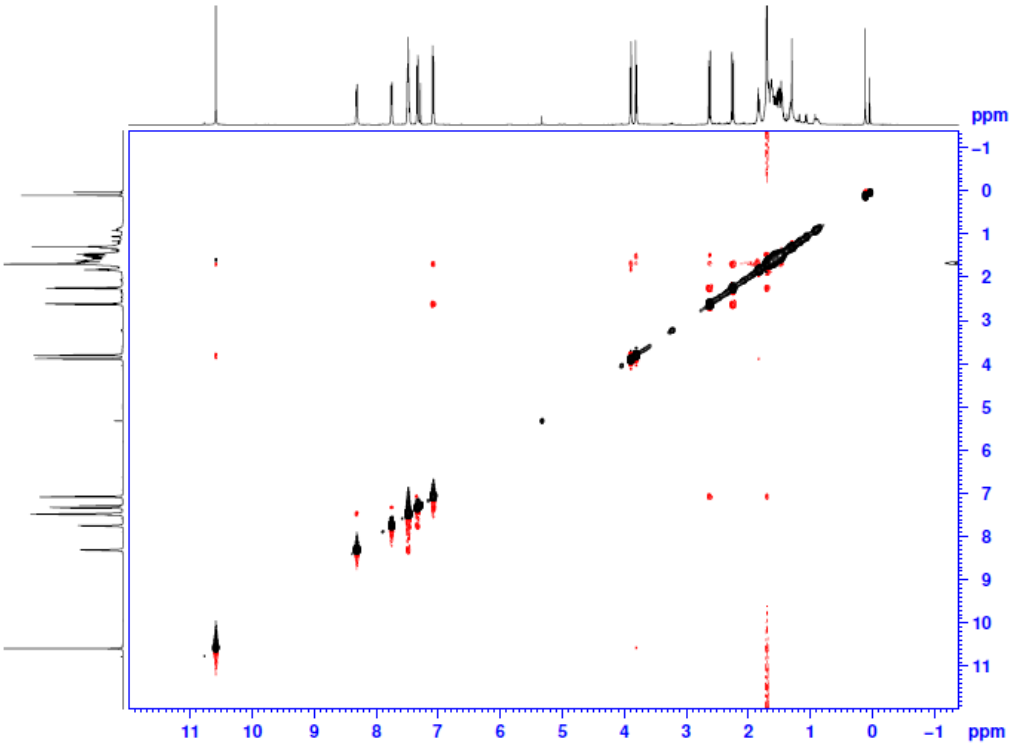
HMBC **(3aa):**

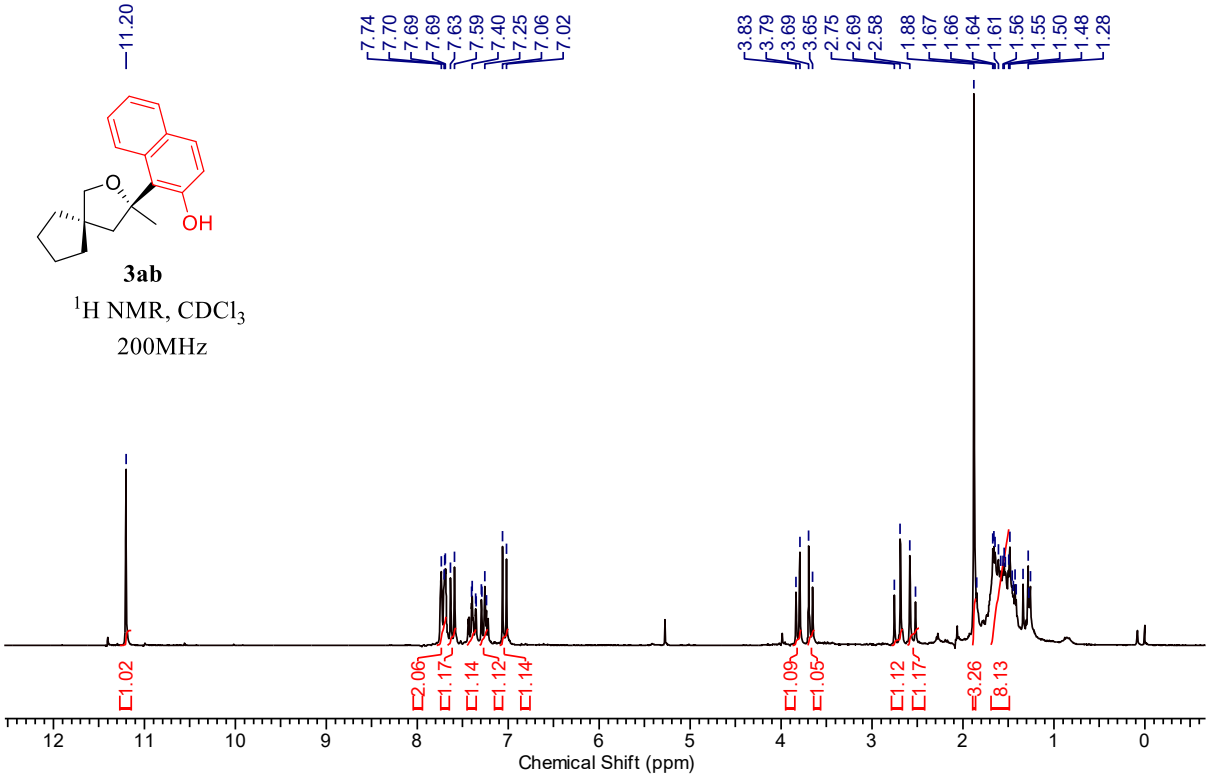

ppm
0
20
40
60
80
100
120
140
11 10 9 8 7 6 5 4 3 2 1 0 -1 ppm

HSQC **(3aa):**



NOESY **(3aa):**

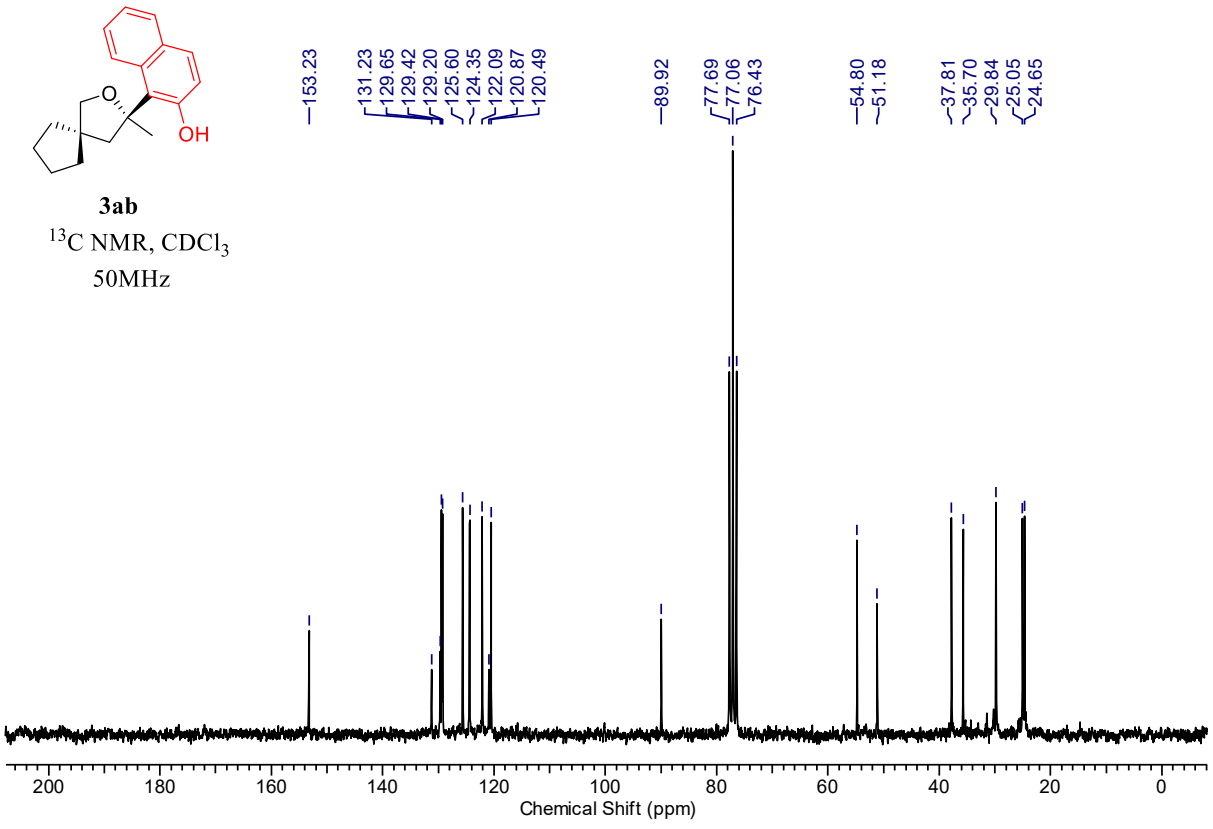




3ab

^{1}H NMR, $CDCl_3$

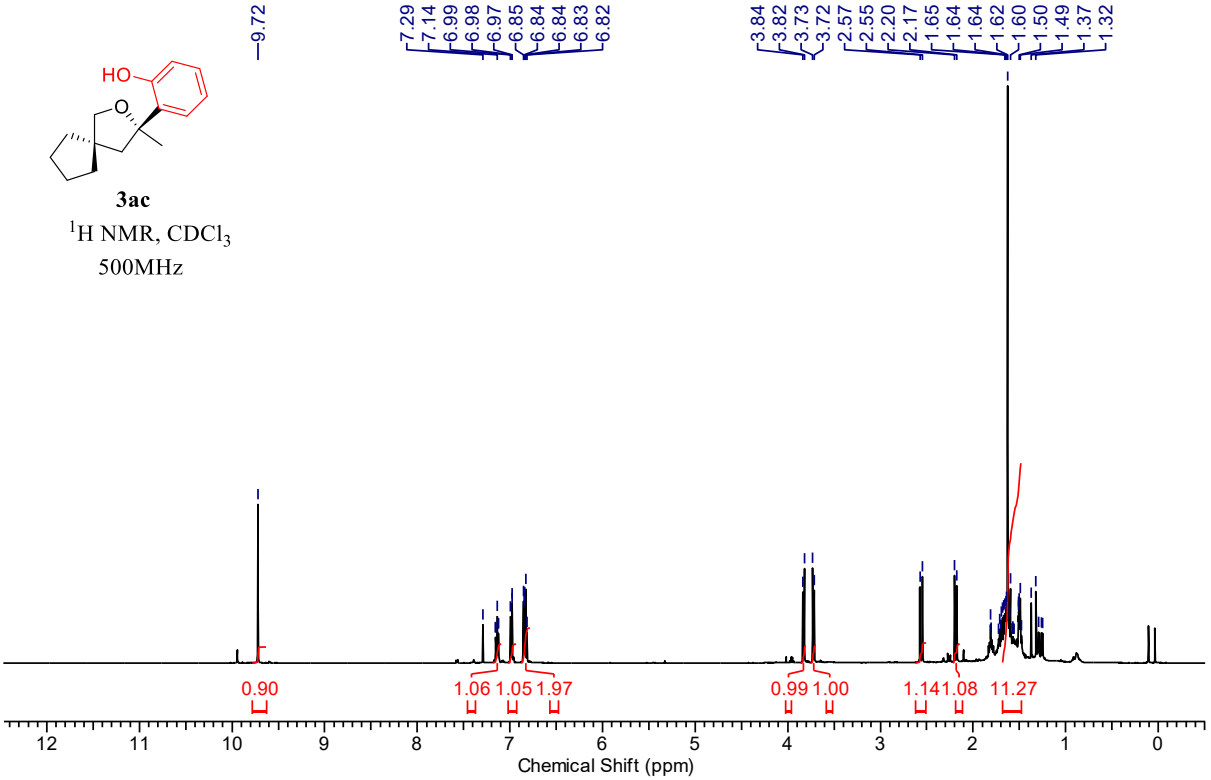
200MHz



3ab

^{13}C NMR, $CDCl_3$

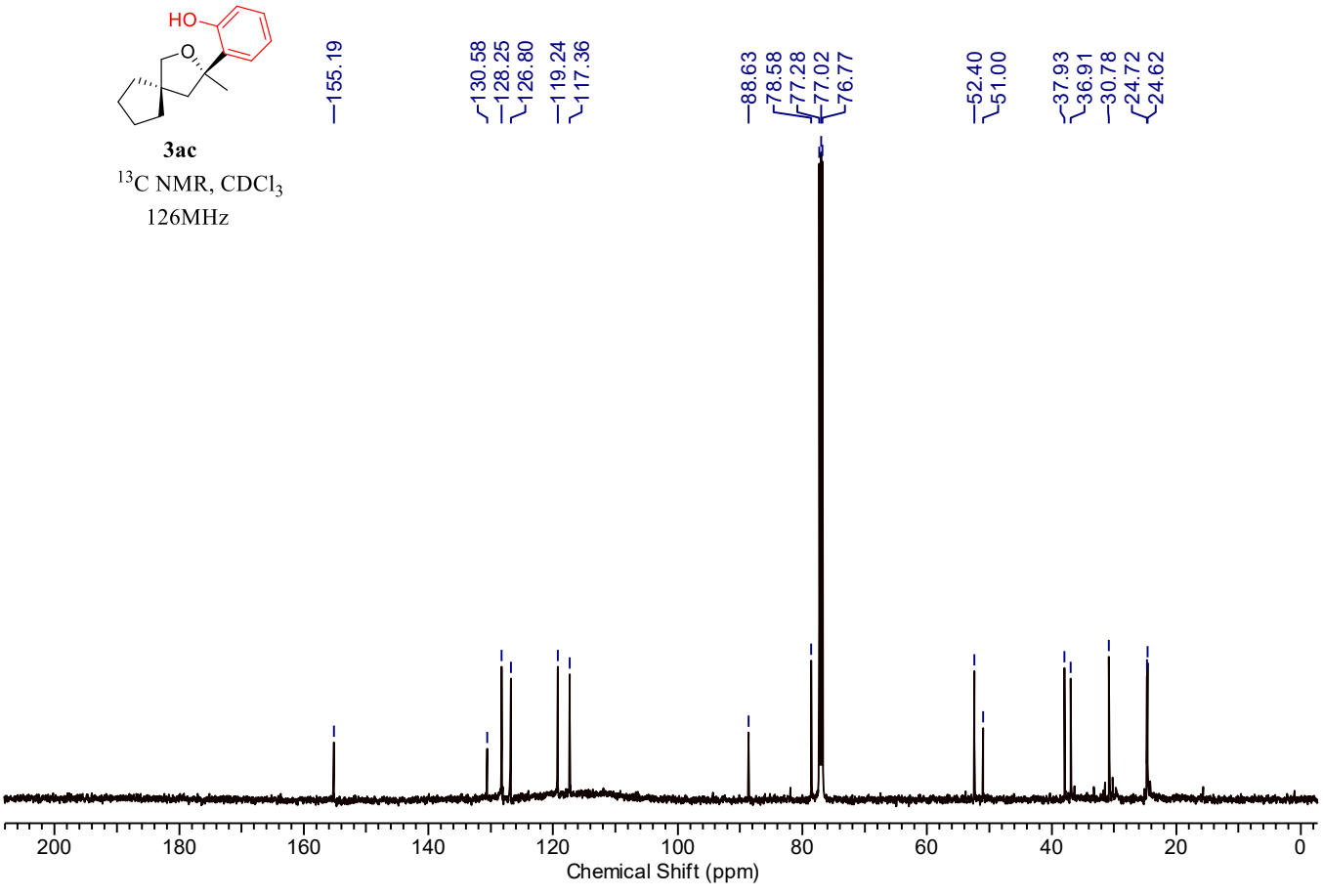
50MHz



3ac

^{1}H NMR, $CDCl_3$

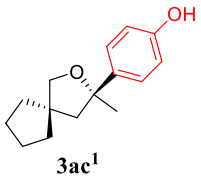
500MHz



3ac

^{13}C NMR, $CDCl_3$

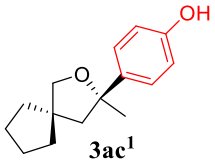
126MHz



3ac[1]

^{1}H NMR, $CDCl_3$

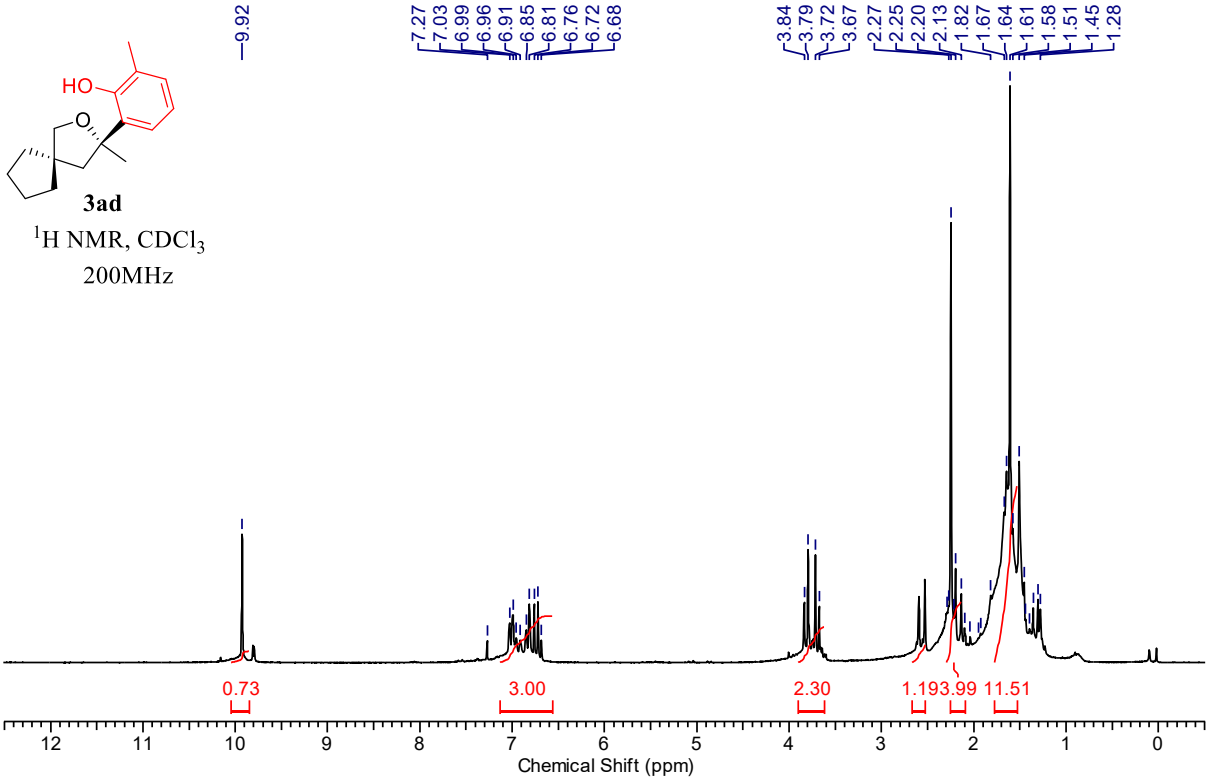
200 MHz

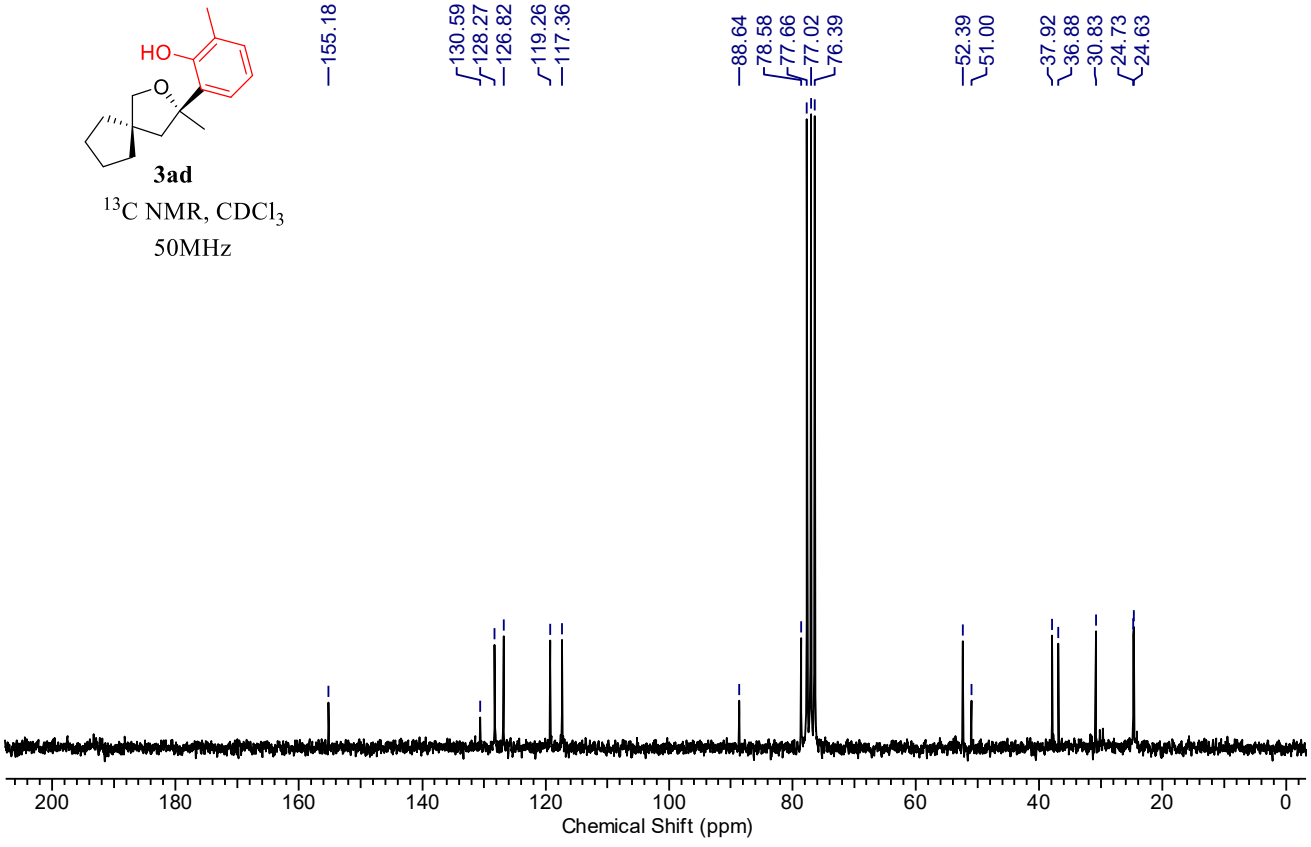


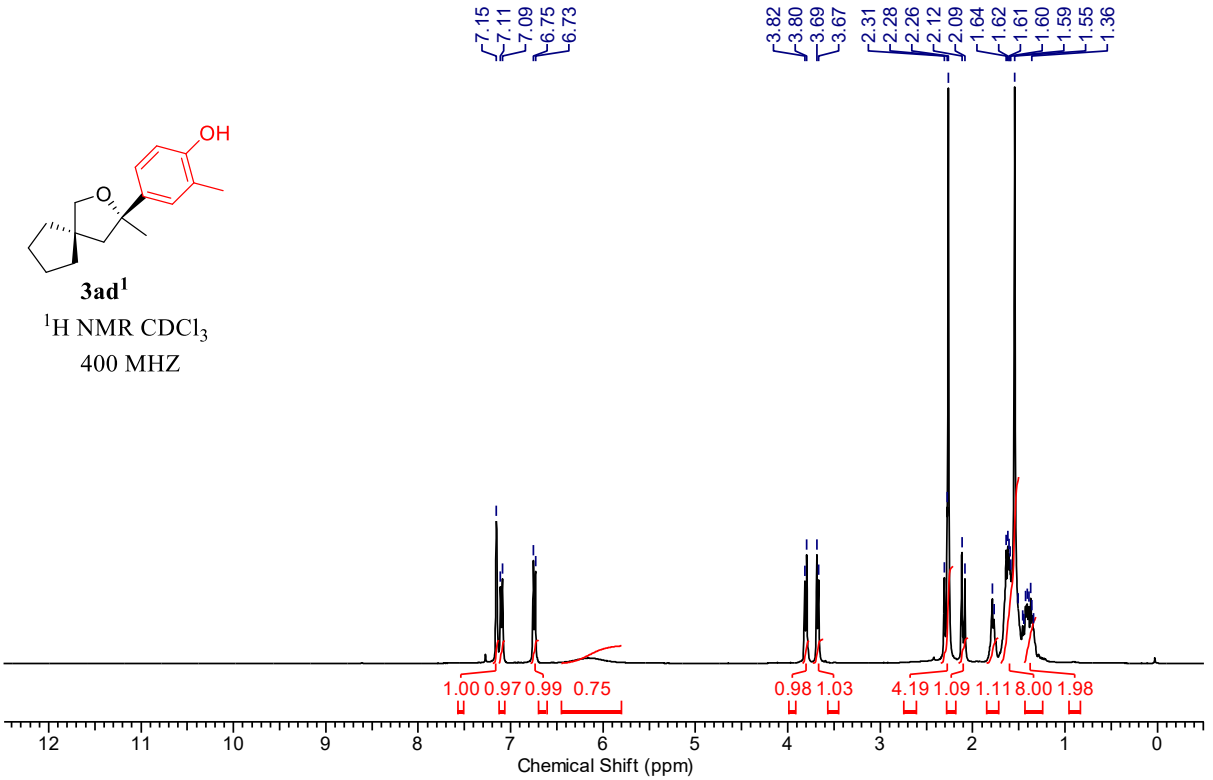
3ac[1]

^{13}C NMR, $CDCl_3$

50 MHz


HO
O
3ad
^{1}H NMR, $CDCl_3$
200MHz
9.92
7.27
7.03
6.99
6.96
6.91
6.85
6.81
6.76
6.72
6.68
3.84
3.79
3.72
3.67
2.27
2.25
2.20
2.13
1.82
1.67
1.64
1.61
1.58
1.51
1.45
1.28
0.73
3.00
2.30
1.19
3.99
11.51
Chemical Shift (ppm)

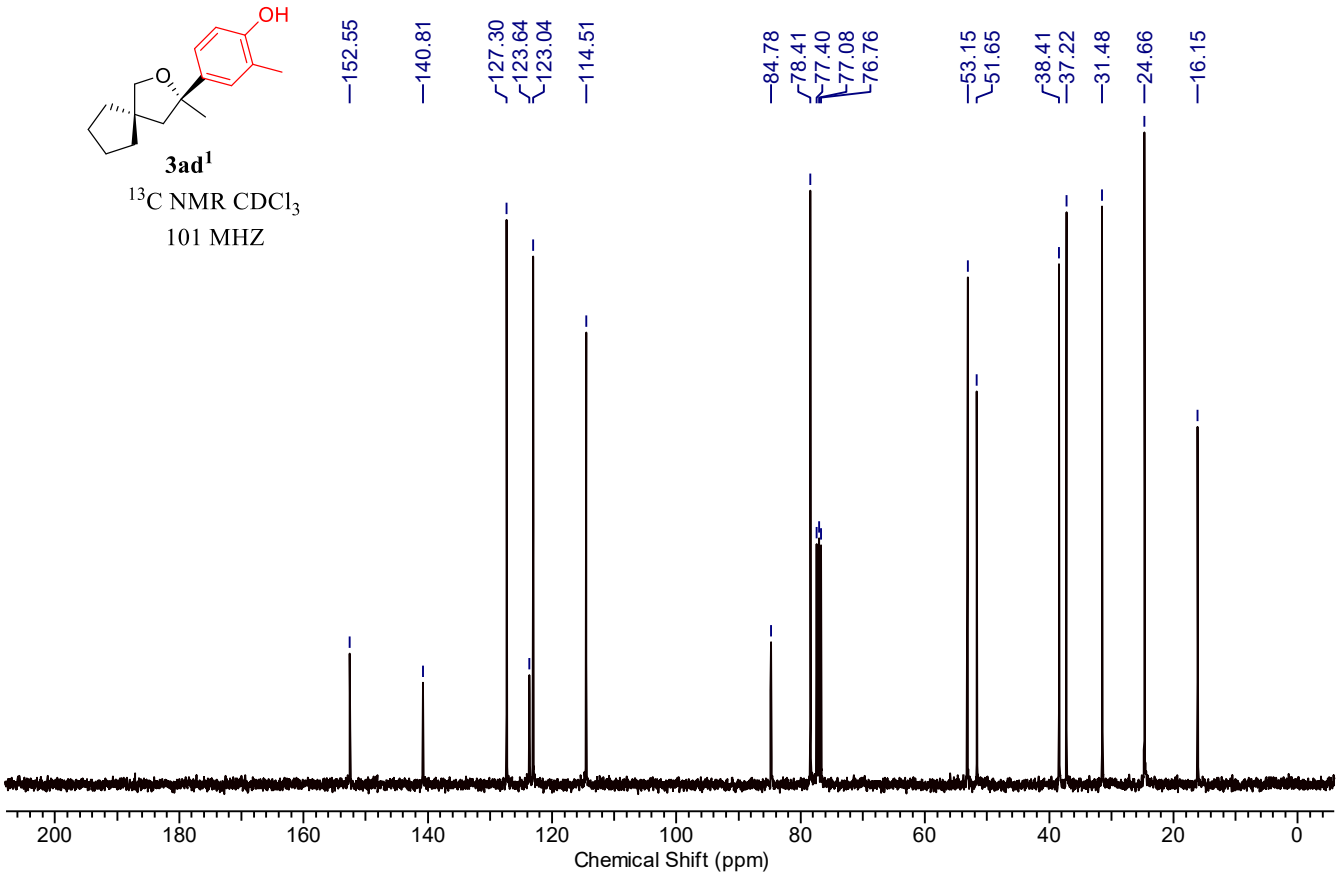

HO
O
3ad
^{13}C NMR, $CDCl_3$
50MHz
155.18
130.59
128.27
126.82
119.26
117.36
88.64
78.58
77.66
77.02
76.39
52.39
51.00
37.92
36.88
30.83
24.73
24.63
Chemical Shift (ppm)



3ad[1]

^{1}H NMR $CDCl_3$

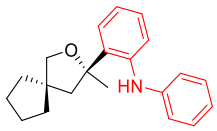
400 MHZ



3ad[1]

^{13}C NMR $CDCl_3$

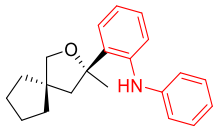
101 MHZ



3ae

^{1}H NMR $CDCl_3$

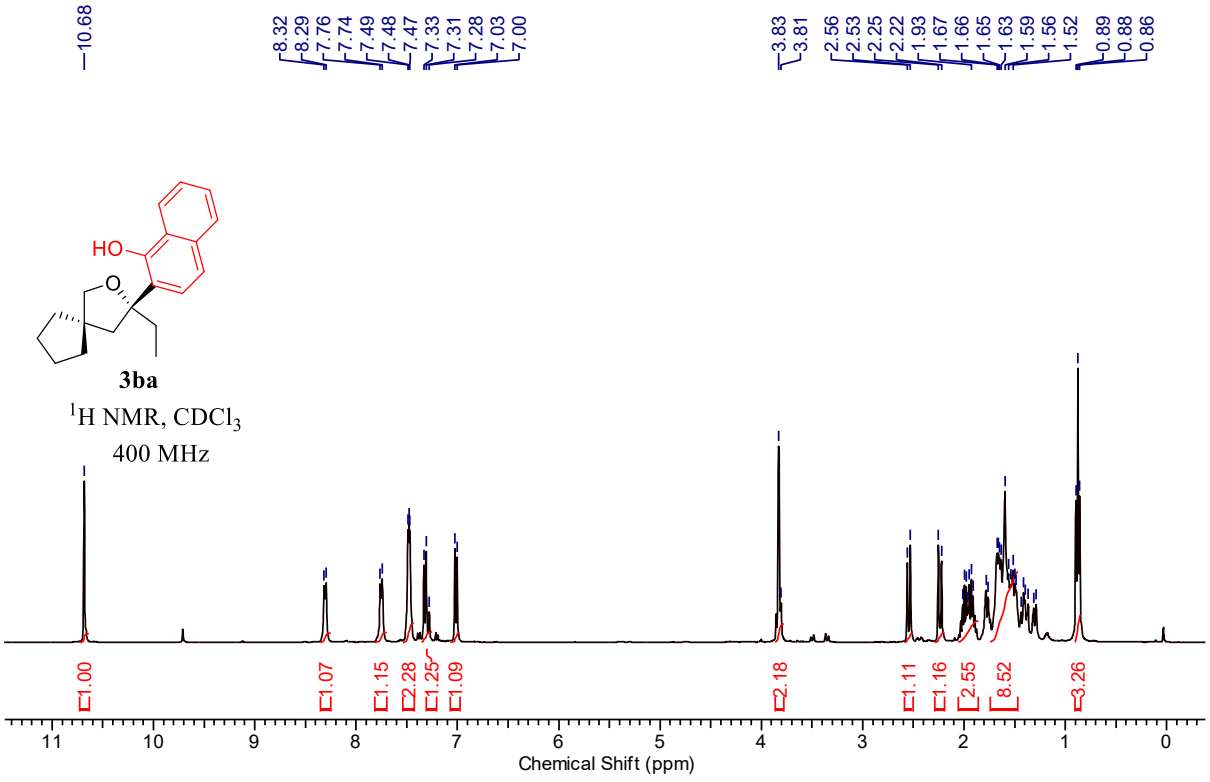
200 MHz

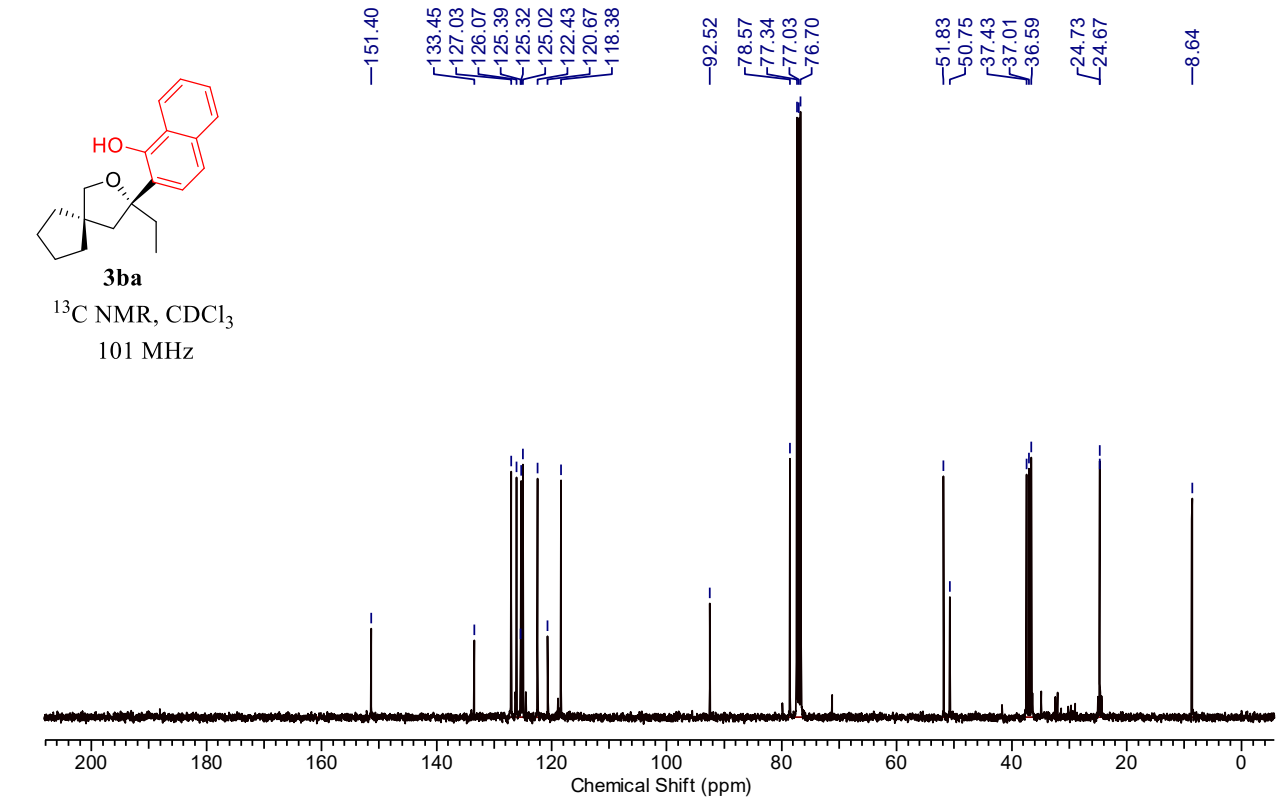


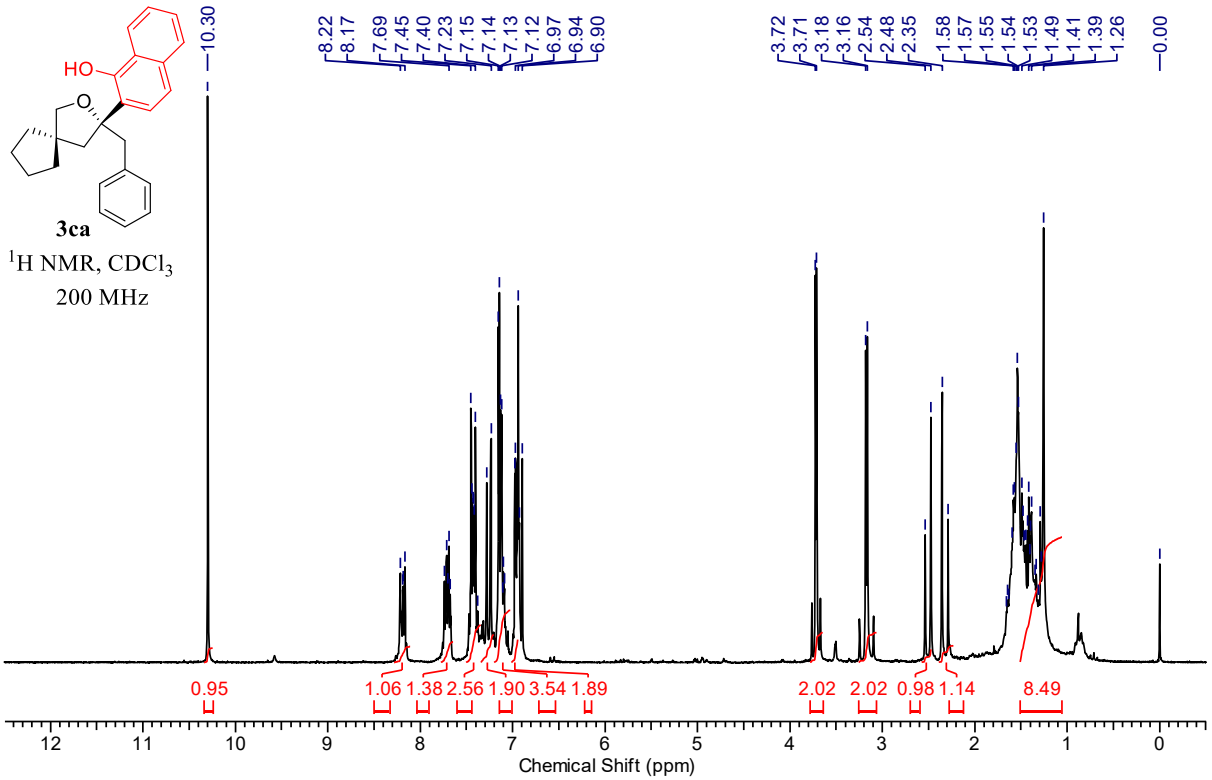
3ae

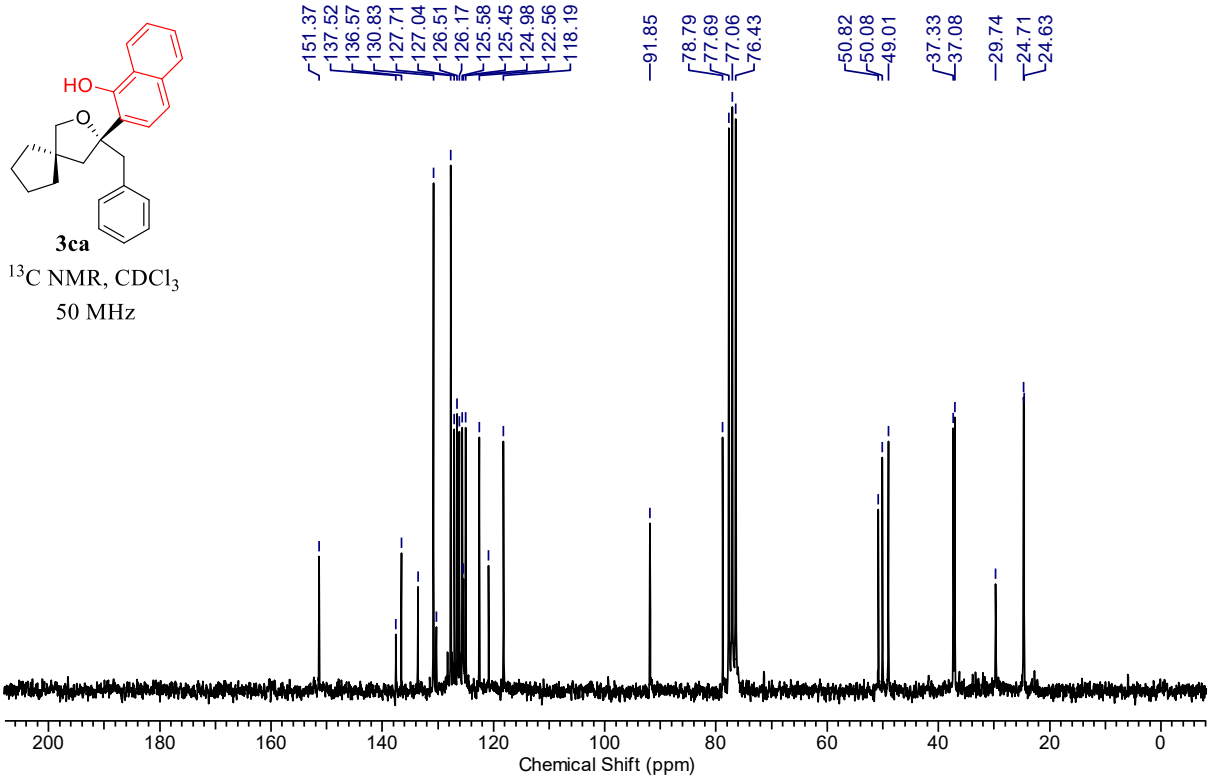
^{13}C NMR $CDCl_3$

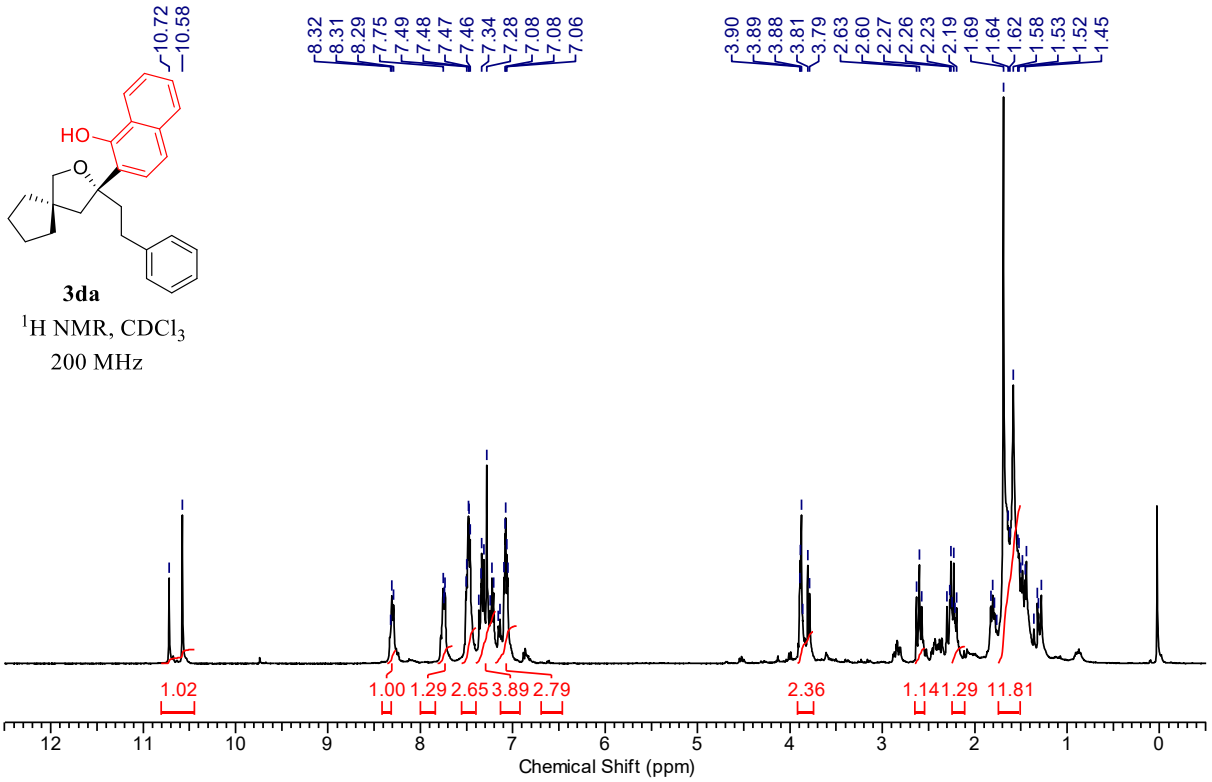
50 MHz


10.68
8.32
8.29
7.76
7.74
7.49
7.48
7.47
7.33
7.31
7.28
7.03
7.00
3.83
3.81
2.56
2.53
2.25
2.22
1.93
1.67
1.66
1.65
1.63
1.59
1.56
1.52
0.89
0.88
0.86
HO
O
3ba
1H NMR, CDCl3
400 MHz
1.00
1.07
1.15
2.28
1.25
1.09
2.18
1.11
1.16
2.55
8.52
3.26
Chemical Shift (ppm)


151.40
133.45
127.03
126.07
125.39
125.32
125.02
122.43
120.67
118.38
92.52
78.57
77.34
77.03
76.70
51.83
50.75
37.43
37.01
36.59
24.73
24.67
8.64
HO
O
3ba
13C NMR, CDCl3
101 MHz
Chemical Shift (ppm)


HO
O
3ca
^{1}H NMR, CDCl$_3$
200 MHz
10.30
8.22
8.17
7.69
7.45
7.40
7.23
7.15
7.14
7.13
7.12
6.97
6.94
6.90
3.72
3.71
3.18
3.16
2.54
2.48
2.35
1.58
1.57
1.55
1.54
1.53
1.49
1.41
1.39
1.26
0.00
0.95
1.06
1.38
2.56
1.90
3.54
1.89
2.02
2.02
0.98
1.14
8.49
Chemical Shift (ppm)

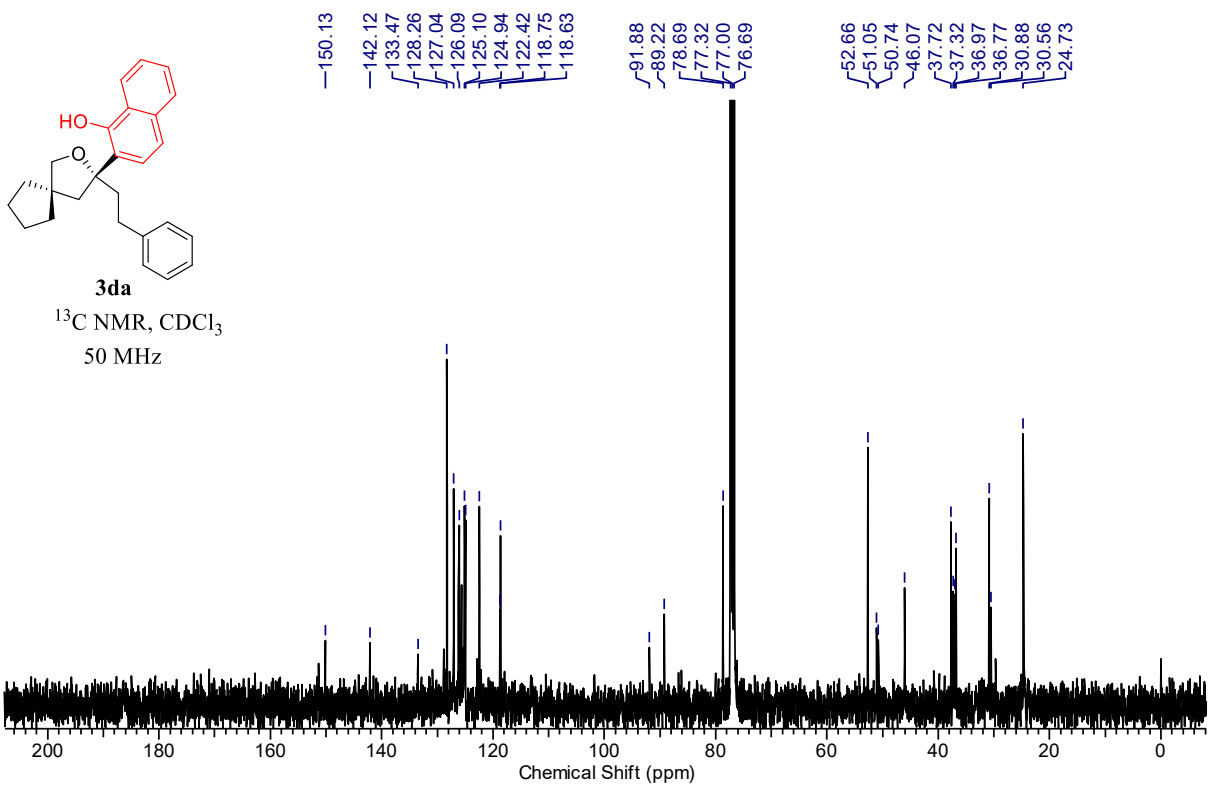

HO
O
3ca
^{13}C NMR, CDCl$_3$
50 MHz
151.37
137.52
136.57
130.83
127.71
127.04
126.51
126.17
125.58
125.45
124.98
122.56
118.19
91.85
78.79
77.69
77.06
76.43
50.82
50.08
49.01
37.33
37.08
29.74
24.71
24.63
Chemical Shift (ppm)



3da

^{1}H NMR, $CDCl_3$

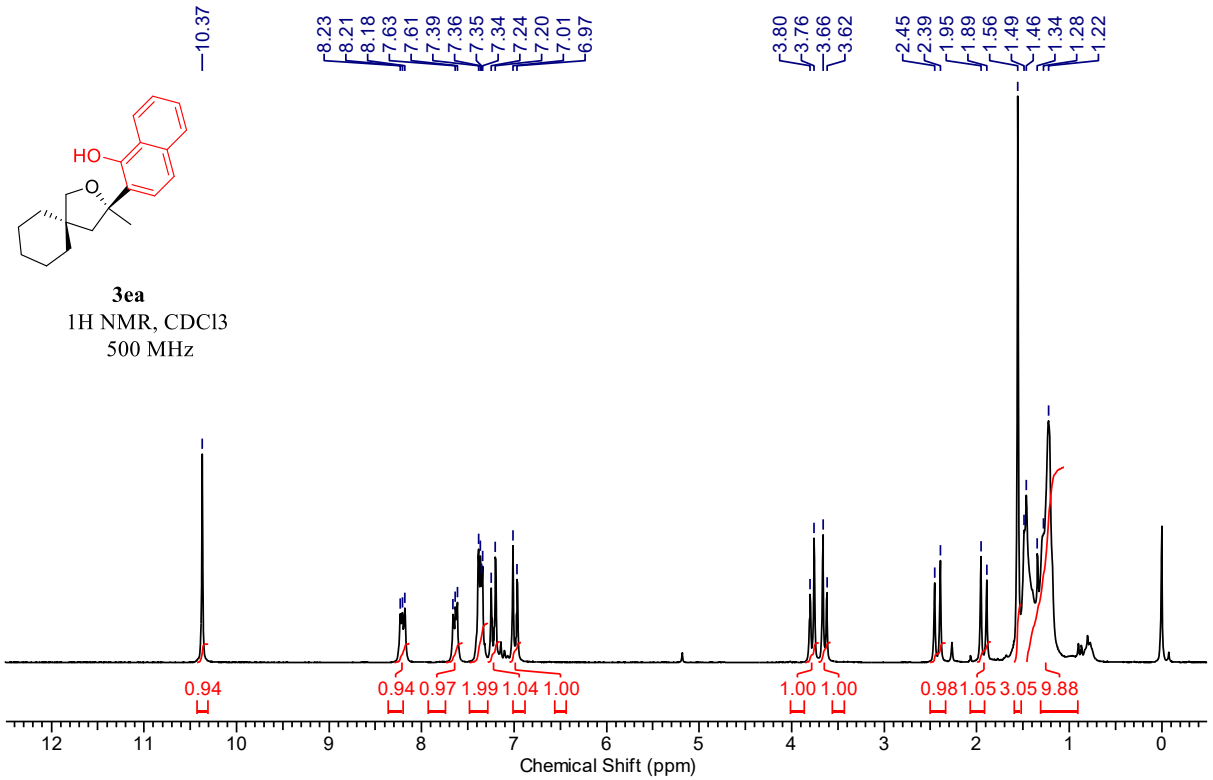
200 MHz

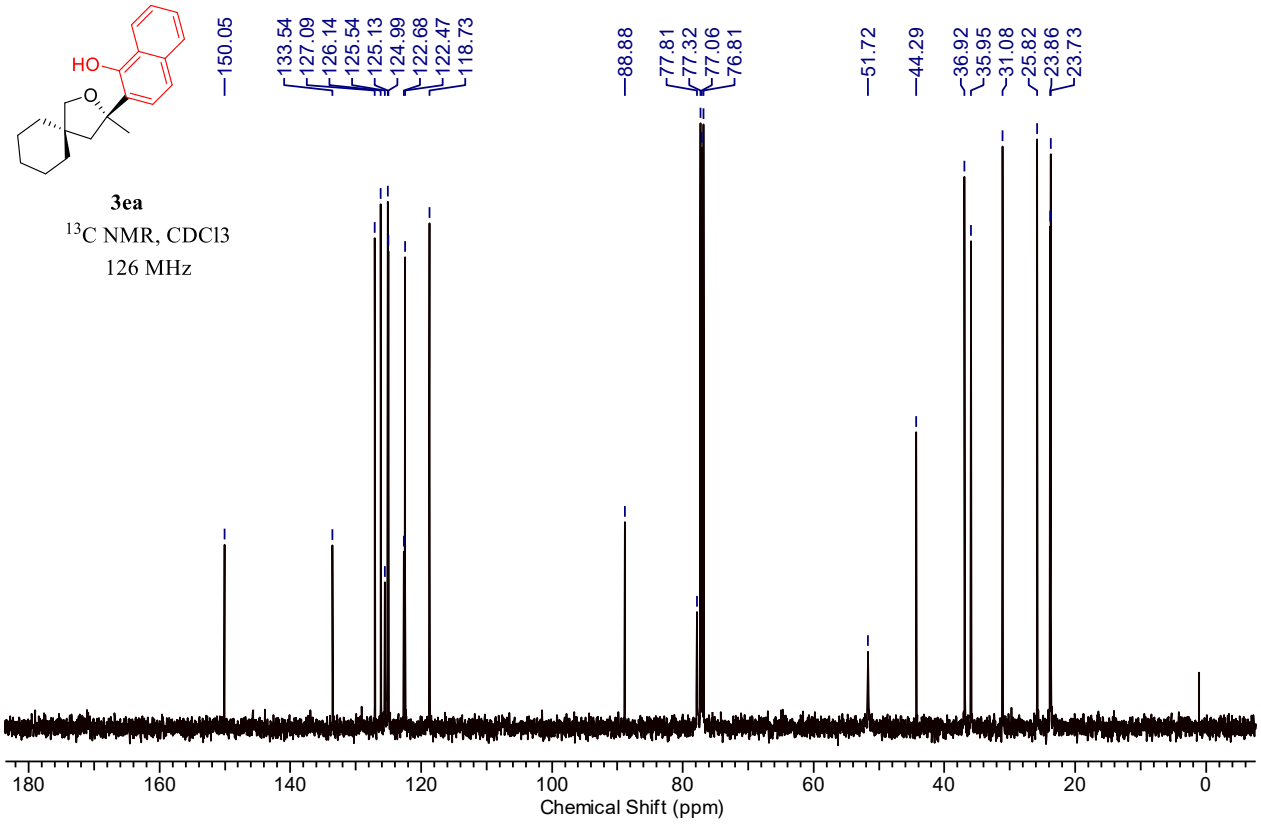


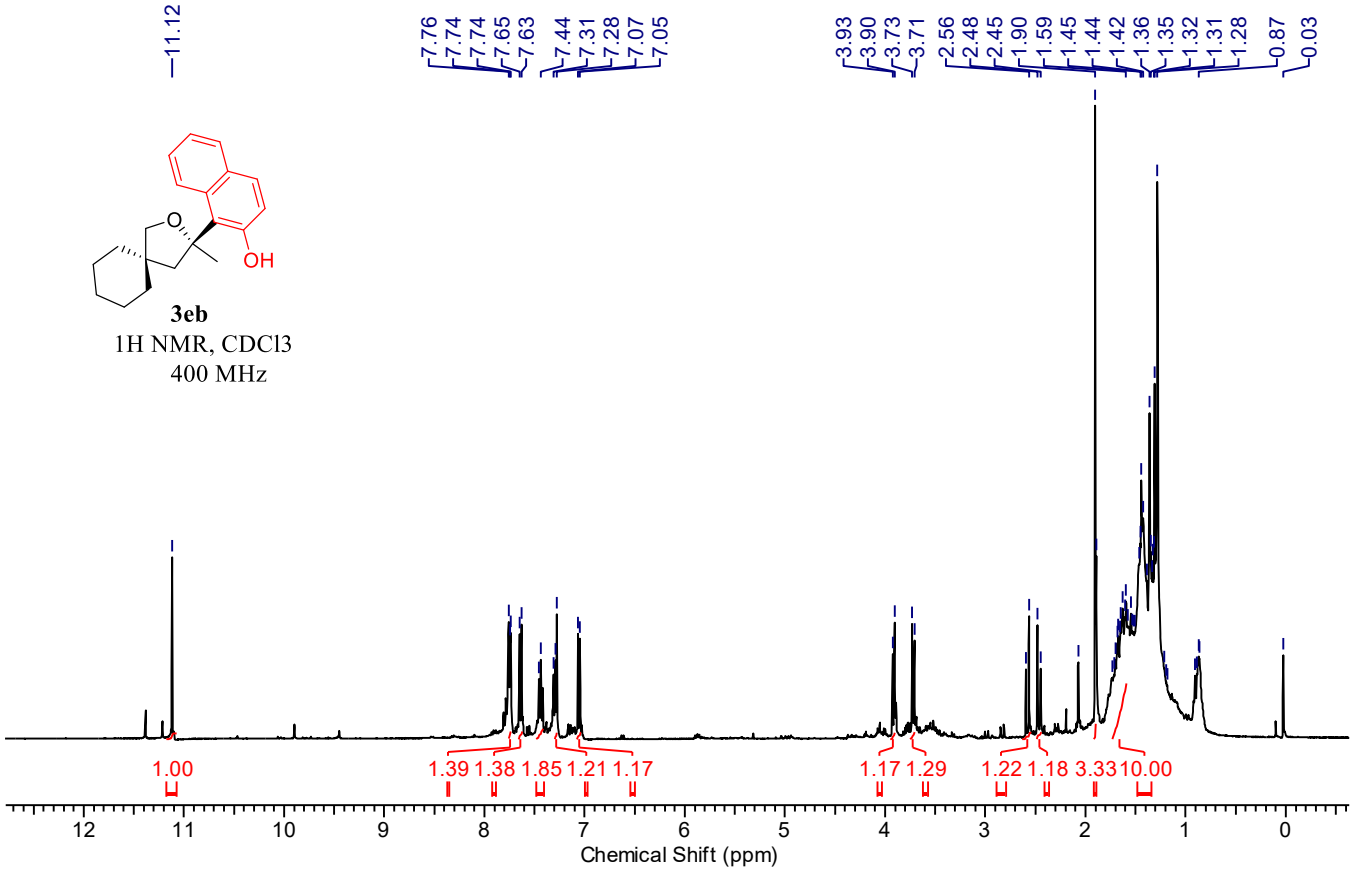
3da

^{13}C NMR, $CDCl_3$

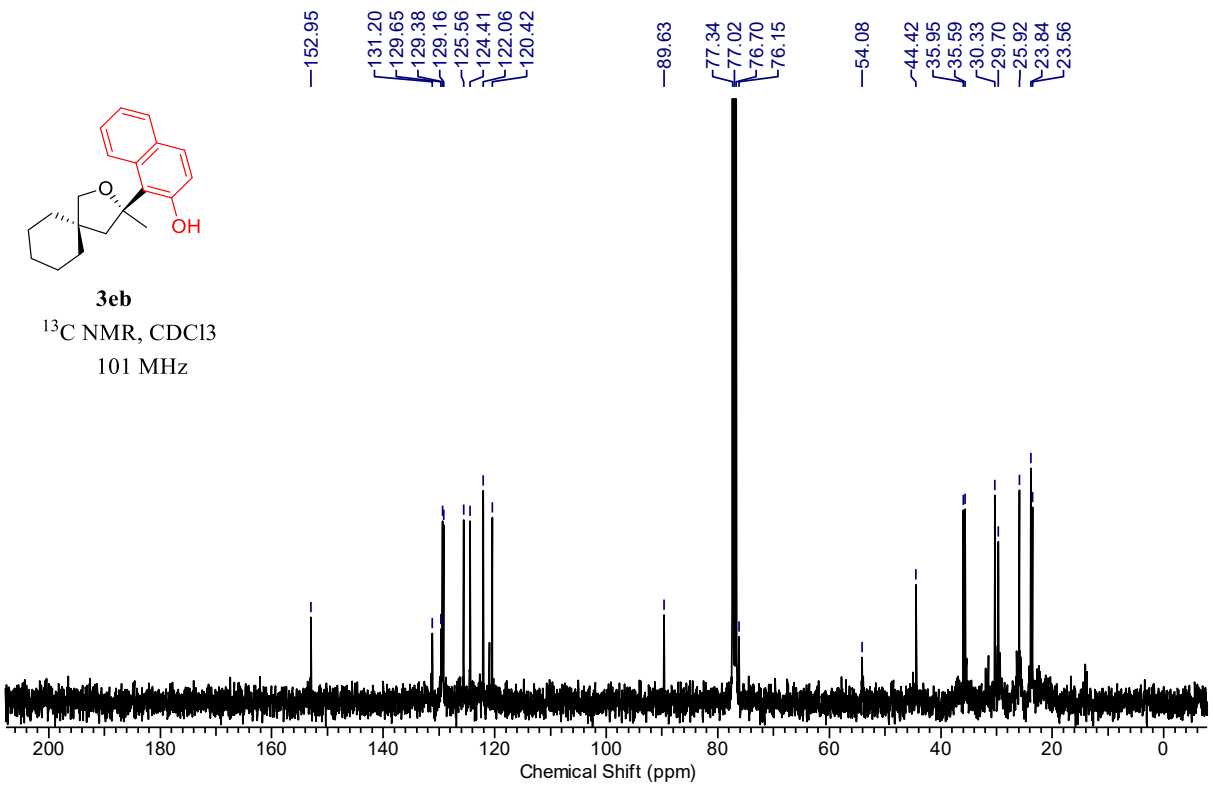
50 MHz


10.37
8.23
8.21
8.18
7.63
7.61
7.39
7.36
7.35
7.34
7.24
7.20
7.01
6.97
3.80
3.76
3.66
3.62
2.45
2.39
1.95
1.89
1.56
1.49
1.46
1.34
1.28
1.22
HO
O
3ea
1H NMR, CDCl3
500 MHz
0.94
0.94
0.97
1.99
1.04
1.00
1.00
1.00
0.98
1.05
3.05
9.88
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

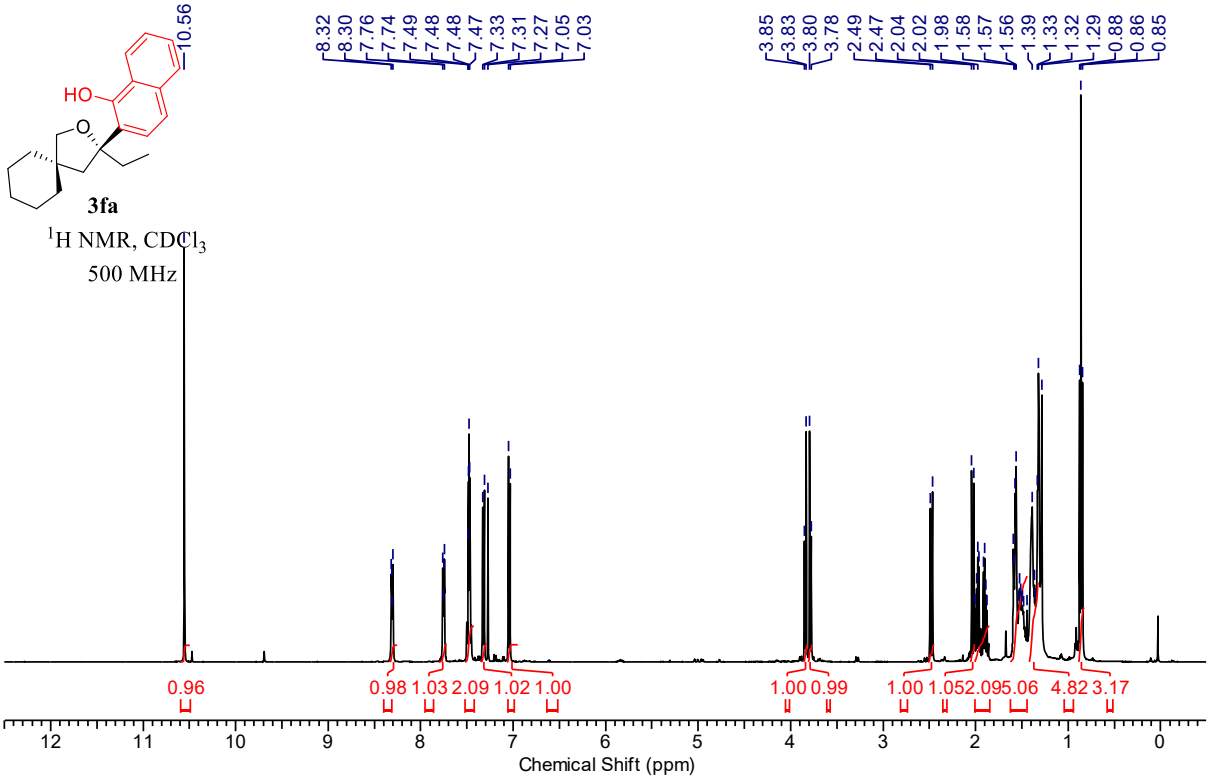

150.05
133.54
127.09
126.14
125.54
125.13
124.99
122.68
122.47
118.73
88.88
77.81
77.32
77.06
76.81
51.72
44.29
36.92
35.95
31.08
25.82
23.86
23.73
HO
O
3ea
13C NMR, CDCl3
126 MHz
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

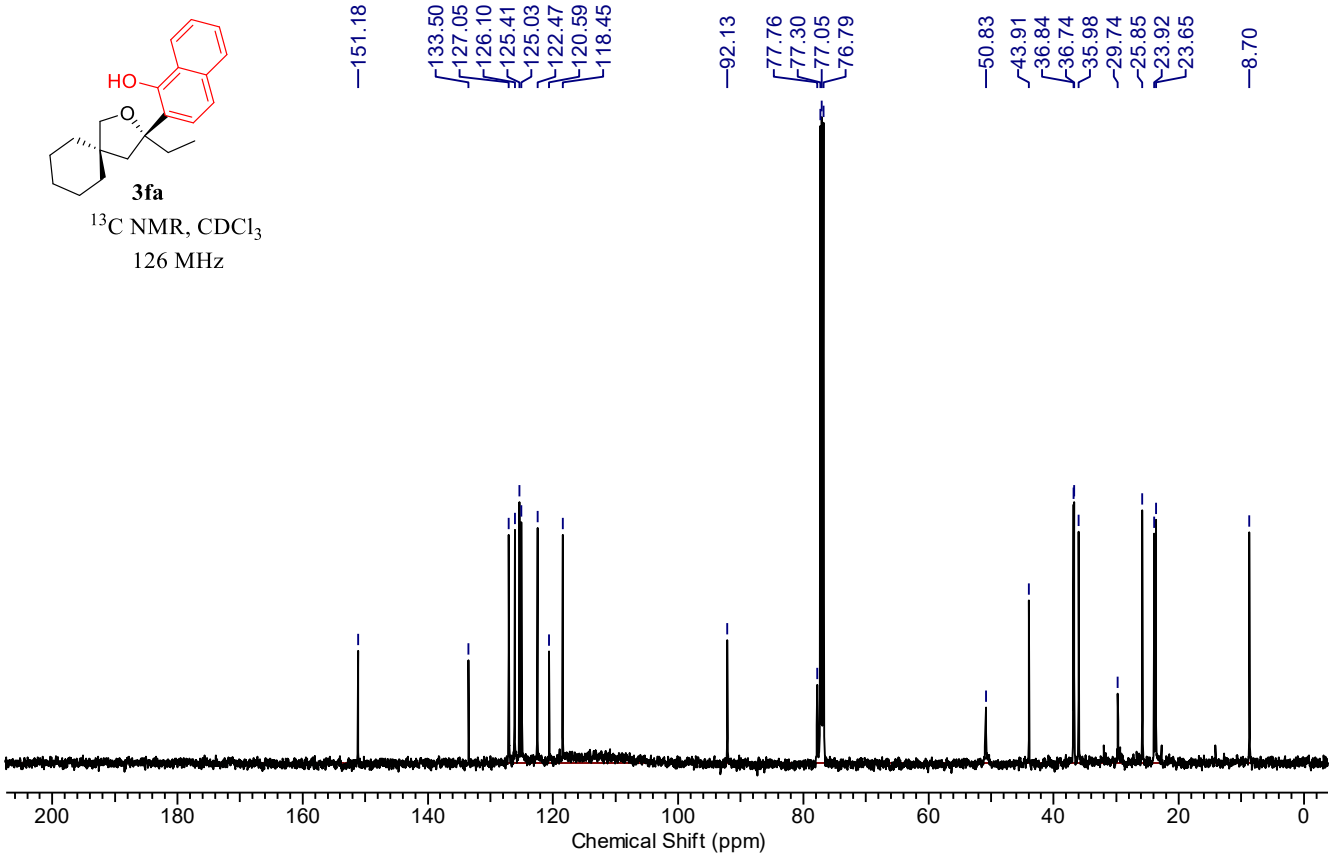


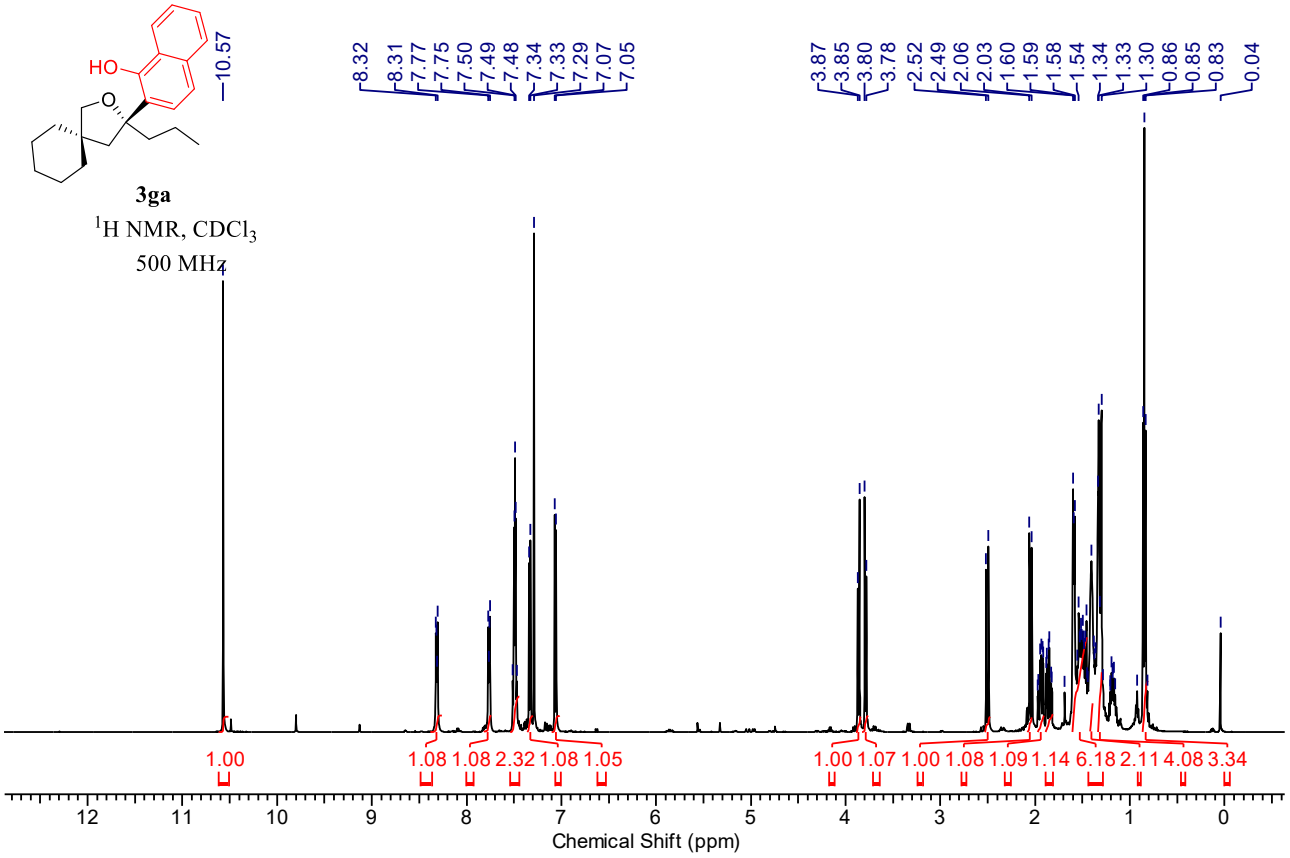
3eb
1H NMR, CDCl3
400 MHz



3eb
^{13}C NMR, CDCl3
101 MHz


HO
O
3fa
^{1}H NMR, $CDCl_3$
500 MHz
10.56
8.32 8.30 7.76 7.74 7.49 7.48 7.48 7.47 7.33 7.31 7.27 7.05 7.03
3.85 3.83 3.80 3.78 2.49 2.47 2.04 2.02 1.98 1.58 1.57 1.56 1.39 1.33 1.32 1.29 0.88 0.86 0.85
0.96 0.98 1.03 2.09 1.02 1.00 1.00 0.99 1.00 1.05 2.09 5.06 4.82 3.17
Chemical Shift (ppm)

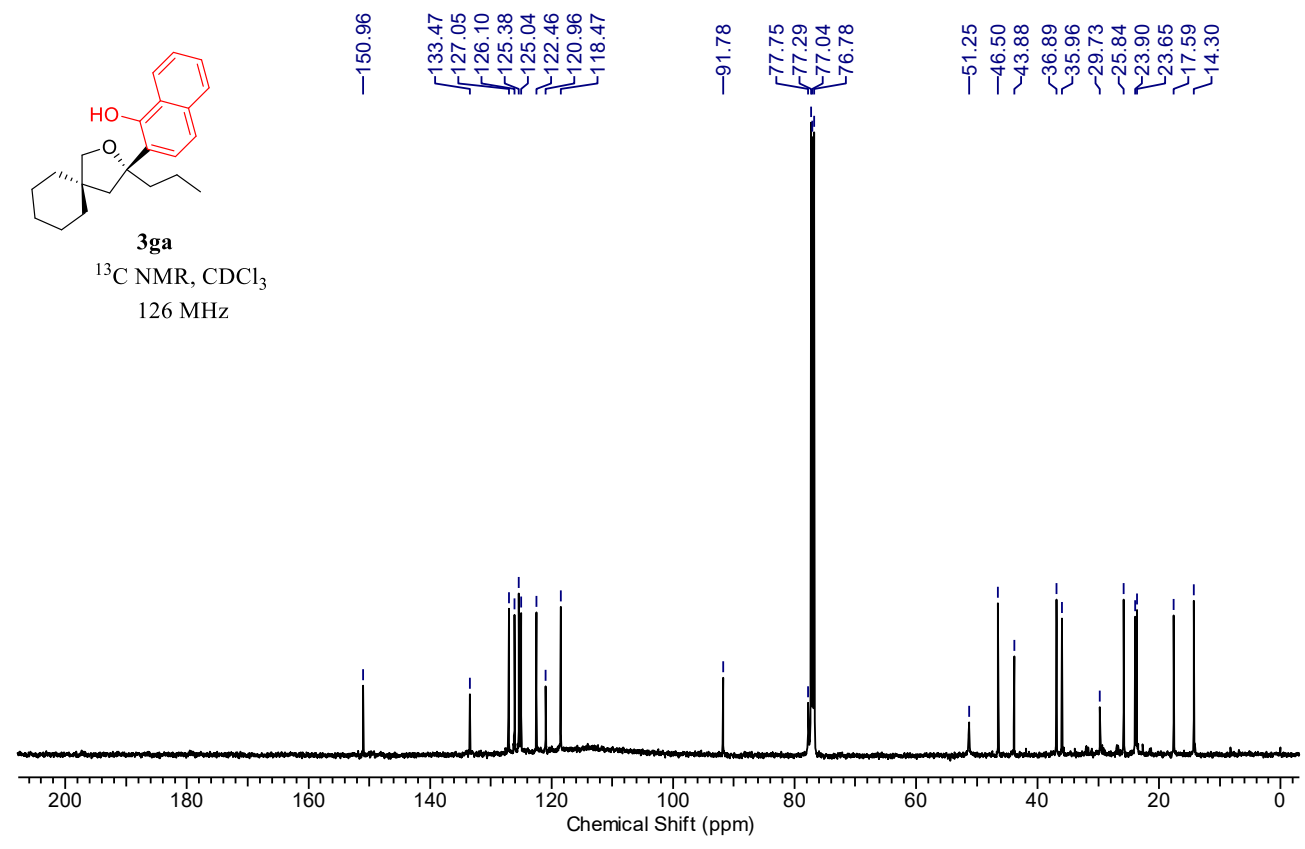

HO
O
3fa
^{13}C NMR, $CDCl_3$
126 MHz
151.18 133.50 127.05 126.10 125.41 125.03 122.47 120.59 118.45 92.13 77.76 77.30 77.05 76.79 50.83 43.91 36.84 36.74 35.98 29.74 25.85 23.92 23.65 8.70
Chemical Shift (ppm)



3ga

^{1}H NMR, $CDCl_3$

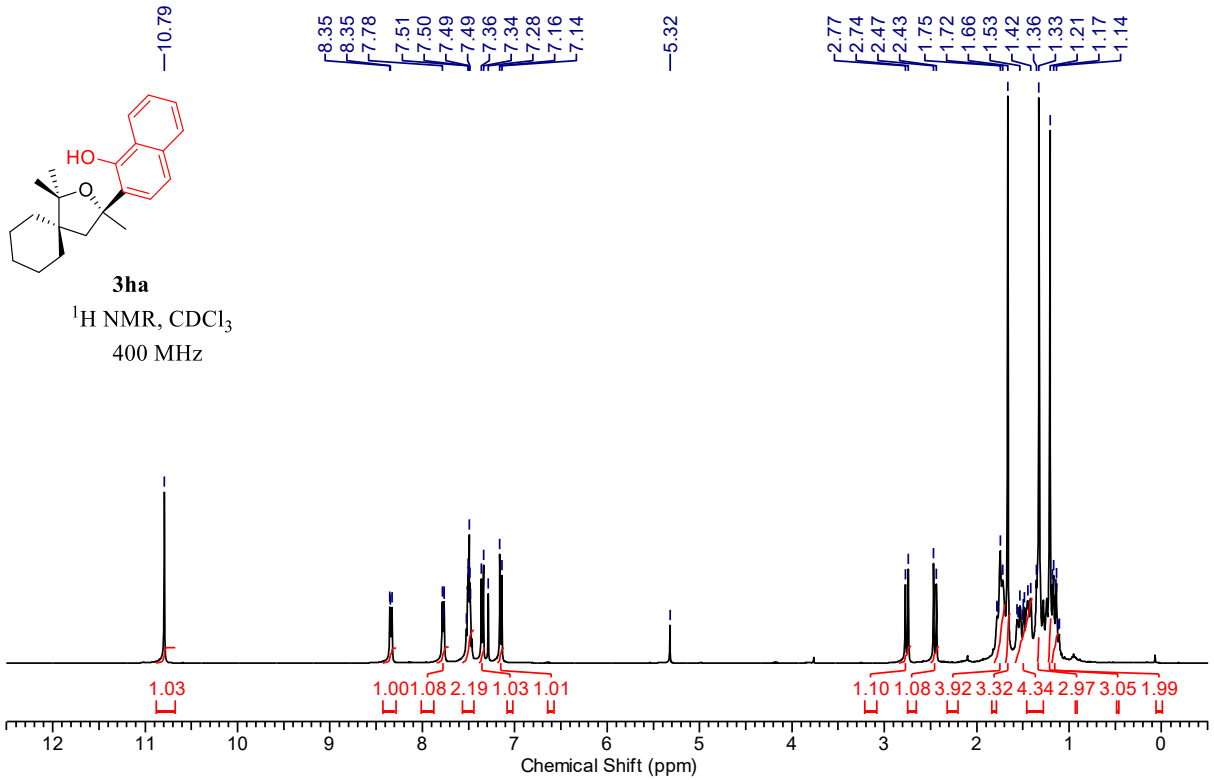
500 MHz



3ga

^{13}C NMR, $CDCl_3$

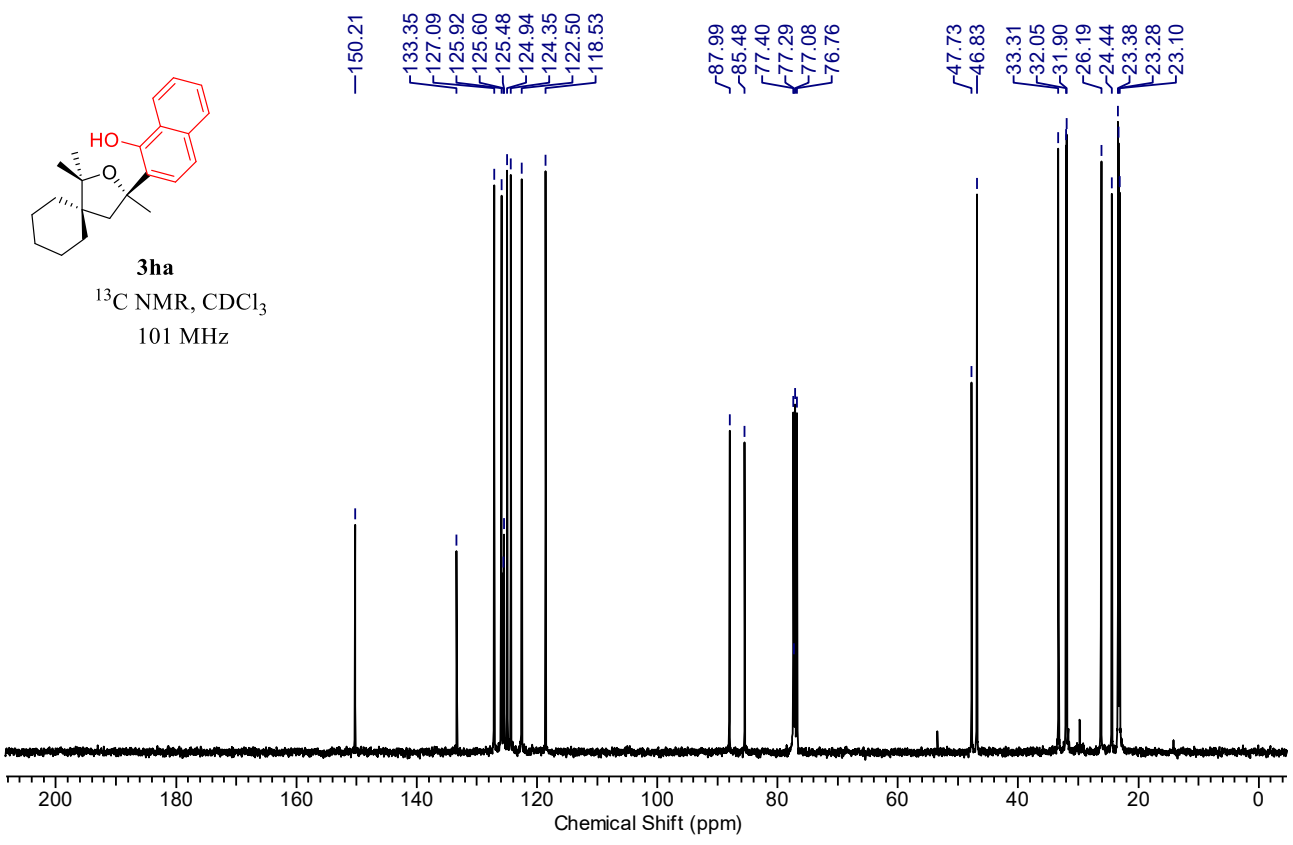
126 MHz



3ha

^{1}H NMR, $CDCl_3$

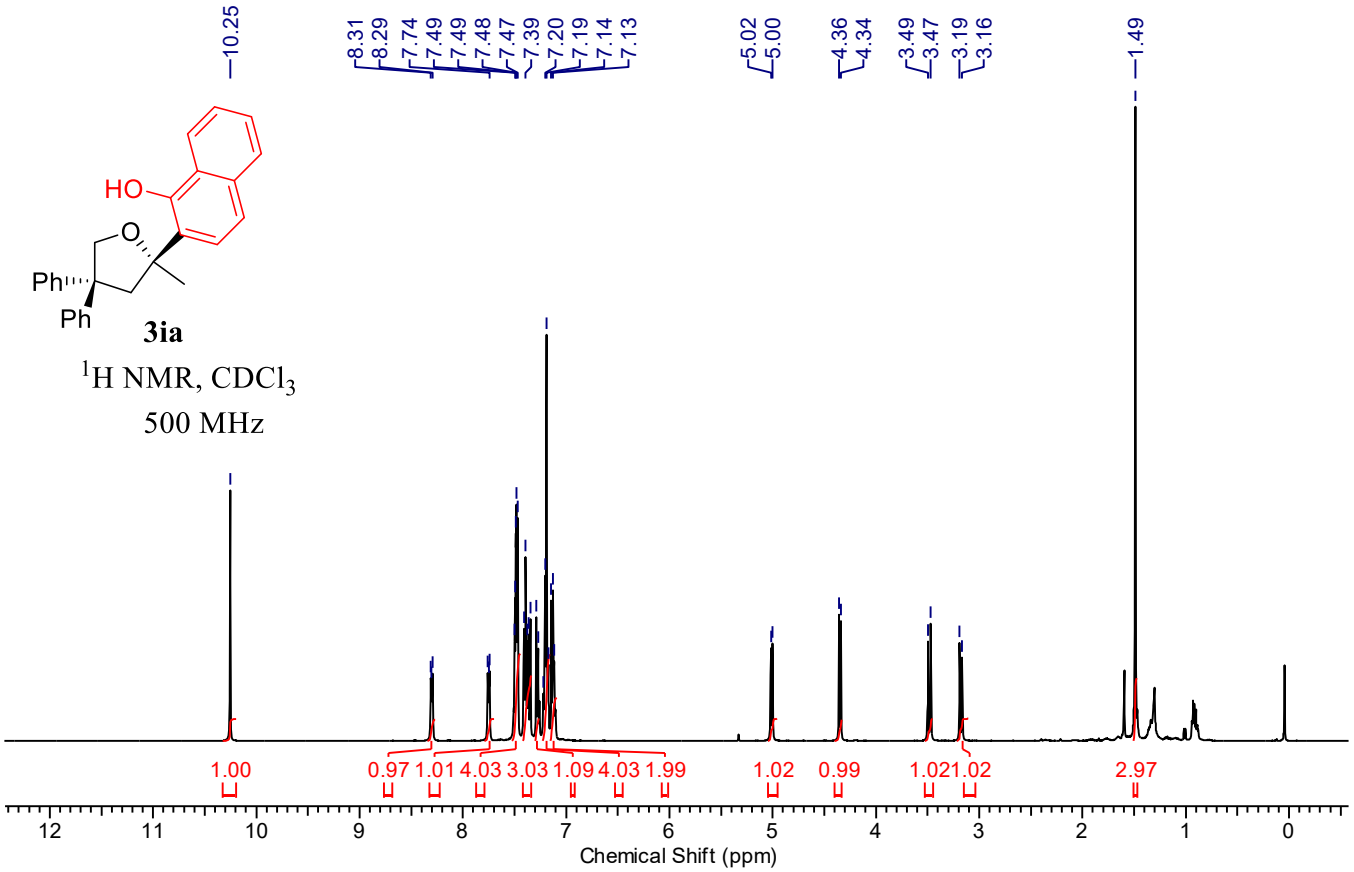
400 MHz

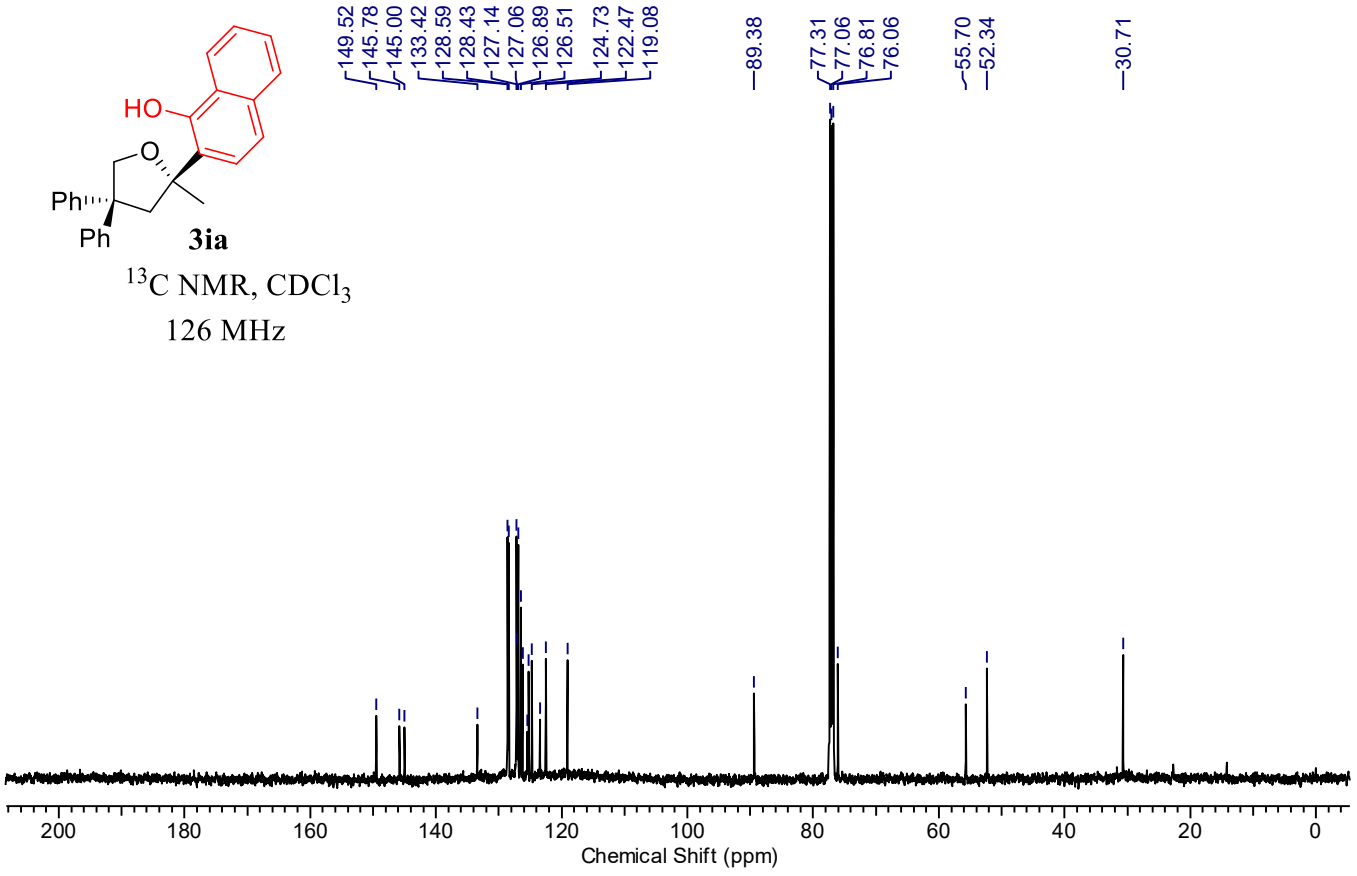


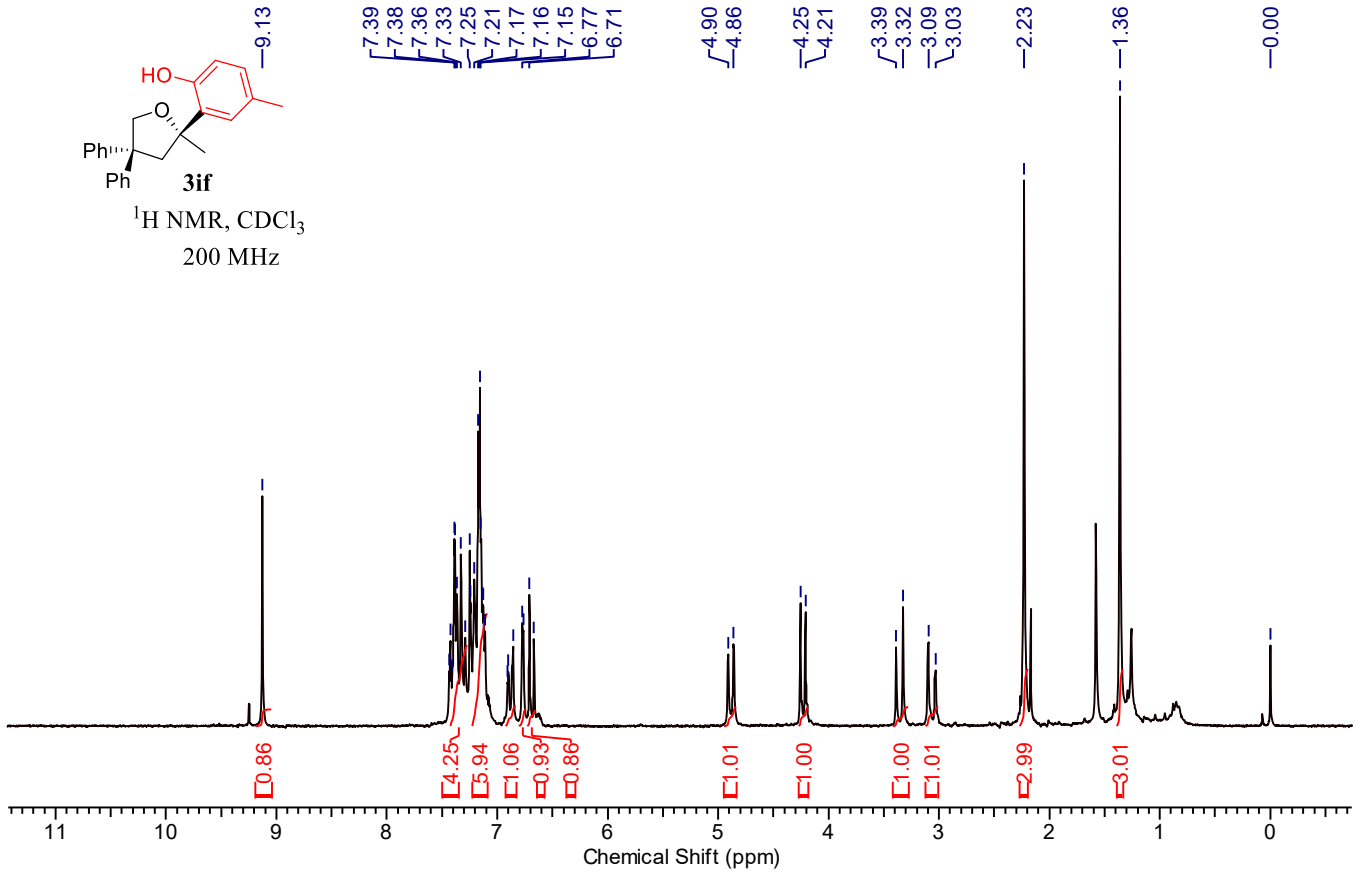
3ha

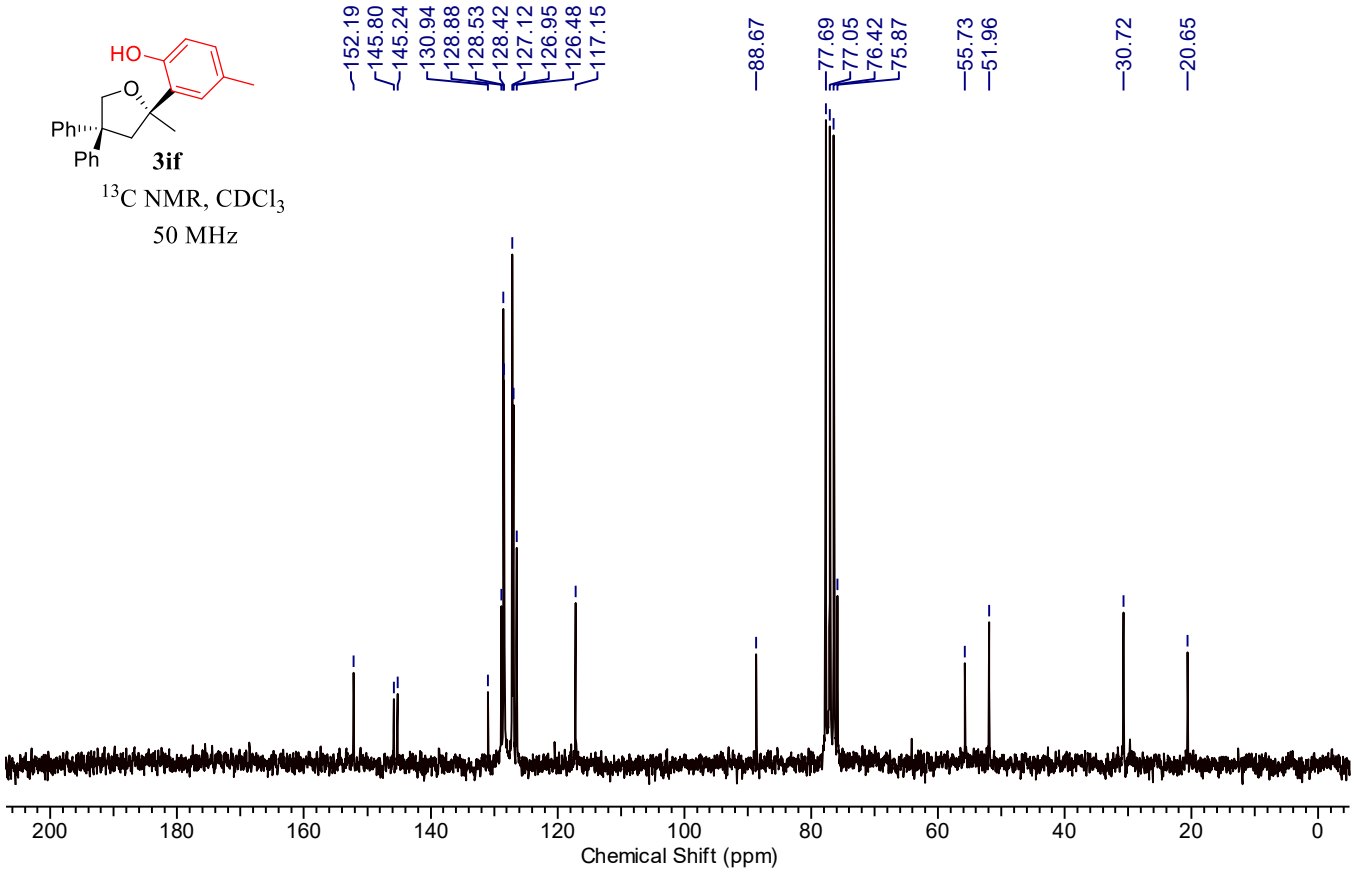
^{13}C NMR, $CDCl_3$

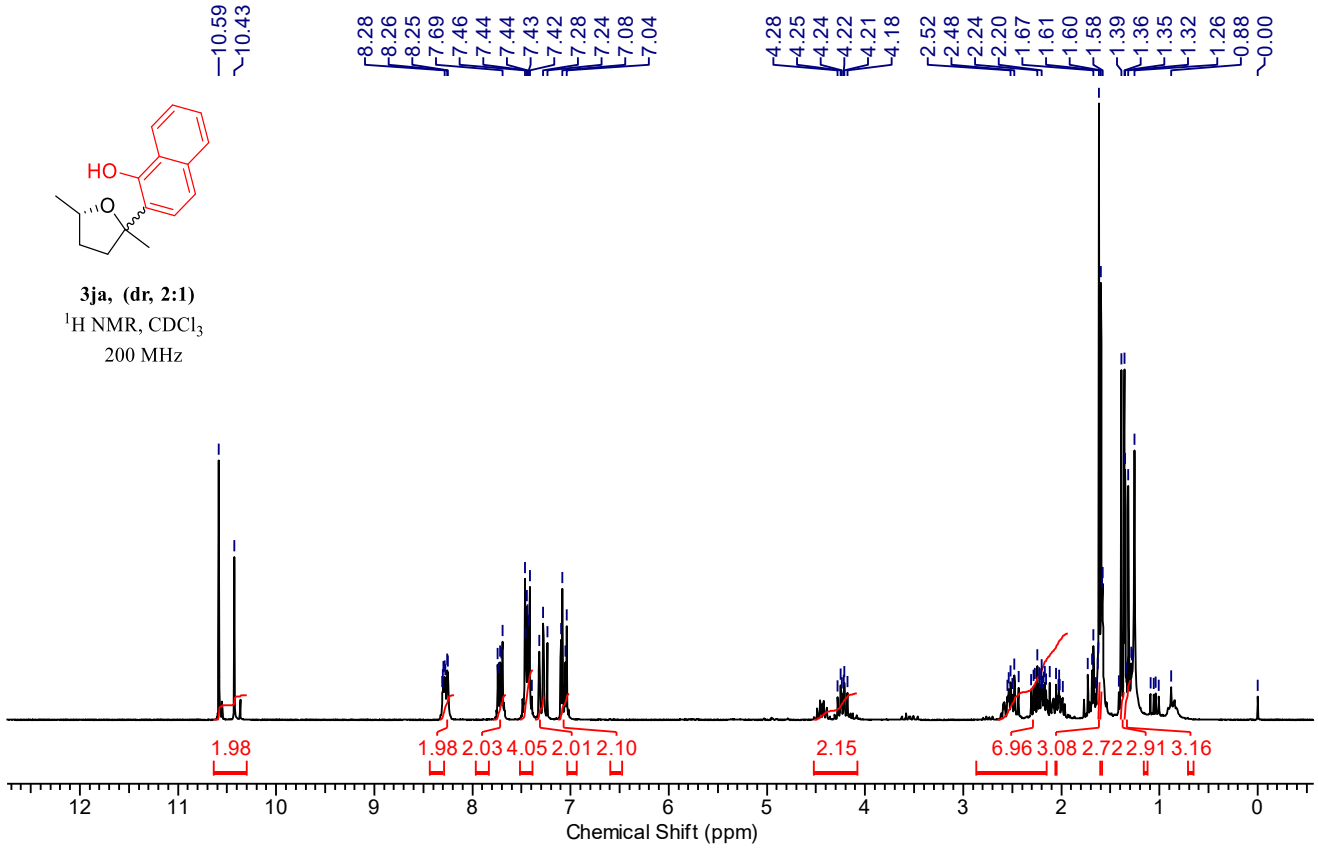
101 MHz


10.25
8.31
8.29
7.74
7.49
7.49
7.49
7.48
7.47
7.39
7.20
7.19
7.14
7.13
5.02
5.00
4.36
4.34
3.49
3.47
3.19
3.16
1.49
HO
O
Ph
Ph
3ia
1H NMR, CDCl3
500 MHz
1.00
0.97
1.01
4.03
3.03
1.09
4.03
1.99
1.02
0.99
1.02
1.02
2.97
Chemical Shift (ppm)

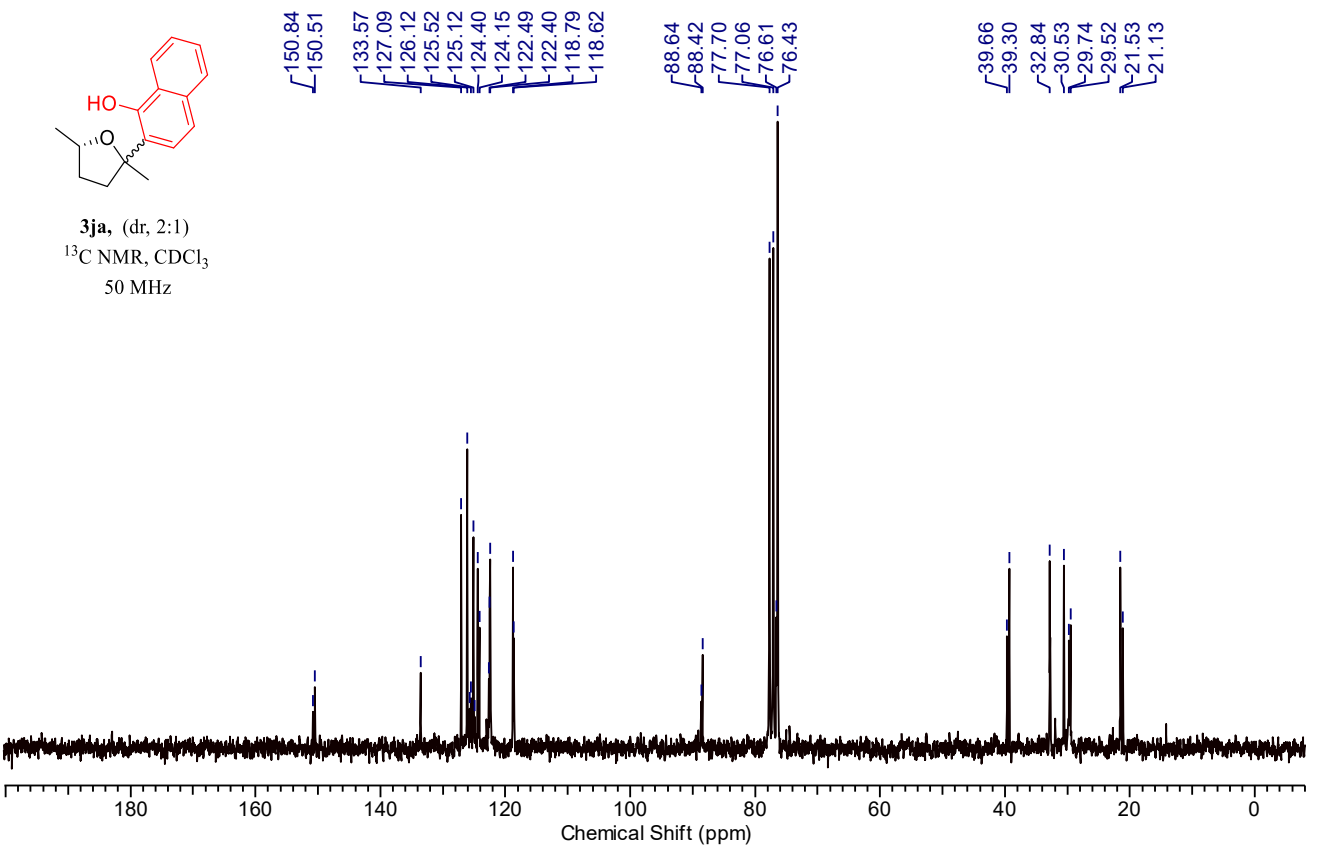

149.52
145.78
145.00
133.42
128.59
128.43
127.14
127.06
126.89
126.51
124.73
122.47
119.08
89.38
77.31
77.06
76.81
76.06
55.70
52.34
30.71
HO
O
Ph
Ph
3ia
13C NMR, CDCl3
126 MHz
Chemical Shift (ppm)


HO
O
Ph
Ph
3if
^{1}H NMR, CDCl$_3$
200 MHz
9.13
7.39
7.38
7.36
7.33
7.25
7.21
7.17
7.16
7.15
6.77
6.71
4.90
4.86
4.25
4.21
3.39
3.32
3.09
3.03
2.23
1.36
0.00
0.86
4.25
5.94
1.06
0.93
0.86
1.01
1.00
1.00
1.01
2.99
3.01
Chemical Shift (ppm)

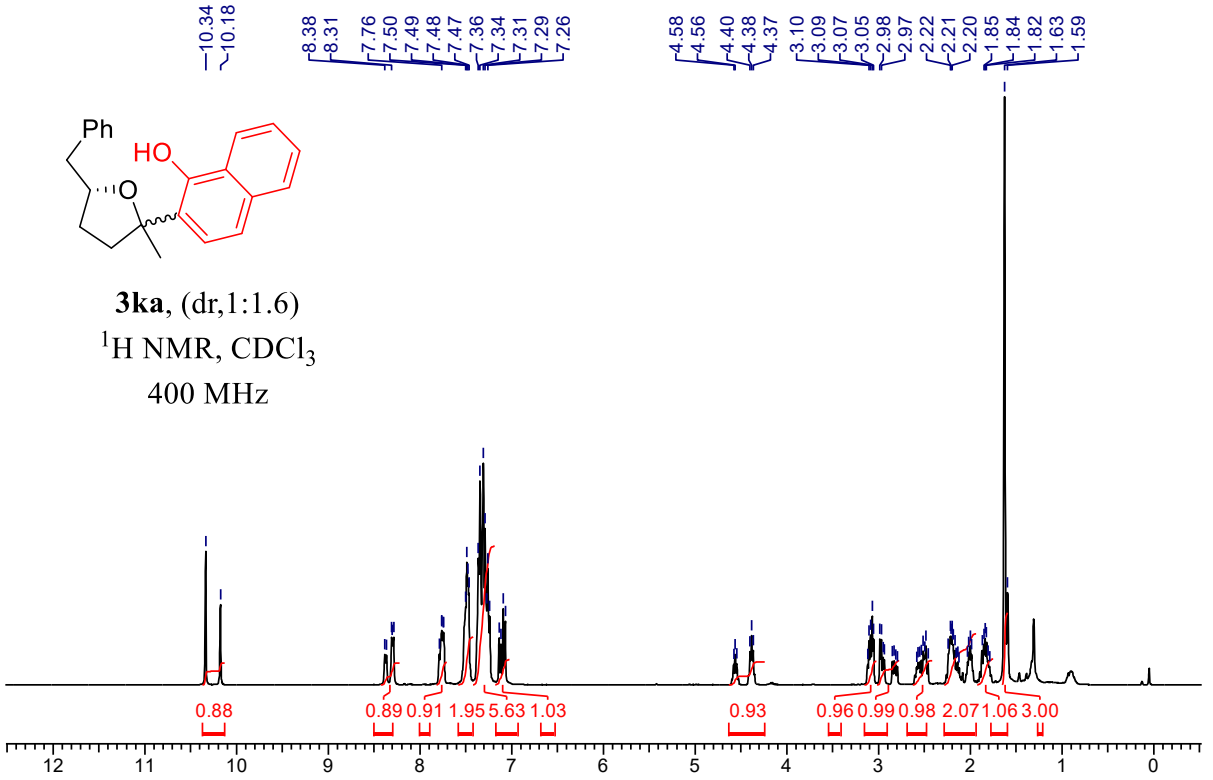

HO
O
Ph
Ph
3if
^{13}C NMR, CDCl$_3$
50 MHz
152.19
145.80
145.24
130.94
128.88
128.53
128.42
127.12
126.95
126.48
117.15
88.67
77.69
77.05
76.42
75.87
55.73
51.96
30.72
20.65
Chemical Shift (ppm)



3ja, (dr, 2:1)
^{1}H NMR, $CDCl_3$
200 MHz



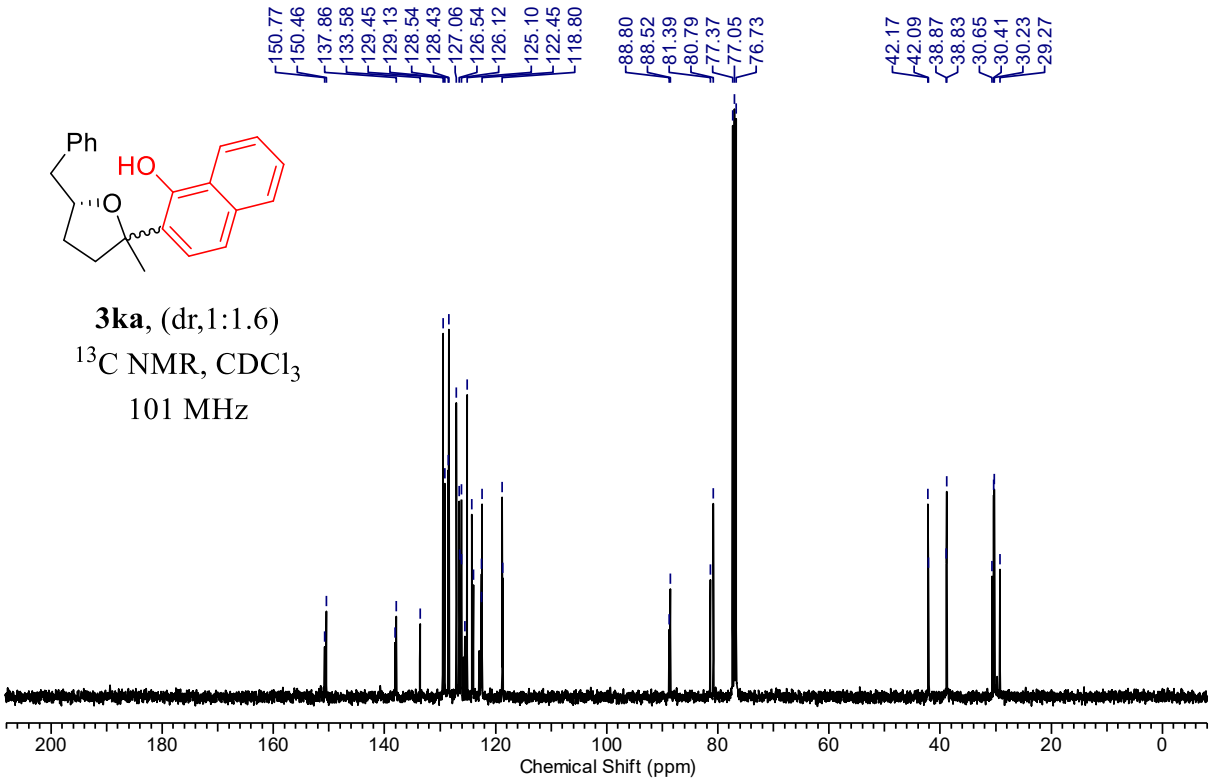
3ja, (dr, 2:1)
^{13}C NMR, $CDCl_3$
50 MHz



3ka, (dr,1:1.6)

^{1}H NMR, $CDCl_3$

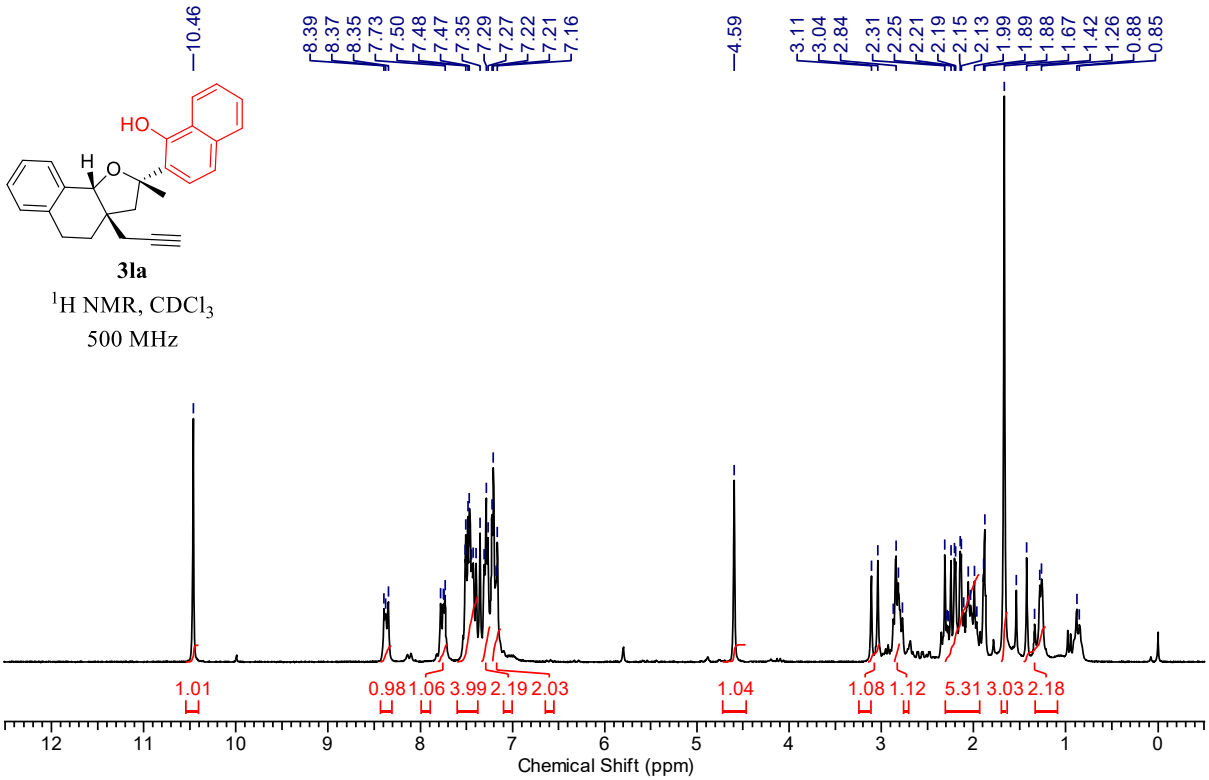
400 MHz



3ka, (dr,1:1.6)

^{13}C NMR, $CDCl_3$

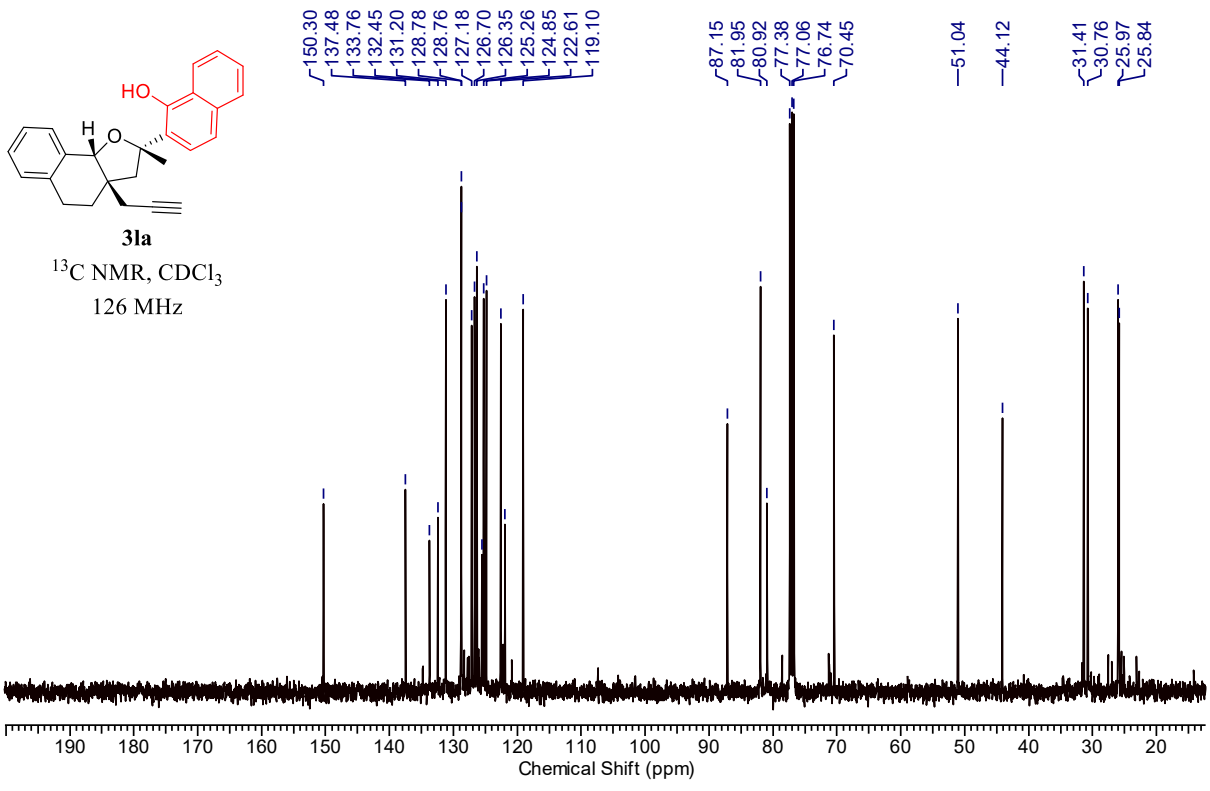
101 MHz



3la

^{1}H NMR, $CDCl_3$

500 MHz

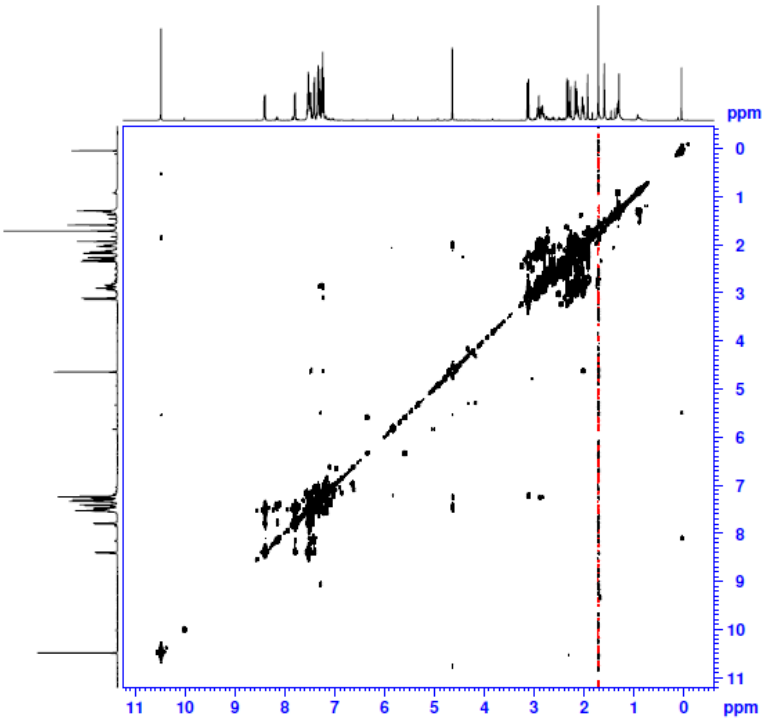


3la

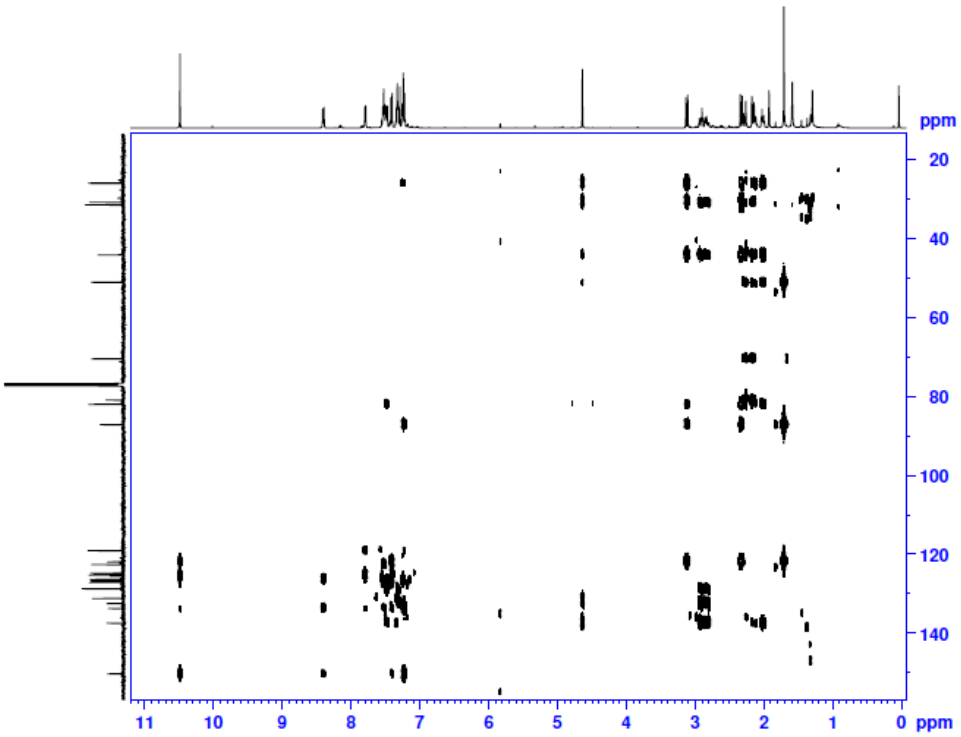
^{13}C NMR, $CDCl_3$

126 MHz

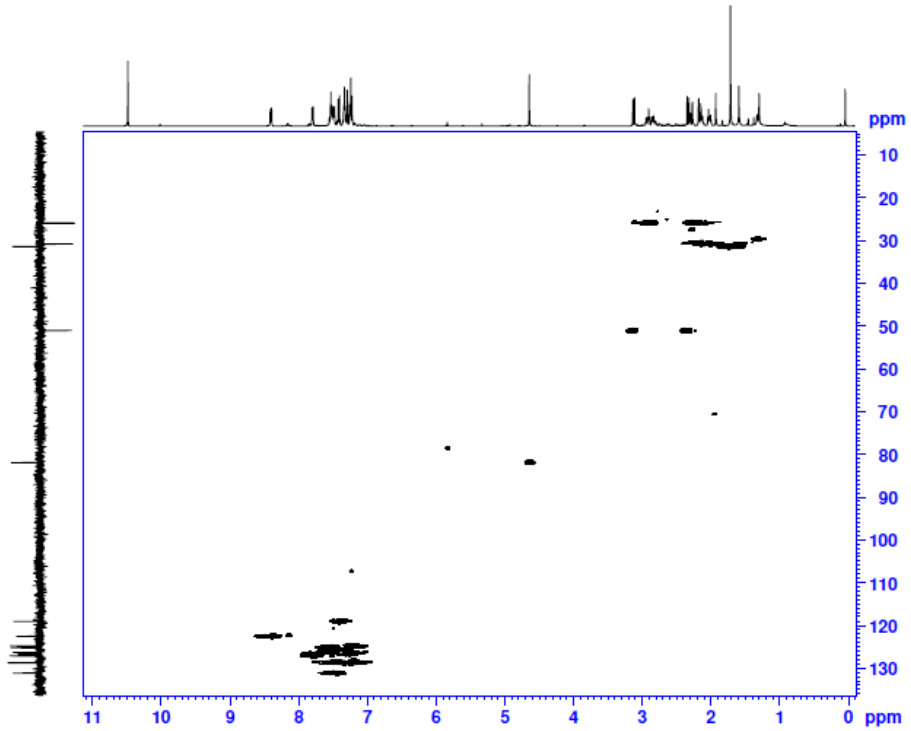
COSY (**3la**):



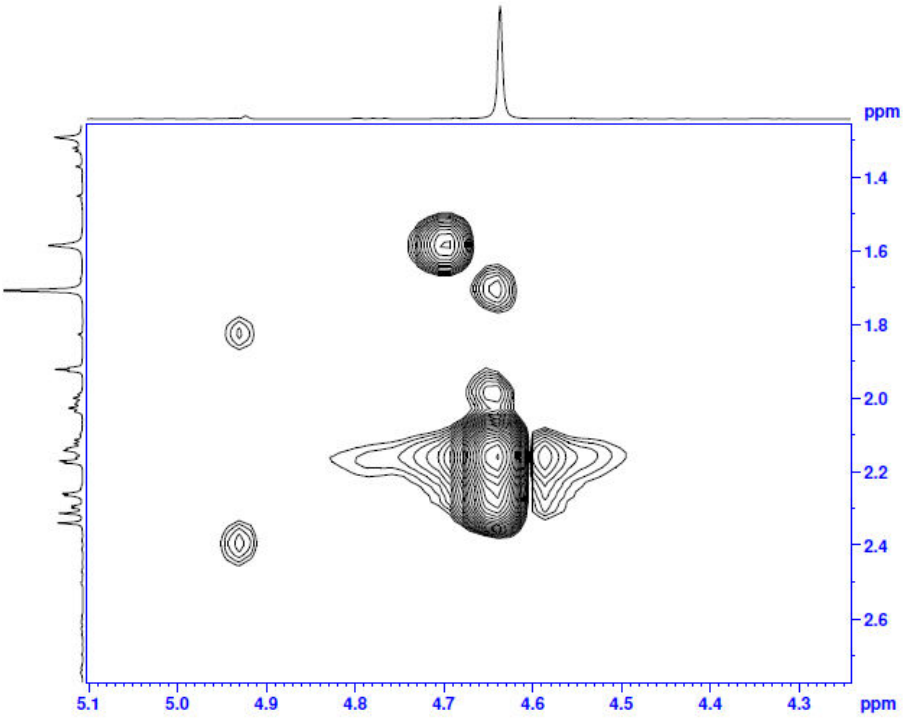
HMBC (**3la**):



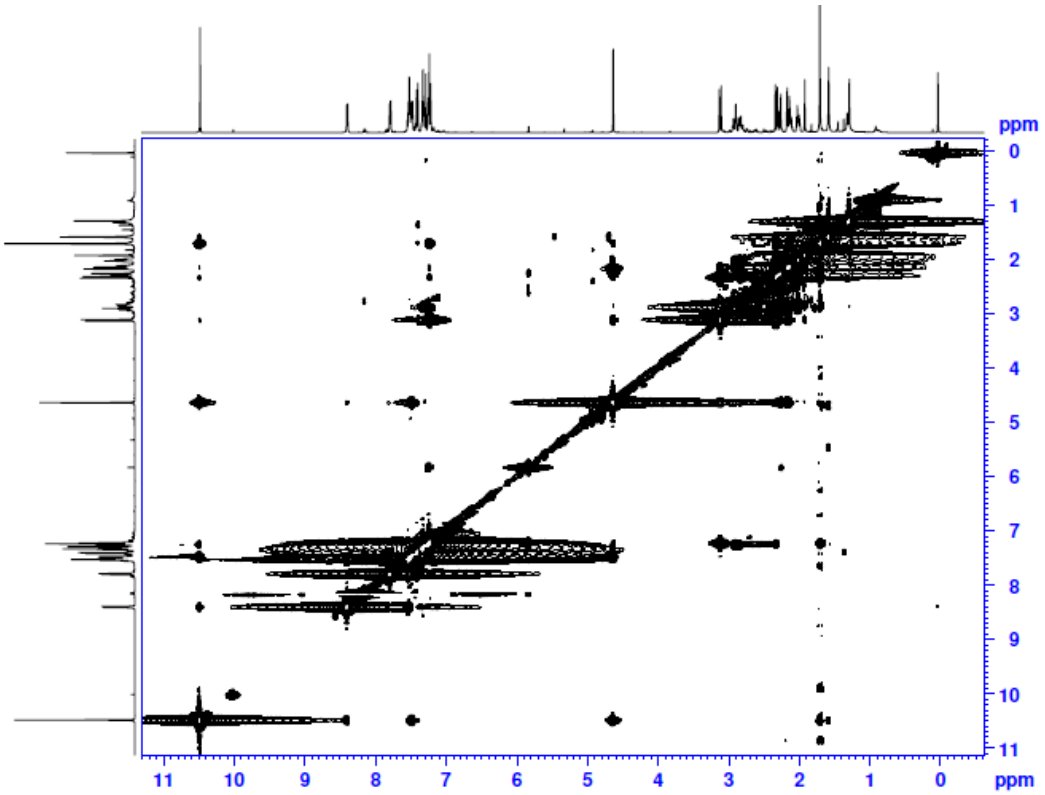
HSQC **(3la):**

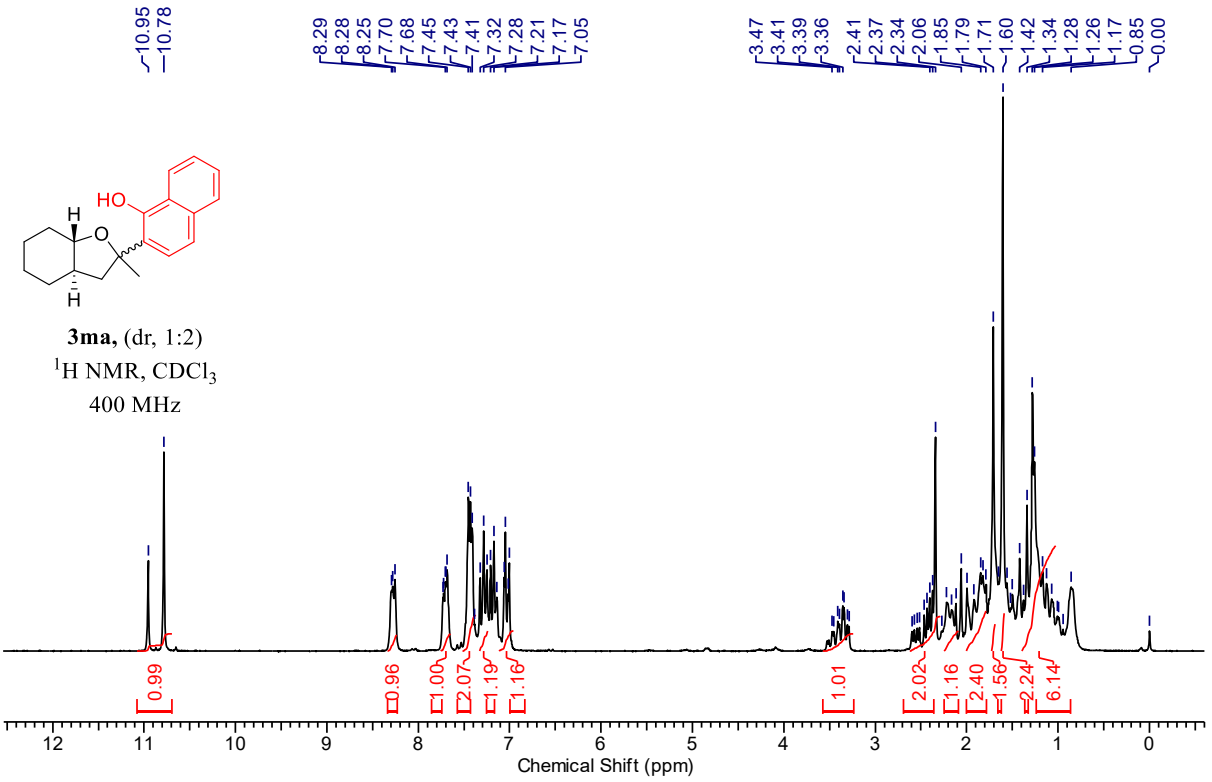


Expanded NOESY **(3la):**

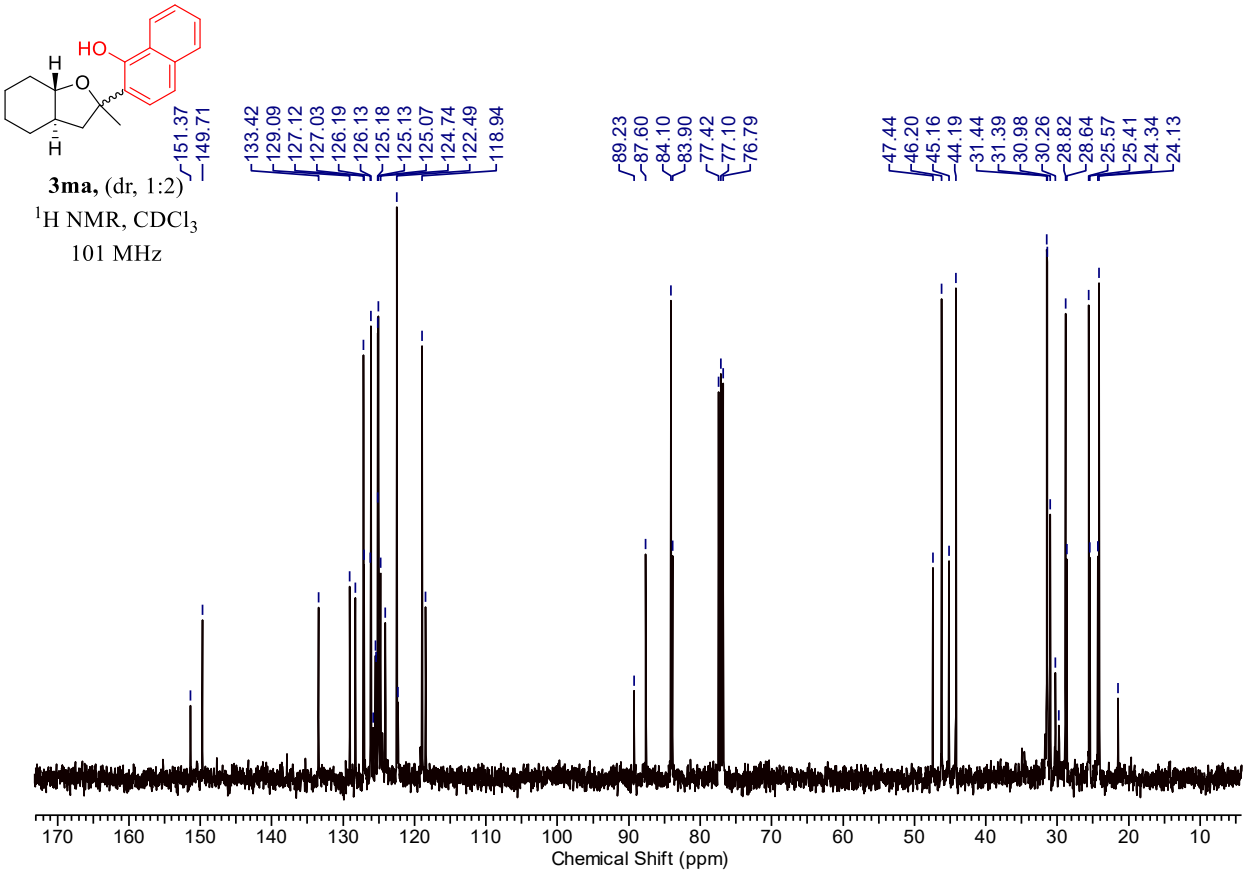


NOESY (**3la**):

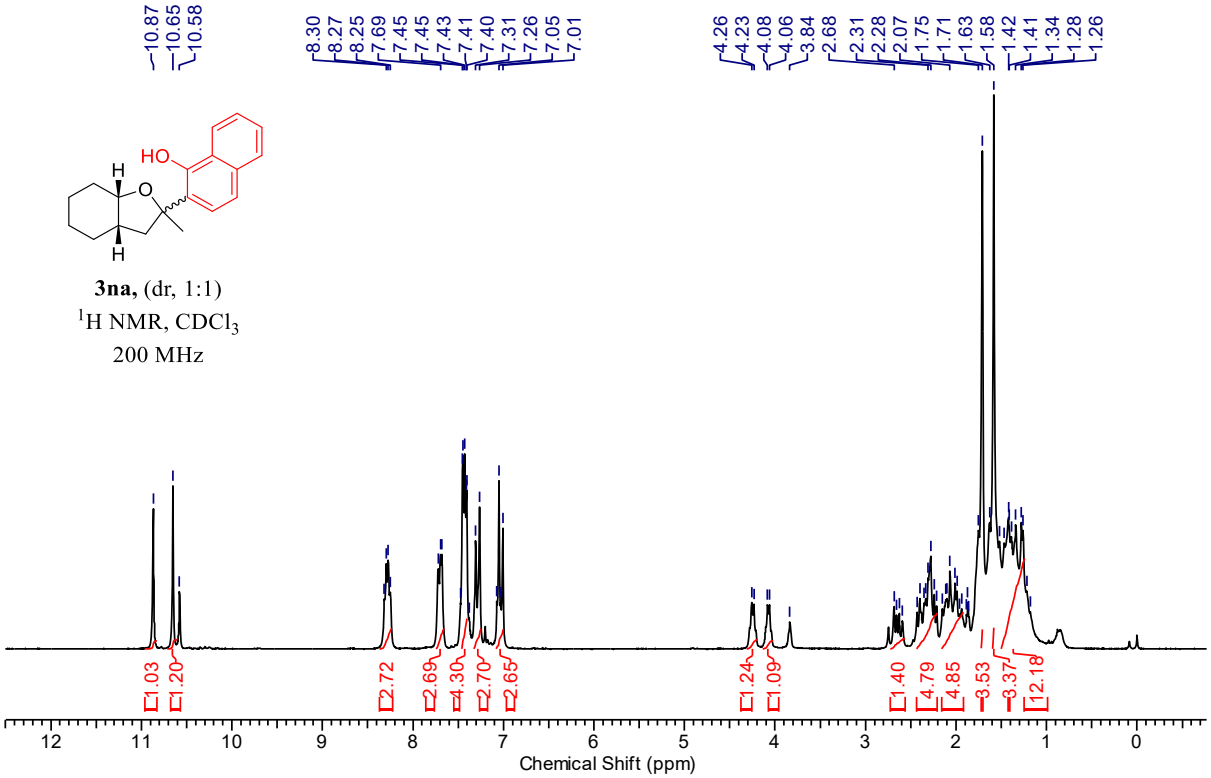




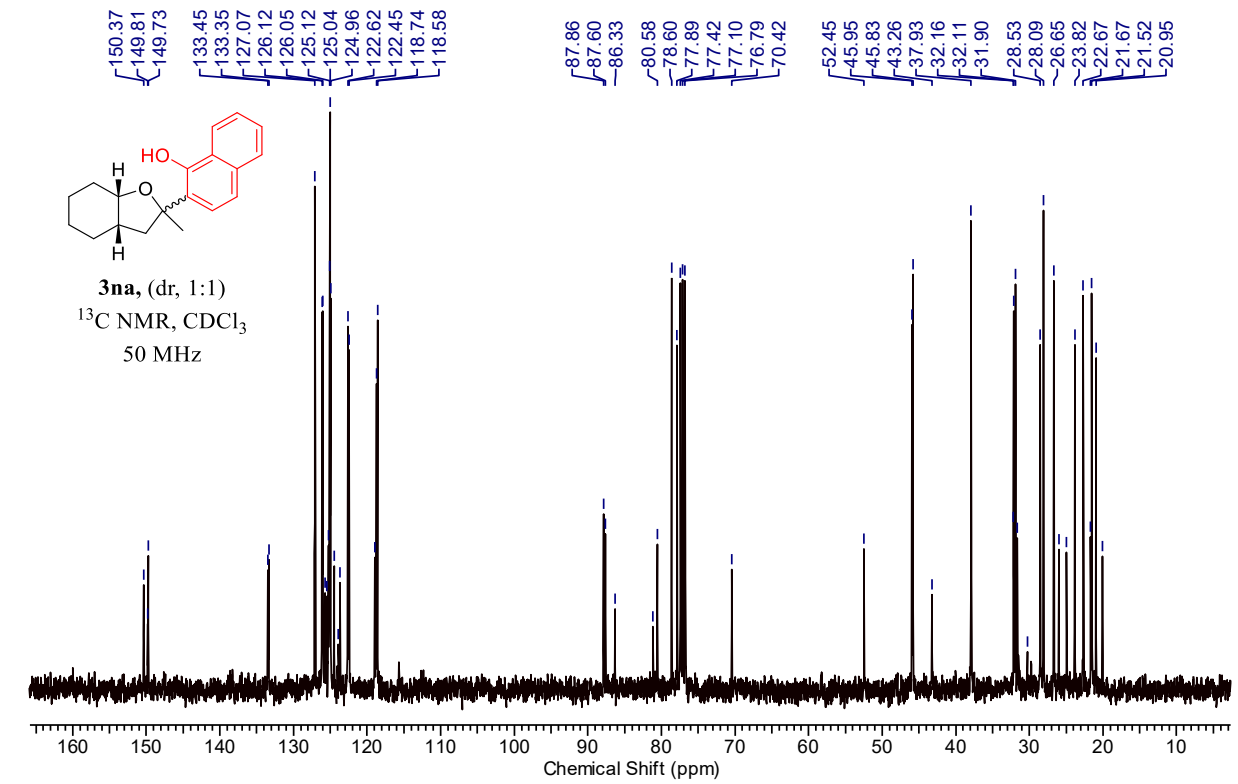
3ma, (dr, 1:2)
^{1}H NMR, $CDCl_3$
400 MHz



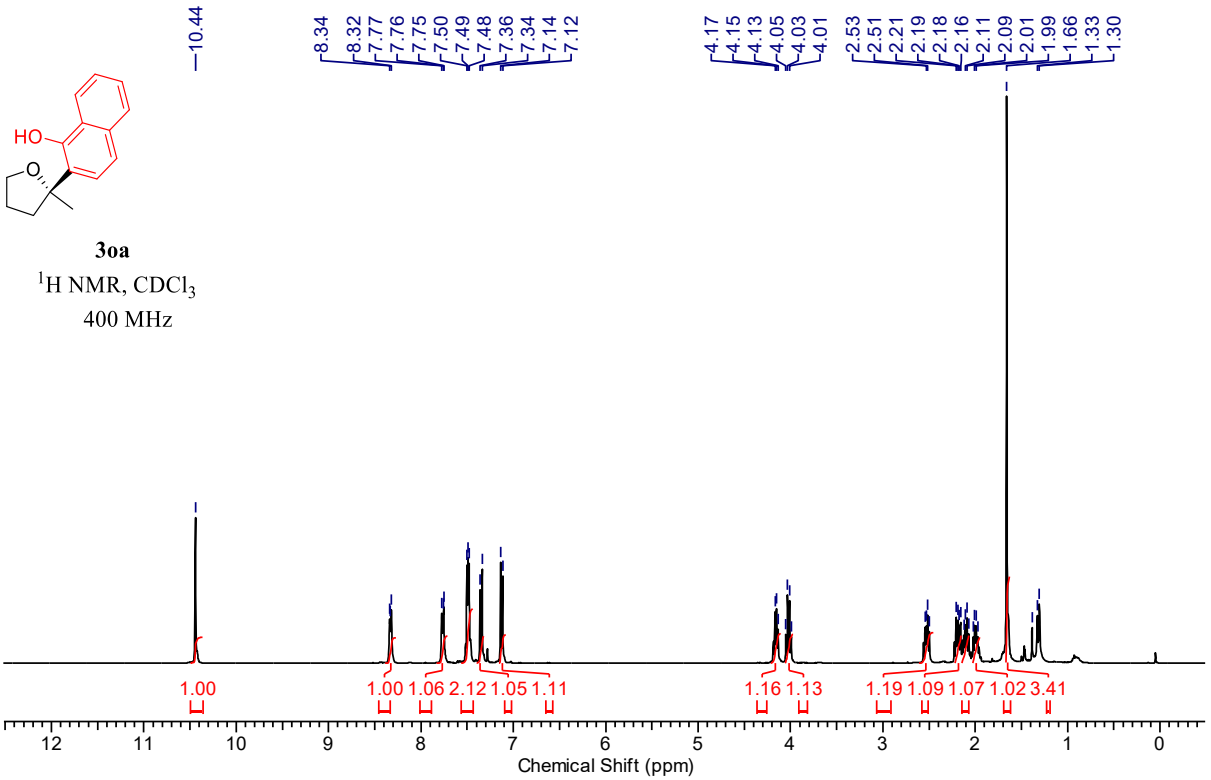
3ma, (dr, 1:2)
^{1}H NMR, $CDCl_3$
101 MHz



3na, (dr, 1:1)
^{1}H NMR, $CDCl_3$
200 MHz



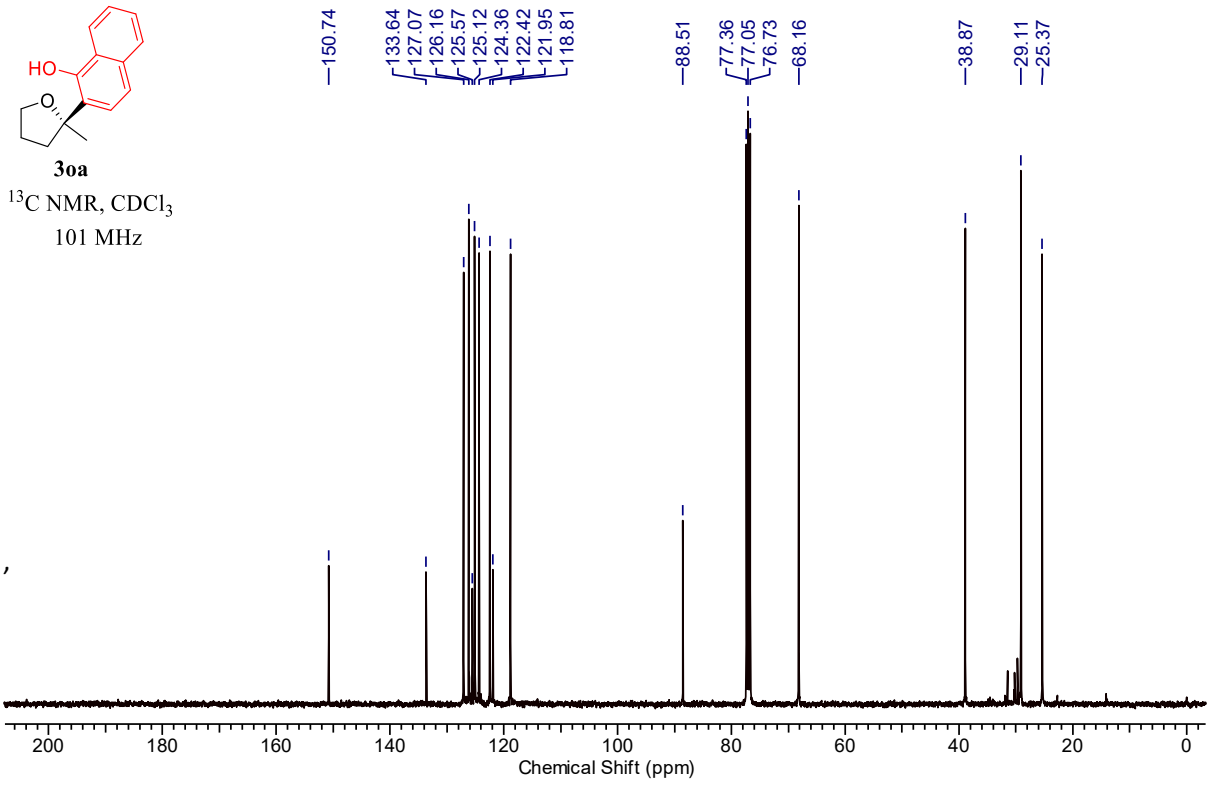
3na, (dr, 1:1)
^{13}C NMR, $CDCl_3$
50 MHz



3oa

^{1}H NMR, $CDCl_3$

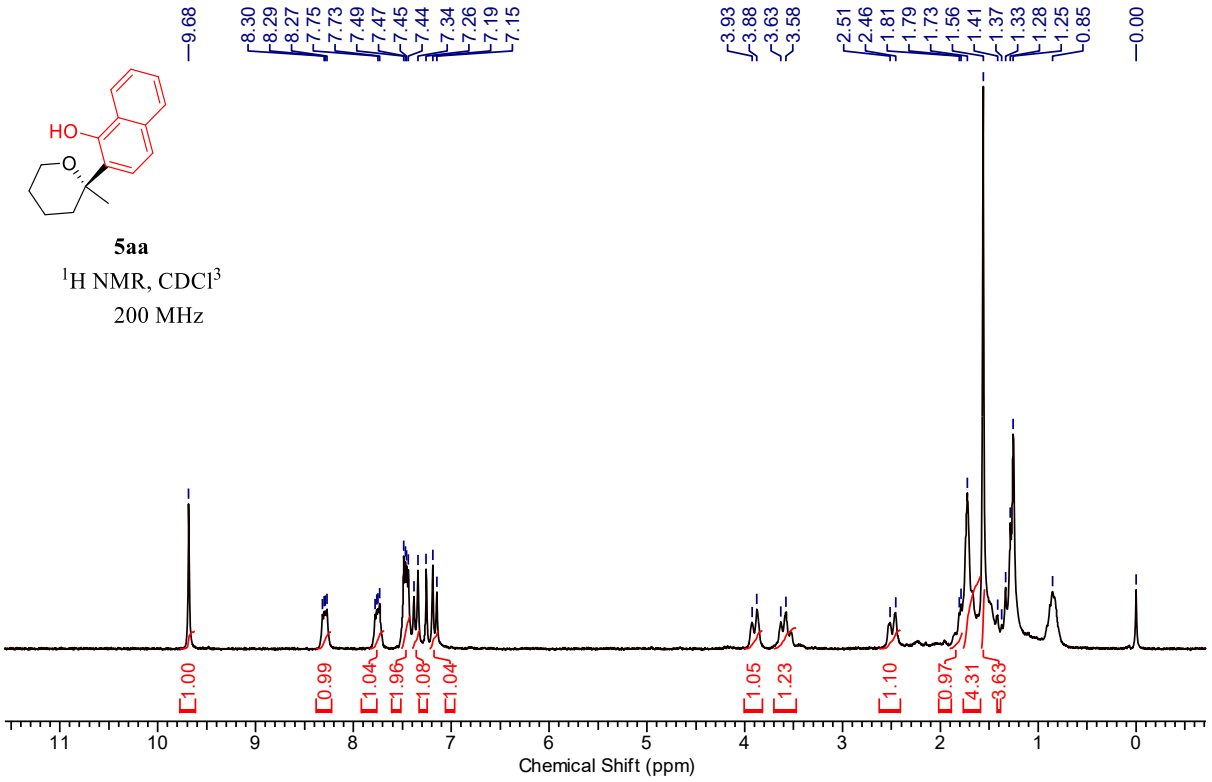
400 MHz



3oa

^{13}C NMR, $CDCl_3$

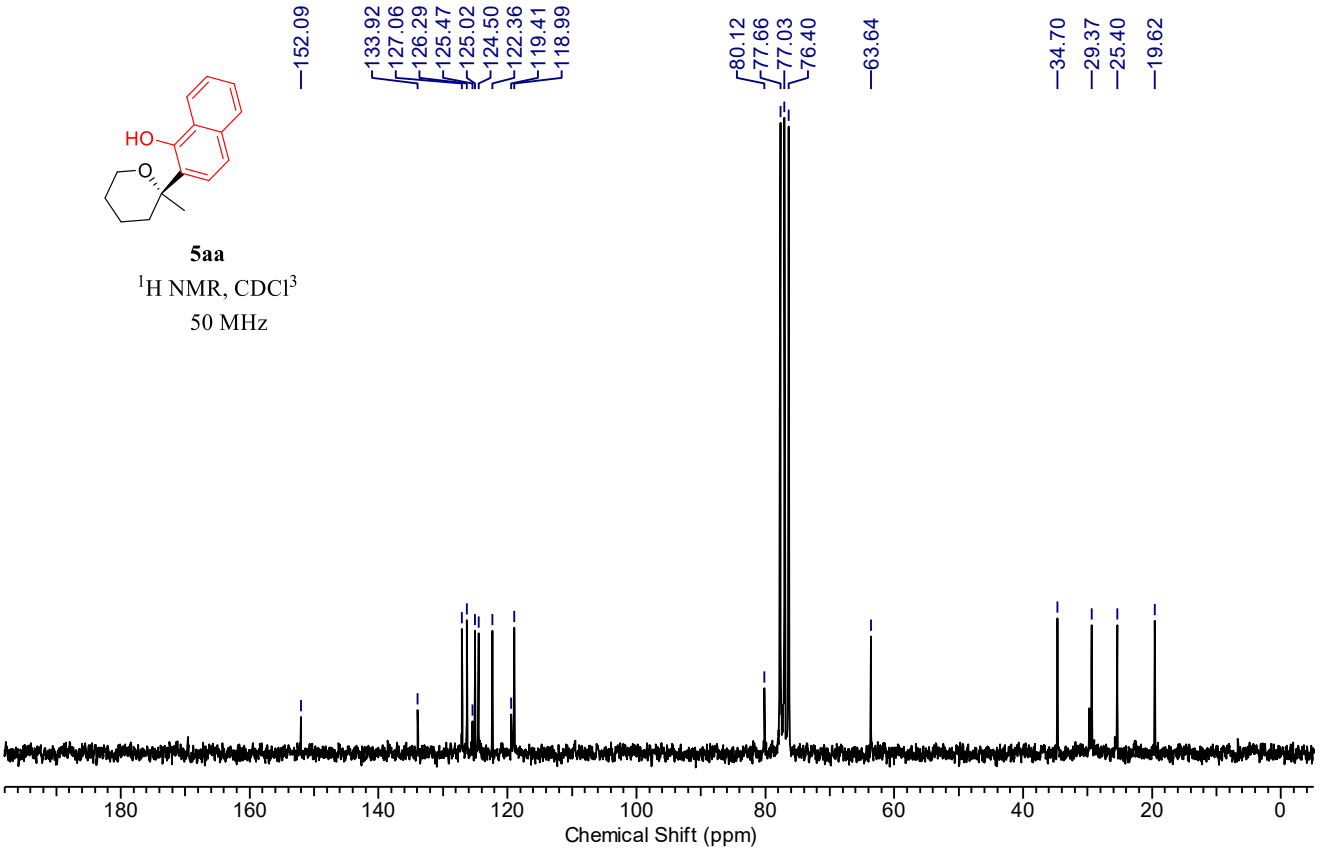
101 MHz



5aa

^{1}H NMR, CDCl^{3}

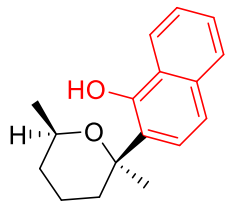
200 MHz



5aa

^{1}H NMR, CDCl^{3}

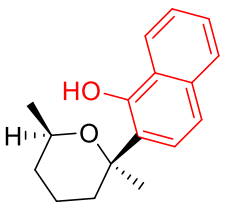
50 MHz



5ba

^{1}H NMR, $CDCl_3$

400MHz

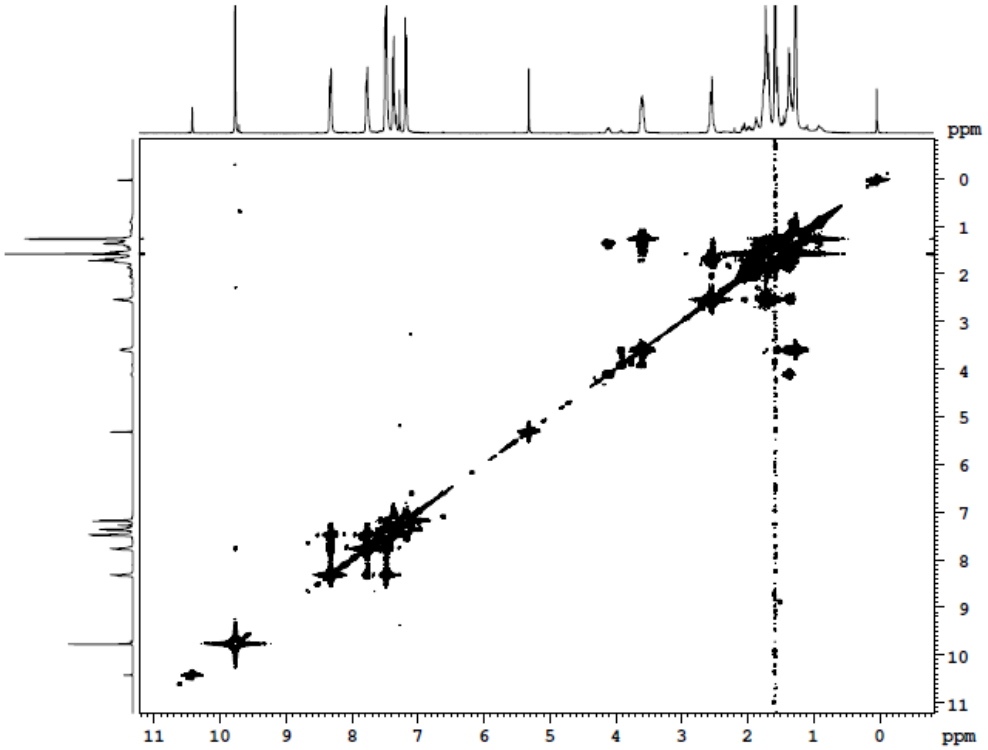


5ba

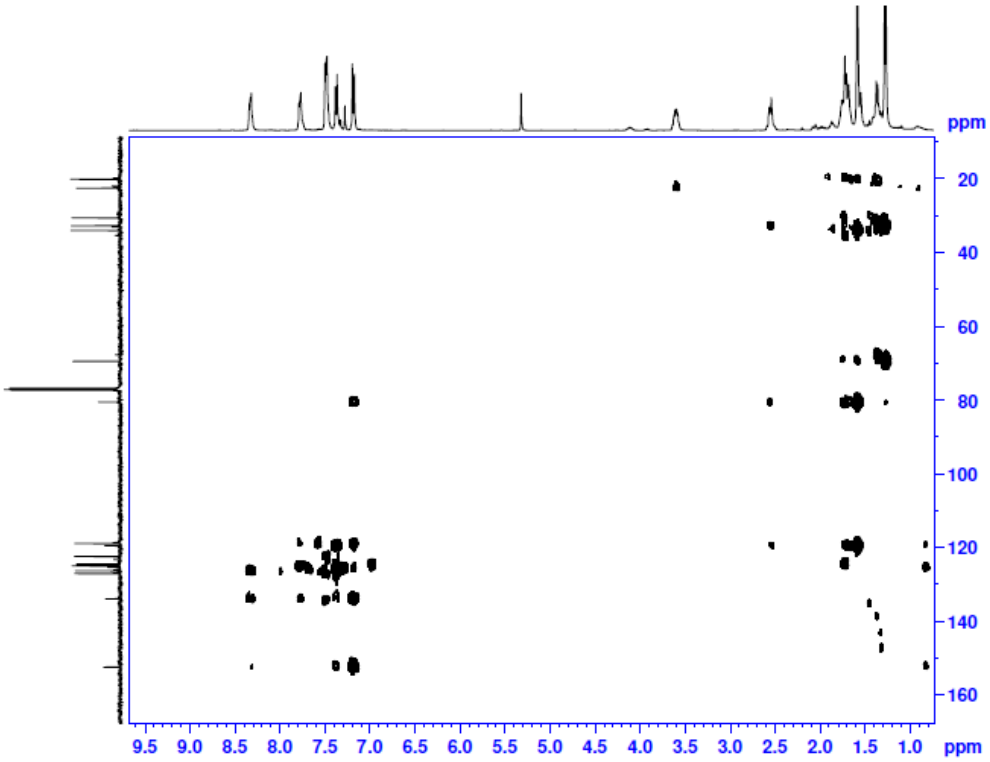
^{13}C NMR, $CDCl_3$

101MHz

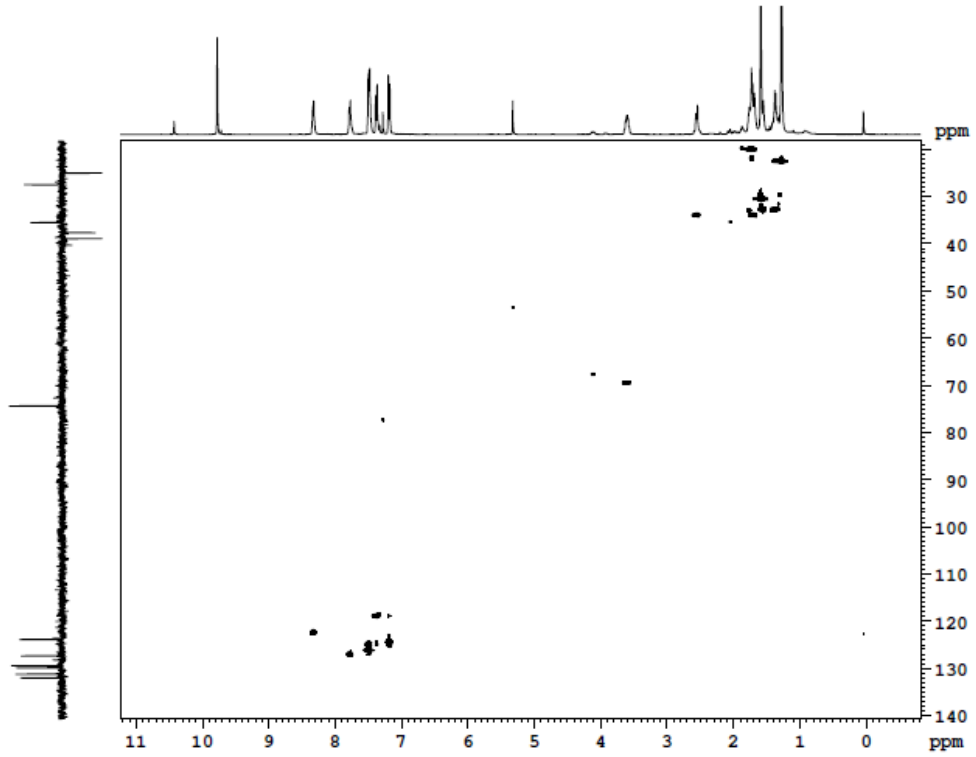
COSY (**5ba**):



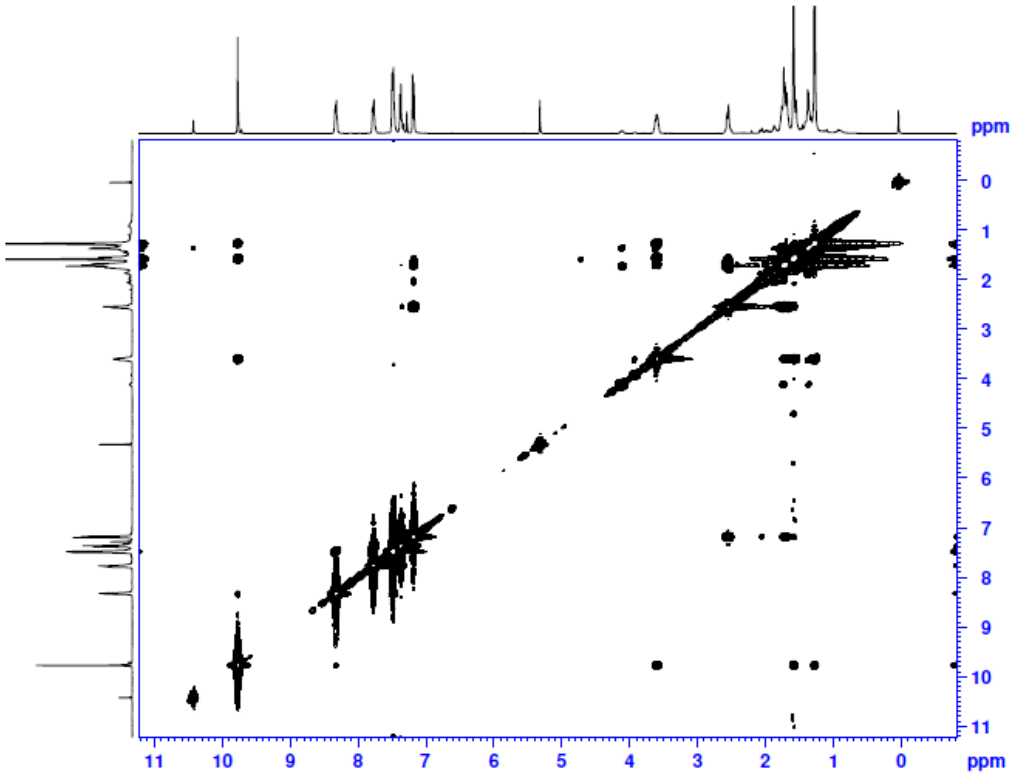
HMBC (**5ba**):



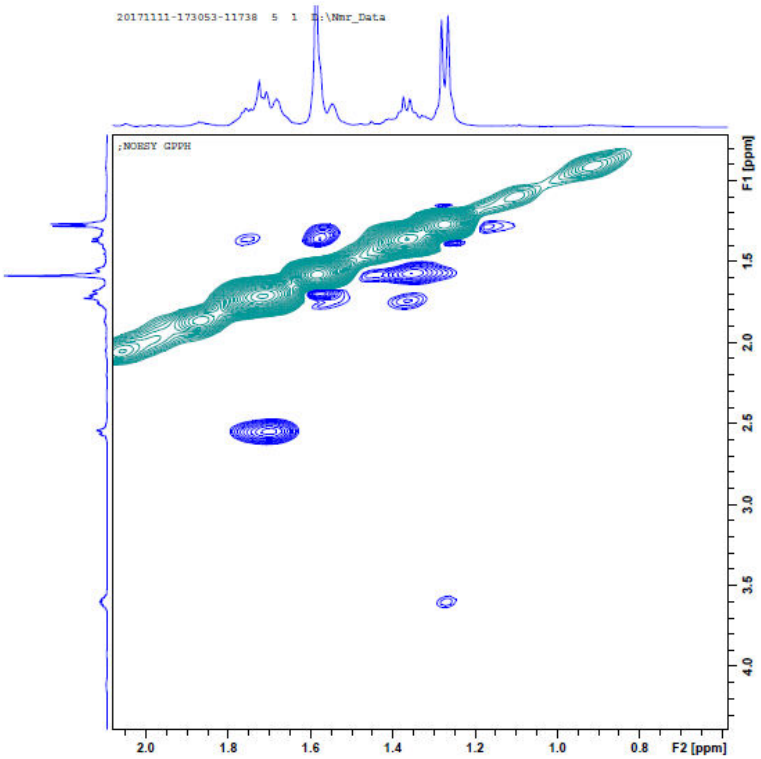
HSQC **(5ba):**

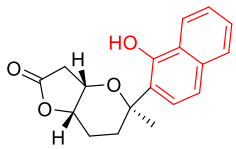


NOESY **(5ba):**



Expanded NOESY **(5ba):**

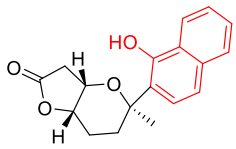




5ca

^{1}H NMR, $CDCl_3$

500 MHz

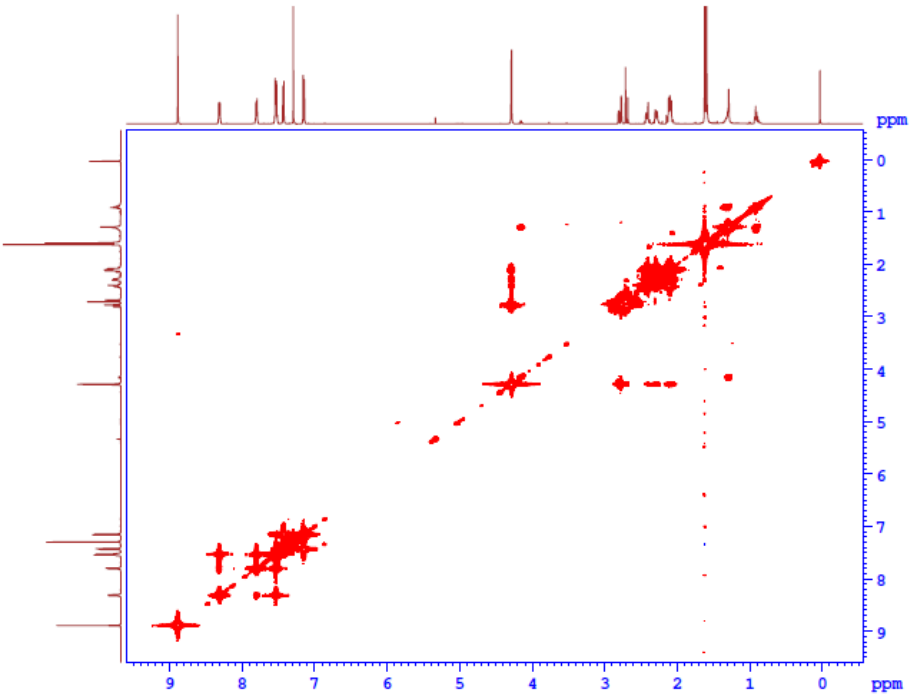


5ca

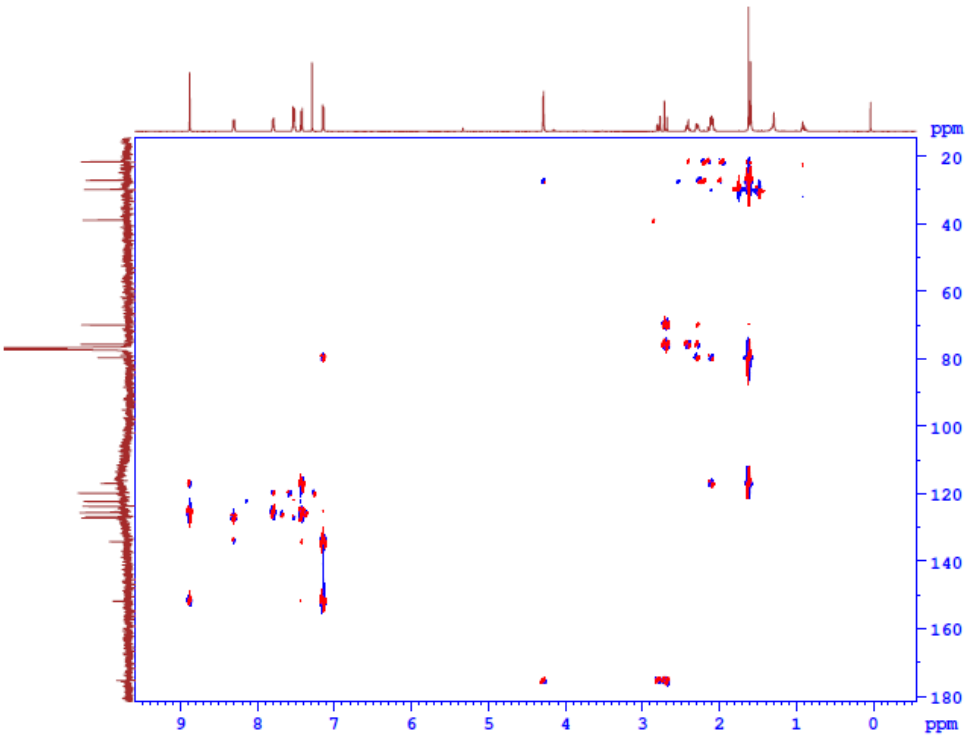
^{13}C NMR, $CDCl_3$

126 MHz

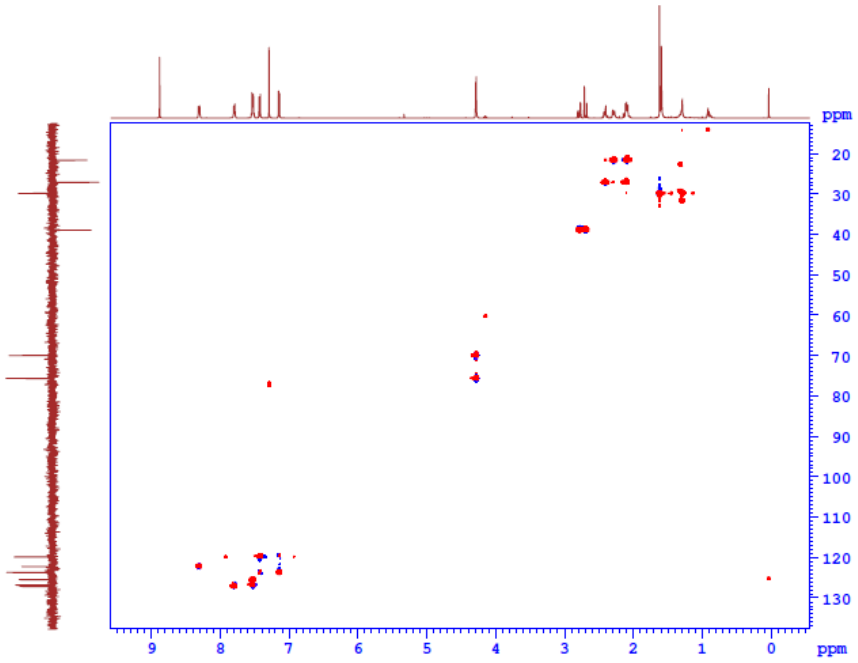
COSY (**5ca**):



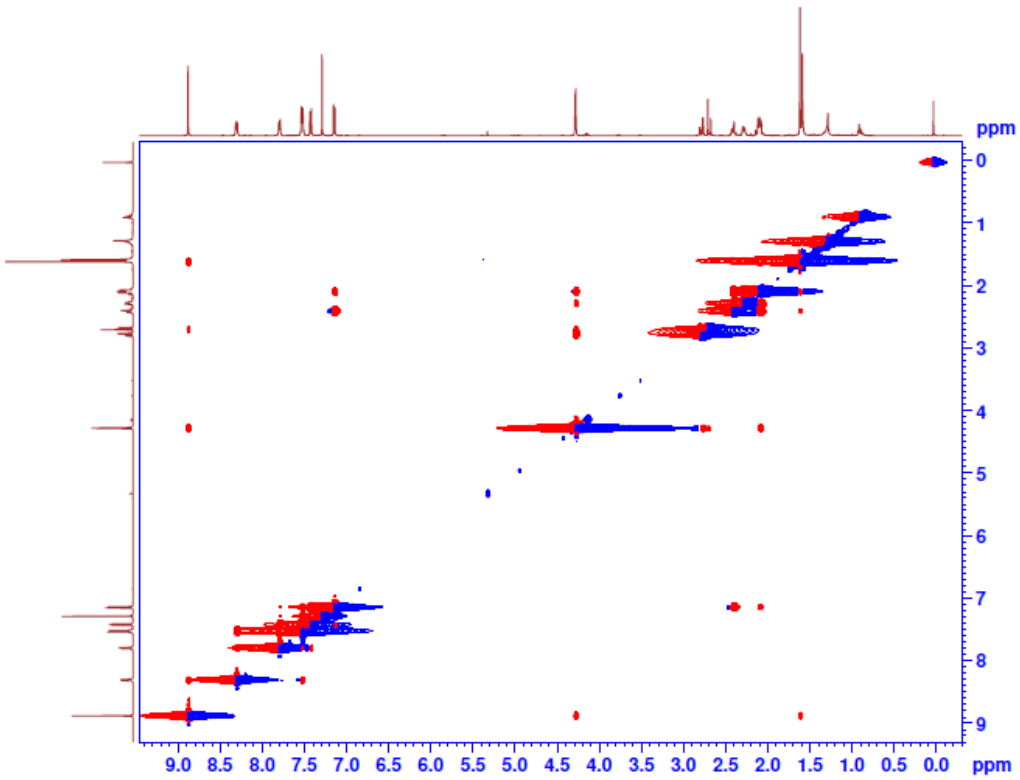
HMBC (**5ca**):



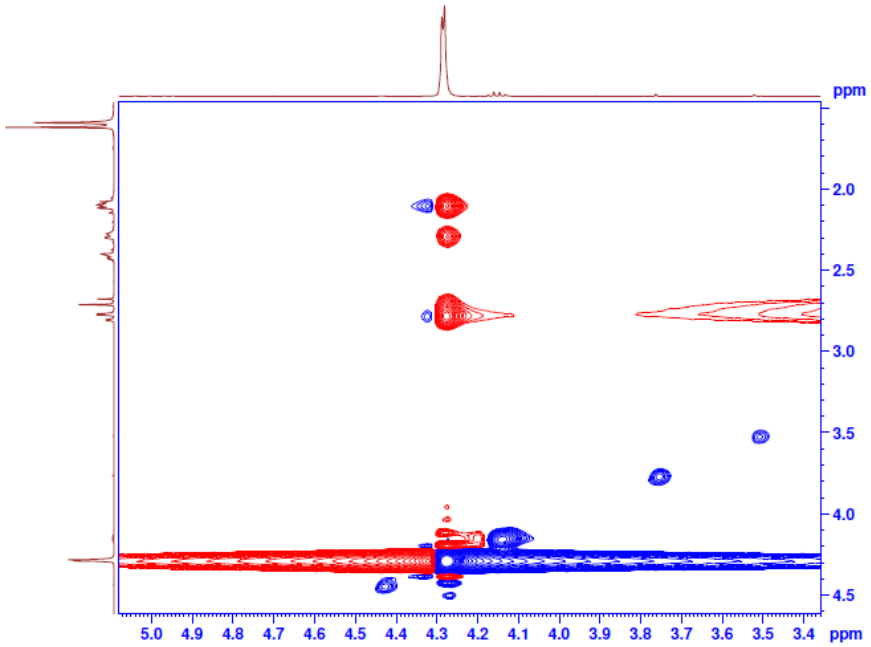
HSQC **(5ca):**

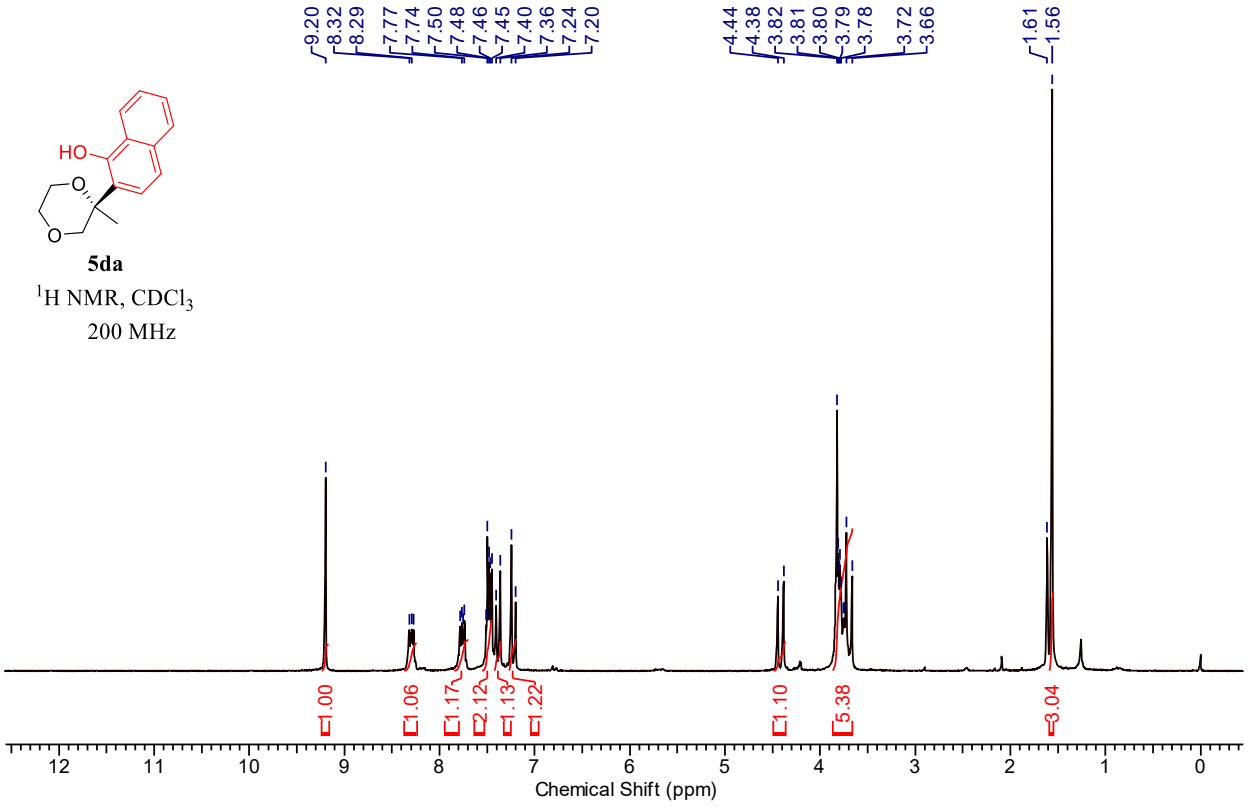


NOESY **(5ca):**



NOESY **(5ca):**

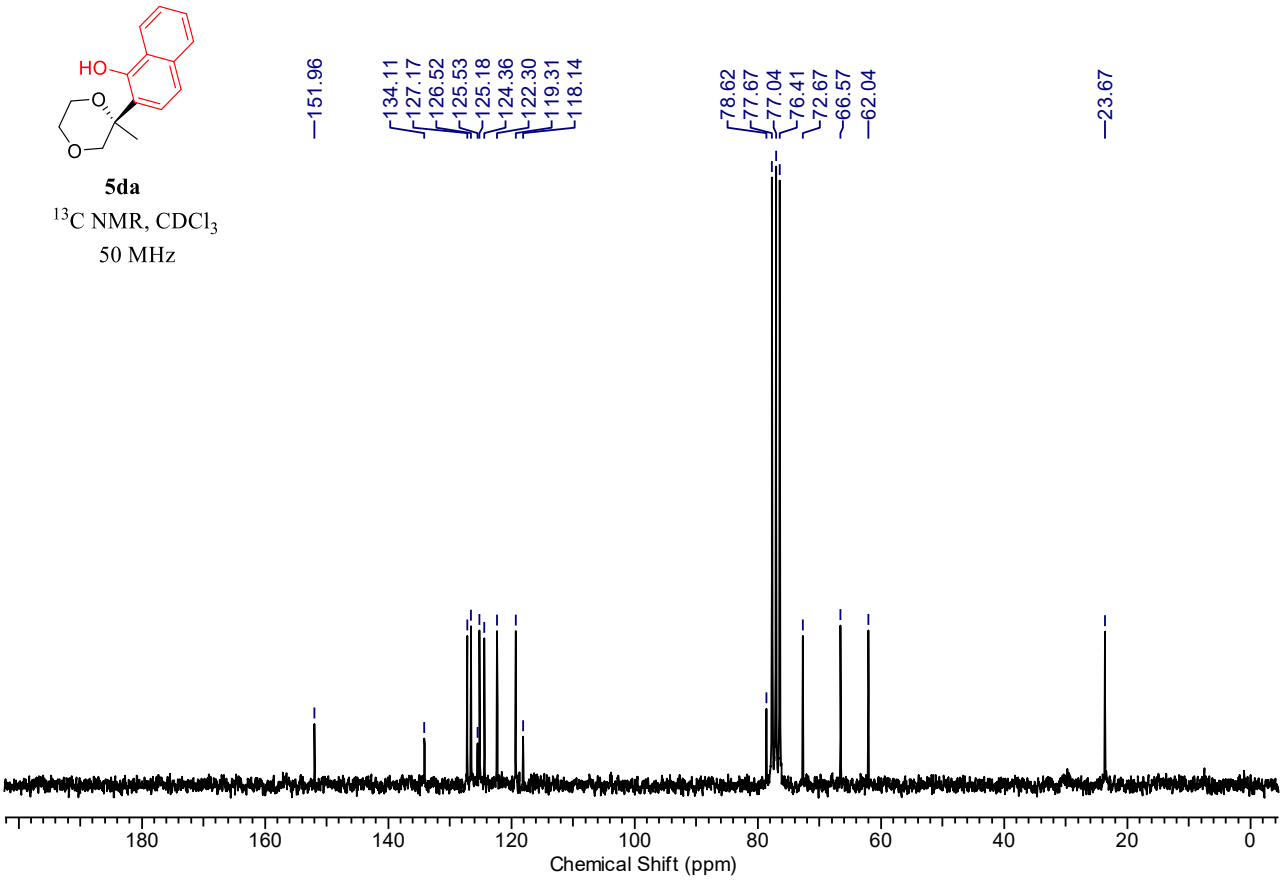

ppm
2.0
2.5
3.0
3.5
4.0
4.5
5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 ppm



5da

^{1}H NMR, $CDCl_3$

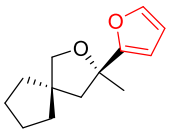
200 MHz



5da

^{13}C NMR, $CDCl_3$

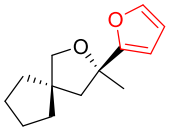
50 MHz



7aa

^{1}H NMR, $CDCl_3$

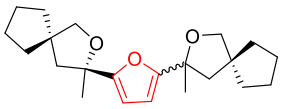
200 MHz



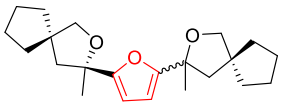
7aa

^{13}C NMR, $CDCl_3$

50 MHz



7aa[1], (dr, 1:3)
^{1}H NMR, $CDCl_3$
200 MHz



7aa[1], (dr, 1:3)
^{13}C NMR, $CDCl_3$
50 MHz

HPLC Analysis Report (7aa[1])

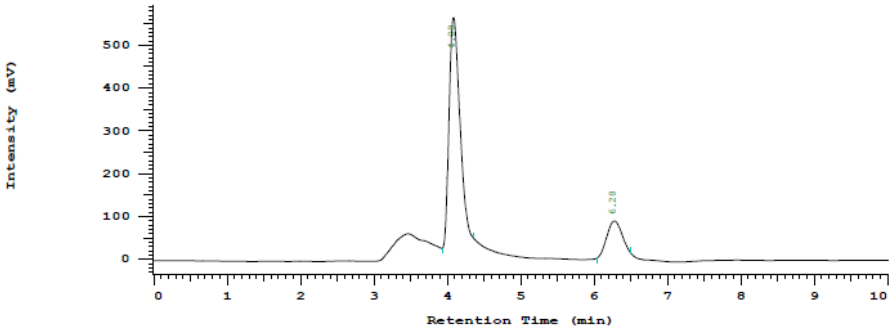
D-7000 HPLC System Manager Report

Analyzed: 11/06/17 04:35 PM
Reported: 11/06/17 05:00 PM
Processed: 11/06/17 04:59 PM

Data Path: C:\WIN32APP\HSM\HPLC\DATA\9916\
Processing Method: cal

System(acquisition): Sys 1
Series:9916
Application: HPLC
Volume: 10.0 ul
Sample Name: AN-03
Injection from this vial: 1 of 1
Sample Description: IPA:PE(01:99)

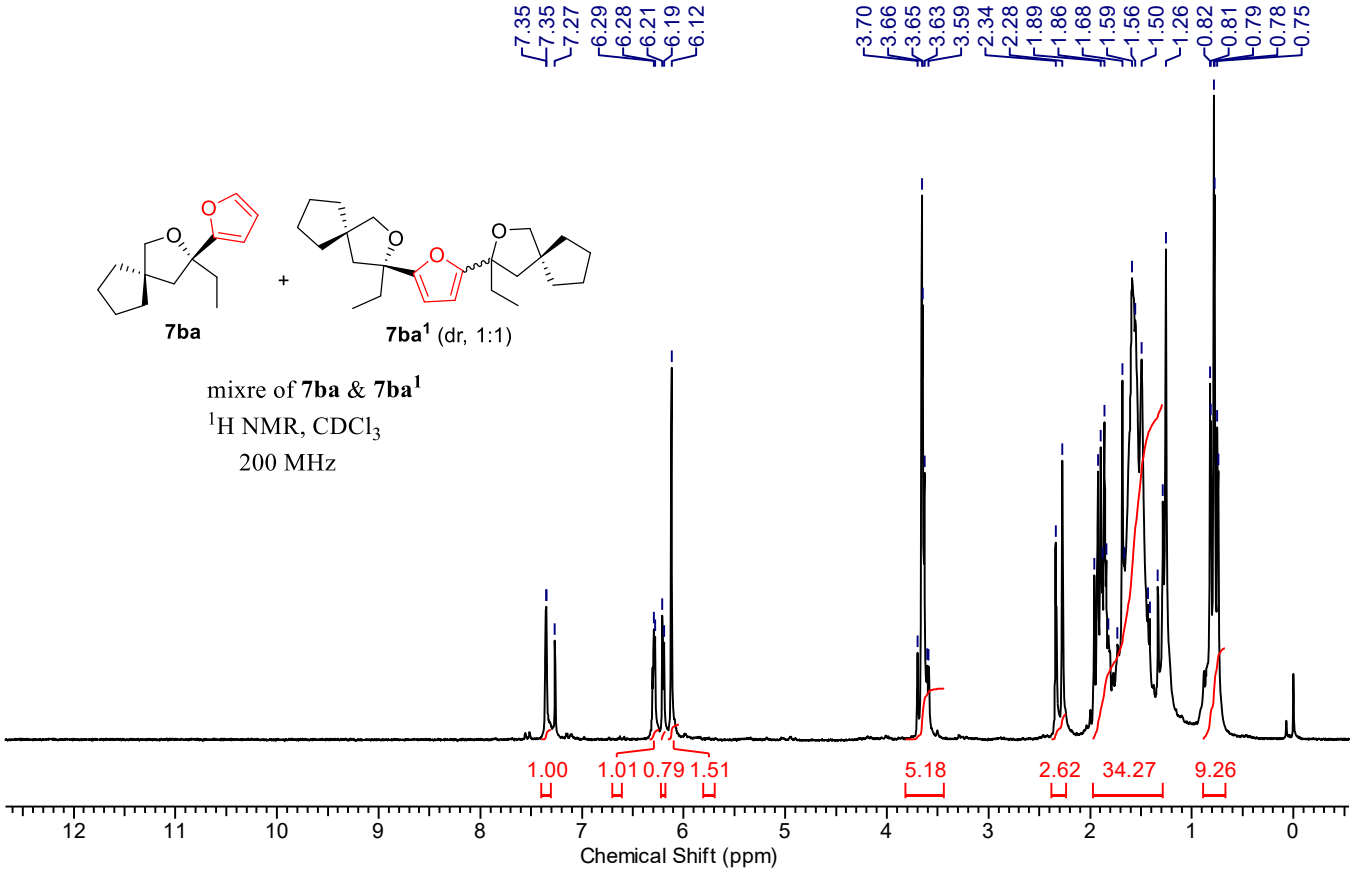
Chrom Type: HPLC Channel : 1

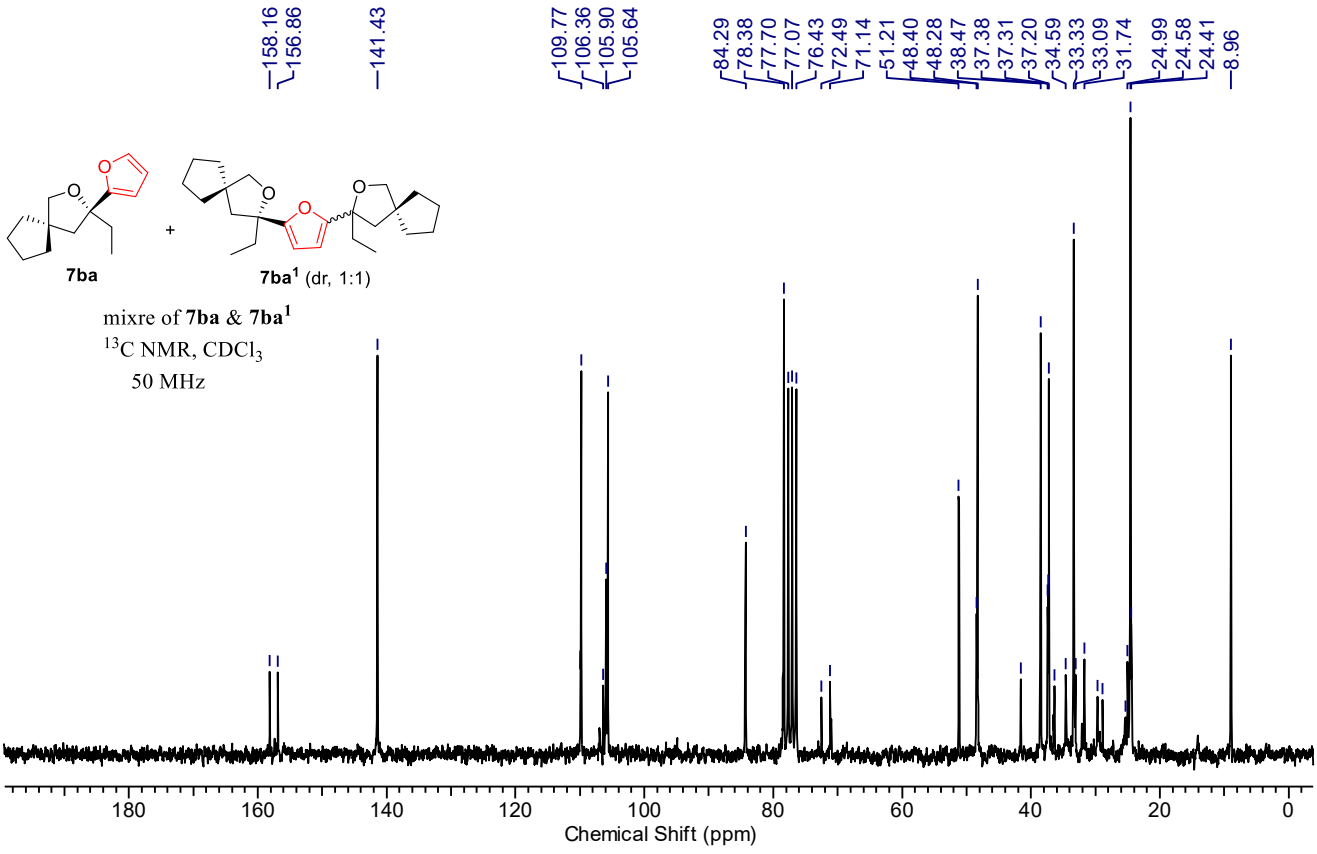


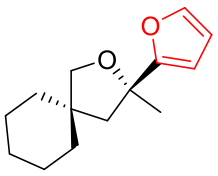
No.	RT	Area	Conc 1	BC
1	4.08	5338034	82.837	BB
2	6.28	1105998	17.163	BB
		6444032	100.000	

Peak rejection level: 0

```
Project Leader: Dr.RAVINDAR kONTHAM
Column     :Chiralcel OJ-H(250 mm x 4.6mm)
Mobile Ph  : IPA:PE(01:99)
Wavelength : 220nm
Flow       : 1 ml/min.
Inject vol: 2ul
```


7.35
7.35
7.27
6.29
6.28
6.21
6.19
6.12
3.70
3.66
3.65
3.63
3.59
2.34
2.28
1.89
1.86
1.68
1.59
1.56
1.50
1.26
0.82
0.81
0.79
0.78
0.75
7ba
7ba1 (dr, 1:1)
mixre of 7ba & 7ba1
1H NMR, CDCl3
200 MHz
1.00
1.01
0.79
1.51
5.18
2.62
34.27
9.26
Chemical Shift (ppm)

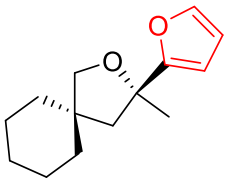

158.16
156.86
141.43
109.77
106.36
105.90
105.64
84.29
78.38
77.70
77.07
76.43
72.49
71.14
51.21
48.40
48.28
38.47
37.38
37.31
37.20
34.59
33.33
33.09
31.74
24.99
24.58
24.41
8.96
7ba
7ba1 (dr, 1:1)
mixre of 7ba & 7ba1
13C NMR, CDCl3
50 MHz
Chemical Shift (ppm)



7ea

^{1}H NMR, $CDCl_3$

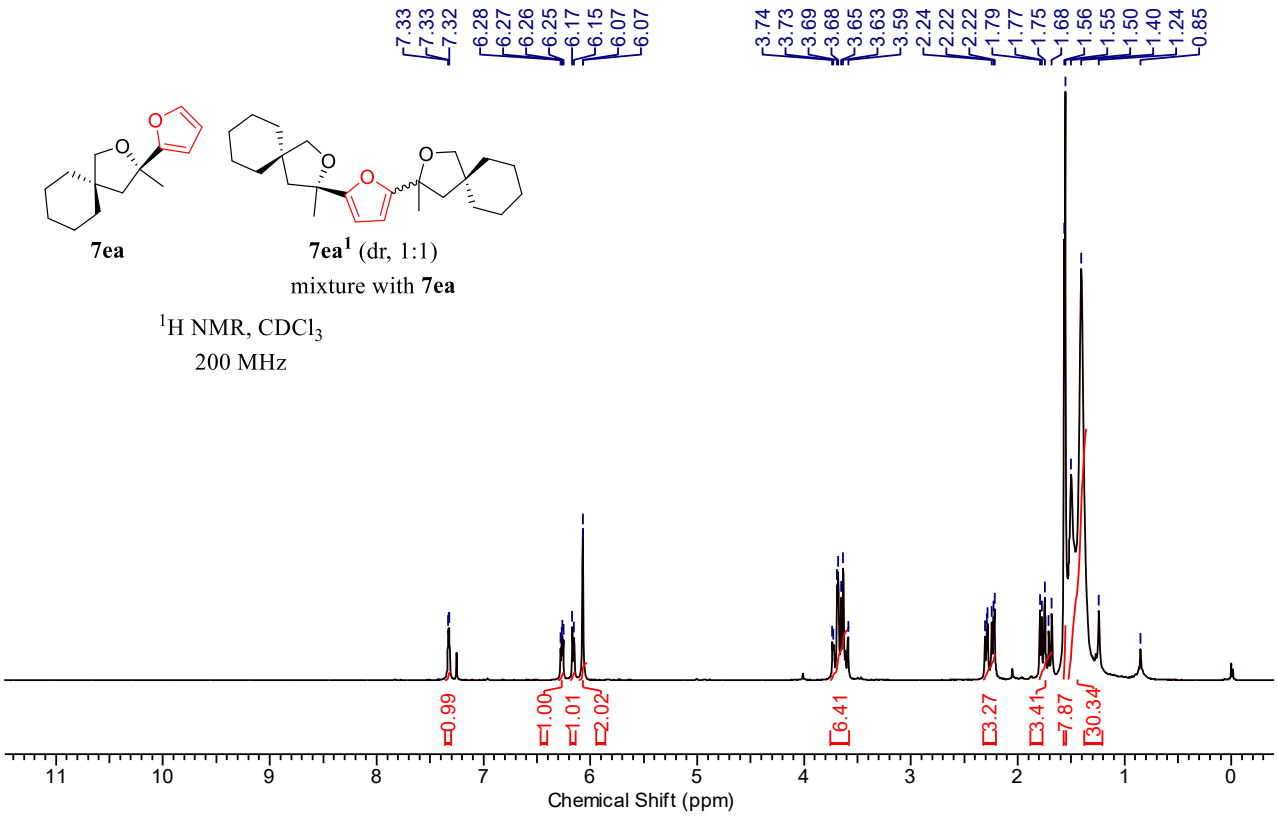
200 MHz



7ea

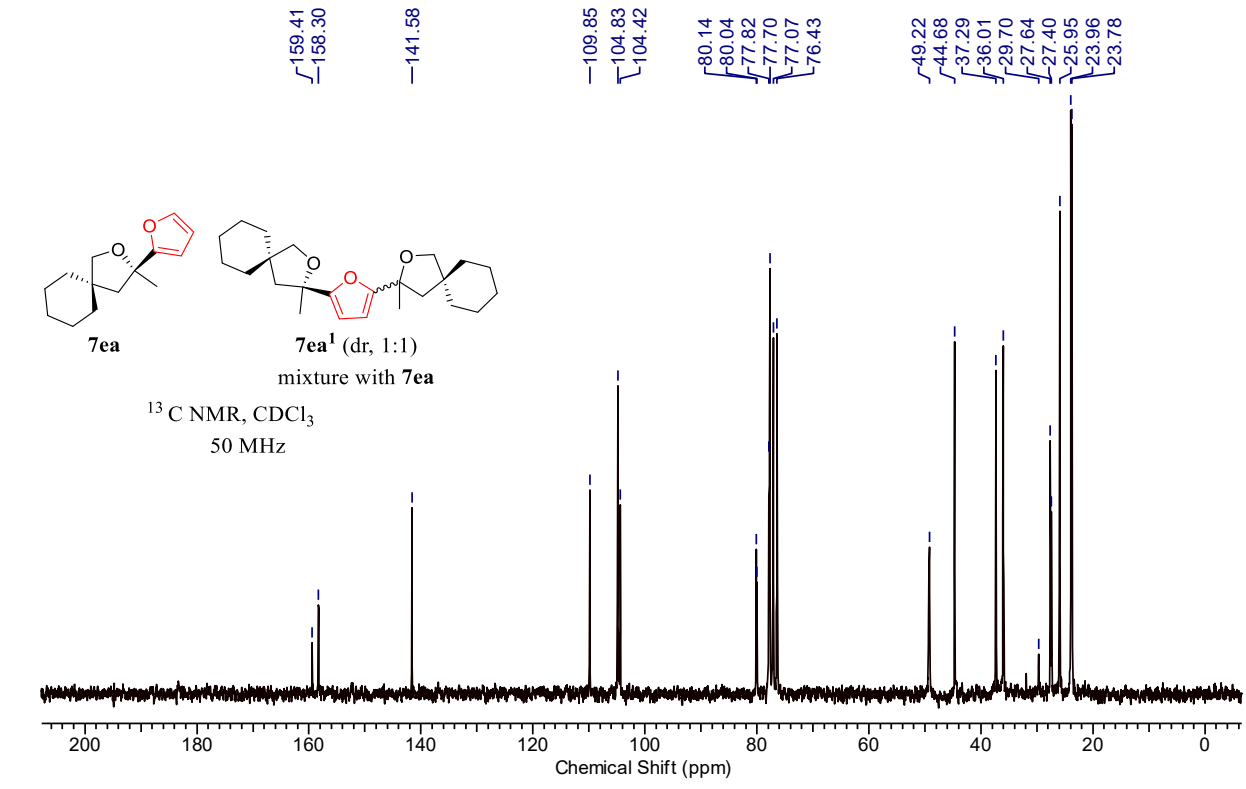
^{13}C NMR, $CDCl_3$

50 MHz



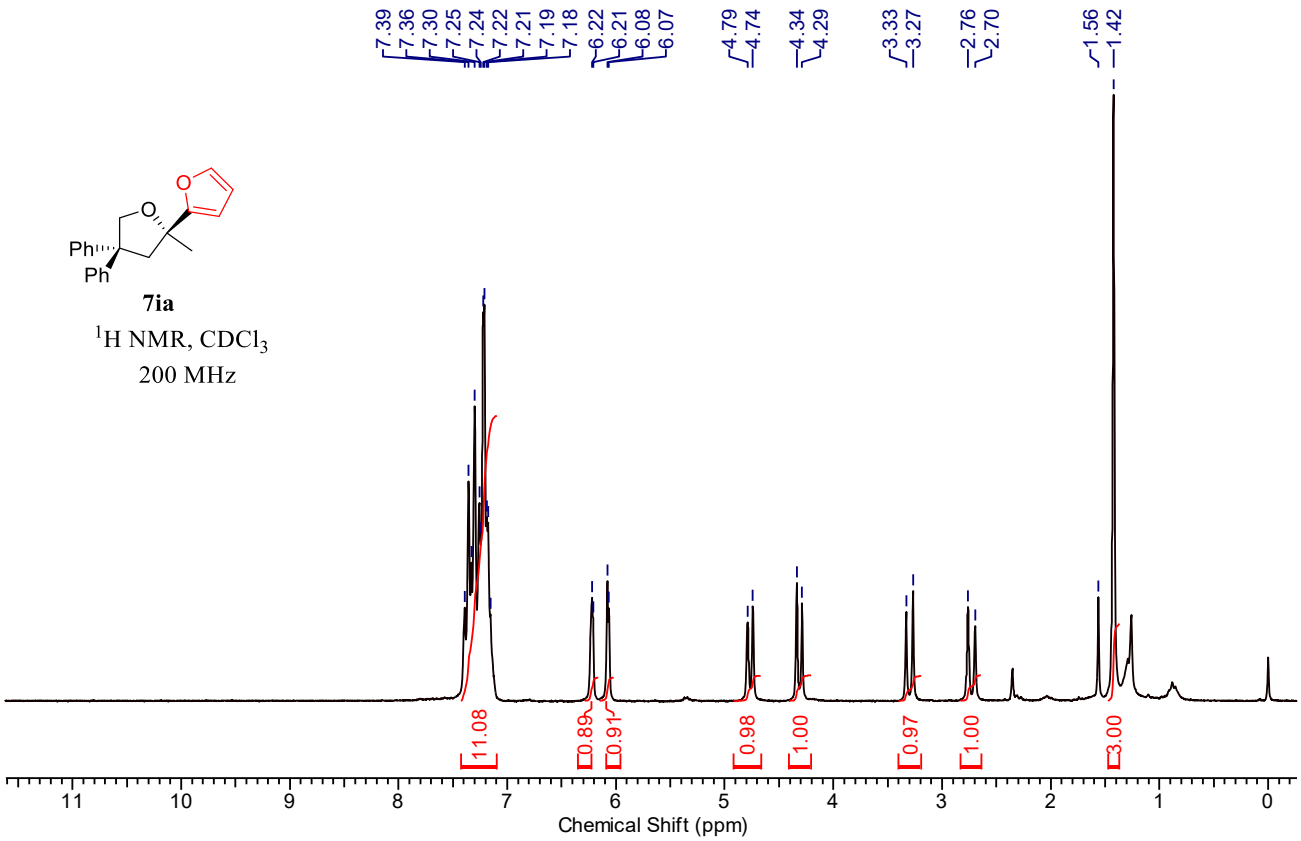
7ea **7ea[1]** (dr, 1:1)
mixture with **7ea**

^{1}H NMR, $CDCl_3$
200 MHz



7ea **7ea[1]** (dr, 1:1)
mixture with **7ea**

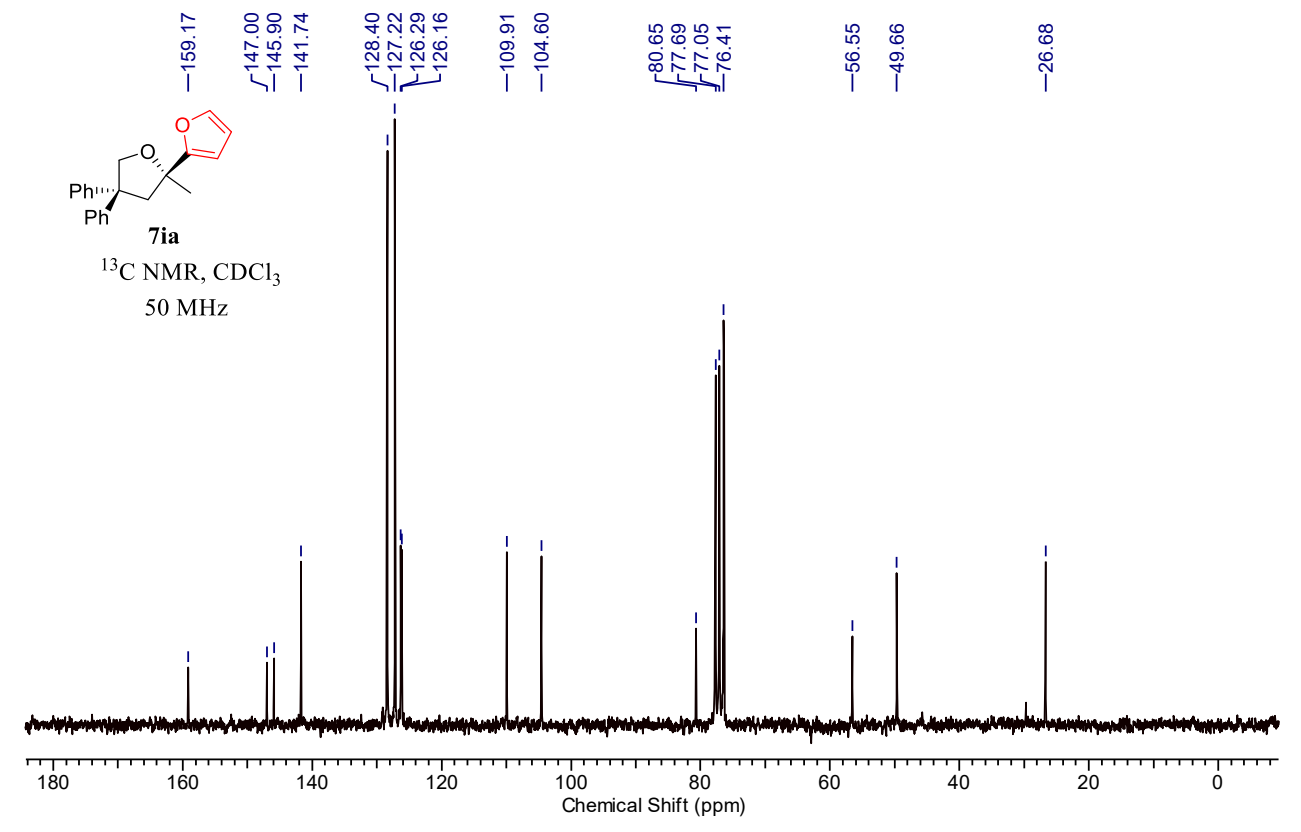
^{13}C NMR, $CDCl_3$
50 MHz



7ia

^{1}H NMR, $CDCl_3$

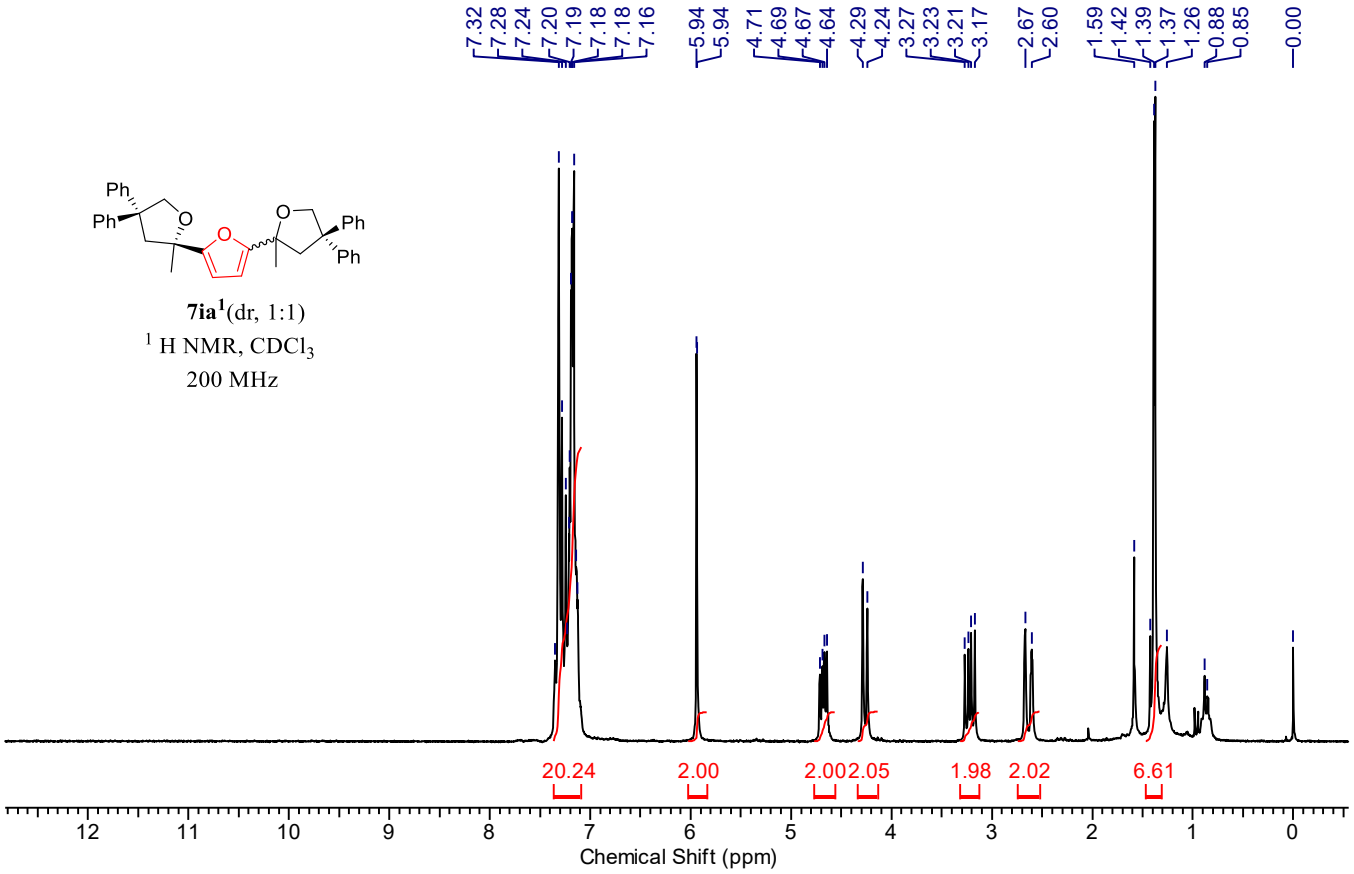
200 MHz



7ia

^{13}C NMR, $CDCl_3$

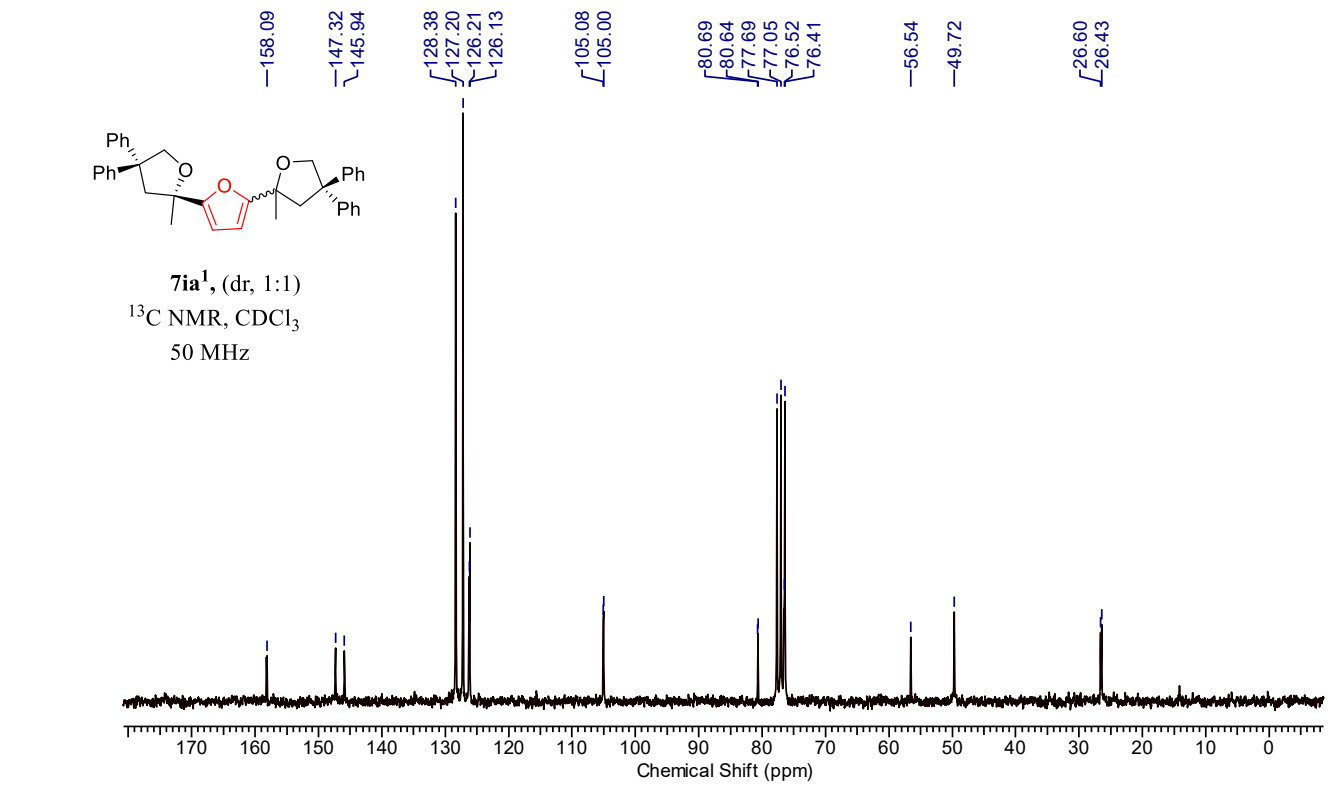
50 MHz



7ia[1](dr, 1:1)

^{1}H NMR, $CDCl_3$

200 MHz



7ia[1], (dr, 1:1)

^{13}C NMR, $CDCl_3$

50 MHz

HPLC Analysis Report (7ia[1])

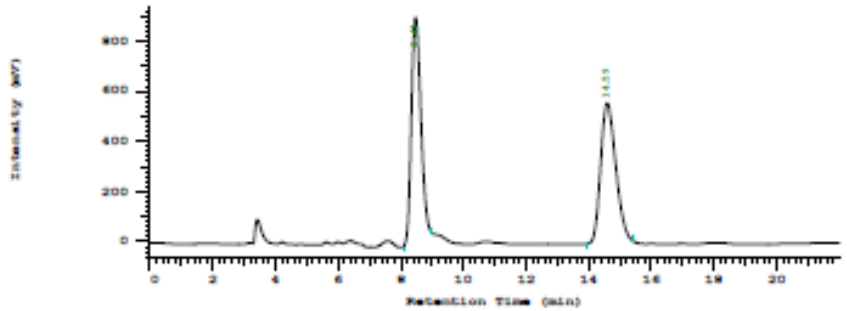
D-7000 HPLC System Manager Report

Analyzed: 11/06/17 02:37 PM
Reported: 11/06/17 03:04 PM
Processed: 11/06/17 03:03 PM

Data Path: C:\WIN32APP\HSM\HPLC\DATA\9910\
Processing Method: cal

System(acquisition): Sys 1
Series:9910
Application: HPLC
Volume: 10.0 ul
Sample Name: AN=04
Injection from this vial: 1 of 1
Sample Description: IPA:PE(02:98)

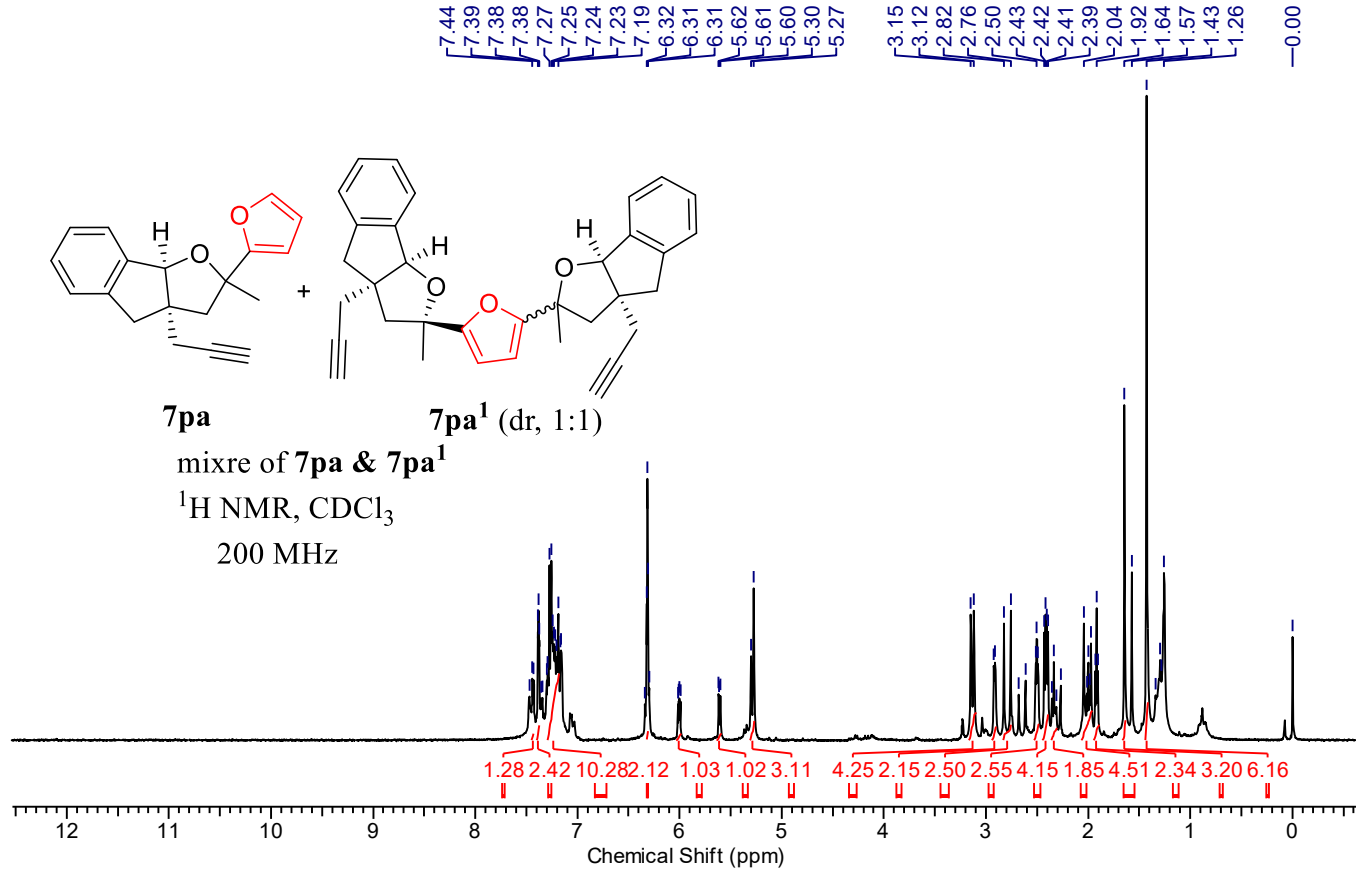
Chrom Type: HPLC Channel : 1

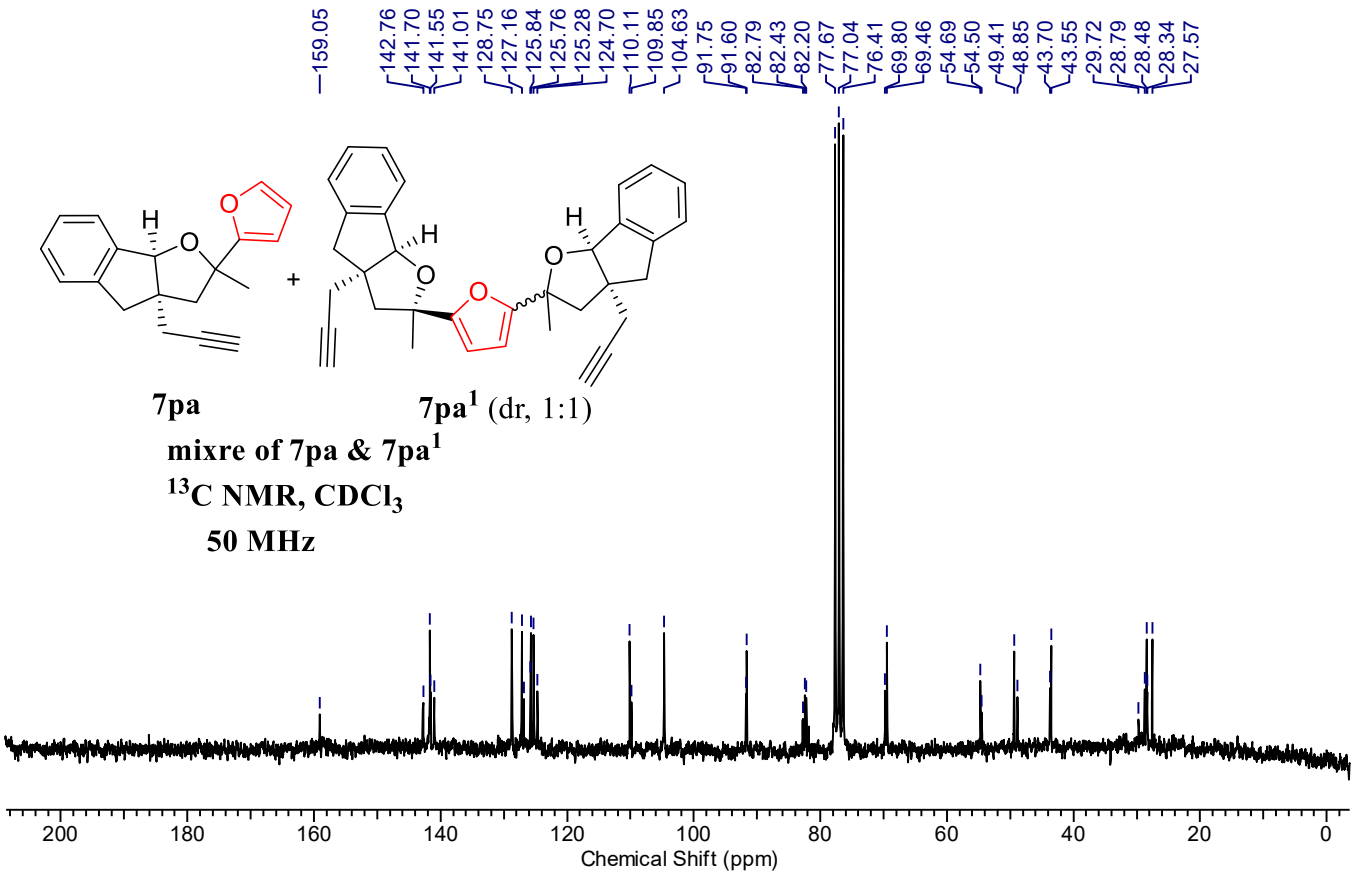


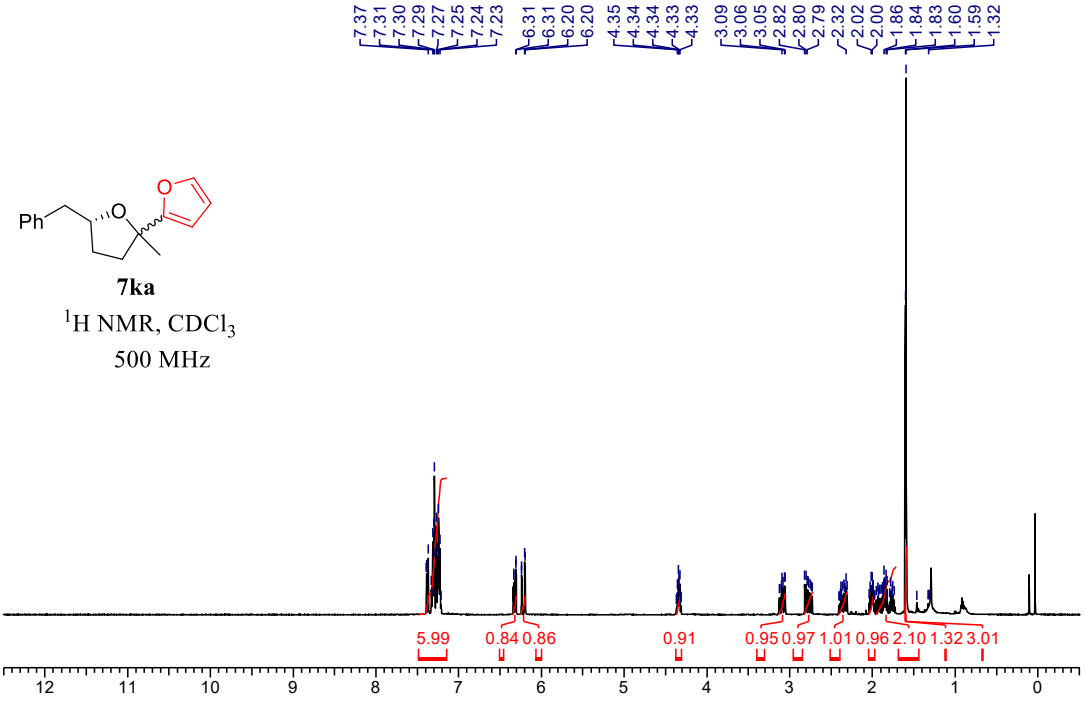
No.	RT	Area	Conc 1	BC
1	8.47	18643153	49.990	BB
2	14.59	18650707	50.010	BB
		37293860	100.000	

Peak rejection level: 0

```
Project Leader: Dr.RAVINDAR kONTHAM
Column     :Kromasil 5-cellucoat(250 mm x 4.6mm)
Mobile Ph  : IPA:PE(02:98)
Wavelength : 220nm
Flow       : 1 ml/min.
Inject vol: 5ul
```


7.44 7.39 7.38 7.38 7.27 7.25 7.24 7.23 7.19 6.32 6.31 6.31 5.62 5.61 5.60 5.30 5.27
3.15 3.12 2.82 2.76 2.50 2.43 2.42 2.41 2.39 2.04 1.92 1.64 1.57 1.43 1.26
0.00
7pa
7pa1 (dr, 1:1)
mixre of 7pa & 7pa1
1H NMR, CDCl3
200 MHz
1.28 2.42 10.28 2.12 1.03 1.02 3.11 4.25 2.15 2.50 2.55 4.15 1.85 4.51 2.34 3.20 6.16
Chemical Shift (ppm)

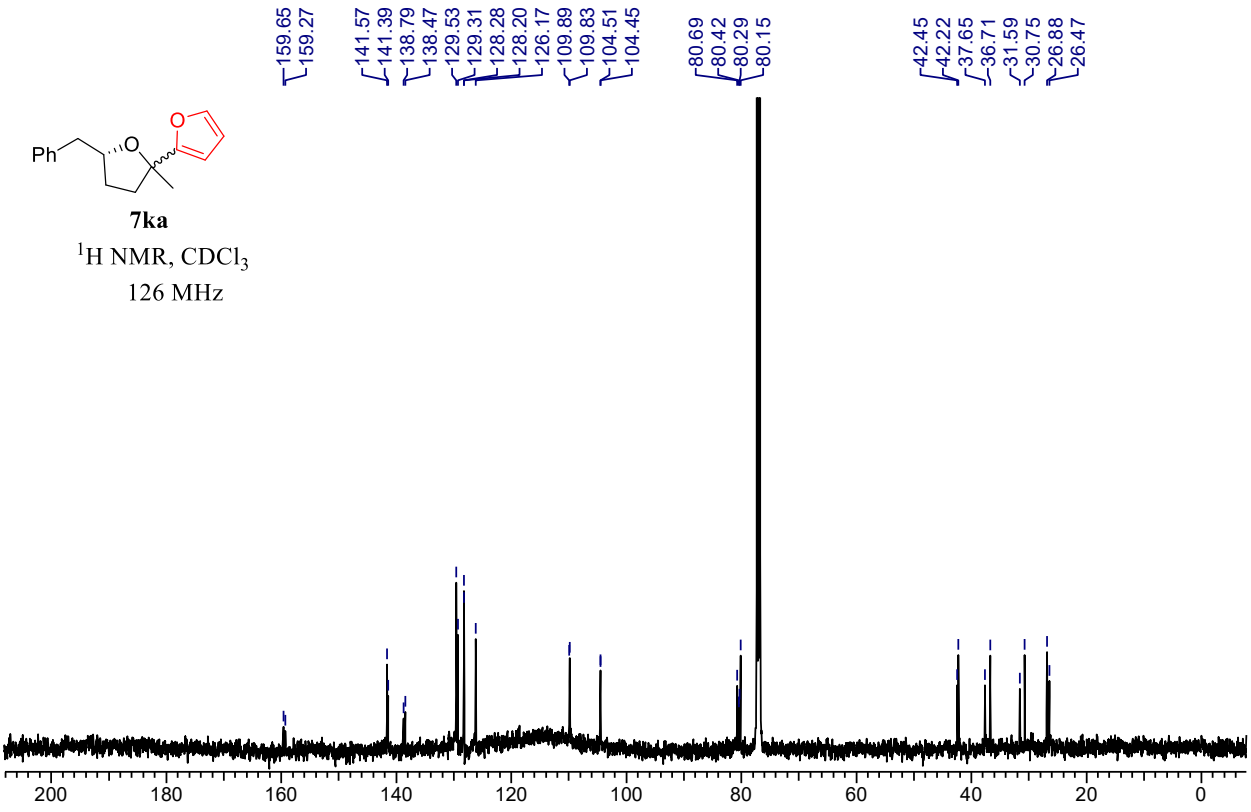

159.05
142.76 141.70 141.55 141.01 128.75 127.16 125.84 125.76 125.28 124.70 110.11 109.85 104.63 91.75 91.60 82.79 82.43 82.20 77.67 77.04 76.41 69.80 69.46 54.69 54.50 49.41 48.85 43.70 43.55 29.72 28.79 28.48 28.34 27.57
7pa
7pa1 (dr, 1:1)
mixre of 7pa & 7pa1
13C NMR, CDCl3
50 MHz
Chemical Shift (ppm)



7ka

^{1}H NMR, $CDCl_3$

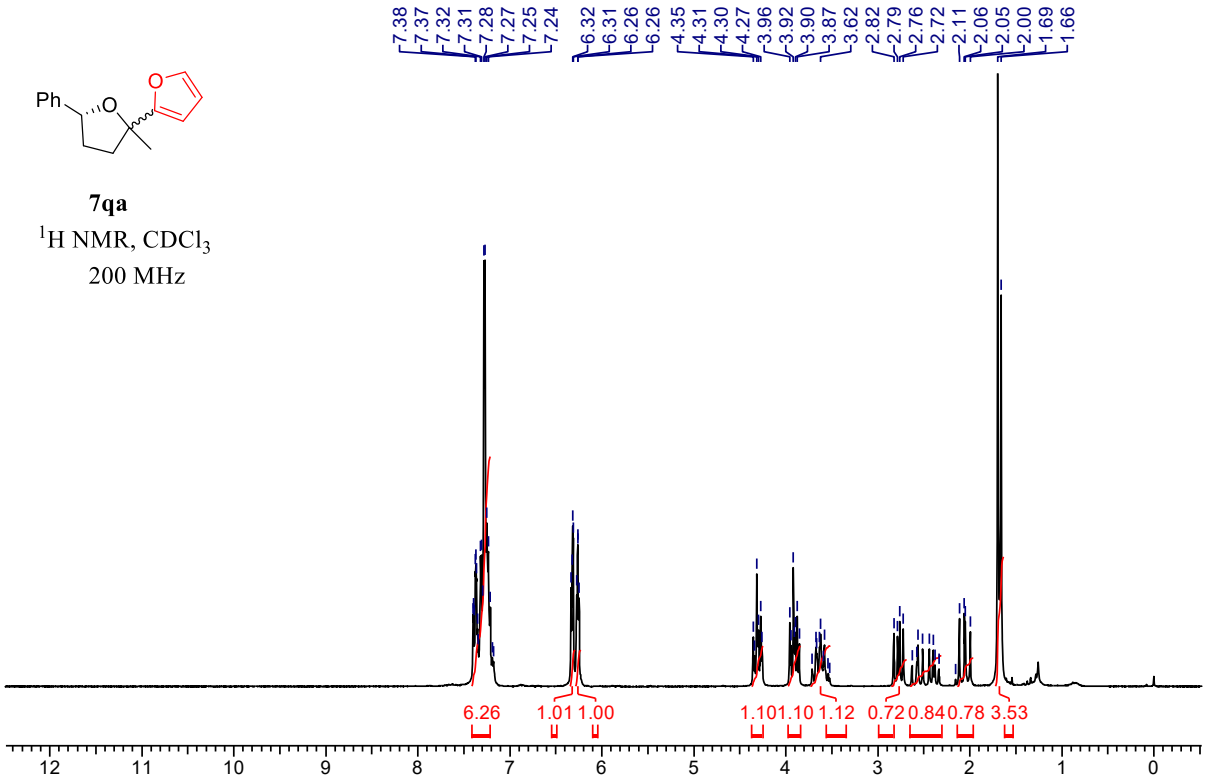
500 MHz



7ka

^{1}H NMR, $CDCl_3$

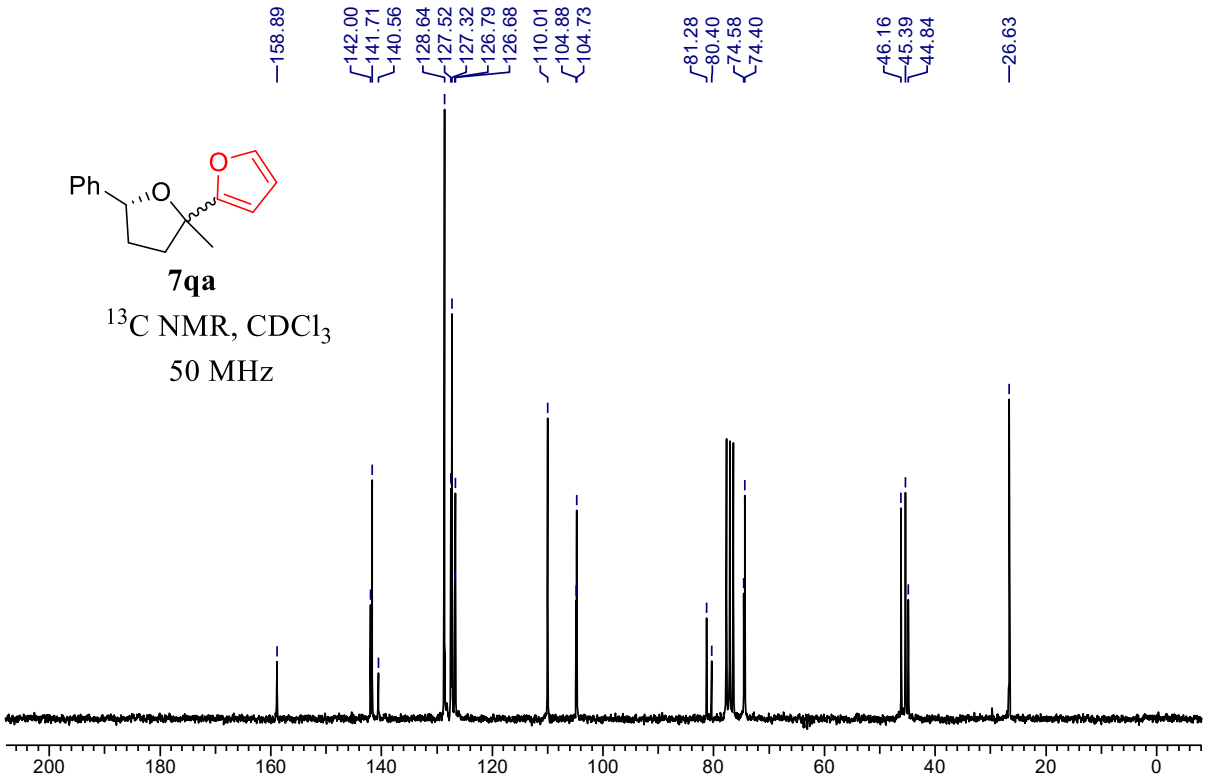
126 MHz



7qa

^{1}H NMR, $CDCl_3$

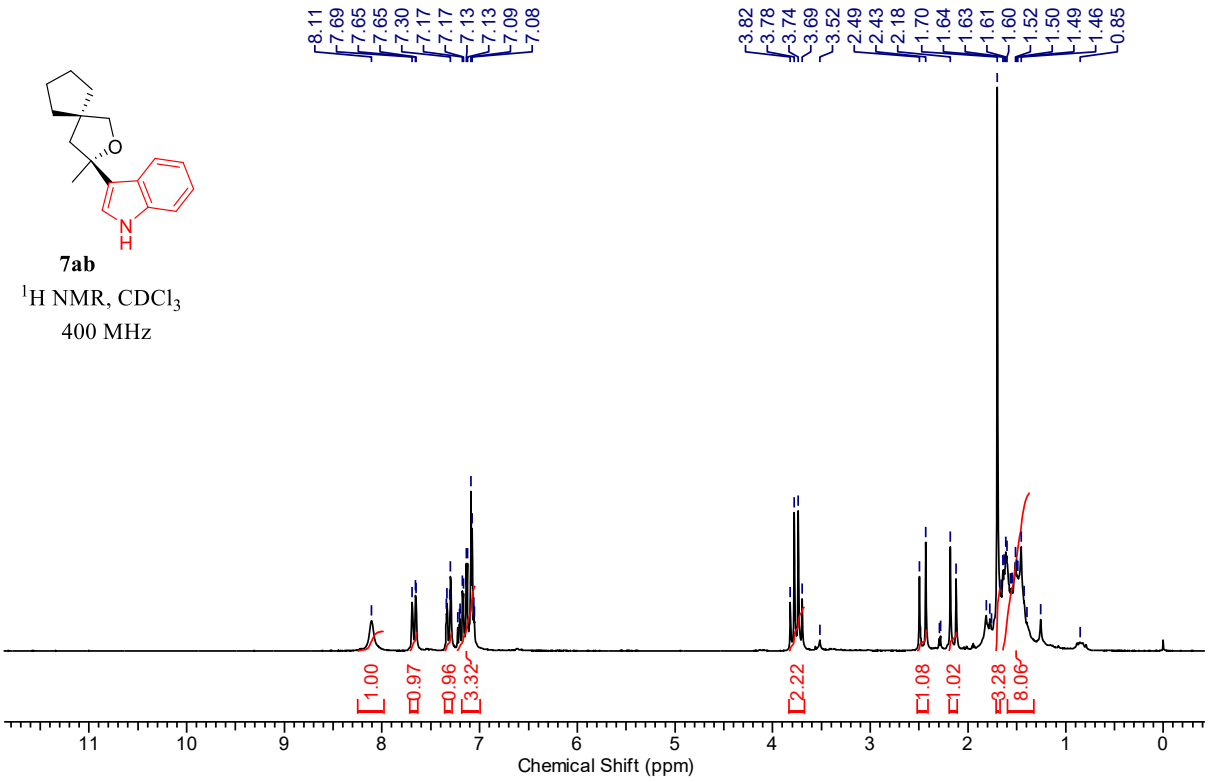
200 MHz



7qa

^{13}C NMR, $CDCl_3$

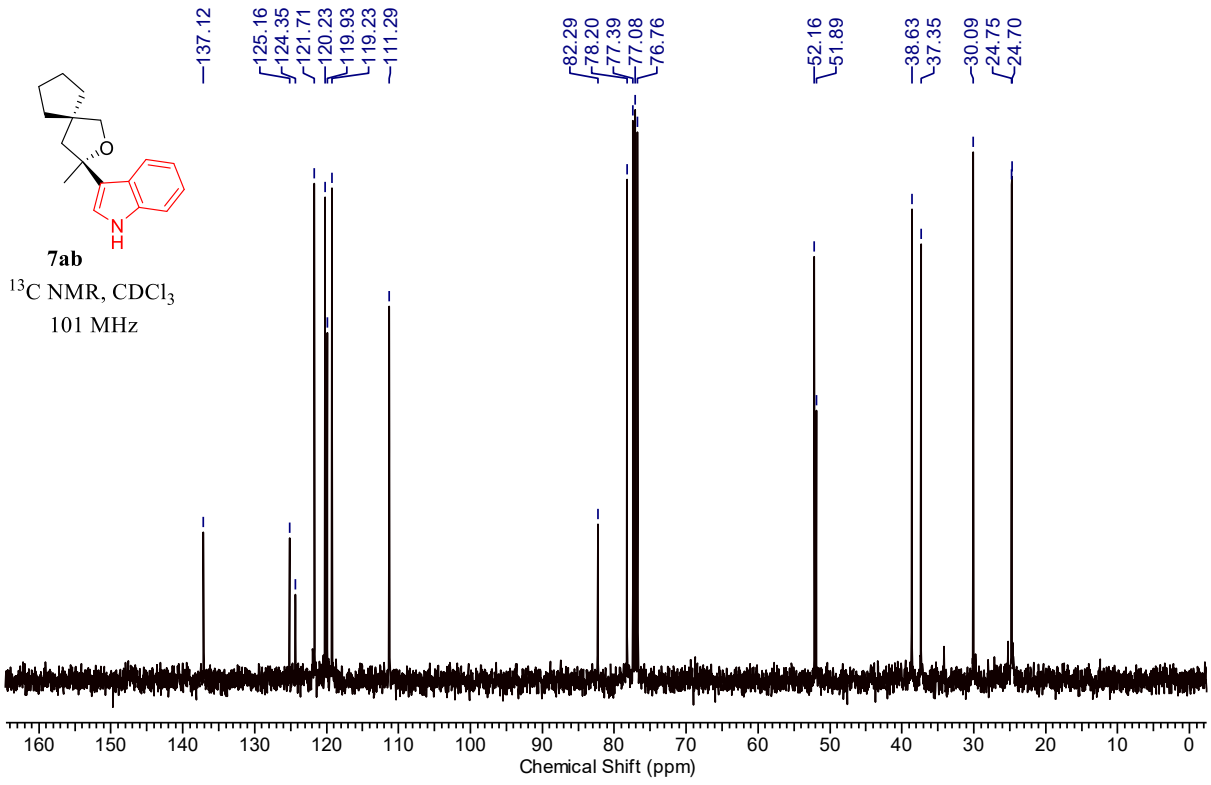
50 MHz



7ab

^{1}H NMR, $CDCl_3$

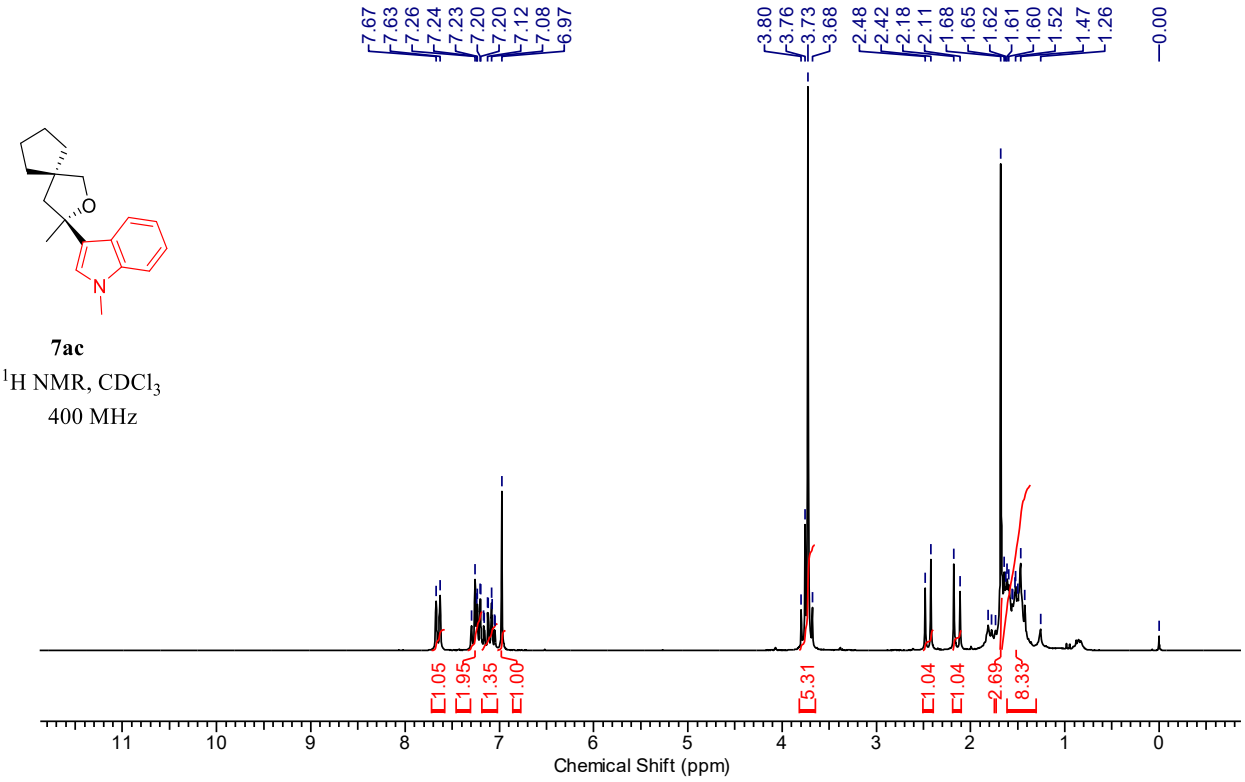
400 MHz



7ab

^{13}C NMR, $CDCl_3$

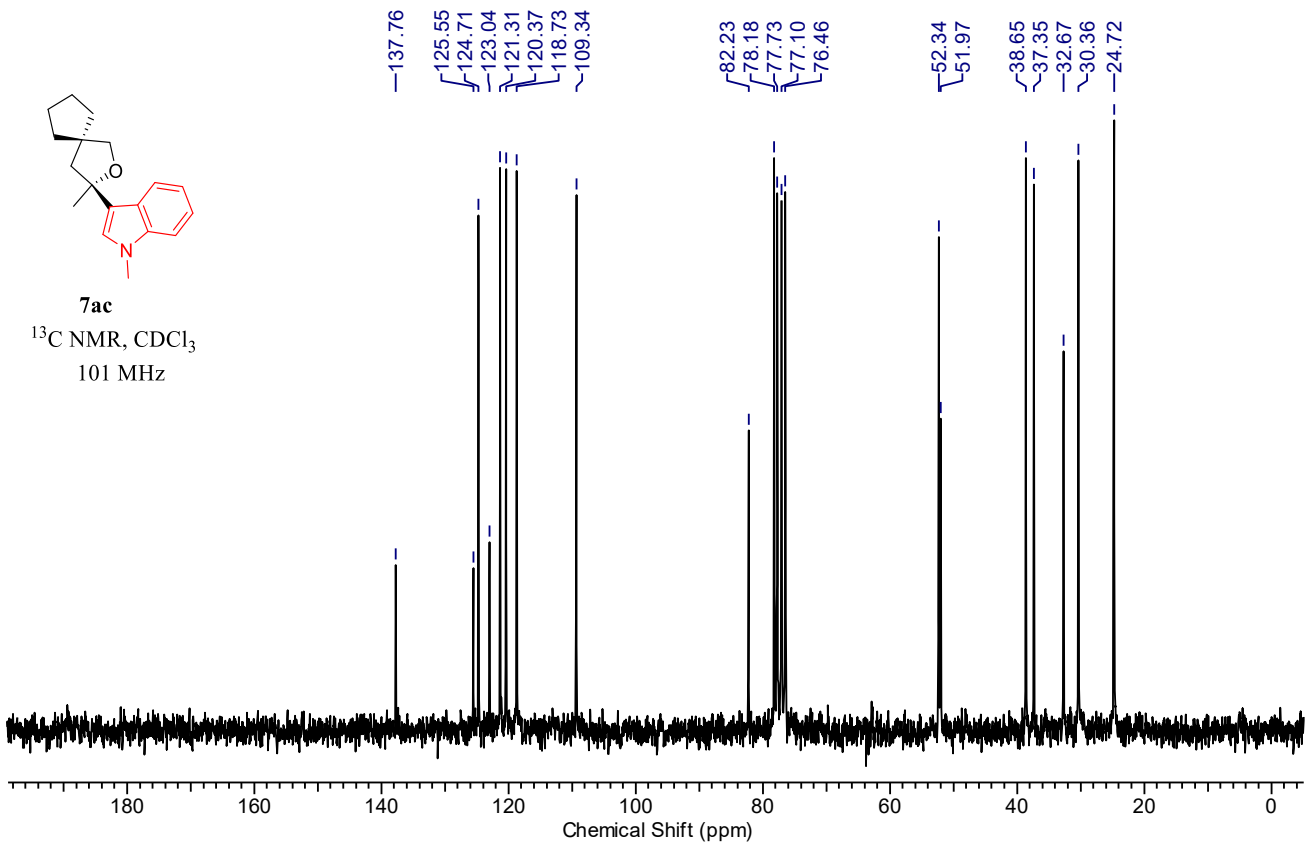
101 MHz



7ac

^{1}H NMR, $CDCl_3$

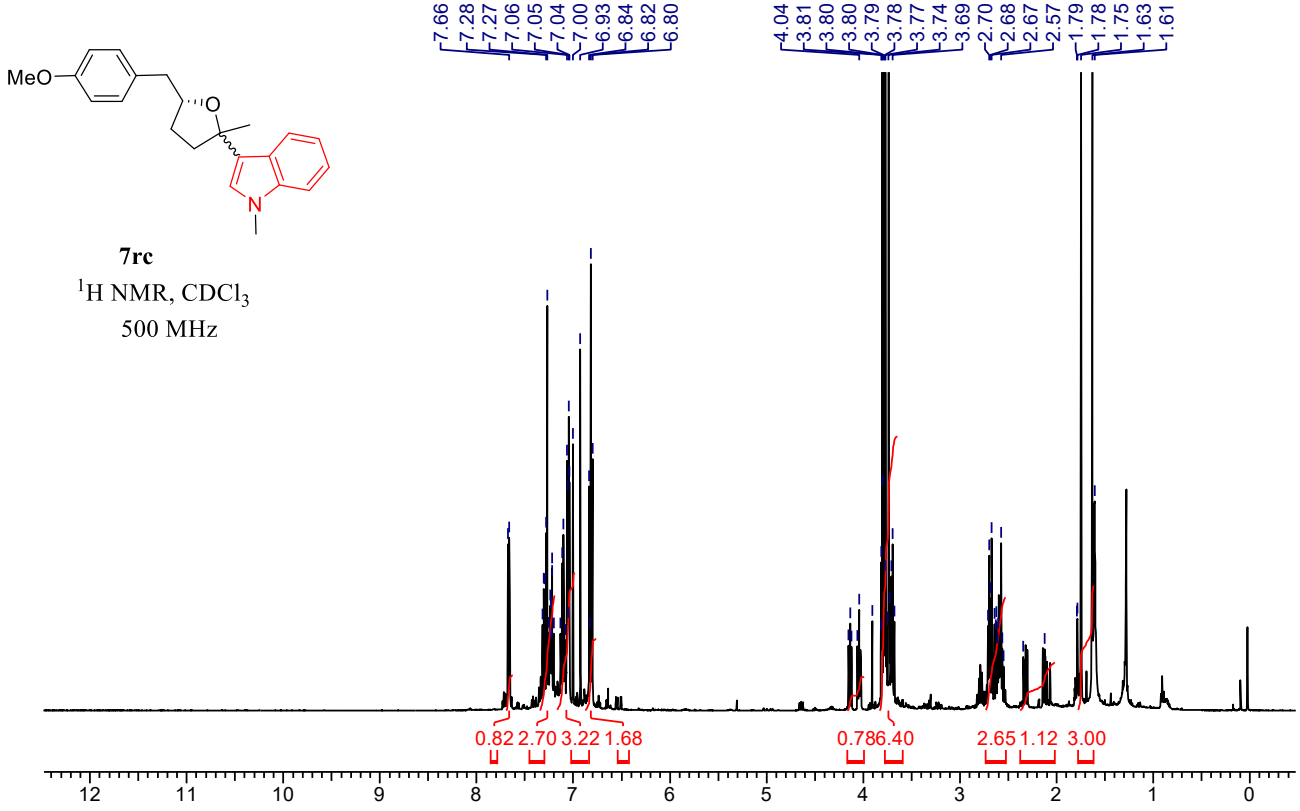
400 MHz



7ac

^{13}C NMR, $CDCl_3$

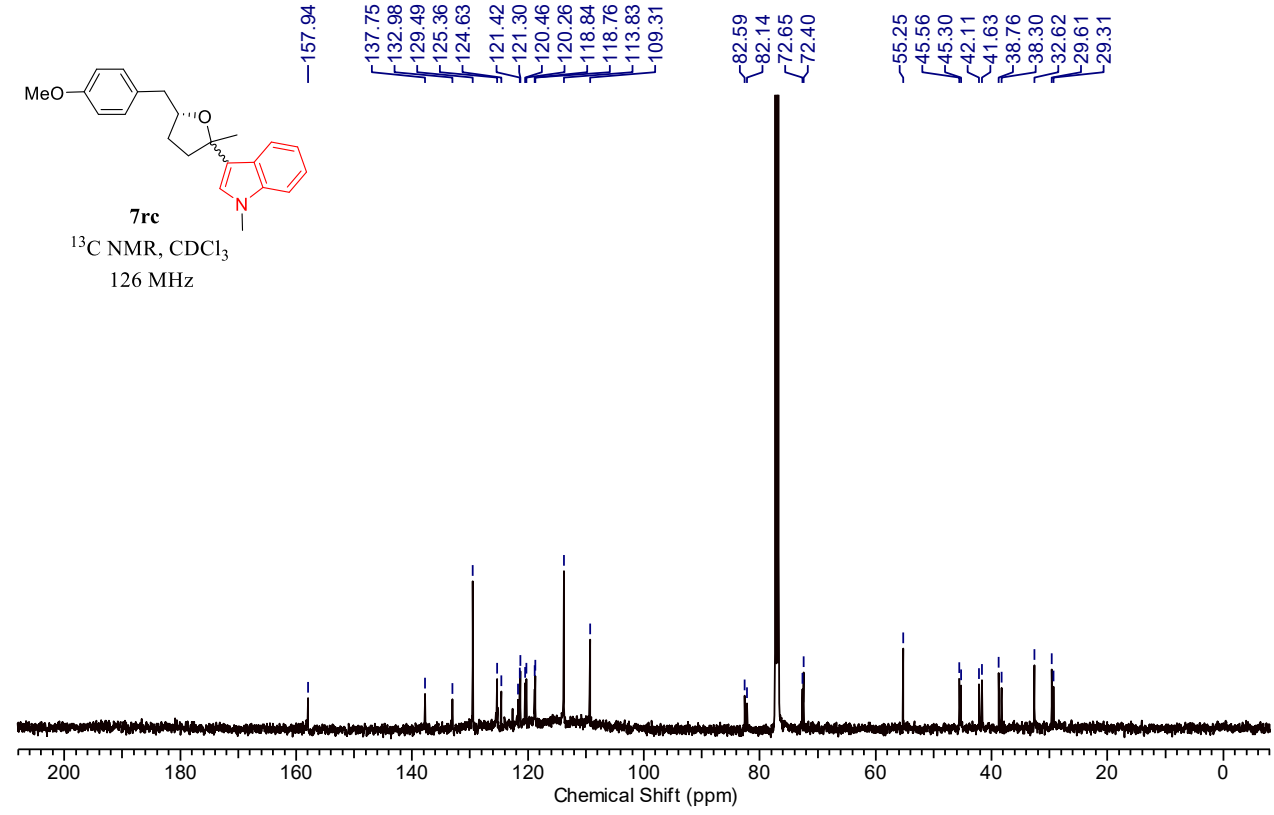
101 MHz



7rc

^{1}H NMR, $CDCl_3$

500 MHz



7rc

^{13}C NMR, $CDCl_3$

126 MHz