

# Sequential Dieckmann Cyclization Enables the Total Synthesis of 7-*epi*-Clusianone, 18-Hydroxy-7-*epi*-clusianone

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## 1. Comparative data for natural product *7-epi-clusianone*

Position	<i>7-epi-clusianone</i> (a) isolated		<i>7-epi-clusianone</i> (a) synthetic	
	$\delta$ C (125 MHz)	$\delta$ H (500 MHz)	$\delta$ C (151 MHz)	$\delta$ H (600 MHz)
1	68.6		68.8	
2	193.7		193.8	
3	115.9		116.0	
4	196.6		196.9	
5	58.4		58.5	
6ax	39.0	2.22 (dd) (14.4, 7.0)	39.1	2.22 (m)
6eq		2.26 (dd) (14.4, 1.8)		2.26 (m)
7	46.3	1.44 (overlapped)	46.4	1.44 (overlapped)
8	48.3		48.5	
9	208.1		208.0	
10	26.2	2.47 (m)	26.5	2.47 (m)
11	120.1	5.12 (m)	119.9	5.13 (m)
12	134.8		135.0	
13	18.1	1.70 (s)	18.1	1.71 (s)
14	26.0	1.66 (s)	26.1	1.67 (s)
15	197.5		197.7	
16	136.8		136.9	
17 21	129.0	7.52 (d, 7.6)	129.1	7.52 (m)
18 20	127.8	7.38 (t, 7.6)	128.0	7.37 (t, 7.6)
19	132.6	7.53 (t, 7.6)	132.8	7.52 (m)
22	30.5	2.62 (m)	30.5	2.62 (m)
23	118.9	5.15 (m)	119.0	5.13 (m)
24	134.7		134.9	
25	18.1	1.67 (s)	18.1	1.65 (s)
26	26.0	1.80 (s)	26.0	1.80 (s)
27	28.9	2.05 (overlapped) 2.16 (overlapped)	28.9	2.05 (overlapped) 2.16 (overlapped)
28	123.5	4.85 (m)	123.4	4.88 (m)
29	132.9		133.0	
30	17.7	1.43 (s)	17.8	1.45 (s)
31	25.7	1.58 (s)	25.8	1.58 (s)
32	27.0	0.97 (s)	27.0	0.98 (s)
33	22.5	1.13 (s)	22.5	1.14 (s)

Position	<i>7-epi-clusianone</i> (b) isolated		<i>7-epi-clusianone</i> (b) synthetic	
	$\delta$ C (125 MHz)	$\delta$ H (500 MHz)	$\delta$ C (151 MHz)	$\delta$ H (600 MHz)
1	65.5		65.5	

2	196.7		196.9	
3	115.5		115.8	
4	193.6		193.7	
5	63.2		63.2	
6ax	40.3	2.01 (dd) (14.4, 7.0)	40.5	2.01 (m)
6eq		2.11 (dd) (14.4, 2.8)		2.11 (m)
7	46.6	1.44 (overlapped)	46.6	1.45 (m)
8	48.8		48.9	
9	208.3		208.2	
10	25.9	2.72 (m)	26.1	2.71 (m)
11	118.6	4.8 (m)	118.7	4.8 (m)
12	134.8		135.0	
13	18.0	1.68 (s)	18.1	1.67 (s)
14	25.8	1.61 (s)	26.1	1.61 (s)
15	197.2		197.4	
16	136.8		136.9	
17 21	128.9	7.55 (d) (7.6)	129.1	7.55 (m)
18 20	127.8	7.40 (t) (7.6)	128.0	7.37 (t) (7.6)
19	132.6	7.53 (t) (7.6)	132.8	7.53 (m)
22	30.7	2.44 (m) 2.52 (m)	30.7	2.44 (m) 2.53 (m)
23	119.7	5.24 (m)	119.8	5.22 (m)
24	134.6		134.9	
25	18.2	1.66 (s)	18.1	1.67 (s)
26	26.1	1.76 (s)	26.0	1.76 (s)
27	28.9	2.00 (overlapped)	28.9	2.00 (overlapped)
28	124.0	4.87 (m)	123.9	4.87 (m)
29	133.0		133.0	
30	17.8	1.50 (s)	17.8	1.51 (s)
31	25.7	1.64 (s)	25.8	1.64 (s)
32	26.9	1.06 (s)	26.9	1.06 (s)
33	22.8	1.30 (s)	22.8	1.30 (s)

## 2. Comparative data for natural product 18-hydroxy-7-*epi*-clusianone

Position	18-hydroxy-7- <i>epi</i> -clusianone (a) isolated		18-hydroxy-7- <i>epi</i> -clusianone (a) synthetic	
	$\delta$ C (125 MHz)	$\delta$ H (500 MHz)	$\delta$ C (151 MHz)	$\delta$ H (600 MHz)
1	68.7		68.7	
2	194.6		194.6	
3	116.0		116.0	
4	197.7	17.63 (br s)	197.8	

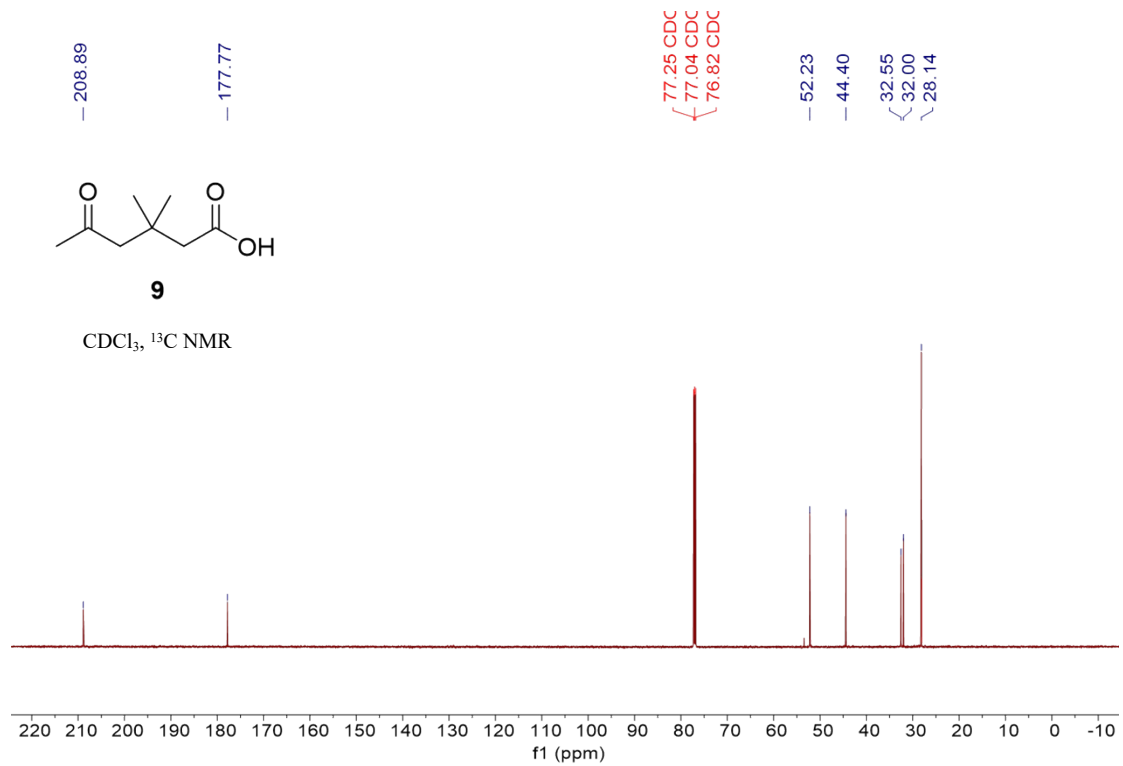
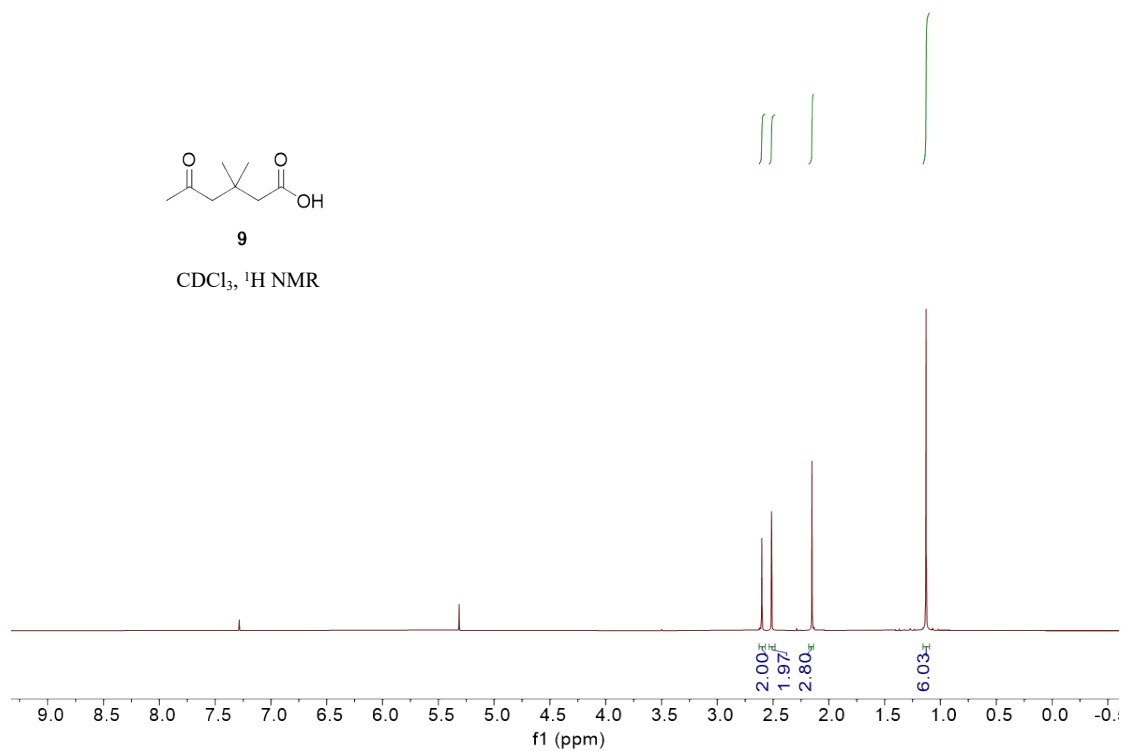
5	58.5		58.5	
6	39.1	2.27 (m) 2.21 (m)	39.1	2.27 (m) 2.21 (m)
7	46.4	1.45 (m)	46.4	1.45 (m)
8	48.4		48.5	
9	207.9		208.0	
10	26.5	2.78 (m)	26.5	2.77 (m)
11	119.8	5.08 (br d; 8)	119.9	5.08 (br d)
12	135.0		135.0	
13	18.1	1.79 (s)	18.1	1.78 (s)
14	26.1	1.68 (s)	26.1	1.68 (s)
15	196.6		196.7	
16	137.9		137.9	
17	115.6	6.95 (br s)	115.6	6.95 (br s)
18	155.7		115.7	
19	119.9	6.86 (m)	119.9	6.87 (m)
20	128.7	7.14(m; W½ 17.5)	128.7	7.14 (m)
21	121.4	7.00 (d; 7.5)	121.4	7.00 (d)
22	30.5	2.62 (t; 8) 2.58 (dd;13.6, 9)	30.5	2.61 (t) 2.58 (dd)
23	118.4	5.14 (br t; 6.9)	118.5	5.13 (br t)
24	134.8		134.9	
25	18.1	1.66 (s)	18.1	1.65 (s)
26	26.0	1.58 (s)	26.0	1.57 (s)
27	28.9	2.09 (m) 2.03 (m)	28.9	2.09 (m) 2.03 (m)
28	123.4	4.88 (m;W½ 15.6)	123.4	4.88 (m)
29	133.0		133.0	
30	17.8	1.46 (s)	17.8	1.45 (s)
31	25.8	1.62 (s)	25.8	1.61 (s)
32	27.0	0.98 (s)	27.0	0.98 (s)
33	22.5	1.16 (s)	22.5	1.15 (s)

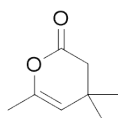
Position	<b>18-hydroxy-7-<i>epi</i>-clusianone (b)</b> isolated		<b>18-hydroxy-7-<i>epi</i>-clusianone (b)</b> synthetic	
	$\delta$ C (125 MHz)	$\delta$ H (500 MHz)	$\delta$ C (151 MHz)	$\delta$ H (600 MHz)
1	65.5		65.5	
2	197.3	17.72 (br s)	197.3	
3	115.8		115.8	
4	194.8		194.7	
5	63.2		63.2	
6	40.5	2.05 (m) 2.17 (m)	40.5	2.05 (m) 2.17 (m)



7	46.6	1.45 (m)	46.6	1.45 (m)
8	48.9		48.9	
9	208.1		208.2	
10	26.1	2.71 (m) 2.73 (m)	26.1	2.71 (m) 2.73 (m)
11	119.4	5.22 (br t; 6)	119.5	5.21 (t)
12	135.0		135.0	
13	18.1	1.76 (s)	18.1	1.76 (s)
14	26.1	1.71 (s)	26.1	1.70 (s)
15	196.4		196.5	
16	138.0		138.0	
17	115.6	6.92 (br s)	115.6	6.92 (br s)
18	155.7		155.7	
19	119.9	6.86 (m)	120.0	6.86 (m)
20	128.9	7.14 (m; W½ 17.5)	128.9	7.14 (m)
21	121.2	7.00 (d; 7.5)	121.2	7.00 (d)
22	30.7	2.55 (m) 2.46 (m)	30.7	2.55 (m) 2.46 (m)
23	118.8	4.79 (m; W½ 13.8)	118.8	4.78 (m)
24	134.8		134.9	
25	18.2	1.71 (s)	18.1	1.70 (s)
26	26.0	1.58 (s)	26.0	1.57 (s)
27	29.0	2.21 (m) 1.89 (m)	28.9	2.21 (m) 1.88 (m)
28	123.9	4.88 (m; W½ 15.6)	123.9	4.87 (m)
29	133.0		133.0	
30	17.8	1.52 (s)	17.8	1.51 (s)
31	26.0	1.69 (s)	26.0	1.70 (s)
32	26.9	1.06 (s)	26.9	1.06 (s)
33	22.8	1.31 (s)	22.8	1.30 (s)

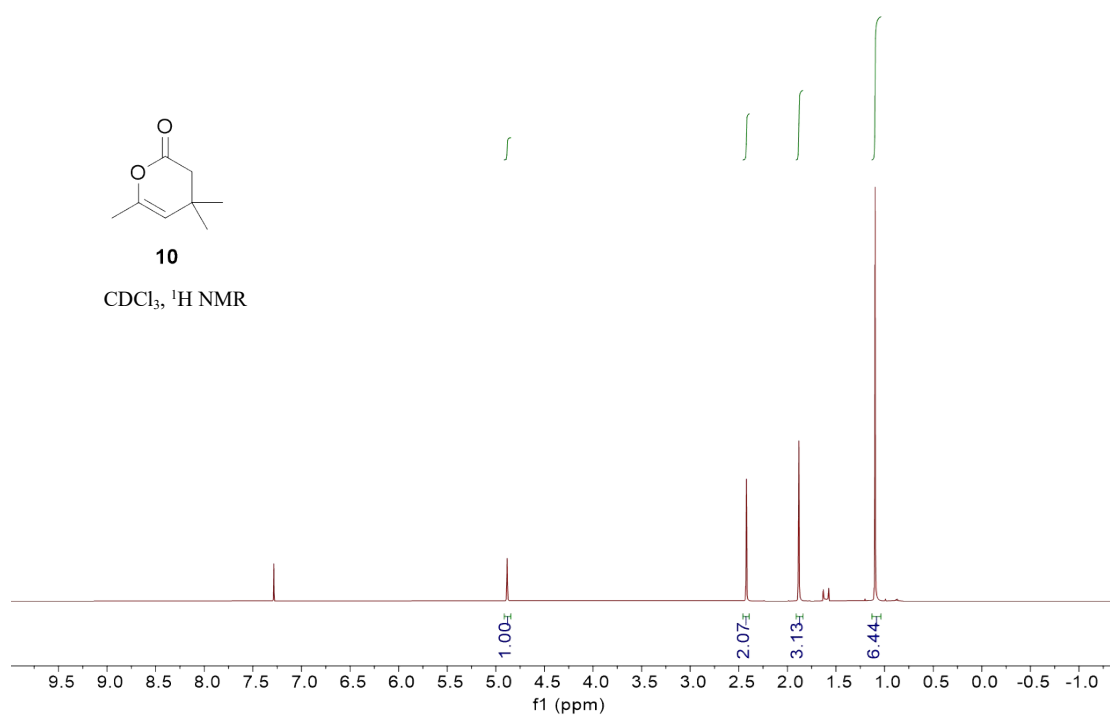
### 3. $^1\text{H}$ NMR and $^{13}\text{C}$ NMR Spectrum for all the compounds





**10**

CDCl<sub>3</sub>, <sup>1</sup>H NMR



— 169.29

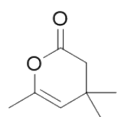
— 147.40

— 111.54  
— 111.24

— 43.28

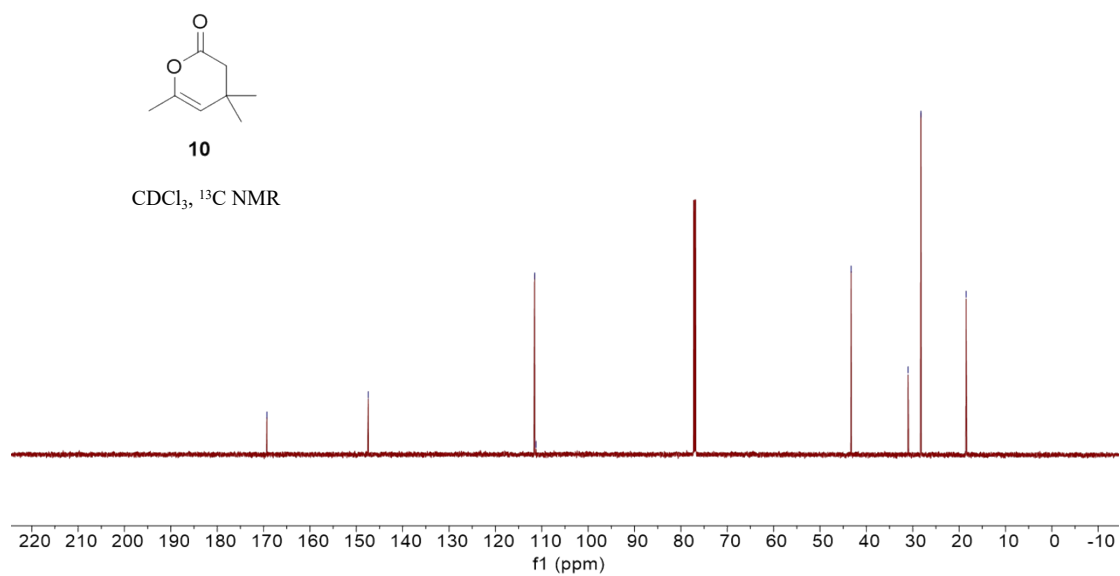
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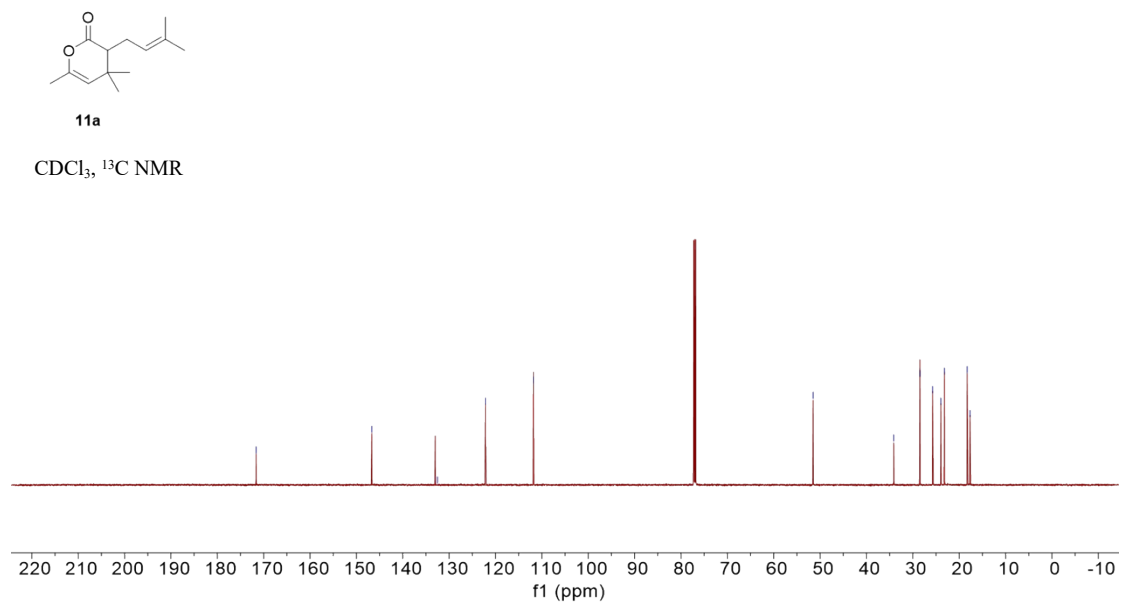
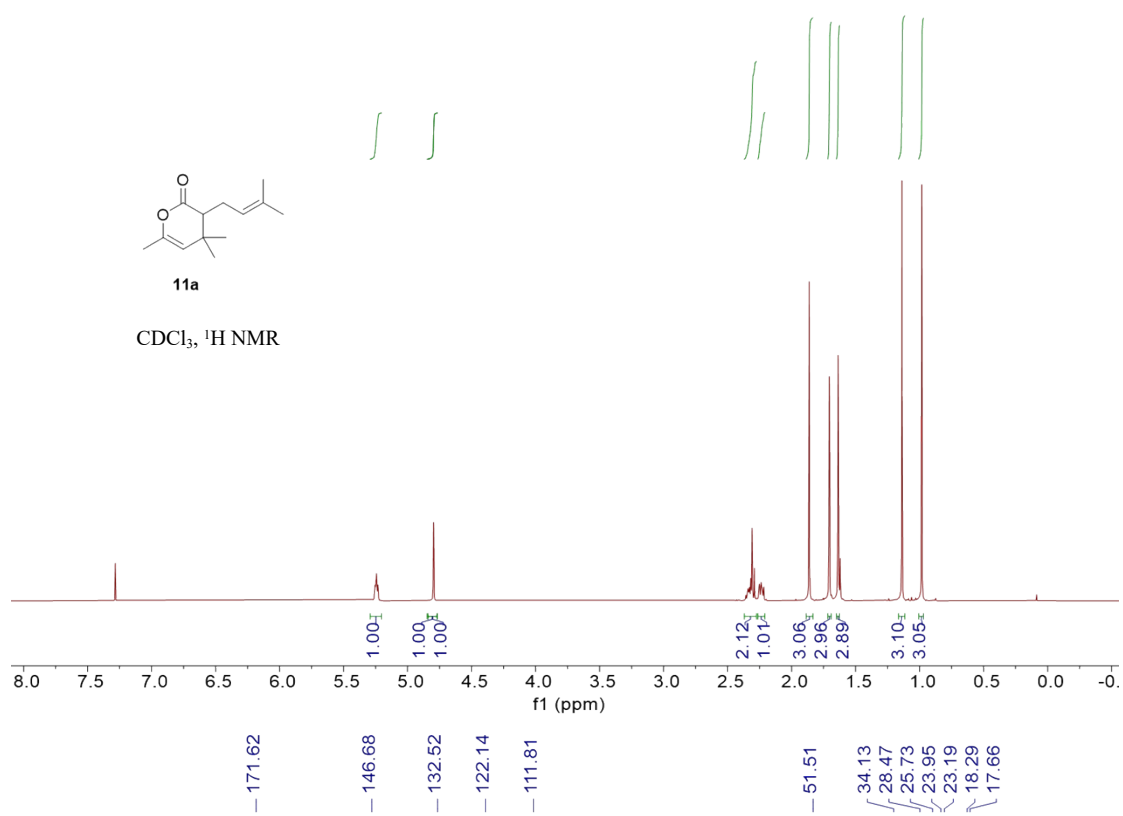
— 18.48

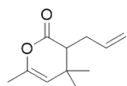


**10**

CDCl<sub>3</sub>, <sup>13</sup>C NMR

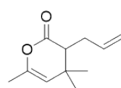
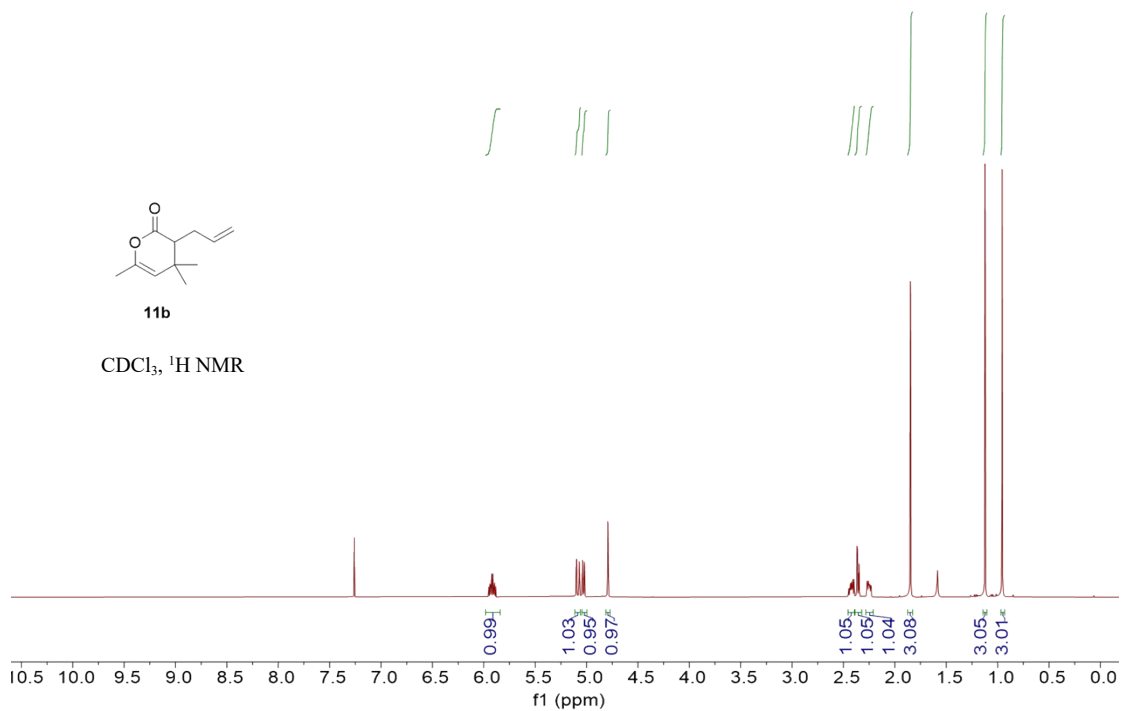






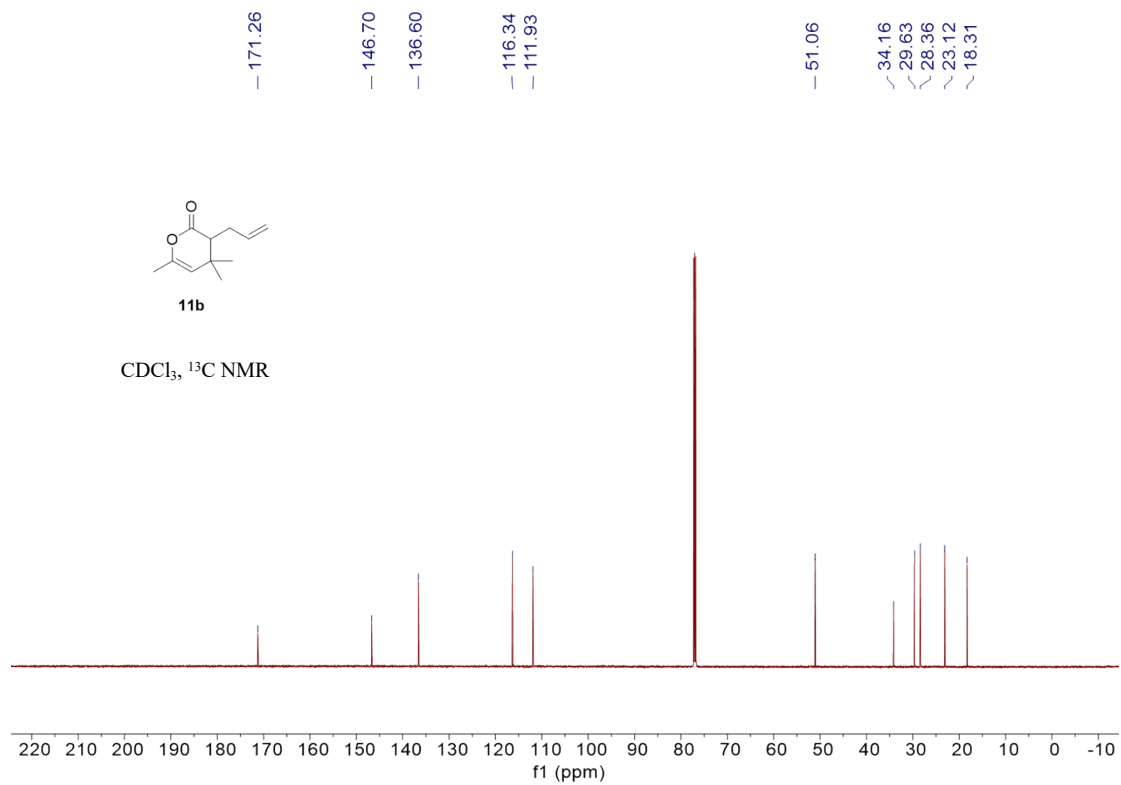
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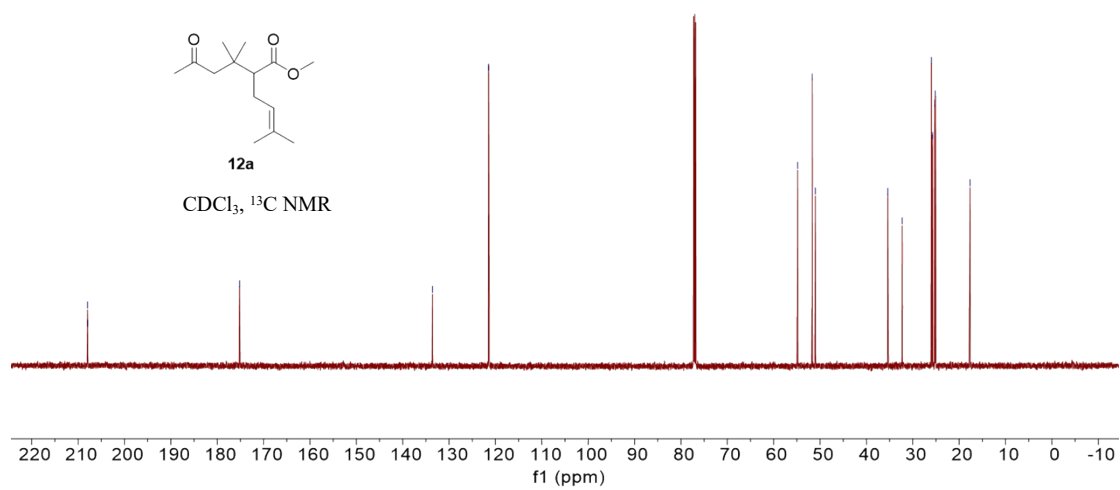
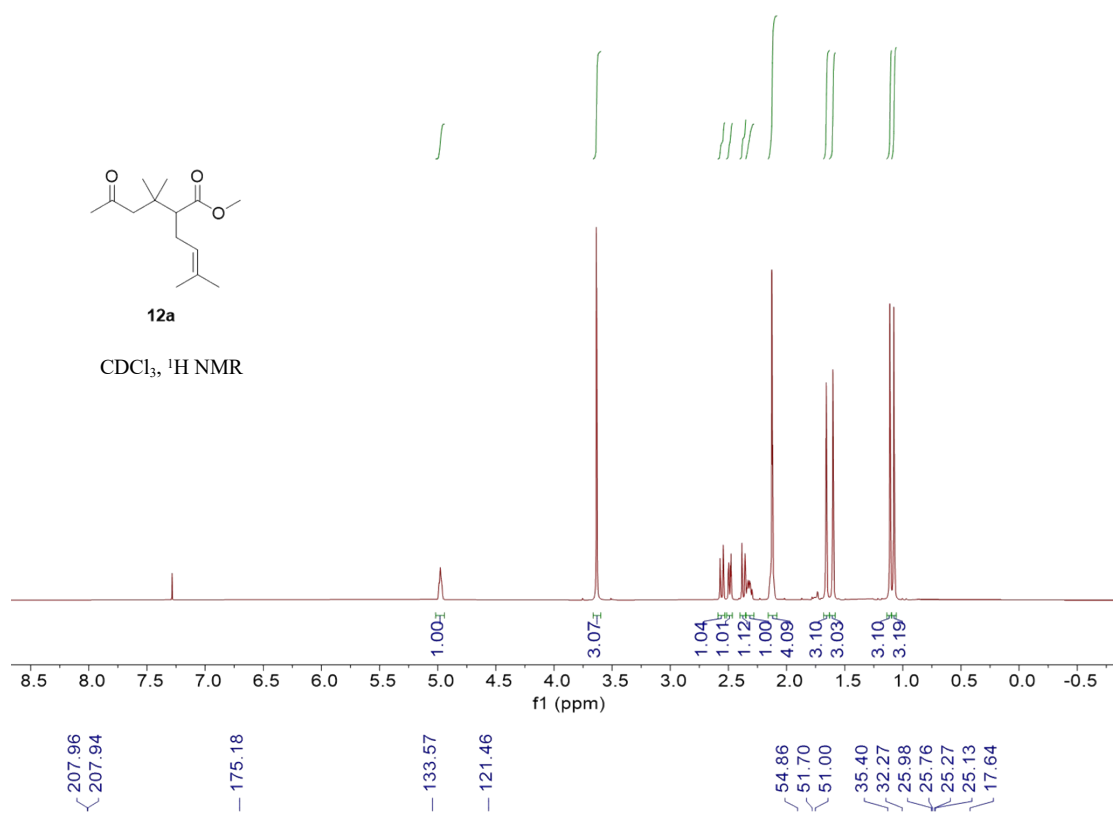
CDCl<sub>3</sub>, <sup>1</sup>H NMR

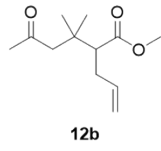


11b

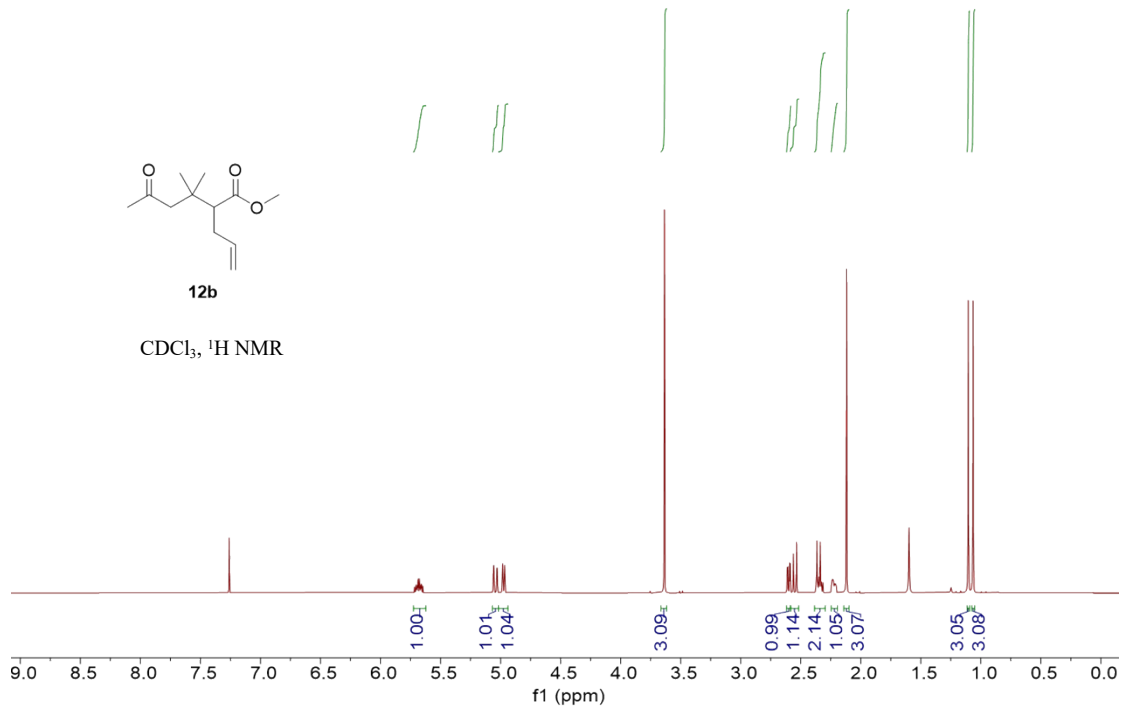
CDCl<sub>3</sub>, <sup>13</sup>C NMR







CDCl<sub>3</sub>, <sup>1</sup>H NMR



-207.88

-174.79

-135.91

-116.59

54.17

51.74

51.03

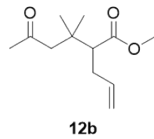
35.42

32.26

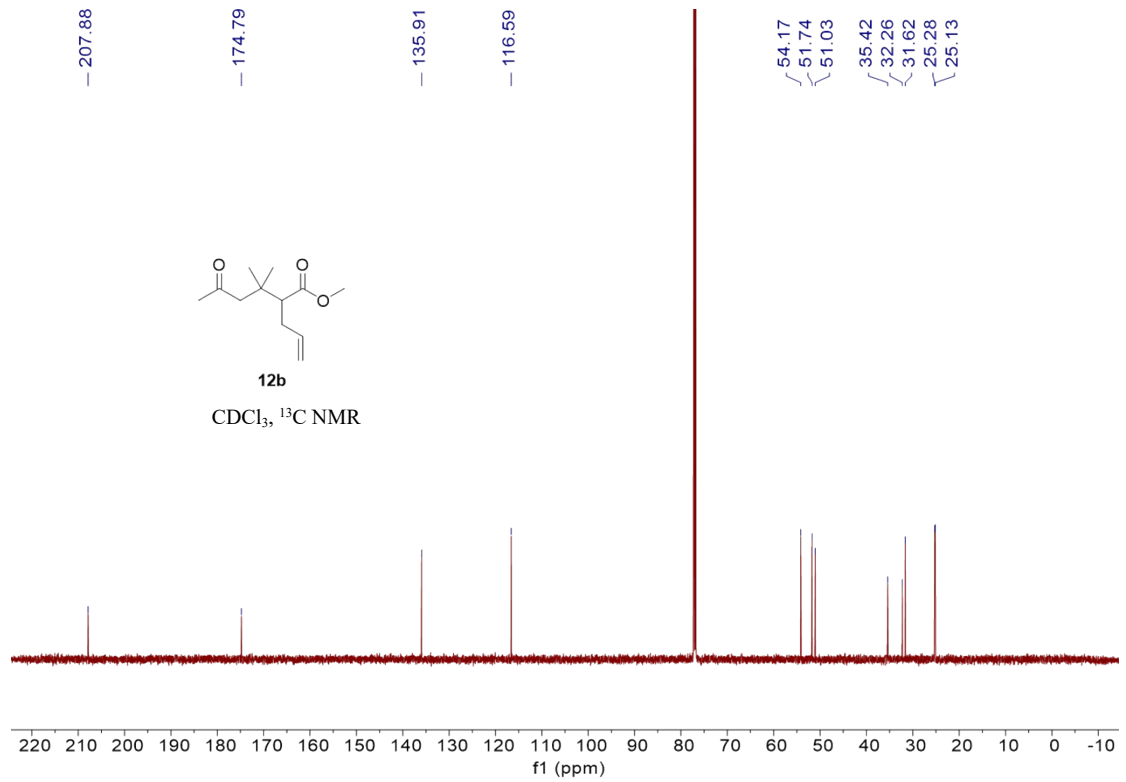
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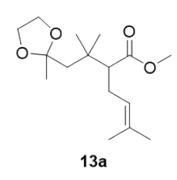
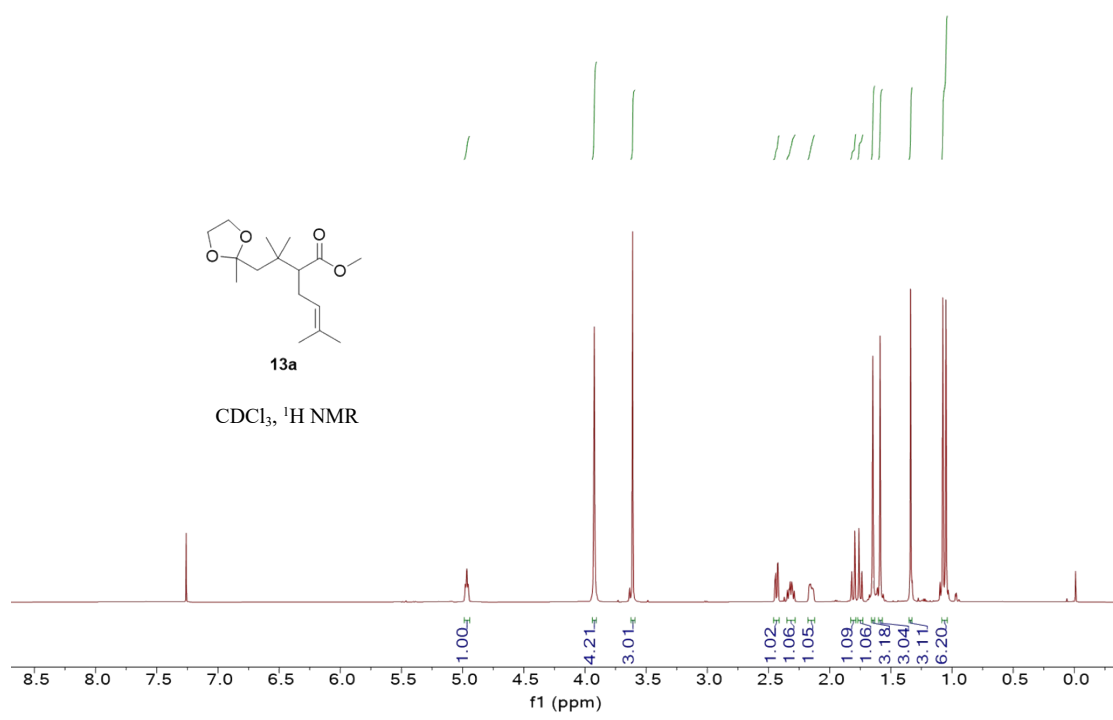
25.28

25.13



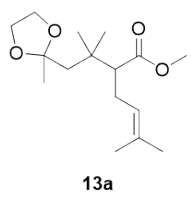
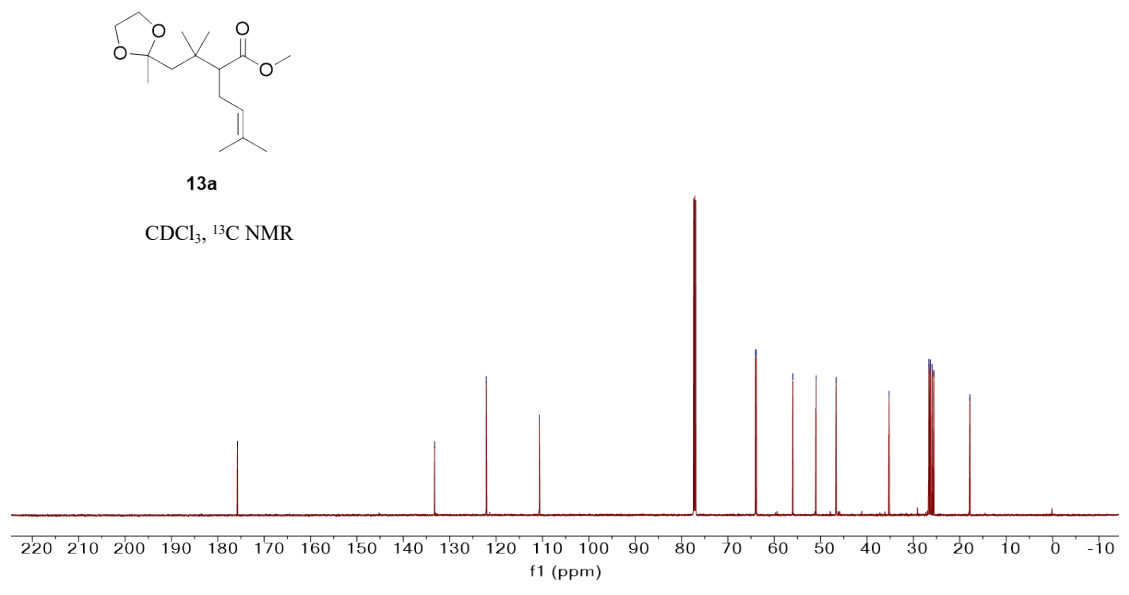
CDCl<sub>3</sub>, <sup>13</sup>C NMR





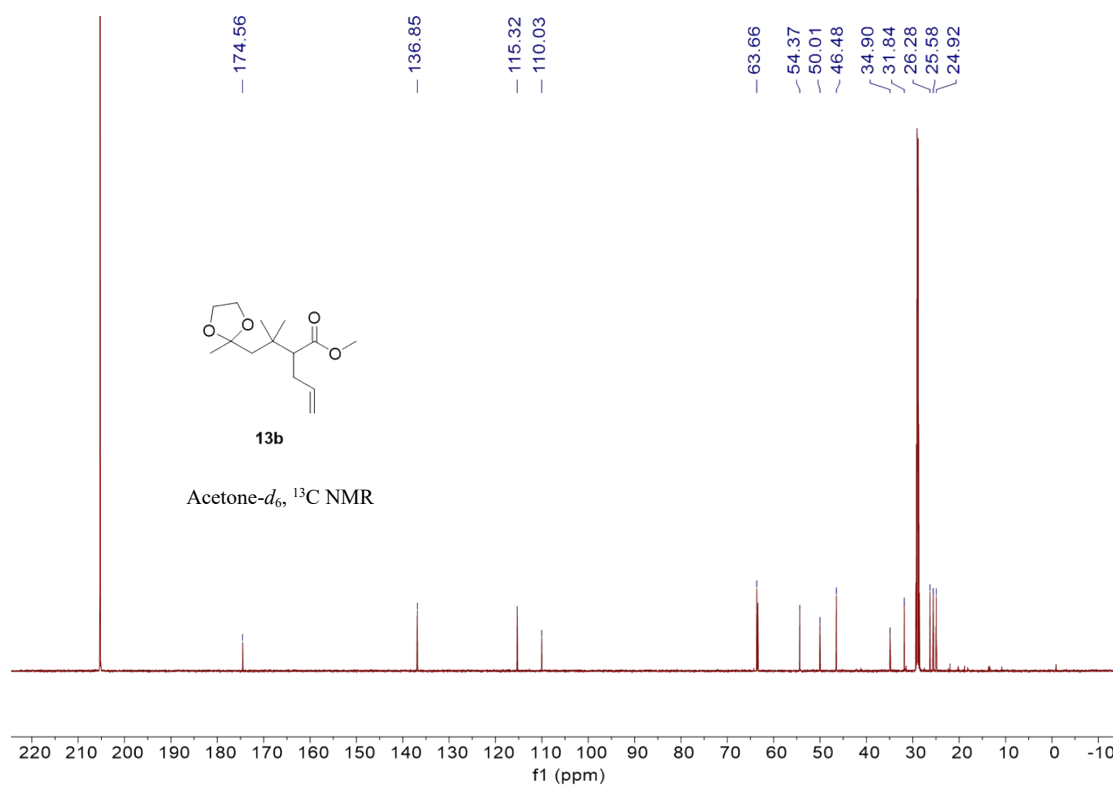
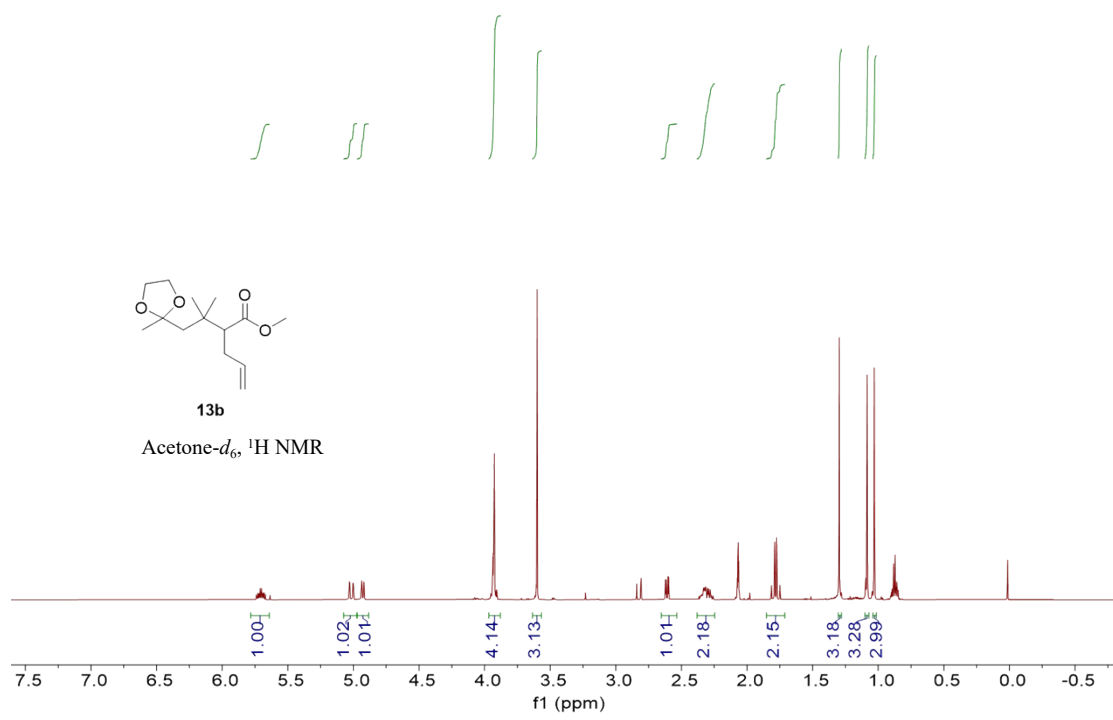
CDCl<sub>3</sub>, <sup>1</sup>H NMR

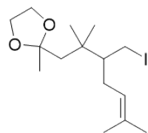
- 175.76
- 133.26
- 122.10
- 110.68
- 64.07
- 63.89
- 55.99
- 51.00
- 46.65
- 35.26
- 26.66
- 26.39
- 26.34
- 25.96
- 25.60
- 17.81



CDCl<sub>3</sub>, <sup>13</sup>C NMR

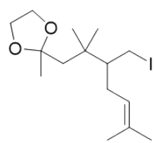
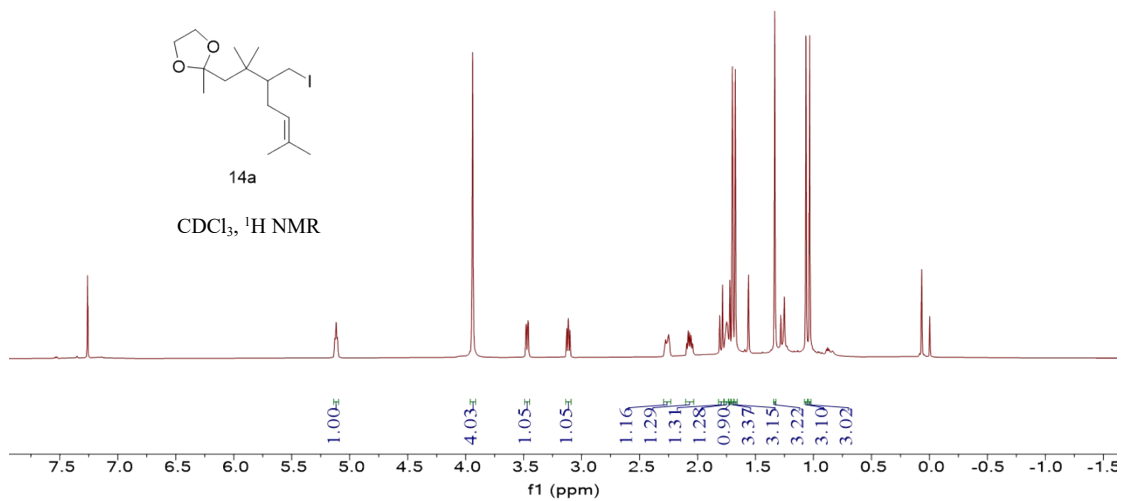






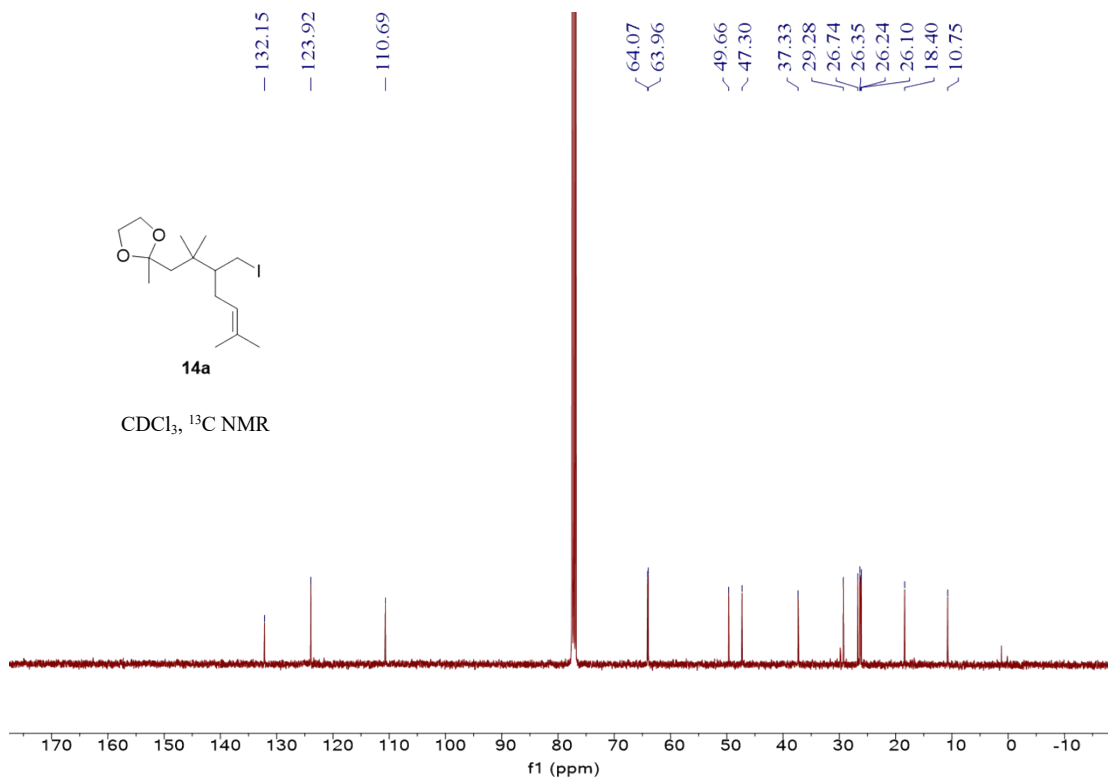
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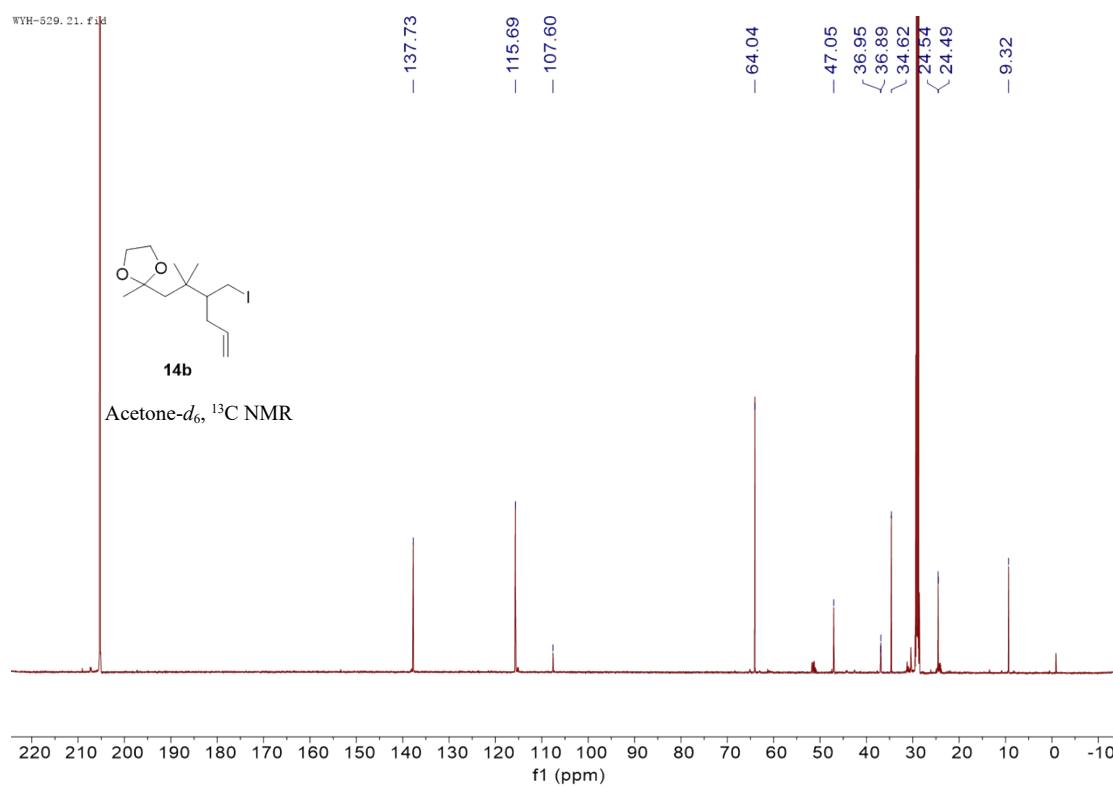
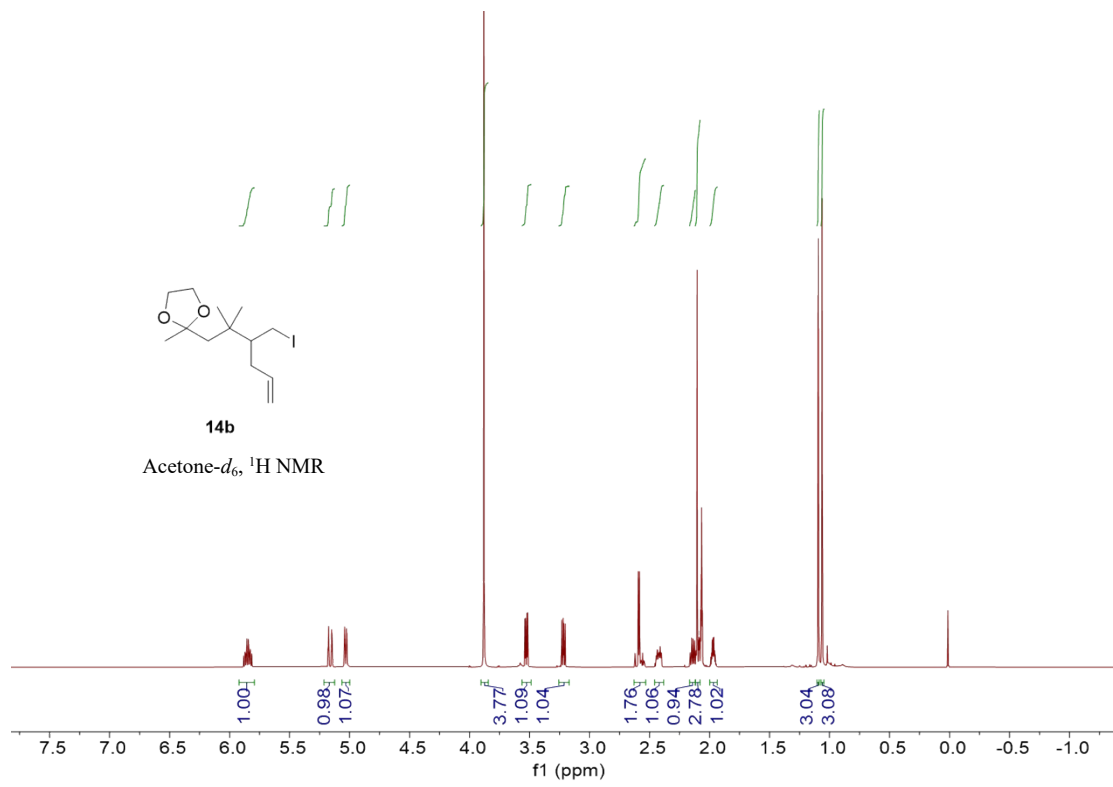
CDCl<sub>3</sub>, <sup>1</sup>H NMR

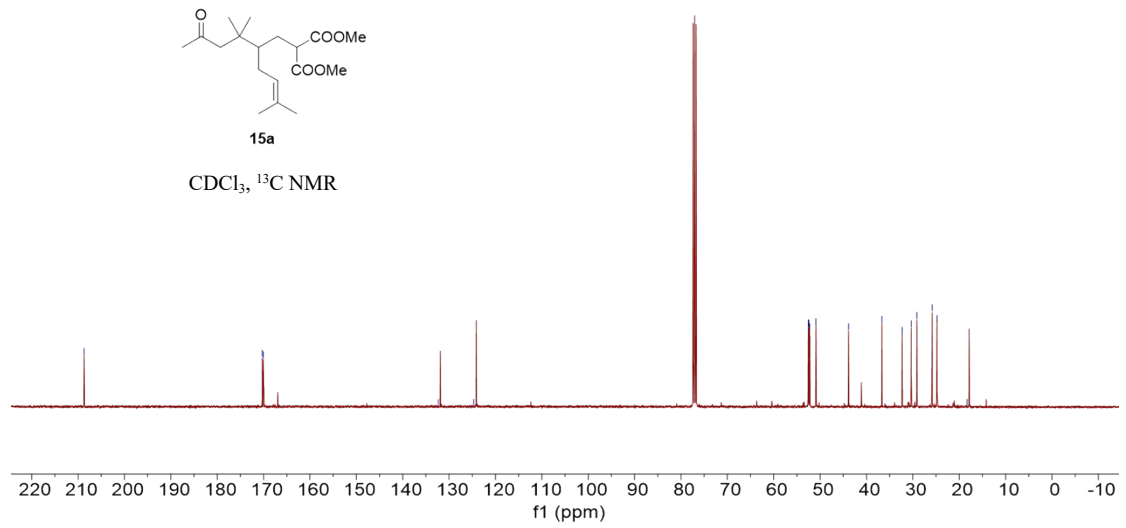
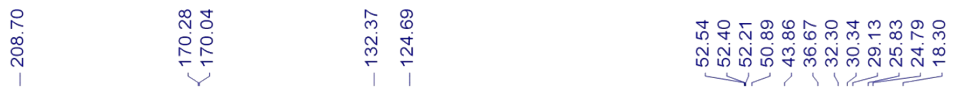
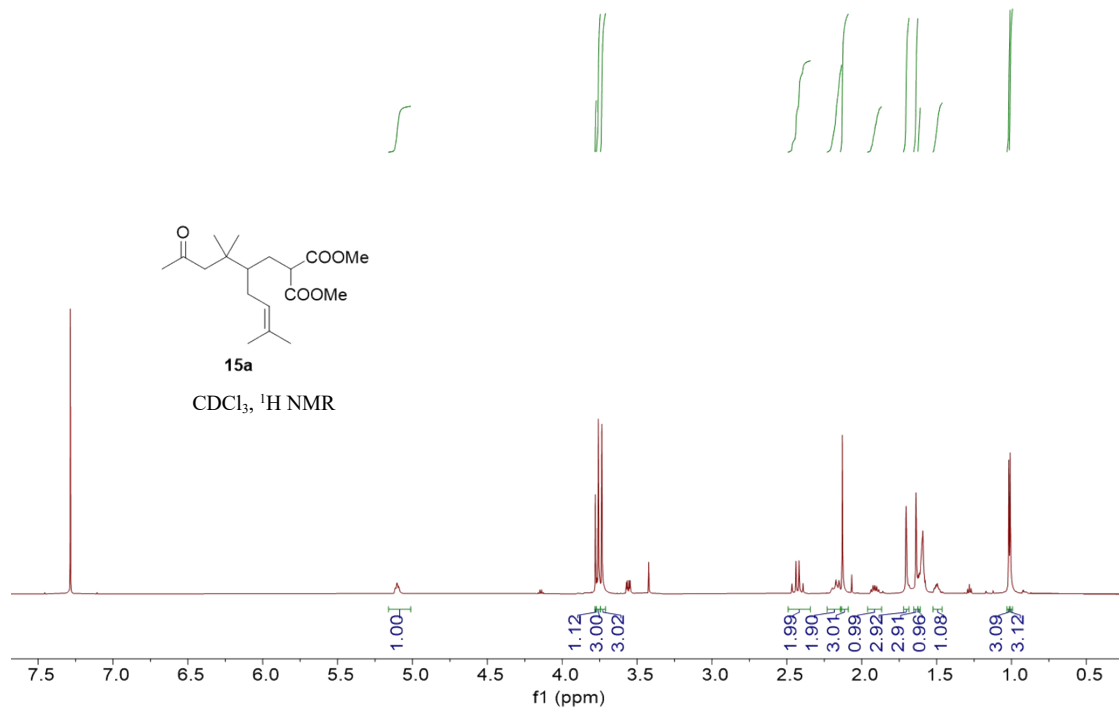


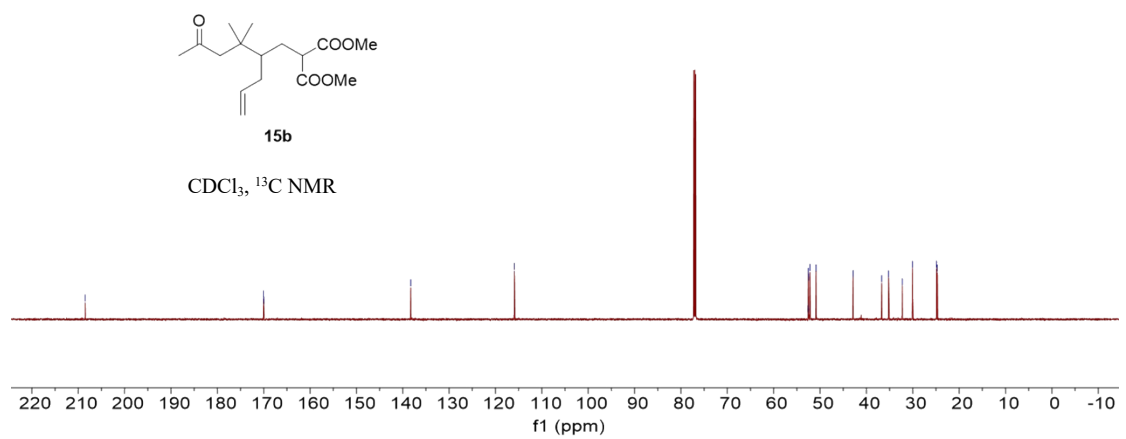
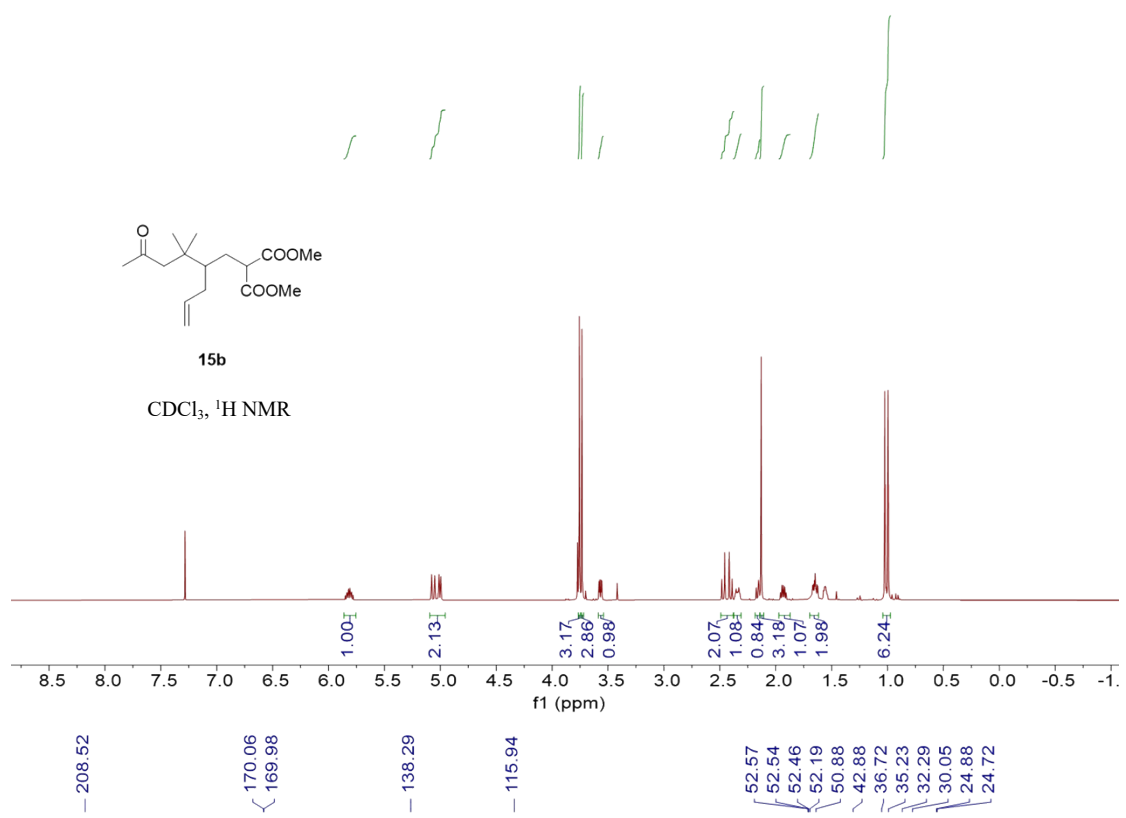
14a

CDCl<sub>3</sub>, <sup>13</sup>C NMR

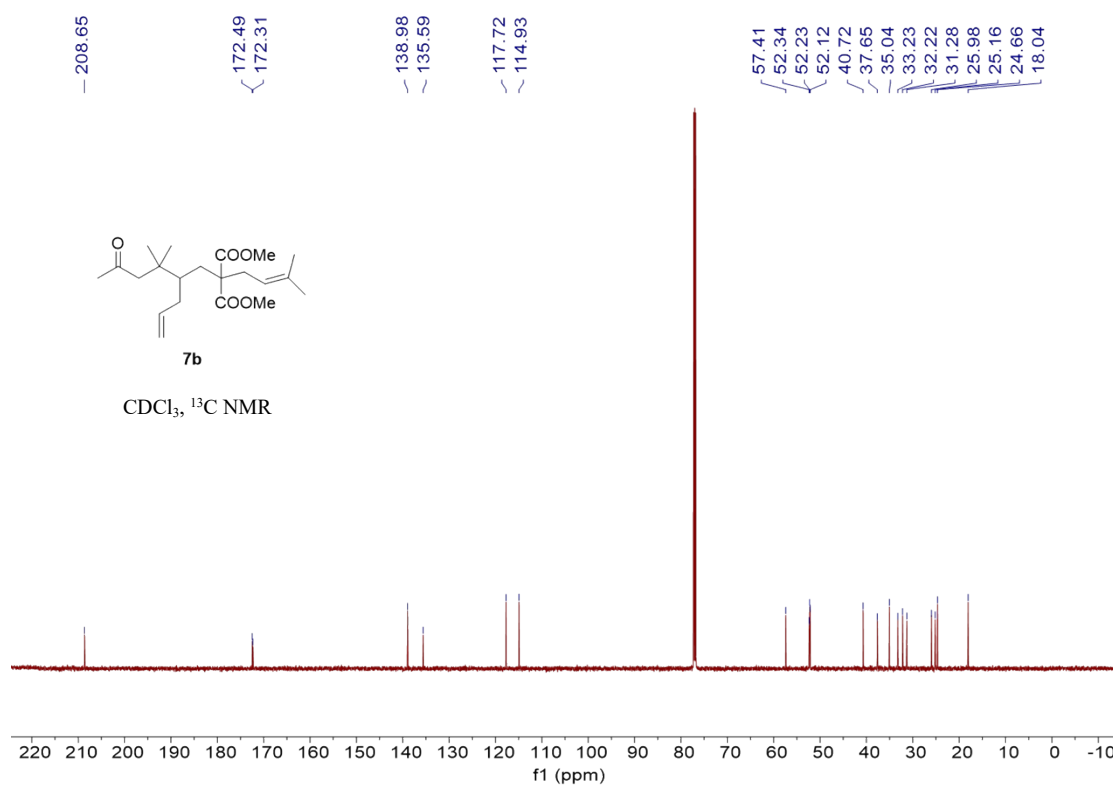
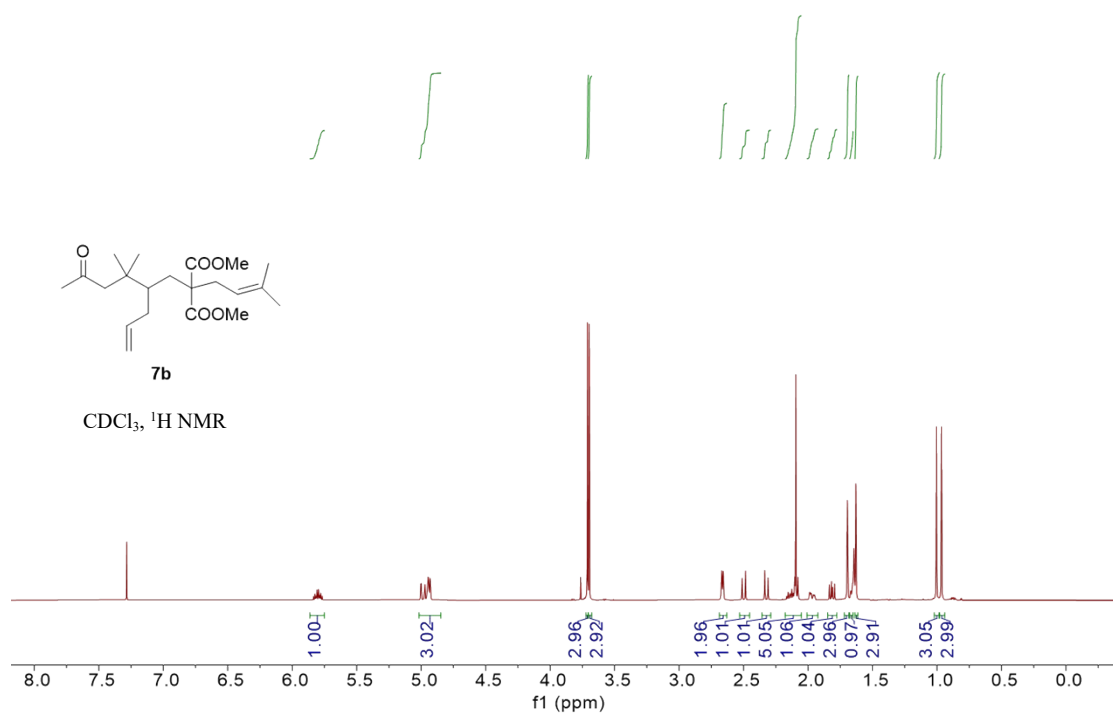


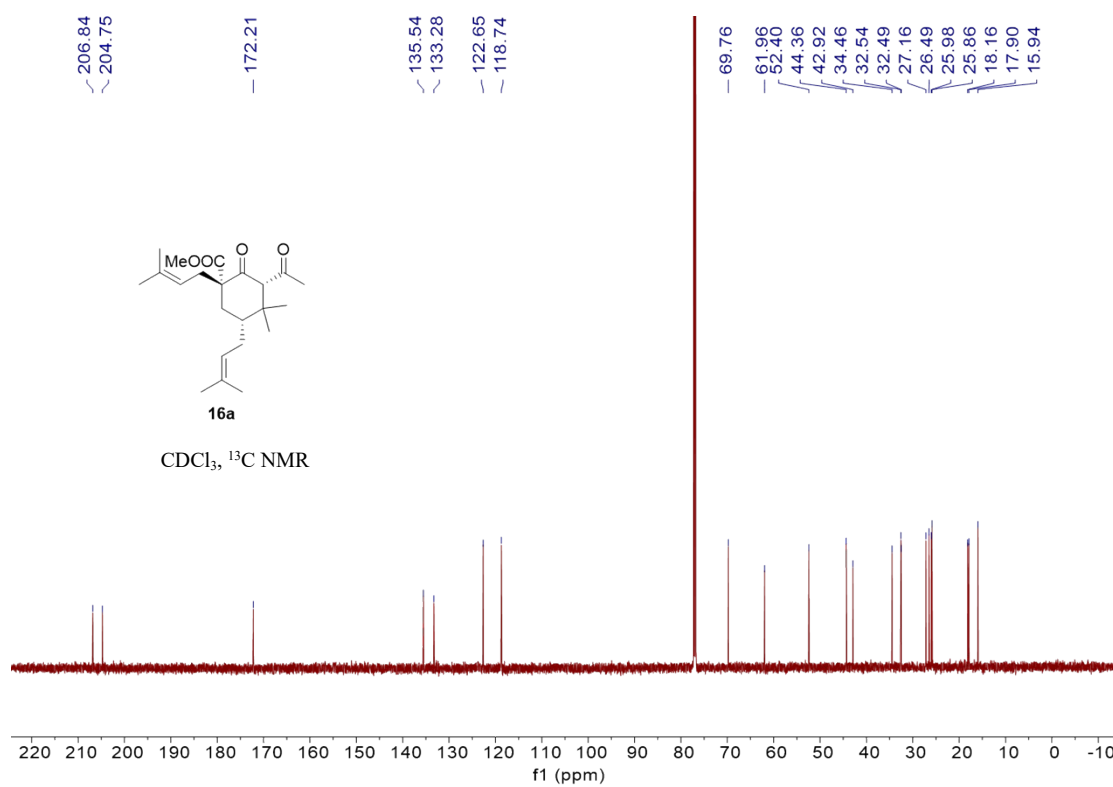
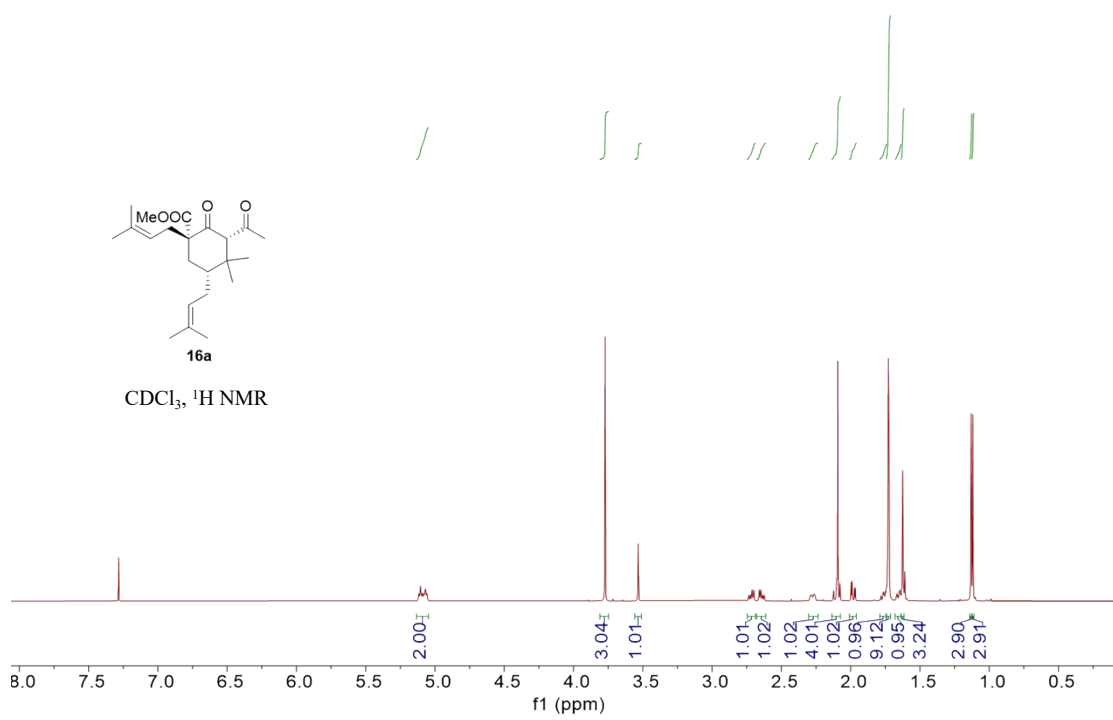




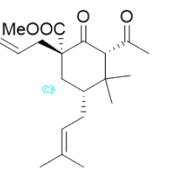
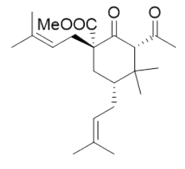
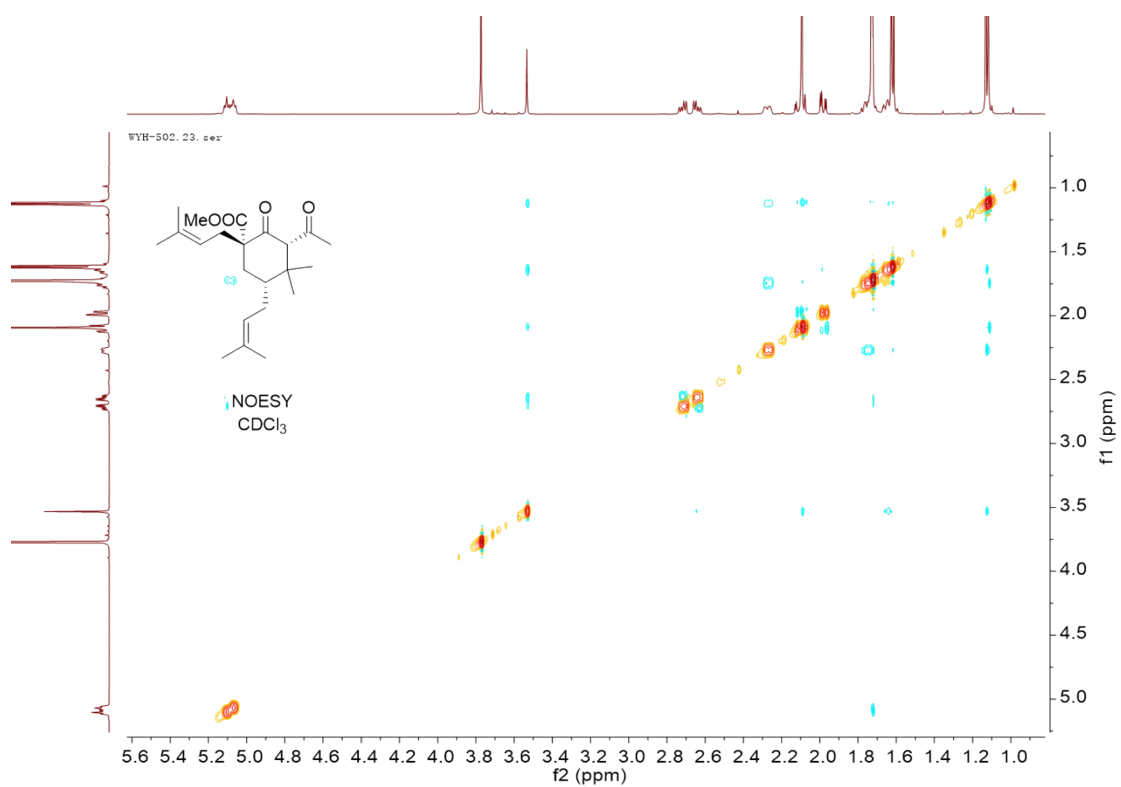
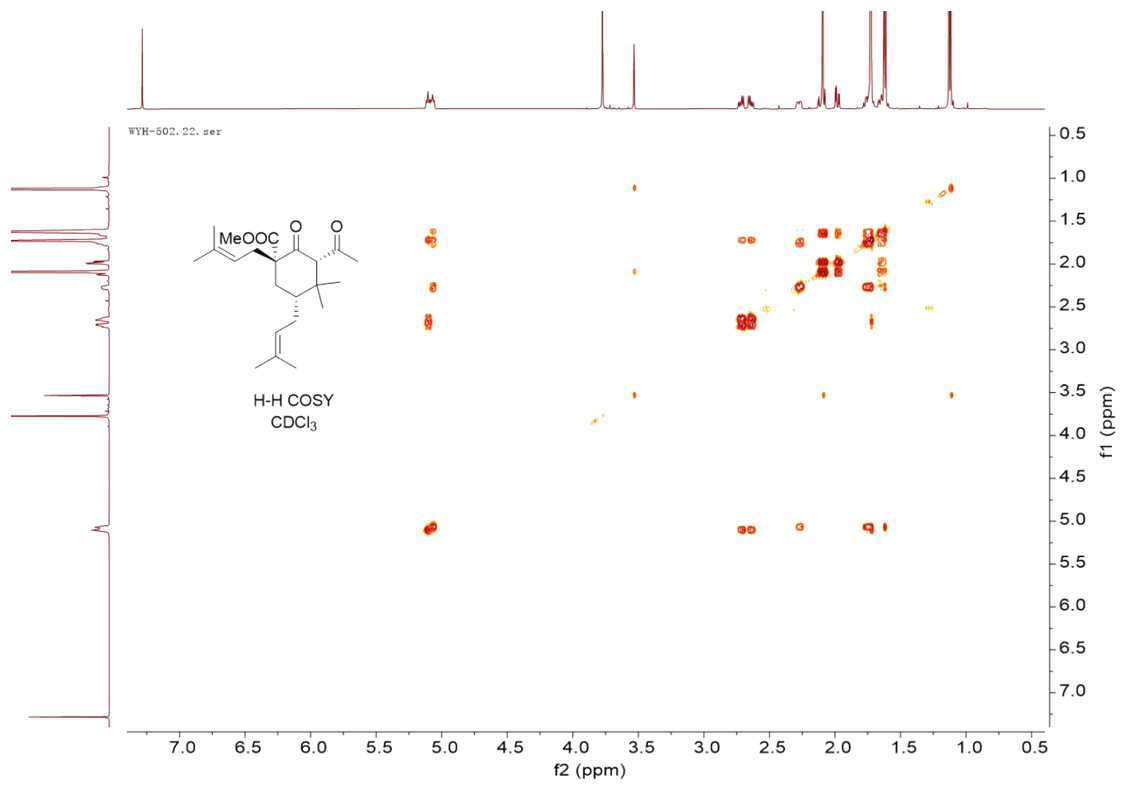


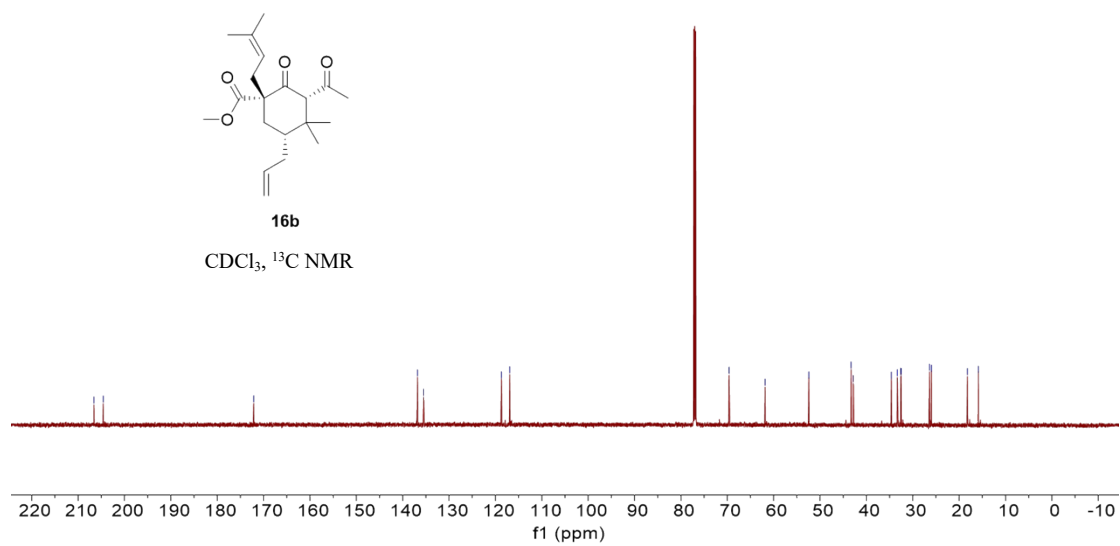
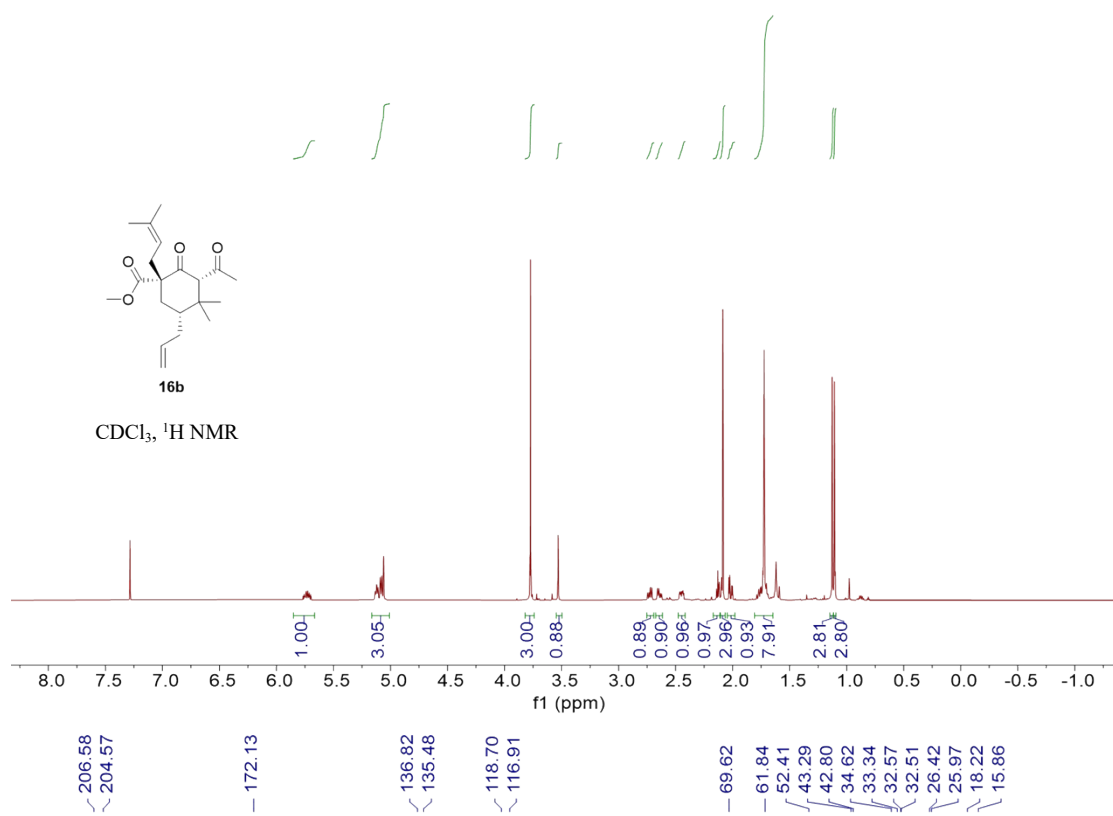


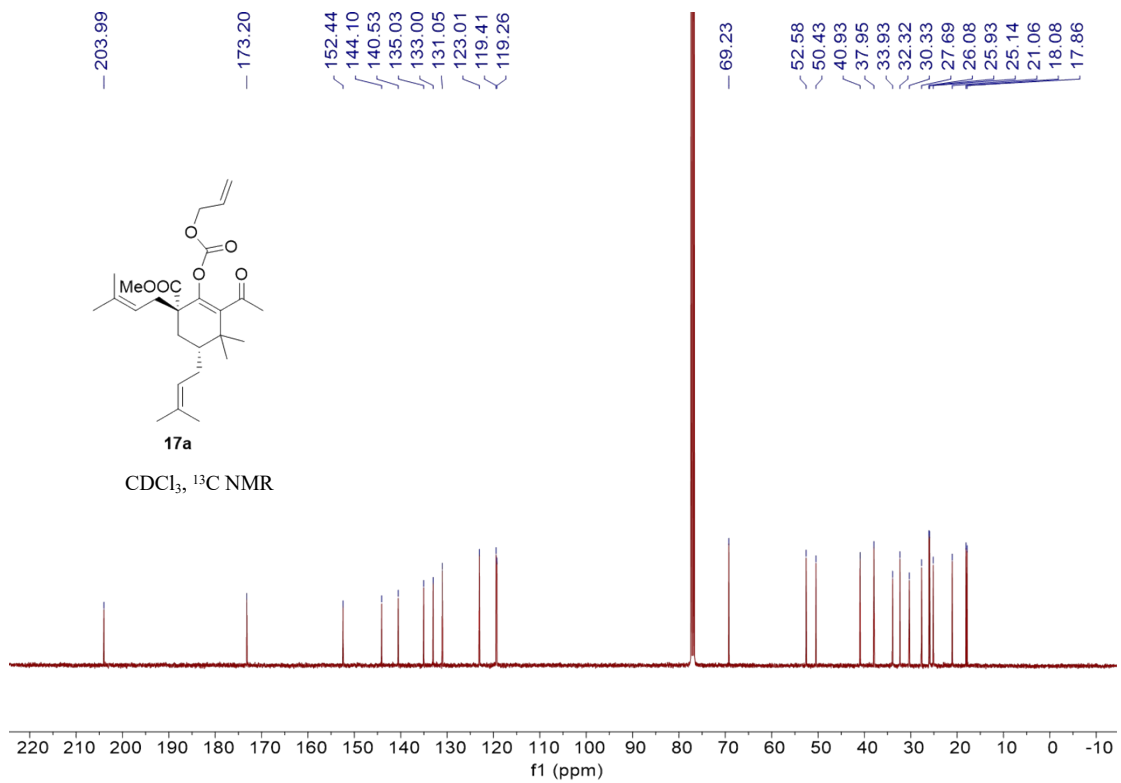
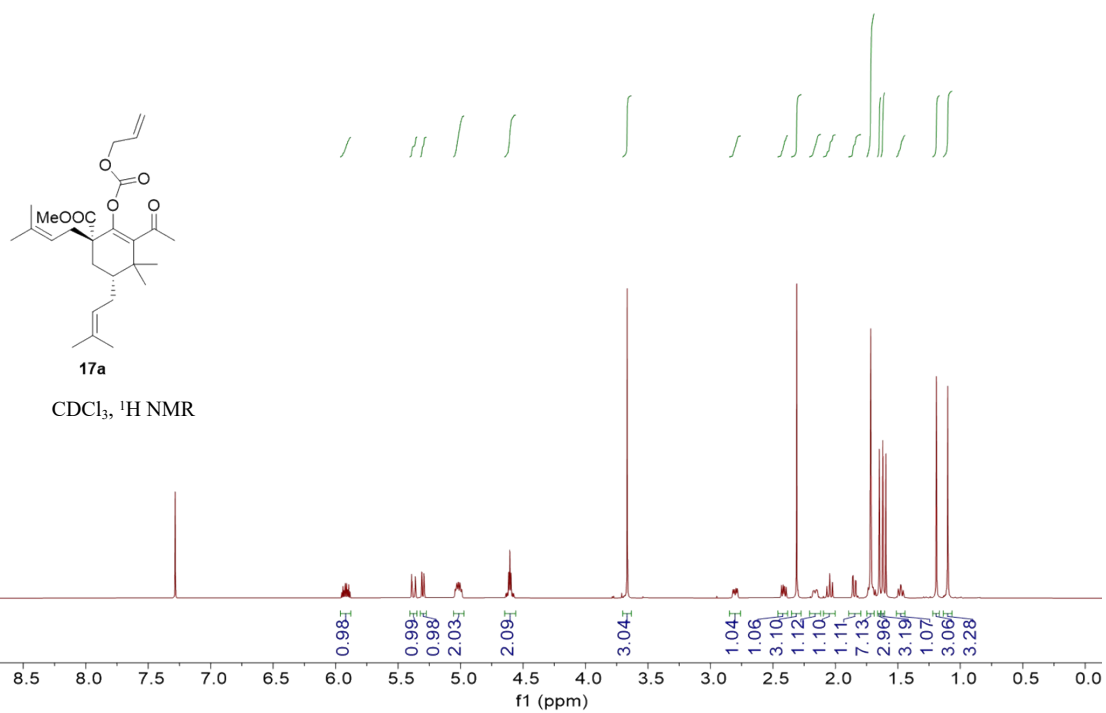


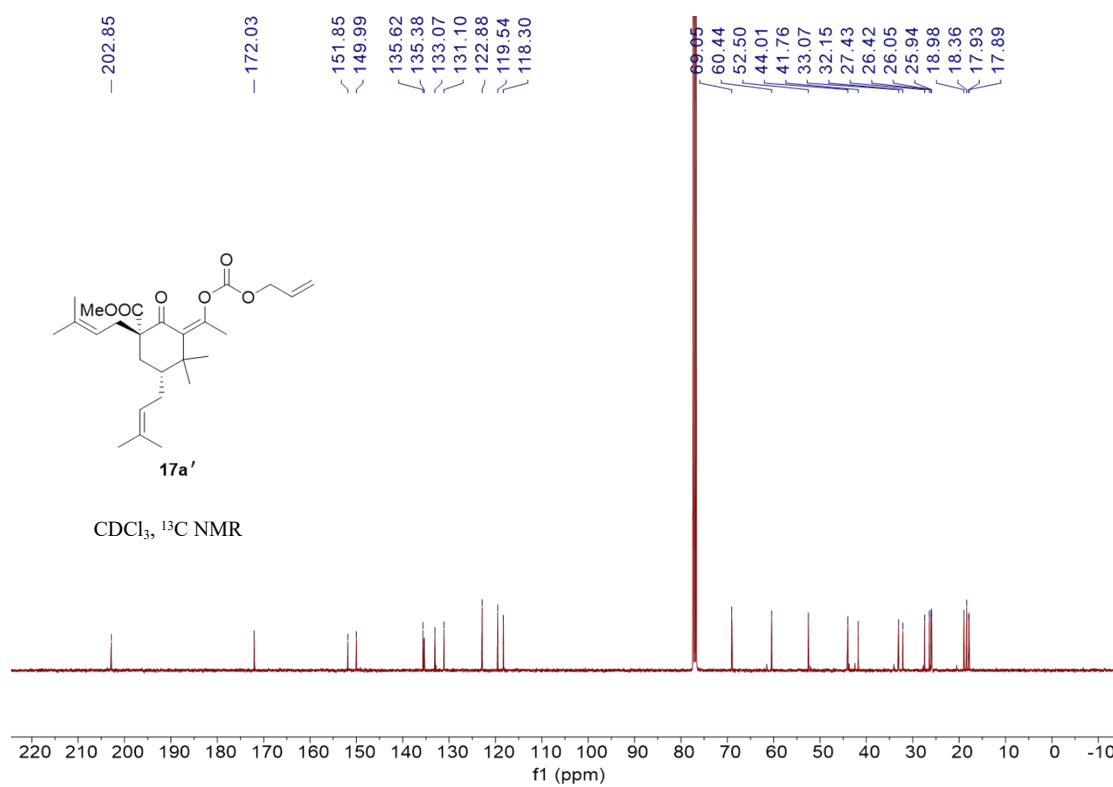
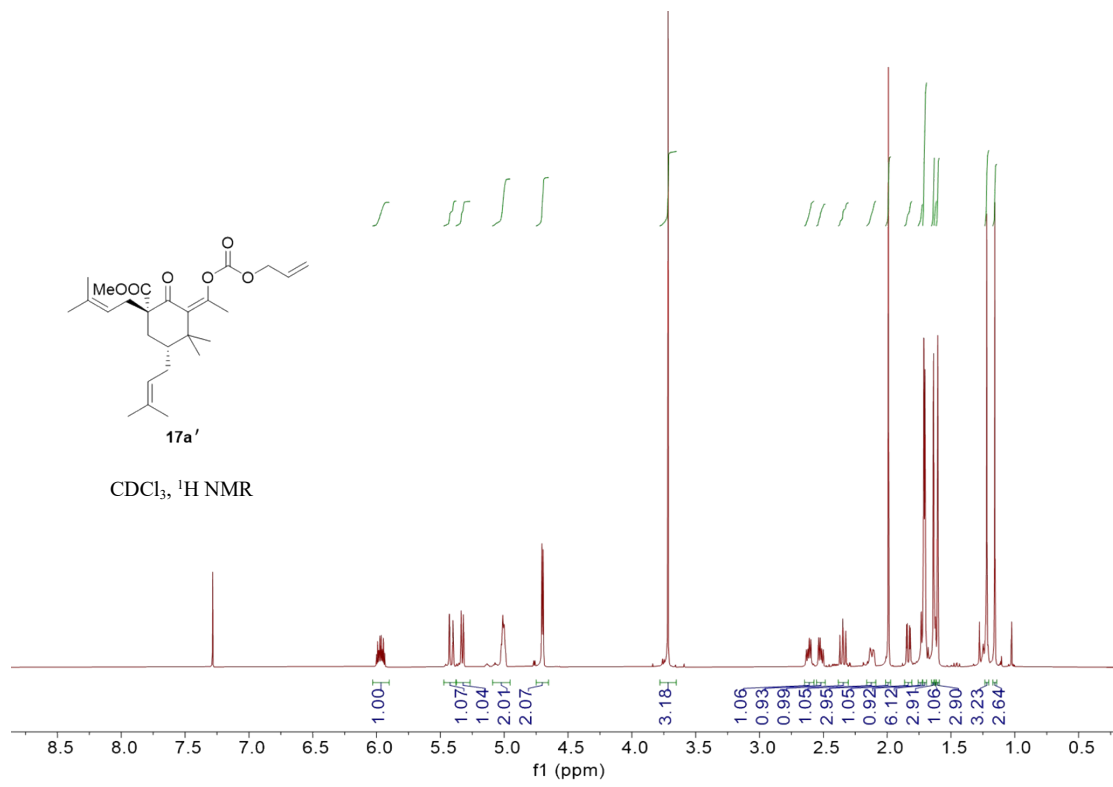


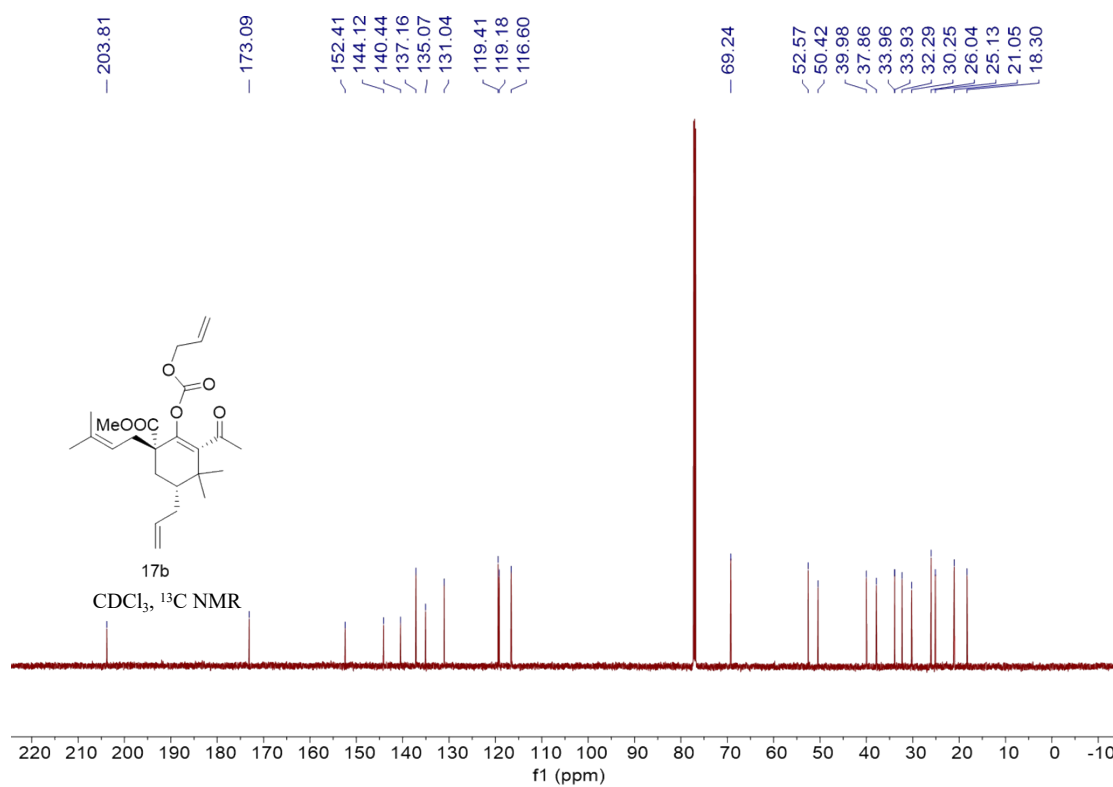
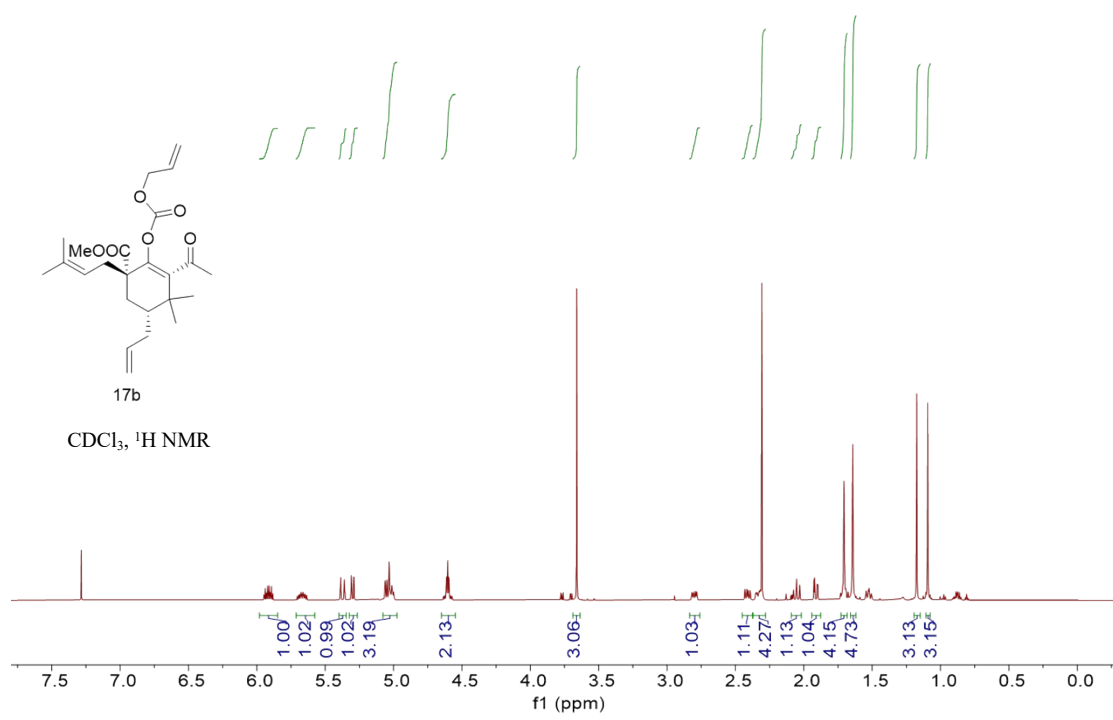


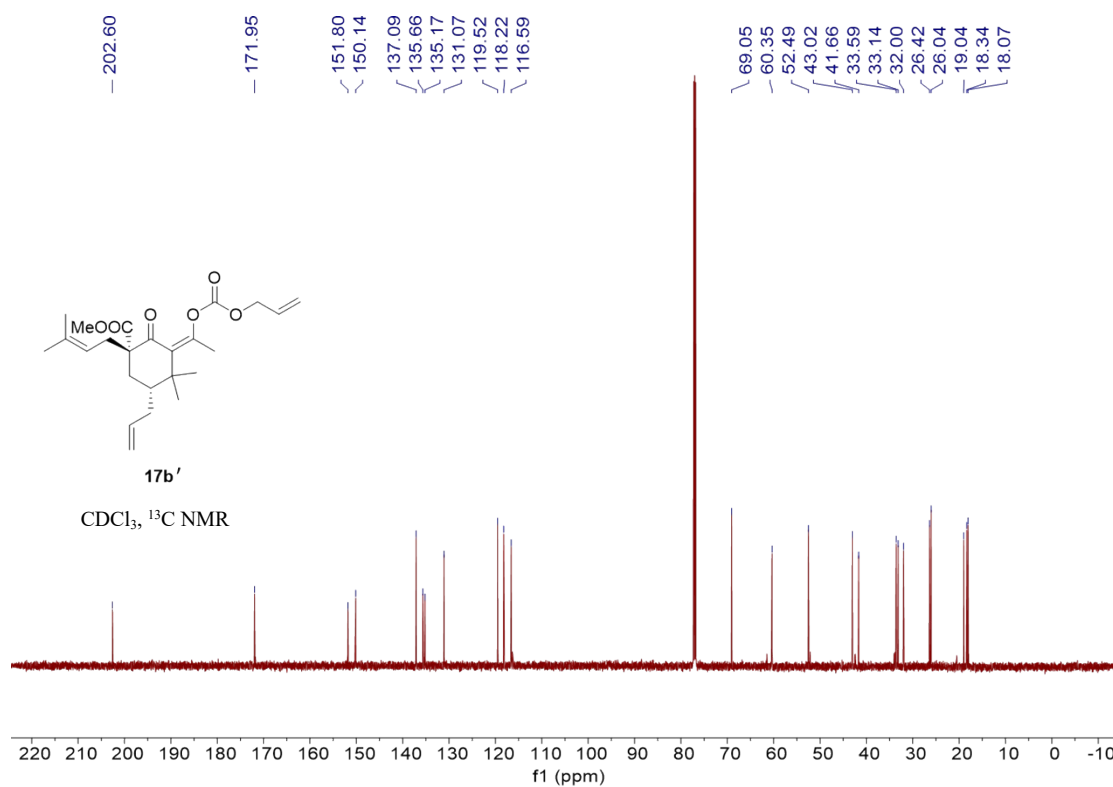
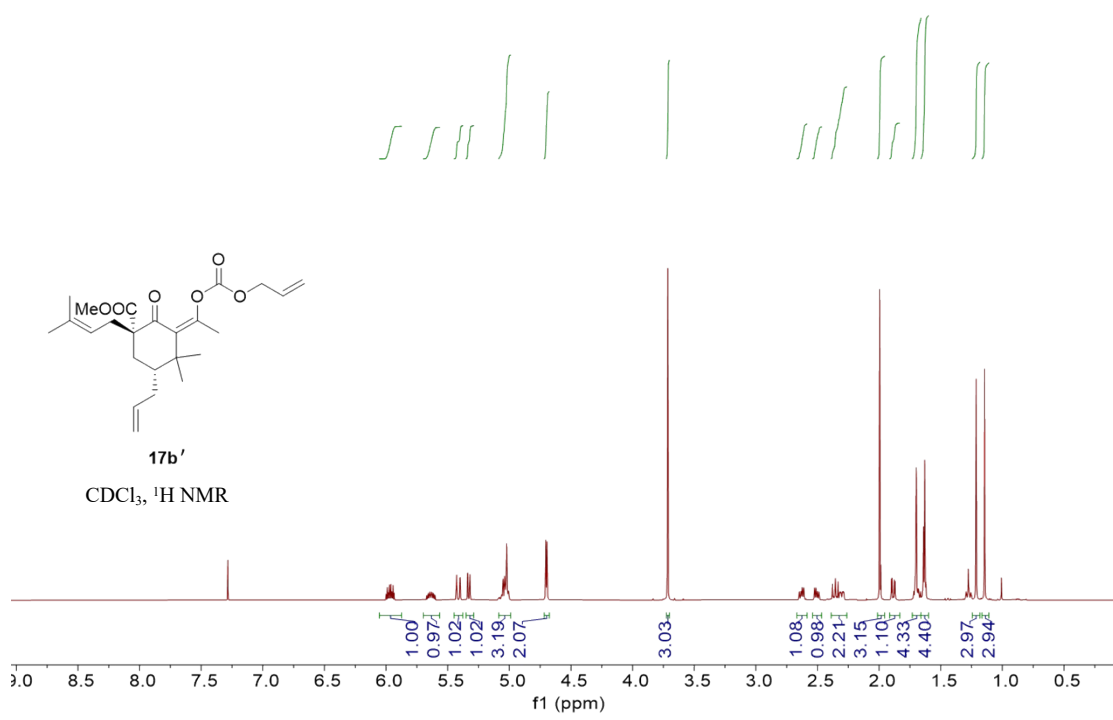


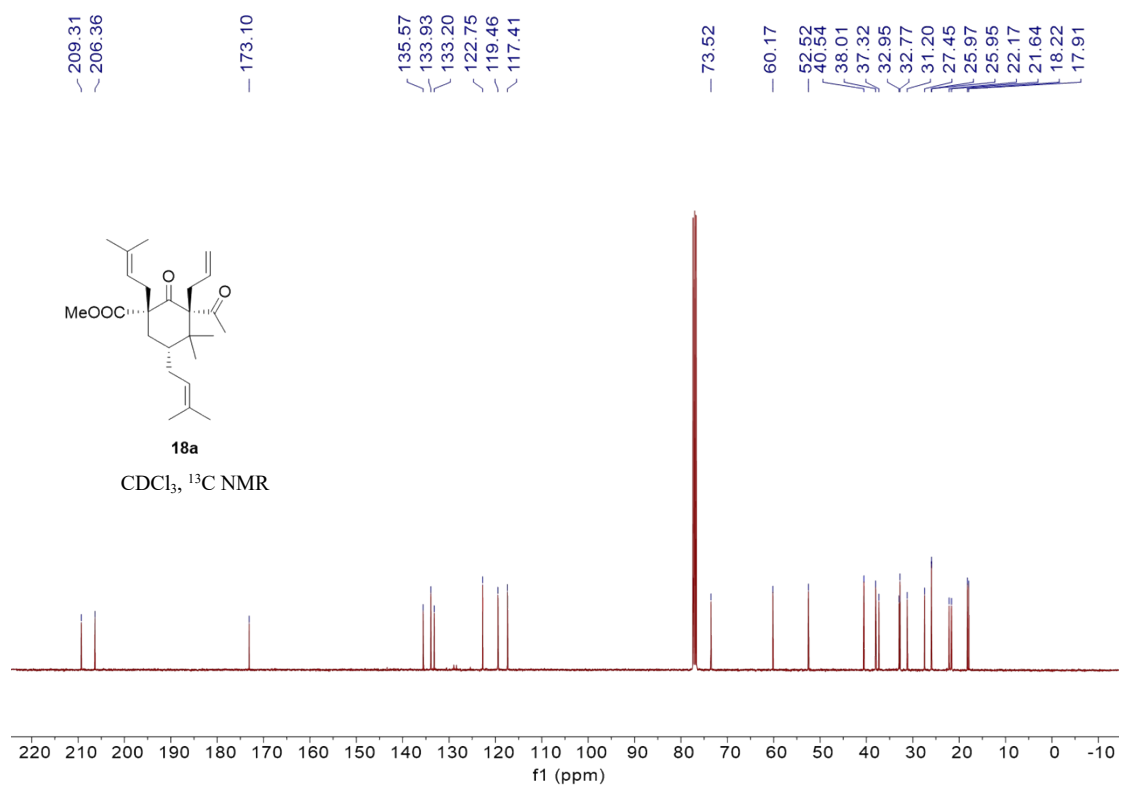
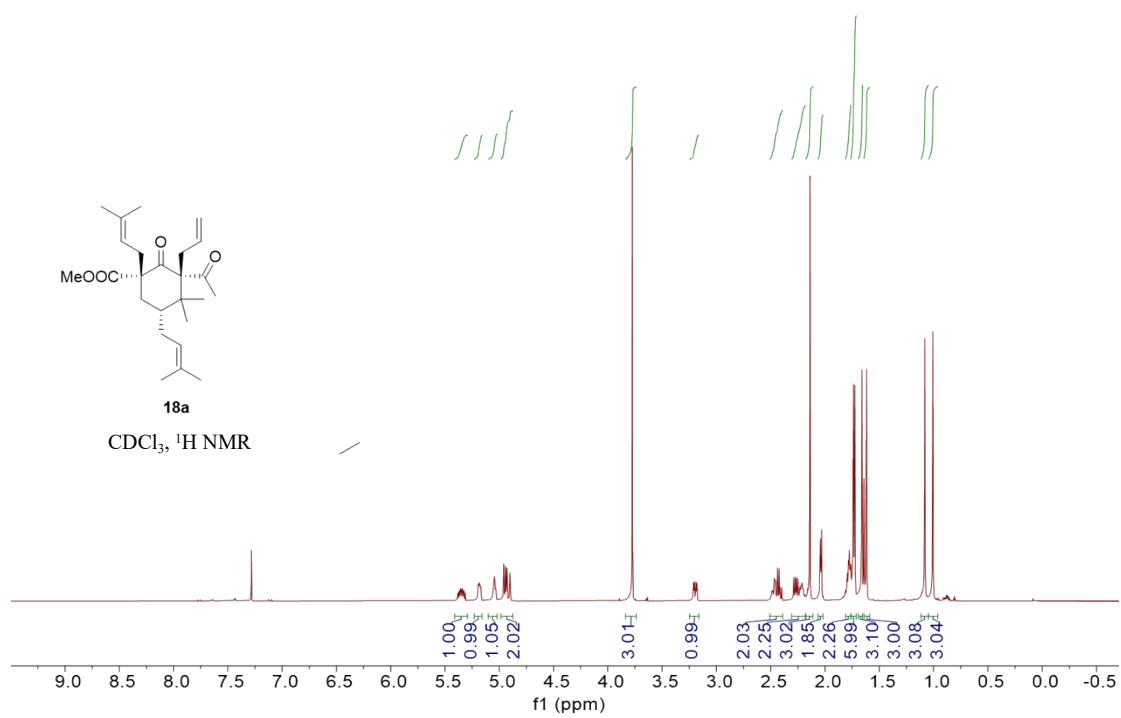


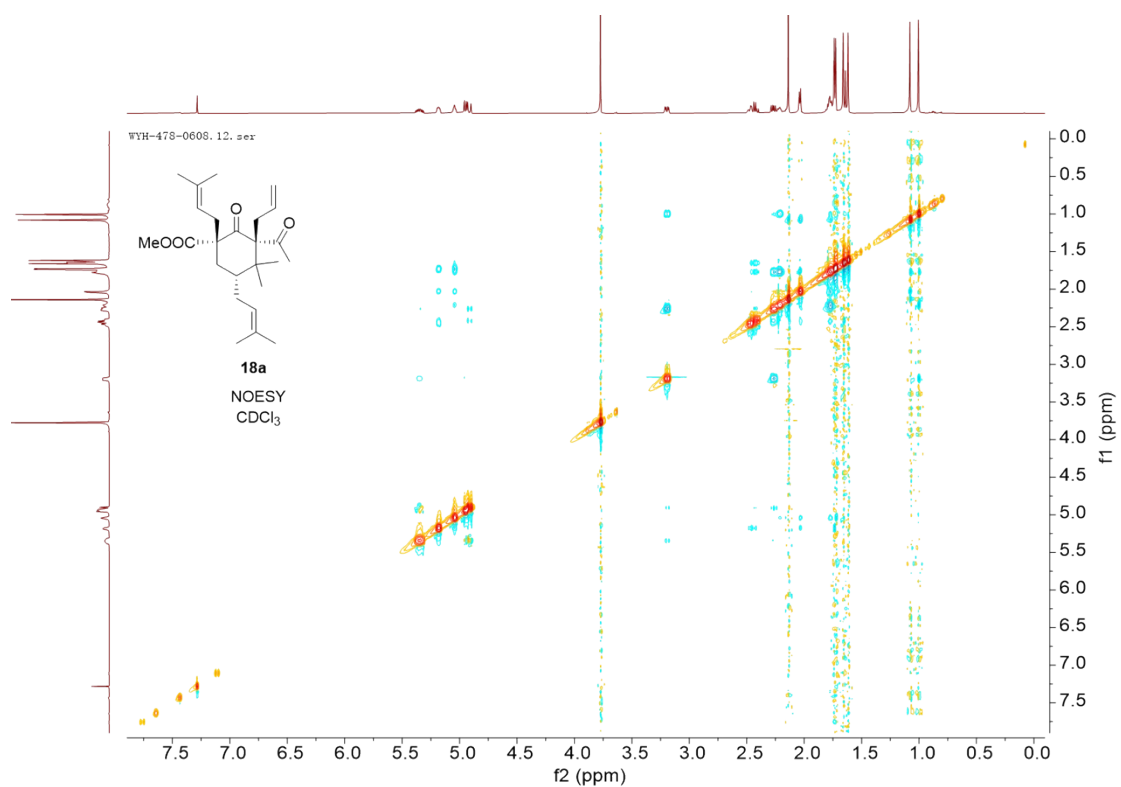
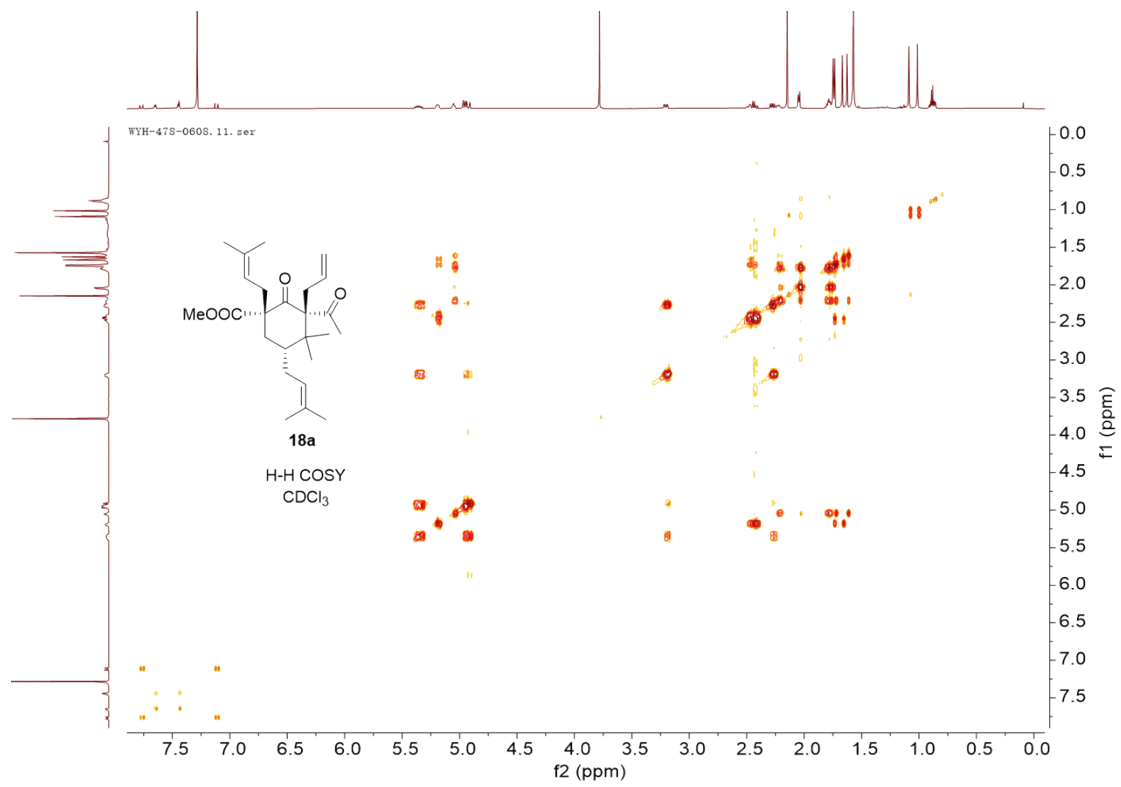




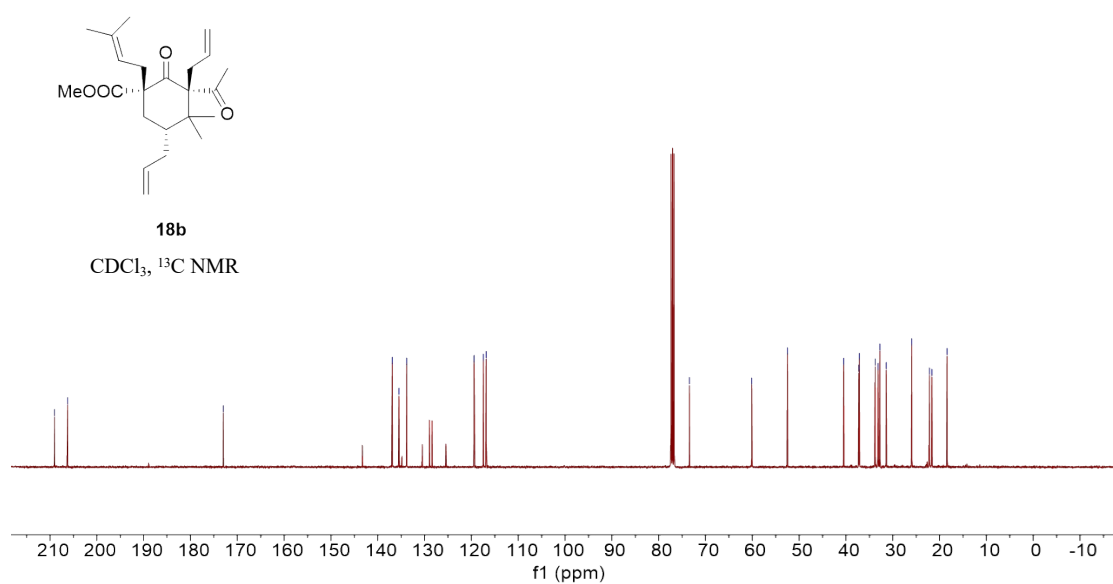
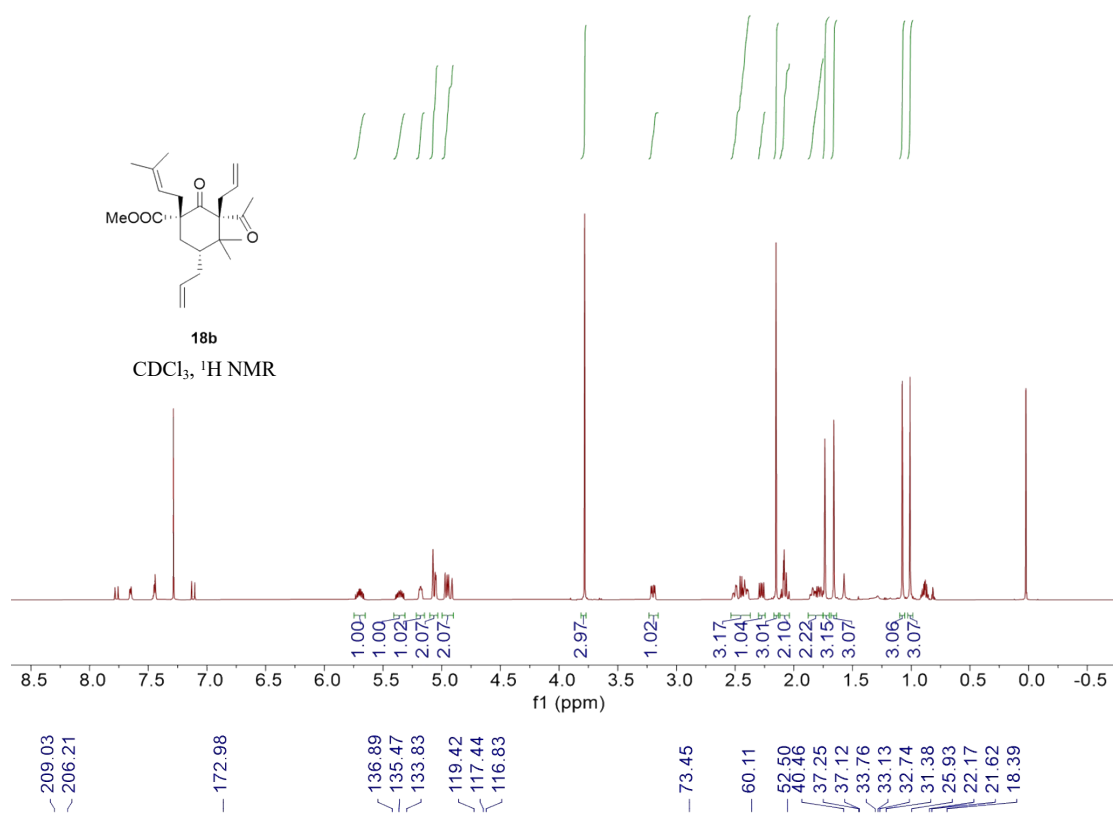


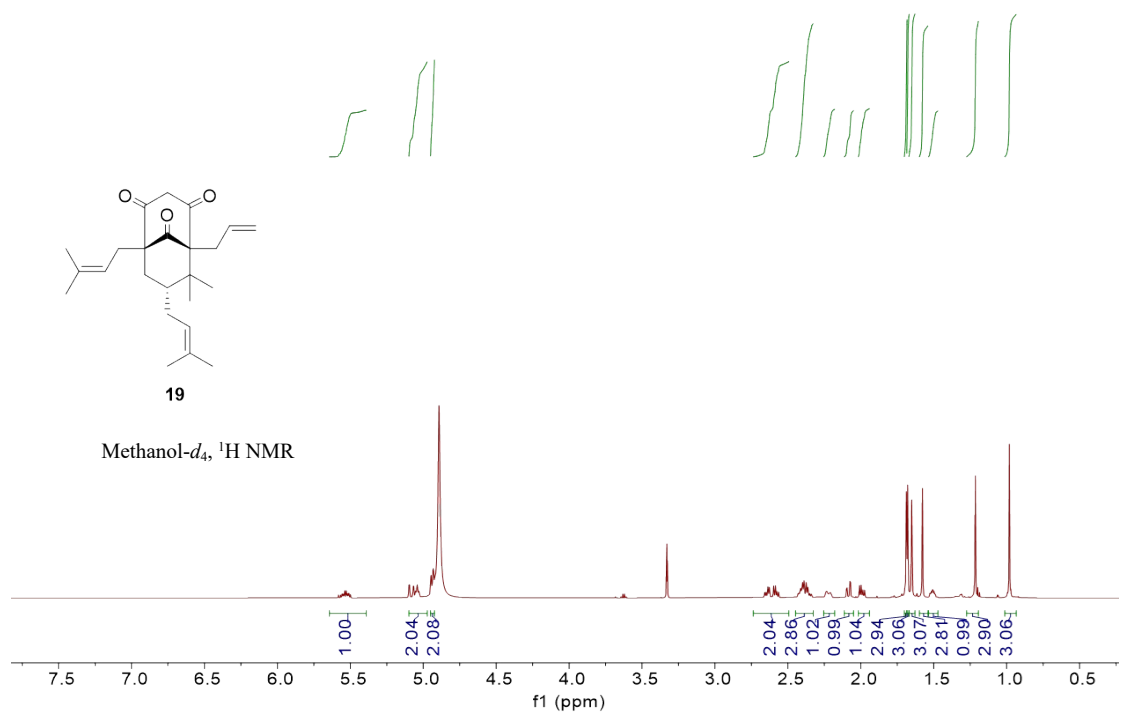
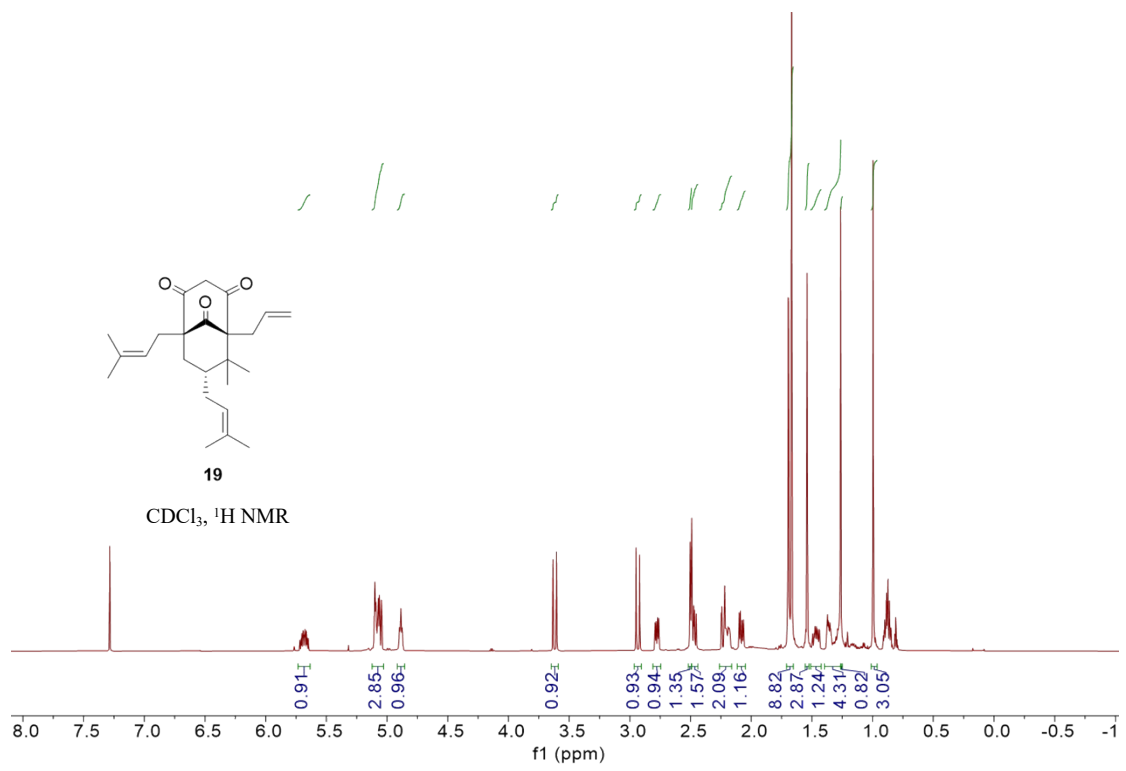


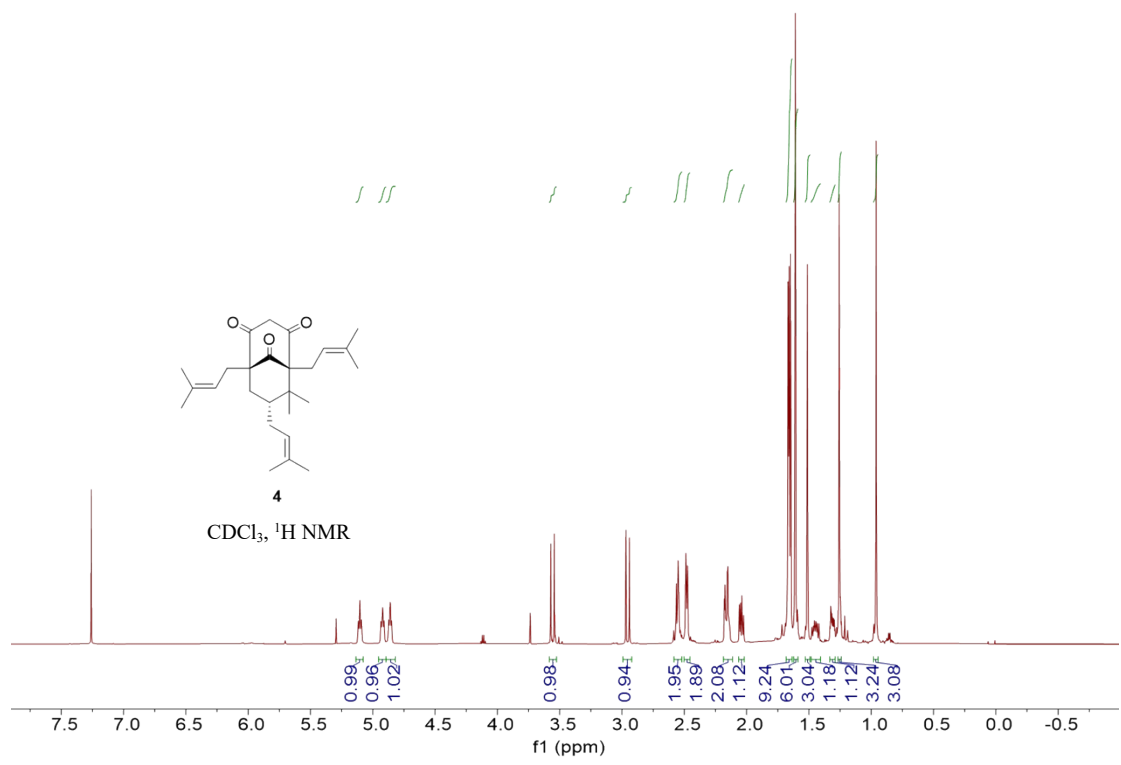
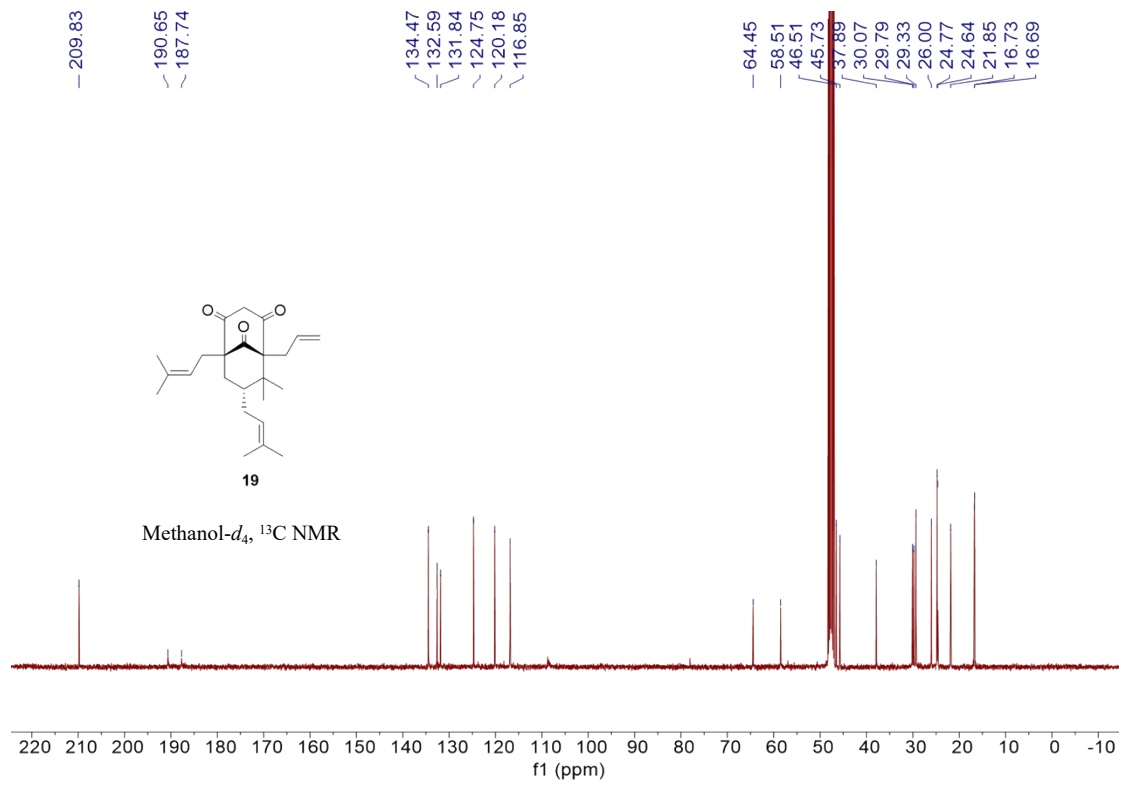


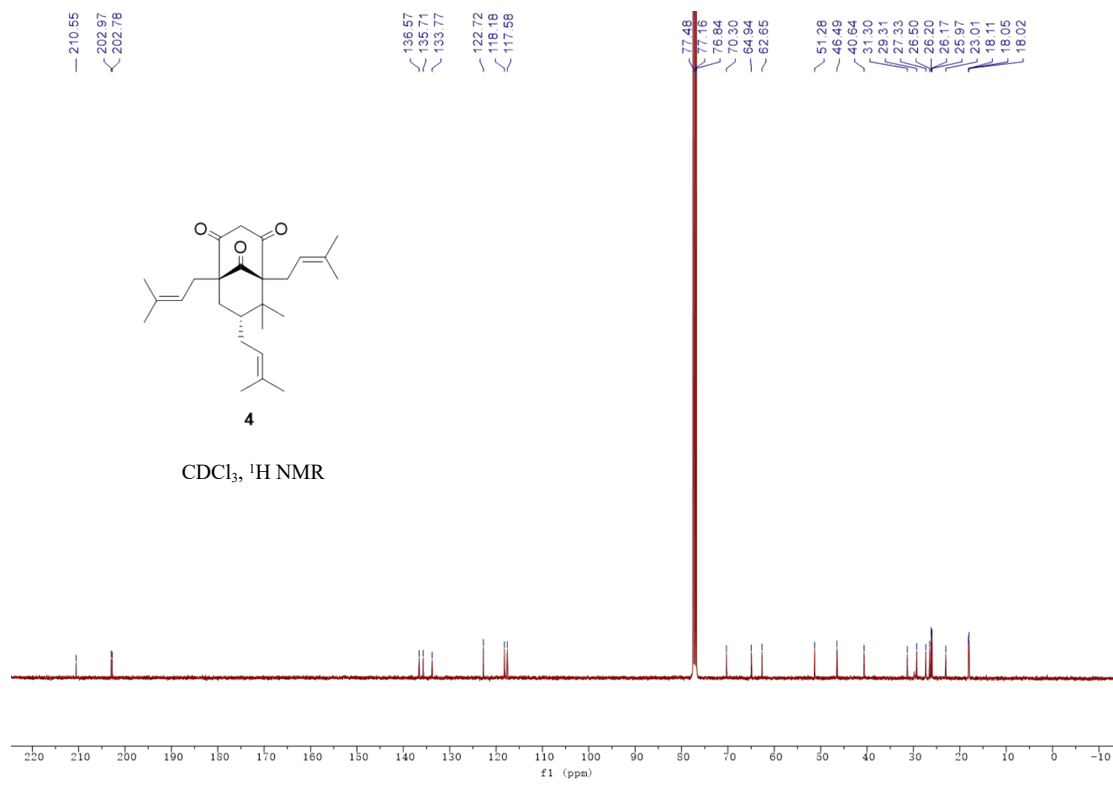




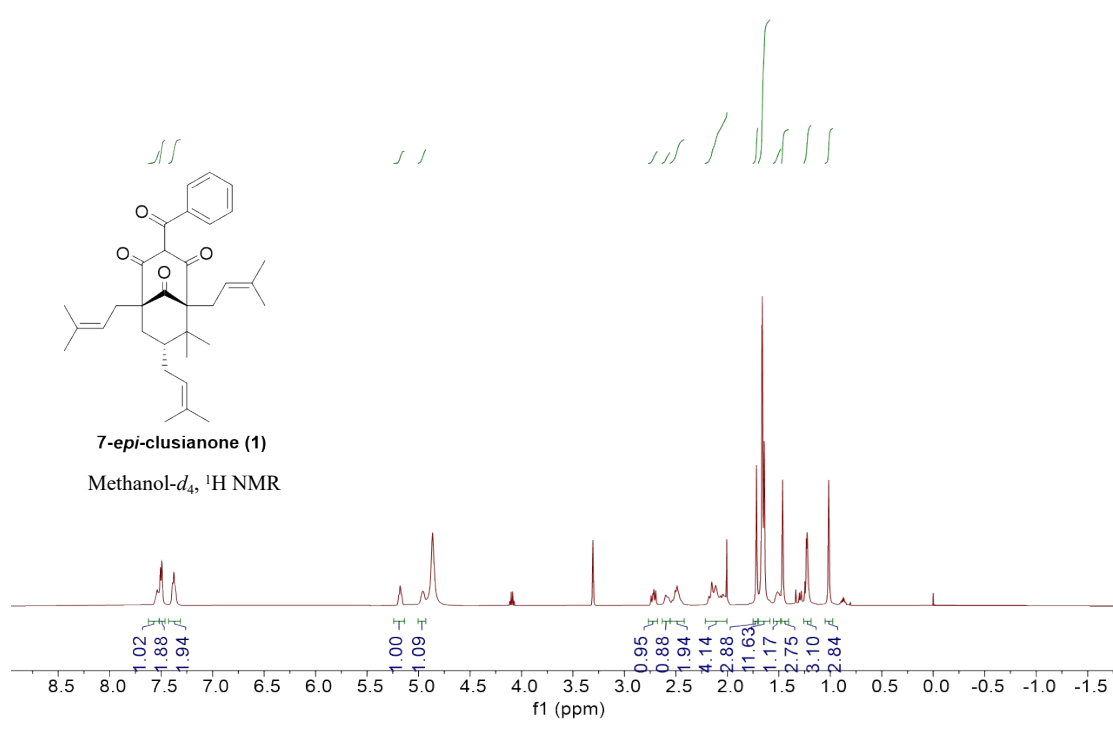


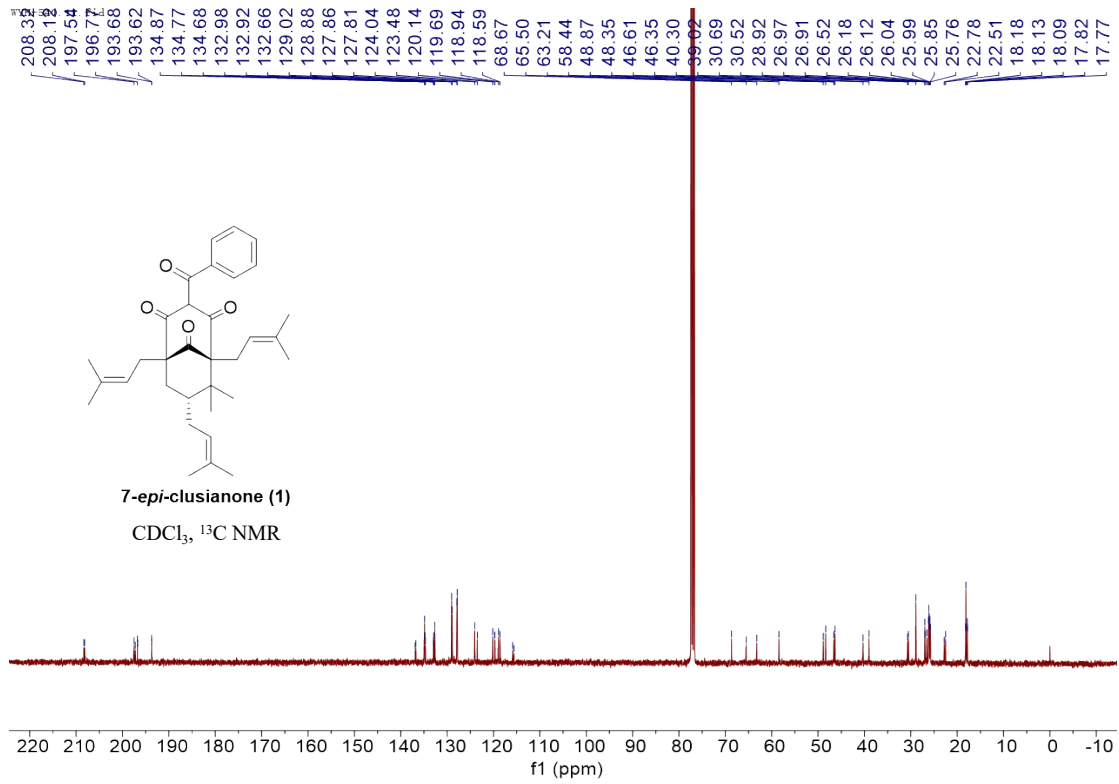
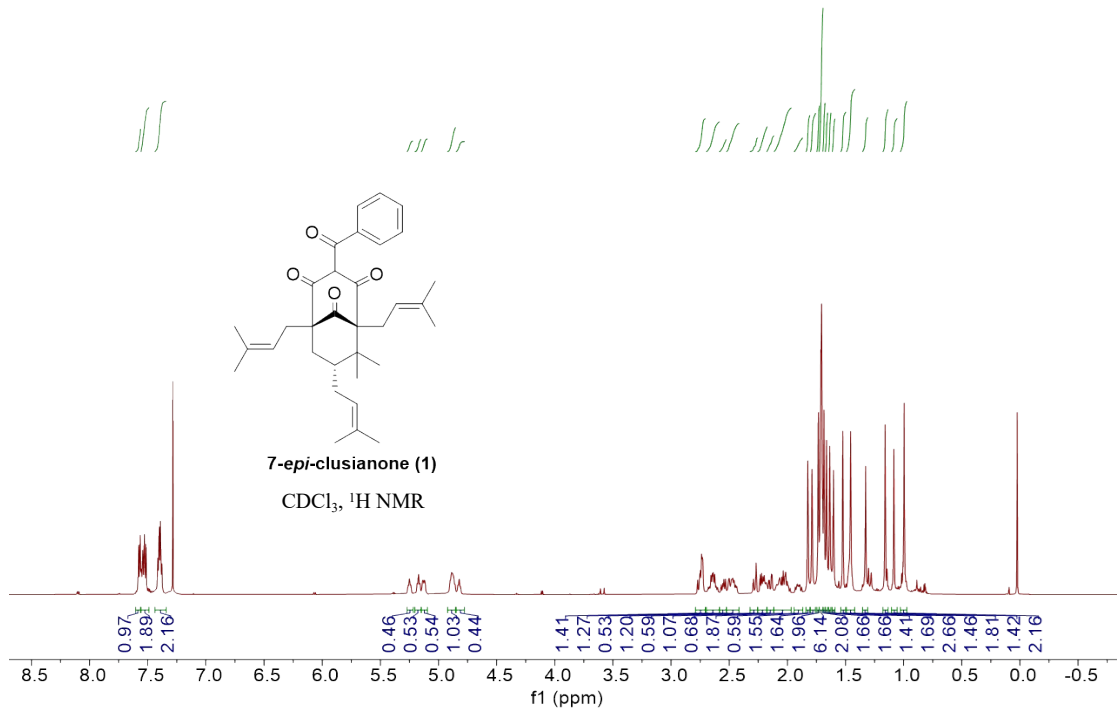




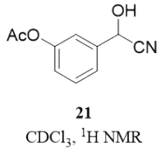
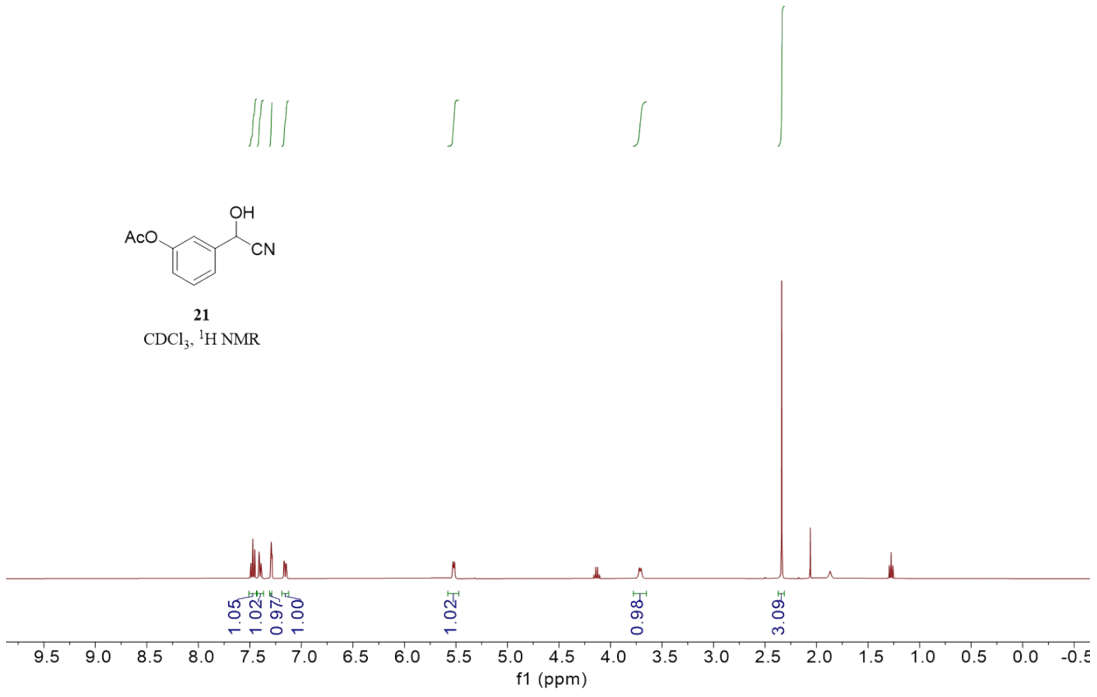


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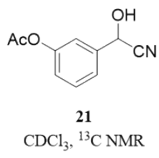
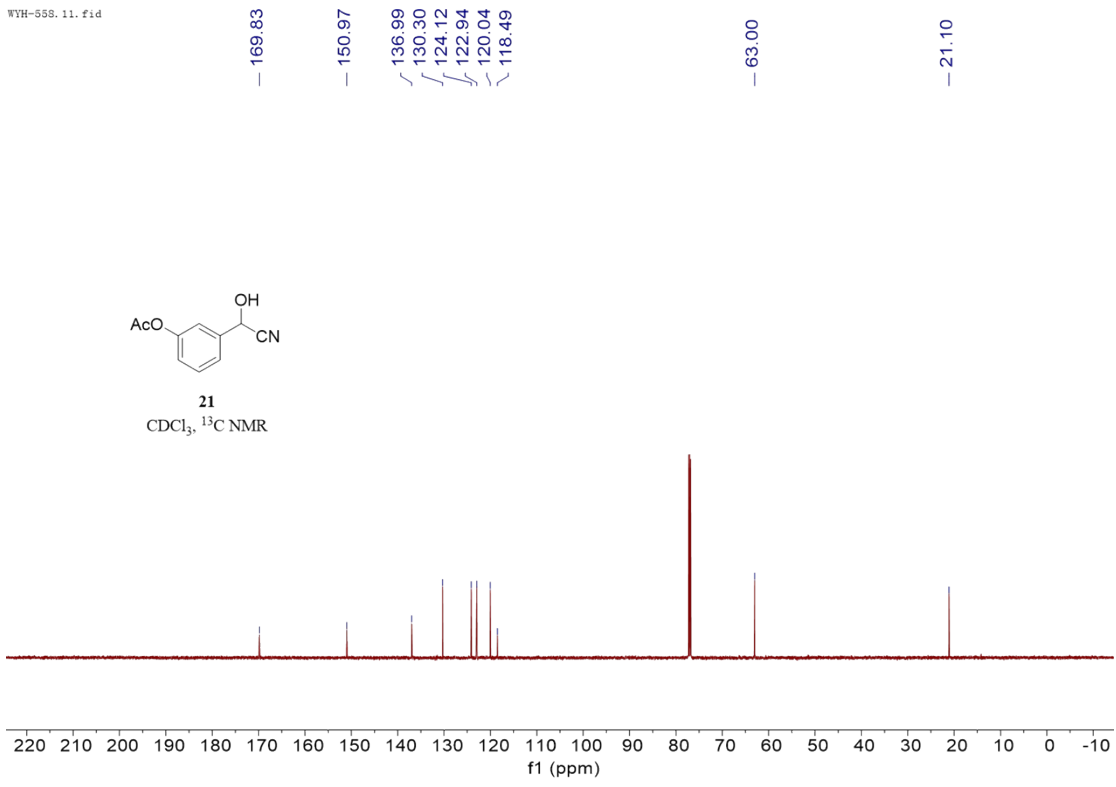


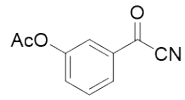


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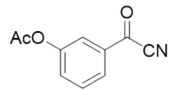
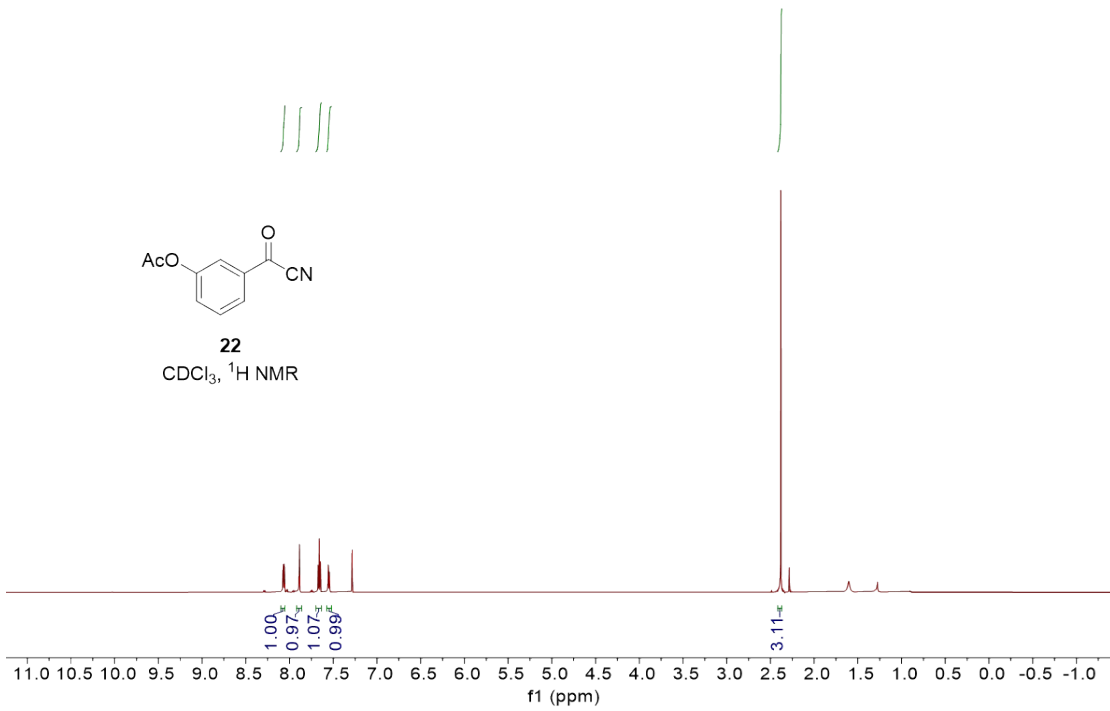
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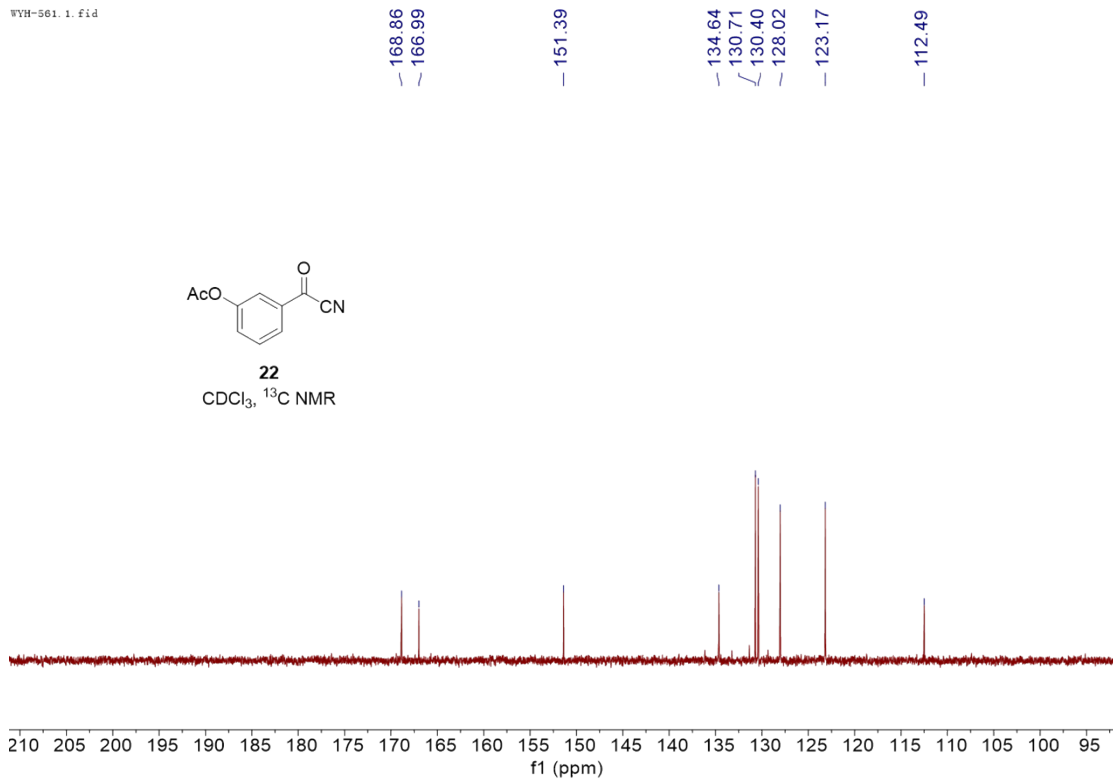
**22**

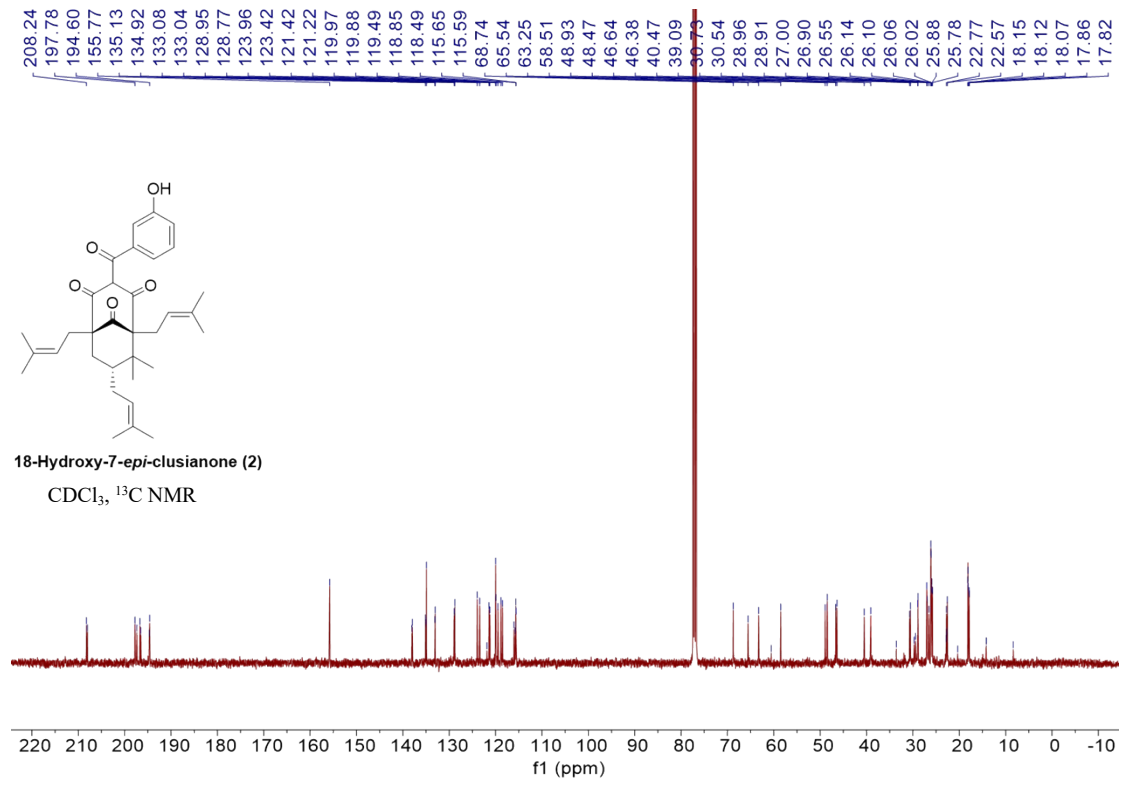
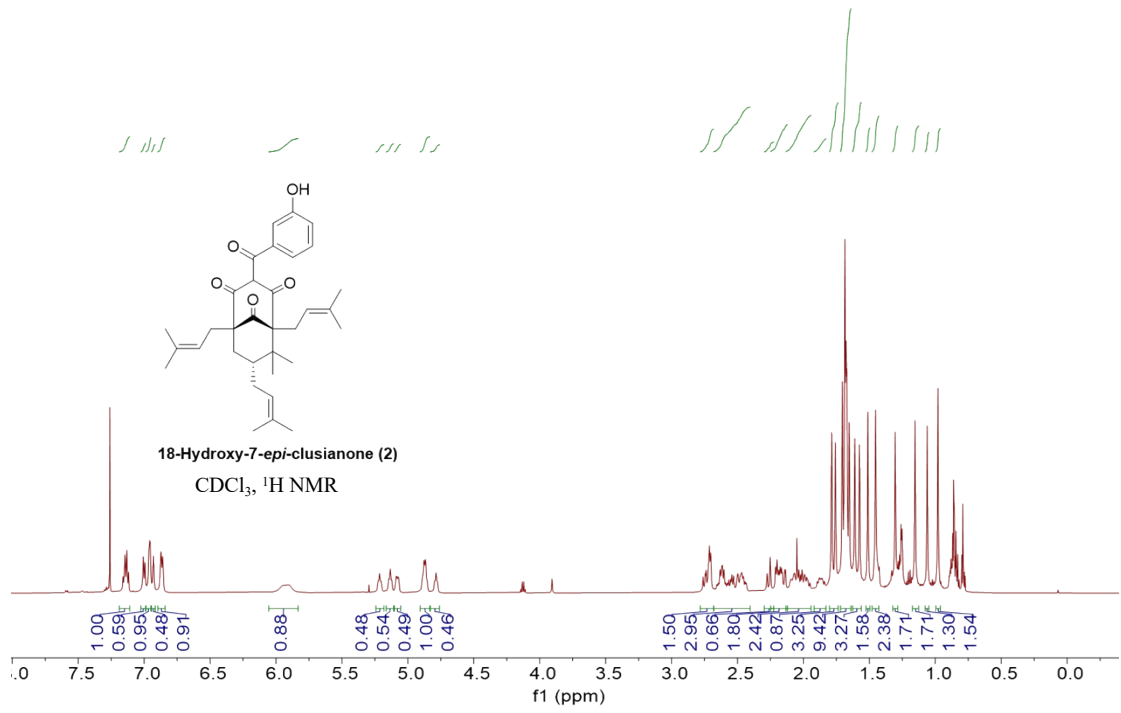
CDCl<sub>3</sub>, <sup>1</sup>H NMR



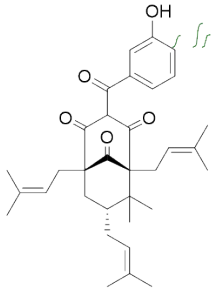
**22**

CDCl<sub>3</sub>, <sup>13</sup>C NMR



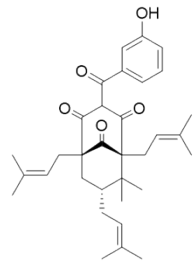
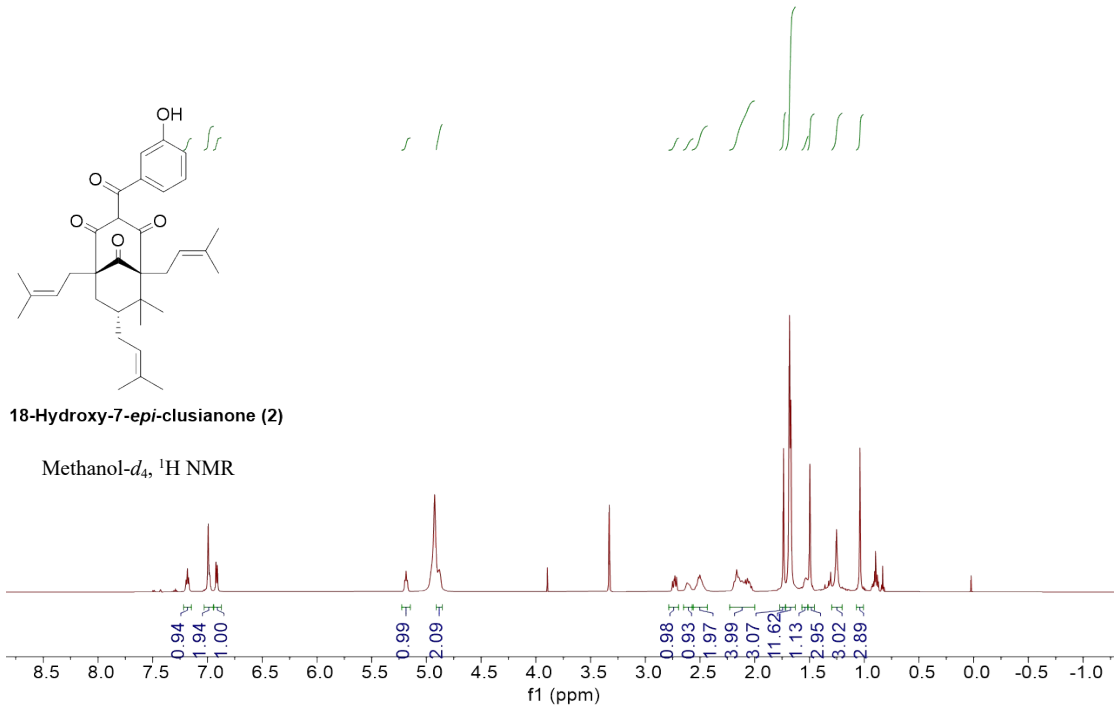






18-Hydroxy-7-epi-clusianone (2)

Methanol-*d*<sub>4</sub>, <sup>1</sup>H NMR



18-Hydroxy-7-epi-clusianone (2)

Methanol-*d*<sub>4</sub>, <sup>13</sup>C NMR

