

## Synthesis of New Triazolopyrazine Antimalarial Compounds

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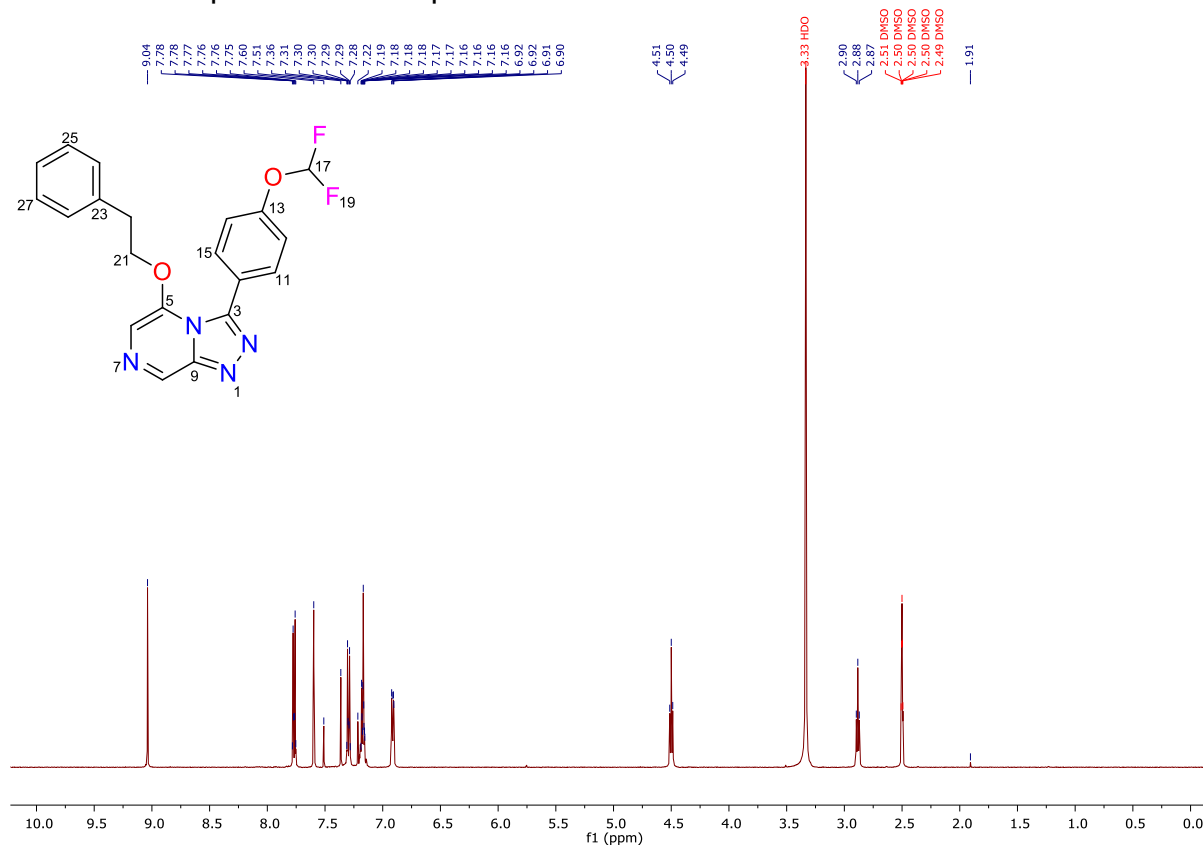
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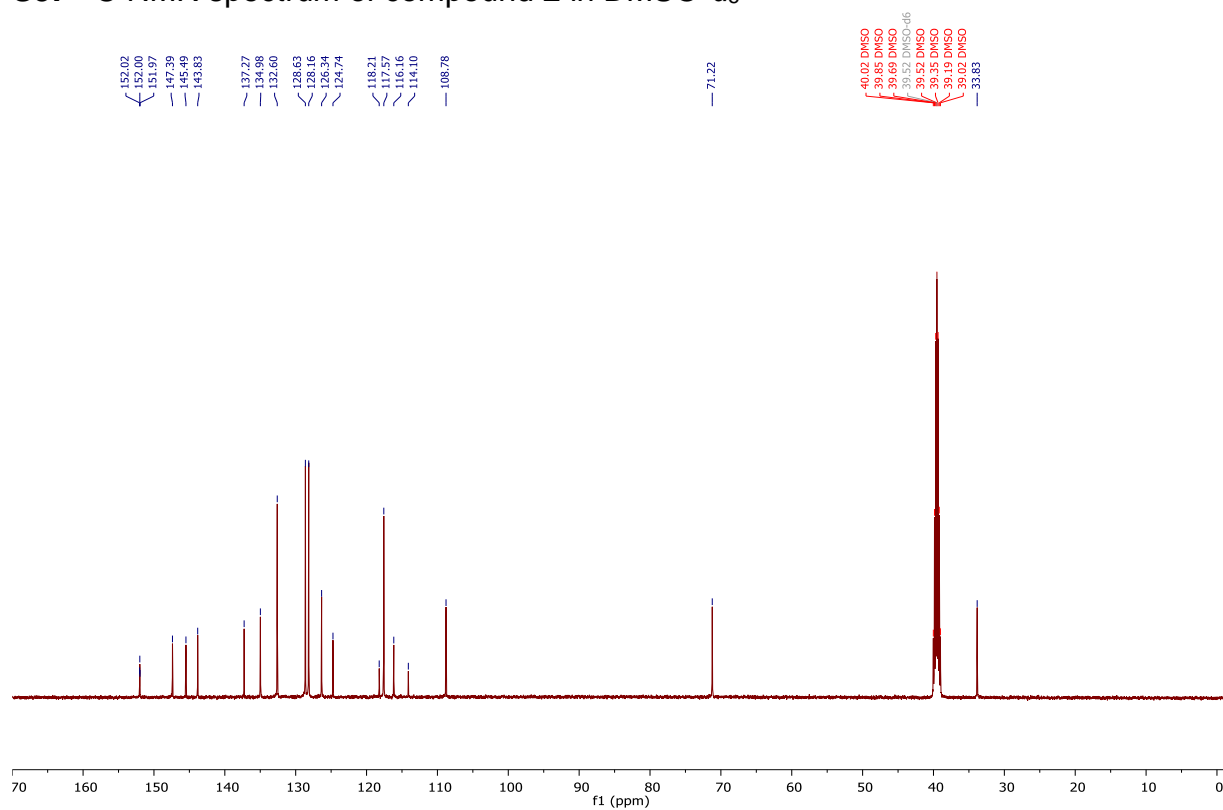
**S1: NMR data of compound 2 in DMSO-*d*<sub>6</sub><sup>a</sup>**

Pos.	δ <sub>H</sub> , mult. ( <i>J</i> in Hz), int.	δ <sub>C</sub> , mult. ( <i>J</i> in Hz)	COSY	HMBC	ROESY
3		145.5, s			
5		143.8, s			
6	7.60, s, 1H	108.8, s		5, 8	21
8	9.04, s, 1H	135.0, s		6, 9	
9		147.4, s			
10		124.7, s			
11	7.77, m, 1H	132.6, s	12	3, 13, 15	12
12	7.30, m, 1H	117.6, s	11	10, 14	11
13		152.0, t (3.2)			
14	7.30, m, 1H	117.6, s	15	10, 12	15
15	7.77, m, 1H	132.6, s	14	3, 11, 13	14
17	7.36, t (73.7), 1H	116.2, t (258.8)		13	
21	4.50, t (6.5), 2H	71.2, s		5, 23	6, 22
22	2.90, t (6.5), 2H	33.8, s		24, 28	21, 24, 28
23		137.3, s			
24	6.91, m, 1H	128.3, s	25	22, 26, 28	22, 25
25	7.18, m, 1H	128.6, s	24	23, 27	24
26	7.16, m, 1H	126.3, s		24, 28	
27	7.18, m, 1H	128.6, s	28	23, 25	28
28	6.91, m, 1H	128.3, s	27	22, 24, 26	22, 27

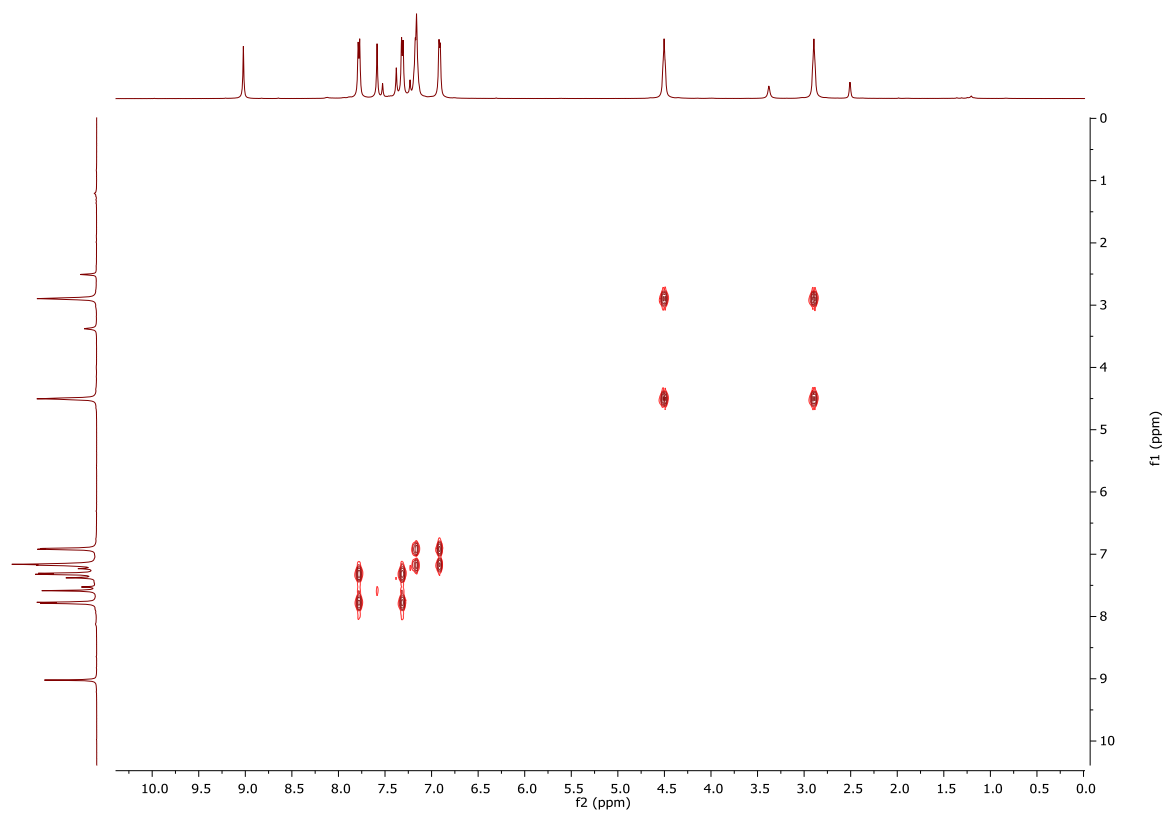
<sup>a</sup> Recorded at 500 MHz (<sup>1</sup>H NMR) and 125 MHz (<sup>13</sup>C NMR) at 25 °C.

**S2: <sup>1</sup>H NMR spectrum of compound 2 in DMSO-*d*<sub>6</sub>**

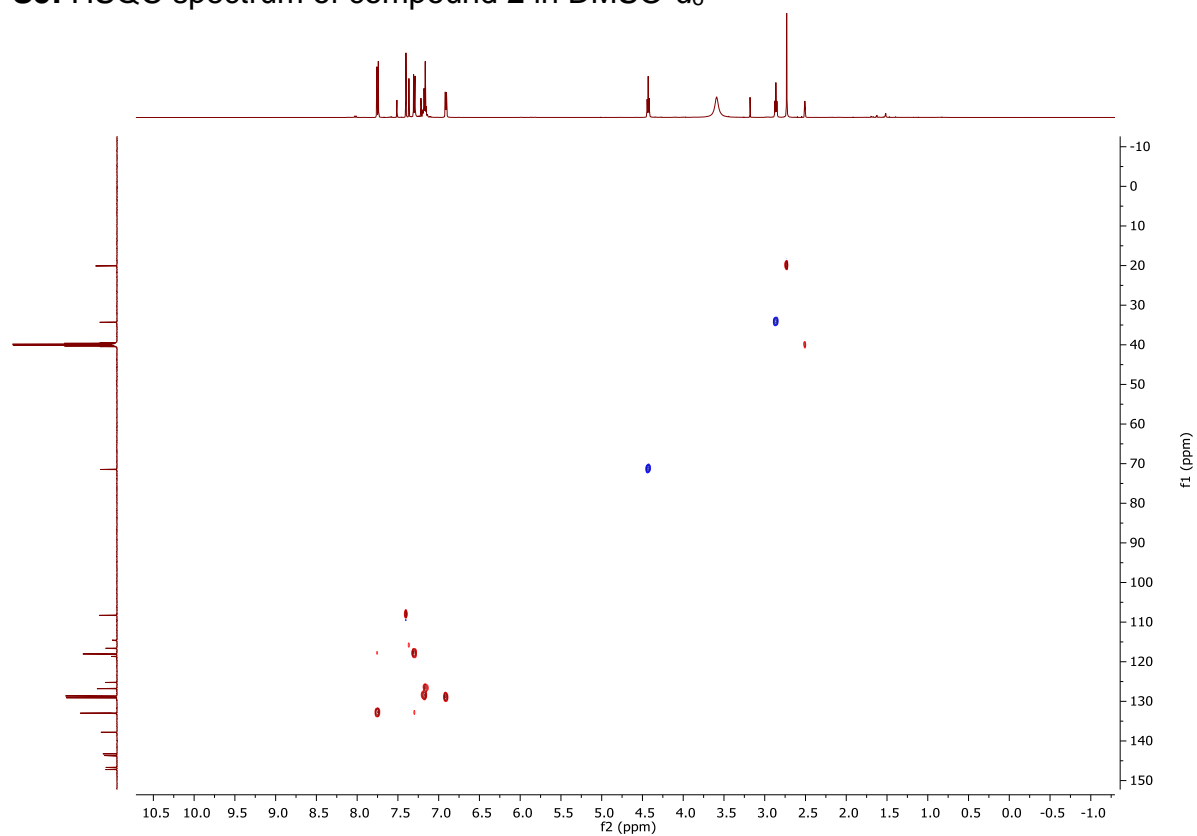
**S3:**  $^{13}\text{C}$  NMR spectrum of compound **2** in  $\text{DMSO-}d_6$



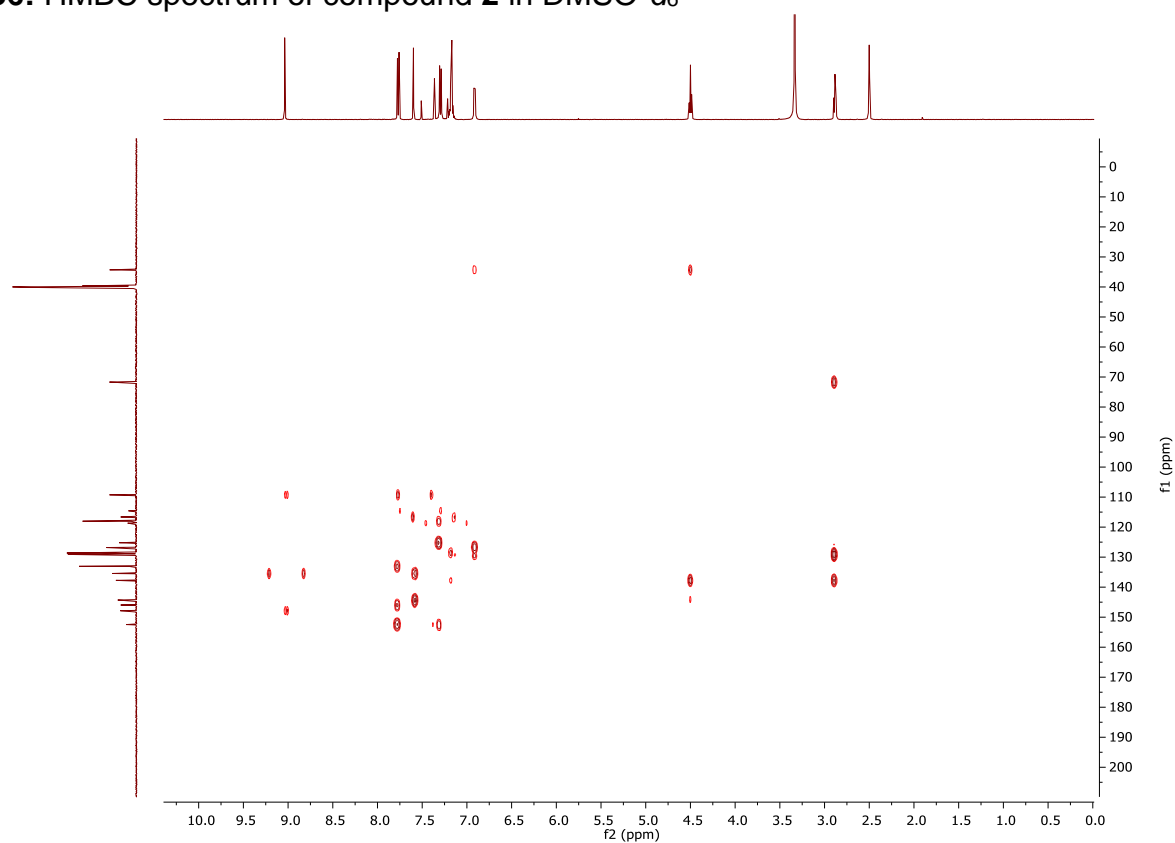
**S4:** COSY spectrum of compound **2** in  $\text{DMSO-}d_6$



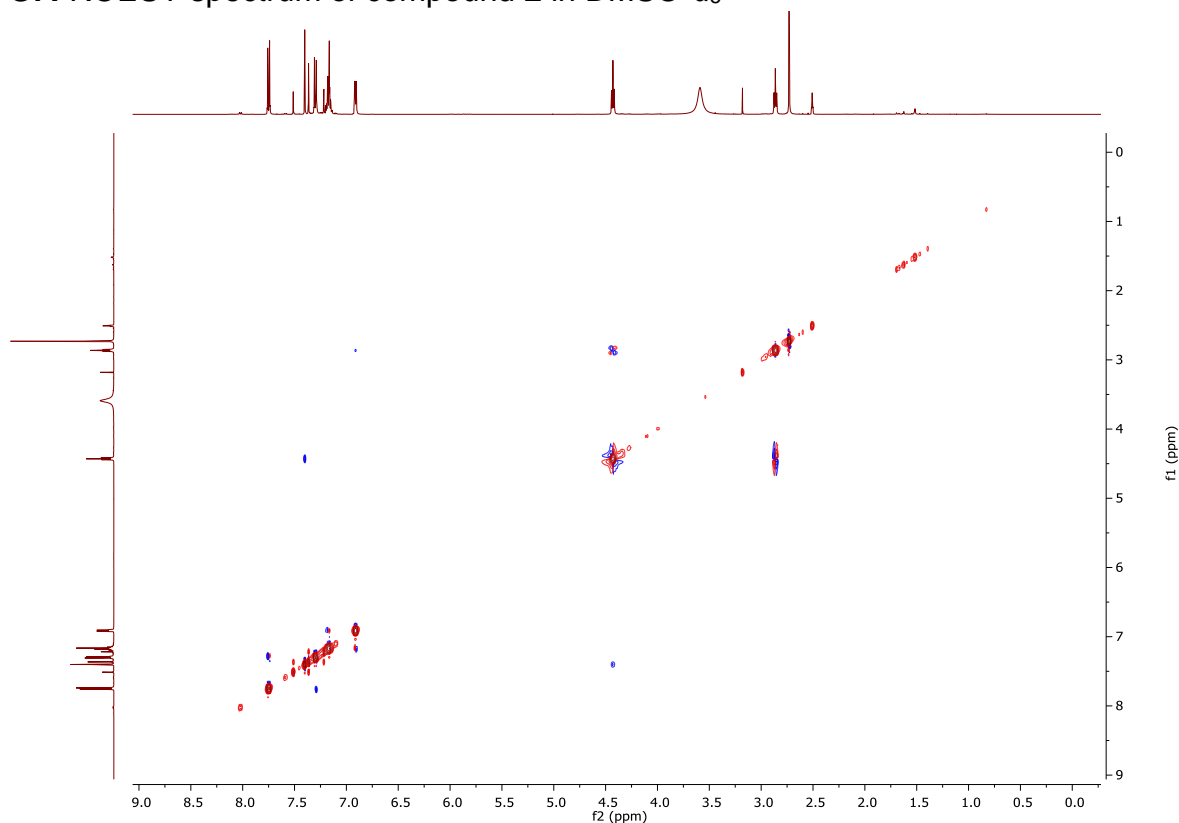
**S5:** HSQC spectrum of compound **2** in DMSO- $d_6$



**S6:** HMBC spectrum of compound **2** in DMSO- $d_6$



**S7: ROESY spectrum of compound 2 in DMSO- $d_6$**



**S8: HRMS of compound 2**



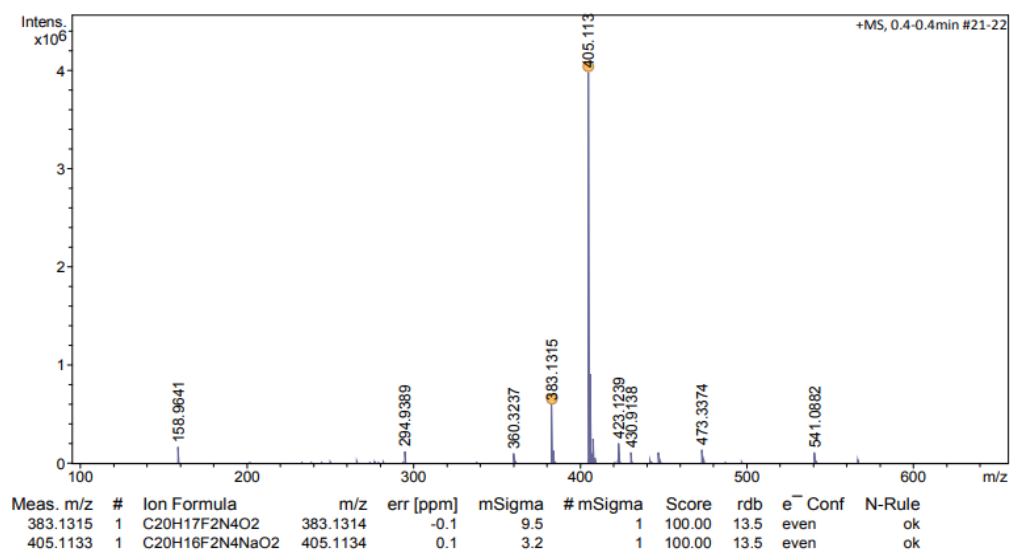
**High Resolution Mass Spectrum**

**Analysis Info**

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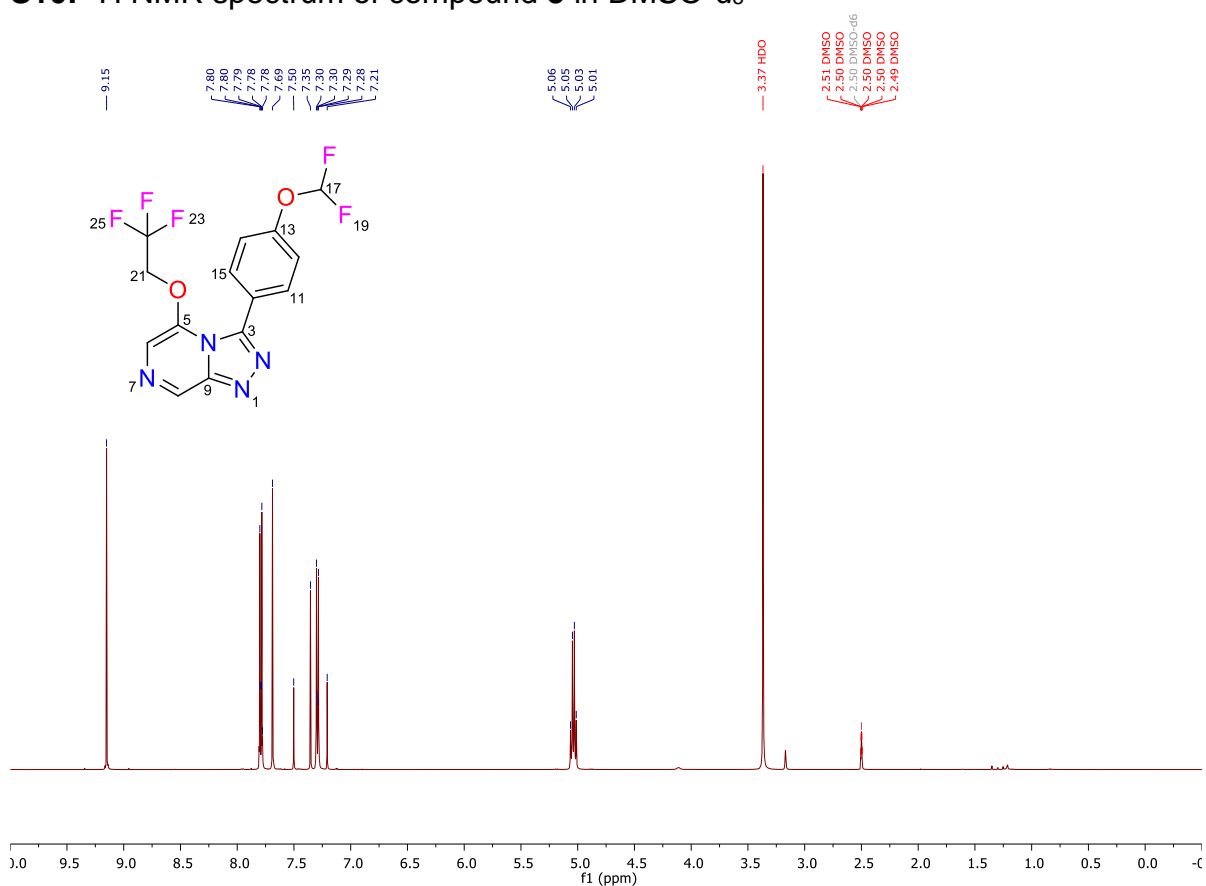


**S9:** NMR data of compound **3** in DMSO- $d_6^a$

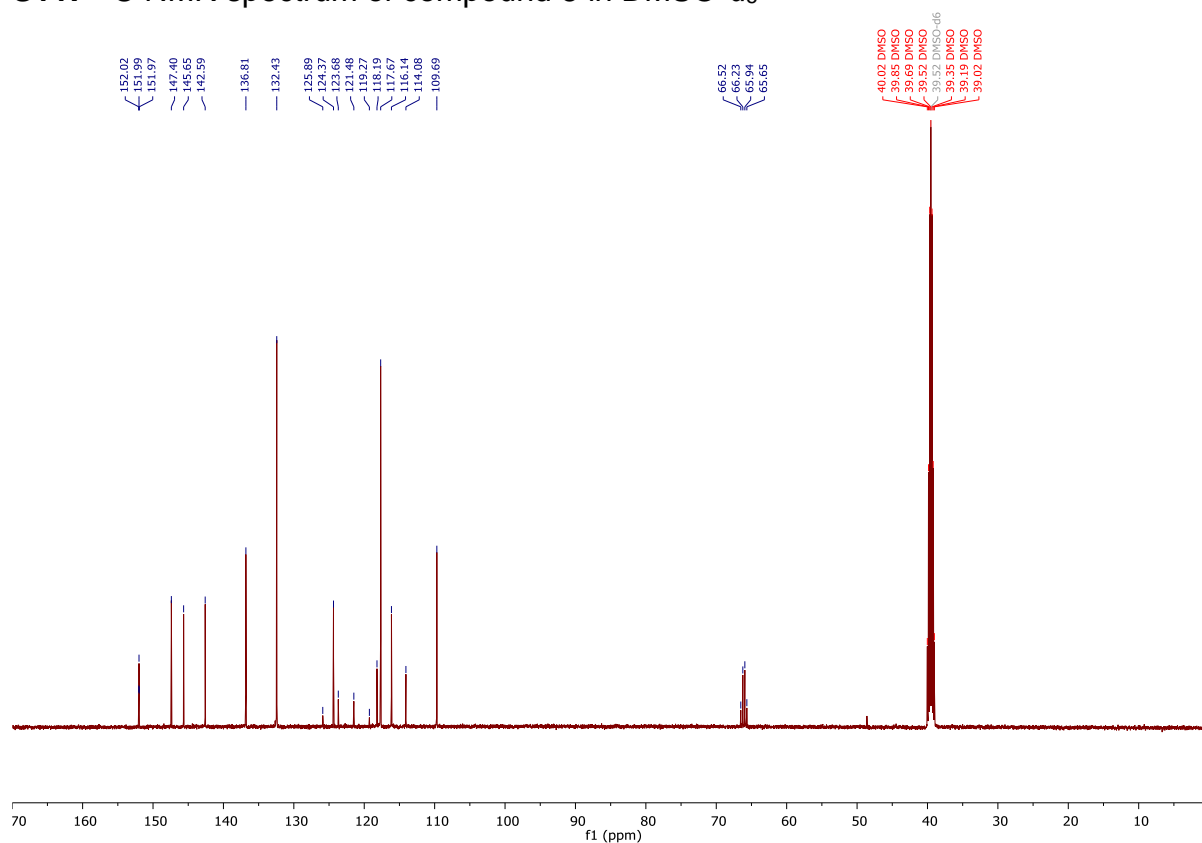
Pos.	$\delta_{\text{H}}$ , mult. ( $J$ in Hz), int.	$\delta_{\text{C}}$ , mult. ( $J$ in Hz)	COSY	HMBC	ROESY
3		145.7, s			
5		142.6, s			
6	7.69, s, 1H	109.7, s		5, 8	21
8	9.15, s, 1H	136.8, s			
9		147.4, s			
10		124.4, s			
11	7.79, m, 1H	132.4, s	12	3, 13,15	12
12	7.29, m, 1H	117.7, s	11	10,14	11
13		152.0, t (3.2)			
14	7.29, m, 1H	117.7, s	15	10, 12	15
15	7.79, m, 1H	132.4, s	14	3, 11, 13	14
17	7.35, t (73.8), 1H	116.1, t (258.8)		13	
21	5.05, q (8.5), 2H	66.1, q (36.2)		5, 22	6
22		122.6, q (277.2)			

<sup>a</sup> Recorded at 500 MHz (<sup>1</sup>H NMR) and 125 MHz (<sup>13</sup>C NMR) at 25 °C.

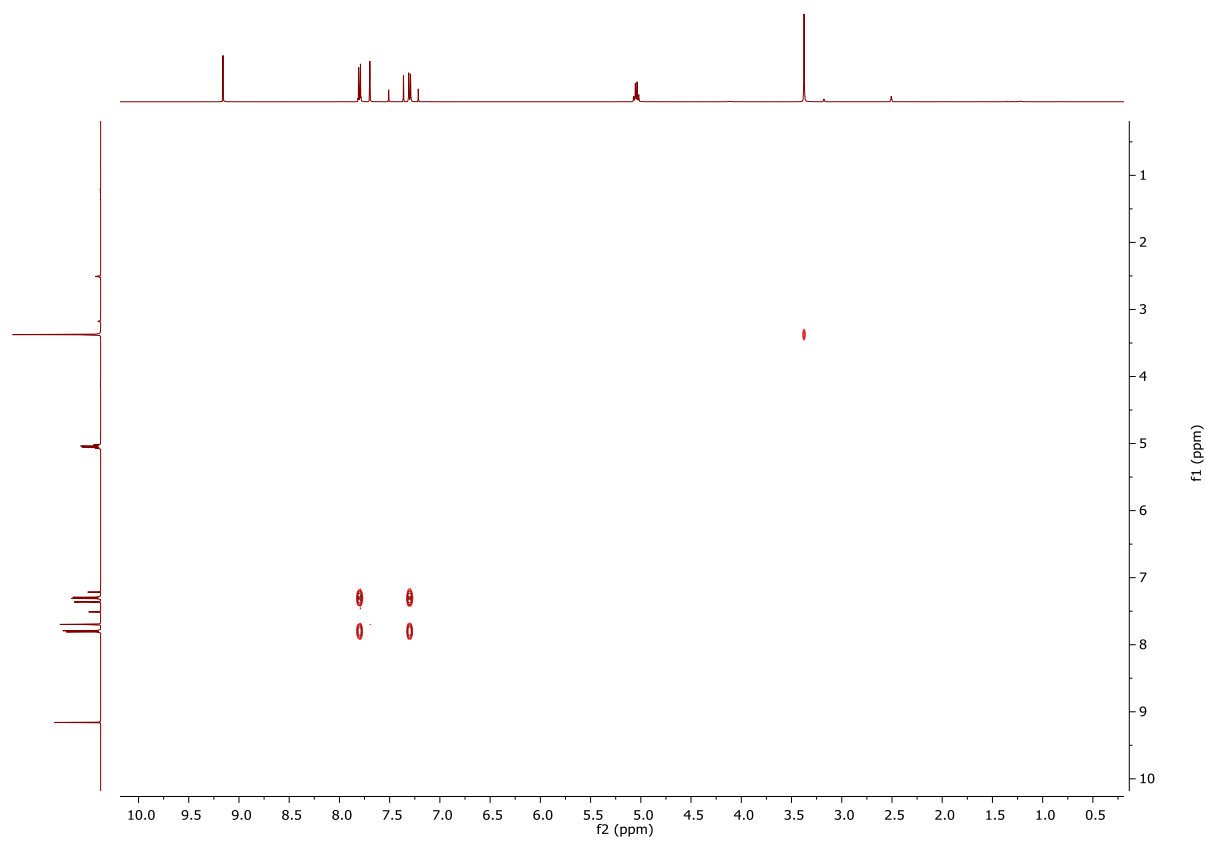
**S10:**  $^1\text{H}$  NMR spectrum of compound **3** in  $\text{DMSO}-d_6$



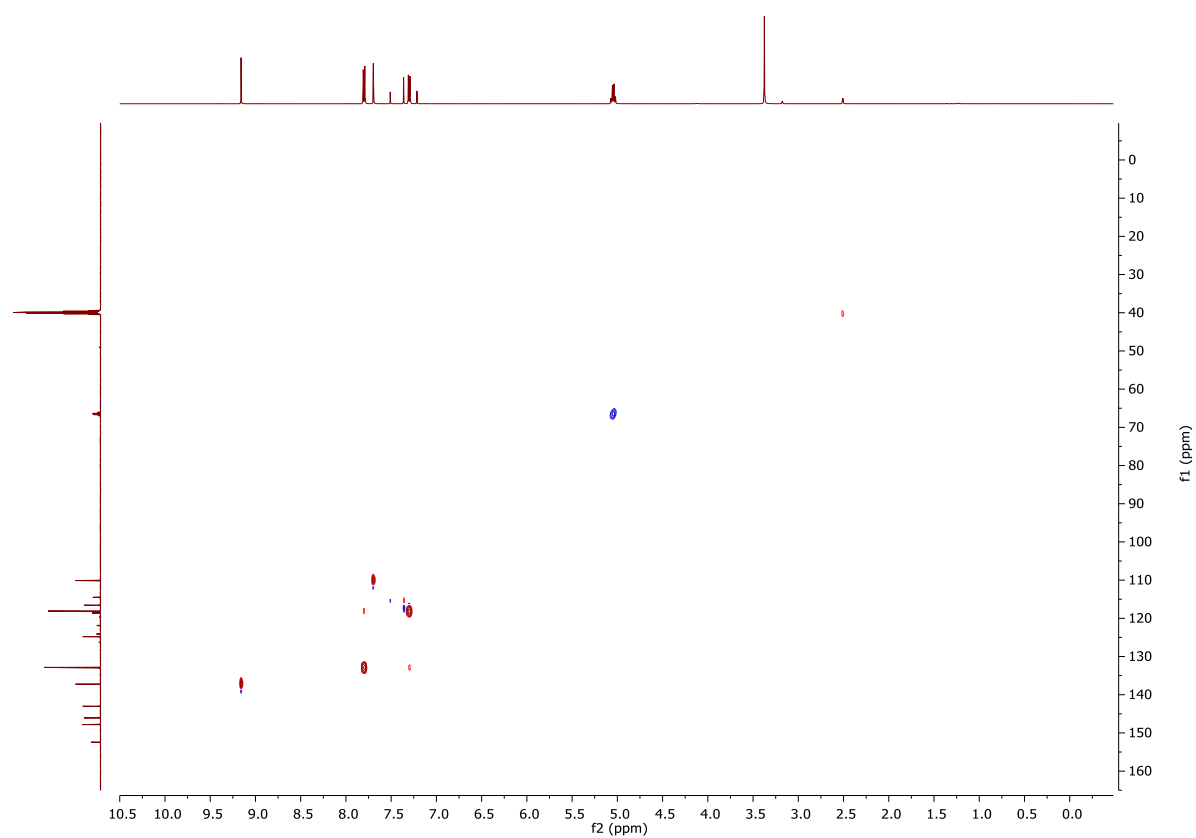
**S11:**  $^{13}\text{C}$  NMR spectrum of compound **3** in  $\text{DMSO}-d_6$



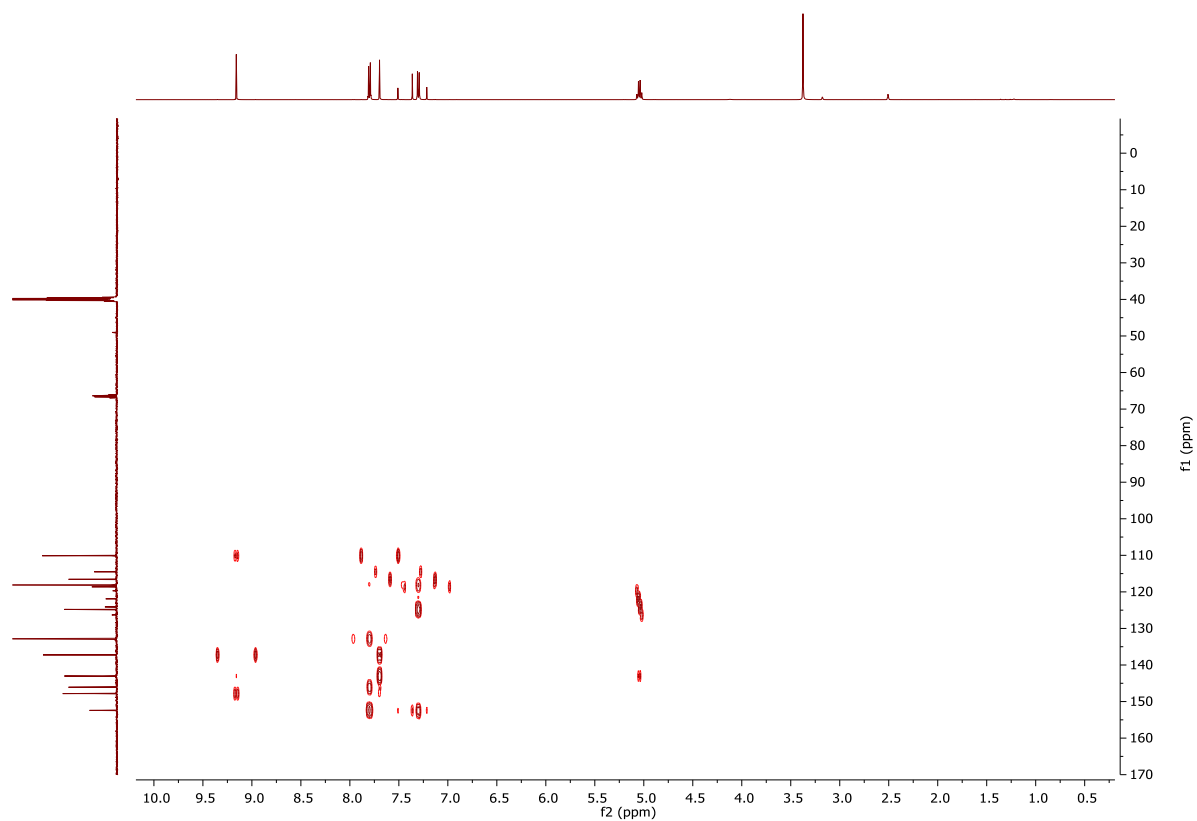
**S12:** COSY spectrum of compound **3** in  $\text{DMSO}-d_6$



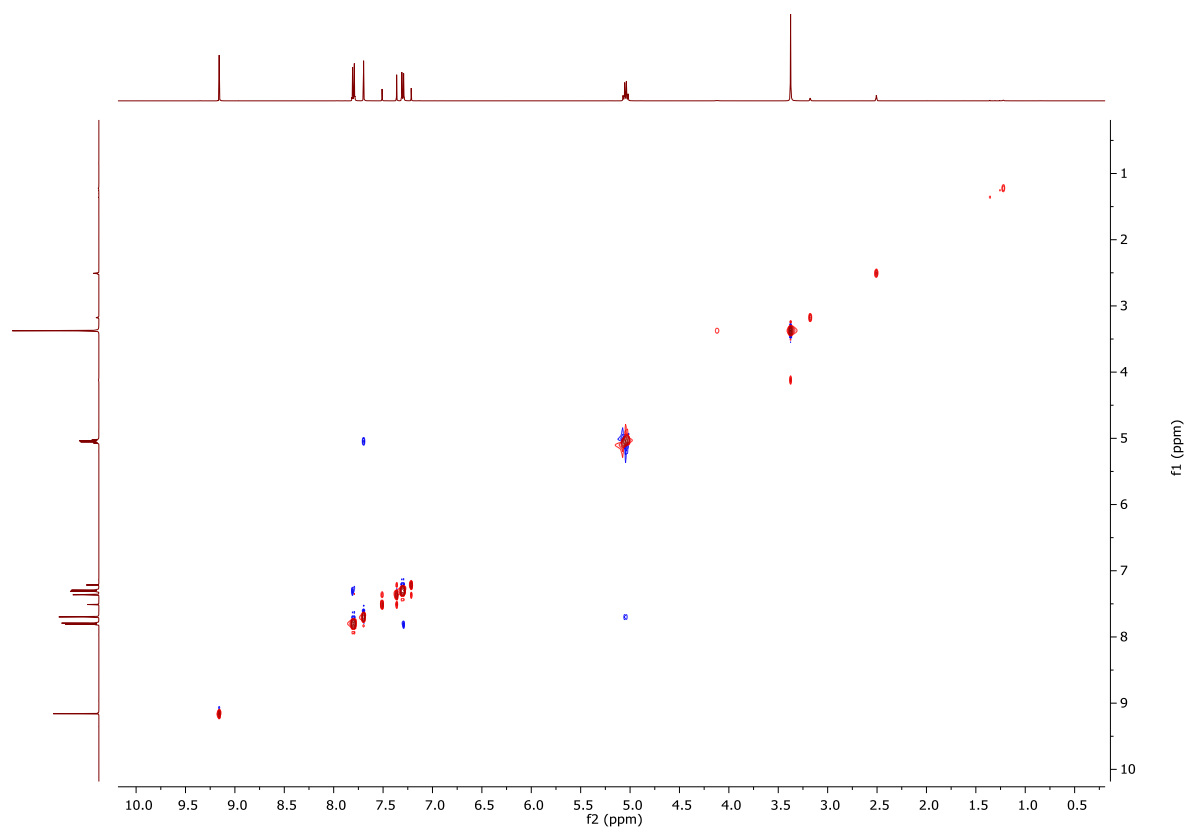
**S13:** HSQC spectrum of compound **3** in DMSO- $d_6$



**S14:** HMBC spectrum of compound **3** in DMSO- $d_6$



**S15:** ROESY spectrum of compound **3** in DMSO- $d_6$



**S16:** HRMS of compound **3**



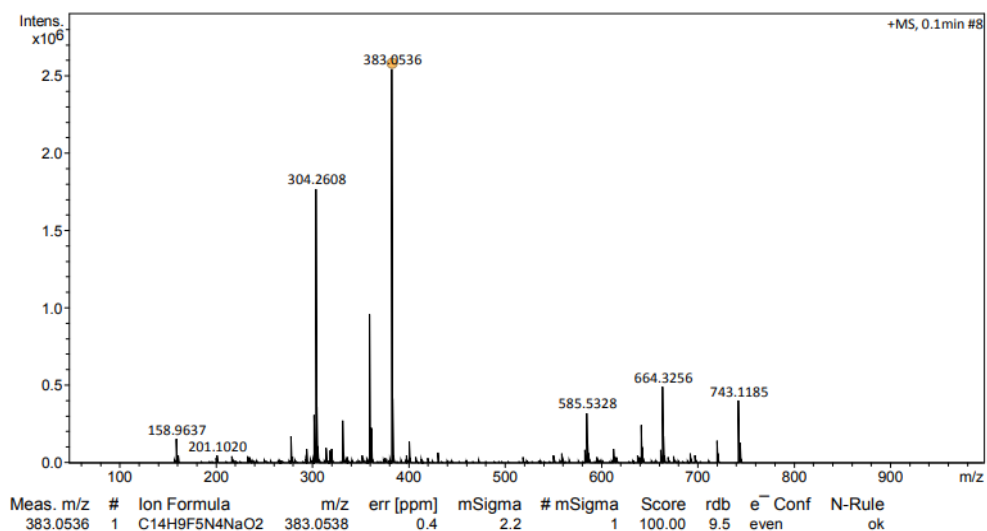
High Resolution Mass Spectrum

**Analysis Info**

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Sample Name RAD863  
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Acquisition Date 5/12/2020 12:03:48 PM  
Instrument maXis II ETD 1823391.22321

**+MS, 0.1min #8**

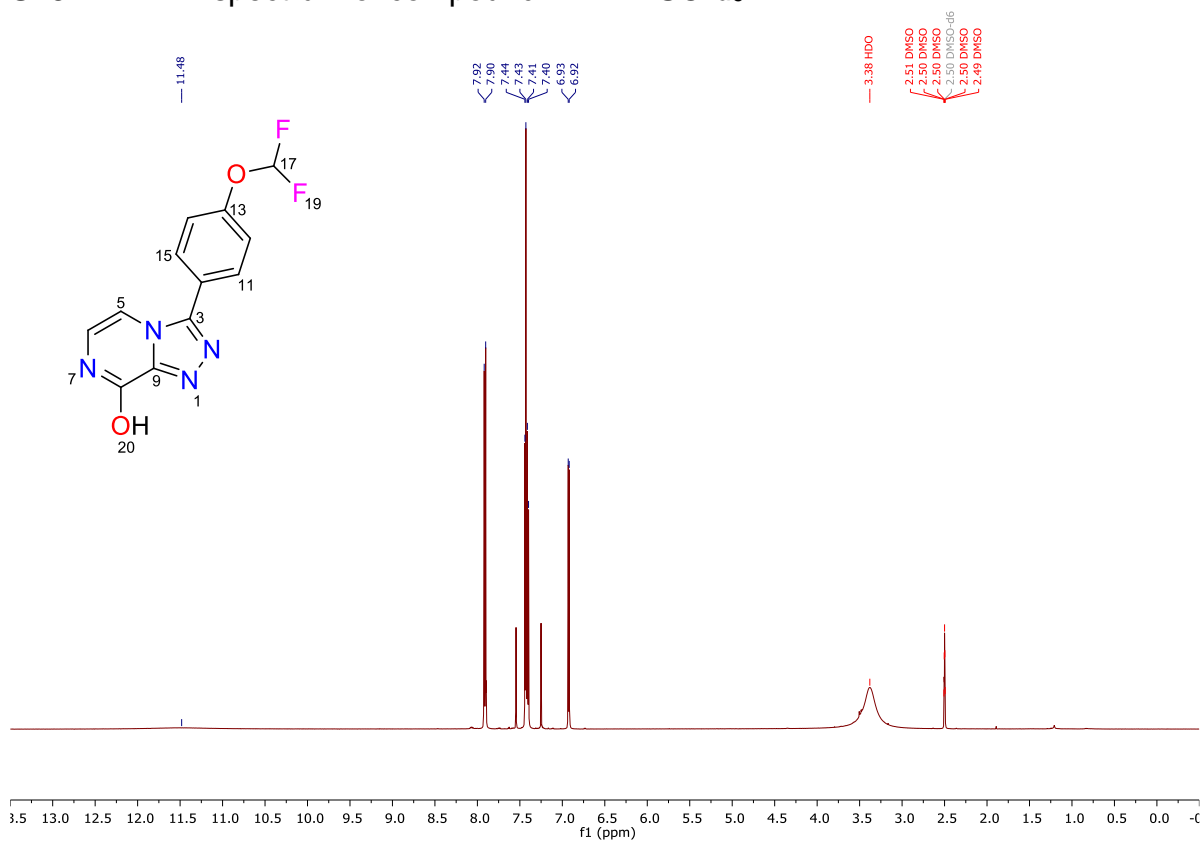




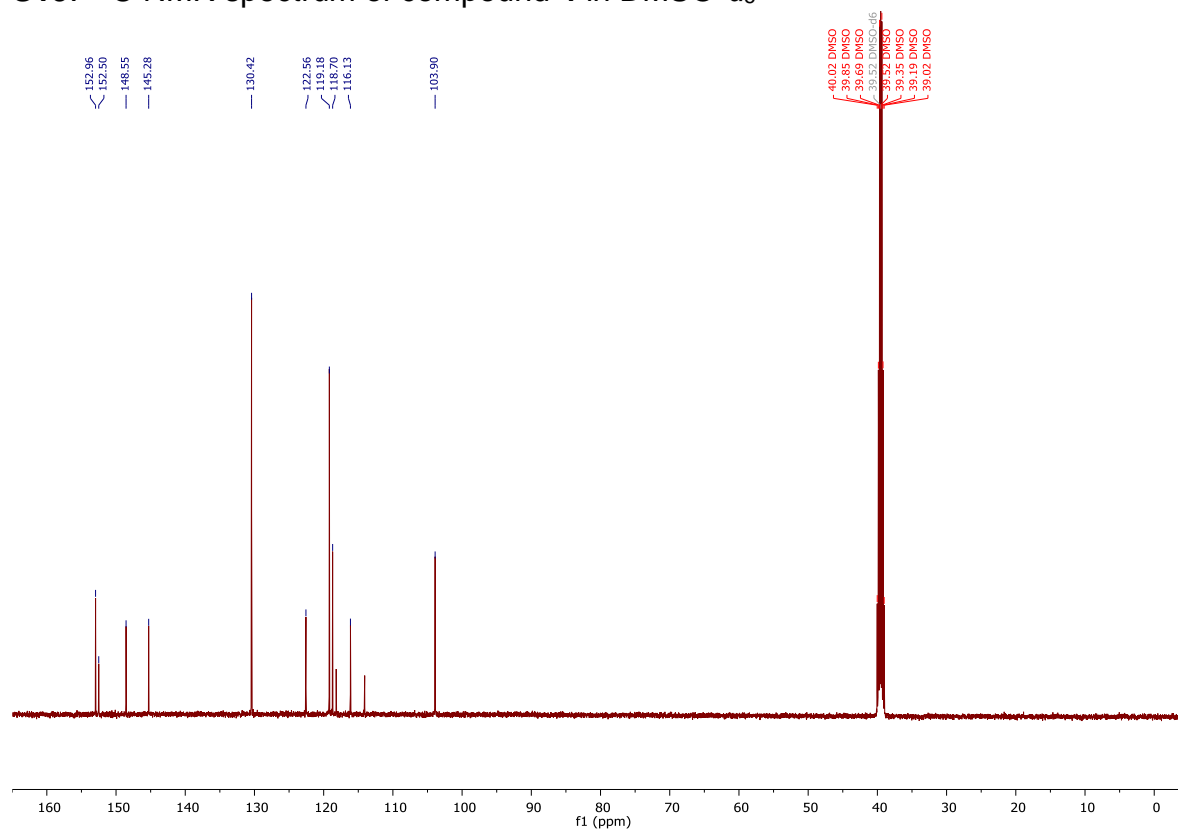
**S17:** NMR data of compound **4** in DMSO-*d*<sub>6</sub><sup>a</sup>

Pos	δ <sub>H</sub> , mult. ( <i>J</i> in Hz), int.	δ <sub>C</sub> , mult. ( <i>J</i> in Hz)	COSY	HMBC
3		148.6, s		
5	7.43, d (5.8), 1H	103.9, s	6	6, 9
6	6.92, d (5.8), 1H	118.7, s	5	5, 8
8		153.0, s		
9		145.3, s		
10		122.6, s		
11	7.91, m, 1H	130.4, s	12	3, 13,15
12	7.42, m, 1H	119.2, s	11	10,14
13		152.5, t (3.3)		
14	7.42, m, 1H	119.2, s	15	10, 12
15	7.91, m, 1H	130.4, s	14	3, 11, 13
17	7.40, t (73.6), 1H	116.1, t (258.7)		13
20-OH	11.48, br s, 1H			

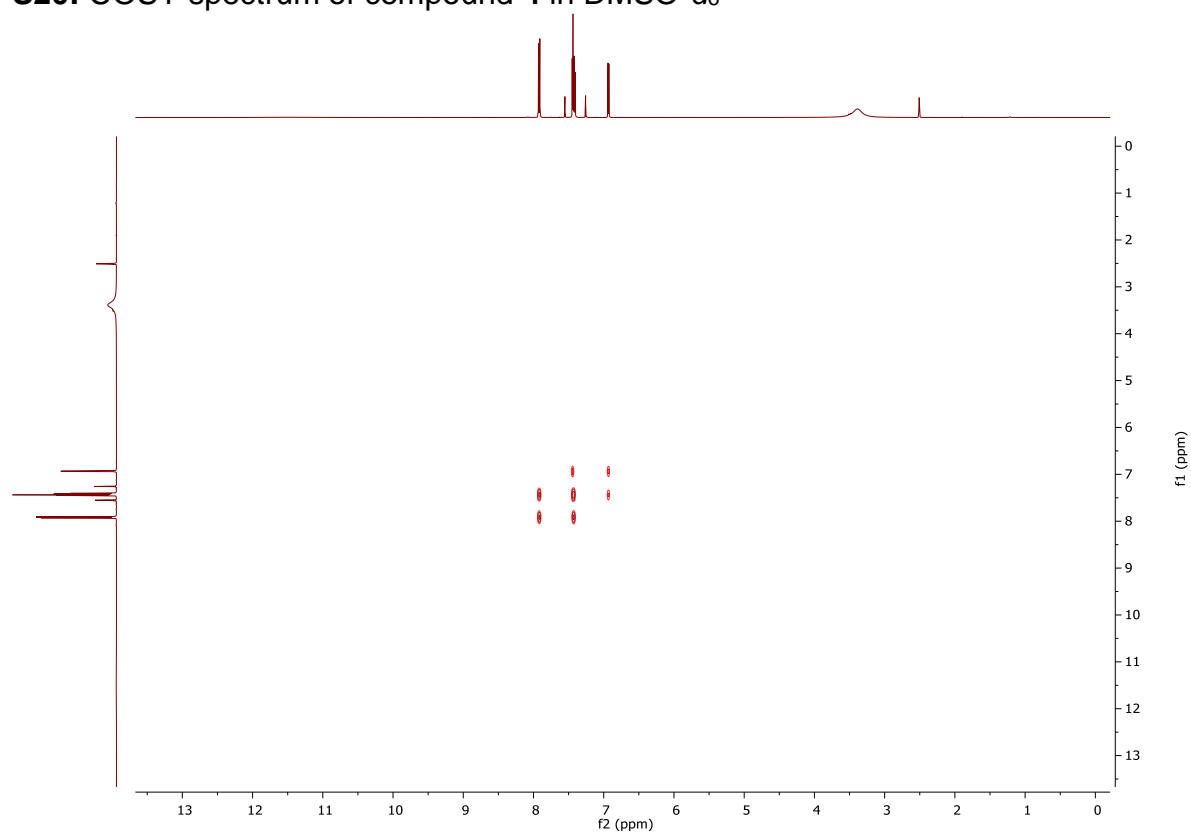
<sup>a</sup> Recorded at 500 MHz (<sup>1</sup>H NMR) and 125 MHz (<sup>13</sup>C NMR) at 25 °C.

**S18:** <sup>1</sup>H NMR spectrum of compound **4** in DMSO-*d*<sub>6</sub>

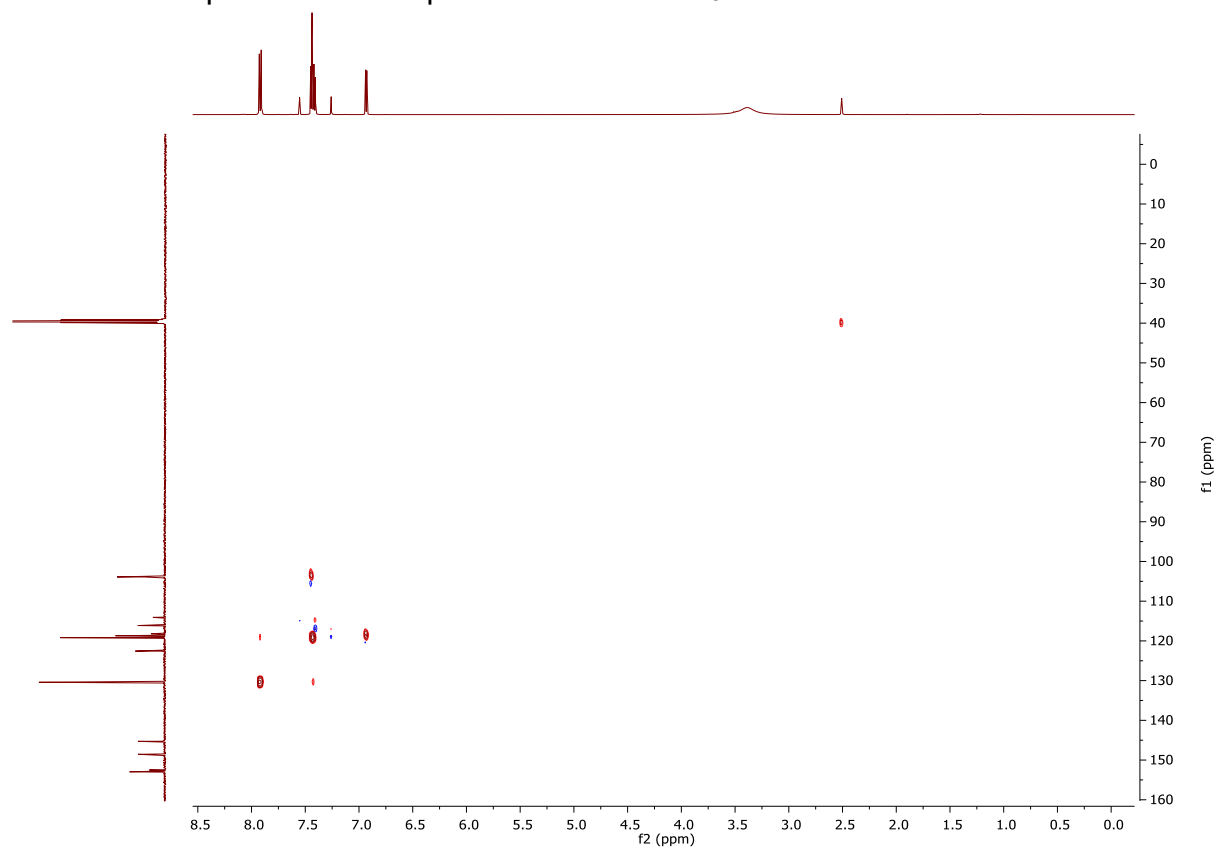
**S19:**  $^{13}\text{C}$  NMR spectrum of compound **4** in  $\text{DMSO}-d_6$



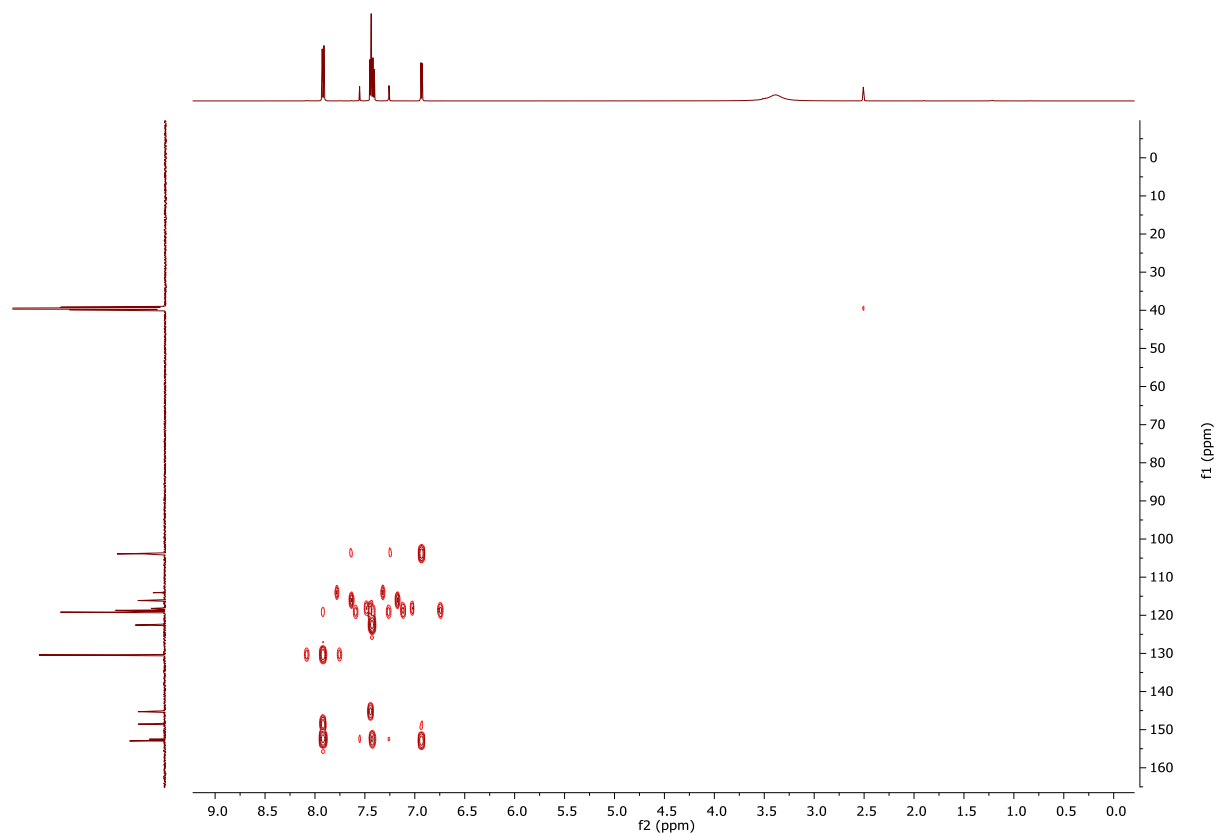
**S20:** COSY spectrum of compound **4** in  $\text{DMSO}-d_6$



**S21:** HSQC spectrum of compound **4** in DMSO- $d_6$



**S22:** HMBC spectrum of compound **4** in DMSO- $d_6$



## S23: HRMS of compound 4



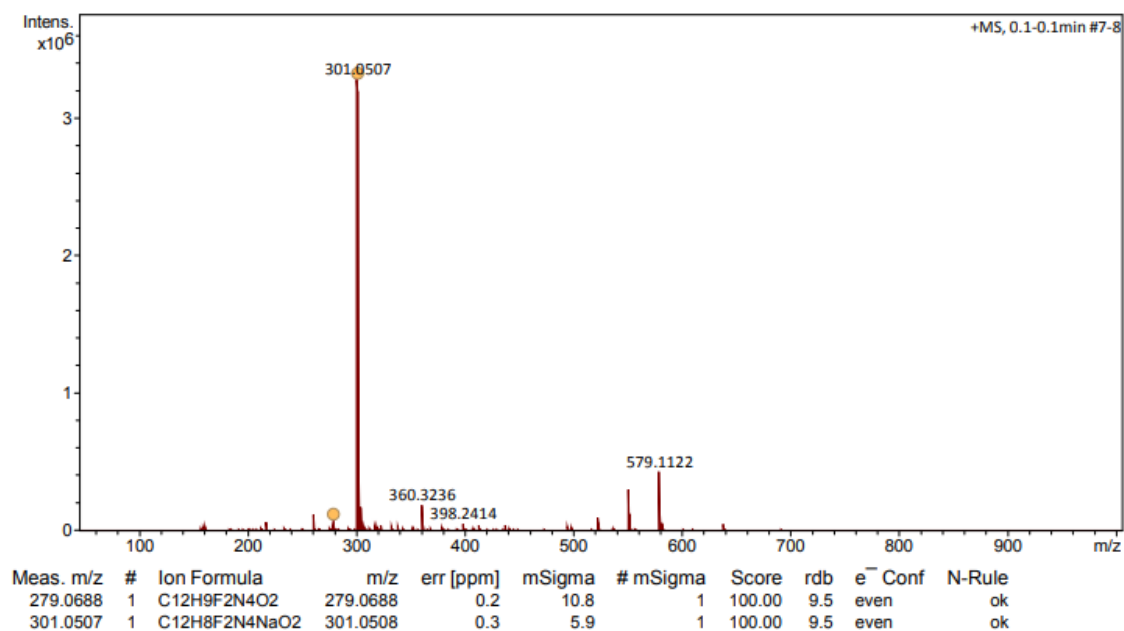
### High Resolution Mass Spectrum

#### Analysis Info

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Instrument maXis II ETD 1823391.22321

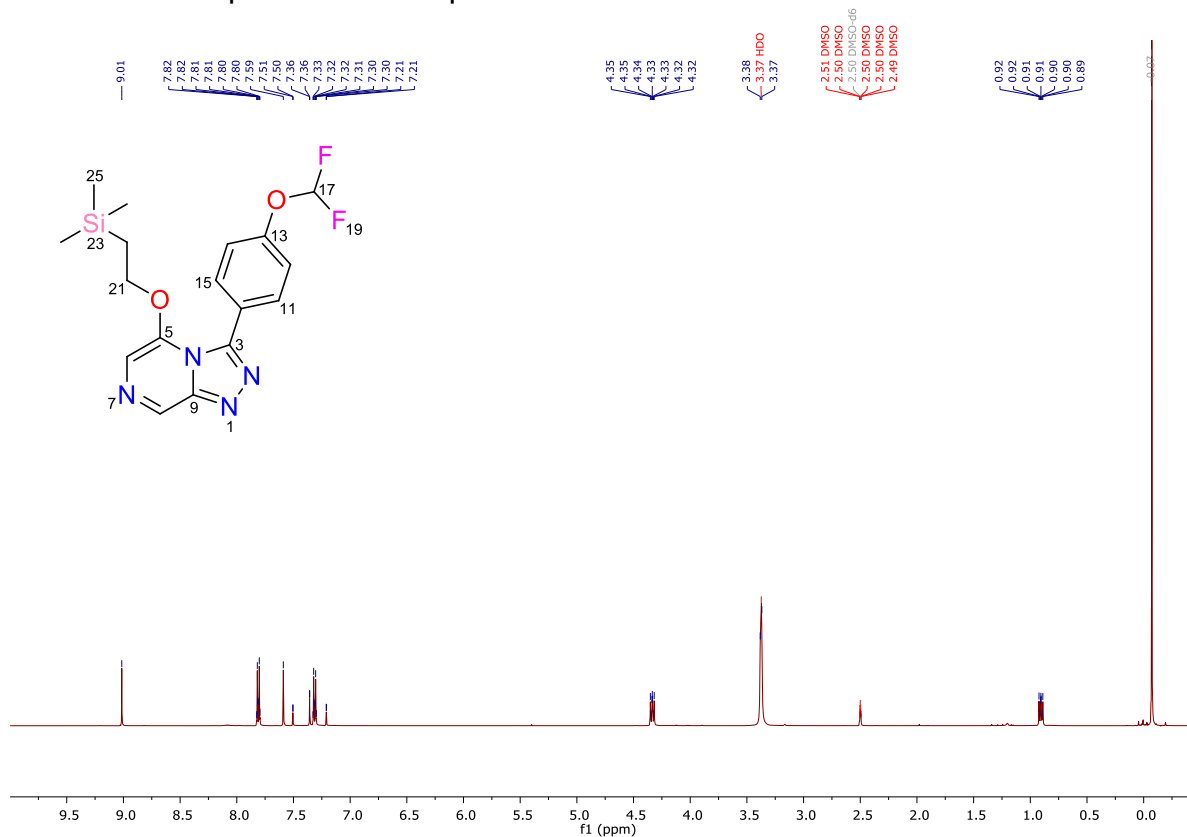
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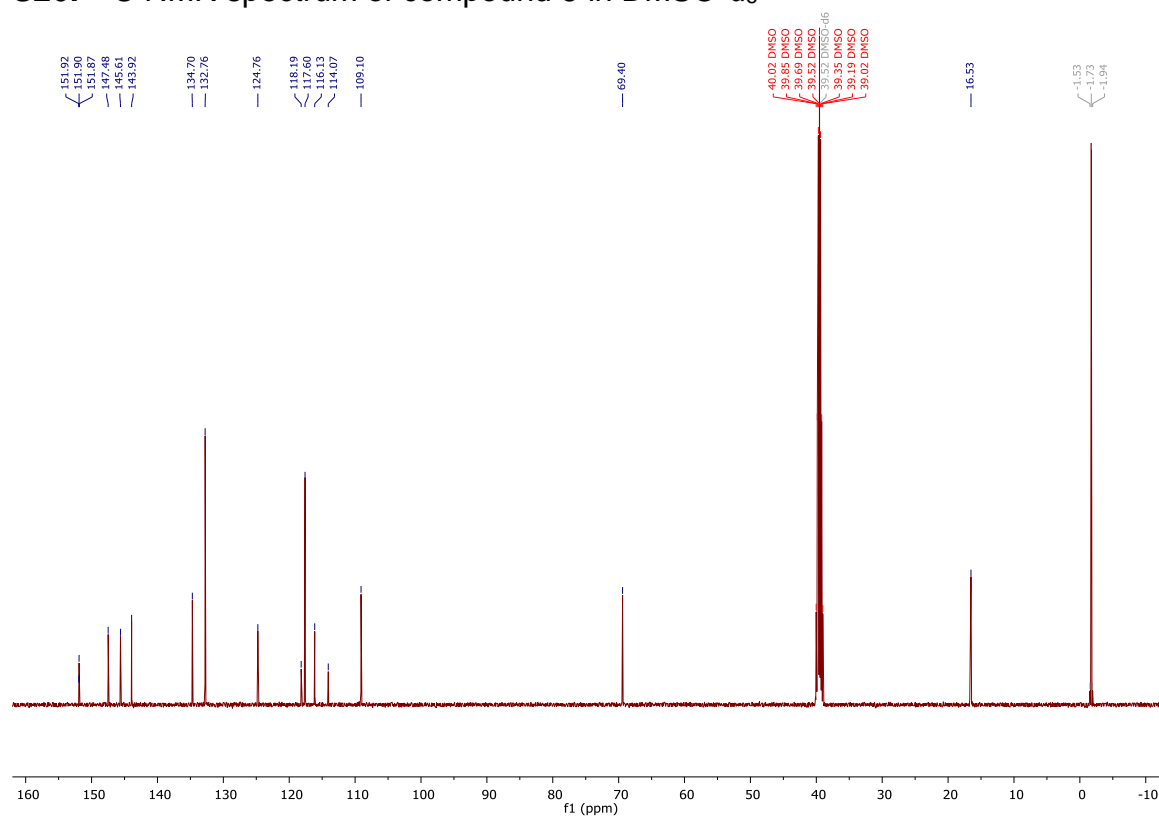
**S24:** NMR data of compound **5** in DMSO-*d*<sub>6</sub><sup>a</sup>

Pos.	δ <sub>H</sub> , mult. ( <i>J</i> in Hz), int.	δ <sub>C</sub> , mult. ( <i>J</i> in Hz)	COSY	HMBC	ROESY
3		145.6, s			
5		143.9, s			
6	7.59, s, 1H	109.1, s		5, 8	21
8	9.01, s, 1H	134.7, s		6, 9	
9		147.5, s			
10		124.8, s			
11	7.81, m, 1H	132.8, s	12	3, 13,15	12
12	7.31, m, 1H	117.6, s	11	10,14	11
13		151.9, t (3.3)			
14	7.31, m, 1H	117.6, s	15	10, 12	15
15	7.81, m, 1H	132.8, s	14	3, 11, 13	14
17	7.36, t (73.6), 1H	116.1, t, (258.5)		13	
21	4.33, m, 2H	69.4, s	22	5, 22	6, 22
22	0.91, m, 2H	16.5, s	21	21, 24, 25, 26	21, 24, 25, 26
24	0.07, s, 3H	-1.7, s		22, 25, 26	22
25	0.07, s, 3H	-1.7, s		22, 24, 26	22
26	0.07, s, 3H	-1.7, s		22, 24, 25	22

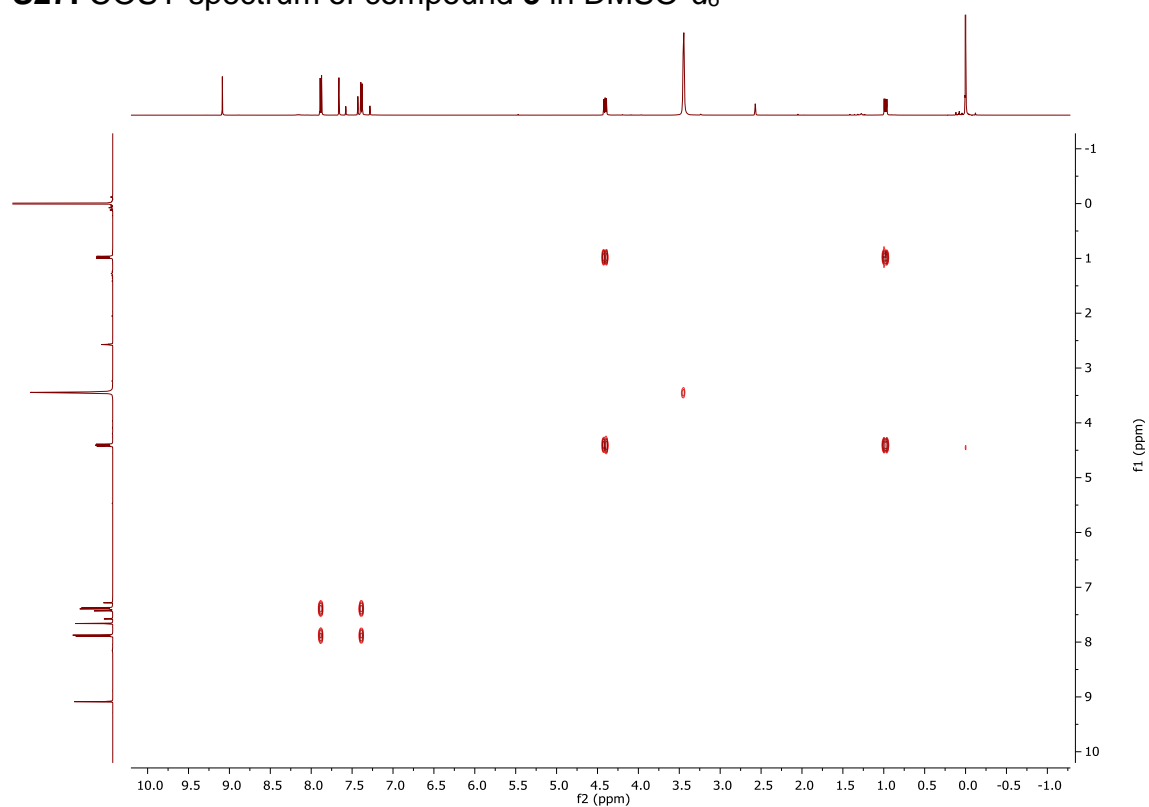
<sup>a</sup> Recorded at 500 MHz (<sup>1</sup>H NMR) and 125 MHz (<sup>13</sup>C NMR) at 25 °C.

**S25:** <sup>1</sup>H NMR spectrum of compound **5** DMSO-*d*<sub>6</sub>

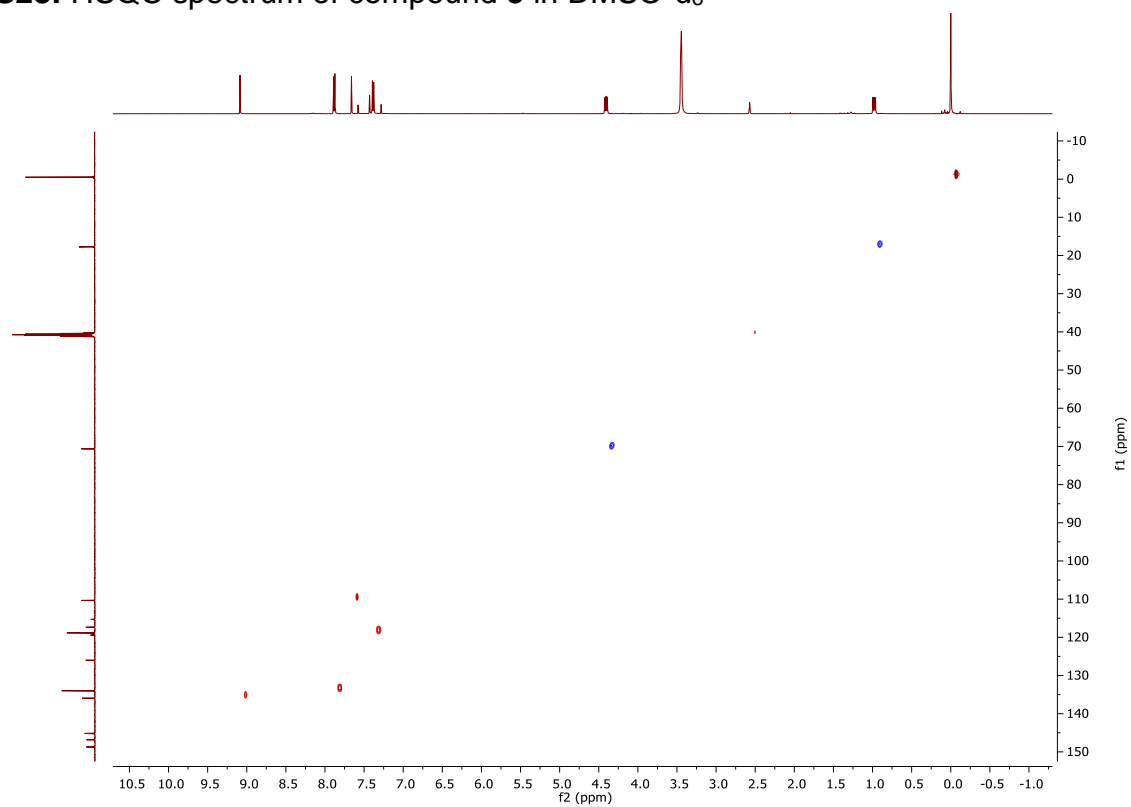
**S26:**  $^{13}\text{C}$  NMR spectrum of compound **5** in  $\text{DMSO}-d_6$



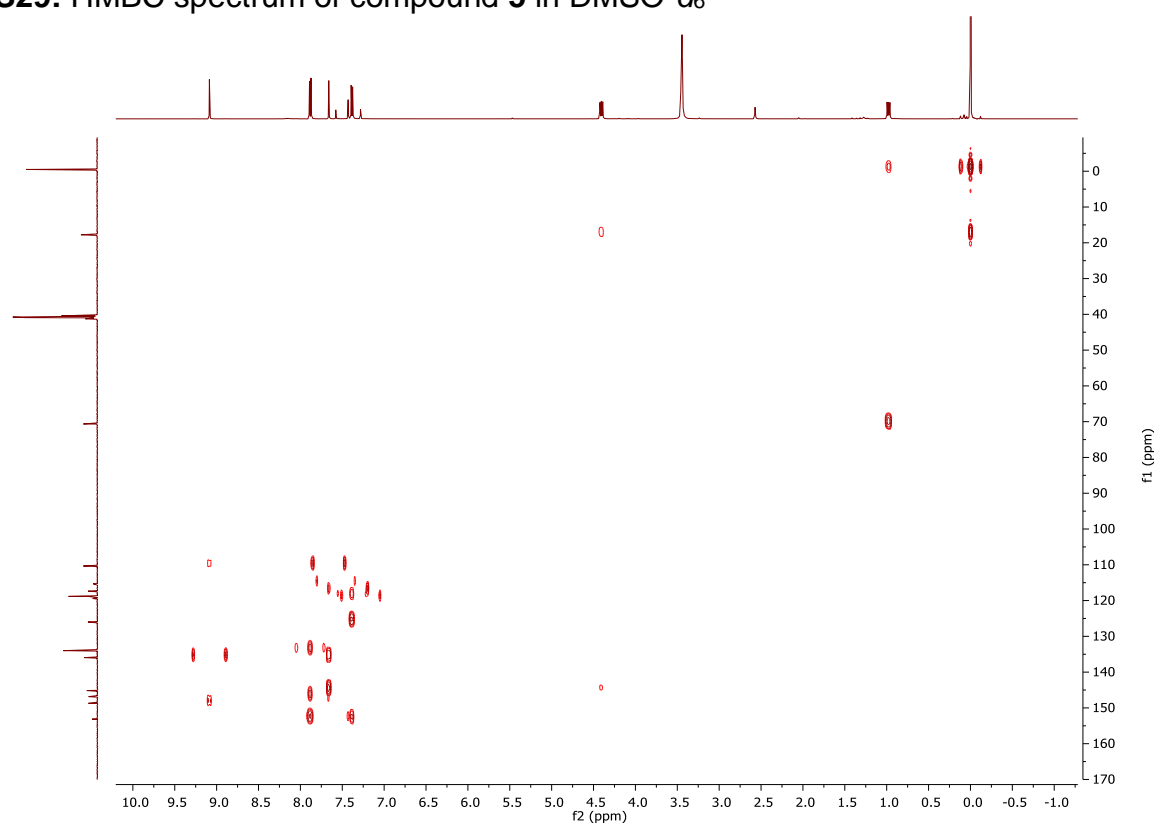
**S27:** COSY spectrum of compound **5** in  $\text{DMSO}-d_6$



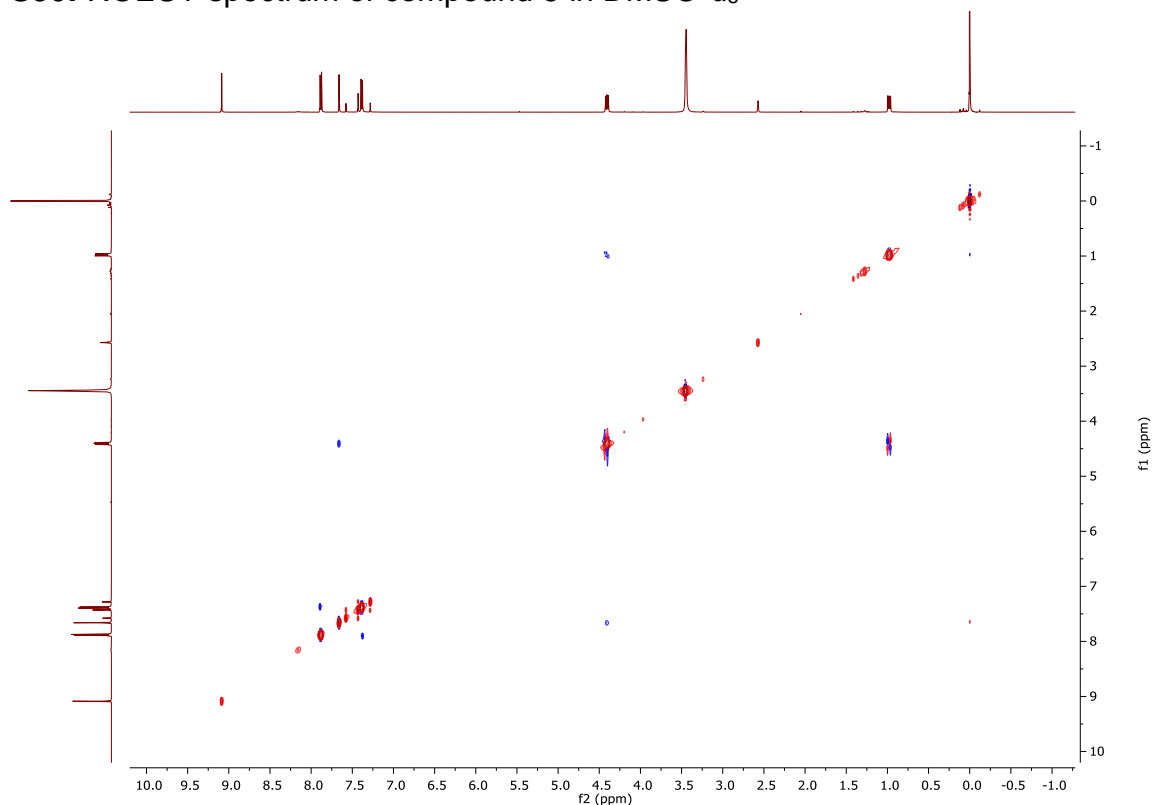
**S28:** HSQC spectrum of compound **5** in DMSO- $d_6$



**S29:** HMBC spectrum of compound **5** in DMSO- $d_6$



**S30:** ROESY spectrum of compound **5** in DMSO-*d*<sub>6</sub>



**S31:** HRMS of compound **5**



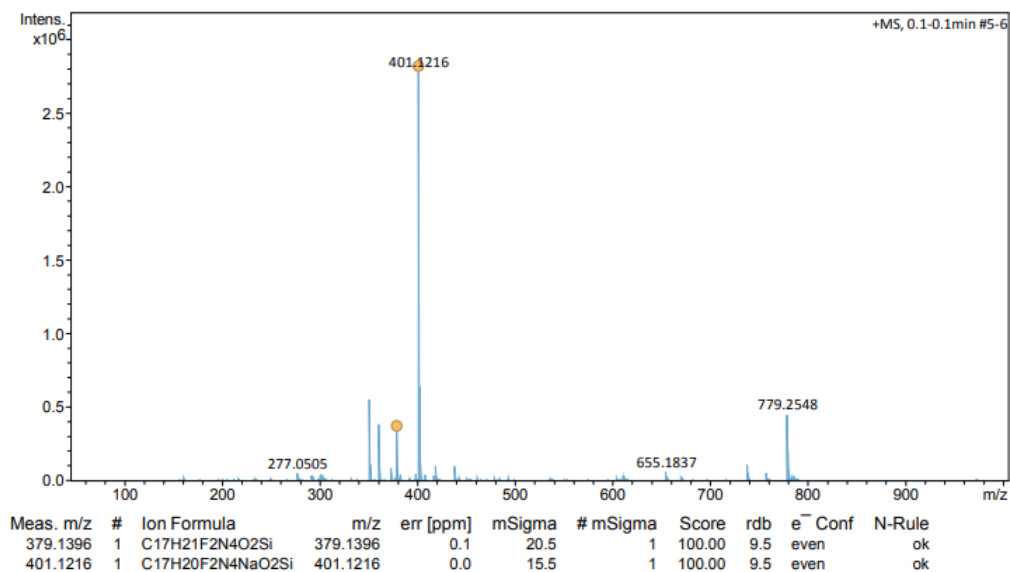
High Resolution Mass Spectrum

**Analysis Info**

Analysis Name D:\Data\KahYean\20200508\RAD860000001.d  
Method DirectInfusion\_2018\_pos.m  
Sample Name RAD860  
Comment

Acquisition Date 5/12/2020 12:13:02 PM  
Instrument maXis II ETD 1823391.22321

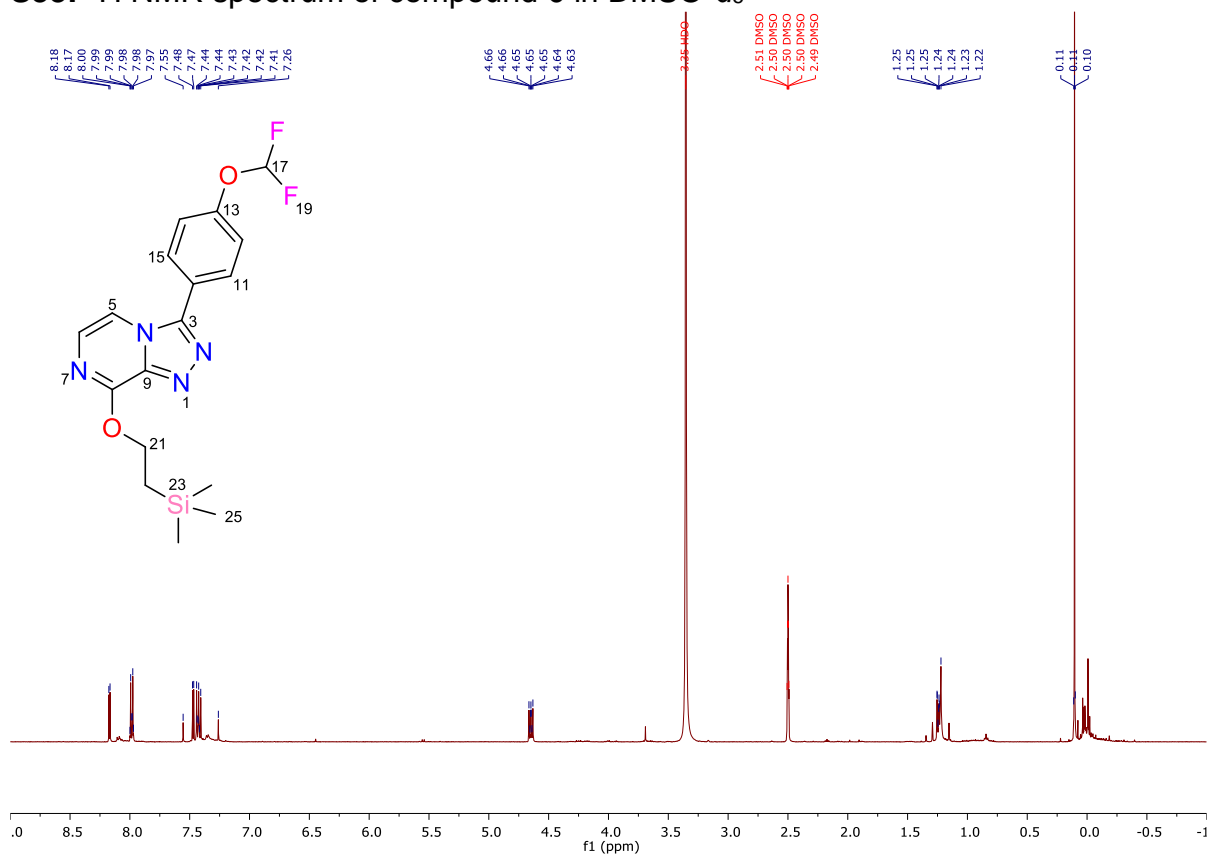
**+MS, 0.1-0.1min #5-6**



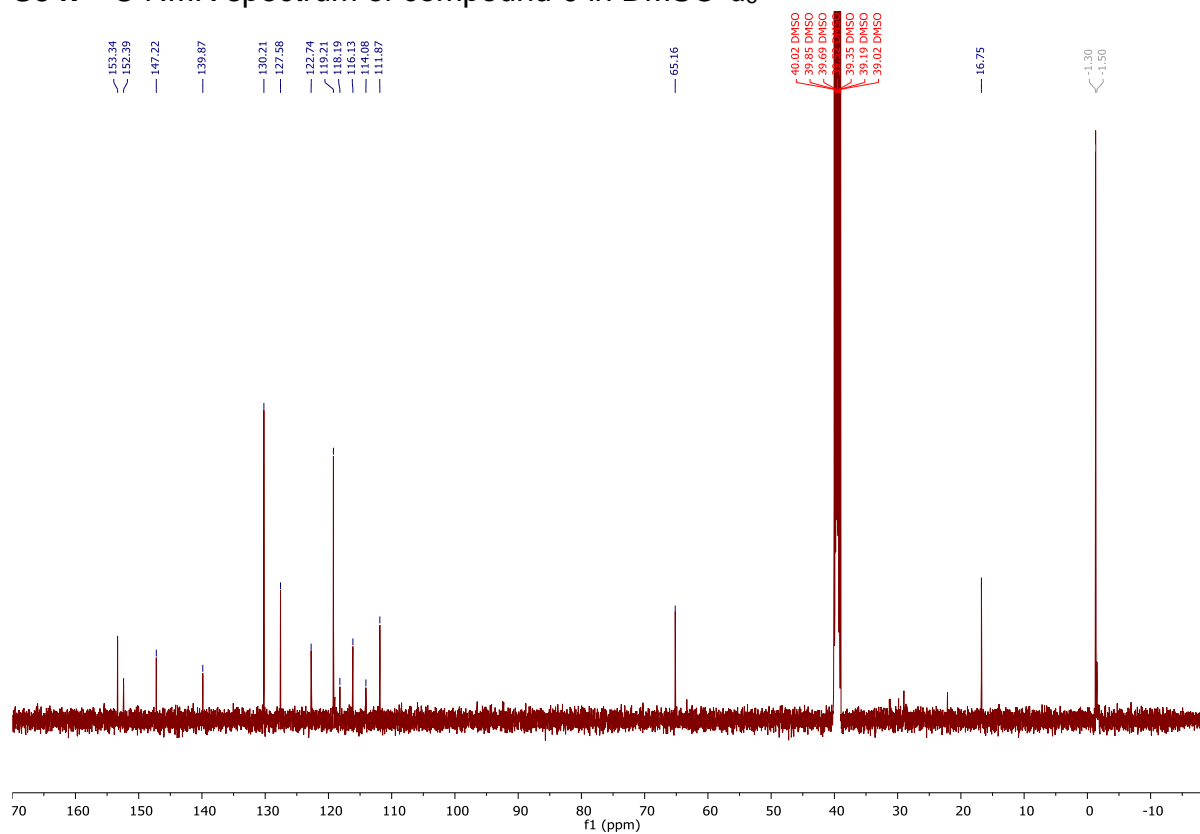


**S32:** NMR data of compound **6** in DMSO-*d*<sub>6</sub><sup>a</sup>

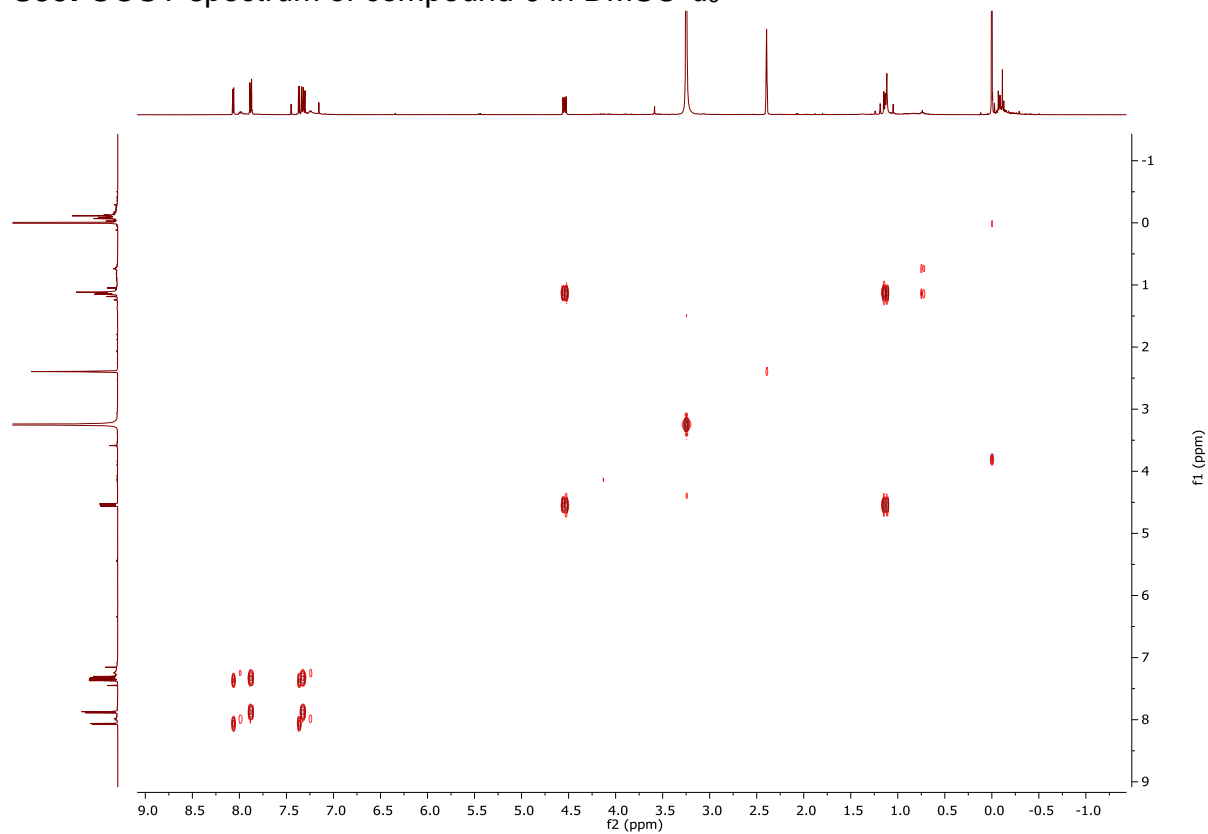
Pos.	δ <sub>H</sub> , mult. ( <i>J</i> in Hz), int.	δ <sub>C</sub> , mult. ( <i>J</i> in Hz)	COSY	HMBC
3		147.2, s		
5	8.17, d (4.9), 1H	111.9, s	6	6, 9
6	7.47, d (4.9), 1H	127.6, s	5	5, 8
8		153.3, s		
9		139.9, s		
10		122.7, s		
11	7.98, m, 1H	130.2, s	12	3, 13, 15
12	7.43, m, 1H	119.2, s	11	10, 14
13		152.4, t (3.3)		
14	7.43, m, 1H	119.2, s	15	10, 12
15	7.98, m, 1H	130.2, s	14	3, 11, 13
17	7.41, t (73.7), 1H	116.1, t (258.4)		13
21	4.65, m, 2H	65.2, s	22	22, 8
22	1.24, m, 2H	16.8, s	21	21, 24, 25, 26
24	0.11, s, 3H	-1.3, s		22, 25, 26
25	0.11, s, 3H	-1.3, s		22, 24, 26
26	0.11, s, 3H	-1.3, s		22, 24, 25

<sup>a</sup> Recorded at 500 MHz (<sup>1</sup>H NMR) and 125 MHz (<sup>13</sup>C NMR) at 25 °C.**S33:** <sup>1</sup>H NMR spectrum of compound **6** in DMSO-*d*<sub>6</sub>

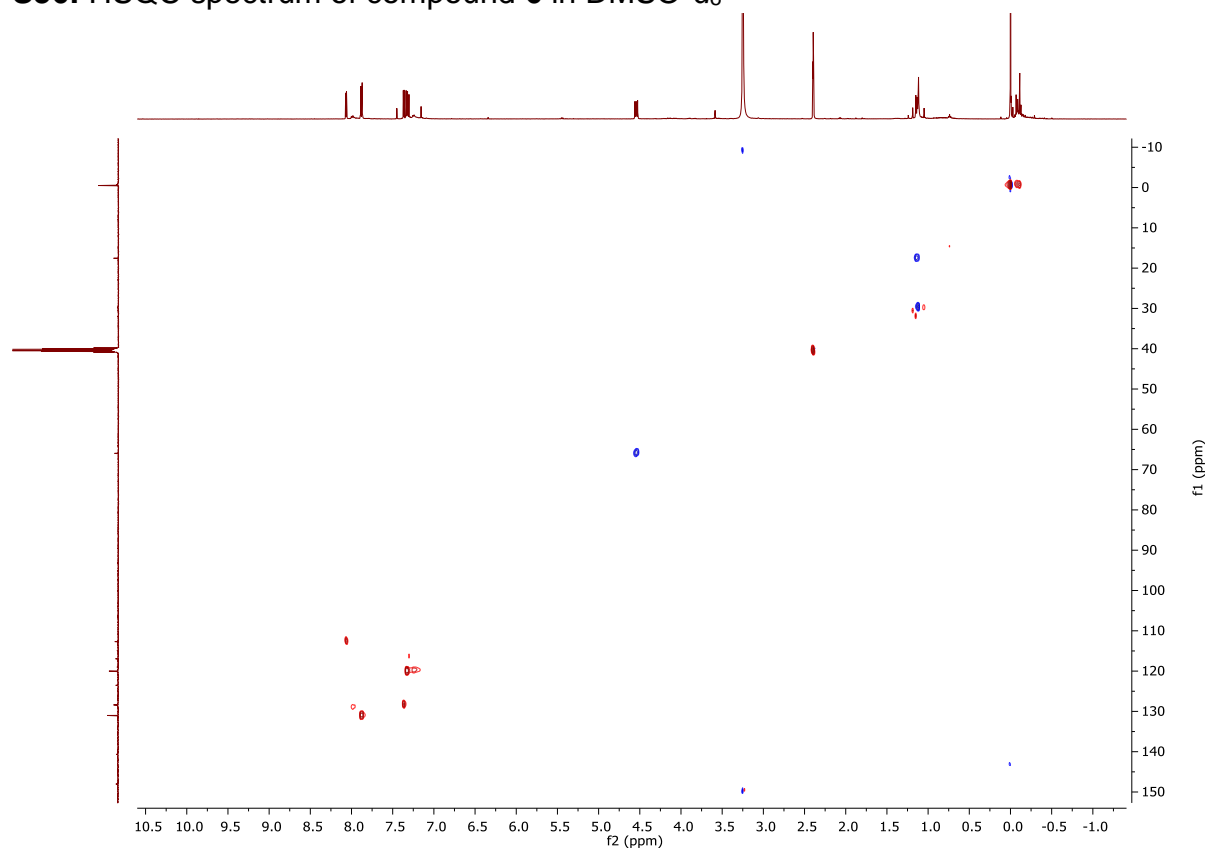
**S34:**  $^{13}\text{C}$  NMR spectrum of compound **6** in  $\text{DMSO}-d_6$



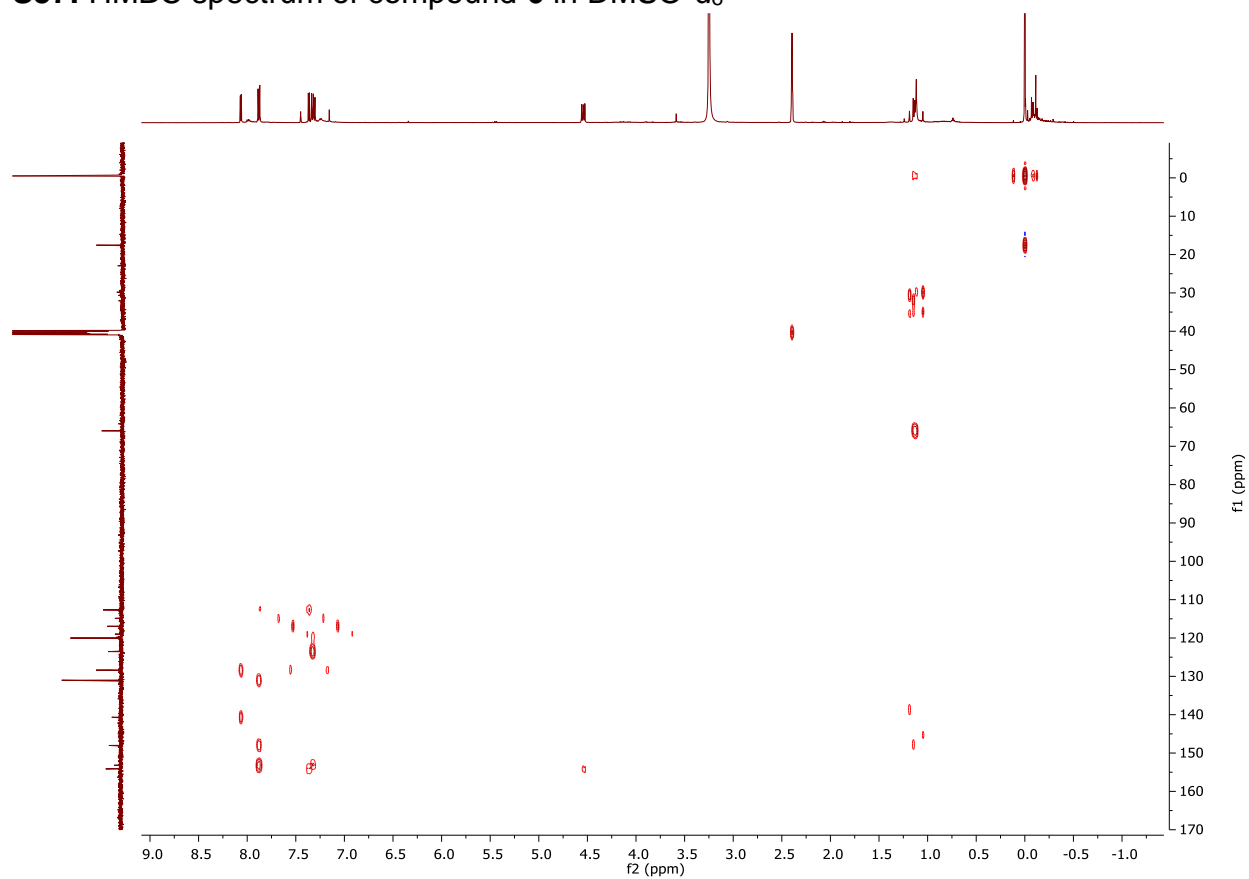
**S35:** COSY spectrum of compound **6** in  $\text{DMSO}-d_6$



**S36:** HSQC spectrum of compound **6** in DMSO- $d_6$



**S37:** HMBC spectrum of compound **6** in DMSO- $d_6$



# S38: HRMS of compound 6



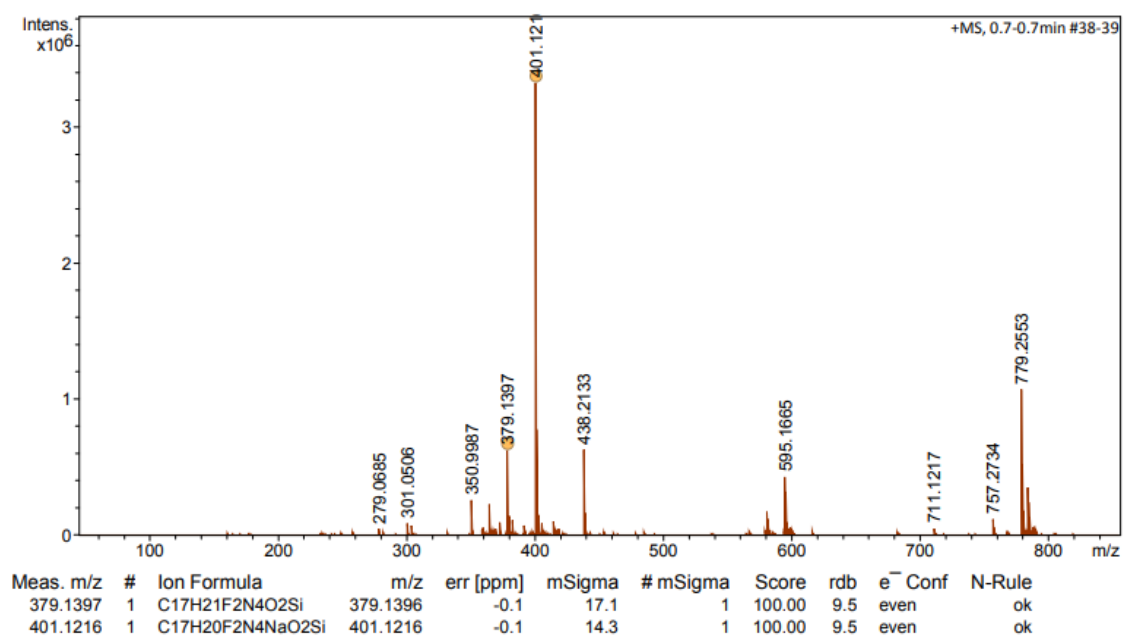
## High Resolution Mass Spectrum

### Analysis Info

Analysis Name D:\Data\KahYean\20200508\RAD861000002.d  
Method DirectInfusion\_2018\_pos.m  
Sample Name RAD861  
Comment

Acquisition Date 5/12/2020 12:26:20 PM  
Instrument maXis II ETD 1823391.22321

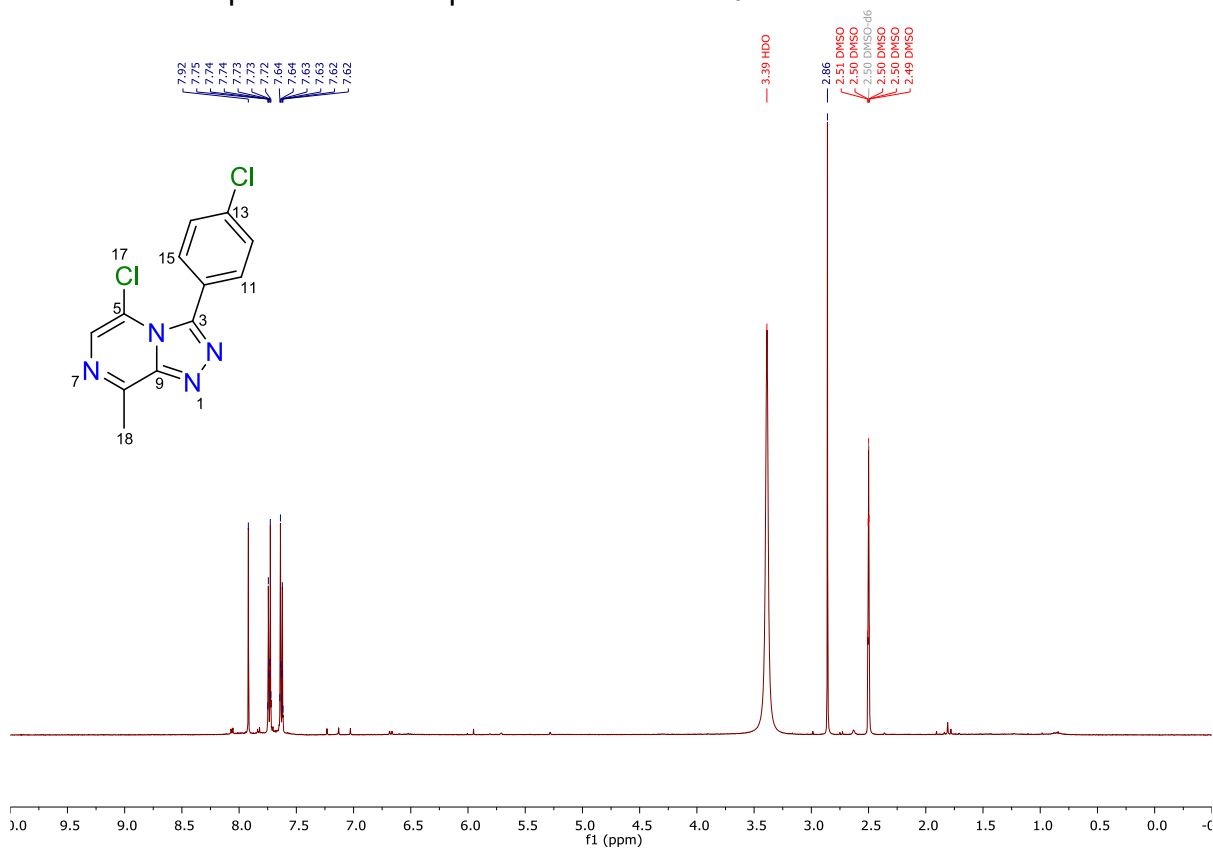
### +MS, 0.7-0.7min #38-39



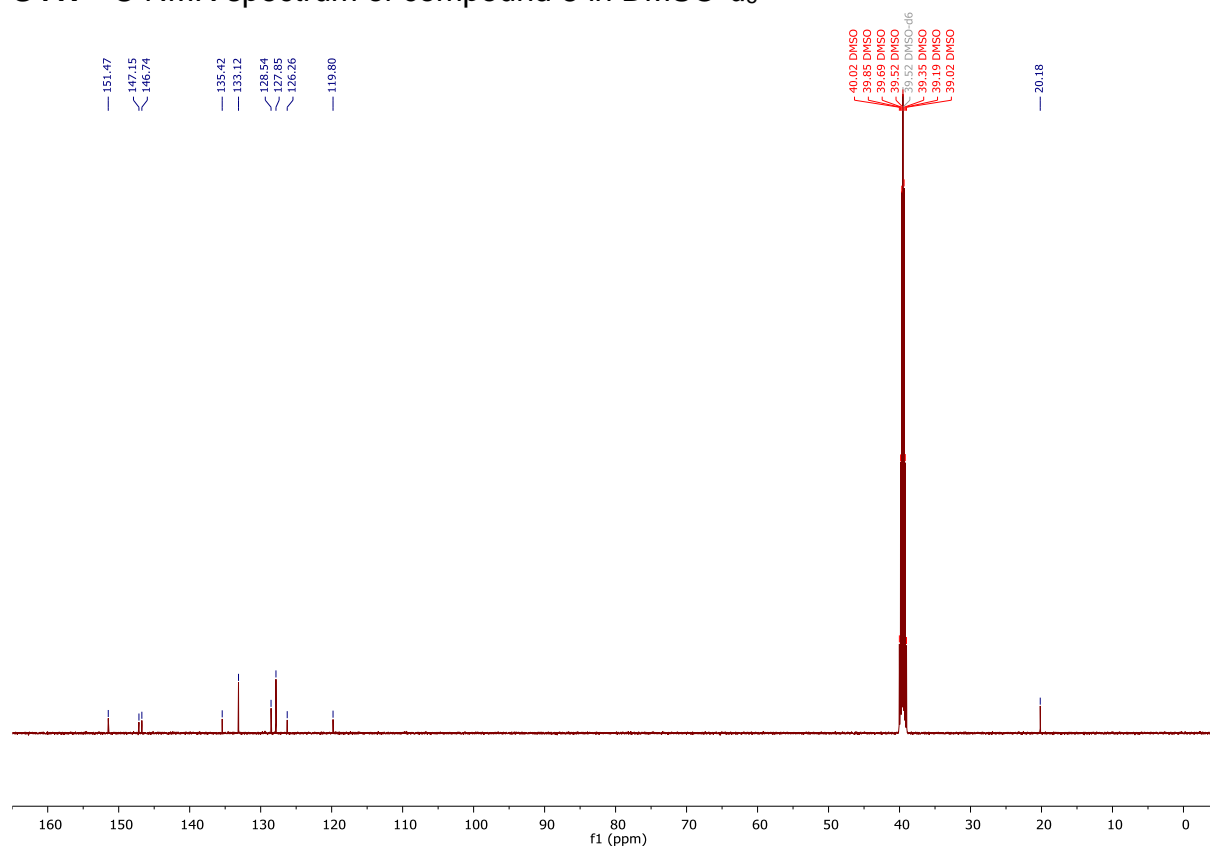
**S39:** NMR data of compound **8** in DMSO-*d*<sub>6</sub><sup>a</sup>

Position	δ <sub>H</sub> , mult. ( <i>J</i> in Hz)	δ <sub>C</sub>	COSY	HMBC
3		147.2		
5		119.8		
6	7.92, s, 1H	128.5		5, 8
8		151.5		
9		146.7		
10		126.3		
11	7.74, m, 1H	133.1	12	3, 13,15
12	7.63, m, 1H	127.9	11	10,14
13		135.4		
14	7.63, m, 1H	127.9	15	10, 12
15	7.74, m, 1H	133.1	14	3, 11, 13
18	2.86, s, 3H	20.2		5, 6, 8, 9

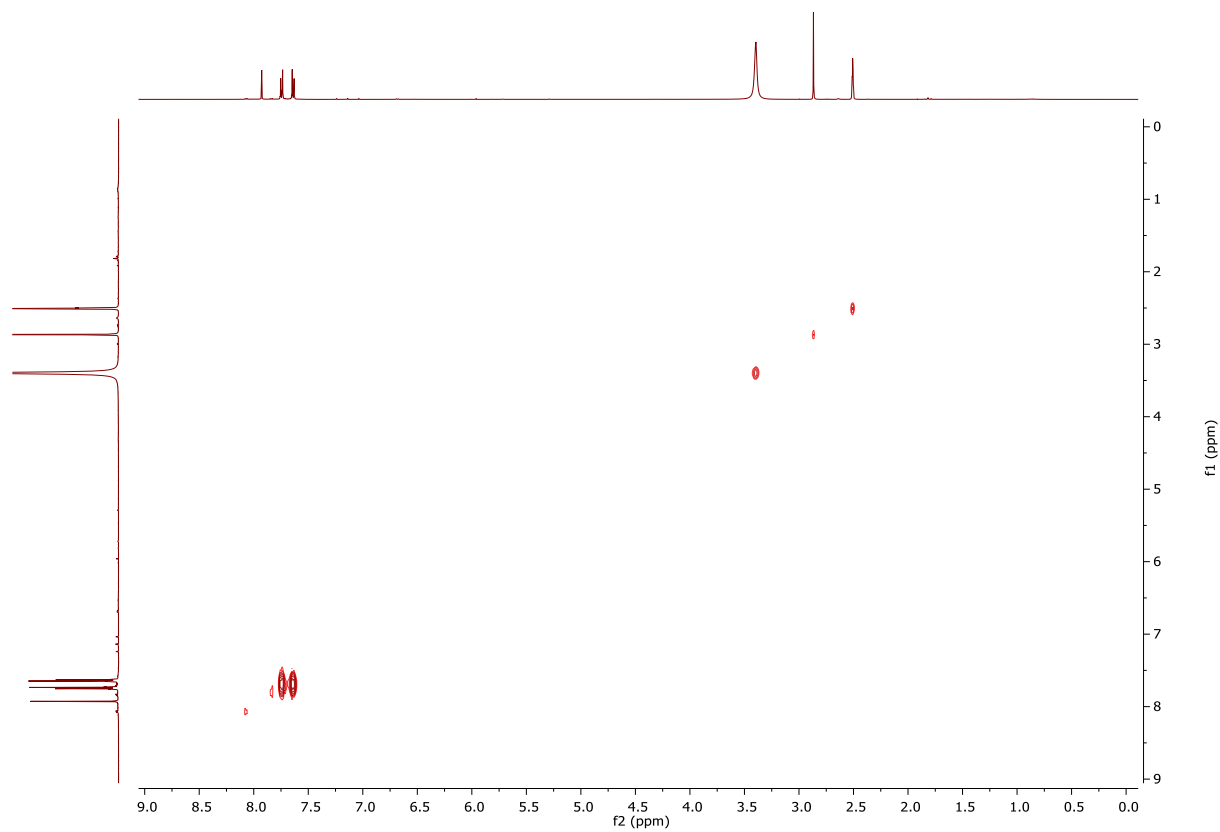
<sup>a</sup> Recorded at 500 MHz (<sup>1</sup>H NMR) and 125 MHz (<sup>13</sup>C NMR) at 25 °C.

**S40:** <sup>1</sup>H NMR spectrum of compound **8** in DMSO-*d*<sub>6</sub>

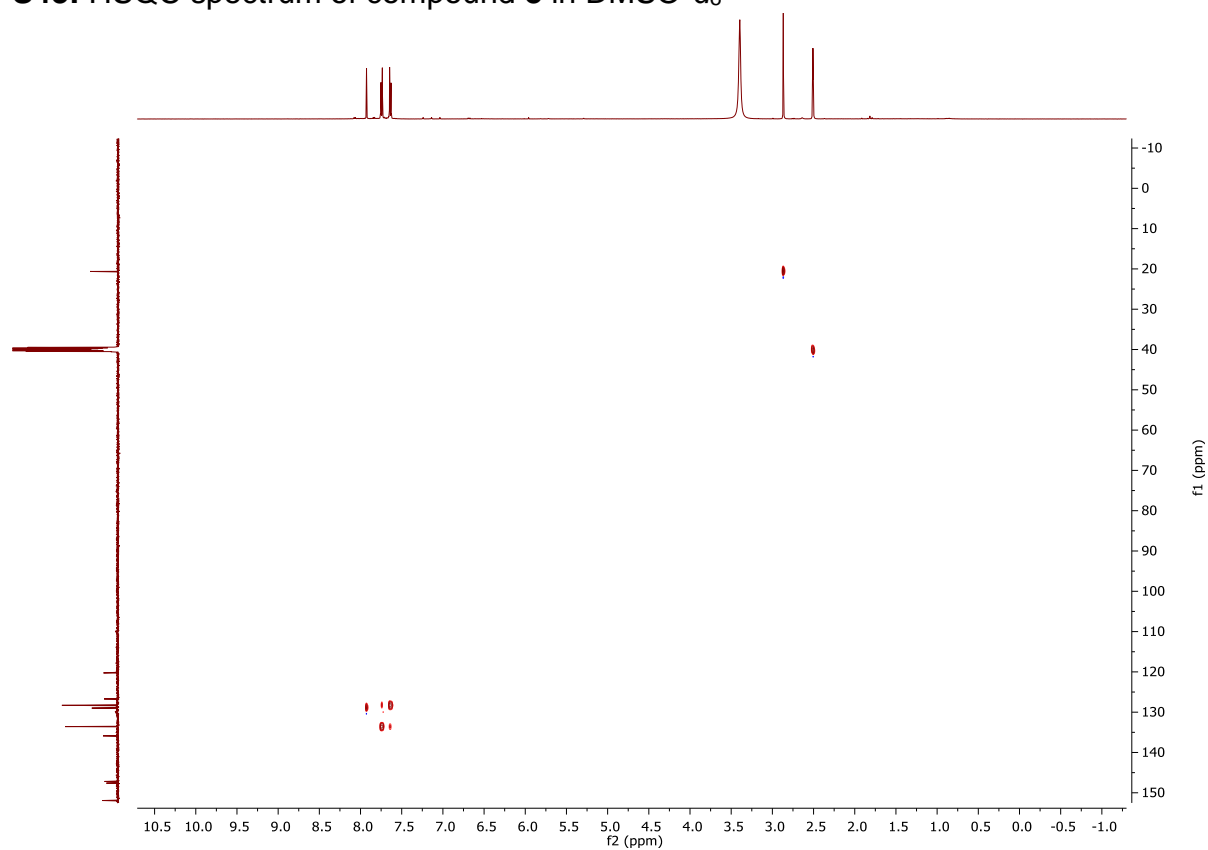
**S41:**  $^{13}\text{C}$  NMR spectrum of compound **8** in  $\text{DMSO}-d_6$



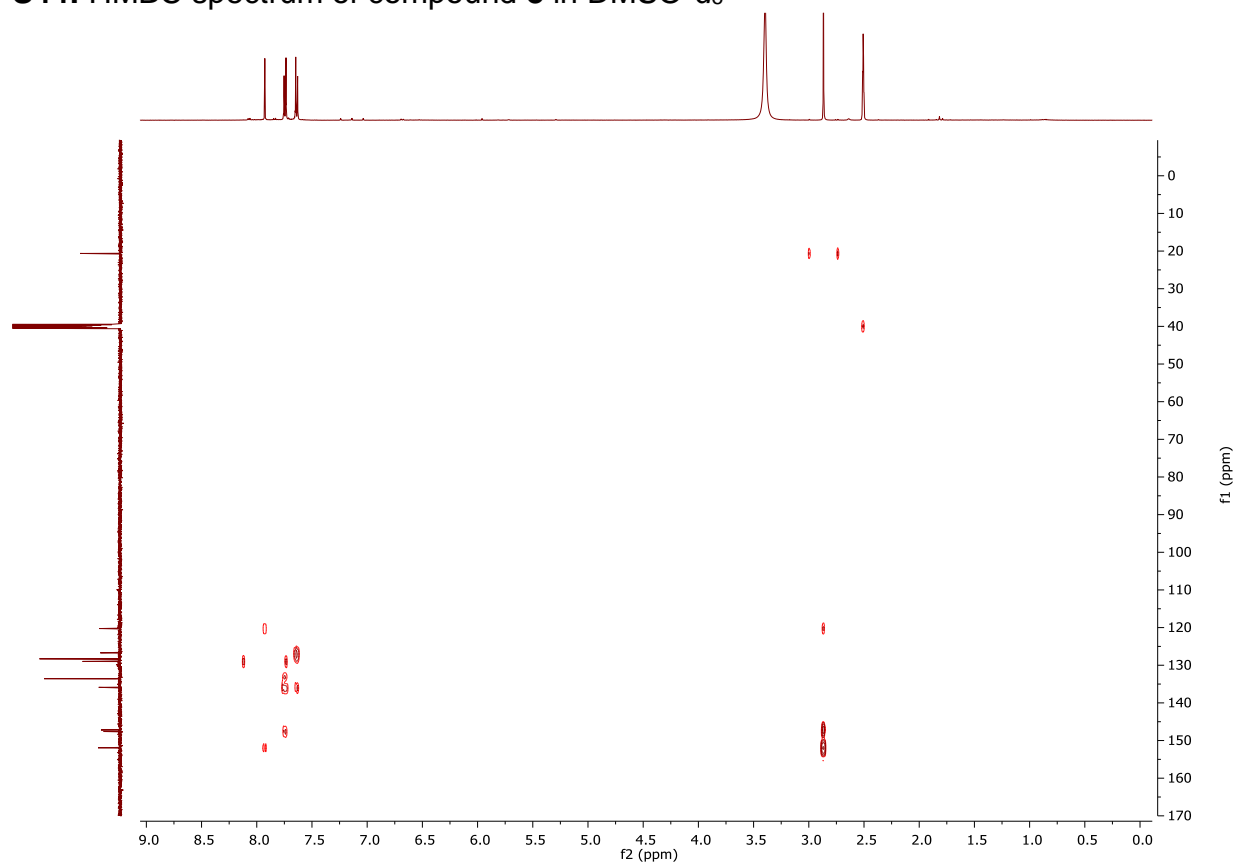
**S42:** COSY spectrum of compound **8** in  $\text{DMSO}-d_6$



**S43:** HSQC spectrum of compound **8** in DMSO- $d_6$



**S44:** HMBC spectrum of compound **8** in DMSO- $d_6$



## S45: HRMS of compound 8



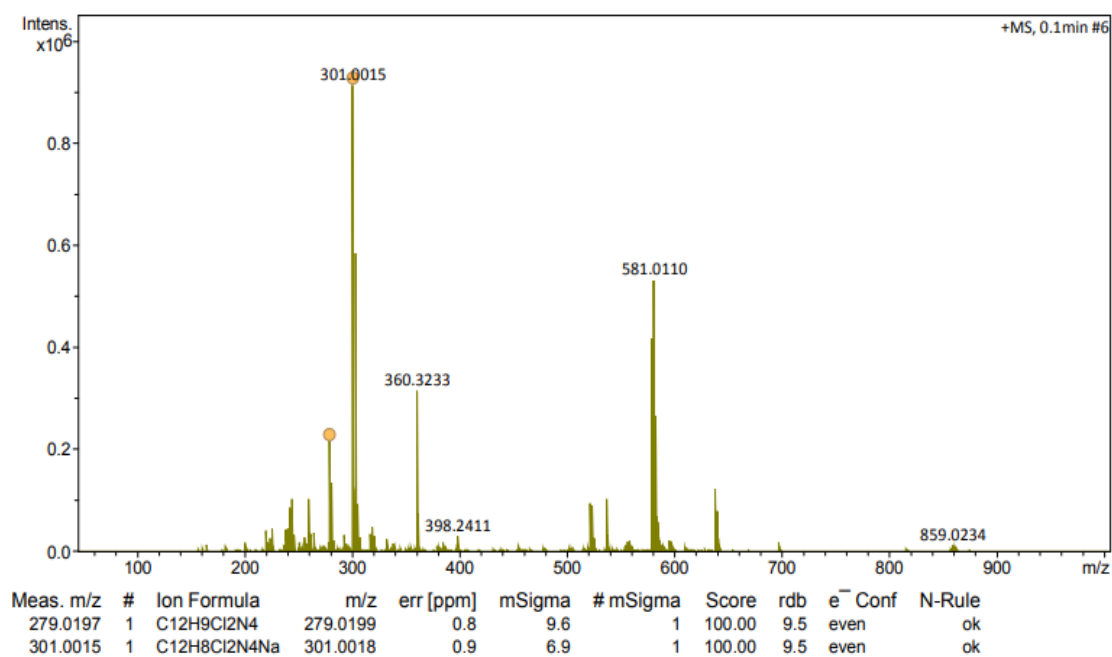
### High Resolution Mass Spectrum

#### Analysis Info

Analysis Name D:\Data\KahYean\20200508\RAD857000003.d  
Method DirectInfusion\_2018\_pos.m  
Sample Name RAD857  
Comment

Acquisition Date 5/12/2020 11:00:21 AM  
Instrument maXis II ETD 1823391.22321

#### +MS, 0.1min #6

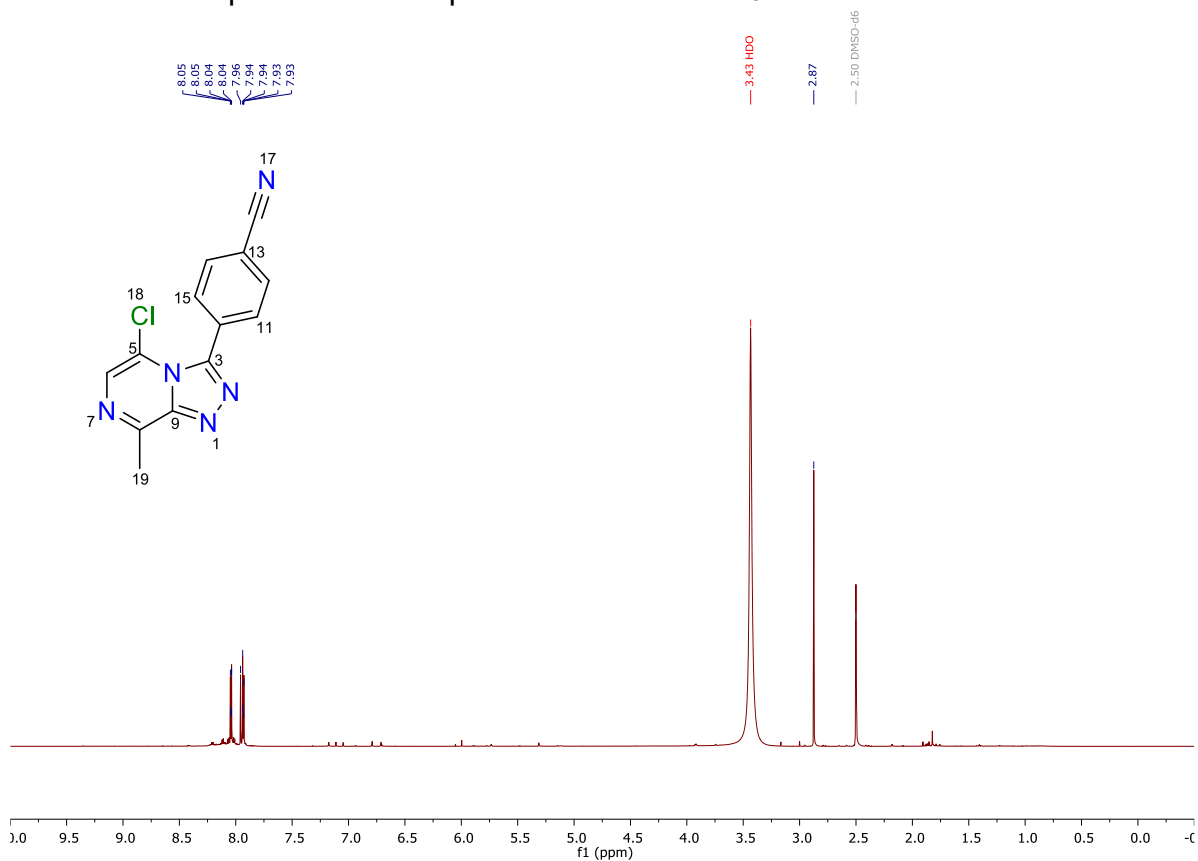




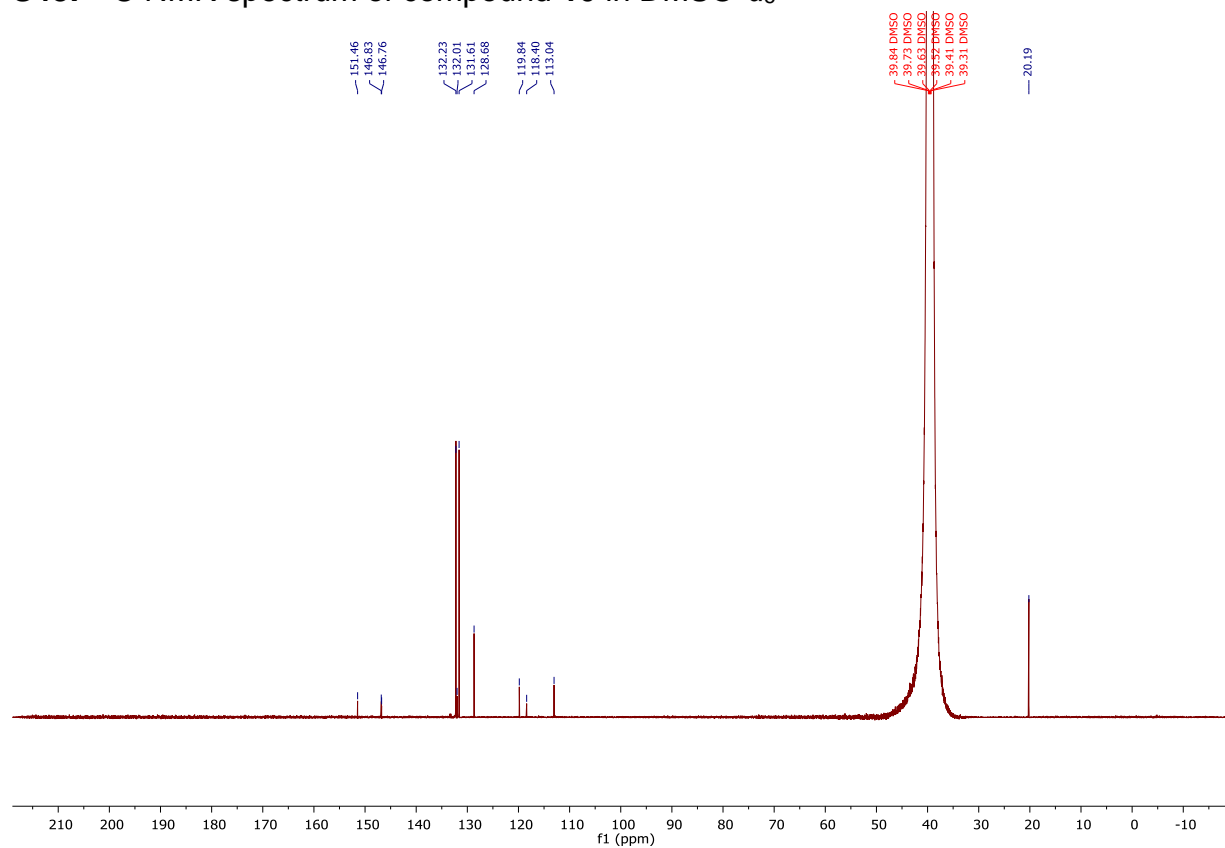
**S46:** NMR data of compound **10** in DMSO-*d*<sub>6</sub><sup>a</sup>

Position	δ <sub>H</sub> , mult. ( <i>J</i> in Hz)	δ <sub>C</sub>	COSY	HMBC
3		146.76 <sup>#</sup>		
5		119.8		
6	7.96, s, 1H	128.7		5, 8
8		151.5		
9		146.83 <sup>#</sup>		
10		132.0		
11	7.93, m, 1H	132.2	12	3, 13, 15
12	8.04, m, 1H	131.6	11	10, 14, 16
13		113.0		
14	8.04, m, 1H	131.6	15	10, 12, 16
15	7.93, m, 1H	132.2	14	3, 11, 13
16		118.4		
19	2.87, s, 3H	20.2		5, 6, 8, 9

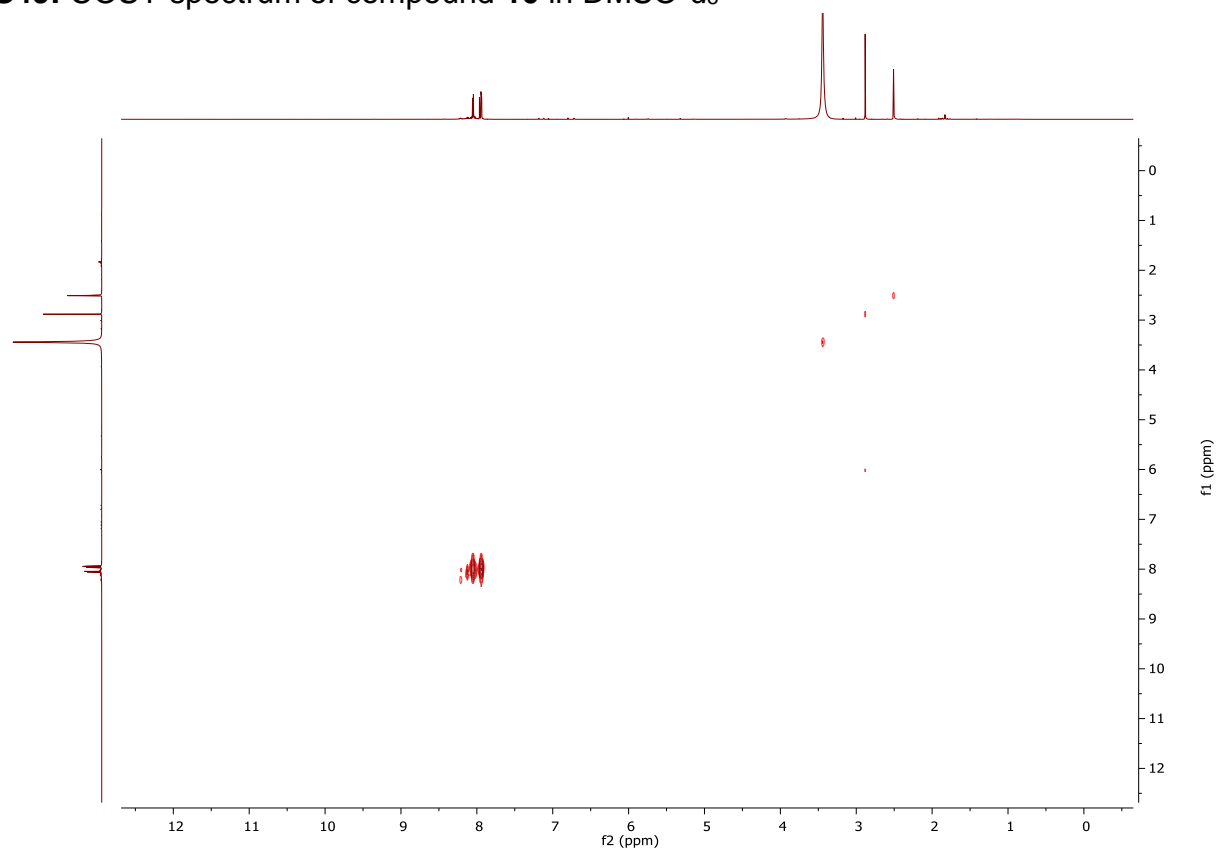
<sup>a</sup> Recorded at 500 MHz (<sup>1</sup>H NMR) and 125 MHz (<sup>13</sup>C NMR) at 25 °C. <sup>#</sup> Interchangeable signals.

**S47:** <sup>1</sup>H NMR spectrum of compound **10** in DMSO-*d*<sub>6</sub>

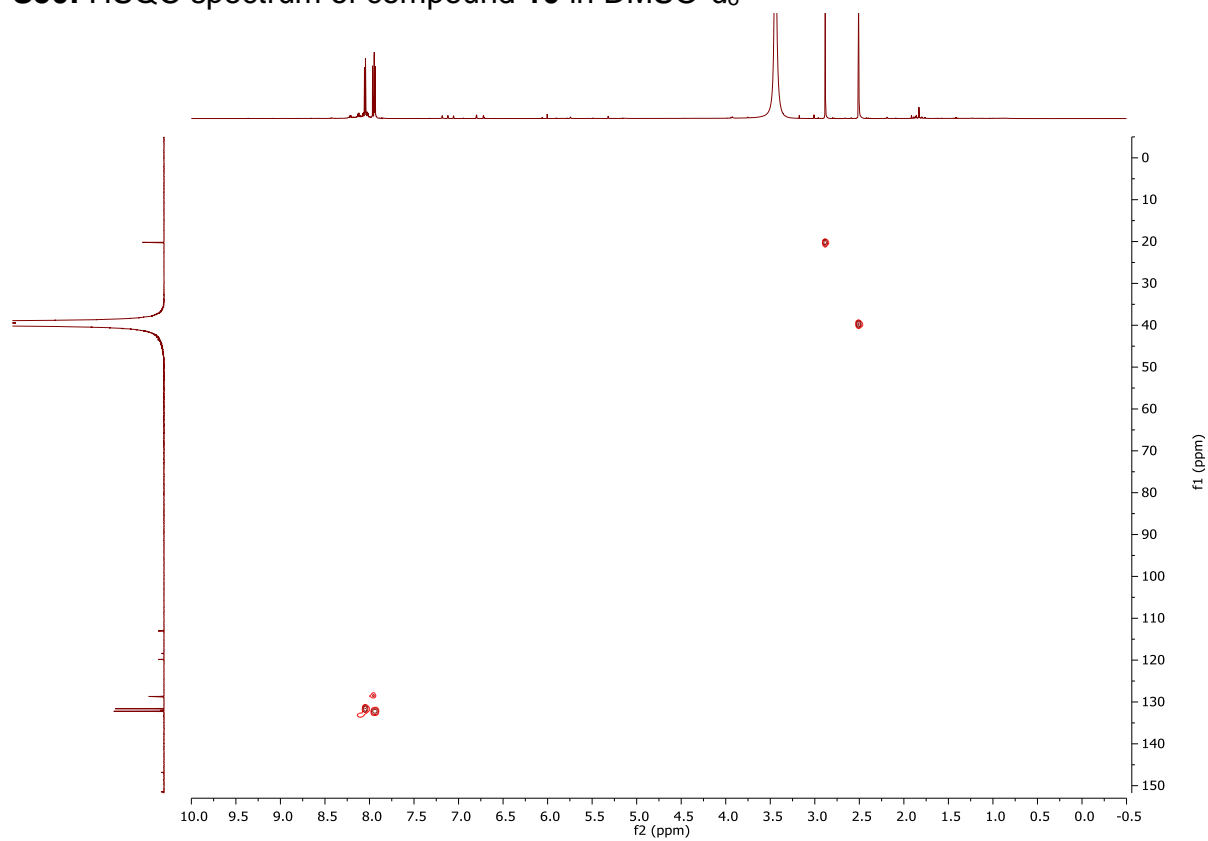
**S48:**  $^{13}\text{C}$  NMR spectrum of compound **10** in  $\text{DMSO}-d_6$



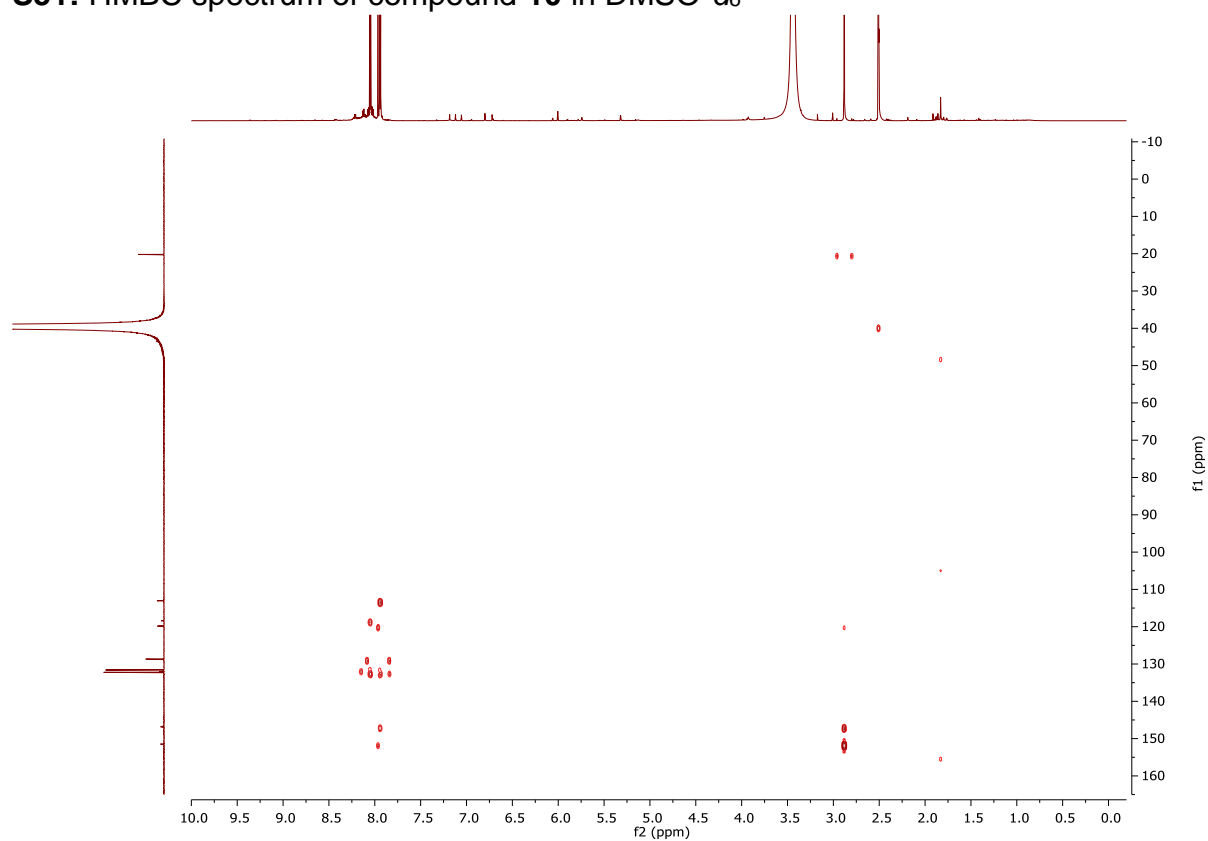
**S49:** COSY spectrum of compound **10** in  $\text{DMSO}-d_6$



**S50:** HSQC spectrum of compound **10** in DMSO- $d_6$



**S51:** HMBC spectrum of compound **10** in DMSO- $d_6$



## S52: HRMS of compound 10



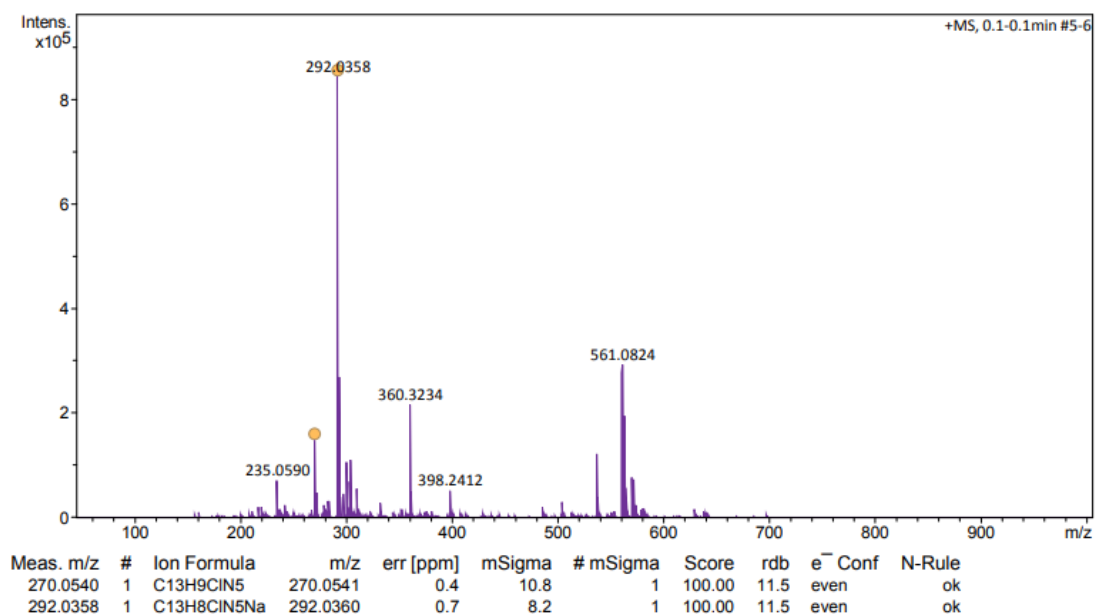
### High Resolution Mass Spectrum

#### Analysis Info

Analysis Name D:\Data\KahYean\20200508\RAD858000001.d  
Method DirectInfusion\_2018\_pos.m  
Sample Name RAD858  
Comment

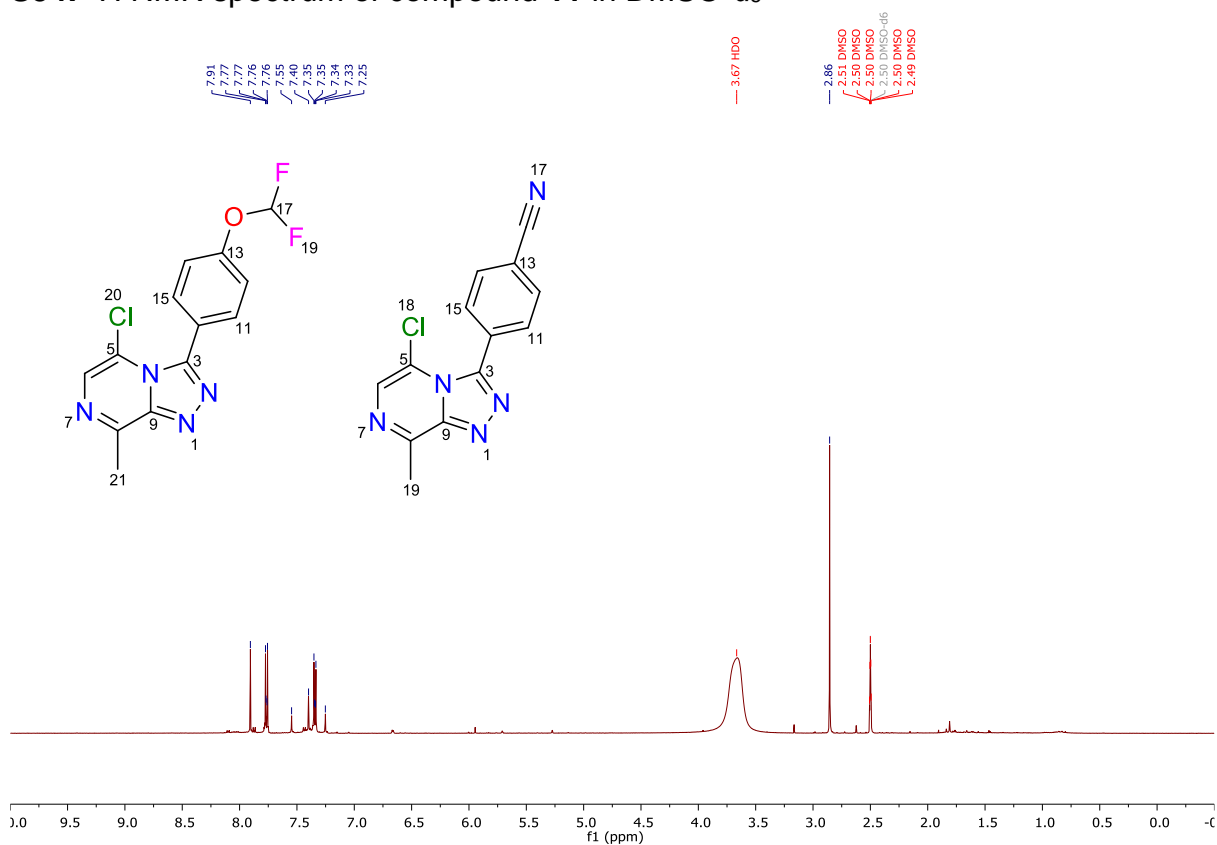
Acquisition Date 5/12/2020 11:09:33 AM  
Instrument maXis II ETD 1823391.22321

#### +MS, 0.1-0.1min #5-6

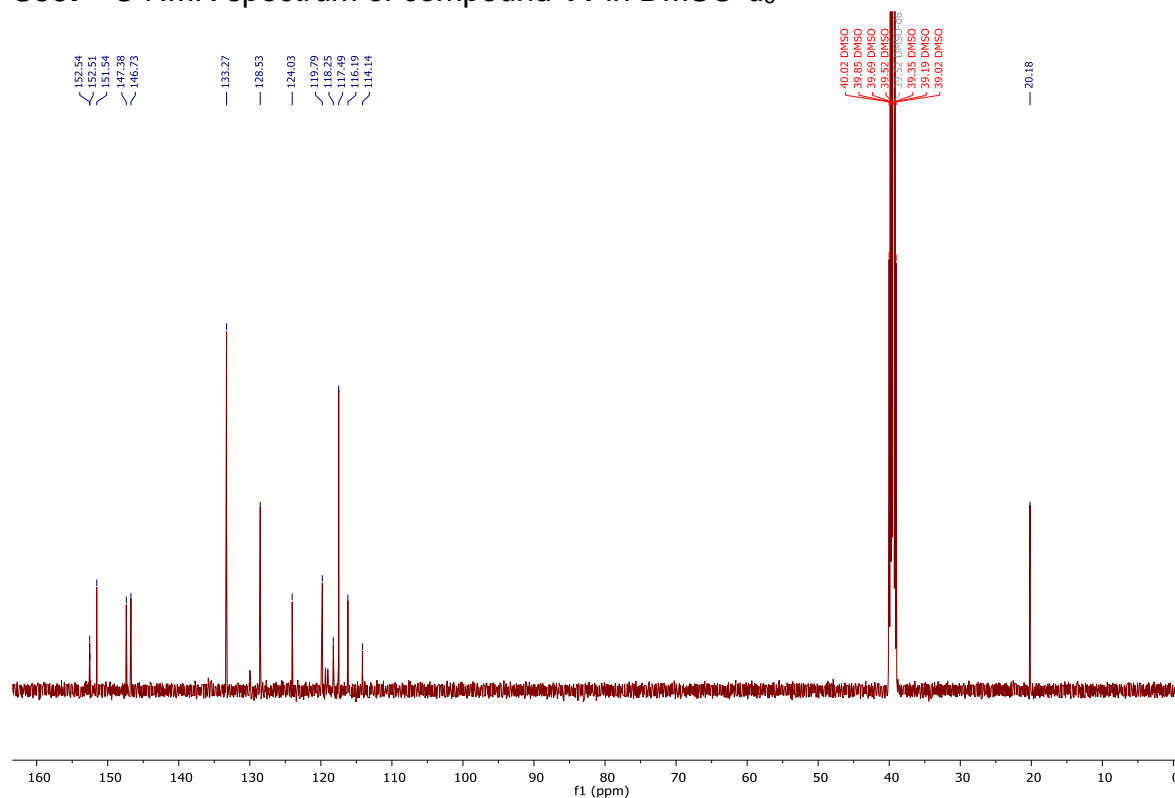


**S53:** NMR data of compound **11** in DMSO-*d*<sub>6</sub><sup>a</sup>

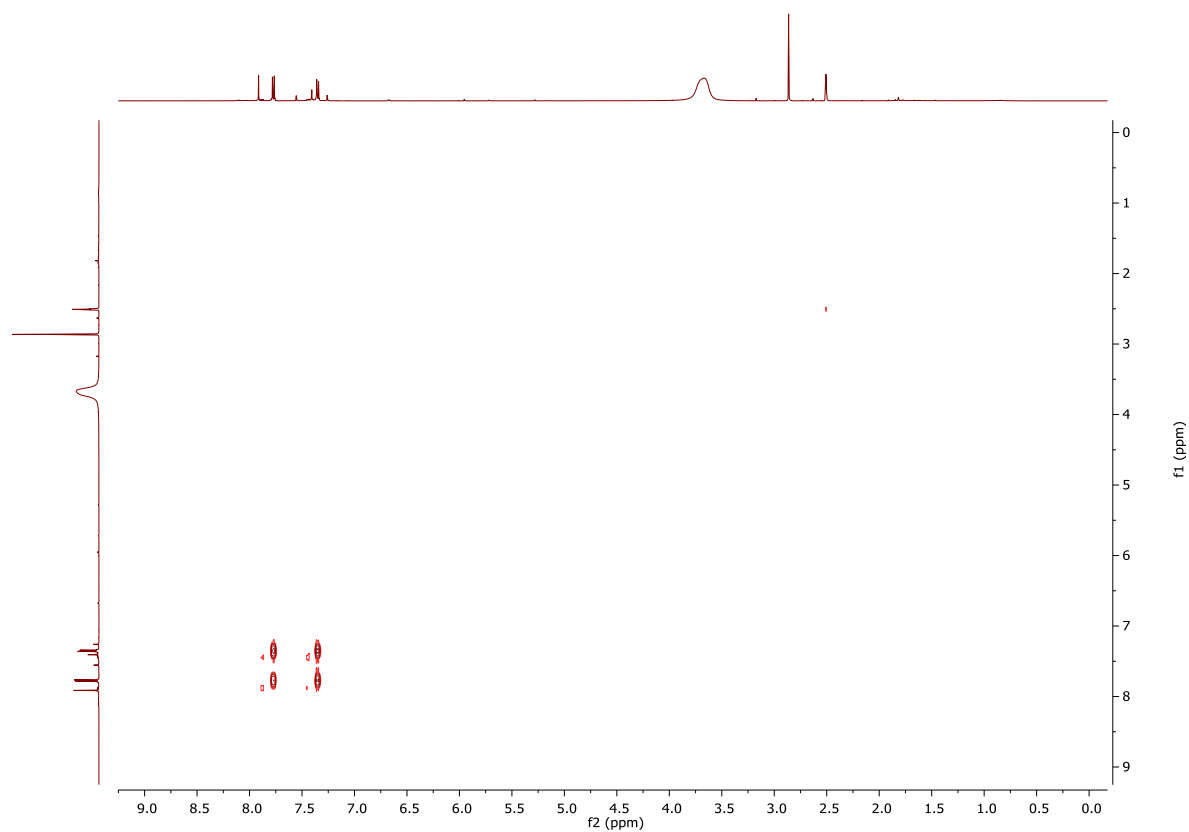
Pos	δ <sub>H</sub> , mult. ( <i>J</i> in Hz), int.	δ <sub>C</sub> , mult. ( <i>J</i> in Hz)	COSY	HMBC
3		147.4, s		
5		119.8, s		
6	7.91, s, 1H	128.5, s		5, 8
8		151.5, s		
9		146.7, s		
10		124.0, s		
11	7.77, m, 1H	133.3, s	12	3, 13, 15
12	7.34, m, 1H	117.5, s	11	10, 14
13		152.5, t (3.3)		
14	7.34, m, 1H	117.5, s	15	10, 12
15	7.77, m, 1H	133.3, s	14	3, 11, 13
17	7.40, t (73.7), 1H	116.2, t (258.5)		13
21	2.86, s, 3H	20.2, s		5, 6, 8, 9

<sup>a</sup> Recorded at 500 MHz (<sup>1</sup>H NMR) and 125 MHz (<sup>13</sup>C NMR) at 25 °C.**S54:** <sup>1</sup>H NMR spectrum of compound **11** in DMSO-*d*<sub>6</sub>

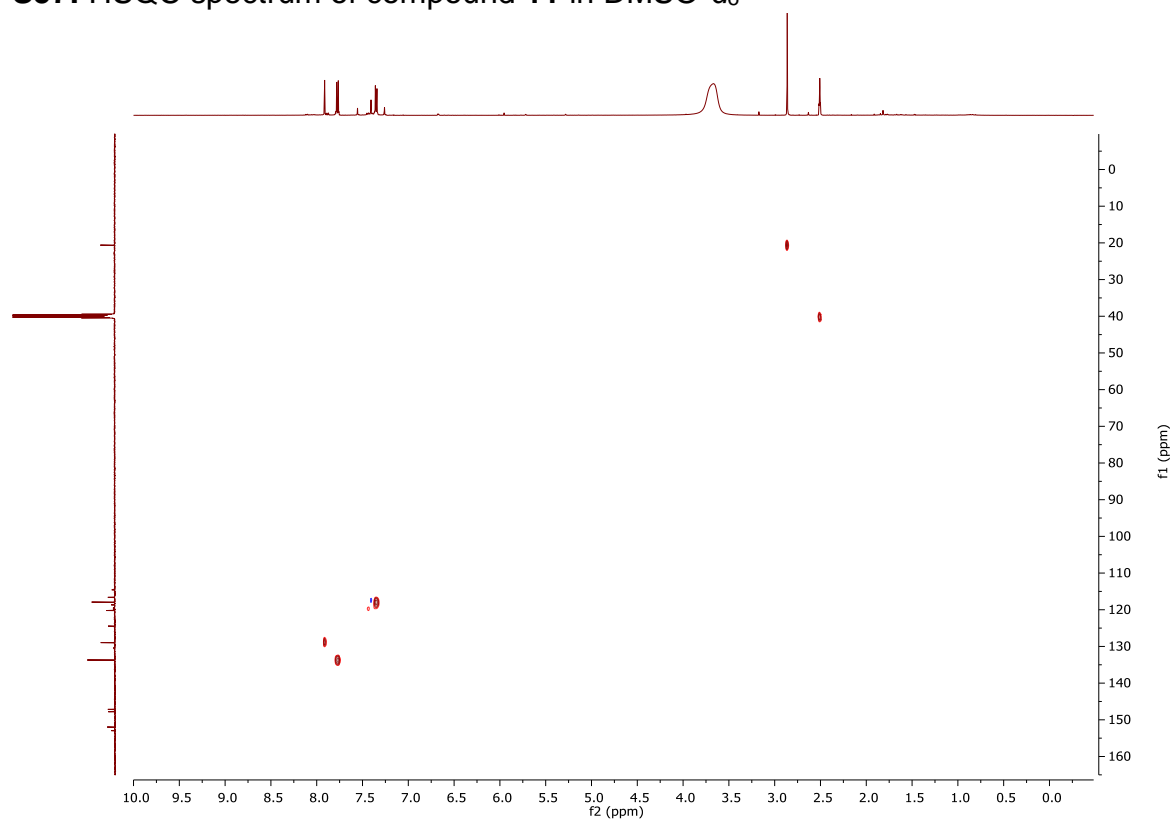
**S55:**  $^{13}\text{C}$  NMR spectrum of compound **11** in  $\text{DMSO}-d_6$



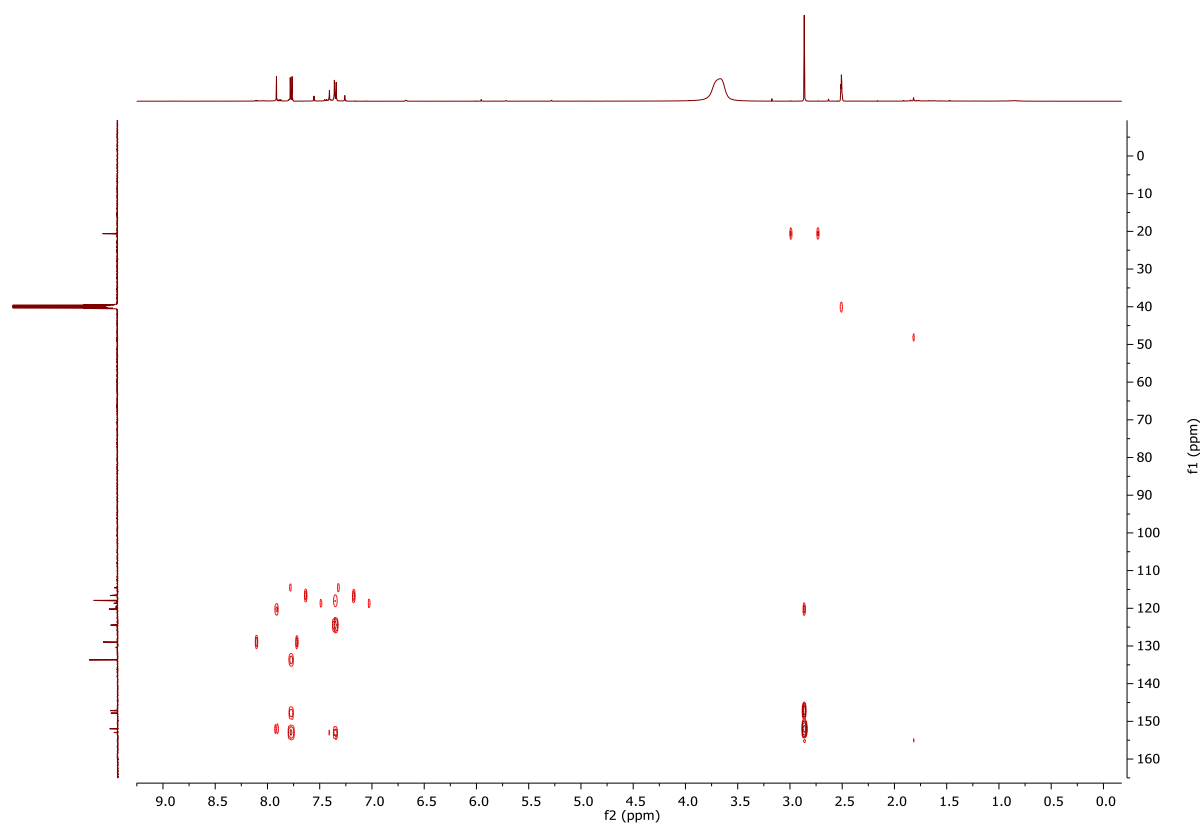
**S56:** COSY spectrum of compound **11** in  $\text{DMSO}-d_6$



**S57:** HSQC spectrum of compound **11** in DMSO- $d_6$



**S58:** HMBC spectrum of compound **11** in DMSO- $d_6$



## S59: HRMS of compound 11



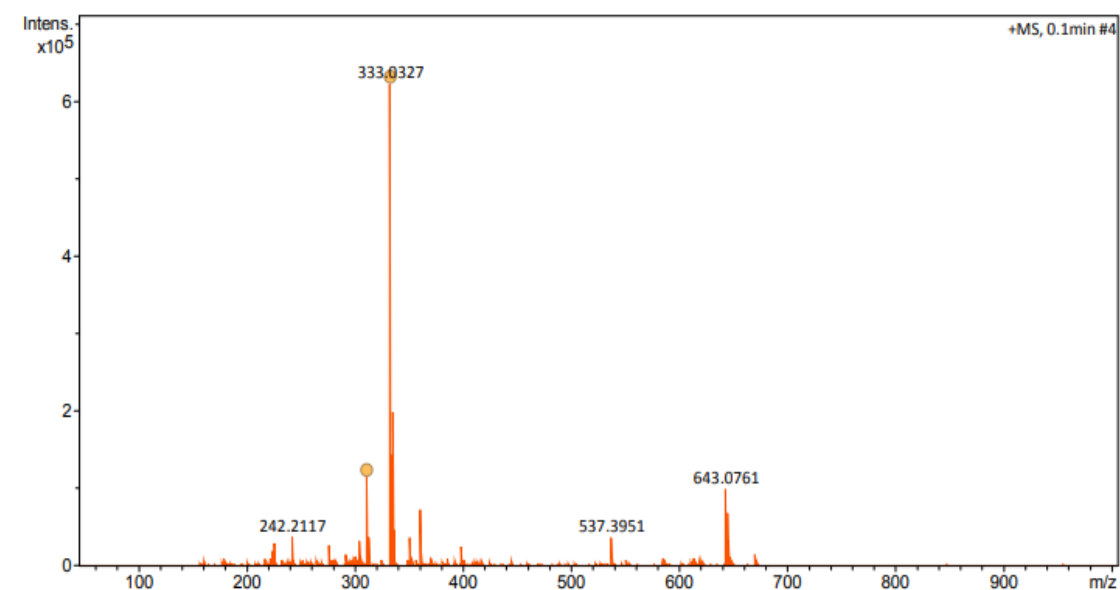
### High Resolution Mass Spectrum

#### Analysis Info

Analysis Name D:\Data\KahYean\20200508\RAD859000001.d  
Method DirectInfusion\_2018\_pos.m  
Sample Name RAD859  
Comment

Acquisition Date 5/12/2020 11:16:52 AM  
Instrument maXis II ETD 1823391.22321

#### +MS, 0.1min #4

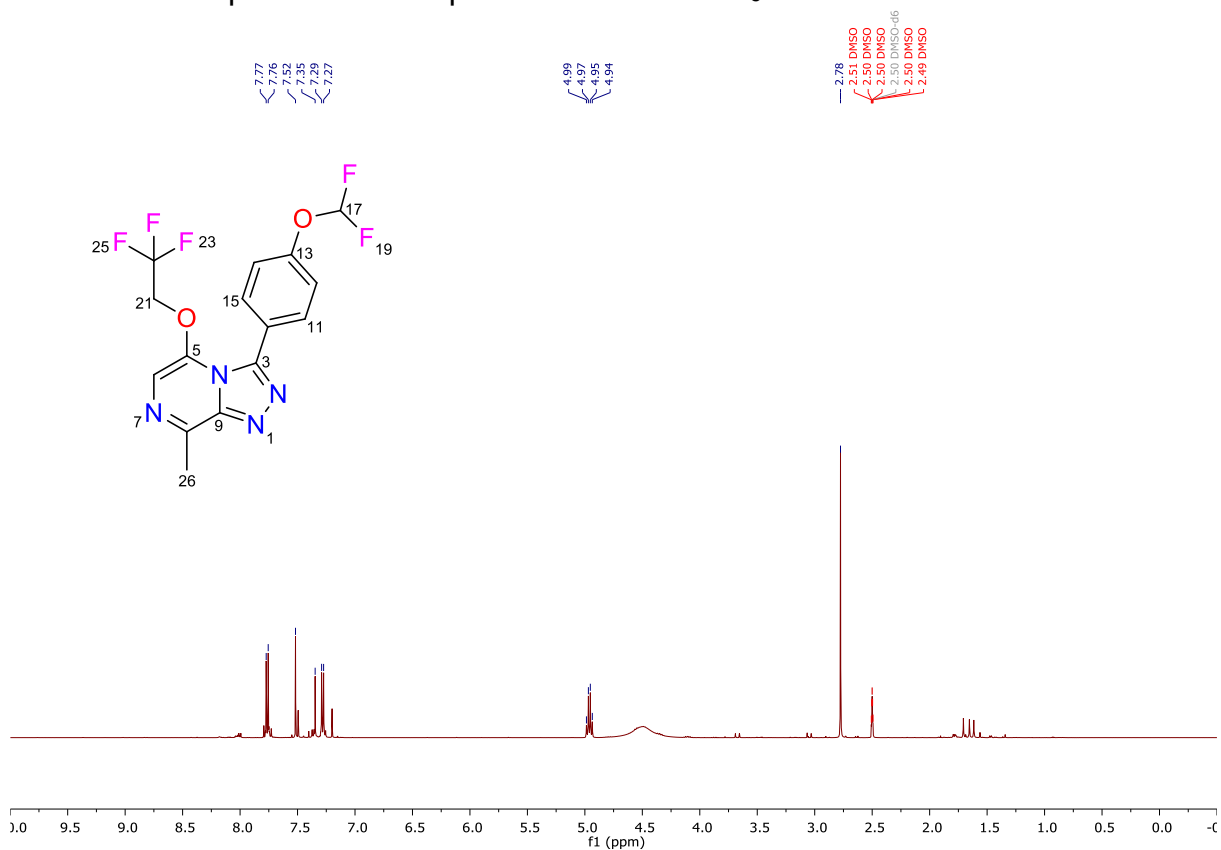


Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e <sup>-</sup> Conf	N-Rule
311.0508	1	C <sub>13</sub> H <sub>10</sub> ClF <sub>2</sub> N <sub>4</sub> O	311.0506	-0.7	40.9	1	100.00	9.5	even	ok
333.0327	1	C <sub>13</sub> H <sub>9</sub> ClF <sub>2</sub> N <sub>4</sub> NaO	333.0325	-0.7	39.6	1	100.00	9.5	even	ok

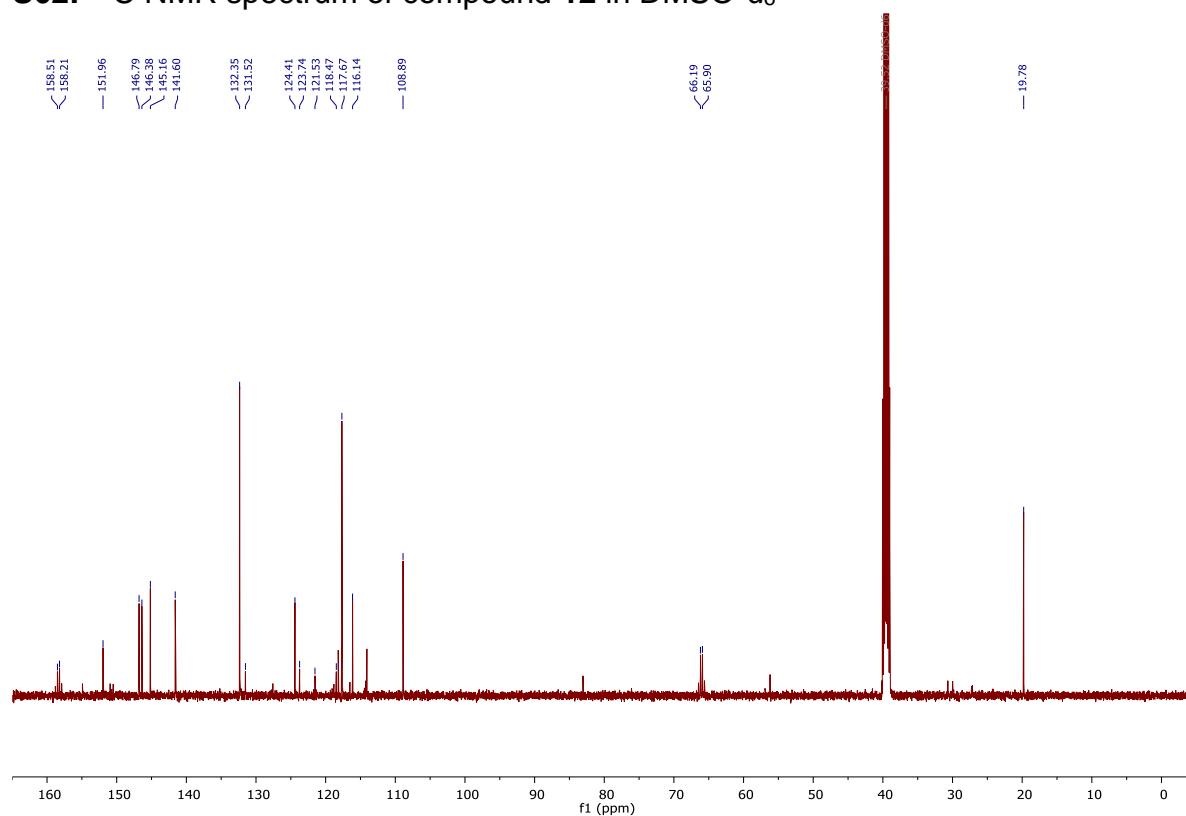


**S60:** NMR data of compound **12** in DMSO-*d*<sub>6</sub><sup>a</sup>

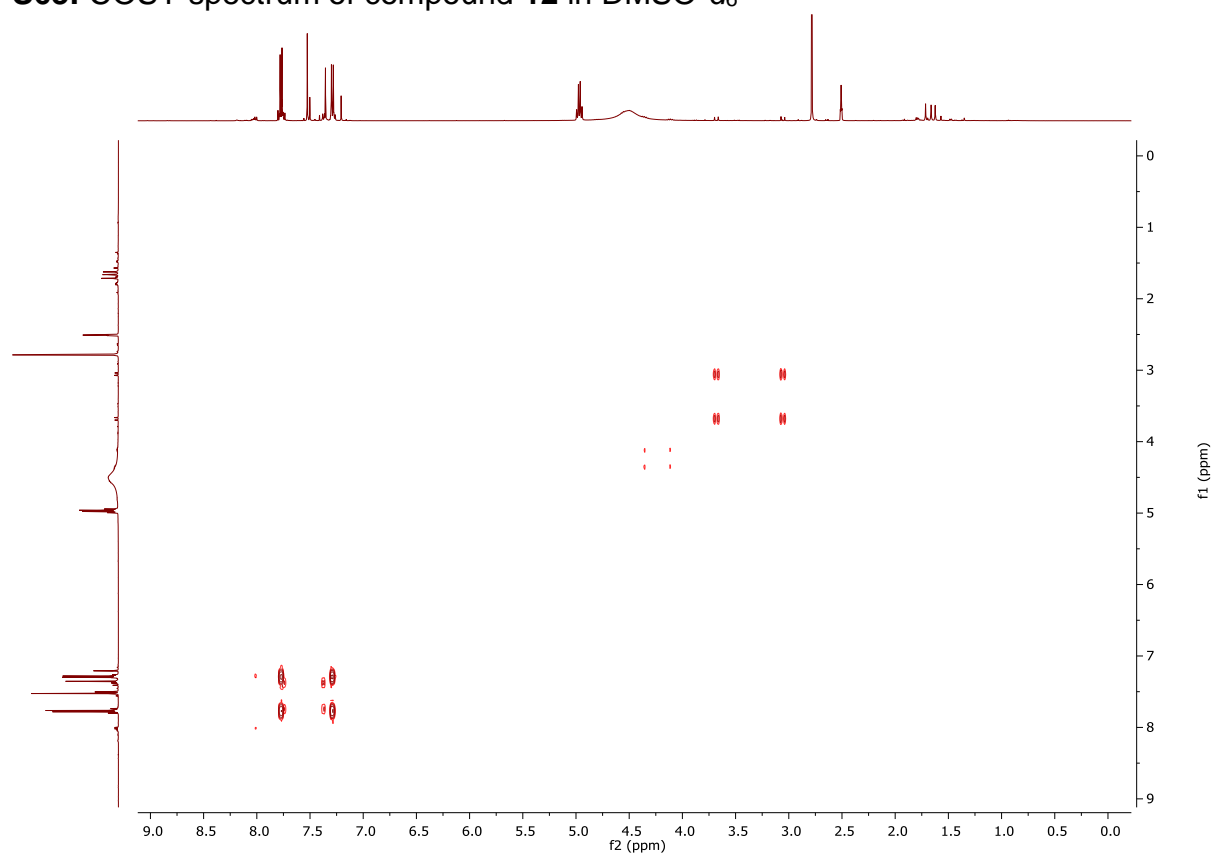
Pos.	δ <sub>H</sub> , mult. ( <i>J</i> in Hz), int.	δ <sub>C</sub> , mult. ( <i>J</i> in Hz)	COSY	HMBC	ROESY
3		146.8, s			
5		141.6, s			
6	7.52, s, 1H	108.9, s		5, 8	21
8		145.1, s			
9		146.4, s			
10		124.4, s			
11	7.76, m, 1H	132.4, s	12	3, 13,15	12
12	7.28, m, 1H	117.7, s	11	10,14	11
13		152.0, t (3.2)			
14	7.28, m, 1H	117.7, s	15	10, 12	15
15	7.76, m, 1H	132.4, s	14	3, 11, 13	14
17	7.35, t (73.7), 1H	116.1, t (258.5)		13	
21	4.96, q (8.5), 2H	66.0, q (35.8)		5, 22	6
22		122.5, q (277.3)			
26	2.78, s	19.8, s		8, 9	

<sup>a</sup> Recorded at 500 MHz (<sup>1</sup>H NMR) and 125 MHz (<sup>13</sup>C NMR) at 25 °C.**S61:** <sup>1</sup>H NMR spectrum of compound **12** in DMSO-*d*<sub>6</sub>

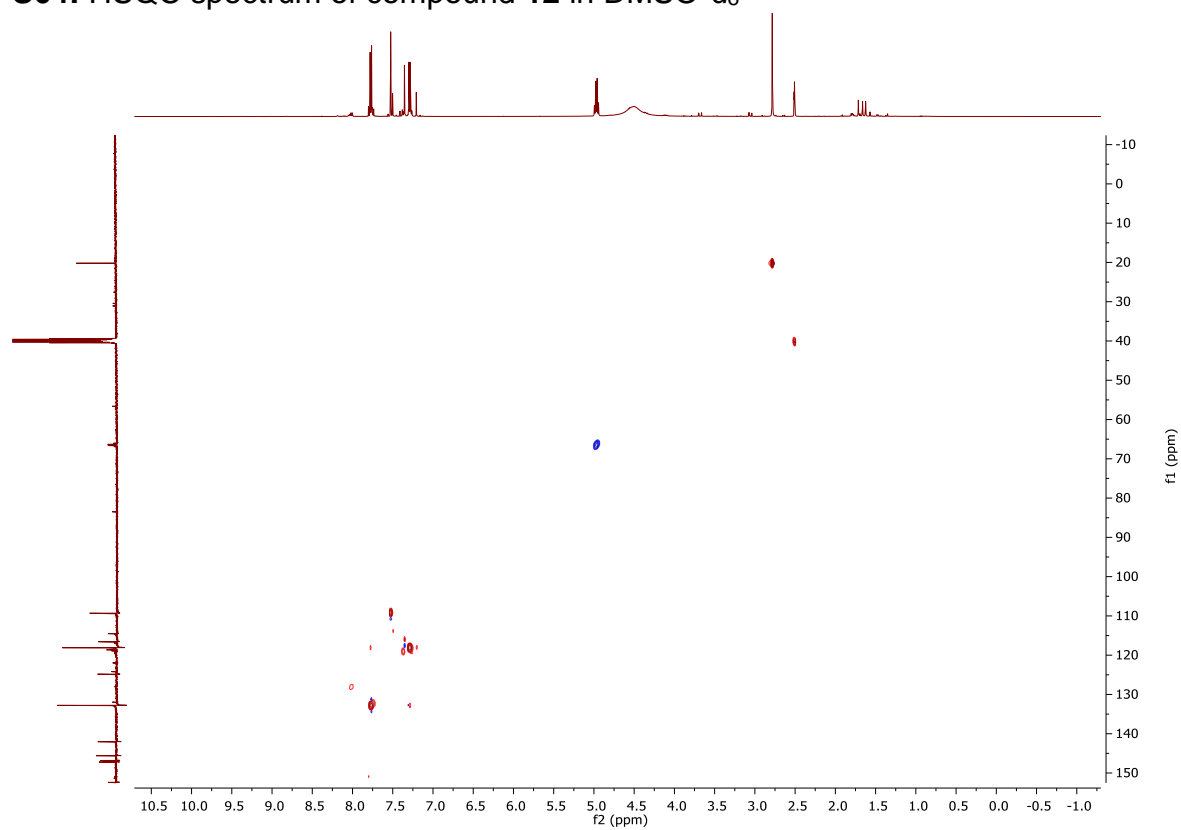
**S62:**  $^{13}\text{C}$  NMR spectrum of compound **12** in  $\text{DMSO}-d_6$



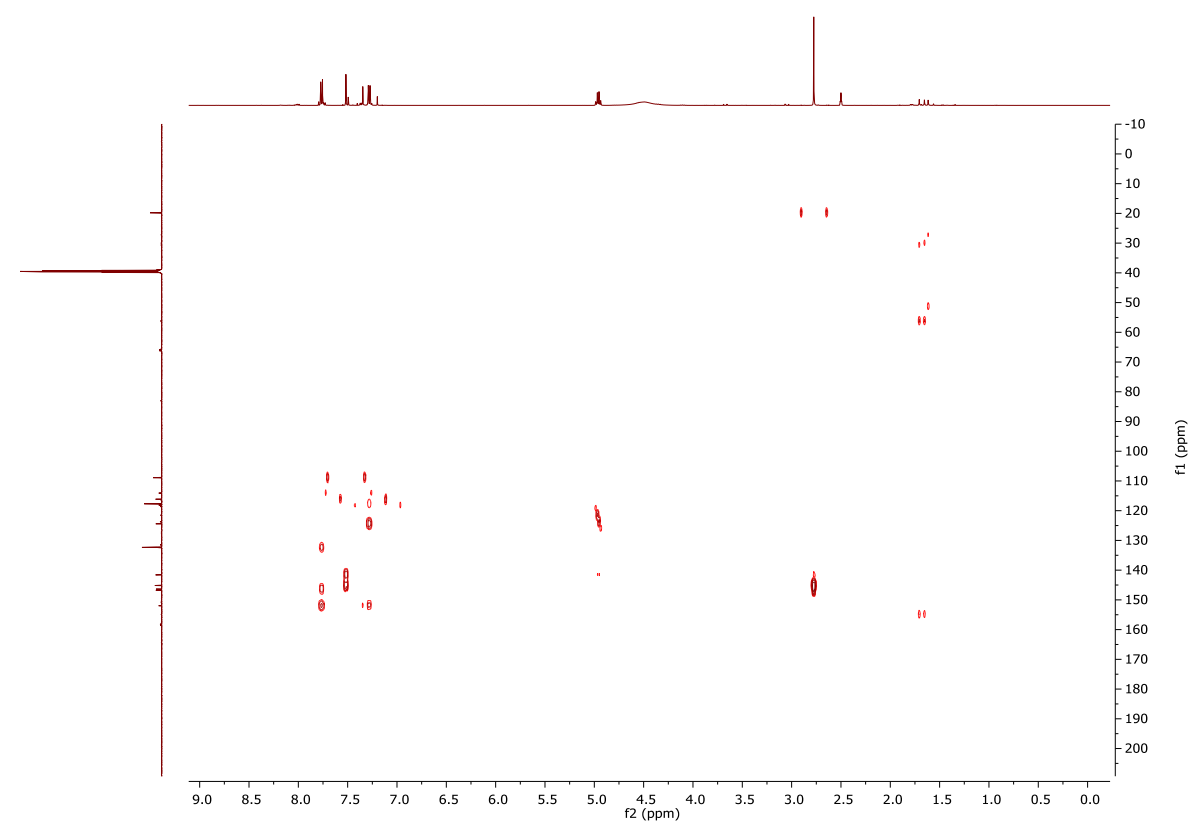
**S63:** COSY spectrum of compound **12** in  $\text{DMSO}-d_6$



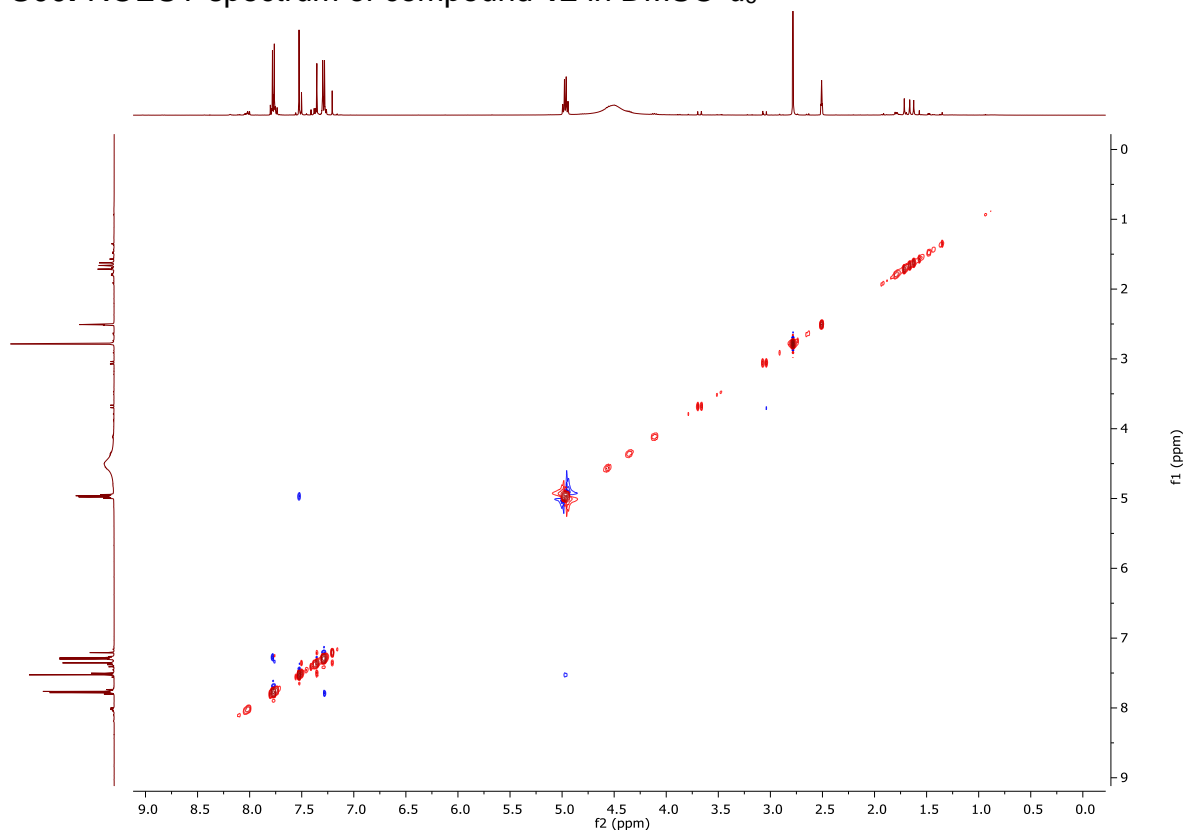
**S64:** HSQC spectrum of compound **12** in DMSO- $d_6$



**S65:** HMBC spectrum of compound **12** in DMSO- $d_6$



**S66: ROESY spectrum of compound 12 in DMSO- $d_6$**



**S67: HRMS of compound 12**



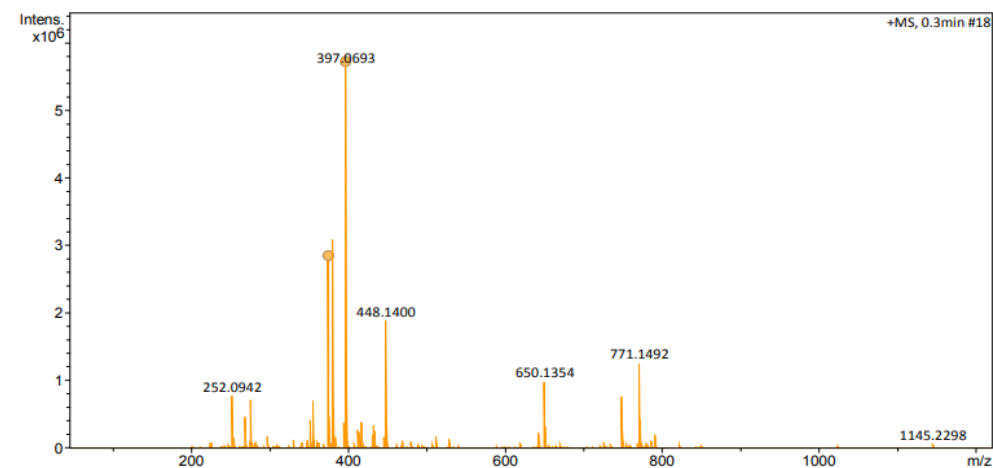
**High Resolution Mass Spectrum**

**Analysis Info**

Analysis Name D:\Data\KahYean\20200904\RAD866000001.d  
 Method DirectInfusion\_2018\_pos.m  
 Sample Name RAD866  
 Comment

Acquisition Date 9/4/2020 11:41:46 AM  
 Instrument maXis II ETD 1823391.22321

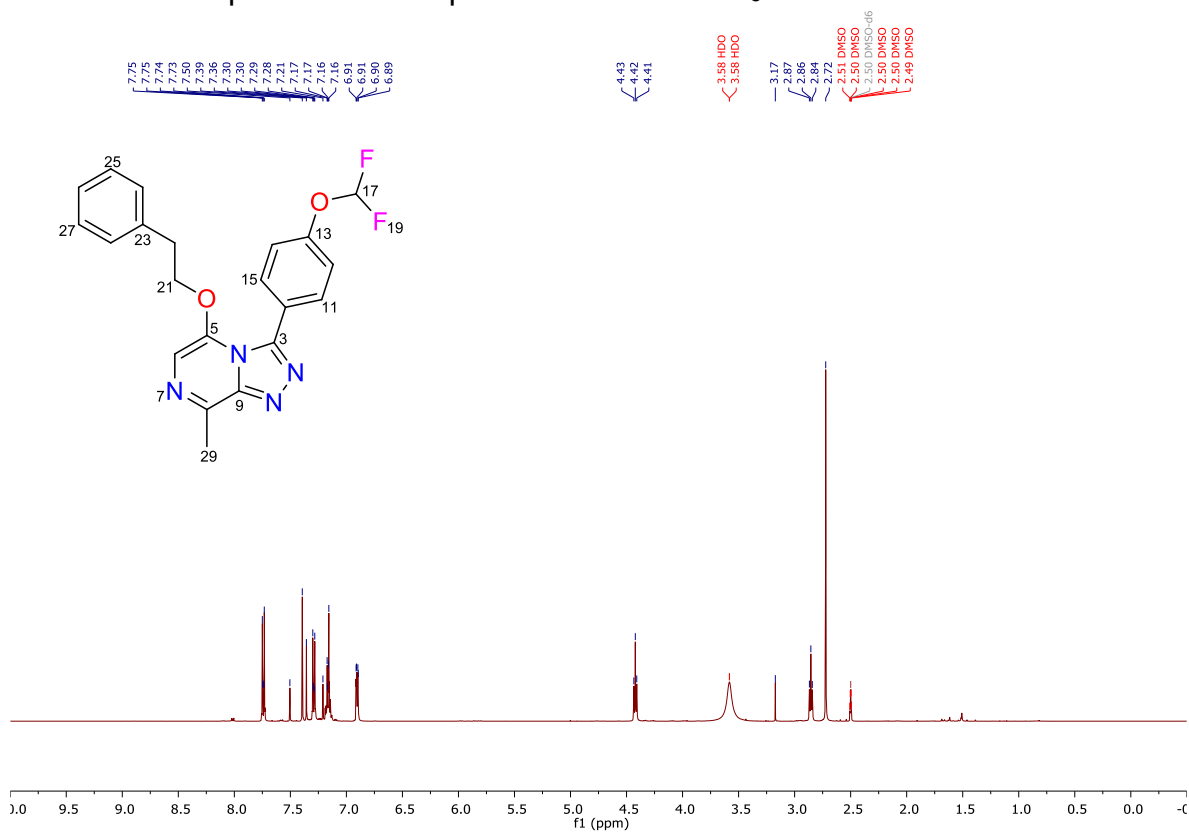
**+MS, 0.3min #18**



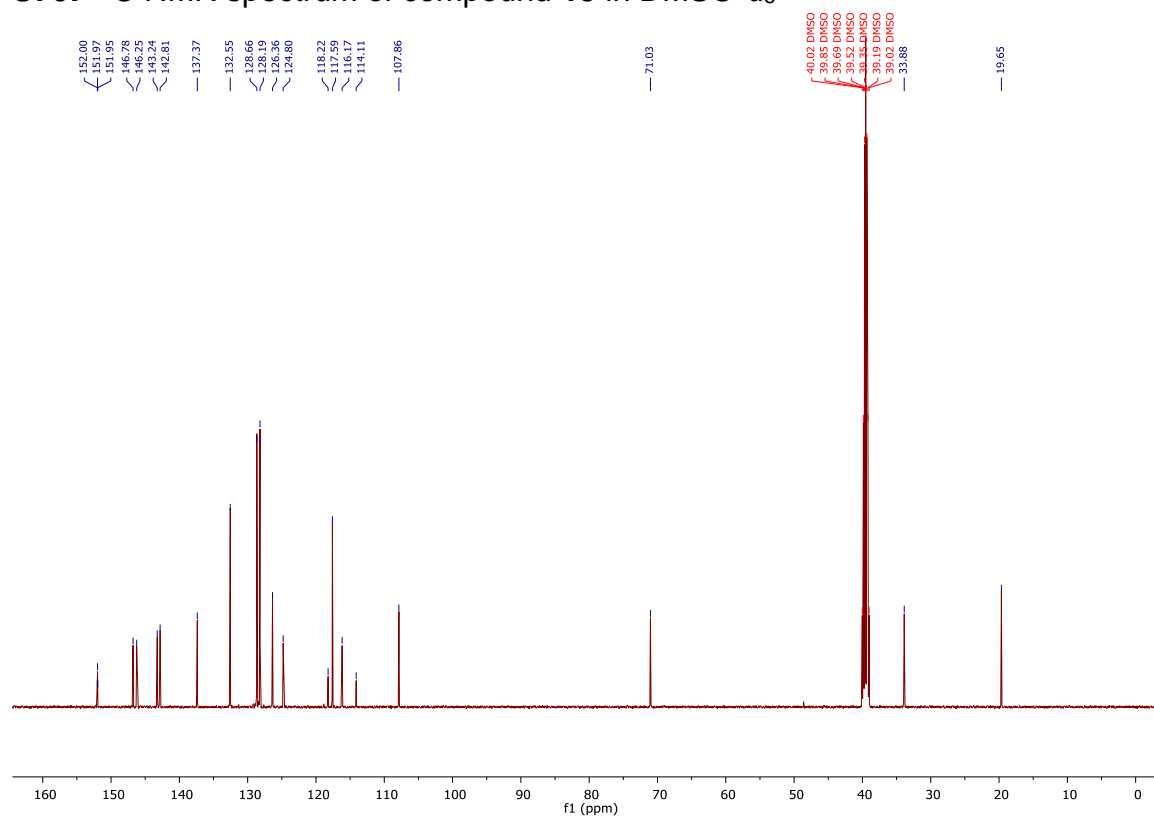
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e <sup>-</sup> Conf	N-Rule
375.0874	1	C15H12F5N4O2	375.0875	0.3	5.5	1	100.00	9.5	even	ok
397.0693	1	C15H11F5N4NaO2	397.0694	0.4	5.0	1	100.00	9.5	even	ok

**S68:** NMR data for compound **13** in DMSO-*d*<sub>6</sub><sup>a</sup>

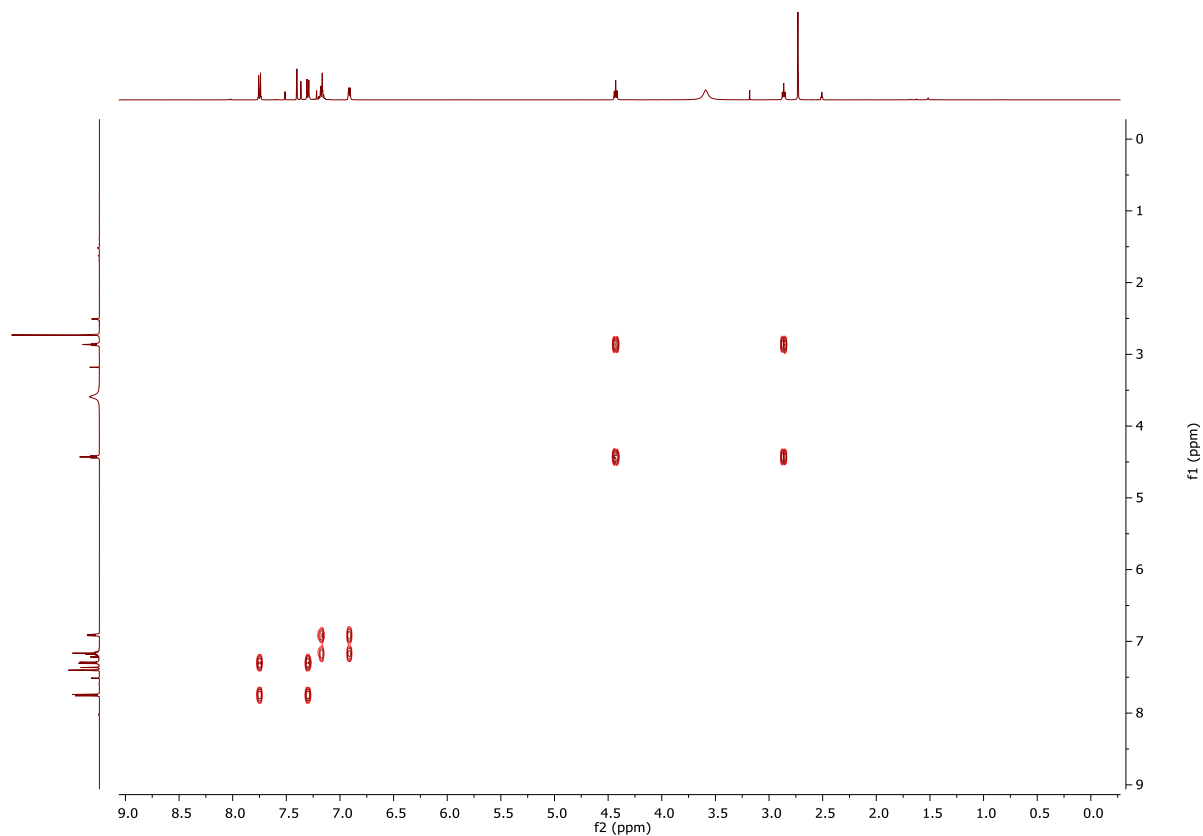
Pos.	δ <sub>H</sub> , mult. ( <i>J</i> in Hz), int.	δ <sub>C</sub> , mult. ( <i>J</i> in Hz)	COSY	HMBC	ROESY
3		146.3, s			
5		142.8, s			
6	7.39, s, 1H	107.9, s		5, 8	
8		143.2, s			
9		146.8, s			
10		124.8, s			
11	7.74, m, 1H	132.6, s	12	3, 13, 15	12
12	7.29, m, 1H	117.6, s	11	10,14	11
13		152.0, t (3.2)			
14	7.29, m, 1H	117.6, s	15	10, 12	15
15	7.74, m, 1H	132.6, s	14	3, 11, 13	14
17	7.36, t (73.7), 1H	116.2, t (258.2)		13	
21	4.42, t (6.5), 2H	71.0, s	22	5, 22, 23	6, 22
22	2.86, t (6.5), 2H	33.9, s	21	21, 23, 24, 28	24, 28
23		137.4, s			
24	6.90, m, 1H	128.7, s	25	22, 26, 28	25
25	7.17, m, 1H	128.2, s	24, 26	23, 27	24, 26
26	7.16, m, 1H	126.4, s	25, 27	24, 28	25, 27
27	7.17, m, 1H	128.2, s	26, 28	23, 25	26, 28
28	6.90, m, 1H	128.7, s	27	22, 24, 26	27
29	2.72, s, 3H	19.7, s		6, 8, 9	

<sup>a</sup> Recorded at 500 MHz (<sup>1</sup>H NMR) and 125 MHz (<sup>13</sup>C NMR) at 25 °C.**S69:** <sup>1</sup>H NMR spectrum of compound **13** in DMSO-*d*<sub>6</sub>

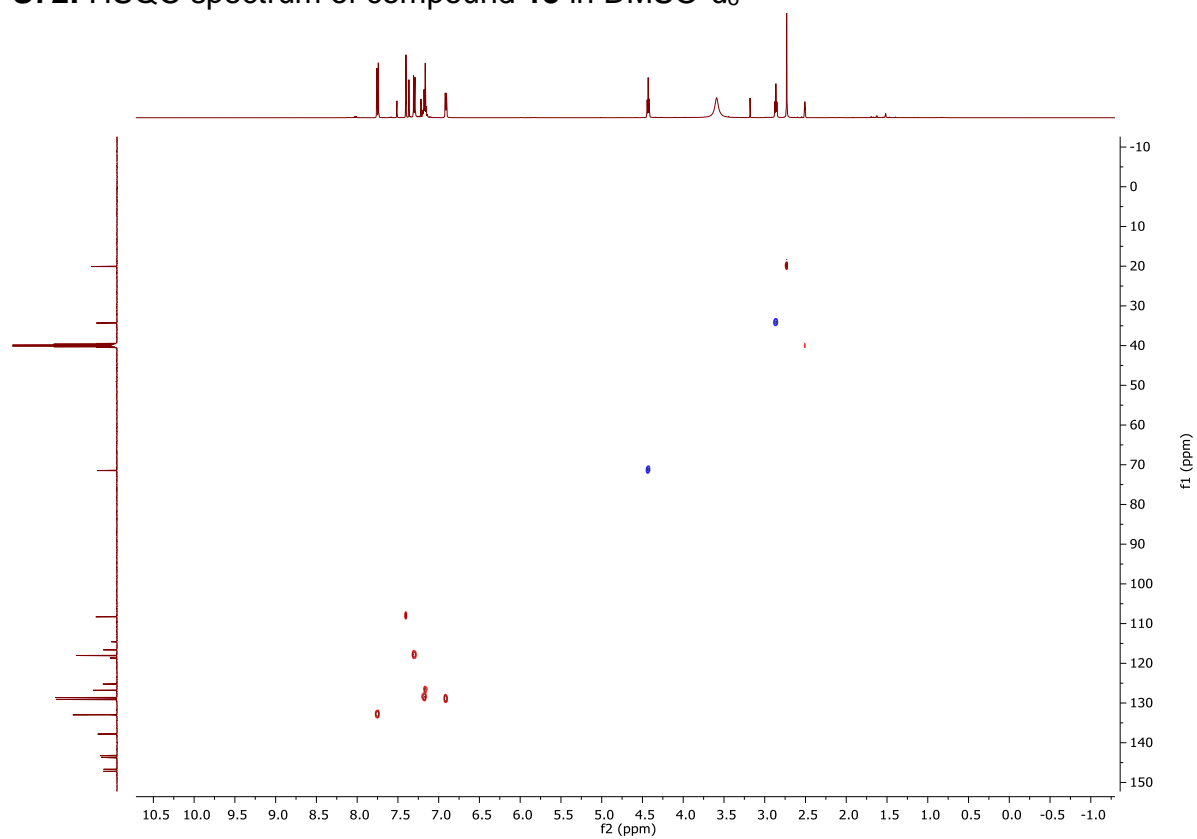
**S70:**  $^{13}\text{C}$  NMR spectrum of compound **13** in  $\text{DMSO}-d_6$



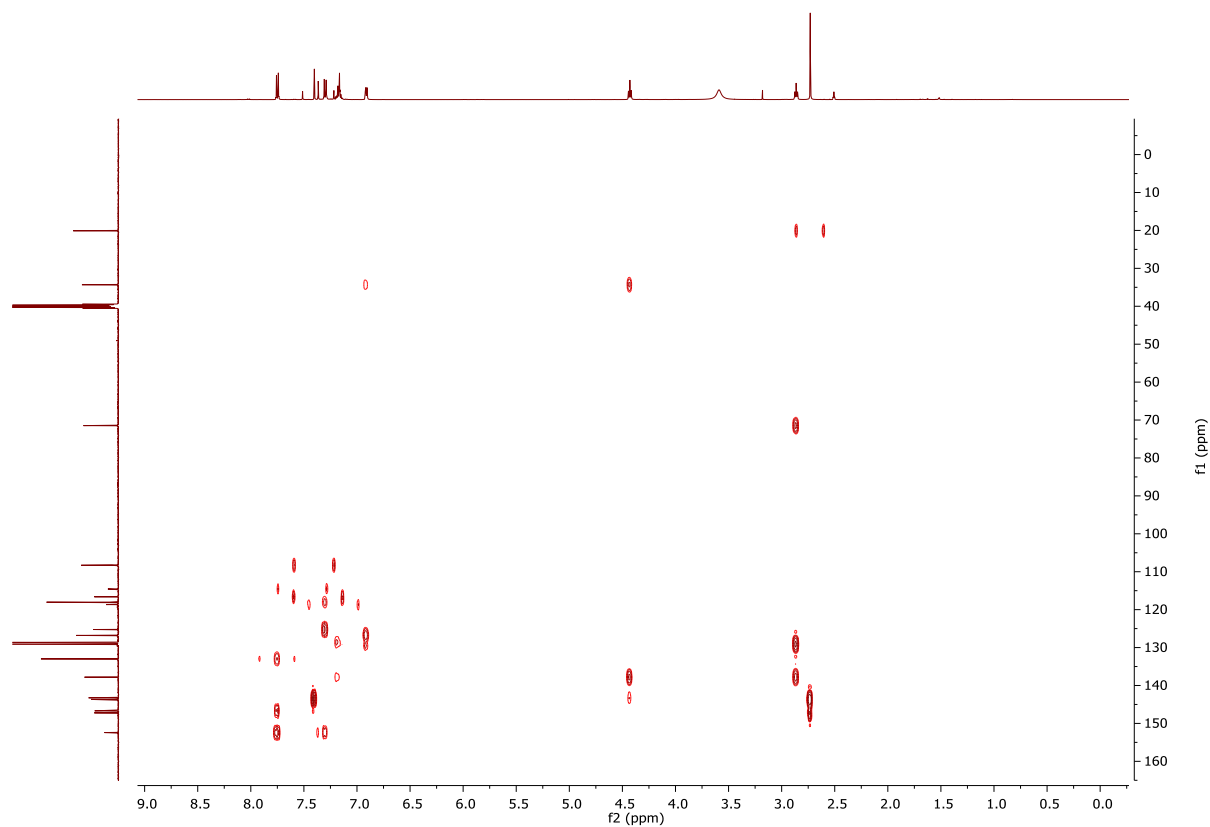
**S71:** COSY spectrum of compound **13** in  $\text{DMSO}-d_6$



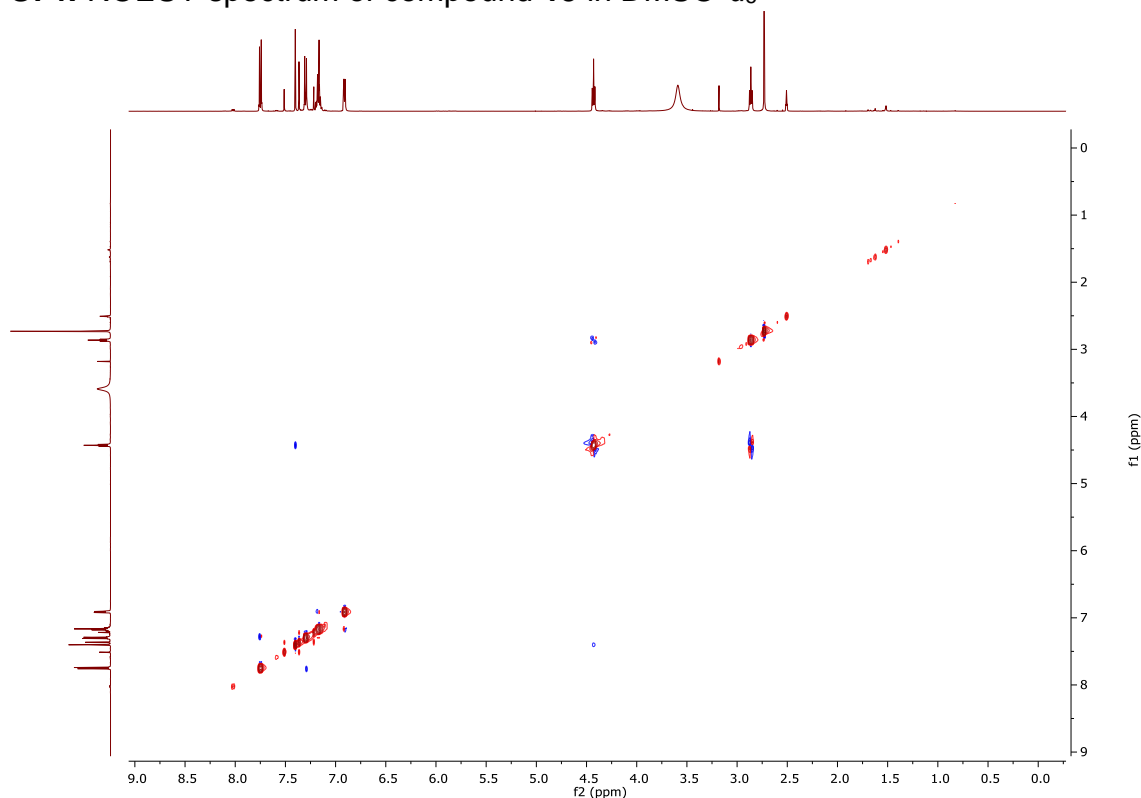
**S72:** HSQC spectrum of compound **13** in DMSO-*d*<sub>6</sub>



**S73:** HMBC spectrum of compound **13** in DMSO-*d*<sub>6</sub>



**S74: ROESY spectrum of compound 13 in DMSO- $d_6$**



**S75: HRMS of compound 13**



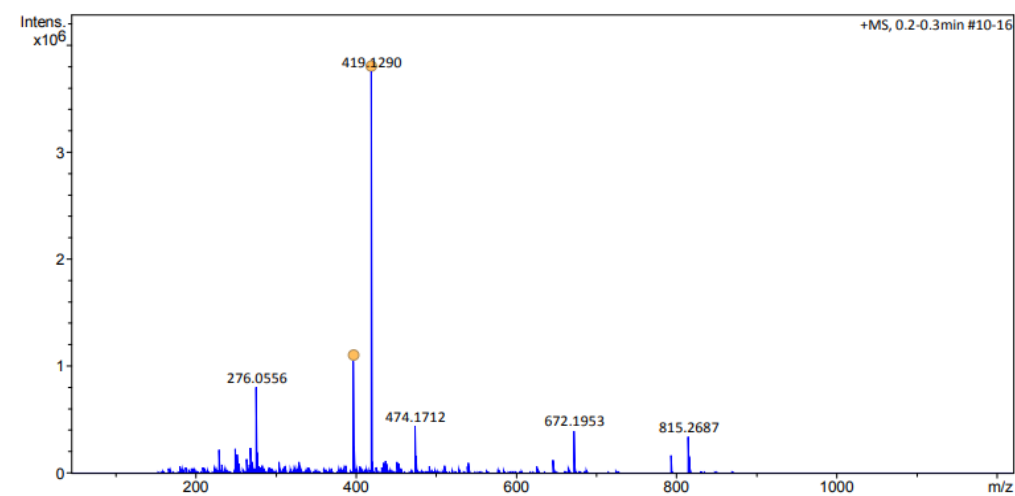
**High Resolution Mass Spectrum**

**Analysis Info**

Analysis Name D:\Data\KahYean\20200904\RAD865000002.d  
 Method DirectInfusion\_2018\_pos.m  
 Sample Name RAD865  
 Comment

Acquisition Date 9/4/2020 11:35:55 AM  
 Instrument maXis II ETD 1823391.22321

**+MS, 0.2-0.3min #10-16**



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e <sup>-</sup> Conf	N-Rule
397.1470	1	C21H19F2N4O2	397.1471	0.0	5.3	1	100.00	13.5	even	ok
419.1290	1	C21H18F2N4NaO2	419.1290	0.0	9.3	1	100.00	13.5	even	ok

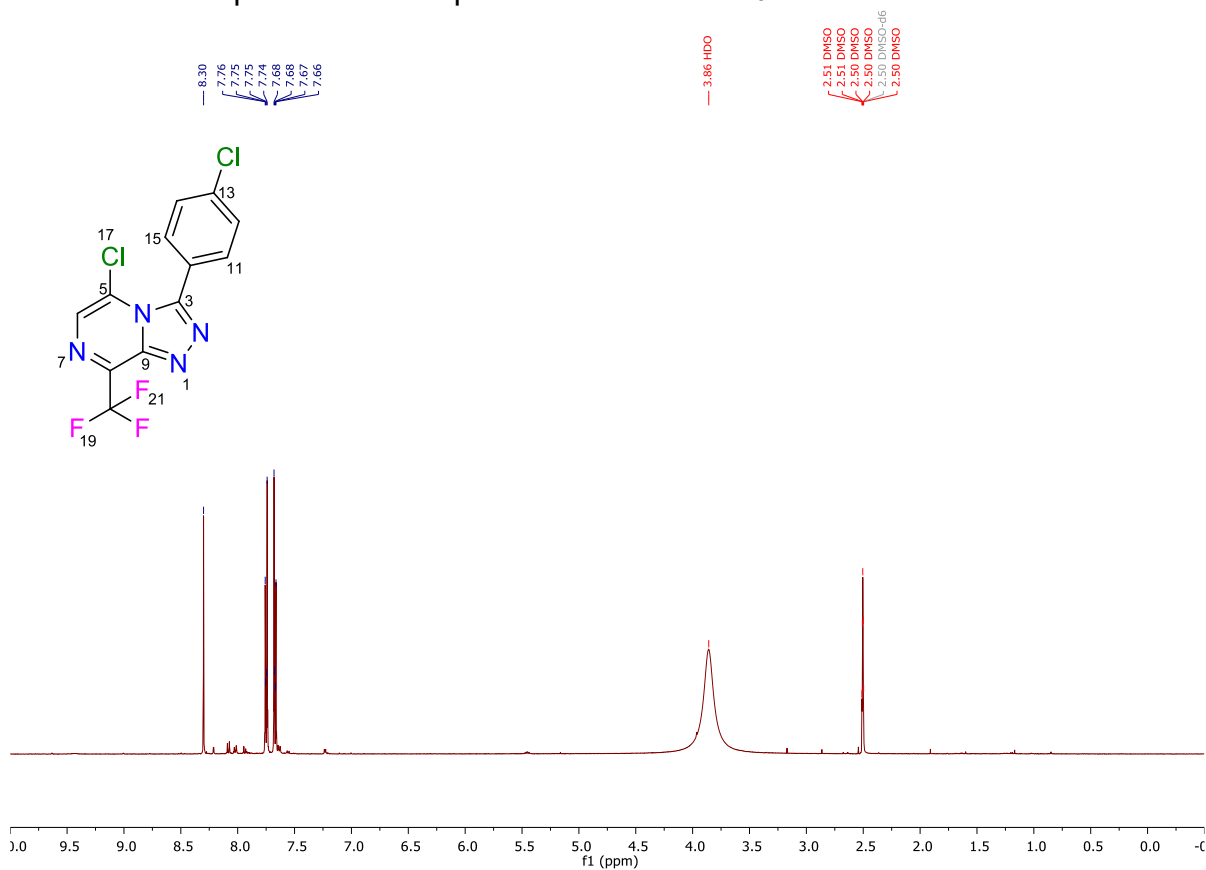


**S76:** NMR data of compound **14** in DMSO-*d*<sub>6</sub><sup>a</sup>

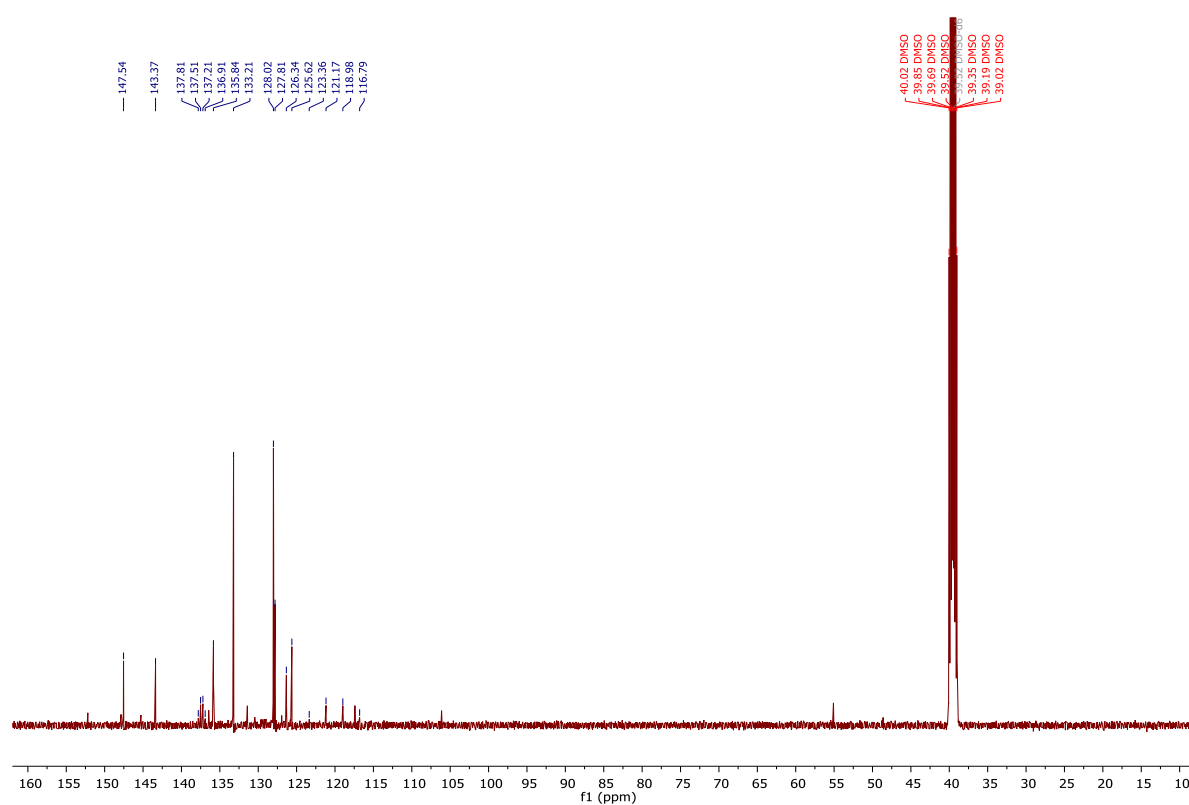
Position	$\delta_{\text{H}}$ , mult. ( <i>J</i> in Hz), int.	$\delta_{\text{C}}$ , mult. ( <i>J</i> in Hz)	COSY	HMBC
3		147.5, s		
5		126.3, s		
6	8.30, s, 1H	127.8, s		5, 8
8		137.4, q (37.9)		
9		143.4, s		
10		125.6, s		
11	7.75, m, 1H	133.2, s	12	3, 13,15
12	7.67, m, 1H	128.0, s	11	10,14
13		135.8, s		
14	7.67, m, 1H	128.0, s	15	10, 12
15	7.75, m, 1H	133.2, s	14	3, 11, 13
18		119.9, q (275.1)		

<sup>a</sup> Recorded at 500 MHz (<sup>1</sup>H NMR) and 125 MHz (<sup>13</sup>C NMR) at 25 °C.

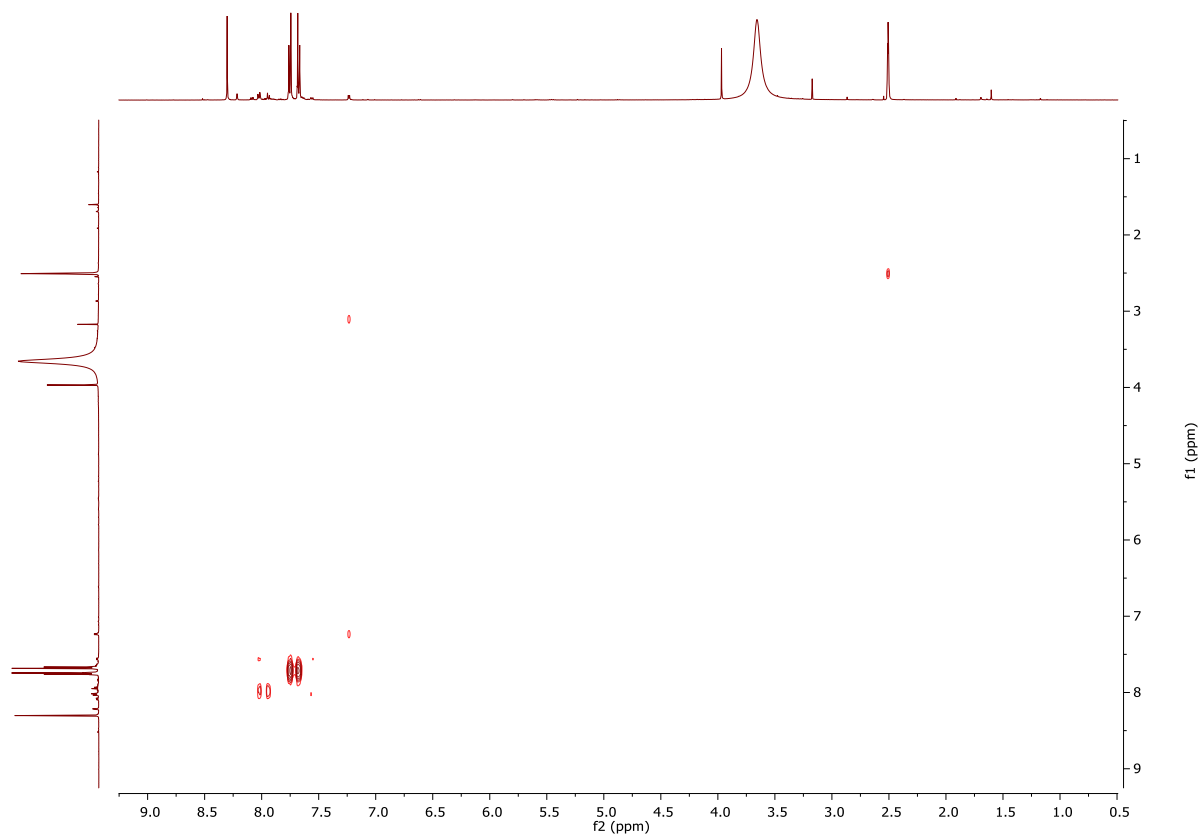
**S77:**  $^1\text{H}$  NMR Spectrum of compound **14** in DMSO- $d_6$



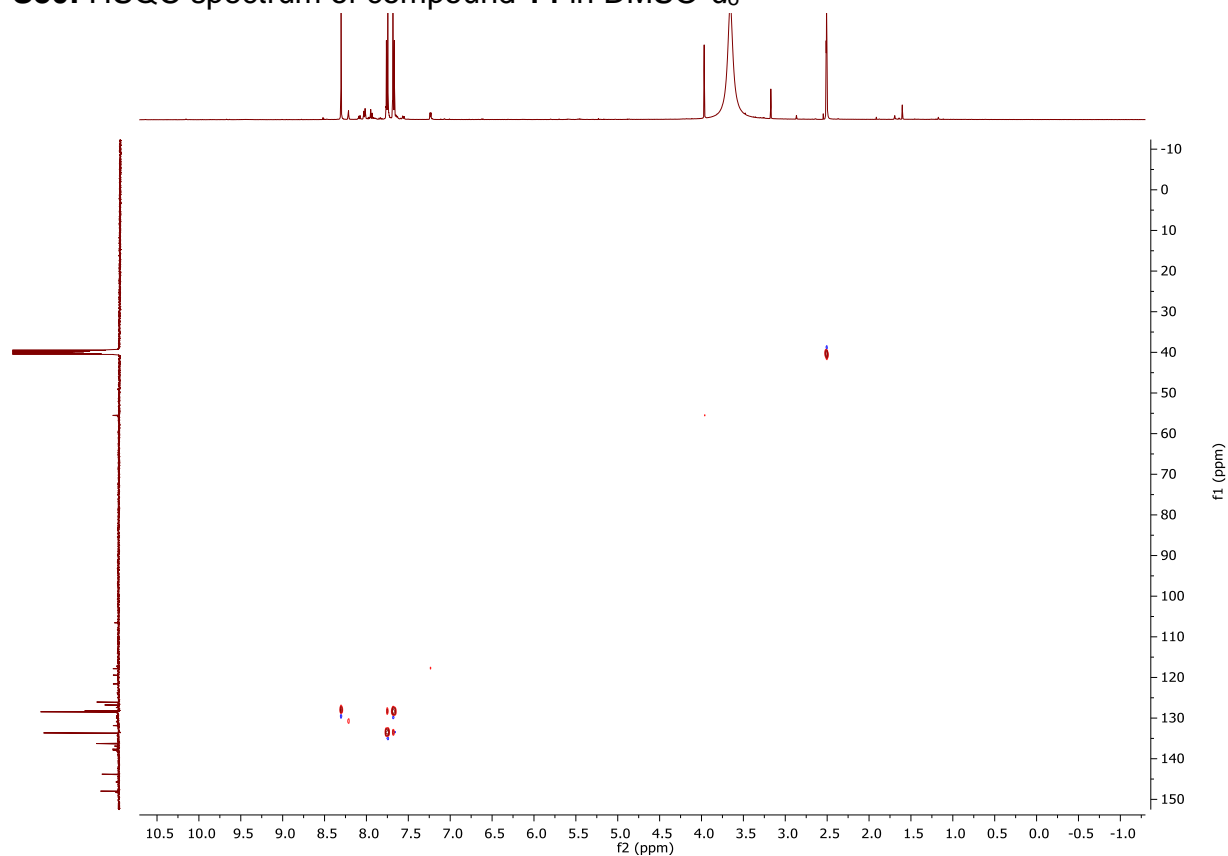
**S78:**  $^{13}\text{C}$  NMR spectrum of compound **14** in  $\text{DMSO}-d_6$



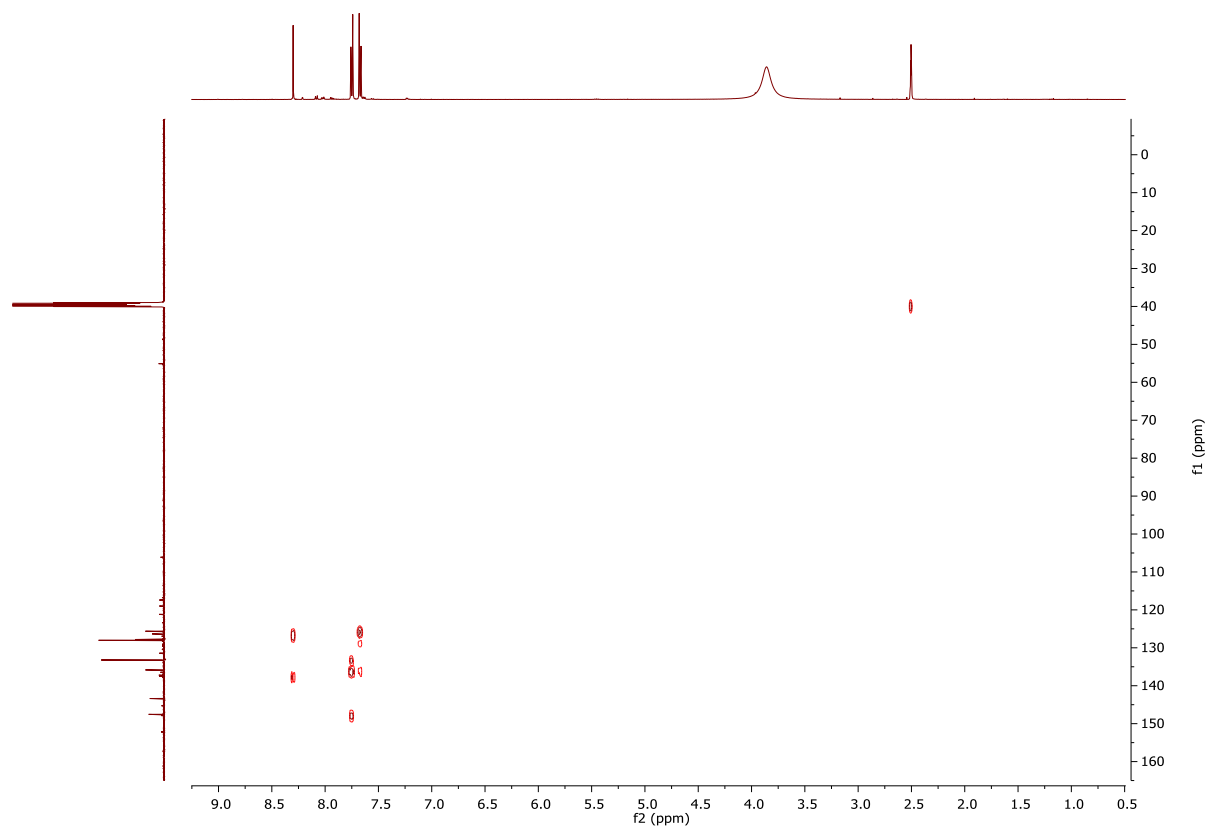
**S79:** COSY spectrum of compound **14** in  $\text{DMSO}-d_6$



**S80:** HSQC spectrum of compound **14** in DMSO- $d_6$



**S81:** HMBC spectrum of compound **14** in DMSO- $d_6$



## S82: HRMS of compound 14



### High Resolution Mass Spectrum

#### Analysis Info

Analysis Name D:\Data\KahYean\20200904\RAD864000002.d

Method DirectInfusion\_2018\_pos.m

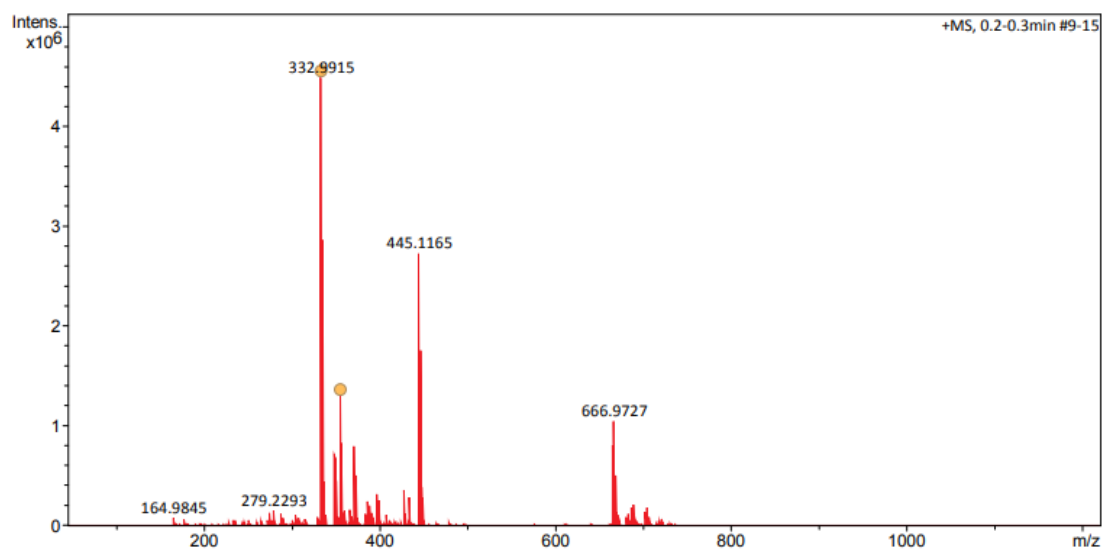
Sample Name RAD864

Comment

Acquisition Date 9/4/2020 10:42:02 AM

Instrument maXis II ETD 1823391.22321

#### +MS, 0.2-0.3min #9-15

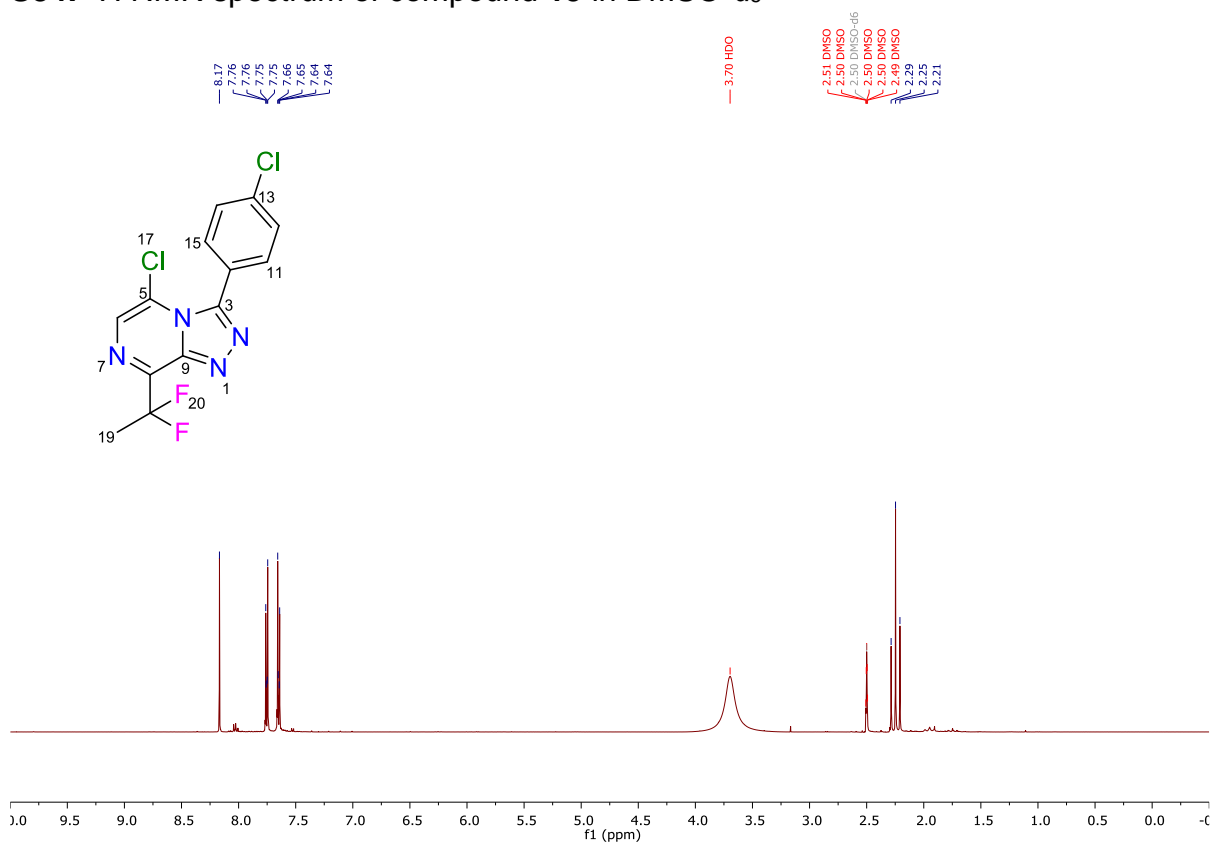


Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdB	e <sup>-</sup> Conf	N-Rule
332.9915	1	C <sub>12</sub> H <sub>6</sub> Cl <sub>2</sub> F <sub>3</sub> N <sub>4</sub>	332.9916	0.5	9.6	1	100.00	9.5	even	ok
	1	C <sub>12</sub> H <sub>8</sub> Cl <sub>2</sub> N <sub>4</sub> NaO <sub>2</sub>	332.9917	0.6	11.5	1	100.00	9.5	even	ok
354.9734	1	C <sub>12</sub> H <sub>5</sub> Cl <sub>2</sub> F <sub>3</sub> N <sub>4</sub> Na	354.9736	0.5	9.9	1	100.00	9.5	even	ok

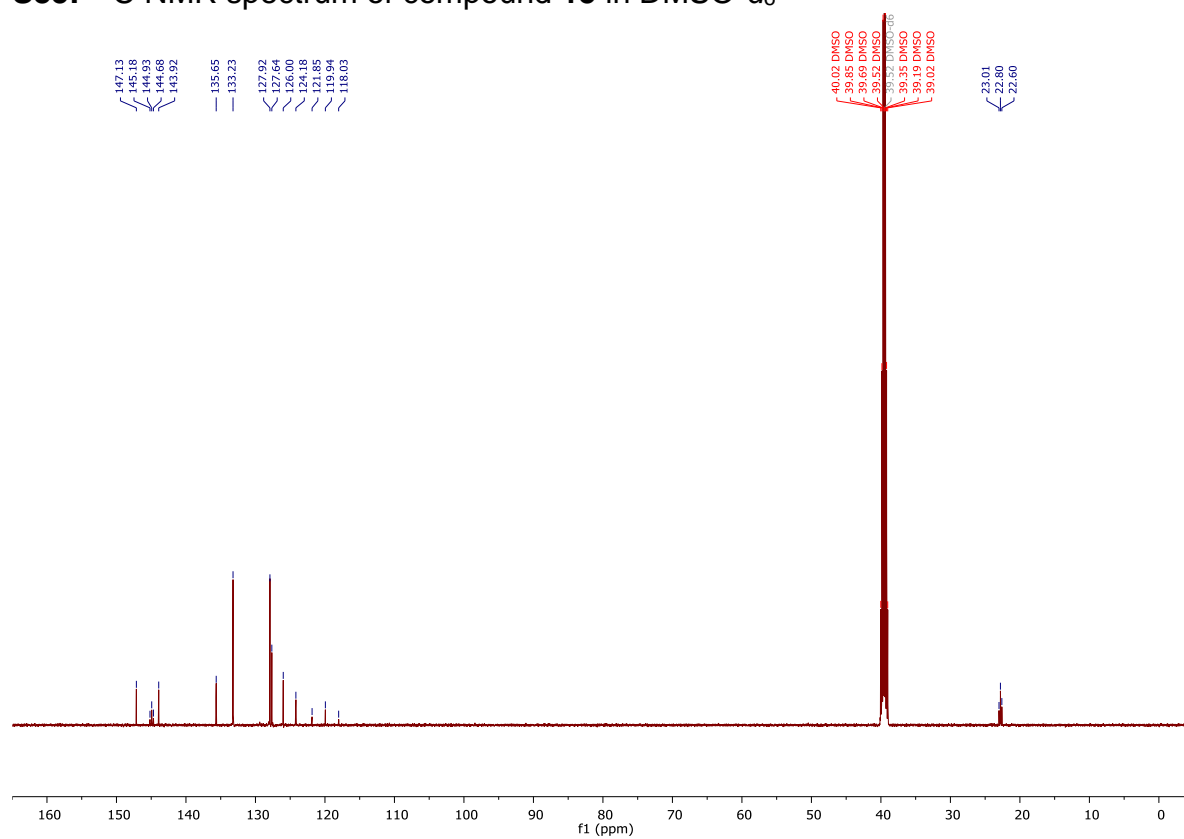
**S83:** NMR data of compound **15** in DMSO-*d*<sub>6</sub><sup>a</sup>

Pos	δ <sub>H</sub> , mult. ( <i>J</i> in Hz), int.	δ <sub>C</sub> , mult. ( <i>J</i> in Hz)	COSY	HMBC
3		147.1, s		
5		124.2, s		
6	8.17, s, 1H	127.6, s		5, 8
8		144.9, t (31.3)		
9		143.9, s		
10		126.0, s		
11	7.75, m, 1H	133.2, s	12	3,13,15
12	7.65, m, 1H	127.9, s	11	10,14
13		135.7, s		
14	7.65, m, 1H	127.9, s	15	10, 12
15	7.75, m, 1H	133.2, s	14	3, 11, 13
18		119.9, t (240.2)		
19	2.25, t, (19.3), 3H	22.8, s		8, 19

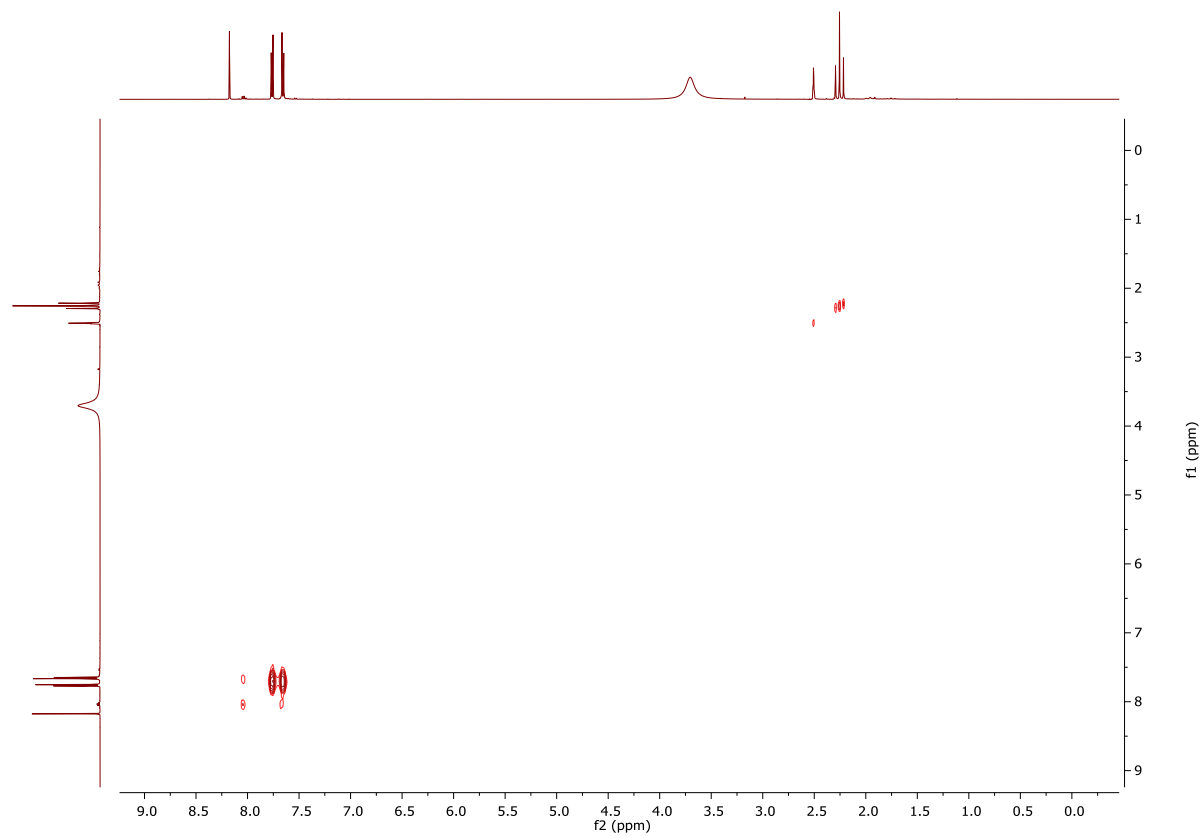
<sup>a</sup> Recorded at 500 MHz (<sup>1</sup>H NMR) and 125 MHz (<sup>13</sup>C NMR) at 25 °C.

**S84:** <sup>1</sup>H NMR spectrum of compound **15** in DMSO-*d*<sub>6</sub>

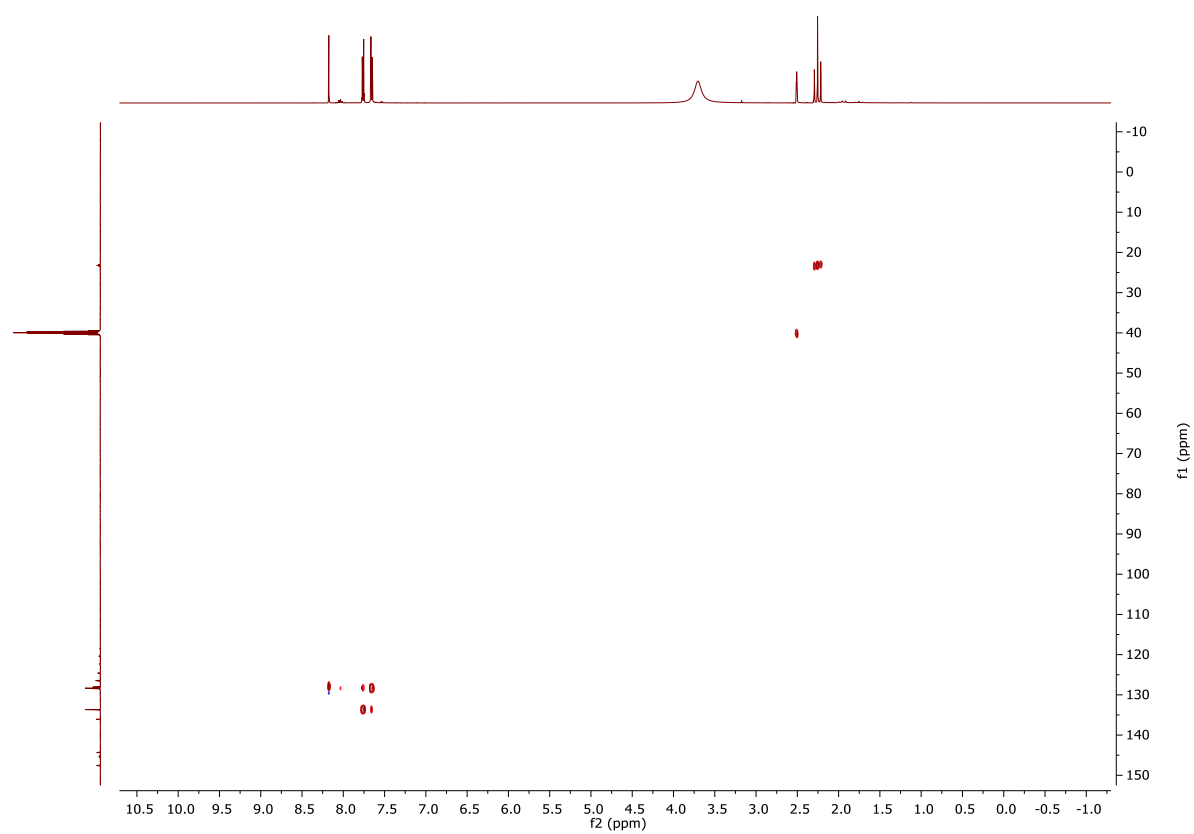
**S85:**  $^{13}\text{C}$  NMR spectrum of compound **15** in  $\text{DMSO}-d_6$



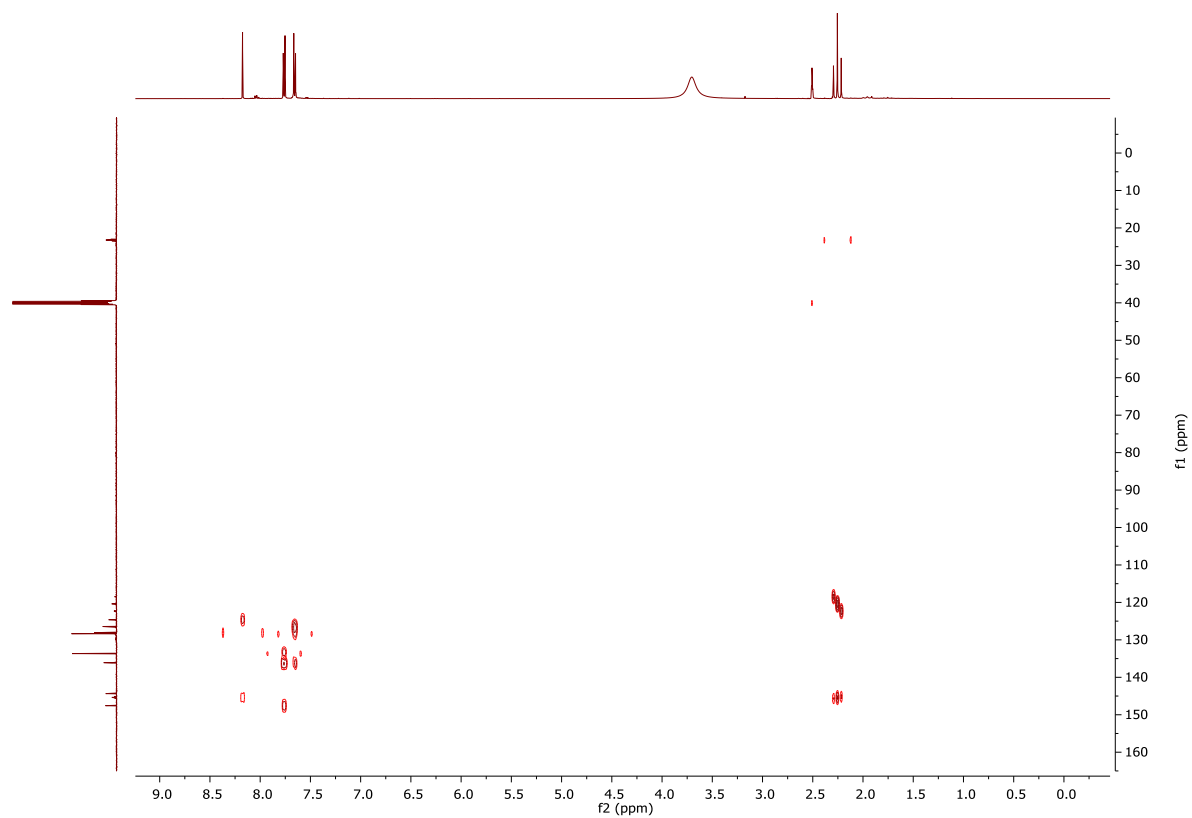
**S86:** COSY spectrum of compound **15** in  $\text{DMSO}-d_6$



**S87:** HSQC spectrum of compound **15** in DMSO- $d_6$



**S88:** HMBC spectrum of compound **15** in DMSO- $d_6$



## S89: HRMS of compound 15



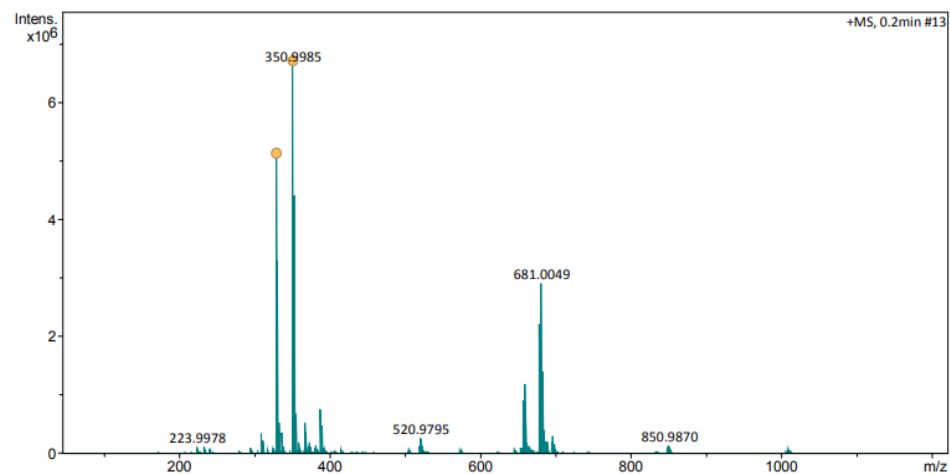
### High Resolution Mass Spectrum

#### Analysis Info

Analysis Name D:\Data\KahYean\20200904\RAD867000001.d  
Method DirectInfusion\_2018\_pos.m  
Sample Name RAD867  
Comment

Acquisition Date 9/4/2020 11:49:35 AM  
Instrument maXis II ETD 1823391.22321

#### +MS, 0.2min #13



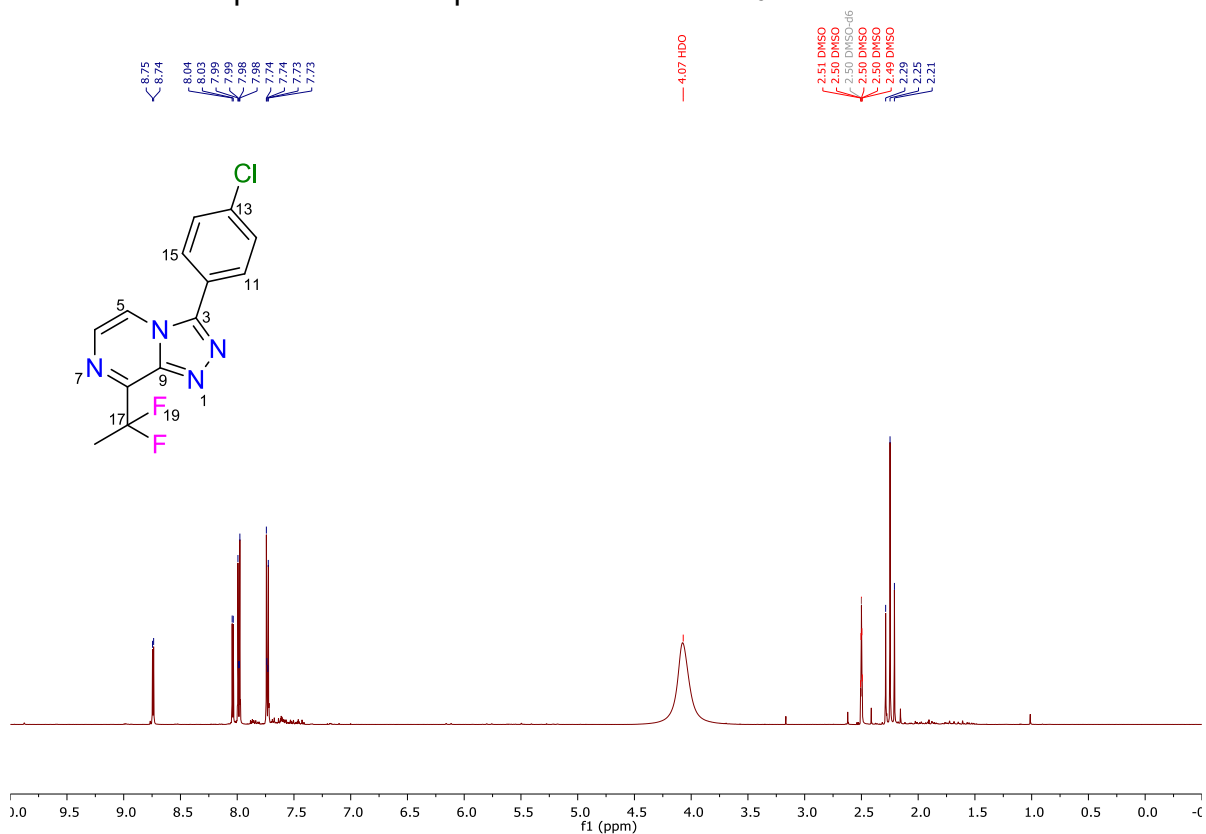
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e <sup>-</sup> Conf	N-Rule
329.0166	1	C <sub>13</sub> H <sub>9</sub> Cl <sub>2</sub> F <sub>2</sub> N <sub>4</sub>	329.0167	0.4	6.3	1	100.00	9.5	even	ok
350.9985	1	C <sub>13</sub> H <sub>8</sub> Cl <sub>2</sub> F <sub>2</sub> N <sub>4</sub> Na	350.9986	0.4	7.6	1	100.00	9.5	even	ok



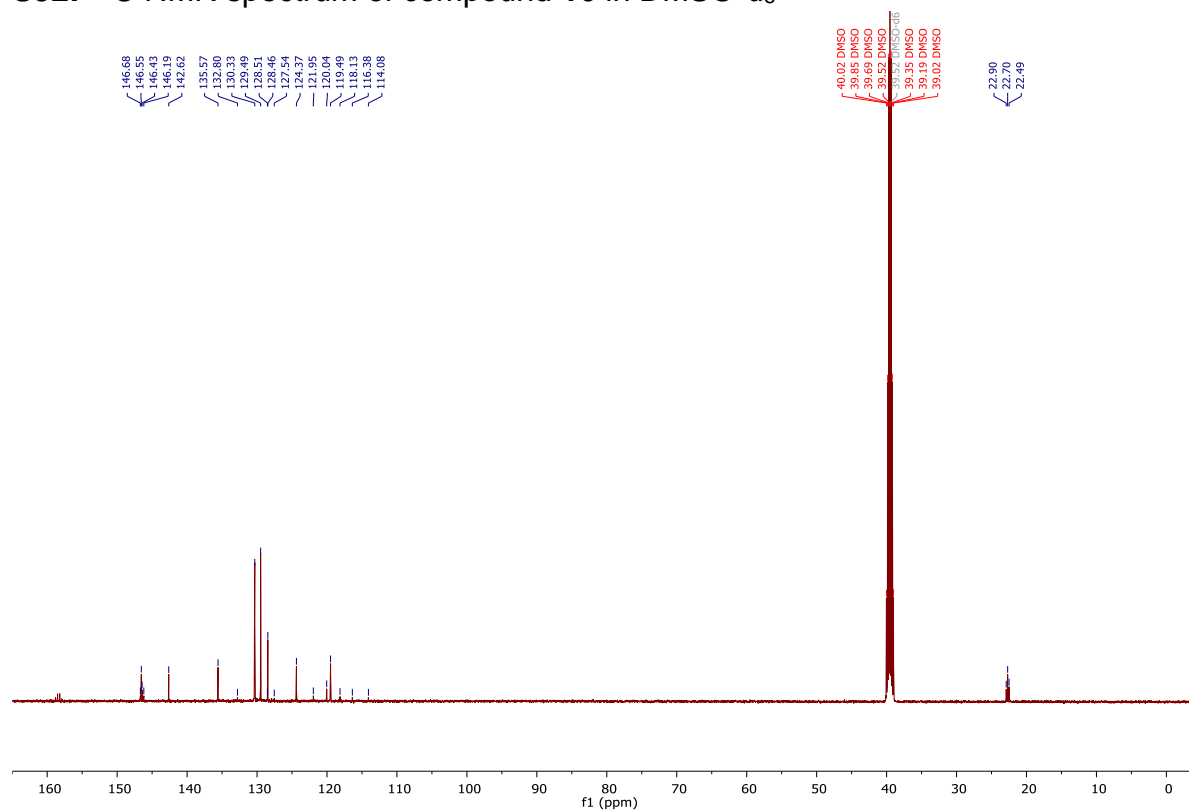
**S90:** NMR data of compound **16** in DMSO-*d*<sub>6</sub><sup>a</sup>

Pos.	δ <sub>H</sub> , mult. (J in Hz), int	δ <sub>C</sub> , mult. (J in Hz)	COSY	HMBC
3		146.4, s		
5	8.74, d (4.8), 1H	119.5, s	6	3, 6, 9
6	8.04, d (4.8), 1H	128.5, s	5	5, 8
8		146.4, t (30.9)		
9		142.6, s		
10		124.4, s		
11	7.98, m, 1H	130.3, s	12	3, 13,15
12	7.73, m, 1H	129.5, s	11	10, 13,14
13		135.6, s		
14	7.73, m, 1H	129.5, s	15	10, 12, 13
15	7.98, m, 1H	130.3, s	14	3 11, 13
17		120.0, t (239.7)		
18	2.25, t (19.2), 3H	22.7, t (25.6)		8, 17

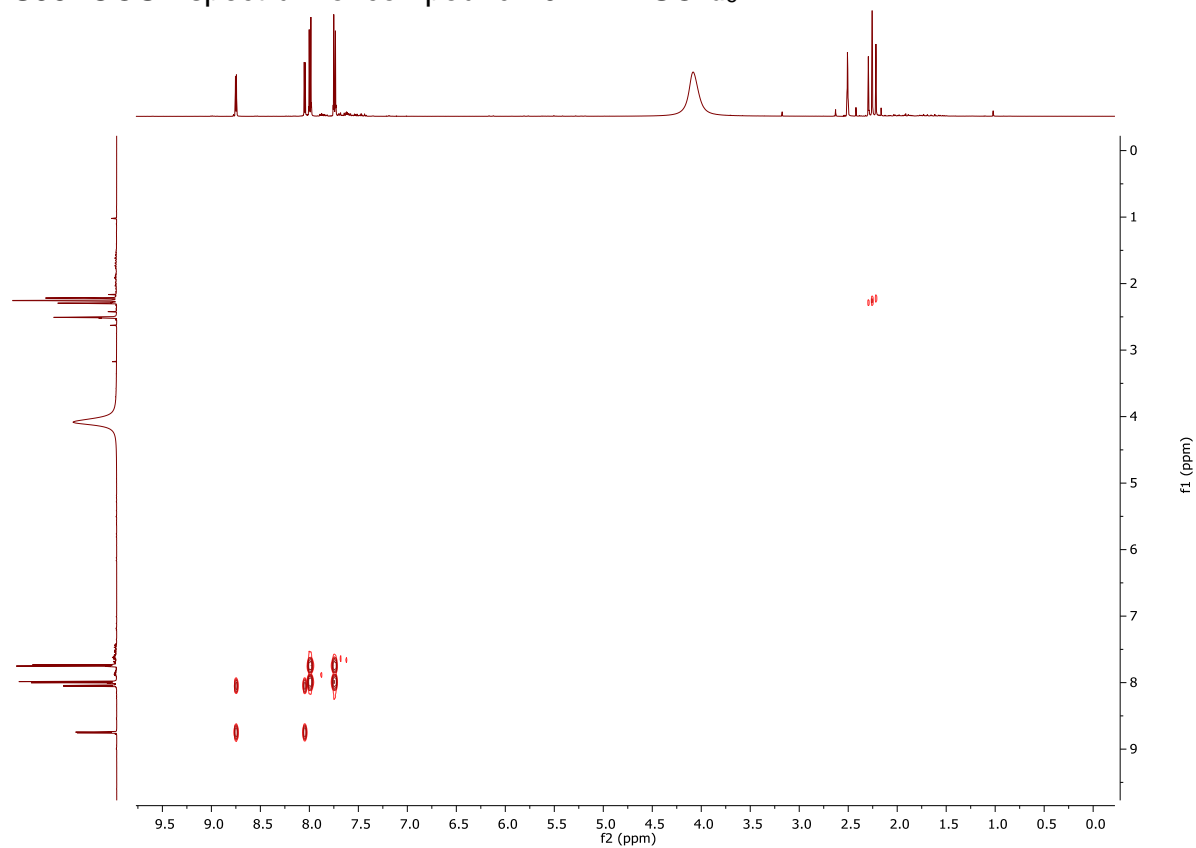
<sup>a</sup> Recorded at 500 MHz (<sup>1</sup>H NMR) and 125 MHz (<sup>13</sup>C NMR) at 25 °C.

**S91:** <sup>1</sup>H NMR Spectrum of compound **16** in DMSO-*d*<sub>6</sub>

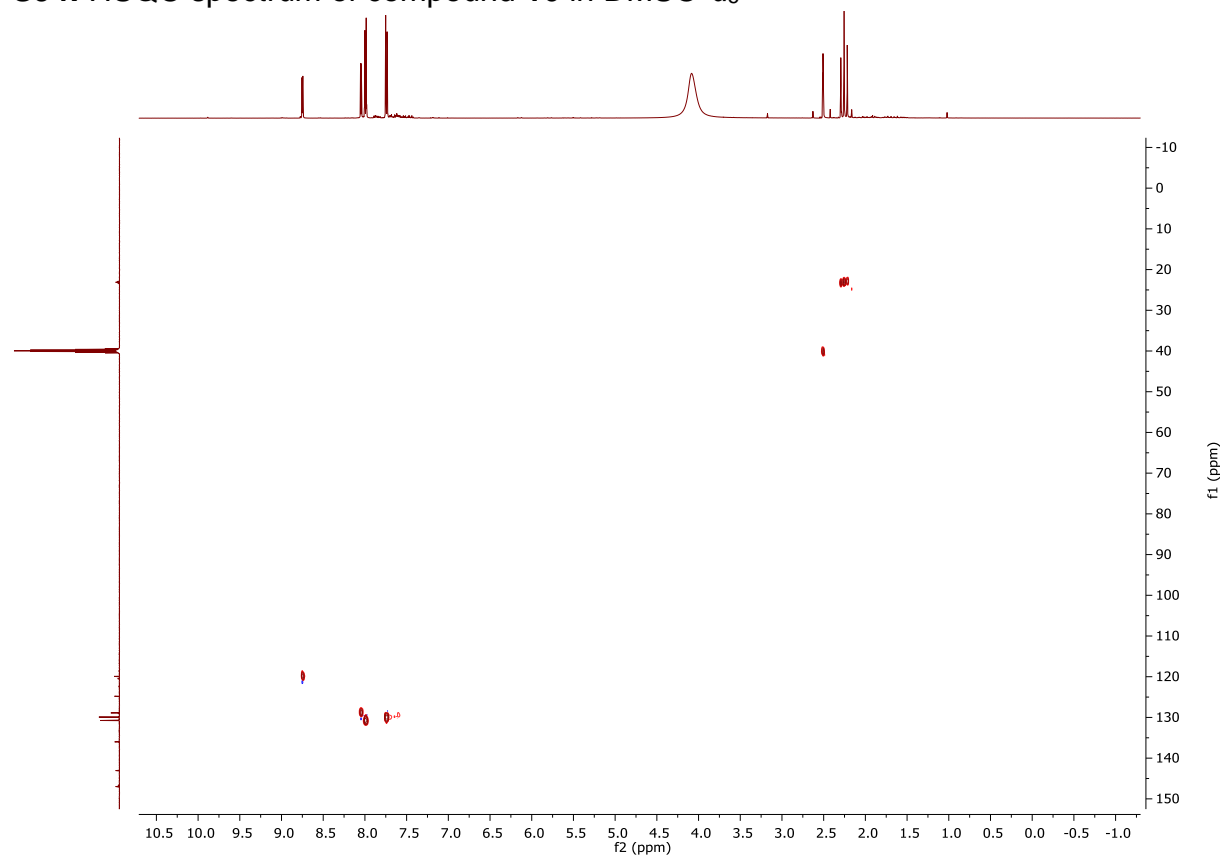
**S92:**  $^{13}\text{C}$  NMR spectrum of compound **16** in  $\text{DMSO}-d_6$



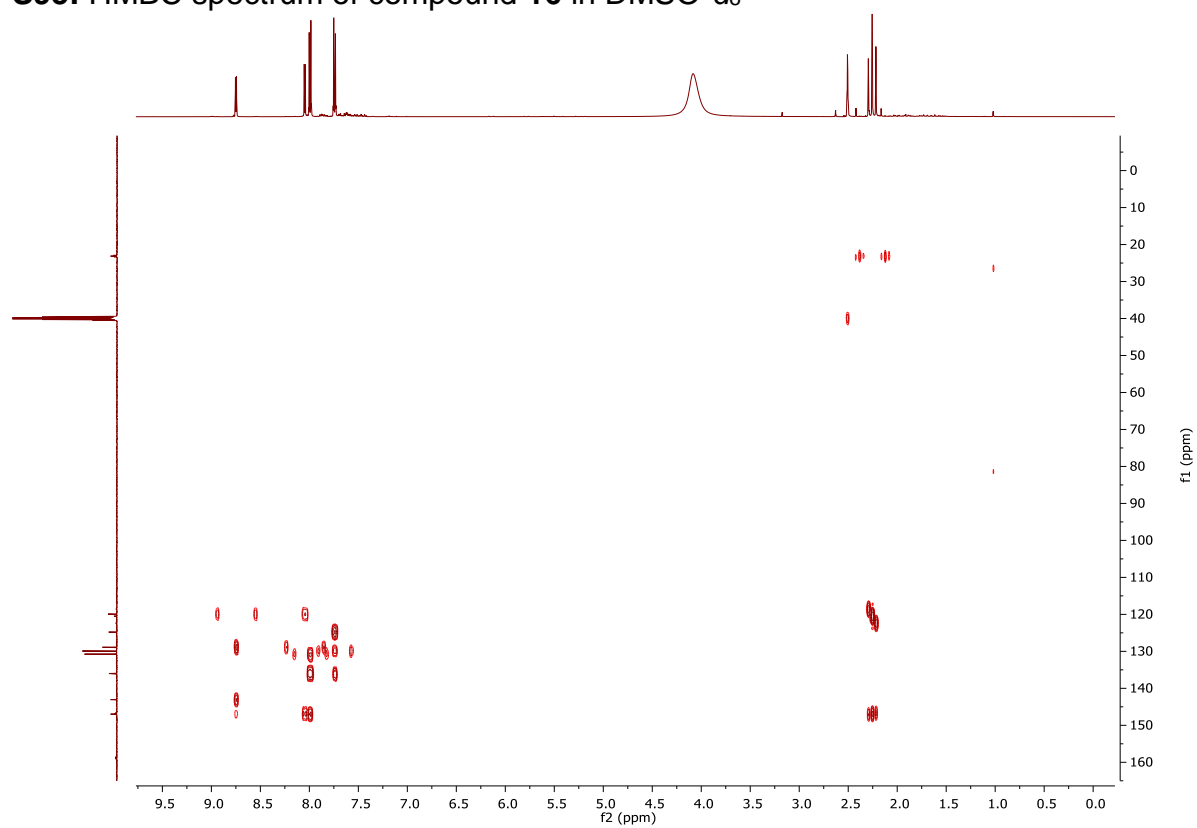
**S93:** COSY spectrum of compound **16** in  $\text{DMSO}-d_6$



**S94:** HSQC spectrum of compound **16** in DMSO- $d_6$



**S95:** HMBC spectrum of compound **16** in DMSO- $d_6$



## S96: HRMS of compound 16



### High Resolution Mass Spectrum

#### Analysis Info

Analysis Name D:\Data\KahYean\20200904\RAD868000002.d

Method DirectInfusion\_2018\_pos.m

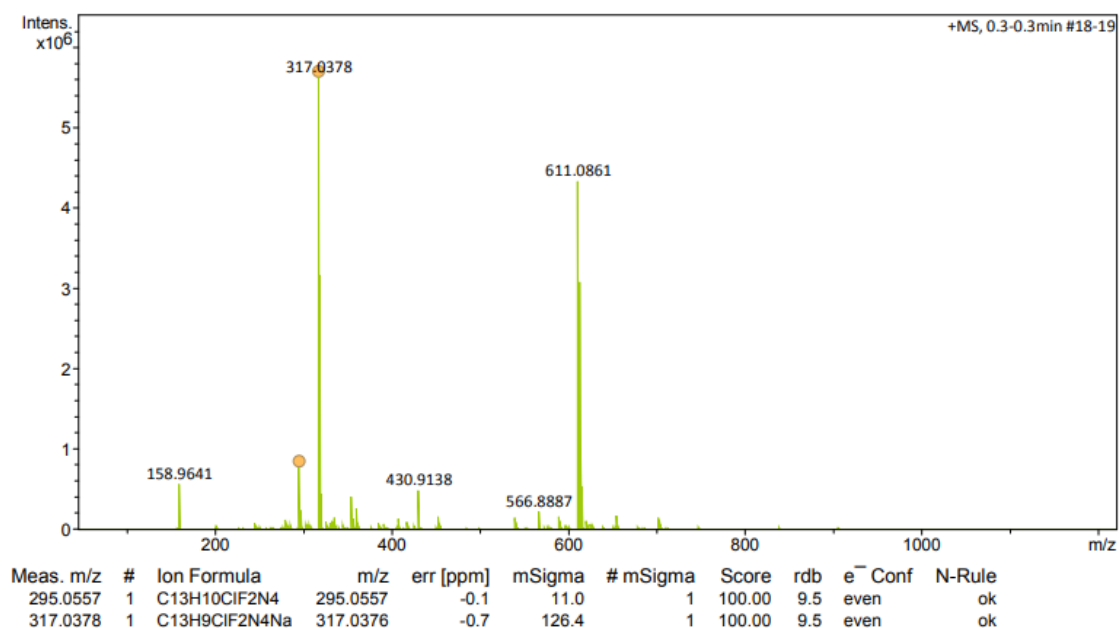
Sample Name RAD868

Comment

Acquisition Date 9/4/2020 12:05:33 PM

Instrument maXis II ETD 1823391.22321

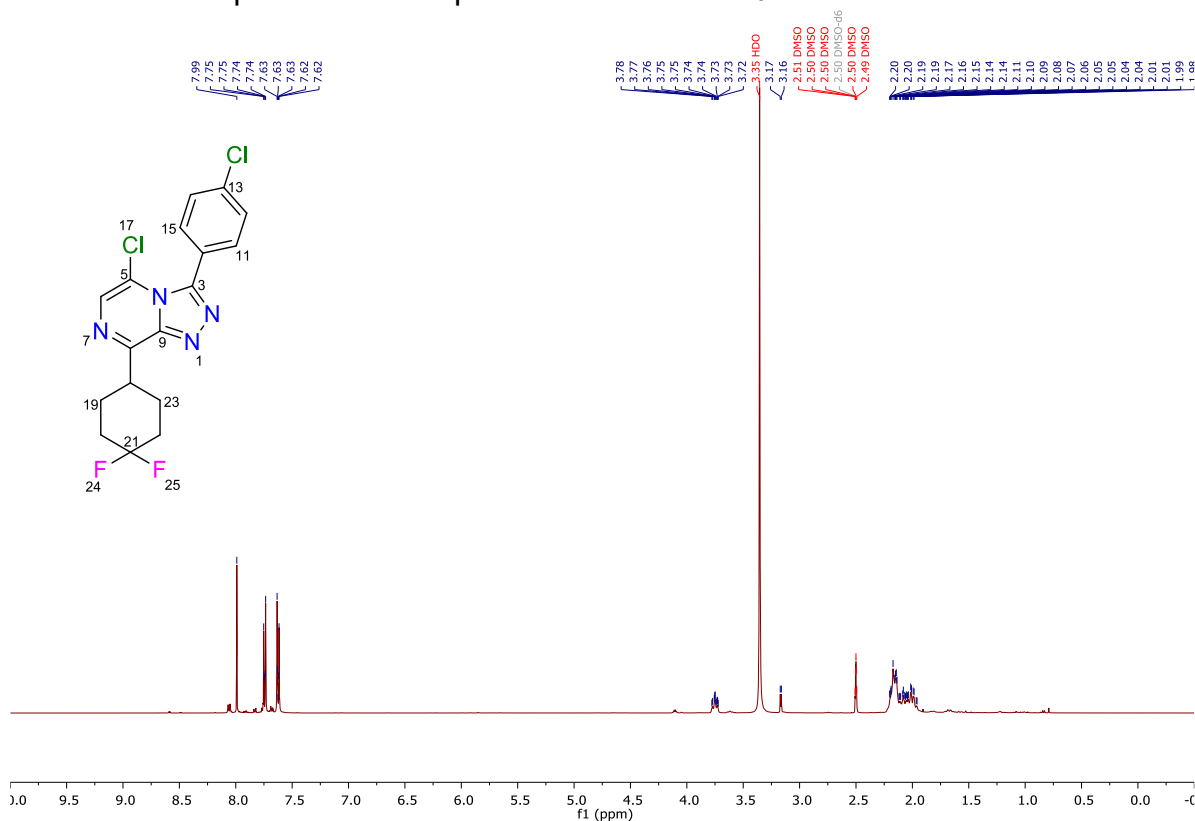
#### +MS, 0.3-0.3min #18-19



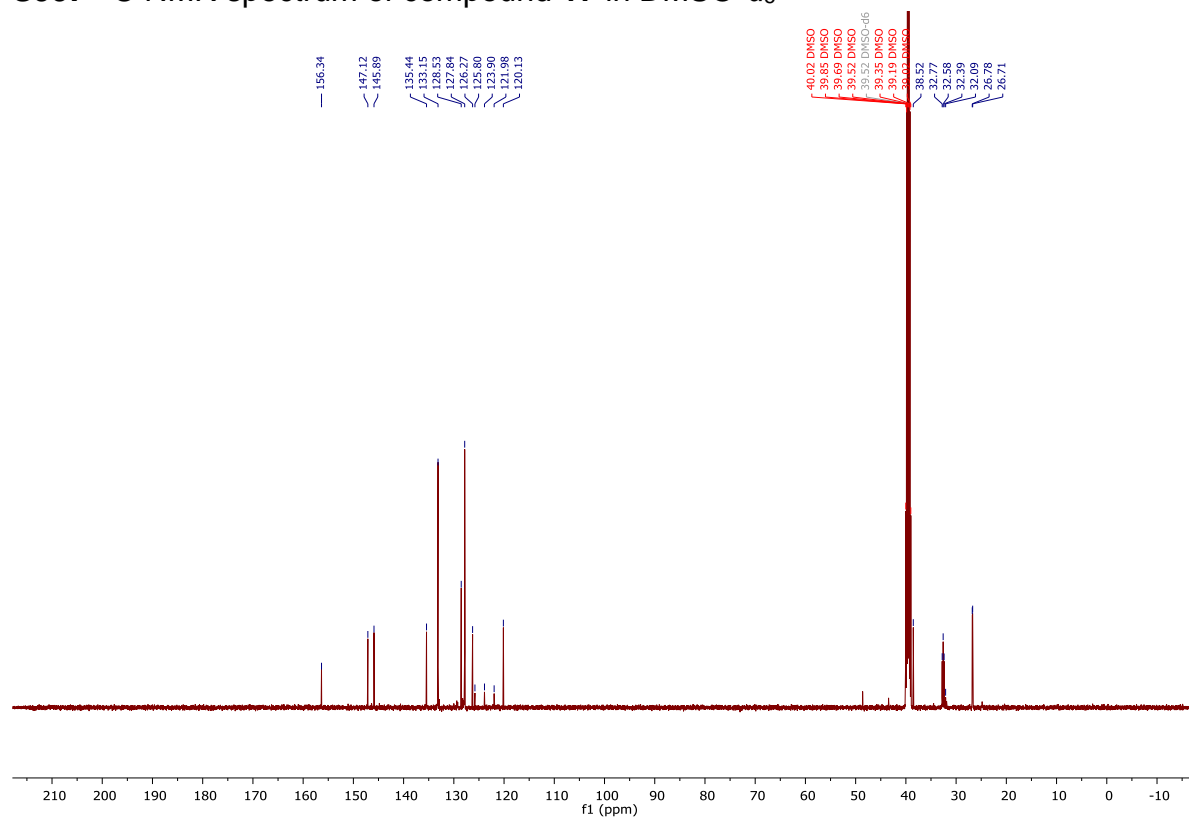
**S97:** NMR data of compound **17** in DMSO-*d*<sub>6</sub><sup>a</sup>

Pos.	δ <sub>H</sub> , mult. ( <i>J</i> in Hz), int.	δ <sub>C</sub> , mult. ( <i>J</i> in Hz)	COSY	HMBC
3		147.1, s		
5		120.1, s		
6	7.99, s, 1H	128.5, s		5, 8, 9
8		156.3, s		
9		145.9, s		
10		126.3, s		
11	7.74, m, 1H	133.2, s	12	3, 13, 15
12	7.62, m, 1H	127.8, s	11	10, 14
13		135.4, s		
14	7.62, m, 1H	127.8, s	15	10, 12
15	7.74, m, 1H	133.2, s	14	3, 11, 13
18	3.75, m, 1H	38.5, s	19, 23	8, 20, 24
19	2.00, 2.14, m, 2H	26.7, d (9.6)	18, 20	18, 20, 21
20	2.08, 2.17, m, 2H	32.6, dd (23.8, 23.8)	19	18, 19, 21
21		123.9, dd (239.3, 241.6)		
22	2.08, 2.17, m, 2H	32.6, dd (23.8, 23.8)	23	18, 21, 23
23	2.00, 2.14, m, 2H	26.7, d (9.6)	18, 22	18, 21, 22

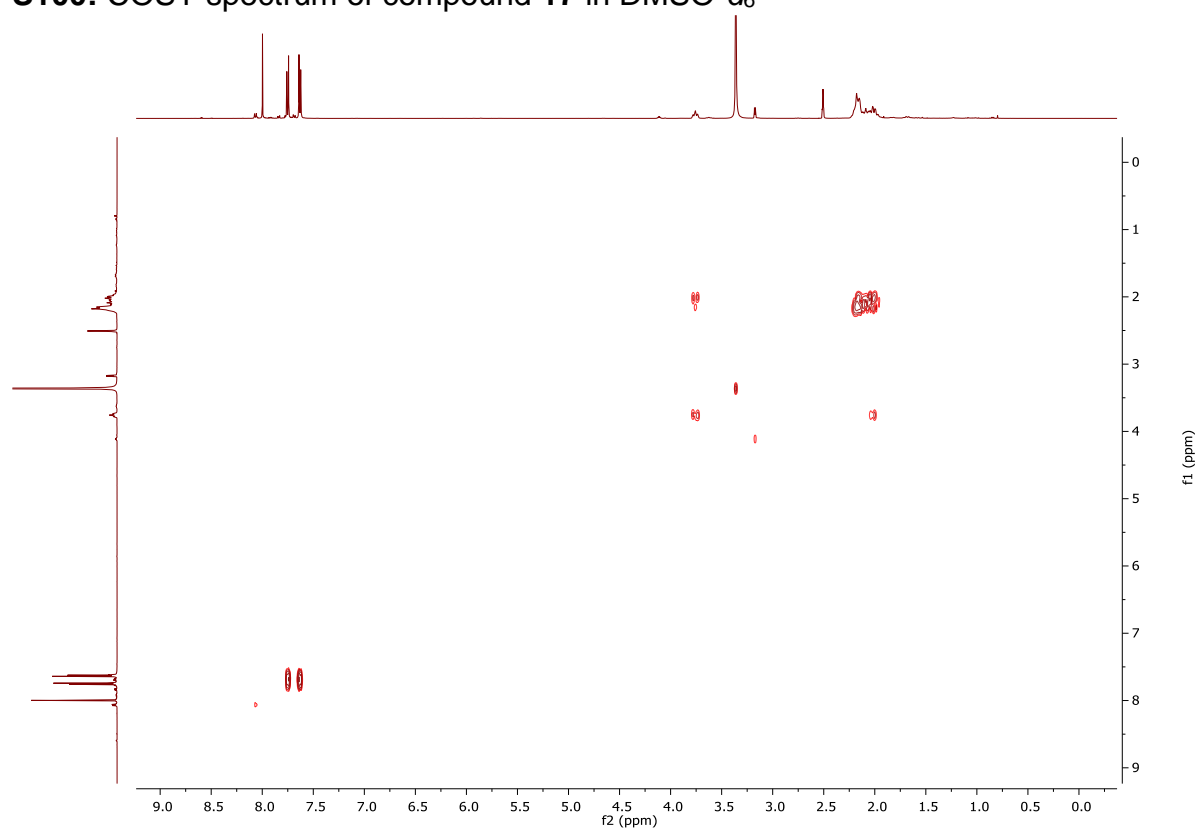
<sup>a</sup> Recorded at 500 MHz (<sup>1</sup>H NMR) and 125 MHz (<sup>13</sup>C NMR) at 25 °C.

**S98:** <sup>1</sup>H NMR Spectrum of compound **17** in DMSO-*d*<sub>6</sub>

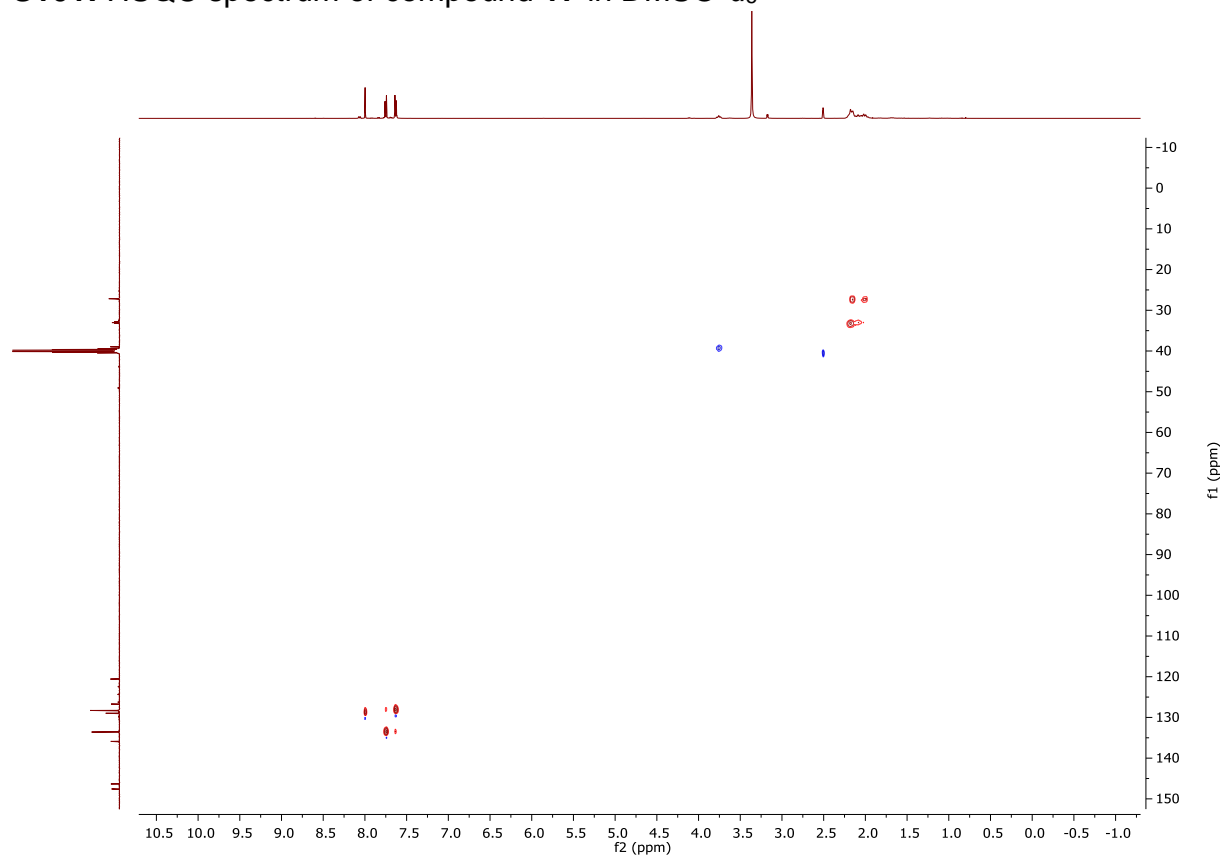
**S99:**  $^{13}\text{C}$  NMR spectrum of compound **17** in  $\text{DMSO}-d_6$



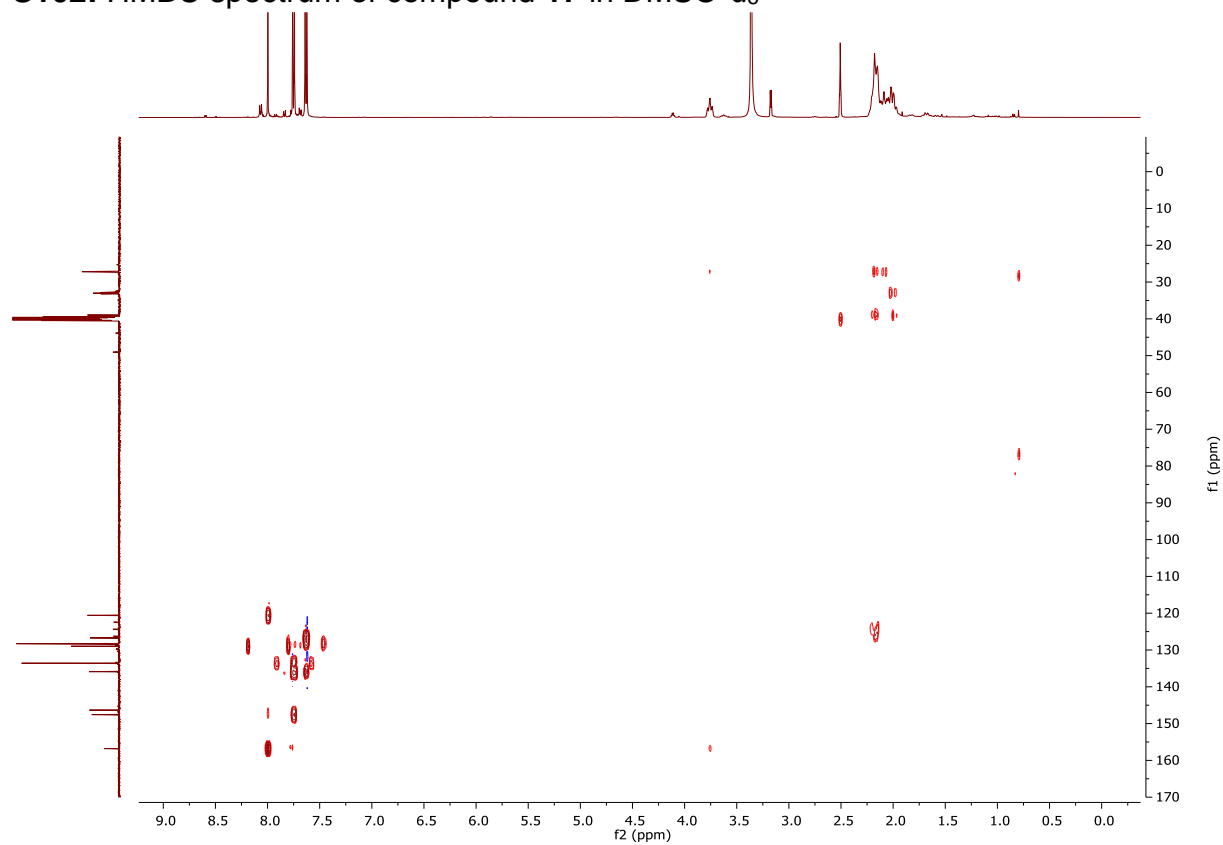
**S100:** COSY spectrum of compound **17** in  $\text{DMSO}-d_6$



**S101:** HSQC spectrum of compound **17** in DMSO- $d_6$



**S102:** HMBC spectrum of compound **17** in DMSO- $d_6$



# S103: HRMS of compound 17



## High Resolution Mass Spectrum

### Analysis Info

Analysis Name D:\Data\KahYean\20200904\RAD869000001.d

Method DirectInfusion\_2018\_pos.m

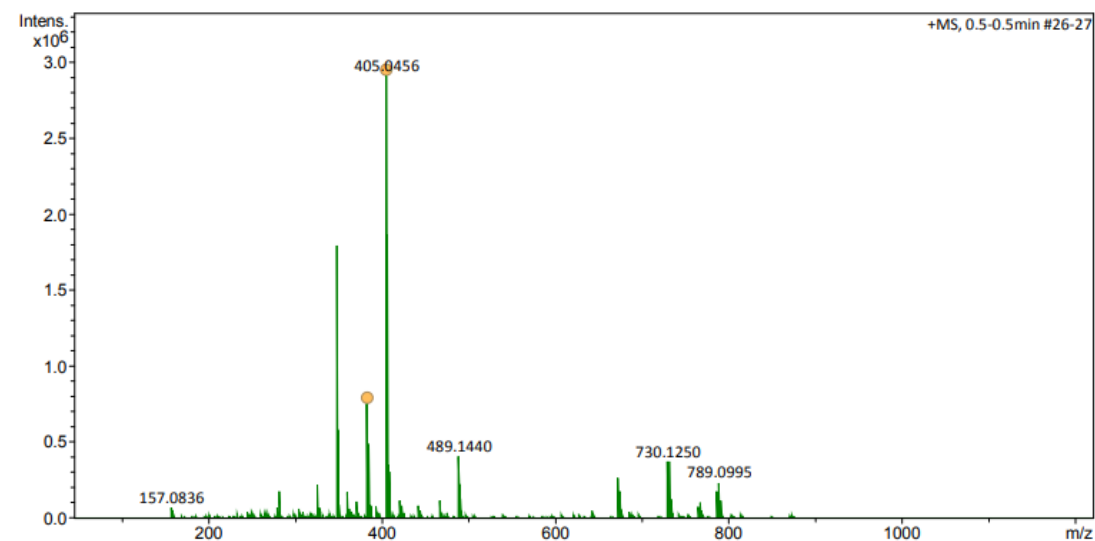
Sample Name RAD869

Comment

Acquisition Date 9/4/2020 12:15:43 PM

Instrument maXis II ETD 1823391.22321

### +MS, 0.5-0.5min #26-27



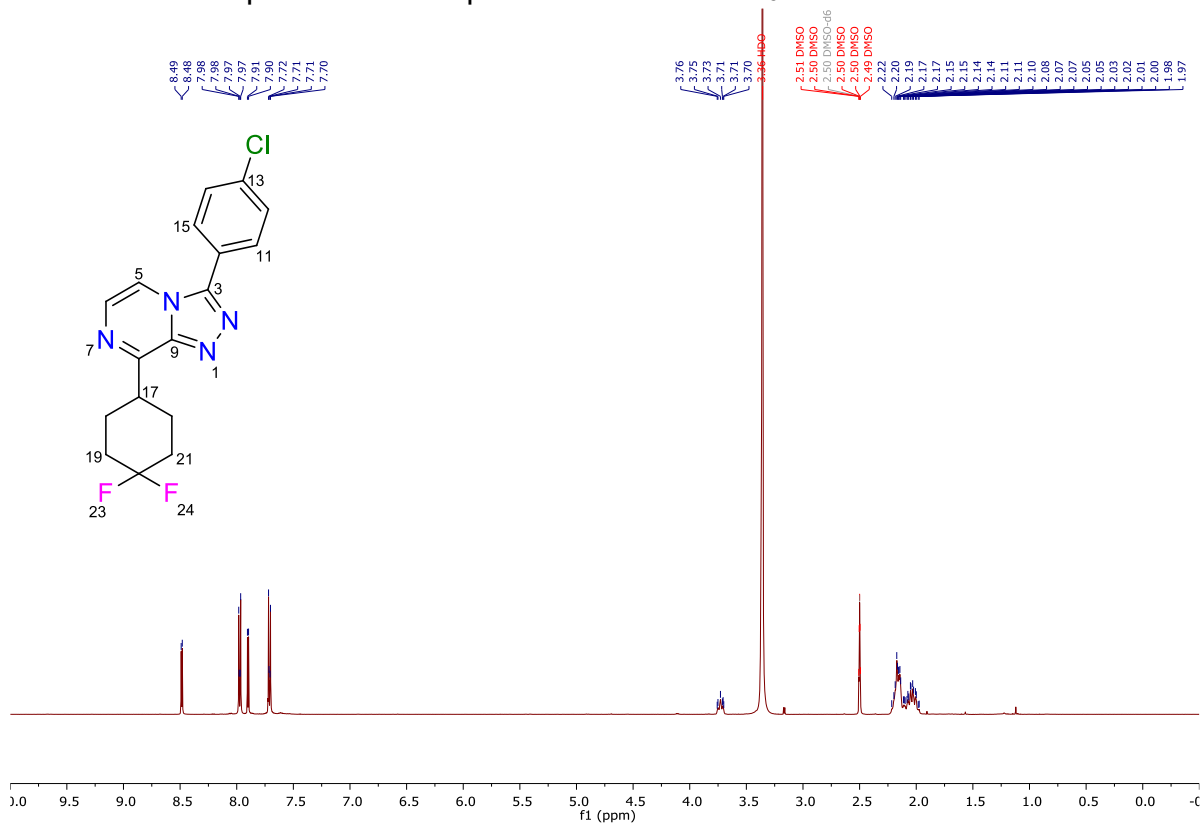
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e <sup>-</sup> Conf	N-Rule
383.0636	1	C <sub>17</sub> H <sub>15</sub> Cl <sub>2</sub> F <sub>2</sub> N <sub>4</sub>	383.0636	-0.0	7.7	1	100.00	10.5	even	ok
405.0456	1	C <sub>17</sub> H <sub>14</sub> Cl <sub>2</sub> F <sub>2</sub> N <sub>4</sub> Na	405.0456	-0.0	9.0	1	100.00	10.5	even	ok



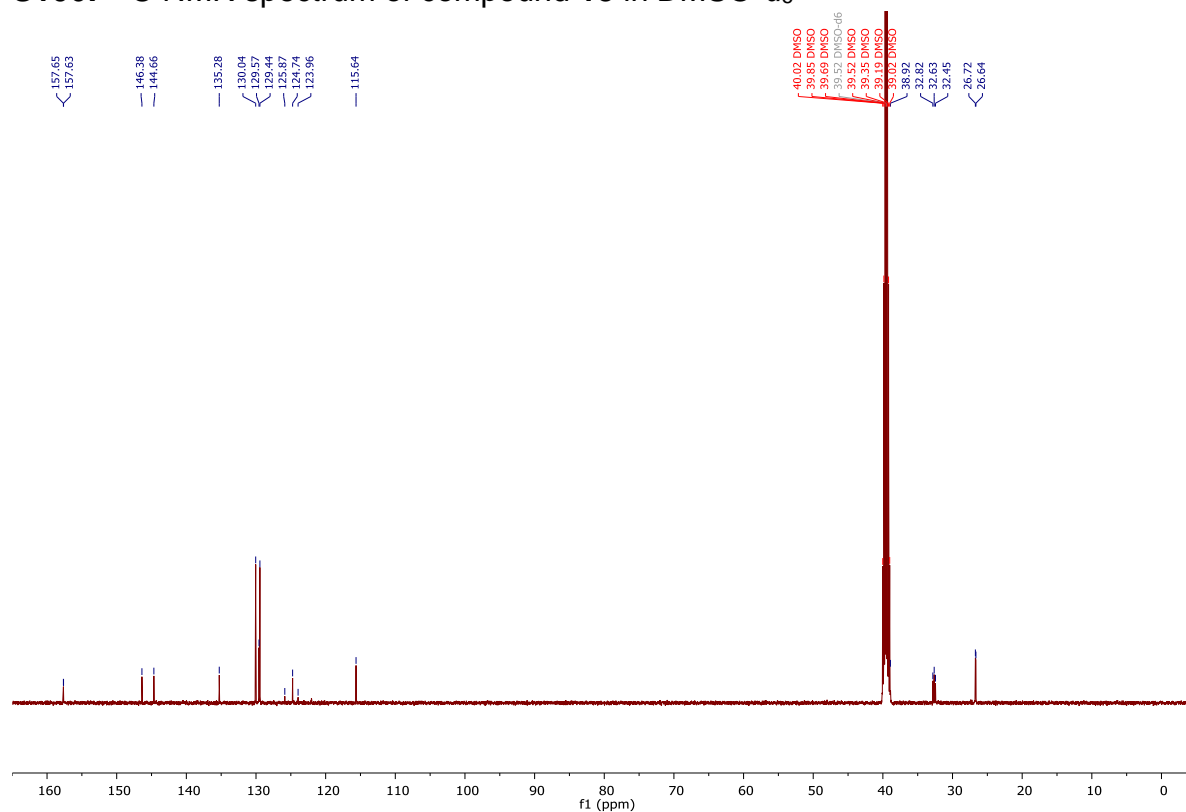
**S104:** NMR data of compound **18** in DMSO-*d*<sub>6</sub><sup>a</sup>

Pos.	δ <sub>H</sub> , mult. ( <i>J</i> in Hz), int.	δ <sub>C</sub> , mult. ( <i>J</i> in Hz)	COSY	HMBC
3		146.4, s		
5	8.49, d (4.9), 1H	115.6, s	6	21
6	7.90, d (4.9), 1H	129.6, s	5	5, 8
8		157.6, s		
9		144.7, s		
10		124.7, s		
11	7.97, m, 1H	130.0, s	12	3, 13,15
12	7.71, m, 1H	129.4, s	11	10,14
13		135.3, s		
14	7.71, m, 1H	129.4, s	15	10, 12
15	7.97, m, 1H	130.0, s	14	3, 11, 13
17	3.75, m, 1H	38.9, s	18, 22	8, 18
18	2.03, 2.15, m, 2H	26.7, d (9.7)	17	17,19, 20, 23
19	2.06, 2.17, m, 2H	32.6, dd (24.5, 23.1)		17, 18, 20, 21
20		123.9, dd (239.5, 241.6)		
21	2.06, 2.17, m, 2H	32.6, dd (24.5, 23.1)		17, 19, 20, 22
22	2.03, 2.15, m, 2H	26.7, d (9.7)	17	17, 18, 20, 21

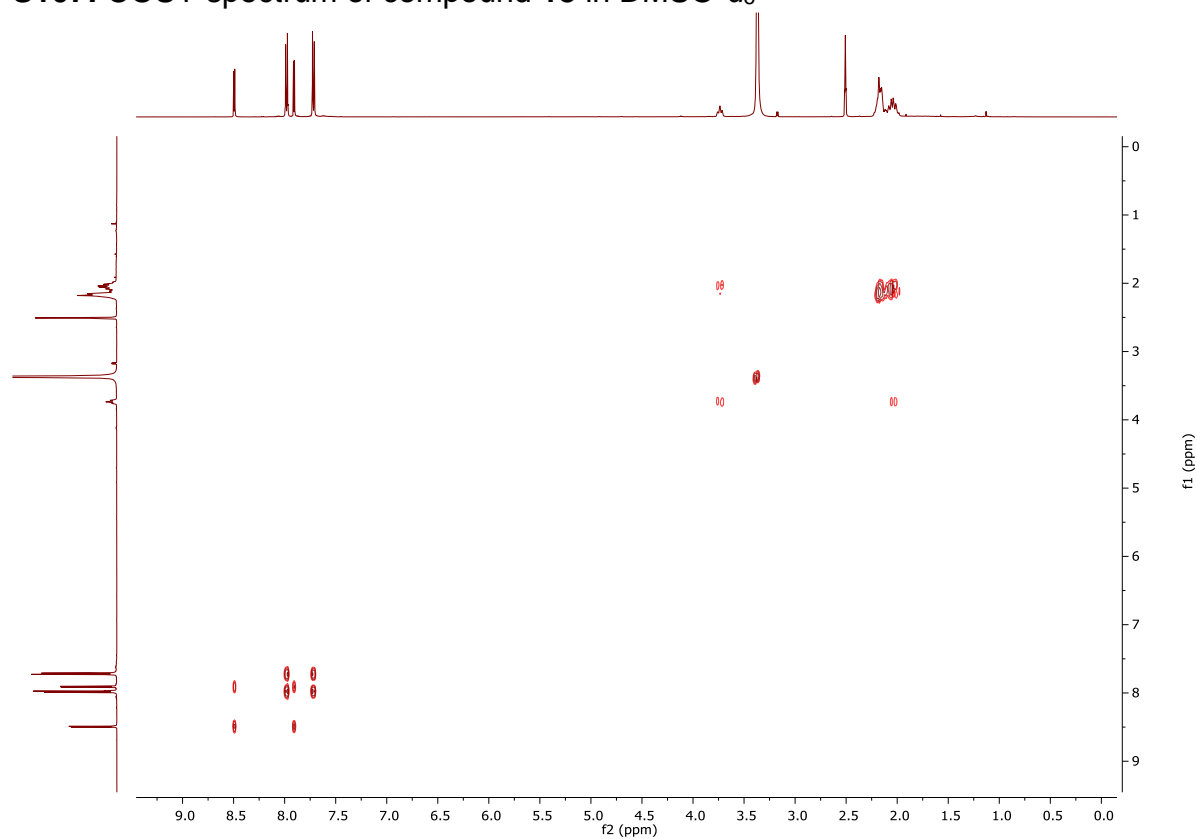
<sup>a</sup> Recorded at 500 MHz (<sup>1</sup>H NMR) and 125 MHz (<sup>13</sup>C NMR) at 25 °C.

**S105:** <sup>1</sup>H NMR spectrum of compound **18** in DMSO-*d*<sub>6</sub>

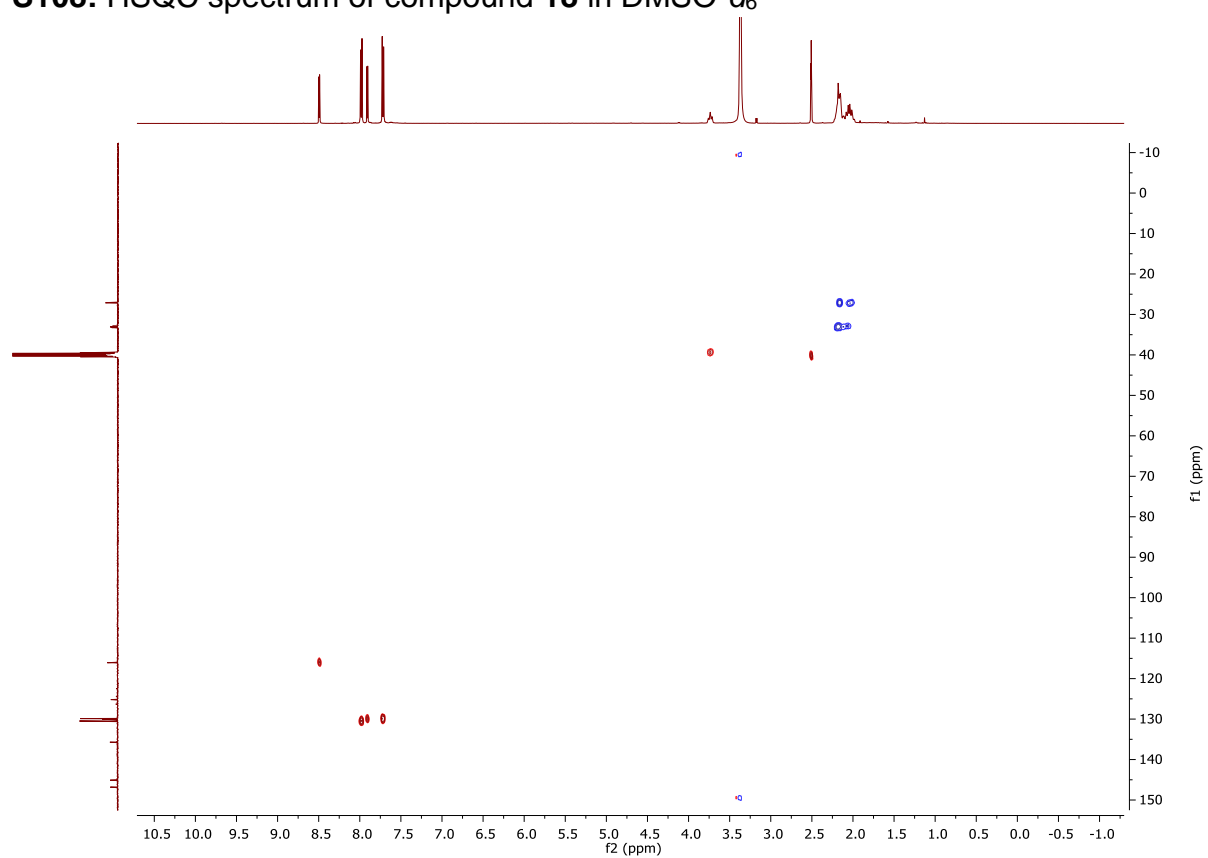
**S106:**  $^{13}\text{C}$  NMR spectrum of compound **18** in  $\text{DMSO}-d_6$



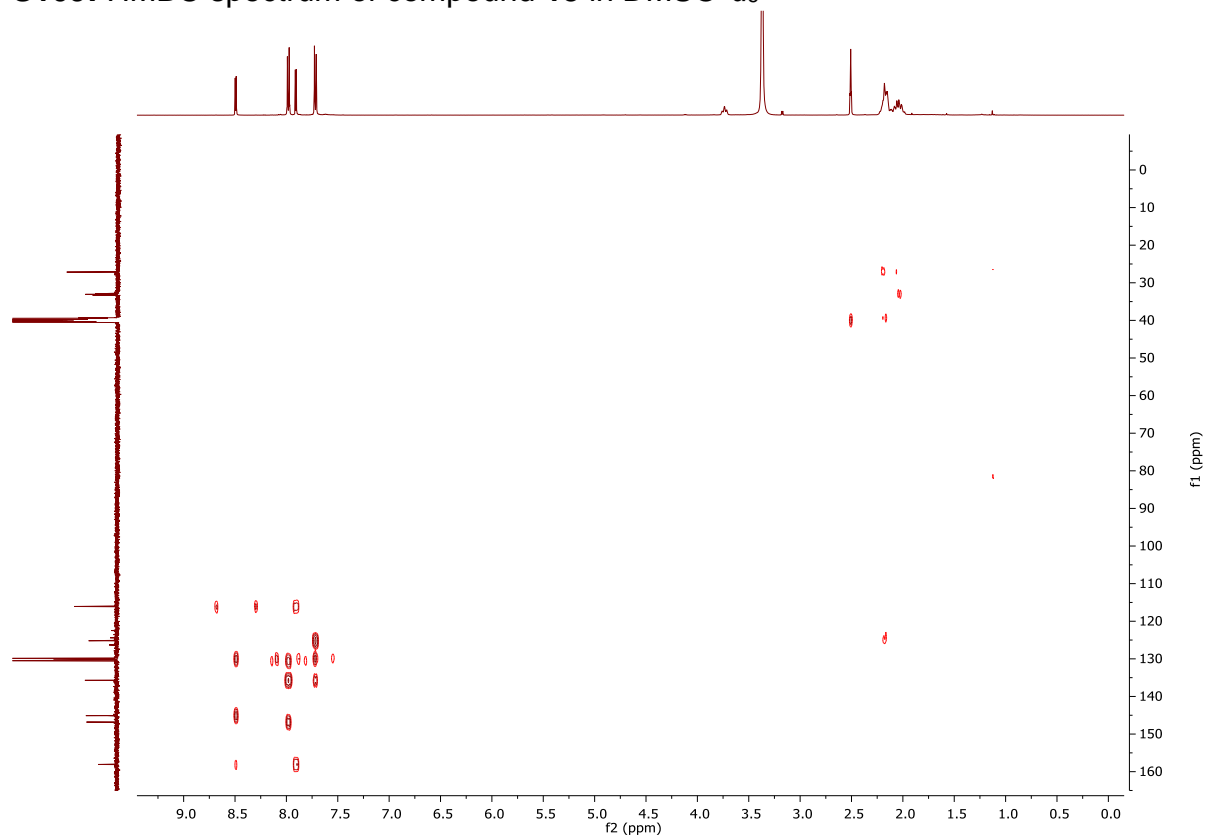
**S107:** COSY spectrum of compound **18** in  $\text{DMSO}-d_6$



**S108:** HSQC spectrum of compound **18** in DMSO- $d_6$



**S109:** HMBC spectrum of compound **18** in DMSO- $d_6$



# S110: HRMS of compound 18



## High Resolution Mass Spectrum

### Analysis Info

Analysis Name D:\Data\KahYean\20200904\RAD870000001.d  
Method DirectInfusion\_2018\_pos.m  
Sample Name RAD870  
Comment

Acquisition Date 9/4/2020 12:22:44 PM  
Instrument maXis II ETD 1823391.22321

### +MS, 0.2-0.2min #13-14

