

## Appendix C. Experimental for Chapter 3

### Supplemental Information Data File

This file contains the supplementary information for the characterization of compounds, as well as the MS data for the HSA photolabeling and competition experiments using **2**, and the MS/MS data used to identify labeled HSA peptide fragments.

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## 1. Compound characterization data

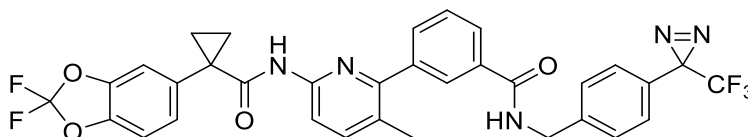
This section contains the relevant characterization data for the series of novel compounds that were generated during the synthesis of compound **2**.

### 1.1. 3-(6-(1-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)cyclopropane-1-carboxamido)-3-methylpyridin-2-yl)-N-(4-(3-(trifluoromethyl)-3H-diazirin-3-yl)benzyl)benzamide (**8**)

Chemical Formula: C<sub>33</sub>H<sub>24</sub>F<sub>5</sub>N<sub>5</sub>O<sub>4</sub>

Molecular Weight: 649.5780

Spectra provided: LC-HRMS, <sup>1</sup>H NMR, <sup>19</sup>F NMR, <sup>13</sup>C NMR, <sup>13</sup>C-APT NMR, COSY, HSQC, HMBC



To a solution of lumacaftor (50 mg, 0.11 mmol), (4-(3-(trifluoromethyl)-3H-diazirin-3-yl)phenyl)methanaminium chloride **129** (26 mg, 0.10 mmol, 0.9 equiv.), HATU (84 mg, 0.22 mmol, 2.2 equiv), DMAP (2 mg, 0.02 mmol, 0.1 equiv), HOBT (15 mg, 0.11 mmol, 1.0 equiv.) in DMF (1.5 mL), was added Et<sub>3</sub>N (60 μL, 0.34 mmol, 3 equiv) and the reaction was stirred overnight at 60 °C. The reaction mixture was concentrated to remove DMF. The crude material was loaded onto a silica cartridge (4 g, 10-100% EtOAc/Hex gradient) to give **8** (49 mg, 0.075 mmol, 68 % isolated yield) as a white residue.

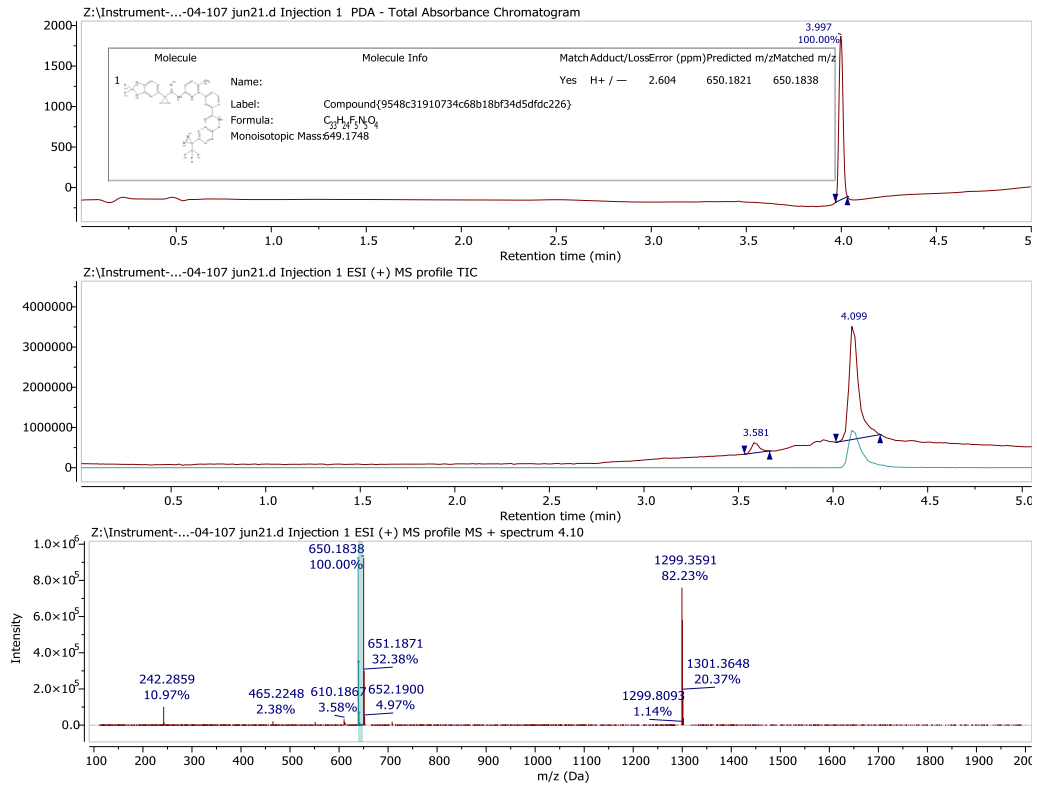
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 8.09 (d, *J* = 8.4 Hz, 1H), 7.82 (d, *J* = 1.8 Hz, 1H), 7.78 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.69 (s, 1H), 7.57 (d, *J* = 8.5 Hz, 1H), 7.54 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 2H), 7.20 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.18 – 7.13 (m, 3H), 7.04 (d, *J* = 8.2 Hz, 1H), 6.63 (t, *J* = 5.9 Hz, 1H), 4.62 (d, *J* = 5.8 Hz, 2H), 2.23 (s, 3H), 1.73 (q, *J* = 3.9 Hz, 2H), 1.15 (q, *J* = 3.9 Hz, 2H).

<sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>) δ -49.6, -65.3.

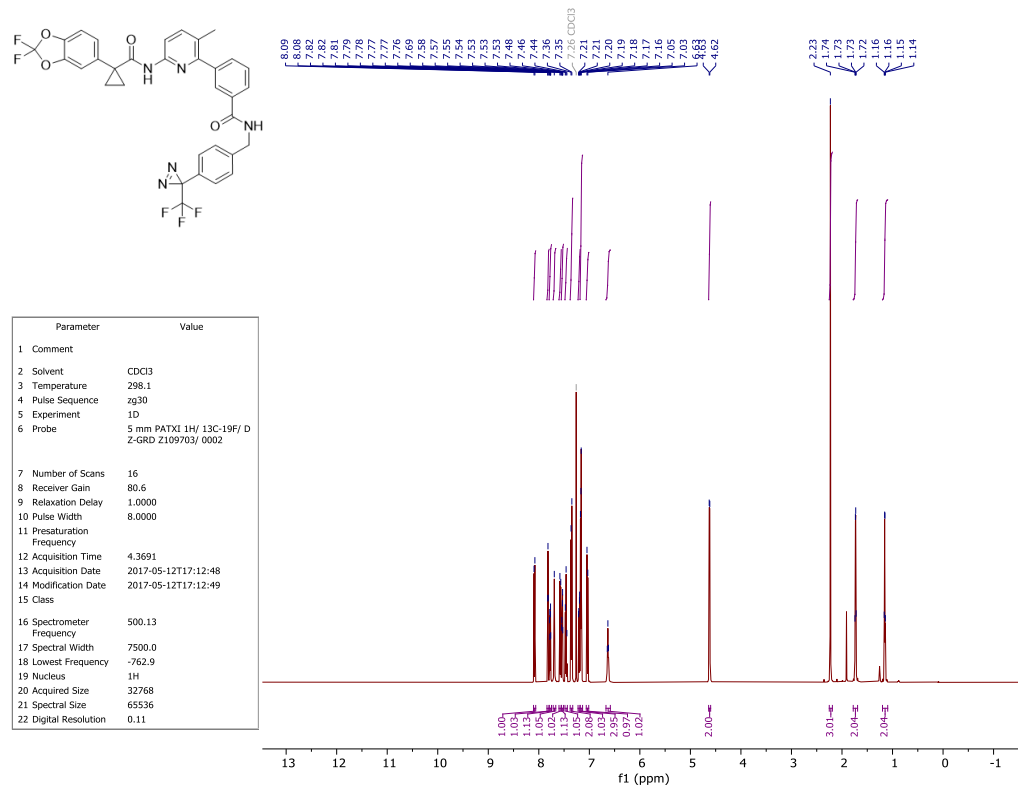
<sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 171.9, 167.3, 155.4, 149.0, 144.3, 143.7, 141.1, 140.4, 140.2, 135.0, 134.4, 132.2, 131.8 (t, <sup>1</sup>*J*<sub>C-F</sub> = 256.3 Hz), 128.7, 128.5, 128.3, 127.7, 127.1, 127.0, 126.8, 126.7, 122.2 (q, <sup>1</sup>*J*<sub>C-F</sub> = 274.7 Hz), 113.2, 112.5, 110.3, 43.6, 31.3, 28.4 (q, <sup>3</sup>*J*<sub>C-F</sub> = 40.5 Hz), 19.2, 17.3.

HRMS: *m/z* calculated for C<sub>33</sub>H<sub>24</sub>F<sub>5</sub>N<sub>5</sub>O<sub>4</sub>: 650.1821 (M+H); found: 650.1838

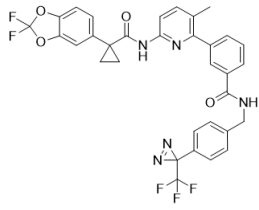
# LC-HRMS



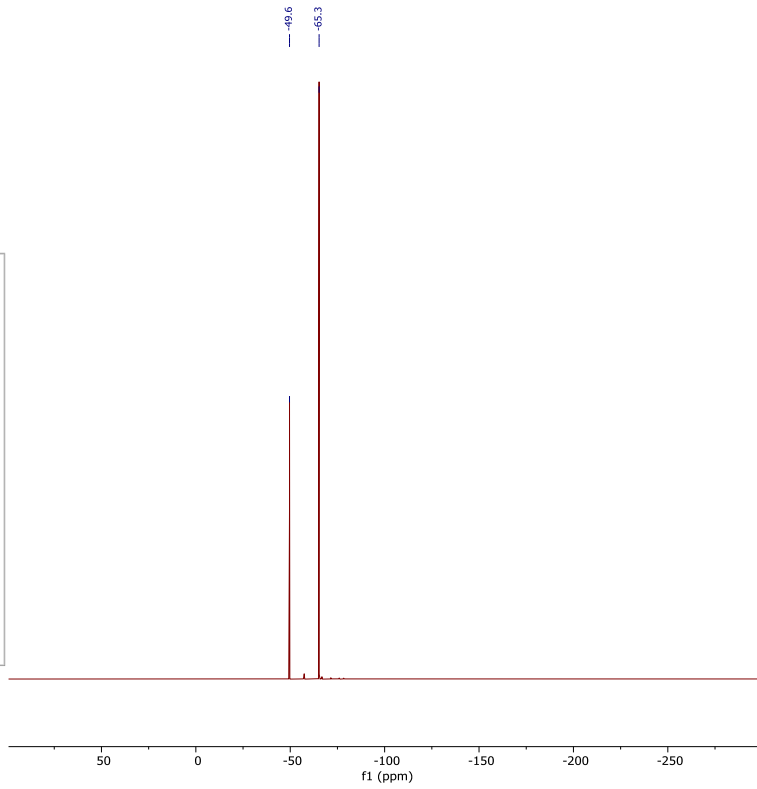
# <sup>1</sup>H NMR



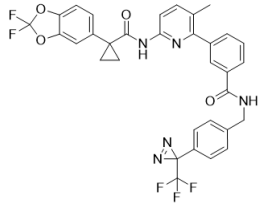
# <sup>19</sup>F NMR



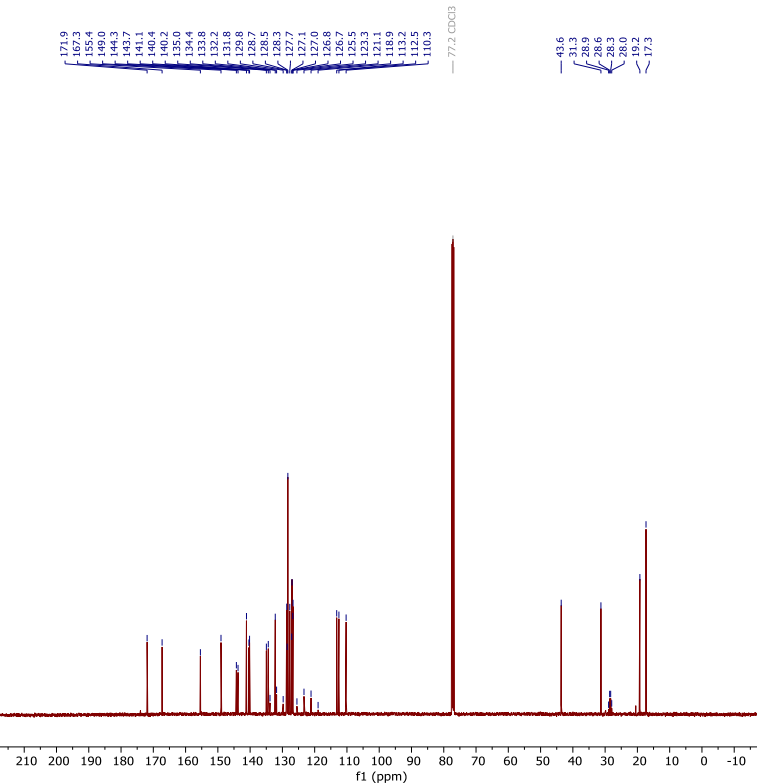
Parameter	Value
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3 Temperature	297.8
4 Pulse Sequence	zgpg30
5 Experiment	1D
6 Probe	5 mm PATXI 1H/ 13C-19F/ D Z-GRD Z109703/ 0002
7 Number of Scans	64
8 Receiver Gain	181.0
9 Relaxation Delay	1.0000
10 Pulse Width	13.5000
11 Presaturation Frequency	
12 Acquisition Time	0.3495
13 Acquisition Date	2017-05-13T22:19:10
14 Modification Date	2017-05-13T22:19:11
15 Class	
16 Spectrometer Frequency	470.55
17 Spectral Width	187500.0
18 Lowest Frequency	-140810.0
19 Nucleus	19F
20 Acquired Size	65536
21 Spectral Size	131072
22 Digital Resolution	1.43



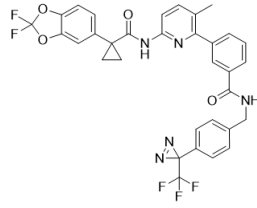
# <sup>13</sup>C NMR



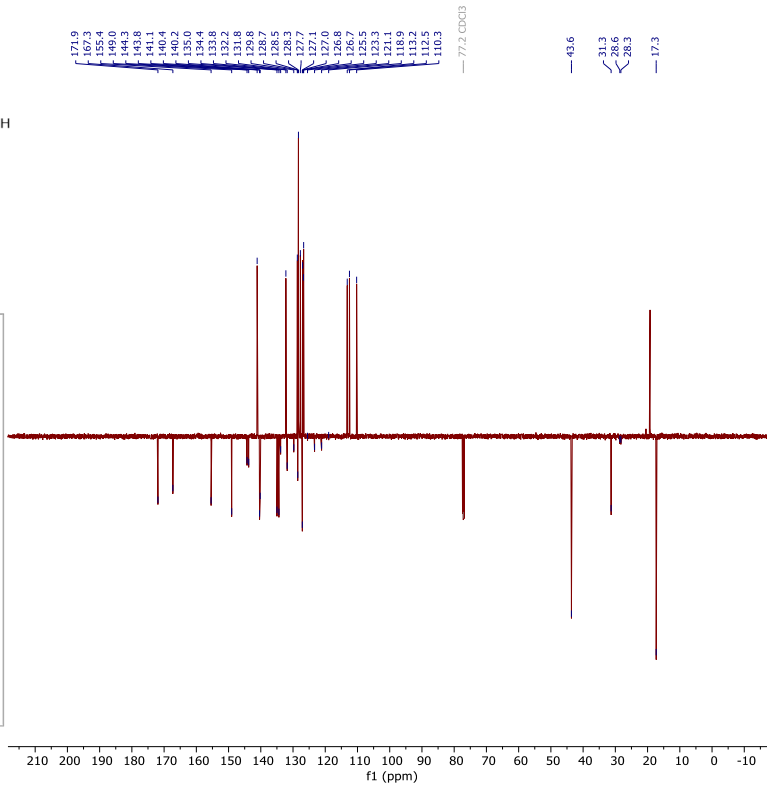
Parameter	Value
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2 Solvent	CDCl3
3 Temperature	298.0
4 Pulse Sequence	zgpg30
5 Experiment	1D
6 Probe	5 mm PATXI 1H/ 13C-19F/ D Z-GRD Z109703/ 0002
7 Number of Scans	5000
8 Receiver Gain	203.0
9 Relaxation Delay	2.0000
10 Pulse Width	10.8000
11 Presaturation Frequency	
12 Acquisition Time	1.1010
13 Acquisition Date	2017-05-13T18:41:40
14 Modification Date	2017-05-13T18:41:41
15 Class	
16 Spectrometer Frequency	125.77
17 Spectral Width	29761.9
18 Lowest Frequency	-2291.4
19 Nucleus	13C
20 Acquired Size	32768
21 Spectral Size	65536
22 Digital Resolution	0.45



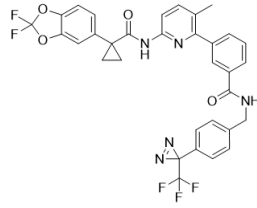
# <sup>13</sup>C-APT NMR



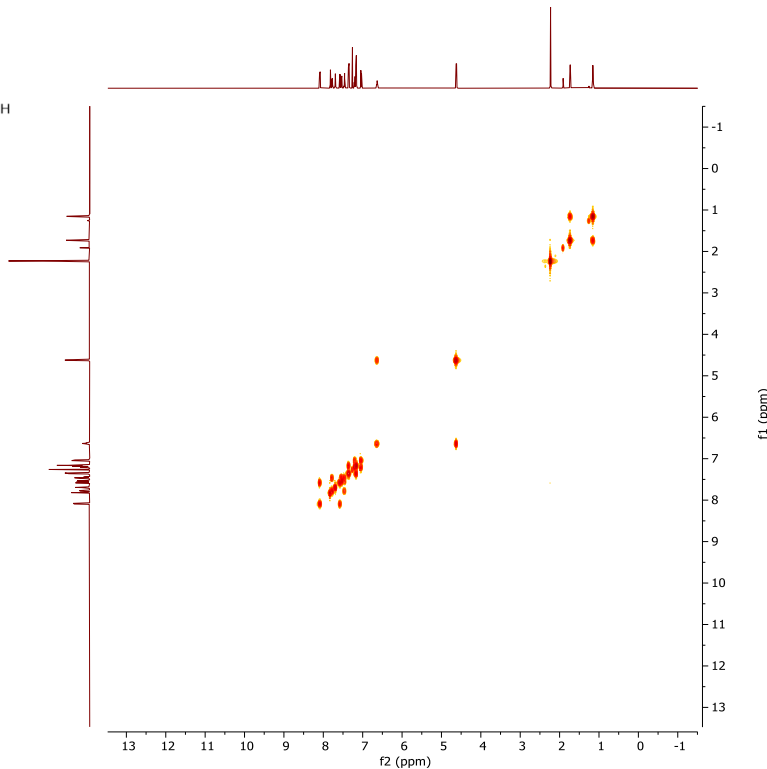
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2 Solvent	CDCl3
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4 Pulse Sequence	jmod
5 Experiment	JMOD
6 Probe	5 mm PATXI 1H/ 13C-19F/ D Z-GRD Z109703/ 0002
7 Number of Scans	2000
8 Receiver Gain	203.0
9 Relaxation Delay	2.0000
10 Pulse Width	10.8000
11 Presaturation	
12 Acquisition Time	1.1010
13 Acquisition Date	2017-05-13T22:16:42
14 Modification Date	2017-05-13T22:16:43
15 Class	
16 Spectrometer	125.77
17 Spectral Width	29761.9
18 Lowest Frequency	-2290.6
19 Nucleus	13C
20 Acquired Size	32768
21 Spectral Size	65536
22 Digital Resolution	0.45



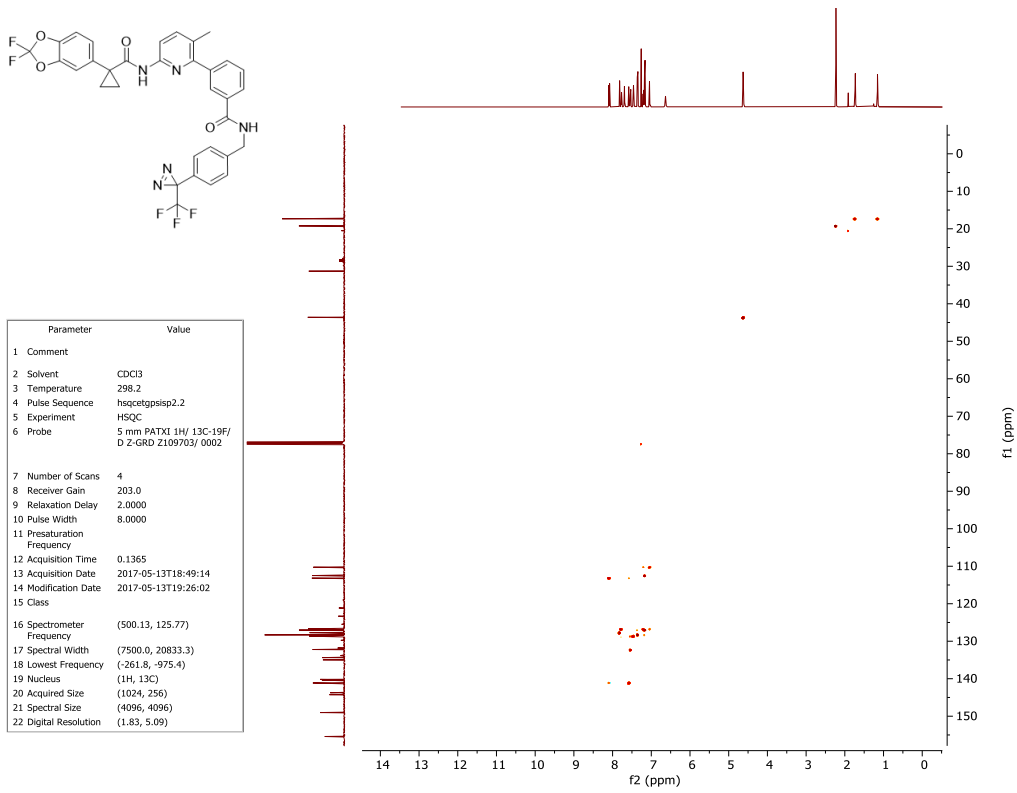
# COSY



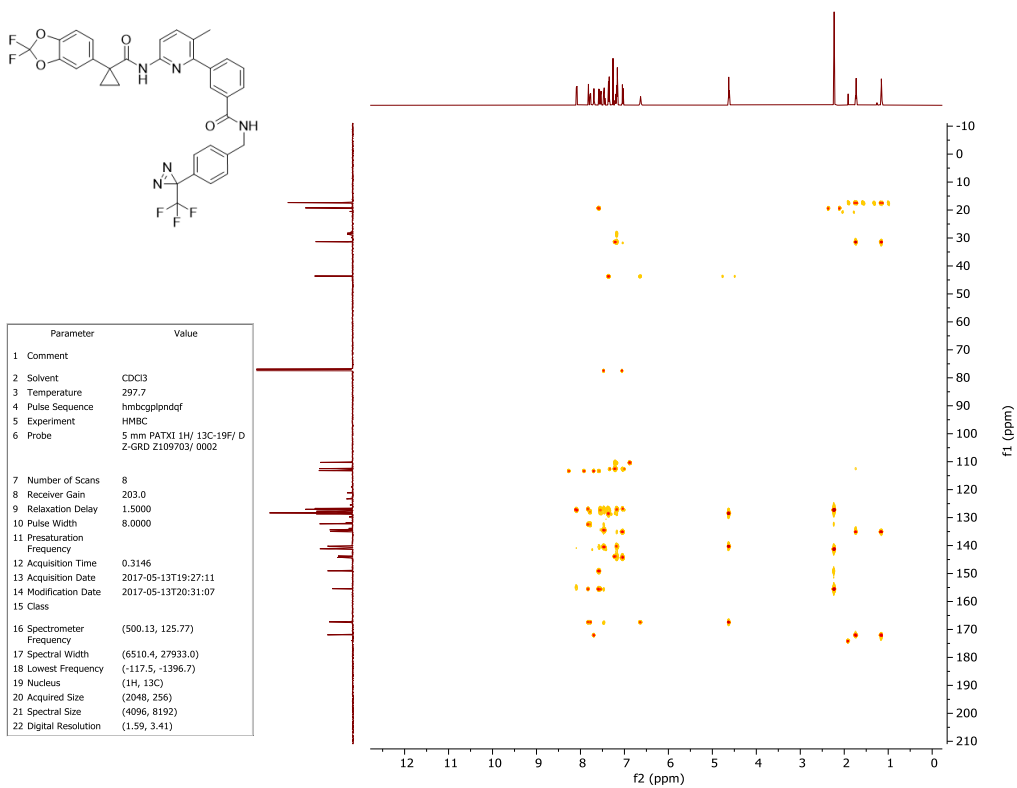
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1 Comment	
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3 Temperature	297.8
4 Pulse Sequence	cosyqpf
5 Experiment	COSY
6 Probe	5 mm PATXI 1H/ 13C-19F/ D Z-GRD Z109703/ 0002
7 Number of Scans	1
8 Receiver Gain	128.0
9 Relaxation Delay	1.2592
10 Pulse Width	8.0000
11 Presaturation	
12 Acquisition Time	0.1365
13 Acquisition Date	2017-05-13T18:42:24
14 Modification Date	2017-05-13T18:48:28
15 Class	
16 Spectrometer	(500.13, 500.13)
17 Spectral Width	(7500.0, 7500.0)
18 Lowest Frequency	(-760.3, -760.3)
19 Nucleus	(1H, 1H)
20 Acquired Size	(1024, 256)
21 Spectral Size	(1024, 1024)
22 Digital Resolution	(7.32, 7.32)



# HSQC



# HMBC

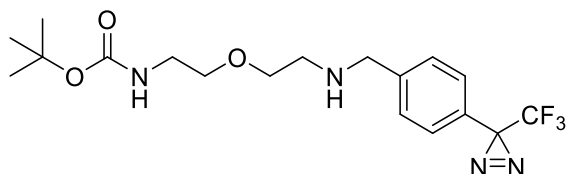


1.2. *tert*-butyl (2-(2-((4-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)benzyl)amino)ethoxy)ethyl)carbamate (**136**)

Chemical Formula: C<sub>18</sub>H<sub>25</sub>F<sub>3</sub>N<sub>4</sub>O<sub>3</sub>

Molecular Weight: 402.4182

Spectra provided: LC-HRMS, <sup>1</sup>H NMR, <sup>19</sup>F NMR, <sup>13</sup>C NMR, <sup>13</sup>C-APT NMR, COSY, HSQC, HMBC



To a solution of *tert*-butyl (2-(2-oxoethoxy)ethyl)carbamate **135** (70 mg, 0.34 mmol, 1.0 equiv.; prepared as described)<sup>132</sup> and diazirine 119 (90 mg, 0.36 mmol, 1.1 equiv.; prepared as described)<sup>133</sup> in 1,2-dichloroethane was added MgSO<sub>4</sub> (50 mg), and stirred for 10 min. NaBH(OAc)<sub>3</sub> (180 mg, 0.85 mmol, 2.5 equiv.) was added and stirred overnight. The reaction was quenched with sat. NaHCO<sub>3</sub>, extracted with EtOAc (10 mL). The organic layer was dried with brine (10 mL), Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo* to give secondary amine **136** (130 mg, 0.32 mmol, 94 % yield) used as a crude product in subsequent reactions. For characterization purposes a portion

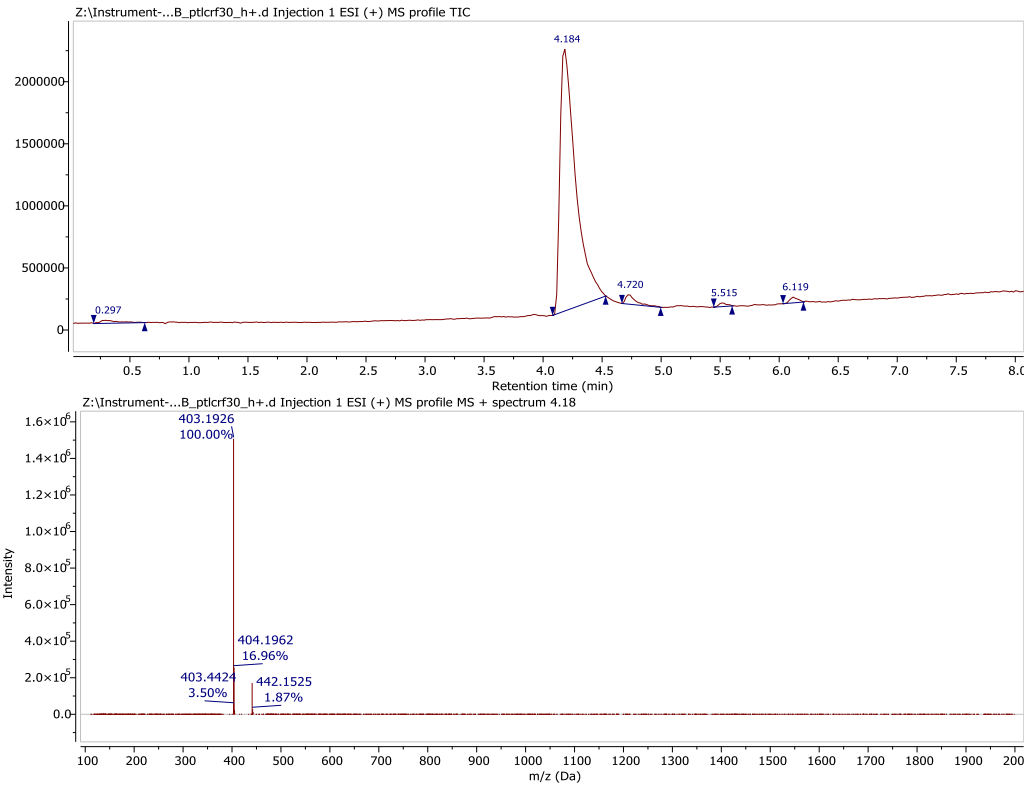
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.40 – 7.34 (m, 1H), 7.16 (d, *J* = 8.0 Hz, 1H), 4.92 (s, 0H), 3.83 (s, 1H), 3.56 (t, *J* = 5.1 Hz, 1H), 3.50 (t, *J* = 5.1 Hz, 1H), 3.31 (q, *J* = 5.3 Hz, 1H), 2.77 (t, *J* = 5.1 Hz, 1H), 1.43 (s, 5H).

<sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>) δ -65.3.

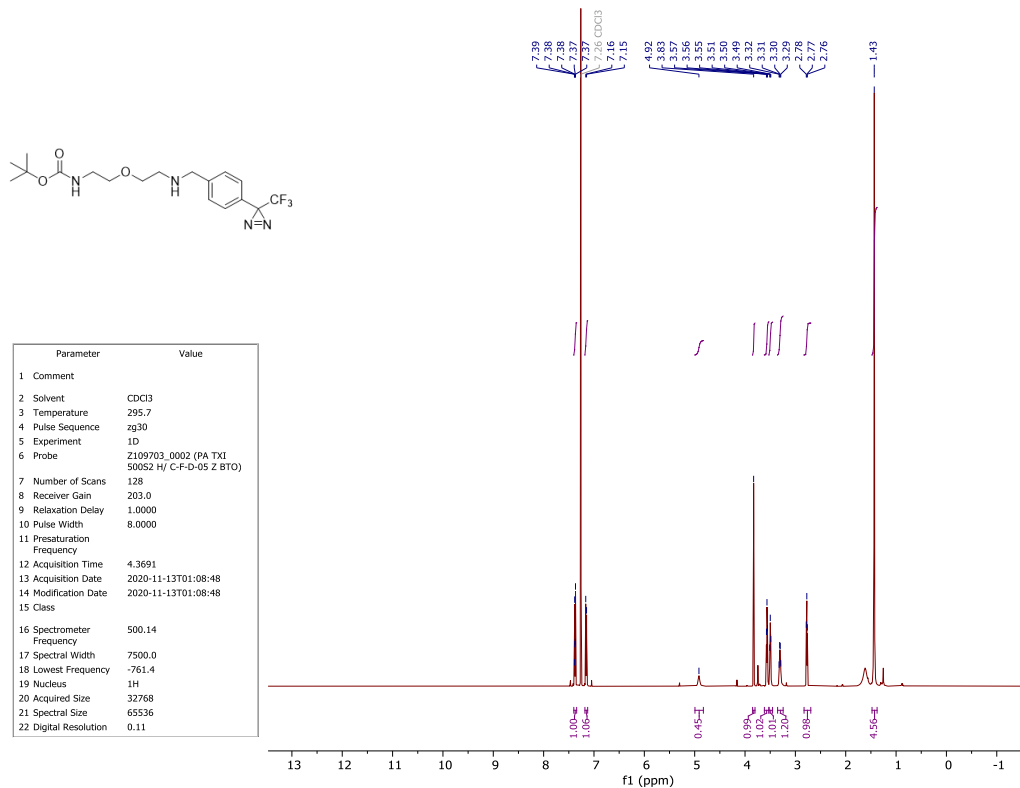
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 156.1, 142.1 (from HMBC), 128.7, 127.9, 126.7, 122.3 (d, *J* = 274.8 Hz), 79.5 (from HMBC), 70.4, 70.2, 53.4, 48.8, 40.5, 28.5, 28.4 (from HMBC, q, *J* = 46 Hz),

HRMS: *m/z* calculated for C<sub>18</sub>H<sub>25</sub>F<sub>3</sub>N<sub>4</sub>O<sub>3</sub>: 403.1952 (M+H); found: 403.1926.

# LC-HRMS

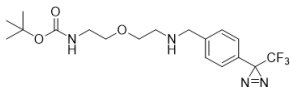


# <sup>1</sup>H NMR

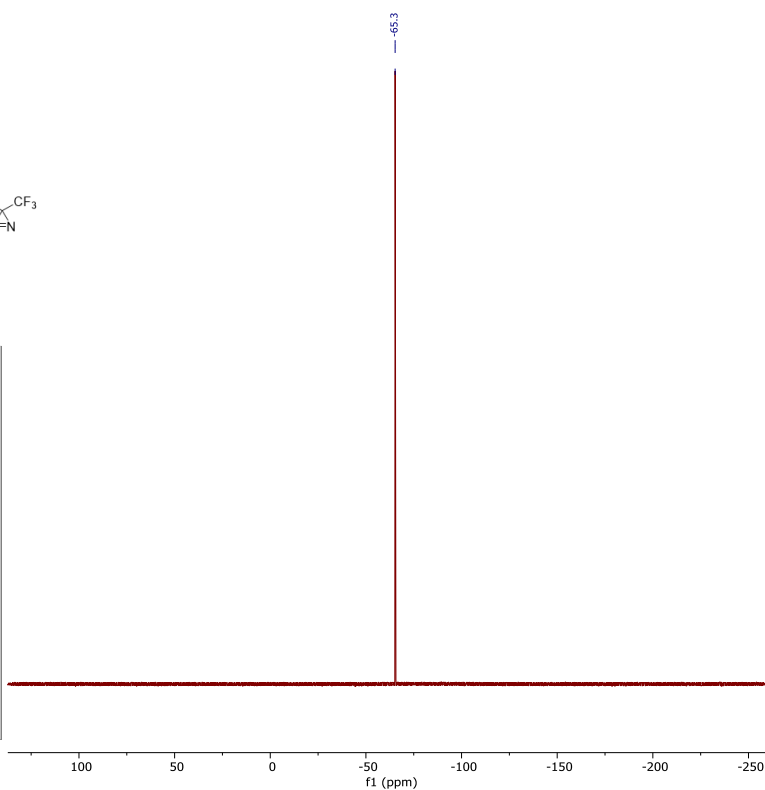




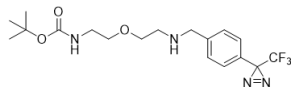
# <sup>19</sup>F NMR



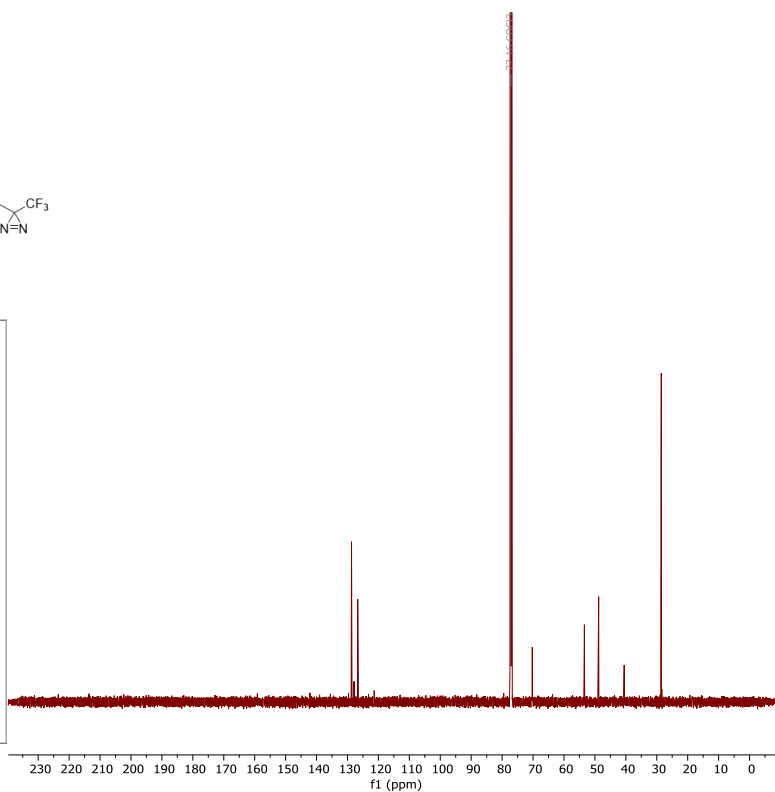
Parameter	Value
1 Comment	
2 Solvent	CDCl3
3 Temperature	295.6
4 Pulse Sequence	zg30
5 Experiment	1D
6 Probe	Z109703_0002 (PA TXI 50052 H/ C-F-D-05 Z BTO)
7 Number of Scans	64
8 Receiver Gain	128.0
9 Relaxation Delay	1.0000
10 Pulse Width	13.5000
11 Presaturation Frequency	
12 Acquisition Time	1.9999
13 Acquisition Date	2020-11-13T01:25:24
14 Modification Date	2020-11-13T01:25:24
15 Class	
16 Spectrometer Frequency	470.57
17 Spectral Width	187500.0
18 Lowest Frequency	-122928.9
19 Nucleus	<sup>19</sup> F
20 Acquired Size	374990
21 Spectral Size	524288
22 Digital Resolution	0.36



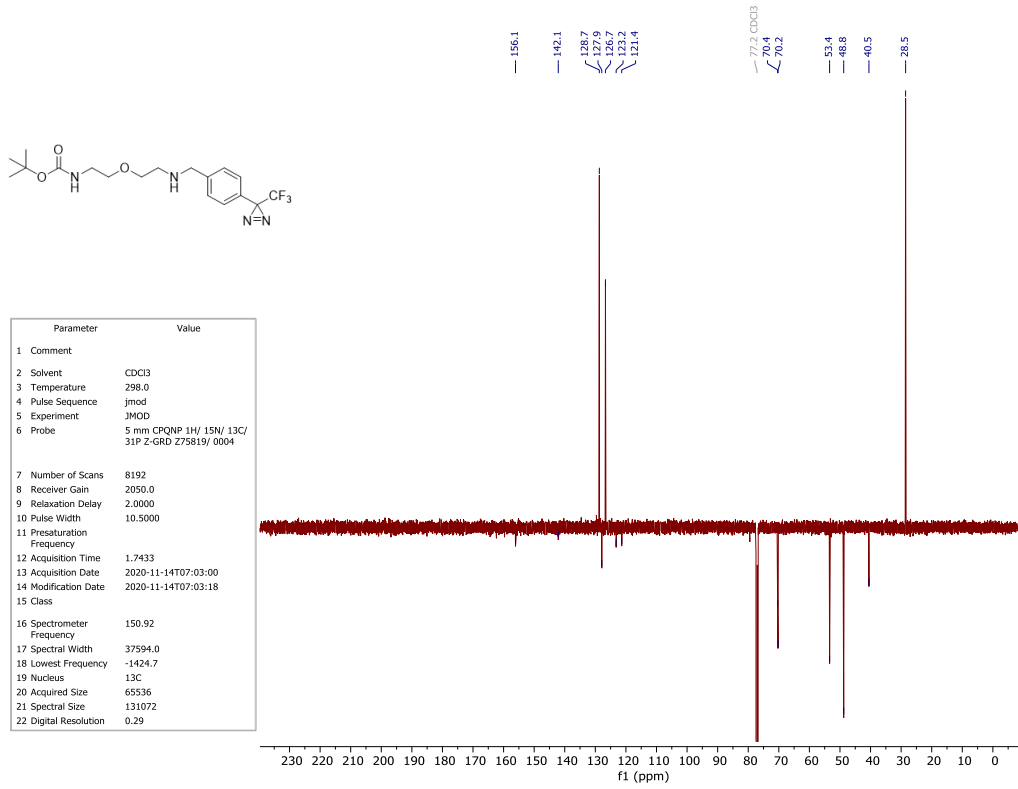
# <sup>13</sup>C NMR



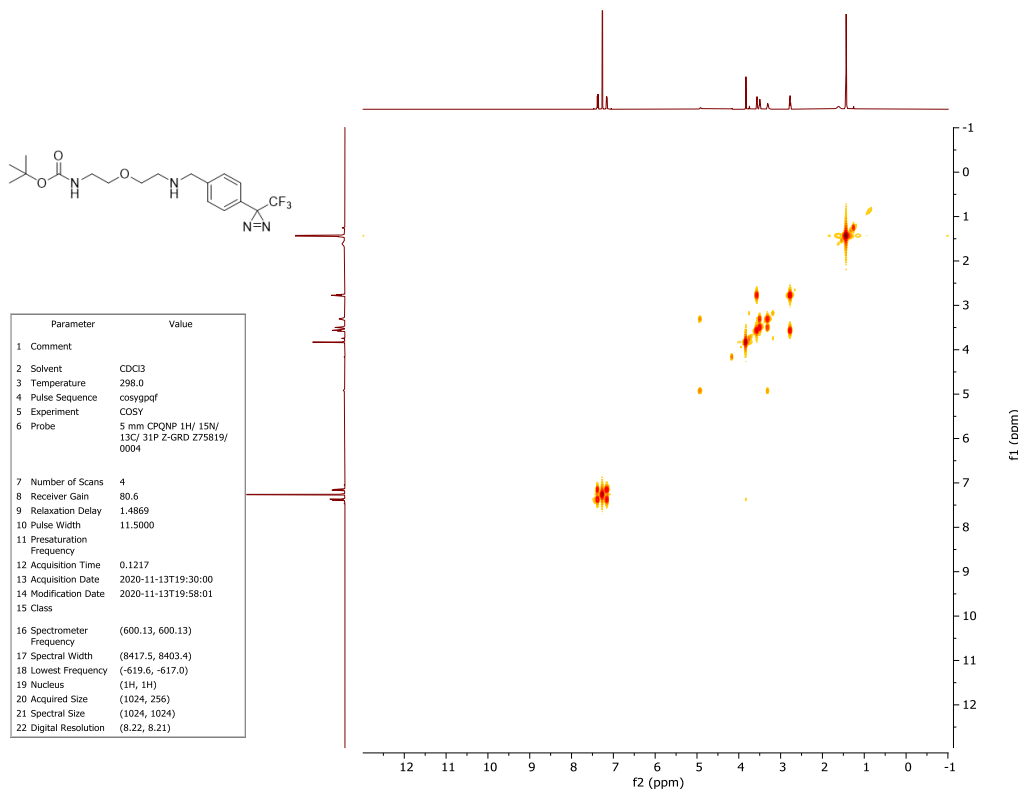
Parameter	Value
1 Comment	
2 Solvent	CDCl3
3 Temperature	298.0
4 Pulse Sequence	zgpg.agf
5 Experiment	1D
6 Probe	5 mm CPQNP 1H/ 15N/ 13C/ 31P Z-GRD Z75819/ 0004
7 Number of Scans	2048
8 Receiver Gain	2050.0
9 Relaxation Delay	2.0000
10 Pulse Width	10.5000
11 Presaturation Frequency	
12 Acquisition Time	1.7433
13 Acquisition Date	2020-11-13T19:28:00
14 Modification Date	2020-11-13T19:28:43
15 Class	
16 Spectrometer Frequency	150.92
17 Spectral Width	37594.0
18 Lowest Frequency	-1424.9
19 Nucleus	<sup>13</sup> C
20 Acquired Size	65536
21 Spectral Size	131072
22 Digital Resolution	0.29



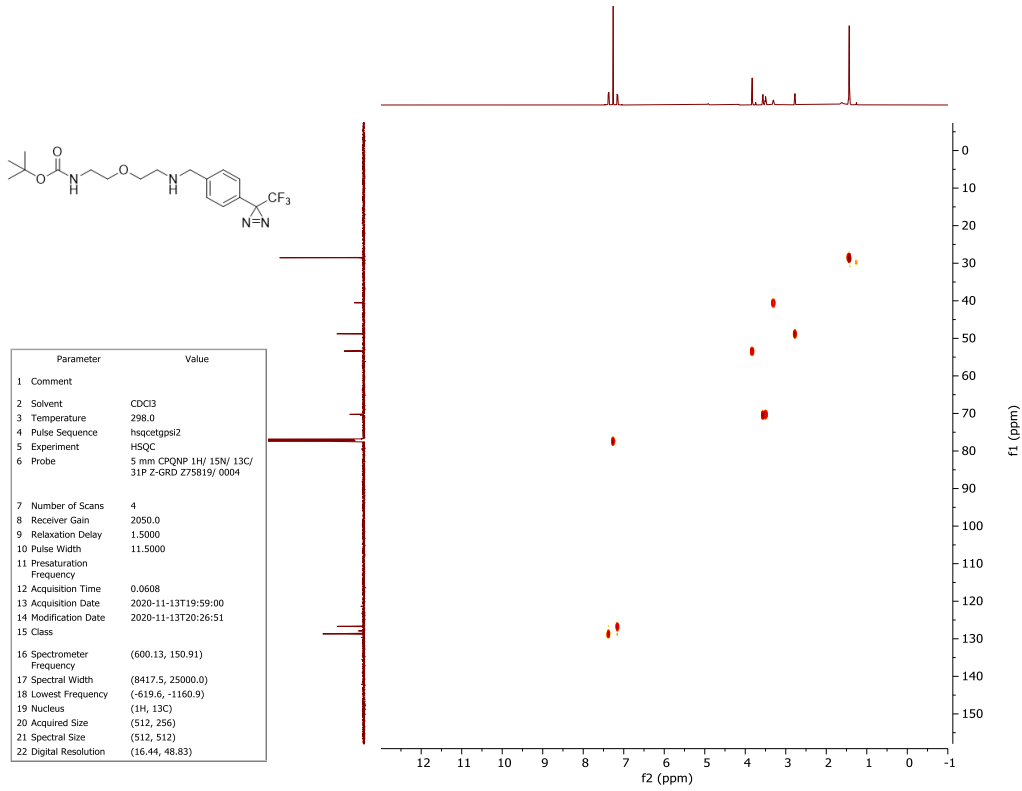
# <sup>13</sup>C-APT NMR



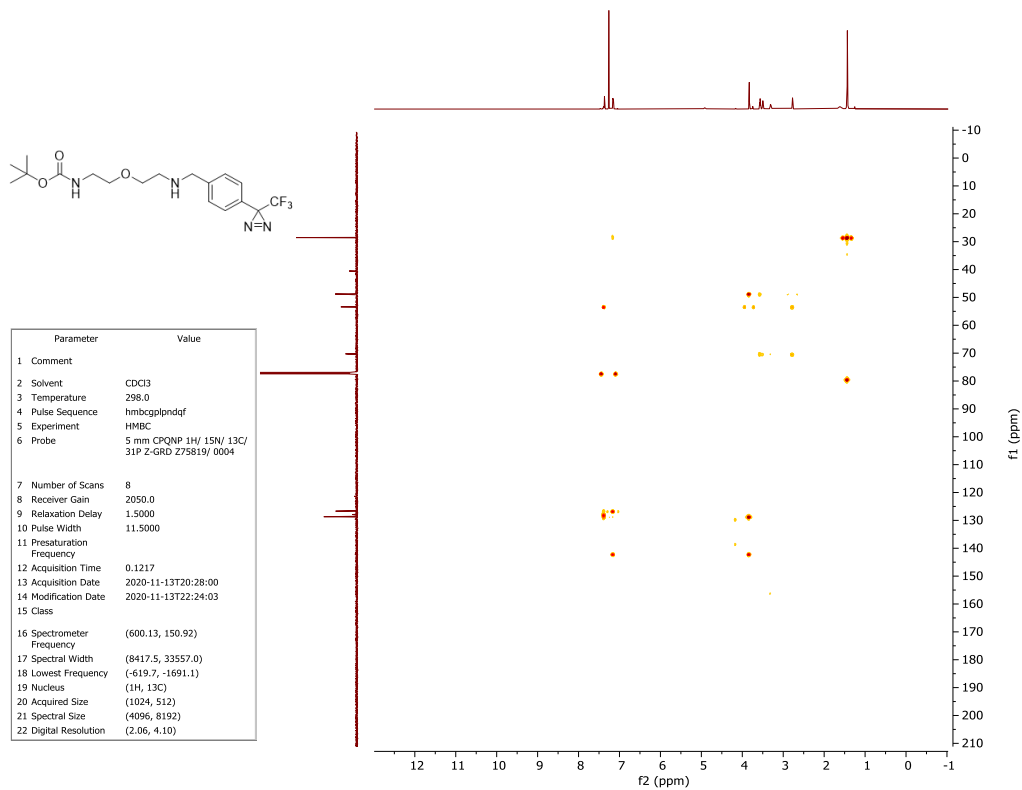
# COSY



# HSQC



# HMBC

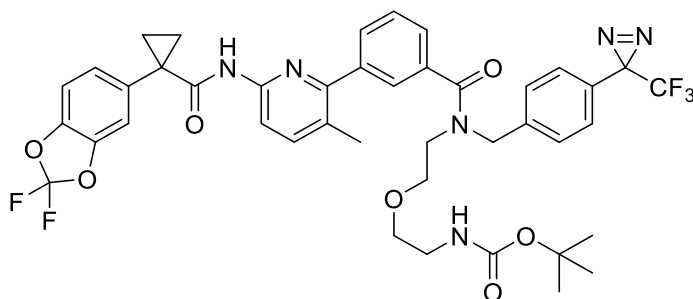


1.3. *tert*-butyl (2-(2-(3-(6-(1-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)cyclopropane-1-carboxamido)-3-methylpyridin-2-yl)-*N*-(4-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)benzyl)benzamido)ethoxy)ethyl)carbamate (**137**)

Chemical Formula:

Molecular Weight

Spectra provided: LC-HRMS, <sup>1</sup>H NMR, <sup>19</sup>F NMR, <sup>13</sup>C NMR, COSY, HSQC, HMBC



Chemical Formula: C<sub>42</sub>H<sub>41</sub>F<sub>5</sub>N<sub>6</sub>O<sub>7</sub>

Molecular Weight: 836.8170

To a solution of lumacaftor (82 mg, 0.18 mmol), amide **136** (73 mg, 0.18 mmol, 1 equiv.), HATU (82 mg, 0.22 mmol, 1.2 equiv.), DMAP (2 mg, 0.02 mmol, 0.1 equiv), HOBT (27 mg, 0.18 mmol, 1 equiv) in DMF (2 mL), was added Et<sub>3</sub>N (95 μL, 0.56 mmol, 3 equiv.) and the reaction was stirred overnight at 40 °C. The reaction mixture was concentrated to remove DMF. The crude material was partitioned between EtOAc and sat. NaHCO<sub>3</sub>, organics were washed with brine, dried with Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. The crude material was loaded onto a silica cartridge (12 g, 10-100% EtOAc/Hex gradient) to give **137** (35 mg, 0.042 mmol, 23 % isolated yield) as a white residue. Compound exhibited rotamers in NMR analysis.

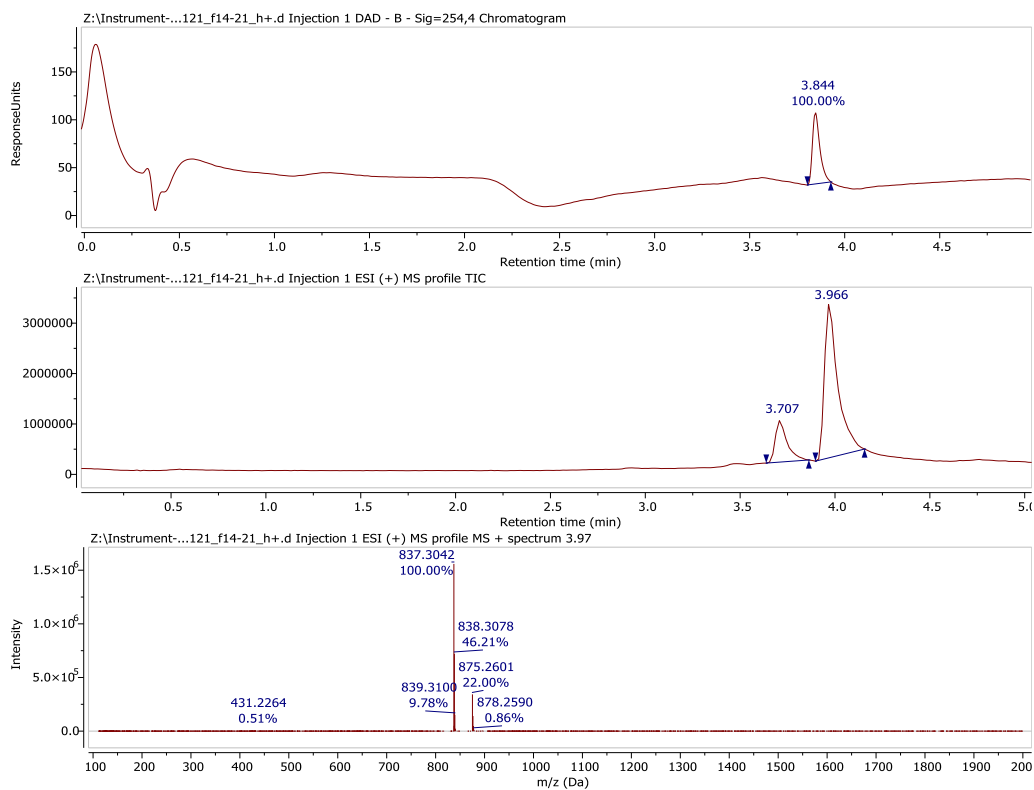
<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 8.08 (d, *J* = 8.3 Hz, 1H), 7.67 (s, 1H), 7.57 (s, 1H), 7.47 (d, *J* = 15.0 Hz, 2H), 7.38 (s, 2H), 7.22 (d, *J* = 8.1 Hz, 1H), 7.18 (d, *J* = 7.6 Hz, 4H), 7.06 (d, *J* = 8.1 Hz, 1H), 4.79 (d, *J* = 43.0 Hz, 2H), 4.66 (s, 1H), 3.66 (d, *J* = 51.8 Hz, 2H), 3.51 – 3.34 (m, 2H), 3.24 (d, *J* = 54.1 Hz, 2H), 2.20 (d, *J* = 59.4 Hz, 3H), 1.74 (q, *J* = 3.8 Hz, 2H), 1.71 (s, OH), 1.42 (s, 9H), 1.28 – 1.22 (m, OH), 1.16 (q, *J* = 3.8 Hz, 2H).

<sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>) δ -49.6, -65.2.

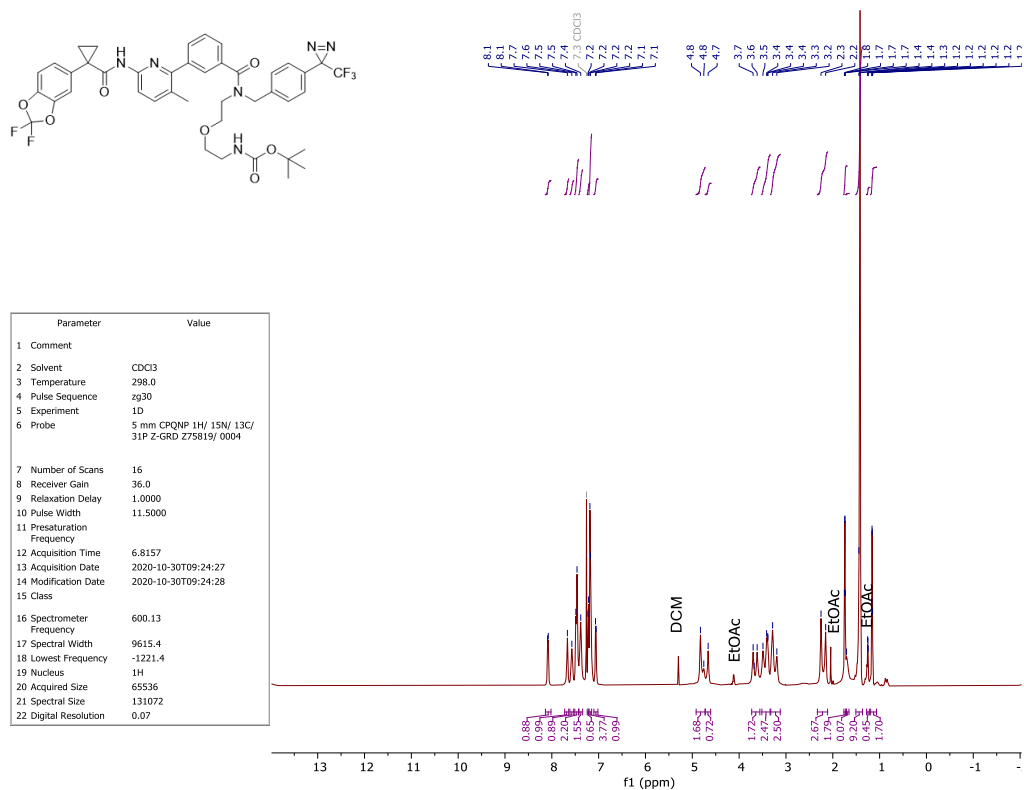
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 172.3, 171.9, 156.0, 155.4, 149.0, 144.2, 143.7, 141.2, 140.3, 139.5, 139.0, 136.2, 135.9, 135.0, 133.5, 131.8, 130.6, 130.3, 130.1, 128.5, 127.8, 127.6, 127.3, 127.1, 127.0, 126.8, 126.3, 123.1, 121.3, 113.1, 112.5, 110.3, 79.5, 70.3, 69.1, 68.7, 60.6, 53.6, 48.5, 48.2, 48.1, 44.8, 40.5, 40.4, 31.3, 29.8, 28.5, 28.3, 19.4, 17.4, 14.3.

HRMS: *m/z* calculated for C<sub>42</sub>H<sub>41</sub>F<sub>5</sub>N<sub>6</sub>O<sub>7</sub>: 837.3030 (M+H); found: 837.3042

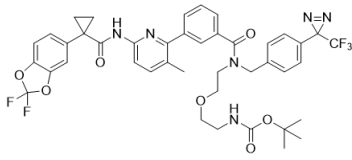
# LC-HRMS



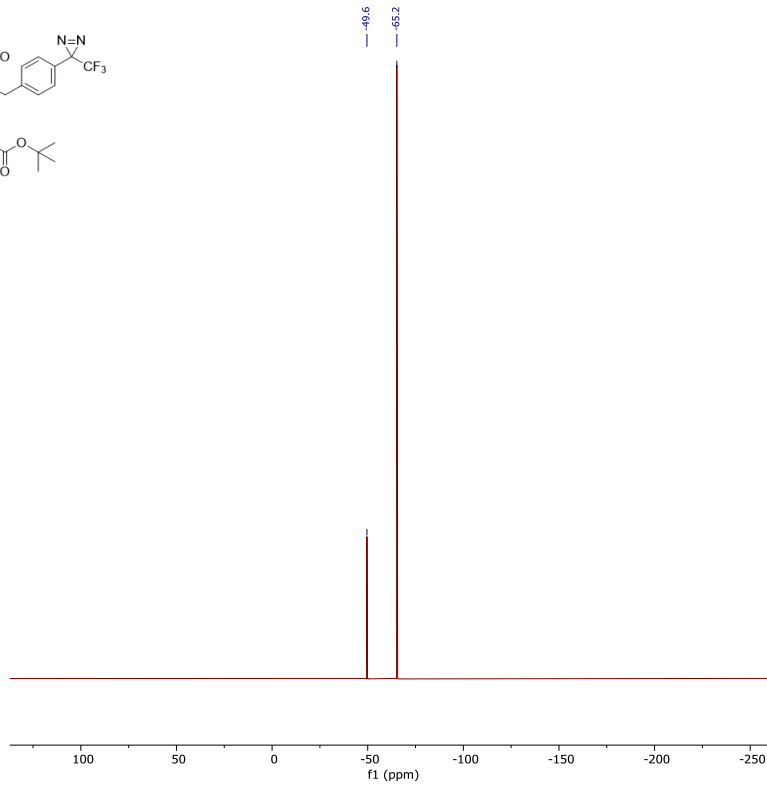
# <sup>1</sup>H NMR



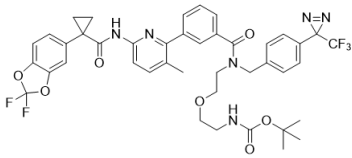
# <sup>19</sup>F NMR



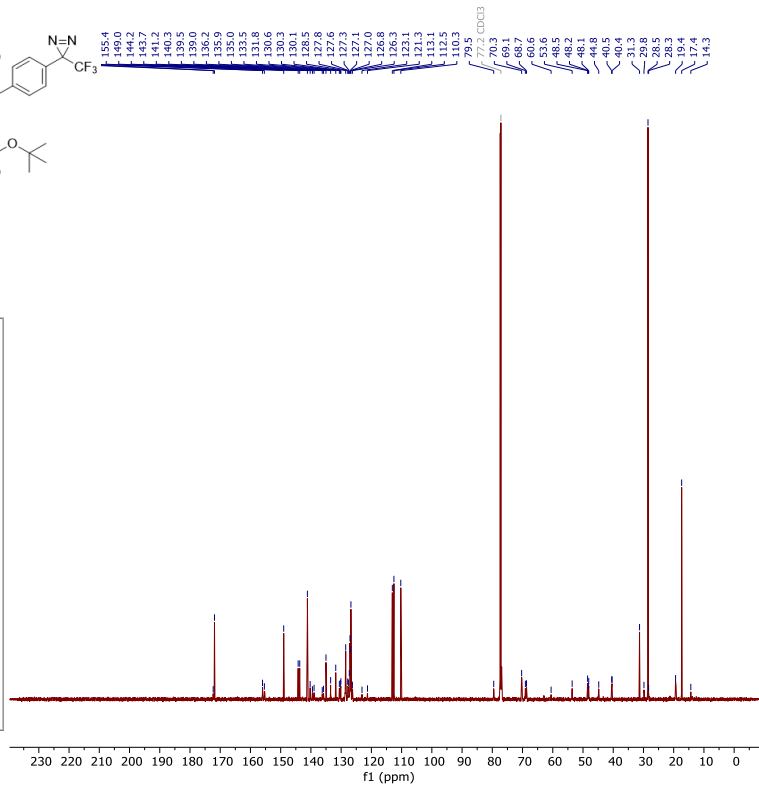
Parameter	Value
1 Comment	
2 Solvent	CDCl3
3 Temperature	296.4
4 Pulse Sequence	zg30s
5 Experiment	1D
6 Probe	Z109703_0002 (PA TXI 50052 H/ C-F-D-05 Z BTO)
7 Number of Scans	64
8 Receiver Gain	128.0
9 Relaxation Delay	1.0000
10 Pulse Width	13.5000
11 Presaturation Frequency	
12 Acquisition Time	1.9999
13 Acquisition Date	2020-10-27T18:01:18
14 Modification Date	2020-10-27T18:01:18
15 Class	
16 Spectrometer Frequency	470.57
17 Spectral Width	187500.0
18 Lowest Frequency	-122928.9
19 Nucleus	<sup>19</sup> F
20 Acquired Size	374990
21 Spectral Size	524288
22 Digital Resolution	0.36



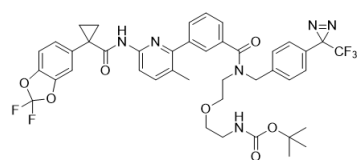
# <sup>13</sup>C NMR



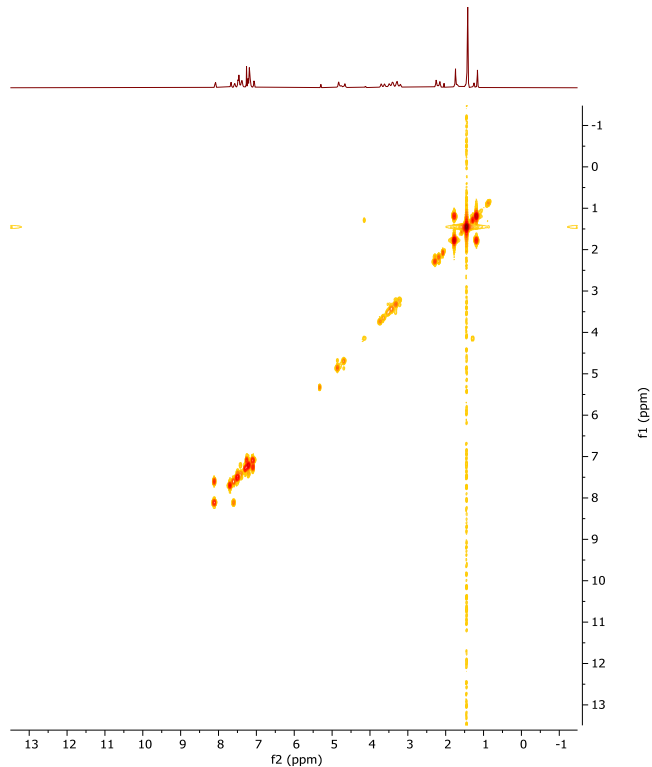
Parameter	Value
1 Comment	
2 Solvent	CDCl3
3 Temperature	298.0
4 Pulse Sequence	zpgp.ar1
5 Experiment	1D
6 Probe	5 mm CPQNP 1H/ 15N/ 13C/ 31P Z-GRD Z75819/ 0004
7 Number of Scans	2048
8 Receiver Gain	2050.0
9 Relaxation Delay	2.0000
10 Pulse Width	10.5000
11 Presaturation Frequency	
12 Acquisition Time	1.7433
13 Acquisition Date	2020-10-30T13:15:32
14 Modification Date	2020-10-30T13:15:33
15 Class	
16 Spectrometer Frequency	150.92
17 Spectral Width	37594.0
18 Lowest Frequency	-1426.4
19 Nucleus	<sup>13</sup> C
20 Acquired Size	65536
21 Spectral Size	131072
22 Digital Resolution	0.29



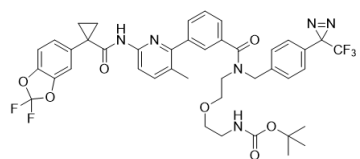
## COSY



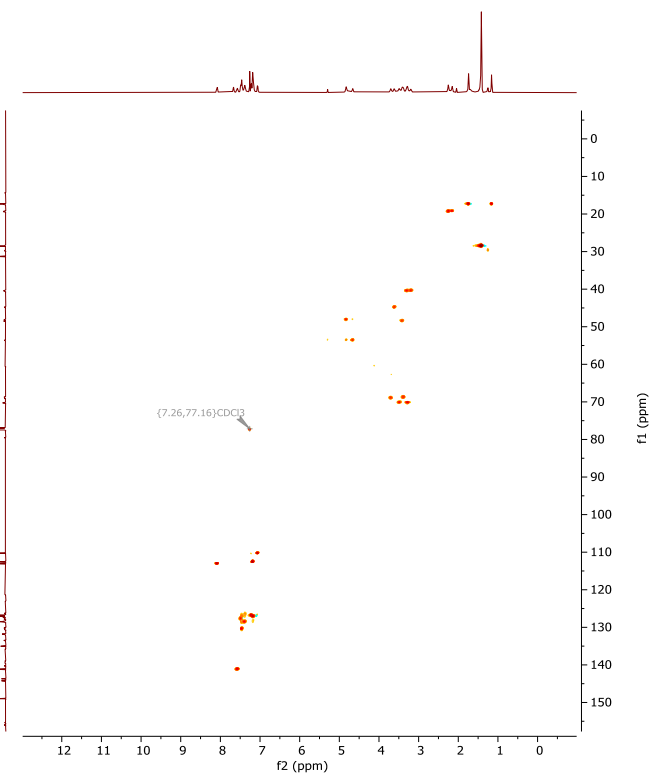
Parameter	Value
1 Comment	
2 Solvent	CDCl3
3 Temperature	295.3
4 Pulse Sequence	cosygpqf
5 Experiment	COSY
6 Probe	2109703_0002 (PA TXI 50652 H/ C-F-D-05.2 BTO)
7 Number of Scans	2
8 Receiver Gain	203.0
9 Relaxation Delay	1.2592
10 Pulse Width	8.0000
11 Presaturation Frequency	0.1365
12 Acquisition Time	
13 Acquisition Date	2020-10-28T10:10:17
14 Modification Date	2020-10-28T10:22:22
15 Class	
16 Spectrometer Frequency	(500.14, 500.14)
17 Spectral Width	(7500.0, 7496.3)
18 Lowest Frequency	(-749.2, -747.3)
19 Nucleus	(1H, 1H)
20 Acquired Size	(1024, 256)
21 Spectral Size	(4096, 4096)
22 Digital Resolution	(1.83, 1.83)



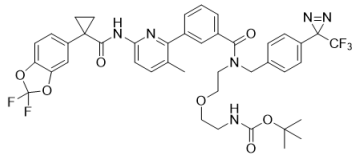
## HSQC



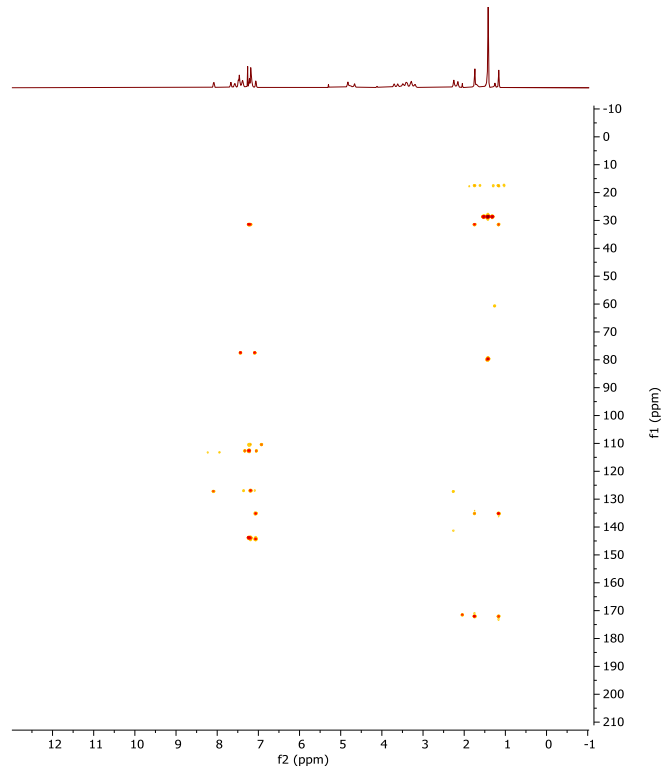
Parameter	Value
1 Comment	
2 Solvent	CDCl3
3 Temperature	298.0
4 Pulse Sequence	hsqcetps2
5 Experiment	HSQC
6 Probe	5 mm CPQNP 1H/ 15N/ 13C/ 31P Z-GRD Z75819/ 0004
7 Number of Scans	4
8 Receiver Gain	2050.0
9 Relaxation Delay	1.5000
10 Pulse Width	11.5000
11 Presaturation Frequency	
12 Acquisition Time	0.0608
13 Acquisition Date	2020-10-30T13:17:29
14 Modification Date	2020-10-30T13:44:23
15 Class	
16 Spectrometer Frequency	(600.13, 150.91)
17 Spectral Width	(8417.5, 25000.0)
18 Lowest Frequency	(-623.9, -1198.1)
19 Nucleus	(1H, 13C)
20 Acquired Size	(512, 256)
21 Spectral Size	(2048, 4096)
22 Digital Resolution	(4.11, 6.10)



# HMBC



Parameter	Value
1 Comment	
2 Solvent	CDCl3
3 Temperature	298.0
4 Pulse Sequence	hmbcgp1pndqf
5 Experiment	HMBC
6 Probe	5 mm CPQNP 1H/ 13N/ 13C/ 31P 2-GRD Z75819/0004
7 Number of Scans	4
8 Receiver Gain	2050.0
9 Relaxation Delay	1.5000
10 Pulse Width	11.5000
11 Presaturation Frequency	
12 Acquisition Time	0.1217
13 Acquisition Date	2020-10-30T13:46:19
14 Modification Date	2020-10-30T14:43:55
15 Class	
16 Spectrometer Frequency	(600.13, 150.92)
17 Spectral Width	(8417.5, 33557.0)
18 Lowest Frequency	(-608.0, -1713.2)
19 Nucleus	(1H, 13C)
20 Acquired Size	(1024, 512)
21 Spectral Size	(1024, 1024)
22 Digital Resolution	(0.22, 32.77)



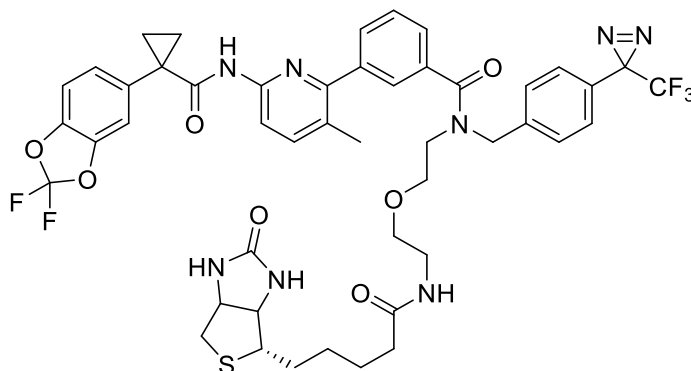


1.4. 3-(6-(1-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)cyclopropane-1-carboxamido)-3-methylpyridin-2-yl)-N-(2-(2-(5-((4S)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanamido)ethoxy)ethyl)-N-(4-(3-(trifluoromethyl)-3H-diazirin-3-yl)benzyl)benzamide (**9**)

Chemical Formula:

Molecular Weight

Spectra provided: LC-HRMS, <sup>1</sup>H NMR, <sup>19</sup>F NMR, <sup>13</sup>C NMR, <sup>13</sup>C-APT NMR, COSY, HSQC, HMBC



Chemical Formula: C<sub>47</sub>H<sub>47</sub>F<sub>5</sub>N<sub>8</sub>O<sub>7</sub>S

Molecular Weight: 962.9940

**137** (2mg, 0.002 mmol) was dissolved in DCM (1 mL) and TFA (1 mL) was added. The solution was stirred 2 hours, then blown dry and concentrated *in vacuo* to generate amine **138** which was used immediately without further purification. To amine 128 was added biotin-NHS ester **139** (6 mg, 0.018 mmol, 8.5 equiv), DMF (1 mL), and Et<sub>3</sub>N (200 μL) and the solution was stirred overnight at room temperature. The reaction mixture was concentrated *in vacuo*, partitioned between EtOAc (5 mL) and sat. bicarb (5 mL). The organic layer was washed with brine, dried with Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. Purification via silica cartridge (4g, 0-15% MeOH/DCM gradient) gave **9** (2 mg, 0.002 mmol, ~95% yield) as a film.

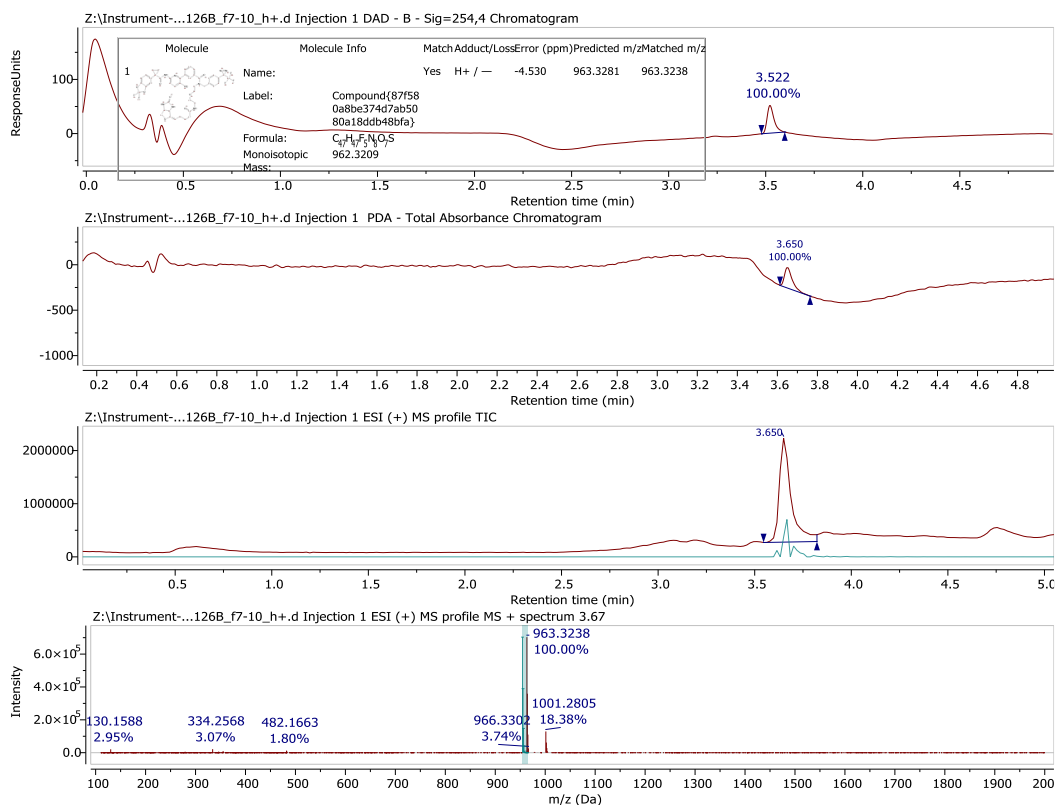
<sup>1</sup>H NMR (601 MHz, CDCl<sub>3</sub>) δ 8.08 (d, *J* = 8.5 Hz, 1H), 8.02 (s, 0H), 7.79 (s, 1H), 7.58 (s, 1H), 7.52 (s, 0H), 7.43 (d, *J* = 44.5 Hz, 4H), 7.23 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.20 (d, *J* = 1.7 Hz, 3H), 7.18 (s, 4H), 7.07 (d, *J* = 8.1 Hz, 1H), 6.51 (s, 1H), 6.07 (d, *J* = 43.7 Hz, 0H), 5.85 (d, *J* = 30.3 Hz, 1H), 5.02 (s, 1H), 4.79 (s, 1H), 4.63 (s, 1H), 4.45 – 4.40 (m, 1H), 4.23 (s, 1H), 3.70 (d, *J* = 21.3 Hz, 1H), 3.61 (d, *J* = 48.2 Hz, 3H), 3.37 (d, *J* = 51.0 Hz, 4H), 3.08 (s, 1H), 2.95 (s, 1H), 2.88 (d, *J* = 0.6 Hz, 1H), 2.87 – 2.81 (m, 1H), 2.67 (d, *J* = 12.9 Hz, 1H), 2.25 (s, 1H), 2.18 – 2.06 (m, 3H), 1.74 (q, *J* = 3.9 Hz, 2H), 1.71 – 1.54 (m, 10H), 1.36 (s, 2H), 1.16 (q, *J* = 4.0 Hz, 2H).

<sup>19</sup>F NMR (565 MHz, CDCl<sub>3</sub>) δ -48.1, -63.7.

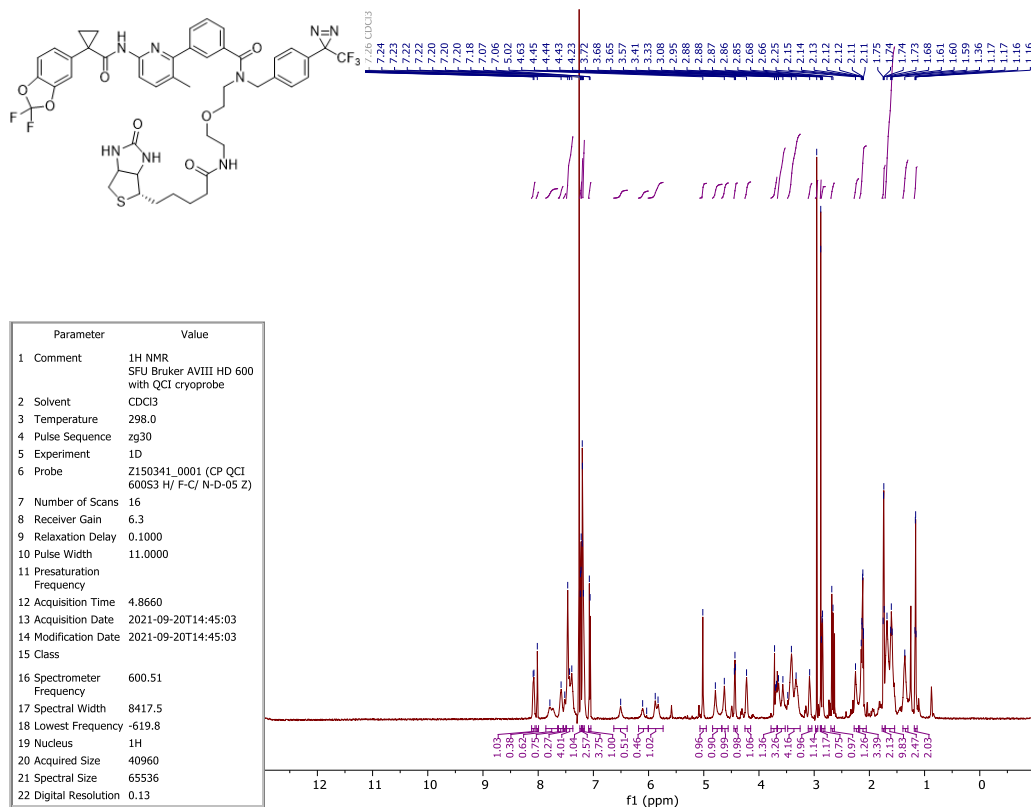
<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 172.4, 171.9, 168.6, 163.4, 162.6, 148.9, 144.1, 143.6, 135.0, 131.7, 127.0, 126.7, 122.1, 113.2, 112.4, 110.2, 63.7, 61.8, 61.7, 60.1, 60.0, 55.3, 55.3, 40.5, 36.5, 35.6, 33.9, 31.9, 31.6, 31.4, 31.2, 30.7, 29.7, 29.7, 28.3, 28.0, 27.9, 27.9, 25.6, 25.4, 24.9, 24.5, 17.2.

HRMS: *m/z* calculated for C<sub>47</sub>H<sub>47</sub>F<sub>5</sub>N<sub>8</sub>O<sub>7</sub>S: 963.3281 (M+H); found: 3238

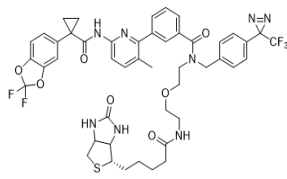
# LC-HRMS:



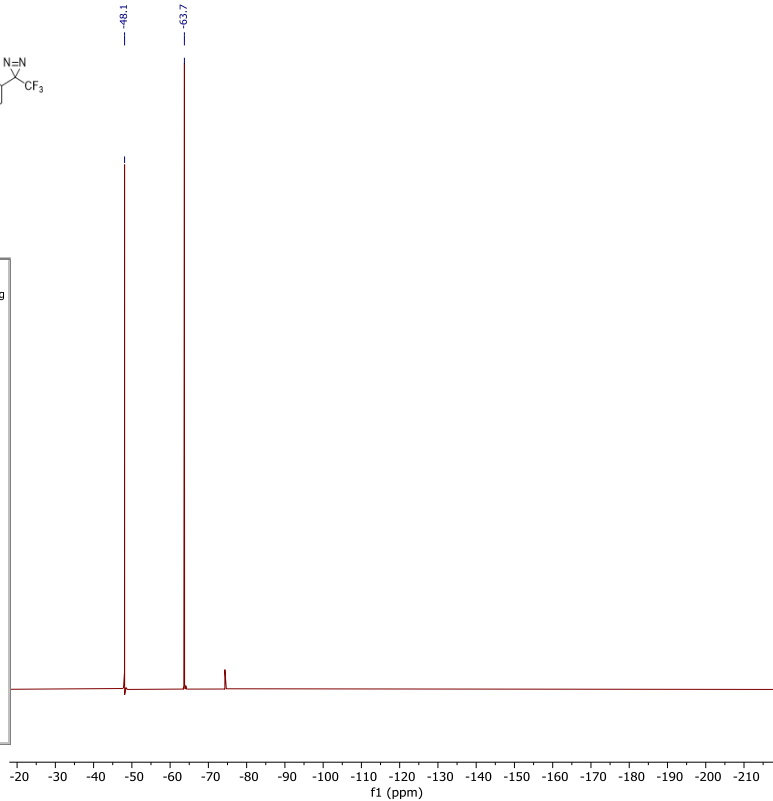
# <sup>1</sup>H NMR



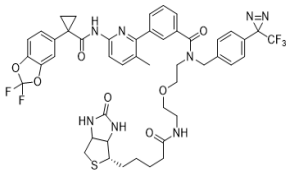
# <sup>19</sup>F NMR



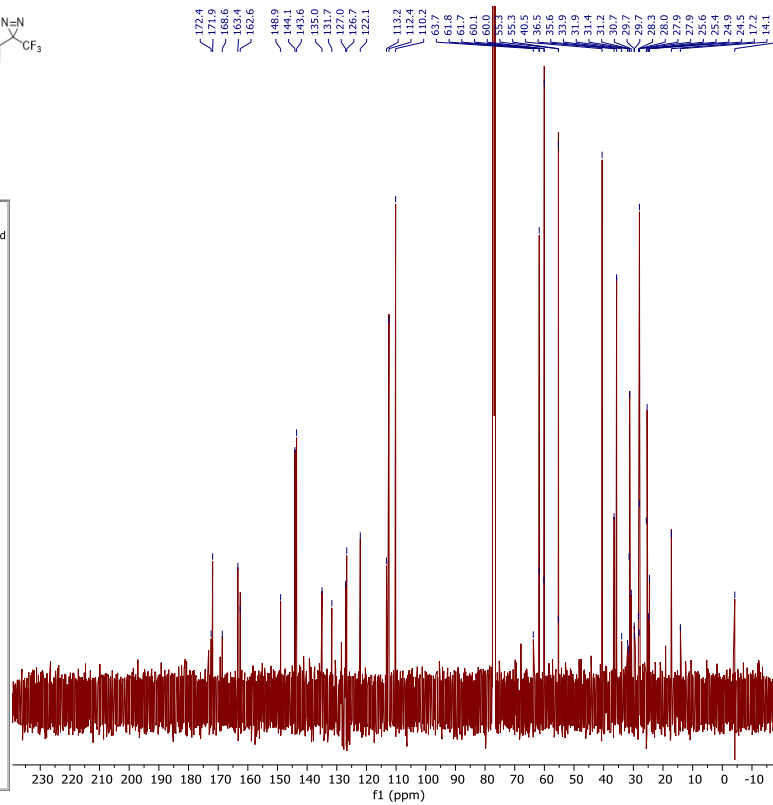
Parameter	Value
1 Comment	<sup>19</sup> F without 1H decoupling SFU AV III HD with 5mm QCI F cryoprobe
2 Solvent	CDCl <sub>3</sub>
3 Temperature	298.0
4 Pulse Sequence	zg30
5 Experiment	1D
6 Probe	Z150341_0001 (CP QCI 600S3 H/ F-C/ N-D-05 Z)
7 Number of Scans	64
8 Receiver Gain	94.8
9 Relaxation Delay	2.0000
10 Pulse Width	12.0000
11 Presaturation Frequency	
12 Acquisition Time	0.5767
13 Acquisition Date	2021-09-20T15:13:09
14 Modification Date	2021-09-20T15:13:09
15 Class	
16 Spectrometer Frequency	564.98
17 Spectral Width	113636.4
18 Lowest Frequency	-123789.9
19 Nucleus	<sup>19</sup> F
20 Acquired Size	65536
21 Spectral Size	131072
22 Digital Resolution	0.87



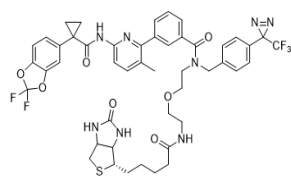
# <sup>13</sup>C NMR



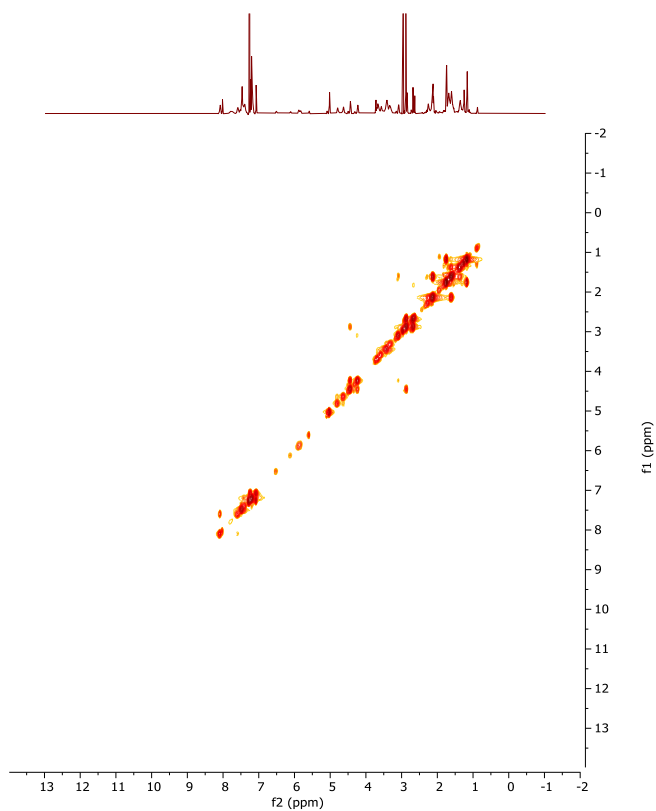
Parameter	Value
1 Comment	<sup>13</sup> C with both power gated 1H decoupling and <sup>19</sup> F inverse gated decoupling both 1H and <sup>19</sup> F channel have 3 db lower than regular one channel decoupling Keep Acquisition Time shorter than 1 second SFU AV III HD with 5mm QCI F cryoprobe
2 Solvent	CDCl <sub>3</sub>
3 Temperature	298.0
4 Pulse Sequence	zpgg30.f2f3dec.ey
5 Experiment	1D
6 Probe	Z150341_0001 (CP QCI 600S3 H/ F-C/ N-D-05 Z)
7 Number of Scans	4096
8 Receiver Gain	1620.0
9 Relaxation Delay	1.0000
10 Pulse Width	11.5000
11 Presaturation Frequency	
12 Acquisition Time	0.8389
13 Acquisition Date	2021-09-20T18:07:05
14 Modification Date	2021-09-20T18:07:05
15 Class	
16 Spectrometer Frequency	151.01
17 Spectral Width	39062.5
18 Lowest Frequency	-2921.5
19 Nucleus	<sup>13</sup> C
20 Acquired Size	32768
21 Spectral Size	65536
22 Digital Resolution	0.60



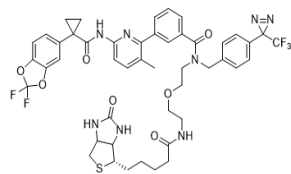
## COSY



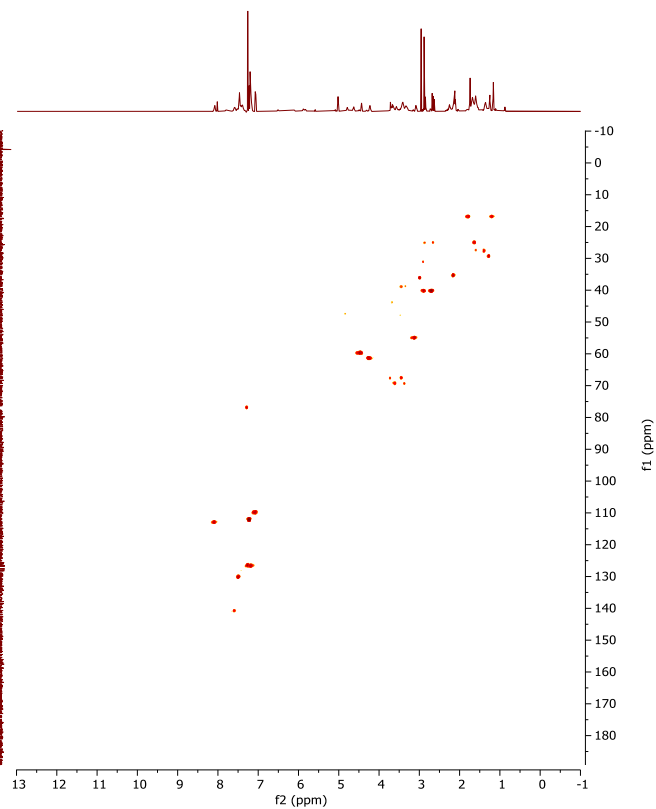
Parameter	Value
1 Comment	1H COSY 45 50% Non uniform sampling SFU AV III HD with 5mm QCIF cryoprobe
2 Solvent	CDCl3
3 Temperature	298.0
4 Pulse Sequence	cosyppppqf
5 Experiment	COSY
6 Probe	Z150341_0001 (CP QCI 600S3 H/ F-C/ N-D-05 Z)
7 Number of Scans	2
8 Receiver Gain	187.3
9 Relaxation Delay	1.2000
10 Pulse Width	11.0000
11 Presaturation Frequency	
12 Acquisition Time	0.1065
13 Acquisition Date	2021-09-20T18:07:36
14 Modification Date	2021-09-20T18:13:22
15 Class	
16 Spectrometer Frequency	(600.51, 600.51)
17 Spectral Width	(9615.4, 9615.4)
18 Lowest Frequency	(-1216.3, -1216.3)
19 Nucleus	(1H, 1H)
20 Acquired Size	(1024, 128)
21 Spectral Size	(2048, 2048)
22 Digital Resolution	(4.70, 4.70)



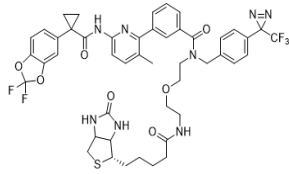
## HSQC



Parameter	Value
1 Comment	1H 2D Edited HSQC CH and CH3 up, CH2 down 50% Non uniform sampling SFU AV III HD with 5mm QCIF cryoprobe
2 Solvent	CDCl3
3 Temperature	298.0
4 Pulse Sequence	hsqcetdgpss
5 Experiment	HSQC-EDITED
6 Probe	Z150341_0001 (CP QCI 600S3 H/ F-C/ N-D-05 Z)
7 Number of Scans	8
8 Receiver Gain	187.3
9 Relaxation Delay	1.5000
10 Pulse Width	11.0000
11 Presaturation Frequency	
12 Acquisition Time	0.1217
13 Acquisition Date	2021-09-20T18:14:09
14 Modification Date	2021-09-20T18:41:57
15 Class	
16 Spectrometer Frequency	(600.51, 151.01)
17 Spectral Width	(8417.5, 30120.5)
18 Lowest Frequency	(-605.8, -1545.8)
19 Nucleus	(1H, 13C)
20 Acquired Size	(1024, 128)
21 Spectral Size	(2048, 4096)
22 Digital Resolution	(4.11, 7.35)



# HMBC



Parameter	Value
1 Comment	1H-13C HMBC 50% Non uniform sampling SFU AV III HD with 5mm QCI cryoprobe
2 Solvent	CDCl3
3 Temperature	298.0
4 Pulse Sequence	hmbcgp1ndqf
5 Experiment	HMBC
6 Probe	Z150341_0001 (CP QCI 600S3 H/ F-C/ N-D-05 Z)
7 Number of Scans	8
8 Receiver Gain	187.3
9 Relaxation Delay	1.5000
10 Pulse Width	11.0000
11 Presaturation Frequency	
12 Acquisition Time	0.1217
13 Acquisition Date	2021-09-20T18:42:45
14 Modification Date	2021-09-20T19:11:30
15 Class	
16 Spectrometer Frequency	(600.51, 151.01)
17 Spectral Width	(8417.5, 36231.9)
18 Lowest Frequency	(-605.7, -3016.3)
19 Nucleus	(1H, 13C)
20 Acquired Size	(1024, 128)
21 Spectral Size	(1024, 1024)
22 Digital Resolution	(8.22, 35.38)

