A Non-Racemic Synthesis of GK-GKRP Disruptor AMG-3969

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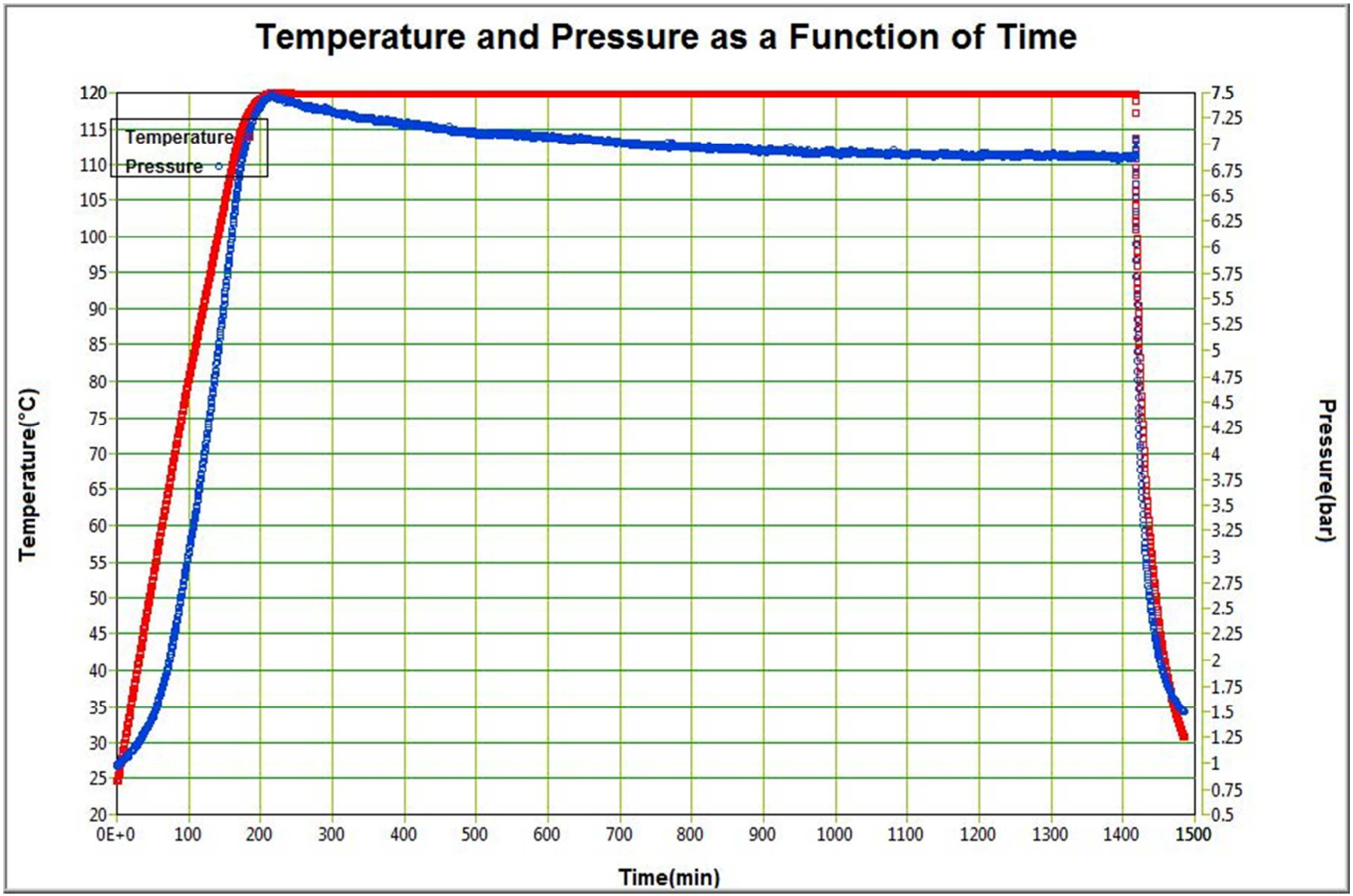
Supporting information

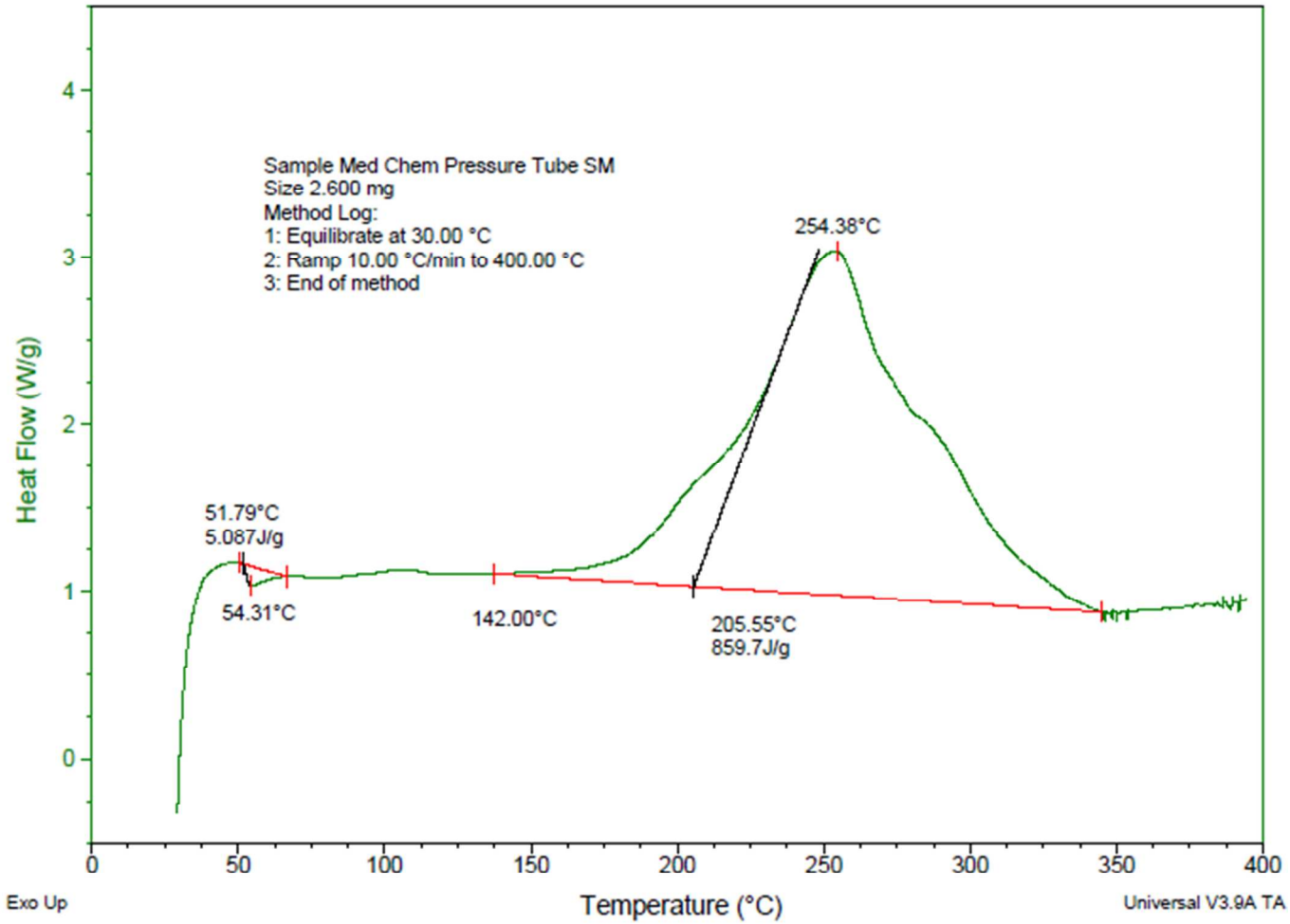
Analysis of conversion of compund 4 to compound 5



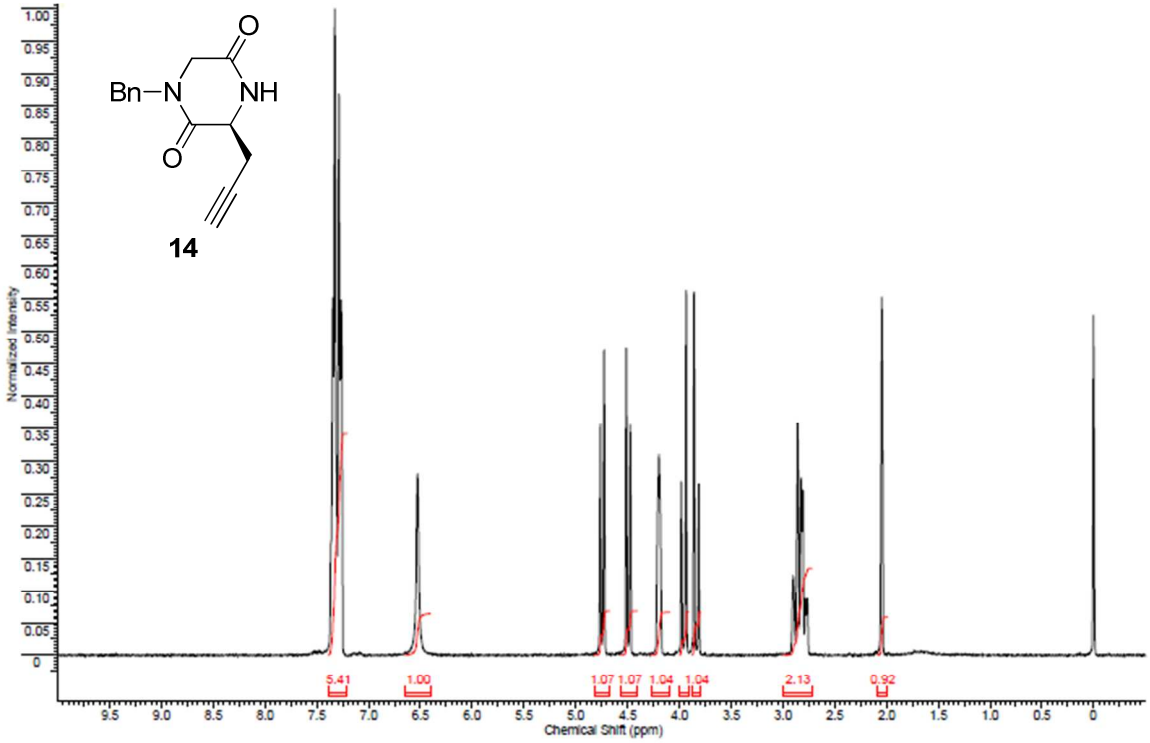
Sample: Med Chem Pressure Tube SM
Size: 2.6000 mg
Method: Ramp
Comment: Research Sample.

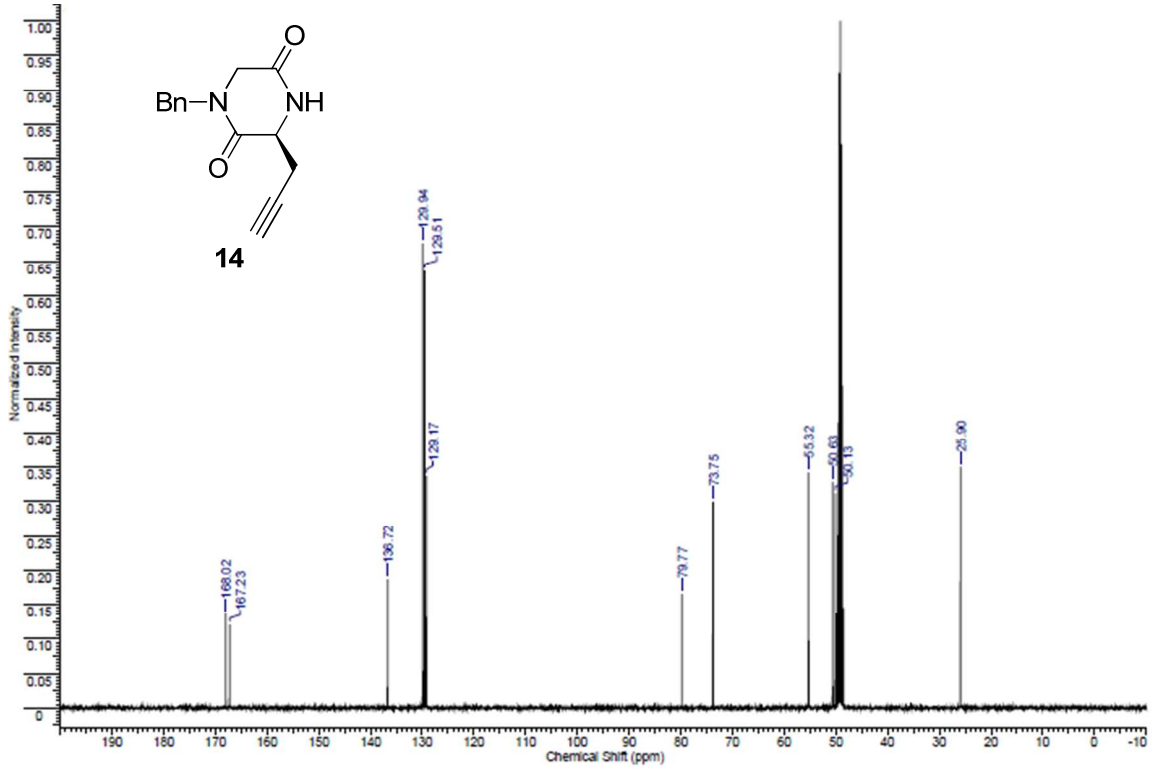
DSC

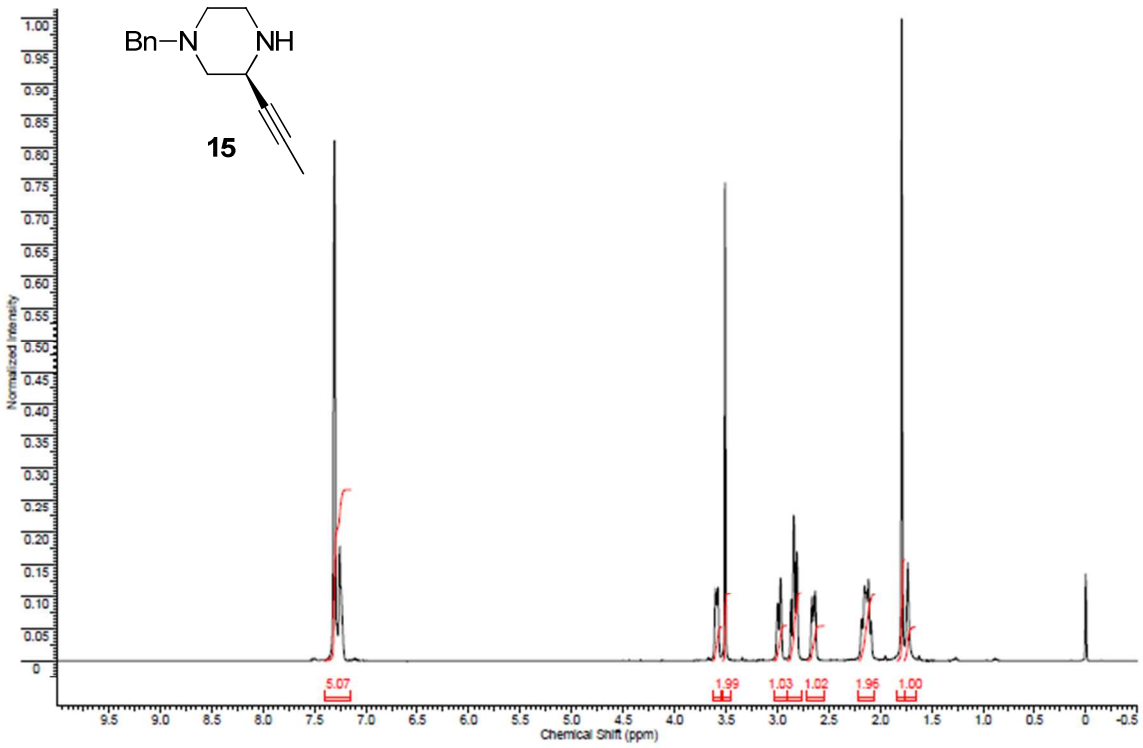
File: MED CHEM PRESSURE TUBE SM
Operator: SMS
Run Date: 14-Sep-11 09:41
Instrument: DSC Q1000 V9.9 Build 303

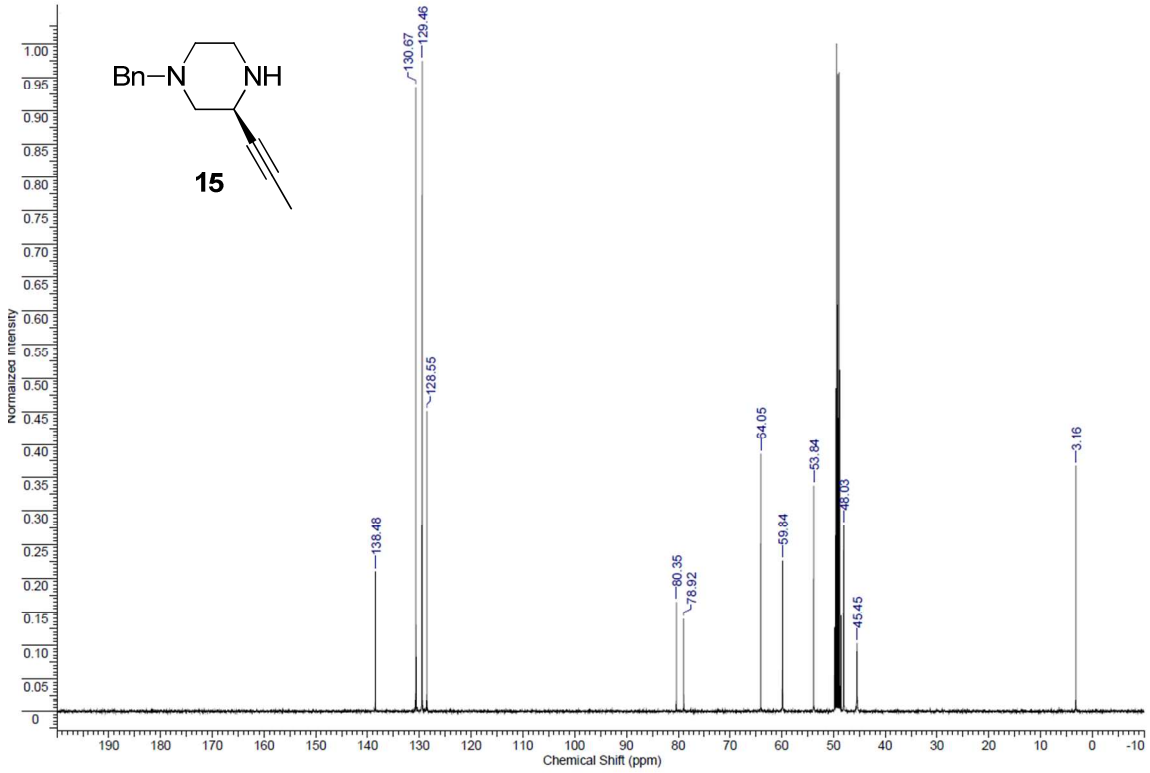


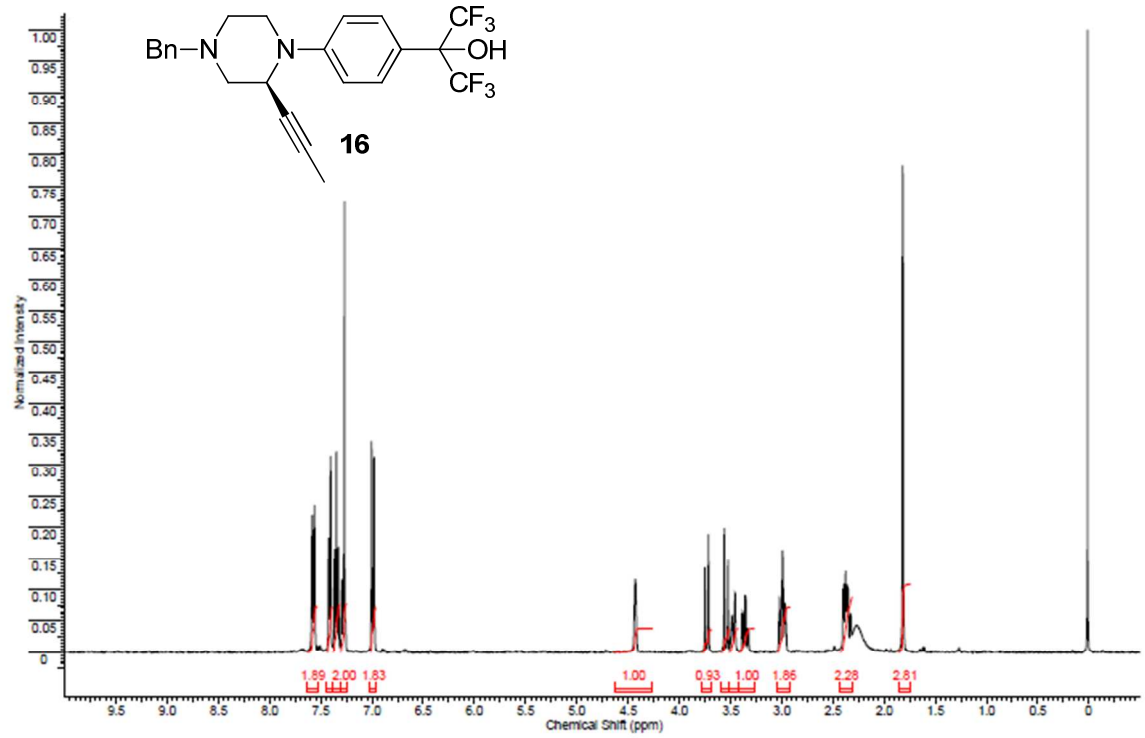
Proton and carbon NMR spectra

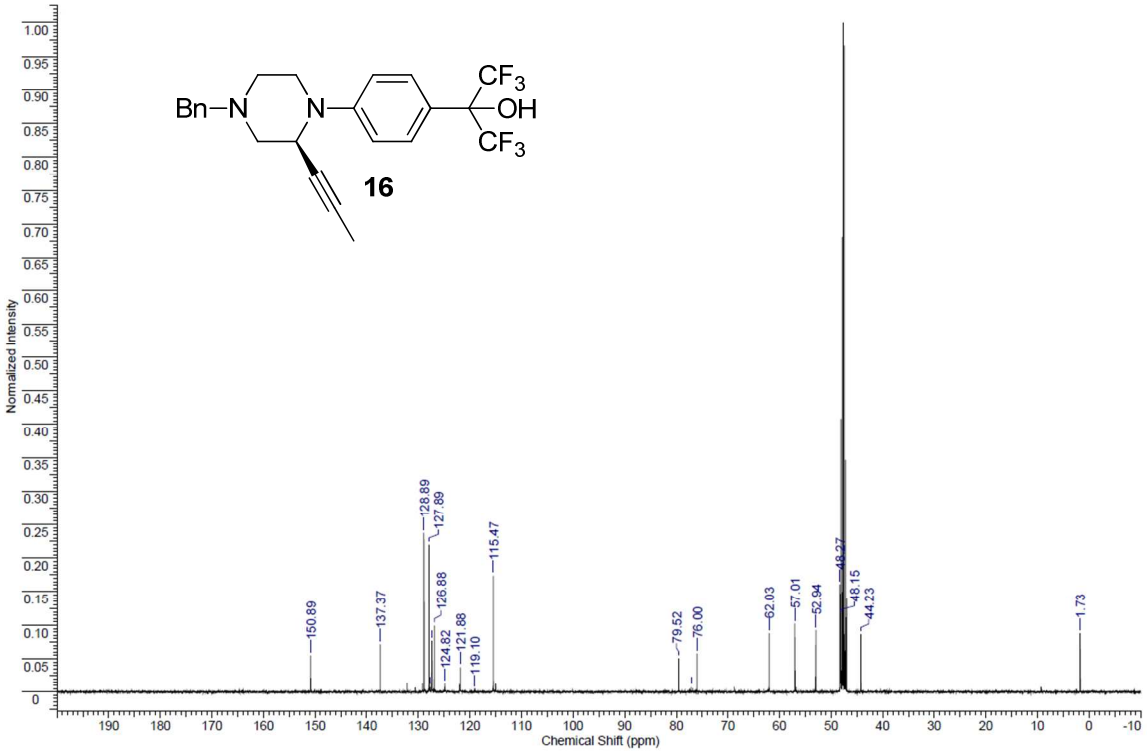


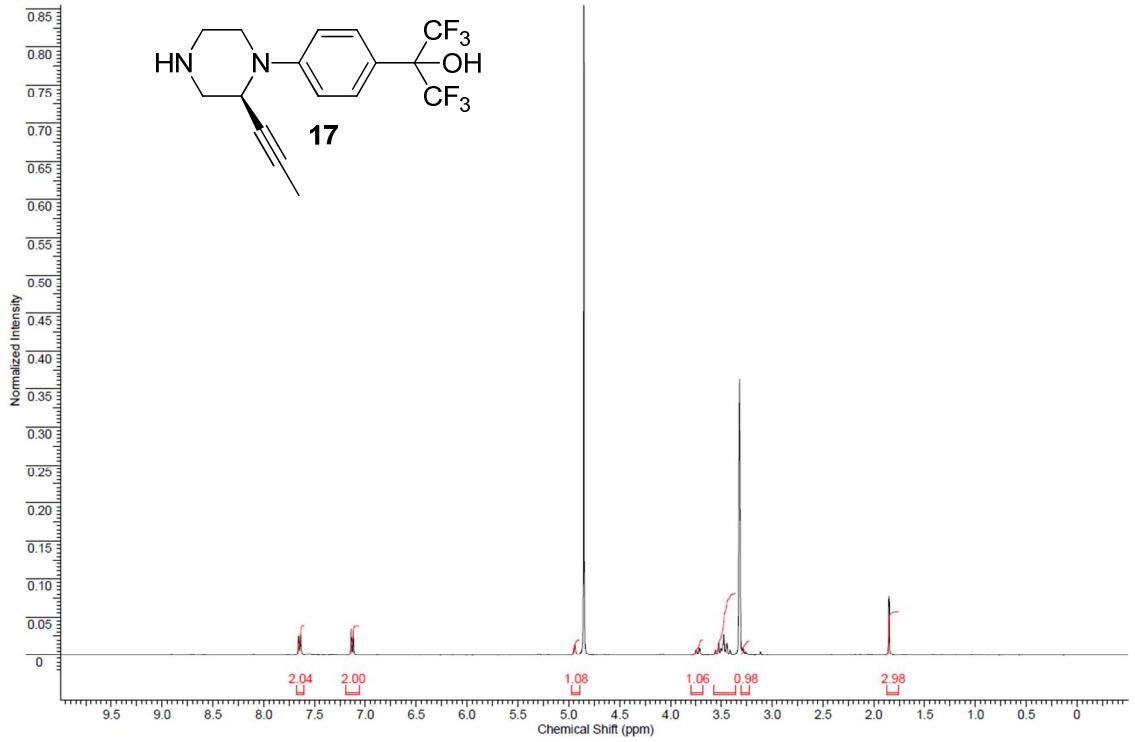

Bn–N
NH
O
O
14
Normalized Intensity
Chemical Shift (ppm)
168.02
167.23
136.72
129.94
129.51
129.17
79.77
73.75
55.32
50.63
50.13
25.90

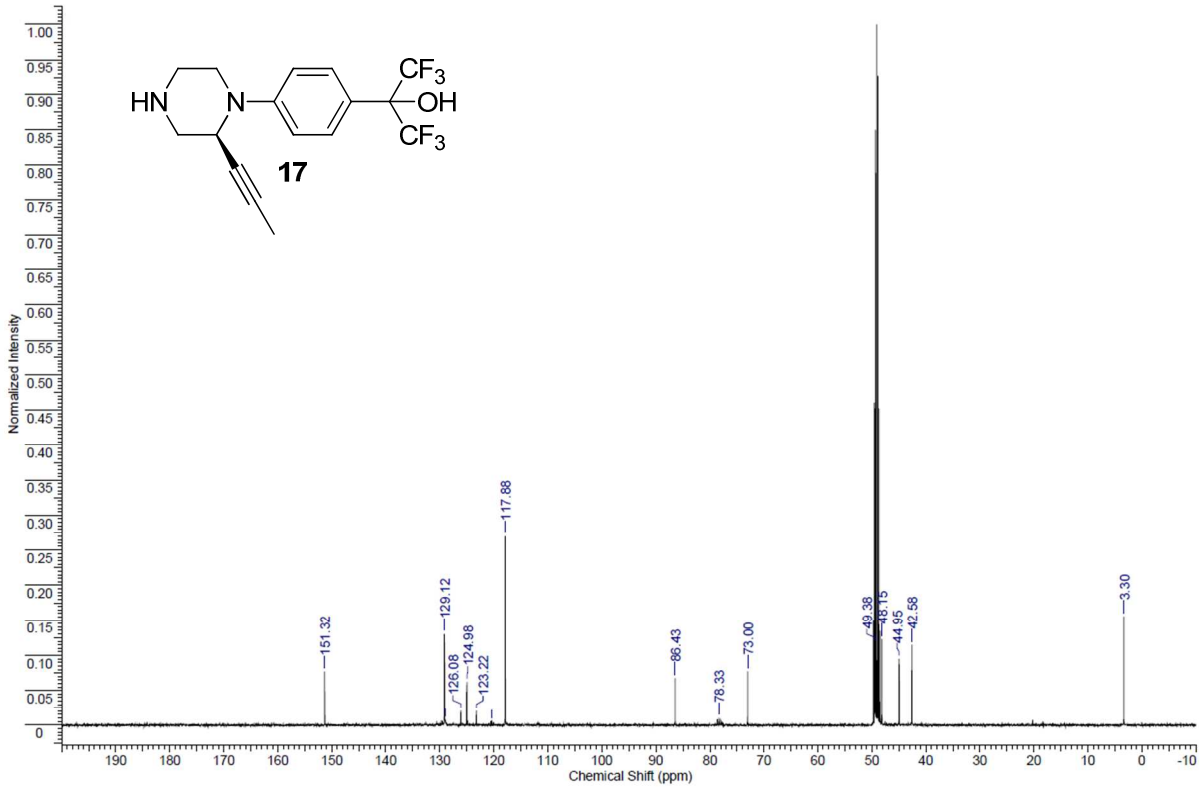

Bn—N
NH
15
Normalized Intensity
Chemical Shift (ppm)
5.07
1.99
1.03
1.02
1.96
1.00

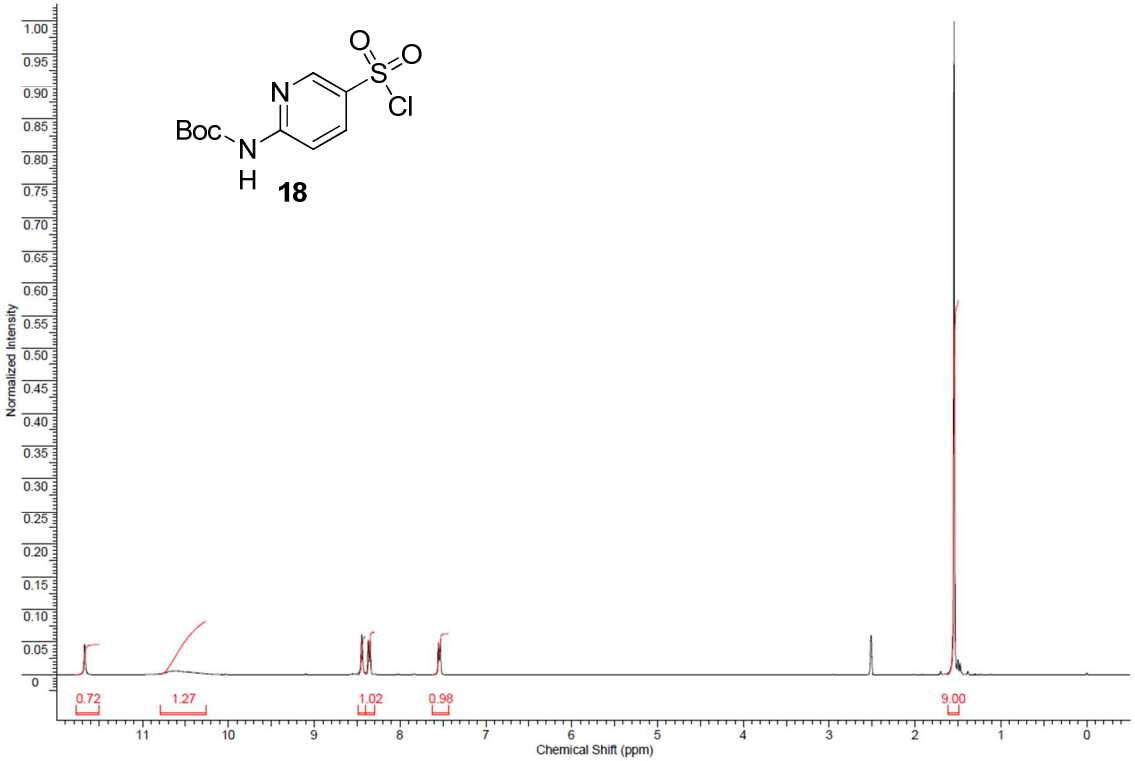

Bn–N
NH
15
Normalized Intensity
Chemical Shift (ppm)
138.48
130.67
129.46
128.55
80.35
78.92
54.05
59.84
53.84
48.03
45.45
3.16

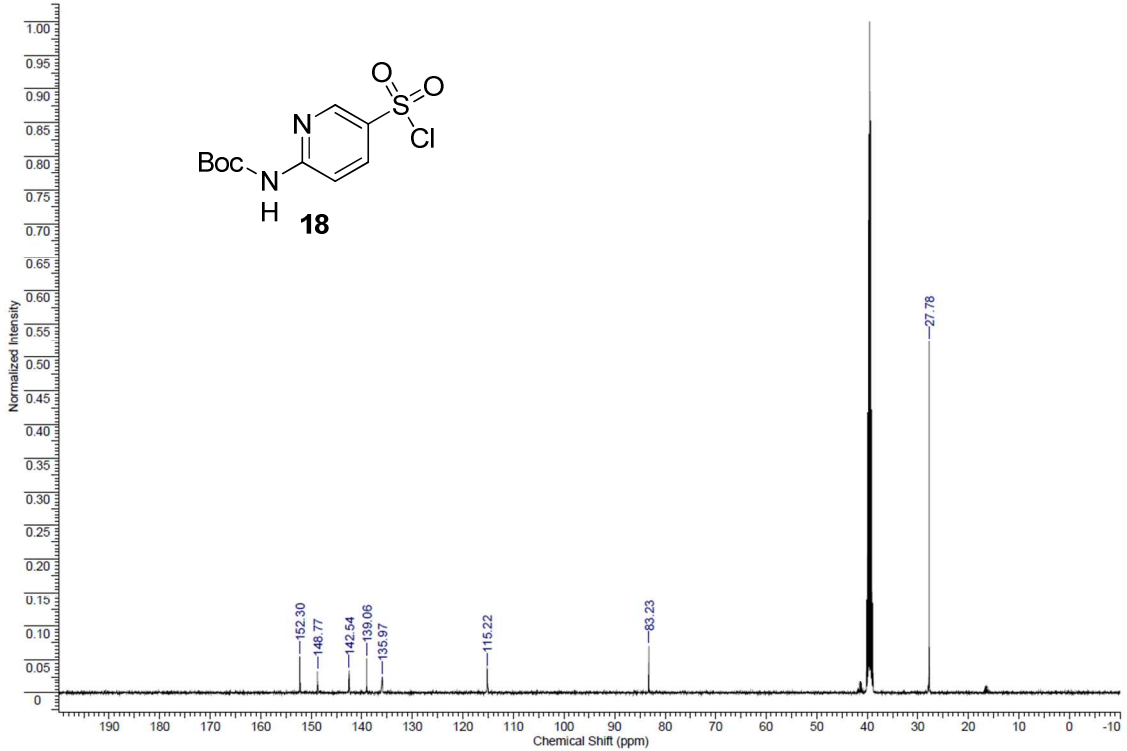

Bn–N
N
CF3
OH
CF3
16
Normalized Intensity
Chemical Shift (ppm)
1.89
2.00
1.83
1.00
0.93
1.00
1.86
2.28
2.81

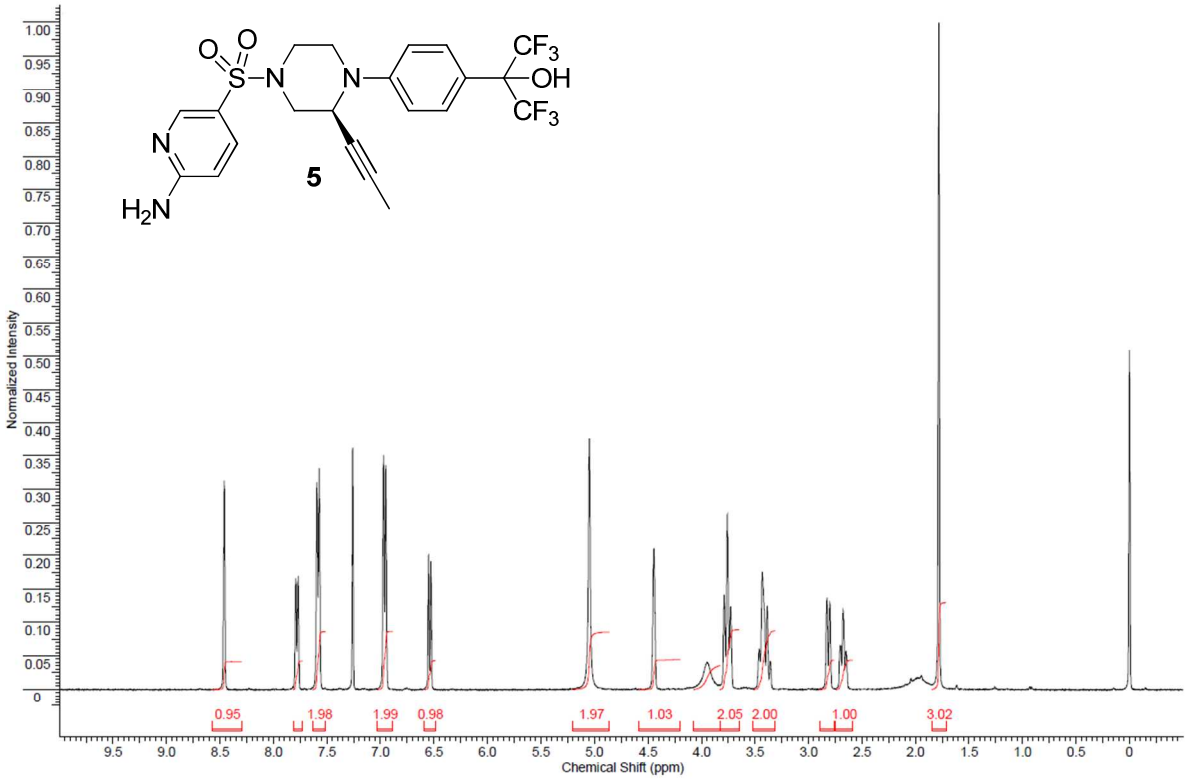

Bn–N
N
CF3
OH
CF3
16
Normalized Intensity
Chemical Shift (ppm)
150.89
137.37
128.89
127.89
126.88
124.82
121.88
119.10
115.47
79.52
76.00
62.03
57.01
52.94
48.27
48.15
44.23
1.73

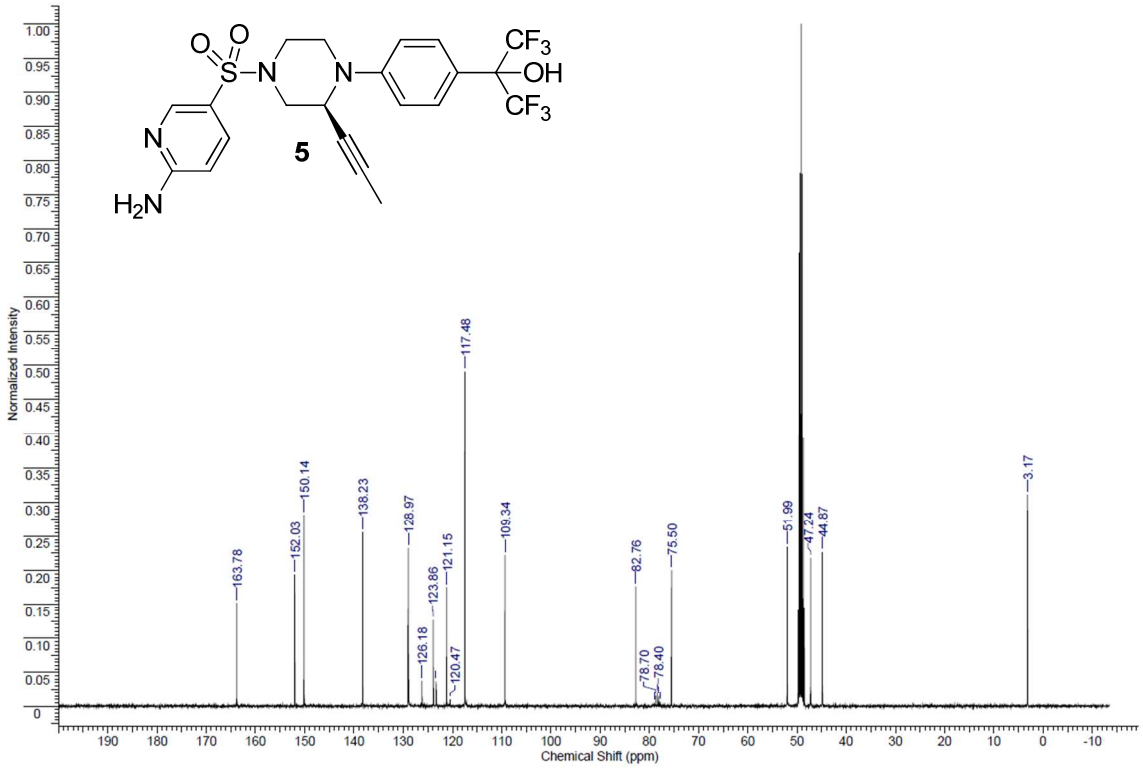

HN
N
CF3
OH
CF3
17
Normalized Intensity
Chemical Shift (ppm)
2.04
2.00
1.08
1.06
0.98
2.98


HN
N
CF3
OH
CF3
17
Normalized Intensity
Chemical Shift (ppm)
151.32
129.12
126.08
124.98
123.22
117.88
86.43
78.33
73.00
49.38
48.15
44.95
42.58
3.30

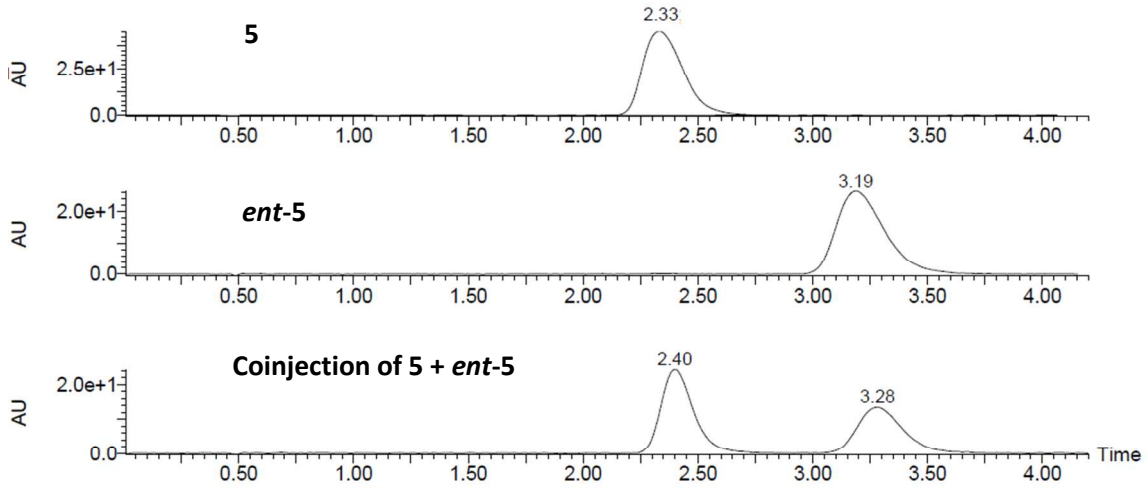

Boc
N
H
N
O
S
O
Cl
18
Normalized Intensity
Chemical Shift (ppm)
0.72
1.27
1.02
0.98
9.00


Boc
N
H
N
O
O
S
Cl
18
Normalized Intensity
Chemical Shift (ppm)
152.30
148.77
142.54
139.06
135.97
115.22
83.23
27.78


5
Normalized Intensity
Chemical Shift (ppm)
0.95
1.98
1.99
0.98
1.97
1.03
2.05
2.00
1.00
3.02


5
Normalized Intensity
Chemical Shift (ppm)
163.78
152.03
150.14
138.23
128.97
126.18
123.86
121.15
120.47
117.48
109.34
82.76
78.70
78.40
75.50
51.99
47.24
44.87
3.17

Chiral SFC Analysis of 5



Analytical SFC conditions: AD (5um, 4.6mm x 15cm) column with 30% MeOH with 20mM ammonia in super critical CO_2; flow rate = 4.0 mL/min, T = 40 °C, pressure = 100 bar. The enantiomeric excess for AMG-3969 was determined to be > 99.5%.