Design, synthesis and evaluation of novel ^{19}F magnetic resonance sensitive protein tyrosine phosphatase inhibitors

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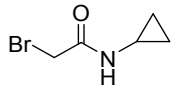
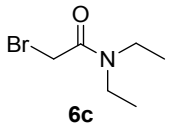
General procedure for preparation of 6a-6r (Using the preparation of **6a** as an example). Bromoacetyl Bromide (2.2 mL, 25.4 mmol) dissolved in dry DCM (10 mL) was added slowly to a solution of propylamine (0.50 g, 8.46 mmol), trimethylamine (1.4 mL, 10.2 mmol) and DMAP (0.10 g, 0.85 mmol) in dry dichloromethane (30 mL) at 0 °C. Then the reaction mixture was stirred overnight at rt. The solution was washed with brine (100 mL x 2) and extracted with DCM (50 mL x 2). The organic layer was dried over anhydrous Na_2SO_4, concentrated under vacuum and purified by flash chromatography on silica gel (30% EtOAc/petroleum ether) to give **6a** as clear oil (1.22 g, 80% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.90-1.02 (m, 3H), 1.47-1.66 (m, 2H), 3.18-3.35 (m, 2H), 3.91 (d, J = 2.4 Hz, 2H).



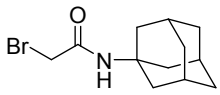
6b

2-Bromo-N-cyclopropylacetamide **6b** was prepared from cyclopropyoamine (0.50 g, 8.76 mmol) by following the general procedure as white wax (0.90 g, 58% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.48-0.70 (m, 2H), 0.74-0.95 (m, 2H), 2.63-2.88 (m, 1H), 3.85 (s, 2H).



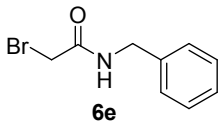
6c

2-Bromo-N,N-diethylacetamide 6c was prepared from diethylamine (0.50 g, 6.84 mmol) by following the general procedure as colourless oil (1.16 g, 87% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.14 (t, J = 7.1 Hz, 3H), 1.26 (t, J = 7.2 Hz, 3H), 3.30-3.49 (m, 4H), 3.85 (s, 2H).



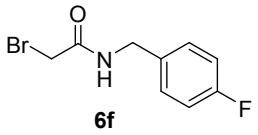
6d

N-((3s,5s,7s)-adamantan-1-yl)-2-bromoacetamide 6d was prepared from amantadine hydrochloride (0.50 g, 2.67 mmol) by following the general procedure except that 3.0 equive of trimethylamine was used. **6d** was obtained as white wax (0.60 g, 82% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.69 (s, 6H), 2.03 (t, J = 7.9 Hz, 6H), 2.10 (s, 3H), 3.78 (s, 2H).



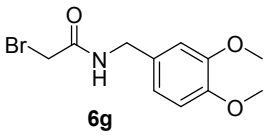
6e

N-benzyl-2-bromoacetamide 6e was prepared from benzylamine (0.50 g, 4.67 mmol) by following the general procedure as white wax (0.83 g, 78% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.93 (s, 2H), 4.48 (d, J = 5.8 Hz, 2H), 7.25-7.41 (m, 5H).



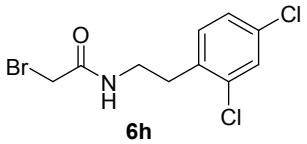
6f

2-Bromo-N-(4-fluorobenzyl)acetamide 6f was prepared from 4-fluorobenzylamine (0.50 g, 4.00 mmol) by following the general procedure as white wax (0.64 g, 65% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.93 (s, 2H), 4.46 (t, J = 6.5 Hz, 2H), 6.96-7.17 (m, 2H), 7.18-7.37 (m, 2H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ -117.68.



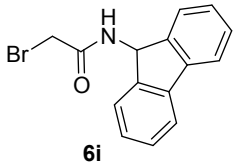
6g

2-Bromo-N-(3,4-dimethoxybenzyl)acetamide 6g was prepared from veratrylamine (0.50 g, 2.99 mmol) by following the general procedure as white wax (0.52 g, 60% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.87 (d, J = 1.9 Hz, 6H), 3.91 (s, 2H), 4.40 (d, J = 5.7 Hz, 2H), 6.83 (d, J = 6.9 Hz, 3H).



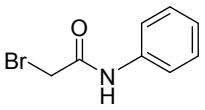
6h

2-Bromo-N-(2,4-dichlorophenethyl)acetamide 6h was prepared from 1-(2,4-dichloro-phenyl)-ethylamine (0.50 g, 2.63 mmol) by following the general procedure as yellow wax (0.51 g, 62% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.97 (t, J = 7.0 Hz, 2H), 3.55 (dd, J = 13.1, 6.9 Hz, 2H), 3.86 (s, 2H), 7.20 (dt, J = 16.4, 5.1 Hz, 2H), 7.40 (d, J = 2.0 Hz, 1H).



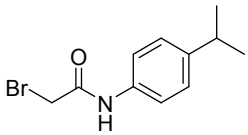
6i

2-Bromo-N-(9H-fluoren-9-yl)acetamide 6i was prepared from 9-aminofluorene hydrochloride (0.50 g, 2.30 mmol) by following the general procedure, except that 3.0 equive of trimethylamine was used. **6i** was obtained as white wax (0.54 g, 78% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.03 (s, 2H), 6.18 (d, J = 8.8 Hz, 1H), 7.34 (dd, J = 10.8, 4.1 Hz, 2H), 7.43 (t, J = 7.4 Hz, 2H), 7.57 (d, J = 7.5 Hz, 2H), 7.72 (d, J = 7.5 Hz, 2H).



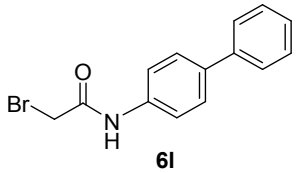
6j

2-Bromo-N-phenylacetamide 6j was prepared from aniline (0.50 g, 5.37 mmol) by following the general procedure as yellow wax (1.04 g, 90% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.03 (s, 2H), 7.12-7.22 (m, 1H), 7.31-7.43 (m, 2H), 7.53 (dd, J = 8.5, 1.0 Hz, 2H).



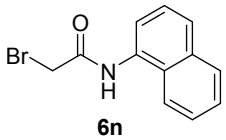
6k

2-Bromo-N-(4-isopropylphenyl)acetamide 6k was prepared from 4-*iso*-propylaniline (0.50 g, 3.70 mmol) by following the general procedure as white wax (0.78 g, 82% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.24 (t, J = 7.1 Hz, 6H), 2.78-3.02 (m, 1H), 4.02 (s, 2H), 7.21 (d, J = 8.5 Hz, 2H), 7.40-7.49 (m, 2H).



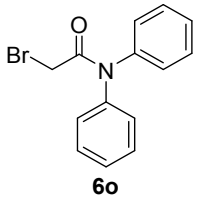
6l

N-([1,1'-biphenyl]-4-yl)-2-bromoacetamide 6l was prepared from 4-aminobiphenyl (0.50 g, 2.95 mmol) by following the general procedure as white wax (0.83 g, 97% yield). ^{1}H NMR (Acetone-d_6, 400 MHz) δ 4.07 (s, 2H), 7.34 (t, J = 8.0 Hz, 1H), 7.39-7.51 (m, 2H), 7.61-7.72 (m, 4H), 7.78 (d, J = 8.5 Hz, 2H).



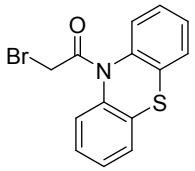
6n

2-Bromo-N-(naphthalen-1-yl)acetamide 6n was prepared from 1-aminonaphthalene (0.50 g, 3.49 mmol) by following the general procedure as white wax (0.86 g, 93% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.20 (s, 2H), 7.46-7.66 (m, 3H), 7.76 (d, J = 8.3 Hz, 1H), 7.85-7.94 (m, 2H), 7.96 (d, J = 7.4 Hz, 1H).



6o

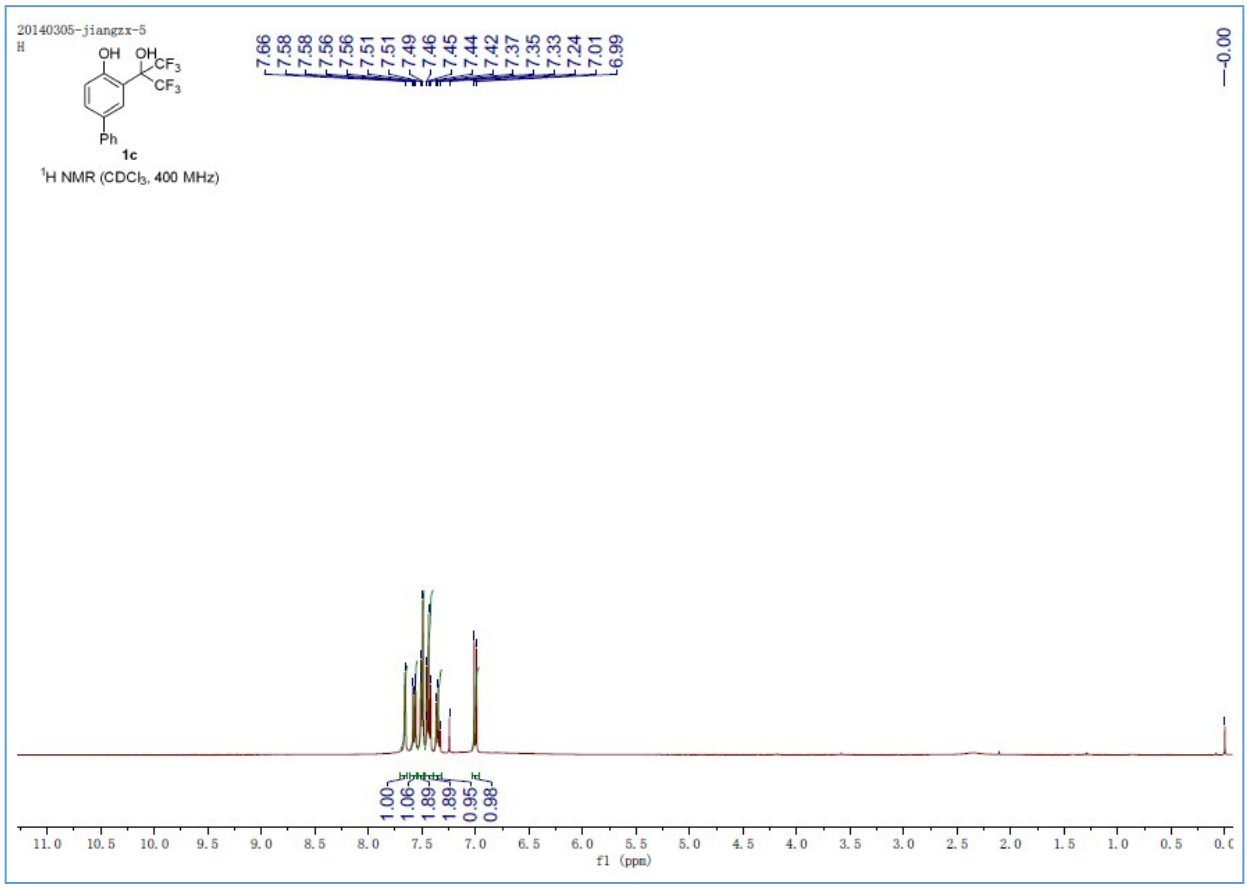
2-Bromo-N,N-diphenylacetamide 6o was prepared from diphenylamine (0.50 g, 2.95 mmol) by following the general procedure as white wax (0.72 g, 84% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.85 (s, 2H), 7.14-7.56 (m, 10H).

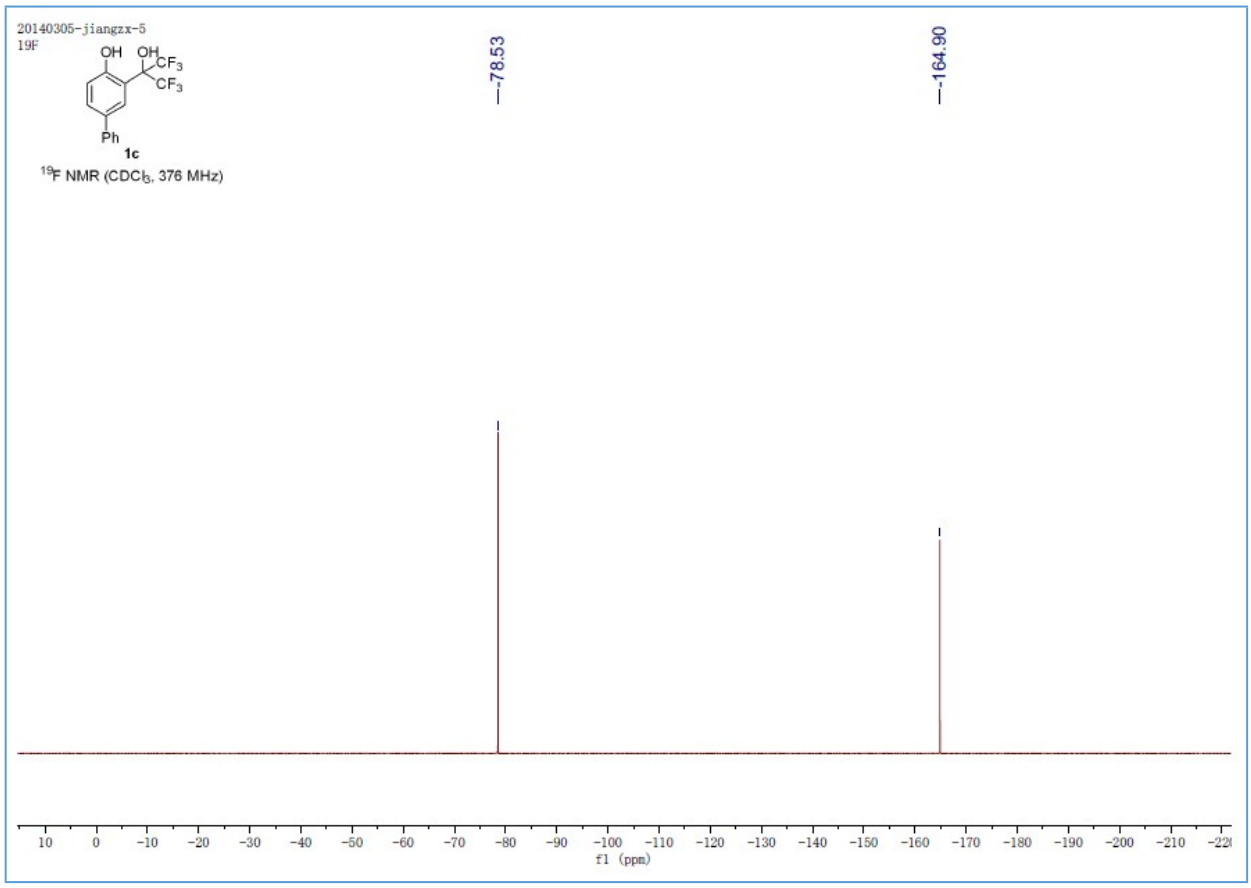


6p

2-Bromo-1-(10H-phenothiazin-10-yl)ethan-1-one 6p was prepared from phenothiazine (0.50 g, 2.51 mmol) by following the general procedure as white wax (0.67 g, 83% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.90 (s, 2H), 7.08-7.17 (m, 2H), 7.22 (td, J = 7.7, 1.4 Hz, 2H), 7.33 (dd, J = 7.7, 1.1 Hz, 2H), 7.49 (d, J = 7.8 Hz, 2H).

1. Copies of ^{1}H NMR, ^{13}C NMR and HRMS spectra of compounds

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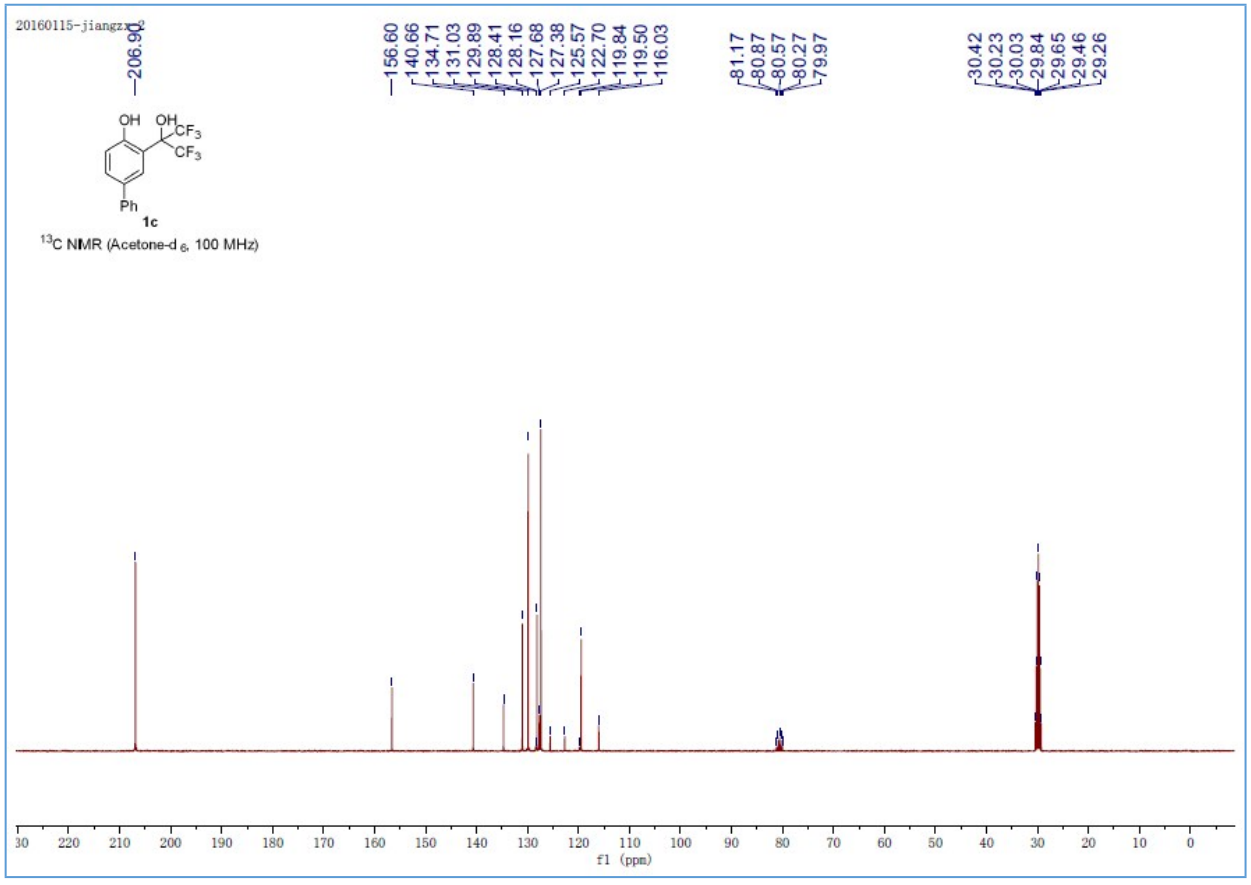
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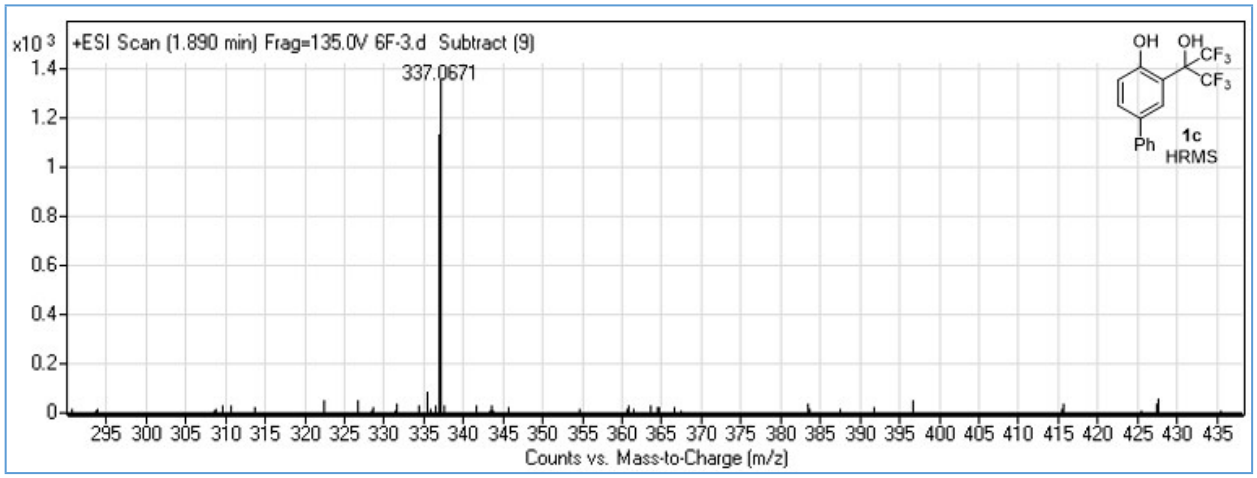
f1 (ppm)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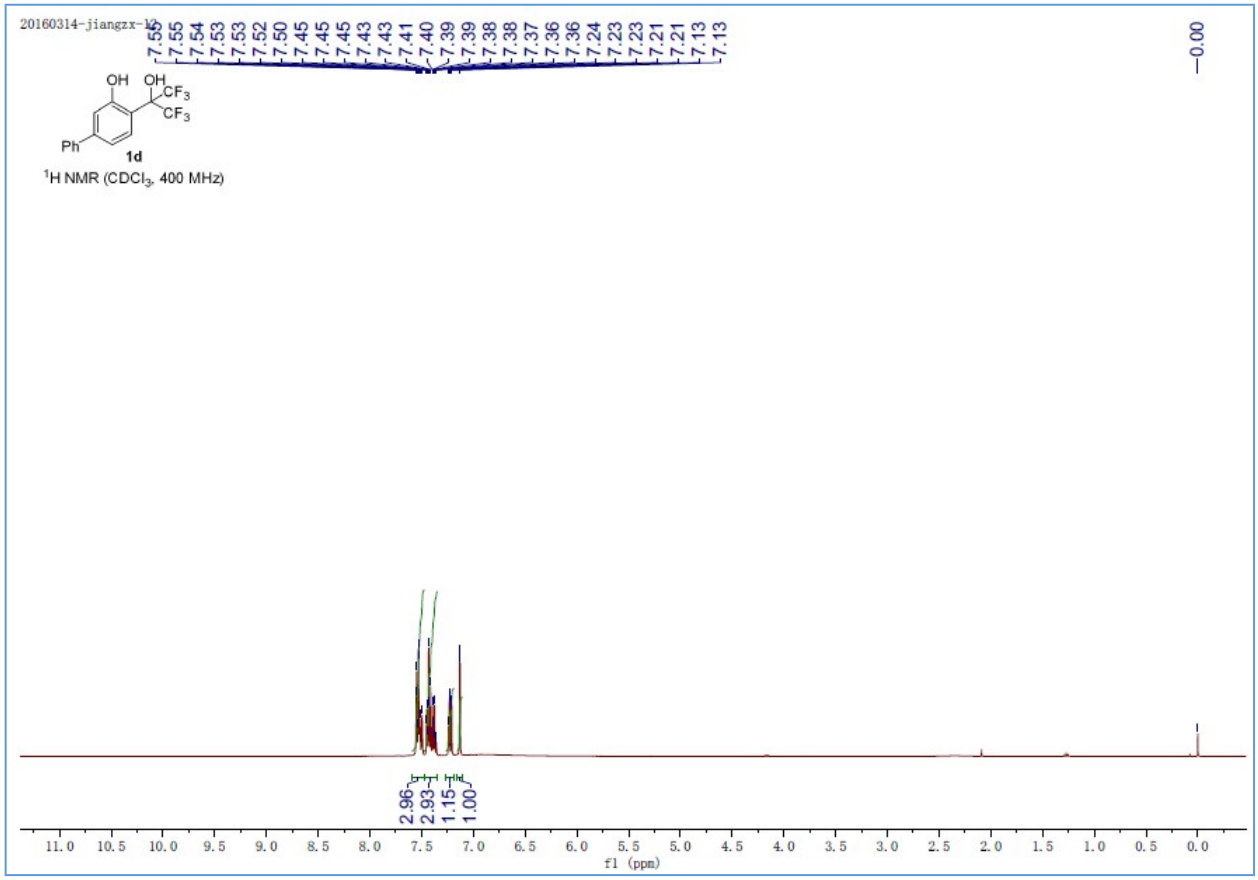
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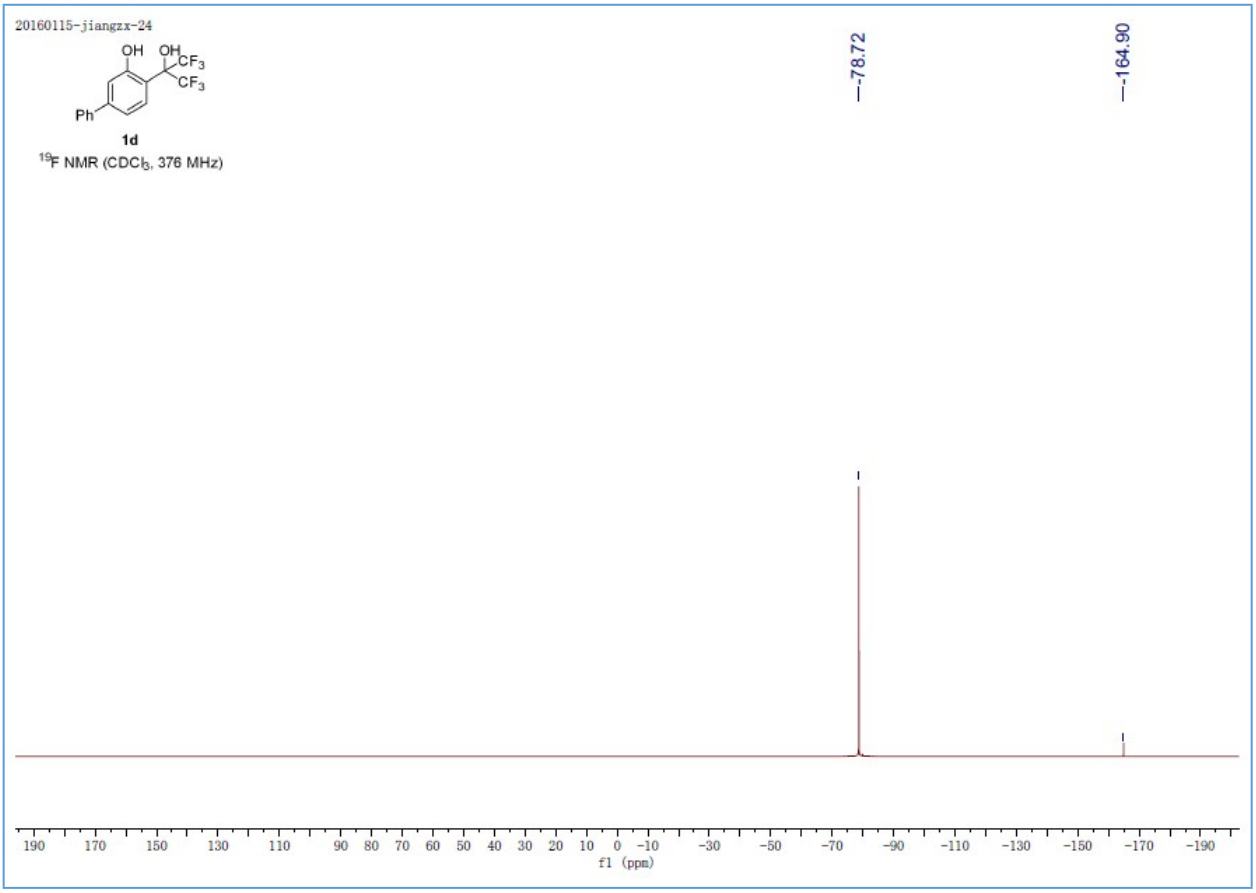
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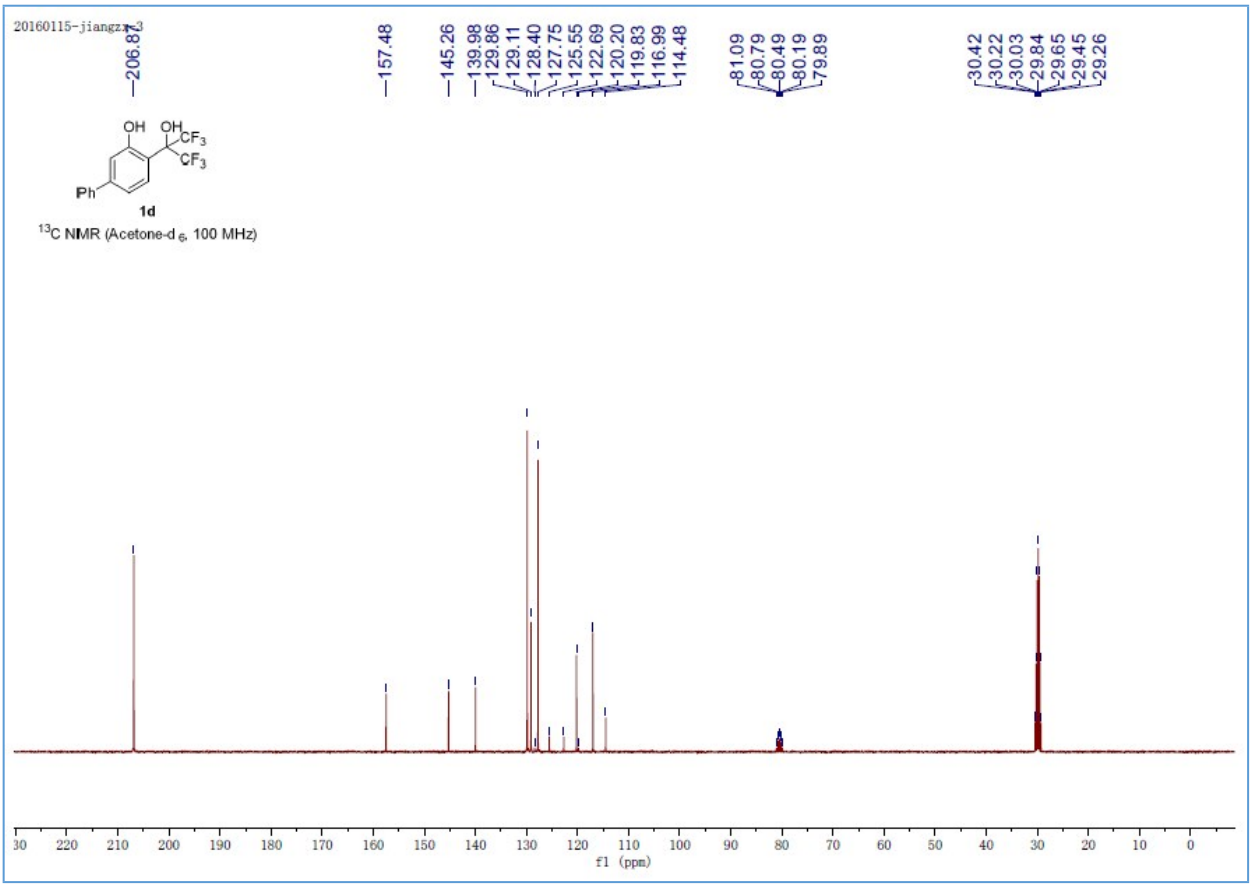
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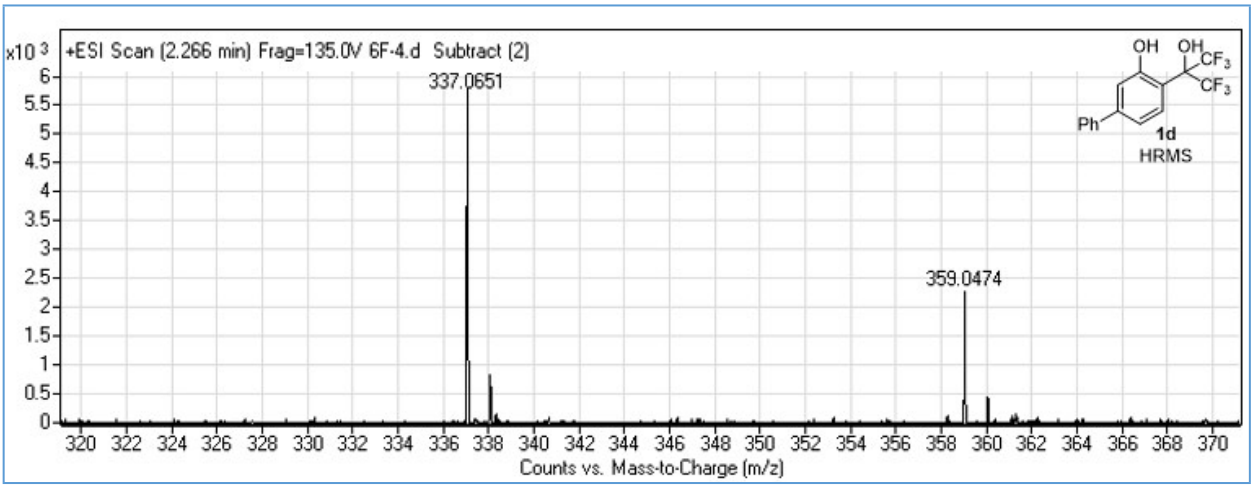
f1 (ppm)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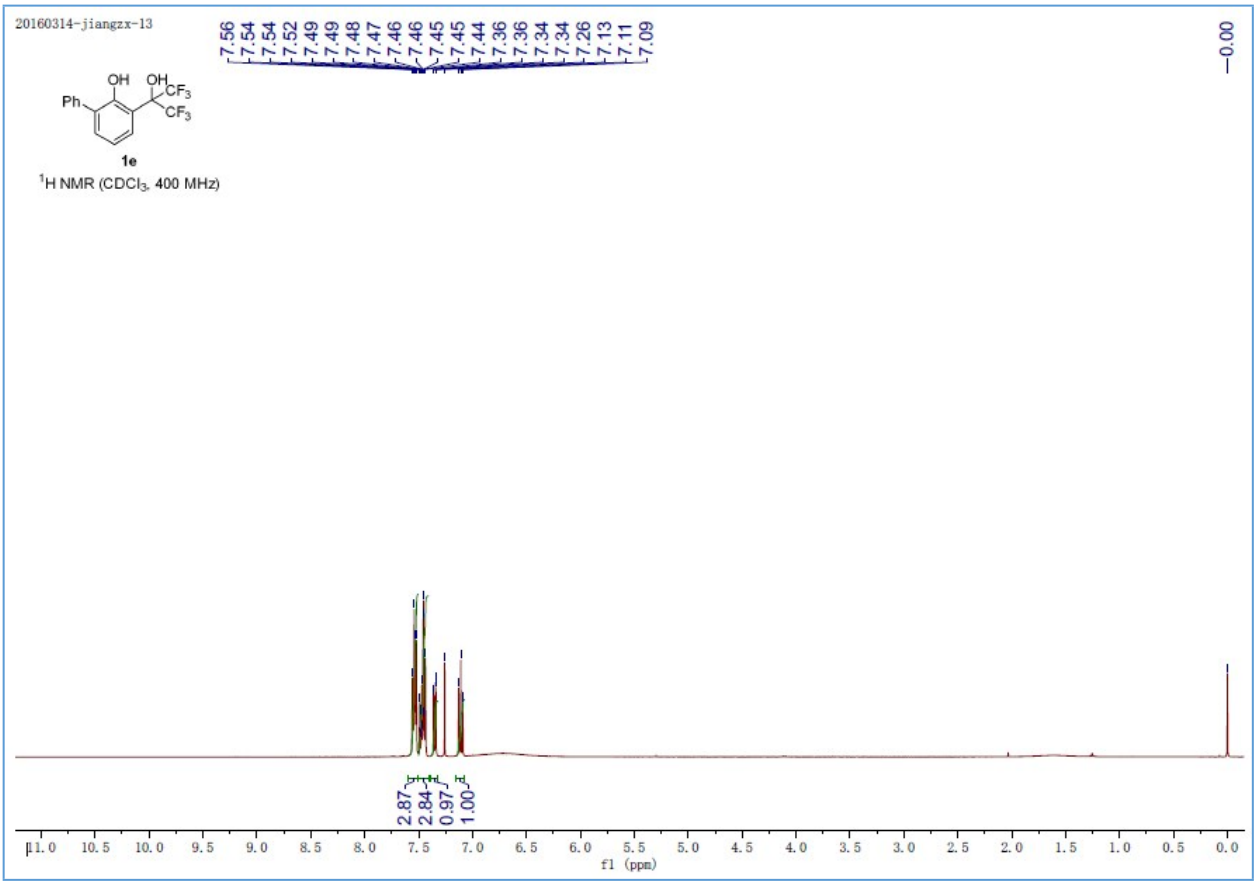
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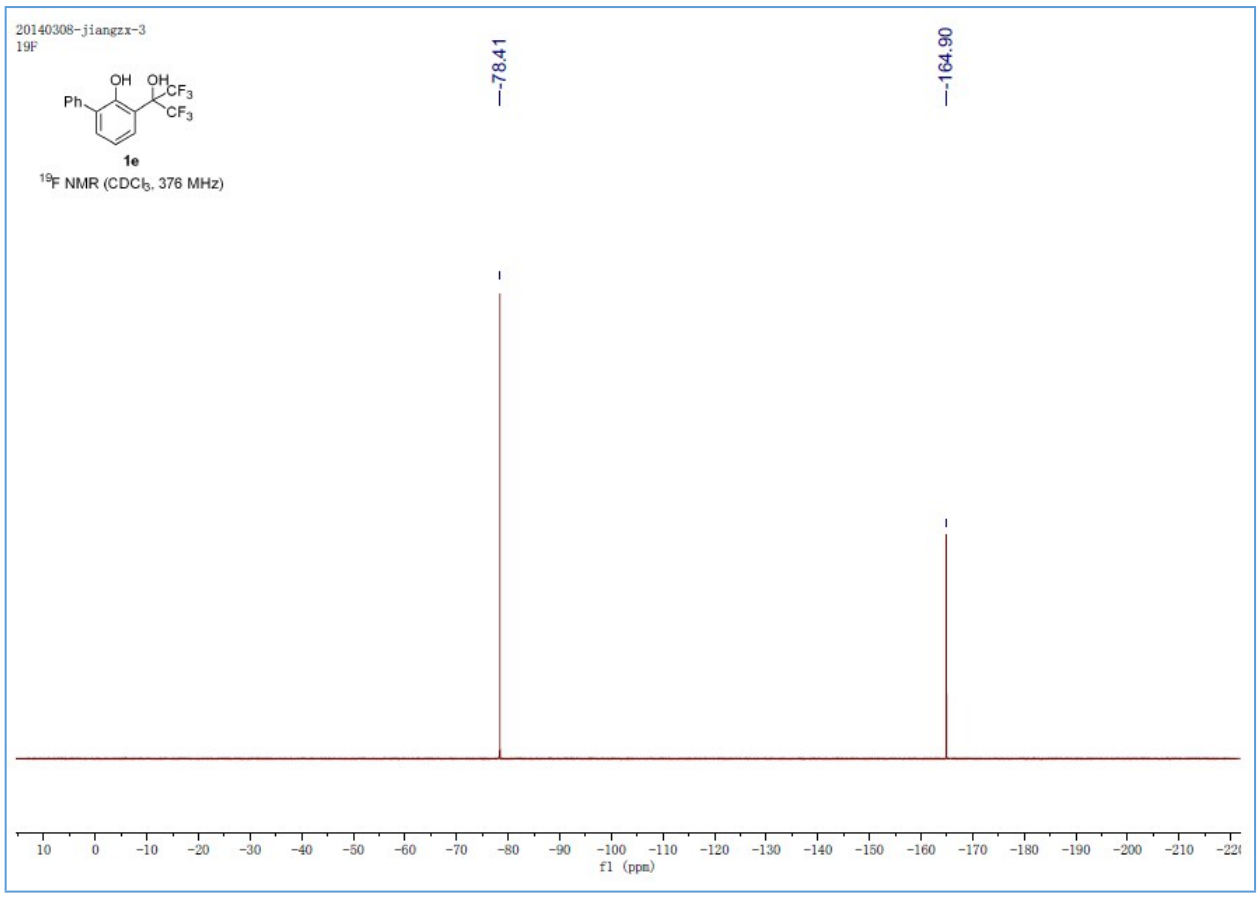
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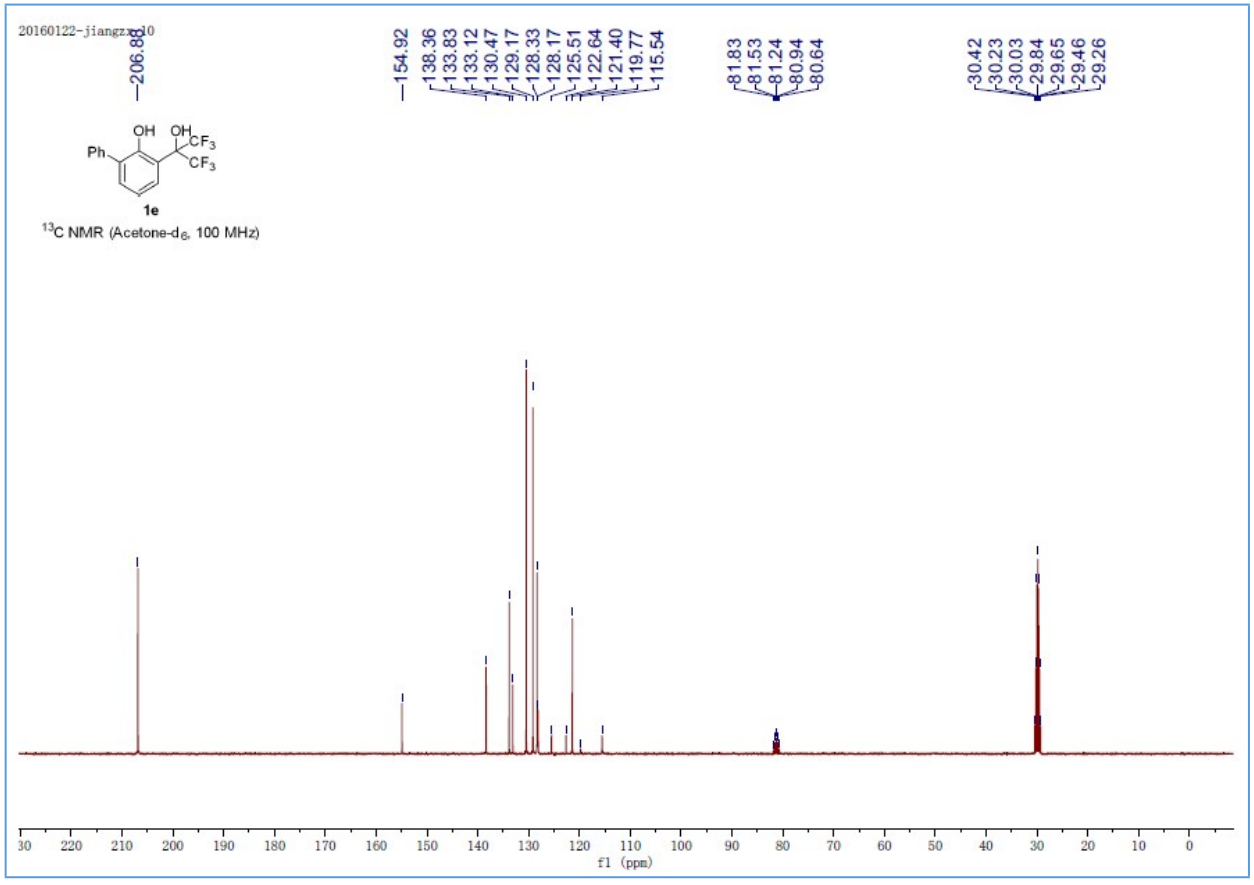
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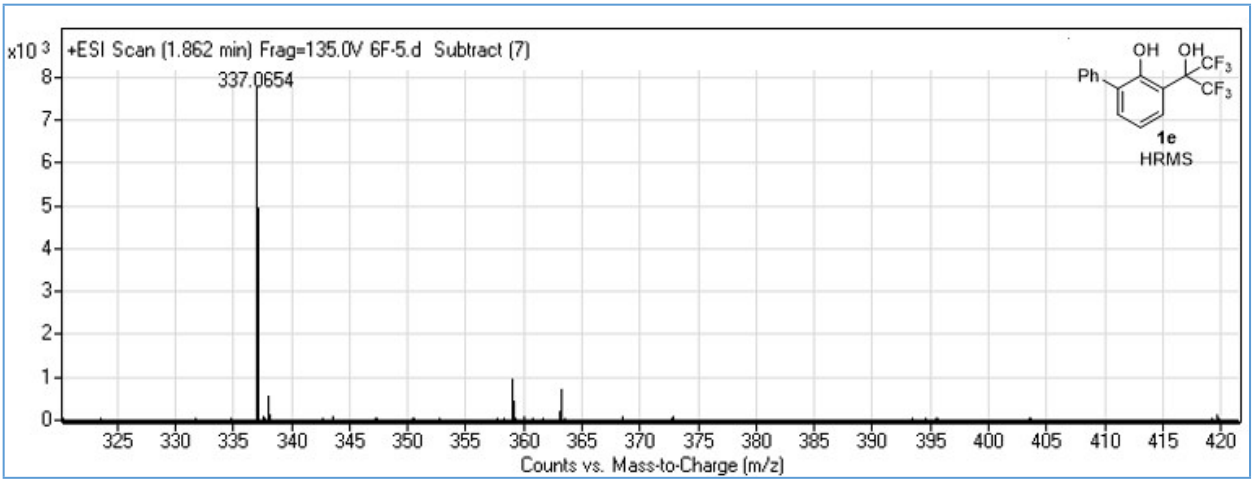
f1 (ppm)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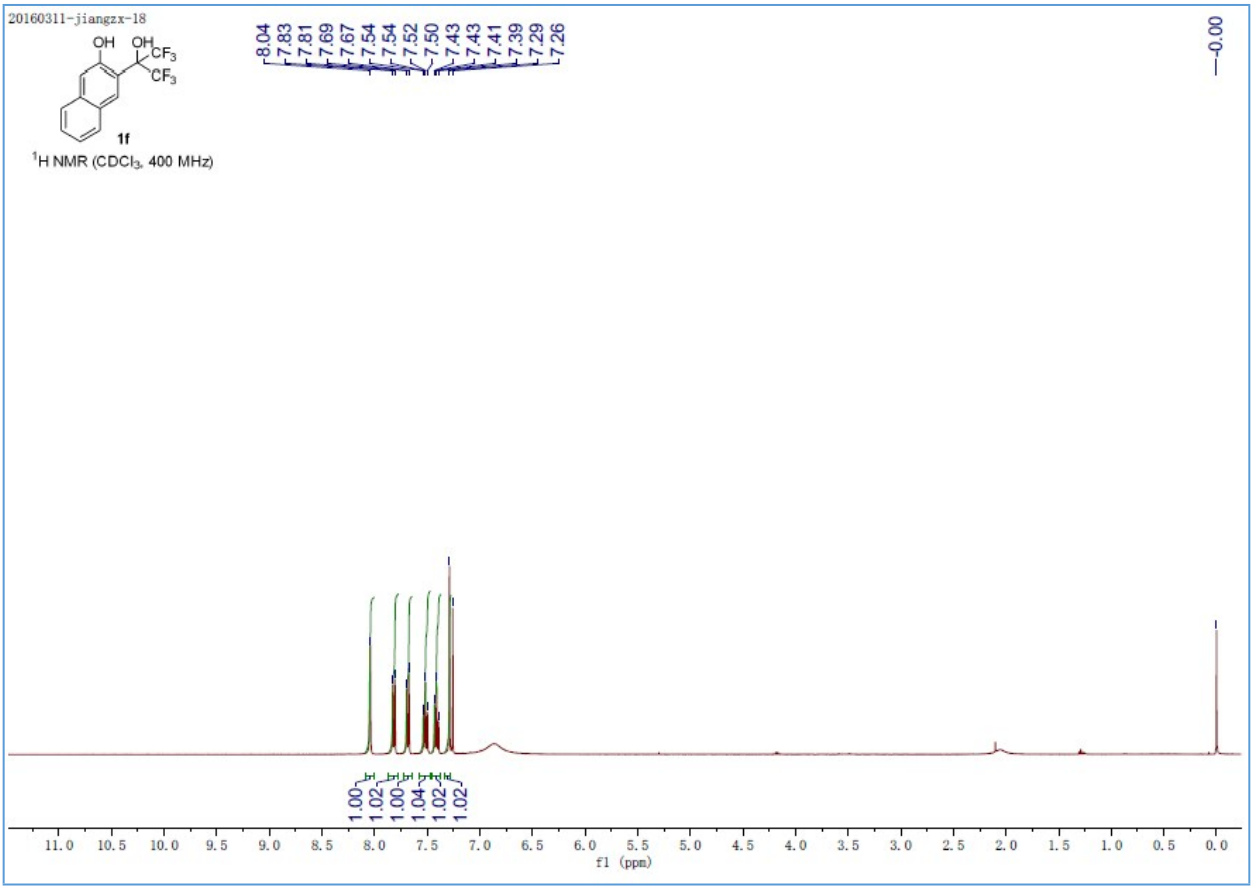
Counts vs. Mass-to-Charge (m/z)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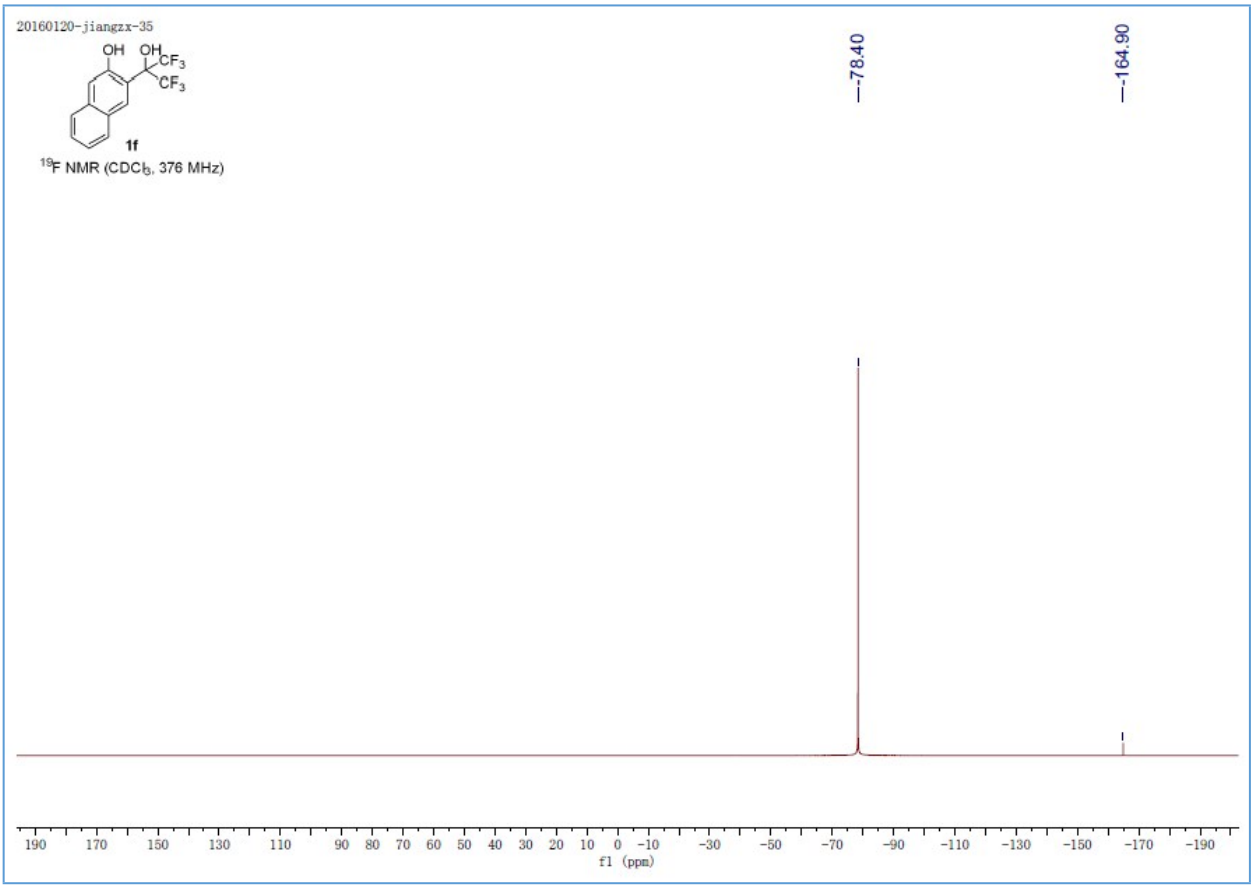
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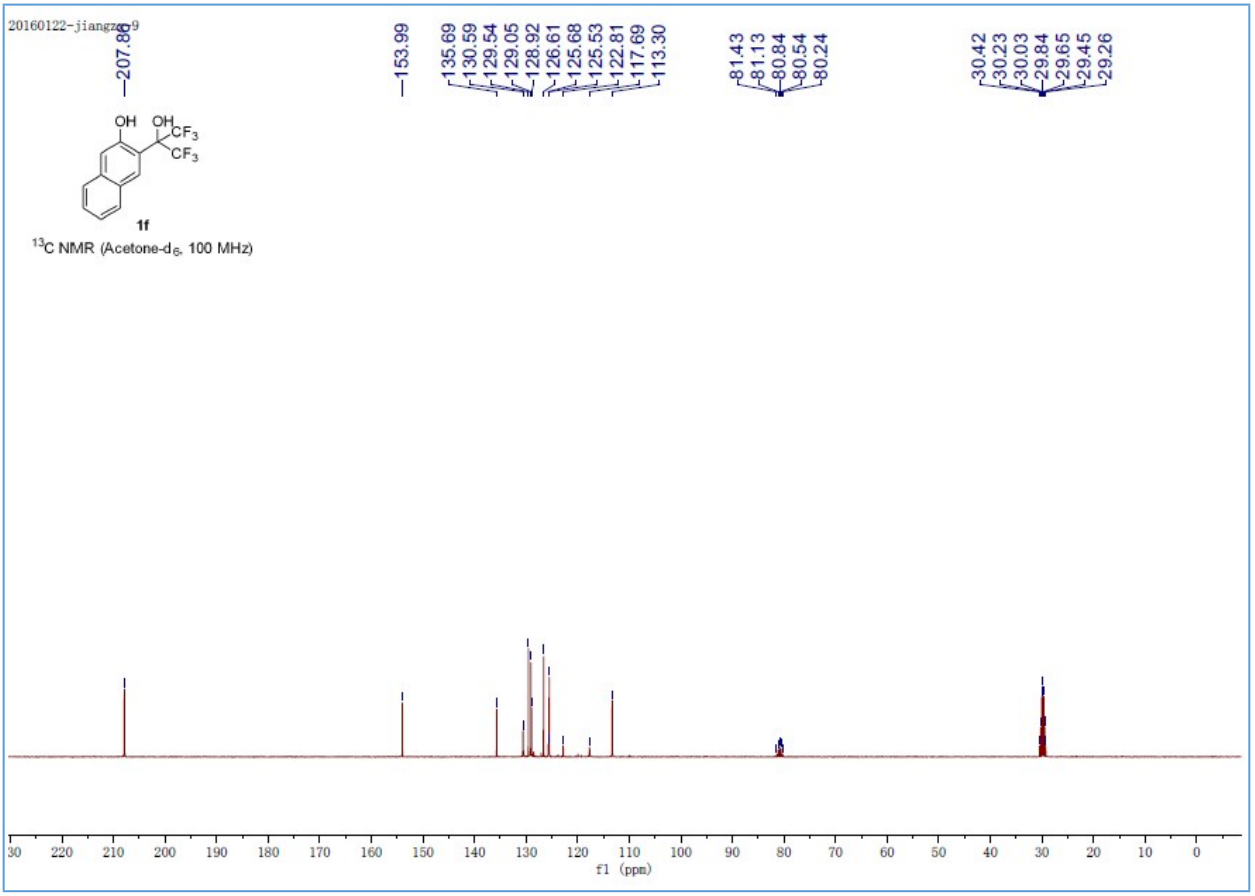
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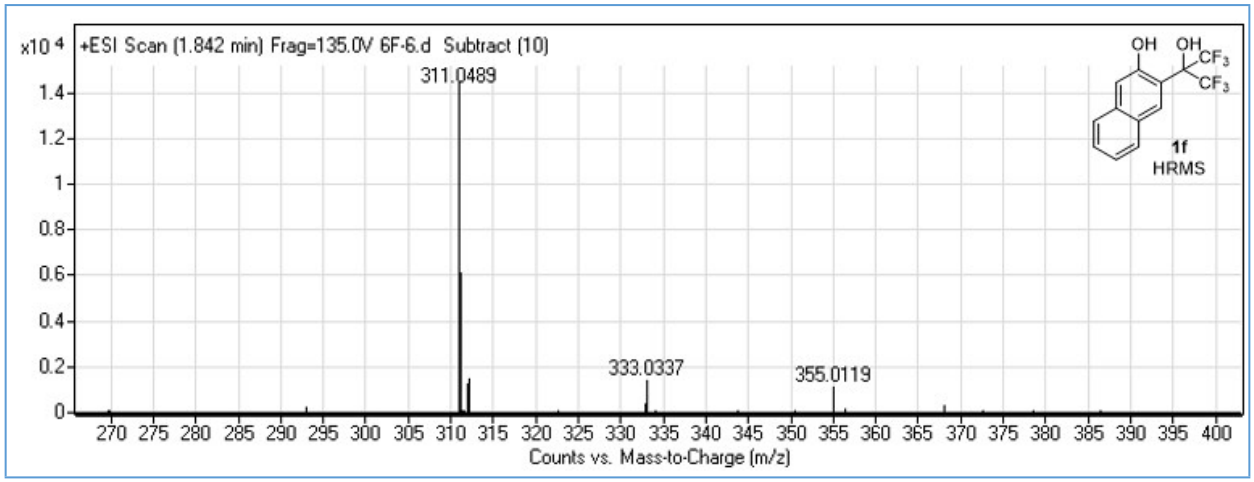
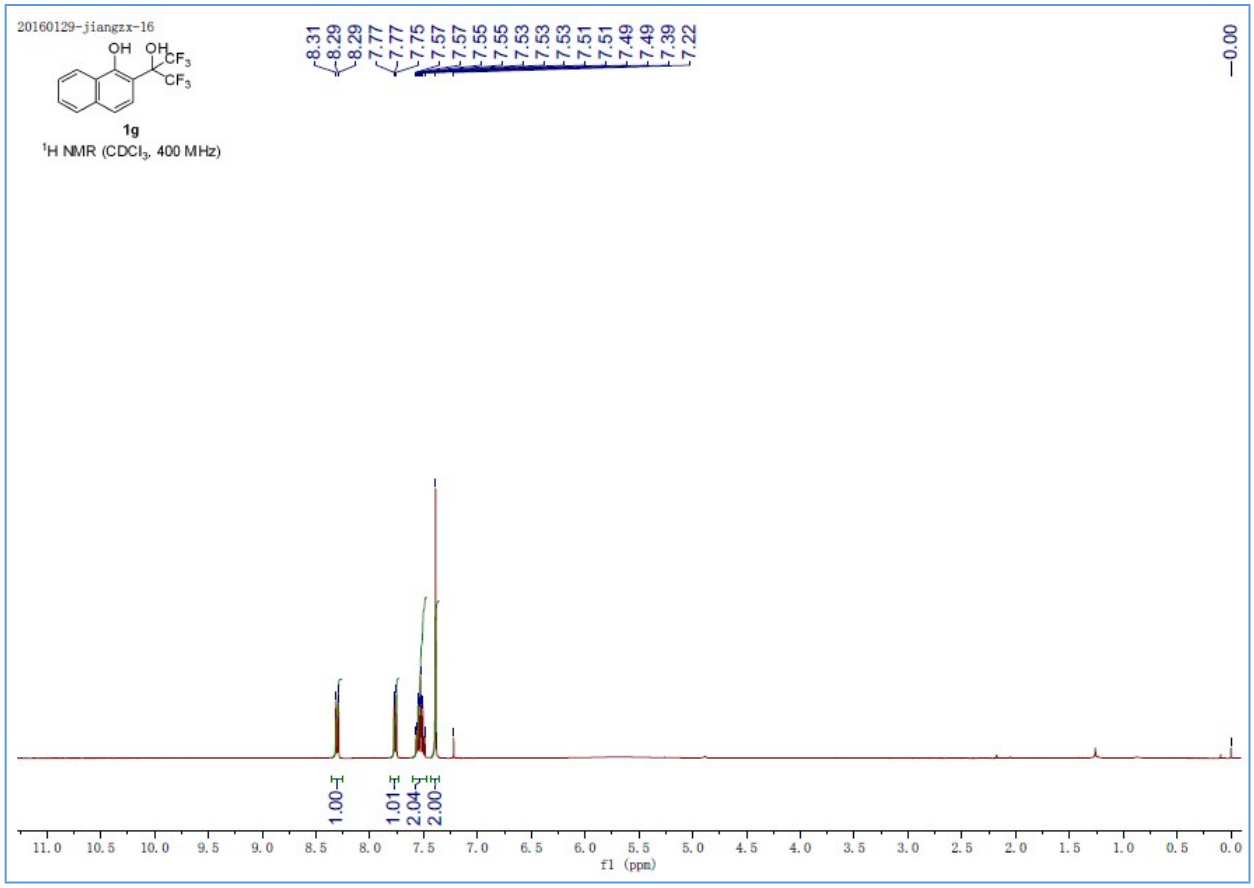
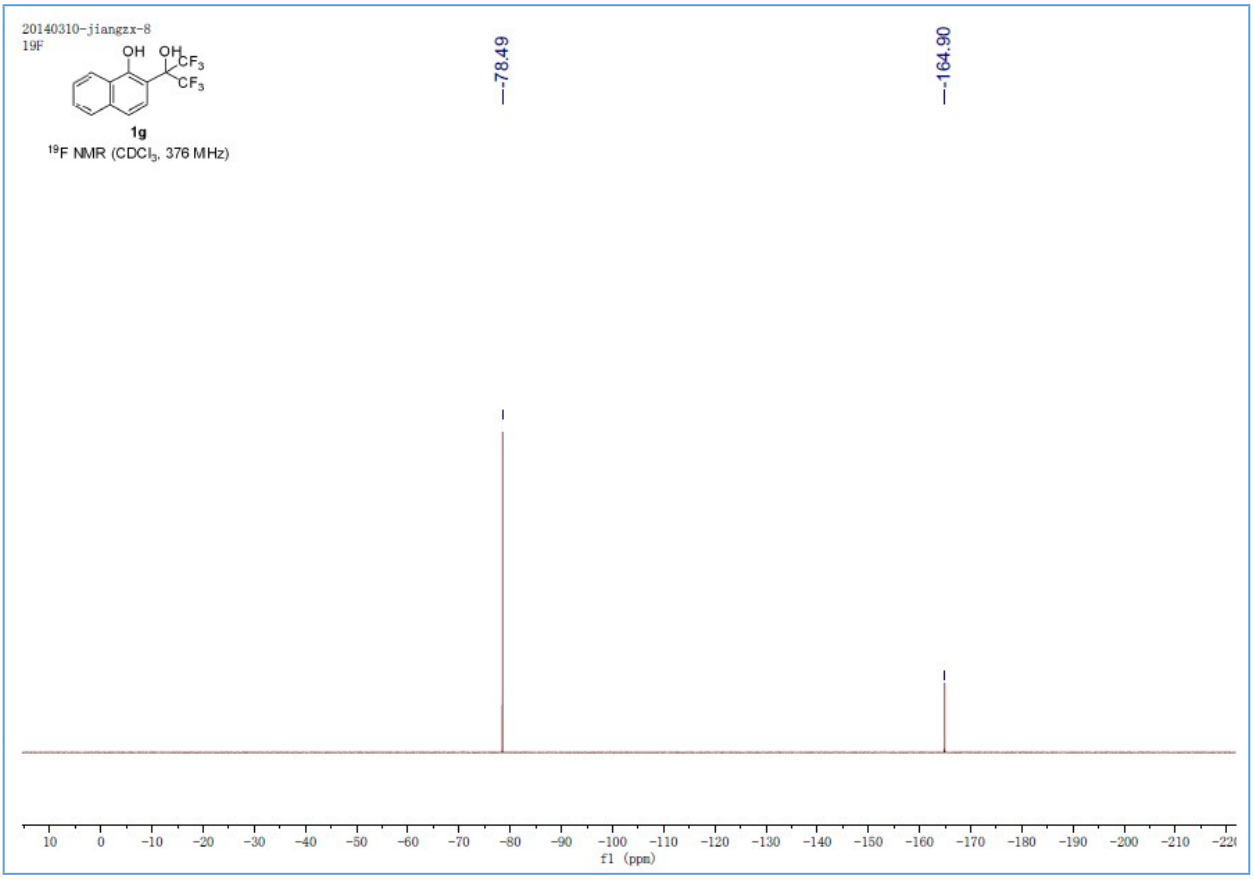
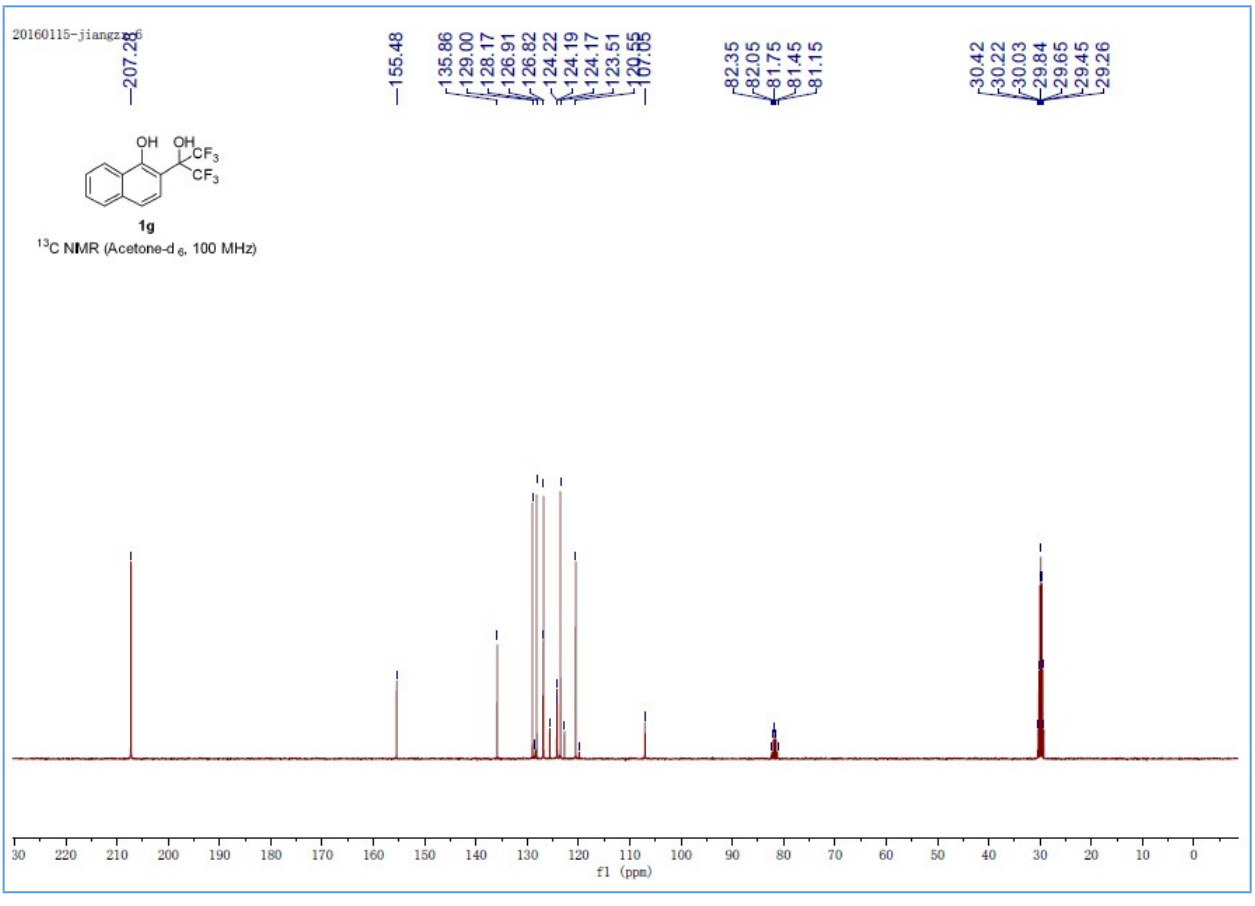
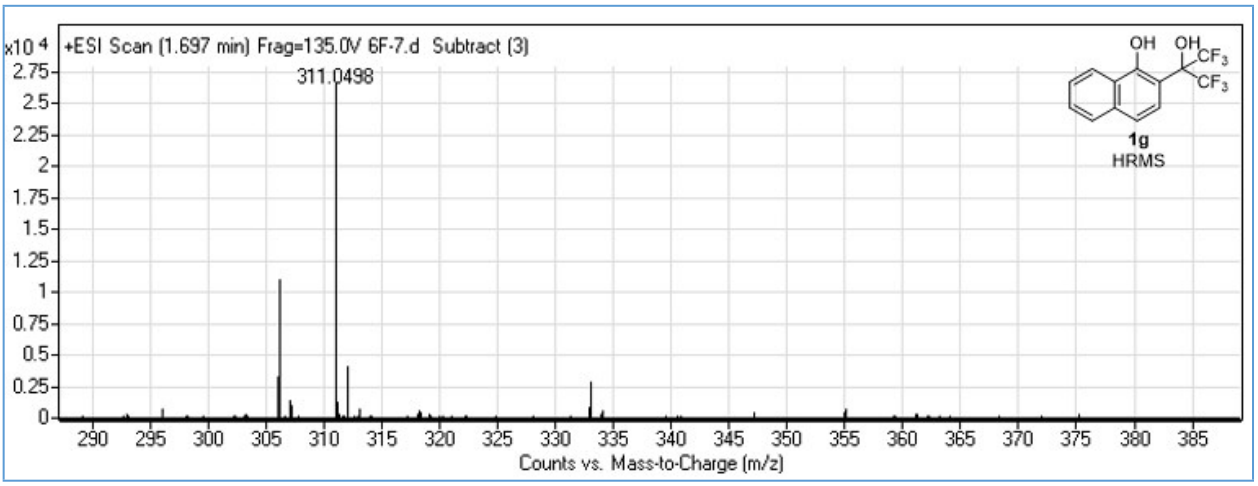
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

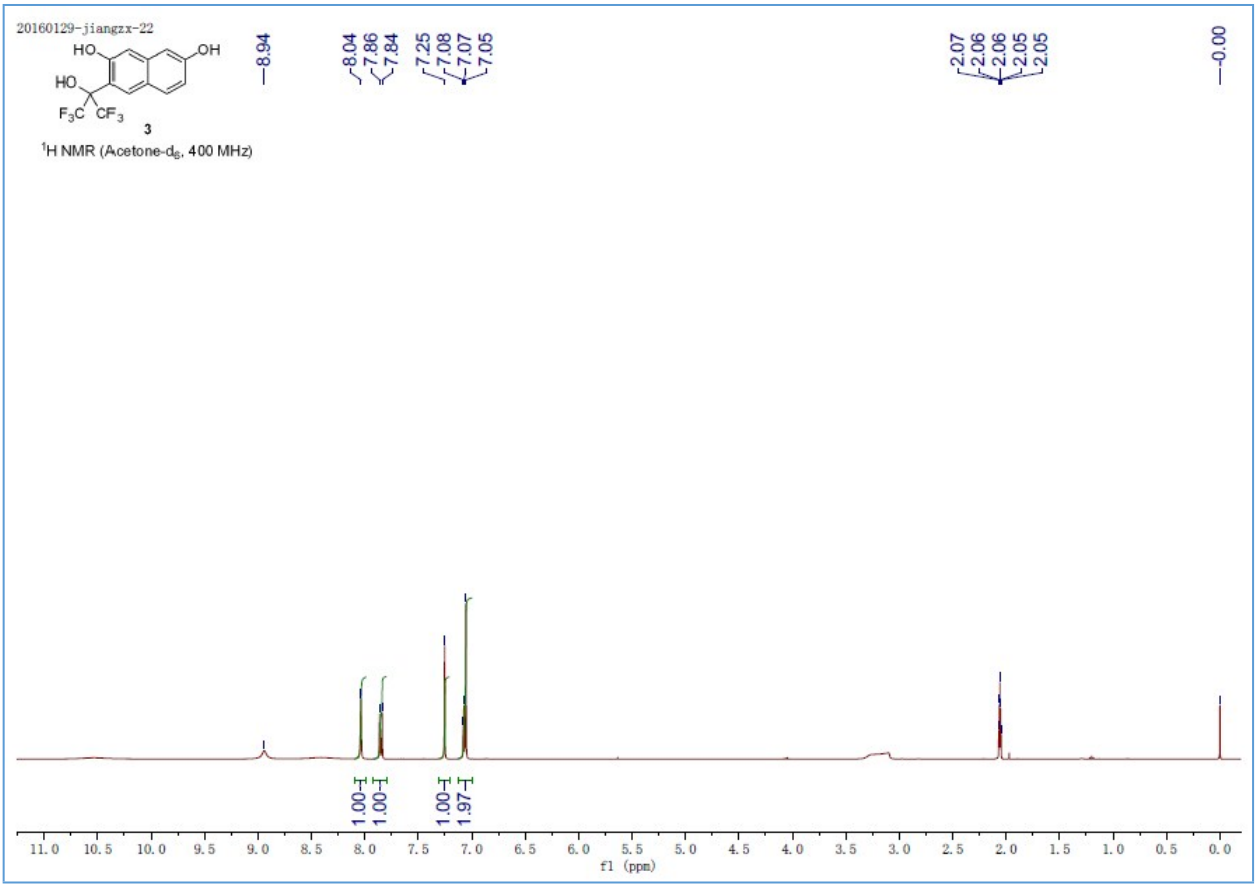

x10 4
+ESI Scan (1.842 min) Frag=135.0V 6F-6.d Subtract (10)
311.0489
333.0337
355.0119
1f
HRMS
Counts vs. Mass-to-Charge (m/z)

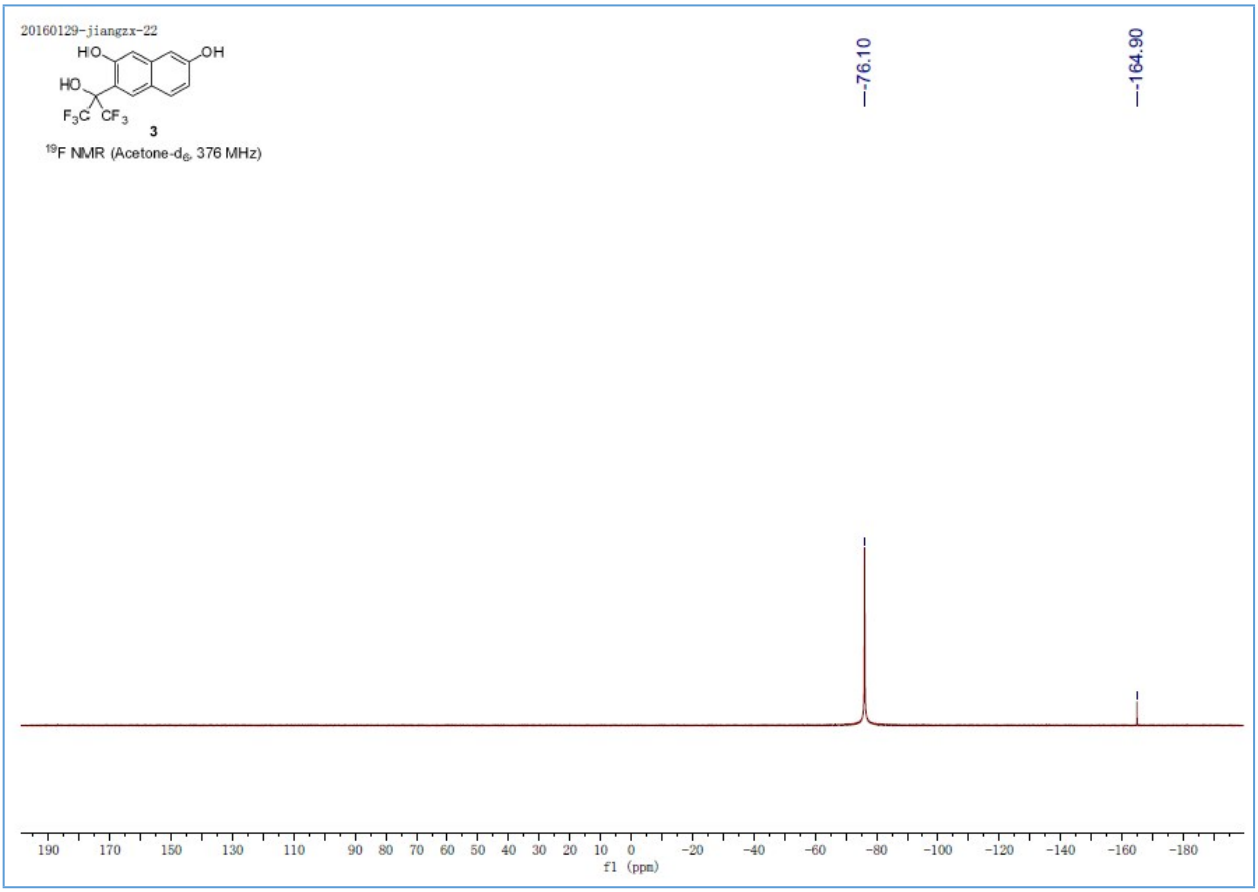

20160129-jiangzx-16
1g
1H NMR (CDCl3, 400 MHz)
f1 (ppm)

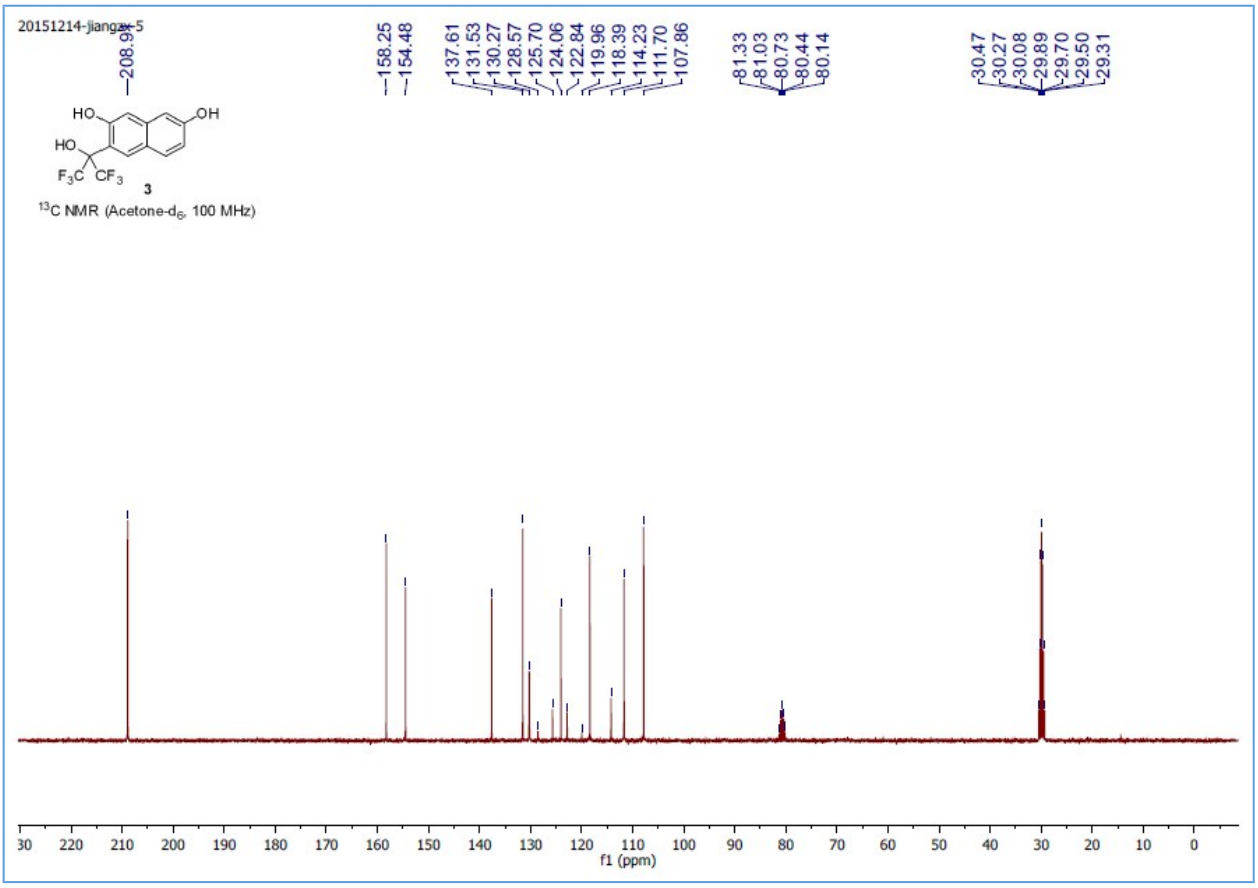

20140310-jiangzx-8
19F
OH
OH
CF3
CF3
1g
19F NMR (CDCl3, 376 MHz)
-78.49
-164.90
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

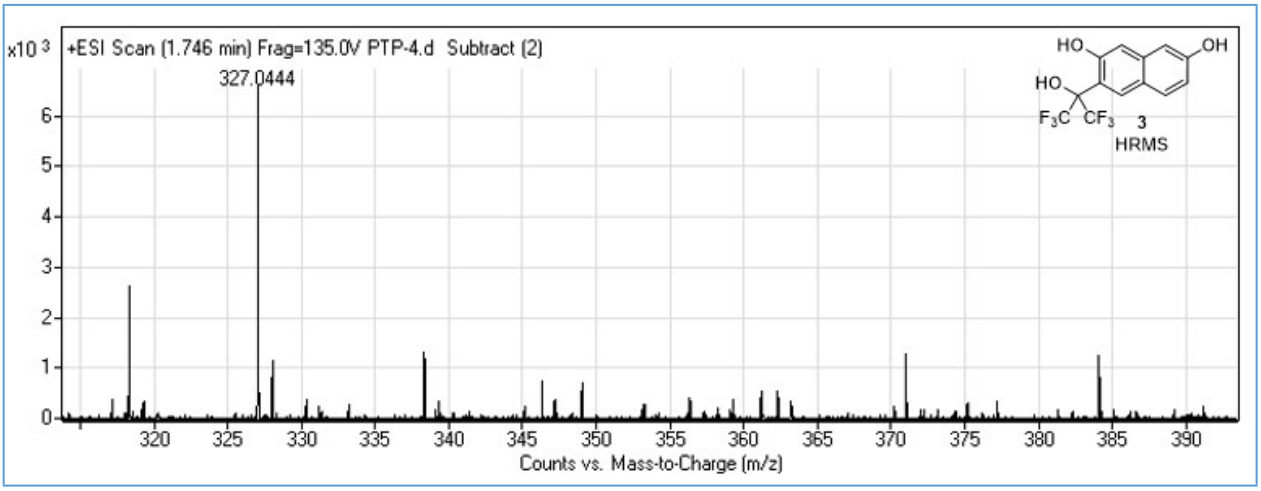

20160115-jiangzx-6
207.28
155.48
135.86
129.00
128.17
126.91
126.82
124.22
124.19
124.17
123.51
82.35
82.05
81.75
81.45
81.15
30.42
30.22
30.03
29.84
29.65
29.45
29.26
OH
OH
CF3
CF3
1g
13C NMR (Acetone-d6, 100 MHz)
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

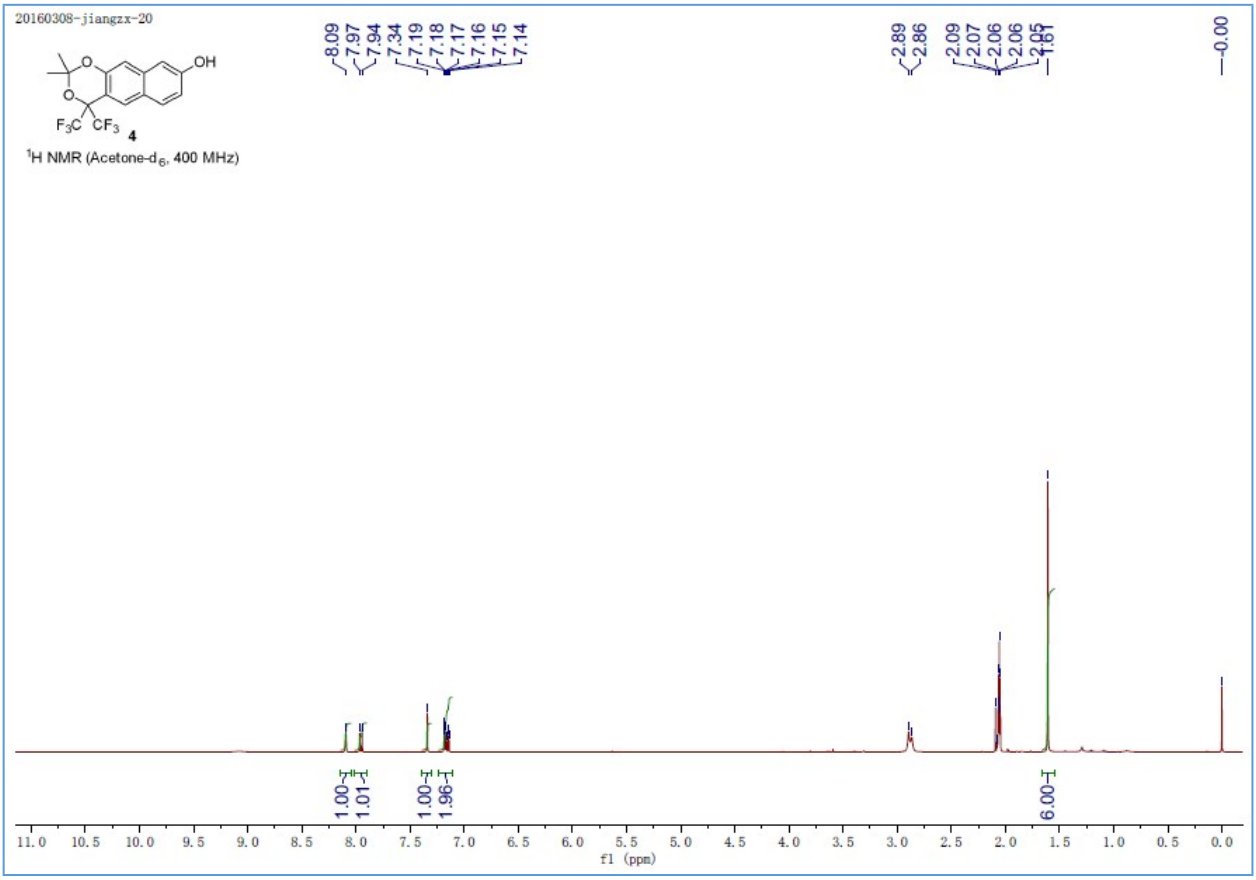

x10 4
+ESI Scan (1.697 min) Frag=135.0V 6F-7.d Subtract (3)
311.0498
OH
OH
CF3
CF3
1g
HRMS
Counts vs. Mass-to-Charge (m/z)

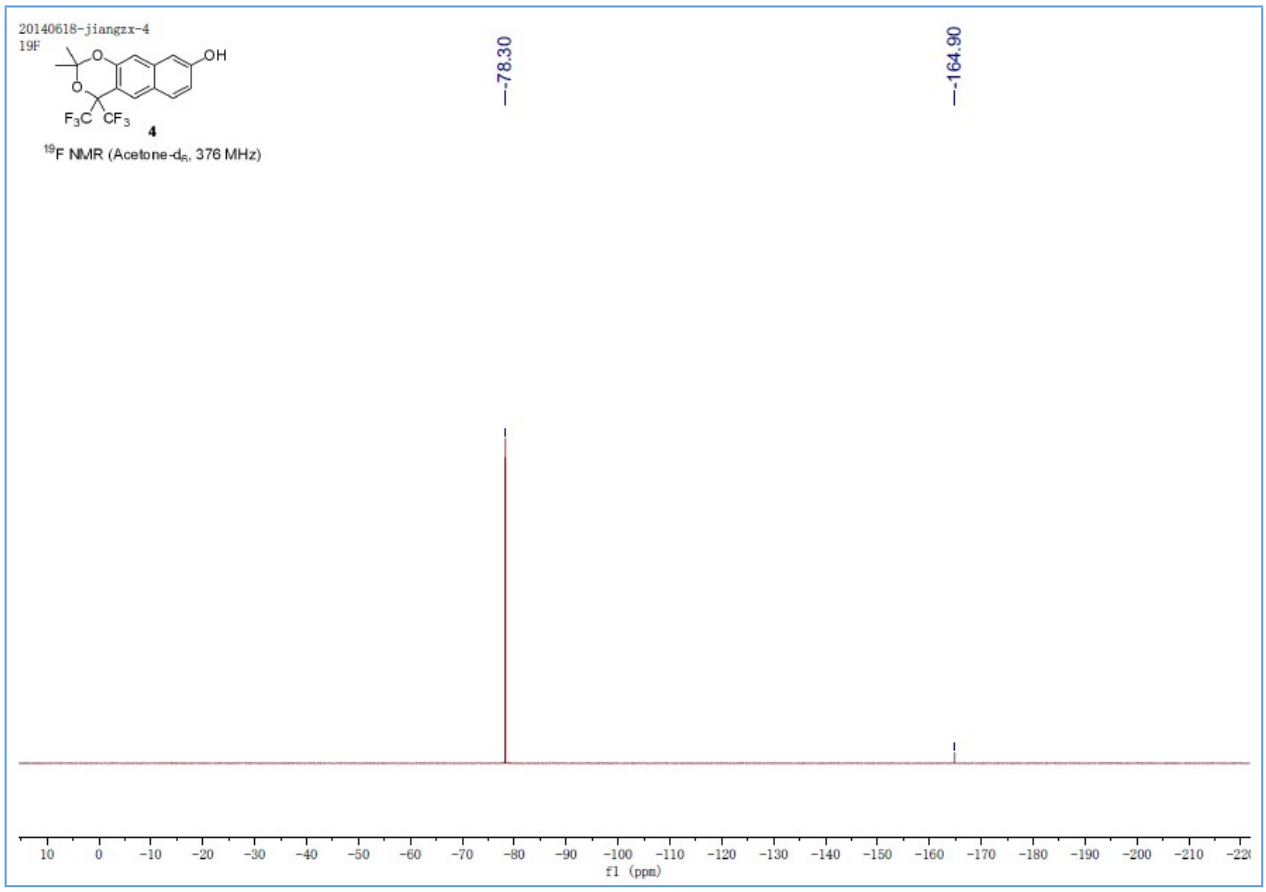

20160129-jiangzx-22
HO
OH
HO
F3C
CF3
3
1H NMR (Acetone-d6, 400 MHz)
8.94
8.04
7.86
7.84
7.25
7.08
7.07
7.05
2.07
2.06
2.06
2.05
2.05
0.00
1.00
1.00
1.00
1.97
f1 (ppm)

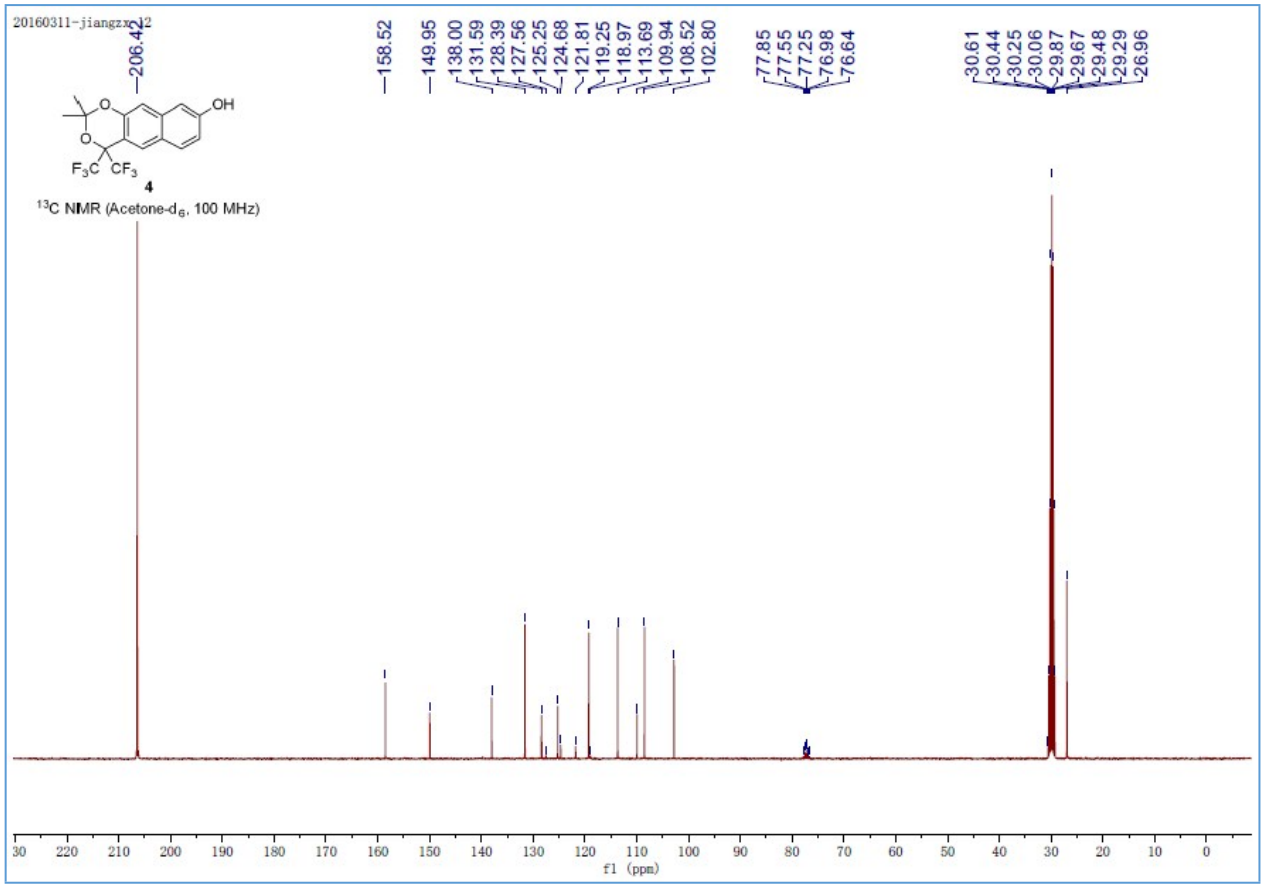

20160129-jiangzx-22
HO
OH
HO
F3C CF3
3
19F NMR (Acetone-d6, 376 MHz)
-76.10
-164.90
190 170 150 130 110 90 80 70 60 50 40 30 20 10 0 -20 -40 -60 -80 -100 -120 -140 -160 -180
f1 (ppm)

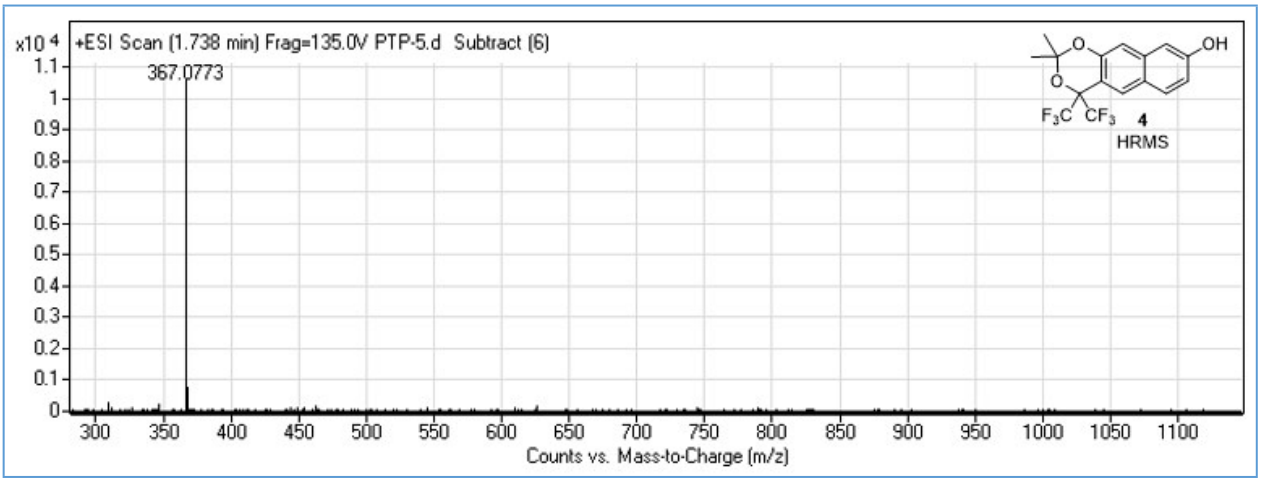

20151214-jiangzx-5
208.99
158.25
154.48
137.61
131.53
130.27
128.57
125.70
124.06
122.84
119.96
118.39
114.23
111.70
107.86
81.33
81.03
80.73
80.44
80.14
30.47
30.27
30.08
29.89
29.70
29.50
29.31
HO
OH
HO
F3C CF3
3
13C NMR (Acetone-d6, 100 MHz)
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

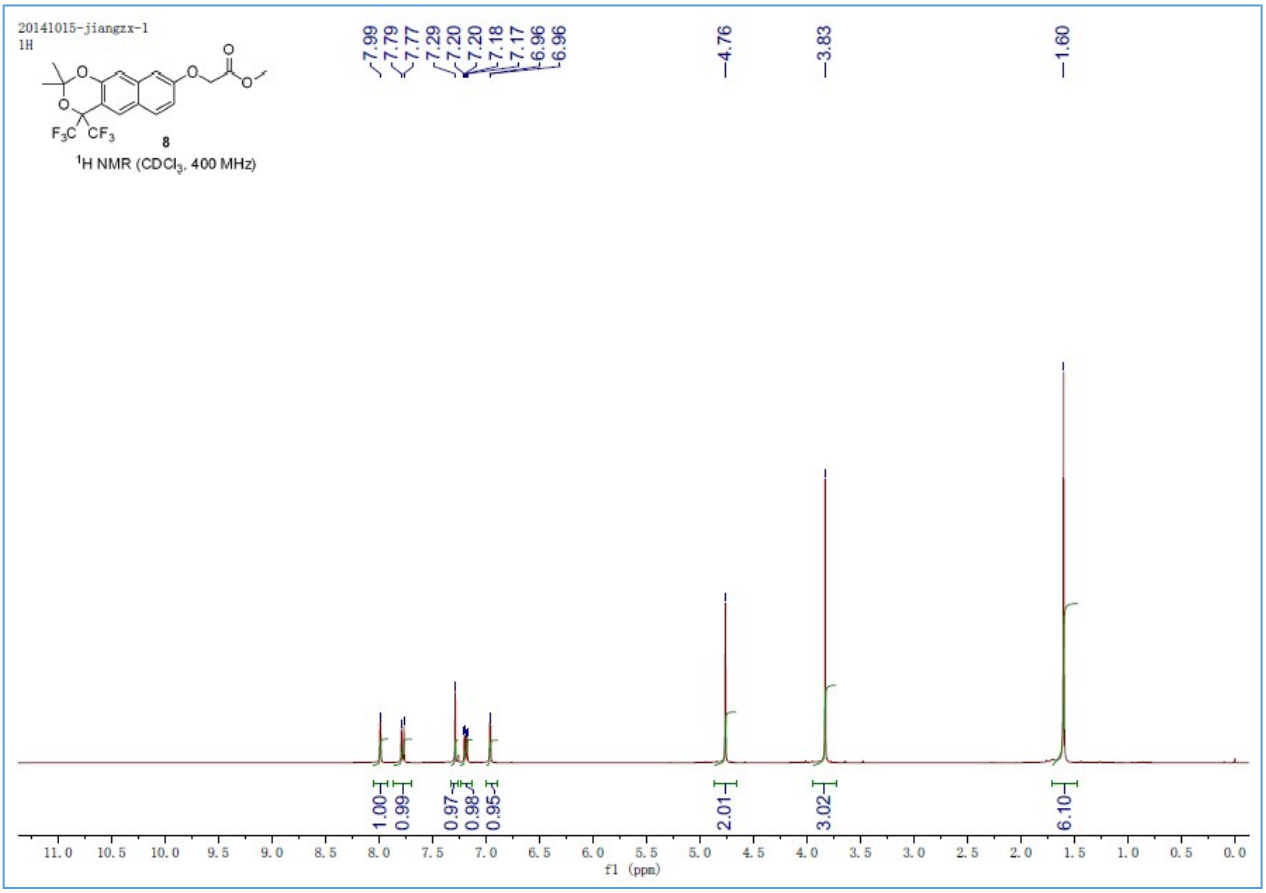

x10 3
+ESI Scan (1.746 min) Frag=135.0V PTP-4.d Subtract (2)
327.0444
HO
OH
HO
F3C CF3
3
HRMS
Counts vs. Mass-to-Charge (m/z)

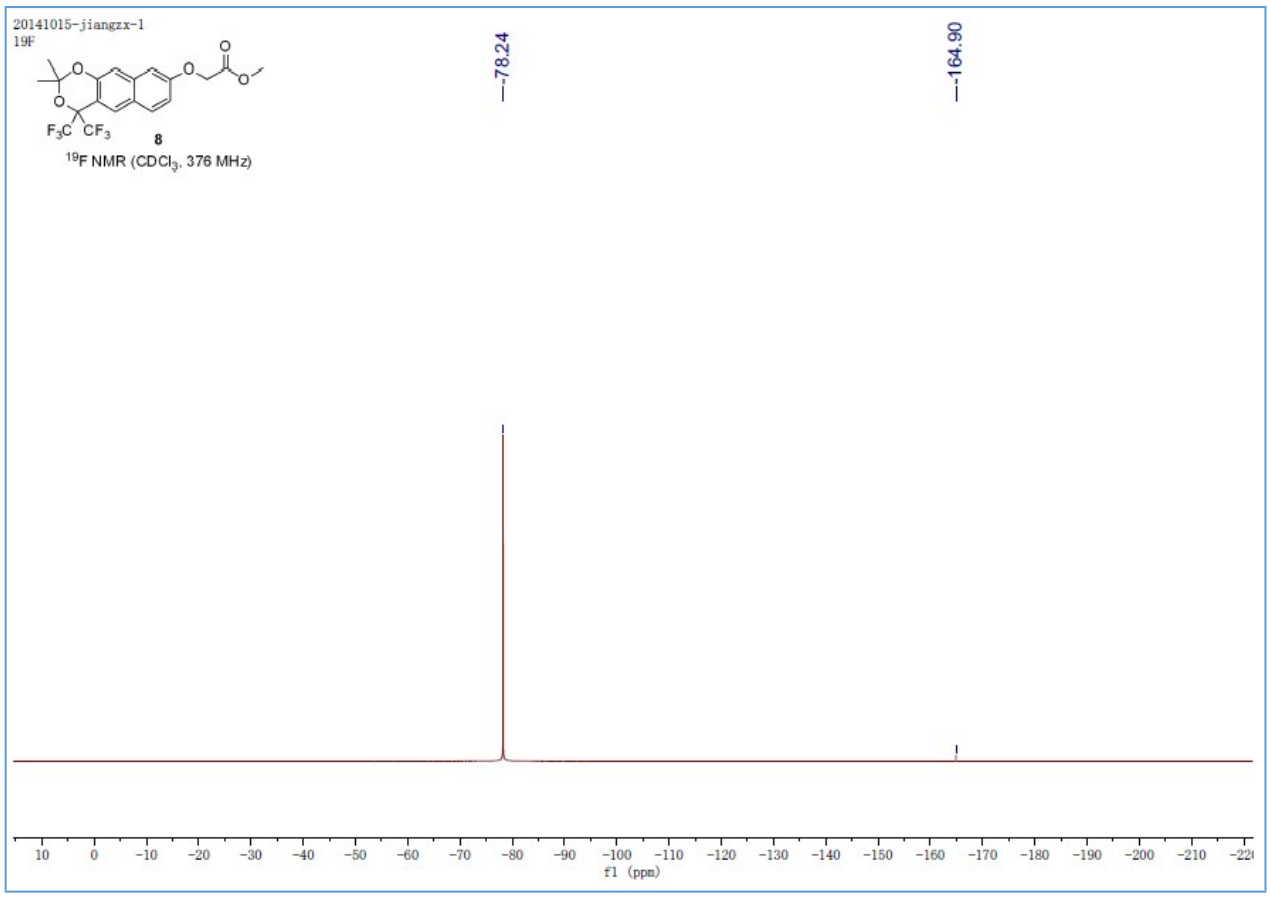

20160308-jiangzx-20
OH
F3C CF3
4
1H NMR (Acetone-d6, 400 MHz)
f1 (ppm)

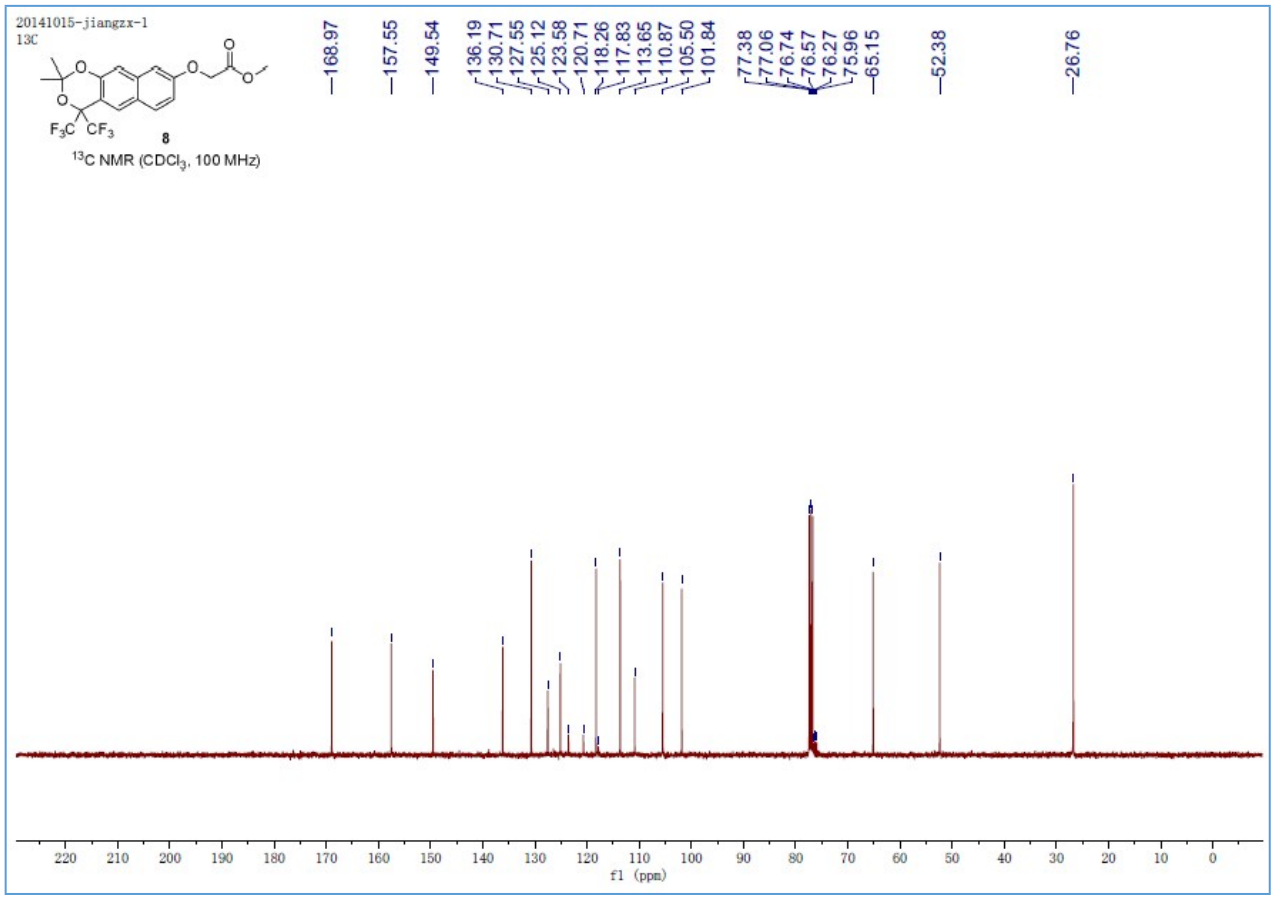

20140618-jiangzx-4
19F
OH
F3C CF3
4
19F NMR (Acetone-d6, 376 MHz)
-78.30
-164.90
f1 (ppm)

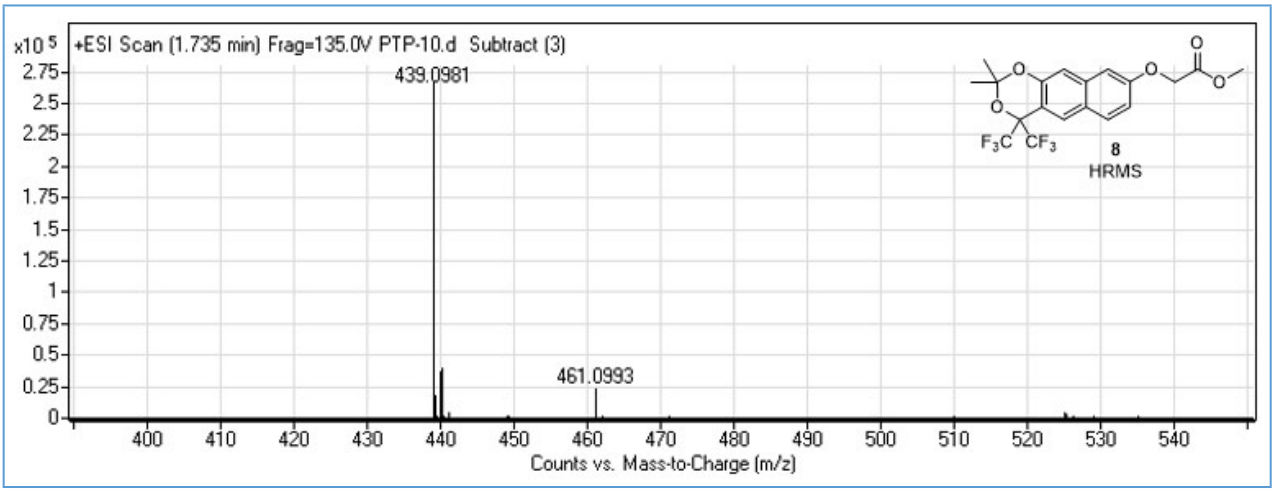

20160311-jiangzx-12
206.42
158.52
149.95
138.00
131.59
128.39
127.56
125.25
124.68
121.81
119.25
118.97
113.69
109.94
108.52
102.80
77.85
77.55
77.25
76.98
76.64
30.61
30.44
30.25
30.06
29.87
29.67
29.48
29.29
26.96
OH
F3C CF3
4
13C NMR (Acetone-d6, 100 MHz)
f1 (ppm)

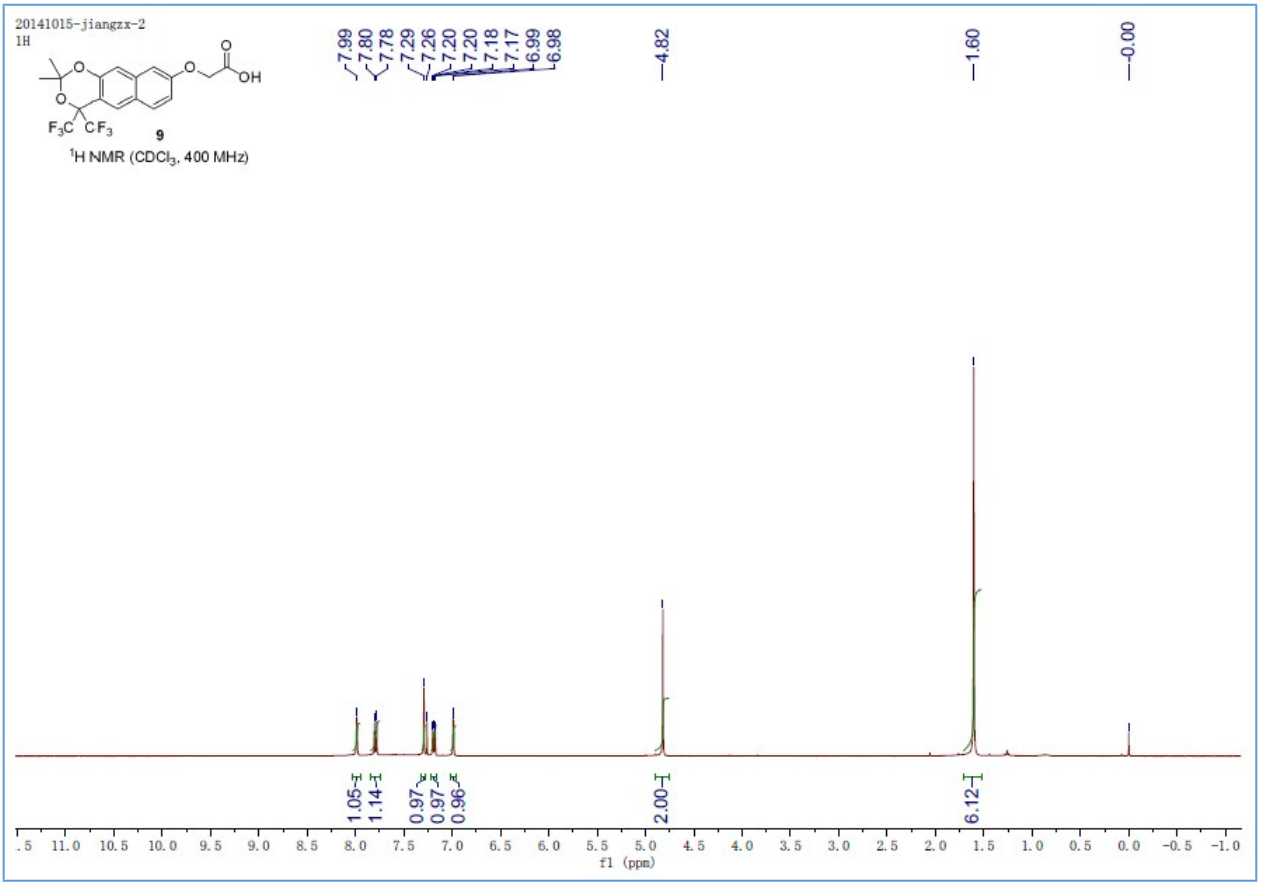

x10 4
+ESI Scan (1.738 min) Frag=135.0V PTP-5.d Subtract (6)
367.0773
OH
F3C CF3
4
HRMS
Counts vs. Mass-to-Charge (m/z)

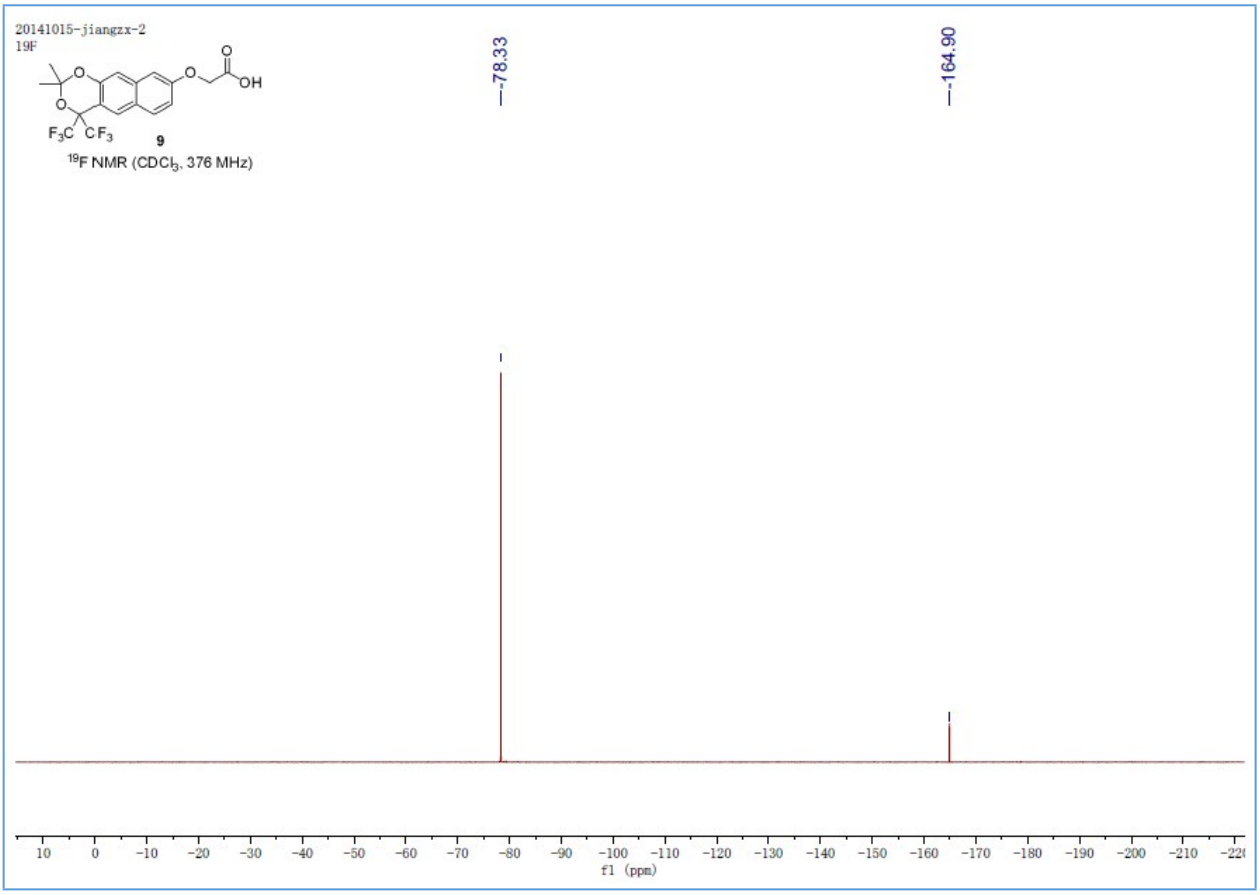

20141015-jiangzx-1
1H
8
1H NMR (CDCl3, 400 MHz)
7.99
7.79
7.77
7.29
7.20
7.20
7.18
7.17
6.96
6.96
4.76
3.83
1.60
1.00
0.99
0.97
0.98
0.95
2.01
3.02
6.10
f1 (ppm)

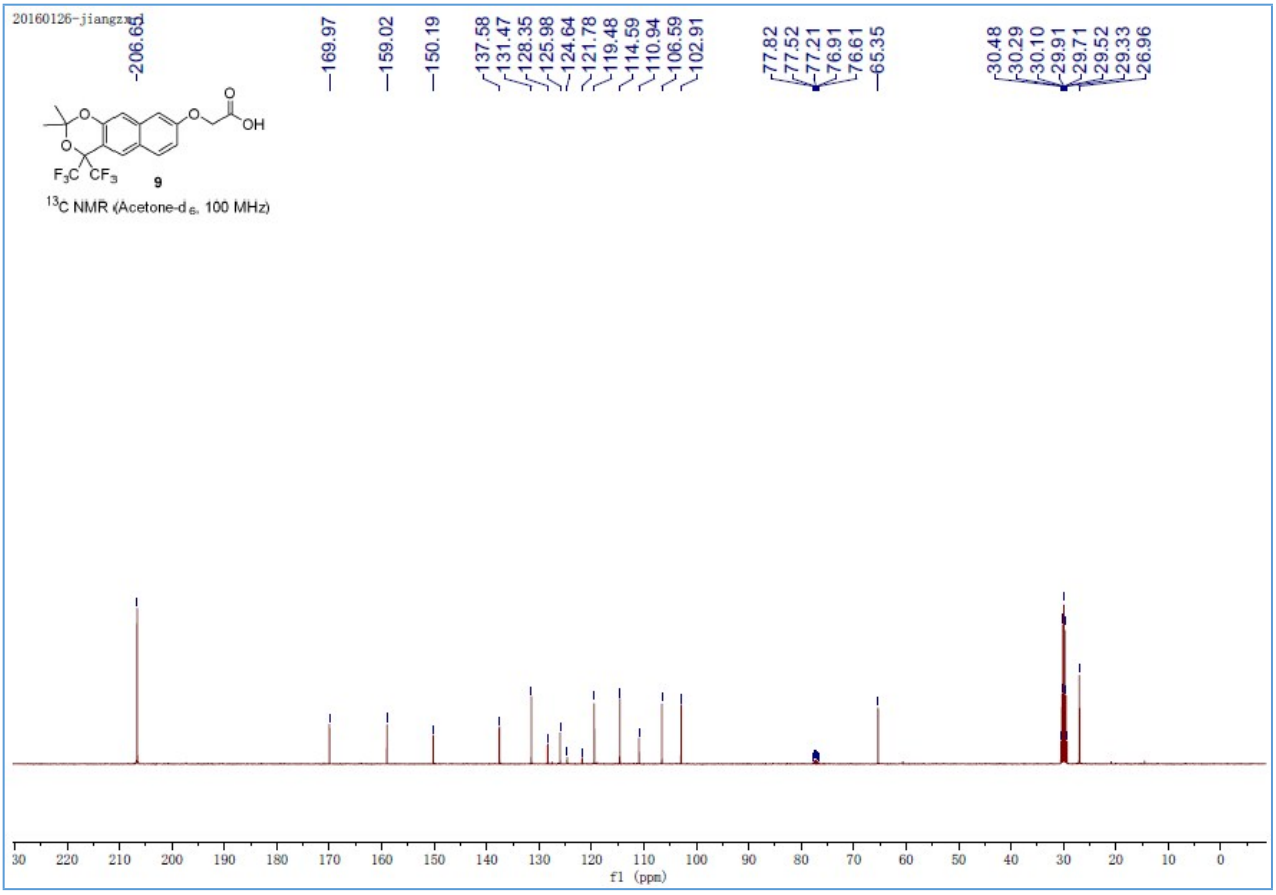

20141015-jiangzx-1
19F
8
^{19}F NMR ($CDCl_3$, 376 MHz)
-78.24
-164.90
f1 (ppm)

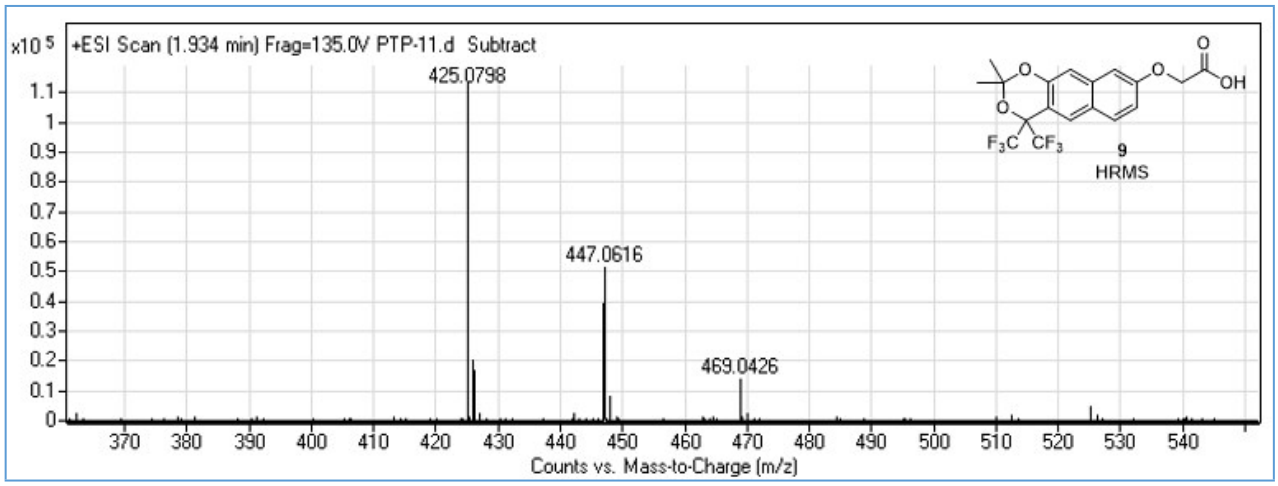

20141015-jiangzx-1
13C
8
^{13}C NMR ($CDCl_3$, 100 MHz)
168.97
157.55
149.54
136.19
130.71
127.55
125.12
123.58
120.71
118.26
117.83
113.65
110.87
105.50
101.84
77.38
77.06
76.74
76.57
76.27
75.96
65.15
52.38
26.76
f1 (ppm)

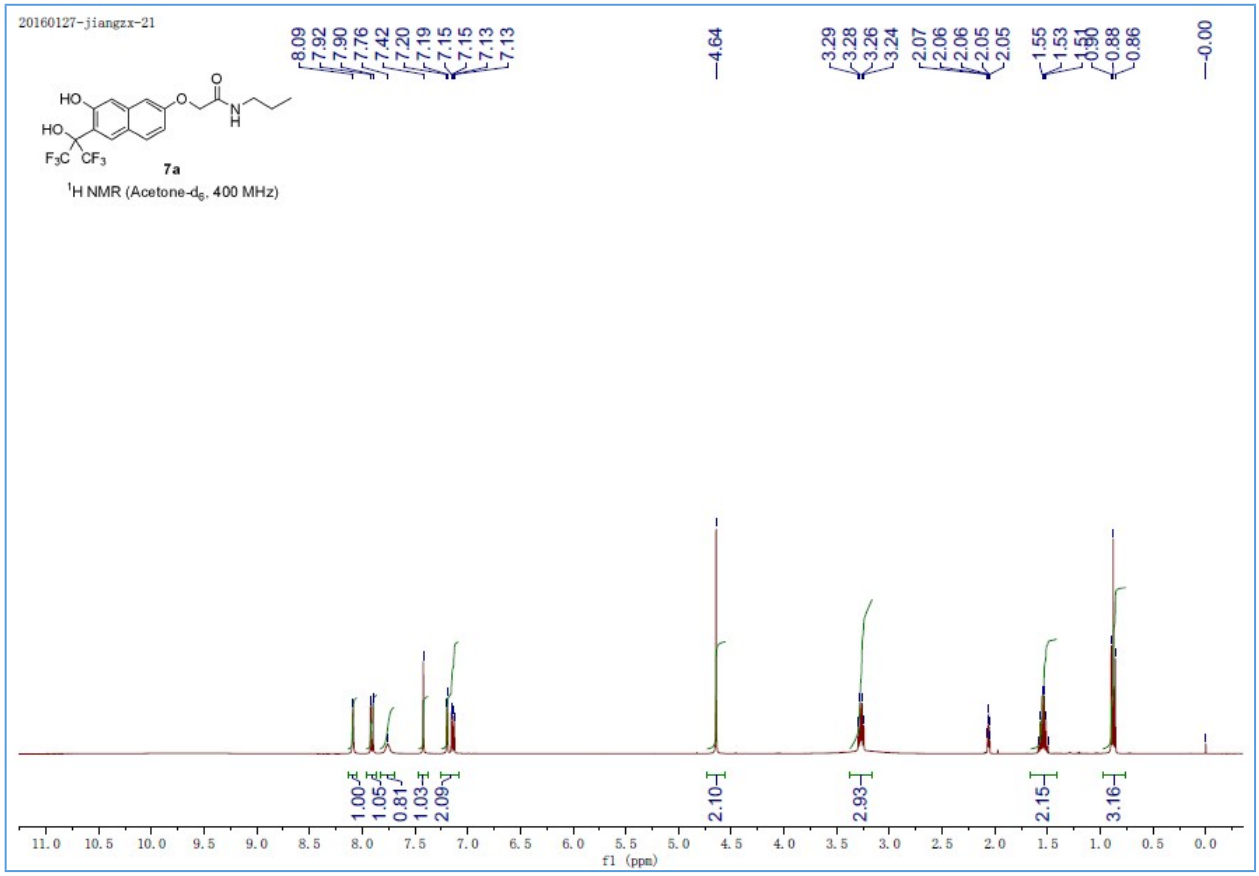

x10 5
+ESI Scan (1.735 min) Frag=135.0V PTP-10.d Subtract (3)
439.0981
461.0993
Counts vs. Mass-to-Charge (m/z)
8
HRMS

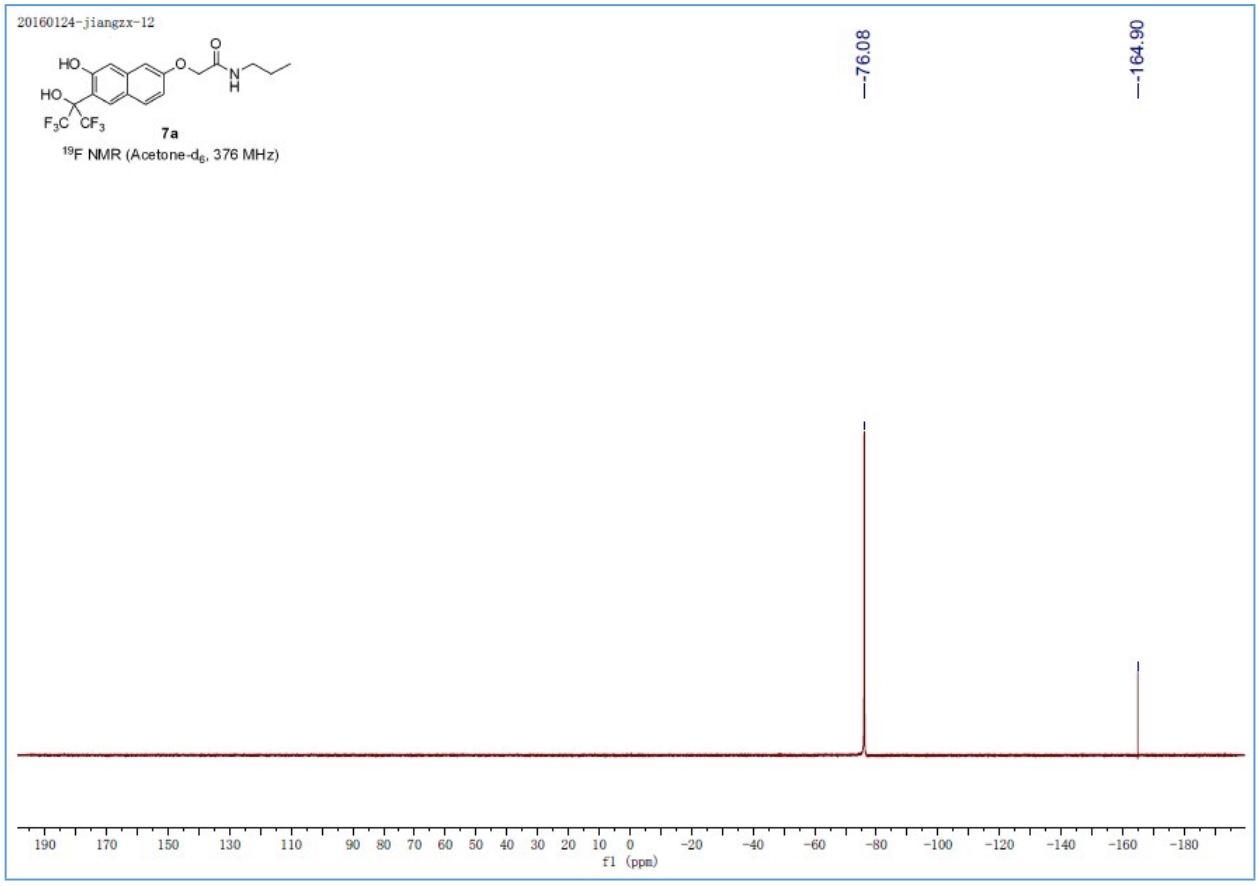

20141015-jiangzx-2
1H
9
1H NMR (CDCl3, 400 MHz)
7.99
7.80
7.78
7.29
7.26
7.20
7.20
7.18
7.17
6.99
6.98
4.82
1.60
0.00
1.05
1.14
0.97
0.97
0.96
2.00
6.12
f1 (ppm)

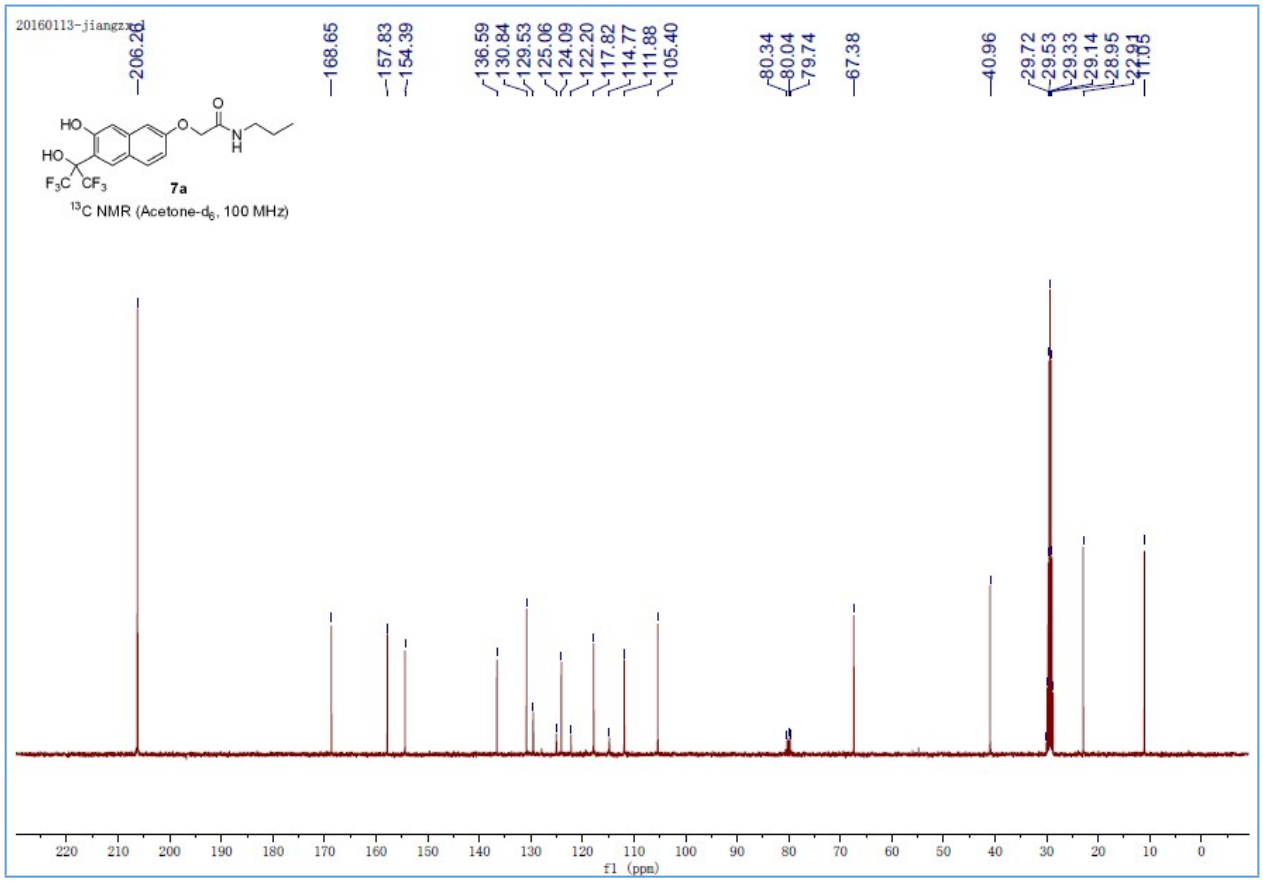

20141015-jiangzx-2
19F
-78.33
-164.90
9
19F NMR (CDCl3, 376 MHz)
f1 (ppm)

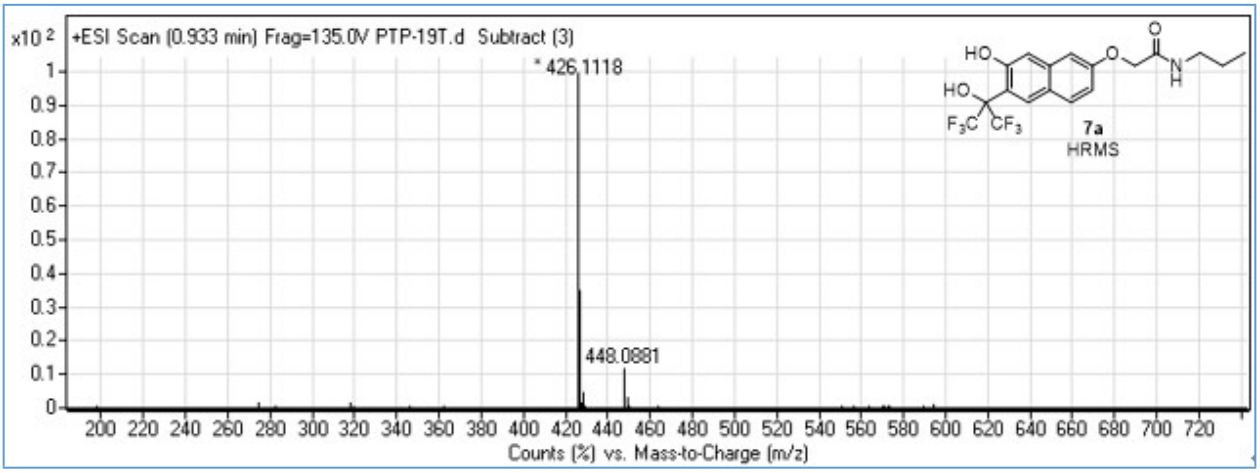

20160126-jiangzx-1
-206.60
169.97
159.02
150.19
137.58
131.47
128.35
125.98
124.64
121.78
119.48
114.59
110.94
106.59
102.91
77.82
77.52
77.21
76.91
76.61
65.35
30.48
30.29
30.10
29.91
29.71
29.52
29.33
26.96
9
13C NMR (Acetone-d6, 100 MHz)
f1 (ppm)

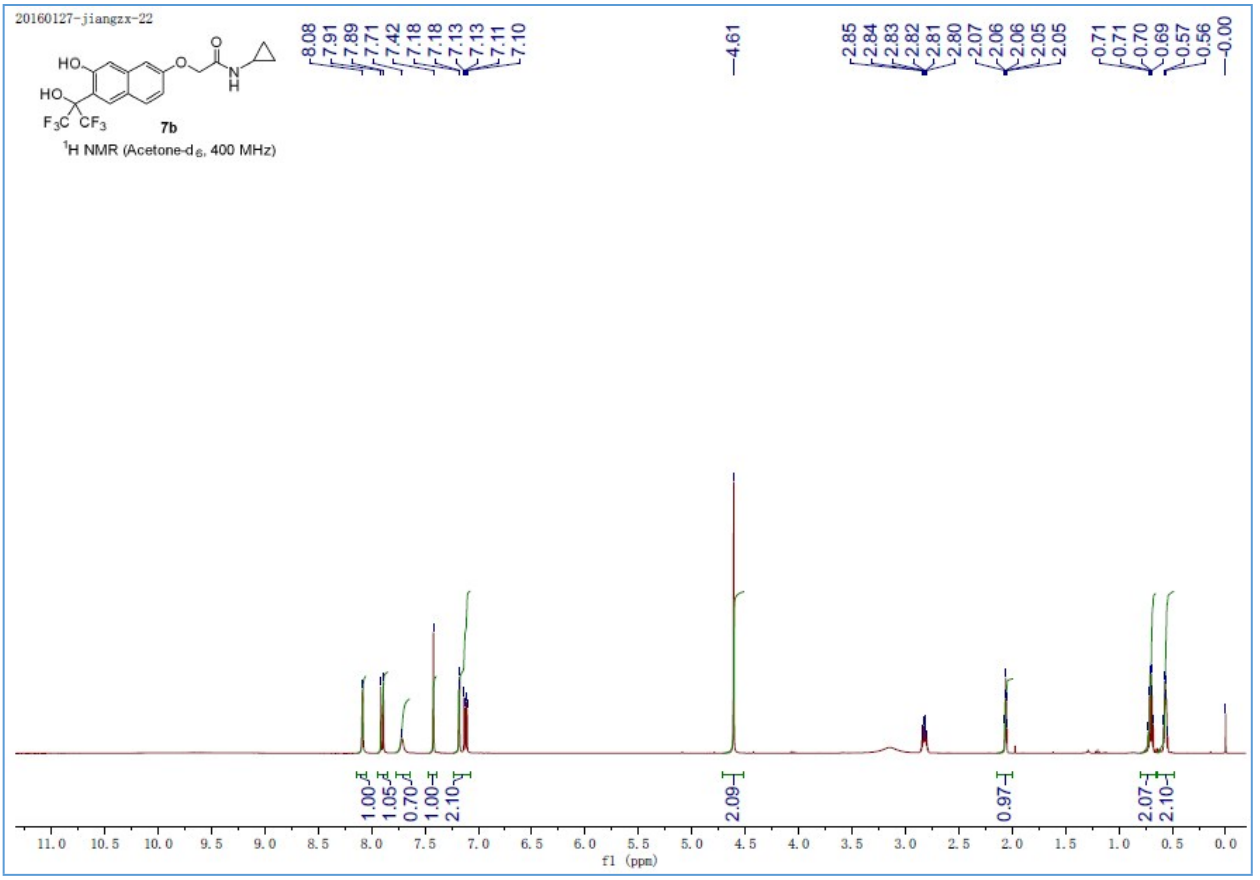

x10 5
+ESI Scan (1.934 min) Frag=135.0V PTP-11.d Subtract
425.0798
447.0616
469.0426
Counts vs. Mass-to-Charge (m/z)
9
HRMS

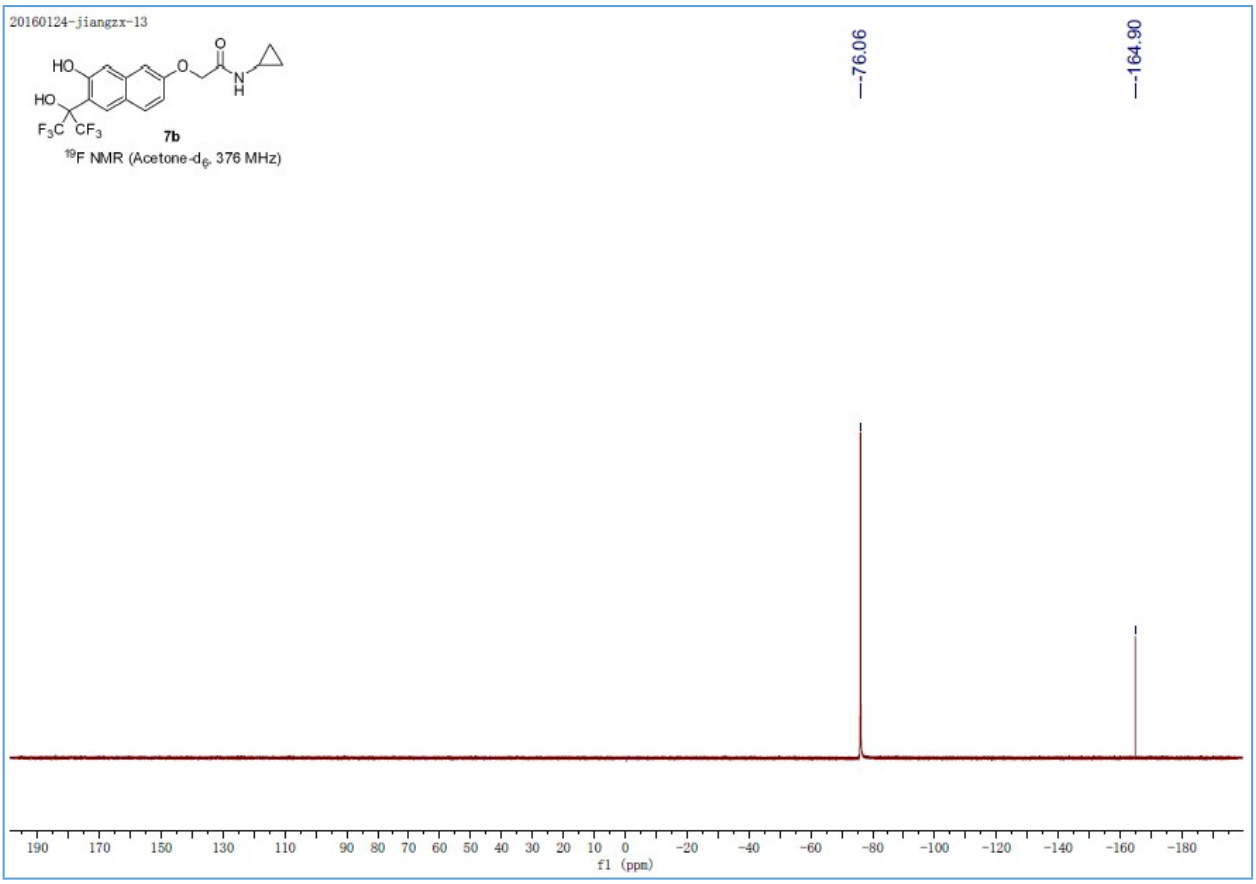

20160127-jiangzx-21
7a
1H NMR (Acetone-d6, 400 MHz)
f1 (ppm)

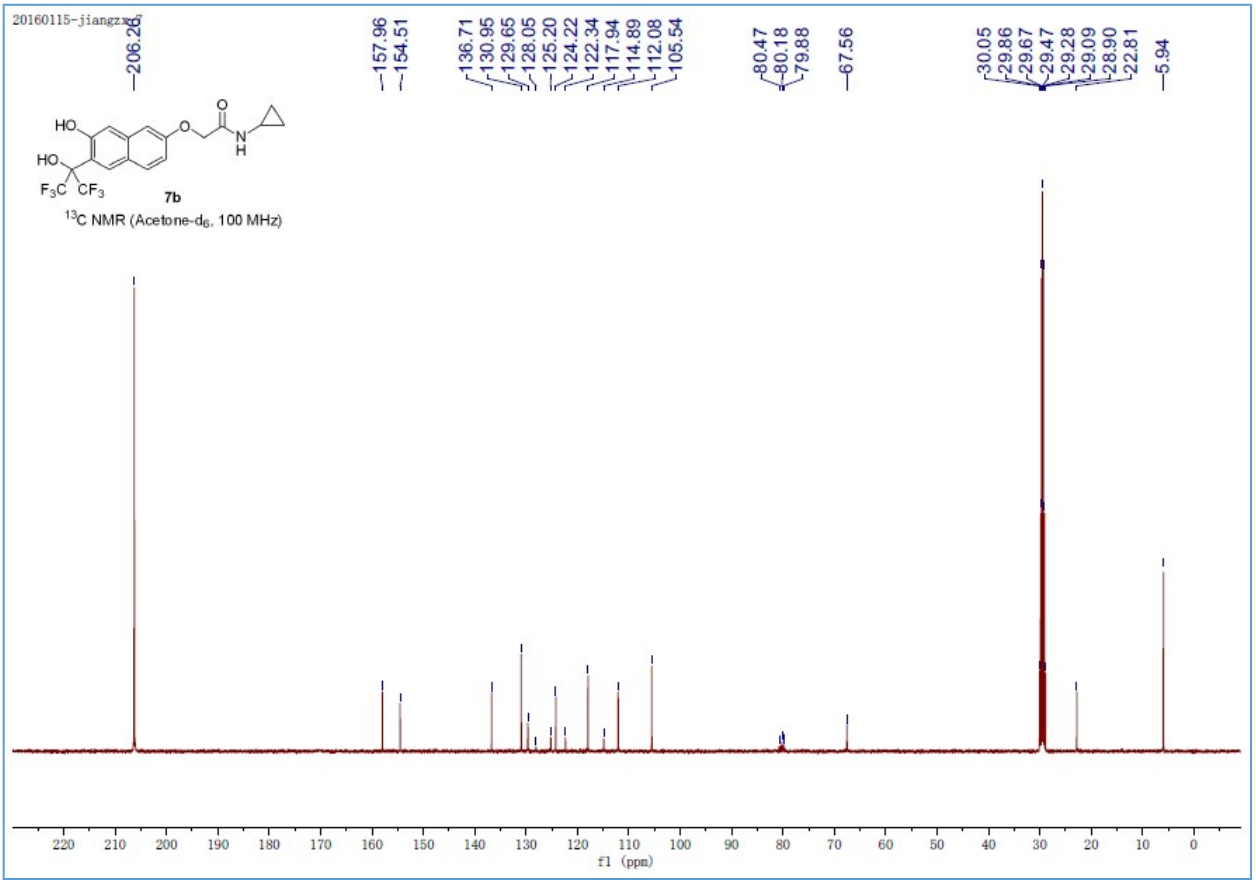

20160124-jiangzx-12
7a
19F NMR (Acetone-d6, 376 MHz)
-76.08
-164.90
f1 (ppm)

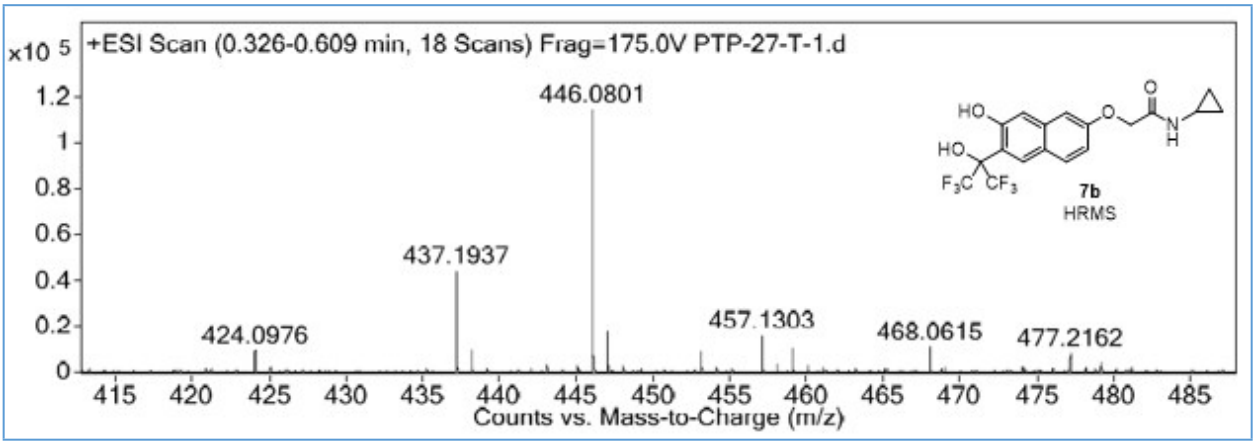

20160113-jiangzx
206.26
168.65
157.83
154.39
136.59
130.84
129.53
125.06
124.09
122.20
117.82
114.77
111.88
105.40
80.34
80.04
79.74
67.38
40.96
29.72
29.53
29.33
29.14
28.95
22.91
11.05
7a
13C NMR (Acetone-d6, 100 MHz)
f1 (ppm)

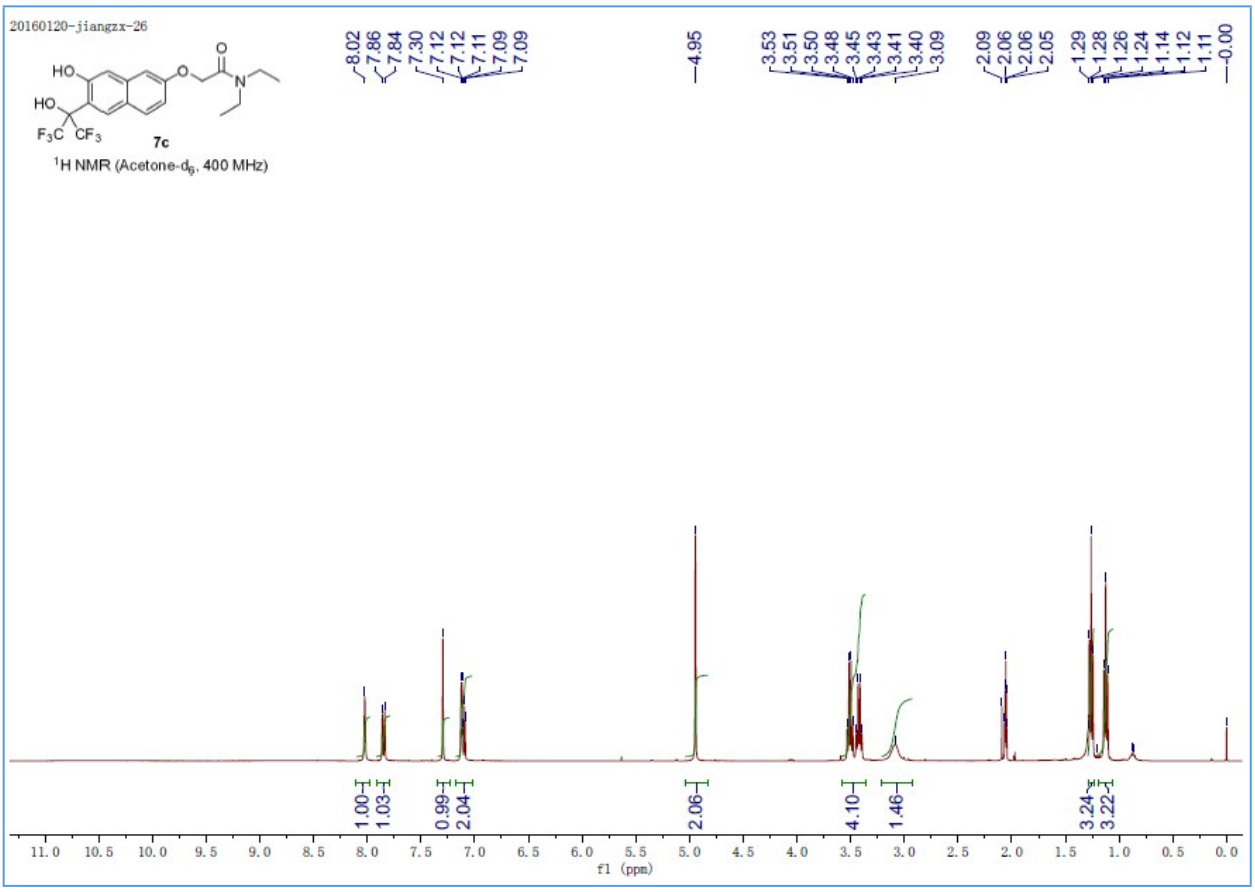

x10 2
+ESI Scan (0.933 min) Frag=135.0V PTP-19T.d Subtract (3)
* 426.1118
448.0881
HO
HO
F3C CF3
7a
HRMS
Counts (%) vs. Mass-to-Charge (m/z)

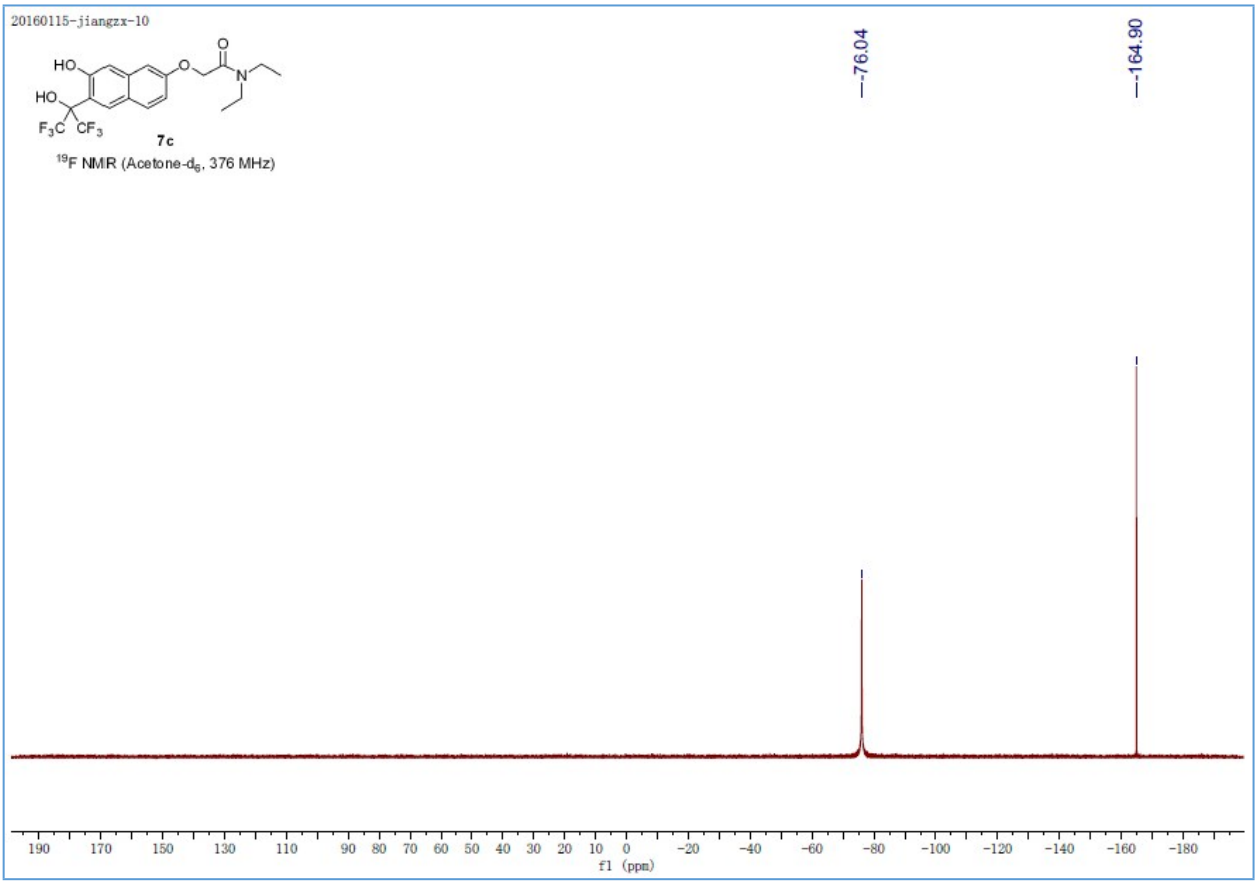

20160127-jiangzx-22
HO
HO
F3C CF3
7b
1H NMR (Acetone-d6, 400 MHz)
8.08
7.91
7.89
7.71
7.42
7.18
7.18
7.13
7.13
7.11
7.10
4.61
2.85
2.84
2.83
2.82
2.81
2.80
2.07
2.06
2.06
2.05
2.05
0.71
0.71
0.70
0.69
0.57
0.56
0.00
1.00
1.05
0.70
1.00
2.10
2.09
0.97
2.07
2.10
f1 (ppm)

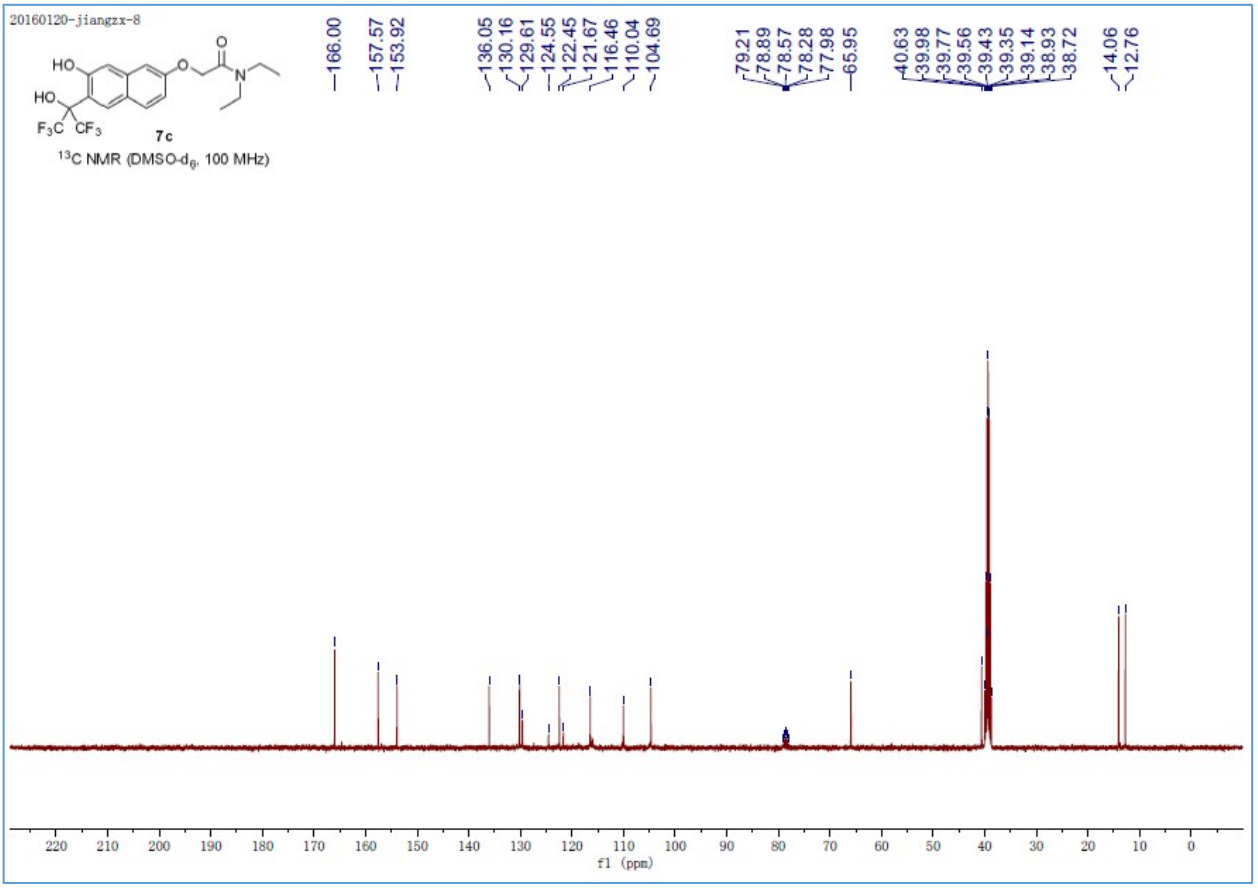

20160124-jiangzx-13
HO
HO
F3C CF3
7b
19F NMR (Acetone-d6, 376 MHz)
-76.06
-164.90
f1 (ppm)

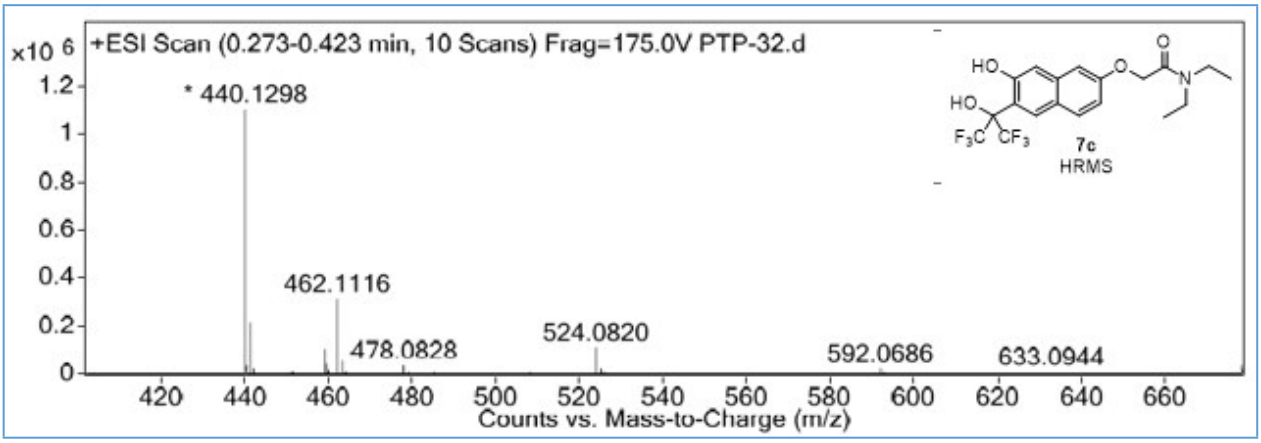

20160115-jiangzx-2
206.26
157.96
154.51
136.71
130.95
129.65
128.05
125.20
124.22
122.34
117.94
114.89
112.08
105.54
80.47
80.18
79.88
67.56
30.05
29.86
29.67
29.47
29.28
29.09
28.90
22.81
5.94
HO
HO
F3C CF3
7b
13C NMR (Acetone-d6, 100 MHz)
f1 (ppm)

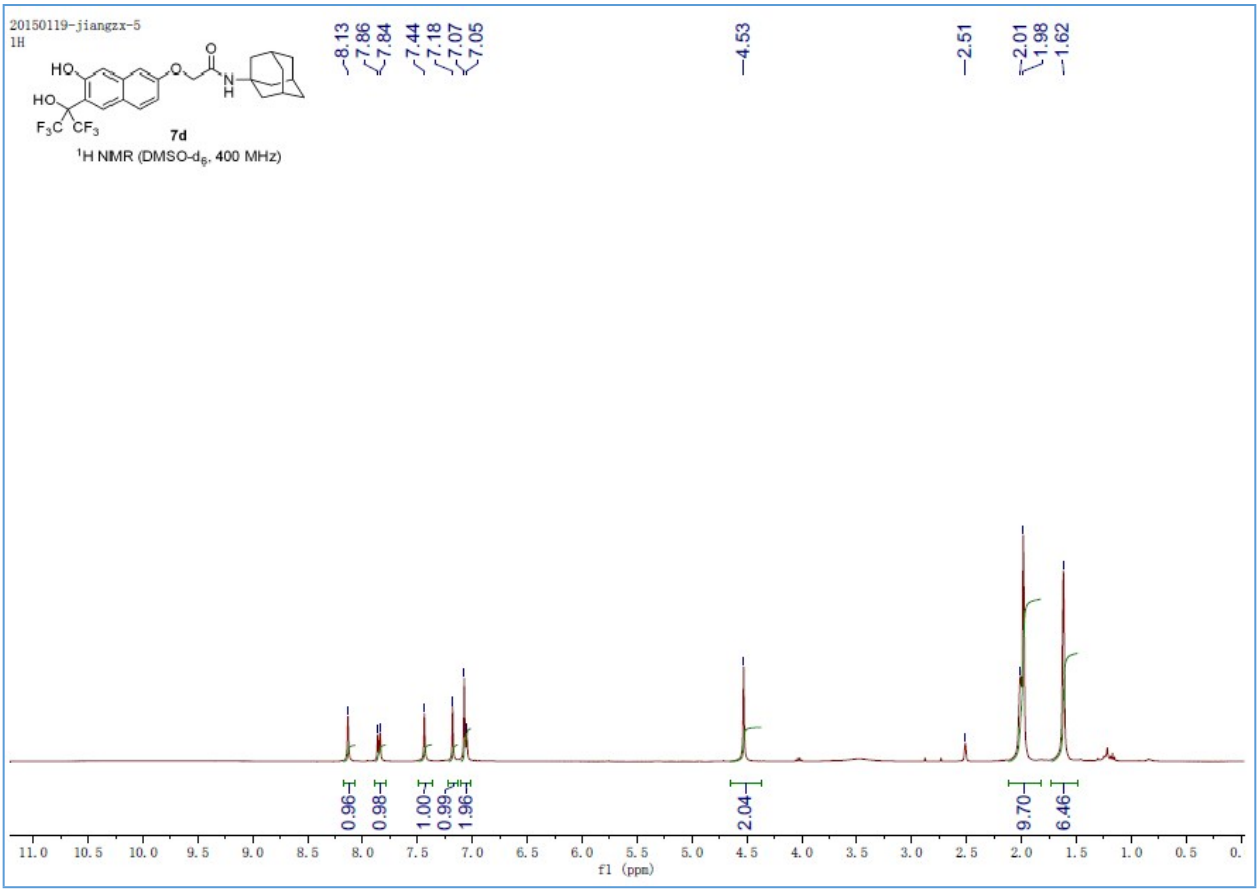

+ESI Scan (0.326-0.609 min, 18 Scans) Frag=175.0V PTP-27-T-1.d
x10 5
446.0801
437.1937
424.0976
457.1303
468.0615
477.2162
Counts vs. Mass-to-Charge (m/z)
7b
HRMS

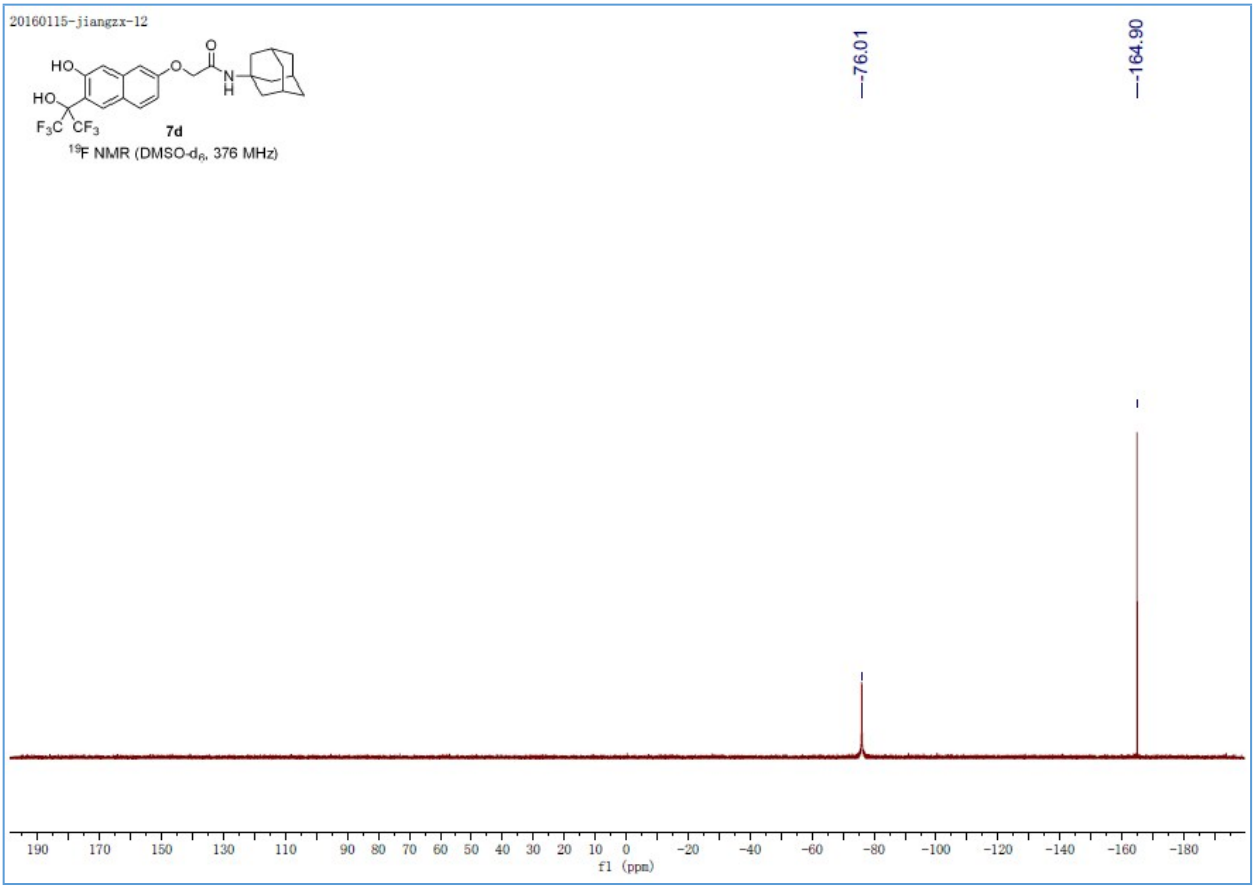

20160120-jiangzx-26
7c
1H NMR (Acetone-d6, 400 MHz)
f1 (ppm)

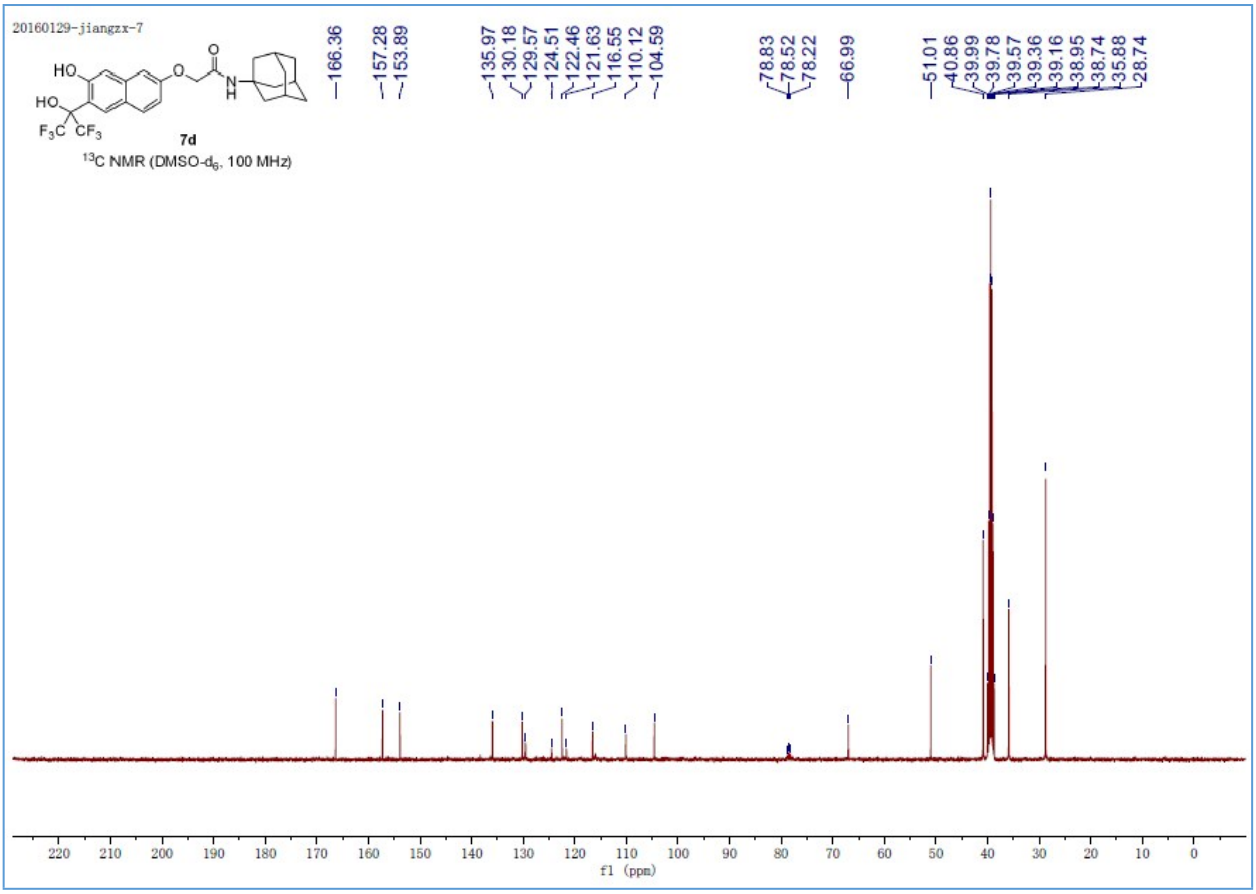

20160115-jiangzx-10
HO
HO
F3C CF3
O
O
N
7c
19F NMR (Acetone-d6, 376 MHz)
-76.04
-164.90
190 170 150 130 110 90 80 70 60 50 40 30 20 10 0 -20 -40 -60 -80 -100 -120 -140 -160 -180
f1 (ppm)

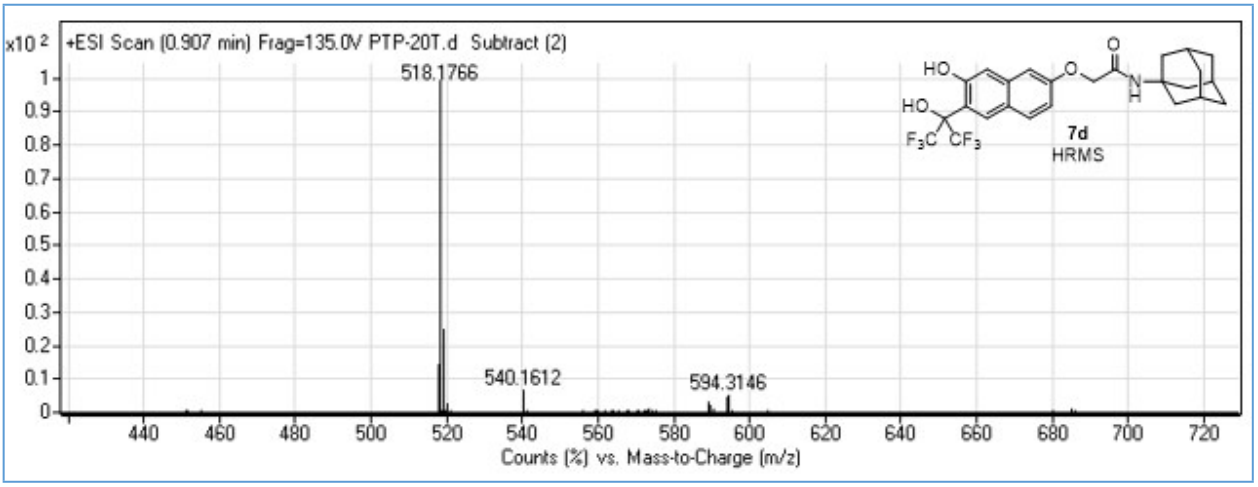

20160120-jiangzx-8
HO
HO
F3C CF3
O
O
N
7c
13C NMR (DMSO-d6, 100 MHz)
166.00
157.57
153.92
136.05
130.16
129.61
124.55
122.45
121.67
116.46
110.04
104.69
79.21
78.89
78.57
78.28
77.98
65.95
40.63
39.98
39.77
39.56
39.43
39.35
39.14
38.93
38.72
14.06
12.76
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

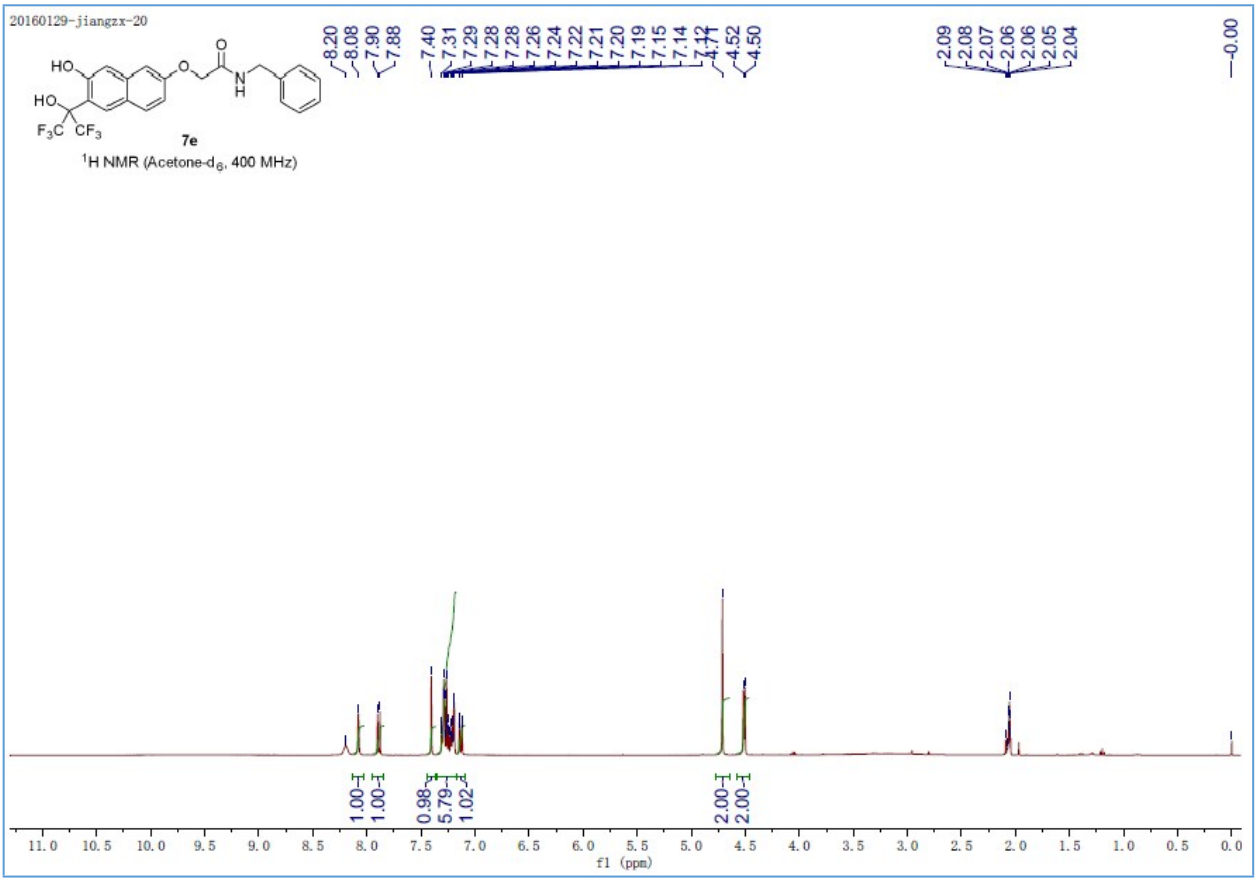

+ESI Scan (0.273-0.423 min, 10 Scans) Frag=175.0V PTP-32.d
x10 6
* 440.1298
462.1116
478.0828
524.0820
592.0686
633.0944
Counts vs. Mass-to-Charge (m/z)
7c
HRMS

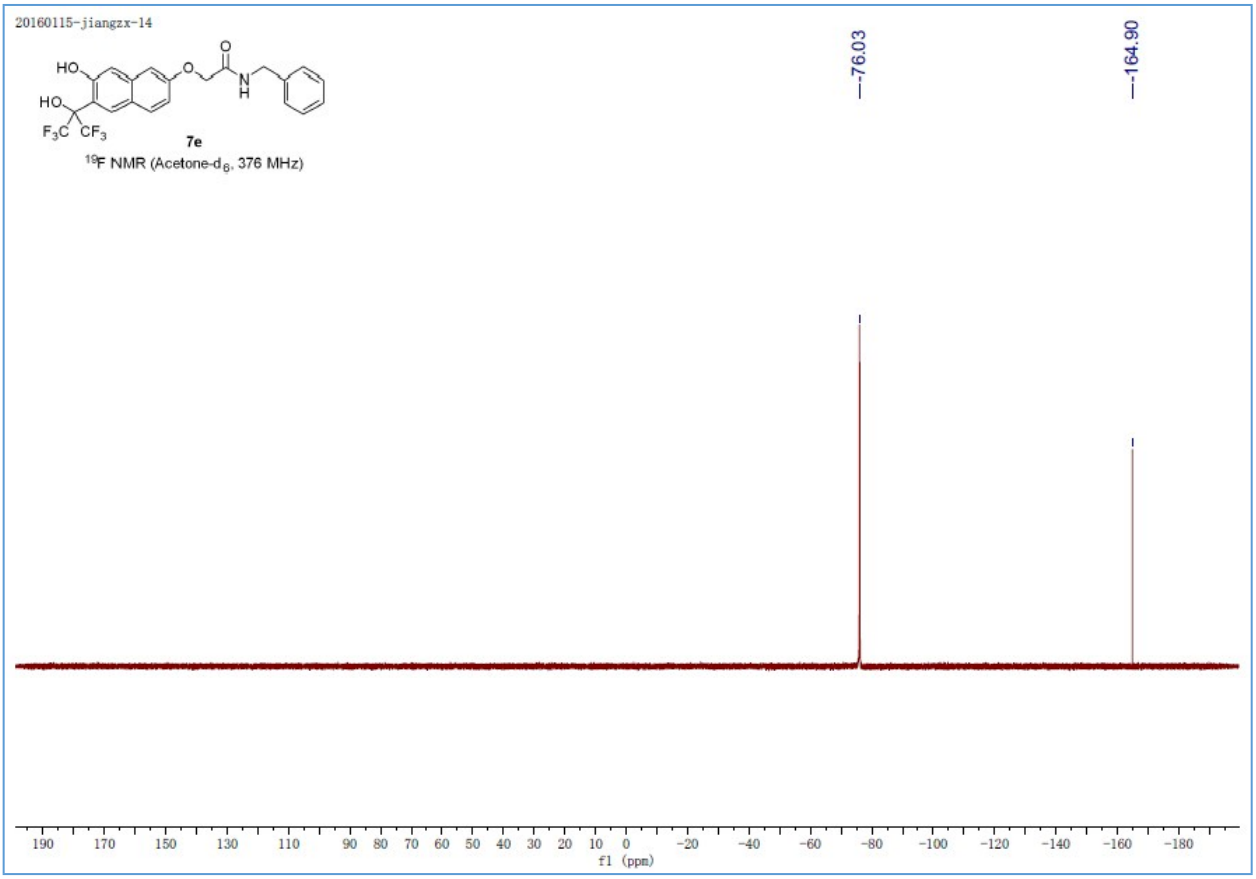

20150119-jiangzx-5
1H
7d
1H NMR (DMSO-d6, 400 MHz)
8.13
7.86
7.84
7.44
7.18
7.07
7.05
4.53
2.51
2.01
1.98
1.62
0.96
0.98
1.00
0.99
1.96
2.04
9.70
6.46
f1 (ppm)

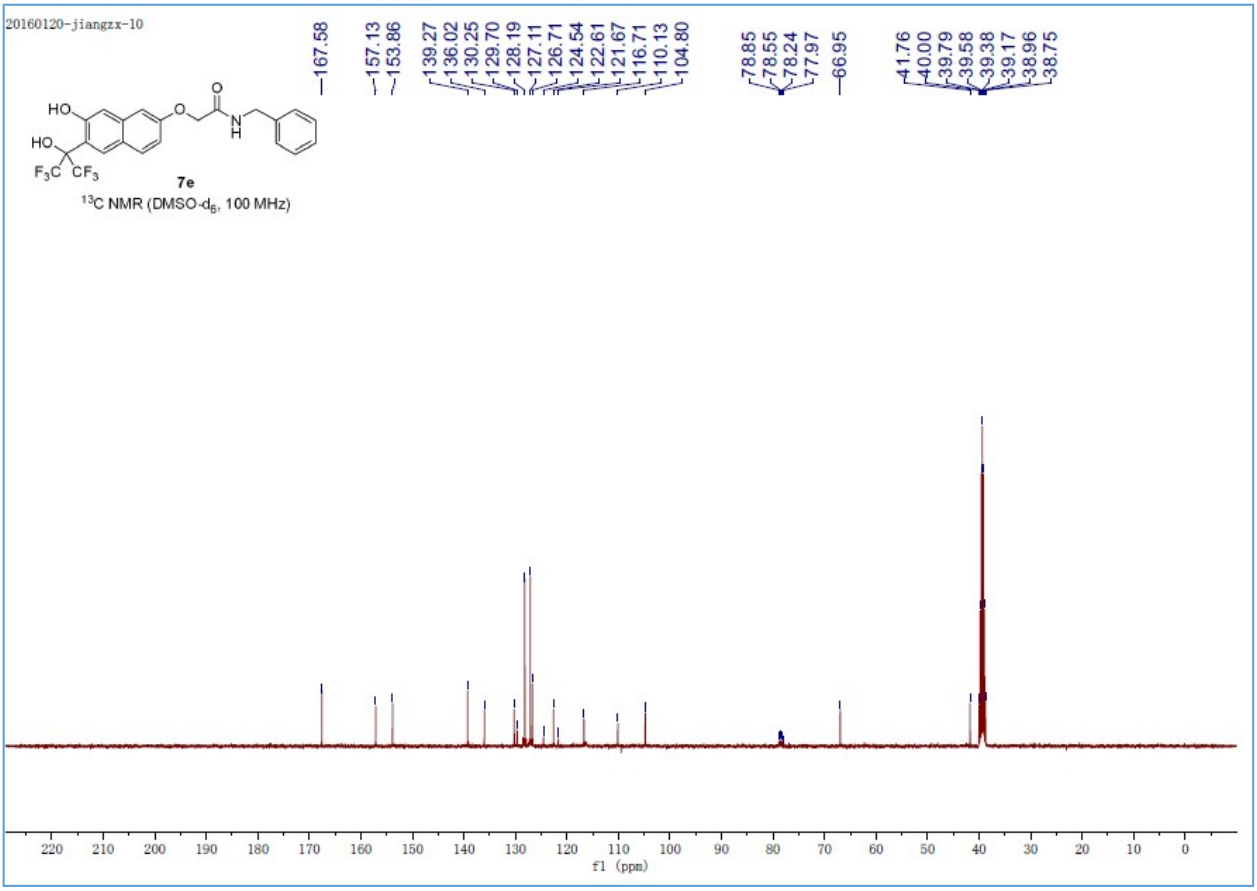

20160115-jiangzx-12
HO
HO
F3C CF3
7d
19F NMR (DMSO-d6, 376 MHz)
-76.01
-164.90
f1 (ppm)

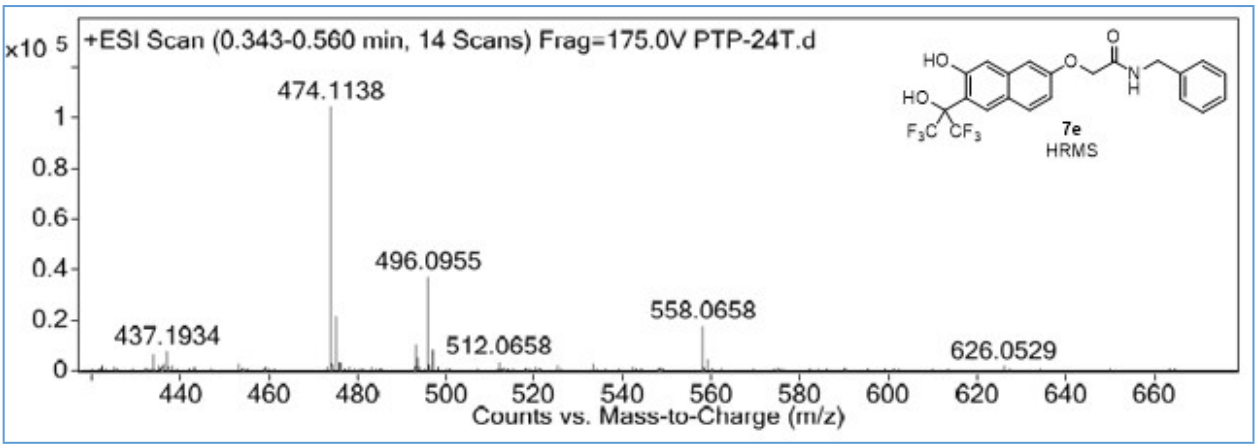

20160129-jiangzx-7
HO
HO
F3C CF3
7d
13C NMR (DMSO-d6, 100 MHz)
166.36
157.28
153.89
135.97
130.18
129.57
124.51
122.46
121.63
116.55
110.12
104.59
78.83
78.52
78.22
66.99
51.01
40.86
39.99
39.78
39.57
39.36
39.16
38.95
38.74
35.88
28.74
f1 (ppm)

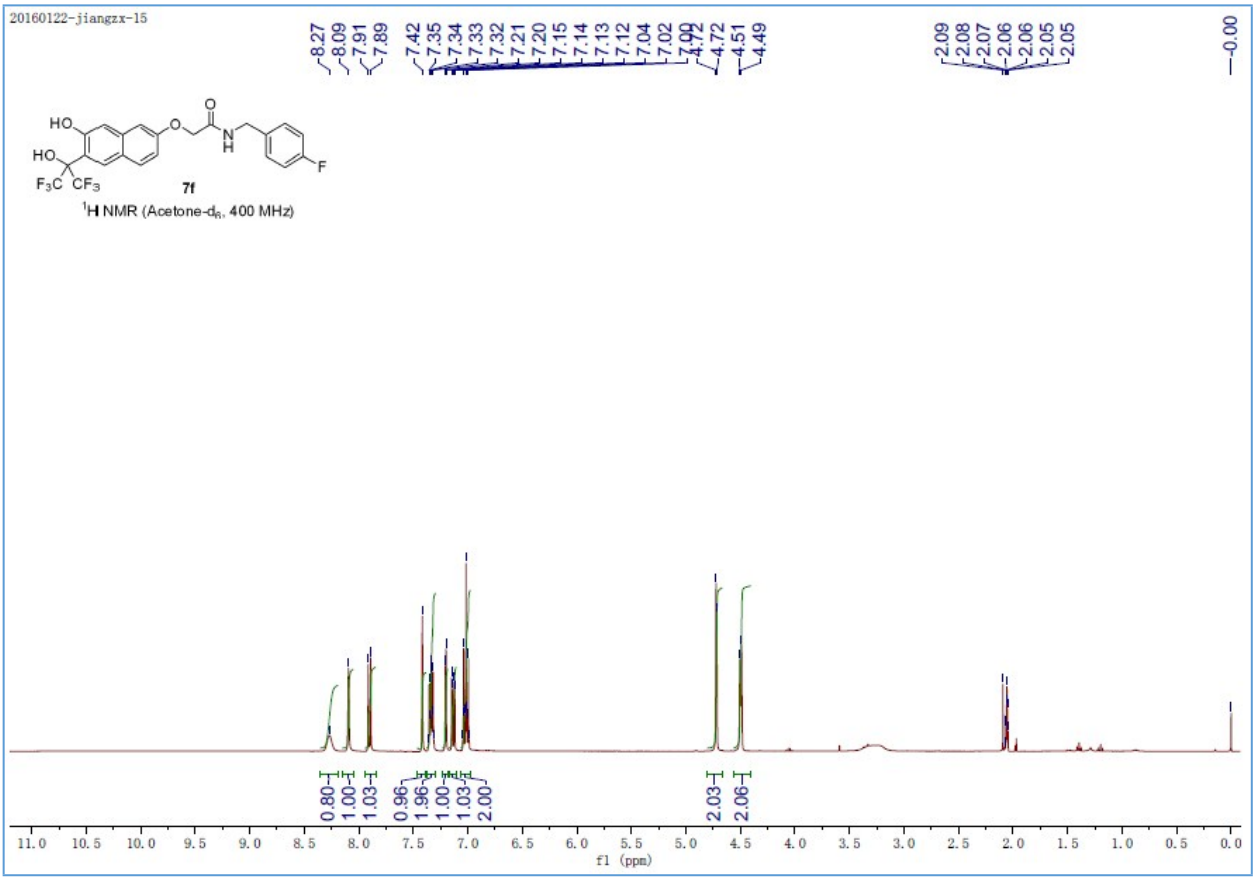

x10 2
+ESI Scan (0.907 min) Frag=135.0V PTP-20T.d Subtract (2)
518.1766
540.1612
594.3146
HO
HO
F3C CF3
O
O
N
H
7d
HRMS
Counts (%) vs. Mass-to-Charge (m/z)

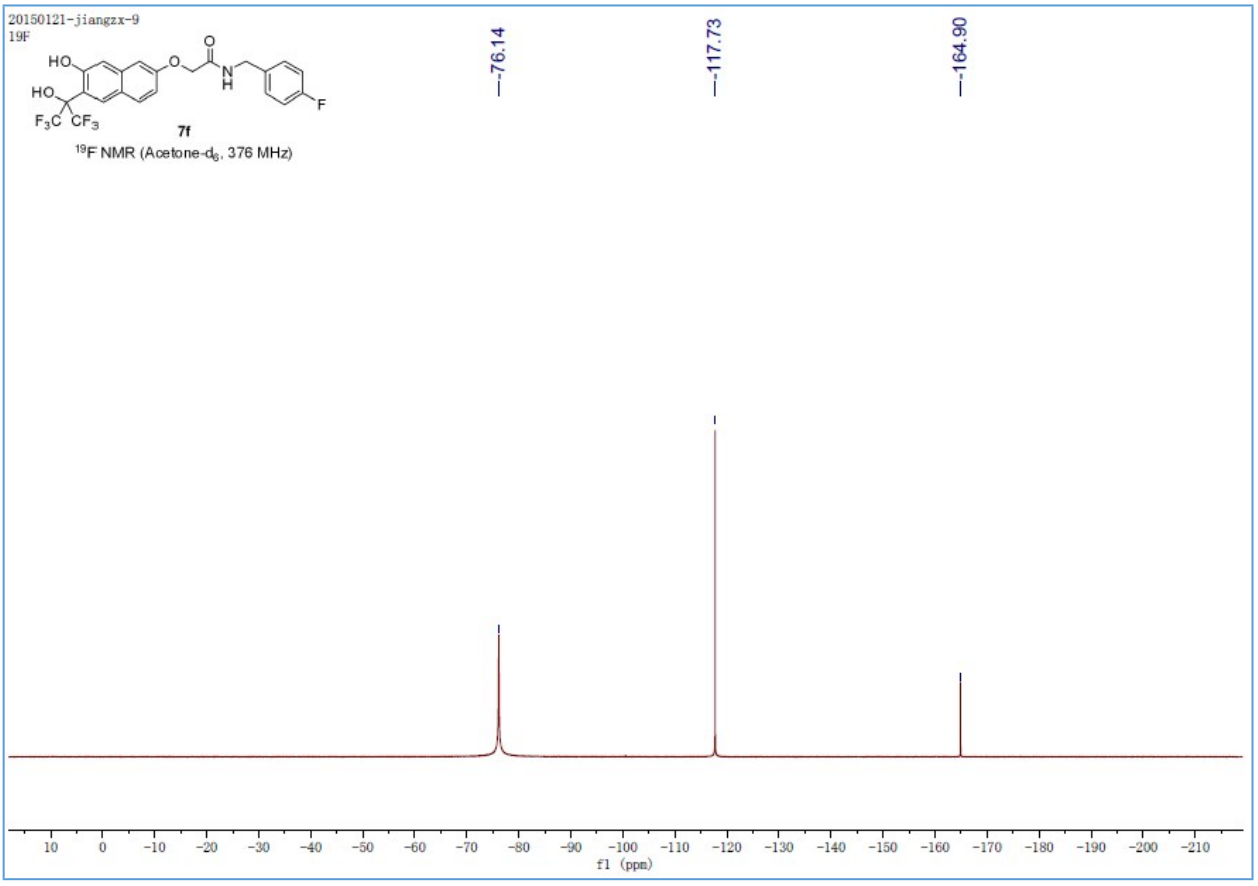

20160129-jiangzx-20
HO
HO
F3C CF3
O
O
N
H
7e
1H NMR (Acetone-d6, 400 MHz)
8.20
8.08
7.90
7.88
7.40
7.31
7.29
7.28
7.28
7.26
7.24
7.22
7.21
7.20
7.19
7.15
7.14
4.52
4.50
2.09
2.08
2.07
2.06
2.06
2.05
2.04
0.00
1.00
1.00
0.98
5.79
1.02
2.00
2.00
f1 (ppm)

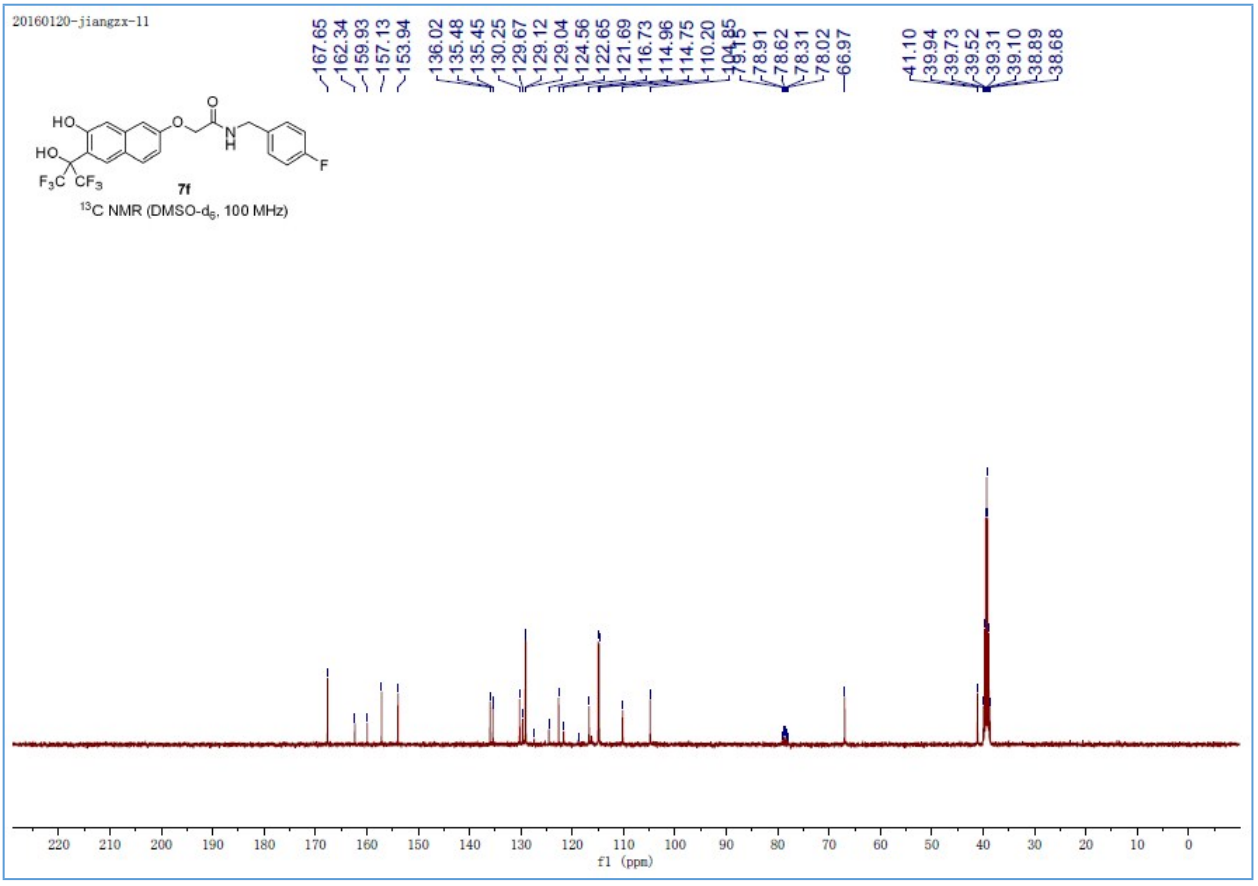

20160115-jiangzx-14
HO
HO
F3C CF3
O
O
N
H
7e
19F NMR (Acetone-d6, 376 MHz)
-76.03
-164.90
190 170 150 130 110 90 80 70 60 50 40 30 20 10 0 -20 -40 -60 -80 -100 -120 -140 -160 -180
f1 (ppm)

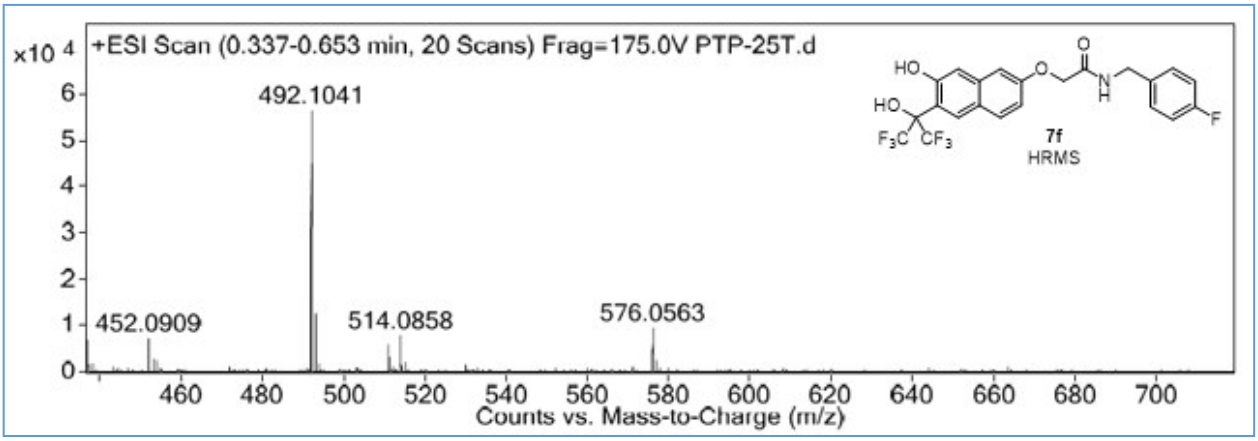

20160120-jiangzx-10
HO
HO
F3C CF3
O
O
N
H
7e
13C NMR (DMSO-d6, 100 MHz)
167.58
157.13
153.86
139.27
136.02
130.25
129.70
128.19
127.11
126.71
124.54
122.61
121.67
116.71
110.13
104.80
78.85
78.55
78.24
77.97
66.95
41.76
40.00
39.79
39.58
39.38
39.17
38.96
38.75
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

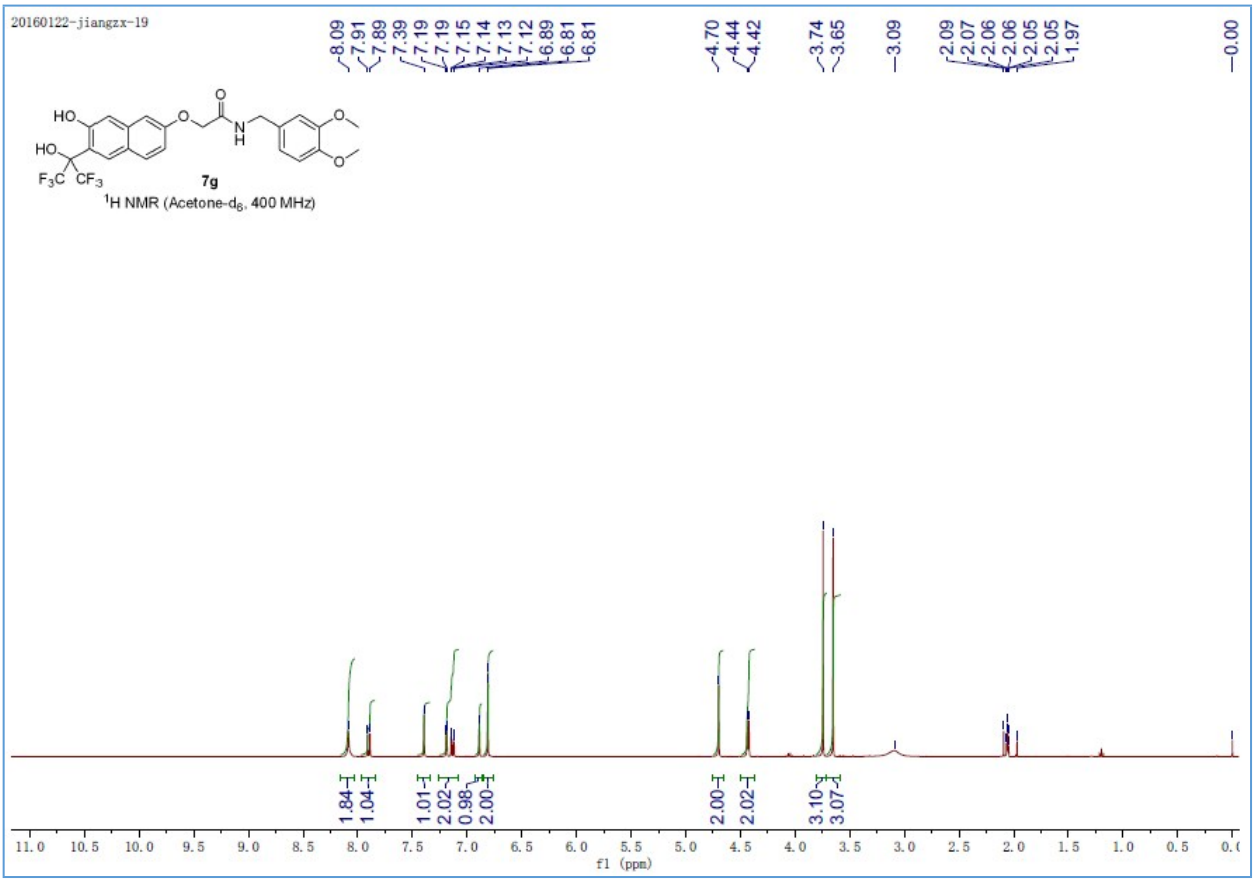

+ESI Scan (0.343-0.560 min, 14 Scans) Frag=175.0V PTP-24T.d
x10 5
474.1138
496.0955
558.0658
437.1934
512.0658
626.0529
Counts vs. Mass-to-Charge (m/z)
7e
HRMS

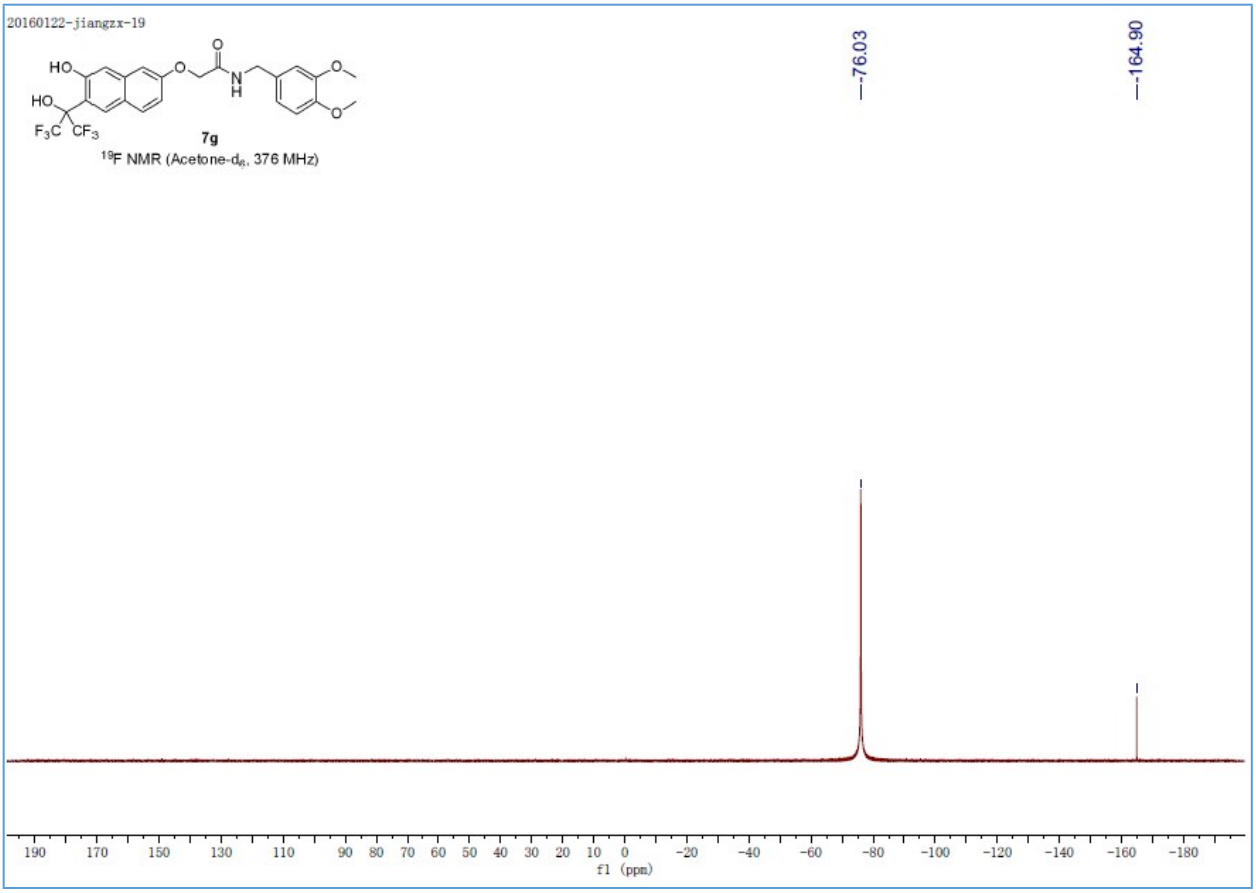

20160122-jiangzx-15
7f
1H NMR (Acetone-d6, 400 MHz)
f1 (ppm)

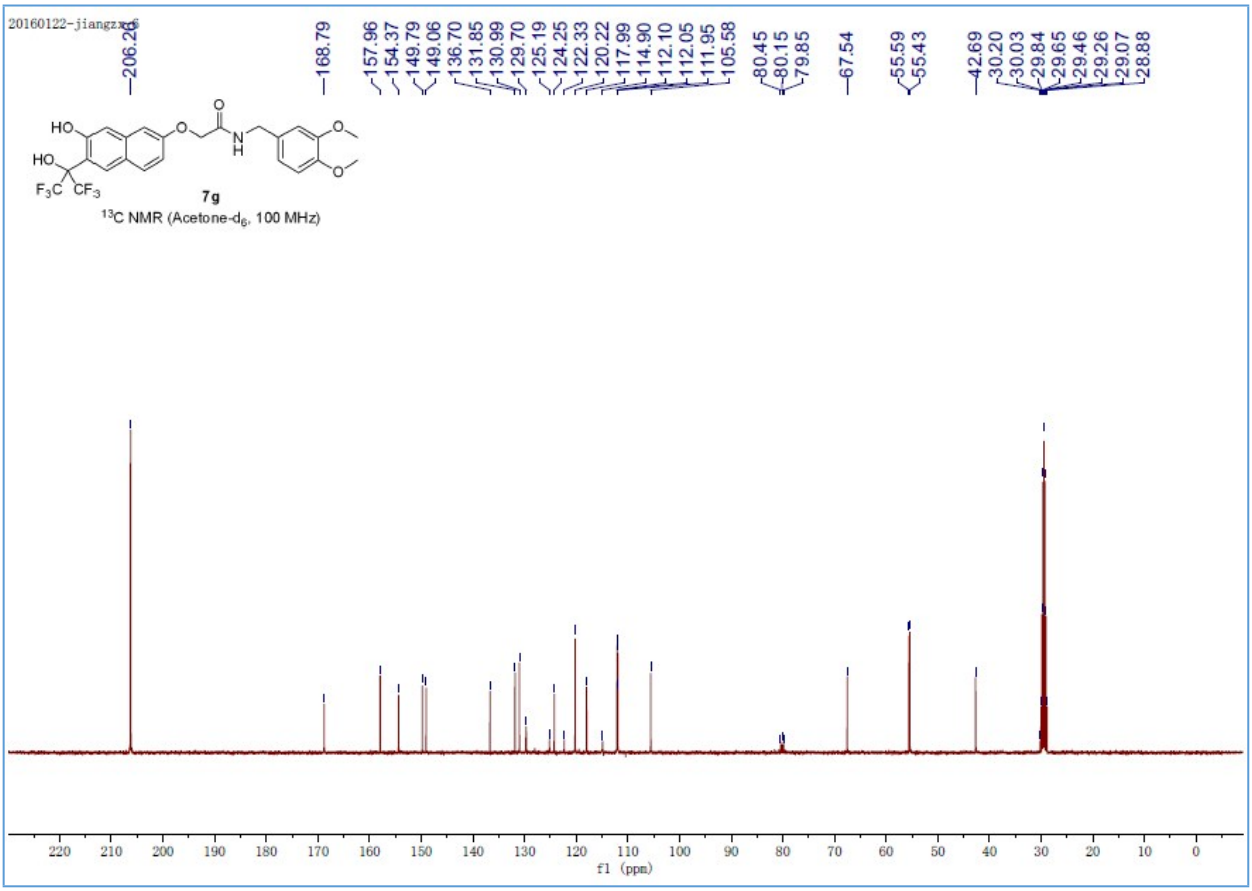

20150121-jiangzx-9
19F
HO
HO
F3C CF3
7f
19F NMR (Acetone-d6, 376 MHz)
-76.14
-117.73
-164.90
f1 (ppm)

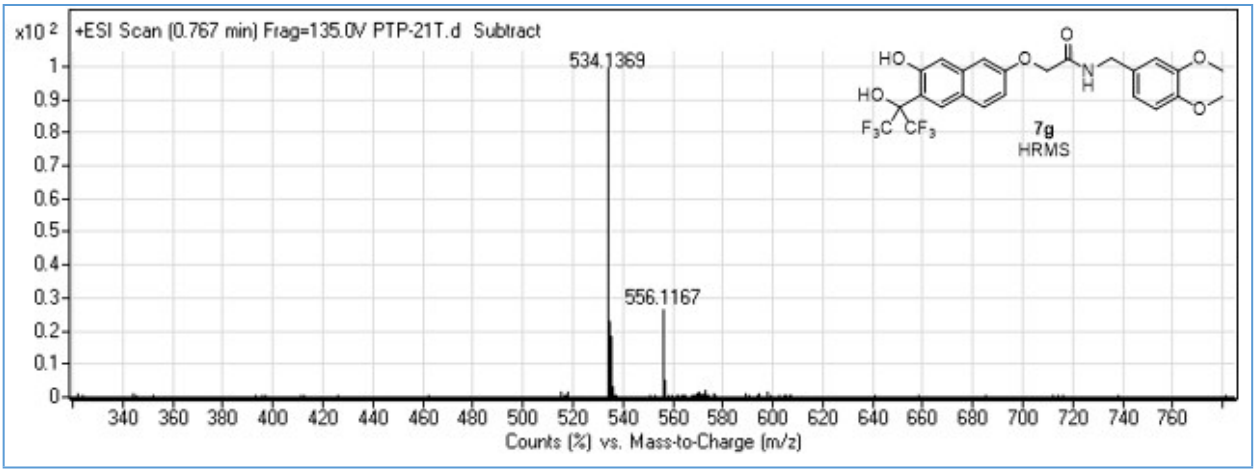

20160120-jiangzx-11
HO
HO
F3C CF3
7f
13C NMR (DMSO-d6, 100 MHz)
167.65
162.34
159.93
157.13
153.94
136.02
135.48
135.45
130.25
129.67
129.12
129.04
124.56
122.65
121.69
116.73
114.96
114.75
110.20
104.85
79.15
78.91
78.62
78.31
78.02
66.97
41.10
39.94
39.73
39.52
39.31
39.10
38.89
38.68
f1 (ppm)

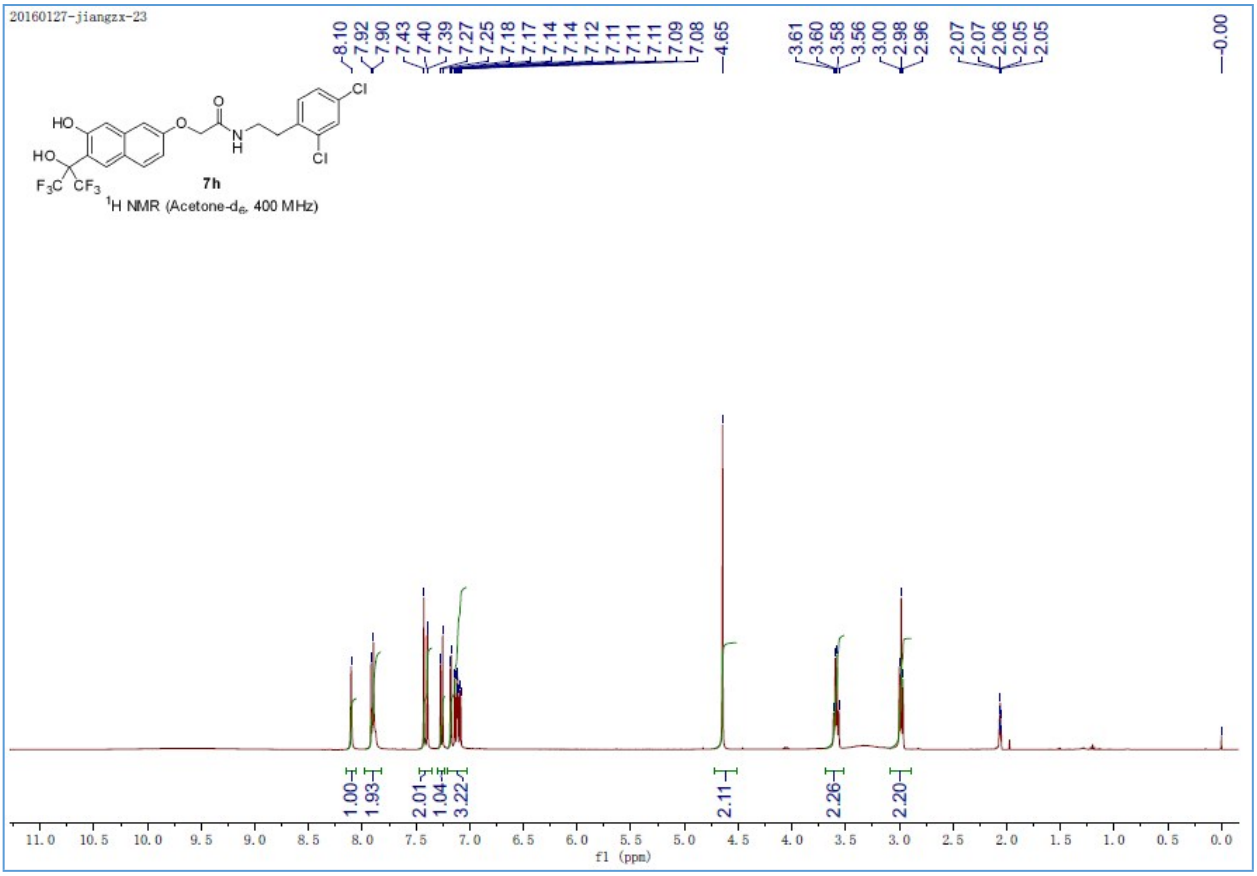

+ESI Scan (0.337-0.653 min, 20 Scans) Frag=175.0V PTP-25T.d
x10 4
492.1041
452.0909
514.0858
576.0563
Counts vs. Mass-to-Charge (m/z)
7f
HRMS

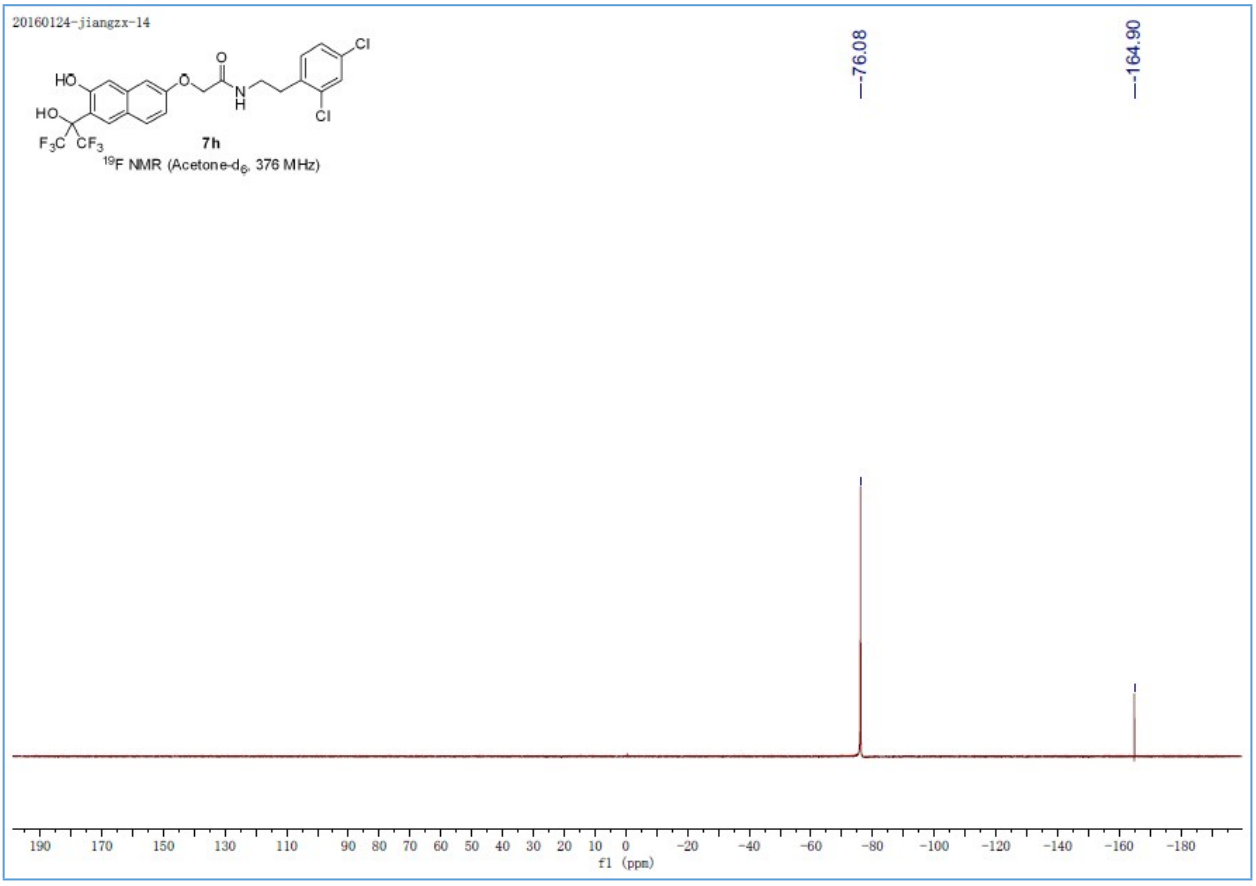

20160122-jiangzx-19
7g
1H NMR (Acetone-d6, 400 MHz)
f1 (ppm)

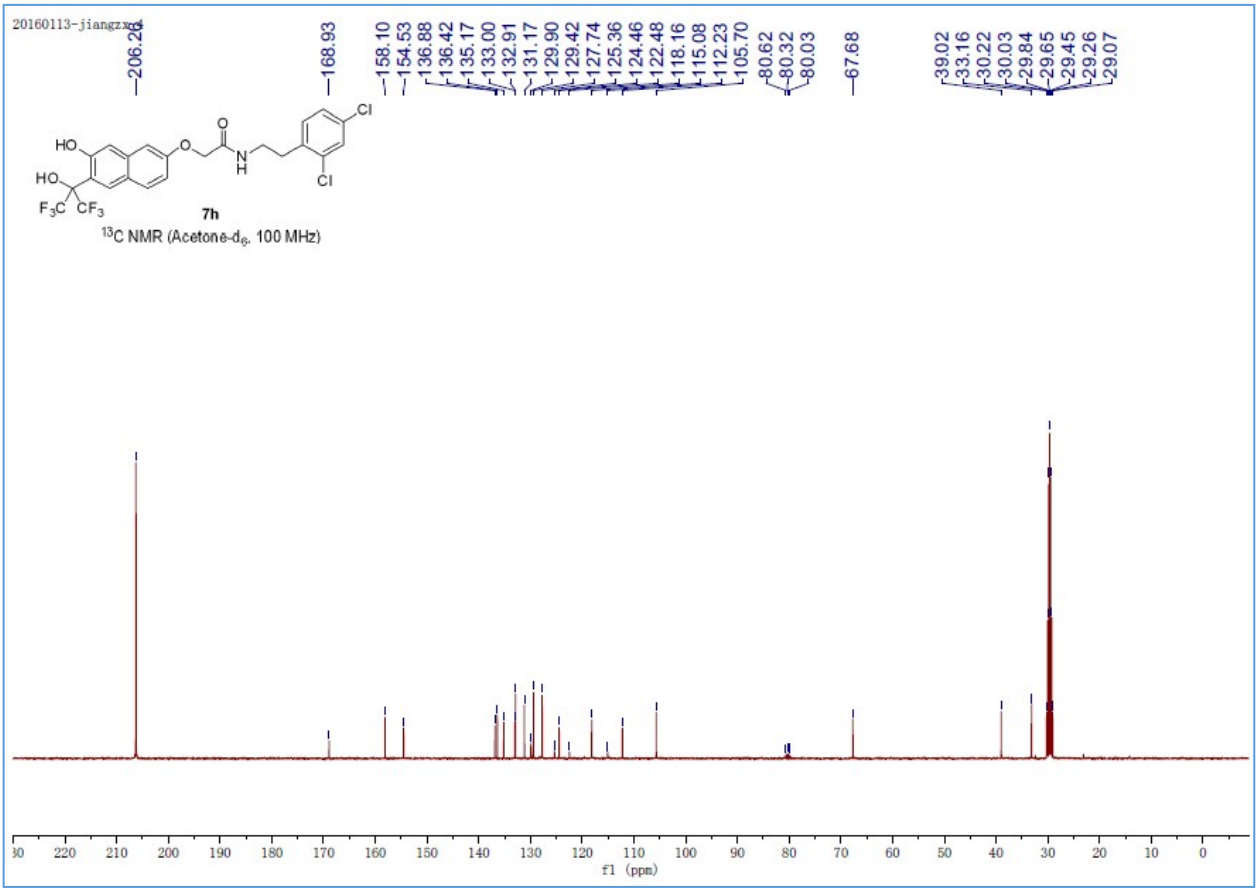

20160122-jiangzx-19
HO
HO
F3C CF3
7g
19F NMR (Acetone-d6, 376 MHz)
-76.03
-164.90
f1 (ppm)

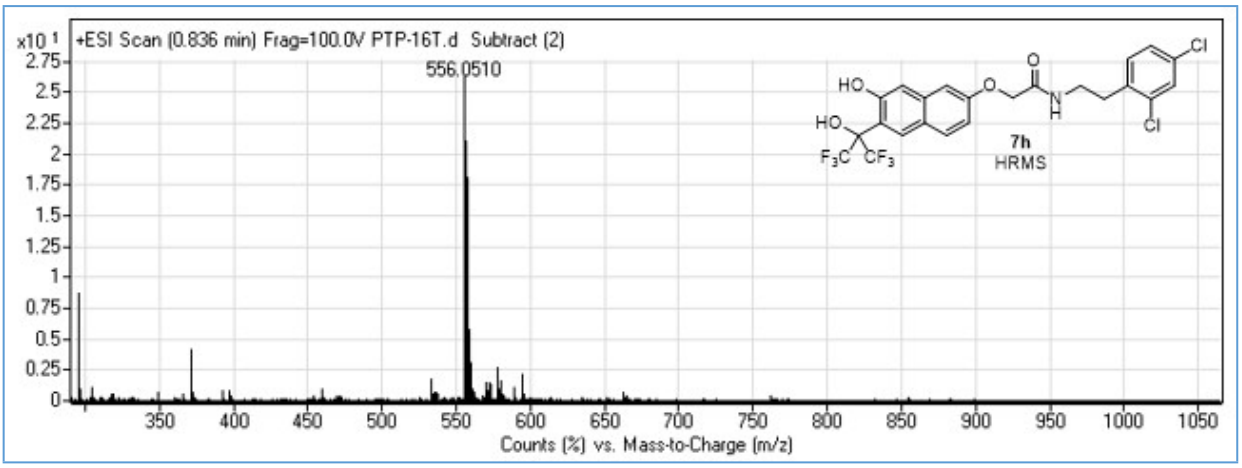

20160122-jiangzx-6
206.26
168.79
157.96
154.37
149.79
149.06
136.70
131.85
130.99
129.70
125.19
124.25
122.33
120.22
117.99
114.90
112.10
112.05
111.95
105.58
80.45
80.15
79.85
67.54
55.59
55.43
42.69
30.20
30.03
29.84
29.65
29.46
29.26
29.07
28.88
HO
HO
F3C CF3
7g
13C NMR (Acetone-d6, 100 MHz)
f1 (ppm)

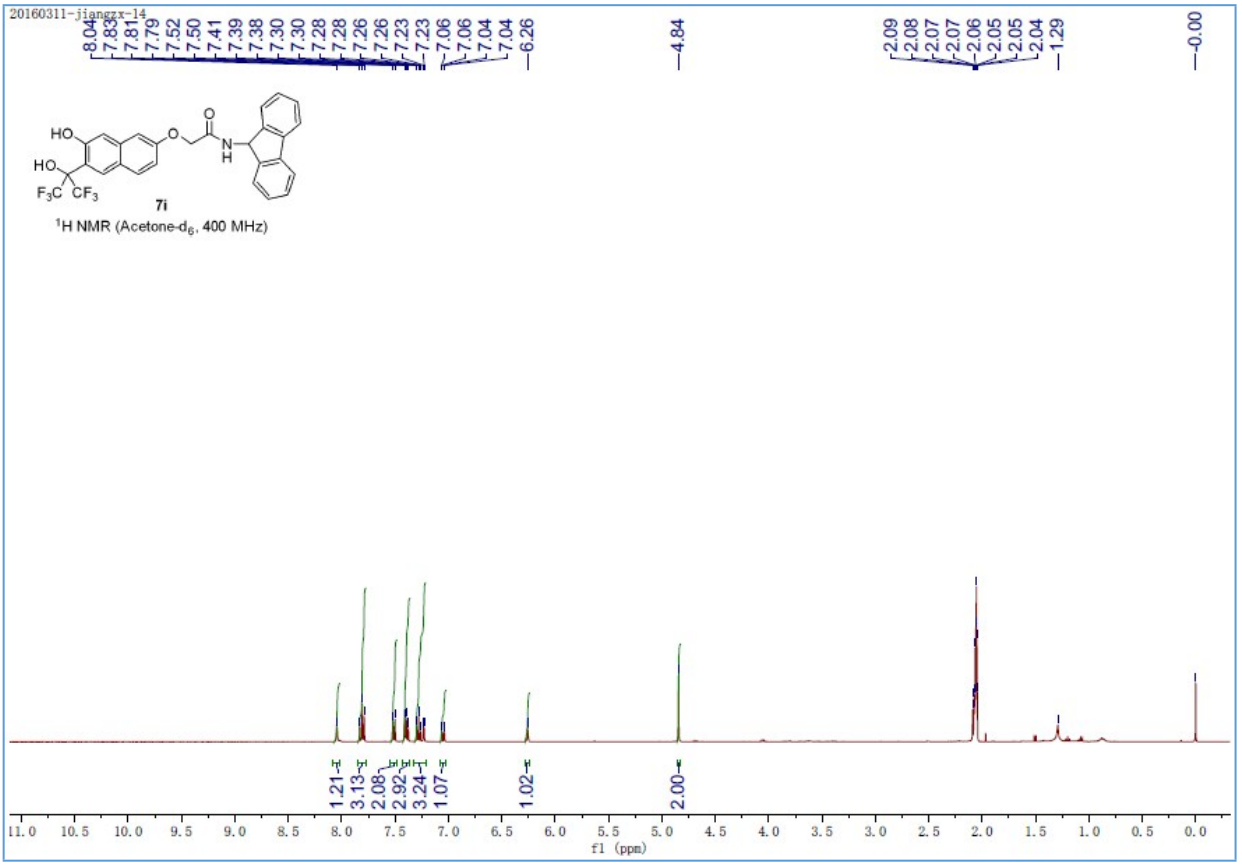

x10 2
+ESI Scan (0.767 min) Frag=135.0V PTP-21T.d Subtract
534.1369
556.1167
Counts (%) vs. Mass-to-Charge (m/z)
7g
HRMS

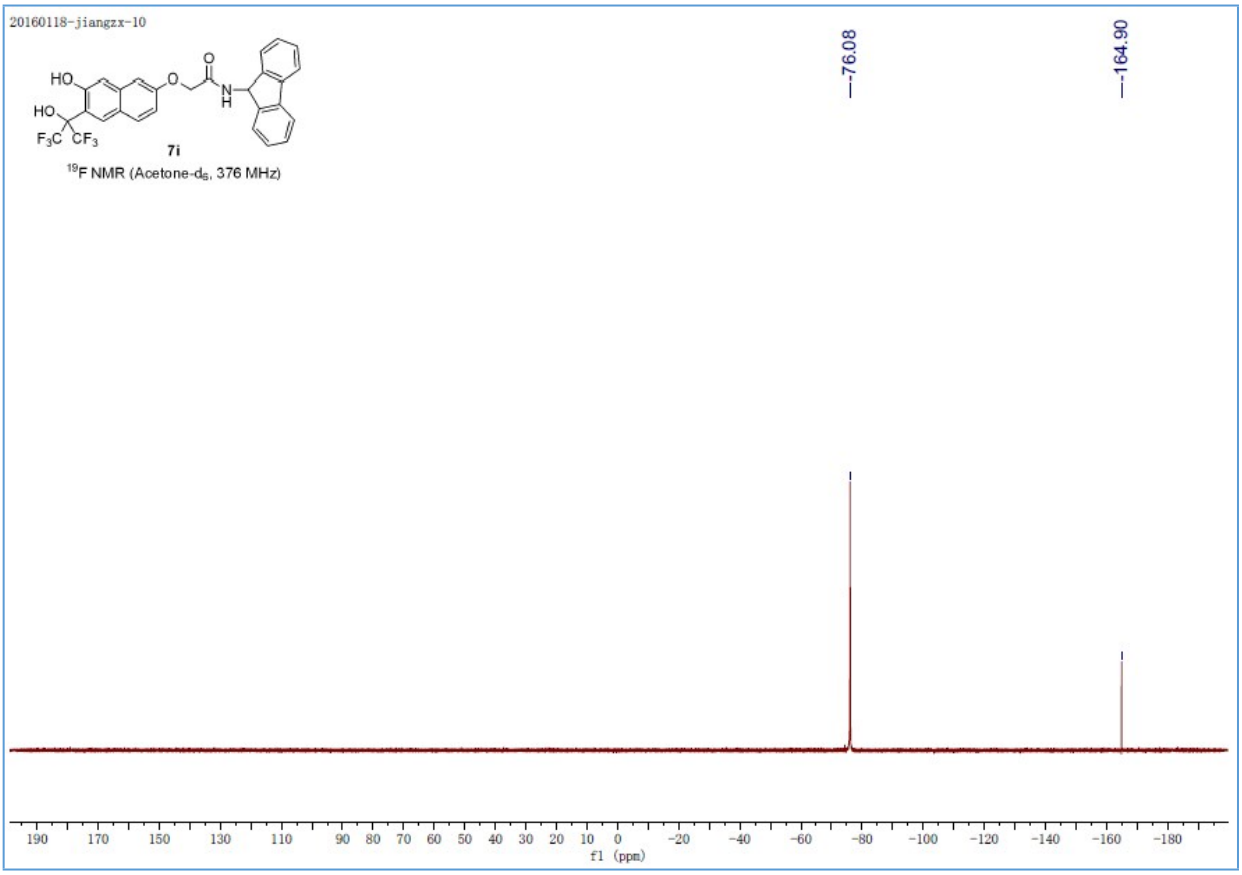

20160127-jiangzx-23
7h
1H NMR (Acetone-d6, 400 MHz)
f1 (ppm)

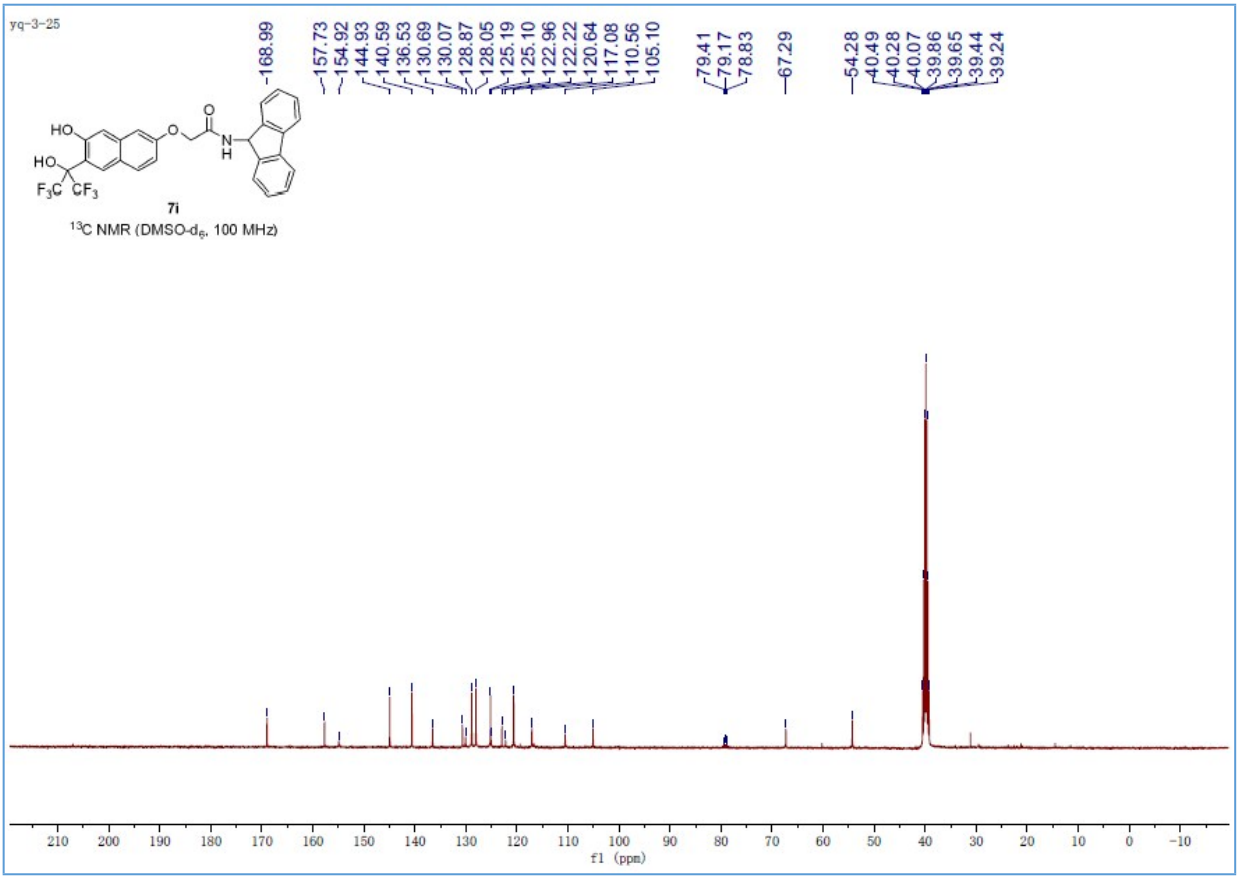

20160124-jiangzx-14
HO
HO
F3C CF3
7h
19F NMR (Acetone-d6, 376 MHz)
-76.08
-164.90
f1 (ppm)

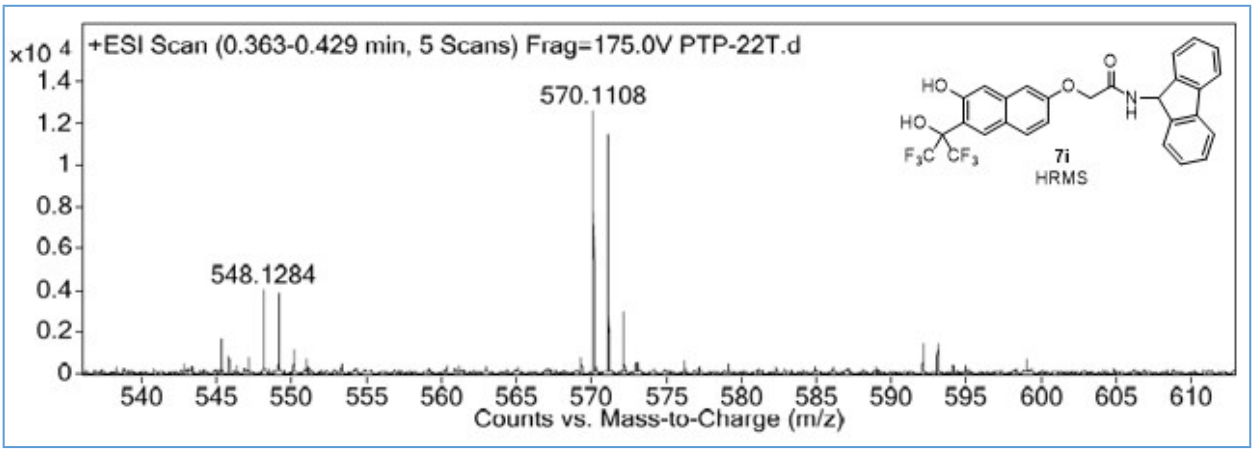

20160113-jiangzx-4
206.26
168.93
158.10
154.53
136.88
136.42
135.17
133.00
132.91
131.17
129.90
129.42
127.74
125.36
124.46
122.48
118.16
115.08
112.23
105.70
80.62
80.32
80.03
67.68
39.02
33.16
30.22
30.03
29.84
29.65
29.45
29.26
29.07
HO
HO
F3C CF3
7h
13C NMR (Acetone-d6, 100 MHz)
f1 (ppm)

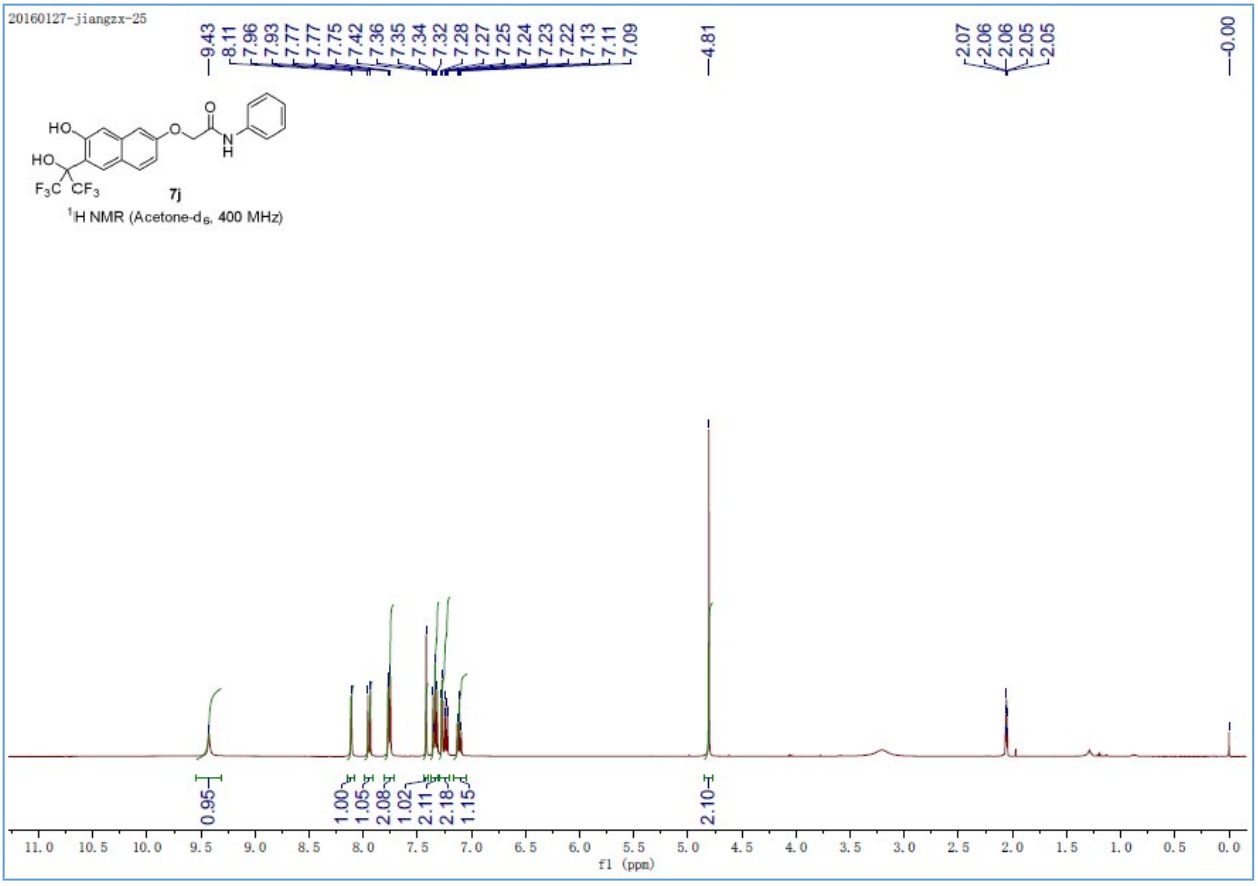

x10 1
+ESI Scan (0.836 min) Frag=100.0V PTP-16T.d Subtract (2)
556.0510
HO
HO
F3C CF3
O
N
H
Cl
Cl
7h
HRMS
Counts (%) vs. Mass-to-Charge (m/z)

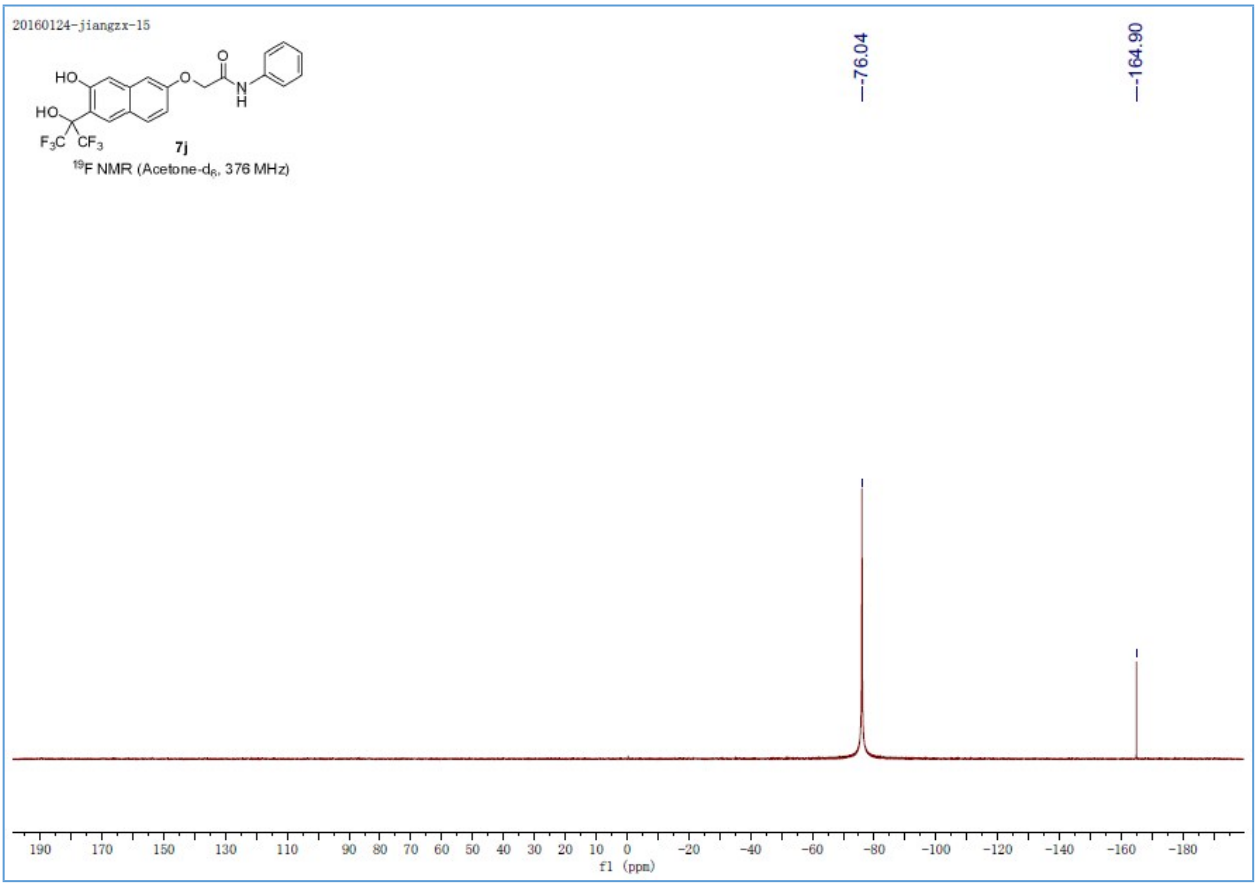

20160311-jiangzx-14
8.04
7.85
7.81
7.79
7.52
7.50
7.41
7.39
7.38
7.30
7.30
7.28
7.26
7.26
7.23
7.23
7.06
7.06
7.04
7.04
6.26
4.84
2.09
2.08
2.07
2.07
2.06
2.05
2.05
2.04
1.29
0.00
HO
HO
F3C CF3
O
N
H
7i
1H NMR (Acetone-d6, 400 MHz)
1.21
3.13
2.08
2.92
3.24
1.07
1.02
2.00
f1 (ppm)

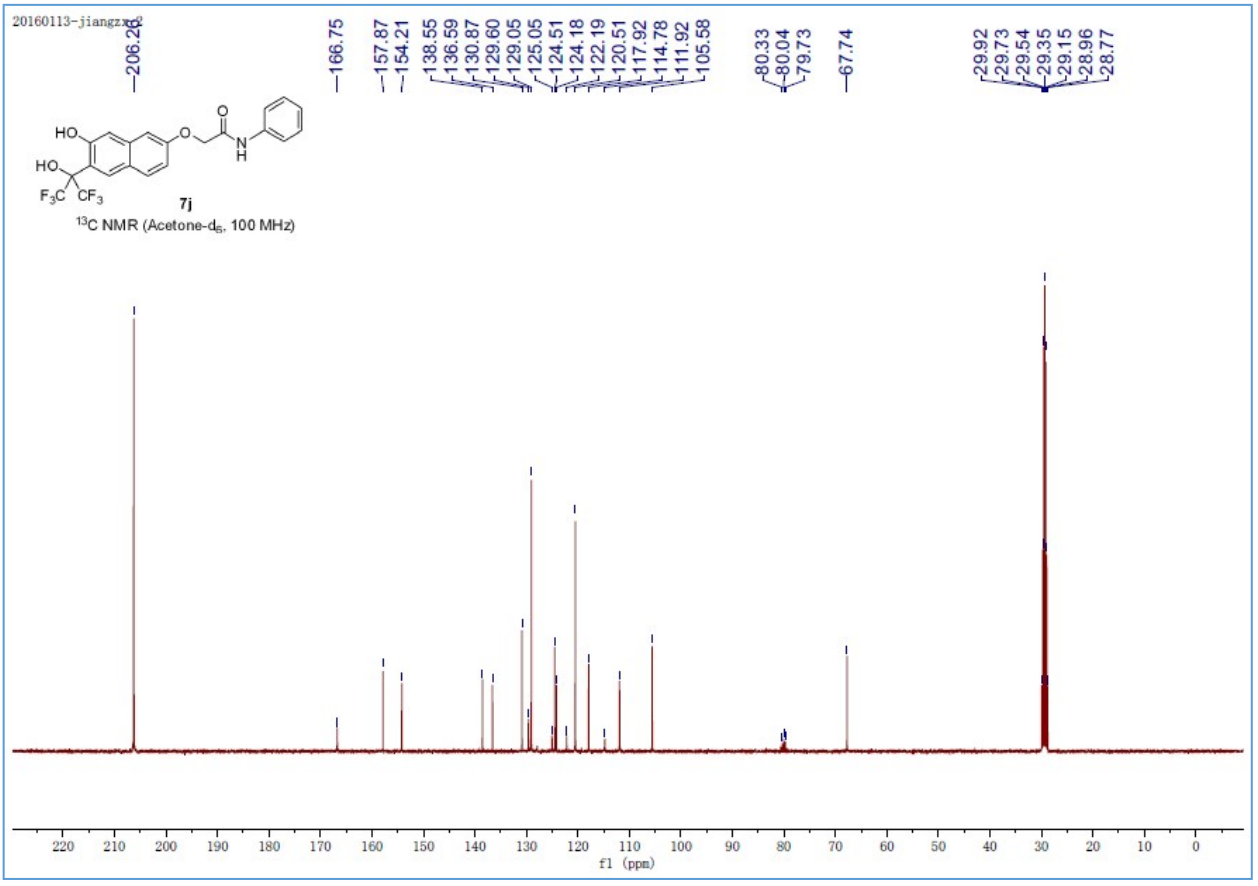

20160118-jiangzx-10
HO
HO
F3C CF3
7i
19F NMR (Acetone-d6, 376 MHz)
-76.08
-164.90
f1 (ppm)

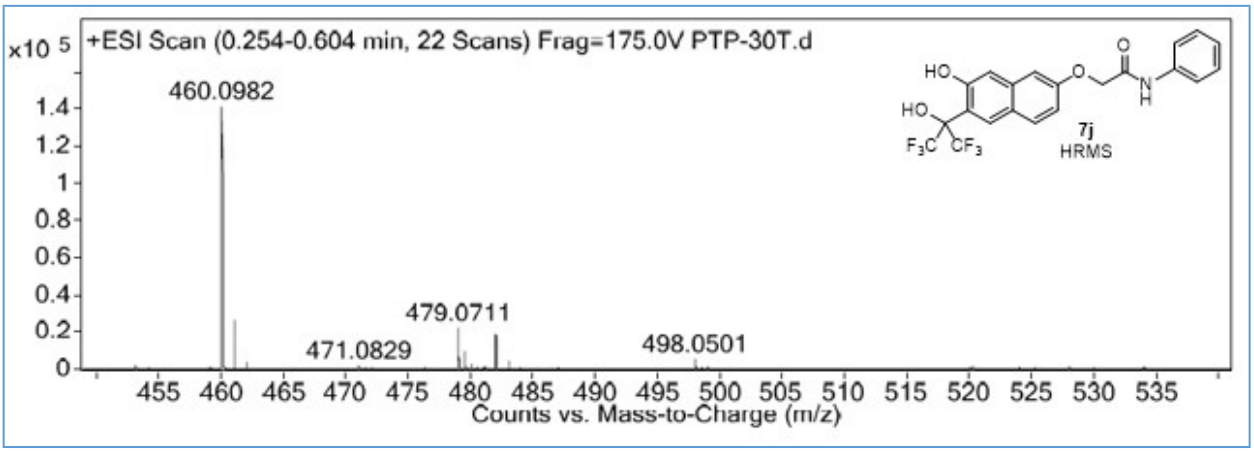

yq-3-25
HO
HO
F3C CF3
7i
13C NMR (DMSO-d6, 100 MHz)
168.99
157.73
154.92
144.93
140.59
136.53
130.69
130.07
128.87
128.05
125.19
125.10
122.96
122.22
120.64
117.08
110.56
105.10
79.41
79.17
78.83
67.29
54.28
40.49
40.28
40.07
39.86
39.65
39.44
39.24
f1 (ppm)

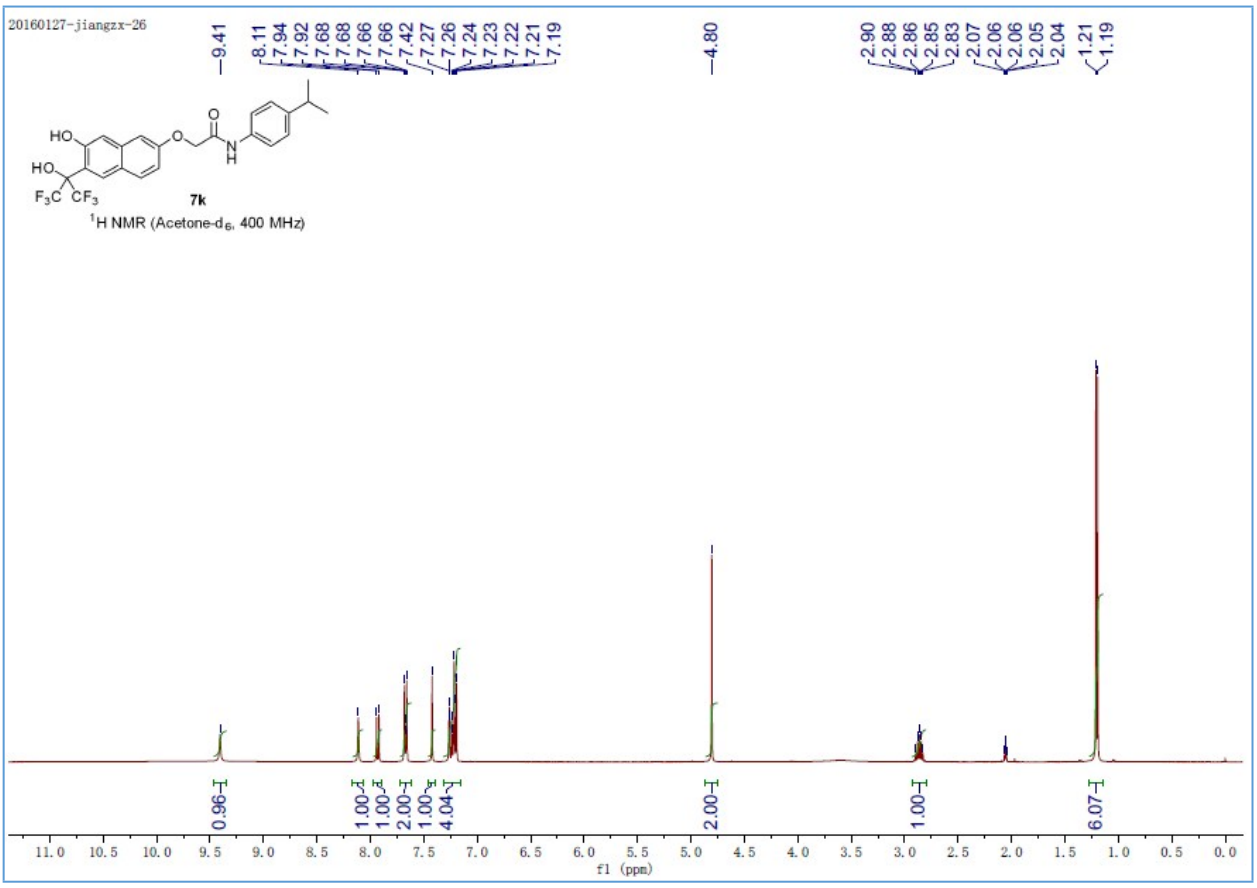

+ESI Scan (0.363-0.429 min, 5 Scans) Frag=175.0V PTP-22T.d
x10 4
570.1108
548.1284
Counts vs. Mass-to-Charge (m/z)
7i
HRMS

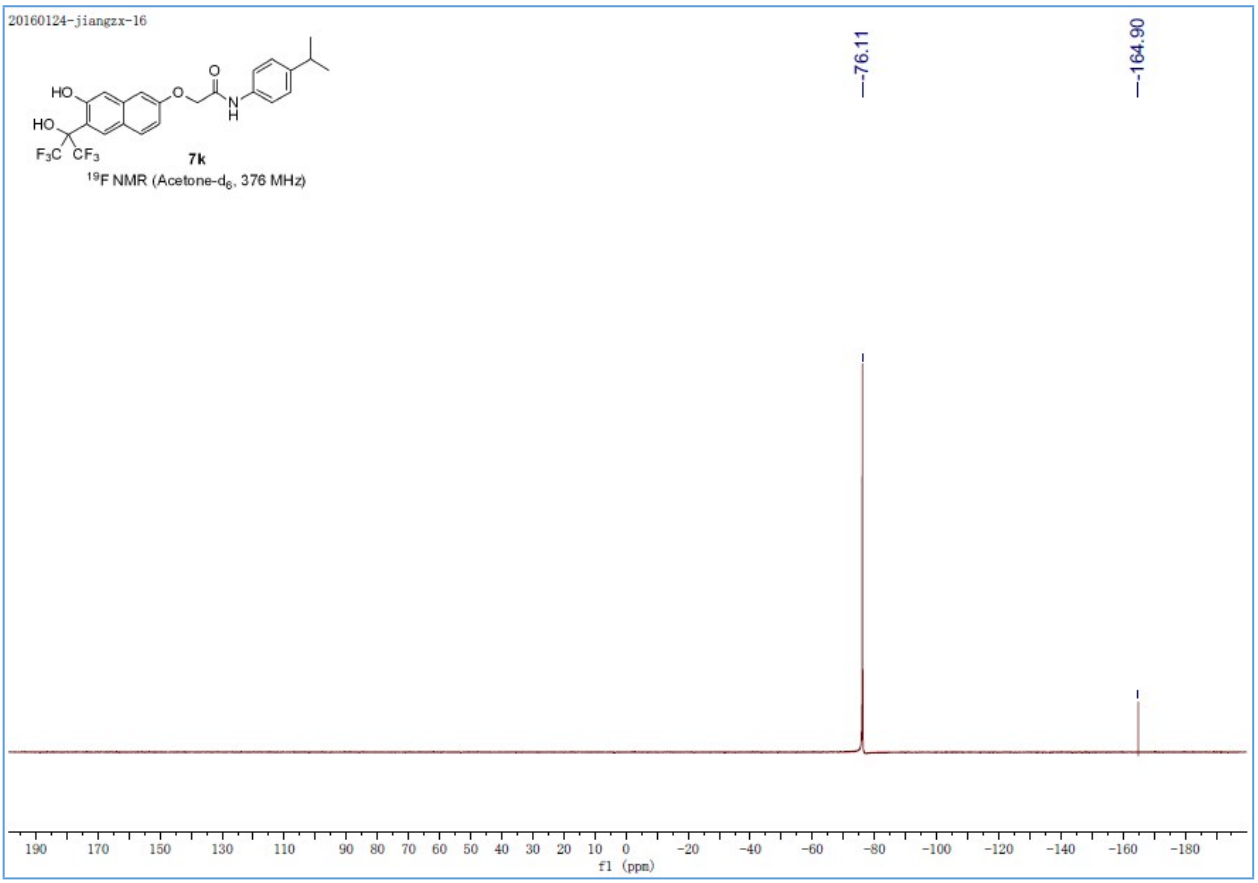

20160127-jiangzx-25
7j
1H NMR (Acetone-d6, 400 MHz)
f1 (ppm)

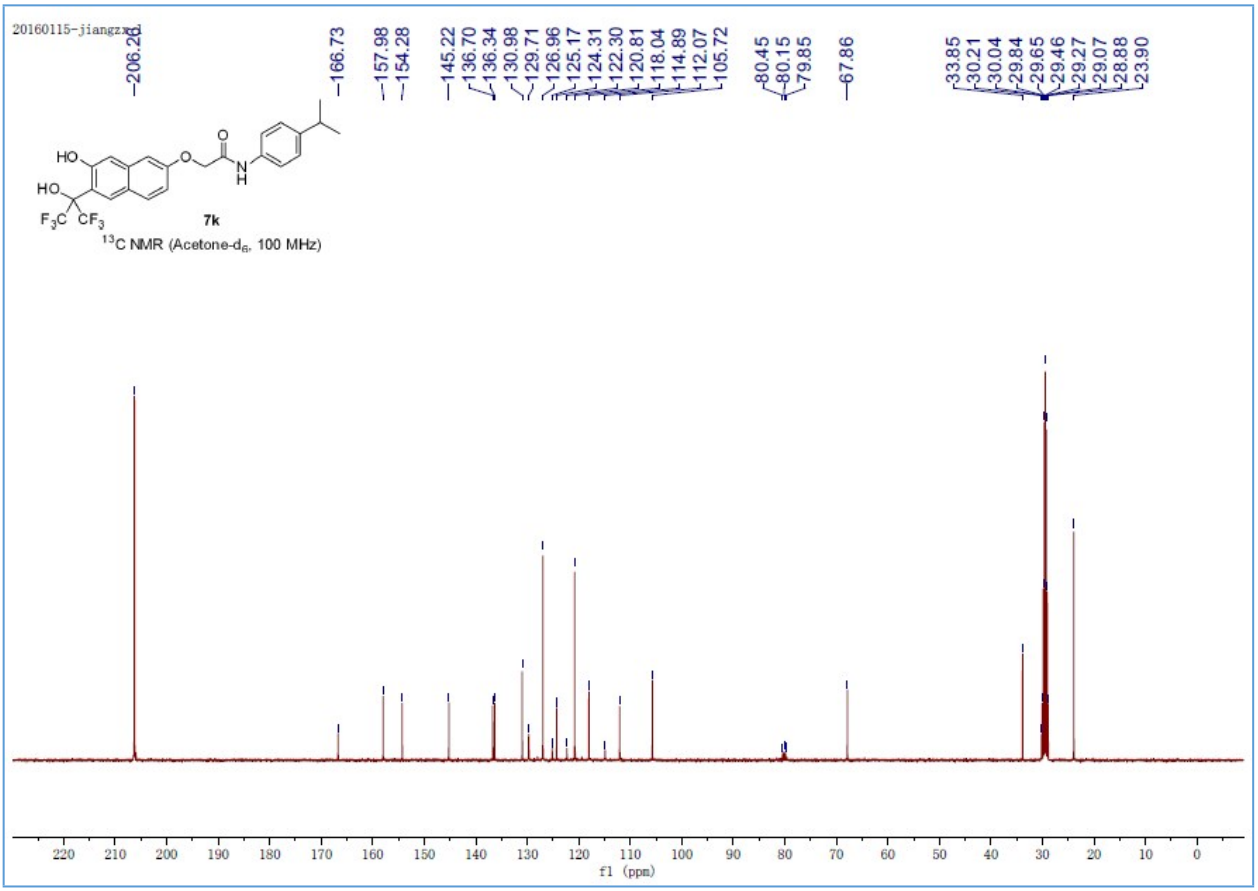

20160124-jiangzx-15
HO
HO
F3C CF3
O
O
N
H
7j
19F NMR (Acetone-d6, 376 MHz)
-76.04
-164.90
190 170 150 130 110 90 80 70 60 50 40 30 20 10 0 -20 -40 -60 -80 -100 -120 -140 -160 -180
f1 (ppm)

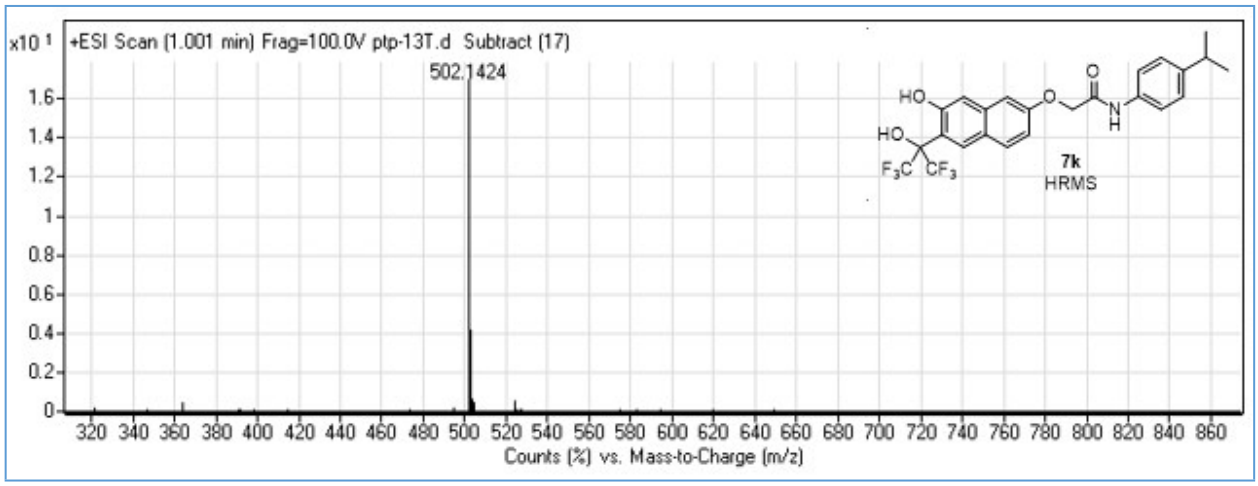

20160113-jiangzx-2
206.26
166.75
157.87
154.21
138.55
136.59
130.87
129.60
129.05
125.05
124.51
124.18
122.19
120.51
117.92
114.78
111.92
105.58
80.33
80.04
79.73
67.74
29.92
29.73
29.54
29.35
29.15
28.96
28.77
HO
HO
F3C CF3
O
O
N
H
7j
13C NMR (Acetone-d6, 100 MHz)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

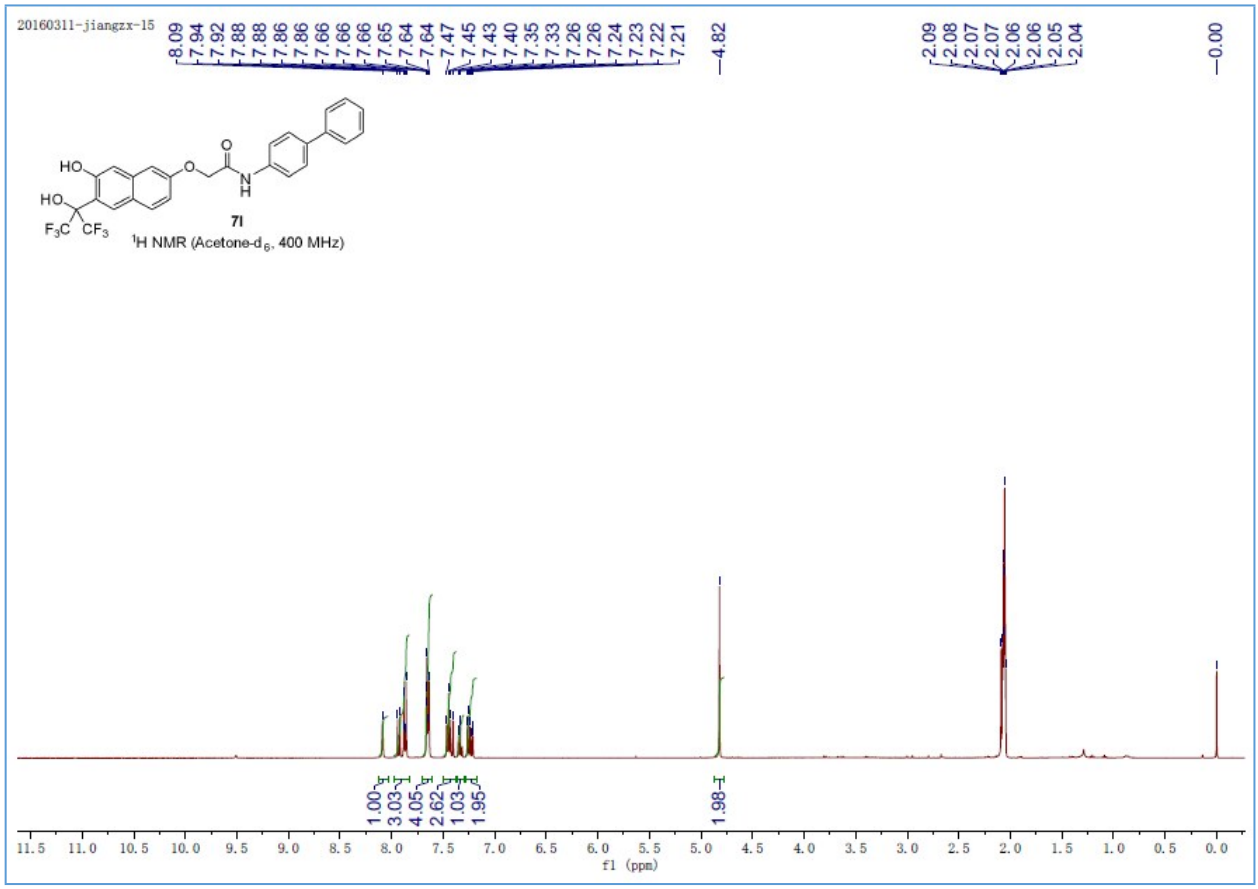

+ESI Scan (0.254-0.604 min, 22 Scans) Frag=175.0V PTP-30T.d
x10 5
460.0982
479.0711
471.0829
498.0501
Counts vs. Mass-to-Charge (m/z)
7j
HRMS

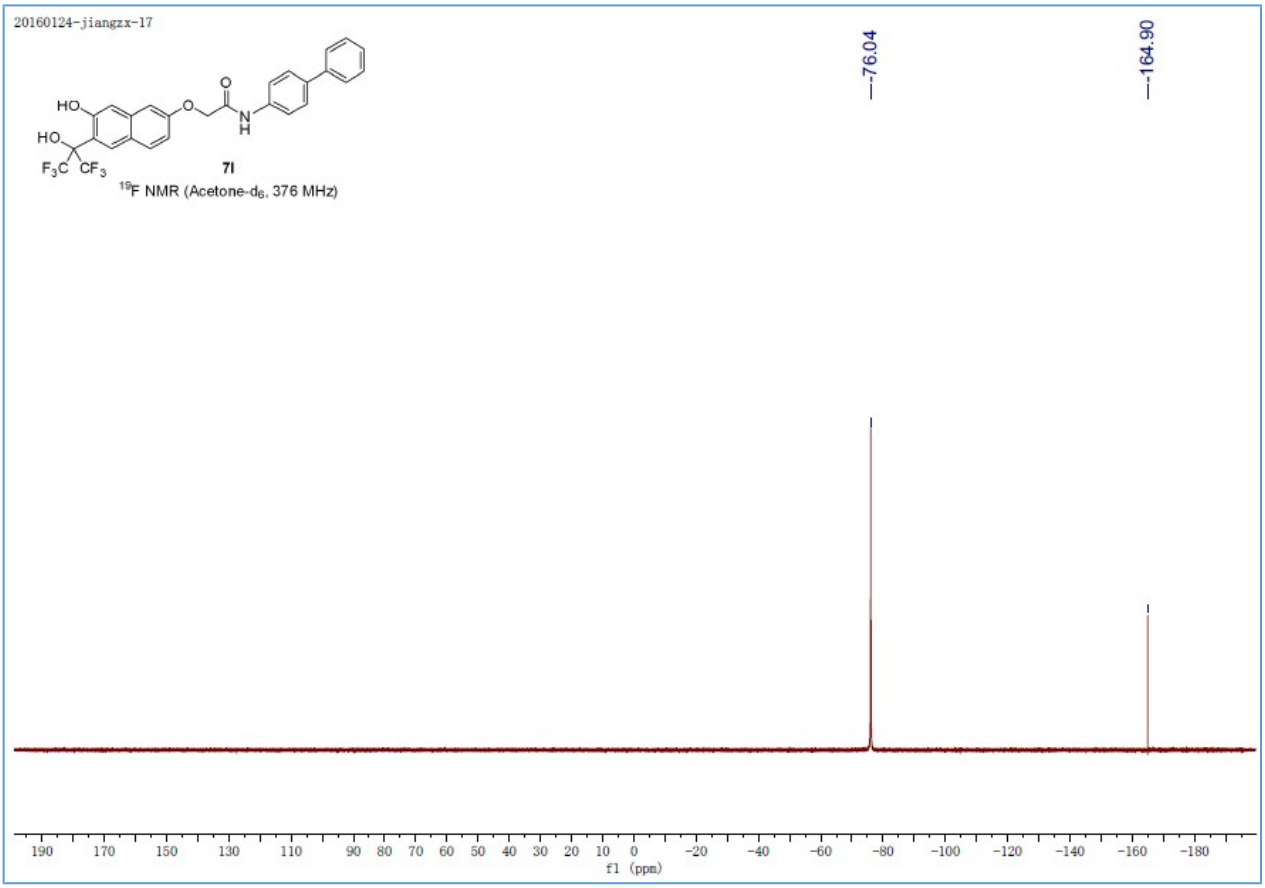

20160127-jiangzx-26
7k
1H NMR (Acetone-d6, 400 MHz)
f1 (ppm)

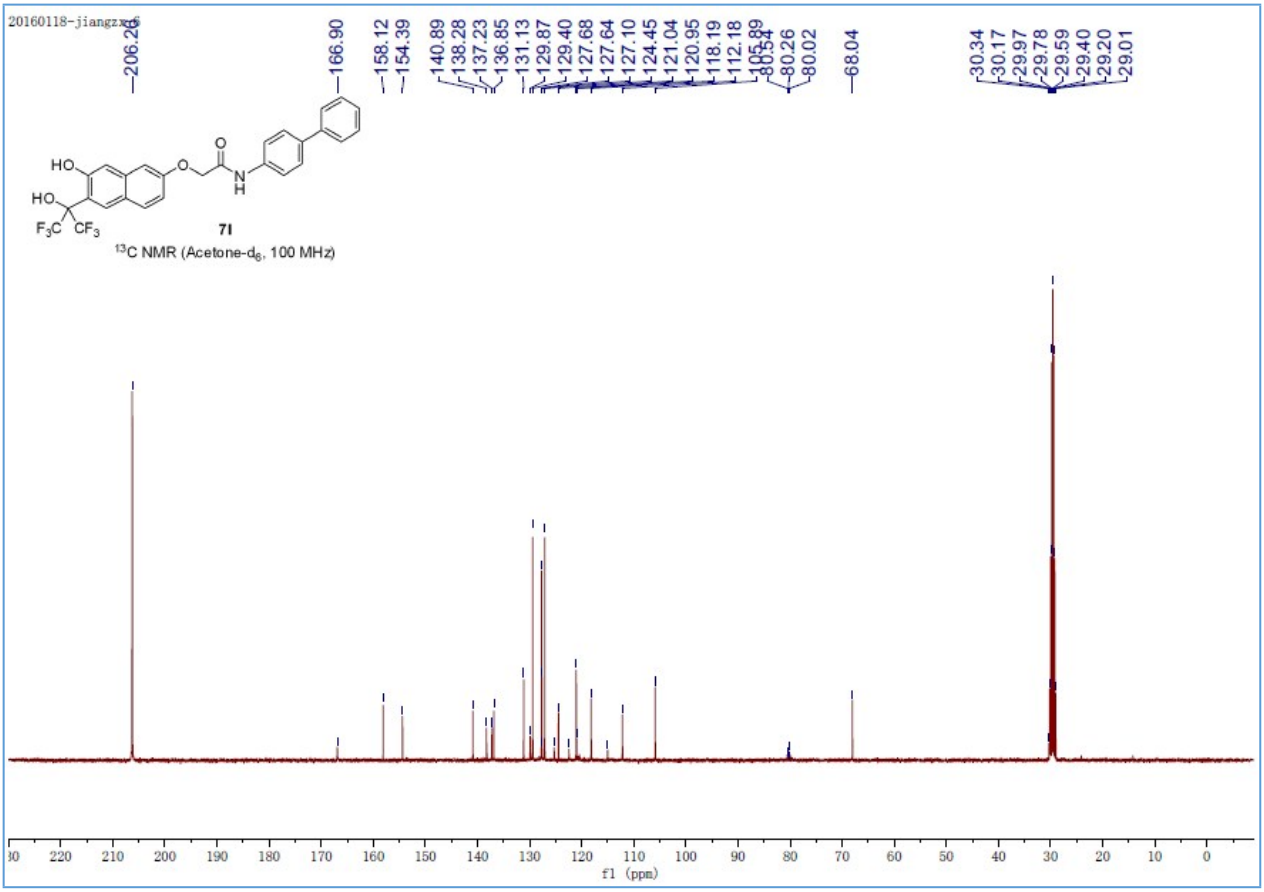

20160124-jiangzx-16
HO
HO
F3C CF3
O
O
N
H
7k
19F NMR (Acetone-d6, 376 MHz)
-76.11
-164.90
f1 (ppm)

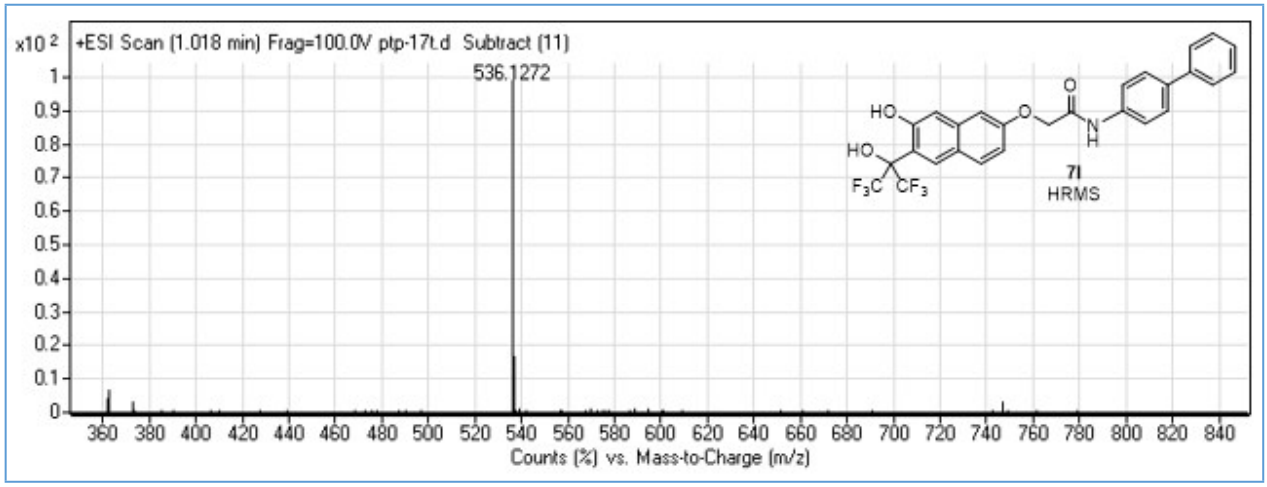

20160115-jiangzx-1
206.26
166.73
157.98
154.28
145.22
136.70
136.34
130.98
129.71
126.96
125.17
124.31
122.30
120.81
118.04
114.89
112.07
105.72
80.45
80.15
79.85
67.86
33.85
30.21
30.04
29.84
29.65
29.46
29.27
29.07
28.88
23.90
HO
HO
F3C CF3
O
O
N
H
7k
13C NMR (Acetone-d6, 100 MHz)
f1 (ppm)

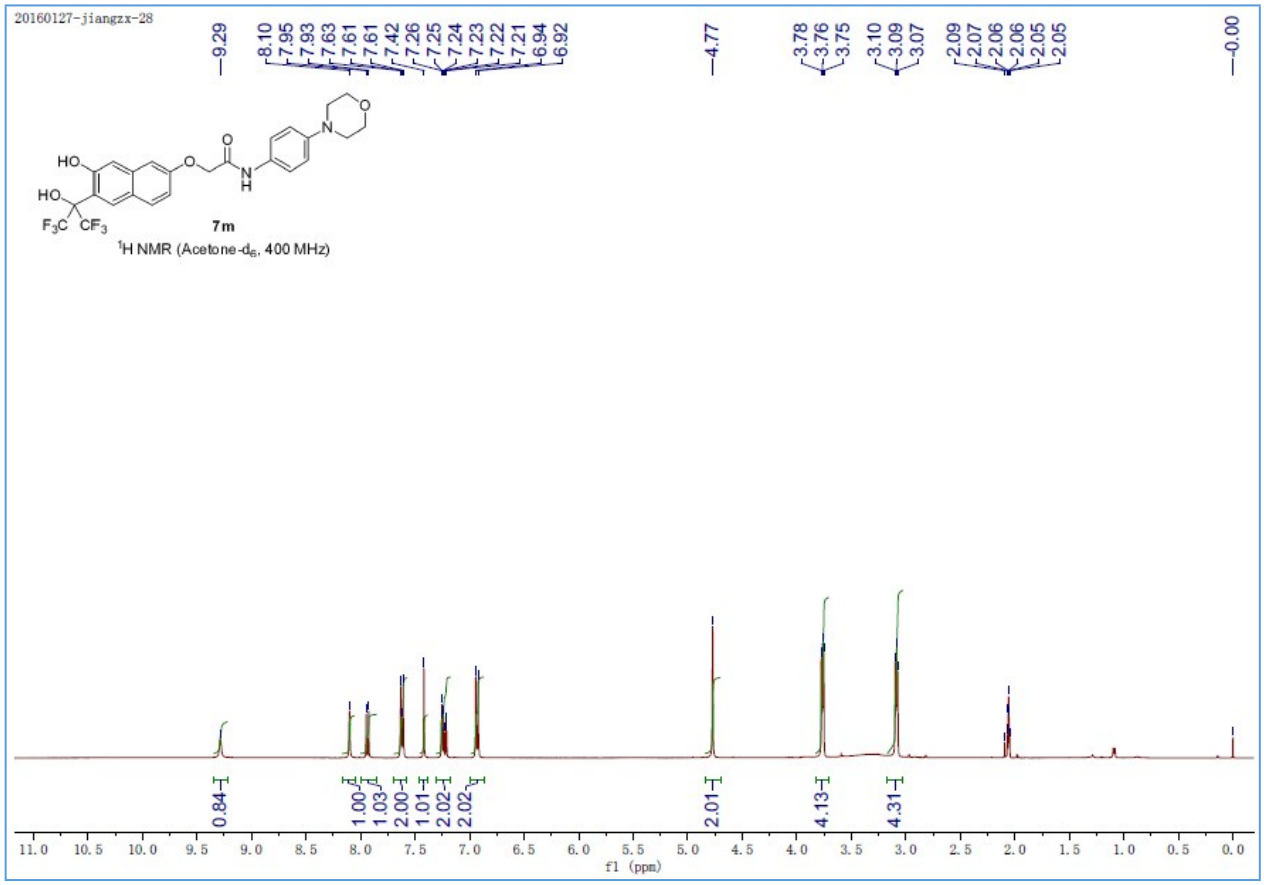

x10 1
+ESI Scan (1.001 min) Frag=100.0V ptp-13T.d Subtract (17)
502.1424
HO
HO
F3C CF3
O
N
H
7k
HRMS
Counts (%) vs. Mass-to-Charge (m/z)

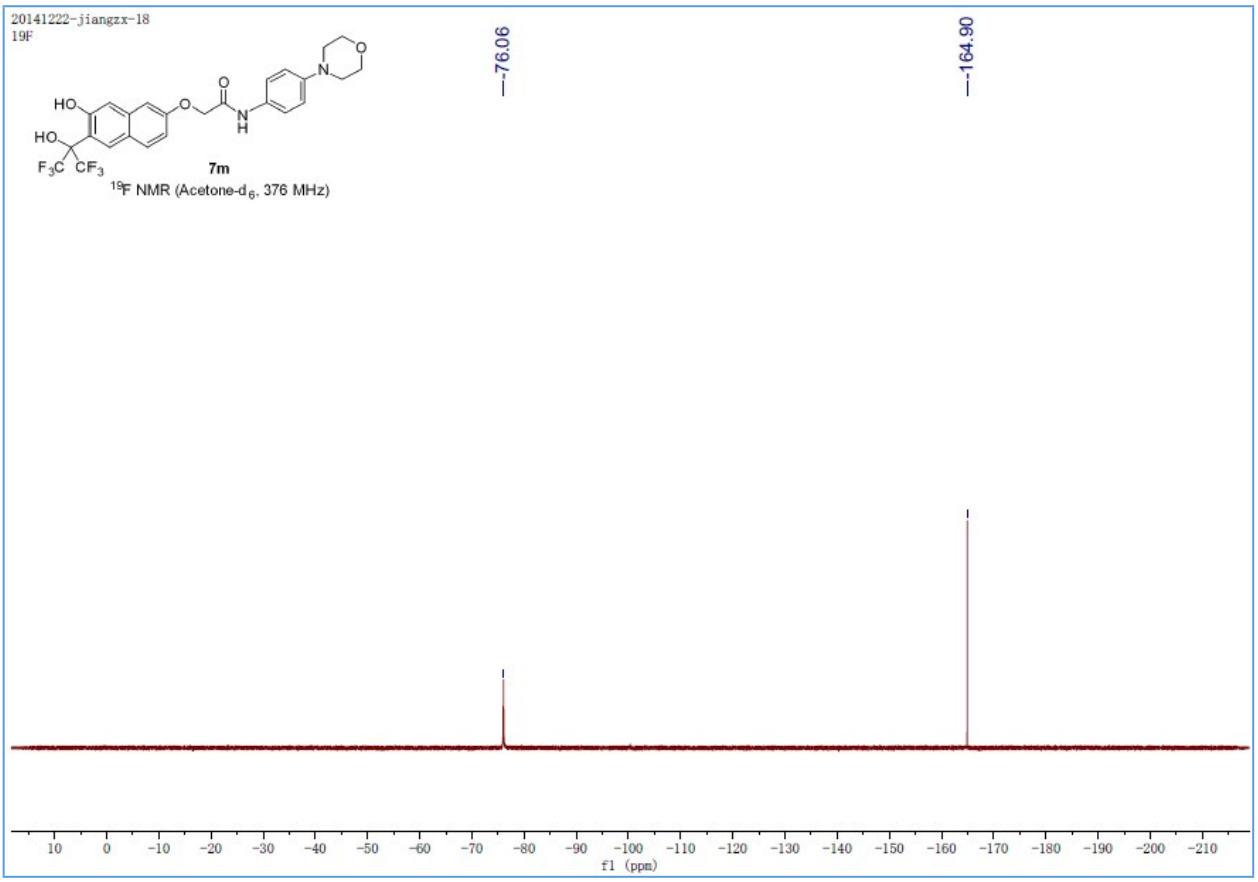

20160311-jiangzx-15
8.09
7.94
7.92
7.88
7.86
7.86
7.66
7.66
7.66
7.65
7.64
7.64
7.47
7.45
7.43
7.40
7.35
7.33
7.26
7.24
7.23
7.22
7.21
4.82
2.09
2.08
2.07
2.07
2.06
2.06
2.05
2.04
0.00
HO
HO
F3C CF3
O
N
H
7l
1H NMR (Acetone-d6, 400 MHz)
1.00
3.03
4.05
2.62
1.03
1.95
1.98
f1 (ppm)

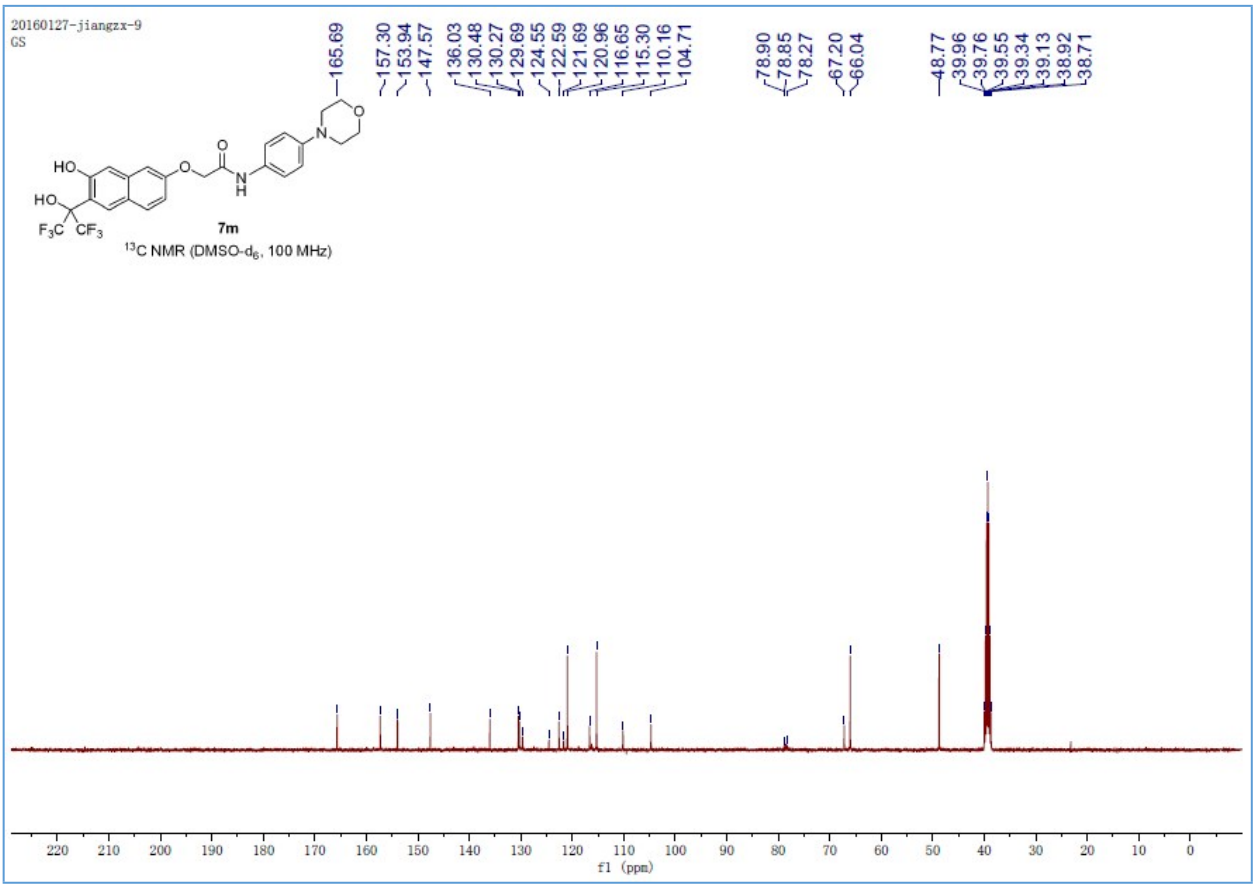

20160124-jiangzx-17
HO
HO
F3C CF3
7l
19F NMR (Acetone-d6, 376 MHz)
-76.04
-164.90
f1 (ppm)

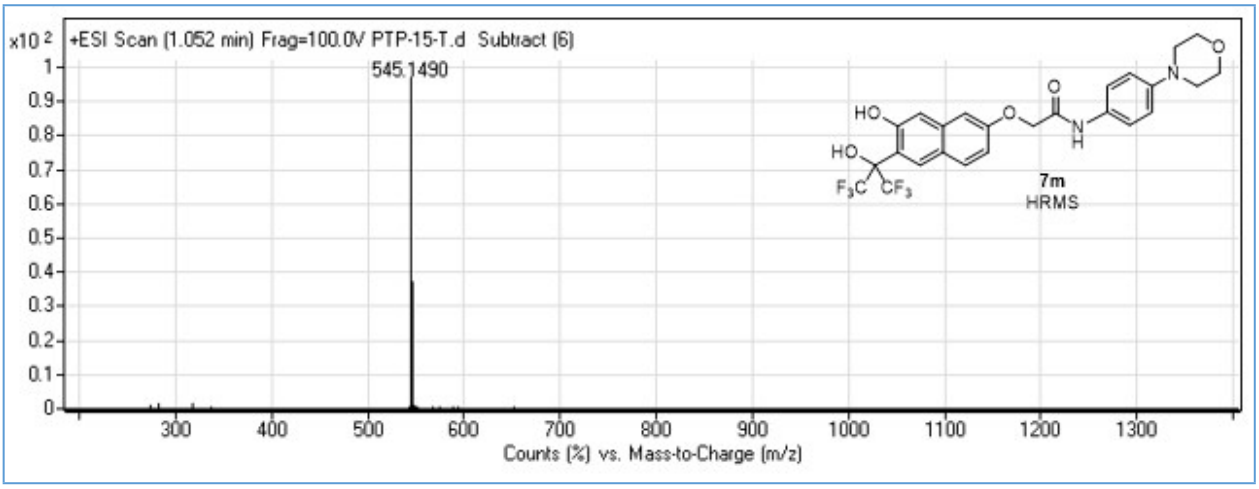

20160118-jiangzx-6
206.26
166.90
158.12
154.39
140.89
138.28
137.23
136.85
131.13
129.87
129.40
127.68
127.64
127.10
124.45
121.04
120.95
118.19
112.18
105.89
80.54
80.26
80.02
68.04
30.34
30.17
29.97
29.78
29.59
29.40
29.20
29.01
HO
HO
F3C CF3
7l
13C NMR (Acetone-d6, 100 MHz)
f1 (ppm)

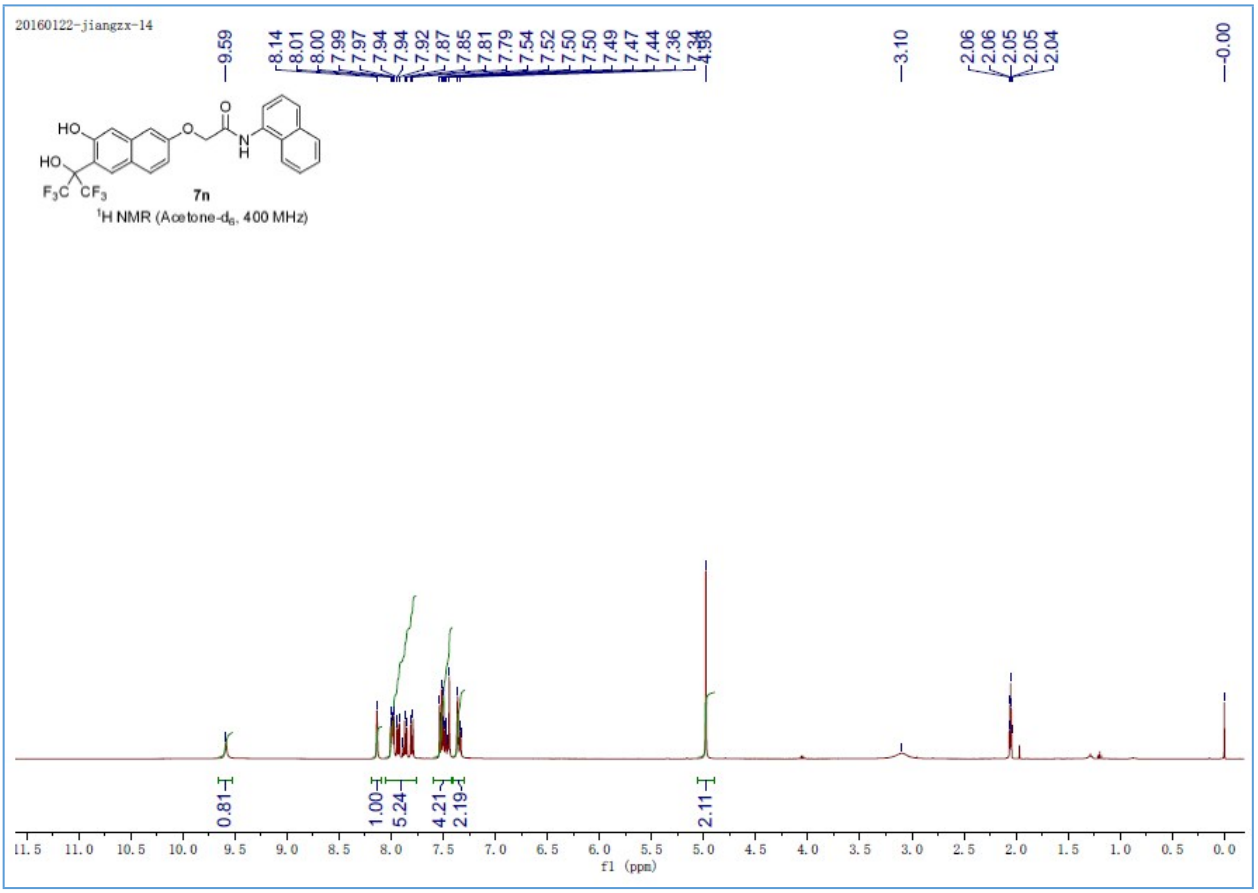

x10 2
+ESI Scan (1.018 min) Frag=100.0V ptp-17t.d Subtract (11)
536.1272
HO
HO
F3C CF3
O
N
H
7l
HRMS
Counts (%) vs. Mass-to-Charge (m/z)

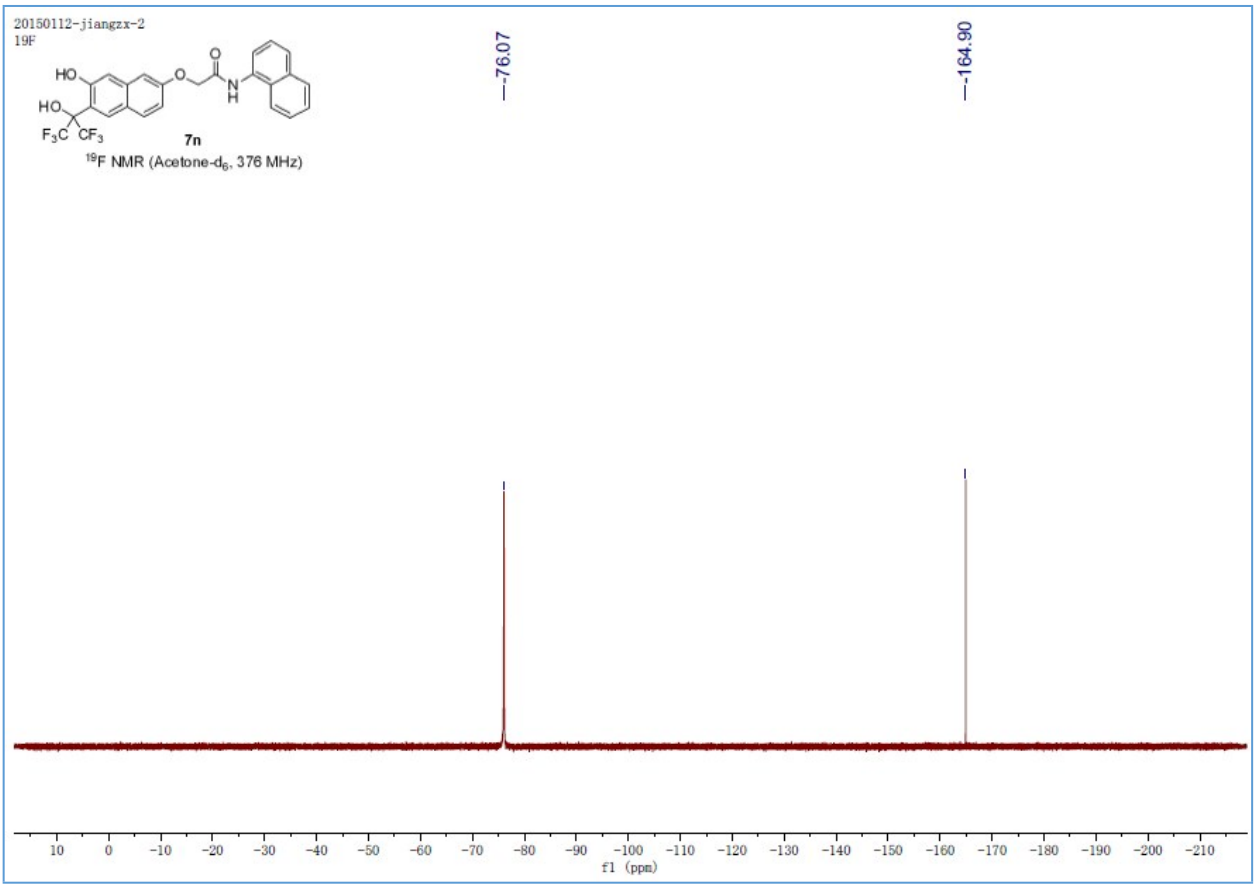

20160127-jiangzx-28
9.29
8.10
7.95
7.93
7.63
7.61
7.61
7.42
7.26
7.25
7.24
7.23
7.22
7.21
6.94
6.92
4.77
3.78
3.76
3.75
3.10
3.09
3.07
2.09
2.07
2.06
2.06
2.05
2.05
0.00
HO
HO
F3C CF3
7m
1H NMR (Acetone-d6, 400 MHz)
0.84
1.00
1.03
2.00
1.01
2.02
2.02
2.01
4.13
4.31
f1 (ppm)

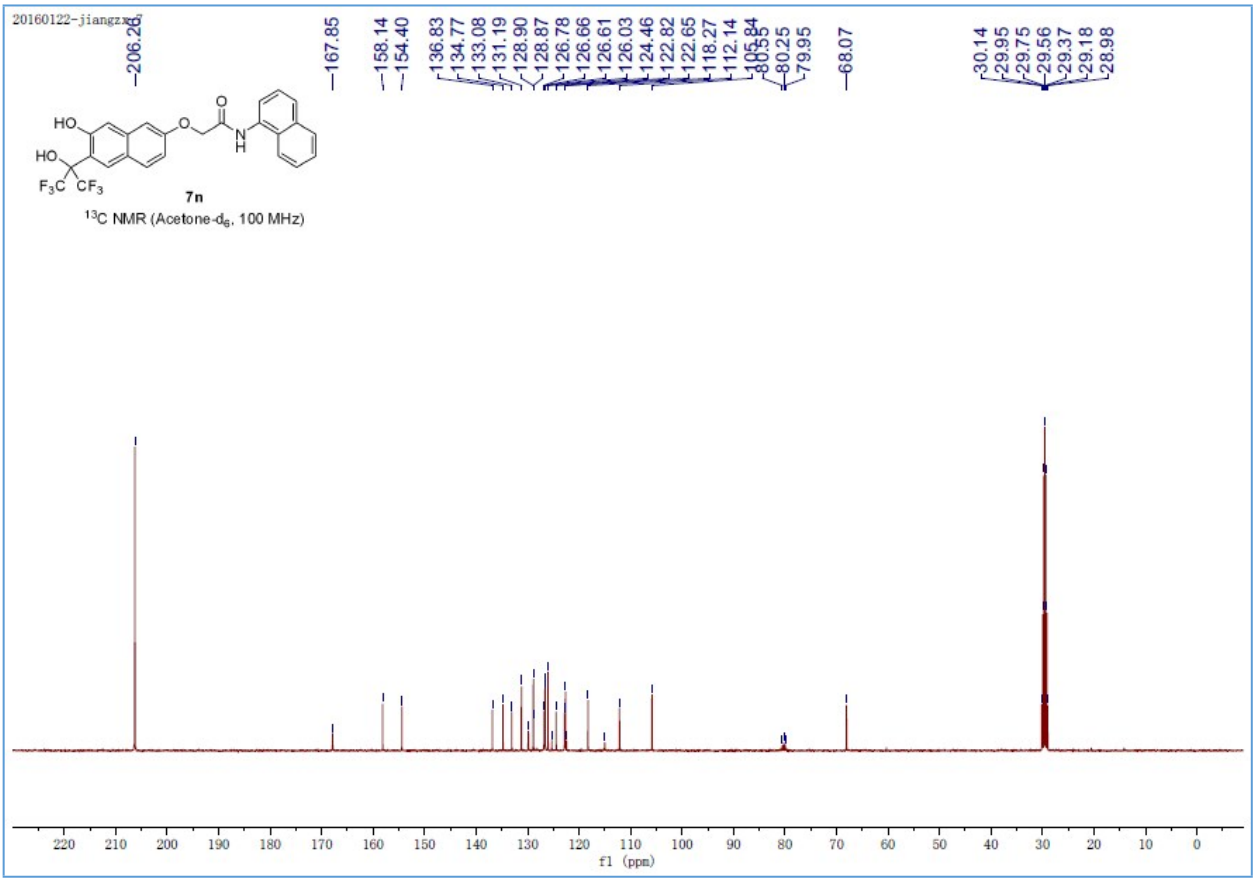

20141222-jiangzx-18
19F
-76.06
-164.90
HO
HO
F3C CF3
7m
19F NMR (Acetone-d6, 376 MHz)
f1 (ppm)

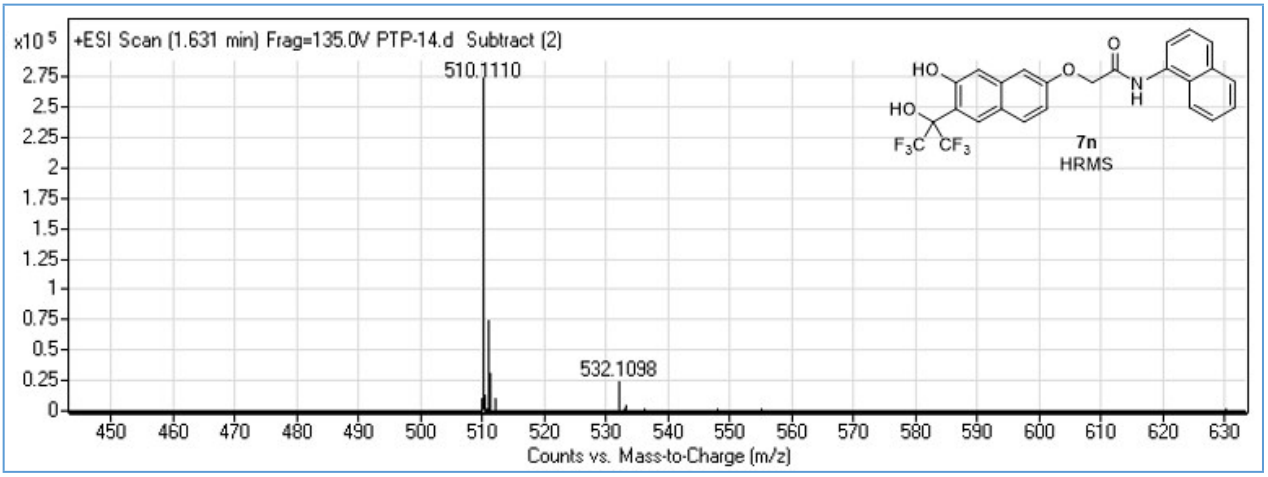

20160127-jiangzx-9
GS
165.69
157.30
153.94
147.57
136.03
130.48
130.27
129.69
124.55
122.59
121.69
120.96
116.65
115.30
110.16
104.71
78.90
78.85
78.27
67.20
66.04
48.77
39.96
39.76
39.55
39.34
39.13
38.92
38.71
HO
HO
F3C CF3
7m
13C NMR (DMSO-d6, 100 MHz)
f1 (ppm)

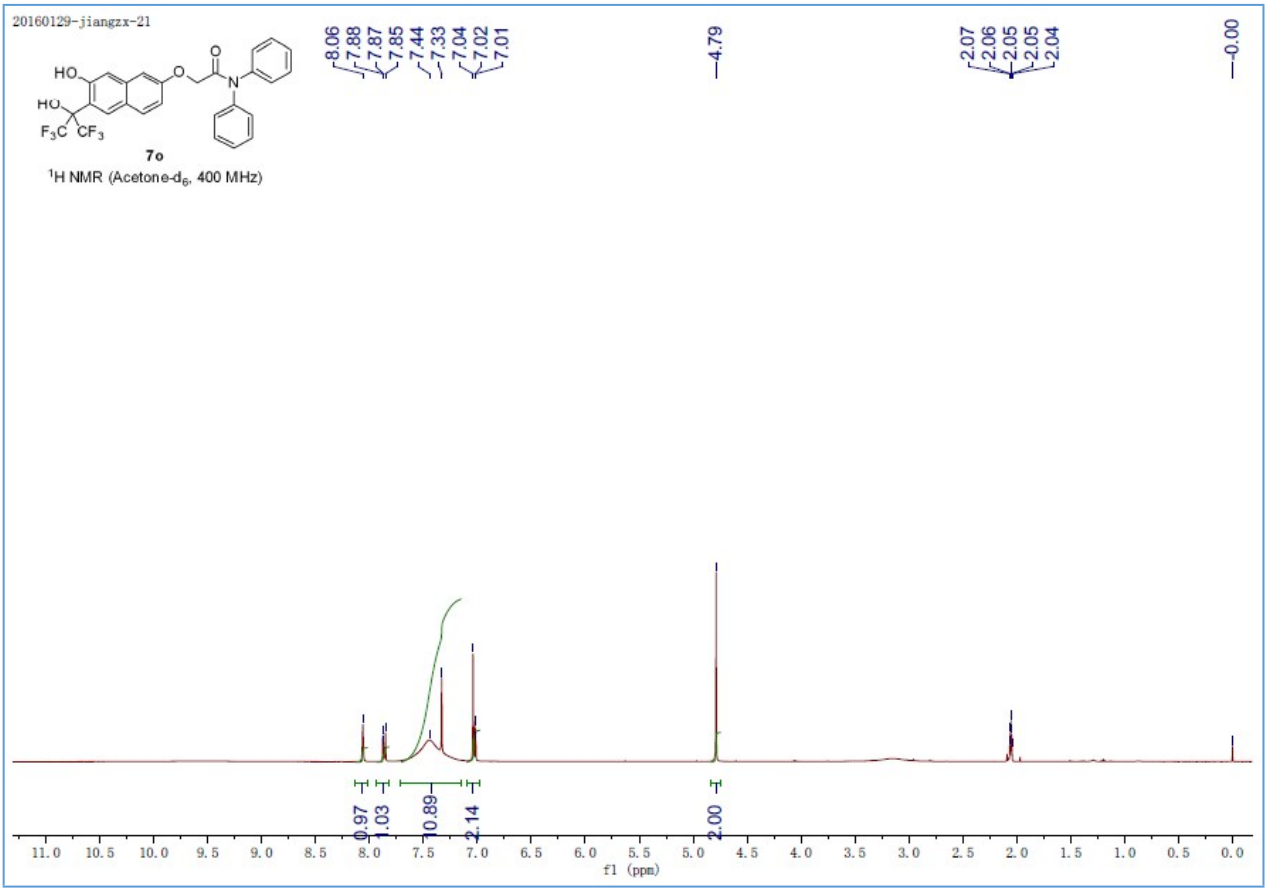

x10 2
+ESI Scan (1.052 min) Frag=100.0V PTP-15-T.d Subtract (6)
545.1490
7m
HRMS
Counts (%) vs. Mass-to-Charge (m/z)

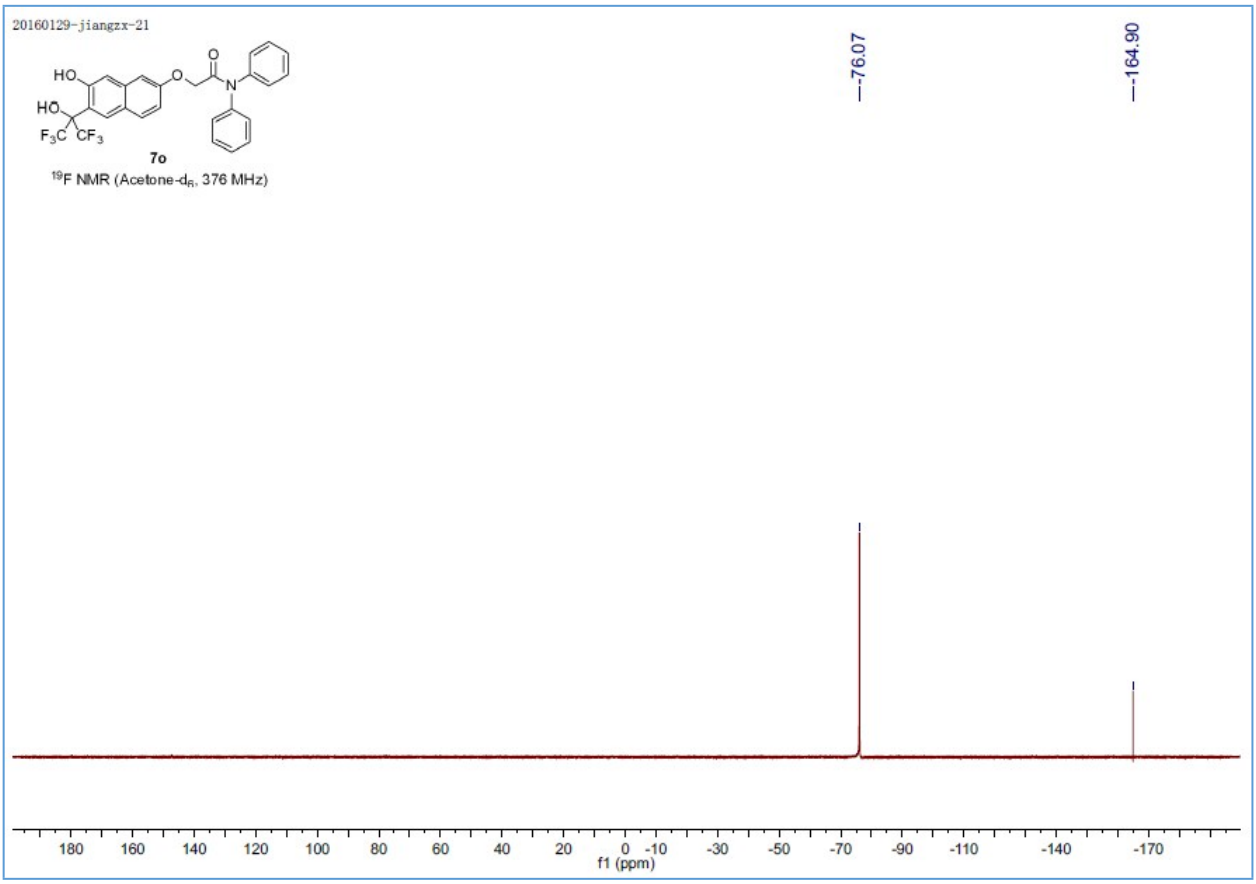

20160122-jiangzx-14
7n
1H NMR (Acetone-d6, 400 MHz)
f1 (ppm)

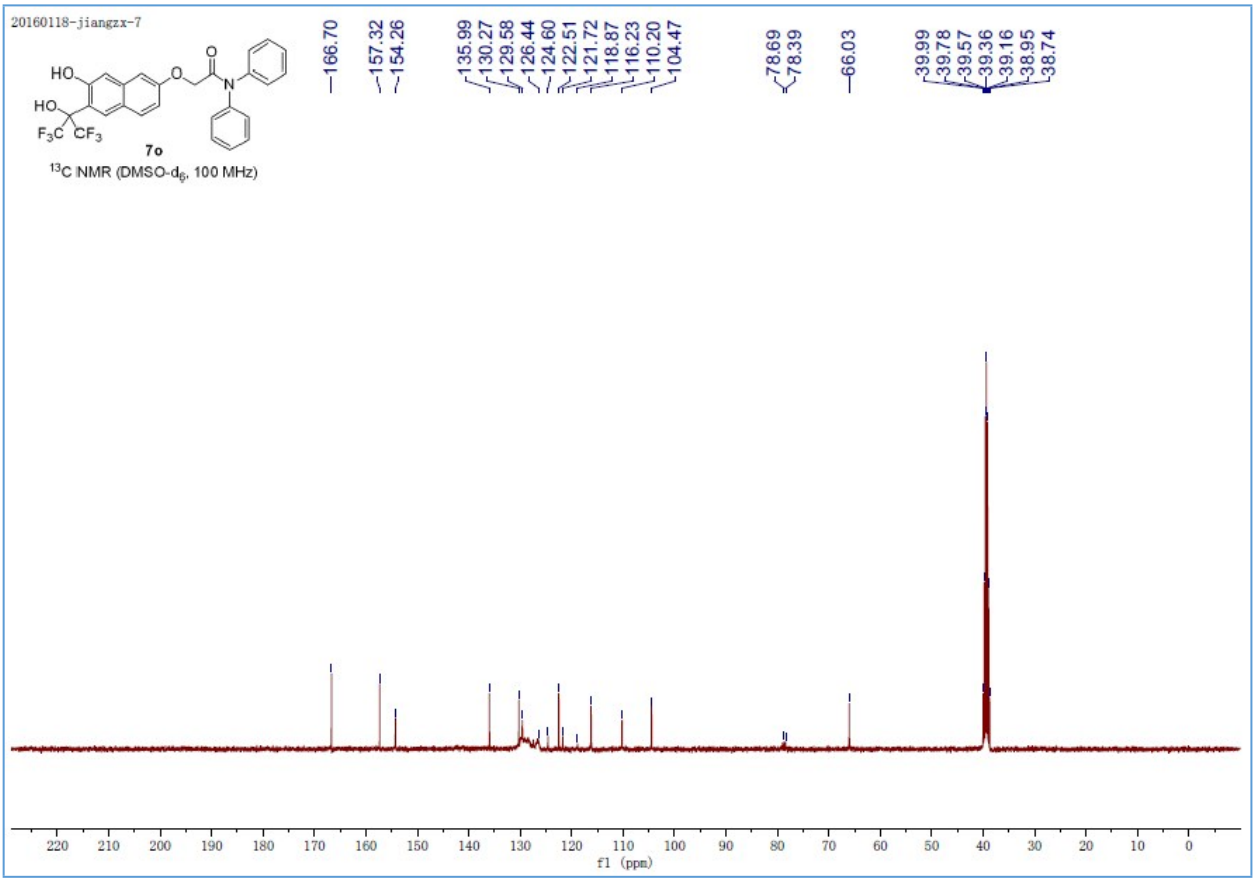

20150112-jiangzx-2
19F
HO
HO
F3C CF3
O
N
H
7n
19F NMR (Acetone-d6, 376 MHz)
-76.07
-164.90
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

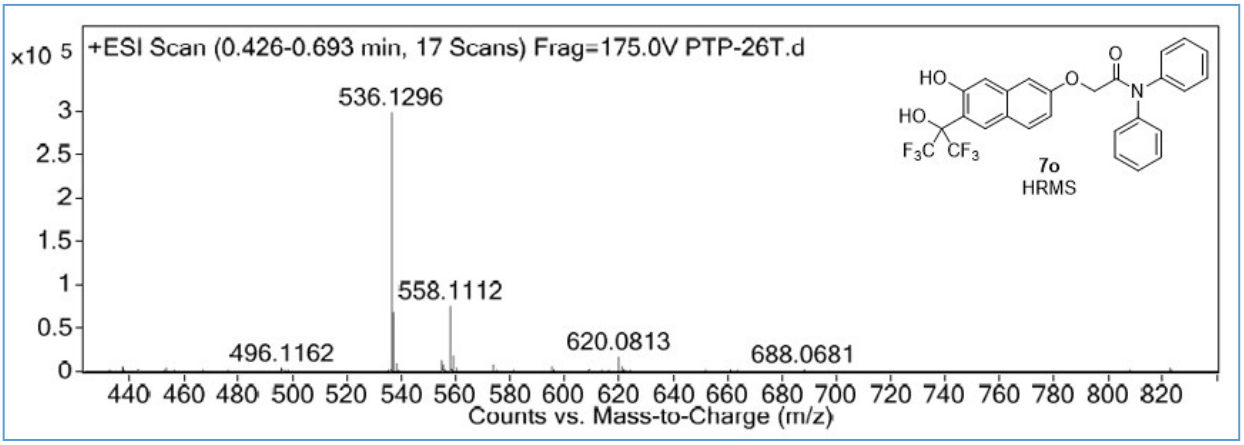

20160122-jiangzx-2
-206.26
-167.85
-158.14
-154.40
136.83
134.77
133.08
131.19
128.90
128.87
126.78
126.66
126.61
126.03
124.46
122.82
122.65
118.27
112.14
105.84
80.55
80.25
79.95
68.07
30.14
29.95
29.75
29.56
29.37
29.18
28.98
HO
HO
F3C CF3
O
N
H
7n
13C NMR (Acetone-d6, 100 MHz)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

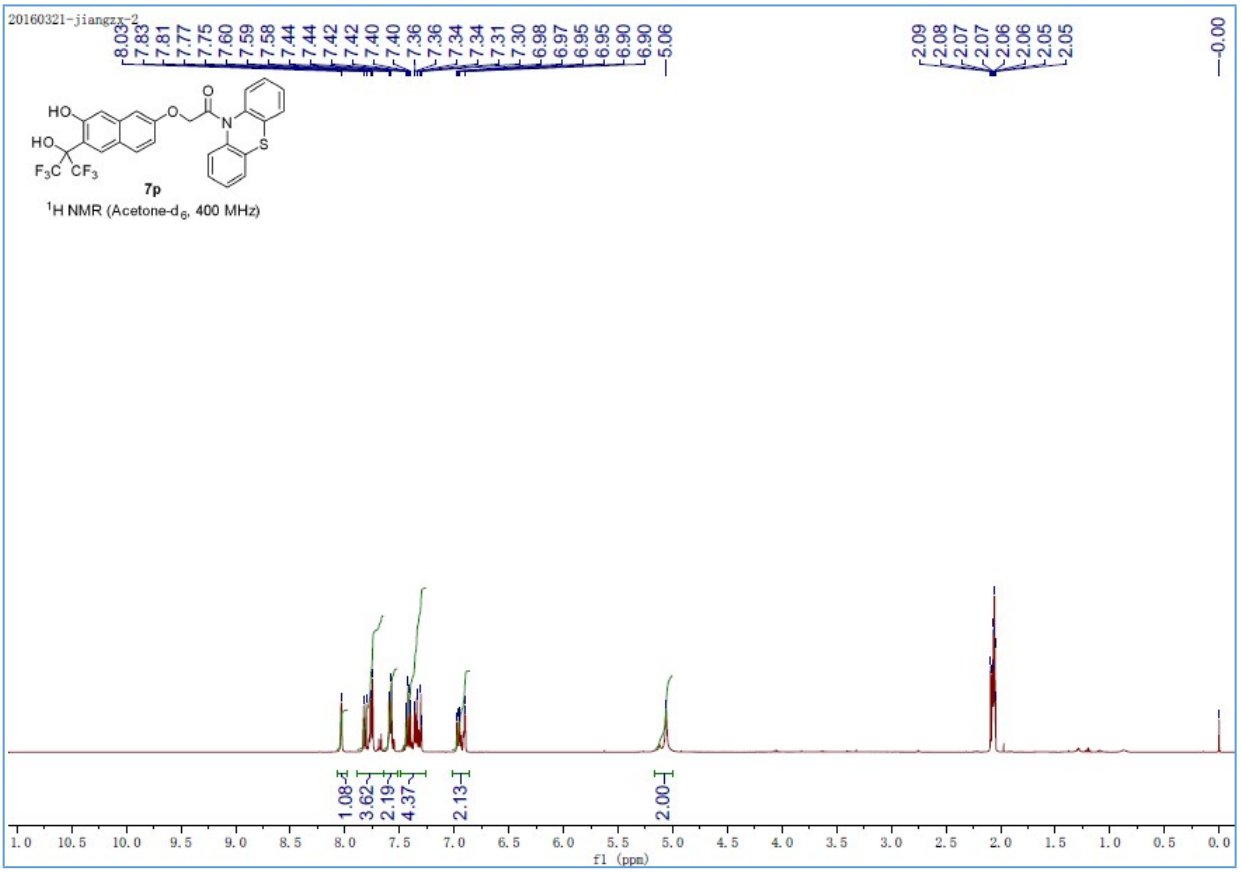

x10 5
+ESI Scan (1.631 min) Frag=135.0V PTP-14.d Subtract (2)
510.1110
532.1098
Counts vs. Mass-to-Charge (m/z)
7n
HRMS

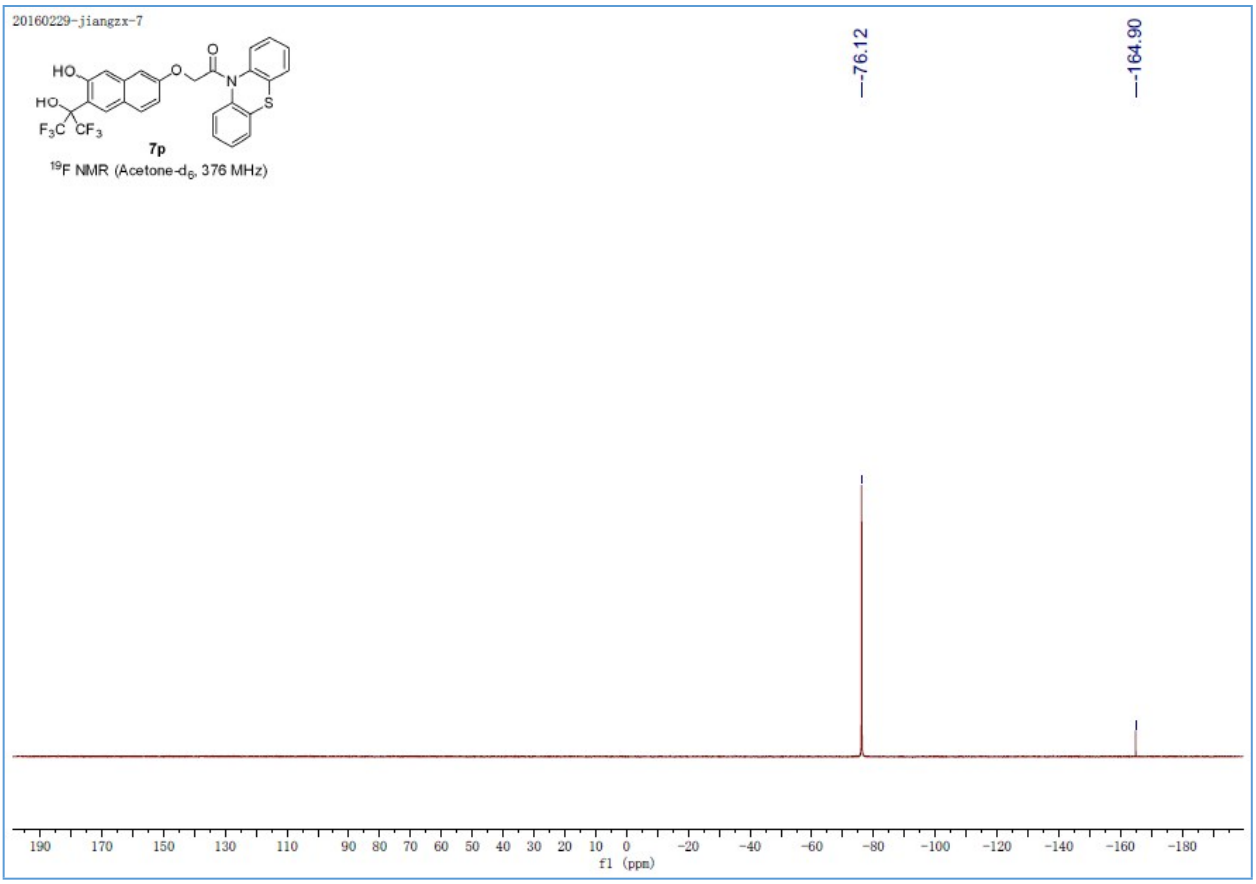

20160129-jiangzx-21
7o
1H NMR (Acetone-d6, 400 MHz)
f1 (ppm)

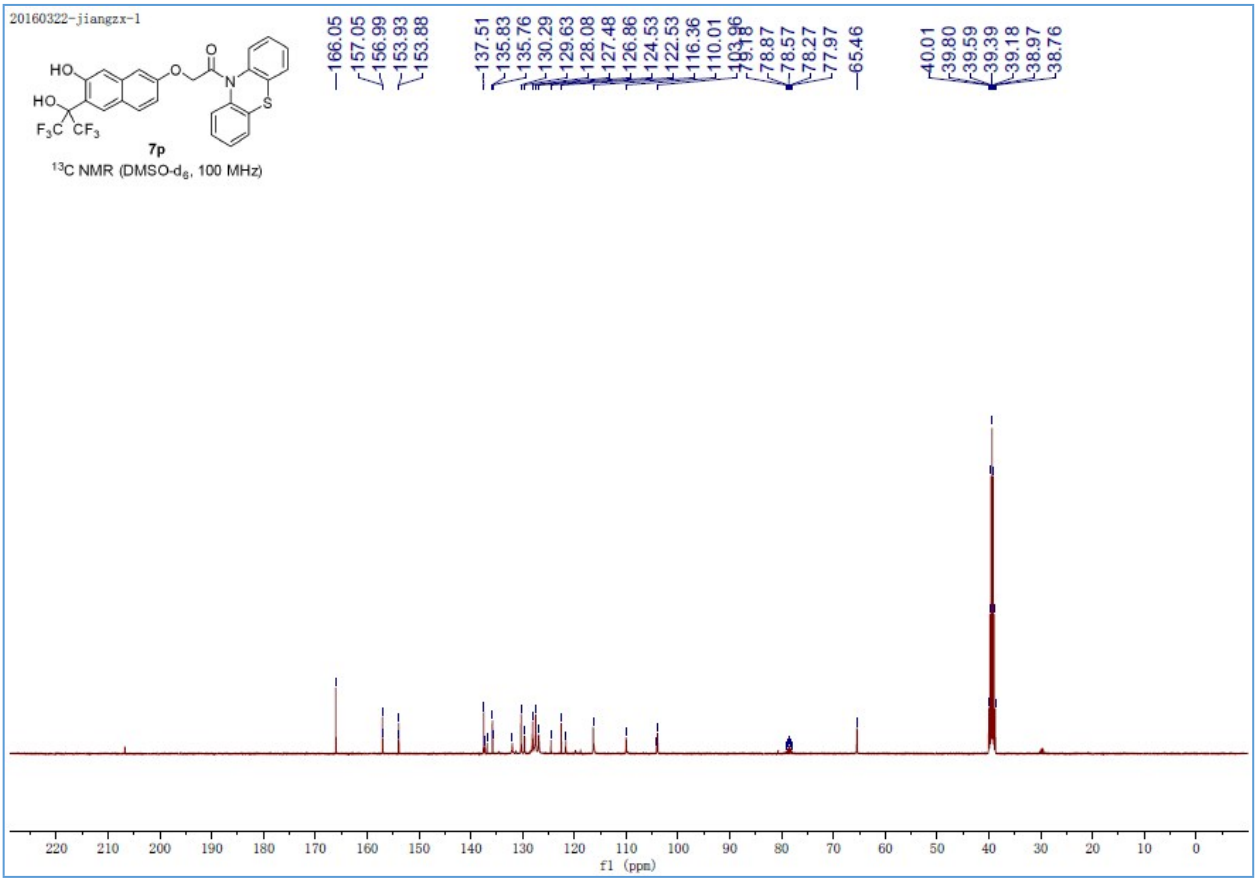

20160129-jiangzx-21
HO
HO
F3C CF3
O
O
N
7o
19F NMR (Acetone-d6, 376 MHz)
-76.07
-164.90
180 160 140 120 100 80 60 40 20 0 -10 -30 -50 -70 -90 -110 -140 -170
f1 (ppm)

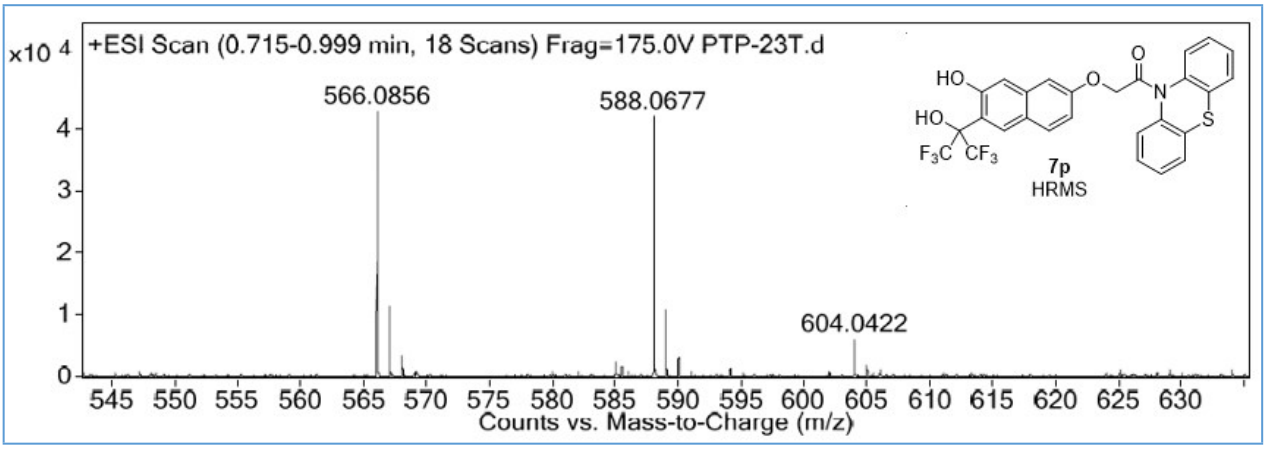

20160118-jiangzx-7
HO
HO
F3C CF3
O
O
N
7o
13C NMR (DMSO-d6, 100 MHz)
166.70
157.32
154.26
135.99
130.27
129.58
126.44
124.60
122.51
121.72
118.87
116.23
110.20
104.47
78.69
78.39
66.03
39.99
39.78
39.57
39.36
39.16
38.95
38.74
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

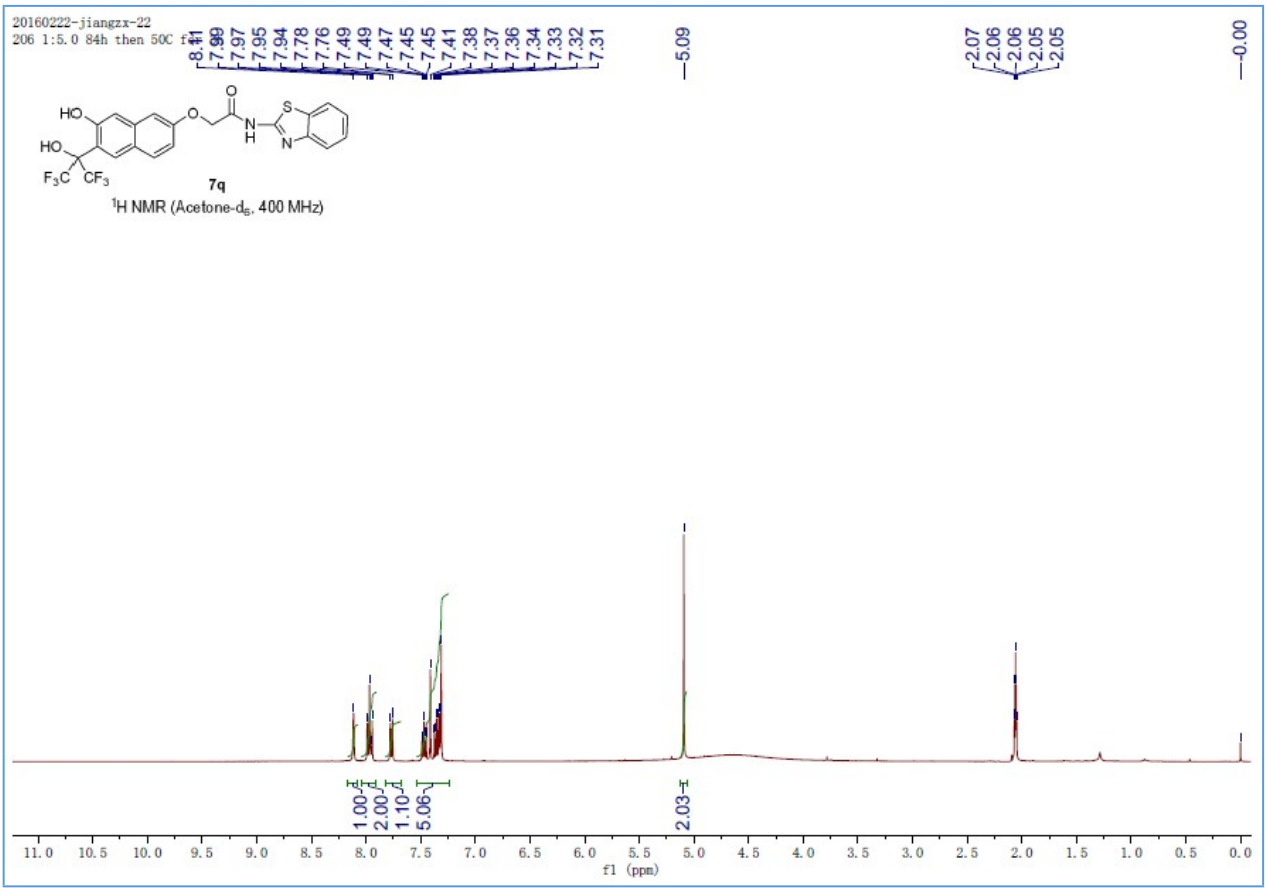

+ESI Scan (0.426-0.693 min, 17 Scans) Frag=175.0V PTP-26T.d
x10 5
536.1296
558.1112
496.1162
620.0813
688.0681
Counts vs. Mass-to-Charge (m/z)
7o
HRMS

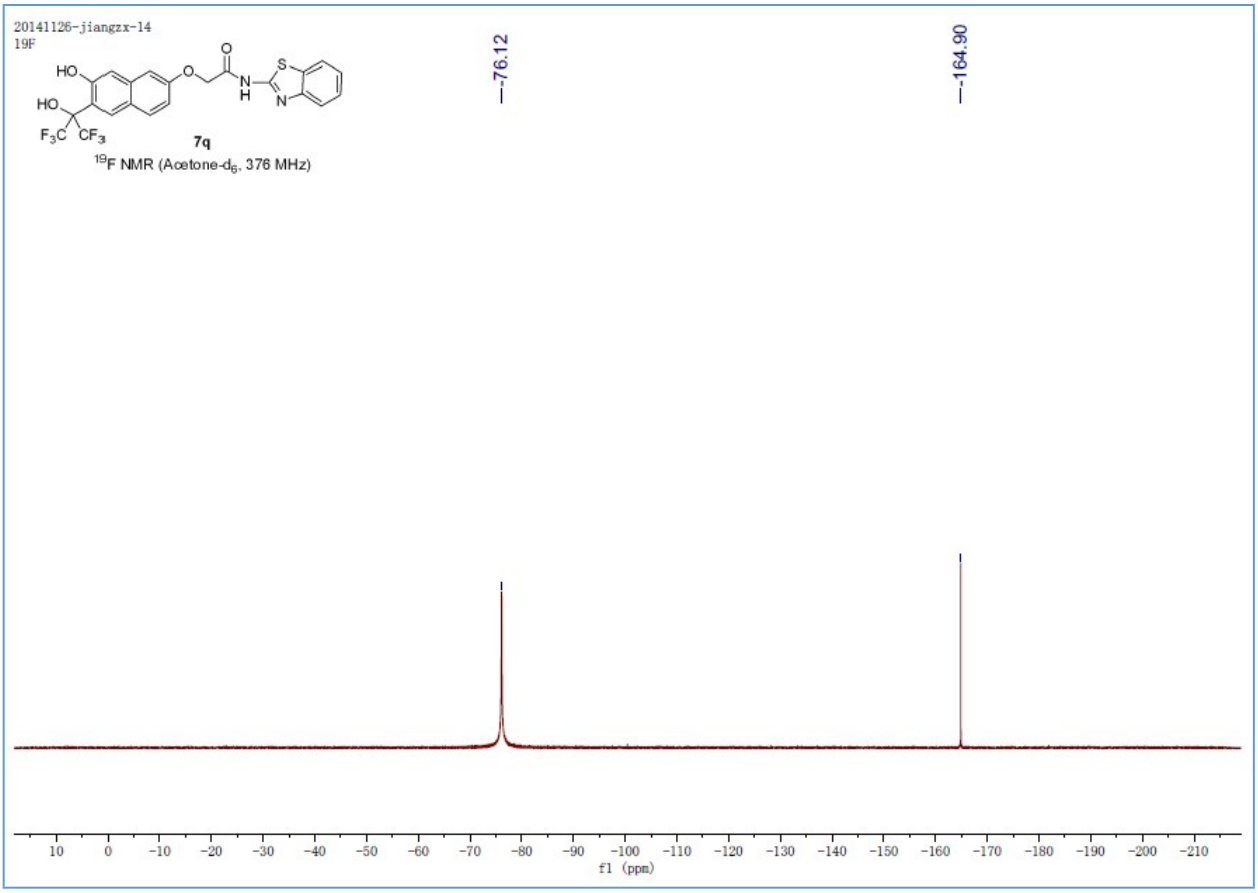

20160321-jiangzx-2
7p
1H NMR (Acetone-d6, 400 MHz)
f1 (ppm)

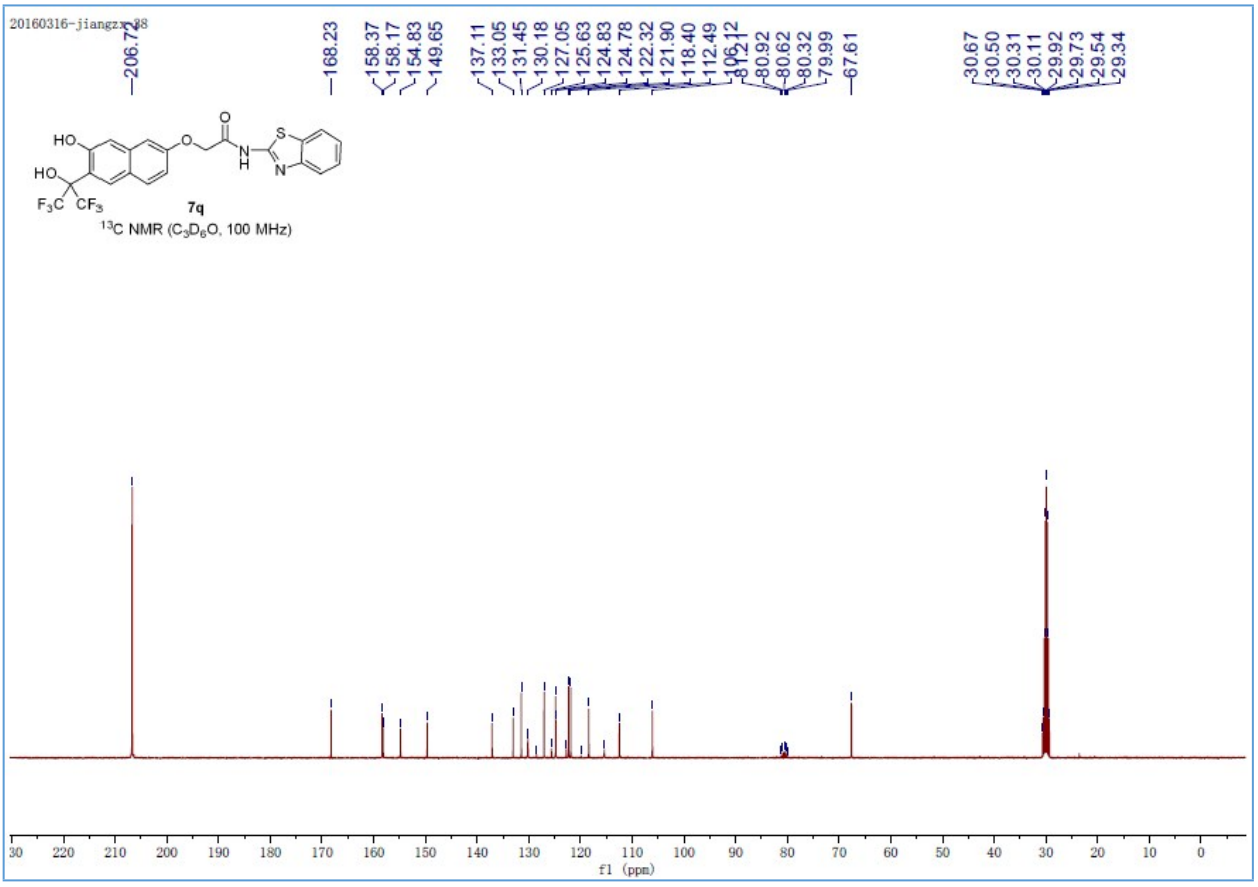

20160229-jiangzx-7
HO
HO
F3C CF3
O
N
S
7p
19F NMR (Acetone-d6, 376 MHz)
-76.12
-164.90
190 170 150 130 110 90 80 70 60 50 40 30 20 10 0 -20 -40 -60 -80 -100 -120 -140 -160 -180
f1 (ppm)

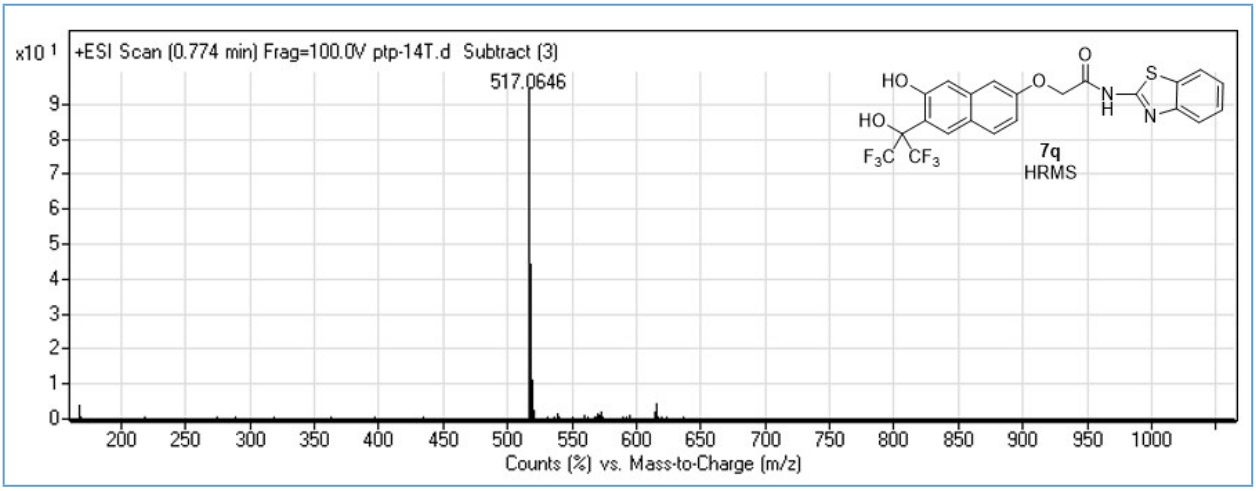

20160322-jiangzx-1
HO
HO
F3C CF3
O
N
S
7p
13C NMR (DMSO-d6, 100 MHz)
166.05
157.05
156.99
153.93
153.88
137.51
135.83
135.76
130.29
129.63
128.08
127.48
126.86
124.53
122.53
116.36
110.01
103.96
79.18
78.87
78.57
78.27
77.97
65.46
40.01
39.80
39.59
39.39
39.18
38.97
38.76
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

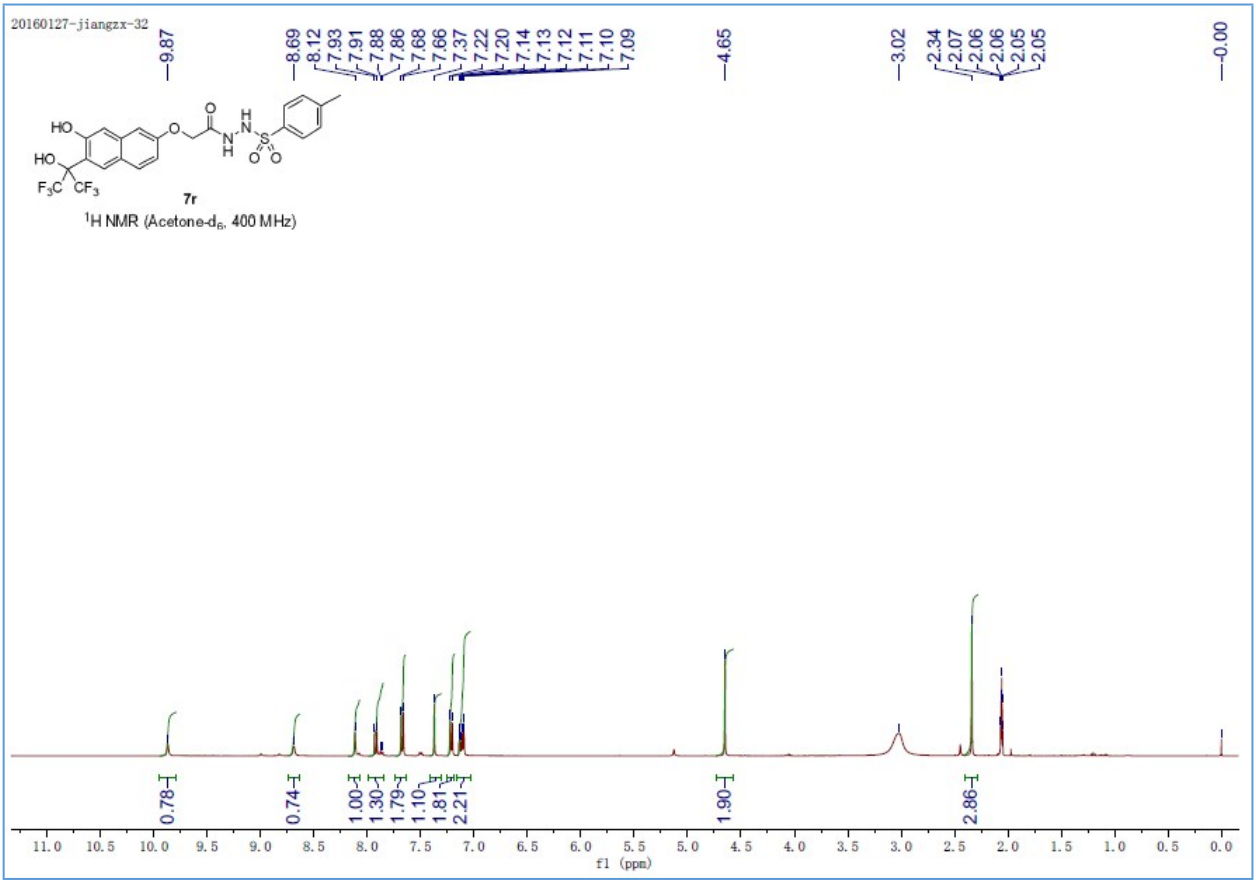

×10 4
+ESI Scan (0.715-0.999 min, 18 Scans) Frag=175.0V PTP-23T.d
566.0856
588.0677
604.0422
HO
HO
F3C CF3
O
N
S
7p
HRMS
Counts vs. Mass-to-Charge (m/z)

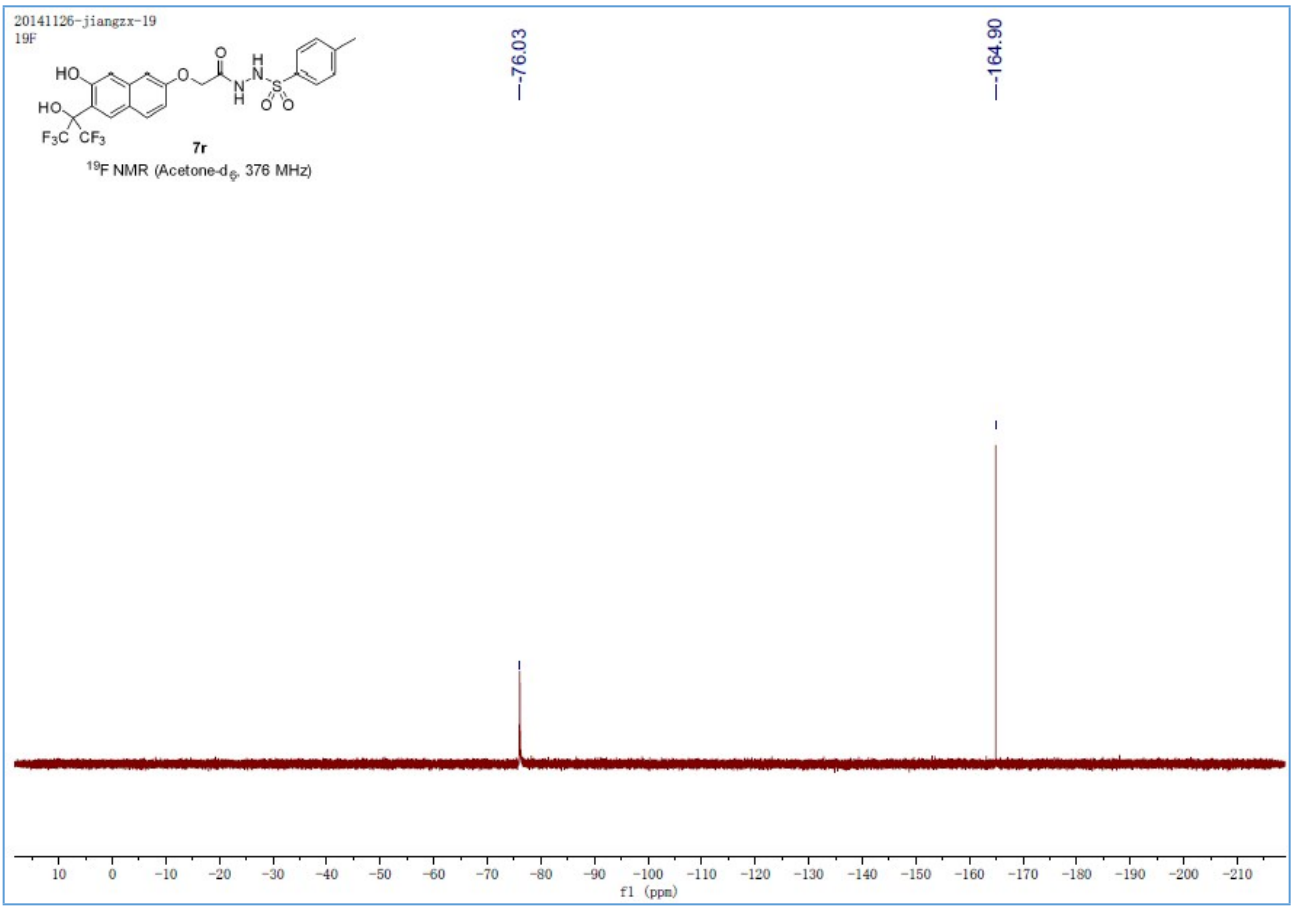

20160222-jiangzx-22
206 1:5.0 84h then 50C f1
HO
HO
F3C CF3
O
N
H
S
N
7q
1H NMR (Acetone-d6, 400 MHz)
f1 (ppm)

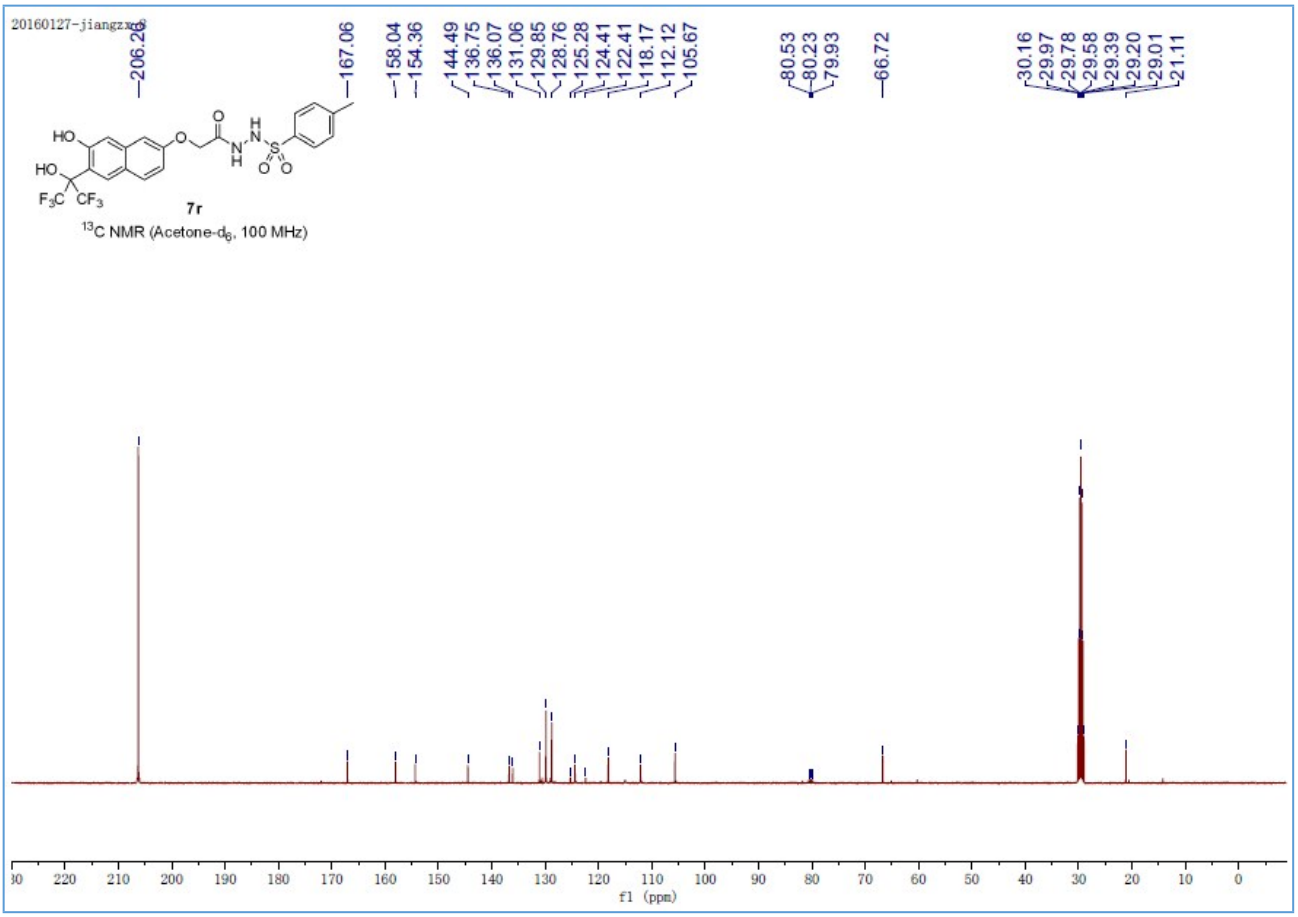

20141126-jiangzx-14
19F
HO
HO
F3C
CF3
7q
19F NMR (Acetone-d6, 376 MHz)
-76.12
-164.90
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

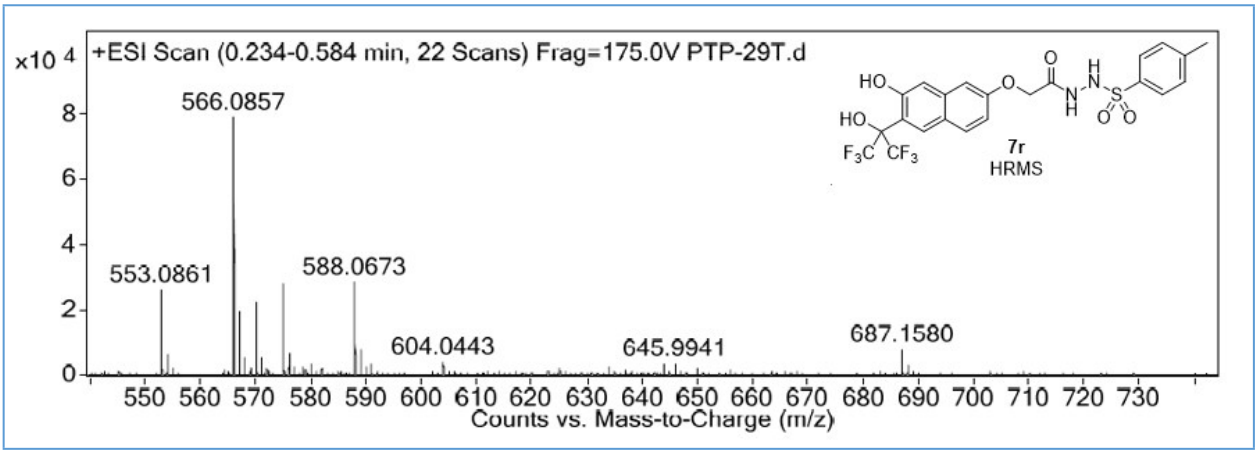

20160316-jiangzx-28
206.72
168.23
158.37
158.17
154.83
149.65
137.11
133.05
131.45
130.18
127.05
125.63
124.83
124.78
122.32
121.90
118.40
112.49
106.12
81.21
80.92
80.62
80.32
79.99
67.61
30.67
30.50
30.31
30.11
29.92
29.73
29.54
29.34
HO
HO
F3C
CF3
7q
13C NMR (C3D6O, 100 MHz)
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


x10 1
+ESI Scan (0.774 min) Frag=100.0V ptp-14T.d Subtract (3)
517.0646
HO
HO
F3C CF3
O
N
H
S
N
7q
HRMS
Counts (%) vs. Mass-to-Charge (m/z)


20160127-jiangzx-32
HO
HO
F3C CF3
7r
1H NMR (Acetone-d6, 400 MHz)
f1 (ppm)


20141126-jiangzx-19
19F
-76.03
-164.90
7r
19F NMR (Acetone-d6, 376 MHz)
f1 (ppm)


20160127-jiangzx-8
206.26
167.06
158.04
154.36
144.49
136.75
136.07
131.06
129.85
128.76
125.28
124.41
122.41
118.17
112.12
105.67
80.53
80.23
79.93
66.72
30.16
29.97
29.78
29.58
29.39
29.20
29.01
21.11
7r
13C NMR (Acetone-d6, 100 MHz)
f1 (ppm)


x10 4
+ESI Scan (0.234-0.584 min, 22 Scans) Frag=175.0V PTP-29T.d
566.0857
553.0861
588.0673
604.0443
645.9941
687.1580
HO
HO
F3C CF3
7r
HRMS
Counts vs. Mass-to-Charge (m/z)

4. Single-crystal X-ray structural data of compound 7c

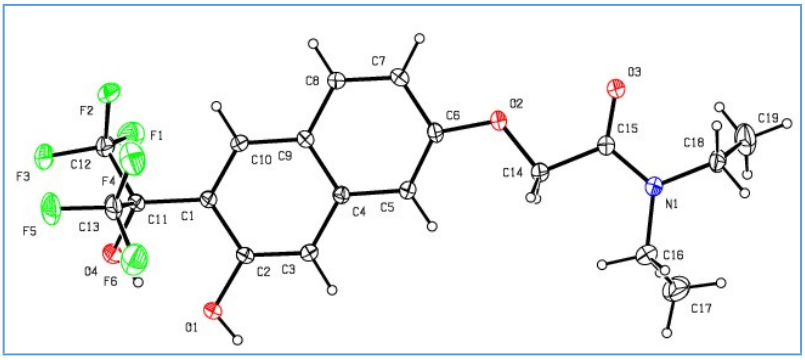


Fig. S1 Single-crystal X-ray structure of **7c** (CCDC 1470244).

Table S1. Bond lengths [Å] and angles [°] of **7c**.

Atom	Bond atom	Bond length (Å)	Angle atom	Angle (°)	2nd Angle atom	2nd Angle (°)
C(5)						
C(13)	C(5)	1.413				
C(3)	C(5)	1.408	C(13)	117.994		
C(6)	C(5)	1.421	C(3)	123.112	C(13)	118.893
C(11)	C(13)	1.408	C(5)	119.135	C(3)	-178.241
C(14)	C(13)	1.405	C(5)	119.251	C(11)	121.607
C(1)	C(14)	1.363	C(13)	122.823	C(5)	-1.484
C(2)	C(3)	1.367	C(5)	121.334	C(6)	178.501
C(8)	C(6)	1.359	C(5)	119.748	C(3)	178.714
C(9)	C(11)	1.349	C(13)	120.836	C(5)	-0.950
C(16)	C(1)	1.530	C(2)	120.665	C(14)	121.837
O(46)	C(8)	1.375	C(6)	126.389	C(9)	112.513
O(44)	C(2)	1.369	C(1)	116.246	C(3)	122.681
C(17)	C(16)	1.538	C(1)	113.187	C(2)	-151.706
C(18)	C(16)	1.533	C(1)	109.079	C(17)	109.730
O(48)	C(16)	1.398	C(1)	113.769	C(17)	102.622
C(19)	O(46)	1.410	C(8)	118.173	C(6)	2.192
C(22)	C(19)	1.520	O(46)	106.873	C(8)	178.151
N(43)	C(22)	1.339	C(19)	117.431	O(46)	-177.506
O(47)	C(22)	1.225	C(19)	121.894	N(43)	120.668
C(23)	N(43)	1.463	C(22)	124.449	C(19)	-4.500
C(30)	N(43)	1.466	C(22)	117.660	C(23)	117.602
C(26)	C(23)	1.499	N(43)	113.875	C(22)	120.548
C(33)	C(30)	1.501	N(43)	113.503	C(22)	-82.241
F(37)	C(17)	1.328	C(16)	111.201	C(1)	49.033
F(38)	C(17)	1.324	C(16)	114.238	F(37)	106.872
F(39)	C(17)	1.333	C(16)	110.877	F(37)	106.944

F(40)	C(18)	1.332	C(16)	112.420	C(1)	58.022
F(41)	C(18)	1.332	C(16)	112.915	F(40)	106.498
F(42)	C(18)	1.329	C(16)	110.602	F(40)	107.578
H(31)	F(42)	13.090	C(18)	102.458	C(16)	59.469
H(32)	F(42)	12.729	C(18)	96.886	C(16)	63.373
H(24)	F(42)	10.035	C(18)	106.730	C(16)	52.806
H(34)	F(42)	13.538	C(18)	96.456	C(16)	51.548
H(35)	F(42)	14.382	C(18)	94.894	C(16)	56.768
H(36)	F(42)	13.190	C(18)	90.976	C(16)	55.151
H(25)	F(42)	11.300	C(18)	109.562	C(16)	57.094
H(21)	F(42)	8.564	C(18)	99.604	C(16)	59.801
H(27)	F(42)	11.661	C(18)	102.793	C(16)	44.427
H(28)	F(42)	11.686	C(18)	110.478	C(16)	44.891
H(29)	F(42)	12.726	C(18)	106.303	C(16)	48.679
H(15)	F(42)	4.217	C(18)	44.375	C(16)	53.870
H(4)	F(42)	4.652	C(18)	104.343	C(16)	34.138
H(10)	F(42)	7.887	C(18)	70.191	C(16)	64.123
H(45)	F(42)	3.522	C(18)	110.668	C(16)	4.947
H(12)	F(42)	6.281	C(18)	57.087	C(16)	63.636
H(20)	F(42)	8.939	C(18)	95.231	C(16)	50.697
H(7)	F(42)	6.584	C(18)	97.246	C(16)	49.846
H(49)	F(42)	2.785	C(18)	74.424	C(16)	-22.395