Supporting Information for
Original article
Discovery of 4-arylthiophene-3-carboxylic acid as inhibitor of ANO1 and its effect as analgesic agent

Yuxi Wang[a,†], Jian Gao[a,†], Song Zhao[b], Yan Song[a], Han Huang[a], Guiwang Zhu[a], Peili Jiao[a], Xiangqing Xu[b], Guisen Zhang[c], Kewei Wang[d,*], Liangren Zhang[a,*], Zhenming Liu[a,*]

[a]*State Key Laboratory of Natural and Biomimetic Drugs, School of Pharmaceutical Sciences, Peking University, Beijing 100191, China*

[b]*Jiangsu Nhwa Pharmaceutical Co., Ltd., Xuzhou 221116, China*

[c]*College of life science and technology, Jiangsu Ocean University, Lianyungang 222005, China*

[d]*Department of Pharmacology, School of Pharmacy, Qingdao University, Qingdao 266021, China*

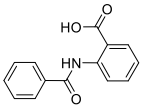
[†]These authors made equal contributions to this work.

Received 13 September 2020; received in revised form 26 October 2020; accepted 4 November 2020

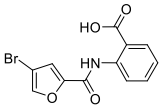
*Corresponding authors. Tel: +86 532 82991070 (Kewei Wang), +86 10 82802567 (Liangren Zhang), +86 10 82805281 (Zhenming Liu).

E-mail addresses: wangkw@qdu.edu.cn (wangkw@qdu.edu.cn), liangren@bjmu.edu.cn (Liangren Zhang), zmliu@bjmu.edu.cn (Zhenming Liu).

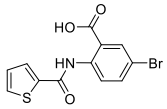
Content



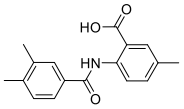
S1



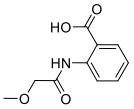
S2



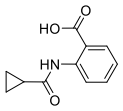
S3



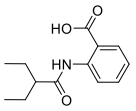
S4



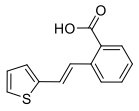
S5



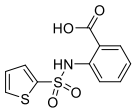
S6



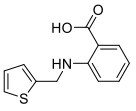
S7



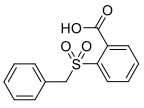
S8



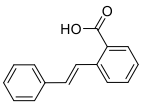
S9



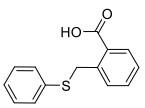
S10



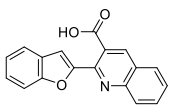
S11



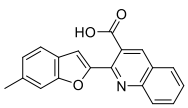
S12



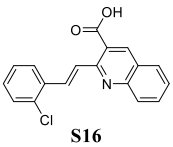
S13



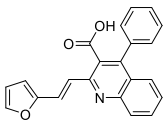
S14



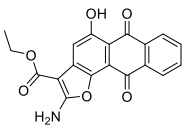
S15



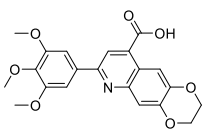
S16



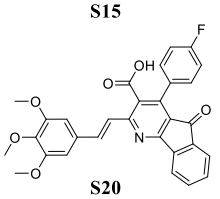
S17



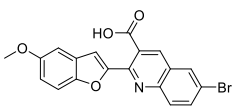
S18



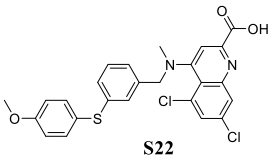
S19



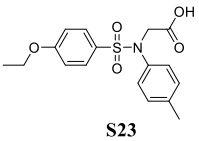
S20



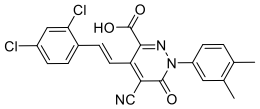
S21



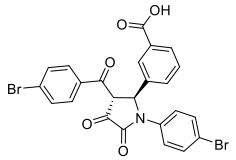
S22



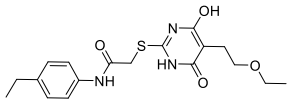
S23



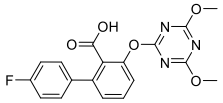
S24



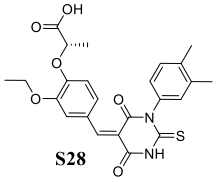
S25



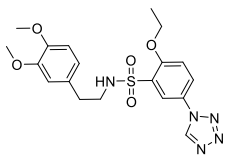
S26



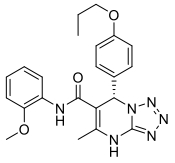
S27



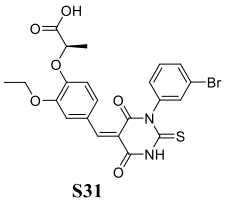
S28



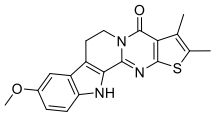
S29



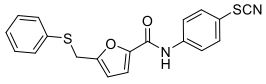
S30



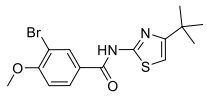
S31



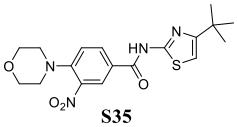
S32



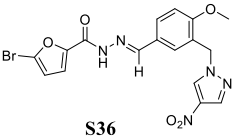
S33



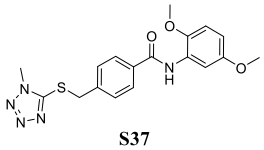
S34



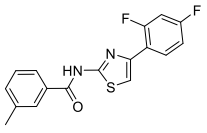
S35



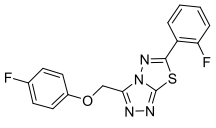
S36



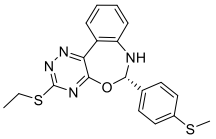
S37



S38



S39



S40

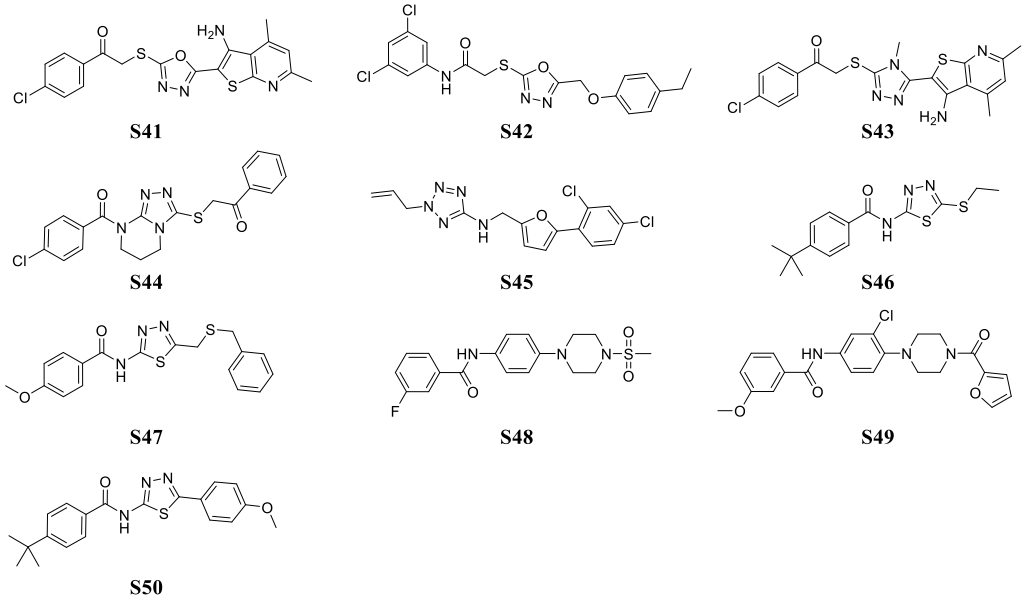
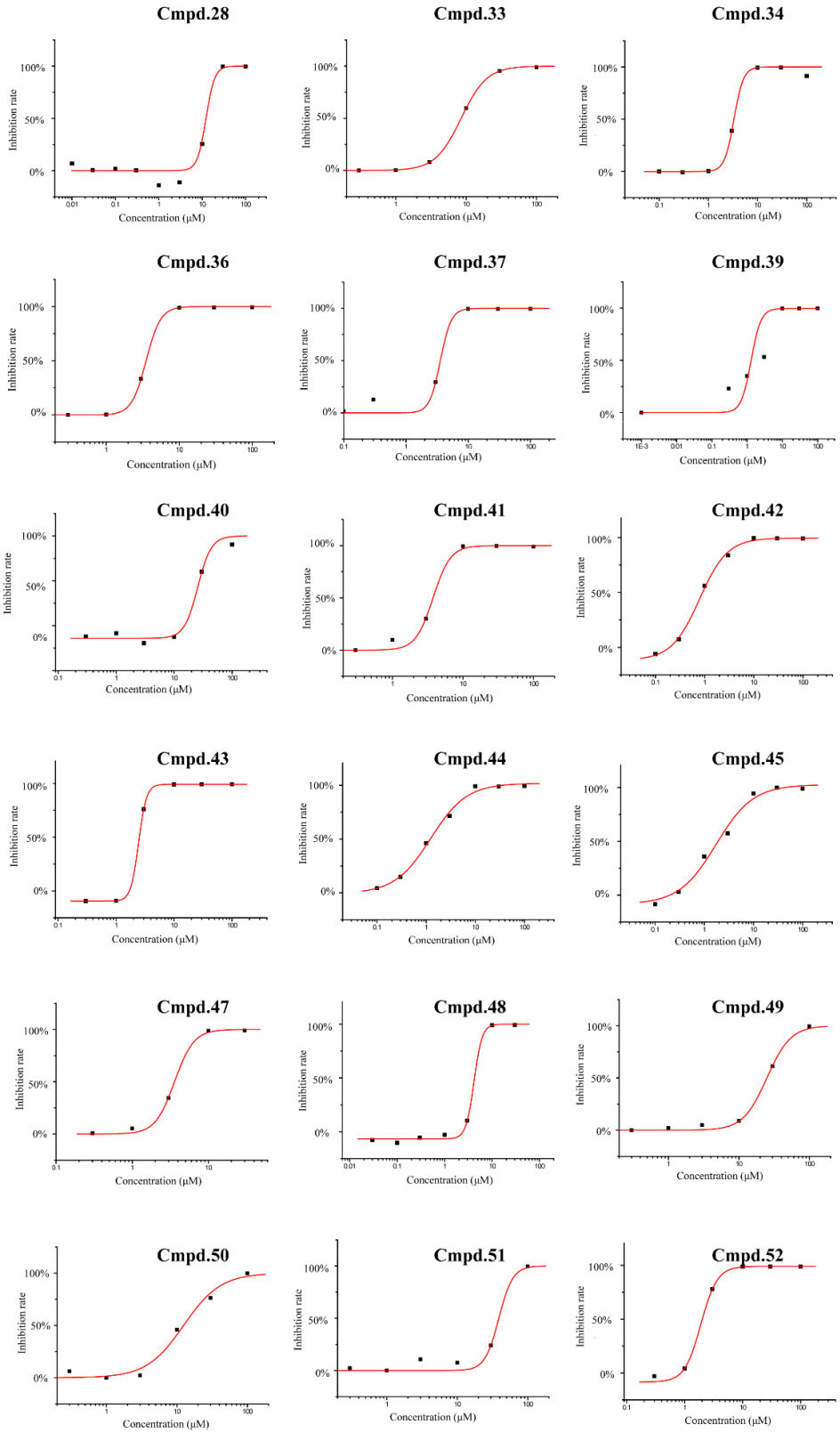


Figure S1 Structures of other compounds in shape and electronic distribution based virtual screening.


Cmpd.28
Cmpd.33
Cmpd.34
Cmpd.36
Cmpd.37
Cmpd.39
Cmpd.40
Cmpd.41
Cmpd.42
Cmpd.43
Cmpd.44
Cmpd.45
Cmpd.47
Cmpd.48
Cmpd.49
Cmpd.50
Cmpd.51
Cmpd.52
Inhibition rate
Concentration (μM)
100%
50%
0%

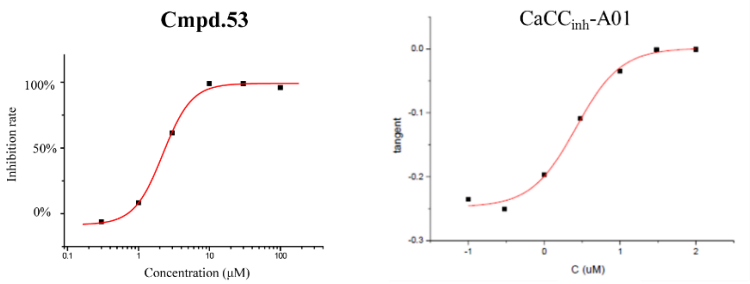


Figure S2 ANO1 inhibitory rate–concentration curve. Compounds **35** and **38** are not represented here because of no significant inhibition effect observed in 100 μmol/L concentration.

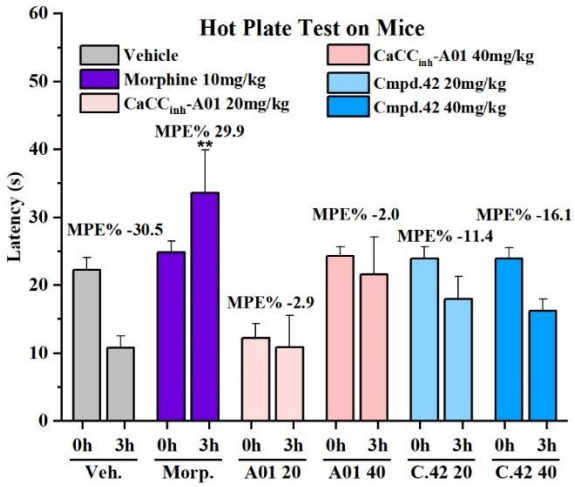


Figure S3 Hot plate test on mice; n=10. The vehicle group was treated with saline by i.g. administration instead of the corresponding compound solution. MPE, maximal possible effect (%). All data are represented by the mean ± SD. Statistical significance was determined by ANOVA, $^{**}P<0.01$ *vs*. vehicle.

In the hot plate test, the latency of pain response appearing (foot licking or jumping) was measured before and 3 h after compound administration. As shown in Fig. S3, the latency of morphine group was significantly prolonged after 10 mg/kg morphine i.p. injection and its maximal possible effect (MPE, %) was about 30. However, no obvious differences in pain response latency were observed among vehicle group, 20 and 40 mg/kg CaCC$_{inh}$-A01 group, and 20 mg/kg compound **42** group.

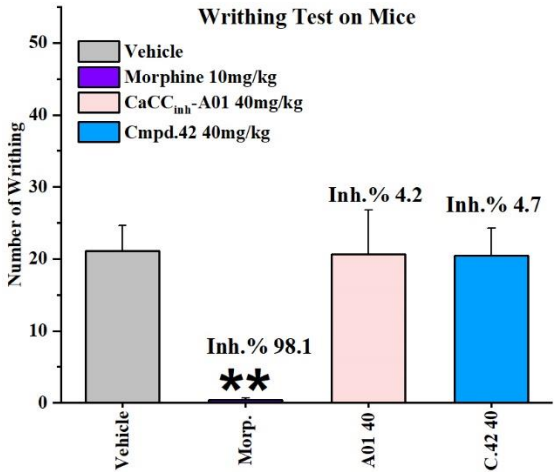


Figure S4 Writhing test on mice; n=10. Inh., the inhibition ratio of pain response (number of writhing) in the corresponding compound group against the vehicle group. All data are represented by the mean ± SD. Statistical significance was determined by ANOVA, $^{**}P<0.01$ compared to vehicle.

In writhing test (Fig. S4), 0.6% (*v*/*v*) acetic acid solution was i.p. injected 1 h after compound administration, then the number of writhing was measured within 15 min immediately. Morphine (10 mg/kg, i.p.) significantly reduce the number of writhing in mice, the inhibition rate of writhing is about 98%. ANO1 inhibitors CaCC$_{inh}$-A01 (20 and 40 mg/kg) and compound **42** (20 mg/kg) displayed no significant analgesic effect on number of writhing.

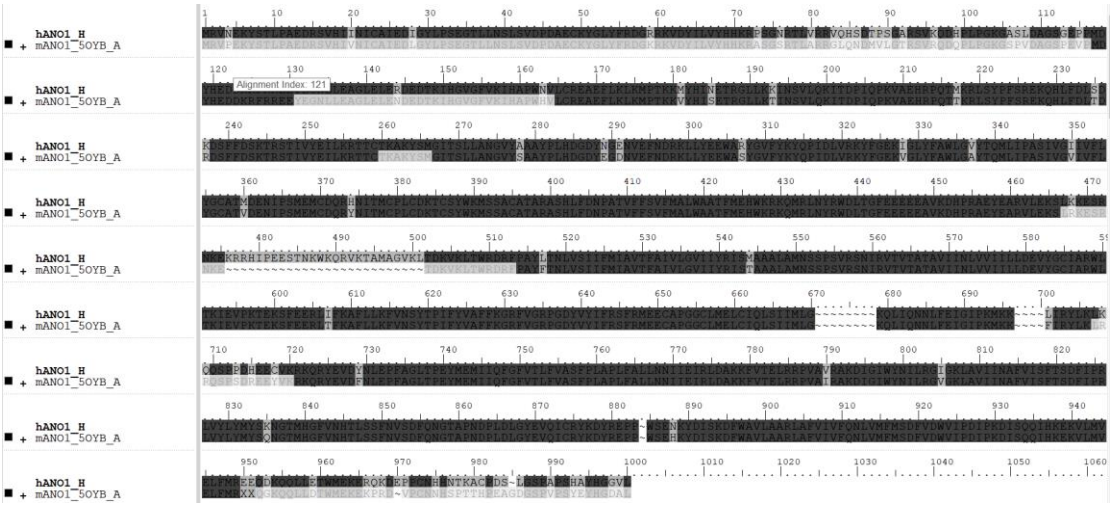
A

	hANO1_H	hANO2_H	hANO3_H	hANO4_H	hANO5_H	hANO6_H	hANO7_H	hANO8_H	hANO9_H	hANO10_H	mhANO_A	mANO1_5OYB_A
hANO1_H	100	56	33	36	34	32	32	10	25	13	12	89
hANO2_H	56	100	33	34	33	29	31	10	25	13	12	56
hANO3_H	33	33	100	60	37	37	30	10	28	15	12	33
hANO4_H	36	34	60	100	38	39	31	10	31	16	13	36
hANO5_H	34	33	37	38	100	48	31	11	28	16	12	35
hANO6_H	32	29	37	39	48	100	30	11	27	17	13	33
hANO7_H	32	31	30	31	31	30	100	11	26	16	13	32
hANO8_H	10	10	10	10	11	11	11	100	11	15	11	10
hANO9_H	25	25	28	31	28	27	26	11	100	15	15	25
hANO10_H	13	13	15	16	16	17	16	15	15	100	16	13
mhANO_A	12	12	12	13	12	13	13	11	15	16	100	12
mANO1_5OYB_A	89	56	33	36	35	33	32	10	25	13	12	100

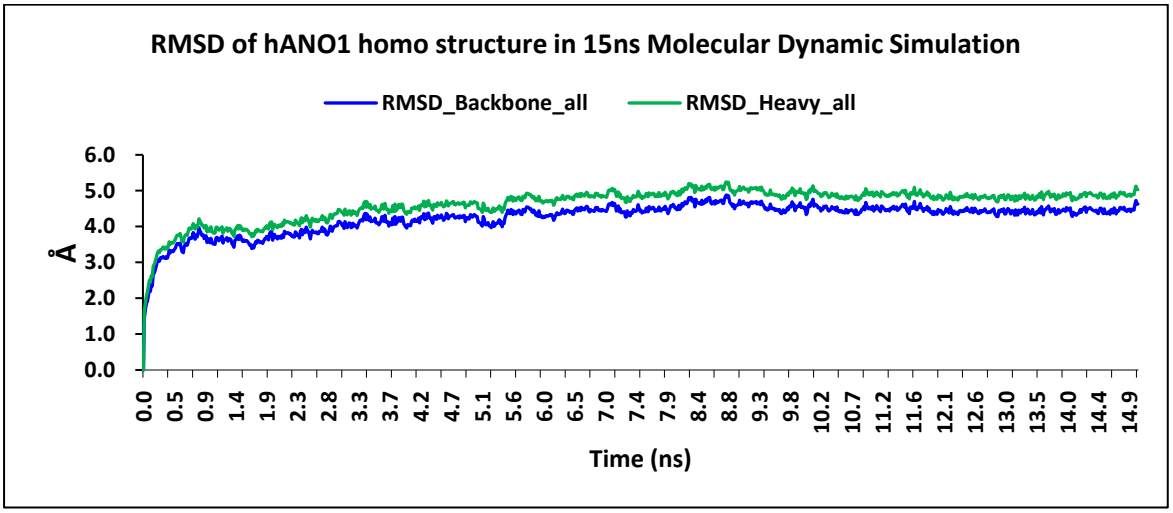
B

	hANO1_H	hANO2_H	hANO3_H	hANO4_H	hANO5_H	hANO6_H	hANO7_H	hANO8_H	hANO9_H	hANO10_H	mhANO_A	mANO1_5OYB_A
hANO1_H	100	70	48	51	50	48	47	20	39	27	25	93
hANO2_H	70	100	49	51	49	45	48	20	38	26	24	70
hANO3_H	48	49	100	73	53	53	47	19	41	27	23	48
hANO4_H	51	51	73	100	57	58	48	20	44	28	24	52
hANO5_H	50	49	53	57	100	66	47	20	43	29	26	51
hANO6_H	48	45	53	58	66	100	46	21	45	30	27	49
hANO7_H	47	48	47	48	47	46	100	20	40	30	25	48
hANO8_H	20	20	19	20	20	21	20	100	21	24	20	21
hANO9_H	39	38	41	44	43	45	40	21	100	30	29	40
hANO10_H	27	26	27	28	29	30	30	24	30	100	31	27
mhANO_A	25	24	23	24	26	27	25	20	29	31	100	26
mANO1_5OYB_A	93	70	48	52	51	49	48	21	40	27	26	100

C



D



E

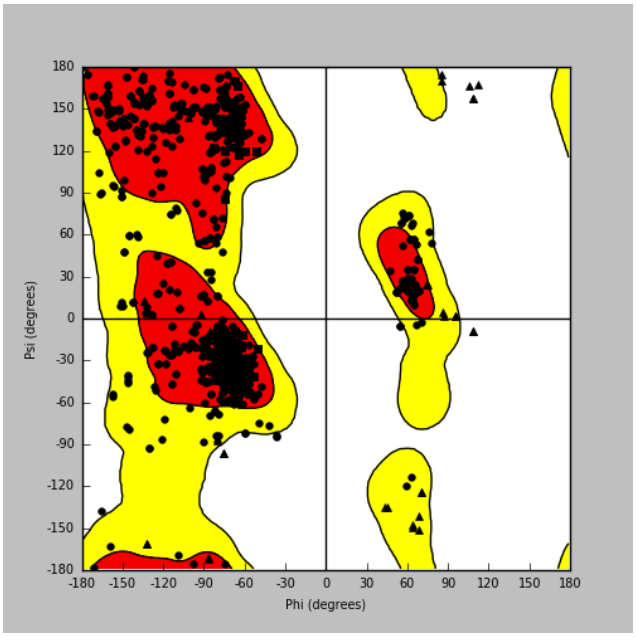


Figure S5 ANO1 homology modeling. (A) Sequence alignment: identity. (B) Sequence alignment: similarity. (C) Sequence alignment of hANO1 and mANO1. (D) 15 ns molecular dynamic optimization of hANO1 homo structure. (E) Ramachandran plot of hANO1 homo structure (Dimer).

Table S1 ANO1 inhibitoty activity of other compounds in shape and electronic distribution based virtual screening.

Compd.	Inh. (%)[a]	Compd.	Inh. (%)[a]
S1	34.5	**S26**	15.7
S2	27.7	**S27**	14.9
S3	88.2	**S28**	5.6
S4	25.7	**S29**	1.9
S5	–1.1	**S30**	–28.2
S6	22.7	**S31**	17.5
S7	11.0	**S32**	17.8
S8	10.5	**S33**	6.1
S9	26.6	**S34**	36.0
S10	7.0	**S35**	23.7
S11	24.1	**S36**	27.3
S12	28.9	**S37**	79.2
S13	7.2	**S38**	28.9
S14	25.1	**S39**	31.7
S15	28.8	**S40**	14.9
S16	12.6	**S41**	35.5
S17	14.2	**S42**	14.4
S18	19.8	**S43**	16.0
S19	–36.7	**S44**	23.6
S20	36.3	**S45**	60.8
S21	18.9	**S46**	18.0
S22	4.3	**S47**	23.3
S23	8.3	**S48**	16.6
S24	61.2	**S49**	26.9
S25	41.5	**S50**	13.4

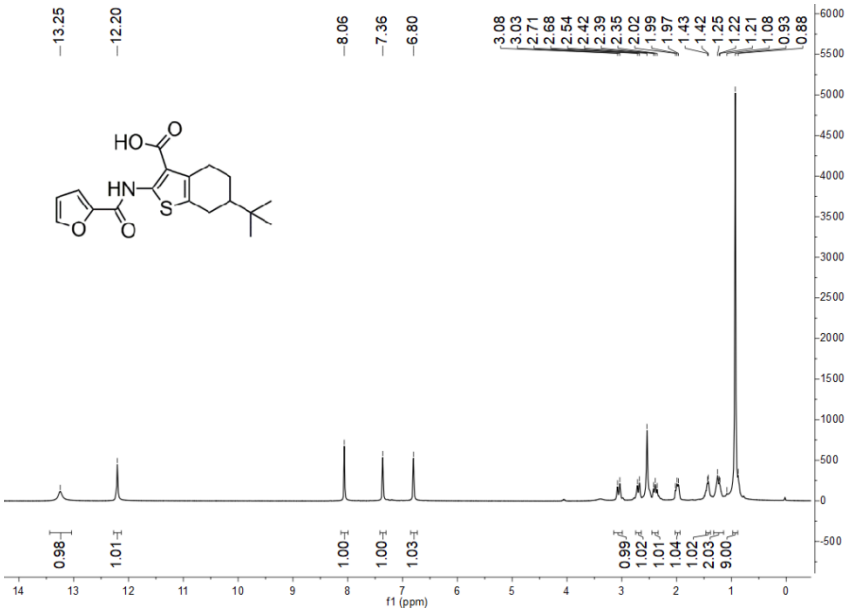
[a]Inh. (%) refers to the ANO1 inhibition rate as determined by in whole cell patch clamp recording at 100 μmol/L; *n*=3.

Structure characterization

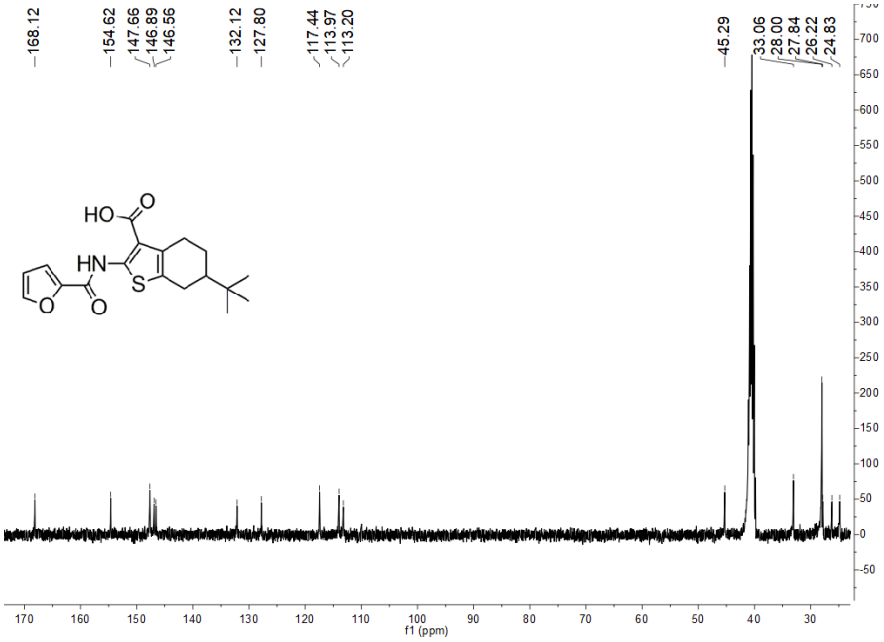
^{1}H and ^{13}C NMR spectra were recorded on Bruker (400 MHz) instruments, using DMSO-d_6 or $CDCl_3$ as solvents. High-resolution mass spectra (HRMS) were recorded on Bruker Apex IV FTMS mass spectrometer using ESI (electrospray ionization).

6-(*tert*-Butyl)-2-(furan-2-carboxamido)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylic acid ($CaCC_{inh}$-A01, **1**)

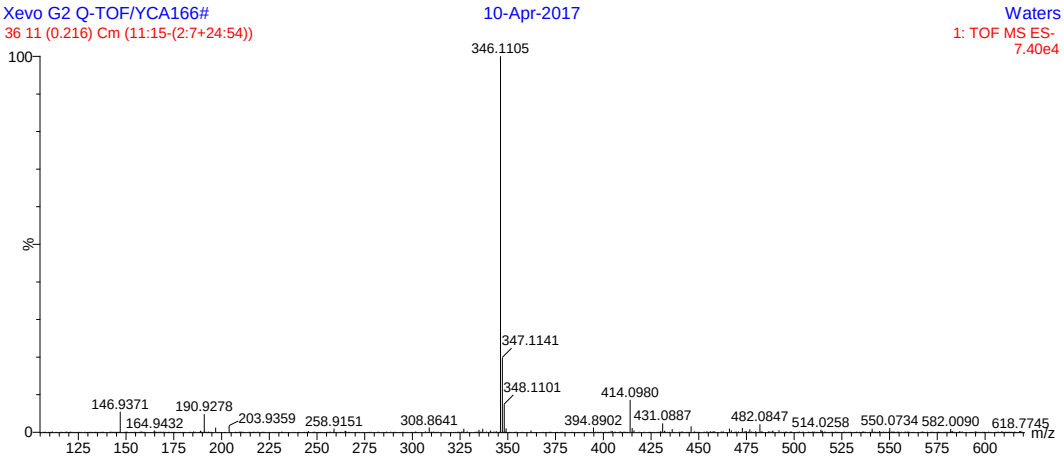
^{1}H-NMR



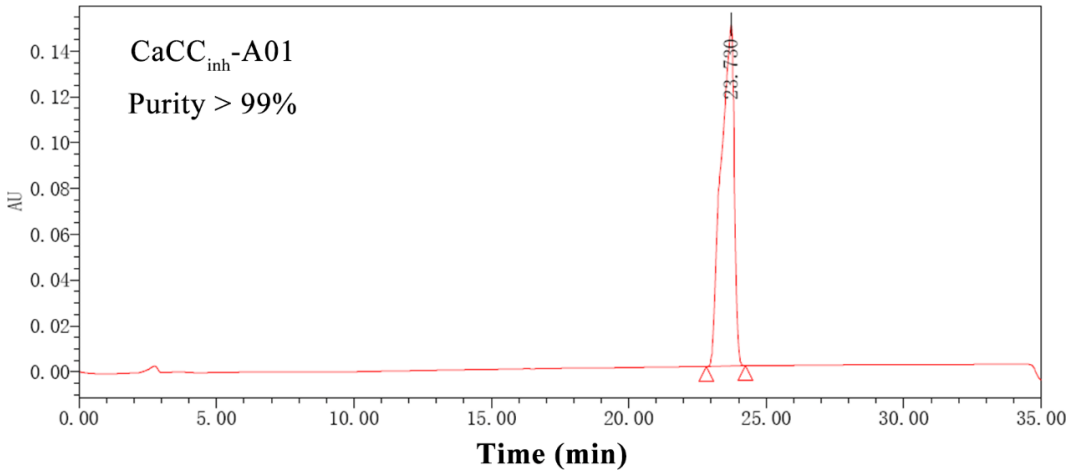
^{13}C-NMR



HRMS



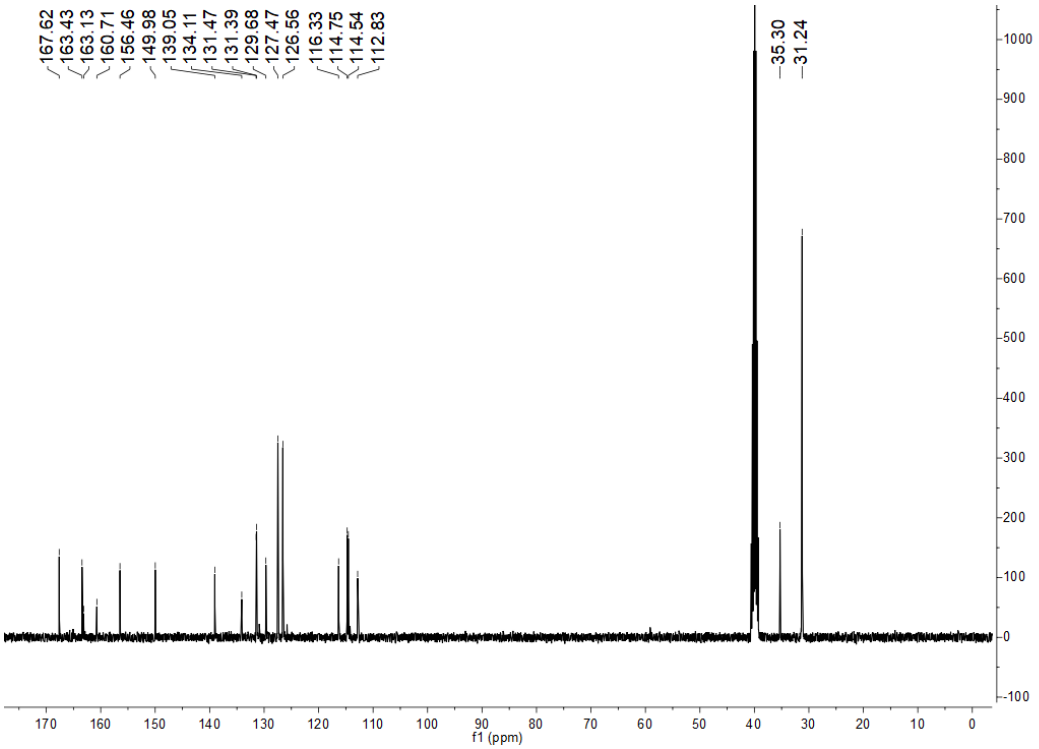
HPLC



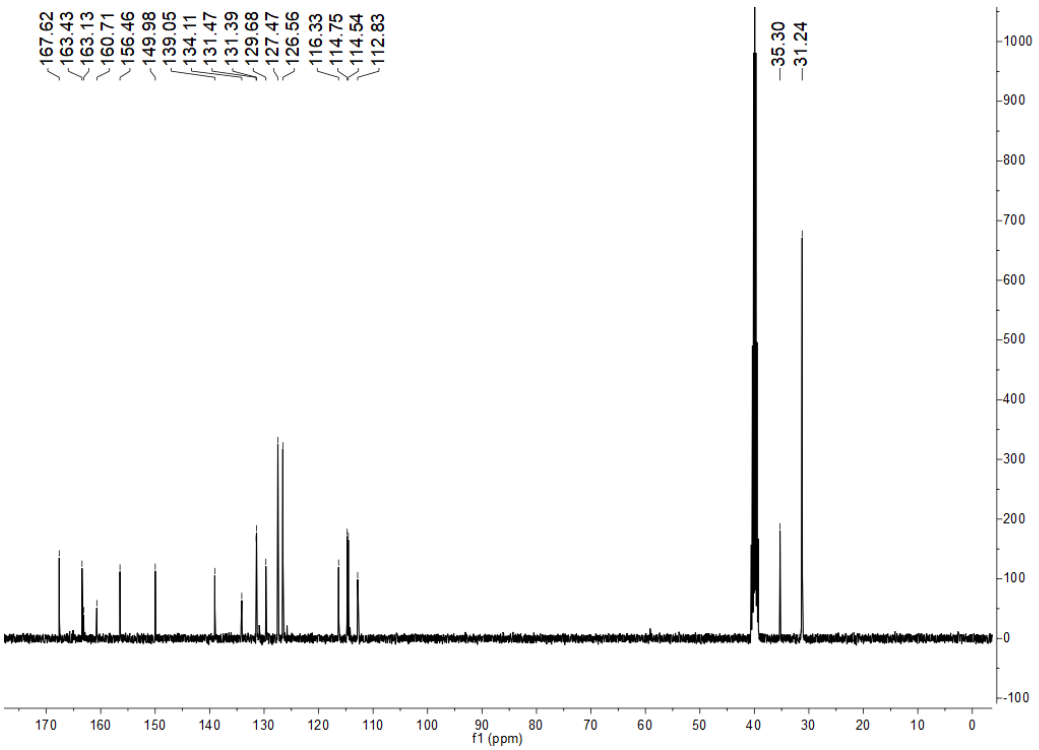
HPLC parameter:
Waters Xbridge C18 column(4.6 mm×250 mm 5 μm i.d.);
Flow rate: 1 mL/min;
Detector: UV 254 nm;
Eluent: A is water containing 0.1%TFA, B is MeOH; 0–5 min: 30% (*v*/*v*) A+70% (*v*/*v*) B, 25–35 min: 5% (*v*/*v*) A+95% (*v*/*v*) B.

2-(4-(*tert*-Butyl) benzamido)-4-(4-fluorophenyl) thiophene-3-carboxylic acid **(33)**

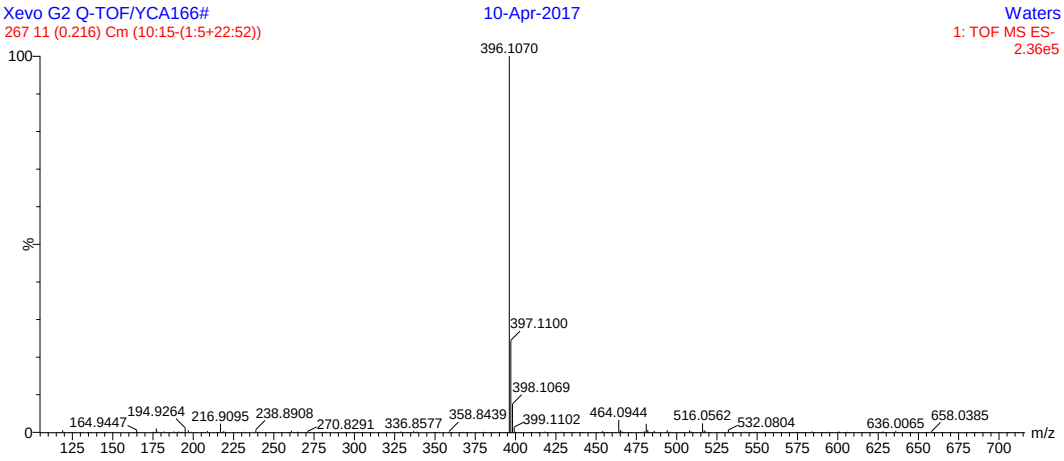
^{1}H-NMR



^{13}C-NMR

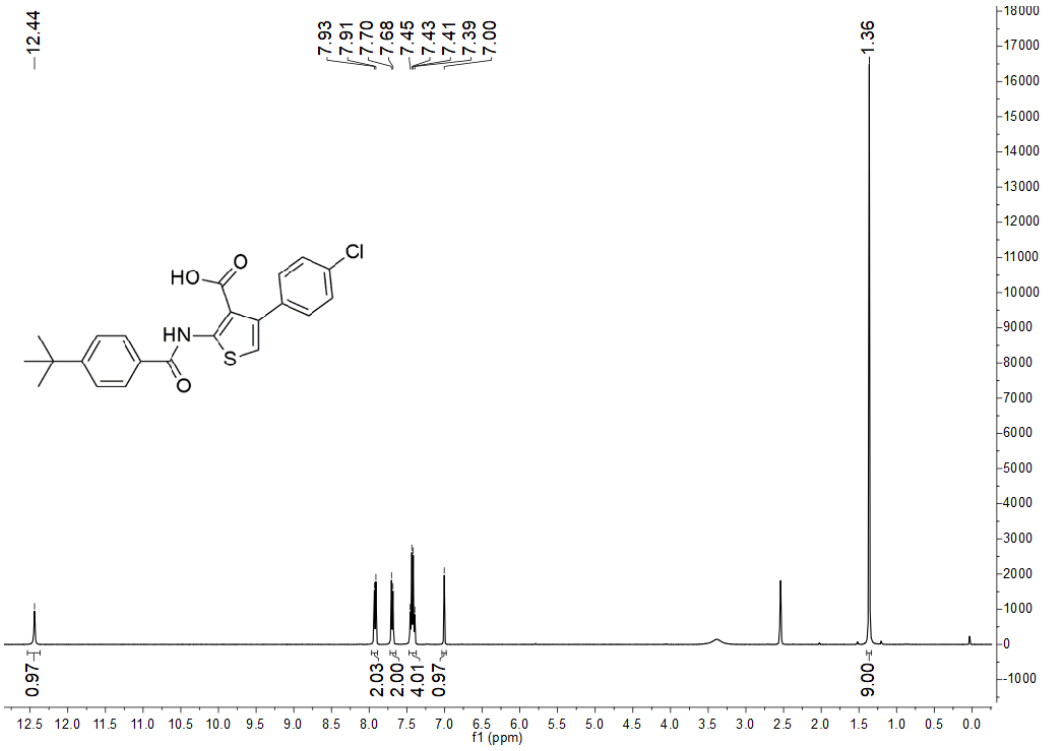


HRMS

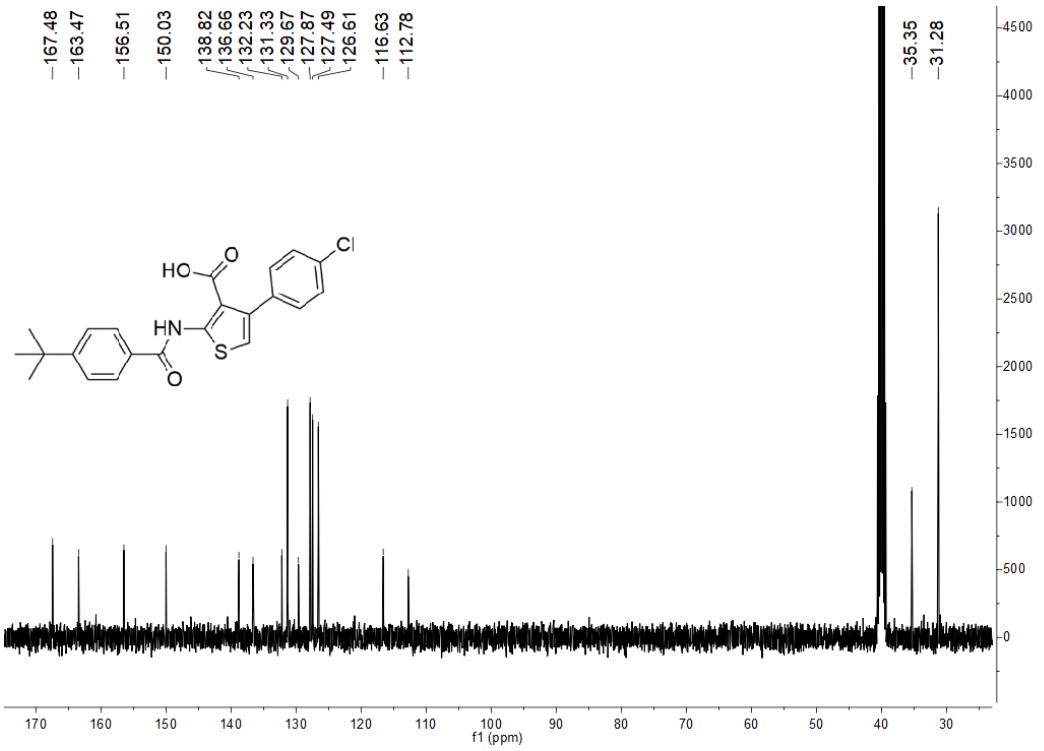


2-(4-(*tert*-Butyl) benzamido)-4-(4-chlorophenyl) thiophene-3-carboxylic acid **(34)**

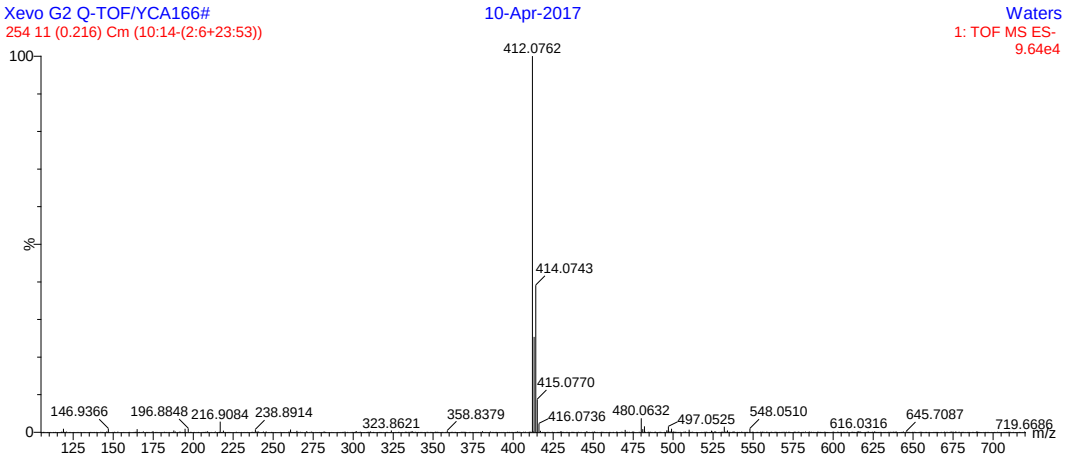
^{1}H-NMR



^{13}C-NMR


167.48
163.47
156.51
150.03
138.82
136.66
132.23
131.33
129.67
127.87
127.49
126.61
116.63
112.78
35.35
31.28
HO
O
HN
S
O
Cl
f1 (ppm)

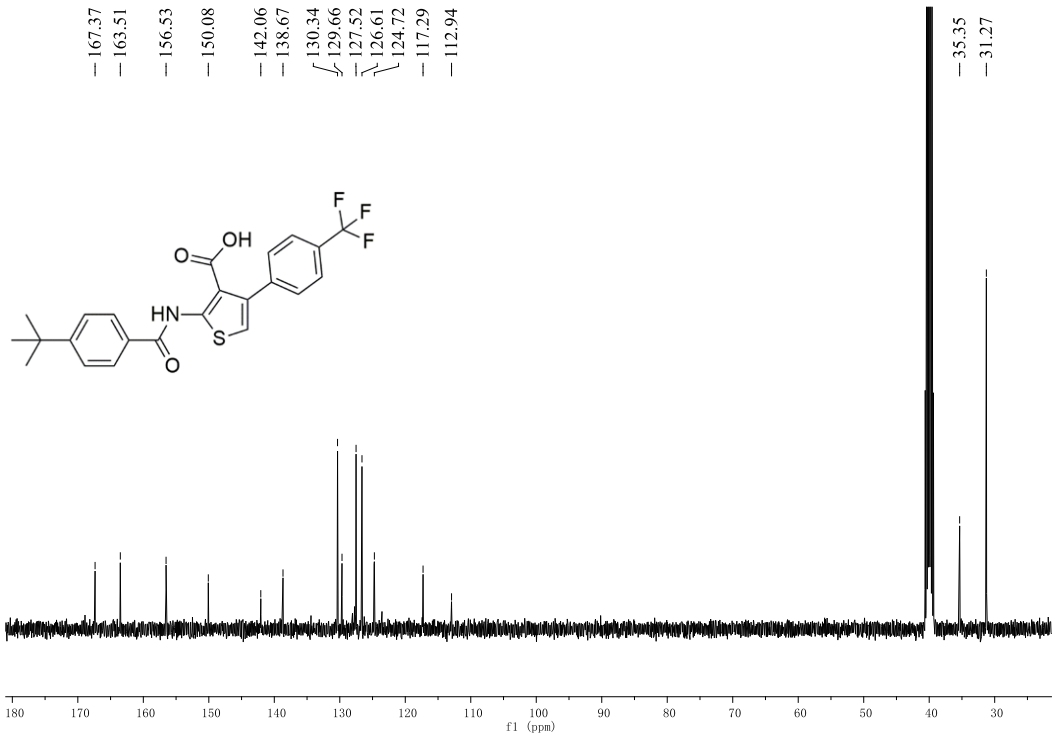
HRMS


Xevo G2 Q-TOF/YCA166#
254 11 (0.216) Cm (10:14-(2:6+23:53))
10-Apr-2017
Waters
1: TOF MS ES-
9.64e4
412.0762
414.0743
415.0770
146.9366
196.8848
216.9084
238.8914
323.8621
358.8379
416.0736
480.0632
497.0525
548.0510
616.0316
645.7087
719.6686
%
m/z

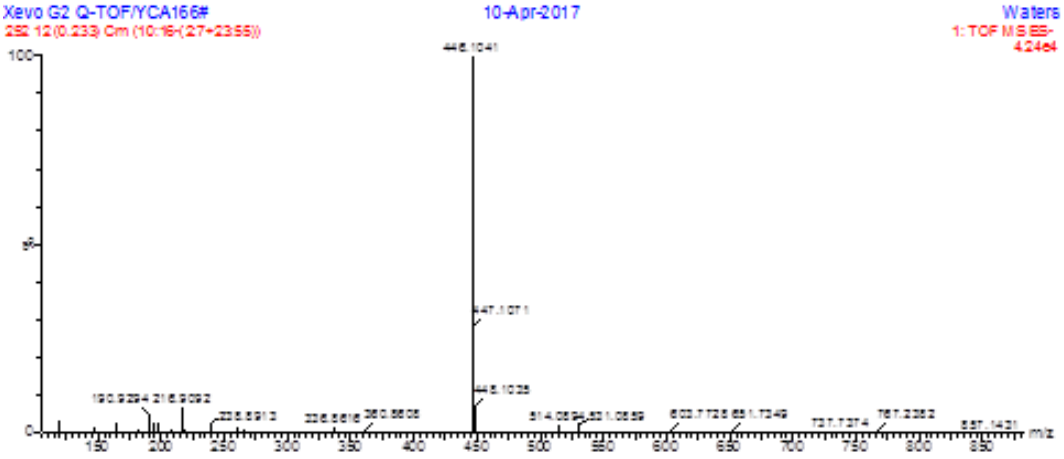
2-(4-(*tert*-Butyl) benzamido)-4-(4-(trifluoromethyl) phenyl) thiophene-3-carboxylic acid **(35)**

^{1}H-NMR

^{13}C-NMR

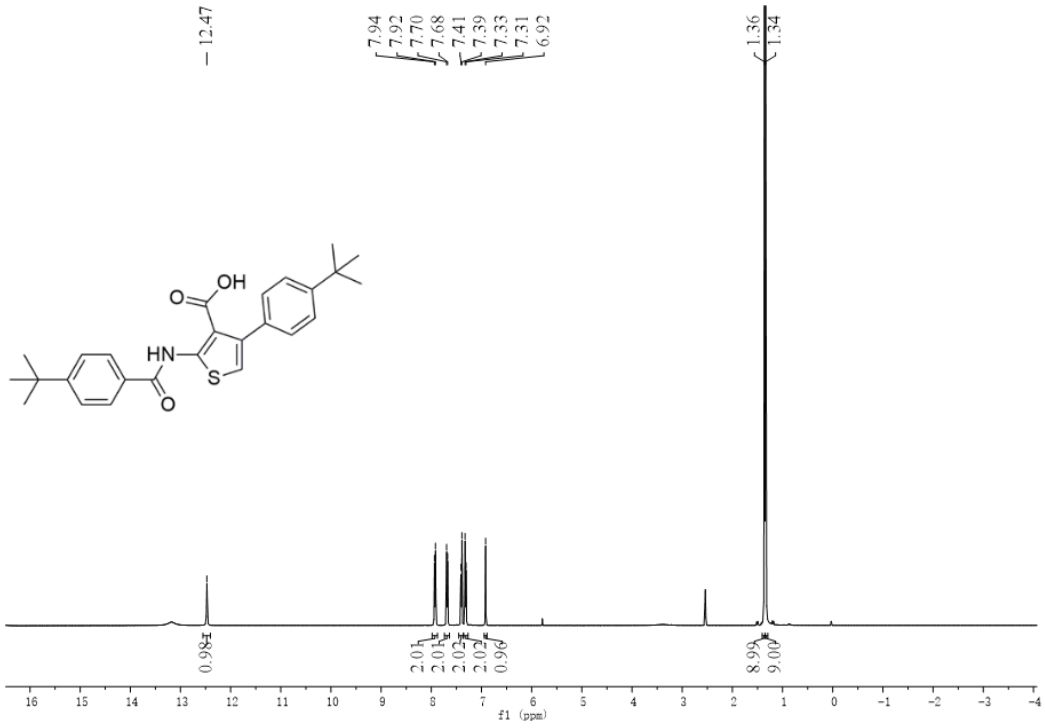


HRMS

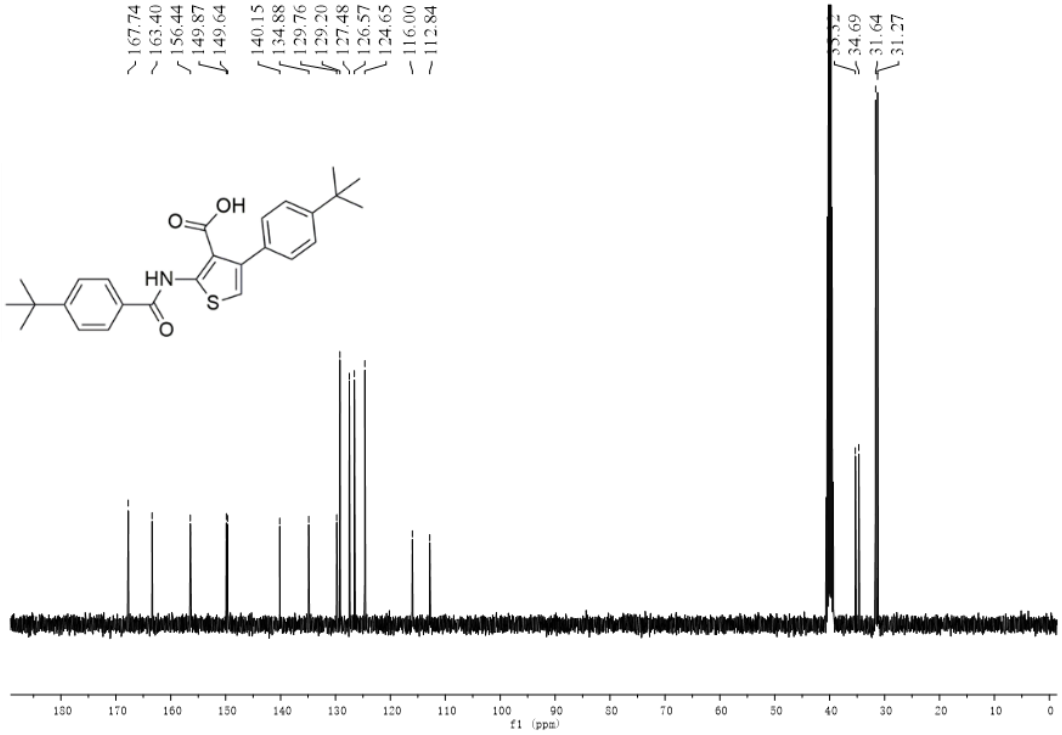


2-(4-(*tert*-Butyl) benzamido)-4-(4-(*tert*-butyl) phenyl) thiophene-3-carboxylic acid **(36)**

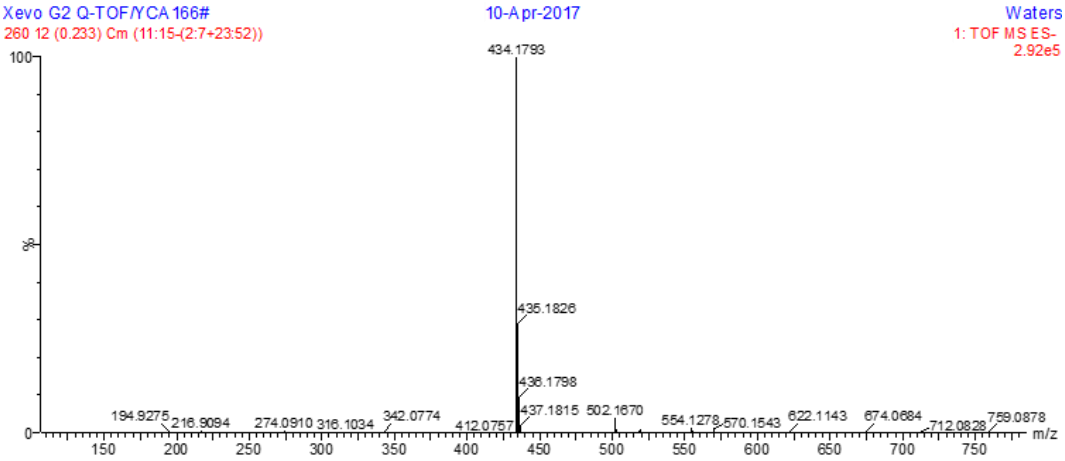
^{1}H-NMR



^{13}C-NMR

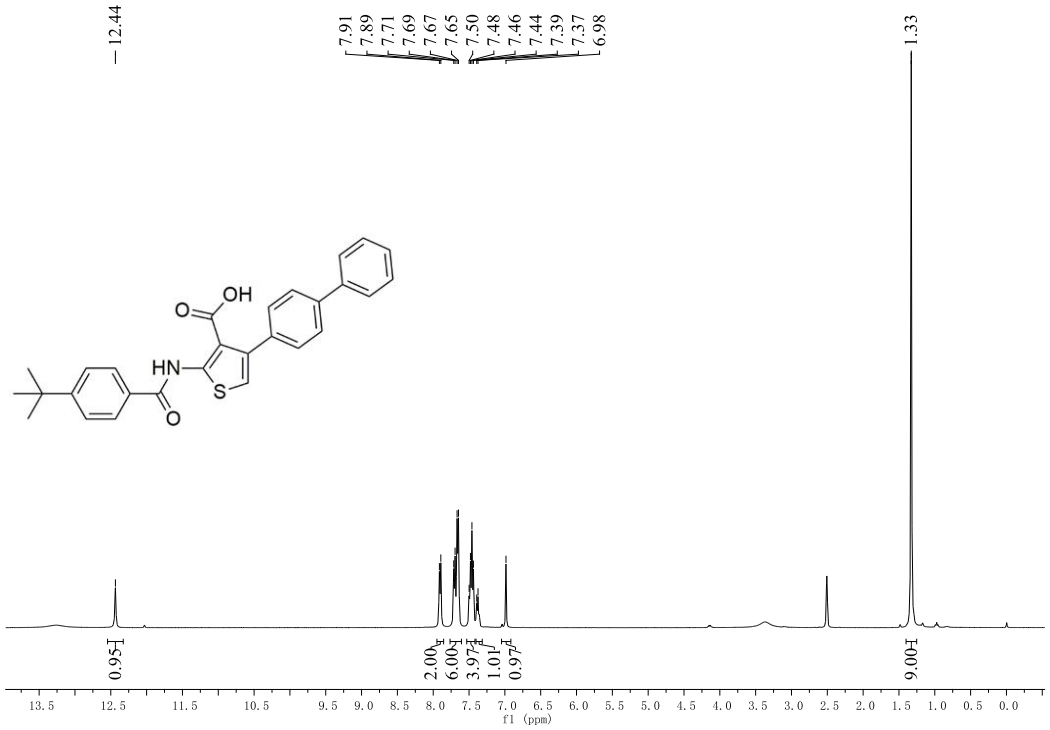

167.74
163.40
156.44
149.87
149.64
140.15
134.88
129.76
129.20
127.48
126.57
124.65
116.00
112.84
33.52
34.69
31.64
31.27
OH
O
HN
S
O
f1 (ppm)

HRMS

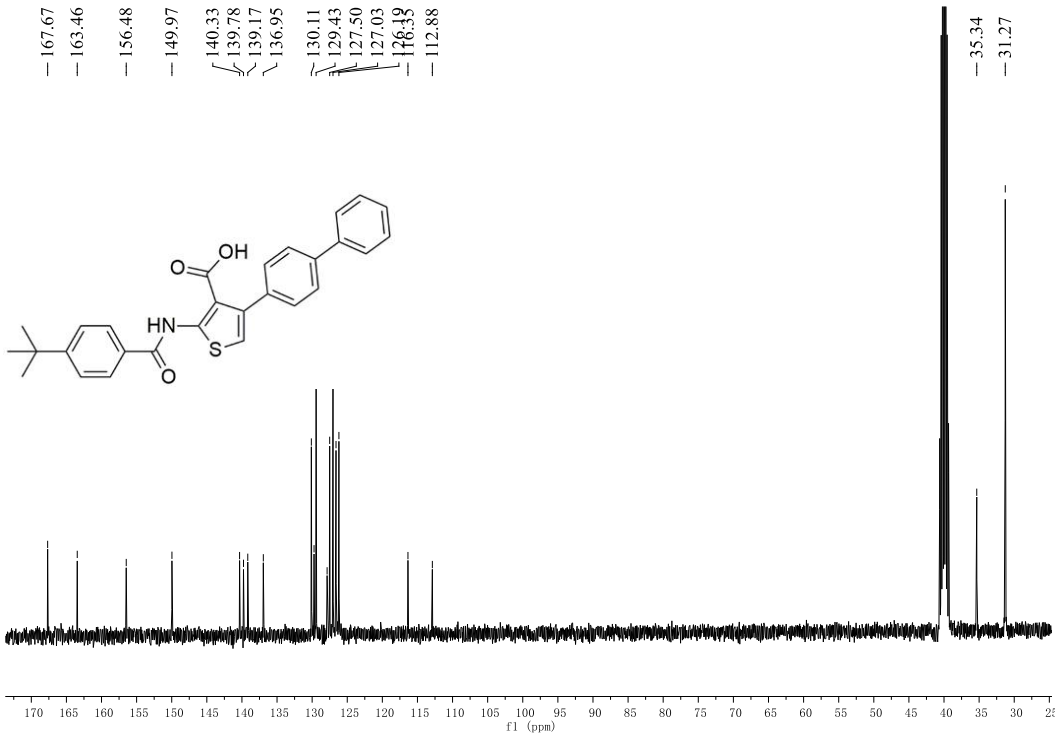

Xevo G2 Q-TOF/YCA166#
260 12 (0.233) Cm (11:15-(2:7+23:52))
10-Apr-2017
Waters
1: TOF MS ES-
2.92e5
100
%
0
434.1793
435.1826
436.1798
437.1815
194.9275
216.9094
274.0910
316.1034
342.0774
412.0757
502.1670
554.1278
570.1543
622.1143
674.0684
712.0828
759.0878
m/z

4-([1,1′-Biphenyl]-4-yl)-2-(4-(*tert*-butyl) benzamido) thiophene-3-carboxylic acid **(37)**

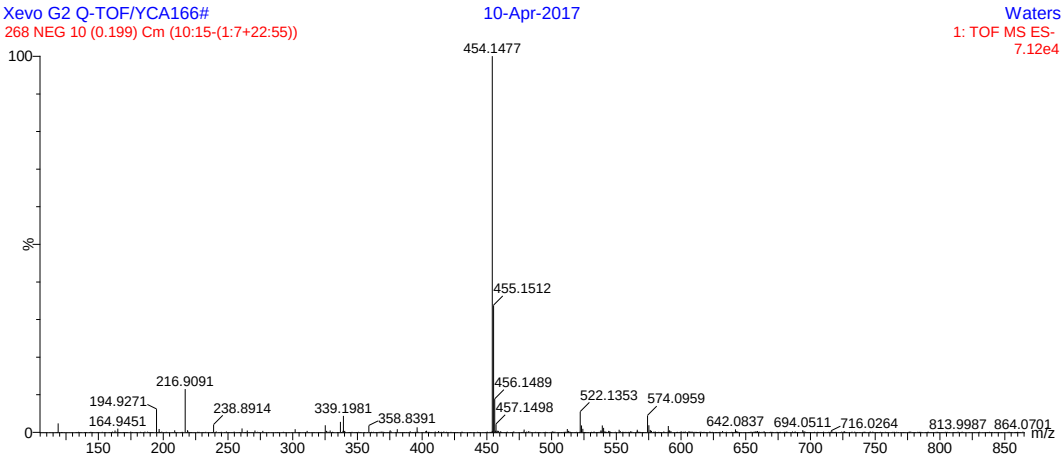
^{1}H-NMR



^{13}C-NMR

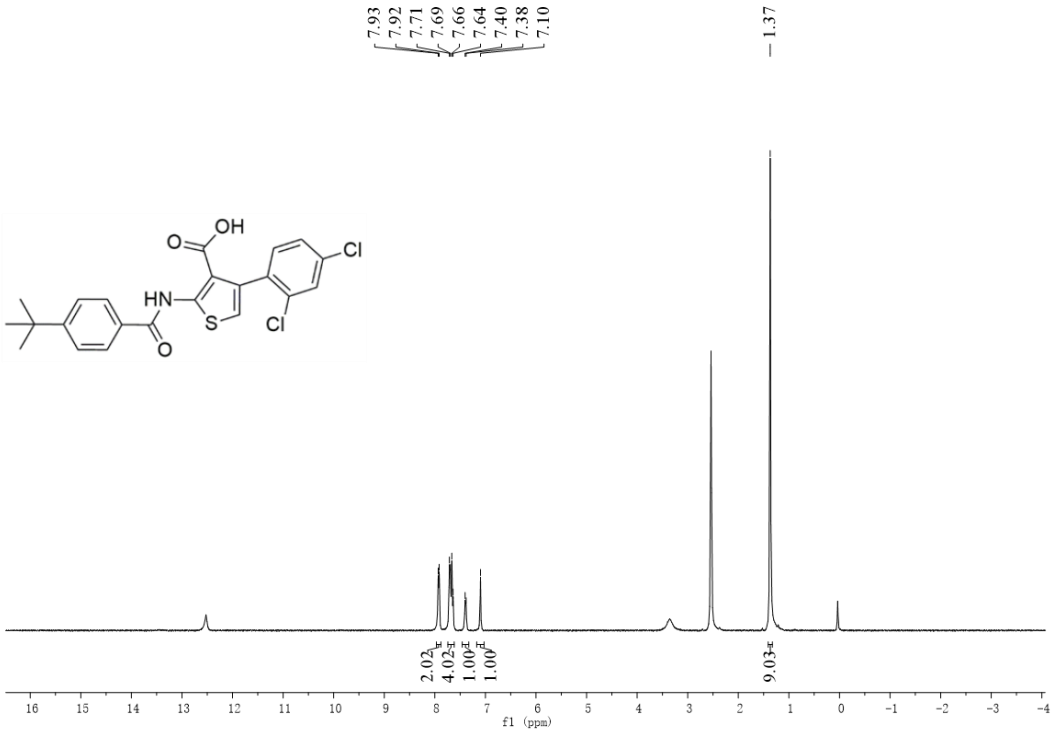


HRMS

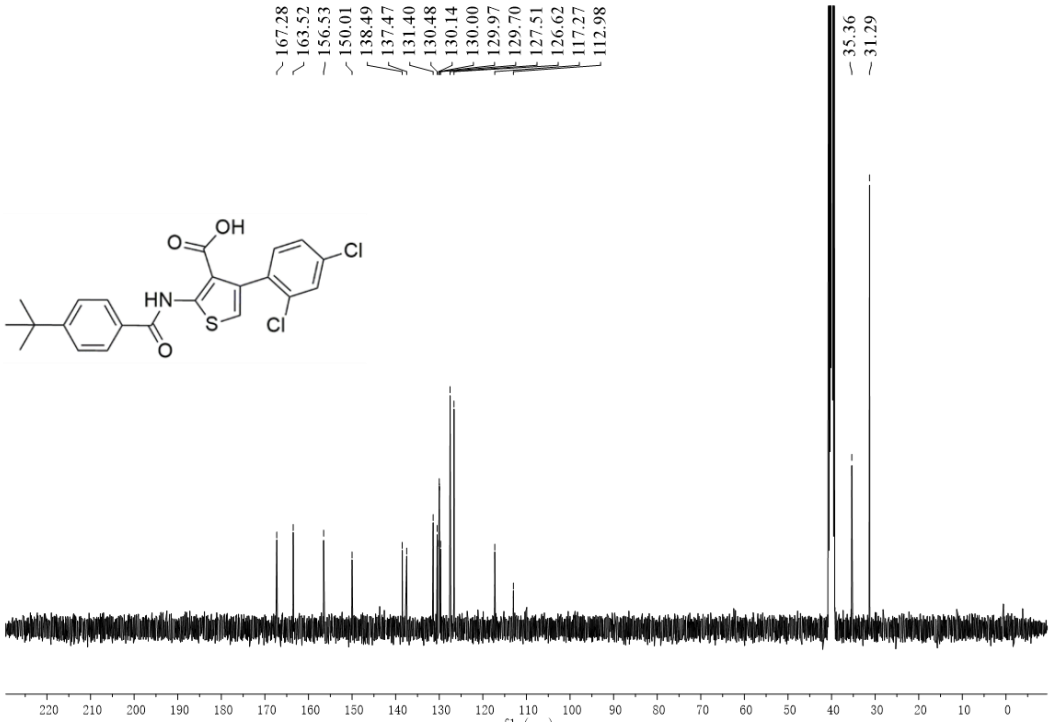


2-(4-(*tert*-Butyl) benzamido)-4-(2, 4-dichlorophenyl) thiophene-3-carboxylic acid **(38)**

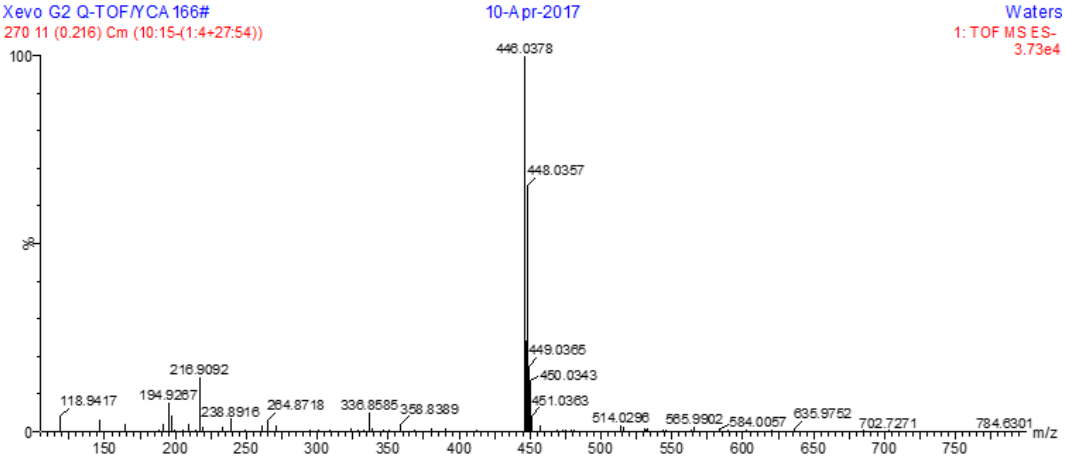
^{1}H-NMR



^{13}C-NMR

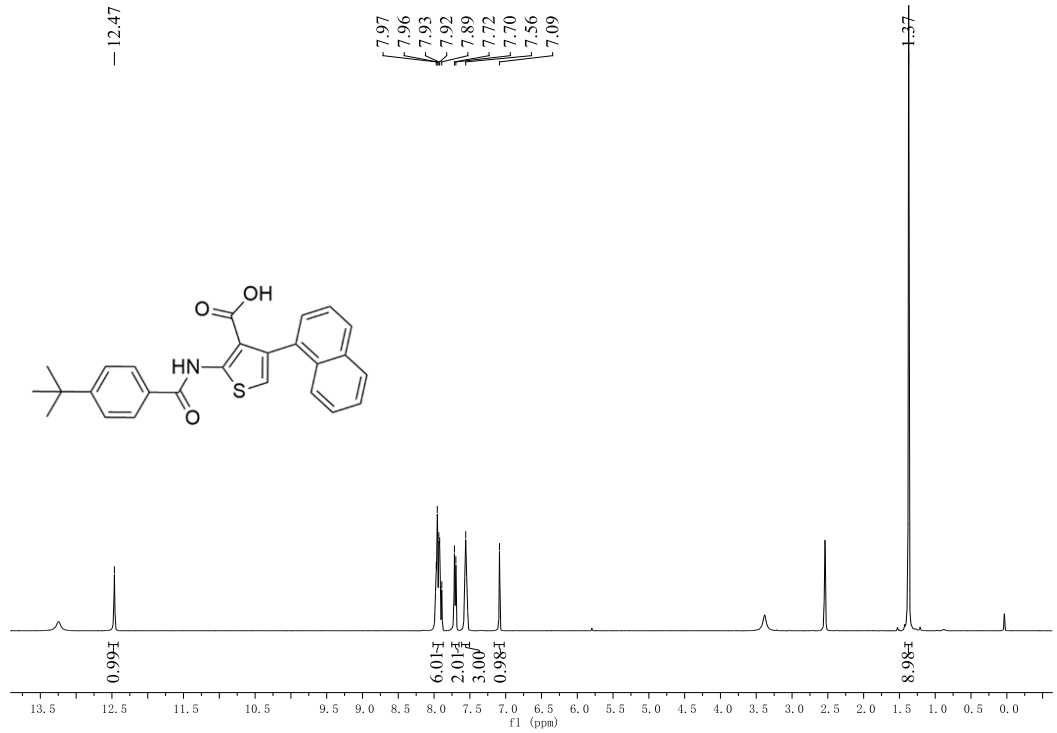

167.28
163.52
156.53
150.01
138.49
137.47
131.40
130.48
130.14
130.00
129.97
129.70
127.51
126.62
117.27
112.98
35.36
31.29
OH
O
HN
S
Cl
Cl
O
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

HRMS

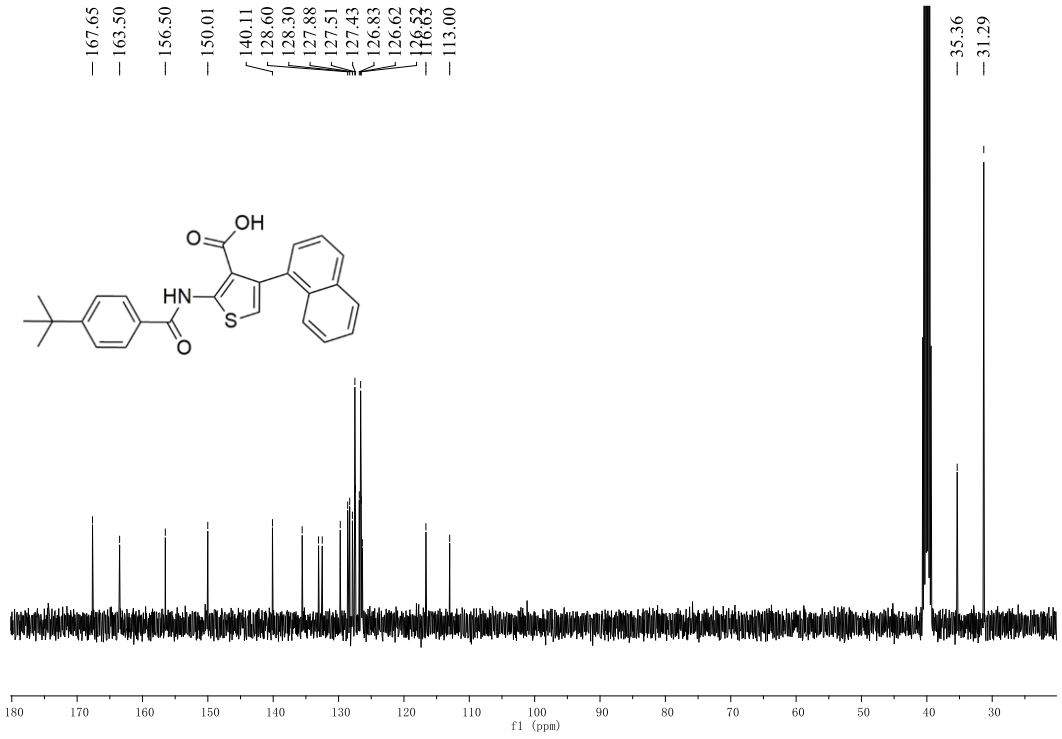

Xevo G2 Q-TOF/YCA166#
270 11 (0.216) Cm (10:15-(1:4+27:54))
10-Apr-2017
Waters
1: TOF MS ES-
3.73e4
100
%
0
446.0378
448.0357
449.0366
450.0343
451.0363
216.9092
194.9267
118.9417
238.8916
264.8718
336.8585
358.8389
514.0296
565.9902
584.0057
635.9752
702.7271
784.6301
150 200 250 300 350 400 450 500 550 600 650 700 750
m/z

2-(4-(*tert*-Butyl) benzamido)-4-(naphthalen-2-yl) thiophene-3-carboxylic acid **(39)**

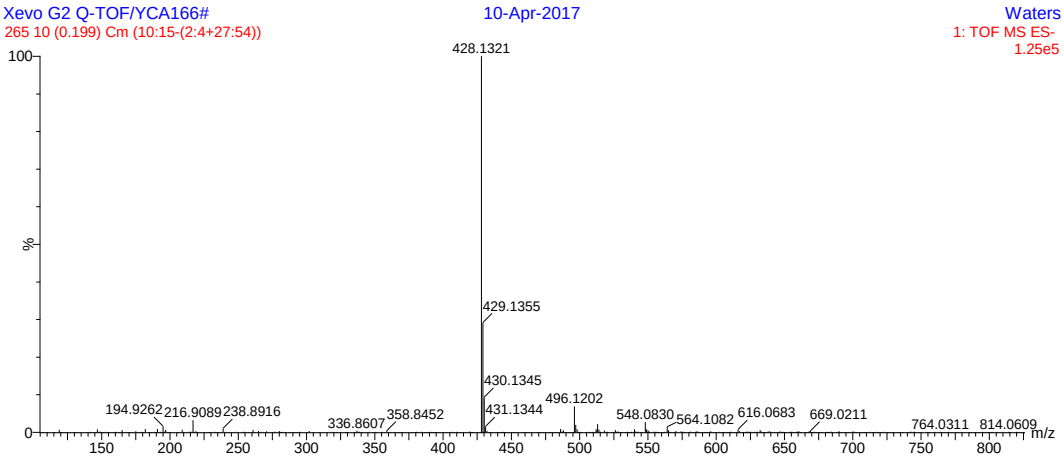
^{1}H-NMR



^{13}C-NMR

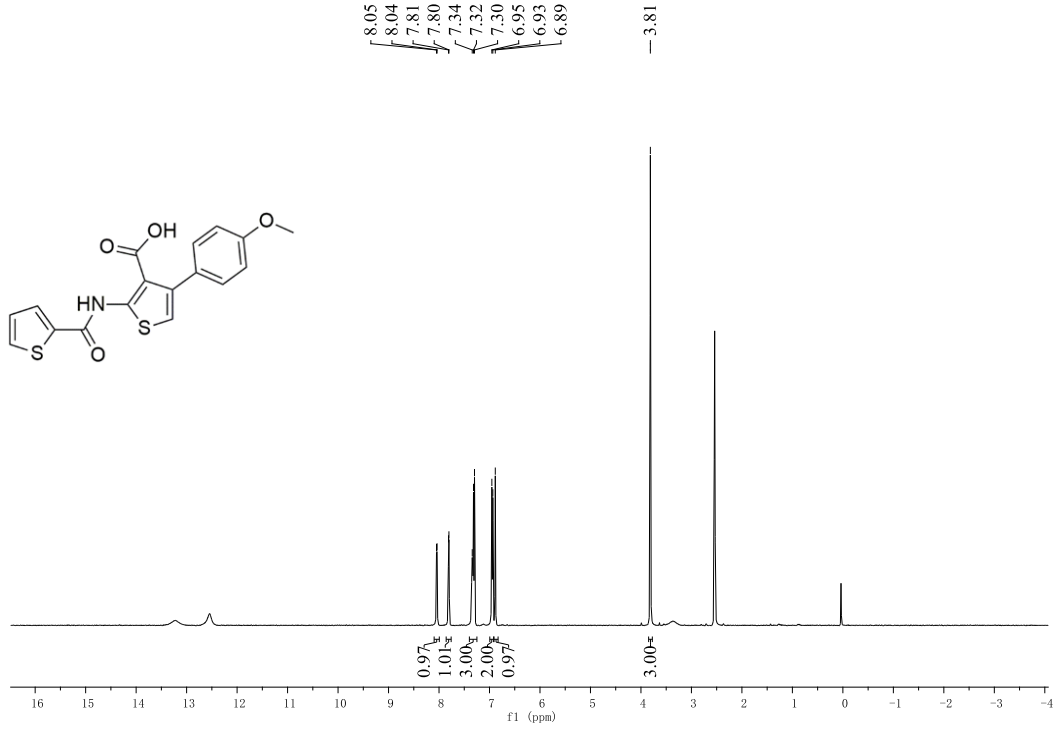


HRMS

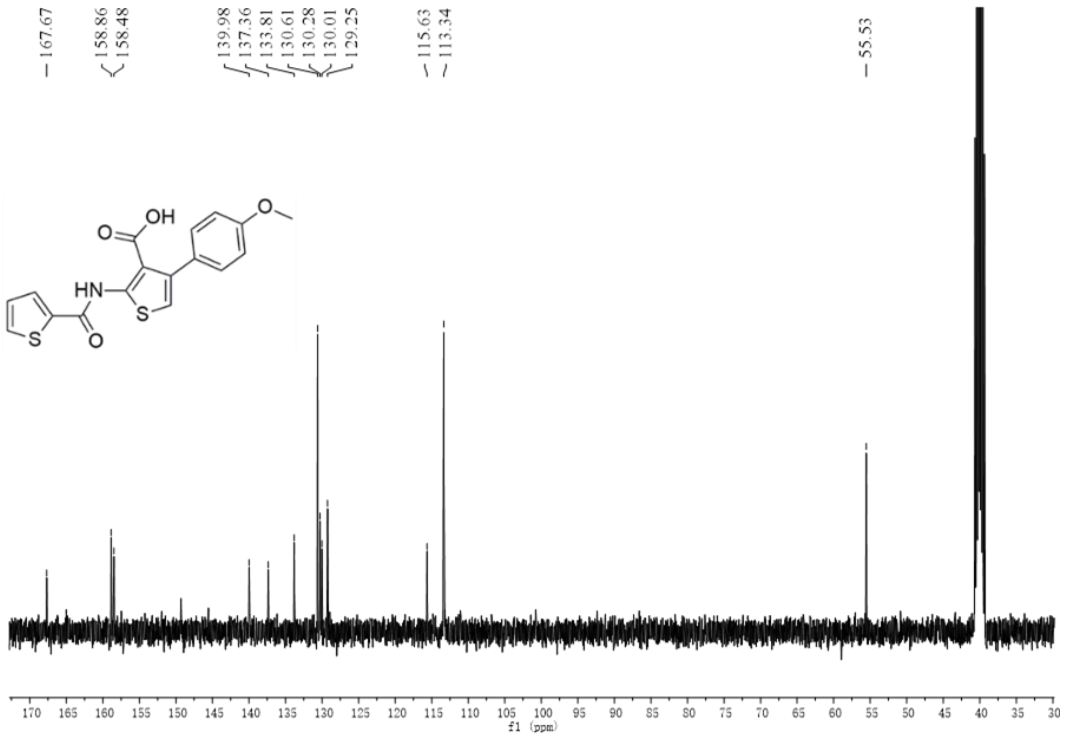


4-(4-Methoxyphenyl)-2-(thiophene-2-carboxamido) thiophene-3-carboxylic acid **(40)**

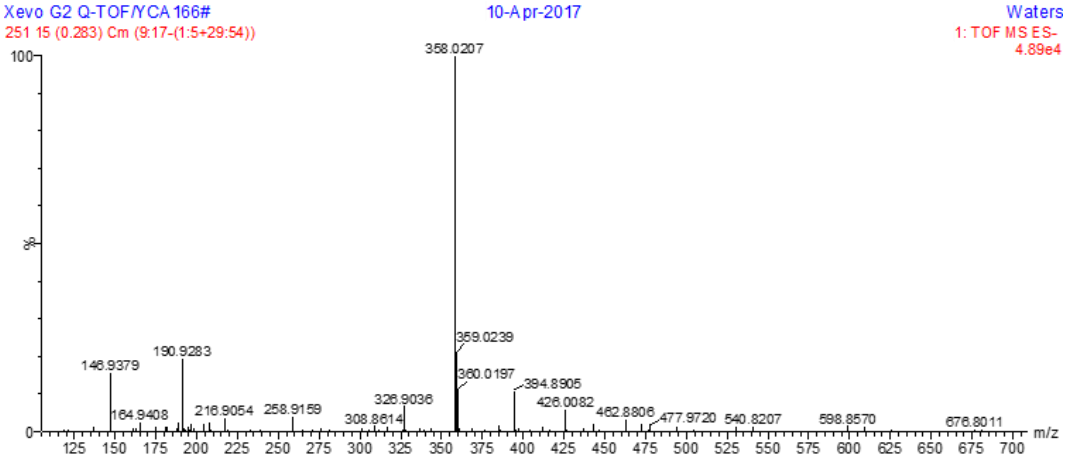
^{1}H-NMR



^{13}C-NMR

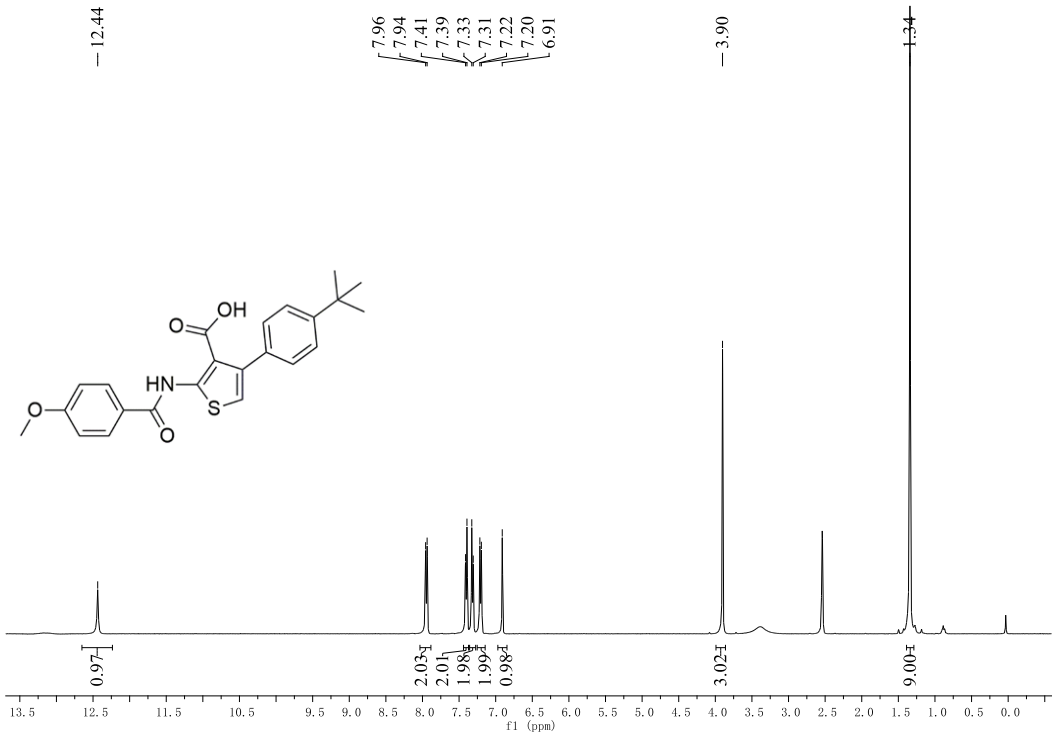

167.67
158.86
158.48
139.98
137.36
133.81
130.61
130.28
130.01
129.25
115.63
113.34
55.53
OH
O
HN
S
S
O
O
f1 (ppm)

HRMS

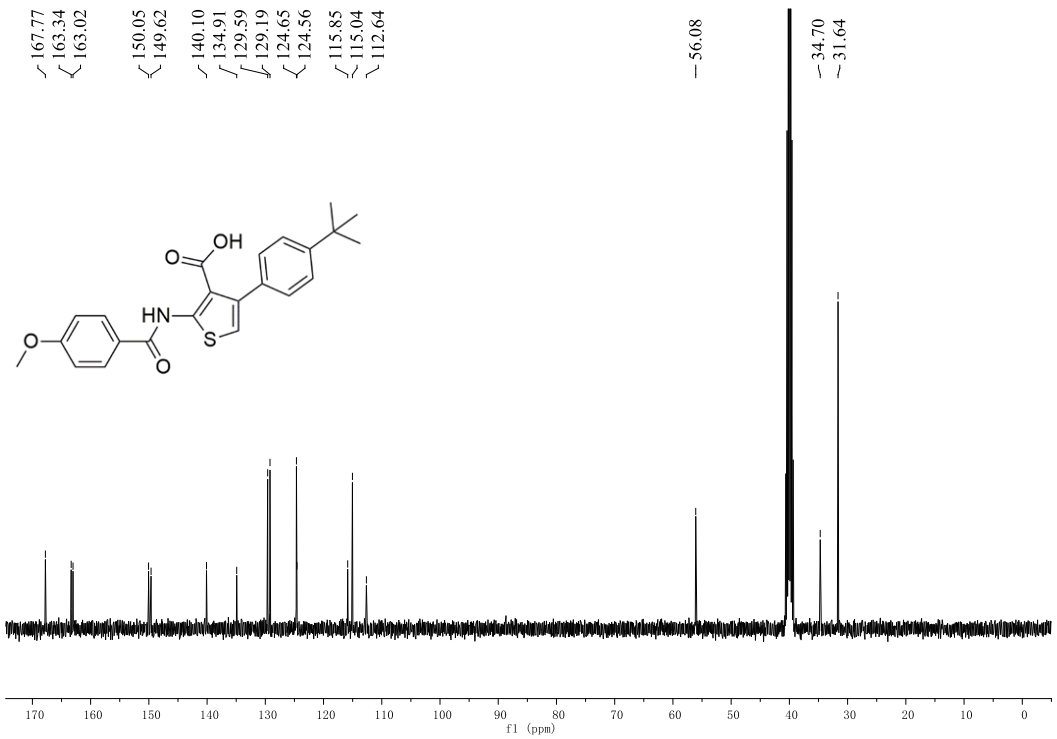

Xevo G2 Q-TOF/YCA166#
251 15 (0.283) Cm (9:17-(1:5+29:54))
10-Apr-2017
Waters
1: TOF MS ES-
4.89e4
100
%
0
358.0207
359.0239
360.0197
190.9283
146.9379
164.9408
216.9054
258.9159
326.9036
308.8614
394.8905
426.0082
462.8806
477.9720
540.8207
598.8570
676.8011
m/z

4-(4-(*tert*-Butyl) phenyl)-2-(4-methoxybenzamido) thiophene-3-carboxylic acid **(41)**

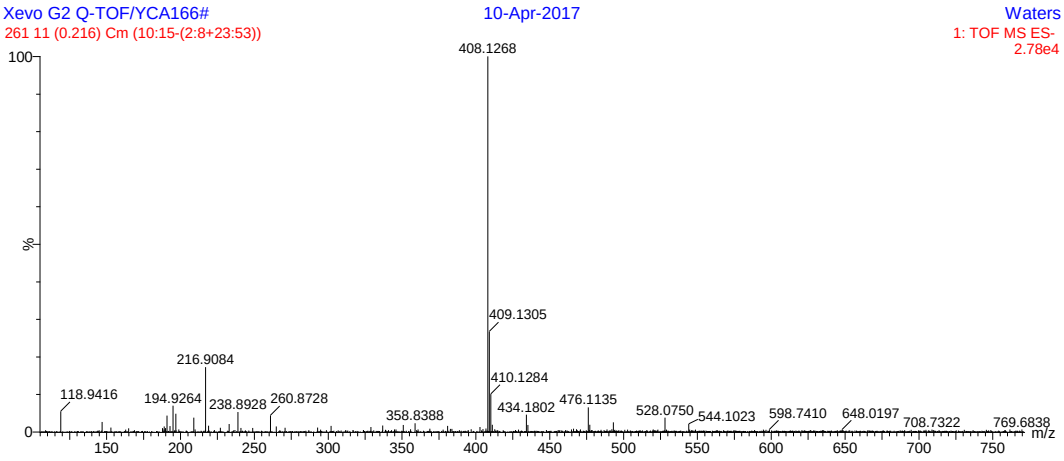
^{1}H-NMR



^{13}C-NMR

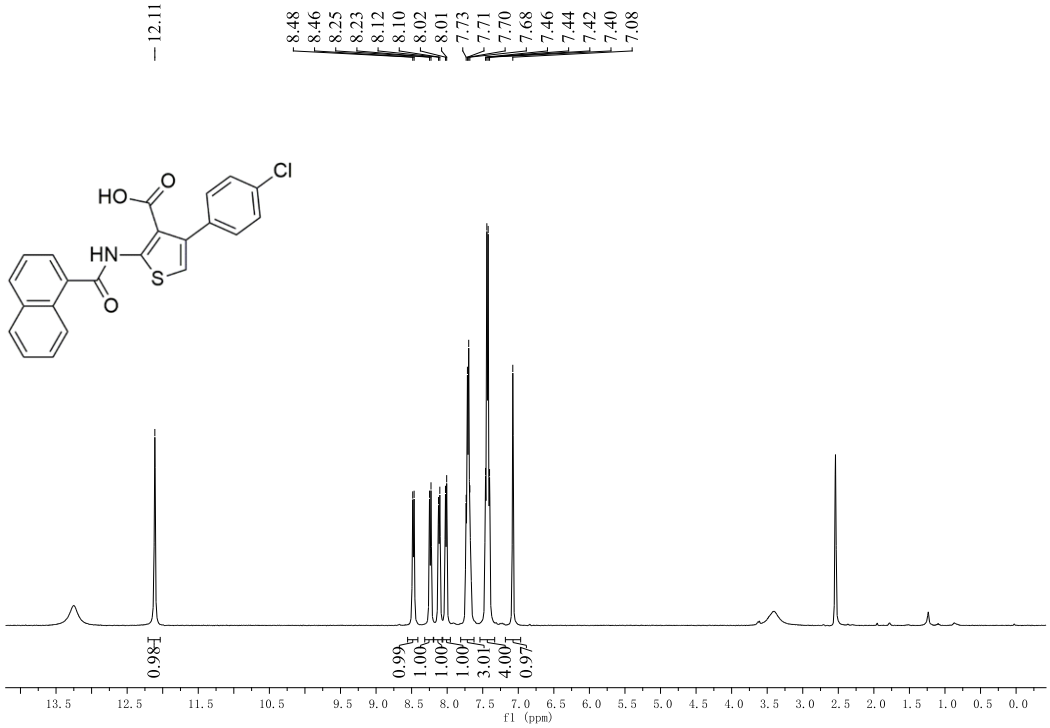


HRMS

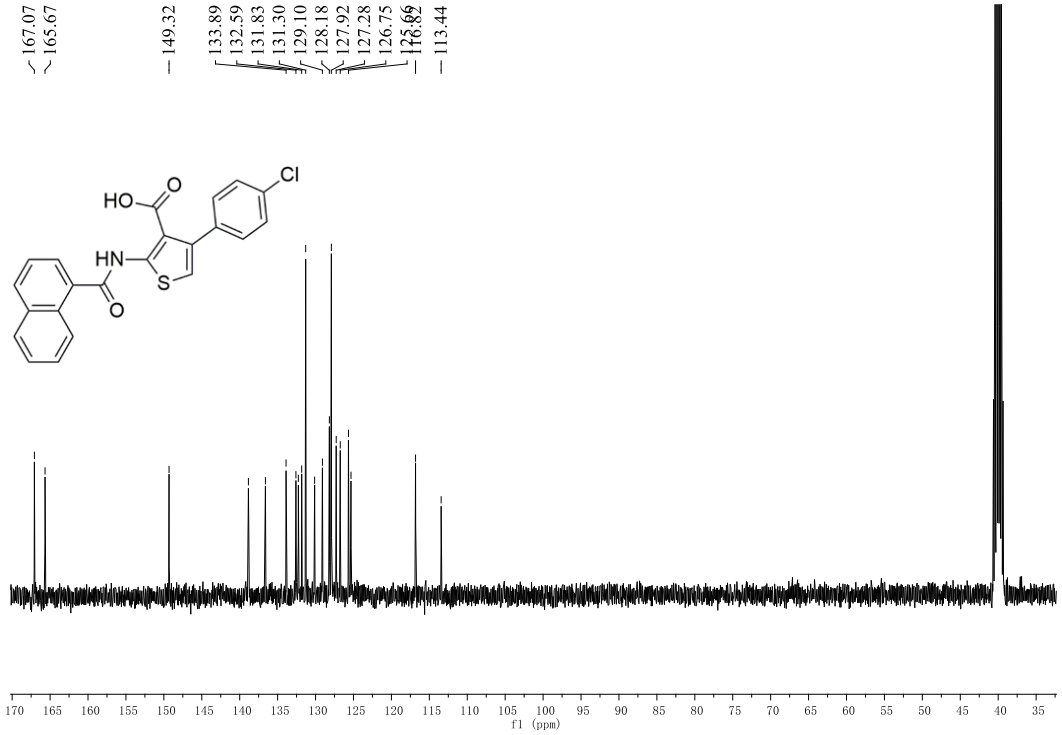


2-(1-Naphthamido)-4-(4-chlorophenyl) thiophene-3-carboxylic acid **(42)**

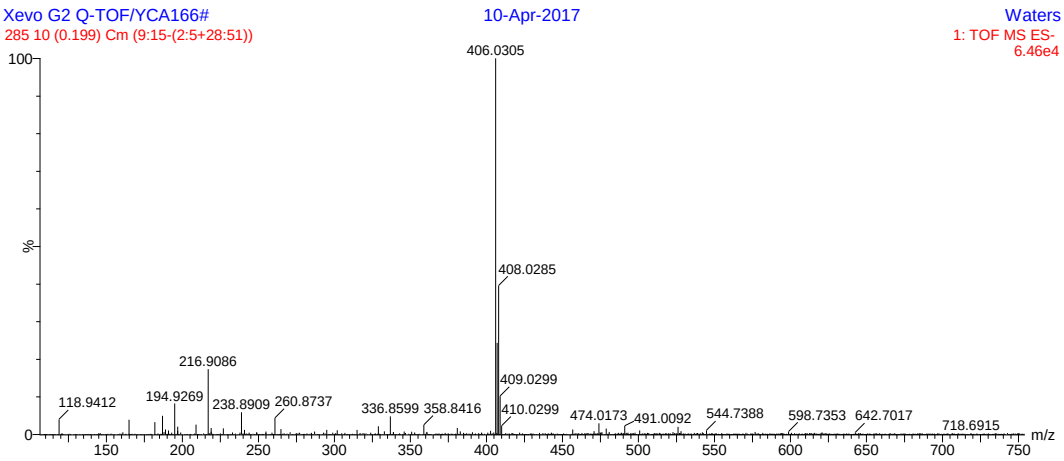
^{1}H-NMR



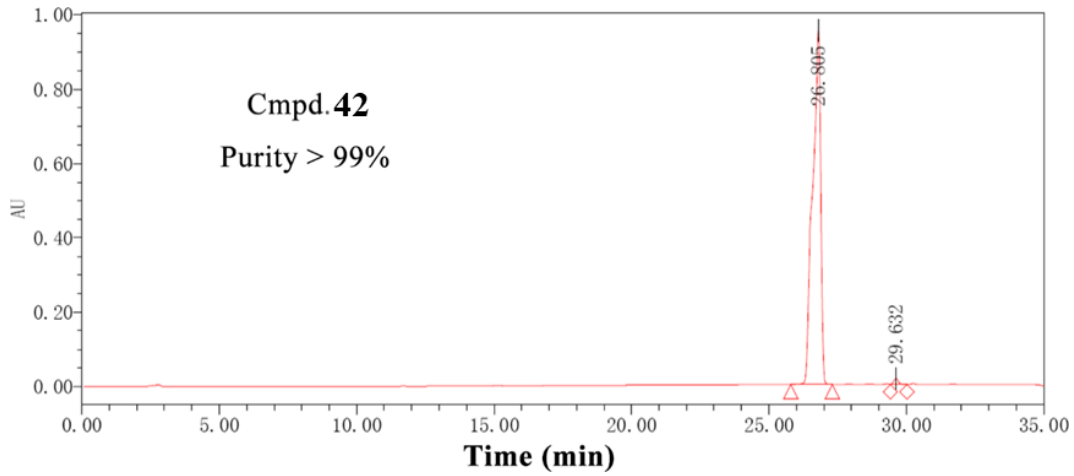
^{13}C-NMR


167.07
165.67
149.32
133.89
132.59
131.83
131.30
129.10
128.18
127.92
127.28
126.75
125.66
118.82
113.44
HO
O
HN
S
O
Cl
170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35
f1 (ppm)

HRMS


Xevo G2 Q-TOF/YCA166#
285 10 (0.199) Cm (9:15-(2:5+28:51))
10-Apr-2017
Waters
1: TOF MS ES-
6.46e4
100
%
0
406.0305
408.0285
409.0299
410.0299
216.9086
194.9269
118.9412
238.8909
260.8737
336.8599
358.8416
474.0173
491.0092
544.7388
598.7353
642.7017
718.6915
150 200 250 300 350 400 450 500 550 600 650 700 750
m/z

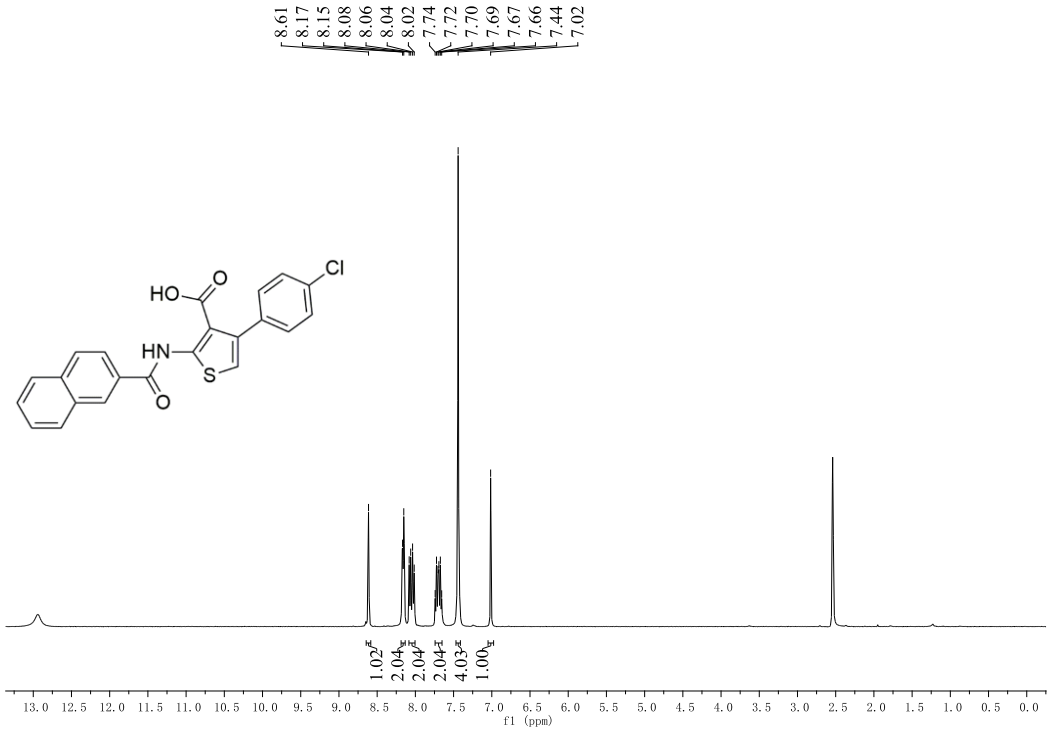
HPLC



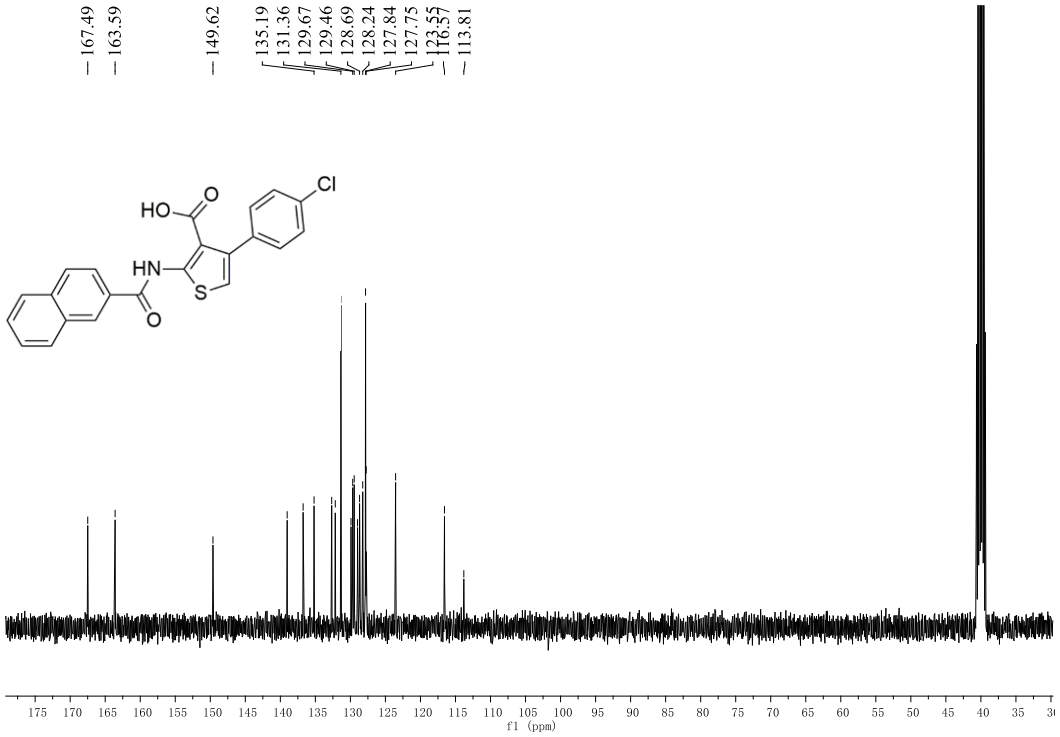
HPLC parameter:
Waters Xbridge C18 column(4.6 mm×250 mm 5 μm i.d.);
Flow rate: 1 mL/min;
Detector: UV 254 nm;
Eluent: A is water containing 0.1% TFA, B is MeOH; 0–5 min: 50% (*v*/*v*) A+50% (*v*/*v*) B, 25–35 min: 5% (*v*/*v*) A+95% (*v*/*v*) B.

2-(2-Naphthamido)-4-(4-chlorophenyl) thiophene-3-carboxylic acid **(43)**

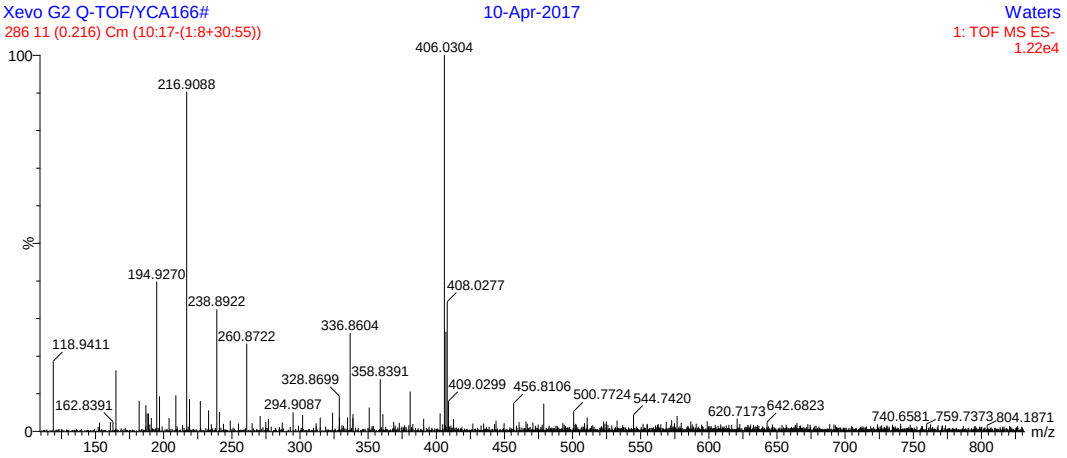
^{1}H-NMR



^{13}C-NMR

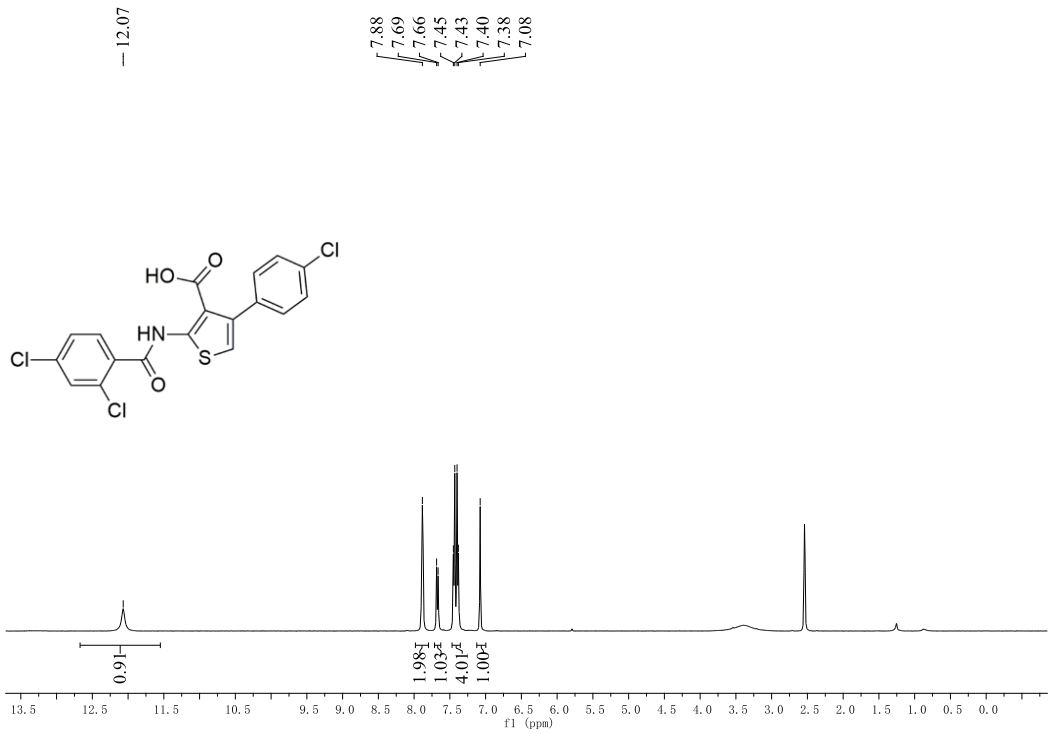

167.49
163.59
149.62
135.19
131.36
129.67
129.46
128.69
128.24
127.84
127.75
123.55
116.57
113.81
HO
O
Cl
HN
S
O
175 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35
f1 (ppm)

HRMS

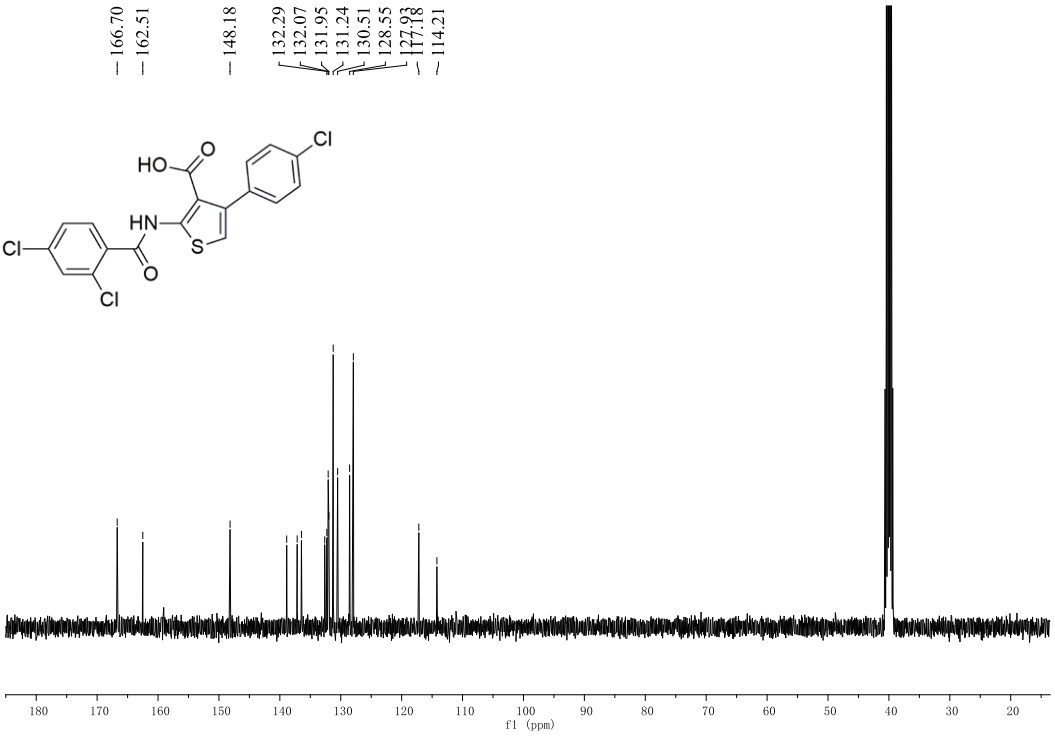

Xevo G2 Q-TOF/YCA166#
286 11 (0.216) Cm (10:17-(1:8+30:55))
10-Apr-2017
Waters
1: TOF MS ES-
1.22e4
100
%
0
406.0304
216.9088
194.9270
238.8922
260.8722
118.9411
336.8604
358.8391
328.8699
294.9087
162.8391
408.0277
409.0299
456.8106
500.7724
544.7420
620.7173
642.6823
740.6581
759.7373
804.1871
150 200 250 300 350 400 450 500 550 600 650 700 750 800
m/z

4-(4-Chlorophenyl)-2-(2,4-dichlorobenzamido)thiophene-3-carboxylic acid **(44)**

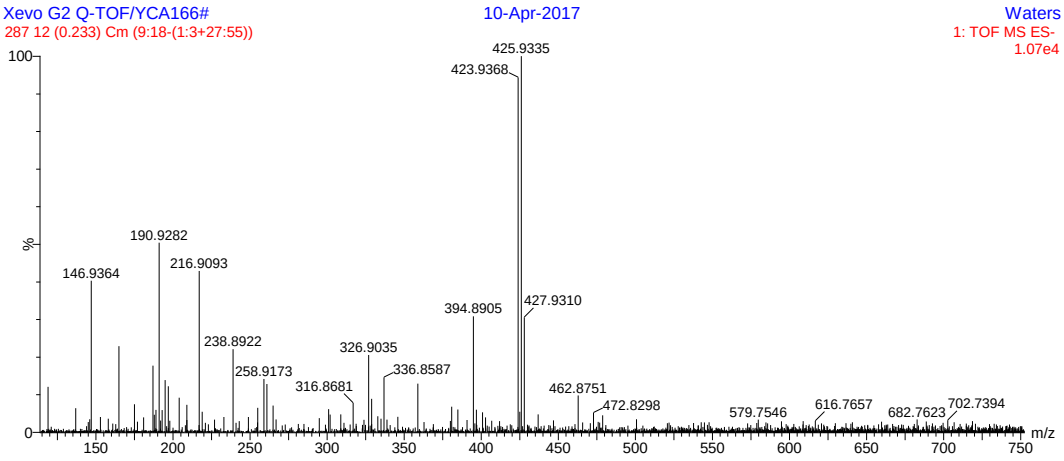
^{1}H-NMR



^{13}C-NMR

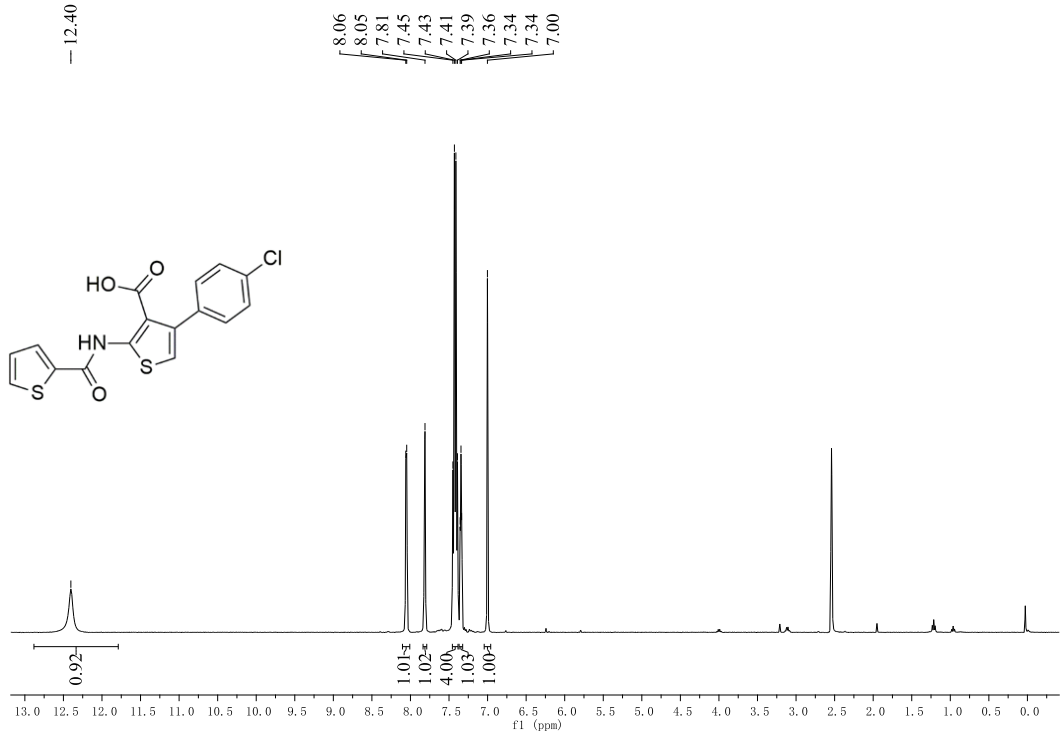


HRMS

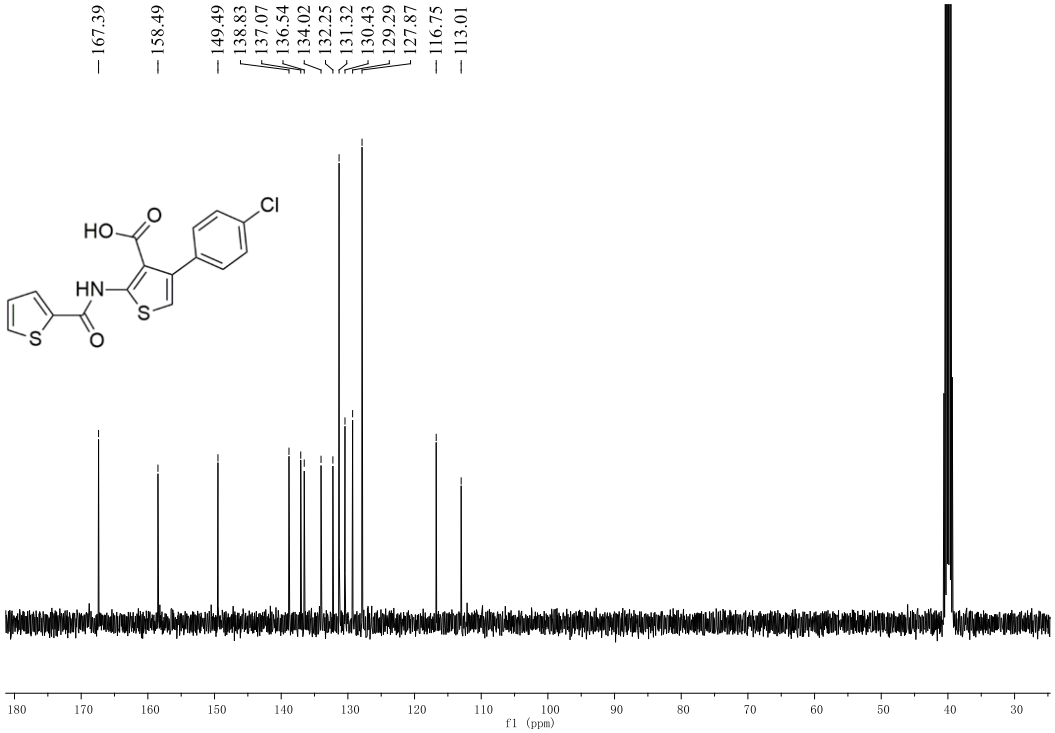


4-(4-Chlorophenyl)-2-(thiophene-2-carboxamido) thiophene-3-carboxylic acid **(45)**

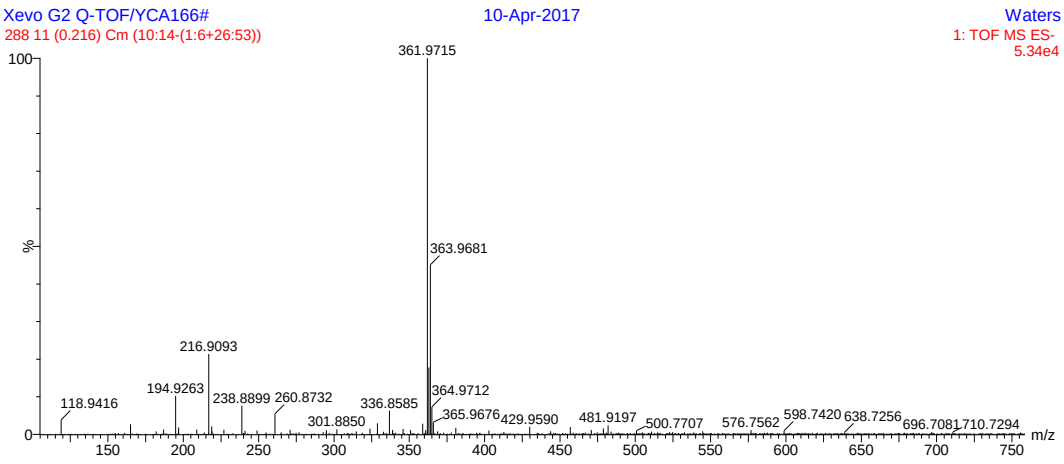
^{1}H-NMR



^{13}C-NMR

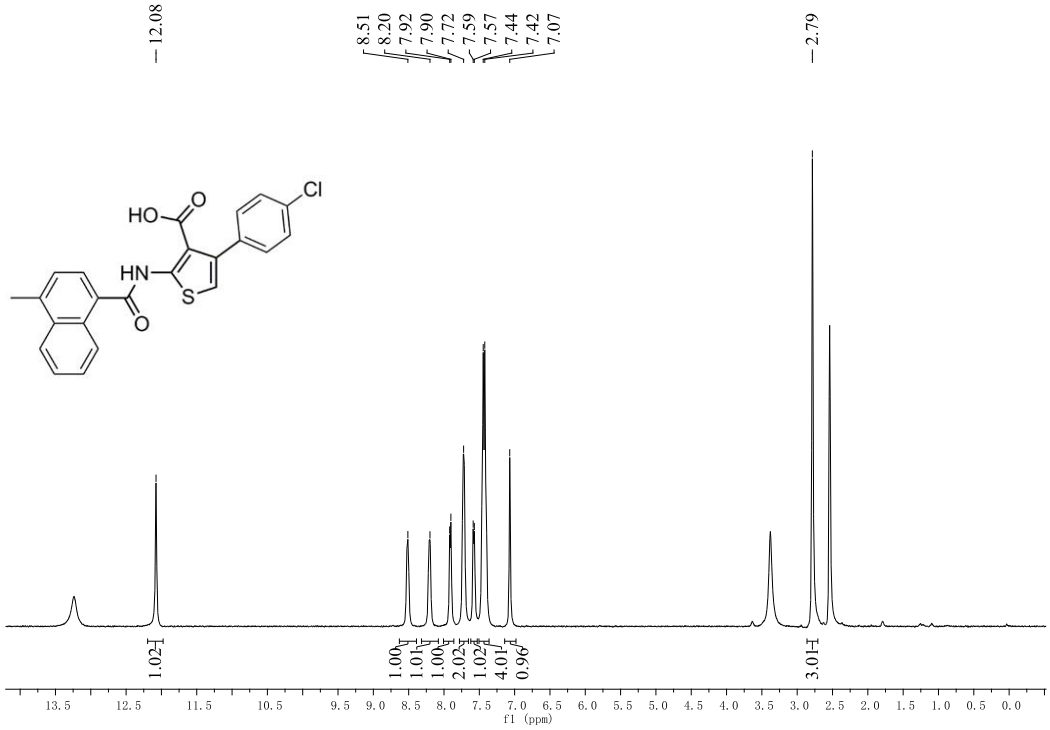

167.39
158.49
149.49
138.83
137.07
136.54
134.02
132.25
131.32
130.43
129.29
127.87
116.75
113.01
HO
O
Cl
HN
S
S
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

HRMS

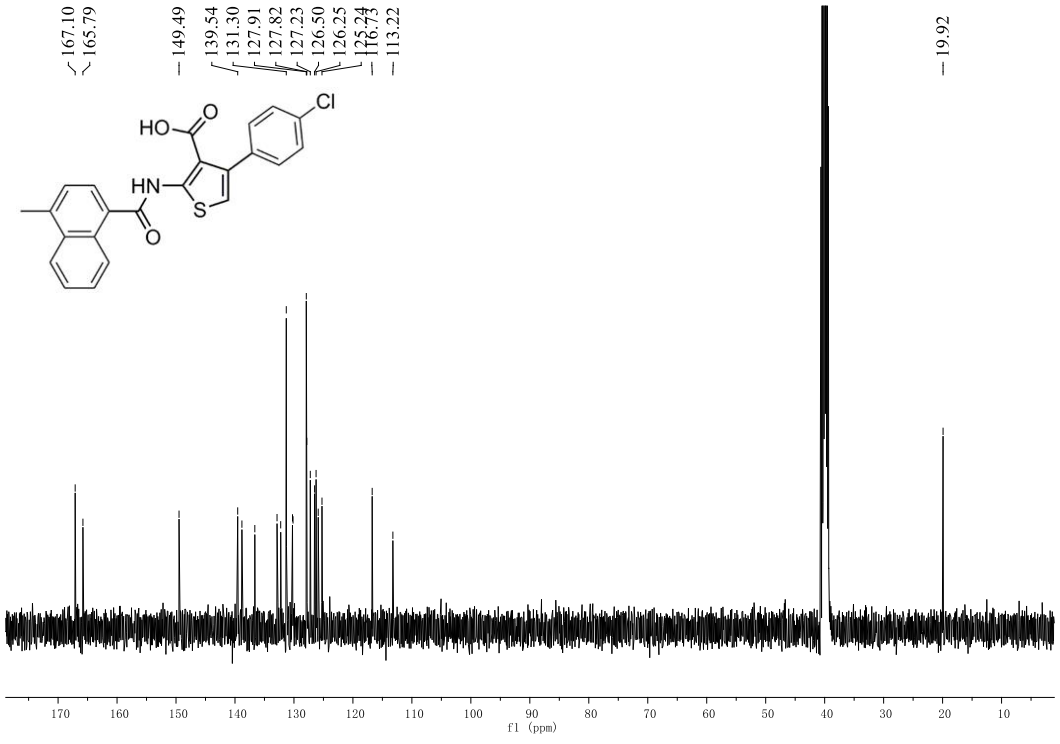

Xevo G2 Q-TOF/YCA166#
288 11 (0.216) Cm (10:14-(1:6+26:53))
10-Apr-2017
Waters
1: TOF MS ES-
5.34e4
100
%
0
361.9715
363.9681
216.9093
194.9263
118.9416
238.8899
260.8732
336.8585
364.9712
301.8850
365.9676
429.9590
481.9197
500.7707
576.7562
598.7420
638.7256
696.7081
710.7294
150
200
250
300
350
400
450
500
550
600
650
700
750
m/z

4-(4-Chlorophenyl)-2-(4-methyl-1-naphthamido) thiophene-3-carboxylic acid **(46)**

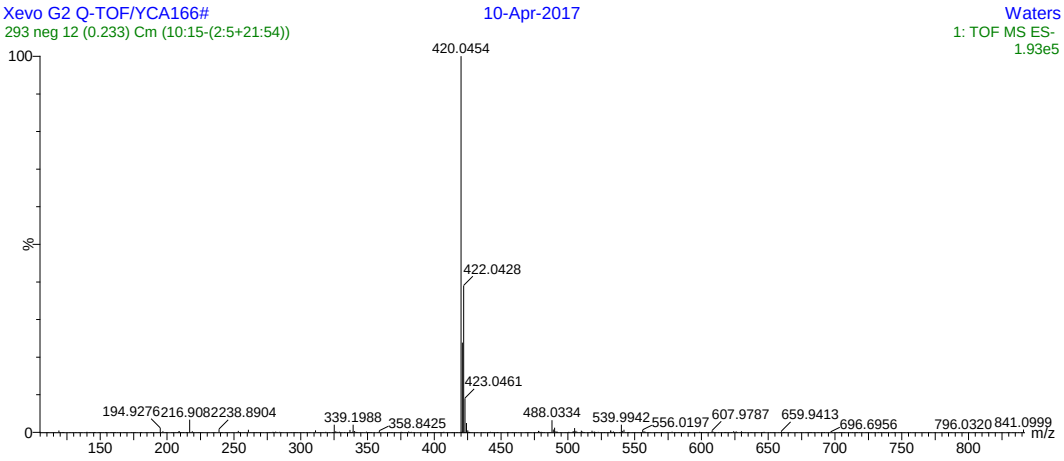
^{1}H-NMR



^{13}C-NMR

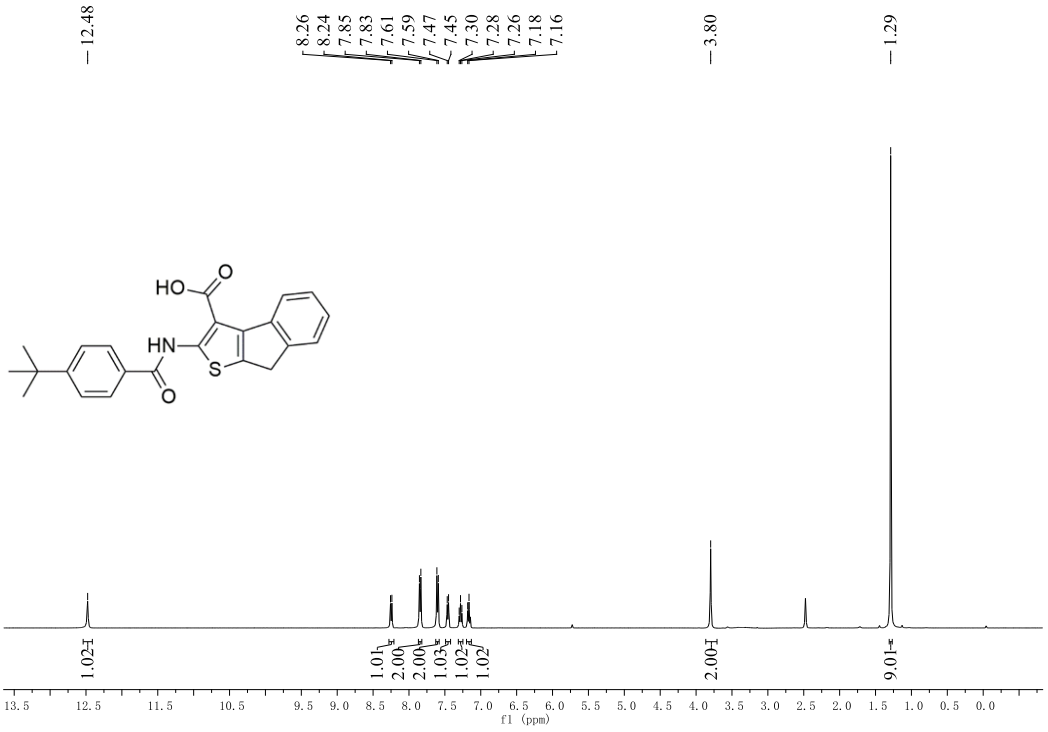


HRMS

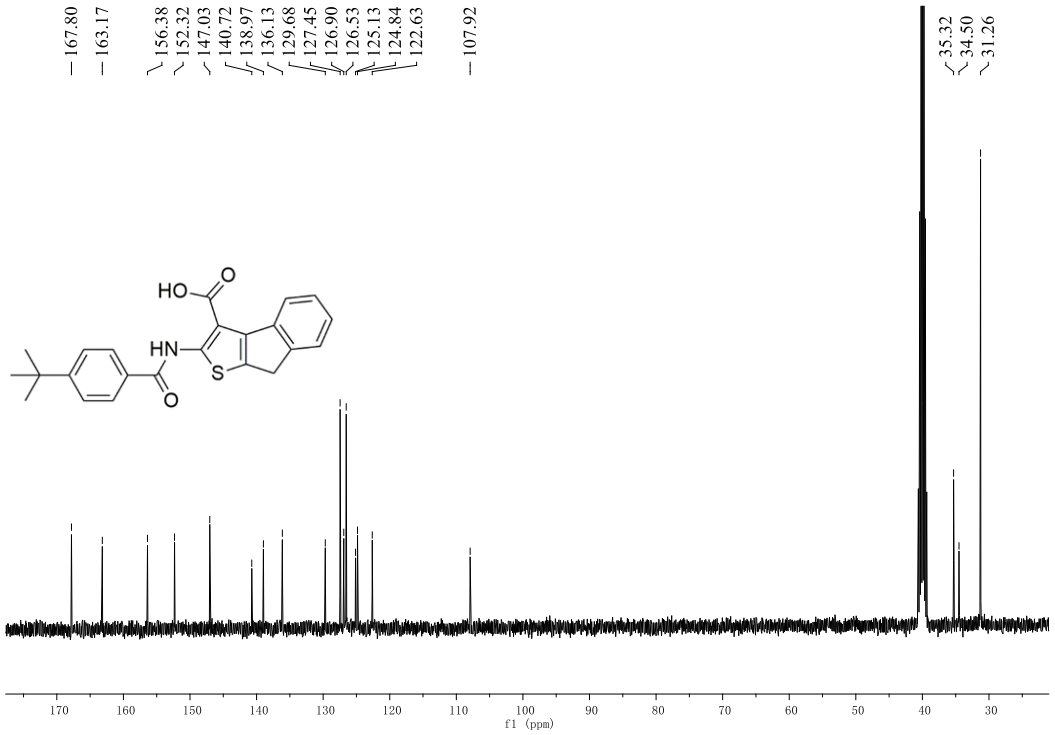


2-(4-(*tert*-Butyl) benzamido)-8*H*-indeno [2,1-*b*] thiophene-3-carboxylic acid **(47)**

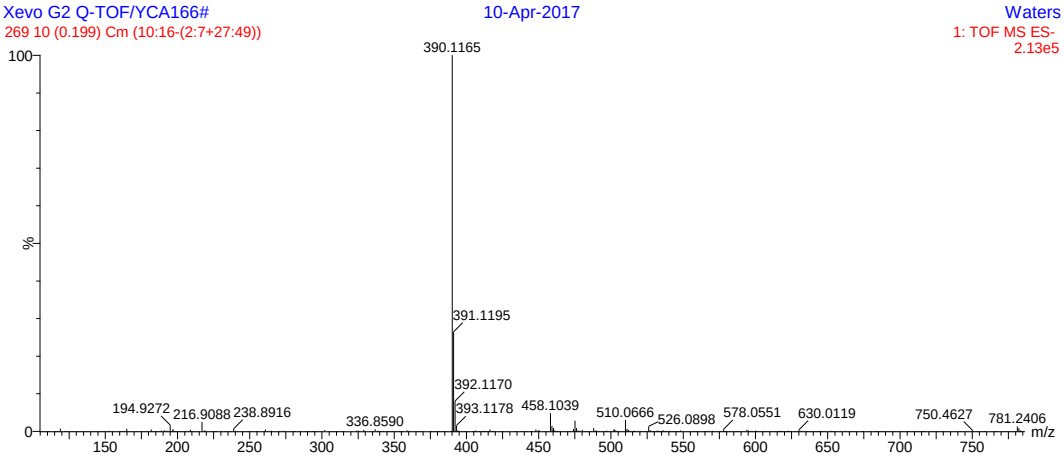
^{1}H-NMR



^{13}C-NMR

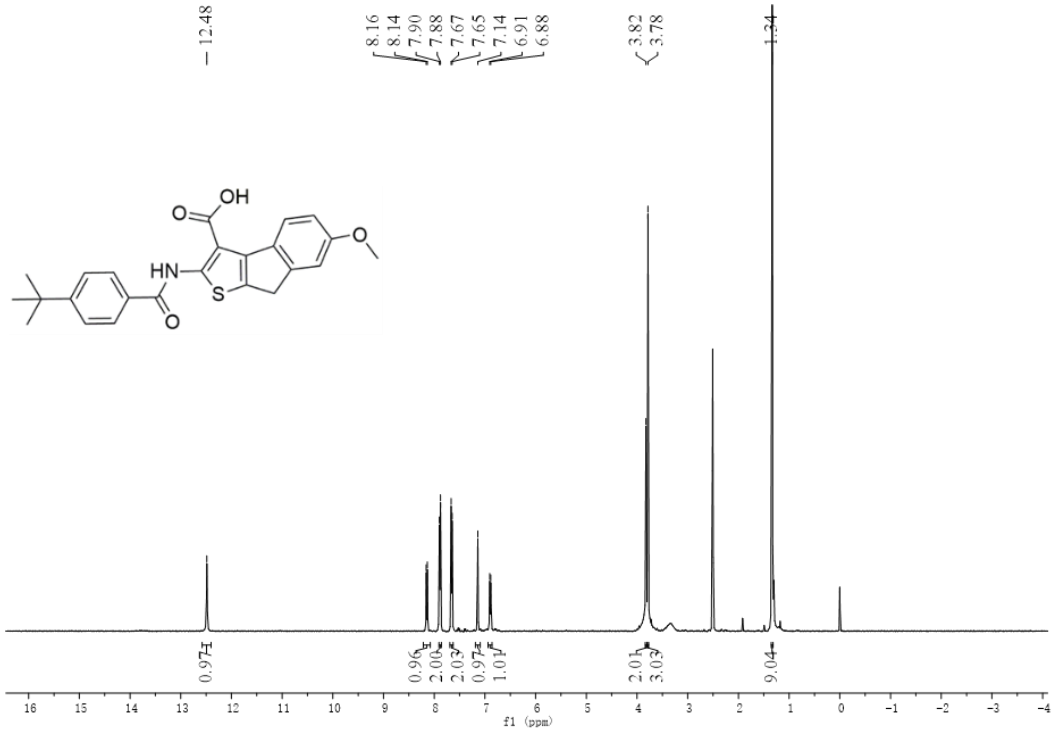

167.80
163.17
156.38
152.32
147.03
140.72
138.97
136.13
129.68
127.45
126.90
126.53
125.13
124.84
122.63
107.92
35.32
34.50
31.26
HO
O
HN
S
O
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

HRMS

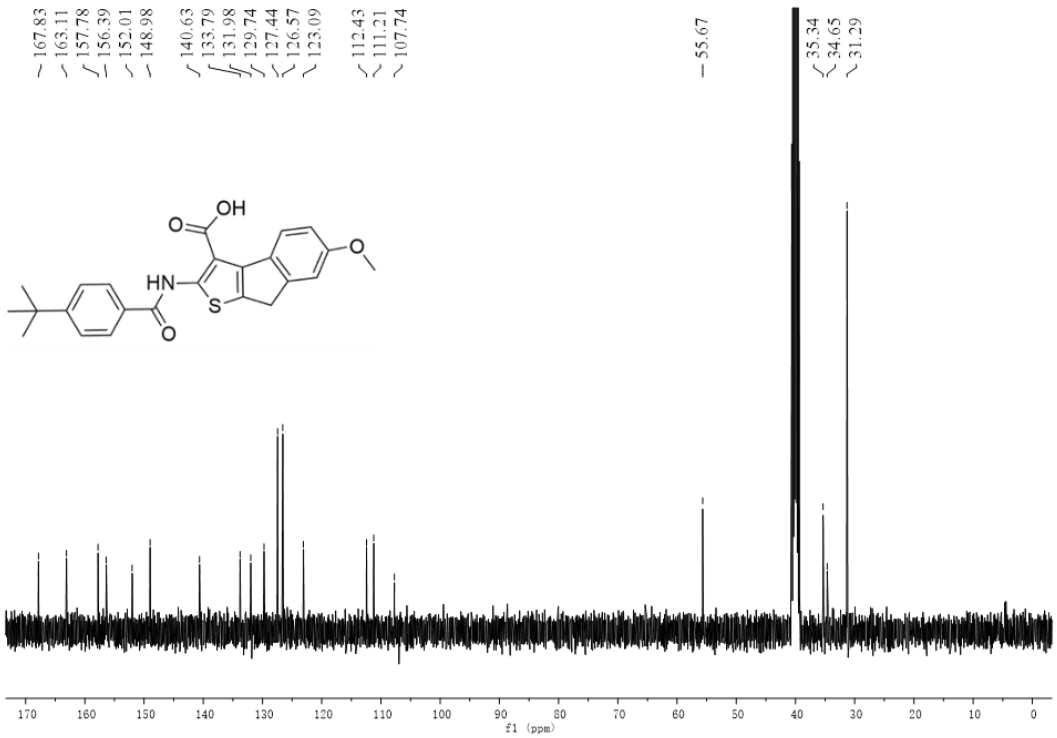

Xevo G2 Q-TOF/YCA166#
269 10 (0.199) Cm (10:16-(2:7+27:49))
10-Apr-2017
Waters
1: TOF MS ES-
2.13e5
100
%
0
390.1165
391.1195
392.1170
393.1178
194.9272
216.9088
238.8916
336.8590
458.1039
510.0666
526.0898
578.0551
630.0119
750.4627
781.2406
150
200
250
300
350
400
450
500
550
600
650
700
750
m/z

2-(4-(*tert*-Butyl) benzamido)-6-methoxy-8*H*-indeno [2,1-*b*] thiophene-3-carboxylic acid **(48)**

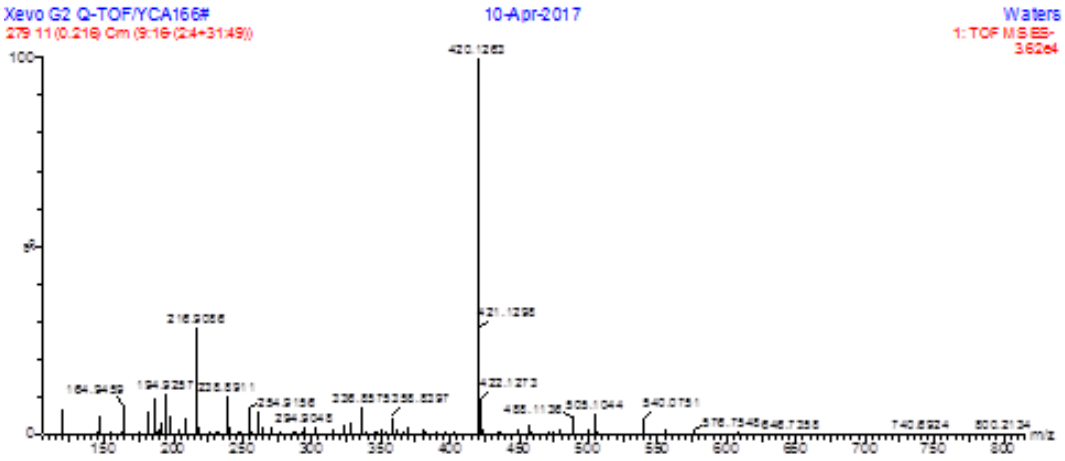
^{1}H-NMR



^{13}C-NMR

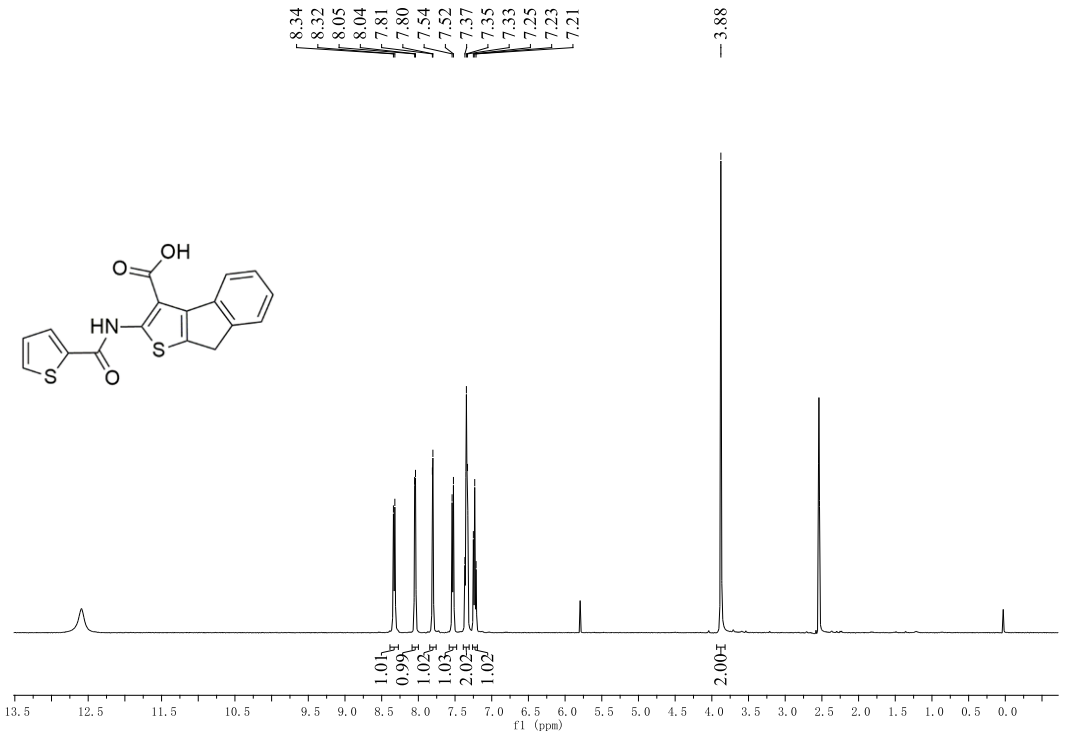


HRMS

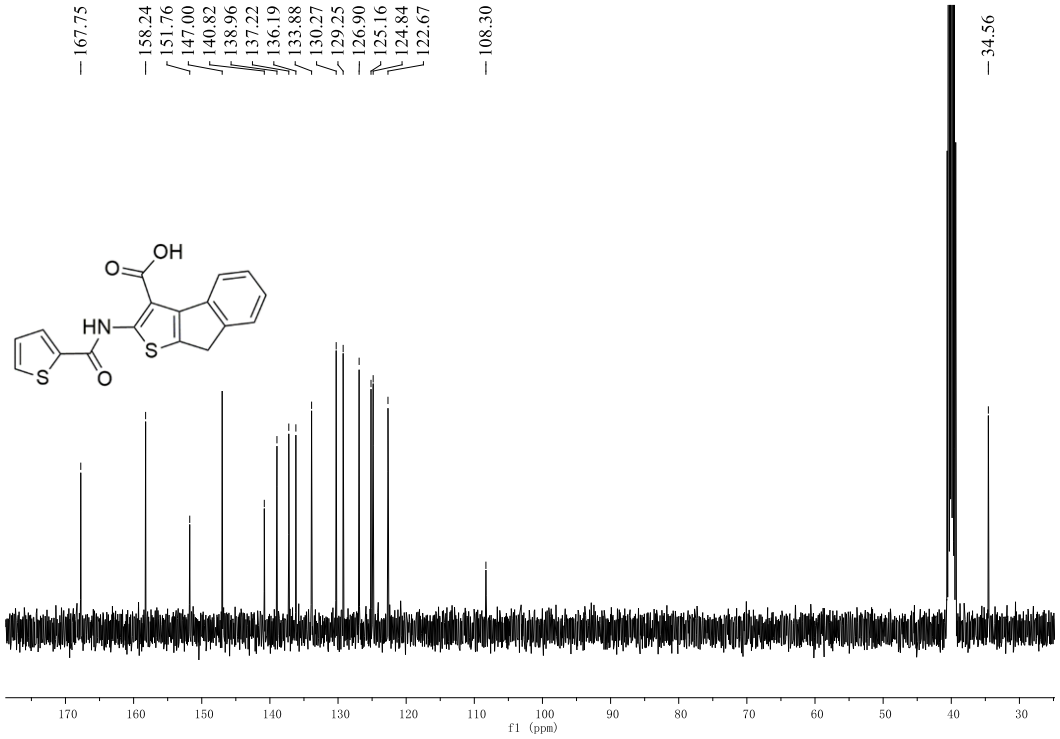


2-(Thiophene-2-carboxamido)-8*H*-indeno [2,1-*b*] thiophene-3-carboxylic acid **(49)**

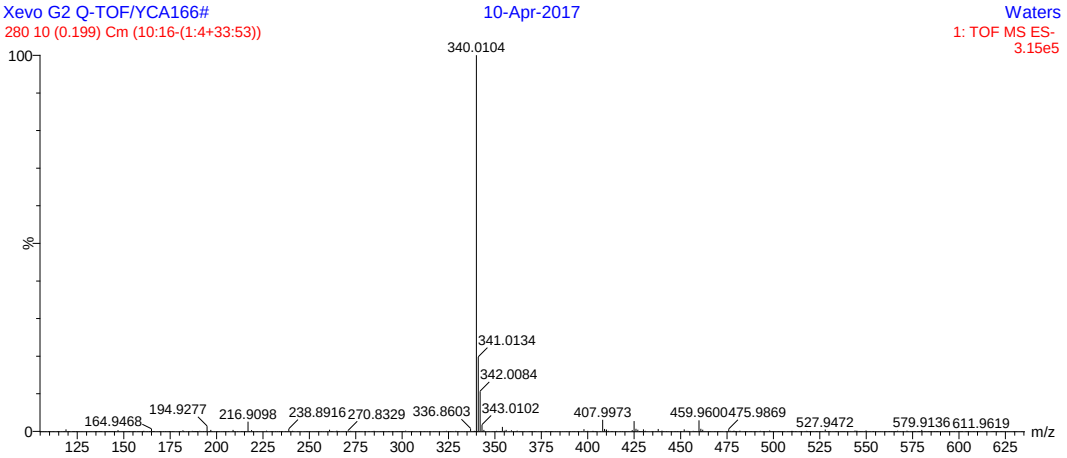
^{1}H-NMR



^{13}C-NMR

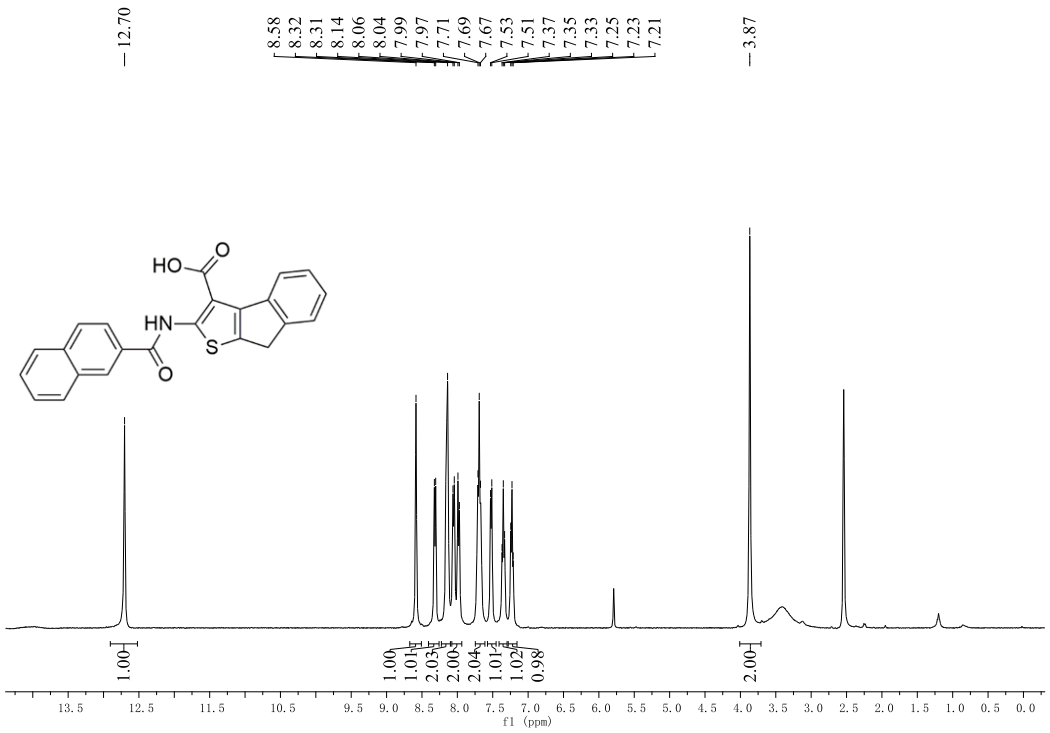

167.75
158.24
151.76
147.00
140.82
138.96
137.22
136.19
133.88
130.27
129.25
126.90
125.16
124.84
122.67
108.30
34.56
OH
O
HN
S
S
O
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

HRMS

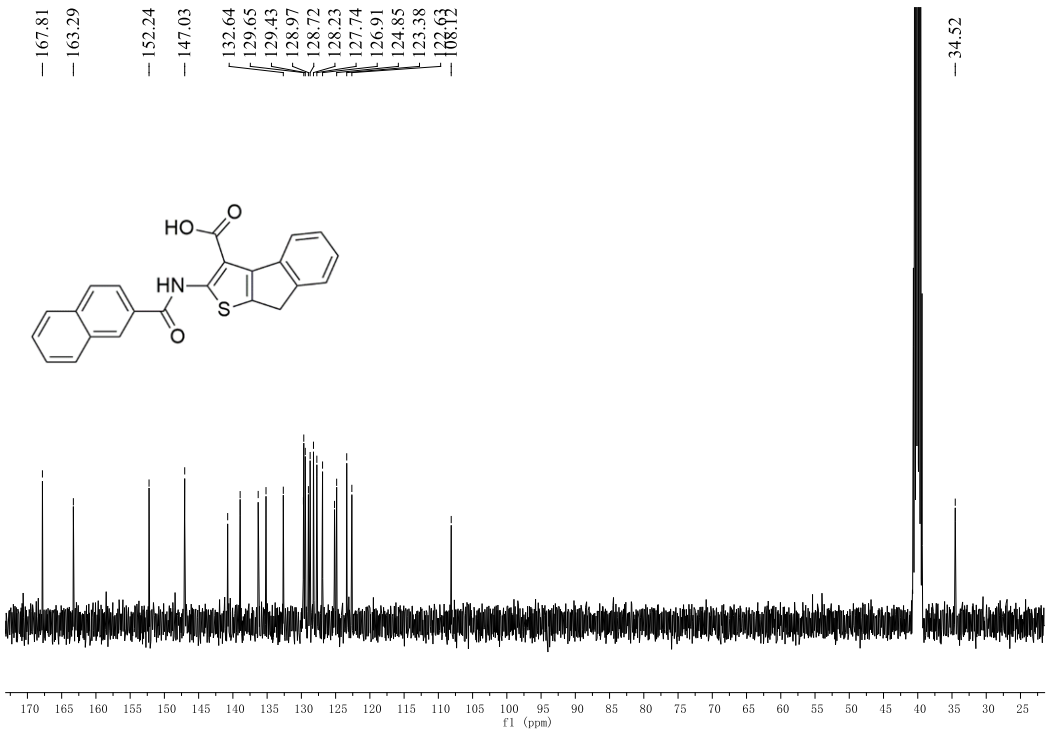

Xevo G2 Q-TOF/YCA166#
280 10 (0.199) Cm (10:16-(1:4+33:53))
10-Apr-2017
Waters
1: TOF MS ES-
3.15e5
100
%
0
340.0104
341.0134
342.0084
343.0102
164.9468
194.9277
216.9098
238.8916
270.8329
336.8603
407.9973
459.9600
475.9869
527.9472
579.9136
611.9619
125
150
175
200
225
250
275
300
325
350
375
400
425
450
475
500
525
550
575
600
625
m/z

2-(2-Naphthamido)-8*H*-indeno [2,1-*b*] thiophene-3-carboxylic acid **(50)**

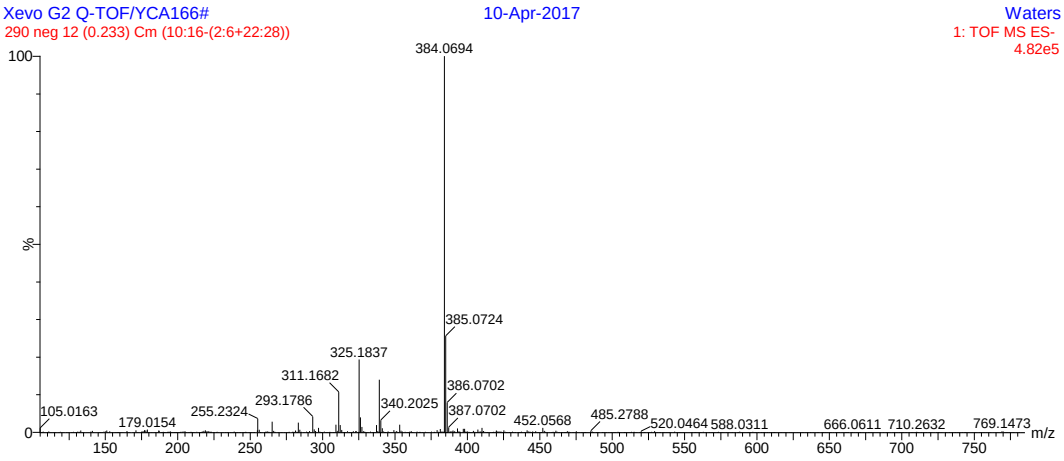
^{1}H-NMR



^{13}C-NMR

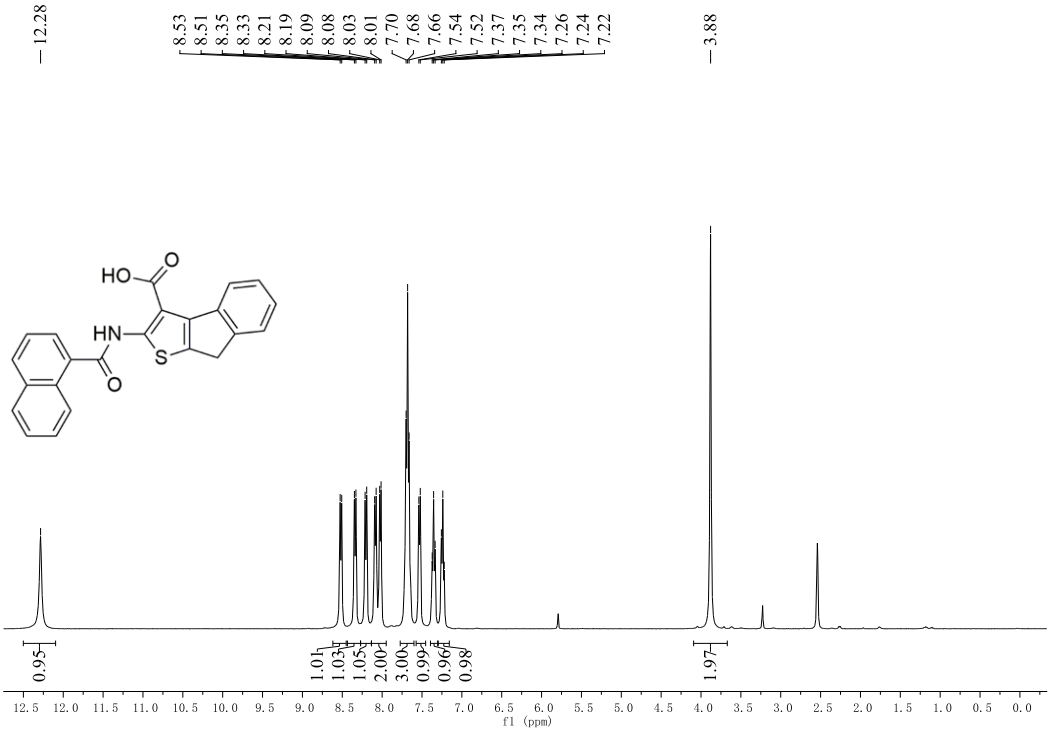


HRMS

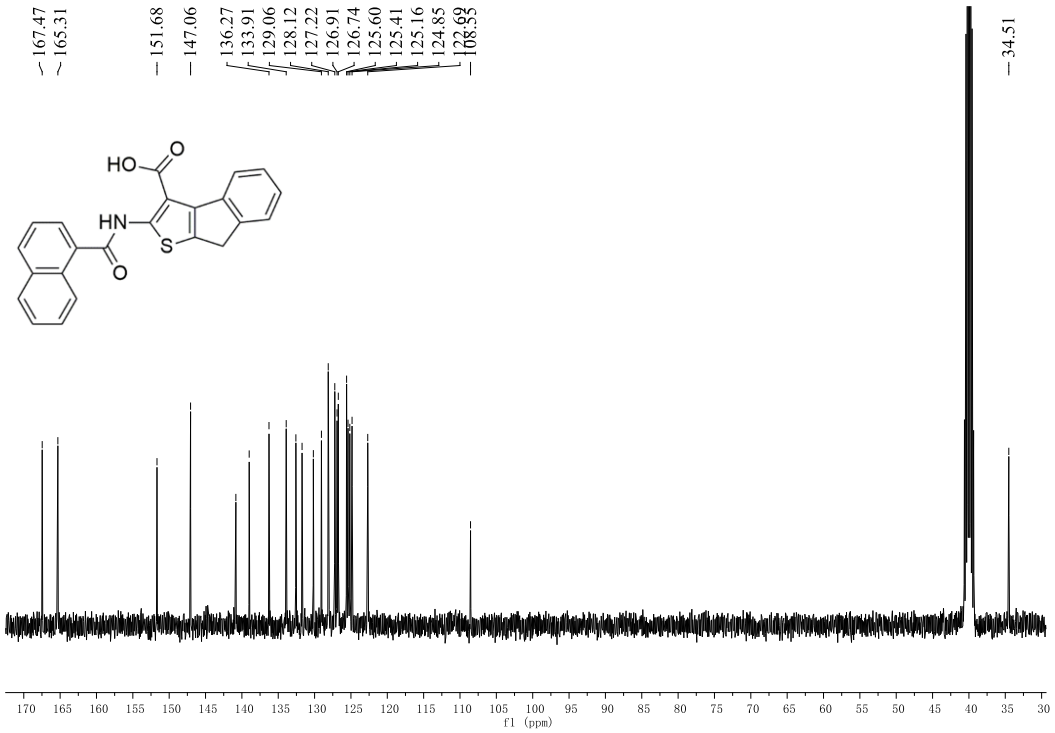


2-(1-Naphthamido)-8*H*-indeno [2,1-*b*] thiophene-3-carboxylic acid **(51)**

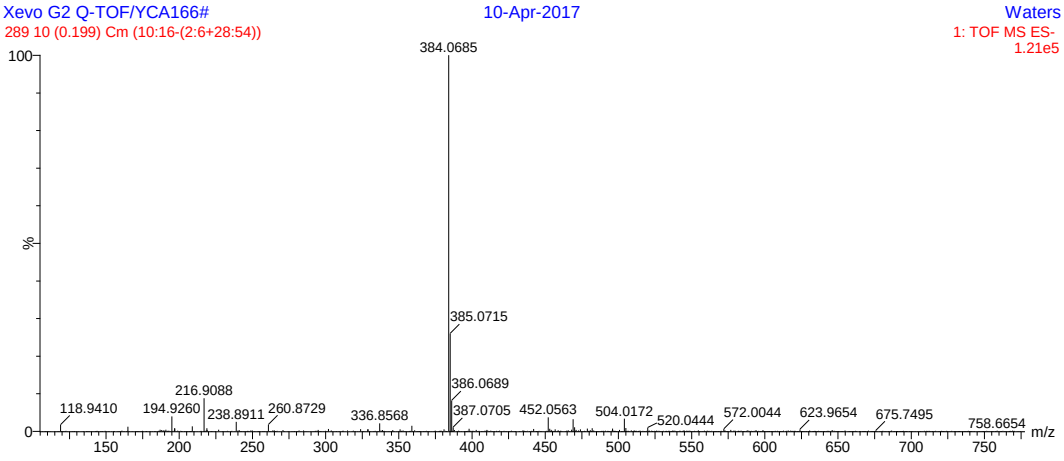
^{1}H-NMR



^{13}C-NMR

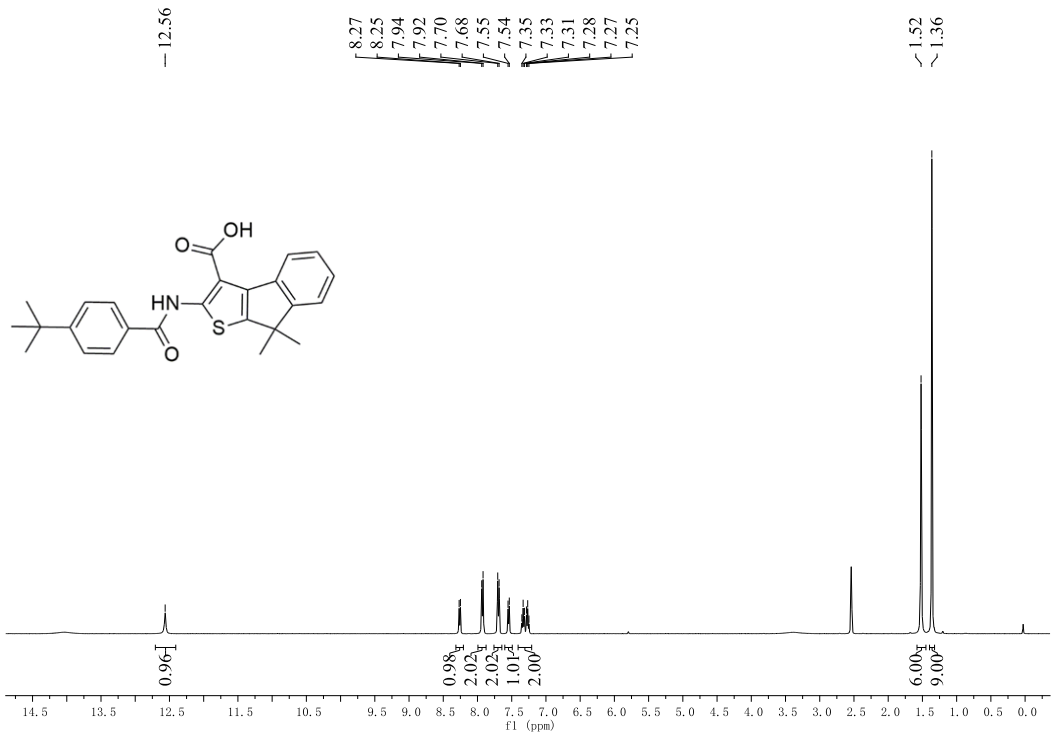

167.47
165.31
151.68
147.06
136.27
133.91
129.06
128.12
127.22
126.91
126.74
125.60
125.41
125.16
124.85
122.69
108.55
34.51
HO
O
HN
S
O
170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30
f1 (ppm)

HRMS

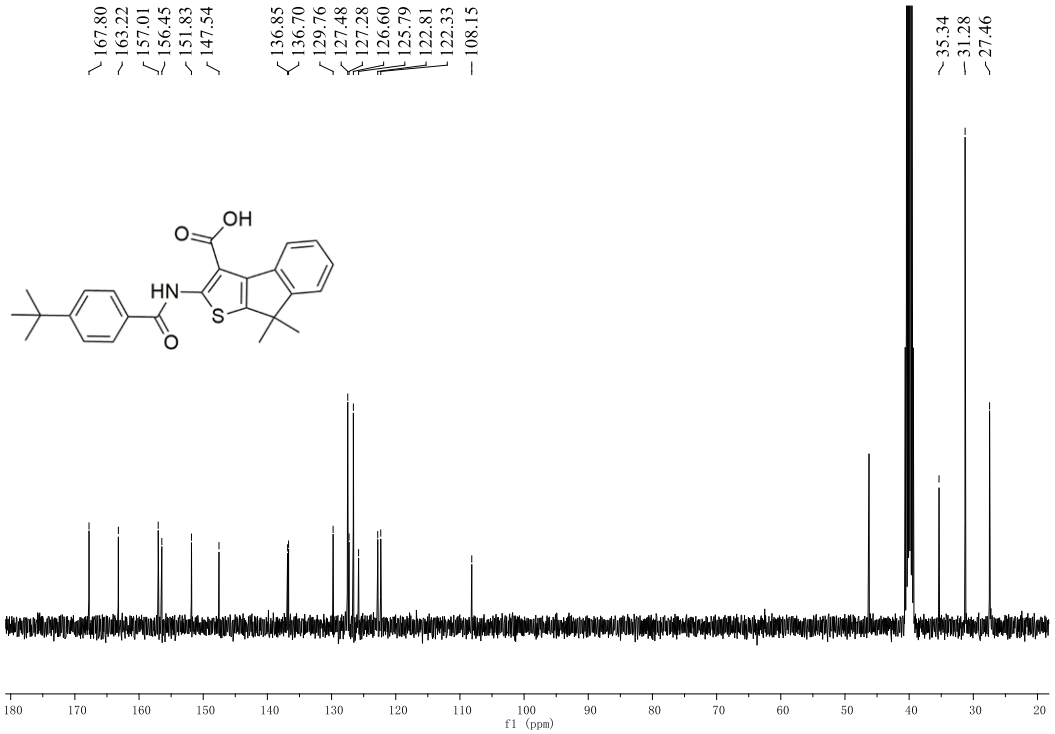

Xevo G2 Q-TOF/YCA166#
289 10 (0.199) Cm (10:16-(2:6+28:54))
10-Apr-2017
Waters
1: TOF MS ES-
1.21e5
100
%
0
384.0685
385.0715
386.0689
387.0705
216.9088
118.9410
194.9260
238.8911
260.8729
336.8568
452.0563
504.0172
520.0444
572.0044
623.9654
675.7495
758.6654
150 200 250 300 350 400 450 500 550 600 650 700 750
m/z

2-(4-(*tert*-Butyl) benzamido)-8,8-dimethyl-8*H*-indeno [2,1-*b*] thiophene-3-carboxylic acid **(52)**

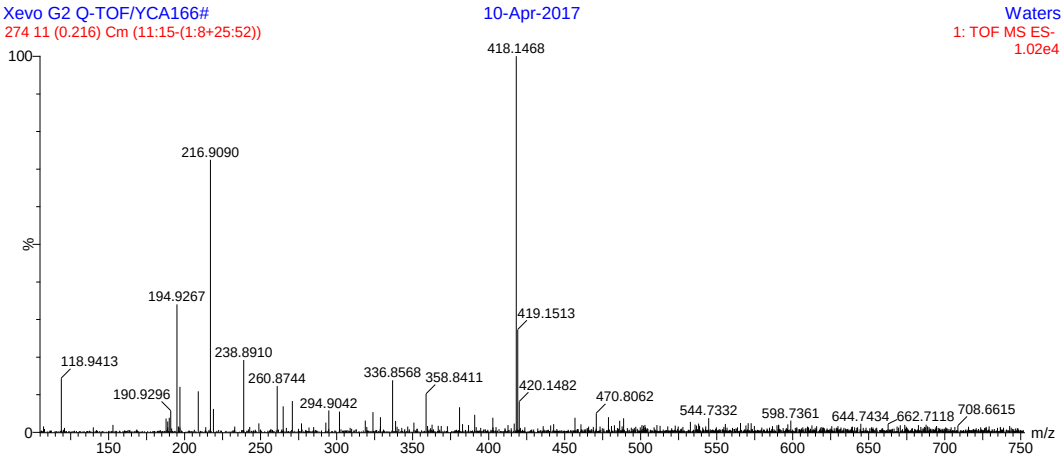
^{1}H-NMR



^{13}C-NMR

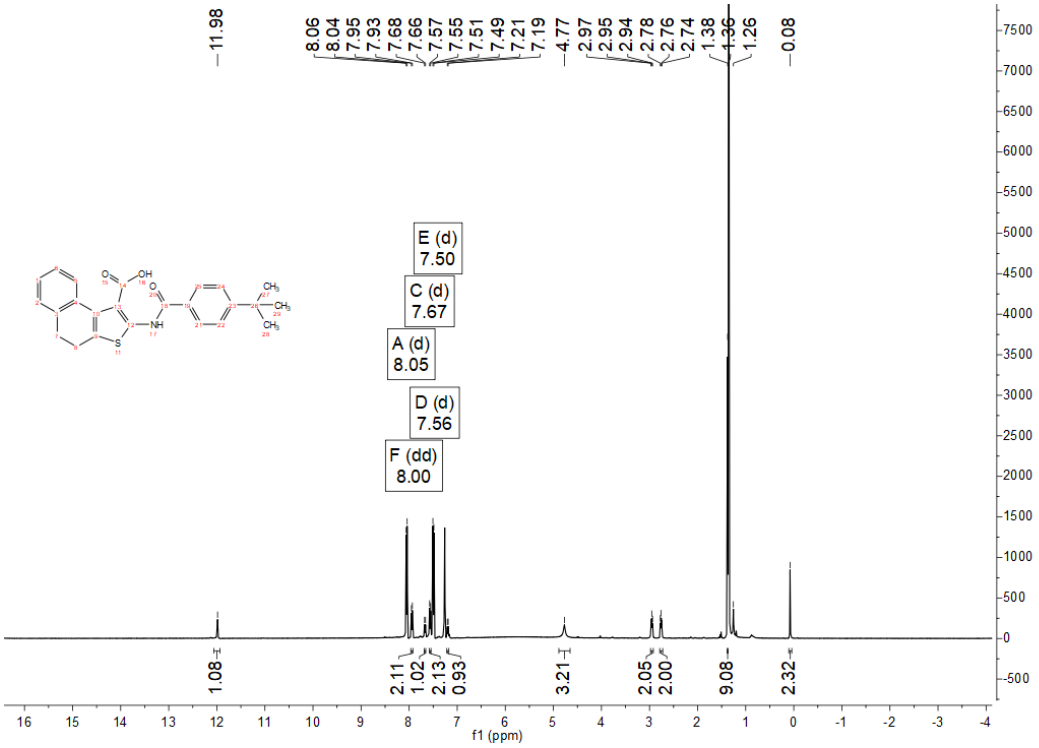


HRMS

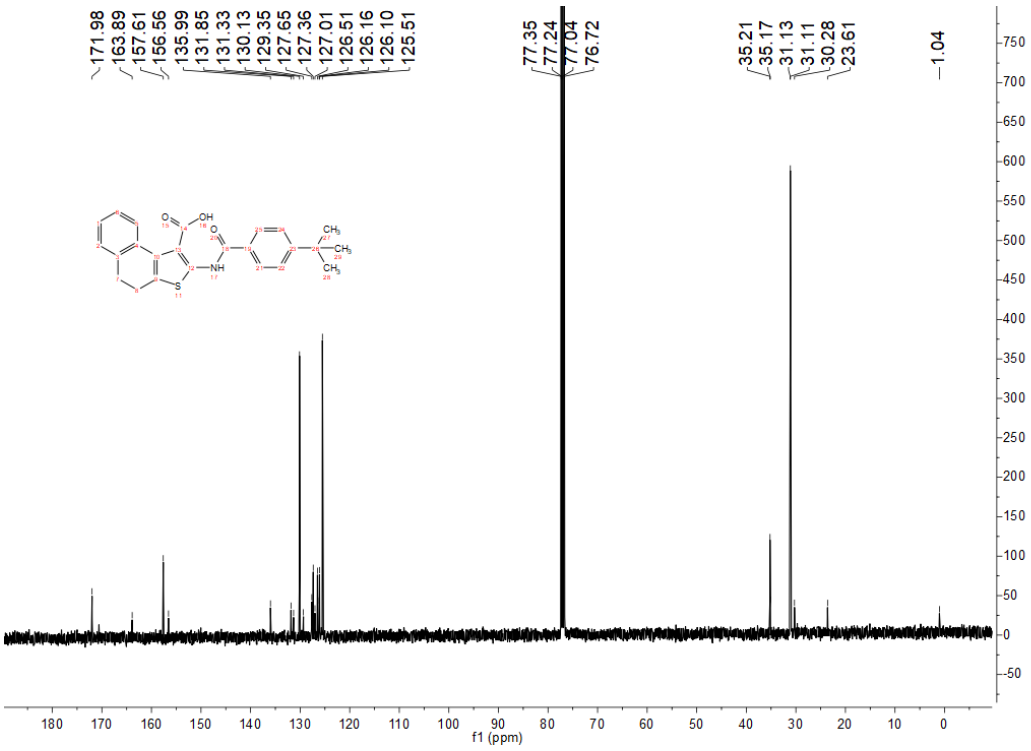


2-(4-(*tert*-Butyl) benzamido)-4,5-dihydronaphtho [2,1-*b*] thiophene-1-carboxylic acid **(53)**

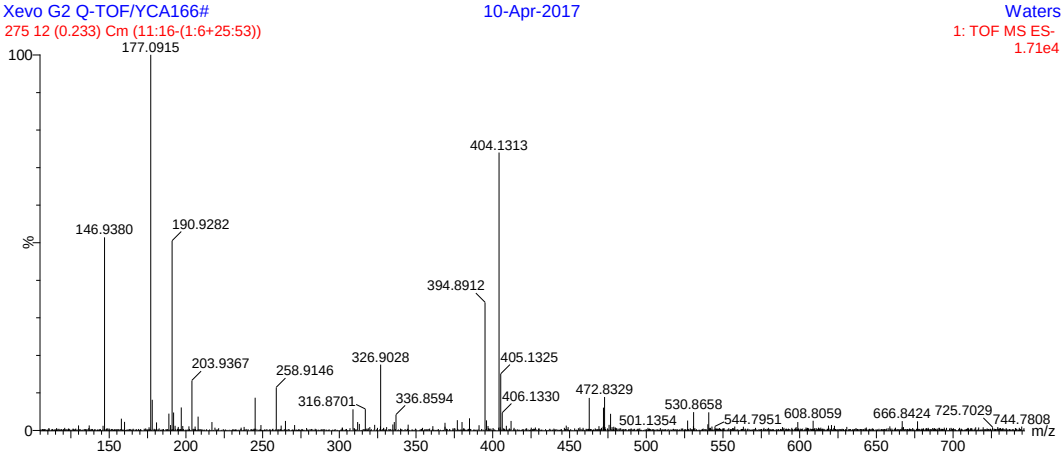
^{1}H-NMR



^{13}C-NMR


171.98
163.89
157.61
156.56
135.99
131.85
131.33
130.13
129.35
127.65
127.36
127.01
126.51
126.16
126.10
125.51
77.35
77.24
77.04
76.72
35.21
35.17
31.13
31.11
30.28
23.61
1.04
f1 (ppm)

HRMS


Xevo G2 Q-TOF/YCA166#
10-Apr-2017
Waters
275 12 (0.233) Cm (11:16-(1:6+25:53))
1: TOF MS ES-
1.71e4
177.0915
404.1313
146.9380
190.9282
394.8912
405.1325
203.9367
258.9146
326.9028
316.8701
336.8594
406.1330
472.8329
530.8658
501.1354
544.7951
608.8059
666.8424
725.7029
744.7808
%
m/z