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Supporting Information

Facile preparation of 3,5-disubstituted-4-aminothiophene-2-carbaldehyde from a novel unexpected domino reaction of vinyl azides and 1,4-dithiane-2,5-diol

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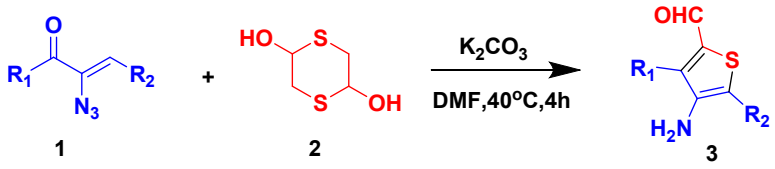
E-mail: guolinzhang@zju.edu.cn
yyu@zju.edu.cn



List of contents

1. General information:

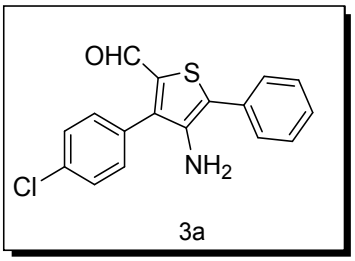
All solvents were purified according to standard methods prior to use. Melting points were recorded on a BÜCHI B-540 melting point apparatus. NMR spectra were recorded for ^{1}H NMR at 500 MHz and ^{13}C NMR at 125 MHz . For ^{1}H NMR, tetramethylsilane (TMS) served as internal standard (δ=0) and data are reported as follows: chemical shift, integration, multiplicity (s=singlet, br. s=broad singlet, d=doublet, t= triplet, q=quartet, m=multiplet), and coupling constant(s) in Hertz. For ^{13}C NMR, TMS (δ=0) or $CDCl_3$ (δ=77.16) was used as internal standard and spectra were obtained with complete proton decoupling. LC-MS and HRMS data was obtained using Agilent Technologies 6224 TOF LC/MS. The starting material vinyl azides **1a-1p** were prepared according to literature methods.[1] The starting material **2** were commercially available.

2. General procedure for the synthesis of 3:

A mixture of α-azidovinylketone **1** (0.4mmol), 1,4-dithiane-2,5-diol **2** (0.4mmol), K_2CO_3 (1.2mmol) was stirred in DMF 2 ml at 40^0C for 4 hours. After the completeness of the reaction, the reaction mixture was diluted with water and extracted three times with ethyl acetate. The combined organic extracts were washed with brine, dried over Na_2SO_4, concentrated and purified by flash chromatography (PE/EA) on silica gel to afford **3a-3m**.

3. Characterization data of 3:

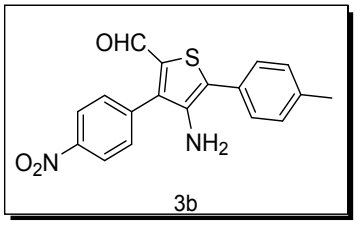
4-Amino-3-(4-chlorophenyl)-5-phenylthiophene-2-carbaldehyde:



3a

Yellow solid; mp: 142 – 144°C; IR (KBr) $\nu_{max,}$ 3461, 3364, 3061, 2852, 1645, 1609, 1545, 1493 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): ^1H NMR (500 MHz, $CDCl_3$) δ 9.61 (s, 1H), 7.62 (d, J = 7.15 Hz, 2H), 7.53 (d, J = 8.45, Hz, 2H), 7.49 (t, J = 7.55Hz, 2H), 7.45 (d, J = 8.50Hz, 2H), 7.39 (t, J = 7.45Hz, 1H), 3.75(s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 183.46, 140.54, 140.33, 136.79, 135.43, 133.23, 131.50, 130.78, 129.54, 129.52, 128.45, 128.16, 126.51; HRMS (ESI): m/z calcd for $C_{17}H_{12}ClNOS$ $[M+H]^+$: 314.0406, found: 314.0402

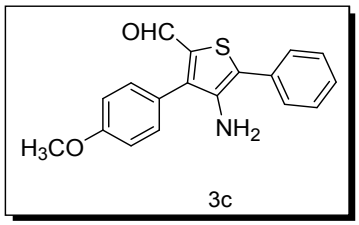
4-Amino-3-(4-nitrophenyl)-5-p-tolylthiophene-2-carbaldehyde:



3b

Red solid; mp: 150 – 152°C; IR (KBr) $\nu_{max,}$ 3416, 3345, 3076, 2864, 1648, 1619, 1595, 1513 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.59(s, 1H), 8.39 (d, J = 8.66Hz, 2H), 7.72 (d, J = 8.65Hz, 2H), 7.50 (d, J = 8.05Hz, 2H), 7.31 (d, J=7.91, 2H), 3.76(s, 2H), 2.42(s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.58, 148.11, 139.96, 139.27, 138.94, 138.49, 136.78, 131.24, 130.32, 129.80, 128.11, 127.86, 124.38, 21.48; HRMS (ESI): m/z calcd for $C_{18}H_{14}N_2O_3S$ $[M+H]^+$: 339.0803, found: 355.0806.

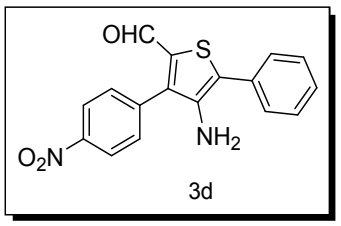
4-Amino-3-(4-methoxyphenyl)-5-phenylthiophene-2-carbaldehyde:



3c

Pale yellow solid; mp: 113 – 115°C; ^1H NMR (500 MHz, $CDCl_3$) δ 9.63(s, 1H), 7.64 (d, J = 7.18Hz, 2H), 7.47 (t, J = 7.58Hz, 2H), 7.43 (d, J = 8.66Hz, 2H), 7.37 (t, J=7.39, 1H) ,7.05(d, J = 8.70Hz, 2H), 3.89 (br. s and s, 5H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 184.17, 160.28, 142.26, 140.58, 136.44, 133.55, 131.48, 129.46, 128.25, 128.11, 125.95, 124.43, 114.66, 55.55 ; HRMS (ESI): m/z calcd for $C_{18}H_{15}NO_2S$ $[M+H]^+$: 310.0902, found: 310.0905.

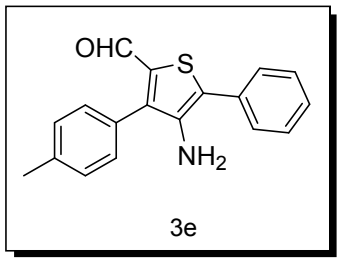
4-Amino-3-(4-nitrophenyl)-5-phenylthiophene-2-carbaldehyde:



3d

Red solid; mp: 123 – 124°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.61(s, 1H), 8.41(d, J = 8.62Hz, 2H), 7.73 (d, J = 8.69Hz, 2H), 7.62 (d, J = 7.25Hz, 2H), 7.51(t, J = 7.53Hz, 2H), 7.41(t, J=7.44, 1H), 3.78(s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.59, 148.12, 140.19, 139.18, 138.47, 137.15, 132.79, 131.24, 129.62, 128.73, 128.23, 127.30, 124.29; HRMS (ESI): m/z calcd for $C_{17}H_{12}N_2O_3S$ $[M+H]^+$: 325.0647, found: 325.0645.

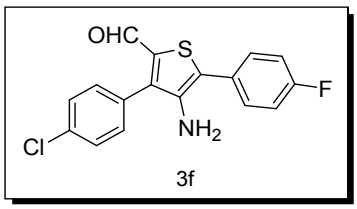
4-Amino-5-phenyl-3-p-tolylthiophene-2-carbaldehyde:



3e

Yellow solid; mp: 125 – 126°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.61(s, 1H), 7.63 (d, J = 7.15Hz, 2H), 7.46 (t, J = 7.51Hz, 2H), 7.38 – 7.32 (m, 5H), 3.79(s, 2H), 2.44(s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 184.10, 142.50, 140.52, 139.17, 136.49, 133.51, 130.02, 129.82, 129.90, 129.42, 128.22, 128.09, 125.94, 21.44; HRMS (ESI): m/z calcd for $C_{18}H_{15}NOS$ $[M+H]^+$: 294.0953, found: 294.0949.

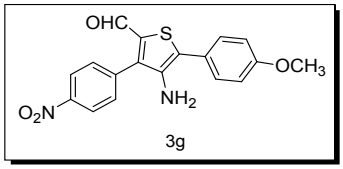
4-Amino-3-(4-chlorophenyl)-5-(4-fluorophenyl)thiophene-2-carbaldehyde:



3f

Yellow solid; mp: 110 – 111°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ9.59(s, 1H), 7.61 – 7.58(m, 2H), 7.52(d, J=8.40Hz, 2H), 7.43(d, J=8.40Hz, 2H), 7.17(t, J=8.55Hz, 2H), 3.74(s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 183.41, 162.60(d, J=249.50Hz), 140.58, 140.30, 136.72, 135.49, 131.45, 130.91, 130.64, 130.06(d, J=8.20 Hz), 129.57, 125.33, 116.61(d, J=21.78Hz); HRMS (ESI): m/z calcd for $C_{17}H_{11}ClFNOS$ $[M+H]^+$: 332.0312, found: 332.0312.

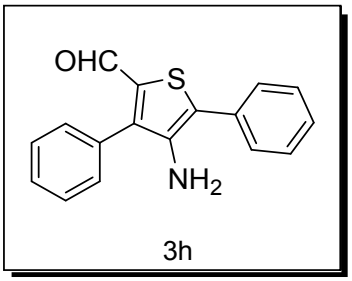
4-Amino-5-(4-methoxyphenyl)-3-(4-nitrophenyl)thiophene-2-carbaldehyde:



3g

Red solid; mp: 143 – 145°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.58(s, 1H), 8.40 (d, J = 8.72Hz, 2H), 7.71 (d, J = 8.77Hz, 2H), 7.55 (d, J = 7.55Hz, 2H), 7.02 (d, J=8.76, 2H), 3.87(s, 3H), 3.70(s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.51, 160.01, 148.09, 139.71, 139.31, 138.55, 136.42, 131.22, 129.63, 127.99, 124.96, 124.37, 115.04, 55.57; HRMS (ESI): m/z calcd for $C_{18}H_{14}N_2O_4S$ $[M+H]^+$: 355.0753, found: 355.0753.

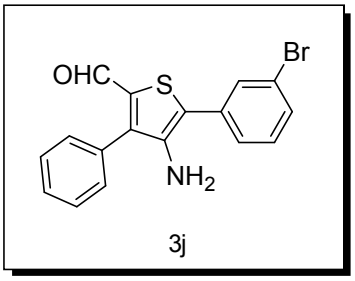
4-Amino-3,5-diphenylthiophene-2-carbaldehyde:



3h

Yellow solid; mp: 132 – 134°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.62(s, 1H), 7.64 (d, J = 7.35Hz, 2H), 7.53 (d, J = 6.31Hz, 2H), 7.50 – 7.46 (m, 5H), 7.37 (t, J=7.45, 1H), 3.81(s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 184.02, 142.28, 140.43, 136.62, 133.42, 132.33, 130.16, 129.46, 129.23, 129.15, 128.30, 128.11, 126.11; HRMS (ESI): m/z calcd for $C_{17}H_{13}NOS$ $[M+H]^+$: 280.0796, found: 280.0795.

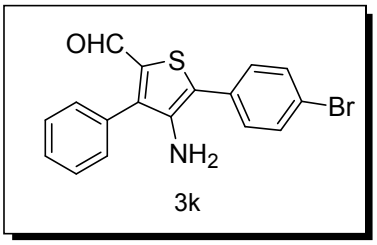
4-Amino-5-(3-bromophenyl)-3-phenylthiophene-2-carbaldehyde:



3j

Yellow solid; mp: 119 – 121°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.61(s, 1H), 7.80(s, 1H), 7.56 – 7.47(m, 7H), 7.33 (t, J = 7.88Hz, 1H), 3.83(s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 183.97, 142.21, 140.91, 137.13, 135.52, 132.05, 131.16, 130.93, 130.79, 130.11, 129.29, 129.27, 126.67, 123.72, 123.51; HRMS (ESI): m/z calcd for $C_{17}H_{12}BrNOS$ $[M+H]^+$: 357.9901, found: 357.9901.

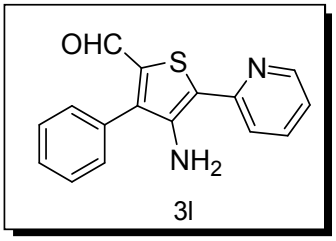
4-Amino-5-(4-bromophenyl)-3-phenylthiophene-2-carbaldehyde:



3k

Yellow solid; mp: 119 – 121°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.61(s, 1H), 7.60 (d, J=8.48, 2H), 7.56 – 7.47(m, 7H), 3.79(s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 183.93, 142.32, 140.69, 136.91, 132.63, 132.42, 132.15, 130.13, 129.58, 129.29, 129.27, 124.46, 122.31; HRMS (ESI): m/z calcd for $C_{17}H_{12}BrNOS$ $[M+H]^+$: 357.9901, found: 357.9901.

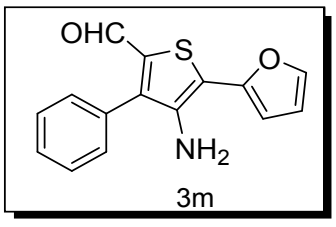
4-Amino-3-phenyl-5-(pyridin-2-yl)thiophene-2-carbaldehyde:



3l

Yellow solid; mp: 110 – 112°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.66(s, 1H), 8.56(d, J=4.87Hz, 1H), 7.70 (t, J=7.80Hz, 1H), 7.58 – 7.48(m, 6H), 7.11(t, J=5.94Hz, 1H), 6.03(s, 2H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 184.38, 154.56, 148.46, 146.13, 142.31, 136.93, 136.57, 131.95, 130.06, 129.26, 129.18, 120.89, 120.67, 118.75; HRMS (ESI): m/z calcd for $C_{16}H_{12}N_2OS$ $[M+H]^+$: 281.0749, found: 281.0745.

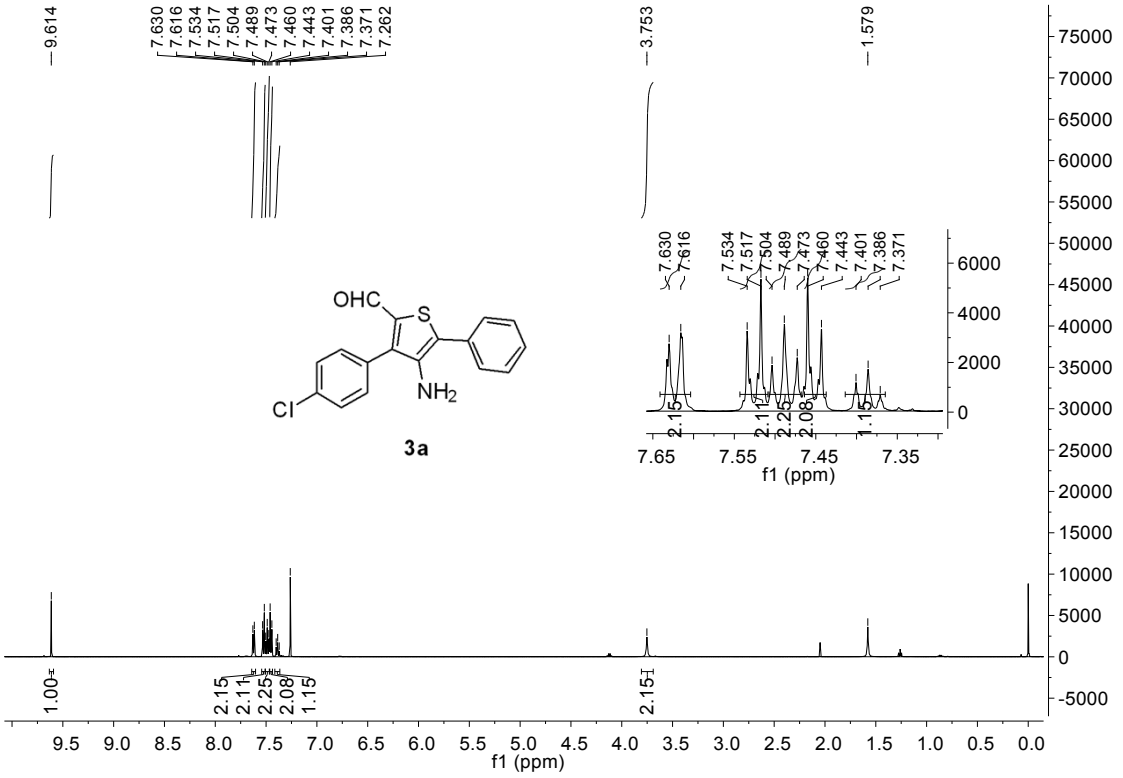
4-Amino-5-(furan-2-yl)-3-phenylthiophene-2-carbaldehyde:

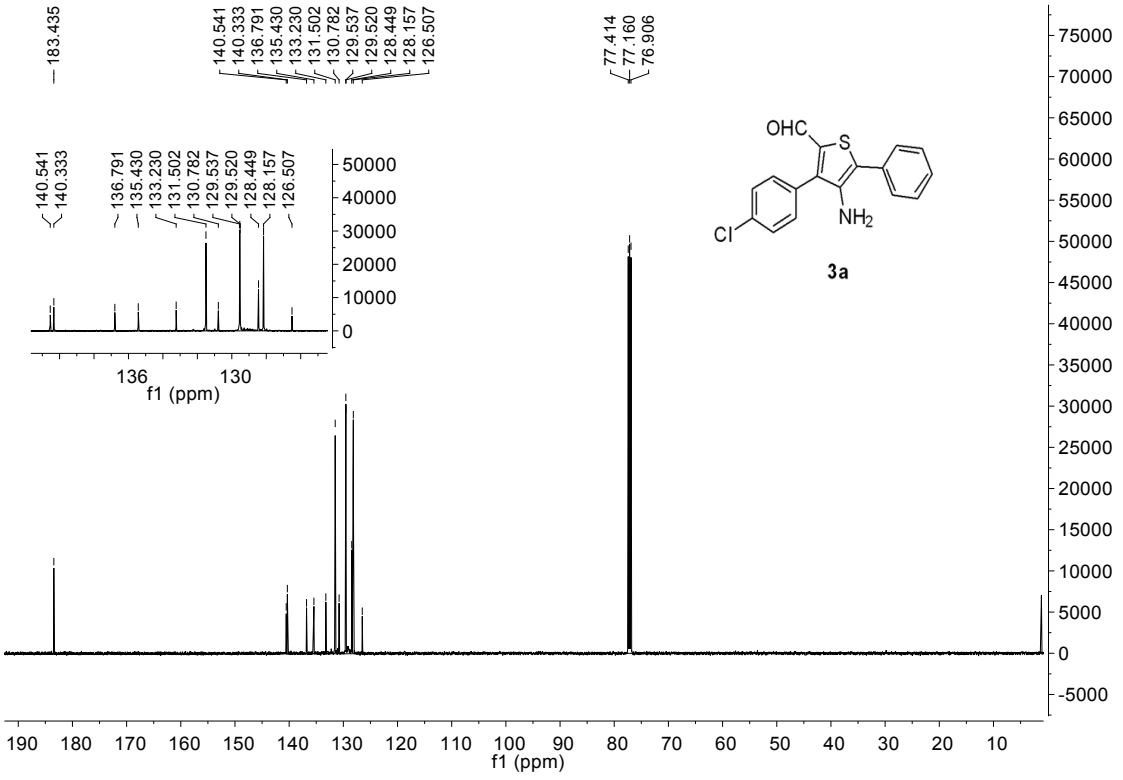


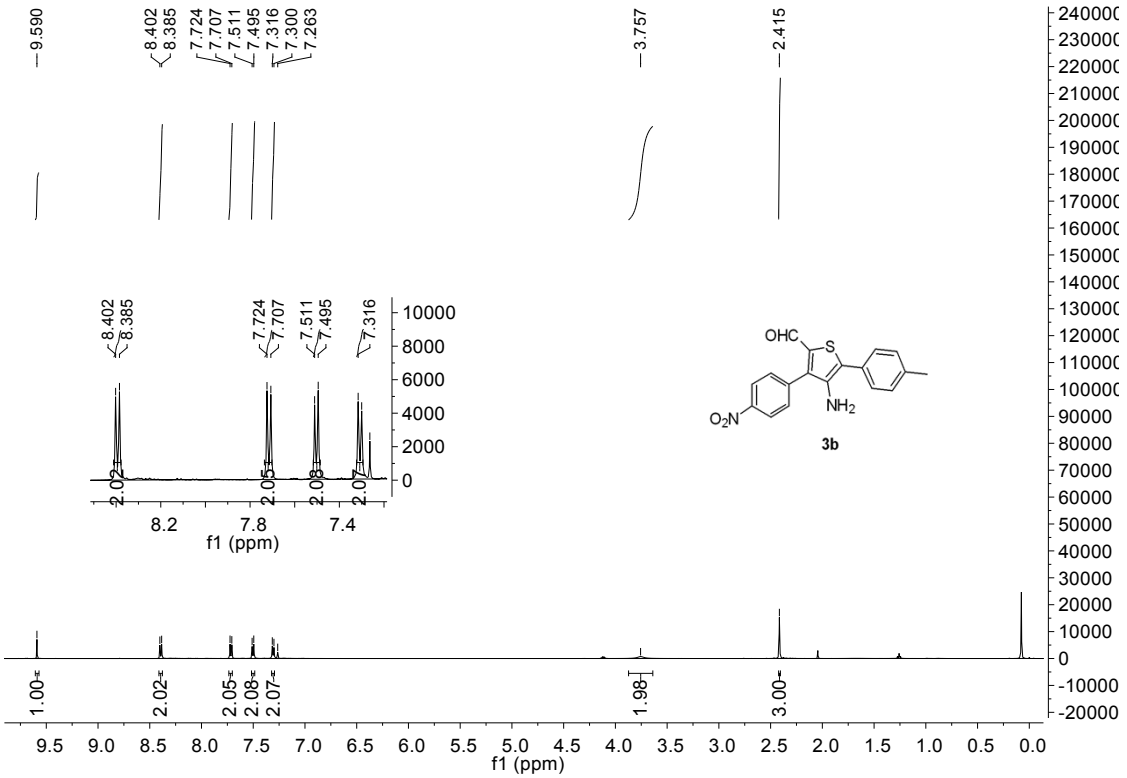
3m

Pale yellow solid; mp: 111 – 113°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.59(s, 1H), 7.55 – 7.49 (m, 6H), 6.59(d, J=3.44, 1H), 6.53(d, J=5.05, 1H), 4.27(s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 183.93, 171.30, 149.05, 142.20, 140.59, 135.81, 131.89, 130.06, 129.30, 129.27, 115.36, 112.13, 107.26; HRMS (ESI): m/z calcd for $C_{15}H_{11}NO_2S$ $[M+H]^+$: 270.0589, found: 270.0587

4. ^{1}H and ^{13}C NMR spectra of 3



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2.02
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2.08
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3.00
f1 (ppm)
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NH2
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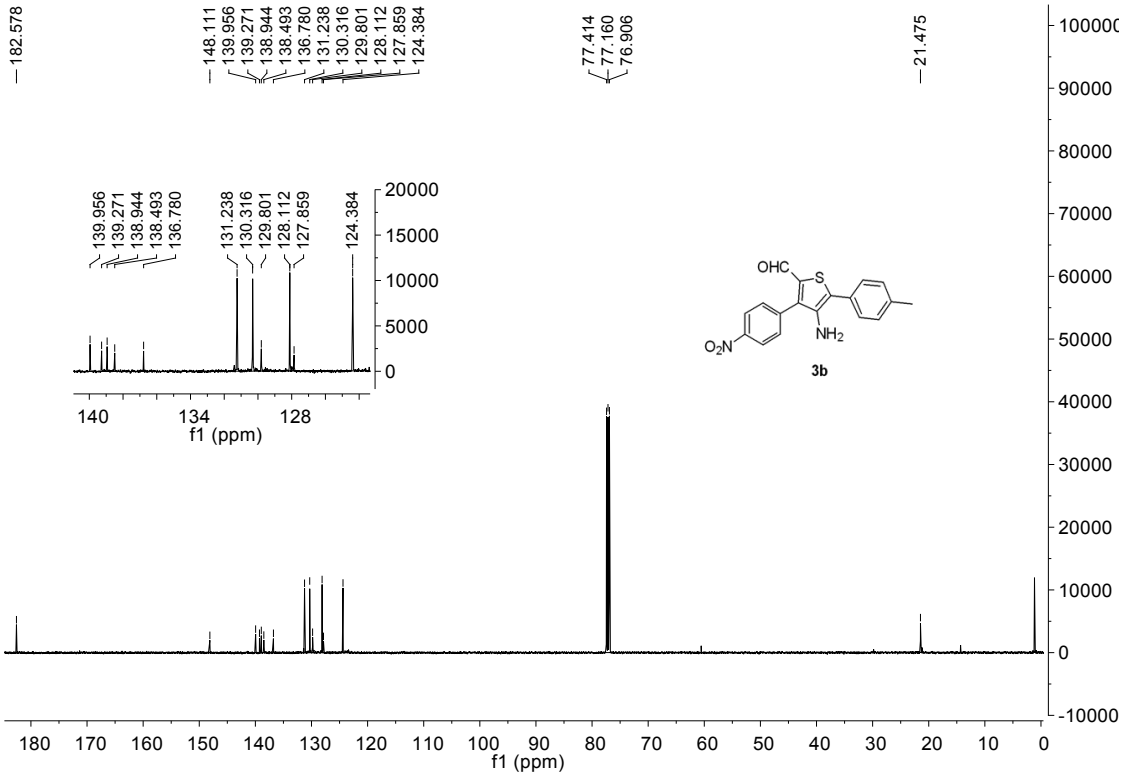
3b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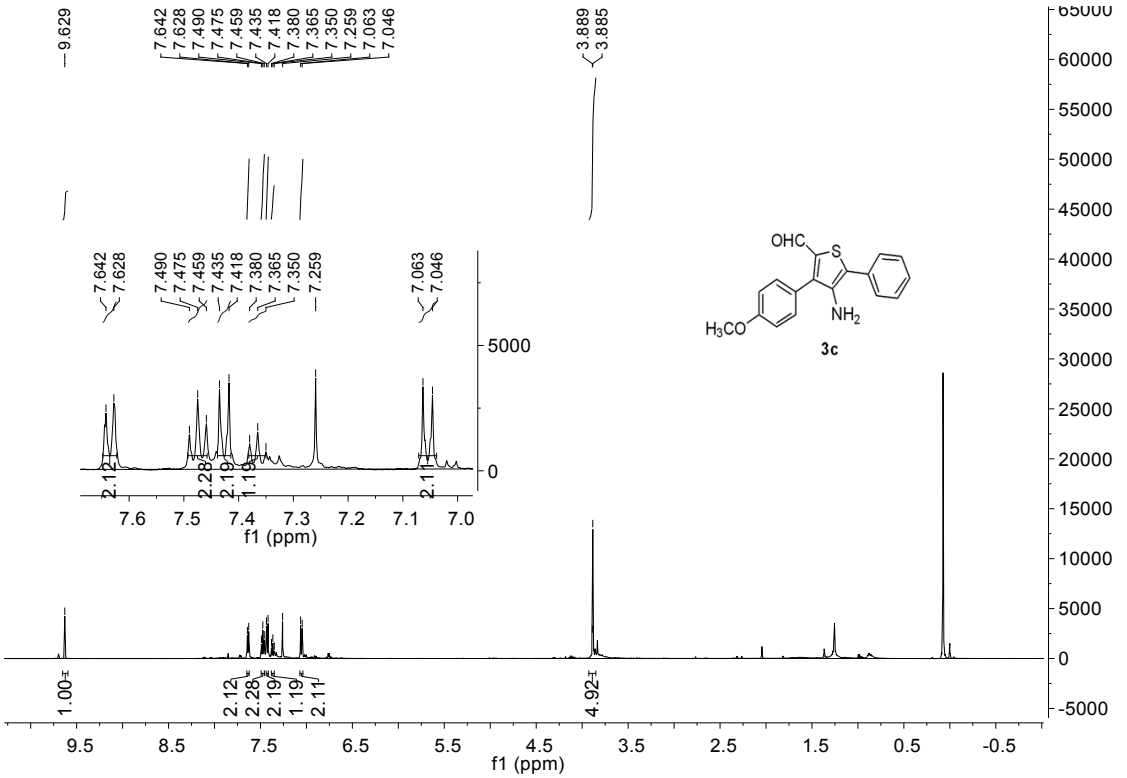
O2N
3b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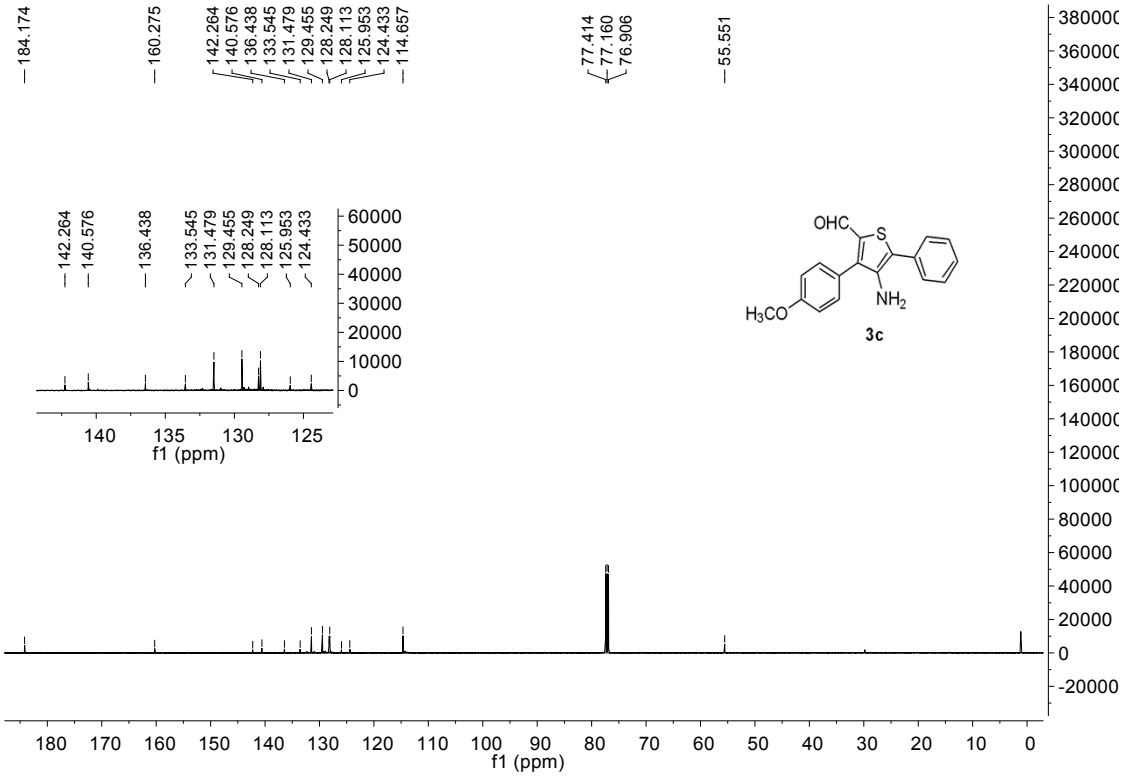
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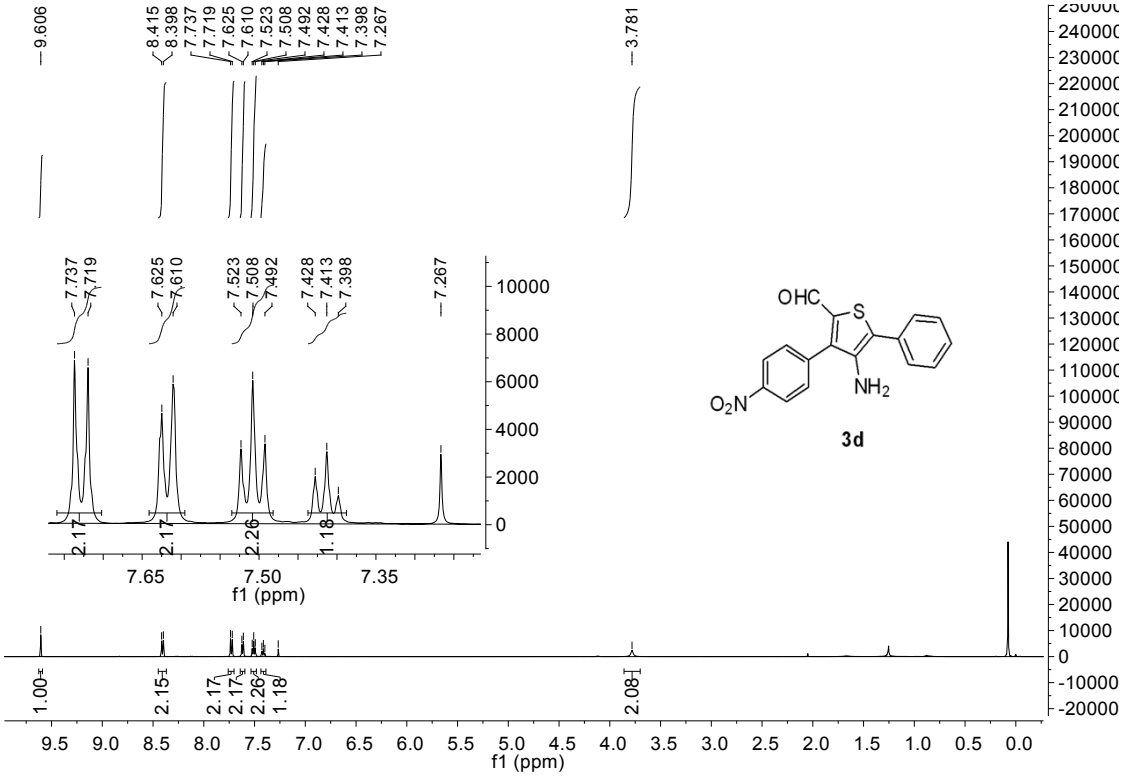
f1 (ppm)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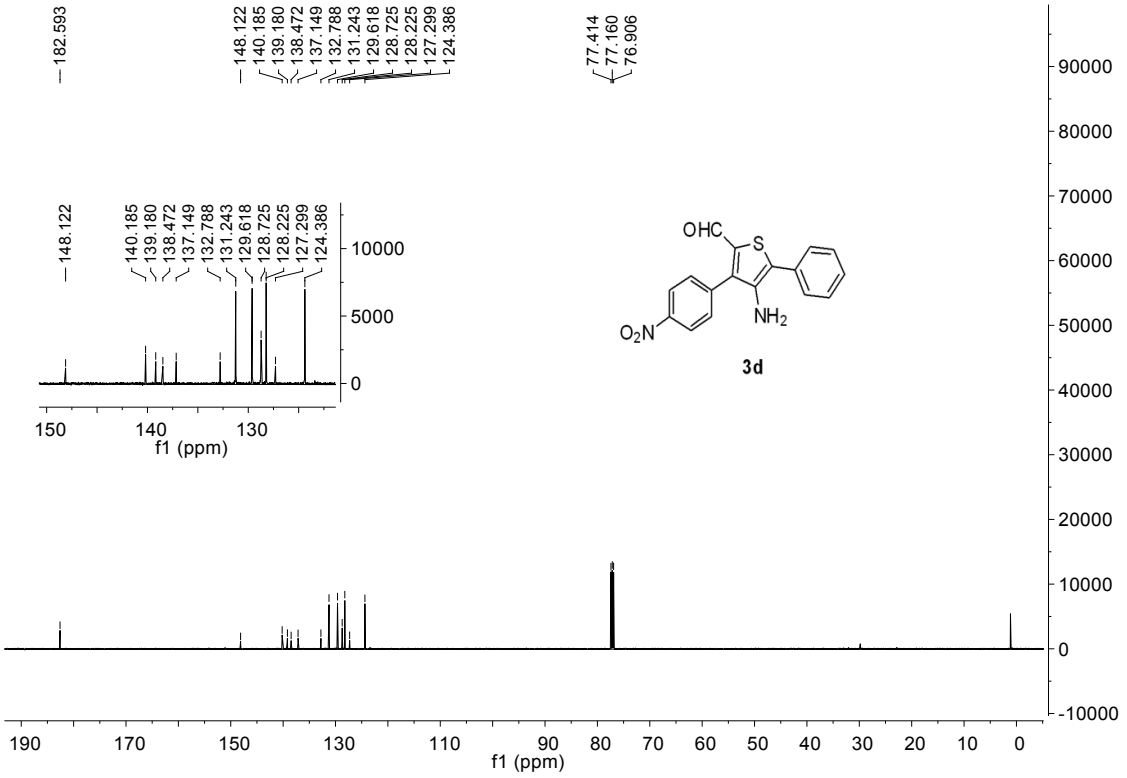
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O2N
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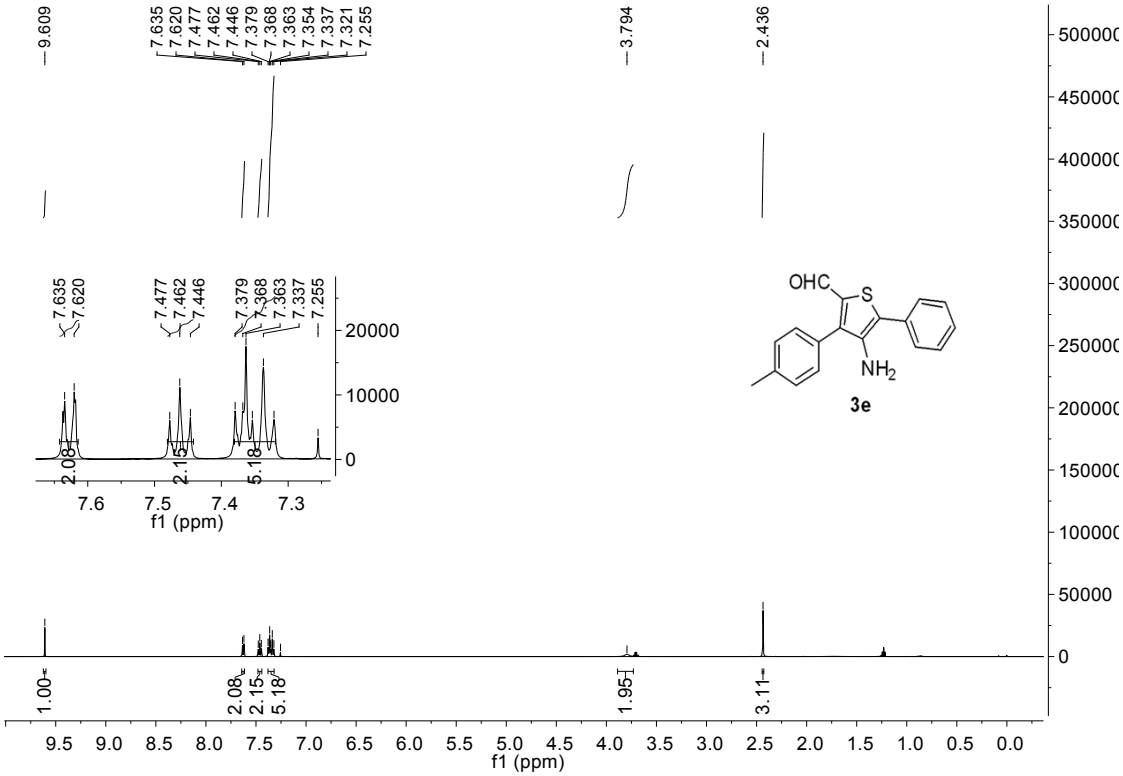
f1 (ppm)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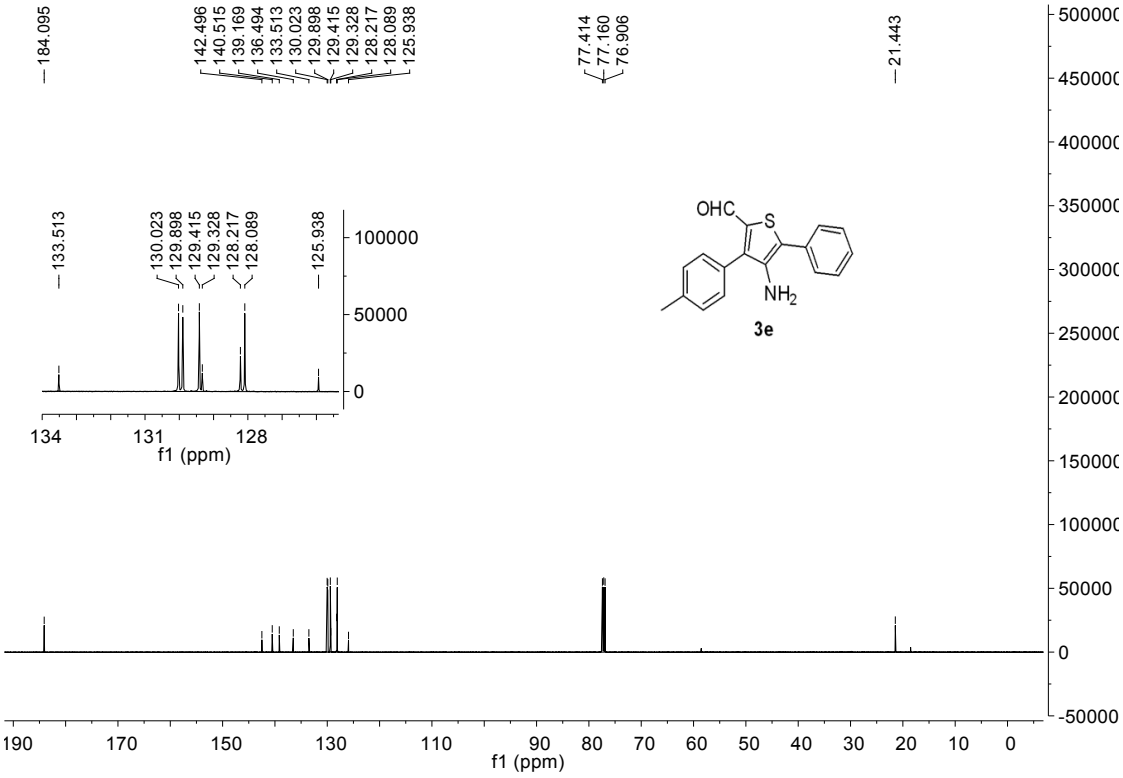
f1 (ppm)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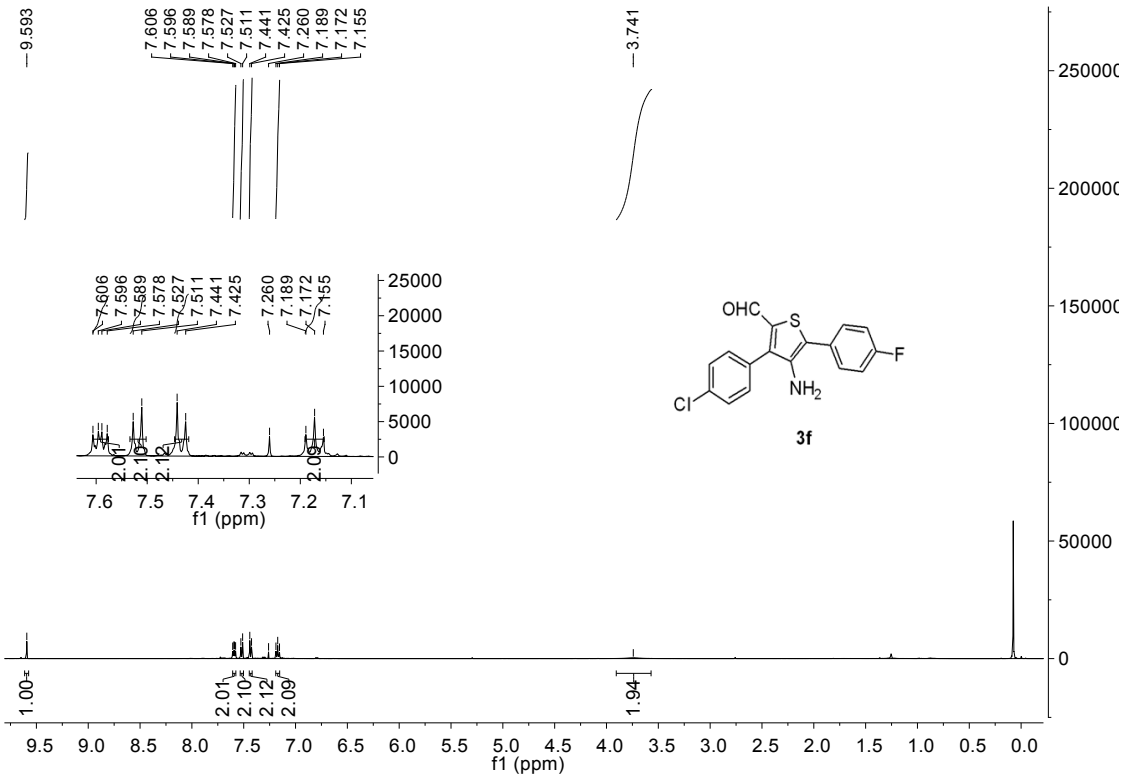
NH2
3e
f1 (ppm)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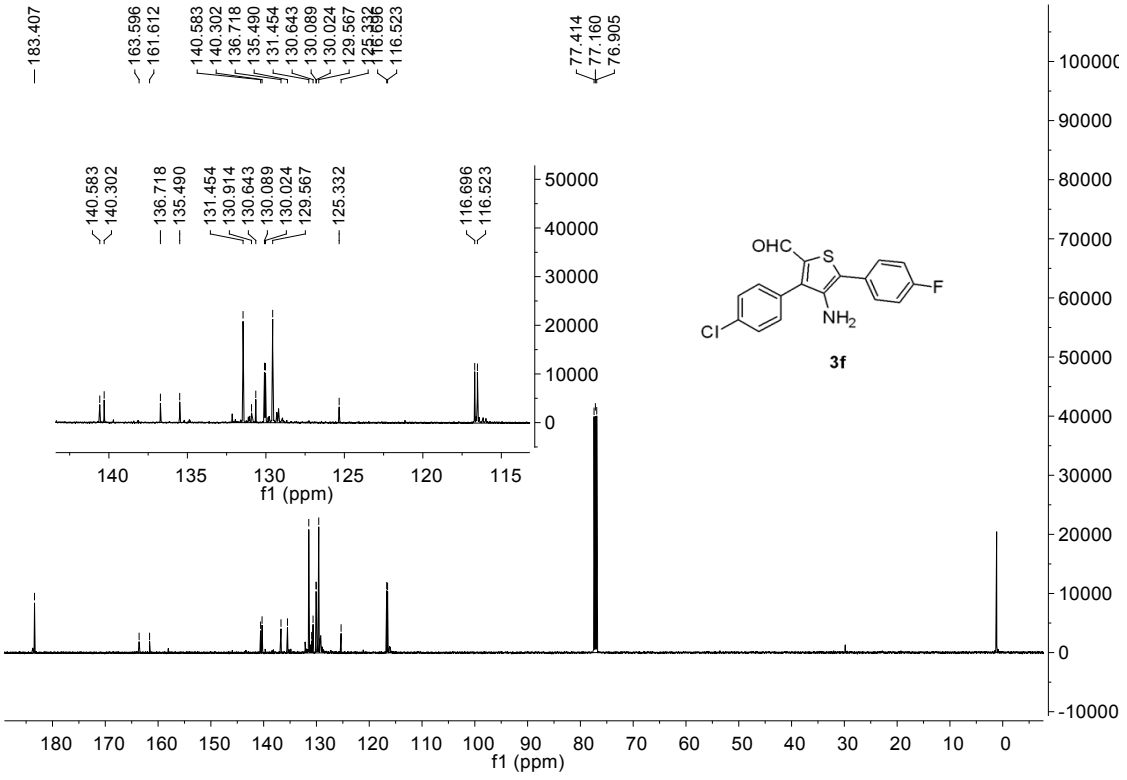
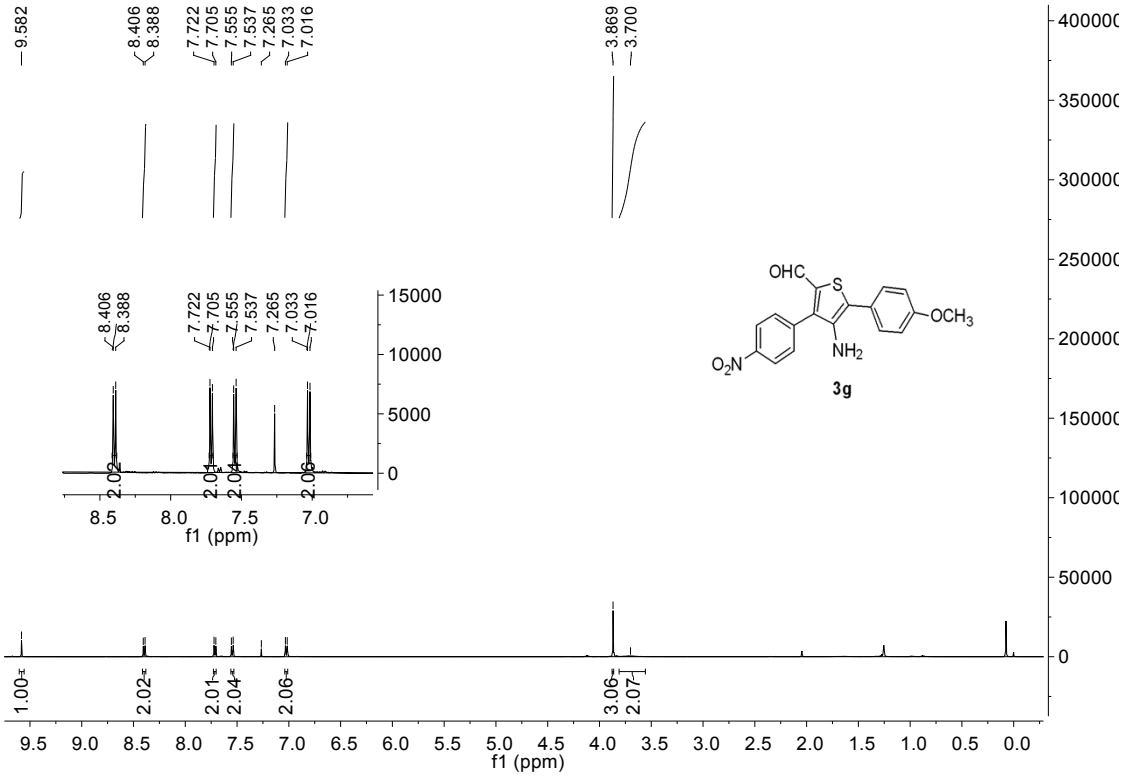
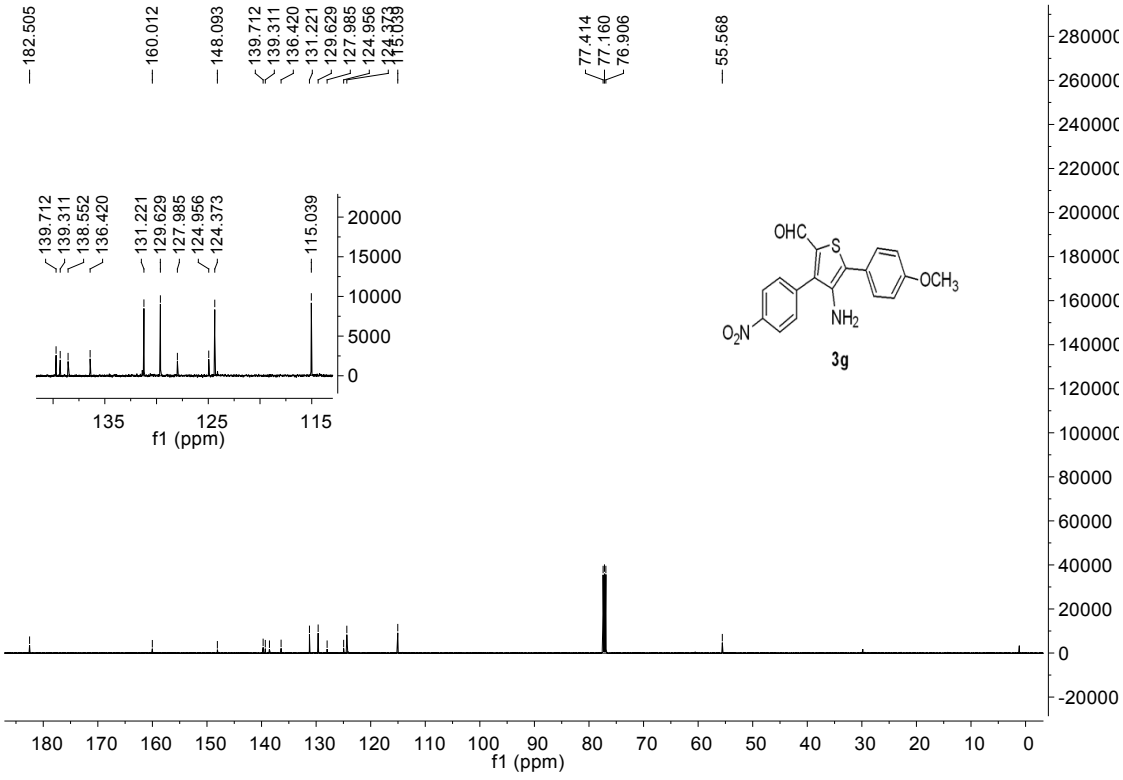
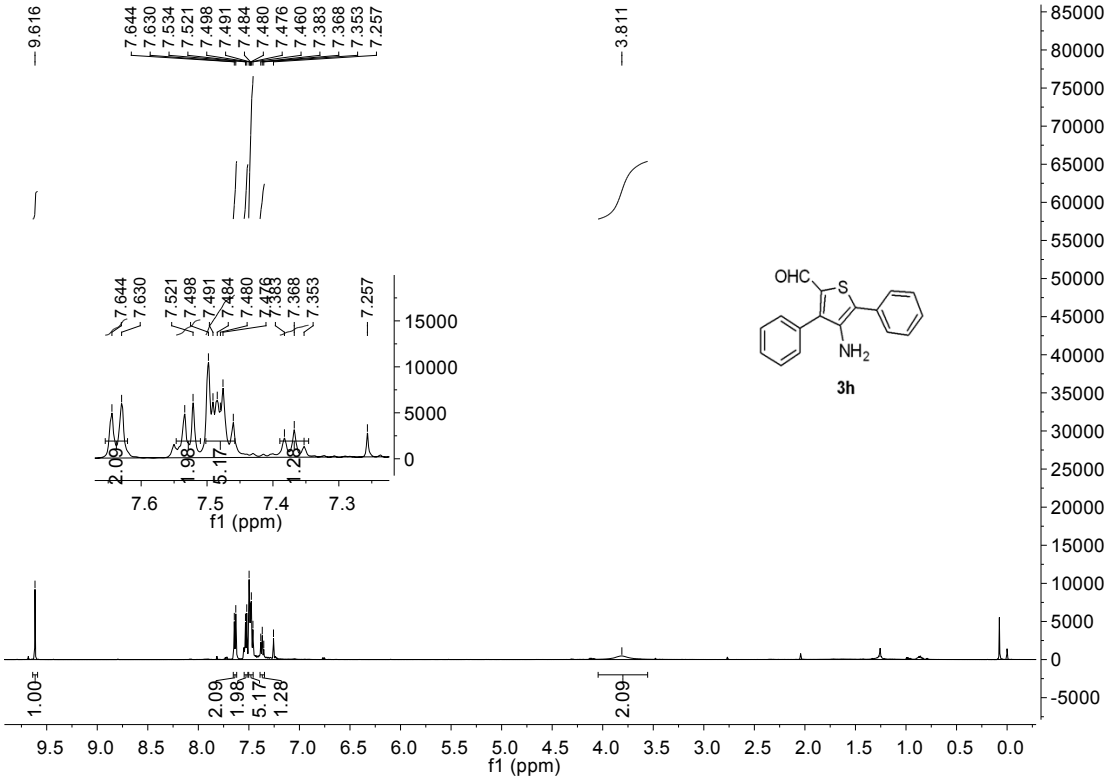
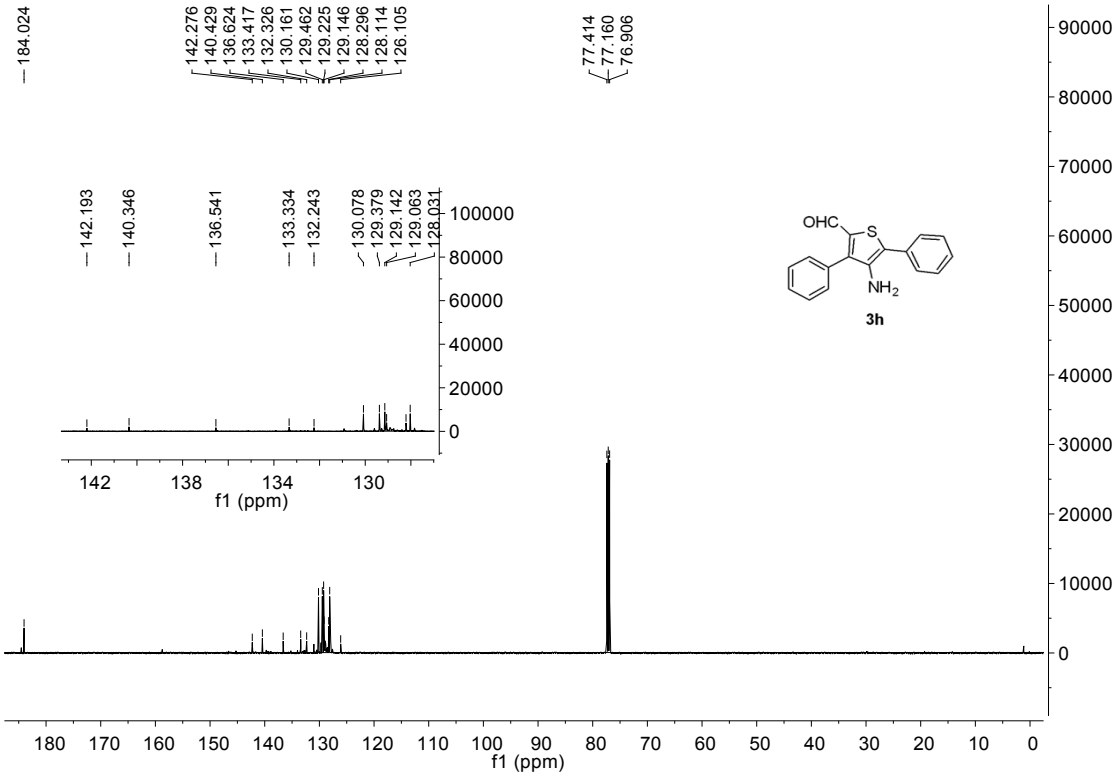
7.155
3.741
OHC
S
F
Cl
NH2
3f
1.00
2.01
2.10
2.12
2.09
1.94
f1 (ppm)

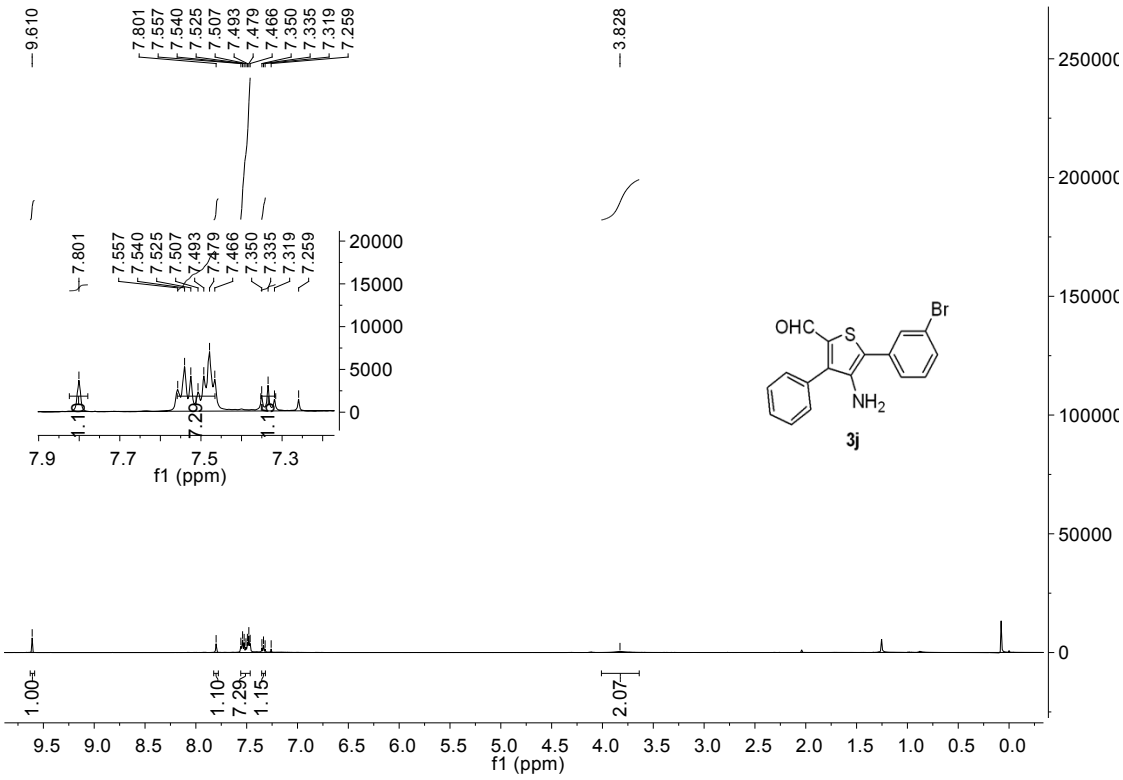

183.407
163.596
161.612
140.583
140.302
136.718
135.490
131.454
130.914
130.643
130.089
130.024
129.567
125.332
116.696
116.523
77.414
77.160
76.905
OHC
S
F
Cl
NH2
3f
f1 (ppm)

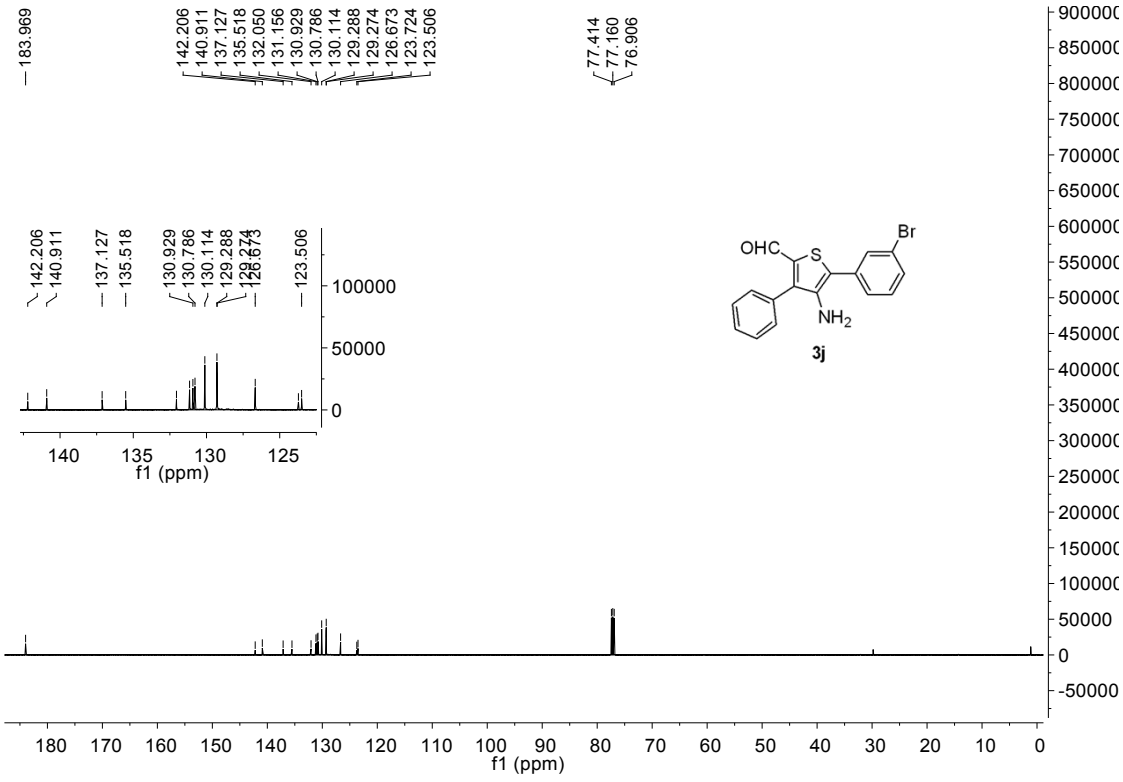

9.582
8.406
8.388
7.722
7.705
7.555
7.537
7.265
7.033
7.016
3.869
3.700
1.00
2.02
2.01
2.04
2.06
3.06
2.07
f1 (ppm)
OHC
S
OCH3
NH2
O2N
3g

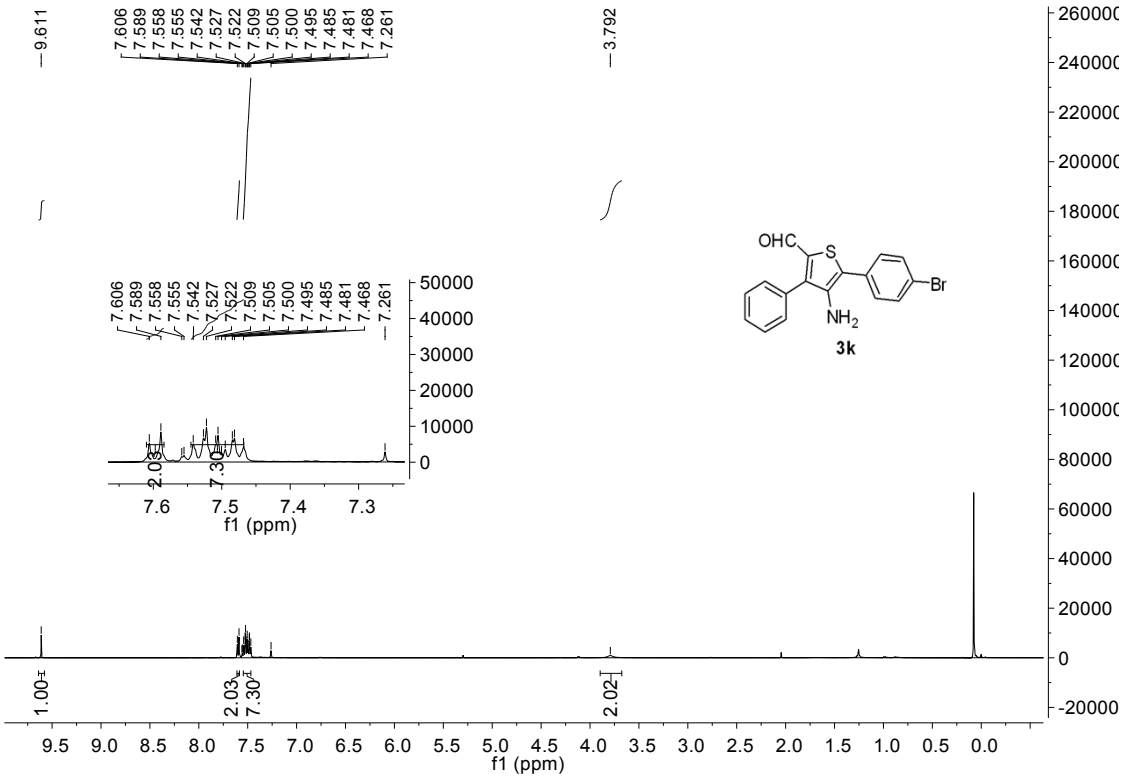

182.505
160.012
148.093
139.712
139.311
136.420
131.221
129.629
127.985
124.956
124.373
115.039
77.414
77.160
76.906
55.568
f1 (ppm)
OHC
S
OCH3
NH2
O2N
3g

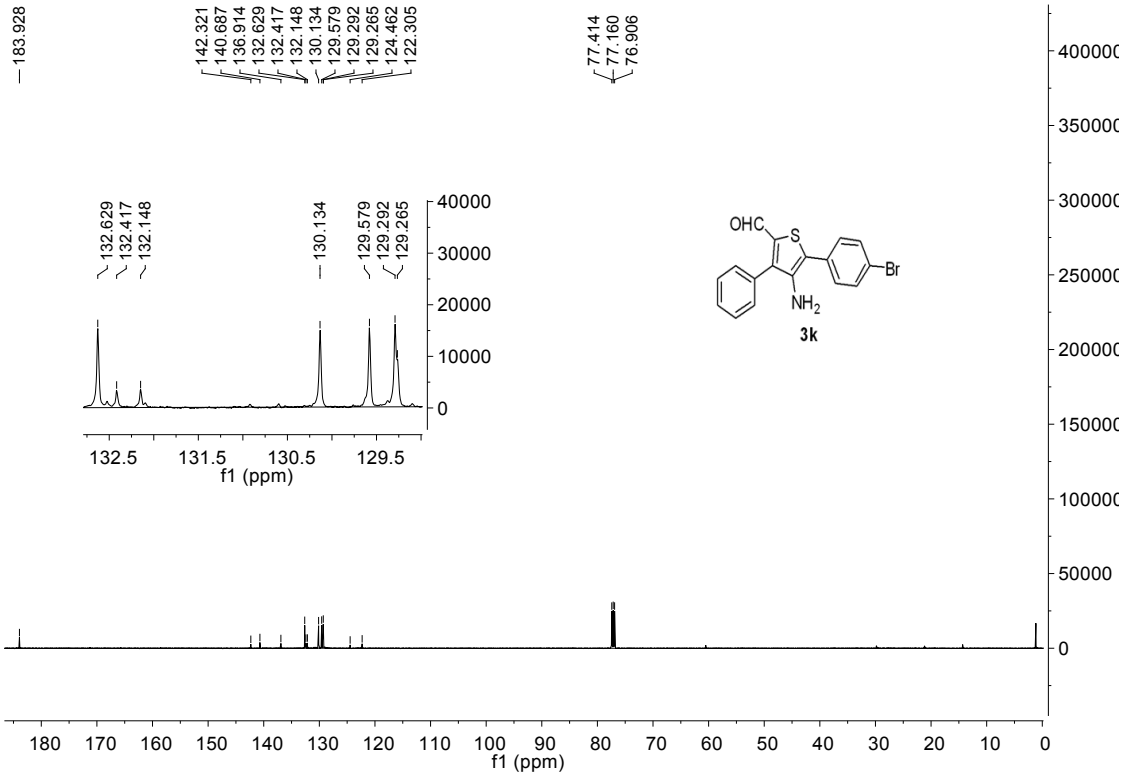

9.616
7.644
7.630
7.534
7.521
7.498
7.491
7.484
7.480
7.476
7.460
7.383
7.368
7.353
7.257
3.811
OHC
S
NH2
3h
1.00
2.09
1.98
5.17
1.28
2.09
f1 (ppm)

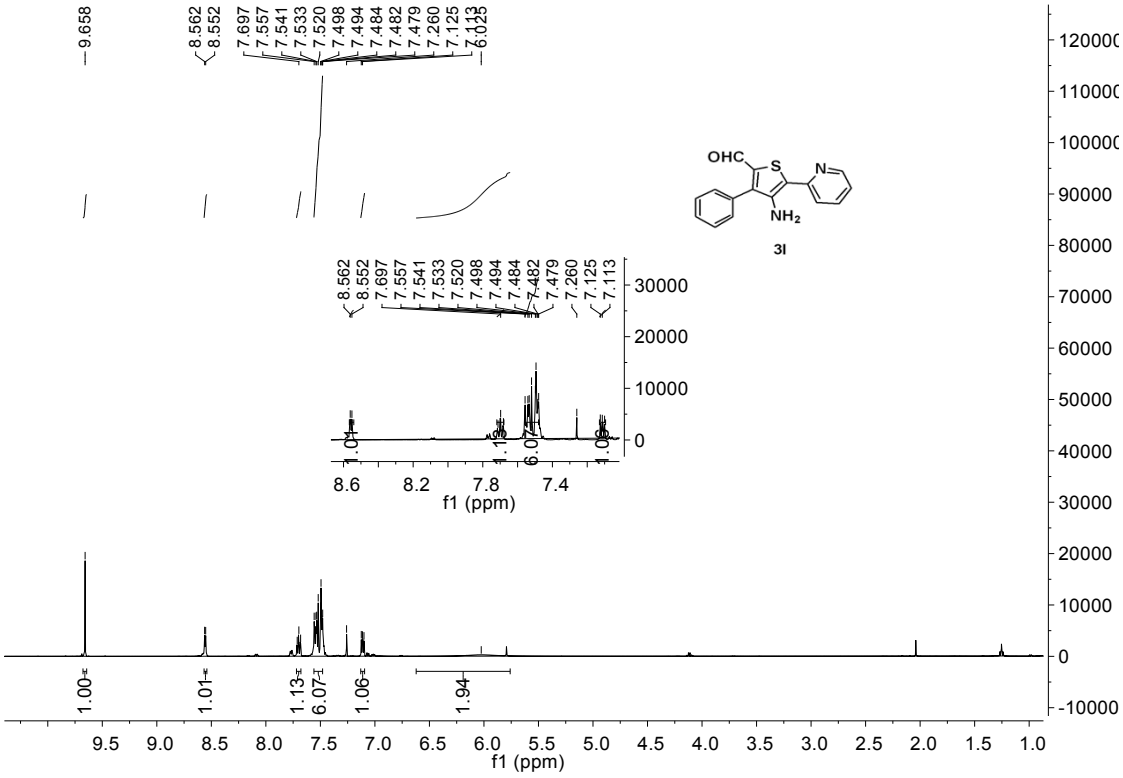

184.024
142.276
140.429
136.624
133.417
132.326
130.161
129.462
129.225
129.146
128.296
128.114
126.105
77.414
77.160
76.906
142.193
140.346
136.541
133.334
132.243
130.078
129.379
129.142
129.063
128.031
OHC
S
NH2
3h
f1 (ppm)

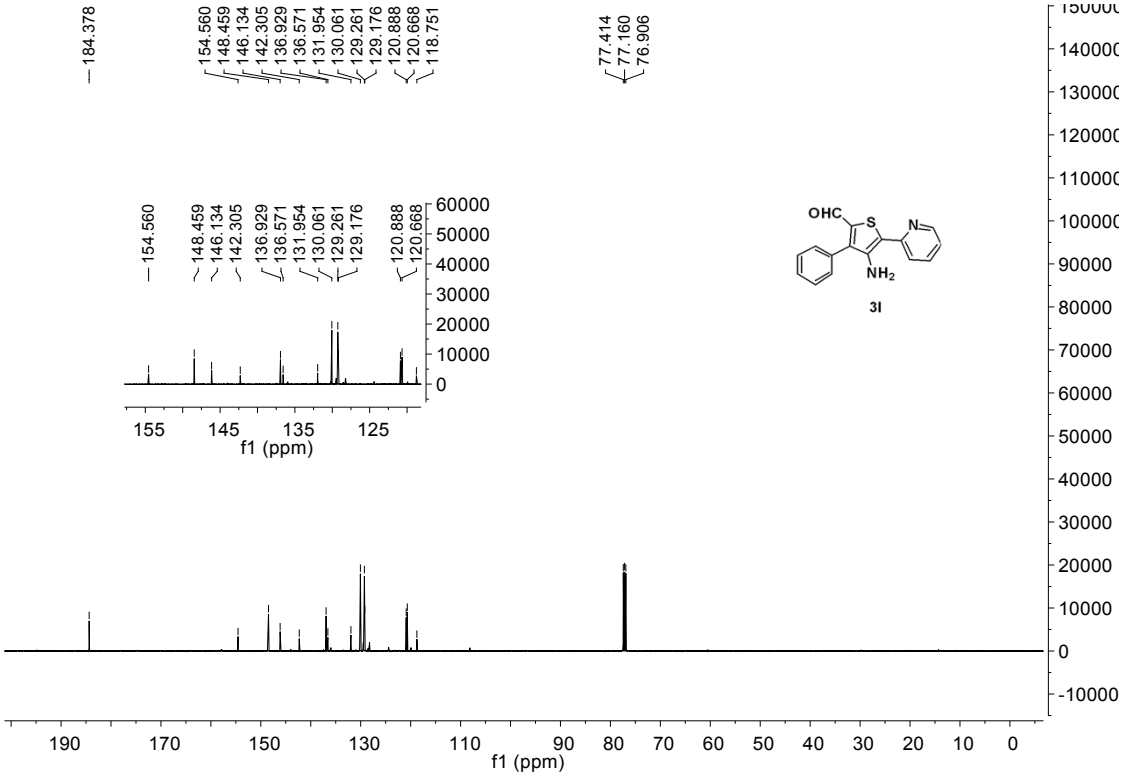

9.610
7.801
7.557
7.540
7.525
7.507
7.493
7.479
7.466
7.350
7.335
7.319
7.259
3.828
OHC
S
Br
NH2
3j
1.00
1.10
7.29
1.15
2.07
f1 (ppm)

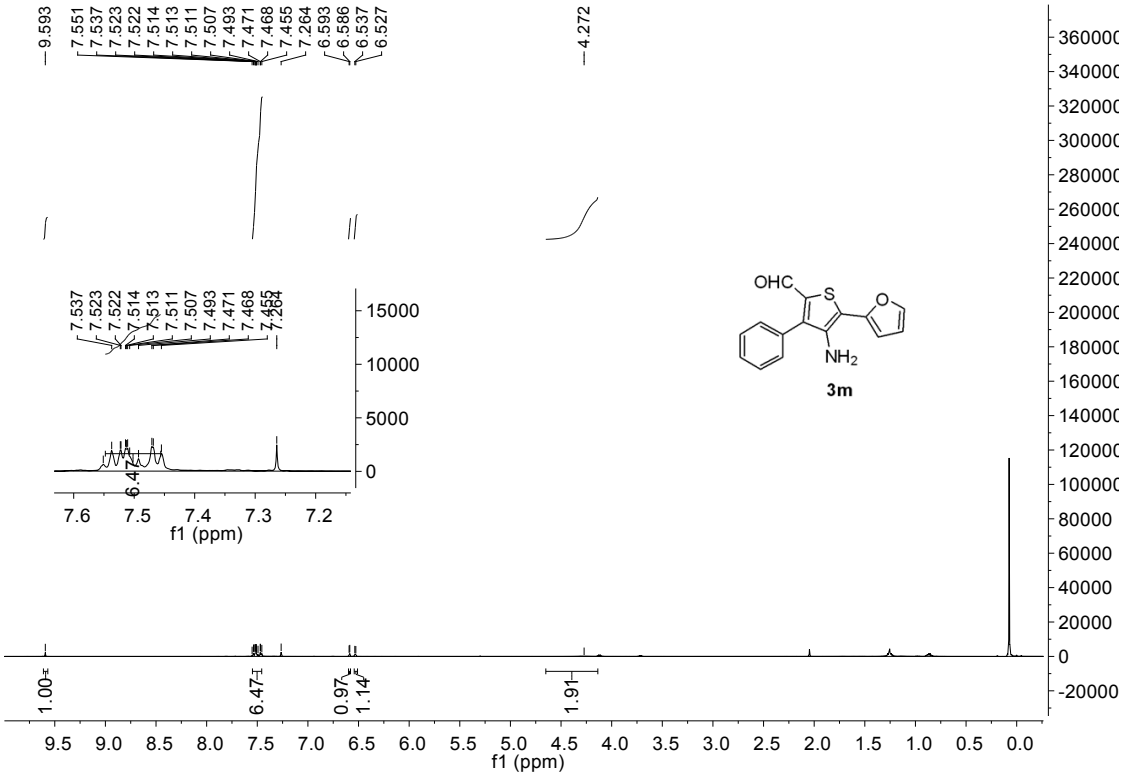

183.969
142.206
140.911
137.127
135.518
132.050
131.156
130.929
130.786
130.114
129.288
129.274
126.673
123.724
123.506
77.414
77.160
76.906
OHC
S
Br
NH2
3j
f1 (ppm)

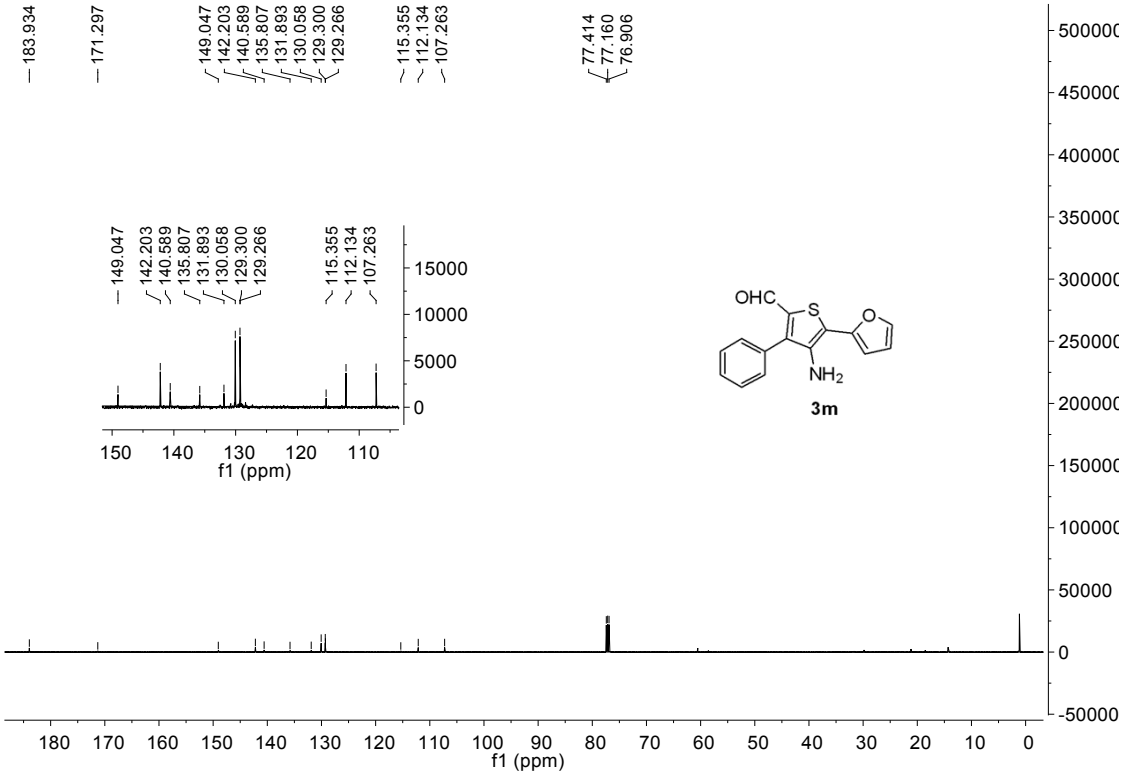

9.611
7.606
7.589
7.558
7.555
7.542
7.527
7.522
7.509
7.505
7.500
7.495
7.485
7.481
7.468
7.261
3.792
OHC
S
Br
NH2
3k
1.00
2.03
7.30
2.02
f1 (ppm)


183.928
142.321
140.687
136.914
132.629
132.417
132.148
130.134
129.579
129.292
129.265
124.462
122.305
77.414
77.160
76.906
OHC
S
Br
NH2
3k
f1 (ppm)

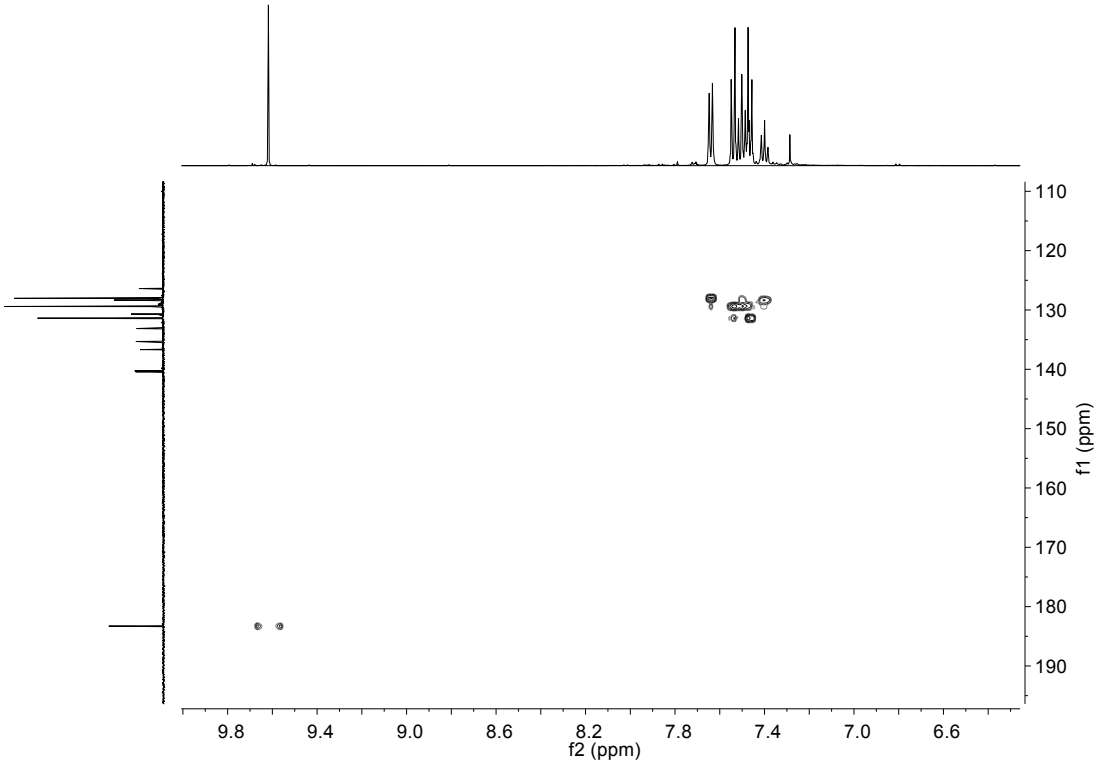

9.658
8.562
8.552
7.697
7.557
7.541
7.533
7.520
7.498
7.494
7.484
7.482
7.479
7.260
7.125
7.113
OHC
S
N
NH2
3l
1.00
1.01
1.13
6.07
1.06
1.94
f1 (ppm)


184.378
154.560
148.459
146.134
142.305
136.929
136.571
131.954
130.061
129.261
129.176
120.888
120.668
118.751
77.414
77.160
76.906
OHC
S
N
NH2
3l
f1 (ppm)


9.593
7.551
7.537
7.523
7.522
7.514
7.513
7.511
7.507
7.493
7.471
7.468
7.455
7.264
6.593
6.586
6.537
6.527
4.272
OHC
S
O
NH2
3m
1.00
6.47
0.97
1.14
1.91
f1 (ppm)


183.934
171.297
149.047
142.203
140.589
135.807
131.893
130.058
129.300
129.266
115.355
112.134
107.263
77.414
77.160
76.906
OHC
S
O
NH2
3m
f1 (ppm)

5. HSQC of 3a:



6. Reference

1 (a) Gilchrist, T. L.; Mendonca, R. *ARKIVOC*. **2000**, 769; (b) Liu, L.; Liebeskind, S. *J. Am. Chem. Soc.* **2008**, *130*, 6918; (c) Khazaei, M. A. *Synthesis.* **2009**, *21*, 3672; (d) Kowalski, C. J.; Weber, A. E.; Fields, K. W. *J. Org. Chem*., **1982**, *47*, 5088; (e) Chiba, S.; Wang, Y. F.; Lapointe, G.; Narasaka, K. *Org. Lett.* **2008**, *10*, 313.