Supplementary Materials: Atom-Economic Synthesis of 4-Pyrones from Diynones and Water

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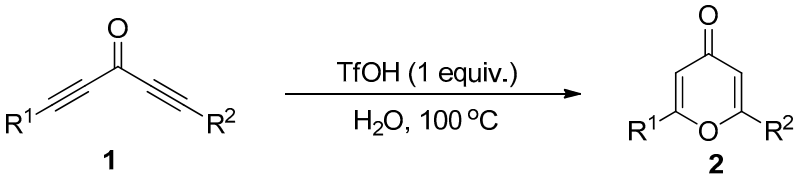
1. General Information

All manipulations were performed under an air atmosphere unless otherwise statement. Column chromatography was performed on silica gel (300–400 mesh). NMR spectra were obtained using a Bruker Avance 500 spectrometer (^{1}H at 500 MHz and ^{13}C at 125 MHz) or NMR spectra were obtained using a Bruker Avance 400 spectrometer (^{1}H at 400 MHz and ^{13}C at 100 MHz). IR spectra were recorded on a FT-IR spectrometer and only major peaks are reported in cm^{-1}. High resolution mass spectra (HRMS) were recorded on the Exactive Mass Spectrometer (Thermo Scientific, USA) equipped with ESI or APCI ionization source.

Materials. Unless stated otherwise, commercial reagents were used without further purification. All reagents were weighed and handled in air at room temperature. **1a–1r** were prepared by the reported methods [1,2].

2. Synthesis of 2



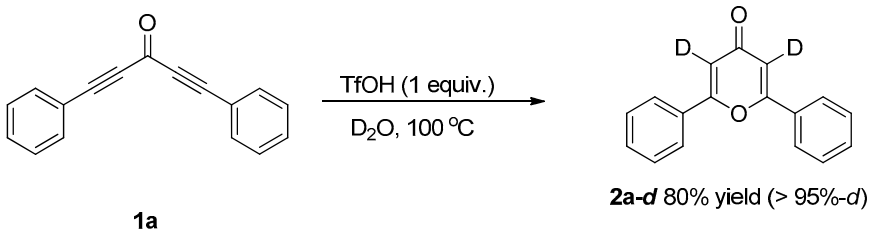
Scheme 1.

The reaction mixture of **1** (0.5 mmol), TfOH (1 equiv.) and H_2O (1 mL) in a 15 mL test tube was stirred at 100 °C for 36 h, and monitored periodically by TLC. Upon completion, the reaction mixture was diluted with water (5 mL) and extracted with ethyl acetate (3 × 5 mL). The combined organic layers were washed with water and brine, dried over $MgSO_4$ and filtered. The solvent was removed under vacuum. The residue was purified by flash column chromatography (petroleum ether and ethyl acetate, *v*/*v* = 5:1 to 2:1) to afford 4-Pyrones **2**.

3. Control Experiments

3.1. Deuterium Labeling Experiment

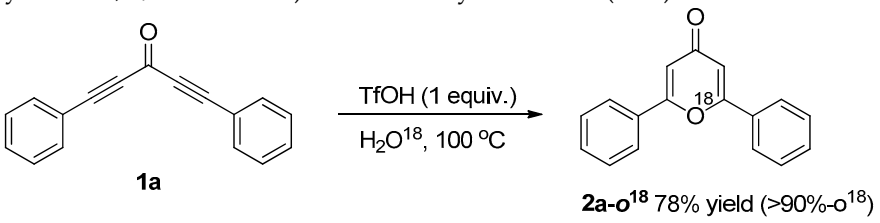
The reaction mixture of **1** (0.5 mmol), TfOH (1 equiv.), and D_2O (1 mL) in a 15 mL test tube was stirred at 100 °C for 36 h, and monitored periodically by TLC. Upon completion, the reaction mixture was diluted with water (5 mL) and extracted with ethyl acetate (3 × 5 mL). The combined organic layers were washed with water and brine, dried over $MgSO_4$ and filtered. The solvent was removed under vacuum. The residue was purified by flash column chromatography (petroleum ether and ethyl acetate, *v*/*v* = 5:1 to 2:1) to afford 4-Pyrone **2a-*d*** (80%).



Scheme 2.

3.2. O^{18}-Labeled Experiment

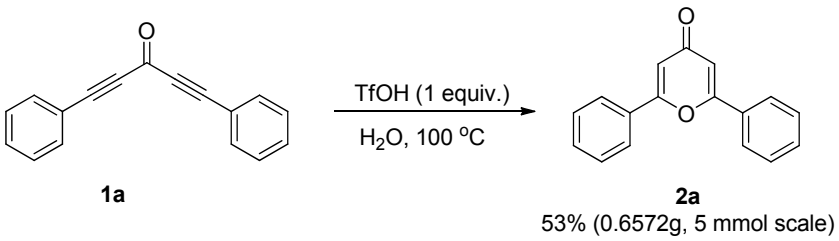
The reaction mixture of **1a** (0.5 mmol), TfOH (1 equiv.), and H_2O^{18} (1 mL) in a 15 mL test tube was stirred at 100 °C for 36 h, and monitored periodically by TLC. Upon completion, the reaction mixture was diluted with water (5 mL) and extracted with ethyl acetate (3 × 5 mL). The combined organic layers were washed with water and brine, dried over $MgSO_4$ and filtered. The solvent was removed under vacuum. The residue was purified by flash column chromatography (petroleum ether and ethyl acetate, *v*/*v* = 5:1 to 2:1) to afford 4-Pyrone **2a-*o*^{18}** (78%).



Scheme 3.

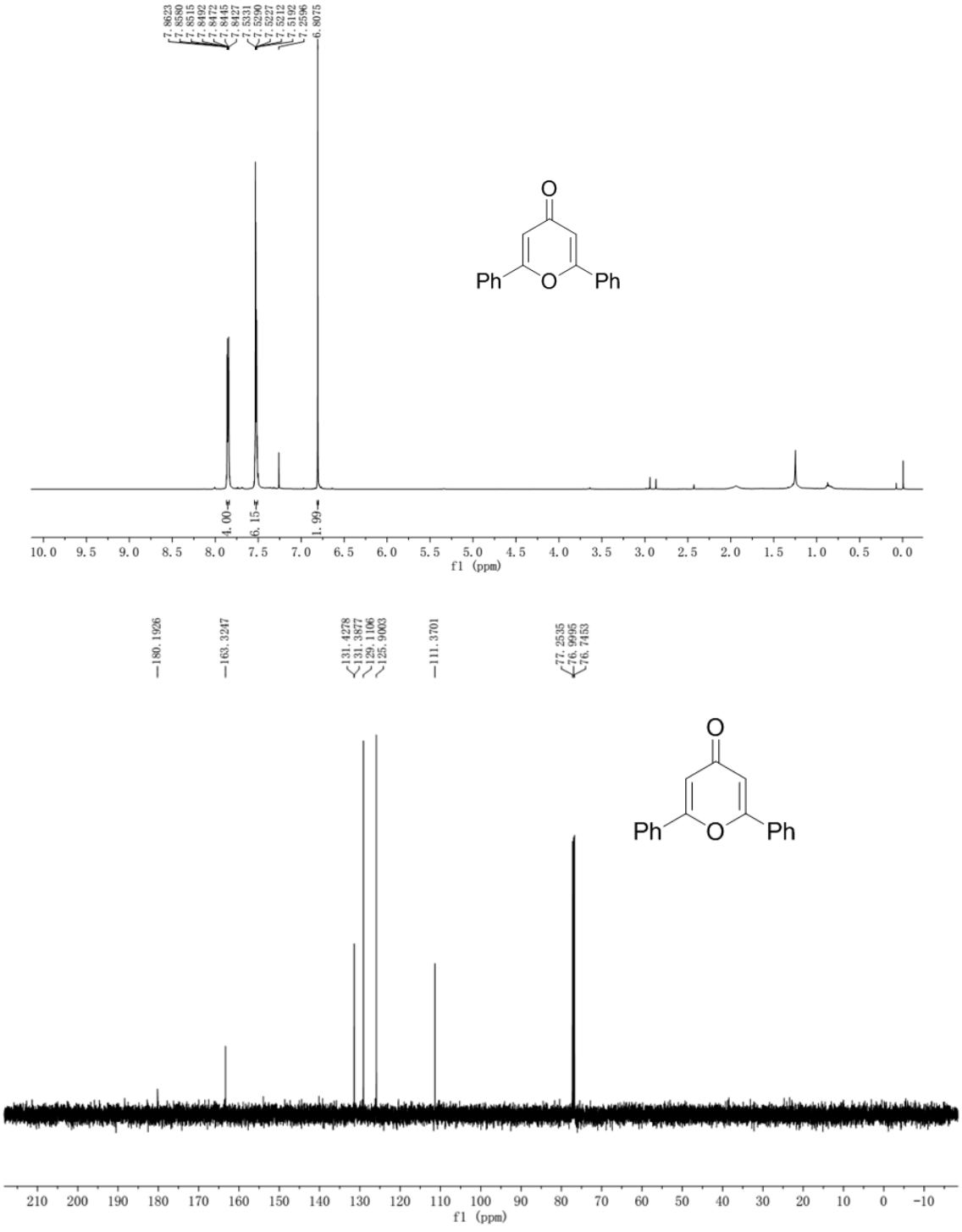
3.3. Gram-Scale Synthesis

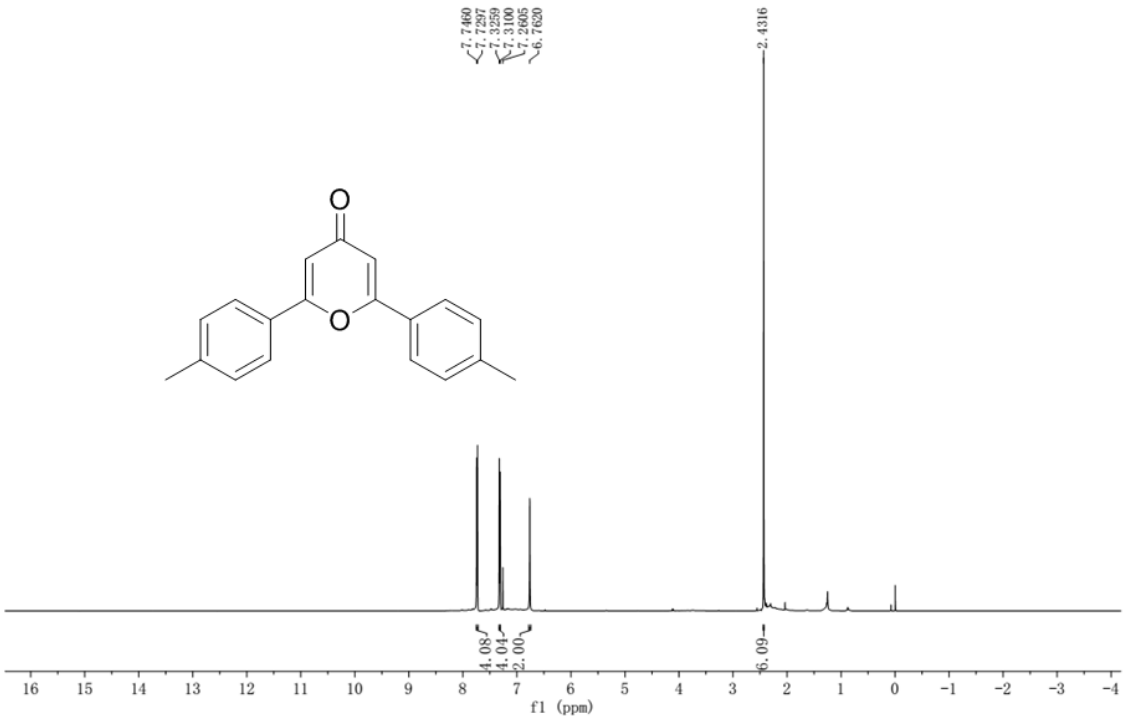
The reaction mixture of **1a** (5 mmol), TfOH (1 equiv.) and H_2O (10 mL) in a 50 mL round-bottom flask was stirred at 100 °C for 36 h, and monitored periodically by TLC. Upon completion, the reaction mixture was diluted with water (30 mL) and extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with water and brine, dried over $MgSO_4$ and filtered. The solvent was removed under vacuum. The residue was purified by flash column chromatography (petroleum ether and ethyl acetate, *v*/*v* = 5:1 to 2:1) to afford 4-Pyrones **2a** (53%).



Scheme 4.

4. Copies of ^{1}H NMR and ^{13}C NMR Spectra of Products

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7.2605
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O
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4.04
2.00
6.09
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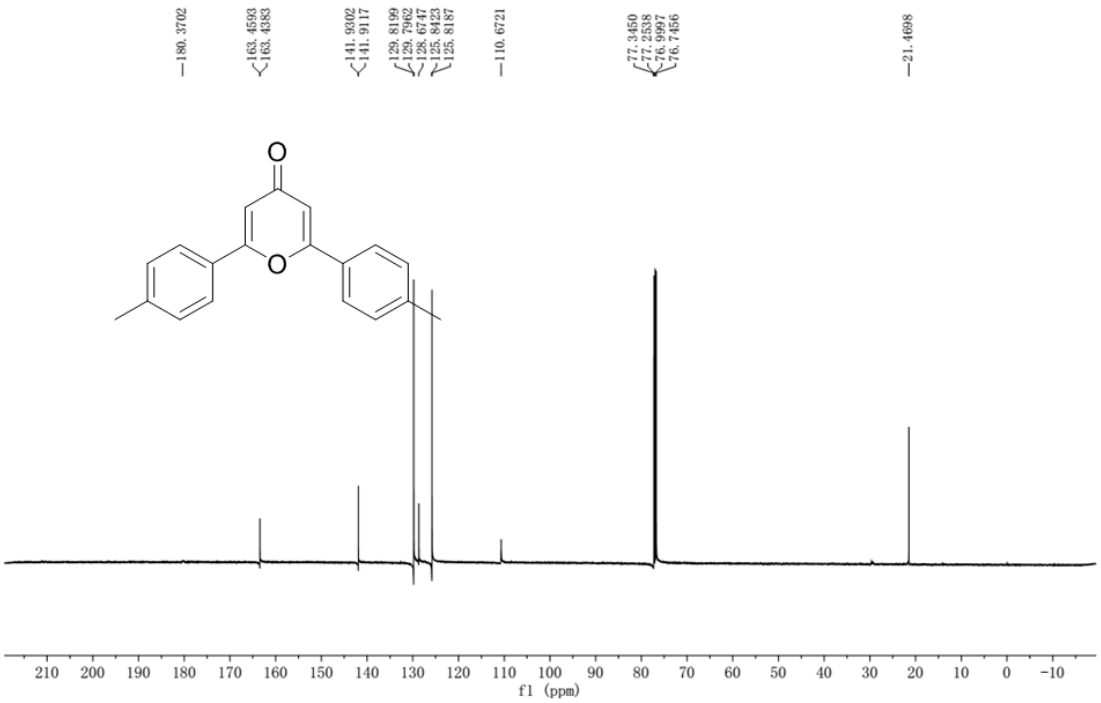
f1 (ppm)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110.6721
77.3450
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O
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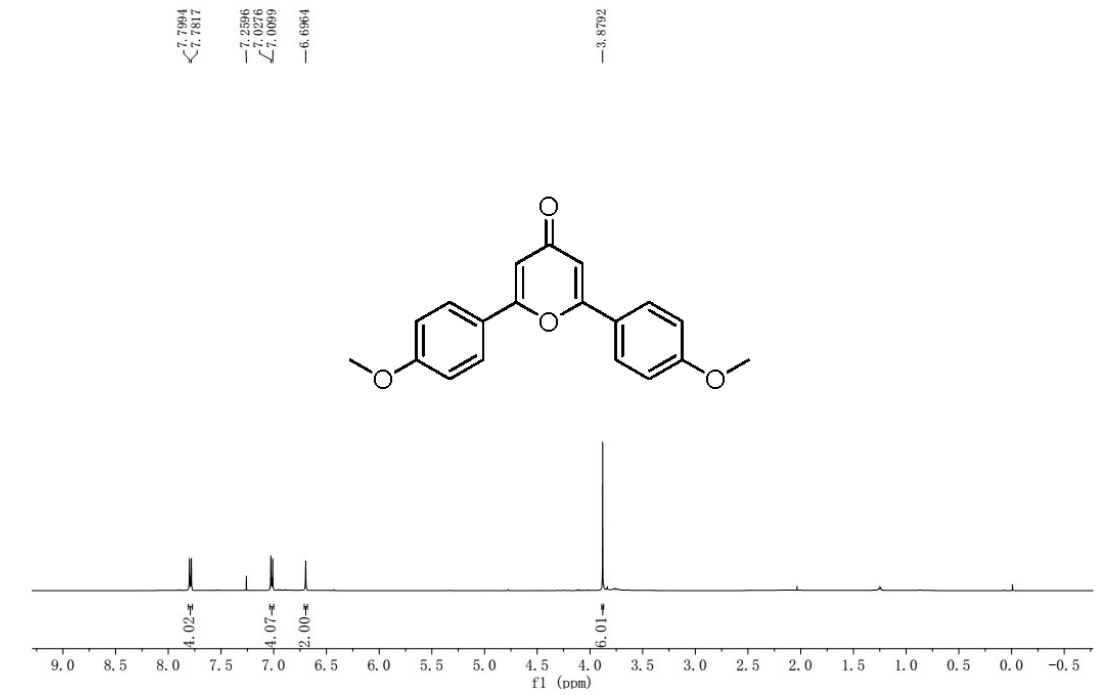
f1 (ppm)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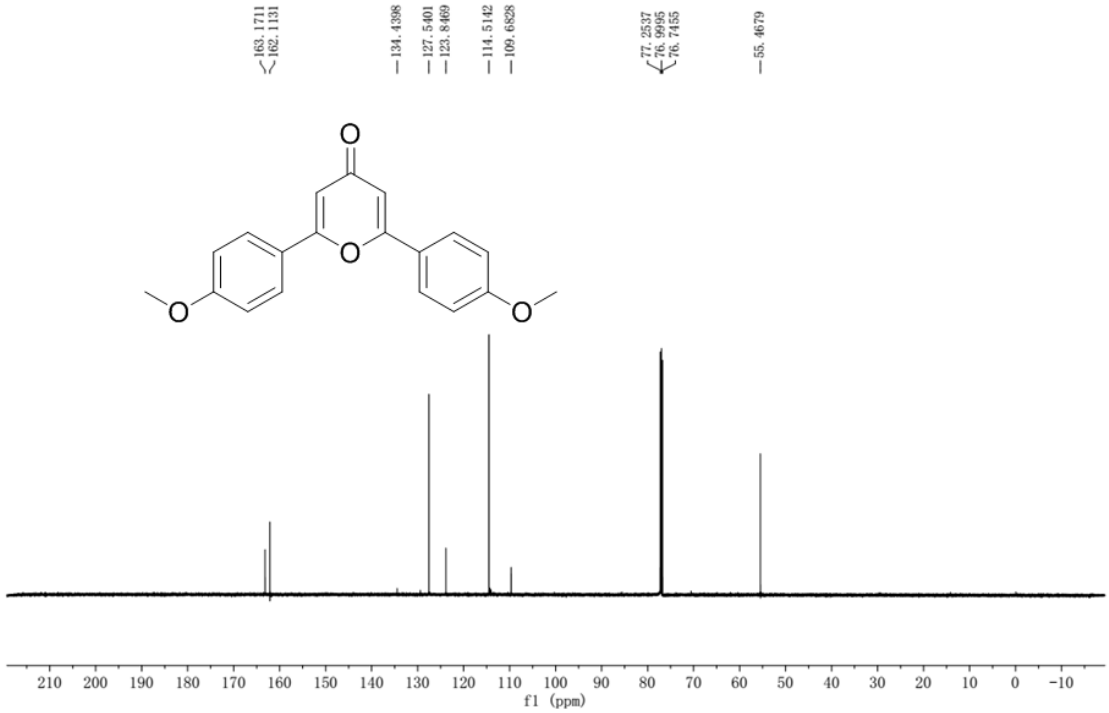
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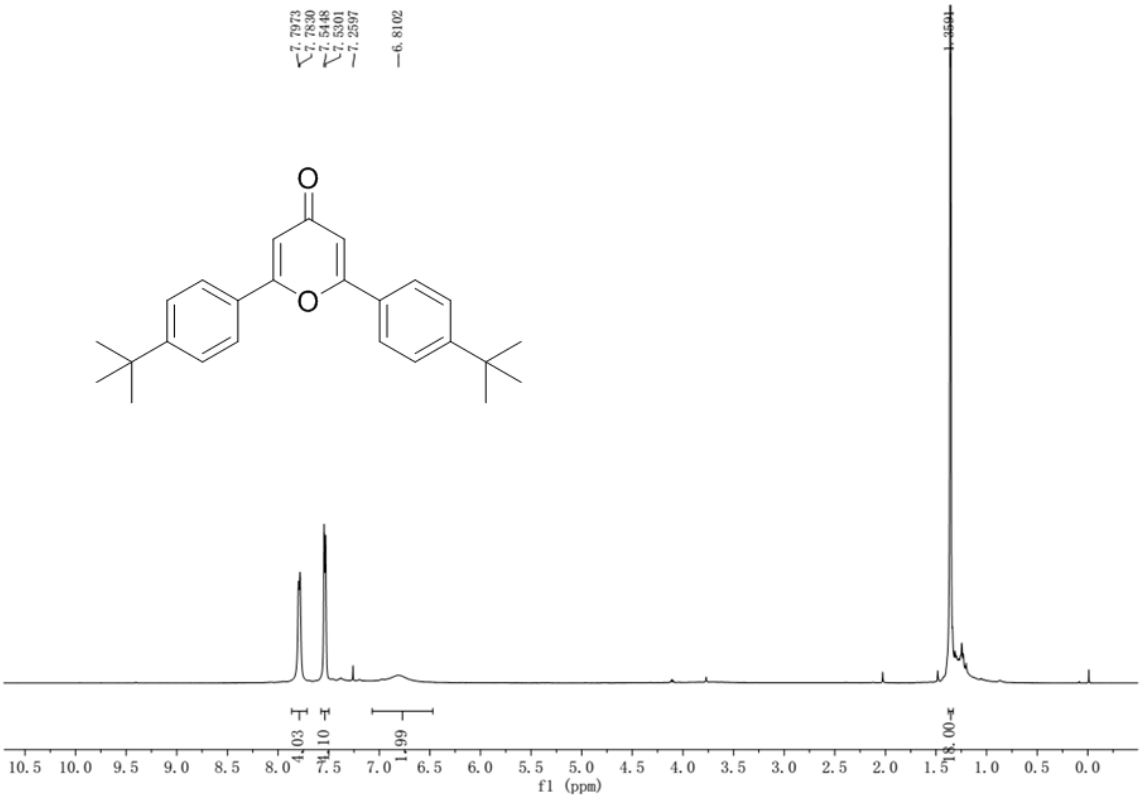
f1 (ppm)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4.10
1.99
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f1 (ppm)


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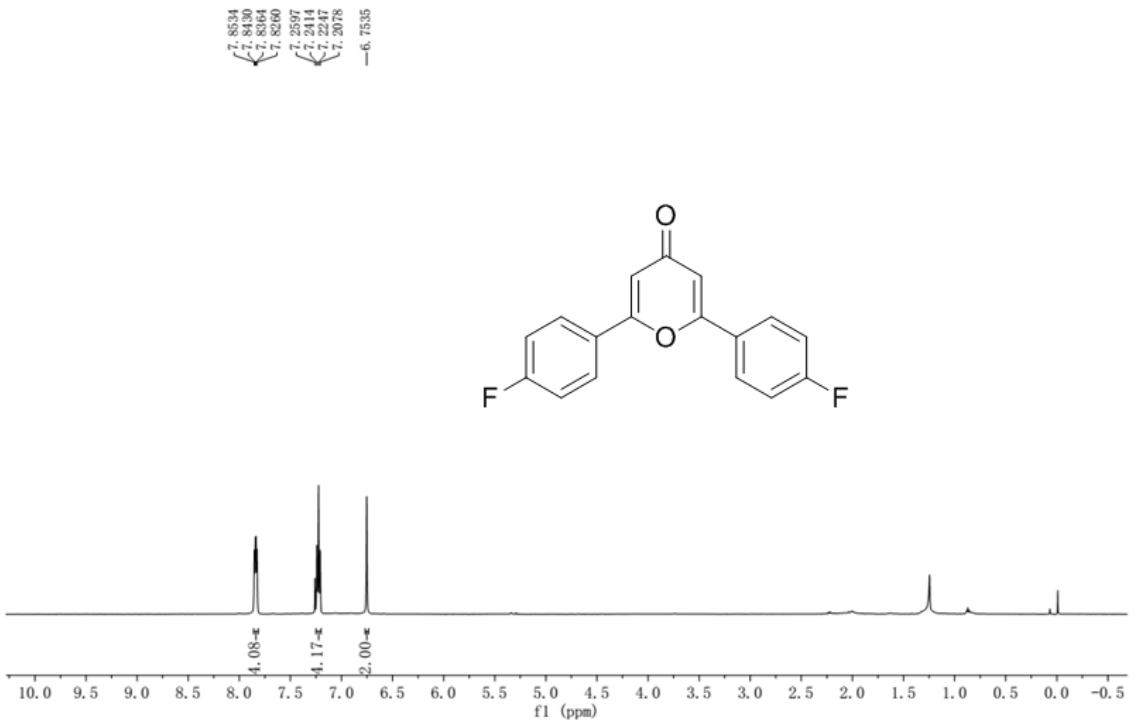
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4.17
2.00
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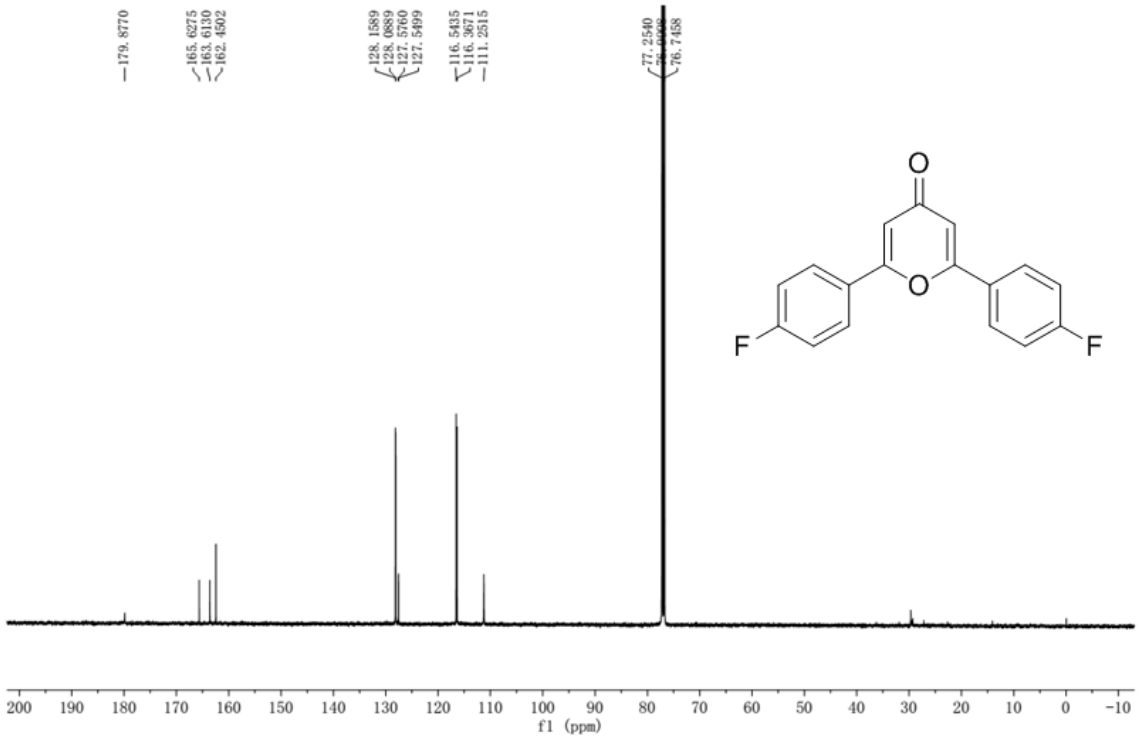
f1 (ppm)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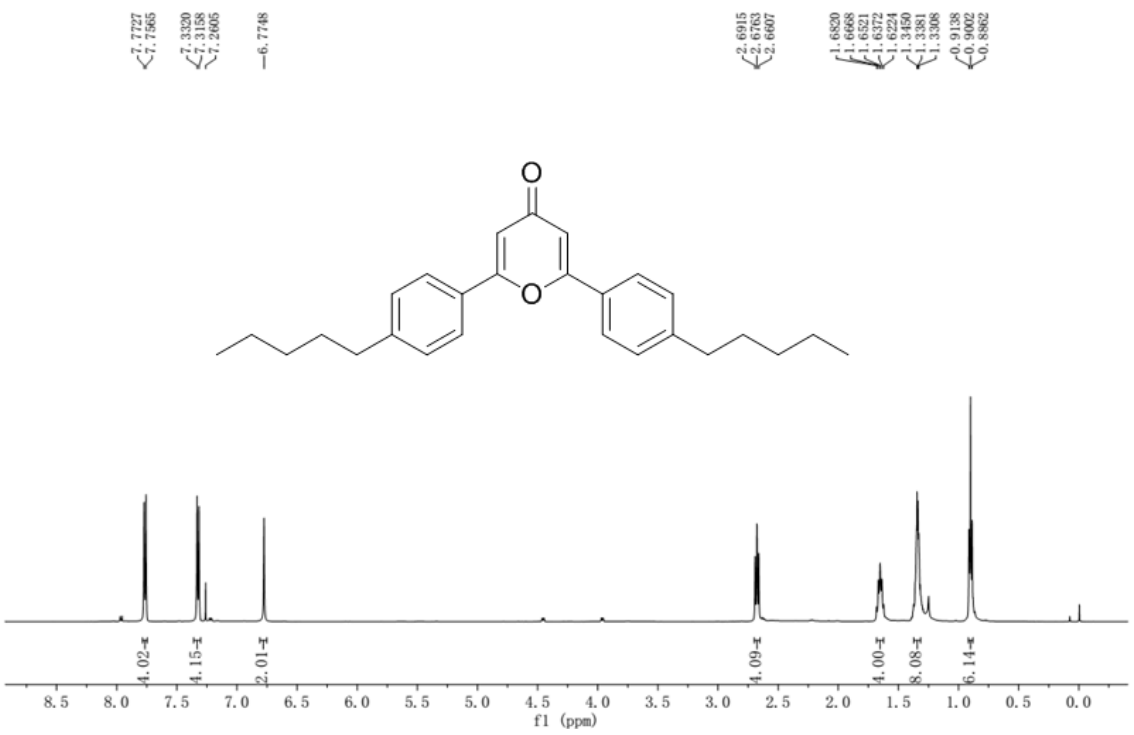
f1 (ppm)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1.6521
1.6372
1.6224
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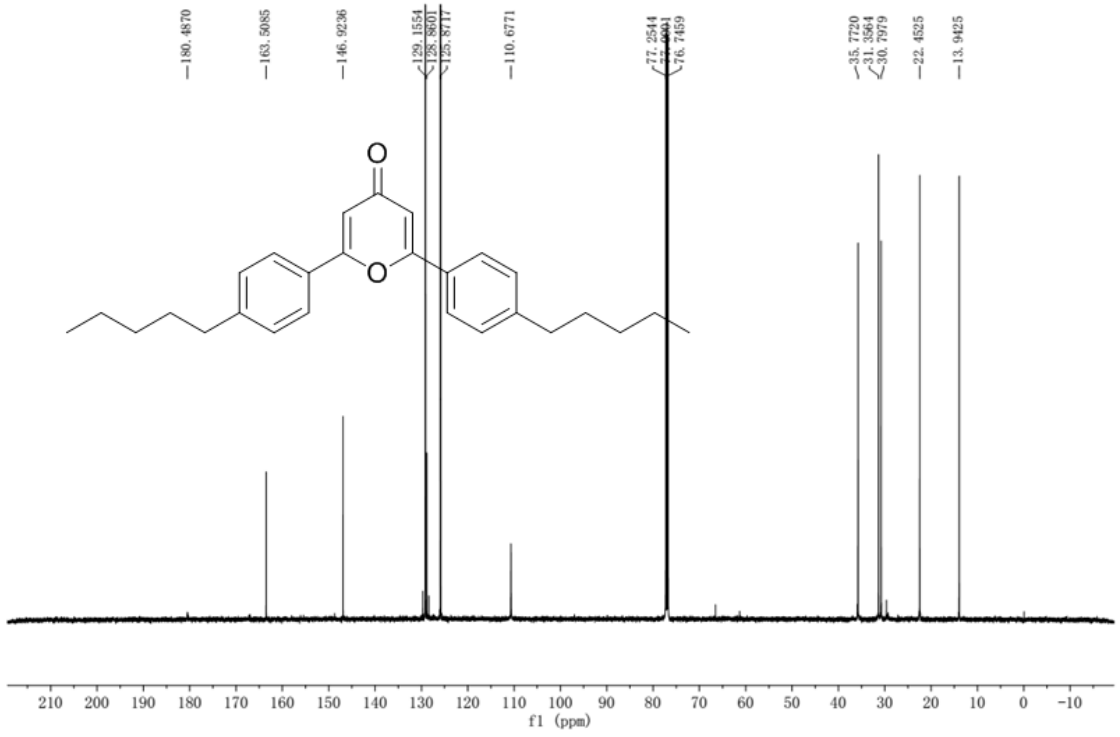
f1 (ppm)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f1 (ppm)


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6.14
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f1 (ppm)


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f1 (ppm)


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4.10
2.09
2.04
2.00
6.10
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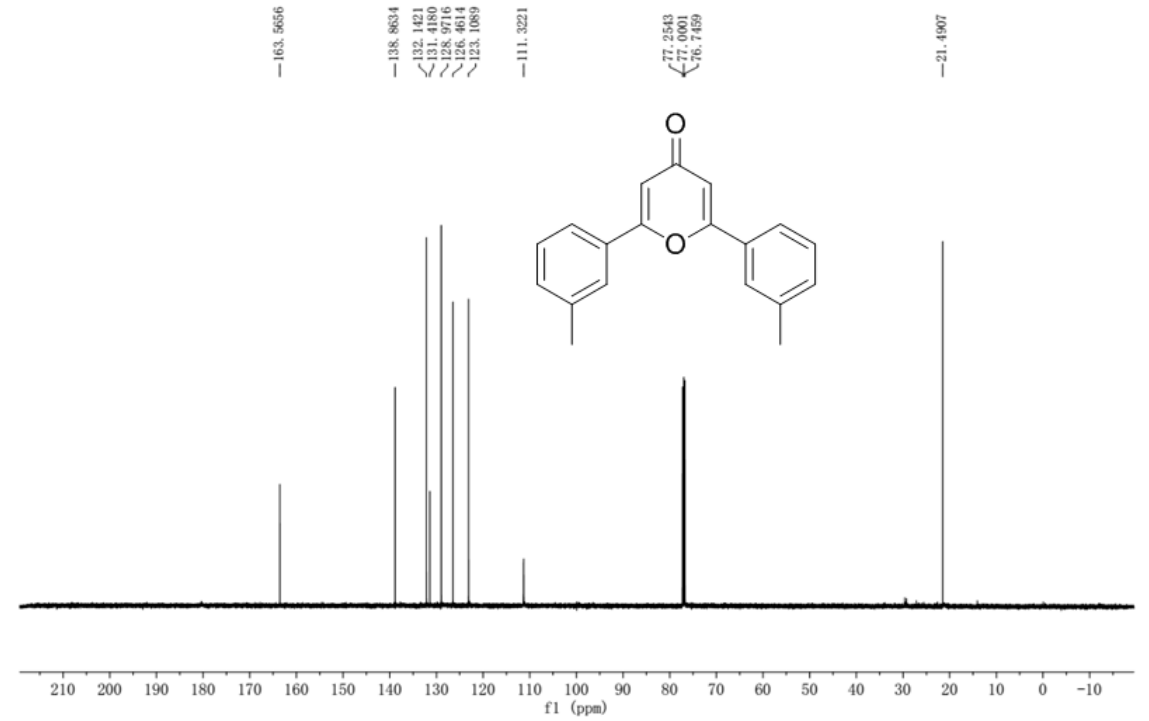
f1 (ppm)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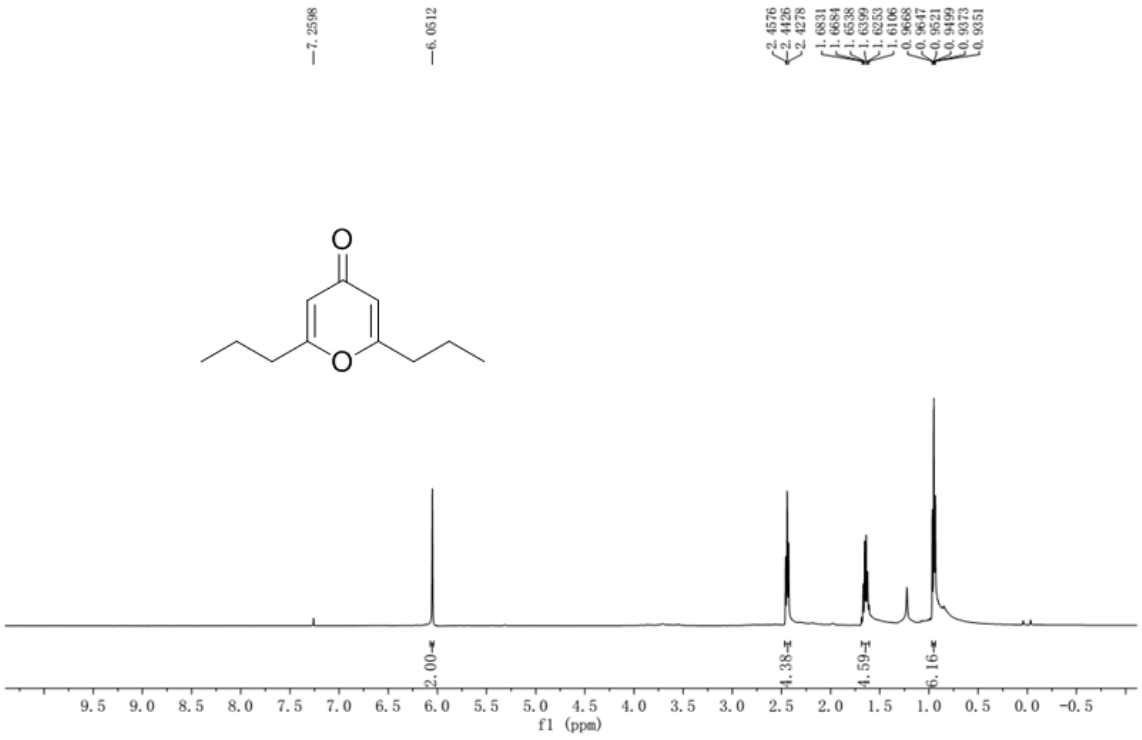
f1 (ppm)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O
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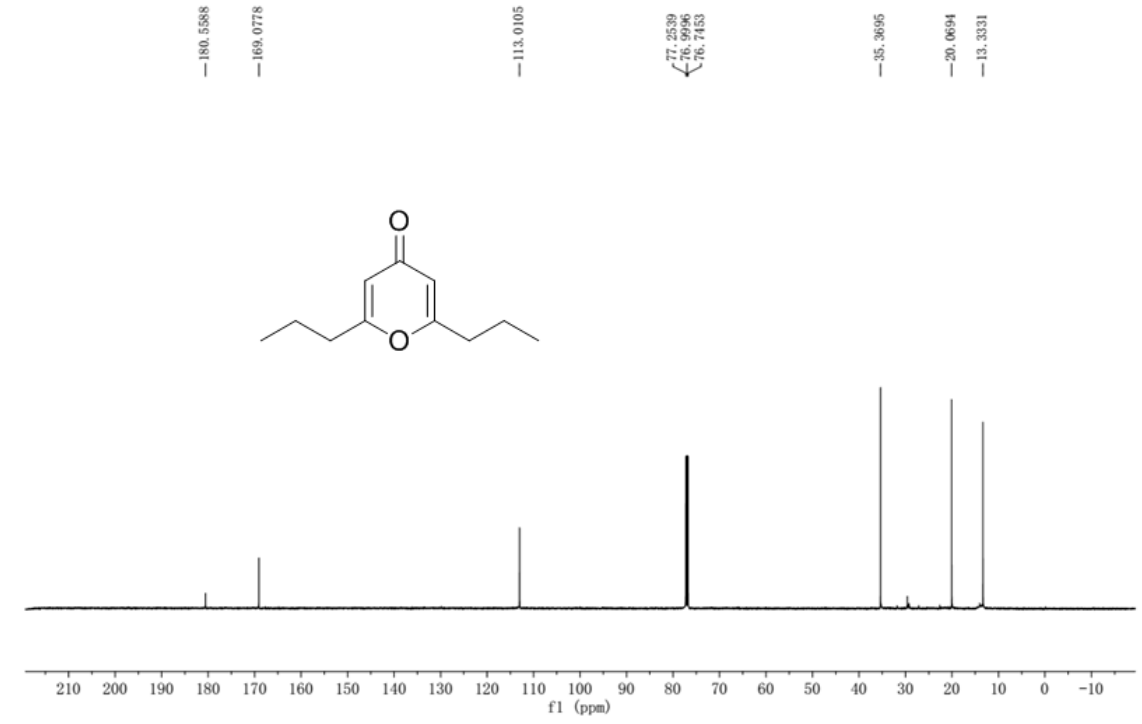
4.59
6.16
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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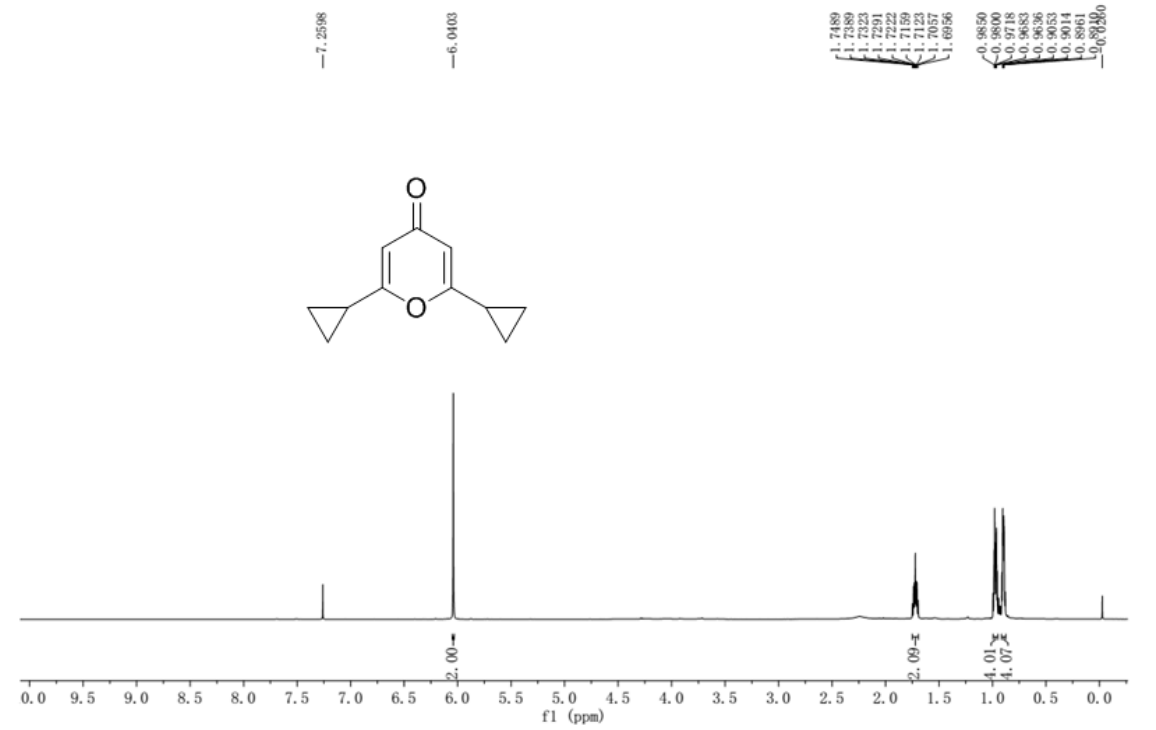
f1 (ppm)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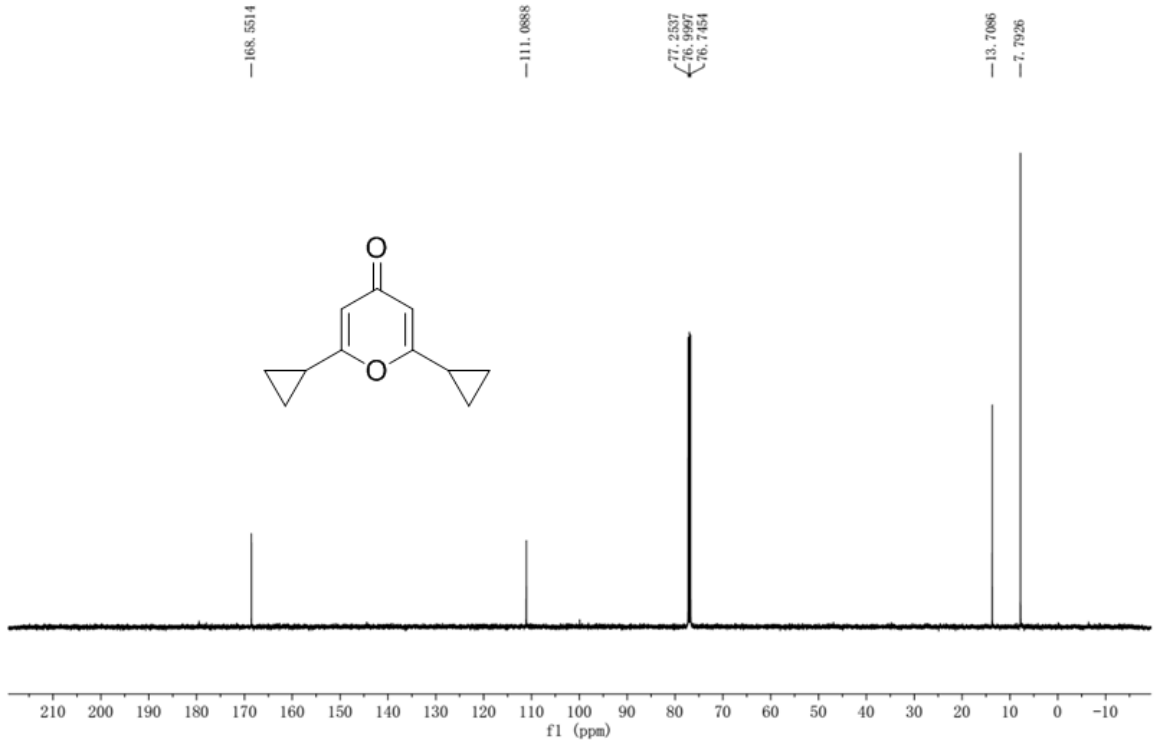
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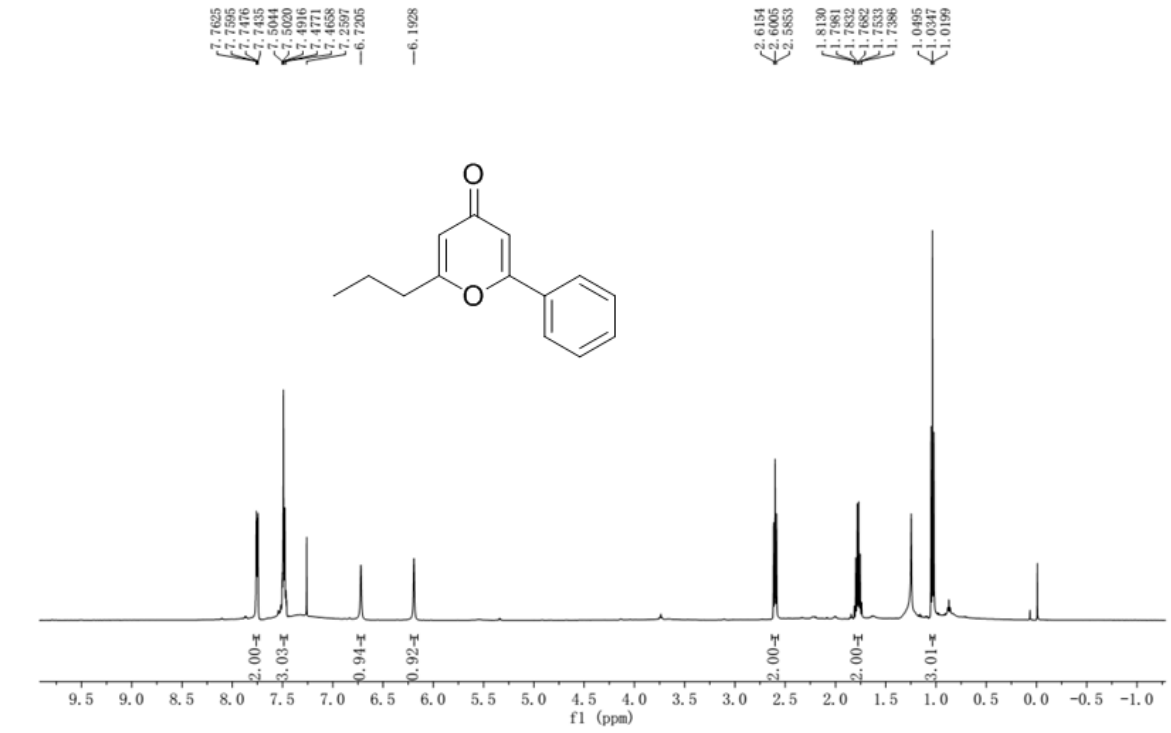
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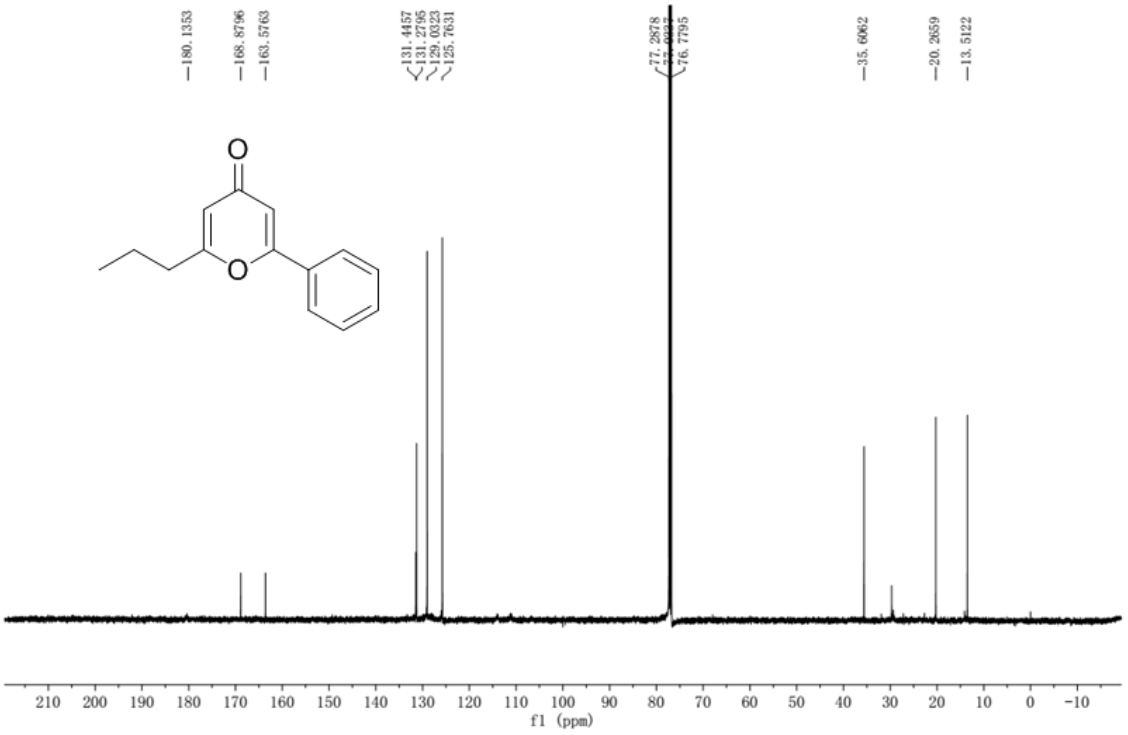
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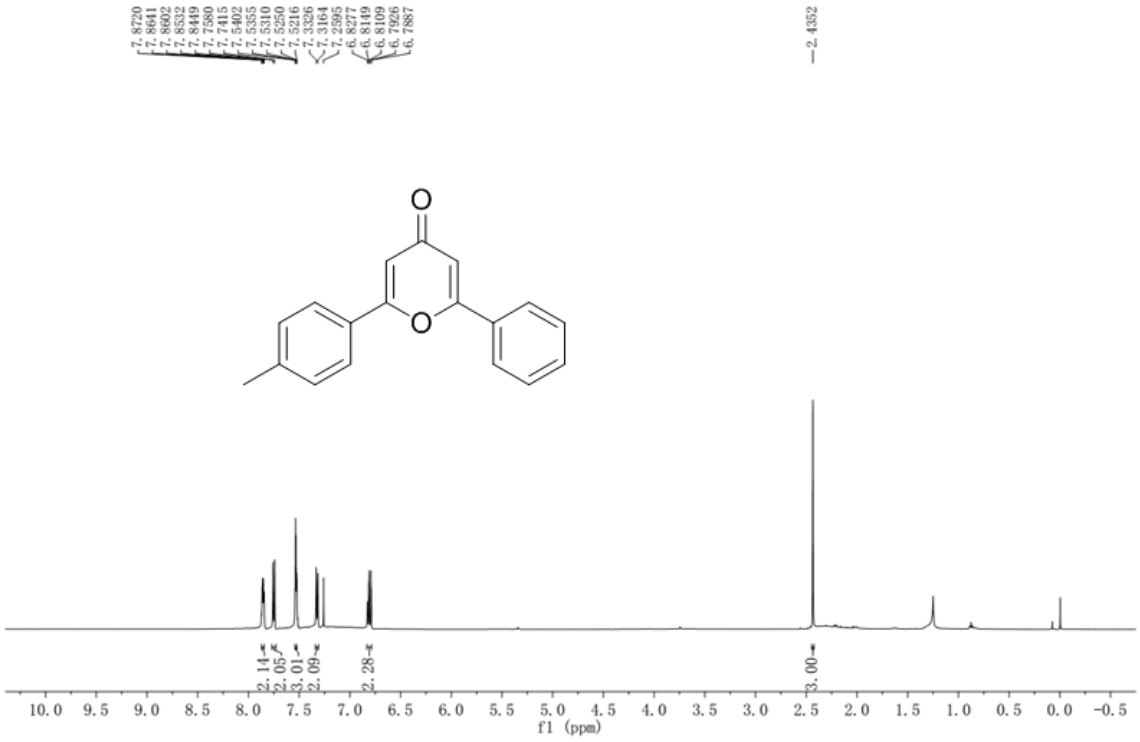
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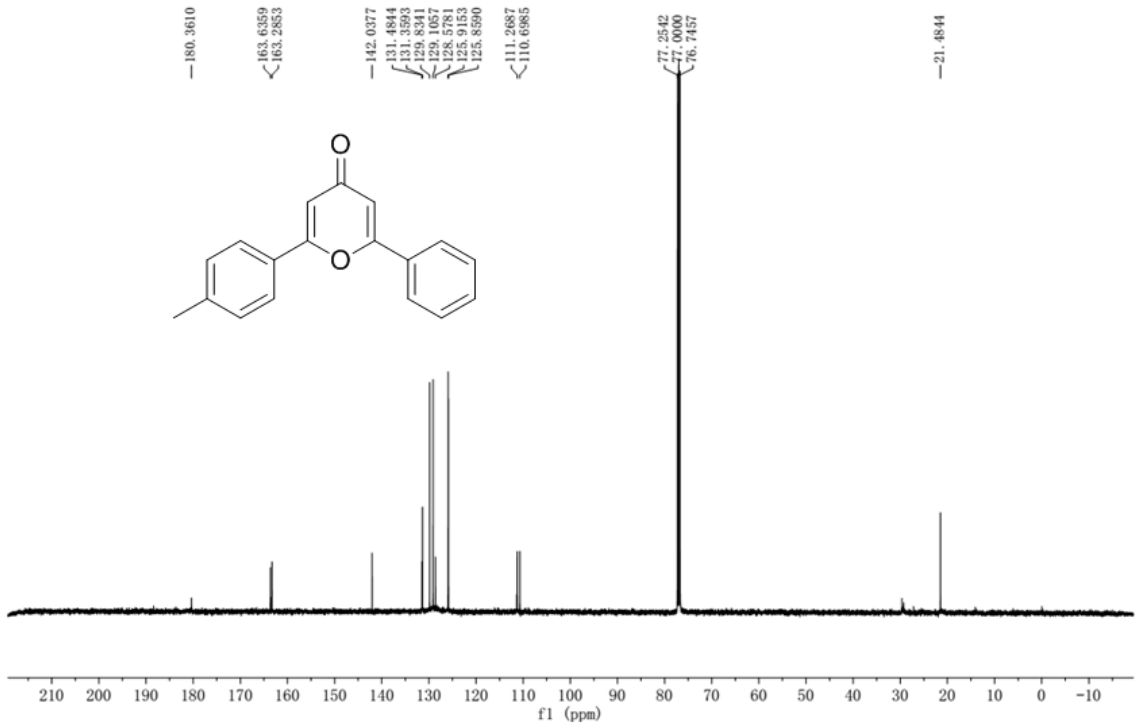
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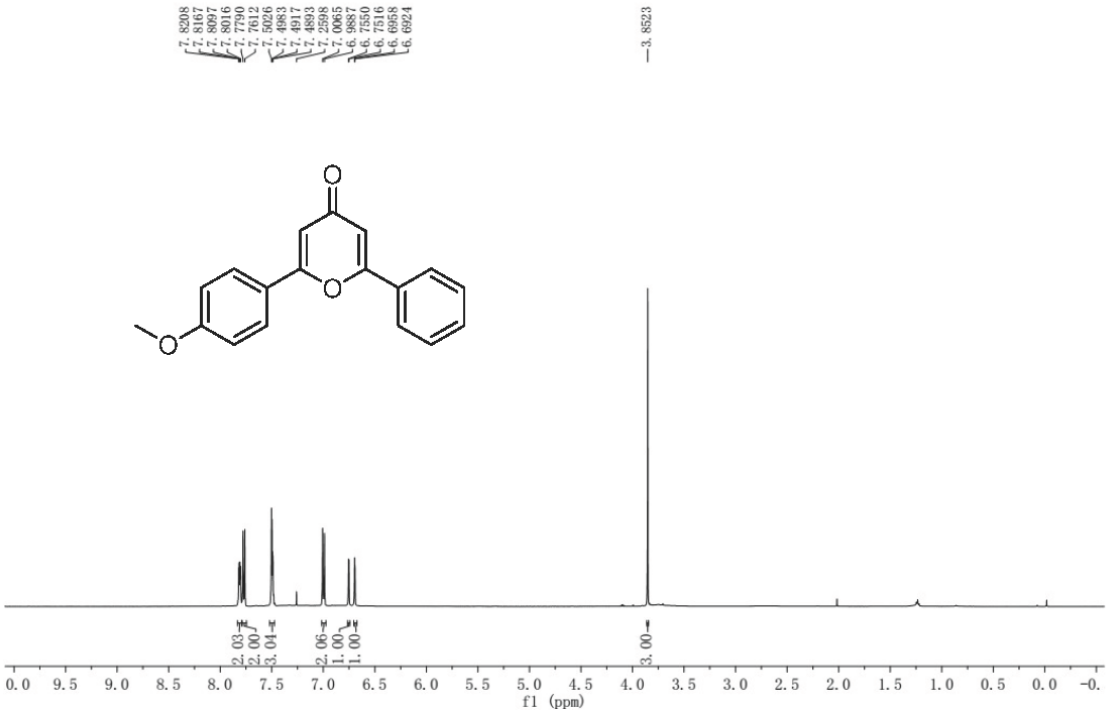
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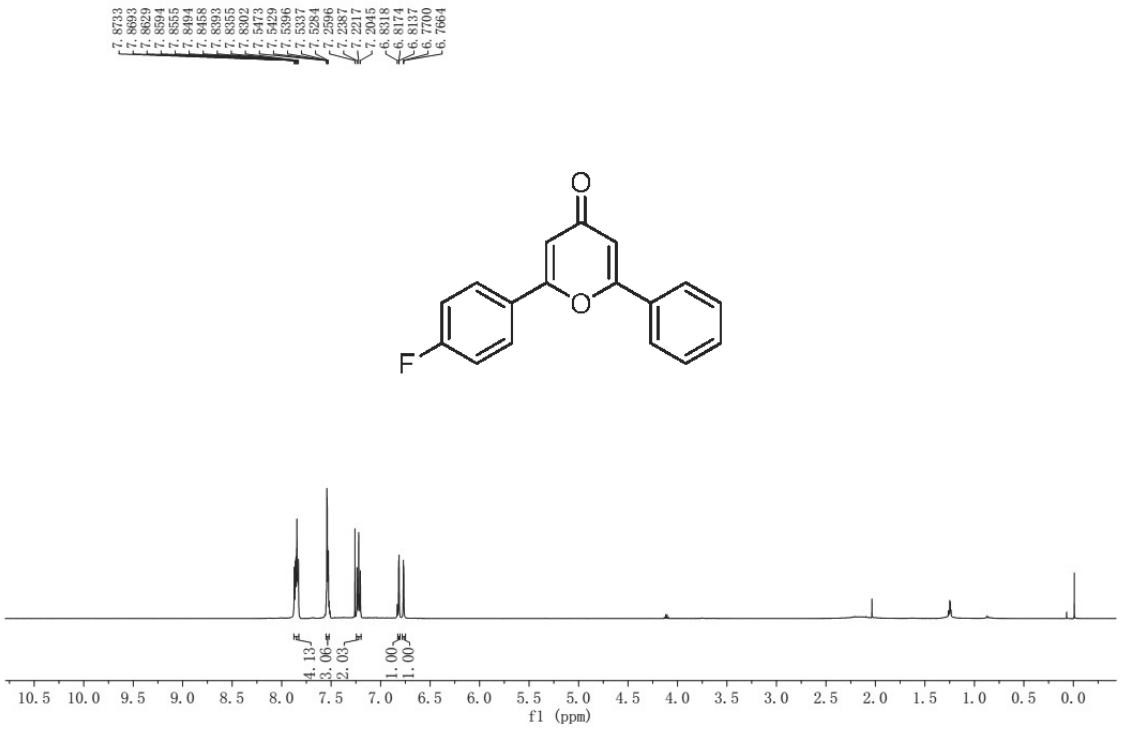
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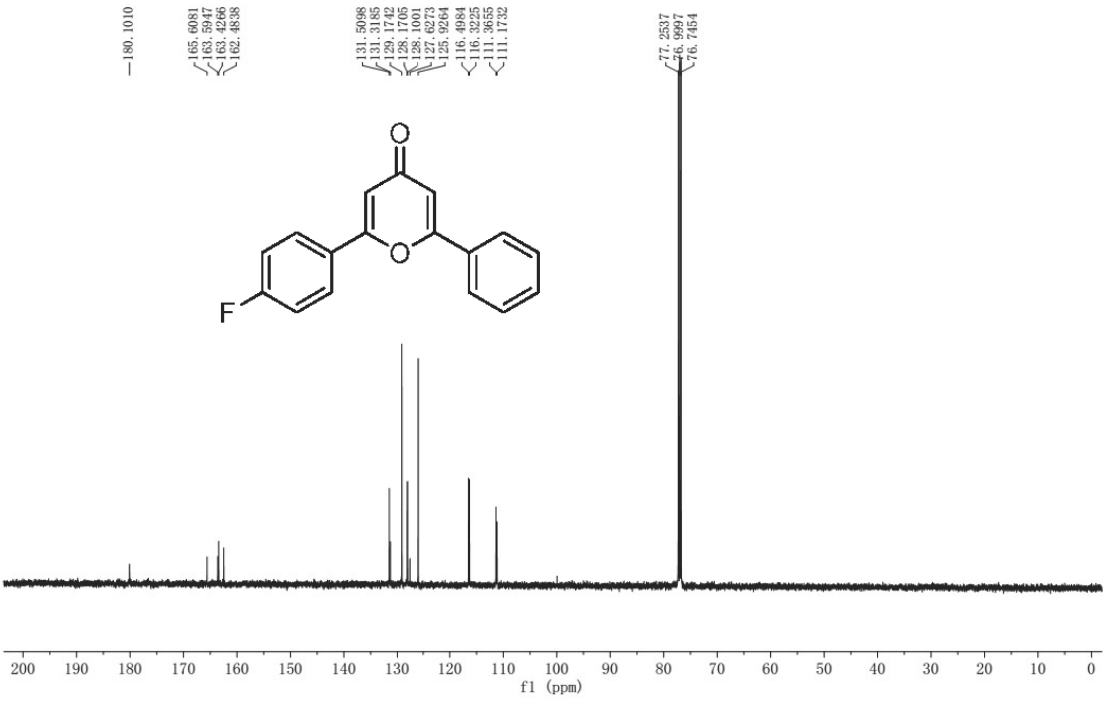
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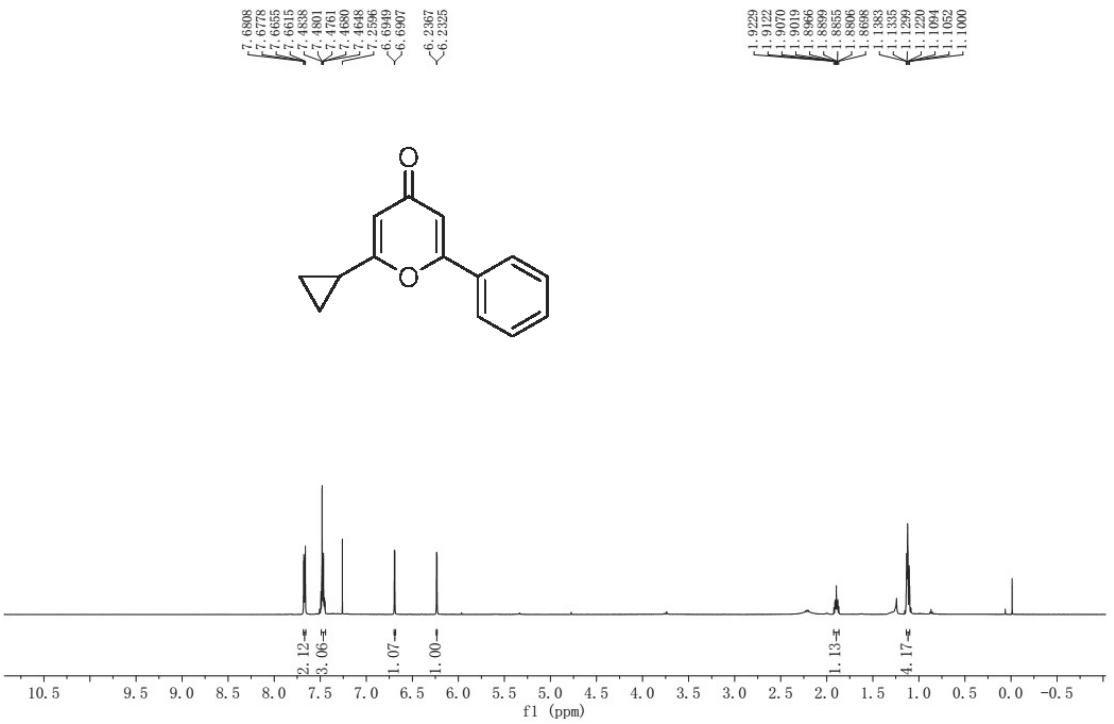
f1 (ppm)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f1 (ppm)


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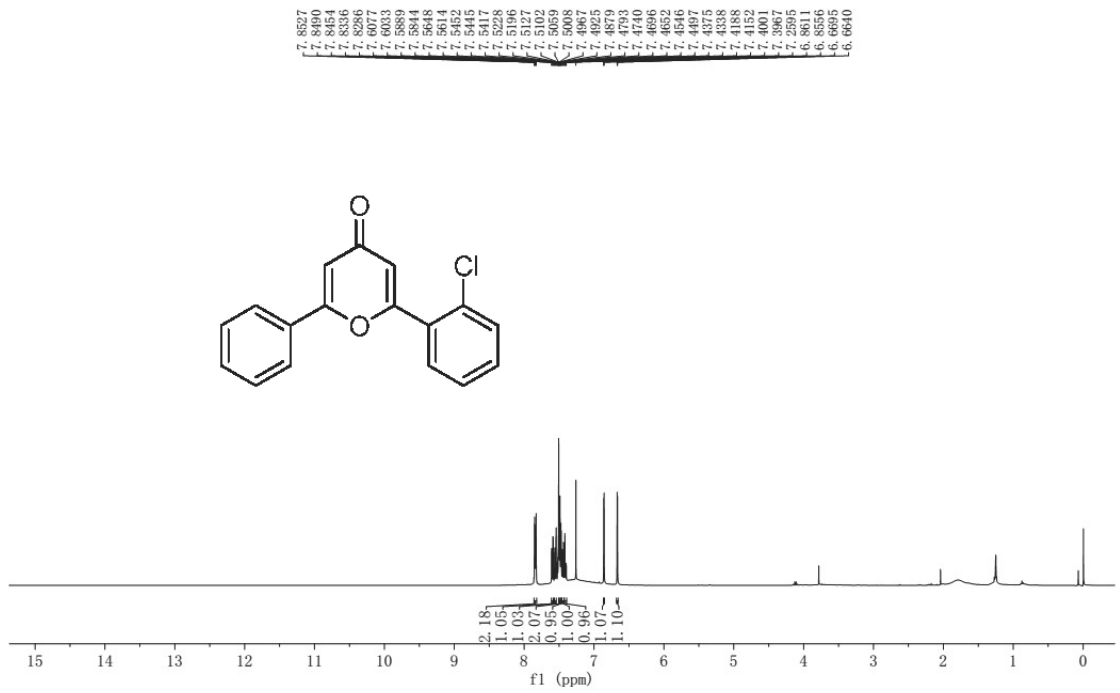
f1 (ppm)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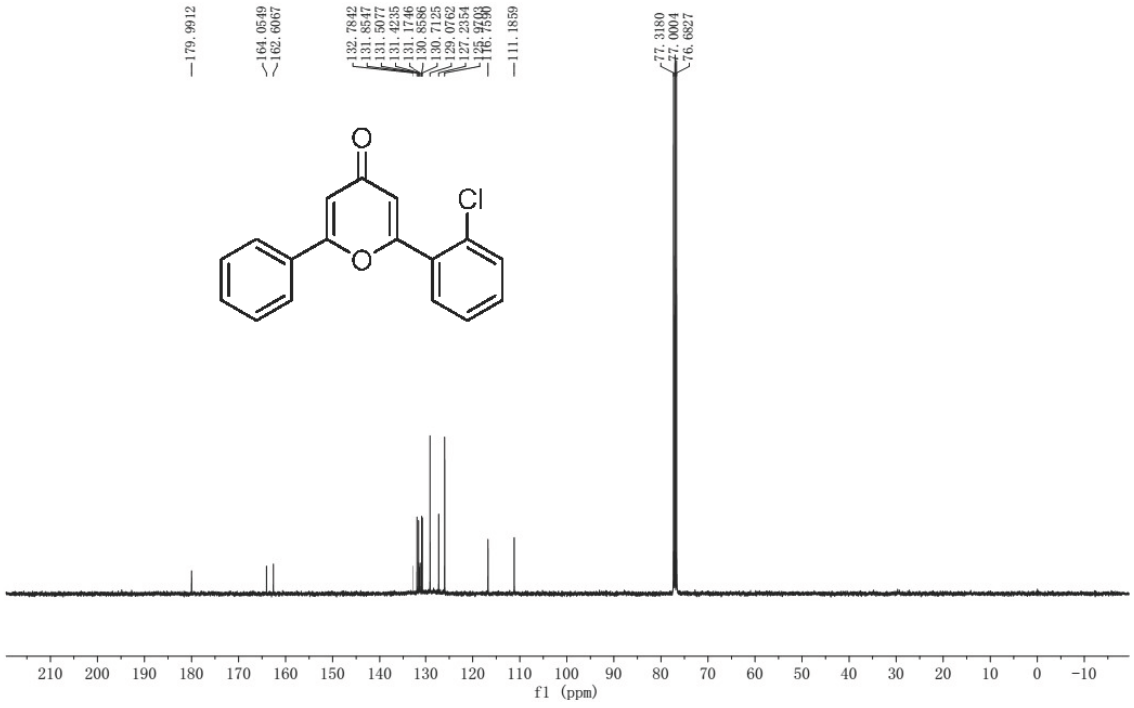
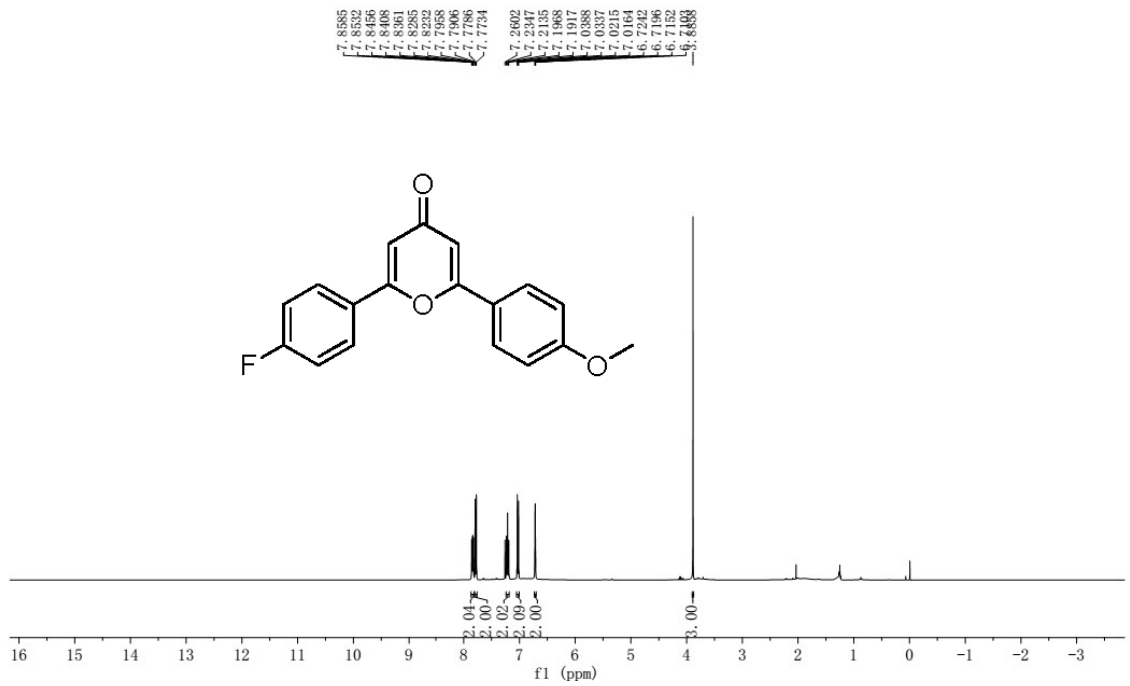
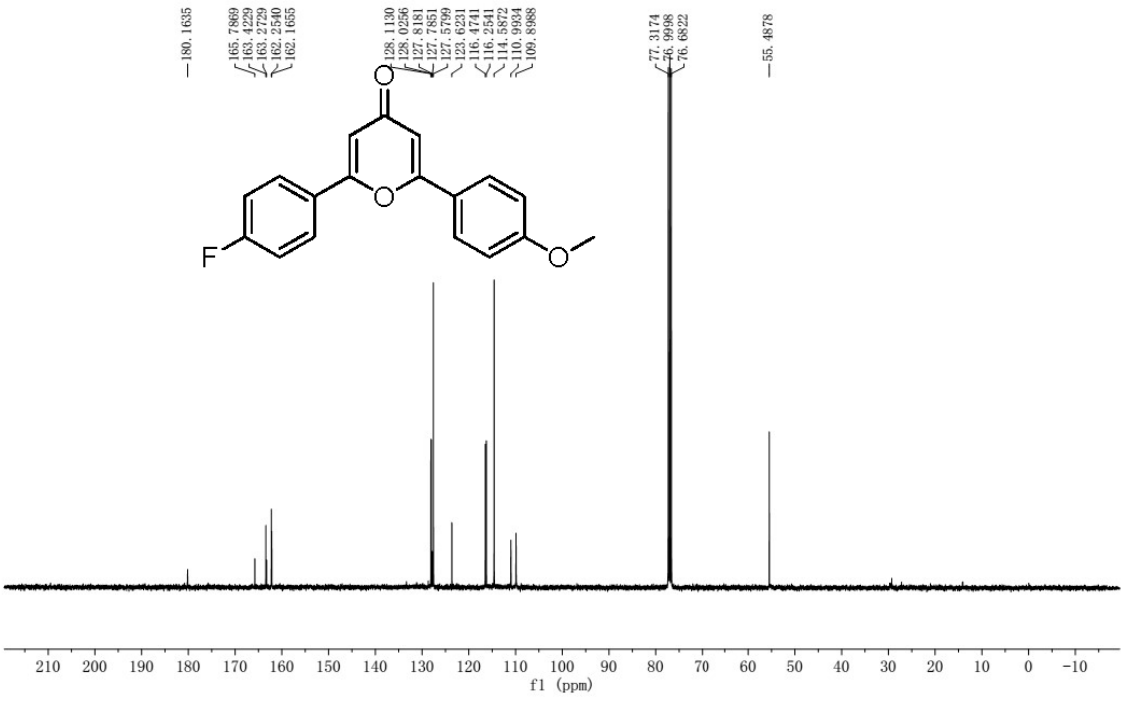
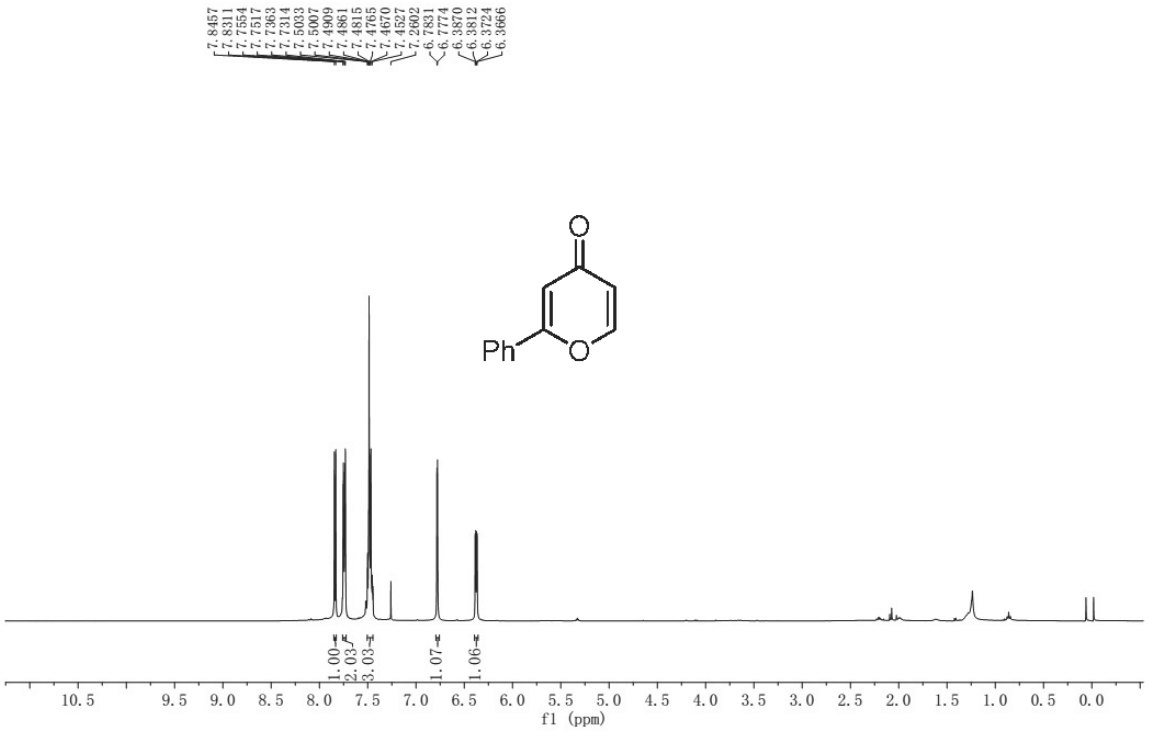
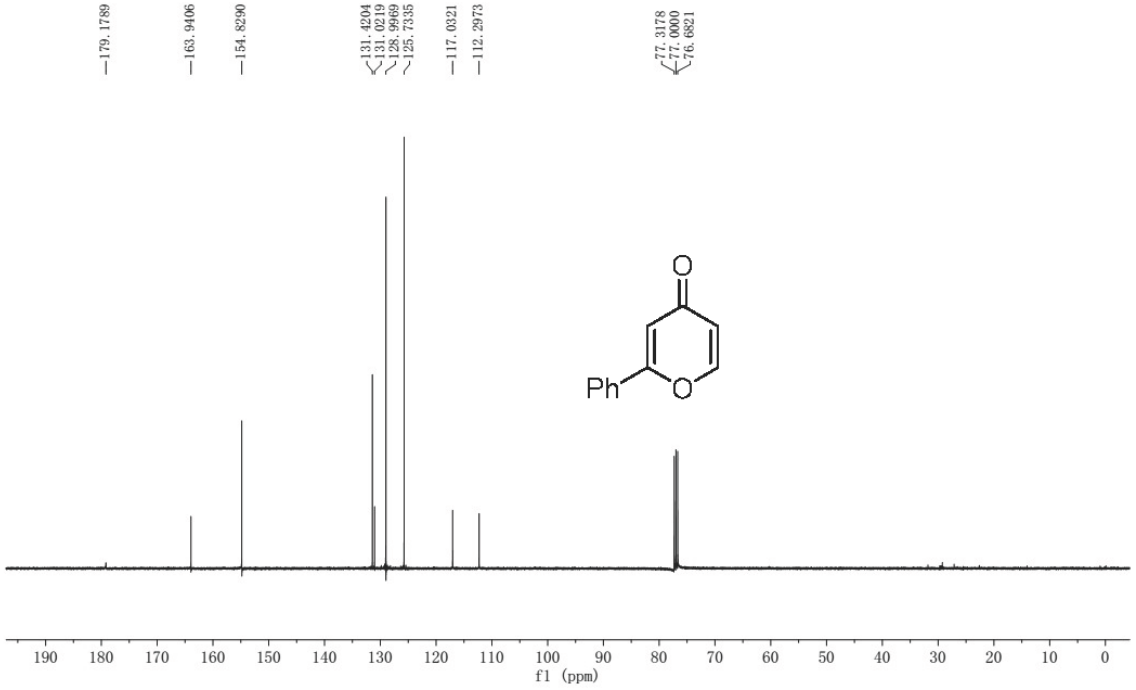
7.8490
7.8454
7.8336
7.8286
7.8077
7.6033
7.5889
7.5844
7.5648
7.5614
7.5452
7.5445
7.5417
7.5298
7.5196
7.5127
7.5102
7.5089
7.4908
7.4867
7.4825
7.4579
7.4733
7.4740
7.4696
7.4652
7.4546
7.4497
7.4375
7.4338
7.4188
7.4152
7.4001
7.3967
7.2595
6.8611
6.8556
6.6695
6.6640
Cl
O
2.18
1.05
1.03
2.07
0.95
1.00
0.96
1.07
1.10
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

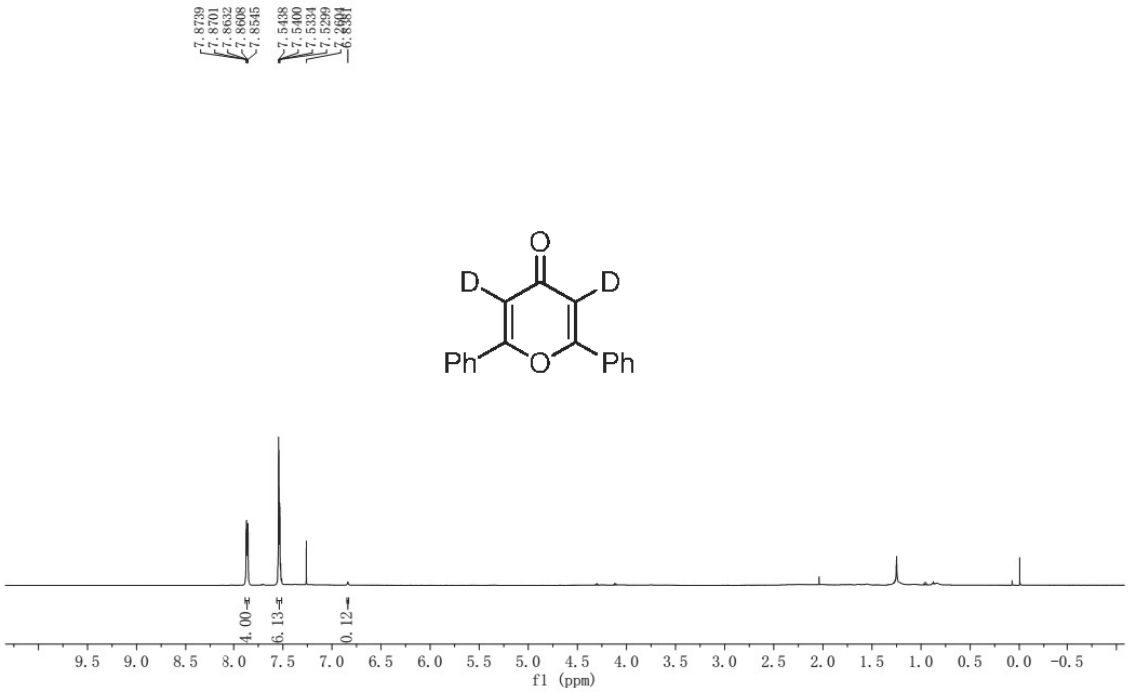

179.9912
164.0549
162.6067
132.7842
131.8547
131.5077
131.4235
131.1746
130.8586
130.7125
129.0762
127.2354
125.7598
116.7590
111.1859
77.3180
77.0004
76.6827
Cl
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.8585
7.8532
7.8456
7.8408
7.8361
7.8285
7.8232
7.7958
7.7906
7.7786
7.7734
7.2602
7.2347
7.2135
7.1968
7.1917
7.0388
7.0337
7.0215
7.0164
6.7242
6.7196
6.7152
3.8858
F
O
2.04
2.00
2.02
2.09
2.00
3.00
f1 (ppm)

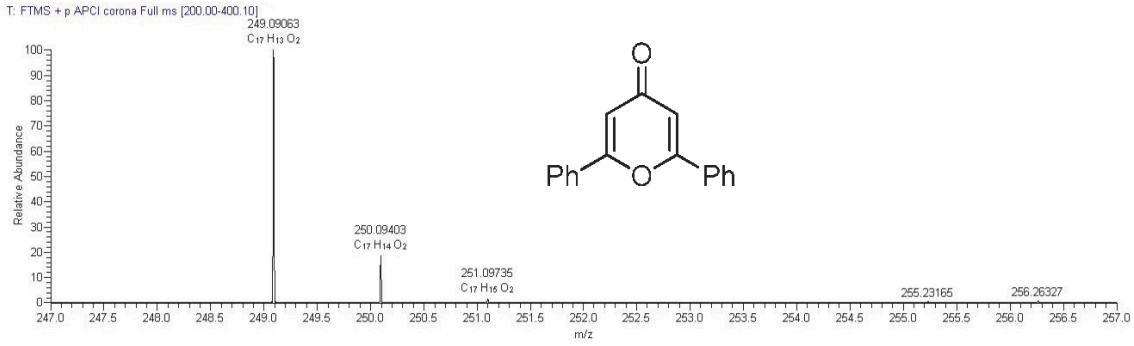

180.1635
165.7869
163.4229
163.2729
162.2540
162.1655
128.1130
128.0256
127.8181
127.7851
127.5799
123.6231
116.4741
116.2541
114.5872
110.9934
109.8988
77.3174
76.9998
76.6822
55.4878
F
O
f1 (ppm)

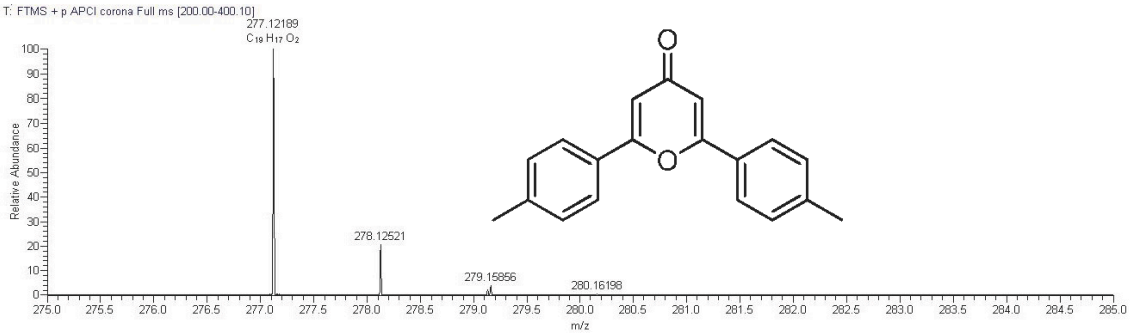

7.8457
7.8311
7.7554
7.7517
7.7363
7.7314
7.5033
7.5007
7.4909
7.4861
7.4815
7.4765
7.4670
7.4527
7.2602
6.7831
6.7774
6.3870
6.3812
6.3724
6.3666
Ph
O
1.00
2.03
3.03
1.07
1.06
f1 (ppm)

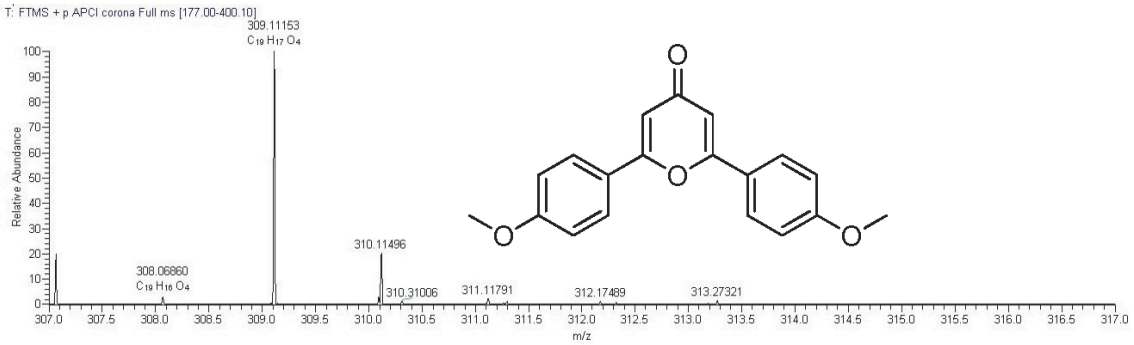

179.1789
163.9406
154.8290
131.4204
131.0219
128.9969
125.7335
117.0321
112.2973
77.3178
77.0000
76.6821
Ph
O
f1 (ppm)

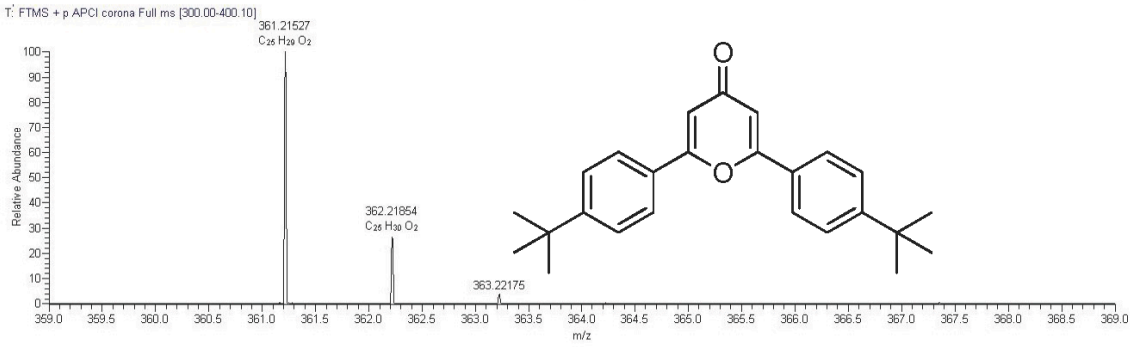

7.8739
7.8701
7.8632
7.8608
7.8545
7.5438
7.5400
7.5334
7.5299
7.2604
6.8381
O
D
D
Ph
O
Ph
4.00
6.13
0.12
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
f1 (ppm)

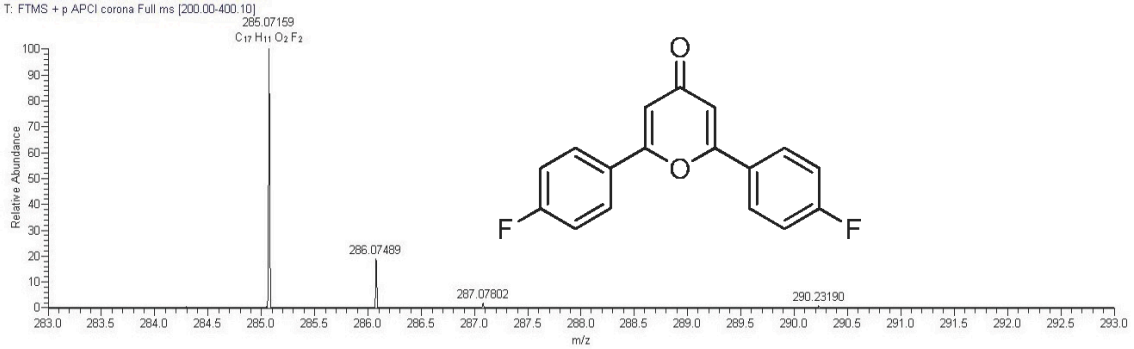
5. Copies of HRMS Spectra of Products

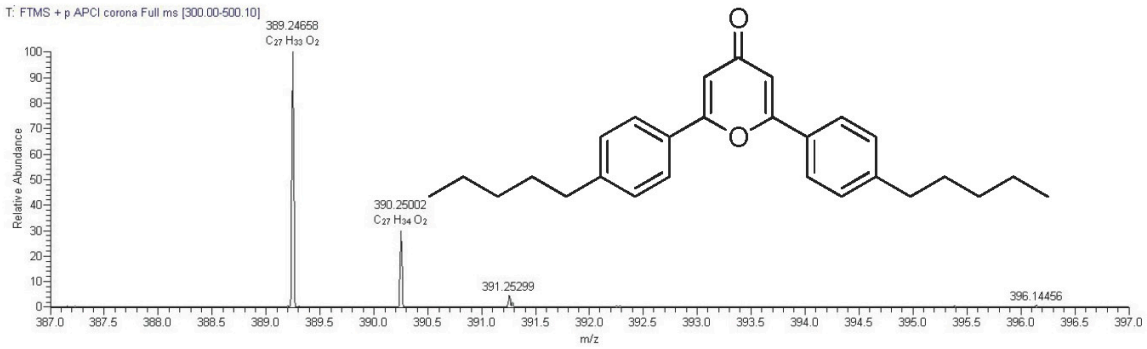


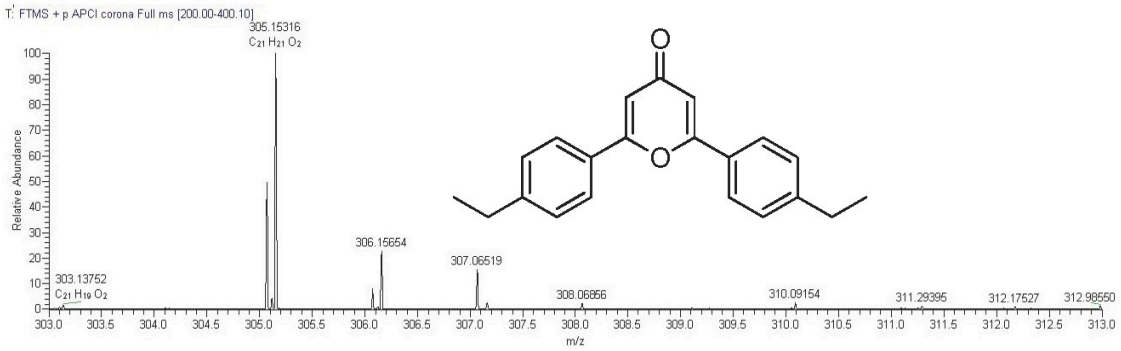


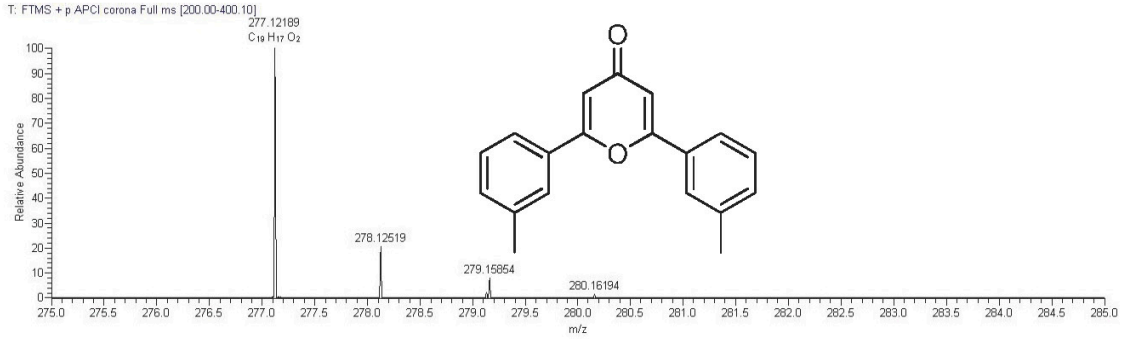


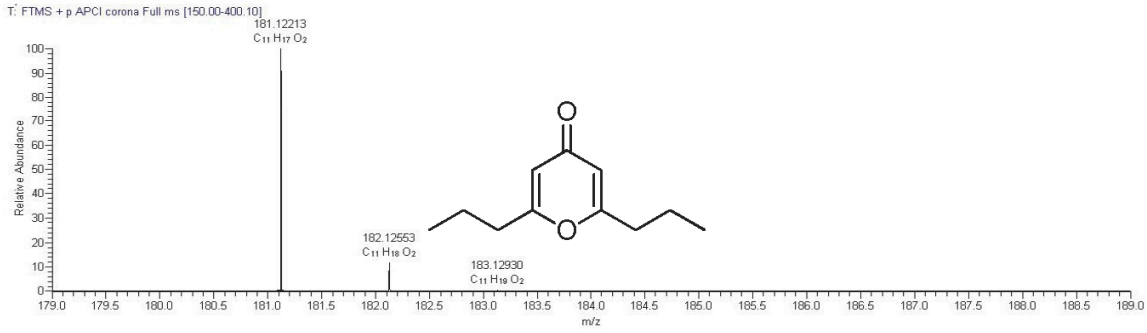


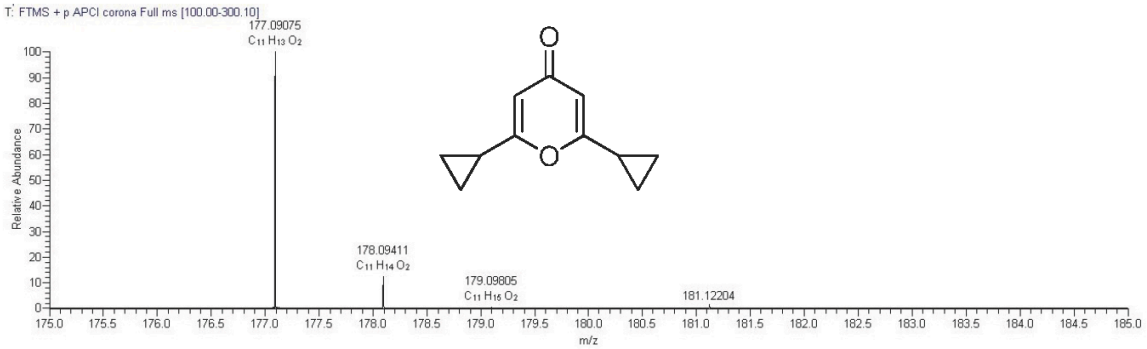


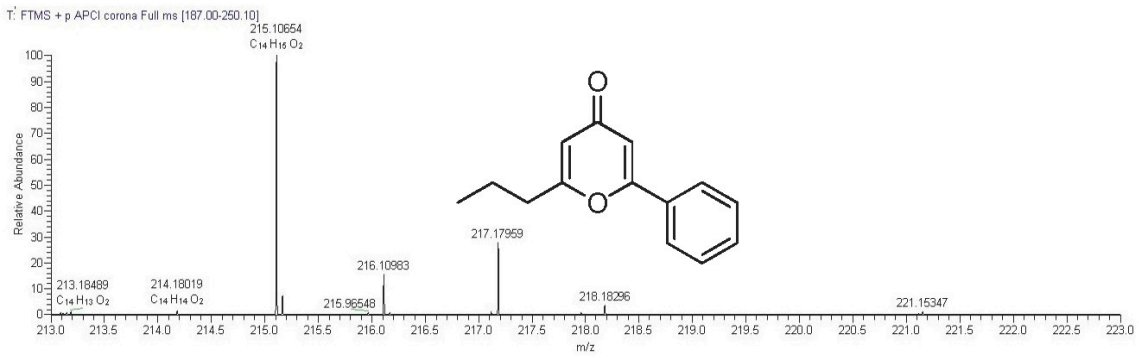

T: FTMS + p APCI corona Full ms [300.00-500.10]
389.24658
C27 H33 O2
390.25002
C27 H34 O2
391.25299
396.14456
Relative Abundance
m/z

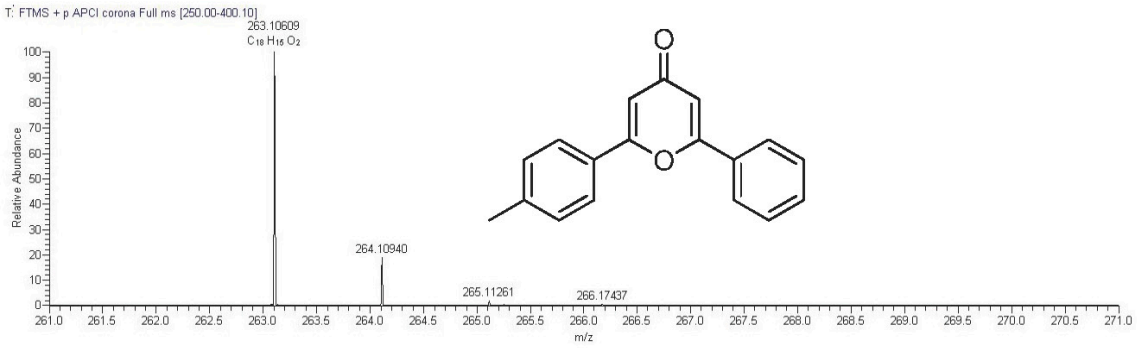

T: FTMS + p APCI corona Full ms [200.00-400.10]
305.15316
C21 H21 O2
306.15654
307.06519
303.13752
C21 H19 O2
308.06856
310.09154
311.29395
312.17527
312.98550
Relative Abundance
m/z

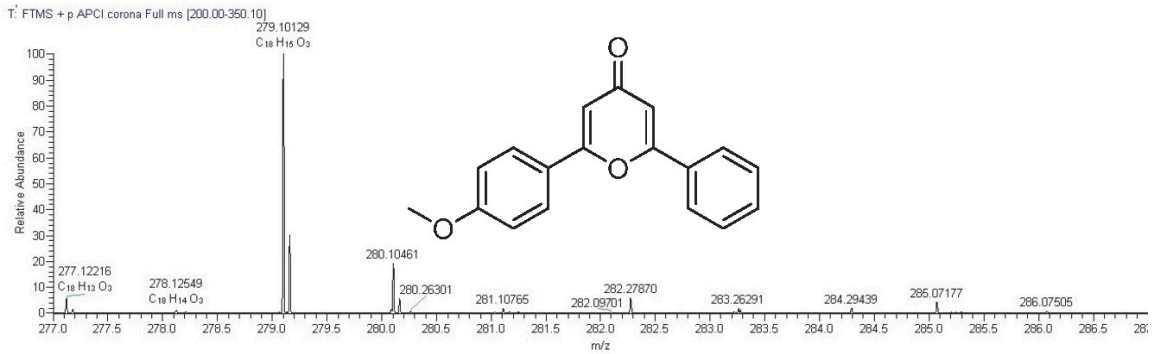

T: FTMS + p APCI corona Full ms [200.00-400.10]
277.12189
C19 H17 O2
278.12519
279.15854
280.16194
Relative Abundance
m/z

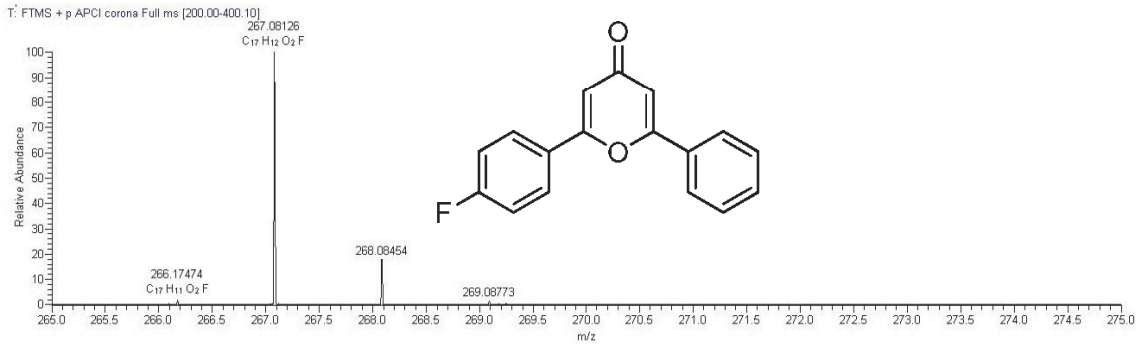

T: FTMS + p APCI corona Full ms [150.00-400.10]
181.12213
C11 H17 O2
182.12553
C11 H18 O2
183.12930
C11 H19 O2
Relative Abundance
m/z

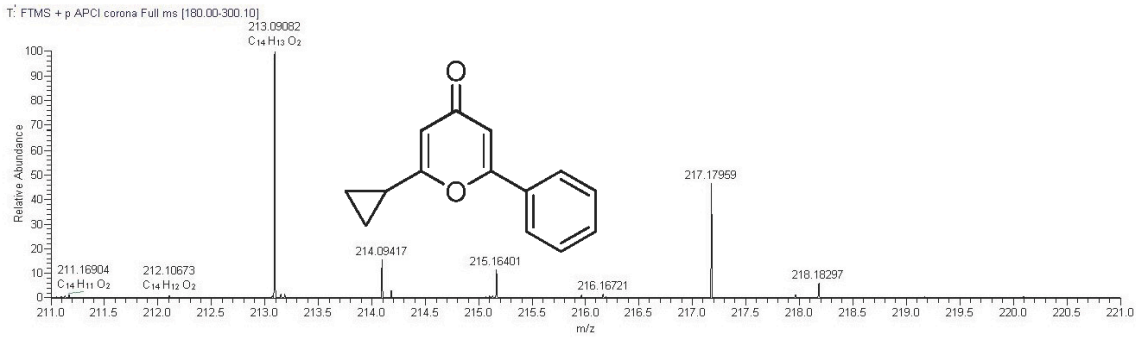

T: FTMS + p APCI corona Full ms [100.00-300.10]
177.09075
C11 H13 O2
178.09411
C11 H14 O2
179.09805
C11 H15 O2
181.12204
Relative Abundance
m/z

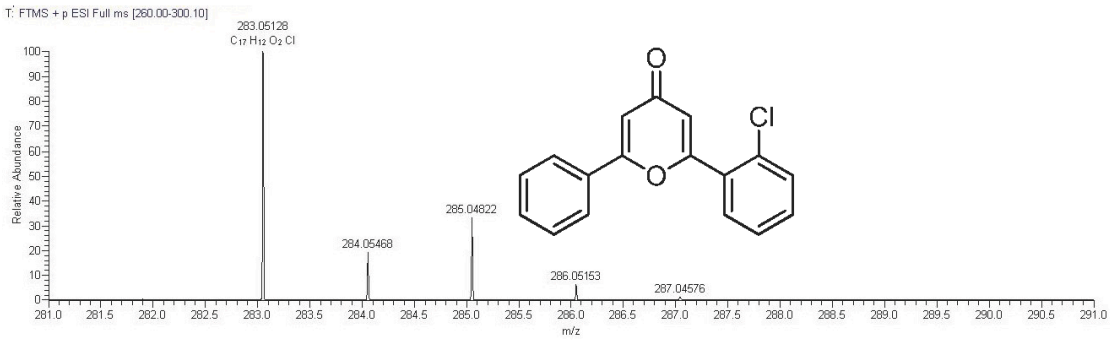

T: FTMS + p APCI corona Full ms [187.00-250.10]
215.10654
C14 H15 O2
217.17959
216.10983
213.18489
C14 H13 O2
214.18019
C14 H14 O2
215.96548
218.18296
221.15347
Relative Abundance
m/z

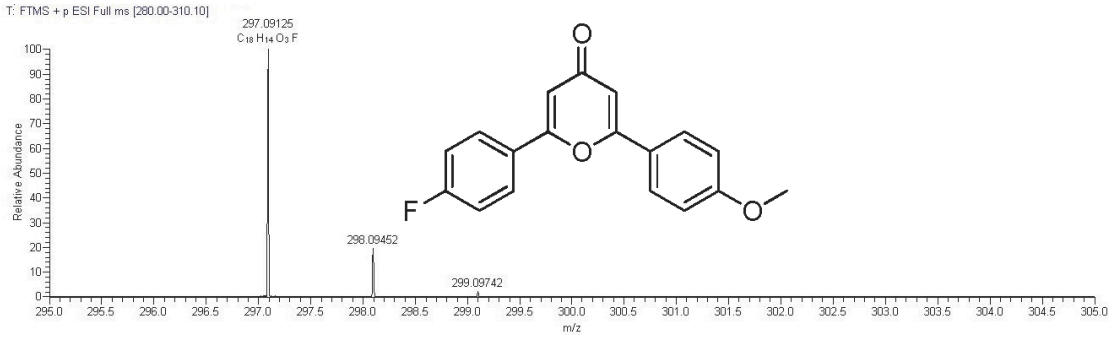

T: FTMS + p APCI corona Full ms [250.00-400.10]
263.10609
C18 H15 O2
264.10940
265.11261
266.17437
Relative Abundance
m/z

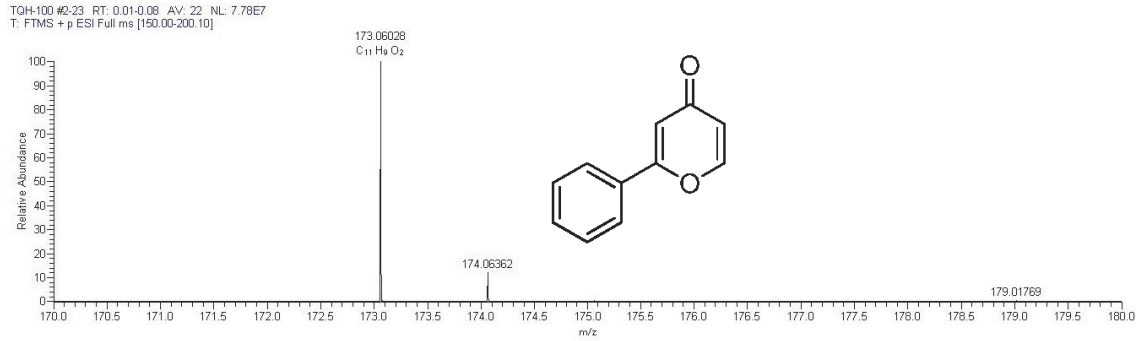

T: FTMS + p APCI corona Full ms [200.00-350.10]
279.10129
C18 H15 O3
280.10461
277.12216
C18 H13 O3
278.12549
C18 H14 O3
280.26301
281.10765
282.09701
282.27870
283.26291
284.29439
285.07177
286.07505
Relative Abundance
m/z

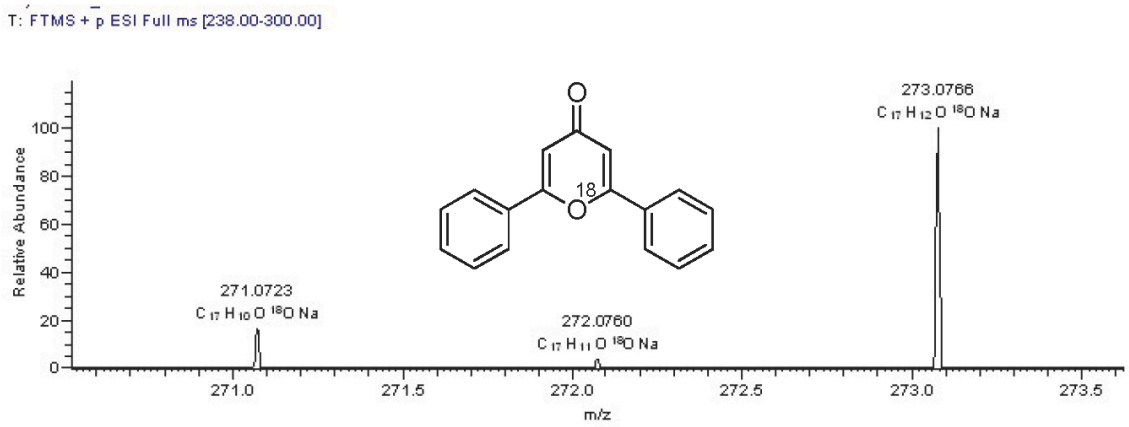

T: FTMS + p APCI corona Full ms [200.00-400.10]
267.08126
C17 H12 O2 F
F
268.08454
266.17474
C17 H11 O2 F
269.08773
Relative Abundance
m/z


T: FTMS + p APCI corona Full ms [180.00-300.10]
213.09082
C14 H13 O2
217.17959
214.09417
215.16401
218.18297
211.16904
C14 H11 O2
212.10673
C14 H12 O2
216.16721
Relative Abundance
m/z









References

1. Qiu, Y.-F.; Yang, F.; Qiu, Z.-H.; Zhong, M.-J.; Wang, L.-J.; Ye, Y.-Y.; Song, B.; Liang, Y.-M. Brønsted Acid Catalyzed and NIS-Promoted Cyclization of Diynones: Selective Synthesis of 4-Pyrone, 4-Pyridone, and 3-Pyrrolone Derivatives. *J. Org. Chem*. **2013**, *78*, 12018–12028.
2. Morisaki, Y.; Luu, T.; Tykwinski, R.R. A One-Pot Synthesis and Functionalization of Polyynes. *Org. Lett*. **2006**, *8*, 689–692.