$AlCl_3$ Catalyzed Coupling of N-benzylic Sulfonamides with 2-Substituted Cyanoacetates through Carbon-Nitrogen Bond Cleavage

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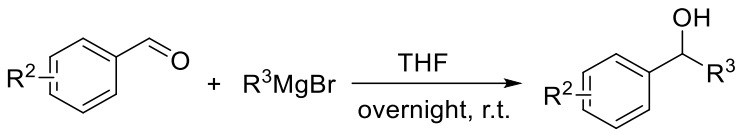
SUPPORTING INFORMATION

contents

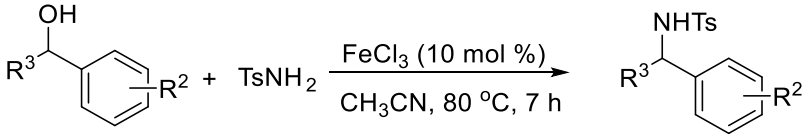
EXPERIMENTAL SECTION

General Information. ^{1}H NMR , ^{13}C NMR and ^{19}F NMR spectra were recorded at 400 MHz , 100 MHz and 376 MHz respectively using tetramethylsilane as an internal reference. Chemical shifts (δ) and coupling constants (J) were expressed in parts per million and hertz, respectively. Melting points were uncorrected. High-resolution mass spectrometry (HRMS) was performed on an ESI-TOF spectrometer. Chemicals were commercially available and used without purification. Chromatography: Column chromatography was performed with silica gel (200-300 mesh ASTM).

1.1 Synthesis of N-benzylic sulfonamides[1]



To an over-dried, argon purged round flask containing the aldehyde (5 mmol) in the THF (10 mL) at room temperature, was added phenylmagnesium bromide (15 mmol) dropwise over 5 minutes. The reaction was then allowed to stir overnight. The reaction mixture was quenched by addition of the saturated aqueous ammonium chloride (40 mL) and extracted with ethyl ether (2× 40 mL). The combined organic layers were washed with brine, dried with Na_2SO_4. Purification was performed by flash column chromatography on silica gel when needed.



To a stirred solution of diphenylmethanol (1 mmol) in 10 mL anhydrous CH_3CN was added 4-methylbenzenesulfonamide (1.1 mmol) and $FeCl_3$ (0.1 mmol) successively at 80 ^{o}C. After 7 hours, the crude product was purified by column chromatography on silica gel to afford the corresponding product.

1.2 Synthesis of substituted cyanoacetates[2]

A solution of cyanoethyl acetate (20 mmol) in 20 mL THF was added to a suspension of sodium hydride (7 mmol) and THF (10 mL) under argon atmosphere at 0 ^{o}C. After 30 min, a solution of hydrocarbon bromide (7 mmol) in THF was slowly added and after stirring the suspension for 15 min at 0 ^{o}C, the reaction mixture was removed to warm temperature and stirring for 8 h. The reaction was then quenched with 1M HCl and extracted using EtOAc (3×50 mL). The organic layer was dried by Na_2SO_4. Purification was performed by flash column chromatography on silica gel when needed.

1.3 Synthesis of 2-nitroesters[3]

The alkyl 2-bromoalkanoate (60 mmol) was added to a suspension of sodium hydride (104 mmol) and phloroglucinol dehydrate (52 mol) in dry DMF (40 mL) at room temperature. After 2.5 h, the reaction was then quenched with ice water (200 mL) and extracted using EtOAc (3×50 mL). The organic layer was dried by Na_2SO_4. Purification was performed by flash column chromatography on silica gel when needed.

1.4 Synthesis of substituted malononitrile [4]

A solution of malononitrile (20 mmol) in 20 mL THF was added to a suspension of sodium hydride (7 mmol) and THF (10 mL) under argon atmosphere at 0 ^{o}C. After 30 min, a solution of hydrocarbon bromide (7 mmol) in THF was slowly added and after stirring the suspension for 15 min at 0 ^{o}C, the reaction mixture was removed to warm temperature and stirring for 8 h. The reaction was then quenched with 1M HCl and extracted using EtOAc (3×50 mL). The organic layer was dried by Na_2SO_4. Purification was performed by flash column chromatography on silica gel when needed.

1.5 Synthesis of substituted diethyl malonate [5]

To a solution of diethyl malonate (20 mmol) in 20 mL THF was added to a suspension of sodium

hydride (7 mmol) and THF (10 mL) under argon atmosphere at 0 ^{o}C. After 30 min, a solution of hydrocarbon bromide (7 mmol) in THF was slowly added and after stirring the suspension for 15 min at 0 ^{o}C, the reaction mixture was removed to warm temperature and stirring for 8 h. The reaction was then quenched with 1M HCl and extracted using EtOAc (3×50 mL). The organic layer was dried by Na_2SO_4. Purification was performed by flash column chromatography on silica gel when needed.

1.6 General Experimental Procedures and Characterizations.

2-subsituted cyanoacetates (0.25 mmol, 1 equiv), *N*-benzylic sulfonamides (0.3 mmol, 1.2 equiv), $AlCl_3$ (100 mol %), dry $CHCl_3$ (1 mL) and a stir bar were added to a sealed tube. After being stirred at 80 ^{o}C for indicated time, the mixture was evaporated under vacuum. The corresponding product was isolated by silica gel column chromatography with a dichloromethane/petroleum ether mixture as eluent.

1.7 Reference

[1] (*a*)H. Li, R.Y. Zhu, W. J. Shi, K. H. He and Z. J. Shi, *Org. Lett.*, 2012, **14**, 4850. (*b*) U. Jana, S. Maiti, S. Biswas, Tetrahedron Lett., 2008, **48**, 858.

[2] (*a*) C. J. Mallia, L. Englert, G. C. Walter and I. R. Baxendale, *Beilstein J. Org. Chem*., 2015, **11**, 875. (*b*) X. Y. Zhang, X. F Jia, L. L. Fang, N. Liu, J. J. Wang and X. S. Fan, *Org. Lett.*, 2011, **13**, 5024.

[3] J. Ram ́ırez, D. P. Huber and A. Togni, *Synlett.*, 2007, **7**, 1143.

[4] A. Schnyder, A. F. Indolese, T. Maetzke, J. Wenger, H. U. Blaser, Synlett, 2006, **18**, 3167.

[5] K. Yoshihisa, C. Werngard and K. Yoshito, *Org. Lett.*, 2003, **5**, 93.

Copies of ^{1}H NMR, ^{13}C NMR and ^{19}F NMR

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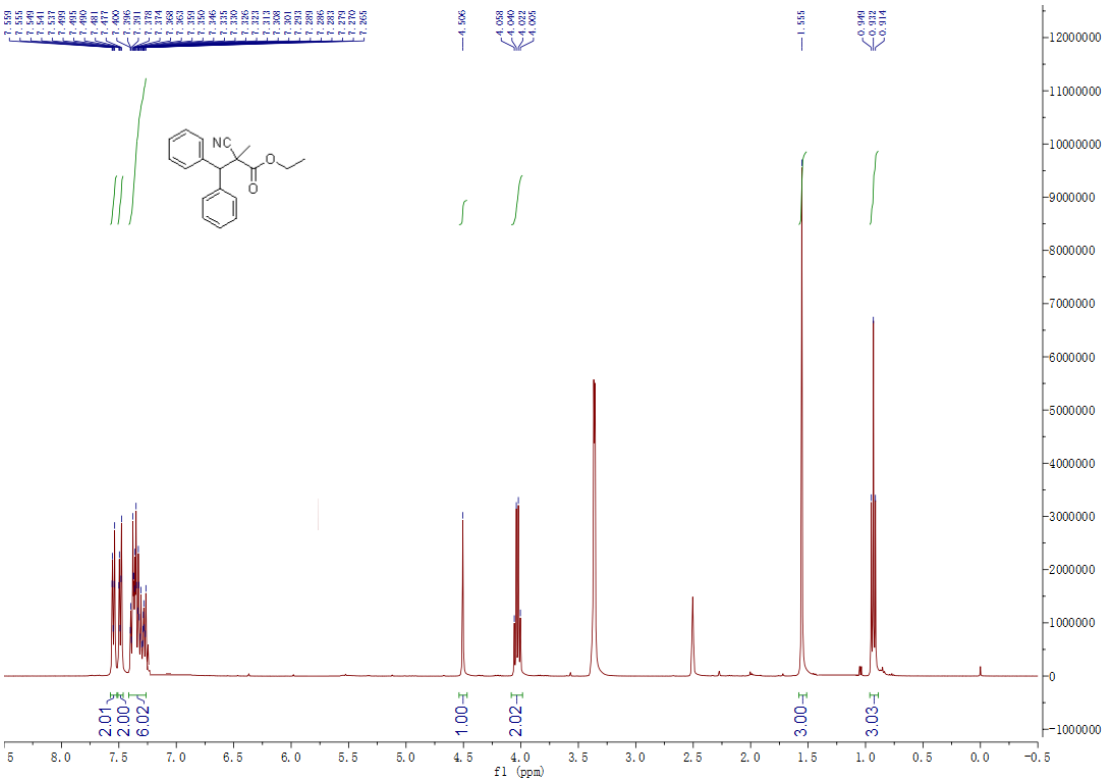

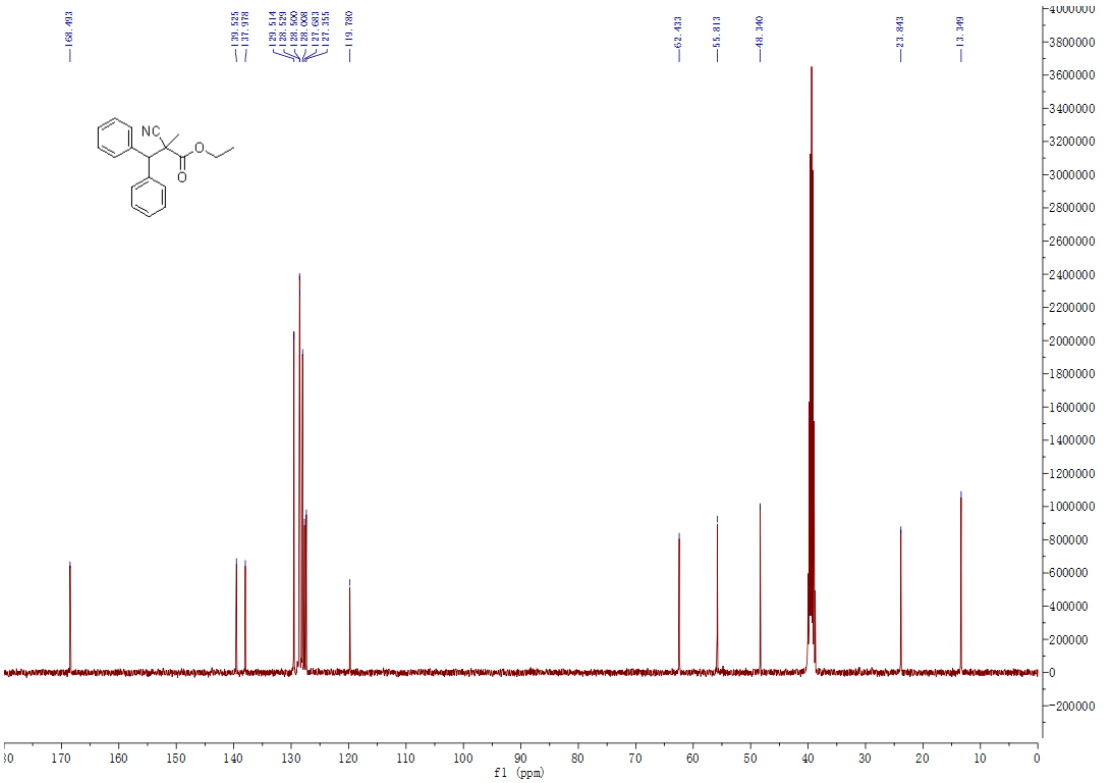

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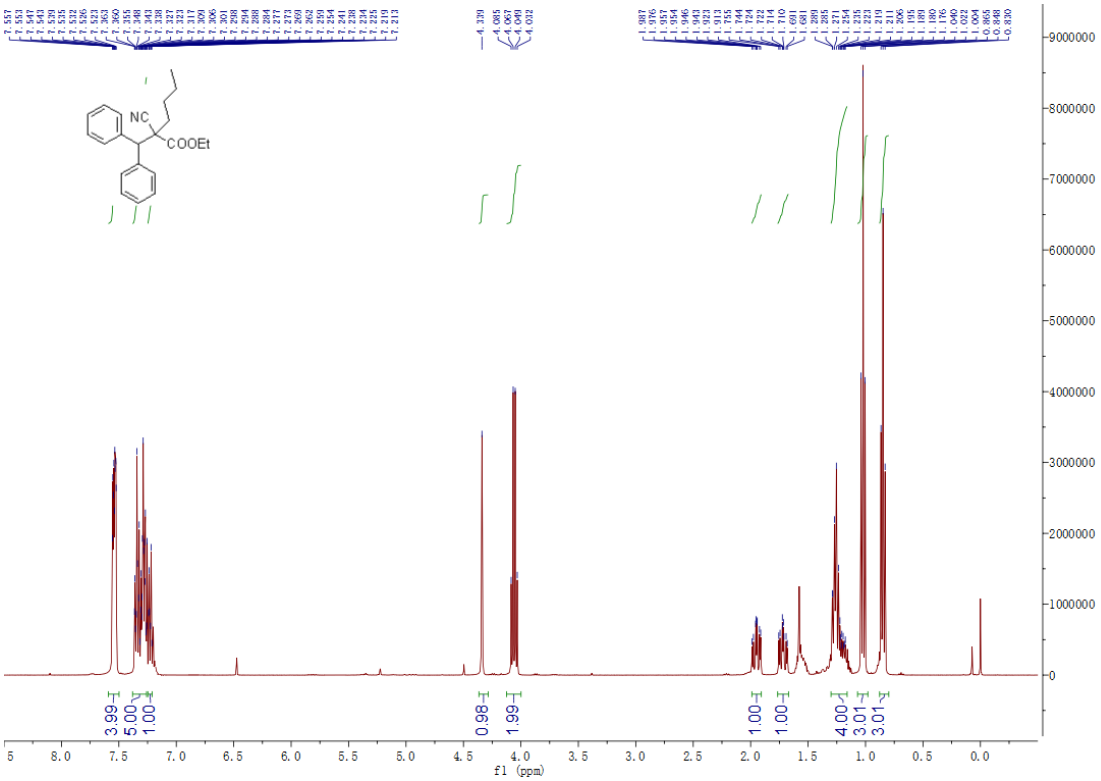
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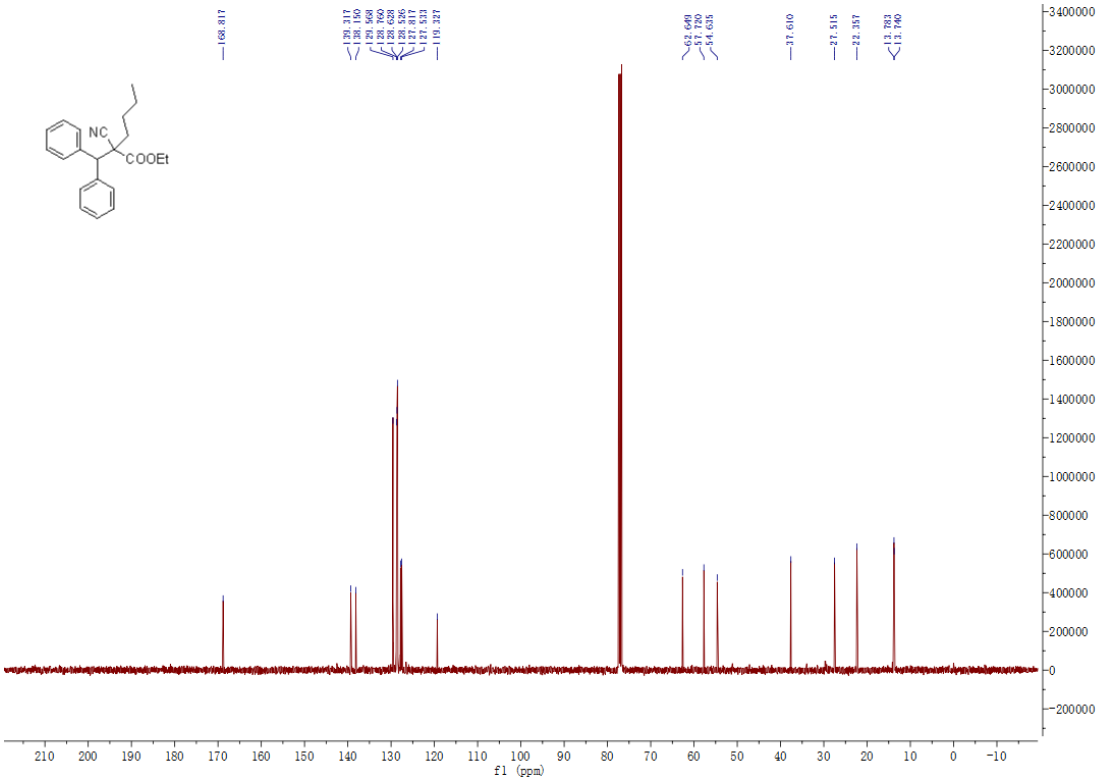
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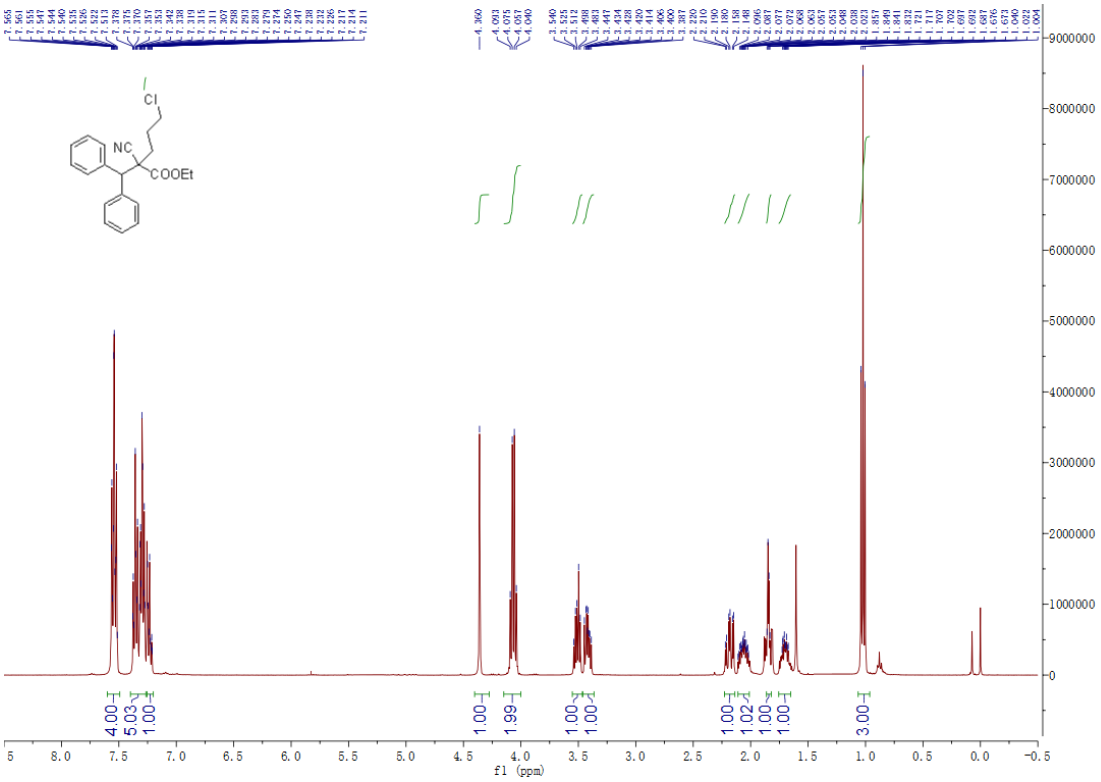
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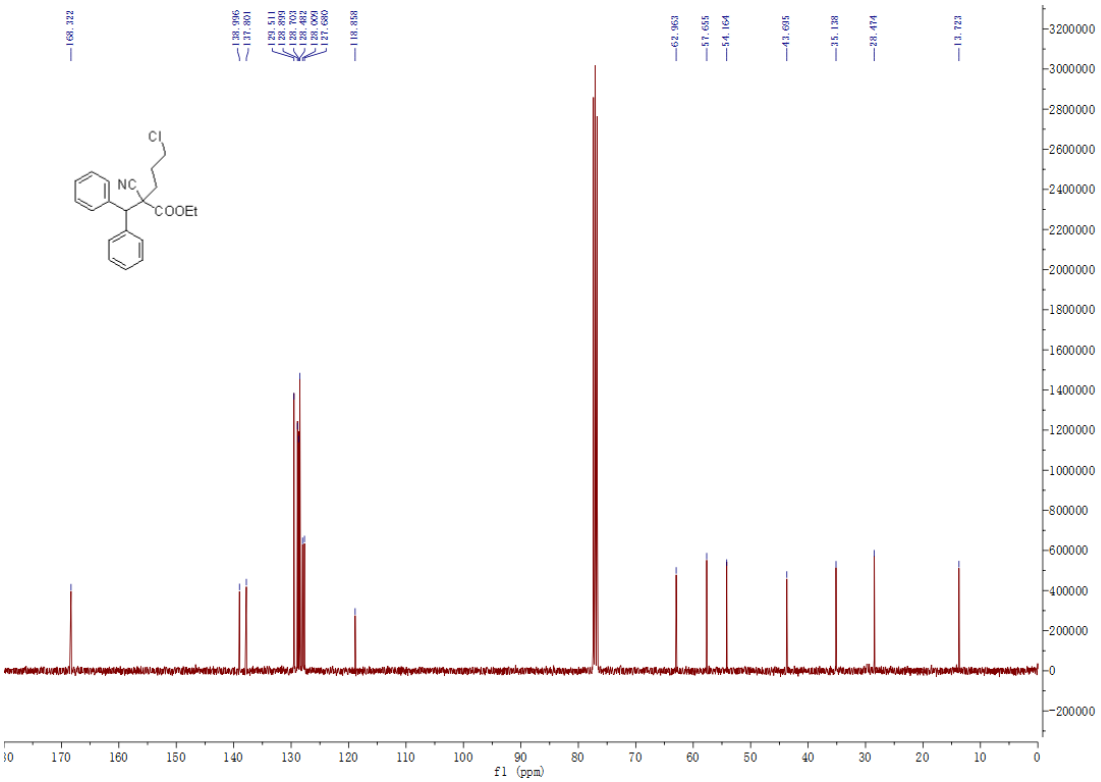
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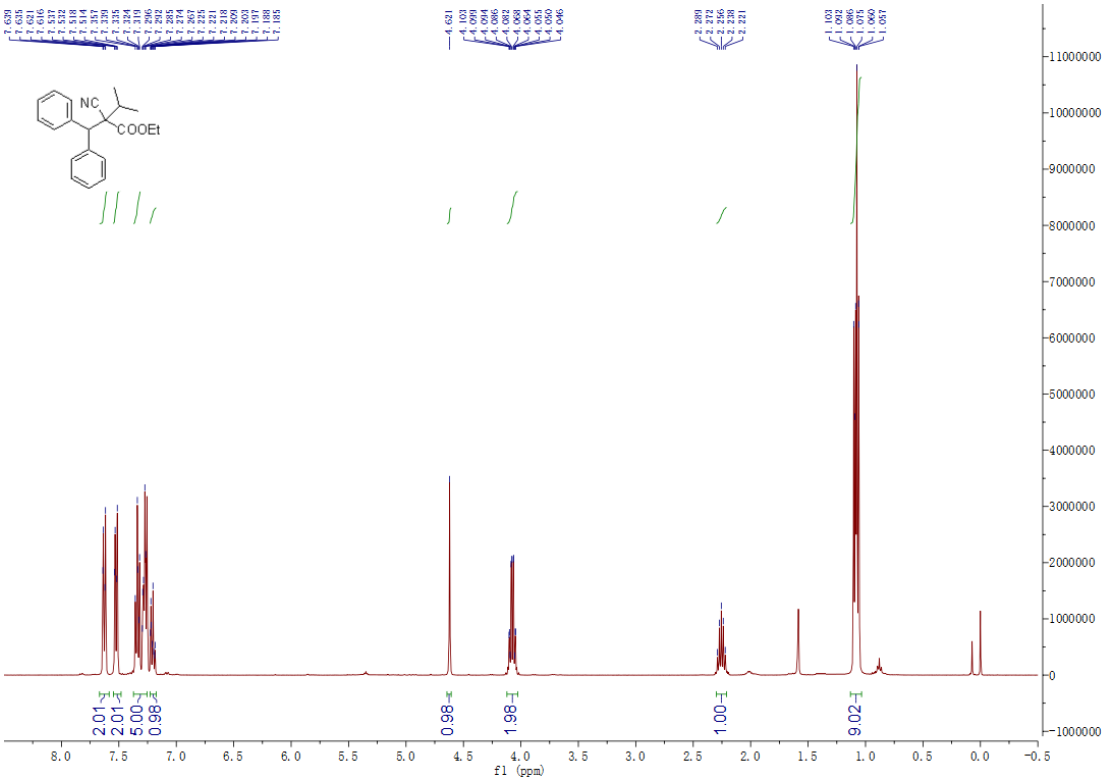

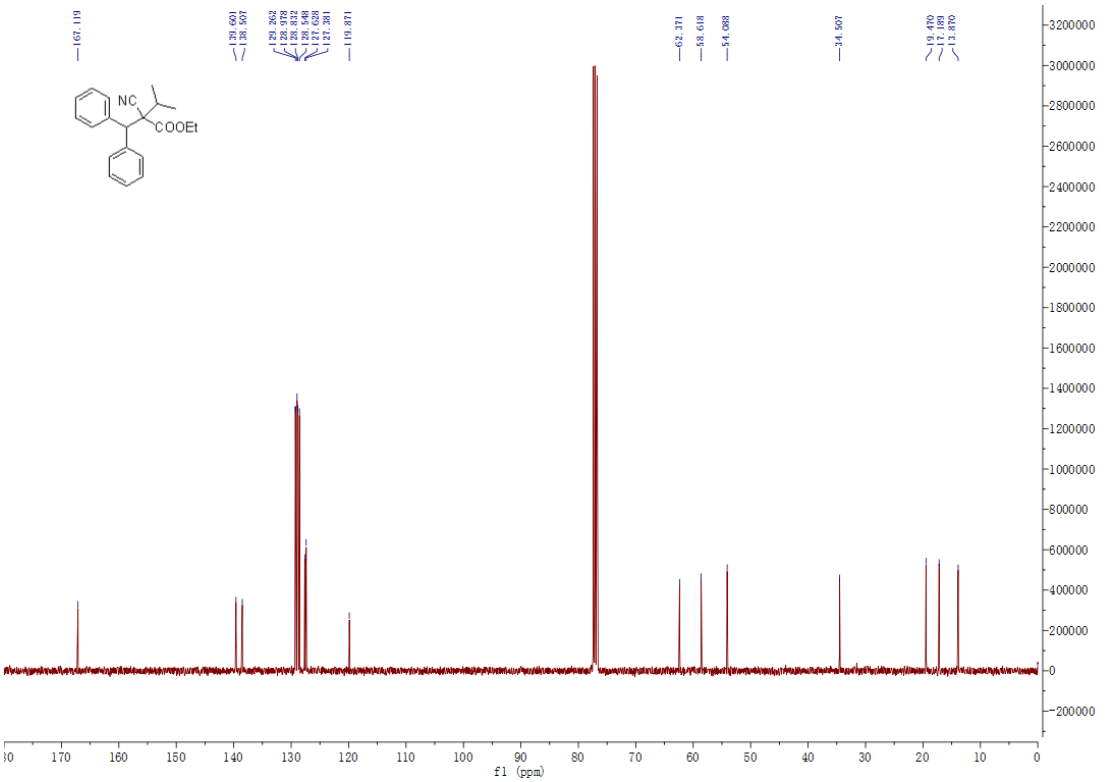

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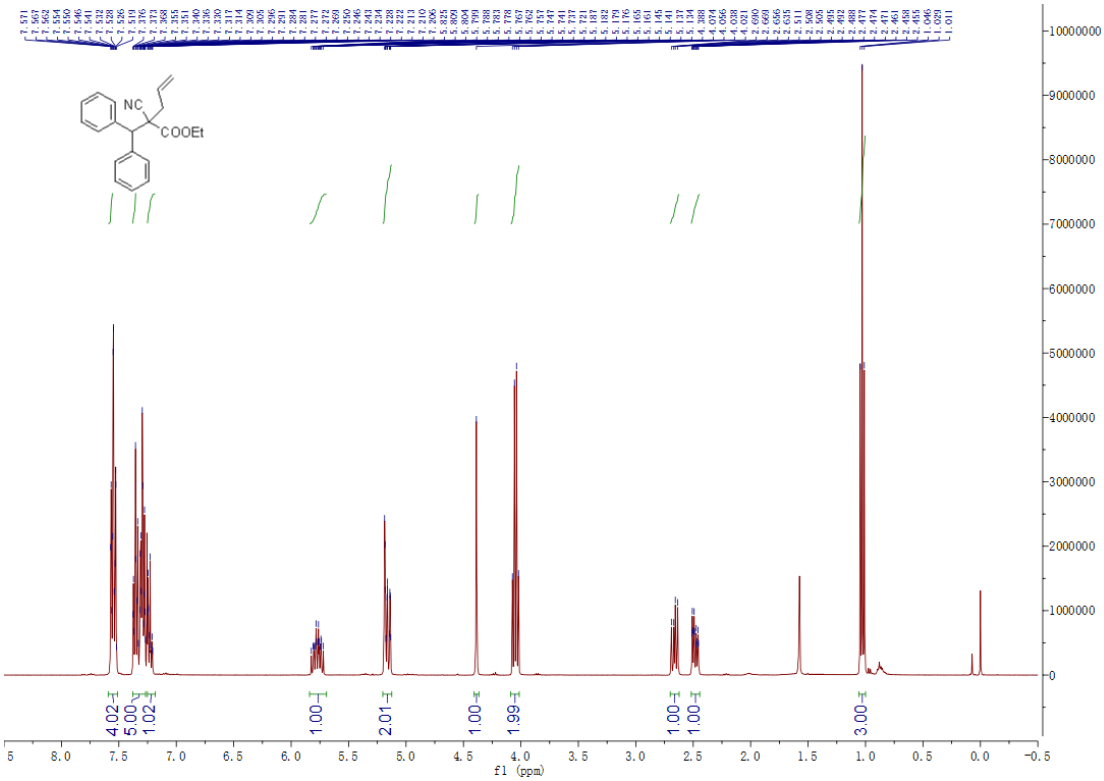
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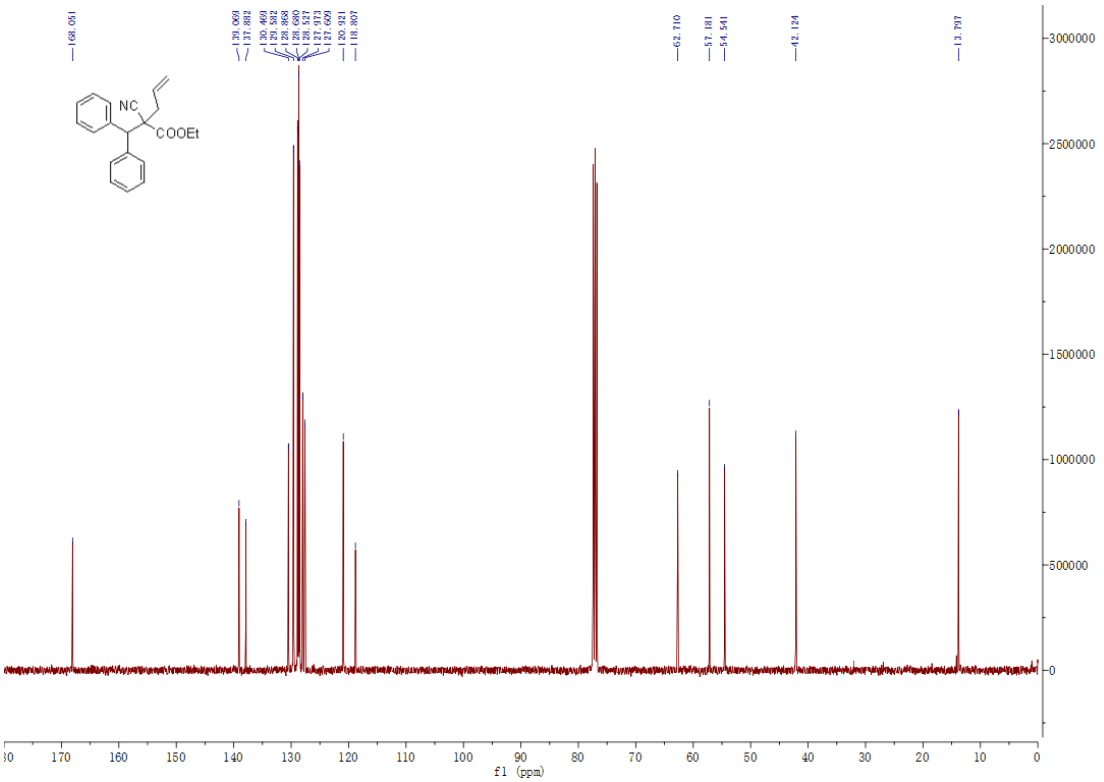
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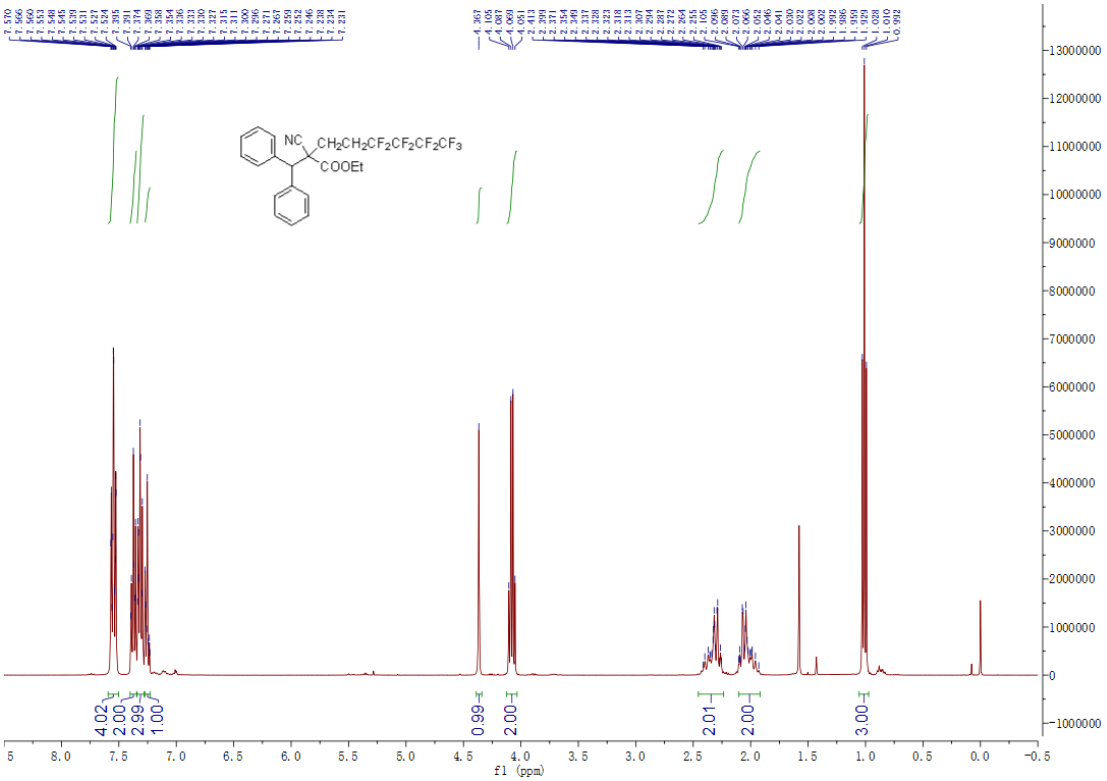
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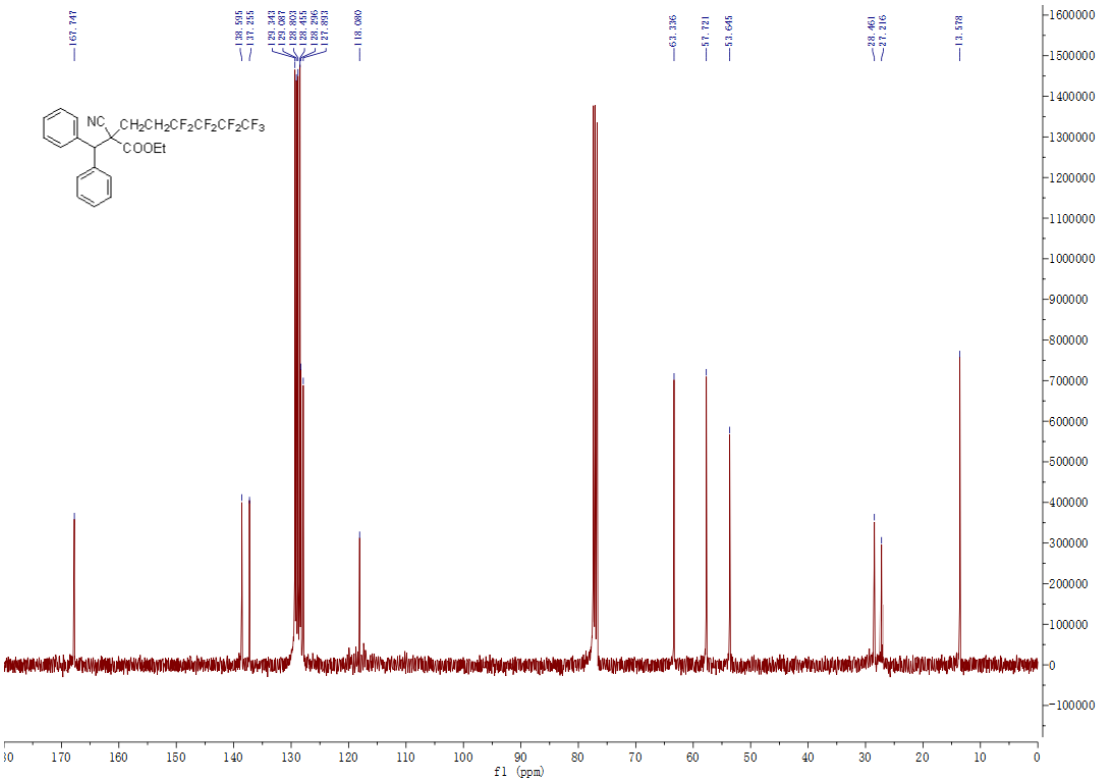
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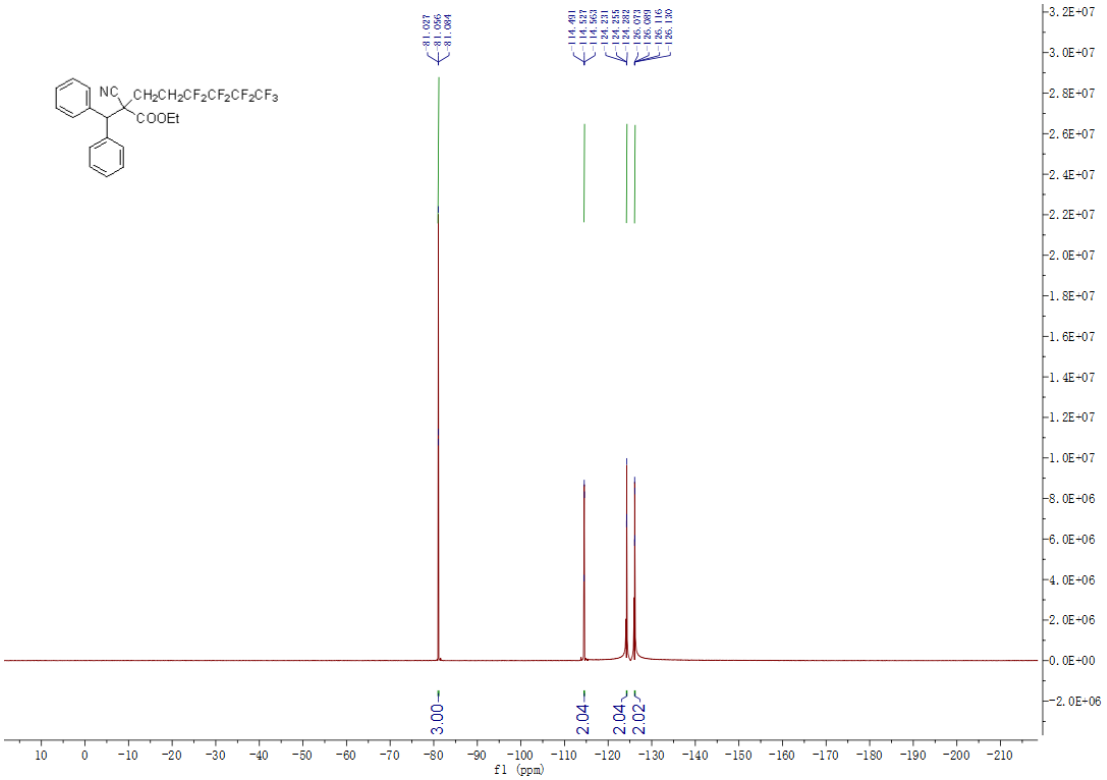

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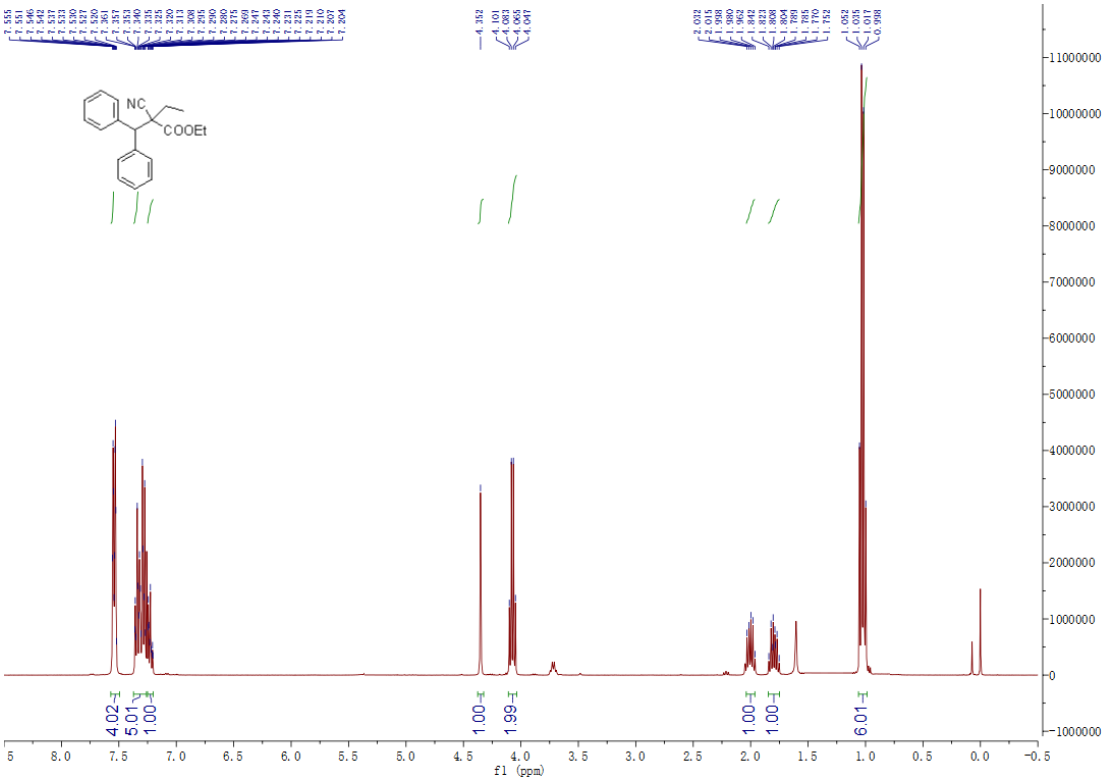

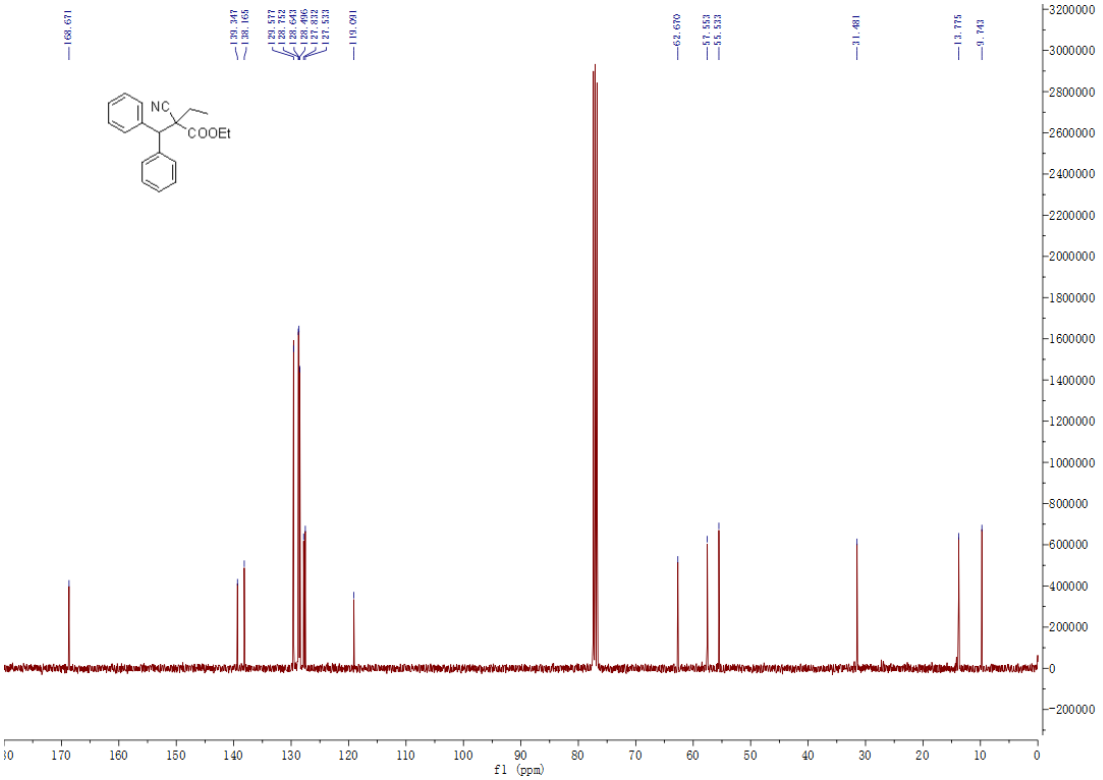
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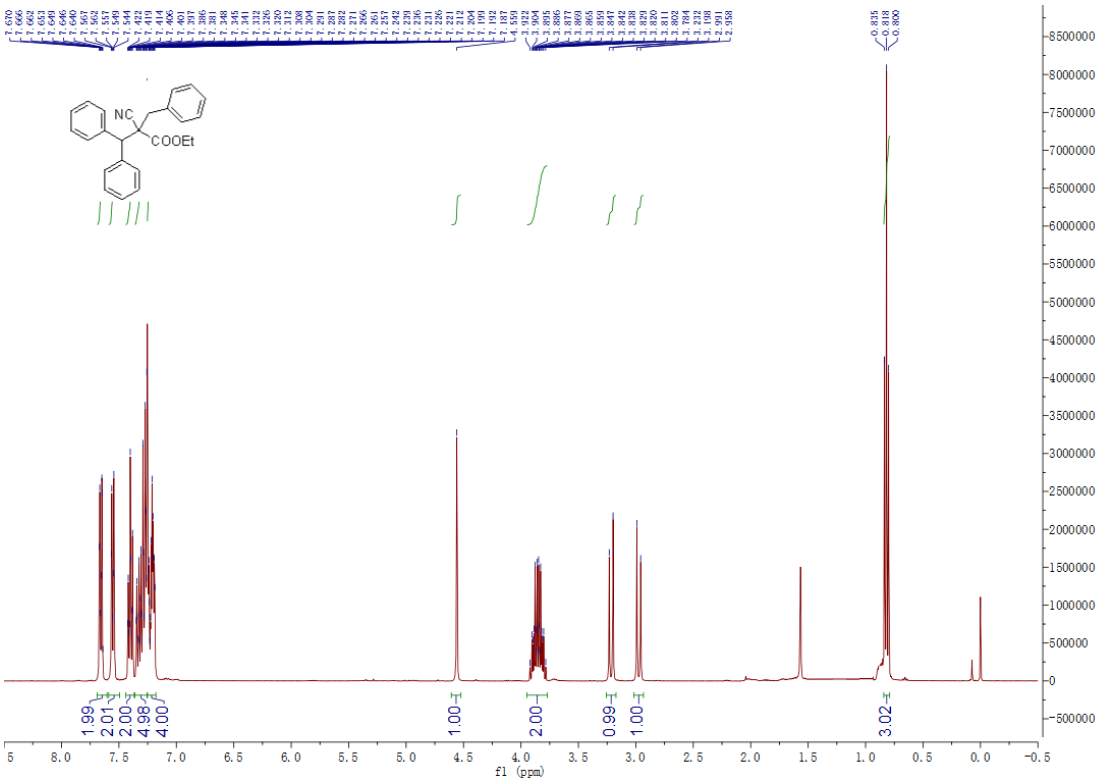
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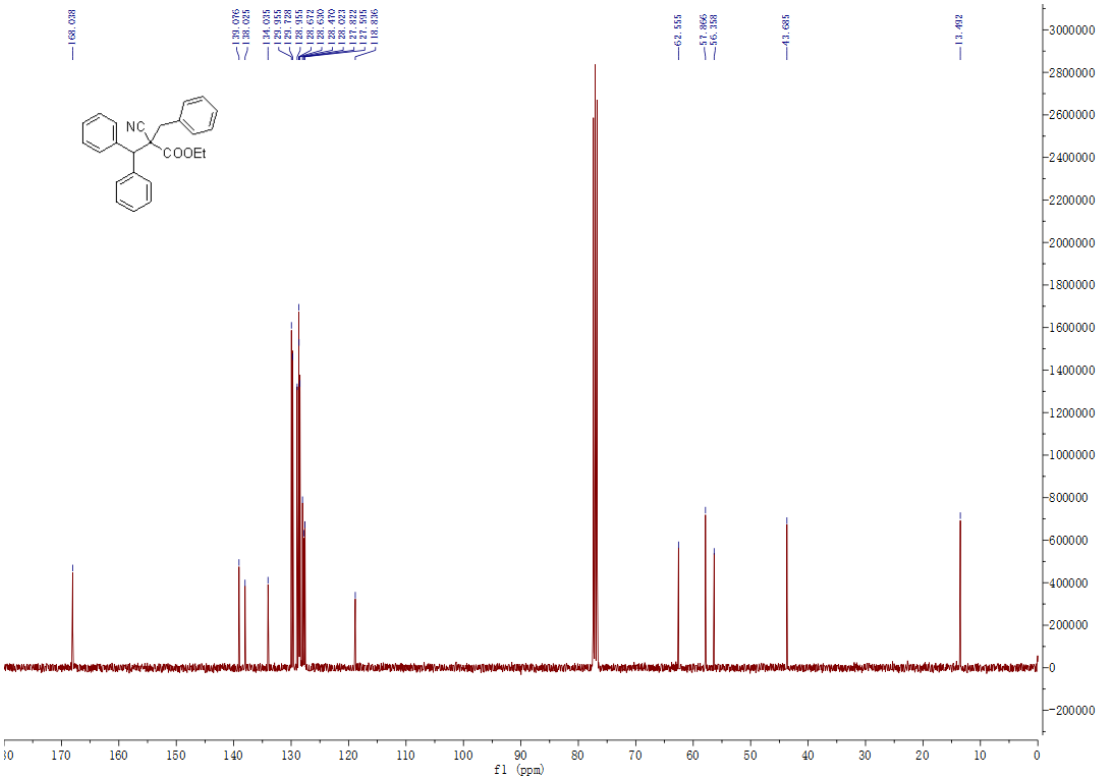

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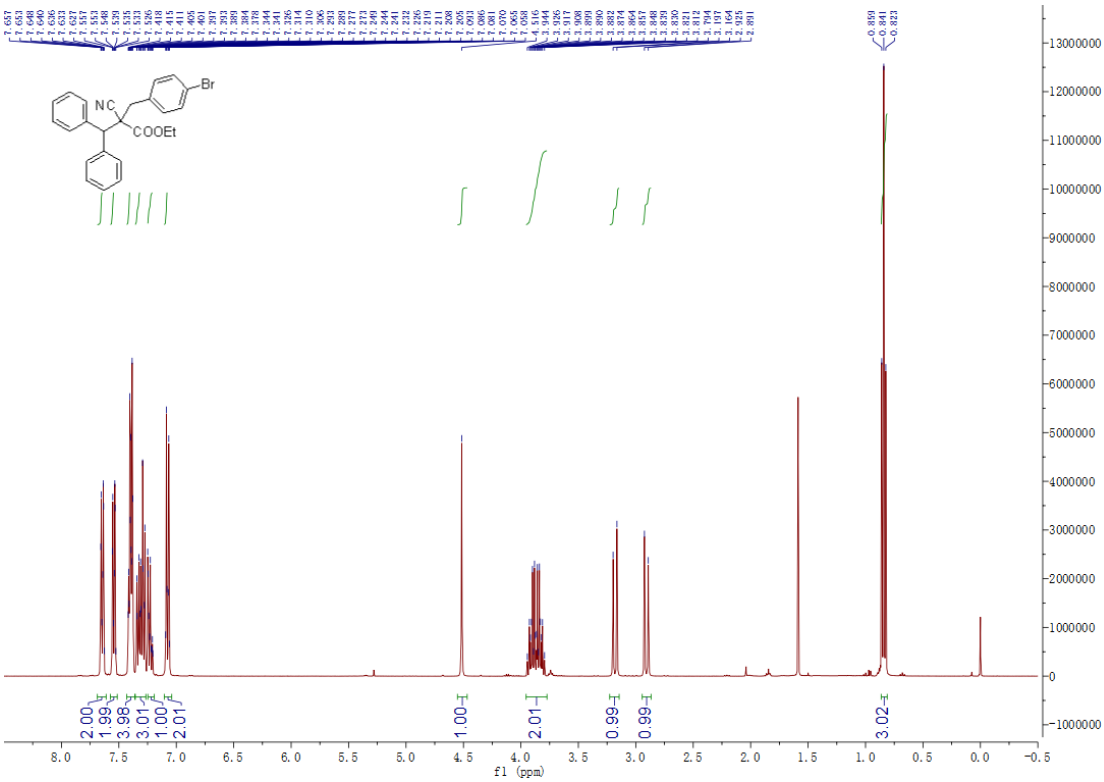

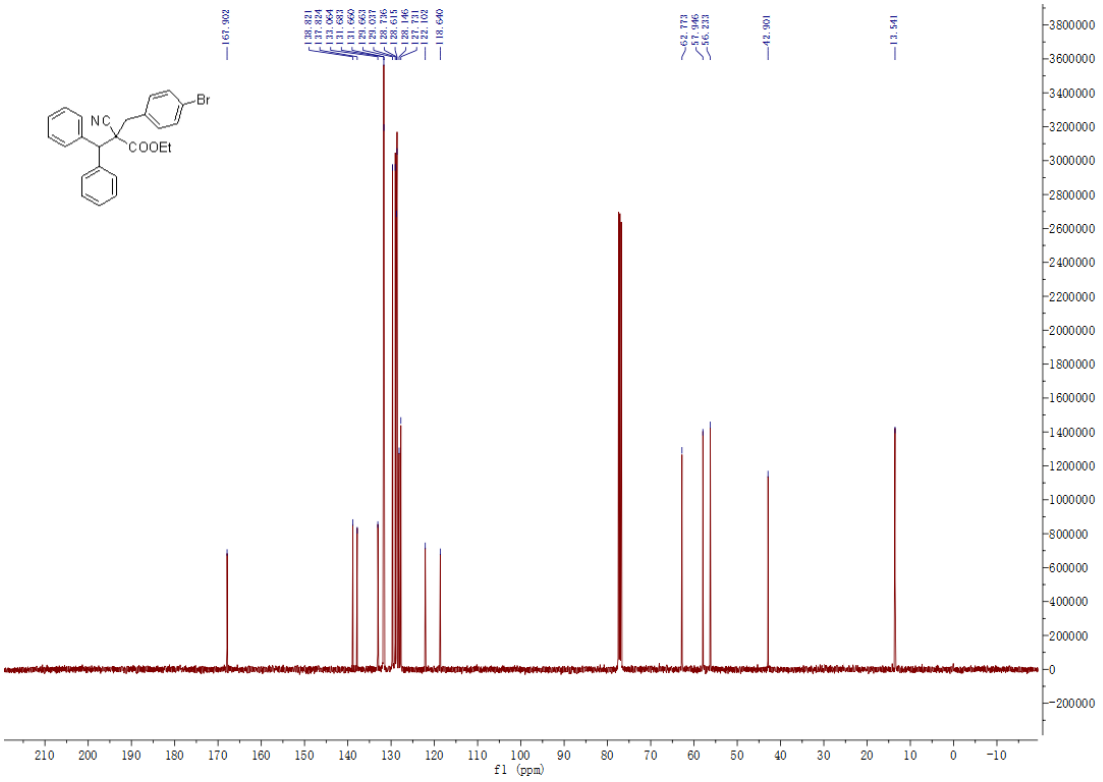
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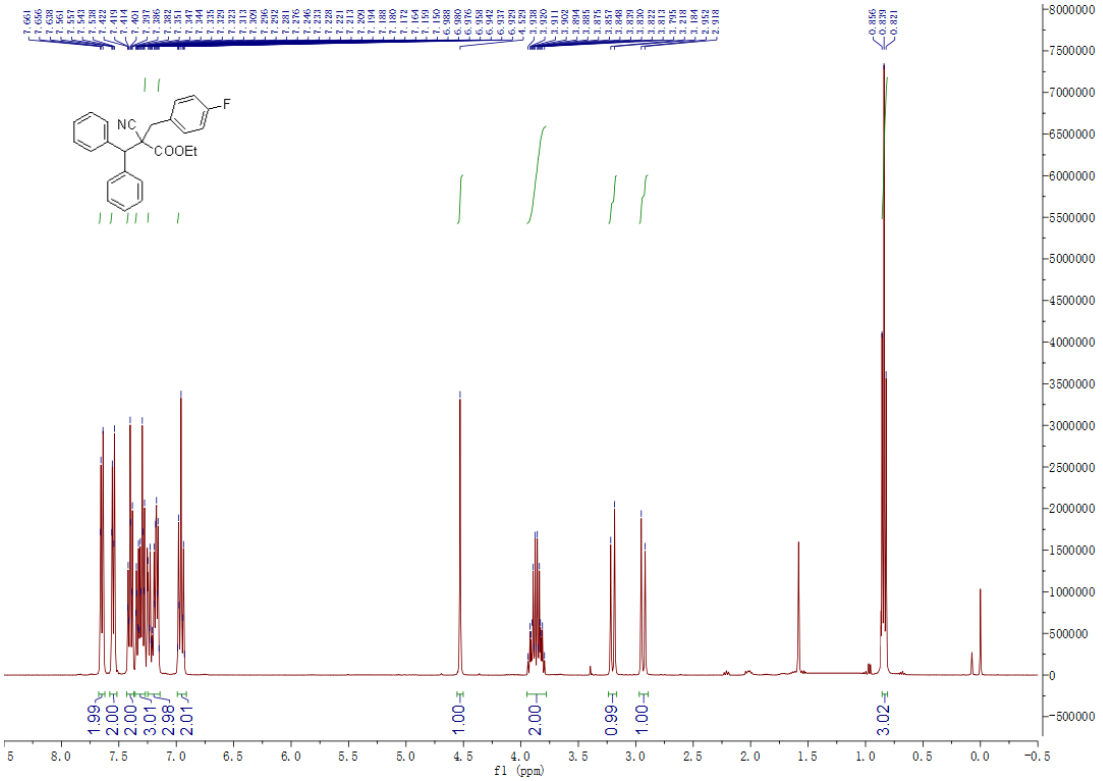
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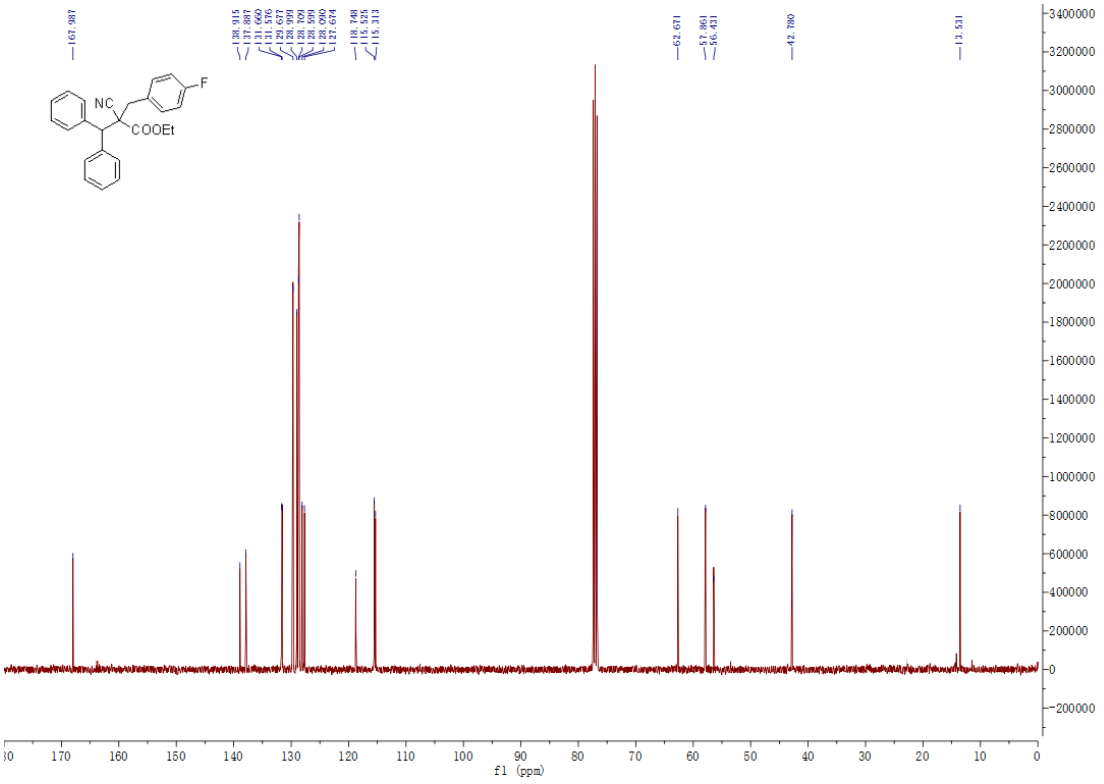
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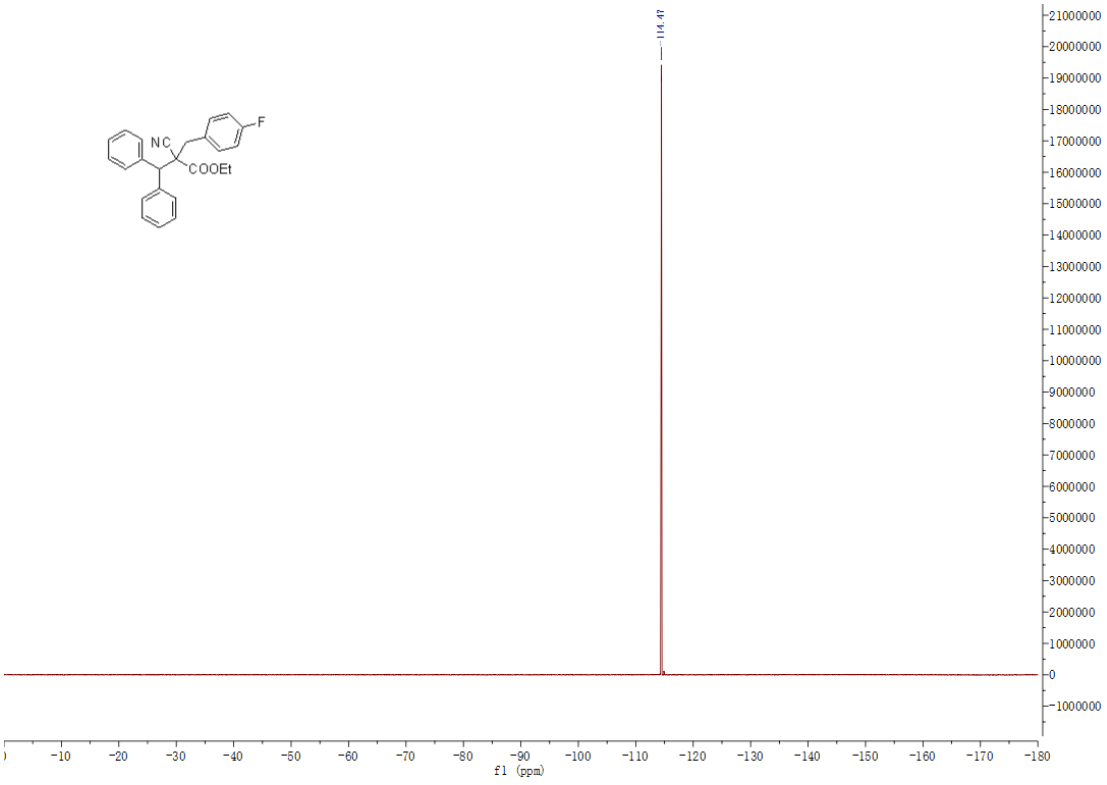
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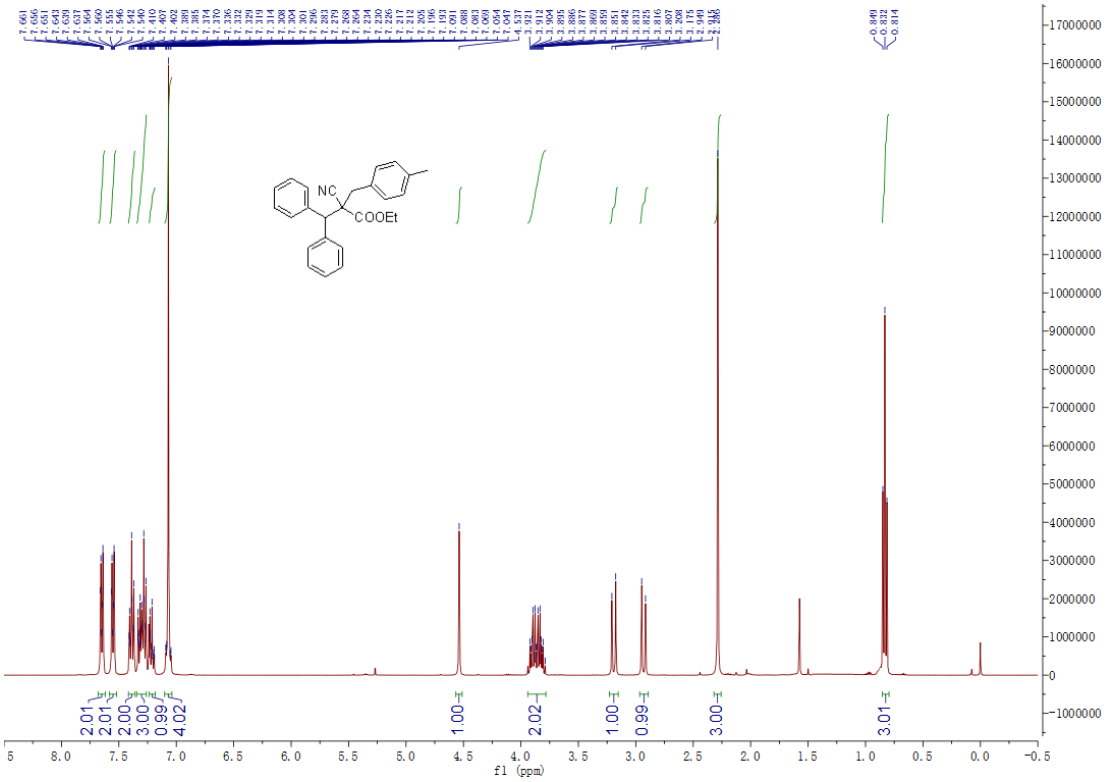
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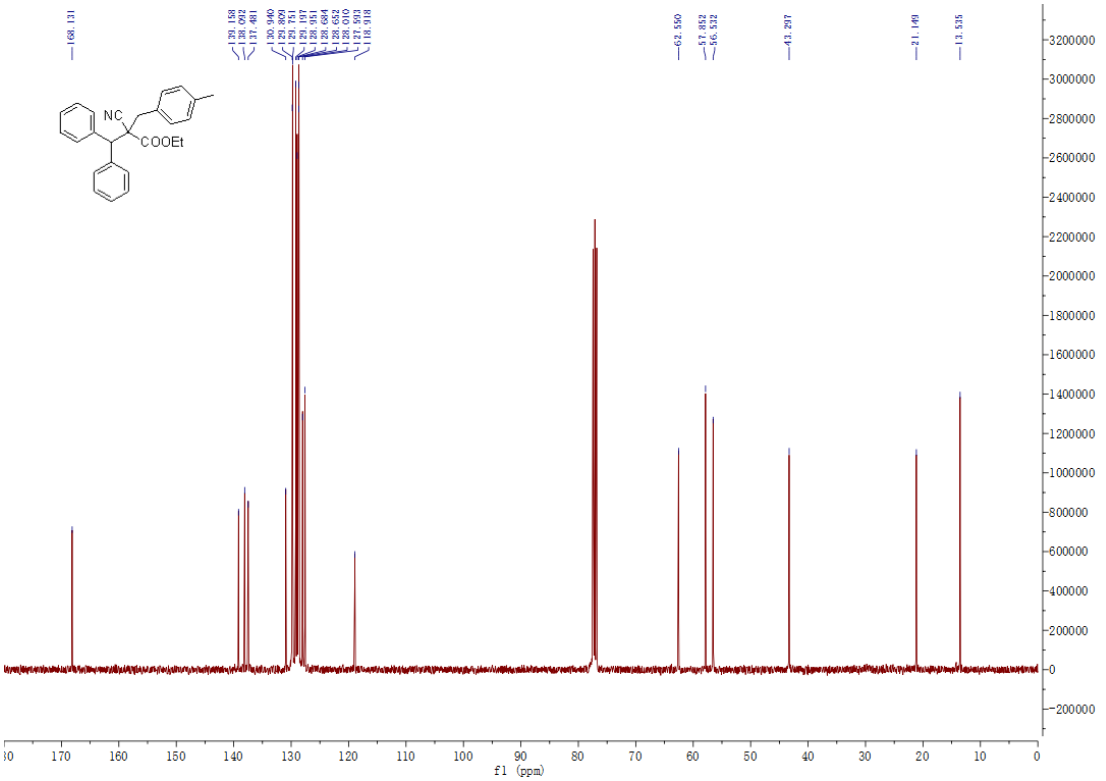
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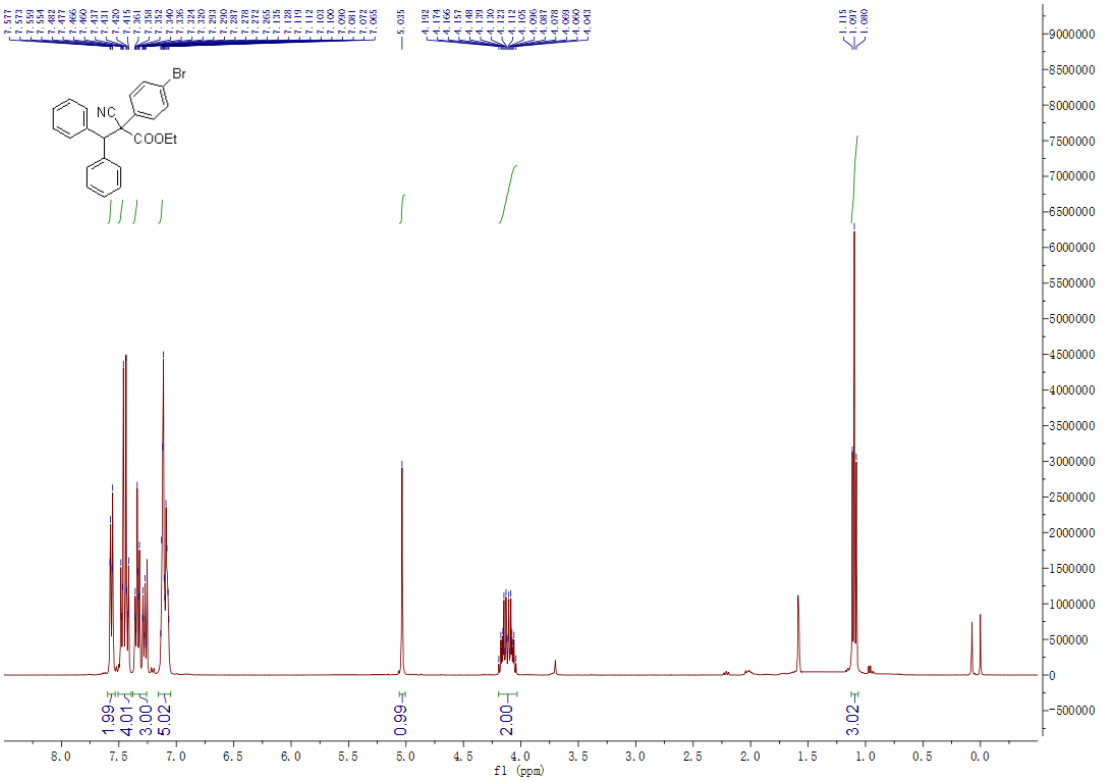

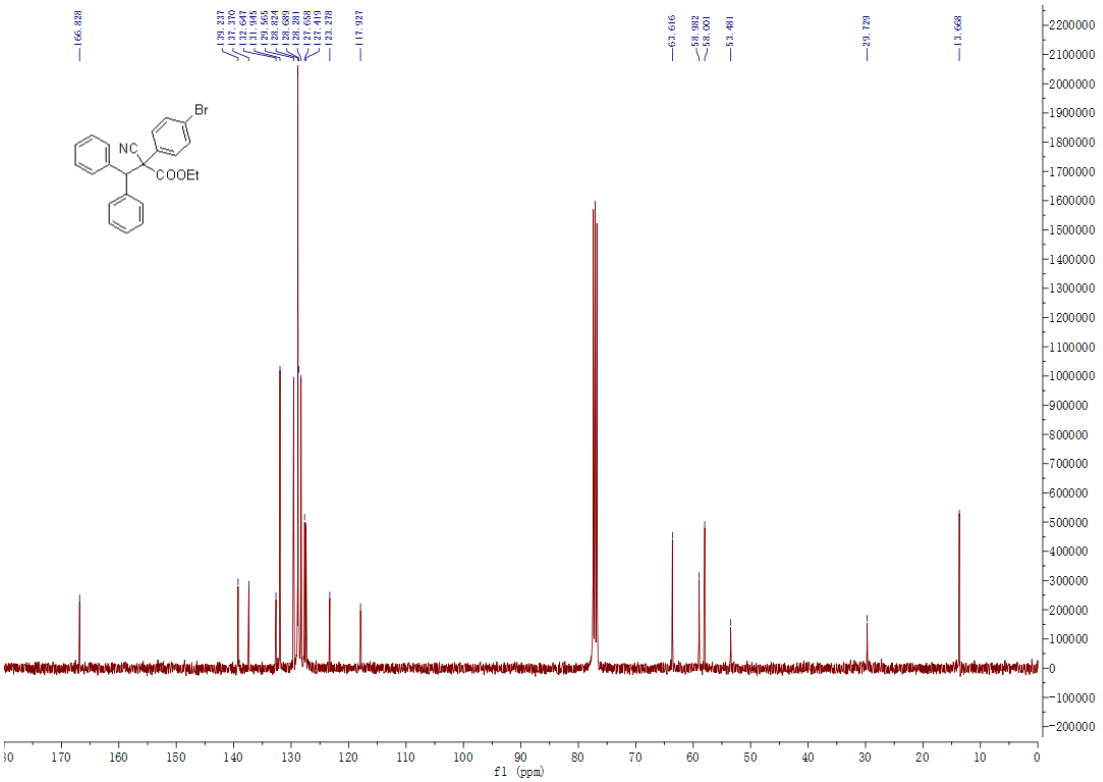

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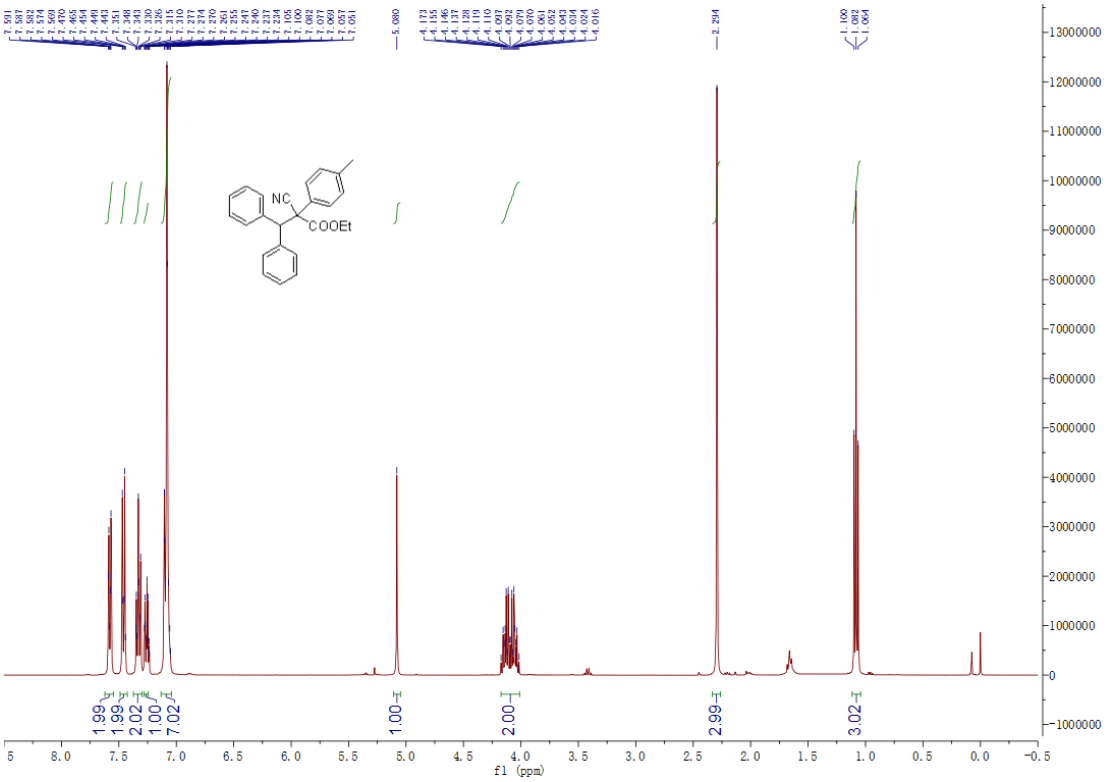
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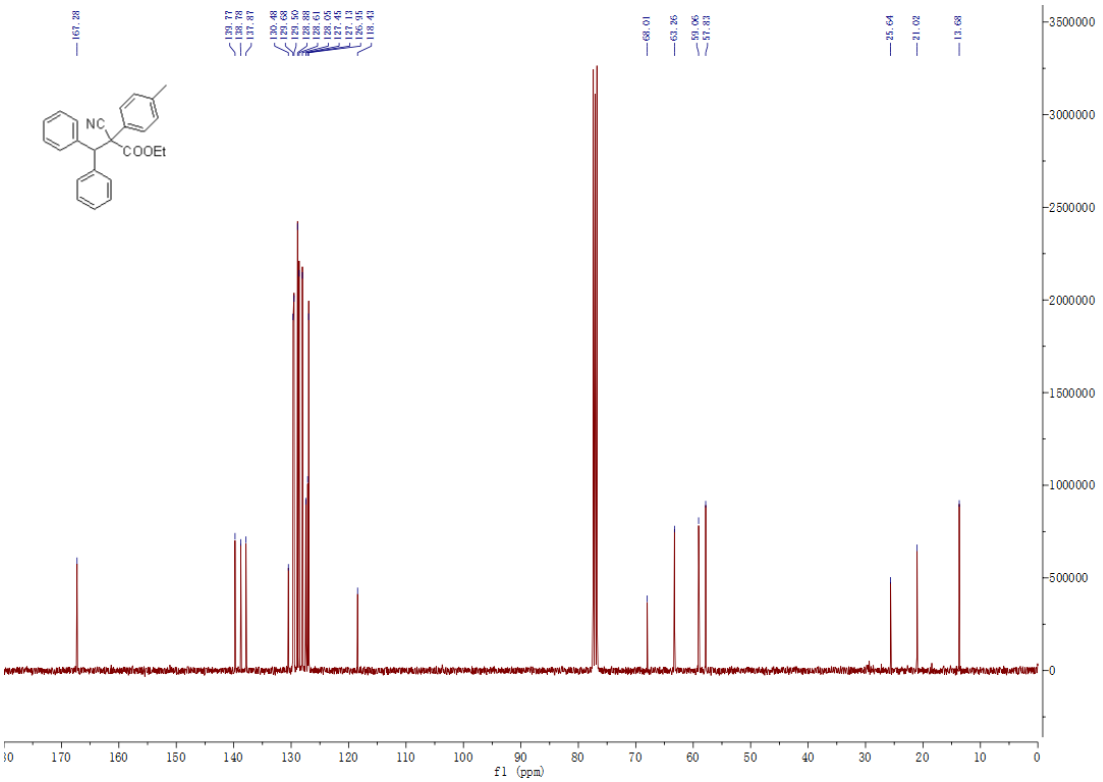
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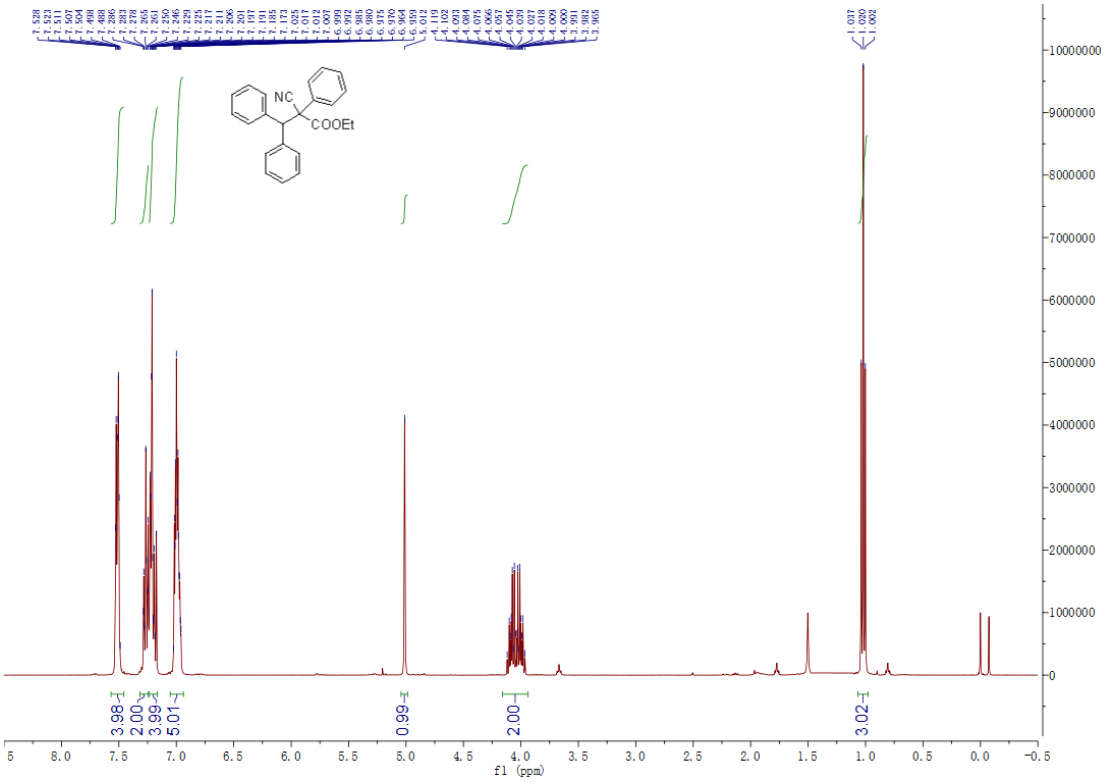

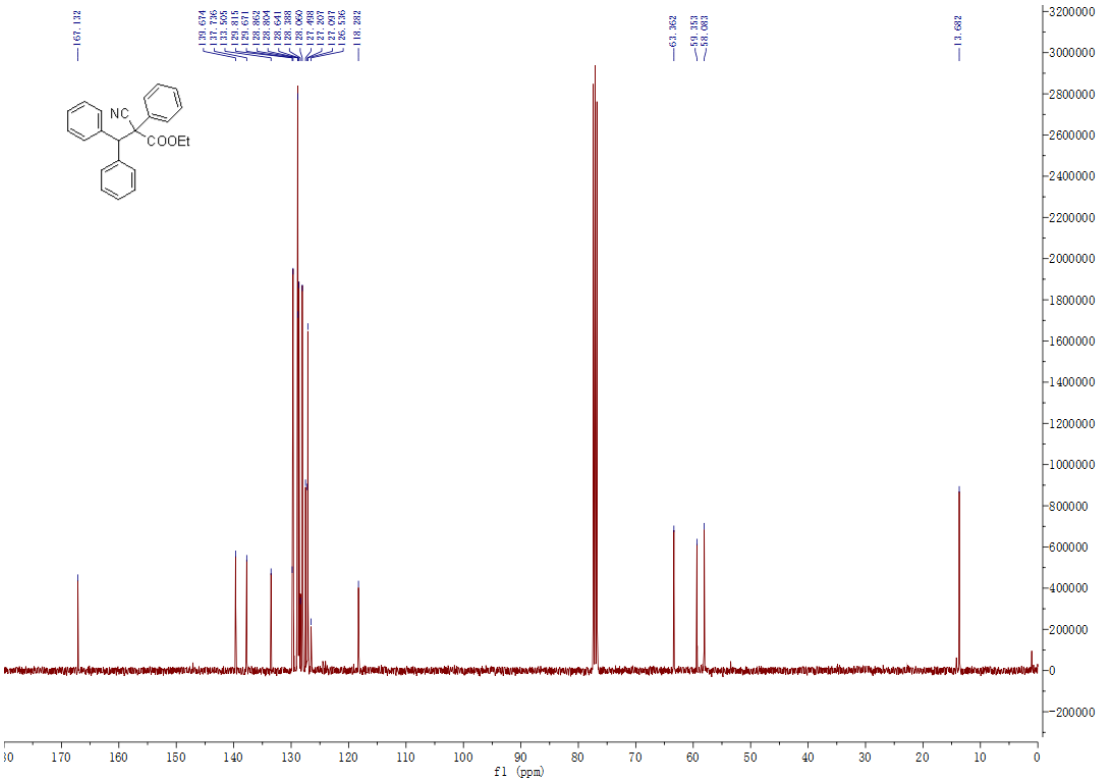

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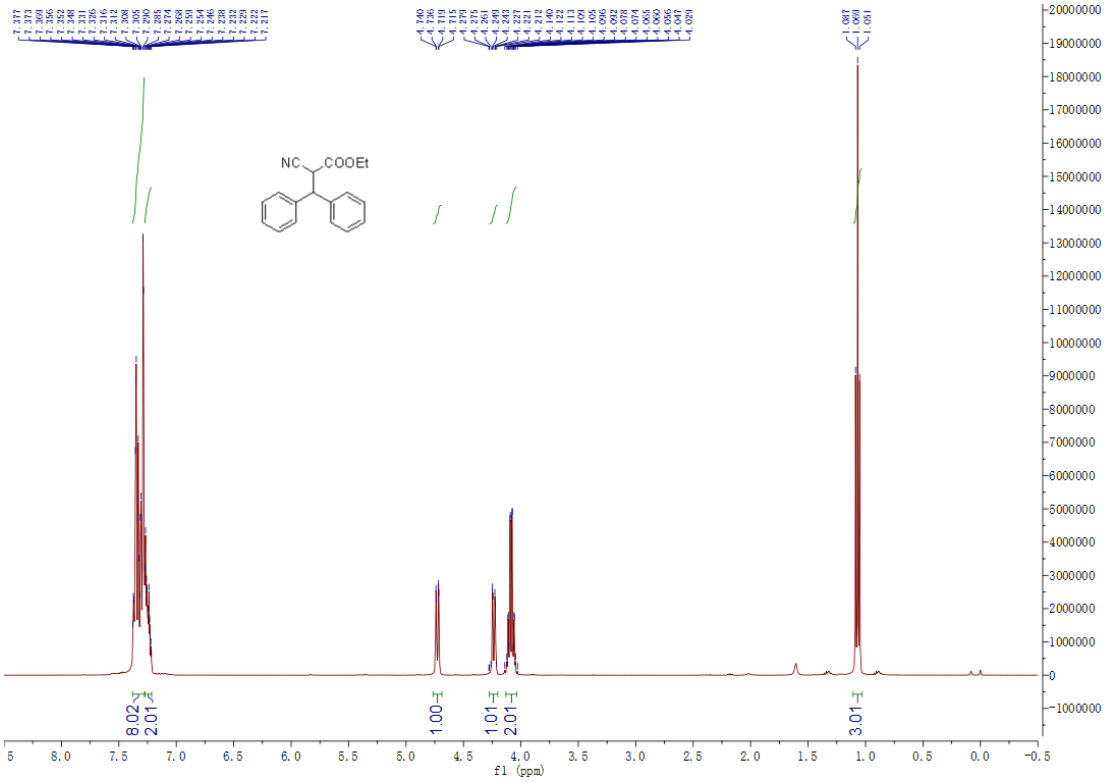
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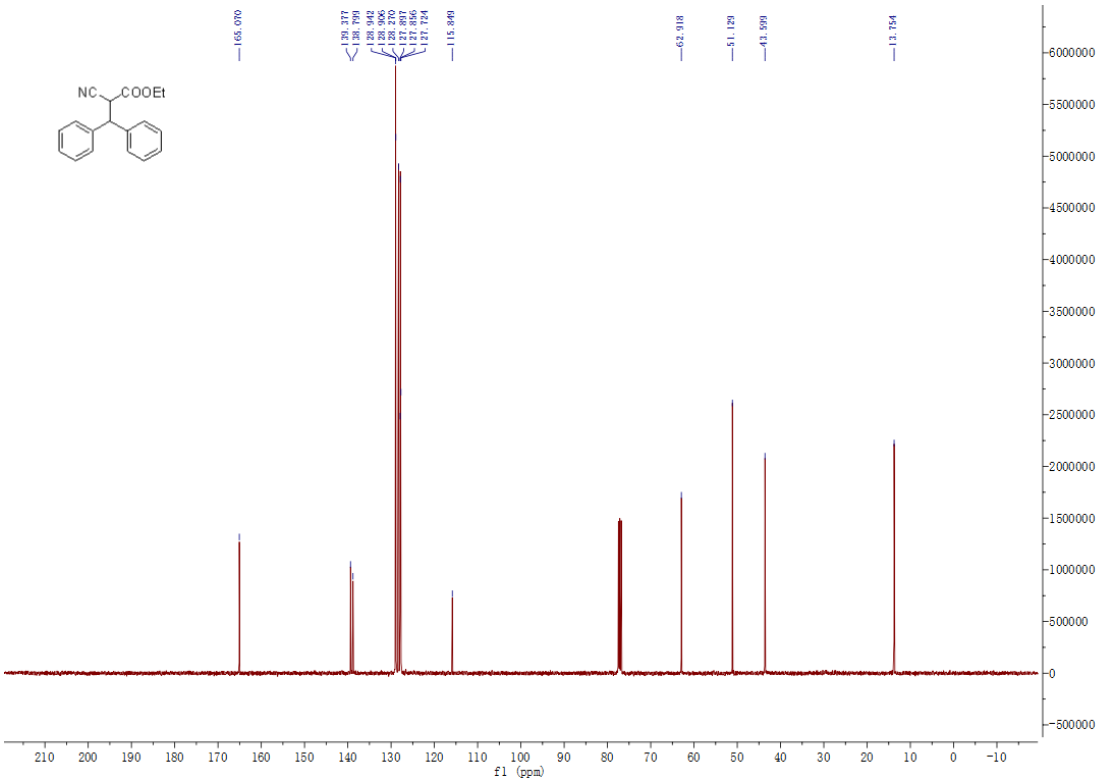
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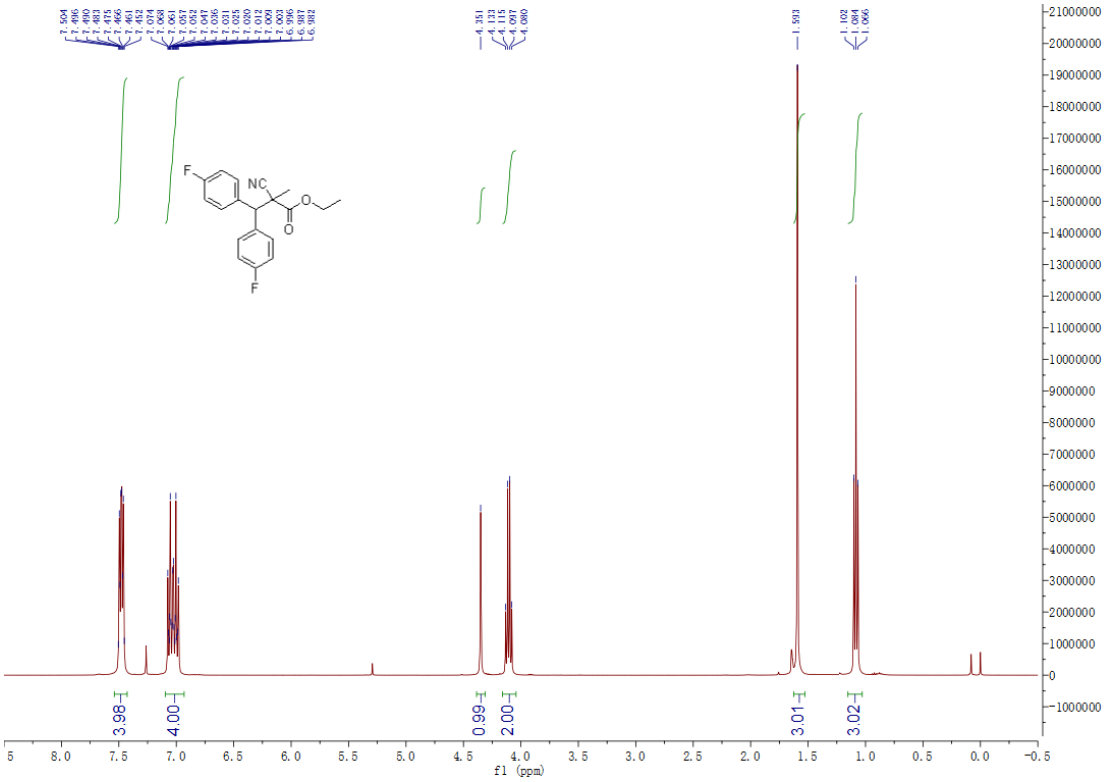

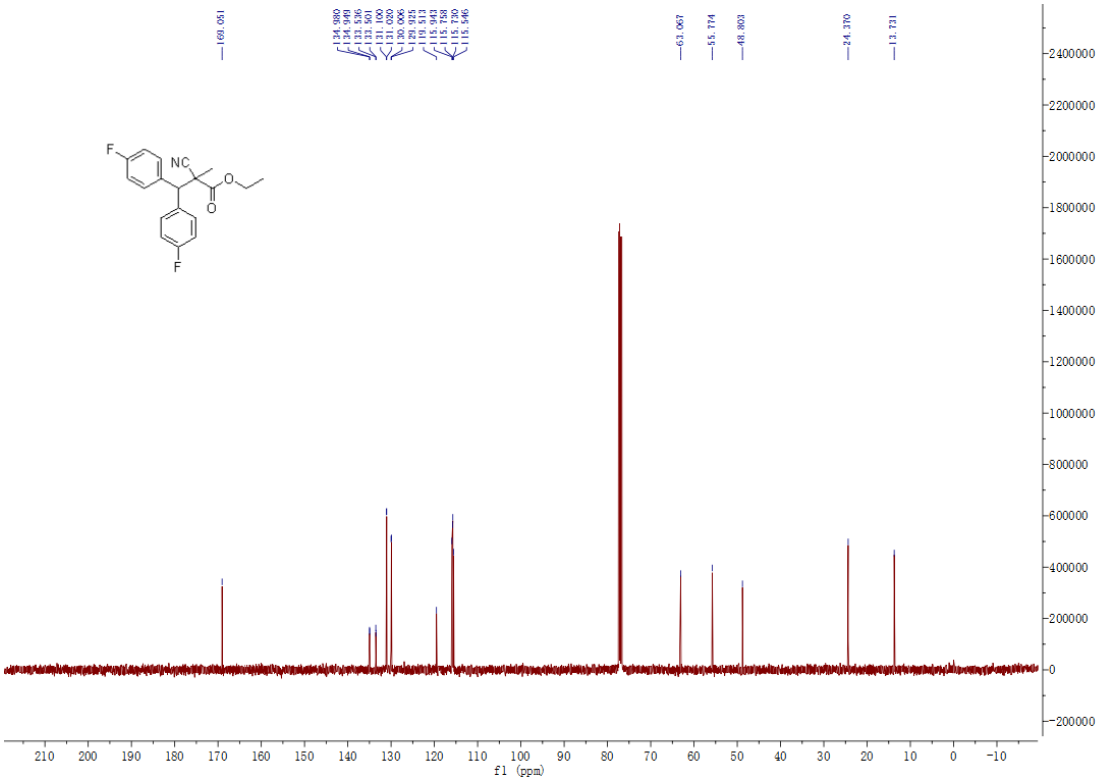

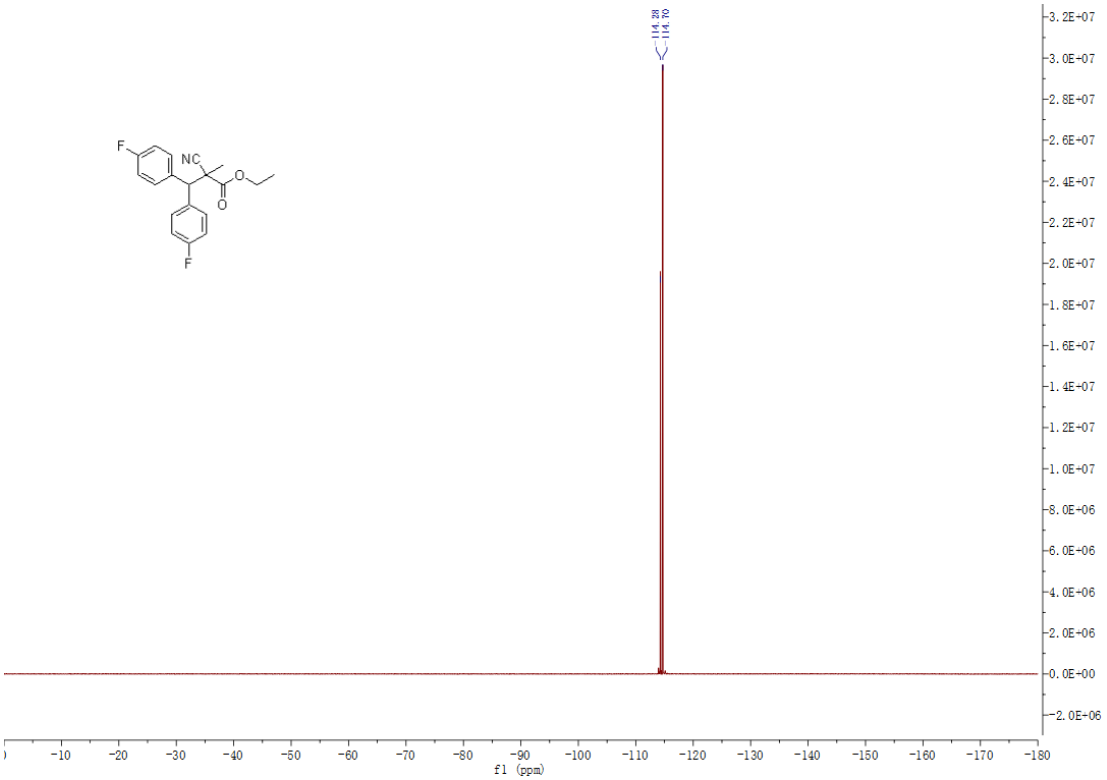
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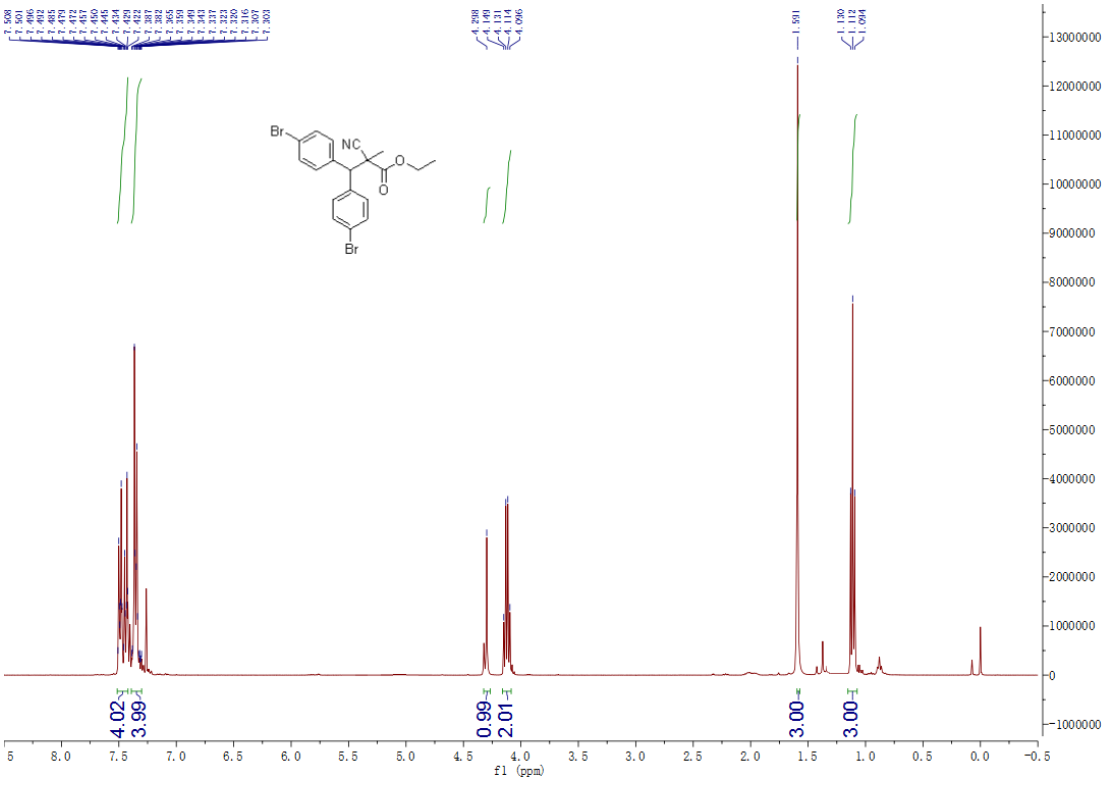
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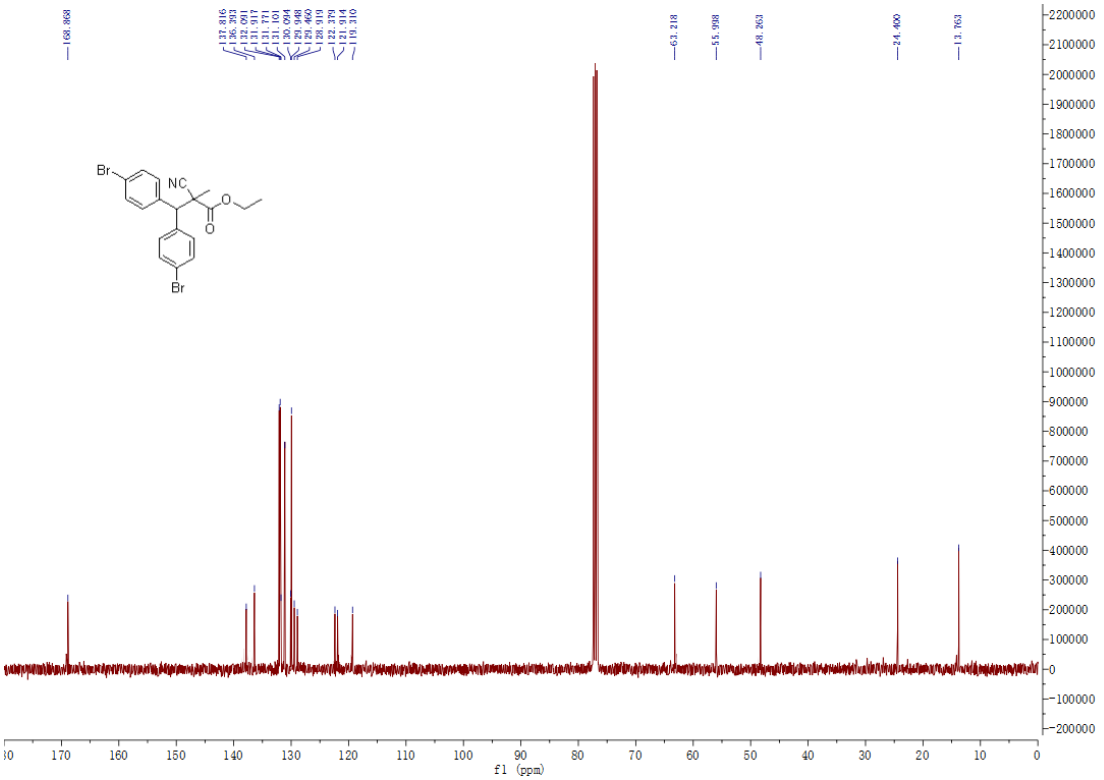
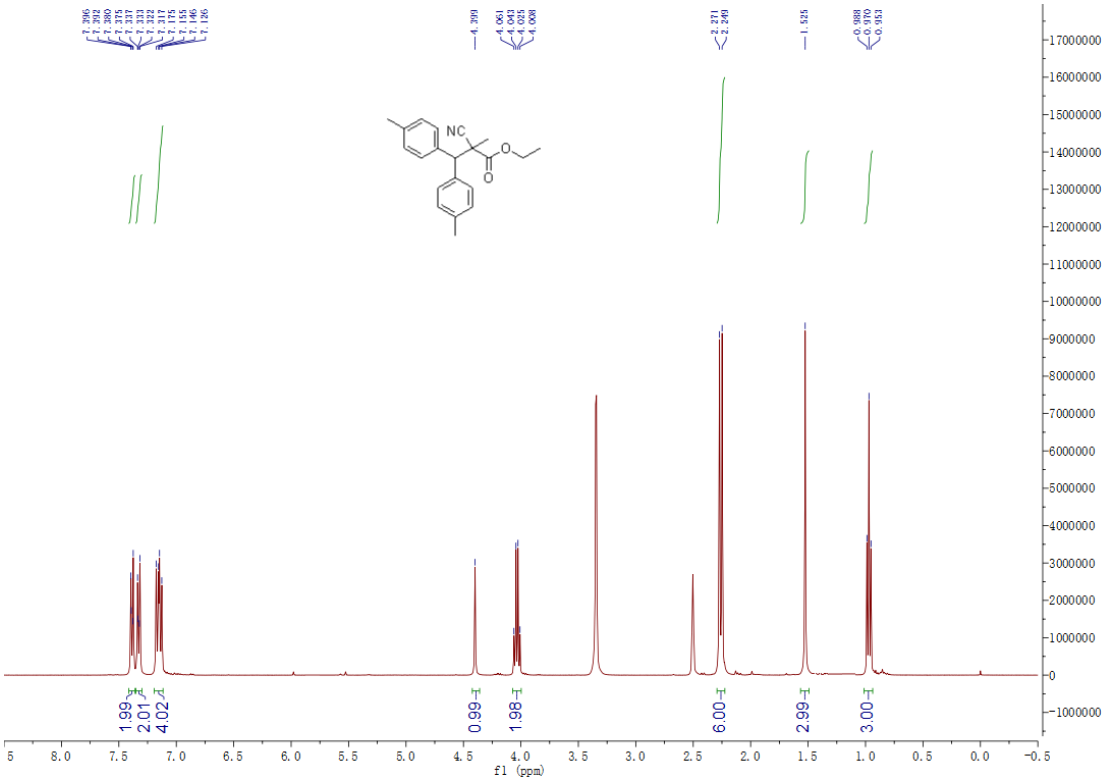
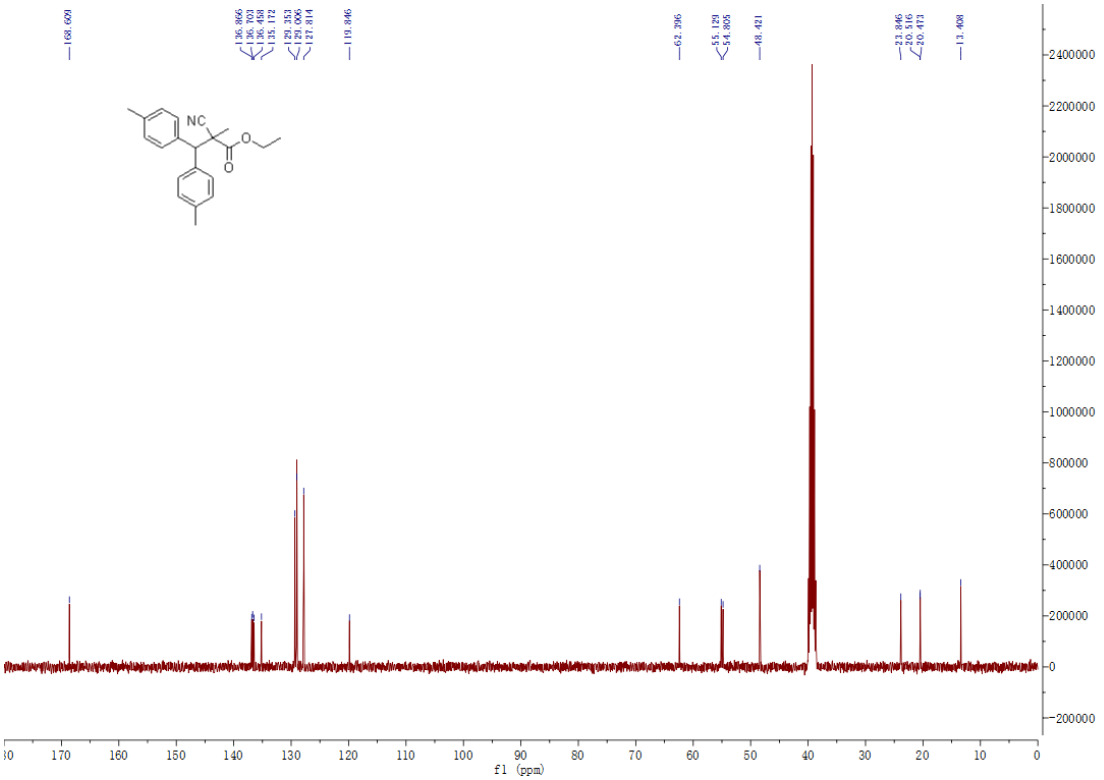
f1 (ppm)

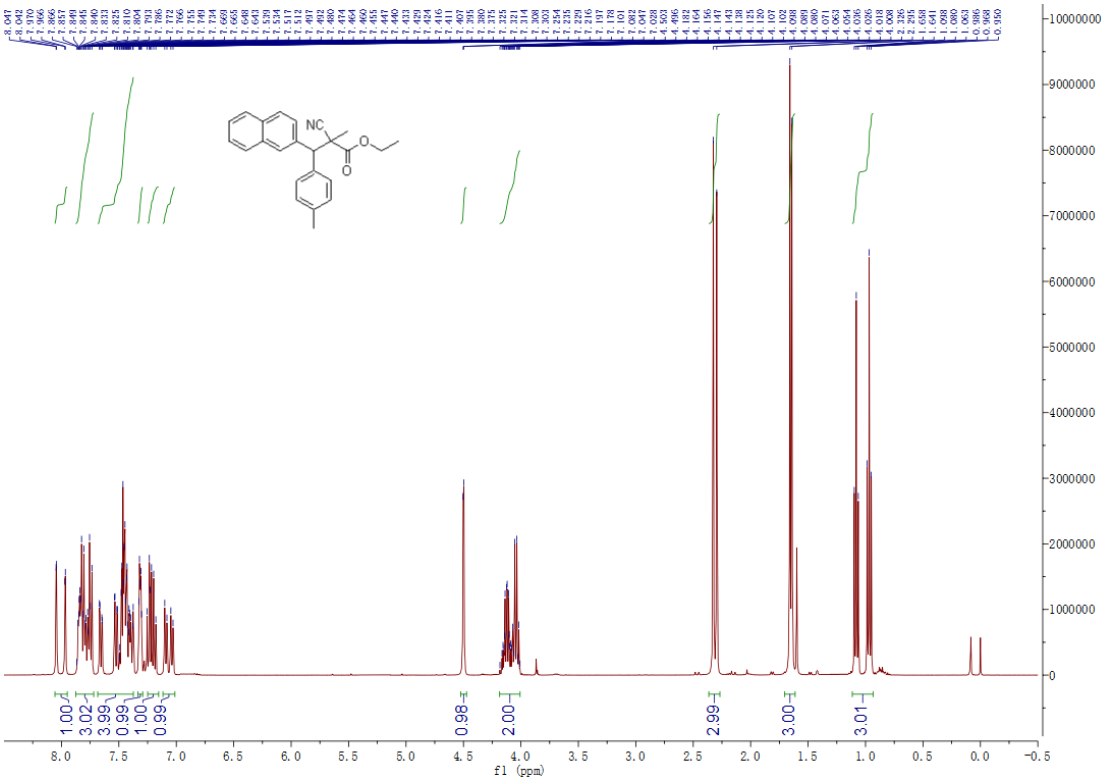

168.868
137.816
136.393
132.691
131.917
131.771
131.101
130.094
129.948
129.460
128.919
122.379
121.914
119.310
63.218
55.998
48.863
24.400
13.763
Br
NC
O
O
Br
f1 (ppm)

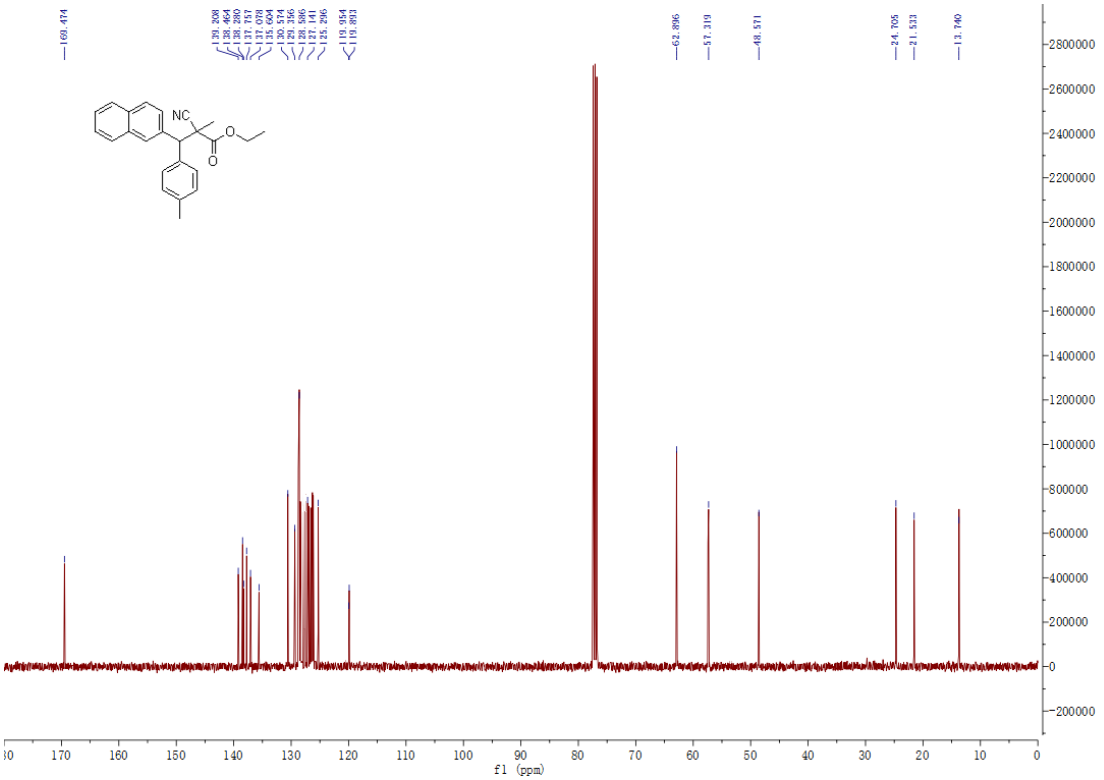
3t


7.396
7.392
7.380
7.375
7.337
7.333
7.322
7.317
7.175
7.155
7.146
7.126
4.399
4.061
4.043
4.025
4.008
2.271
2.249
1.925
0.988
0.970
0.953
NC
O
O
1.99
2.01
4.02
0.99
1.98
6.00
2.99
3.00
f1 (ppm)

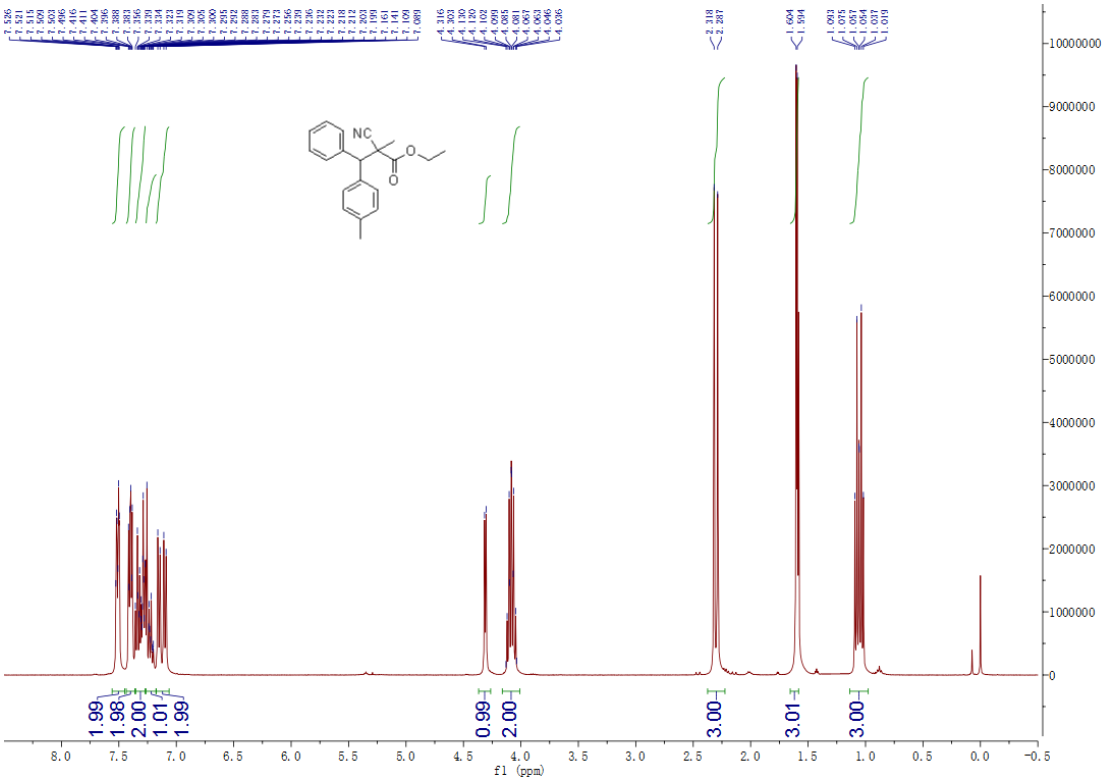

168.609
136.866
136.703
136.458
135.172
129.353
129.006
127.914
119.846
62.396
55.129
54.805
48.421
23.846
20.516
20.473
13.408
NC
O
O
f1 (ppm)

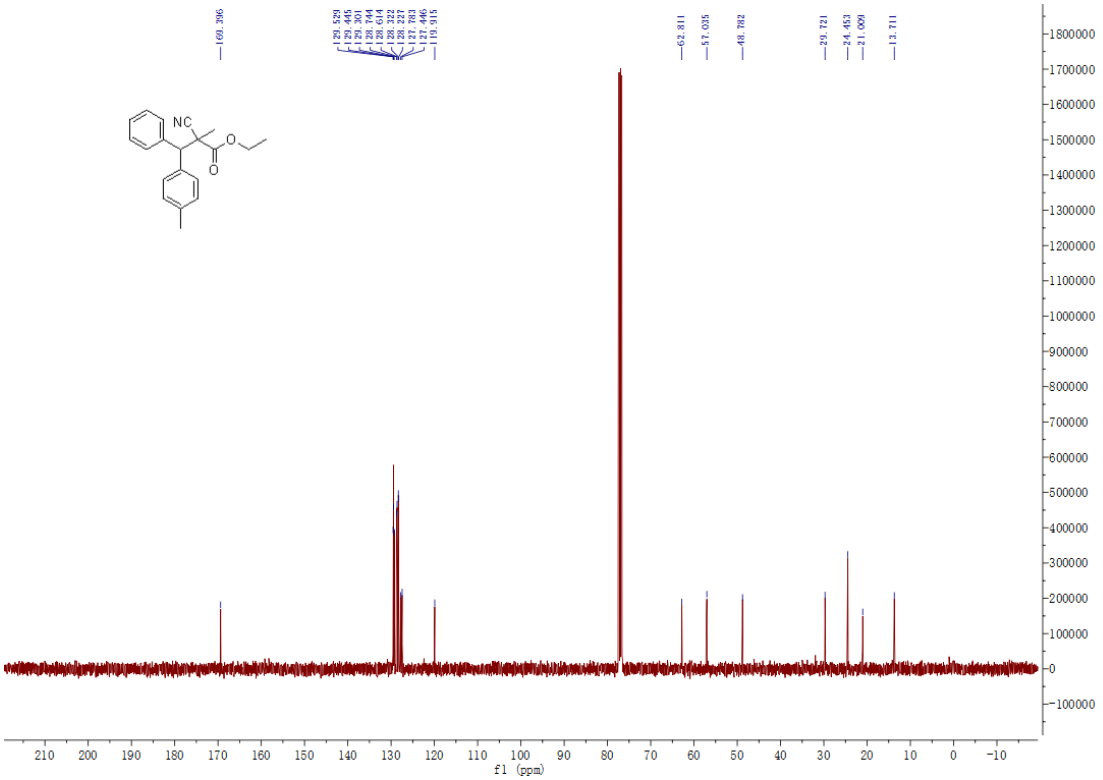
3u


NC
O
O
1.00
3.02
3.99
0.99
1.00
0.99
0.98
2.00
2.99
3.00
3.01
f1 (ppm)

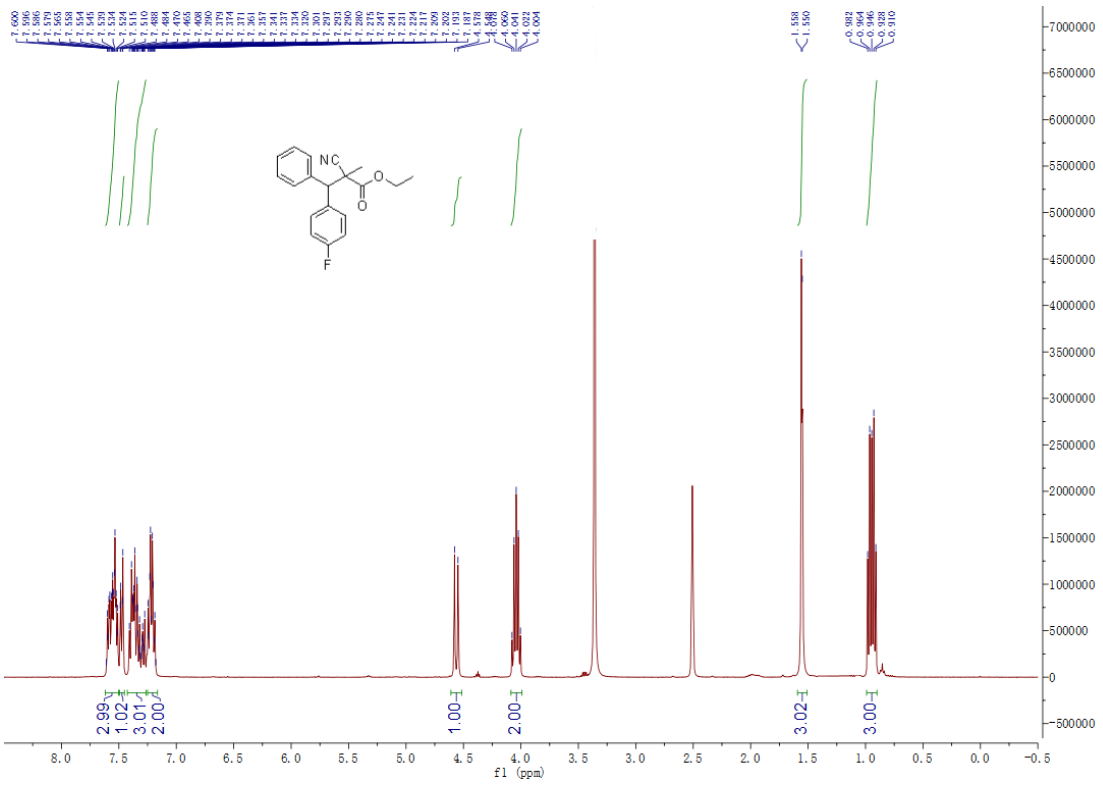


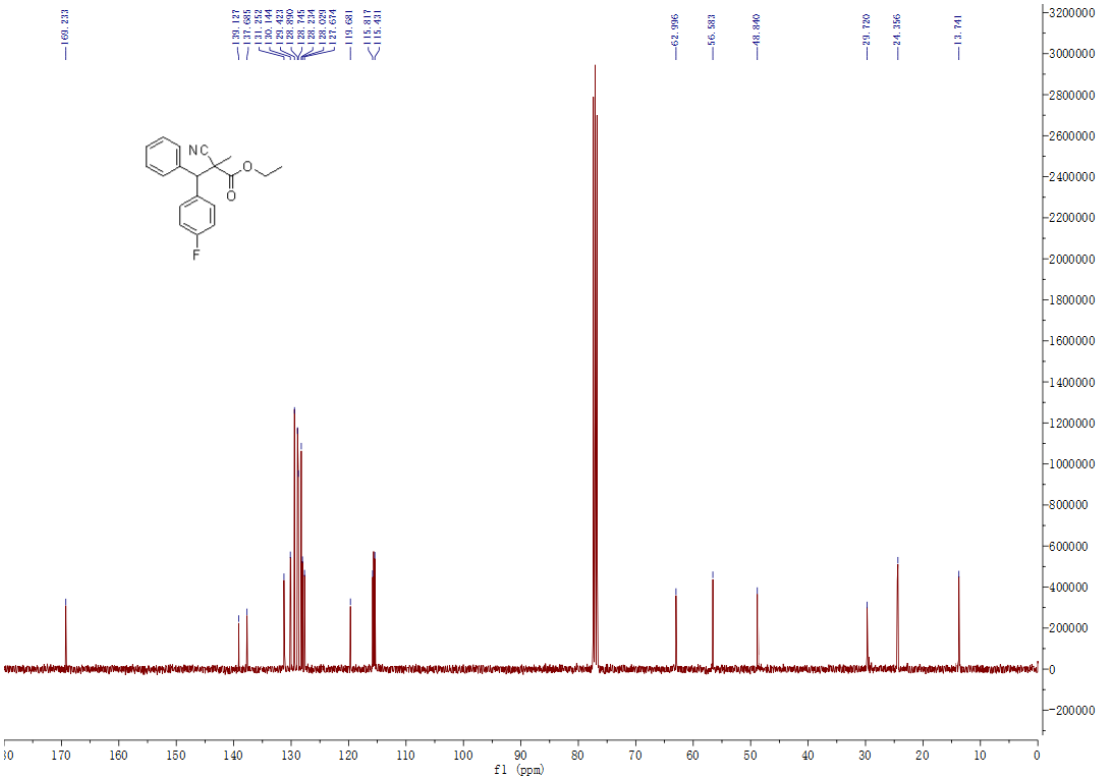
3v

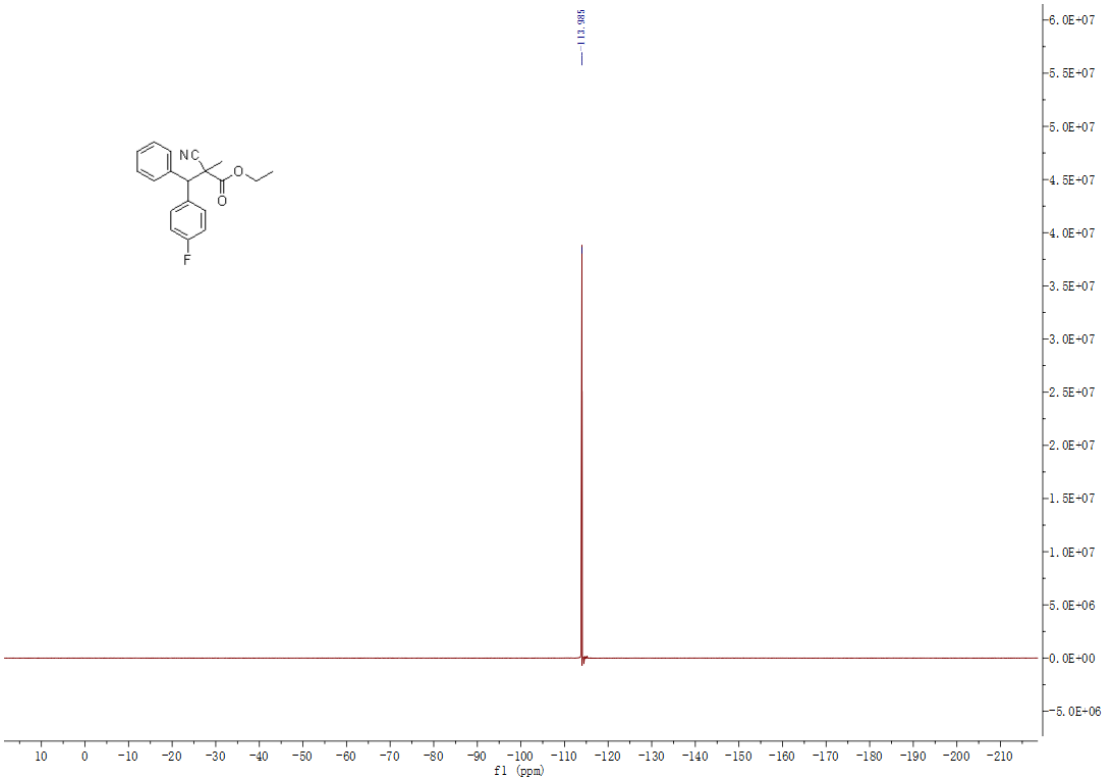



169.396
129.529
129.445
129.301
128.744
128.644
128.322
128.227
127.783
127.446
119.915
62.811
57.035
48.782
29.721
24.453
21.009
13.711
NC
O
O
f1 (ppm)

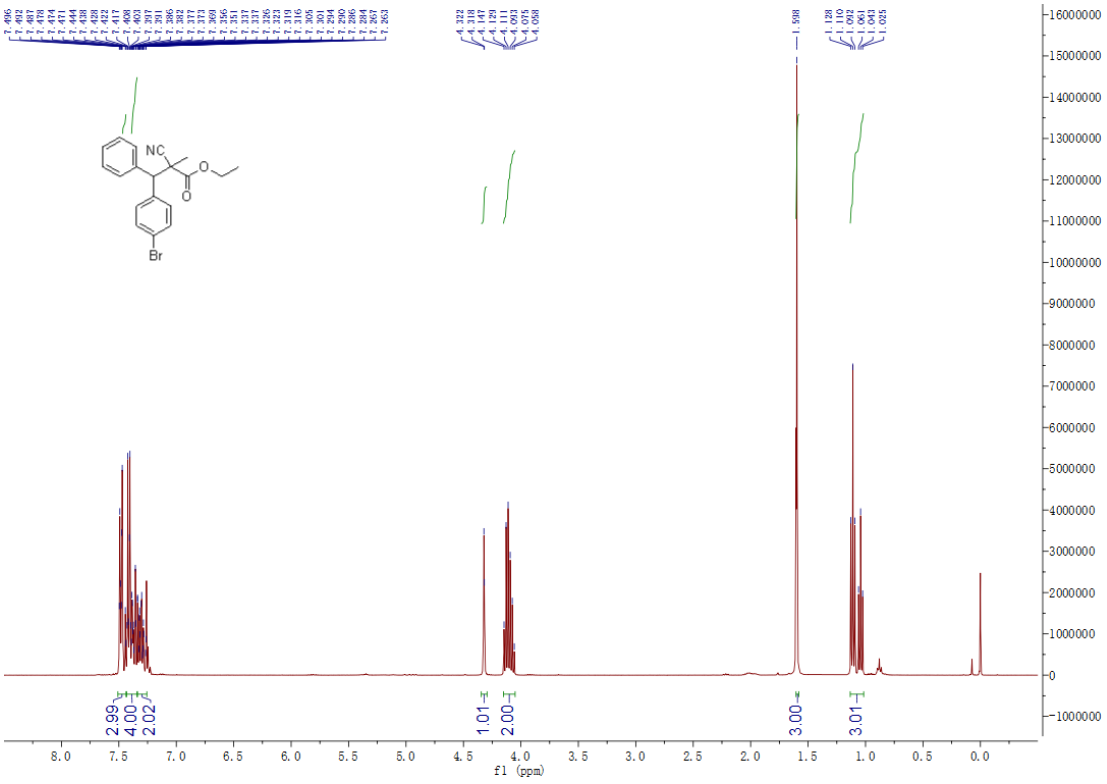
3w

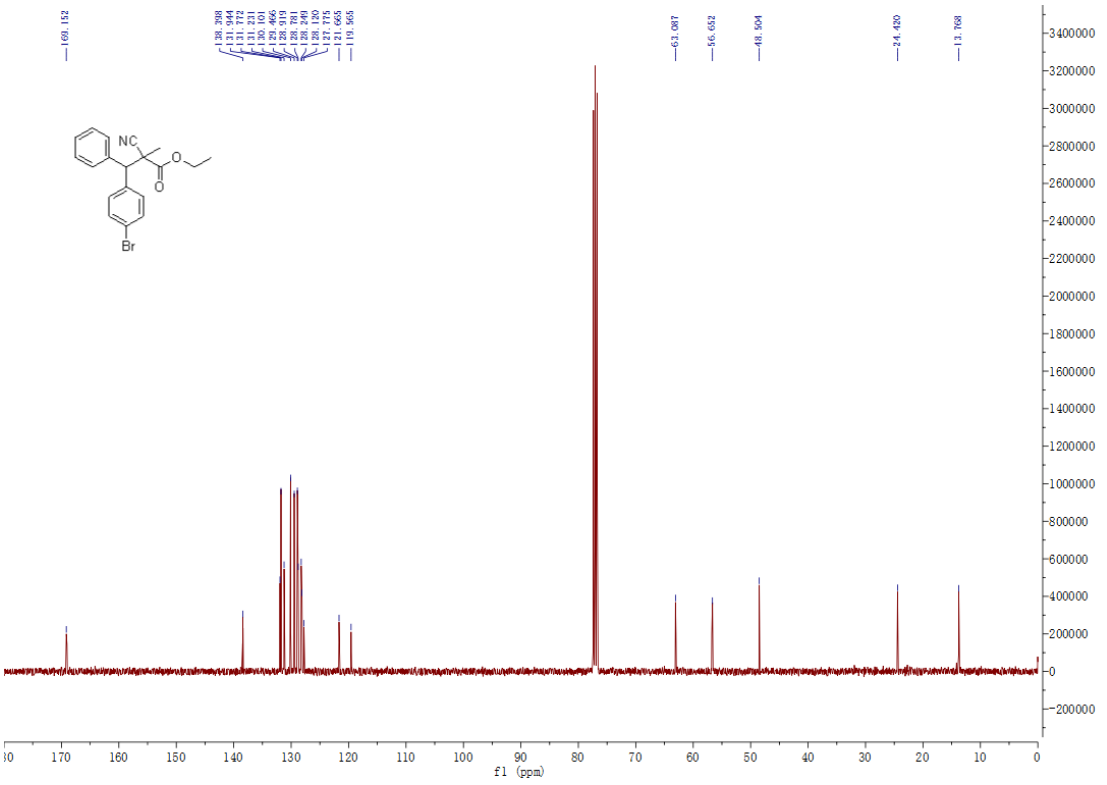

NC
O
O
F
1.558
1.550
0.982
0.964
0.946
0.928
0.910
2.99
1.02
3.01
2.00
1.00
2.00
3.02
3.00
f1 (ppm)


169.233
139.127
137.685
131.252
130.144
129.423
128.890
128.745
128.234
128.050
127.674
119.681
115.817
115.411
62.996
56.883
48.840
29.720
24.356
13.741
NC
O
O
F
f1 (ppm)

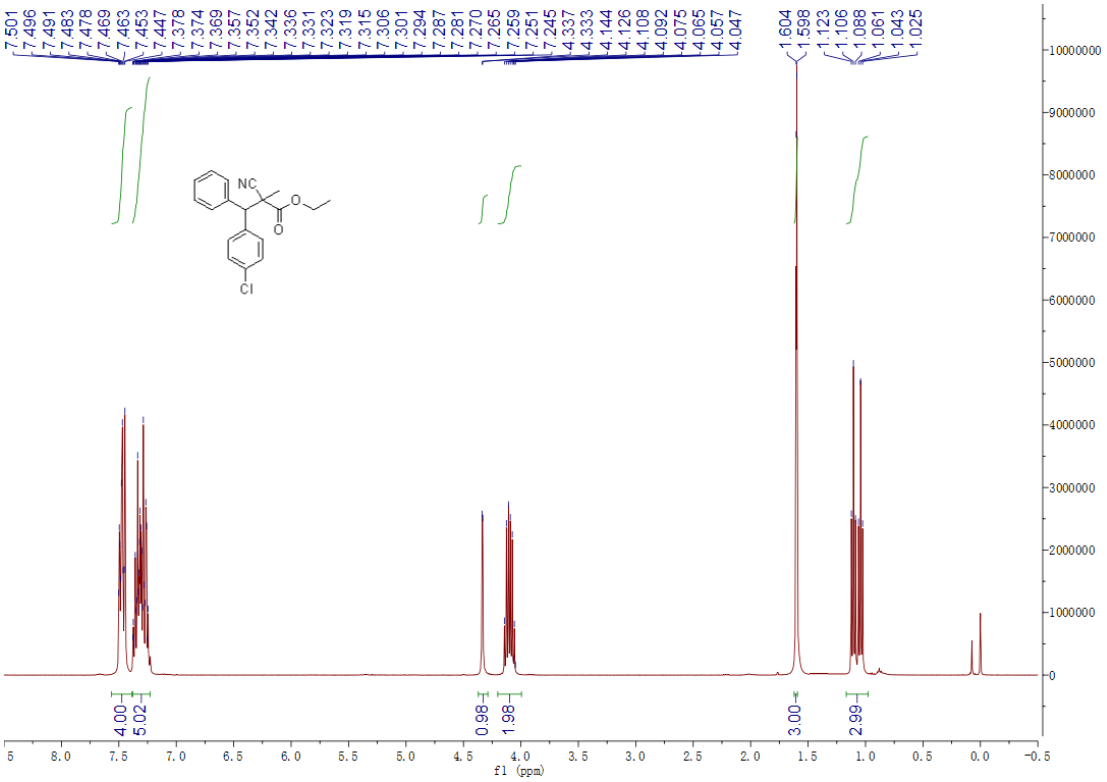

-112.985
NC
O
O
F
f1 (ppm)

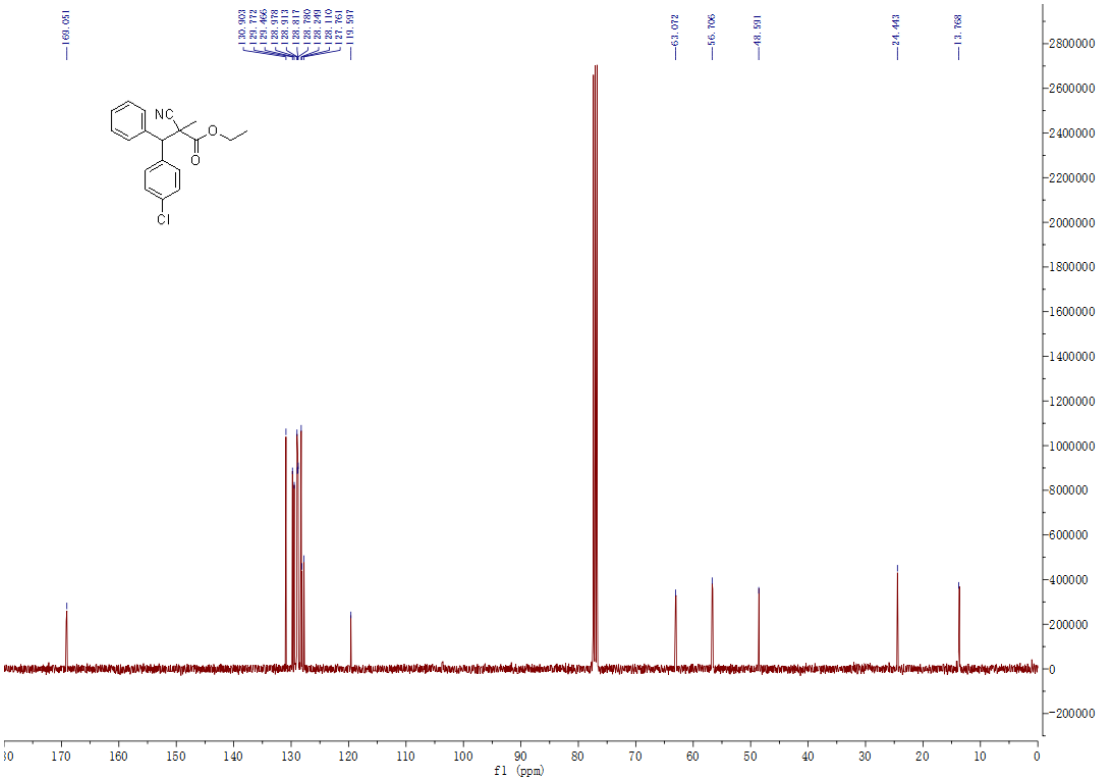
3x


NC
O
O
Br
2.99
4.00
2.02
1.01
2.00
3.00
3.01
f1 (ppm)

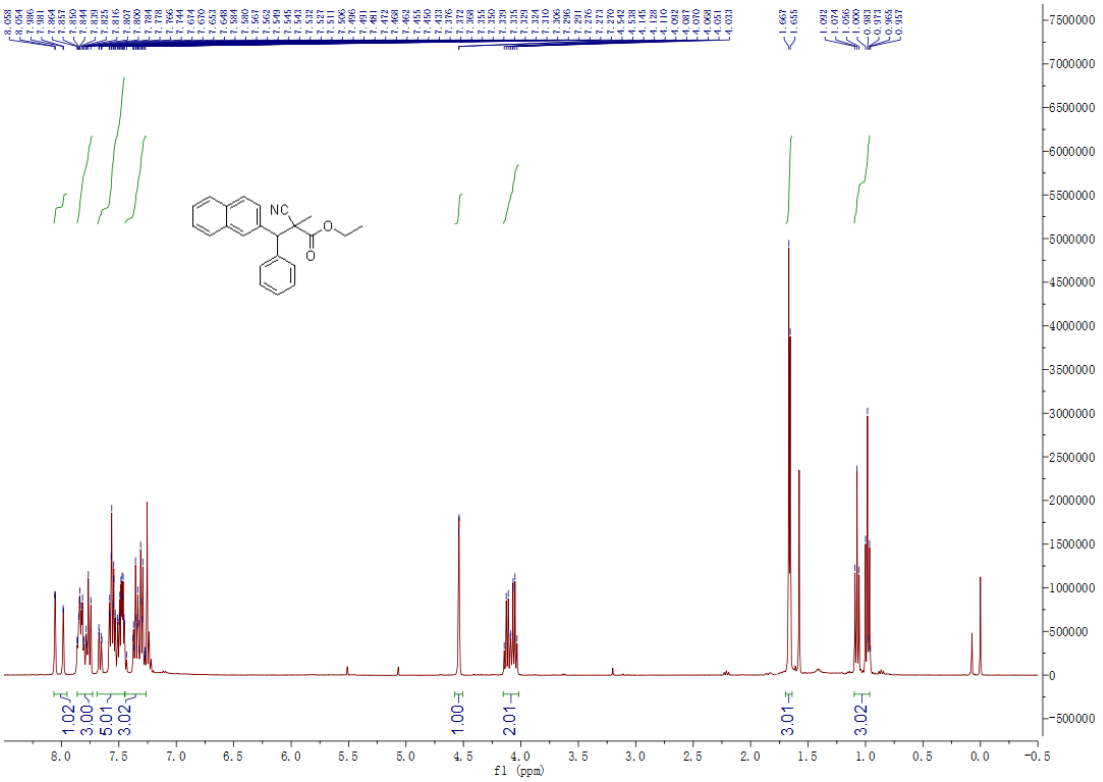

169.152
138.398
131.944
131.572
131.231
130.101
129.466
128.919
128.701
128.249
128.120
127.775
121.666
119.565
63.087
56.652
48.504
24.420
13.768
NC
O
O
Br
f1 (ppm)

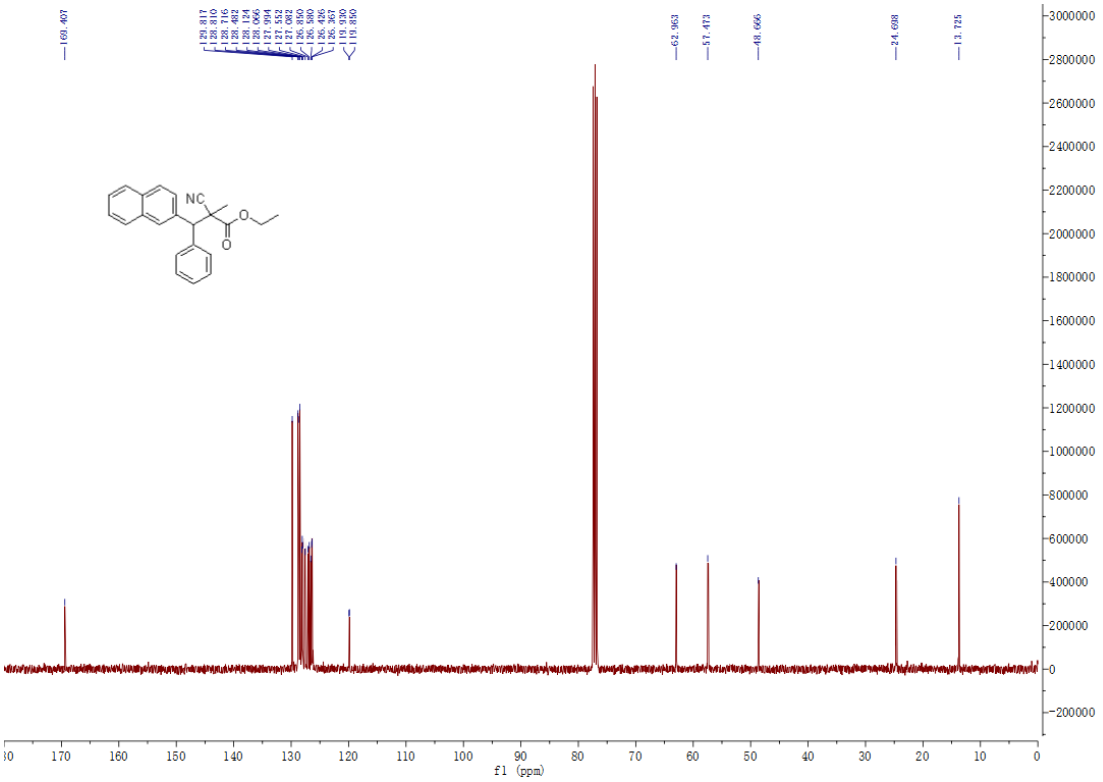
3y


7.501
7.496
7.491
7.483
7.478
7.469
7.463
7.453
7.447
7.378
7.374
7.369
7.357
7.352
7.342
7.336
7.331
7.323
7.319
7.315
7.306
7.301
7.294
7.287
7.281
7.270
7.265
7.259
7.251
7.245
4.337
4.333
4.144
4.126
4.108
4.092
4.075
4.065
4.057
4.047
1.604
1.598
1.123
1.106
1.088
1.061
1.043
1.025
NC
O
O
Cl
4.00
5.02
0.98
1.98
3.00
2.99
f1 (ppm)

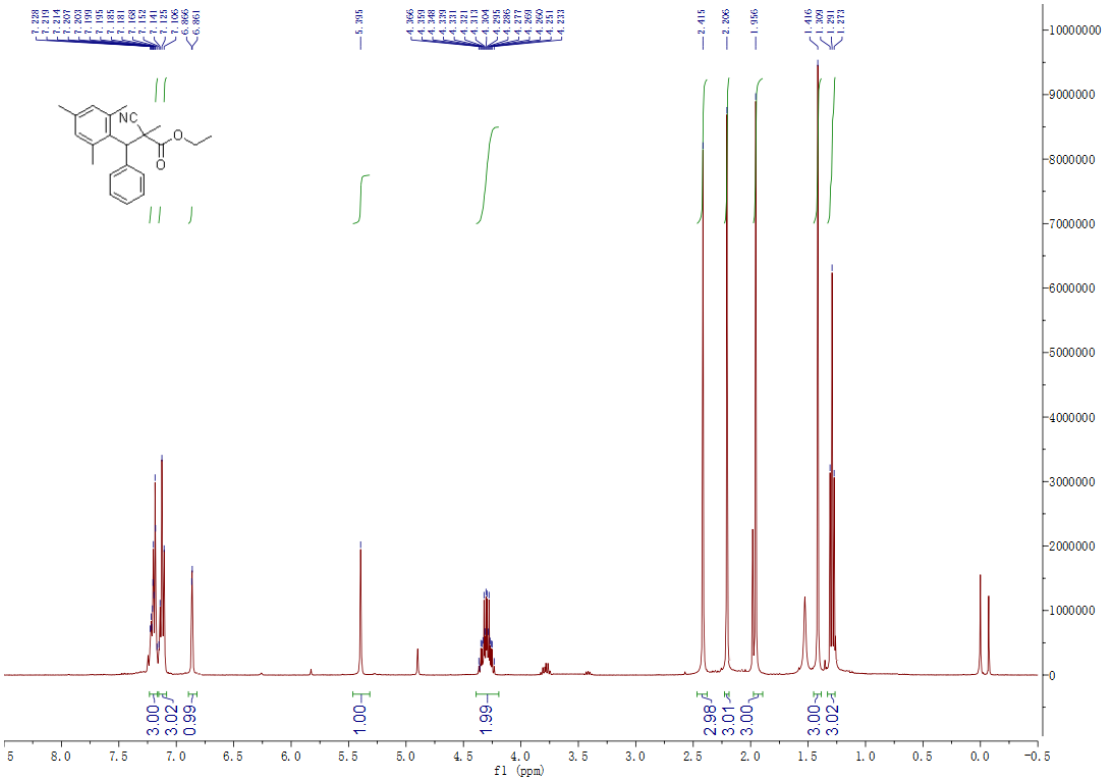

169.051
130.903
129.978
129.466
128.978
128.913
128.847
128.780
128.399
128.110
123.591
119.597
63.072
56.706
48.591
24.443
13.768
NC
O
O
Cl
f1 (ppm)

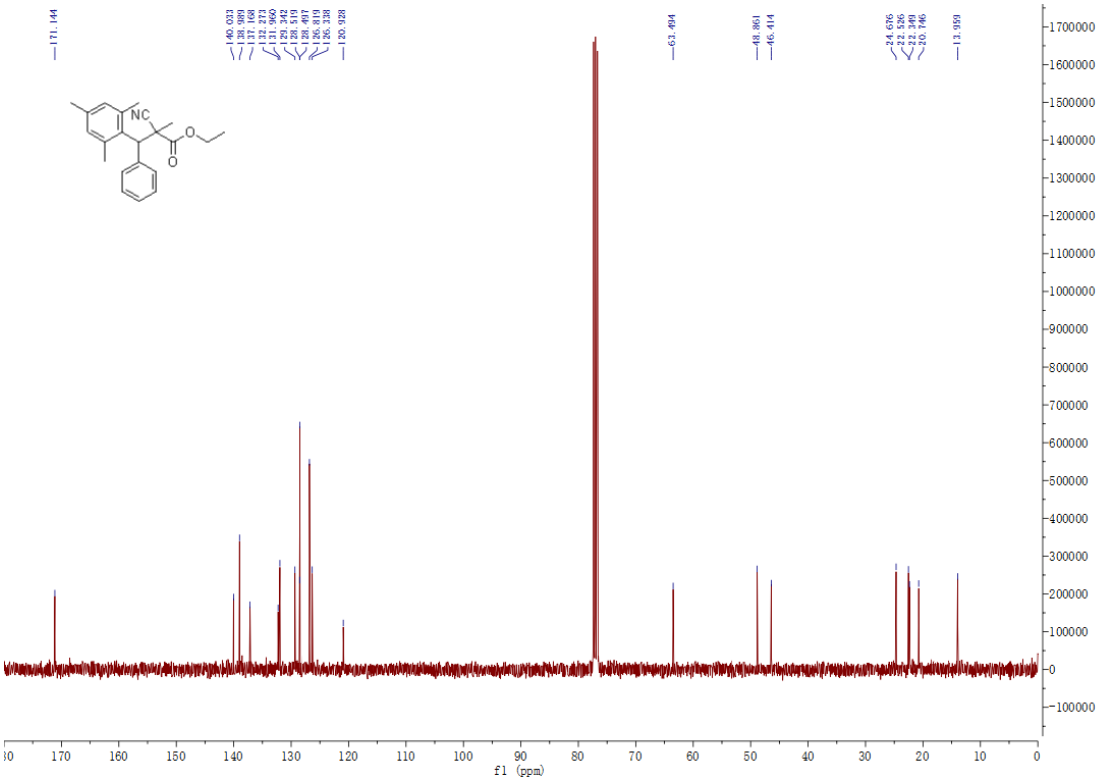
3z


NC
O
O
1.02
3.00
5.01
3.02
1.00
2.01
3.01
3.02
f1 (ppm)

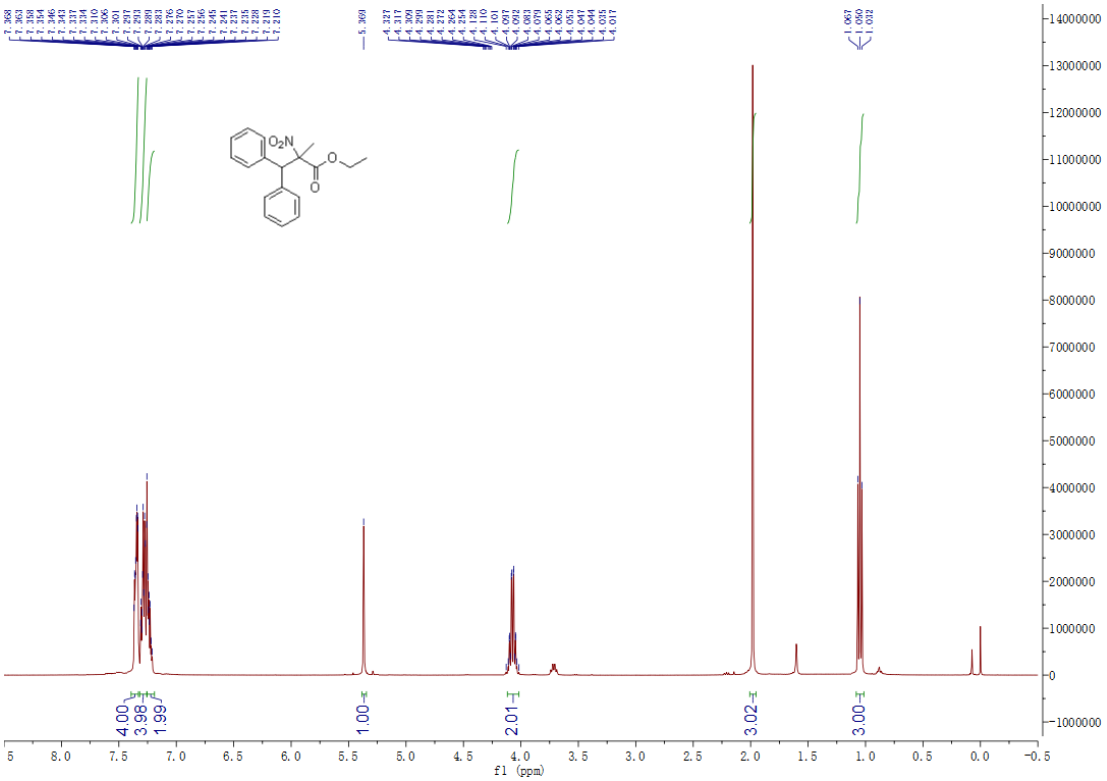

169.407
62.963
57.473
48.666
24.688
13.725
NC
O
O
f1 (ppm)

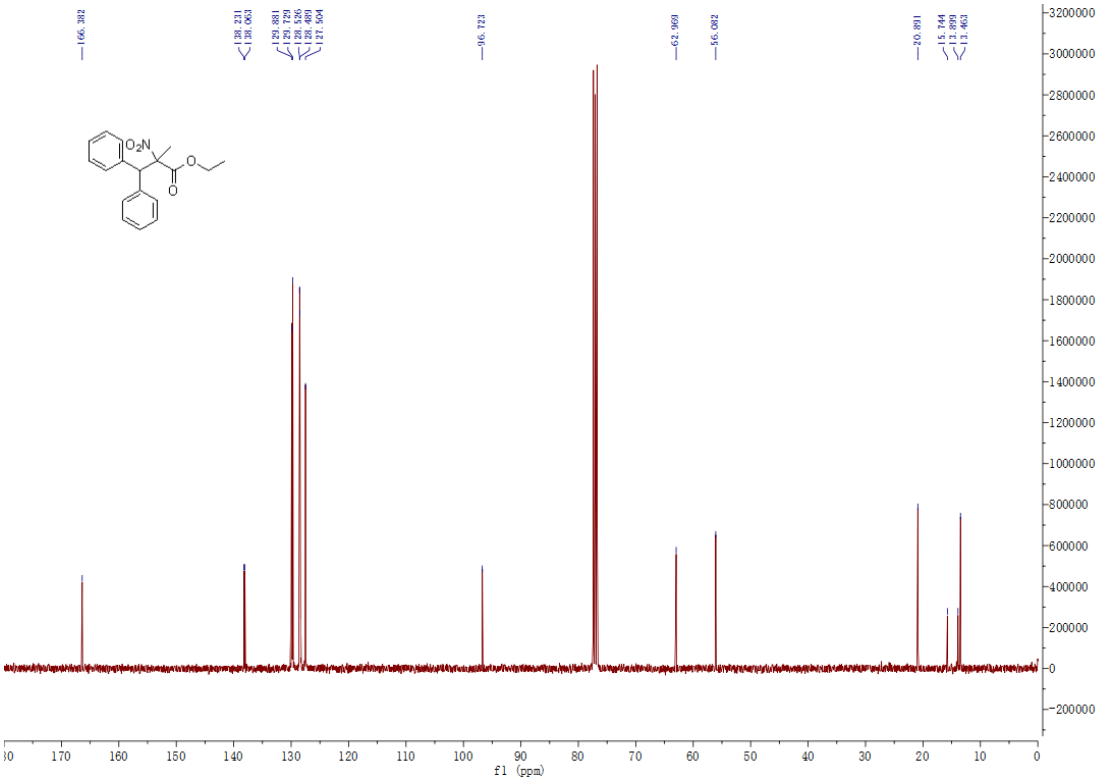
3aa



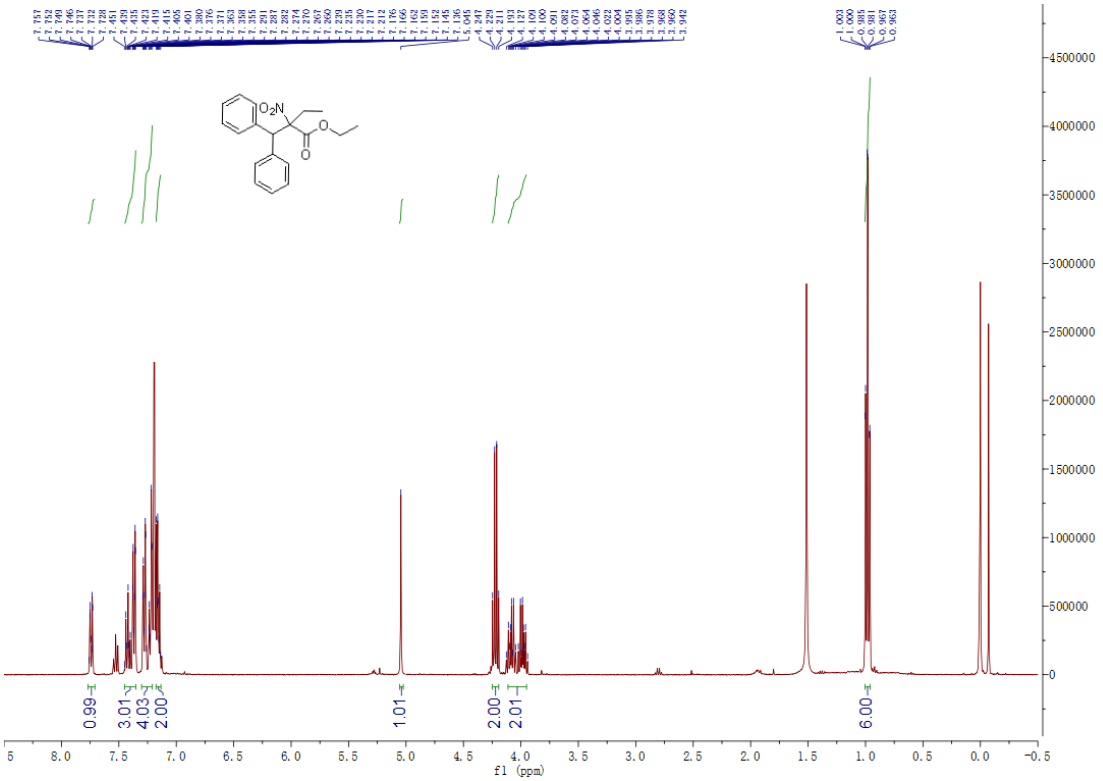


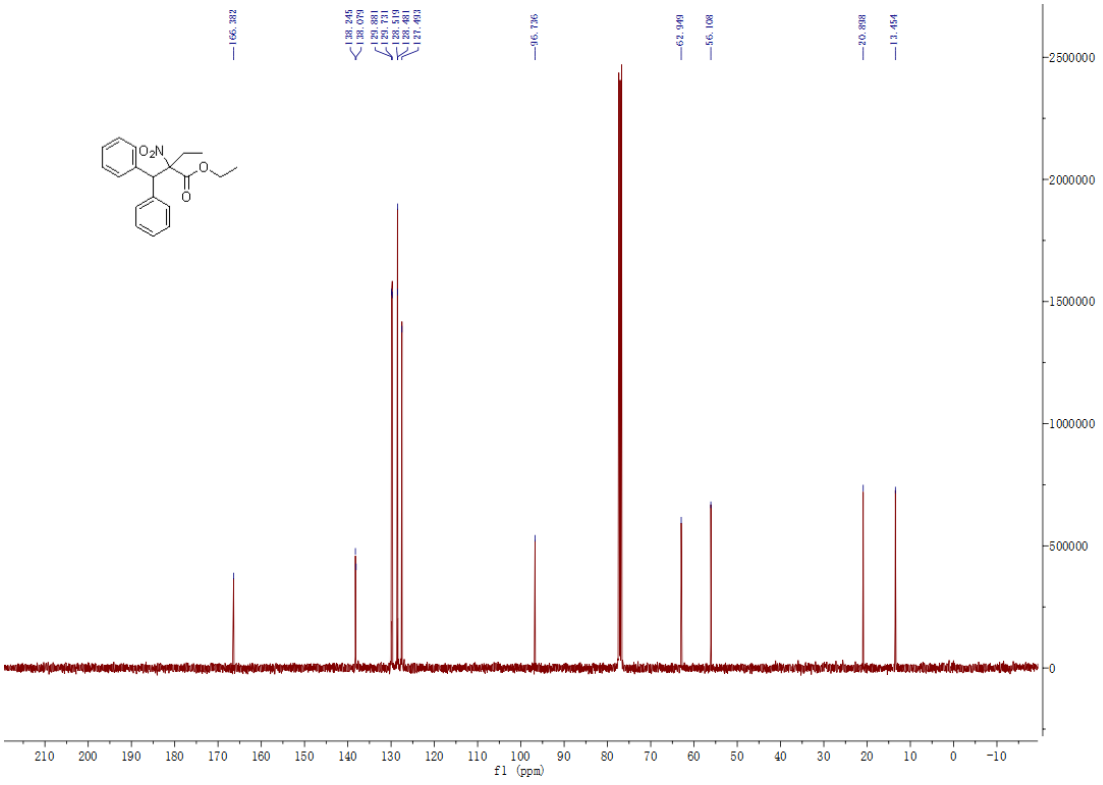
5a



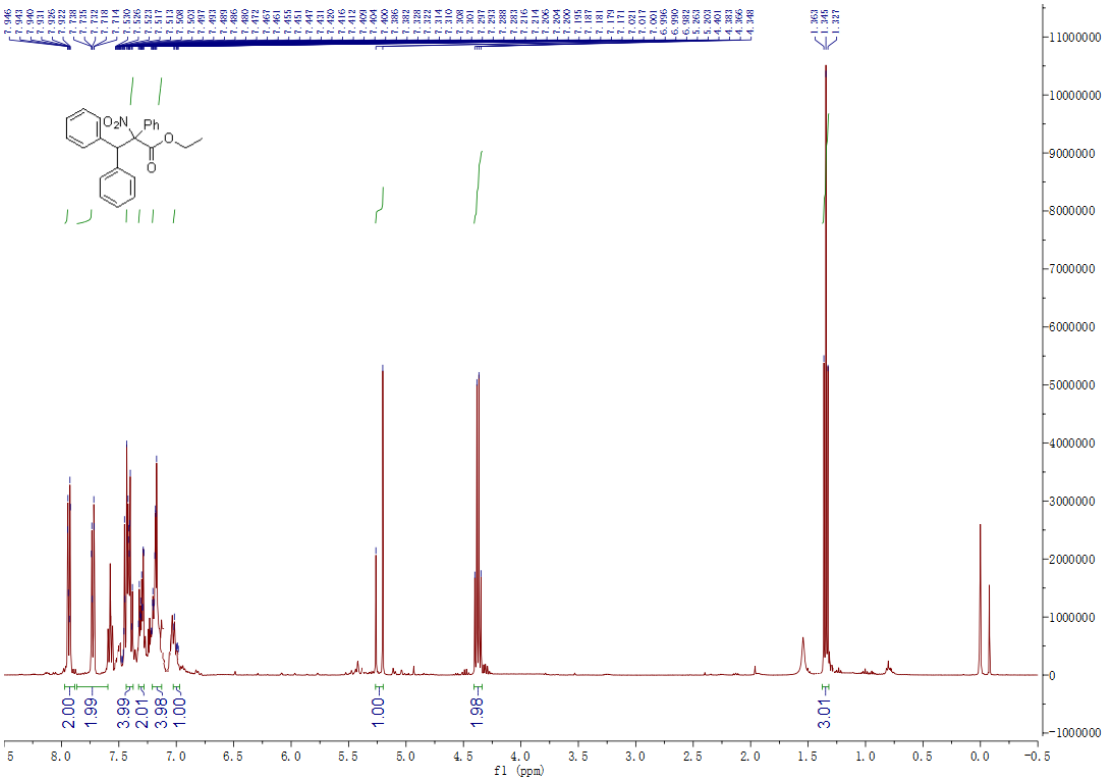


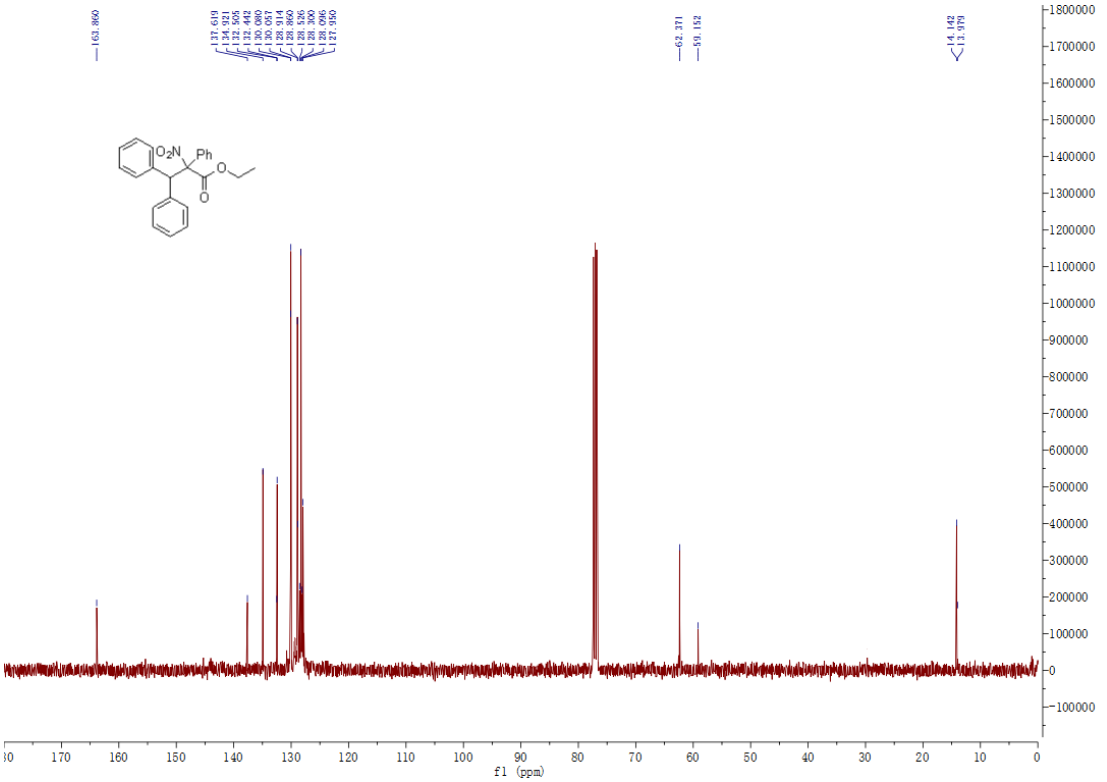
5b



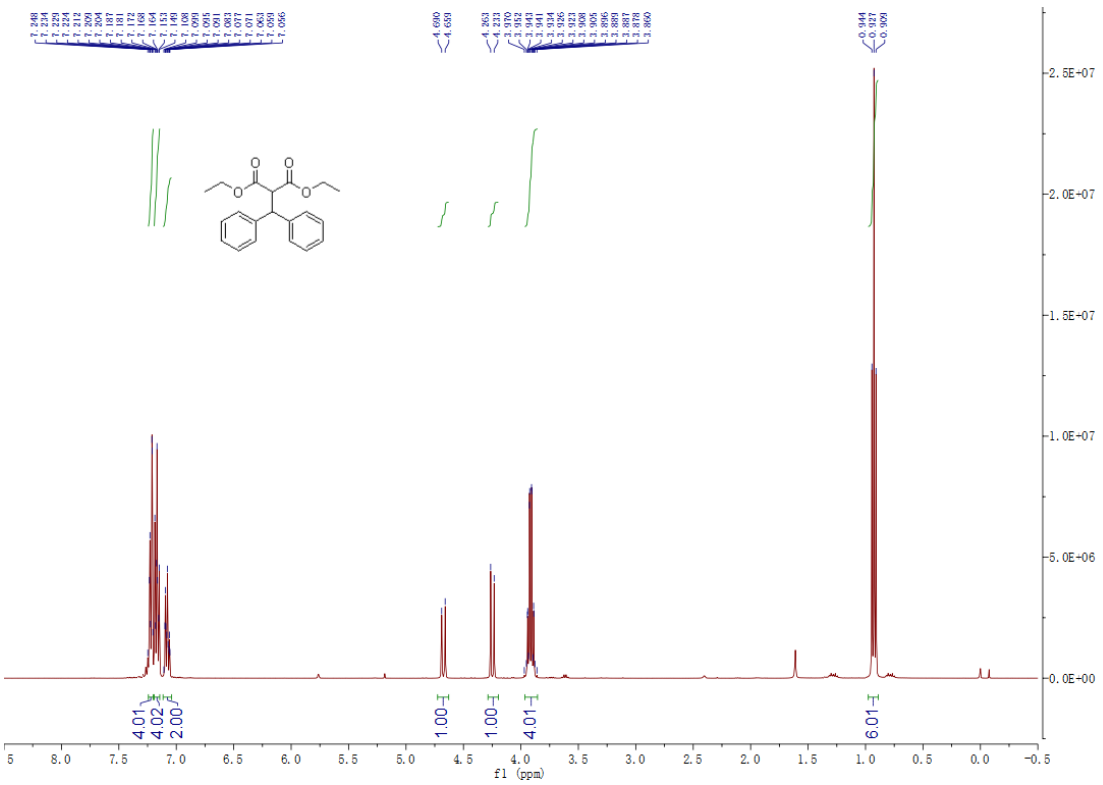


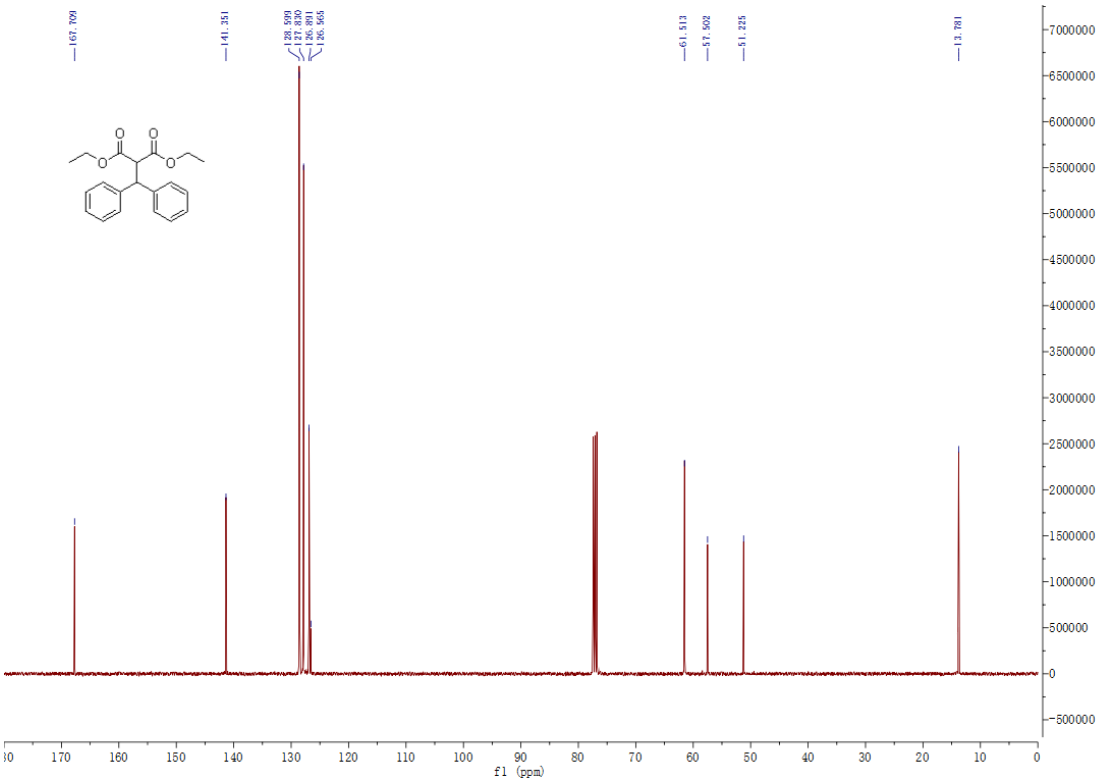
5c


O2N
Ph
O
O
2.00
1.99
3.99
2.01
3.98
1.00
1.00
1.98
3.01
f1 (ppm)

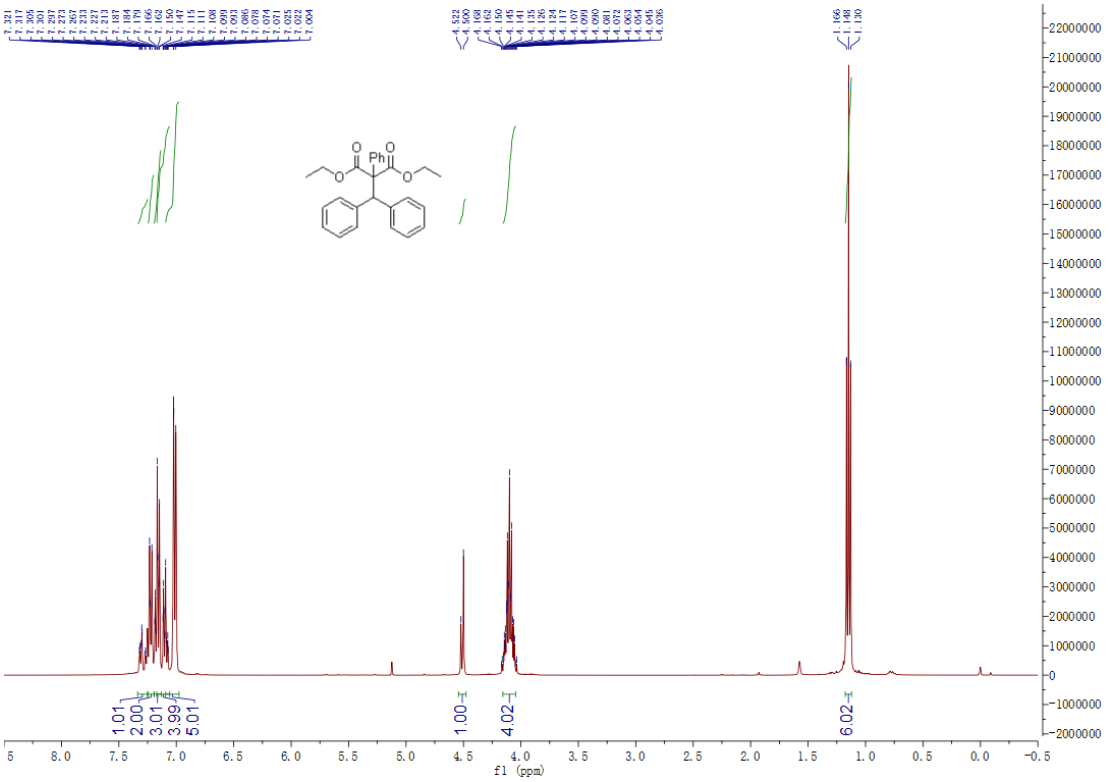

163.860
137.619
134.971
132.505
132.442
130.080
129.954
128.914
128.860
128.526
128.300
128.066
127.950
62.371
59.152
14.142
13.979
O2N
Ph
O
O
f1 (ppm)

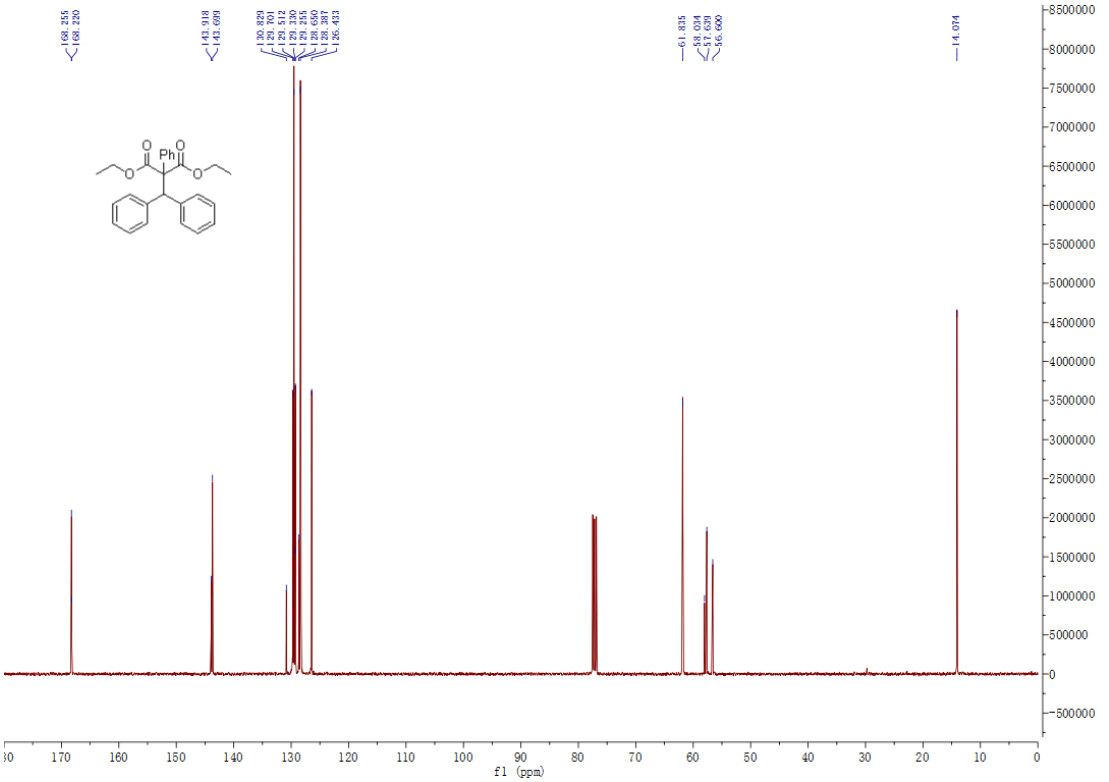
7a



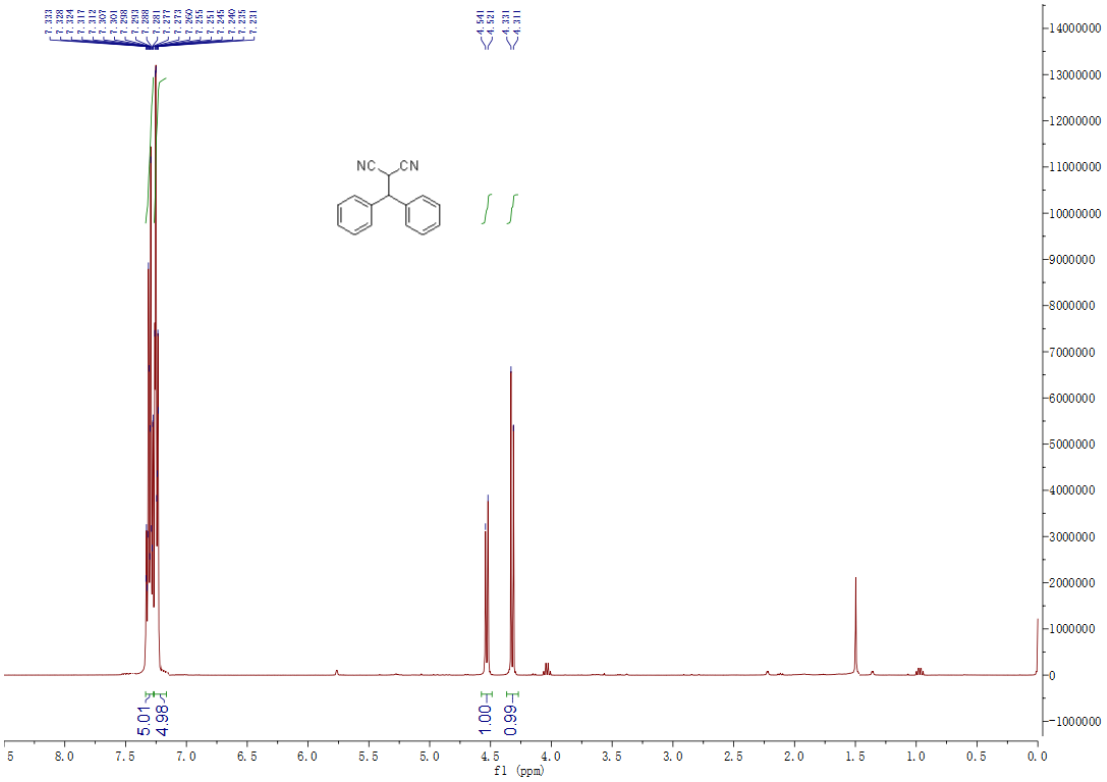


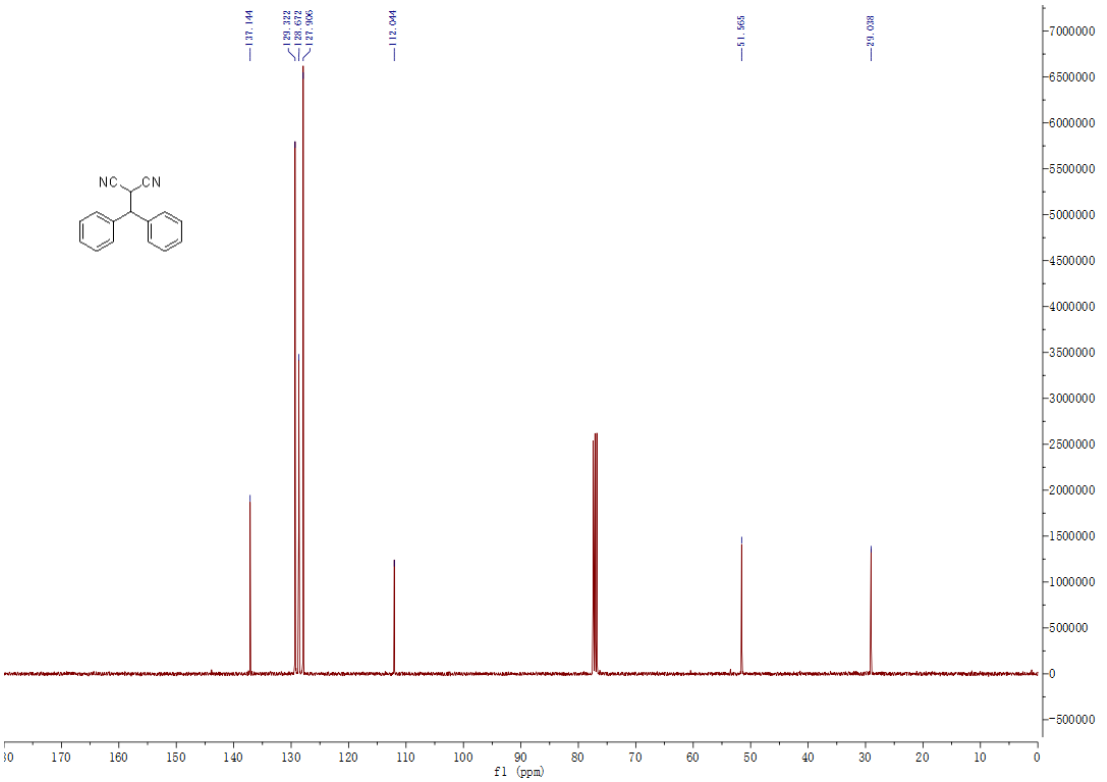
7c



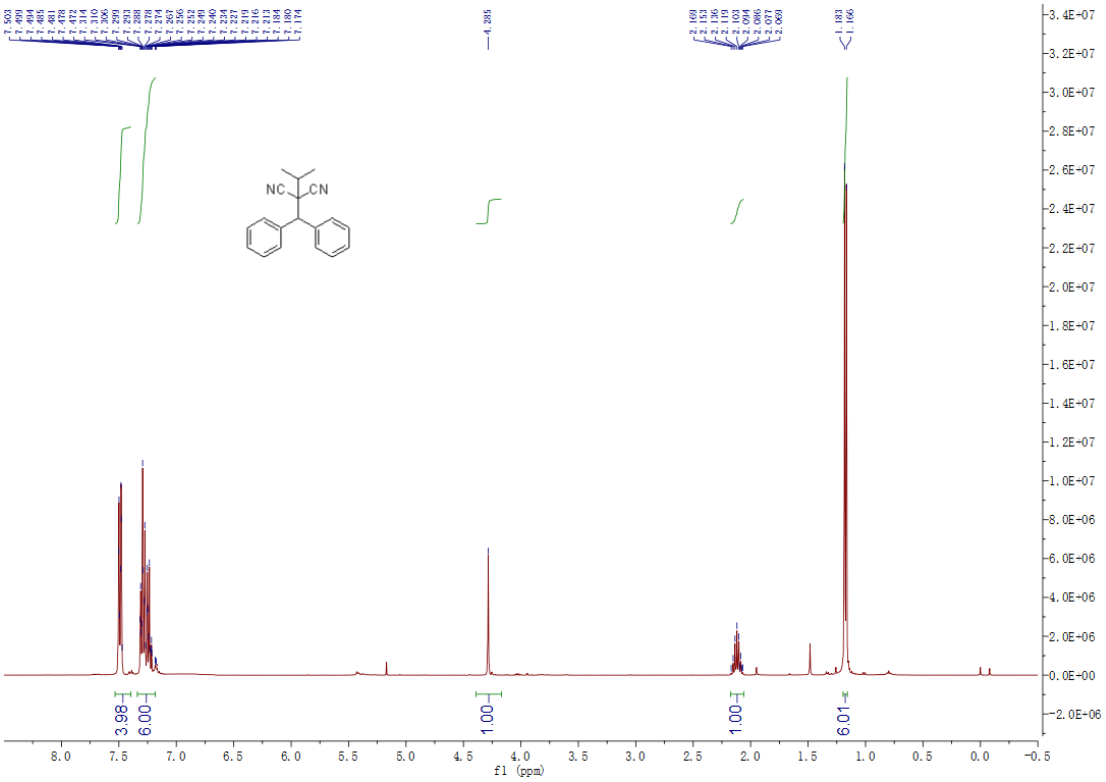


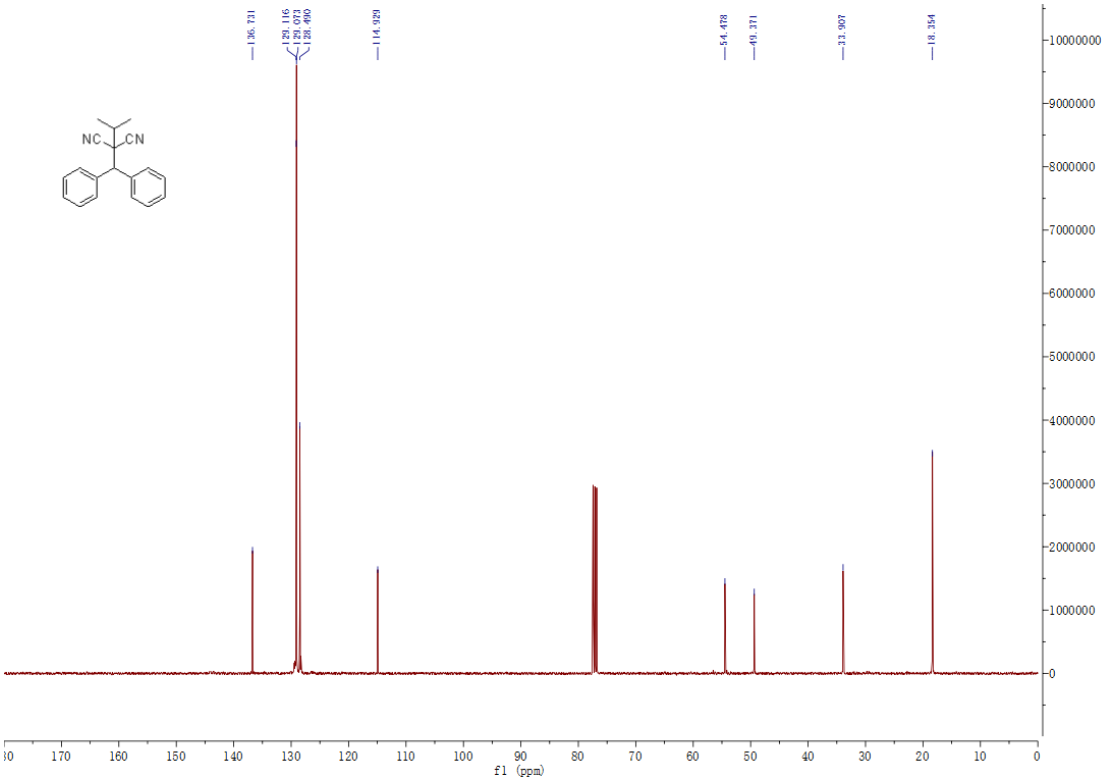
9a


NC
CN
5.01
4.98
1.00
0.99
f1 (ppm)

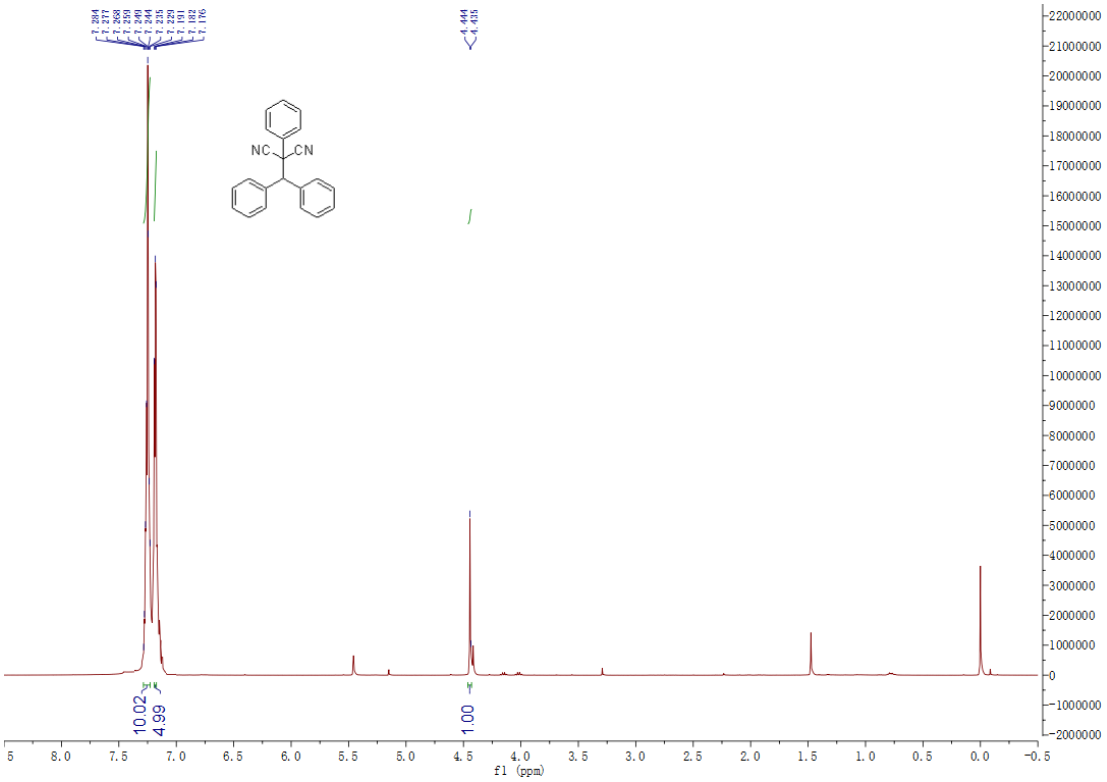

137.144
129.322
128.672
127.966
112.044
51.565
29.038
NC
CN
f1 (ppm)

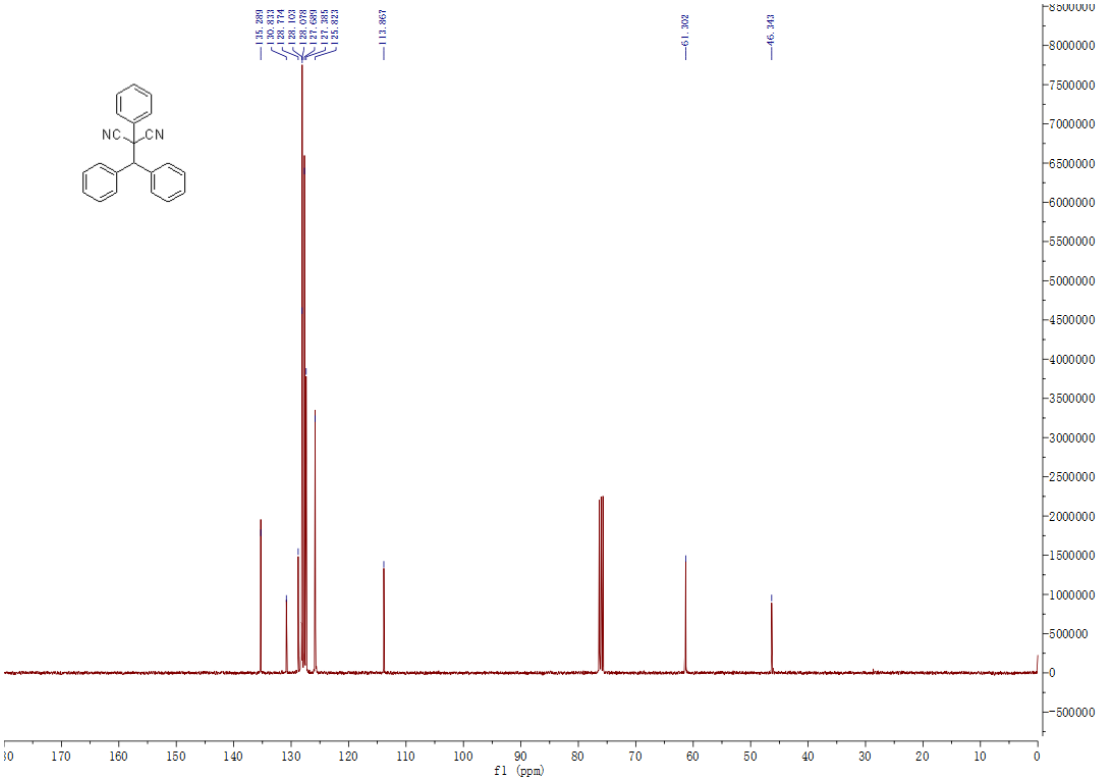
9b


NC
CN
3.98
6.00
1.00
1.00
6.01
f1 (ppm)

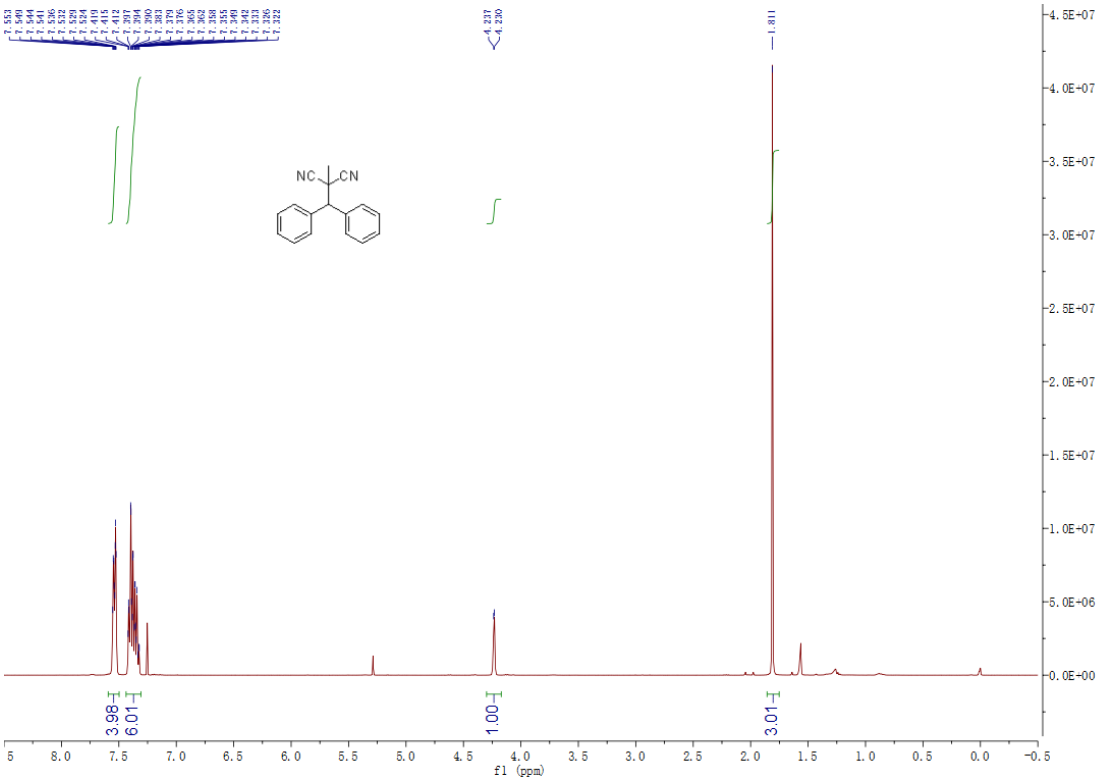

NC
CN
136.731
129.116
128.693
128.409
114.929
54.478
49.371
33.907
18.354
f1 (ppm)

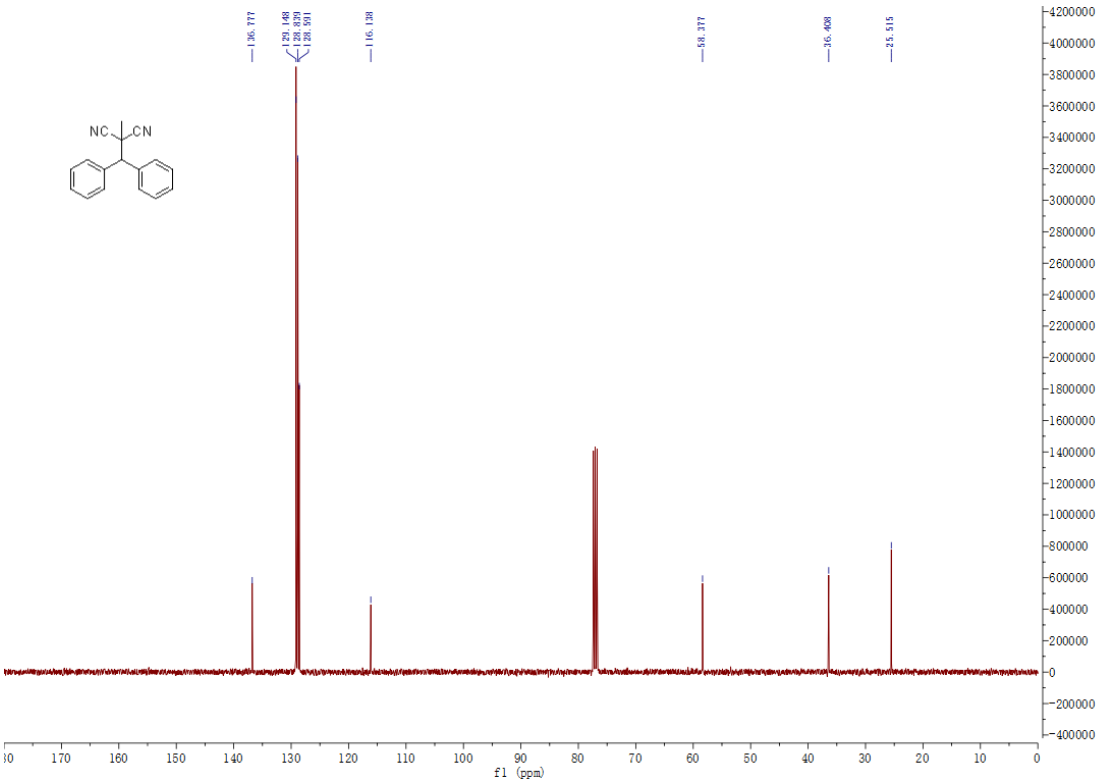
9c


7.284
7.277
7.268
7.259
7.250
7.240
7.244
7.235
7.229
7.191
7.182
7.176
4.444
4.435
NC
CN
10.02
4.99
1.00
f1 (ppm)

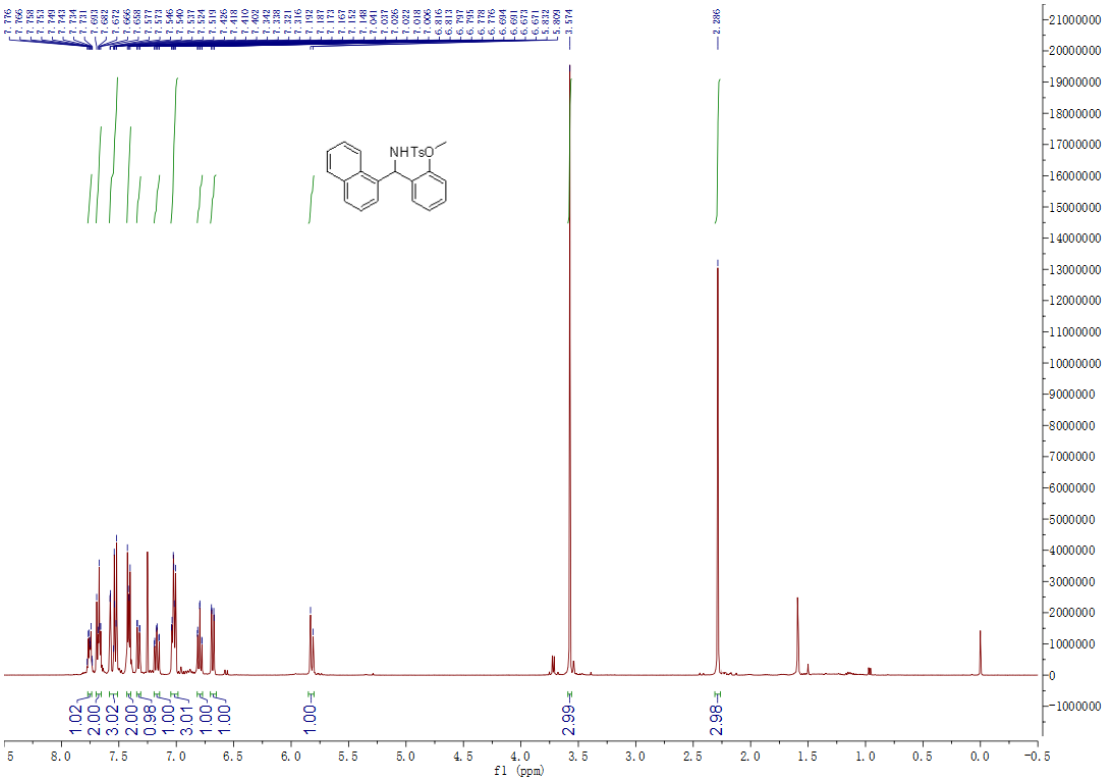

135.289
130.833
128.974
128.103
128.078
127.689
127.385
125.823
113.867
61.302
46.343
NC
CN
f1 (ppm)

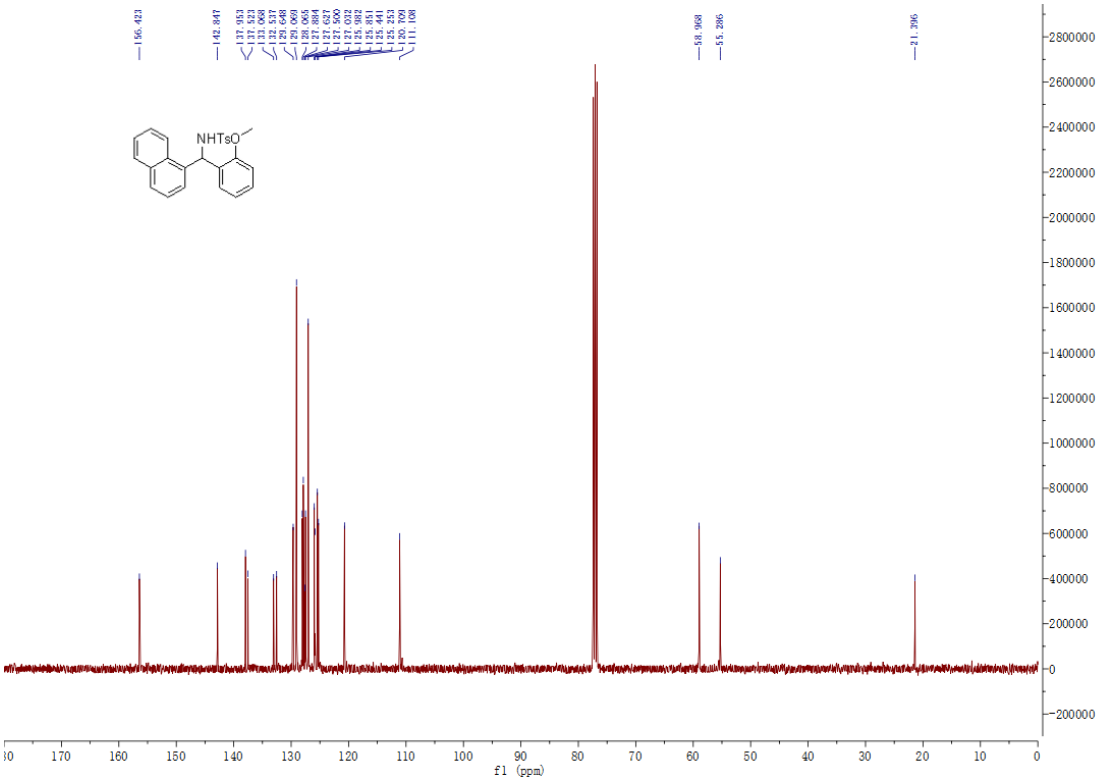
9d


7.553
7.540
7.541
7.532
7.526
7.524
7.415
7.412
7.397
7.394
7.390
7.383
7.379
7.376
7.365
7.362
7.358
7.355
7.340
7.342
7.333
7.326
7.322
4.237
4.230
1.811
NC
CN
3.98
6.01
1.00
3.01
f1 (ppm)

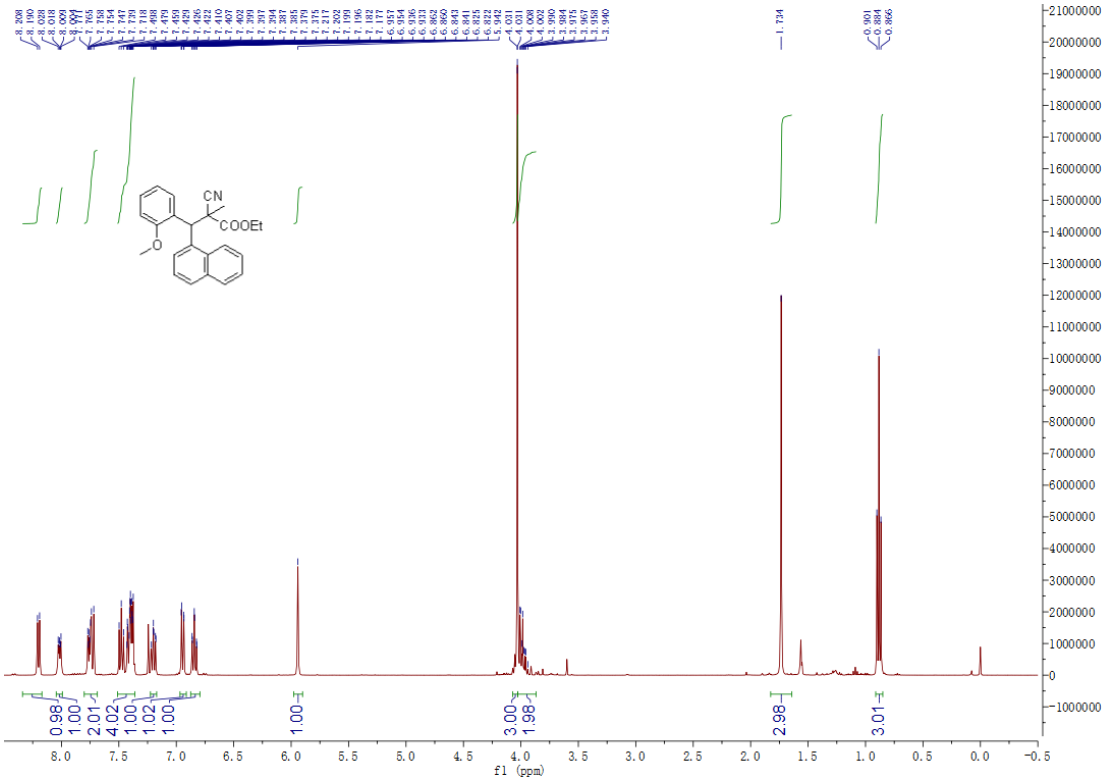

136.777
129.148
128.939
128.601
116.138
58.377
36.408
25.515
NC
CN
f1 (ppm)

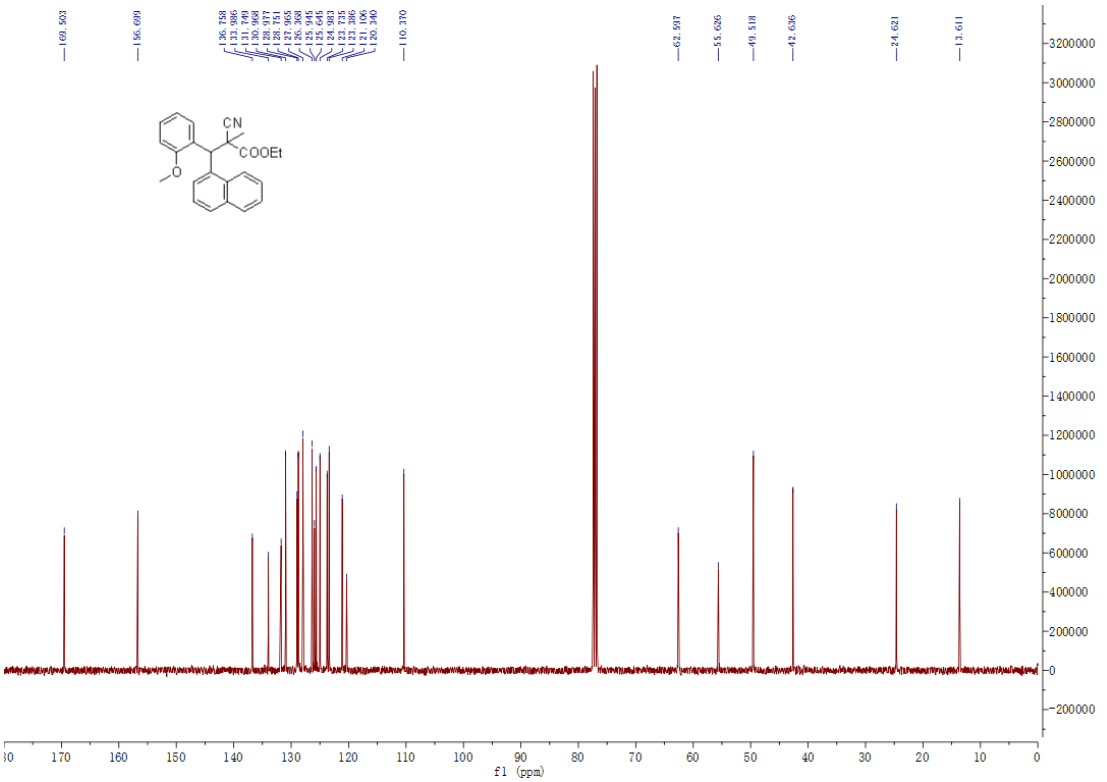
10



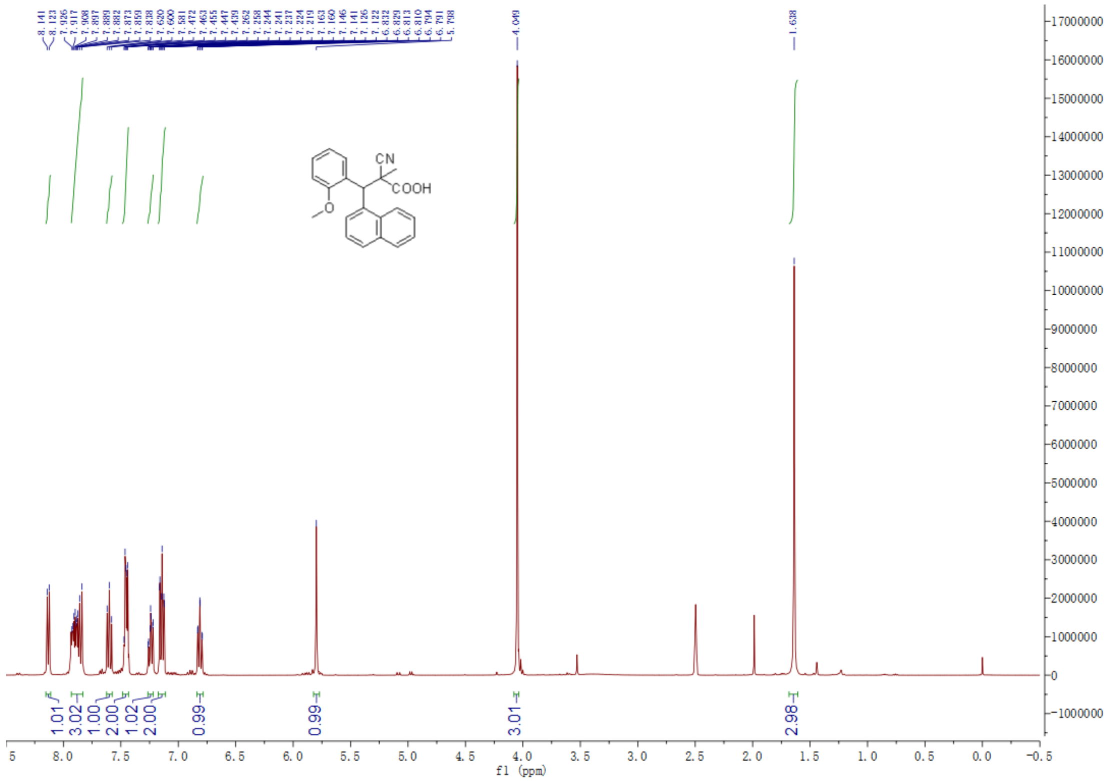


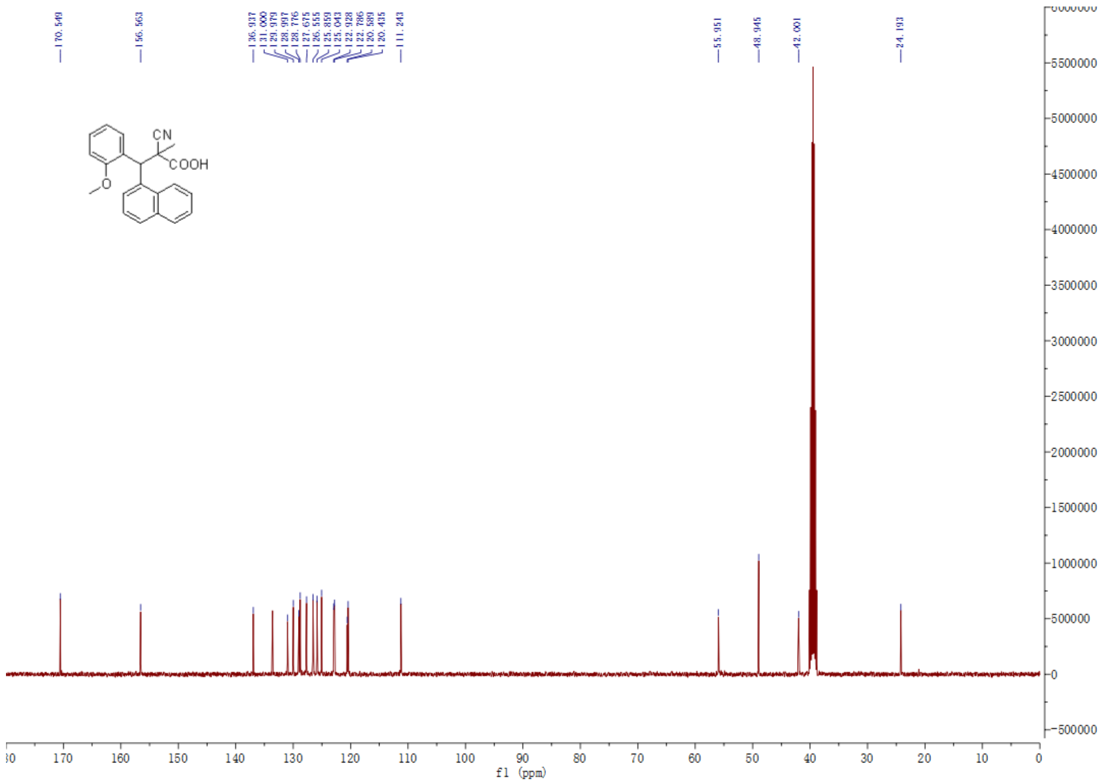
11


CN
COOEt
O
1.734
0.901
0.884
0.865
0.98
1.00
2.01
4.02
1.00
1.02
1.00
1.00
3.00
1.98
2.98
3.01
f1 (ppm)


169.503
156.699
136.758
133.386
131.740
130.999
128.977
128.751
127.965
126.368
125.966
125.645
124.983
123.735
121.986
121.106
120.340
110.370
62.937
55.626
49.518
42.636
24.621
13.611
CN
COOEt
O
f1 (ppm)

12





13