Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Directed Arene/alkyne Annulation Reactions via Aerobic Copper Catalysis

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Supporting Information

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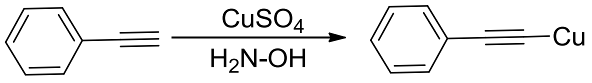
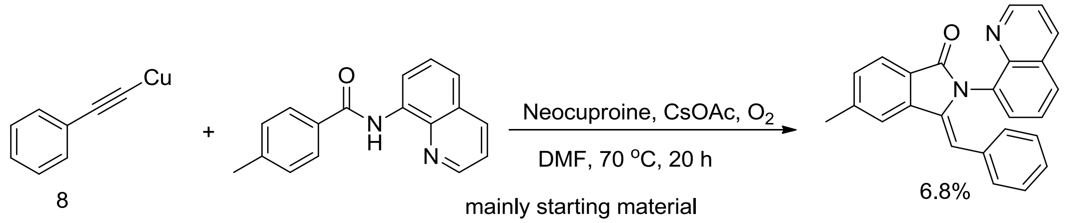
General Methods and Materials:

All reactions were carried out using anhydrous solvents. All other reagents were purchased and used without further purification unless specified otherwise. Flash chromatography was performed using 200-300 mesh silica gel (Qingdao Haiyang Chemical HG/T2354-92) with the indicated solvent system according to standard techniques. Analytical thin-layer chromatography (TLC) was performed using Huanghai silica gel plates with HSGF 254. ^{1}H NMR and ^{13}C NMR data were recorded on Bruker 400M or 300M nuclear resonance spectrometers unless otherwise specified. Chemical shifts (δ) in ppm are reported as quoted relative to the residual signals of chloroform (^{1}H 7.26 ppm or ^{13}C 77.16 ppm). Multiplicities are described as: s (singlet), bs (broad singlet), d (doublet), t (triplet), q (quartet), m (multiplet); and coupling constants (*J*) are reported in Hertz (Hz). ^{13}C NMR spectra were recorded with total proton decoupling. HRMS (ESI) analysis was performed by The Analytical Instrumentation Center at Peking University; Shenzhen Graduate School and the data were reported with ion mass/charge (m/z) ratios as values in atomic mass units.

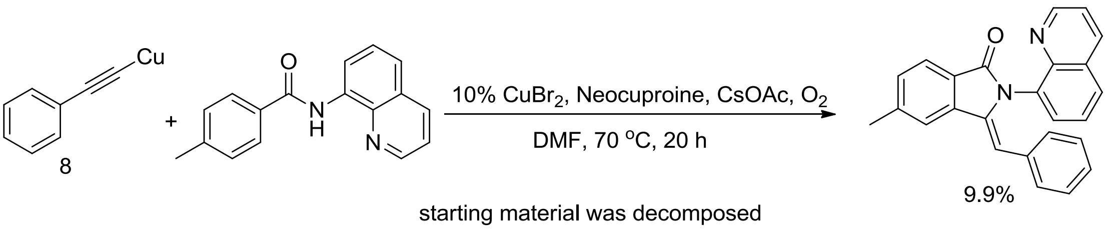
Mechanistic Studies



General procedure for the synthesis of copper phenacetylides: To an ice-cooled mixture of copper sulfate pentahydrate (1.25g, 5 mmol), 28% aqueous ammonia (5 mL), water (50 mL) and hydroxylamine hydrochloride (0.7 g, 10 mmol) was added a solution of the phenylacetylene (5 mmol) in ethanol (30 mL), and the reaction was stirred for 5 min. The precipitate was filtered, washed with water (10 mL), ethanol (10 mL) and diethyl ether (2 x 20 mL), and dried in vacuo for 12 h.



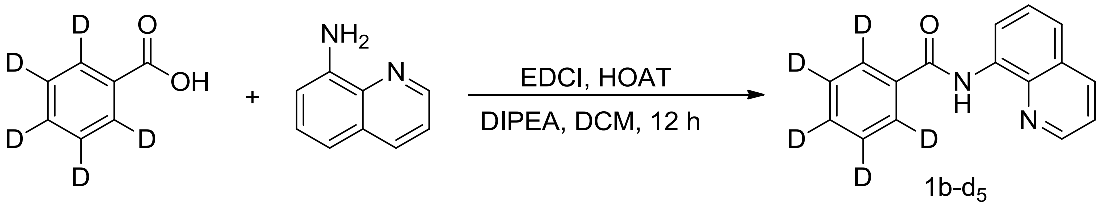
(3)



(4)

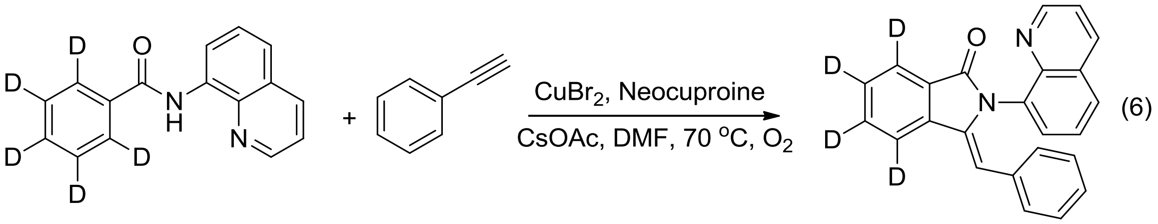
A 1 dram vial equipped with a magnetic stir bar was charged with 4-methyl-N-(quinolin-8-yl)benzamide (0.2 mmol, 1 equiv), cupric bromide (0.02 mmol, 0.1 equiv) (for eqn 4), 2,9-dimethyl-1,10-phenanthroline (0.04 mmol, 0.2 equiv), CsOAc (0.24 mmol, 1.2 equiv). To this mixture was added anhydrous DMF (1.0 mL), alkyne (0.3 mmol, 1.5 equiv), and then transferred to preheated oil bath for indicated time under an oxygen balloon. The yields were determined by GC using biphenyl as the internal standard.

KIE Experiment for Isotope Effect



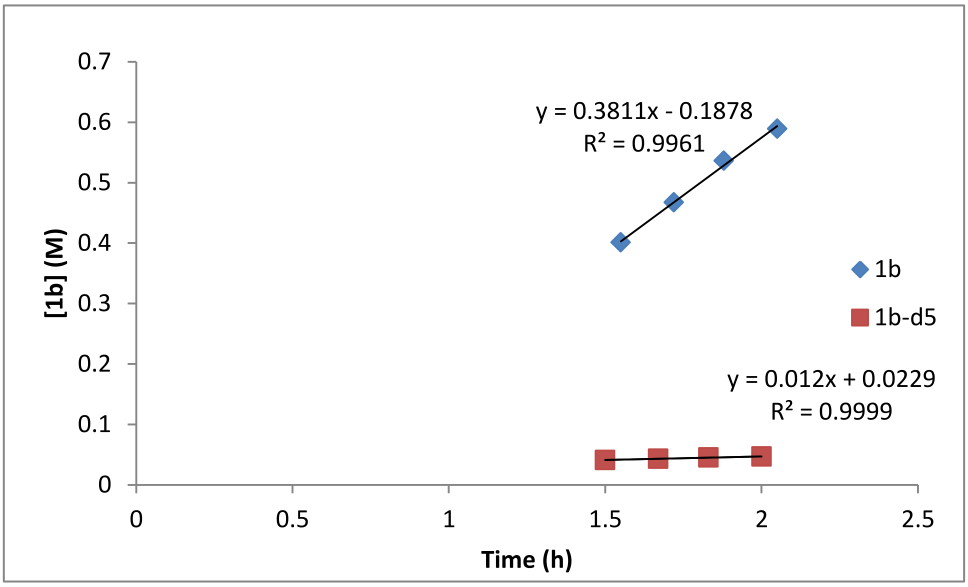
(5)

Benzoic Acid-d_5 (509 mg, 4 mmol, 1 equiv) and 8-Aminoquinoline (865 mg, 6 mmol, 1.5 equiv) were dissolved in DCM (25 mL). HOAT (0.59 g, 4.4 mmol, 1.1 equiv) and EDCI (0.84 g, 11 mmol, 1.1 equiv) were added sequentially, followed by DIPEA (1.55 g, 12 mmol, 3 equiv). The reaction mixture was stirred at R. T. for 24 h, washed using sat. $NaHCO_3$, and extracted with DCM three times. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by silica gel flash column chromatograph (EtOAc:Hexane = 1:10) to give compound **1b-d_5**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.76 (s, 1H), 8.95 (dd, *J* = 7.5, 1.2 Hz, 1H), 8.86 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.67 – 7.52 (m, 2H), 7.48 (dd, *J* = 8.3, 4.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.49, 148.31, 138.82, 136.41, 135.03, 134.63, 128.55, 128.30, 128.03, 127.49, 127.15, 126.67, 121.70, 116.57.

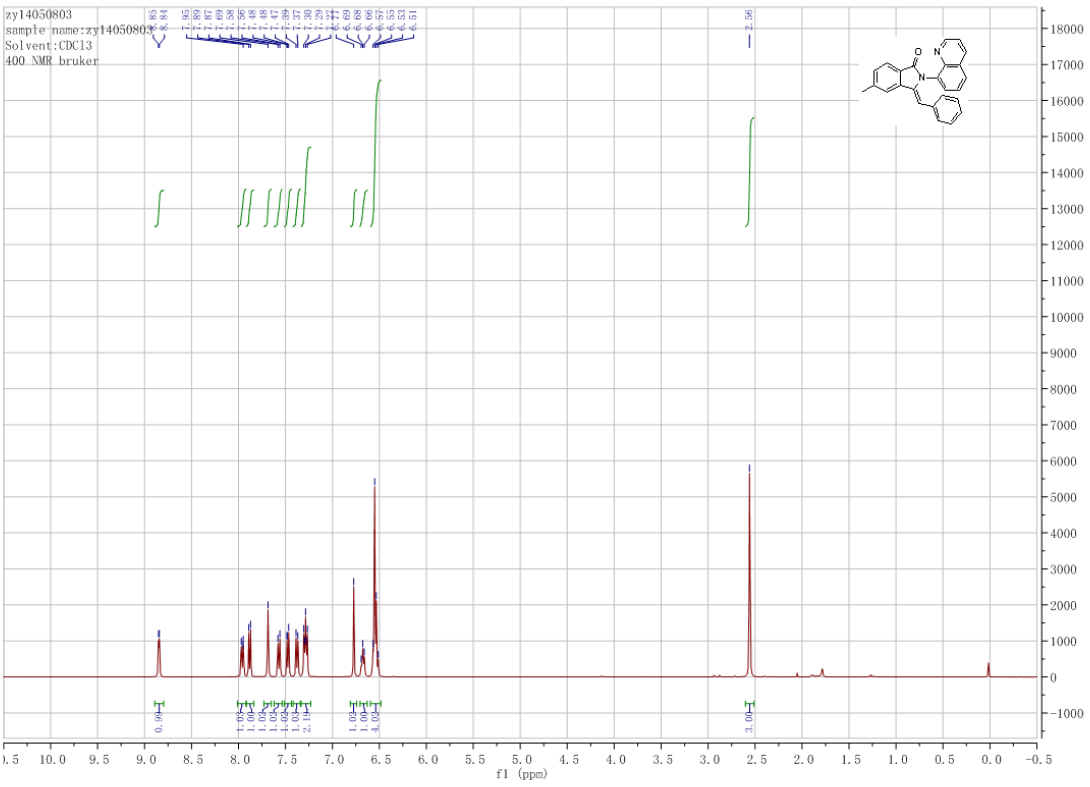


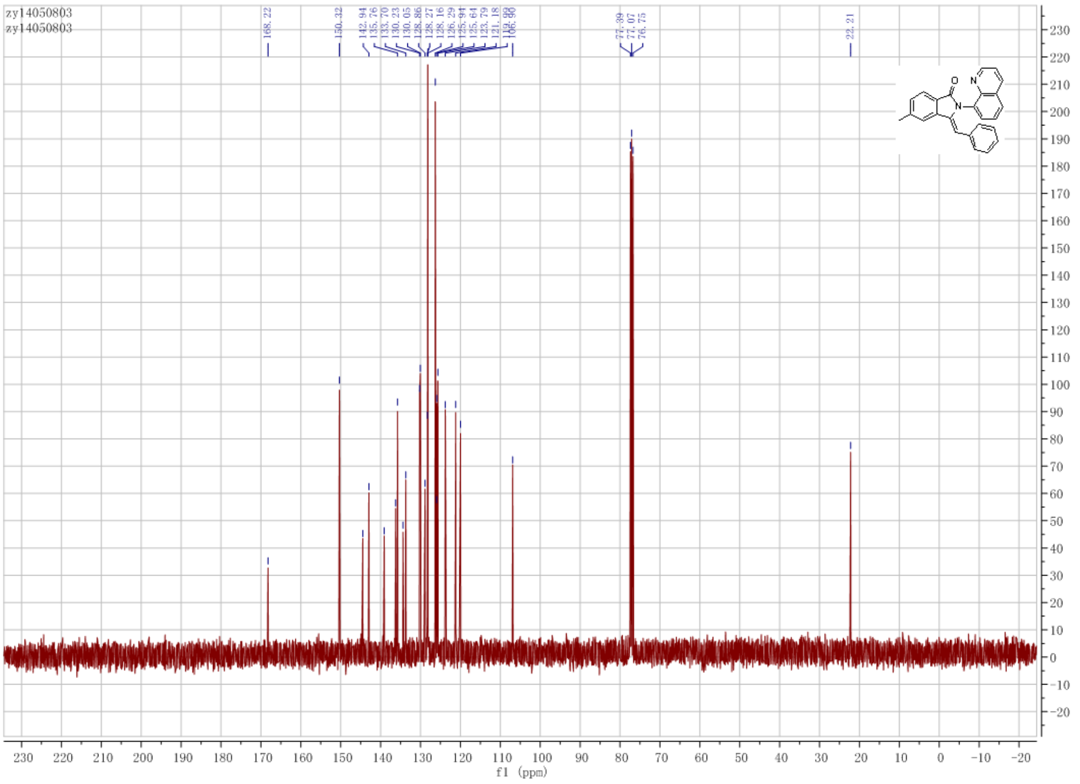
A sample experimental set-up is as follows: A 1 dram vial equipped with a magnetic stir bar was charged with 1b (49.6 mg, 0.2 mmol, or 1b-d_5: 50.6 mg, 0.2 mmol), cupric bromide (0.02 mmol, 0.1 equiv), 2,9-dimethyl-1,10-phenanthroline (0.04 mmol, 0.2 equiv), CsOAc (0.24 mmol, 1.2 equiv), diphenyl (0.2 mmol, as internal standard). To this mixture was added anhydrous DMF (1.0 mL, for 1b-d_5, DMF-D_7 was used), alkyne (0.3 mmol, 1.5 equiv) and then transferred to preheated oil bath (70 °C) under an oxygen balloon. Aliquots (~10 uL) were taken at 90 min intervals. Each aliquot was filtered through a plug of silica gel and analyzed by GC. A sample plot of the conversion vs time for both reactions using 1b and 1b-d_5 are shown below.

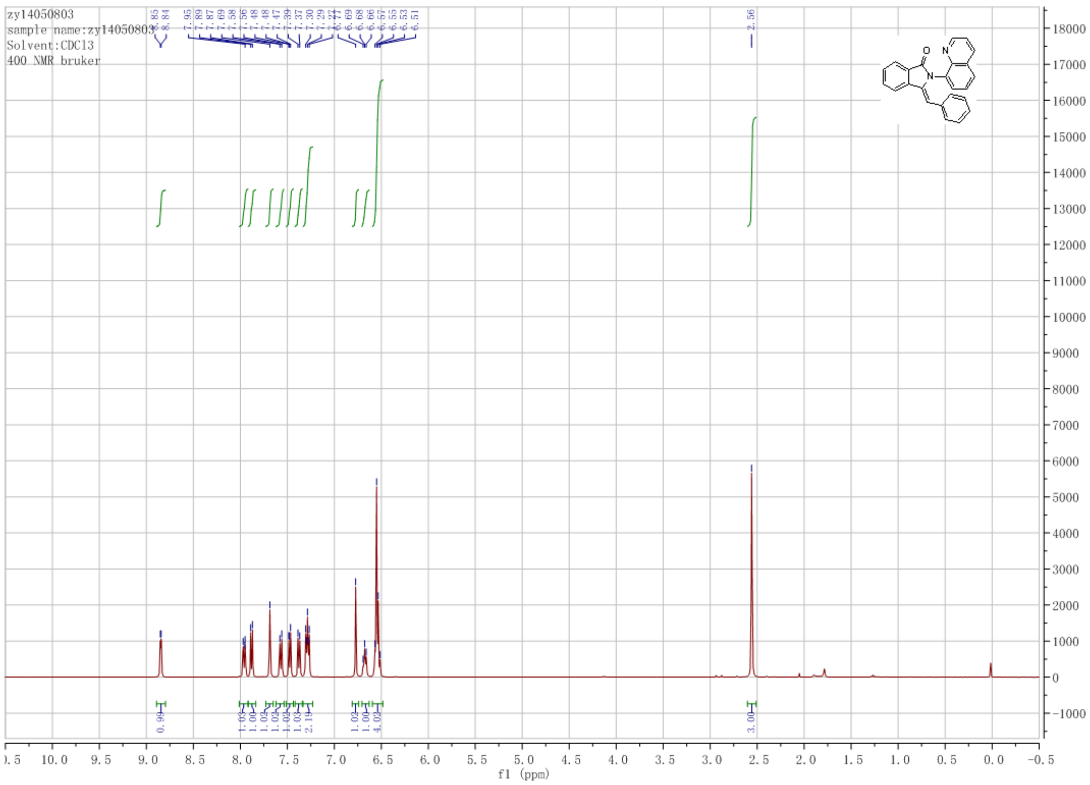
Chart S1. Plot of initial rates for DKIE measurements.



NMR Spectra Images of products



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6.51
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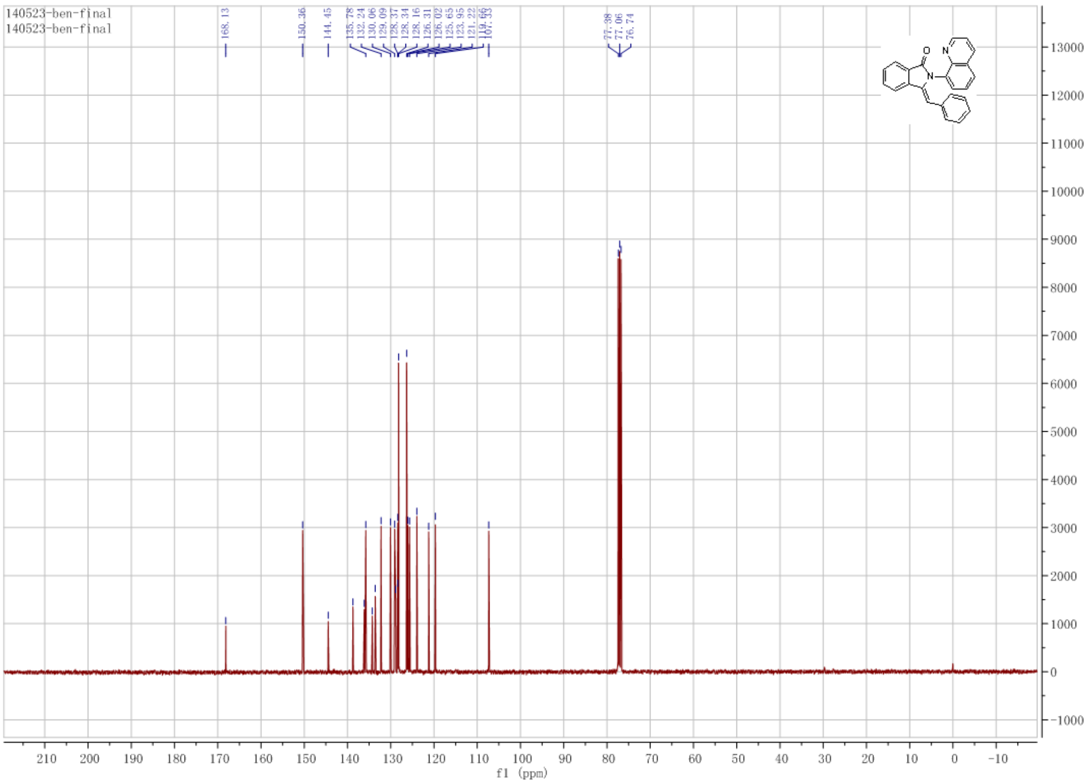
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140523-ben-final
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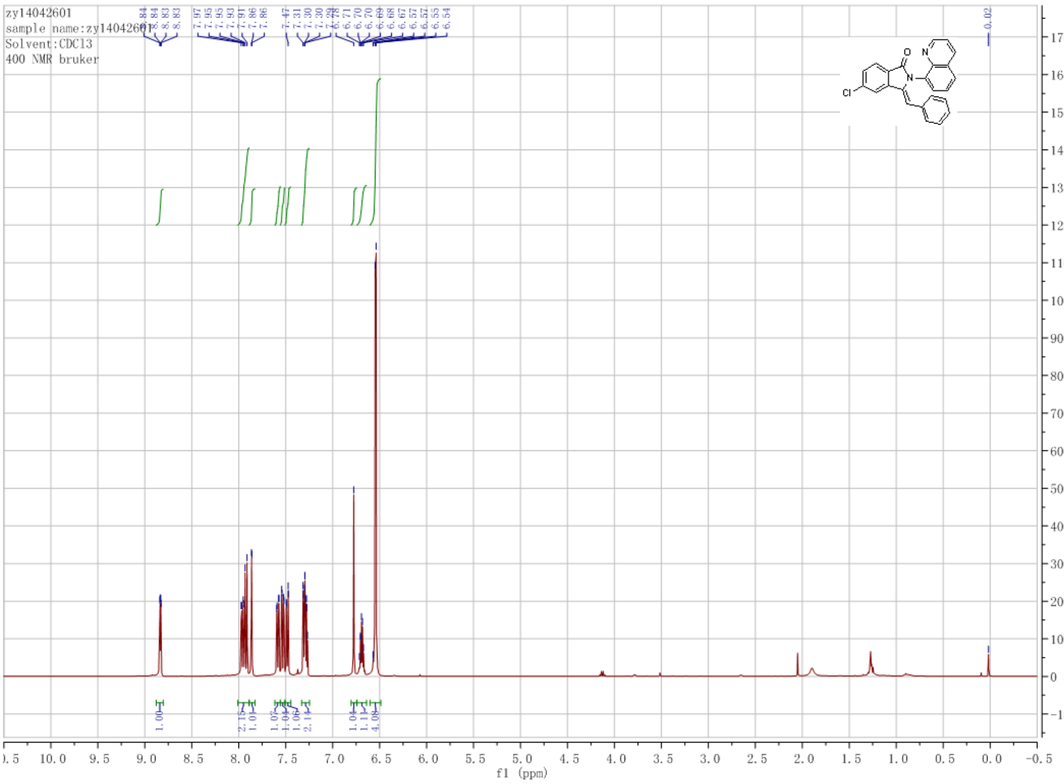
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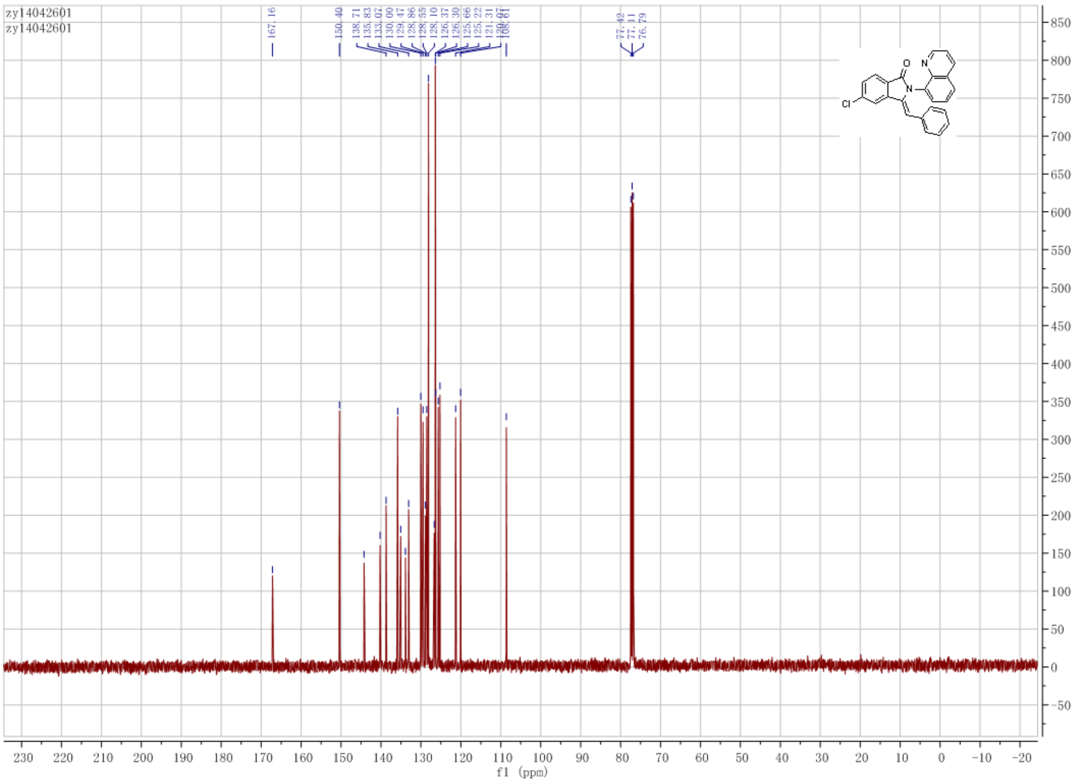
Cl
f1 (ppm)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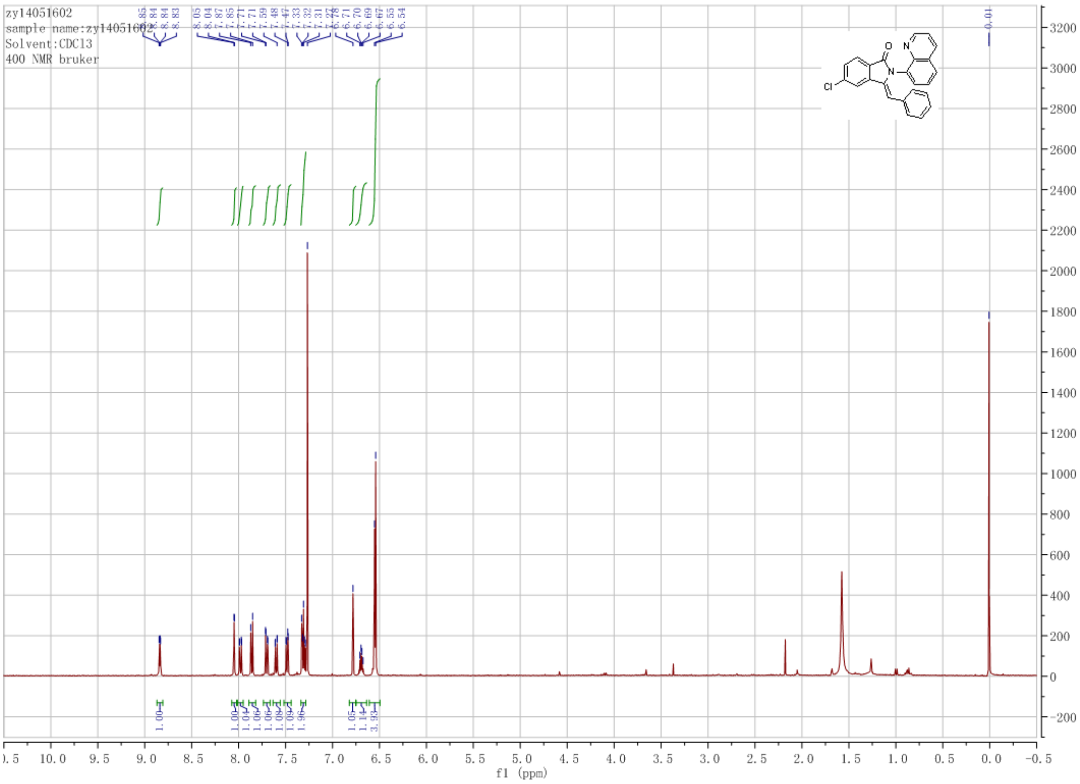
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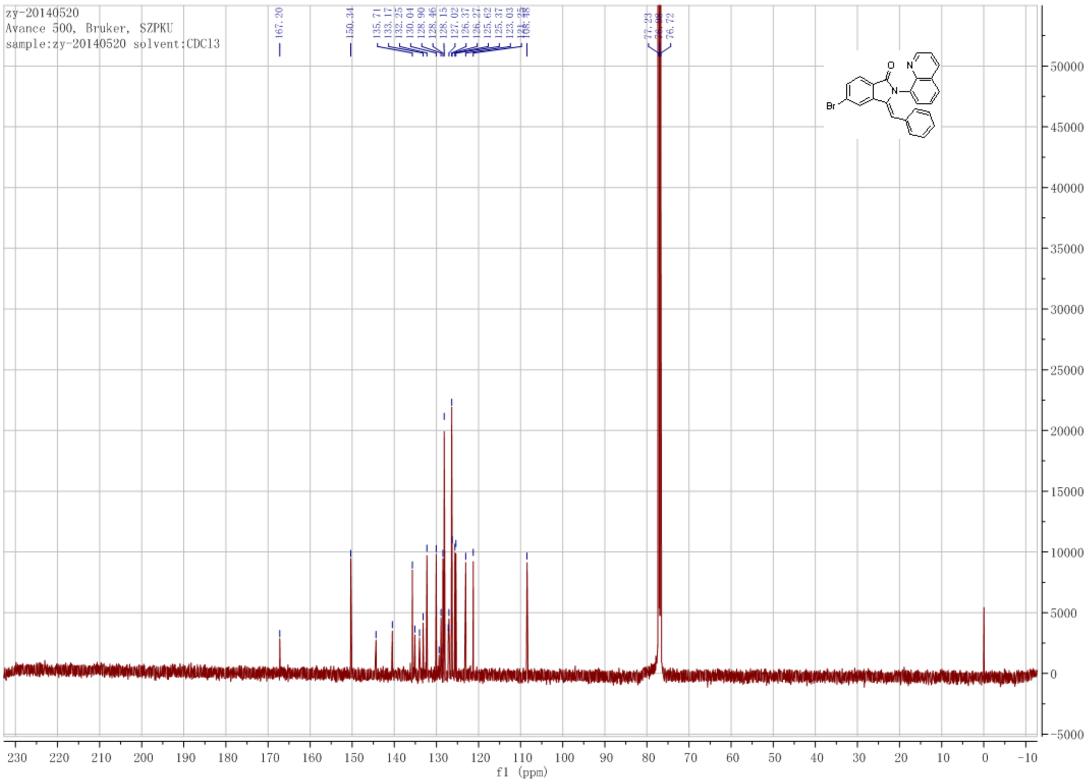
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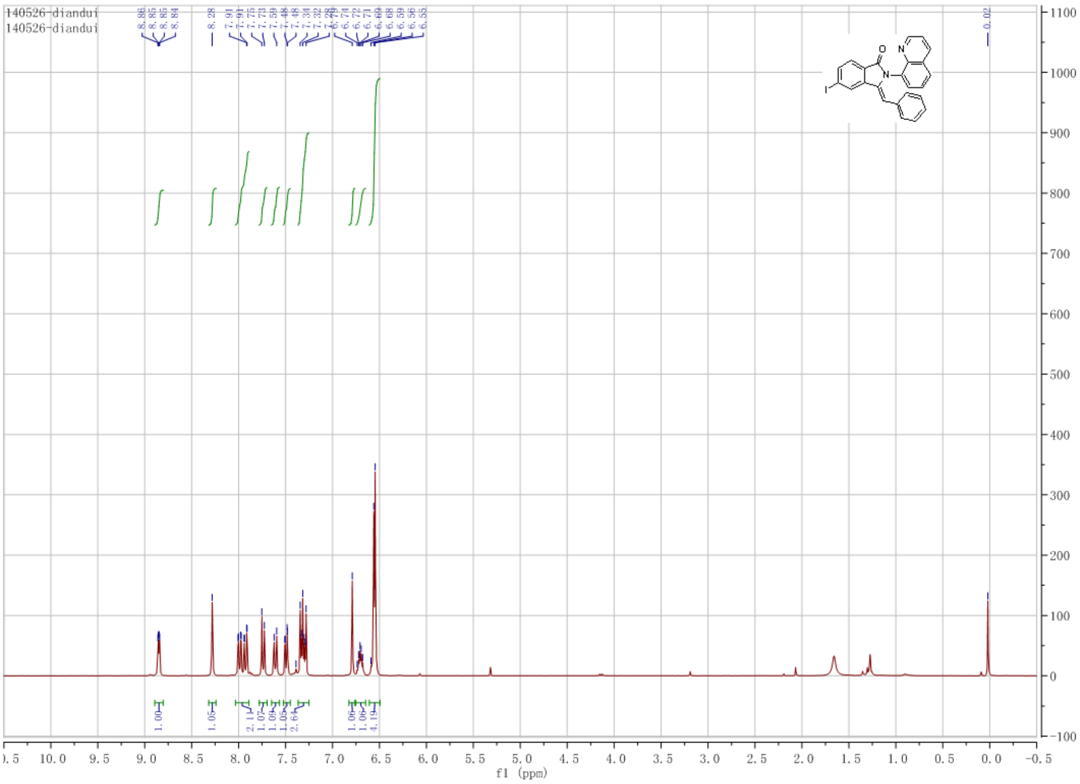
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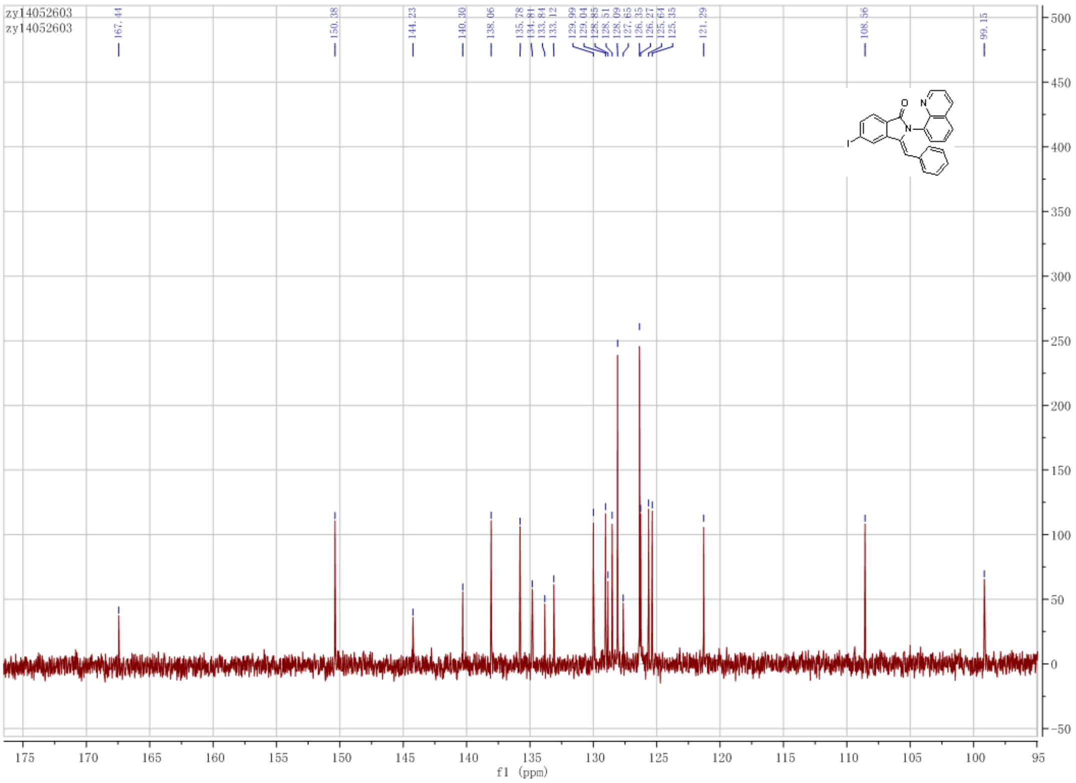
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N
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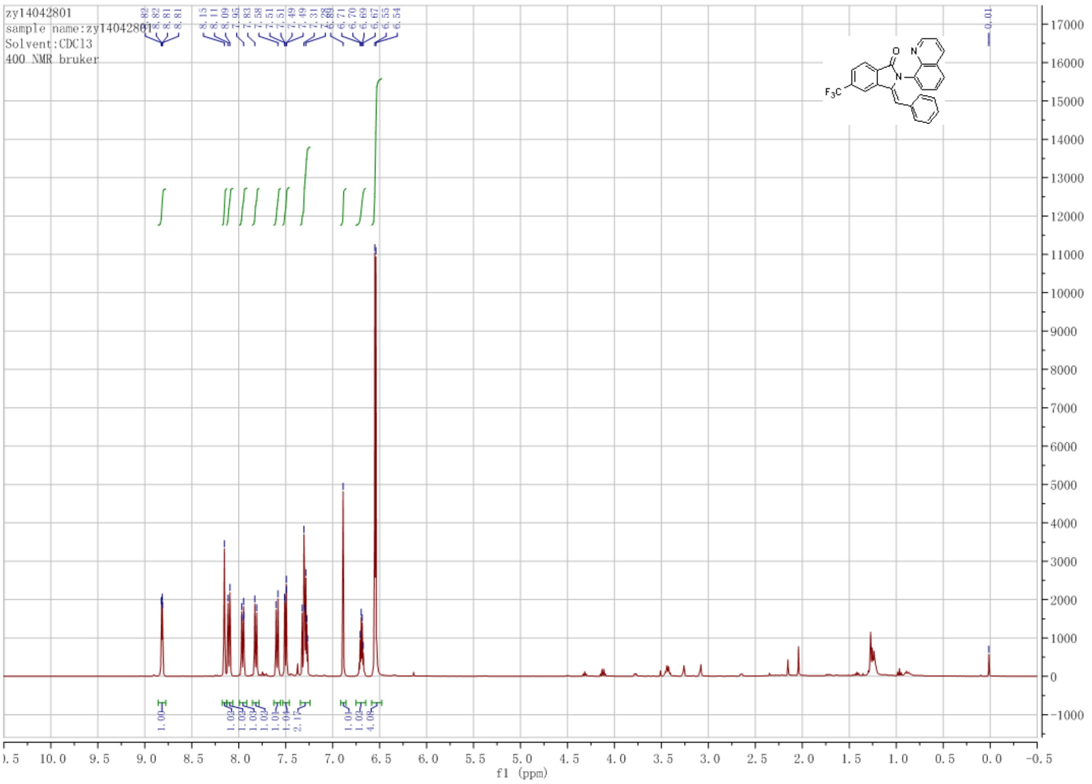
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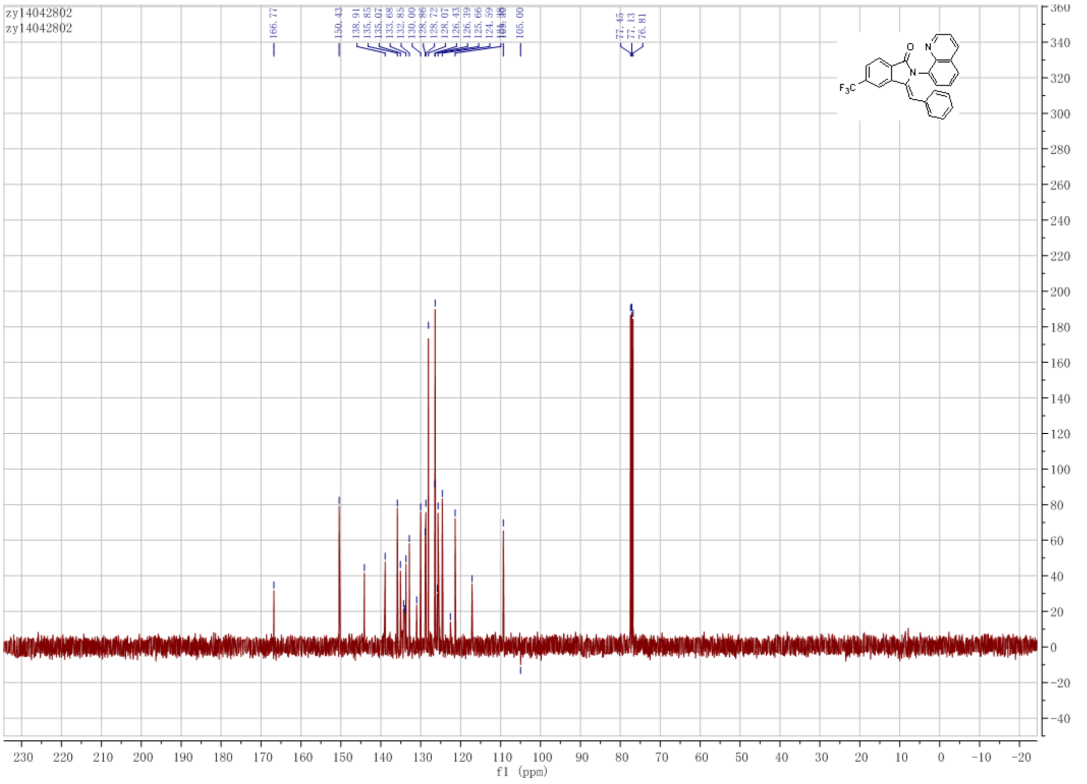
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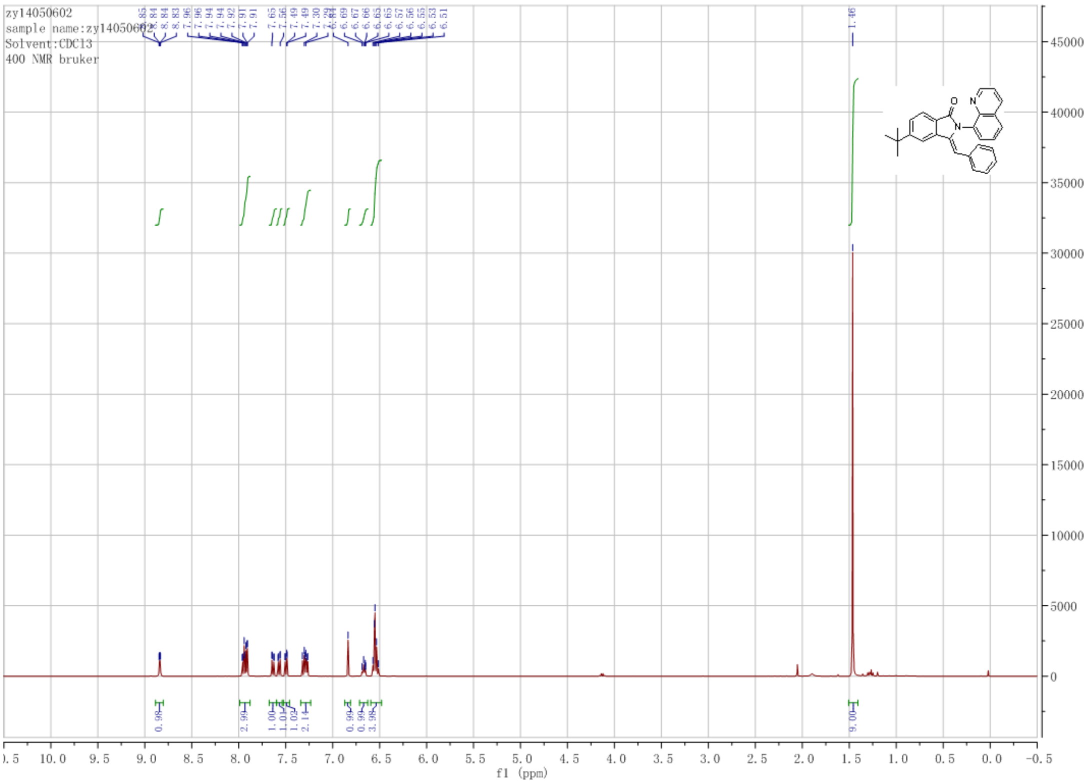
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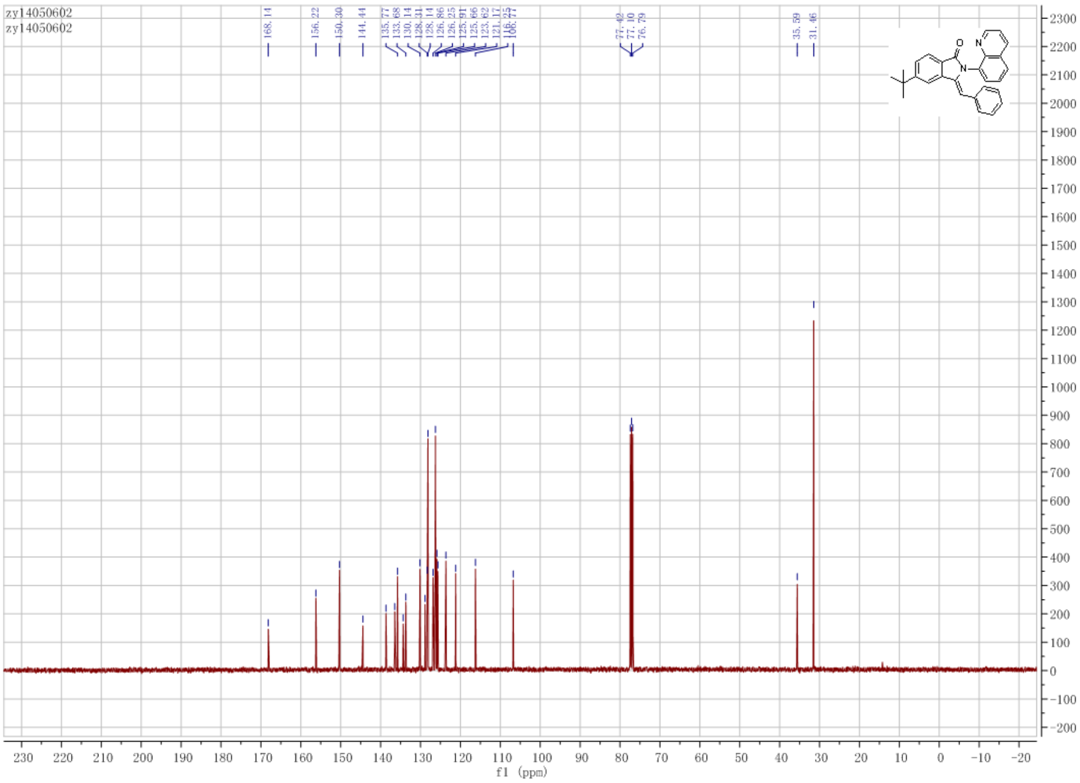
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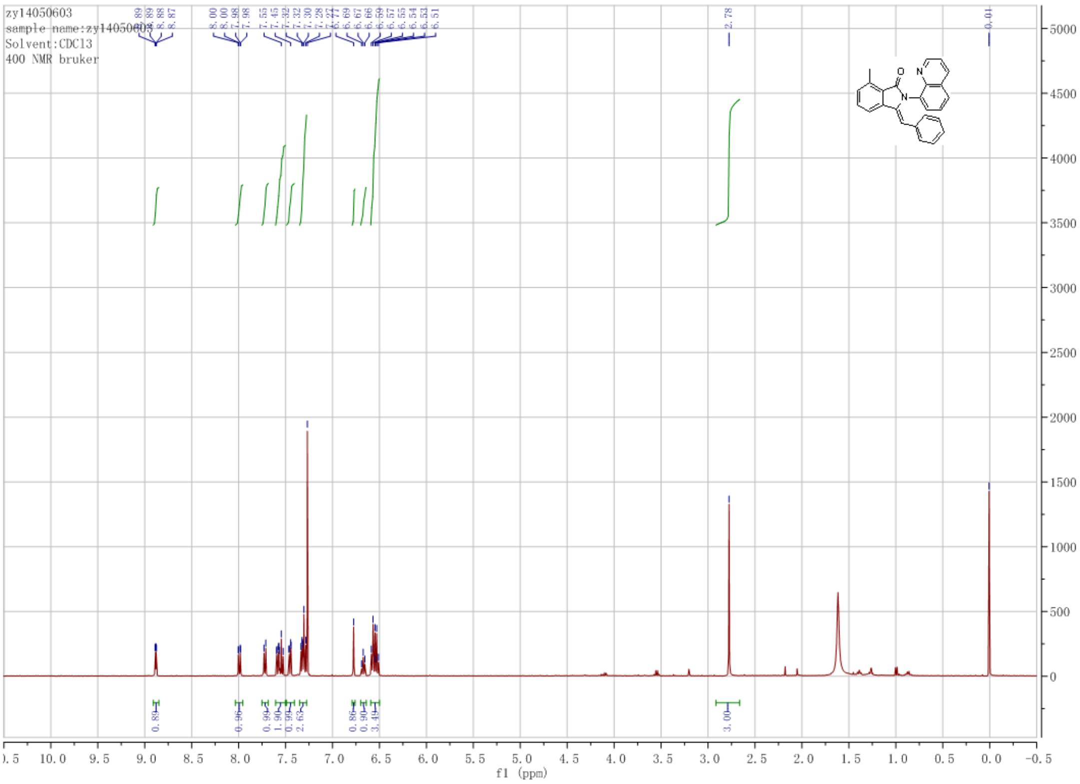
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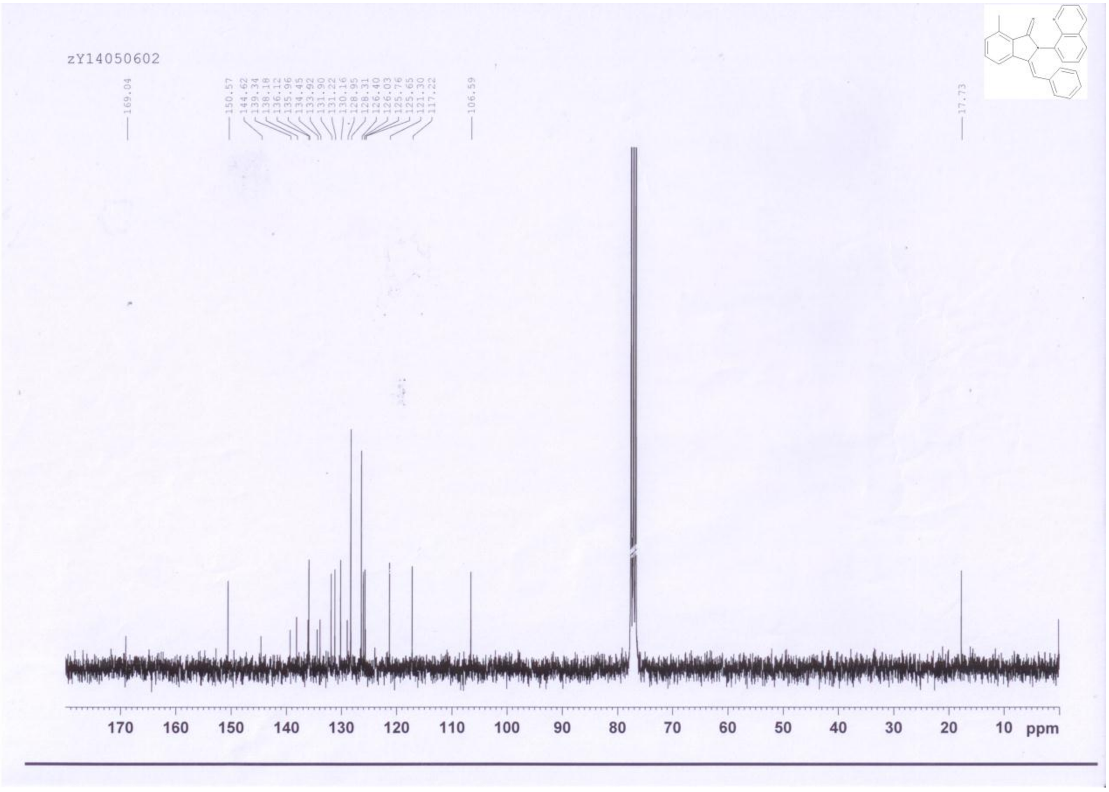
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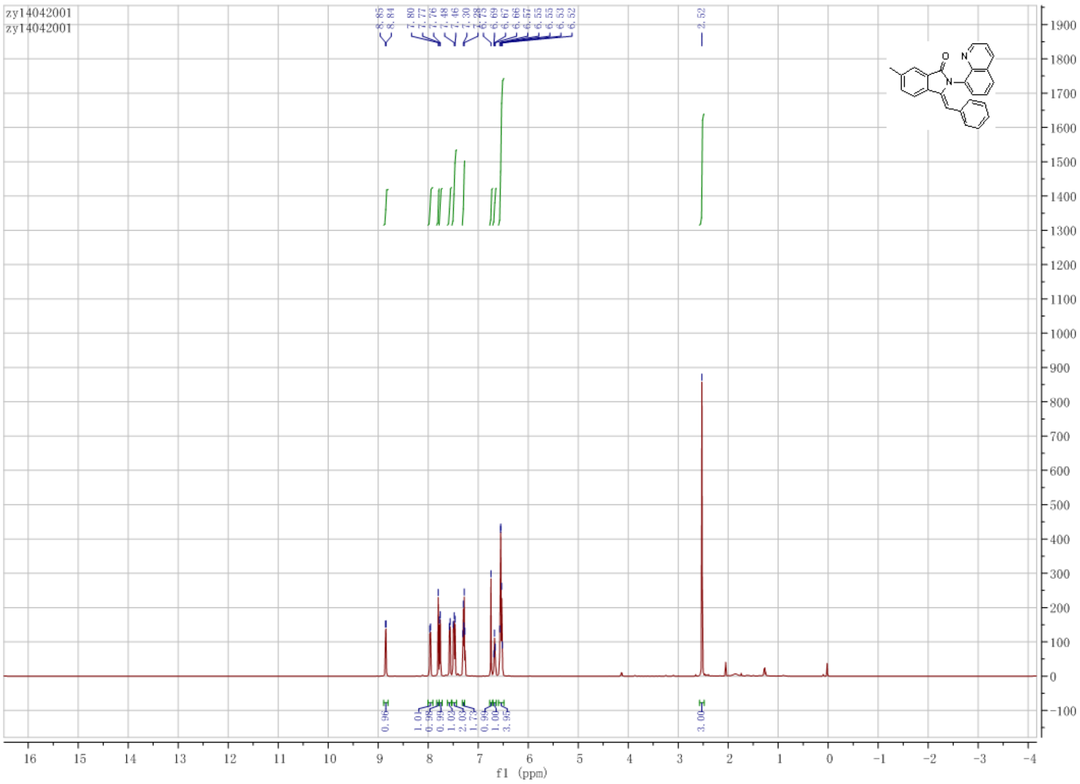
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3.00
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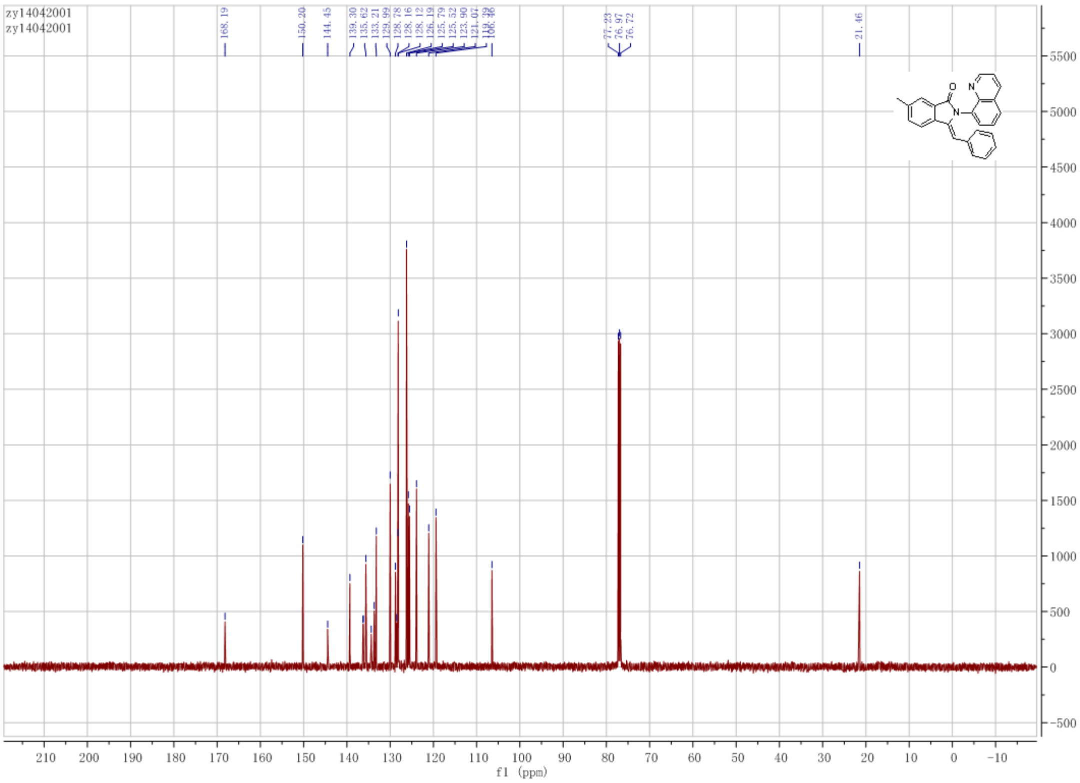
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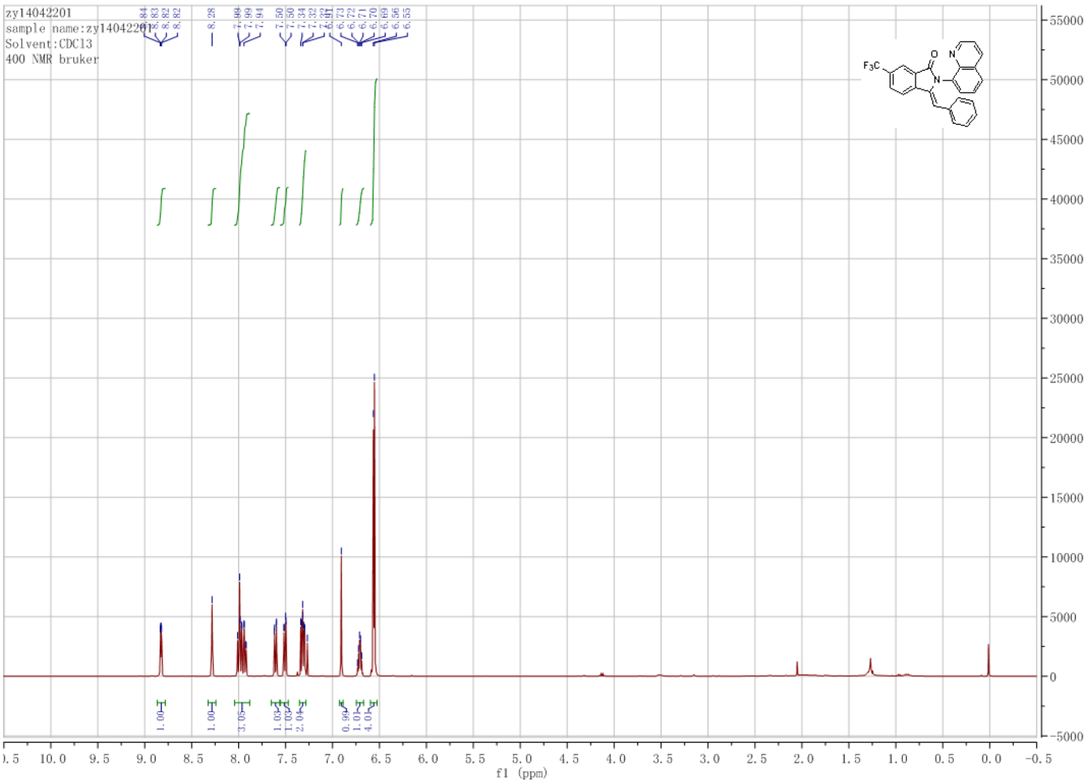
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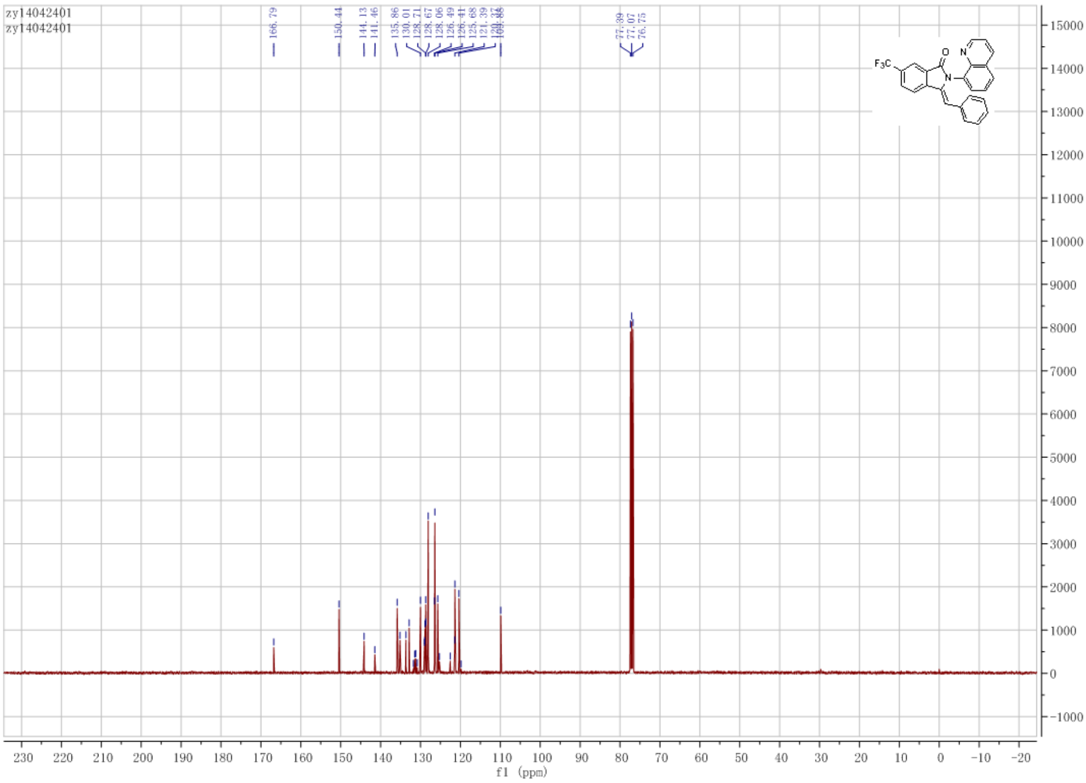
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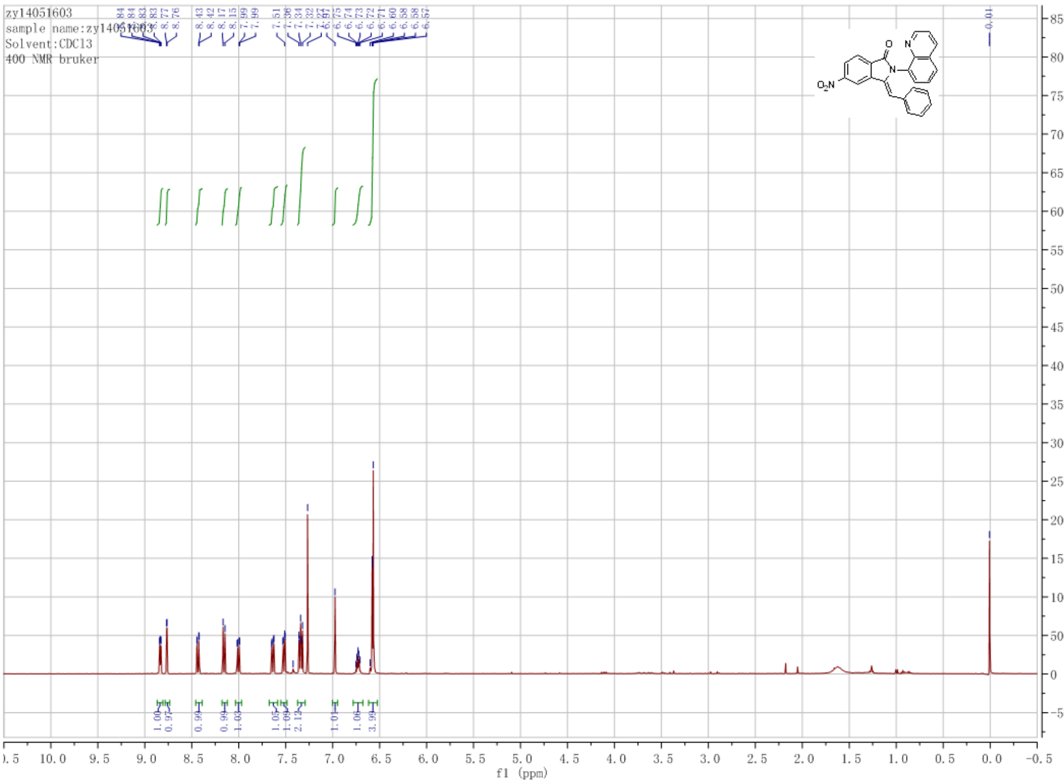
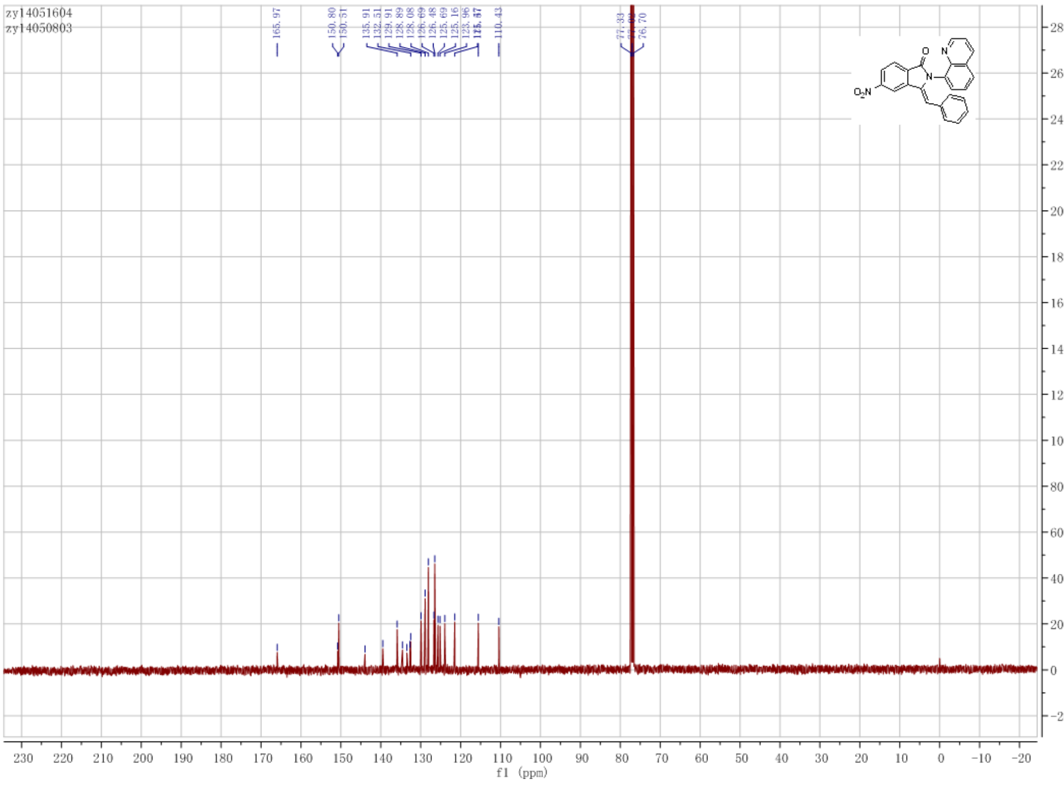
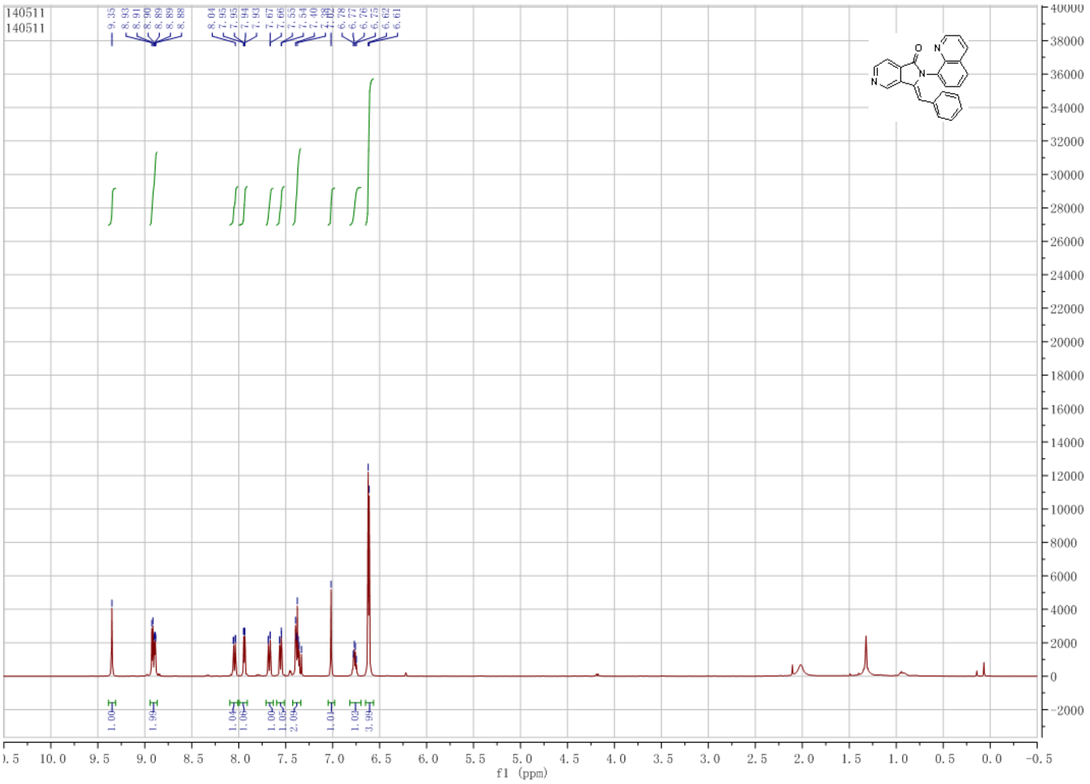
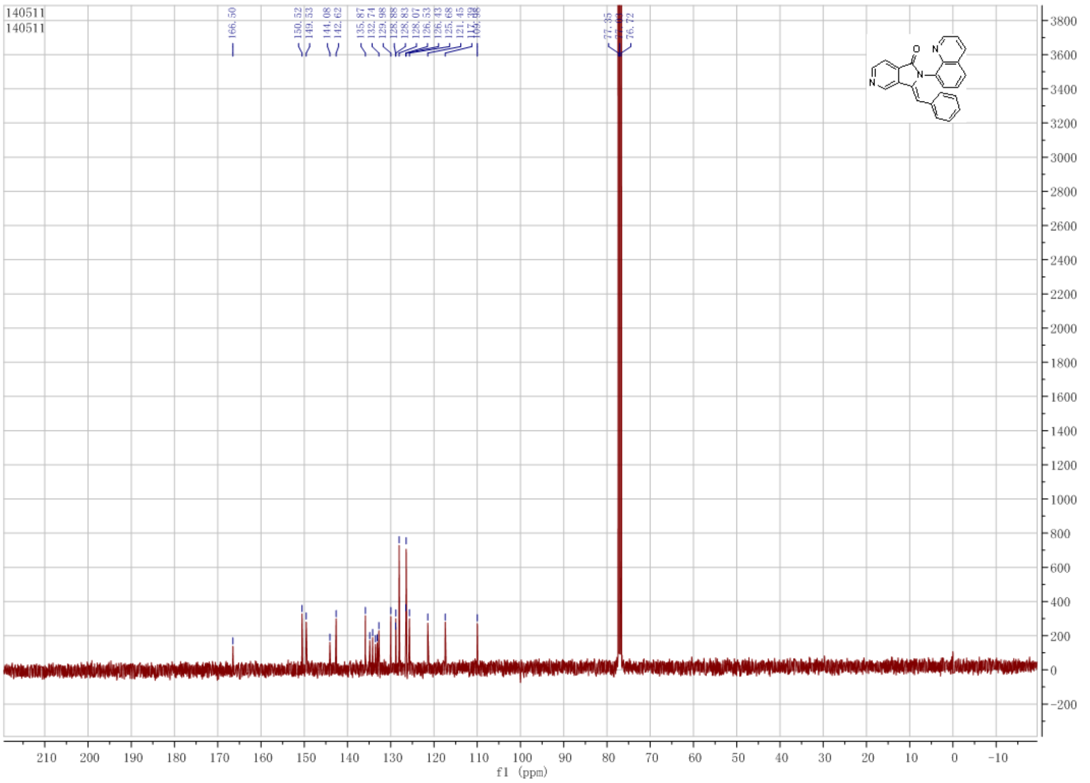
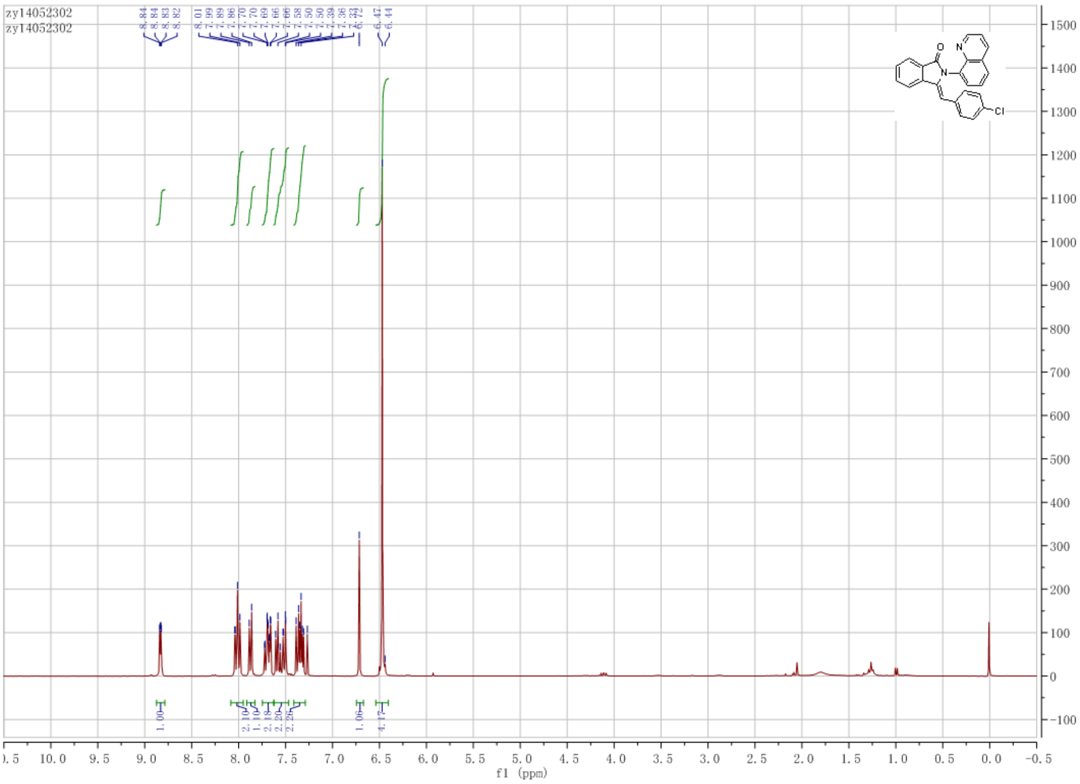
150.44
144.13 141.46
135.86 130.01 128.71 128.67 128.06 126.49 126.41 125.68 121.39 120.37 109.88
77.39 77.07 76.75
F3C
O
N
f1 (ppm)

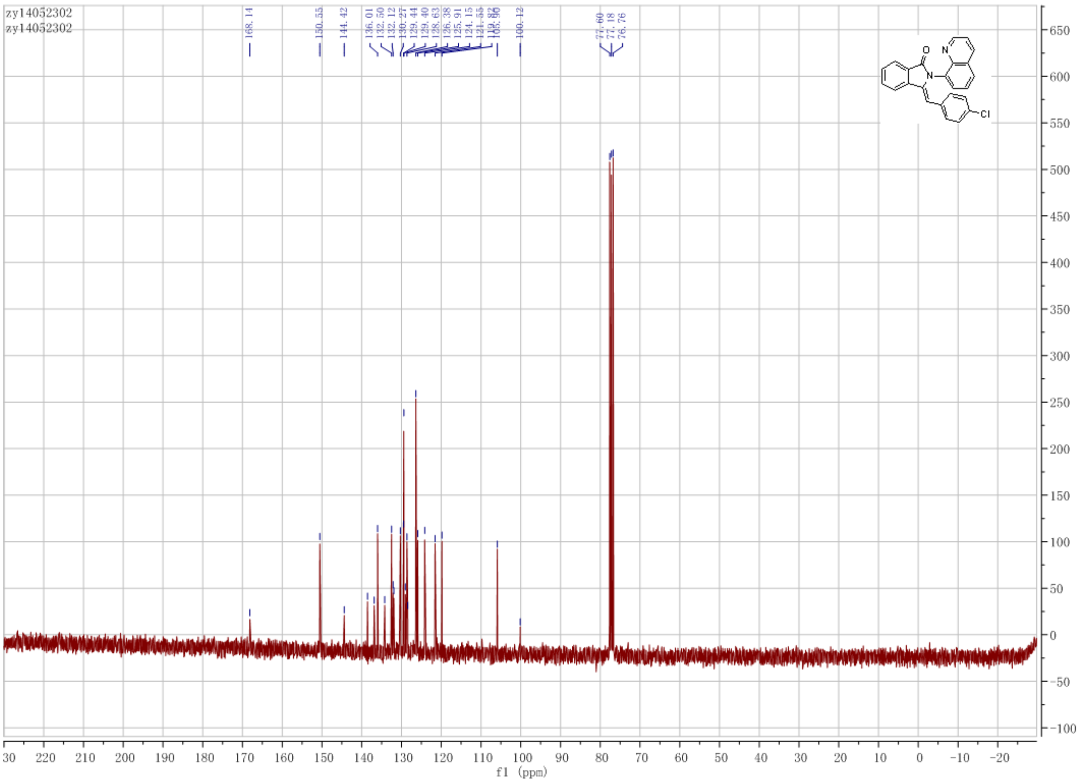

zy14051603
sample name:zy14051603
Solvent:CDCl3
400 NMR bruker
8.84 8.84 8.83 8.83 8.77 8.76 8.43 8.42 8.17 8.15 7.99 7.99 7.51 7.36 7.34 7.32 7.27 6.97 6.75 6.74 6.73 6.72 6.71 6.60 6.58 6.58 6.57
-0.01
1.00 0.97 0.99 0.99 1.03 1.05 1.09 2.12 1.01 1.06 3.99
O
N
N
O2N
f1 (ppm)

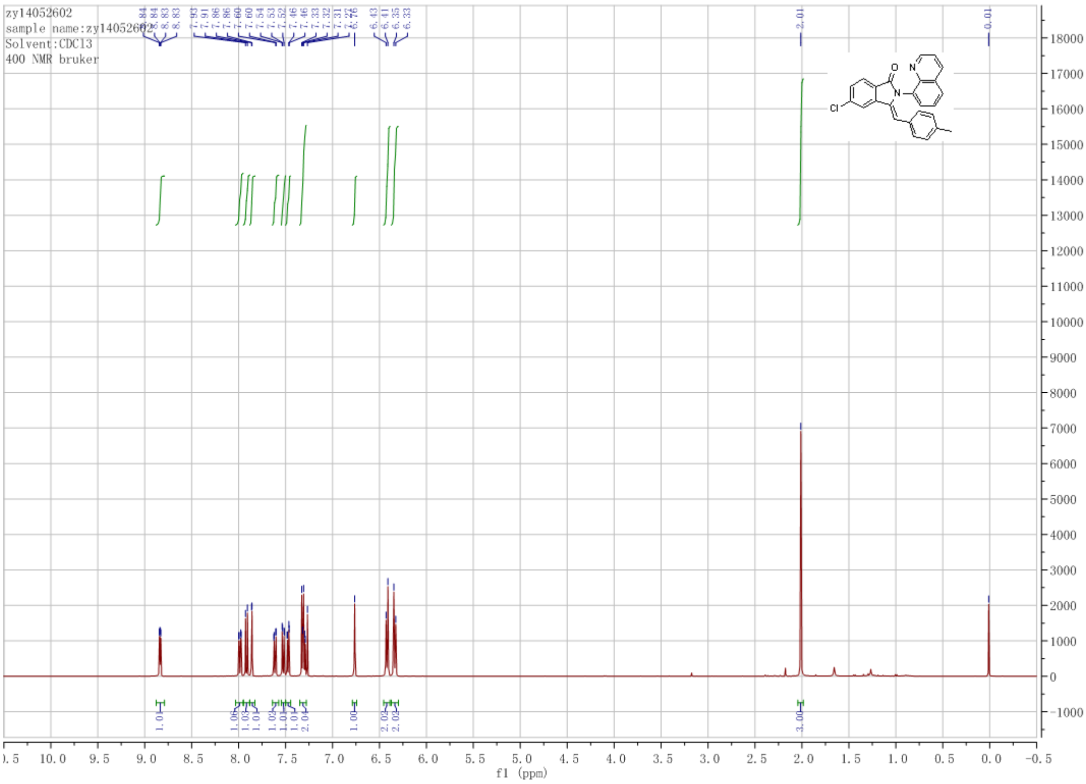

zy14051604
zy14050803
165.97
150.80 150.51
135.91 132.51 129.91 128.89 128.08 126.69 126.48 125.69 125.16 123.96 115.47 115.37 110.43
77.33 77.02 76.70
O
N
N
O2N
f1 (ppm)

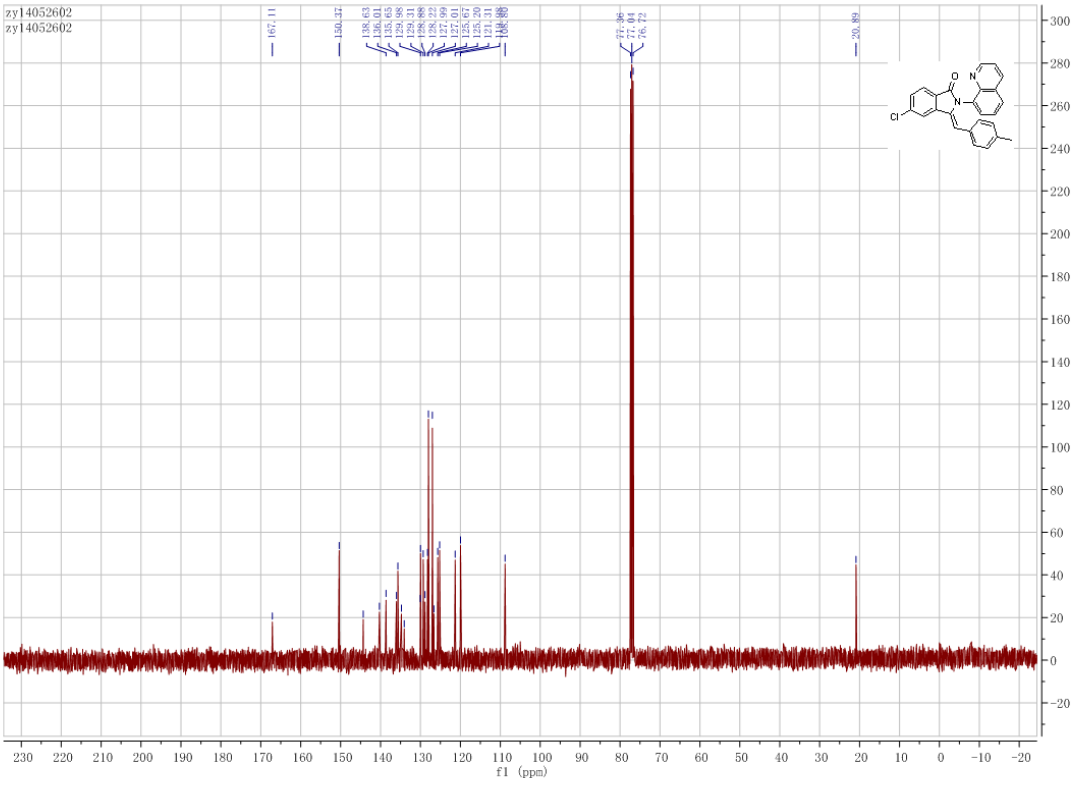

140511
140511
9.35
8.93
8.91
8.90
8.89
8.89
8.88
8.04
7.95
7.95
7.94
7.93
7.67
7.66
7.55
7.54
7.40
7.38
6.78
6.77
6.76
6.75
6.62
6.61
1.00
1.99
1.04
1.06
1.00
1.05
2.04
1.01
1.02
3.99
O
N
N
N
f1 (ppm)

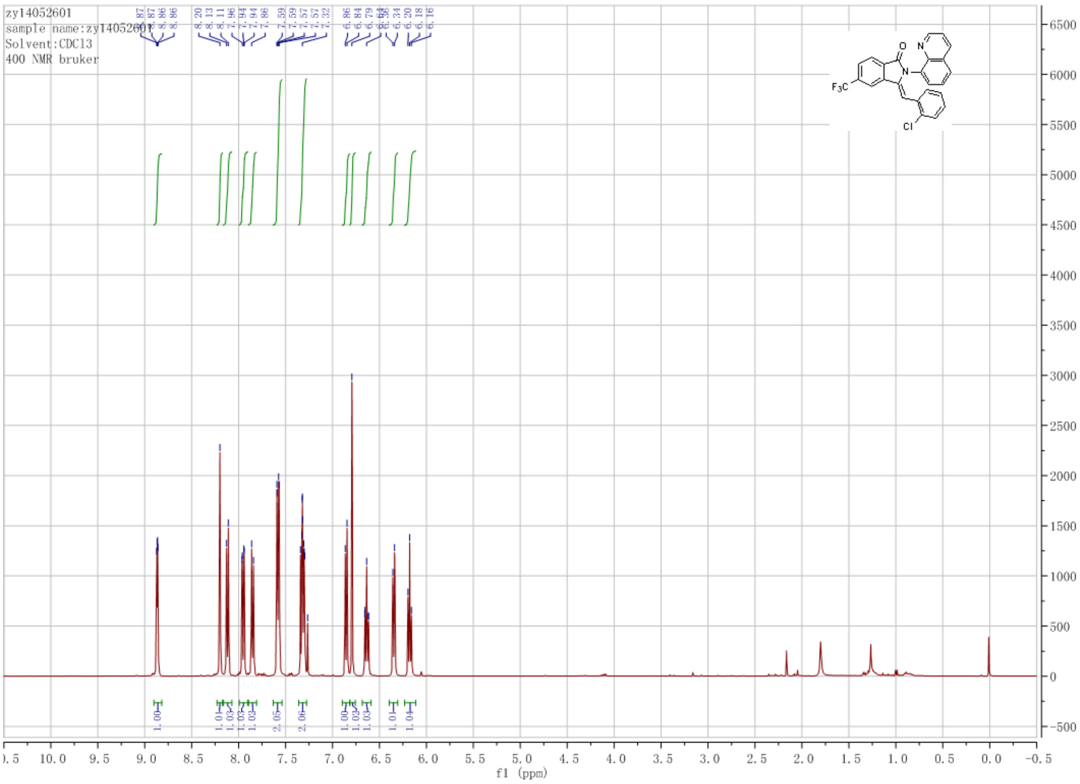

140511
140511
166.50
150.52
149.53
144.08
142.62
135.87
132.74
129.98
128.88
128.83
128.07
126.53
126.43
125.68
121.45
77.35
76.72
O
N
N
N
f1 (ppm)

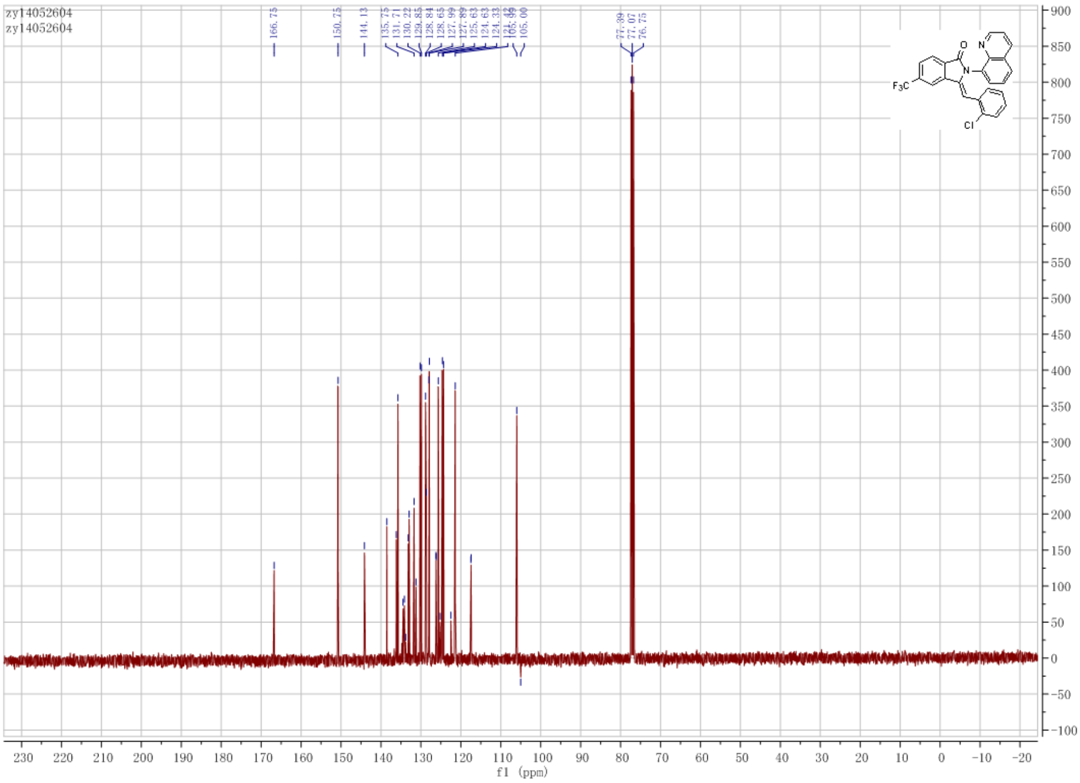

zy14052302
zy14052302
8.84
8.84
8.83
8.82
8.01
7.99
7.89
7.86
7.70
7.70
7.69
7.66
7.66
7.58
7.50
7.50
7.39
7.36
7.33
6.72
6.47
6.44
1.00
2.10
1.10
2.18
2.20
2.26
1.06
4.17
O
N
N
Cl
f1 (ppm)

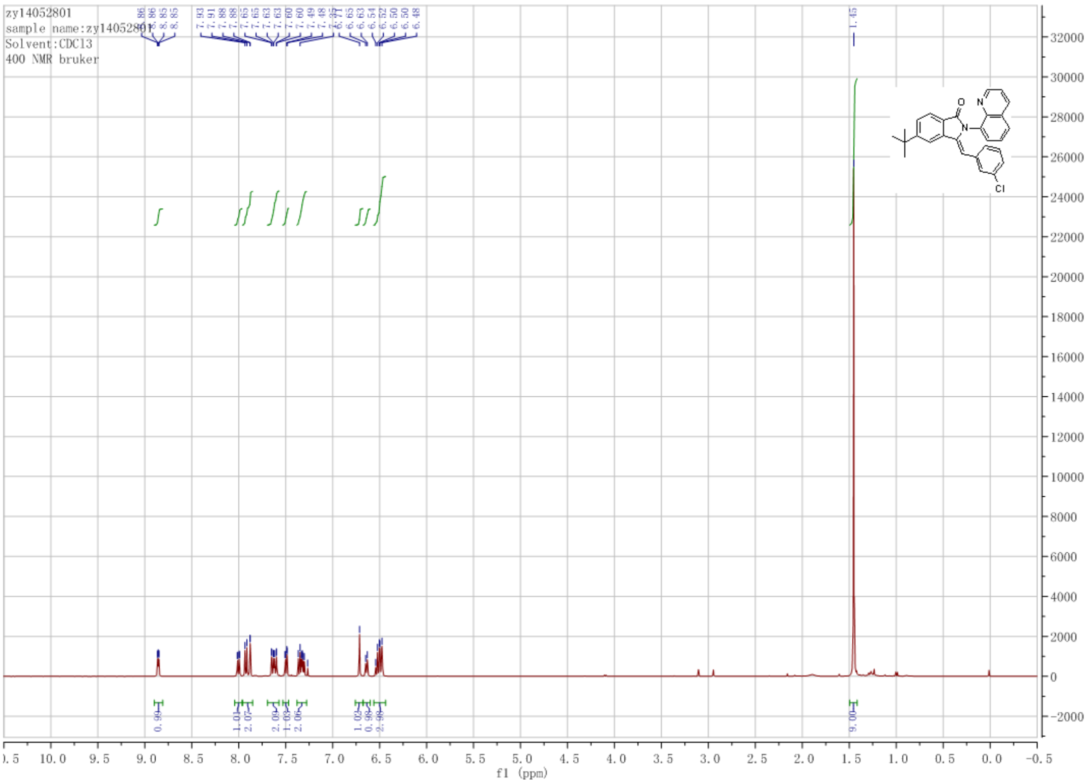

zy14052302
zy14052302
168.14
150.55
144.42
136.01
132.50
132.12
130.27
129.44
129.40
128.63
126.38
125.91
124.15
121.55
119.82
105.96
100.12
77.60
77.18
76.76
O
N
N
Cl
f1 (ppm)

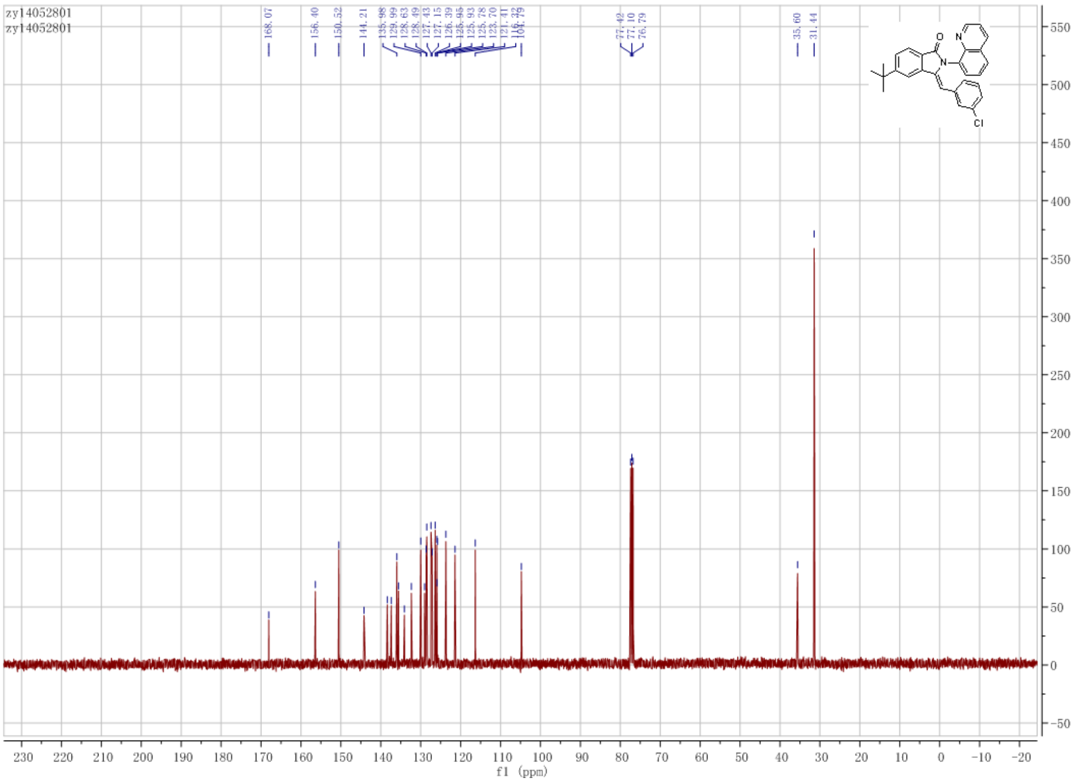

zy14052602
sample name:zy14052602
Solvent:CDCl3
400 NMR bruker
8.84
8.84
8.83
8.83
7.93
7.91
7.86
7.86
7.60
7.60
7.54
7.53
7.52
7.46
7.46
7.33
7.32
7.31
7.27
6.76
6.43
6.41
6.35
6.33
2.01
0.01
1.04
1.06
1.03
1.04
1.02
1.01
1.01
2.04
1.00
2.02
2.02
3.00
Cl
O
N
N
f1 (ppm)

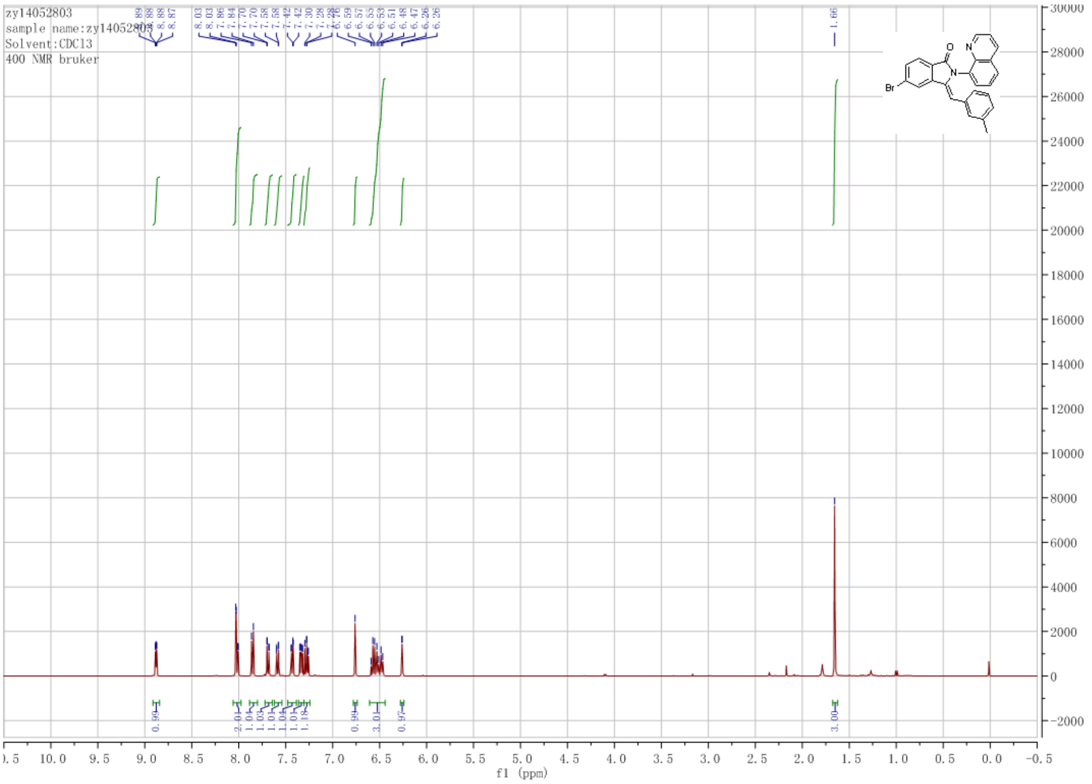

zy14052602
zy14052602
167.11
150.37
138.63
136.01
135.65
129.98
129.31
128.88
128.22
127.99
127.01
125.67
125.20
121.31
108.80
77.36
77.04
76.72
20.89
Cl
O
N
N
f1 (ppm)

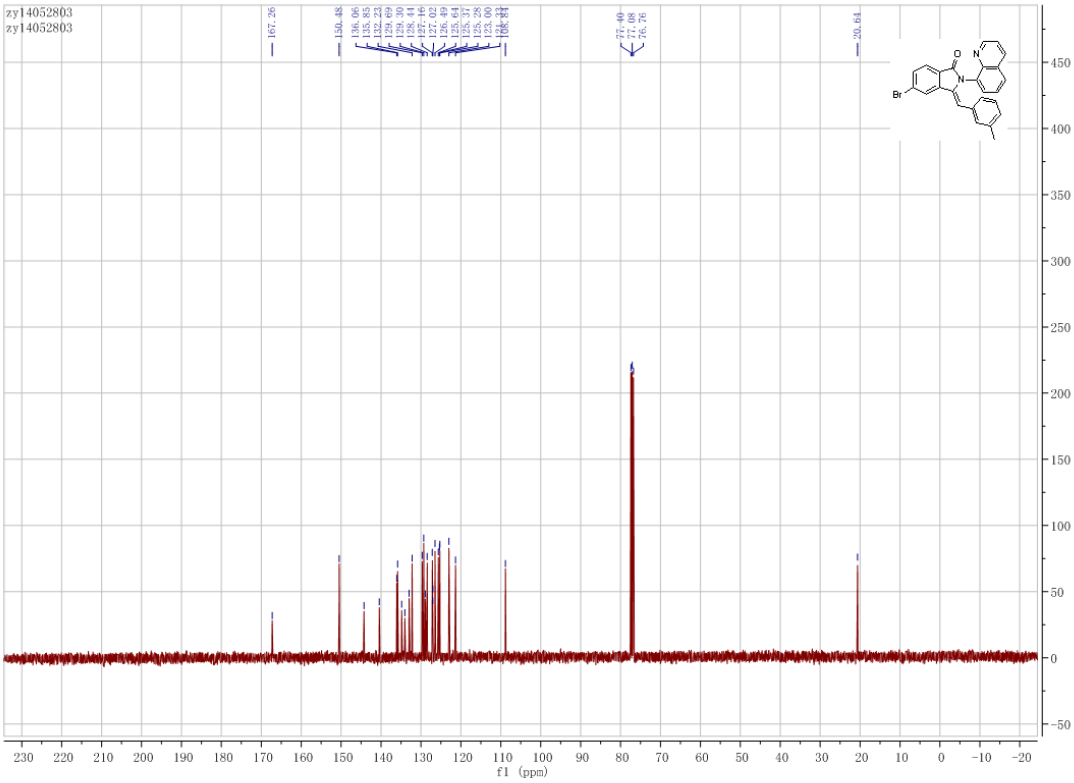

zy14052601
sample name:zy14052601
Solvent:CDC13
400 NMR bruker
8.87 8.87 8.86 8.86 8.20 8.13 8.11 7.96 7.94 7.94 7.86 7.59 7.59 7.57 7.57 7.32 6.86 6.84 6.79 6.64 6.36 6.34 6.20 6.18 6.16
1.00 1.01 1.03 1.03 1.02 2.05 2.06 1.00 1.02 1.03 1.01 1.04
F3C
O
N
N
Cl
f1 (ppm)

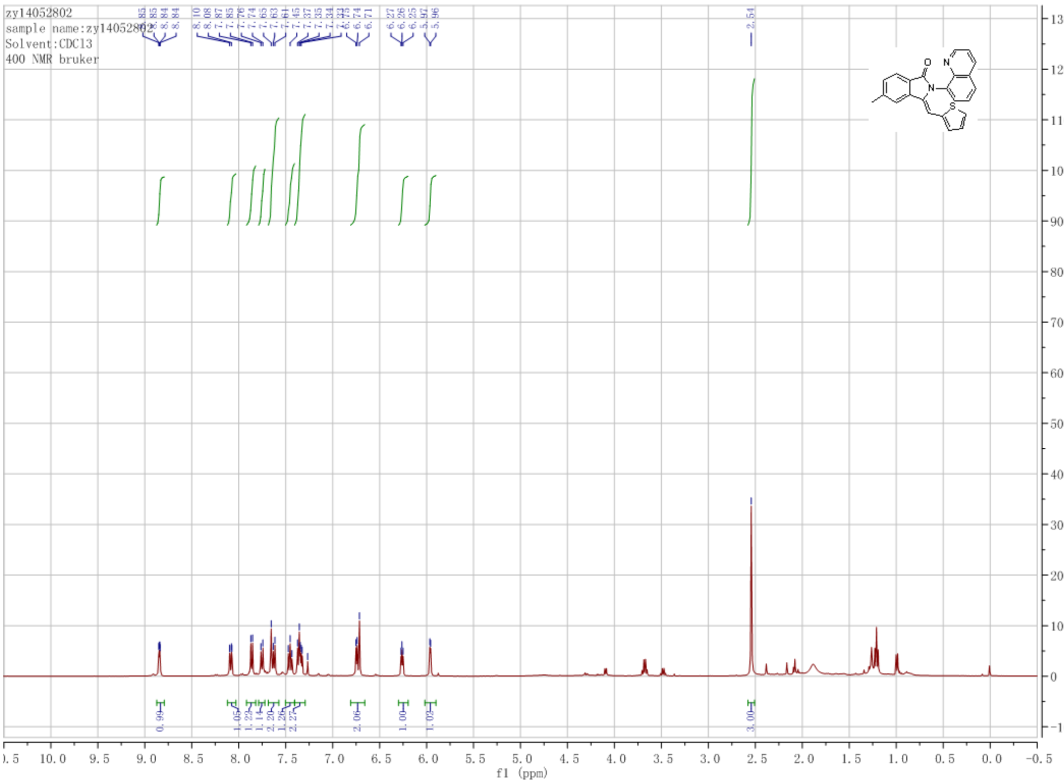

zy14052604
zy14052604
166.75 150.75 144.13 135.75 131.71 130.22 129.85 128.84 128.65 127.99 127.89 125.63 124.63 124.33 121.42 105.99 105.00 77.39 77.07 76.75
F3C
O
N
N
Cl
f1 (ppm)

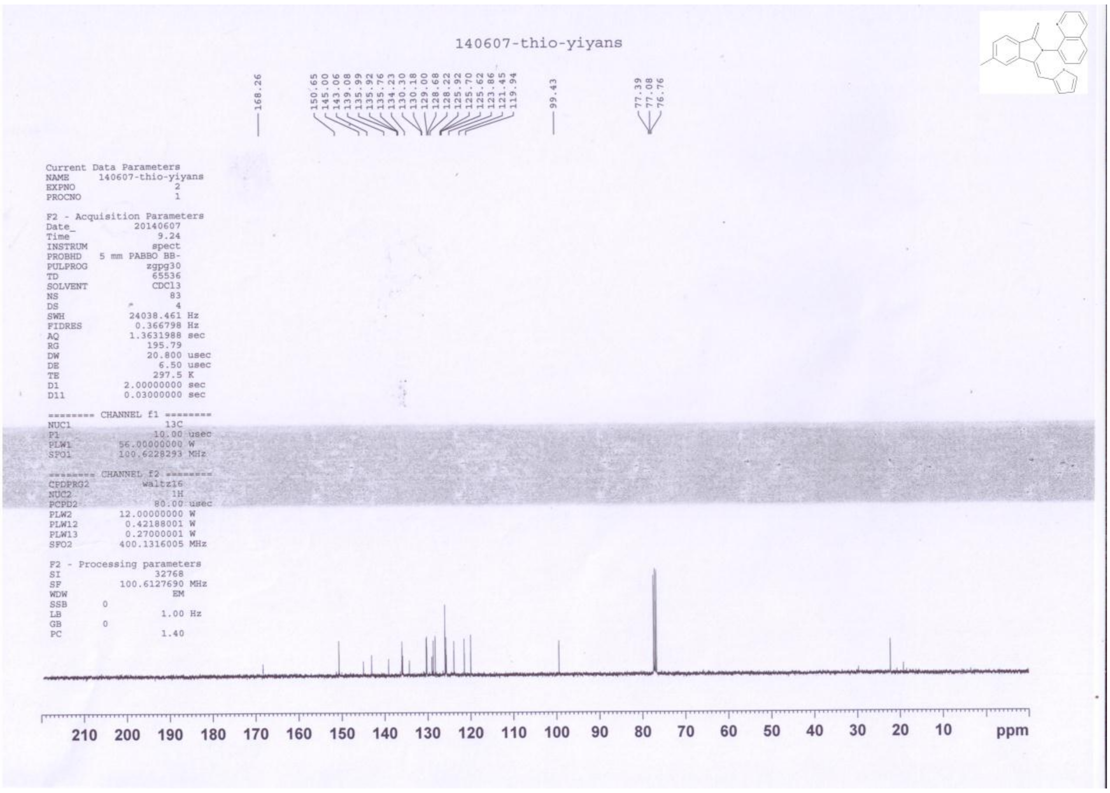

zy14052801
sample name:zy14052801
Solvent:CDCl3
400 NMR bruker
8.86 8.86 8.85 8.85
7.93 7.91 7.88 7.88 7.65 7.65 7.63 7.63 7.60 7.60 7.49 7.48 7.35
6.71 6.65 6.63 6.54 6.52 6.50 6.50 6.48
1.45
0.99 1.01 2.07 2.09 1.03 2.06 1.02 0.98 2.98 9.00
O
N
N
Cl
f1 (ppm)

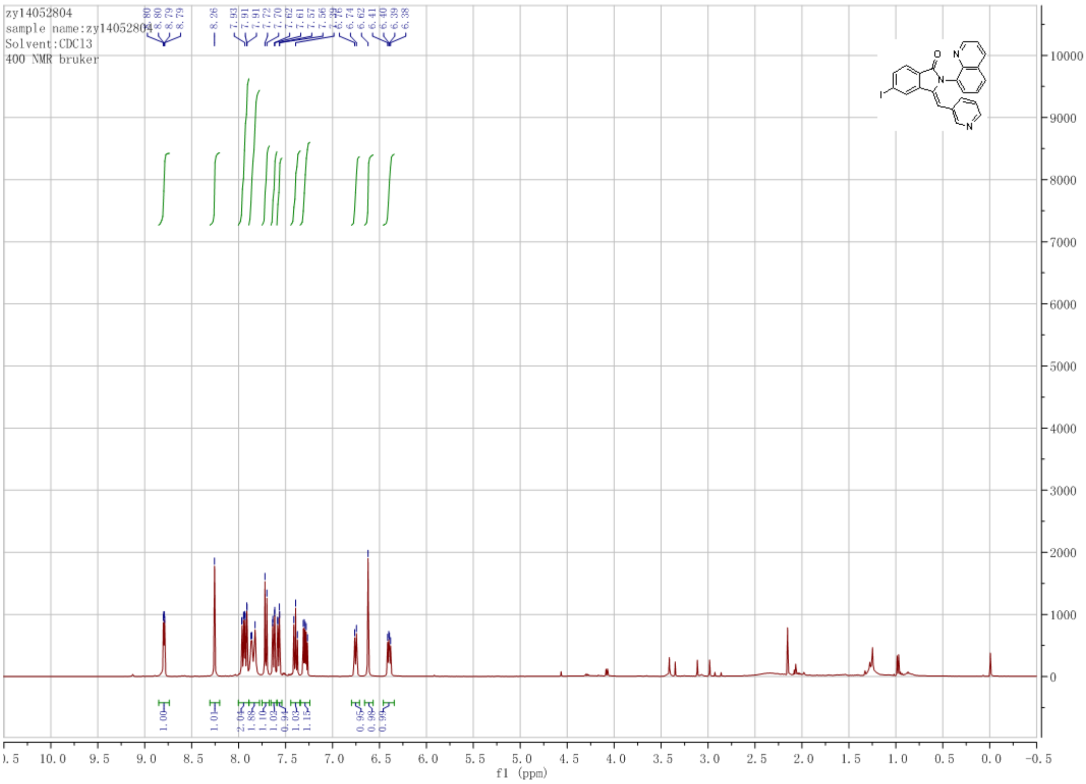

zy14052801
zy14052801
168.07
156.40
150.52
144.21
135.98 129.99 128.63 128.49 127.43 127.15 126.39 125.95 125.93 125.78 123.70 121.41 116.32 104.79
77.42 77.10 76.79
35.60
31.44
O
N
N
Cl
f1 (ppm)

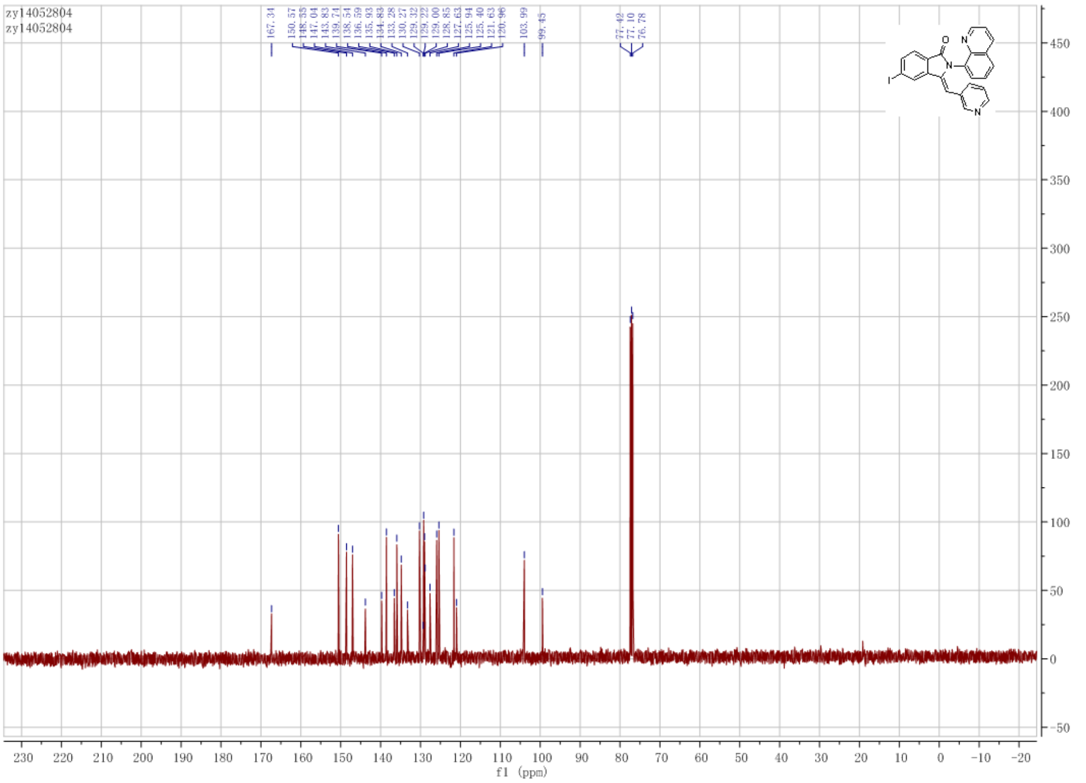

zy14052803
sample name:zy14052803
Solvent:CDCl3
400 NMR bruker
8.89
8.88
8.88
8.87
8.03
8.03
7.86
7.84
7.70
7.70
7.58
7.58
7.42
7.42
7.30
7.28
7.28
6.76
6.59
6.57
6.55
6.53
6.51
6.48
6.47
6.26
6.26
1.66
0.99
2.01
1.04
1.03
1.01
1.04
1.01
1.18
0.99
3.01
0.97
3.00
O
N
N
Br
f1 (ppm)
10.0
9.5
9.0
8.5
8.0
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
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000


zy14052803
zy14052803
167.26
150.48
136.06
135.85
132.23
129.69
129.30
128.44
127.16
127.02
126.49
125.64
125.37
125.28
123.00
121.33
108.84
77.40
77.08
76.76
20.64
O
N
N
Br
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
450
400
350
300
250
200
150
100
50
0
-50


zy14052802
sample name:zy14052802
Solvent:CDCl3
400 NMR bruker
8.85
8.85
8.84
8.84
8.10
8.08
7.87
7.85
7.76
7.74
7.65
7.63
7.61
7.45
7.37
7.35
7.34
7.33
6.75
6.74
6.71
6.27
6.26
6.25
5.97
5.96
2.54
0.99
1.05
1.23
1.14
2.20
1.20
2.27
2.06
1.00
1.03
3.00
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.5
10.0
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)
O
N
N
S


140607-thio-yiyans
168.26
150.65
145.00
143.06
139.08
135.99
135.92
135.76
134.23
130.30
130.18
129.00
128.68
128.22
125.92
125.70
125.62
123.86
121.45
119.94
99.43
77.39
77.08
76.76
Current Data Parameters
NAME 140607-thio-yiyans
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140607
Time 9.24
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 83
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 195.79
DW 20.800 usec
DE 6.50 usec
TE 297.5 K
D1 2.00000000 sec
D11 0.03000000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 10.00 usec
PLW1 56.00000000 W
SFO1 100.6228293 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PLW2 12.00000000 W
PLW12 0.42188001 W
PLW13 0.27000001 W
SFO2 400.1316005 MHz
F2 - Processing parameters
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


zy14052804
sample name:zy14052804
Solvent:CDCl3
400 NMR bruker
8.80
8.80
8.79
8.79
8.26
7.93
7.91
7.91
7.72
7.70
7.62
7.61
7.57
7.56
7.39
6.76
6.74
6.62
6.41
6.40
6.39
6.38
1.00
1.01
2.04
1.88
1.10
1.02
0.94
1.03
1.15
0.95
0.98
0.99
O
N
N
I
N
f1 (ppm)


zy14052804
zy14052804
167.34
150.57
148.55
147.04
143.83
139.74
138.54
136.59
135.93
134.83
133.28
130.27
129.32
129.22
129.00
128.85
127.63
125.94
125.40
121.63
120.96
103.99
99.45
77.42
77.10
76.78
O
N
N
I
N
f1 (ppm)