Supporting Information

Pd/C-catalyzed Transfer Hydrogenation of *N*-H Indoles with Trifluoroethanol and Tetrahydroxydiboron as Hydrogen Source

Xiao-Yu Zhou and Xia Chen*

School of Chemistry and Materials Engineering, Liupanshui Normal University, Liupanshui, 553004, China

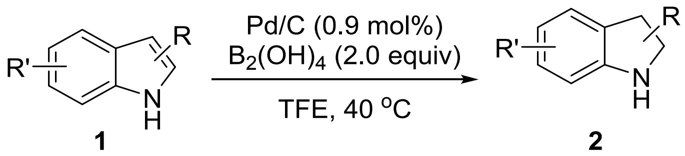
xia811@live.cn (X. Chen)

Table of Contents

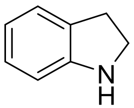
1. General and Materials.

All reagents and solvents were of pure analytical grade. Pd/C (Type 394) is 10 wt% palladium on activated carbon paste with 50 wt% water that purchased from Johnson Matthey (product code: 113390). Thin layer chromatography (TLC) was performed on HSGF254 silica gel, pre-coated on glass-backed plates coated with 0.2 mm silica and revealed with either a UV lamp (λ_{max} = 254 nm). The products were purified by flash column chromatography on silica gel 200-300 mesh. ^{1}H and ^{13}C NMR spectra were recorded on a 600 MHz spectrometer (^{1}H 600 MHz, ^{13}C 151 MHz) using $CDCl_3$ or d^6-DMSO as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature. Chemical shifts are in δ (ppm) relative to TMS. The coupling constants (J) are in Hz.

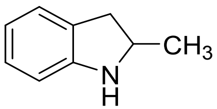
2. The Typical Procedure for Pd/C-catalyzed Transfer Hydrogenation of Indoles



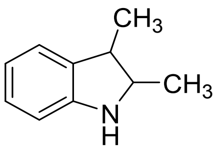
The Typical Procedure for Pd/C Catalyzed Transfer Hydrogenation of Indoles: A mixture of indole **1** (0.50 mmol), Pd/C (10.0 mg, 10 wt% palladium on activated carbon paste and 50% moisture, 0.9 mol% [Pd] based on starting material **1**) in 2,2,2-trifluoroethanol (3 mL) was added into a Schlenk flask (25 mL) and stirred at room temperature. Then $B_2(OH)_4$ (90 mg, 1.0 mmol, 2.0 equiv) was added and the mixture was stirred at 40 °C. When the reaction was complete monitored by TLC, the solvent was evaporated under reduced pressure and the residue was purified by column chromatography (petroleum ether/ethyl acetate 50:1 to 20:1) to provide indolines **2**.



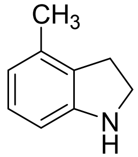
Indoline (2a):[1] Yield: 99%, 59.2 mg, colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21 (d, J = 7.2 Hz, 1H), 7.11 (t, J = 7.6 Hz, 1H), 6.80 (t, J = 7.3 Hz, 1H), 6.72 (d, J = 7.8 Hz, 1H), 3.78 (s, 1H), 3.61 (t, J = 8.4 Hz, 2H), 3.11 (t, J = 8.4 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 151.7, 129.4, 127.3, 124.7, 118.7, 109.5, 47.4, 29.9.



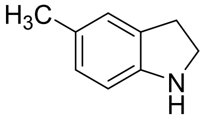
2-methylindoline (2b):[1] Yield: >99%, 66.5 mg, colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.19 (d, J = 7.3 Hz, 1H), 7.13 (t, J = 7.6 Hz, 1H), 6.81 (t, J = 7.4 Hz, 1H), 6.70 (d, J = 7.8 Hz, 1H), 4.11-4.02 (m, 1H), 3.81 (s, 1H), 3.24 (dd, J = 15.4, 8.5 Hz, 1H), 2.74 (dd, J = 15.4, 7.8 Hz, 1H), 1.38 (d, J = 6.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 151.1, 129.0, 127.3, 124.8, 118.6, 109.3, 55.3, 37.9, 22.4.



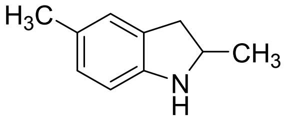
2,3-dimethylindoline (2c):[1] Yield: 99%, 73.0 mg, colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.13 (dd, *J* = 14.3, 7.4 Hz, 2H), 6.83 (t, *J* = 7.4 Hz, 1H), 6.69 (d, *J* = 7.7 Hz, 1H), 3.81 (s, 1H), 3.54-3.51 (m, 1H), 2.97-2.85 (m, 1H), 1.40 (dd, *J* = 6.6, 3.3 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 150.6, 134.4, 127.4, 123.3, 118.7, 109.2, 64.0, 44.4, 20.6, 17.3.



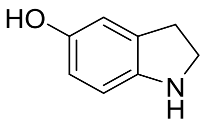
4-methylindoline (2d):[4] Yield: 96%, 64.1 mg, colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.05 (t, *J* = 7.6 Hz, 1H), 6.66 (d, *J* = 7.6 Hz, 1H), 6.59 (d, *J* = 7.7 Hz, 1H), 3.76 (s, 1H), 3.64 (t, *J* = 8.4 Hz, 2H), 3.06 (t, *J* = 8.4 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 151.5, 134.3, 128.2, 127.4, 119.9, 107.0, 47.1, 28.7, 18.9.



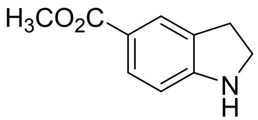
5-methylindoline (2e):[1] Yield: >99%, 66.4 mg, colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.02 (s, 1H), 6.90 (d, *J* = 7.8 Hz, 1H), 6.63 (d, *J* = 7.8 Hz, 1H), 3.63 (brs, 1H), 3.58 (t, *J* = 8.3 Hz, 2H), 3.06 (t, *J* = 8.3 Hz, 2H), 2.33 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.2, 129.8, 128.1, 127.6, 125.5, 109.5, 47.6, 30.0, 20.8.



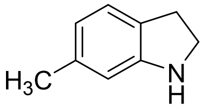
2,5-dimethylindoline (2f):[2] Yield: 98%, 72.0 mg, colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.96 (s, 1H), 6.87 (d, *J* = 7.8 Hz, 1H), 6.57 (d, *J* = 7.8 Hz, 1H), 4.03-3.98 (m, 1H), 3.55 (brs, 1H), 3.15 (dd, *J* = 15.3, 8.4 Hz, 1H), 2.65 (dd, *J* = 15.3, 7.8 Hz, 1H), 2.29 (s, 3H), 1.33 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 148.5, 129.3, 128.0, 127.5, 125.6, 109.3, 55.5, 37.9, 22.3, 20.8.



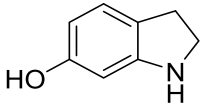
indolin-5-ol (2g):[5] Yield: 90%, 60.6 mg, brown solid, m.p. 113-115 °C. ^{1}H NMR (600 MHz, DMSO) δ 6.60 (dd, *J* = 1.7, 1.0 Hz, 1H), 6.44 (d, *J* = 1.8 Hz, 2H), 3.43-3.39 (m, 2H), 2.88 (dd, *J* = 12.2, 4.4 Hz, 2H). ^{13}C NMR (151 MHz, DMSO) δ 150.3, 143.6, 131.0, 113.3, 112.3, 110.4, 47.4, 30.2.



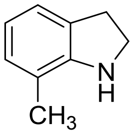
methyl indoline-5-carboxylate (2h):[1] Yield: 92%, 81.2 mg, colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.77 (dd, J = 4.0, 2.7 Hz, 2H), 6.55 (d, J = 8.6 Hz, 1H), 4.30 (brs, 1H), 3.86 (s, 3H), 3.66 (t, J = 8.6 Hz, 2H), 3.07 (t, J = 8.5 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.5, 156.0, 130.7, 128.7, 126.1, 119.6, 107.4, 51.5, 47.3, 28.9.



6-methylindoline (2i):[3] Yield: 98%, 65.2 mg, colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.09 (d, J = 7.3 Hz, 1H), 6.62 (d, J = 7.3 Hz, 1H), 6.56 (s, 1H), 3.69 (s, 1H), 3.60 (t, J = 8.3 Hz, 2H), 3.06 (t, J = 8.3 Hz, 2H), 2.36 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 151.9, 137.1, 126.5, 124.3, 119.4, 110.5, 47.6, 29.6, 21.5.



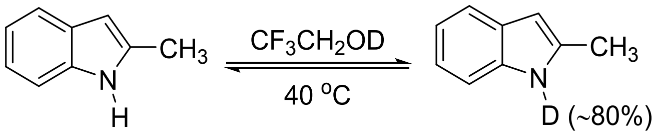
indolin-6-ol (2j):[5] Yield: 89%, 59.8 mg, brown solid, m.p. 102-104 ^{o}C. ^{1}H NMR (600 MHz, DMSO) δ 8.75 (s, 1H), 6.76 (d, J = 7.8 Hz, 1H), 5.9-5.934 (m, 2H), 5.33 (s, 1H), 3.36 (t, J = 8.3 Hz, 2H), 2.76 (t, J = 8.3 Hz, 2H). ^{13}C NMR (151 MHz, DMSO) δ 157.4, 154.2, 124.7, 119.4, 104.0, 97.0, 47.4, 28.9.



7-methylindoline (2k):[4] Yield: 99%, 65.9 mg, colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.06 (d, J = 7.3 Hz, 1H), 6.93 (d, J = 7.5 Hz, 1H), 6.73 (t, J = 7.4 Hz, 1H), 3.62 (t, J = 8.4 Hz, 2H), 3.52 (brs, 1H), 3.12 (t, J = 8.4 Hz, 2H), 2.20 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 150.1, 128.7, 128.2, 122.2, 119.0, 118.9, 47.2, 30.2, 16.9.

3. Mechanism Study

1H NMR Study: 2-methylindole (66 mg, 0.50 mmol) was added to CF_3CH_2OD (1.5 mL) and stirred for 6 h at 40 ^{o}C. The solvent was evaporated under reduced pressure at 40 ^{o}C and the residue was obtained.



According to ^{1}H-NMR spectrum, it was indicated that hydrogen-deuterium exchange process existed between CF_3CH_2OD and 2-methylindole to form 2-methyl-1*H*-indole-1-*d* (**Figure 1**).

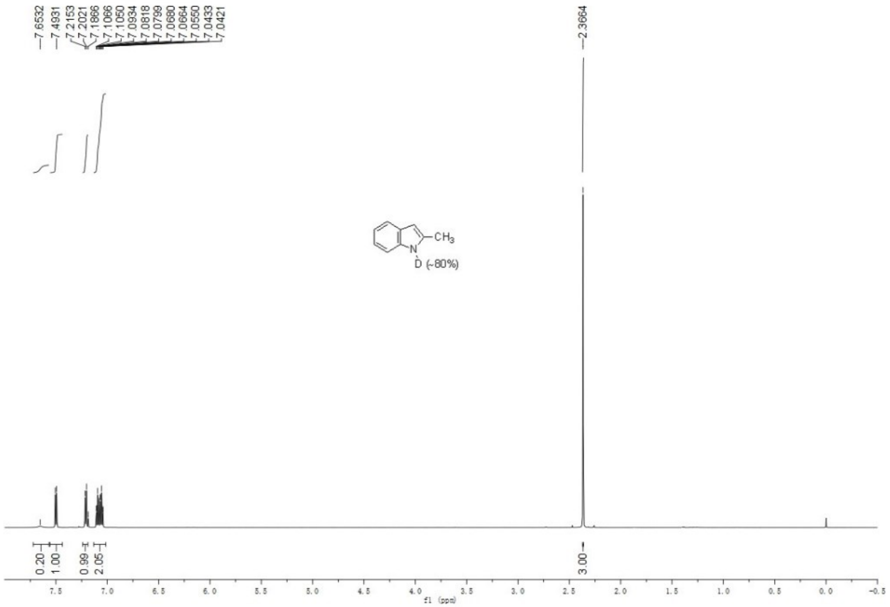


Figure 1. ^{1}H NMR of 2-methylindole in CF_3CH_2OD

Pd/C Catalyzed Transfer Hydrogenation of 2-methylindole in TFE: A mixture of 2-methylindole **1b** (66 mg, 0.50 mmol), Pd/C (10.0 mg, 10 wt% palladium on activated carbon paste and 50% moisture, 0.9 mol% [Pd] based on **1b**) in TFE (3 mL) was added into a Schlenk flask (25 mL) and stirred at room temperature. Then $B_2(OH)_4$ (90 mg, 1.0 mmol, 2.0 equiv) was added and the mixture was stirred at 40 °C. When the reaction was complete monitored by TLC (24 h), the reaction solution was filtered.

The analysis of ^{19}F NMR of the filtrate showed that the peak at δ -76.06 was a new fluorine-containing compound. It was suggested that $CF_3CH_2OB(OH)_2$ might be formed in the reaction system (**Figure 2**).

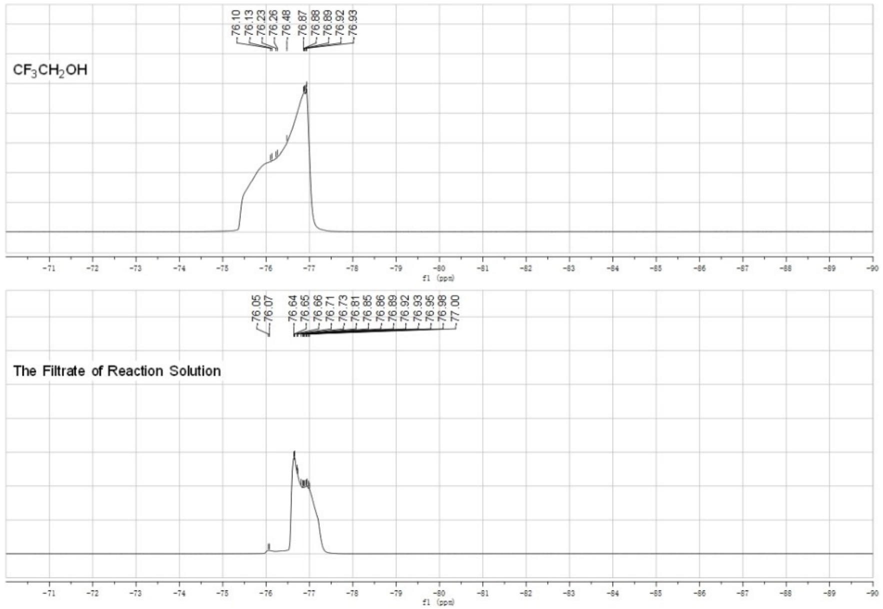
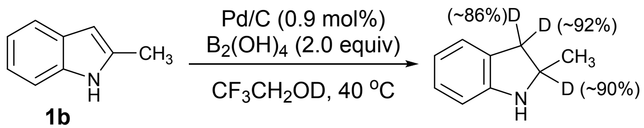


Figure 2. ^{19}F NMR of CF_3CH_2OH and Reaction Solution

Pd/C Catalyzed Transfer Hydrogenation of 2-methylindole in 2,2,2-trifluoroethan-1-ol-*d* (CF_3CH_2OD): A mixture of 2-methylindole **1b** (66 mg, 0.50 mmol), Pd/C (10.0 mg, 10 wt% palladium on activated carbon paste and 50% moisture, 0.9 mol% [Pd] based on **1b**) in CF_3CH_2OD (3 mL) was added into a Schlenk flask (25 mL) and stirred at room temperature. Then $B_2(OH)_4$ (90 mg, 1.0 mmol, 2.0 equiv) was added and the mixture was stirred at 40 °C. When the reaction was complete monitored by TLC (48 h), the solvent was evaporated under reduced pressure and the residue was purified by column chromatography (petroleum ether/ethyl acetate 50:1 to 30:1) to provide 2-methylindoline (colorless oil, 45.2 mg).



The analysis of ^{1}H NMR of the product showed that three deuterium atoms were imported to the 2- (~86% and ~92%) and 3-position (~90%). A hydrogen-deuterium exchange process existed between CF_3CH_2OD and $B_2(OH)_4$ to form $B_2(OD)_4$. The two deuterium atoms of 3-position suggested that a reversible process of protonation and deprotonation existed (**Figure 3**).

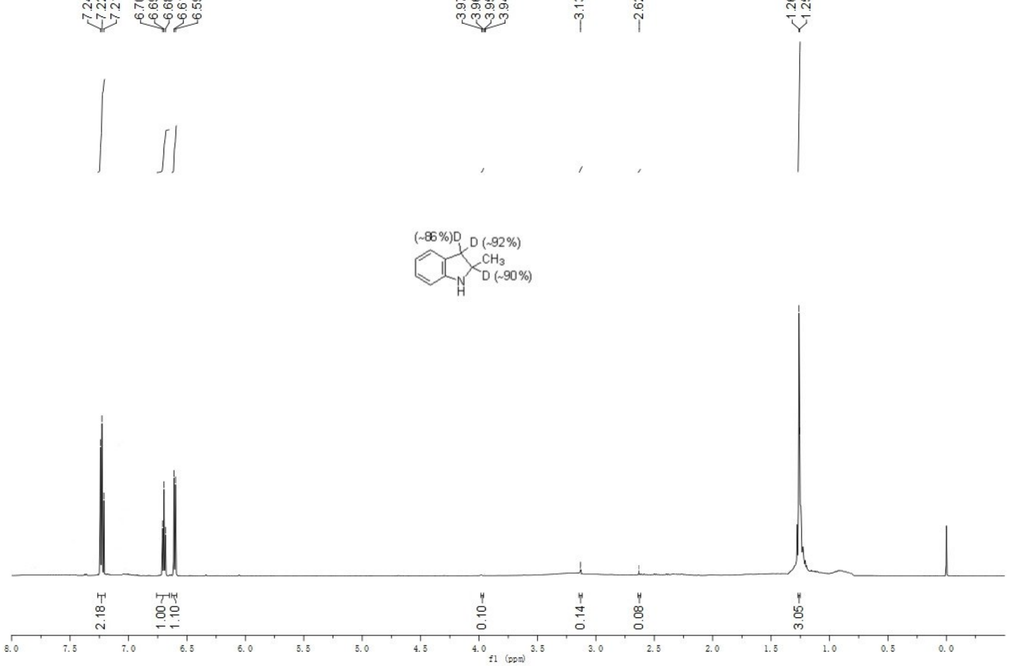


Figure 3. ^{1}H NMR of Product 1b in CF_3CH_2OD

4. References

(1) Kulkarni, A.; Zhou, W.; Török, B. *Org. Lett.* **2011**, *13*, 5124.

(2) Wang, D.-S.; Chen, Q.-A.; Li, W.; Yu, C.-B.; Zhou, Y.-G.; Zhang, X. *J. Am. Chem. Soc.* **2010**, *132*, 8909.

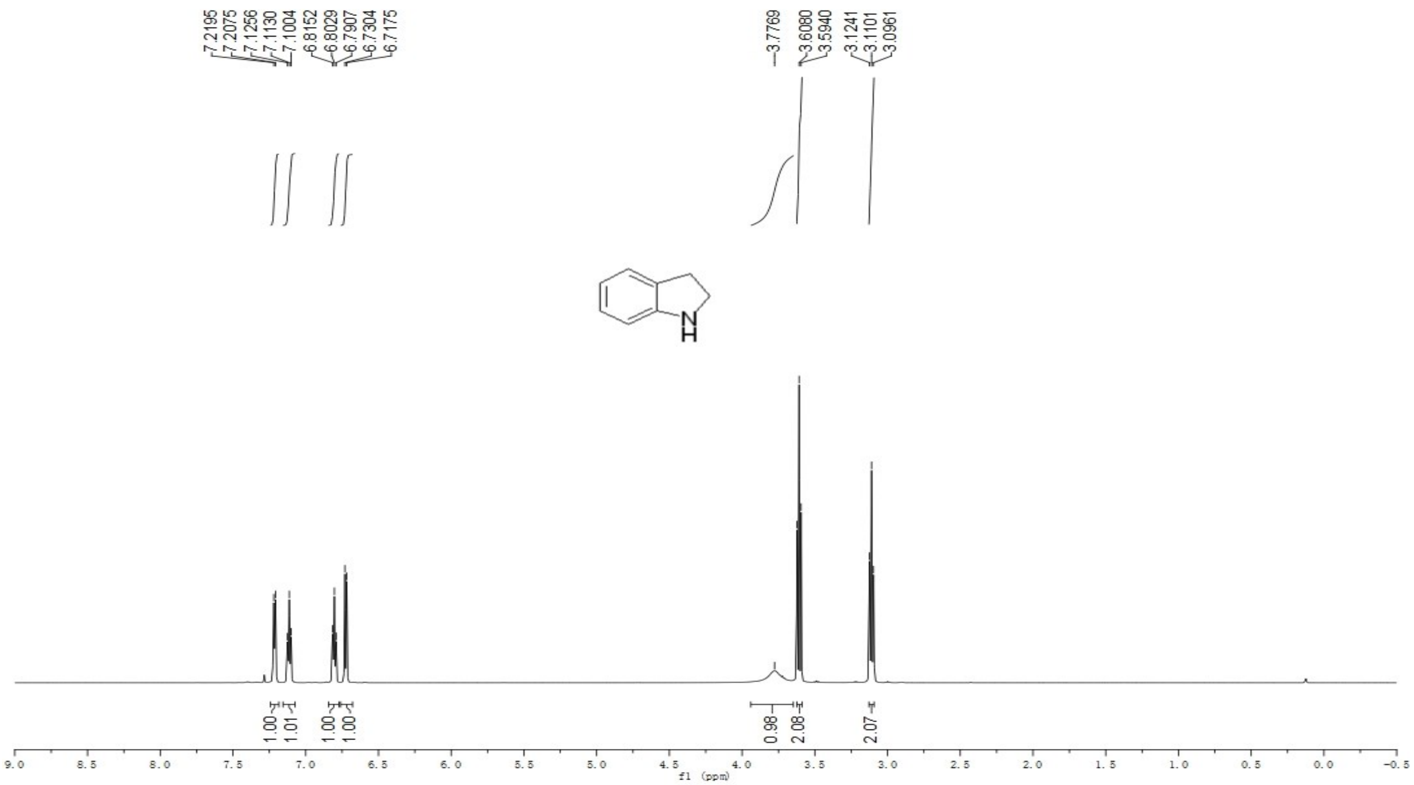
(3) Walkington, A.; Gray, M.; Hossner, F.; Kitteringham, J.; Voyle, M. *Synth. Commun.* **2003**, *33*, 2229.

(4) Sato, K.; Sugimoto, H.; Rikimaru, K.; Imoto, H.; Kamaura, M.; Negoro, N.; Tsujihata, Y.; Miyashita, H.; Odani, T.; Murata, T. *Bioorgan. Med. Chem.* **2014**, *22*, 1649.

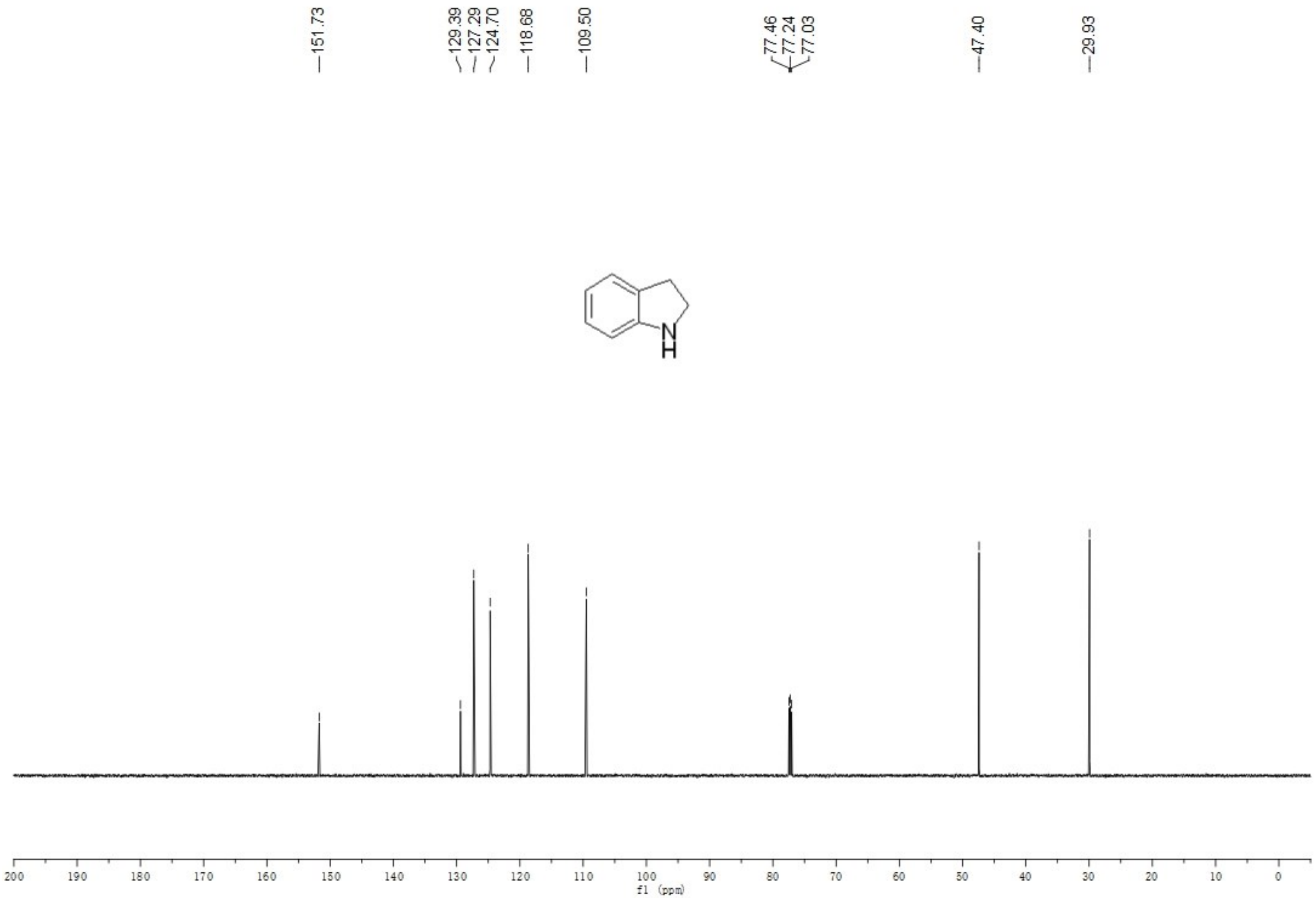
(5) Berrier, C.; Jacquesy, J.-C.; Jouannetaud, M.-P.; Renoux, A. *Tetrahedron Lett.* **1986**, *27*, 4565.

5. Copy of NMR for the Indolines

^{1}H-NMR of 2a

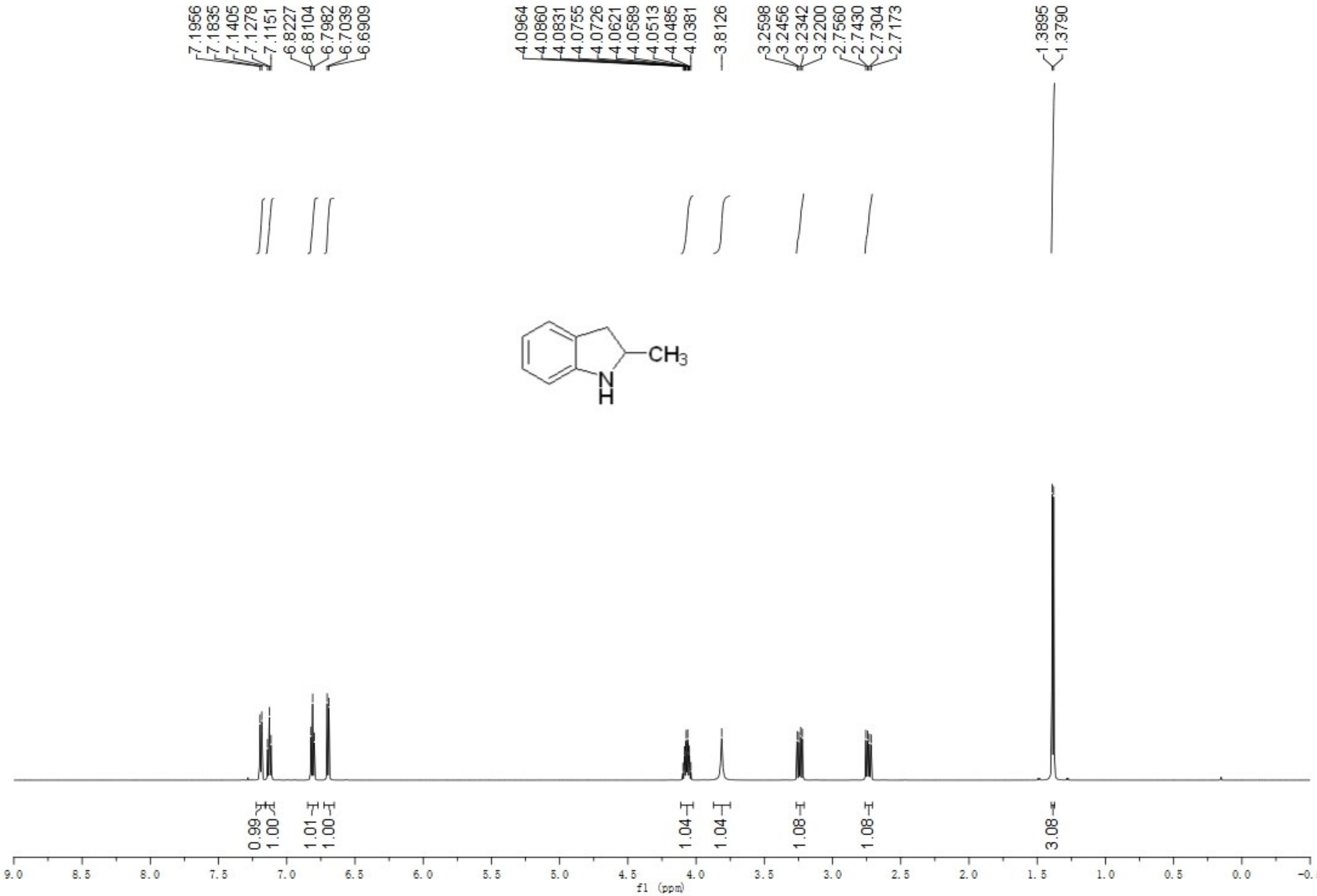


^{13}C-NMR of 2a



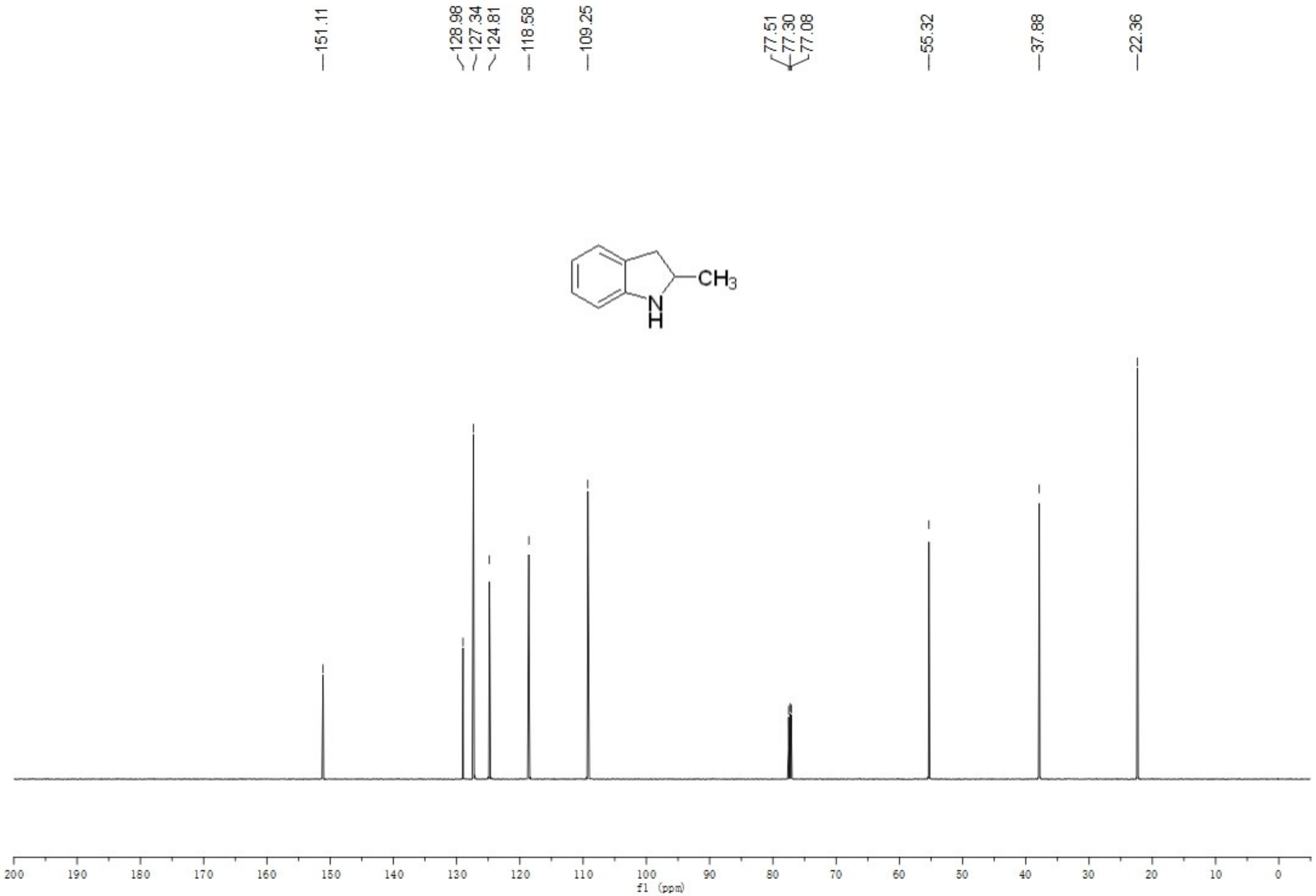
151.73
129.39
127.29
124.70
118.68
109.50
77.46
77.24
77.03
47.40
29.93
N
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^1H-NMR of 2b



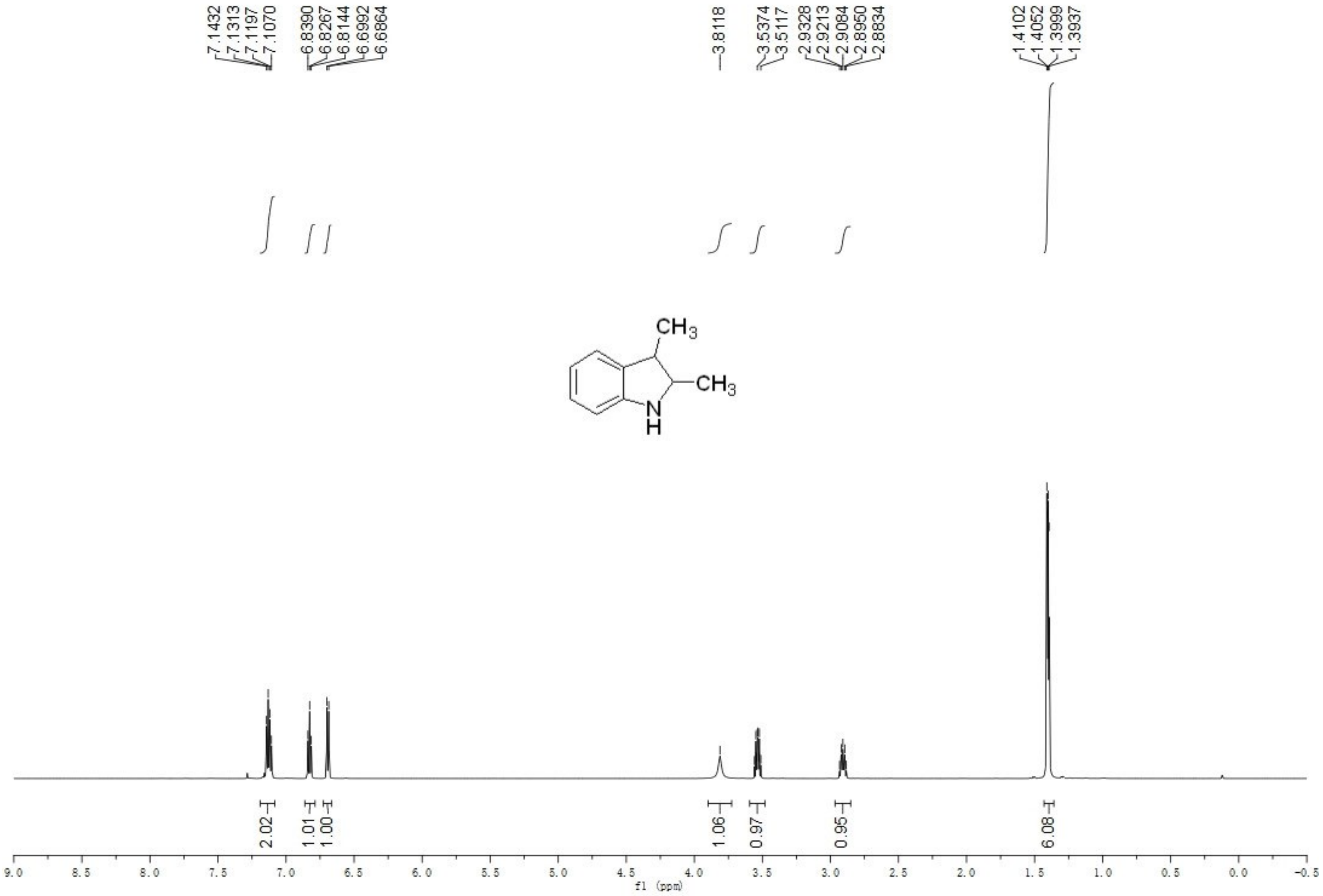
7.1956
7.1835
7.1405
7.1278
7.1151
6.8227
6.8104
6.7982
6.7039
6.6909
4.0964
4.0860
4.0831
4.0755
4.0726
4.0621
4.0589
4.0513
4.0485
4.0381
3.8126
3.2598
3.2456
3.2342
3.2200
2.7560
2.7430
2.7304
2.7173
1.3895
1.3790
CH3
N
H
0.99
1.00
1.01
1.00
1.04
1.04
1.08
1.08
3.08
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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)

^{13}C-NMR of 2b

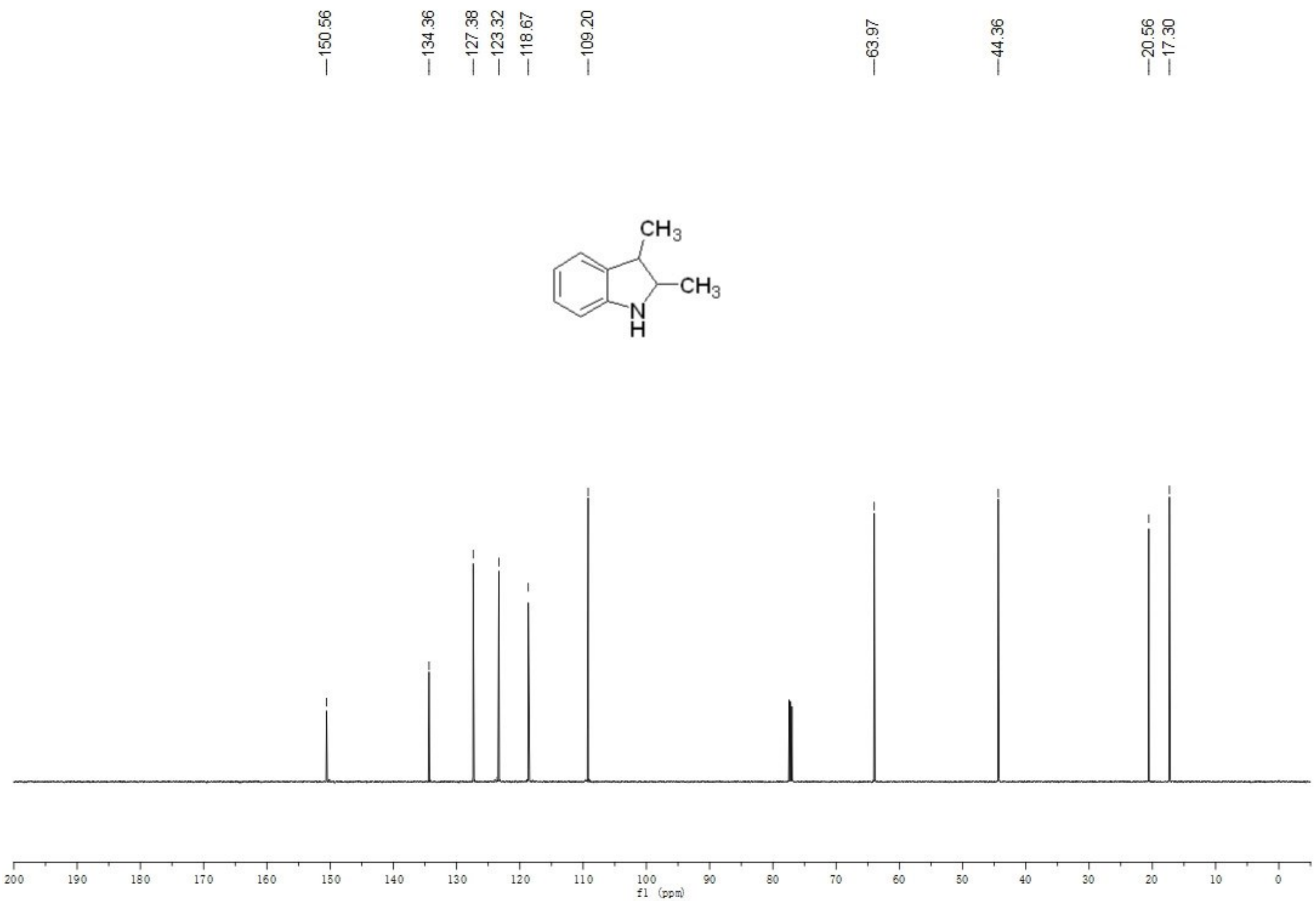


151.11
128.98
127.34
124.81
118.58
109.25
77.51
77.30
77.08
55.32
37.88
22.36
CH3
N
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

[1]H-NMR of 2c

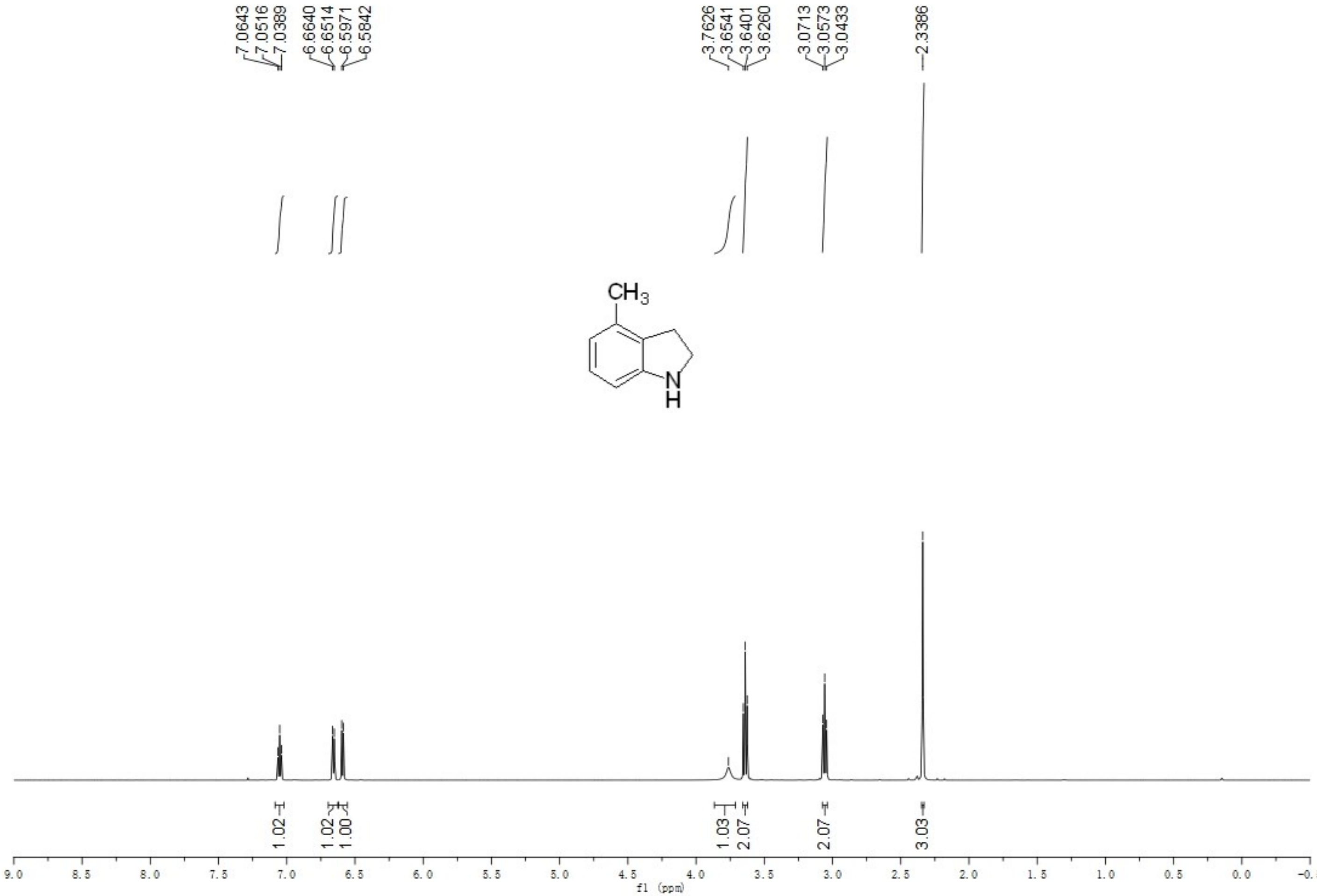

7.1432
7.1313
7.1197
7.1070
6.8390
6.8267
6.8144
6.6992
6.6864
3.8118
3.5374
3.5117
2.9328
2.9213
2.9084
2.8950
2.8834
1.4102
1.4052
1.3999
1.3937
CH3
CH3
N
H
2.02
1.01
1.00
1.06
0.97
0.95
6.08
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

^{13}C-NMR of 2c

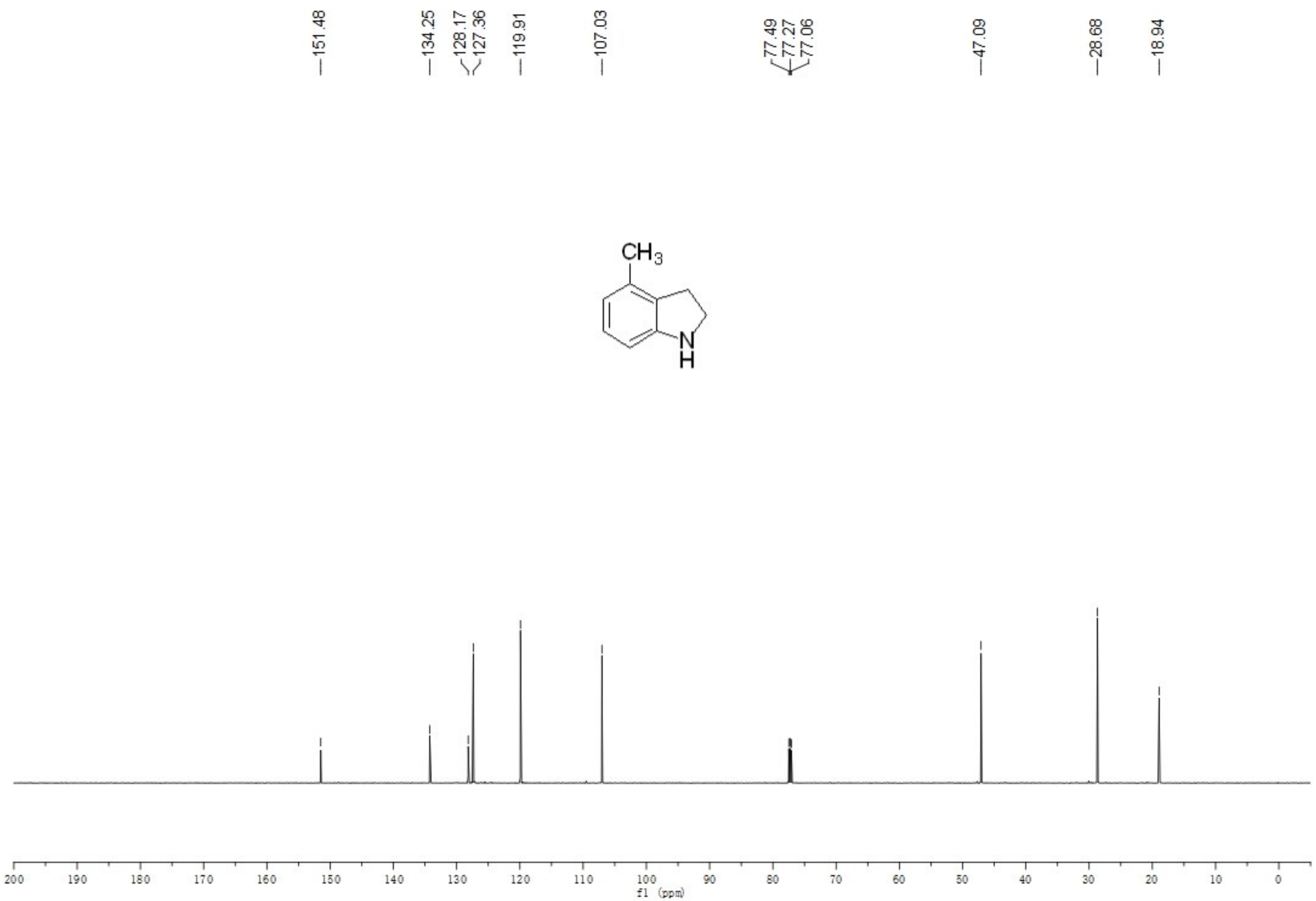


150.56
134.36
127.38
123.32
118.67
109.20
63.97
44.36
20.56
17.30
CH3
CH3
N
H
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

[1]H-NMR of 2d

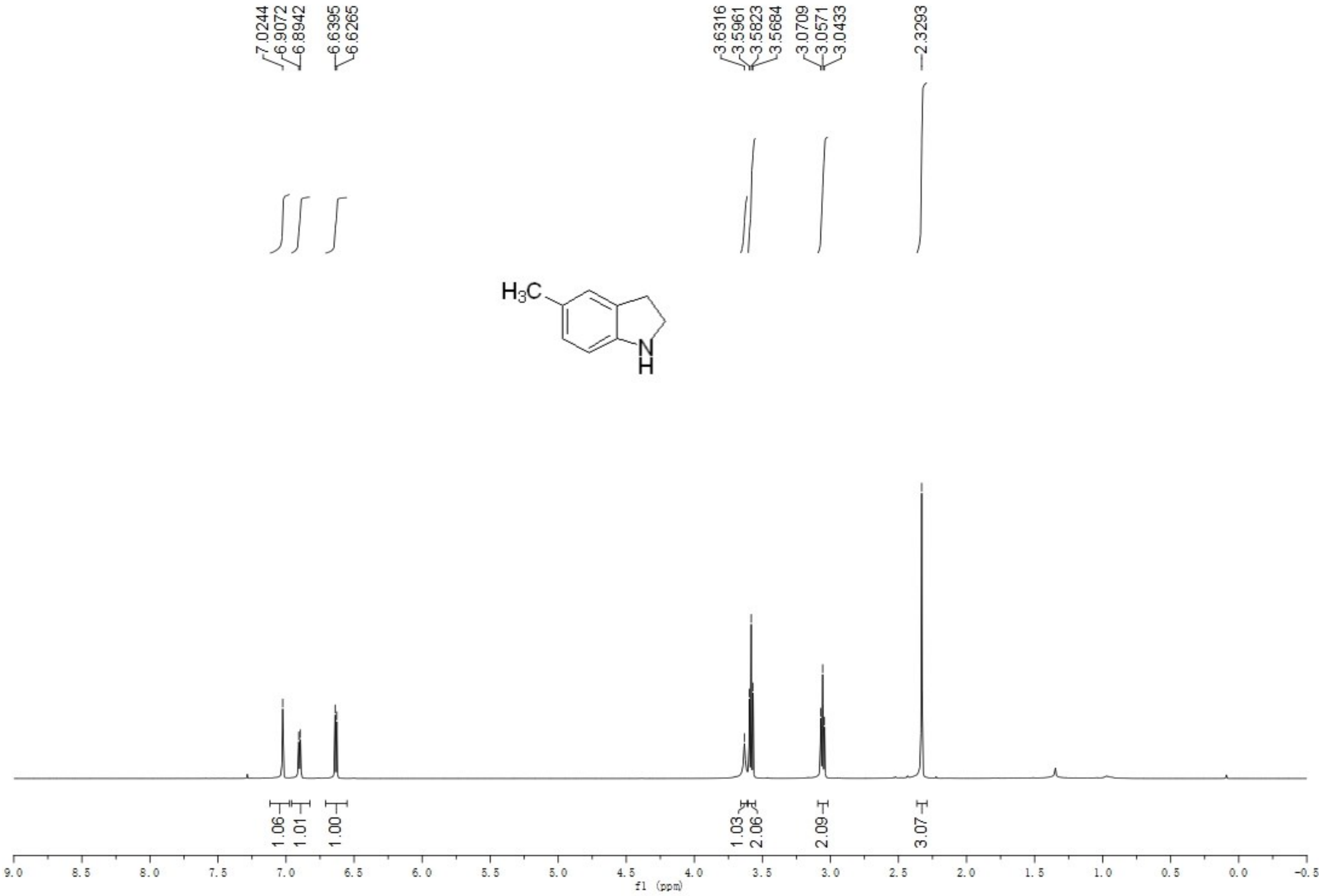

7.0643
7.0516
7.0389
6.6640
6.6514
6.5971
6.5842
3.7626
3.6541
3.6401
3.6260
3.0713
3.0573
3.0433
2.3386
CH3
N
H
1.02
1.02
1.00
1.03
2.07
2.07
3.03
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

^{13}C-NMR of 2d

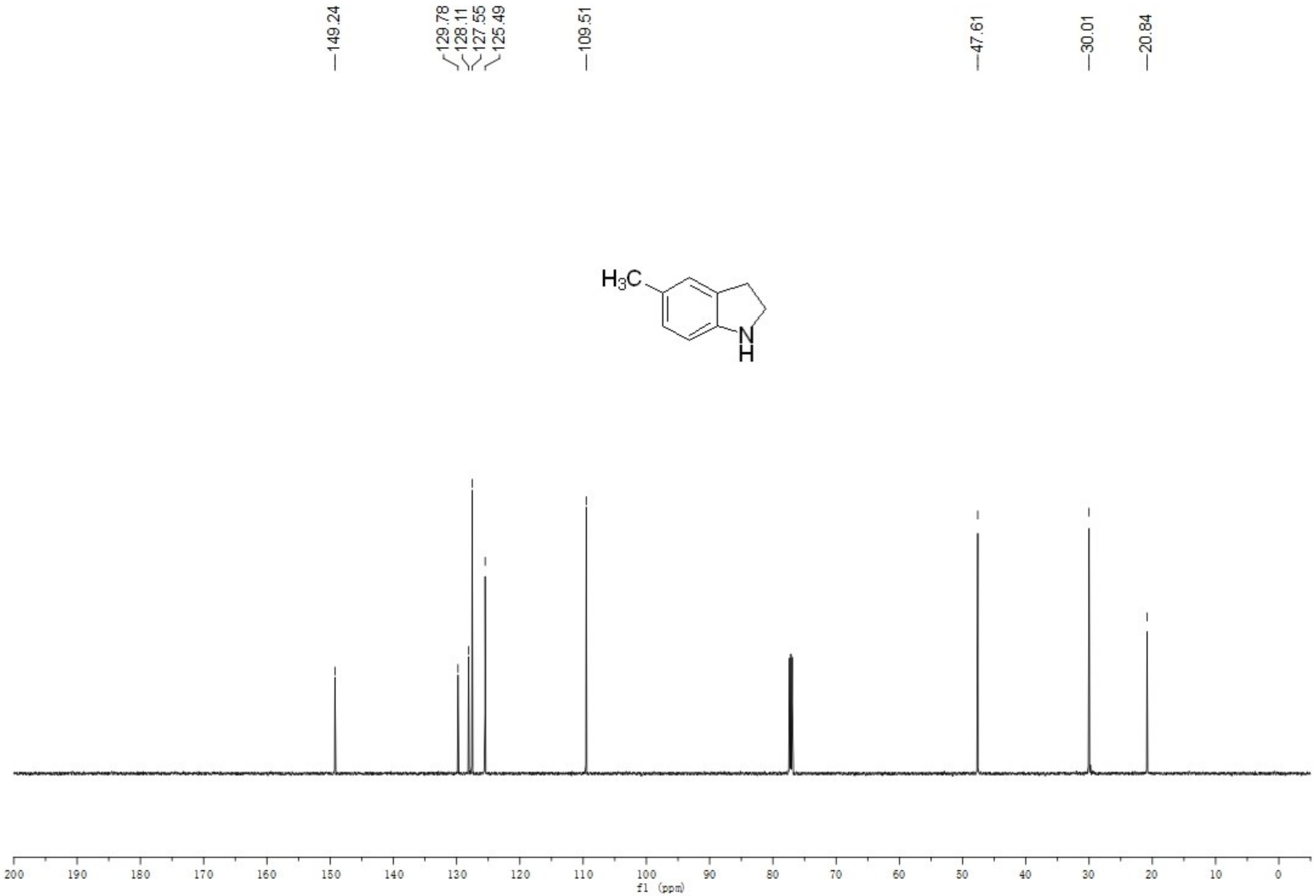


151.48
134.25
128.17
127.36
119.91
107.03
77.49
77.27
77.06
47.09
28.68
18.94
CH3
N
H
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

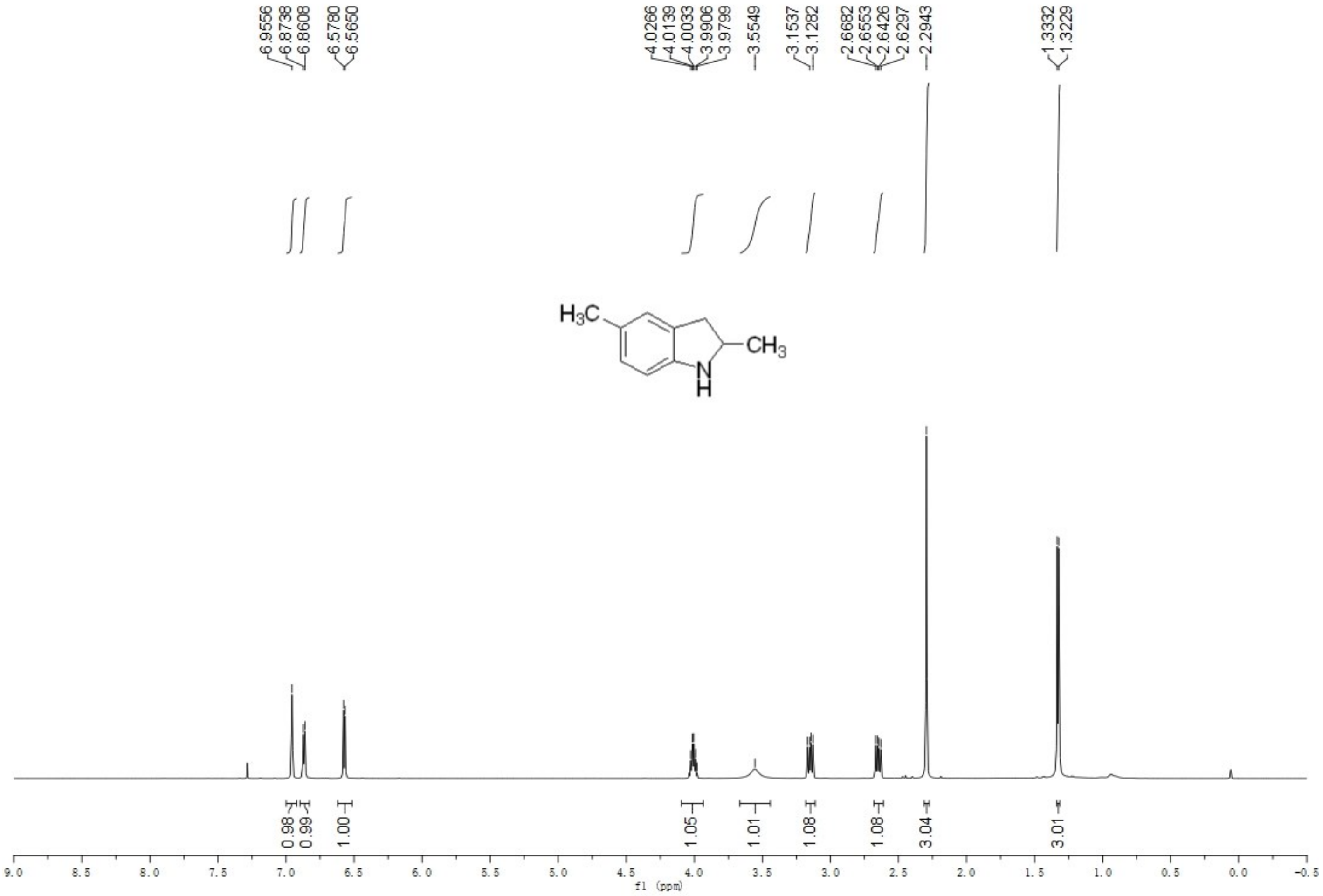
[1]H-NMR of 2e


7.0244
6.9072
6.8942
6.6395
6.6265
3.6316
3.5961
3.5823
3.5684
3.0709
3.0571
3.0433
2.3293
H3C
N
H
1.06
1.01
1.00
1.03
2.06
2.09
3.07
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)

^{13}C-NMR of 2e

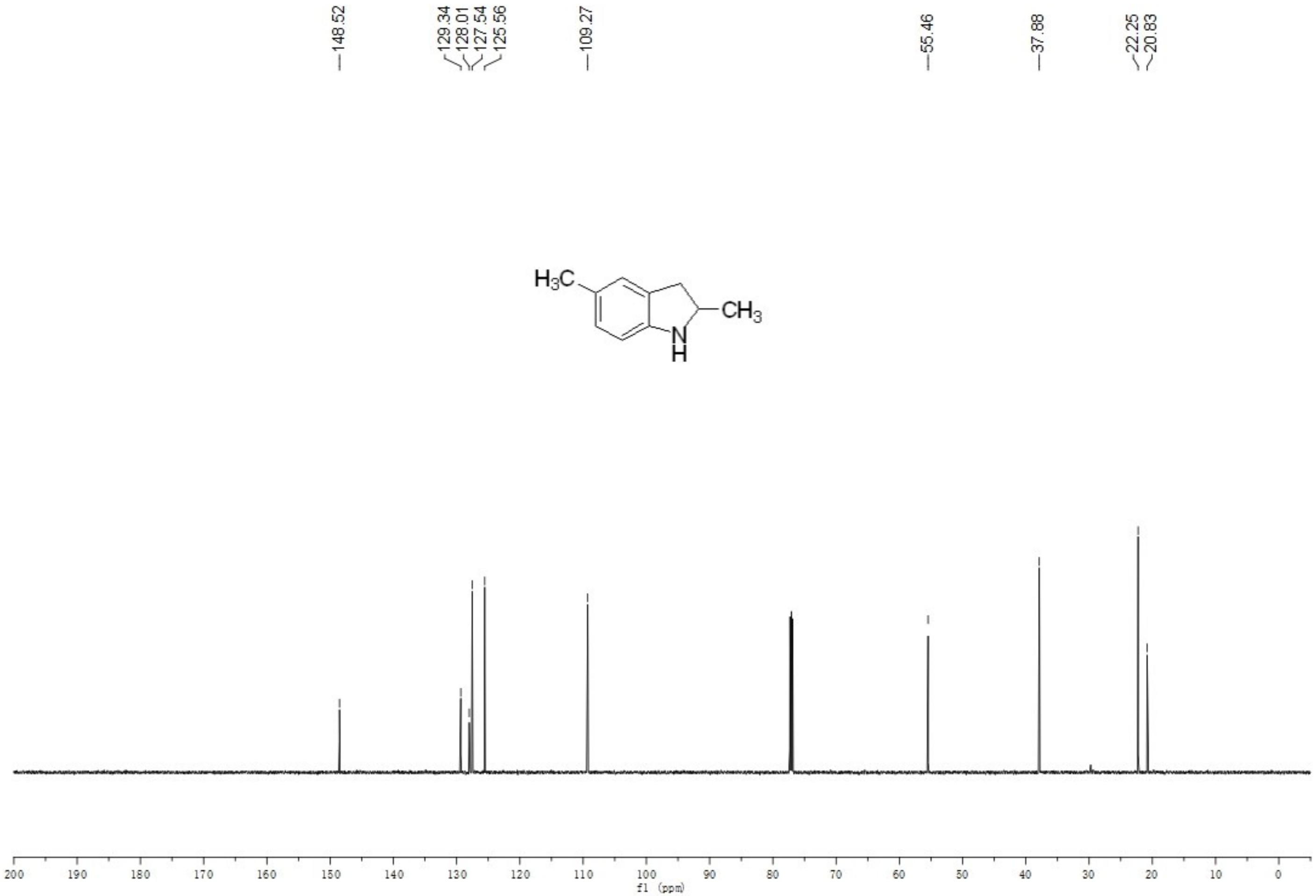

149.24
129.78
128.11
127.55
125.49
109.51
47.61
30.01
20.84
H_3C
N
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

¹H-NMR of 2f



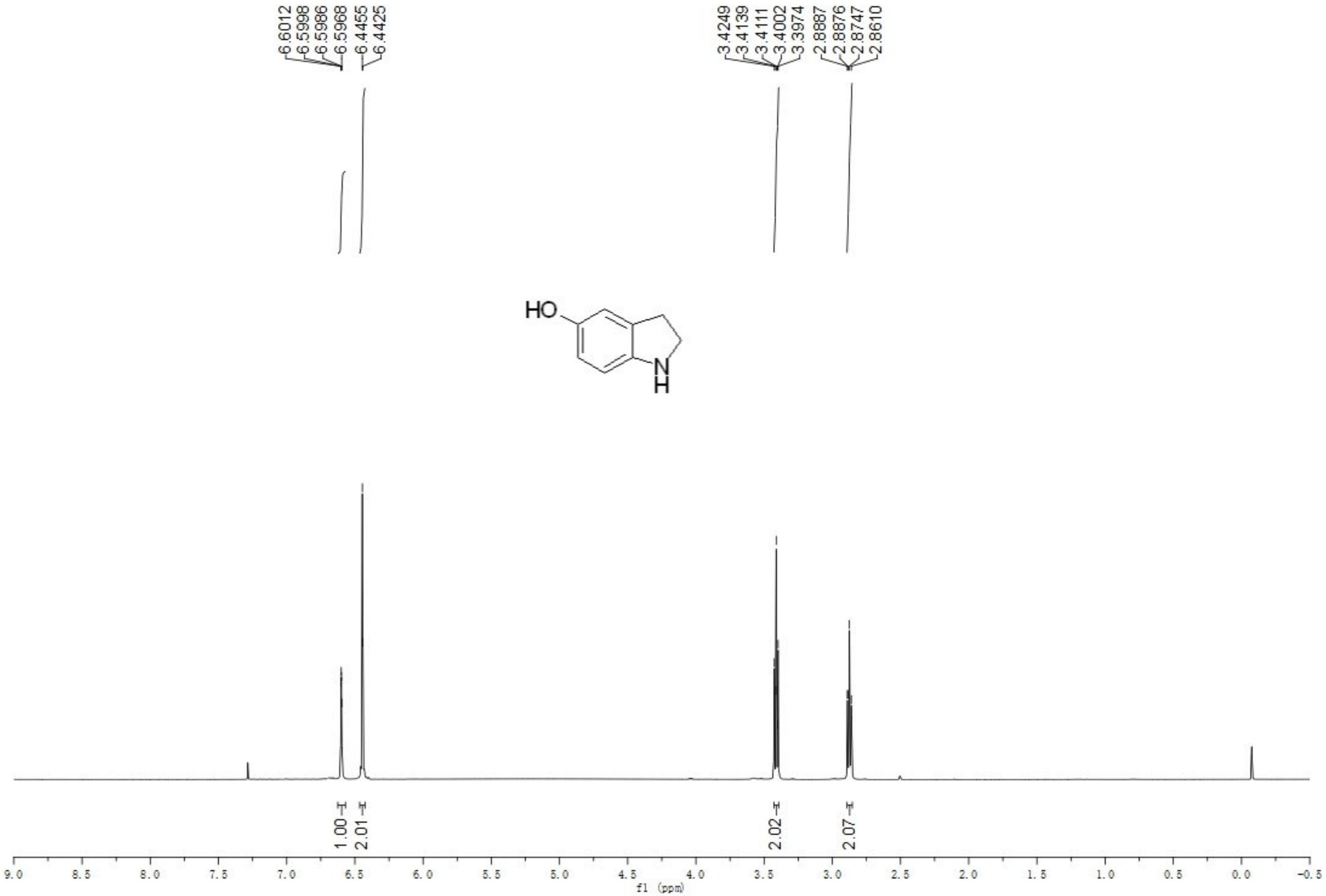
6.9556
6.8738
6.8608
6.5780
6.5650
4.0266
4.0139
4.0033
3.9906
3.9799
3.5549
3.1537
3.1282
2.6682
2.6553
2.6426
2.6297
2.2943
1.3332
1.3229
H3C
CH3
N
H
0.98
0.99
1.00
1.05
1.01
1.08
1.08
3.04
3.01
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

^{13}C-NMR of 2f

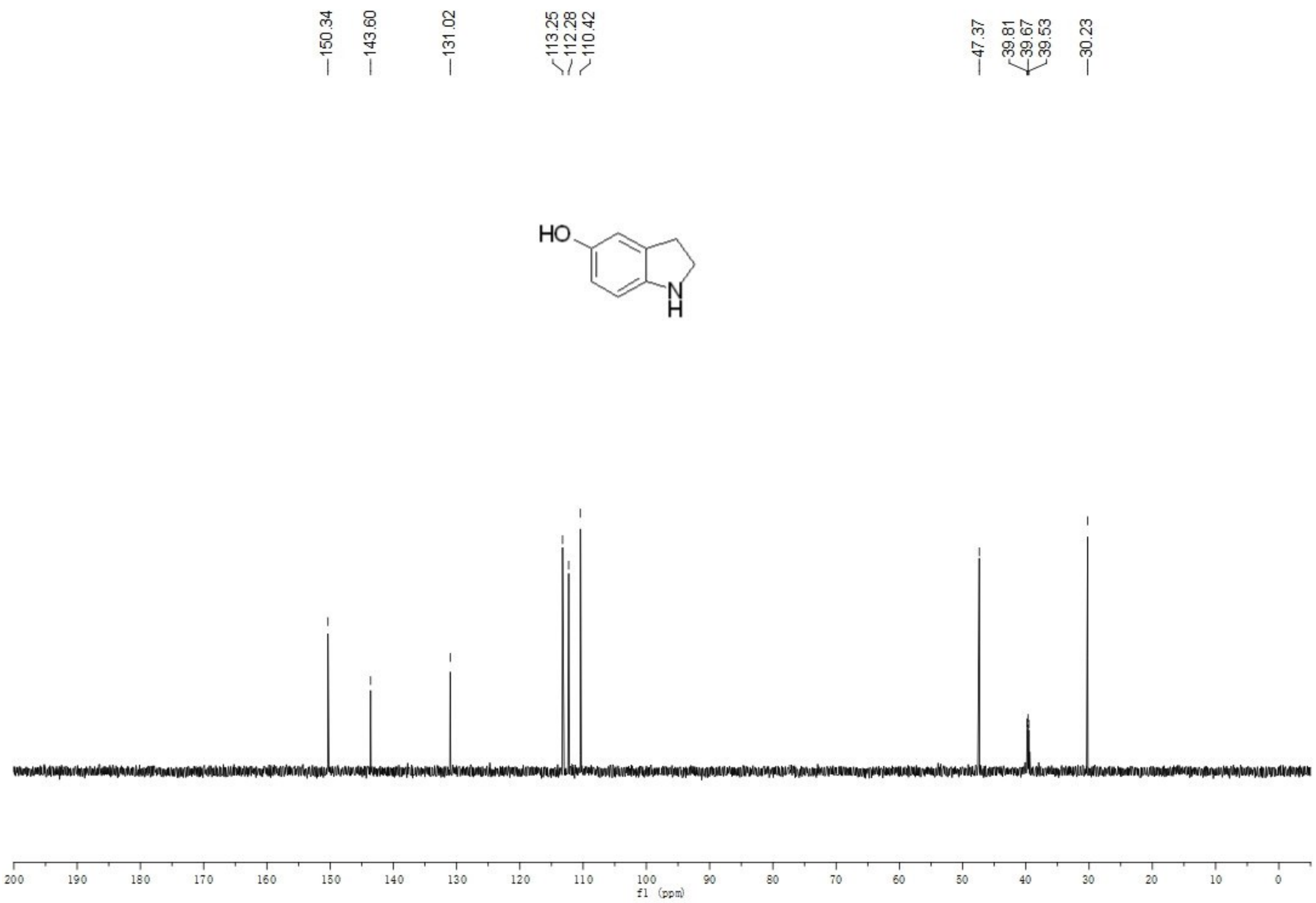


148.52
129.34
128.01
127.54
125.56
109.27
55.46
37.88
22.25
20.83
H_3C
CH_3
N
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

[1]H-NMR of 2g

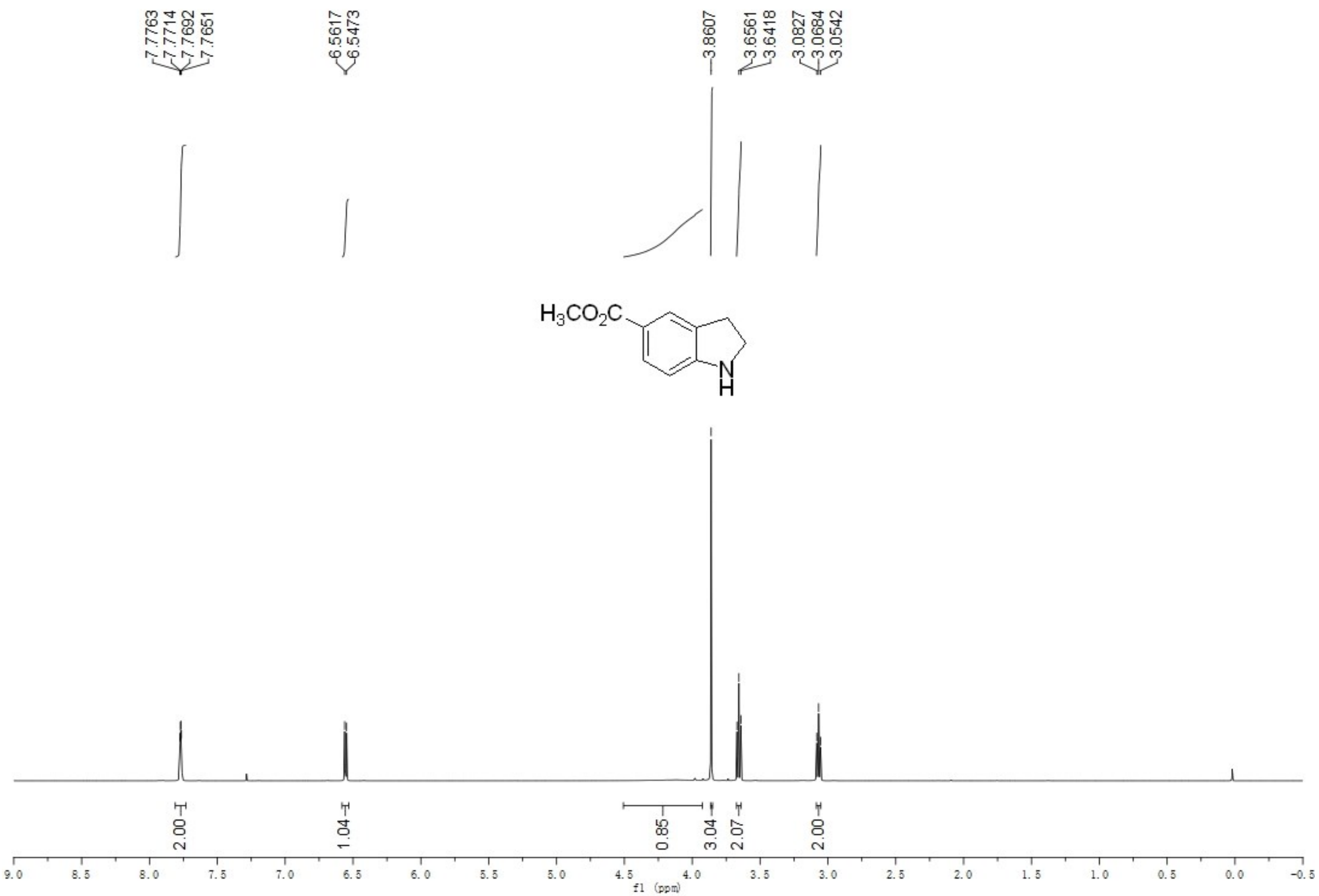

6.6012
6.5998
6.5986
6.5968
6.4455
6.4425
3.4249
3.4139
3.4111
3.4002
3.3974
2.8887
2.8876
2.8747
2.8610
HO
N
H
1.00
2.01
2.02
2.07
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

^{13}C-NMR of 2g

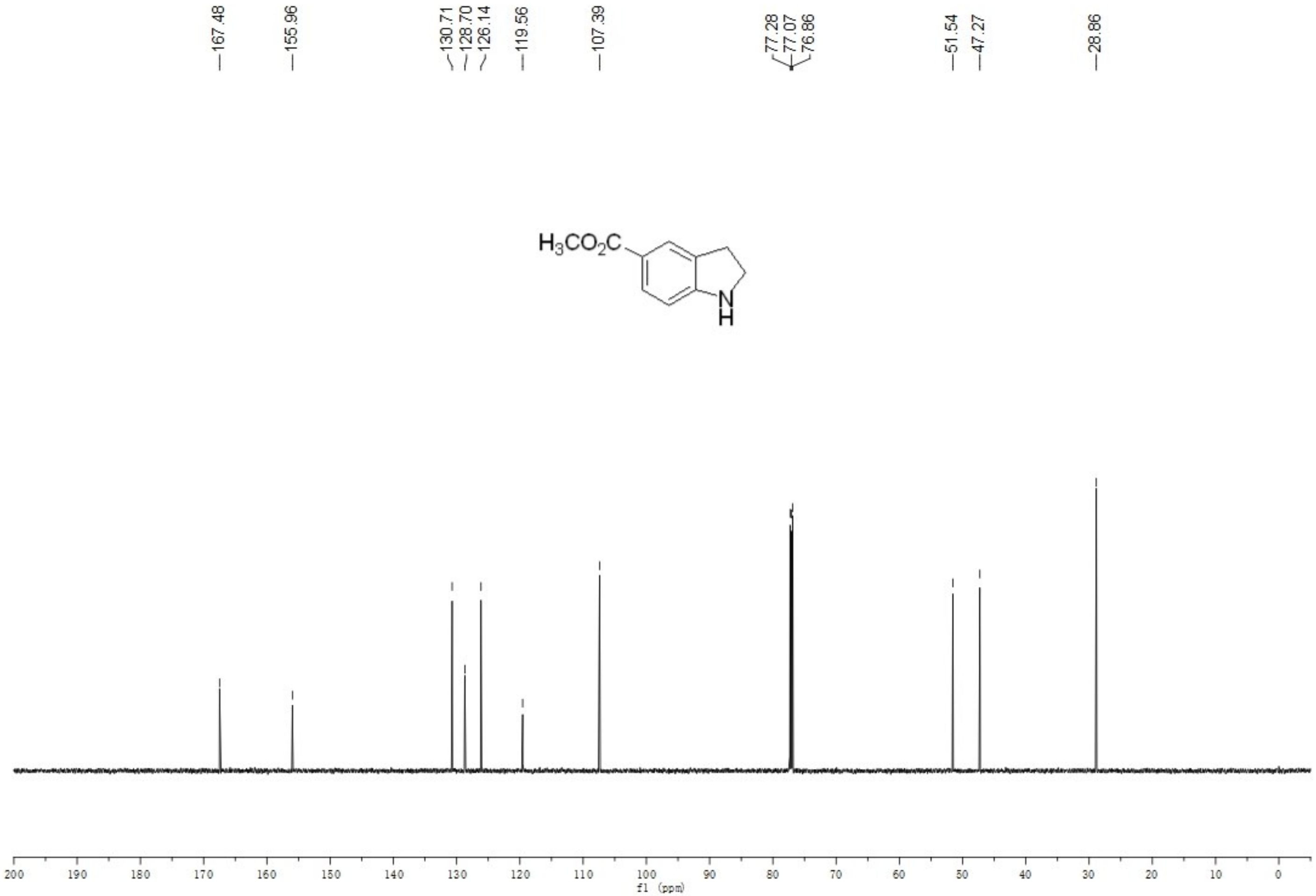


150.34
143.60
131.02
113.25
112.28
110.42
47.37
39.81
39.67
39.53
30.23
HO
N
H
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

[1]H-NMR of 2h

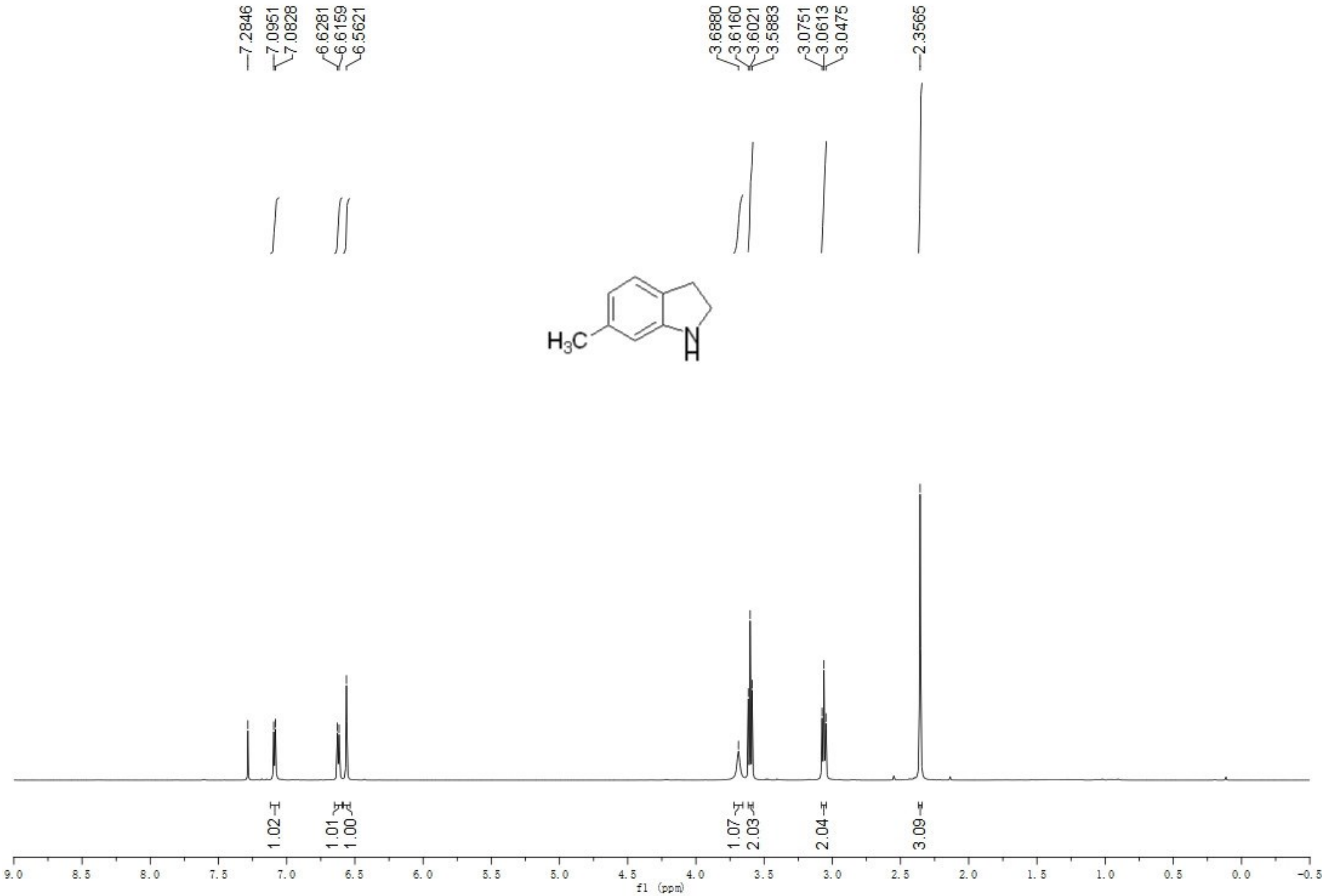

7.7763
7.7714
7.7692
7.7651
6.5617
6.5473
3.8607
3.6561
3.6418
3.0827
3.0684
3.0542
H3CO2C
N
H
2.00
1.04
0.85
3.04
2.07
2.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

^{13}C-NMR of 2h



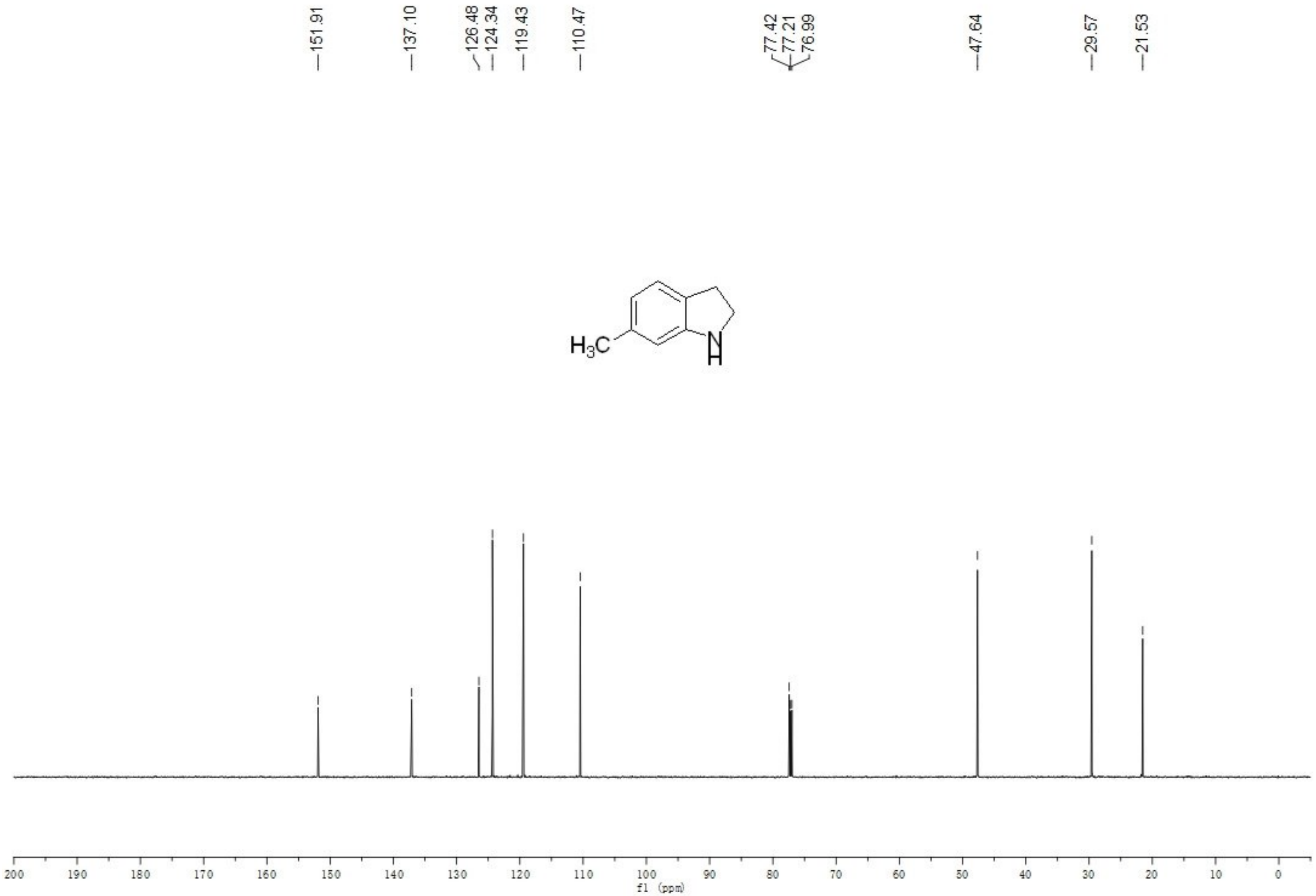
167.48
155.96
130.71
128.70
126.14
119.56
107.39
77.28
77.07
76.86
51.54
47.27
28.86
H3CO2C
N
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{1}H-NMR of 2i



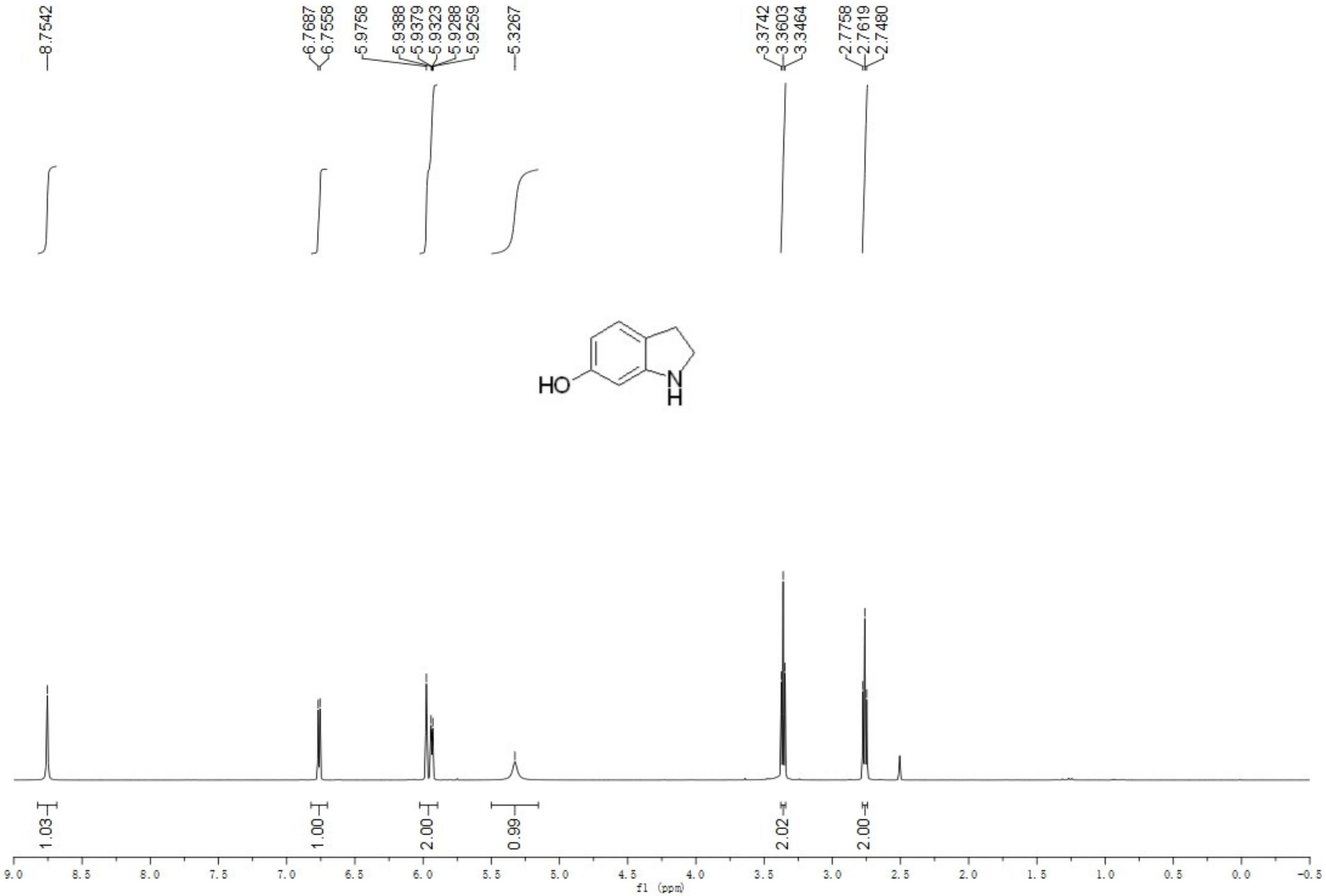
7.2846
7.0951
7.0828
6.6281
6.6159
6.5621
3.6880
3.6160
3.6021
3.5883
3.0751
3.0613
3.0475
2.3565
H3C
N
H
1.02
1.01
1.00
1.07
2.03
2.04
3.09
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

^{13}C-NMR of 2i

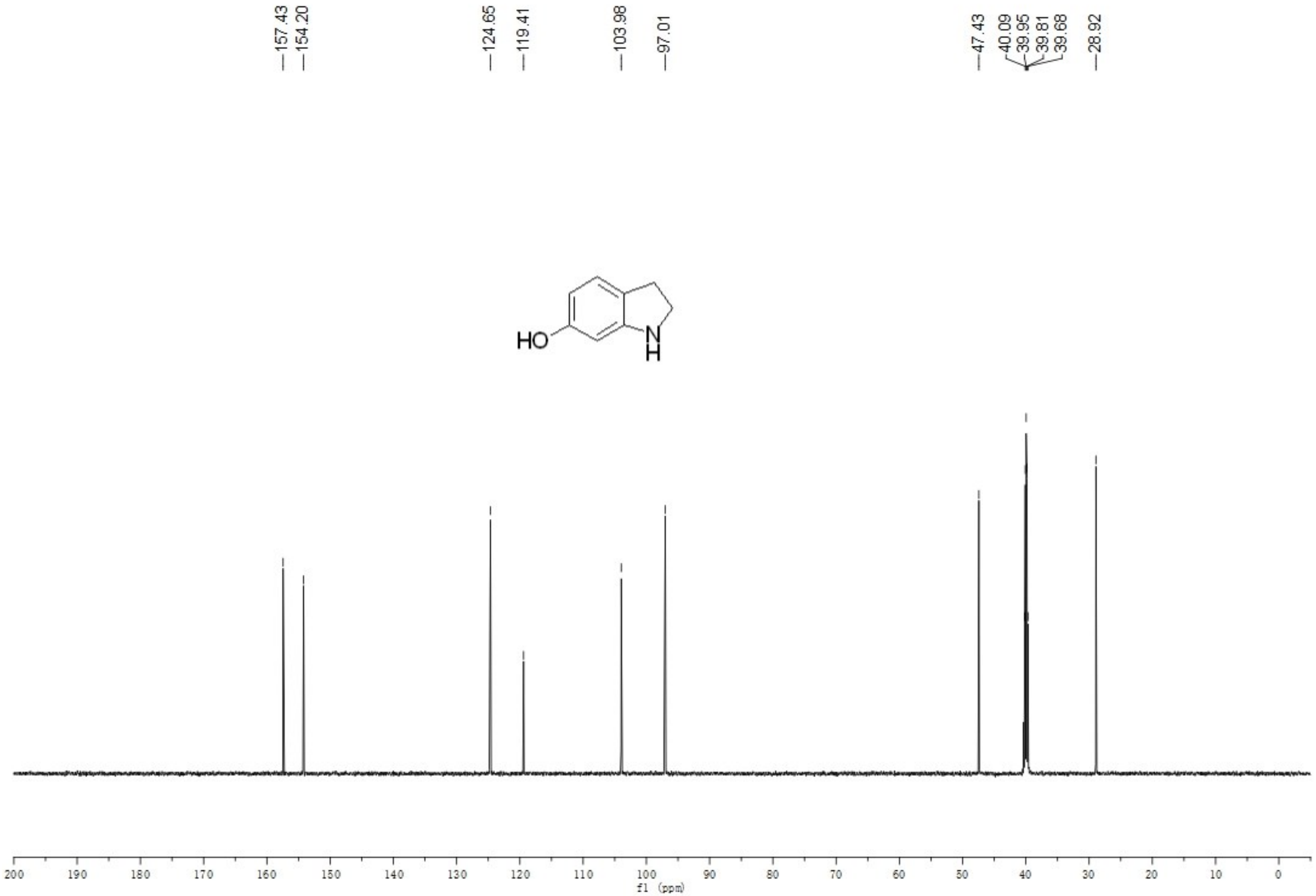


151.91
137.10
126.48
124.34
119.43
110.47
77.42
77.21
76.99
47.64
29.57
21.53
H_3C
N
H
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

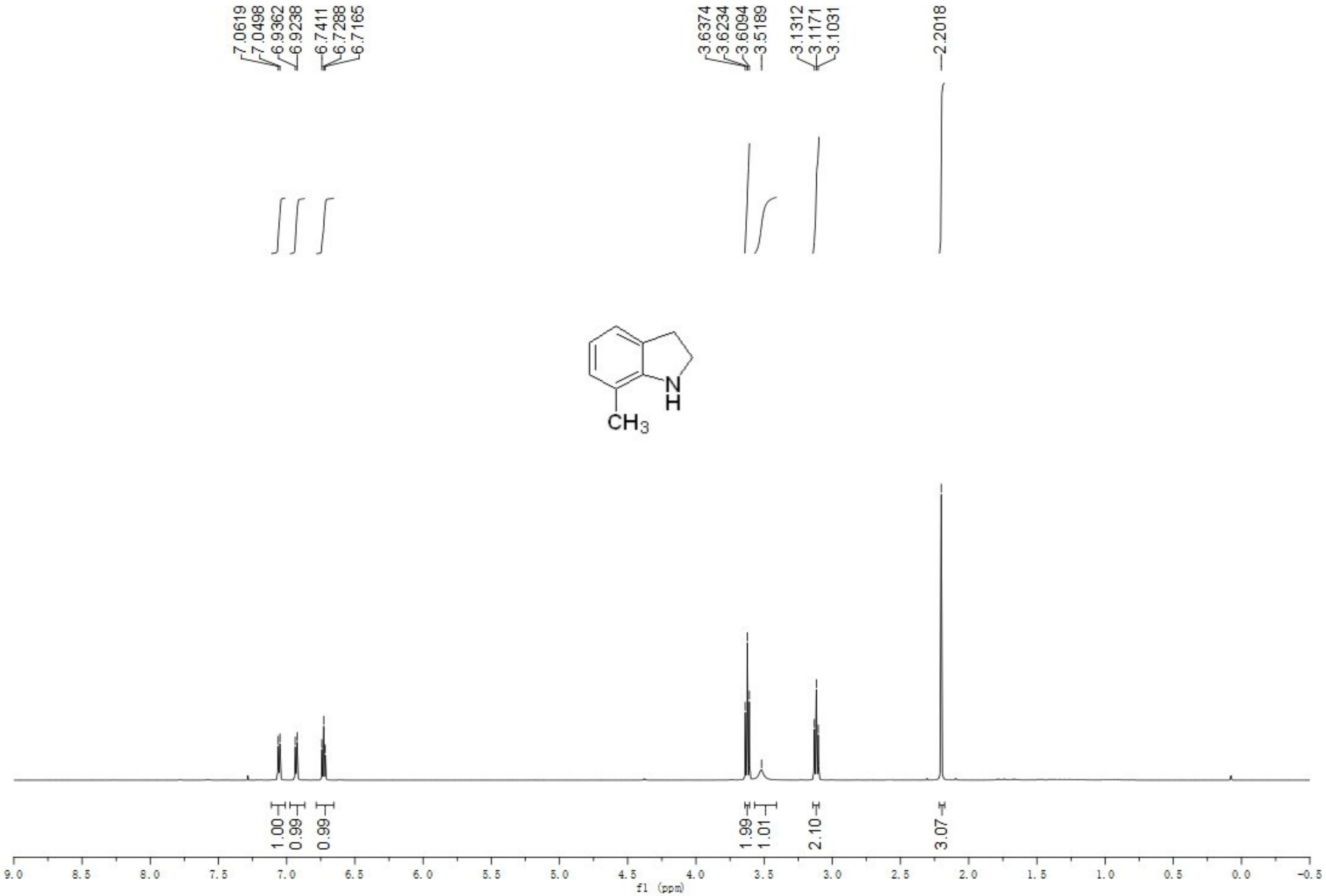
[1]H-NMR of 2j


8.7542
6.7687
6.7558
5.9758
5.9388
5.9379
5.9323
5.9288
5.9259
5.3267
3.3742
3.3603
3.3464
2.7758
2.7619
2.7480
HO
N
H
1.03
1.00
2.00
0.99
2.02
2.00
fl (ppm)

^{13}C-NMR of 2j

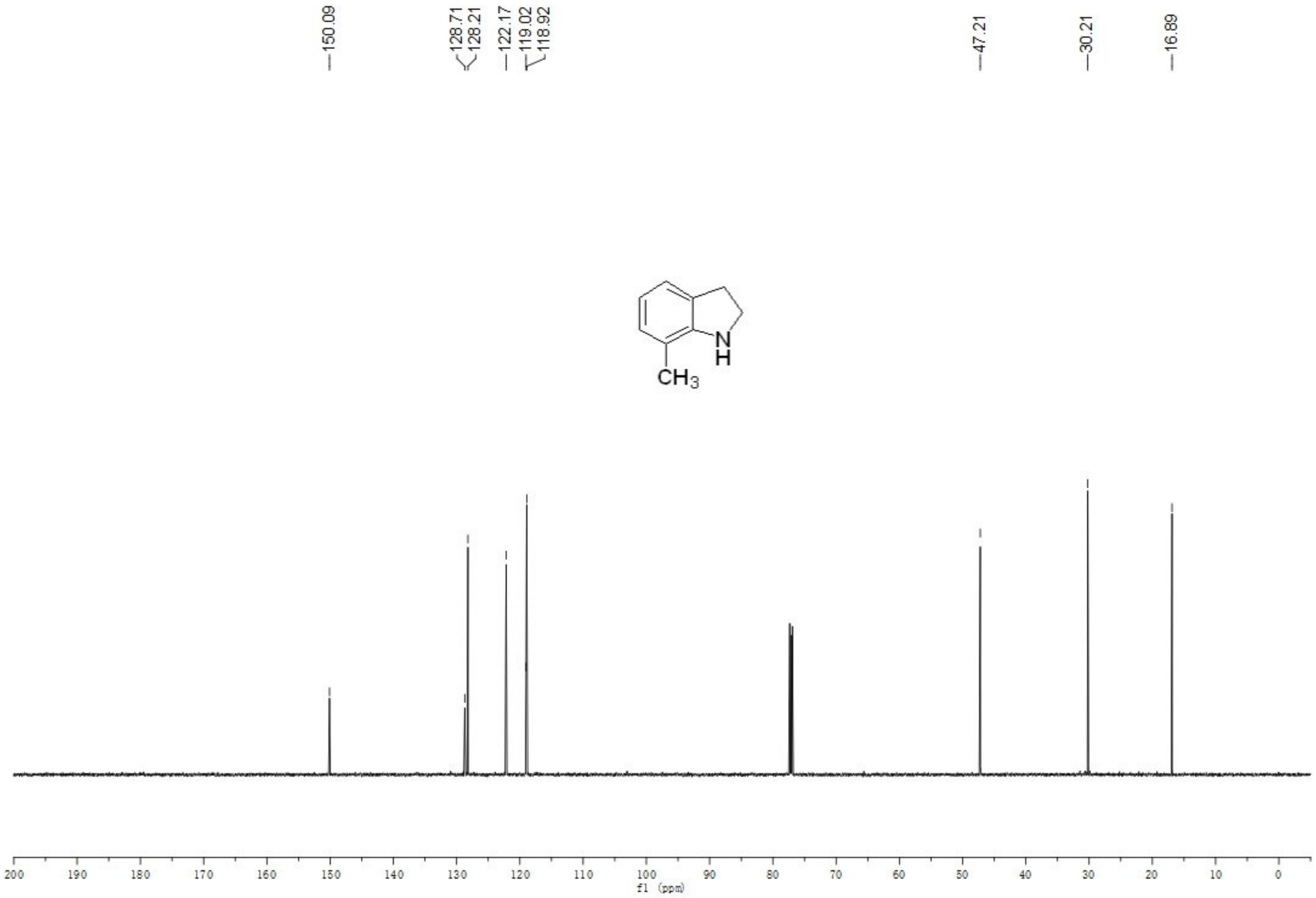

157.43
154.20
124.65
119.41
103.98
97.01
47.43
40.09
39.95
39.81
39.68
28.92
HO
N
H
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

[1]H-NMR of 2k



7.0619
7.0498
6.9362
6.9238
6.7411
6.7288
6.7165
3.6374
3.6234
3.6094
3.5189
3.1312
3.1171
3.1031
2.2018
N
H
CH3
1.00
0.99
0.99
1.99
1.01
2.10
3.07
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)

^{13}C-NMR of 2k



150.09
128.71
128.21
122.17
119.02
118.92
47.21
30.21
16.89
H
N
CH_3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)