Supporting Information

Novel pyrrolo[2,1-*a*]isoquinoline aryl ketones attenuate carbon nanotube-induced acute lung injury through NF-κB pathway inhibition

Guo-Liang Qiu,[1] Jing Zhang,[2] Zongze Yao,[2] Wei Shao,[4] Jiahong Ma,[3] Hua-Li Qin,[3] Wenjian Tang[2,4]

[1] *Department of Pharmacy, Anhui No.2 Provincial People's Hospital, Hefei 230041, China*

[2] *Anhui Province Key Laboratory of Occupational Health, Anhui No.2 Provincial People's Hospital, Hefei 230041, China*

[3] *School of Chemistry, Chemical Engineering and Life Science, Wuhan University of Technology, Wuhan 430070, China*

[4] *School of Pharmacy, Anhui Medical University, Hefei 230032, China*

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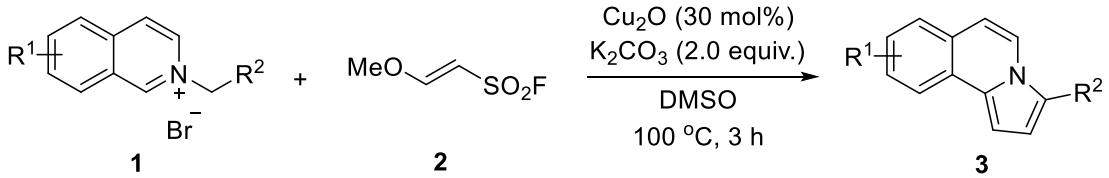
1. General Information

All reactions were carried out under an air atmosphere unless otherwise specified. Oil bath was used for the heating reactions. NMR spectra were recorded in $CDCl_3$ on a 500 MHz (for ^1H), 471 MHz (for ^{19}F), 126 MHz (for ^{13}C) spectrometer. All chemical shifts are reported in ppm relative to TMS (0 ppm) as an internal standard. The following abbreviations were used to explain the multiplicities: *s* = singlet, *d* = doublet, *t* = triplet, *q* = quartet, *m* = multiplet. The coupling constants were reported in Hertz (Hz). All reagents used in the reactions were all purchased from commercial sources and used without further purification. The product spots on the thin layer chromatography (TLC) were visualized under ultraviolet light (254 nm or 365 nm).

2. General procedure for preparation of **3a–3q**



1 **2** **3**

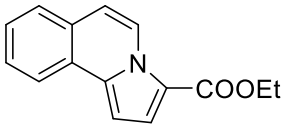
An oven-dried reaction tube equipped with a magnetic stirring bar was charged with isoquinolinium *N*-ylides (**1**, 1.0 mmol), Cu_2O (30 mol%, 43.0 mg), K_2CO_3 (2.0 mmol, 2.0 equiv., 276.0 mg), DMSO (5.0 mL) and 2-methoxyethene-1-sulfonyl fluoride (MESF, 3.0 mmol, 3.0 equiv., 420.0 mg). Then the mixture was stirred at 100 ℃ for 3 h. After the reaction was completed, the mixture was extracted with ethyl acetate (3 × 20 mL) and the combined organic layers were further washed with brine, and dried over anhydrous sodium sulfate. The solvent was concentrated under reduced pressure and the residue was further purified by flash silica gel chromatography using a mixture of petroleum ether, dichloromethane and ethyl acetate as eluent to afford the title products **3a–3q**.

3. The preparation of **3g** and **3k** as samples for animal experiments

An oven-dried reaction tube equipped with a magnetic stirring bar was charged with isoquinolinium *N*-ylides (**1**, 10.0 mmol), Cu_2O (30 mol%, 429.0 mg), K_2CO_3 (20.0

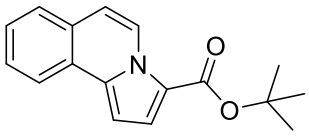
mmol, 2.0 equiv., 2.76 g), DMSO (45.0 mL) and 2-methoxyethene-1-sulfonyl fluoride (MESF, 50.0 mmol, 30 equiv., 4.20 g). Then the mixture was stirred at 60 ℃ for 24 h. After the reaction was completed, the mixture was extracted with ethyl acetate (3 × 150 mL) and the combined organic layers were further washed with brine, and dried over anhydrous sodium sulfate. The solvent was concentrated under reduced pressure and the residue was further purified by flash silica gel chromatography using a mixture of petroleum ether and ethyl acetate as eluent to afford products **3g** and **3k**, their yields were 72% and 81%, respectively.

4. Characterization data of **3a–3q**



3a

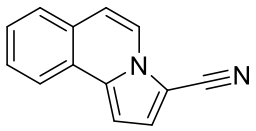
Ethyl pyrrolo[2,1-a]isoquinoline-3-carboxylate (**3a**). White solid, 187 mg, 78% yield. Purified by column chromatography on silica gel using petroleum ether / ethyl acetate = 10:1 (v/v) as eluent, purity, 98.84%. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.23 (d, J = 7.5 Hz, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.66 (d, J = 7.5 Hz, 1H), 7.55-7.48 (m, 3H), 7.00 (d, J = 5.0 Hz, 2H), 4.40 (q, J = 7.0 Hz, 2H), 1.43 (t, J = 7.0 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.5, 135.4, 127.9, 127.6, 127.3, 126.9, 125.2, 125.0, 123.2, 120.6, 116.7, 112.6, 101.0, 60.0, 14.6.



3b

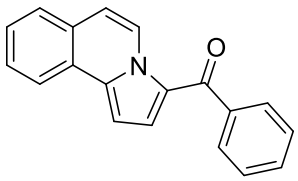
Tert-butyl pyrrolo[2,1-a]isoquinoline-3-carboxylate (**3b**). White solid, 200 mg, 75% yield. Purified by column chromatography on silica gel using petroleum ether / ethyl acetate = 10:1 (v/v) as eluent, purity, 98.02%. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.22 (d, J = 7.5 Hz, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.65 (d, J = 7.5 Hz, 1H), 7.54-7.43 (m, 3H), 6.97 (d, J = 8.0 Hz, 2H), 1.65 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.2, 135.1,

127.8, 127.6, 127.2, 126.9, 125.4, 125.1, 123.1, 120.5, 118.0, 112.4, 100.7, 80.7, 28.7.



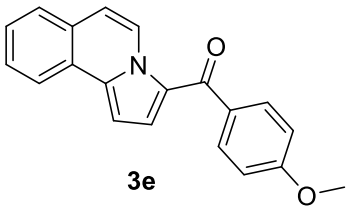
3c

Pyrrolo[2,1-a]isoquinoline-3-carbonitrile (**3c**). White solid, 115 mg, 60% yield. Purified by column chromatography on silica gel using petroleum ether / ethyl acetate = 10:1 (v/v) as eluent, purity, 99.89%. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.03 (d, J = 8.0 Hz, 1H), 7.97 (d, J = 7.5 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.56-7.47 (m, 2H), 7.25 (d, J = 4.0 Hz, 1H), 6.97 (d, J = 7.0 Hz, 1H), 6.90 (d, J = 4.0 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 134.3, 128.5, 127.9, 127.7, 127.4, 125.1, 123.1, 122.6, 121.9, 113.8, 113.7, 101.5, 97.8.



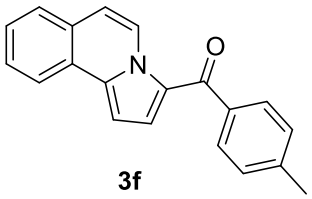
3d

Phenyl(pyrrolo[2,1-a]isoquinolin-3-yl)methanone (**3d**). Yellow solid, 190 mg, 70% yield. Purified by column chromatography on silica gel using petroleum ether / dichloromethane = 1:1 (v/v) as eluent, purity, 99.99%. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.62 (d, J = 7.5 Hz, 1H), 8.18 (d, J = 7.5 Hz, 1H), 7.86 (d, J = 7.5 Hz, 2H), 7.73 (d, J = 7.0 Hz, 1H), 7.59-7.49 (m, 5H), 7.32 (d, J = 4.5 Hz, 1H), 7.12 (d, J = 7.5 Hz, 1H), 7.05 (d, J = 4.0 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 185.5, 140.7, 137.1, 131.2, 129.2, 129.0, 128.3, 128.1, 127.8, 127.0, 126.0, 125.9, 124.8, 123.7, 113.5, 102.0. Note: In the ^{13}C NMR spectrum of **3k**, theoretically, there should be seventeen peaks. Due to the compact overlaying, it is difficult to specify the overlaying peaks.



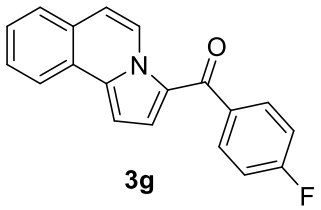
3e

(4-Methoxyphenyl)(pyrrolo[2,1-a]isoquinolin-3-yl)methanone (**3e**). Yellow solid, 151 mg, 50 % yield. Purified by column chromatography on silica gel using petroleum ether / dichloromethane = 1:1 (v/v) as eluent, purity, 98.81%. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.54 (d, J = 8.0 Hz, 1H), 8.17 (d, J = 7.5 Hz, 1H), 7.89-7.86 (m, 2H), 7.72-7.71 (m, 1H), 7.59-7.52 (m, 2H), 7.32 (d, J = 4.5 Hz, 1H), 7.09 (d, J = 7.5 Hz, 1H), 7.05 (d, J = 4.5 Hz, 1H), 7.02-6.99 (m, 2H), 3.90 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 184.6, 162.4, 136.7, 133.2, 131.5, 129.0, 128.0, 127.8, 127.0, 126.0, 125.3, 124.9, 123.7, 113.6, 113.3, 101.8, 55.6. Note: In the ^{13}C NMR spectrum of **3m**, theoretically, there should be eighteen peaks. Due to the compact overlaying, it is difficult to specify the overlaying peaks.



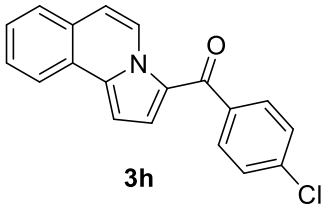
3f

Pyrrolo[2,1-a]isoquinolin-3-yl(p-tolyl)methanone (**3f**). Yellow solid, 257 mg, 90% yield. Purified by column chromatography on silica gel using petroleum ether / dichloromethane = 1:1 (v/v) as eluent, purity, 95.08%. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.59 (d, J = 7.5 Hz, 1H), 8.17 (d, J = 7.5 Hz, 1H), 7.77 (d, J = 8.0 Hz, 2H), 7.73-7.71 (m, 1H), 7.59-7.53 (m, 2H), 7.33-7.30 (m, 3H), 7.11 (d, J = 8.0 Hz, 1H), 7.05 (d, J = 4.0 Hz, 1H), 2.46 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 185.5, 141.8, 138.0, 136.9, 129.4, 129.0, 129.0, 128.1, 127.8, 127.0, 126.0, 125.8, 125.0, 124.9, 123.7, 113.4, 101.9, 21.7.



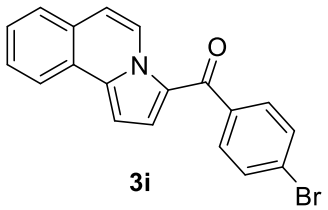
3g

(4-Fluorophenyl)(pyrrolo[2,1-a]isoquinolin-3-yl)methanone (**3g**). Yellow solid, 119 mg, 41% yield. Purified by column chromatography on silica gel using petroleum ether / dichloromethane = 1:1 (v/v) as eluent, purity, 99.99%. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.57 (d, J = 7.0 Hz, 1H), 8.19 (d, J = 7.5 Hz, 1H), 7.89-7.87 (m, 2H), 7.75-7.73 (m, 1H), 7.61-7.55 (m, 2H), 7.29 (d, J = 4.5 Hz, 1H), 7.20-7.17 (m, 2H), 7.14 (d, J = 7.5 Hz, 1H), 7.07 (d, J = 4.5 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 183.9, 164.7 (d, J = 252.0 Hz), 137.1, 136.8 (d, J = 3.7 Hz), 131.5 (d, J = 8.2 Hz), 129.0, 128.1, 127.8, 127.0, 125.8, 125.7, 124.7, 124.5, 123.7, 115.3 (d, J = 21.8 Hz), 113.5, 102.0.



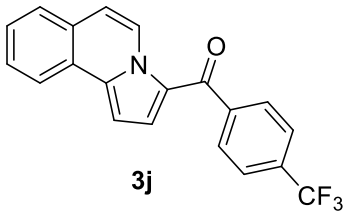
3h

(4-Chlorophenyl)(pyrrolo[2,1-a]isoquinolin-3-yl)methanone (**3h**). Yellow solid, 122 mg, 40% yield. Purified by column chromatography on silica gel using petroleum ether / dichloromethane = 1:1 (v/v) as eluent, purity, 98.90%. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.58 (d, J = 7.5 Hz, 1H), 8.19 (d, J = 7.5 Hz, 1H), 7.80 (d, J = 8.5 Hz, 2H), 7.75-7.73 (m, 1H), 7.61-7.56 (m, 2H), 7.48 (d, J = 8.5 Hz, 2H), 7.28 (d, J = 4.5 Hz, 1H), 7.14 (d, J = 7.5 Hz, 1H), 7.07 (d, J = 4.5 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 184.0, 165.9, 139.1, 137.5, 137.4, 130.6, 129.1, 128.6, 128.3, 128.0, 127.1, 125.9, 124.7, 124.5, 123.8, 113.7, 102.3.



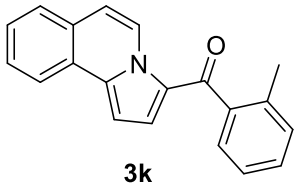
3i

(4-Bromophenyl)(pyrrolo[2,1-a]isoquinolin-3-yl)methanone (**3i**). Yellow solid, 122 mg, 48% yield. Purified by column chromatography on silica gel using petroleum ether / dichloromethane = 1:1 (v/v) as eluent, purity, 99.99%. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.58 (d, J = 7.5 Hz, 1H), 8.20-8.18 (m, 1H), 7.75-7.71 (m, 3H), 7.66-7.63 (m, 2H), 7.61-7.55 (m, 2H), 7.28 (d, J =4.5 Hz, 1H), 7.14 (d, J = 7.5 Hz, 1H), 7.06 (d, J = 4.5 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 184.1, 139.5, 137.4, 131.6, 130.8, 129.1, 128.3, 128.0, 127.1, 125.9, 125.9, 124.7, 124.5, 123.8, 113.7, 102.3. Note: In the ^{13}C NMR spectrum of **3q**, theoretically, there should be seventeen peaks. Due to the compact overlaying, it is difficult to specify the overlaying peaks.



3j

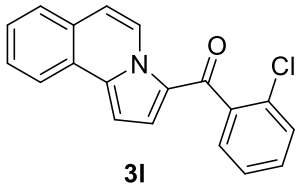
Pyrrolo[2,1-a]isoquinolin-3-yl(4-(trifluoromethyl)phenyl)methanone (**3j**). Yellow solid, 110 mg, 32% yield. M.p. 236-238 ℃. Purified by column chromatography on silica gel using petroleum ether / dichloromethane = 1:1 (v/v) as eluent, purity, 98.19%. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.64 (d, J = 7.5 Hz, 1H), 8.23-8.21 (m, 1H), 7.96 (d, J = 8.0 Hz, 2H), 7.80-7.77 (m, 3H), 7.65-7.59 (m, 2H), 7.29 (d, J = 4.0 Hz, 1H), 7.20(d, J = 7.5 Hz, 1H), 7.10 (d, J = 5.0 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 183.9, 144.0, 137.8, 132.9, 132.6, 129.4, 129.3, 128.5, 128.1, 127.2, 126.4, 125.9, 125.4 (q, J = 3.7 Hz), 125.1, 124.7, 124.4, 123.9, 122.9, 114.0, 102.6. **HRMS-ESI** (m/z) calcd. for $[C_{20}H_{13}F_3NO]^+$ ($[M+H]^+$): 340.0944, found: 340.0951.



3k

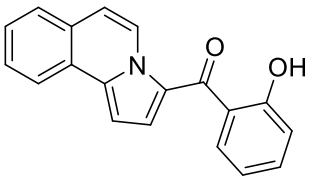
Pyrrolo[2,1-a]isoquinolin-3-yl(o-tolyl)methanone (**3k**). Yellow solid, 177 mg, 62% yield. M.p. 87-89 ℃. Purified by column chromatography on silica gel using petroleum

ether / dichloromethane = 1:1 (v/v) as eluent, purity, 99.85%. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.73 (d, J = 7.5 Hz, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 7.0 Hz, 1H), 7.60-7.55 (m, 2H), 7.45 (d, J = 7.5 Hz, 1H), 7.39 (t, J = 7.5 Hz, 1H), 7.31-7.27(m, 2H), 7.15 (d, J = 7.5 Hz, 1H), 7.05 (d, J = 4.5 Hz, 1H), 7.01 (d, J = 4.5 Hz, 1H), 2.43 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 187.5, 140.7, 137.3, 136.2, 130.8, 129.6, 129.2, 128.3, 128.2, 127.9, 127.1, 126.5, 126.1, 125.6, 125.2, 124.8, 123.8, 113.7, 102.2, 19.8. **HRMS-ESI** (m/z) calcd. for $[C_{20}H_{16}NO]^+$ ($[M+H]^+$): 286.1227, found: 286.1234.



3l

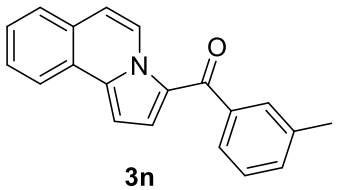
(2-Chlorophenyl)(pyrrolo[2,1-a]isoquinolin-3-yl)methanone (**3l**). Yellow solid, 116 mg, 38% yield. Purified by column chromatography on silica gel using petroleum ether / dichloromethane = 1:1 (v/v) as eluent, purity, 99.83%. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.69 (d, J = 7.5 Hz, 1H), 8.18-8.16 (m, 1H), 7.75-7.74 (m, 1H), 7.60-7.56 (m, 2H), 7.50-7.48 (m, 2H), 7.43-7.40 (m, 1H), 7.38-7.35 (m, 1H), 7.17 (d, J = 7.5 Hz, 1H), 7.03-7.00 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 183.3, 140.0, 137.8, 131.5, 130.6, 130.1, 129.3, 129.2, 128.4, 128.0, 127.1, 126.6, 126.5, 126.0, 124.7, 124.6, 123.9, 113.9, 102.7.



3m

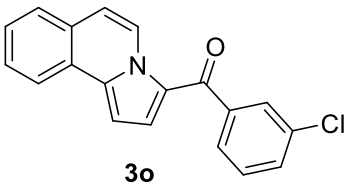
(2-Hydroxyphenyl)(pyrrolo[2,1-a]isoquinolin-3-yl)methanone (**3m**). Yellow solid, 161 mg, 56% yield. M.p. 142-144 °C. Purified by column chromatography on silica gel using petroleum ether / ethyl acetate = 10:1 (v/v) as eluent, purity, 98.51%. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 11.57 (s, 1H), 9.31 (d, J = 7.5 Hz, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 7.0 Hz, 1H), 7.61-7.55 (m, 2H), 7.49-7.44 (m, 2H), 7.11-7.06 (m, 3H), 6.96 (t, J = 7.5 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 187.1, 162.0,

137.6, 134.6, 132.1, 129.1, 128.4, 128.0, 127.1, 126.1, 125.8, 124.8, 124.2, 123.8, 121.5, 118.8, 118.2, 113.6, 102.6. **HRMS-ESI** (m/z) calcd. for $[C_{19}H_{14}NO_2]^+$ ($[M+H]^+$): 288.1020, found: 288.1015.



3n

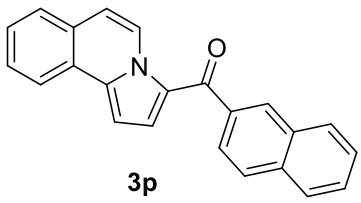
Pyrrolo[2,1-a]isoquinolin-3-yl(m-tolyl)methanone (**3n**). Yellow solid, 185 mg, 65% yield. M.p. 123-125 ℃. Purified by column chromatography on silica gel using petroleum ether / dichloromethane = 1:1 (v/v) as eluent, purity, 99.84%. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.61 (d, J = 7.0 Hz, 1H), 8.19-8.18 (m, 1H), 7.74-7.72 (m, 1H), 7.66-7.63 (m, 2H), 7.60-7.54 (m, 2H), 7.40-7.37 (m, 2H), 7.32(d, J = 4.0 Hz, 1H), 7.12 (d, J = 7.5 Hz, 1H), 7.05 (d, J = 4.5 Hz, 1H), 2.46 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 185.8, 140.8, 138.1, 137.0, 132.0, 129.8, 129.1, 128.1, 127.9, 127.1, 126.5, 126.0, 124.9, 124.9, 123.8, 113.5, 102.0, 21.6. Note: In the ^{13}C NMR spectrum of **3v**, theoretically, there should be twenty peaks. Due to the compact overlaying, it is difficult to specify the overlaying peaks. **HRMS-ESI** (m/z) calcd. for $[C_{20}H_{16}NO]^+$ ($[M+H]^+$): 286.1227, found: 286.1225.



3o

(3-Chlorophenyl)(pyrrolo[2,1-a]isoquinolin-3-yl)methanone (**3o**). Yellow solid, 128 mg, 42% yield. Purified by column chromatography on silica gel using petroleum ether / dichloromethane = 1:1 (v/v) as eluent, purity, 99.38%. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.59 (d, J = 7.5 Hz, 1H), 8.21-8.19 (m, 1H), 7.82 (t, J = 2.0 Hz, 1H), 7.76-7.71 (m, 2H), 7.62-7.56 (m, 2H), 7.54-7.52 (m, 1H), 7.44 (t, J = 7.5 Hz, 1H), 7.30 (d, J = 5.0 Hz, 1H), 7.16 (d, J = 7.5 Hz, 1H), 7.07 (d, J = 4.5 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 183.7, 142.4, 137.6, 134.5, 131.2, 129.6, 129.2, 129.2, 128.4, 128.0, 127.3, 127.1, 126.2, 125.9,

124.7, 124.4, 123.9, 113.8, 102.4.

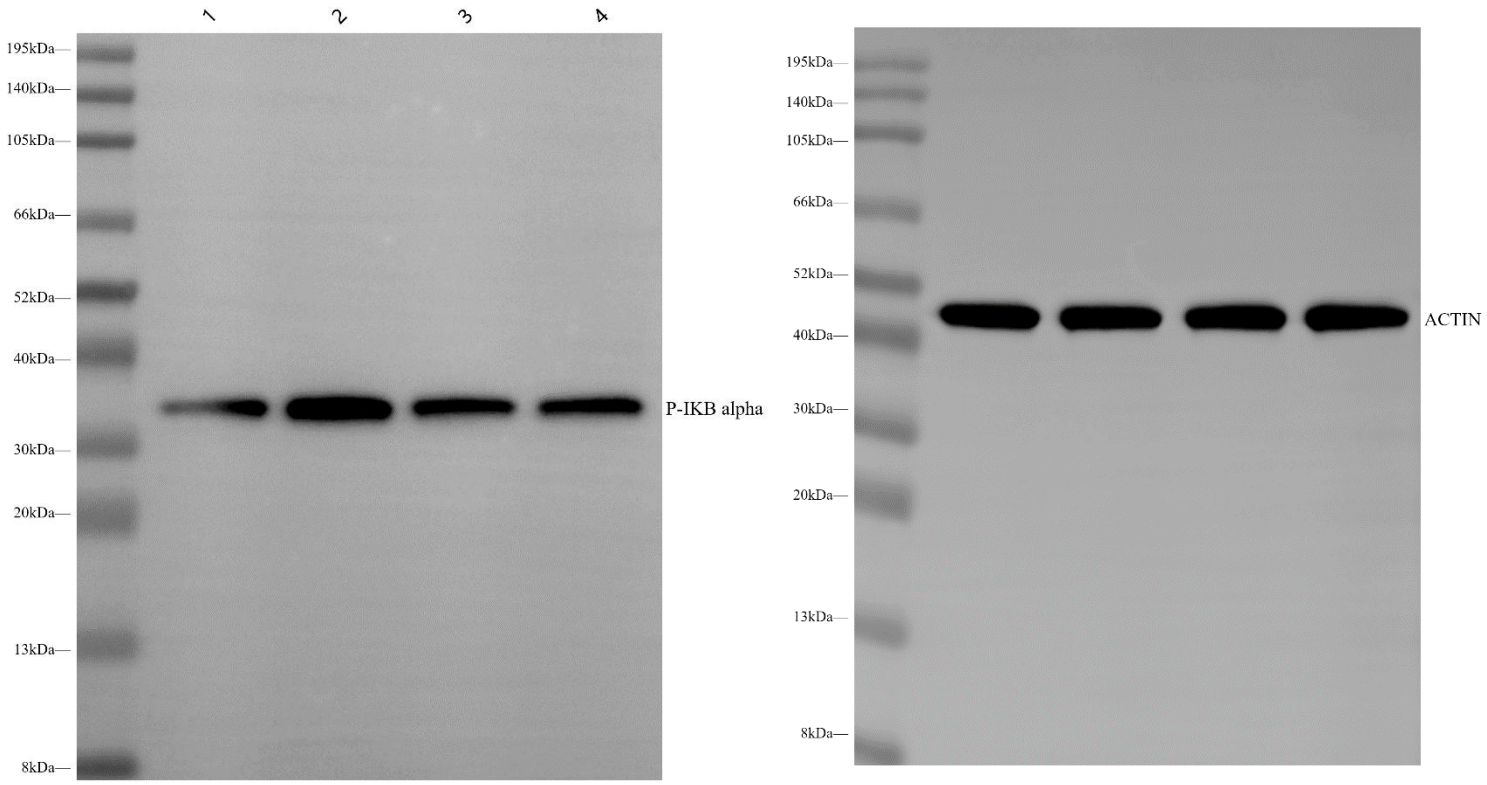


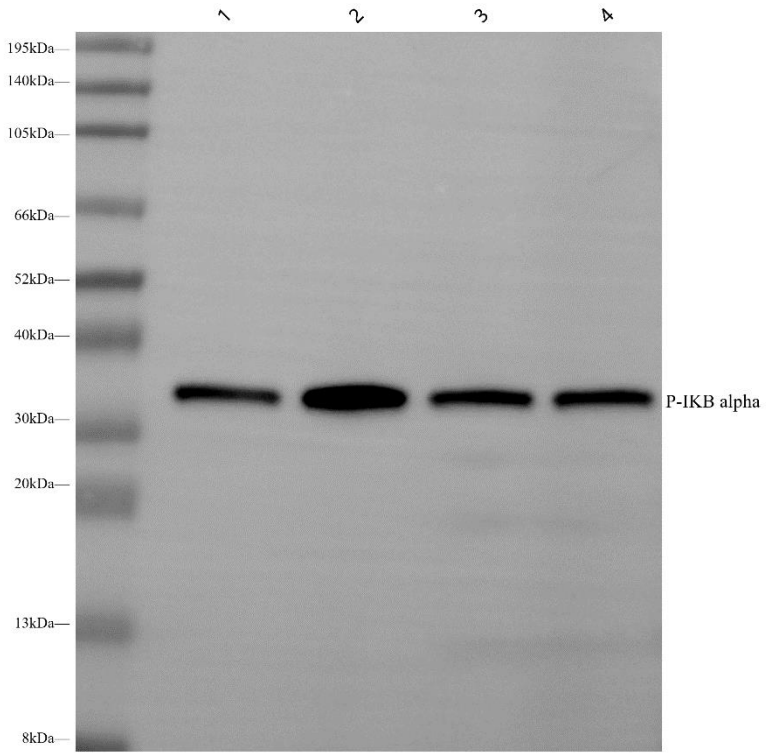
3p

Naphthalen-2-yl(pyrrolo[2,1-a]isoquinolin-3-yl)methanone (**3p**). Yellow solid, 167 mg, 52% yield. Purified by column chromatography on silica gel using petroleum ether / dichloromethane = 1:1 (v/v) as eluent, purity, 98.65%. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.65 (d, J = 7.5 Hz, 1H), 8.36 (s, 1H), 8.22-8.20 (m, 1H), 7.98-7.93 (m, 4H), 7.76-7.74 (m, 1H), 7.62-7.56 (m, 4H), 7.39 (d, J = 5.0 Hz, 1H), 7.16 (d, J = 7.5 Hz, 1H), 7.09 (d, J = 4.5 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 185.5, 138.0, 137.2, 134.9, 132.6, 130.0, 129.3, 129.1, 128.2, 128.2, 128.0, 127.9, 127.8, 127.1, 126.8, 126.2, 126.0, 125.9, 125.1, 124.9, 123.8, 113.6, 102.2.

Raw data of Western blotting:

P-IKB alpha and ACTIN

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105kDa
66kDa
52kDa
40kDa
30kDa
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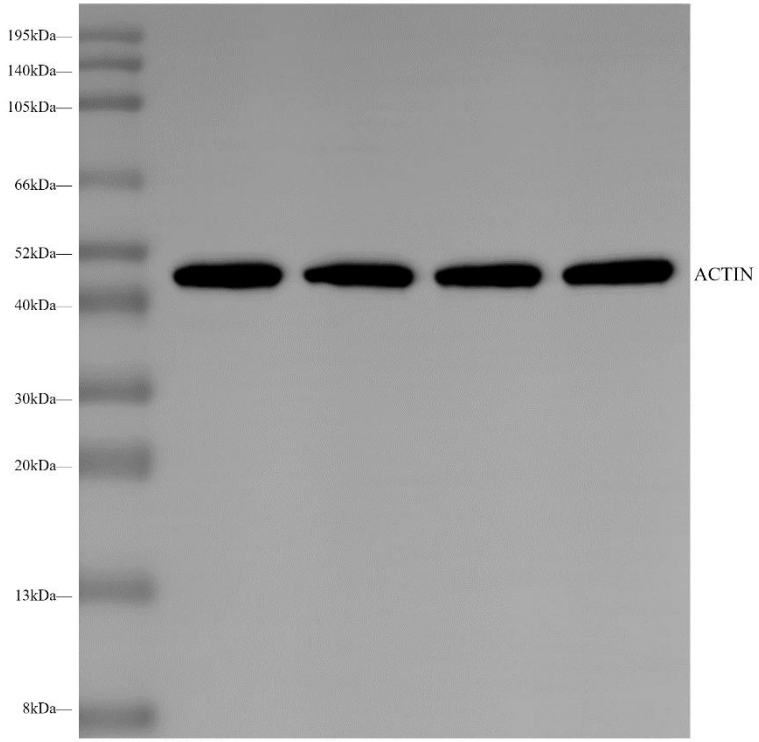
13kDa
8kDa
P-IKB alpha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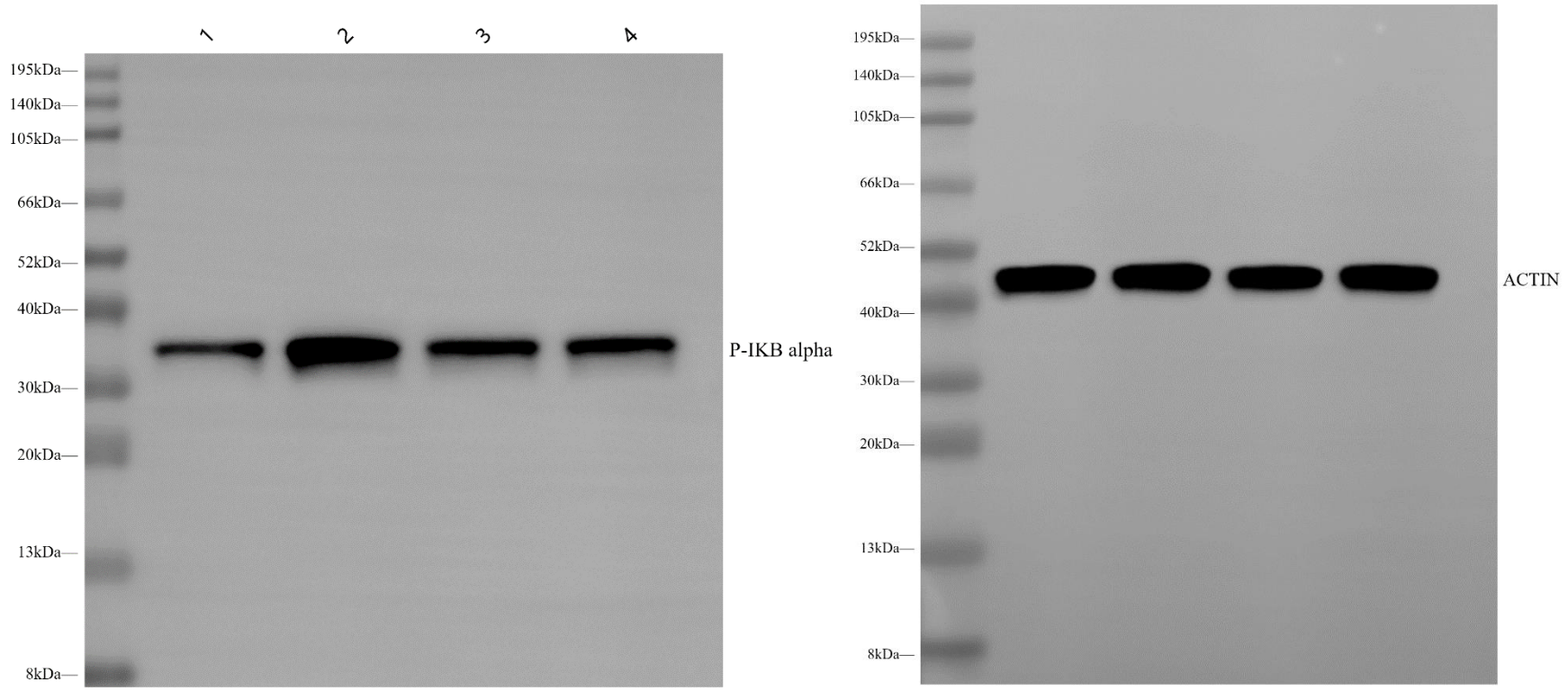
ACTIN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40kDa—
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8kDa—
P-IKB alpha
195kDa—
140kDa—
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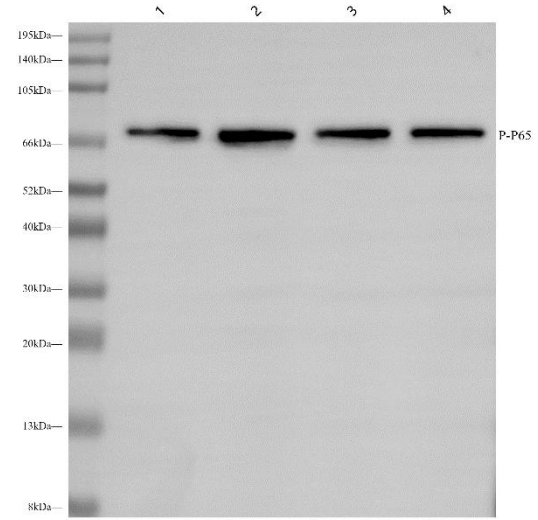
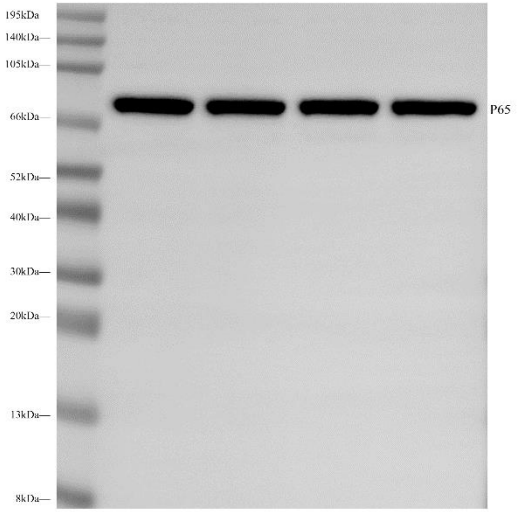
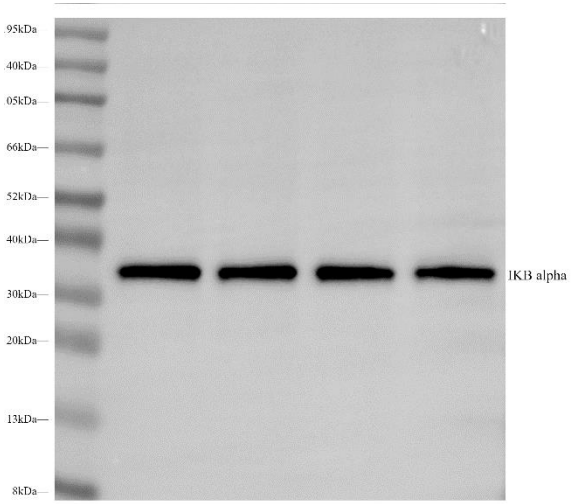
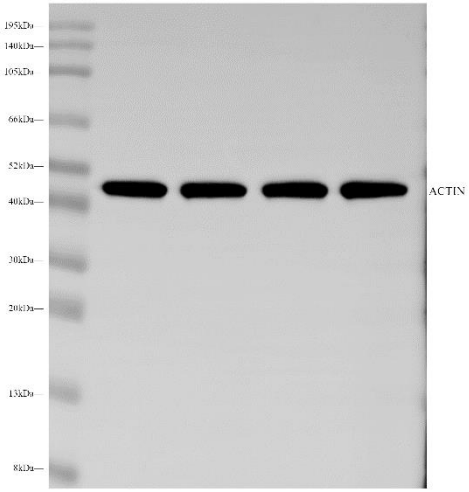
40kDa—
30kDa—
20kDa—
13kDa—
8kDa—
ACTIN

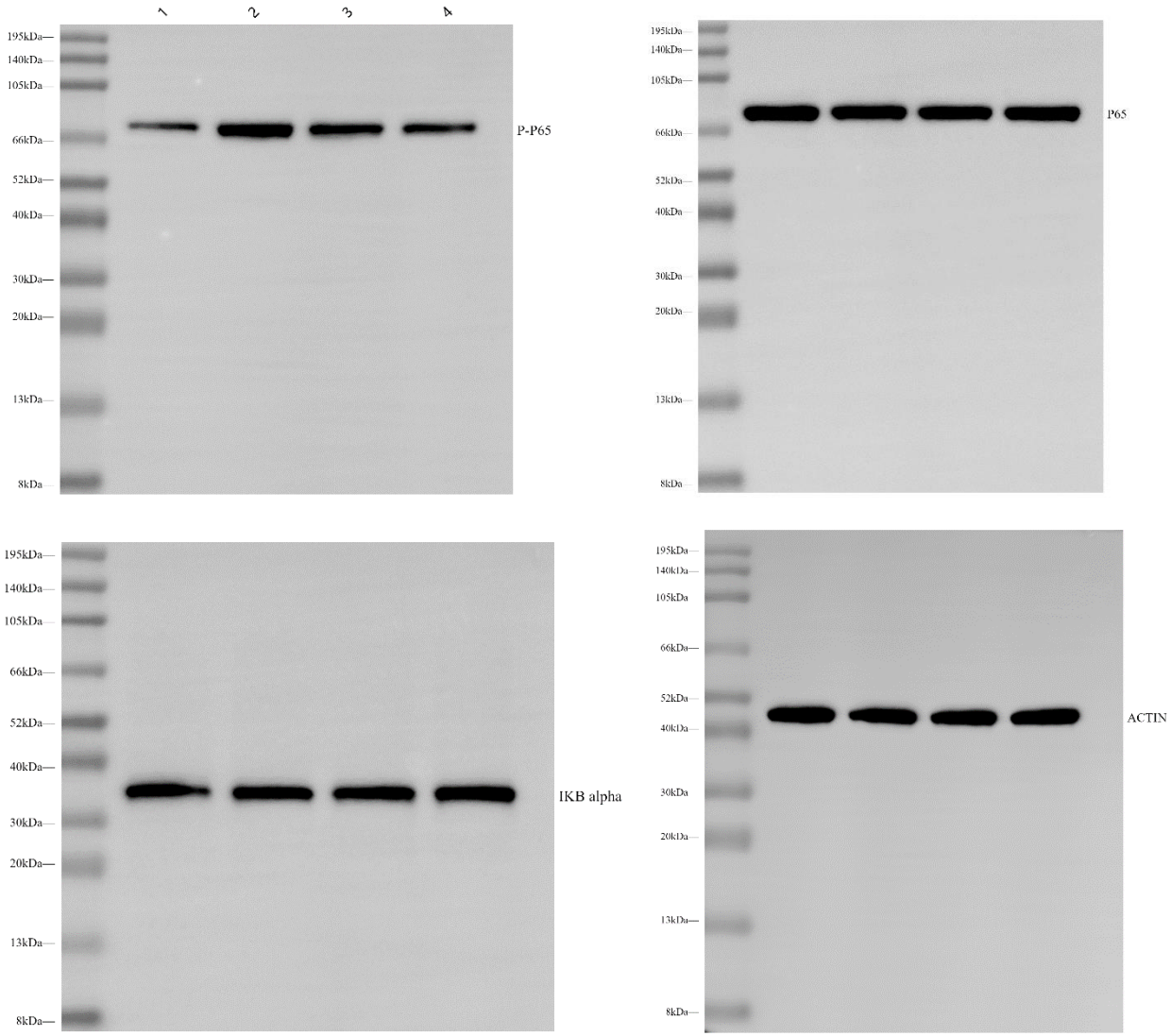
Raw data: P-P65, P65, IKB alpha and ACTIN







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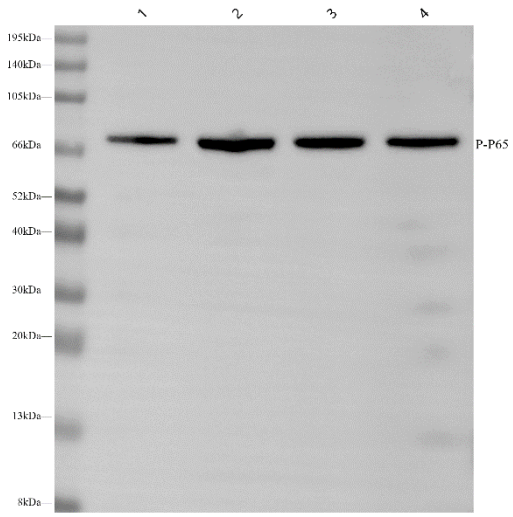
8kDa
P-P65
P65
IKB alpha
ACTIN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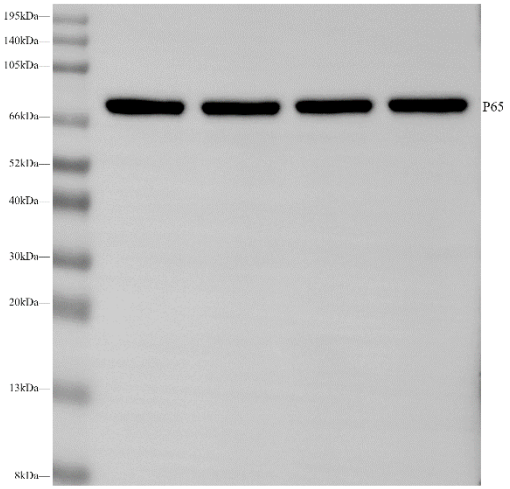
P-P65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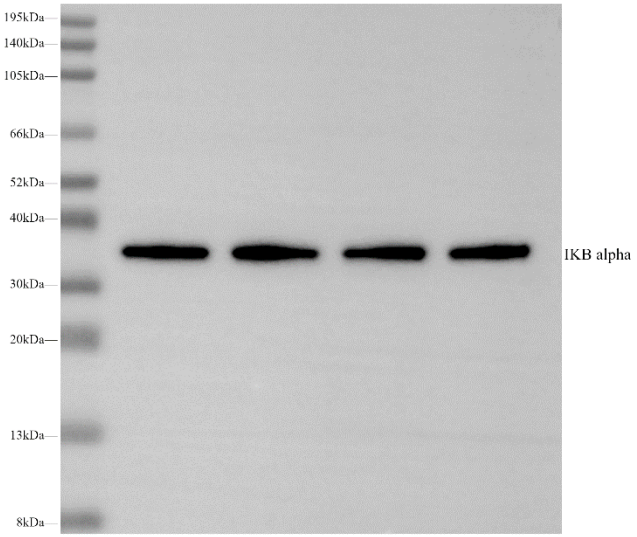
8kDa
P65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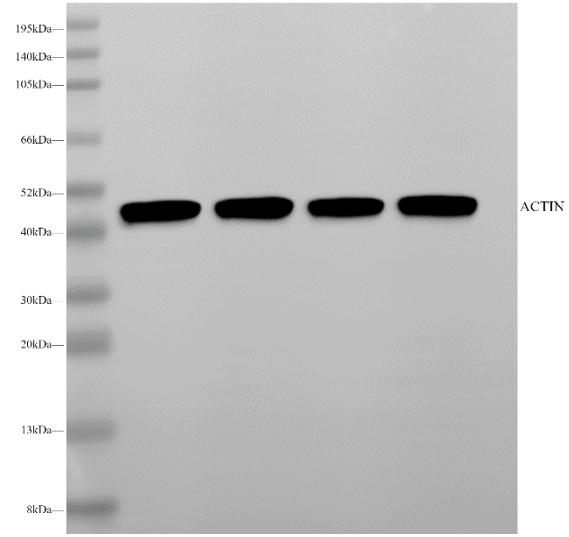
13kDa
8kDa
IKB alpha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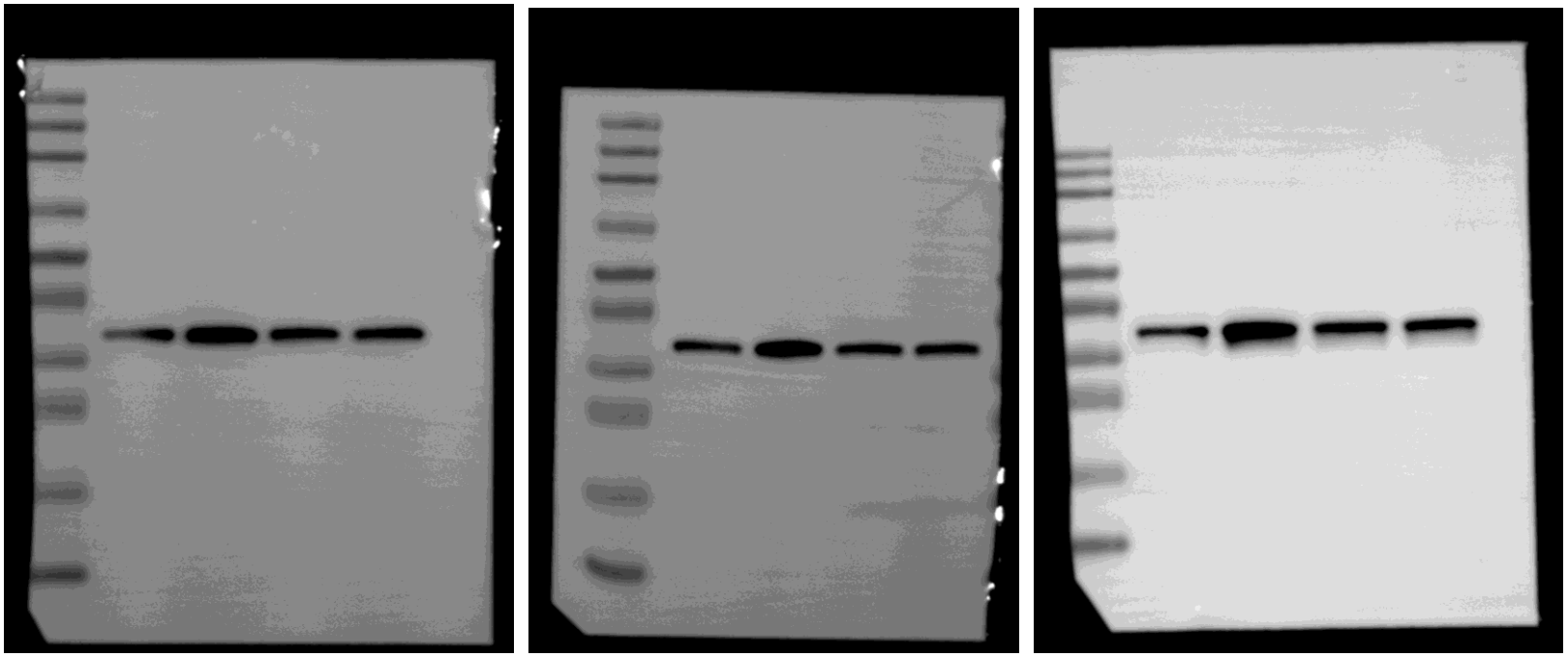
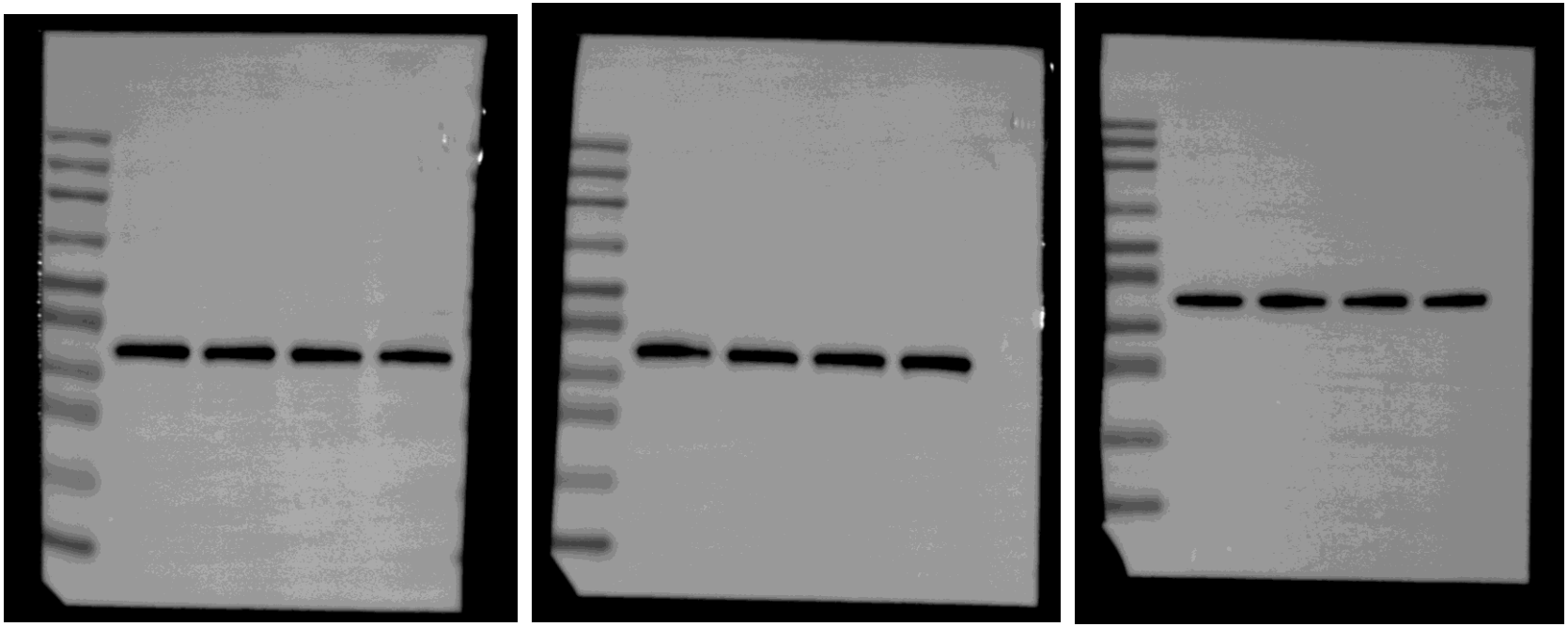
66kDa
52kDa
40kDa
30kDa
20kDa
13kDa
8kDa
ACTIN

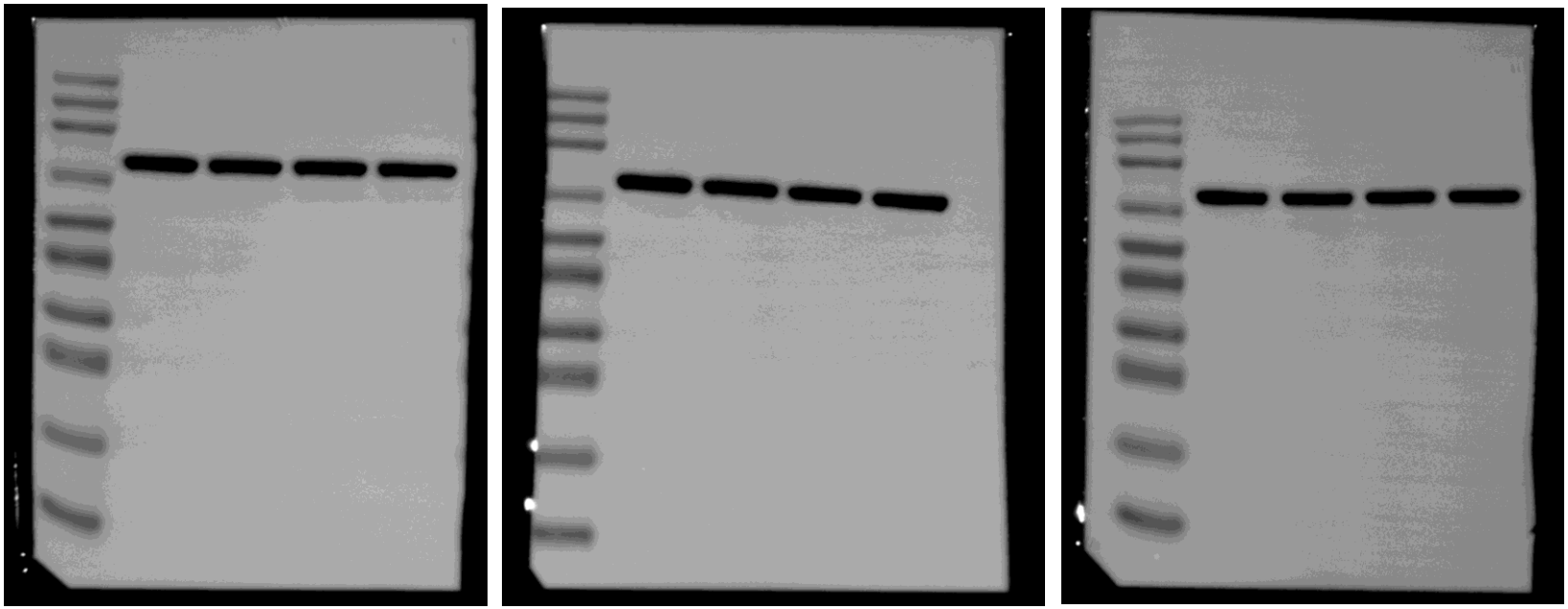
Raw data: P-IKB alpha (n = 3)



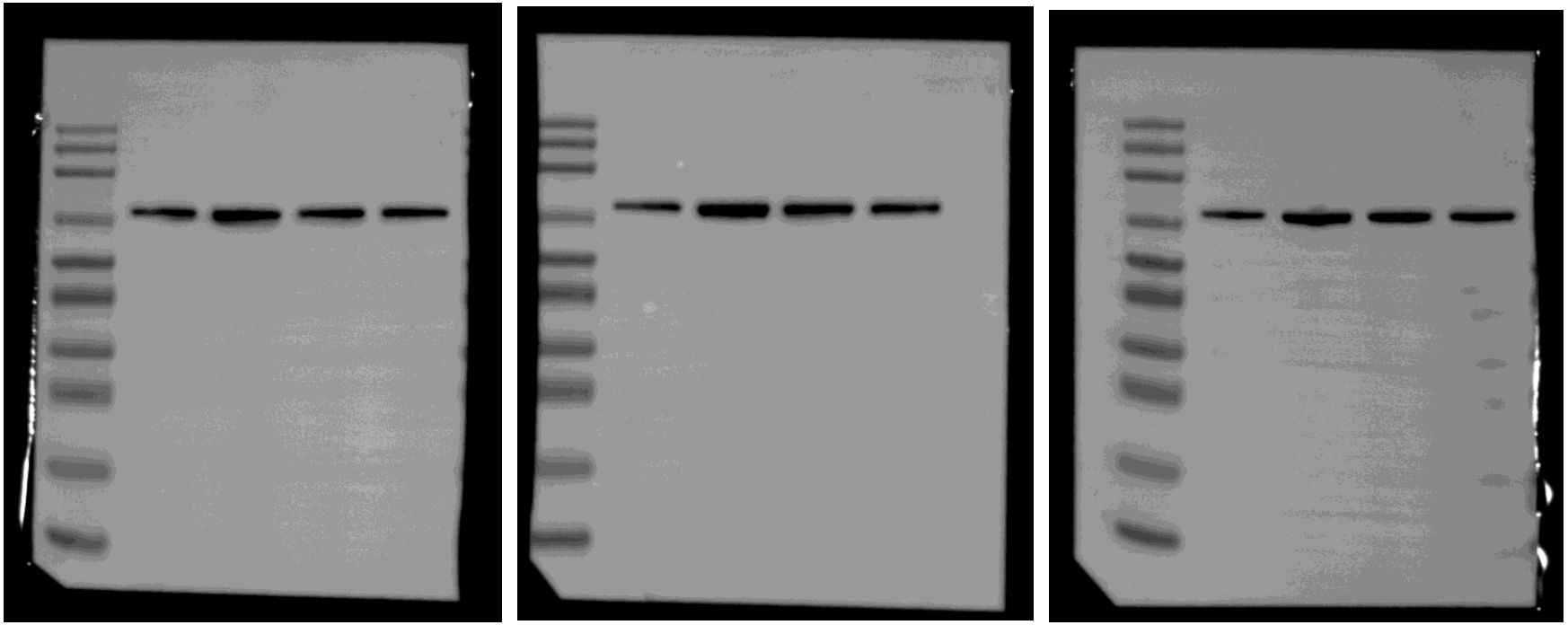
Raw data: IKB alpha (n = 3)



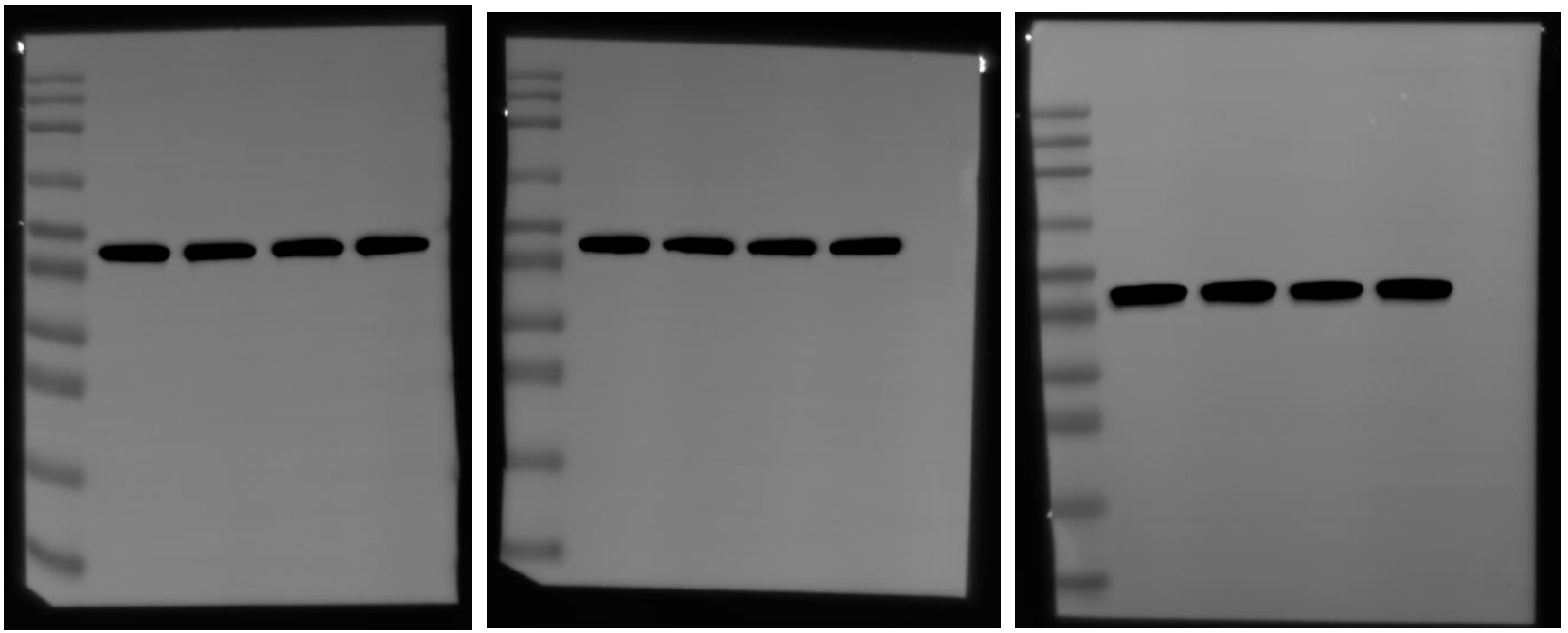
Raw data: P65 (n = 3)



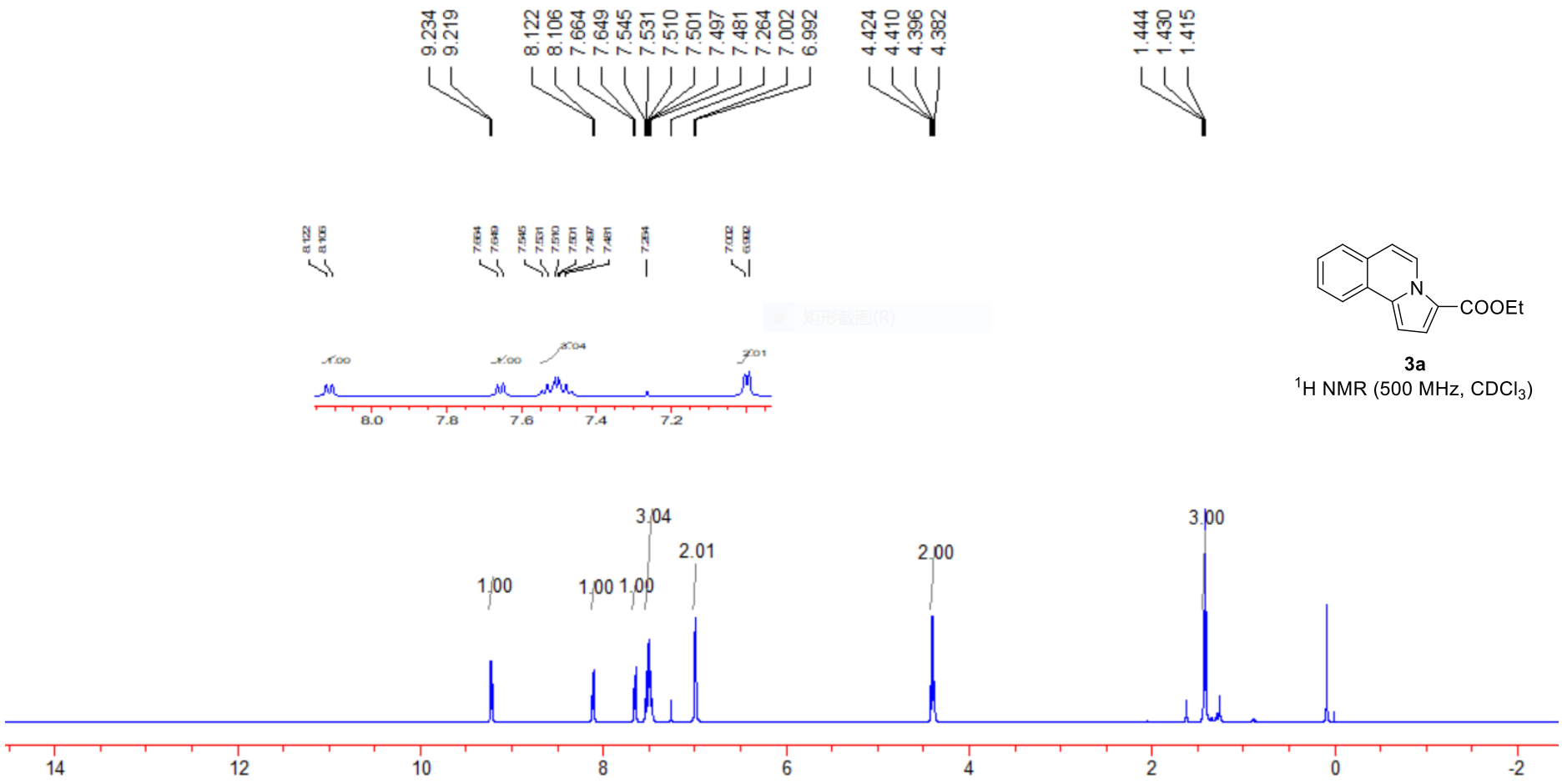
Raw data: P-P65 (n = 3)

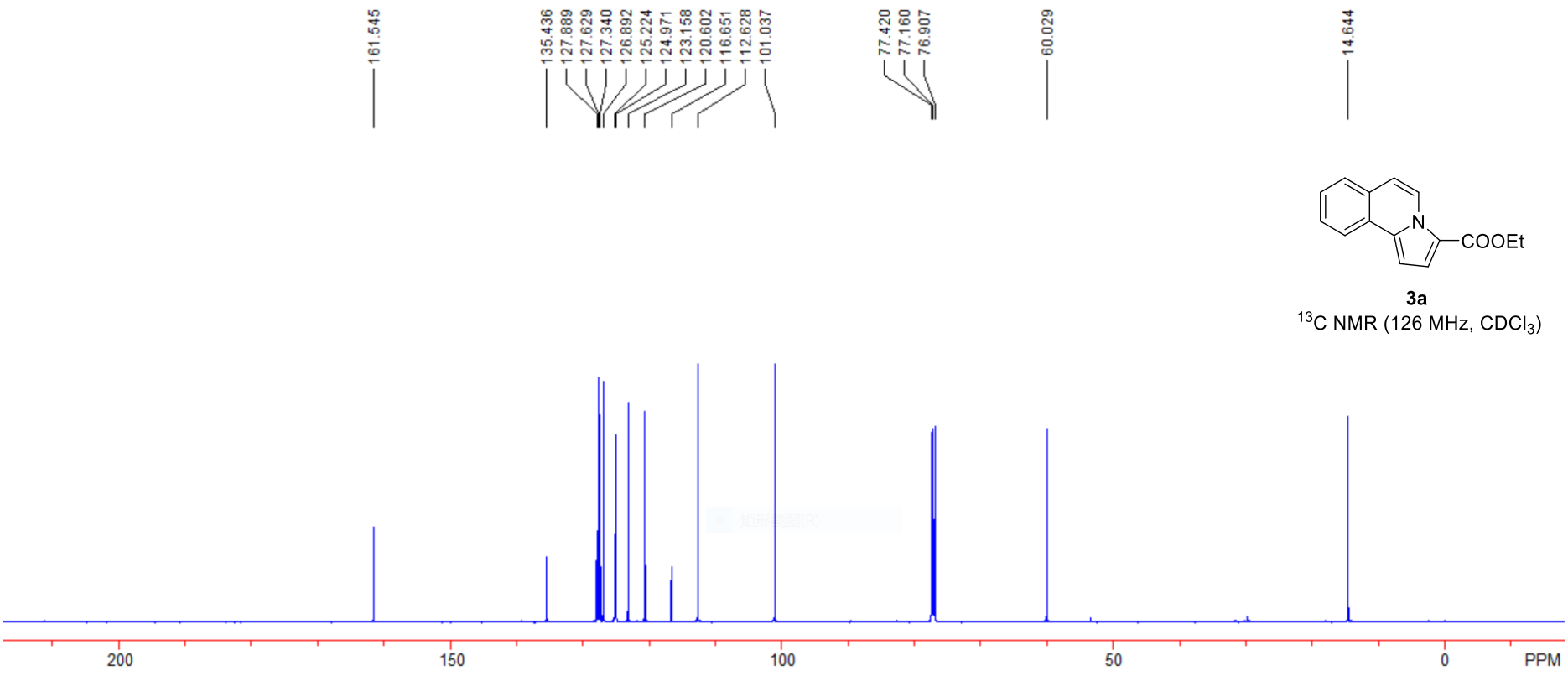


Raw data: ACTIN (n = 3)



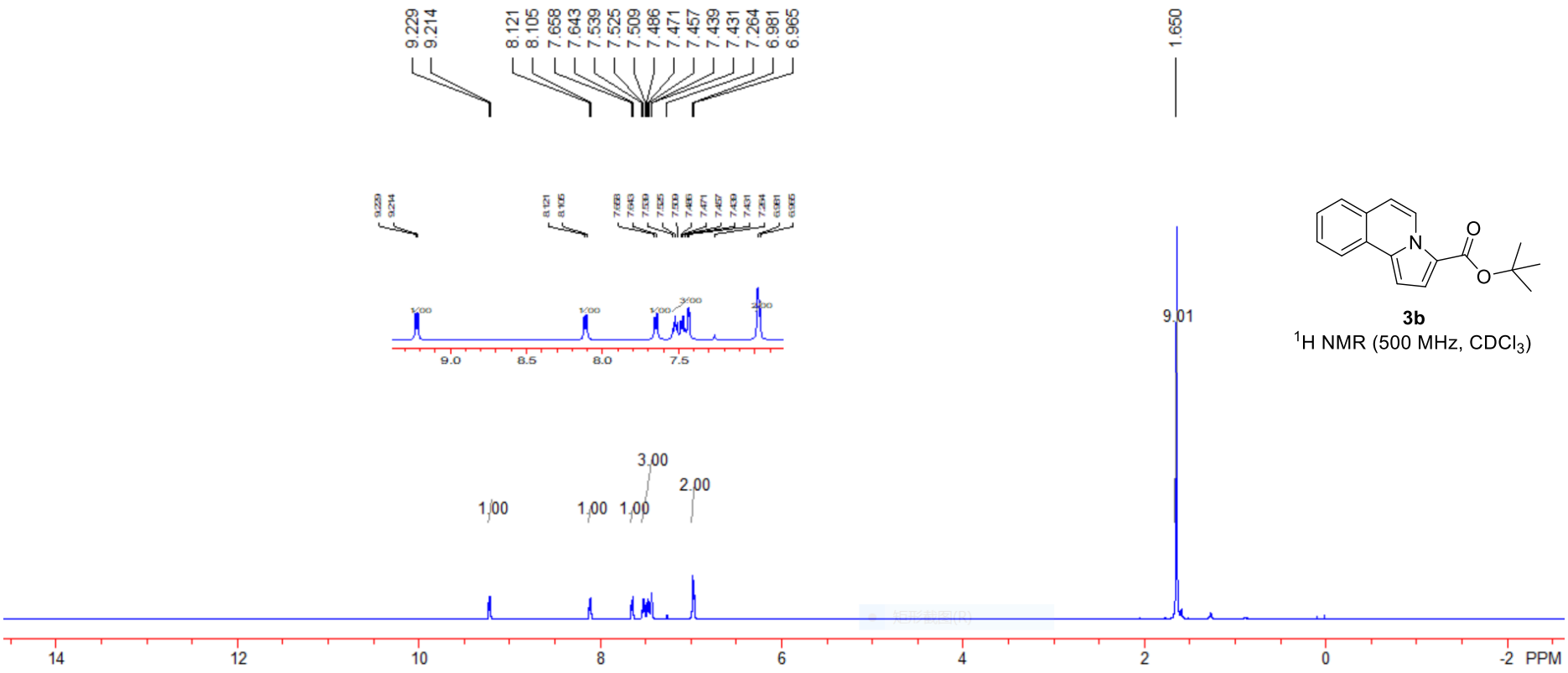
7. NMR and HPLC spectra





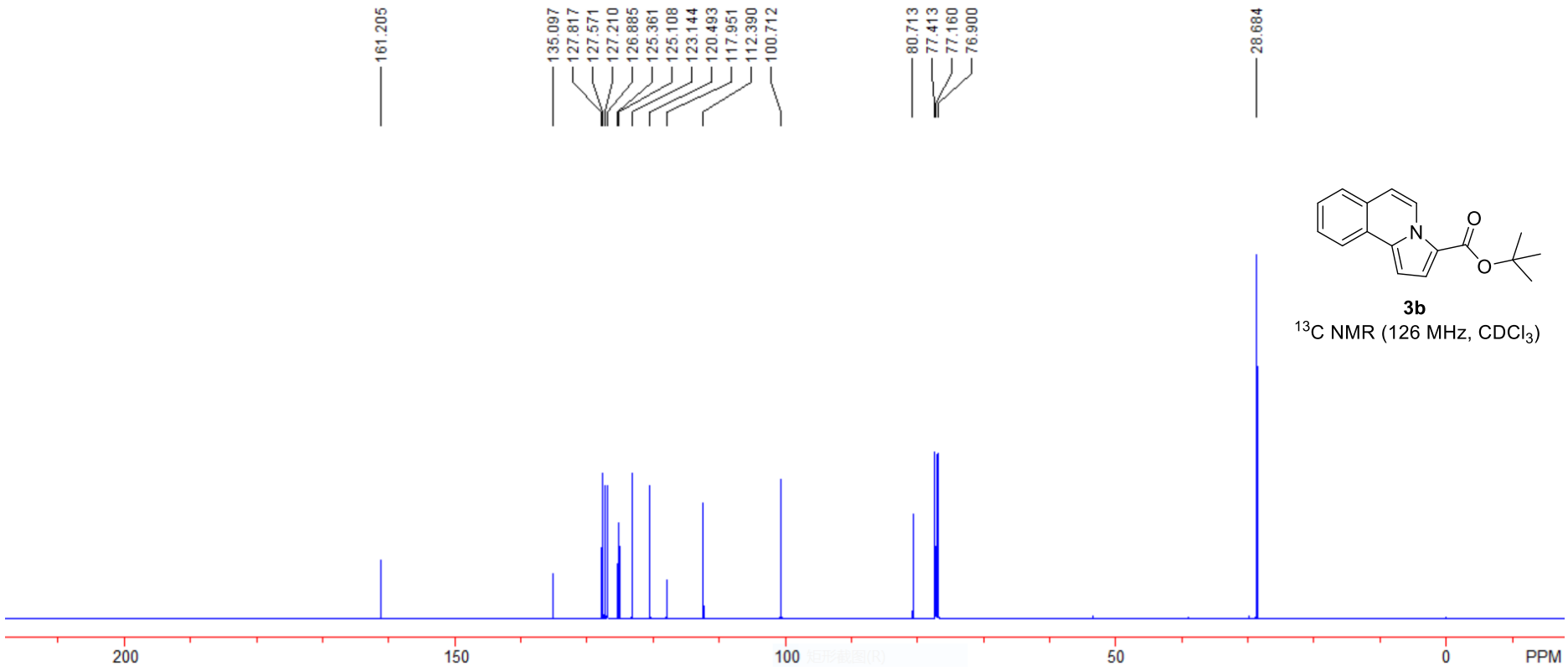
3a

^{13}C NMR (126 MHz, $CDCl_3$)



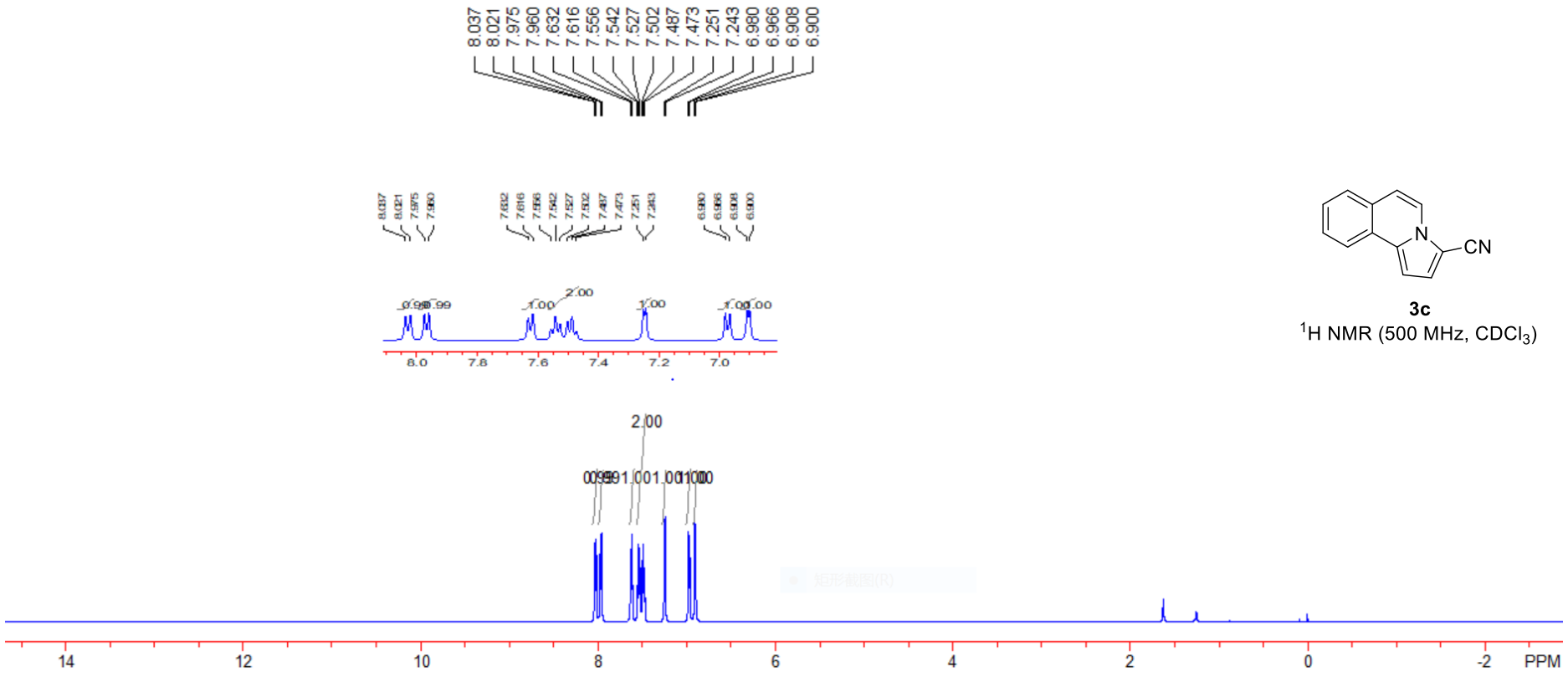
3b

^{1}H NMR (500 MHz, $CDCl_3$)



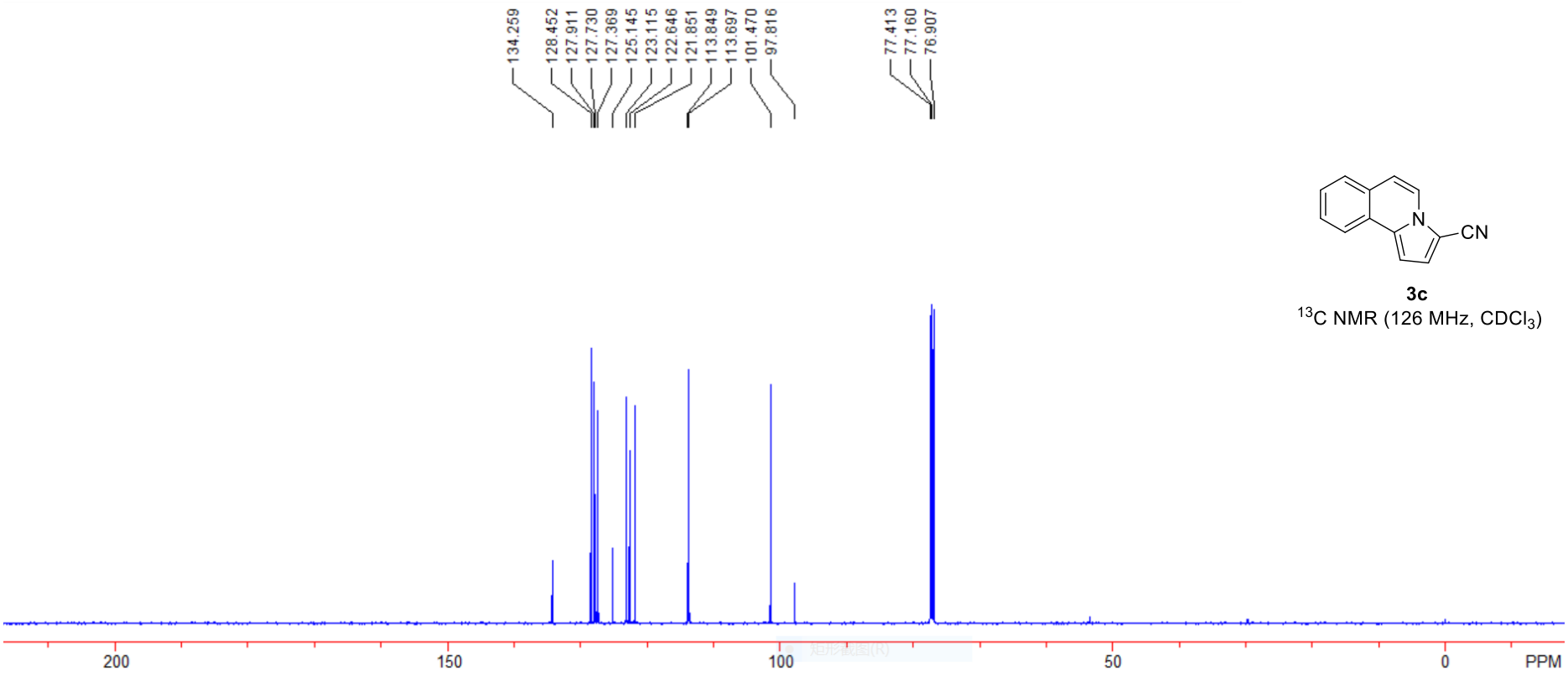
3b

^{13}C NMR (126 MHz, $CDCl_3$)



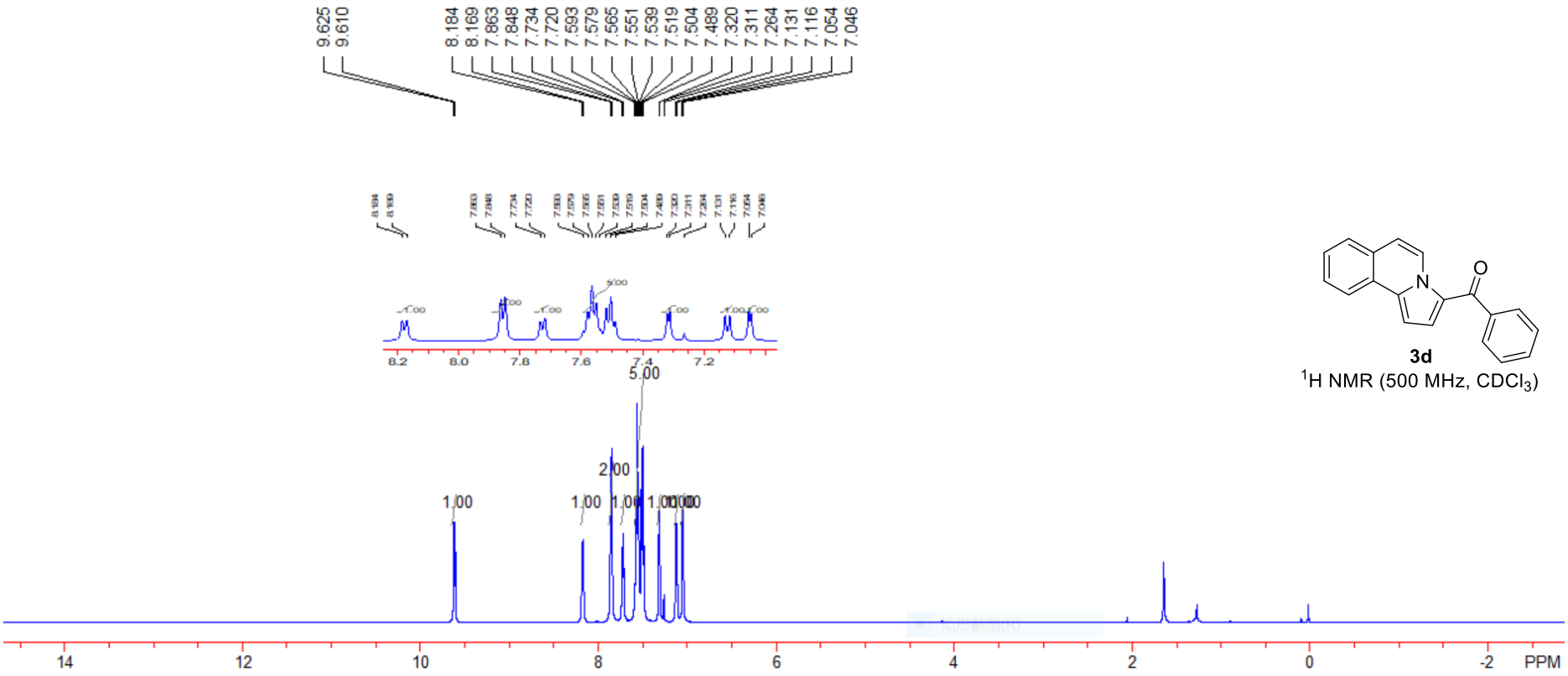
3c

^{1}H NMR (500 MHz, $CDCl_3$)



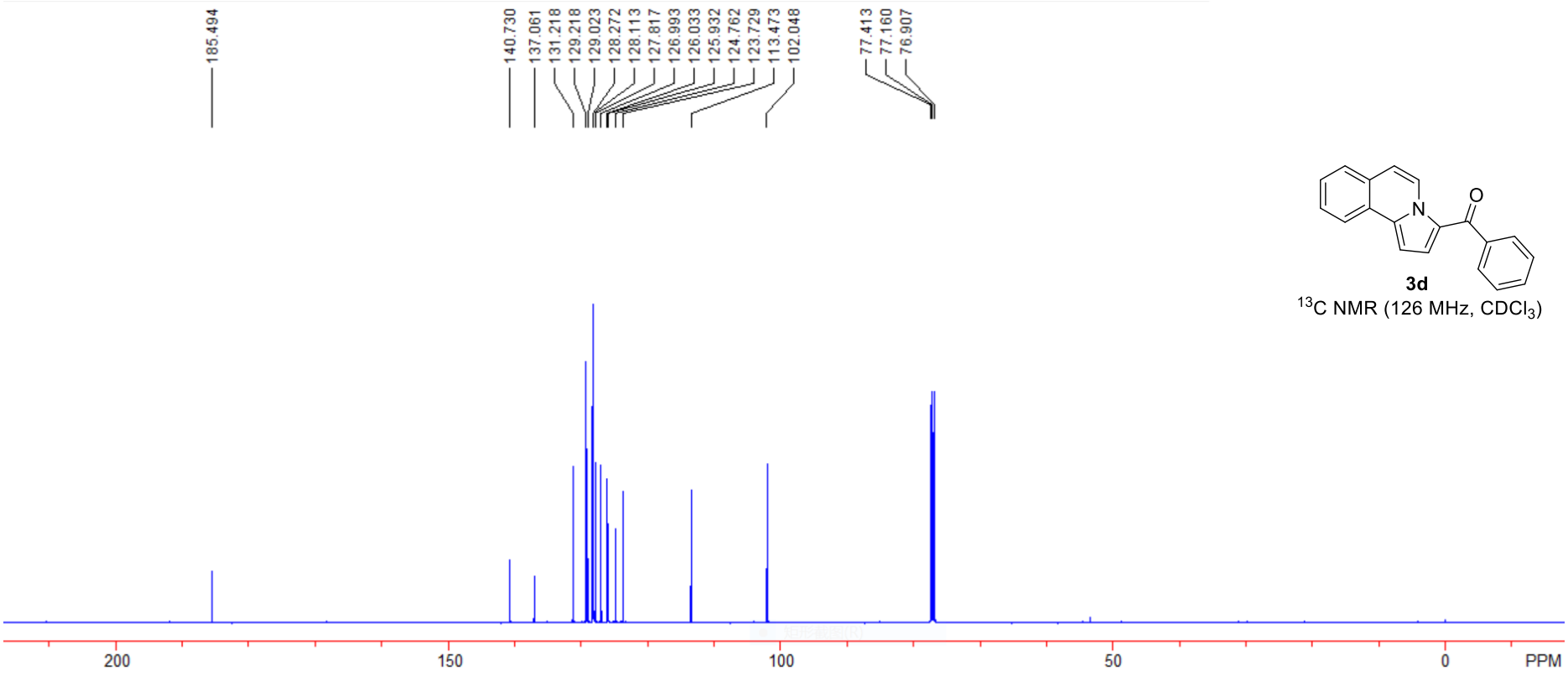
3c

^{13}C NMR (126 MHz, $CDCl_3$)



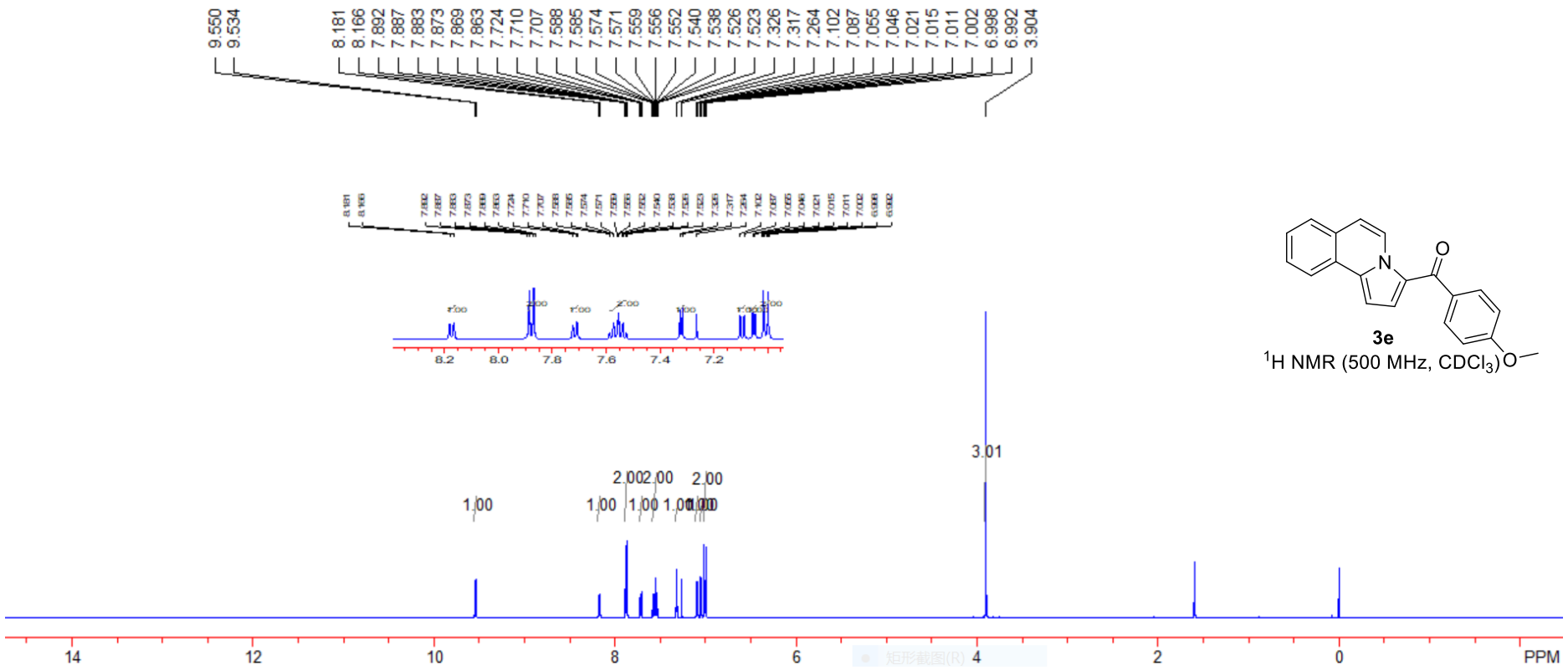
3d

^{1}H NMR (500 MHz, $CDCl_3$)



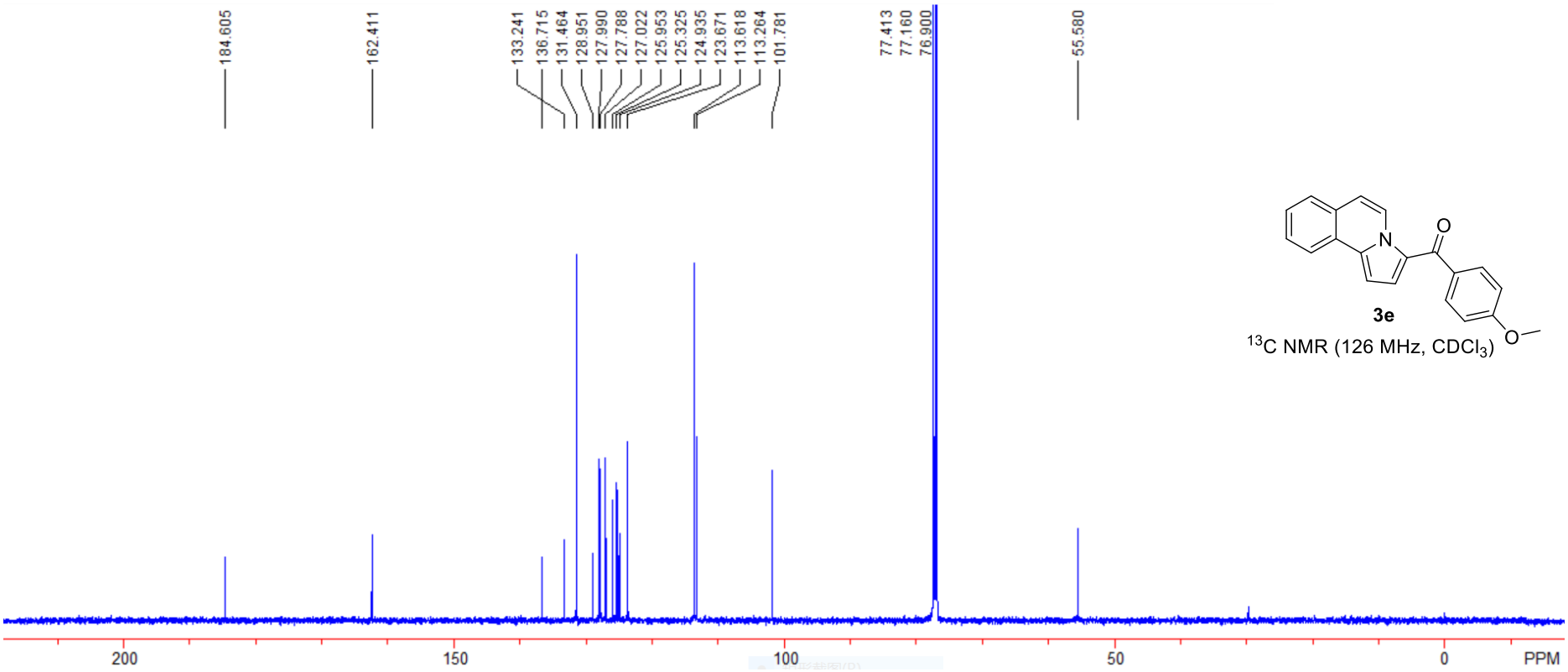
3d

^{13}C NMR (126 MHz, $CDCl_3$)



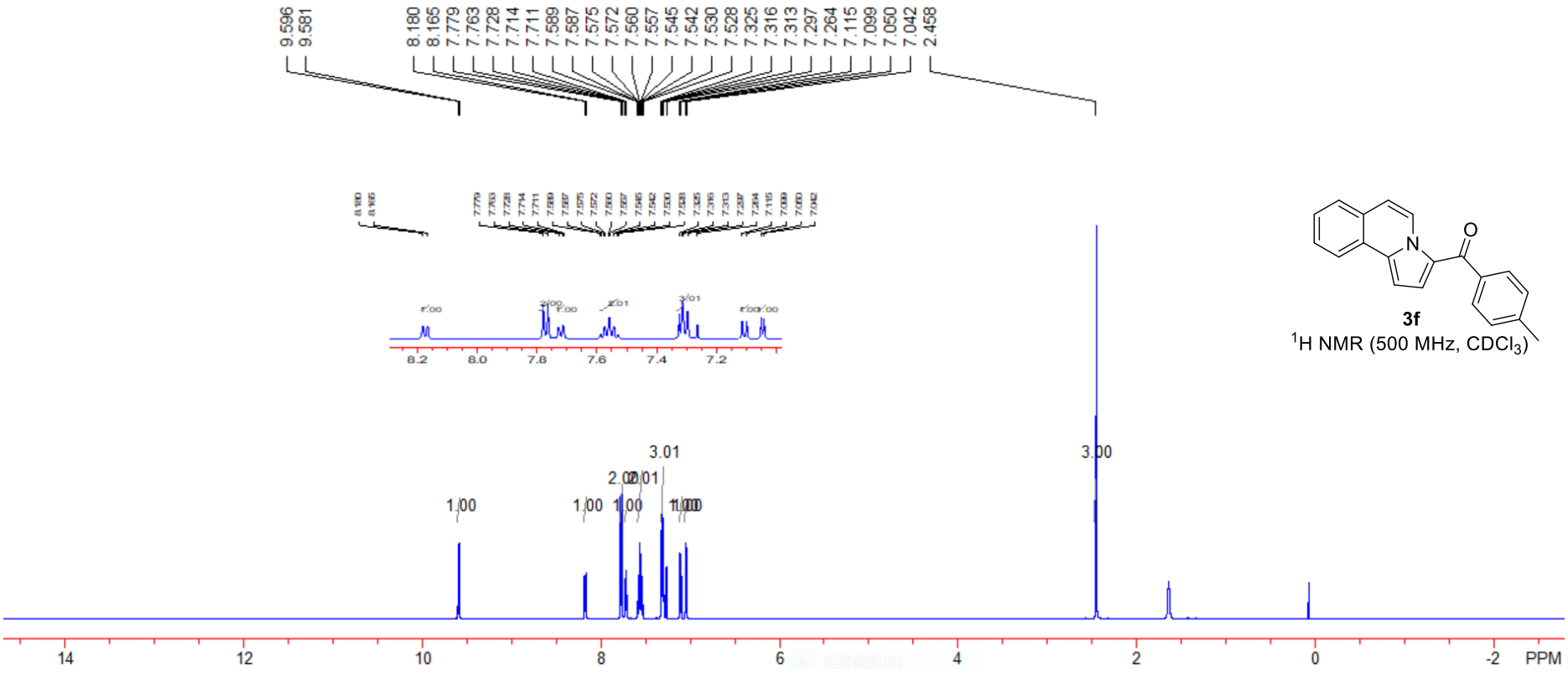
3e

^{1}H NMR (500 MHz, $CDCl_3$)



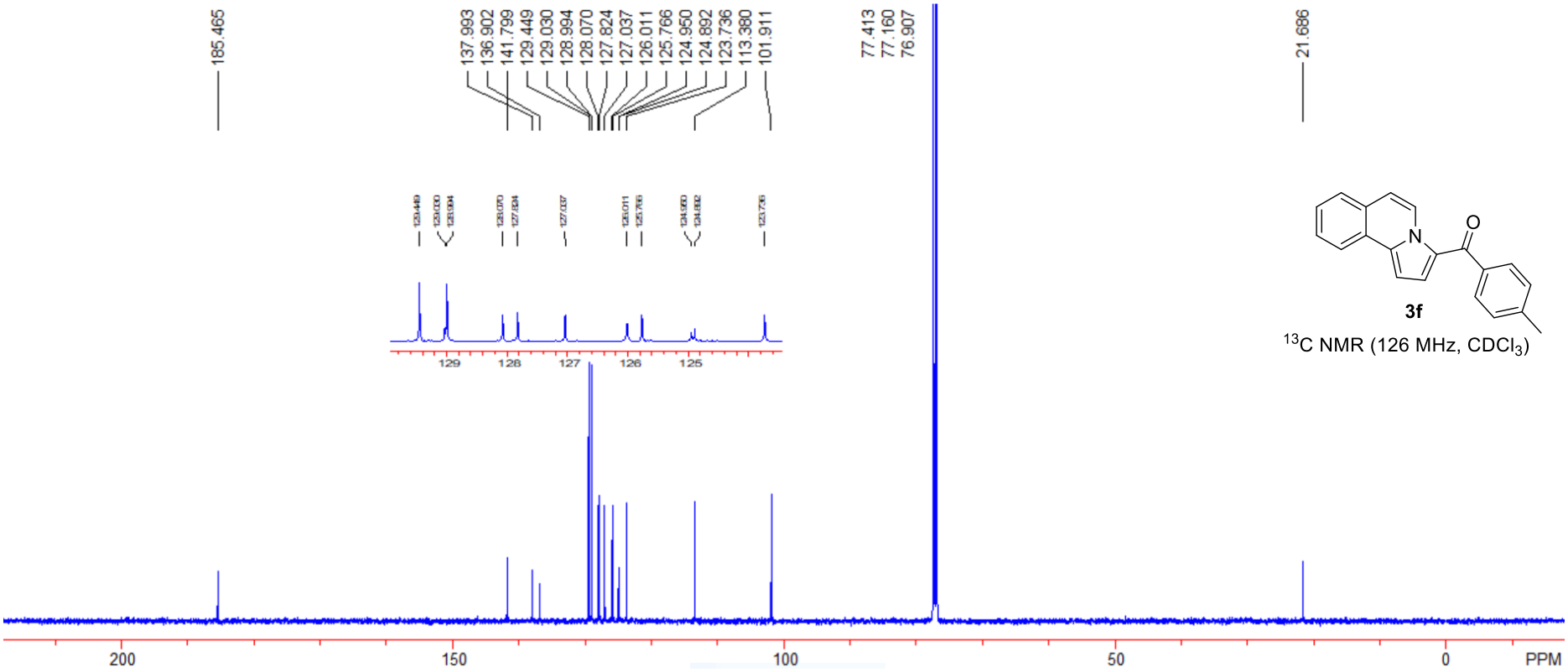
3e

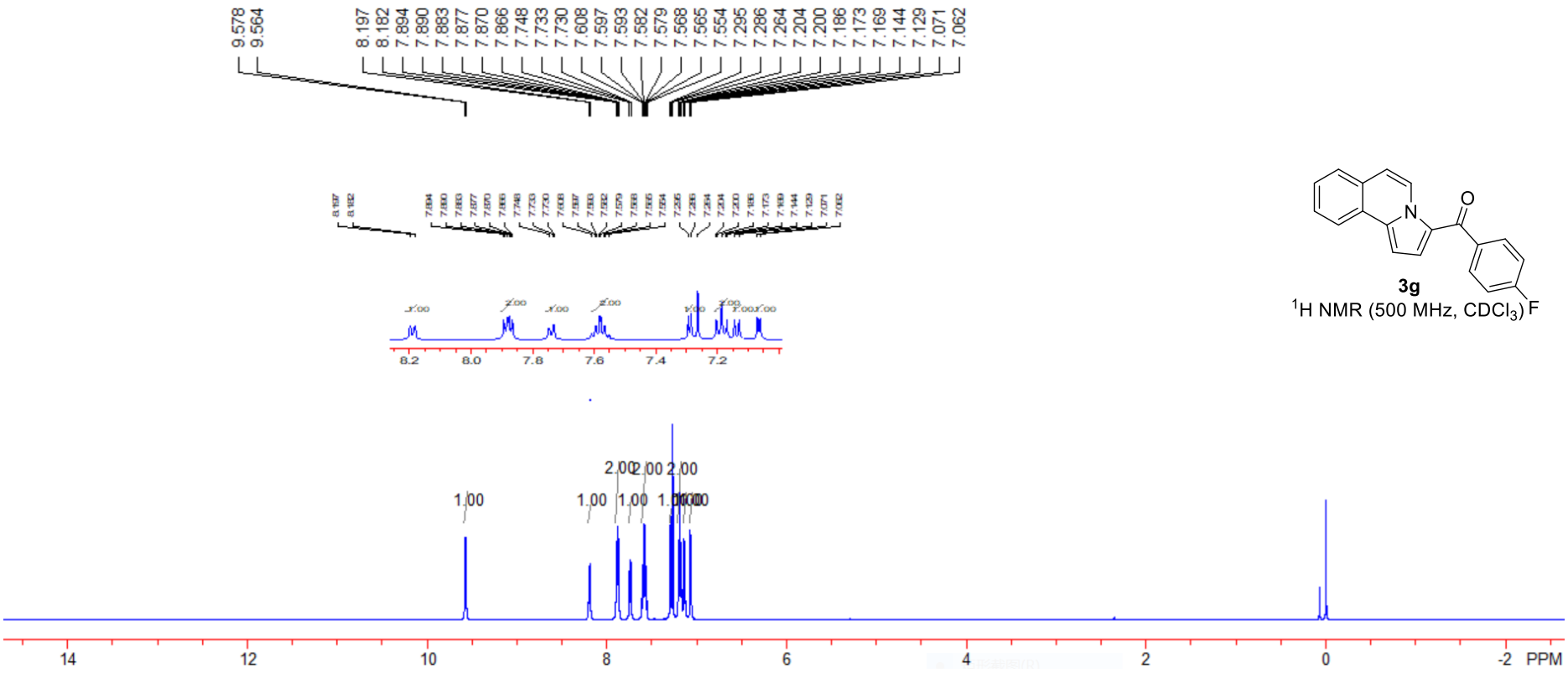
^{13}C NMR (126 MHz, $CDCl_3$)



3f

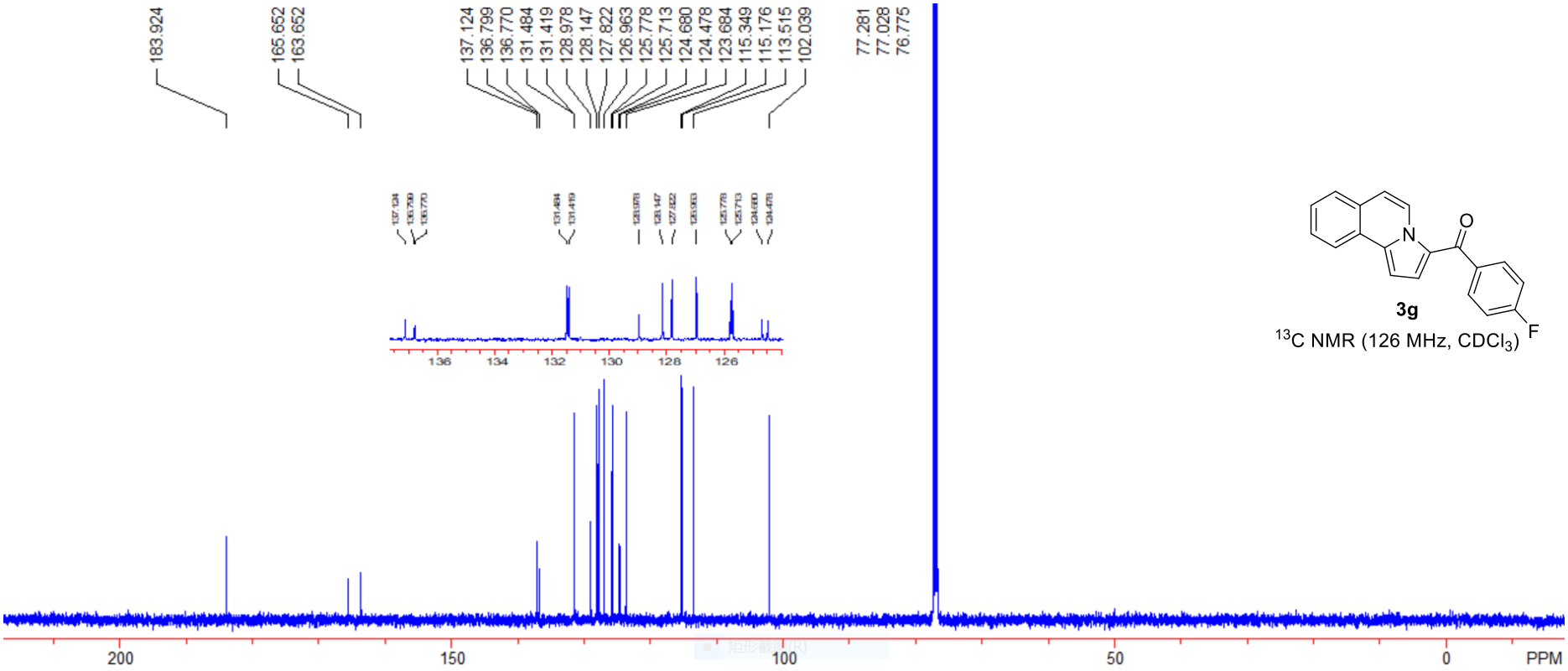
^{1}H NMR (500 MHz, $CDCl_3$)

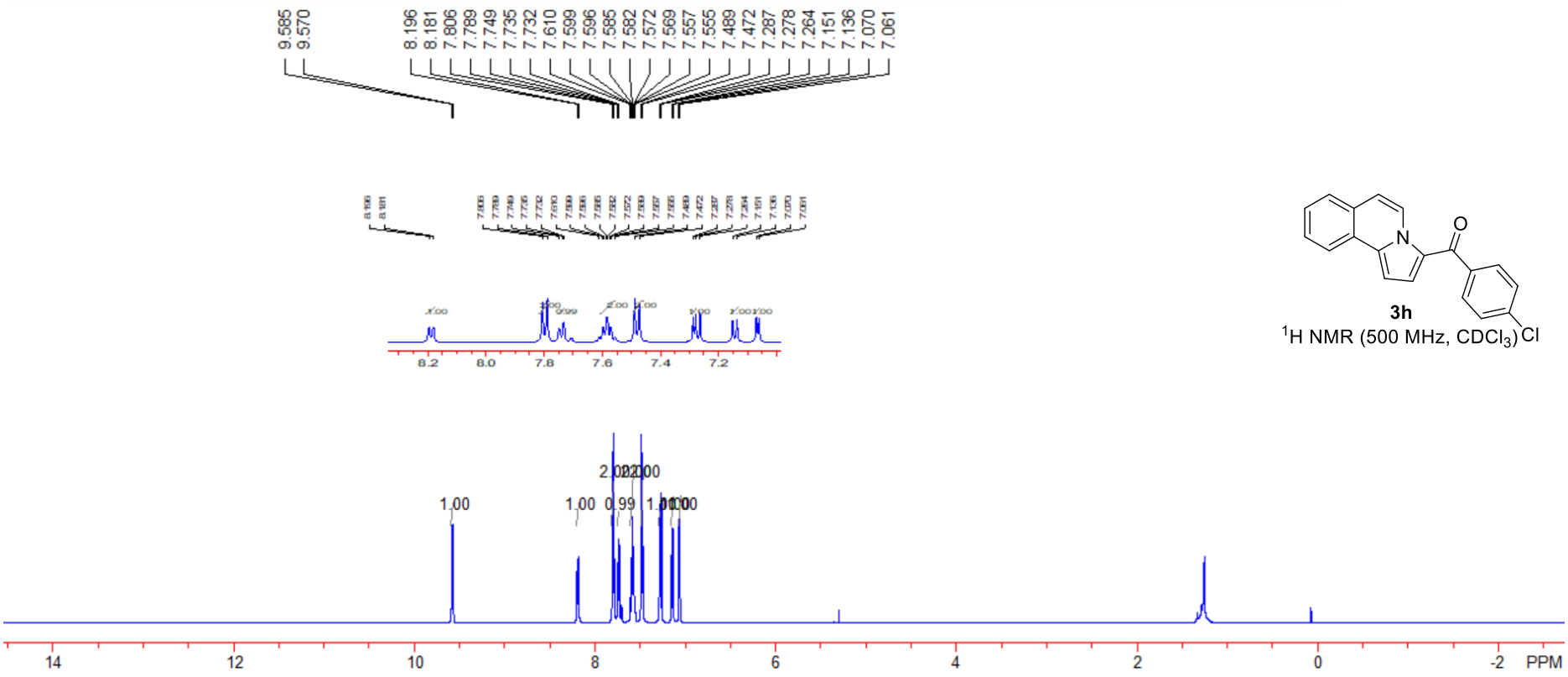

185.465
137.993
136.902
141.799
129.449
129.030
128.994
128.070
127.824
127.037
126.011
125.766
124.950
124.892
123.736
113.380
101.911
77.413
77.160
76.907
21.686
129
128
127
126
125
200
150
100
50
0
PPM
O
N
3f
^{13}C NMR (126 MHz, CDCl$_3$)



3g

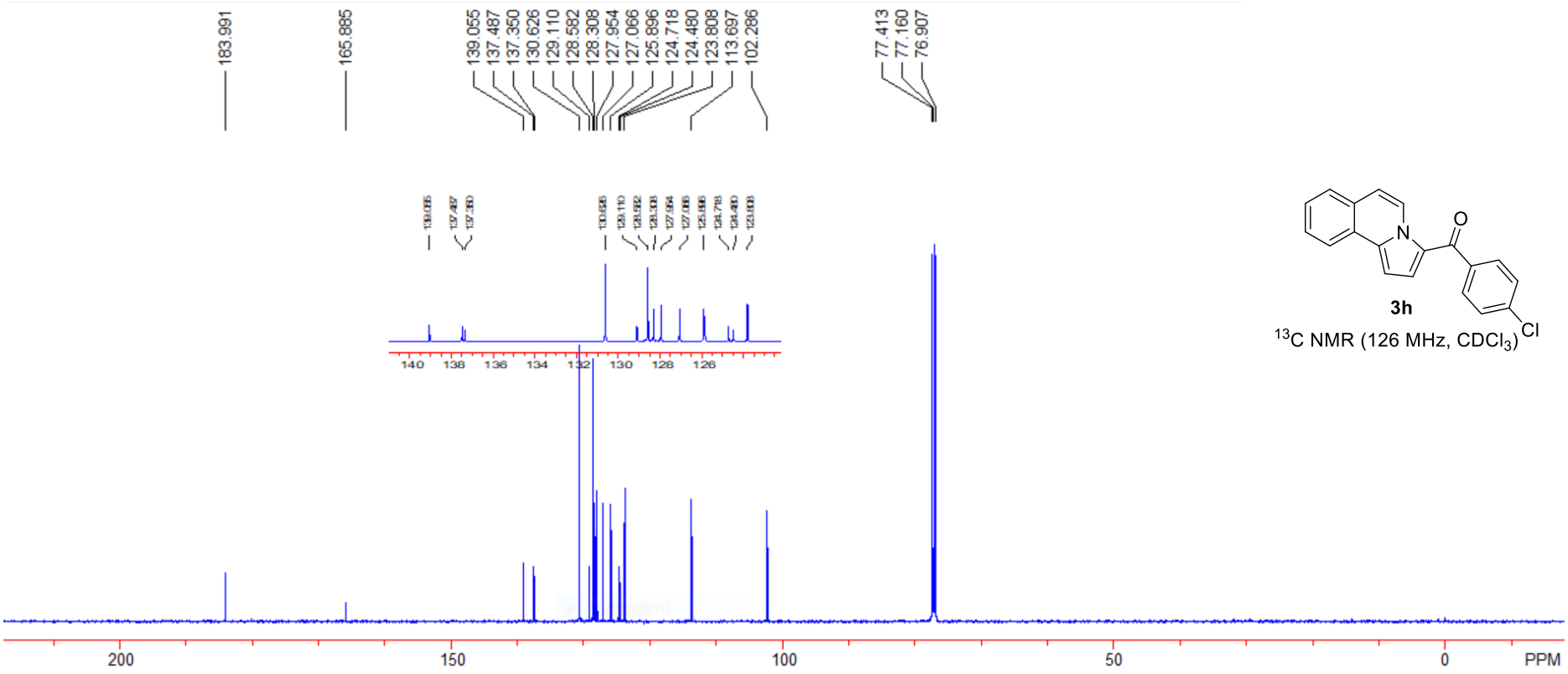
^{1}H NMR (500 MHz, $CDCl_3$)


183.924
165.652
163.652
137.124
136.799
136.770
131.484
131.419
128.978
128.147
127.822
126.963
125.778
125.713
124.680
124.478
123.684
115.349
115.176
113.515
102.039
77.281
77.028
76.775
136
134
132
130
128
126
200
150
100
50
0
PPM
O
N
F
3g
^{13}C NMR (126 MHz, CDCl$_3$)



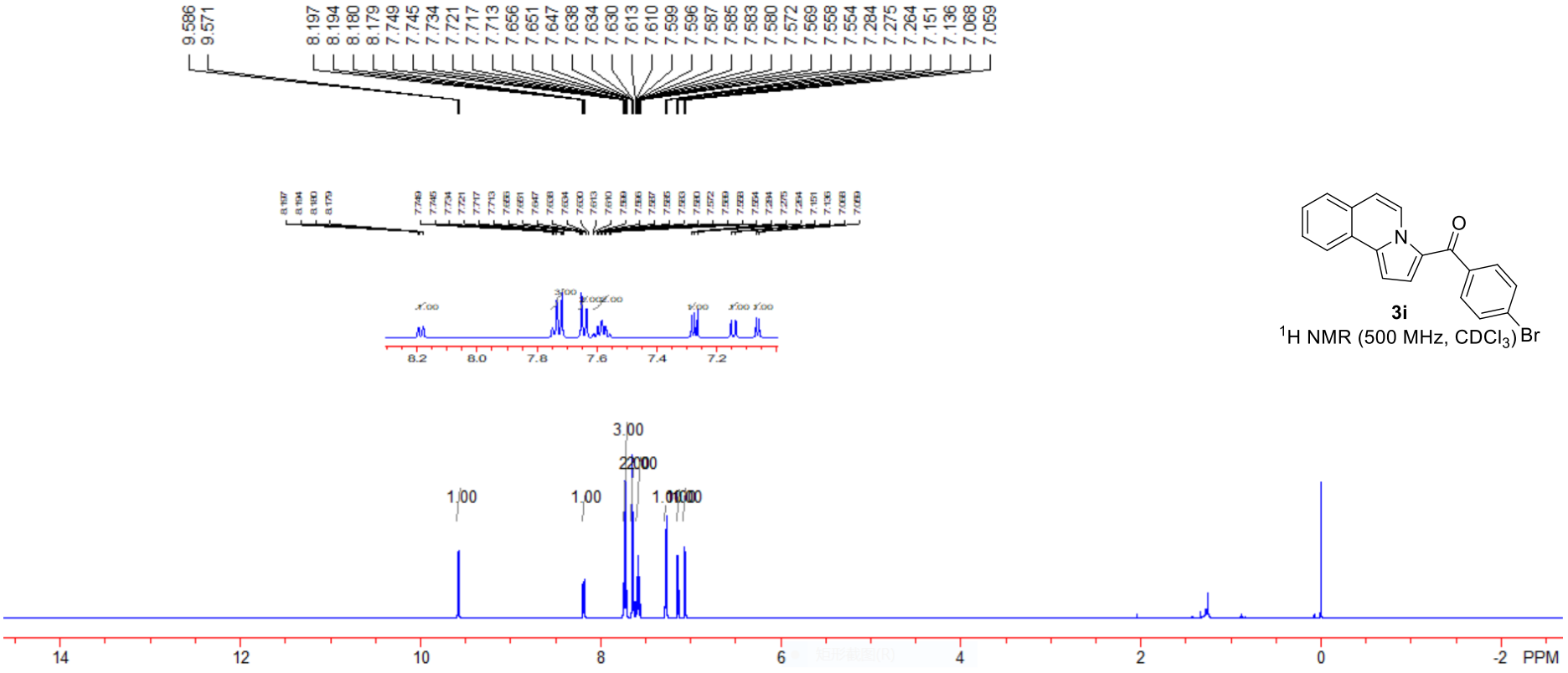
3h

^{1}H NMR (500 MHz, $CDCl_3$)



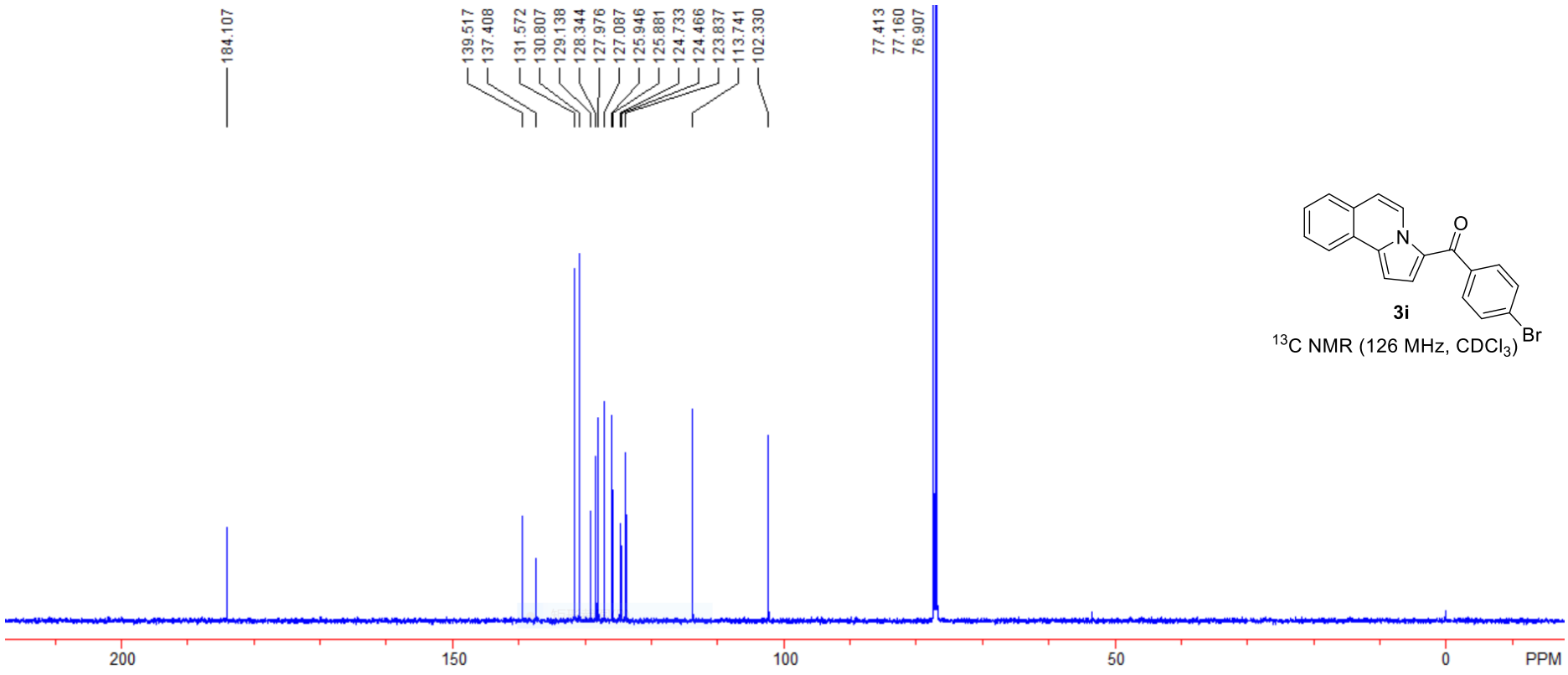
3h

^{13}C NMR (126 MHz, $CDCl_3$)



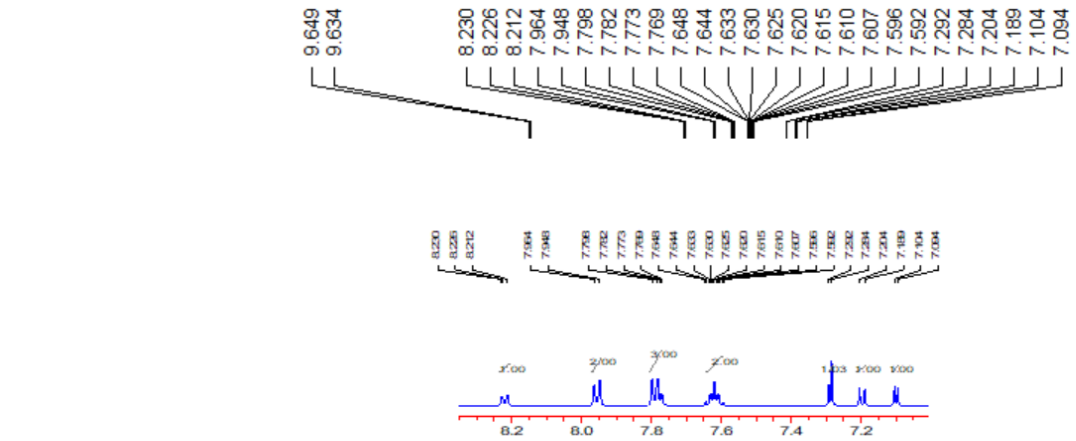
3i

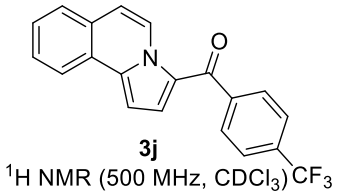
^{1}H NMR (500 MHz, $CDCl_3$)



3i

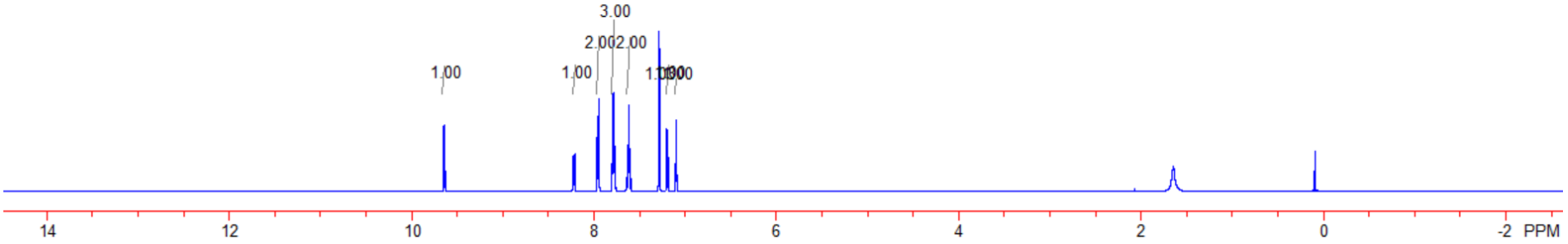
^{13}C NMR (126 MHz, $CDCl_3$)

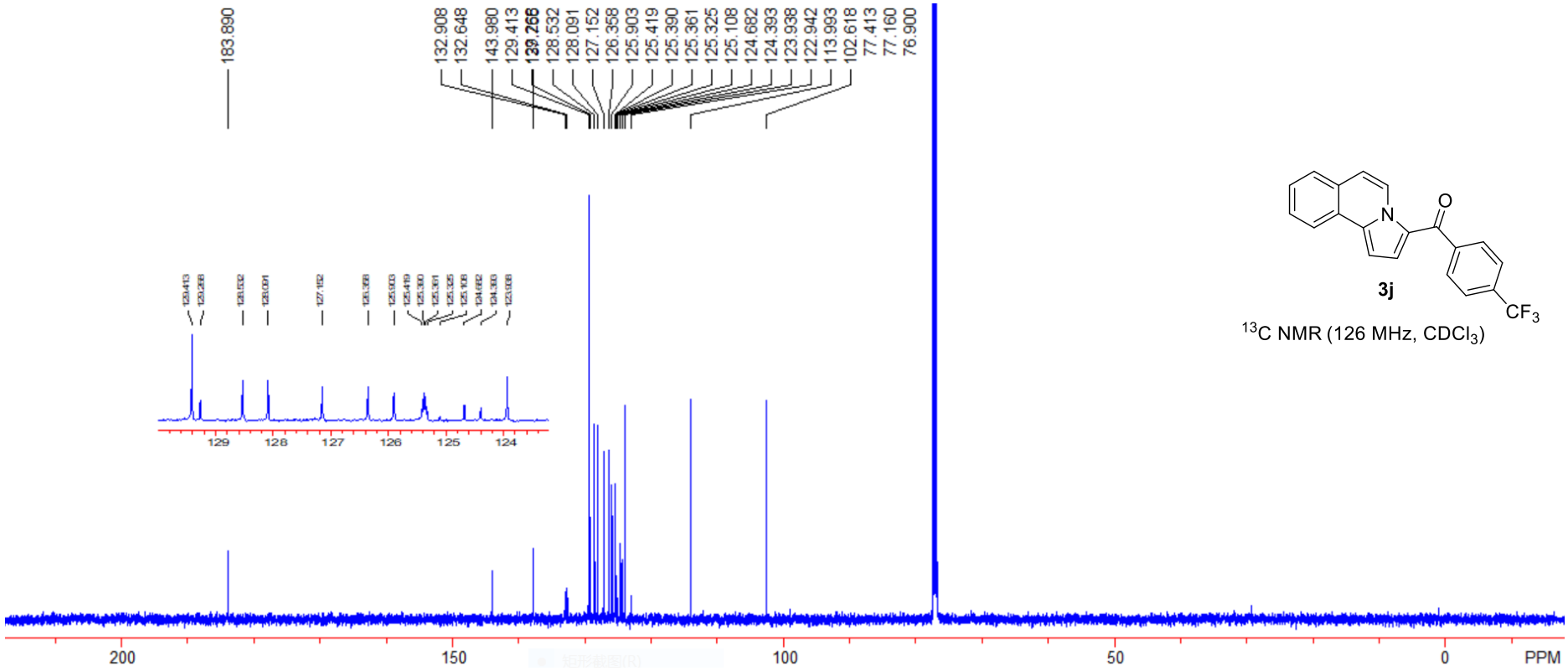


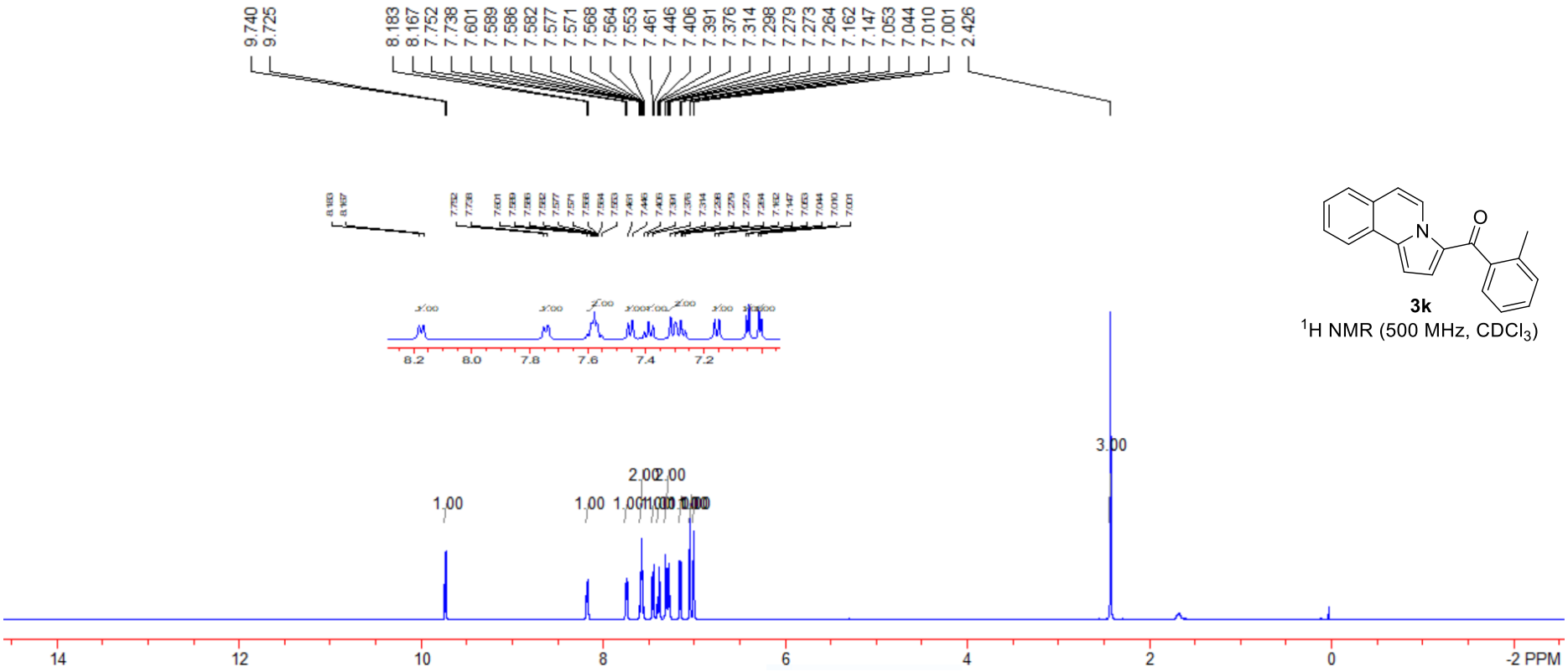


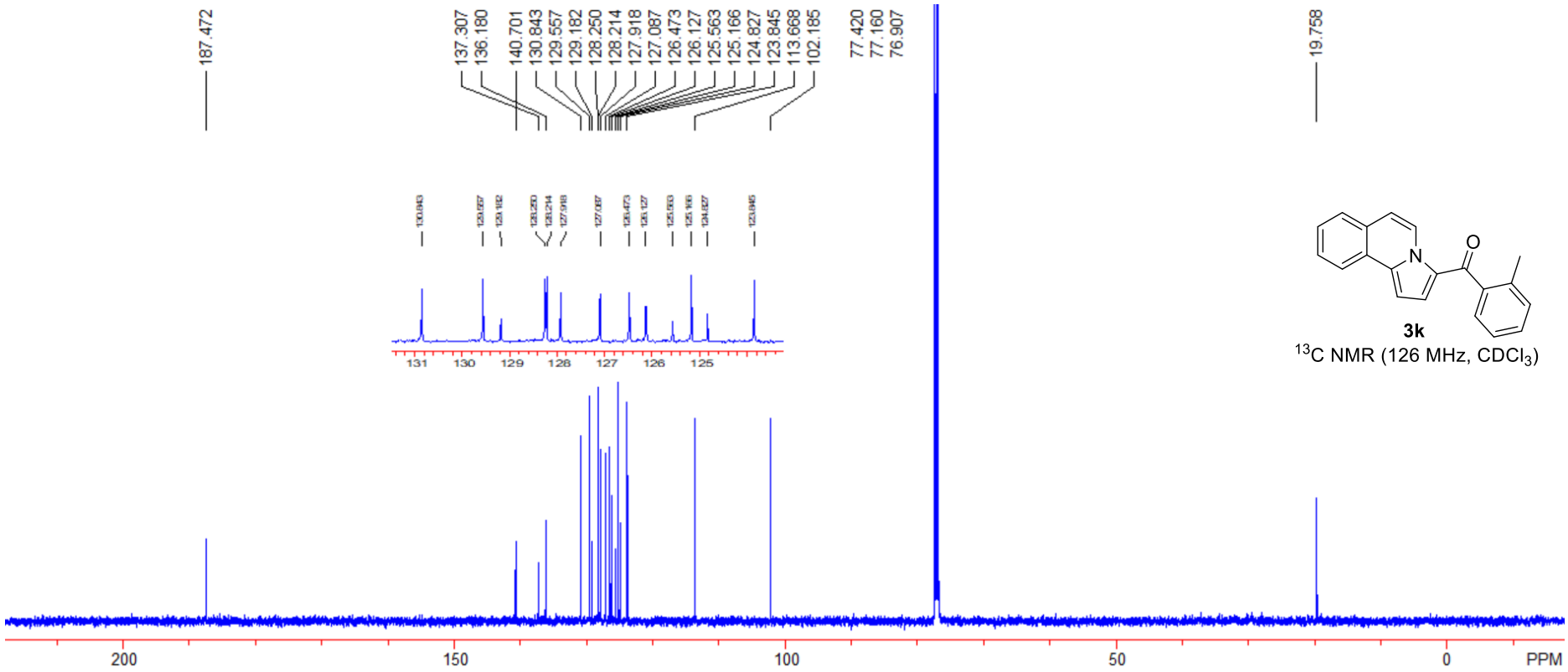
3j

^{1}H NMR (500 MHz, $CDCl_3$)



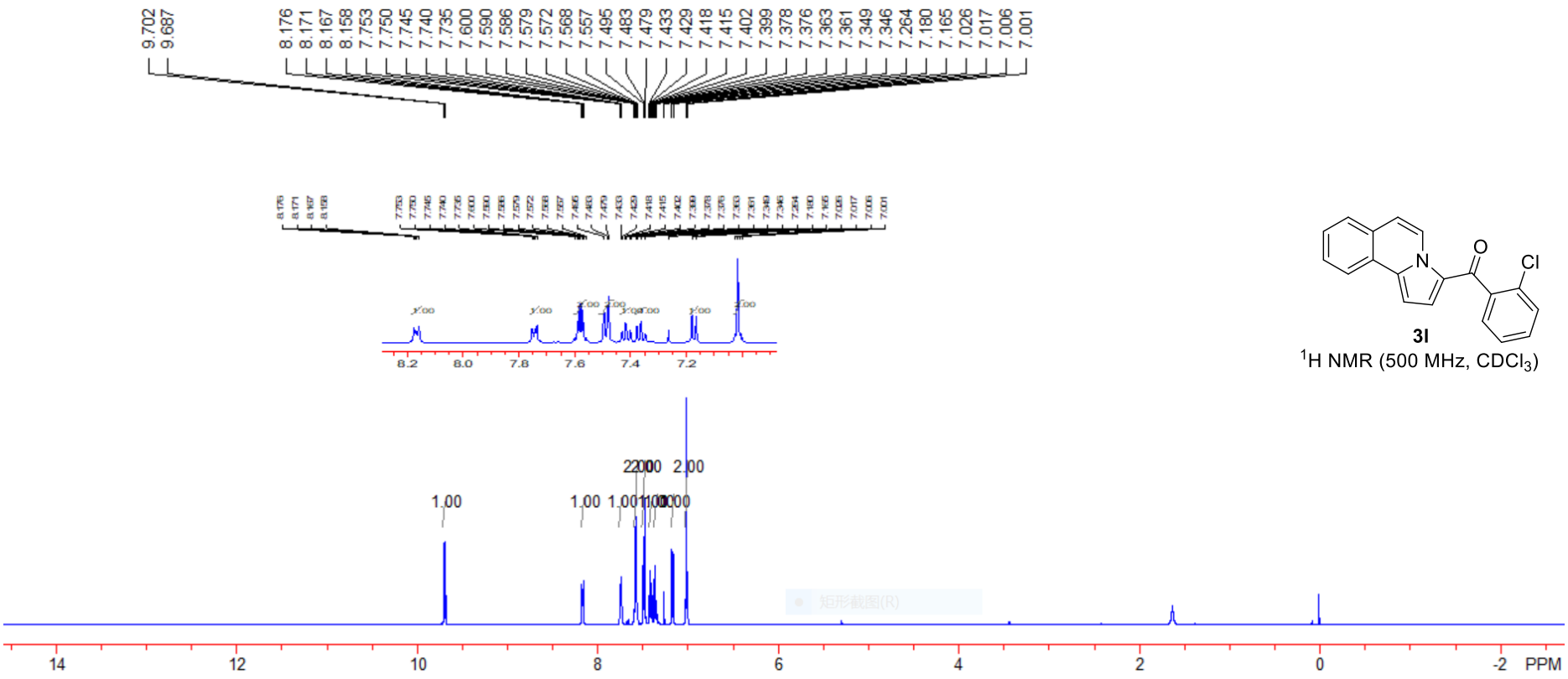

183.890
132.908
132.648
143.980
129.413
128.532
128.091
127.152
126.358
125.903
125.419
125.390
125.361
125.325
125.108
124.682
124.393
123.938
122.942
113.993
102.618
77.413
77.160
76.900
O
N
CF3
3j
13C NMR (126 MHz, CDCl3)
200
150
100
50
0
PPM
129
128
127
126
125
124


9.740
9.725
8.183
8.167
7.752
7.738
7.601
7.589
7.586
7.582
7.577
7.571
7.568
7.564
7.553
7.461
7.446
7.406
7.391
7.376
7.314
7.298
7.279
7.273
7.264
7.162
7.147
7.053
7.044
7.010
7.001
2.426
N
O
3k
1H NMR (500 MHz, CDCl3)
1.00
1.00
2.00
2.00
3.00
14
12
10
8
6
4
2
0
-2 PPM



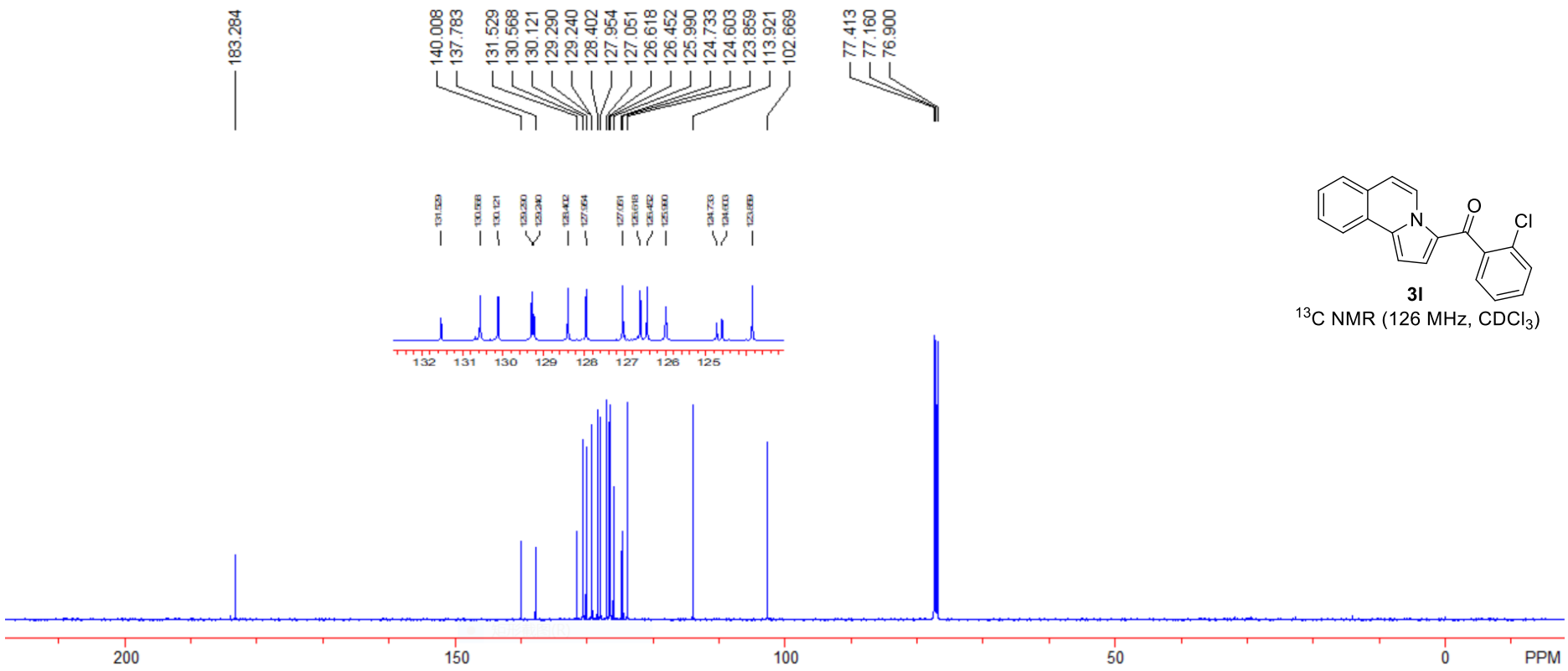
3k

^{13}C NMR (126 MHz, $CDCl_3$)



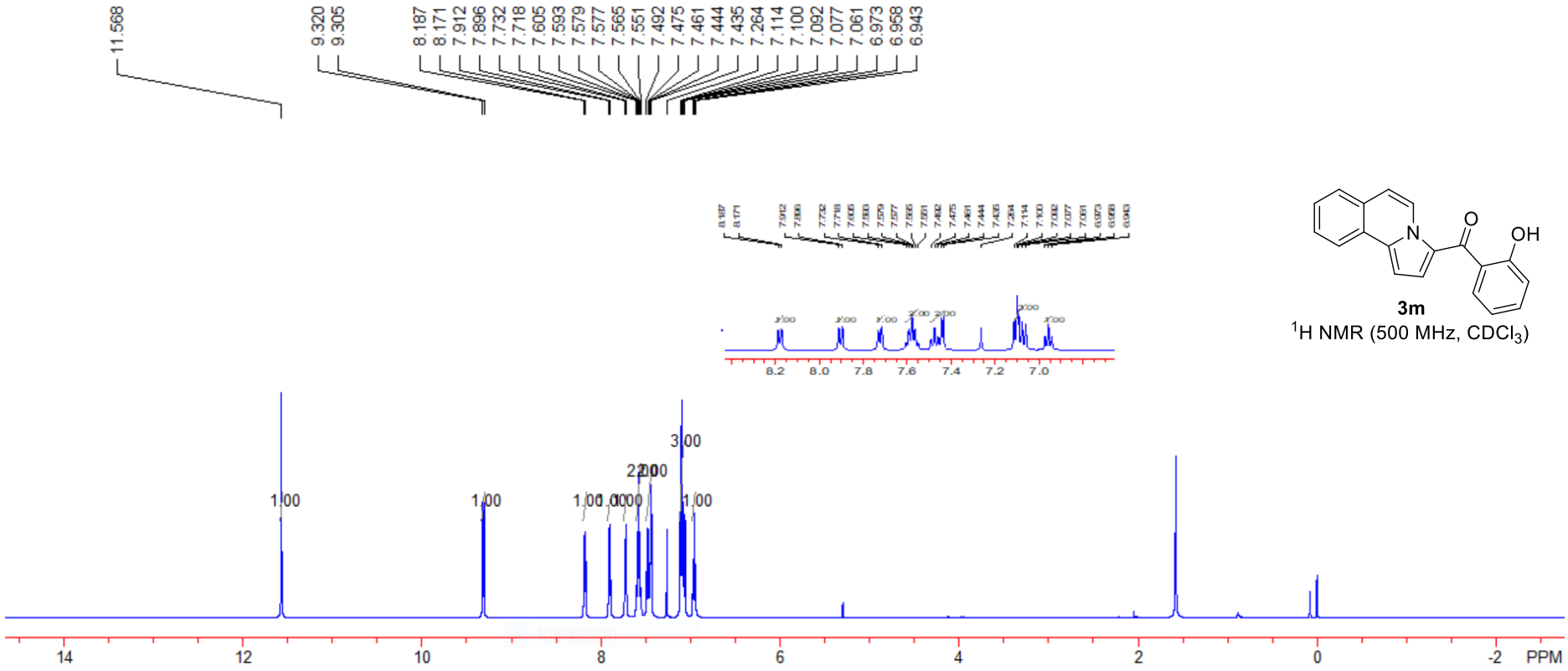
3l

^{1}H NMR (500 MHz, $CDCl_3$)



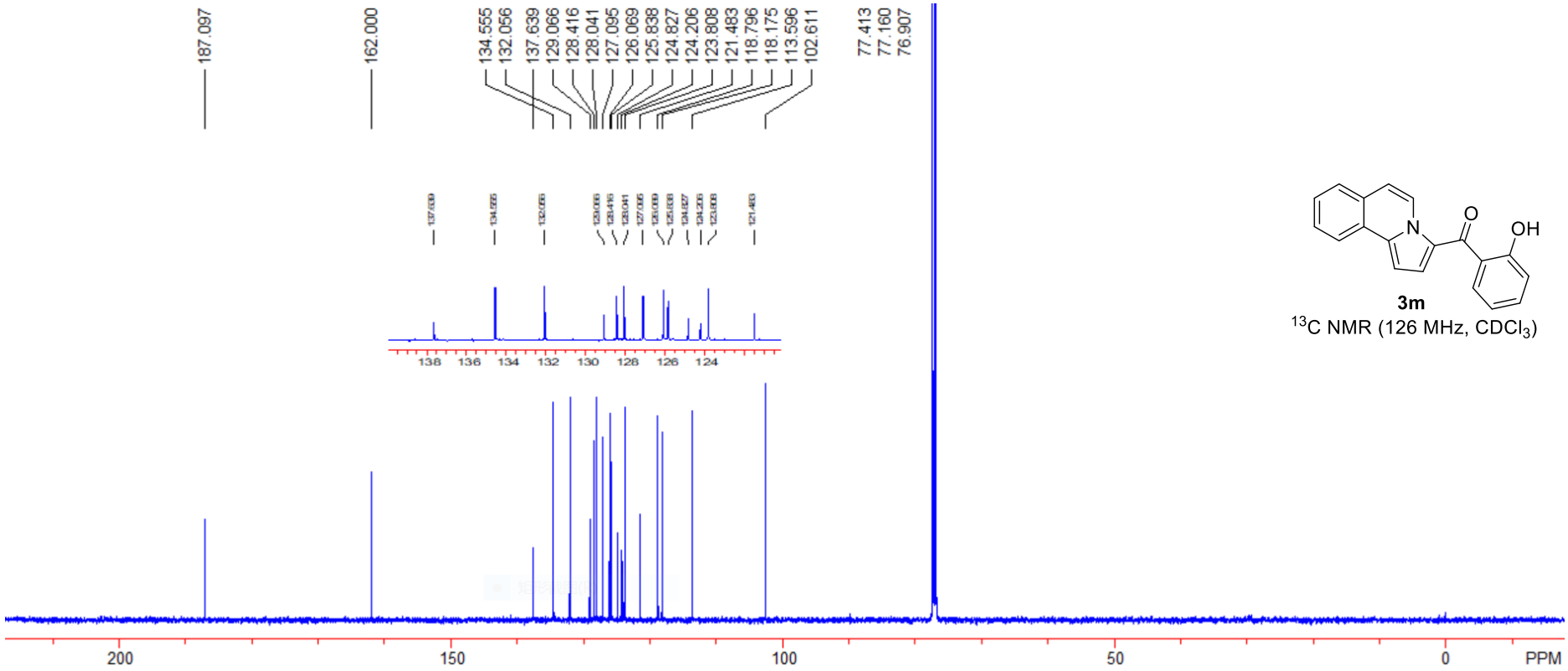
3l

^{13}C NMR (126 MHz, $CDCl_3$)



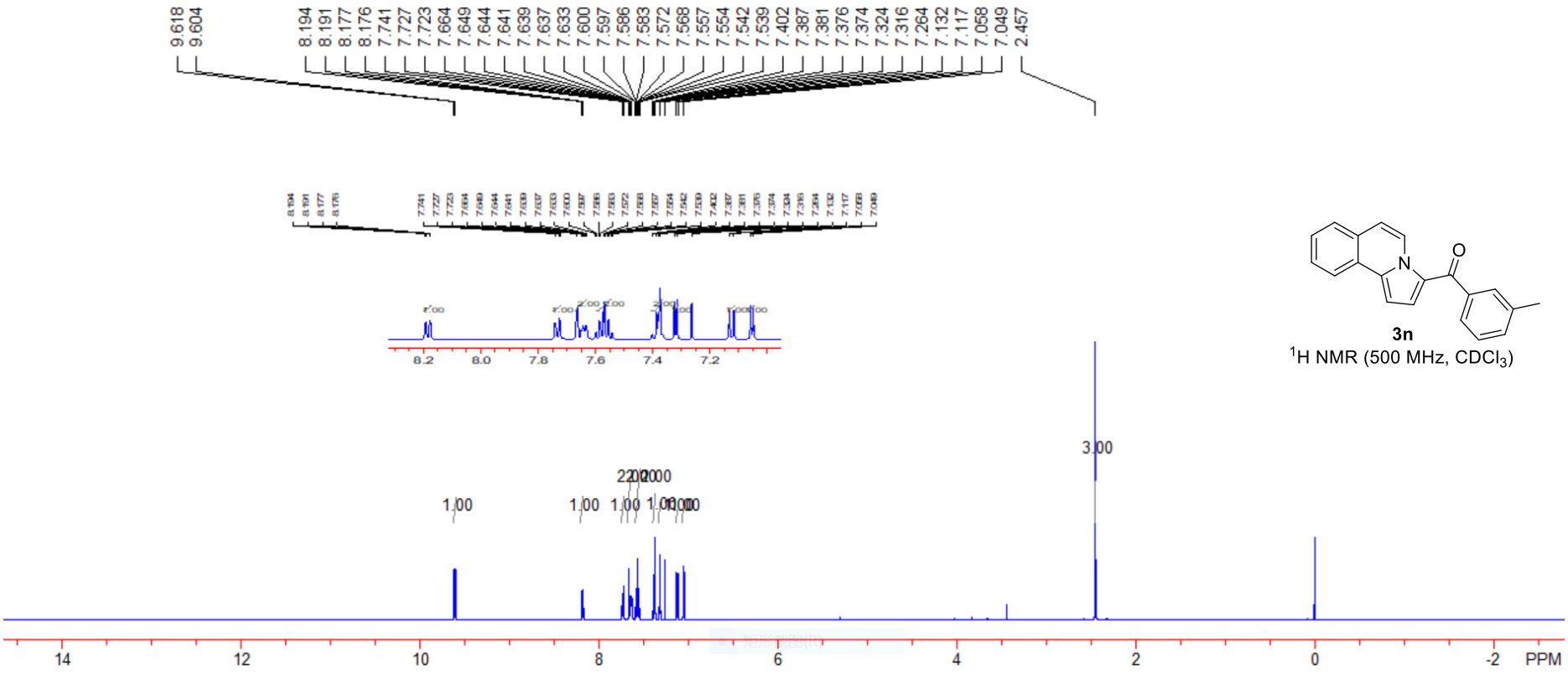
3m

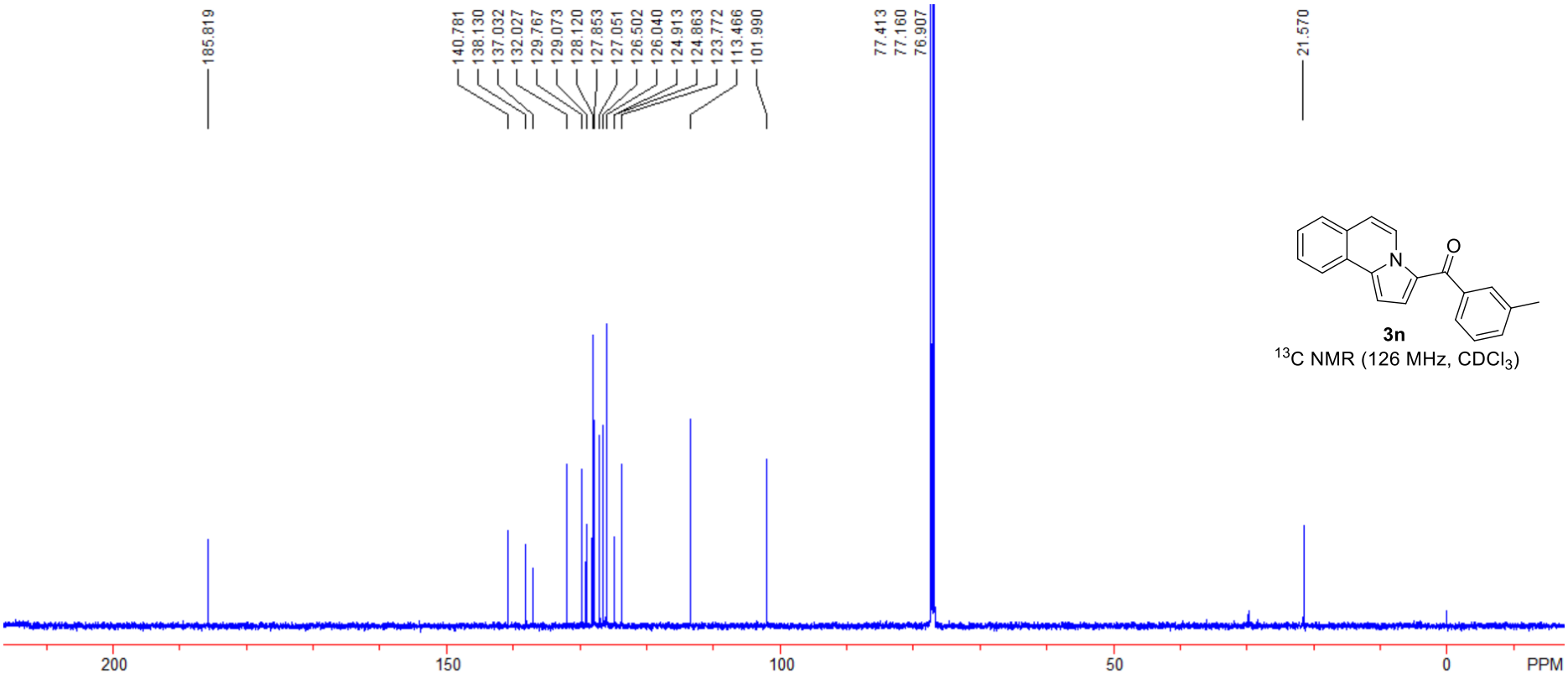
^{1}H NMR (500 MHz, $CDCl_3$)



3m

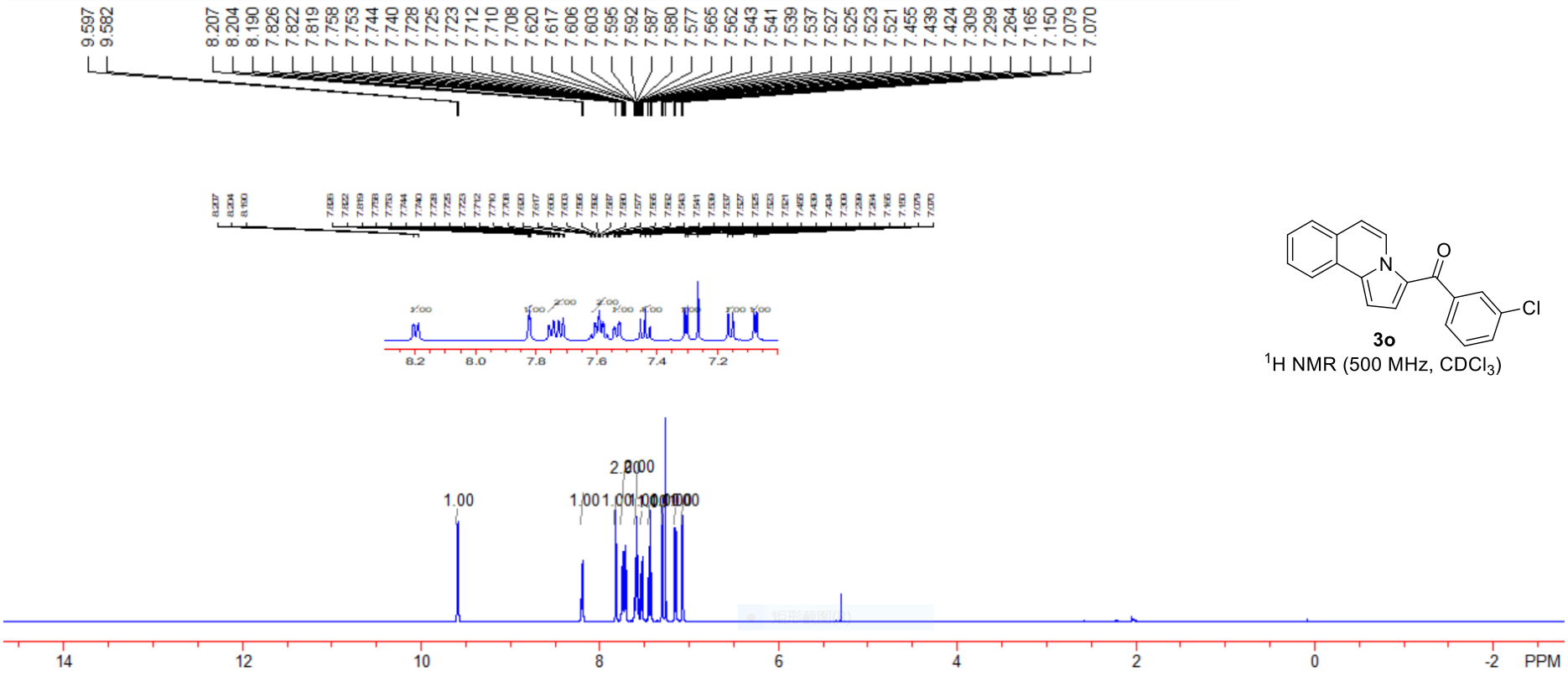
^{13}C NMR (126 MHz, $CDCl_3$)


9.618
9.604
8.194
8.191
8.177
8.176
7.741
7.727
7.723
7.664
7.649
7.644
7.641
7.639
7.637
7.633
7.600
7.597
7.586
7.583
7.572
7.568
7.557
7.554
7.542
7.539
7.402
7.387
7.381
7.376
7.374
7.324
7.316
7.264
7.132
7.117
7.058
7.049
2.457
O
N
3n
1H NMR (500 MHz, CDCl3)
3.00
1.00
1.00
1.00
1.00
14
12
10
8
6
4
2
0
-2
PPM



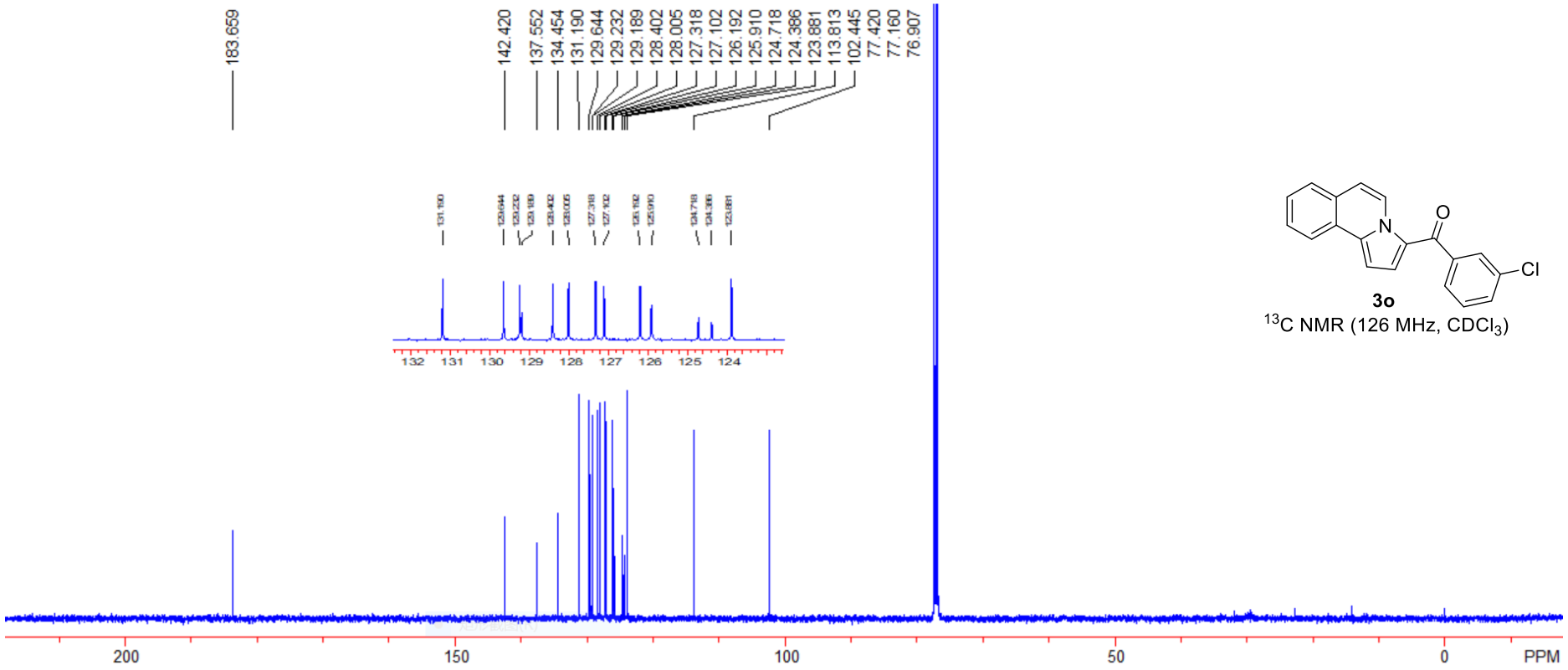
3n

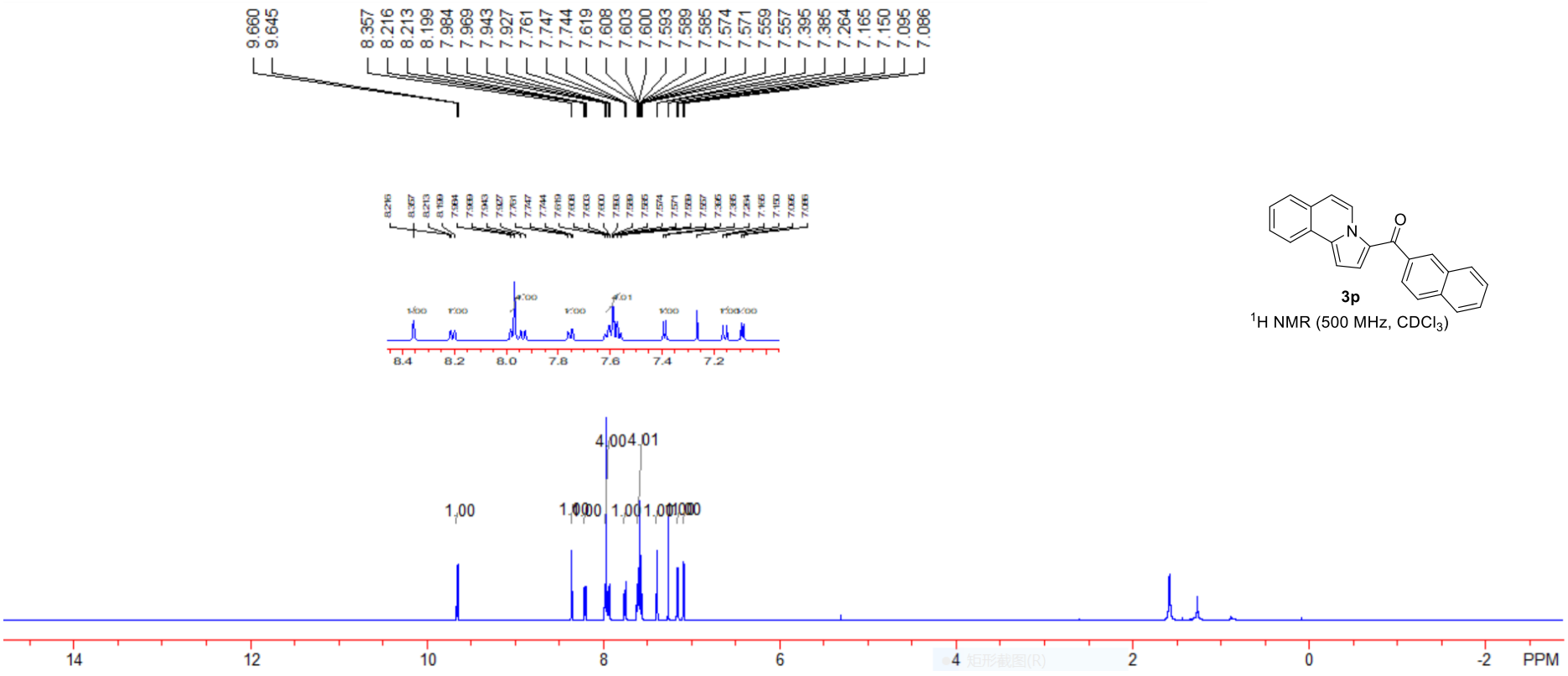
^{13}C NMR (126 MHz, $CDCl_3$)



3o

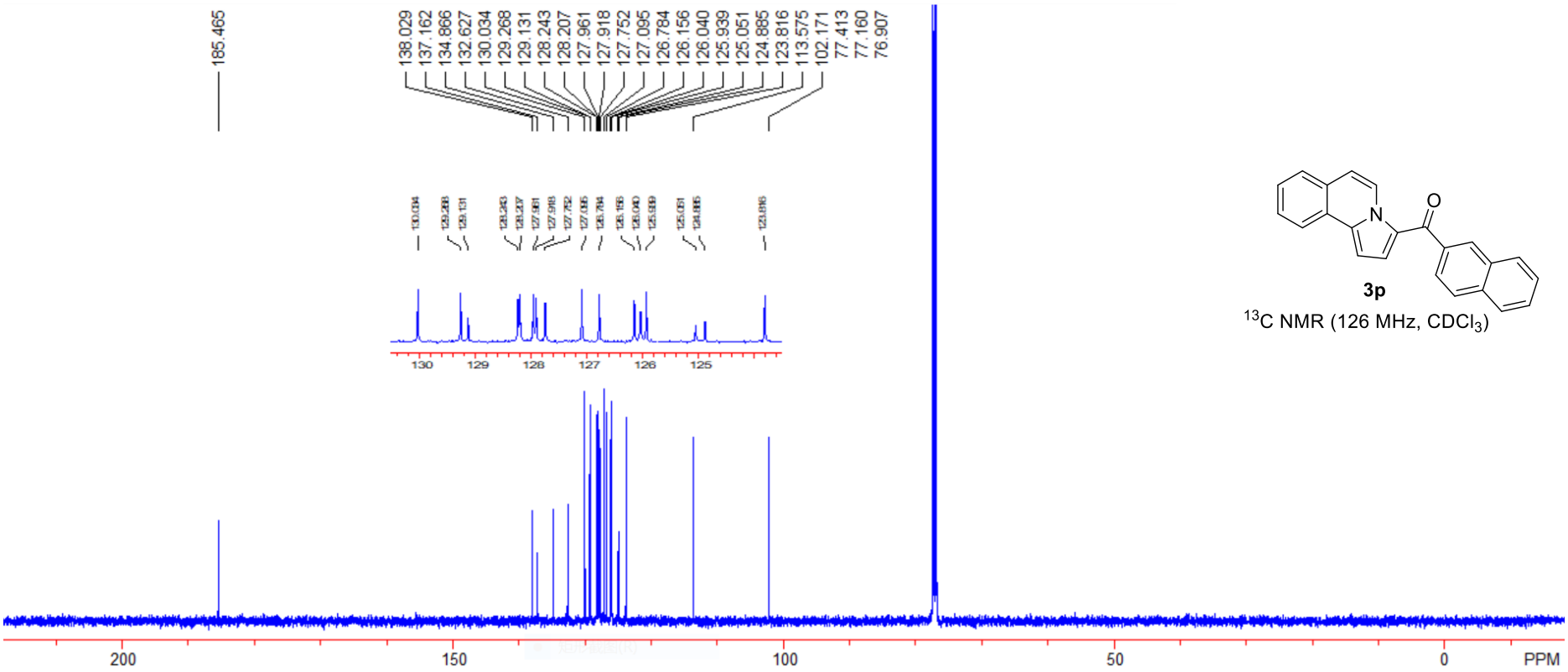
^{1}H NMR (500 MHz, $CDCl_3$)


183.659
142.420
137.552
134.454
131.190
129.644
129.232
129.189
128.402
128.005
127.318
127.102
126.192
125.910
124.718
124.386
123.881
113.813
102.445
77.420
77.160
76.907
O
N
Cl
3o
^{13}C NMR (126 MHz, CDCl$_3$)
132
131
130
129
128
127
126
125
124
200
150
100
50
0
PPM



3p

^{1}H NMR (500 MHz, $CDCl_3$)



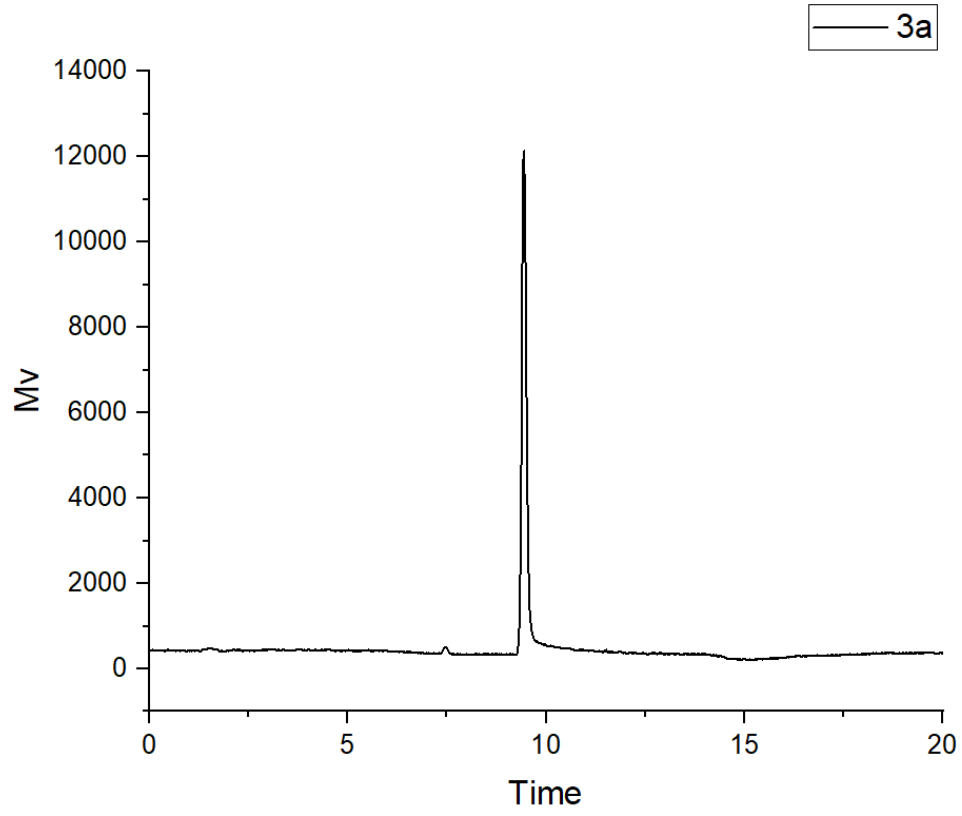
3p

^{13}C NMR (126 MHz, $CDCl_3$)

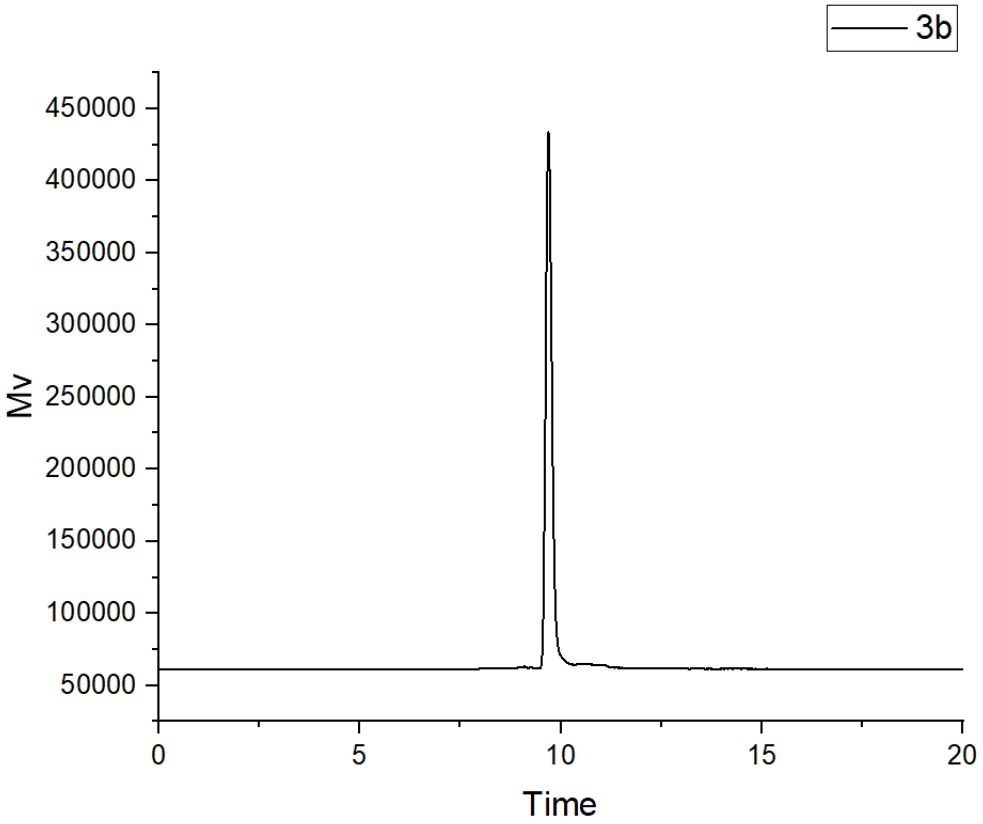
The purity of compounds **3a–3q** by HPLC.

Compounds	RT (min)	Area (%)
3a	9.058	98.84
3b	9.694	98.02
3c	8.676	99.89
3d	7.195	99.99
3e	9.083	98.81
3f	8.030	95.08
3g	9.509	99.99
3h	9.130	98.90
3i	8.508	99.99
3j	8.991	98.19
3k	7.709	99.85
3l	8.012	99.83
3m	8.491	98.51
3n	8.030	99.84
3o	9.175	99.38
3p	9.439	98.65

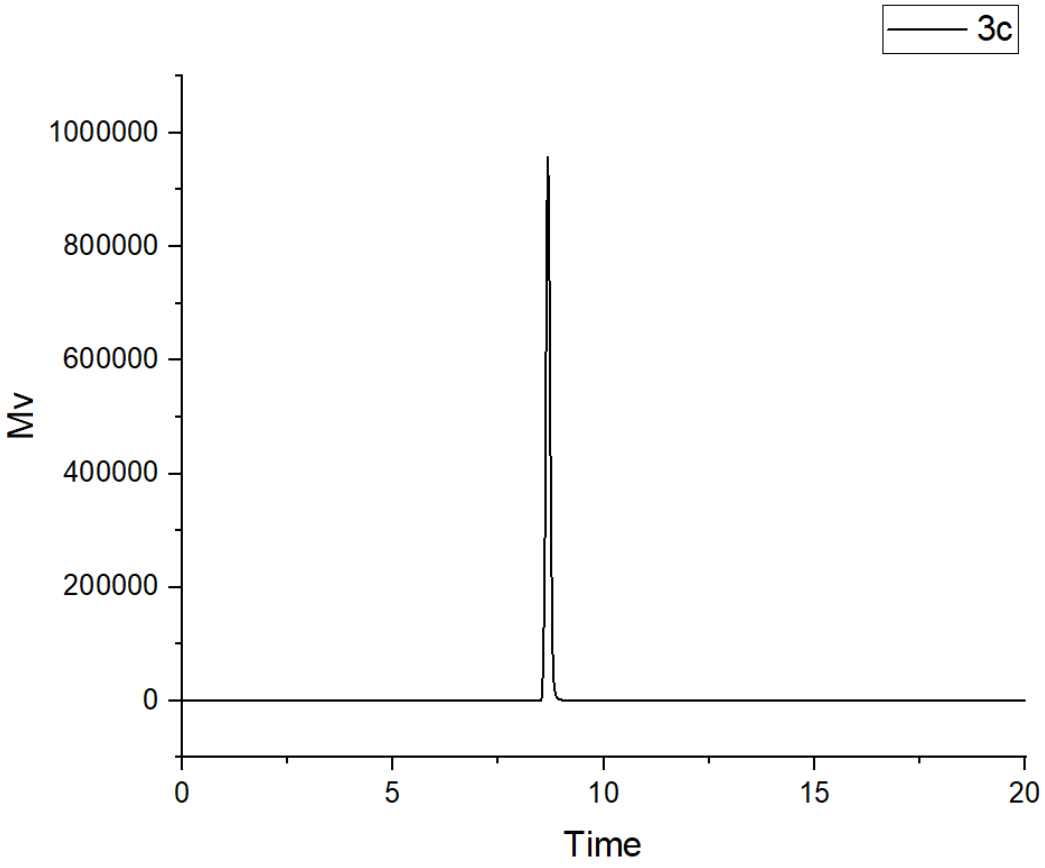
3a


3a
14000
12000
10000
8000
6000
4000
2000
0
Mv
0
5
10
15
20
Time

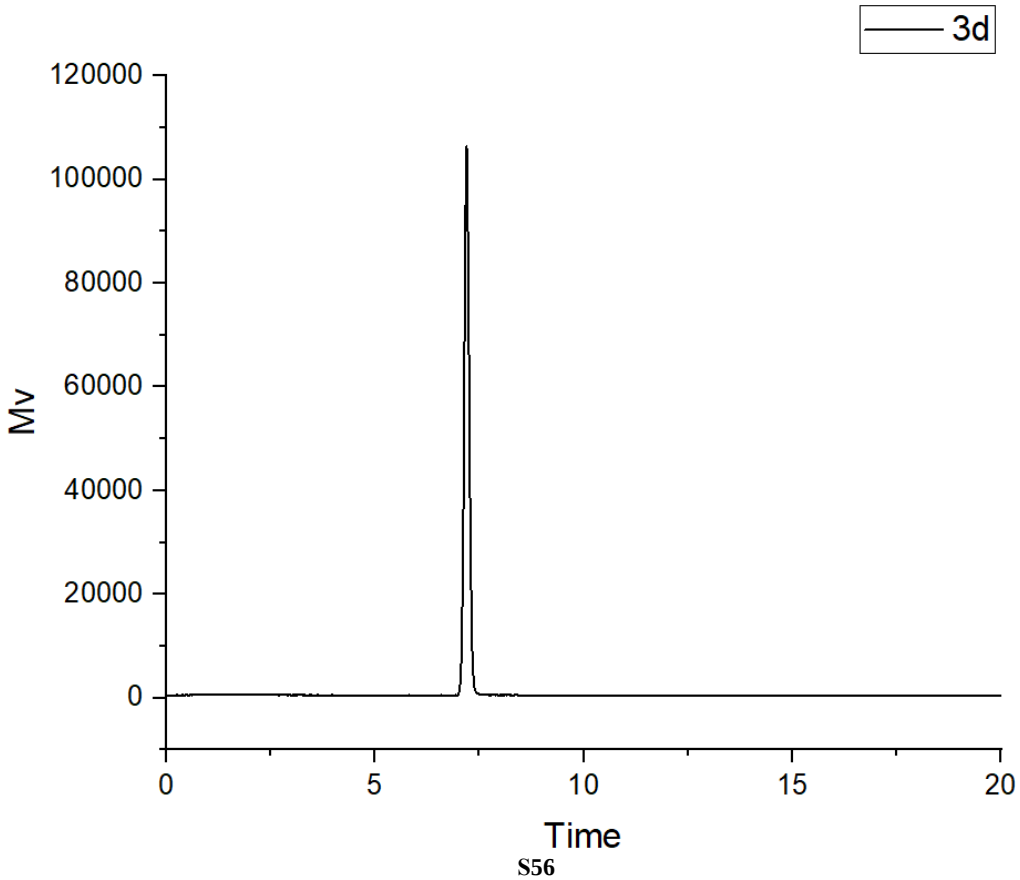
3b


3b
450000
400000
350000
300000
250000
200000
150000
100000
50000
Mv
0
5
10
15
20
Time

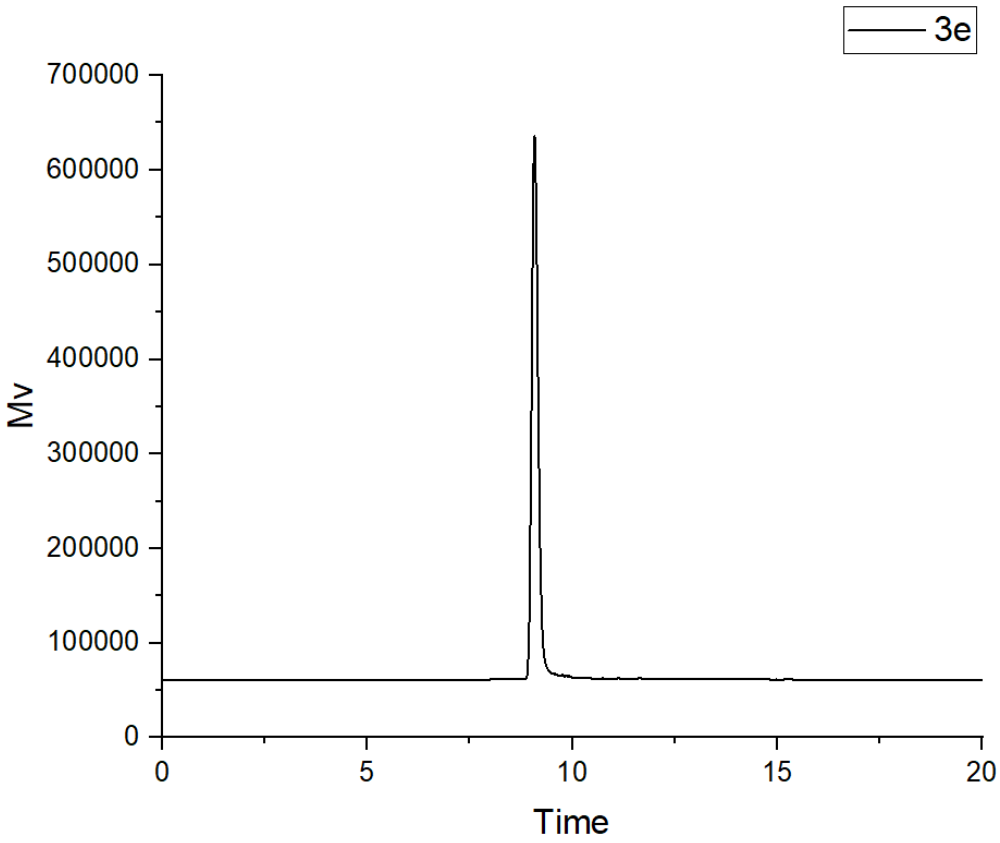
3c


3c
1000000
800000
600000
400000
200000
0
Mv
0
5
10
15
20
Time

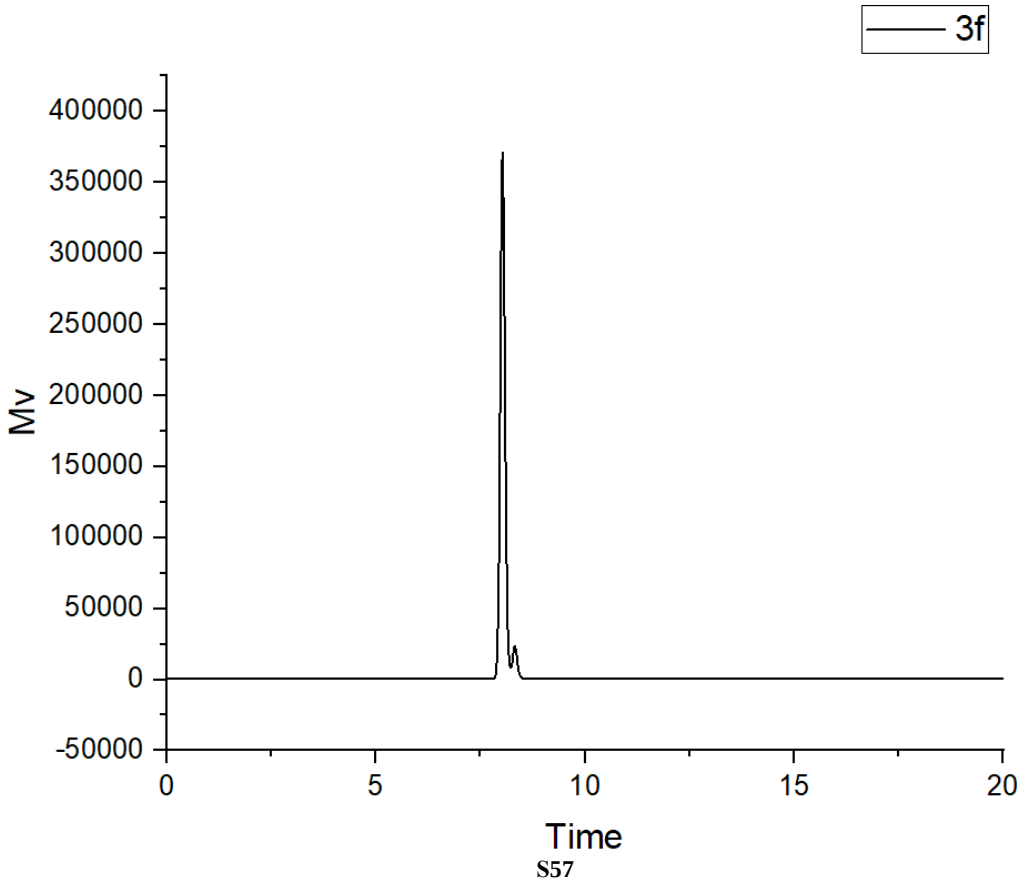
3d


3d
120000
100000
80000
60000
40000
20000
0
Mv
0
5
10
15
20
Time

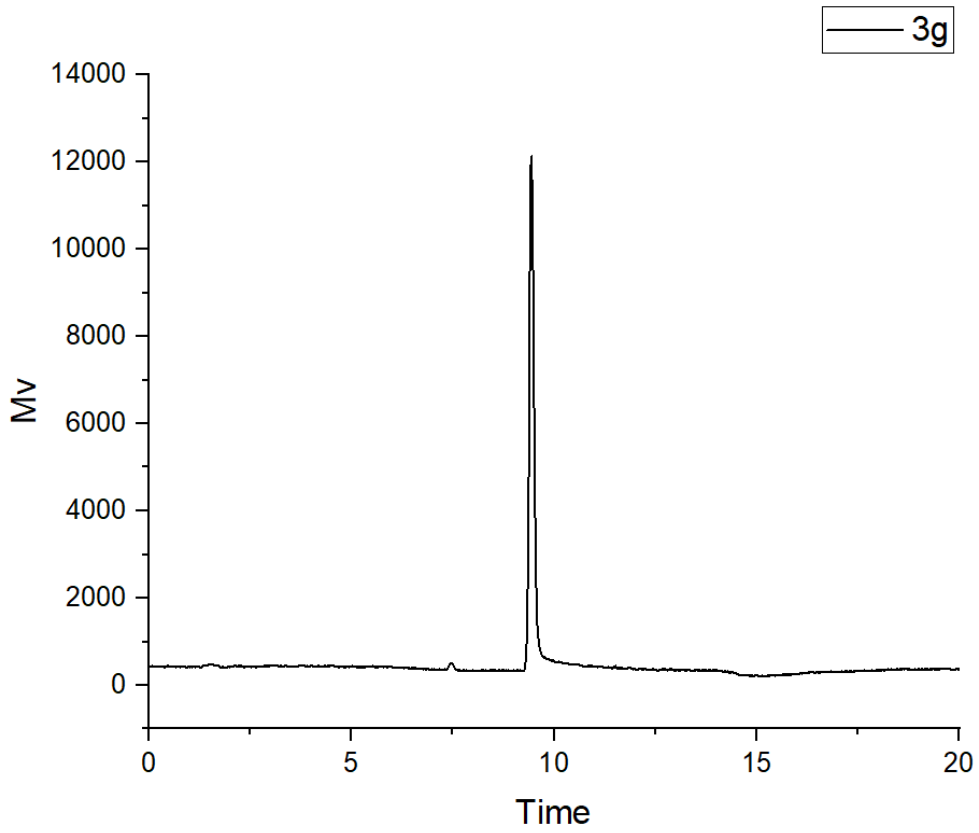
3e


3e
700000
600000
500000
400000
300000
200000
100000
0
Mv
0
5
10
15
20
Time

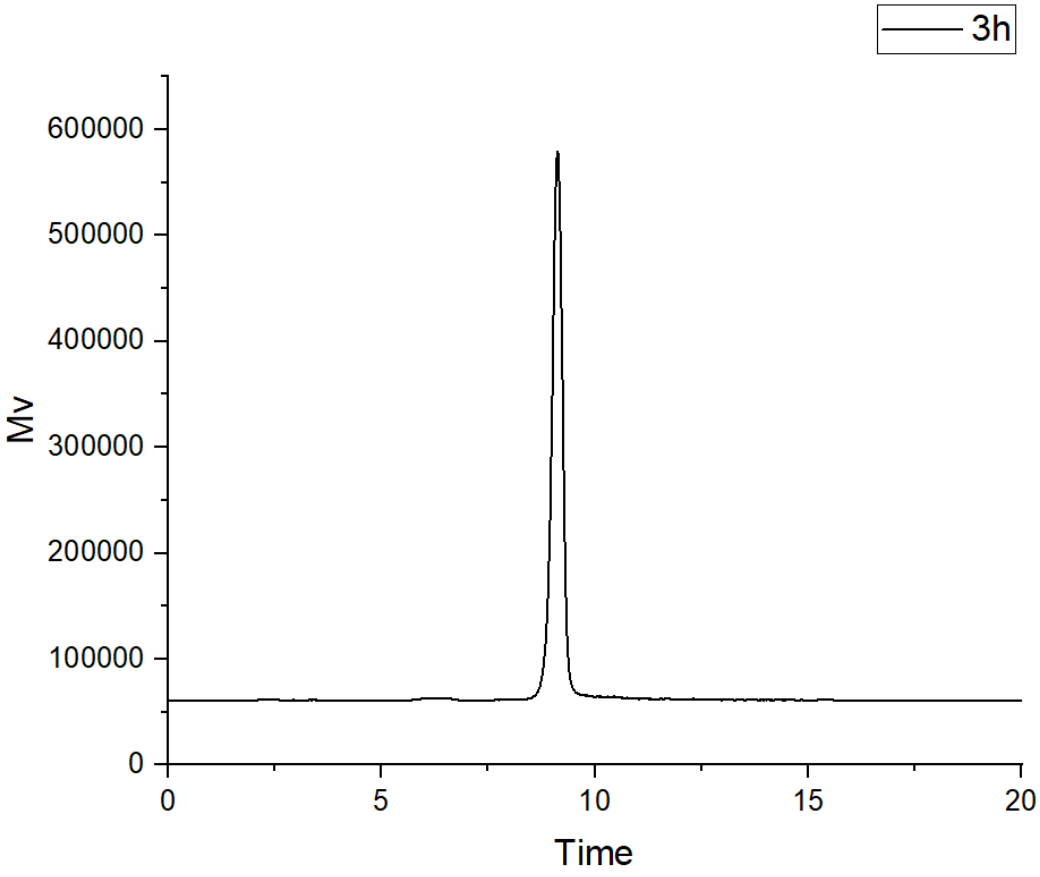
3f


3f
400000
350000
300000
250000
200000
150000
100000
50000
0
-50000
Mv
0
5
10
15
20
Time

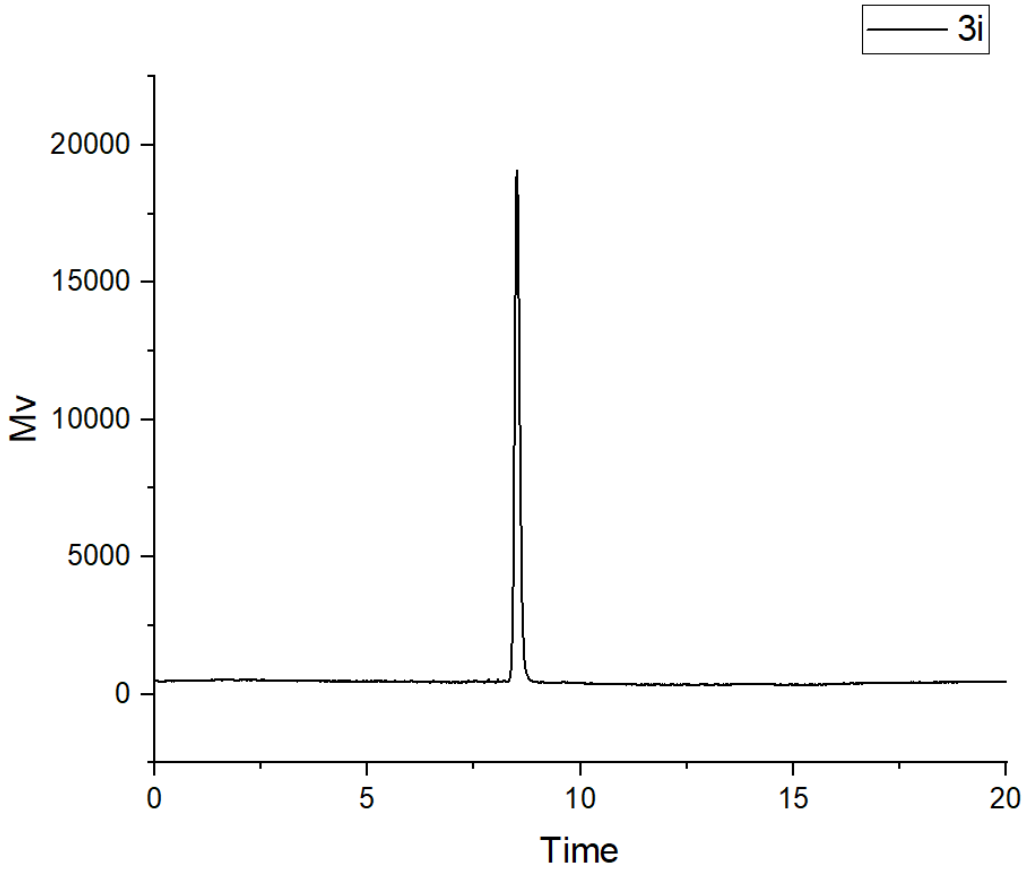
3g


3g
14000
12000
10000
8000
6000
4000
2000
0
Mv
0
5
10
15
20
Time

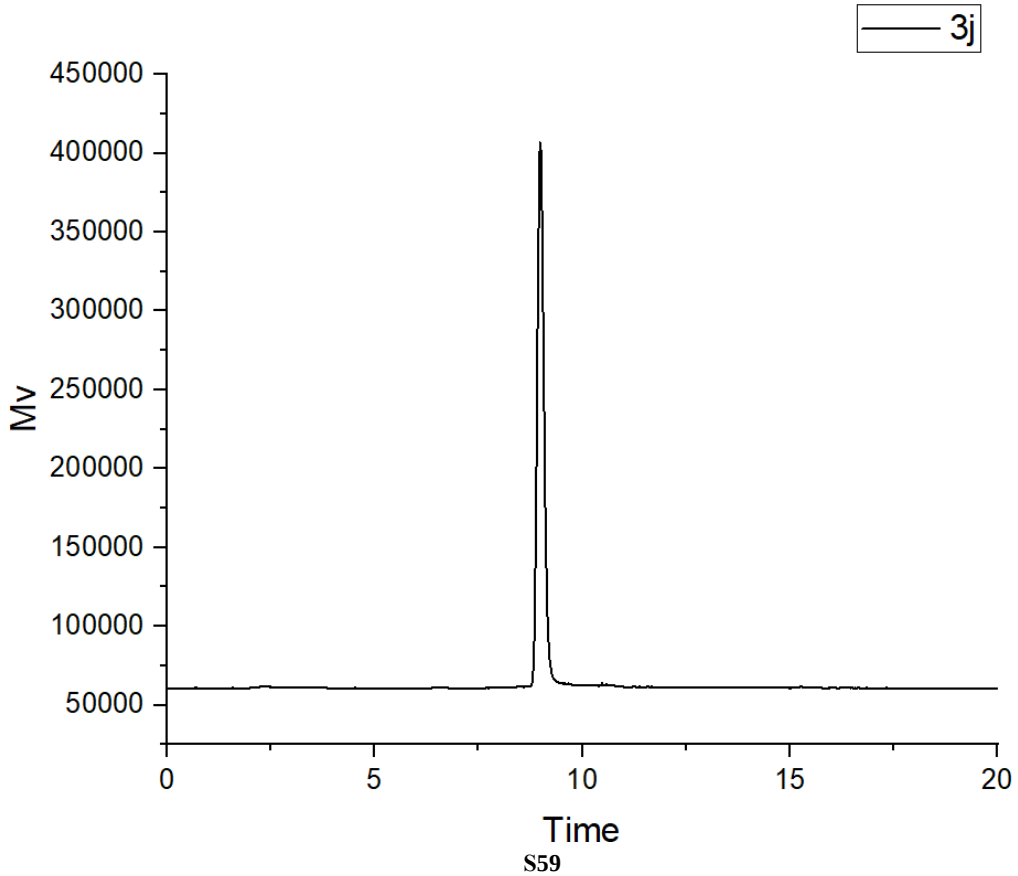
3h


3h
600000
500000
400000
300000
200000
100000
0
Mv
0
5
10
15
20
Time

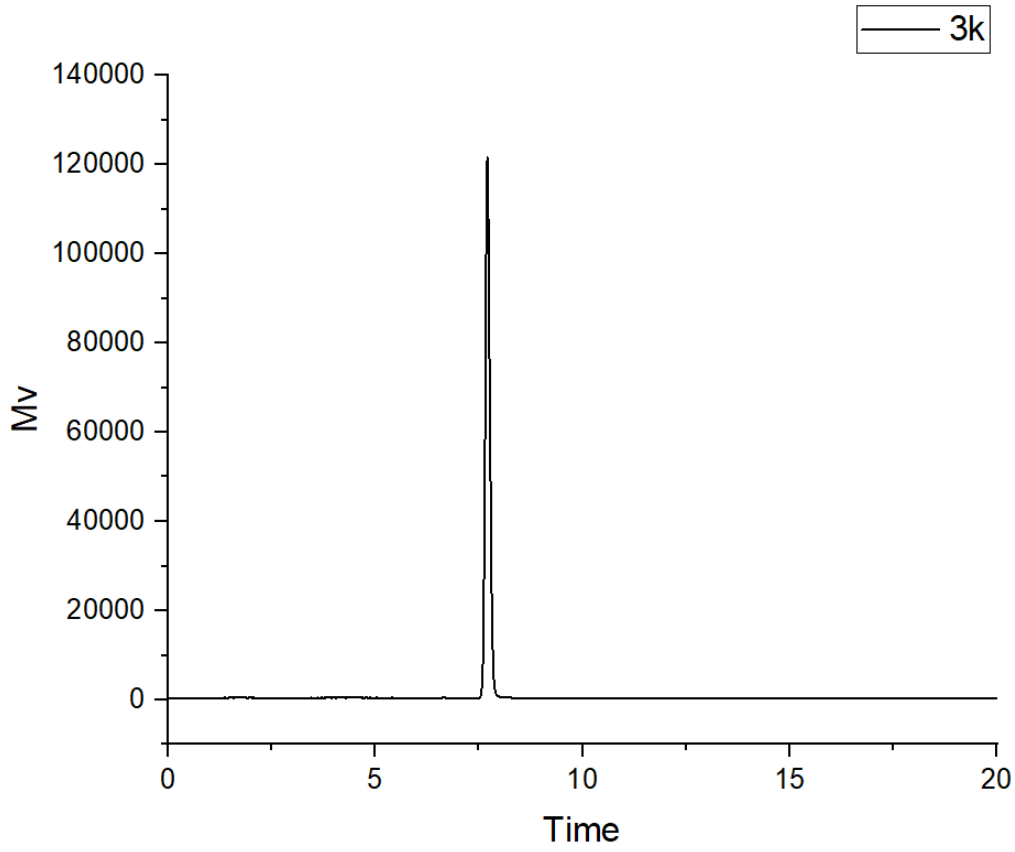
3i


3i
20000
15000
10000
5000
0
Mv
0
5
10
15
20
Time

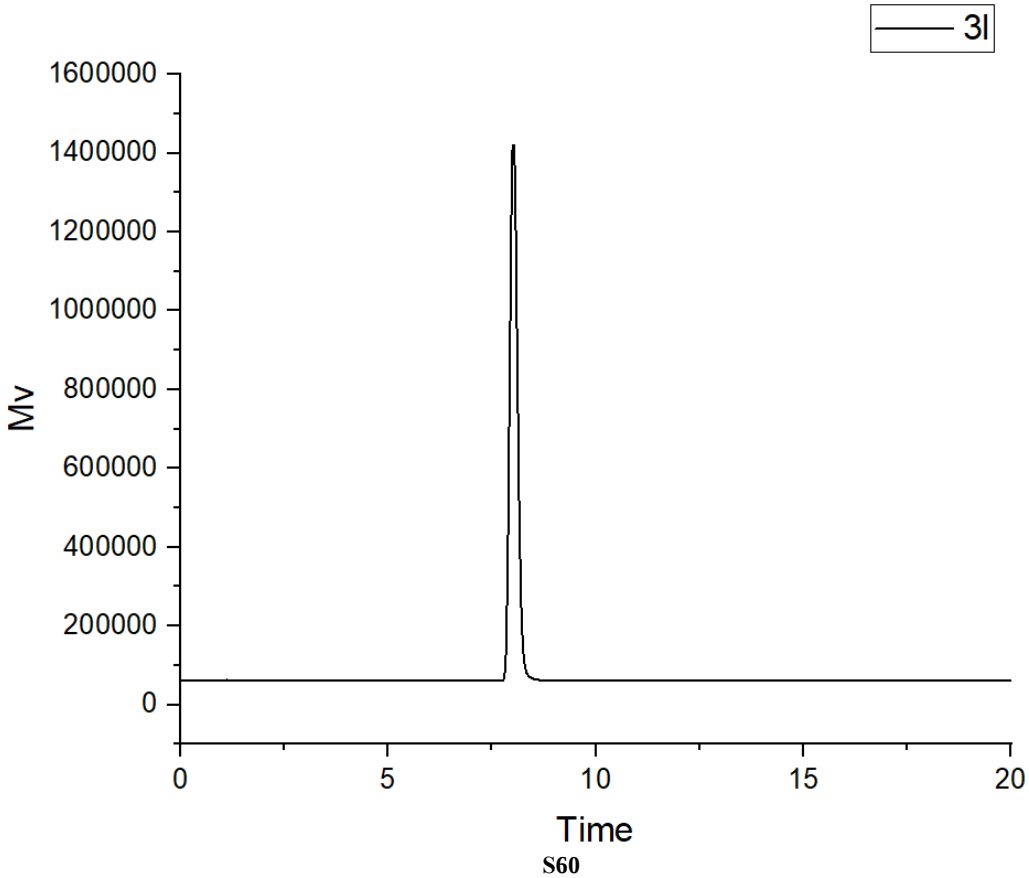
3j


3j
450000
400000
350000
300000
250000
200000
150000
100000
50000
Mv
0
5
10
15
20
Time

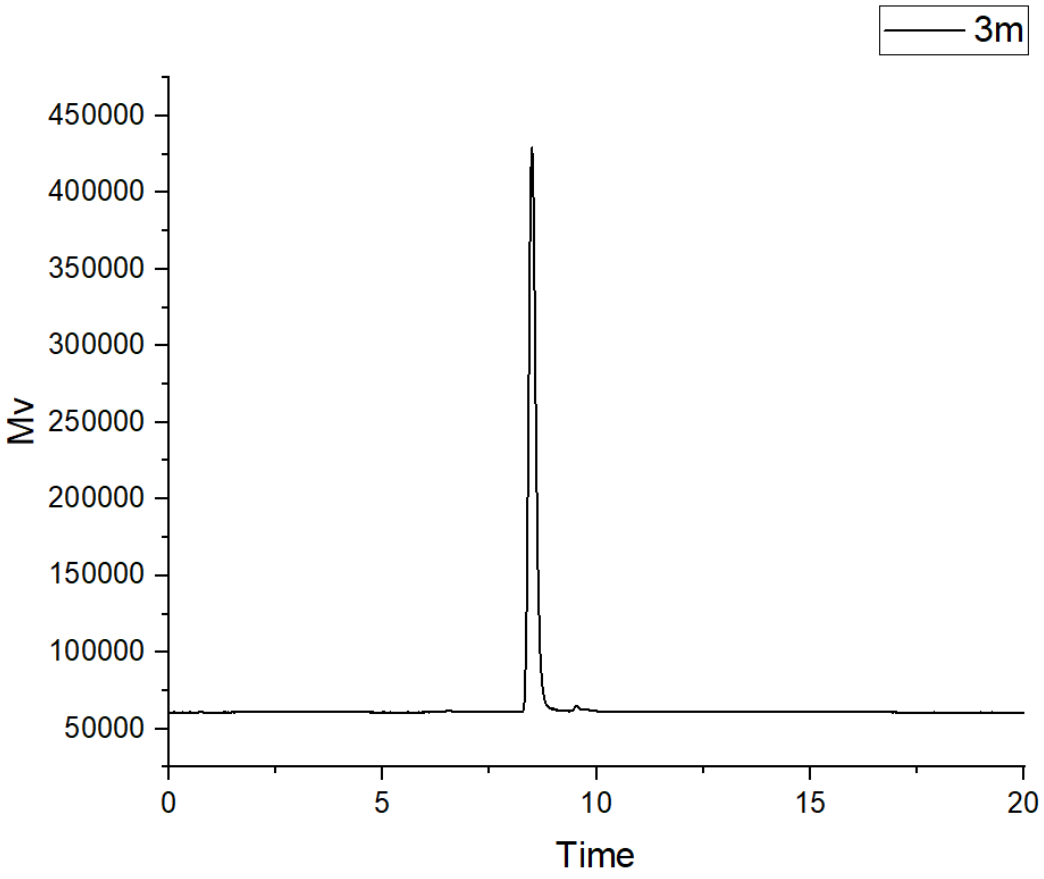
3k


3k
140000
120000
100000
80000
60000
40000
20000
0
Mv
0
5
10
15
20
Time

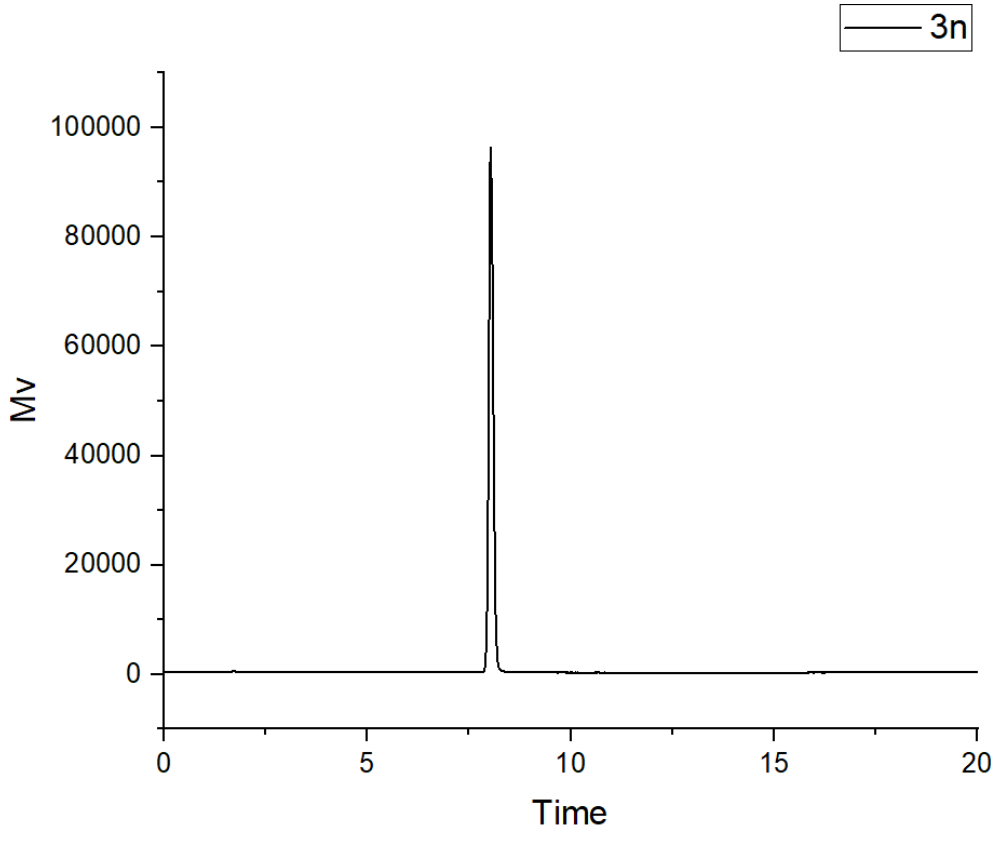
3l


3l
1600000
1400000
1200000
1000000
800000
600000
400000
200000
0
Mv
0
5
10
15
20
Time

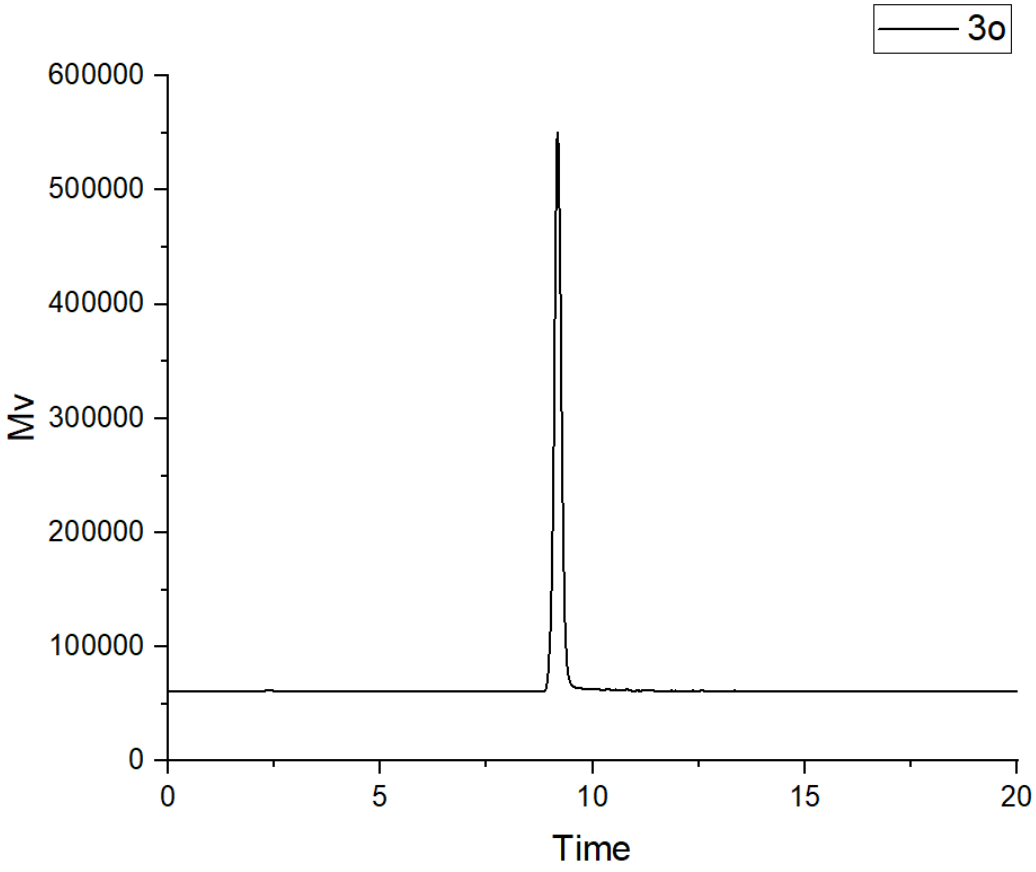
3m


3m
450000
400000
350000
300000
250000
200000
150000
100000
50000
Mv
0
5
10
15
20
Time

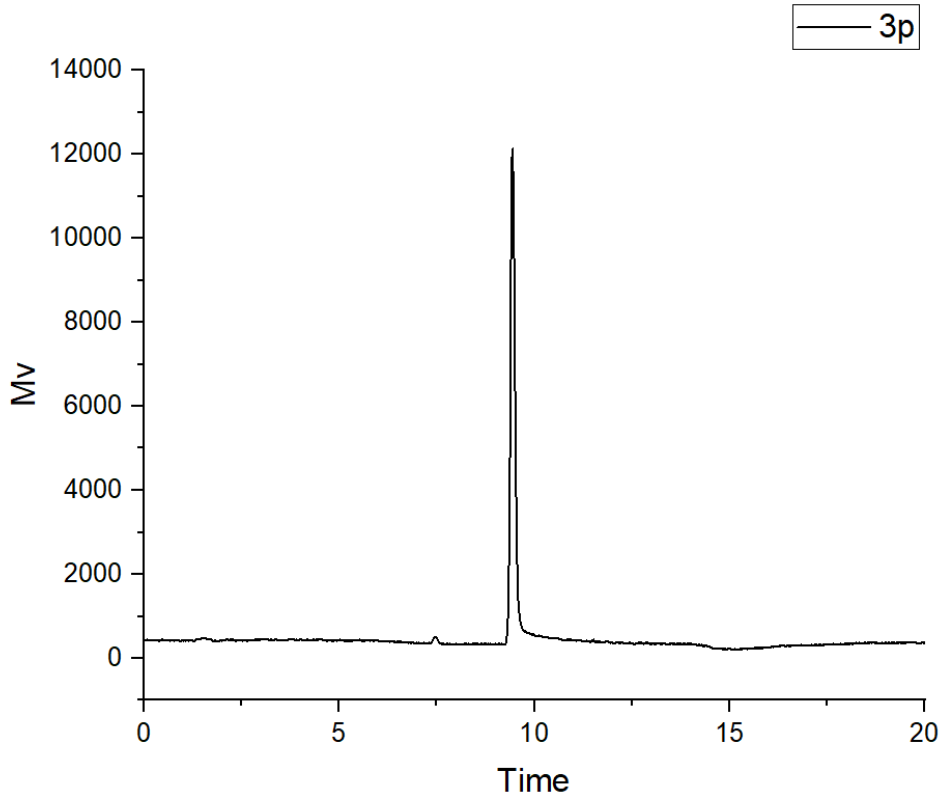
3n


3n
100000
80000
60000
40000
20000
0
Mv
0
5
10
15
20
Time

3o


3o
600000
500000
400000
300000
200000
100000
0
Mv
0
5
10
15
20
Time

3p


3p
14000
12000
10000
8000
6000
4000
2000
0
Mv
0
5
10
15
20
Time