

Formal [4+2] annulation of Enaminones and Cyanomethyl sulfur ylide : One-pot Access to Polysubstituted Pyridin-2(1*H*)-ones

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Electronic Supplementary Information

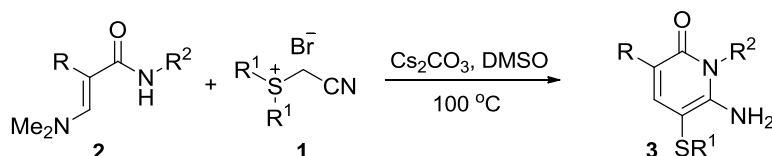
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I. General information

All reagents were purchased from commercial sources and used without treatment, unless otherwise indicated. The products were purified by column chromatography over silica gel. ^1H NMR and ^{13}C NMR spectra were recorded at 25 °C at 300 MHz, 400 MHz and 100 MHz, respectively, with TMS as internal standard. IR spectra (KBr) were recorded on FTIR-spectrophotometer in the range of 400-4000 cm^{-1} . All melting points were determined in open capillary tubes in a Thiele apparatus and are uncorrected.

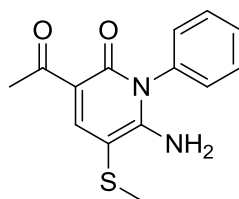
II. Synthesis and analytical data of compounds 3



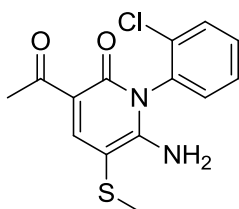
Typical procedure for the synthesis of substituted pyridin-2(1H)-ones 3a-3m and 3o-3q (3a as an example): The sulfur ylide was prepared by adding Cs_2CO_3 (3.0 mmol) in one portion into a solution of sulfonium bromide salt **1a** (1.2 mmol) in DMSO (4.0 mL) under stirring for 15 min at room temperature. To the above sulfur ylide was then added **2a** (1.0 mmol), which was heated to 100 °C and stirred for 1.5 h. After the reaction was completed, the resulting mixture was poured into saturated aqueous NaCl (100 mL), which was extracted with dichloromethane (3×30 mL). The combined organic phase was washed with water, dried over anhydrous MgSO_4 , filtered, and evaporated *in vacuo*. The crude product was purified by flash silica gel chromatography to give **3a** as a yellow solid (85%).

Typical procedure for the synthesis of 3n: The sulfur ylide was prepared by adding Cs_2CO_3 (3.0 mmol) in one portion into a solution of sulfonium bromide salt **1b** (1.2 mmol) in DMSO (4.0 mL) at room temperature under stirring for 15 min under nitrogen. To the above sulfur ylide was then added **2b** (1.0 mmol), which was heated to 100 °C and stirred for 2.0 h under nitrogen. After the reaction was completed, the resulting mixture was poured into saturated aqueous NaCl (100 mL), which was extracted with dichloromethane (3×30 mL). The combined organic phase was washed with water, dried over anhydrous MgSO_4 , filtered, and evaporated *in vacuo*. The crude product was purified by flash silica gel chromatography to give **3m** as a white solid.

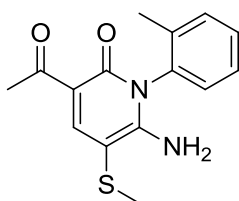
Analytical data of compounds 3



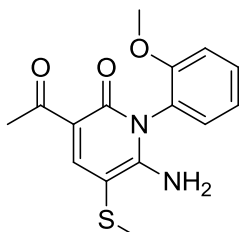
(3a) Yellow solid, m.p. 218-219 °C; $^1\text{H-NMR}$ (300 MHz, DMSO) δ 2.23 (s, 3H), 2.36 (s, 3H), 7.03 (s, 2H), 7.27 (d, $J = 7.2$ Hz, 2H), 7.50-7.60 (m, 3H), 8.20 (s, 1H); $^{13}\text{C-NMR}$ (100 MHz, DMSO): δ 20.5, 31.5, 94.5, 112.1, 129.8, 130.4, 131.3, 137.1, 151.7, 158.8, 162.1, 194.3; **IR** (KBr): $\nu = 3445, 3059, 2920, 1676, 1584, 1545, 1489, 1459, 1367, 1334, 1262$ cm^{-1} ; **Anal. Calcd** for $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_2\text{S}$: C, 61.29; H, 5.14; N, 10.21. Found: C, 61.04; H, 5.06; N, 10.36.



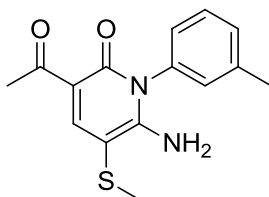
(3b) Light yellow solid, m.p. 190-191 °C; $^1\text{H-NMR}$ (300 MHz, DMSO): δ 2.22 (s, 3H), 2.35 (s, 3H), 7.38 (s, 2H), 7.44-7.47 (m, 1H), 7.52-7.58 (m, 2H), 7.69-7.72 (m, 1H), 8.21 (s, 1H); $^{13}\text{C-NMR}$ (100 MHz, DMSO): δ 19.8, 30.7, 93.8, 111.0, 129.5, 131.1, 131.4, 131.7, 132.2, 134.0, 151.4, 157.8, 160.6, 193.5; **IR** (KBr): ν = 3383, 3164, 2918, 1672, 1633, 1600, 1542, 1493, 1475, 1369, 1338, 1279 cm^{-1} ; **Anal. Calcd** for $\text{C}_{14}\text{H}_{13}\text{ClN}_2\text{O}_2\text{S}$: C, 54.46; H, 4.24; N, 9.07. Found: C, 54.62; H, 4.30; N, 9.21. **HRMS** (ESI) m/z calculated for $\text{C}_{14}\text{H}_{13}\text{ClN}_2\text{O}_2\text{S} [\text{M} + \text{Na}]^+$: 331.0284. Found: 331.0276.



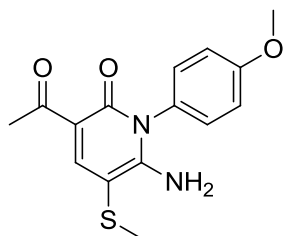
(3c) Light yellow solid, m.p. 149-151 °C; $^1\text{H-NMR}$ (300 MHz, DMSO): δ 1.98 (s, 3H), 2.22 (s, 3H), 2.35 (s, 3H), 7.04 (s, 2H), 7.17 (d, J = 6.9 Hz, 1H), 7.37-7.44 (m, 3H), 8.21 (s, 1H); $^{13}\text{C-NMR}$ (100 MHz, DMSO): δ 17.2, 19.8, 30.8, 93.7, 111.4, 128.3, 129.0, 130.0, 132.0, 135.5, 135.8, 151.1, 157.7, 160.8, 193.7; **IR** (KBr): ν = 3389, 3165, 2915, 1666, 1636, 1593, 1544, 1491, 1369, 1340, 1267 cm^{-1} ; **Anal. Calcd** for $\text{C}_{15}\text{H}_{16}\text{N}_2\text{O}_2\text{S}$: C, 62.48; H, 5.59; N, 9.71. Found: C, 62.75; H, 5.65; N, 9.52.



(3d) Light yellow solid, m.p. 219-222 °C; $^1\text{H-NMR}$ (300 MHz, DMSO): δ 2.21 (s, 3H), 2.34 (s, 3H), 3.74 (s, 3H), 7.07 (m, 2H), 7.09-7.12 (m, 1H), 7.18-7.25 (m, 2H), 7.47-7.52 (m, 1H), 8.18 (s, 1H); $^{13}\text{C-NMR}$ (100 MHz, DMSO): δ 19.8, 30.7, 56.2, 93.5, 111.2, 113.6, 121.9, 124.4, 130.3, 131.4, 151.1, 155.2, 158.2, 160.9, 193.6; **IR** (KBr): ν = 3376, 3163, 2916, 1670, 1630, 1597, 1543, 1503, 1368, 1343, 1255 cm^{-1} ; **Anal. Calcd** for $\text{C}_{15}\text{H}_{16}\text{N}_2\text{O}_3\text{S}$: C, 59.19; H, 5.30; N, 9.20. Found: C, 59.44; H, 5.20; N, 9.01.

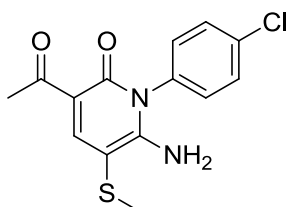


(3e) Yellow solid, m.p. 215-216 °C; ¹H-NMR (300 MHz, DMSO): δ 2.22 (s, 3H), 2.35 (s, 3H), 2.38 (s, 3H), 7.01 (s, 2H), 7.05-7.10 (m, 2H), 7.32 (d, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 8.20 (s, 1H); ¹³C-NMR (100 MHz, DMSO): δ 19.8, 21.3, 30.8, 93.7, 111.4, 125.9, 129.4, 130.4(2), 136.3, 140.2, 150.9, 158.1, 161.3, 193.7; IR (KBr): ν = 3436, 3166, 2922, 1669, 1587, 1543, 1489, 1455, 1366, 1338, 1267 cm⁻¹; Anal. Calcd for C₁₅H₁₆N₂O₂S: C, 62.48; H, 5.59; N, 9.71. Found: C, 62.29; H, 5.49; N, 9.51.

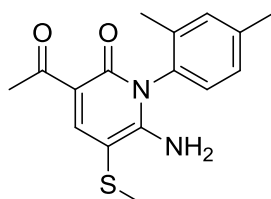


(3f) Yellow solid, m.p. 238-240 °C; ¹H-NMR (300 MHz, DMSO): δ 2.21 (s, 3H), 2.35 (s, 3H), 3.83 (s, 3H), 7.04 (s, 2H), 7.08 (d, *J* = 8.7 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 2H), 8.18 (s, 1H); ¹³C-NMR (100 MHz, DMSO): δ 19.7, 30.6, 55.8, 93.5, 111.5, 115.8, 128.8, 130.1, 150.8, 158.4, 160.6, 161.4, 193.6; IR (KBr): ν = 3442, 3171, 2908, 1651, 1599, 1543, 1552, 1504, 1362, 1337, 1267 cm⁻¹; Anal. Calcd for C₁₅H₁₆N₂O₃S: C, 59.19; H, 5.30; N, 9.20. Found: C, 59.47; H, 5.19; N, 9.34.

Crystal data for 3f: C₁₅H₁₆N₂O₃S, white crystal, *M* = 304.36, orthorhombic, *p c c n*, *a* = 18.861(15) Å, *b* = 9.284(8) Å, *c* = 16.581(14) Å, α = 90.00°, β = 90.00°, γ = 90.00°, *V* = 2903.5(4) Å³, *Z* = 8, *T* = 293 K, *F*000 = 1280.0, *F*000^o = 1281.54, *R* = 0.0458 (2001), *wR*2 = 0.1181 (2579). CCDC deposition number: 1013387. These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 (0)1223 762911; or deposit@ccdc.cam.ac.uk).

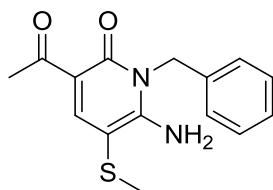


(3g) Yellow solid, m.p. 254-256 °C; ¹H-NMR (300 MHz, DMSO): δ 2.22 (s, 3H), 2.35 (s, 3H), 7.26 (s, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 8.20 (s, 1H); ¹³C-NMR (100 MHz, DMSO): δ 19.8, 30.8, 94.0, 111.1, 130.7, 131.2, 134.4, 135.5, 151.1, 158.2, 161.3, 193.5; IR (KBr): ν = 3420, 2921, 1696, 1608, 1582, 1542, 1503, 1463, 1277 cm⁻¹; Anal. Calcd for C₁₄H₁₃ClN₂O₂S: C, 54.46; H, 4.24; N, 9.07. Found: C, 54.19; H, 4.34; N, 9.22.

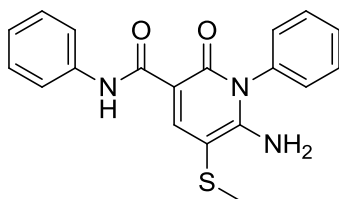


(3h) Yellow solid, m.p. 168-170 °C; ¹H-NMR (300 MHz, DMSO): δ 1.94 (s, 3H), 2.21 (s, 3H), 2.36 (s, 6H), 7.04 (s, 2H), 7.07 (s, 1H), 7.17 (d, *J* = 8.1 Hz, 1H), 7.26 (s, 1H), 8.21 (s, 1H); ¹³C-NMR (100 MHz,

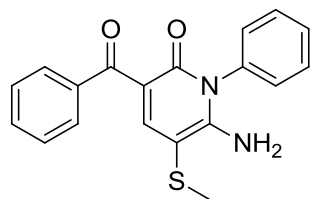
DMSO): δ 17.1, 19.8, 21.2, 30.7, 93.7, 111.4, 128.7, 128.8, 132.5, 132.8, 135.5, 139.2, 151.0, 157.8, 160.8, 193.7; **IR** (KBr): ν = 3396, 3166, 2922, 1581, 1544, 1493, 1355, 1267 cm^{-1} ; **Anal. Calcd** for $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_2\text{S}$: C, 63.55; H, 6.00; N, 9.26. Found: C, 63.26; H, 5.94; N, 9.13.



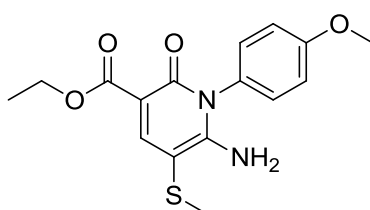
(3i) Yellow solid, m.p. 188-189 $^{\circ}\text{C}$; **$^1\text{H-NMR}$** (300 MHz, DMSO): δ 2.19 (s, 3H), 2.42 (s, 3H), 5.36 (s, 2H), 7.13 (d, J = 7.2 Hz, 2H), 7.25-7.27 (m, 1H), 7.31-7.35 (m, 2H), 7.80 (s, 2H), 8.16 (s, 1H); **$^{13}\text{C-NMR}$** (100 MHz, DMSO): δ 19.7, 30.9, 44.9, 94.3, 110.7, 126.8, 127.4, 128.9, 136.2, 150.2, 157.8, 161.0, 194.0; **IR** (KBr): ν = 3401, 3171, 2921, 1655, 1607, 1543, 1456, 1365, 1247 cm^{-1} ; **Anal. Calcd** for $\text{C}_{15}\text{H}_{16}\text{N}_2\text{O}_2\text{S}$: C, 62.48; H, 5.59; N, 9.71. Found: C, 62.70; H, 5.66; N, 9.54.



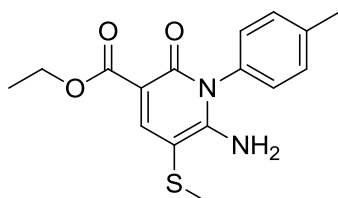
(3j) Yellow solid, m.p. 248-249 $^{\circ}\text{C}$; **$^1\text{H-NMR}$** (300 MHz, DMSO): δ 2.26 (s, 3H), 7.00 (m, 2H), 7.27 (t, J = 7.8 Hz, 2H), 7.35-7.37 (m, 2H), 7.57-7.63 (m, 6H), 8.41 (s, 1H), 11.47 (s, 1H); **$^{13}\text{C-NMR}$** (100 MHz, DMSO): δ 19.6, 94.4, 104.5, 119.6, 123.3, 129.0, 129.3, 130.0, 130.7, 136.0, 139.6, 151.0, 157.0, 162.3, 162.8; **IR** (KBr): ν = 3316, 3024, 2913, 1669, 1583, 1539, 1482, 1441, 1359, 1254 cm^{-1} ; **Anal. Calcd** for $\text{C}_{19}\text{H}_{17}\text{N}_3\text{O}_2\text{S}$: C, 64.94; H, 4.88; N, 11.96. Found: C, 64.74; H, 4.94; N, 11.79.



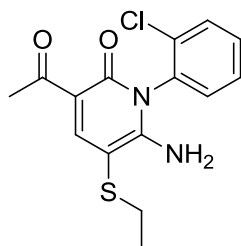
(3k) Yellow solid, m.p. 223-225 $^{\circ}\text{C}$; **$^1\text{H-NMR}$** (400 MHz, DMSO): δ 2.25 (s, 3H), 6.95 (s, 2H), 7.28 (d, J = 7.6 Hz, 2H), 7.28-7.34 (m, 2H), 7.42 (d, J = 7.2 Hz, 1H), 7.49 (d, J = 7.2 Hz, 1H), 7.51-7.56 (m, 4H), 8.02 (s, 1H); **$^{13}\text{C-NMR}$** (100 MHz, DMSO): δ 19.8, 92.8, 111.8, 128.0, 128.9, 129.1, 129.7, 130.6, 131.3, 136.4, 140.5, 152.4, 157.9, 160.3, 192.5; **Anal. Calcd** for $\text{C}_{19}\text{H}_{16}\text{N}_2\text{O}_2\text{S}$: C, 67.84; H, 4.79; N, 8.33. Found: C, 64.60; H, 4.83; N, 8.46.



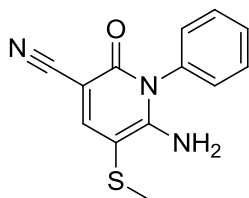
(3l) Yellow solid, m.p. 258-259 °C; $^1\text{H-NMR}$ (300 MHz, DMSO): δ 1.19 (t, $J = 7.2$ Hz, 3H), 2.20 (s, 3H), 3.82 (s, 3H), 4.05-4.12 (q, $J = 7.2$ Hz, 2H), 6.86 (s, 2H), 7.07 (d, $J = 9.0$ Hz, 2H), 7.13 (d, $J = 9.0$ Hz, 2H), 8.15 (s, 1H); $^{13}\text{C-NMR}$ (100 MHz, DMSO): δ 14.9, 19.8, 55.8, 59.5, 91.3, 102.4, 115.8, 128.9, 130.2, 152.7, 158.1, 159.1, 160.0, 164.9; **Anal. Calcd** for $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_4\text{S}$: C, 57.47; H, 5.43; N, 8.38. Found: C, 57.73; H, 5.35; N, 8.22.



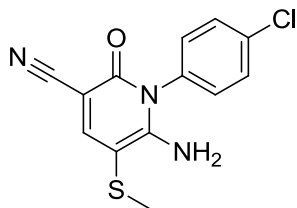
(3m) Yellow solid, m.p. 219-220 °C; $^1\text{H-NMR}$ (400 MHz, DMSO): δ 1.20 (t, $J = 7.2$ Hz, 3H), 2.21 (s, 3H), 2.40 (s, 3H), 4.07-4.12 (q, $J = 7.2$ Hz, 2H), 6.81 (s, 2H), 7.10 (d, $J = 8.0$ Hz, 2H), 7.36 (d, $J = 8.0$ Hz, 2H), 8.17 (s, 1H); $^{13}\text{C-NMR}$ (100 MHz, DMSO): δ 14.9, 19.8, 21.3, 59.5, 91.3, 102.5, 128.7, 131.1, 133.8, 139.0, 152.7, 157.8, 158.9, 164.9; **Anal. Calcd** for $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_3\text{S}$: C, 60.36; H, 5.70; N, 8.80. Found: C, 60.06; H, 5.81; N, 8.92.



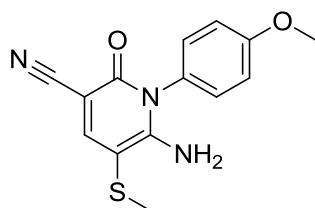
(3n) White solid, m.p. 182-183 °C; $^1\text{H-NMR}$ (400 MHz, DMSO): δ 1.51 (t, $J = 7.2$ Hz, 3H), 2.35 (s, 3H), 2.61 (q, $J = 7.2$ Hz, 2H), 7.32 (s, 2H), 7.45-7.48 (d, $J = 6.8$ Hz, 1H), 7.51-7.57 (m, 2H), 7.69-7.71 (d, $J = 6.8$ Hz, 1H), 8.18 (s, 1H); $^{13}\text{C-NMR}$ (100 MHz, DMSO): δ 14.7, 29.7, 30.7, 91.3, 111.0, 129.5, 131.1, 131.4, 131.7, 132.1, 134.0, 152.3, 158.4, 160.6, 193.5; **IR** (KBr): $\nu = 3164, 2947, 1682, 1611, 1543, 1509, 1475, 1366, 1336, 1249$ cm^{-1} ; **Anal. Calcd** for $\text{C}_{15}\text{H}_{15}\text{ClN}_2\text{O}_2\text{S}$: C, 55.81; H, 4.68; N, 8.68. Found: C, 55.50; H, 4.60; N, 8.80.



(3o) Yellow solid, m.p. 235-237 °C; $^1\text{H-NMR}$ (400 MHz, DMSO): δ 2.23 (s, 3H), 7.10 (s, 2H), 7.29 (d, $J = 7.2$ Hz, 2H), 7.53-7.60 (m, 3H), 8.00 (s, 1H); $^{13}\text{C-NMR}$ (100 MHz, DMSO): δ 19.7, 85.0, 93.3, 118.5, 128.9, 130.1, 130.7, 135.6, 153.4, 157.8, 160.6; **IR** (KBr): $\nu = 3399, 3175, 2916, 2204, 1649, 1601, 1559, 1511, 1455, 1356, 1279$ cm^{-1} ; **Anal. Calcd** for $\text{C}_{13}\text{H}_{11}\text{N}_3\text{OS}$: C, 60.68; H, 4.31; N, 16.33. Found: C, 60.40; H, 4.38; N, 16.21. **HRMS** (ESI) m/z calculated for $\text{C}_{13}\text{H}_{11}\text{N}_3\text{OS}$ $[\text{M} + \text{Na}]^+$: 280.0521. Found: 280.0583.



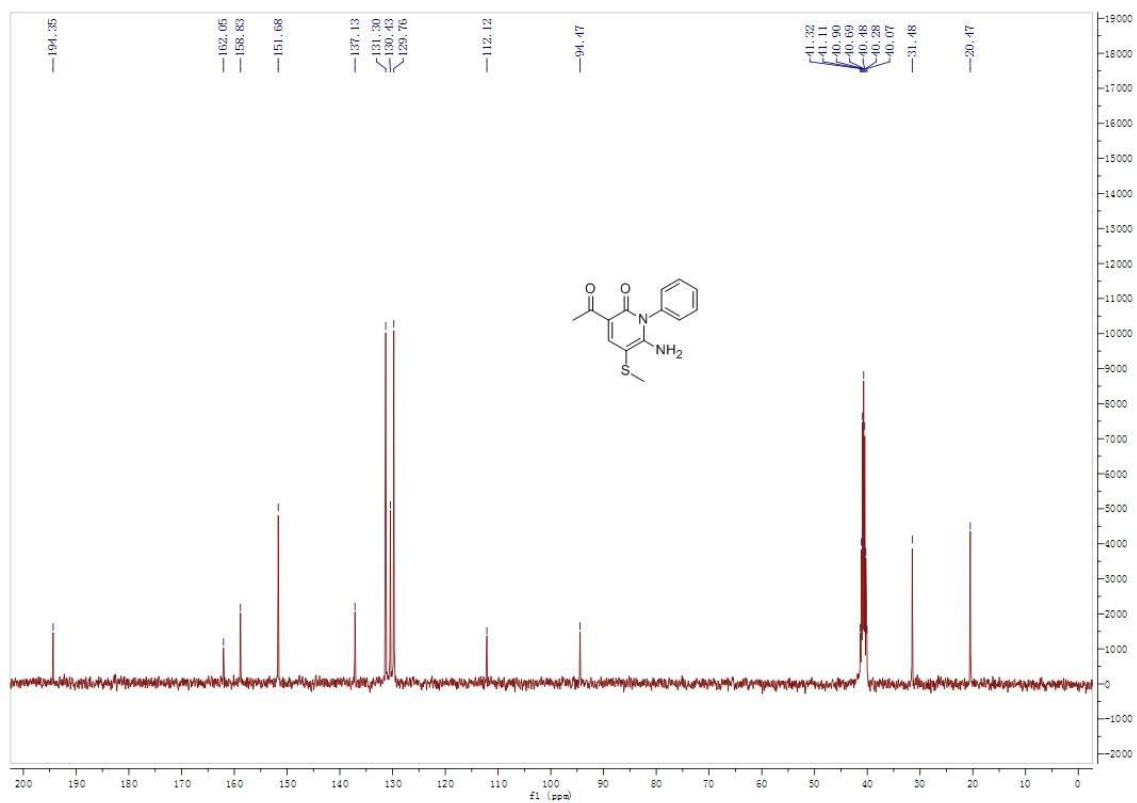
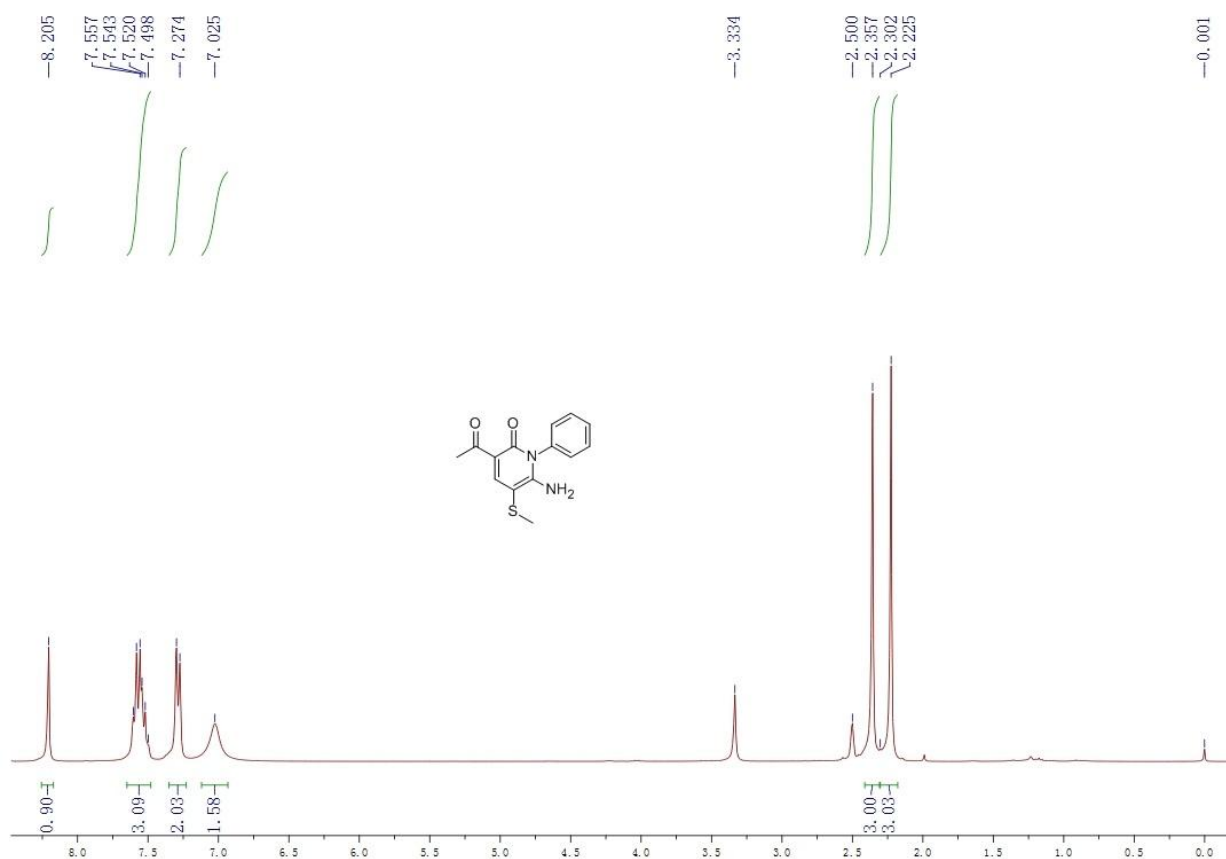
(3p) Light yellow solid, m.p. 252-255 °C; **¹H-NMR** (300 MHz, DMSO): δ 2.22 (s, 3H), 7.32 (s, 2H), 7.33 (d, $J = 8.7$ Hz, 2H), 7.60 (d, $J = 8.4$ Hz, 2H), 7.99 (s, 1H); **¹³C-NMR** (100 MHz, DMSO): δ 19.7, 84.7, 93.5, 118.5, 130.8, 131.0, 134.6, 134.7, 153.5, 157.8, 160.6; **IR** (KBr): $\nu = 3405, 3178, 2921, 2206, 1646, 1602, 1557, 1508, 1277$ cm⁻¹; **Anal. Calcd** for C₁₃H₁₀ClN₃OS: C, 53.52; H, 3.45; N, 14.40. Found: C, 53.20; H, 3.40; N, 14.22.



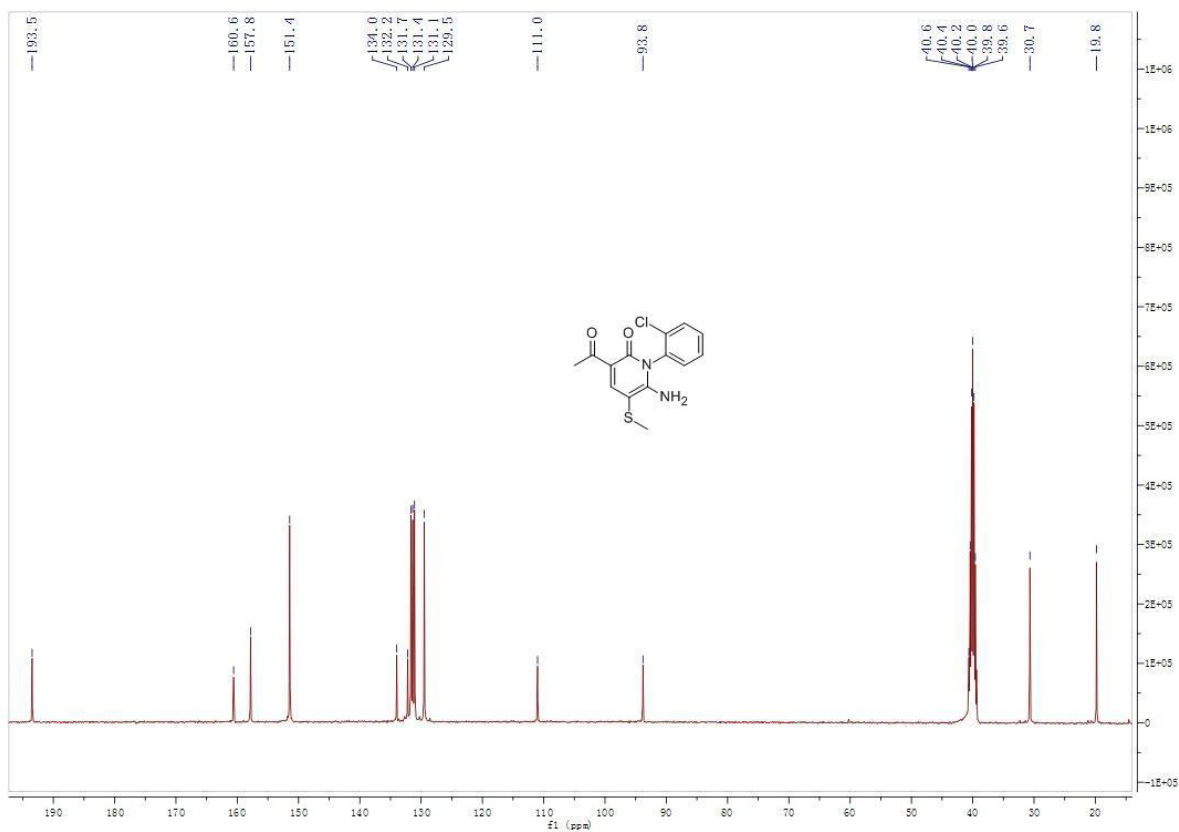
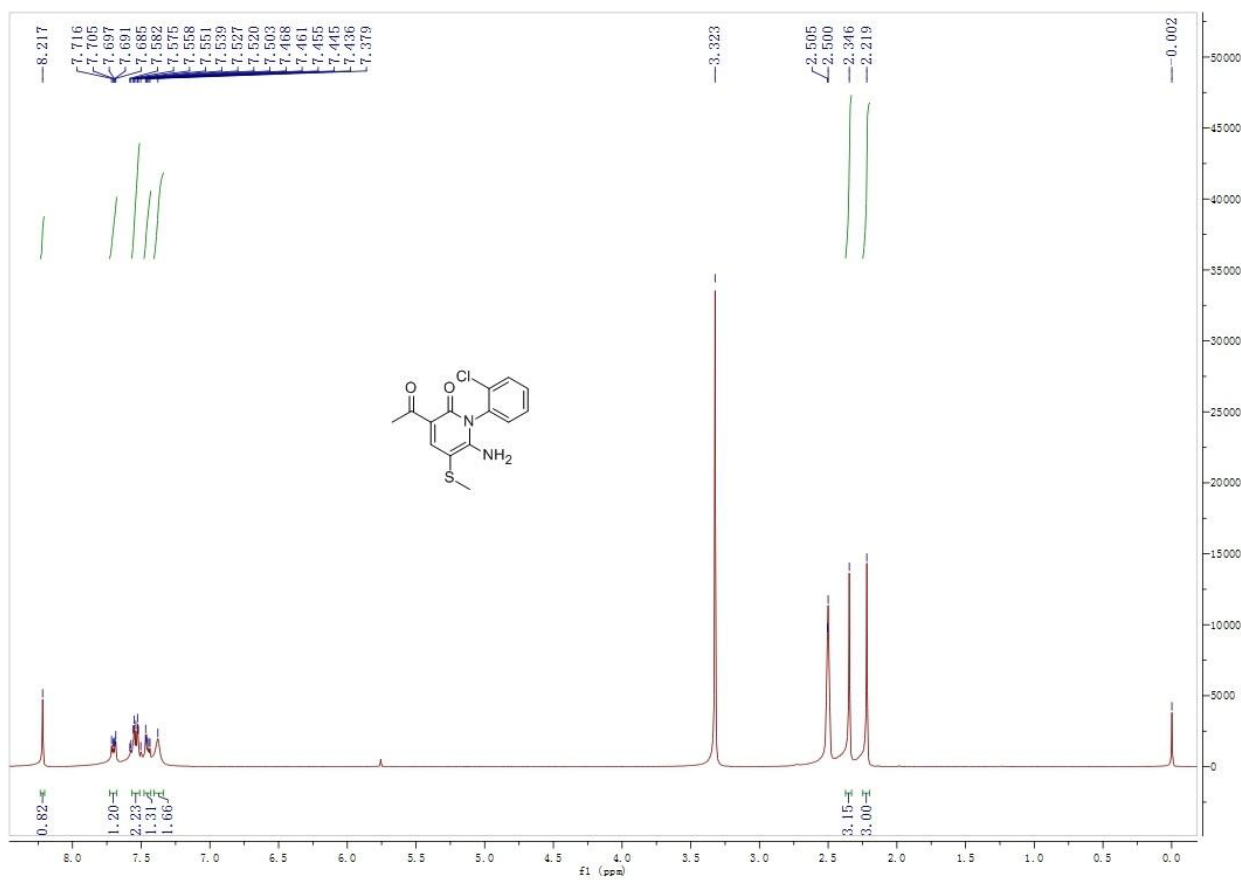
(3q) Yellow solid, m.p. 254-257 °C; **¹H-NMR** (300 MHz, DMSO): δ 2.21 (s, 3H), 3.82 (s, 3H), 7.08-7.12 (m, 4H), 7.18 (d, $J = 7.5$ Hz, 2H), 7.97 (s, 1H); **¹³C-NMR** (100 MHz, DMSO): δ 19.7, 55.8, 84.9, 93.1, 115.9, 118.6, 128.0, 130.0, 153.2, 158.2, 160.3, 160.8; **IR** (KBr): $\nu = 3403, 3168, 2913, 2201, 1646, 1601, 1558, 1510, 1248$ cm⁻¹; **Anal. Calcd** for C₁₄H₁₃N₃O₂S: C, 58.52; H, 4.56; N, 14.62. Found: C, 58.75; H, 4.49; N, 14.43.

III. NMR spectra copes

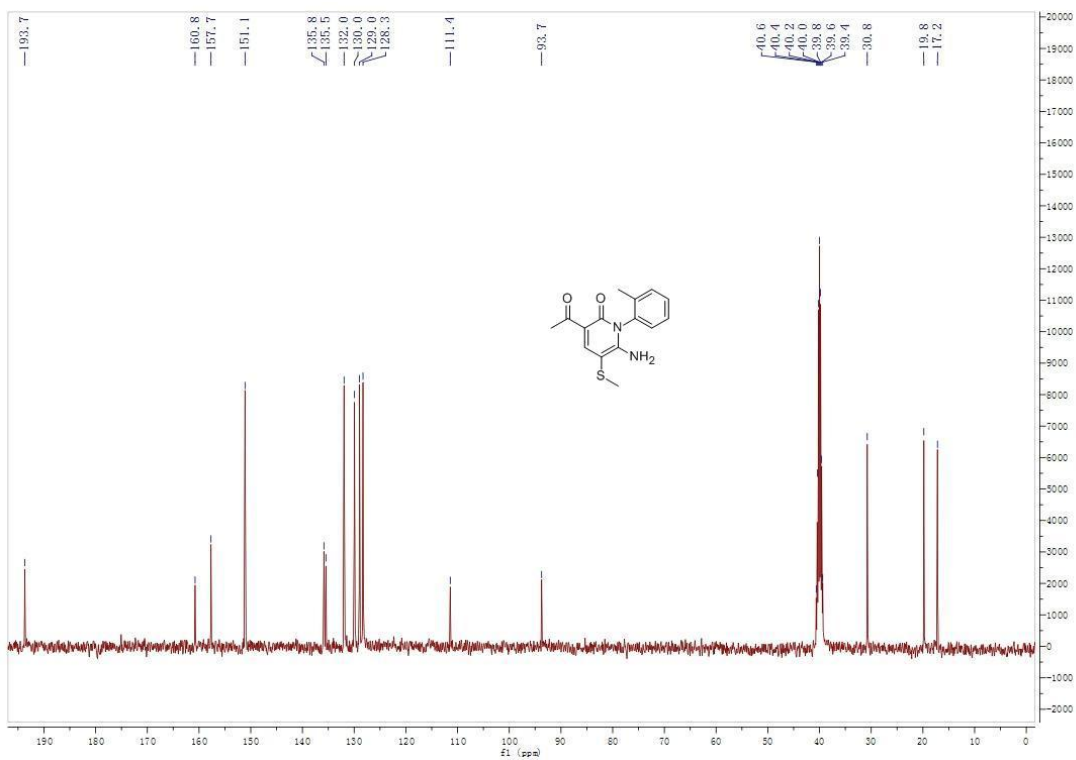
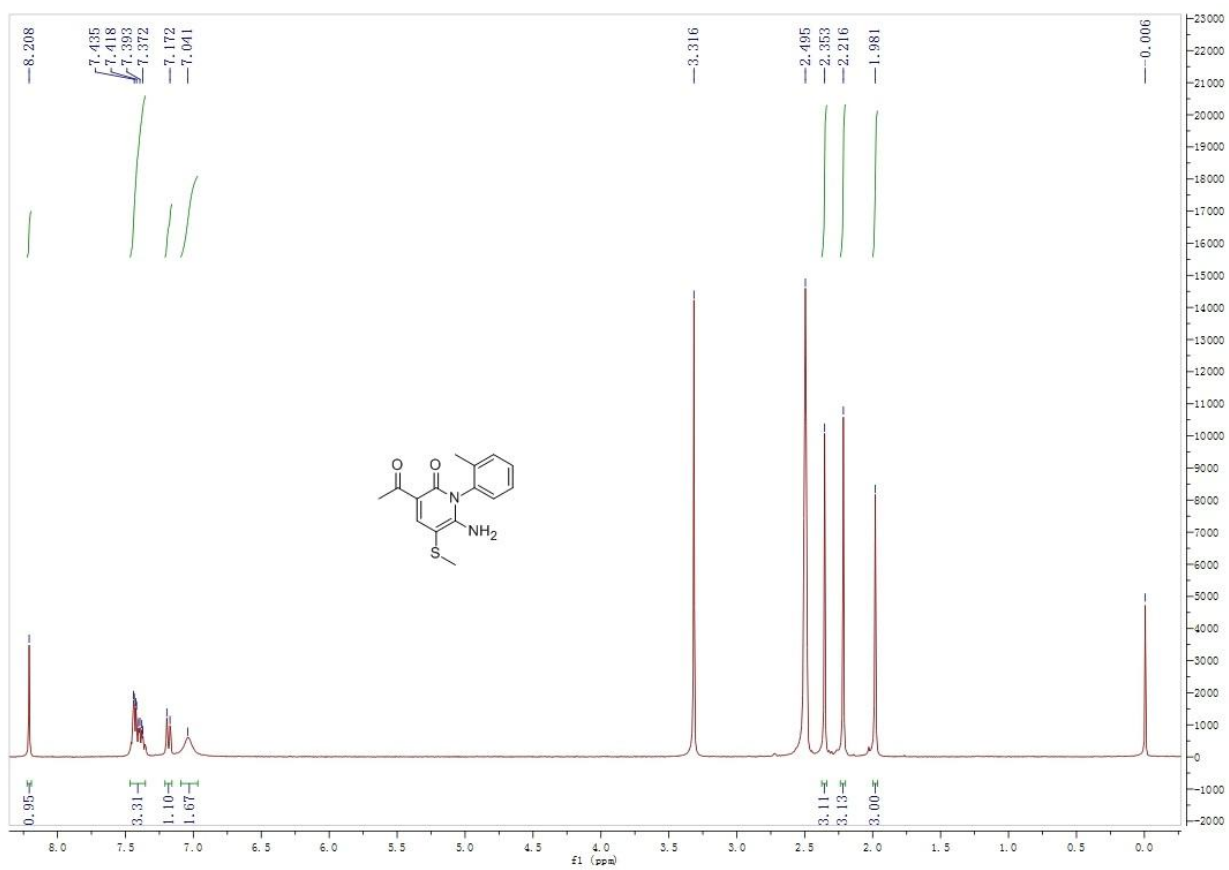
3a



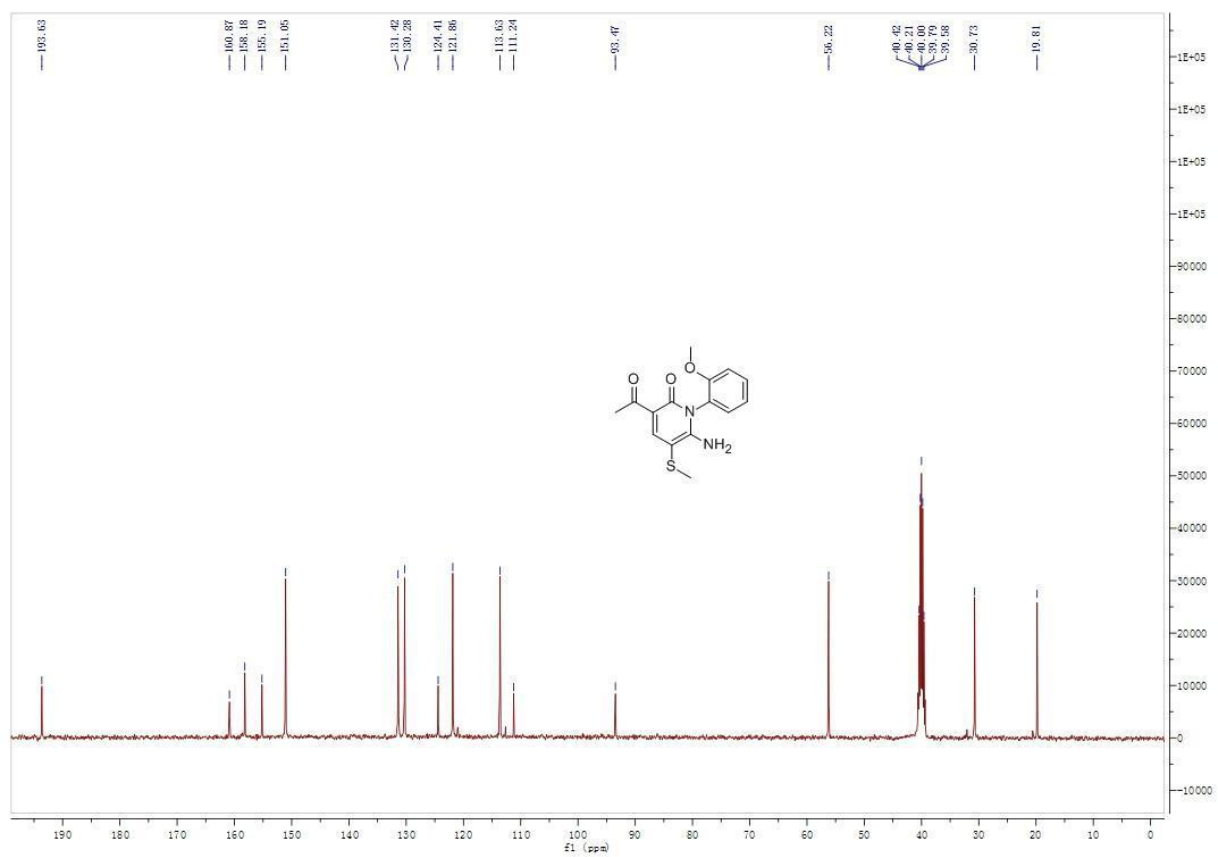
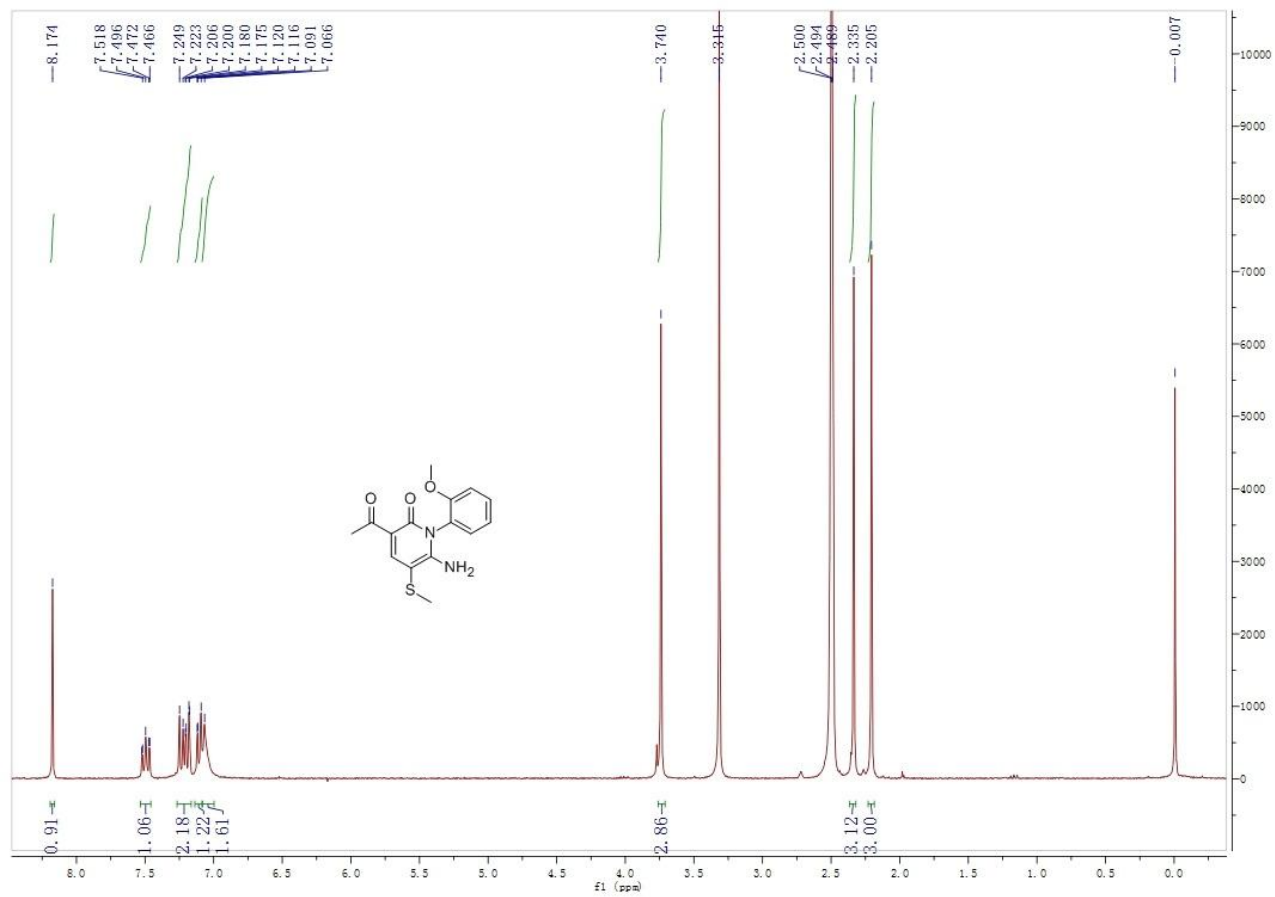
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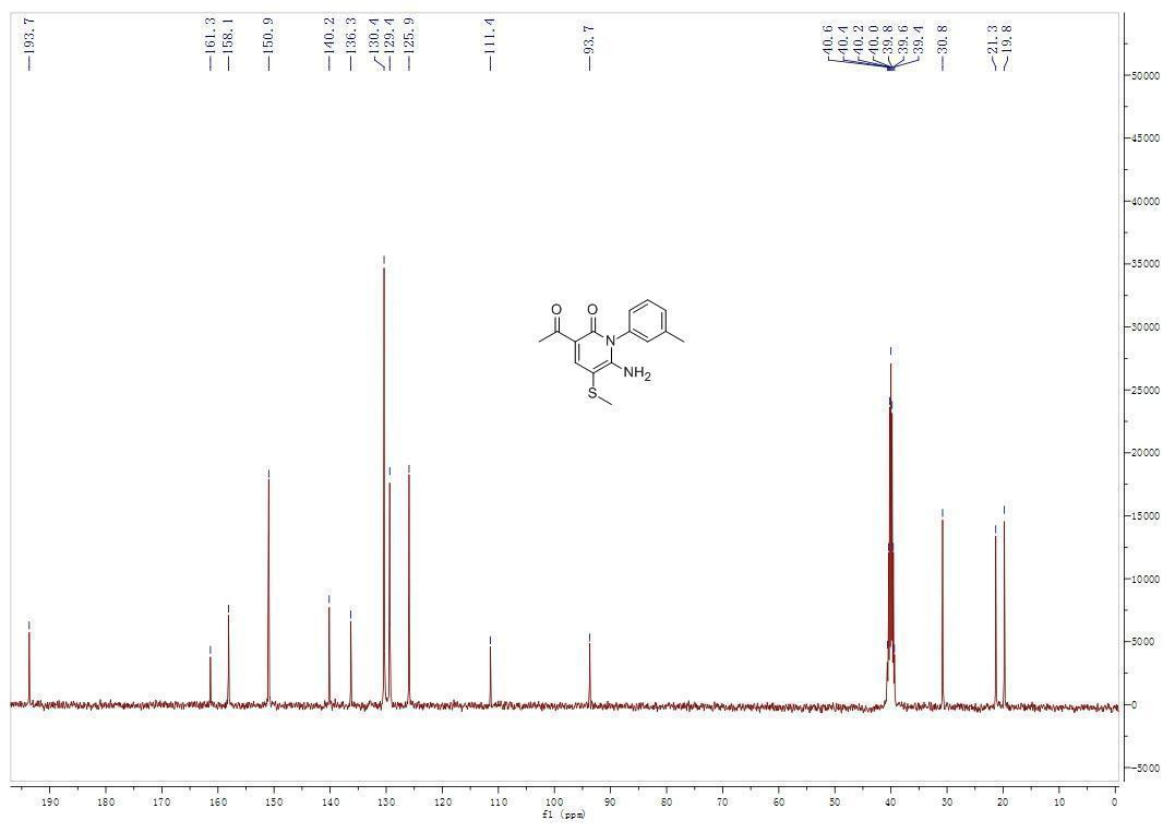
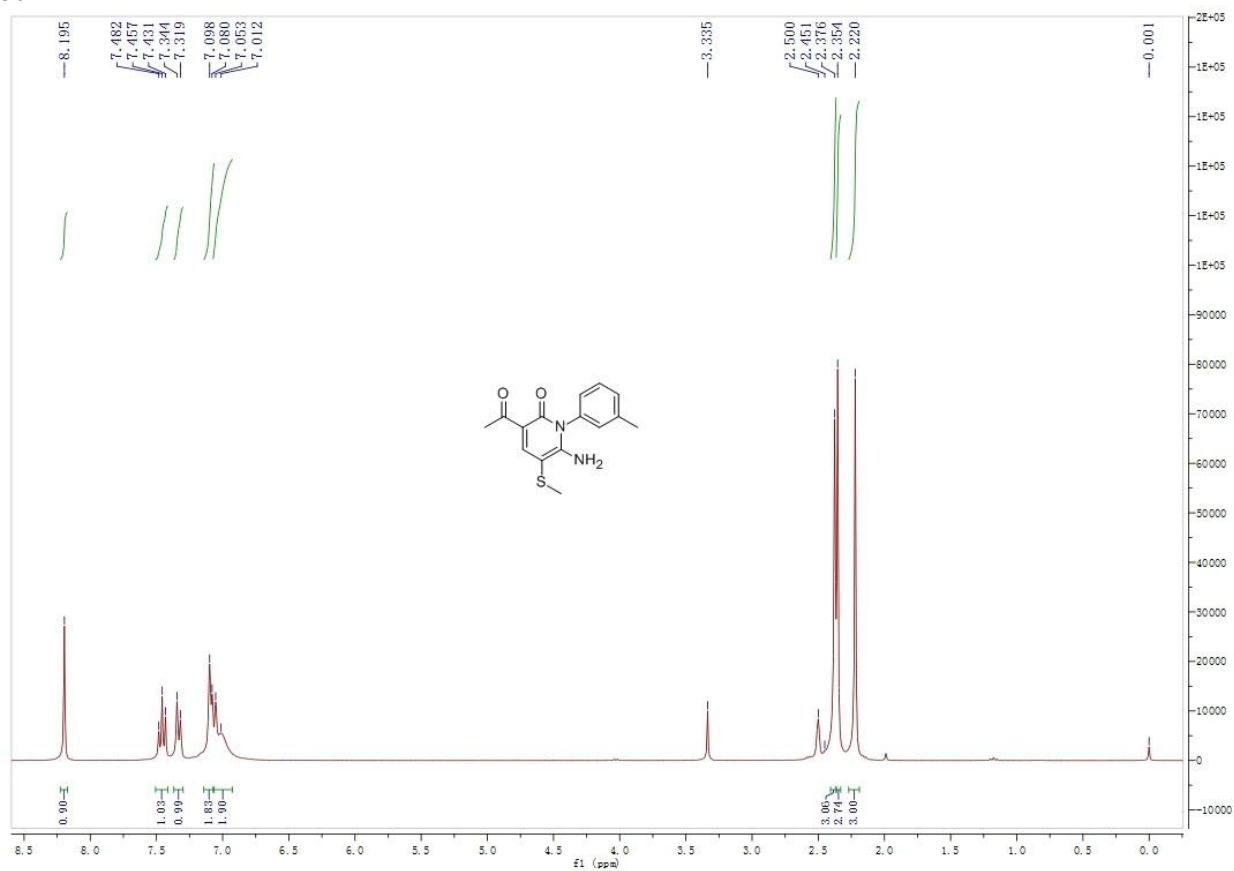
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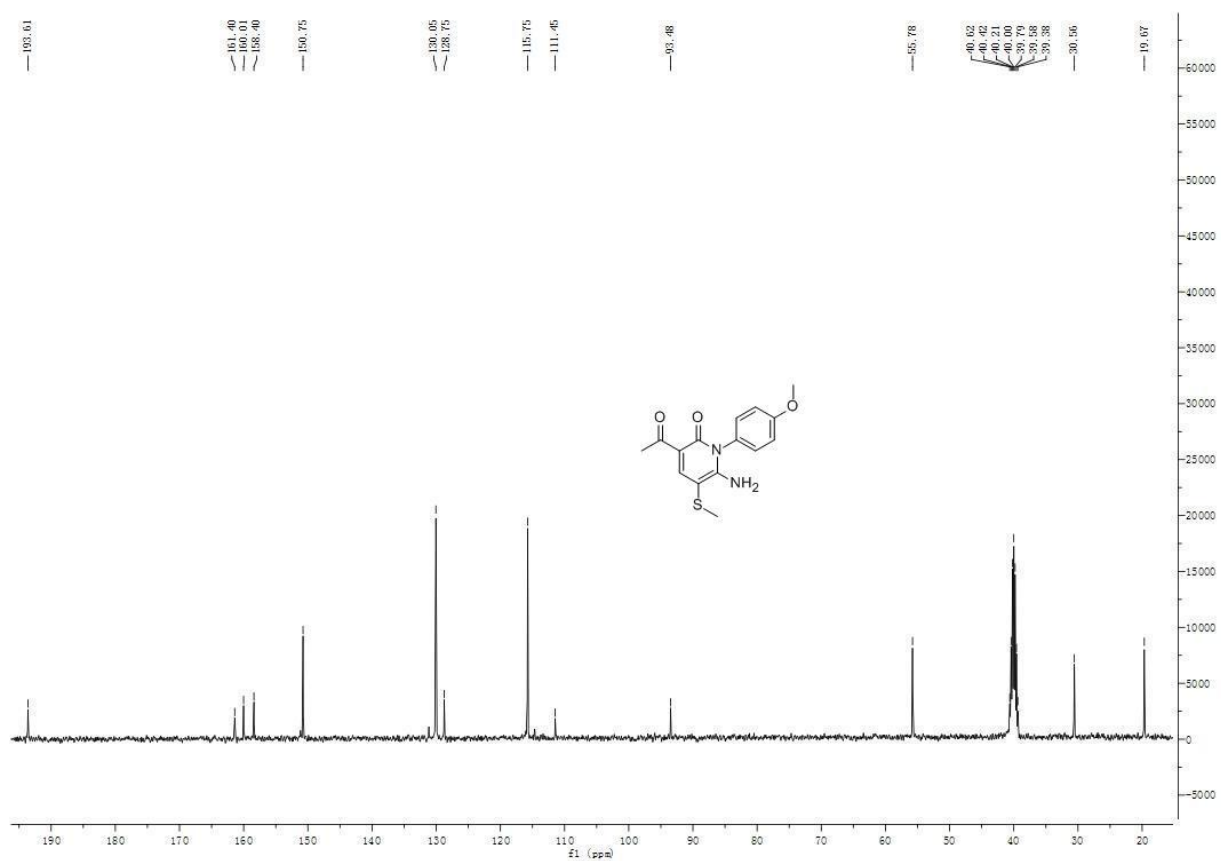
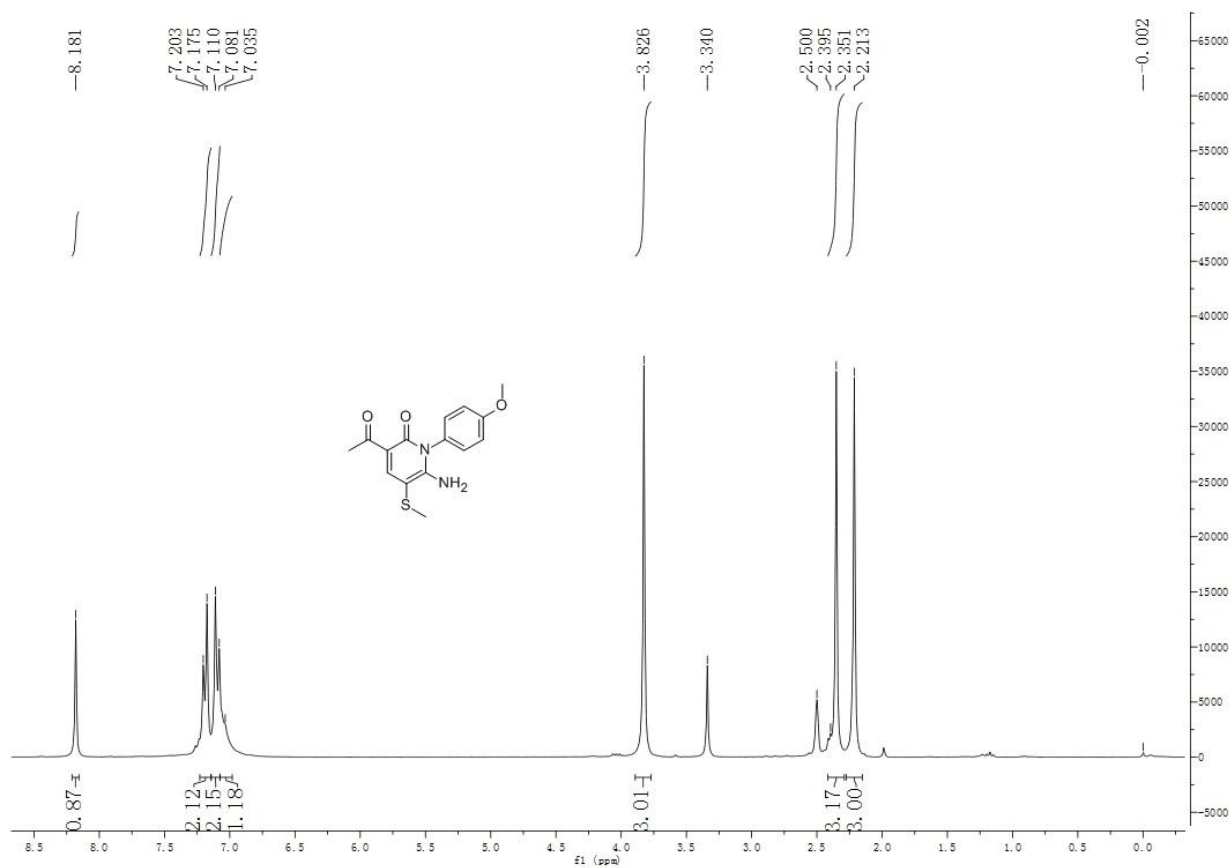
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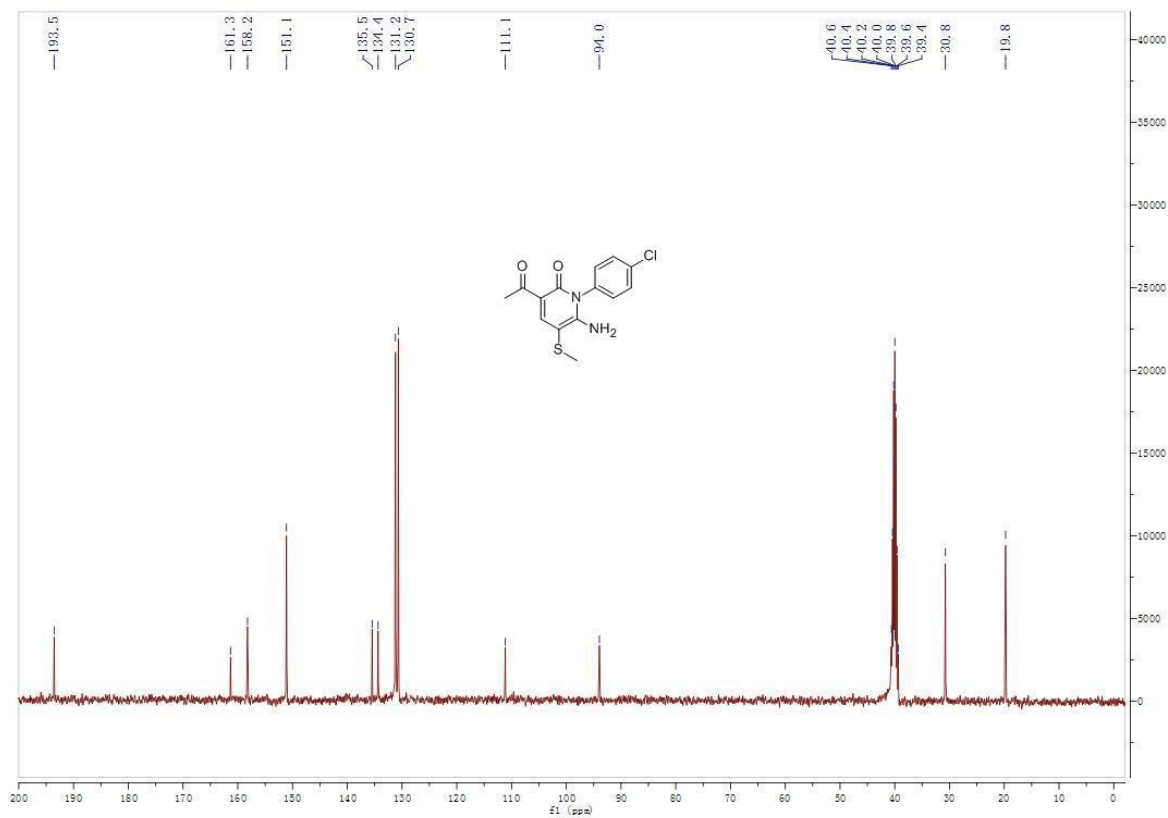
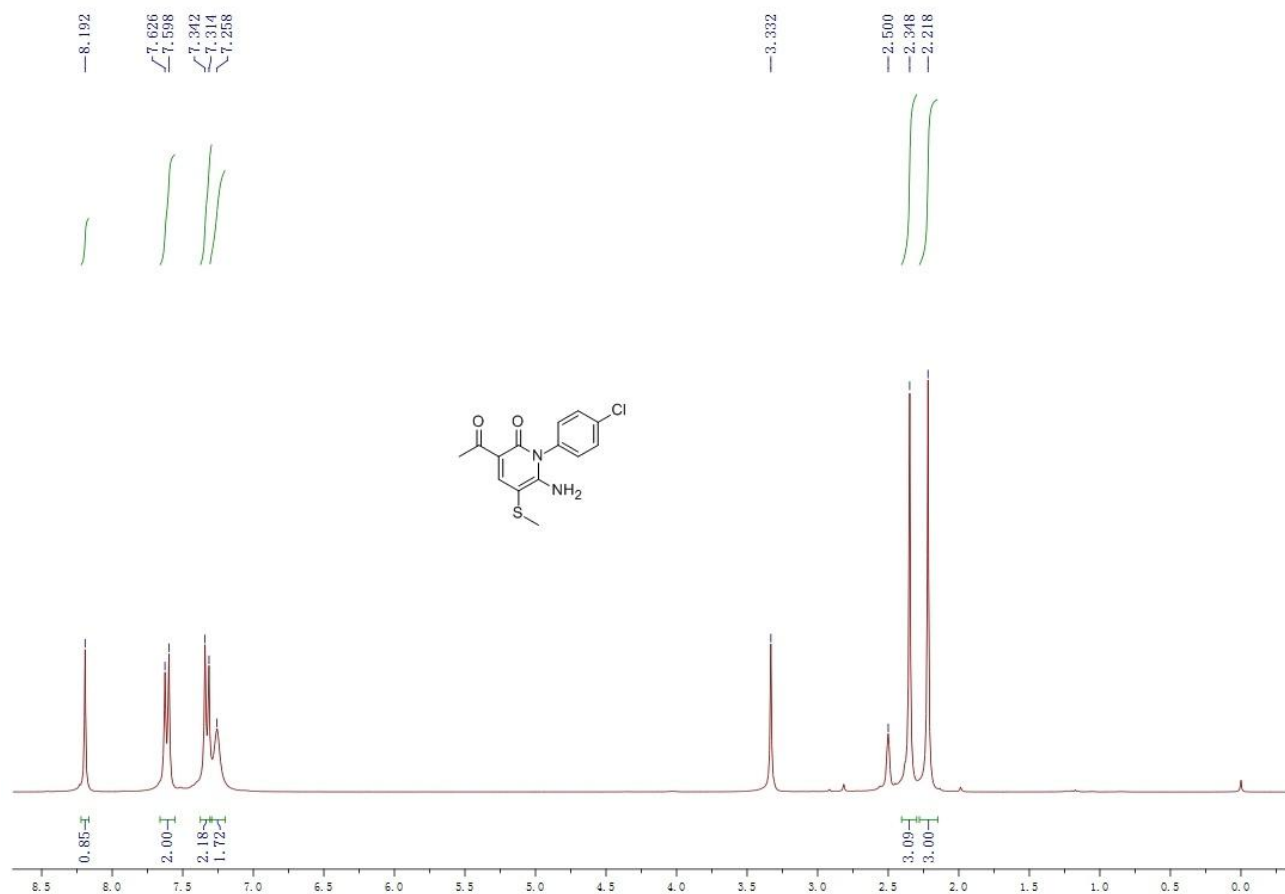
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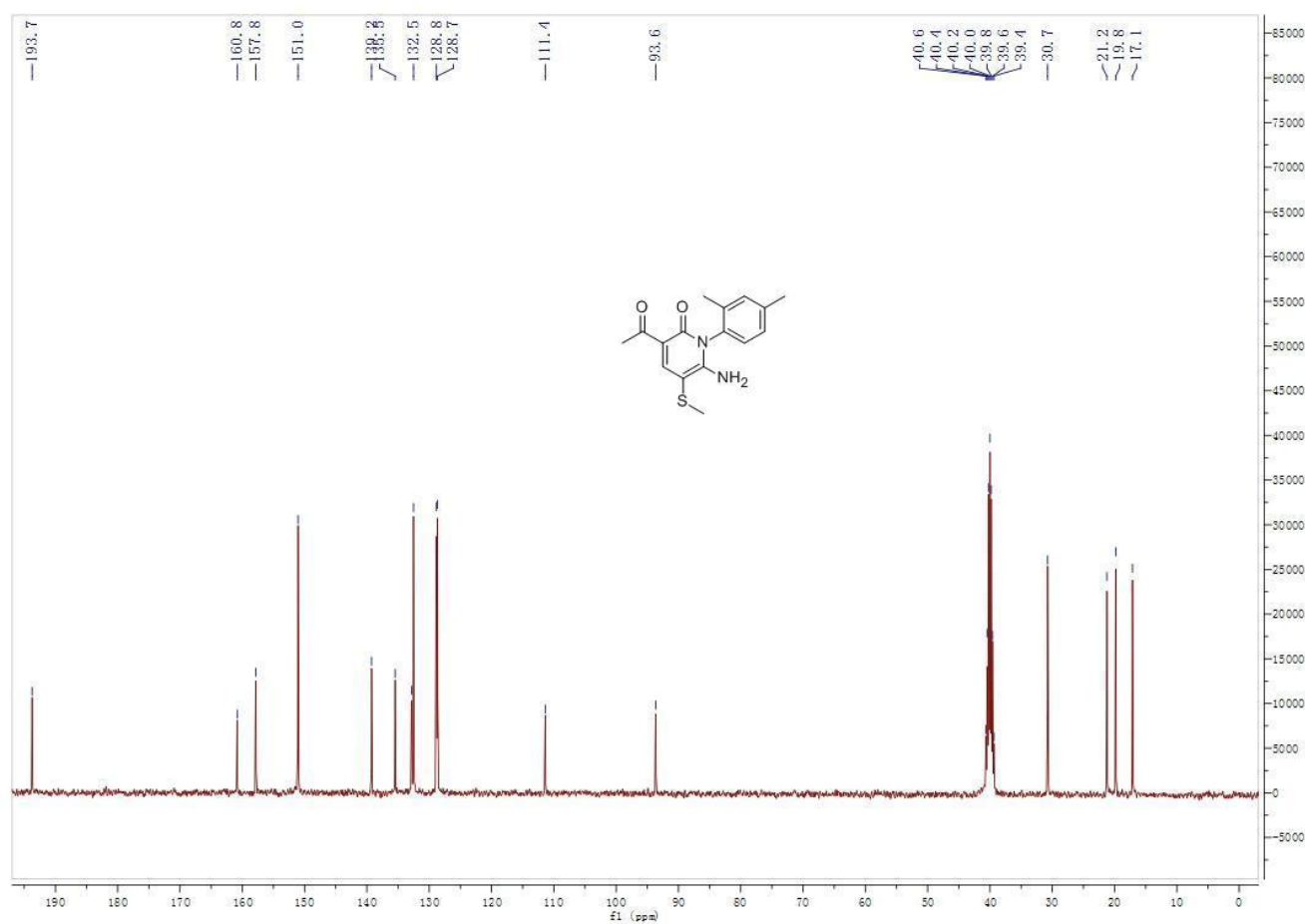
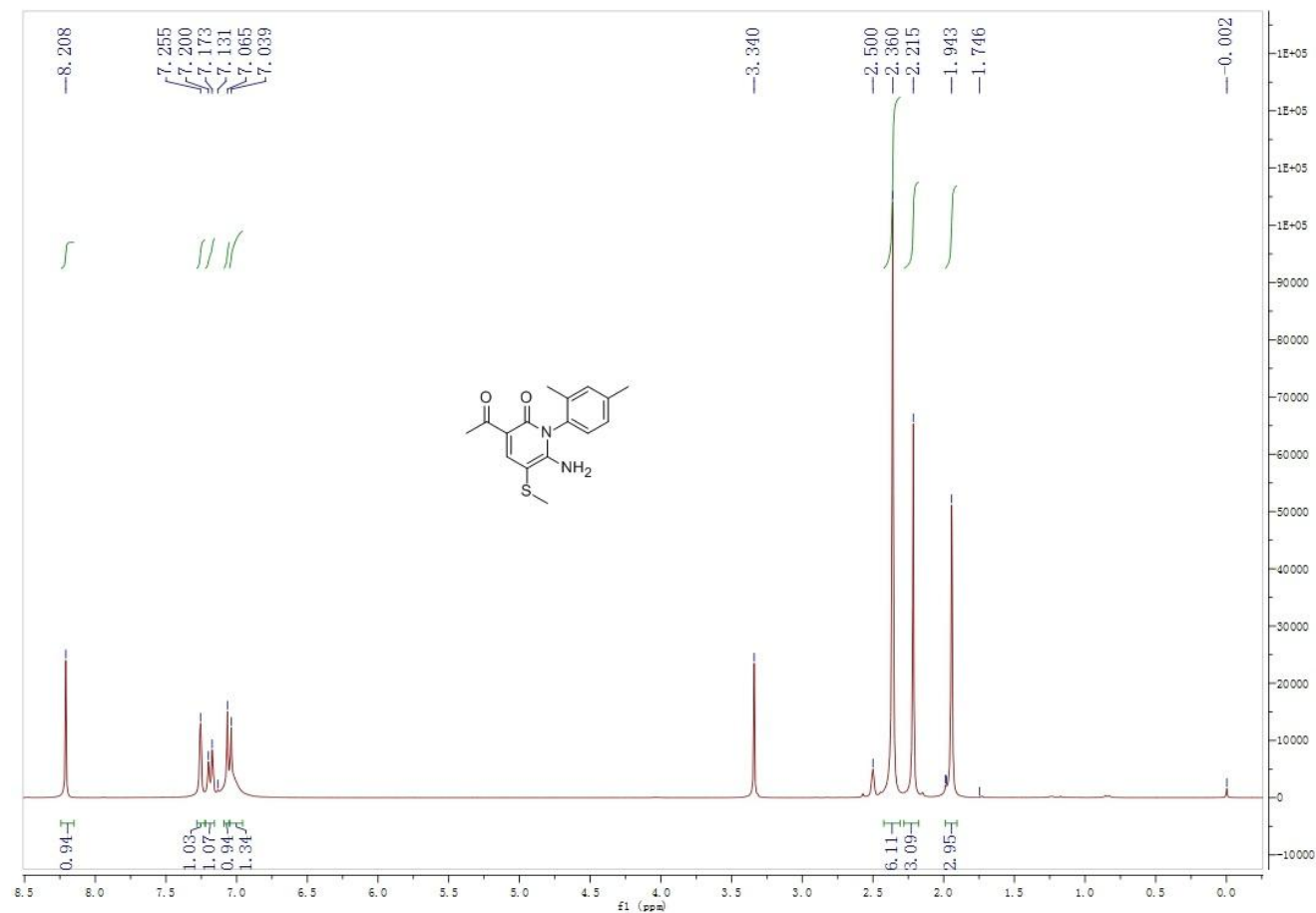
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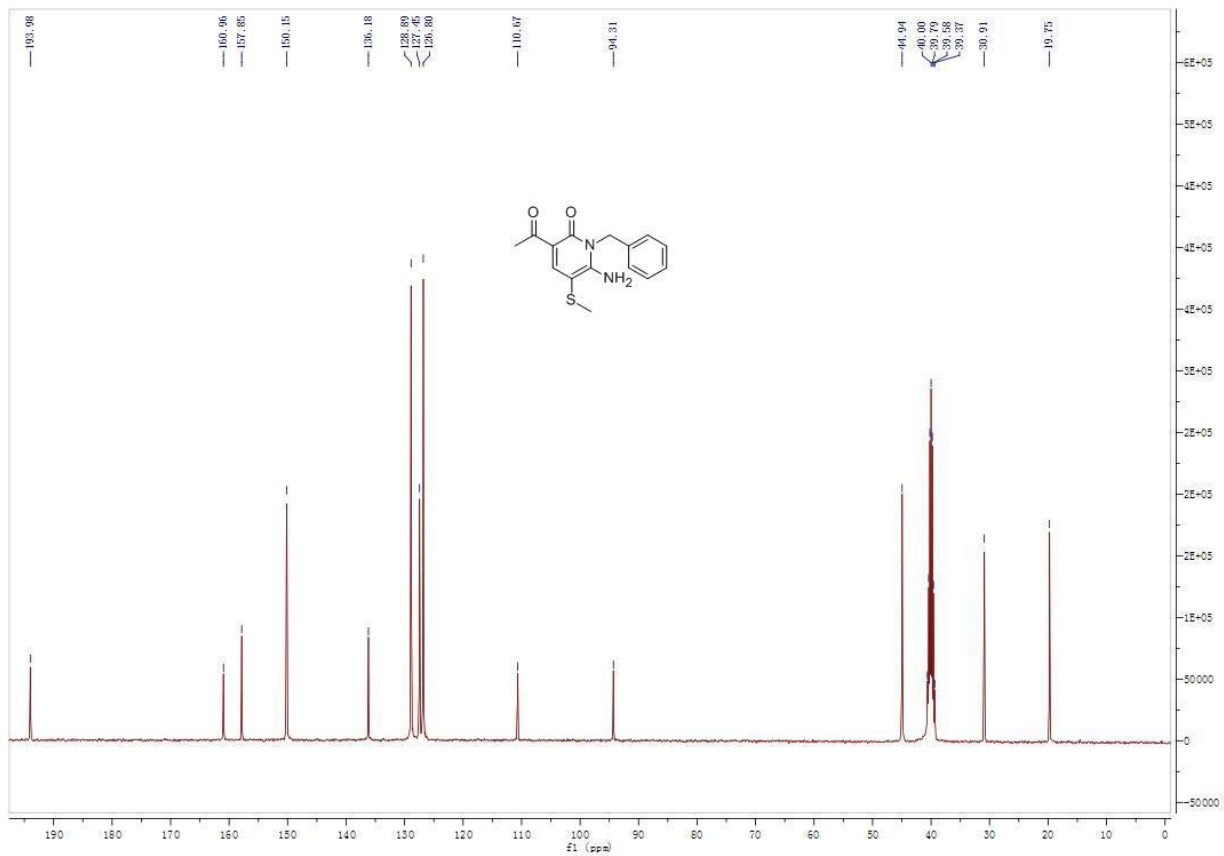
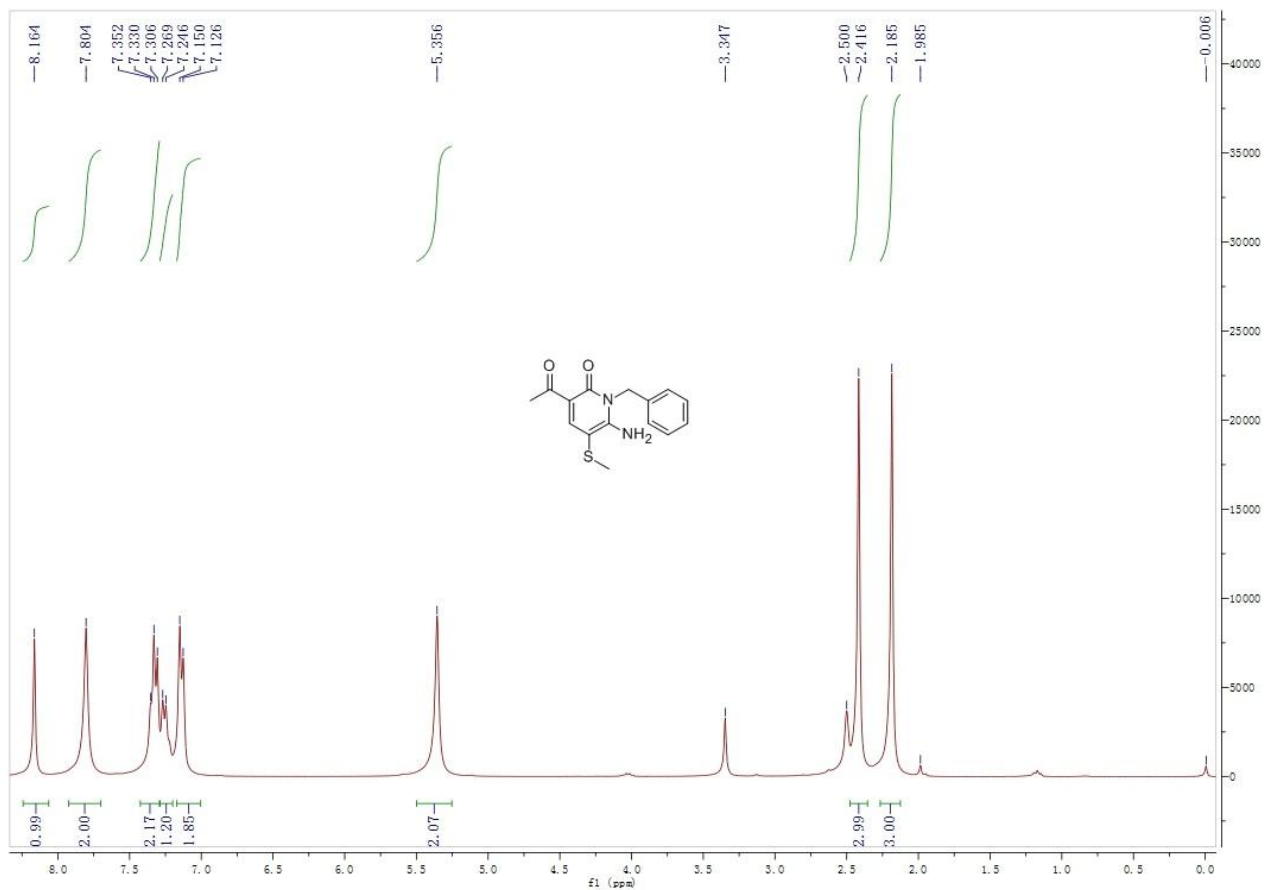
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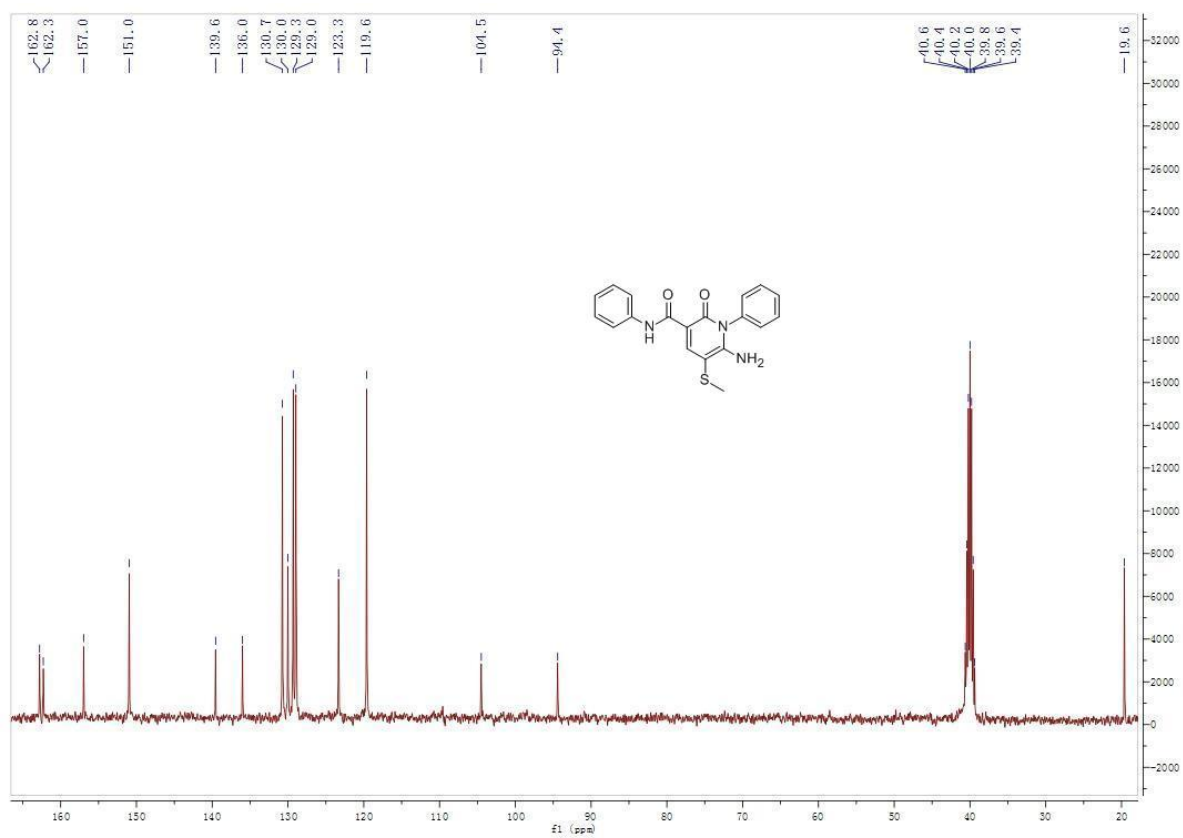
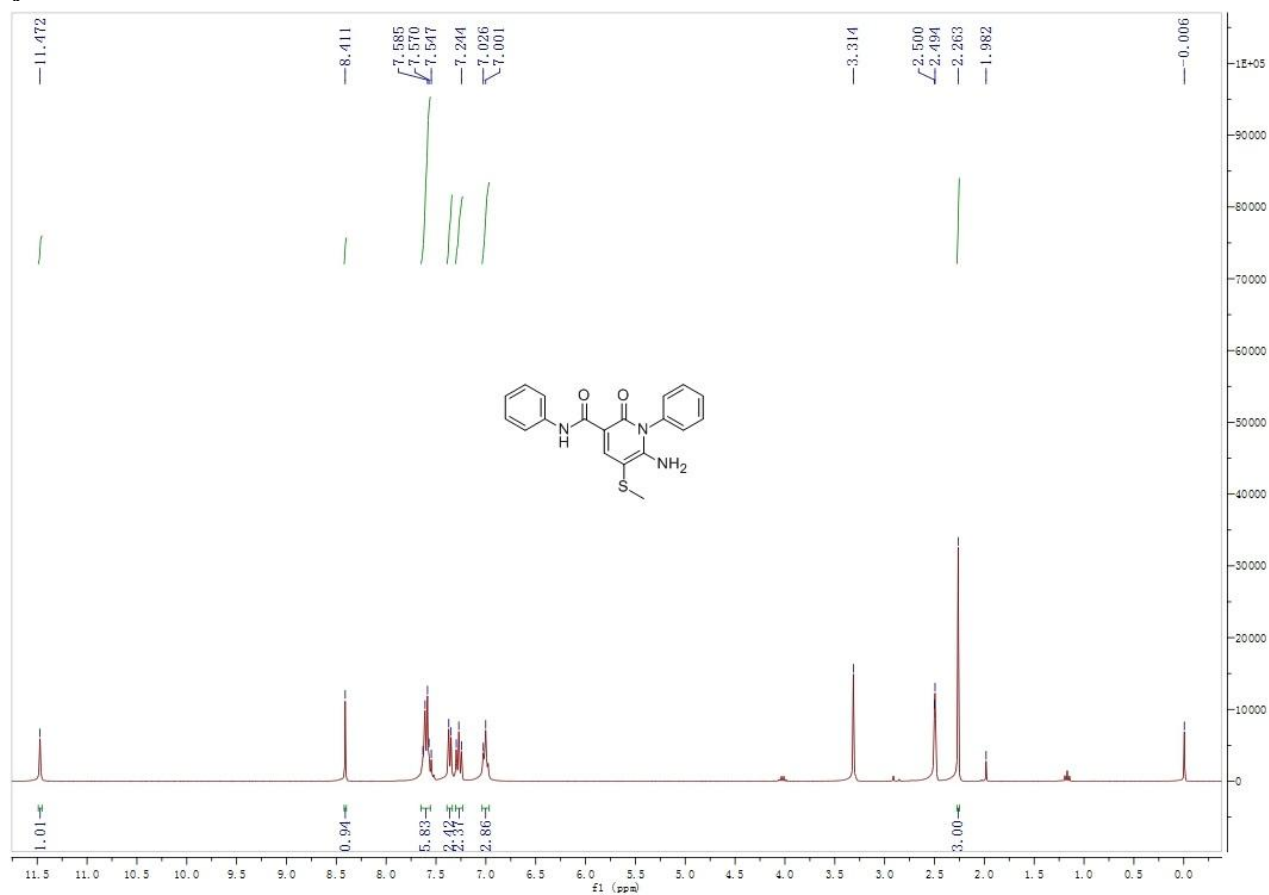
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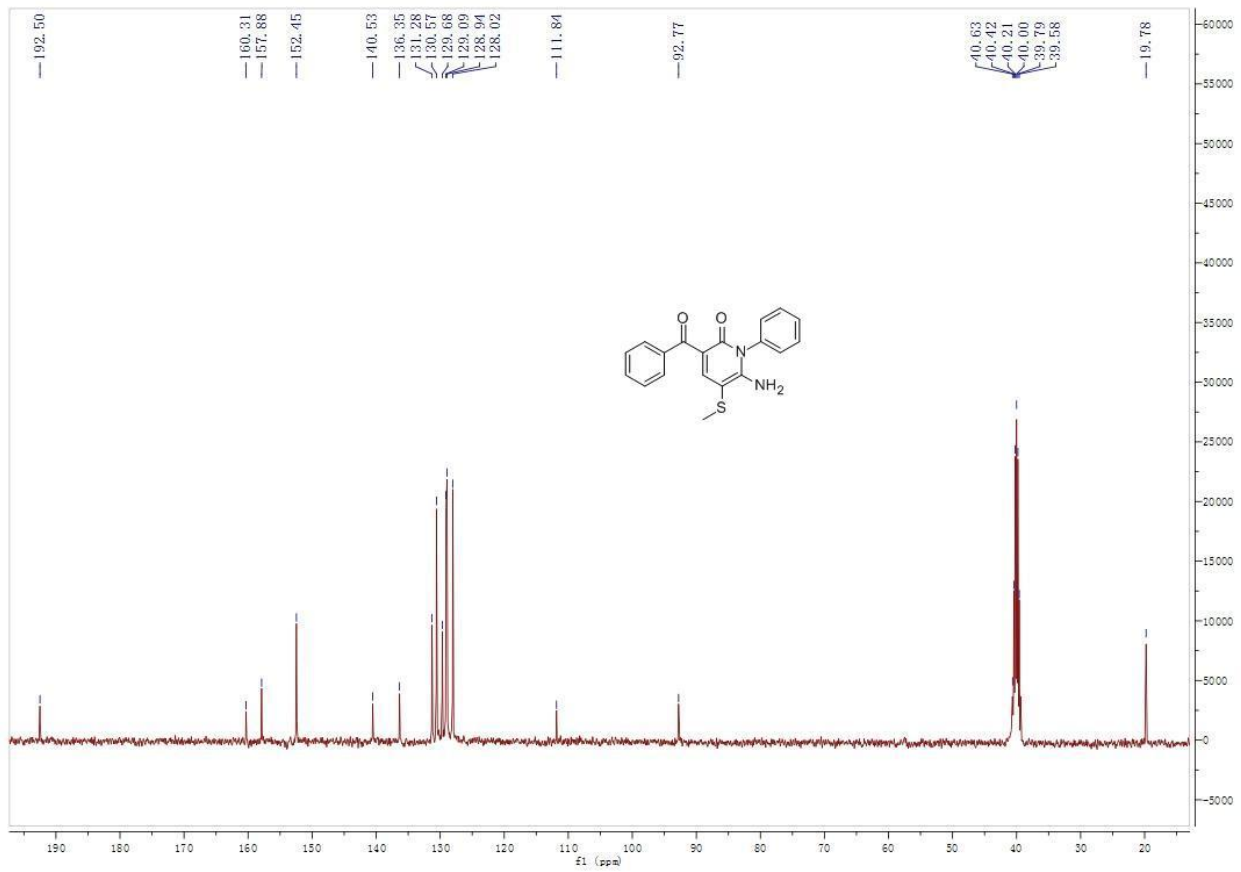
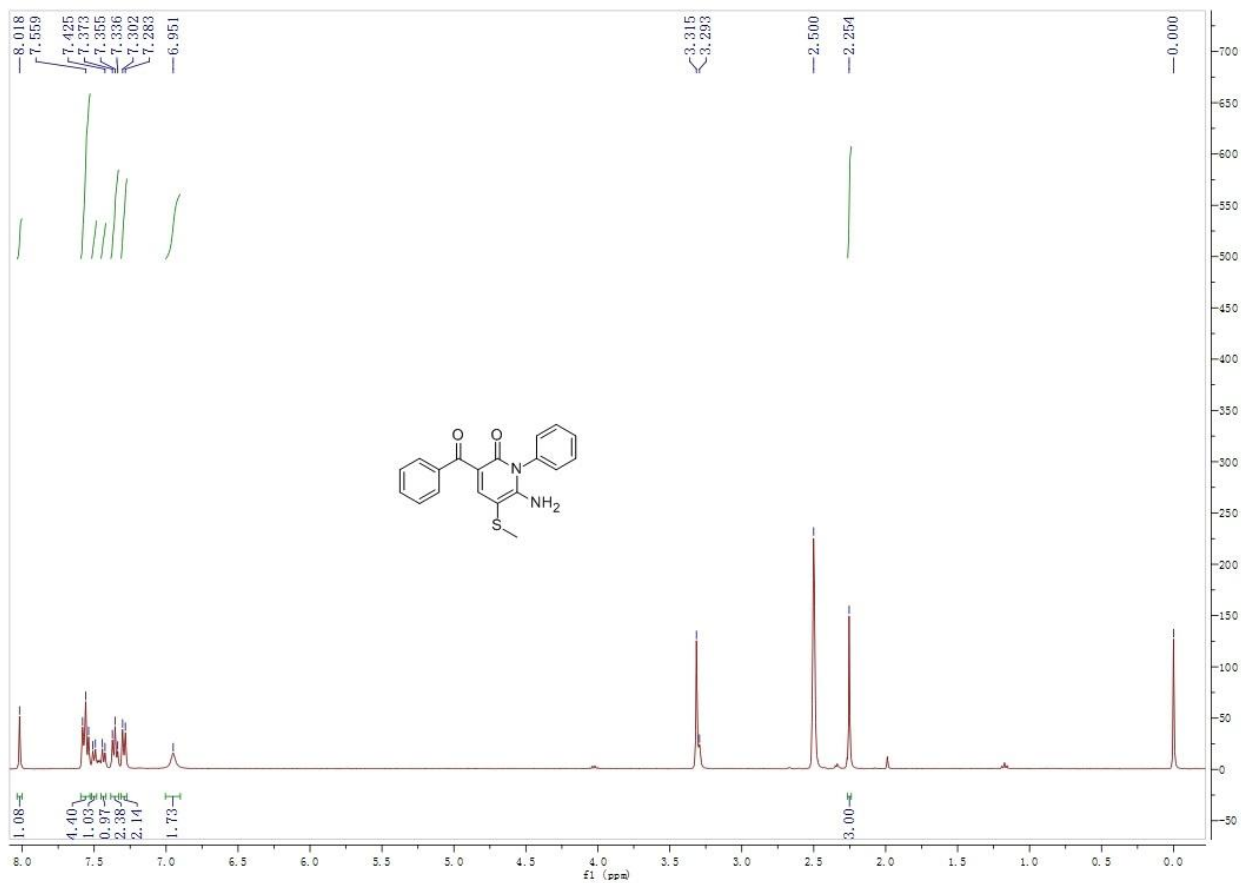
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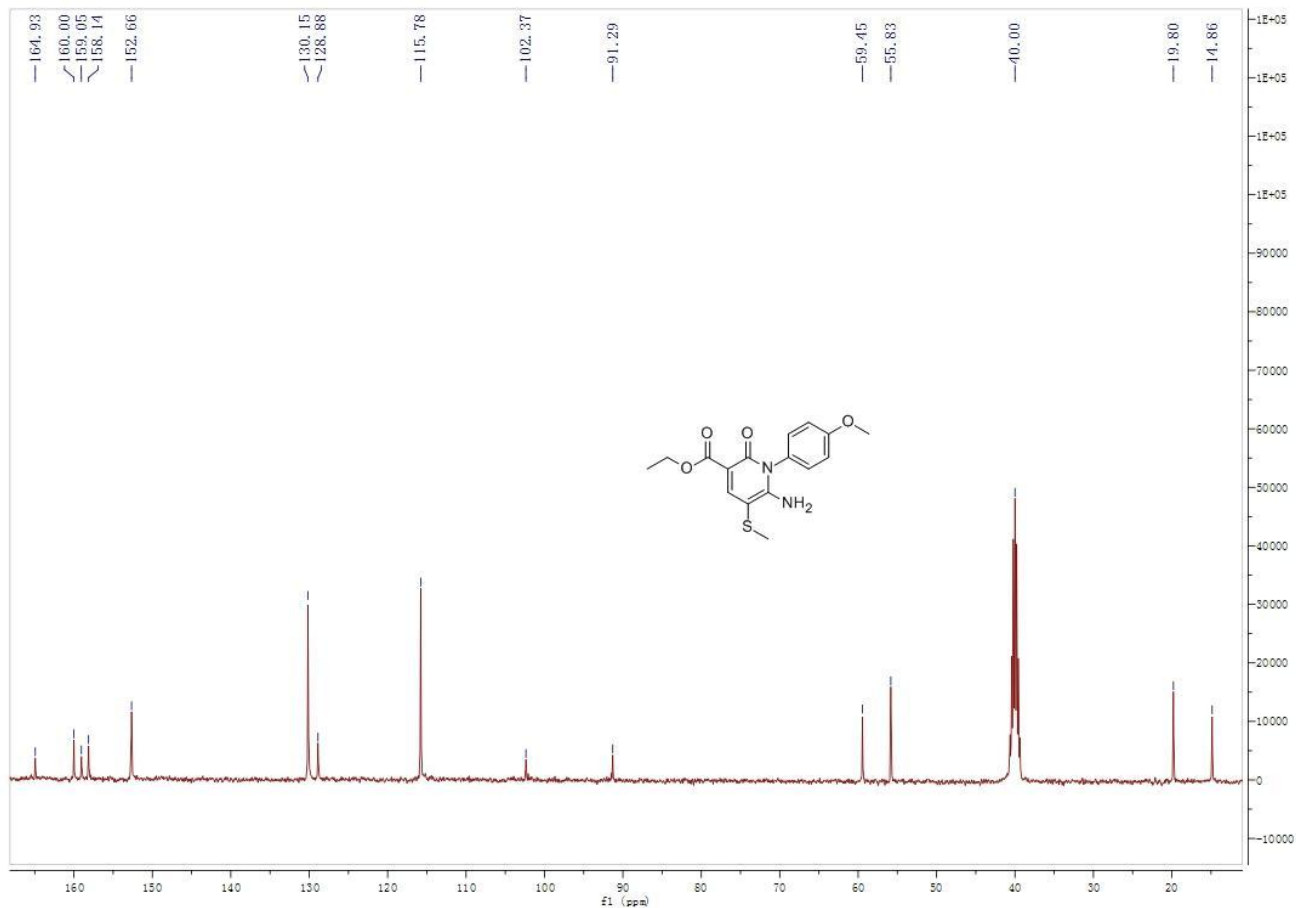
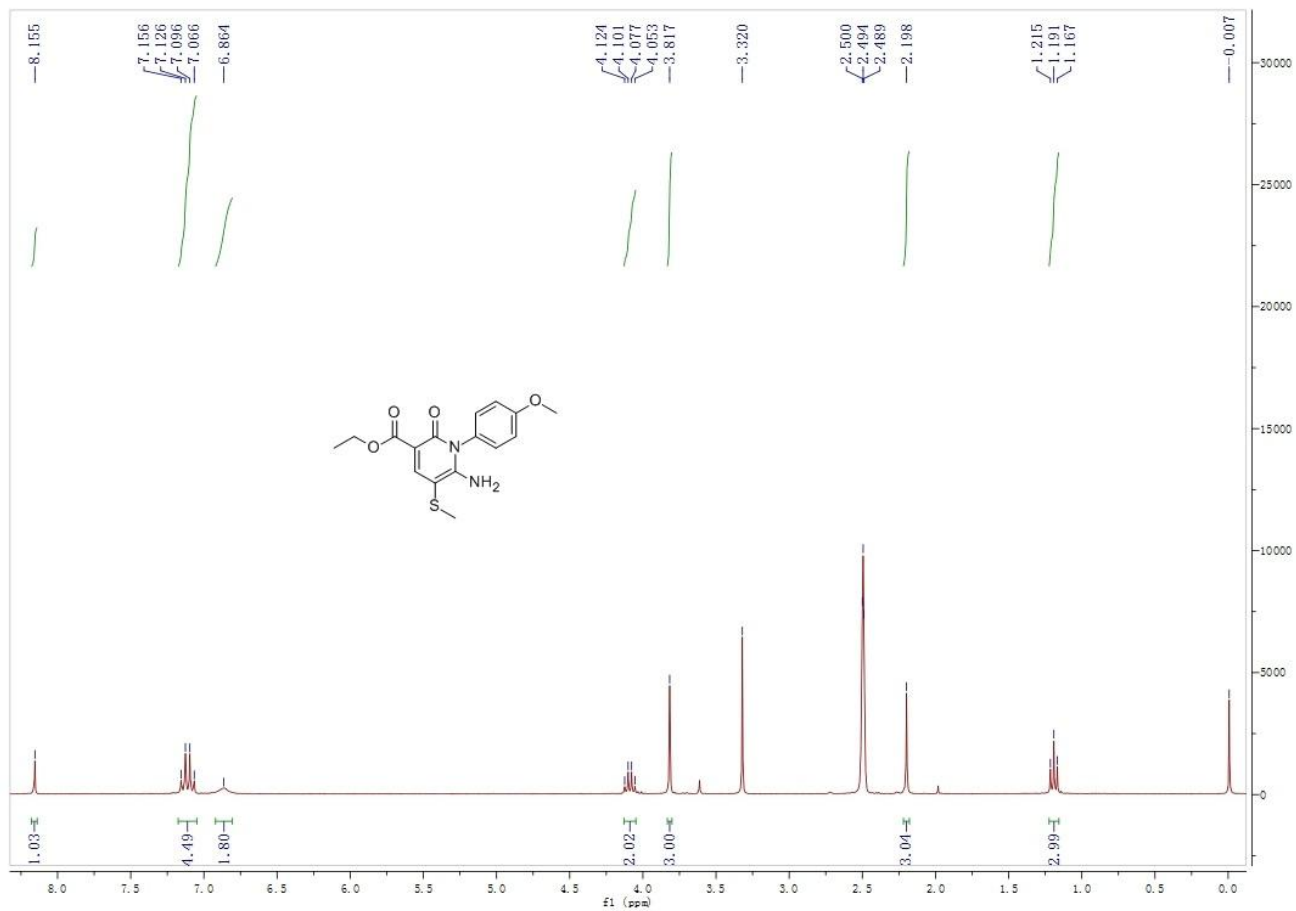


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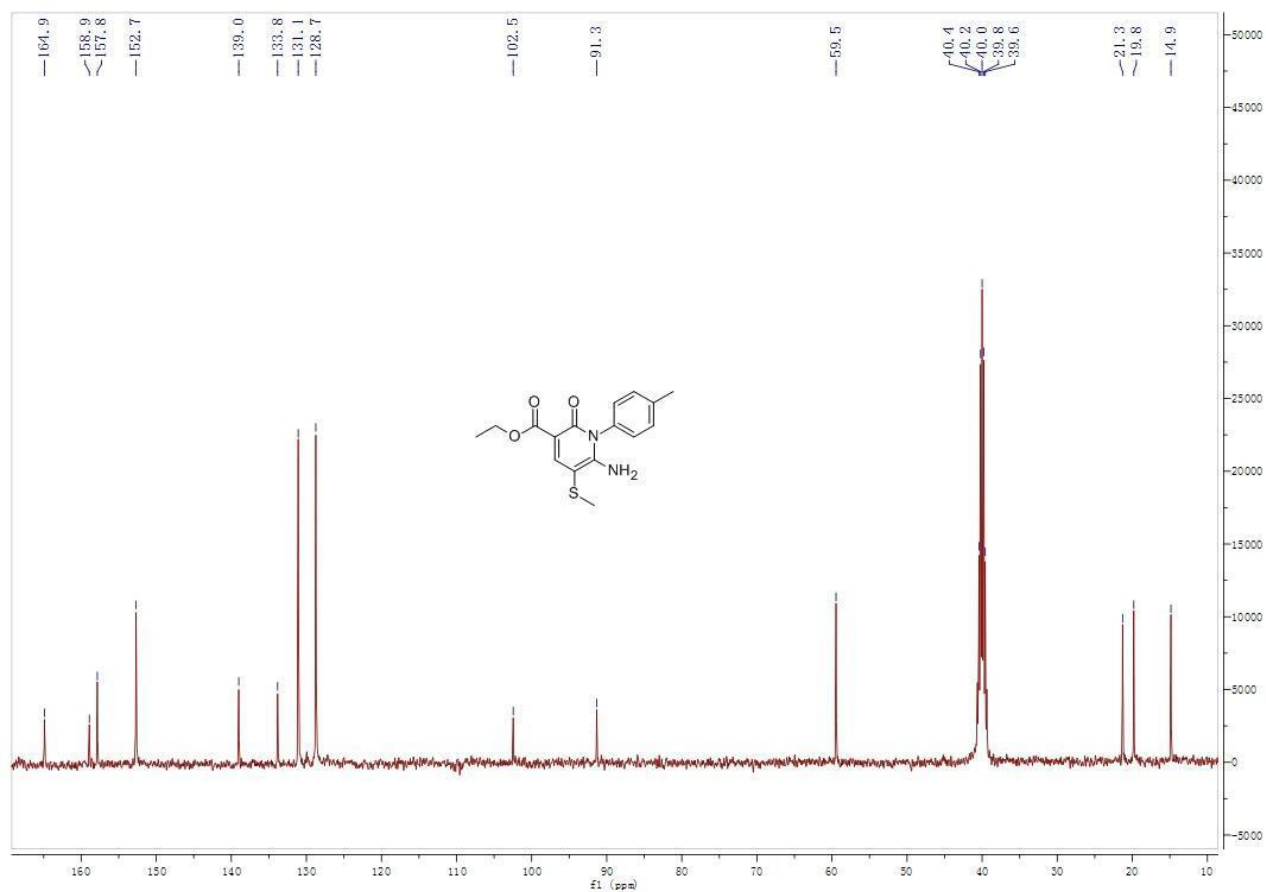
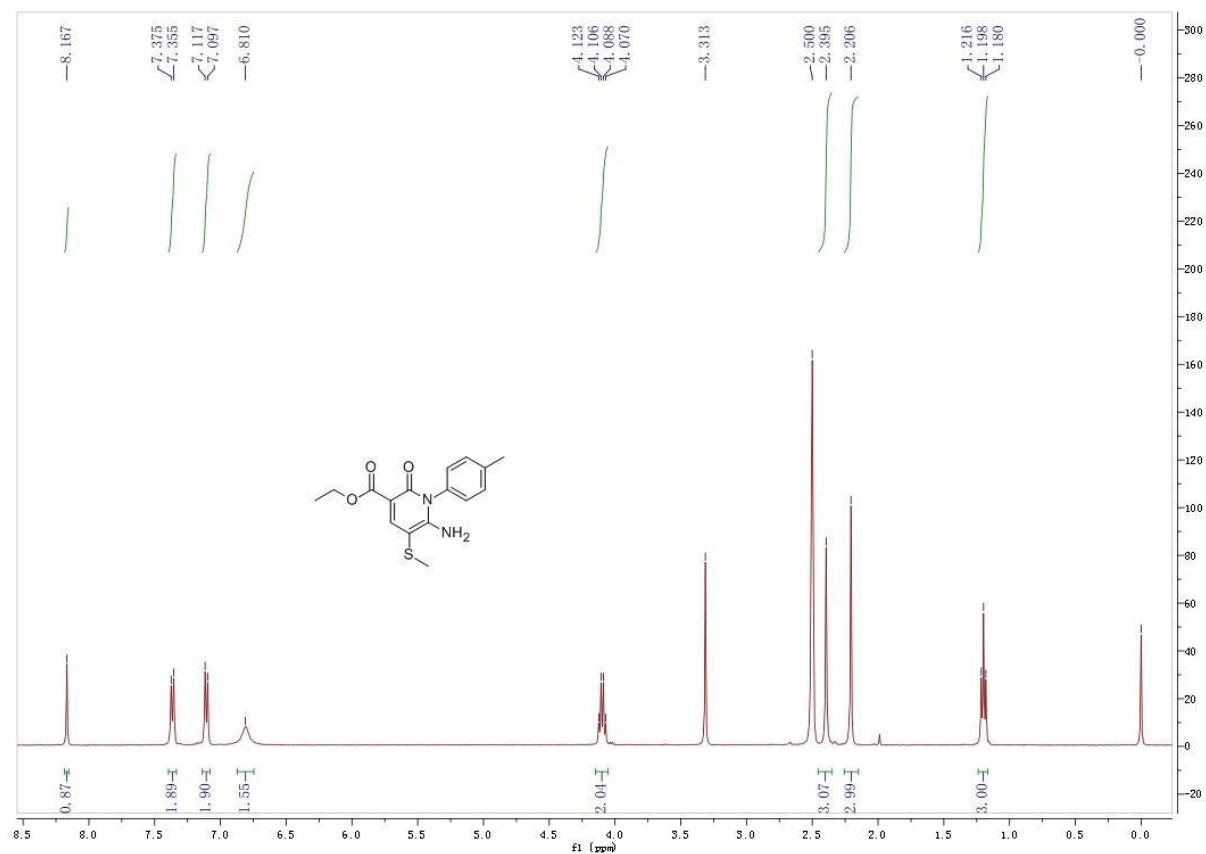


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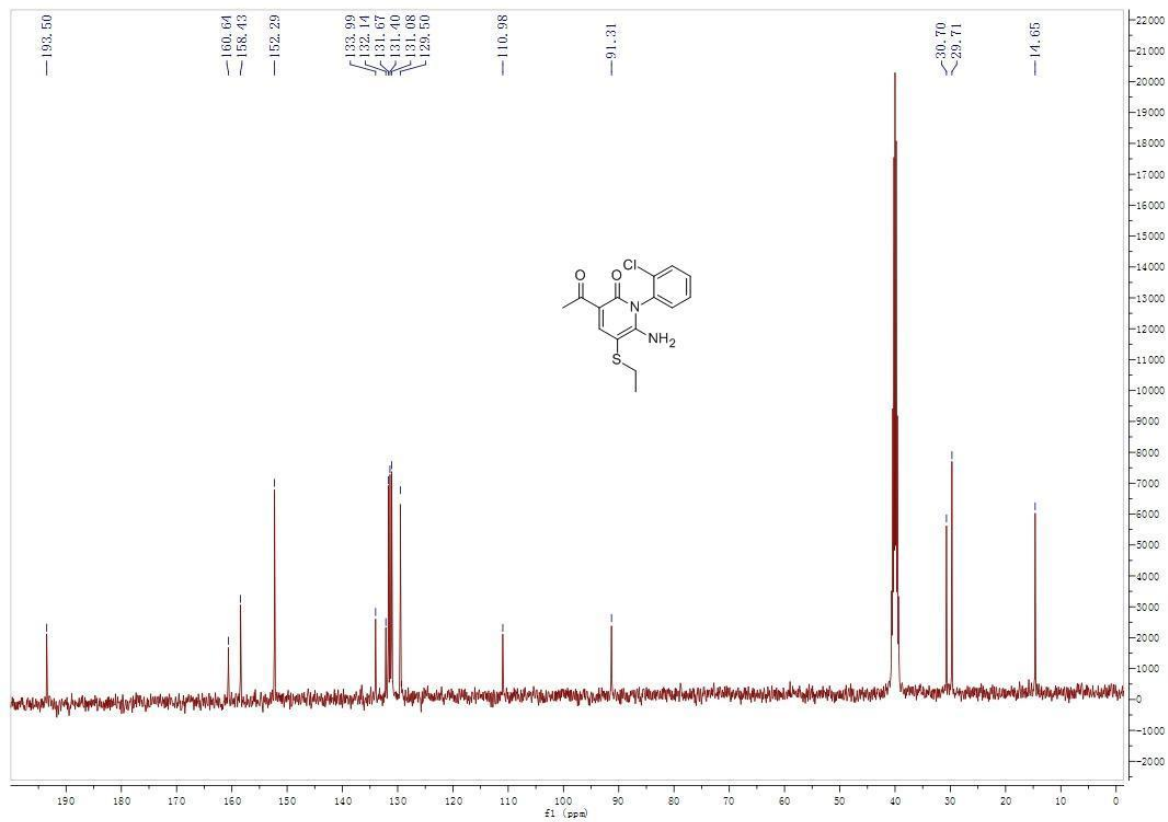
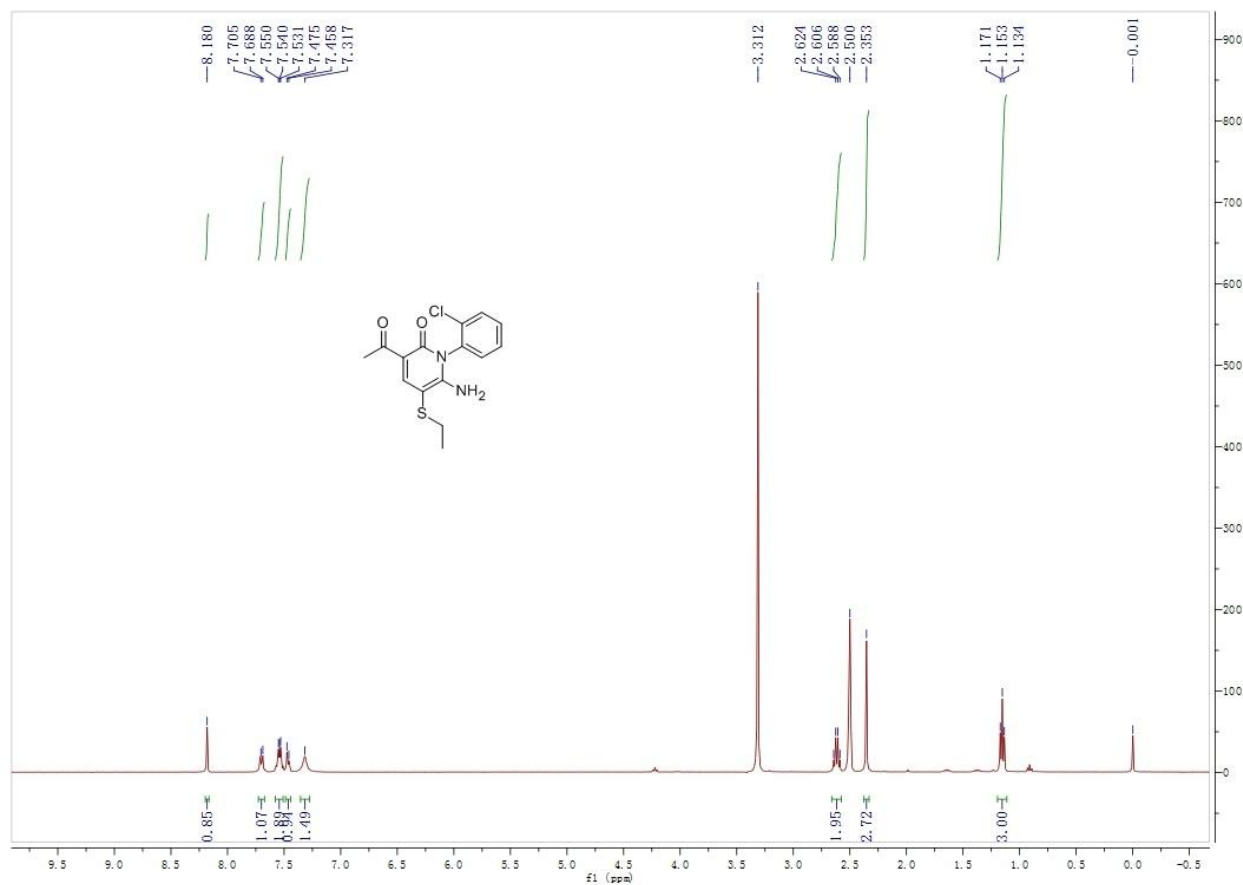


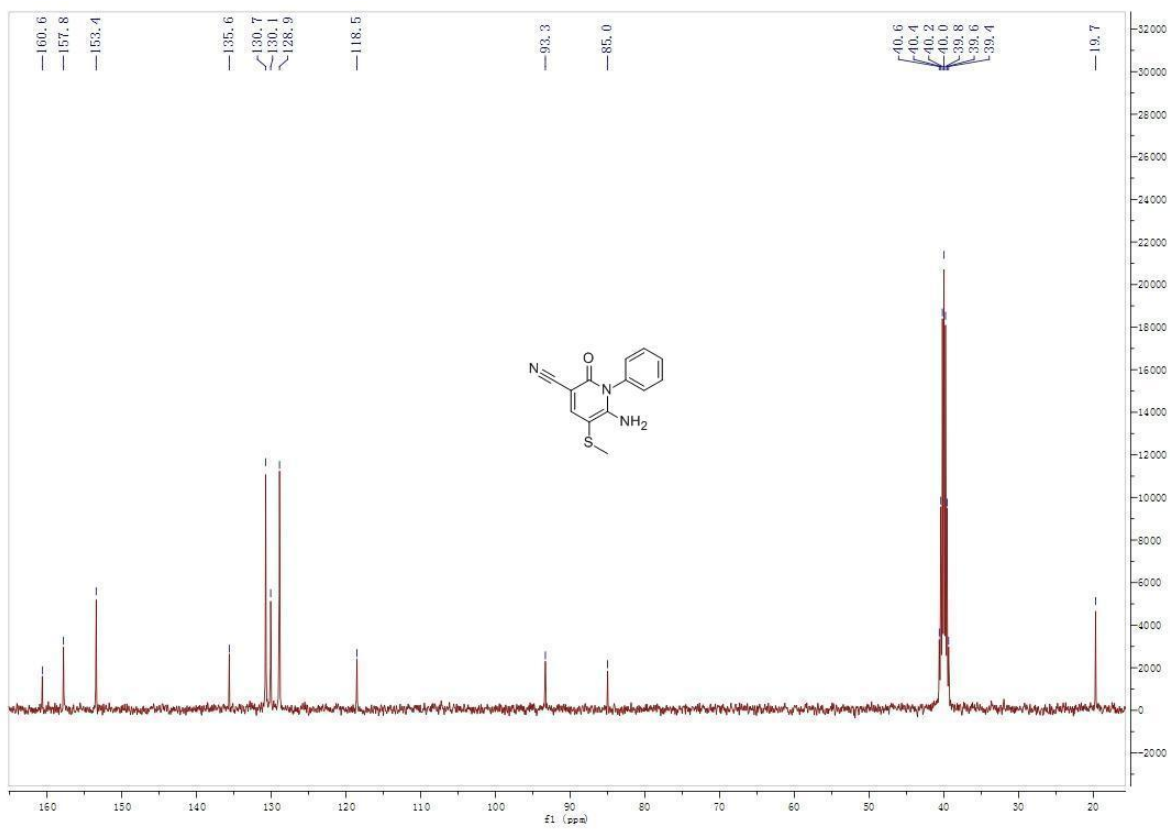
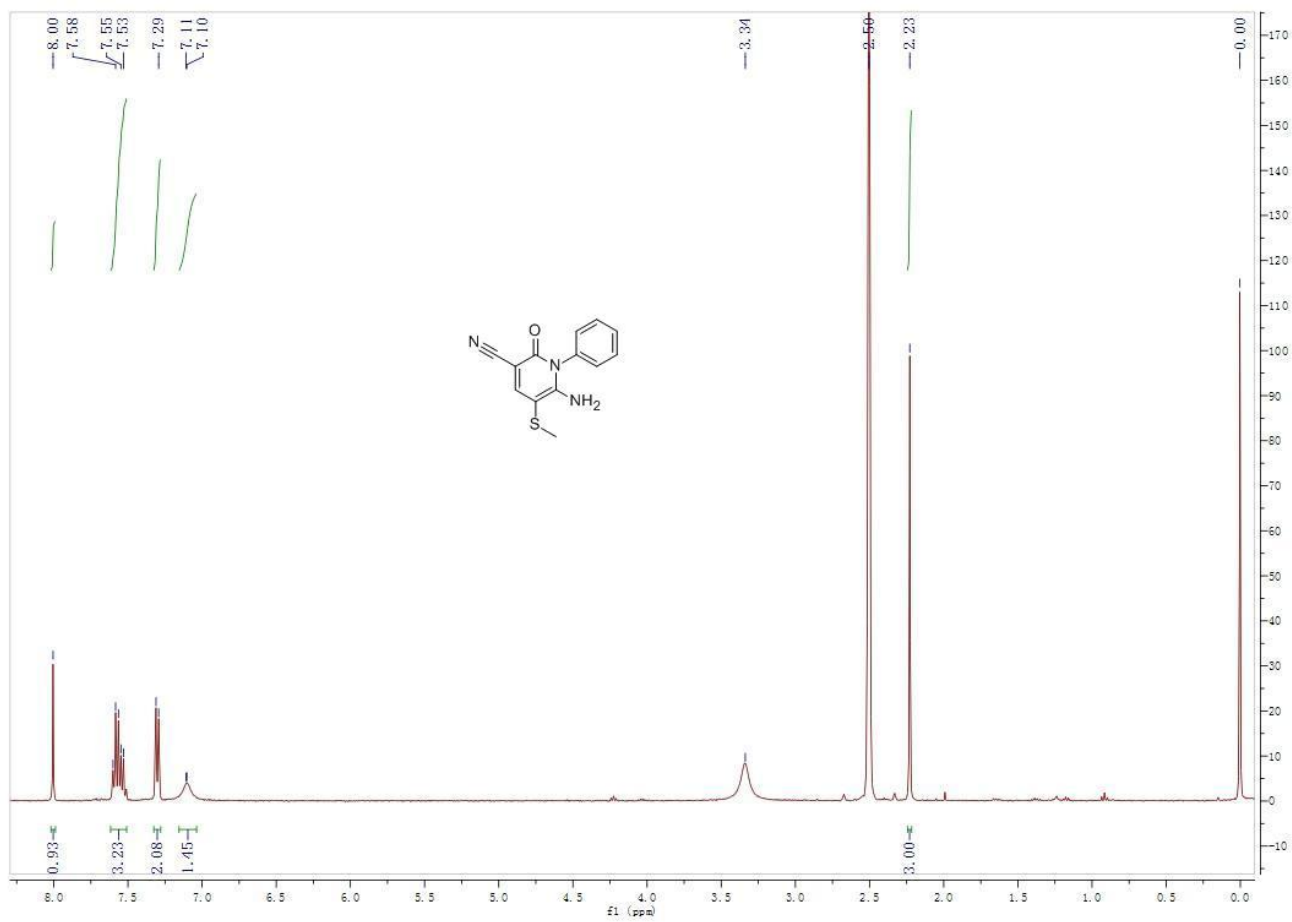


3m

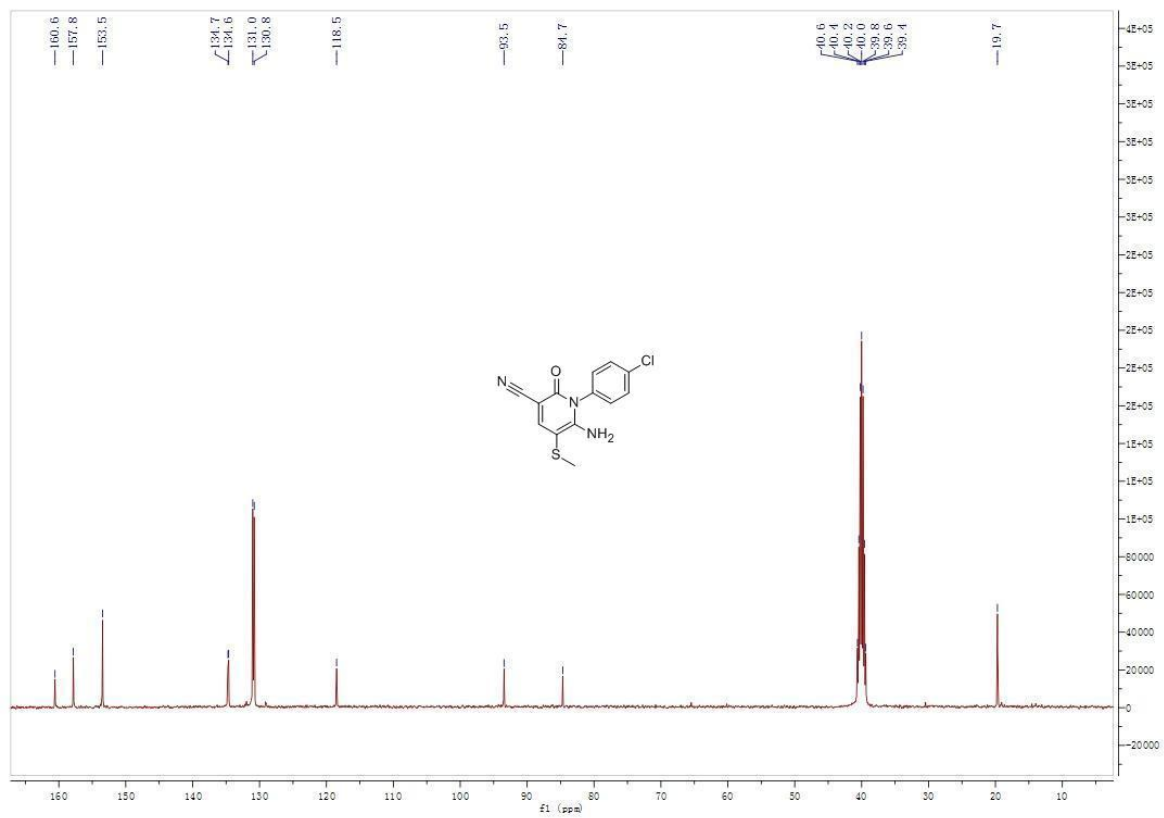
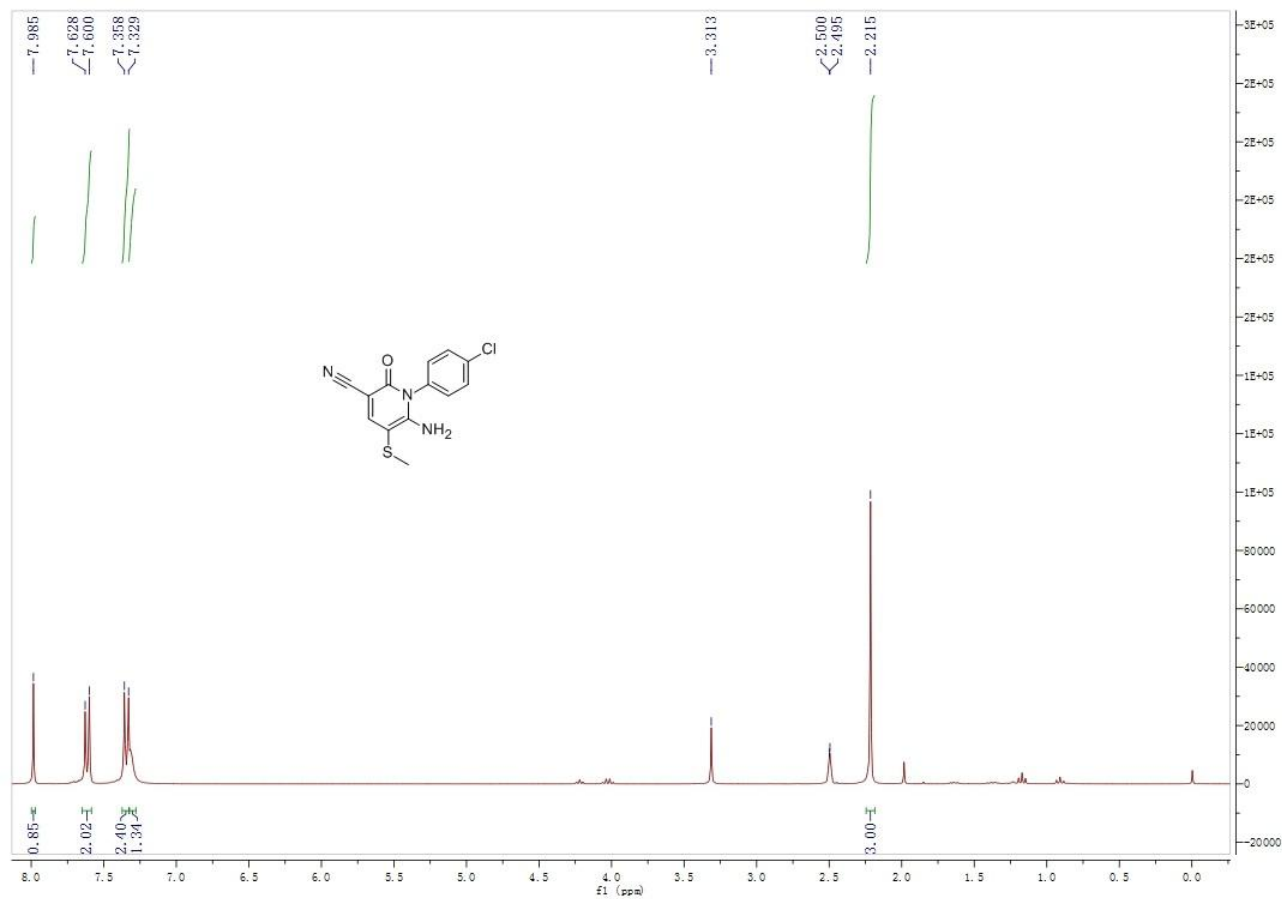


3n





3p



3q

