

Supplementary Information

Cyanomethylative cyclization of unactivated alkenes with acetonitrile for the synthesis of cyano-containing ring-fused quinazolinones

Han Liu, Zixian Yang, Gao Huang, Jin-Tao Yu* and Changduo Pan*

Email: yujintao@cczu.edu.cn; panchangduo@jsut.edu.cn

Table of Contents

1. General Considerations	S2
2. General Synthetic Procedures	S2
3. Mechanism Studies	S4
4. Characterization Data for the Products	S6
5. References	S19
6. Copies of the ¹H NMR and ¹³C NMR Spectra	S20

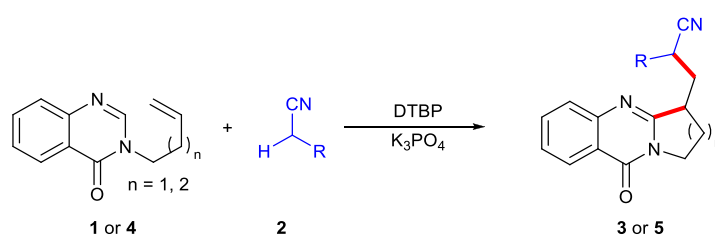
1. General Considerations

General Information: Unless otherwise noted, all chemicals were purchased and used without further purification. ^1H NMR and ^{13}C NMR spectra were recorded at ambient temperature on a 300 or 400 MHz NMR spectrometer (75 or 100 MHz for ^{13}C). NMR experiments are reported in δ units, parts per million (ppm), and were referenced to CDCl_3 (d 7.26 or 77.0) as the internal standard. The coupling constants J are given in Hz. Column chromatography was performed using EM Silica gel 60 (300-400 mesh).

2. General Synthetic Procedures

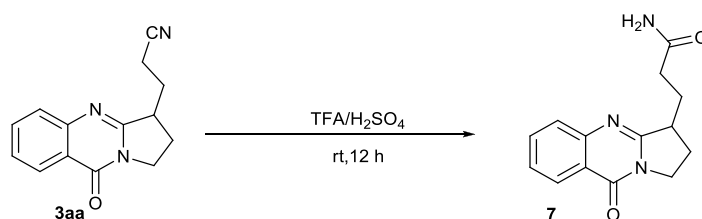
All quinazolinone derivatives **1** and **4** were prepared according to the previous reports.¹

General procedure for the synthesis of ring-fused quinazolinones (3 or 5):



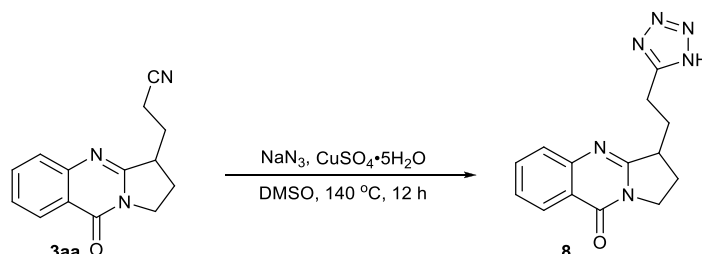
Under air, the mixture of **1** or **4** (0.2 mmol), DTBP (3 equiv.), K_3PO_4 (2 equiv.) and alkyl nitrile **2** (2 mL) were added into a Schlenk tube and sealed. The mixture was stirred at $140\text{ }^\circ\text{C}$ for 16 hours. Then, the solvent was evaporated under reduced pressure, and the residue was purified by silica gel flash column chromatography to obtain product **3** or **5**.

Derivatization of the cyanomethylated ring-fused quinazolinone products

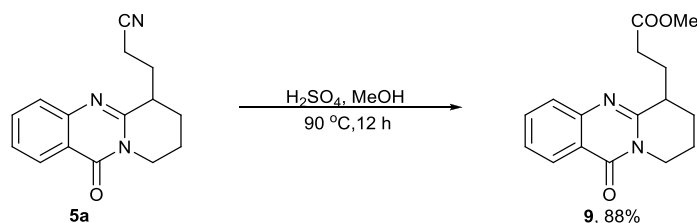


A mixture of **3aa** (48 mg, 0.2 mmol) in 2.0 mL of $\text{TFA}-\text{H}_2\text{SO}_4$ (4:1, v/v) was stirred overnight at room temperature.² After completion of the reaction, the mixture

was poured into ice water and neutralized with 1 M NaOH. The mixture was extracted with EtOAc, dried over anhydrous sodium sulfate, evaporated under vacuum and purified by silica gel flash column chromatography to give **7** (43.6 mg, 85% yield) as a white solid.



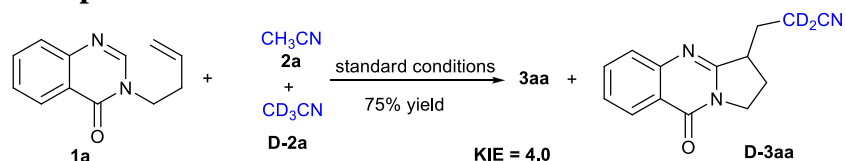
A mixture of **3aa** (48 mg, 0.2 mmol), sodium azide (26 mg, 0.4 mmol), cupric sulfate pentahydrate (2 mol%) in DMSO (2 mL) were stirred at $140\text{ }^\circ\text{C}$ for 12 h.³ After completion of the reaction, the mixture was cooled and extracted with EtOAc, dried over anhydrous sodium sulfate, evaporated under vacuum and purified by silica gel flash column chromatography to give compound **8** as colorless oil (28.0 mg 50% yield).



Compound **5a** (51 mg, 0.2 mmol) was treated with 0.4 mL concd H_2SO_4 in 4 mL methanol at $90\text{ }^\circ\text{C}$ for 12 h.⁴ After completion, the mixture was neutralized by saturated NaHCO_3 , extracted with EtOAc, dried over anhydrous sodium sulfate, evaporated under vacuum and purified by silica gel flash column chromatography to give compound **9** (50.4 mg, 88% yield).

2. Mechanism Studies

2.1 The KIE experiment:



The mixture of **1a** (0.1 mmol), DTBP (3 equiv), K_3PO_4 (2 equiv), CH_3CN (0.5 mL) and CD_3CN (0.5 mL) was added to a sealed tube. The mixture was stirred at 140 °C for 16 hours. Then, the solvent was evaporated under reduced pressure, and the residue was purified by silica gel flash column chromatography to obtain product **3aa** and **D-3aa** in 75% yield. A KIE value of 4.0 was observed.

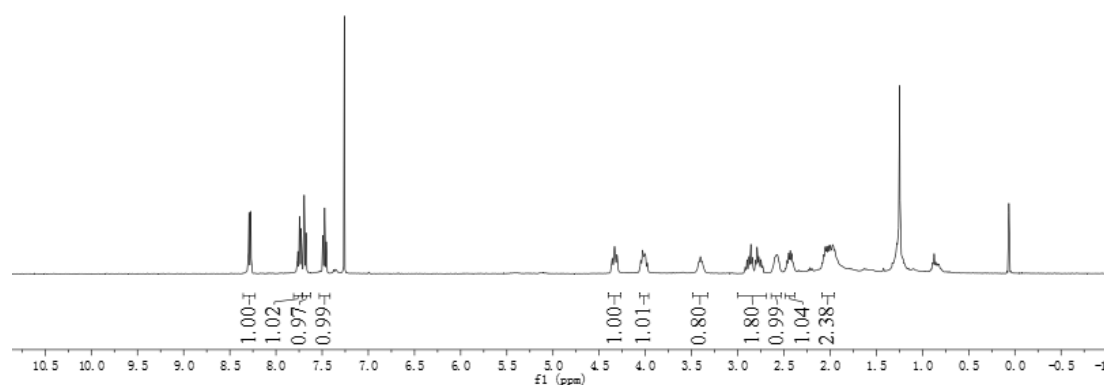


Figure S1 ^1H NMR spectrum of the KIE experiment

2.2 Radical inhibiting and trapping experiment

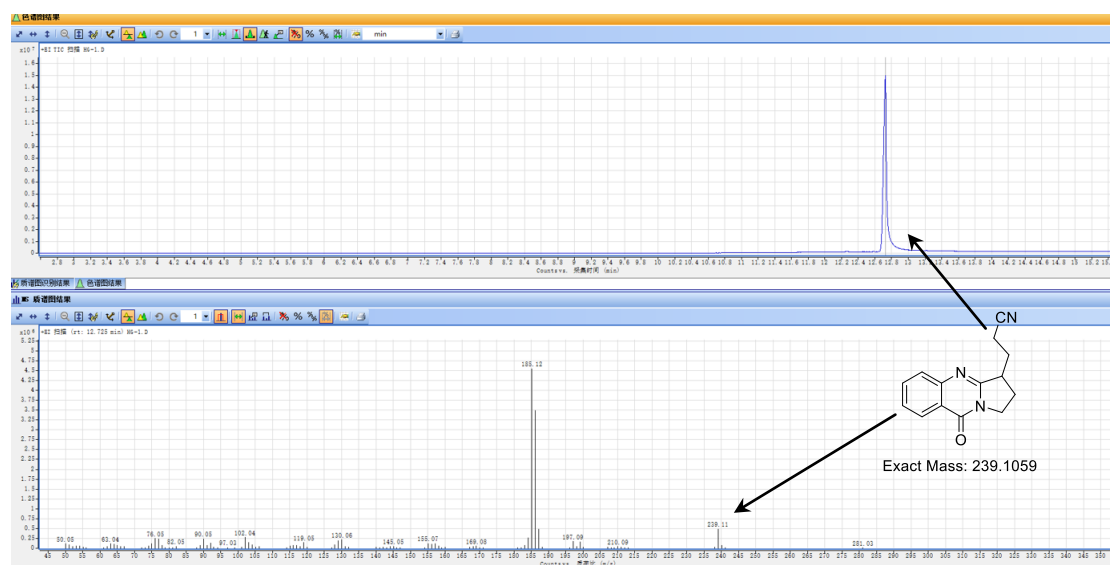


Figure S2 GC-MS spectra of **3aa**.

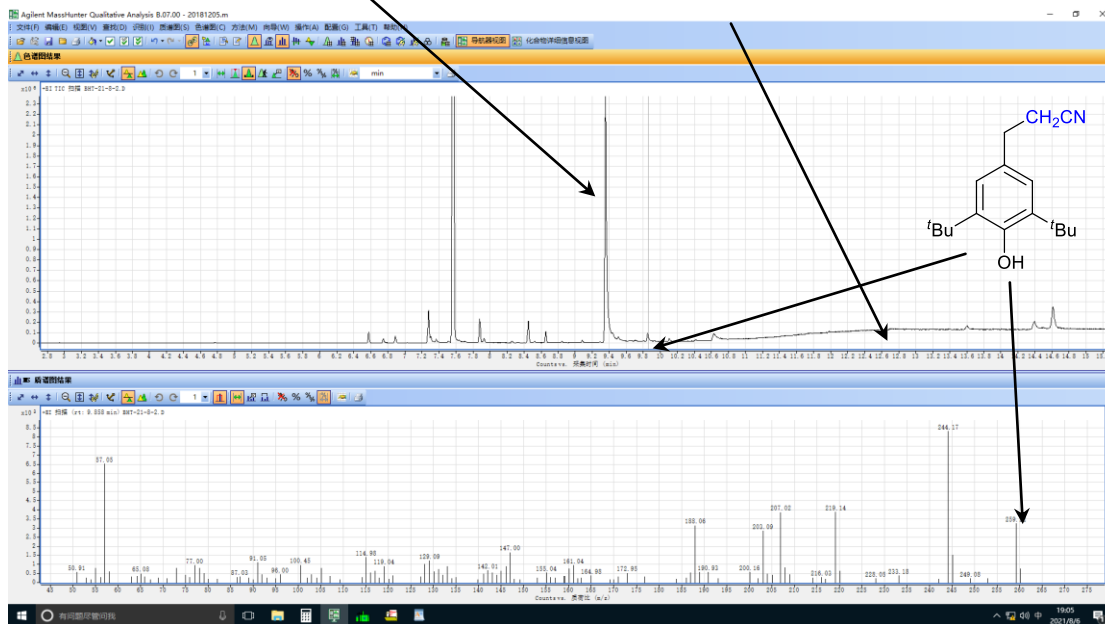
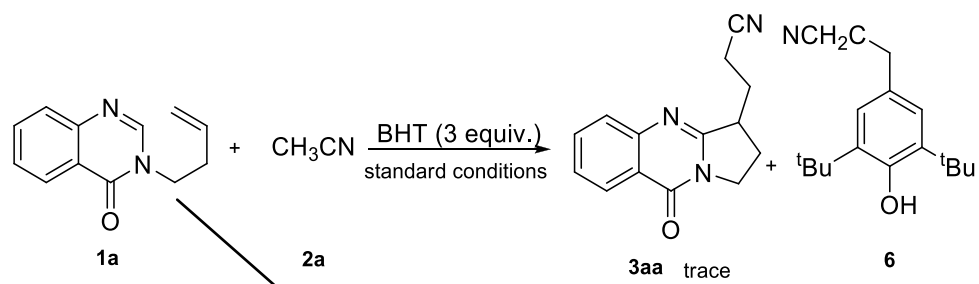
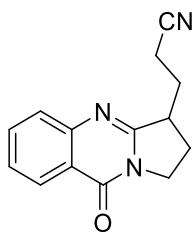
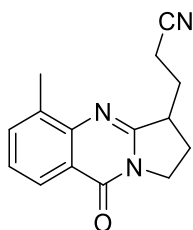


Figure S3 GC spectrum of the reaction mixture and MS spectrum of adduct 6.

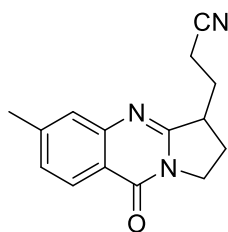
4. Characterization Data for the Products



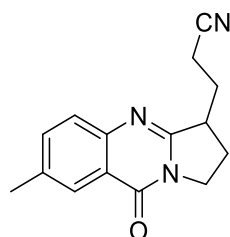
3-(9-Oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanenitrile (3aa, 37 mg, 77% yield), yellow oil; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.20 (dd, $J = 8.0, 1.6$ Hz, 1H), 7.70-7.66 (m, 1H), 7.59 (dd, $J = 8.3, 1.2$ Hz, 1H), 7.42-7.38 (m, 1H), 4.29-4.23 (m, 1H), 3.97-3.90 (m, 1H), 3.35-3.27 (m, 1H), 2.86-2.68 (m, 2H), 2.55-2.47 (m, 1H), 2.40-2.31 (m, 1H), 2.02-1.84 (m, 2H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 160.5, 160.0, 148.8, 134.0, 127.0, 126.3, 126.1, 120.6, 119.4, 44.5, 42.1, 27.8, 26.4, 15.2; HRMS (ESI-TOF) m/z calcd for $\text{C}_{14}\text{H}_{13}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 262.0951, found 262.0948.



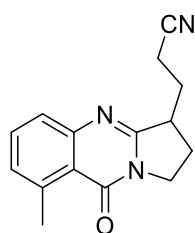
3-(5-Methyl-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanenitrile (3ba, 33.2 mg, 65% yield), yellow solid, mp: 149-151 $^\circ\text{C}$; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 8.08 (dd, $J = 8.0, 1.5$ Hz, 1H), 7.55 (d, $J = 7.2$ Hz, 1H), 7.31 (t, $J = 7.6$ Hz, 1H), 4.32-4.24 (m, 1H), 4.00-3.90 (m, 1H), 3.40-3.29 (m, 1H), 3.02-2.78 (m, 2H), 2.55 (m, 4H), 2.38-2.26 (m, 1H), 2.09-1.83 (m, 2H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 161.1, 158.7, 147.3, 135.5, 134.9, 126.1, 124.0, 120.6, 119.5, 44.5, 42.0, 28.3, 26.8, 17.6, 15.3; HRMS (ESI-TOF) m/z calcd for $\text{C}_{15}\text{H}_{15}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 276.1107, found 276.1105.



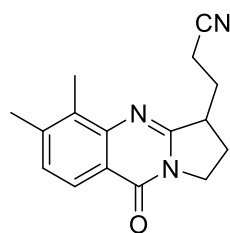
3-(6-Methyl-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanenitrile (3ca, 35.6 mg, 70% yield), yellow oil; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.13 (d, $J = 8.1$ Hz, 1H), 7.43 (s, 1H), 7.26 (dd, $J = 8.2, 1.5$ Hz, 1H), 4.31-4.26 (m, 1H), 4.00-3.92 (m, 1H), 3.37-3.29 (m, 1H), 2.89-2.71 (m, 2H), 2.58-2.50 (m, 1H), 2.47 (s, 3H), 2.47-2.33 (m, 1H), 2.05-1.89 (m, 2H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 160.7, 159.9, 148.8, 145.3, 128.2, 126.8, 126.2, 119.3, 118.3, 44.6, 42.3, 28.0, 26.6, 21.9, 15.3; HRMS (ESI-TOF) m/z calcd for $\text{C}_{15}\text{H}_{15}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 276.1107, found 276.1108.



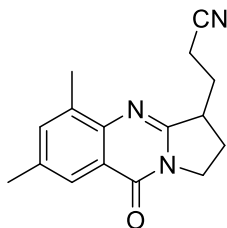
3-(7-Methyl-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanenitrile (3da), 29.5 mg, 58% yield), yellow solid, mp: 158-160 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.05 (s, 1H), 7.56 (t, $J = 2.7$ Hz, 2H), 4.34-4.28 (m, 1H), 4.03-3.96 (m, 1H), 3.39-3.33 (m, 1H), 2.90-2.73 (m, 2H), 2.60-2.55 (m, 1H), 2.48 (s, 3H), 2.44-2.38 (m, 1H), 2.05-1.92 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 160.8, 159.0, 146.7, 136.8, 135.7, 126.8, 125.8, 120.5, 119.3, 44.6, 42.2, 28.0, 26.7, 21.3, 15.3; HRMS (ESI-TOF) m/z calcd for $\text{C}_{15}\text{H}_{15}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 276.1107, found 276.1104.



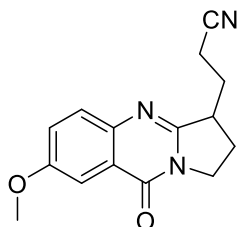
3-(8-Methyl-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanenitrile (3ea), 32.9 mg, 65% yield), yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 7.53 (t, $J = 7.7$ Hz, 1H), 7.46 (d, $J = 8.1$ Hz, 1H), 7.17 (d, $J = 7.2$ Hz, 1H), 4.26-4.21 (m, 1H), 3.96-3.89 (m, 1H), 3.34-3.30 (m, 1H), 2.84-2.71 (m, 5H), 2.55-2.48 (m, 1H), 2.41-2.32 (m, 1H), 2.03-1.87 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 161.5, 159.4, 150.5, 141.0, 133.3, 129.2, 125.3, 119.3, 119.2, 44.6, 42.2, 28.0, 26.5, 23.0, 15.3; HRMS (ESI-TOF) m/z calcd for $\text{C}_{15}\text{H}_{15}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 276.1107, found 276.1110.



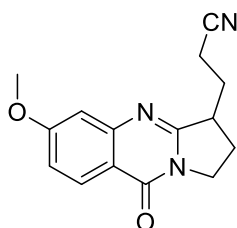
3-(5,6-Dimethyl-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanenitrile (3fa), 35.2 mg, 66% yield), yellow solid, mp: 175-176 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.98 (d, $J = 8.1$ Hz, 1H), 7.22 (d, $J = 8.1$ Hz, 1H), 4.30-4.24 (m, 1H), 3.97-3.90 (m, 1H), 3.37-3.29 (m, 1H), 2.99-2.79 (m, 2H), 2.56-2.50 (m, 1H), 2.48 (s, 3H), 2.40 (s, 3H), 2.36-2.29 (m, 1H), 2.07-1.98 (m, 1H), 1.94-1.84 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 161.2, 158.4, 147.2, 143.2, 133.4, 128.4, 123.1, 119.5, 118.6, 44.4, 42.1, 28.3, 26.8, 21.0, 15.3, 13.3; HRMS (ESI-TOF) m/z calcd for $\text{C}_{16}\text{H}_{17}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 290.1264, found 290.1268.



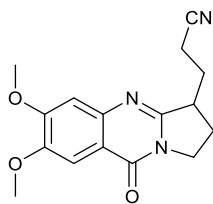
3-(5,7-Dimethyl-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanenitrile (3ga), 33.8 mg, 63% yield), yellow solid, mp: 180-182 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.88-7.87 (m, 1H), 7.38-7.37 (m, 1H), 4.31-4.25 (m, 1H), 3.98-3.91 (m, 1H), 3.37-3.29 (m, 1H), 3.00-2.80 (m, 2H), 2.56-2.49 (m, 4H), 2.41 (s, 3H), 2.36-2.27 (m, 1H), 2.07-1.98 (m, 1H), 1.95-1.85 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 161.1, 157.8, 145.5, 136.4, 136.1, 135.2, 123.4, 120.4, 119.5, 44.4, 41.9, 28.3, 26.9, 21.2, 17.4, 15.3; HRMS (ESI-TOF) m/z calcd for $\text{C}_{16}\text{H}_{17}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 290.1264, found 290.1265.



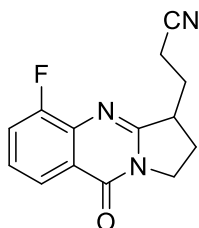
3-(7-Methoxy-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanenitrile (3ha), 33.1 mg, 62% yield), yellow oil; ^1H NMR (400 MHz, CDCl_3) δ 7.57 (d, $J = 3.0$ Hz, 1H), 7.53 (d, $J = 8.9$ Hz, 1H), 7.29-7.26 (m, 1H), 4.30-4.24 (m, 1H), 3.99-3.92 (m, 1H), 3.87 (s, 3H), 3.35-3.27 (m, 1H), 2.86-2.68 (m, 2H), 2.56-2.48 (m, 1H), 2.40-2.30 (m, 1H), 2.02-1.85 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 160.5, 158.2, 157.7, 143.2, 128.4, 124.4, 121.5, 119.3, 105.9, 55.8, 44.7, 42.0, 28.0, 26.7, 15.3; HRMS (ESI-TOF) m/z calcd for $\text{C}_{15}\text{H}_{15}\text{N}_3\text{O}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ 292.1056, found 292.1061.



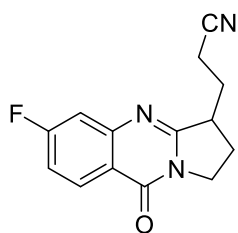
3-(6-Methoxy-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanenitrile (3ia), 34.8 mg, 65% yield), yellow oil; ^1H NMR (400 MHz, CDCl_3) δ 8.15-8.13 (m, 1H), 7.02-6.99 (m, 2H), 4.31-4.25 (m, 1H), 4.00-3.92 (m, 1H), 3.90 (s, 3H), 3.38-3.30 (m, 1H), 2.88-2.70 (m, 2H), 2.58-2.50 (m, 1H), 2.43-2.35 (m, 1H), 2.05-1.87 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 164.5, 160.6, 160.3, 151.1, 127.8, 119.2, 116.6, 114.2, 107.9, 55.7, 44.6, 42.4, 28.0, 26.6, 15.4; HRMS (ESI-TOF) m/z calcd for $\text{C}_{15}\text{H}_{15}\text{N}_3\text{O}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ 292.1056, found 292.1060.



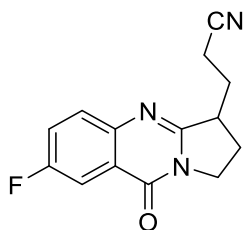
3-(6,7-Dimethoxy-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propane nitrile (3ja), 33.5 mg, 56% yield), yellow oil; ^1H NMR (400 MHz, CDCl_3) δ 7.56 (s, 1H), 7.04 (s, 1H), 4.33-4.27 (m, 1H), 4.01-3.94 (m, 7H), 3.38-3.30 (m, 1H), 2.87-2.70 (m, 2H), 2.58-2.51 (m, 1H), 2.42-2.34 (m, 1H), 2.05-1.88 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 160.1, 158.6, 154.7, 148.8, 145.1, 119.2, 114.0, 107.5, 105.3, 56.3, 56.3, 44.7, 42.2, 28.1, 26.7, 15.3; HRMS (ESI-TOF) m/z calcd for $\text{C}_{16}\text{H}_{17}\text{N}_3\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 322.1162, found 322.1159.



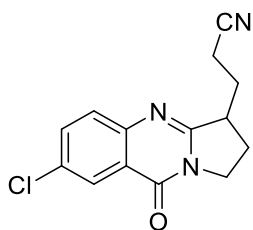
3-(5-Fluoro-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanenitrile (3ka), 37.5 mg, 73% yield), yellow oil; ^1H NMR (400 MHz, CDCl_3) δ 7.97 (d, $J = 7.8$ Hz, 1H), 7.43-7.32 (m, 2H), 4.32-4.26 (m, 1H), 4.01-3.94 (m, 1H), 3.42-3.34 (m, 1H), 2.89-2.70 (m, 2H), 2.61-2.53 (m, 1H), 2.46-2.38 (m, 1H), 2.04-1.90 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 160.6, 159.8, 156.8 (d, $J_{\text{C-F}} = 256.0$ Hz), 138.3 (d, $J_{\text{C-F}} = 11.8$ Hz), 126.6 (d, $J_{\text{C-F}} = 8.0$ Hz), 122.7, 121.8 (d, $J_{\text{C-F}} = 4.2$ Hz), 119.7 (d, $J_{\text{C-F}} = 19.8$ Hz), 119.2, 44.8, 42.5, 28.0, 26.6, 15.3; HRMS (ESI-TOF) m/z calcd for $\text{C}_{14}\text{H}_{12}\text{FN}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 280.0857, found 280.0855.



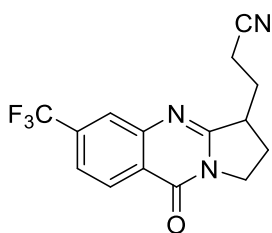
3-(6-Fluoro-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanenitrile (3la), 37.6 mg, 73% yield), yellow oil; ^1H NMR (400 MHz, CDCl_3) δ 8.23 (dd, $J = 8.8, 6.1$ Hz, 1H), 7.26 (dd, $J = 9.8, 2.5$ Hz, 1H), 7.16-7.11 (m, 1H), 4.31-4.25 (m, 1H), 3.99-3.92 (m, 1H), 3.39-3.31 (m, 1H), 2.89-2.69 (m, 2H), 2.59-2.52 (m, 1H), 2.42-2.33 (m, 1H), 2.04-1.88 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.4 (d, $J_{\text{C-F}} = 252.4$ Hz), 161.3, 160.00, 151.0 (d, $J_{\text{C-F}} = 13.0$ Hz), 129.0 (d, $J_{\text{C-F}} = 10.6$ Hz), 119.2, 117.5 (d, $J_{\text{C-F}} = 2.0$ Hz), 115.3 (d, $J_{\text{C-F}} = 23.4$ Hz), 112.5 (d, $J_{\text{C-F}} = 21.9$ Hz), 44.6, 42.3, 27.9, 26.6, 15.3; HRMS (ESI-TOF) m/z calcd for $\text{C}_{14}\text{H}_{12}\text{FN}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 280.0857, found 280.0854.



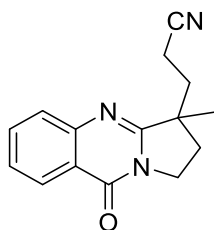
3-(7-Fluoro-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanenitrile (3ma), 35.4 mg, 69% yield), yellow oil; ^1H NMR (400 MHz, CDCl_3) δ 7.87 (dd, $J = 8.5, 3.0$ Hz, 1H), 7.64 (dd, $J = 8.9, 4.8$ Hz, 1H), 7.46-7.41 (m, 1H), 4.33-3.27 (m, 1H), 4.01-3.94 (m, 1H), 3.39-3.31 (m, 1H), 2.90-2.71 (m, 2H), 2.61-2.53 (m, 1H), 2.43-2.30 (m, 1H), 2.06-1.89 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 160.7 (d, $J_{\text{C-F}} = 248.9$ Hz), 160.0 (d, $J_{\text{C-F}} = 3.5$ Hz), 159.3 (d, $J_{\text{C-F}} = 2.2$ Hz), 145.4 (d, $J_{\text{C-F}} = 2.0$ Hz), 129.4 (d, $J_{\text{C-F}} = 8.3$ Hz), 122.7 (d, $J_{\text{C-F}} = 24.2$ Hz), 122.0 (d, $J_{\text{C-F}} = 8.6$ Hz), 119.2, 111.3 (d, $J_{\text{C-F}} = 23.6$ Hz), 44.7, 42.1, 27.9, 26.7, 15.3; HRMS (ESI-TOF) m/z calcd for $\text{C}_{14}\text{H}_{12}\text{FN}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 280.0857, found 280.0856.



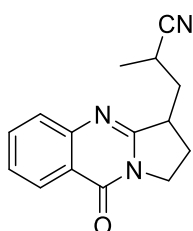
3-(7-Chloro-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanenitrile (3na), 16.9 mg, 31% yield), yellow oil; ^1H NMR (400 MHz, CDCl_3) δ 8.22, (d, $J = 2.2$ Hz, 1H), 7.68-7.62 (m, 2H), 4.36-4.30 (m, 1H), 4.05-3.98 (m, 1H), 3.46-3.38 (m, 1H), 2.91-2.72 (m, 2H), 2.63-2.56 (m, 1H), 2.50-2.39 (m, 1H), 2.08-1.93 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 160.2, 159.7, 147.4, 134.6, 132.4, 128.7, 125.7, 121.9, 119.2, 44.8, 42.2, 27.9, 26.7, 15.4; HRMS (ESI-TOF) m/z calcd for $\text{C}_{14}\text{H}_{12}\text{ClN}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 296.0561, found 296.0559.



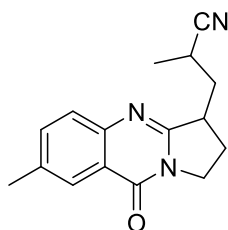
3-(9-Oxo-6-(trifluoromethyl)-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanenitrile (3oa), 38.4 mg, 62% yield), yellow solid, mp: 158-159 $^{\circ}\text{C}$; ^1H NMR (300 MHz, CDCl_3) δ 8.33 (d, $J = 8.3$ Hz, 1H), 7.90 (d, $J = 1.6$ Hz, 1H), 7.62 (dd, $J = 8.4, 1.7$ Hz, 1H), 4.36-4.27 (m, 1H), 4.04-3.94 (m, 1H), 3.44-3.33 (m, 1H), 2.94-2.68 (m, 2H), 2.64-2.53 (m, 1H), 2.44-2.32 (m, 1H), 2.08-1.89 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 161.4, 159.9, 148.9, 135.7 (q, $J_{\text{C-F}} = 32.6$ Hz), 127.5, 124.7 (q, $J_{\text{C-F}} = 4.0$ Hz), 123.4 (q, $J_{\text{C-F}} = 271.4$ Hz), 123.1, 122.5 (q, $J_{\text{C-F}} = 3.4$ Hz), 119.1, 44.8, 42.3, 27.8, 26.6, 15.3; HRMS (ESI-TOF) m/z calcd for $\text{C}_{15}\text{H}_{12}\text{F}_3\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 330.0825, found 330.0823.



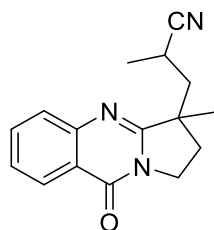
3-(3-Methyl-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanenitrile (3pa), 39.1 mg, 77% yield), colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 8.25 (dt, $J = 8.0, 1.8$ Hz, 1H), 7.73-7.64 (m, 2H), 7.45-7.41 (m, 1H), 4.21-4.15 (m, 1H), 4.10-4.03 (m, 1H), 2.70-2.62 (m, 1H), 2.57-2.49 (m, 1H), 2.24-2.08 (m, 4H), 1.42 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 162.3, 160.9, 149.0, 134.2, 127.2, 126.6, 126.4, 120.8, 119.6, 45.8, 43.1, 33.9, 33.2, 23.6, 12.7; HRMS (ESI-TOF) m/z calcd for $\text{C}_{15}\text{H}_{15}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 276.1107, found 276.1104.



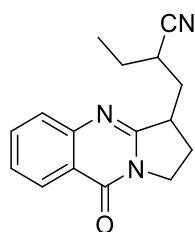
2-Methyl-3-(9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanenitrile (3ab), 41.6 mg, 82% yield), yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 8.19-8.15 (m, 1H), 7.65-7.54 (m, 2H), 7.39-7.34 (m, 1H), 4.30-4.18 (m, 1H), 3.94-3.84 (m, 1H), 3.45-3.28 (m, 1.45H), 2.97-2.89 (m, 0.45H), 2.59-2.44 (m, 1.55H), 2.20-2.12 (m, 0.55H), 1.96-1.66 (m, 2H), 1.37 (dd, $J = 10.8, 6.9$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 160.8, 160.2, 159.9, 149.0, 148.9, 134.2, 134.1, 127.1, 127.0, 126.5, 126.5, 126.3, 126.3, 122.9, 122.1, 120.8, 44.6, 41.8, 41.3, 37.0, 36.0, 27.4, 26.6, 24.2, 23.3, 18.6, 18.1; HRMS (ESI-TOF) m/z calcd for $\text{C}_{15}\text{H}_{15}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 276.1107, found 276.1109.



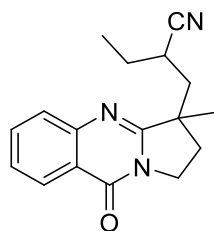
2-Methyl-3-(7-methyl-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanenitrile (3db), 39.1 mg, 73% yield), yellow oil; ^1H NMR (400 MHz, CDCl_3) δ 8.02 (s, 1H), 7.52 (t, $J = 2.7$ Hz, 2H), 4.34-4.25 (m, 1H), 3.99-3.90 (m, 1H), 3.50-3.34 (m, 1.50H), 3.03-2.94 (m, 0.50H), 2.64-2.50 (m, 1.52H), 2.45 (s, 3H), 2.25-2.18 (m, 0.48H), 2.00-1.84 (m, 1.48H), 1.80-1.73 (m, 0.52H), 1.46-1.40 (m, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 160.7, 160.7, 159.4, 159.1, 146.8, 146.7, 136.7, 135.7, 135.6, 126.8, 126.7, 125.8, 125.8, 122.9, 122.1, 120.4, 44.7, 44.6, 41.7, 41.2, 37.1, 36.0, 27.4, 26.6, 24.2, 23.3, 21.2, 18.6, 18.1; HRMS (ESI-TOF) m/z calcd for $\text{C}_{16}\text{H}_{17}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 290.1264, found 290.1261.



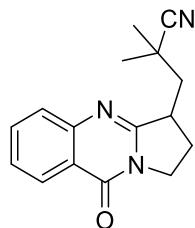
2-Methyl-3-(3-methyl-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanenitrile (3pb), 50.2 mg, 94% yield), yellow oil; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.27 (d, $J = 8.0$ Hz, 1H), 7.73-7.65 (m, 2H), 7.46-7.42 (m, 1H), 4.29-4.19 (m, 1H), 4.10-4.01 (m, 1H), 3.11-3.02 (m, 0.59H), 2.75-2.66 (m, 0.41H), 2.49-2.23 (m, 2H), 2.18-2.01 (m, 2H), 1.47 (d, $J = 7.1$ Hz, 3H), 1.39 (dd, $J = 7.1, 3.7$ Hz, 3H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 163.3, 162.6, 160.9, 160.9, 149.2, 149.1, 134.2, 134.2, 127.2, 126.5, 126.5, 126.4, 126.4, 123.3, 123.1, 120.9, 120.8, 77.5, 77.1, 76.7, 46.6, 46.0, 43.4, 43.2, 42.6, 42.1, 33.8, 32.0, 25.5, 23.1, 21.5, 21.0, 20.1, 19.8; HRMS (ESI-TOF) m/z calcd for $\text{C}_{16}\text{H}_{17}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 290.1264, found 290.1267.



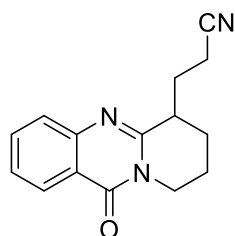
2-((9-Oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)methyl)butanenitrile (3ac), 34.5 mg, 65% yield), yellow oil; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.26-8.22 (m, 1H), 7.70-7.62 (m, 2H), 7.44-7.41 (m, 1H), 4.35-4.25 (m, 1H), 4.00-3.91 (m, 1H), 3.50-3.29 (m, 1.47H), 2.80-2.74 (m, 0.50H), 2.64-2.52 (m, 1.53H), 2.27-2.20 (m, 0.58H), 2.01-1.83 (m, 1.60H), 1.80-1.67 (m, 2.41H), 1.16-1.12 (m, 3H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 160.8, 160.3, 159.9, 148.9, 148.8, 134.2, 134.1, 127.1, 127.0, 126.5, 126.4, 126.3, 122.1, 121.2, 120.8, 44.7, 41.9, 41.5, 35.0, 34.0, 31.8, 31.0, 27.5, 26.6, 26.1, 25.7, 11.6, 11.5; HRMS (ESI-TOF) m/z calcd for $\text{C}_{16}\text{H}_{17}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 290.1264, found 290.1265.



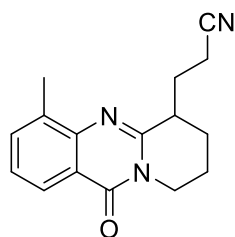
2-((3-Methyl-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)methyl)butanenitrile (3pc), 45.0 mg, 80% yield), yellow oil; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.27 (d, $J = 8.0$ Hz, 1H), 7.74-7.65 (m, 2H), 7.46-7.42 (m, 1H), 4.29-4.19 (m, 1H), 4.10-4.02 (m, 1H), 2.97-2.90 (m, 0.61H), 2.56-2.01 (m, 4.39H), 1.72-1.64 (m, 2H), 1.47 (d, $J = 5.0$ Hz, 3H), 1.12-1.06 (m, 3H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 163.4, 162.6, 160.9, 149.1, 149.0, 134.2, 127.1, 127.1, 126.5, 126.4, 122.5, 122.3, 120.9, 120.8, 46.6, 45.9, 43.4, 43.2, 40.6, 40.1, 33.8, 32.0, 28.9, 28.4, 27.3, 27.2, 25.6, 23.0, 11.4, 11.3; HRMS (ESI-TOF) m/z calcd for $\text{C}_{17}\text{H}_{19}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 304.1420, found 304.1423.



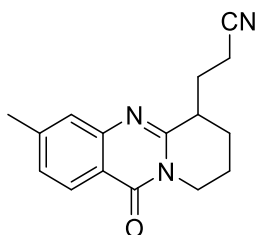
2,2-Dimethyl-3-(9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanenitrile (3ad), 17.6 mg, 33% yield), colourless oil; ^1H NMR (400 MHz, CDCl_3) δ 8.31 (d, $J = 7.8$ Hz, 1H), 7.78-7.72 (m, 2H), 7.51-7.47 (m, 1H), 4.44-4.38 (m, 1H), 4.03-3.95 (m, 1H), 3.51-3.43 (m, 1H), 2.88-2.80 (m, 1H), 2.67 (dd, $J = 14.2, 2.6$ Hz, 1H), 2.20-2.10 (m, 1H), 1.95-1.82 (m, 1H), 1.55 (d, $J = 5.4$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 160.8, 160.4, 148.8, 134.2, 126.9, 126.6, 126.5, 124.9, 120.8, 44.9, 42.9, 41.1, 31.2, 28.5, 28.2, 26.0; HRMS (ESI-TOF) m/z calcd for $\text{C}_{16}\text{H}_{17}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 290.1264, found 290.1267.



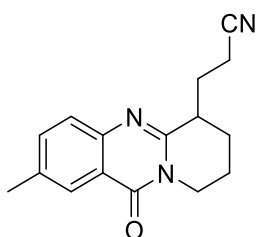
3-(11-Oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-*b*]quinazolin-6-yl)propanenitrile (5a), 31.7 mg, 63% yield), yellow oil; ^1H NMR (400 MHz, CDCl_3) δ 8.23 (dd, $J = 8.1, 1.5$ Hz, 1H), 7.72-7.68 (m, 1H), 7.59 (dd, $J = 8.4, 1.2$ Hz, 1H), 7.44-7.40 (m, 1H), 4.41-4.35 (m, 1H), 3.87-3.80 (m, 1H), 2.99-2.92 (m, 1H), 2.86-2.67 (m, 2H), 2.52-2.43 (m, 1H), 2.20-2.12 (m, 1H), 2.06-1.93 (m, 3H), 1.66-1.56 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 161.8, 155.9, 146.9, 134.2, 126.9, 126.7, 126.5, 120.3, 119.8, 41.0, 38.7, 28.6, 25.4, 20.5, 15.7; HRMS (ESI-TOF) m/z calcd for $\text{C}_{15}\text{H}_{15}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 276.1107, found 276.1105.



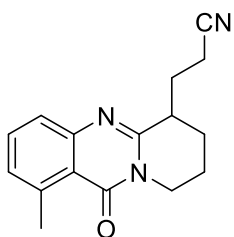
3-(4-Methyl-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-*b*]quinazolin-6-yl)propane nitrile (5b), 30.7 mg, 57% yield), colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 8.08 (dd, $J = 8.0, 1.5$ Hz, 1H), 7.56-7.54 (m, 1H), 7.31 (t, $J = 7.6$ Hz, 1H), 4.42-4.35 (m, 1H), 3.87-3.80 (m, 1H), 3.01-2.87 (m, 2H), 2.81-2.73 (m, 1H), 2.56 (s, 3H), 2.52-2.43 (m, 1H), 2.22-2.13 (m, 1H), 2.07-1.95 (m, 3H), 1.65-1.56 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 162.2, 154.7, 145.4, 135.3, 134.7, 126.1, 124.3, 120.2, 119.9, 40.9, 38.8, 28.8, 25.8, 20.7, 17.4, 15.8; HRMS (ESI-TOF) m/z calcd for $\text{C}_{16}\text{H}_{17}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 290.1264, found 290.1267.



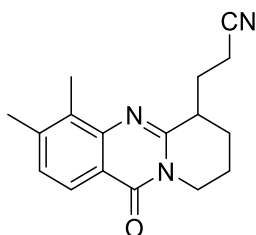
3-(3-Methyl-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-*b*]quinazolin-6-yl)propane nitrile (5c), 30.7 mg, 57% yield), colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 8.10 (d, $J = 8.1$ Hz, 1H), 7.39 (s, 1H), 7.24 (d, $J = 8.1$ Hz, 1H), 4.40-4.33 (m, 1H), 3.85-3.78 (m, 1H), 2.97-2.90 (m, 1H), 2.86-2.67 (m, 2H), 2.50-2.41 (m, 4H), 2.19-2.11 (m, 1H), 2.05-1.92 (m, 3H), 1.65-1.55 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 161.7, 156.0, 146.9, 145.2, 128.2, 126.5, 126.5, 119.8, 117.9, 40.9, 38.7, 28.7, 25.4, 21.9, 20.5, 15.7; HRMS (ESI-TOF) m/z calcd for $\text{C}_{16}\text{H}_{17}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 290.1264, found 290.1262.



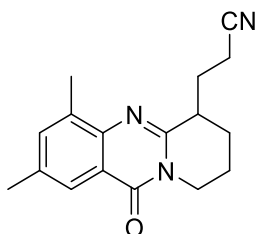
3-(2-Methyl-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-*b*]quinazolin-6-yl)propane nitrile (5d), 32.0 mg, 60% yield), colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 8.01 (t, $J = 1.4$ Hz, 1H), 7.53-7.48 (m, 2H), 4.41-4.34 (m, 1H), 3.86-3.79 (m, 1H), 2.98-2.90 (m, 1H), 2.85-2.66 (m, 2H), 2.51-2.42 (m, 4H), 2.20-2.11 (m, 1H), 2.06-1.94 (m, 3H), 1.63-1.57 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 161.8, 155.0, 144.9, 136.7, 135.7, 126.7, 126.0, 120.0, 119.9, 41.0, 38.7, 28.6, 25.4, 21.3, 20.5, 15.7; HRMS (ESI-TOF) m/z calcd for $\text{C}_{16}\text{H}_{17}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 290.1264, found 290.1261.



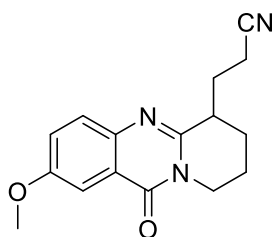
3-(1-Methyl-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-*b*]quinazolin-6-yl)propane nitrile (5e), 32.2 mg, 60% yield), yellow oil; ^1H NMR (400 MHz, CDCl_3) δ 7.54-7.51 (m, 1H), 7.42 (dd, $J = 8.2, 1.4$ Hz, 1H), 7.17-7.15 (m, 1H), 4.30-4.23 (m, 1H), 3.84-3.77 (m, 1H), 2.96-2.89 (m, 1H), 2.85-2.77 (m, 4H), 2.73-2.66 (m, 1H), 2.50-2.41 (m, 1H), 2.18-2.10 (m, 1H), 2.04-1.95 (m, 3H), 1.65-1.55 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 162.4, 155.5, 148.4, 140.9, 133.3, 129.1, 125.1, 119.9, 118.9, 40.9, 38.7, 28.7, 25.4, 23.2, 20.6, 15.7; HRMS (ESI-TOF) m/z calcd for $\text{C}_{16}\text{H}_{17}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 290.1264, found 290.1265.



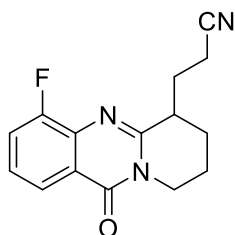
3-(3,4-Dimethyl-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-*b*]quinazolin-6-yl)propanenitrile (5f), 28.0 mg, 50% yield), colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 7.99 (d, $J = 8.1$ Hz, 1H), 7.23 (d, $J = 8.1$ Hz, 1H), 4.41-4.35 (m, 1H), 3.85-3.78 (m, 1H), 3.02-2.94 (m, 1H), 2.91-2.72 (m, 2H), 2.53-2.44 (m, 4H), 2.41 (s, 3H), 2.21-2.13 (m, 1H), 2.08-1.95 (m, 3H), 1.65-1.56 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 162.2, 154.4, 145.1, 143.1, 133.1, 128.6, 123.5, 119.9, 118.2, 40.8, 38.8, 28.7, 25.7, 21.0, 20.6, 15.7, 13.0; HRMS (ESI-TOF) m/z calcd for $\text{C}_{17}\text{H}_{19}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 304.1420, found 304.1417.



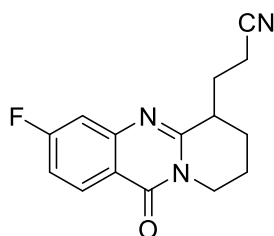
3-(2,4-Dimethyl-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-*b*]quinazolin-6-yl)propanenitrile (5g), 27.0 mg, 48% yield), colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 7.88 (s, 1H), 7.39 (s, 1H), 4.42-4.35 (m, 1H), 3.87-3.80 (m, 1H), 2.99-2.87 (m, 2H), 2.81-2.73 (m, 1H), 2.53 (s, 3H), 2.49-2.43 (m, 1H), 2.42 (s, 3H), 2.21-2.13 (m, 1H), 2.06-1.93 (m, 3H), 1.65-1.55 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 162.1, 153.7, 143.5, 136.3, 136.1, 135.0, 123.7, 120.0, 119.9, 40.9, 38.7, 28.8, 25.8, 21.3, 20.7, 17.3, 15.8 HRMS (ESI-TOF) m/z calcd for $\text{C}_{17}\text{H}_{19}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 304.1420, found 304.1421.



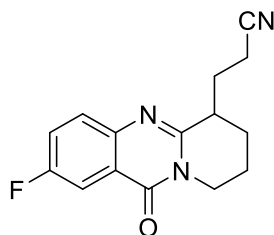
3-(2-Methoxy-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-*b*]quinazolin-6-yl)propanenitrile (5h), 27.4 mg, 48% yield), yellow oil; ^1H NMR (400 MHz, CDCl_3) δ 7.58 (t, $J = 2.4$ Hz, 1H), 7.53 (dd, $J = 8.9, 1.6$ Hz, 1H), 7.31-7.28 (m, 1H), 4.41-4.34 (m, 1H), 3.91-3.81 (m, 4H), 2.98-2.91 (m, 1H), 2.85-2.66 (m, 2H), 2.50-2.41 (m, 1H), 2.20-2.12 (m, 1H), 2.04-1.95 (m, 3H), 1.65-1.56 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 161.7, 158.2, 153.6, 141.6, 128.5, 124.6, 121.0, 119.8, 105.8, 55.8, 41.1, 38.6, 28.7, 25.5, 20.6, 15.7. HRMS (ESI-TOF) m/z calcd for $\text{C}_{16}\text{H}_{17}\text{N}_3\text{O}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ 306.1213, found 306.1210.



3-(4-Fluoro-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-*b*]quinazolin-6-yl)propane nitrile (5i), 35.3 mg, 65% yield), yellow solid, mp: 152-154 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.97 (dd, *J* = 7.8, 3.0 Hz, 1H), 7.42-7.31 (m, 2H), 4.37-4.29 (m, 1H), 3.89-3.82 (m, 1H), 3.02-2.87 (m, 2H), 2.78-2.70 (m, 1H), 2.52-2.43 (m, 1H), 2.22-2.14 (m, 1H), 2.07-1.95 (m, 3H), 1.67-1.57 (m, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 160.9 (d, *J*_{C-F} = 3.2 Hz), 156.7 (d, *J*_{C-F} = 256.5 Hz), 156.7, 136.5 (d, *J*_{C-F} = 11.8 Hz), 126.4 (d, *J*_{C-F} = 7.6 Hz), 122.2, 122.1 (d, *J*_{C-F} = 4.4 Hz), 119.8, 119.4 (d, *J*_{C-F} = 18.8 Hz), 41.3, 39.0, 28.7, 25.4, 20.5, 15.8; HRMS (ESI-TOF) *m/z* calcd for C₁₅H₁₄FN₃ONa [M+Na]⁺ 294.1013, found 294.1011.

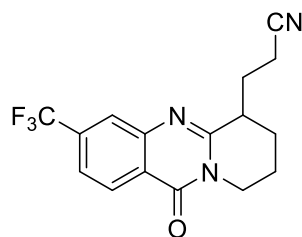


3-(3-Fluoro-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-*b*]quinazolin-6-yl)propane nitrile (5j), 34.2 mg, 63% yield), yellow oil; ¹H NMR (300 MHz, CDCl₃) δ 8.19 (dd, *J* = 8.9, 6.1 Hz, 1H), 7.19 (dd, *J* = 9.3, 2.9 Hz, 1H), 7.12-7.05 (m, 1H), 4.36-4.27 (m, 1H), 3.82-3.73 (m, 1H), 2.96-2.86 (m, 1H), 2.82-2.58 (m, 2H), 2.47-2.36 (m, 1H), 2.18-2.06 (m, 1H), 2.02-1.89 (m, 3H), 1.63-1.50 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 166.4 (d, *J*_{C-F} = 252.5 Hz), 161.1, 157.5, 148.9 (d, *J*_{C-F} = 13.1 Hz), 129.5 (d, *J*_{C-F} = 10.6 Hz), 119.7, 117.0 (d, *J*_{C-F} = 2.0 Hz), 115.5 (d, *J*_{C-F} = 23.5 Hz), 112.0 (d, *J*_{C-F} = 21.5 Hz), 41.0, 38.8, 28.5, 25.3, 20.4, 15.7; HRMS (ESI-TOF) *m/z* calcd for C₁₅H₁₄FN₃ONa [M+Na]⁺ 294.1013, found 294.1015.

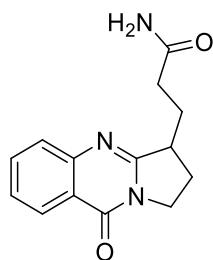


3-(2-Fluoro-11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-*b*]quinazolin-6-yl)propane nitrile (5k), 32.4 mg, 60% yield), yellow solid; mp: 148-149 °C ¹H NMR (400 MHz, CDCl₃) δ 7.86-7.82 (m, 1H), 7.64-7.60 (m, 1H), 7.45-7.40 (m, 1H), 4.41-4.34 (m, 1H), 3.88-3.81 (m, 1H), 3.01-2.94 (m, 1H), 2.85-2.66 (m, 2H), 2.52-2.43 (m, 1H), 2.22-2.13 (m, 1H), 2.08-1.94 (m, 3H), 1.67-1.58 (m, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 161.1 (d, *J*_{C-F} = 3.4 Hz), 160.7 (d, *J*_{C-F} = 248.5 Hz), 155.4, 143.4, 129.2 (d, *J*_{C-F} = 8.1 Hz), 122.9 (d, *J*_{C-F} = 24.2 Hz), 121.4 (d, *J*_{C-F} = 8.8 Hz), 119.7, 111.4 (d, *J*_{C-F} = 23.5 Hz), 41.2, 38.6, 28.6, 25.3, 20.4, 15.7; HRMS (ESI-TOF) *m/z* calcd for

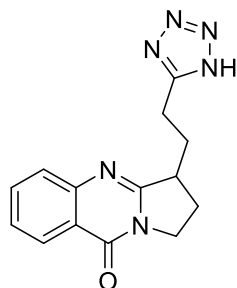
C₁₅H₁₄FN₃ONa [M+Na]⁺ 294.1013, found 294.1010.



3-(11-Oxo-3-(trifluoromethyl)-6,8,9,11-tetrahydro-7H-pyrido[2,1-*b*]quinazolin-6-yl)propanenitrile (51), 33.8 mg, 53% yield), colourless oil; ¹H NMR (400 MHz, CDCl₃) δ 8.32 (d, *J* = 8.4 Hz, 1H), 7.87 (s, 1H), 7.60 (dd, *J* = 8.3, 1.8 Hz, 1H), 4.43-4.36 (m, 1H), 3.88-3.81 (m, 1H), 3.02-2.94 (m, 1H), 2.88-2.80 (m, 1H), 2.74-2.66 (m, 1H), 2.53-2.44 (m, 1H), 2.24-2.16 (m, 1H), 2.10-1.95 (m, 3H), 1.67-1.58 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 161.0, 157.6, 146.8, 135.7 (q, *J*_{C-F} = 32.6 Hz), 127.9, 124.5 (q, *J*_{C-F} = 4.0 Hz), 123.4 (q, *J*_{C-F} = 271.4 Hz), 122.5, 122.4 (q, *J*_{C-F} = 3.4 Hz), 119.6, 41.2, 38.8, 28.4, 25.3, 20.4, 15.7; HRMS (ESI-TOF) *m/z* calcd for C₁₆H₁₄F₃N₃ONa [M+Na]⁺ 344.0981, found 344.0982.

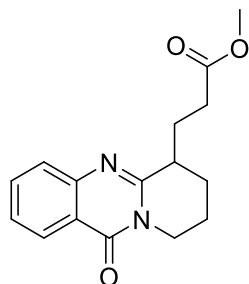


3-(9-Oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanamide (7), 43.6 mg, 85% yield), white solid, mp: 233-235 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.26 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.95-7.91 (m, 1H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.64-7.60 (m, 1H), 7.50 (s, 1H), 6.95 (s, 1H), 4.30-4.24 (m, 1H), 4.07-4.00 (m, 1H), 3.42-3.35 (m, 1H), 2.56-2.48 (m, 1H), 2.44-2.38 (m, 3H), 2.03-1.93 (m, 1H), 1.89-1.81 (m, 1H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 174.4, 162.5, 160.4, 149.5, 134.5, 127.3, 126.5, 126.1, 120.8, 45.1, 43.1, 32.9, 27.8, 26.2; HRMS (ESI-TOF) *m/z* calcd for C₁₄H₁₅N₃O₂Na [M+Na]⁺ 280.1056, found 280.1053.



3-(2-(2H-Tetrazol-5-yl)ethyl)-2,3-dihydropyrrolo[2,1-*b*]quinazolin-9(1H)-one (8), 28.0 mg, 50% yield), colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 8.23 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.76-7.71 (m, 1H), 7.65 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.50-7.46 (m, 1H), 4.27-4.20 (m, 1H), 4.13-4.07 (m, 1H), 3.70 (s, 1H), 2.83-2.67 (m, 2H), 2.52-2.33 (m, 3H), 2.23-2.15 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 166.0, 165.1, 154.1, 139.5,

132.5, 131.8, 131.0, 126.1, 83.0, 48.0, 38.5, 37.7, 16.4; HRMS (ESI-TOF) m/z calcd for $C_{14}H_{14}N_6ONa$ $[M+Na]^+$ 305.1121, found 305.1124.

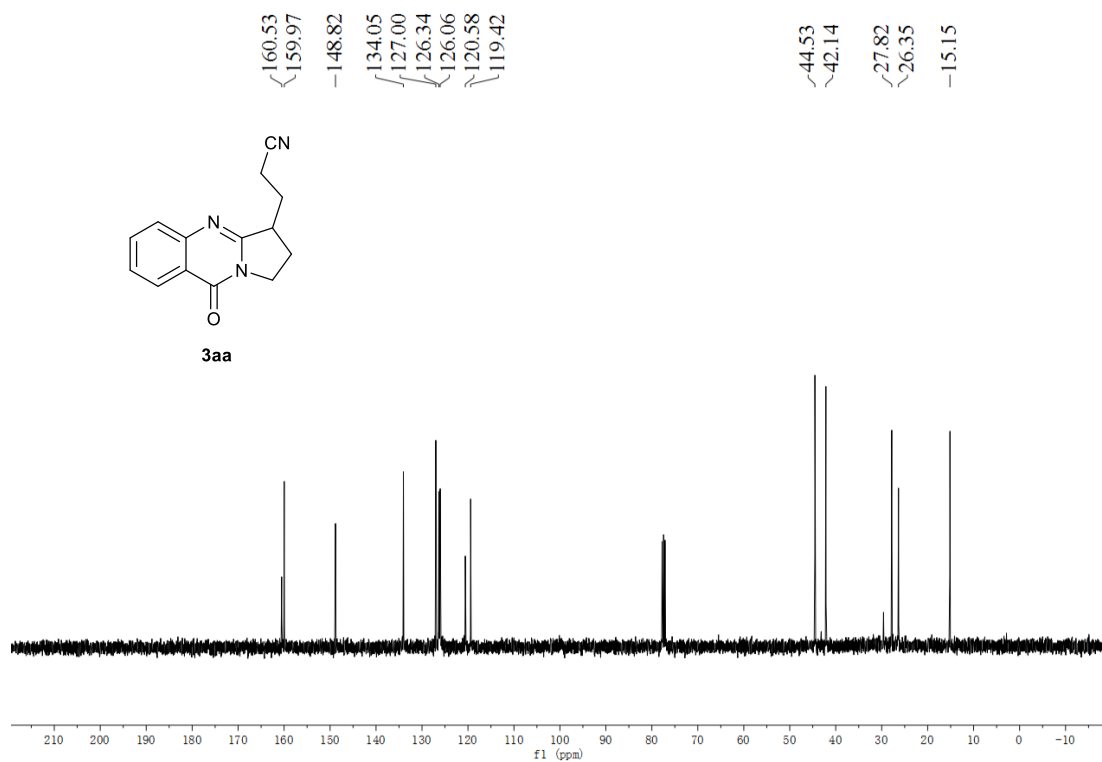
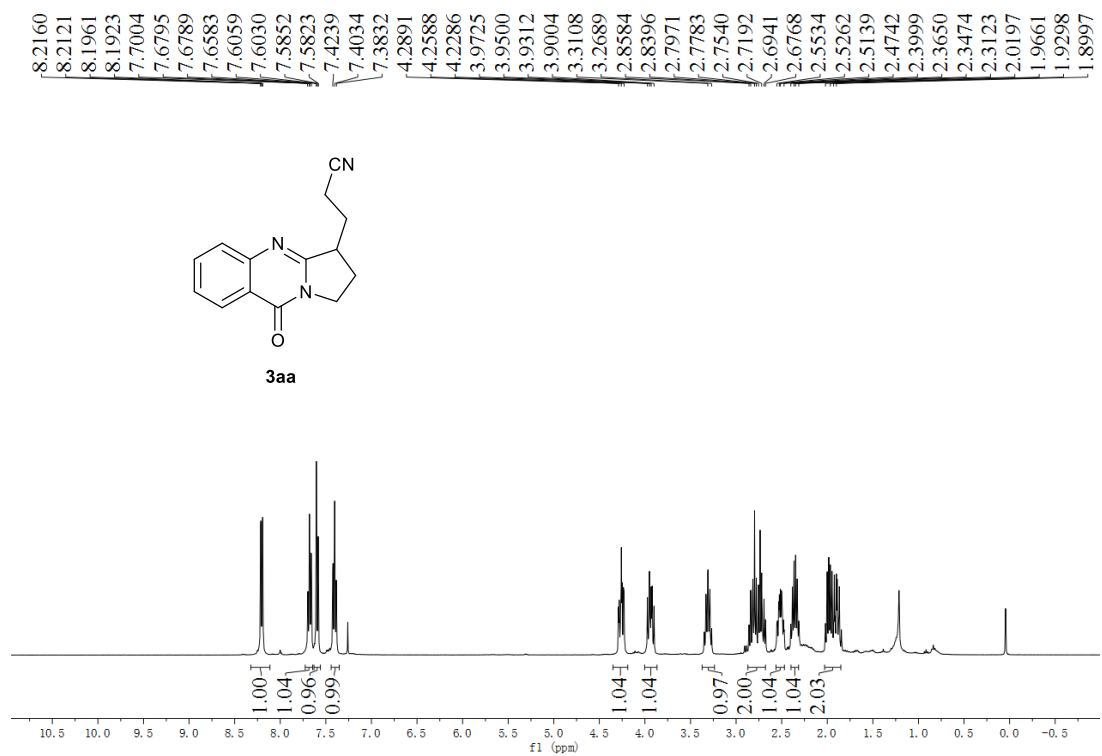


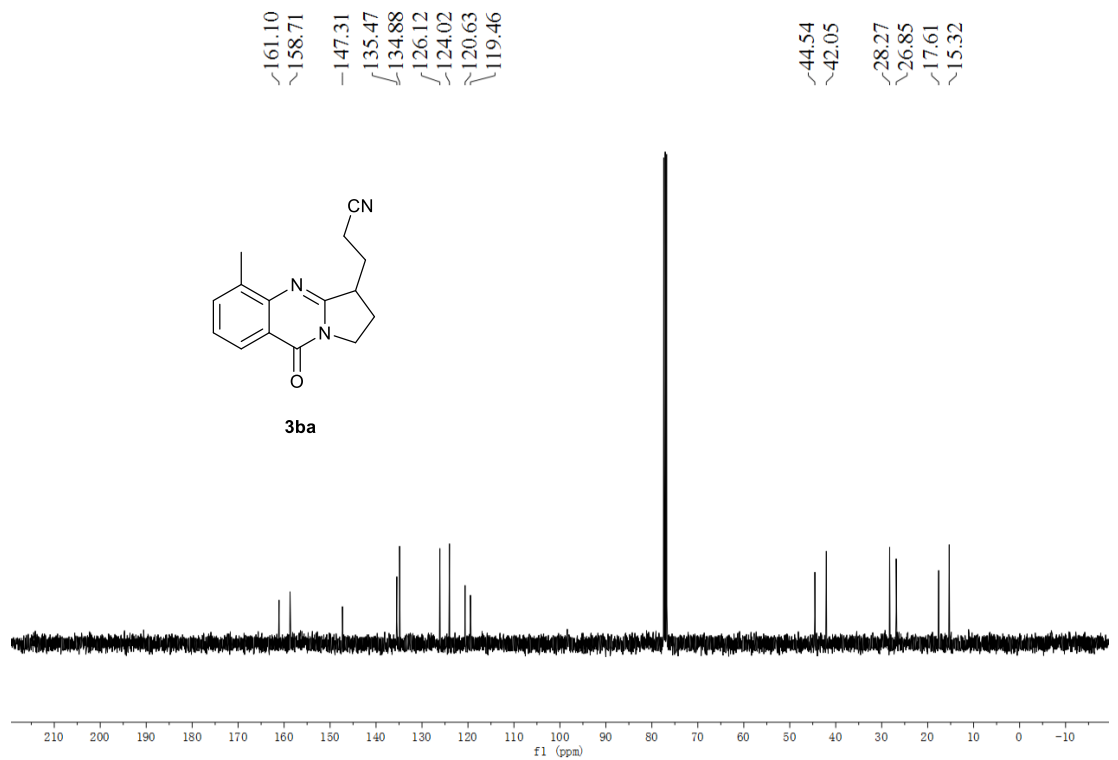
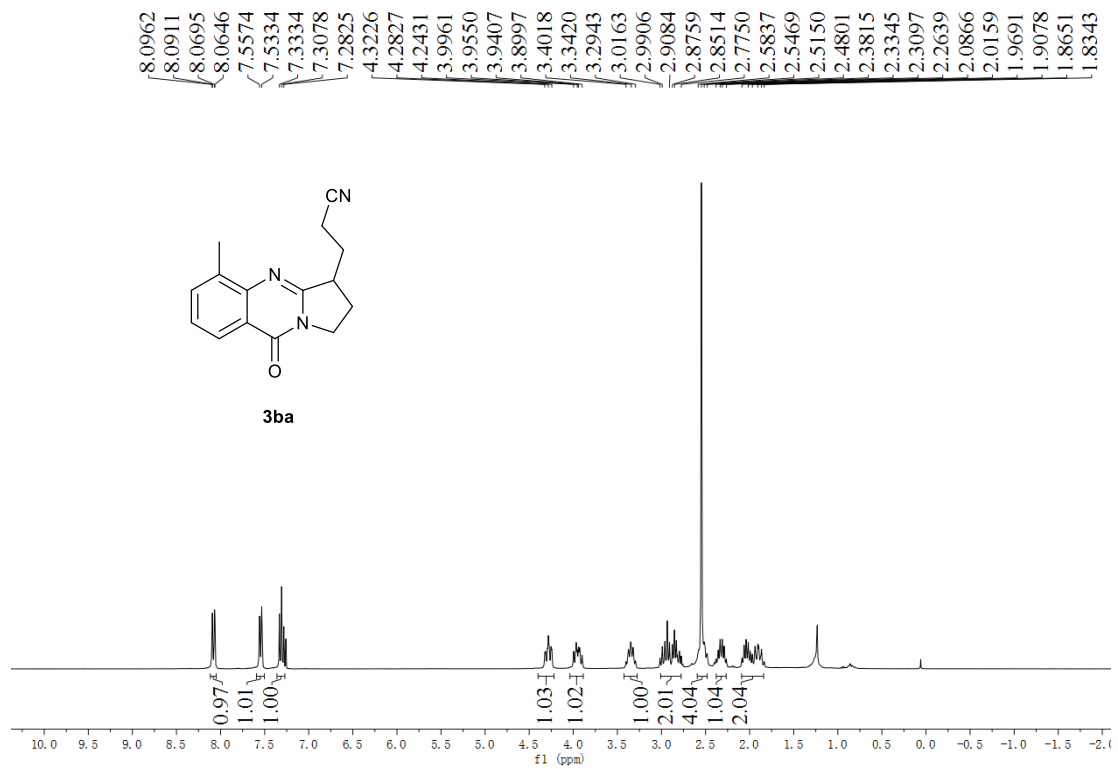
Methyl 3-(11-oxo-6,8,9,11-tetrahydro-7H-pyrido[2,1-*b*]quinazolin-6-yl)propanoate (9), 50.4 mg, 88% yield), colourless oil; 1H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, $J = 8.1$ Hz, 1H), 7.70-7.66 (m, 1H), 7.60 (d, $J = 8.3$ Hz, 1H), 7.42-7.37 (m, 1H), 4.30-4.23 (m, 1H), 3.92-3.85 (m, 1H), 3.62 (s, 3H), 2.95-2.88 (m, 1H), 2.61-2.56 (m, 2H), 2.47-2.38 (m, 1H), 2.15-2.07 (m, 1H), 2.05-1.93 (m, 3H), 1.67-1.58 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 162.1, 156.9, 147.1, 134.0, 126.9, 126.6, 126.2, 120.2, 51.6, 41.5, 39.5, 31.8, 28.3, 25.1, 20.2; HRMS (ESI-TOF) m/z calcd for $C_{16}H_{18}N_2O_3Na$ $[M+Na]^+$ 309.1210, found 309.1213.

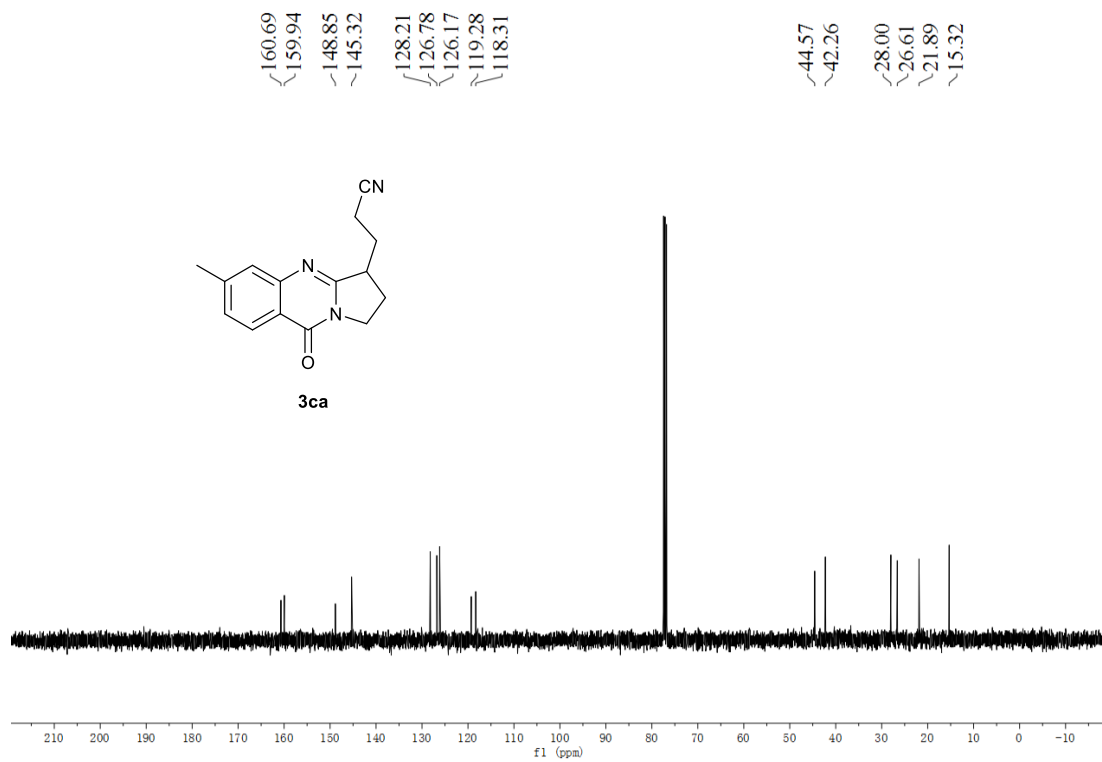
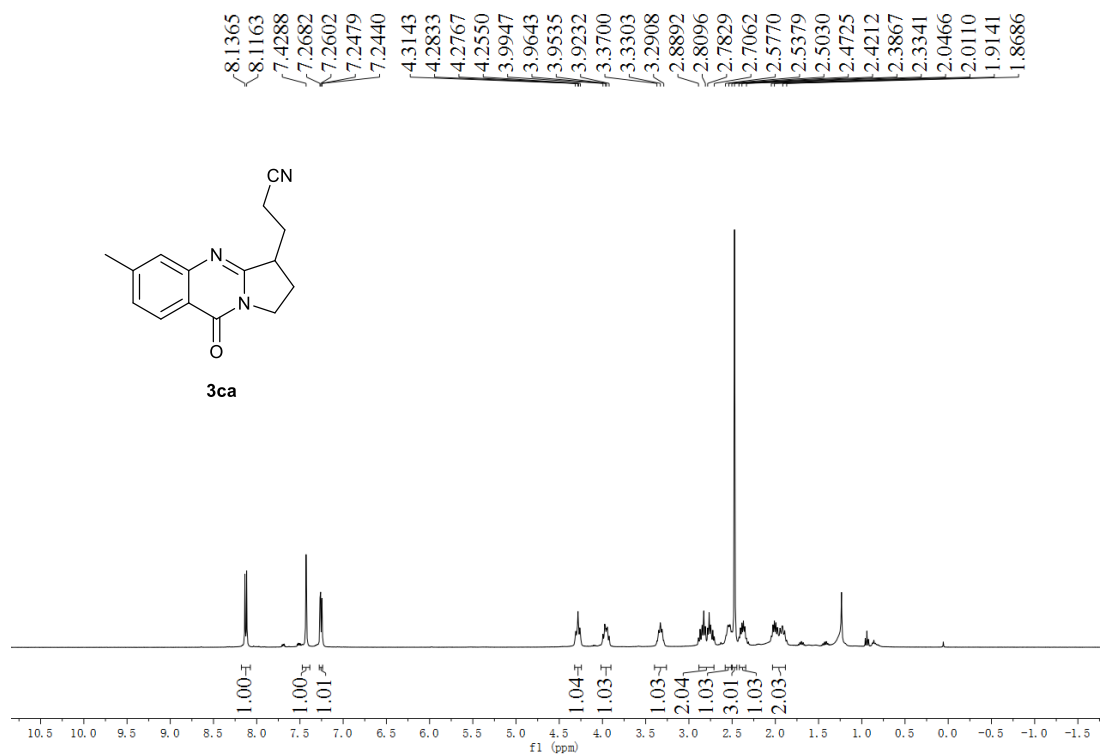
5. References

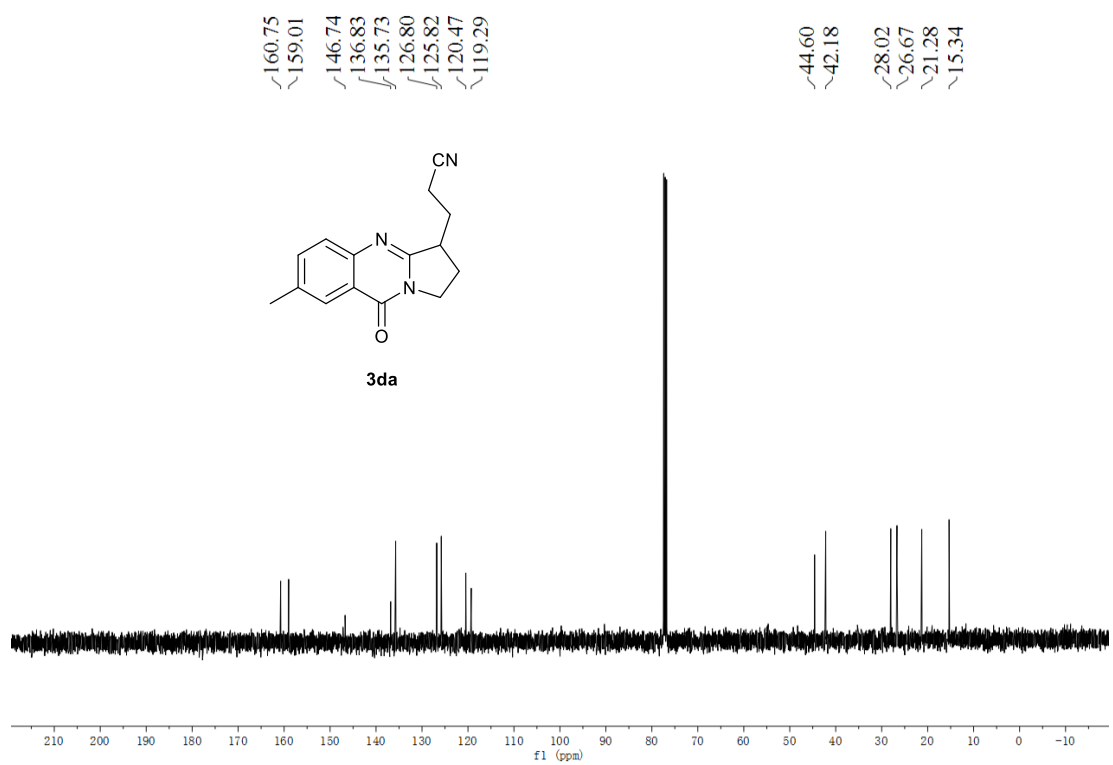
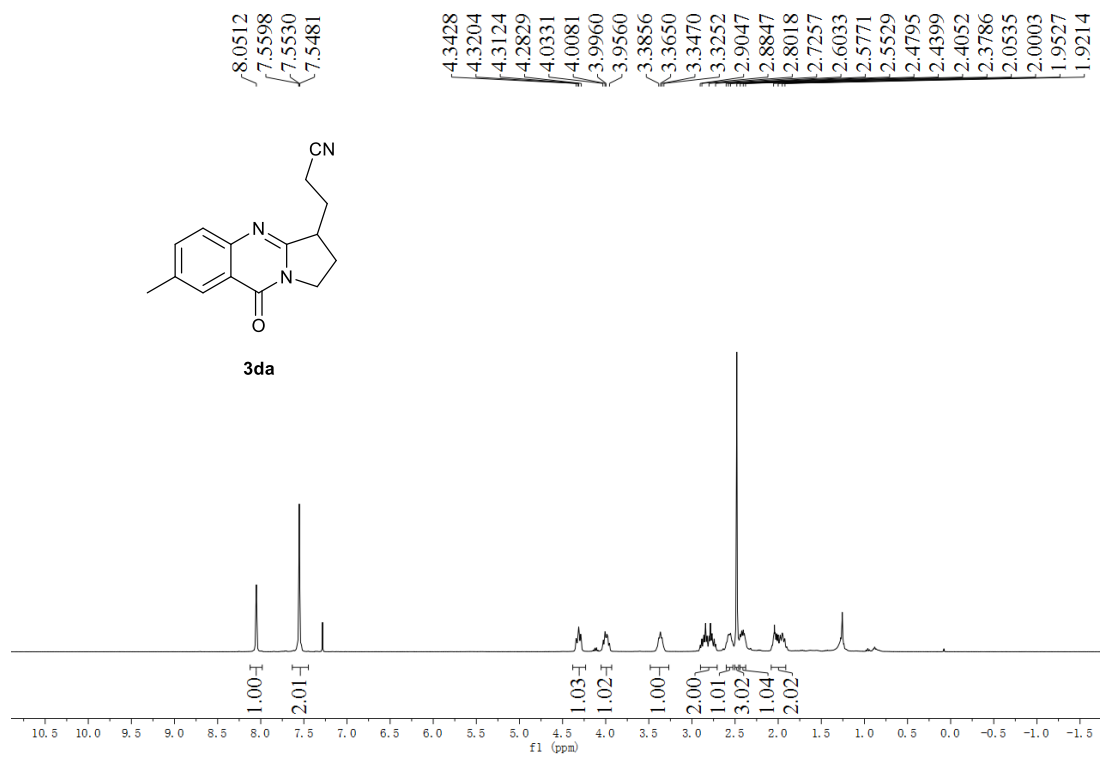
1. (a) J. Yang, B. Sun, H. Ding, P.-Y. Huang, X.-L. Tang, R.-C. Shi, Z.-Y. Yan, C.-M. Yu and C. Jin, *Green Chem.*, 2021, **23**, 575. (b) B. Sun, P. Huang, Z. Yan, X. Shi, X. Tang, J. Yang and C. Jin, *Org. Lett.*, 2021, **23**, 1026.
2. J. N. Moorthy and N. Singhal, *J. Org. Chem.*, 2005, **70**, 1926.
3. B. Akhlaghinia and S. Rezazadeh, *J. Braz. Chem. Soc.*, 2012, **23**, 2197.
4. Y. Yu, Z. Cai, W. Yuan, P. Liu and P. Sun, *J. Org. Chem.*, 2017, **82**, 8148.

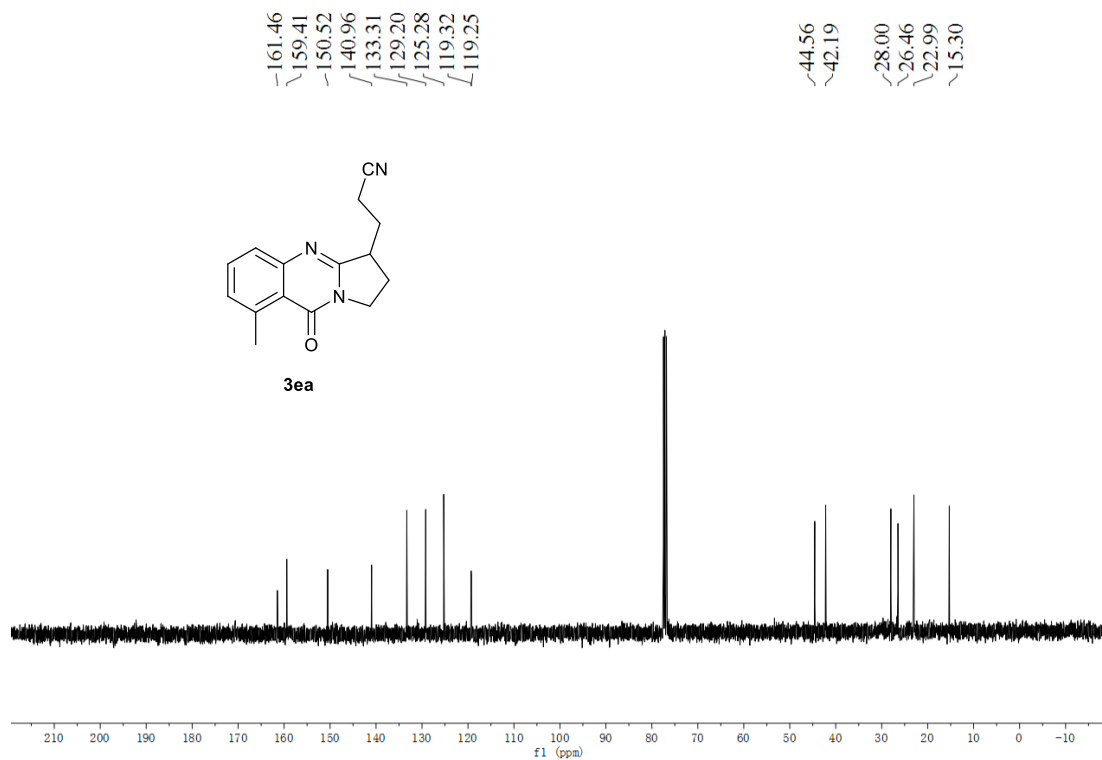
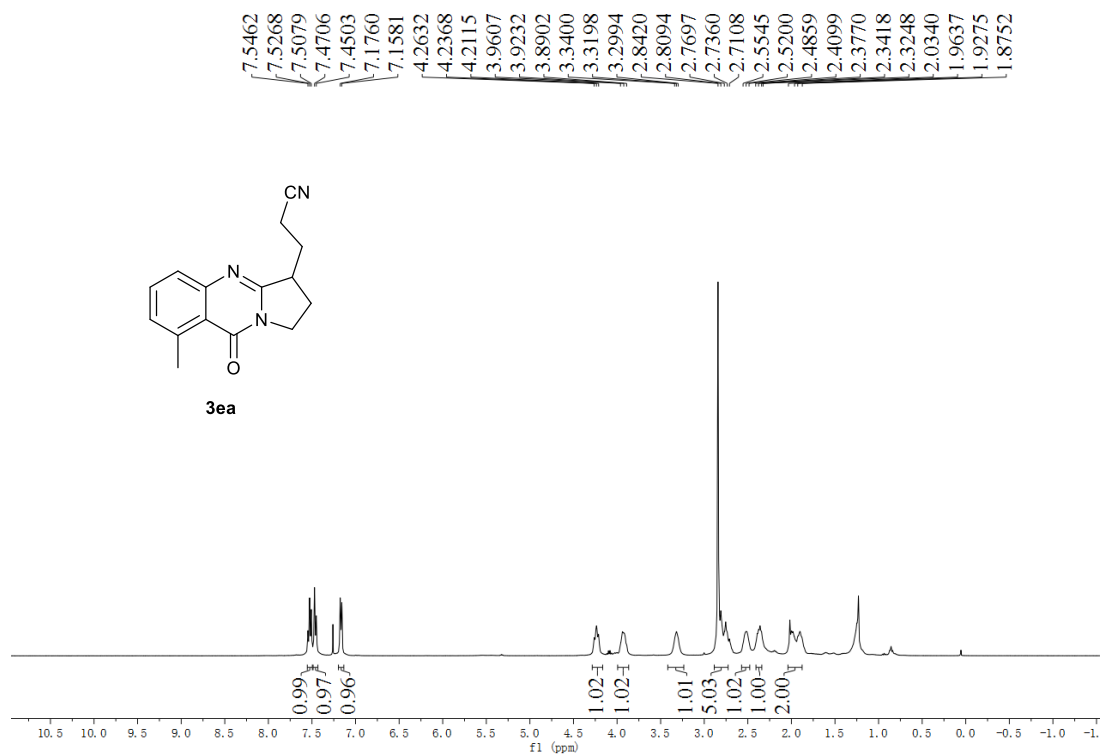
6. Copies of the ^1H NMR and ^{13}C NMR Spectra

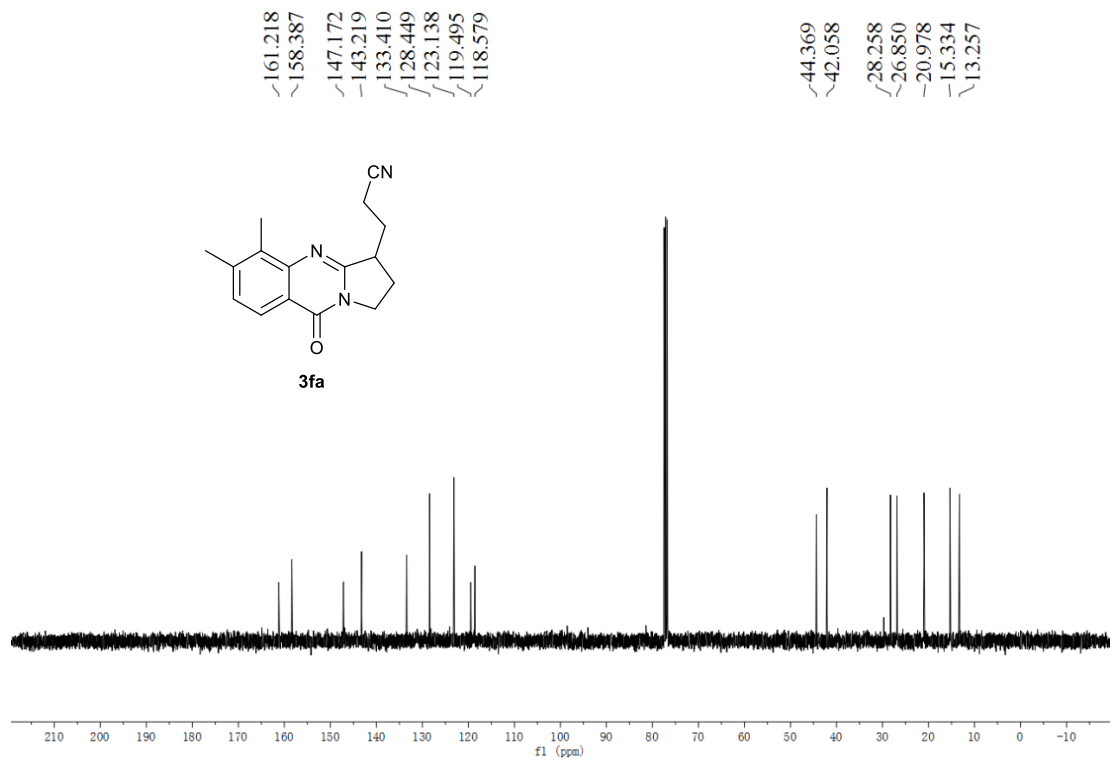
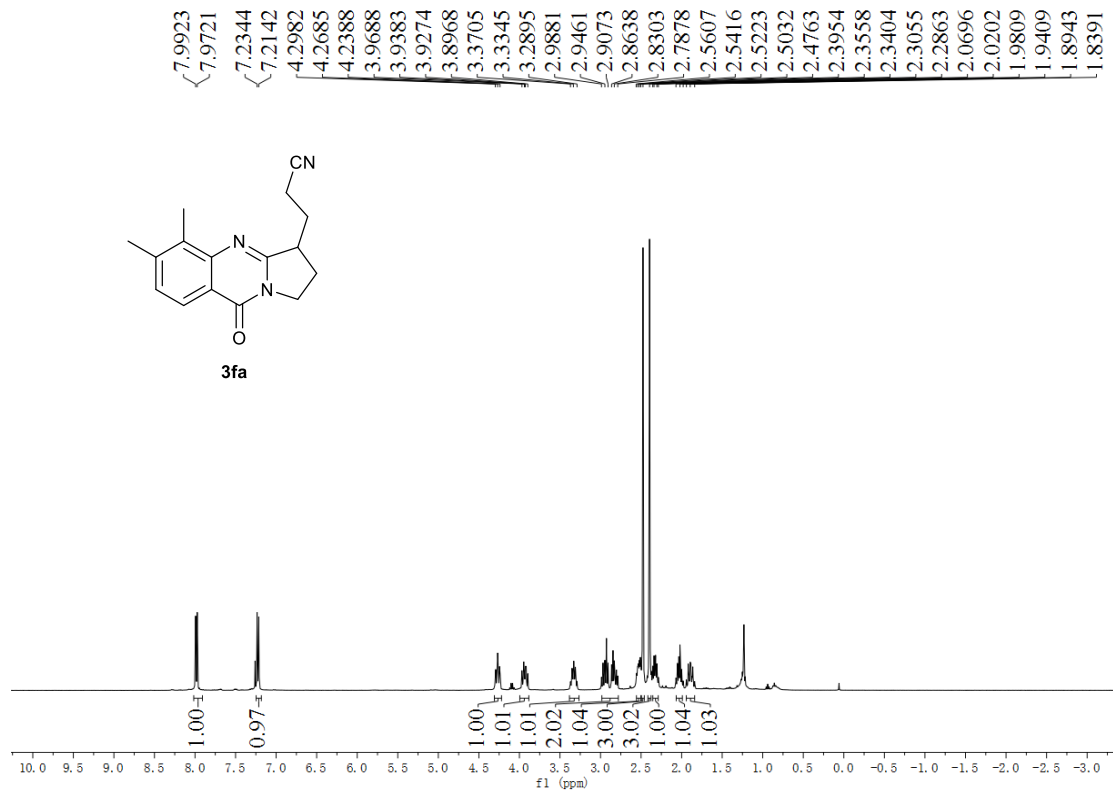


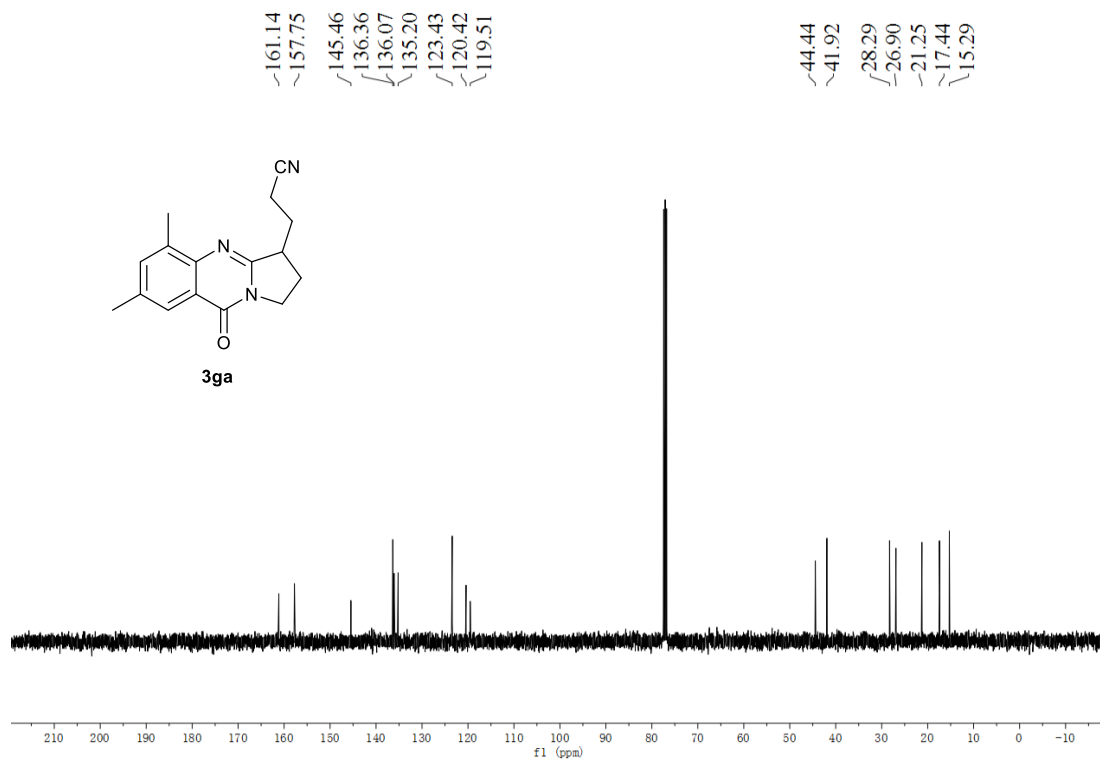
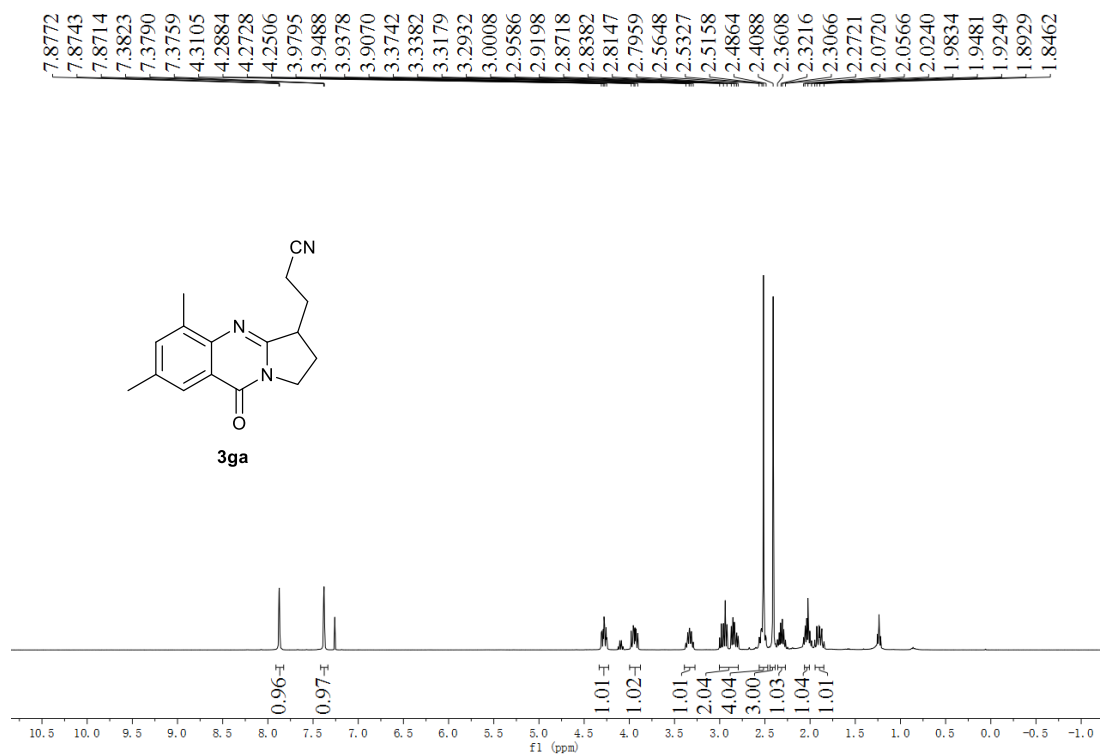


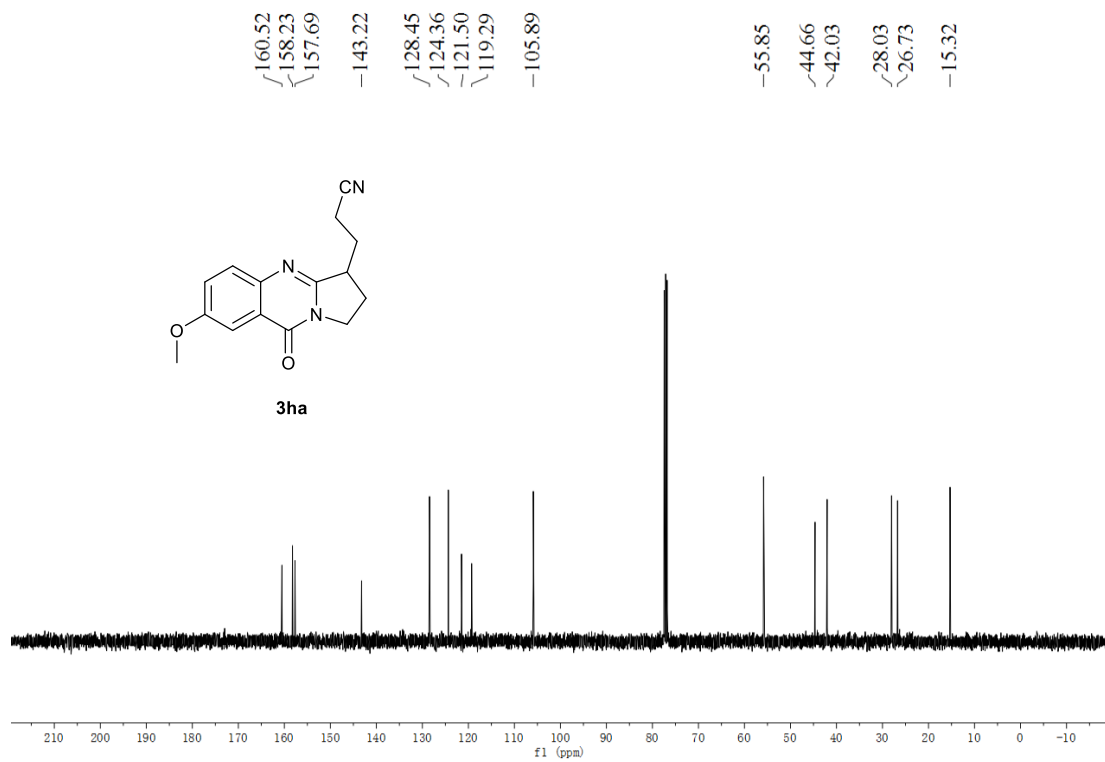
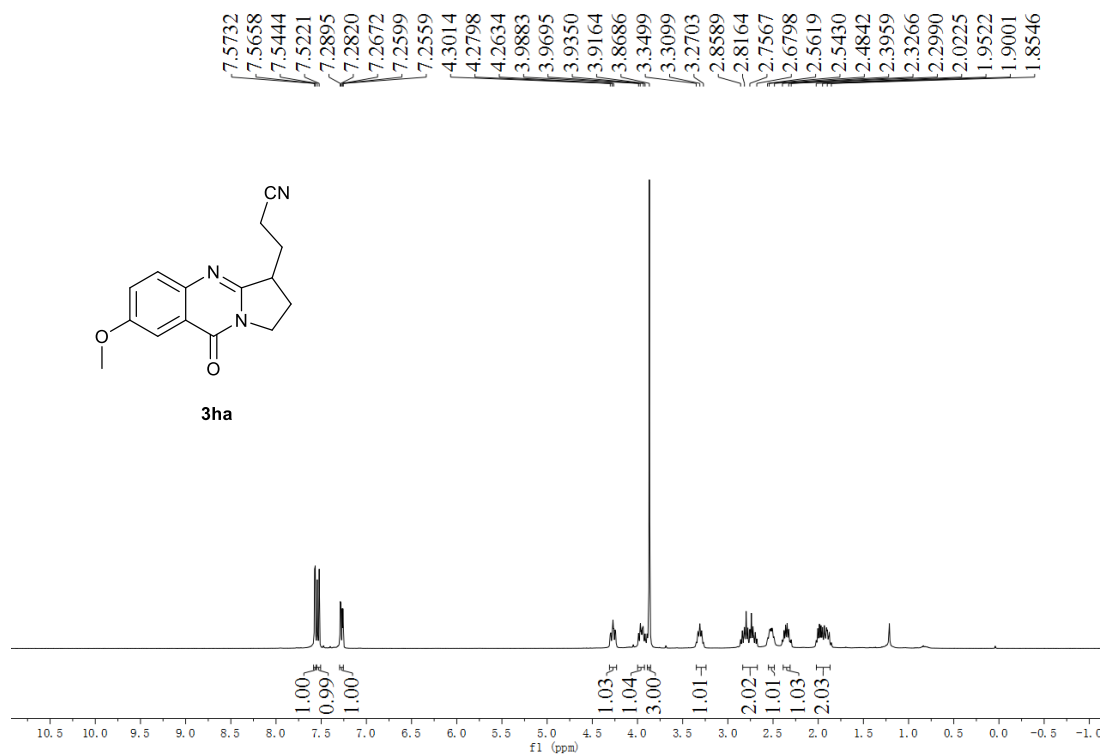


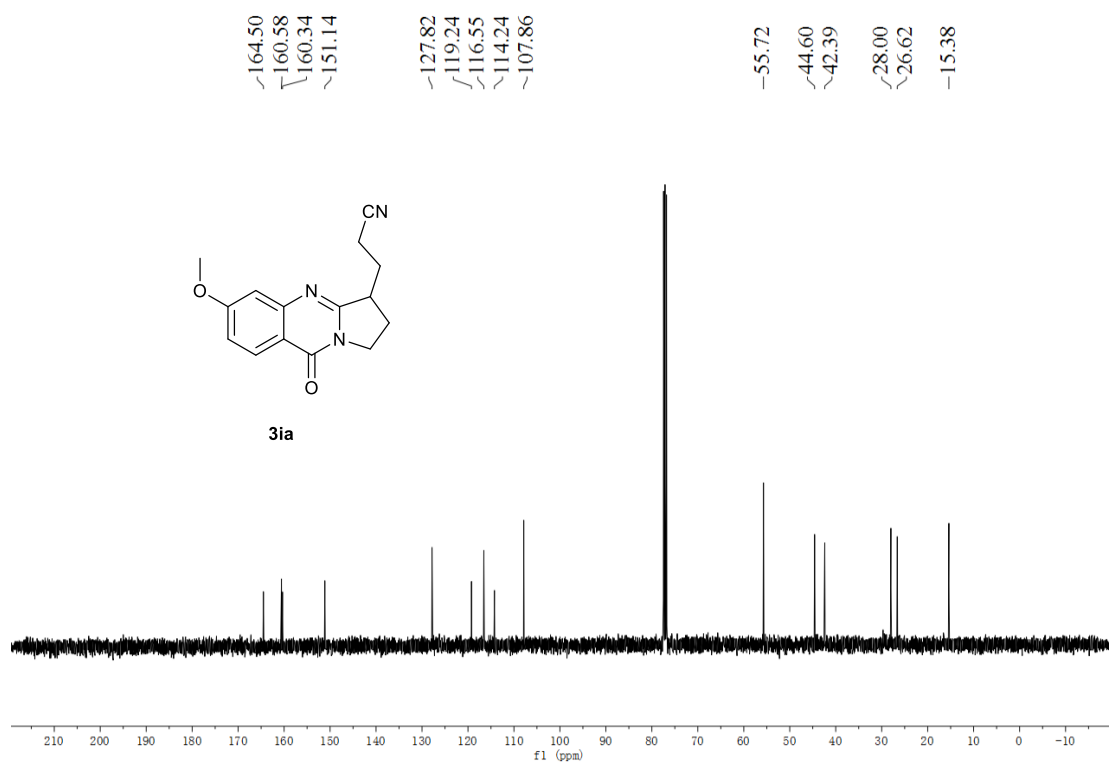
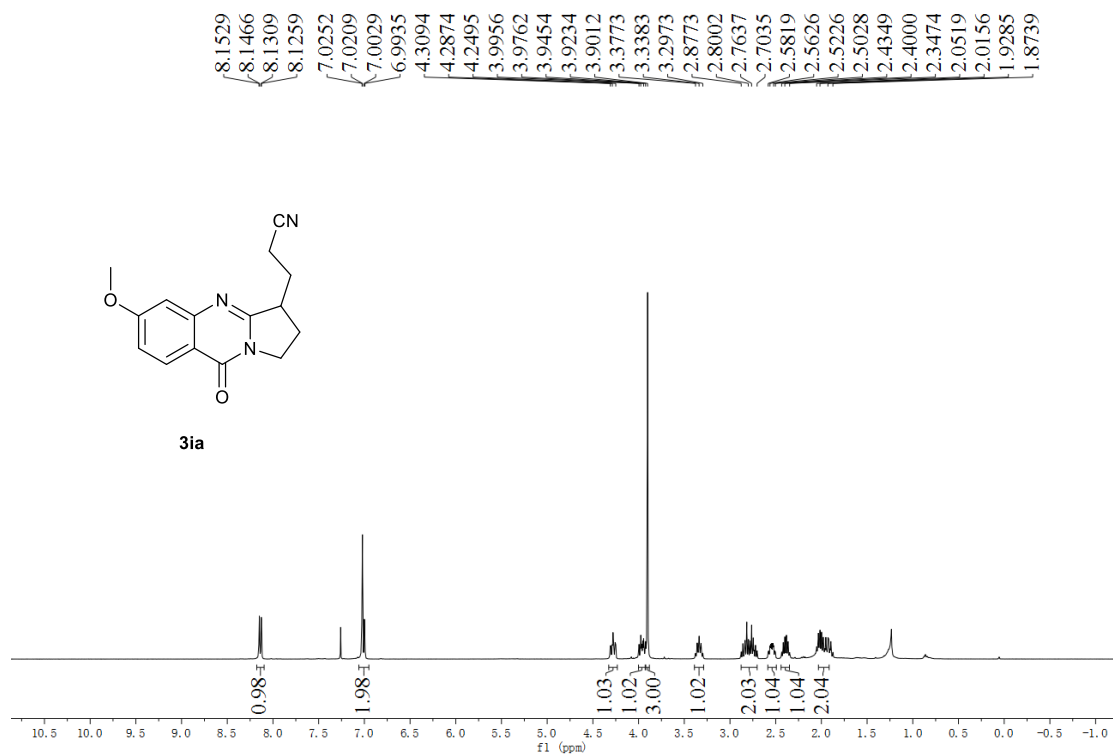


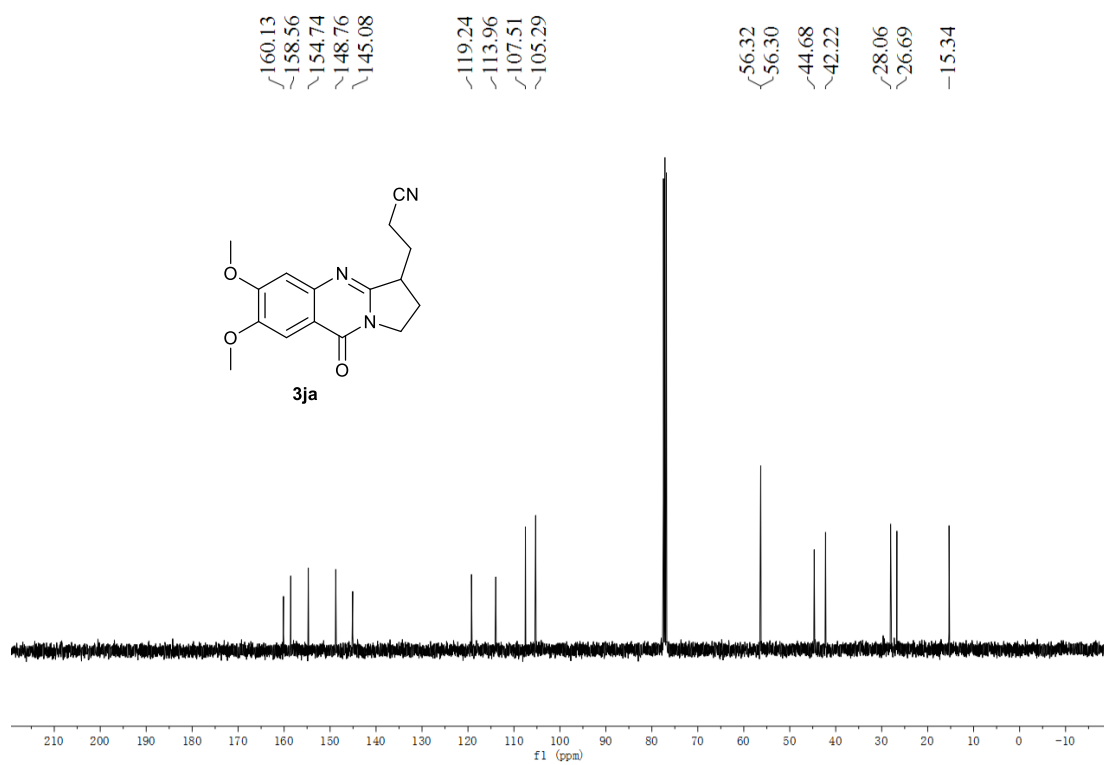
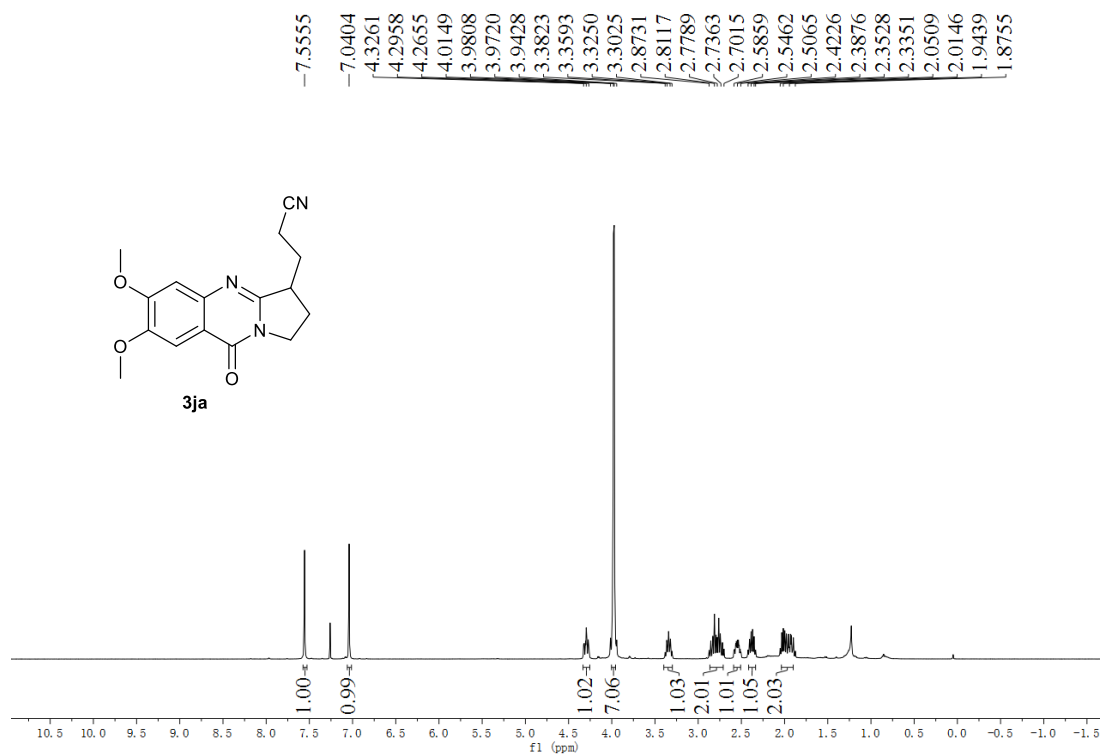


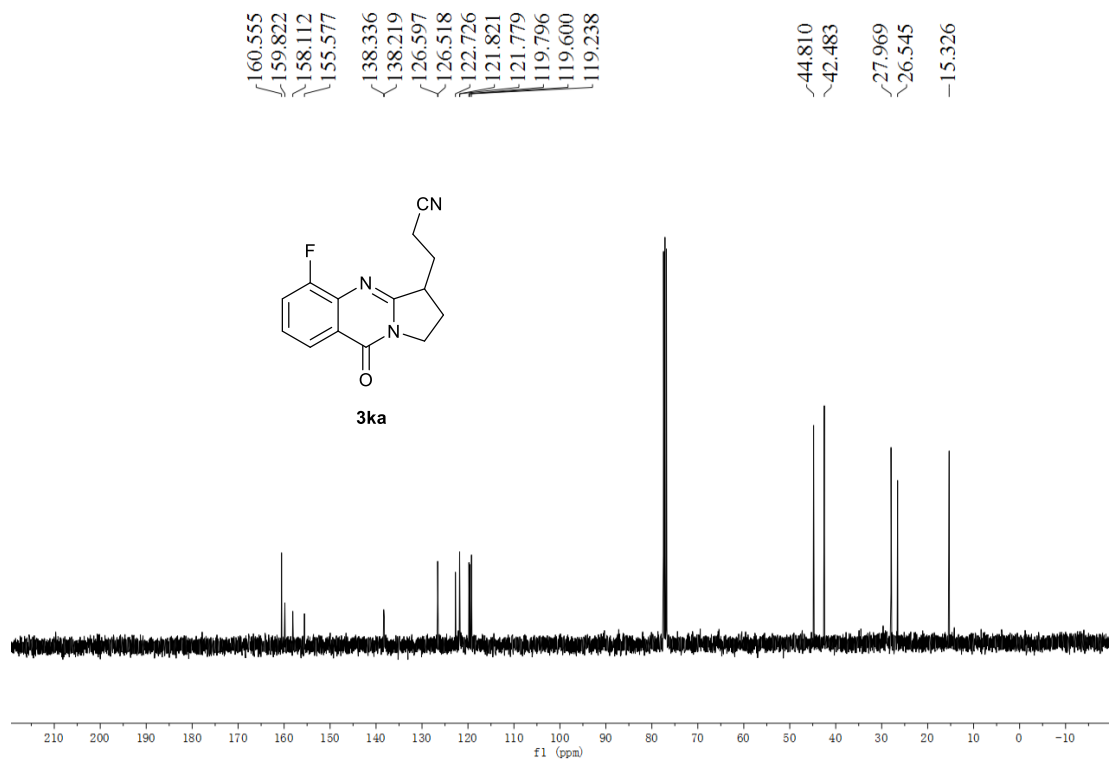
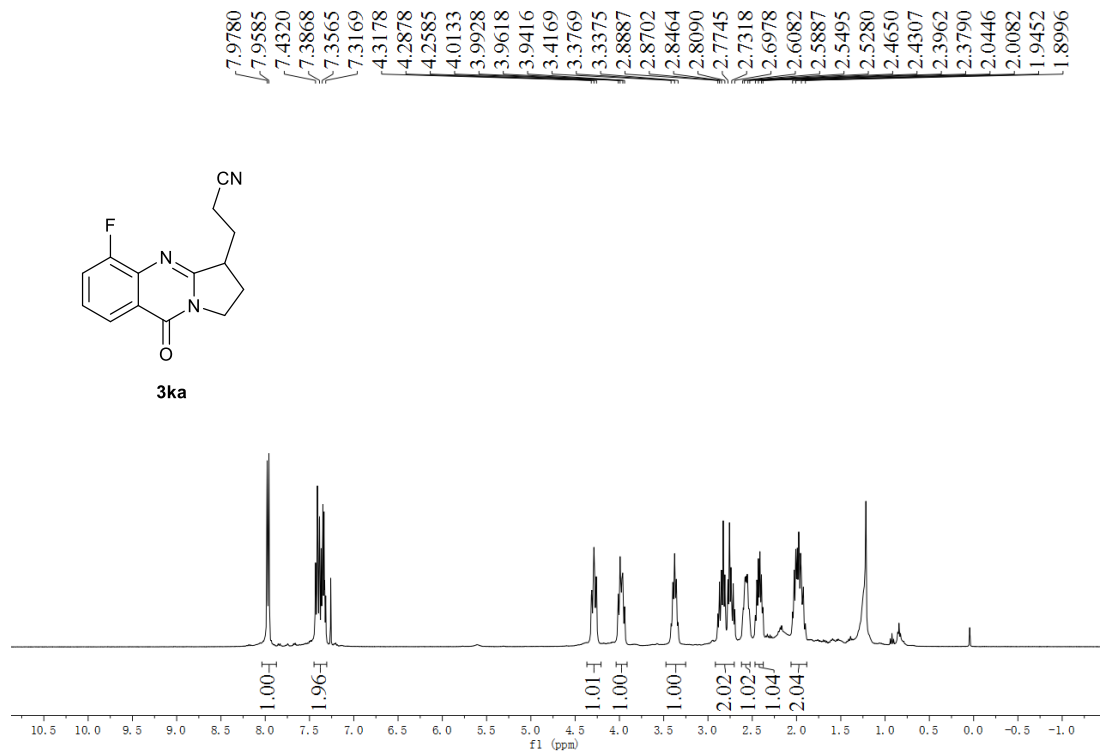


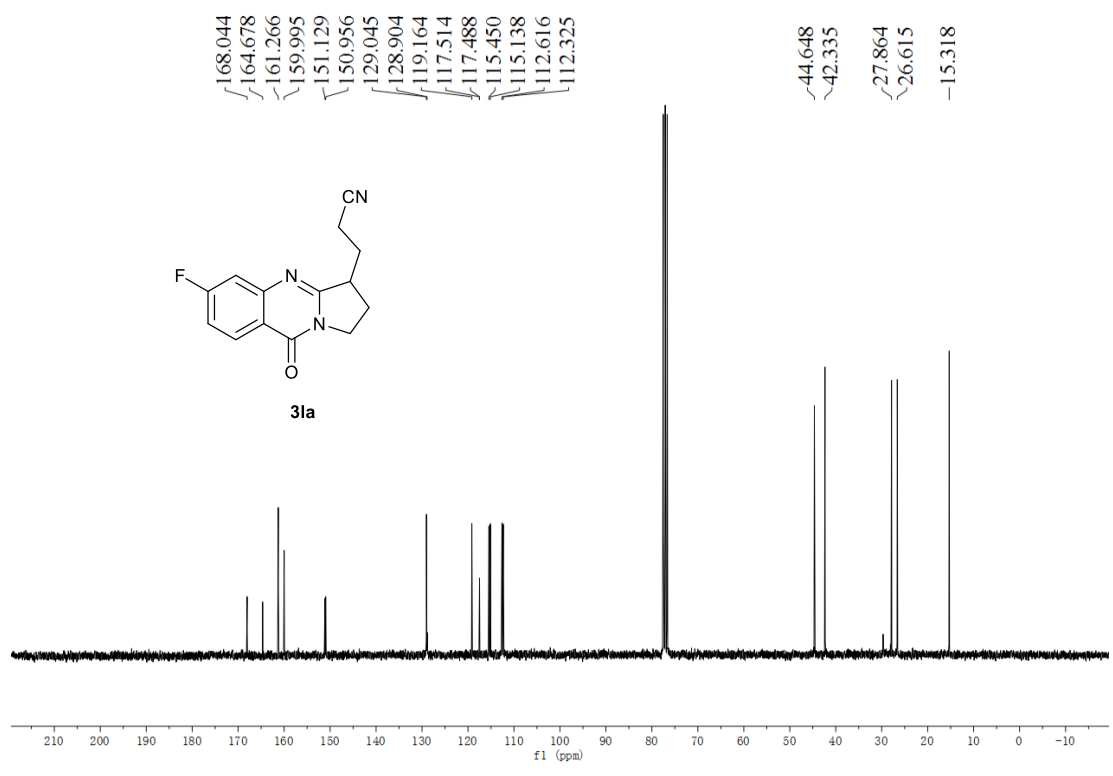
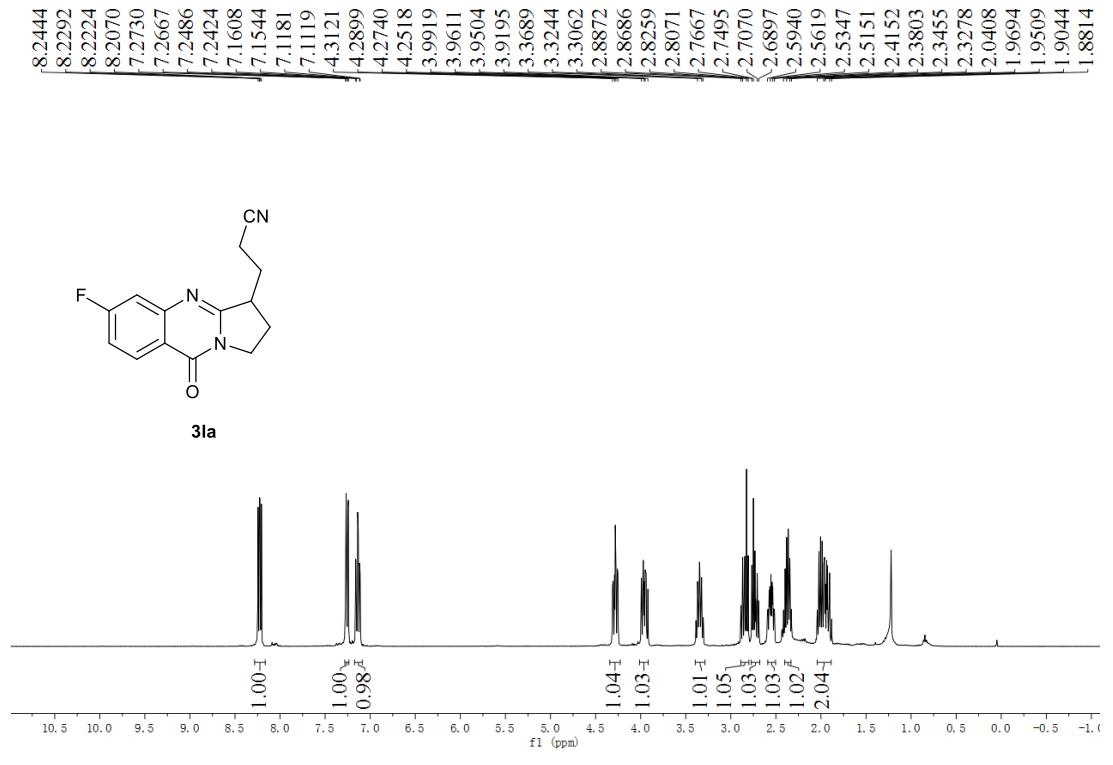




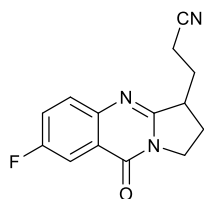




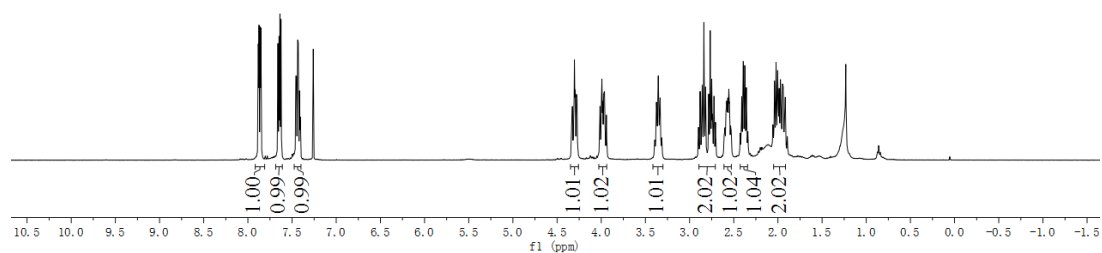




7.8814
7.8740
7.8602
7.8528
7.6595
7.6474
7.6372
7.6251
7.4574
7.4290
7.4075
4.3339
4.3037
4.2737
4.0141
3.9832
3.9632
3.9418
3.3946
3.3545
3.3145
2.8992
2.8805
2.8193
2.7835
2.7663
2.7067
2.6067
2.5799
2.5558
2.5283
2.4271
2.3925
2.3749
2.3400
2.0567
1.9857
1.9168
1.8938

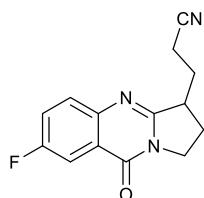


3ma

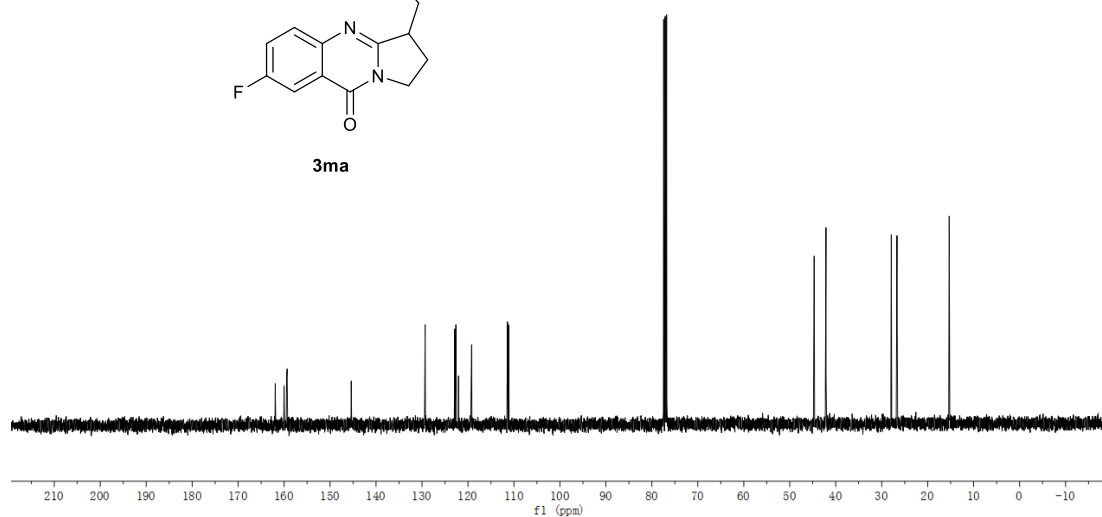


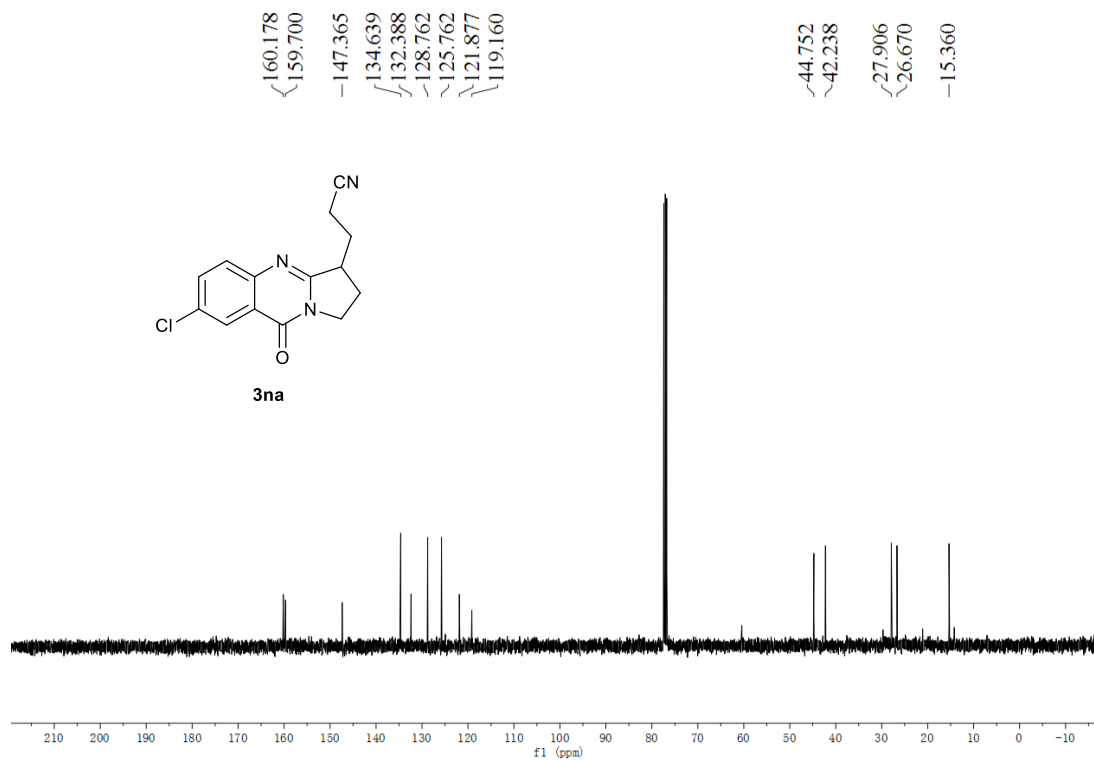
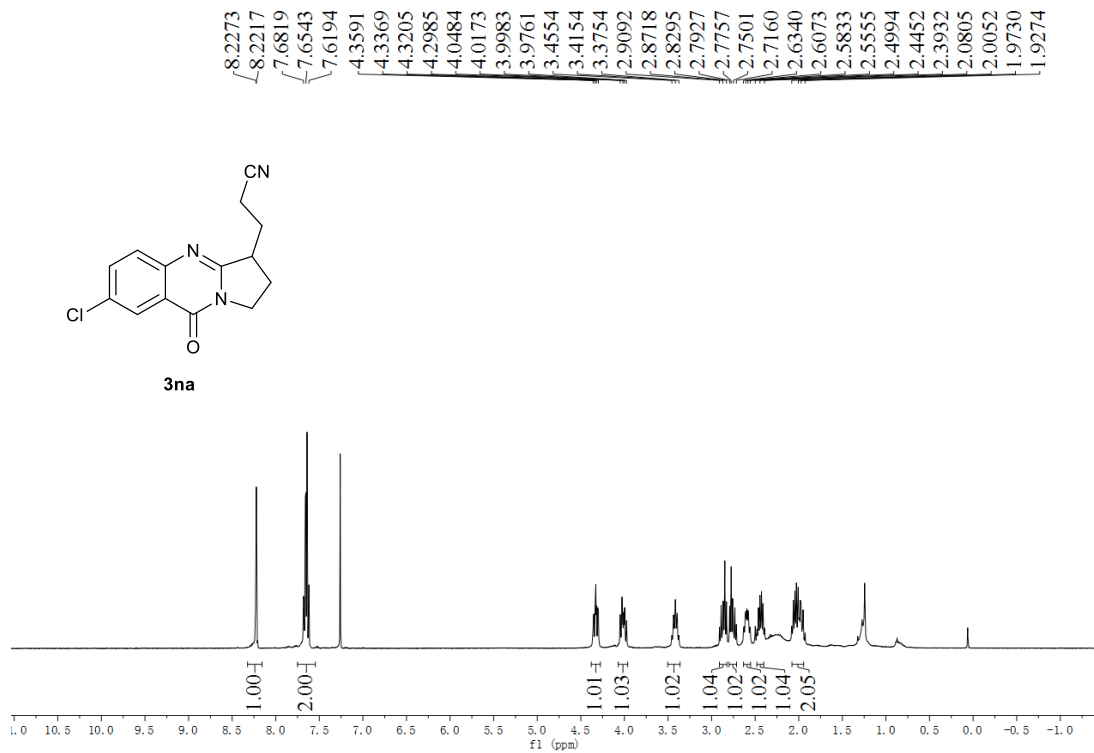
161.934
160.002
159.967
159.469
159.346
159.324
145.398
145.378
129.400
129.318
122.868
122.629
122.061
121.976
119.209
111.396
111.162

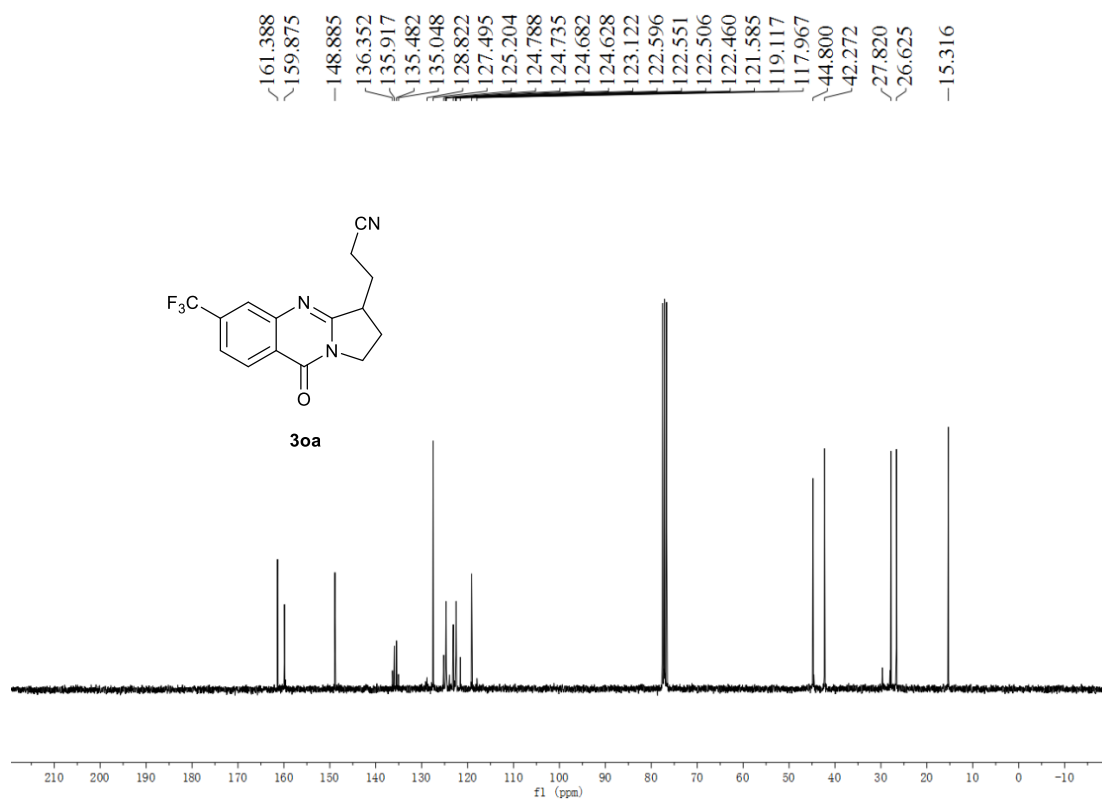
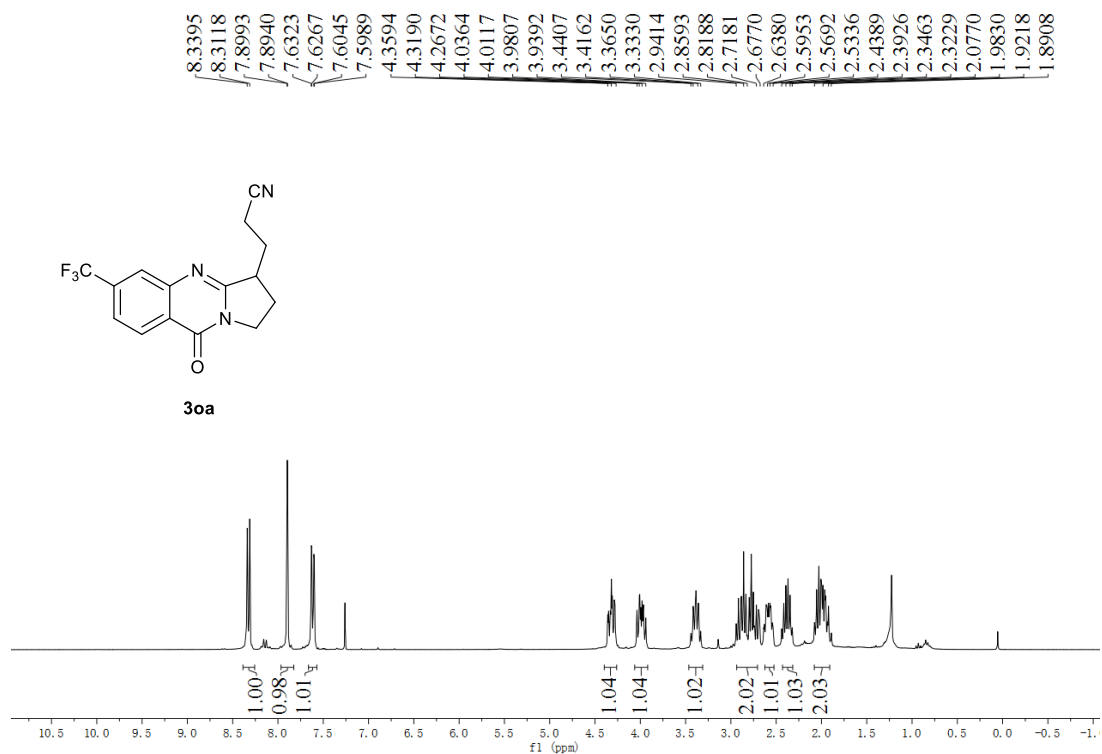
44.693
42.120
27.921
26.672
15.321



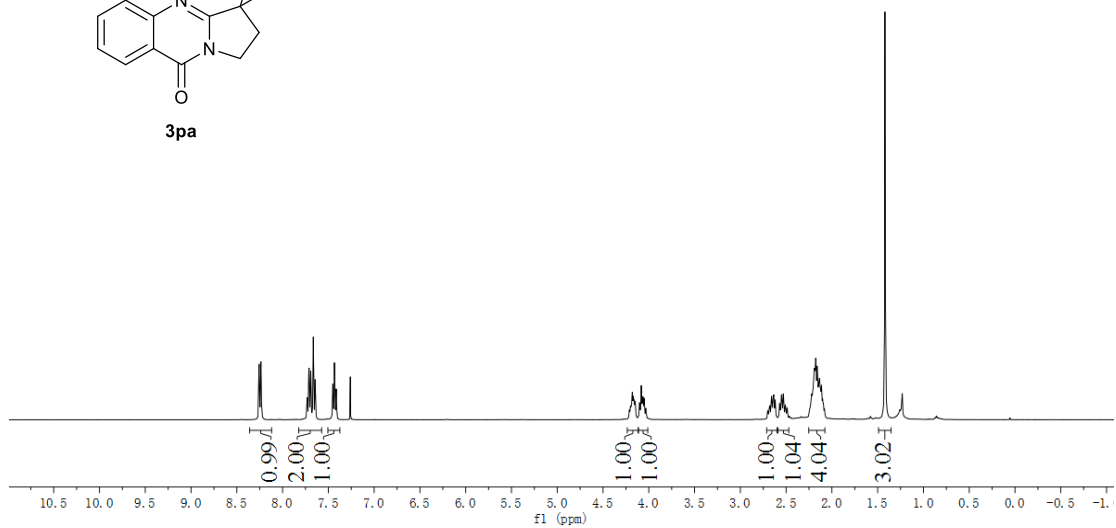
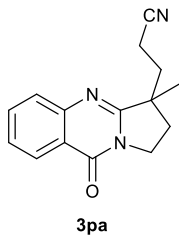
3ma



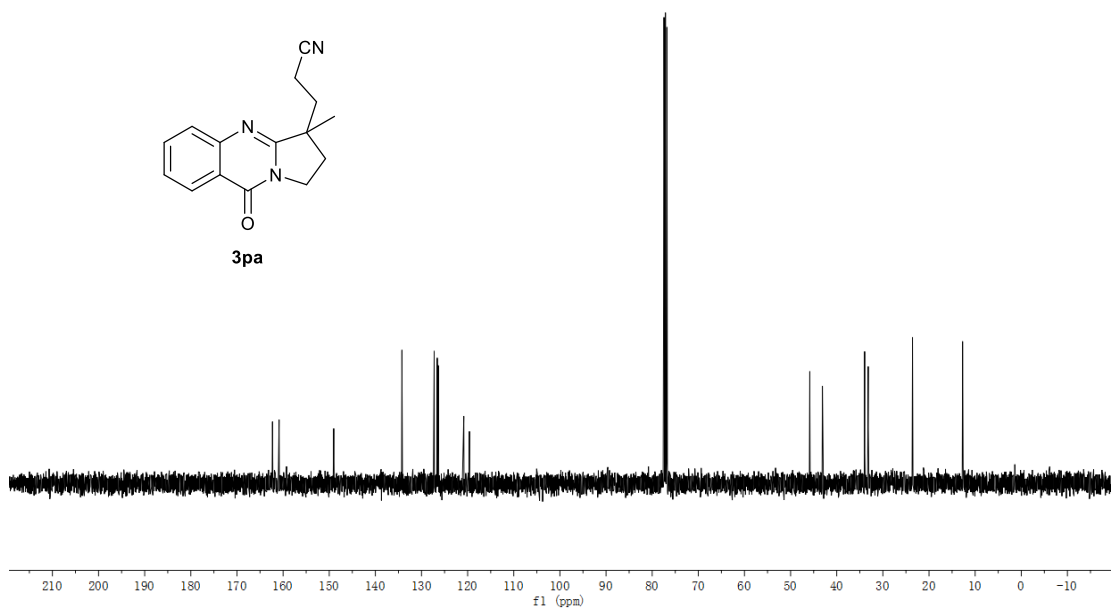
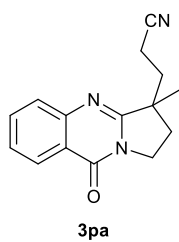


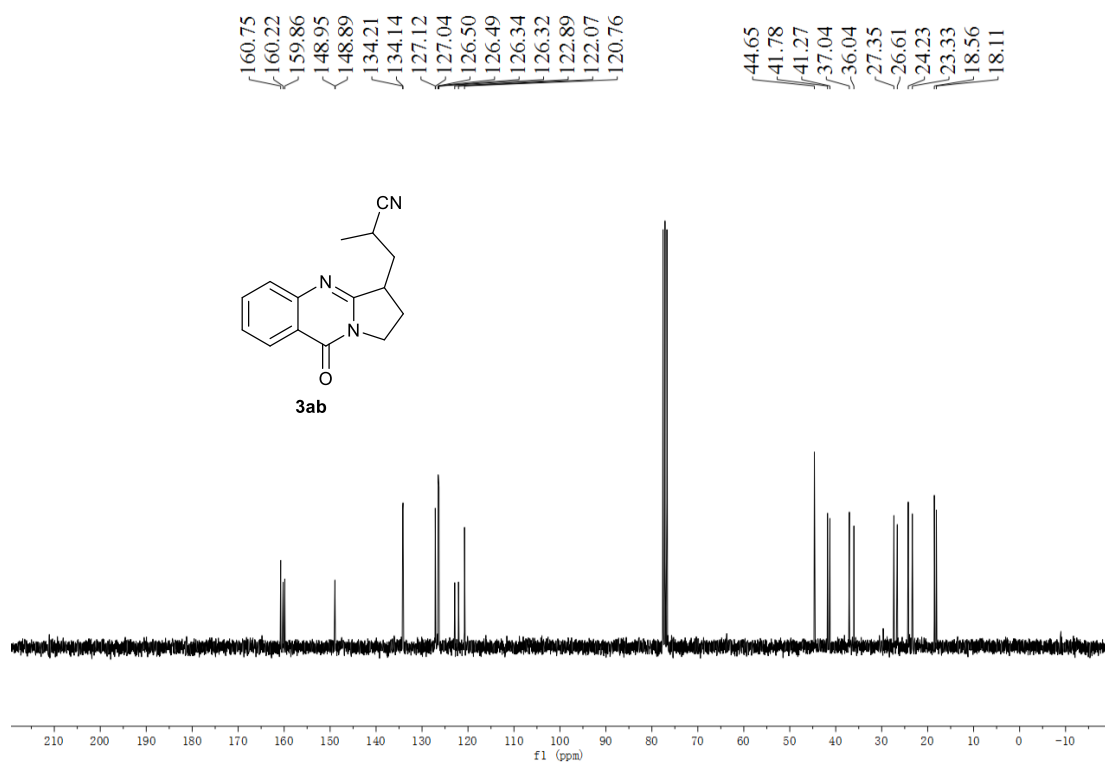
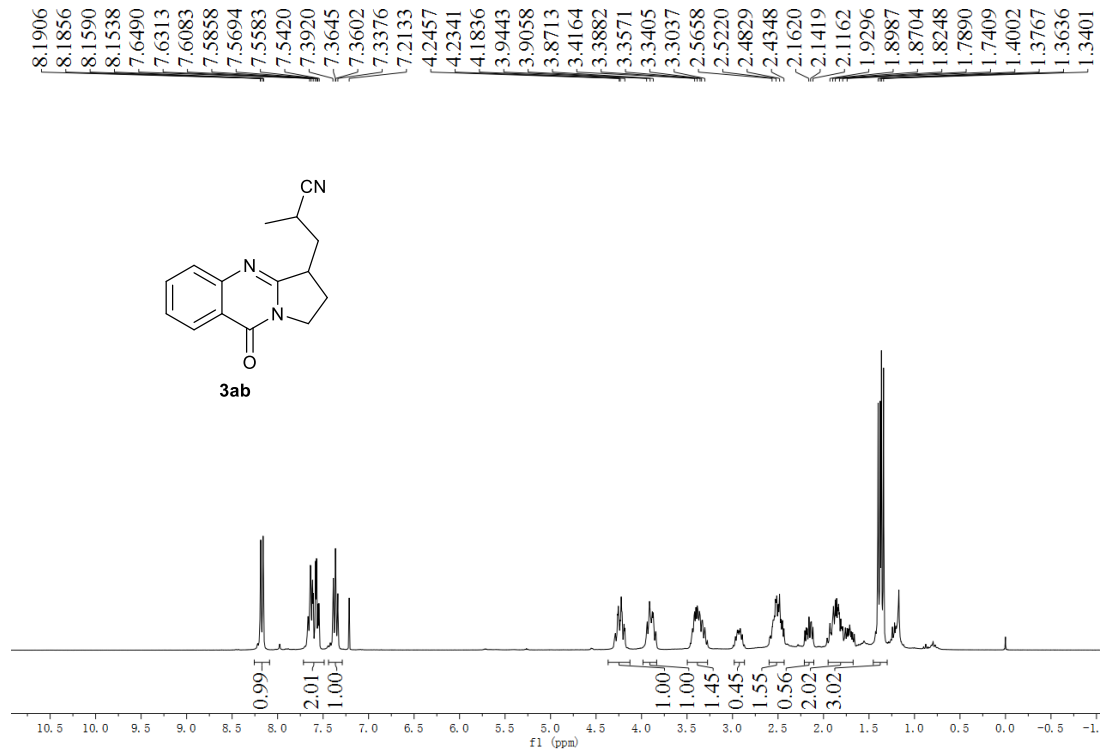


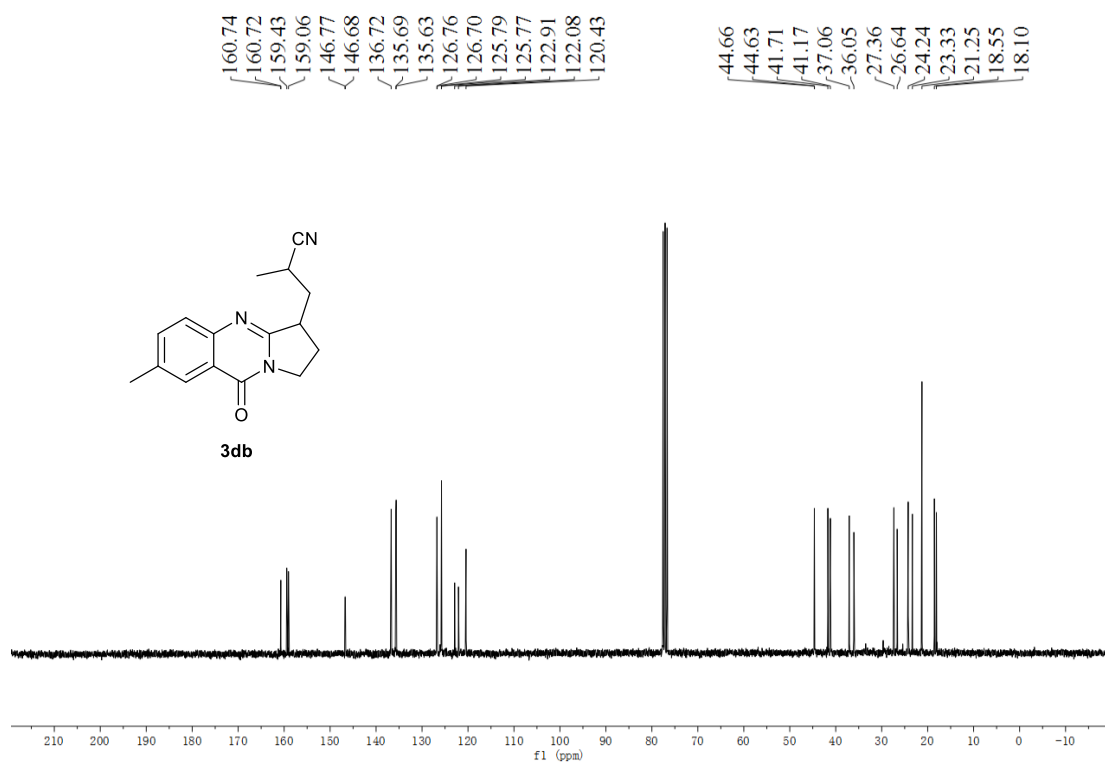
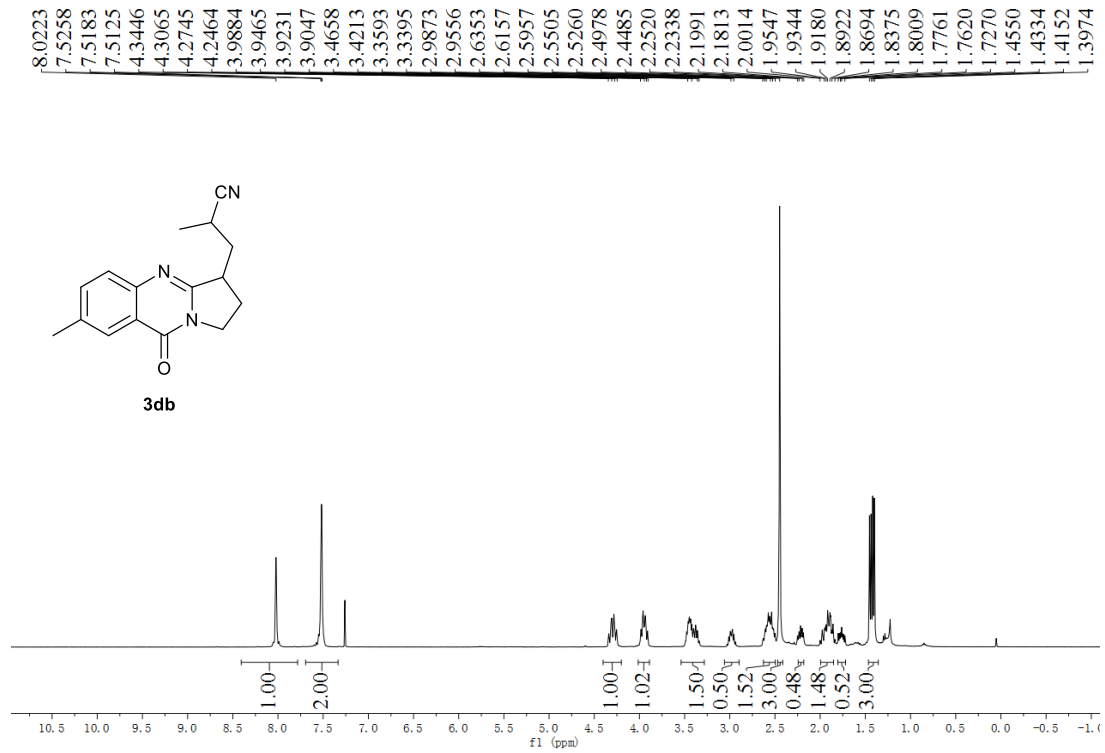
8.2605
8.2565
8.2519
8.2408
8.2366
8.2318
7.7340
7.6887
7.6643
7.6438
7.4548
7.4376
7.4103
4.2126
4.1696
4.1487
4.1011
4.0707
4.0510
4.0324
2.7002
2.6632
2.6589
2.6199
2.5709
2.5303
2.5122
2.4890
2.2425
2.2107
2.1375
2.0931
2.0812
1.4209

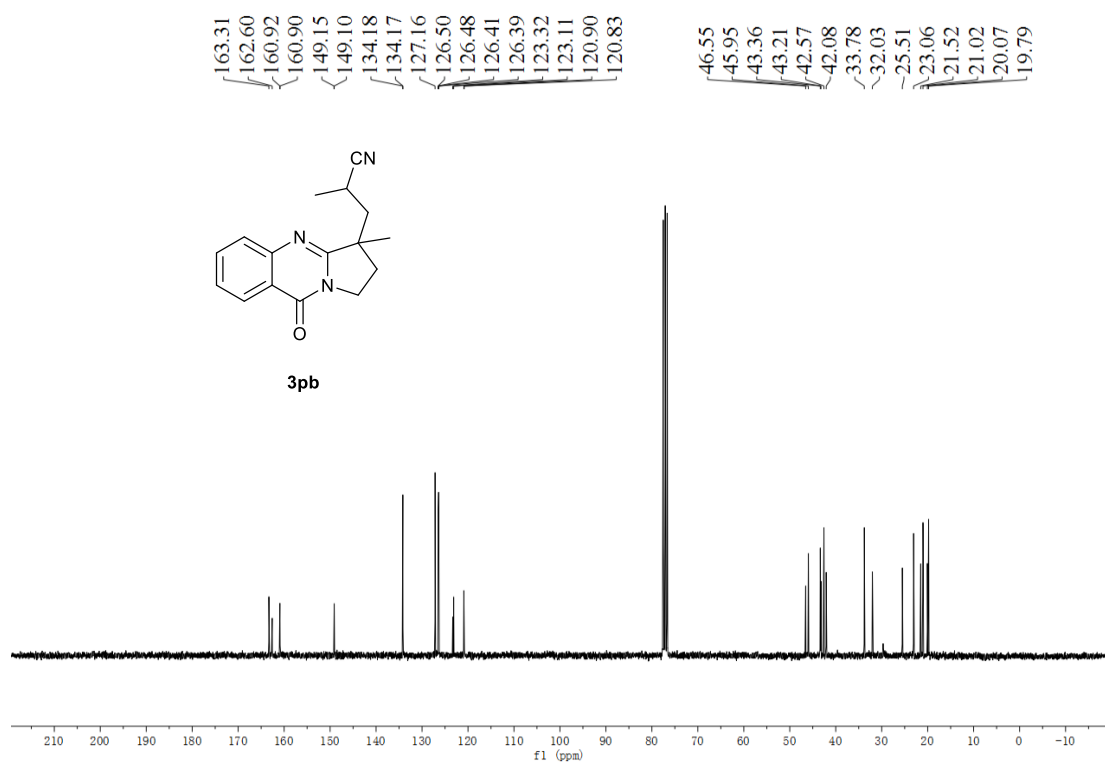
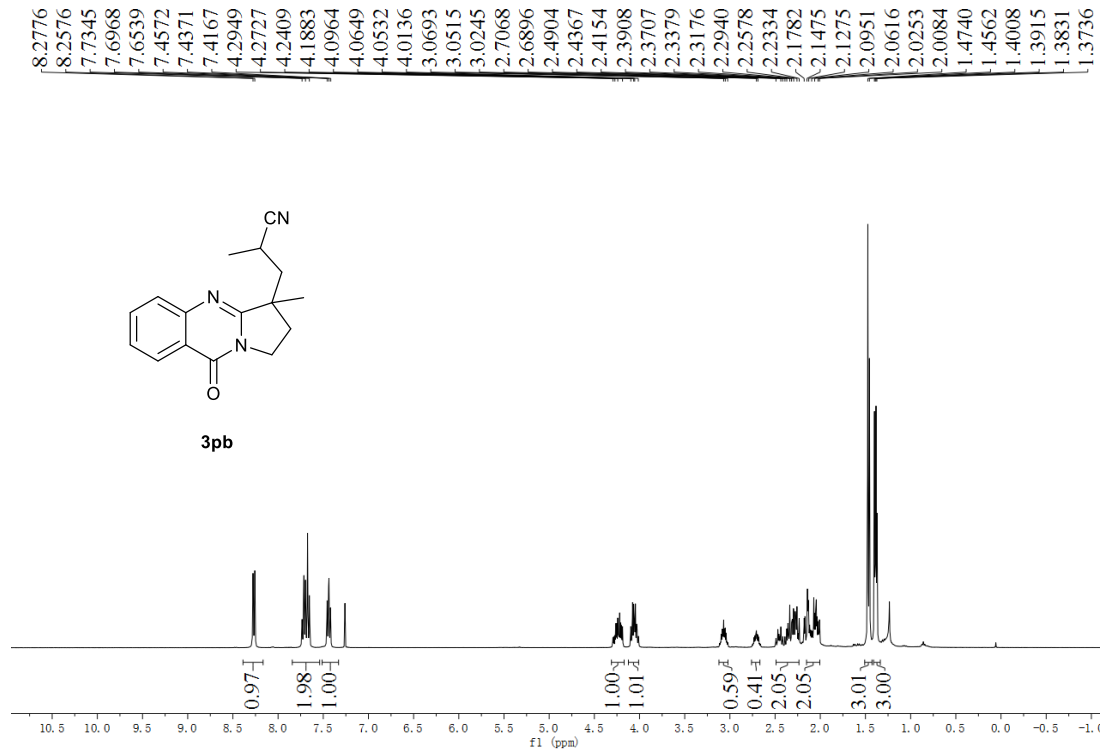


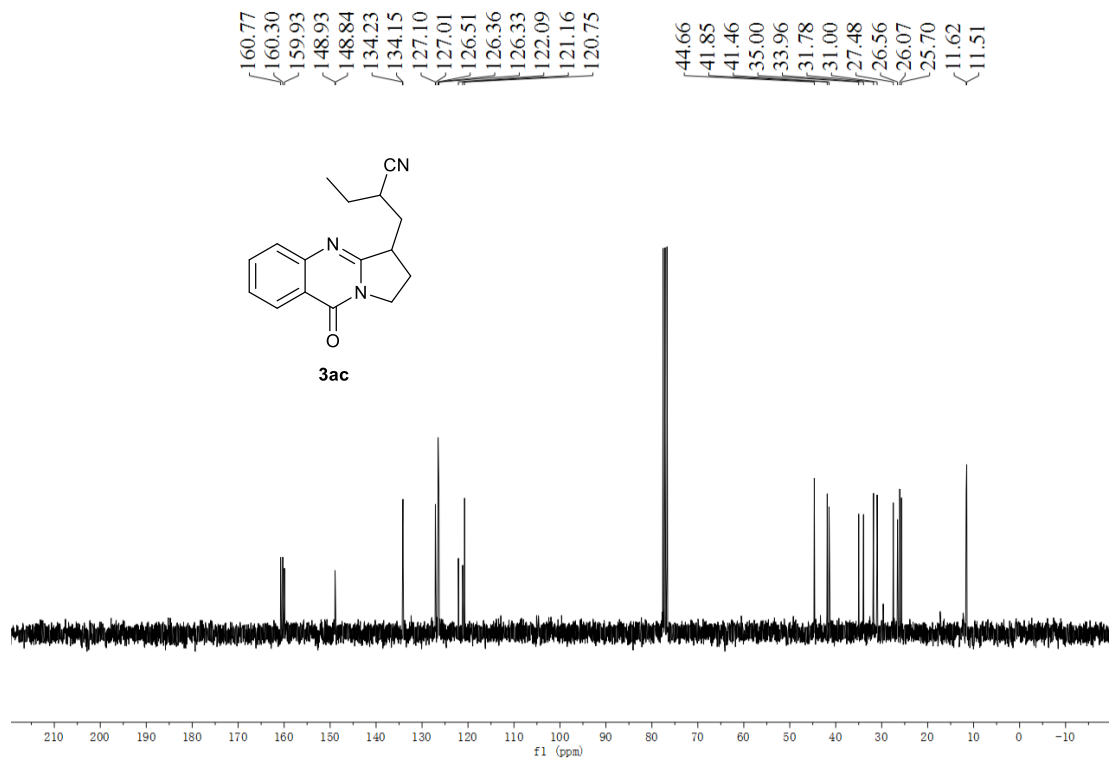
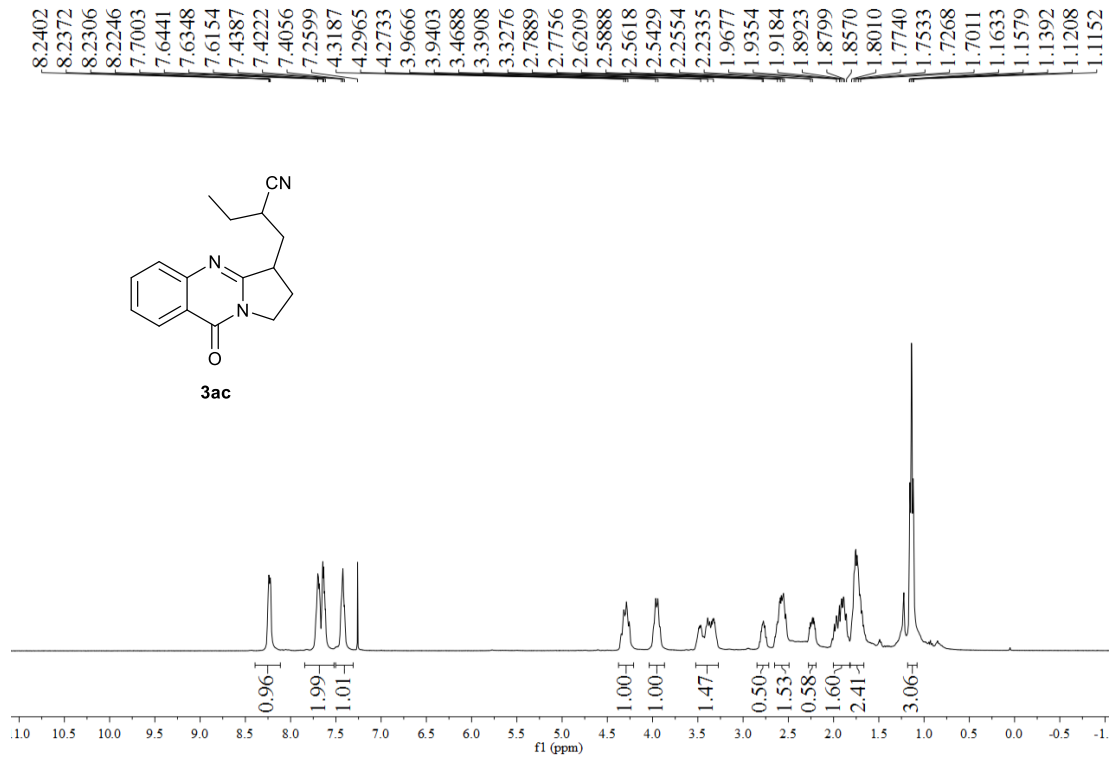
162.31
160.87
-149.02
134.25
127.25
126.58
126.37
120.83
119.61
45.85
43.10
33.95
33.17
23.58
12.72

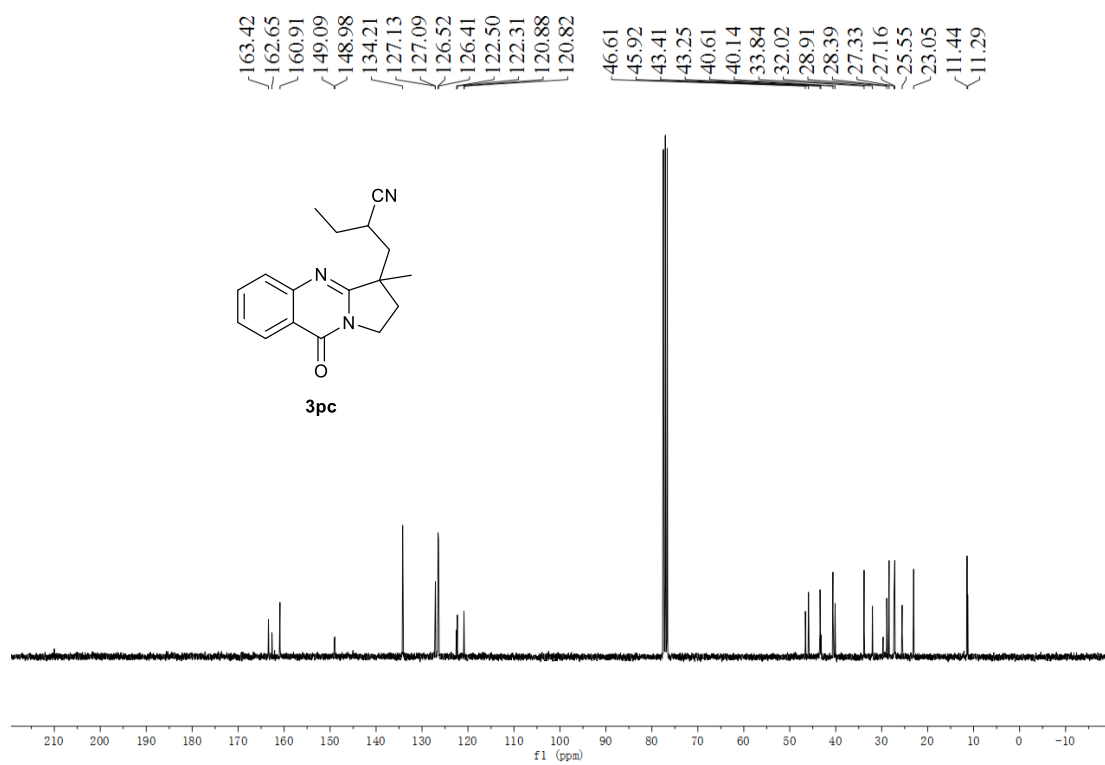
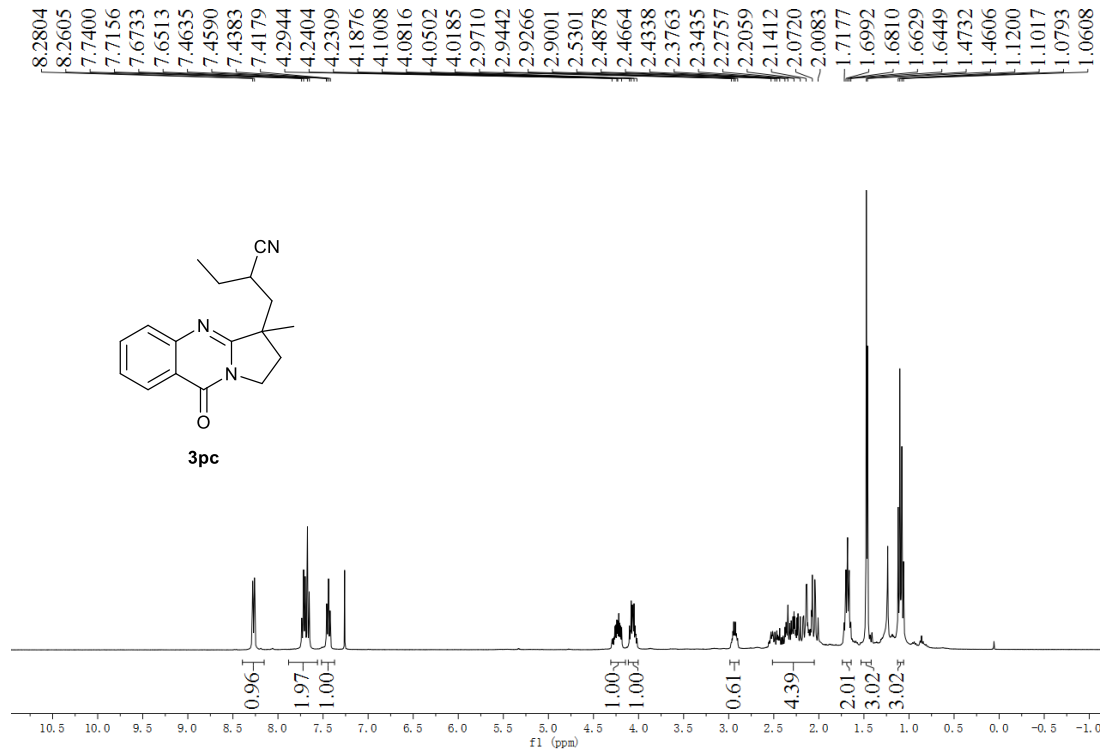


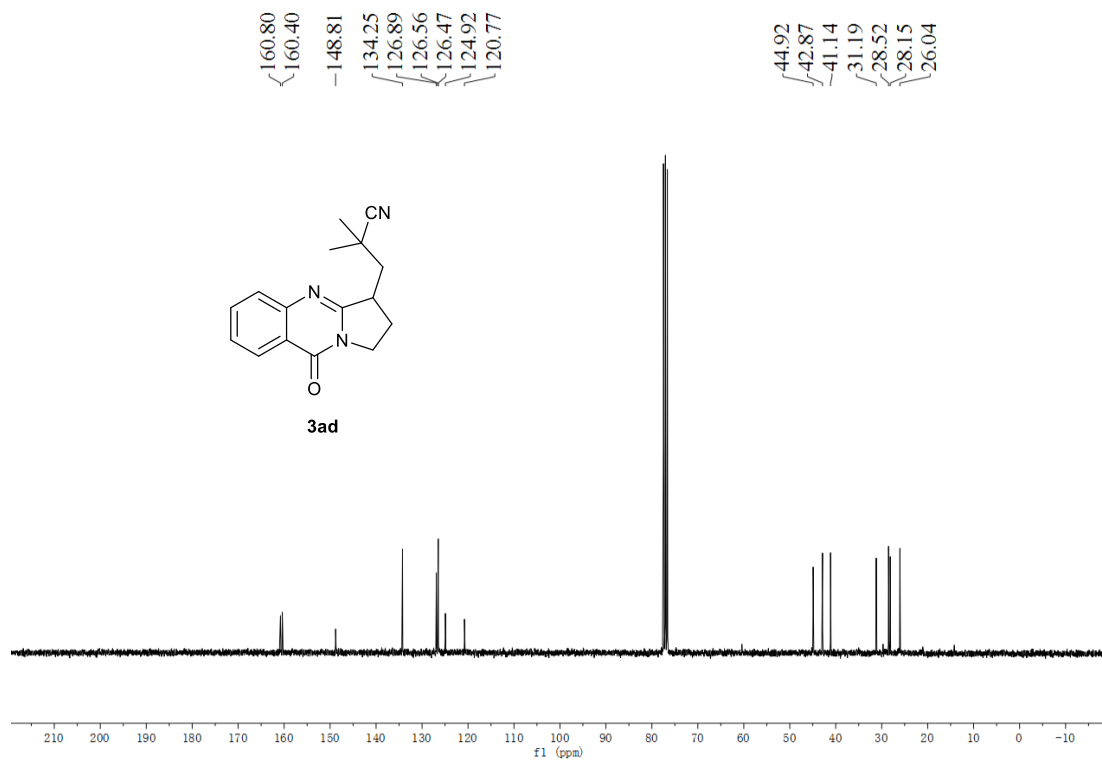
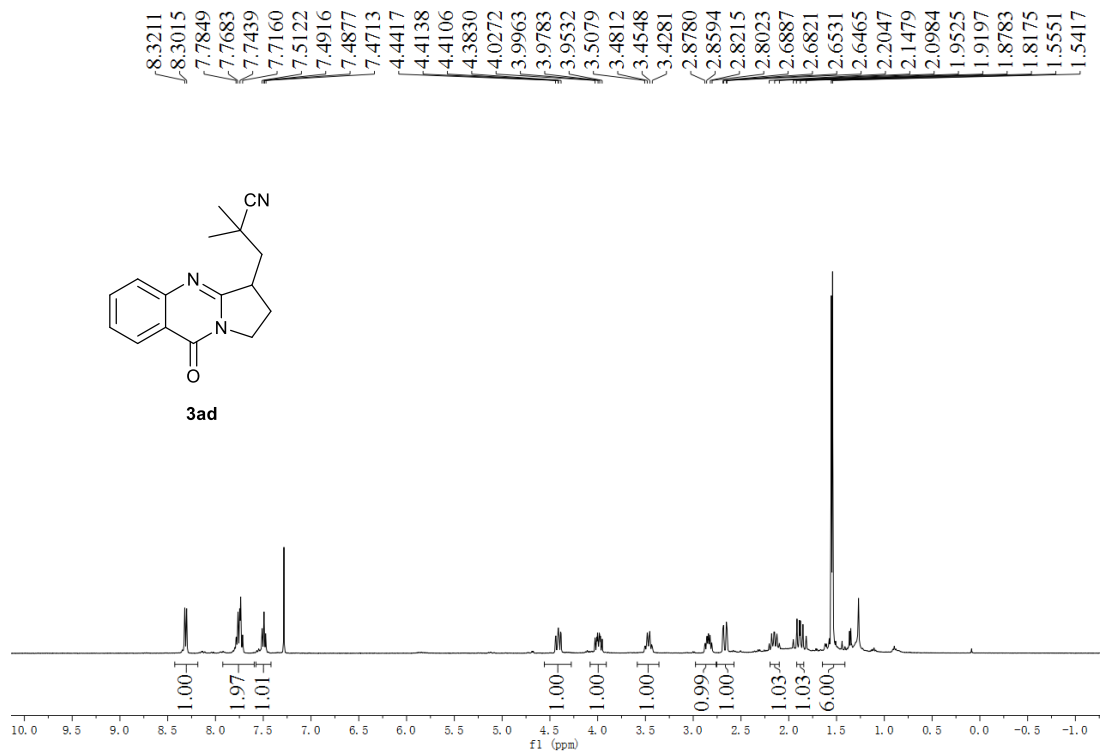


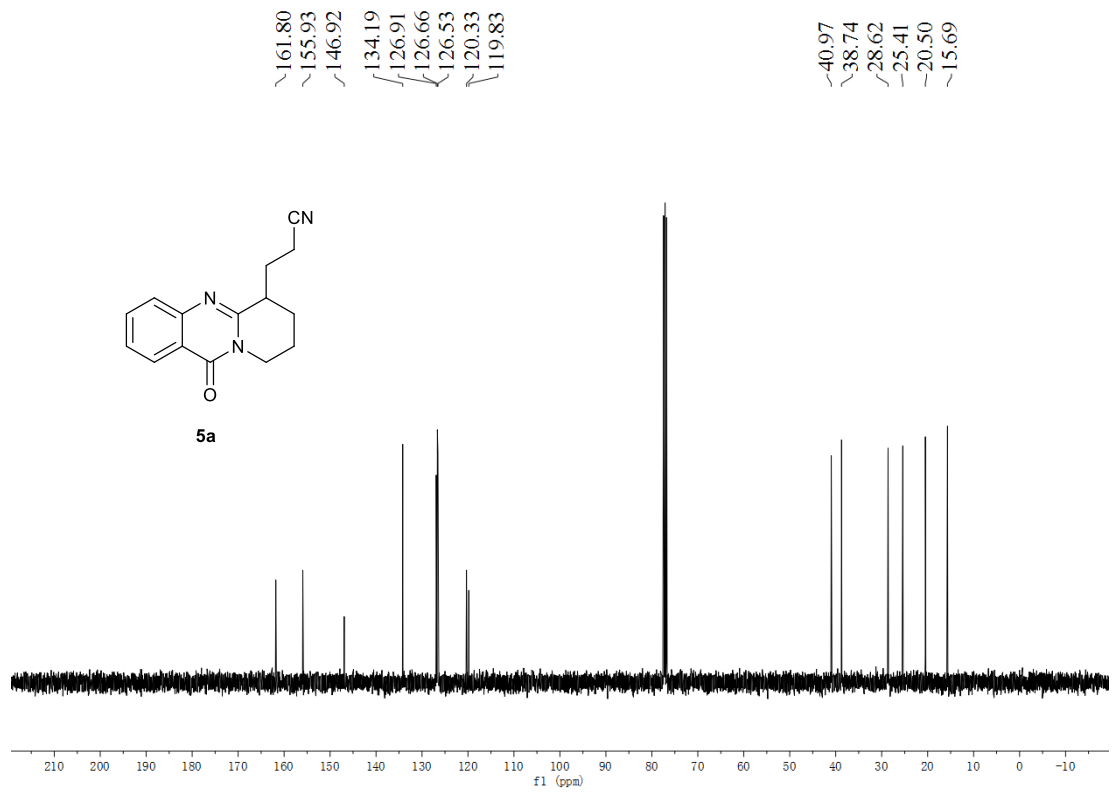
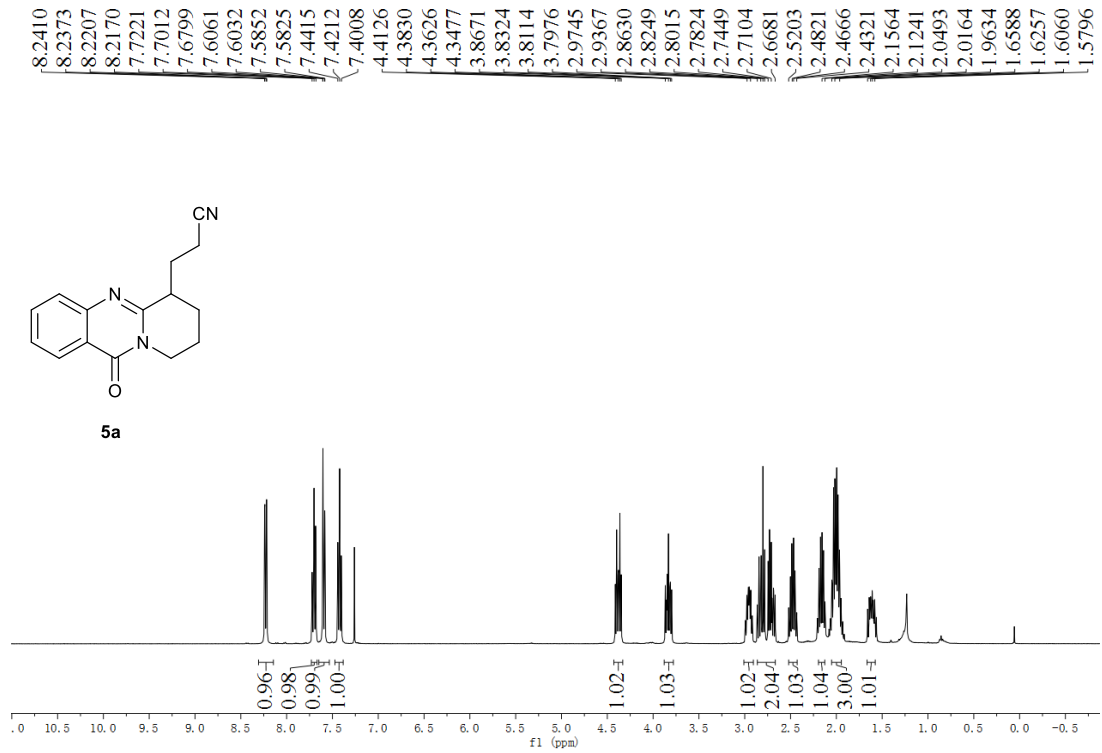


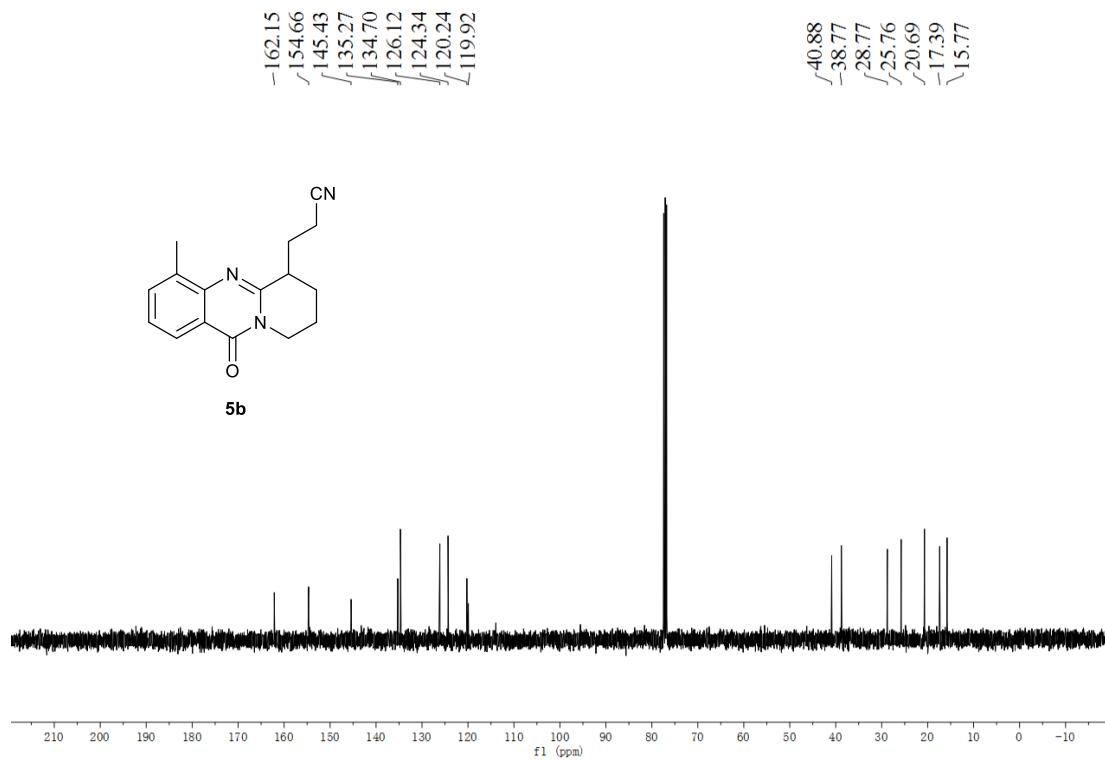
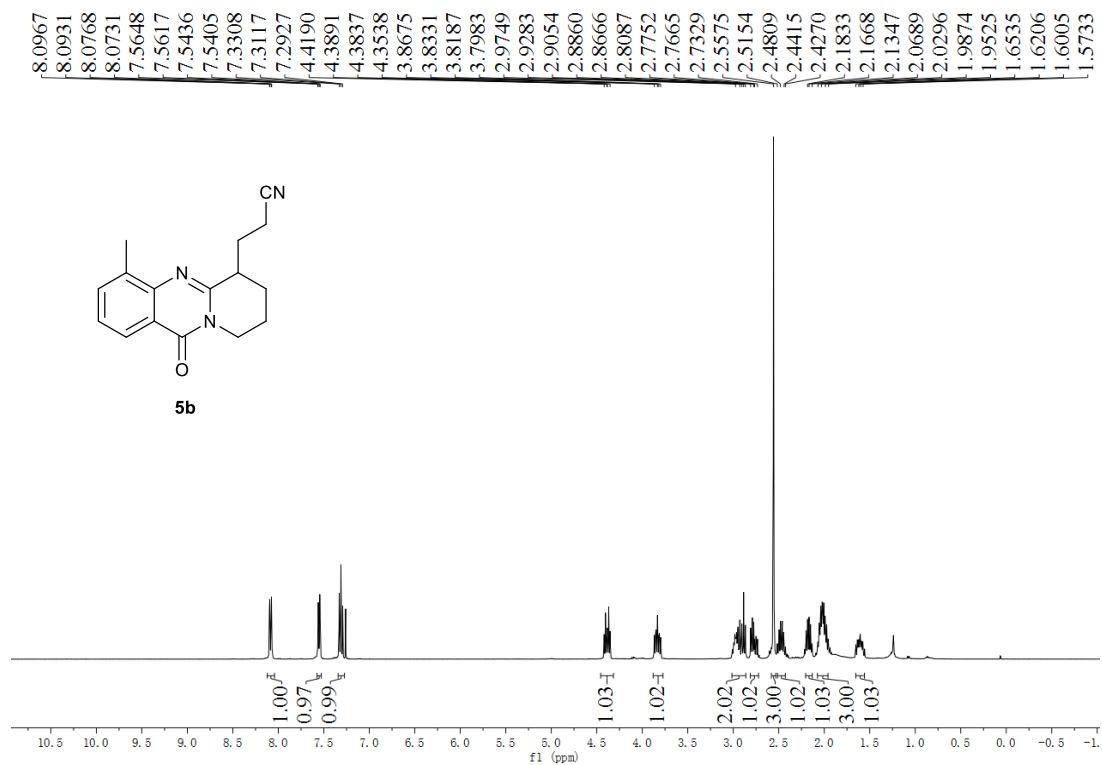


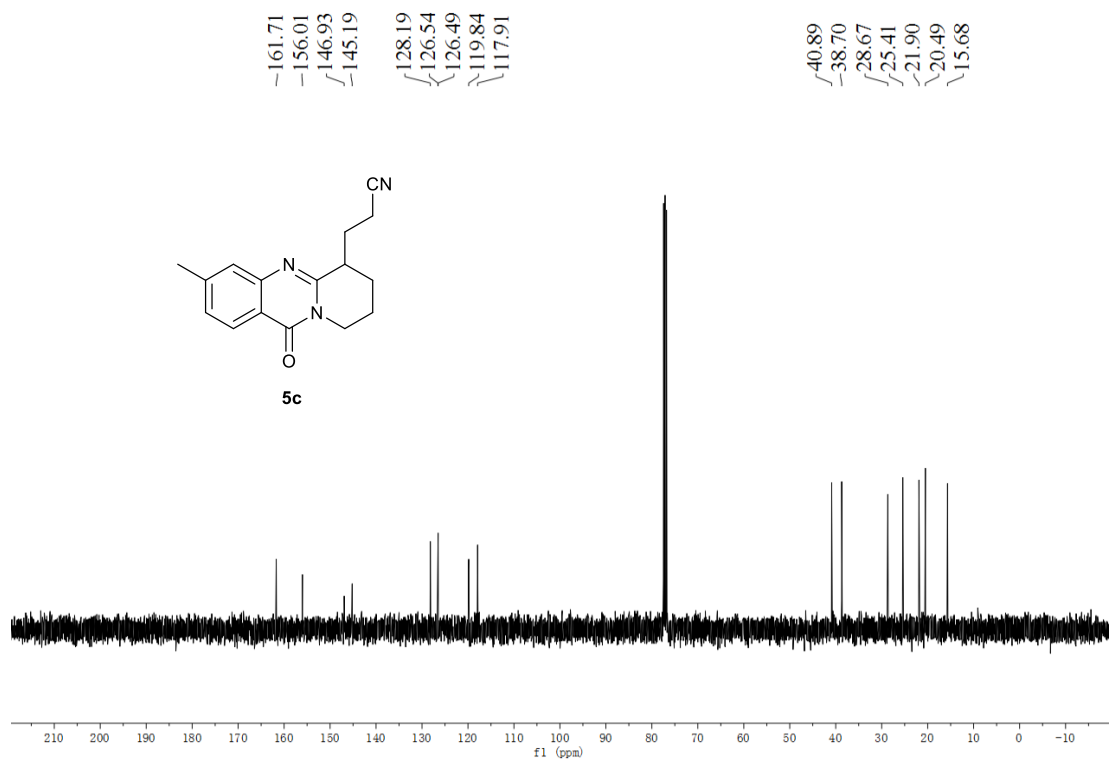
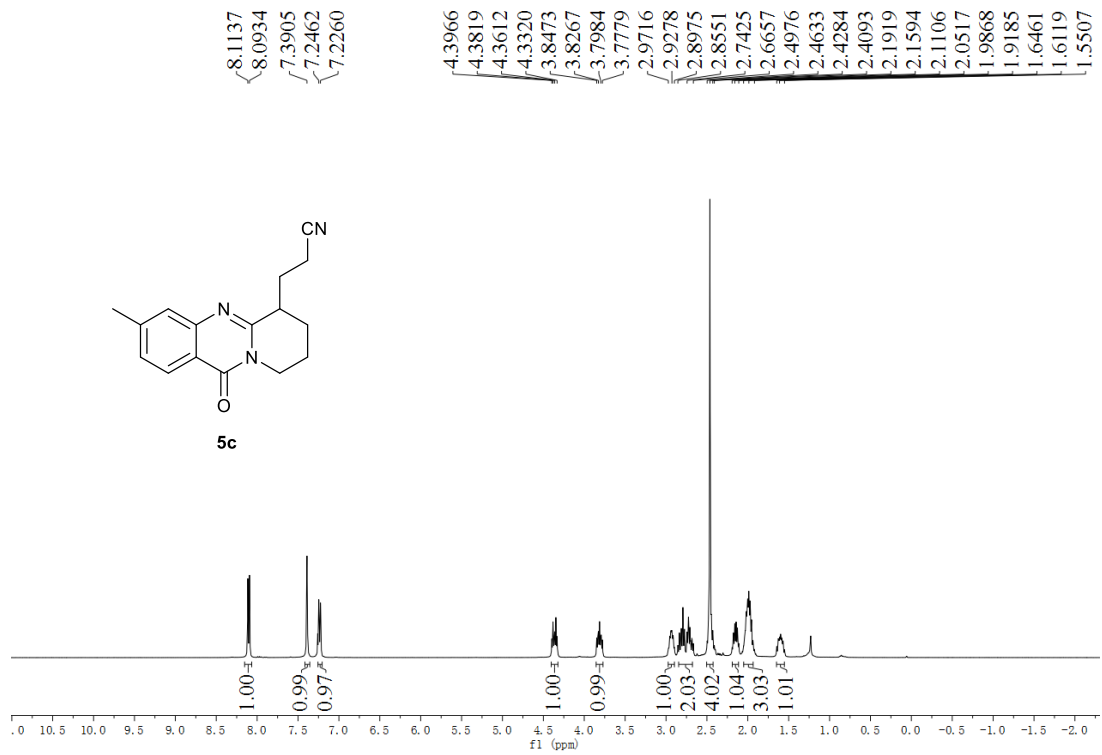


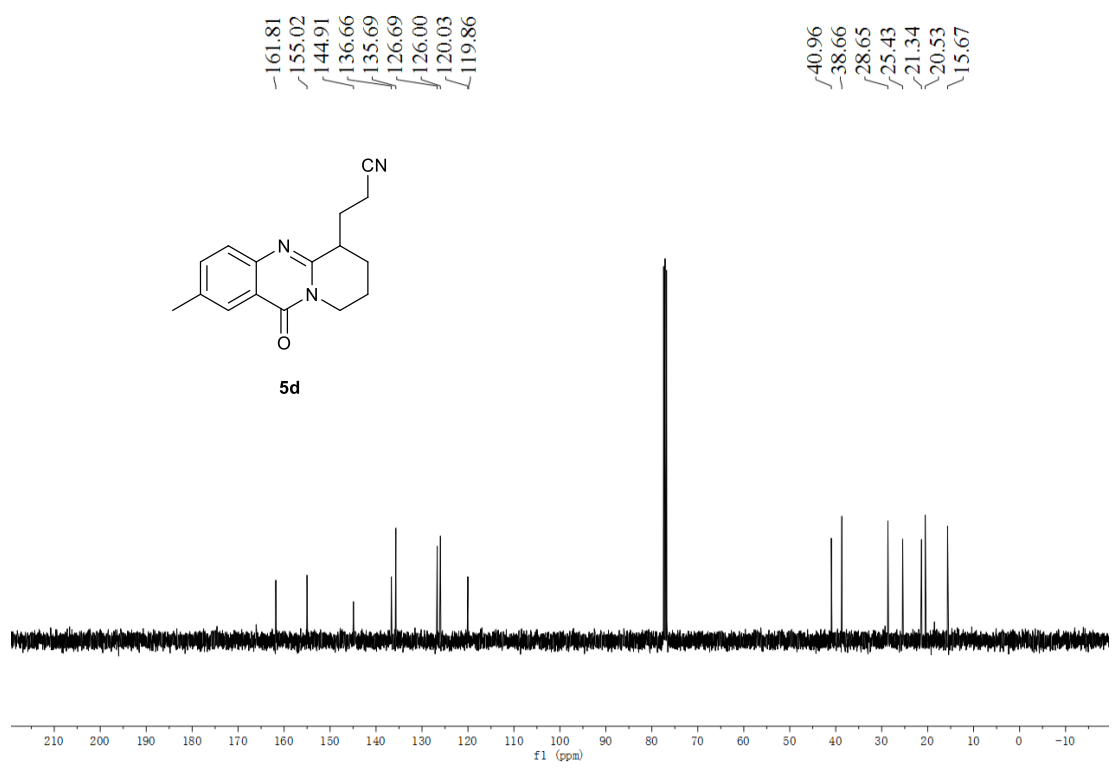
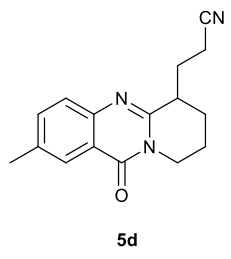
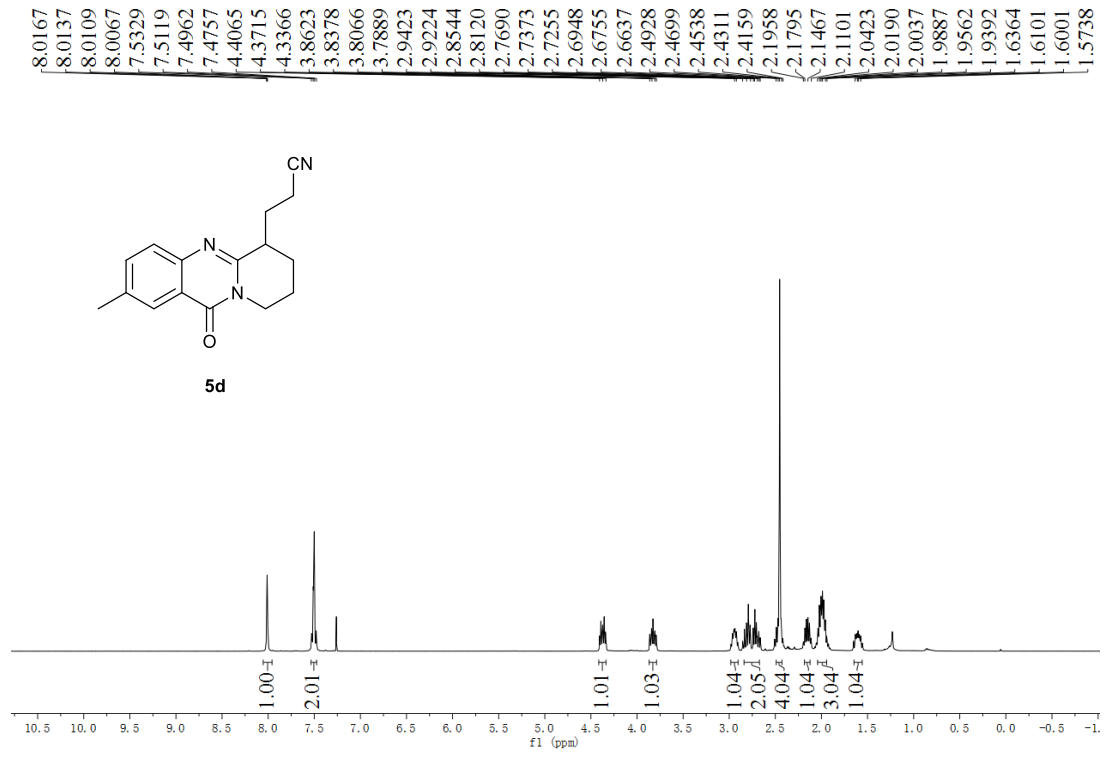


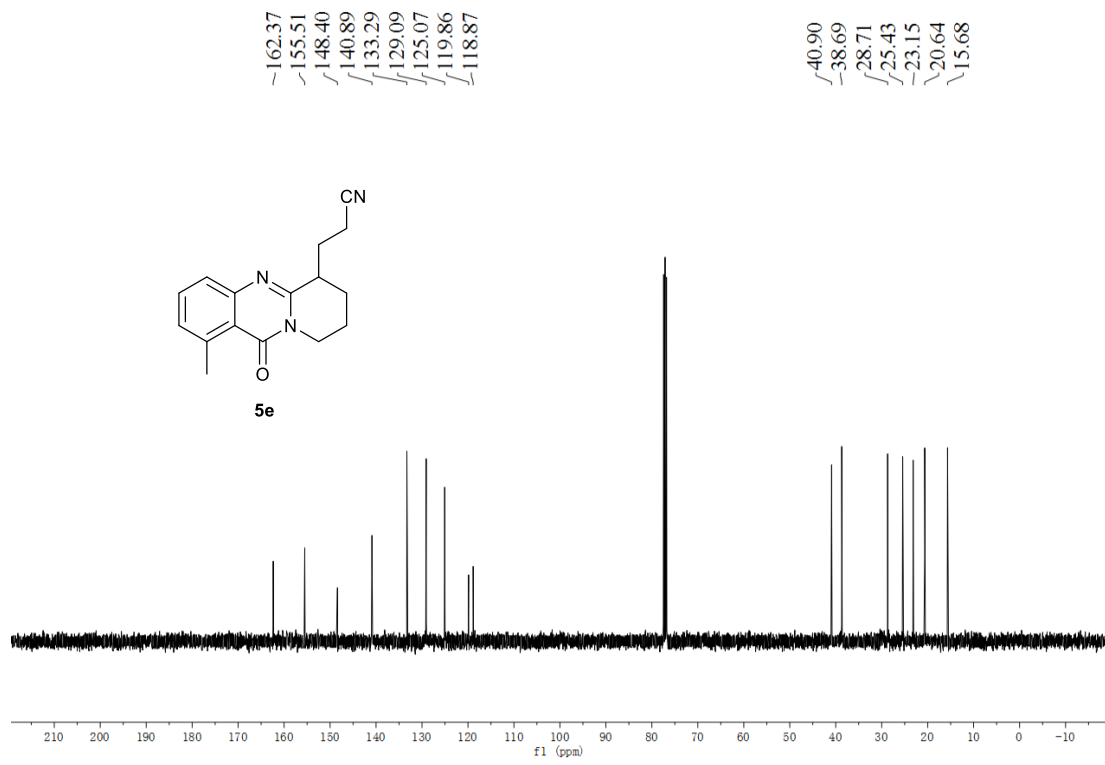
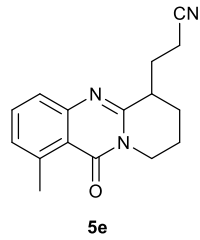
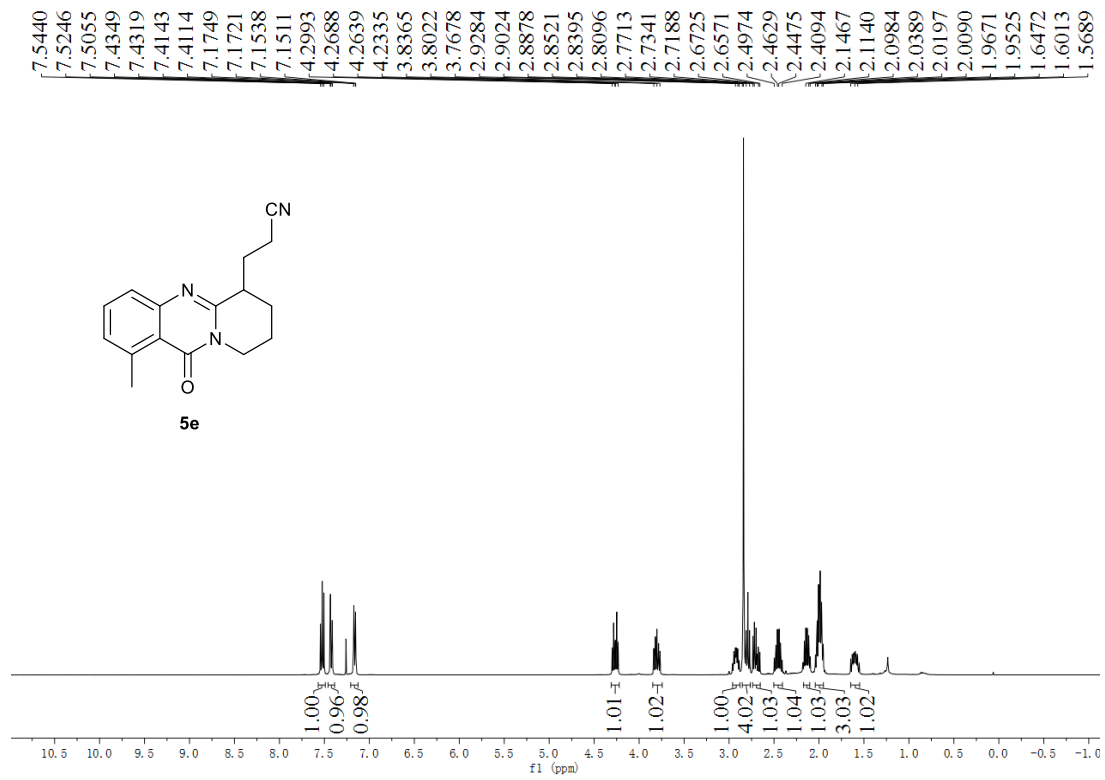


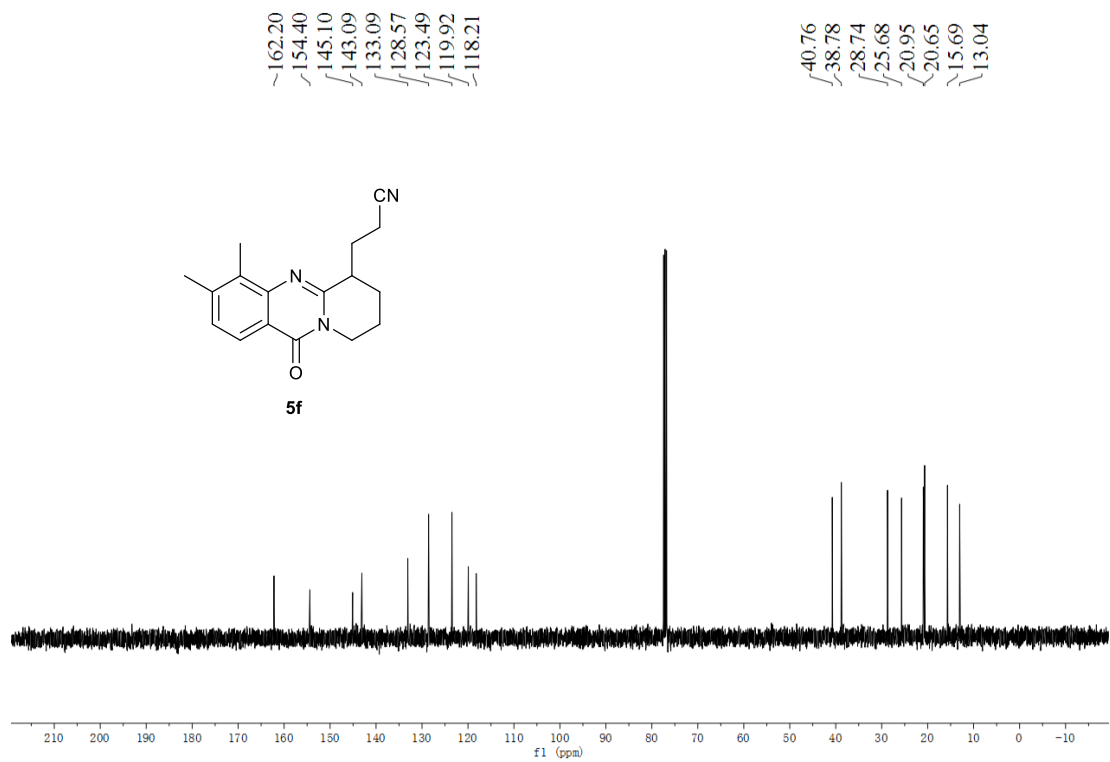
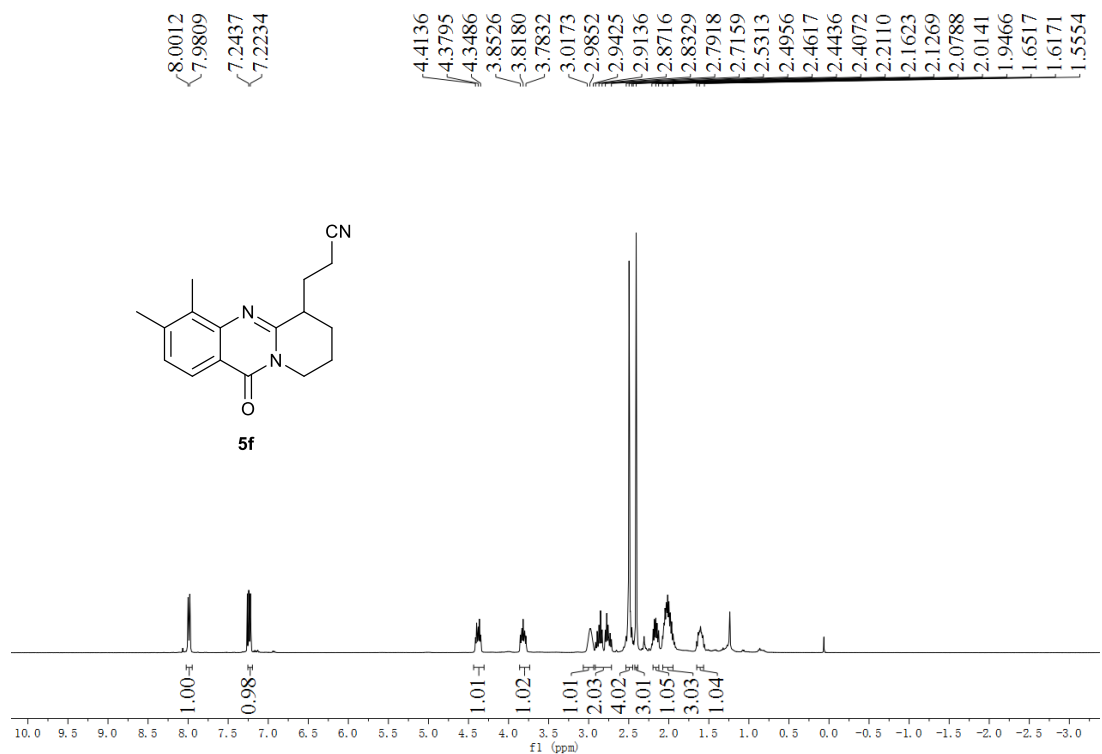


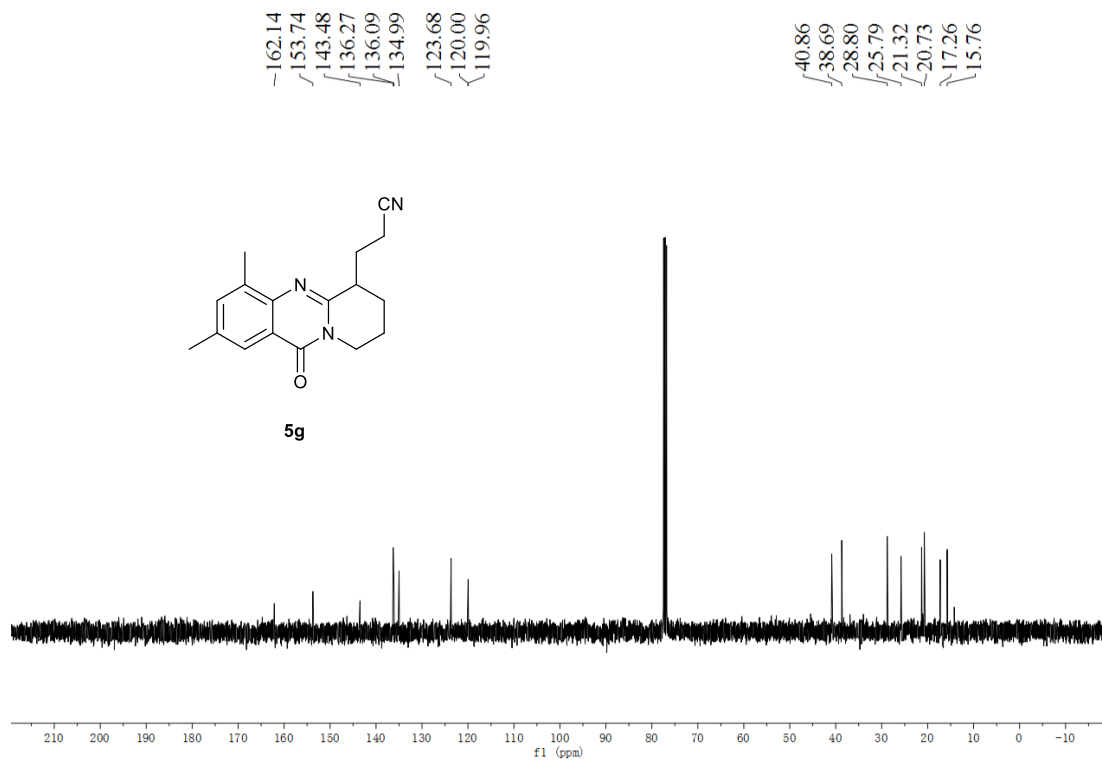
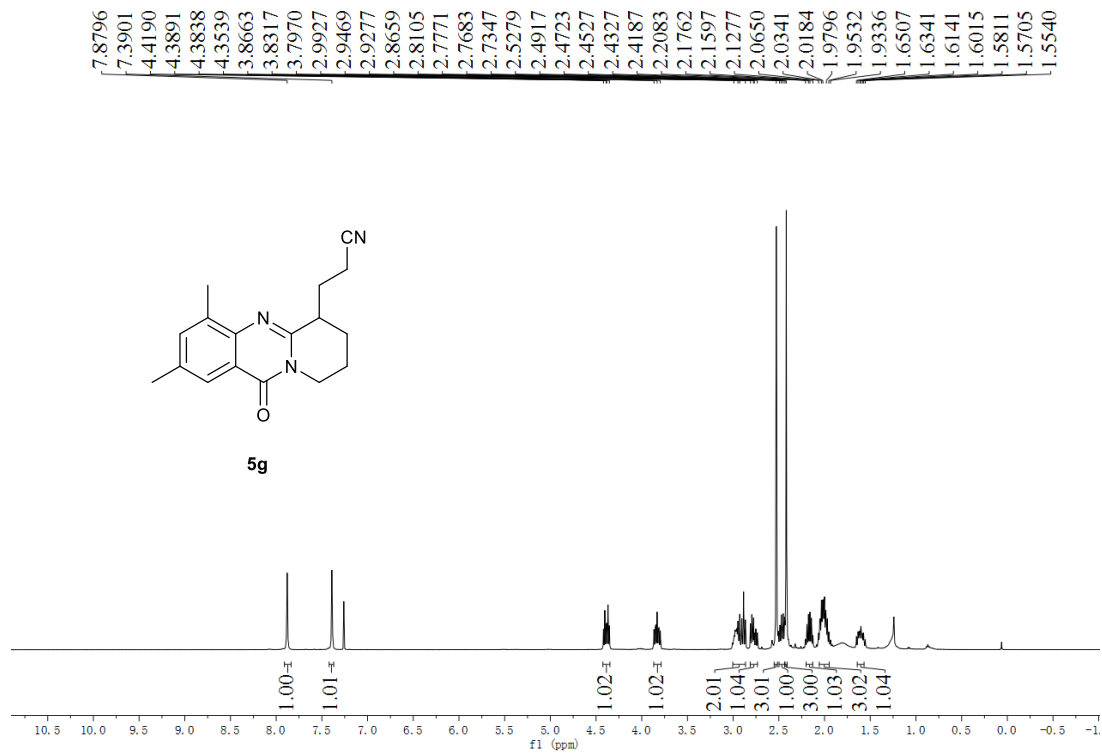


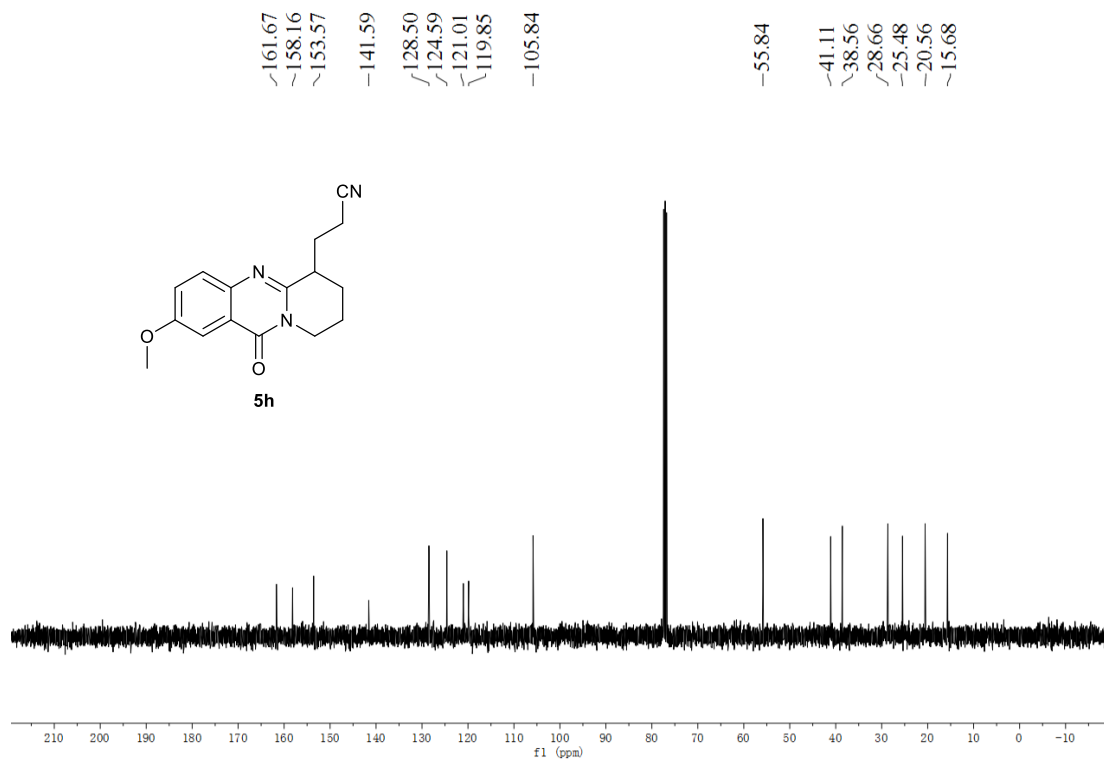
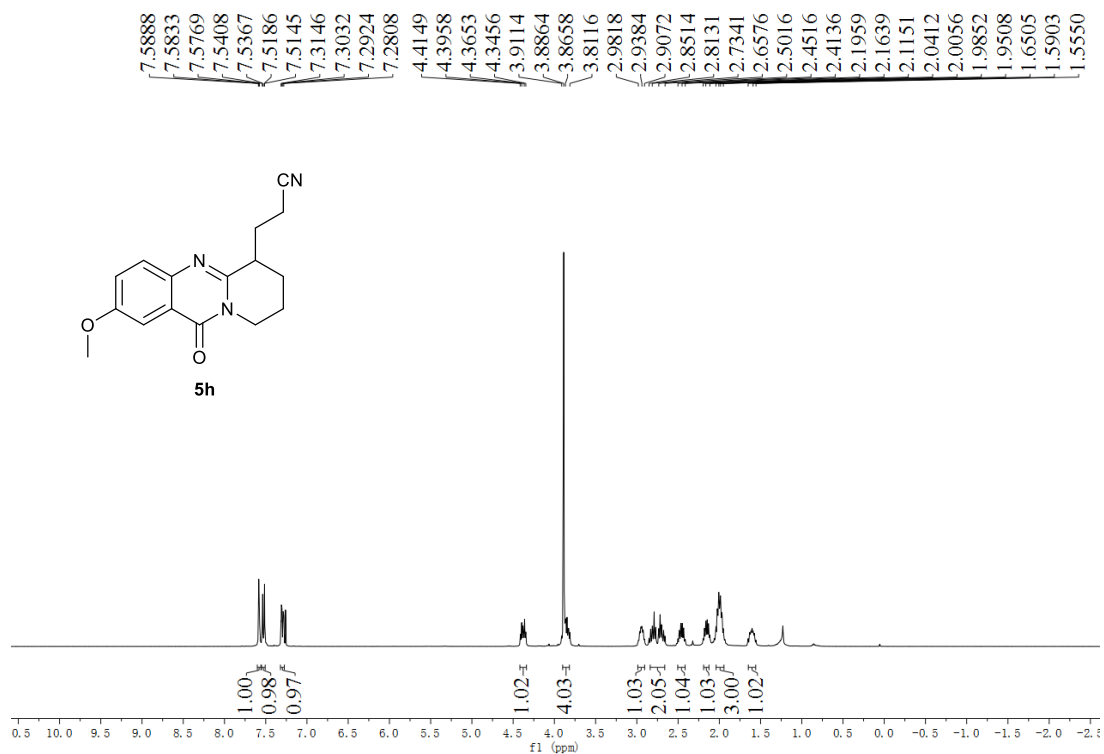


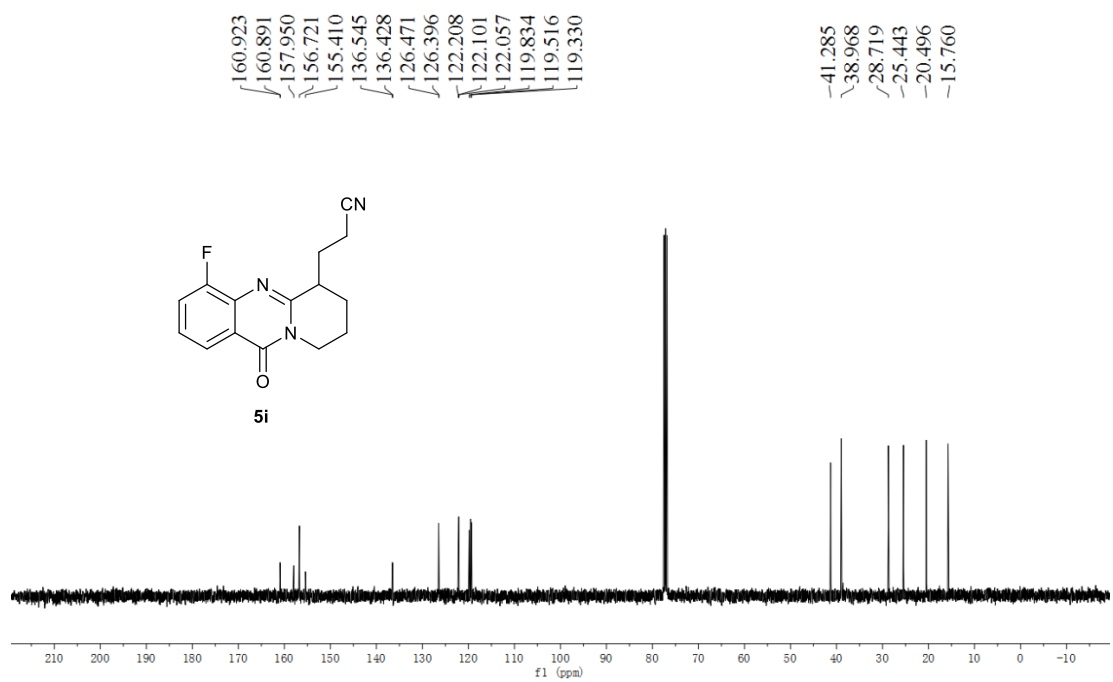
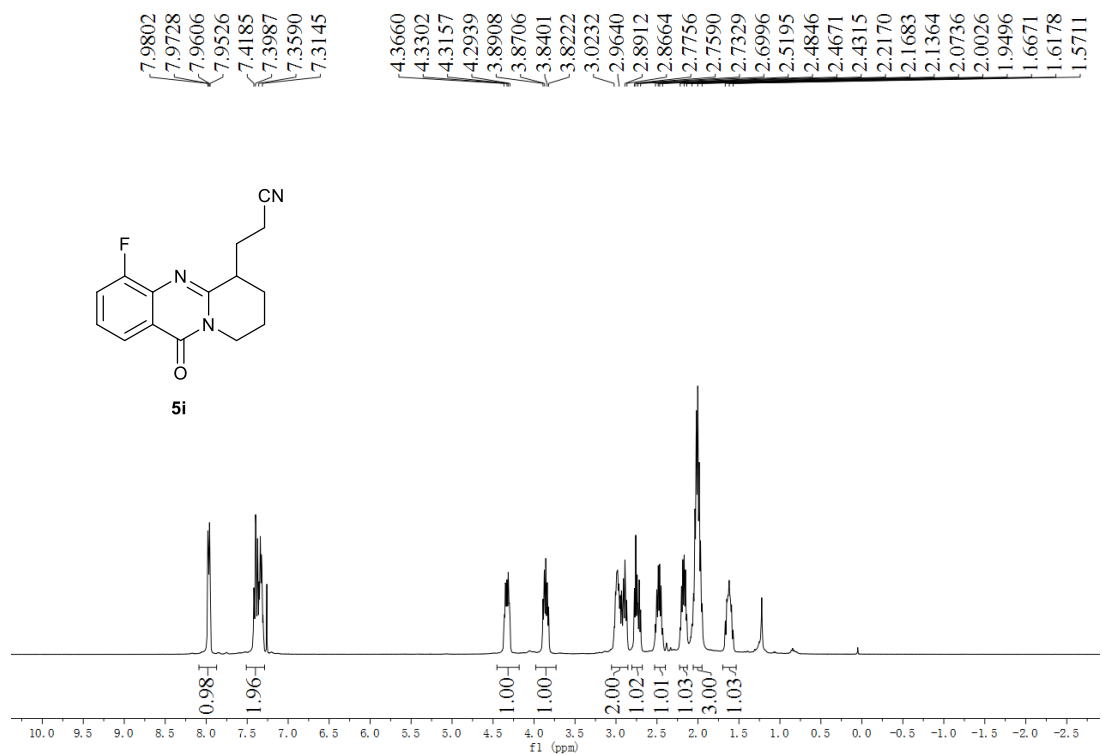




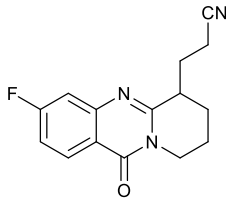




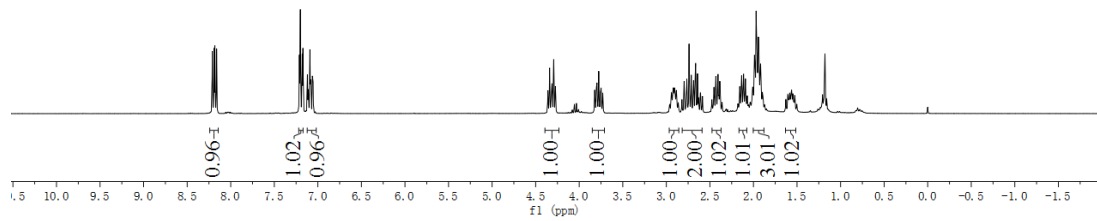




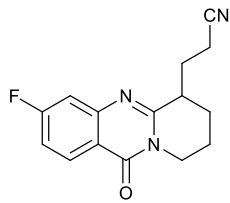
8.2115
8.1912
8.1820
8.1616
7.2117
7.2010
7.1796
7.1714
7.1198
7.1115
7.0627
7.0544
4.3593
4.3201
4.3122
4.2730
3.8222
3.7760
3.7297
2.9617
2.9199
2.8212
2.7392
2.6308
2.5857
2.4774
2.4311
2.3608
2.1787
2.1355
2.1136
2.0563
2.0176
1.9437
1.8915
1.6283
1.5845
1.5021



5j



168.093
164.726
161.056
157.457
148.959
148.784
129.545
129.403
119.657
117.040
117.014
115.622
115.309
112.156
111.869
41.031
38.757
28.533
25.260
20.400
15.695



5j

