

## Supporting Information

### Divergent application of 5-amino-isoxazoles for construction of nitrogen heterocycles via hydride transfer strategy

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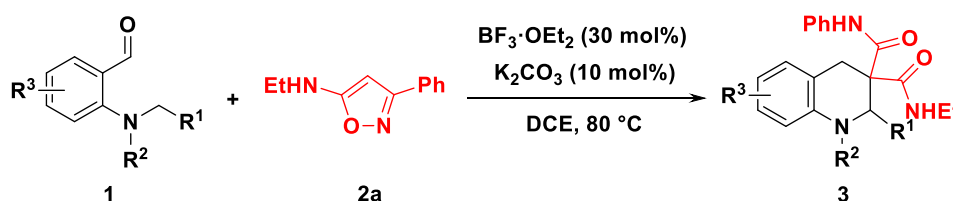
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## 1. General Information

Unless otherwise noted, all reagents and solvents were purchased from the commercial sources (from Adamas-beta) and used as received. Thin layer chromatography (TLC) was used to monitor the reaction on Merck 60 F254 precoated silica gel plate (0.2 mm thickness). TLC spots were visualized by UV-light irradiation on Spectroline Model ENF-24061/F 254 nm. The products were purified by flash column chromatography (200-300 mesh silica gel) eluted with the gradient of petroleum ether and ethyl acetate. Proton nuclear magnetic resonance spectra ( $^1\text{H}$  NMR) were recorded on a Bruker 500 MHz or 400 MHz NMR spectrometer ( $\text{CDCl}_3$ ). The chemical shifts were reported in parts per million (ppm), downfield from  $\text{SiMe}_4$  ( $\delta$  0.0) and relative to the signal of chloroform-*d* ( $\delta$  7.26, singlet). Multiplicities were afforded as: s (singlet); d (doublet); t (triplet); q (quartet); dd (doublets of doublet) or m (multiplets). The number of protons for a given resonance is indicated by nH. Coupling constants were reported as a *J* value in Hz. Carbon nuclear magnetic resonance spectra ( $^{13}\text{C}$  NMR) was referenced to the appropriate residual solvent peak. Conventional heating was performed with a standard hot plate/magnetic stirrer, using a silicone oil bath. The type of the device that used for the crystal measurement was "X calibur, Eos, Gemini". High resolution mass spectral analysis (HRMS) was performed on Waters XEVO G2 Q-TOF. 3-Phenylisoxazol-5-amine and N-ethyl-3-phenylisoxazol-5-amine were prepared according to literature.<sup>1</sup>

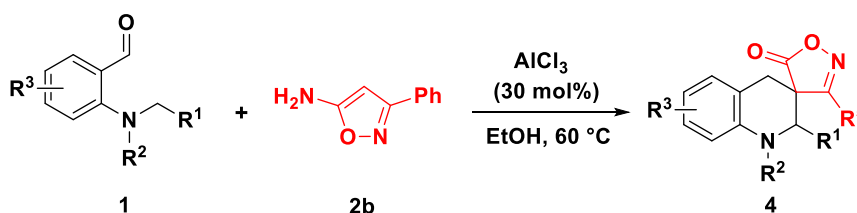
## 2. General Procedure

### 2.1 General Procedure for Construction of 3



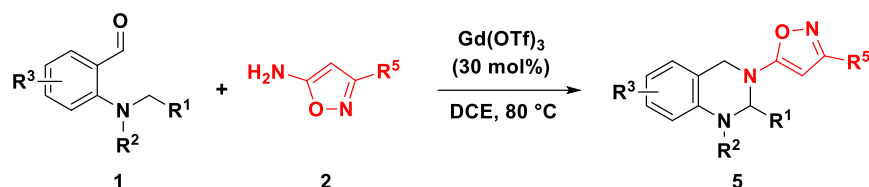
A sealed tube was charged with **1** (0.1 mmol, 1.0 equiv.), **2a** (0.15 mmol, 1.5 equiv.),  $\text{BF}_3 \cdot \text{OEt}_2$  (30 mol%, 0.3 equiv.),  $\text{K}_2\text{CO}_3$  (10 mol%, 0.1 equiv.) and DCE (1.0 mL). The mixture was stirred at  $80^\circ\text{C}$  in oil bath. Upon completion of the reaction as indicated by TLC analysis, the mixture was concentrated in vacuum and the residue was directly purified by flash column chromatography on silica gel (petroleum ether: EtOAc = 10:1) to afford the desired **3a-1**.

### 2.2 General Procedure for Construction of 4



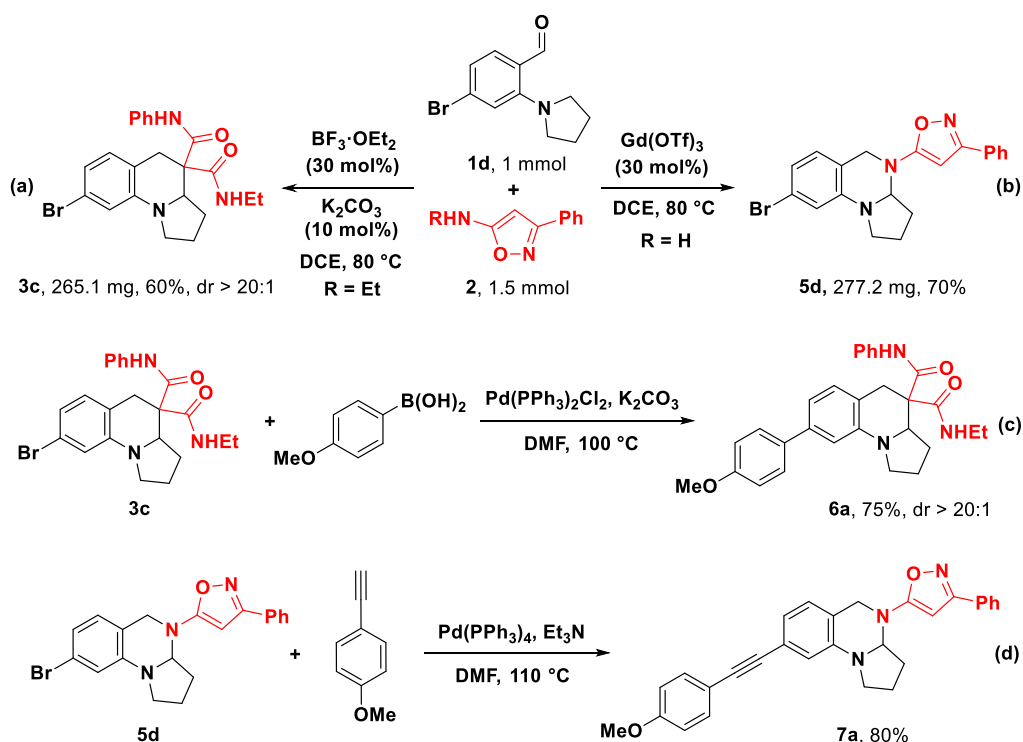
A sealed tube was charged **1** (0.1 mmol, 1.0 equiv.), **2b** (0.15 mmol, 1.5 equiv.), AlCl<sub>3</sub> (30 mol%, 0.3 equiv.), and EtOH (1.0 mL). The mixture was stirred at 60 °C in oil bath. Upon completion of the reaction as indicated by TLC analysis, the mixture was concentrated in vacuum and the residue was directly purified by flash column chromatography on silica gel (petroleum ether: EtOAc = 30:1) to afford the desired **4a-k**.

### 2.3 General Procedure for Construction of **5**



A sealed tube was charged with **1** (0.1 mmol, 1.0 equiv.), **2** (0.15 mmol, 1.5 equiv.), Gd(OTf)<sub>3</sub> (30 mol%, 0.3 equiv.), and DCE (1.0 mL). The mixture was stirred at 60 °C in oil bath. Upon completion of the reaction as indicated by TLC analysis, the mixture was concentrated in vacuum and the residue was directly purified by flash column chromatography on silica gel (petroleum ether: EtOAc = 30:1) to afford the desired **5a-n**.

### 2.4 Large-scale Synthesis and Derivatization



A round-bottom flask was charged with **1d** (1.0 mmol, 1.0 equiv.), **2b** (1.5 mmol, 1.5 equiv.), BF<sub>3</sub>·OEt<sub>2</sub> (30 mol%, 0.3 equiv.), K<sub>2</sub>CO<sub>3</sub> (10 mol%, 0.1 equiv.) in 10.0 mL of DCE. The mixture was stirred at 80 °C in oil bath. Upon completion of the reaction as indicated by TLC analysis, the mixture was concentrated in vacuum and the residue was directly purified by flash column chromatography on silica gel (petroleum ether: EtOAc = 10:1) to give the desired product **3c** in

60% yield.

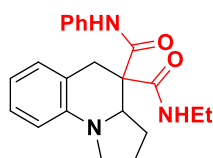
A sealed tube was charged with **1d** (0.1 mmol, 1.0 equiv.), **2a** (0.15 mmol, 1.5 equiv.), Gd(OTf)<sub>3</sub> (30 mol%, 0.3 equiv.), and DCE (1.0 mL). The mixture was stirred at 60 °C in oil bath. Upon completion of the reaction as indicated by TLC analysis, the mixture was concentrated in vacuum and the residue was directly purified by flash column chromatography on silica gel (petroleum ether: EtOAc = 30:1) to afford the desired **5d** in 70% yield.

Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (2.1 mg, 0.003 mmol) and K<sub>2</sub>CO<sub>3</sub> (14 mg, 0.1 mmol) were degassed in a flame-dried round-bottom flask, and then 4-methoxyphenylboronic acid (45 mg, 0.3 mmol), and compound **3c** (39.7 mg, 0.1 mmol). Then, DMF (2.0 mL) were added to the mixture under N<sub>2</sub>. The reaction mixture was heated at 100 °C for 4h and then allowed to cool to room temperature. The black solution was washed with water (3 x 10 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 x 10 mL). All organic phases were combined, dried over sodium sulfate, filtered and concentrated in vacuo to obtain the crude product. The residue was purified by flash column chromatography on silica gel (petroleum ether: EtOAc = 10:1) to afford **6a** (35.2 mg, 0.075 mmol, 75%).

Pd(PPh<sub>3</sub>)<sub>4</sub> (5.7 mg, 0.005 mmol) and CuI (1.9 mg, 0.01 mmol) were degassed in a flame-dried round-bottom flask, and then Et<sub>3</sub>N (0.4 mL), DMF (2.0 mL) and compound **5d** (39.6 mg, 0.1 mmol) were added. The solution was degassed again before 4-ethynylanisole (19.8 mg, 0.15 mmol) was added. The reaction mixture was heated at 110 °C for 6h and then allowed to cool to room temperature. The black solution was washed with water (3 x 10 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 x 10 mL). All organic phases were combined, dried over sodium sulfate, filtered and concentrated in vacuo to obtain the crude product. The residue was purified by flash column chromatography on silica gel (petroleum ether: EtOAc = 30:1) to afford **7a** (35.8 mg, 0.08 mmol, 80%).

### 3. Characterization of Products

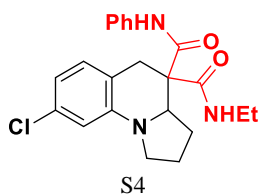
#### N-ethyl-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (**3a**).



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 10:1) afforded the product as a white solid (26.4 mg, 73% yield, dr > 20:1).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 9.01 (s, 1H), 8.81 (s, 1H), 7.35 – 6.98 (m, 8H), 6.83 – 6.59 (m, 2H), 3.91 – 3.81 (m, 2H), 3.50 (q, *J* = 7.6 Hz, 1H), 3.43 – 3.31 (m, 2H), 3.29 – 3.25 (m, 1H), 3.11 (d, *J* = 17.4 Hz, 1H), 2.18 (q, *J* = 8.5, 7.6 Hz, 1H), 2.06 – 1.96 (m, 3H), 1.21 (t, *J* = 7.2 Hz, 3H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 171.3, 170.1, 143.5, 137.1, 129.2, 129.0, 128.1, 124.9, 120.7, 120.0, 118.2, 112.4, 62.7, 51.4, 46.9, 36.5, 34.8, 27.4, 22.4, 14.7. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>22</sub>H<sub>26</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup> 364.2020; Found 364.2024.

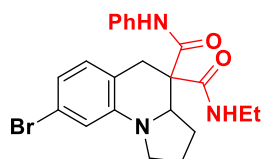
#### 8-chloro-N-ethyl-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (**3b**).



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 10:1) afforded the product as a white solid (25.4 mg, 64% yield, dr > 20:1).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 8.72 (t, *J* = 5.6 Hz, 1H), 8.61 (s, 1H), 7.27 – 7.23 (m, 2H), 7.13 – 7.10 (m, 2H), 7.10 – 7.05 (m, 2H), 6.72 (dd, *J* = 8.1, 2.1 Hz, 1H), 6.60 (d, *J* = 2.0 Hz, 1H), 3.85 – 3.80 (m, 2H), 3.47 – 3.38 (m, 2H), 3.35 – 3.25 (m, 2H), 3.07 (d, *J* = 17.5 Hz, 1H), 2.21 – 2.16 (m, 1H), 2.10 – 2.02 (m, 2H), 2.01 – 1.91 (m, 1H), 1.20 (t, *J* = 7.3 Hz, 3H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 170.9, 169.7, 144.4, 136.8, 133.7, 130.1, 129.0, 125.1, 120.8, 118.1, 117.7, 112.0, 62.6, 51.2, 46.9, 35.7, 34.9, 27.4, 22.4, 14.7. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>22</sub>H<sub>25</sub>ClN<sub>3</sub>O<sub>2</sub><sup>+</sup> 398.1630; Found 398.1635.

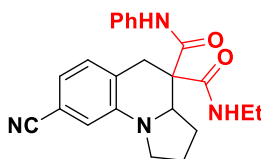
**8-bromo-N-ethyl-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (3c).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 10:1) afforded the product as a white solid (27.3 mg, 62% yield, dr > 20:1).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 8.75 – 8.69 (m, 1H), 8.61 (s, 1H), 7.28 – 7.24 (m, 2H), 7.13 – 7.07 (m, 3H), 7.01 (d, *J* = 8.0 Hz, 1H), 6.87 (dd, *J* = 8.0, 1.9 Hz, 1H), 6.75 (d, *J* = 1.9 Hz, 1H), 3.85 – 3.78 (m, 2H), 3.49 – 3.21 (m, 5H), 3.06 (d, *J* = 17.5 Hz, 1H), 2.22 – 2.15 (m, 1H), 2.13 – 2.03 (m, 2H), 2.00 – 1.97 (m, 1H), 1.20 (t, *J* = 7.2 Hz, 3H), 0.88 (t, *J* = 7.1 Hz, 2H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 170.8, 169.7, 144.6, 136.8, 130.4, 129.1, 125.1, 121.8, 120.8, 120.6, 118.6, 114.9, 62.6, 51.2, 46.9, 35.8, 34.9, 27.4, 22.4, 14.7. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>22</sub>H<sub>26</sub>BrN<sub>3</sub>O<sub>2</sub><sup>+</sup> 442.1125; Found 442.1126.

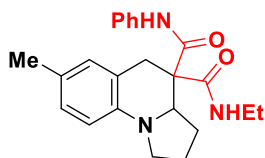
**8-cyano-N-ethyl-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (3d).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 7:1) afforded the product as a white solid (25.2 mg, 65% yield, dr > 20:1).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 8.53 (t, *J* = 5.4 Hz, 1H), 8.33 (s, 1H), 7.19 (dd, *J* = 9.7, 6.4 Hz, 3H), 7.03 (t, *J* = 7.2 Hz, 3H), 6.95 (d, *J* = 7.7 Hz, 1H), 6.76 (s, 1H), 3.86 – 3.77 (m, 2H), 3.39 (d, *J* = 8.4 Hz, 1H), 3.35 – 3.29 (m, 1H), 3.29 – 3.23 (m, 2H), 3.09 (d, *J* = 18.0 Hz, 1H), 2.14 (dd, *J* = 9.2, 6.2 Hz, 1H), 2.09 – 2.00 (m, 2H), 1.98 – 1.91 (m, 1H), 1.14 (t, *J* = 7.3 Hz, 3H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 170.3, 169.3, 143.7, 136.6, 129.7, 129.1, 125.3, 125.2, 121.1, 120.7, 119.3, 114.6, 111.7, 62.8, 51.0, 46.9, 36.3, 35.0, 27.5, 22.5, 14.7. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>23</sub>H<sub>25</sub>N<sub>4</sub>O<sub>2</sub><sup>+</sup> 389.1972; Found 389.1977.

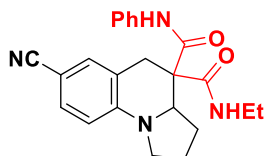
**N-ethyl-7-methyl-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (3e).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 10:1) afforded the product as a white solid (12.4 mg, 33% yield, dr > 20:1).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 9.02 (s, 1H), 8.72 (t, *J* = 5.5 Hz, 1H), 7.18 – 7.14 (m, 2H), 7.07 – 7.03 (m, 2H), 7.01 – 6.93 (m, 2H), 6.52 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.39 (d, *J* = 1.5 Hz, 1H), 3.79 – 3.70 (m, 2H), 3.47 – 3.40 (m, 1H), 3.35 – 3.22 (m, 2H), 3.20 – 3.16 (m, 1H), 3.00 (d, *J* = 17.2 Hz, 1H), 2.24 (s, 3H), 2.14 – 2.07 (m, 1H), 2.01 – 1.86 (m, 3H), 1.13 (t, *J* = 7.2 Hz, 3H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 171.4, 170.3, 143.3, 137.8, 137.2, 129.1, 129.0, 124.8, 120.8, 119.2, 117.0, 113.2, 62.6, 51.5, 46.9, 36.2, 34.8, 27.3, 22.3, 21.6, 14.7. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>23</sub>H<sub>28</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup> 378.2176; Found 378.2173.

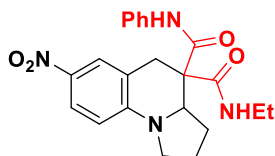
**7-cyano-N-ethyl-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (3f).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 7:1) afforded the product as a white solid (24.8 mg, 64% yield, dr > 20:1).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 8.59 (t, *J* = 5.6 Hz, 1H), 8.40 (s, 1H), 7.26 (dd, *J* = 10.3, 6.0 Hz, 3H), 7.10 (dd, *J* = 7.8, 4.5 Hz, 3H), 7.02 (d, *J* = 7.7 Hz, 1H), 6.83 (s, 1H), 3.94 – 3.80 (m, 2H), 3.49 – 3.30 (m, 4H), 3.16 (d, *J* = 18.0 Hz, 1H), 2.24 – 2.18 (m, 1H), 2.17 – 2.06 (m, 2H), 2.01 (q, *J* = 10.9, 9.5 Hz, 1H), 1.21 (t, *J* = 7.3 Hz, 3H). **<sup>13</sup>C NMR** (125 MHz, CDCl<sub>3</sub>) δ 170.2, 169.3, 143.7, 136.6, 129.7, 129.1, 125.3, 125.2, 121.1, 120.7, 119.3, 114.6, 111.7, 62.8, 51.0, 47.0, 36.3, 35.0, 27.5, 22.5, 14.6. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>23</sub>H<sub>25</sub>N<sub>4</sub>O<sub>2</sub><sup>+</sup> 389.1972; Found 389.1971.

**N-ethyl-7-nitro-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (3g).**

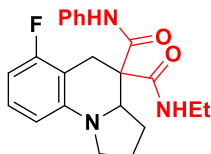


Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 5:1) afforded the product as a yellow solid (25.7 mg, 63% yield, dr > 20:1).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 8.17 (t, *J* = 5.5 Hz, 1H), 8.04 (d, *J* = 2.7 Hz, 1H), 8.02 (dd, *J* = 9.0, 2.6 Hz, 1H), 7.81 (s, 1H), 7.15 (t, *J* = 7.9 Hz, 2H), 7.03 – 6.97 (m, 3H), 6.42 (d, *J* = 9.0 Hz, 1H), 3.87 (dd, *J* = 9.9, 6.2 Hz, 1H), 3.82 (d, *J* = 17.4 Hz, 1H), 3.48 – 3.44 (m, 1H), 3.39 – 3.31 (m, 2H), 3.29 – 3.23 (m, 1H), 3.12 (d, *J* = 17.4 Hz, 1H), 2.29 – 2.21 (m, 1H), 2.21 – 2.14 (m, 1H), 2.07 – 2.00 (m, 1H), 1.96 – 1.88 (m, 1H), 1.14 (t, *J* = 7.3 Hz, 3H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 169.2, 168.8, 148.3, 137.3, 136.4, 129.1, 125.5, 125.5, 125.1, 120.8, 118.5, 110.1, 63.7, 51.2, 47.5, 35.1.

29.7, 27.9, 22.9, 14.6. **HRMS (ESI) m/z:**  $[M + H]^+$  Calcd for  $C_{23}H_{25}N_4O_4^+$  409.1870; Found 409.1874.

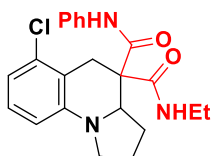
**N-ethyl-6-fluoro-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (3h).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 10:1) afforded the product as a white solid (26.2 mg, 69% yield, dr > 20:1).

**$^1H$  NMR** (500 MHz,  $CDCl_3$ )  $\delta$  8.83 (s, 1H), 8.77 (s, 1H), 7.35 – 7.17 (m, 3H), 7.14 (d,  $J = 7.8$  Hz, 3H), 7.08 (t,  $J = 7.4$  Hz, 1H), 6.52 (t,  $J = 8.7$  Hz, 1H), 6.44 (d,  $J = 8.2$  Hz, 1H), 3.84 (t,  $J = 7.4$  Hz, 1H), 3.61 (d,  $J = 17.9$  Hz, 1H), 3.52 (q,  $J = 7.6$  Hz, 1H), 3.42 – 3.33 (m, 2H), 3.33 – 3.27 (m, 2H), 2.21 (dd,  $J = 9.6, 5.5$  Hz, 1H), 2.08 – 1.97 (m, 3H), 1.21 (t,  $J = 7.3$  Hz, 3H).  **$^{13}C$  NMR** (100 MHz,  $CDCl_3$ )  $\delta$  171.0, 169.9, 161.3 (d,  $J = 243.8$  Hz), 144.9 (d,  $J = 7.1$  Hz), 136.9, 129.0, 128.6 (d,  $J = 10.5$  Hz), 125.0, 120.8, 108.0 (d,  $J = 3.0$  Hz), 107.7 (d,  $J = 19.2$  Hz), 104.7 (d,  $J = 22.2$  Hz), 62.2, 50.8, 47.3, 34.9, 29.7, 27.4, 22.4, 14.7. **HRMS (ESI) m/z:**  $[M + H]^+$  Calcd for  $C_{22}H_{25}FN_3O_2^+$  382.1925; Found 382.1928.

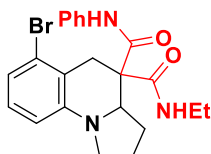
**6-chloro-N-ethyl-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (3i).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 10:1) afforded the product as a white solid (27.8 mg, 70% yield, dr > 20:1).

**$^1H$  NMR** (500 MHz,  $CDCl_3$ )  $\delta$  8.73 (t,  $J = 5.7$  Hz, 1H), 8.68 (s, 1H), 7.28 – 7.24 (m, 2H), 7.16 – 7.13 (m, 2H), 7.12 – 7.06 (m, 2H), 6.84 (d,  $J = 7.9$  Hz, 1H), 6.55 (d,  $J = 8.1$  Hz, 1H), 3.82 (dd,  $J = 9.1, 6.4$  Hz, 1H), 3.68 (d,  $J = 18.2$  Hz, 1H), 3.52 – 3.47 (m, 1H), 3.41 (q,  $J = 7.4$  Hz, 2H), 3.37 – 3.25 (m, 2H), 2.24 – 2.15 (m, 1H), 2.14 – 2.04 (m, 2H), 2.03 – 1.97 (m, 1H), 1.22 (t,  $J = 7.3$  Hz, 3H).  **$^{13}C$  NMR** (100 MHz,  $CDCl_3$ )  $\delta$  170.9, 169.8, 144.9, 136.9, 134.8, 129.0, 128.4, 125.0, 120.8, 118.8, 118.0, 110.7, 62.4, 51.6, 47.4, 34.9, 34.3, 27.4, 22.6, 14.7. **HRMS (ESI) m/z:**  $[M + H]^+$  Calcd for  $C_{22}H_{25}ClN_3O_2^+$  398.1630; Found 398.1627.

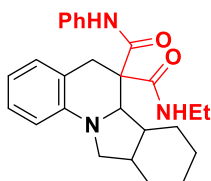
**6-bromo-N-ethyl-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (3j).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 10:1) afforded the product as a white solid (33.1 mg, 75% yield, dr > 20:1).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 8.70 (t, *J* = 5.6 Hz, 1H), 8.59 (s, 1H), 7.26 – 7.23 (m, 2H), 7.16 – 7.13 (m, 2H), 7.08 (m, 1H), 7.05 – 7.00 (m, 2H), 6.58 (dd, *J* = 6.7, 2.7 Hz, 1H), 3.82 (dd, *J* = 9.2, 6.5 Hz, 1H), 3.69 (d, *J* = 18.2 Hz, 1H), 3.48 – 3.28 (m, 5H), 2.21 – 2.15 (m, 1H), 2.15 – 2.09 (m, 1H), 2.08 – 1.96 (m, 2H), 1.22 (t, *J* = 7.3 Hz, 3H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 170.9, 169.7, 145.0, 136.9, 129.0, 128.9, 125.4, 125.0, 121.9, 120.8, 119.4, 111.3, 62.6, 51.9, 47.3, 37.0, 34.9, 27.4, 22.7, 14.7. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>22</sub>H<sub>26</sub>BrN<sub>3</sub>O<sub>2</sub><sup>+</sup> 442.1125; Found 442.1122.

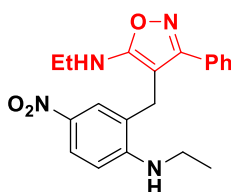
**N-ethyl-N-phenyl-6a,6b,7,8,9,10,10a,11-octahydroisindolo[2,1-a]quinoline-6,6(5H)-dicarboxamide (3k).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 10:1) afforded the product as a white solid (25.9 mg, 62% yield, dr > 20:1).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 8.86 (t, *J* = 5.5 Hz, 1H), 7.89 (s, 1H), 7.14 – 7.08 (m, 4H), 6.99 – 6.94 (m, 1H), 6.93 – 6.89 (m, 2H), 6.64 (t, *J* = 7.3 Hz, 1H), 6.48 (d, *J* = 8.1 Hz, 1H), 3.97 (d, *J* = 8.4 Hz, 1H), 3.87 (d, *J* = 17.2 Hz, 1H), 3.34 – 3.22 (m, 2H), 3.17 (dd, *J* = 9.1, 6.3 Hz, 1H), 3.12 (dd, *J* = 9.2, 3.5 Hz, 1H), 2.96 (d, *J* = 17.3 Hz, 1H), 2.36 – 2.31 (m, 1H), 2.11 – 2.04 (m, 1H), 1.61 – 1.48 (m, 4H), 1.43 – 1.29 (m, 3H), 1.13 (t, *J* = 7.3 Hz, 3H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 171.7, 170.3, 143.5, 137.0, 129.2, 129.0, 128.6, 124.9, 120.4, 117.9, 116.5, 111.1, 63.4, 52.3, 50.3, 39.8, 36.4, 36.2, 34.9, 27.9, 26.0, 24.3, 22.0, 14.5. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>26</sub>H<sub>32</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup> 418.2489; Found 418.2485.

**N-ethyl-4-(2-(ethylamino)-5-nitrobenzyl)-3-phenylisoxazol-5-amine (3l).**

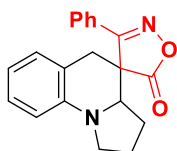


Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 5:1) afforded the product as a yellow solid (25.2 mg, 69% yield, dr > 20:1).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 7.95 (dd, *J* = 9.0, 2.8 Hz, 1H), 7.80 (d, *J* = 2.8 Hz, 1H), 7.39 – 7.29 (m, 5H), 6.44 (d, *J* = 9.0 Hz, 1H), 4.20 – 4.14 (m, 2H), 3.40 (s, 2H), 3.28 (p, *J* = 6.9 Hz, 2H), 3.12 – 3.07 (m, 2H), 1.08 (q, *J* = 6.8 Hz, 6H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 167.5, 163.7, 151.3, 137.4, 129.6, 129.5, 128.9, 128.2, 125.4, 124.6, 121.2, 108.6, 83.9, 38.2, 24.3, 15.8, 14.2. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>23</sub>N<sub>4</sub>O<sub>3</sub><sup>+</sup> 367.1765; Found 367.1770.

**3-phenyl-1',2',3',3a'-tetrahydro-5H,5'H-spiro[isoxazole-4,4'-pyrrolo[1,2-a]quinolin]-5-one (4a).**

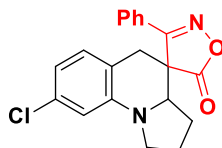




Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as a white solid (25.4 mg, 80% yield, dr = 1.3:1).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.72 – 7.69 (m, 1H), 7.56 – 7.47 (m, 2H), 7.25 (d, *J* = 3.2 Hz, 1H), 7.13 – 7.07 (m, 3H), 6.70 – 6.67 (m, 1H), 6.63 (d, *J* = 8.1 Hz, 1H), 6.21 (d, *J* = 8.1 Hz, 1H), 4.06 (dd, *J* = 9.4, 6.0 Hz, 1H), 3.71 (dd, *J* = 9.3, 6.3 Hz, 1H), 3.64 (d, *J* = 16.2 Hz, 1H), 3.55 (d, *J* = 17.2 Hz, 1H), 3.42 – 3.55 (m, 1H), 3.30 – 3.21 (m, 2H), 3.07 (d, *J* = 16.4 Hz, 1H), 2.59 (q, *J* = 8.2 Hz, 1H), 2.14 – 2.05 (m, 2H), 1.92 (d, *J* = 5.3 Hz, 1H), 1.58 (q, *J* = 5.1, 3.7 Hz, 1H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 179.4, 175.4, 169.6, 167.2, 143.3, 143.0, 131.6, 130.7, 129.4, 129.0, 128.5, 128.3, 128.2, 128.2, 128.0, 127.6, 127.3, 117.3, 116.8, 116.7, 114.5, 111.5, 111.3, 62.4, 60.1, 50.6, 48.8, 48.0, 46.3, 34.8, 33.7, 28.7, 27.5, 23.2, 22.9. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>19</sub>N<sub>2</sub>O<sub>2</sub><sup>+</sup> 319.1441; Found 319.1444.

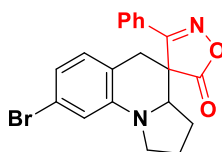
**8'-chloro-3-phenyl-1',2',3',3a'-tetrahydro-5H,5'H-spiro[isoxazole-4,4'-pyrrolo[1,2-a]quinolin]-5-one (4b).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as a yellow solid (23.6 mg, 67% yield, dr = 2:1).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.68 (dd, *J* = 7.1, 1.9 Hz, 1H), 7.57 – 7.53 (m, 1H), 7.49 (dd, *J* = 8.3, 6.5 Hz, 1H), 7.33 – 7.27 (m, 1H), 7.12 (t, *J* = 7.8 Hz, 2H), 7.07 – 6.97 (m, 3H), 6.93 (d, *J* = 8.0 Hz, 1H), 6.63 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.57 (d, *J* = 2.0 Hz, 1H), 6.17 (d, *J* = 2.0 Hz, 1H), 4.04 (dd, *J* = 9.7, 5.8 Hz, 1H), 3.68 (dd, *J* = 9.6, 6.2 Hz, 1H), 3.59 – 3.51 (m, 1H), 3.46 (dd, *J* = 17.0, 1.3 Hz, 1H), 3.33 (m, 1H), 3.26 – 3.16 (m, 2H), 3.03 (d, *J* = 16.4 Hz, 1H), 2.62 – 2.52 (m, 1H), 2.16 – 1.91 (m, 5H), 1.62 – 1.52 (m, 2H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 179.1, 175.1, 169.3, 167.0, 144.2, 143.9, 133.8, 133.7, 131.7, 130.9, 129.9, 129.4, 129.4, 128.1, 128.0, 127.5, 127.5, 127.2, 116.6, 116.4, 115.7, 113.0, 111.2, 111.0, 62.2, 59.9, 50.3, 48.5, 48.0, 46.4, 34.3, 33.3, 28.6, 27.5, 23.2, 22.9. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>18</sub>ClN<sub>2</sub>O<sub>2</sub><sup>+</sup> 353.1051; Found 353.1053.

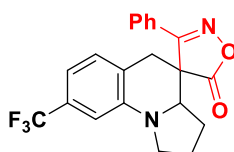
**8'-bromo-3-phenyl-1',2',3',3a'-tetrahydro-5H,5'H-spiro[isoxazole-4,4'-pyrrolo[1,2-a]quinolin]-5-one (4c).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as a white solid (26.9 mg, 68% yield, dr = 1.25:1).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.67 (dd, *J* = 7.1, 1.8 Hz, 2H), 7.58 – 7.43 (m, 2H), 7.32 – 7.26 (m, 1H), 7.11 (t, *J* = 7.8 Hz, 2H), 7.03 (dd, *J* = 8.2, 1.5 Hz, 2H), 6.93 (d, *J* = 8.0 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 1H), 6.78 – 6.74 (m, 2H), 6.70 (d, *J* = 1.9 Hz, 1H), 6.30 (d, *J* = 1.9 Hz, 1H), 4.02 (dd, *J* = 9.7, 5.8 Hz, 1H), 3.65 (dd, *J* = 9.5, 6.2 Hz, 1H), 3.56 – 3.46 (m, 2H), 3.41 (dd, *J* = 17.1, 1.2 Hz, 1H), 3.30 (m, 1H), 3.23 – 3.12 (m, 2H), 2.99 (d, *J* = 16.5 Hz, 1H), 2.56 (q, *J* = 8.4 Hz, 1H), 2.16 – 1.94 (m, 4H), 1.91 (dd, *J* = 7.7, 3.2 Hz, 2H), 1.62 – 1.49 (m, 2H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 179.0, 175.1, 169.3, 167.1, 144.4, 144.1, 131.8, 130.9, 130.2, 129.7, 129.4, 128.1, 128.0, 127.5, 127.5, 127.3, 121.9, 121.7, 119.4, 119.2, 116.2, 114.0, 113.9, 113.6, 62.2, 59.9, 50.22, 48.4, 48.1, 46.5, 34.3, 33.4, 28.6, 27.5, 23.2, 22.9. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>18</sub>BrN<sub>2</sub>O<sub>2</sub><sup>+</sup> 397.0546; Found 397.0549.

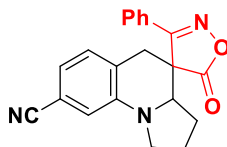
**3-phenyl-8'-(trifluoromethyl)-1',2',3',3a'-tetrahydro-5H,5'H-spiro[isoxazole-4,4'-pyrrolo[1,2-a]quinolin]-5-one (4d).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 20:1) afforded the product as a white solid (29.0 mg, 75% yield, dr = 4:1).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.59 – 7.47 (m, 1H), 7.29 – 7.24 (m, 1H), 7.19 (d, *J* = 7.8 Hz, 1H), 7.14 – 7.04 (m, 2H), 6.99 (dd, *J* = 8.0, 1.4 Hz, 2H), 6.94 – 6.86 (m, 1H), 6.35 (d, *J* = 1.7 Hz, 1H), 3.74 (dd, *J* = 9.6, 6.2 Hz, 1H), 3.67 – 3.60 (m, 1H), 3.57 – 3.52 (m, 1H), 3.34 – 3.25 (m, 2H), 2.64 – 2.58 (m, 1H), 2.22 – 1.99 (m, 2H), 1.99 – 1.93 (m, 1H), 1.66 – 1.57 (m, 1H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 178.9, 169.2, 143.1, 130.9, 130.5 (d, *J* = 32.3 Hz), 129.5, 128.8, 128.1, 127.5, 124.2 (q, *J* = 272.2 Hz), 120.8, 113.0 (q, *J* = 3.9 Hz), 107.5 (q, *J* = 3.9 Hz), 62.4, 50.0, 46.5, 34.6, 27.6, 22.9. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>18</sub>F<sub>3</sub>N<sub>2</sub>O<sub>2</sub><sup>+</sup> 387.1315; Found 387.1310.

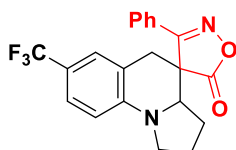
**5-oxo-3-phenyl-1',2',3',3a'-tetrahydro-5H,5'H-spiro[isoxazole-4,4'-pyrrolo[1,2-a]quinoline]-8'-carbonitrile (4e).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 20:1) afforded the product as a white solid (24.7 mg, 72% yield, dr = 4:1).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.69 (dd, *J* = 7.1, 1.9 Hz, 2H), 7.61 – 7.48 (m, 3H), 7.10 (d, *J* = 7.9 Hz, 2H), 6.94 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.80 (d, *J* = 1.5 Hz, 1H), 4.10 (dd, *J* = 9.7, 5.8 Hz, 1H), 3.67 – 3.57 (m, 2H), 3.40 – 3.25 (m, 2H), 3.12 (d, *J* = 16.8 Hz, 1H), 2.22 – 2.06 (m, 2H), 2.06 – 1.96 (m, 1H), 1.65 – 1.55 (m, 1H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 175.0, 168.9, 166.7, 143.6, 143.1, 131.9, 131.1, 129.6, 129.5, 129.1, 128.2, 127.7, 127.4, 127.2, 127.2, 122.4, 120.0, 119.8, 119.8, 119.6, 119.3, 114.0, 113.7, 111.8, 111.6, 77.3, 62.3, 60.0, 49.8, 48.1, 46.5, 34.6, 33.8, 29.7, 28.6, 27.6, 23.2, 22.9. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>18</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup> 344.1394; Found 344.1399.

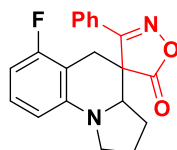
**3-phenyl-7'-(trifluoromethyl)-1',2',3',3a'-tetrahydro-5H,5'H-spiro[isoxazole-4,4'-pyrrolo[1,2-a]quinolin]-5-one (4f).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 20:1) afforded the product as a white solid (24.3 mg, 63% yield, dr = 1.25:1).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 7.61 (d, *J* = 7.6 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.33 (d, *J* = 8.6 Hz, 1H), 7.24 (s, 1H), 7.18 (q, *J* = 6.6, 4.9 Hz, 3H), 7.00 (t, *J* = 7.7 Hz, 2H), 6.91 (d, *J* = 7.7 Hz, 2H), 6.54 (d, *J* = 8.5 Hz, 1H), 6.10 (d, *J* = 8.5 Hz, 1H), 4.01 (dd, *J* = 9.8, 5.9 Hz, 1H), 3.67 (dd, *J* = 9.8, 6.2 Hz, 1H), 3.58 – 3.53 (m, 2H), 3.45 (d, *J* = 16.9 Hz, 1H), 3.30 (d, *J* = 8.3 Hz, 1H), 3.26 – 3.16 (m, 2H), 3.01 (d, *J* = 16.4 Hz, 1H), 2.55 (d, *J* = 8.4 Hz, 1H), 2.13 – 1.93 (m, 4H), 1.93 – 1.88 (m, 2H), 1.56 – 1.48 (m, 2H). **<sup>13</sup>C NMR** (125 MHz, CDCl<sub>3</sub>) δ 178.8, 175.0, 169.1, 166.9, 145.6, 145.2, 131.8, 130.8, 129.5, 128.1, 127.5 (d, *J* = 40.0 Hz), 127.4, 127.4, 127.2, 126.1 (d, *J* = 3.0 Hz), 125.5 (d, *J* = 15.1 Hz), 125.4 (d, *J* = 3.0 Hz), 121.3 (q, *J* = 242.0 Hz), 117.0, 114.4, 110.8, 110.6, 62.4, 60.0, 49.9, 48.3, 48.0, 46.6, 34.6, 33.5, 28.6, 27.6, 23.2, 22.9. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>18</sub>F<sub>3</sub>N<sub>2</sub>O<sub>2</sub><sup>+</sup> 387.1315; Found 387.1318.

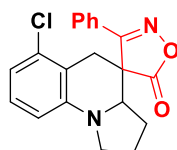
**6'-fluoro-3-phenyl-1',2',3',3a'-tetrahydro-5H,5'H-spiro[isoxazole-4,4'-pyrrolo[1,2-a]quinolin]-5-one (4g).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as a white solid (23.5 mg, 70% yield, dr = 1.4:1).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.70 – 7.58 (m, 1H), 7.50 – 7.39 (m, 2H), 7.19 (d, *J* = 7.6 Hz, 2H), 7.06 – 6.91 (m, 5H), 6.42 – 6.27 (m, 2H), 5.90 (d, *J* = 8.2 Hz, 1H), 3.97 (dd, *J* = 9.4, 6.0 Hz, 1H), 3.61 (dd, *J* = 9.4, 6.3 Hz, 1H), 3.56 – 3.51 (m, 1H), 3.39 (dd, *J* = 17.7, 1.7 Hz, 1H), 3.34 – 3.29 (m, 1H), 3.28 – 3.11 (m, 3H), 2.52 (q, *J* = 8.3 Hz, 1H), 2.16 – 1.89 (m, 3H), 1.88 – 1.83 (m, 2H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 179.2, 175.3, 169.2, 167.0, 161.4 (d, *J* = 241.0 Hz), 160.9 (d, *J* = 241.0 Hz), 144.7 (d, *J* = 5.6 Hz), 144.3 (d, *J* = 7.1 Hz), 131.8, 130.8, 129.4, 128.7 (d, *J* = 11.1 Hz), 128.7 (d, *J* = 11.1 Hz), 128.1, 127.7 (d, *J* = 64.1 Hz), 127.4, 127.2, 107.2 (d, *J* = 2.5 Hz), 106.8 (d, *J* = 2.5 Hz), 104.8 (d, *J* = 19.2 Hz), 103.1 (d, *J* = 21.2 Hz), 103.0 (d, *J* = 22.2 Hz), 102.3 (d, *J* = 20.2 Hz), 62.0, 59.6, 49.8, 48.3, 48.1, 46.7, 28.7, 27.9, 27.9, 27.5, 26.7, 26.7, 23.1, 22.9. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>18</sub>FN<sub>2</sub>O<sub>2</sub><sup>+</sup> 337.1347; Found 337.1343.

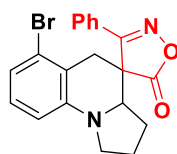
**6'-chloro-3-phenyl-1',2',3',3a'-tetrahydro-5H,5'H-spiro[isoxazole-4,4'-pyrrolo[1,2-a]quinolin]-5-one (4h).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as a yellow solid (25.3 mg, 72% yield, dr = 2.5:1).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.75 – 7.70 (m, 1H), 7.58 – 7.48 (m, 1H), 7.30 – 7.25 (m, 1H), 7.14 – 7.08 (m, 2H), 7.04 – 6.94 (m, 3H), 6.77 – 6.73 (m, 1H), 6.07 (dd, *J* = 8.3, 1.0 Hz, 1H), 3.67 (dd, *J* = 9.3, 6.3 Hz, 1H), 3.62 – 3.53 (m, 1H), 3.38 – 3.26 (m, 2H), 3.25 – 3.20 (m, 1H), 2.62 – 2.51 (m, 1H), 2.21 – 1.95 (m, 3H), 1.95 – 1.90 (m, 1H), 1.66 – 1.57 (m, 1H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 179.0, 175.4, 169.2, 166.7, 144.6, 144.3, 134.5, 134.0, 131.8, 130.8, 129.4, 128.5, 128.1, 128.1, 127.4, 127.3, 127.2, 117.3, 117.3, 115.4, 112.9, 110.1, 109.6, 61.9, 59.5, 50.6, 49.0, 48.2, 46.7, 32.5, 31.1, 28.6, 27.5, 23.2, 23.0. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>18</sub>ClN<sub>2</sub>O<sub>2</sub><sup>+</sup> 353.1051; Found 353.1047.

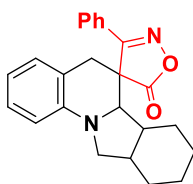
**6'-bromo-3-phenyl-1',2',3',3a'-tetrahydro-5H,5'H-spiro[isoxazole-4,4'-pyrrolo[1,2-a]quinolin]-5-one (4i).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as a white solid (33.7 mg, 85% yield, dr = 3:1).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 7.73 (d, *J* = 7.7 Hz, 1H), 7.58 – 7.49 (m, 1H), 7.27 (d, *J* = 6.9 Hz, 2H), 7.11 (t, *J* = 7.7 Hz, 2H), 7.02 (d, *J* = 7.9 Hz, 2H), 6.96 – 6.88 (m, 2H), 6.11 (d, *J* = 7.8 Hz, 1H), 3.68 (dd, *J* = 9.3, 6.4 Hz, 1H), 3.62 – 3.51 (m, 1H), 3.50 – 3.38 (m, 1H), 3.38 – 3.27 (m, 2H), 3.25 – 3.21 (m, 1H), 2.57 (q, *J* = 8.3 Hz, 1H), 2.19 – 2.07 (m, 2H), 2.00 – 1.90 (m, 3H), 1.65 – 1.57 (m, 1H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 178.9, 175.3, 169.2, 166.6, 144.7, 144.4, 131.8, 130.8, 129.4, 128.9, 128.9, 128.1, 127.4, 127.3, 127.2, 125.3, 124.7, 120.6, 120.5, 116.9, 114.5, 110.7, 110.2, 62.0, 59.6, 50.9, 49.3, 48.2, 46.6, 35.4, 34.0, 28.6, 27.4, 23.2, 23.0. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>18</sub>BrN<sub>2</sub>O<sub>2</sub><sup>+</sup> 397.0546; Found 397.0541.

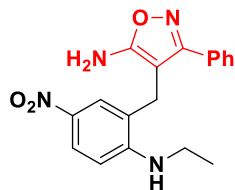
**3'-phenyl-6a,6b,7,8,9,10,10a,11-octahydro-5H,5'H-spiro[isoindolo[2,1-a]quinoline-6,4'-isoxazol]-5'-one (4j).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as a yellow solid (20.5 mg, 55% yield, dr > 20:1).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 7.20 – 7.16 (m, 1H), 7.01 – 6.95 (m, 4H), 6.94 – 6.90 (m, 2H), 6.55 – 6.52 (m, 1H), 6.08 (dd, *J* = 8.3, 1.1 Hz, 1H), 3.46 – 3.38 (m, 2H), 3.31 (dd, *J* = 8.7, 7.4 Hz, 1H), 3.13 (d, *J* = 16.8 Hz, 1H), 2.04 (dd, *J* = 10.5, 8.6 Hz, 1H), 1.87 – 1.70 (m, 4H), 1.63 – 1.57 (m, 2H), 1.31 – 1.03 (m, 5H), 1.01 – 0.91 (m, 1H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 179.7, 170.1, 142.8, 130.6, 128.5, 128.3, 128.2, 128.0, 127.9, 116.3, 116.0, 110.3, 66.7, 50.6, 49.1, 47.4, 43.1, 35.7, 28.9, 28.3, 25.5, 25.4. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>24</sub>H<sub>25</sub>F<sub>3</sub>N<sub>2</sub>O<sub>2</sub><sup>+</sup> 373.1911; Found 373.1914.

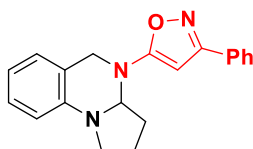
#### 4-(2-(ethylamino)-5-nitrobenzyl)-3-phenylisoxazol-5-amine (4k).



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 5:1) afforded the product as a yellow solid (22.6 mg, 67% yield).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 8.06 – 7.87 (m, 2H), 7.62 (s, 2H), 7.39 (s, 3H), 6.84 (d, *J* = 9.2 Hz, 1H), 4.24 (s, 2H), 3.93 (d, *J* = 9.1 Hz, 2H), 1.36 – 1.24 (m, 3H). **<sup>13</sup>C NMR** (125 MHz, CDCl<sub>3</sub>) δ 162.0, 160.9, 143.6, 141.9, 130.0, 129.3, 129.0, 127.1, 126.3, 124.1, 122.1, 112.4, 86.9, 39.2, 26.1, 12.7. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>18</sub>H<sub>19</sub>N<sub>4</sub>O<sub>3</sub><sup>+</sup> 339.1452; Found 339.1454.

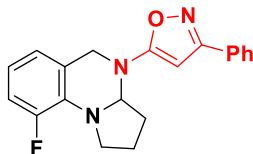
#### 3-phenyl-5-(1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)isoxazole (5a).



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as a white solid (26.3 mg, 83% yield).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.78 – 7.70 (m, 2H), 7.44 – 7.38 (m, 3H), 7.19 – 7.15 (m, 1H), 7.05 (dd, *J* = 7.4, 1.4 Hz, 1H), 6.76 – 6.72 (m, 1H), 6.59 (dd, *J* = 8.1, 1.1 Hz, 1H), 5.58 (s, 1H), 4.61 (dd, *J* = 8.1, 5.7 Hz, 1H), 4.54 (d, *J* = 15.1 Hz, 1H), 4.43 (d, *J* = 15.1 Hz, 1H), 3.42 – 3.31 (m, 2H), 2.62 – 2.52 (m, 1H), 2.30 – 2.20 (m, 1H), 2.17 – 2.08 (m, 1H), 2.04 – 1.91 (m, 1H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 171.1, 163.2, 143.4, 129.8, 129.7, 128.8, 128.3, 126.6, 126.0, 119.3, 117.6, 112.1, 82.5, 74.7, 51.5, 46.4, 31.8, 21.9. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>20</sub>N<sub>3</sub>O<sup>+</sup> 318.1601; Found 318.1597.

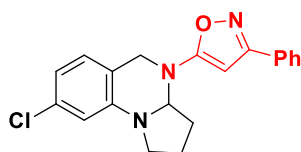
#### 5-(9-fluoro-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)-3-phenylisoxazole (5b).



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as a white solid (25.1 mg, 75% yield).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.82 – 7.70 (m, 2H), 7.42 – 7.39 (m, 3H), 6.95 – 6.90 (m, 1H), 6.88 – 6.71 (m, 2H), 5.57 (s, 1H), 4.79 (t, *J* = 5.7 Hz, 1H), 4.53 (d, *J* = 15.6 Hz, 1H), 4.37 (d, *J* = 15.6 Hz, 1H), 3.89 – 3.76 (m, 1H), 3.31 – 3.26 (m, 1H), 2.40 – 2.28 (m, 2H), 2.06 – 1.92 (m, 2H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 170.9, 163.3, 153.6 (d, *J* = 254.4 Hz), 132.6 (d, *J* = 12.1 Hz), 129.9, 129.7, 128.8, 126.6, 125.5 (d, *J* = 4.1 Hz), 121.7 (d, *J* = 3.0 Hz), 120.3 (d, *J* = 8.1 Hz), 114.9 (d, *J* = 20.2 Hz), 82.8, 75.2, 51.1 (d, *J* = 6.8 Hz), 49.6 (d, *J* = 2.6 Hz), 30.3, 22.9 (d, *J* = 1.6 Hz). **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>19</sub>FN<sub>3</sub>O<sup>+</sup> 336.1507; Found 336.1503.

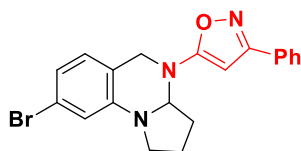
**5-(8-chloro-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)-3-phenylisoxazole (5c).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as a yellow solid (27.0 mg, 77% yield).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.79 – 7.69 (m, 2H), 7.41 (dd, *J* = 5.0, 2.0 Hz, 3H), 7.27 – 7.24 (m, 1H), 7.06 – 6.98 (m, 1H), 6.92 (t, *J* = 7.7 Hz, 1H), 5.46 (s, 1H), 4.91 (dd, *J* = 5.6, 4.3 Hz, 1H), 4.54 (d, *J* = 15.3 Hz, 1H), 4.32 – 4.28 (m, 1H), 4.05 (d, *J* = 9.3 Hz, 1H), 3.10 – 3.00 (m, 1H), 2.37 – 2.26 (m, 2H), 2.07 – 1.97 (m, 2H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 170.0, 163.5, 142.2, 129.8, 129.7, 129.4, 128.8, 127.6, 126.6, 124.7, 123.1, 80.0, 74.7, 51.9, 47.2, 31.3, 23.2. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>19</sub>ClN<sub>3</sub>O<sup>+</sup> 352.1211; Found 352.1216.

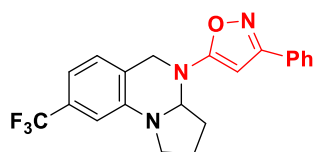
**5-(8-bromo-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)-3-phenylisoxazole (5d).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as a white solid (30.3 mg, 76% yield).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.74 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.42 (dd, *J* = 4.9, 2.0 Hz, 3H), 6.89 (d, *J* = 7.9 Hz, 1H), 6.83 (dd, *J* = 8.0, 1.8 Hz, 1H), 6.68 (d, *J* = 1.8 Hz, 1H), 5.62 (s, 1H), 4.67 (dd, *J* = 8.2, 5.6 Hz, 1H), 4.47 (d, *J* = 15.6 Hz, 1H), 4.38 (d, *J* = 15.4 Hz, 1H), 3.39 – 3.31 (m, 2H), 2.61 – 2.54 (m, 1H), 2.31 – 2.22 (m, 1H), 2.18 – 2.09 (m, 1H), 2.05 – 1.95 (m, 1H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 170.9, 163.3, 144.2, 129.9, 129.5, 128.8, 127.3, 126.6, 121.9, 119.9, 117.5, 114.4, 83.7, 74.8, 51.7, 46.4, 31.7, 22.0. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>19</sub>BrN<sub>3</sub>O<sup>+</sup> 396.0706; Found 396.0711.

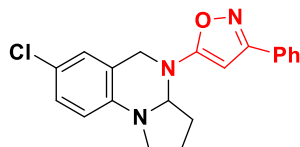
**3-phenyl-5-(8-(trifluoromethyl)-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)isoxazole (5e).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 20:1) afforded the product as a white solid (28.9 mg, 75% yield).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.78 – 7.72 (m, 2H), 7.42 (dd, *J* = 5.0, 1.9 Hz, 3H), 7.11 (d, *J* = 7.8 Hz, 1H), 6.96 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.74 (d, *J* = 1.7 Hz, 1H), 5.64 (s, 1H), 4.71 (dd, *J* = 8.2, 5.6 Hz, 1H), 4.58 – 4.44 (m, 2H), 3.46 – 3.36 (m, 2H), 2.63 – 2.56 (m, 1H), 2.33 – 2.24 (m, 1H), 2.20 – 2.12 (m, 1H), 2.06 – 1.97 (m, 1H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 170.8, 163.3, 143.2, 130.6 (q, *J* = 32.3 Hz), 130.0, 129.5, 128.8, 126.6, 126.3, 124.3 (q, *J* = 272.3 Hz), 122.0, 113.6 (q, *J* = 4.0 Hz), 108.0 (q, *J* = 4.0 Hz), 83.9, 74.9, 51.8, 46.4, 31.8, 22.0. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>19</sub>F<sub>3</sub>N<sub>3</sub>O<sup>+</sup> 386.1475; Found 386.1472.

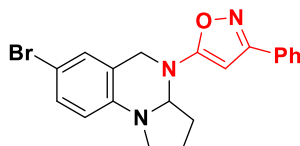
**5-(7-chloro-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)-3-phenylisoxazole (5f).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as a yellow solid (28.1 mg, 80% yield).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 7.70 – 7.62 (m, 2H), 7.35 – 7.32 (m, 3H), 7.02 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.93 (d, *J* = 2.4 Hz, 1H), 6.39 (d, *J* = 8.5 Hz, 1H), 5.52 (s, 1H), 4.55 (dd, *J* = 8.1, 5.8 Hz, 1H), 4.41 (d, *J* = 15.3 Hz, 1H), 4.29 (d, *J* = 15.4 Hz, 1H), 3.30 – 3.23 (m, 2H), 2.49 – 2.44 (m, 1H), 2.21 – 2.13 (m, 1H), 2.06 – 1.99 (m, 1H), 1.93 – 1.83 (m, 1H). **<sup>13</sup>C NMR** (125 MHz, CDCl<sub>3</sub>) δ 170.9, 163.3, 141.9, 129.9, 128.8, 128.1, 126.6, 125.9, 122.2, 120.5, 113.1, 83.5, 74.9, 51.5, 46.6, 31.6, 22.0. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>19</sub>ClN<sub>3</sub>O<sup>+</sup> 352.1211; Found 352.1209.

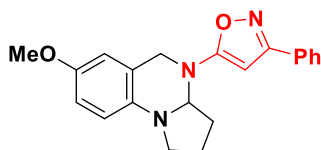
**5-(7-bromo-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)-3-phenylisoxazole (5g).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as a white solid (30.0 mg, 76% yield).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 7.66 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.34 (dd, *J* = 5.1, 2.0 Hz, 3H), 7.18 – 7.15 (m, 1H), 7.07 (d, *J* = 2.3 Hz, 1H), 6.35 (d, *J* = 8.5 Hz, 1H), 5.53 (s, 1H), 4.56 (dd, *J* = 8.0, 5.9 Hz, 1H), 4.42 (d, *J* = 15.4 Hz, 1H), 4.30 (d, *J* = 15.4 Hz, 1H), 3.31 – 3.23 (m, 2H), 2.50 – 2.44 (m, 1H), 2.23 – 2.13 (m, 1H), 2.06 – 2.02 (m, 1H), 1.94 – 1.85 (m, 1H). **<sup>13</sup>C NMR** (125 MHz, CDCl<sub>3</sub>) δ 170.9, 163.3, 142.3, 131.0, 129.9, 129.5, 128.8, 128.7, 126.6, 120.8, 113.5, 109.2, 83.6, 74.9, 51.4, 46.5, 31.6, 22.0. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>19</sub>BrN<sub>3</sub>O<sup>+</sup> 396.0706; Found 396.0707.

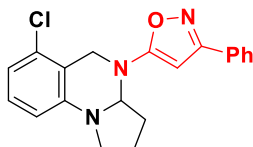
**5-(7-methoxy-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)-3-phenylisoxazole (5h).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as a yellow oil (17.0 mg, 49% yield).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 7.68 – 7.65 (m, 2H), 7.34 (dd, *J* = 5.2, 2.0 Hz, 3H), 6.70 (dd, *J* = 8.7, 2.9 Hz, 1H), 6.61 (d, *J* = 2.8 Hz, 1H), 6.53 (d, *J* = 8.7 Hz, 1H), 5.46 (s, 1H), 4.49 – 4.42 (m, 2H), 4.35 (d, *J* = 15.2 Hz, 1H), 3.68 (s, 4H), 3.32 – 3.27 (m, 1H), 3.25 – 3.20 (m, 1H), 2.49 – 2.44 (m, 1H), 2.18 – 2.13 (m, 1H), 2.06 – 2.00 (m, 1H), 1.93 – 1.87 (m, 1H). **<sup>13</sup>C NMR** (125 MHz, CDCl<sub>3</sub>) δ 170.8, 163.3, 152.6, 138.1, 129.8, 129.7, 128.8, 126.6, 121.8, 114.1, 113.6, 112.1, 81.6, 75.0, 55.8, 50.8, 47.2, 31.4, 21.8. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>22</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup> 348.1707; Found 348.1710.

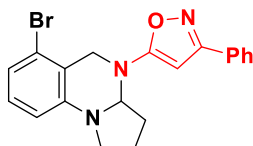
**6-(6-chloro-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)-3-phenylisoxazole (5i).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as a white solid (27.4 mg, 78% yield).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.78 – 7.72 (m, 2H), 7.45 – 7.39 (m, 3H), 7.08 (t, *J* = 8.1 Hz, 1H), 6.75 (dd, *J* = 8.0, 1.0 Hz, 1H), 6.45 (dd, *J* = 8.1, 1.0 Hz, 1H), 5.67 (s, 1H), 4.69 – 4.57 (m, 2H), 4.40 (d, *J* = 16.1 Hz, 1H), 3.44 – 3.34 (m, 2H), 2.63 – 2.55 (m, 1H), 2.38 – 2.28 (m, 1H), 2.18 – 2.08 (m, 1H), 2.04 – 1.94 (m, 1H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 171.2, 163.2, 144.3, 132.0, 129.9, 129.5, 128.8, 128.7, 126.6, 117.7, 116.1, 110.2, 83.9, 74.4, 50.3, 46.6, 31.8, 22.2. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>19</sub>ClN<sub>3</sub>O<sup>+</sup> 352.1211; Found 352.1214.

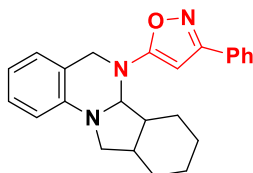
**5-(6-bromo-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)-3-phenylisoxazole (5j).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as a white solid (34.4 mg, 87% yield, dr > 20:1).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.82 – 7.71 (m, 2H), 7.45 – 7.40 (m, 3H), 7.01 (t, *J* = 8.0 Hz, 1H), 6.93 (dd, *J* = 8.0, 1.1 Hz, 1H), 6.49 (dd, *J* = 8.0, 1.1 Hz, 1H), 5.67 (s, 1H), 4.66 (dd, *J* = 8.0, 5.7 Hz, 1H), 4.58 (d, *J* = 16.0 Hz, 1H), 4.40 (d, *J* = 16.1 Hz, 1H), 3.41 – 3.36 (m, 2H), 2.63 – 2.56 (m, 1H), 2.39 – 2.29 (m, 1H), 2.17 – 2.12 (m, 1H), 2.07 – 1.88 (m, 1H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 171.1, 163.2, 144.5, 129.9, 129.5, 129.1, 128.8, 126.6, 122.2, 120.8, 117.7, 110.8, 84.0, 74.5, 52.9, 46.6, 31.7, 22.2. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>19</sub>BrN<sub>3</sub>O<sup>+</sup> 396.0706; Found 396.0703.

**5-(6a,6b,7,8,9,10,10a,11-octahydroisindolo[2,1-a]quinazolin-6(5H)-yl)-3-phenylisoxazole (5k).**



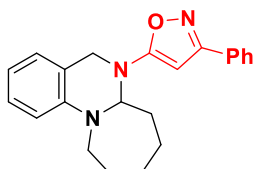
Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as a yellow solid (29.7 mg, 80% yield, dr = 1.7:1).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.80 – 7.76 (m, 1H), 7.67 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.43 (dd, *J* = 5.2, 2.0 Hz, 2H), 7.40 – 7.35 (m, 3H), 7.21 – 7.17 (m, 1H), 7.16 – 7.12 (m, 1H), 7.04 (dd, *J* = 7.4, 1.4 Hz, 1H), 7.01 (dd, *J* = 7.4, 1.5 Hz, 1H), 6.73 – 6.65 (m, 2H), 6.57 (d, *J* = 8.0 Hz, 1H), 6.48 (d, *J* = 8.1 Hz, 1H), 5.58 (s, 1H), 5.57 (s, 1H), 4.89 (d, *J* = 8.1 Hz, 1H), 4.76 – 4.67 (m, 2H), 4.44 (q, *J* = 14.5 Hz, 1H), 4.28 (d, *J* = 16.1 Hz, 1H), 3.42 (t, *J* = 8.9 Hz, 1H), 3.32 (dd, *J* = 8.9, 6.3 Hz, 1H),



3.26 – 3.19 (m, 2H), 2.74 – 2.60 (m, 2H), 2.23 (m, 1H), 1.94 – 1.89 (m, 1H), 1.82 – 1.52 (m, 8H), 1.49 – 1.13 (m, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  171.7, 170.6, 163.4, 163.2, 143.8, 143.3, 129.8, 129.8, 129.8, 129.6, 128.8, 128.7, 128.5, 128.4, 126.7, 126.5, 126.3, 125.7, 118.8, 118.3, 116.8, 116.6, 111.7, 110.6, 87.7, 79.4, 76.5, 54.0, 52.9, 50.0, 47.0, 42.4, 40.4, 35.4, 33.7, 28.3, 25.2, 24.5, 24.4, 24.2, 22.2, 21.3, 20.8. HRMS (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{24}\text{H}_{26}\text{N}_3\text{O}^+$  372.2070; Found 372.2073.

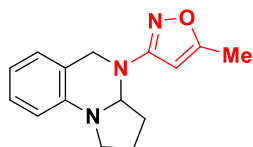
**5-(6a,7,8,9,10,11-hexahydroazepino[1,2-a]quinazolin-6(5H)-yl)-3-phenylisoxazole (5l).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as an oil liquid (21.7 mg, 63% yield).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.77 – 7.70 (m, 2H), 7.44 – 7.36 (m, 3H), 7.16 – 7.09 (m, 1H), 7.02 (dd,  $J = 7.4, 1.5$  Hz, 1H), 6.73 – 6.60 (m, 2H), 5.38 (s, 1H), 5.09 (dd,  $J = 10.5, 4.2$  Hz, 1H), 4.64 – 4.49 (m, 2H), 3.92 – 3.87 (m, 1H), 3.31 – 3.25 (m, 1H), 2.19 – 2.08 (m, 1H), 2.02 – 1.84 (m, 2H), 1.74 – 1.62 (m, 3H), 1.59 – 1.50 (m, 1H), 1.39 – 1.33 (m, 1H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  170.0, 163.7, 141.8, 129.9, 129.7, 128.7, 128.3, 126.6, 126.6, 116.3, 116.1, 110.7, 77.8, 72.3, 47.3, 44.8, 32.7, 26.6, 25.6, 24.4. HRMS (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{22}\text{H}_{24}\text{N}_3\text{O}^+$  346.1914; Found 346.1918.

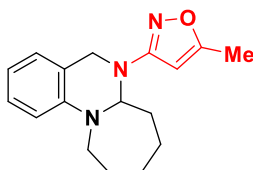
**3-methyl-5-(1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)isoxazole (5m).**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as an oil liquid (17.3 mg, 68% yield).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.08 – 7.05 (m, 1H), 6.92 (dd,  $J = 7.5, 1.4$  Hz, 1H), 6.62 – 6.59 (m, 1H), 6.48 (dd,  $J = 8.1, 1.1$  Hz, 1H), 5.70 (d,  $J = 1.0$  Hz, 1H), 4.50 (dd,  $J = 8.2, 5.2$  Hz, 1H), 4.30 (s, 2H), 3.32 – 3.28 (m, 2H), 2.59 – 2.54 (m, 1H), 2.24 (d,  $J = 0.9$  Hz, 3H), 2.06 – 1.98 (m, 1H), 1.96 – 1.83 (m, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  169.0, 166.5, 143.3, 128.1, 125.9, 119.7, 117.0, 111.7, 95.9, 74.8, 52.0, 46.6, 32.2, 22.0, 12.6. HRMS (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{15}\text{H}_{18}\text{N}_3\text{O}_2^+$  256.1444; Found 256.1448.

**3-(6a,7,8,9,10,11-hexahydroazepino[1,2-a]quinazolin-6(5H)-yl)-5-methylisoxazole (5n).**

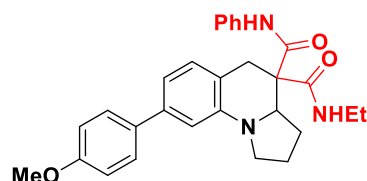


Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the

product as an oil liquid (16.4 mg, 58% yield).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 7.11 – 7.07 (m, 1H), 6.99 (dd, *J* = 7.5, 1.4 Hz, 1H), 6.66 – 6.56 (m, 2H), 5.67 (d, *J* = 0.9 Hz, 1H), 4.93 (dd, *J* = 10.5, 4.1 Hz, 1H), 4.53 – 4.42 (m, 2H), 3.91 – 3.86 (m, 1H), 3.29 – 3.23 (m, 1H), 2.32 – 2.28 (m, 3H), 2.15 – 2.10 (m, 1H), 1.95 – 1.90 (m, 1H), 1.88 – 1.82 (m, 1H), 1.70 – 1.59 (m, 3H), 1.55 – 1.47 (m, 1H), 1.38 – 1.32 (m, 1H). **<sup>13</sup>C NMR** (125 MHz, CDCl<sub>3</sub>) δ 169.4, 165.7, 142.0, 128.0, 126.6, 116.8, 115.8, 110.4, 93.0, 72.6, 47.2, 44.7, 32.1, 26.5, 25.8, 24.5, 12.7. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>22</sub>H<sub>24</sub>N<sub>3</sub>O<sup>+</sup> 284.1757; Found 284.1755.

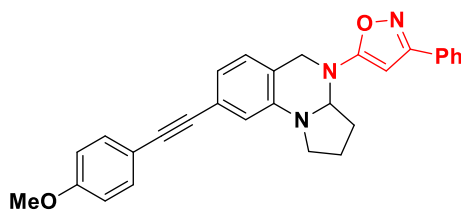
**N-ethyl-8-(4-methoxyphenyl)-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (6a)**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 10:1) afforded the product as a white solid (35.2 mg, 75% yield, dr > 20:1).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 8.97 (s, 1H), 8.72 (t, *J* = 5.4 Hz, 1H), 7.46 – 7.43 (m, 2H), 7.15 – 7.12 (m, 2H), 7.12 – 7.06 (m, 2H), 7.05 – 7.03 (m, 2H), 6.98 – 6.94 (m, 1H), 6.89 – 6.86 (m, 3H), 6.72 (d, *J* = 1.8 Hz, 1H), 3.81 – 3.77 (m, 2H), 3.75 (s, 3H), 3.51 – 3.46 (m, 1H), 3.34 – 3.24 (m, 3H), 3.06 (d, *J* = 17.4 Hz, 1H), 2.15 – 2.09 (m, 1H), 1.99 – 1.88 (m, 3H), 1.13 (t, *J* = 7.3 Hz, 3H). **<sup>13</sup>C NMR** (125 MHz, CDCl<sub>3</sub>) δ 171.3, 170.2, 159.3, 143.8, 140.9, 137.1, 133.9, 129.6, 129.0, 128.1, 124.9, 120.8, 118.6, 116.8, 114.2, 110.7, 62.8, 55.4, 51.6, 47.0, 36.3, 34.9, 27.4, 22.4, 14.7. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>29</sub>H<sub>32</sub>N<sub>3</sub>O<sub>3</sub><sup>+</sup> 470.2438; Found 470.2435.

**5-(8-((4-methoxyphenyl)ethynyl)-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)-3-phenylisoxazole (7a)**



Flash column chromatography on a silica gel (petroleum ether: ethyl acetate, 30:1) afforded the product as a white solid (35.8 mg, 80% yield).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 7.70 – 7.63 (m, 2H), 7.40 – 7.37 (m, 2H), 7.34 (dd, *J* = 5.2, 2.0 Hz, 3H), 6.93 (d, *J* = 7.7 Hz, 1H), 6.85 – 6.78 (m, 3H), 6.64 (d, *J* = 1.5 Hz, 1H), 5.53 (s, 1H), 4.58 (dd, *J* = 8.2, 5.7 Hz, 1H), 4.50 – 4.32 (m, 2H), 3.74 (s, 3H), 3.32 (dd, *J* = 8.1, 5.9 Hz, 2H), 2.53 – 2.48 (m, 1H), 2.23 – 2.13 (m, 1H), 2.09 – 2.04 (m, 1H), 1.98 – 1.87 (m, 1H). **<sup>13</sup>C NMR** (125 MHz, CDCl<sub>3</sub>) δ 171.0, 163.3, 159.59, 143.1, 133.1, 129.9, 129.6, 128.8, 126.6, 126.0, 123.2, 120.8, 119.2, 115.4, 114.5, 114.0, 88.7, 88.5, 83.2, 74.8, 55.3, 51.7, 46.4, 31.7, 21.9. **HRMS (ESI) m/z:** [M + H]<sup>+</sup> Calcd for C<sub>29</sub>H<sub>26</sub>N<sub>3</sub>O<sub>2</sub><sup>+</sup> 448.2020; Found 448.2022.

## Reference

1. H. Liu, Y. Yan, M. Li, X. Zhang, An enantioselective aza-Friedel–Crafts reaction of 5-aminoisoxazoles with isatin-derived N-Boc ketimines, *Org. Biomol. Chem.*, **2021**, *19*, 3820-3824.

#### 4. Crystal Structures and Data

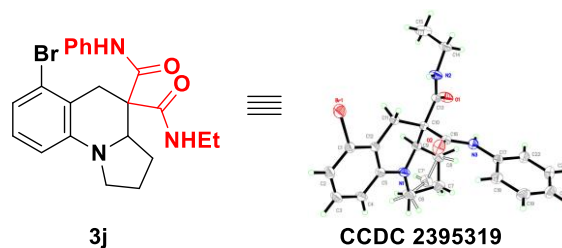


Table 1. Crystal data and structure refinement for **3j**.

Identification code	<b>3j</b>
Empirical formula	C <sub>22</sub> H <sub>24</sub> BrN <sub>3</sub> O <sub>2</sub>
Formula weight	442.35
Temperature	273(2) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 9.9945(5) Å    alpha = 90.047(2) deg. b = 10.0580(5) Å    beta = 98.948(2) deg. c = 10.3299(5) Å    gamma = 102.789(2) deg.
Volume	999.65(9) Å <sup>3</sup>
Z, Calculated density	2, 1.470 Mg/m <sup>3</sup>
Absorption coefficient	2.079 mm <sup>-1</sup>
F(000)	456
Crystal size	0.401 x 0.333 x 0.319 mm
Theta range for data collection	2.078 to 25.020 deg.
Limiting indices	-11 ≤ h ≤ 11, -11 ≤ k ≤ 11, -12 ≤ l ≤ 12
Reflections collected / unique	15553 / 3474 [R(int) = 0.0181]
Completeness to theta = 25.020	98.8 %
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	3474 / 36 / 264
Goodness-of-fit on F <sup>2</sup>	1.026
Final R indices [I > 2σ(I)]	R1 = 0.0268, wR2 = 0.0674
R indices (all data)	R1 = 0.0321, wR2 = 0.0704
Extinction coefficient	n/a
Largest diff. peak and hole	0.245 and -0.367 e.Å <sup>-3</sup>

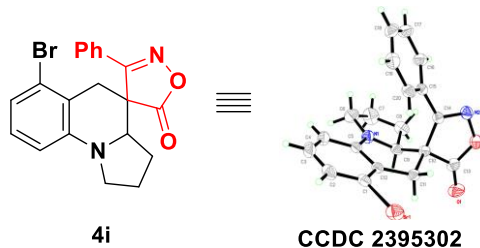
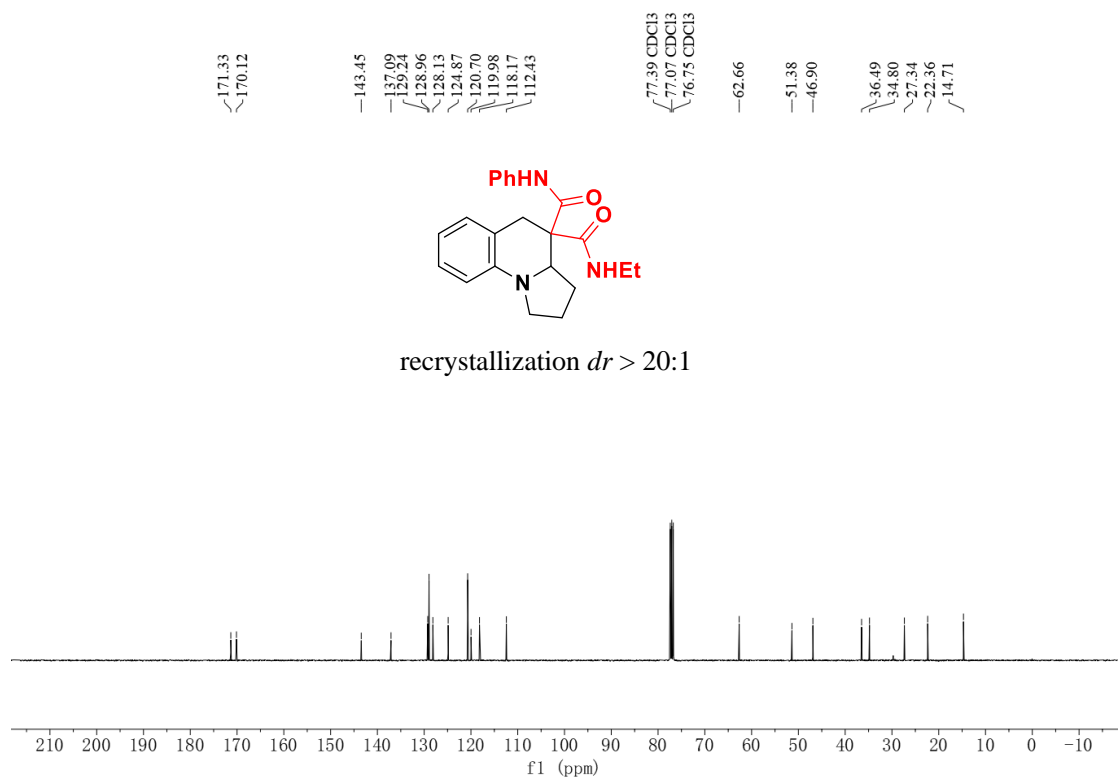
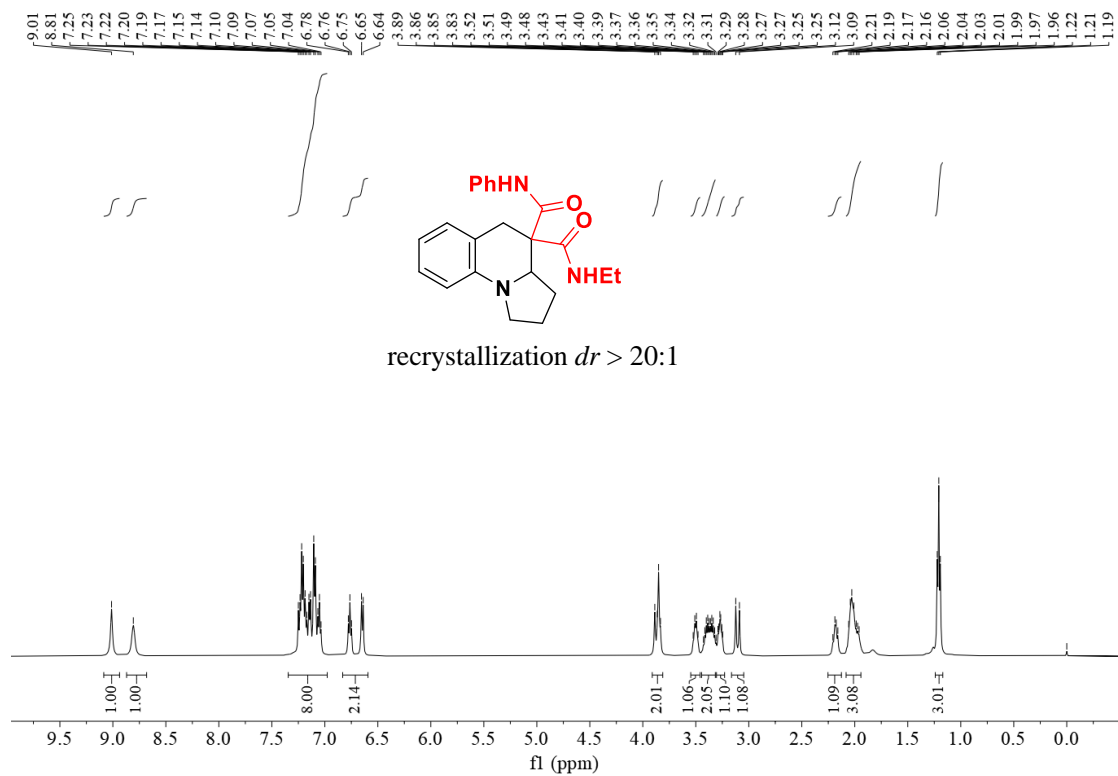


Table 1. Crystal data and structure refinement for **4i**.

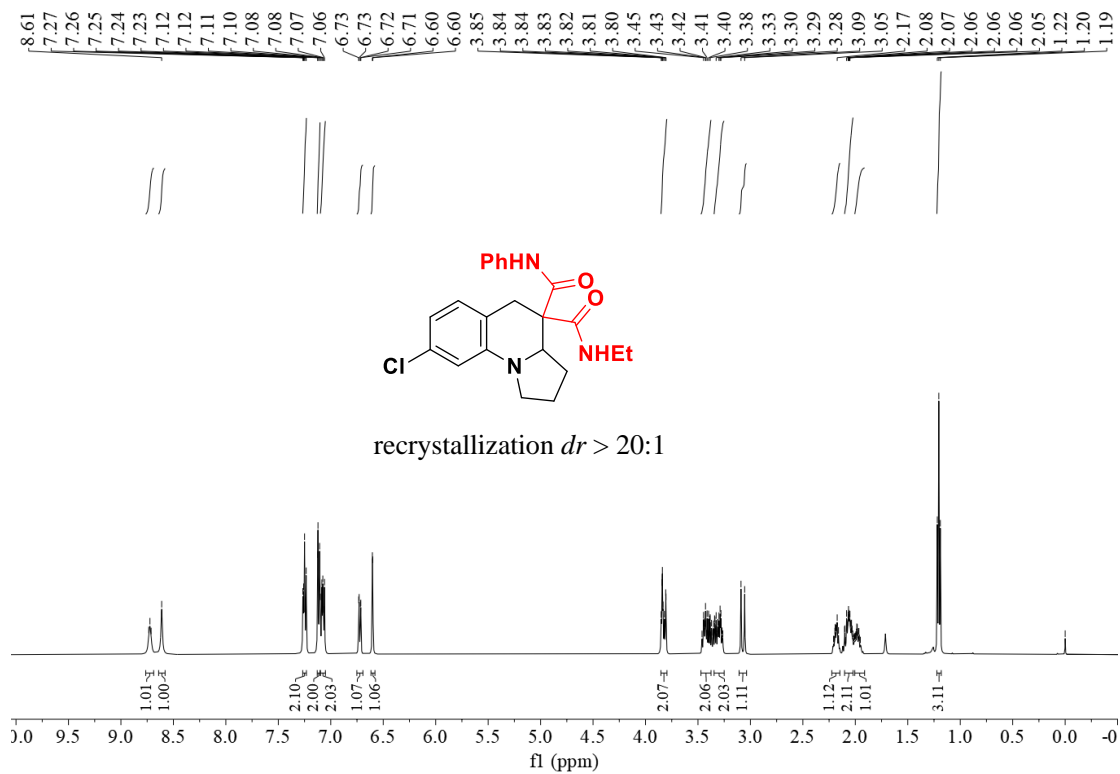
Identification code	<b>4i</b>
Empirical formula	C <sub>20</sub> H <sub>17</sub> BrN <sub>2</sub> O <sub>2</sub>
Formula weight	397.26
Temperature	273(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/n
Unit cell dimensions	a = 9.3775(13) Å    alpha = 90 deg. b = 9.8418(13) Å    beta = 96.999(5) deg. c = 18.943(3) Å    gamma = 90 deg.
Volume	1735.2(4) Å <sup>3</sup>
Z, Calculated density	4, 1.521 Mg/m <sup>3</sup>
Absorption coefficient	2.385 mm <sup>-1</sup>
F(000)	808
Crystal size	0.492 x 0.477 x 0.425 mm
Theta range for data collection	2.557 to 25.020 deg.
Limiting indices	-11 ≤ h ≤ 11, -11 ≤ k ≤ 11, -20 ≤ l ≤ 22
Reflections collected / unique	19651 / 3042 [R(int) = 0.0238]
Completeness to theta = 25.020	99.3 %
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	3042 / 0 / 226
Goodness-of-fit on F <sup>2</sup>	1.049
Final R indices [I > 2σ(I)]	R1 = 0.0283, wR2 = 0.0694
R indices (all data)	R1 = 0.0372, wR2 = 0.0732
Extinction coefficient	n/a
Largest diff. peak and hole	0.315 and -0.438 e.Å <sup>-3</sup>

## 5. <sup>1</sup>H and <sup>13</sup>C NMR Spectra

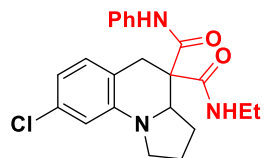
### N-ethyl-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (3a).



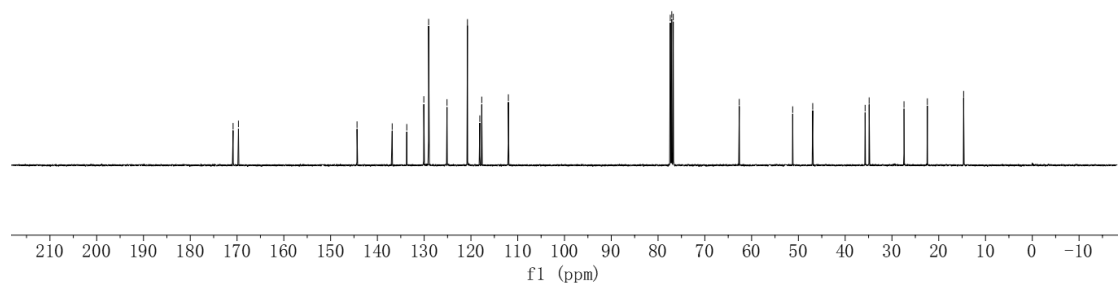
**8-chloro-N-ethyl-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (3b).**



170.85  
169.70  
144.35  
136.83  
133.72  
130.07  
129.04  
125.12  
120.75  
118.10  
117.69  
112.00  
77.39 CDCl3  
77.07 CDCl3  
76.75 CDCl3  
62.64  
51.22  
46.94  
35.73  
34.88  
27.43  
22.43  
14.68



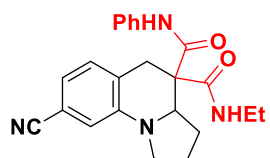
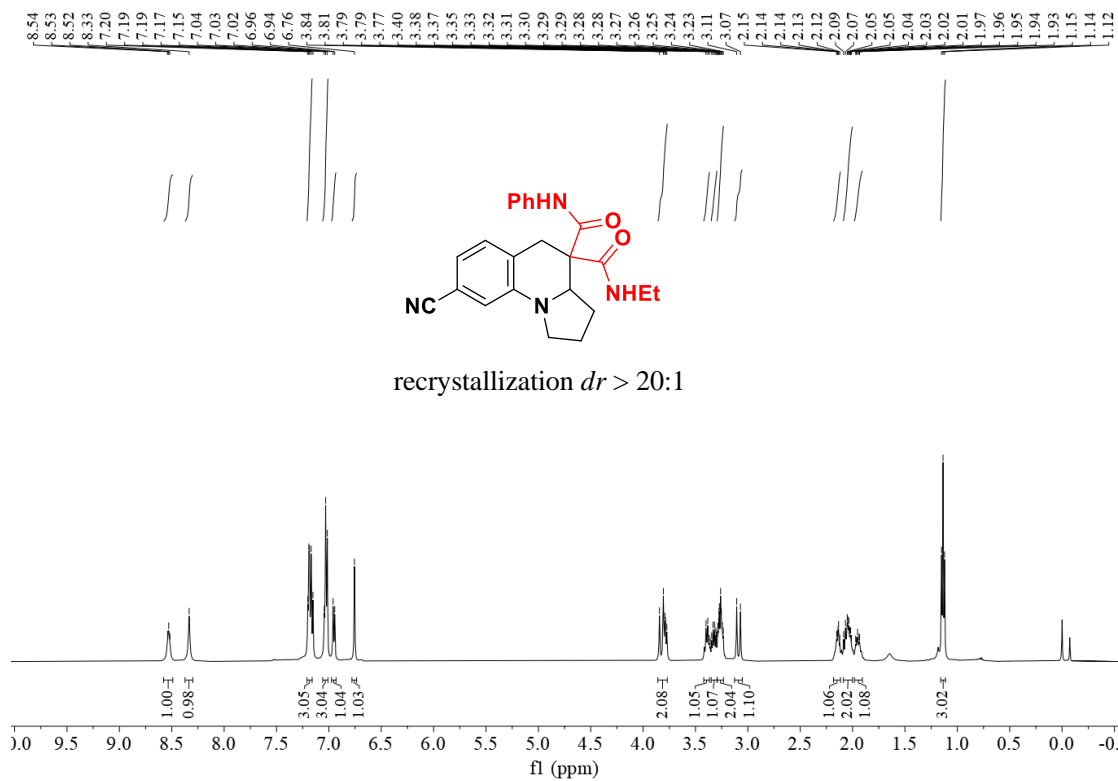
recrystallization *dr* > 20:1



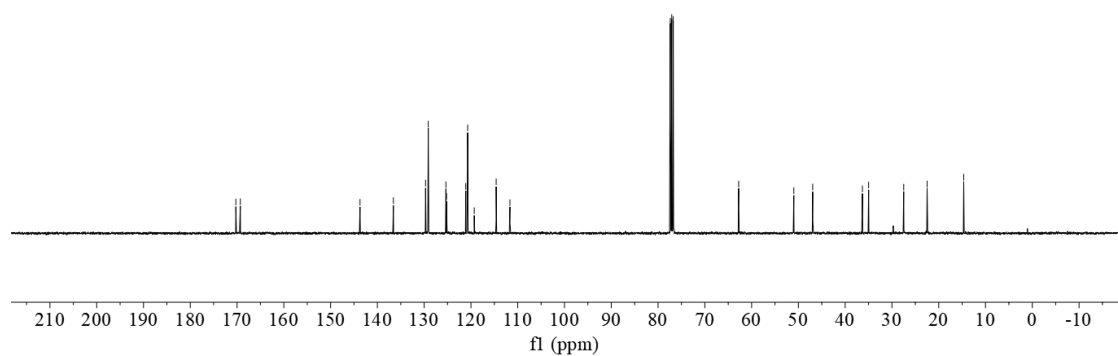




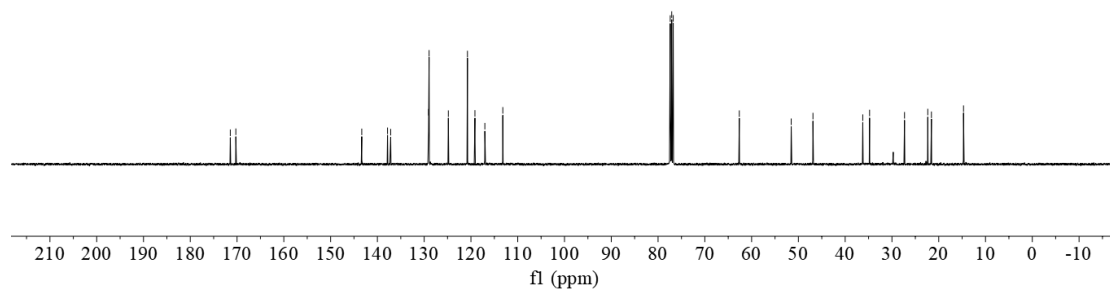
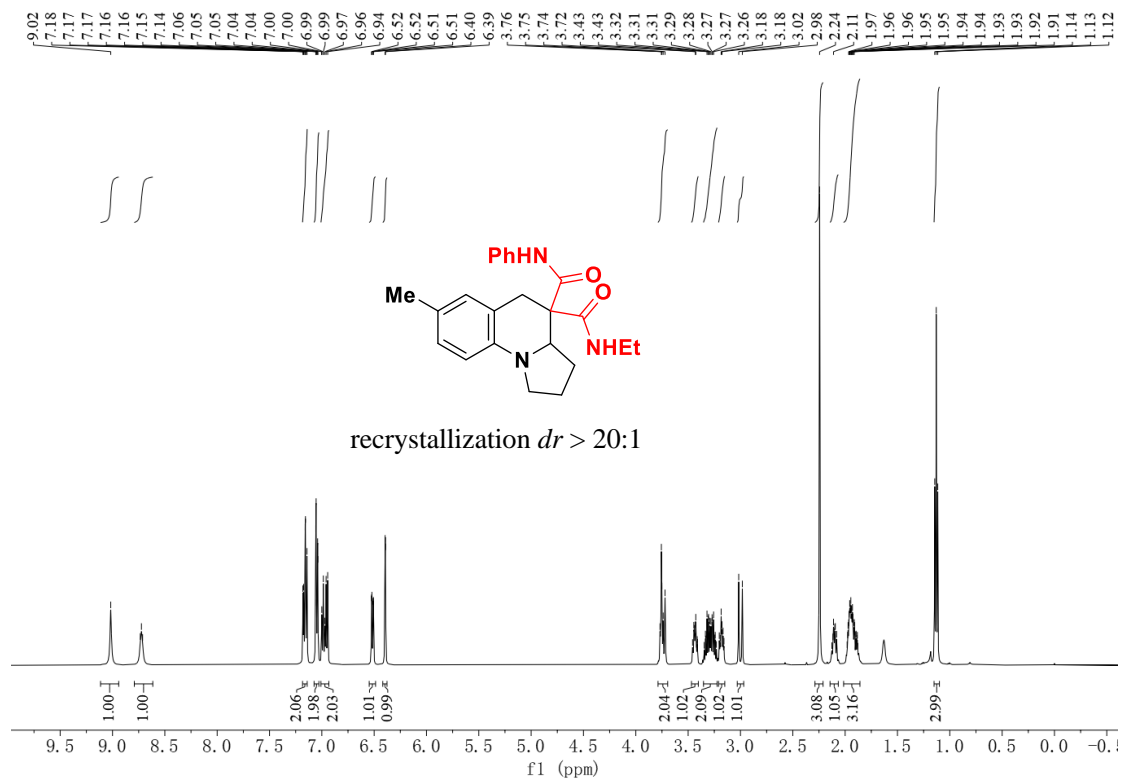
**8-cyano-N-ethyl-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (3d).**



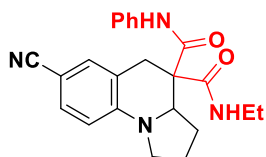
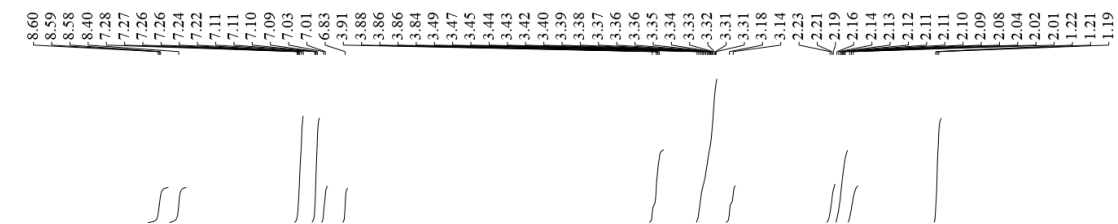
recrystallization  $dr > 20:1$



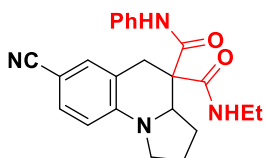
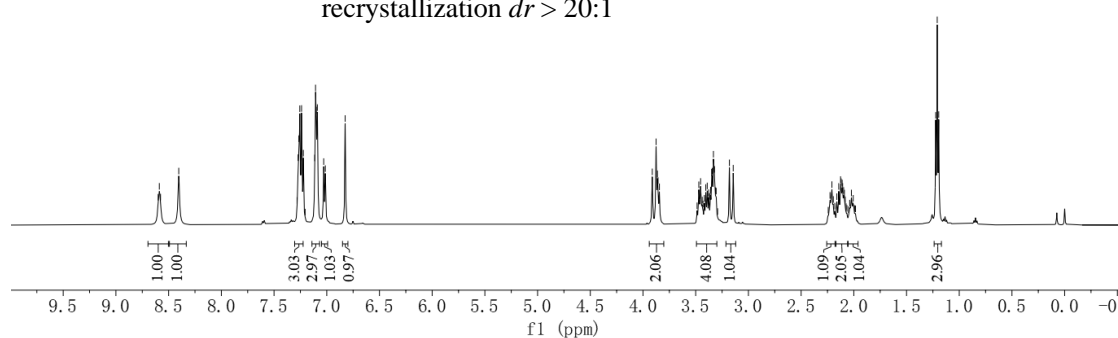
**N-ethyl-7-methyl-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (3e).**



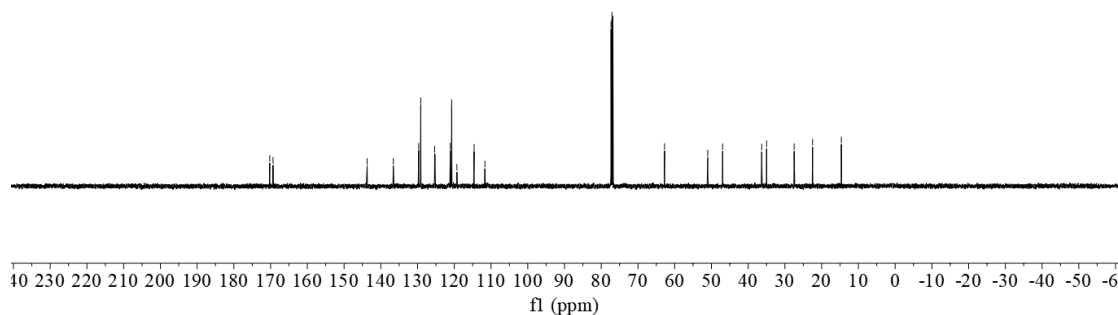
**7-cyano-N-ethyl-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (3f).**



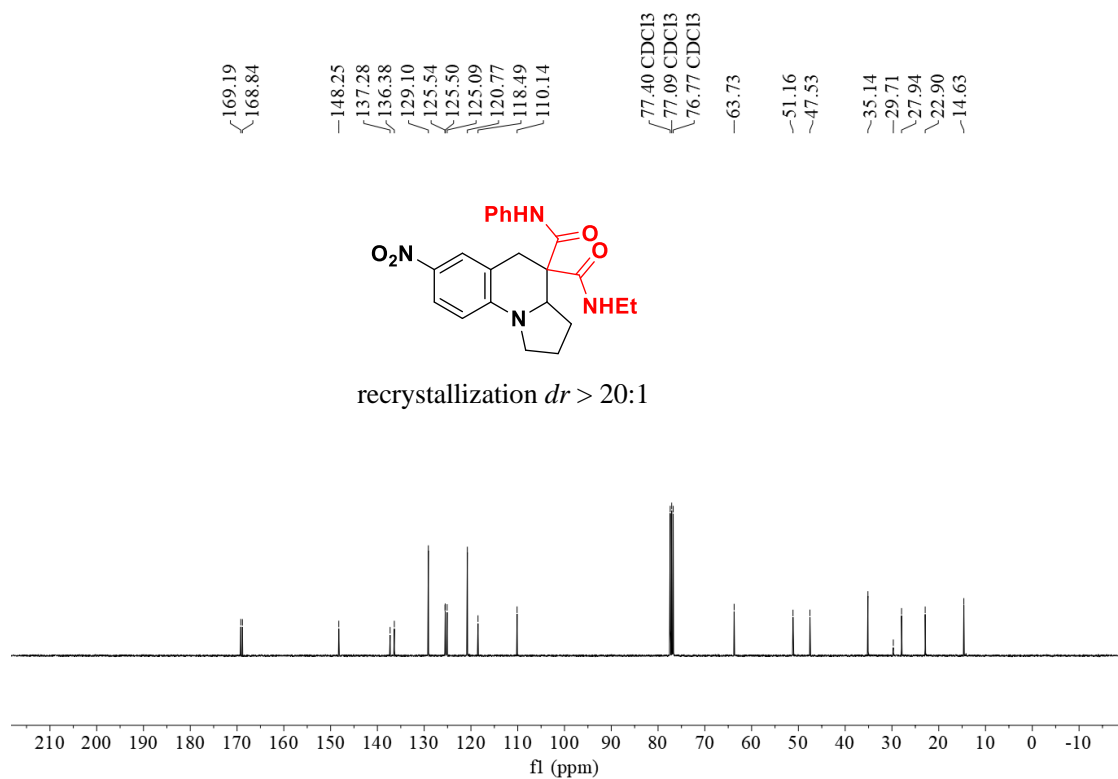
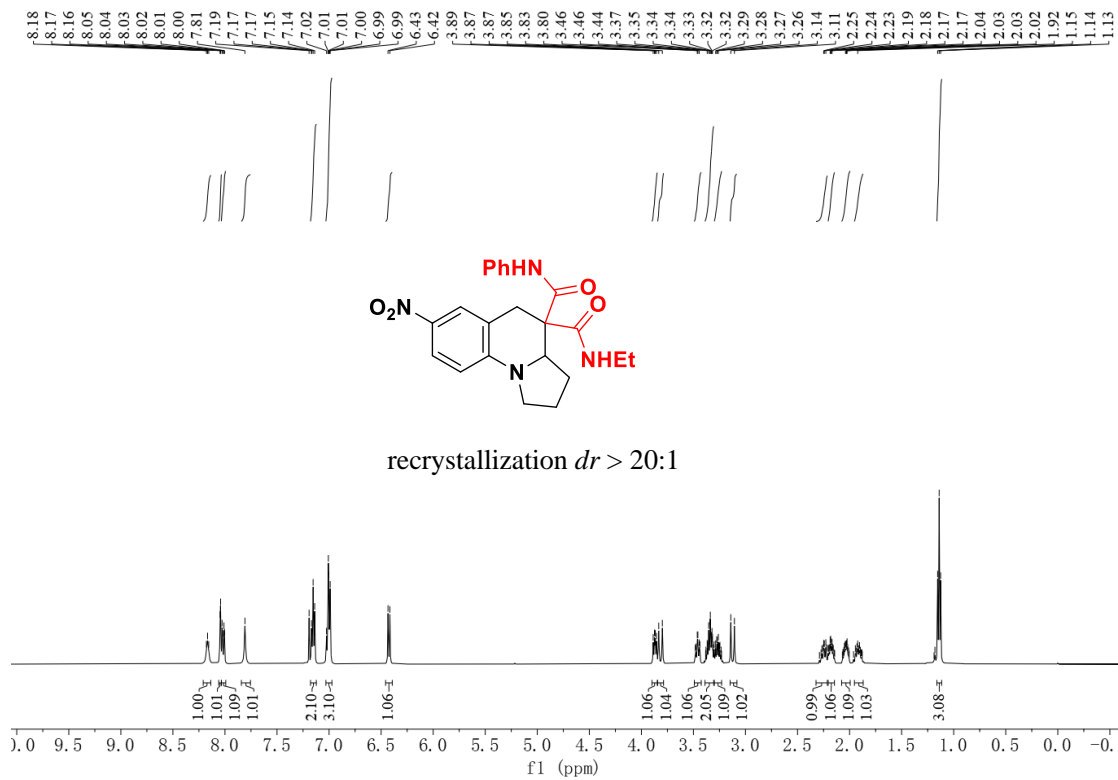
recrystallization  $dr > 20:1$



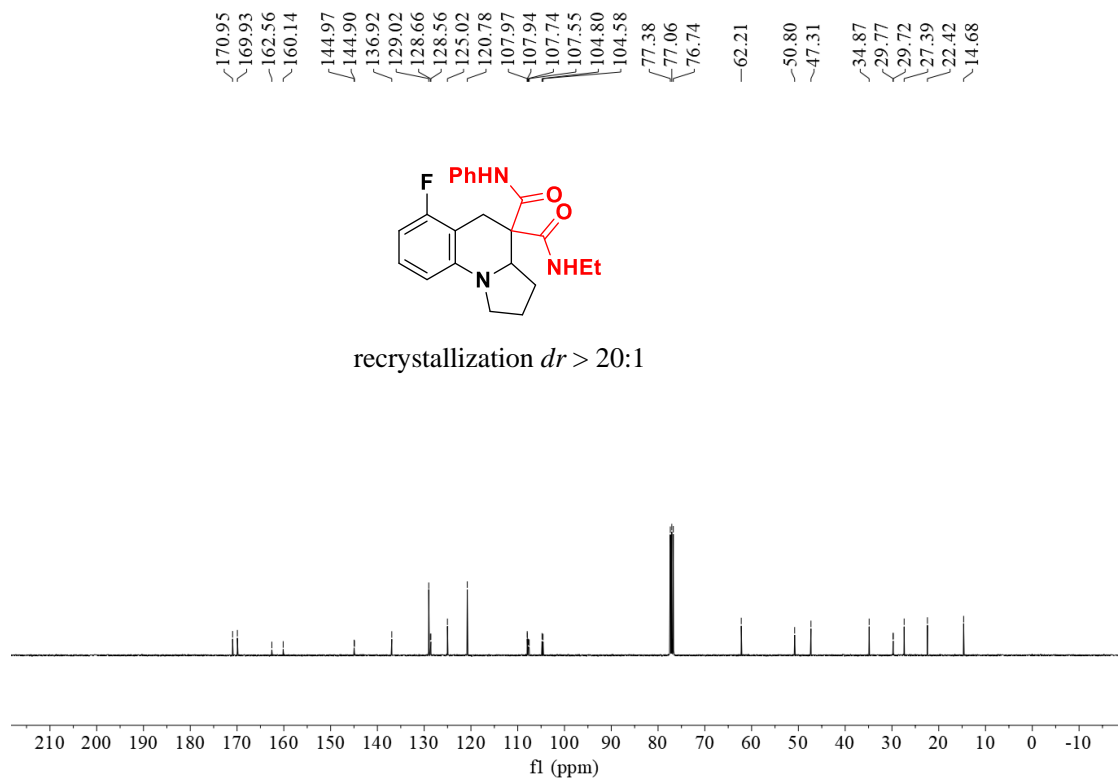
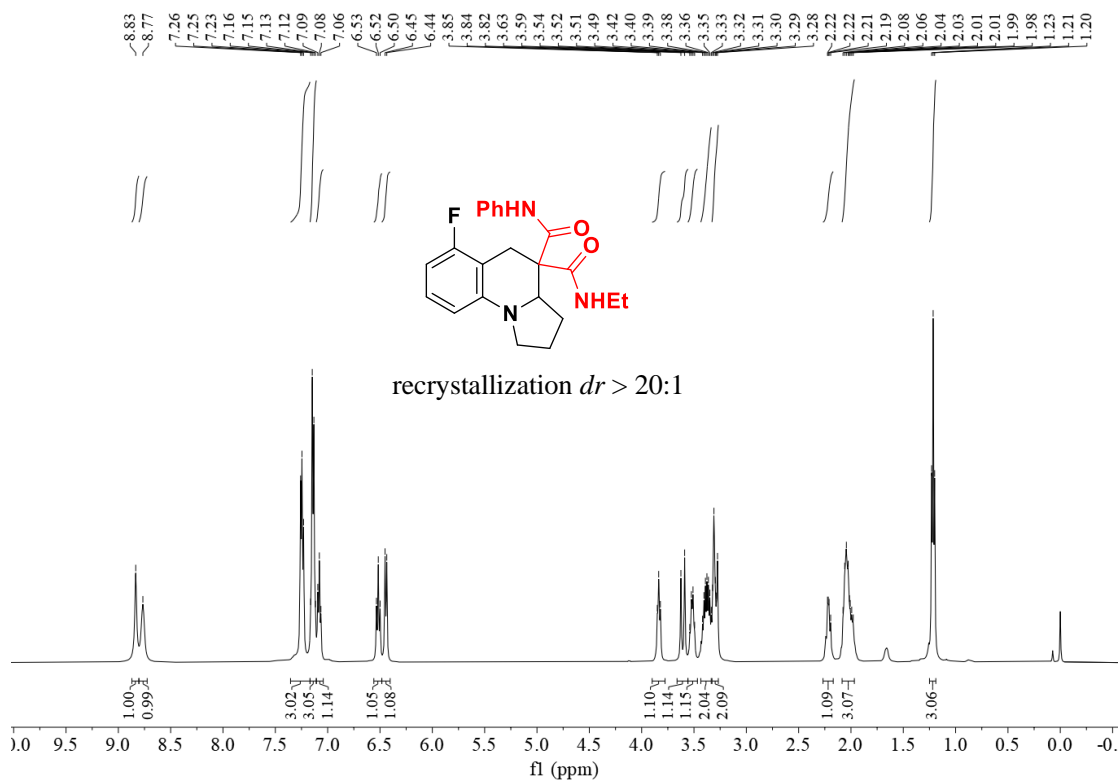
recrystallization  $dr > 20:1$



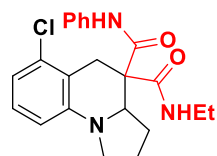
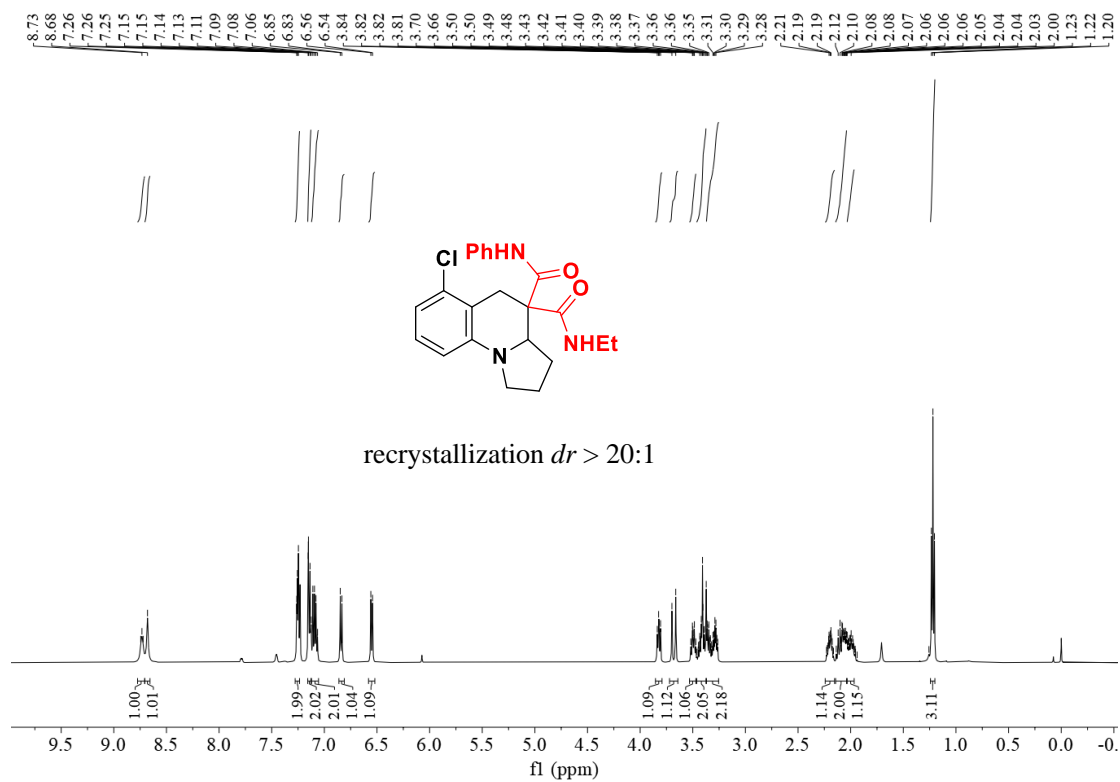
**N-ethyl-7-nitro-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (3g).**



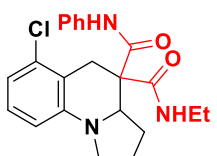
**N-ethyl-6-fluoro-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (3h).**



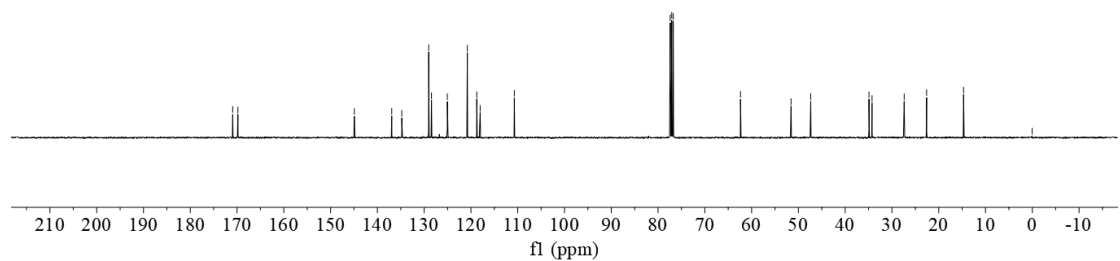
**6-chloro-N-ethyl-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (3i).**



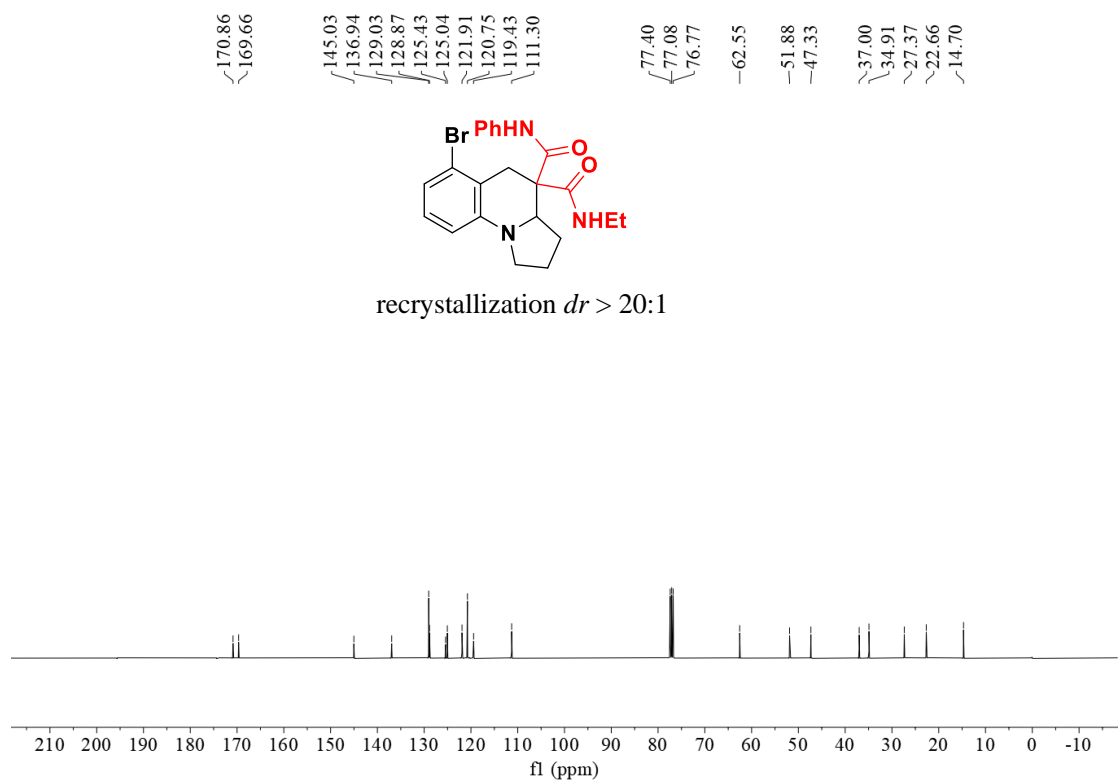
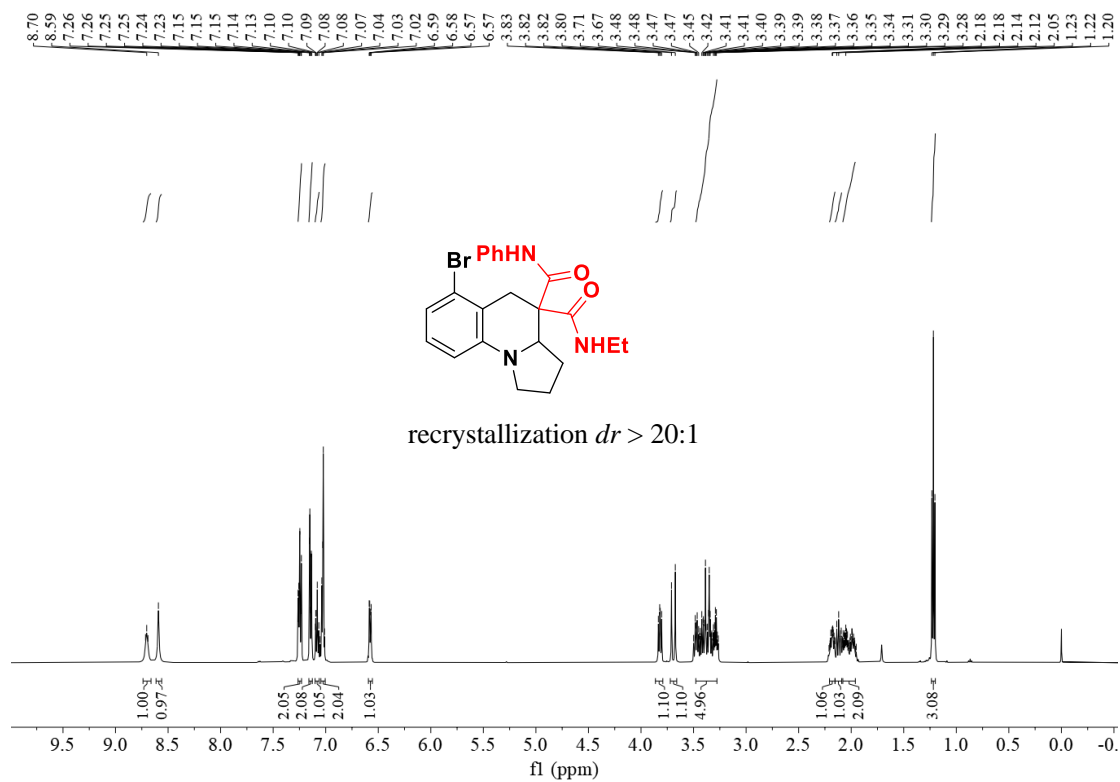
recrystallization *dr* > 20:1



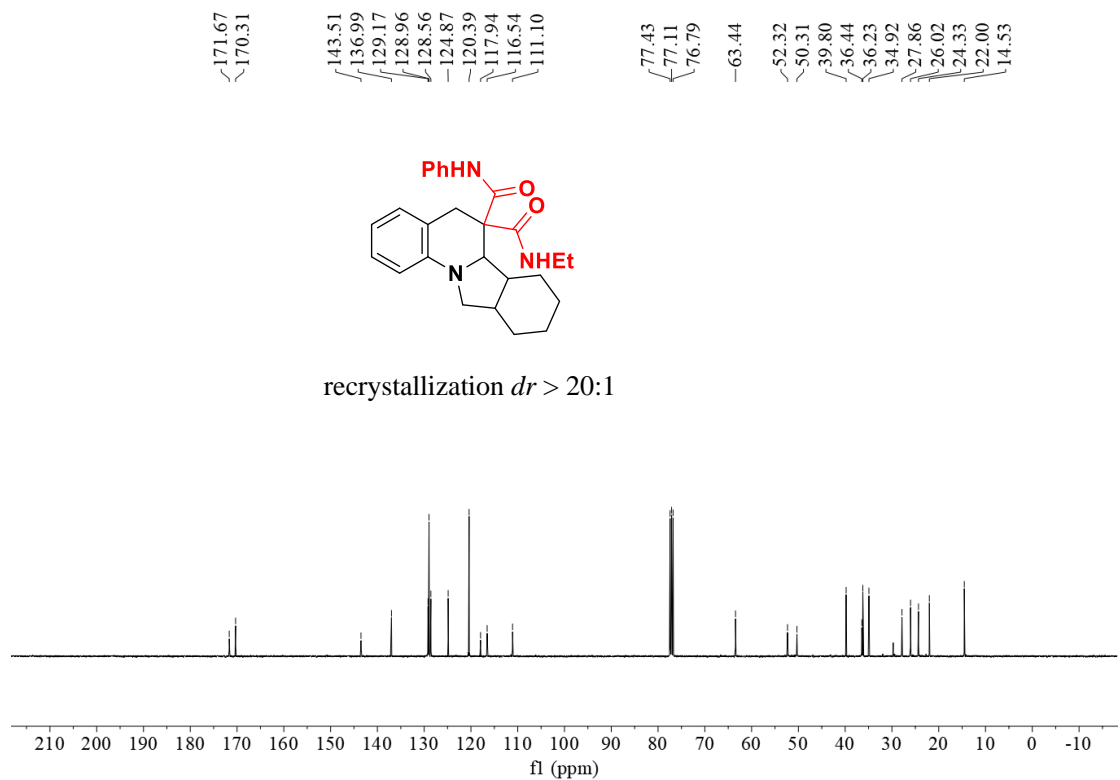
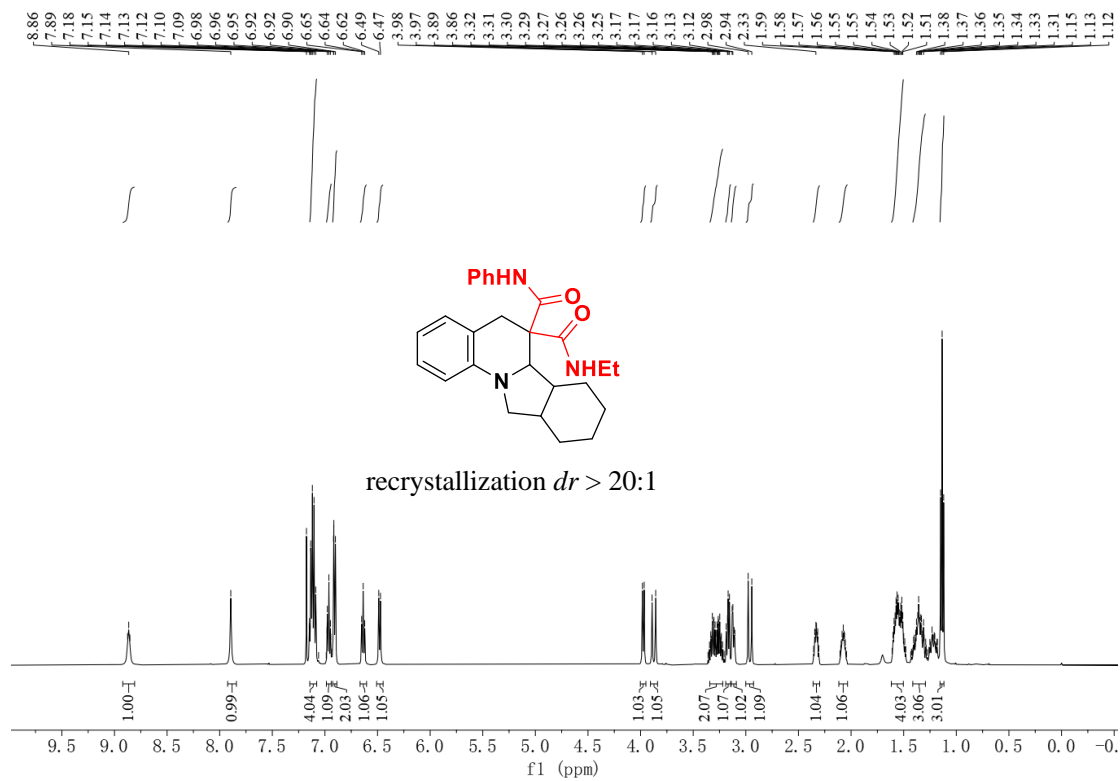
recrystallization *dr* > 20:1



**6-bromo-N-ethyl-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (3j).**

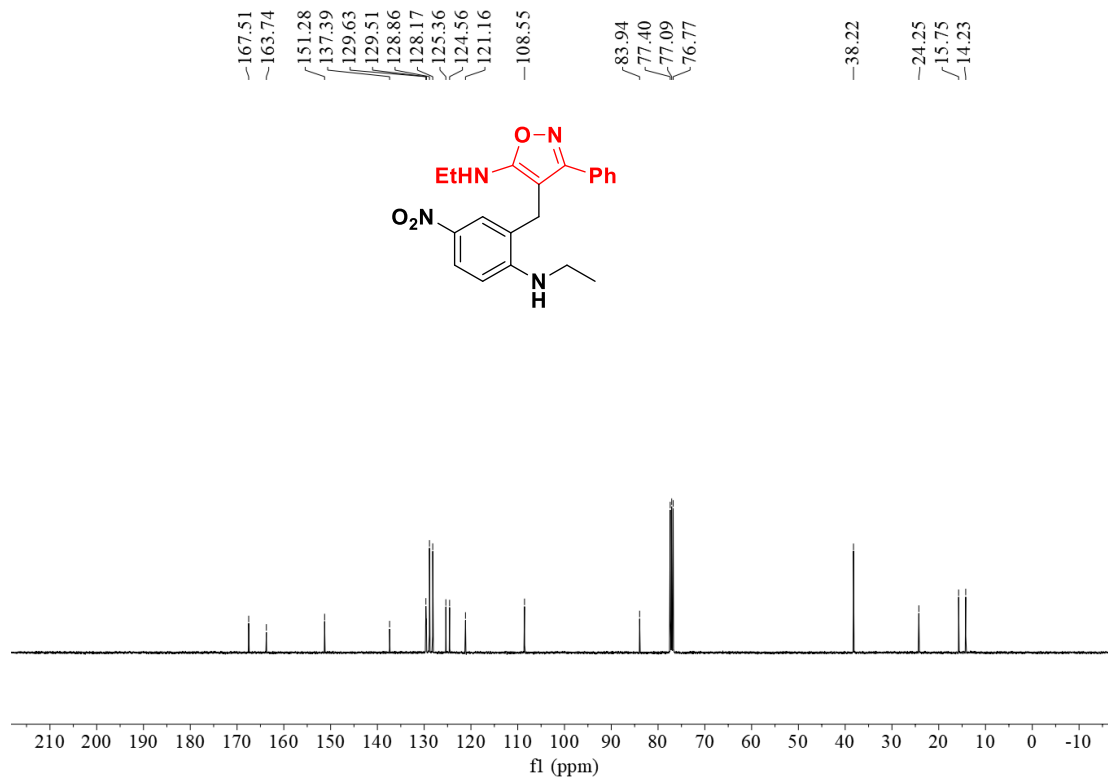
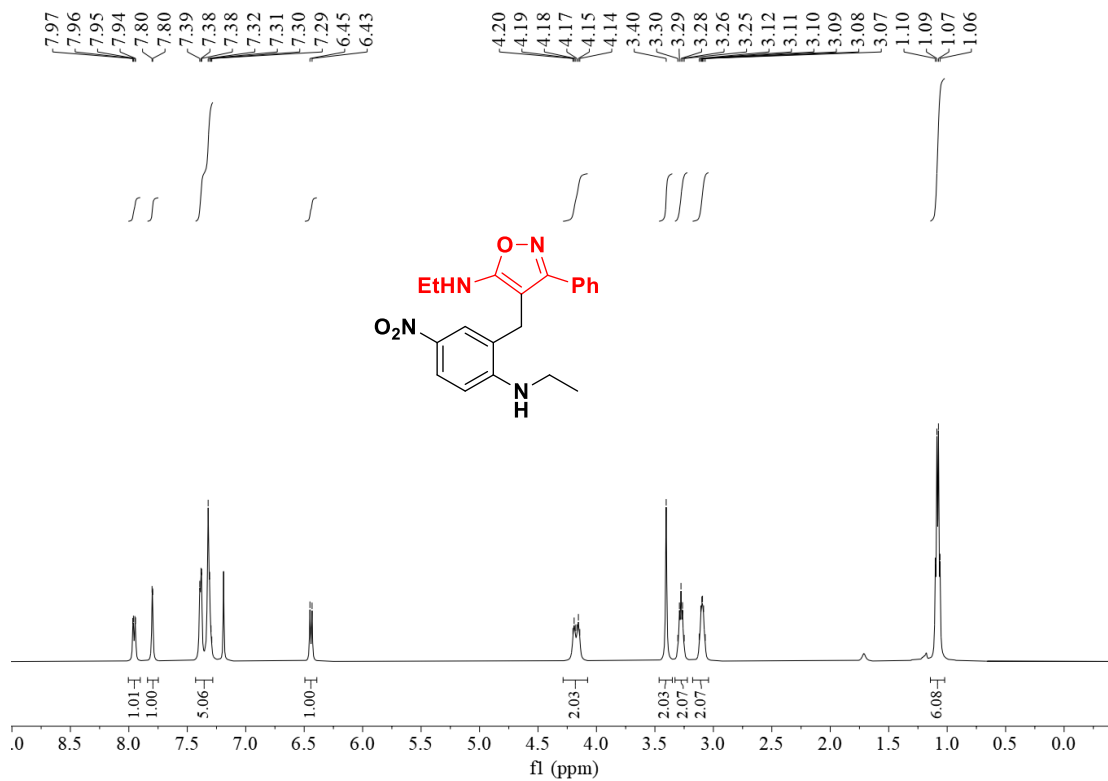


**N-ethyl-N-phenyl-6a,6b,7,8,9,10,10a,11-octahydroisindolo[2,1-a]quinoline-6,6(5H)-dicarboxamide (3k).**

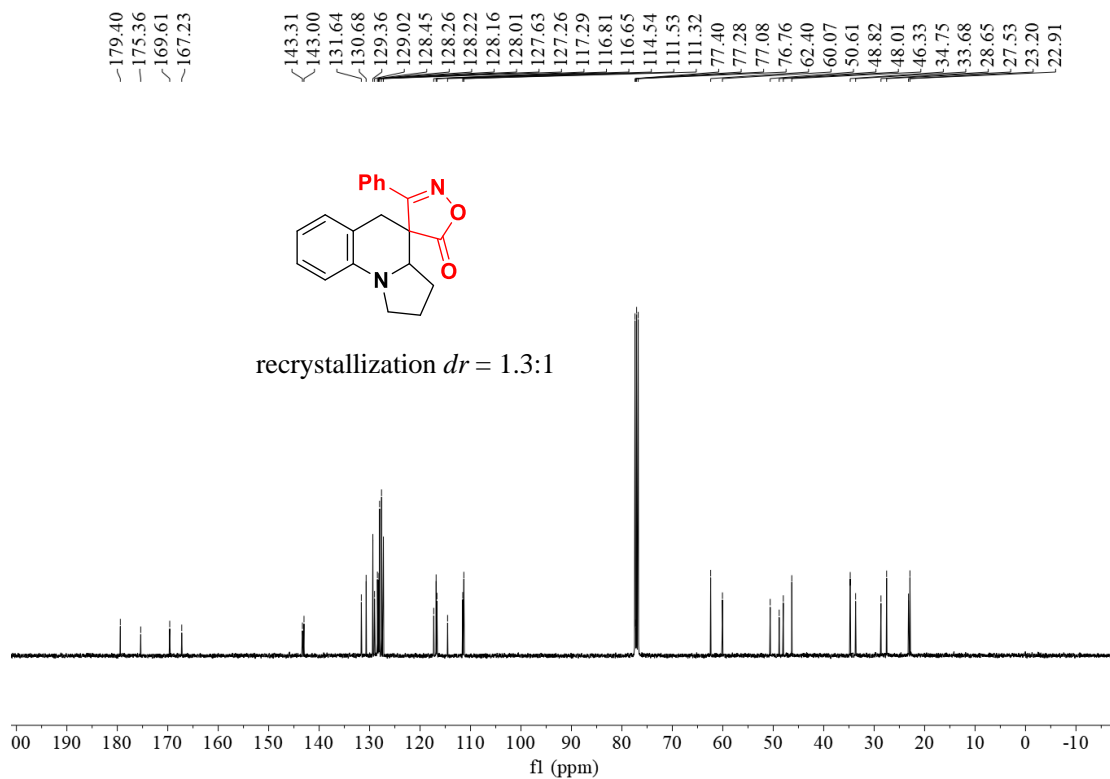
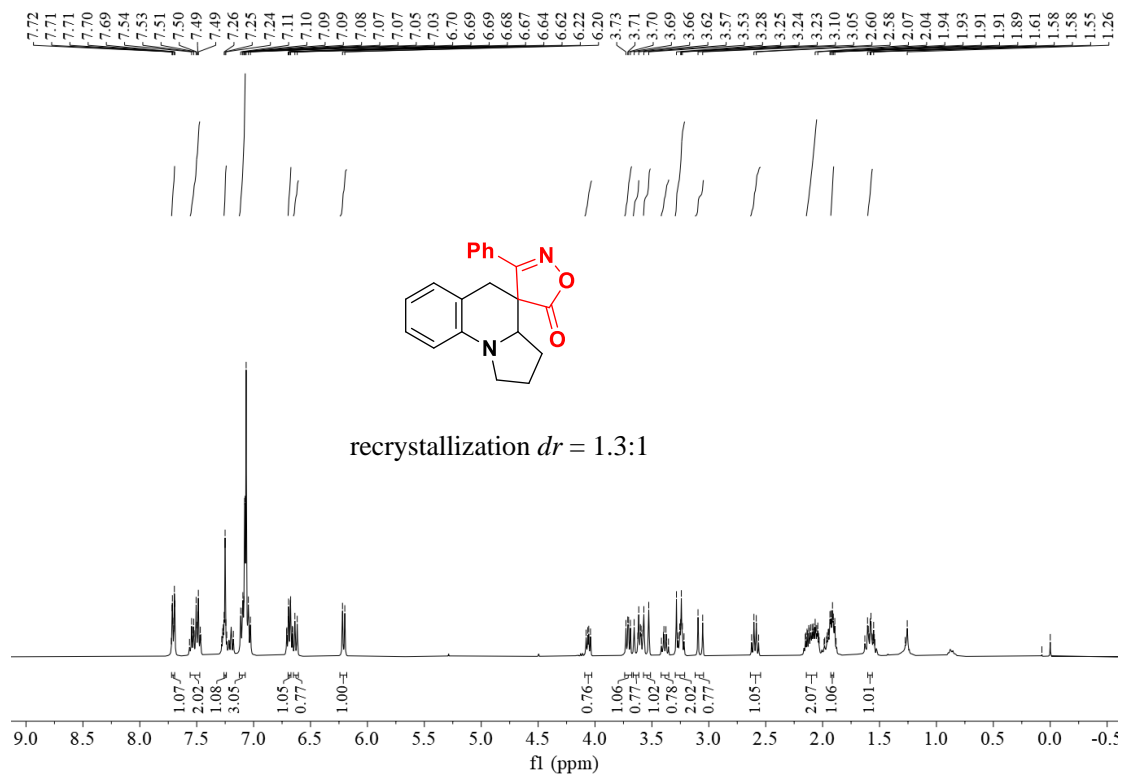




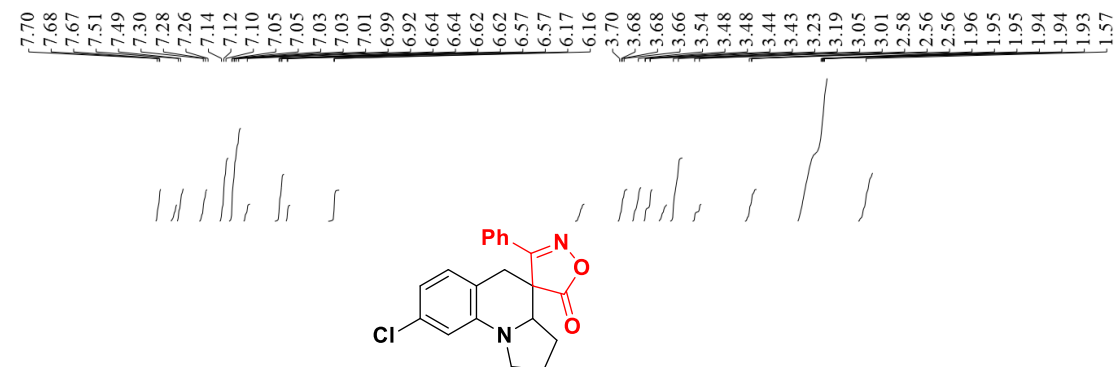
**N-ethyl-4-(2-(ethylamino)-5-nitrobenzyl)-3-phenylisoxazol-5-amine (31).**



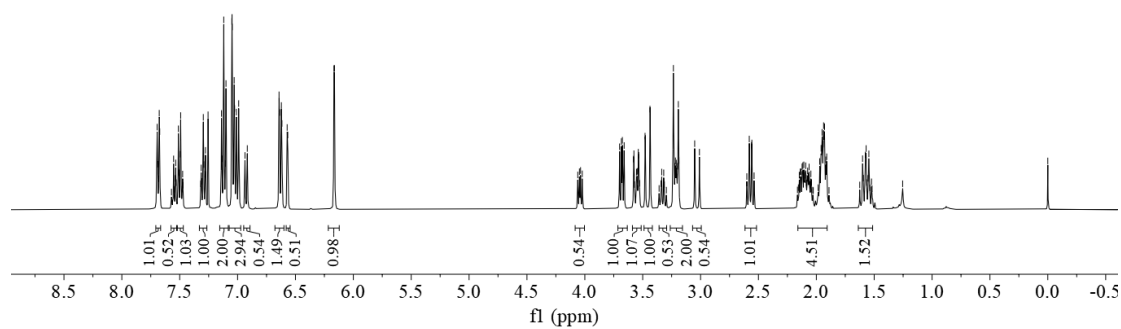
**3-phenyl-1',2',3',3a'-tetrahydro-5H,5'H-spiro[isoxazole-4,4'-pyrrolo[1,2-a]quinolin]-5-one (4a).**



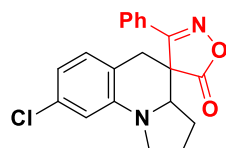
**8'-chloro-3-phenyl-1',2',3',3a'-tetrahydro-5H,5'H-spiro[isoxazole-4,4'-pyrrolo[1,2-a]quinolin]-5-one (4b).**



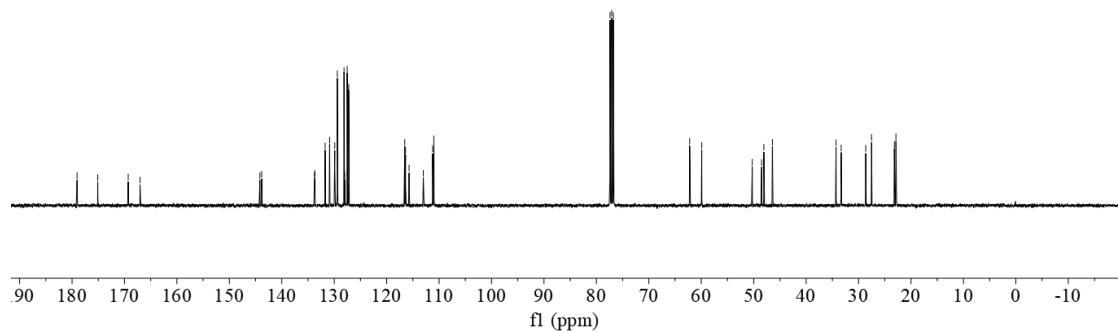
recrystallization  $dr = 2:1$



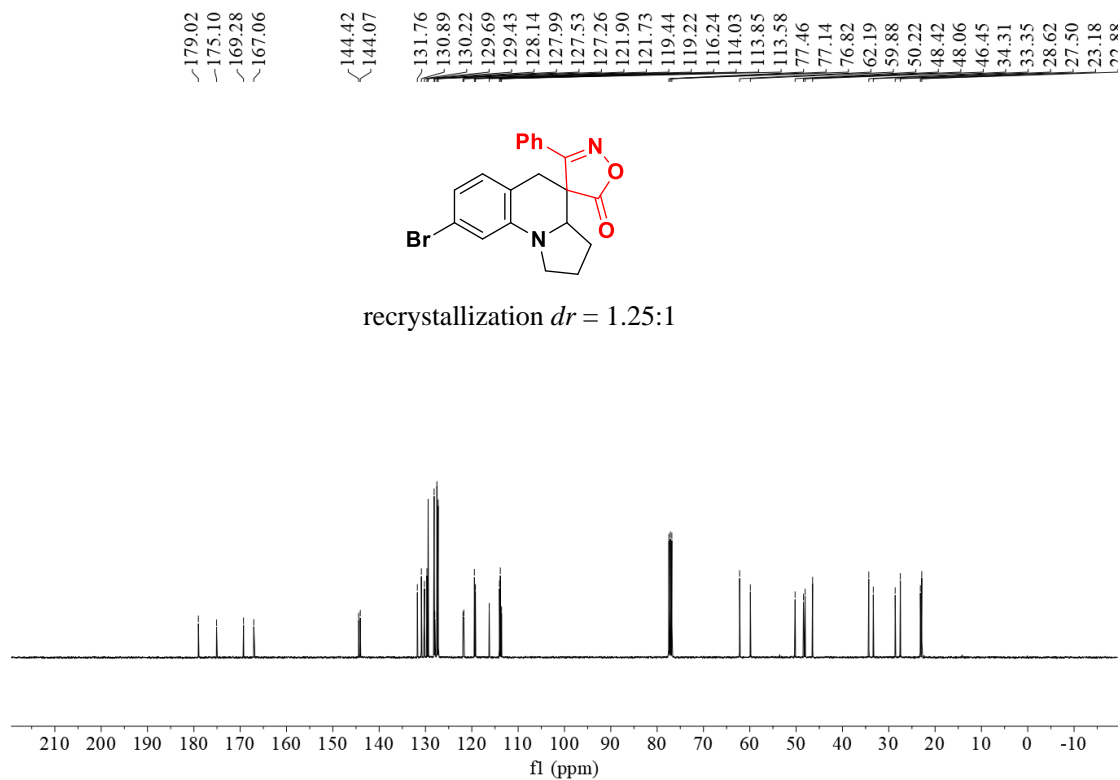
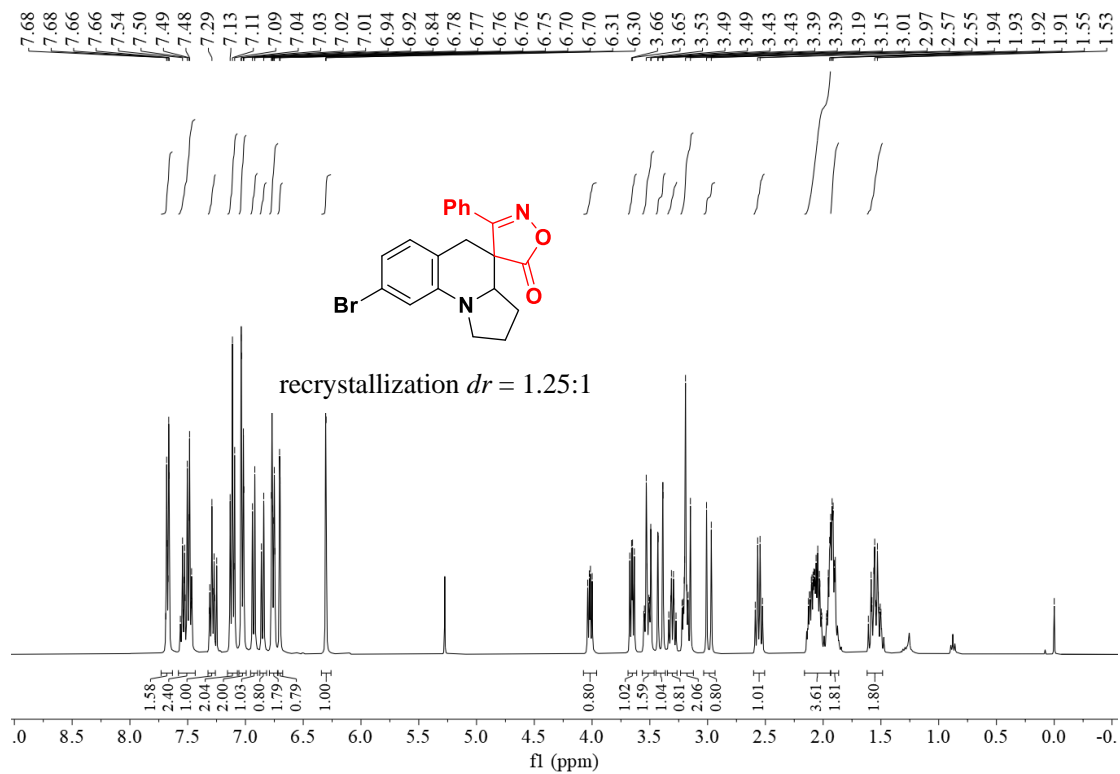
179.05  
175.10  
169.30  
167.04  
144.18  
143.85  
133.78  
133.69  
131.74  
130.88  
129.90  
129.41  
129.38  
128.13  
128.01  
127.53  
127.48  
127.24  
116.55  
116.40  
115.73  
113.01  
111.24  
110.99  
110.99  
77.39  
77.08  
76.76  
62.21  
59.91  
50.28  
48.49  
48.06  
46.43  
34.29  
33.32  
28.63  
27.52  
23.18  
22.87



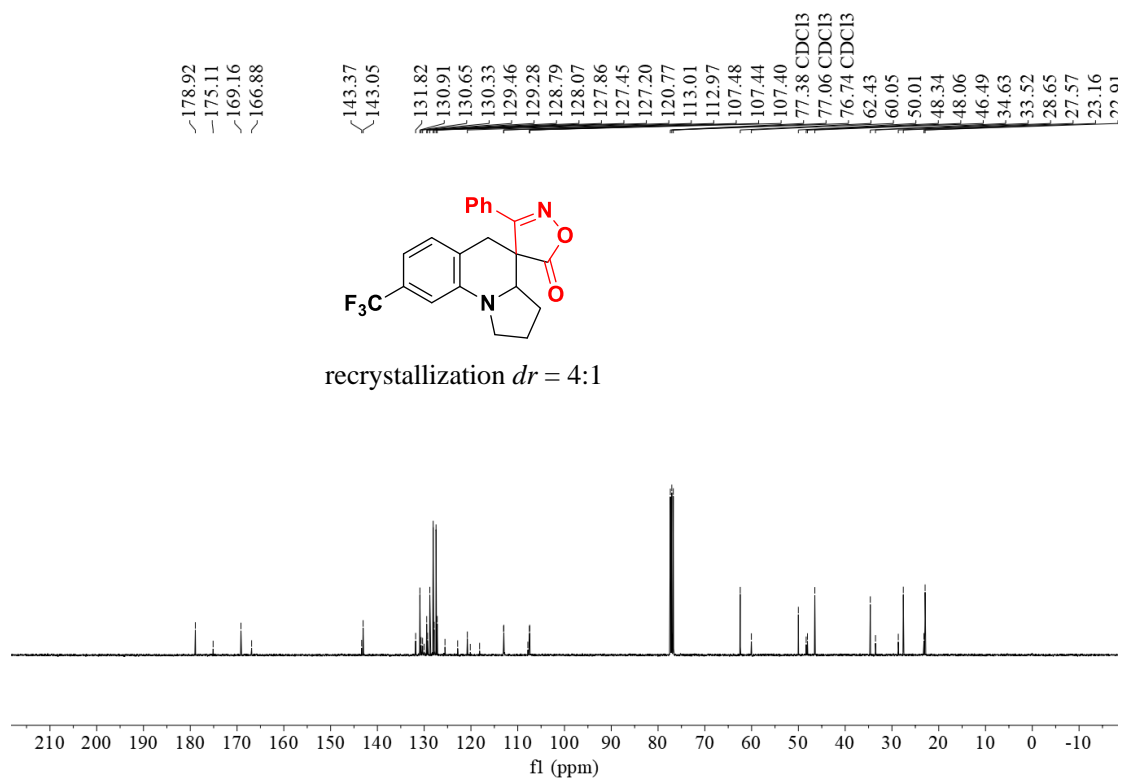
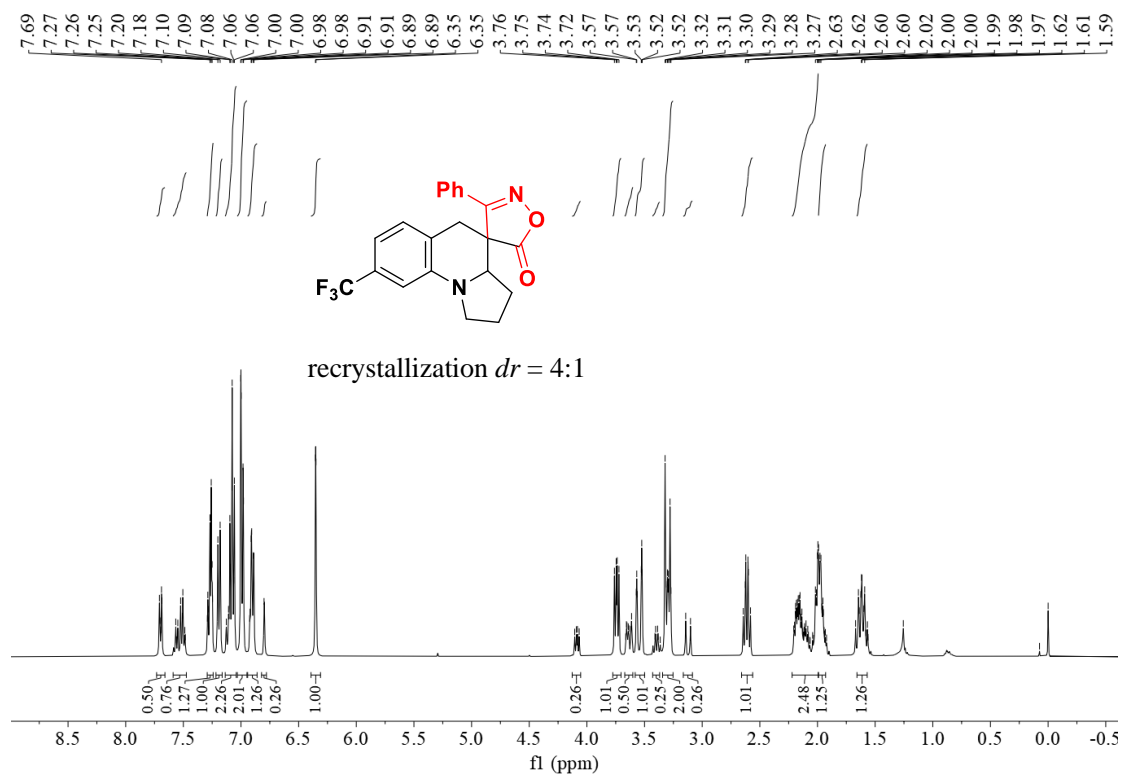
recrystallization  $dr = 2:1$



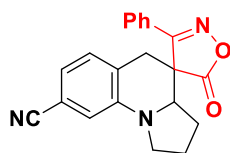
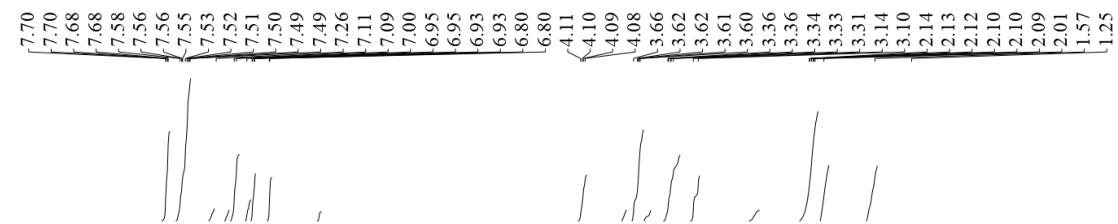
**8'-bromo-3-phenyl-1',2',3',3a'-tetrahydro-5H,5'H-spiro[isoxazole-4,4'-pyrrolo[1,2-a]quinolin]-5-one (4c).**



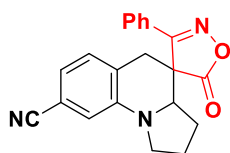
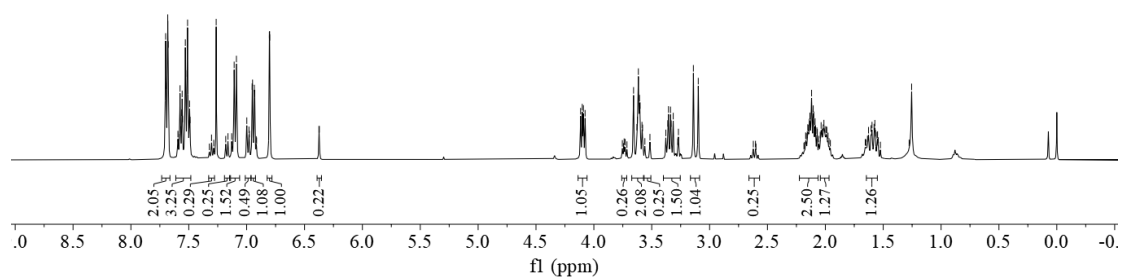
**3-phenyl-8'-(trifluoromethyl)-1',2',3',3a'-tetrahydro-5H,5'H-spiro[isoxazole-4,4'-pyrrolo[1,2-a]quinolin]-5-one (4d).**



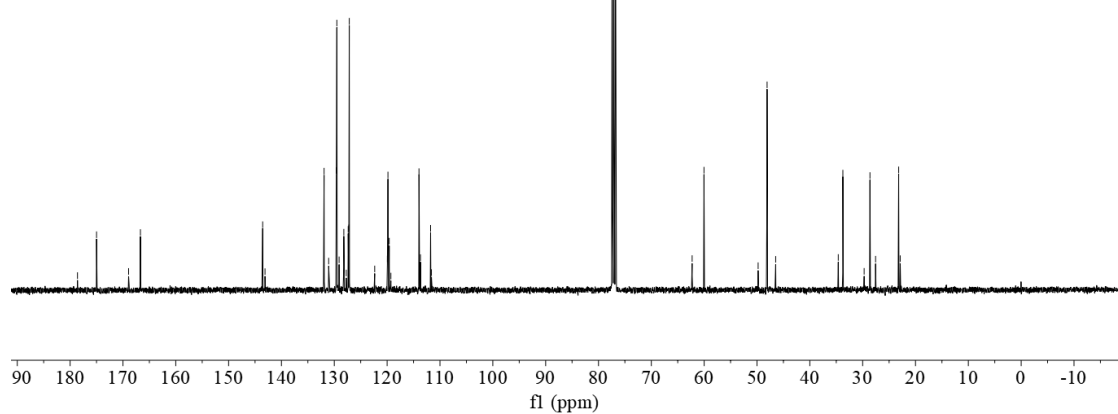
**5-oxo-3-phenyl-1',2',3',3a'-tetrahydro-5H,5'H-spiro[isoxazole-4,4'-pyrrolo[1,2-a]quinoline]-8'-carbonitrile (4e).**



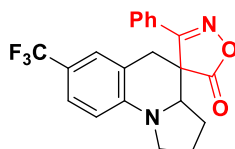
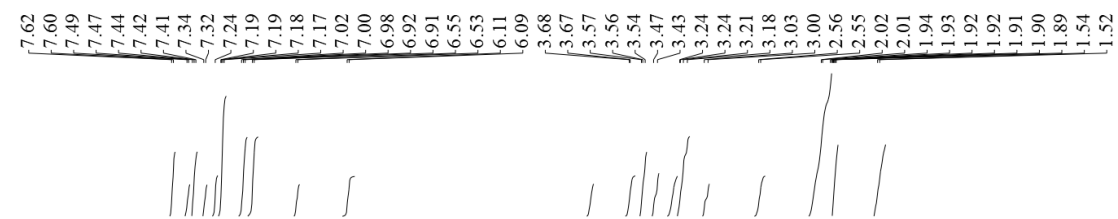
recrystallization  $dr = 4:1$



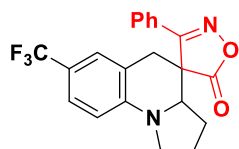
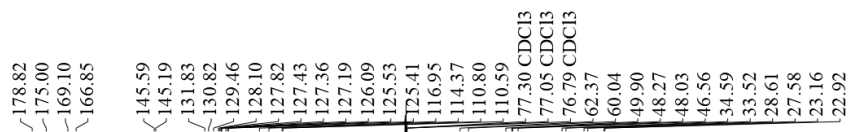
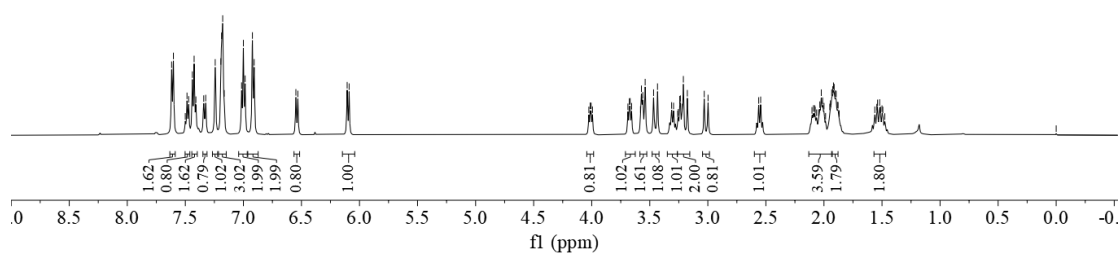
recrystallization  $dr = 4:1$



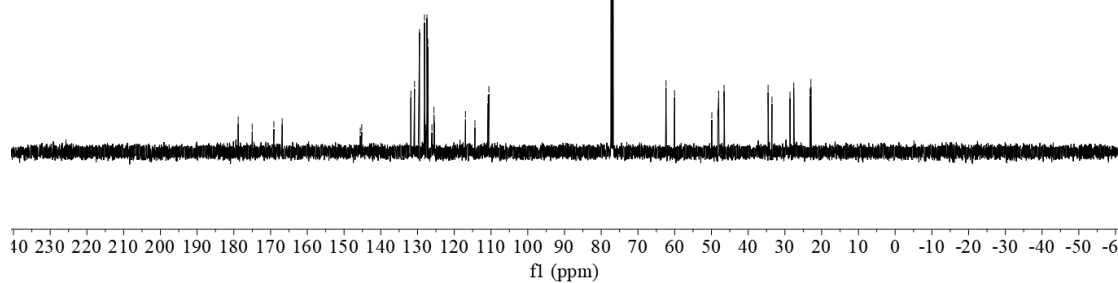
**3-phenyl-7-(trifluoromethyl)-1',2',3',3a'-tetrahydro-5H,5'H-spiro[isoxazole-4,4'-pyrrolo[1,2-a]quinolin]-5-one (4f).**



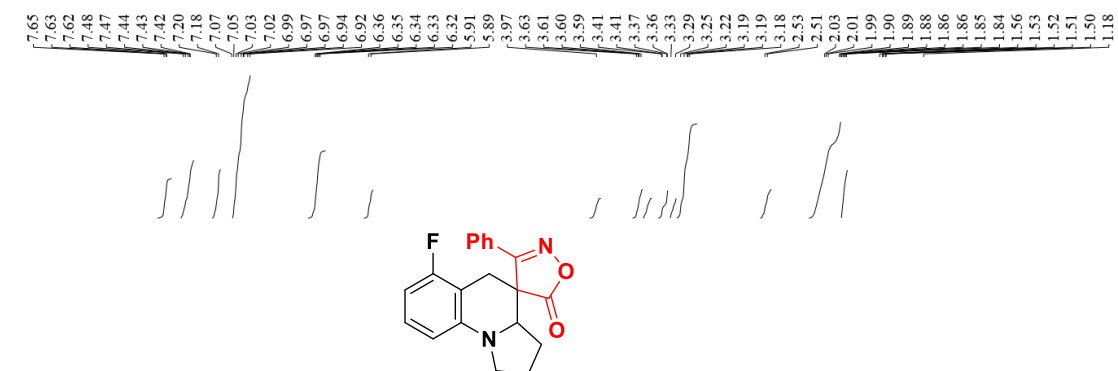
recrystallization  $dr = 1.25:1$



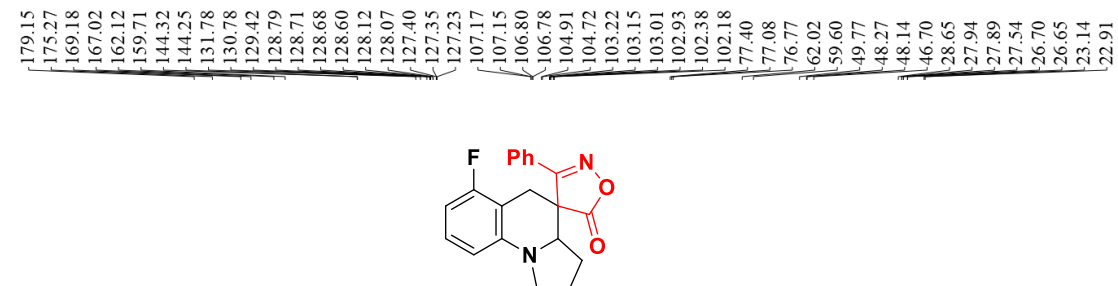
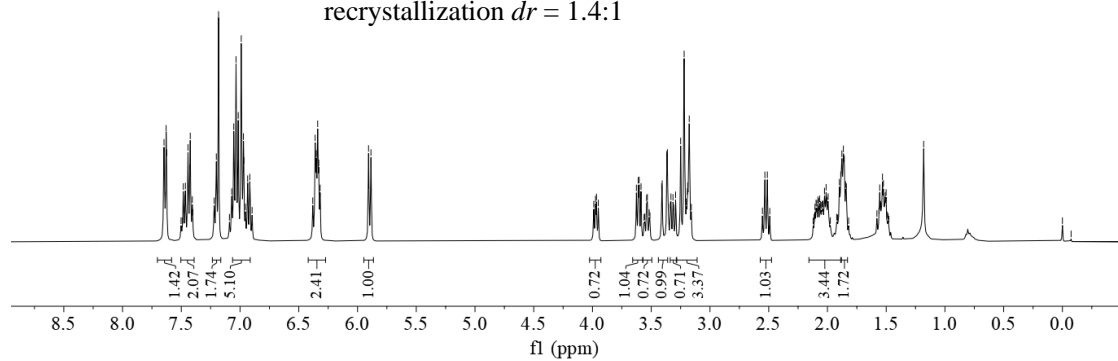
recrystallization  $dr = 1.25:1$



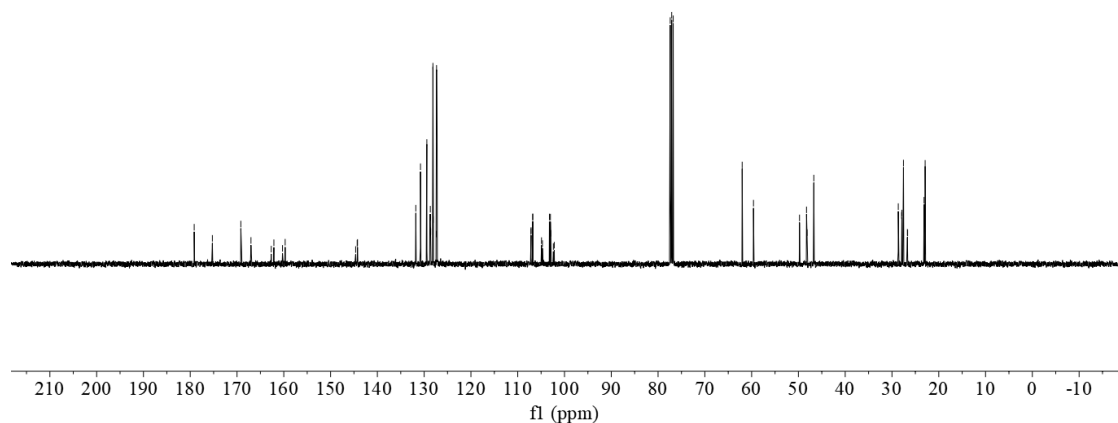
**6'-fluoro-3-phenyl-1',2',3',3a'-tetrahydro-5H,5'H-spiro[isoxazole-4,4'-pyrrolo[1,2-a]quinolin]-5-one (4g).**



recrystallization  $dr = 1.4:1$

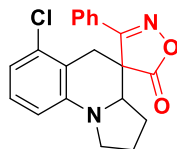
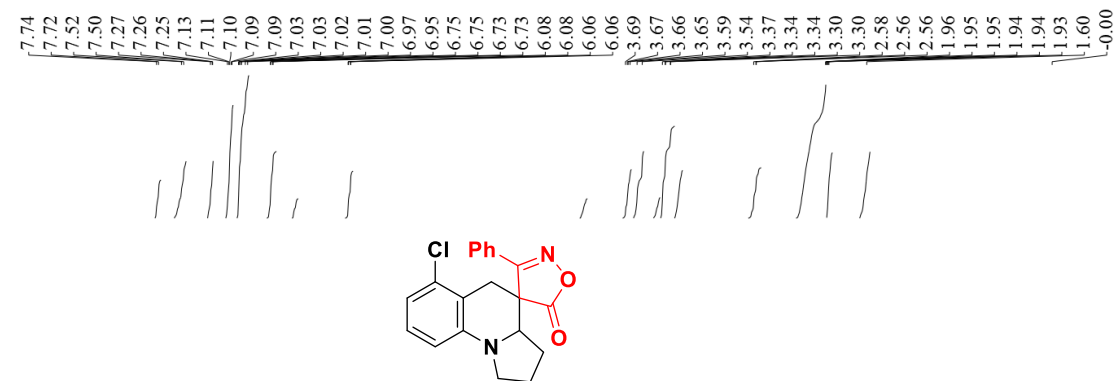


recrystallization  $dr = 1.4:1$

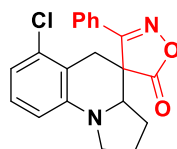
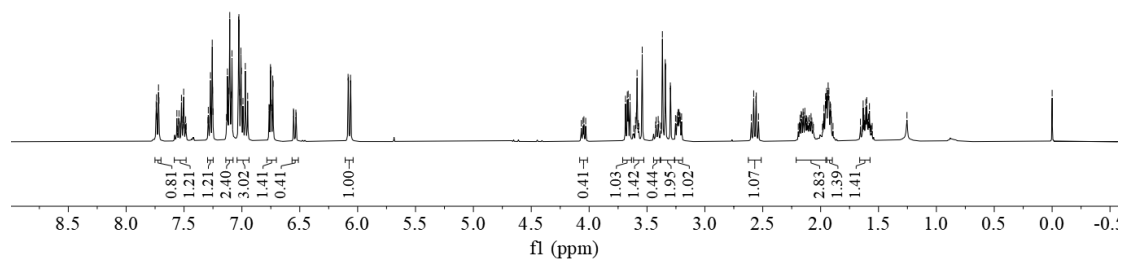




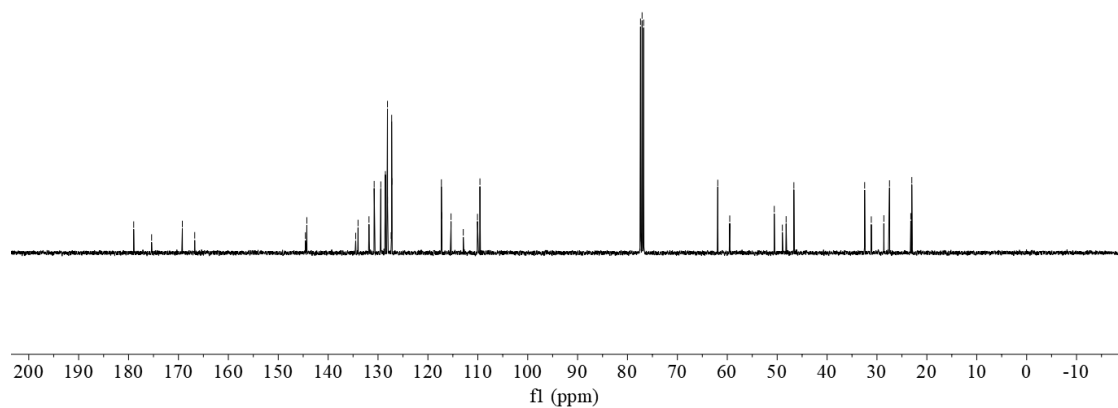
**6'-chloro-3-phenyl-1',2',3',3a'-tetrahydro-5H,5'H-spiro[isoxazole-4,4'-pyrrolo[1,2-a]quinolin]-5-one (4h).**



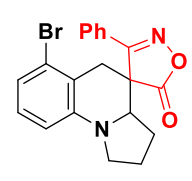
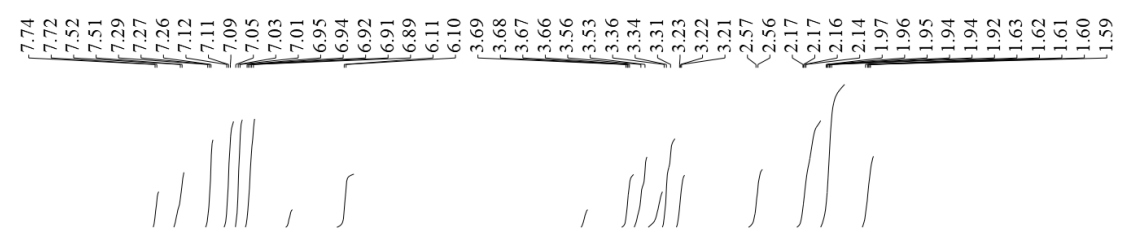
recrystallization  $dr = 2.5:1$



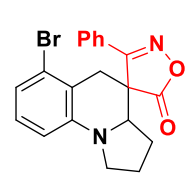
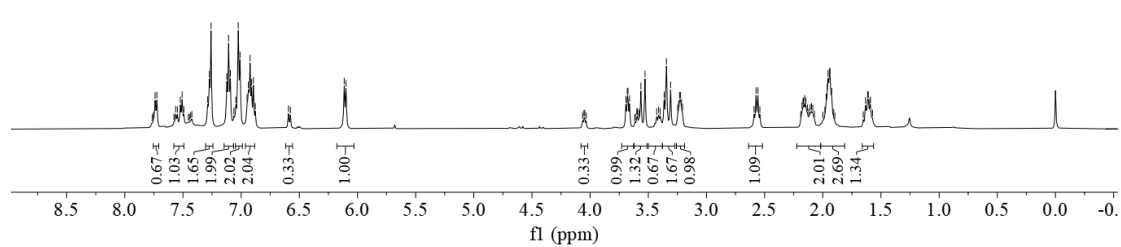
recrystallization  $dr = 2.5:1$



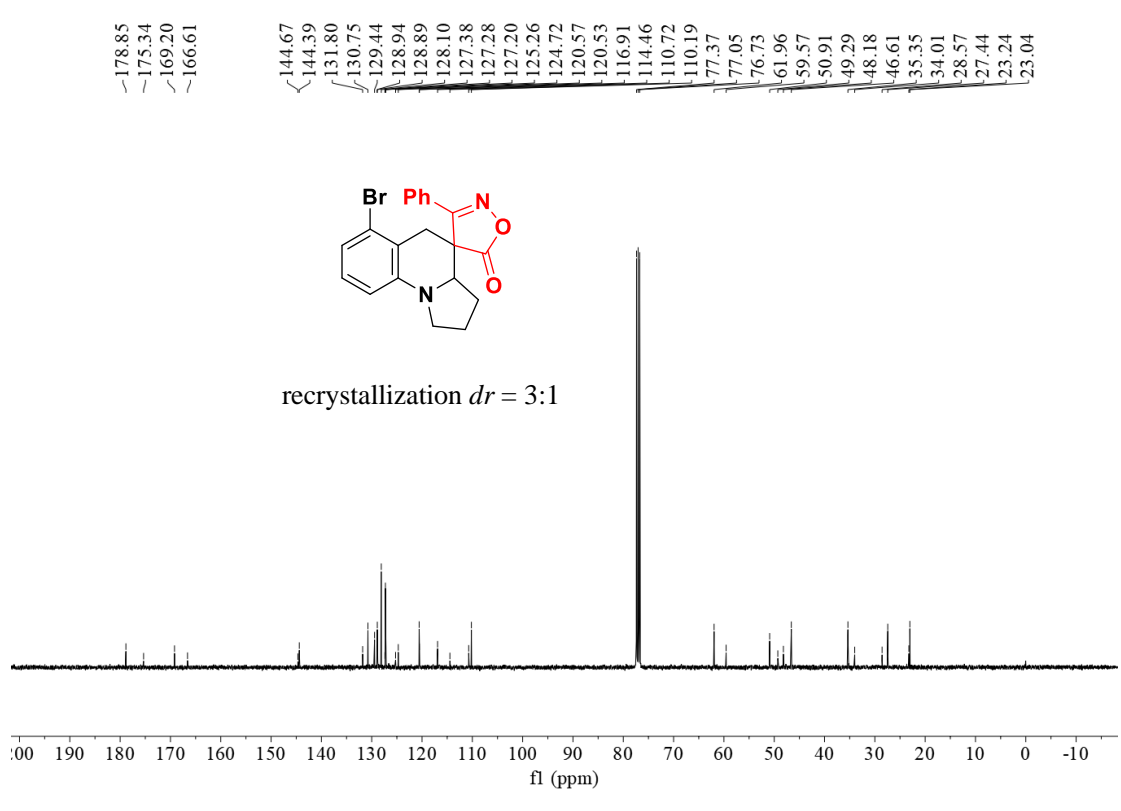
**6'-bromo-3-phenyl-1',2',3',3a'-tetrahydro-5H,5'H-spiro[isoxazole-4,4'-pyrrolo[1,2-a]quinolin]-5-one (4i).**



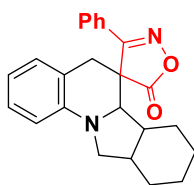
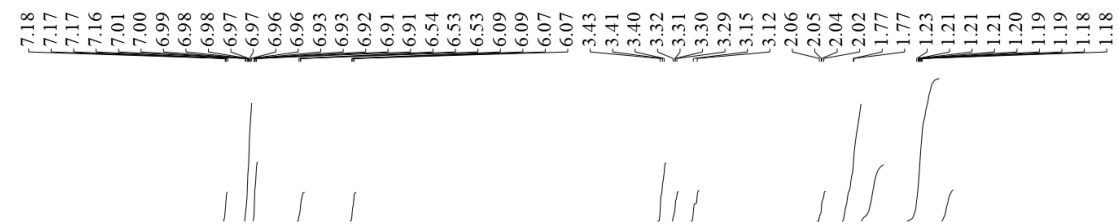
recrystallization  $dr = 3:1$



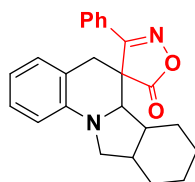
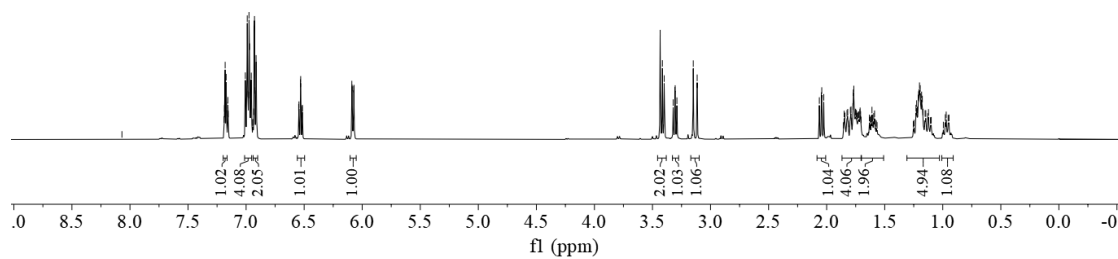
recrystallization  $dr = 3:1$



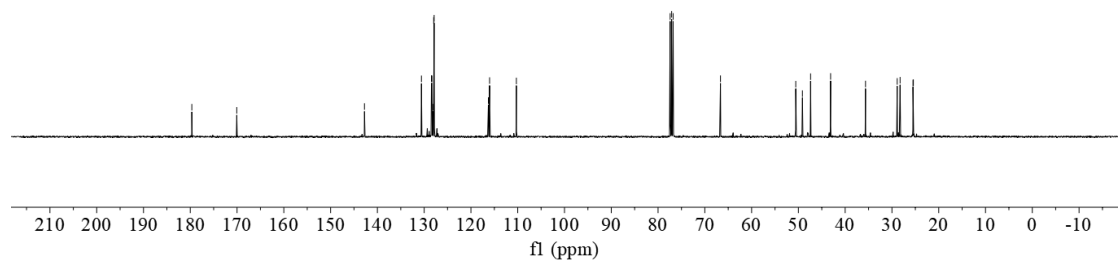
**3'-phenyl-6a,6b,7,8,9,10a,11-octahydro-5H,5'H-spiro[isindolo[2,1-a]quinoline-6,4'-isoxazol]-5'-one (4j).**



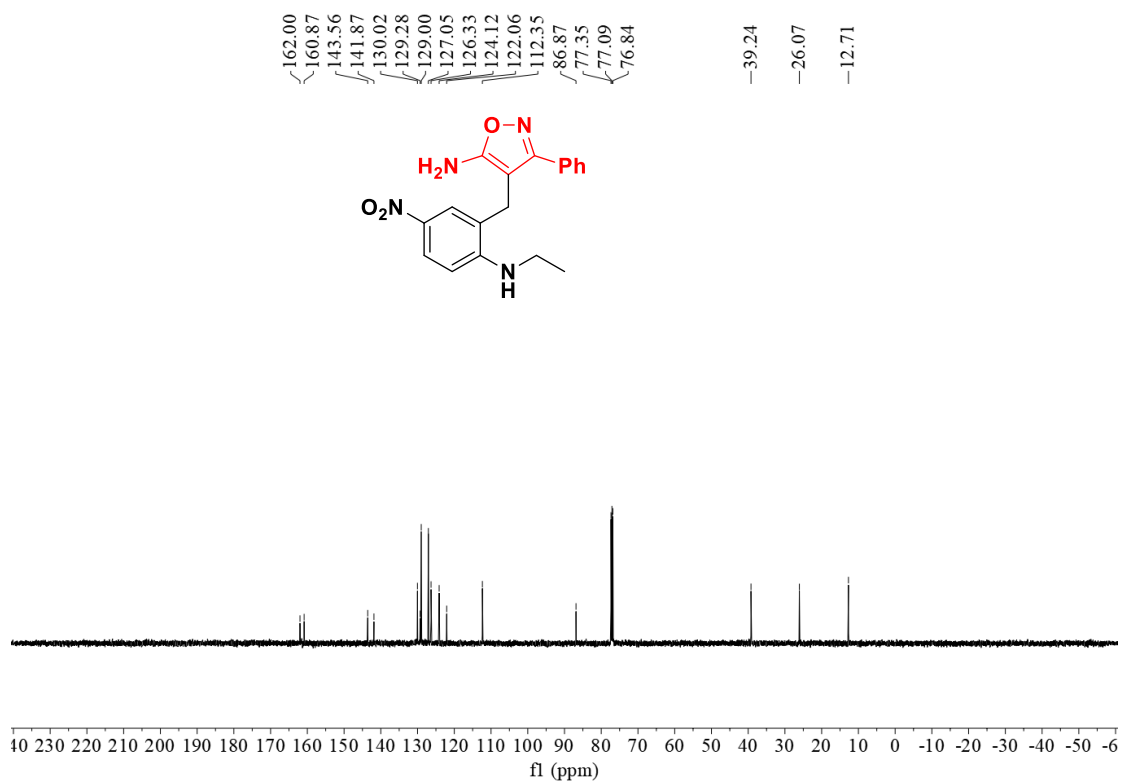
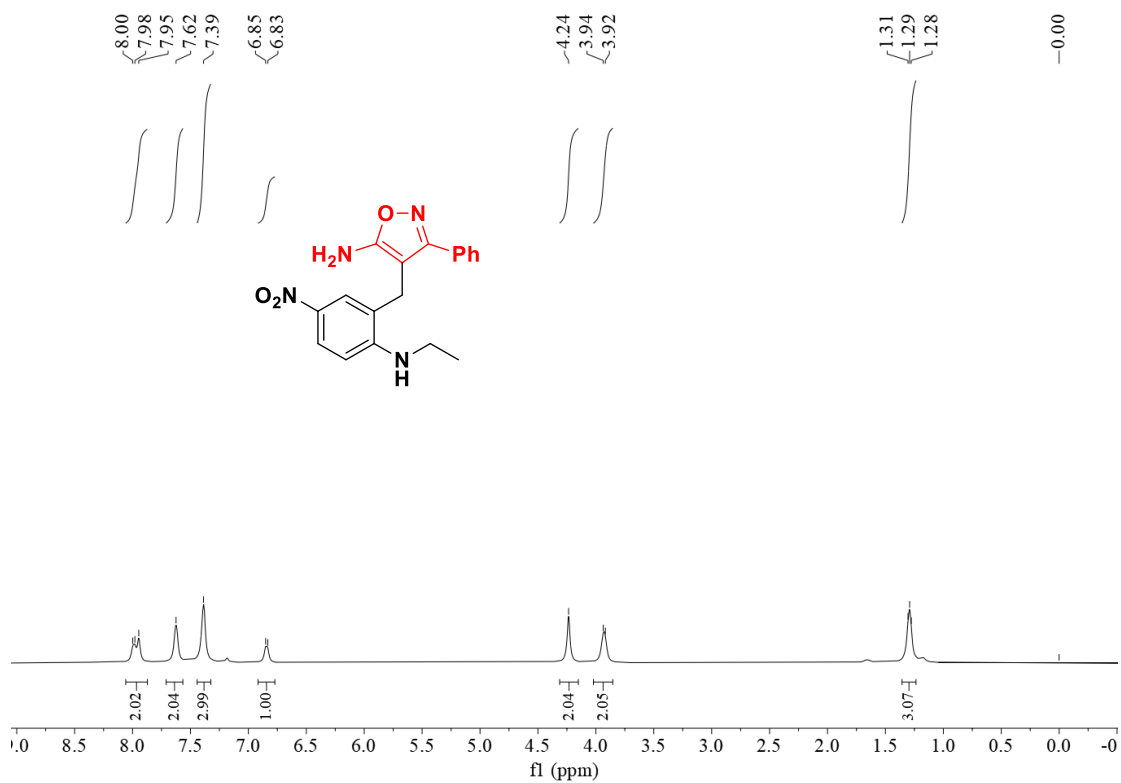
recrystallization  $dr > 20:1$



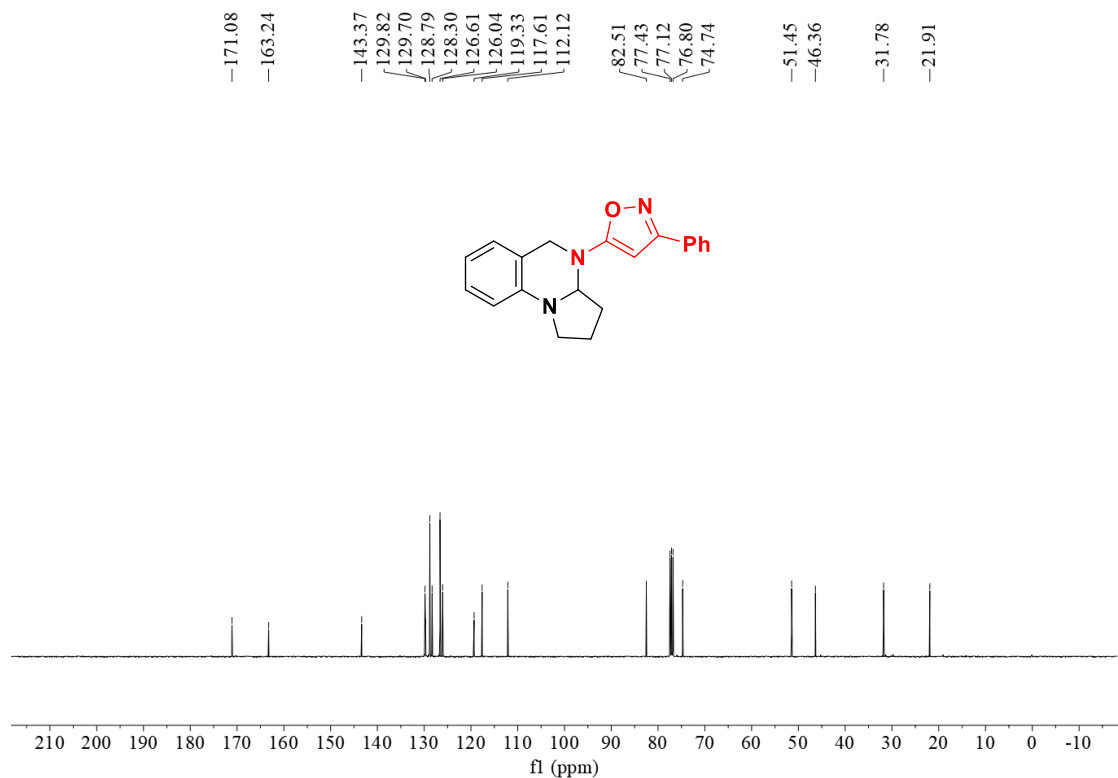
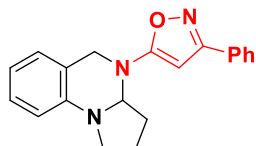
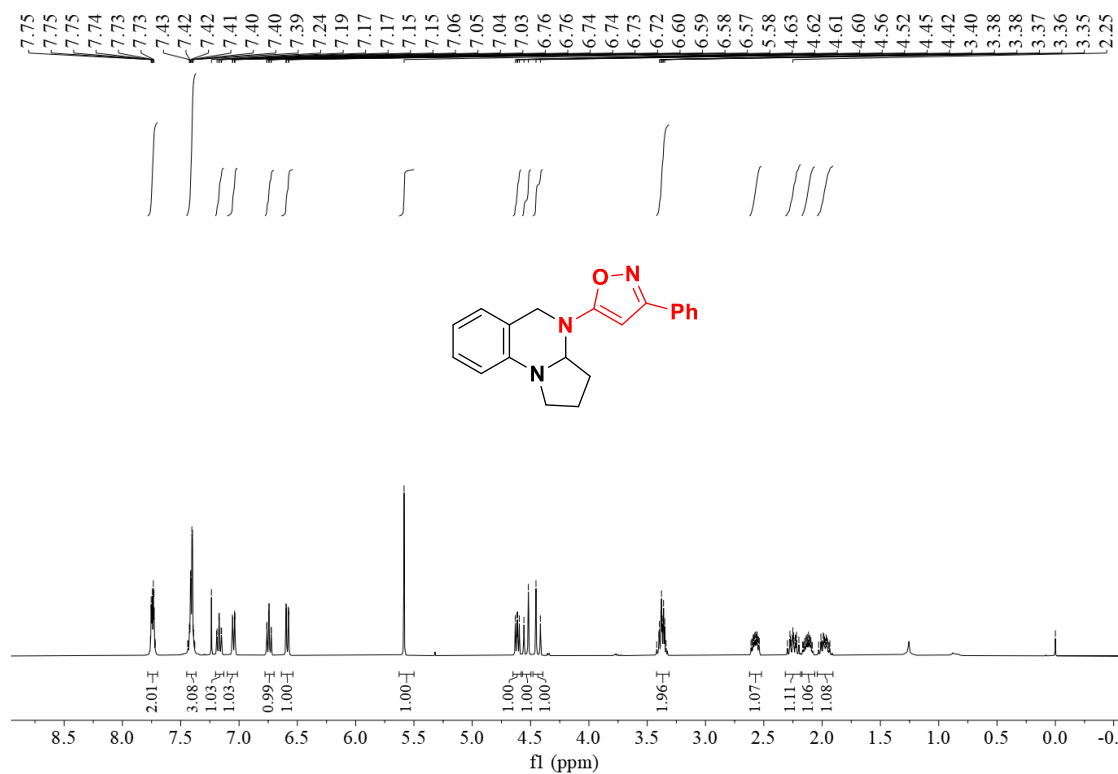
recrystallization  $dr > 20:1$



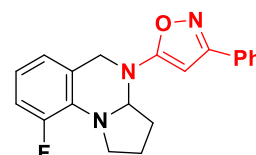
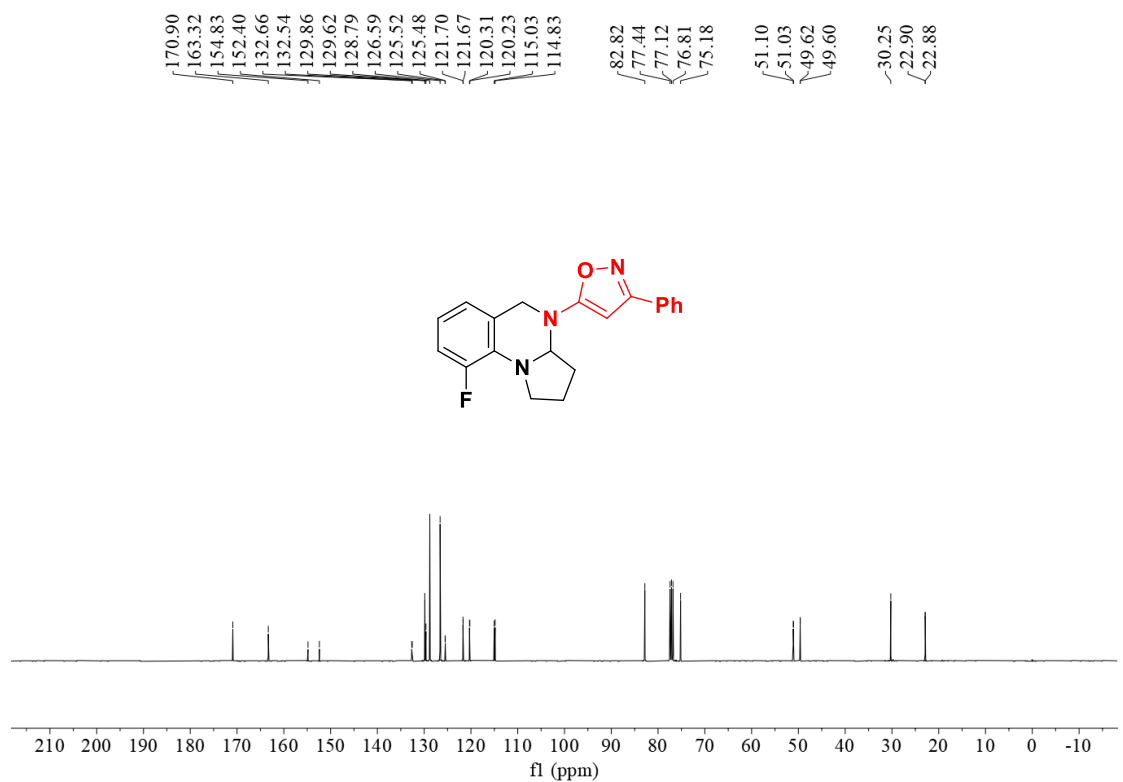
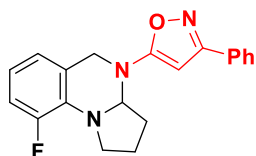
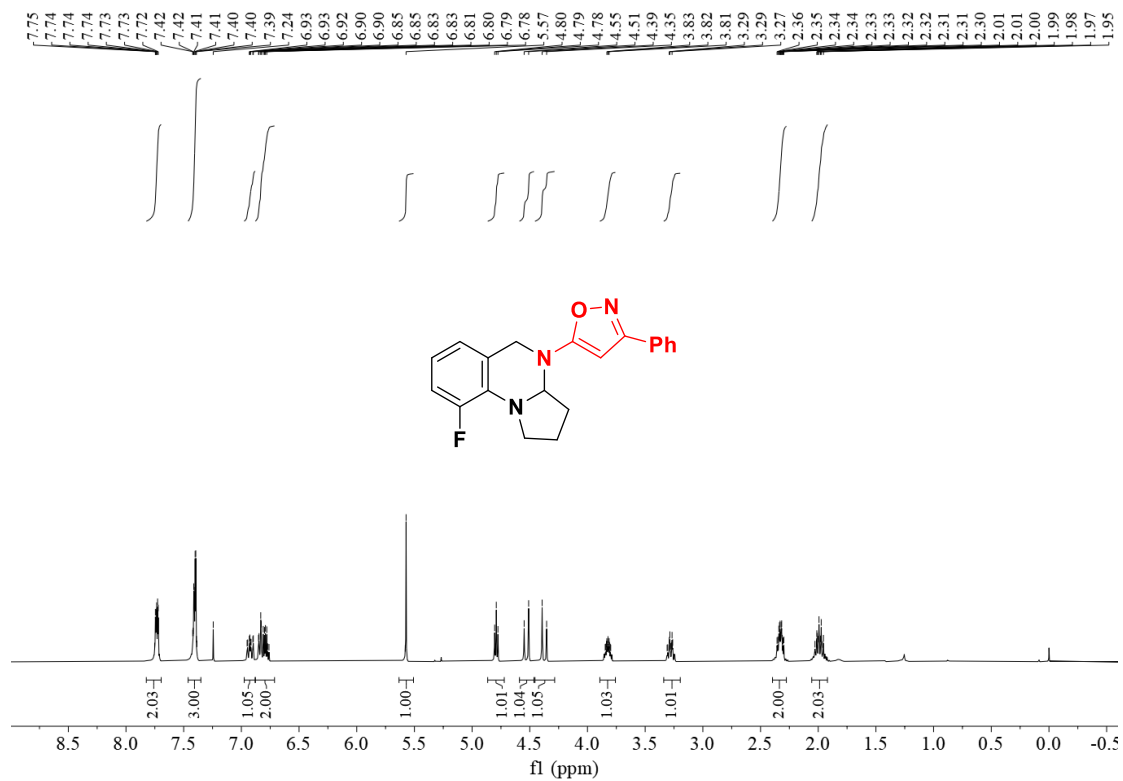
**4-(2-(ethylamino)-5-nitrobenzyl)-3-phenylisoxazol-5-amine (4k).**



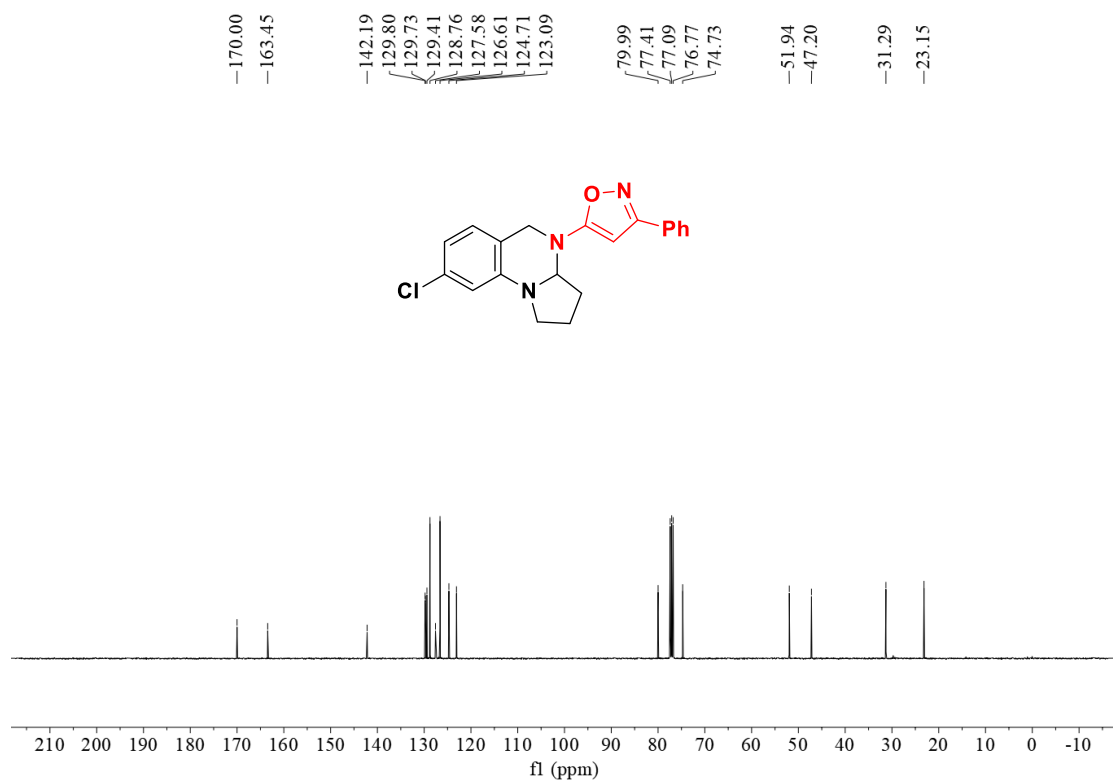
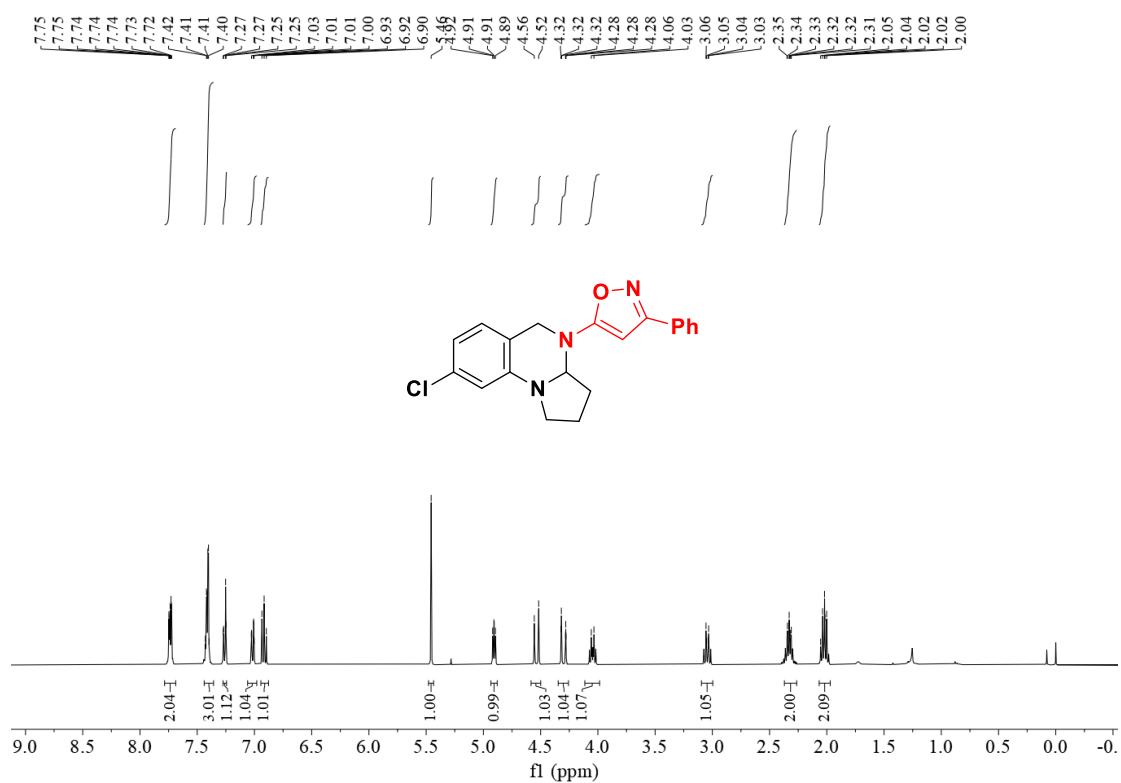
**3-phenyl-5-(1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)isoxazole (5a).**



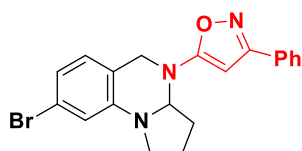
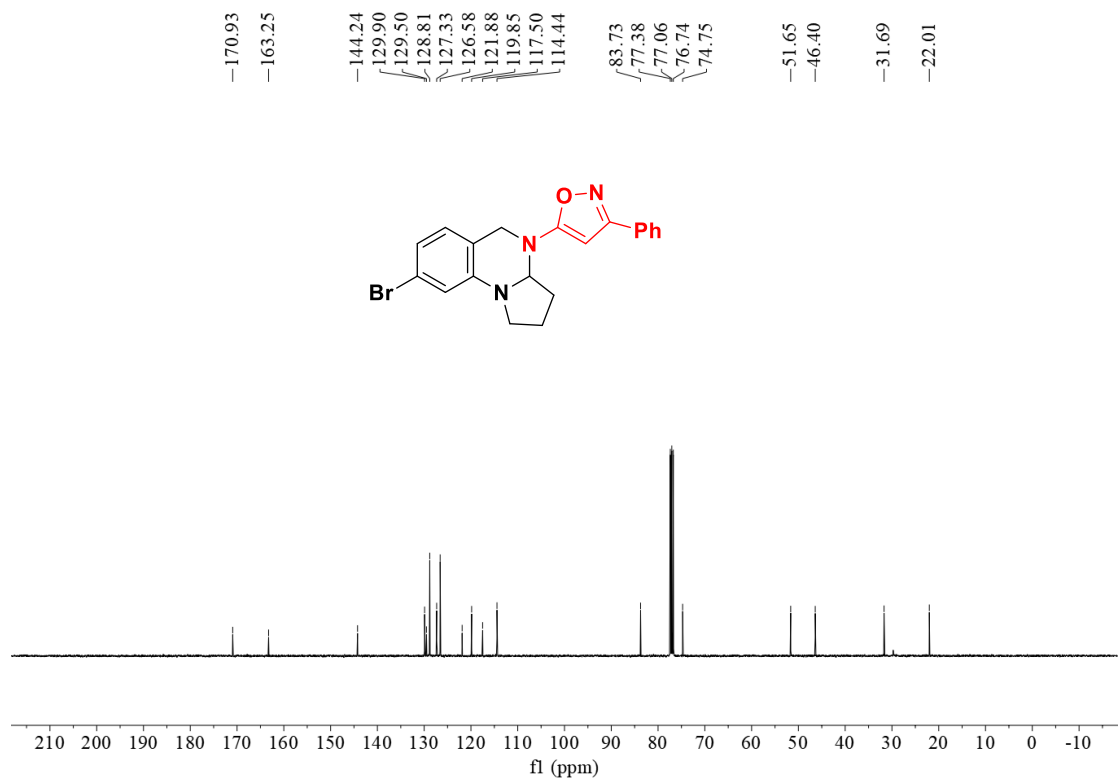
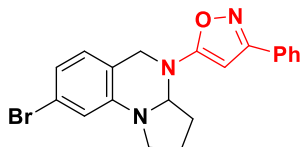
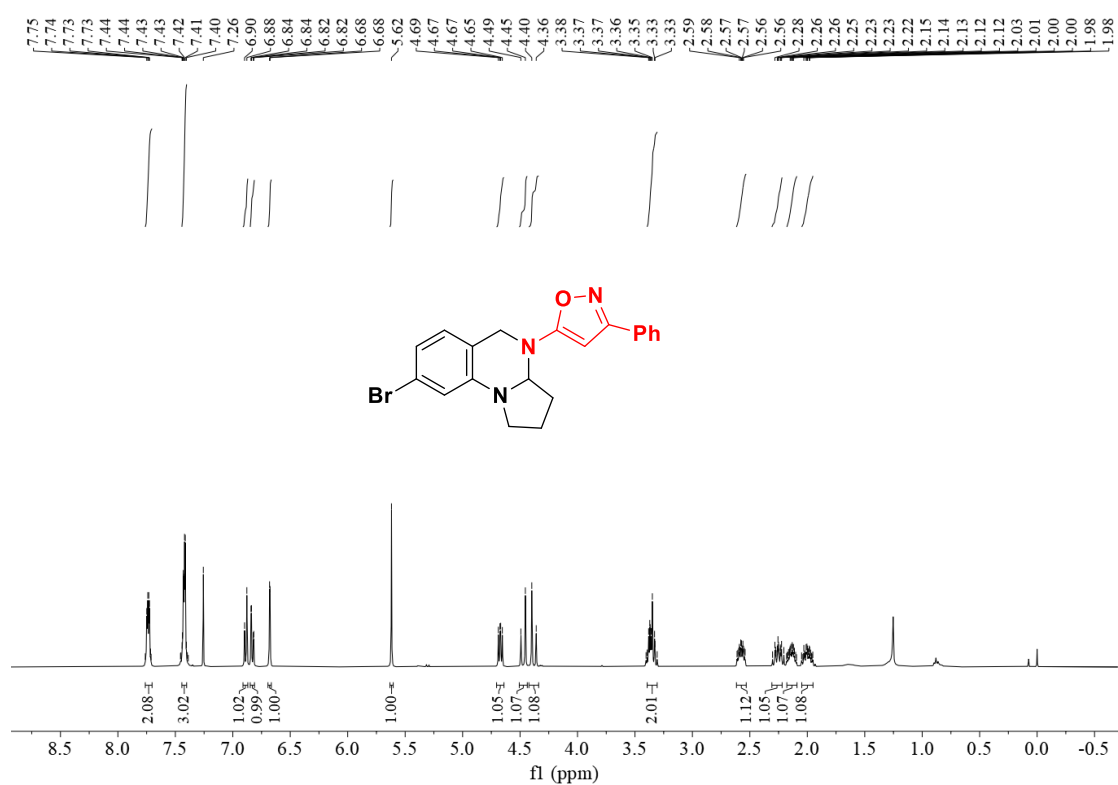
**5-(9-fluoro-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)-3-phenylisoxazole (5b).**



**5-(8-chloro-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)-3-phenylisoxazole (5c).**

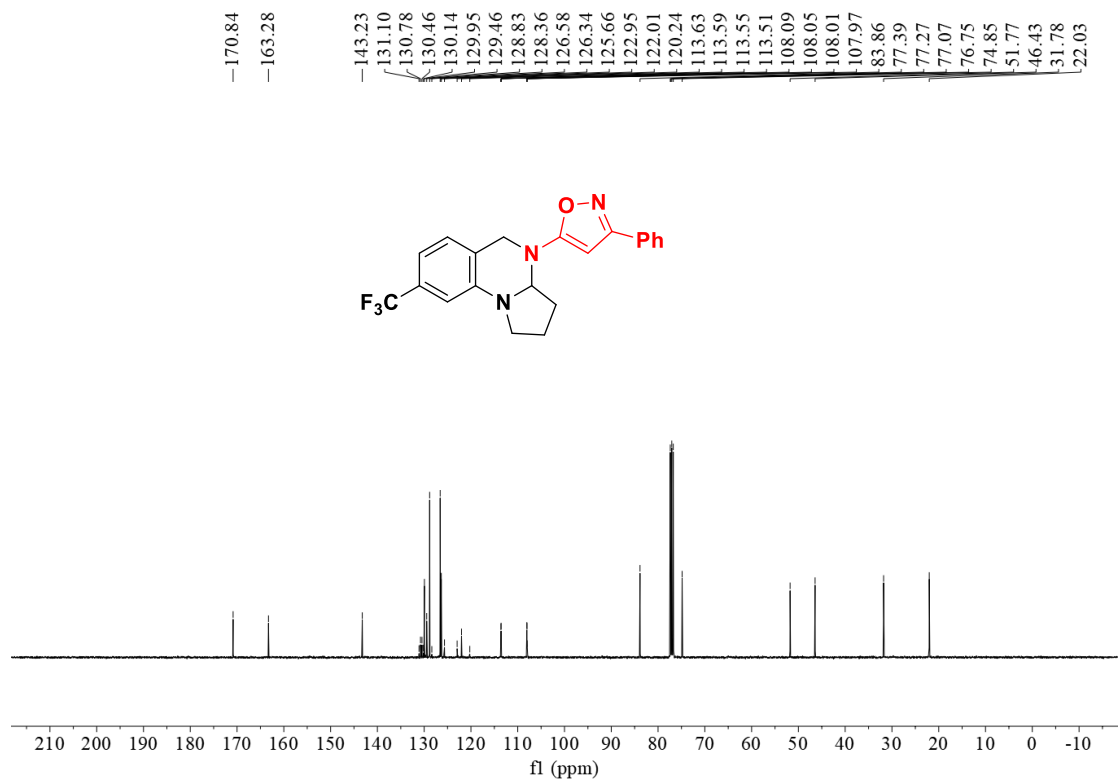
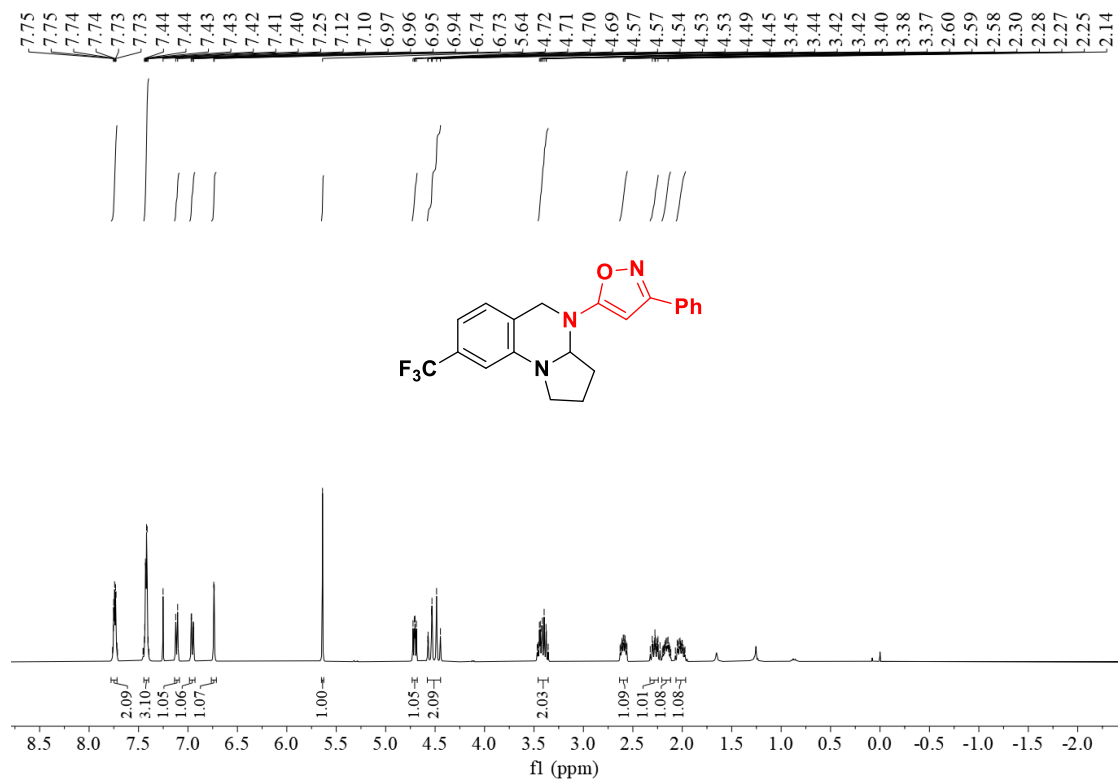


**5-(8-bromo-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)-3-phenylisoxazole (5d).**

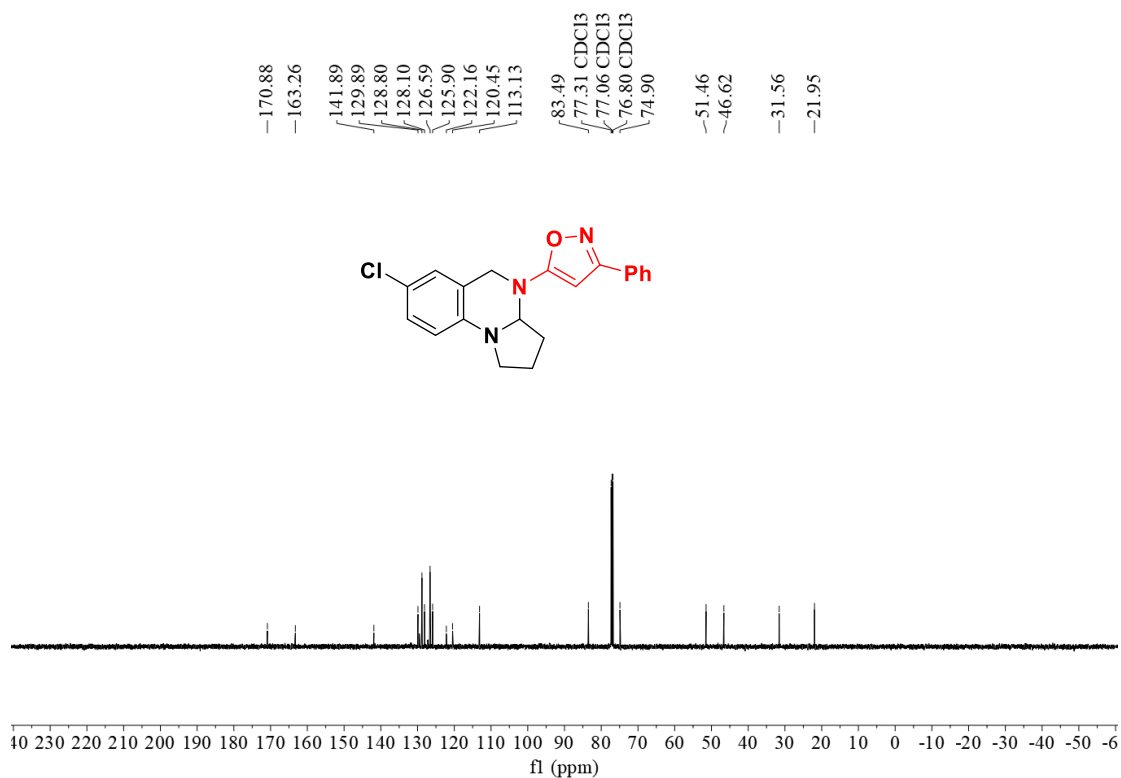
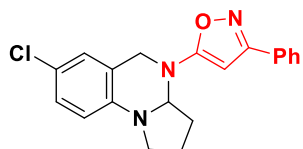
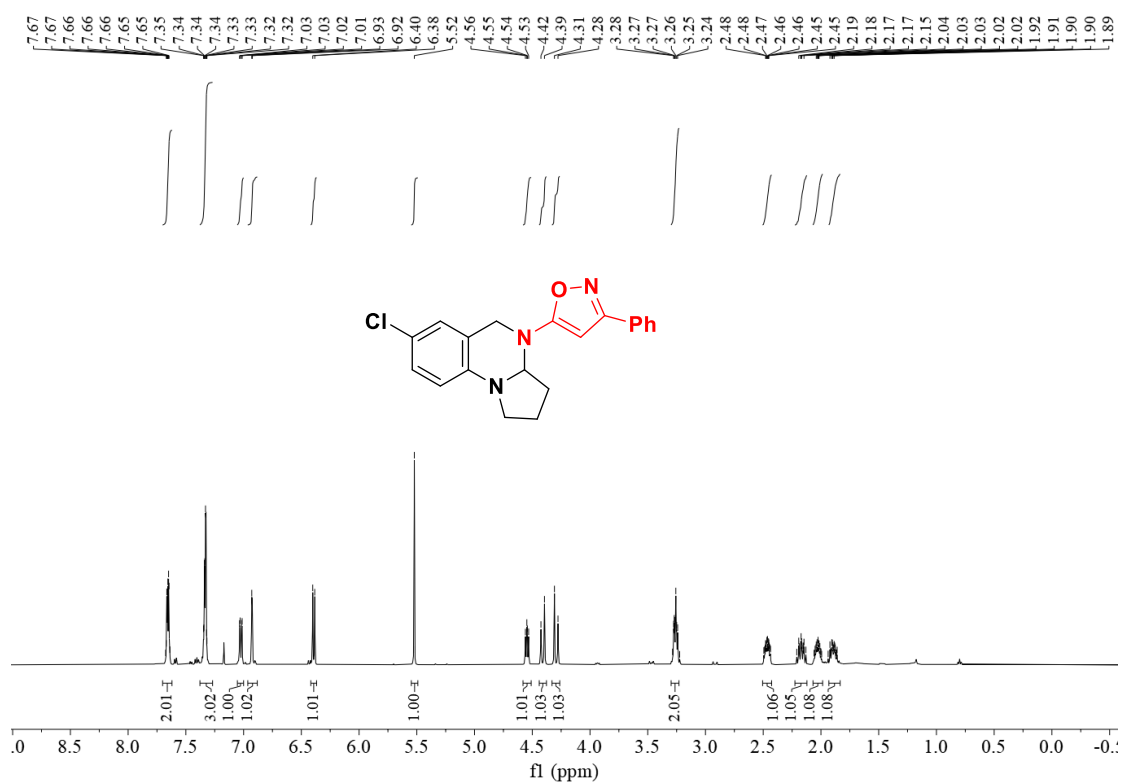




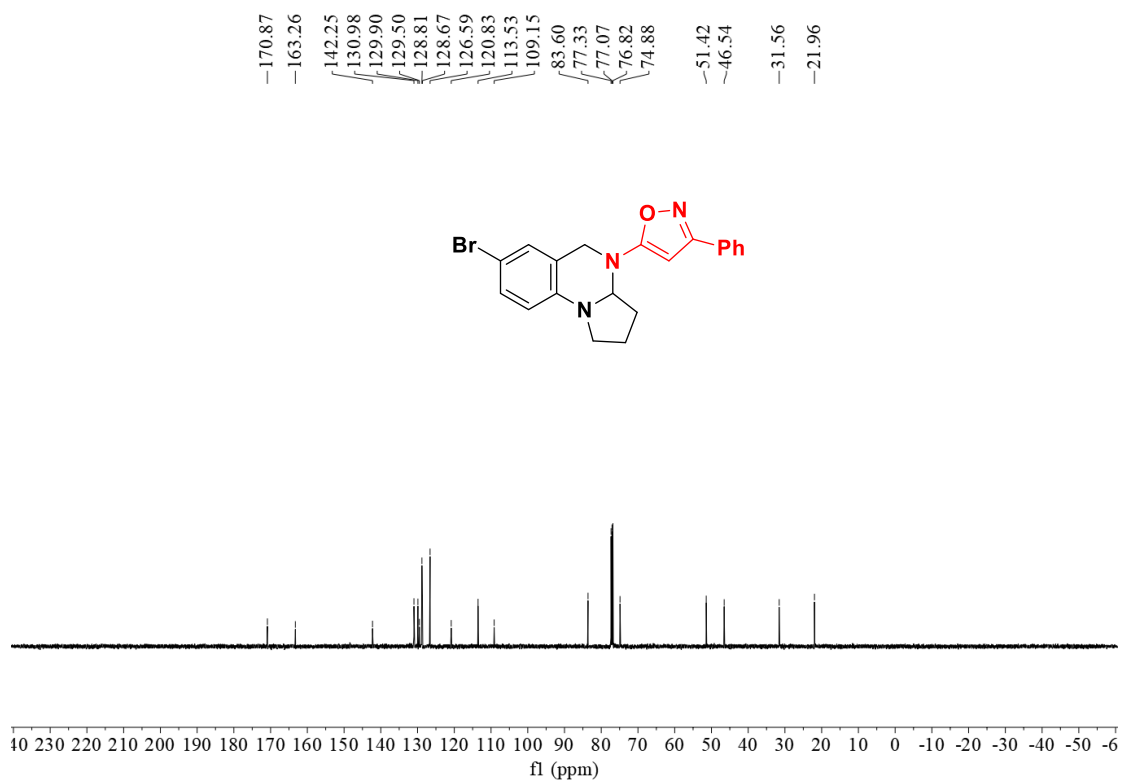
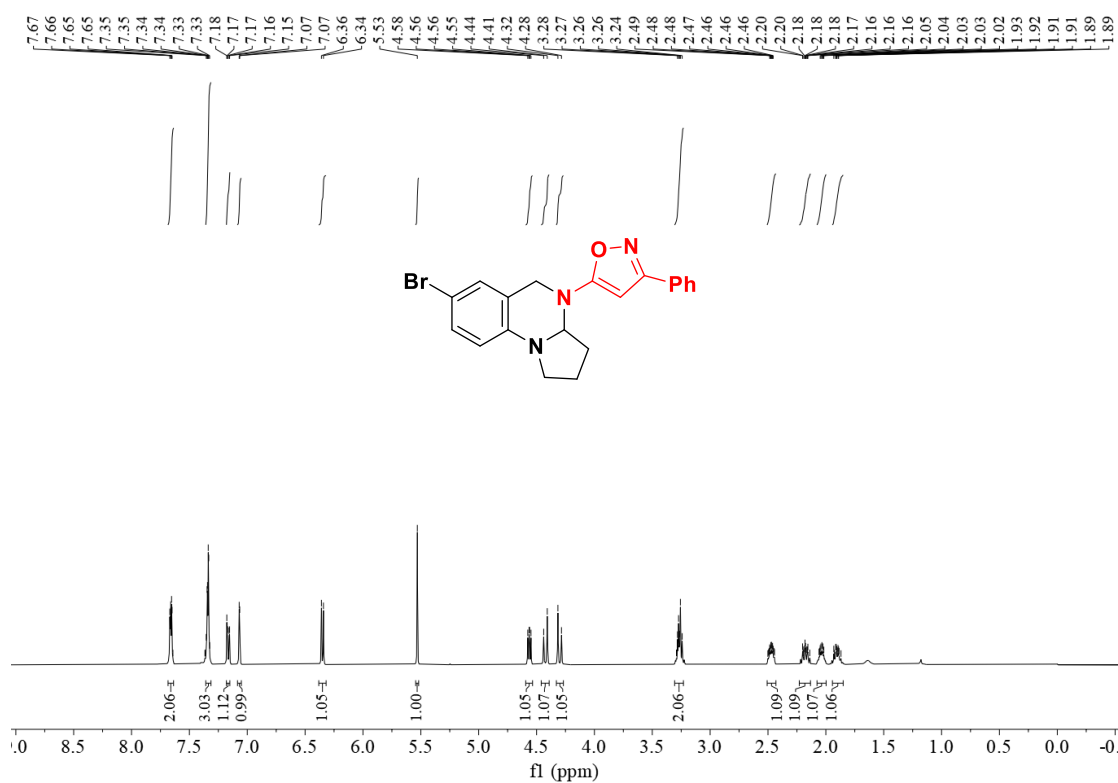
**3-phenyl-5-(8-(trifluoromethyl)-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)isoxazole (5e).**



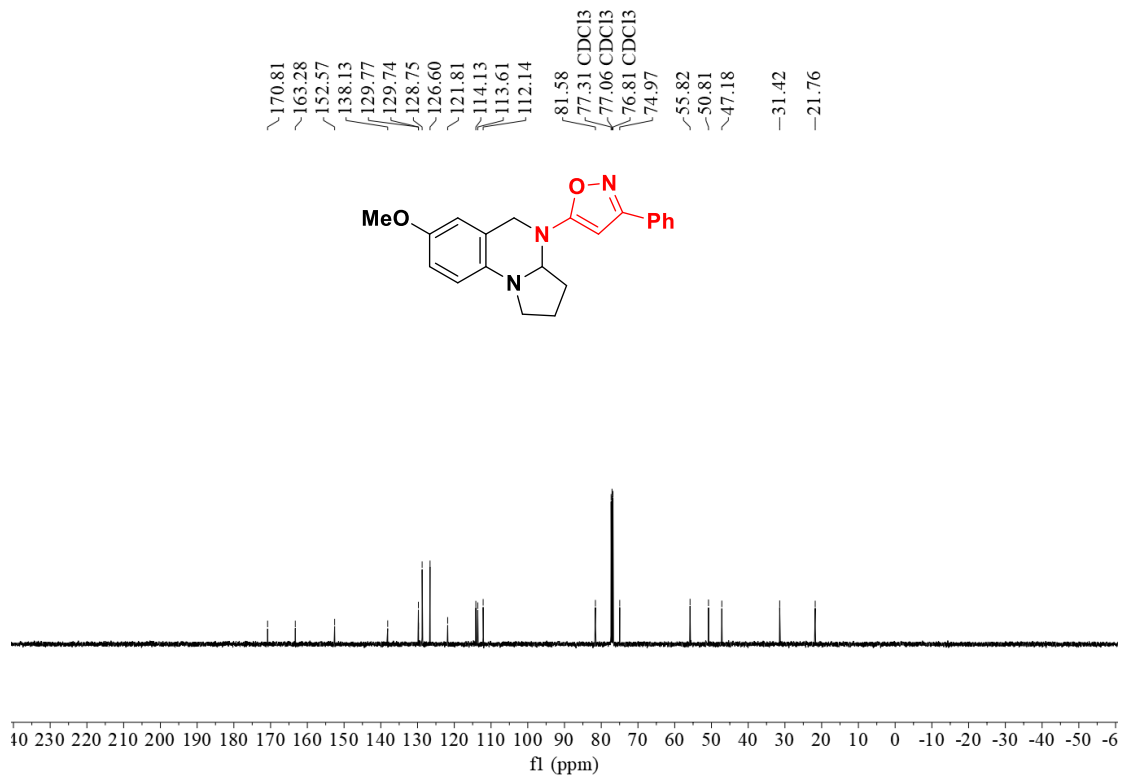
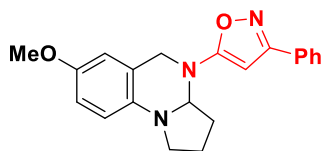
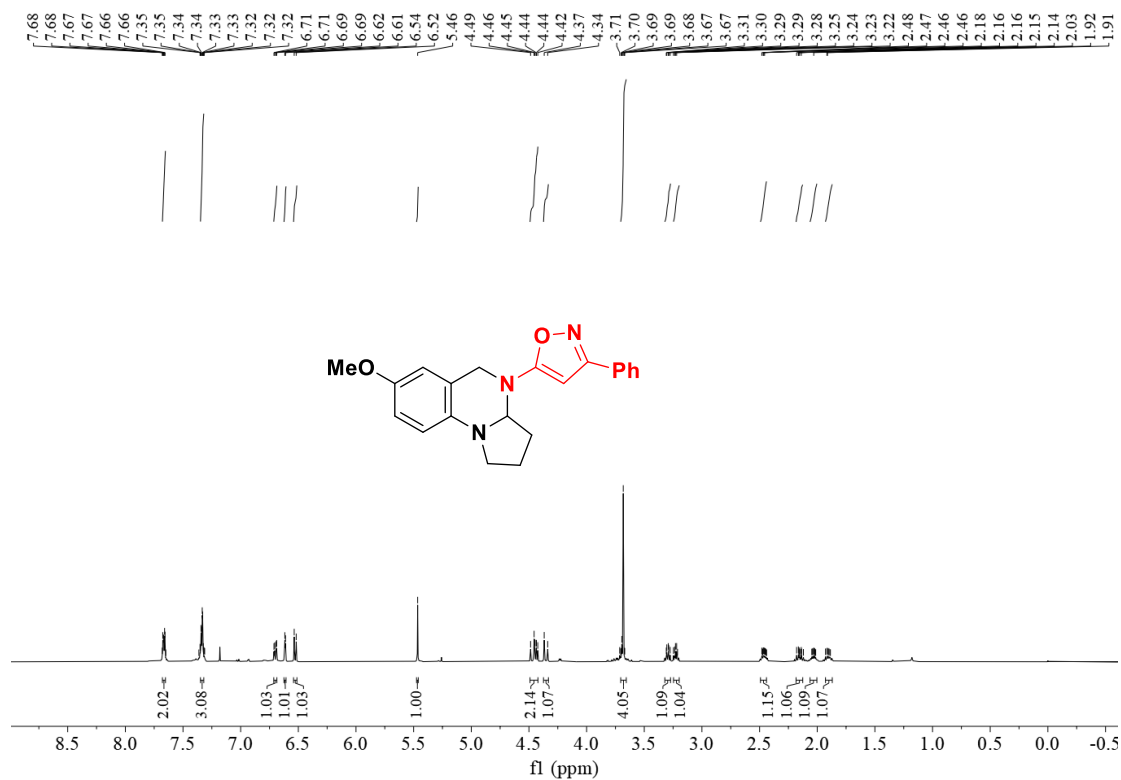
**5-(7-chloro-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)-3-phenylisoxazole (5f).**



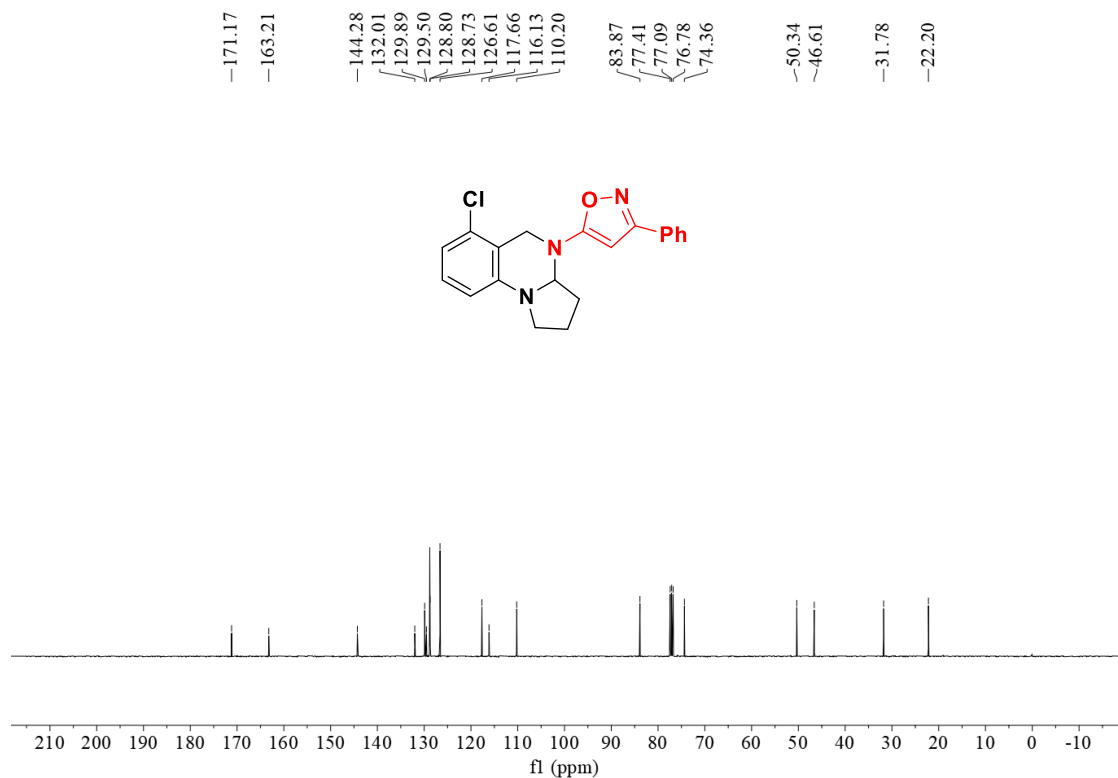
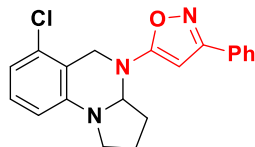
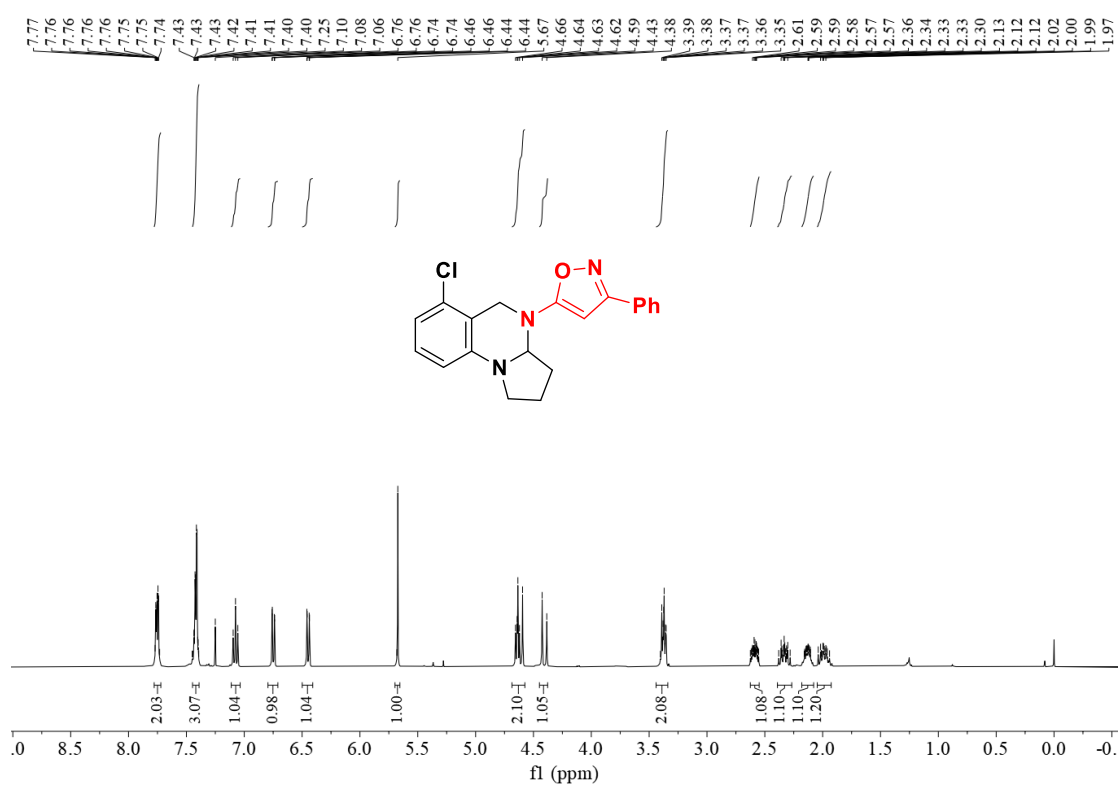
**5-(7-bromo-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)-3-phenylisoxazole (5g).**



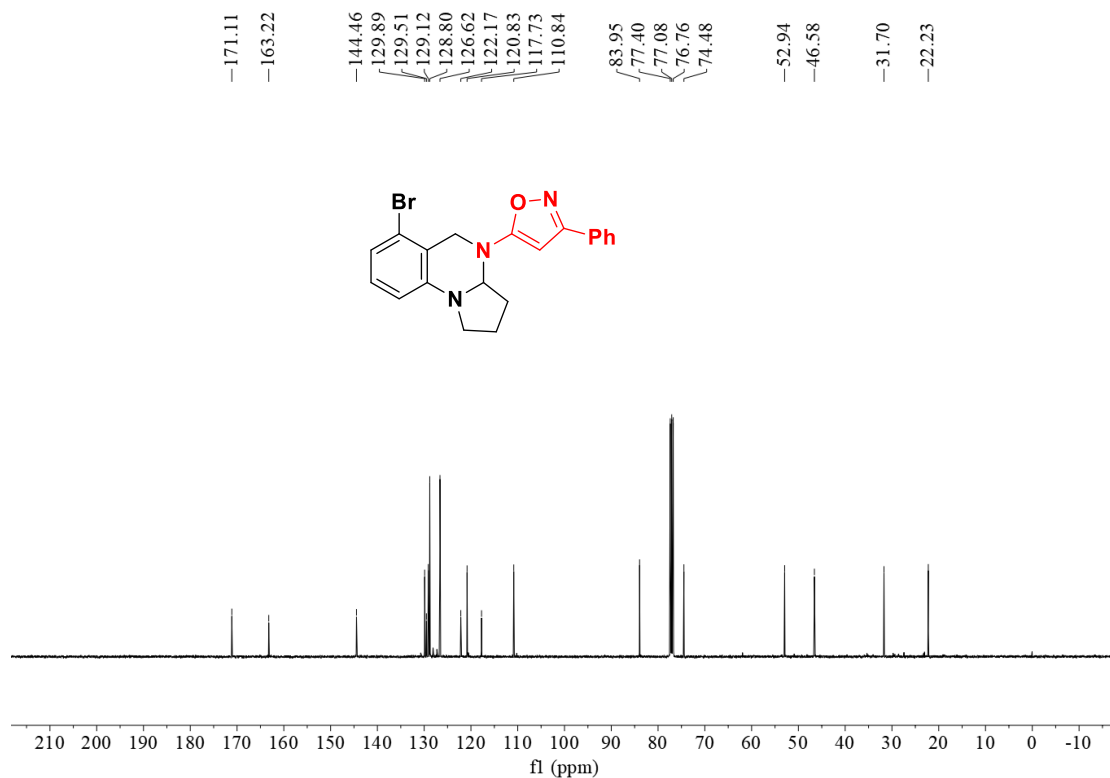
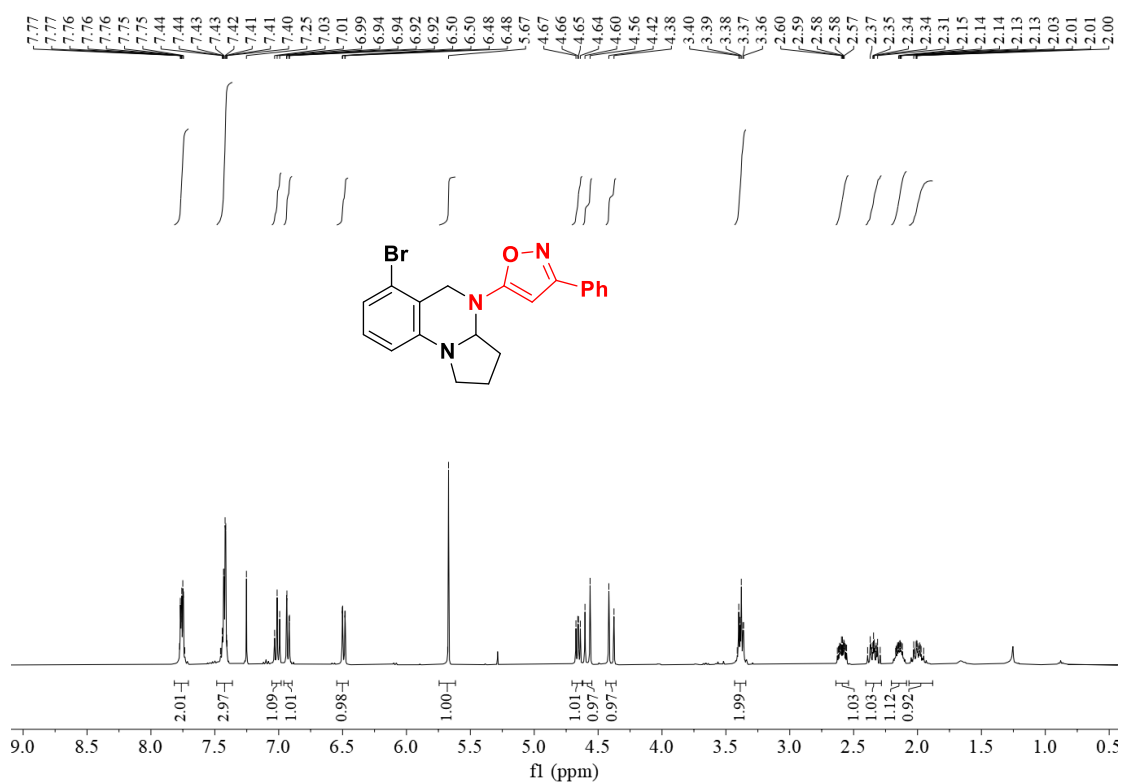
**5-(7-methoxy-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)-3-phenylisoxazole (5h).**



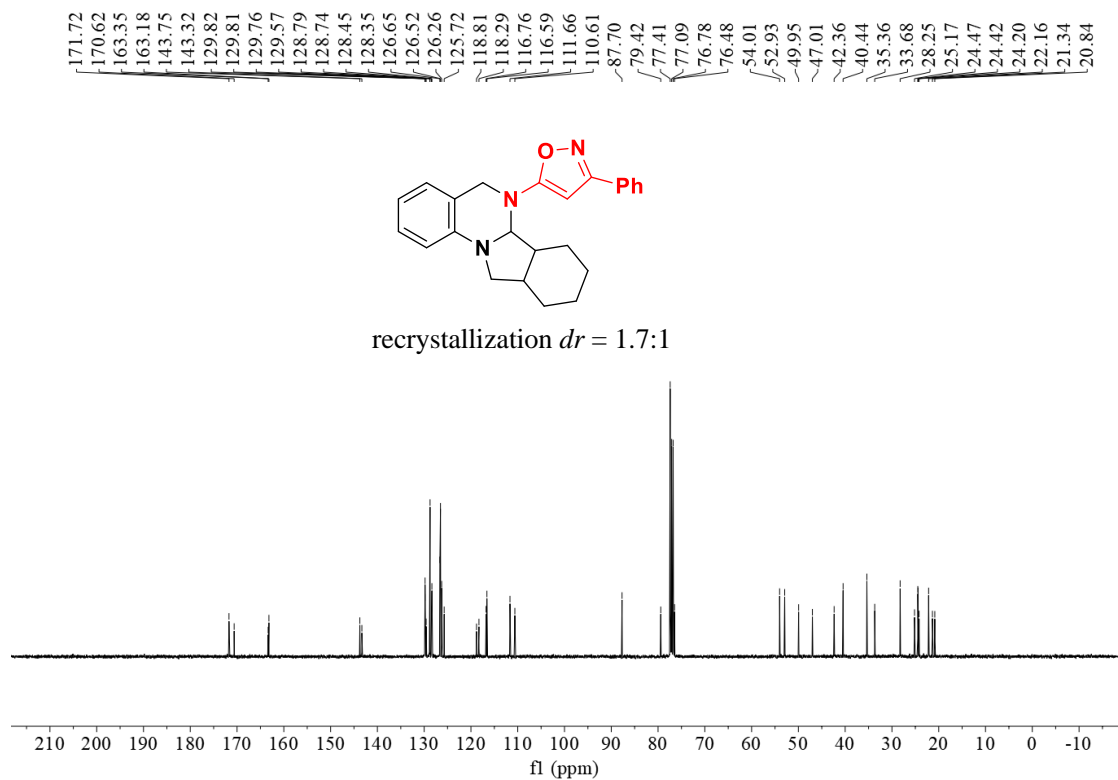
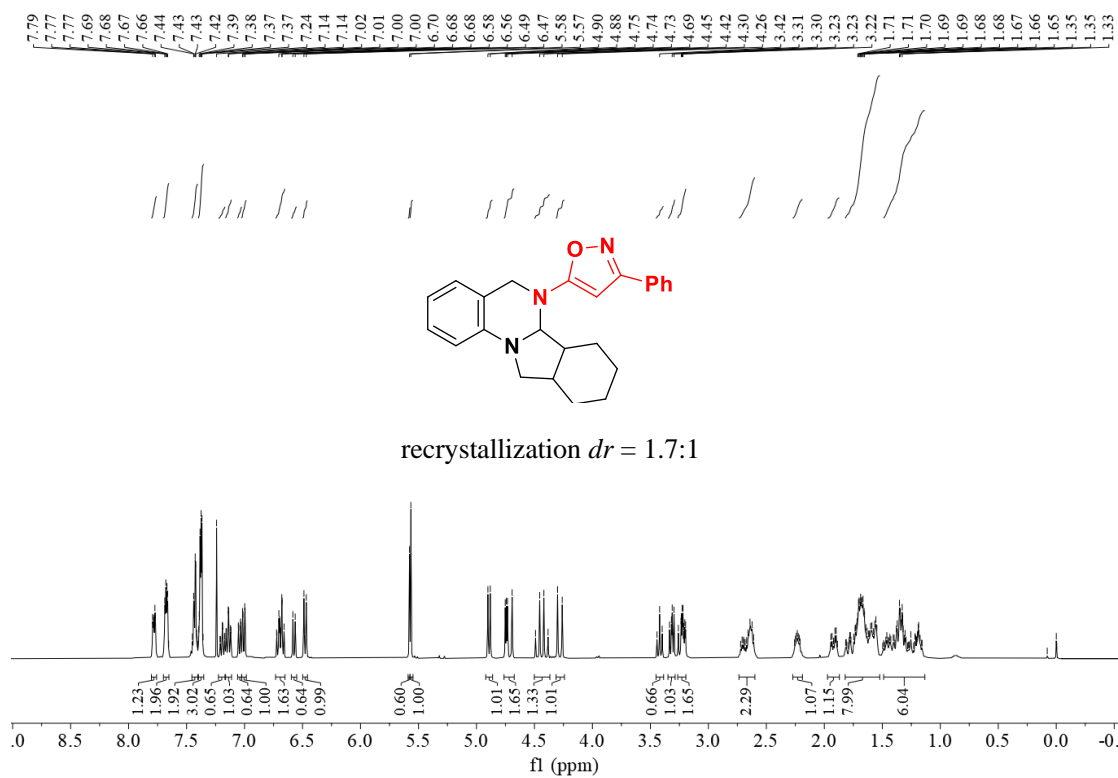
**6-(6-chloro-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)-3-phenylisoxazole (5i).**



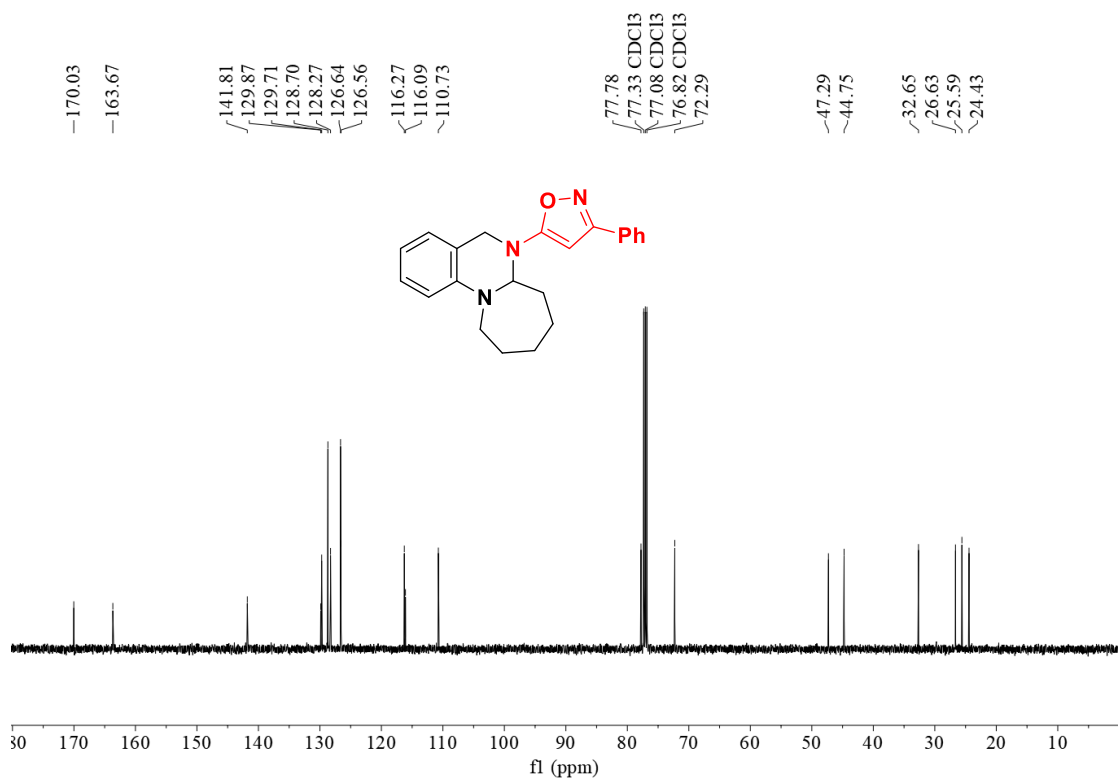
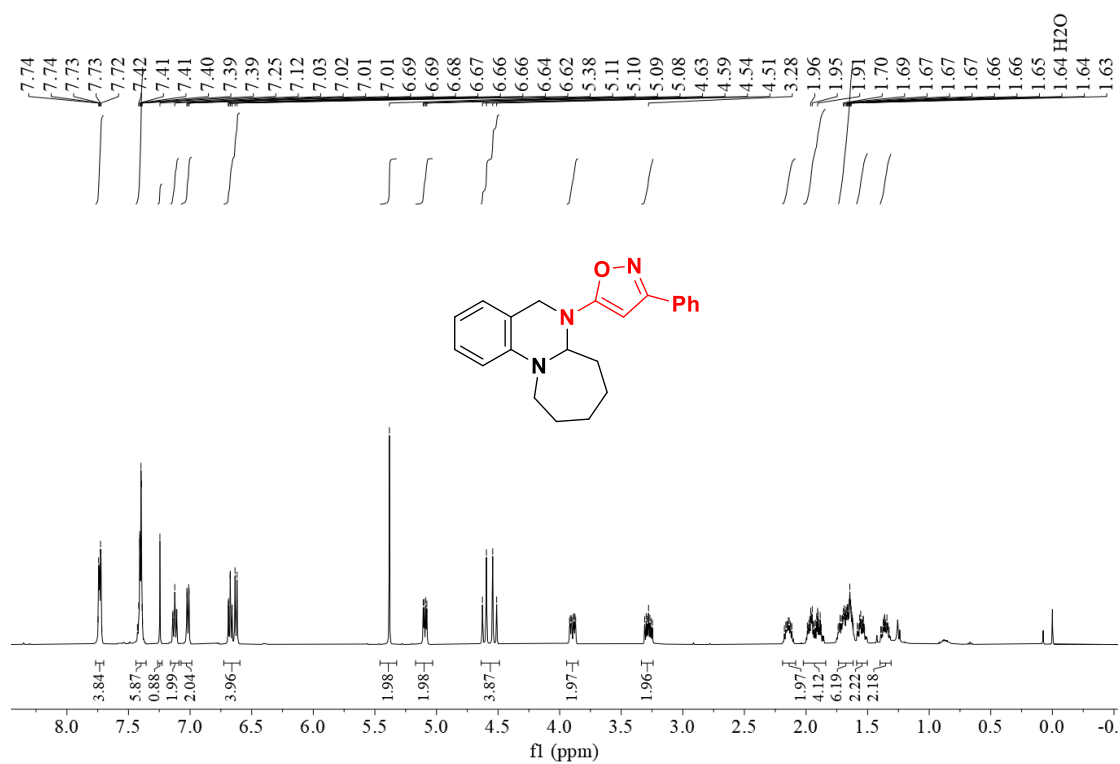
**5-(6-bromo-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)-3-phenylisoxazole (5j).**



5-(6a,6b,7,8,9,10,10a,11-octahydroisoindolo[2,1-a]quinazolin-6(5H)-yl)-3-phenyloxazole  
(5k).

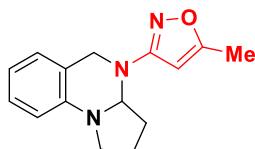
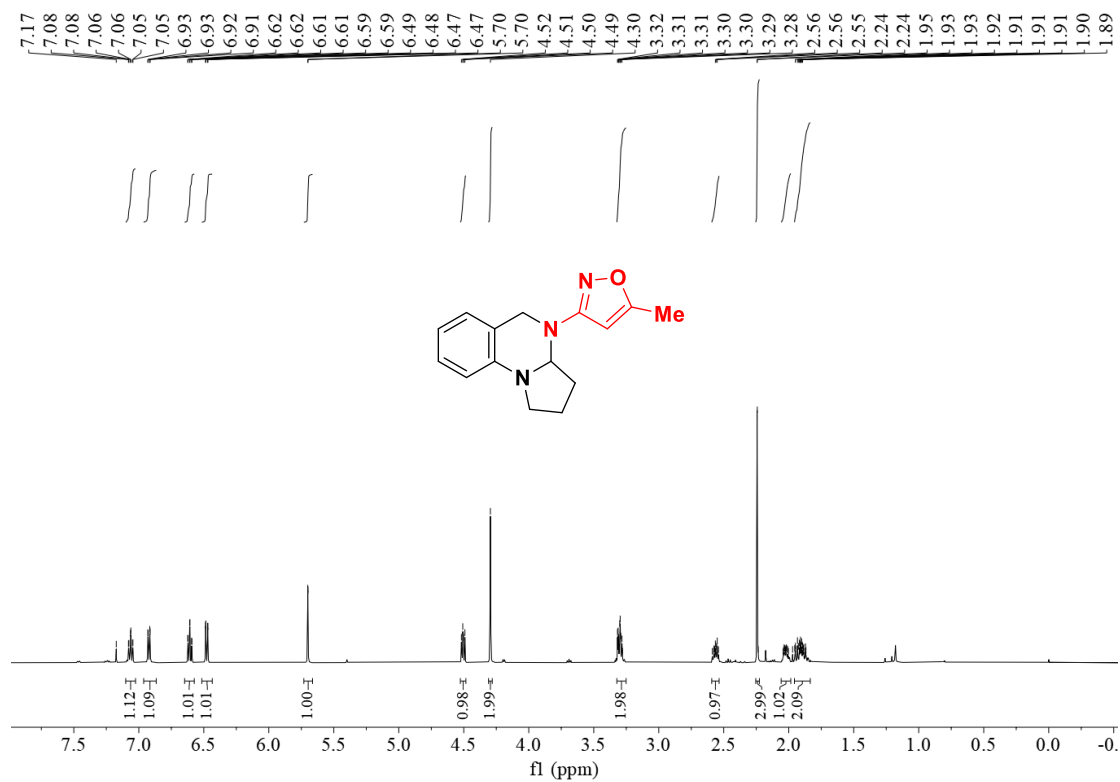


5-(6a,7,8,9,10,11-hexahydroazepino[1,2-a]quinazolin-6(5H)-yl)-3-phenylisoxazole (5I).

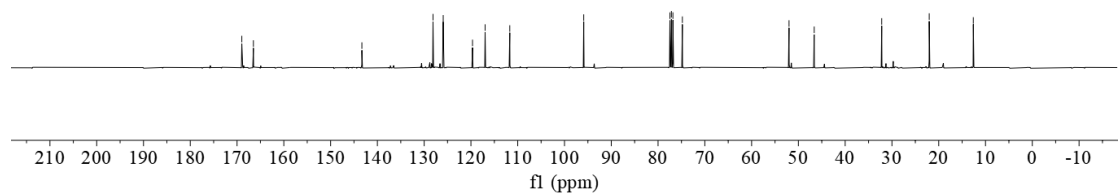
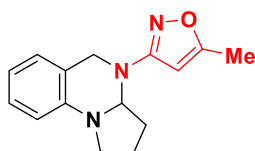




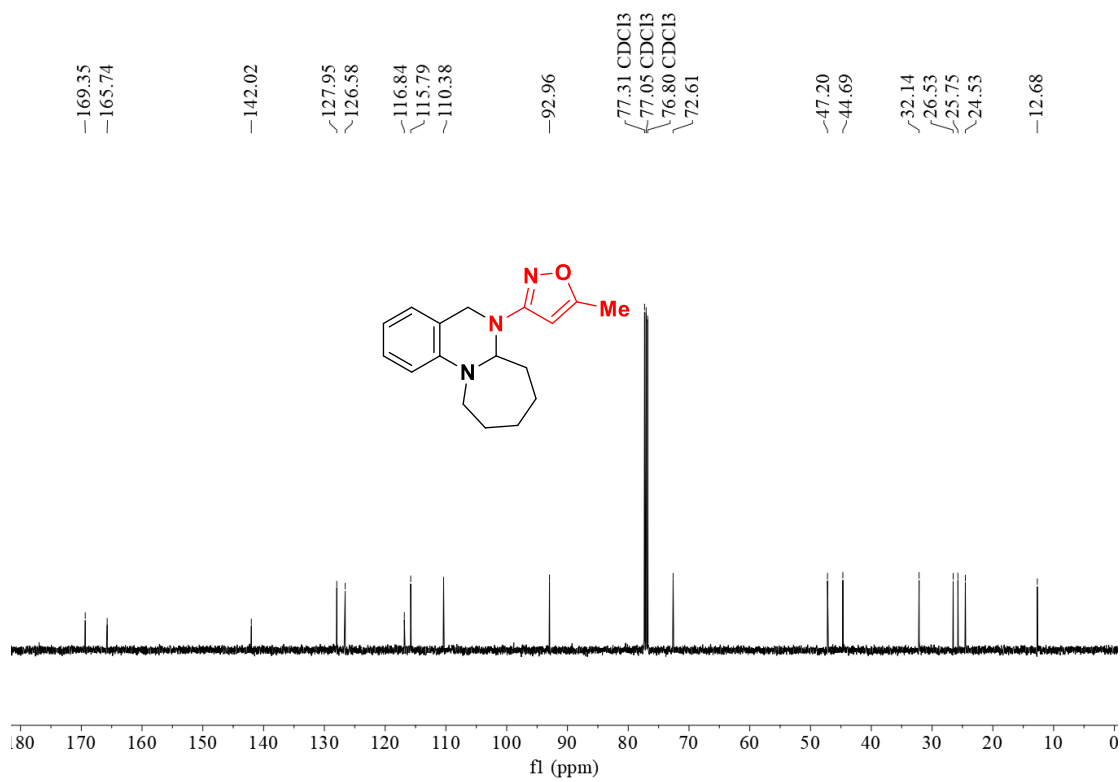
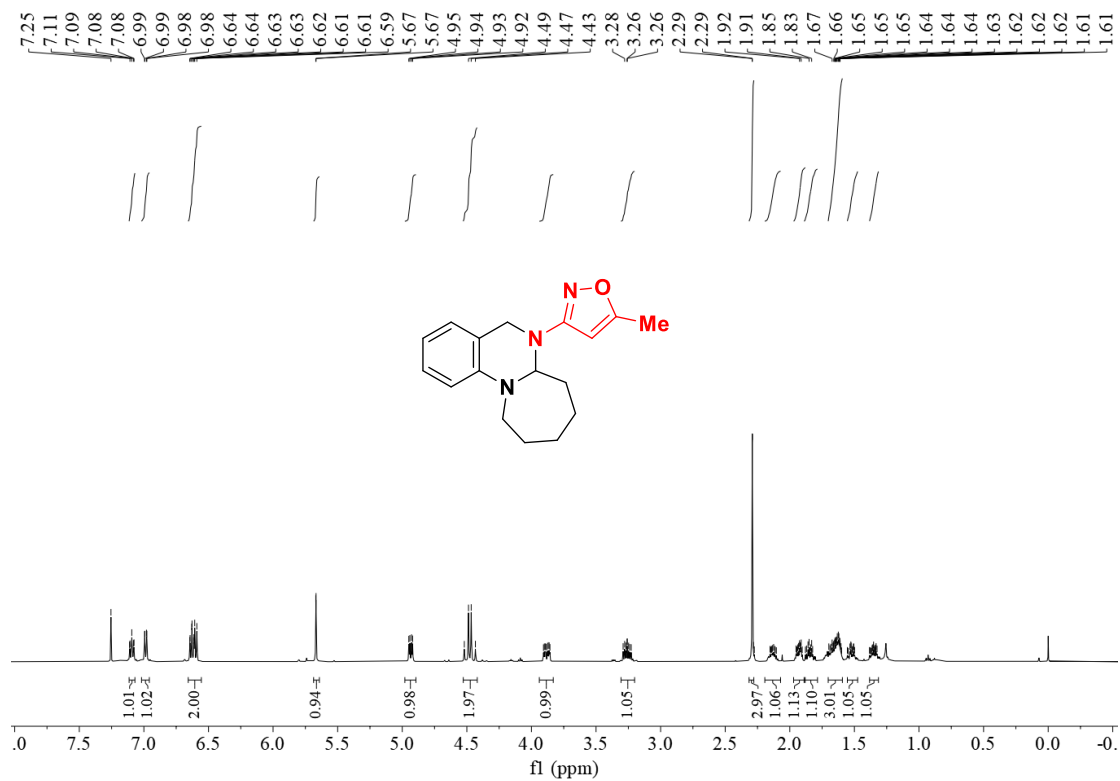
**3-methyl-5-(1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)isoxazole (5m).**



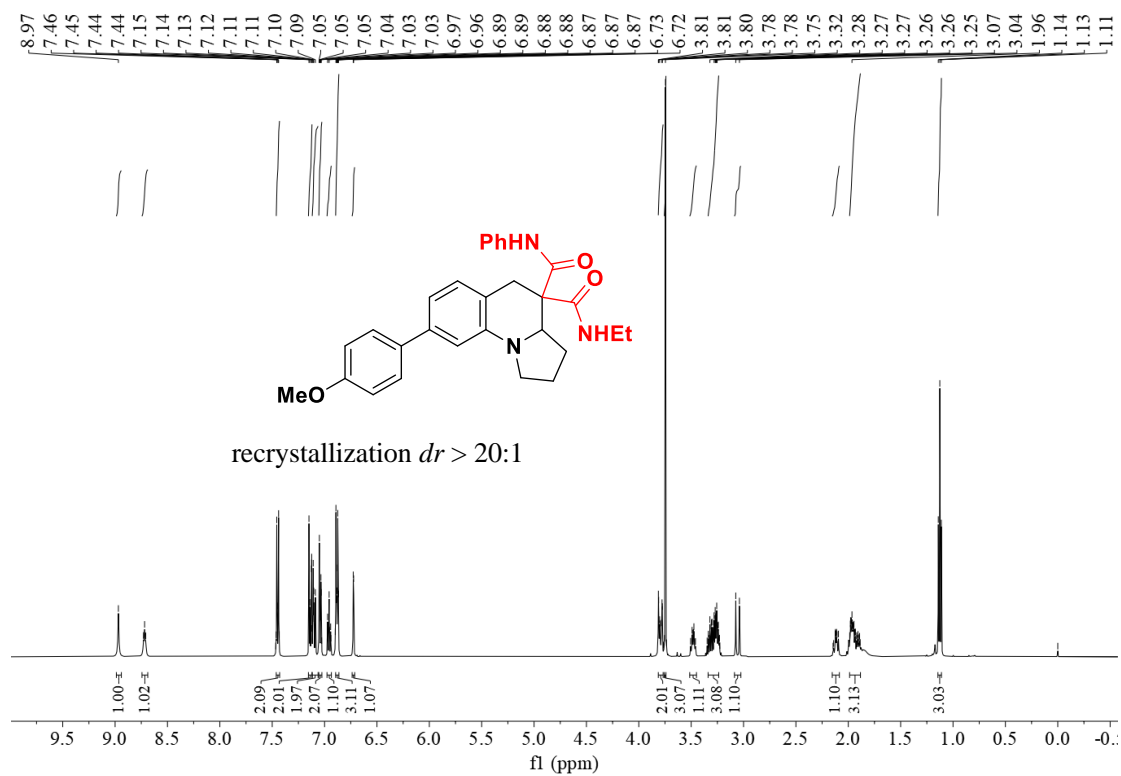
168.98  
166.50  
143.31  
128.11  
125.93  
119.66  
116.97  
111.70  
95.89  
77.46  
77.14  
76.82  
74.80  
52.00  
46.62  
32.19  
22.03  
12.60



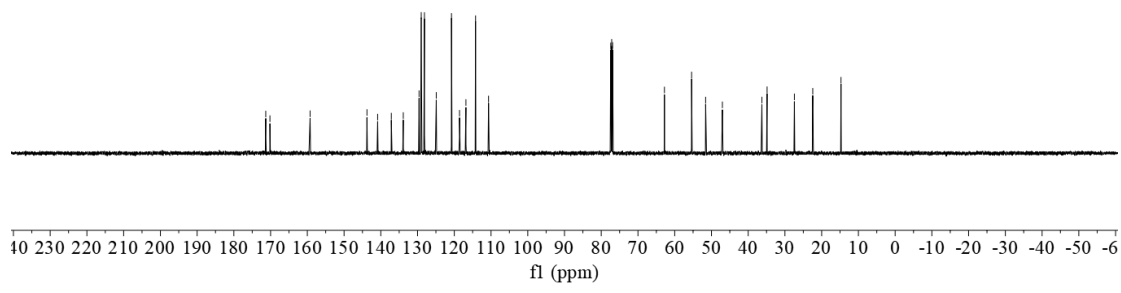
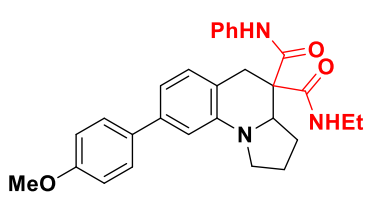
**3-(6a,7,8,9,10,11-hexahydroazepino[1,2-a]quinazolin-6(5H)-yl)-5-methylisoxazole (5n).**



**N-ethyl-8-(4-methoxyphenyl)-N-phenyl-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinoline-4,4(5H)-dicarboxamide (6a)**



- 171.52
- 170.18
- 159.25
- 143.77
- 140.86
- 137.14
- 133.88
- 129.59
- 129.00
- 128.12
- 124.90
- 120.76
- 118.57
- 116.83
- 114.21
- 110.68
- 77.41
- 77.16
- 76.90
- 62.80
- 55.40
- 51.58
- 47.02
- 36.27
- 34.86
- 27.42
- 22.43
- 14.73



**5-(8-((4-methoxyphenyl)ethynyl)-1,2,3,3a-tetrahydropyrrolo[1,2-a]quinazolin-4(5H)-yl)-3-phenylisoxazole (7a)**

