



## Supporting Information

for

### **Lewis acid-promoted direct synthesis of isoxazole derivatives**

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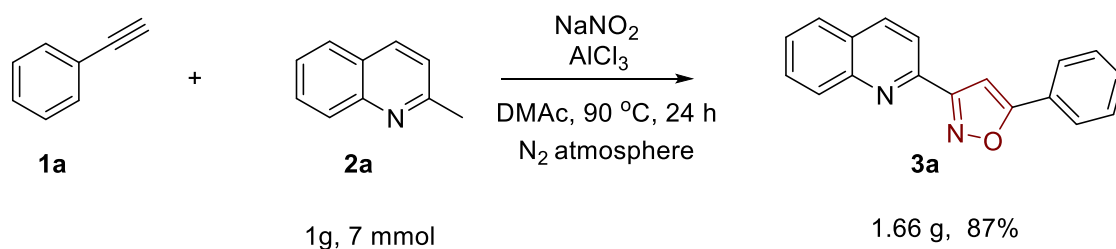
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### **Characterization data and copies of spectra**

## General information:

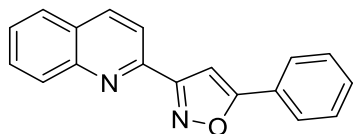
Unless otherwise noted, all reagents and solvents were obtained from commercial suppliers and used without further purification.  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, and  $^{19}\text{F}$  NMR spectra were obtained with an Agilent Technologies 400 or 500 spectrometer in  $\text{CDCl}_3$  or  $\text{DMSO}-d_6$  with TMS as an internal standard. Mass spectra were obtained on a Bruker Dalton maxis instrument. All reactions were carried out under a nitrogen atmosphere. All reactions under standard conditions were monitored by thin-layer chromatography (TLC) on gel F254 plates. Flash column chromatography was carried out using 300–400 mesh silica gel at medium pressure.

## Gram-scale synthesis of 3a



To a flame-dried 100 mL Schlenk tube filled with nitrogen, 2-methylquinoline (**2a**, 1.0 g, 7 mmol), phenylacetylene (**1a**, 0.36 g, 3.5 mmol),  $\text{AlCl}_3$  (1.4 g, 10.5 mmol), sodium nitrite (2.4 g, 35 mmol), and absolute dry DMAc (30 mL) were added under nitrogen. The formed mixture was stirred at 90 °C under nitrogen for 24 h and monitored by TLC. After work-up, 1.66 g (87%) of product **3a** were obtained.

## Characterization of the products

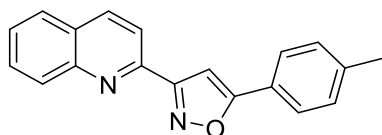


**5-Phenyl-3-(quinolin-2-yl)isoxazole (3a)**<sup>[1,2,3]</sup>. Yield: 92%. yellow solid. Mp: 128-130 °C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**: δ 8.30 – 8.15 (m, 3H), 7.93 – 7.82 (m, 3H), 7.76 (ddd, J = 8.5, 6.9, 1.5 Hz, 1H), 7.58 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 7.53 – 7.45 (m, 3H), 7.39 (s, 1H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)**: δ 170.6, 164.2, 148.7, 148.0, 136.9, 130.3, 129.9, 129.7, 129.0, 128.4, 127.7, 127.5, 127.3, 125.9, 119.1, 98.6.

**HRMS (ESI) m/z**: [M+H]<sup>+</sup> calcd. for: C<sub>18</sub>H<sub>13</sub>N<sub>2</sub>O<sup>+</sup> : 273.1022; found 273.1027.

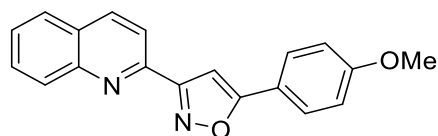


**3-(Quinolin-2-yl)-5-(p-tolyl)isoxazole (3b)**<sup>[1,2]</sup>. Yield: 76%. yellow solid. Mp: 150-152 °C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**: δ 8.28 – 8.16 (m, 3H), 7.86 (dd, J = 7.8, 1.3 Hz, 1H), 7.81 – 7.73 (m, 3H), 7.59 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 7.34 (s, 1H), 7.30 (dt, J = 7.8, 0.8 Hz, 2H), 2.42 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)**: δ 170.9, 164.1, 148.8, 148.0, 140.6, 136.9, 129.9, 129.7, 129.7, 128.4, 127.7, 127.3, 125.8, 124.8, 119.1, 98.0, 21.5.

**HRMS (ESI) m/z**: [M+H]<sup>+</sup> calcd. for: C<sub>19</sub>H<sub>15</sub>N<sub>2</sub>O<sup>+</sup> : 287.1179; found 287.1182.

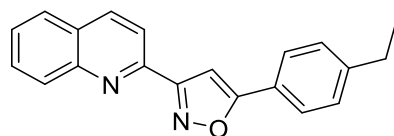


**5-(4-Methoxyphenyl)-3-(quinolin-2-yl)isoxazole (3c)** <sup>[1,2]</sup>. Yield: 73%. yellow solid.  
Mp: 140-142°C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.3 – 8.15 (m, 3H), 7.9 – 7.81 (m, 3H), 7.78 – 7.73 (m, 1H), 7.71 – 7.66 (m, 1H), 7.60 – 7.55 (m, 1H), 7.3 (s, 1H), 7.0 – 6.9 (m, 2H), 3.9 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 170.6, 164.1, 161.1, 148.8, 148.2, 148.0, 137.5, 136.9, 131.3, 130.0, 129.9, 129.7, 129.5, 128.4, 127.8, 127.7, 127.5, 127.3, 123.3, 120.3, 119.1, 114.4, 97.2, 55.4.

**HRMS (ESI) m/z:** [M+Na]<sup>+</sup> calcd. for: C<sub>19</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub><sup>+</sup>: 325.0953; found 325.0943.

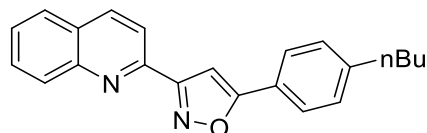


**5-(4-Ethylphenyl)-3-(quinolin-2-yl)isoxazole (3d)** <sup>[1,2]</sup>. Yield: 72%. yellow solid.  
Mp: 112-114°C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.29 – 8.16 (m, 3H), 7.89 – 7.81 (m, 3H), 7.76 (td, J = 6.9, 1.6 Hz, 1H), 7.62 – 7.56 (m, 1H), 7.37 – 7.30 (m, 3H), 2.72 (q, J = 7.7 Hz, 2H), 1.29 (t, J = 7.6 Hz, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 170.9, 164.1, 148.8, 148.0, 146.8, 136.9, 129.9, 129.7, 128.5, 128.4, 127.7, 127.3, 125.9, 125.0, 119.1, 98.0, 28.8, 15.3.

**HRMS (ESI) m/z:** [M+H]<sup>+</sup> calcd. for: C<sub>20</sub>H<sub>17</sub>N<sub>2</sub>O<sup>+</sup>: 301.1335; found 301.1338.

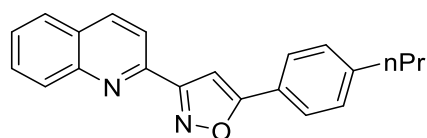


**5-(4-Butylphenyl)-3-(quinolin-2-yl)isoxazole (3e)** <sup>[1]</sup>. Yield: 70%. yellow solid. Mp: 58-61°C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.28 – 8.15 (m, 3H), 7.86 (d, J = 8.1 Hz, 1H), 7.81 (dd, J = 8.1, 1.4 Hz, 2H), 7.78 – 7.74 (m, 1H), 7.61 – 7.56 (m, 1H), 7.34 (d, J = 1.3 Hz, 1H), 7.33 – 7.29 (m, 2H), 2.67 (t, J = 7.8 Hz, 2H), 1.67 – 1.61 (m, 2H), 1.38 (q, J = 7.0 Hz, 2H), 0.95 (td, J = 7.3, 1.3 Hz, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 170.9, 164.1, 148.8, 148.0, 145.6, 136.9, 129.9, 129.7, 129.2, 129.1, 128.4, 127.7, 127.3, 125.9, 124.9, 119.2, 98.0, 35.6, 33.4, 22.3, 13.9.

**HRMS (ESI) m/z:** [M+H]<sup>+</sup>calcd. for: C<sub>20</sub>H<sub>22</sub>N<sub>2</sub>NaO<sup>+</sup>; 351.1473, found 351.1463.

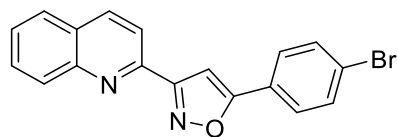


**5-(4-Propylphenyl)-3-(quinolin-2-yl)isoxazole (3f)** <sup>[2]</sup>. Yield: 65%. yellow solid. Mp: 88-90°C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.28 – 8.16 (m, 3H), 7.86 (d, J = 8.2 Hz, 1H), 7.81 (d, J = 8.2 Hz, 2H), 7.78 – 7.74 (m, 1H), 7.58 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 7.34 (s, 1H), 7.33 – 7.29 (m, 2H), 2.65 (t, 2H), 1.69 (dd, J = 7.5 Hz, 2H), 0.97 (t, J = 7.3 Hz, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 170.9, 164.1, 148.8, 148.0, 145.3, 136.9, 129.9, 129.7, 129.1, 128.4, 127.7, 127.3, 125.9, 125.0, 119.2, 98.0, 38.0, 24.3, 13.8.

**HRMS (ESI) m/z:** [M+H]<sup>+</sup>calcd. for: C<sub>21</sub>H<sub>19</sub>N<sub>2</sub>O<sup>+</sup>; 315.1492; found 315.1499.

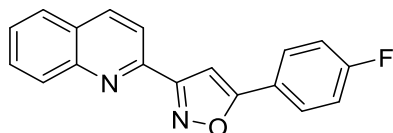


**5-(4-Bromophenyl)-3-(quinolin-2-yl)isoxazole (3g)** <sup>[2]</sup>. Yield: 84%. yellow solid. Mp: 200-202°C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.27 – 8.13 (m, 3H), 7.87 – 7.82 (m, 1H), 7.78 – 7.70 (m, 3H), 7.64 – 7.55 (m, 3H), 7.37 (d, J = 1.6 Hz, 1H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 169.5, 164.2, 148.4, 148.0, 137.0, 132.3, 130.0, 129.7, 128.4, 127.7, 127.4, 127.3, 126.3, 124.6, 119.0, 99.1, 99.0.

**HRMS (ESI) m/z:** [M+H]<sup>+</sup>calcd. for: C<sub>18</sub>H<sub>12</sub>BrN<sub>2</sub>O<sup>+</sup> : 351.0128; found 351.0133.



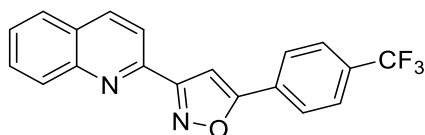
**5-(4-Fluorophenyl)-3-(quinolin-2-yl)isoxazole (3h)** <sup>[1,2]</sup>. Yield: 75%. white solid. Mp: 164-166°C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.27 – 8.14 (m, 3H), 7.90 – 7.83 (m, 3H), 7.76 (t, J = 8.4, 6.9, 1.4 Hz, 1H), 7.58 (t, J = 8.1, 6.9, 1.2 Hz, 1H), 7.33 (s, 1H), 7.18 (t, J = 8.6 Hz, 2H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 169.6, 165.0, 164.6 (d, J = 250.0 Hz), 148.5, 148.0, 137.0, 130.0, 129.7, 128.4, 127.9 (d, J = 9.0 Hz), 127.7, 127.3, 123.8 (d, J=3.0Hz), 119.1, 116.3 (d, J = 23.0 Hz), 98.4.

**<sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>):** δ -109.4.

**HRMS (ESI) m/z:** [M+H]<sup>+</sup>calcd. for: C<sub>18</sub>H<sub>12</sub>FN<sub>2</sub>O<sup>+</sup> : 291.0928; found 291.0932.



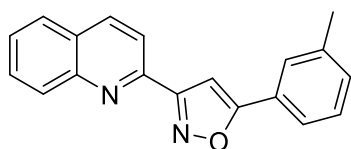
**3-(Quinolin-2-yl)-5-(4-(trifluoromethyl)phenyl)isoxazole (3i)** <sup>[1]</sup>. Yield: 73%. yellow solid. Mp: 172-175°C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.22 – 8.11 (m, 3H), 7.93 (d, J = 8.1 Hz, 2H), 7.81 (d, J = 8.2 Hz, 1H), 7.76 – 7.67 (m, 3H), 7.59 – 7.52 (m, 1H), 7.44 (s, 1H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 168.8, 164.3, 148.2, 148.0, 136.9, 131.7 (q, J=32.0 Hz), 130.4, 130.0, 129.7, 128.4, 127.7, 127.4, 126.0, 125.9, 123.7 (q, J=271.0 Hz), 118.9, 100.1.

**<sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>):** δ -62.9.

**HRMS (ESI) m/z:** [M+H]<sup>+</sup>calcd. for: C<sub>19</sub>H<sub>12</sub>F<sub>3</sub>N<sub>2</sub>O<sup>+</sup> : 341.0902; found 341.0908.

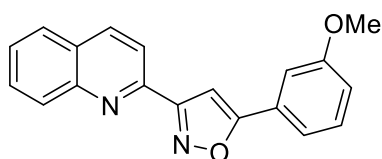


**3-(Quinolin-2-yl)-5-(m-tolyl)isoxazole (3j)** <sup>[1,2]</sup>. Yield: 53%. Yellow solid. Mp: 109-111 °C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.29 – 8.15 (m, 3H), 7.87 (dd, J = 8.1, 1.5 Hz, 1H), 7.79 – 7.69 (m, 3H), 7.59 (t, J = 8.1, 6.8, 1.2 Hz, 1H), 7.41 – 7.36 (m, 2H), 7.28 (d, J = 7.6 Hz, 1H), 2.45 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 170.8, 164.1, 148.7, 148.1, 138.8, 136.9, 131.1, 129.9, 129.7, 128.9, 128.4, 127.7, 127.4, 127.3, 126.5, 123.1, 119.1, 98.5, 21.5.

**HRMS (ESI) m/z:** [M+H]<sup>+</sup> calcd. for: C<sub>19</sub>H<sub>15</sub>N<sub>2</sub>O<sup>+</sup> : 287.1179; found 287.1188.

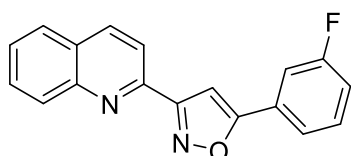


**5-(3-Methoxyphenyl)-3-(quinolin-2-yl)isoxazole (3k)** <sup>[1]</sup>. Yield: 81%. yellow solid. Mp: 104-106 °C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.29 – 8.16 (m, 3H), 7.86 (dd, J = 8.1, 1.5 Hz, 1H), 7.79 – 7.71 (m, 1H), 7.61 – 7.55 (m, 1H), 7.48 (dt, J = 7.6, 1.3 Hz, 1H), 7.45 – 7.35 (m, 3H), 7.03 – 6.98 (m, 1H), 3.89 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 170.5, 164.2, 160.0, 148.6, 148.0, 136.9, 130.2, 129.9, 129.7, 128.6, 128.4, 127.7, 127.3, 119.1, 118.4, 116.4, 110.9, 98.9, 55.4, 55.4.

**HRMS (ESI) m/z:** [M+H]<sup>+</sup> calcd. for: C<sub>19</sub>H<sub>15</sub>N<sub>2</sub>O<sub>2</sub><sup>+</sup> : 303.1134; found 303.1138.



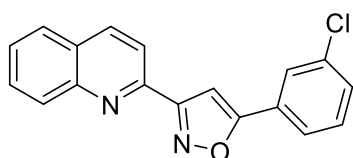
**5-(3-Fluorophenyl)-3-(quinolin-2-yl)isoxazole (3l)** <sup>[1,2]</sup>. Yield: 71%. yellow solid. Mp: 125-127 °C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.29 – 8.15 (m, 3H), 7.86 (dd, J = 8.2, 1.6 Hz, 1H), 7.76 (tt, J = 6.8, 1.5 Hz, 1H), 7.67 (dq, J = 7.8, 1.3 Hz, 1H), 7.63 – 7.55 (m, 2H), 7.50 – 7.44 (m, 1H), 7.41 (d, J = 1.4 Hz, 1H), 7.20 – 7.11 (m, 1H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 169.2, 164.3, 162.9 (d, J = 246.0 Hz), 148.2 (d, J = 36.0 Hz), 137.0, 130.8, 130.7, 130.0, 129.7, 129.3 (d, J = 7.0 Hz), 128.4, 127.7, 127.4, 121.6 (d, J = 4.0 Hz), 119.0, 117.2 (d, J = 21.0 Hz), 112.8 (d, J = 23.0 Hz), 99.5.

**<sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>):** δ -111.5.

**HRMS (ESI) m/z:** [M+H]<sup>+</sup>calcd. for: C<sub>18</sub>H<sub>12</sub>FN<sub>2</sub>O<sup>+</sup> : 291.0934; found 291.0933.

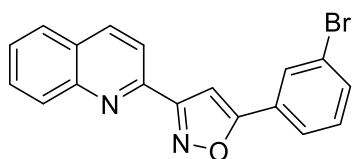


**5-(3-Chlorophenyl)-3-(quinolin-2-yl)isoxazole (3m)**<sup>[1]</sup>. Yield: 75%. yellow solid. Mp: 138-141 °C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.26 – 8.12 (m, 3H), 7.87 – 7.81 (m, 2H), 7.78 – 7.71 (m, 2H), 7.57 (ddd, J = 7.9, 7.0, 1.2 Hz, 1H), 7.45 – 7.34 (m, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 169.0, 164.2, 148.3, 148.0, 136.9, 135.1, 130.3, 130.2, 130.0, 129.7, 129.0, 128.4, 127.7, 127.4, 125.9, 125.9, 123.9, 119.0, 99.5, 99.5.

**HRMS (ESI) m/z:** [M+H]<sup>+</sup>calcd. for: C<sub>18</sub>H<sub>12</sub>ClN<sub>2</sub>O<sup>+</sup> : 307.0638; found 307.0644.



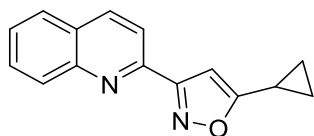
**5-(3-Bromophenyl)-3-(quinolin-2-yl)isoxazole (3n)**<sup>[1]</sup>. Yield: 85%. yellow solid. Mp: 147-149 °C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.23 (q, J = 8.5 Hz, 2H), 8.16 (d, J = 8.5 Hz, 1H), 8.03 (t, J = 1.8 Hz, 1H), 7.87 – 7.72 (m, 3H), 7.62 – 7.55 (m, 2H), 7.40 (s, 1H), 7.36 (t, J = 7.9 Hz, 1H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 168.9, 164.2, 148.3, 148.0, 137.0, 133.1, 130.6, 130.0, 129.7, 129.2, 128.8, 128.4, 127.7, 127.4, 124.4, 123.1, 119.0, 99.5, 99.5.



**HRMS (ESI) m/z:**  $[M+H]^+$  calcd. for:  $C_{18}H_{12}BrN_2O^+$  : 351.0133; found 351.0139.

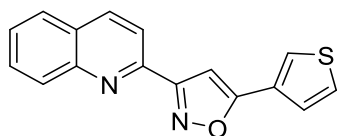


**5-Cyclopropyl-3-(quinolin-2-yl)isoxazole (3o)** <sup>[1,2]</sup>. Yield: 76%. yellow oil .

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):**  $\delta$  8.21 (dd,  $J = 8.6, 0.8$  Hz, 1H), 8.17 – 8.10 (m, 2H), 7.83 (dd,  $J = 8.1, 1.5$  Hz, 1H), 7.73 (ddd,  $J = 8.5, 6.9, 1.5$  Hz, 1H), 7.56 (ddd,  $J = 8.1, 6.9, 1.2$  Hz, 1H), 6.72 (s, 1H), 2.19 – 2.08 (m, 1H), 1.13 – 1.02 (m, 4H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):**  $\delta$  175.9, 163.6, 148.9, 148.0, 136.8, 129.8, 129.7, 128.3, 127.7, 127.2, 119.1, 97.6, 8.6, 8.2.

**HRMS (ESI) m/z:**  $[M+H]^+$  calcd. for:  $C_{15}H_{13}N_2O^+$  : 237.1022; found 237.1027.

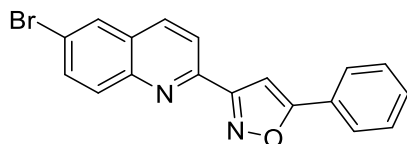


**3-(Quinolin-2-yl)-5-(thiophen-3-yl)isoxazole (3p)** <sup>[1]</sup>. Yield: 81%. yellow solid. Mp: 155-157°C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):**  $\delta$  8.30 – 8.20 (m, 2H), 8.17 (d,  $J = 8.5$  Hz, 1H), 7.90 – 7.82 (m, 2H), 7.79 – 7.83 (m, 1H), 7.59 (ddd,  $J = 8.3, 4.9, 1.6$  Hz, 1H), 7.52 (dq,  $J = 4.9, 1.5$  Hz, 1H), 7.45 (ddd,  $J = 4.8, 3.0, 1.5$  Hz, 1H), 7.24 (t,  $J = 1.6$  Hz, 1H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):**  $\delta$  166.8, 164.0, 148.6, 148.0, 136.9, 130.0, 129.9, 129.7, 128.9, 128.4, 127.7, 127.3, 127.1, 125.5, 124.4, 119.2, 98.4.

**HRMS (ESI) m/z:**  $[M+H]^+$  calcd. for:  $C_{16}H_{11}N_2OS^+$  : 279.0592; found 279.0599.

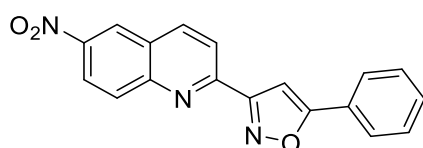


**3-(6-Bromoquinolin-2-yl)-5-phenylisoxazole (4a)** <sup>[1,2]</sup>. Yield: 92%. yellow solid. Mp: 177-179°C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.22 (dd, *J* = 8.6, 2.5 Hz, 1H), 8.14 (dd, *J* = 8.6, 2.4 Hz, 1H), 8.03 – 7.99 (m, 2H), 7.90 – 7.86 (m, 2H), 7.80 (dt, *J* = 8.9, 2.4 Hz, 1H), 7.54 – 7.45 (m, 3H), 7.33 (d, *J* = 2.6 Hz, 1H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 170.8, 163.8, 149.0, 146.6, 135.9, 133.4, 131.4, 130.3, 129.8, 129.4, 129.0, 127.3, 125.9, 121.3, 120.0, 98.5.

**HRMS (ESI) m/z:** [M+H]<sup>+</sup> calcd. for: C<sub>18</sub>H<sub>12</sub>BrN<sub>2</sub>O<sup>+</sup> : 351.0128; found 351.0131.

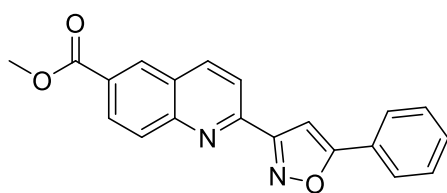


**3-(6-Nitroquinolin-2-yl)-5-phenylisoxazole (4b)** . Yield: 41%. yellow solid. Mp: 233-237 °C.

**<sup>1</sup>H NMR (400 MHz, DMSO):** δ 9.04 (d, *J* = 2.6 Hz, 1H), 8.80 (d, *J* = 8.6 Hz, 1H), 8.45 (dd, *J* = 9.3, 2.6 Hz, 1H), 8.24 (dd, *J* = 16.1, 8.9 Hz, 2H), 7.95 (dd, *J* = 7.4, 2.1 Hz, 2H), 7.63 (s, 1H), 7.52 (q, *J* = 4.9 Hz, 3H).

**<sup>13</sup>C NMR (400 MHz, DMSO):** δ 171.0, 163.7, 151.6, 149.7, 145.8, 140.4, 131.4, 131.2, 129.7, 127.5, 126.9, 126.2, 125.5, 124.0, 120.9, 99.5.

**HRMS (ESI) m/z:** [M+H]<sup>+</sup> calcd. for: C<sub>18</sub>H<sub>12</sub>N<sub>3</sub>O<sub>3</sub><sup>+</sup> : 318.0879; found 317.0885.

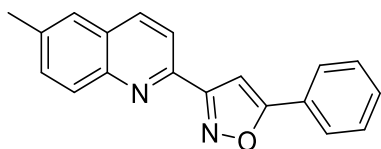


**Methyl 2-(5-phenylisoxazol-3-yl)quinoline-6-carboxylate (4c)**<sup>[2]</sup>. Yield: 90%. yellow solid. Mp: 172-174 °C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.60 (d, *J* = 1.9 Hz, 1H), 8.36 – 8.27 (m, 3H), 8.21 – 8.17 (m, 1H), 7.91 – 7.88 (m, 2H), 7.52 – 7.46 (m, 3H), 7.38 (s, 1H), 4.00 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 170.9, 166.5, 163.8, 150.7, 149.8, 138.2, 130.7, 130.4, 130.0, 129.4, 129.1, 128.6, 127.5, 127.3, 125.9, 119.8, 98.6, 98.6, 52.5.

**HRMS (ESI) m/z:** [M+H]<sup>+</sup> calcd. for: C<sub>20</sub>H<sub>15</sub>N<sub>2</sub>O<sub>3</sub><sup>+</sup> : 331.1077; found 331.1080.

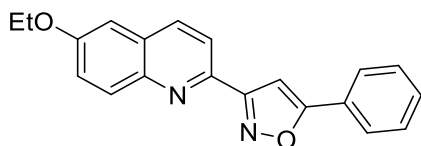


**3-(6-Methylquinolin-2-yl)-5-phenylisoxazole (4d)**<sup>[1,2]</sup>. Yield: 83%. yellow solid. Mp: 129-131°C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**: δ 8.21 – 8.14 (m, 2H), 8.06 (d, *J* = 8.5 Hz, 1H), 7.91 – 7.87 (m, 2H), 7.62 – 7.56 (m, 2H), 7.52 – 7.43 (m, 3H), 7.37 (s, 1H), 2.55 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)**: δ 170.5, 164.2, 147.8, 146.6, 137.4, 136.2, 132.2, 130.2, 129.4, 129.0, 128.5, 127.5, 126.6, 125.9, 119.1, 98.6, 21.7.

**HRMS (ESI) m/z**: [M+H]<sup>+</sup> calcd. for: C<sub>19</sub>H<sub>15</sub>N<sub>2</sub>O<sup>+</sup> : 287.1179; found 287.1185.

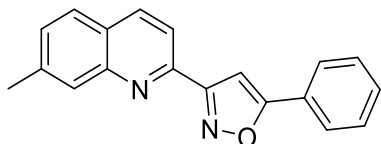


**3-(6-Ethoxyquinolin-2-yl)-5-phenylisoxazole (4e)**<sup>[2]</sup>. Yield: 62%. yellow solid. Mp: 205-207°C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**: δ 8.19 – 8.11 (m, 2H), 8.06 (dd, *J* = 9.2, 1.4 Hz, 1H), 7.90 (dt, *J* = 7.9, 1.7 Hz, 2H), 7.52 – 7.45 (m, 3H), 7.40 (dt, *J* = 9.2, 2.2 Hz, 1H), 7.37 – 7.35 (m, 1H), 7.27 – 7.24 (m, 1H), 4.22 – 4.13 (m, 2H), 1.53 – 1.48 (m, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)**: δ 170.5, 164.2, 157.8, 146.2, 144.0, 135.5, 131.1, 130.2, 129.6, 129.0, 127.5, 125.9, 123.0, 119.4, 105.9, 98.5, 63.9, 14.7.

**HRMS (ESI) m/z**: [M+H]<sup>+</sup> calcd. for: C<sub>19</sub>H<sub>15</sub>N<sub>2</sub>O<sub>2</sub><sup>+</sup> : 303.1134; found 303.1138.

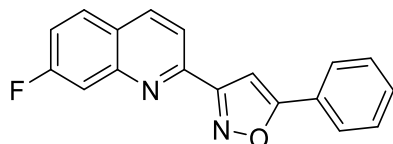


**3-(7-Methylquinolin-2-yl)-5-phenylisoxazole (4f)**. Yield: 80%. yellow solid. Mp: 131-133°C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**: δ 8.14 – 8.06 (m, 2H), 8.01 – 7.89 (m, 2H), 7.82 – 7.78 (m, 2H), 7.66 (d, *J* = 8.8 Hz, 1H), 7.19 (dt, *J* = 8.9, 2.6 Hz, 1H), 7.14 (q, *J* = 2.7 Hz, 1H), 4.47 (dd, *J* = 18.1, 2.4 Hz, 1H), 4.16 (dd, *J* = 18.1, 2.3 Hz, 1H), 3.97 – 3.88 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 158.6, 158.5, 148.6, 146.3, 135.5, 134.7, 133.5, 131.3, 130.5, 130.0, 129.8, 129.3, 128.2, 127.4, 126.2, 124.3, 121.8, 119.9, 119.7, 105.5, 55.4.

**HRMS (ESI) m/z:** [M+Na]<sup>+</sup> calcd. for: C<sub>19</sub>H<sub>14</sub>N<sub>2</sub>NaO<sup>+</sup> : 309.1004; found 309.0991.



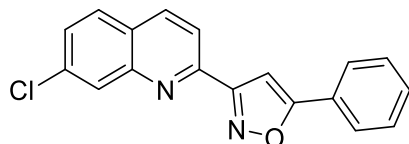
**3-(7-Fluoroquinolin-2-yl)-5-phenylisoxazole (4g)**<sup>[1]</sup>. Yield: 80%. yellow solid. Mp: 131-133°C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.26 – 8.17 (m, 2H), 7.91 – 7.77 (m, 4H), 7.49 (qd, J = 7.8, 6.8, 3.7 Hz, 3H), 7.40 – 7.34 (m, 2H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 170.7, 163.9, 163.2 (d, J = 250.0 Hz), 149.6, 149.0, 148.9, 136.8, 130.3, 129.7 (d, J = 10.0 Hz), 129.0, 127.4, 125.9, 125.4, 118.5, 118.4, 117.8 (d, J = 25.0 Hz), 113.3 (d, J = 10.0 Hz), 98.6.

**<sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>):** δ -108.8.

**HRMS (ESI) m/z:** [M+H]<sup>+</sup> calcd. for: C<sub>18</sub>H<sub>12</sub>FN<sub>2</sub>O<sup>+</sup> : 291.0934; found 291.0935.

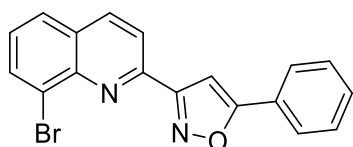


**3-(7-Chloroquinolin-2-yl)-5-phenylisoxazole (4h)**<sup>[1,2]</sup>. Yield: 75%. white solid. Mp: 146-148°C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.22 (s, 2H), 8.16 (d, J = 2.1 Hz, 1H), 7.90 – 7.87 (m, 2H), 7.78 (dd, J = 8.7, 0.5 Hz, 1H), 7.54 – 7.47 (m, 4H), 7.34 (s, 1H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 170.8, 163.8, 149.6, 148.3, 136.7, 135.8, 130.3, 129.0, 128.9, 128.7, 128.3, 127.3, 126.7, 125.9, 119.3, 98.6, 98.5.

**HRMS (ESI) m/z:** [M+H]<sup>+</sup> calcd. for: C<sub>18</sub>H<sub>12</sub>ClN<sub>2</sub>O<sup>+</sup> : 307.0633; found 307.0638.

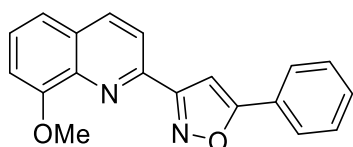


**3-(8-Bromoquinolin-2-yl)-5-phenylisoxazole (4i)** <sup>[1]</sup>. Yield: 54%. white solid. Mp: 142-144 °C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.27 (q, J = 8.5 Hz, 2H), 8.08 (dd, J = 7.5, 1.3 Hz, 1H), 7.93 – 7.90 (m, 2H), 7.81 (dd, J = 8.1, 1.3 Hz, 1H), 7.53 – 7.40 (m, 5H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 170.7, 164.0, 149.4, 144.9, 137.4, 133.6, 130.3, 129.6, 129.0, 127.7, 127.6, 127.4, 126.0, 125.5, 119.8, 99.0, 98.9.

**HRMS (ESI) m/z:** [M+H]<sup>+</sup> calcd. for: C<sub>18</sub>H<sub>12</sub>BrN<sub>2</sub>O<sup>+</sup> : 351.0133; found 351.0139.

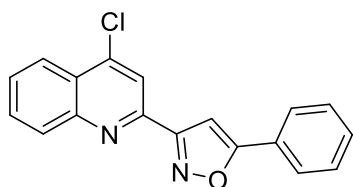


**3-(8-Methoxyquinolin-2-yl)-5-phenylisoxazole(4j)** <sup>[2]</sup>. Yield: 72%. white solid. Mp: 129-131 °C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.29 – 8.22 (m, 2H), 7.92 – 7.88 (m, 2H), 7.54 – 7.43 (m, 6H), 7.10 (dd, J = 7.7, 1.3 Hz, 1H), 4.13 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 170.5, 164.2, 155.5, 147.6, 139.9, 137.0, 130.2, 129.6, 129.0, 127.6, 127.5, 125.9, 119.7, 119.6, 108.4, 99.0, 99.0, 56.2.

**HRMS (ESI) m/z:** [M+H]<sup>+</sup> calcd. for: C<sub>19</sub>H<sub>15</sub>N<sub>2</sub>O<sub>2</sub><sup>+</sup>: 303.1128; found 303.1135.

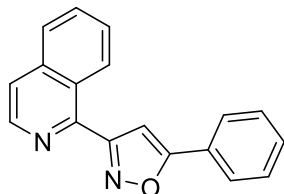


**3-(4-Chloroquinolin-2-yl)-5-phenylisoxazole (4k)** <sup>[2]</sup>. Yield: 34%. yellow solid. Mp: 149-151 °C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 8.31 (s, 1H), 8.24 (dd, J = 8.4, 1.4 Hz, 1H), 8.17 (dd, J = 8.4, 1.1 Hz, 1H), 7.87 (dd, J = 7.7, 1.8 Hz, 2H), 7.82 – 7.76 (m, 1H), 7.70 – 7.64 (m, 1H), 7.50 – 7.46 (m, 3H), 7.34 (s, 1H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 170.9, 163.3, 148.7, 148.5, 143.3, 130.8, 130.5, 130.4, 130.1, 129.0, 128.2, 127.3, 126.5, 125.9, 124.2, 119.2, 98.5, 98.5.

**HRMS (ESI) m/z:** [M+H]<sup>+</sup>calcd. for: C<sub>19</sub>H<sub>15</sub>N<sub>2</sub>O<sub>2</sub><sup>+</sup>: 307.0633; found 307.0637.



**3-(Isoquinolin-1-yl)-5-phenylisoxazole (4l)**<sup>11,21</sup>. Yield: 93%. yellow solid. Mp: 96-98 °C.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 9.19 (d, J = 8.6 Hz, 1H), 8.65 (d, J = 5.5 Hz, 1H), 7.94 – 7.87 (m, 3H), 7.77 – 7.69 (m, 3H), 7.53 – 7.45 (m, 3H), 7.29 (s, 1H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 169.6, 164.4, 148.5, 142.0, 136.9, 130.5, 130.2, 129.0, 128.4, 127.7, 127.3, 127.0, 126.8, 125.9, 122.2, 101.0.

**HRMS (ESI) m/z:** [M+H]<sup>+</sup>calcd. for: C<sub>18</sub>H<sub>13</sub>N<sub>2</sub>O<sup>+</sup>: 273.1022, found 273.1028.

## Single crystal X-ray diffraction

Crystals of compound **3i** were obtained by slow diffusion from a solution of the compound in  $\text{CHCl}_3$  layered with petroleum ether at room temperature for several days (Figure S1). Crystal data and details of the structure determination are presented in Table S1.

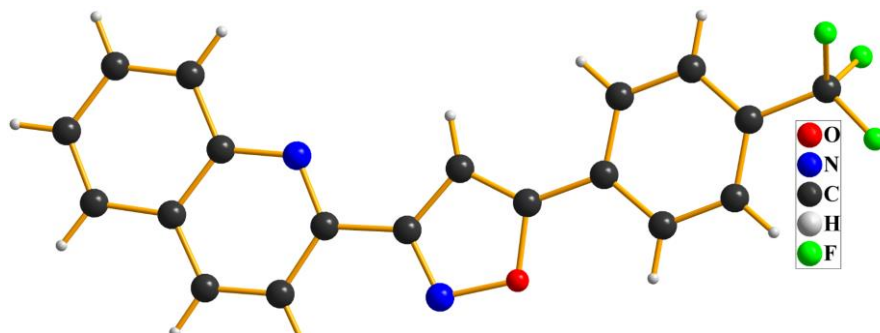


Figure S1. Crystal structure of **3i**

**Table S1:** The single crystal data of compounds **3i**

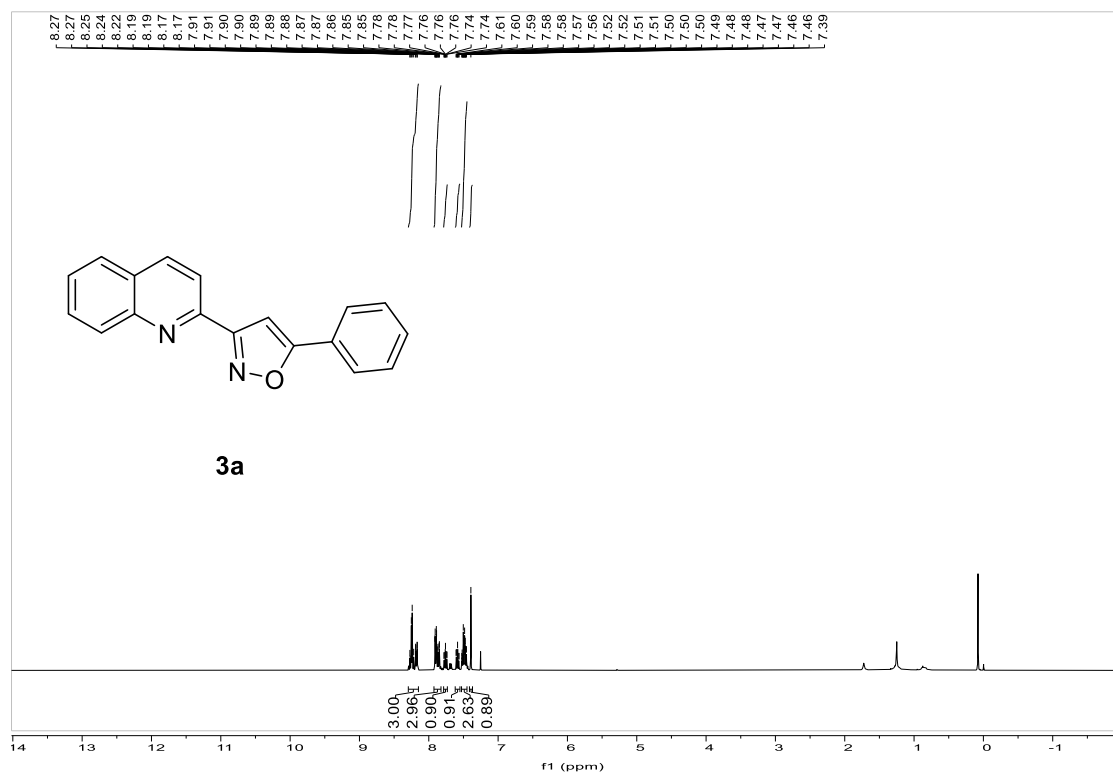
Phase	<b>3i</b>
Identification code	20230826a_a
Empirical formula	C <sub>19</sub> H <sub>11</sub> F <sub>3</sub> N <sub>2</sub> O
Formula weight	340.30
Temperature/K	296
Crystal system	triclinic
Space group	P-1
a/Å	7.2105(9)
b/Å	9.3278(11)
c/Å	12.3469(14)
$\alpha$ /°	90.218(4)
$\beta$ /°	104.858(4)
$\gamma$ /°	102.493(4)
Volume/Å <sup>3</sup>	782.11(16)
Z	2
$\rho_{\text{calc}}/\text{cm}^3$	1.445
$\mu/\text{mm}^{-1}$	0.115
F(000)	348.0
Crystal size/mm <sup>3</sup>	0.2 × 0.18 × 0.08
Radiation	MoK $\alpha$ ( $\lambda$ = 0.71073)
2 $\Theta$ range for data collection/°	3.42 to 55.174
Index ranges	-9 ≤ h ≤ 9, -12 ≤ k ≤ 9, -16 ≤ l ≤ 16
Reflections collected	11926
Independent reflections	3612 [ $R_{\text{int}}$ = 0.0347, $R_{\text{sigma}}$ = 0.0439]
Data/restraints/parameters	3612/0/226
Goodness-of-fit on F <sup>2</sup>	1.033
Final R indexes [ $I \geq 2\sigma(I)$ ]	$R_1$ = 0.0690, $wR_2$ = 0.1686
Final R indexes [all data]	$R_1$ = 0.1190, $wR_2$ = 0.1972
Largest diff. peak/hole / e Å <sup>-3</sup>	0.40/-0.29



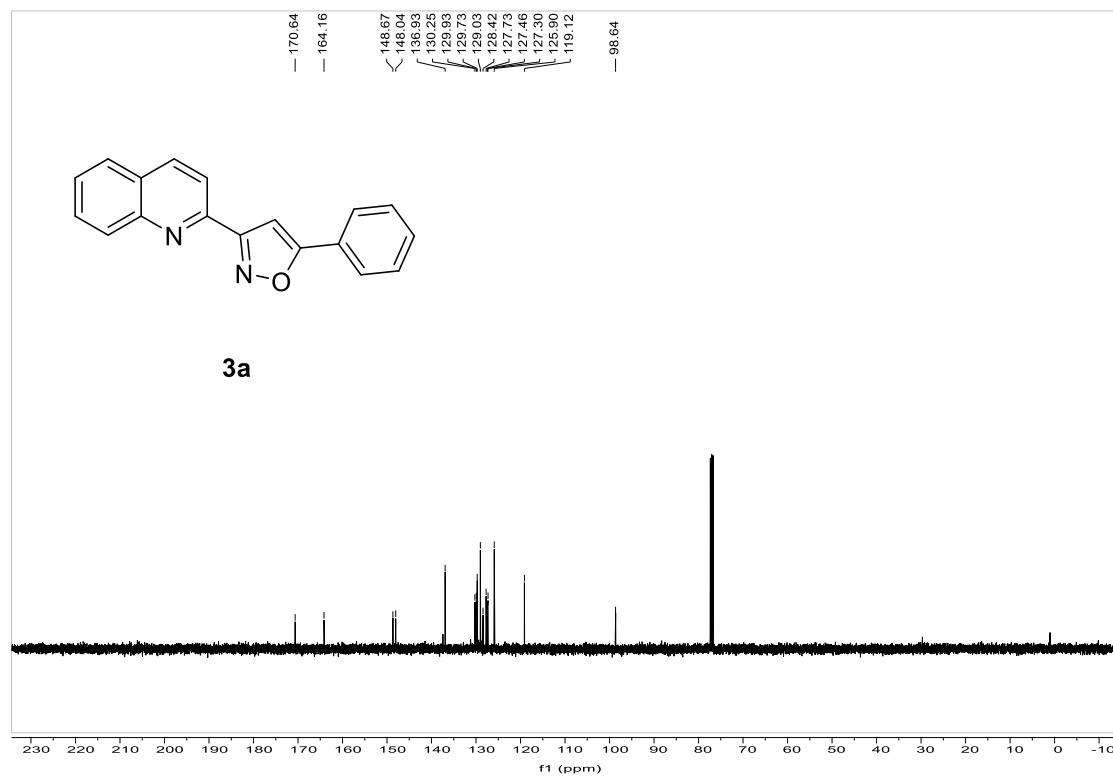
## References

1. Meng, L.; Zhang S.W.; Jia X.D.; Lv I.Z.; Yuan Y. *Tetrahedron Letters*, **2019**, 60, 1443-1447.
2. D, H, Wang.; F, Zhang.; F, H, Xiao.; G,J, Deng.; *Org. Biomol. Chem*, **2019**, 17, 9163-9168.
3. J, M. Pérez.; D, J, Ramón. *ACS Sustainable Chem. Eng.* **2015**, 9, 2343–2349.

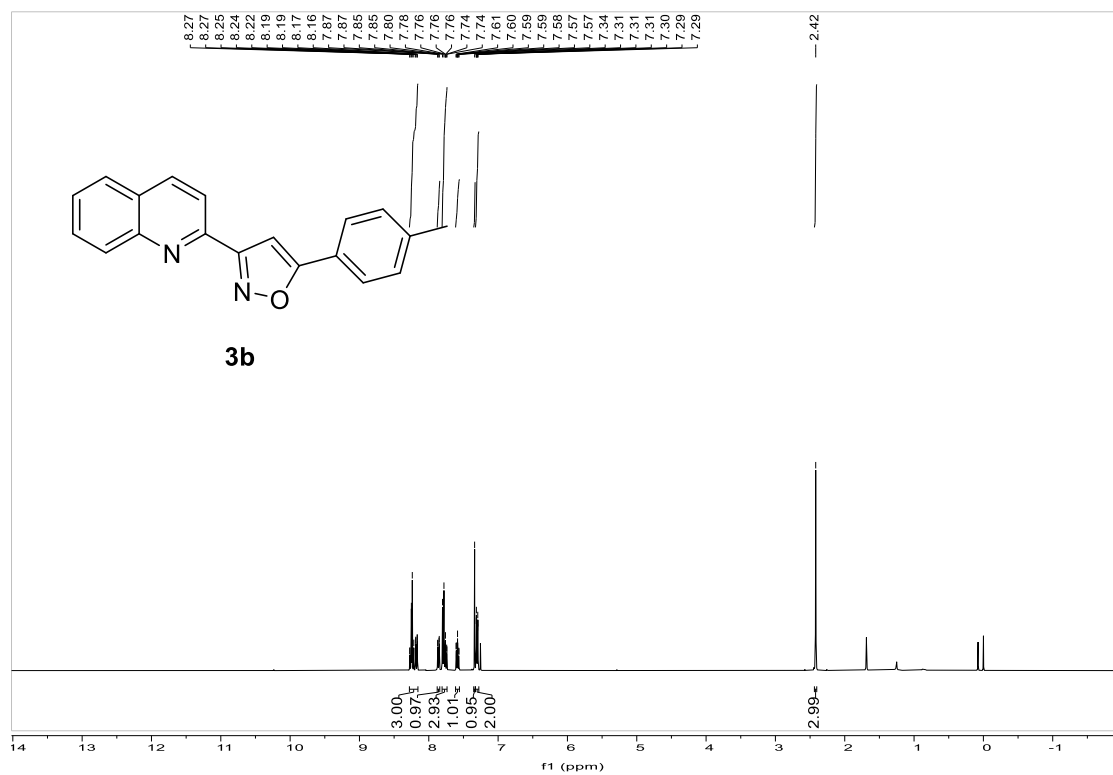
### $^1\text{H}$ NMR spectra of compound **3a**



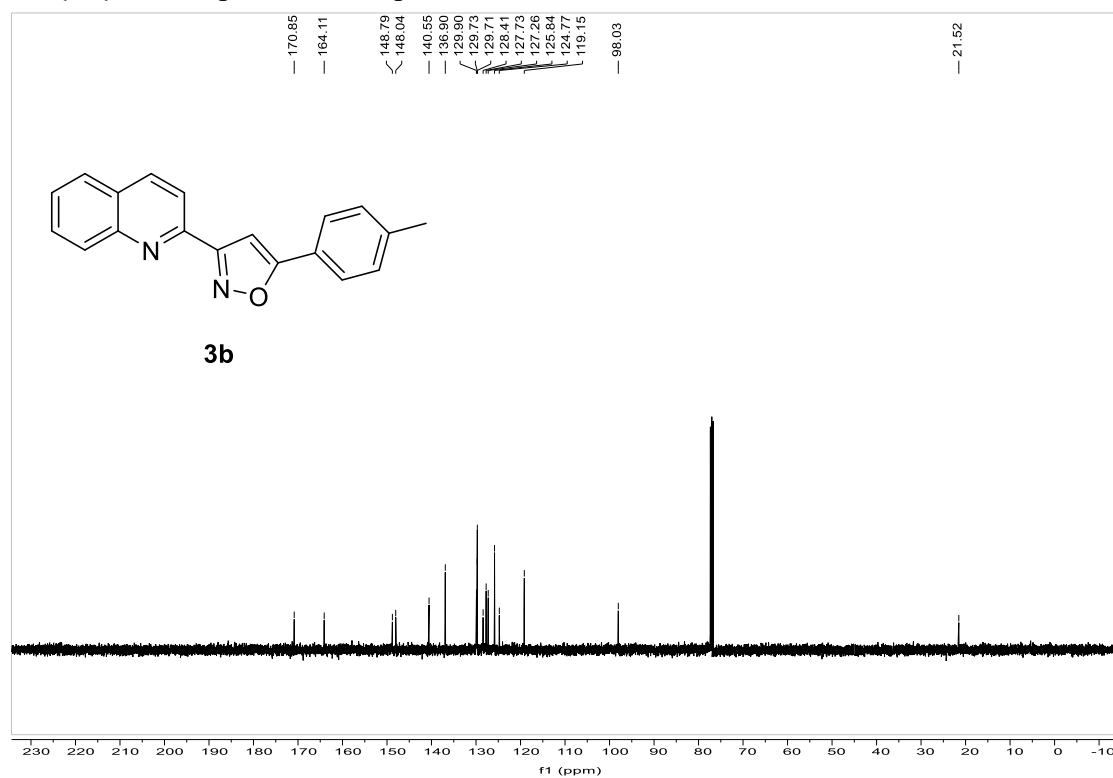
### $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of compound **3a**



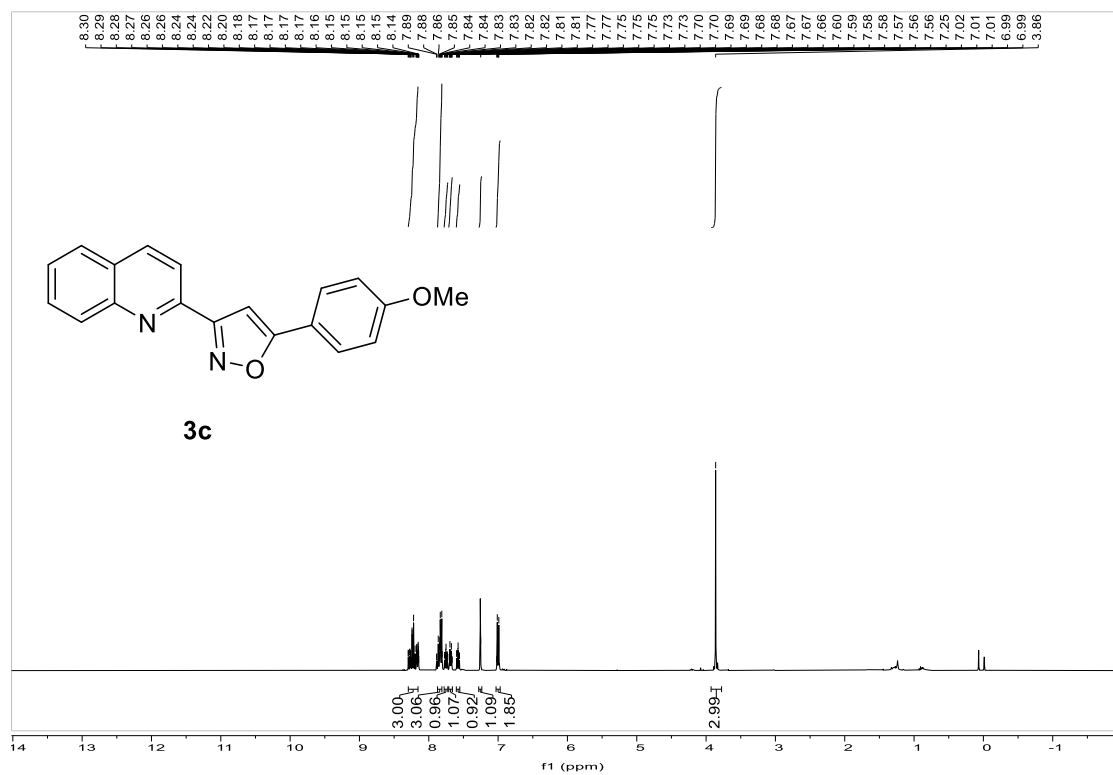
### $^1\text{H}$ NMR spectra of compound **3b**



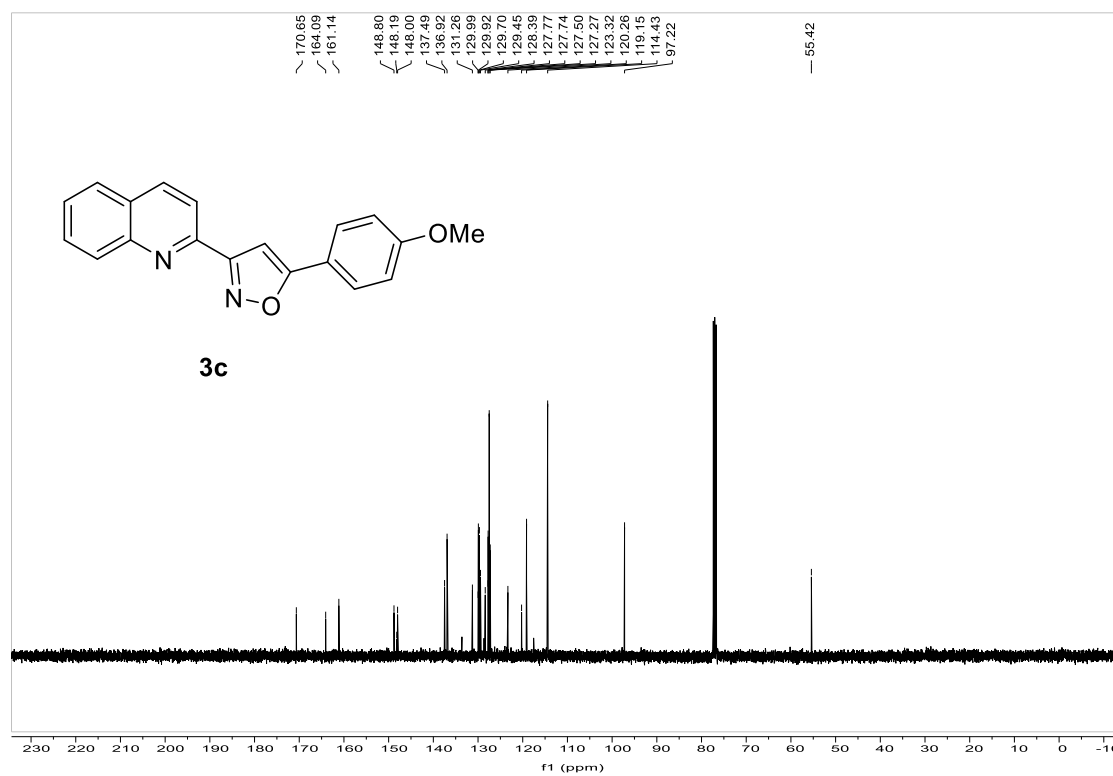
### $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of compound **3b**



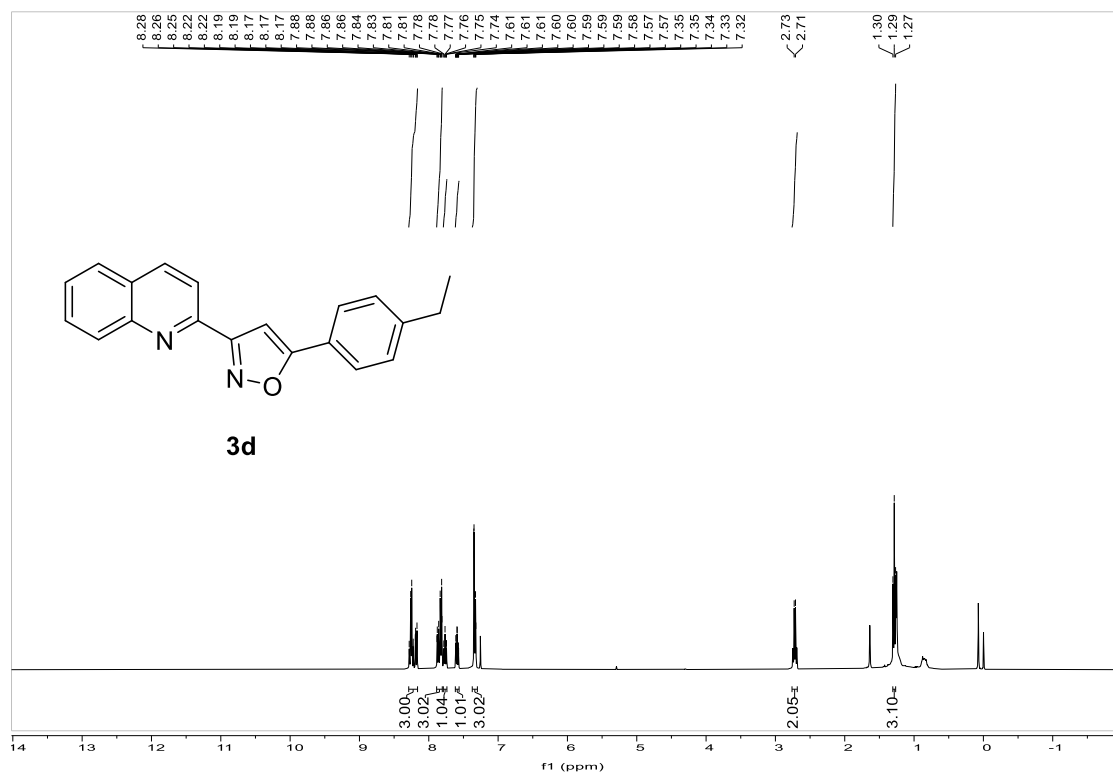
### $^1\text{H}$ NMR spectra of compound **3c**



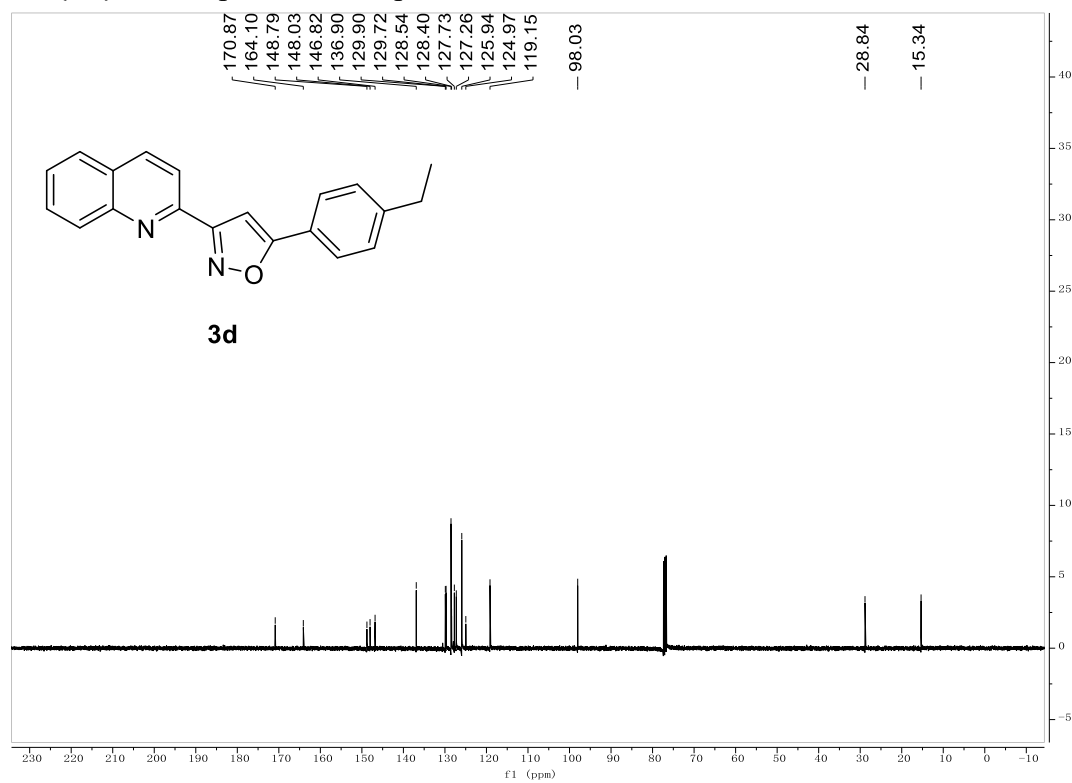
### $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of compound **3c**



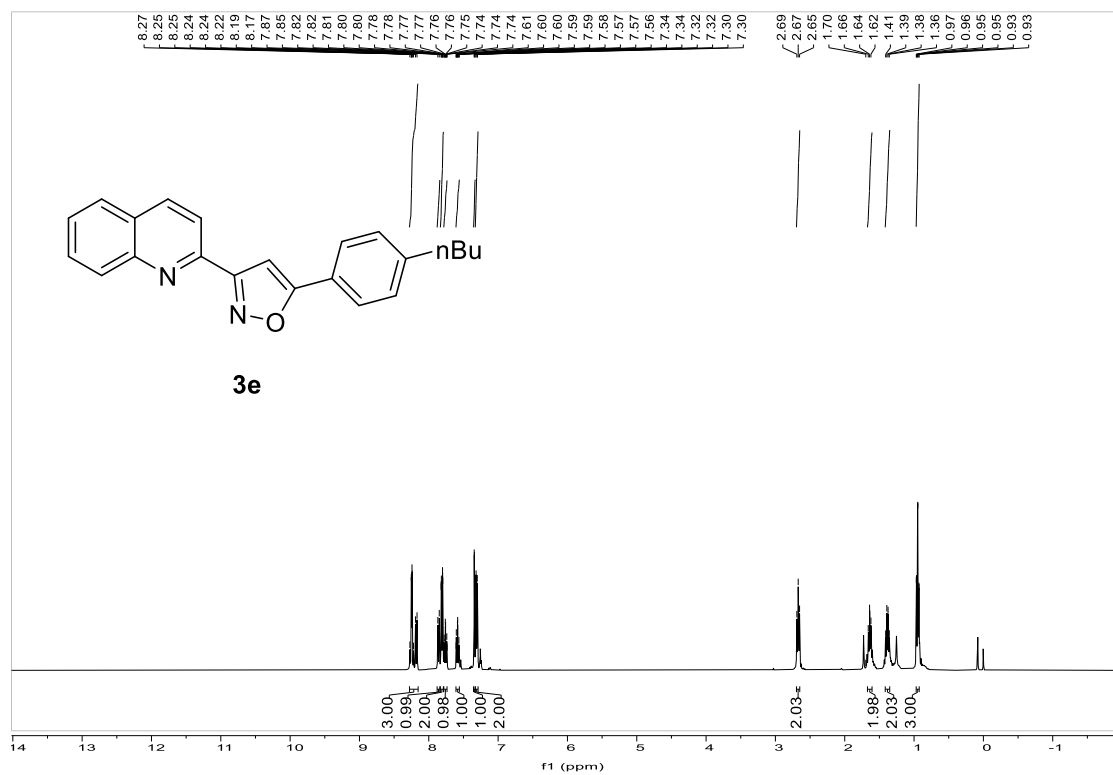
$^1\text{H}$  NMR spectra of compound **3d**



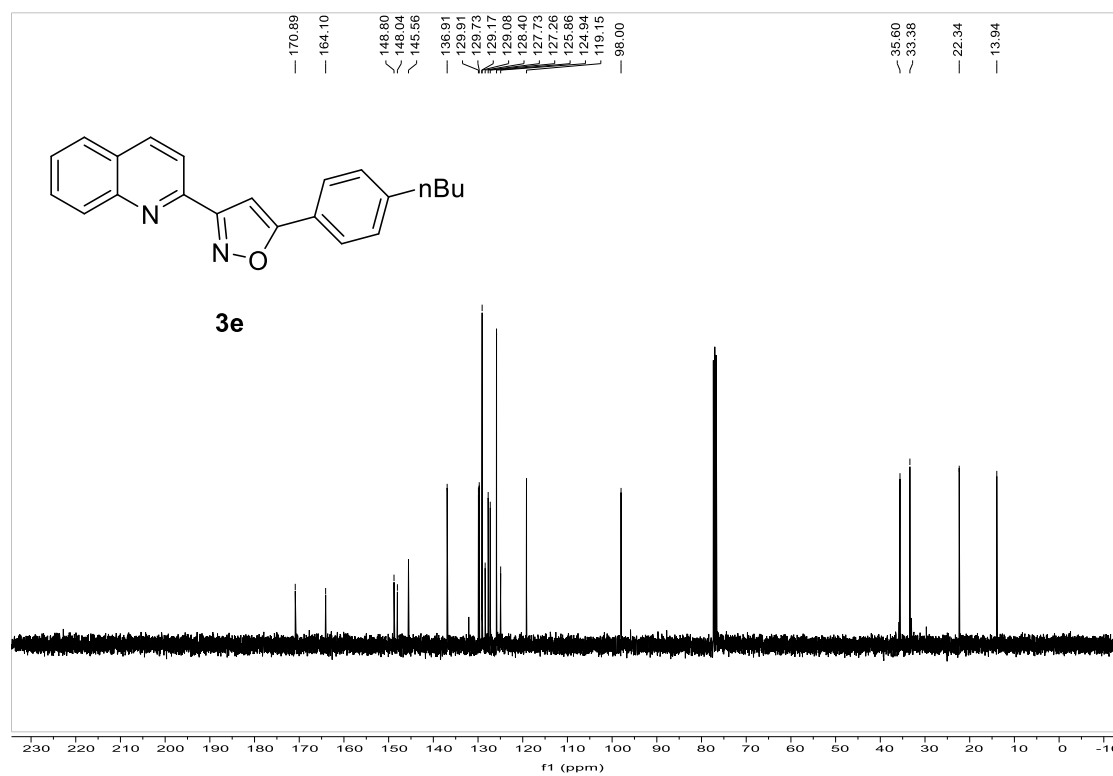
$^{13}\text{C}\{^1\text{H}\}$  NMR spectra of compound **3d**



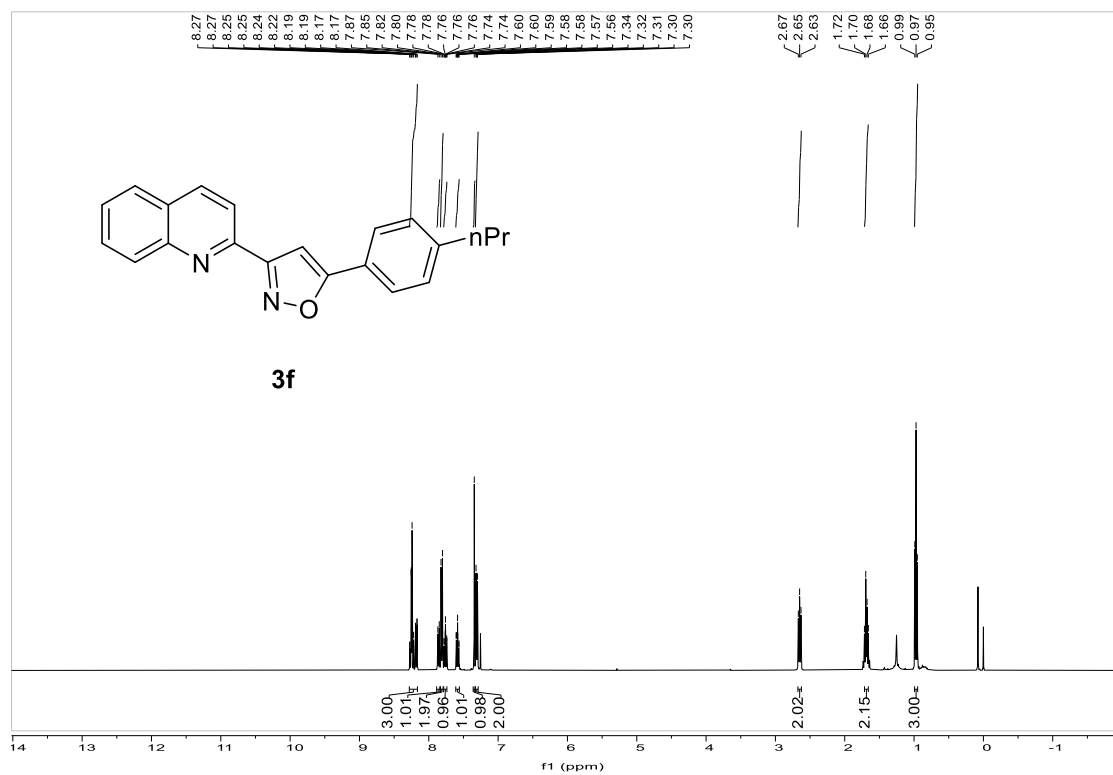
$^1\text{H}$  NMR spectra of compound **3e**



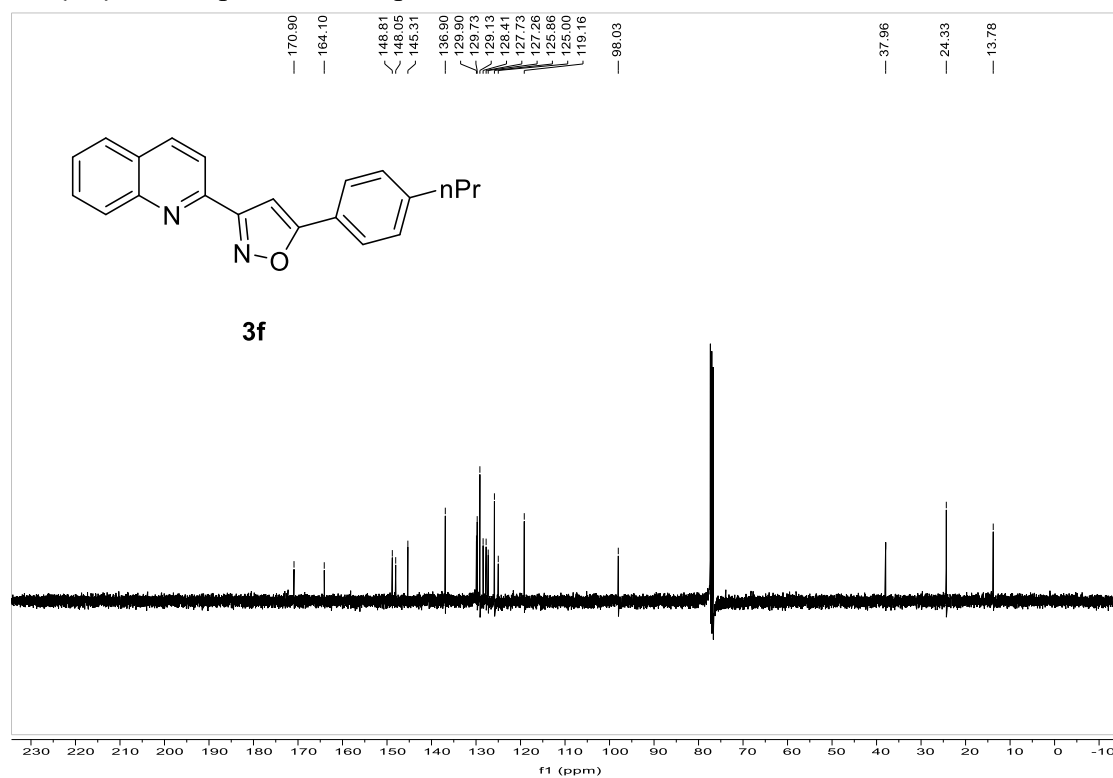
$^{13}\text{C}\{^1\text{H}\}$  NMR spectra of compound **3e**



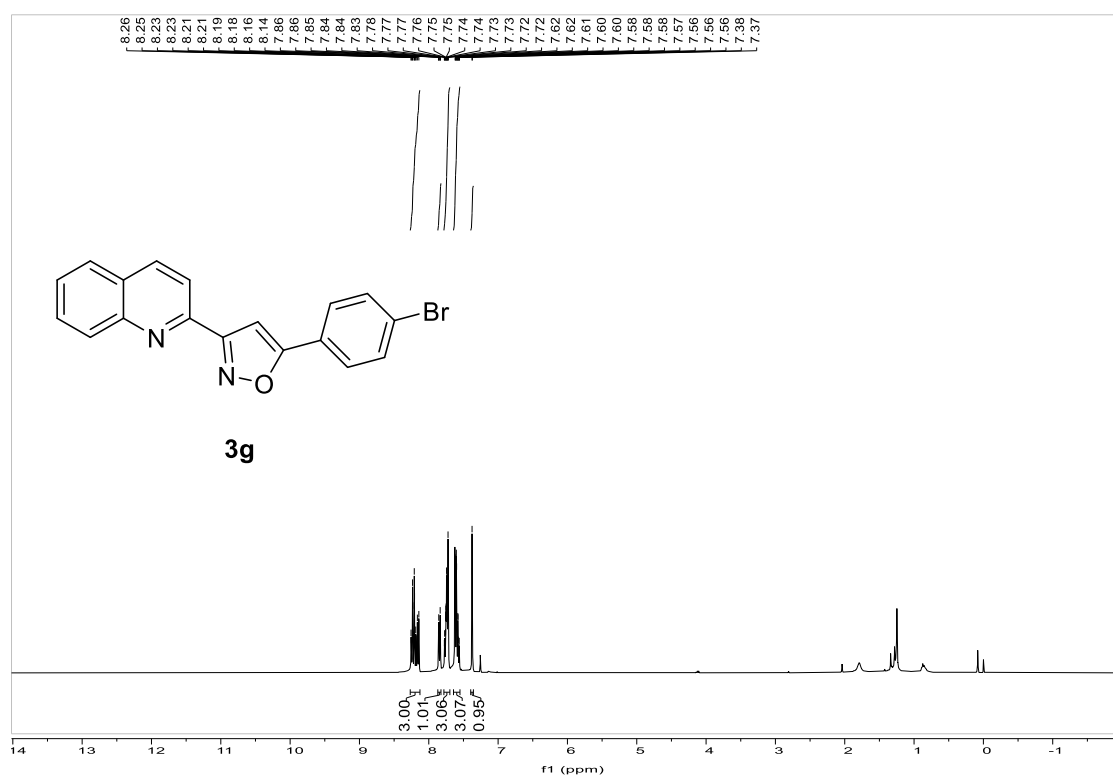
### $^1\text{H}$ NMR spectra of compound **3f**



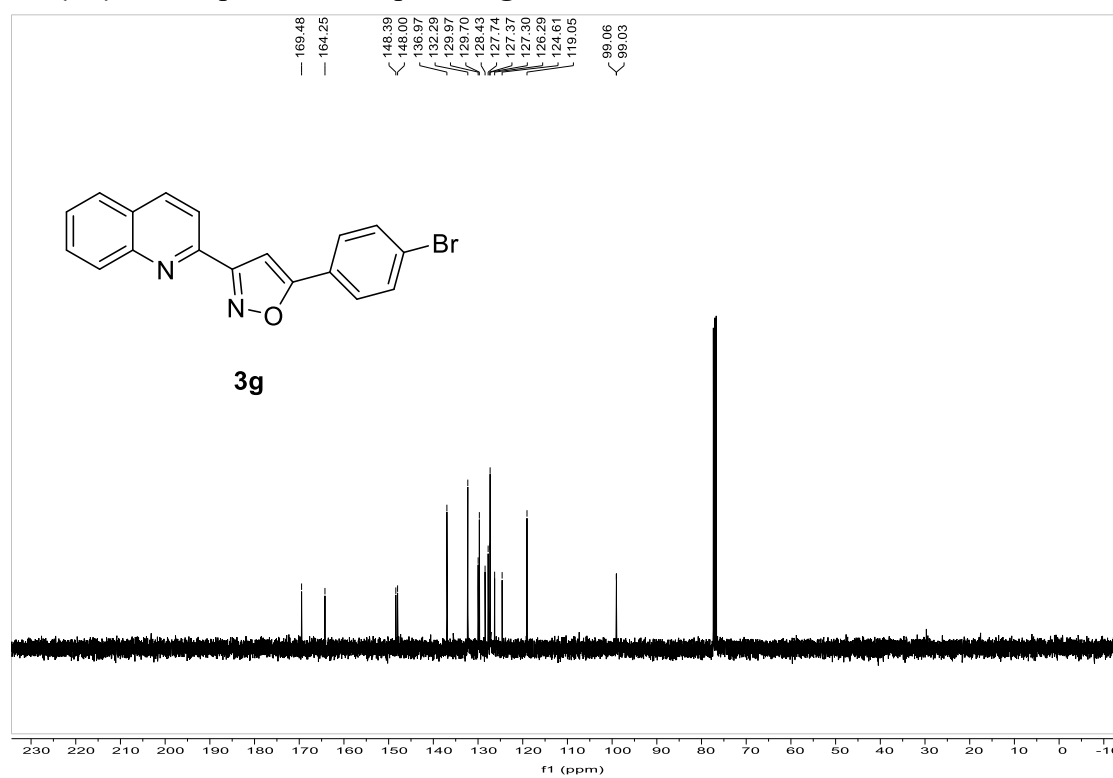
### $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of compound **3f**



### $^1\text{H}$ NMR spectra of compound **3g**

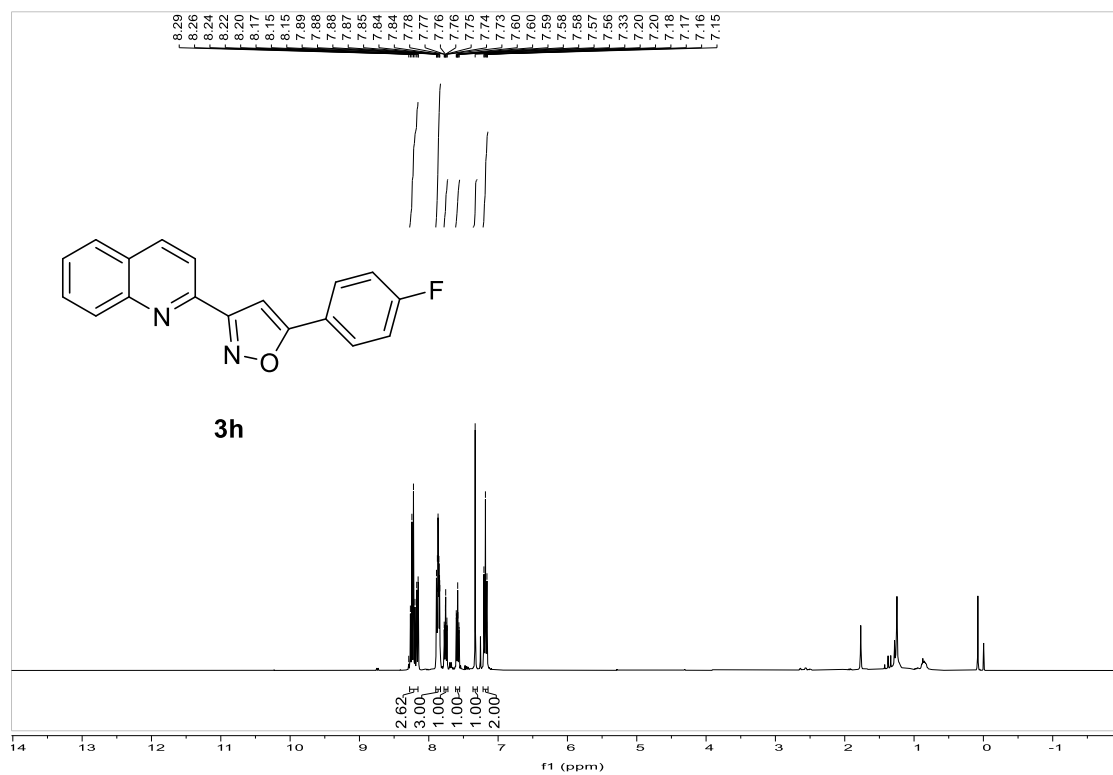


### $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of compound **3g**

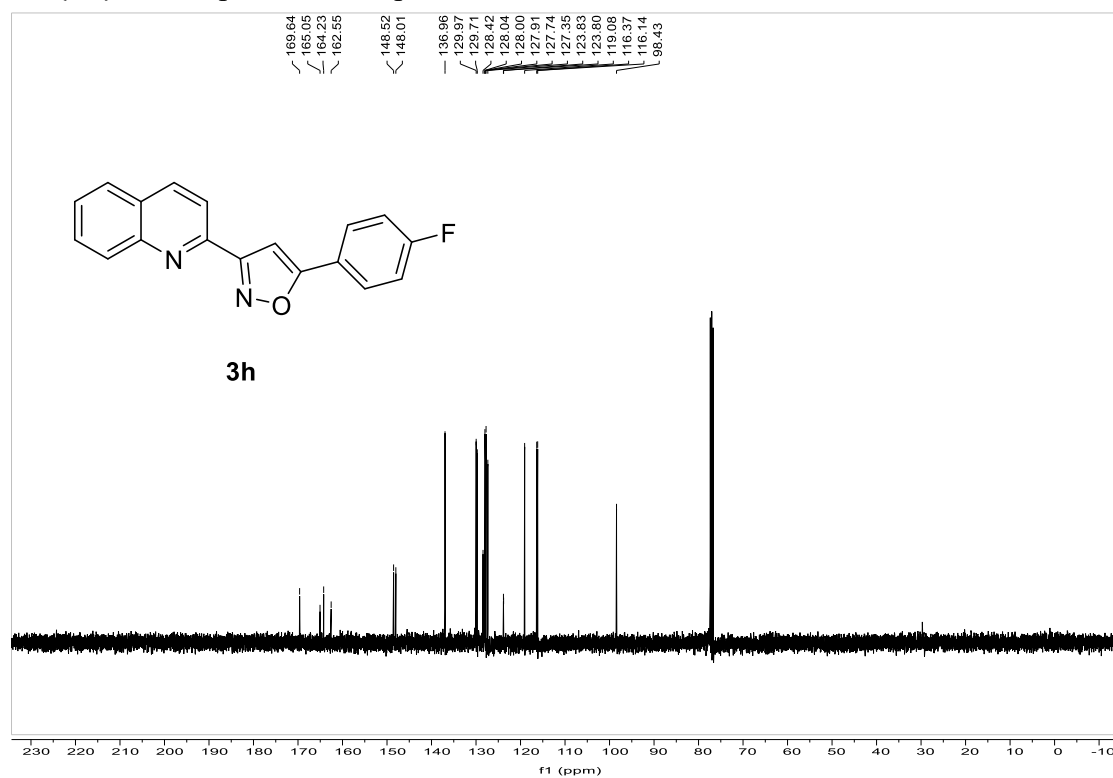




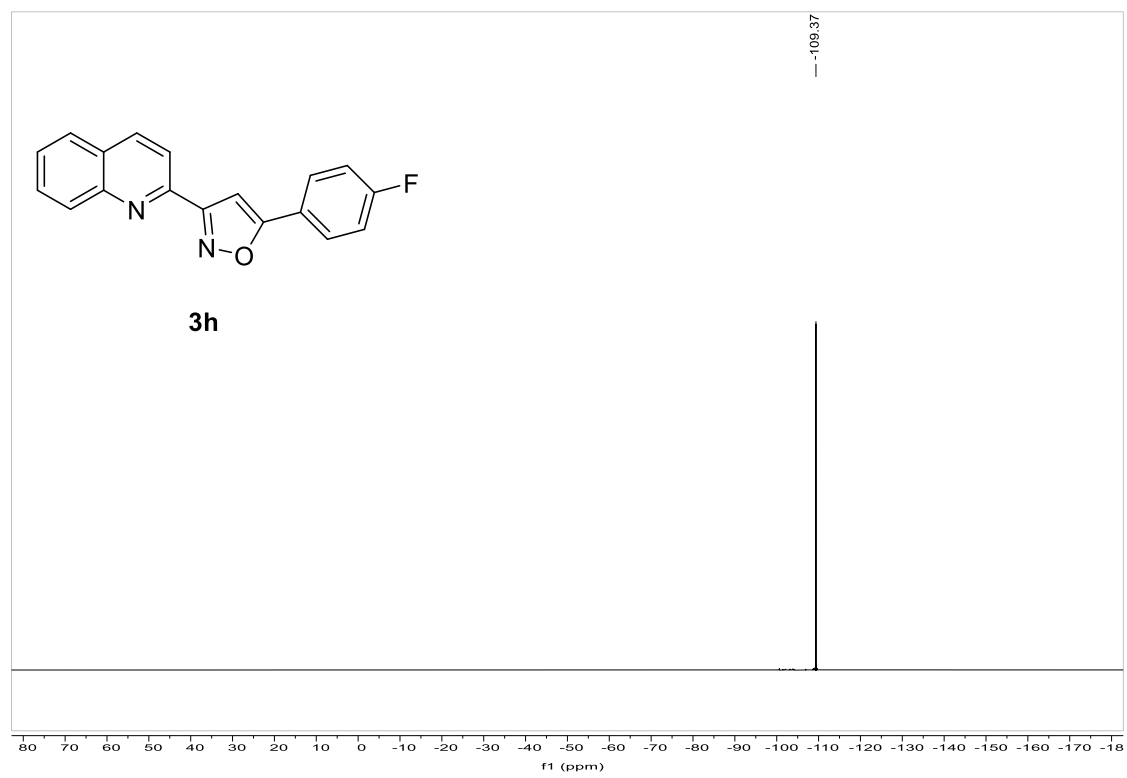
### $^1\text{H}$ NMR spectra of compound **3h**



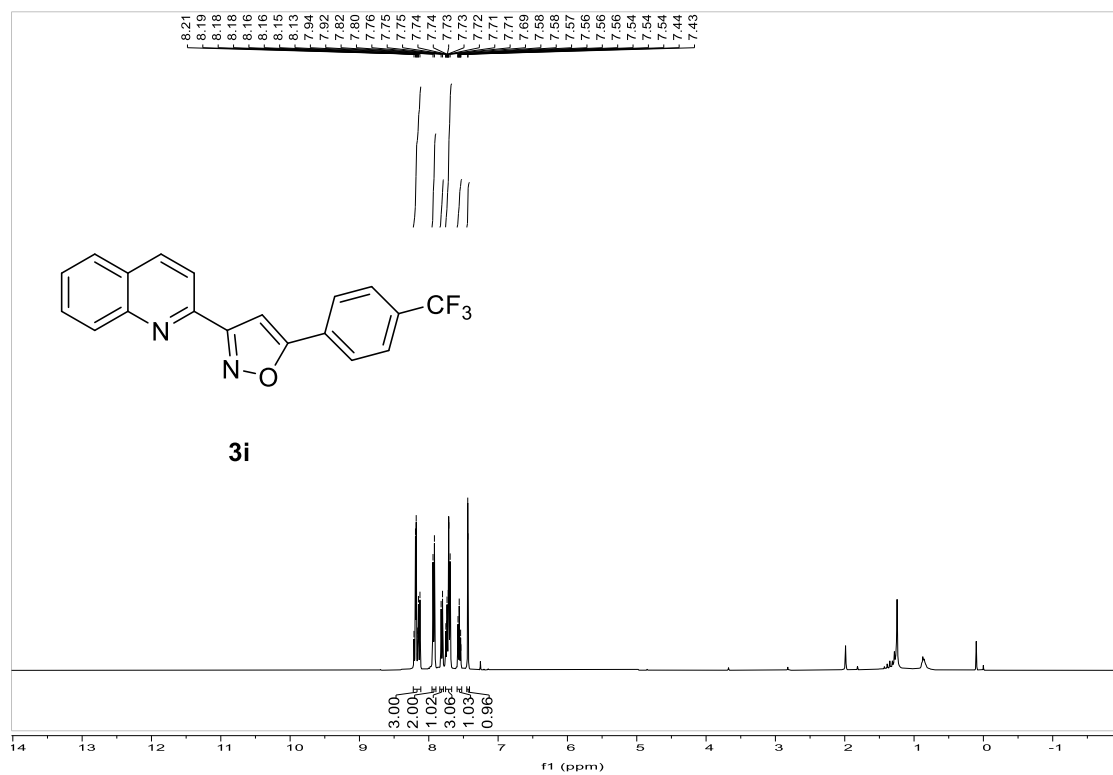
### $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of compound **3h**



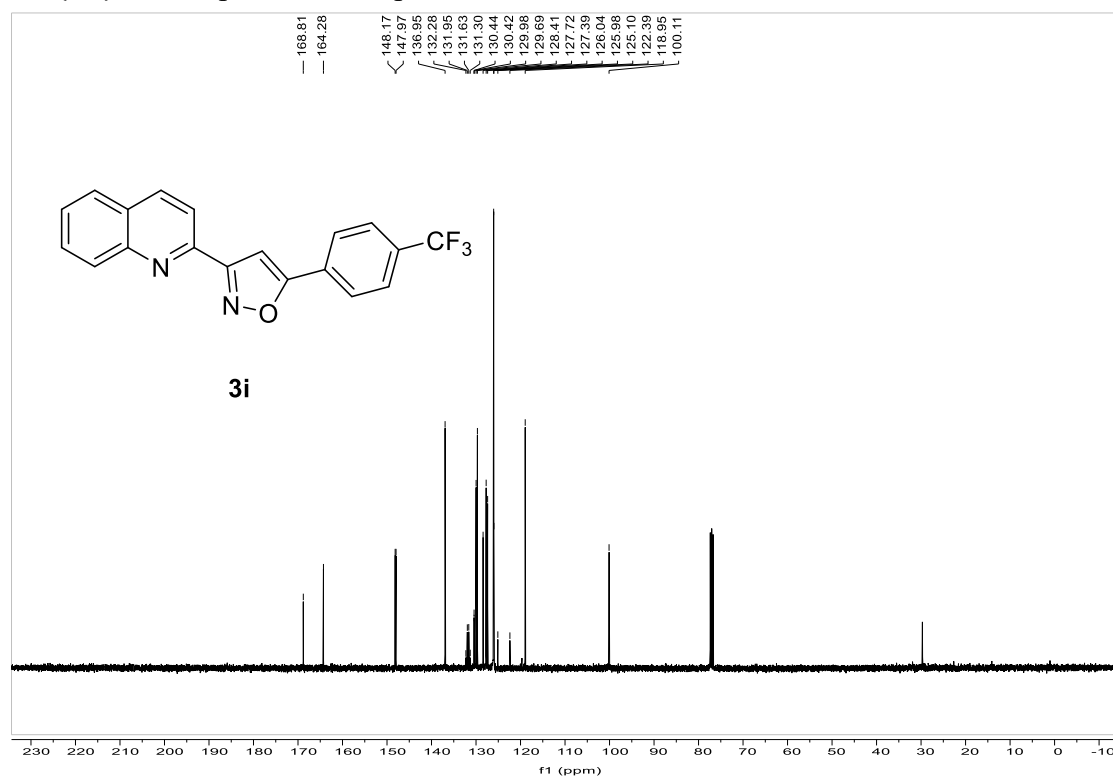
<sup>19</sup>F NMR spectra of compound **3h**



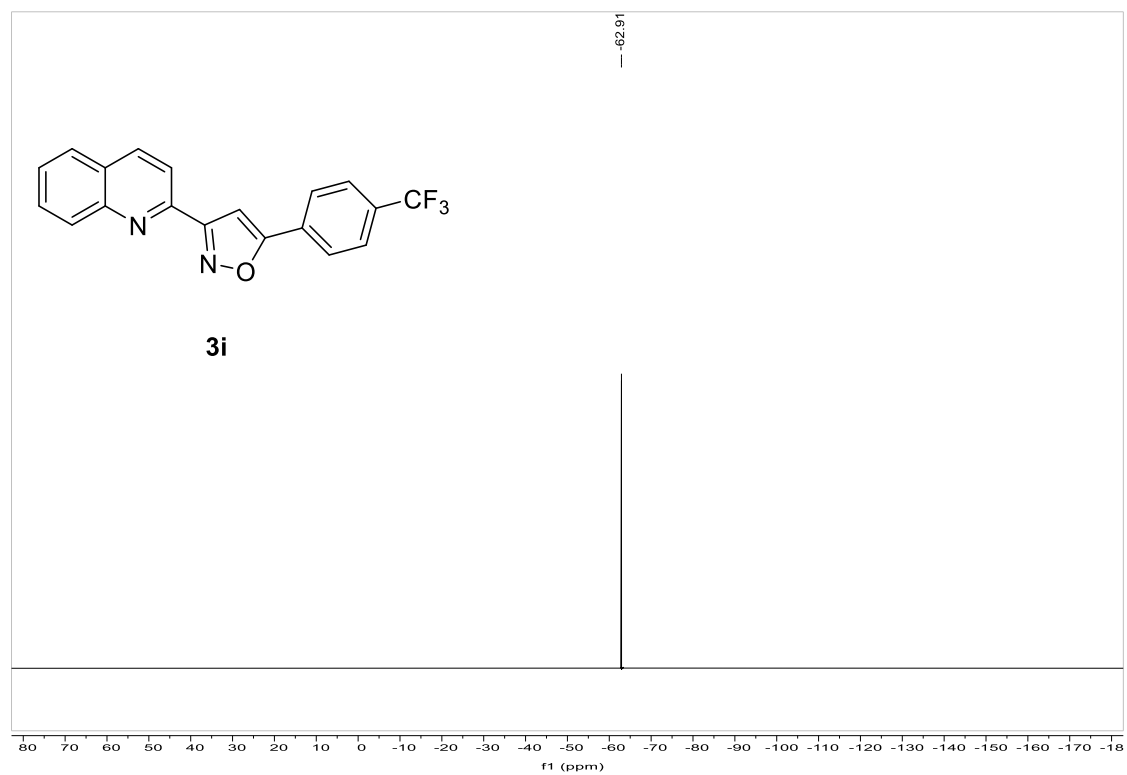
<sup>1</sup>H NMR spectra of compound **3i**



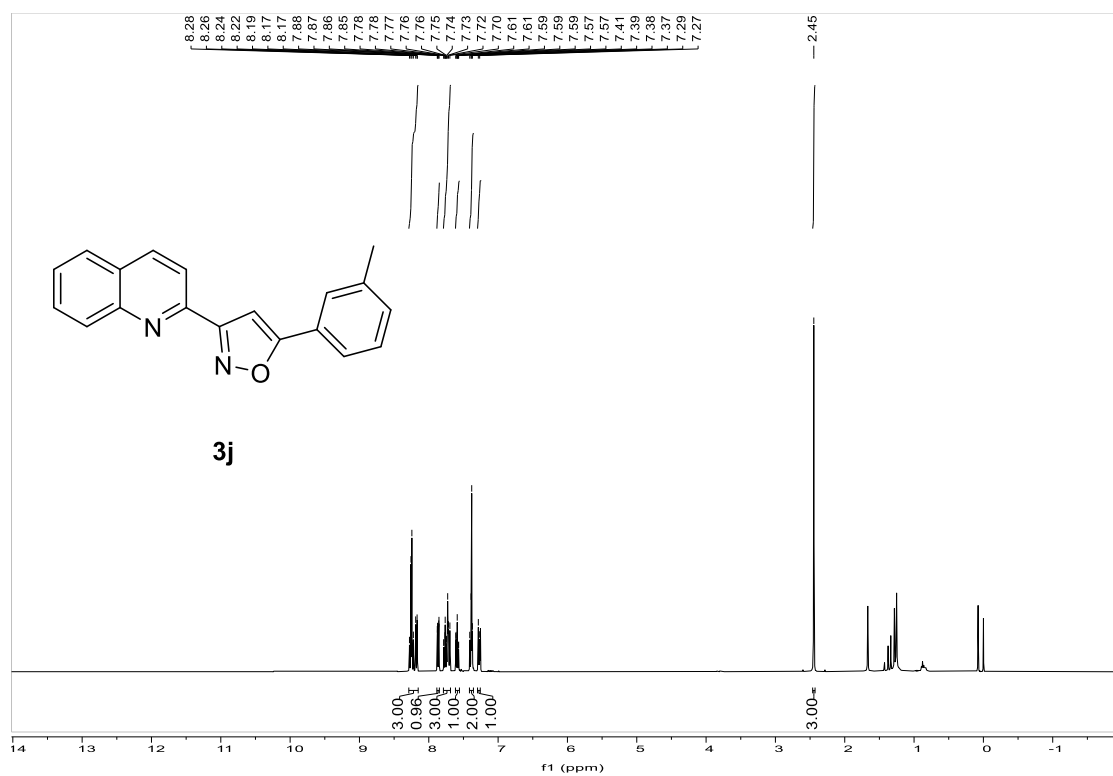
<sup>13</sup>C{<sup>1</sup>H} NMR spectra of compound **3i**



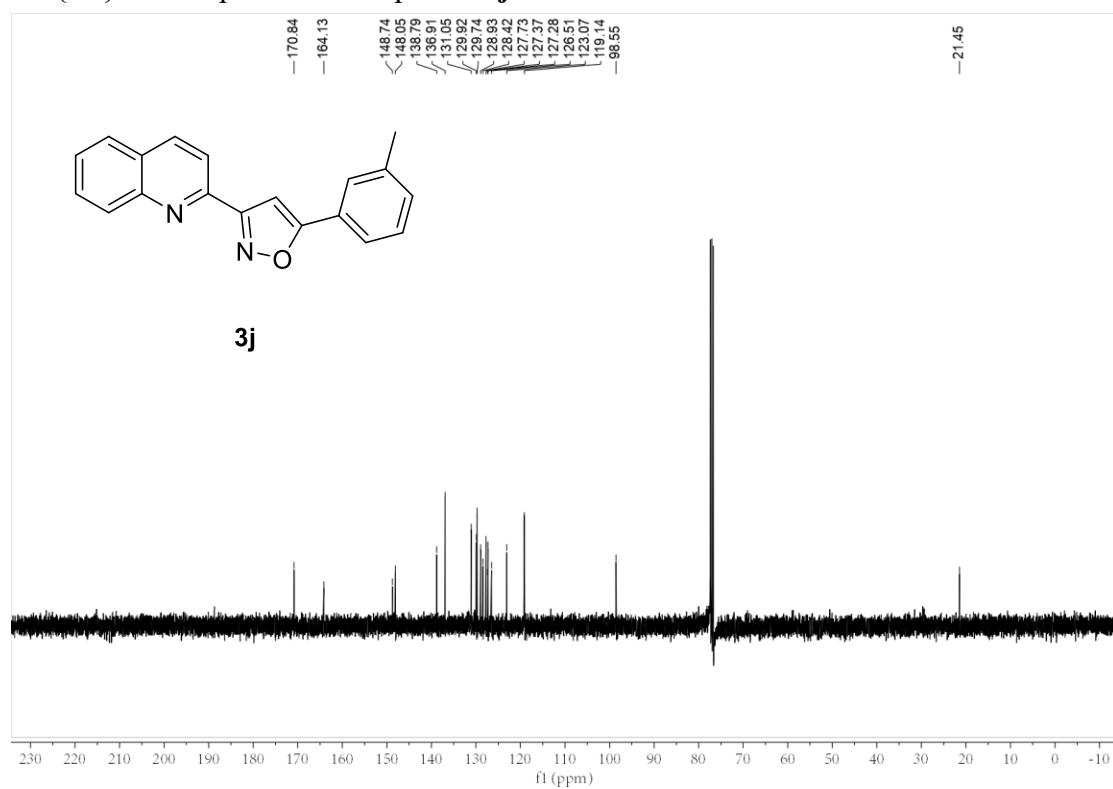
<sup>19</sup>F NMR spectra of compound **3i**



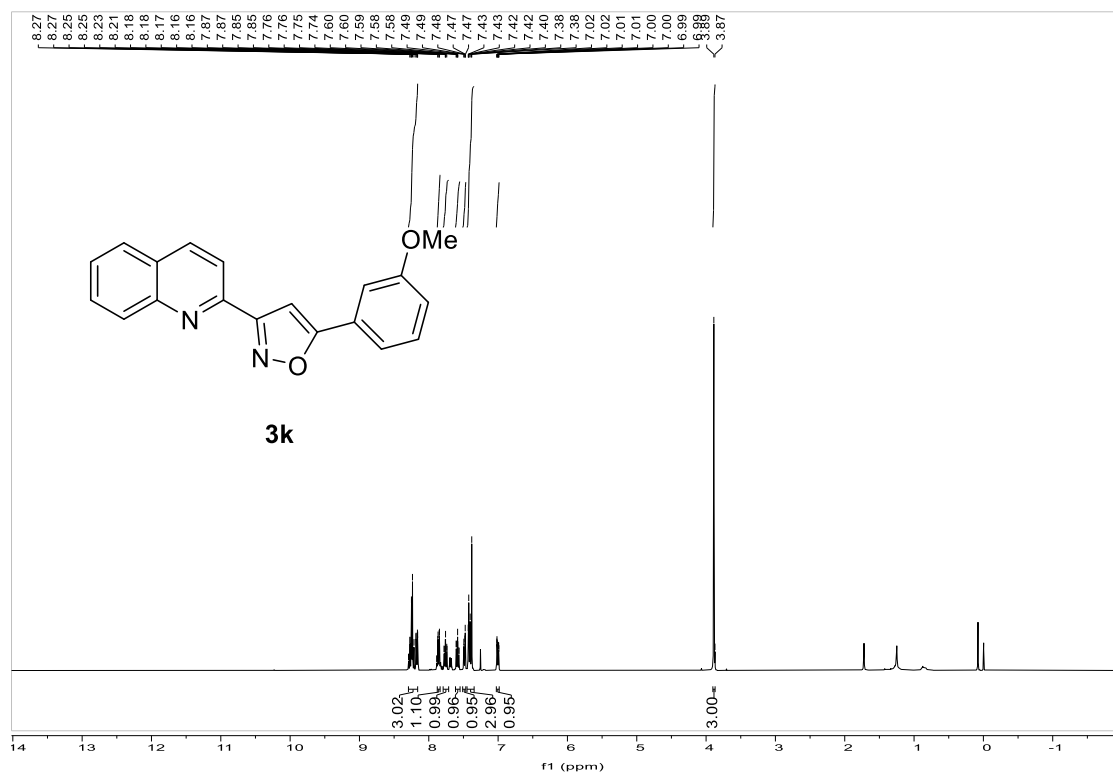
### $^1\text{H}$ NMR spectra of compound **3j**



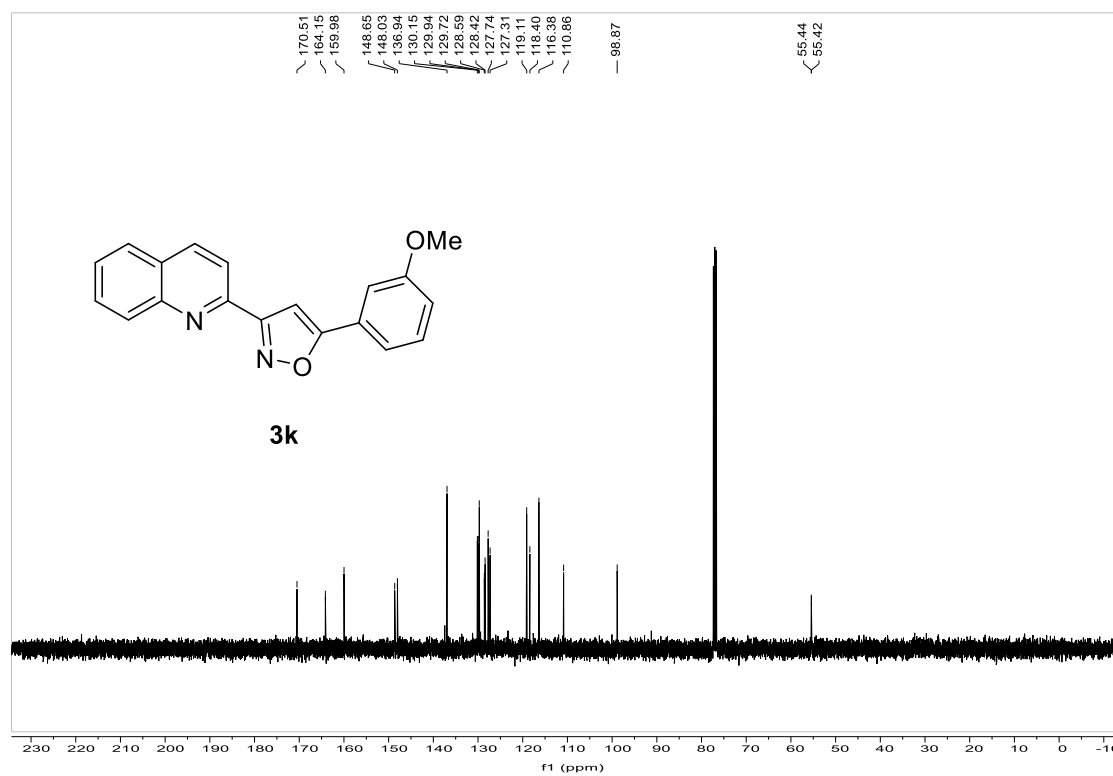
### $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of compound **3j**



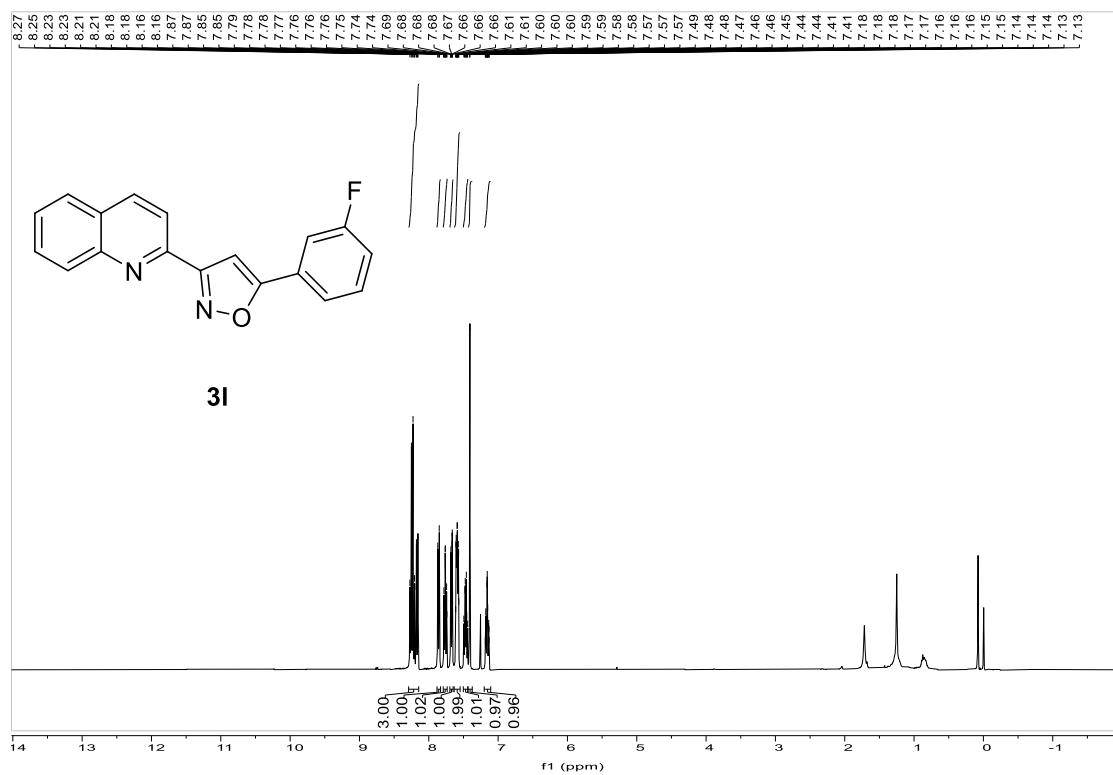
$^1\text{H}$  NMR spectra of compound **3k**



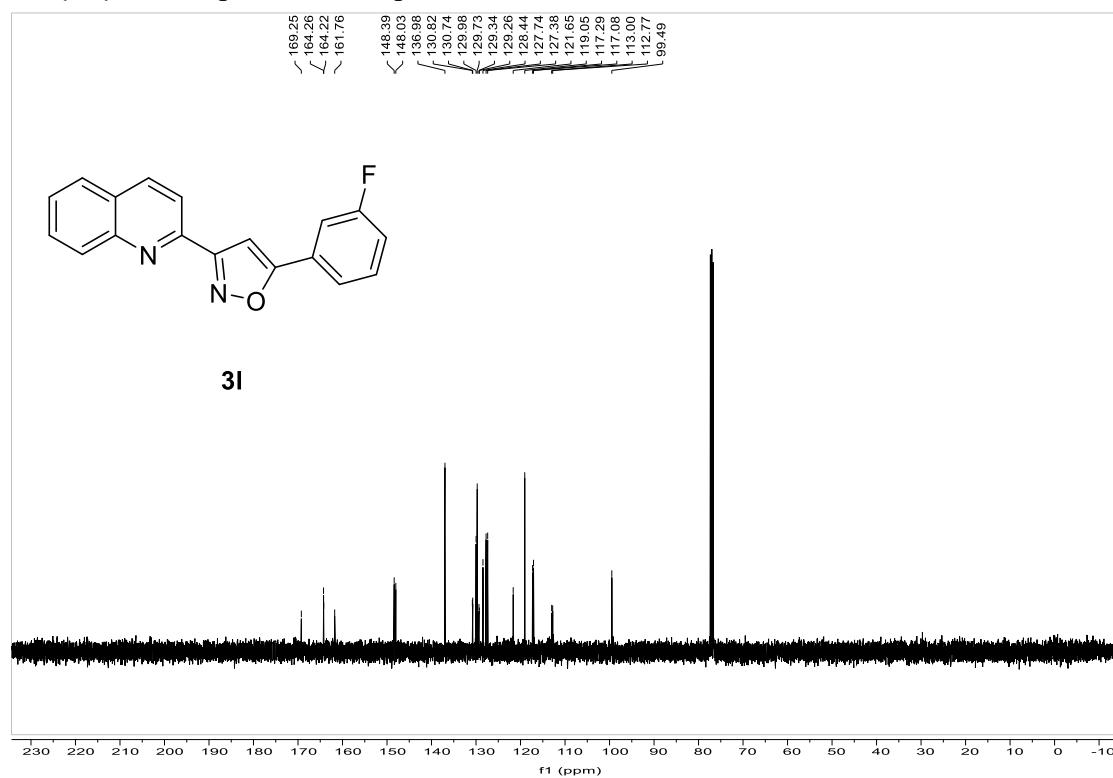
$^{13}\text{C}\{^1\text{H}\}$  NMR spectra of compound **3k**



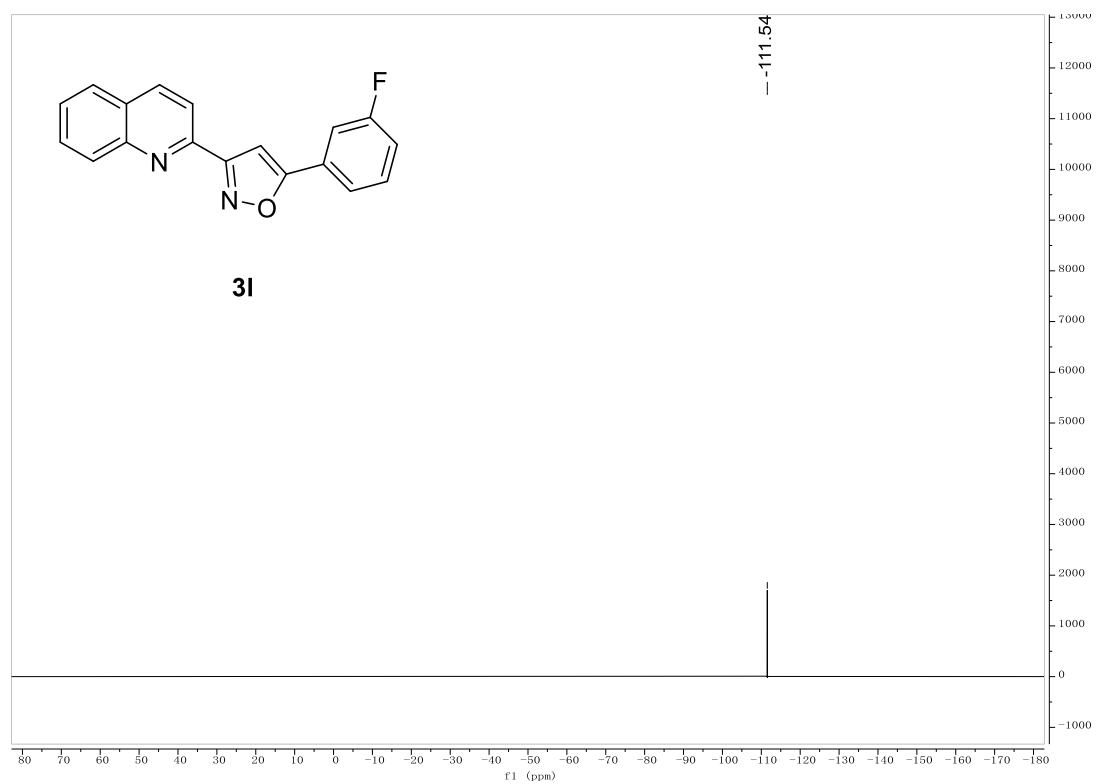
### $^1\text{H}$ NMR spectra of compound **3I**



### $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of compound **3I**

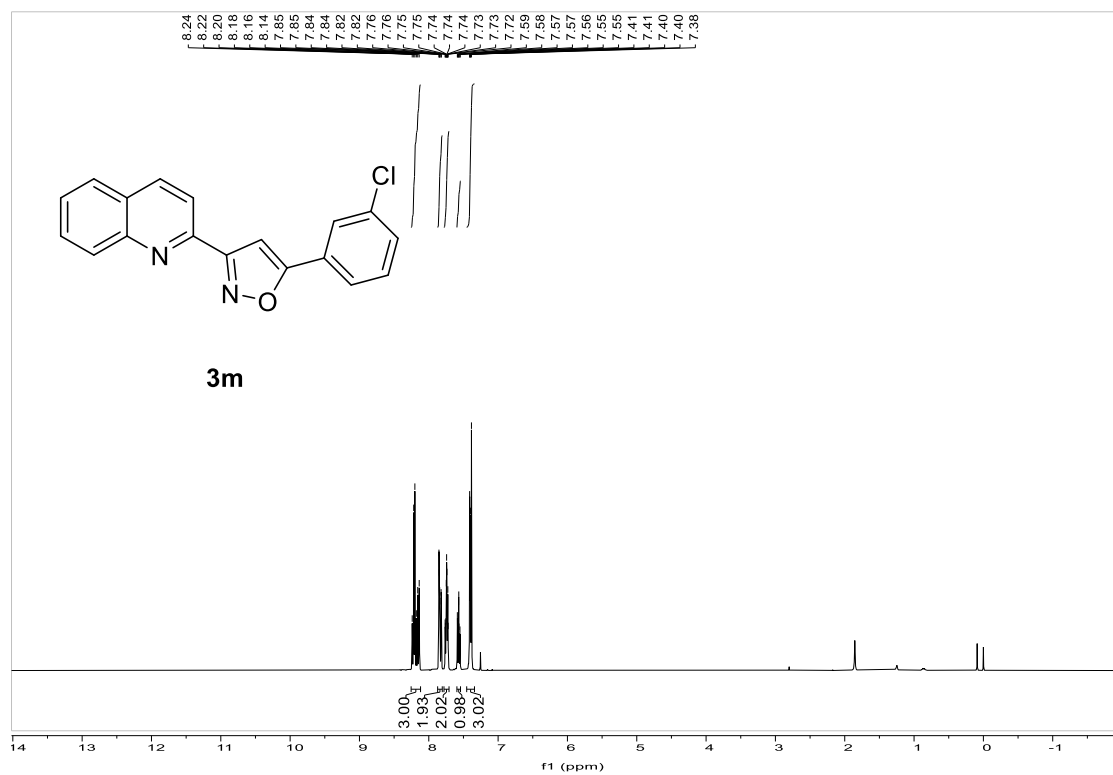


<sup>19</sup>F NMR spectra of compound 31

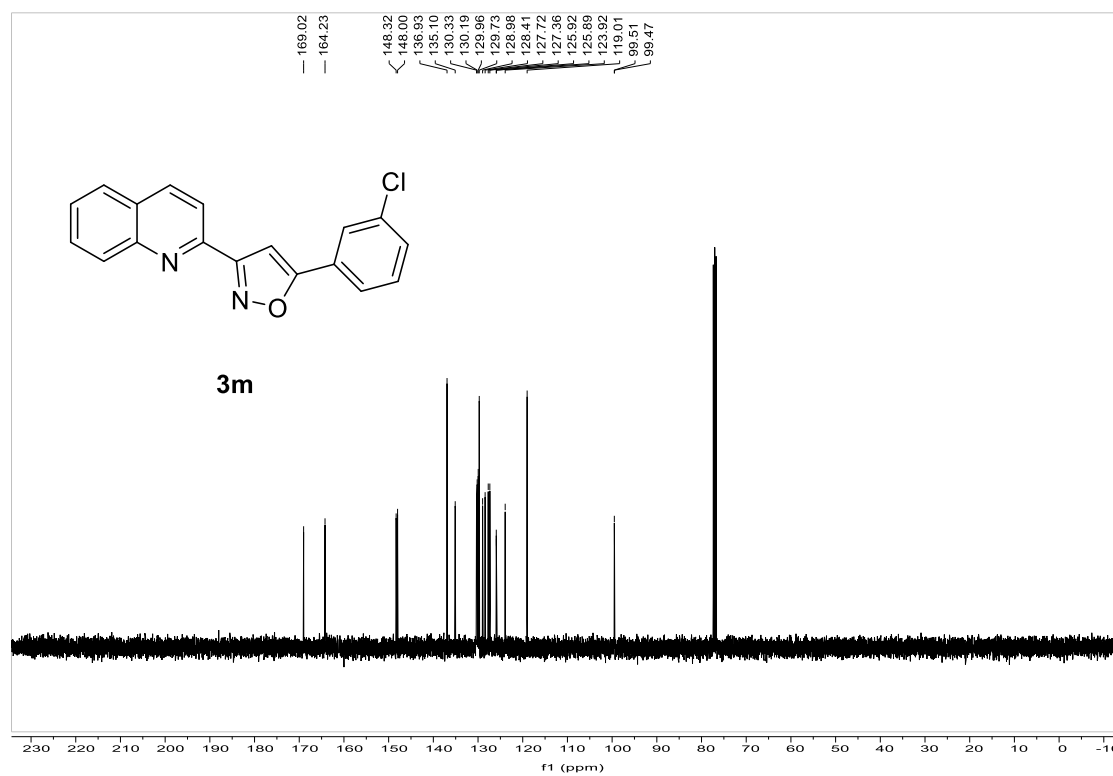




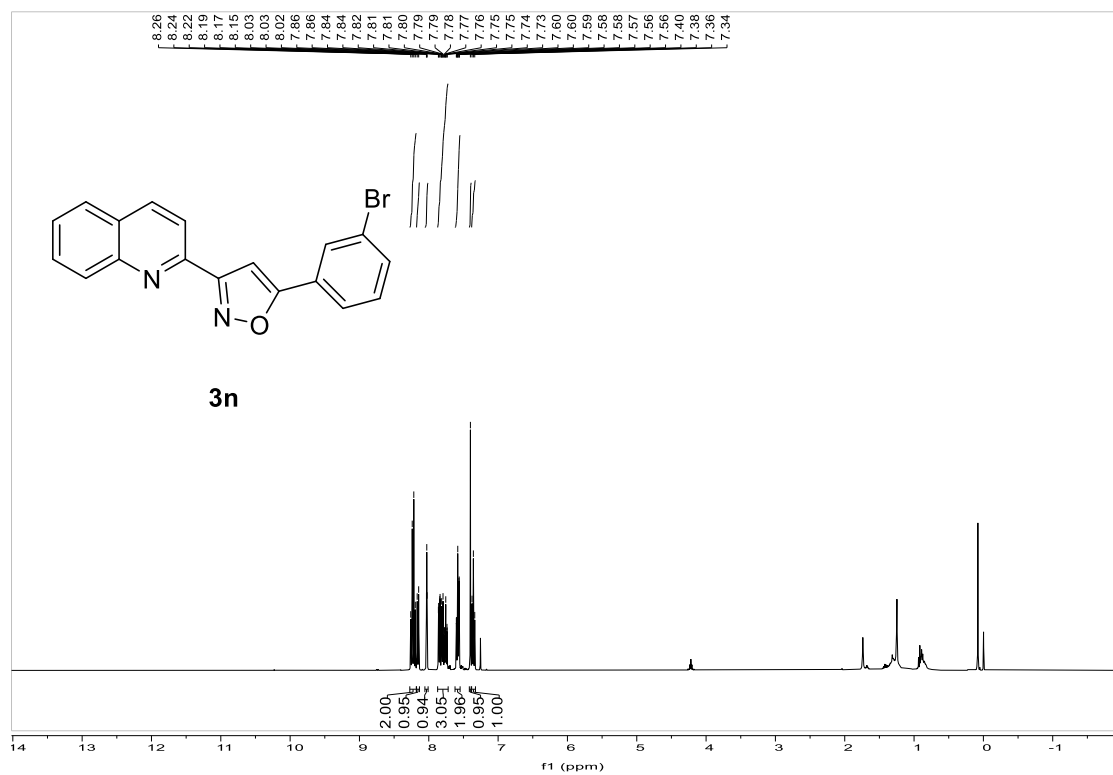
### $^1\text{H}$ NMR spectra of compound **3m**



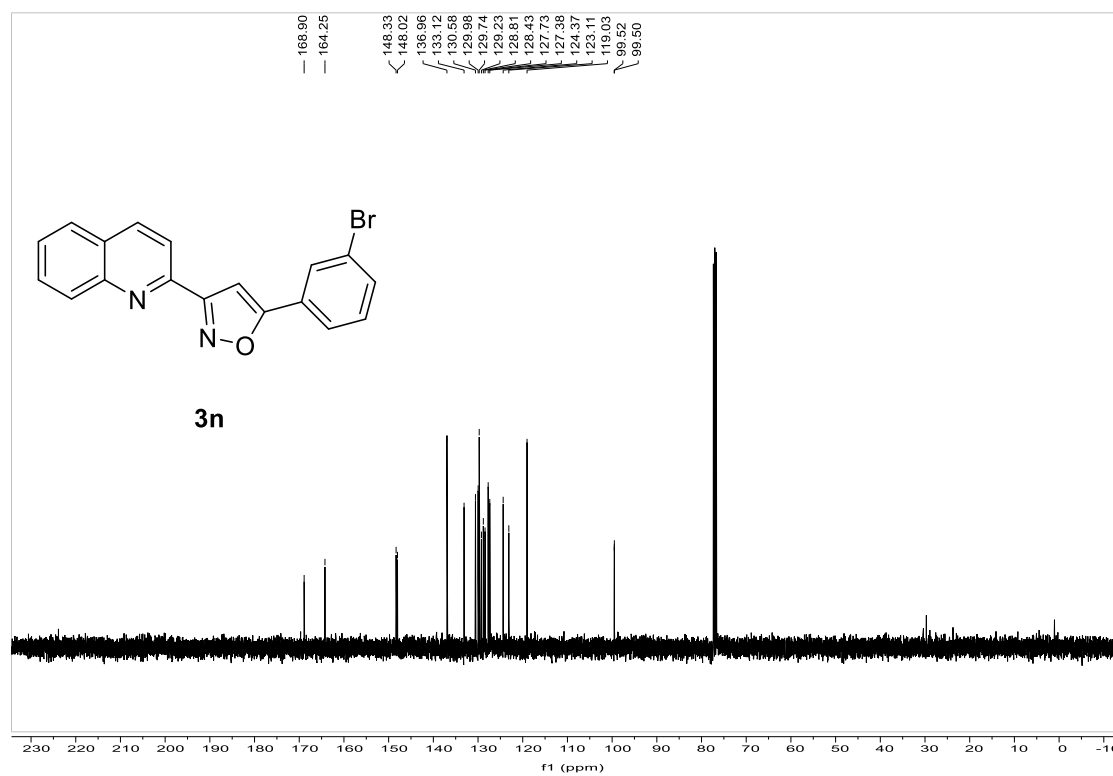
### $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of compound **3m**



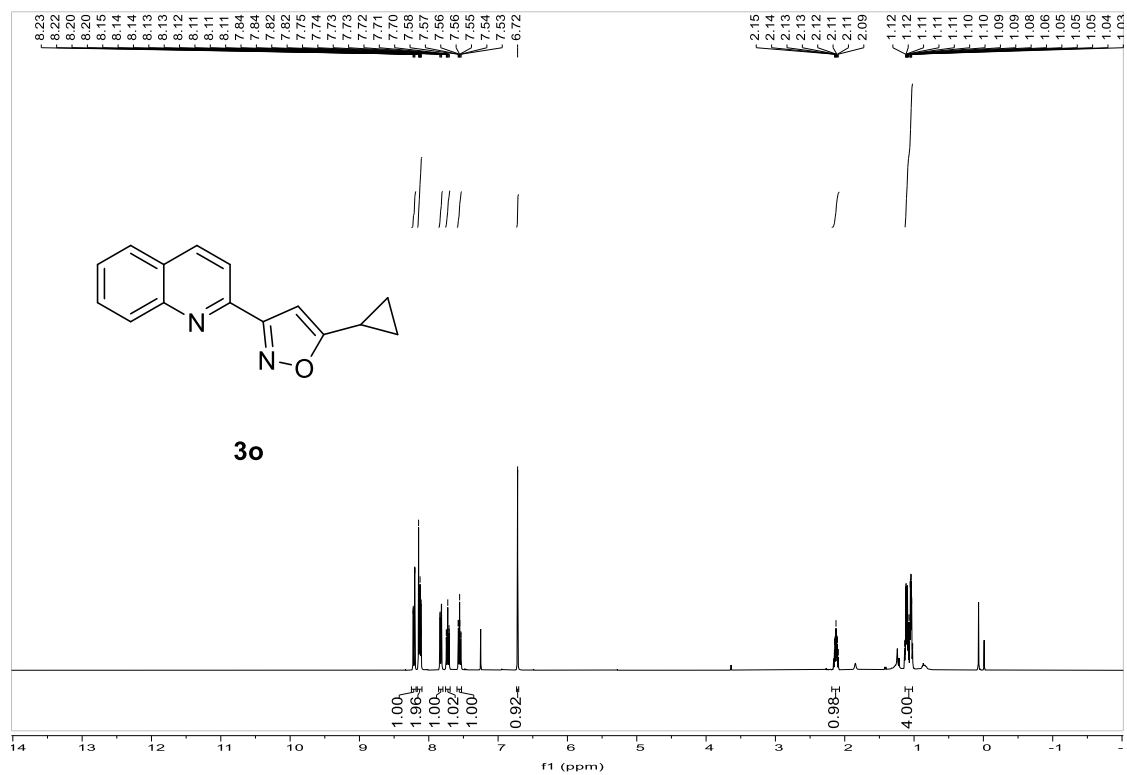
### $^1\text{H}$ NMR spectra of compound **3n**



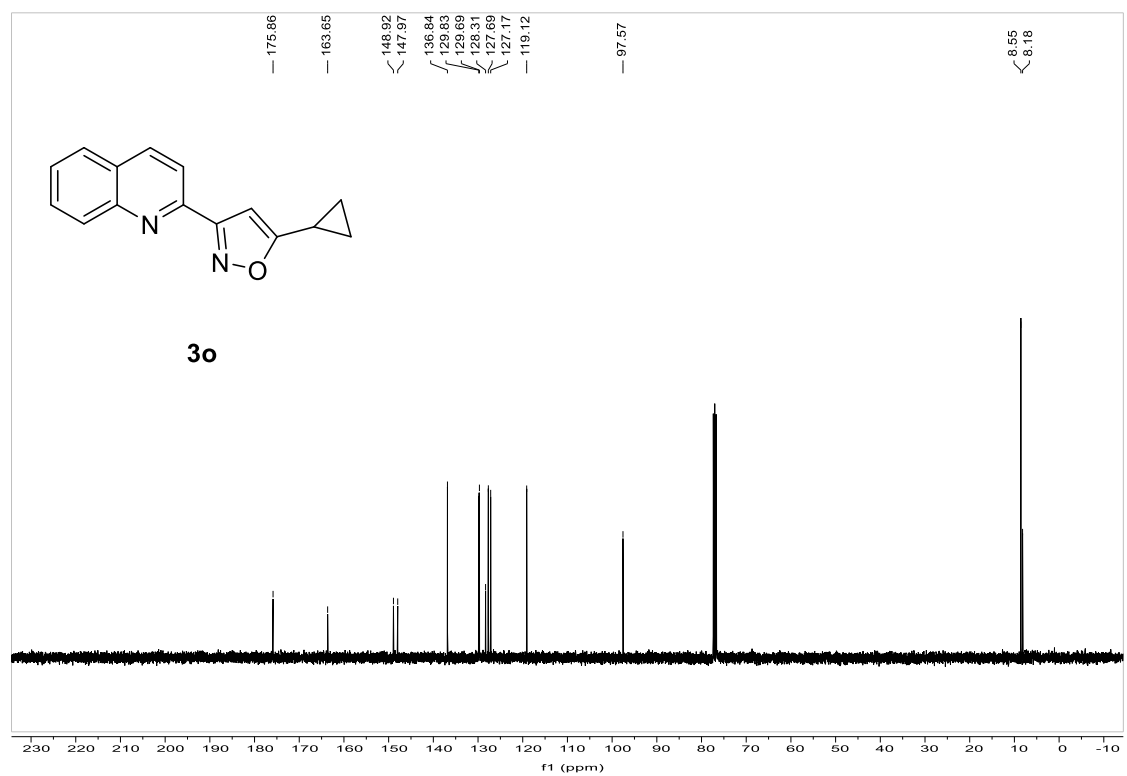
### $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of compound **3n**



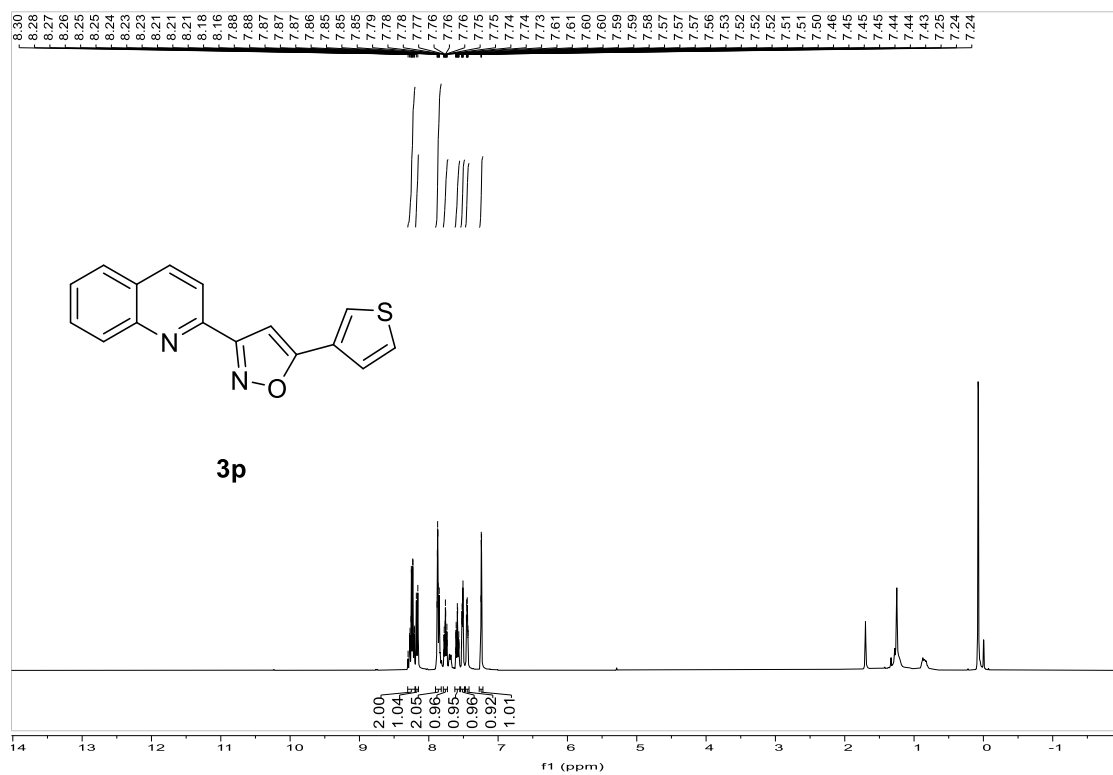
$^1\text{H}$  NMR spectra of compound **3o**



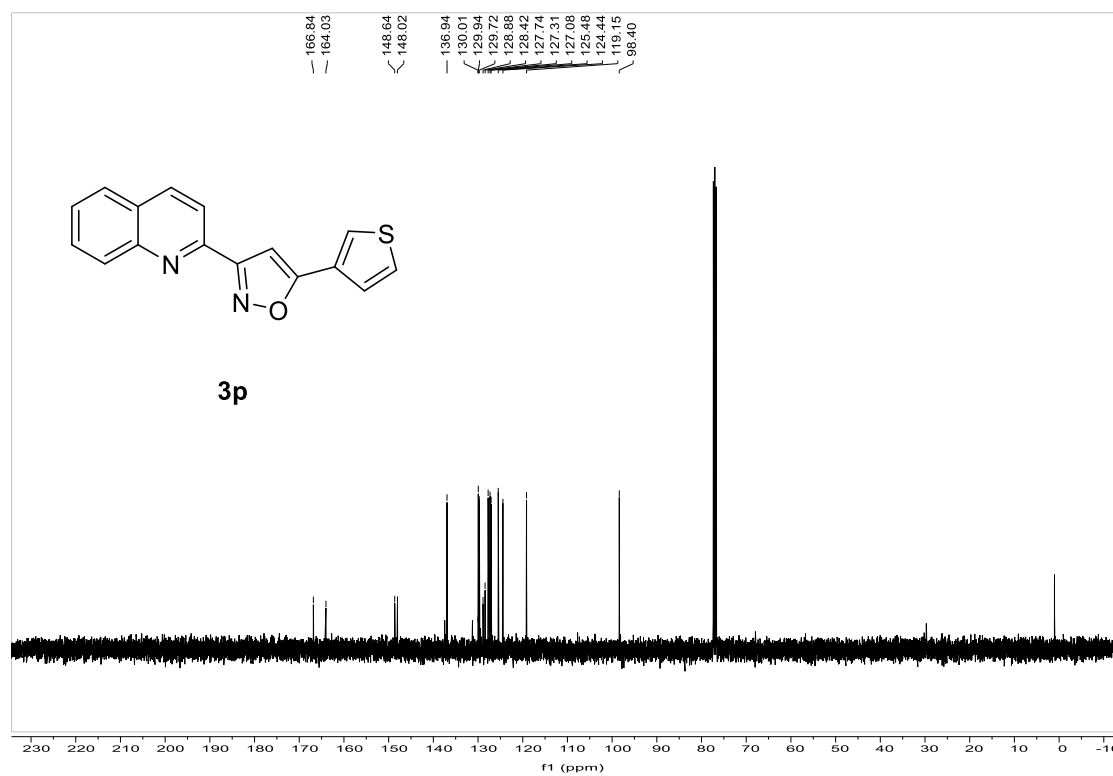
$^{13}\text{C}\{^1\text{H}\}$  NMR spectra of compound **3o**



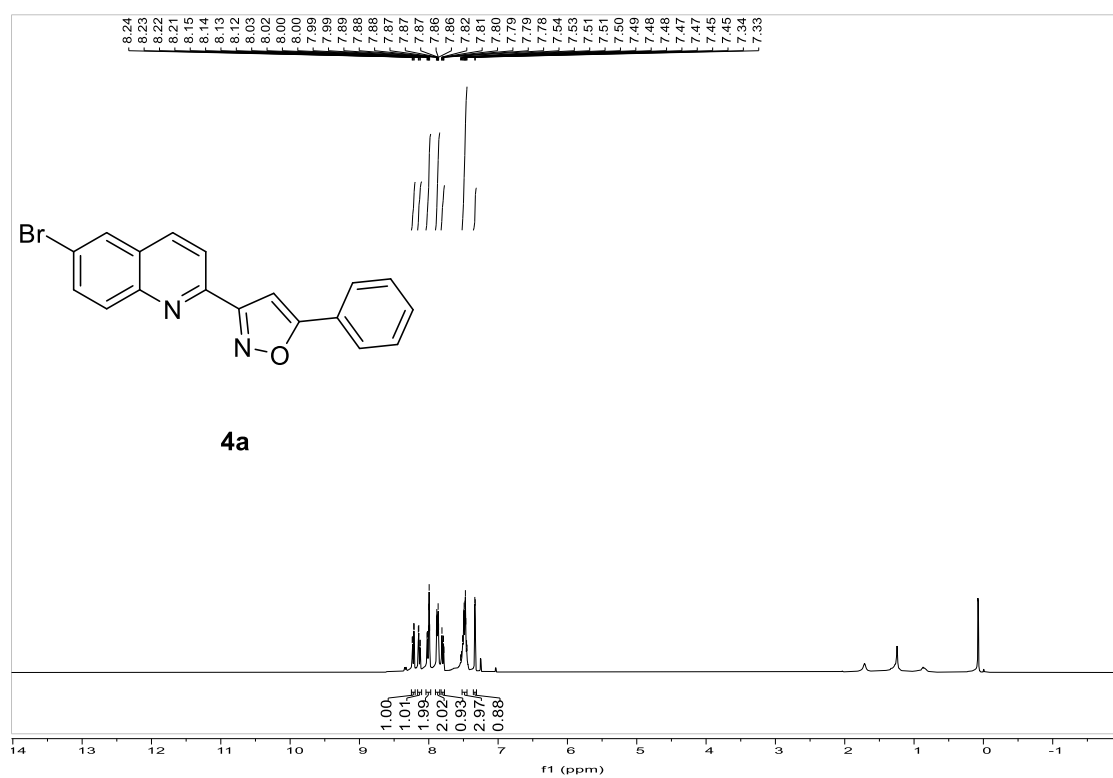
### $^1\text{H}$ NMR spectra of compound **3p**



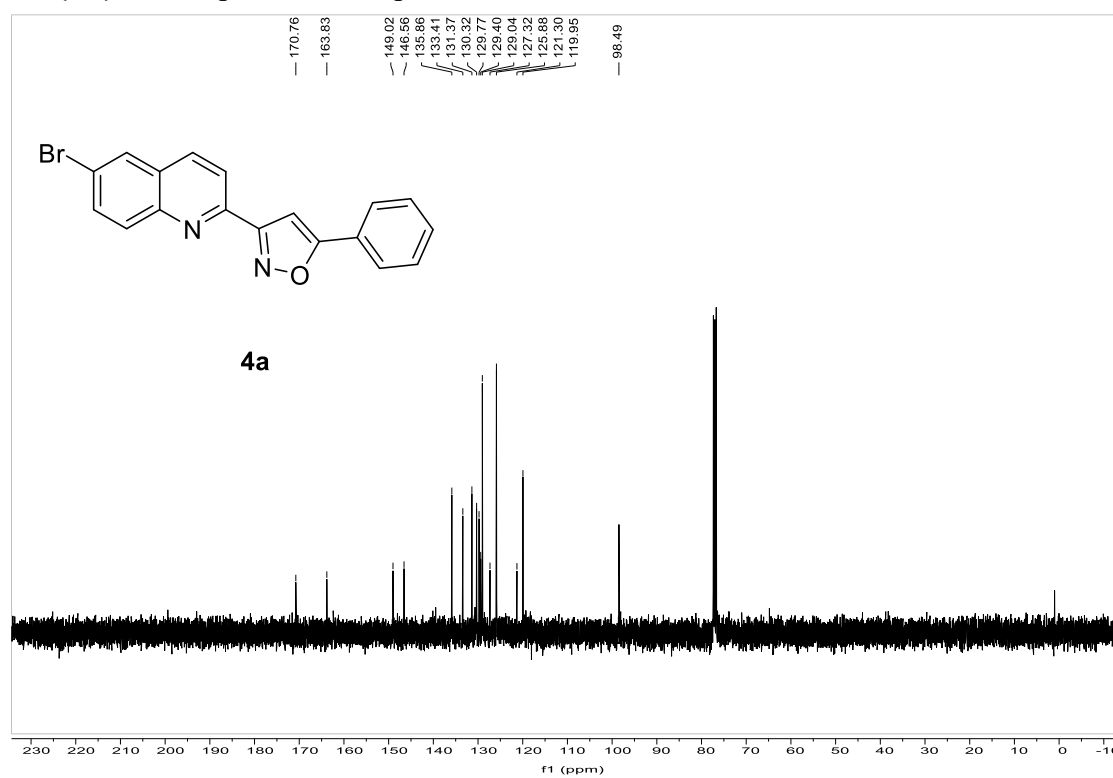
### $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of compound **3p**



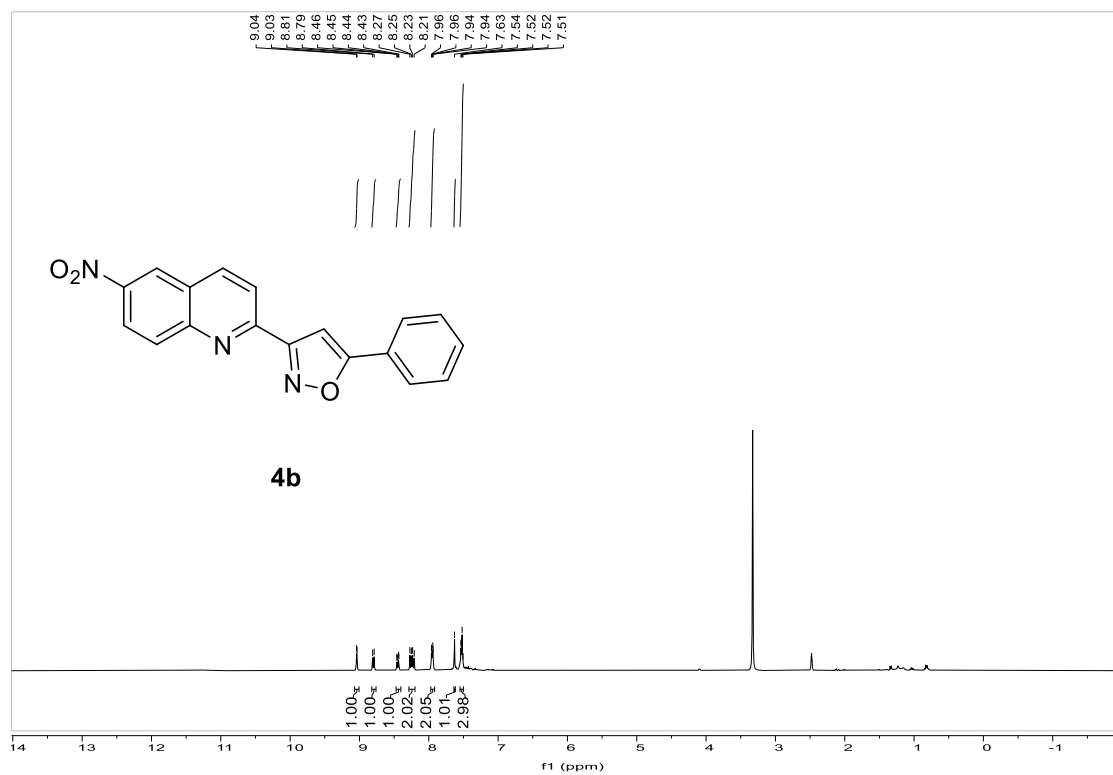
### $^1\text{H}$ NMR spectra of compound **4a**



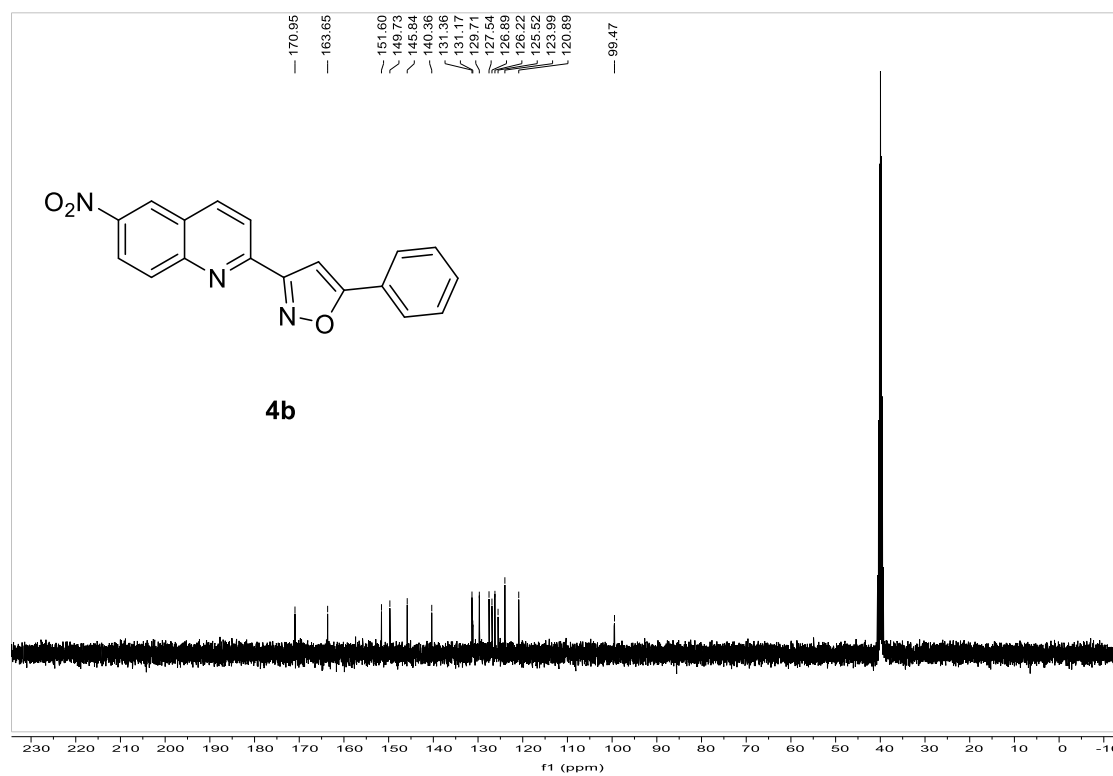
### $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of compound **4a**



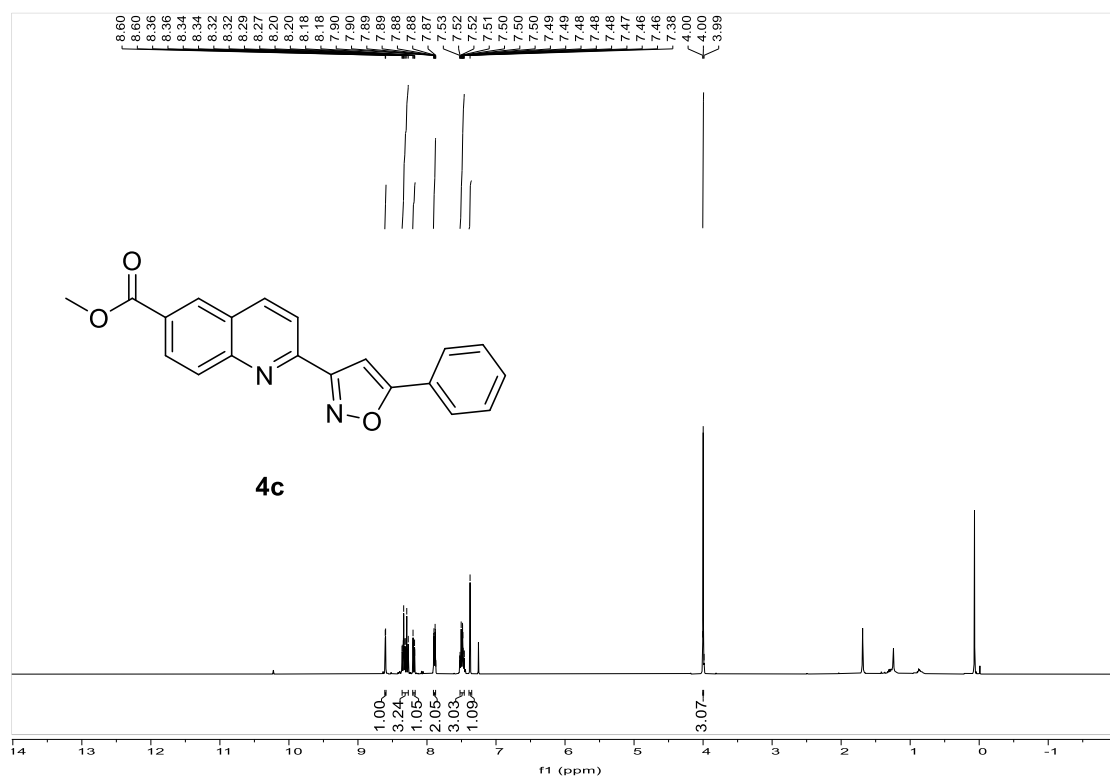
$^1\text{H}$  NMR spectra of compound **4b**



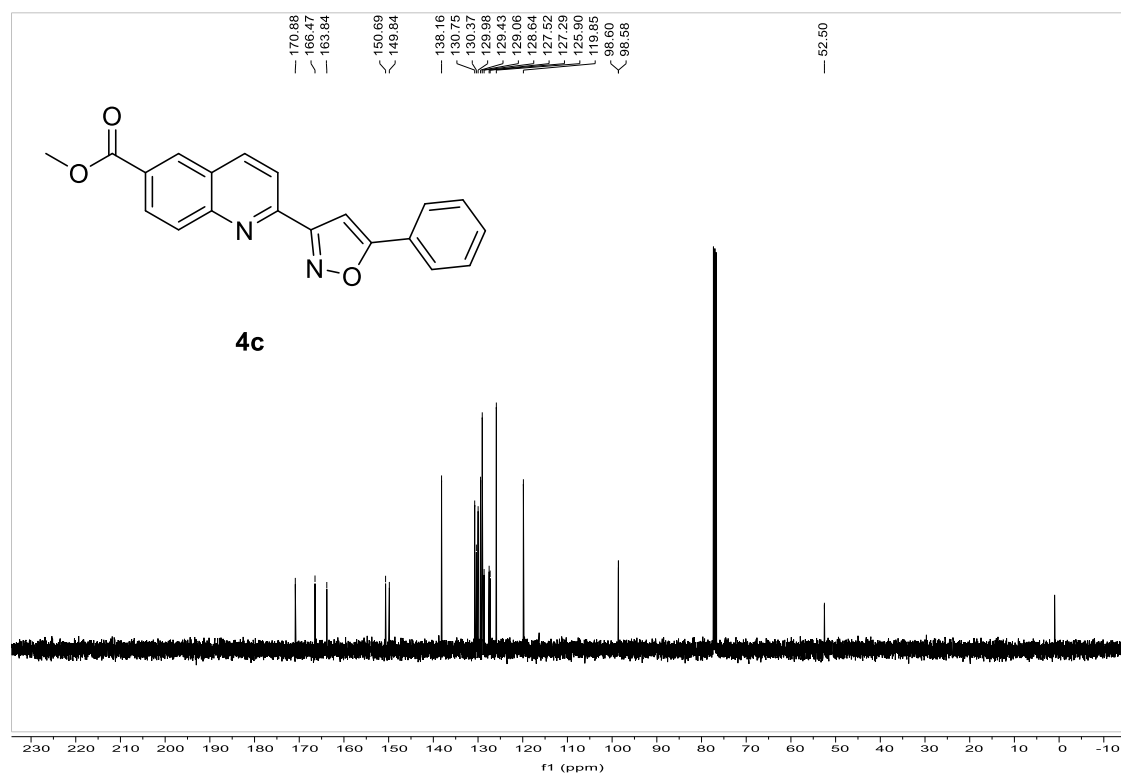
$^{13}\text{C}\{^1\text{H}\}$  NMR spectra of compound **4b**



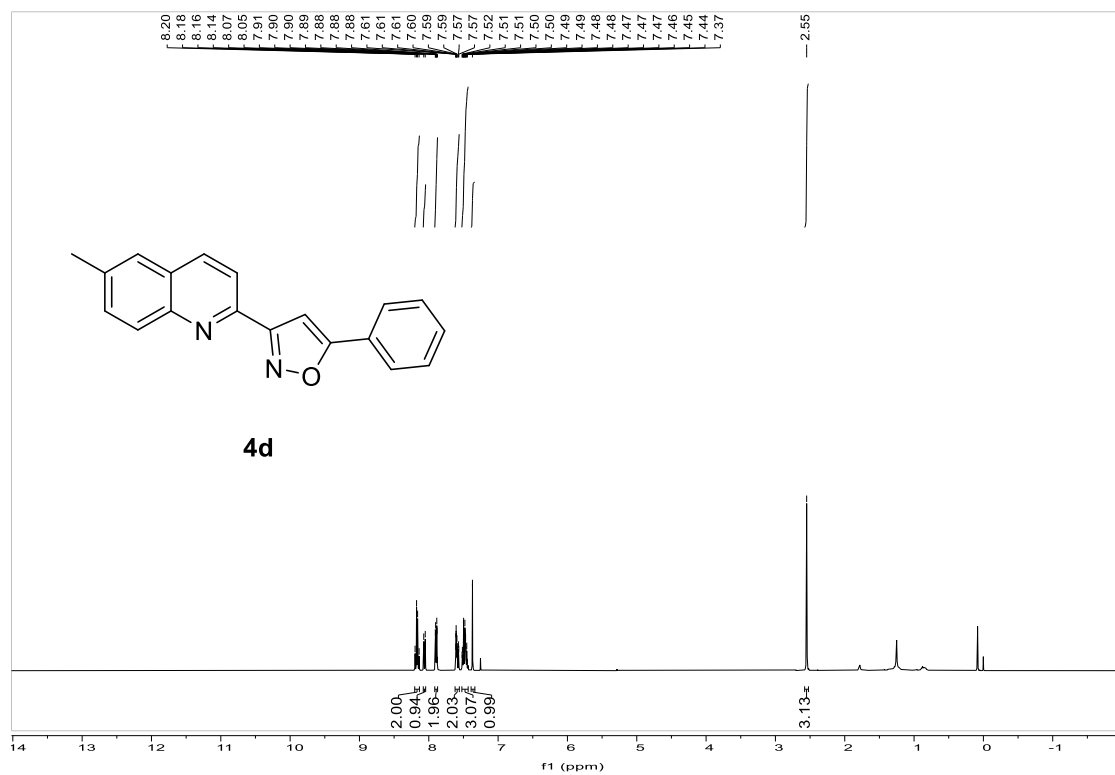
$^1\text{H}$  NMR spectra of compound **4c**



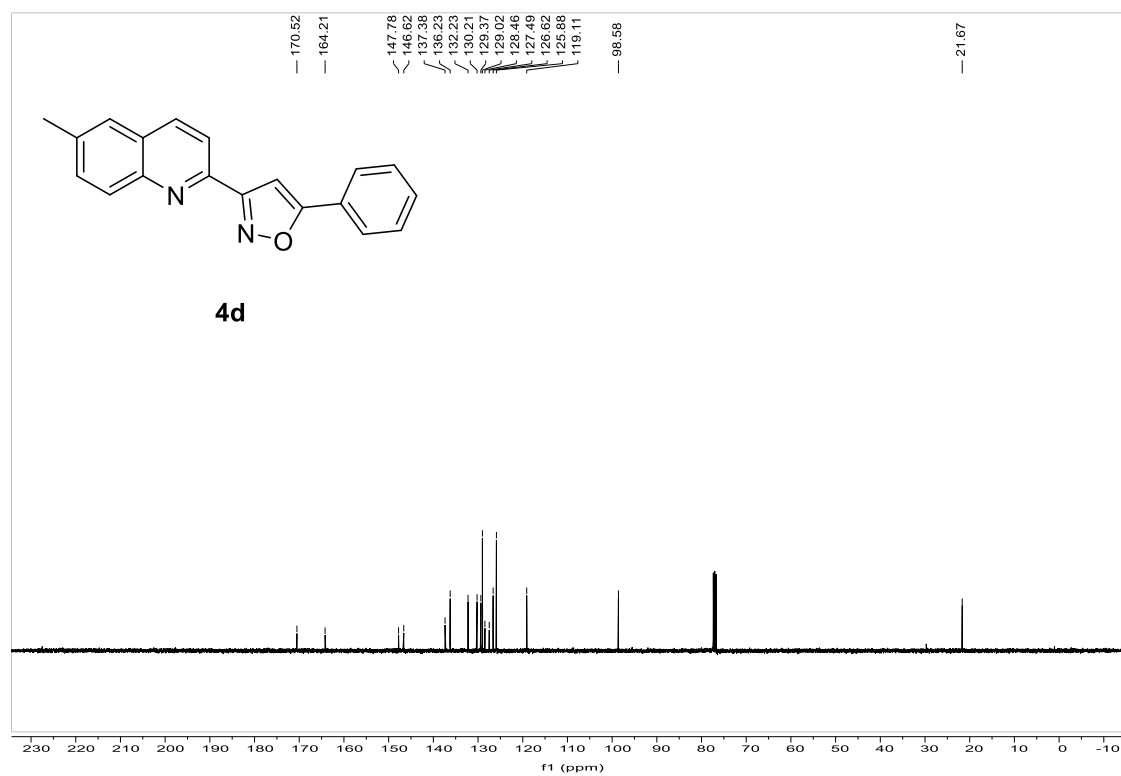
$^{13}\text{C}\{^1\text{H}\}$  NMR spectra of compound **4c**



# $^1\text{H}$ NMR spectra of compound **4d**



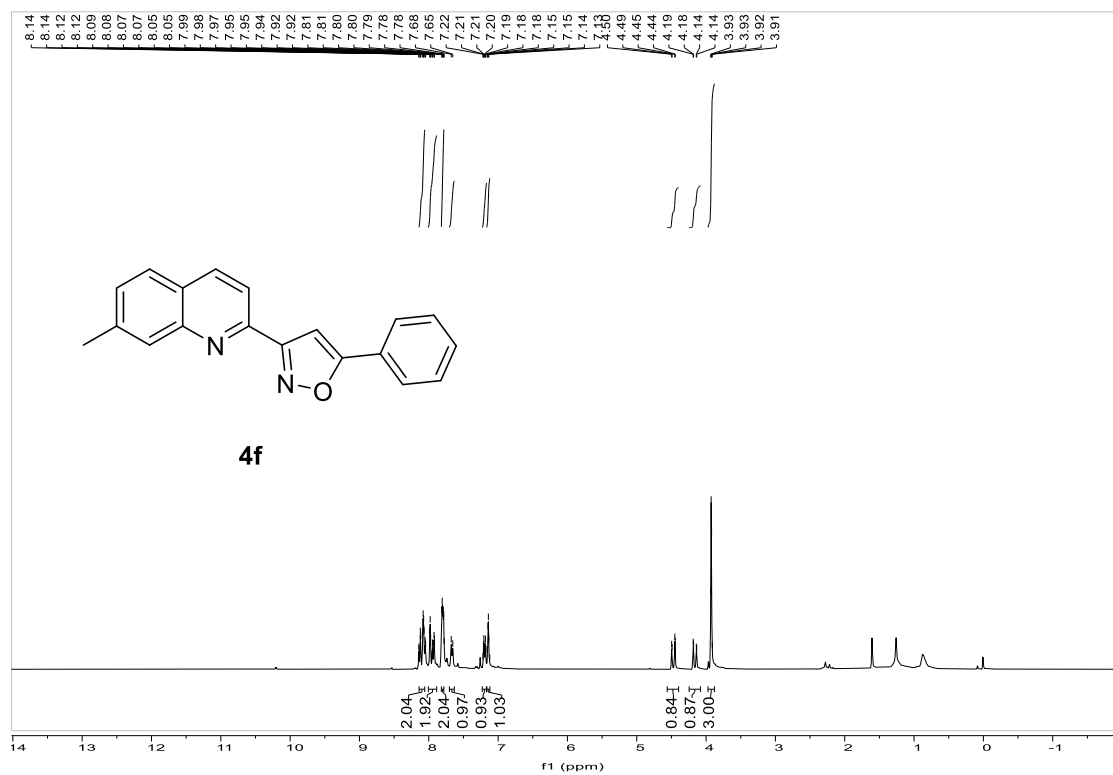
# $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of compound **4d**



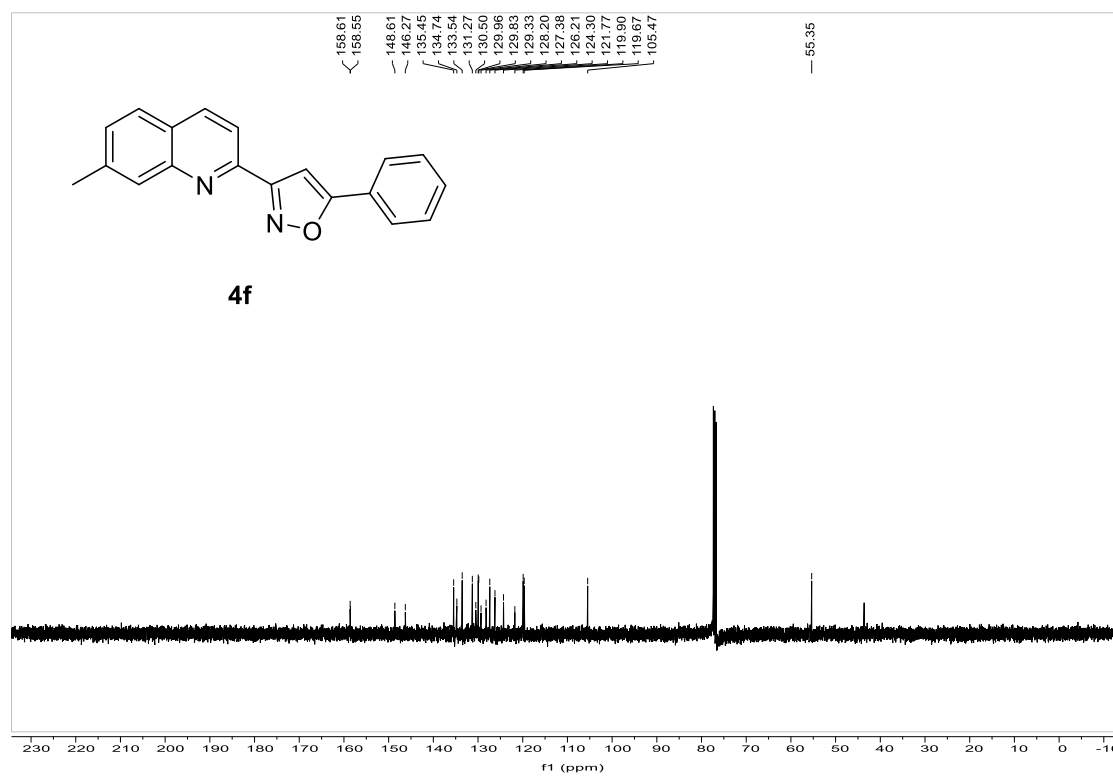




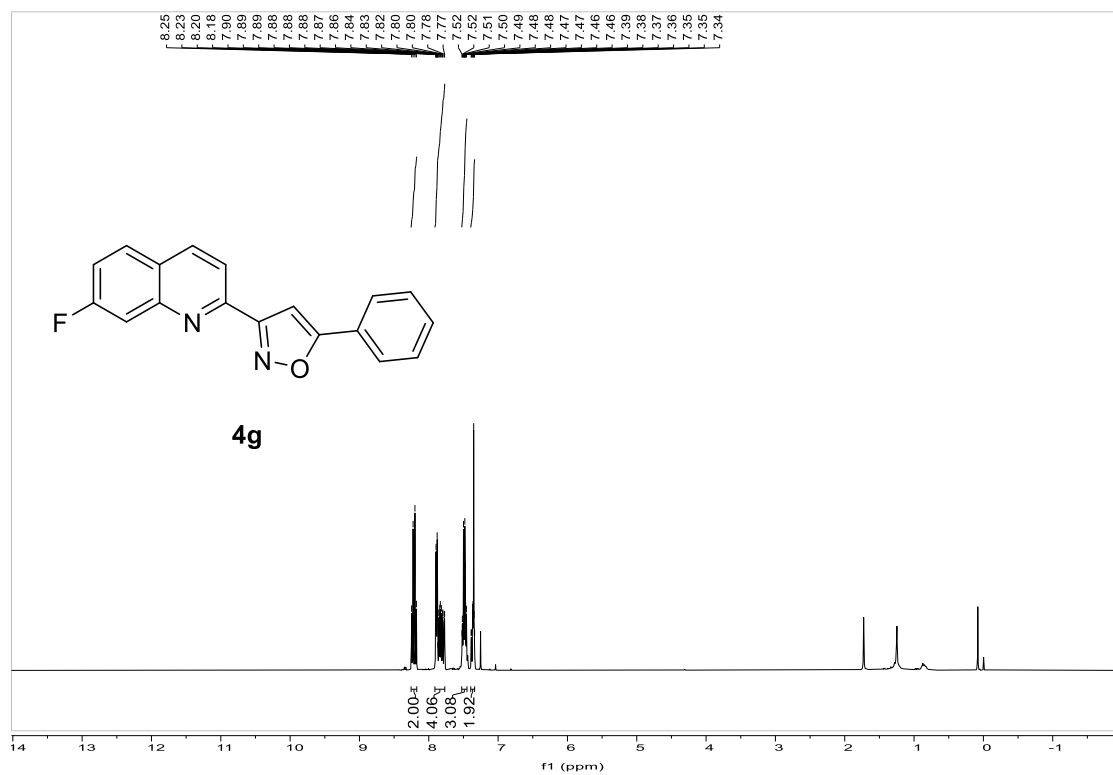
$^1\text{H}$  NMR spectra of compound **4f**



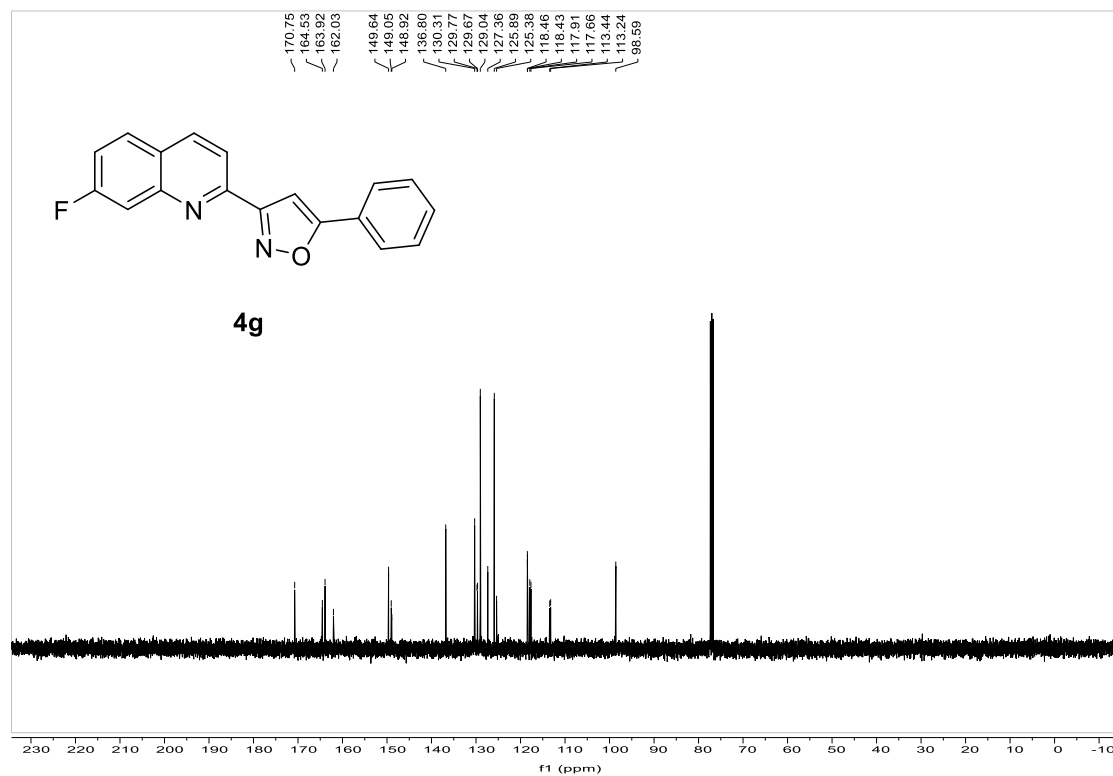
$^{13}\text{C}\{^1\text{H}\}$  NMR spectra of compound **4f**



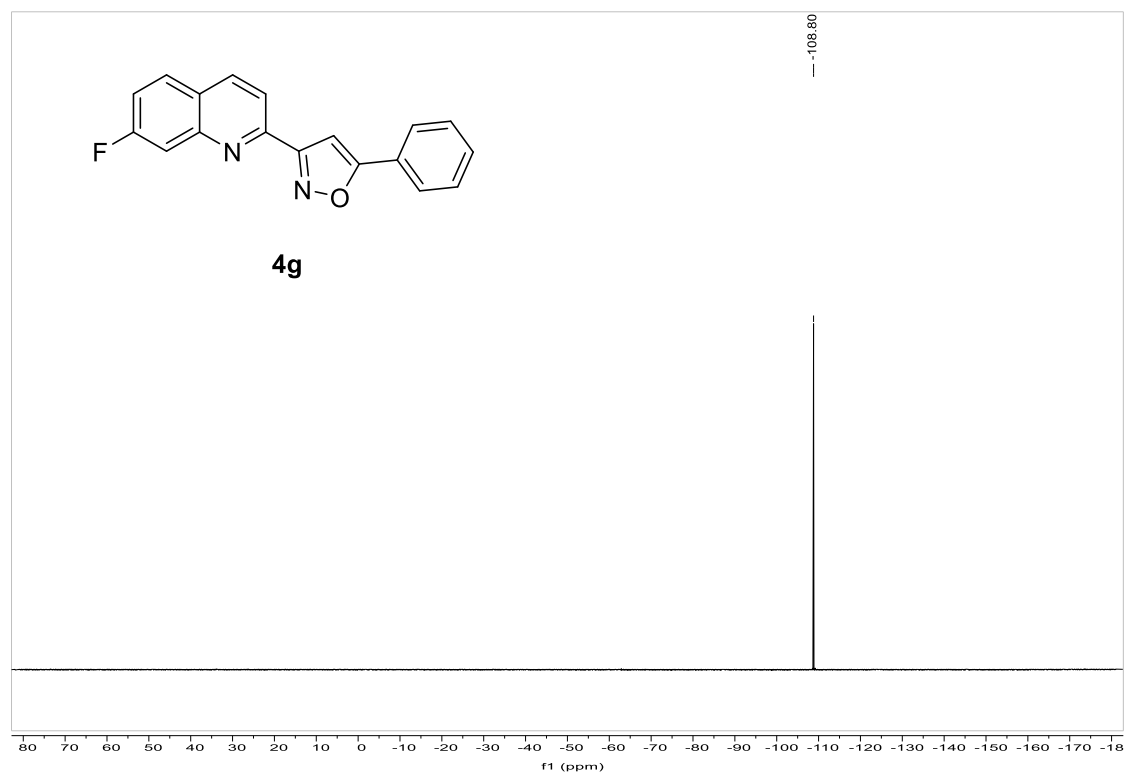
### $^1\text{H}$ NMR spectra of compound **4g**



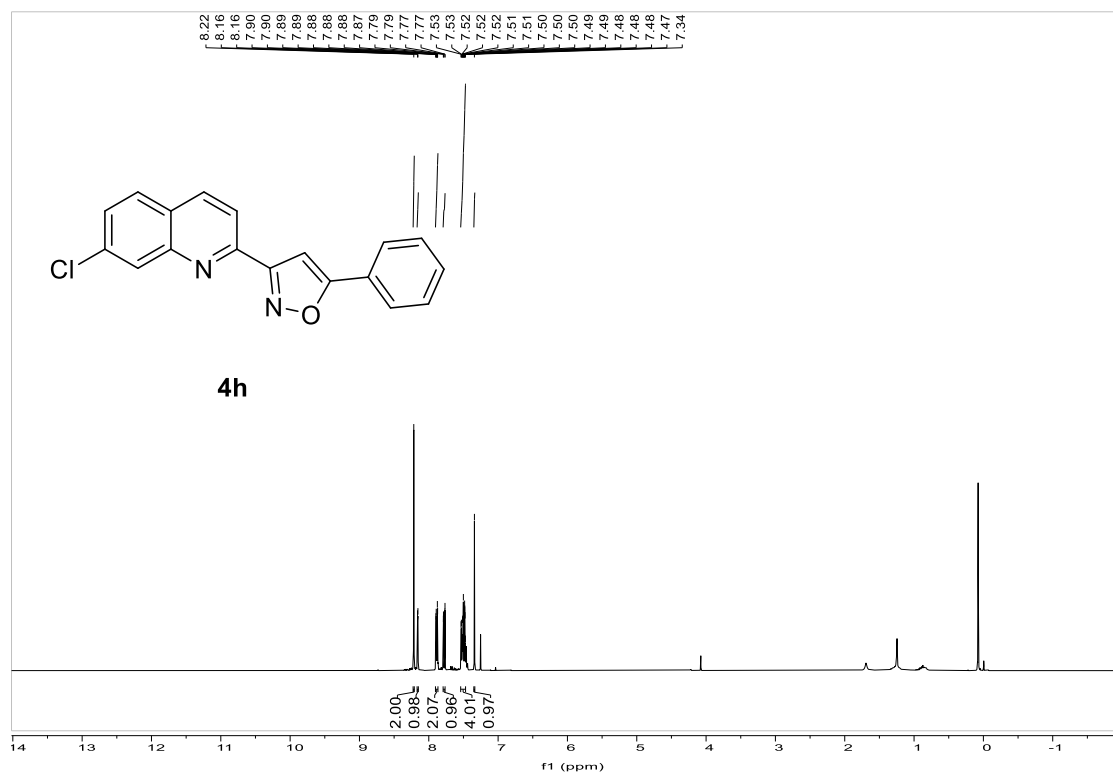
### $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of compound **4g**



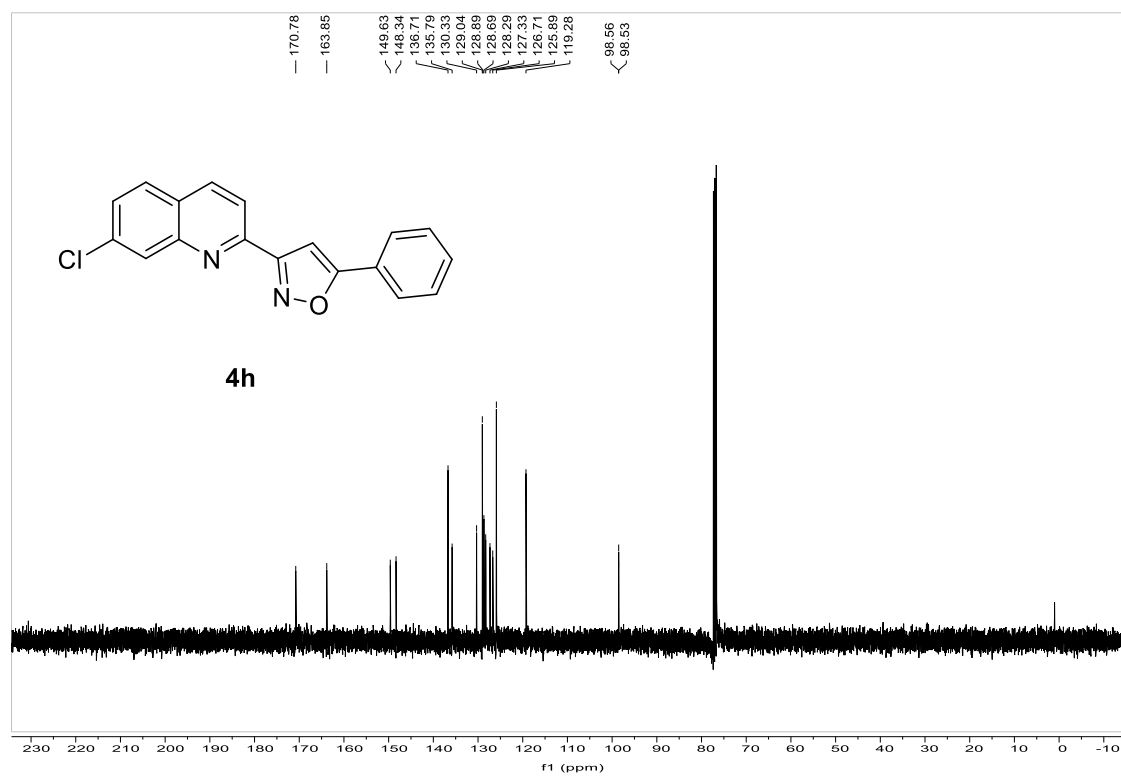
<sup>19</sup>F NMR spectra of compound **4g**



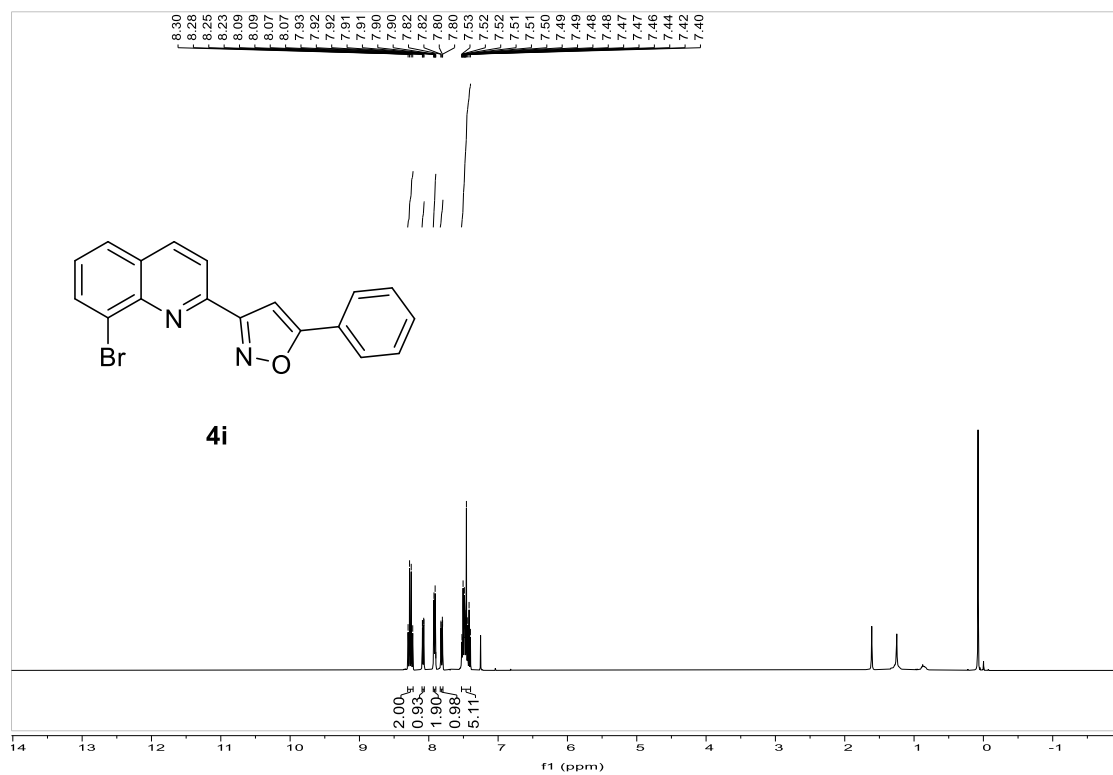
### $^1\text{H}$ NMR spectra of compound **4h**



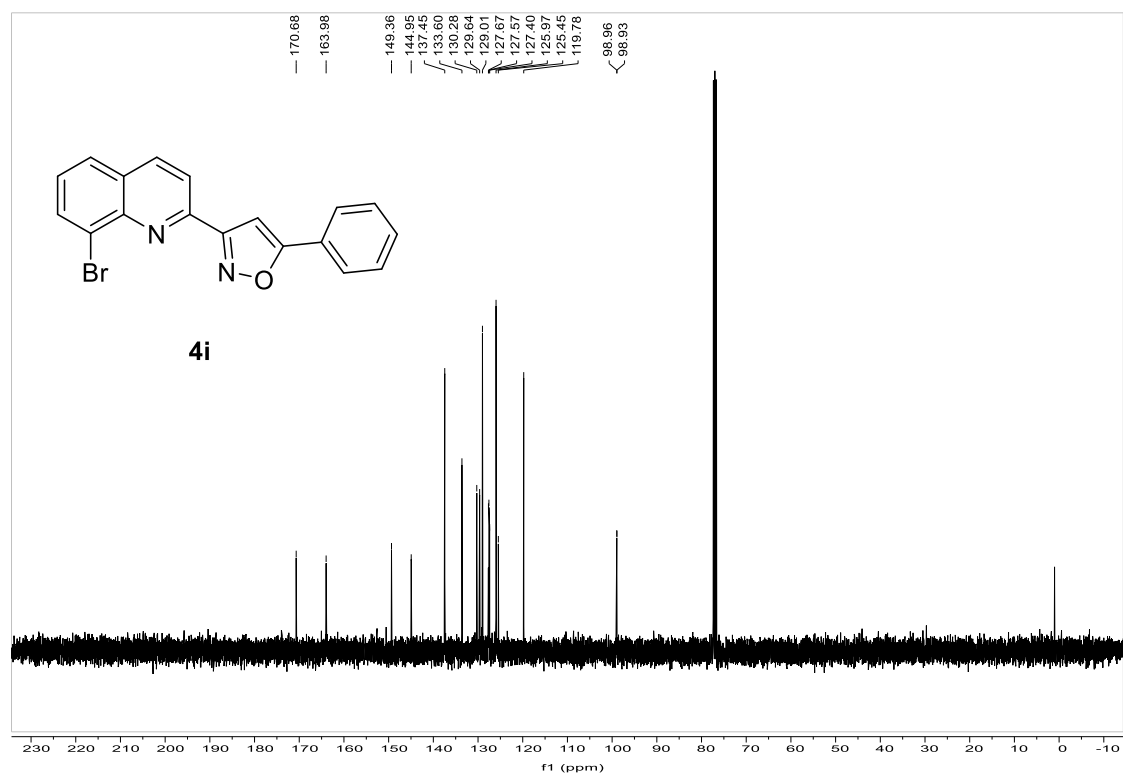
### $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of compound **4h**



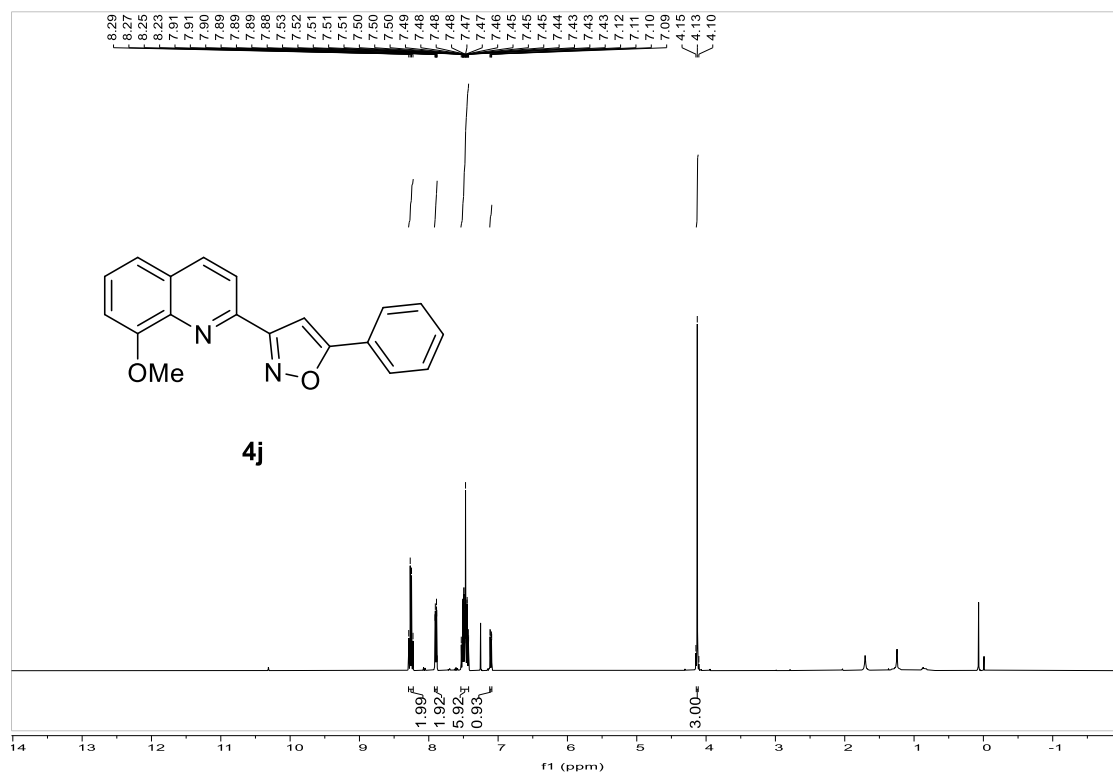
### $^1\text{H}$ NMR spectra of compound **4i**



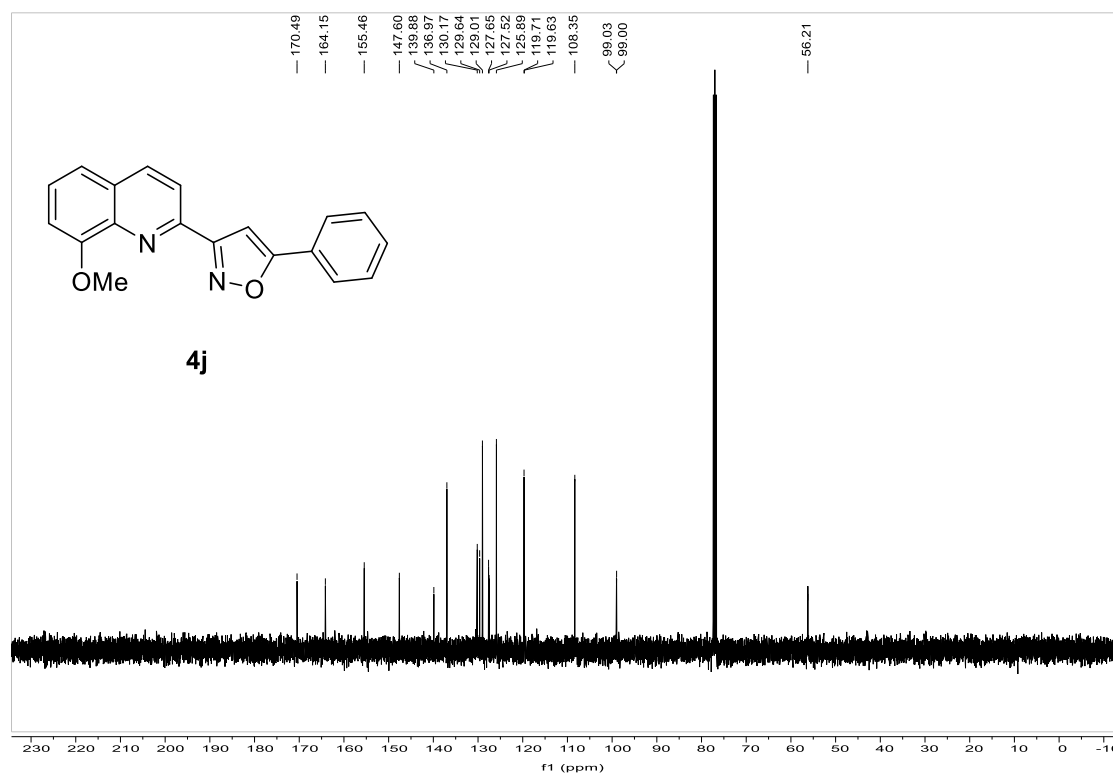
### $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of compound **4i**



### $^1\text{H}$ NMR spectra of compound **4j**



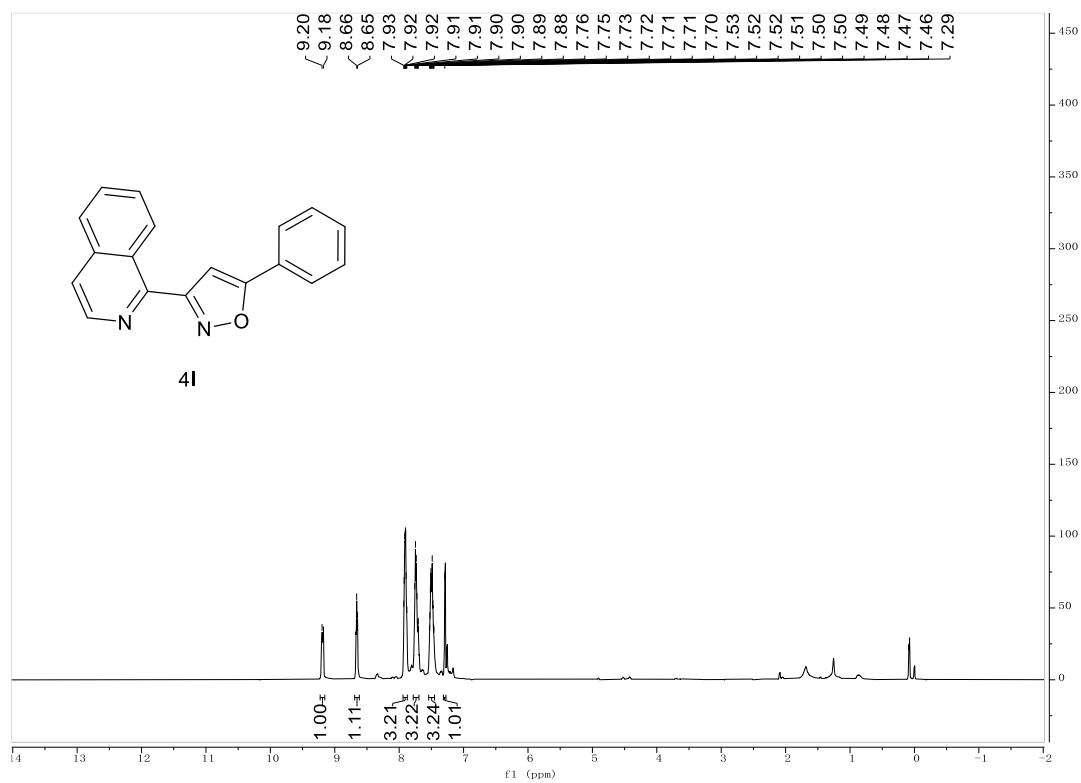
### $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of compound **4j**







### $^1\text{H}$ NMR spectra of compound **4I**



### $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of compound **4I**

