

Electronic Supplementary Information

**Catalyst-Free and Selective Synthesis of 2-Aminothiophenes and 2-Amino-4,5-dihydrothiophenes from 4-Thiazolidinones in Water**

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**General Information**

Aryl isothiocyanates were obtained according to reported procedures.<sup>[1]</sup> All other solvents and reagents were purchased directly from commercial suppliers and used as received without further purification. Melting points (m.p.) were recorded on Büchi B540 apparatus (Büchi Labortechnik AG, Flawil, Switzerland) and are uncorrected. <sup>1</sup>H NMR, <sup>19</sup>F NMR and <sup>13</sup>C NMR spectra were recorded on Bruker AM-400 (<sup>1</sup>H at 400 MHz, <sup>13</sup>C at 100 MHz, <sup>19</sup>F at 376 MHz) spectrometer and HMQC spectra were recorded on Bruker AM-500 spectrometer with DMSO-*d*<sub>6</sub> as the solvent and TMS as the internal standard. Chemical shifts are reported in  $\delta$  (parts per million) values. High-resolution electron mass spectra (ESI-TOF) were performed on a Micromass LC-TOF spectrometer. High Resolution Mass Spectrometry (HRMS) EI were recorded under electron impact (70 eV) condition using a MicroMass GCT CA 055 instrument. Analytical thin-layer chromatography (TLC) was carried out on precoated plates (silica gel 60 F254) and spots were visualized with ultraviolet (UV) light. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, coupling constant (Hz) and integration. X-ray diffraction was performed with a Bruker Smart 1000. Chromatographic analysis was performed using an ACQUITY UPLC-H Class system (Waters Corp., USA), equipped with BEH C18 reversed phase column with 50 mm×2.1 mm i.d. and 1.7

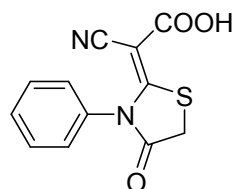
$\mu\text{m}$  particle size, equipped with a quaternary solvent delivery system, a 48-vial autosampler (10  $\mu\text{L}$  loop), and a photodiode array detector (PDA). The UPLC separations were carried out using gradient separation at a flow rate of 0.4  $\text{mL min}^{-1}$ . The mobile phase was a mixture of MilliQ ultrapure 0.01% TFA solution (A) and acetonitrile (B). The following elution gradient totally lasted 15 min: initial mobile-phase composition, 90:10 (v/v) phase A:B; 0-8 min, linear change from 10 to 100% B; 8-10 min 100% B; 10-11 min, linear change from 100 to 10% B. The column and injection chamber were maintained at 40 and 25  $^{\circ}\text{C}$ , respectively. The sample injection volume was 3  $\mu\text{L}$  and the detector was set at 220 nm for **10a** and 284 nm for **11a**.

### General Procedure for the Synthesis of tert-butyl 2-cyano-2-(4-oxo-3-arylthiazolidin-2-ylidene)acetates (**8a–8n**)<sup>[2]</sup>

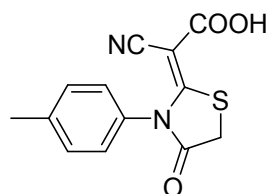
Tert-butyl cyanoacetate (10 mmol) followed by a solution of aryl isothiocyanate **5** (10 mmol) in anhydrous DMF (10 mL) were added to a cold suspension of powdered KOH (20 mmol) in dry DMF (10 mL). The mixture was stirred at room temperature for 0.5 h, then cooled again to 0 $^{\circ}\text{C}$ , treated with a solution of appropriate 2-halogen acyl chloride **7** (15 mmol) in anhydrous DMF (10 mL) and stirred at room temperature overnight. The mixture was poured into ice-cold water, and the resulting precipitate was filtered off, dried, and crystallized from DCM-EtOH to give compounds **8a–8n** in yield of 68%–80%.

### General Procedure for the Synthesis of 2-cyano-2-(4-oxo-3-arylthiazolidin-2-ylidene)acetic acid (**9a–9n**)

To a solution of tert-butyl acetate derivative **8** (5 mmol) in DCM (50 mL) was added a mixture of TFA (7.5 mL) and DCM (75 mL). The mixture was stirred at room temperature until the reaction was complete as indicated by TLC (typically 24 h). The solvent was evaporated under reduced pressure. The residual solid was further crystallized from DCM-MeOH to afford the compounds **9a–9n** in yield of 84%–91%.

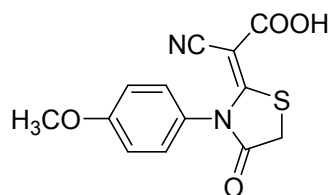


**(Z)-2-cyano-2-(4-oxo-3-phenylthiazolidin-2-ylidene)acetic acid (9a)**: yellow solid; yield: 88%; m.p.: 226.8–227.7  $^{\circ}\text{C}$ ;  $^1\text{H NMR}$  (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$ : 13.12 (s, 1H), 7.54–7.46 (m, 3H), 7.40–7.37 (m, 2H), 4.01 (s, 2H) ppm;  $^{13}\text{C NMR}$  (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$ : 173.5, 171.6, 166.6, 134.9, 130.4, 129.3, 129.2, 112.6, 76.8, 32.0 ppm; HRMS (EI) calc. for  $\text{C}_{12}\text{H}_8\text{N}_2\text{O}_3\text{S}^+$  260.0256, found 260.0255.

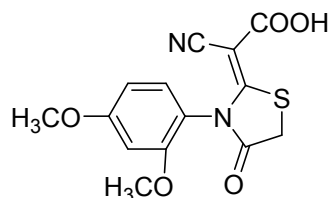


**(Z)-2-cyano-2-(4-oxo-3-(p-tolyl)thiazolidin-2-ylidene)acetic acid (9b)**: yellow solid; yield: 87%; m.p.: 239.8–240.7  $^{\circ}\text{C}$ ;  $^1\text{H NMR}$  (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$ : 13.11 (s, 1H), 7.29 (d,  $J = 8.4$  Hz, 2H),

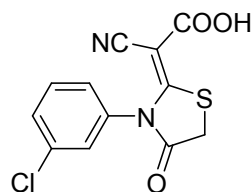
7.24 (d,  $J = 8.4$  Hz, 2H), 4.00 (s, 2H), 2.36 (s, 3H) ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$ : 173.5, 171.8, 166.6, 139.9, 132.3, 129.7, 129.0, 112.6, 76.7, 31.9, 20.9 ppm; HRMS (EI) calc. for  $\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}_3\text{S}^+$  274.0412, found 274.0415.



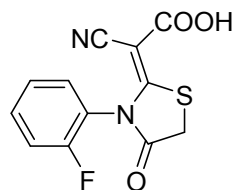
**(Z)-2-cyano-2-(3-(4-methoxyphenyl)-4-oxothiazolidin-2-ylidene)acetic acid (9c)**: yellow solid; yield: 90%; m.p.: 243.0–243.2 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$ : 13.09 (s, 1H), 7.29 (d,  $J = 8.8$  Hz, 2H), 7.02 (d,  $J = 8.8$  Hz, 2H), 3.99 (s, 2H), 3.80 (s, 3H) ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$ : 173.6, 172.2, 166.6, 160.5, 130.5, 127.5, 114.4, 112.8, 76.7, 55.4, 31.9 ppm; HRMS (EI) calc. for  $\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}_4\text{S}^+$  290.0361, found 290.0362.



**(Z)-2-cyano-2-(3-(2,4-dimethoxyphenyl)-4-oxothiazolidin-2-ylidene)acetic acid (9d)**: yellow solid; yield: 89%; m.p.: 222.7–223.1 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$ : 13.14 (s, 1H), 7.22 (d,  $J = 8.8$  Hz, 1H), 6.67 (d,  $J = 2.8$  Hz, 1H), 6.60 (dd,  $J = 8.8, 2.8$  Hz, 1H), 4.07 (ABq,  $J_{gem} = 18.4$  Hz, 2H), 3.81 (s, 3H), 3.77 (s, 3H) ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$ : 173.2, 171.5, 166.6, 162.4, 156.9, 131.1, 115.5, 112.6, 105.3, 98.9, 76.5, 56.0, 55.5, 31.4 ppm; HRMS (EI) calc. for  $\text{C}_{14}\text{H}_{12}\text{N}_2\text{O}_5\text{S}^+$  320.0467, found 320.0464.

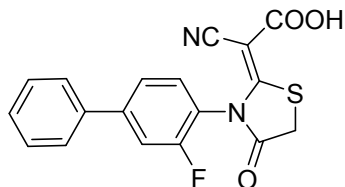


**(Z)-2-(3-(3-chlorophenyl)-4-oxothiazolidin-2-ylidene)-2-cyanoacetic acid (9e)**: yellow solid; yield: 86%; m.p.: 143.0–143.6 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$ : 13.18 (s, 1H), 7.63–7.59 (m, 2H), 7.53 (t,  $J = 8.0$  Hz, 1H), 7.42 (d,  $J = 8.0$ , 1H), 4.00 (ABq,  $J_{gem} = 18.4$  Hz, 2H) ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$ : 173.3, 171.4, 166.4, 136.2, 133.3, 130.8, 130.5, 129.5, 128.4, 112.9, 76.7, 32.0 ppm; HRMS (EI) calc. for  $\text{C}_{12}\text{H}_7\text{ClN}_2\text{O}_3\text{S}^+$  293.9866, found 293.9861.

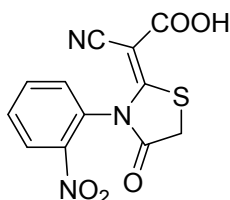


**(Z)-2-cyano-2-(3-(2-fluorophenyl)-4-oxothiazolidin-2-ylidene)acetic acid (9f)**: yellowish solid;

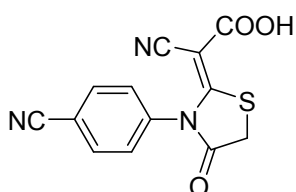
yield: 85%; m.p.: 237.9–238.7 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 13.32 (s, 1H), 7.59 (dt, *J* = 15.6, 7.6 Hz, 2H), 7.42 (t, *J* = 8.8 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 4.14 (ABq, *J*<sub>gem</sub> = 18.8 Hz, 2H) ppm; <sup>19</sup>F NMR (376 MHz, DMSO-*d*<sub>6</sub>) δ: -122.69 – -122.75 (m) ppm; HRMS (ES-) calcd for C<sub>12</sub>H<sub>6</sub>N<sub>2</sub>O<sub>3</sub>FS (M-H)<sup>-</sup>; 277.0083; found, 277.0087.



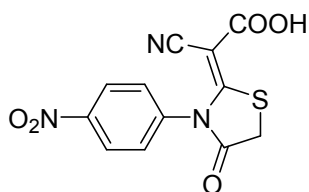
**(Z)-2-cyano-2-(3-(3-fluoro-[1,1'-biphenyl]-4-yl)-4-oxothiazolidin-2-ylidene)acetic acid (9g):** yellow solid; yield: 87%; m.p.: 225.8–226.7 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 13.37 (s, 1H), 7.84–7.77 (m, 3H), 7.73–7.62 (m, 2H), 7.56–7.49 (m, 2H), 7.48–7.42 (m, 1H), 4.18 (ABq, *J*<sub>gem</sub> = 18.4 Hz, 2H) ppm; <sup>19</sup>F NMR (376 MHz, DMSO-*d*<sub>6</sub>) δ: -121.97 – -122.04 (m) ppm; HRMS (EI) calc. for C<sub>18</sub>H<sub>11</sub>FN<sub>2</sub>O<sub>3</sub>S<sup>+</sup> 354.0474, found 354.0480.



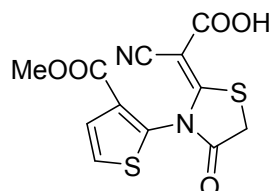
**(Z)-2-cyano-2-(3-(2-nitrophenyl)-4-oxothiazolidin-2-ylidene)acetic acid (9h):** yellow solid; yield: 84%; m.p.: 217.7–217.9 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 13.43 (s, 1H), 8.31 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.96 (td, *J* = 7.6, 1.2 Hz, 1H), 7.88 (td, *J* = 8.0, 1.2 Hz, 1H), 7.83 (dd, *J* = 8.0, 1.2 Hz, 1H), 4.17 (ABq, *J*<sub>gem</sub> = 18.4 Hz, 2H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 173.1, 170.5, 166.1, 146.5, 135.4, 132.7, 132.4, 128.0, 125.8, 112.9, 77.3, 31.8 ppm; HRMS (EI) calc. for C<sub>12</sub>H<sub>7</sub>N<sub>3</sub>O<sub>5</sub>S<sup>+</sup> 305.0106, found 305.0107.



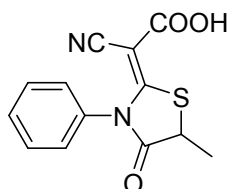
**(Z)-2-cyano-2-(3-(4-cyanophenyl)-4-oxothiazolidin-2-ylidene)acetic acid (9i):** yellow solid; yield: 87%; m.p.: 235.0–235.9 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 13.25 (s, 1H), 8.03 (d, *J* = 8.4 Hz, 2H), 7.69 (d, *J* = 8.4 Hz, 2H), 4.02 (s, 2H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 173.2, 171.2, 166.3, 139.1, 133.4, 130.8, 118.2, 113.1, 113.0, 76.7, 32.2 ppm; HRMS (EI) calc. for C<sub>13</sub>H<sub>7</sub>N<sub>3</sub>O<sub>3</sub>S<sup>+</sup> 285.0208, found 285.0207.



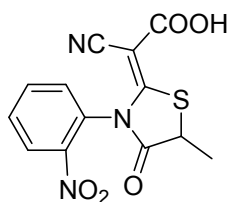
**(Z)-2-cyano-2-(3-(4-nitrophenyl)-4-oxothiazolidin-2-ylidene)acetic acid (9j):** white solid; yield: 84%; m.p.: 243.1–243.3 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 13.25 (s, 1H), 8.40 (d, *J* = 8.8 Hz, 2H), 7.78 (d, *J* = 8.8 Hz, 2H), 4.03 (s, 2H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 173.3, 171.2, 166.3, 148.4, 140.7, 131.3, 124.5, 113.1, 76.7, 32.2 ppm; HRMS (EI) calc. for C<sub>12</sub>H<sub>7</sub>N<sub>3</sub>O<sub>5</sub>S<sup>+</sup> 305.0106, found 305.0103.



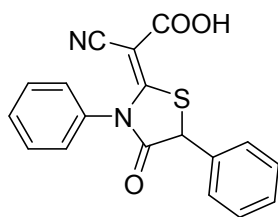
**(Z)-2-cyano-2-(4-oxo-3,5-diphenylthiazolidin-2-ylidene)acetic acid (9l):** gray solid; yield: 86%; m.p.: 206.3–207.3 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 13.34 (s, 1H), 7.84 (d, *J* = 5.6 Hz, 1H), 7.46 (d, *J* = 5.6 Hz, 1H), 4.11 (ABq, *J*<sub>gem</sub> = 18.8 Hz, 2H), 3.76 (s, 3H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 172.8, 171.2, 166.2, 160.9, 139.2, 131.0, 129.0, 126.9, 112.3, 77.4, 52.2, 31.5 ppm; HRMS (EI) calc. for C<sub>12</sub>H<sub>8</sub>N<sub>2</sub>O<sub>5</sub>S<sub>2</sub><sup>+</sup> 323.9875, found 323.9872.



**(Z)-2-cyano-2-(5-methyl-4-oxo-3-phenylthiazolidin-2-ylidene)acetic acid (9i):** white solid; yield: 91%; m.p.: 206.5–207.0 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 13.17 (s, 1H), 7.54–7.39 (m, 5H), 4.25 (q, *J* = 7.2 Hz, 1H), 1.59 (d, *J* = 7.2 Hz, 3H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 176.4, 170.0, 166.5, 135.1, 130.4, 129.4, 129.3, 129.2, 129.1, 112.65, 76.8, 40.0, 17.5 ppm; HRMS (EI) calc. for C<sub>13</sub>H<sub>10</sub>N<sub>2</sub>O<sub>3</sub>S<sup>+</sup> 274.0412, found 274.0413.



**(Z)-2-cyano-2-(5-methyl-4-oxo-3-(4-nitrophenyl)thiazolidin-2-ylidene)acetic acid (9m):** yellow solid; yield: 90%; m.p.: 202.3–203.3 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 13.36 (s, 1H), 8.34–8.30 (m, 1H), 8.00–7.84 (m, 3H), 4.46 and 4.32 (2\*q, *J* = 7.2 Hz, 1H), 1.62 and 1.56 (2\*d, *J* = 7.2 Hz, 3H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 176.0, 175.9, 169.0, 168.9, 166.0, 165.9, 146.4, 146.2, 135.5, 135.4, 132.8, 132.6, 128.1, 128.0, 125.9, 125.8, 112.9, 112.8, 77.4, 77.0, 40.2, 39.9, 18.0, 17.5 ppm; HRMS (EI) calc. for C<sub>13</sub>H<sub>9</sub>N<sub>3</sub>O<sub>5</sub>S<sup>+</sup> 319.0263, found 319.0263.



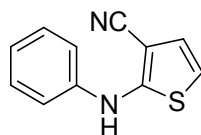
**(Z)-2-cyano-2-(4-oxo-3,5-diphenylthiazolidin-2-ylidene)acetic acid (9n):** white solid; yield: 88%; m.p.: 284.1–184.8 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$ : 13.37 (s, 1H), 7.59–7.49 (m, 7H), 7.46–7.36 (m, 3H), 5.55 (s, 1H) ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$ : 174.2, 169.1, 166.6, 135.4, 135.0, 130.6, 129.5, 129.4, 129.3, 129.2, 129.1, 129.0, 128.6, 112.5, 77.5, 49.2 ppm; HRMS (EI) calc. for  $\text{C}_{18}\text{H}_{12}\text{N}_2\text{O}_3\text{S}^+$  336.0569, found 336.0576.

### References and notes

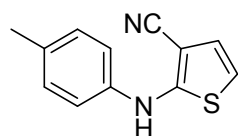
- 1 (a) Khatik, G. L.; Pal, A.; Mobin, S. M.; Nair, V. A. *Tetrahedron Lett.* **2010**, 51 (28): 3654;(b) Liu, P.; Li, C.; Zhang, J.; Xu, X. *Synth. Commun.* **2013**, 43 (24): 3342.
- 2 Kaminsky, D.; Gzella, A. K.; Lesyk, R. *Synth. Commun.* **2014**, 44 (2): 231.

### General Procedure for the Synthesis of 2-aminothiophenes (10a–10n)

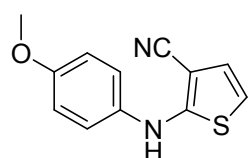
Carboxylic acid compound **9** (0.5 mmol) was added to a solution of NaBH<sub>4</sub> (1 mmol) in water (2.5 mL) at 15 °C. The reaction mixture was stirred at 15 °C until the reaction was complete as determined by TLC analysis (typically 0.5–24 h). The reaction mixture was quenched with 1 M HCl, and the product precipitated was filtered. The solid was purified by silica gel column chromatography (PE : EA = 5:1) to afford the compounds **10a–10n**.



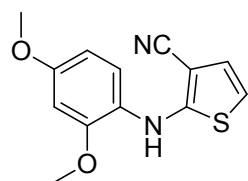
**2-(phenylamino)thiophene-3-carbonitrile (10a)**: white solid; yield: 83%; m.p.: 125.1–125.6 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 9.53 (s, 1H), 7.32 (t, *J* = 7.8 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.10–7.06 (m, 1H), 7.00 (t, *J* = 7.2 Hz, 1H), 6.91 (dd, *J* = 5.8, 2.6 Hz, 1H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 158.7, 142.5, 129.4, 126.2, 122.2, 117.5, 115.6, 113.7, 92.0 ppm; HRMS (EI) calc. for C<sub>11</sub>H<sub>8</sub>N<sub>2</sub>S<sup>+</sup> 200.0408, found 200.0409.



**2-(p-tolylamino)thiophene-3-carbonitrile (10b)**: red solid; yield: 68%; m.p.: 106.8–107.4 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 9.49 (s, 1H), 7.17–7.10 (m, 4H), 7.04 (d, *J* = 5.8 Hz, 1H), 6.82 (d, *J* = 5.8 Hz, 1H), 2.26 (s, 3H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 159.8, 139.9, 131.7, 129.8, 126.2, 118.3, 115.8, 112.5, 90.2, 20.3 ppm; HRMS (EI) calc. for C<sub>12</sub>H<sub>10</sub>N<sub>2</sub>S<sup>+</sup> 214.0565, found 214.0564.



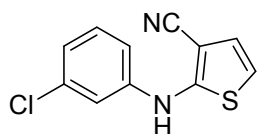
**2-((4-methoxyphenyl)amino)thiophene-3-carbonitrile (10c)**: gray solid; yield: 79%; m.p.: 125.9–126.5 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 9.40 (s, 1H), 7.18–2.24 (m, 2H), 6.98 (d, *J* = 5.8 Hz, 1H), 6.95–6.89 (m, 2H), 6.70 (d, *J* = 5.8 Hz, 1H), 3.74 (s, 3H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 161.6, 155.5, 135.5, 126.2, 121.2, 116.0, 114.6, 111.1, 87.9, 55.2 ppm; HRMS (EI) calc. for C<sub>12</sub>H<sub>10</sub>N<sub>2</sub>OS<sup>+</sup> 230.0514, found 230.0513.



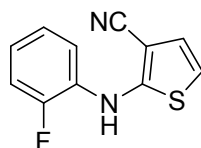
**2-((2,4-dimethoxyphenyl)amino)thiophene-3-carbonitrile (10d)**: gray solid; yield: 28%; m.p.: 86.7–87.1 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 8.83 (s, 1H), 7.13 (d, *J* = 8.8 Hz, 1H), 6.87 (d, *J* = 5.6 Hz, 1H), 6.66 (d, *J* = 2.4 Hz, 1H), 6.58–6.47 (m, 2H), 3.77 (s, 6H) ppm; <sup>13</sup>C NMR (100



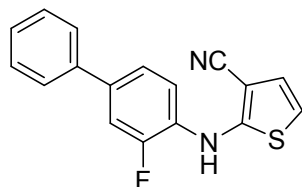
MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 164.4, 158.4, 154.2, 126.2, 125.7, 123.3, 116.1, 110.3, 104.7, 99.6, 85.0, 55.6, 55.3 ppm; HRMS (EI) calc. for C<sub>13</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>S<sup>+</sup> 260.0619, found 260.0620.



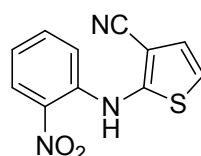
**2-((3-chlorophenyl)amino)thiophene-3-carbonitrile (10e):** white solid; yield: 72%; m.p.: 212.3–213.2 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 9.63 (s, 1H), 7.33 (t, *J* = 8.0 Hz, 1H), 7.19–7.17 (m, 1H), 7.16–7.11 (m, 2H), 7.07 (d, *J* = 5.6 Hz, 1H), 7.01 (d, *J* = 7.6 Hz, 1H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 157.0, 144.4, 133.7, 131.0, 126.4, 121.3, 116.3, 115.9, 115.1, 94.6 ppm; HRMS (EI) calc. for C<sub>11</sub>H<sub>7</sub><sup>35</sup>CIN<sub>2</sub><sup>+</sup> 234.0018, found 234.0019; calc. for C<sub>11</sub>H<sub>7</sub><sup>37</sup>CIN<sub>2</sub><sup>+</sup> 235.9989, found 235.9996.



**2-((2-fluorophenyl)amino)thiophene-3-carbonitrile (10f):** white solid; yield: 82%; m.p.: 73.9–74.3 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 9.26 (s, 1H), 7.32–7.20 (m, 2H), 7.16 (t, *J* = 7.0 Hz, 1H), 7.13–7.06 (m, 2H), 6.97 (d, *J* = 5.6 Hz, 1H) ppm; <sup>19</sup>F NMR (376 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : -125.37 – -125.45 (m) ppm; HRMS (EI) calc. for C<sub>11</sub>H<sub>7</sub>FN<sub>2</sub>S<sup>+</sup> 218.0314, found 218.0313.



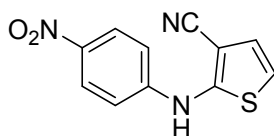
**2-((3-fluoro-[1,1'-biphenyl]-4-yl)amino)thiophene-3-carbonitrile (10g):** White solid; yield: 80%; m.p.: 122.5–123.0 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 9.38 (s, 1H), 7.70 (d, *J* = 7.2 Hz, 2H), 7.65 (dd, *J* = 12.8, 1.6 Hz, 1H), 7.54–7.42 (m, 3H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.30 (t, *J* = 8.6 Hz, 1H), 7.13 (d, *J* = 5.8 Hz, 1H), 7.03 (d, *J* = 5.8 Hz, 1H) ppm; <sup>19</sup>F NMR (376 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : -125.11 (dd, *J* = 12.2, 9.2 Hz) ppm; HRMS (EI) calc. for C<sub>17</sub>H<sub>11</sub>FN<sub>2</sub>S<sup>+</sup> 294.0627, found 294.0626.



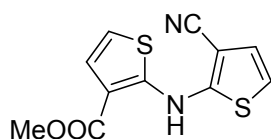
**2-((2-nitrophenyl)amino)thiophene-3-carbonitrile (10h):** Red solid; yield: 39%; m.p.: 133.4–134.2 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 9.74 (s, 1H), 8.15 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.68–7.60 (m, 1H), 7.48 (d, *J* = 5.8 Hz, 1H), 7.34 (d, *J* = 5.8 Hz, 1H), 7.12–7.06 (m, 2H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 153.6, 140.2, 136.2, 135.2, 126.8, 126.2, 122.4, 120.5, 117.8, 114.2, 102.9 ppm; HRMS (EI) calc. for C<sub>11</sub>H<sub>7</sub>N<sub>3</sub>O<sub>2</sub>S<sup>+</sup> 245.0259, found 245.0261.



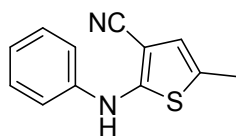
**2-((4-cyanophenyl)amino)thiophene-3-carbonitrile (10i):** White solid; yield: 61%; m.p.: 193.1–193.8 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 9.92 (s, 1H), 7.72 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 5.8 Hz, 1H), 7.25 (d, *J* = 5.8 Hz, 1H), 7.20 (d, *J* = 8.4 Hz, 2H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 154.6, 147.2, 133.8, 126.7, 119.3, 118.7, 115.6, 114.7, 102.1, 98.3 ppm; HRMS (EI) calc. for C<sub>12</sub>H<sub>7</sub>N<sub>3</sub>S<sup>+</sup> 225.0361, found 225.0363.



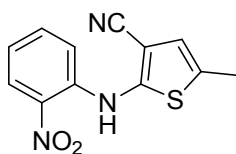
**2-((4-nitrophenyl)amino)thiophene-3-carbonitrile (10j):** Yellow solid; yield: 77%; m.p.: 212.3–213.2 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 10.16 (s, 1H), 8.19 (d, *J* = 9.2 Hz, 2H), 7.38 (d, *J* = 5.8 Hz, 1H), 7.30 (d, *J* = 5.8 Hz, 1H), 7.19 (d, *J* = 9.2 Hz, 2H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 153.8, 149.5, 140.0, 126.8, 126.0, 120.1, 114.7, 114.5, 99.8 ppm; HRMS (EI) calc. for C<sub>11</sub>H<sub>7</sub>N<sub>3</sub>O<sub>2</sub>S<sup>+</sup> 245.0259, found 245.0258.



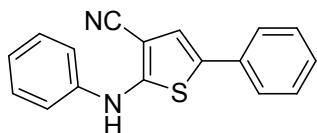
**methyl 2-((3-cyanothiophen-2-yl)amino)thiophene-3-carboxylate (10k):** Yellow solid; yield: 36%; m.p.: 192.2–193.1 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 10.67 (s, 1H), 7.29–7.25 (m, 2H), 7.19 (d, *J* = 5.6 Hz, 1H), 6.97 (d, *J* = 5.6 Hz, 1H), 3.84 (s, 3H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 164.7, 155.1, 154.9, 126.2, 125.6, 117.5, 114.3, 112.8, 110.2, 94.7, 51.7 ppm; HRMS (EI) calc. for C<sub>11</sub>H<sub>8</sub>N<sub>2</sub>O<sub>2</sub>S<sub>2</sub><sup>+</sup> 264.0027, found 263.9998.



**5-methyl-2-(phenylamino)thiophene-3-carbonitrile (10l):** White solid; yield: 45%; m.p.: 110.1–110.4 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 9.38 (s, 1H), 7.29 (t, *J* = 7.8 Hz, 2H), 7.16 (d, *J* = 7.8 Hz, 2H), 6.96 (t, *J* = 7.4 Hz, 1H), 6.77 (s, 1H), 2.31 (s, 3H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 156.5, 142.9, 129.3, 127.2, 123.0, 121.7, 116.9, 115.5, 92.4, 14.8 ppm; HRMS (EI) calc. for C<sub>12</sub>H<sub>10</sub>N<sub>2</sub>S<sup>+</sup> 214.0565, found 214.0566.



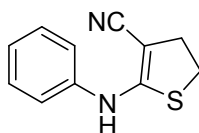
**5-methyl-2-((2-nitrophenyl)amino)thiophene-3-carbonitrile (10m):** Yellow solid; yield: 81%; m.p.: 112.5–113.0 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 9.65 (s, 1H), 8.15 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.65–7.58 (m, 1H), 7.08–7.01 (m, 3H), 2.44 (s, 3H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 150.8, 140.8, 136.2, 136.1, 134.7, 126.1, 124.1, 120.0, 117.3, 114.1, 103.7, 15.1 ppm; HRMS (EI) calc. for C<sub>12</sub>H<sub>9</sub>N<sub>3</sub>O<sub>2</sub>S<sup>+</sup> 259.0415, found 259.0419.



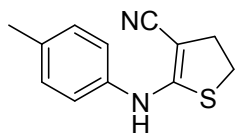
**5-phenyl-2-(phenylamino)thiophene-3-carbonitrile (10n):** White solid; yield: 45%; m.p.: 194.3–195.1 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 9.80 (s, 1H), 7.57 (s, 1H), 7.55 (s, 2H), 7.42–7.23 (m, 7H), 7.06 (t, *J* = 6.8 Hz, 1H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 158.0, 142.0, 132.5, 129.5, 129.1, 128.4, 127.4, 124.7, 122.9, 122.2, 118.2, 115.4, 91.8 ppm; HRMS (EI) calc. for C<sub>17</sub>H<sub>12</sub>N<sub>2</sub>S<sup>+</sup> 276.0721, found 276.0722.

#### General Procedure for the Synthesis of 2-amino-4,5-dihydrothiophenes (11a–11n)

Carboxylic acid compound **9** (0.5 mmol) was added to a solution of KBH<sub>4</sub> (5 mmol) in water (5 mL) at 60 °C. The reaction mixture was stirred at 60 °C for 0.5 h. The reaction mixture was cooled to room temperature and quenched with 1 M HCl. The aqueous layer was extracted with EtOAc (3×2 mL). The combined organic phases were washed once with brine, dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>, vacuum-filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (PE : EA = 3:1) to afford the corresponding 2-amino-4,5-dihydrothiophenes **11a–11m**.

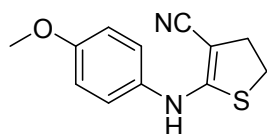


**2-(phenylamino)-4,5-dihydrothiophene-3-carbonitrile (11a):** White solid; yield: 81%; m.p.: 126.8–127.5 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 9.46 and 4.54–4.50 (s and m, 1H, NH and CN-CH), 7.39 and 7.29 (2\*t, *J* = 7.8 Hz, 2H, Ar H-3,5), 7.16 and 7.04 (2\*t, *J* = 7.2 Hz, 1H, Ar H-4), 7.14 and 6.93 (2\*d, *J* = 7.6 Hz, 2H, Ar H-2,6), 3.35–3.31 and 3.28 (m and t, *J* = 8.0 Hz, 2H, S-CH<sub>2</sub>), 2.89, 2.70–2.64 and 2.37–2.27 (t, *J* = 8.0 Hz, 2\*m, 2H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 168.5, 160.7, 150.9, 141.0, 129.3, 128.8, 124.9, 123.4, 120.8, 119.5, 118.0, 117.7, 73.1, 40.4, 33.4, 31.7, 31.1, 30.8 ppm; HRMS (EI) calc. for C<sub>11</sub>H<sub>10</sub>N<sub>2</sub>S<sup>+</sup> 202.0565, found 202.0566.

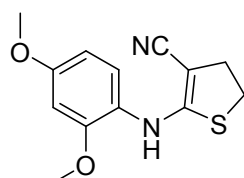


**2-(p-tolylamino)-4,5-dihydrothiophene-3-carbonitrile (11b):** Pink solid; yield: 80%; m.p.: 110.7–111.9 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 9.37 and 4.52–4.47 (s and m, 1H, NH and CN-CH), 7.19 and 7.10 (2\*d, *J* = 8.4 Hz, 2H, Ar H-2,6), 7.04 and 6.84 (2\*d, *J* = 8.4 Hz, 2H, Ar H-3,5), 3.34–3.29 and 3.25 (m and t, *J* = 8.0 Hz, 2H, S-CH<sub>2</sub>), 2.88, 2.68–2.63 and 2.35–2.31 (t, *J* = 8.0 Hz, 2\*m, 2H, CH<sub>2</sub>), 2.29 and 2.25 (2\*s, 3H, CH<sub>3</sub>) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ:

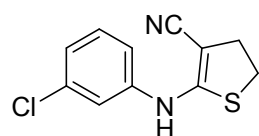
167.7, 161.2, 148.2, 138.5, 134.0, 132.8, 129.7, 129.2, 121.4, 119.6, 118.1, 117.9, 71.5, 40.4, 33.4, 31.6, 31.0, 30.7, 20.5, 20.4 ppm; HRMS (EI) calc. for C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>S<sup>+</sup> 216.0721, found 216.0723.



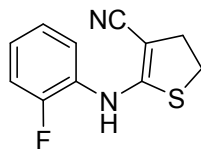
**2-((4-methoxyphenyl)amino)-4,5-dihydrothiophene-3-carbonitrile (11c):** Pink solid; yield: 75%; m.p.: 105.4–106.1 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 9.27 and 4.51–4.45 (s and m, 1H, NH and CN-CH), 7.09 and 6.95 (d, *J* = 8.4 Hz, s, 2H, Ar H-2,6), 6.95 and 6.87 (d, *J* = 8.4 Hz, 2H, Ar H-3,5), 3.75 and 3.73 (2\*s, 3H, OCH<sub>3</sub>), 3.34–3.30 and 3.22 (m and t, *J* = 7.6 Hz, 2H, S-CH<sub>2</sub>), 2.87, 2.68–2.61 and 2.34–2.23 (t, *J* = 7.6 Hz, 2\*m, 2H, CH<sub>2</sub>) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 166.7, 162.2, 156.6, 156.2, 143.5, 134.0, 124.0, 121.2, 118.1, 114.4, 113.9, 69.5, 55.2, 40.5, 33.5, 31.7, 31.0, 30.5 ppm; HRMS (EI) calc. for C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>OS<sup>+</sup> 232.0670, found 232.0669.



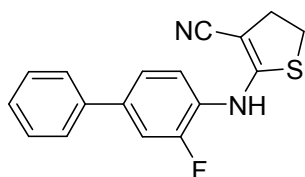
**2-((2,4-dimethoxyphenyl)amino)-4,5-dihydrothiophene-3-carbonitrile (11d):** Yellow oil; yield: 68%; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 8.57 and 4.50–4.44 (s and m, 1H, NH and CN-CH), 7.02 and 6.75 (2\*d, *J* = 8.4 Hz, 1H, Ar H-6), 6.61 and 6.58 (2\*d, *J* = 2.0 Hz, 1H, Ar H-3), 6.50 and 6.45 (2\*dd, *J* = 8.4, 2.4 Hz, 1H, Ar H-5), 3.78 and 3.75 (2\*s, 3H, OCH<sub>3</sub>), 3.75 and 3.73 (2\*s, 3H, OCH<sub>3</sub>), 3.31–3.26 and 3.16 (m and t, *J* = 8.0 Hz, 2H, S-CH<sub>2</sub>), 2.85, 2.67–2.59 and 2.35–2.25 (t, *J* = 8.0 Hz, 2\*m, 2H, CH<sub>2</sub>) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 168.1, 163.7, 158.9, 157.6, 155.3, 150.7, 133.5, 127.9, 122.3, 119.8, 118.2, 118.1, 104.5, 104.1, 99.7, 99.0, 66.4, 55.6, 55.5, 55.3, 55.2, 40.0, 34.2, 31.3, 31.0, 30.7 ppm; HRMS (EI) calc. for C<sub>13</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub>S<sup>+</sup> 262.0776, found 262.0777.



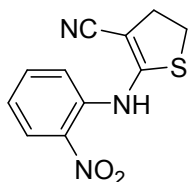
**2-((3-chlorophenyl)amino)-4,5-dihydrothiophene-3-carbonitrile (11e):** Colourless oil; yield: 78%; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 9.61 and 4.57–4.51 (s and m, 1H, NH and CN-CH), 7.42 and 7.31 (2\*t, *J* = 8.0 Hz, 1H, Ar H-5), 7.23 and 7.11 (2\*dd, *J* = 8.0, 1.2 Hz, 1H, Ar H-4), 7.18 and 6.99 (2\*t, *J* = 1.2 Hz, 1H, Ar H-2), 7.07 and 6.91 (2\*dd, *J* = 8.0, 1.2 Hz, 1H, Ar H-6), 3.39–3.34 and 3.32 (m and t, *J* = 8.0 Hz, 2H, S-CH<sub>2</sub>), 2.92, 2.74–2.66 and 2.40–2.29 (t, *J* = 8.0 Hz, 2\*m, 2H, CH<sub>2</sub>) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 170.6, 159.6, 152.4, 142.6, 133.6, 133.1, 131.1, 130.4, 124.7, 122.6, 119.7, 119.3, 118.6, 118.4, 117.8, 117.3, 75.8, 40.4, 33.3, 31.9, 31.2, 30.9 ppm; HRMS (EI) calc. for C<sub>11</sub>H<sub>9</sub><sup>35</sup>ClN<sub>2</sub>S<sup>+</sup> 236.0175, found 236.0173; calc. for C<sub>11</sub>H<sub>9</sub><sup>37</sup>ClN<sub>2</sub>S<sup>+</sup> 238.0145, found 238.0144.



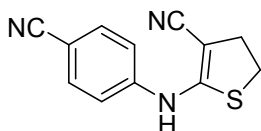
**2-((2-fluorophenyl)amino)-4,5-dihydrothiophene-3-carbonitrile (11f):** White solid; yield: 82%; m.p.: 132.8–133.7 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 9.23 and 4.64–4.59 (s and m, 1H, NH and CN-CH), 7.31–7.13 and 7.03–6.98 (2\*m, 4H, Ar H), 3.39–3.34 and 3.25 (m and t, *J* = 8.0 Hz, 2H, S-CH<sub>2</sub>), 2.90, 2.75–2.67 and 2.42–2.31 (t, *J* = 7.9 Hz, 2\*m, 2H, CH<sub>2</sub>) ppm; <sup>19</sup>F NMR (376 MHz, DMSO-*d*<sub>6</sub>) δ: -122.89 – -122.96 (m), -126.02 – -126.09 (m) ppm; HRMS (EI) calc. for C<sub>11</sub>H<sub>9</sub>FN<sub>2</sub>S<sup>+</sup> 220.0470, found 220.0471.



**2-((3-fluoro-[1,1'-biphenyl]-4-yl)amino)-4,5-dihydrothiophene-3-carbonitrile (11g):** Yellowish solid; yield: 75%; m.p.: 95.0–95.5 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 9.32 and 4.68–4.62 (s and m, 1H, NH and CN-CH), 7.71 (t, *J* = 6.8 Hz, 2H, Ar H), 7.66–7.50 (m, 2H, Ar H), 7.47 (t, *J* = 7.2 Hz, 2H, Ar H), 7.38 (t, *J* = 7.2 Hz, 1H, Ar H), 7.33 and 7.11 (2\*t, *J* = 8.4 Hz, 1H, Ar H), 3.41–3.38 and 3.28 (m and t, *J* = 8.0 Hz, 2H, S-CH<sub>2</sub>), 2.93, 2.74–2.72 and 2.45–2.34 (t, *J* = 7.6 Hz, 2\*m, 2H, CH<sub>2</sub>) ppm; <sup>19</sup>F NMR (376 MHz, DMSO-*d*<sub>6</sub>) δ: -122.38 – -122.44 (m), -125.15 – -125.22 (m) ppm; HRMS (EI) calc. for C<sub>17</sub>H<sub>13</sub>FN<sub>2</sub>S<sup>+</sup> 296.0783, found 296.0784.



**2-((2-nitrophenyl)amino)-4,5-dihydrothiophene-3-carbonitrile (11h):** Pink oil; yield: 76%; m.p.: 91.6–92.4 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 9.64 and 4.65–4.60 (s and m, 1H, NH and CN-CH), 8.08–8.03 (m, 1H, Ar H-3), 7.77–7.68 (m, 1H, Ar H-5), 7.47 and 7.12 (2\*d, *J* = 7.6 Hz, 1H, Ar H-6), 7.39 and 7.29 (2\*t, *J* = 7.6 Hz, 1H, Ar H-4), 3.42–3.38 and 3.34 (m and t, *J* = 8.0 Hz, 2H, S-CH<sub>2</sub>), 2.94, 2.76–2.71 and 2.43–2.32 (t, *J* = 8.0 Hz, 2\*m, 2H, CH<sub>2</sub>) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ: 172.4, 159.5, 144.7, 140.2, 139.8, 135.5, 135.0, 134.6, 125.6, 125.5, 125.0, 124.4, 124.2, 121.4, 117.3, 116.6, 78.6, 40.4, 33.5, 32.3, 31.5, 31.4 ppm; HRMS (EI) calc. for C<sub>11</sub>H<sub>9</sub>N<sub>3</sub>O<sub>2</sub>S<sup>+</sup> 247.0415, found 247.0414.

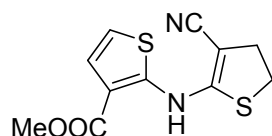


**2-((4-cyanophenyl)amino)-4,5-dihydrothiophene-3-carbonitrile (11i):** White solid; yield: 78%; m.p.: 142.3–143.0 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ: 9.92 and 4.62–4.57 (s and m, 1H, NH

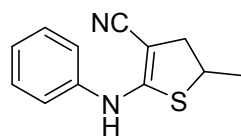
and CN-CH), 7.87 and 7.73 (2\*d,  $J = 8.0$  Hz, 2H, Ar H-3,5), 7.24 and 7.10 (2\*d,  $J = 8.0$  Hz, 2H, Ar H-2,6), 3.37 (t,  $J = 7.6$  Hz, 2H, S-CH<sub>2</sub>), 2.95, 2.75–2.68 and 2.42–2.31 (t,  $J = 7.6$  Hz, 2\*m, 2H, CH<sub>2</sub>) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 171.3, 158.2, 154.9, 154.6, 145.4, 133.8, 133.2, 120.5, 119.1, 118.8, 116.7, 115.6, 107.2, 103.5, 80.3, 40.5, 33.3, 32.1, 31.4, 31.0 ppm; HRMS (EI) calc. for C<sub>12</sub>H<sub>9</sub>N<sub>3</sub>S<sup>+</sup> 227.0517, found 227.0516.



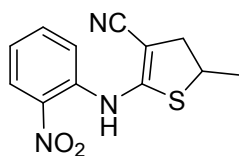
**2-((4-nitrophenyl)amino)-4,5-dihydrothiophene-3-carbonitrile (11j):** Yellow solid; yield: 61%; m.p.: 154.1–154.8 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 10.16 and 4.67–4.61 (s and m, 1H, NH and CN-CH), 8.28 and 8.18 (2\*d,  $J = 8.8$  Hz, 2H, Ar H-3,5), 7.27 and 7.16 (2\*d,  $J = 8.8$  Hz, 2H, Ar H-2,6), 3.41 (t,  $J = 8.0$  Hz, 2H, S-CH<sub>2</sub>), 2.98, 2.77–2.71 and 2.44–2.33 (t,  $J = 8.0$  Hz, 2\*m, 2H, CH<sub>2</sub>) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 157.8, 153.8, 147.5, 144.1, 141.0, 125.9, 125.4, 125.2, 120.5, 117.9, 116.5, 114.7, 82.2, 40.6, 33.3, 32.3, 31.5, 31.0 ppm; HRMS (EI) calc. for C<sub>11</sub>H<sub>9</sub>N<sub>3</sub>O<sub>2</sub>S<sup>+</sup> 247.0415, found 247.0414.



**methyl 2-((3-cyano-4,5-dihydrothiophen-2-yl)amino)thiophene-3-carboxylate (11k):** Yellow solid; yield: 66%; m.p.: 130.5–131.3 °C; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 10.53 and 4.67–4.62 (s and m, 1H, NH and CN-CH), 7.37 and 7.16 (2\*d,  $J = 5.6$  Hz, 1H, Ar H-5), 7.28 and 7.02 (2\*d,  $J = 5.6$  Hz, 1H, Ar H-4), 3.82 and 3.74 (2\*s, 3H, CH<sub>3</sub>), 3.50–3.43 (m, 2H, S-CH<sub>2</sub>), 2.94, 2.75–2.68 and 2.42–2.32 (t,  $J = 8.0$  Hz, 2\*m, 2H, CH<sub>2</sub>) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 172.9, 164.5, 162.2, 158.4, 156.9, 152.5, 127.5, 125.3, 120.2, 119.9, 117.5, 116.4, 115.8, 113.4, 76.9, 51.9, 51.5, 41.1, 33.3, 33.1, 32.5, 31.1 ppm; HRMS (EI) calc. for C<sub>11</sub>H<sub>10</sub>N<sub>2</sub>O<sub>2</sub>S<sub>2</sub><sup>+</sup> 266.0184, found 266.0185.

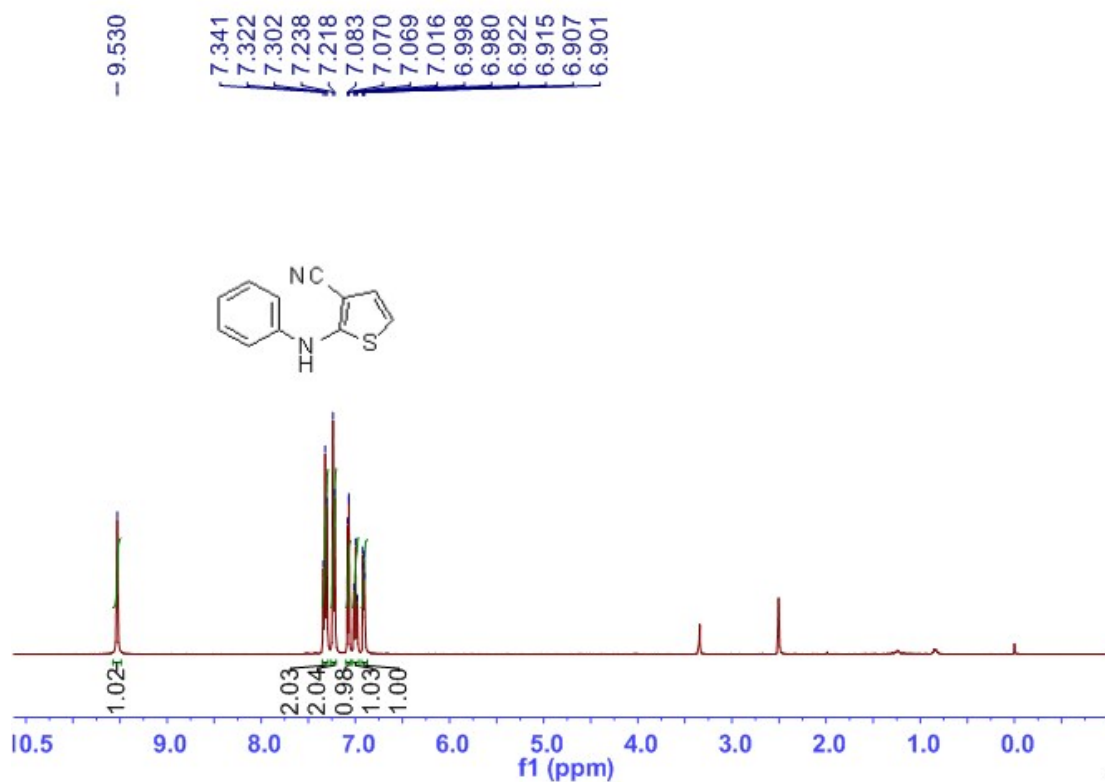


**5-methyl-2-(phenylamino)-4,5-dihydrothiophene-3-carbonitrile (11l):** Yellowish oil; yield: 75%; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 9.43, 4.77–4.73 and 4.65–4.59 (s and 2\*m, 1H, NH and CN-CH), 7.38 and 7.29 (2\*t,  $J = 8.0$  Hz, 2H, Ar H-3,5), 7.18–7.12 and 6.99–6.97 (2\*m, 2H, Ar H-2,6), 7.16 and 7.04 (2\*t,  $J = 7.6$  Hz, 1H, Ar H-4), 4.02–3.96 and 3.91–3.83 (2\*m, 1H, S-CH), 3.10–3.04, 2.81–2.74, 2.71–2.66, 2.60–2.53, 2.33–2.27, 2.19–2.11 and 2.05–1.95 (7\*m, 2H, CH<sub>2</sub>), 1.40–1.35 (m, 3H, CH<sub>3</sub>) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 168.0, 159.8, 150.8, 150.7, 141.0, 129.3, 128.7, 124.9, 124.8, 123.3, 120.8, 119.6, 119.5, 118.2, 117.9, 117.8, 77.7, 71.9, 43.6, 43.5, 43.2, 41.2, 41.1, 39.7, 38.7, 37.4, 21.5, 21.3, 19.8, 19.5 ppm; HRMS (EI) calc. for C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>S<sup>+</sup> 216.0721, found 216.0723.

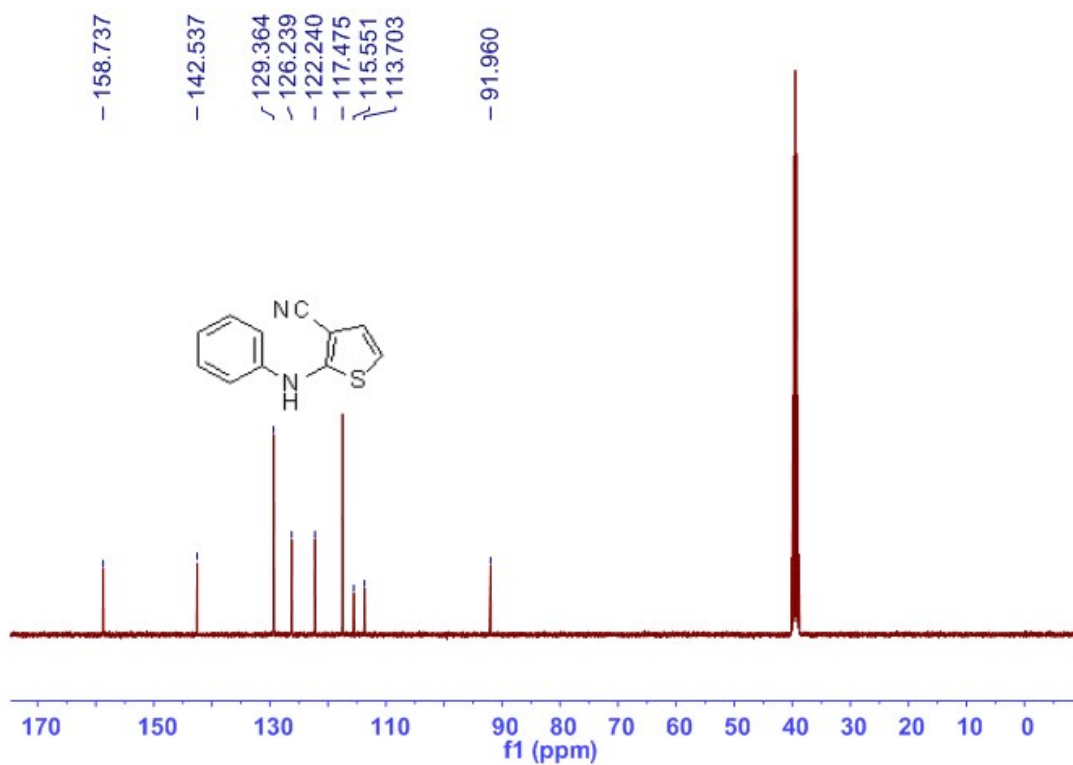


**5-methyl-2-((2-nitrophenyl)amino)-4,5-dihydrothiophene-3-carbonitrile (11m):** Yellow solid; yield: 75%; m.p.: 73.8–74.5 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$ : 9.64, 4.88–4.84 and 4.76–4.71 (s and 2\*m, 1H, NH and CN-CH), 8.08–8.02 (m, 1H, Ar H), 7.76–7.67 (m, 1H, Ar H), 7.46–7.37 (m, 1H, Ar H), 7.29 and 7.11 (2\*t,  $J = 8.0$  Hz, 1H, Ar H), 4.11–4.04 and 4.01–3.90 (2\*m, 1H, S-CH), 3.15–3.09, 2.88–2.81, 2.65–2.57, 2.42–2.35 and 2.12–1.02 (5\*m, 2H,  $\text{CH}_2$ ), 1.41 and 1.38 (2\*d,  $J = 6.8$  Hz, 3H,  $\text{CH}_3$ ) ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$ : 171.9, 171.8, 158.7, 144.6, 140.2, 139.9, 139.7, 135.6, 134.9, 134.6, 125.7, 125.5, 125.0, 124.3, 124.1, 121.5, 121.4, 117.5, 117.3, 116.8, 77.5, 44.6, 43.8, 41.1, 38.1, 21.4, 21.2, 19.7 ppm; HRMS (EI) calc. for  $\text{C}_{12}\text{H}_{11}\text{N}_3\text{O}_2\text{S}^+$  261.0572, found 261.0573.

$^1\text{H}$ ,  $^{19}\text{F}$  and  $^{13}\text{C}$  NMR Spectra of Compounds 10a–10n

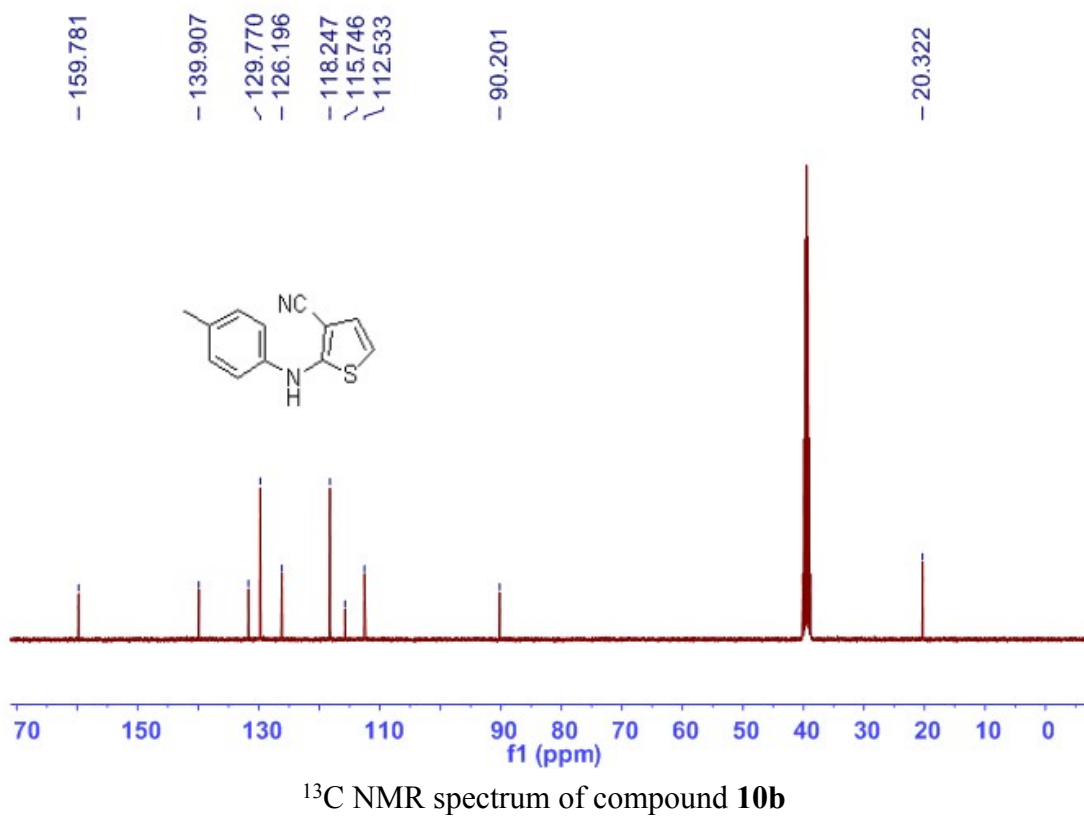
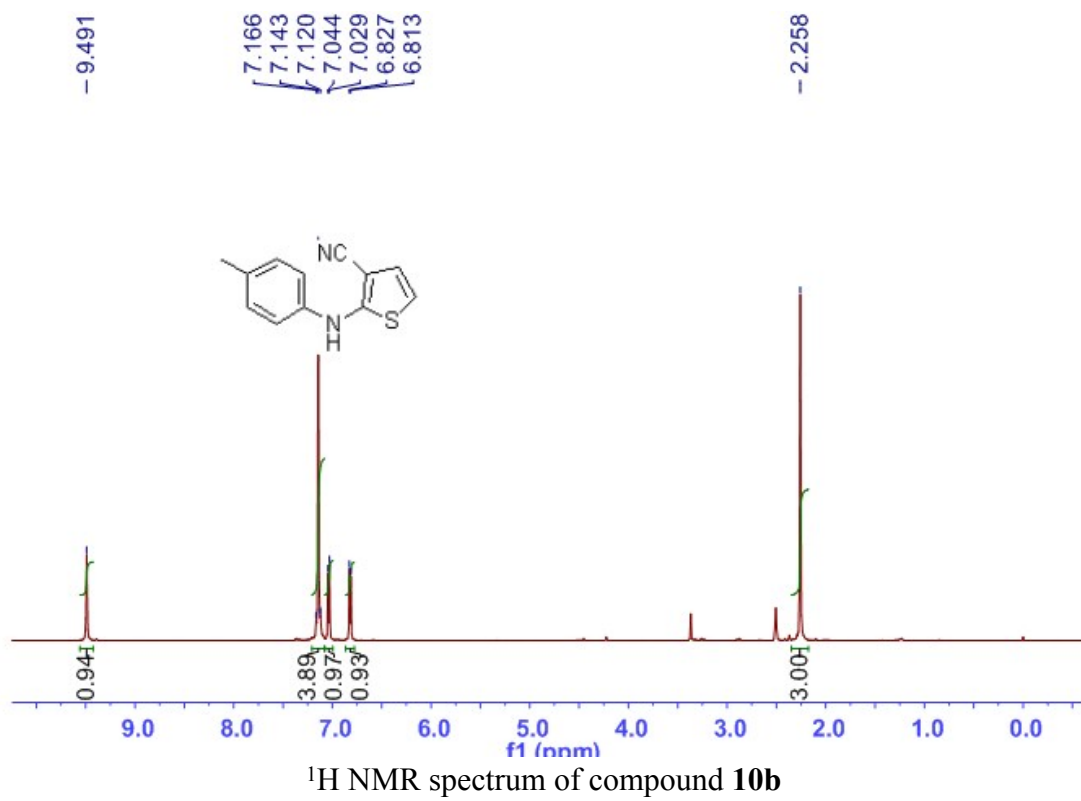


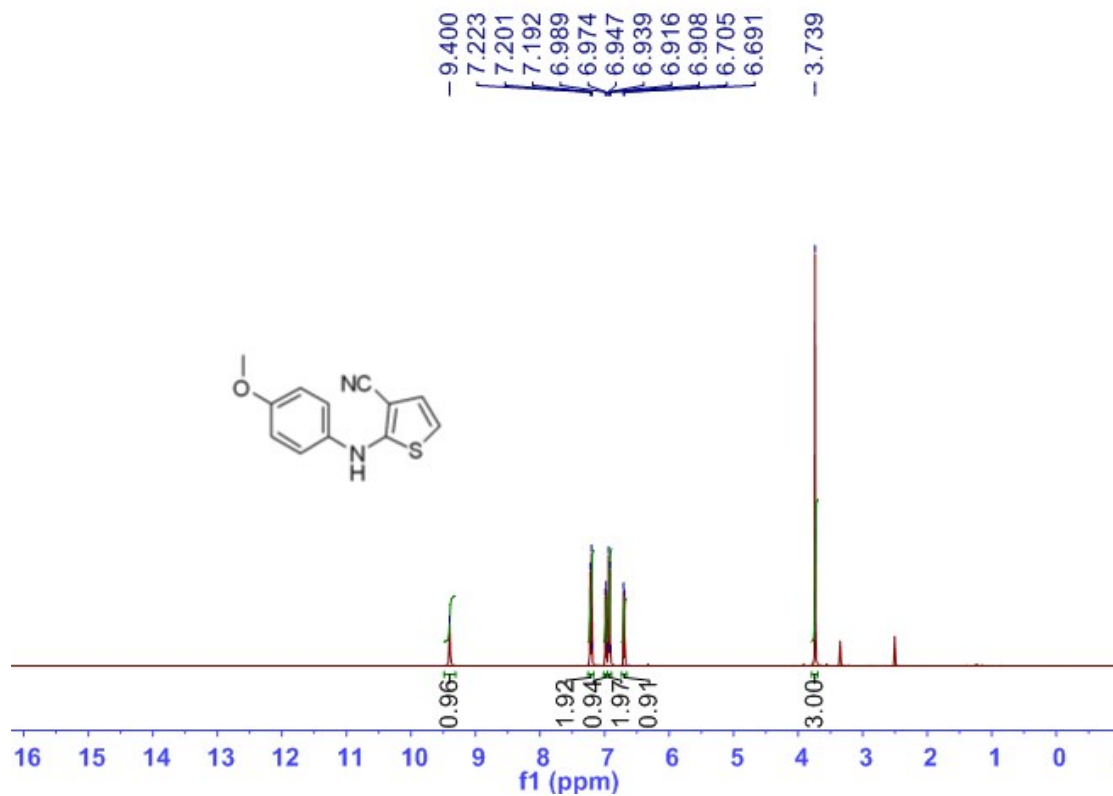
$^1\text{H}$  NMR spectrum of compound 10a



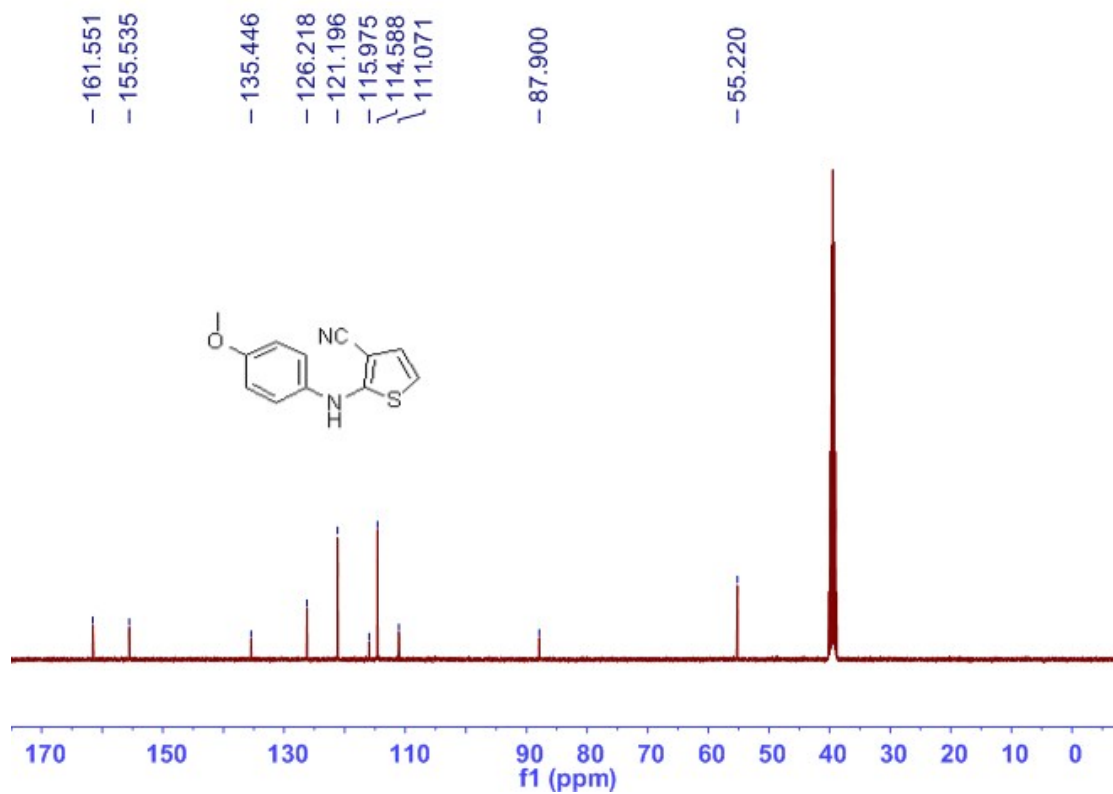
$^{13}\text{C}$  NMR spectrum of compound 10a



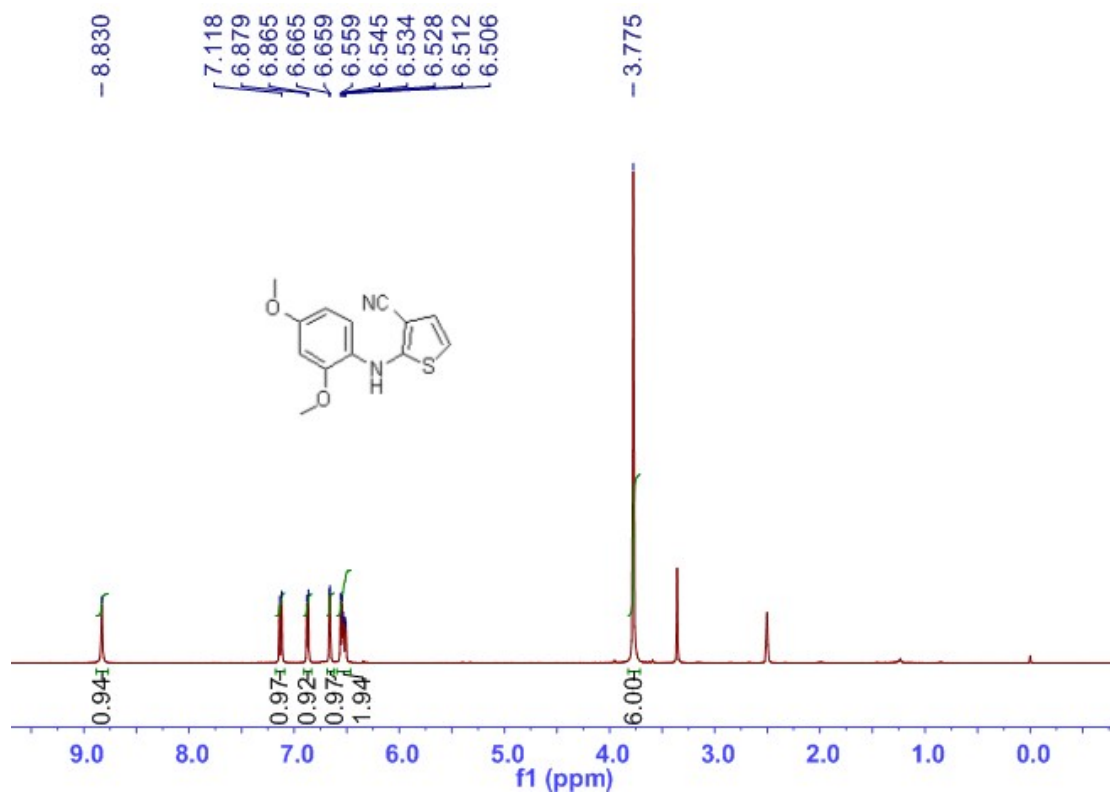




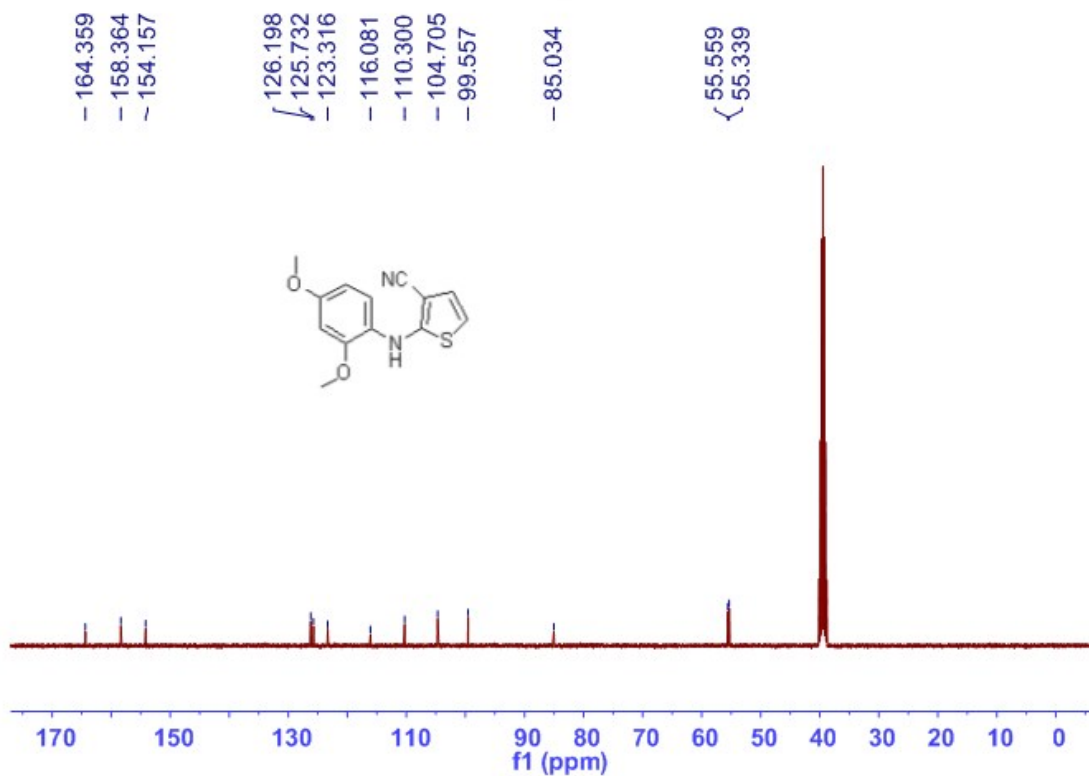
<sup>1</sup>H NMR spectrum of compound **10c**



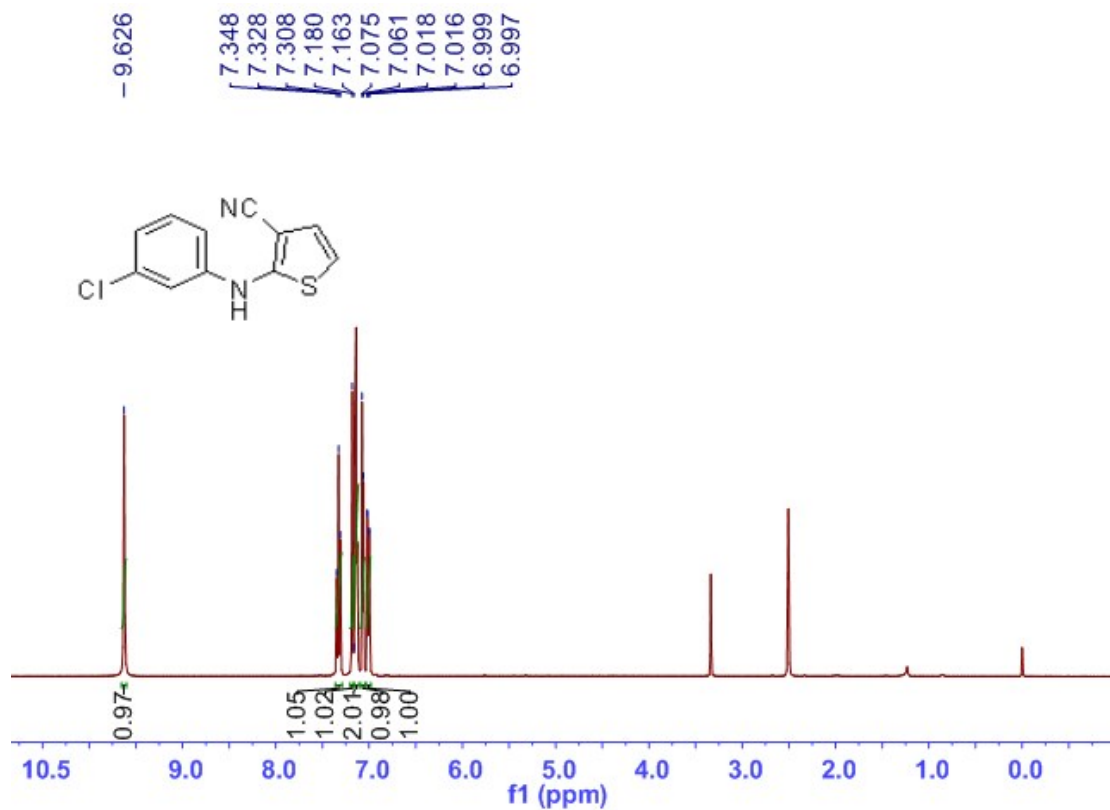
<sup>13</sup>C NMR spectrum of compound **10c**



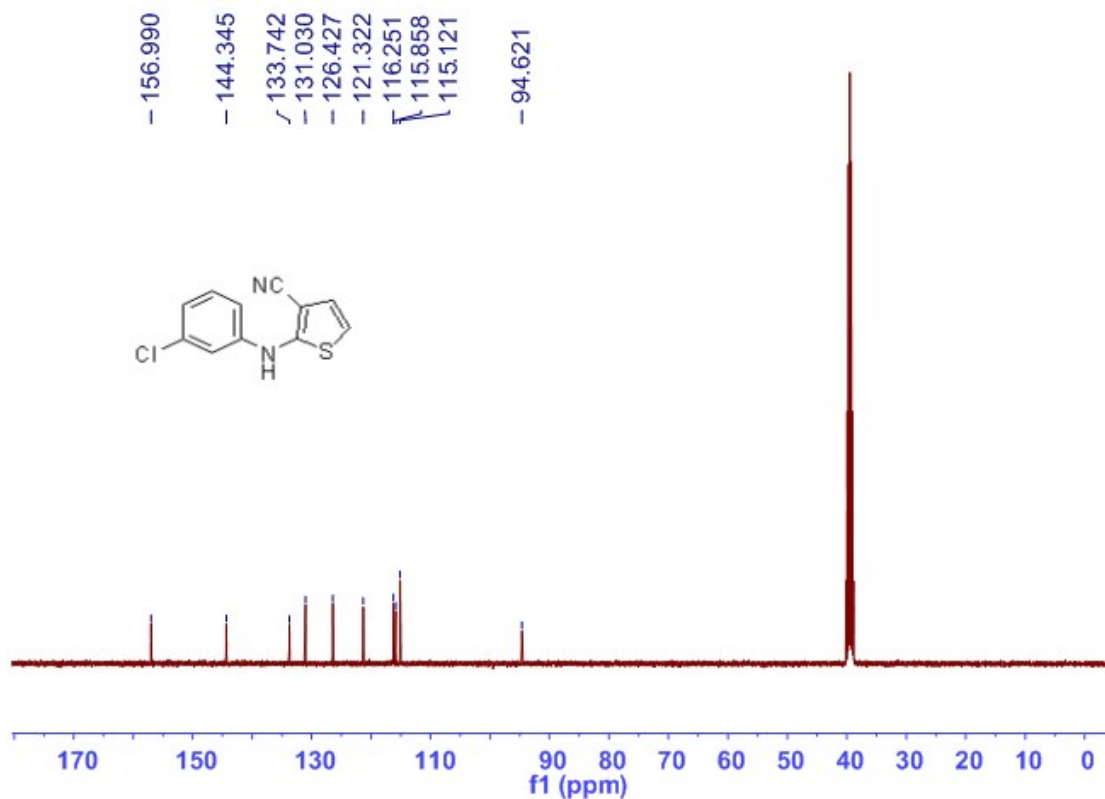
<sup>1</sup>H NMR spectrum of compound 10d



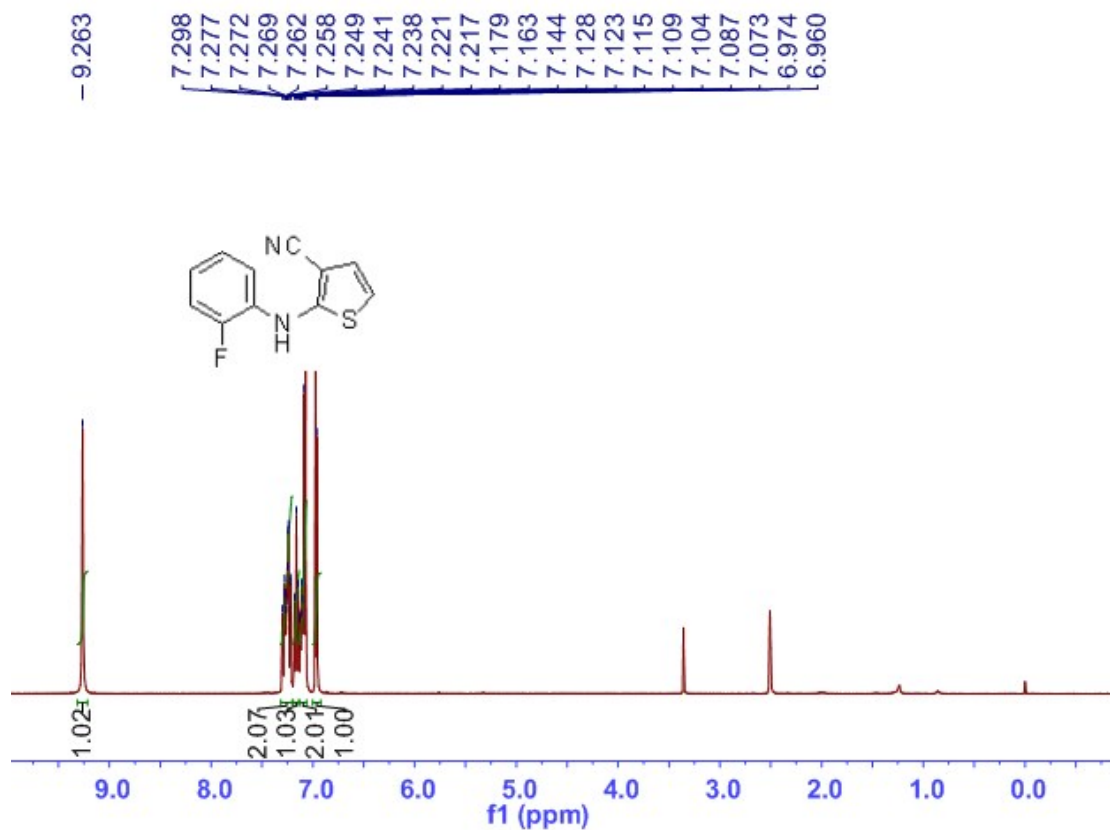
<sup>13</sup>C NMR spectrum of compound 10d



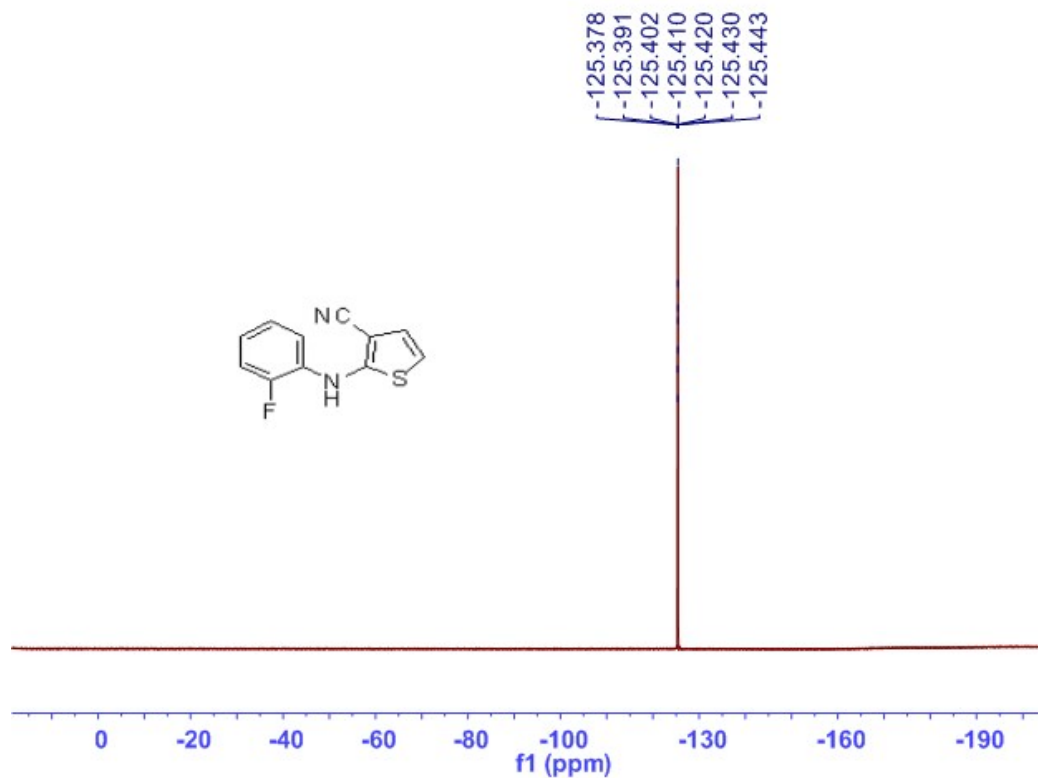
<sup>1</sup>H NMR spectrum of compound **10e**



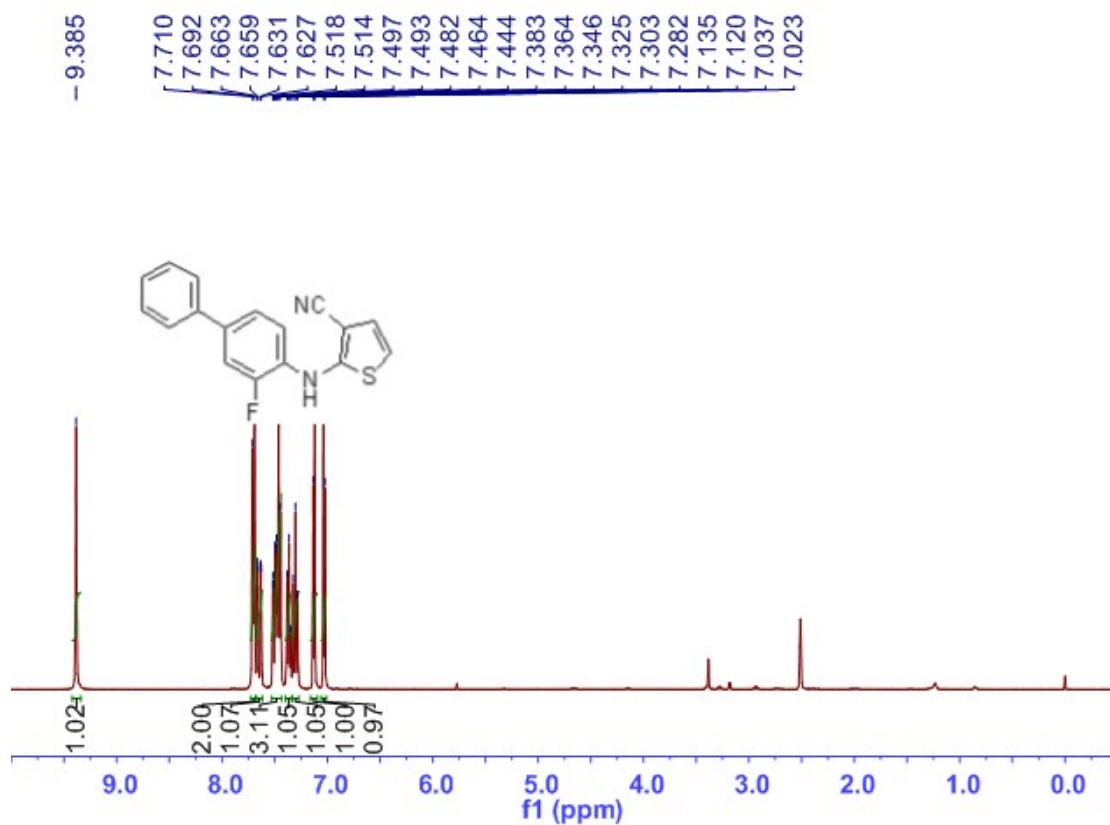
<sup>13</sup>C NMR spectrum of compound **10e**



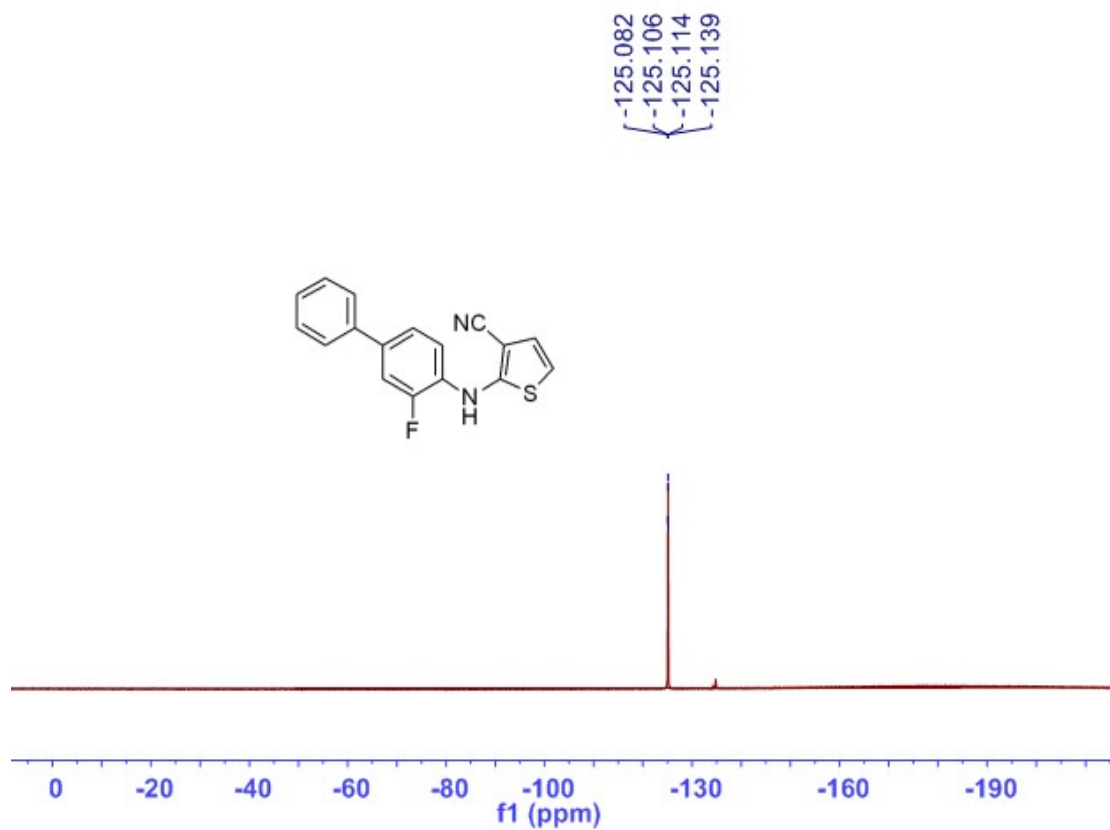
<sup>1</sup>H NMR spectrum of compound **10f**



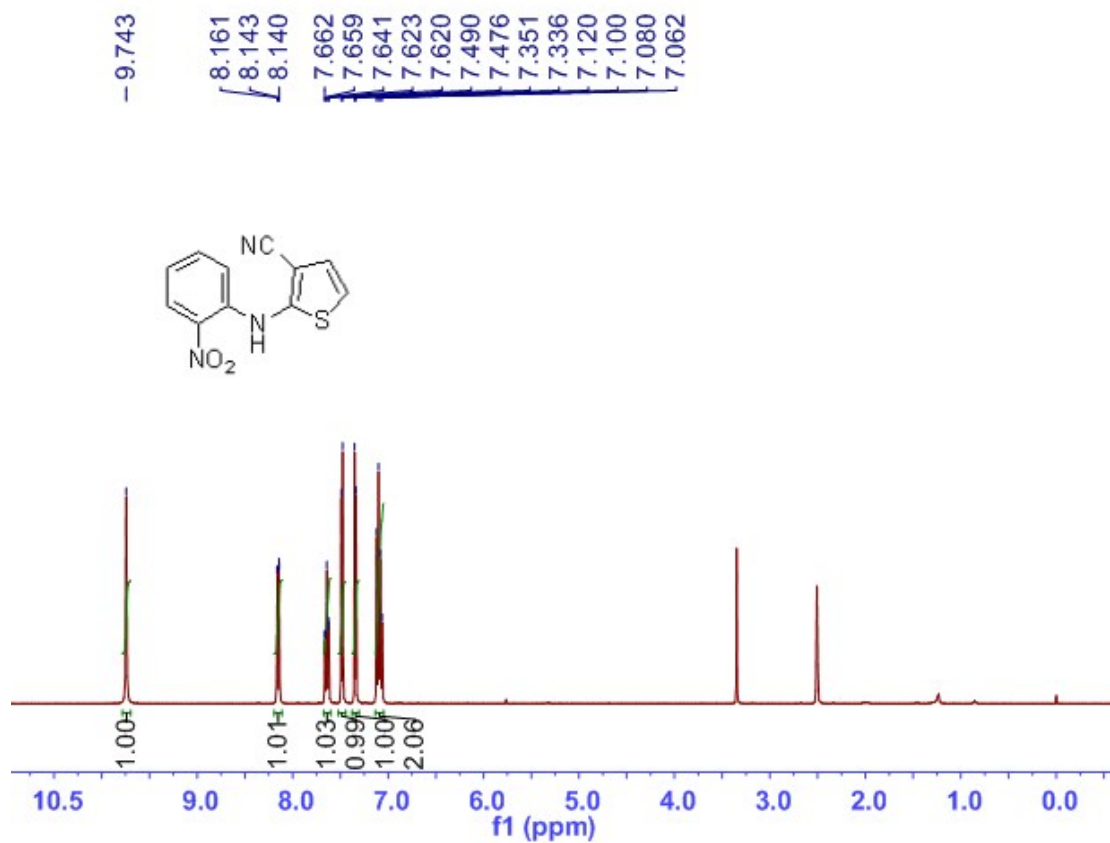
<sup>19</sup>F NMR spectrum of compound **10f**



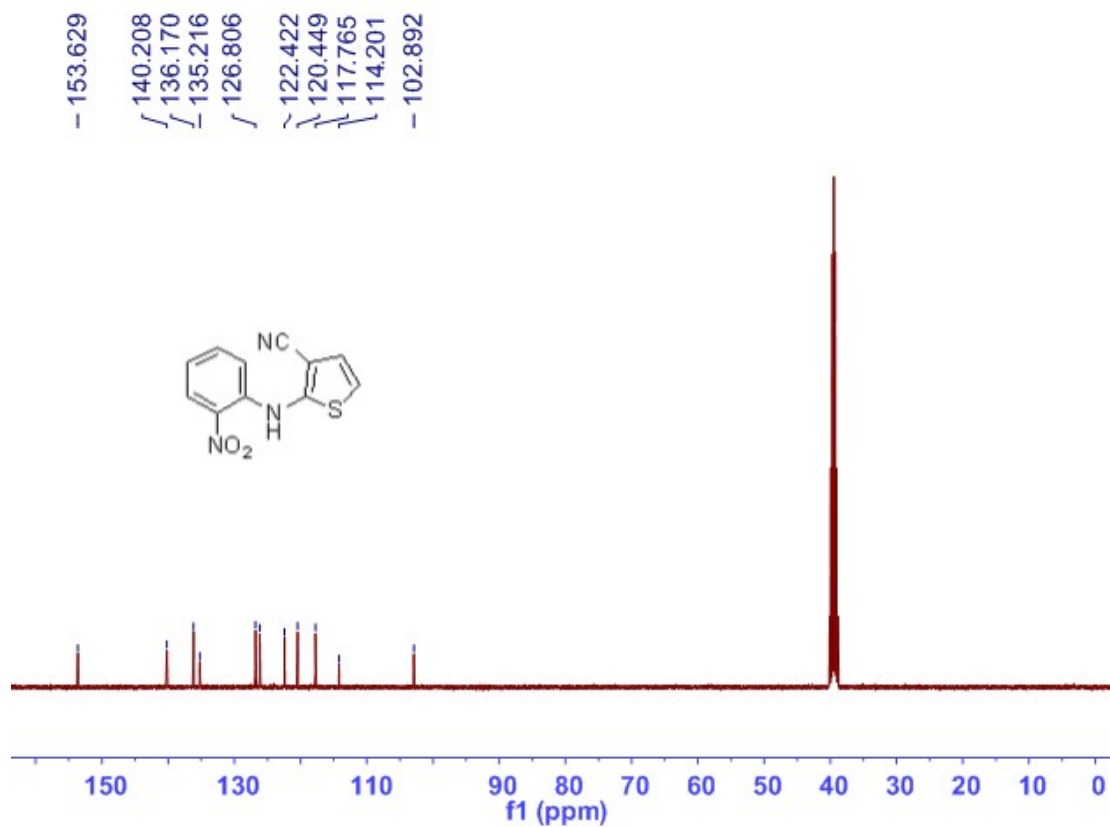
<sup>1</sup>H NMR spectrum of compound **10g**



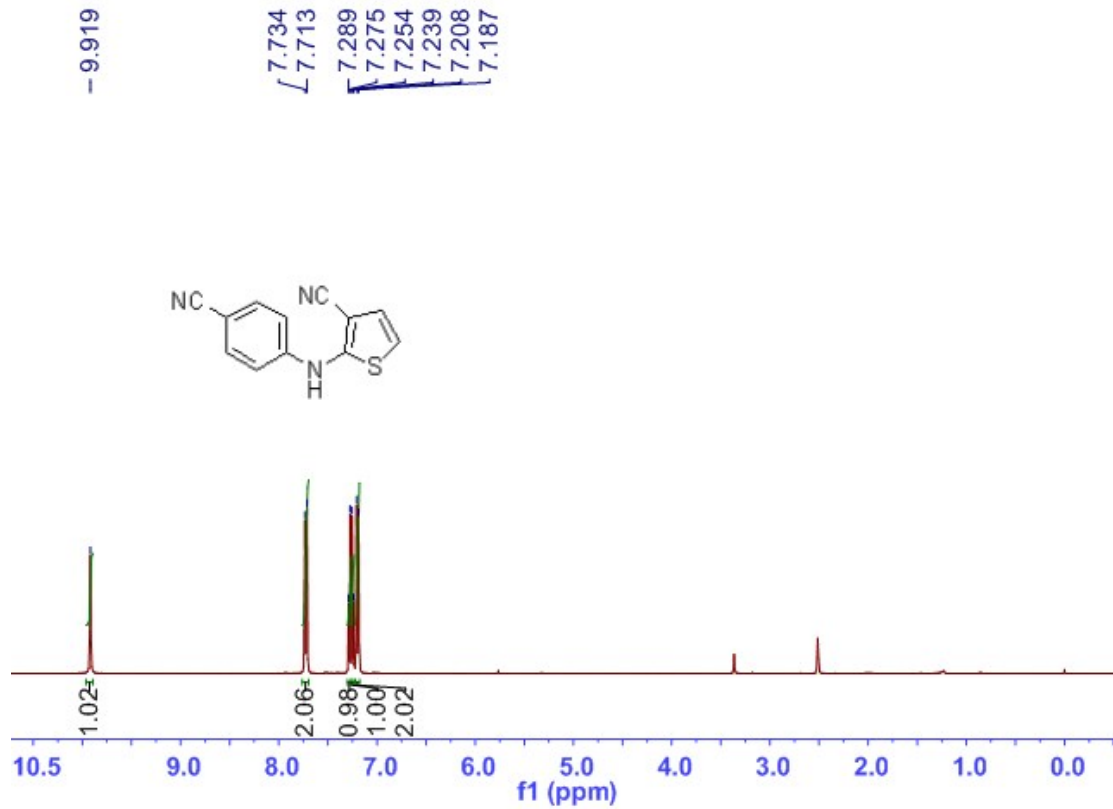
<sup>19</sup>F NMR spectrum of compound **10g**



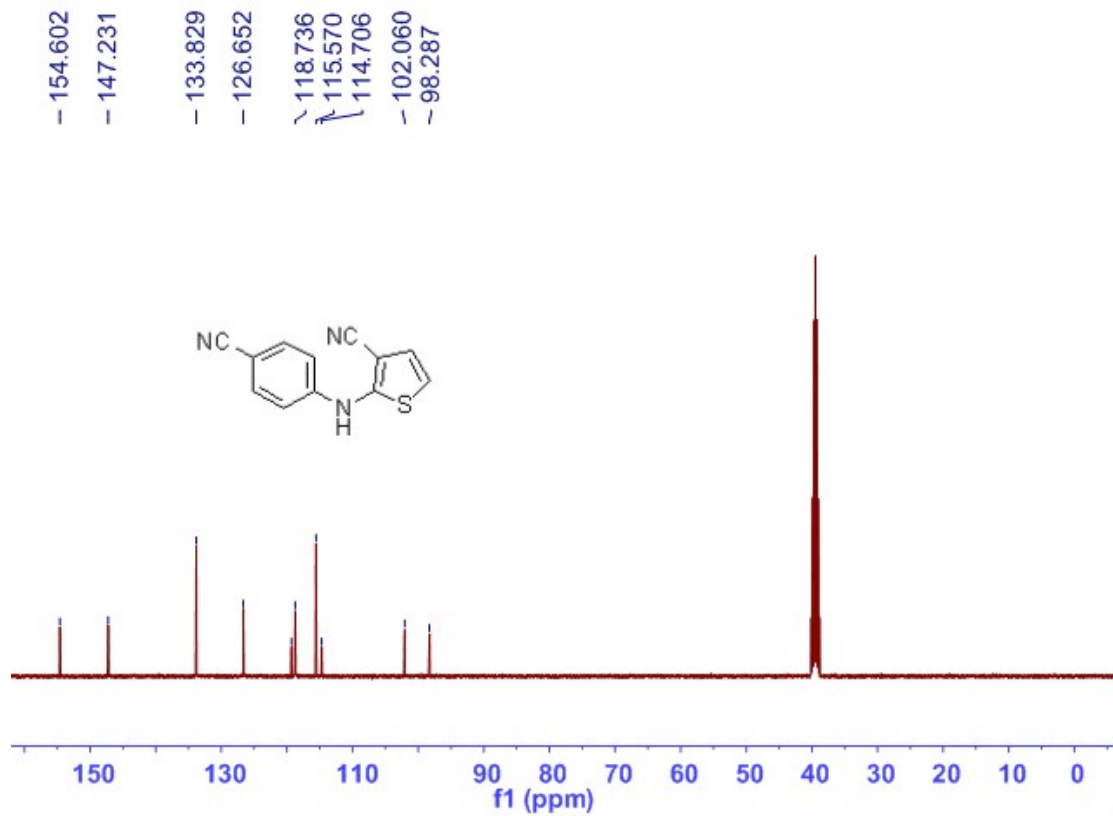
<sup>1</sup>H NMR spectrum of compound **10h**



<sup>13</sup>C NMR spectrum of compound **10h**

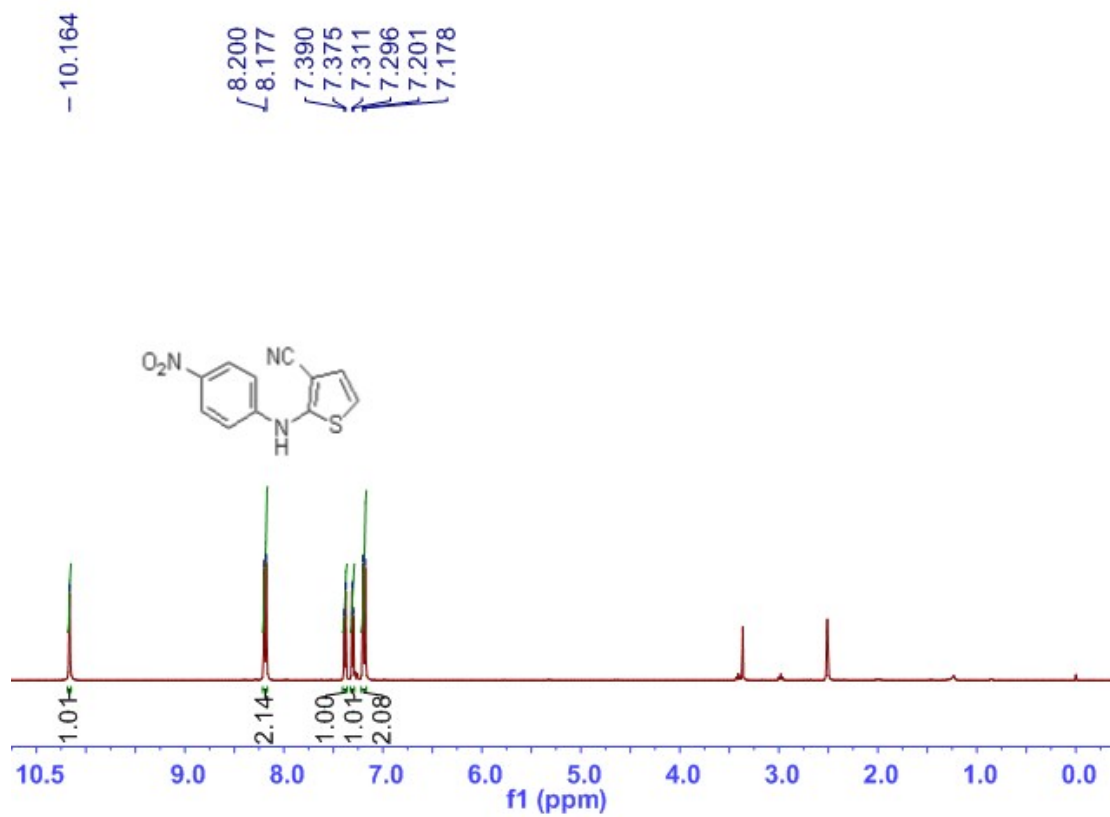


<sup>1</sup>H NMR spectrum of compound **10i**

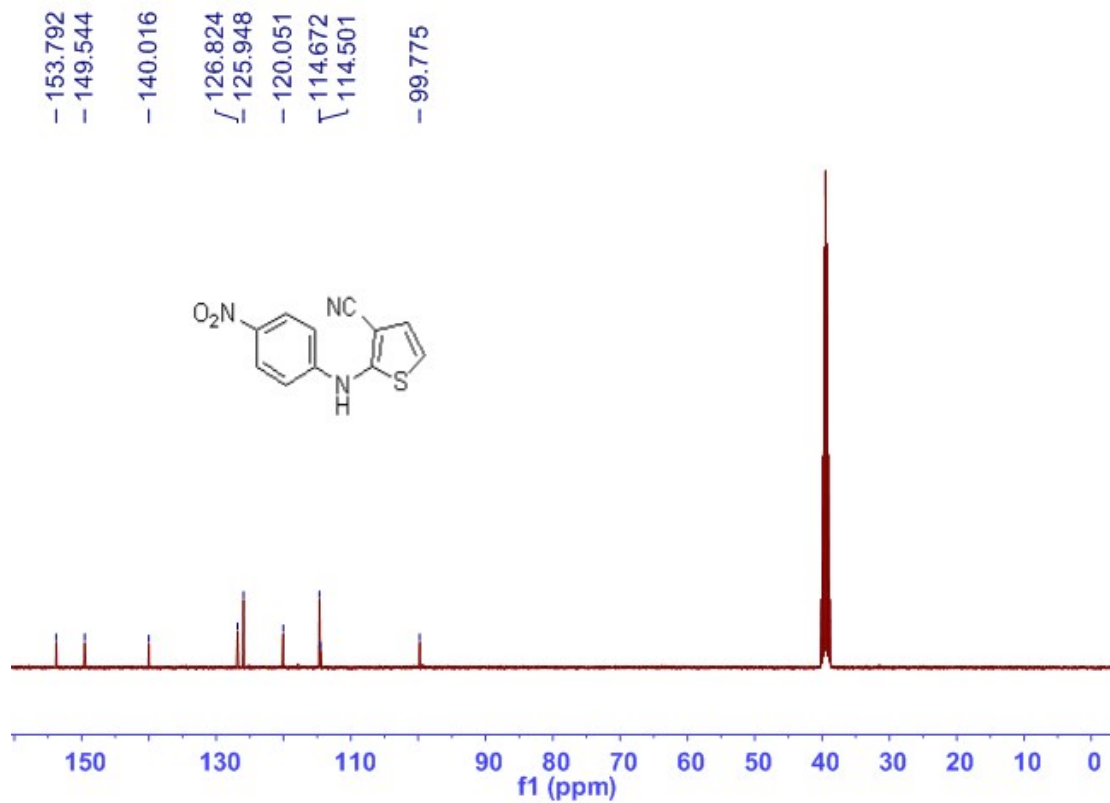


<sup>13</sup>C NMR spectrum of compound **10i**

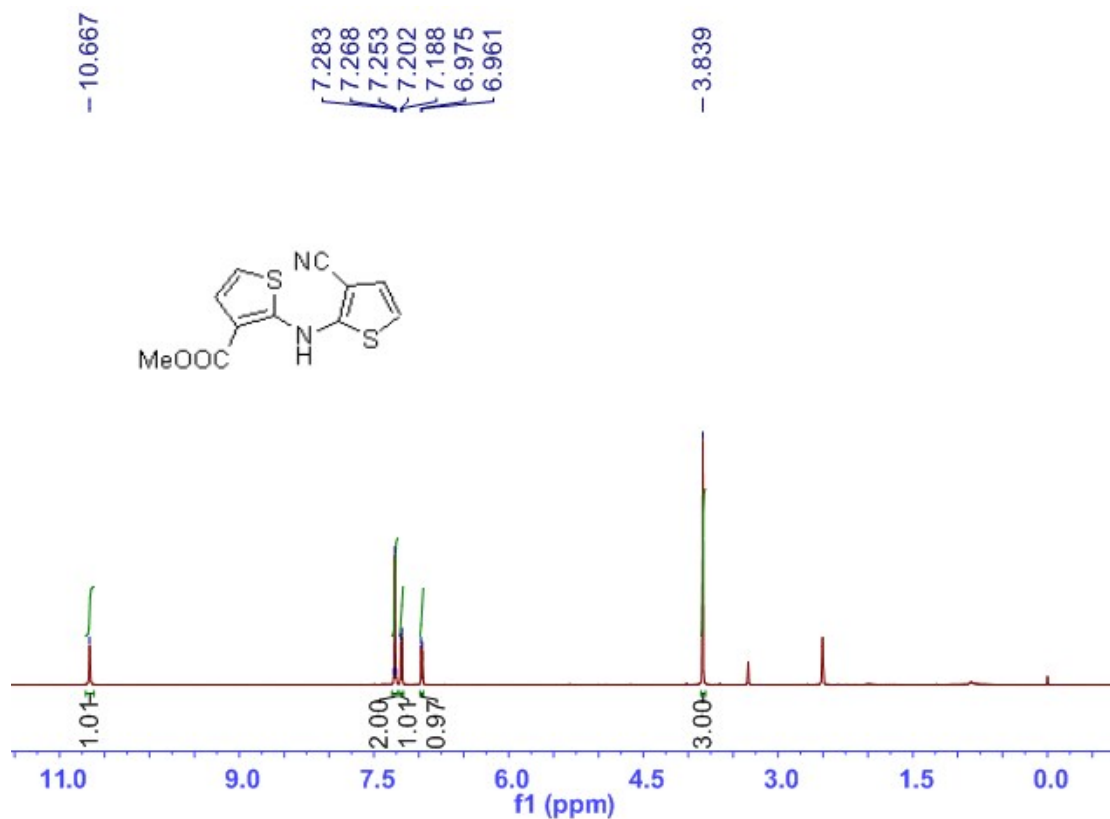




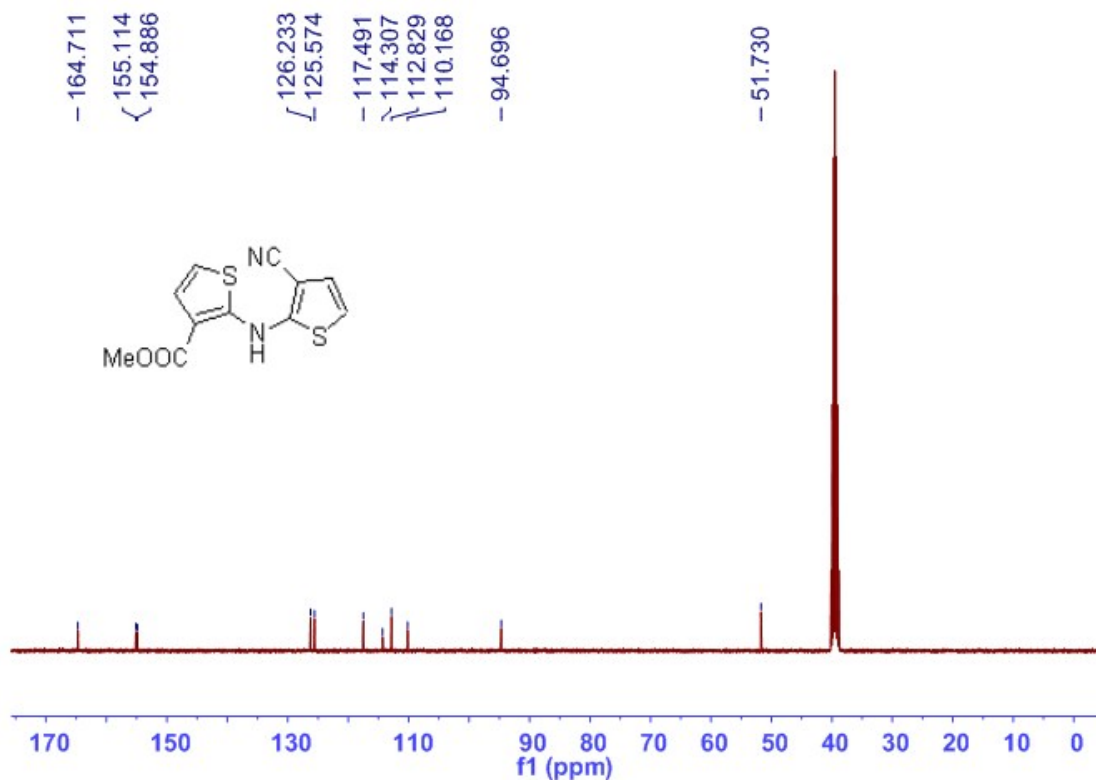
$^1\text{H}$  NMR spectrum of compound **10j**



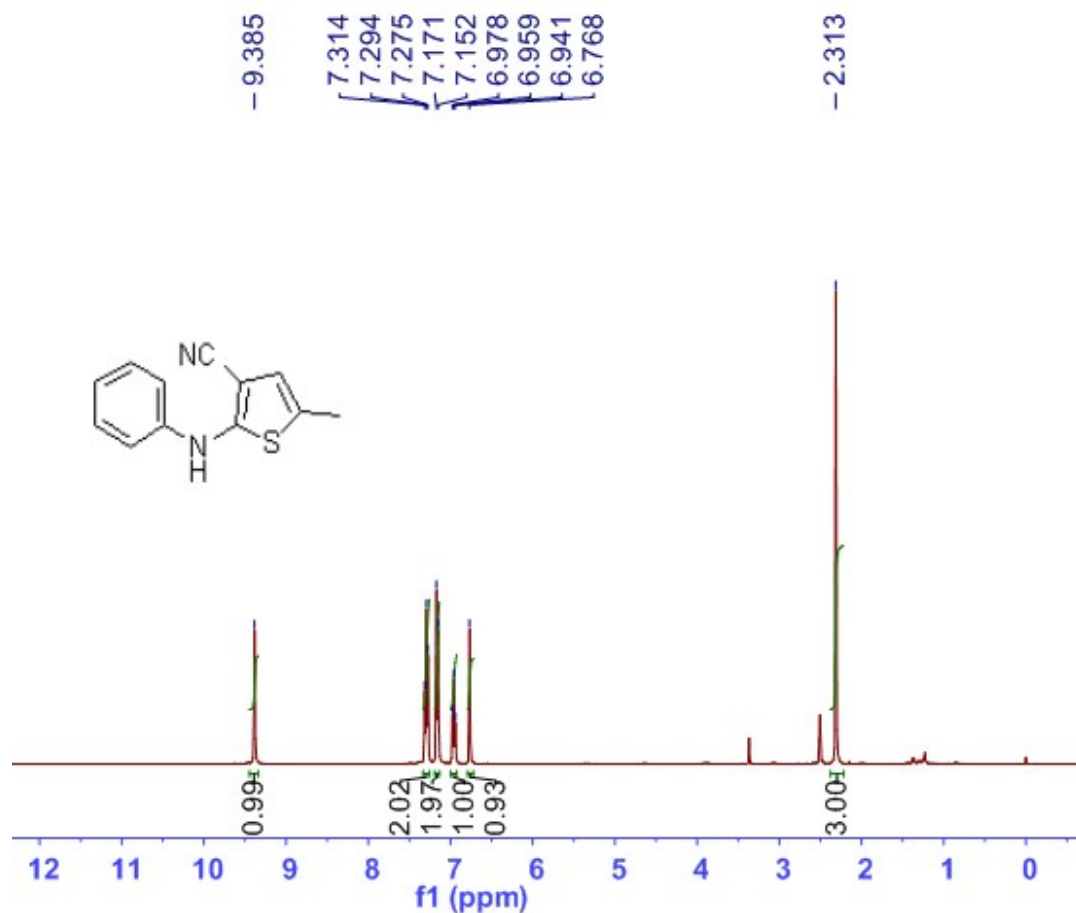
$^{13}\text{C}$  NMR spectrum of compound **10j**



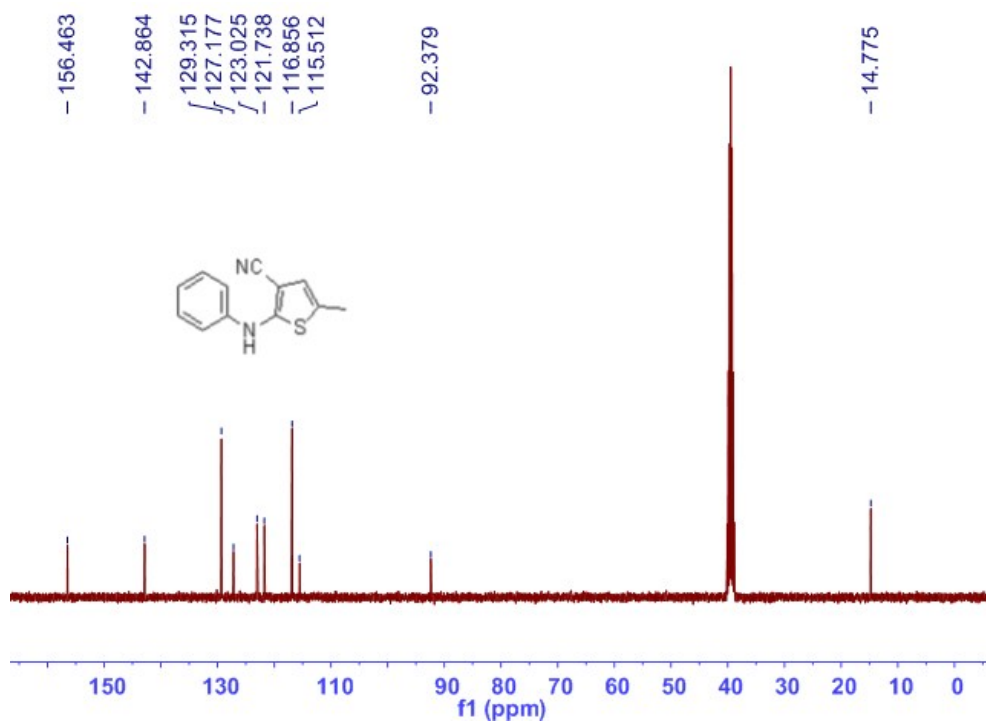
<sup>1</sup>H NMR spectrum of compound **10k**



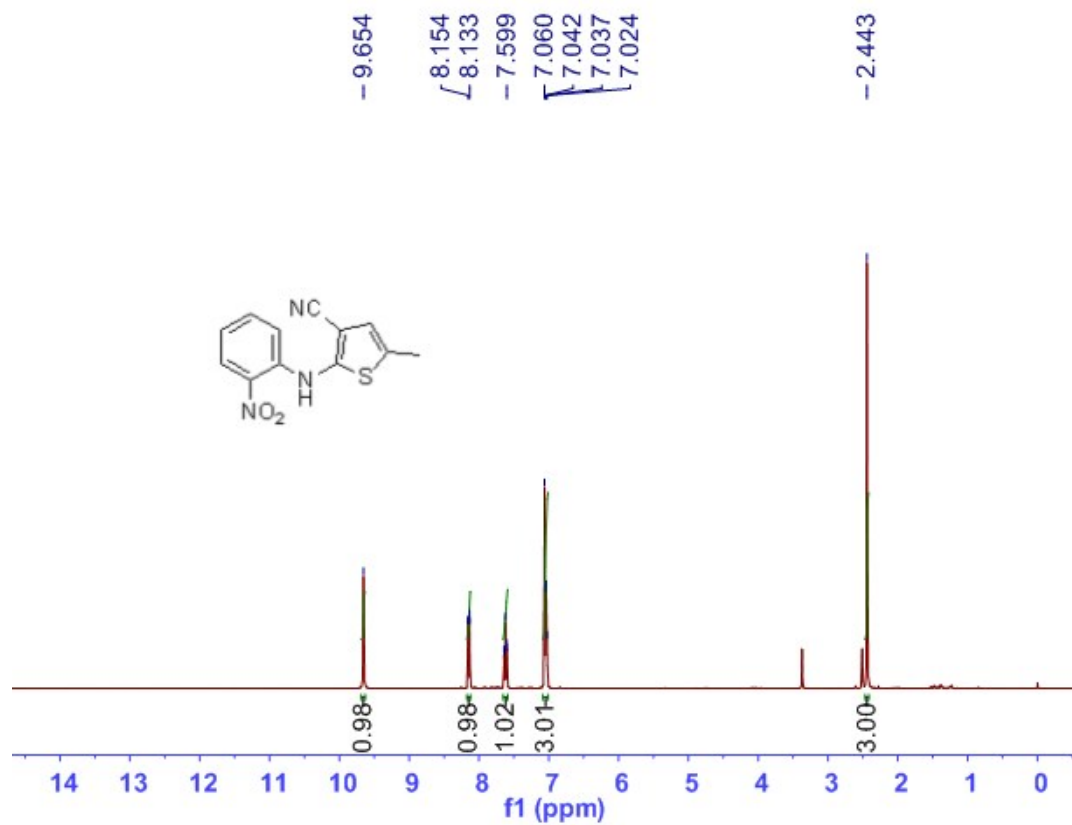
<sup>13</sup>C NMR spectrum of compound **10k**



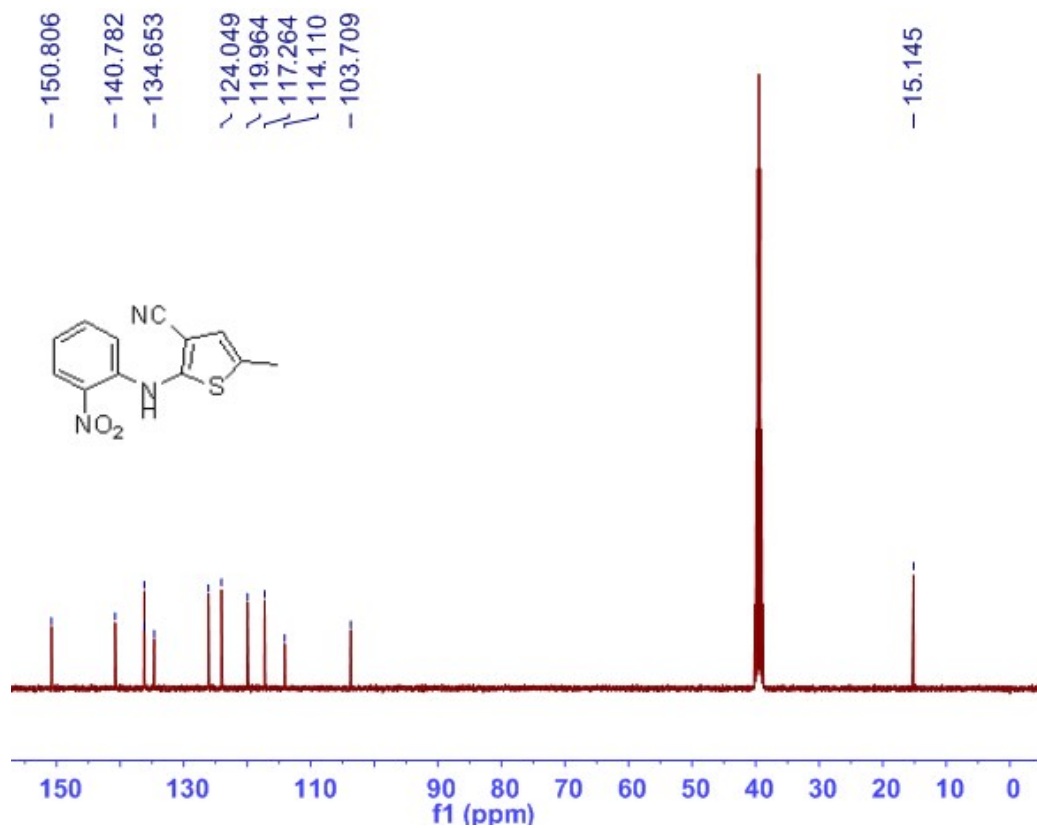
$^1\text{H}$  NMR spectrum of compound **101**



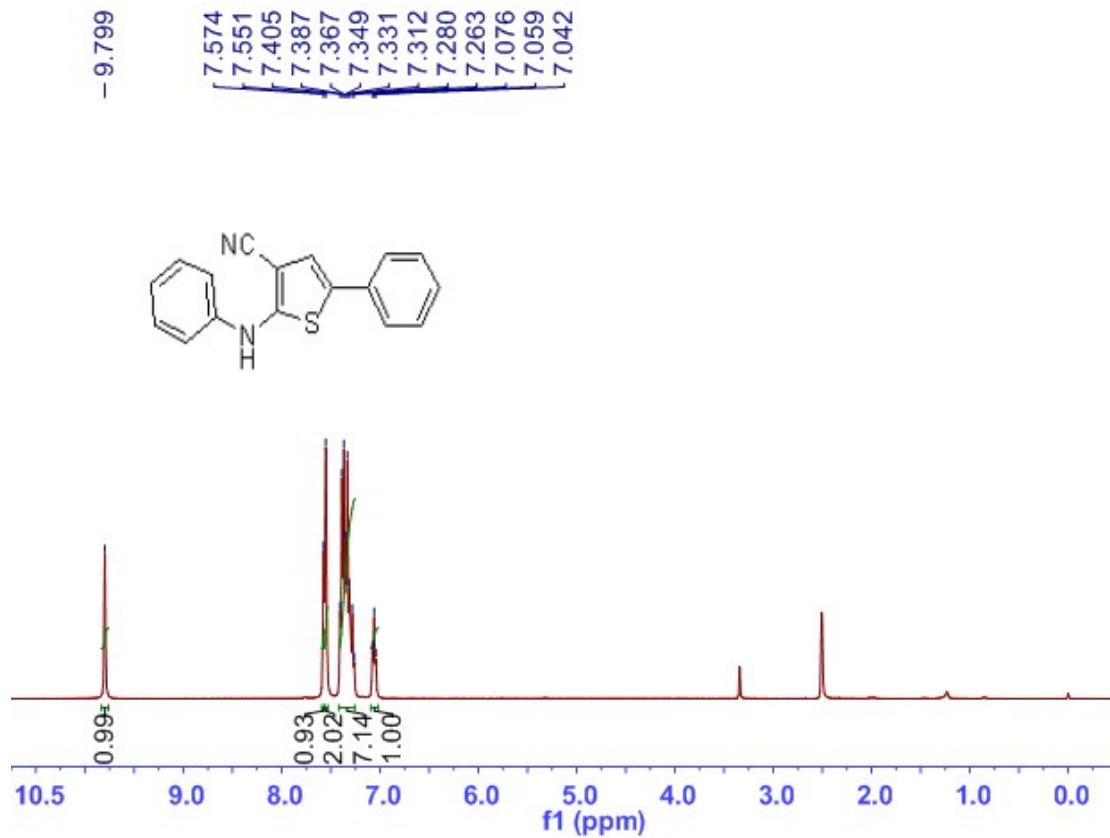
$^{13}\text{C}$  NMR spectrum of compound **101**



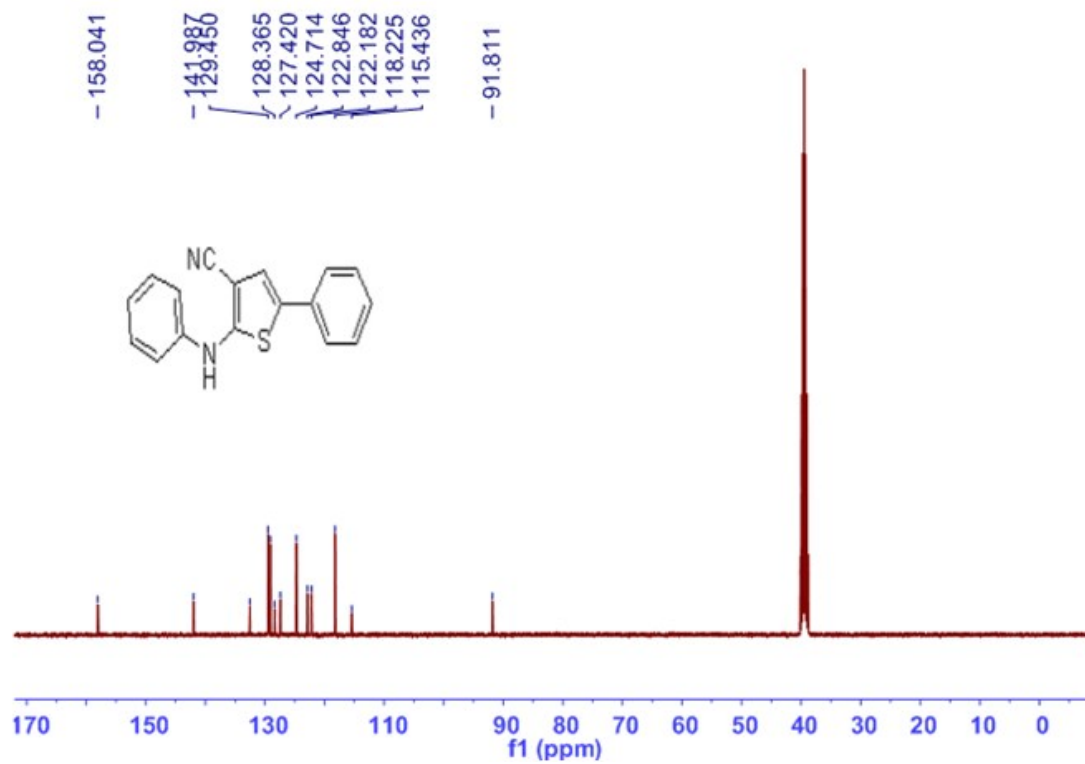
<sup>1</sup>H NMR spectrum of compound **10m**



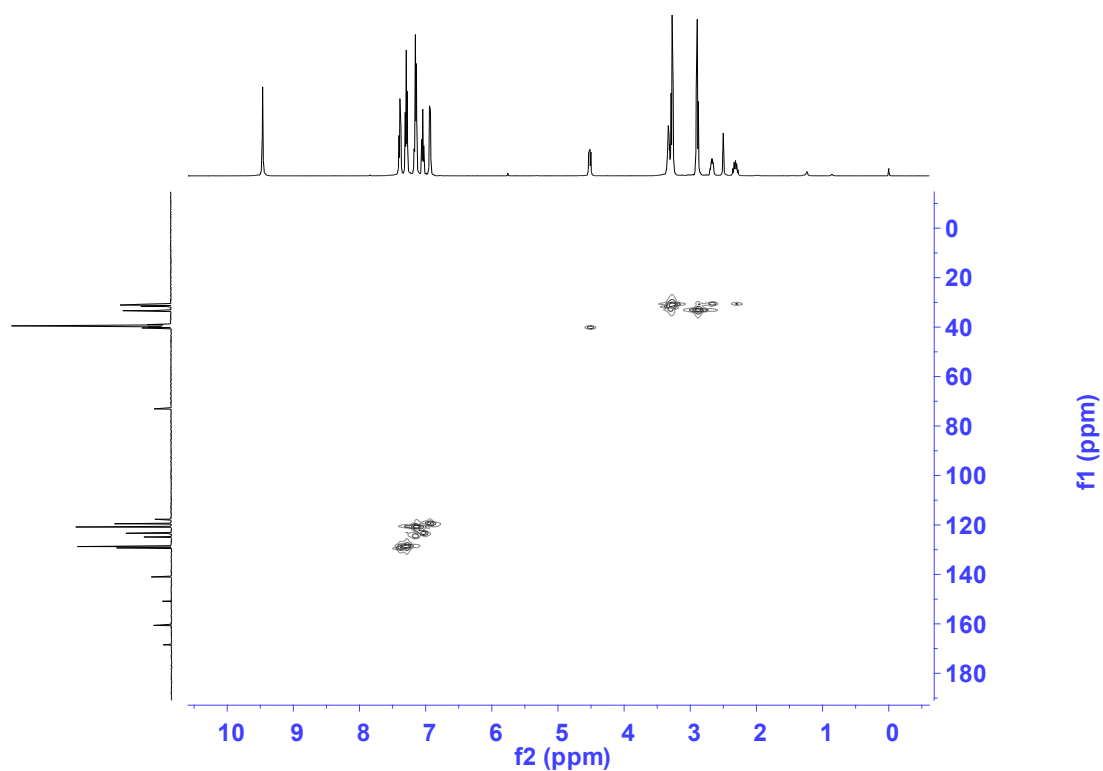
<sup>13</sup>C NMR spectrum of compound **10m**



<sup>1</sup>H NMR spectrum of compound **10n**

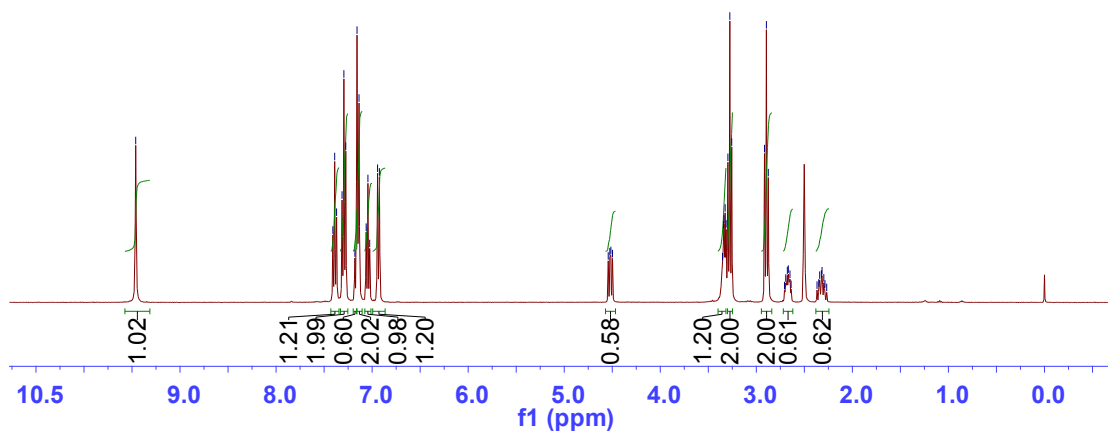
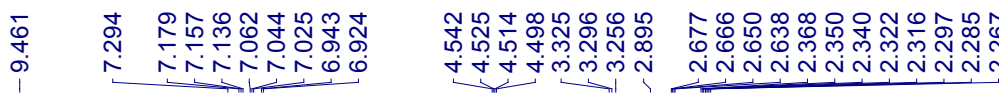


<sup>13</sup>C NMR spectrum of compound **10n**

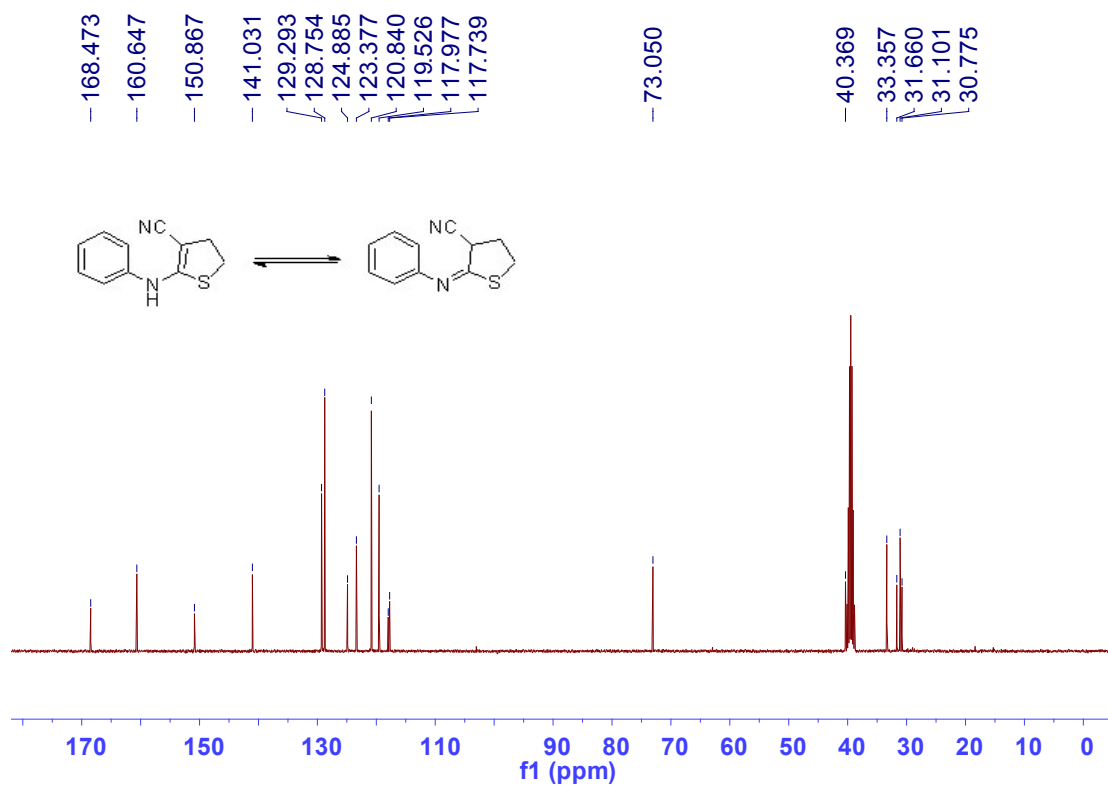


HMQC spectra of compound **11a**

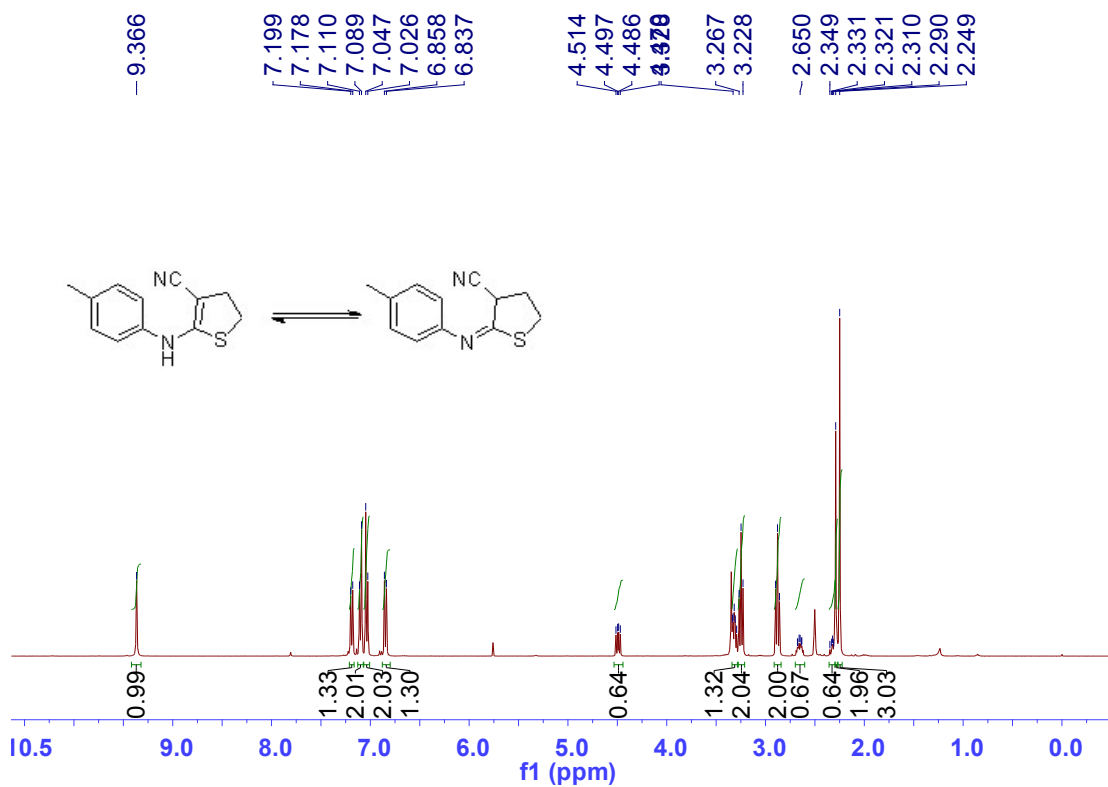
**<sup>1</sup>H, <sup>19</sup>F and <sup>13</sup>C NMR Spectra of Compounds 11a–11m**



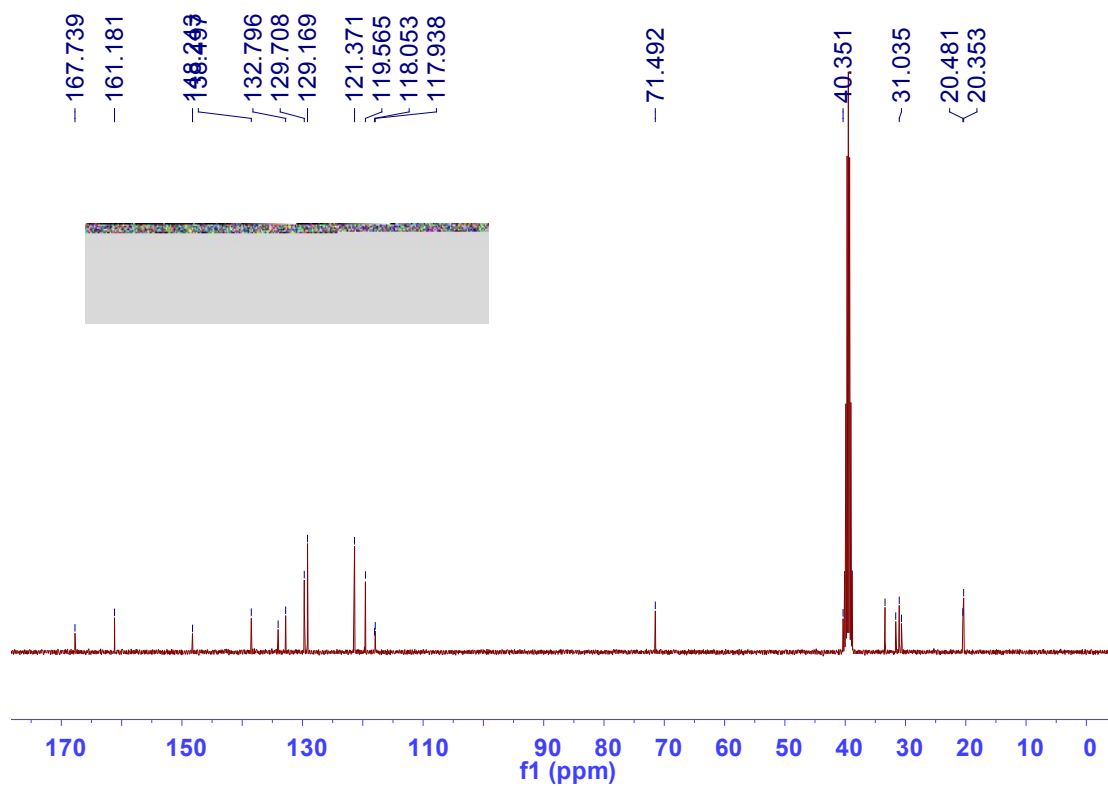
<sup>1</sup>H NMR spectrum of compound **11a**



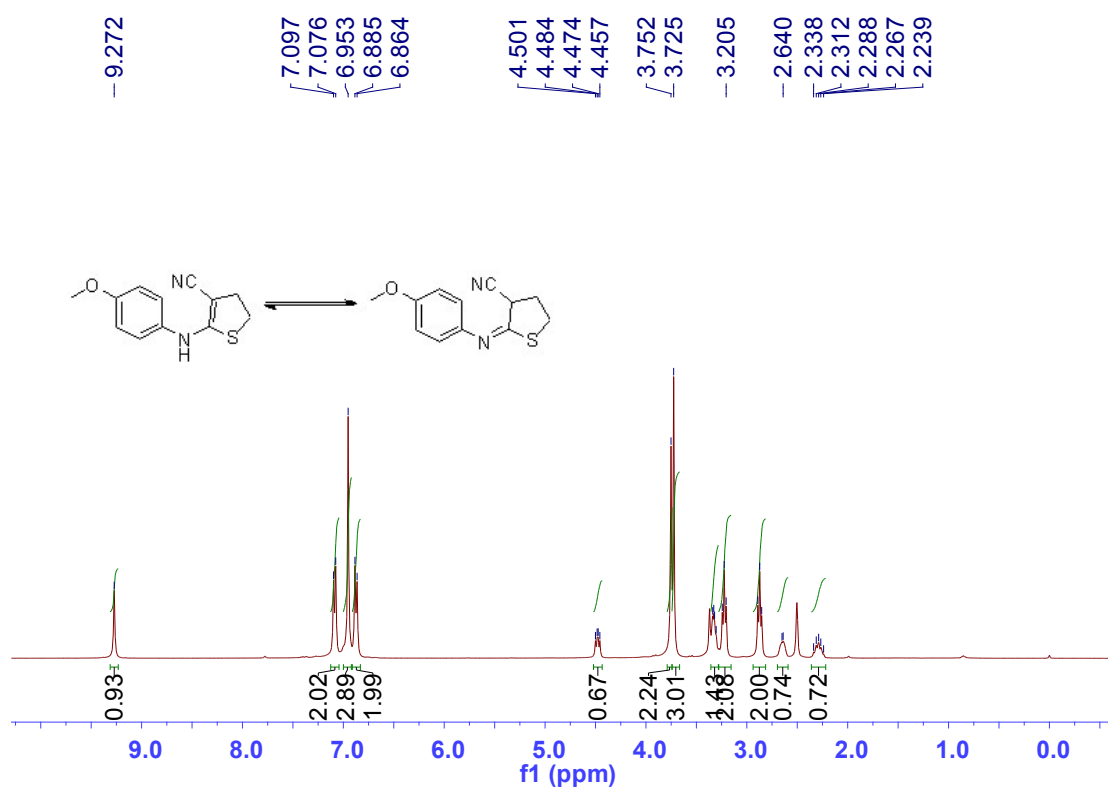
<sup>13</sup>C NMR spectrum of compound 11a



<sup>1</sup>H NMR spectrum of compound 11b

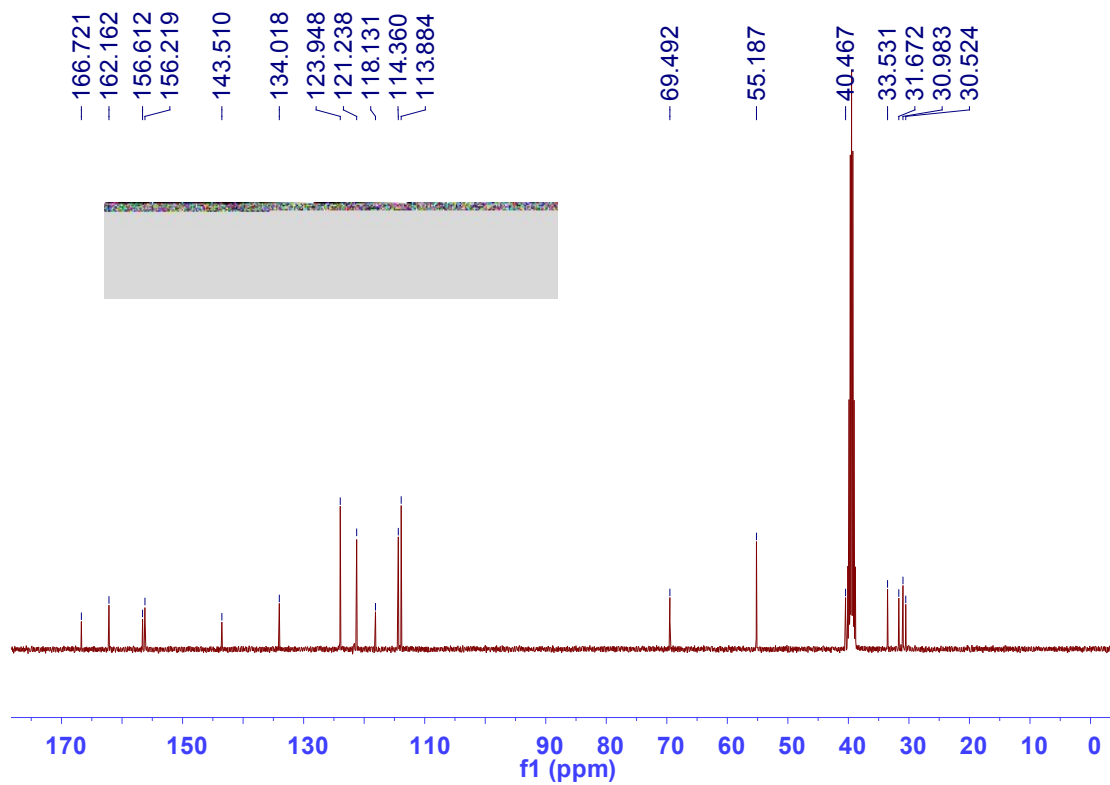


<sup>13</sup>C NMR spectrum of compound 11b

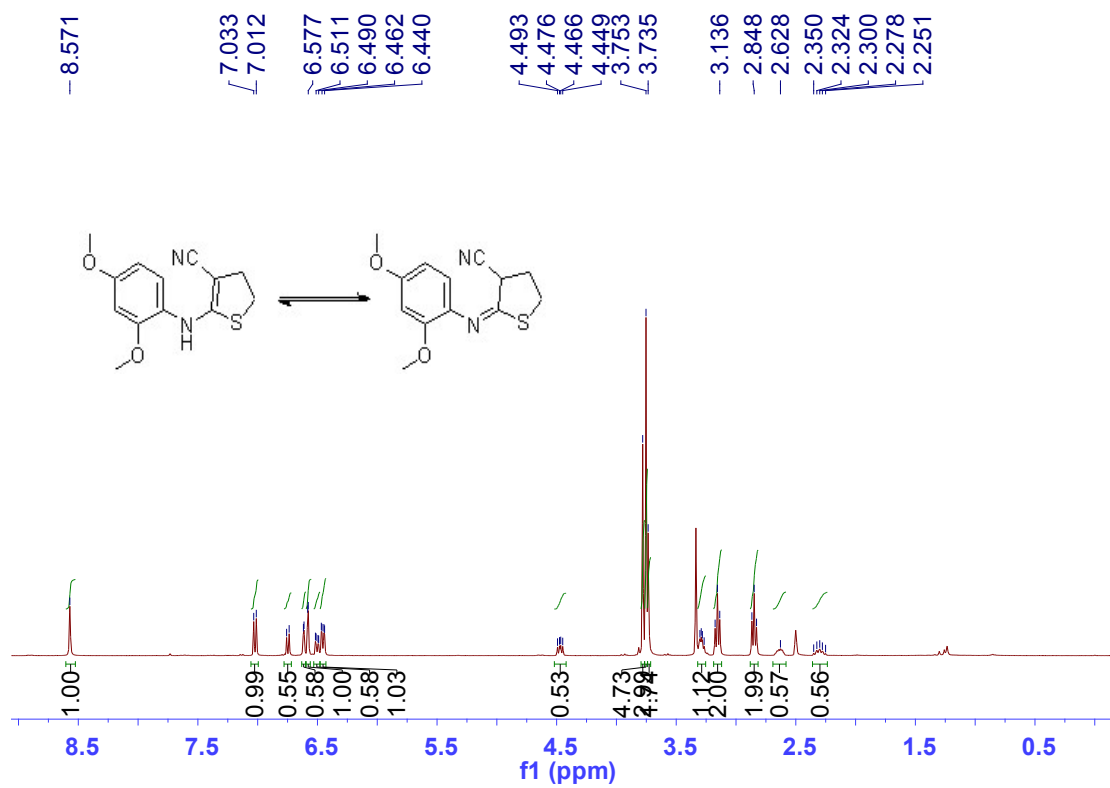


<sup>1</sup>H NMR spectrum of compound 11c

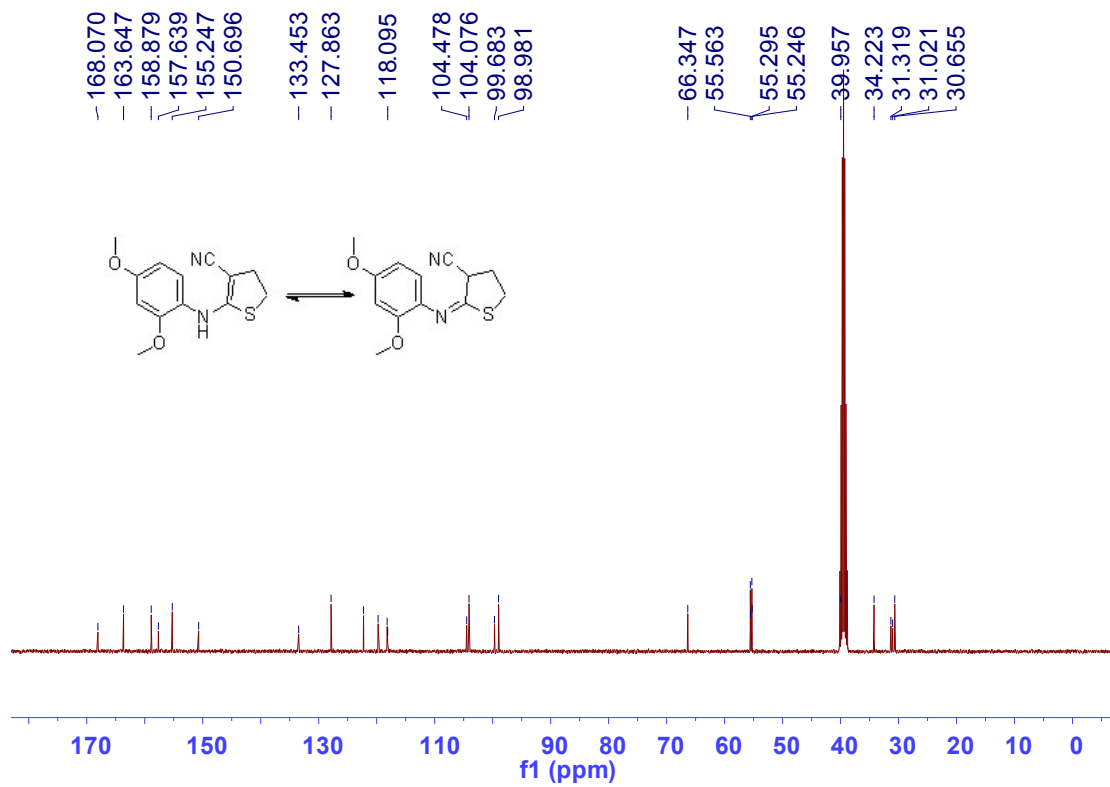




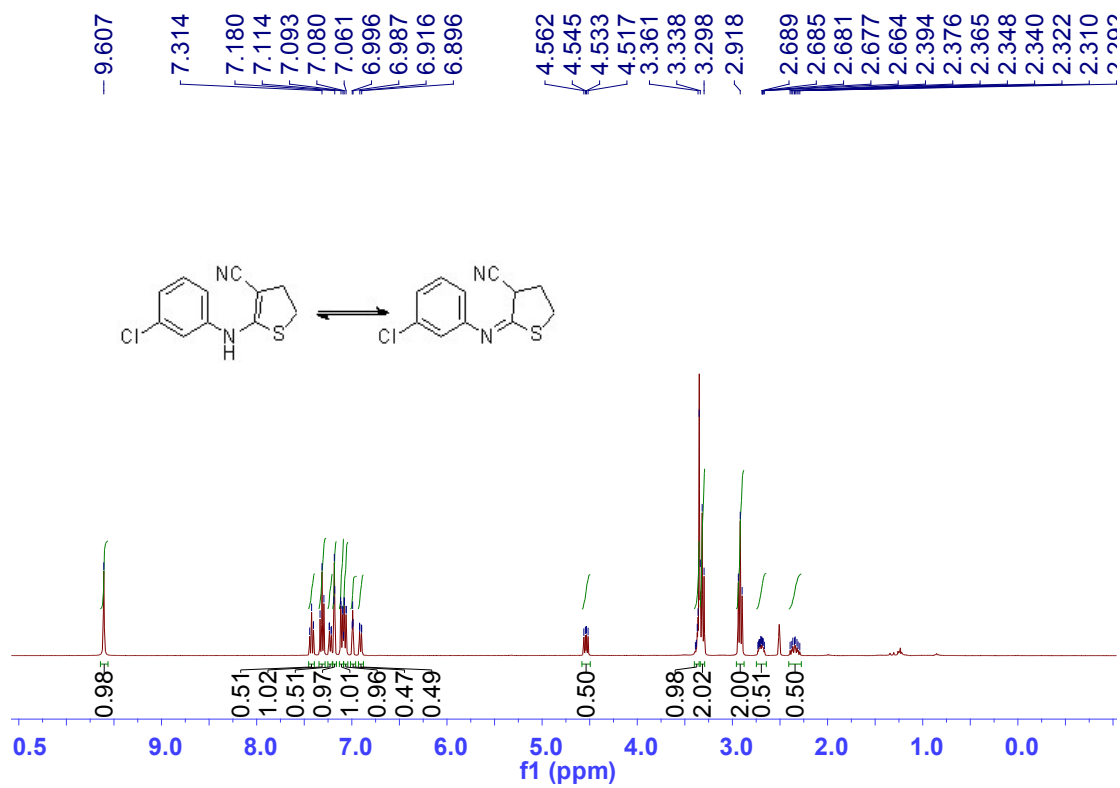
<sup>13</sup>C NMR spectrum of compound **11c**



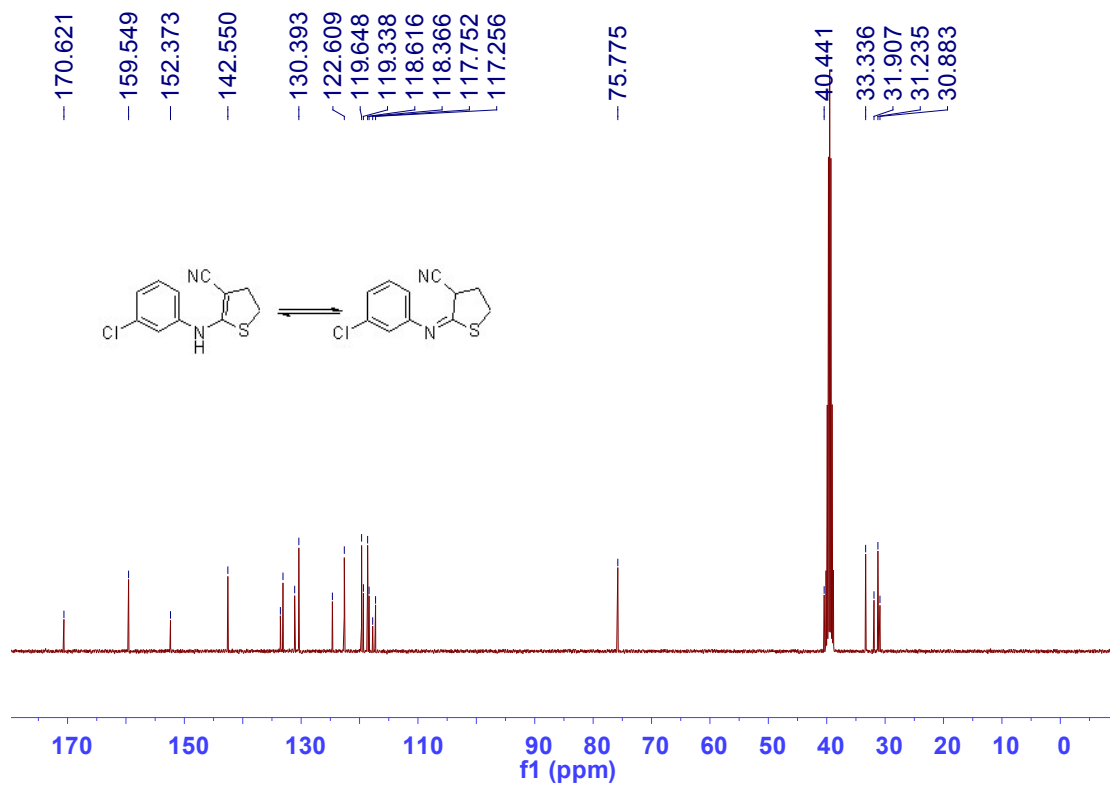
<sup>1</sup>H NMR spectrum of compound **11d**



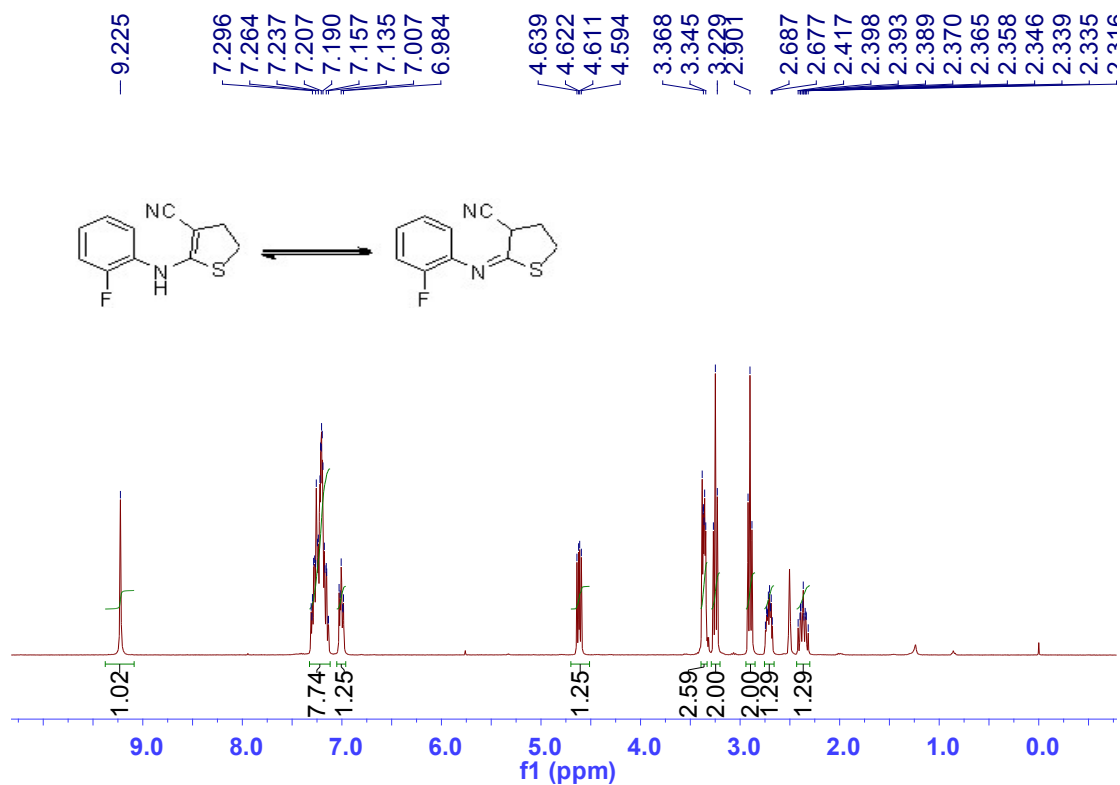
<sup>13</sup>C NMR spectrum of compound 11d



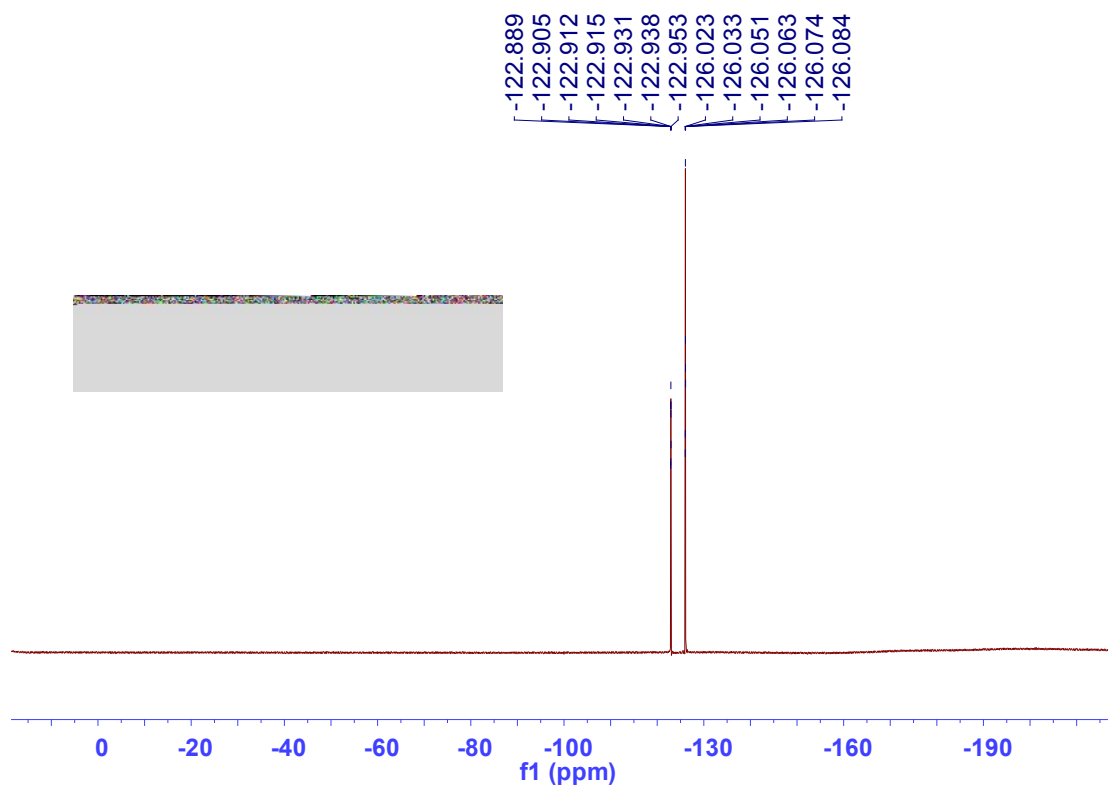
<sup>1</sup>H NMR spectrum of compound 11e



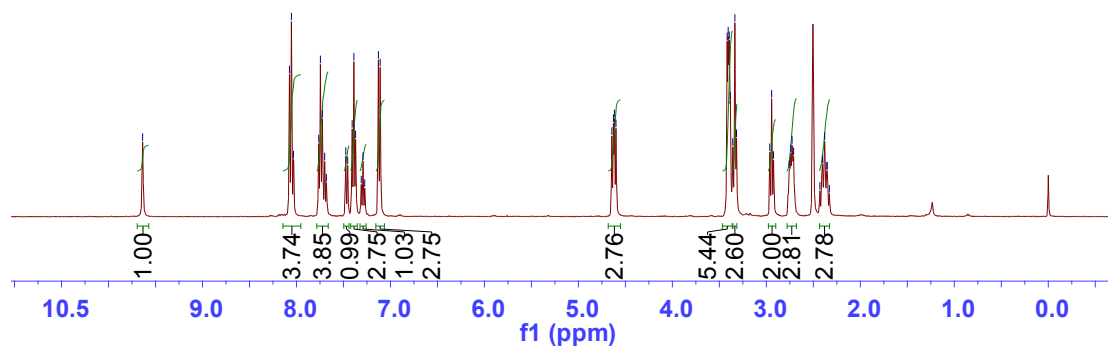
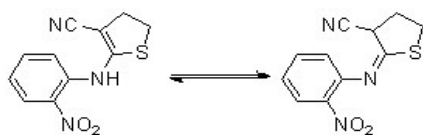
<sup>13</sup>C NMR spectrum of compound **11e**



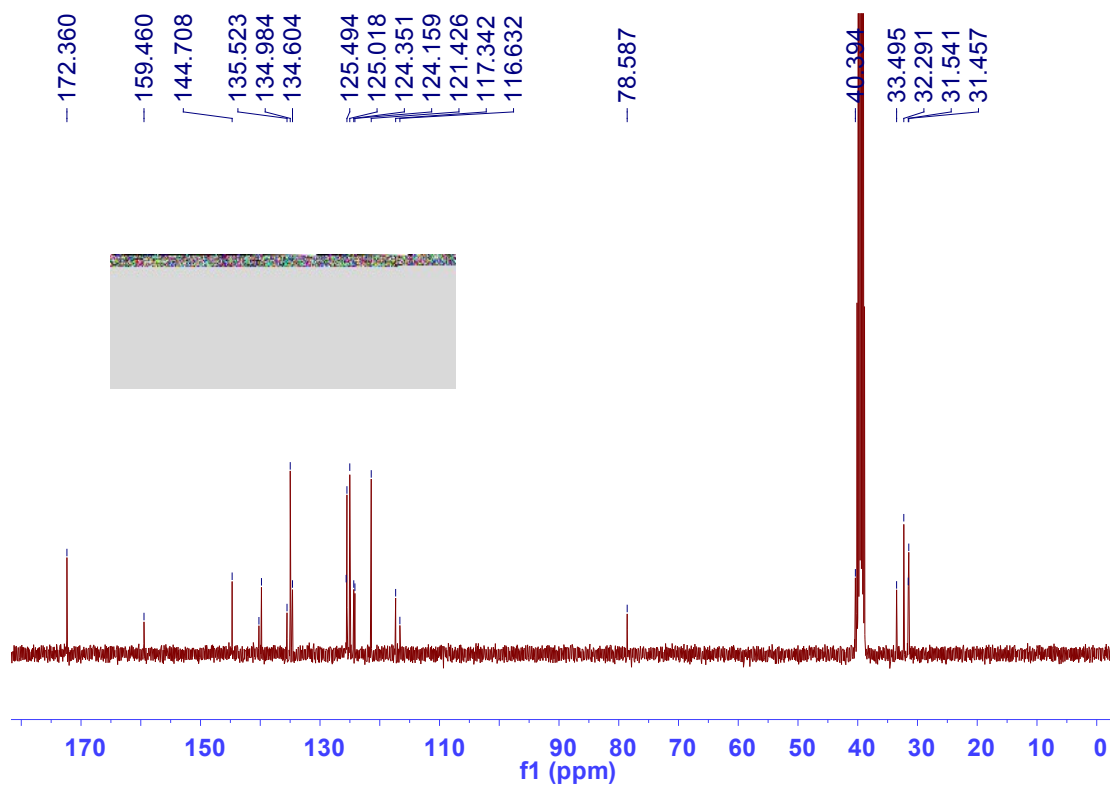
<sup>1</sup>H NMR spectrum of compound **11f**



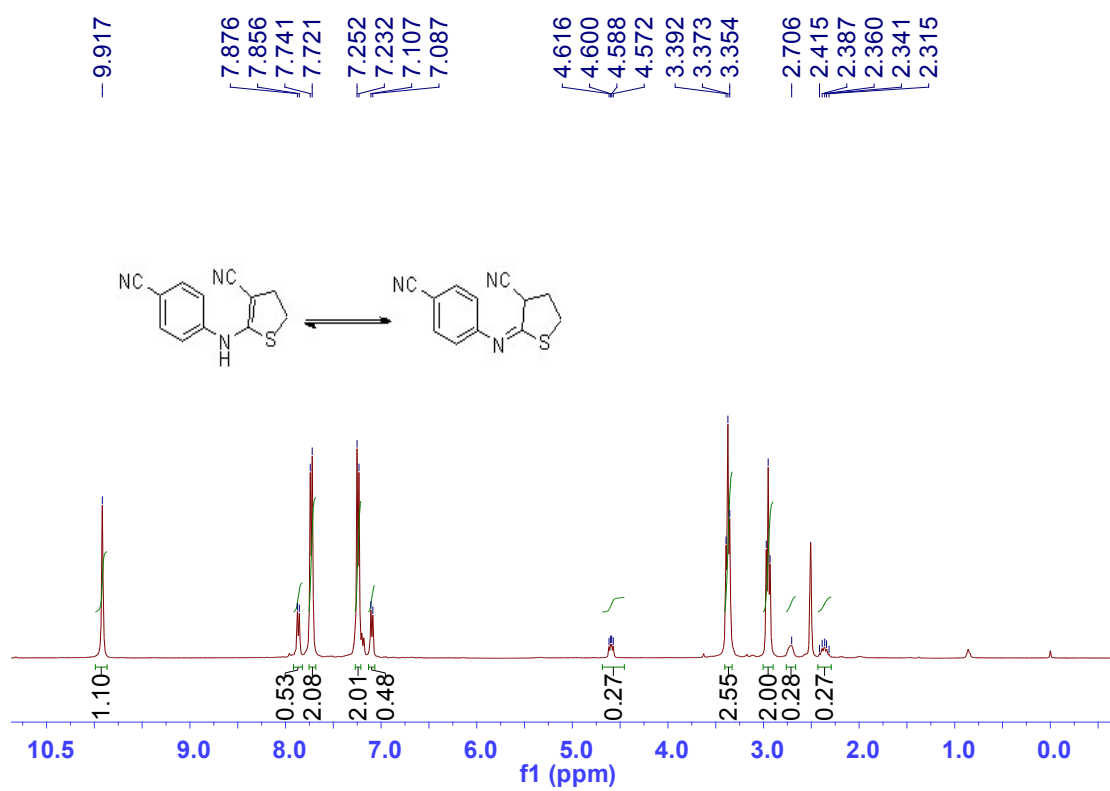
<sup>19</sup>F NMR spectrum of compound **11f**



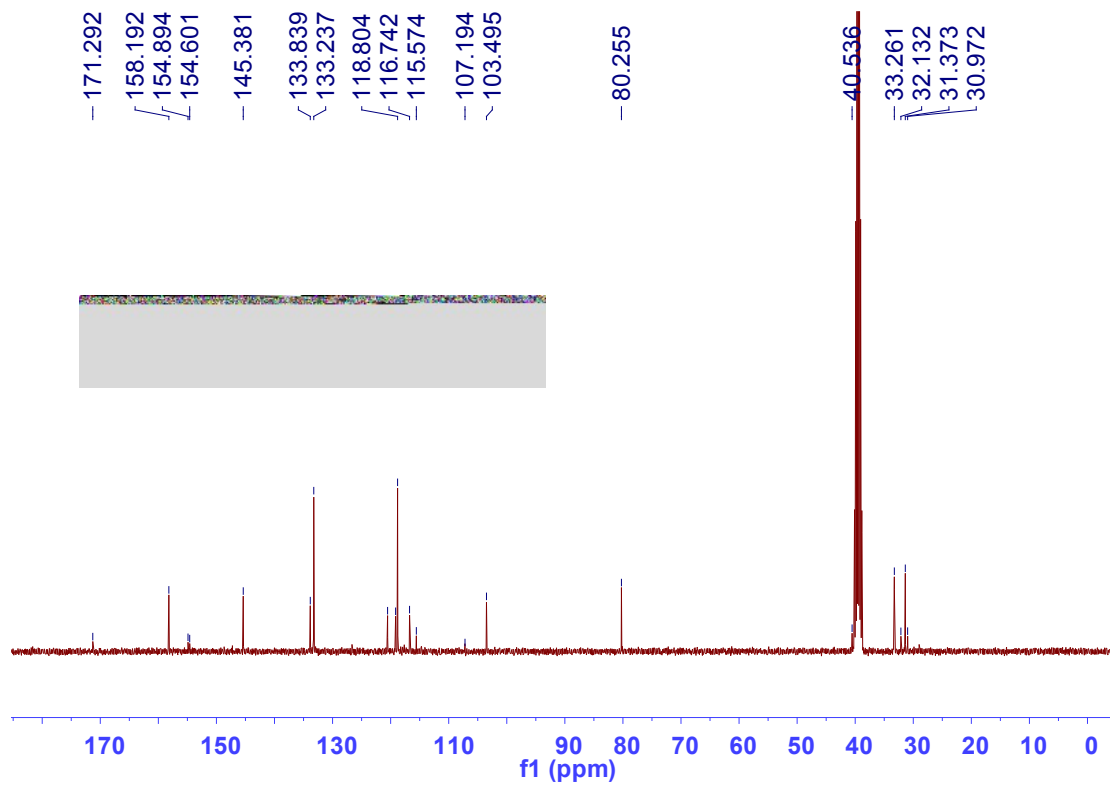
<sup>1</sup>H NMR spectrum of compound **11g**



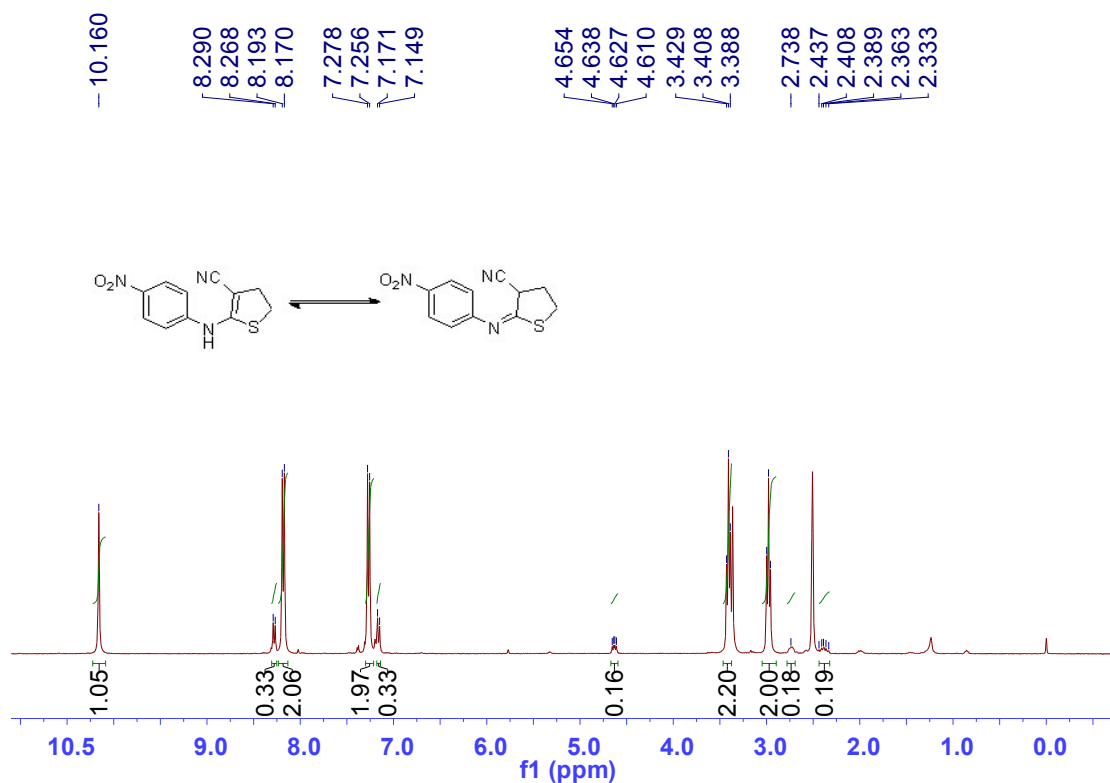
<sup>13</sup>C NMR spectrum of compound **11g**



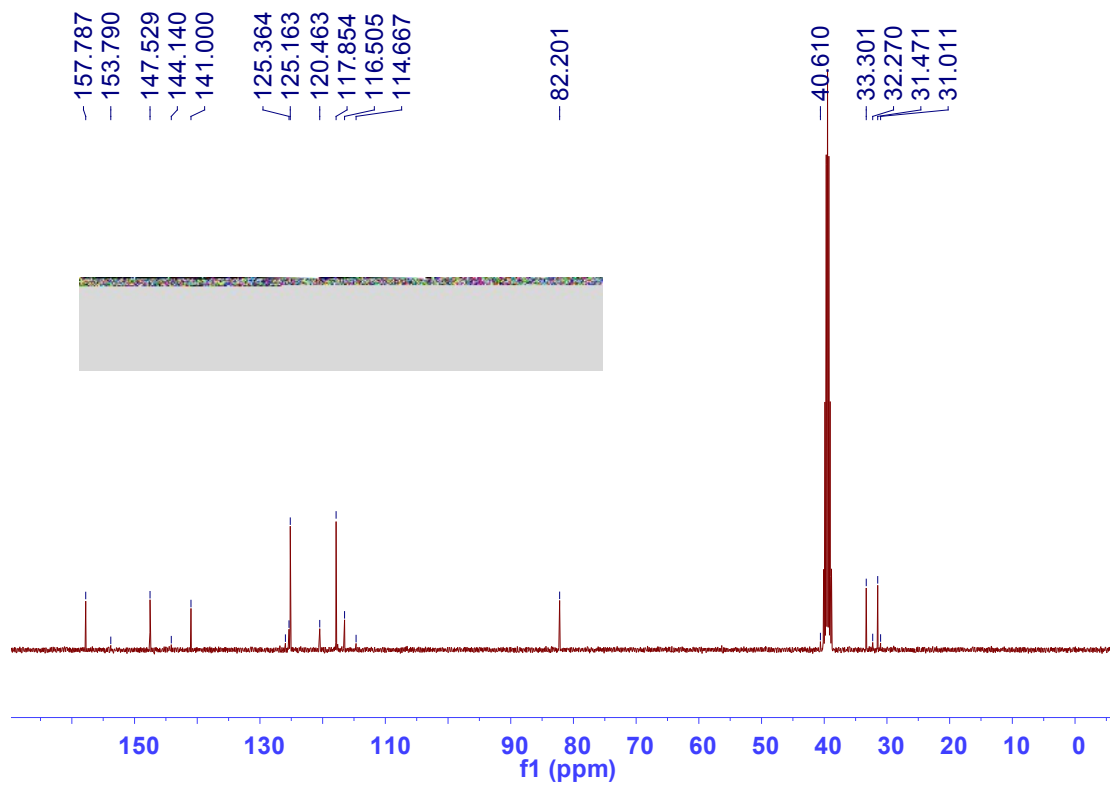
<sup>1</sup>H NMR spectrum of compound **11h**



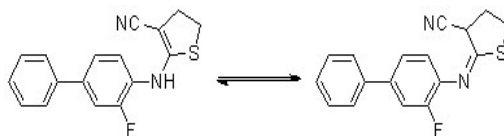
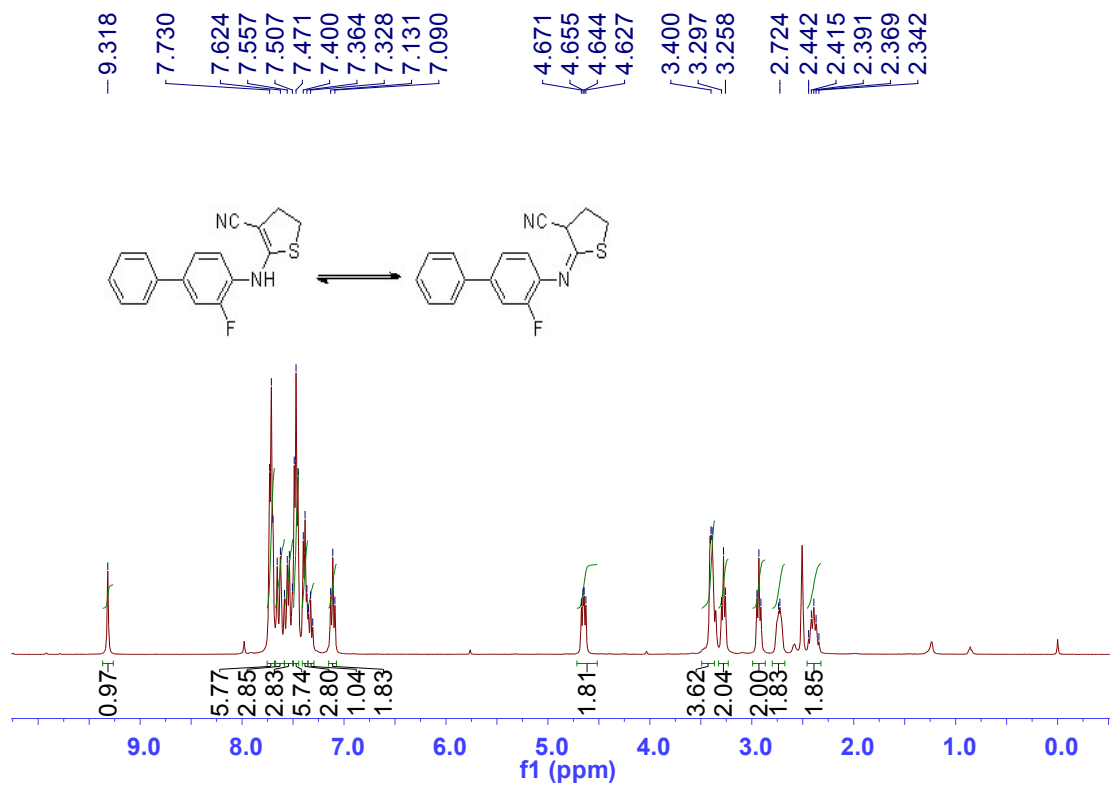
<sup>13</sup>C NMR spectrum of compound **11h**



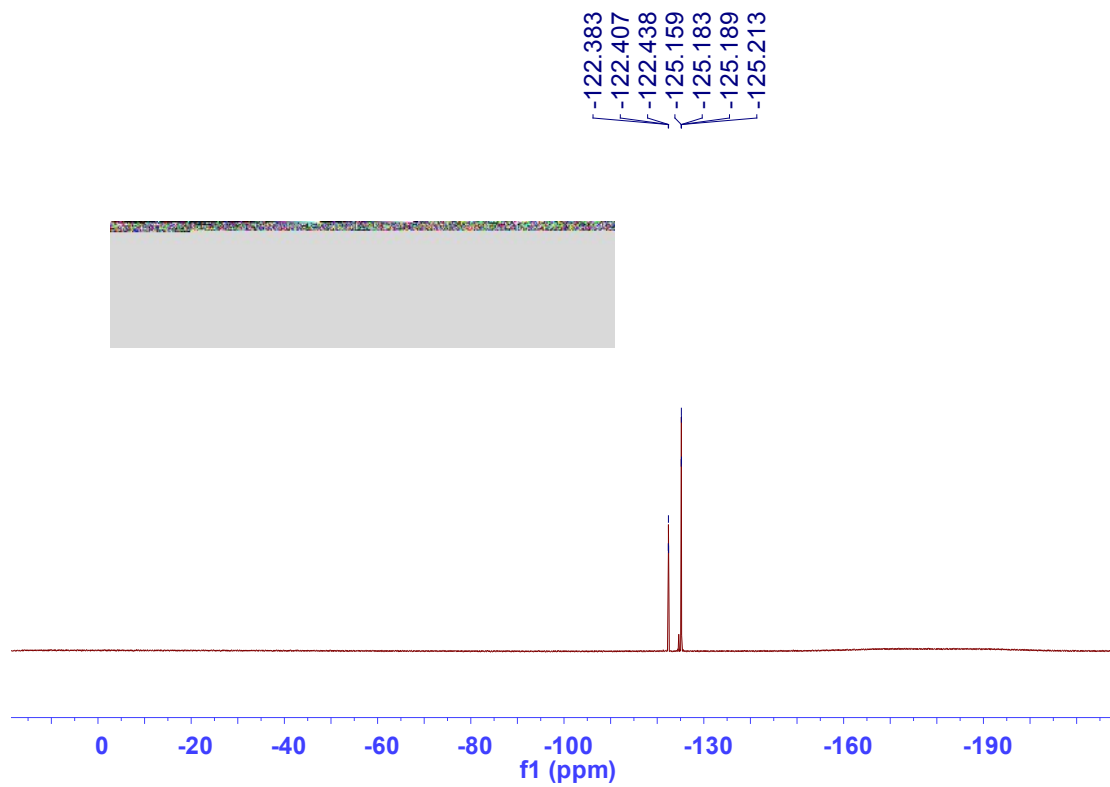
<sup>1</sup>H NMR spectrum of compound **11i**



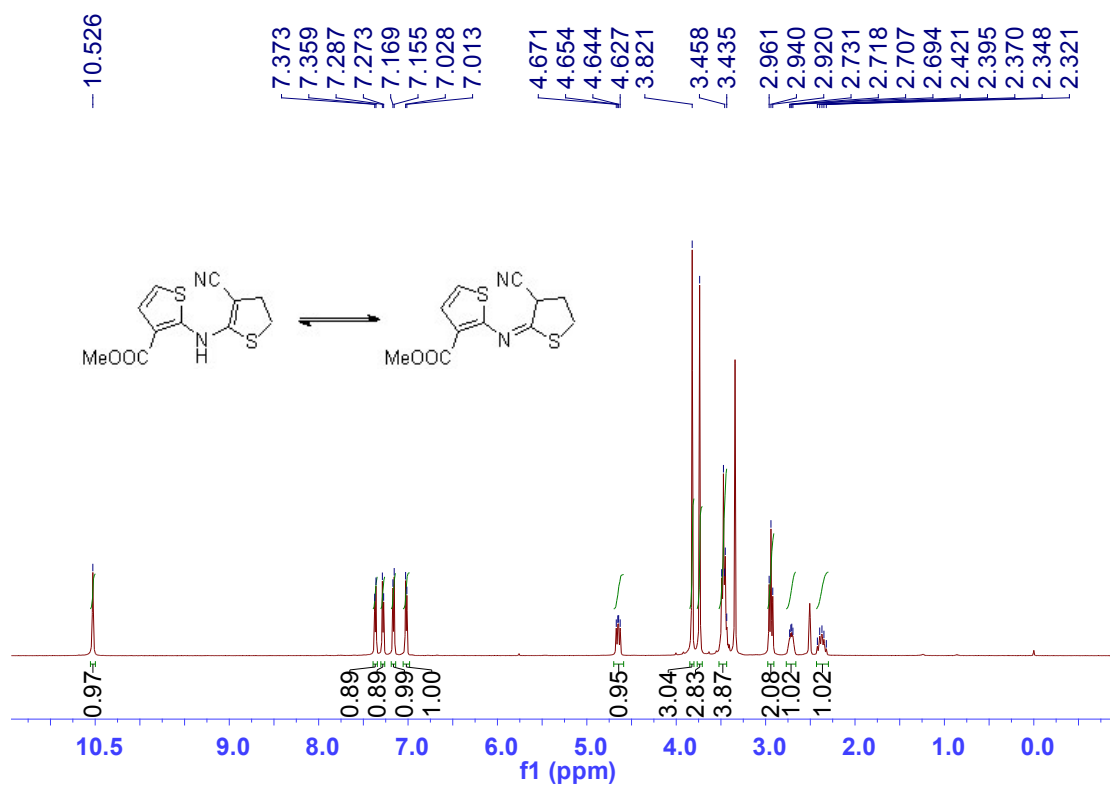
<sup>13</sup>C NMR spectrum of compound **11i**



<sup>1</sup>H NMR spectrum of compound **11j**

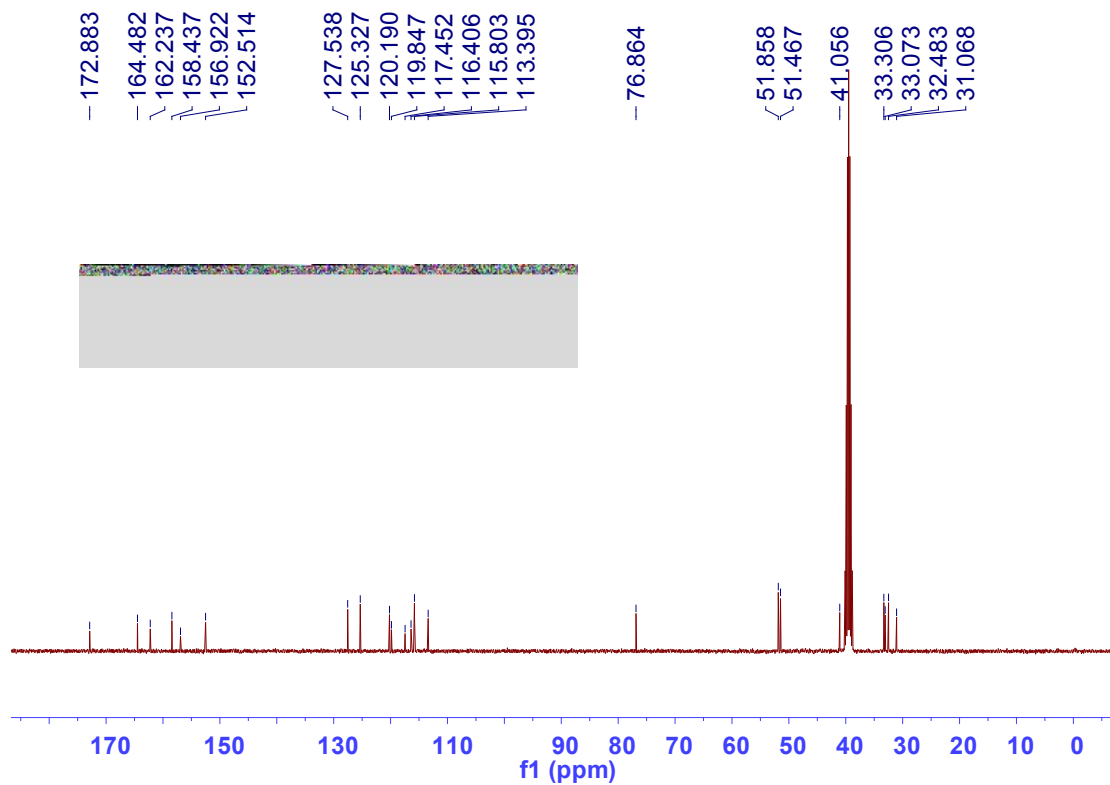


<sup>19</sup>F NMR spectrum of compound **11j**

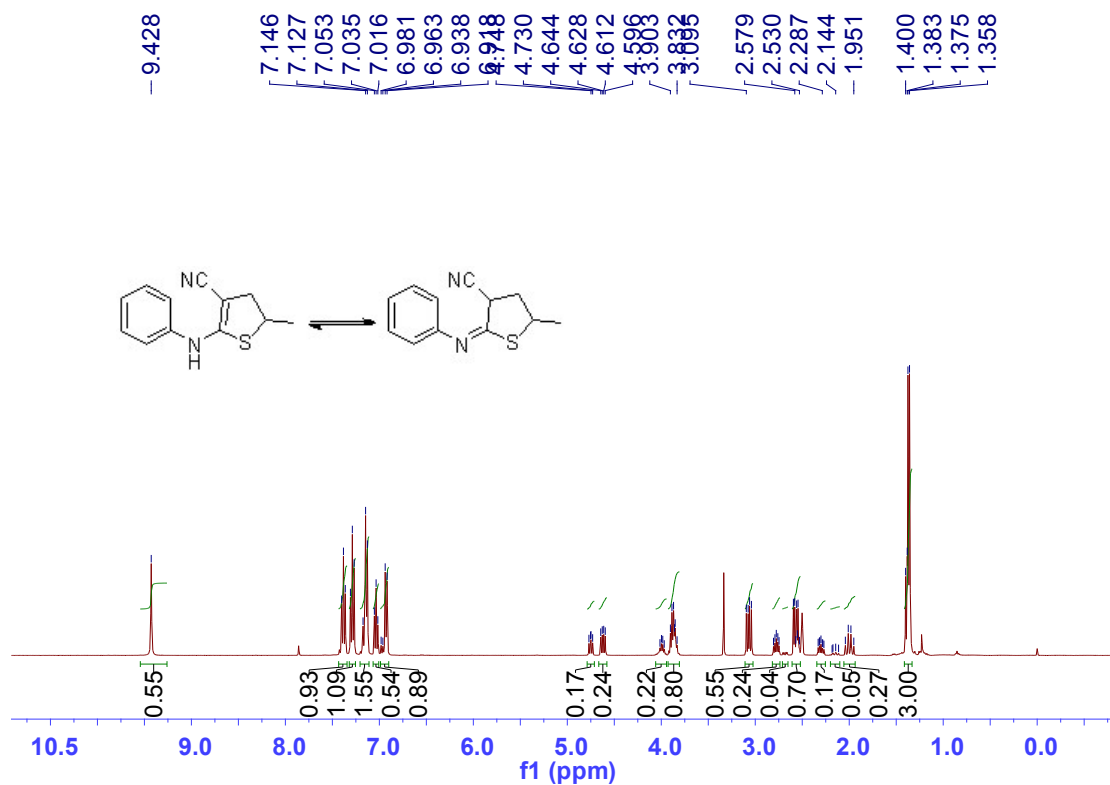


<sup>1</sup>H NMR spectrum of compound **11k**

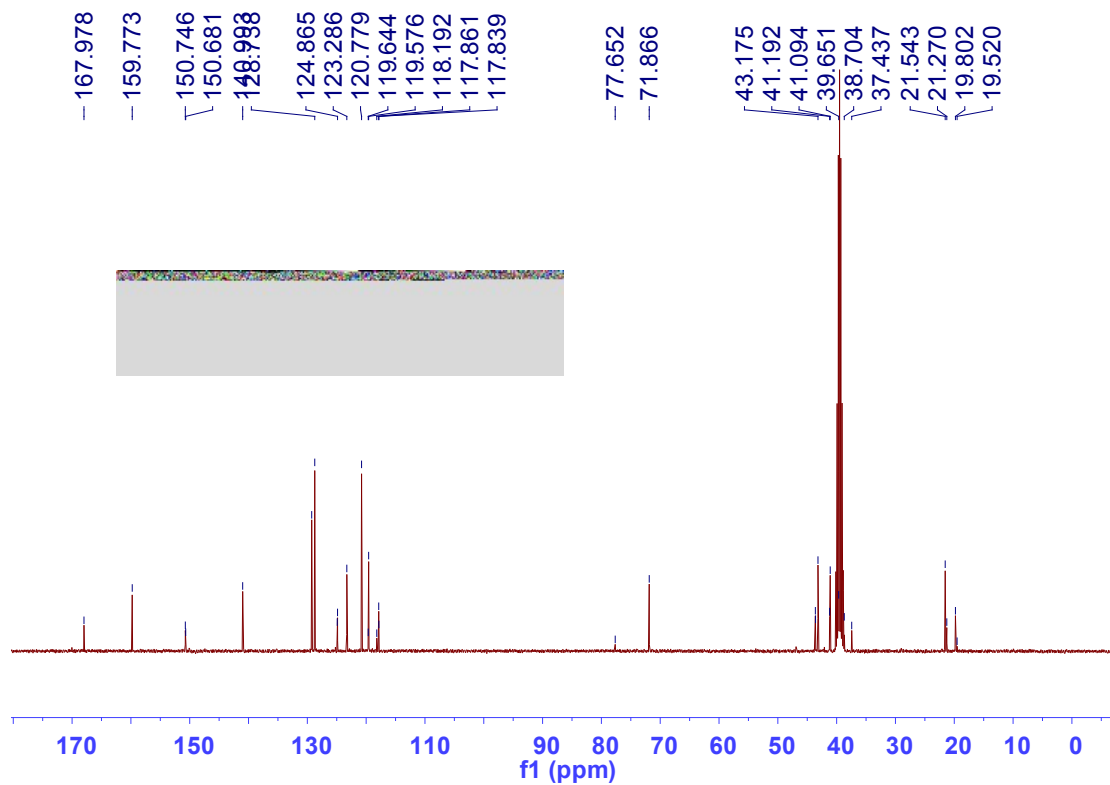




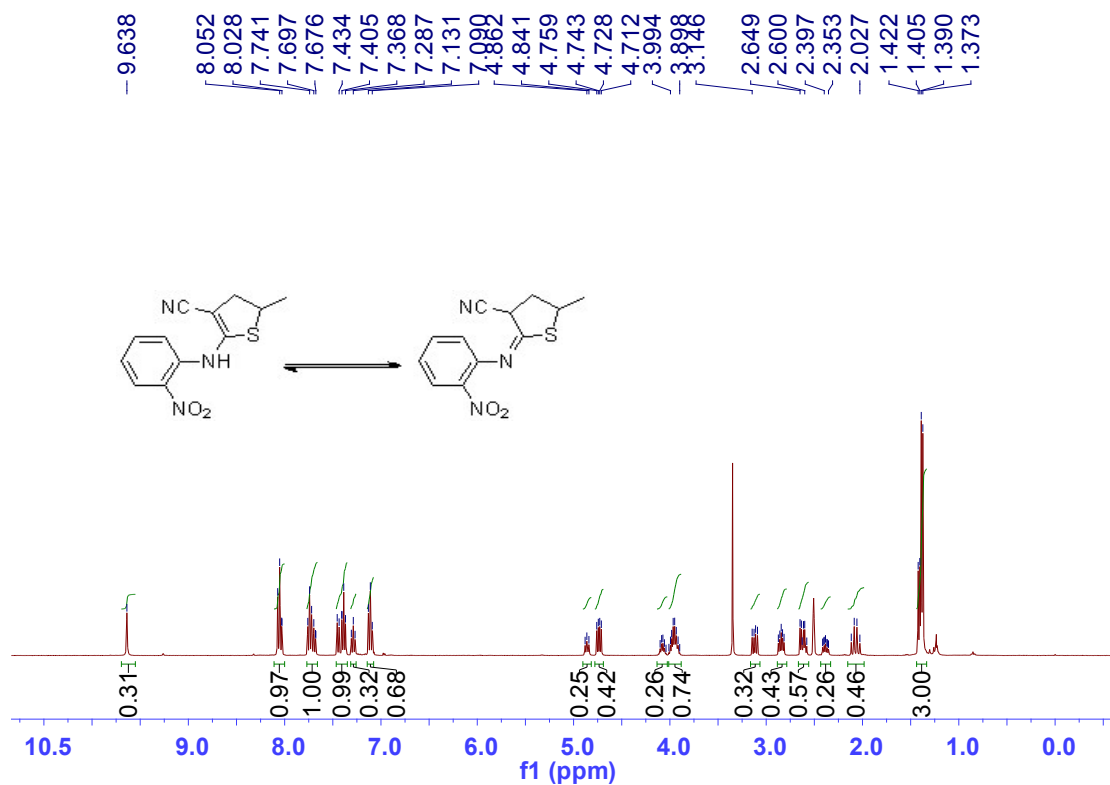
<sup>13</sup>C NMR spectrum of compound 11k



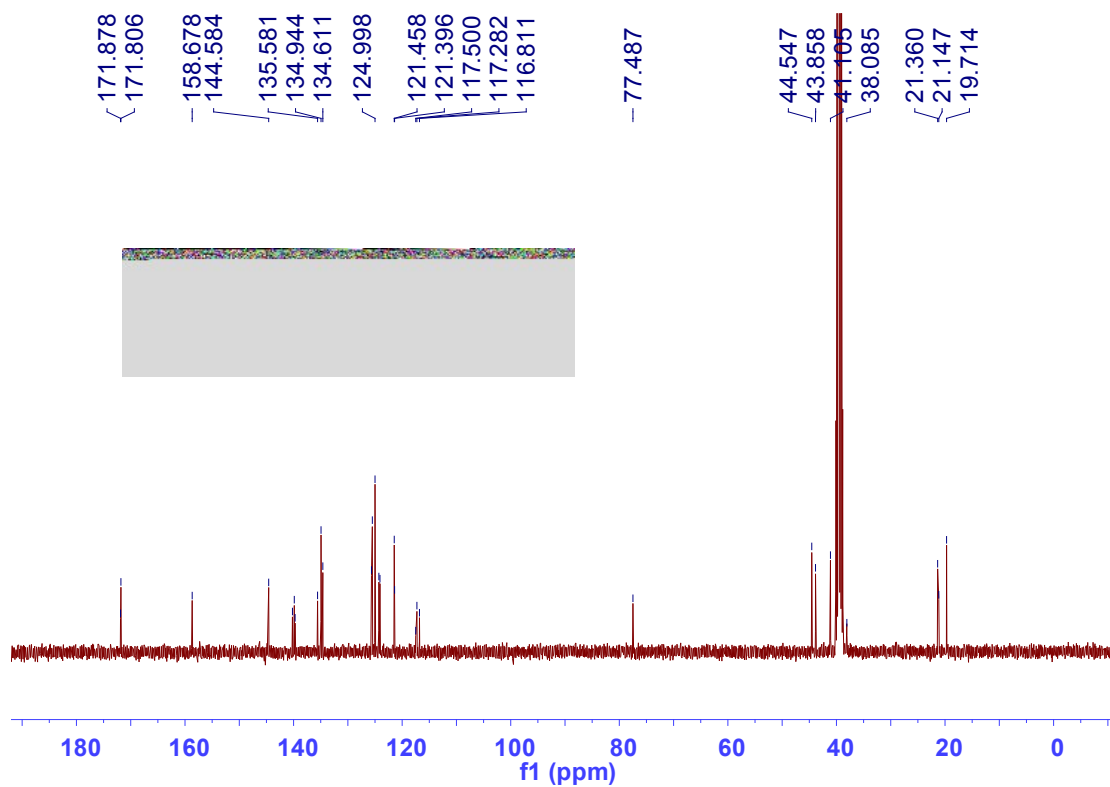
<sup>1</sup>H NMR spectrum of compound 11l



$^{13}\text{C}$ NMR spectrum of compound **11l**



$^1\text{H}$  NMR spectrum of compound **11m**



$^{13}\text{C}$  NMR spectrum of compound **11m**