

A New Mumm-type Rearrangement with Dithiocarbamates via Isocyanide- Based Multicomponent Reaction under Ultrasound Irradiation: Synthesis of Polysubstituted Pyrrolidine Compounds

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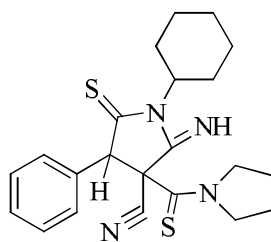
Experimental Section

All materials used are commercially available and were purchased from Merck and used without any additional purification. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker (Avance DRX-500) spectrometer using CDCl_3 , DMSO-d_6 , and Acetone-d_6 as solvent at room temperature. Chemical shifts δ were reported in ppm relative to tetramethylsilane as an internal standard. FTIR spectra of samples were taken using an ABB Bomem MB-100 FTIR spectrophotometer.

General procedure for the formation of product 5:

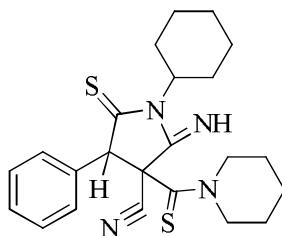
To a mixture of secondary amines 1 (1.00 mmol), carbon disulfide 2 (2.00 mmol) in MeOH (1.5 mL), *gem*-dicyano olefins 3 (1.00 mmol) and alkyl isocyanide 4 was added and the mixture subjected to ultrasound irradiation (45 kHz) for 45-120 min at room temperature. After completion of the reaction (45- 120 min), as monitored by TLC (ethyl acetate: *n*-hexane, 1:3), the product was filtered and washed with water and EtOH. The products with high purity were obtained in most cases and did not require further purification by column chromatography.

Characterization Data of Products (5a-5l)



3-cyano-1-cyclohexyl-N, N-diethyl-2-imino-4-phenyl-5-thioxopyrrolidine-3-carbothioamide (5a)

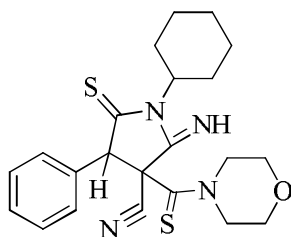
5a: White solid; mp: 181-182 °C; yield 82% (338 mg); ^1H NMR (500 MHz, Acetone- d_6) δ 1.29 (t, $J=7.4$ Hz, 4H), 1.40 (t, $J=7.0$ Hz, 5H), 1.70-1.73 (m, 1H), 1.81-1.84 (m, 1H), 1.88-1.94 (m, 3H), 2.67-2.75 (m, 1H), 2.78-2.84 (m, 1H), 3.83-4.12 (m, 4H), 4.54 (s, 1H), 5.04 (t, $J=12.0$ Hz, 1H), 7.33 (d, $J=7.2$ Hz, 2H), 7.42-7.49 (m, 3H), 9.70 (s, 1H) ppm; ^{13}C NMR (100 MHz, Acetone- d_6) δ 9.7, 11.8, 25.3, 25.7, 25.9, 26.0, 27.6, 48.3, 49.0, 58.4, 62.1, 66.4, 115.4, 128.1, 129.1, 129.4, 136.9, 154.0, 188.8, 203.1 ppm; IR (KBr): ν 3715, 3270, 2923, 1720, 1666, 1498, 1398, 1183, 1068 cm^{-1} ; Anal. calcd for $\text{C}_{22}\text{H}_{28}\text{N}_4\text{S}_2$: C, 64.04; H, 6.84; N, 13.58; Found: C, 64.01; H, 7.07; N, 13.21%.



1-cyclohexyl-2-imino-4-phenyl-3-(piperidine-1-carbonothioyl)-5-thioxopyrrolidine-3-carbonitrile (5b)

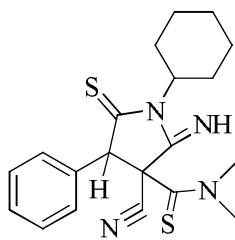
5b: Orange solid; mp: 156-158 °C; yield 89% (378 mg); ^1H NMR (500 MHz, DMSO- d_6) δ 1.14-1.39 (m, 6H), 1.61-1.85 (m, 8H), 2.59-2.72 (m, 1H), 3.35-3.37 (m, 1H), 3.55-3.57 (m, 1H), 3.74-3.78 (m, 1H), 3.93-3.96 (m, 1H), 4.71 (s, 1H), 4.75-7.78 (m, 1H), 4.89-4.94 (m, 1H), 7.20 (d, $J=5.0$ Hz, 2H), 7.39-7.47 (m, 3H), 10.45 (s, 1H) ppm; ^{13}C NMR (100 MHz, DMSO- d_6) δ 23.5, 24.0, 25.3, 25.5, 25.9, 26.1, 26.3, 27.9, 53.3, 53.9, 58.4, 61.6, 65.2, 115.7, 128.4, 129.5, 129.8, 137.1, 162.6, 187.8, 203.4 ppm; IR (KBr): ν 3280, 2993, 2858, 2664,

2240, 1665, 1449, 1390 cm^{-1} ; Anal. calcd for $\text{C}_{23}\text{H}_{28}\text{N}_4\text{S}_2$: C, 65.06; H, 6.65; N, 13.19; Found: C, 64.78 ; H, 6.68; N, 12.92%.



1-cyclohexyl-2-imino-3-(morpholine-4-carbonothioyl)-4-phenyl-5-thioxopyrrolidine-3-carbonitrile (5c)

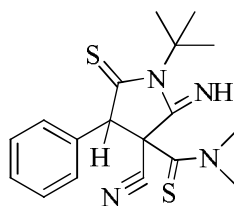
5c: White solid; mp: 198-200 °C; yield 94% (401 mg); ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ 1.27-1.43 (m, 3H), 1.70-1.83 (m, 2H), 1.89-1.94 (m, 3H), 2.67-2.78 (m, 2H), 3.74-4.13 (m, 8H), 4.61 (s, 1H), 5.04 (t, $J = 12$ Hz, 1H), 7.29 (d, $J = 5.0$ 2H), 7.42-7.48 (m, 3H), 9.70 (s, 1H), ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 25.4 , 25.8 , 26.1 , 26.3 , 27.9 , 52.1 , 53.6 , 58.4 , 61.3, 65.0, 66.0, 115.9, 128.5, 129.5, 129.9, 136.9 , 162.4, 189.2, 203.4 ppm; IR (KBr): ν 3281, 3031, 2929, 2856, 2247, 1905, 1664, 1440, 1388 cm^{-1} ; Anal. calcd for $\text{C}_{22}\text{H}_{26}\text{N}_4\text{OS}_2$: C, 61.94; H, 6.14; N, 13.13; Found: C, 61.76; H, 6.19; N, 12.77%.



3-cyano-1-cyclohexyl-2-imino-N,N-dimethyl-4-phenyl-5-thioxopyrrolidine-3-carbothioamide (5d)

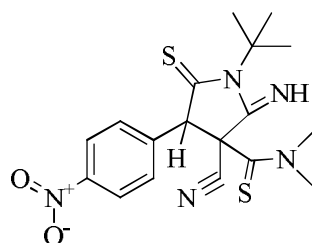
5d: Pale yellow solid; mp: 220-222 °C; yield 71% (273 mg); ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ 1.17-1.32 (m, 3H), 1.65-1.88 (m, 5H), 2.59-2.72 (m, 2H), 3.32 (s, 3H), 3.39 (s, 3H), 4.87 (s, 1H), 4.89-4.94 (m, 1H), 7.24 (d, $J = 10.0$ Hz , 2H), 7.38-7.46 (m, 3H), 10.36 (s, 1H) ppm; ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 25.5, 25.8, 26.1, 26.3, 27.9, 45.3, 46.3, 58.4, 61.0, 64.7, 72.3, 115.4, 128.4, 129.4, 129.8, 137.3, 162.7, 188.6, 203.7 ppm; IR (KBr): ν

3272, 2930, 2055, 2241, 1665, 1516, 1390 cm^{-1} ; Anal. calcd for $\text{C}_{20}\text{H}_{24}\text{N}_4\text{S}_2$: C, 62.47; H, 6.29; N, 14.57; Found: C, 62.24; H, 6.74; N, 14.41%.



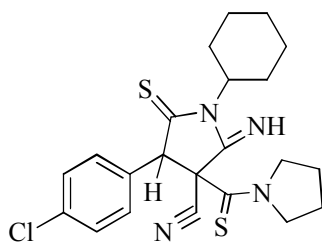
1-(tert-butyl)-3-cyano-2-imino-N,N-dimethyl-4-phenyl-5-thioxopyrrolidine-3-carbothioamide (5e)

5e: Yellow solid; mp: 168-170 $^{\circ}\text{C}$; yield 92% (330 mg); ^1H NMR (500 MHz, CDCl_3) δ 1.98 (s, 9H), 3.49 (s, 3H), 3.53 (s, 3H), 4.31 (s, 1H), 7.19-7.20 (m, 2H), 7.43-7.44 (m, 3H), 9.14 (brs, 1H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 28.1, 44.4, 45.9, 59.9, 65.0, 66.7, 114.7, 127.7, 129.4, 129.7, 136.7, 165.0, 189.1, 202.3 ppm; IR (KBr): ν 3112, 3073, 3019, 2834, 2034, 1895, 1602, 1525 cm^{-1} ; Anal. calcd for $\text{C}_{18}\text{H}_{22}\text{N}_4\text{S}_2$: C, 60.30; H, 6.19; N, 15.63; Found: C, 60.14; H, 6.31; N, 15.48%.



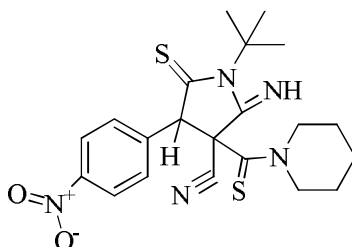
1-(tert-butyl)-3-cyano-2-imino-N,N-dimethyl-4-(4-nitrophenyl)-5-thioxopyrrolidine-3-carbothioamide (5f)

5f: Pale yellow solid; mp: 180-182 $^{\circ}\text{C}$; yield 96% (387 mg); ^1H NMR (500 MHz, CDCl_3) δ 1.95(s, 9H), 3.52 (s, 3H), 3.54 (s, 3H), 4.60 (s, 1H), 7.39 (d, $J = 10$ Hz, 2H), 8.29 (d, $J = 10$ Hz, 2H), 9.16 (brs, 1H) ppm; ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ 28.1, 45.2, 46.4, 64.3, 64.4, 64.9, 115.0, 124.9, 130.5, 144.9, 148.0, 162.5, 187.5, 202.3 ppm; IR (KBr): ν 3738, 3362, 3085, 2984, 1691, 1609, 1527, 1421 cm^{-1} ; Anal. calcd for $\text{C}_{18}\text{H}_{21}\text{N}_5\text{O}_2\text{S}_2$: C, 53.58; H, 5.25; N, 17.36; Found: C, 53.44; H, 5.51; N, 16.93%.



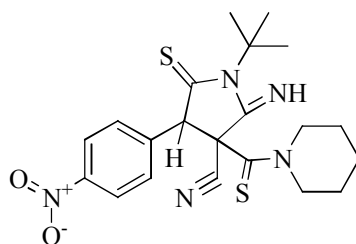
4-(4-chlorophenyl)-1-cyclohexyl-2-imino-3-(pyrrolidine-1-carbonothioyl)-5-thioxopyrrolidine-3-carbonitrile (5g)

5g: White solid; mp: 181-182 °C; yield 71% (316 mg); ^1H NMR (500 MHz, DMSO $-d_6$) δ 1.18-1.32 (m, 4H), 1.65-2.21 (m, 9H), 2.61-2.64 (m, 1H), 3.61-3.76 (m, 4H), 4.89-4.96 (m, 1H), 5.09 (s, 1H), 7.28 (d, $J = 10.0$ Hz, 2H), 7.52 (d, $J = 10.0$ Hz, 2H), 10.44 (s, 1H) ppm; ^{13}C NMR (100 MHz, DMSO $-d_6$) 23.6, 25.5, 25.8, 26.1, 26.3, 27.0, 53.9, 57.4, 58.4, 63.8, 115.2, 129.7, 130.6, 134.0, 136.7, 162.4, 185.3, 203.6 ppm; IR (KBr): ν 3081, 3007, 2932, 2834, 1901, 1605, 1525, 1474, 1245 cm^{-1} ; Anal. calcd for $\text{C}_{22}\text{H}_{25}\text{ClN}_4\text{S}_2$: C, 59.37; H, 5.66; N, 12.59; Found: C, 59.12; H, 5.76; N, 12.29%.



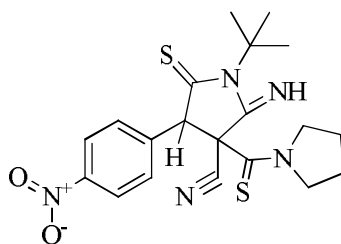
1-(tert-butyl)-2-imino-4-(4-nitrophenyl)-3-(piperidine-1-carbonothioyl)-5-thioxopyrrolidine-3-carbonitrile (5h)

5h: White solid; mp: 198-200 °C; yield 96% (428 mg); ^1H NMR (500 MHz, CDCl_3) δ 1.94 (s, 9H), 3.86-4.04 (m, 8H), 4.64 (s, 1H), 7.37 (d, $J = 8.0$ Hz, 2H), 8.30 (d, $J = 8.0$ Hz, 2H), 9.38 (brs, 1H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 28.0, 52.1, 52.2, 52.7, 53.0, 66.20, 66.2, 114.8, 124.8, 129.3, 143.1, 148.3, 155.3, 188.4, 200.3 ppm; IR (KBr): ν 3383, 3279, 3077, 2975, 2926, 1936, 1668, 1604, 1529, 1359 cm^{-1} ; Anal. calcd for $\text{C}_{20}\text{H}_{23}\text{N}_5\text{O}_3\text{S}_2$: C, 53.91; H, 5.20; N, 15.72; Found: C, 53.77; H, 5.49; N, 15.47%.



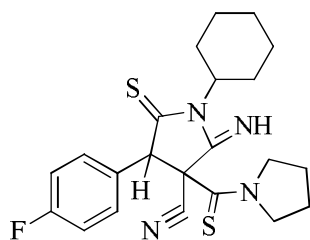
1-(tert-butyl)-2-imino-4-(4-nitrophenyl)-3-(piperidine-1-carbonothioyl)-5-thioxopyrrolidine-3-carbonitrile (5i)

5i: White solid; mp: 168-170 °C; yield 77% (342 mg); ^1H NMR (500 MHz, CDCl_3) δ 1.79-1.85 (m, 6H), 1.97 (s, 9H), 3.57-3.93 (m, 3H), 4.47 (s, 1H), 4.55-4.61 (m, 1H), 7.36 (d, $J = 5.0$ Hz, 2H), 8.29 (d, $J = 5.0$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 23.3, 23.6, 25.2, 25.7, 28.0, 52.3, 53.7, 66.2, 114.8, 123.1, 124.8, 129.1, 130.6, 143.5, 187.2, 200.3 ppm; IR (KBr): ν 3315, 3273, 2931, 2856, 2241, 1998, 1666, 1518, 1391 cm^{-1} ; Anal. calcd for $\text{C}_{21}\text{H}_{25}\text{N}_5\text{O}_2\text{S}_2$: C, 56.86; H, 5.68; N, 15.79; Found: C, 56.64; H, 5.97; N, 15.63%.



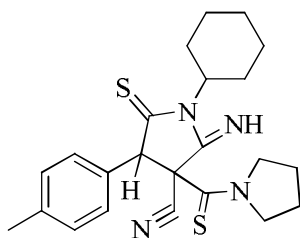
1-(tert-butyl)-2-imino-4-(4-nitrophenyl)-3-(pyrrolidine-1-carbonothioyl)-5-thioxopyrrolidine-3-carbonitrile (5j)

5j: White solid; mp: 188-190 °C; yield 84% (361 mg); ^1H NMR (500 MHz, CDCl_3) δ 1.94 (s, 9H), 2.07-2.21 (m, 4H), 3.75-4.06 (m, 4H), 4.88 (s, 1H), 7.40 (d, $J = 8.0$ Hz, 2H), 8.28 (d, $J = 8.0$ Hz, 2H), 9.12 (s, 1H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 23.5, 27.2, 28.0, 53.1, 57.0, 66.6, 114.2, 124.7, 129.2, 143.6, 148.2, 163.9, 184.4, 200.5 ppm; IR (KBr): 3070, 2954, 2873, 1685, 1575, 1431, 1337 cm^{-1} ; Anal. calcd for $\text{C}_{20}\text{H}_{23}\text{N}_5\text{O}_2\text{S}_2$: C, 55.92; H, 5.40; N, 16.30; Found: C, 55.89; H, 5.57; N, 16.05%.



1-cyclohexyl-4-(4-fluorophenyl)-2-imino-3-(pyrrolidine-1-carbonothioyl)-5-thioxopyrrolidine-3-carbonitrile (5k)

5k: White solid; mp: 200-202 °C; yield 84% (360 mg); ^1H NMR (500 MHz, CDCl_3) δ 1.30-1.43 (m, 3H), 1.71-1.74 (m, 1H), 1.83-2.19 (m, 8H), 2.53-2.68 (m, 2H), 3.62-3.99 (m, 4H), 4.52 (s, 1H), 4.99 (t, $J = 15.0$ Hz, 1H), 7.13 (t, $J = 10.0$ Hz, 2H), 7.19 (t, $J = 5.0$ Hz, 2H), 8.82 (s, 1H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 23.6, 25.2, 25.8, 26.0, 26.5, 27.2, 27.9, 53.5, 56.8, 58.9, 65.8, 114.7, 116.6, 116.8, 129.8, 132.1, 164.1, 185.7, 202.3 ppm; IR (KBr): ν 3081, 3007, 2932, 2834, 1901, 1605, 1525, 1474, 1245 cm^{-1} ; Anal. calcd for $\text{C}_{22}\text{H}_{25}\text{FN}_4\text{S}_2$: C, 61.65; H, 5.88; N, 13.07; Found: C, 61.44; H, 6.12; N, 12.71%.



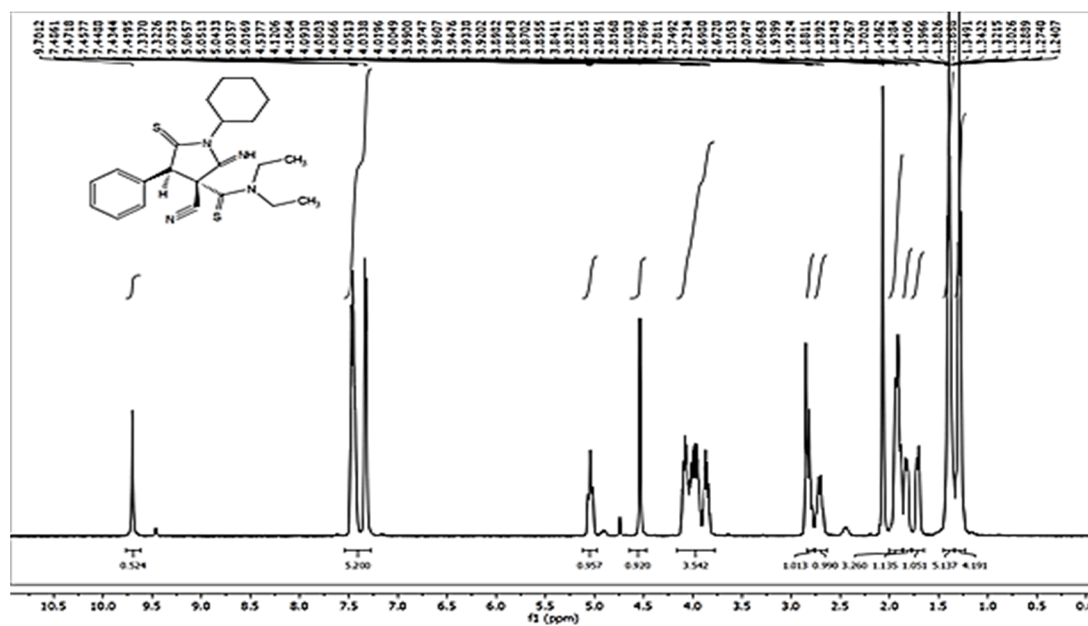
1-cyclohexyl-2-imino-3-(pyrrolidine-1-carbonothioyl)-5-thio-4-(p-tolyl)pyrrolidine-3-carbonitrile (5l)

5l: White solid; mp: 195-197 °C; yield 56% (238 mg); ^1H NMR (500 MHz, CDCl_3) δ 1.28-1.46 (m, 3H), 1.72 (d, $J = 10.0$ Hz, 1H), 1.85-1.98 (m, 5H), 2.09-2.17 (m, 3H), 2.37 (s, 3H), 2.56-2.74 (m, 2H), 3.57-3.96 (m, 4H), 4.38 (s, 1H), 5.00 (t, $J = 10.0$ Hz, 1H), 7.08 (d, $J = 10.0$ Hz, 2H), 7.23 (d, $J = 5.0$ Hz, 2H), 8.73 (brs, 1H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 21.2, 23.6, 25.3, 25.9, 26.0, 26.4, 27.2, 27.9, 53.5, 56.7, 58.9, 62.7, 66.3, 114.8, 127.5, 130.3,

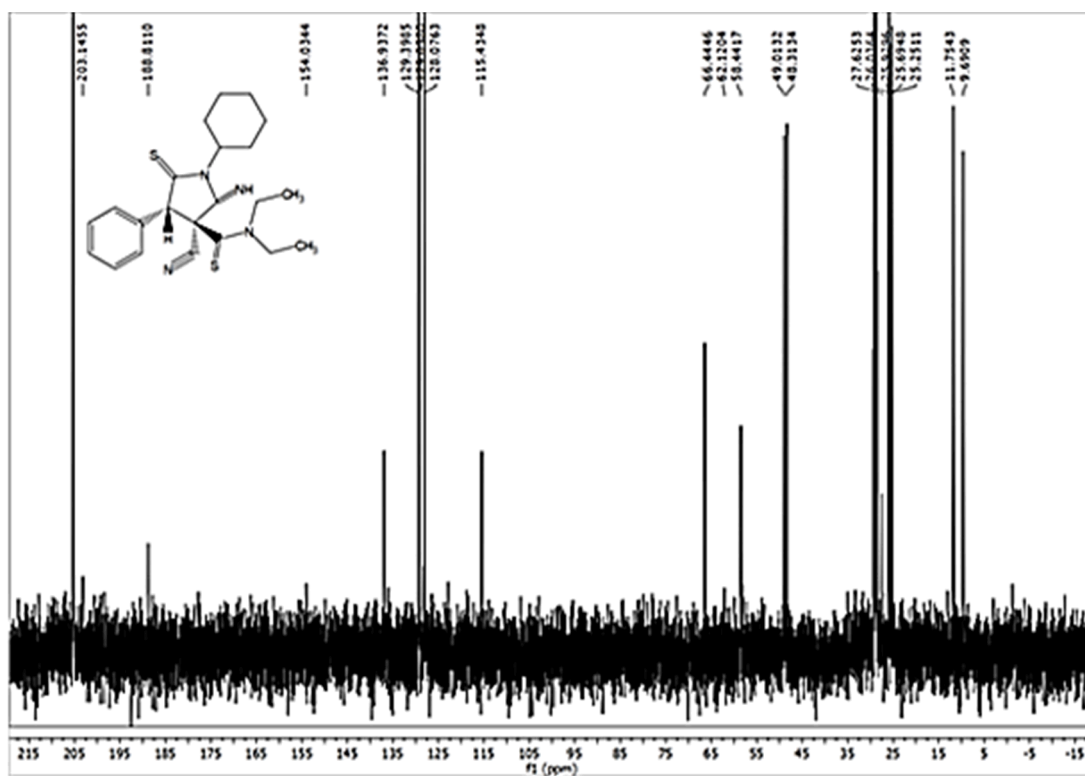
133.3, 139.5, 164.4, 185.9, 202.9 ppm; IR (KBr): ν 3277, 3024, 2929, 2854, 1670, 1511, 1474, 1444, 1347, 1173 cm^{-1} ; Anal. calcd for $\text{C}_{23}\text{H}_{28}\text{N}_4\text{S}_2$: C, 65.06; H, 6.65; N, 13.19 Found: C, 64.85; H, 6.92; N, 12.98%.

Characterization Data of Products (5a-5l)

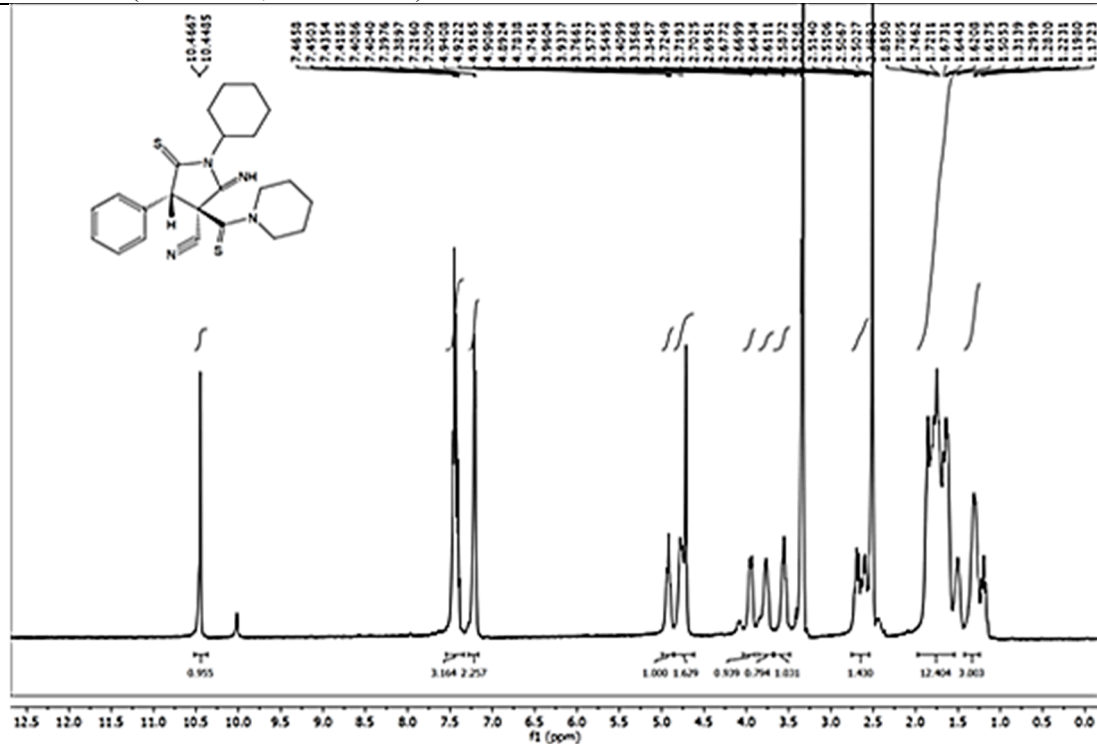
5a: ^1H NMR (500MHz, Acetone- d_6)



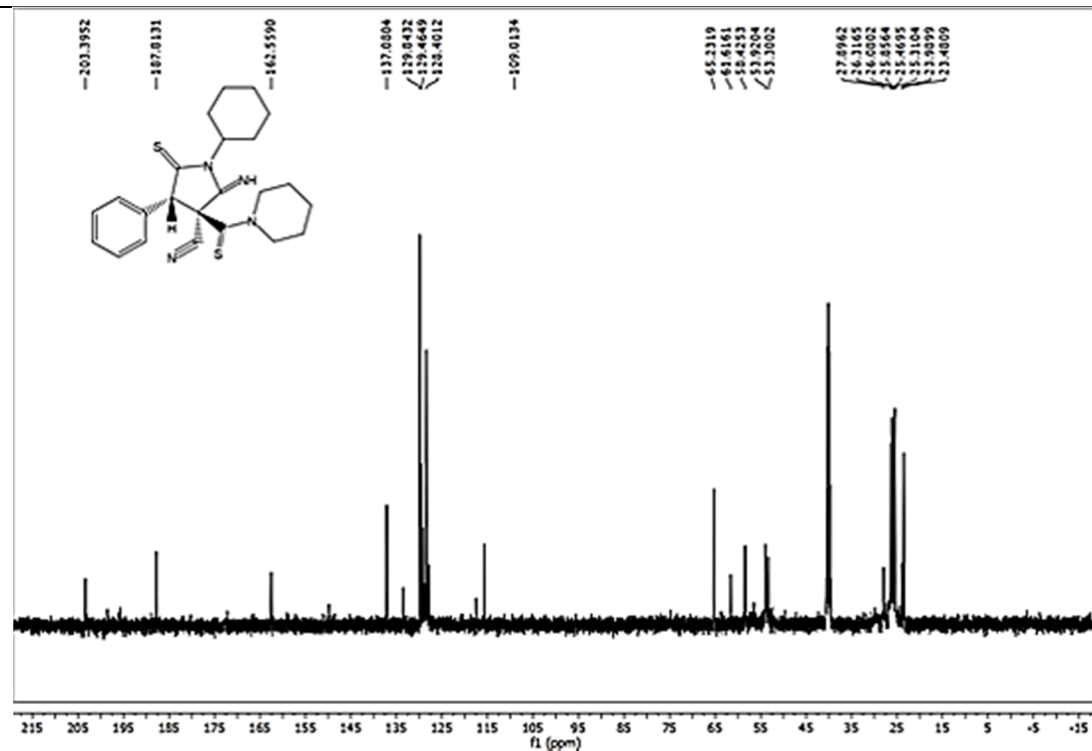
5a: ^{13}C NMR (100MHz, Acetone - d_6)



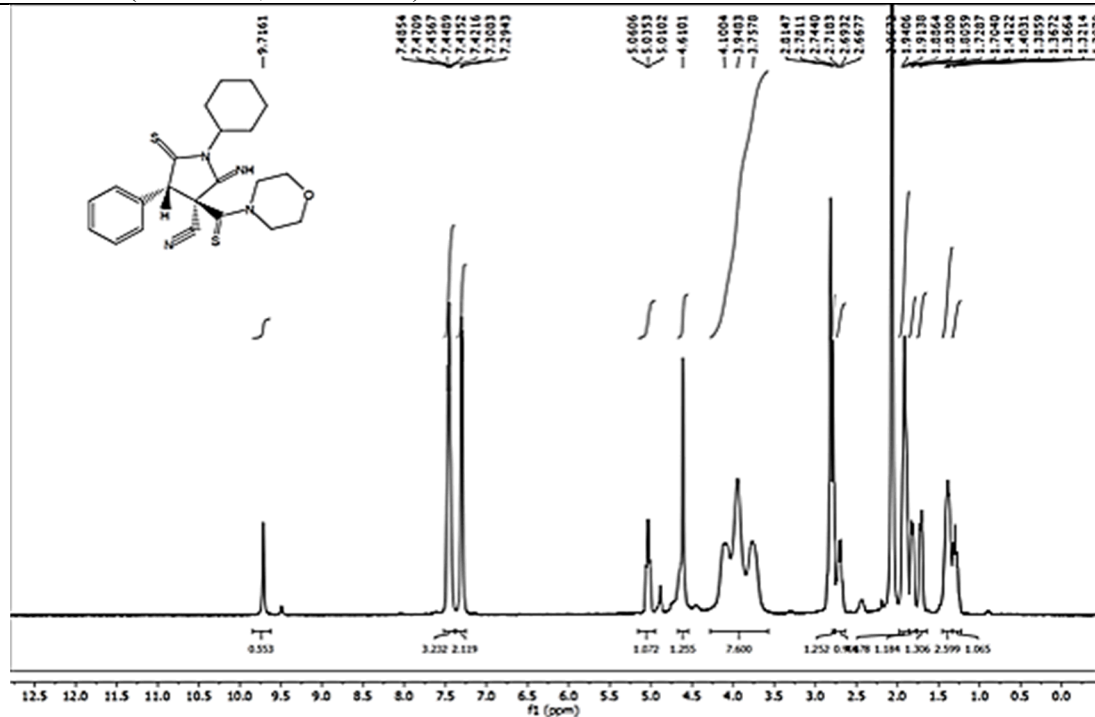
5b: ^1H NMR (500 MHz, $\text{DMSO-}d_6$)



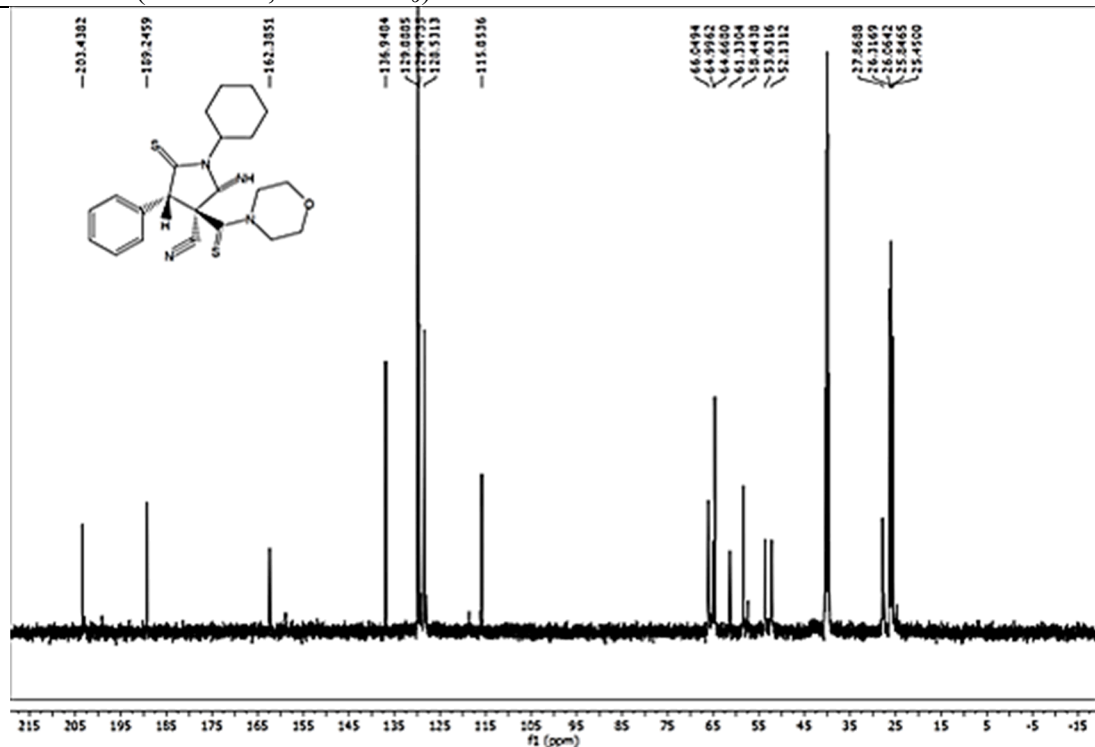
5b: ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$)



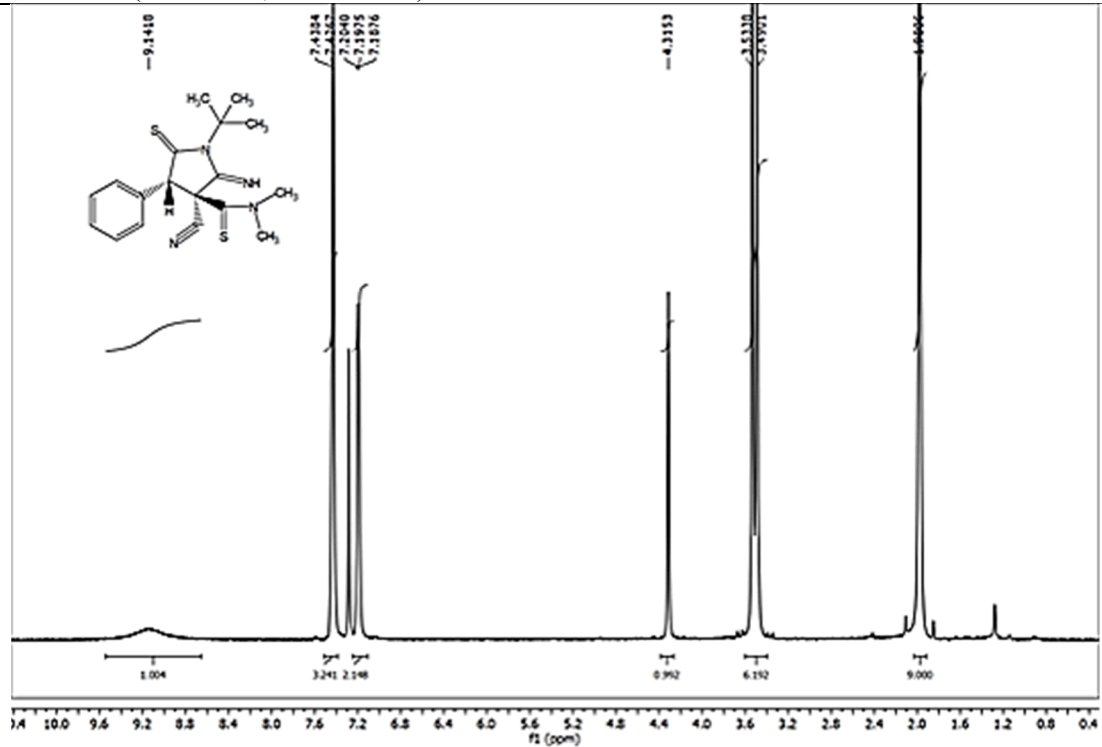
5c: ^1H NMR (500 MHz, $\text{DMSO-}d_6$)



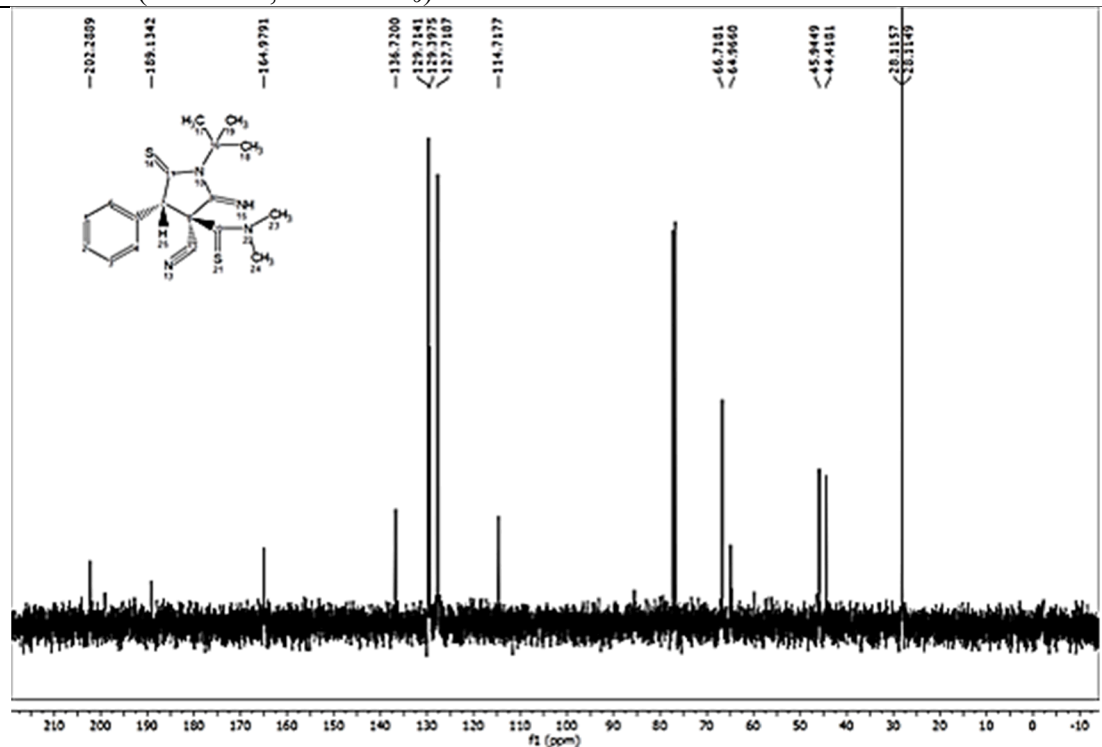
5c: ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$)



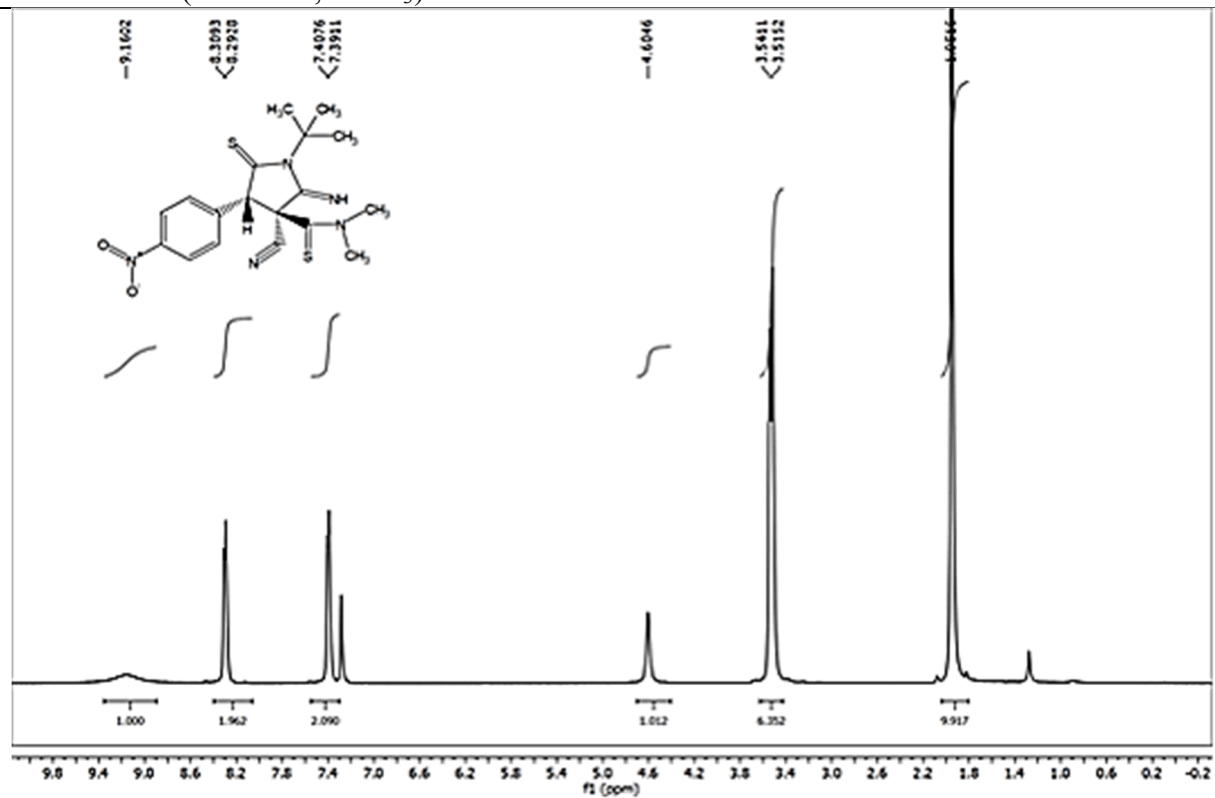
5d: ^1H NMR (500 MHz, $\text{DMSO-}d_6$)



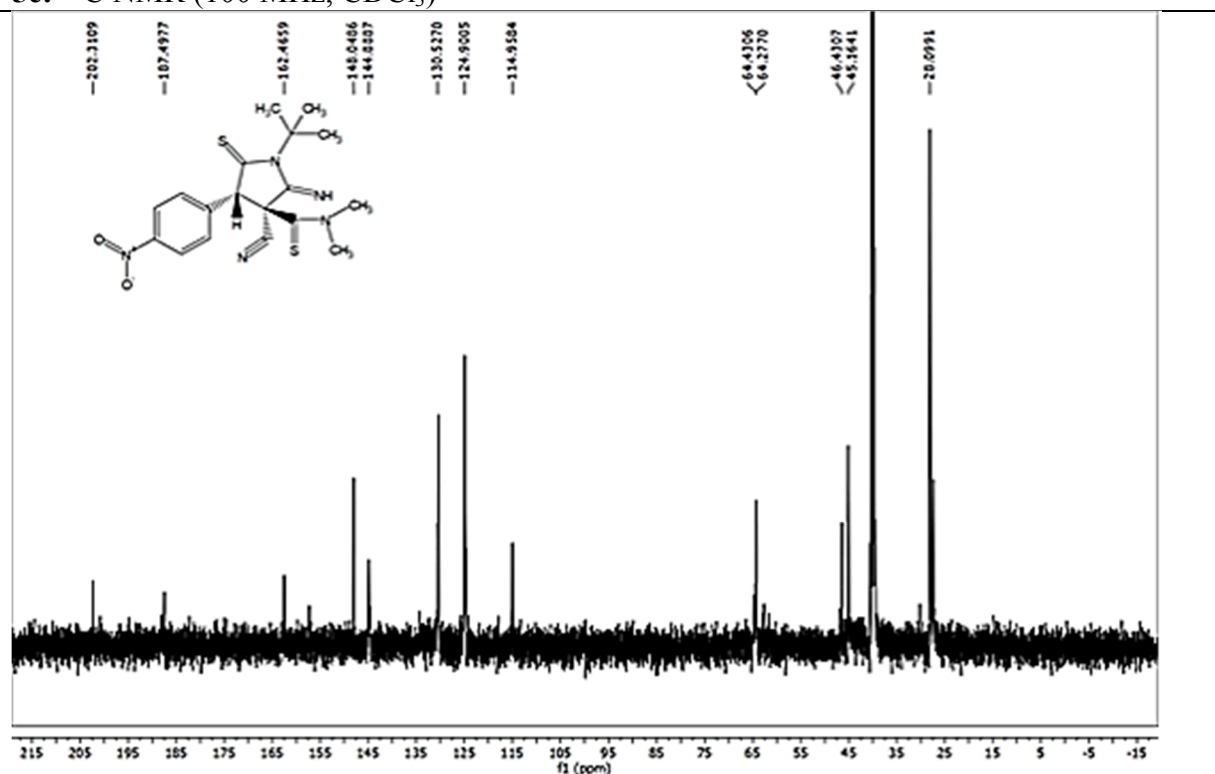
5d: ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$)



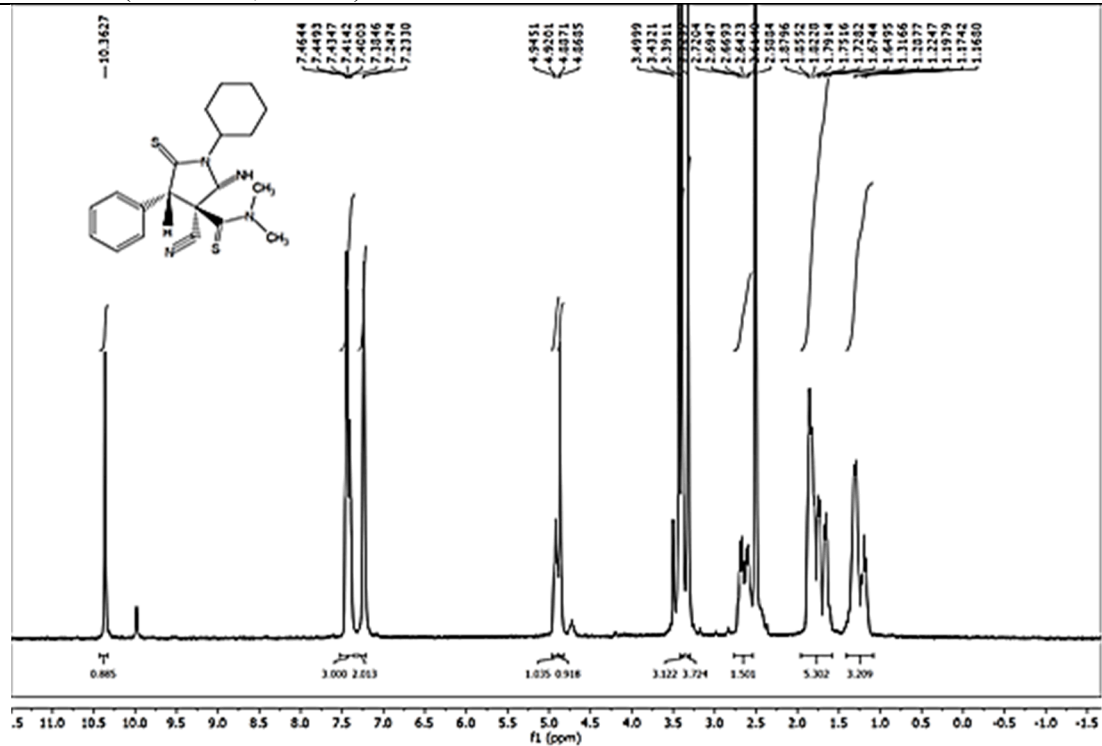
5e: ^1H NMR (500 MHz, CDCl_3)



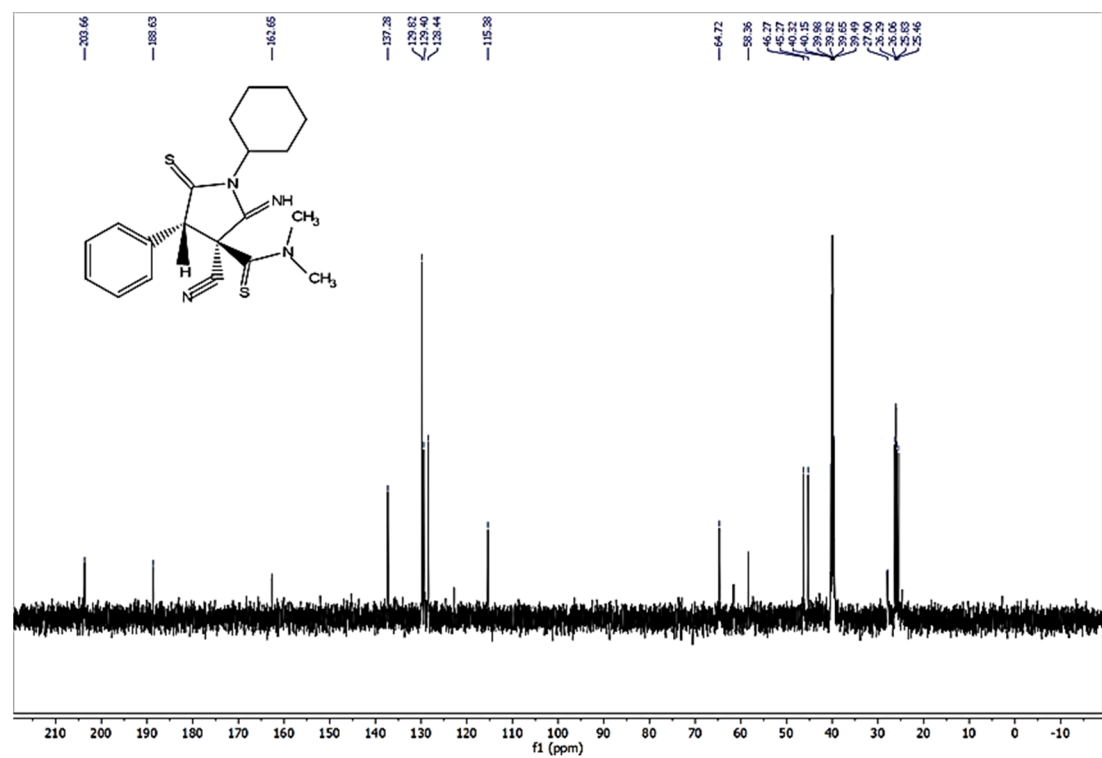
5e: ^{13}C NMR (100 MHz, CDCl_3)



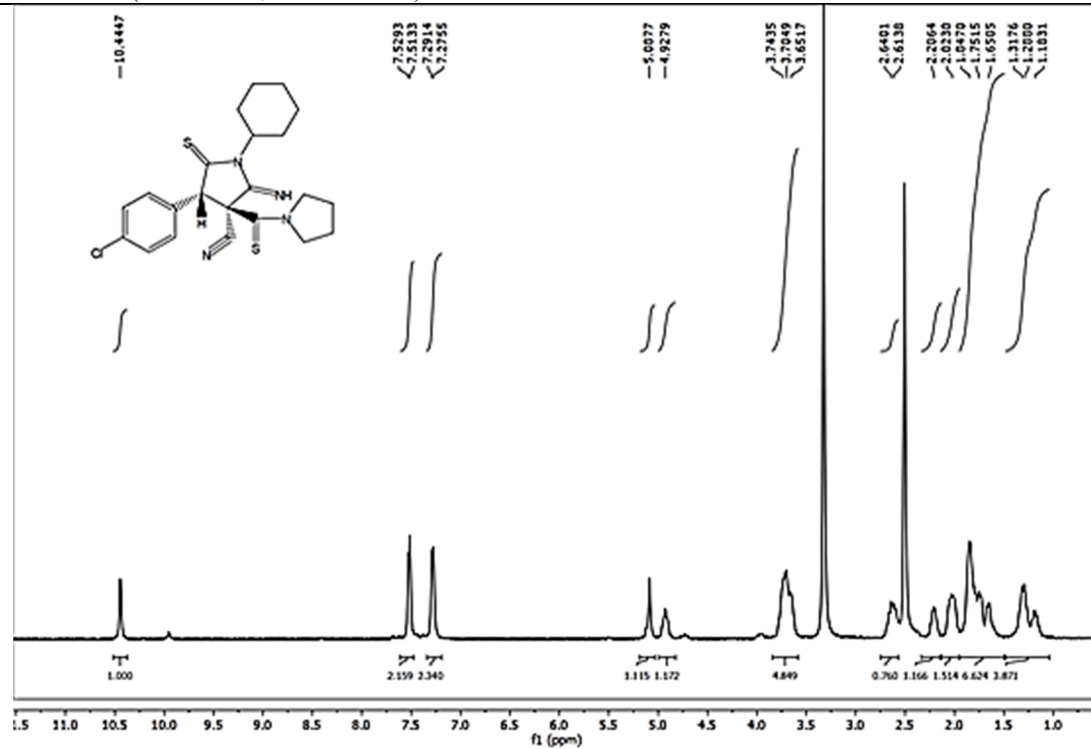
5f: ^1H NMR (500 MHz, CDCl_3)



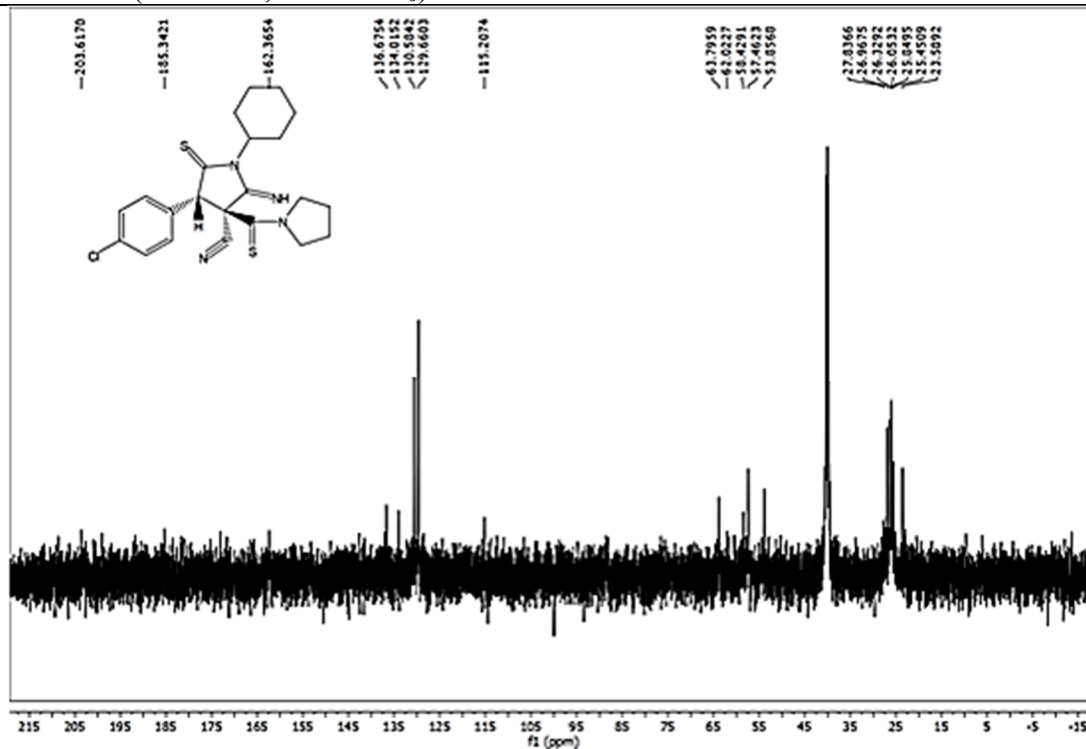
5f: ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$)



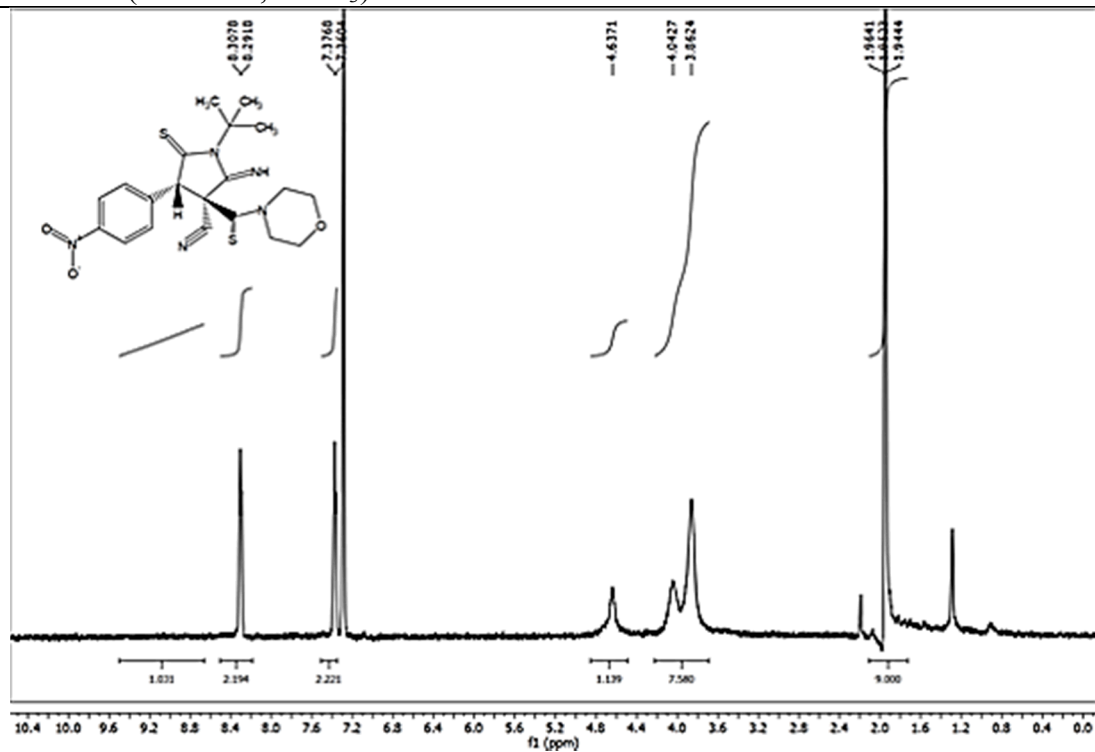
5g: ^1H NMR (500 MHz, $\text{DMSO}-d_6$)



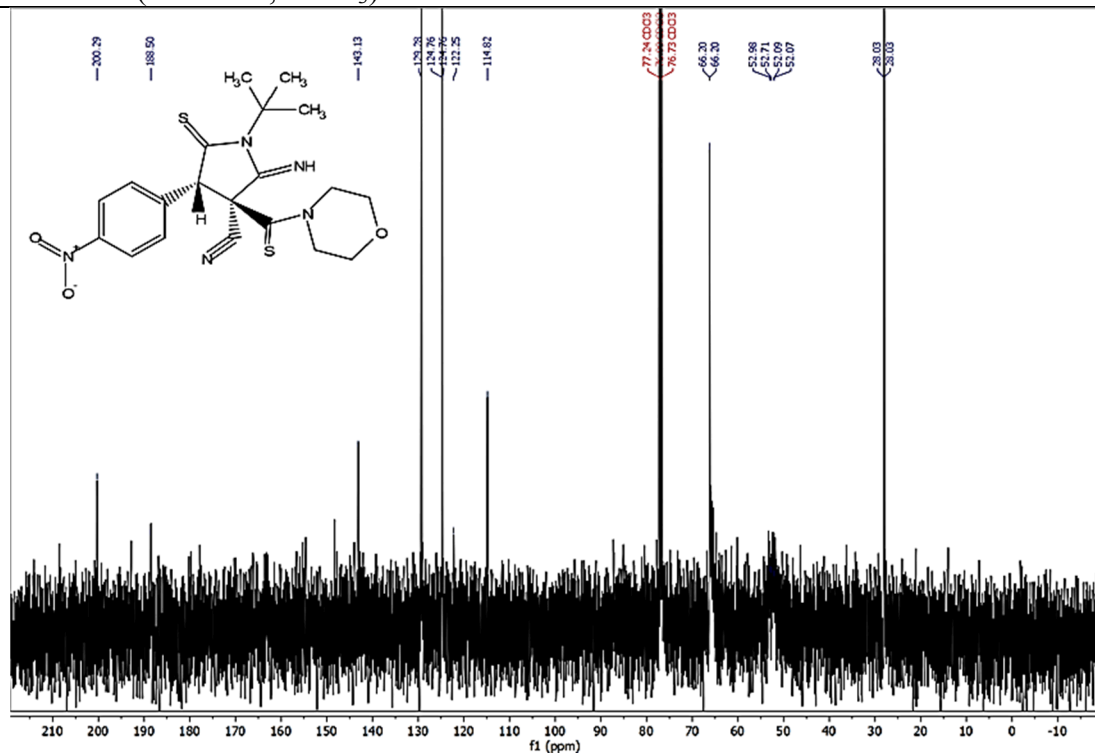
5g: ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$)



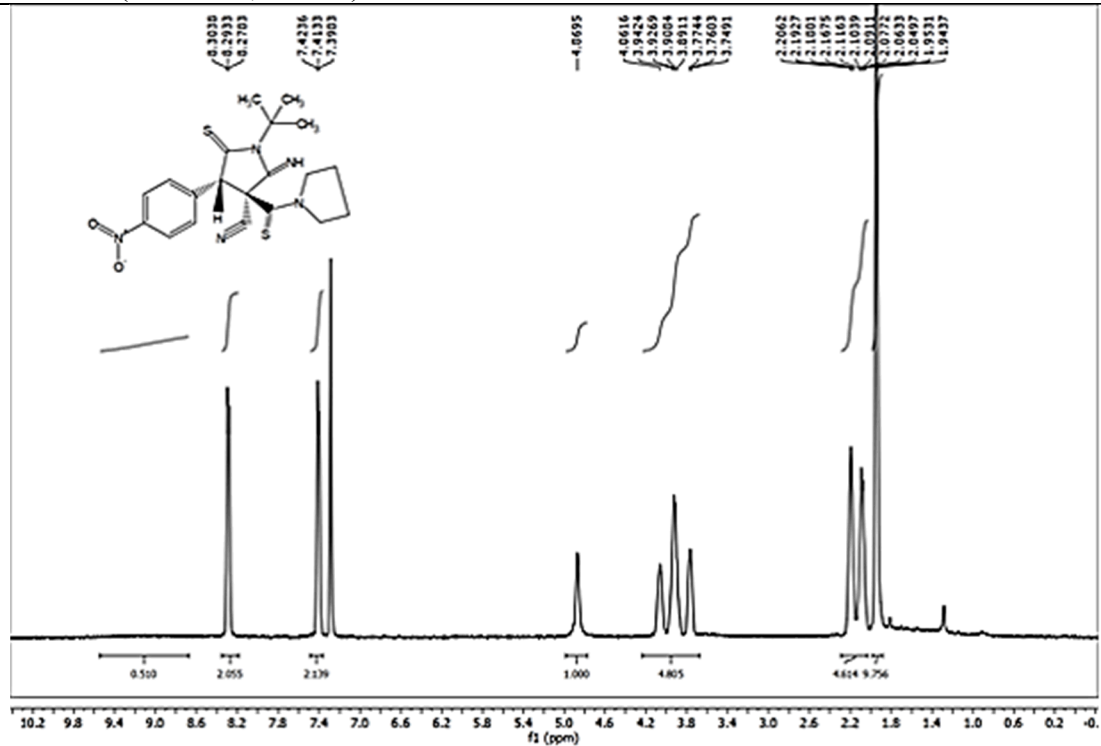
5h: ^1H NMR (500 MHz, CDCl_3)



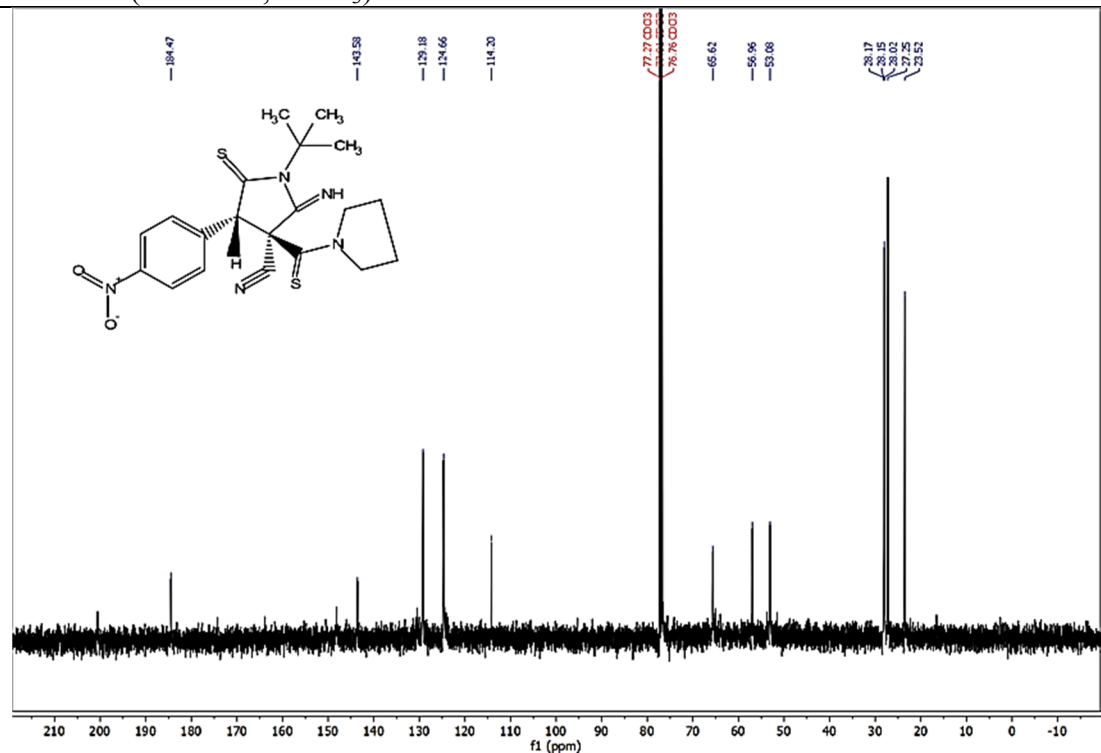
5h: ^{13}C NMR (100 MHz, CDCl_3)



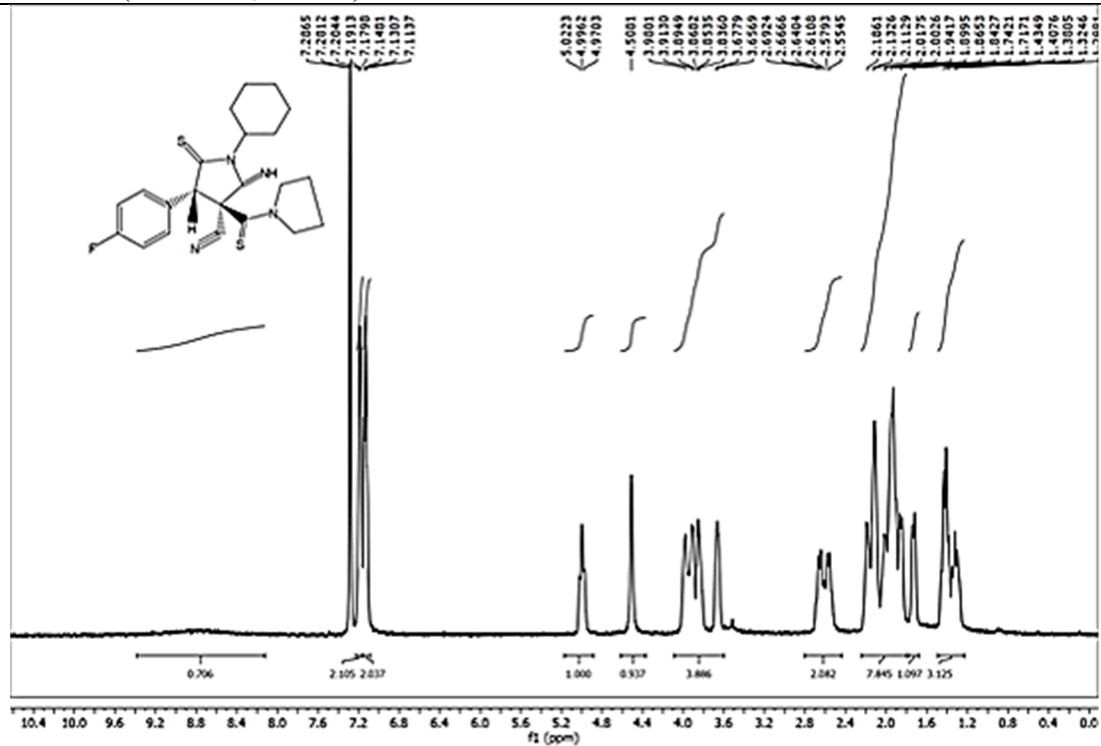
5i: ^1H NMR (500 MHz, CDCl_3)



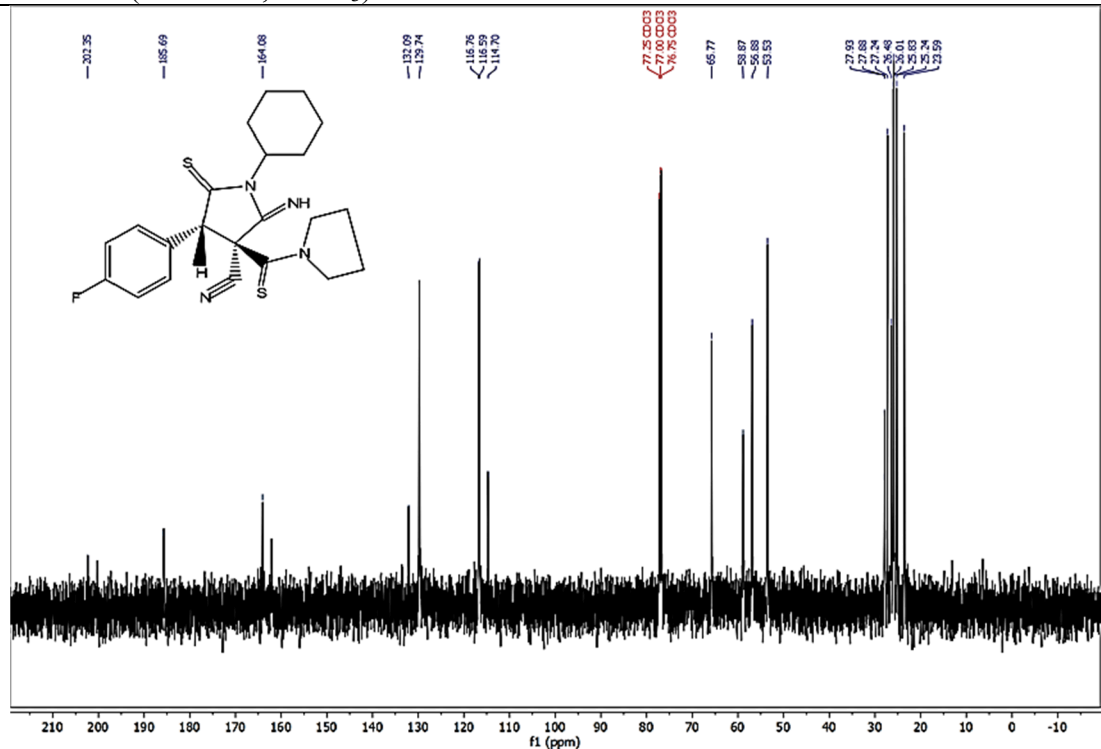
5i: ^{13}C NMR (100 MHz, CDCl_3)



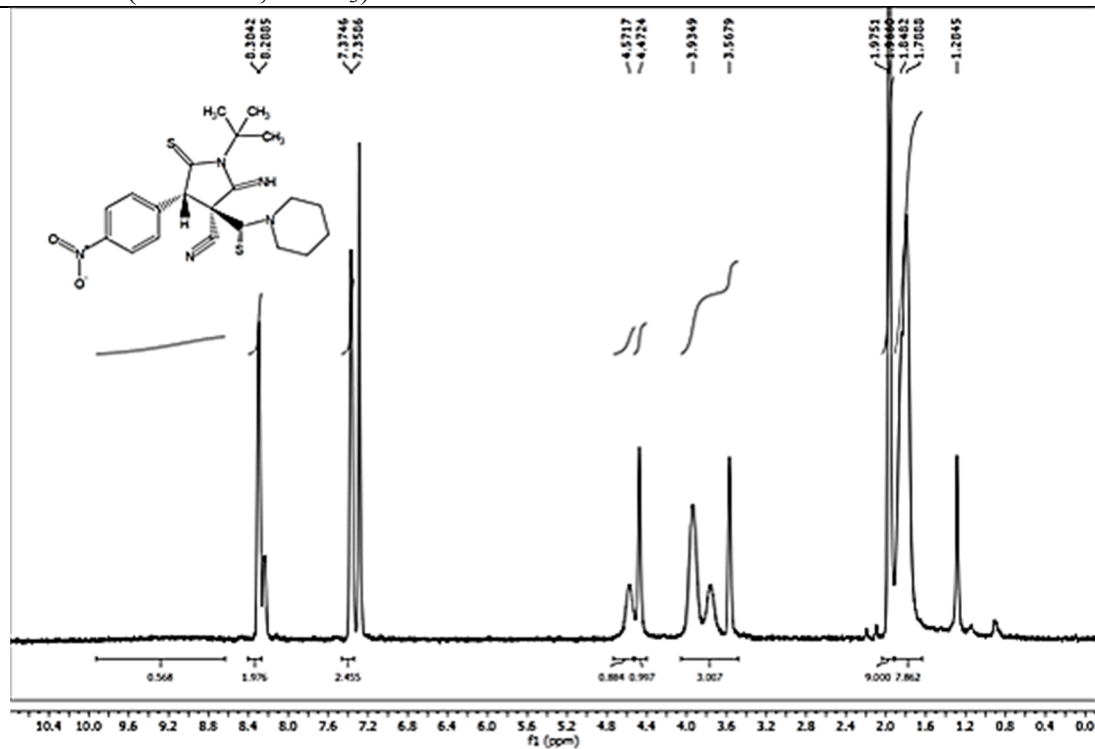
5j: ^1H NMR (500 MHz, CDCl_3)



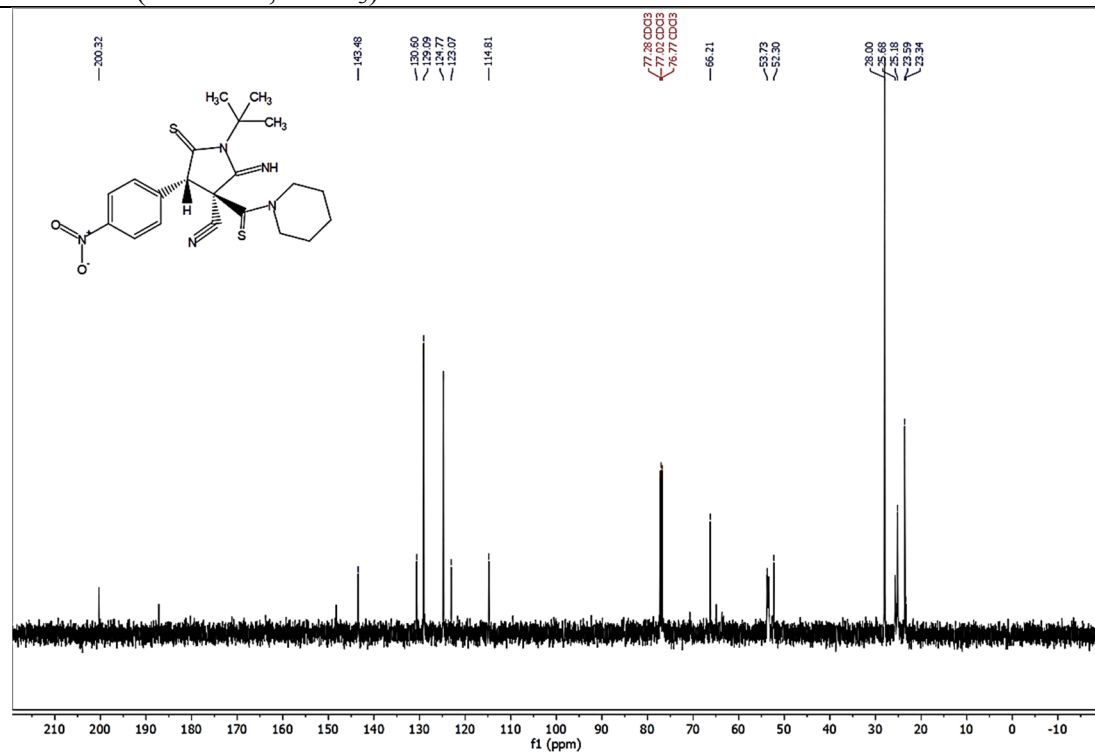
5j: ^{13}C NMR (100 MHz, CDCl_3)



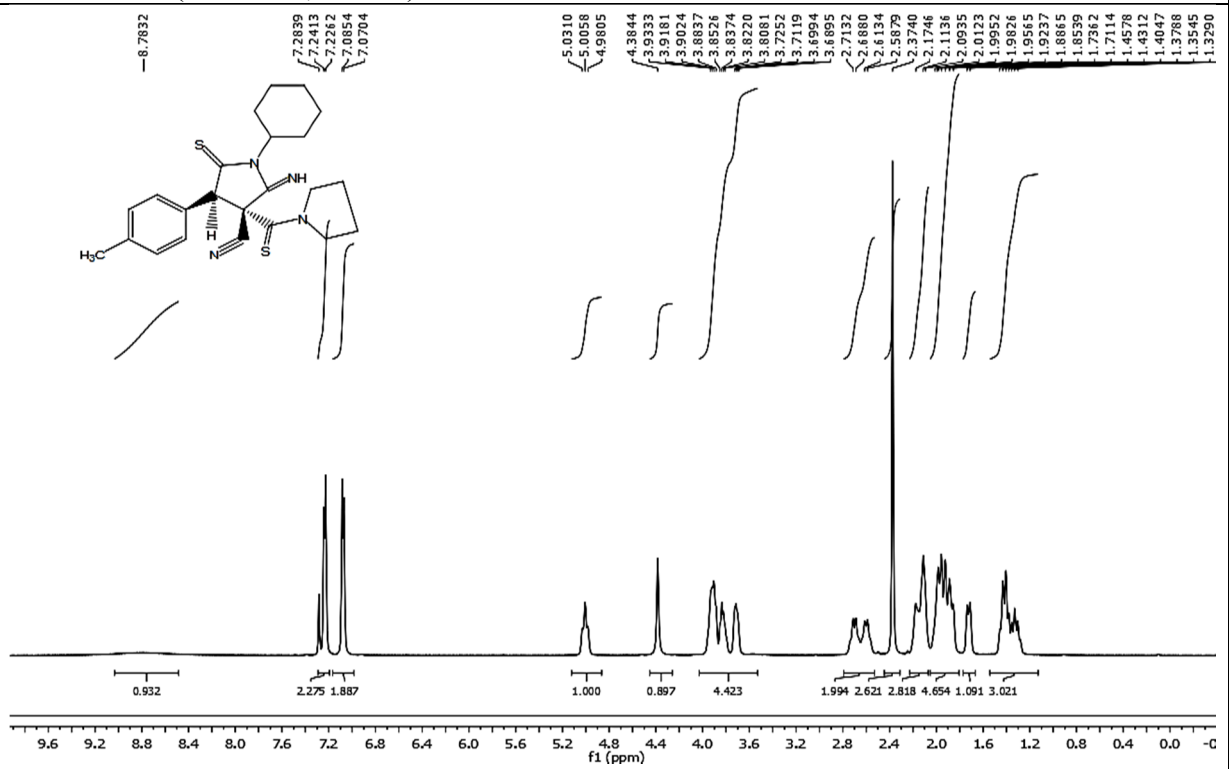
5k: ^1H NMR (500 MHz, CDCl_3)



5k: ^{13}C NMR (100 MHz, CDCl_3)



5l: ^1H NMR (500 MHz, CDCl_3)



5l: ^{13}C NMR (100 MHz, CDCl_3)

