Chapter 2

MATERIALS AND METHODS

2.1 Materials

2.1.1 Chemicals

Chemicals used in the present work were procured from various companies, such as Himedia, Sigma Aldrich, CDH, Rankem, Spectrochem, Alfa aesar etc. Solvents used for the chemical synthesis, acquired from commercial sources, were of analytical grade and used without further purification.

2.2 Instruments

- All the melting points reported in the present work were taken in open capillaries and are reported uncorrected.
- The elemental analysis (Carbon, Hydrogen, Nitrogen and Sulphur) was performed on Carlo Erba-1108 Elemental Analyser and Euro EA 3000 Elemental Analyser.
- Infrared spectra (IR) were recorded on ABB FTIR spectrometer and the results are reported in cm\(^{-1}\). Only principle absorption peaks of interest are reported.
- \(^1\)H NMR spectra were recorded in CDCl\(_3\) and DMSO-d\(_6\) on a BRUKER AVANCE II 400 MHz spectrometer. The chemical shift values are expressed in \(\delta\) values (ppm) using tetramethylsilane (TMS) as an internal standard. \(^{13}\)C NMR spectra were recorded on the same instrument with complete noise decoupling.
- The mass spectra were recorded on WATERS, Q-TOF MICROMASS (LC-MS) and GC-MS QP-2010 Ultra Shimadzu instrument. The relative intensities of the peaks are given in the parenthesis.
• Thin layer chromatography (TLC) was performed on TLC grade silica gel ‘G’ (60-120 mesh) using pet ether-ethylacetate (4:1), pet ether-chloroform (7:3), pet ether-acetone (3:2) etc. as eluents. The spots were made visible by exposing to iodine vapours.

• Column Chromatography was performed with silica gel (Alpha-Chem, 60-120 mesh) and eluted with ethyl acetate: pet ether (4:1) mixtures unless otherwise stated.

• X-ray diffraction was performed on X Calibur EOS OXFORD Diffractometer.

• DFT studies were carried out on Jaguar software package version 6.5112 and Gaussian 09 W software package by using B3LYP exchange correlation function using 6-31G, 6-31G** and 6-31G(d) basis sets.

• Electronic absorption spectra were recorded on Shimadzu UV 1800 spectrophotometer (190–1100 nm).

• Fluorescence measurements were carried out on a Perkin Elmer LS-55 luminescence spectrophotometer equipped with quartz cuvettes with a path length of 10 mm at 25.0 ± 0.1 °C. Fluorescence spectra were registered with excitation at 360 nm.

2.3 3,4-Dihydrornaphthalen-1(2H)ylidene-hydrazone-thiazolidin-4-one (3)

2.3.1 Synthesis of ionic liquid N-methylpyridinium tosylate

Pyridine (1.1 mol) was added to methyl-4-toluene sulfonate (1.0 mol) at 0-10 °C. After completion of the addition, the mixture was stirred at room temperature (15 °C) for 1 h. The solid of N-methylpyridinium tosylate was filtered, washed with ethyl acetate and dried. mp 28-30 °C; 1H NMR (400 MHz, DMSO-d6): δ 2.29 (s, 3H, CH3), 4.37 (s, 3H, NCH3), 7.11 (d, 2H, C6H4, J = 7.9 Hz) 7.54 (d, 2H, C6H4, J = 8.0 Hz), 8.08 (t, 2H, pyridine ring, J = 7.1 Hz), 8.54 (t, 1H, pyridine ring, J = 7.8 Hz), 9.06 (d, 2H, pyridine ring,
$J = 5.8 \text{ Hz}$). $^1\text{H}$ NMR spectral data of the above synthesized ionic liquid sample was compared with authentic sample obtained from commercial source. The data is in good agreement with the authentic sample.

### 2.3.2 General procedure for synthesis of hydrazinecarbothioamide 2

A mixture of 1-tetralone/6-methoxy-1-tetralone 1 (0.03 mol), thiosemicarbazide (2.73 g, 0.03 mol) and concentrated HCl (0.8 mL) in absolute ethanol (40 mL) was stirred at room temperature for 3 h. The mixture was poured into ice cold water. The resultant white solid was filtered, dried and crystallized from ethanol.

#### 2.3.2.1 (E)-2(3,4-Dihyronaphthalen-1(2H)-ylidene)hydrazinecarbothioamide (2a)

Bright white needles; yield 91 %; mp 202–206 °C. IR (cm$^{-1}$): 3410, 3217, 3140 (NH), 1597 (C=N), 1489 (C=C), 1288 (C=S). $^1\text{H}$ NMR (400 MHz, CDCl$_3$): $\delta$ 1.95-2.01 (m, 2H, CH$_2$), 2.61 (t, 2H, CH$_2$, $J = 6.6$ Hz), 2.8 (t, 2H, CH$_2$, $J = 6.2$ Hz), 6.51 (br, 1H, NH exchanged with D$_2$O), 7.15-7.32 (m, 3H, C$_6$H$_5$), 7.4 (br, 1H, NH$_2$ exchangeable with D$_2$O), 7.99 (d, 1H, C$_6$H$_5$, $J = 6.8$ Hz), 8.8 (br, 1H, NH$_2$ exchangeable with D$_2$O). Anal. Calcd. (%) for C$_{11}$H$_{13}$N$_3$S: C, 60.27; H, 5.98; N, 19.12; S, 14.62. Found (%): C, 60.22; H, 5.90; N, 19.22; S, 14.58.

#### 2.3.2.2 (E)-2-(6-Methoxy-3,4-dihyronaphthalen-1(2H)-ylidene)hydrazine carbothioamide (2b)

Light brown crystals; yield 86.5 %; mp 198–200 °C. IR (cm$^{-1}$): 3433, 3194, 3117 (NH), 1582 (C=N), 1489 (C=C), 1250 (C=S). $^1\text{H}$ NMR (400 MHz, CDCl$_3$): $\delta$ 1.87-1.93 (m, 2H, CH$_2$), 2.51 (t, 2H, CH$_2$, $J = 6.6$ Hz), 2.7 (t, 2H, CH$_2$, $J = 6.2$ Hz), 3.75 (s, 3H, OCH$_3$), 6.3 (br, 1H, NH exchangeable with D$_2$O), 6.59 (d, 1H, C$_6$H$_5$, $J = 2.6$ Hz), 6.70-6.73 (m, 1H, C$_6$H$_5$), 7.28 (br, 1H, NH$_2$ exchangeable with D$_2$O), 7.86 (d, 1H, C$_6$H$_5$, $J = 8.8$ Hz), 8.66 (br, 1H,
NH₂ exchangeable with D₂O). Anal. Calcd. (%) for C₁₂H₁₅N₃SO: C, 57.91; H, 6.05; N, 16.88; S, 12.86. Found (%): C, 57.80; H, 5.98; N, 16.82; S, 12.81.

2.3.3 Solvent free general procedure for synthesis of 3

An equimolar mixture of 2 (0.025 mol) and chloroacetic acid/2-bromopropionic acid (0.025 mol) in premolten ionic liquid, N-methylpyridinium tosylate (2.0 g) was stirred at 80-90 °C for 3-4 h. The reaction was monitored by TLC. After completion the mixture was poured into ice cold water and the resultant solid was filtered, dried and crystallized from ethanol.

2.3.4 Conventional procedure for synthesis of 3

A mixture of 2 (0.005 mol), chloroacetic acid/2-bromopropionic acid (0.005 mol), anhydrous sodium acetate (0.8 g, 0.01 mol), glacial acetic acid (3.0 mL) and acetic anhydride (1.0 mL) was heated under reflux for 4 h. The reaction mixture was cooled to room temperature and then poured into ice cold water. The resultant solid was filtered, washed with water and crystallized from ethanol.

2.3.4.1 (Z)-2-((E)-3,4-Dihyronaphthalen-1(2H)ylidene)hydrazono)-thiazolidin-4-one (3a’)

Light yellow crystals; yield 90 %; mp 206–208 °C. IR (cm⁻¹): 2800 (NH), 1705 (N=C=O), 1605 (C=N). ¹H NMR (400 MHz, CDCl₃): δ 1.85-1.91 (m, 2H, CH₂), 2.81 (t, 2H, CH₂, J= 6.2 Hz), 2.88 (t, 2H, CH₂, J= 6.6 Hz), 3.79 (s, 2H, SCH₂), 7.15 (d, 1H, C₆H₅, J= 7.5 Hz), 7.22-7.32 (m, 2H, C₆H₅), 8.21-8.24 (m, 1H, C₆H₅). ¹³C NMR (100 MHz, CDCl₃): δ 173.5 (C=O), 162.5 (C=N), 162.1 (C=N), 140.9, 132.3, 130.1, 128.6, 126.3, 125.5 (C₆H₅), 33.1 (SCH₂), 29.9 (CH₂), 27.4 (CH₂), 22.2 (CH₂). MS, m/z 260.1 (M+H⁺, 100 %), 144 (M-C₃H₃N₂SO, 29 %). Anal. Calcd. (%) for C₁₃H₁₃N₃SO: C, 60.32; H, 5.11; N, 16.24; S, 12.38. Found (%): C, 60.20; H, 5.04; N, 16.18; S, 12.32.
2.3.4.2 2-\{(E)-[3,4-Dihydro-2H-naphthalen-1(E)-ylidene]-hydrazono\}-5-methyl thiazolidin-4-one (3a"")

Grey color solid; yield 78%; mp 158-160 °C. IR (cm\(^{-1}\)): 3132 (NH), 1713 (N-C=O), 1612 (C=N). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta \) 1.68 (d, 3H, CH\(_3\), \(J=7.0\) Hz), 1.89-1.94 (m, 2H, CH\(_2\)), 2.81 (t, 2H, CH\(_2\), \(J=6.0\) Hz), 2.89 (t, 2H, CH\(_2\), \(J=7.0\) Hz), 4.06 (q, 1H, SCH, \(J=7.0\) Hz), 7.15 (d, 1H, ArH, \(J=7.0\) Hz), 7.23 (d, 1H, ArH, \(J=7.0\) Hz), 7.3 (t, 1H, ArH, \(J=7.0\) Hz), 8.21 (dd, 1H, ArH, \(J=1.0, 7.0\) Hz). \(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta \) 175.9 (C=O), 162.2 (C=N), 140.9, 132.1, 130.2, 128.7, 126.4, 125.5 (ArC), 42.5 (SCH), 29.8 (CH\(_2\)), 27.5 (CH\(_2\)), 22.1 (CH\(_2\)), 19.1 (CH\(_3\)). MS, m/z 274.1 (M+H\(^+\), 100%). Anal. Calcd. (%) for C\(_{14}\)H\(_{15}\)N\(_3\)SO: C, 61.53; H, 5.49; N, 15.38; S, 11.72. Found (%): C, 61.58; H, 5.60; N, 15.49; S, 11.83.

2.3.4.3 (Z)-2-\{(E)-[6-Methoxy-3,4-dihydronaphthalen-1(2H)-ylidene]hydrazono\} thiazolidin-4-one (3b')

Shining white crystals; yield 88%; mp 224–226 °C. IR (cm\(^{-1}\)): 3124 (NH), 1697 (N-C=O), 1597 (C=N). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta \) 1.78-1.84 (m, 2H, CH\(_2\)), 2.72-2.78 (m, 4H, 2CH\(_2\)), 3.72 (s, 2H, SCH\(_2\)), 3.76 (s, 3H, OCH\(_3\)), 6.64 (d, 1H, C\(_6\)H\(_5\), \(J=2.5\) Hz), 6.72-6.75 (m, 1H, C\(_6\)H\(_5\)), 8.02 (d, 1H, C\(_6\)H\(_5\), \(J=8.6\) Hz), 11.73 (br, 1H, NH). \(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta \) 173.5 (C=O), 160.3 (C=N), 159.5 (C=N), 142, 128.6, 126.5 (C\(_6\)H\(_5\)), 54.9 (OCH\(_3\)), 32.7 (SCH\(_2\)), 29.7 (CH\(_2\)), 26.8 (CH\(_2\)), 21.8 (CH\(_2\)). Anal. Calcd (%) for C\(_{14}\)H\(_{15}\)N\(_3\)O\(_2\): C, 58.23; H, 5.22; N, 14.58; S, 11.17. Found (%): C, 58.10; H, 5.14; N, 14.56; S, 11.02.

2.3.4.4 2-\{(E)-[6-Methoxy-3,4-dihydronaphthalen-1(2H)-ylidene]hydrazono\}-5-methyl-thiazolidin-4-one (3b'')

Light green solid; yield 76%; mp 172-174 °C. IR (cm\(^{-1}\)): 3070 (NH), 1705 (N-C=O), 1597 (C=N). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \(\delta \) 1.57 (d, 3H, CH\(_3\), \(J=7.0\) Hz), 1.86 (t, 2H, CH\(_2\), \(J=6.0\) Hz), 2.76-2.84 (m, 4H, 2CH\(_2\)), 3.81 (s, 3H, OCH\(_3\)), 3.98 (q, 1H, SCH, \(J=7.0\) Hz), 6.66 (s,
1H, ArH), 6.76 (d, 1H, ArH, J = 9.0 Hz), 8.08 (d, 1H, ArH, J = 9.0 Hz). $^{13}$C NMR (100 MHz, DMSO-d$_6$): δ 181.7 (C=O), 165.5 (C=N), 164.9 (C- OCH$_3$), 147.2, 131.7, 130.1, 117.9, 117.3 (ArC), 60 (OCH$_3$), 34.9 (SCH), 34.9 (CH$_2$), 32 (CH$_2$), 27 (CH$_2$), 24.1 (CH$_3$). MS, m/z 304.1 (M+H$^+$, 100 %). Anal. Calcd. (%) for C$_{15}$H$_{17}$N$_3$O$_2$: C, 59.40; H, 5.61; N, 13.86; S, 10.56. Found (%): C, 59.49; H, 5.69; N, 13.91; S, 10.86.

2.3.5 Solvent-free general procedure for synthesis of 4

A mixture of 2 (0.001 mol) and p-substituted phenacyl bromide (0.001 mol) was grinded in a pestle mortar without a solvent for 15–20 min at room temperature. The progress of the reaction was monitored by TLC. After completion of the reaction, the product was extracted with ethyl acetate. The solvent was removed under reduced pressure to obtain the crude solid that was crystallized from ethanol.

2.3.6 Conventional procedure for synthesis of 4

A mixture of 2 (0.001 mol) and p-substituted phenacyl bromide (0.001 mol) in absolute ethanol (5.0 mL) was stirred at room temperature for 15 min. The resultant solid was filtered, washed with ethanol and crystallized from ethanol.

2.3.6.1 (E)-4-(4-Chlorophenyl)-2-(2-(3,4-dihyronaphthalen-1(2H)-ylidene) hydrazinyl)thiazole (4a’)

Dark brown needles; yield 95 %; mp 232–235 °C. IR (cm$^{-1}$): 3204 (NH), 1605 (C=N), 1481 (C=C), 733 (C-Cl). $^1$H NMR (400 MHz, CDCl$_3$): δ 2.02-2.05 (m, 2H, CH$_2$), 2.83 (t, 2H, CH$_2$, J = 6.1 Hz), 2.92 (t, 2H, CH$_2$, J = 6.6 Hz), 6.75 (s, 1H, CH), 7.19-7.70 (m, 7H, C$_6$H$_5$), 8.07-8.09 (m, 1H, C$_6$H$_5$), 12.59 (br, 1H, NH exchangeable with D$_2$O). Anal. Calcd. (%) for C$_{19}$H$_{16}$N$_3$SCl: C, 64.48; H, 4.62; N, 11.92; S, 9.14. Found (%): C, 64.56; H, 4.56; N, 11.84; S, 9.04.
2.3.6.2 (E)-2-(2-(3,4-Dihyronaphthalen-1(2H)-ylidene)hydrazinyl)-4-(4-nitrophenyl)thiazole (4a"")

Light yellow needles; yield 92%; mp 195-197 °C. IR (cm⁻¹): 3310 (NH), 1597 (C=N), 1558, 1335 (NO₂), 1504 (C=C). ¹H NMR (400 MHz, CDCl₃): δ 1.97-2.03 (m, 2H, CH₂), 2.6 (t, 2H, CH₂, J = 6.6 Hz), 2.79 (t, 2H, CH₂, J = 6.2 Hz), 7.12 (s, 1H, CH), 7.14-8.27 (m, 8H, C₆H₅), 8.89 (br, 1H, NH exchangeable with D₂O). Anal. Calcd. (%) for C₁₉H₁₆N₄SO₂: C, 62.76; H, 4.44; N, 15.38; S, 8.89. Found (%): C, 62.65; H, 4.36; N, 15.32; S, 8.76.

2.3.6.3 (E)-4-(4-Chlorophenyl)-2-(2-(6-methoxy-3,4-dihyronaphthalen-1(2H)-ylidene)hydrazinyl)thiazole (4b')

White crystals; yield 94%; mp 218-220 °C. IR (cm⁻¹): 3040 (NH), 1620 (C=N), 1497 (C=C), 748 (C-Cl). ¹H NMR (400 MHz, CDCl₃): δ 1.89 (t, 2H, CH₂, J = 6.2 Hz), 2.5 (t, 2H, CH₂, J = 6.0 Hz), 2.66-2.74 (m, 4H, CH₂), 3.76 (s, 3H, OCH₃), 6.63 (d, 1H, C₆H₅, J = 2.0 Hz), 6.73-6.76 (m, 1H, C₆H₅), 7.13 (s, 1H, CH), 7.36 (d, 1H, C₆H₅, J = 8.4 Hz), 7.63 (d, 1H, C₆H₅, J = 8.0 Hz), 7.72 (d, 2H, C₆H₅, J = 8.5 Hz), 7.98 (br, 1H, NH exchanged with D₂O). Anal. Calcd. (%) for C₂₀H₁₈N₃SClO: C, 62.76; H, 4.69; N, 10.98; S, 8.41. Found (%): C, 62.62; H, 4.64; N, 10.92; S, 8.32.

2.3.6.4 (E)-2-(2-(6-Methoxy-3,4-dihyronaphthalen-1(2H)-ylidene)-hydrazinyl)-4-(4-nitrophenyl)thiazole (4b"")

Light brown crystals; yield 93%; mp 211-212 °C. IR (cm⁻¹): 3348 (NH), 1597 (C=N), 1558, 1342 (NO₂), 1512 (C=C). ¹H NMR (400 MHz, DMSO-d₆): δ 1.84-1.90 (m, 2H, CH₂), 2.5 (t, 2H, CH₂, J = 6.1 Hz), 2.64-2.72 (m, 4H, 2CH₂), 3.75 (s, 3H, OCH₃), 6.61 (d, 1H, C₆H₅, J = 2.4 Hz), 6.72-6.75 (dd, 1H, C₆H₅, J = 6.1 Hz, J = 2.6 Hz), 7.9 (s, 1H, CH of thiazole ring), 7.94 (d, 1H, C₆H₅, J = 8.8 Hz), 8.0 (d, 2H, C₆H₅, J = 2.0 Hz), 8.16 (d, 2H, C₆H₅, J = 2.2 Hz),
10.87 (br, 1H, NH exchanged with D₂O). Anal. Calcd. (%) for C₂₀H₁₈N₆O₃S: C, 60.94; H, 4.62; N, 14.12; S, 8.14. Found (%): C, 60.89; H, 4.52; N, 14.18; S, 8.09.

2.3.7 Solvent-free procedure for synthesis of 5

An equimolar mixture of 2 (0.025 mol), 3-chloropropionic acid (2.71 g, 0.025 mol) and the ionic liquid, N-methylpyridinium tosylate (2.0 g) was stirred at 100 °C for 6 h. After the reaction was completed, as monitored by TLC, the mixture was poured into ice-cold water. The resultant precipitate of 5 was filtered, dried and crystallized from ethanol.

2.3.8 Conventional procedure for synthesis of 5

A mixture of 2 (0.005 mol), 3-chloropropionic acid (0.54 g, 0.005 mol), anhydrous sodium acetate (0.8 g, 0.01 mol), glacial acetic acid (3.0 mL) and acetic anhydride (1.0 mL) was heated under reflux for 14 h. The mixture was cooled to room temperature and poured into ice cold water. The gummy product obtained was extracted with ethyl acetate (2×25 mL). The extract was washed with water, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The solid residue of 5 was crystallized from ethyl acetate.

2.3.8.1 2-[(E)-[3,4-Dihyronaphthalene-1(2H)-ylidene]hydrazono]-perhydro-1,3-thiazin-4-one (5a)

Light grey solid; yield 75 %; mp 154–56 °C. IR (cm⁻¹): 1697 (N=O), 1589 (C=N), 1543 (C=C). ¹H NMR (400 MHz, CDCl₃): δ 1.89-1.94 (m, 2H, CH₂), 2.79-3.07 (m, 8H, 4CH₂), 7.15 (t, 1H, ArH, J= 7.0 Hz), 7.21-7.34 (m, 2H, ArH), 8.24 (dd, 1H, ArH, J= 7.0 Hz, J= 2.0 Hz), 9.72 (br, 1H, NH exchangeable with D₂O). ¹³C NMR (100 MHz, CDCl₃): δ 169.4 (C=O), 162.4 (C=N), 140.9, 132.5, 130.3, 128.8, 126.3, 125.4 (ArC), 34.3 (SCH₂), 29.9, 27.4, 23.2, 22.7, 22.1 (CH₂). MS, m/z 274.1 (M+H⁺, 20 %), 231 (M-CONH, 100 %). Anal.
Calcd. (%) for C_{14}H_{13}N_{3}SO: C, 61.53; H, 5.49; N, 15.38; S, 11.72. Found (%): C, 61.45; H, 5.44; N, 15.32; S, 11.80.

2.3.8.2 2-\{(E)-[6-Methoxy-3,4-dihydronaphthalen-1(2H)-ylidene]hydrazono\}-perhydro-1,3-thiazin-4-one (5b)

Light yellow solid; yield 74 %; mp 139-140 °C. IR (cm^{-1}): 1697 (N=C=O), 1589 (C=N), 1551 (C=C). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \( \delta \) 1.85-2.17 (m, 2H, CH\textsubscript{2}), 2.76-3.16 (m, 6H, 3CH\textsubscript{2}), 3.83 (s, 3H, OCH\textsubscript{3}), 6.64-6.66 (m, 1H, ArH), 6.79 (dd, 1H, ArH, \( J = 6.0 \) Hz, \( J = 3.0 \) Hz), 8.13-8.21 (m, 1H, ArH), 9.74 (br, 1H, NH exchangeable with D\textsubscript{2}O). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): \( \delta \) 169.5 (C=O), 162.6 (C=N), 140.8, 132.1, 130.1, 127.2, 125.1, 123.4 (ArC), 58.9 (OCH\textsubscript{3}), 33.4 (SCH\textsubscript{2}), 28.9, 27.2, 23.1, 22.4, 22.6 (CH\textsubscript{2}). MS, m/z 304.1 (M+H\textsuperscript{+}, 20 %). Anal. Calcd (%) for C_{15}H_{17}N_{3}O_{2}S: C, 59.40; H, 5.61; N, 13.86; S, 10.56. Found (%): C, 59.33; H, 5.56; N, 13.78; S, 10.45.

2.3.9 General procedure for synthesis of 6

An equimolar mixture of 2 (0.001 mol) and ethyl bromopyruvate (0.001 mol) in absolute ethanol (5.0 mL) was stirred at room temperature for 15 min. The resultant solid was filtered, washed with ethanol and crystallized from ethanol.

2.3.9.1 (E)-Ethyl 2-(2-(3,4-dihydronaphthalen-1(2H)-ylidene)hydrazinyl)thiazole-4-carboxylate (6a)

Light yellow needles; yield 72 %; mp 194-196 °C. IR (cm^{-1}): 3206 (NH), 1702 (C=O), 1642 (C=N). \textsuperscript{1}H NMR (400 MHz, DMSO-d\textsubscript{6}): \( \delta \) 1.32 (t, 3H, CH\textsubscript{3}, \( J = 7.1 \) Hz ), 1.84-1.90 (m, 2H, CH\textsubscript{2}), 2.66 (t, 2H, CH\textsubscript{2}, \( J = 6.4 \) Hz), 2.74 (t, 2H, CH\textsubscript{2}, \( J = 5.9 \) Hz), 4.26 (q, 2H, CH\textsubscript{2}, \( J = 7.0 \) Hz), 7.14–7.17 (m, 1H, C\textsubscript{6}H\textsubscript{5}), 7.20–7.25 (m, 2H, C\textsubscript{6}H\textsubscript{5}), 7.69 (s, 1H, CH of thiazole ring), 7.94-8.0 (m, 1H, C\textsubscript{6}H\textsubscript{5}), 11.39 (br, 1H, NH). MS, m/z 316.1 (M+H\textsuperscript{+}, 100 %). Anal. Calcd.
(%) for C_{16}H_{17}N_{3}O_{2}S: C, 70.04; H, 5.62; N, 13.58; S, 10.34. Found (%): C, 60.93; H, 5.43; N, 13.32; S, 10.17.

2.3.9.2 (E)-Ethyl 2-(2-(6-methoxy-3,4-dihyronaphthalen-1(2H)-ylidene)hydrazinyl)thiazole-4-carboxylate (6b)

Light orange needles; yield 69%; mp 208-210 °C. IR (cm⁻¹): 3208 (NH), 1692 (C=O), 1638 (C=N). ¹H NMR (400 MHz, DMSO-d₆):  δ 1.34 (t, 3H, CH₃, J = 7.0 Hz), 1.84-1.87 (m, 2H, CH₂), 2.64 (t, 2H, CH₂, J = 5.8 Hz), 2.72 (t, 2H, CH₂, J = 6.4 Hz), 3.78 (s, 3H, OCH₃), 4.25 (q, 2H, CH₂, J = 6.5 Hz), 6.70-6.81 (m, 2H, C₆H₅), 7.66 (s, 1H, CH of thiazole ring), 7.89-7.93 (m, 1H, C₆H₅), 11.32 (br, 1H, NH). Anal. Calcd. (%) for C_{17}H_{19}N₃O₃S: C, 59.34; H, 5.72; N, 12.29; S, 9.34. Found (%): C, 59.11; H, 5.54; N, 12.17; S, 9.28.

2.4 Dihydrobenzofuranyl-hydrazone-thiazolidin-4-one (9) and analogs

2.4.1 General procedure for synthesis of 7

6,7-Dihydrobenzofuran-4(5H)-one 7a was prepared from furan and succinic anhydride following the reported procedure [Sen et al., 1999] and 6,7-dihydrobenzo[b]thiophen-4(5H)-one 7b was procured from Sigma.

2.4.2 General procedure for synthesis of 8

Compound 8 was prepared from condensation of compound 7 with thiosemicarbazide in presence of conc. HCl by the literature [Venkateswarlu and Vasireddy, 2005] procedure.

2.4.2.1 2-(6,7-Dihydrobenzofuran-4(5H)-ylidene)hydrazinecarbothioamide (8a)

White solid; yield 90%; mp 156-58 °C. IR (cm⁻¹): 3402, 3202, 3114 (NH), 1628 (C=N), 1589 (C=C), 1234 (C=S). ¹H NMR (400 MHz, CDCl₃):  δ 2.06-2.12 (m, 2H, CH₂), 2.51 (t, 2H
CH$_2$, $J$ = 5.8 Hz), 2.78 (t, 2H, CH$_2$, $J$ = 6.2 Hz), 6.35 (br, 1H, NH), 6.6 (s, 1H, CH furen ring), 7.31 (s, 1H, CH furen ring), 8.76 (br, 1H, NH$_2$). Anal. Calcd. (%) for C$_9$H$_{11}$N$_3$SO: C, 51.67; H, 5.26; N, 20.09; S, 15.31; Found (%): C, 51.54; H, 5.20; N, 19.96; S, 15.24.

2.4.2.2 2-(6,7-Dihydrobenzo[b]thiophen-4(5H)-ylidene)hydrazinecarbothioamide (8b)

Shining white solid; yield 86 %; mp 160-62 °C. IR (cm$^{-1}$): 3400, 3216, 3128 (NH), 1620 (C=N), 1585 (C=C), 1246 (C=S). $^1$H NMR (400 MHz, CDCl$_3$): δ 2.05-2.10 (m, 2H, CH$_2$), 2.5 (t, 2H, CH$_2$, $J$ = 5.6 Hz), 2.77 (t, 2H, CH$_2$, $J$ = 6.5 Hz), 6.32 (br, 1H, NH), 6.58 (s, 1H, CH thiophene ring), 7.29 (s, 1H, CH thiophene ring), 8.72 (br, 1H, NH$_2$). Anal. Calcd. (%) for C$_9$H$_{11}$N$_3$S$_2$: C, 47.97; H, 4.92; N, 18.65; S, 28.46. Found (%): C, 48.12; H, 5.09; N, 18.86; S, 28.65.

2.4.3 N-Methylpyridinium tosylate mediated general procedure for synthesis of 9 and 10

An equimolar mixture of 8 (0.12 mmol) and chloroacetic acid or 2-bromopropionic acid (0.12 mmol) in premolten ionic liquid 2.0 g was stirred at 90-100 °C for 2-3 h. The progress of the reaction was monitored by TLC. After completion of the reaction the mixture was poured in to ice cold water, filtered the solid obtained, dried and recrystallized from ethanol.

2.4.4 Conventional procedure for synthesis of 9 and 10

A mixture of 8 (0.1 mmol), chloroacetic acid or 2- bromopropionic acid (0.1 mmol), anhydrous sodium acetate (0.2 mmol), in absolute ethanol (5.0 mL) was heated under reflux for 7–8 h. The reaction mixture was cooled to room temperature and then poured into ice cold water. The solid thus separated was filtered, washed with water and recrystallized from ethanol.
2.4.4.1 \((Z)-2-((E)-(6,7\text{Dihydrobenzofuran-4(5H)}-\text{ylidene})\text{hydrazono})\text{thiazolidin-4-one}\) (9a)

Shining white solid; yield 84 %; mp 168-170 °C. IR (cm\(^{-1}\)): 3117 (NH), 1713 (N-C=O), 1620 (C=N). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 1.96-2.03\) (m, 2H, CH\(_2\)), 2.73-2.80 (m, 4H, 2CH\(_2\)), 3.78 (s, 2H, SCH\(_2\)), 6.73 (d, 1H, CH furan ring, \(J = 1.9\) Hz), 7.3 (d, 1H, CH furan ring, \(J = 2.0\) Hz). \(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 173\) (C=O), 159.6 (C=N), 159.6 (C=N), 142, 141.1, 118.2, 106.5 (C\(_6\)H\(_6\)), 33 (SCH\(_2\)), 25.6 (CH\(_2\)), 23.1 (CH\(_2\)), 22.3 (CH\(_2\)). MS, m/z 250.1 (M+H\(^+\), 100 %). Anal. Calcd. (%) for C\(_{11}\)H\(_{11}\)N\(_3\)SO\(_2\): C, 53.01; H, 4.41; N, 16.86; S, 12.85. Found (%): C, 53.12; H, 4.36; N, 16.78; S, 12.76.

2.4.4.2 \((Z)-2-((E)-(6,7\text{Dihydrobenzo[b]}\text{thiophen-4(5H)}-\text{ylidene})\text{hydrazono})\text{thiazolidin-4-one}\) (9b)

White solid; yield 80 %; mp 192-94 °C. IR (cm\(^{-1}\)): 3134 (NH), 1708 (N-C=O), 1620 (C=N). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 2.16-2.20\) (m, 2H, CH\(_2\)), 2.81-2.85 (m, 4H, CH\(_2\)), 3.94 (s, 2H, SCH\(_2\)), 6.86 (d, 1H, CH thiophene ring, \(J = 2.2\) Hz), 7.39 (d, 1H, CH thiophene ring, \(J = 2.1\) Hz). \(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 168.1\) (C=O), 161 (C=N), 159.5 (C=N), 142, 140.6, 120.3, 110.7 (C\(_6\)H\(_6\)), 38 (SCH\(_2\)), 24.6 (CH\(_2\)), 23.1 (CH\(_2\)), 22.4 (CH\(_2\)). Anal. Calcd. (%) for C\(_{11}\)H\(_{11}\)N\(_3\)OS\(_2\): C, 49.79; H, 4.18; N, 15.84; S, 24.16. Found (%): C, 50.02; H, 4.46; N, 15.98; S, 24.32.

2.4.4.3 \((Z)-2-((E)-(6,7\text{Dihydrobenzofuran-4(5H)}-\text{ylidene})\text{hydrazono})\text{-5-methyl thiazolidin-4-one}\) (10a)

Light yellow solid; yield 82 %; mp 130-32 °C. IR (cm\(^{-1}\)): 3155 (NH), 1697 (N-C=O), 1620 (C=N). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 1.66\) (d, 3H, CH\(_3\), \(J = 7.2\) Hz), 1.95-2.03 (m, 2H, CH\(_2\)), 2.74-2.82 (m, 4H, 2CH\(_2\)), 4.03 (q, 1H, SCH, \(J = 7.2\) Hz), 6.72 (d, 1H, CH furan ring, \(J = 2.0\) Hz), 7.3 (d, 1H, CH furan ring, \(J = 2.0\) Hz). \(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 176.1\) (C=O),
159.6 (C=N), 159.6 (C=N), 142, 118.2, 106.5 (C=H), 42.4 (SCH), 25.6 (CH₃), 23.1 (CH₂),
22.3 (CH₂), 19.2 (CH₂). MS, m/z 264.1 (M+H⁺, 100 %). Anal. Calcd. (%) for C₁₂H₁₃N₃S₂O₂:
C, 54.75; H, 4.94; N, 15.96; S, 12.16. Found (%): C 54.68; H 4.90; N 15.86; S 12.10.

2.4.4.4 (Z)-2-(((E)-(6,7-Dihydrobenzo[b]thiophen-4(5H)-ylidene)hydrazono)-5-methyl
thiazolidin-4-one (10b)

White solid; yield 76 %; mp 168-70 °C. IR (cm⁻¹): 3145 (NH), 1695 (N-C=O), 1615 (C=N).

¹H NMR (400 MHz, CDCl₃): δ 1.69 (d, 3H, CH₃, J = 7.2 Hz), 2.06-2.08 (m, 2H, CH₂), 2.78-
2.81 (m, 4H, 2CH₂), 4.15 (q, 1H, SCH, J = 7.2 Hz), 6.78 (d, 1H, CH thiophene ring, J = 2.1
Hz), 7.35 (d, 1H, CH thiophene ring, J = 2.0 Hz). ¹³C NMR (100 MHz, CDCl₃): δ 173.7
(C=O), 160.5 (C=N), 158.4 (C=N), 144.1, 120.3, 110.5, 44.3 (SCH), 25.9 (CH₃), 24.4 (CH₂),
21.6 (CH₂), 18.2 (CH₂). Anal. Calcd. (%) for C₁₂H₁₃N₃S₂: C, 51.59; H, 4.69; N, 15.04; S,
22.95. Found (%): C, 60.02; H, 4.86; N, 15.21; S, 23.09.

2.4.5 General procedure for synthesis of 11 under grinding conditions

To an equimolar mixture of 8 (0.12 mmol) and p-substituted phenacyl bromide
(0.12 mmol), ionic liquid (2.0 g) is added and the reaction mixture was grinded in
pestle mortar in a solvent free environment for 10–15 min at ambient temperature.
The progress of the reaction was monitored by TLC. After completion of reaction, the
product was extracted by ethyl acetate. The solvent was removed under reduced
pressure to obtain the crude solid. The crude product was recrystallized from ethanol.

2.4.6 Conventional procedure for synthesis of 11

An equimolar mixture of 8 (0.12 mmol) and p-substituted phenacyl bromide
(0.12 mmol) in absolute ethanol (5.0 mL) was heated under reflux for 30 min. Cooled
and the solid thus separated was filtered and washed with ethanol. The crude solid was recrystallized from ethanol.

2.4.6.1 (E)-4-(4-Chlorophenyl)-2-(2-(6,7-dihydrobenzo[4(5H)-ylidene)hydrazinyl])thiazole (11a)

Orange solid; yield 82 %; mp 198-200 °C. IR (cm⁻¹): 3070 (NH), 1612 (C=N), 1489 (C=C), 741 (C-Cl). ¹H NMR (400 MHz, CDCl₃): δ 2.08-2.11 (m, 2H, CH₂) 2.76-2.82 (m, 4H, CH₂), 6.6 (d, 1H, CH furan ring, J = 1.9 Hz), 6.71 (s, 1H, CH of thiazole ring) 7.21 (d, 1H, C₆H₅, J = 7.9 Hz), 7.32 (d, 1H, CH furan ring, J = 2.0 Hz), 7.41 (d, 1H, C₆H₅, J = 1.8 Hz), 7.65 (d, 1H, C₆H₅, J = 2.5 Hz), 7.81 (d, 1H, C₆H₅, J = 6.5 Hz), 13.07 (br, 1H, NH). Anal. Calcd. (%) for C₁₇H₁₄N₃O₃S: C, 59.47; H, 4.08; N, 12.24; S, 9.32. Found (%): C, 59.42; H, 4.04; N, 12.20; S, 9.28.

2.4.6.2 (E)-2-(2-(6,7-Dihydrobenzo[4(5H)-ylidene)hydrazinyl]-4-(4-nitrophenyl)thiazole (11a')

Brown solid; yield 85 %; mp 210-211 °C. IR (cm⁻¹): 3340 (NH), 1651 (C=N), 1504 (C=C), 1558, 1355 (NO₂), 1512 (C=C). ¹H NMR (400 MHz, CDCl₃): δ 2.09-2.12 (m, 2H, CH₂) 2.57 (t, 2H, CH₂, J = 6.5 Hz), 2.78 (t, 2H, CH₂, J = 6.2 Hz), 6.7 (d, 1H, CH furan ring, J = 1.8 Hz), 7.06 (s, 1H, CH thiazole ring) 7.32 (d, 1H, CH furan ring, J = 1.8 Hz), 7.93 (d, 2H, C₆H₅, J = 8.9 Hz), 8.27 (d, 2H, C₆H₅, J = 8.9 Hz). Anal. Calcd. (%) for C₁₇H₁₄N₄O₅S: C, 57.62; H, 3.95; N, 15.81; S, 9.03. Found (%): C, 57.60; H, 3.90; N, 15.78; S, 9.01.

2.4.6.3 (E)-4-(4-Chlorophenyl)-2-(2-(6,7-dihydrobenzo[b]thiophen-4(5H)-ylidene)hydrazinyl)thiazole (11b)

White solid; yield 80 %; mp 210-12 °C. IR (cm⁻¹): 3078 (NH), 1621 (C=N), 1480 (C=C), 736 (C-Cl). ¹H NMR (400 MHz, CDCl₃): δ 2.16-2.18 (m, 2H, CH₂), 2.82-2.84 (m, 4H, 2CH₂), 6.63 (d, 1H, CH thiophene ring, J = 1.9 Hz), 6.76 (s, 1H, CH of thiazole ring) 7.19
(d, 1H, $C_6H_5$, $J= 7.8$ Hz), 7.36 (d, 1H, CH thiophene ring, $J= 2.1$ Hz), 7.47 (d, 1H, $C_6H_5$, $J= 1.9$ Hz), 7.73 (d, 1H, $C_6H_5$, $J= 2.6$ Hz), 7.92 (d, 1H, $C_6H_5$, $J= 6.8$ Hz), 12.9 (br, 1H, NH).

Anal. Calcd. (%) For $C_{17}H_{14}ClN_3S_2$: C, 56.74; H, 3.92; N, 11.68; S, 17.82. Found (%): C, 56.91; H, 4.12; N, 11.92; S, 17.98.

2.4.6.4 (E)-2-(2-[6,7-Dihydrobenzo[b]thiophen-4(5H)-ylidene]hydrazinyl)-4-(4-nitrophenyl)thiazole (11b’)

Shining orange solid; yield 84 %; mp 222-24 °C. IR (cm$^{-1}$): 3328 (NH), 1636 (C=N), 1496 (C=C), 1539, 1346 (NO$_2$). $^1$H NMR (400 MHz, CDCl$_3$): δ 2.06-2.10 (m, 2H, CH$_2$), 2.65 (t, 2H, CH$_2$, $J= 6.7$ Hz), 2.83 (t, 2H, CH$_2$, $J= 6.4$ Hz), 6.77 (d, 1H, CH thiophene ring, $J= 1.9$ Hz), 7.24 (s, 1H, CH thiazole ring), 7.44 (d, 1H, CH thiophene ring, $J= 2.0$ Hz), 7.96 (d, 2H, $C_6H_5$, $J= 8.8$ Hz), 8.23 (d, 2H, $C_6H_5$, $J= 8.6$ Hz). Anal. Calcd. (%) For $C_{17}H_{14}N_4O_2S_2$: C, 55.12; H, 3.81; N, 15.12; S, 17.31. Found (%): C, 55.41; H, 4.09; N, 15.32; S, 17.43.

2.5 2,3-Dihydro-1H-carbazol-4(9H)-ylidene-hydrazono-thiazolidin-4-one (16) and derivatives

2.5.1 2,3-Dihydro-1H-carbazol-4(9H)-one (13)

Compound 13 was obtained from oxidation of tetrahydrocarbazole 12 with DDQ in wet dioxane by the reported procedure [Kunihide and Kameji, 1978].

White crystals; yield 62 %; mp 216-18 °C [Literature (Kunihide and Kameji, 1978) mp 219-21 °C]. IR (cm$^{-1}$): 1690 (C=O). $^1$H NMR (400 MHz, DMSO-d$_6$): δ 2.18-2.23 (m, 2H, CH$_2$), 2.51 (t, 2H, CH$_2$, $J= 6.2$ Hz), 2.98 (t, 2H, CH$_2$, $J= 6.0$ Hz), 7.13-7.16 (m, 2H, ArH), 7.35-7.37 (m, 1H, ArH), 8.05- 8.07 (m, 1H, ArH), 11.4 (br, 1H, NH). $^{13}$C NMR (100 MHz, DMSO d$_6$): δ 193.3 (C=O), 135.7, 124.3, 122.1, 121.2, 111.9, 110.9 (ArC), 40.2 (CH$_2$),
37.7 (CH$_2$), 22.8 (CH$_2$). MS, m/z 186.1 (M+H$^+$, 100 %). Anal. Calcd. (%) for C$_{12}$H$_{11}$NO: C, 78.39; H, 6.53; N, 7.03. Found (%): C, 78.29; H, 6.49; N, 6.92.

2.5.2 General procedure for synthesis of 14

A mixture of 13 (1.0 mmol) and DMF-DMA (10 mmol) in DMF (5.0 mL) was refluxed for 1 h. The reaction mixture was cooled and extracted with ethyl acetate (2X25 mL). The organic layer was separated and washed with brine solution. The organic layer was dried over anhydrous Na$_2$SO$_4$. The solvent was removed under reduced pressure and the solid obtained was recrystallized from ethanol.

2.5.2.1 9-Methyl-2,3-dihydro-1H-carbazol-4(9H)-one (14)

White needles; yield 71 %; mp 190-92 °C. IR (cm$^{-1}$): 1695 (C=O). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 2.25 (t, 2H, CH$_2$, $J$ = 6.2 Hz), 2.57 (t, 2H, CH$_2$, $J$ = 6.0 Hz), 2.92 (t, 2H, CH$_2$, $J$ = 6.2 Hz), 3.7 (s, 3H, NCH$_3$), 7.27-7.30 (m, 3H, Ph), 8.24-8.26 (m, 1H, Ph). Anal. Calcd. (%) for C$_{13}$H$_{13}$NO: C, 78.39; H, 6.53; N, 7.03. Found (%): C, 78.29; H, 6.49; N, 6.92.

2.5.3 General procedure for synthesis of 15

A mixture of 14 (0.16 g, 0.825 mol), thiosemicarbazide (0.075 g, 0.825 mol) and conc. HCl (0.4 mL) in ethanol (10 mL) was stirred at room temperature for 3 h. The reaction mixture was poured into ice cold water. The solid obtained was filtered, dried and recrystallized from ethanol.

2.5.3.1 2-(2,3-Dihydro-1H-carbazol-4(9H)-ylidene)hydrazinecarbothioamide (15a)

White crystals; yield 81 %; mp 185-86 °C. IR (cm$^{-1}$): 3240, 3178 (NH), 1574 (C=N), 1504 (C=C), 1273 (C=S). $^1$H NMR (400 MHz, DMSO-d$_6$): $\delta$ 2.18-2.23 (m, 2H, CH$_2$), 2.51 (t, 2H, CH$_2$, $J$ = 6.5 Hz), 2.98 (t, 2H, CH$_2$, $J$ = 6.0 Hz), 7.10-7.18 (m, 2H, ArH), 7.33-7.37 (m, 1H, ArH), 8.05-8.07 (m, 1H, ArH), 9.59 (br, 1H, NH), 11.0 (br, 1H, NH), 11.38 (br, 1H, NH).
Anal. Calcd. (%) for C$_{13}$H$_{14}$N$_{4}$S: C, 60.46; H, 5.42; N, 21.70; S, 12.40. Found (%): C, 60.42; H, 5.36; N, 21.61; S, 12.28.

2.5.3.2 2-(9-Methyl-2,3-dihydro-1H-carbazol-4(9H)-ylidene)hydrazinecarbothioamide (15b)
White crystals; yield 81%; mp 190-92 °C. IR (cm$^{-1}$): 3240, 3178 (NH), 1574 (C=N), 1504 (C=C), 1273 (C=S). $^1$H NMR (400 MHz, DMSO-d$_6$): δ 2.05 (t, 2H, CH$_2$, J = 6.3 Hz), 2.72 (t, 2H, CH$_2$, J = 6.2 Hz), 2.88 (t, 2H, CH$_2$, J = 6.1 Hz), 3.7 (s, 3H, NCH$_3$), 7.11-7.24 (m, 3H, Ph), 7.40 (d, 1H, Ph, J = 7.9 Hz), 8.07 (br, 2H, NH$_2$), 10.1 (br, 1H, NH). Anal. Calcd. (%) for C$_{14}$H$_{16}$N$_{4}$S: C, 61.76; H, 5.88; N, 20.58; S, 11.76. Found (%): C, 61.69; H, 5.76; N, 20.51; S, 11.71.

2.5.4 Solvent free general procedure for synthesis of 16
An equimolar mixture of 15 (0.025 mol) and chloroacetic acid or 2-bromopropionic acid (0.025 mol) in premolten ionic liquid 2.0 g was stirred at 100 °C for 1-2 h. The reaction was monitored by TLC, poured in to ice cold water, filtered the solid obtained, dried and recrystallized from ethanol.

2.5.5 Conventional procedure for synthesis of 16
A mixture of 15 (0.625 mmol), chloroacetic acid or 2-bromopropionic acid (0.625 mmol) and anhydrous sodium acetate (1.25 mmol) in absolute ethanol (5.0 mL) was refluxed on water bath for 7-8 h. The progress of the reaction was monitored by TLC. The solvent was removed under reduced pressure. The solid thus obtained was recrystallized from ethanol.

2.5.6 DCC mediated general procedure for the synthesis of 16
A mixture of thiosemicarbazone 15 (1.0 mmol), chloroacetic acid / 2-bromopropionic acid (1.0 mmol) in THF (15 mL) was stirred at 0 °C for 5 min. and then
DCC (1.2 mmol) was added to the reaction mixture at 0 °C and reaction mixture was stirred for additional 50 min. at room temp. The progress of the reaction was monitored by TLC. Dicyclohexyl urea (DCU) was removed by filtration and the filtrate was concentrated to dryness under reduced pressure and the residue was extracted in ethyl acetate. The organic layer was successively washed with 10 % aq. citric acid, water, 10 % aq. sodium hydrogen carbonate and then finally with brine. The organic layer was dried over sodium sulphate and solvent was removed under reduced pressure to get a crude product, which was recrystallized from ethanol.

2.5.6.1 \((Z)-2-((E)-(2,3-Dihydro-1H-carbazol-4(9H)-ylidene)hydrazono)thiazolidin-4-one\) (16a)

White crystalline powder; yield 85 %; mp >250 °C. IR (cm\(^{-1}\)): 3364 (NH), 1713 (N-C=O), 1589 (C=N). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \(\delta\) 2.04 (t, 2H, CH\(_2\), \(J= 6.2\) Hz), 2.88-2.92 (m, 4H, CH\(_2\)), 3.75 (s, 2H, SCH\(_2\)), 7.10-7.12 (m, 2H, ArH), 7.31-7.34 (m, 1H, ArH), 8.19-8.21 (m, 1H, ArH), 10.95 (br, 1H, NH), 11.61 (br, 1H, NH). \(^13\)C NMR (100 MHz, DMSO-d\(_6\)): \(\delta\) 176 (C=O), 160 (C=N), 159.6 (C=N), 135, 128.1, 121.2, 119.5, 118, 111 (ArC), 36 (SCH\(_2\)), 31 (CH\(_2\)), 25 (CH\(_2\)), 23 (CH\(_2\)). MS, m/z 299.1 (M+H\(^+\), 100 %). Anal. Calcd. (%) for C\(_{15}\)H\(_{14}\)N\(_4\)SO: C, 60.40; H, 4.69; N, 18.79; S, 10.73. Found (%): C, 60.28; H, 4.65; N, 18.68; S, 10.68.

2.5.6.2 \((Z)-2-((E)-(2,3-Dihydro-1H-carbazol-4(9H)-ylidene)hydrazono)-5-methyl thiazolidin-4-one\) (16b)

Light yellow crystals; yield 83 %; mp 232-34 °C. IR (cm\(^{-1}\)): 3286 (NH), 3286 (NH), 1705 (N-C=O), 1612 (C=N). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \(\delta\) 1.57 (d, 3H, CH\(_2\), \(J= 7.2\) Hz), 1.98-2.05 (m, 2H, CH\(_2\)), 2.52-2.54 (m, 2H, CH\(_2\)), 2.84-2.89 (m, 2H, CH\(_2\)), 4.05 (q, 1H, SCH, \(J= 7.2\) Hz), 7.06-7.12 (m, 2H, ArH), 7.30-7.33 (m, 1H, ArH), 8.13-8.16 (m, 1H, ArH), 11.27 (br, 1H, NH). \(^13\)C NMR (100 MHz, DMSO-d\(_6\)): \(\delta\) 176 (C=O), 160 (C=N), 159.4 (C=N), 136, 126,
121, 119, 118, 111 (ArC), 31 (CH₃), 25 (CH₂), 24.5 (CH₂), 23 (CH₂). MS, m/z 313.1 (M+H⁺, 100 %). Anal. Calcd. (%) for C₁₆H₁₆N₄SO: C, 61.53; H, 5.12; N, 17.94; S, 10.25. Found (%): C, 61.42; H, 5.06; N, 17.88; S, 10.21.

2.5.6.3 (Z)-2-((E)-(9-Methyl-2,3-dihydro-1H-carbazol-4(9H)-ylidene)hydrazono) thiazolidin-4-one (16c)

Green crystals; yield 65 %; mp 226-28 °C. IR (cm⁻¹): 1697 (C=O), 1605 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 2.03 (t, 2H, CH₂, J = 6.1 Hz), 2.85-2.93 (m, 4H, 2CH₂), 3.71 (s, 3H, NCH₃), 3.78 (s, 2H, SCH₂), 7.11-7.20 (m, 2H, Ph), 7.38 (d, 1H, Ph, J = 7.8 Hz), 8.21 (d, 1H, Ph, J = 7.3 Hz), 11.7 (br, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆): δ 176 (C=O), 160 (C=N), 159.4 (C=N), 136, 126, 121, 119, 118, 111 (C₆H₆), 31 (CH₃), 25 (CH₂), 24.5 (CH₂), 23 (CH₂). MS, m/z 313.1 (M+H⁺, 100 %). Anal. Calcd. (%) for C₁₆H₁₆N₄SO: C, 61.53; H, 5.12; N, 17.94; S, 10.25. Found (%): C, 61.42; H, 5.06; N, 17.88; S, 10.21.

2.5.6.4 (Z)-5-Methyl-2-((E)-(9-methyl-2,3-dihydro-1H-carbazol-4(9H)-ylidene)hydrazono) thiazolidin-4-one (16d)

Yellow crystals; yield 68 %; mp 208-10 °C. IR (cm⁻¹): 1720 (C=O), 1620 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 1.56 (d, 3H, CH₃, J = 7.2 Hz), 2.03 (t, 2H, CH₂, J = 6.1 Hz), 2.83-2.91 (m, 4H, 2CH₂), 3.68 (s, 3H, NCH₃), 4.07 (q, 1H, Hₐ, J = 7.1 Hz, J = 7.2 Hz), 7.12-7.20 (m, 2H, Ph), 7.38 (d, 1H, Ph, J = 7.5 Hz), 8.19 (t, 1H, Ph, J = 6.9 Hz), 11.6 (br, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆): δ 176.5 (C=O), 162 (C=N), 159.6 (C=N), 145.1, 137.2, 124.1, 121.8, 121.6, 120.6, 109.1, 108.5, 41.7, 35.8, 30.7, 29.2, 25.6, 22.2, 21.4, 19. MS, m/z 327.1 (M+H⁺, 100 %). Anal. Calcd. (%) for C₁₇H₁₈N₄SO: C, 62.57; H, 5.52; N, 17.17; S, 9.81. Found (%): C, 62.52; H, 5.44; N, 17.08; S, 9.70.
2.5.7 Solvent free synthesis of 17

A mixture of 15 (2.5 mmol) and phenacyl bromide (2.5 mmol) was grinded in a pestle mortar for 5-10 min. The reaction was monitored by TLC. The residue was extracted with ethyl acetate. After removal of solvent under reduced pressure the solid obtained was recrystallized from ethanol-DMF (3:1) mixture.

2.5.8 Conventional procedure for synthesis of 17

An equimolar mixture of 15 (2.5 mmol) and phenacyl bromide (2.5 mmol) in absolute ethanol (5.0 mL) was heated under reflux for 20 min. The reaction mixture was cooled and the solid thus separated was filtered and washed with ethanol. The crude solid was recrystallized from ethanol-DMF (3:1) mixture.

2.5.8.1 (E)-2-(2-(2,3-Dihydro-1H-carbazol-4(9H)-ylidene)hydrazinyl)-4-phenylthiazole (17a)

Brown solid; yield 80 %; mp > 250 °C. IR (cm⁻¹): 3110 (NH), 1597 (C=N), 1490 (C=C). ¹H NMR (400 MHz, DMSO-d₆): δ 2.08-2.12 (m, 2H, CH₂), 2.79 (t, 2H, CH₂, J = 7.1 Hz), 2.89 (t, 2H, CH₂, J = 6.1 Hz), 7.12 (s, 1H, =CH of thiazole ring), 7.18-7.20 (m, 2H, ArH), 7.37-7.38 (m, 4H, ArH), 7.47 (d, 2H, ArH, J = 7.9 Hz), 7.75 (br, 1H, NH), 8.08 (d, 1H, ArH, J = 3.4 Hz), 11.09 (br, 1H, NH). Anal. Calcd. (%) for C₂₁H₁₈N₄S: C, 70.36; H, 5.06; N, 15.63; S, 8.95. Found (%): C, 70.59; H, 5.22; N, 15.90; S, 9.10.

2.5.8.2 (E)-4-(4-Chlorophenyl)-2-(2-(2,3-dihydro-1H-carbazol-4(9H)-ylidene)hydrazinyl) thiazol (17b)

Yellow solid; yield 88 %; mp 222-24 °C. IR (cm⁻¹): 3112 (NH), 1601 (C=N), 1494 (C=C), 728 (C-Cl). ¹H NMR (400 MHz, DMSO-d₆): δ 2.16-2.19 (m, 2H, CH₂), 2.91 (t, 2H, CH₂, J = 7.0 Hz), 2.93 (t, 2H, CH₂, J = 5.9 Hz), 7.15 (s, 1H, =CH of thiazole ring), 7.18-7.20 (m, 2H, ArH), 7.37-7.39 (m, 1H, ArH), 7.46 (d, 2H, ArH, J = 8.4 Hz), 7.74 (br, 1H, NH), 8.08 (d,
1H, ArH, J = 3.2 Hz), 11.26 (br, 1H, NH). Anal. Calcd. (%) for C_{21}H_{17}N_{4}SCl: C, 64.20; H, 4.36; N, 14.26; S, 8.16. Found (%): C, 64.09; H, 4.32; N, 14.20; S, 8.10.

2.5.8.3 (E)-2-(2-(2,3-Dihydro-1H-carbazol-4(9H)-ylidene)hydrazinyl)-4-(4-nitrophenyl) thiazol (17c)

Light brown solid; yield 90 %; mp 232-34 °C. IR (cm⁻¹): 3342 (NH), 1641 (C=N), 1494 (C=C), 1558, 1328 (NO₂), 1509 (C=C). ¹H NMR (400 MHz, DMSO-d₆): δ 2.16-2.17 (m, 2H, CH₂), 2.93 (t, 2H, CH₂, J = 5.8 Hz), 2.98 (t, 2H, CH₂, J = 5.7 Hz), 7.14-7.20 (m, 2H, ArH), 7.32-7.42 (m, 2H, ArH), 8.01-8.05 (m, 2H, ArH), 8.15-8.17 (m, 1H, ArH), 8.27-8.34 (m, 1H, ArH), 11.35 (br, 1H, NH). MS, m/z 404.2 (M+H⁺, 100 %). Anal. Calcd. (%) for C_{21}H_{17}N_{4}SO₂: C, 62.52; H, 4.25; N, 17.36; S, 7.96. Found (%): C, 62.56; H, 4.21; N, 17.30; S, 7.92.

2.5.8.4 (E)-2-(2-(9-Methyl-2,3-dihydro-1H-carbazol-4(9H)-ylidene)hydrazinyl)-4-phenyl thiazole (17d)

Brown solid; yield 78 %; mp >250 °C. IR (cm⁻¹): 3112 (NH), 1601 (C=N), 1494 (C=C). ¹H NMR (400 MHz, DMSO-d₆): δ 2.13 (t, 2H, CH₂, J = 6.2 Hz), 2.81 (t, 2H, CH₂, J = 6.2 Hz), 3.11 (t, 2H, CH₂, J = 6.3 Hz), 3.75 (s, 3H, NCH₃), 7.16-7.62 (m, 5H, Ph), 8.14-8.45 (m, 4H, Ph). Anal. Calcd. (%) for C_{22}H_{20}N₄S: C, 70.96; H, 5.37; N, 15.05; S, 8.60. Found (%): C, 70.89; H, 5.31; N, 14.98; S, 8.49.

2.5.8.5 (E)-4-(4-Chlorophenyl)-2-(2-(9-methyl-2,3-dihydro-1H-carbazol-4(9H)-ylidene) hydrazinyl)thiazole (17e)

Grey solid; yield 75 %; mp 218-20 °C. IR (cm⁻¹): 3112 (NH), 1601 (C=N), 1494 (C=C), 728 (C-Cl). ¹H NMR (400 MHz, DMSO-d₆): δ 2.13 (d, 2H, CH₂, J = 6.1 Hz), 2.88-3.12 (m, 4H, 2CH₂), 3.74 (s, 3H, NCH₃), 7.11-7.78 (m, 5H, Ph), 7.92-8.36 (m, 4H, Ph). Anal. Calcd. (%)
for C$_{22}$H$_{19}$N$_4$S$_2$: C, 65.02; H, 4.67; N, 13.79; S, 7.88. Found (%): C, 64.95; H, 4.58; N, 13.71; S, 7.79.

2.5.8.6 (E)-2-(2-(9-Methyl-2,3-dihydro-1H-carbazol-4(9H)-ylidene)hydrazinyl)-4-(4-nitrophenyl)thiazole (17f)

Yellow solid; yield 71 %; mp >250 °C. IR (cm$^{-1}$): 3342 (NH), 1641 (C=N), 1494 (C=C), 1558, 1328 (NO$_2$). $^1$H NMR (400 MHz, DMSO-d$_6$): δ 2.11 (d, 2H, CH$_2$, J = 6.3 Hz), 2.94-3.01 (m, 4H, 2CH$_2$), 3.76 (s, 3H, NCH$_3$), 6.86-7.42 (m, 4H, Ph), 7.80-8.52 (m, 5H, Ph).

An. Calcd. (%) for C$_{22}$H$_{19}$N$_5$SO$_2$: C, 63.30; H, 4.55; N, 16.78; S, 7.67. Found (%): C, 63.25; H, 4.48; N, 16.71; S, 7.59.

2.5.9 General procedure for the synthesis of 18

An equimolar mixture of 15b (0.001 mol) and ethyl bromo pyruvate (0.001 mol) in ethanol (5.0 mL) was stirred at room temperature for 1h. The solid obtained was filtered, dried and recrystallized from ethanol.

2.5.9.1 Ethyl(E)-2-(2-(9-methyl-1,2,3,9-tetrahydro-4H-carbazol-4-ylidene)hydrazinyl)thiazole-4-carboxylate (18)

Green solid; yield 64 %; mp 198-200 °C. IR (cm$^{-1}$): 1720 (C=O), 1612 (C=N). $^1$H NMR (400 MHz, DMSO-d$_6$): δ 1.31 (t, 3H, CH$_3$, J = 7.1 Hz), 2.04-2.07 (m, 2H, CH$_2$), 2.69 (t, 2H, CH$_2$, J = 6.2 Hz), 2.88 (t, 2H, CH$_2$, J = 6.2 Hz), 3.7 (s, 3H, N-CH$_3$), 4.25 (q, 2H, CH$_2$, J = 7.1 Hz), 7.13-7.21 (m, 2H, Ph), 7.36 (s, 1H, CH of thiazole ring), 7.43 (d, 1H, Ph, J = 7.3 Hz), 8.18 (d, 1H, Ph, J = 5.5 Hz), 11.16 (br, 1H, NH). An. Calcd. (%) for C$_{19}$H$_{20}$N$_4$O$_2$: C, 61.94; H, 5.47; N, 15.21; S, 8.70. Found (%): C, 62.12; H, 5.64; N, 15.38; S, 8.91.
2.5.10 General procedure for the synthesis of 20

A mixture of 15b (0.001 mol) and dimethylacetylene dicarboxylate DMAD (0.001 mol) in water (10 mL) was stirred at room temperature for 30 minutes. The solid obtained was filtered, dried and recrystallized from ethanol.

2.5.10.1 Dimethyl(\(E\))-4-(((2Z,5Z)-5-(2-methoxy-2-oxoethylidene)-4-oxothiazolidin-2-ylidene)hydrazono)-9-methyl-1,2,3,4-tetrahydro-9H-4a,9a-ethenocarbazole-10,11-dicarboxylate (20)

Light orange solid; yield 62 %; mp 182-184 °C. IR (cm\(^{-1}\)): 1724 (C=O), 1689 (C=O), 1630 (C=N). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): δ 2.01 (t, 2H, CH\(_2\), J= 6.2 Hz), 2.74-2.76 (m, 2H, CH\(_2\)), 2.92 (t, 2H, CH\(_2\), J= 6.0 Hz), 3.69 (s, 3H, CH\(_3\)), 3.73 (s, 3H, CH\(_3\)), 3.85 (s, 3H, CH\(_3\)), 3.86 (s, 3H, CH\(_3\)), 6.87 (s, 1H, =CH), 7.23-7.26 (m, 2H, Ph), 7.48-7.50 (m, 1H, Ph), 8.13-8.16 (m, 1H, Ph). MS, m/z 525.5 (M+H\(^+\), 100 %). Anal. Calcd. (%) for C\(_{25}\)H\(_{24}\)N\(_4\)O\(_7\)S: C, 57.24; H, 4.61; N, 10.68; S, 6.11. Found (%): C, 57.42; H, 4.86; N, 10.88; S, 6.32.

2.6 3,3a,4,5-Tetrahydro-2H-benzo[g]indazol-2-yl-thiazol-4(5H)-one (25)

2.6.1 General procedure for synthesis of 22

Compound 22 was prepared by refluxing a mixture of 1-tetralone and aromatic aldehyde in aq. NaOH by the reported procedure [Pal et al., 1994].

2.6.1.1 (\(E\))-2-Benzylidene-3,4-dihyronaphthalen-1(2H)-one (22a)

Greyish white solid; yield 82 %; mp 103-105 °C. [Pal et al., 1994, mp 105 °C].

2.6.1.2 (\(E\))-2-(4-Chlorobenzylidene)-3,4-dihyronaphthalen-1(2H)-one (22b)

White solid; yield 86 %; mp 128-32 °C. [Pal et al., 1994, mp 134 °C].

2.6.1.3 (\(E\))-2-Benzylidene-6-methoxy-3,4-dihyronaphthalen-1(2H)-one (22c)

Light brown solid; yield 88 %; mp 100-02 °C. IR (cm\(^{-1}\)): 1712 (C=O). \(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 2.91 (t, 2H, CH\(_2\), J= 6.7 Hz), 3.1 (t, 2H, CH\(_2\), J= 6.8 Hz), 3.87 (s, 3H, OCH\(_3\)), 6.7
(d, 1H, Ar-H, J= 2.4 Hz), 6.86-6.89 (m, 1H, Ar-H), 7.34-7.42 (m, 5H, Ar-H), 7.83 (s, 1H, =CH), 8.12 (d, 1H, Ar-H, J= 8.7 Hz).

2.6.1.4  (E)-2-(4-Chlorobenzylidene)-6-methoxy-3,4-dihyronaphthalen-1(2H)-one (22d)
White solid; yield 90 %; mp 125-27 °C. IR (cm$^{-1}$): 1715 (C=O). $^1$H NMR (400 MHz, DMSO-d$_6$): δ 2.96 (t, 2H, CH$_2$, J= 6.8 Hz), 3.11 (t, 2H, CH$_2$, J = 6.9 Hz), 3.9 (s, 3H, OCH$_3$), 6.88-6.9 (m, 1H, Ar-H), 7.38-7.44 (m, 5H, Ar-H), 7.86 (s, 1H, =CH), 8.15 (d, 1H, Ar-H, J= 7.8 Hz).

2.6.2 General procedure for synthesis of 23
To a solution of 2-arylidene-3,4-dihyronaphthalen-1(2H)-ones 22 (1.0 mol) and semicarbazide or thiosemicarbazide (1.0 mol) in absolute ethanol (20 mL), 1.0 g of KOH was added and the reaction mixture was heated at 70-80 °C for 3-4 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the volume of the reaction mixture was reduced to half and kept overnight. The solid obtained was filtered and washed with ice cold ethanol. Recrystallization from 95 % ethanol furnished a pure mixture of two diastereoisomers. The mixture (23a and 24a) was separated by preparative TLC using Pet. ether: ethyl acetate (4:1) as eluent. Compound 23b-e was obtained in pure state by recrystallization from ethanol.

2.6.2.1  (3S,3aS)-3-Phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carboxamide (23a)
White solid; yield 55 %; mp 238-40 °C. IR (cm$^{-1}$): 3483, 3276, 3215 (NH), 1684 (C=O), 1571 (C=N). $^1$H NMR (400 MHz, DMSO-d$_6$): δ 0.81-0.85 (m, 1H, CH$_2$), 1.72-1.76 (m, 1H, CH$_2$), 2.87-2.92 (m, 1H, CH$_2$), 3.15-3.19 (m, 1H, CH$_2$), 3.72-3.75 (m, 1H, H-3a), 5.51 (d, 1H, H-3, J= 10.9 Hz), 6.48 (br, 2H, NH$_2$), 7.1 (d, 2H, C$_6$H$_5$, J= 7.1 Hz), 7.17-7.33 (m, 6H,
C₆H₃), 7.98-8.0 (m, 1H, C₆H₅). ¹³C NMR (100 MHz, DMSO-d₆): δ 154.6, 151.6, 139.1, 138.3, 129.8, 128.2, 127.3, 126.4, 125.7, 124.2, 62.8, 61.2, 60.6, 48.1, 28.5, 23.5, 15.3. MS, m/z 292.2 (M+H⁺, 80 %). Anal. Calcd. (%) for C₁₈H₁₇N₃O: C, 74.20; H, 5.88; N, 14.42. Found (%): C, 74.36; H, 5.97; N, 14.68.

2.6.2.2 (3S,3aS)-3-Phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carbothioamide (23b)
Light yellow crystals; yield 65 %; mp 208-210 °C. IR (cm⁻¹): 3443, 3263, 3144 (NH), 1590 (C=N), 1347 (C=S). ¹H NMR (400 MHz, DMSO-d₆): δ 0.8-0.91 (m, 1H, CH₂), 1.78-1.82 (m, 1H, CH₂), 2.78-2.94 (m, 2H, CH₂), 3.73-3.80 (m, 1H, H-3a), 6.06 (d, 1H, H-3, J= 10.6 Hz), 7.02 (d, 2H, C₆H₅, J= 7.2 Hz), 7.16-7.35 (m, 6H, C₆H₅), 7.49 (br, 1H, NH₂), 7.81 (br, 1H, NH₂), 8.07 (d, 1H, C₆H₅, J= 7.6 Hz). ¹³C NMR (100 MHz, DMSO-d₆): δ 178.4, 175.4, 156.1, 155.1, 143.4, 139.8, 137.4, 130.6, 128.9, 125.9, 124.8, 69.6, 48.2, 28.6, 27.5, 23.7, 18.3. MS, m/z 308.1 (M+H⁺, 40 %), 330.1 (M+Na⁺, 100 %). Anal. Calcd. (%) for C₁₈H₁₇N₃S: C, 70.33; H, 5.57; N, 13.67; S, 10.43. Found (%): C, 70.58; H, 5.77; N, 13.87; S, 10.67.

2.6.2.3 (3S,3aS)-3-(4-Chlorophenyl)-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carbothioamide (23c)
Yellow solid; yield 62 %; mp 178-80 °C. IR (cm⁻¹): 3435, 3263, 3119 (NH), 1598 (C=N), 1246 (C=S). ¹H NMR (400 MHz, DMSO-d₆): δ 0.81-0.85 (m, 1H, CH₂), 1.78-1.82 (m, 1H, CH₂), 2.82-2.93 (m, 2H, CH₂), 3.76-3.83 (m, 1H, H-3a), 6.04 (d, 1H, H-3, J= 10.7 Hz), 7.02 (d, 2H, C₆H₅, J= 7.7 Hz), 7.17-7.66 (m, 4H, C₆H₅), 7.94 (br, 1H, NH₂), 8.03 (br, 1H, NH₂), 8.07 (d, 2H, C₆H₅, J= 7.6 Hz). ¹³C NMR (100 MHz, DMSO-d₆): δ 175.4, 156, 155, 142.3, 139.8, 136.5, 131.8, 130.6, 128.9, 127.5, 126.5, 124.8, 69.0, 65.7, 48.1, 28.6, 27.3, 23.8. MS, m/z 342.1 (M+H⁺, 35Cl, 100 %), 344.1 (MH+2, 37Cl, 35 %). Anal. Calcd. (%) for
C_{18}H_{16}ClN_{3}S: C, 63.24; H, 4.72; N, 12.29; S, 9.38. Found (%): C, 63.46; H, 4.82; N, 12.54; S, 9.49.

2.6.2.4 (3S,3aS)-7-Methoxy-3-phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carbothioamide (23d)

Light brown solid; yield 72%; mp 160-62 °C. IR (cm⁻¹): 3470, 3204, 3146 (NH), 1590 (C=N), 1250 (C=S). ¹H NMR (400 MHz, DMSO-d₆): δ 0.81-0.86 (m, 1H, CH₂), 1.77-1.80 (m, 1H, CH₂), 2.54-2.56 (m, 2H, CH₂), 3.69-3.75 (m, 1H, H-3a), 3.79 (s, 3H, OCH₃), 6.03 (d, 1H, H-3, J= 10.5 Hz), 6.69 (d, 1H, C₆H₅, J= 2.3 Hz), 6.79-6.90 (m, 1H, C₆H₅), 7.02 (d, 2H, C₆H₅, J= 7.2 Hz), 7.19-7.29 (m, 3H, C₆H₅), 7.44 (br, 1H, NH₂), 7.7 (br, 1H, NH₂), 7.98 (d, 1H, C₆H₅, J= 2.9 Hz). ¹³C NMR (DMSO-d₆): δ 178.3, 161.2, 156.2, 147.8, 142, 137.5, 128.2, 126.8, 125.7, 124.4, 119.1, 113.4, 69.4, 66.1, 55, 48.3, 29.2, 25.6, 21.3. MS, m/z 338.1 (M+H⁺, 100%). Anal. Calcd. (%) for C_{19}H_{18}N_{3}S: C, 67.63; H, 5.68; N, 12.45; S, 9.50. Found (%): C, 67.91; H, 5.79; N, 12.68; S, 9.63.

2.6.2.5 (3S,3aS)-3-(4-Chlorophenyl)-7-methoxy-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carbothioamide (23e)

White solid; yield 68%; mp 182-84 °C. IR (cm⁻¹): 3441, 3215, 3125 (NH), 1602 (C=N), 1276 (C=S). ¹H NMR (400 MHz, DMSO-d₆): δ 0.77-0.86 (m, 1H, CH₂), 1.76-1.79 (m, 1H, CH₂), 2.75-2.91 (m, 2H, CH₂), 3.70-3.78 (m, 1H, H-3a), 3.80 (s, 3H, OCH₃), 6.01 (d, 1H, H-3, J= 10.6 Hz), 6.71-6.76 (m, 1H, C₆H₅), 6.83-6.86 (m, 1H, C₆H₅), 7.01 (d, 2H, C₆H₄, J= 7.8 Hz), 7.24-7.33 (m, 2H, C₆H₅), 7.54 (br, 1H, NH₂), 7.91 (br, 1H, NH₂), 7.98 (d, 1H, C₆H₄, J= 3.7 Hz). ¹³C NMR (100 MHz, DMSO-d₆): δ 175, 161.3, 156.1, 142, 136.5, 131.8, 128.1, 127.5, 126.6, 119, 113.5, 112.7, 65.5, 48.2, 28.9, 23.8. MS, m/z 372.1 (M+H⁺, 35Cl, 100%), 374.1 (MH+2, 37Cl, 38%). Anal. Calcd. (%) for C_{19}H_{18}ClN_{3}OS: C, 61.36; H, 4.88; N, 11.30; S, 8.62. Found (%): C, 61.68; H, 4.98; N, 11.58; S, 8.76.
2.6.2.6 (3R,3aS)-3-Phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carboxamide (24a)

White solid; yield 46%; mp >250 °C. IR (cm⁻¹): 3476, 3248, 3205 (NH), 1668 (C=O), 1580 (C=N). ¹H NMR (400 MHz, DMSO-d₆): 1.89-1.93 (m, 1H, CH₂), 2.13-2.16 (m, 1H, CH₂), 2.87-2.92 (m, 2H, CH₂), 3.12-3.19 (m, 1H, H-3a), 4.8 (d, 1H, H-3, J= 11.1 Hz), 6.51 (br, 2H, NH₂), 7.23-7.37 (m, 8H, C₆H₅), 7.90-7.92 (m, 1H, C₆H₅). ¹³C NMR (100 MHz, DMSO-d₆): δ 162.1, 156.9, 152.1, 143, 139.3, 129.1, 128.3, 127.1, 125.8, 124.2, 99.5, 67.8, 61.1, 55.1, 15. MS, m/z 292.2 (M+H⁺, 88%), 314.2 (M+Na⁺, 100%). Anal. Calcd. (%) for C₁₈H₁₇N₃O: C, 74.20; H, 5.88; N, 14.42. Found (%): C, 74.36; H, 5.92; N, 14.68.

2.6.3 General procedure for the synthesis of 25(a-h)

An equimolar mixture of 23b-e (0.001 mol), chloroacetic acid or 2-bromopropionic acid (0.001 mol) and anhydrous sodium acetate (0.16 g, 0.002 mol) in ethanol (10 mL) was heated under reflux for 4-5 h. The progress of the reaction was monitored by TLC. After completion of the reaction volume of the reaction mixture was reduced to half under vacuum and kept overnight. The solid, thus obtained was filtered, dried and recrystallized from ethanol-DMF mixture (3:1).

2.6.3.1 2-[[3S,3aS]-3-Phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]thiazol-4(5H)-one (25a)

Yellow crystalline solid; yield 64%; mp 258-60 °C. IR (cm⁻¹): 1697 (C=O), 1597 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 0.90-0.94 (m, 1H, CH₂), 1.80-1.84 (m, 1H, CH₂), 2.79-3.01 (m, 2H, CH₂), 3.88 (s, 2H, SCH₂), 3.95-4.02 (m, 1H, H-3a), 5.93 (d, 1H, H-3, J= 10.5 Hz), 7.07 (d, 2H, C₆H₅, J= 7.1 Hz), 7.25-7.43 (m, 6H, C₆H₅), 8.03 (dd, 1H, C₆H₅, J= 6.6 Hz, J= 1.0 Hz). ¹³C NMR (100 MHz, DMSO-d₆): δ 186.5 (C=N), 180.7 (C=O), 177.1 (C=N), 161.1, 140.3, 135.3, 135.1, 131.5, 129, 128.5, 127.7, 126.6, 125.7, 125.1, 66.8, 49.2, 28.5,
23.7. MS, m/z 348.1 (M+H\(^+\), 54 %), 370.1 (M+Na\(^+\), 100 %). Anal. Calcd. (%) for C\(_{20}\)H\(_{17}\)N\(_3\)SO: C, 69.14; H, 4.93; N, 12.09; S, 9.23. Found (%): C, 69.04; H, 4.89; N, 11.98; S, 9.12.

2.6.3.2 5-Methyl-2-[[3S,3aS]-3-phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]thiazol-4(5H)-one (25b)

White solid; yield 62 %; mp 218-220 °C. IR (cm\(^{-1}\)): 1705 (C=O), 1594 (C=N). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): δ 0.82-0.88 (m, 1H, CH\(_2\)), 1.5 (d, 3H, CH\(_3\), J= 7.2 Hz), 1.79 (m, 1H, CH\(_2\)), 2.82-2.91 (m, 2H, CH\(_2\)), 3.97-4.05 (m, 1H, H-3a), 4.14 (q, 1H, SCHCH\(_3\), J= 7.1 Hz), 5.94 (d, 1H, H-3, J= 10.8 Hz), 7.07 (d, 2H, C\(_6\)H\(_5\), J= 7.4 Hz), 7.24-7.45 (m, 6H, C\(_6\)H\(_5\)), 7.99 (d, 1H, C\(_6\)H\(_5\), J= 7.0 Hz). \(^1\)C NMR (100 MHz, DMSO-d\(_6\)): δ 189.3 (C=O), 175.4, 160.9 (C=N), 140.5, 135.5, 131.6, 129.1, 128.6, 127.7, 126.7, 125.8, 125.7, 125, 66.7, 49.2, 48.8, 28.5, 23.7, 18.8. MS, m/z 362.1 (M+H\(^+\), 100 %). Anal. Calcd. (%) for C\(_{21}\)H\(_{19}\)N\(_3\)SO: C, 69.78; H, 5.30; N, 11.63; S, 8.87. Found (%): C, 69.88; H, 5.39; N, 11.78; S, 8.98.

2.6.3.3 2-[[3S,3aS]-3-[4-Chlorophenyl]-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]thiazol-4(5H)-one (25c)

Greyish solid; yield 78 %; mp 238-40 °C. IR (cm\(^{-1}\)): 1707 (C=O), 1605 (C=N). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): δ 0.89-0.92 (m, 1H, CH\(_2\)), 1.79-1.82 (m, 1H, CH\(_2\)), 2.51-2.53 (m, 2H, CH\(_2\)), 3.85 (s, 2H, SCH\(_2\)), 3.98-4.05 (m, 1H, H-3a), 5.95 (d, 1H, H-3, J= 10.6 Hz), 7.10 (d, 2H, C\(_6\)H\(_5\), J= 8.1 Hz), 7.24-7.45 (m, 5H, C\(_6\)H\(_5\)), 8.0 (d, 1H, C\(_6\)H\(_5\), J= 6.7 Hz). \(^1\)C NMR (100 MHz, DMSO-d\(_6\)): δ 186.4 (C=O), 177.1, 160.8 (C=N), 140.4, 134.4, 132.6, 131.6, 129.1, 128.6, 127.7, 126.7, 125.6, 66.1, 49.2, 28.5, 23.7. MS, m/z 382.1 (M+H\(^+\), \(^{35}\)Cl, 100 %), 384.1 (MH+2, \(^{37}\)Cl, 38 %). Anal. Calcd. (%) for C\(_{20}\)H\(_{16}\)ClN\(_3\)OS: C, 62.90; H, 4.22; N, 11.00; S, 8.40. Found (%): C, 62.84; H, 4.19; N, 10.98; S, 8.32.
2.6.3.4 2-[(3S,3aS)-3-(4-Chlorophenyl)-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]-5-methylthiazol-4(5H)-one (25d)

Greyish solid; yield 72%; mp 218-20 °C. IR (cm⁻¹): 1695 (C=O), 1595 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 0.86-0.95 (m, 1H, CH₂), 1.50 (d, 3H, CH₃, J= 7.2 Hz), 1.79-1.83 (m, 1H, CH₂), 2.76-3.0 (m, 2H, CH₂), 3.97-4.05 (m, 1H, H-3a), 4.14 (q, 1H, SCHCH₃, J= 7.6 Hz, J= 7.3 Hz), 5.95 (d, 1H, H-3, J= 10.6 Hz), 7.09 (d, 2H, C₆H₅, J= 8.0 Hz), 7.24-7.44 (m, 5H, C₆H₅), 7.99 (d, 1H, C₆H₅, J= 7.4 Hz). ¹³C NMR (100 MHz, DMSO-d₆): δ 189.3 (C=O), 175.5, 160.8 (C=N), 140.4, 139.4, 132.6, 131.6, 129.1, 128.6, 127.7, 126.6, 125.6, 124.1, 48.9, 28.5, 23.7. MS, m/z 396.1 (M+H⁺, 35Cl, 100%), 398.1 (MH⁺2, 37Cl, 38%). Anal. Calcd. (%) for C₂₁H₁₈ClN₃O₃: C, 63.71; H, 4.58; N, 10.61; S, 8.10. Found (%): C, 63.74; H, 4.49; N, 10.58; S, 8.02.

2.6.3.5 2-[(3S,3aS)-7-Methoxy-3-phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl] thiazol-4(5H)-one (25e)

Light yellow solid; yield 84%; mp 208-10 °C. IR (cm⁻¹): 1705 (C=O), 1594 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 0.86-0.91 (m, 1H, CH₂), 1.79-1.83 (m, 1H, CH₂), 2.76-2.98 (m, 2H, CH₂), 3.77 (s, 3H, OCH₃), 3.82 (s, 2H, SCH₂), 3.89-3.96 (m, 1H, H-3a), 5.9 (d, 1H, H-3, J= 10.4 Hz), 6.76 (s, 1H, C₆H₅), 6.88-6.91 (m, 1H, C₆H₅), 7.06-7.07 (m, 2H, C₆H₅), 7.27-7.34 (m, 4H, C₆H₅). ¹³C NMR (100 MHz, DMSO-d₆): δ 186.4 (C=O), 176.5, 161.9 (C=N), 142.6, 135.3, 128.9, 127.6, 125.7, 118.3, 113.8, 112.8, 66.6, 55.1, 49.3, 35.8, 30.7, 28.9, 23.6. MS, m/z 378.1 (M+H⁺, 100%). Anal. Calcd. (%) for C₂₁H₁₉N₃O₃S: C, 66.82; H, 5.07; N, 11.13; S, 8.49. Found (%): C, 66.74; H, 4.99; N, 11.01; S, 8.32.
2.6.3.6  2-[(3S,3aS)-7-Methoxy-3-phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]-5-methylthiazol-4(5H)-one (25f)

Orange crystalline solid; yield 80%; mp 218-20 °C. IR (cm⁻¹): 1697 (C=O), 1602 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 0.79-0.81 (m, 1H, CH₂), 1.49 (d, 3H, CH₃), J = 7.2 Hz), 1.78-1.82 (m, 1H, CH₂), 2.88-2.94 (m, 2H, CH₂), 3.8 (s, 3H, OCH₃), 3.91-3.98 (m, 1H, H-3a), 4.1 (q, 1H, SCHCH₃, J = 7.2 Hz), 5.9 (d, 1H, H-3, J = 10.4 Hz), 6.77-6.78 (m, 1H, C₆H₅), 6.89-6.91 (m, 1H, C₆H₅), 7.05-7.07 (m, 2H, C₆H₅), 7.25-7.35 (m, 3H, C₆H₅), 7.95 (m, 1H, C₆H₅). ¹³C NMR (100 MHz, DMSO-d₆): δ 189.2 (C=O), 175, 162 (C=N), 135.5, 128.5, 127.6, 125.8, 118.3, 113.8, 112.9, 66.4, 55.2, 49.2, 48.8, 35.8, 30.7, 28.9, 23.7, 18.8. MS, m/z 392.1 (M+H⁺, 100%). Anal. Calcd. (%) for C₂₂H₂₁N₃O₂S: C, 67.50; H, 5.41; N, 10.73; S, 8.19. Found (%): C, 67.48; H, 5.28; N, 10.71; S, 8.08.

2.6.3.7  2-[(3S,3aS)-3-(4-Chlorophenyl)-7-methoxy-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]thiazol-4(5H)-one (25g)

Yellow solid; yield 68%; mp 210-12 °C. IR (cm⁻¹): 1702 (C=O), 1610 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 0.86-0.94 (m, 1H, CH₂), 1.79-1.83 (m, 1H, CH₂), 2.75-2.97 (m, 2H, CH₂), 3.82 (s, 3H, OCH₃), 3.86 (s, 2H, SCH₂), 3.91-3.99 (m, 1H, H-3a), 5.91 (d, 1H, H-3, J = 10.5 Hz), 6.81-6.82 (m, 1H, C₆H₅), 6.88-6.91 (m, 1H, C₆H₅), 7.07-7.10 (m, 1H, C₆H₅), 7.33-7.40 (m, 2H, C₆H₅), 7.93-7.95 (m, 2H, C₆H₅). ¹³C NMR (100 MHz, DMSO-d₆): δ 186.3 (C=O), 162, 160.6 (C=N), 142.6, 134.4, 132.6, 128.5, 127.6, 118.2, 113.8, 112.9, 65.9, 55.2, 49.2, 35.8, 30.7, 28.9, 23.7. MS, m/z 412.1 (M+H⁺, ³⁵Cl, 100%), 414.1 (MH+2, ³⁷Cl, 38%). Anal. Calcd. (%) for C₂₃H₁₈ClN₃O₂S: C, 61.23; H, 4.40; N, 10.20; S, 7.78. Found (%): C, 67.38; H, 5.18; N, 10.68; S, 7.98.
2.6.3.8 2-[(3S,3aS)-3-(4-Chlorophenyl)-7-methoxy-3,3a,4,5-tetrahydro-2H-benzo[g] indazol-2-yl]-5-methylthiazol-4(5H)-one (25h)

Orange solid; yield 80 %; mp 162-64 °C. IR (cm⁻¹): 1705 (C=O), 1598 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 0.84-0.89 (m, 1H, CH₂), 1.48 (d, 3H, CH₃, J = 7.3 Hz), 1.77-1.85 (m, 1H, CH₂), 2.75-2.91 (m, 2H, CH₂), 3.81 (s, 3H, OCH₃), 3.91-3.98 (m, 1H, H-3a), 4.08 (q, 1H, SCHCH₃, J = 7.2 Hz), 5.91 (d, 1H, H-3, J = 10.4 Hz), 6.71-6.72 (m, 1H, C₆H₅), 6.77-6.80 (m, 1H, C₆H₅), 6.89-6.92 (m, 1H, C₆H₅), 7.08 (d, 1H, C₆H₅, J = 8.0 Hz), 7.35-7.38 (m, 1H, C₆H₅), 7.9 (d, 1H, C₆H₅, J = 8.7 Hz), 8.03 (d, 1H, C₆H₅, J = 8.8 Hz). ¹³C NMR (100 MHz, DMSO-d₆): δ 189.2 (C=O), 176.5, 160.7 (C=N), 142.7, 132.6, 128.6, 126.9, 124.9, 118.2, 112.9, 55.2, 41.6, 29.5, 26.8, 21.8, 18.9. MS, m/z 426.1 (M+H⁺, 35Cl, 100 %), 428.1 (MH+2, 37Cl, 28 %). Anal. Calcd. (%) for C₂₂H₂₀ClN₃O₂S: C, 62.04; H, 4.73; N, 9.87; S, 7.53. Found (%): C, 62.08; H, 4.68; N, 9.78; S, 7.48.

2.7 Ferrocenyl-hydrazono-thiazolidin-4-one (29) and derivatives

2.7.1 General procedure for the synthesis of compound 28

This compound was prepared from reaction of 2-acetyl ferrocene 27 and thiosemicarbazide by the reported procedure [Casas et al., 2002] and recrystallized from dichloromethane-hexane (1:1) mixture.

2.7.1.1 (2-(1-(2-Carbamothiolyldrazono)ethyl)cyclopenta-2,4-dien-1-yl)(cyclopenta-1,3-dien-1-yl)iron (28)

Orange crystals; yield 81 %; mp 164-66 °C [Casas et al., 2002, mp 169 °C]. ¹H NMR (400 MHz, CDCl₃): δ 2.18 (s, 3H, CH₃), 4.17 (s, 4H, ferrocene ring), 4.39 (s, 2H, ferrocene ring), 4.59 (s, 2H, ferrocene ring), 5.30 (s, 1H, ferrocene ring), 6.28 (br, 1H, NH), 8.62 (br, 1H, NH), 10.19 (br, 1H, NH). Anal. Calcd. (%) for C₁₃H₁₅FeN₃S: C, 51.84; H, 5.02; N, 13.95; S, 10.65. Found (%): C, 51.58; H, 4.67; N, 14.16; S, 10.32.
2.7.2 General procedure for the synthesis of compounds 29

A mixture of 28 (0.8 mmol), chloroacetic acid or 2-bromopropionic acid (0.8 mmol), anhydrous sodium acetate (0.13 g, 1.6 mmol) in ethanol (8.0 mL) was refluxed for 8 h. The solvent was removed under reduced pressure. The solid thus separated was recrystallized from ethanol-DMF (3:1) mixture.

2.7.2.1 Cyclopenta-2,4-dien-1-yl(2-((E)-1-((E)-(4-oxothiazolidin-2-ylidene)hydrazono)ethyl)cyclopenta-2,4-dien-1-yl)iron (29a)

Dark orange crystals; yield 68 %; mp 216-18 ⁰C. IR (cm⁻¹): 3325 (NH), 1728 (C=O), 1566 (C=N), 1265 (C=S). ¹H NMR (400 MHz, DMSO-d₆): δ 2.25 (s, 3H, CH₃), 3.72 (s, 2H, SCH₂), 4.13 (s, 5H, unsubstituted cyclopentadiene ring), 4.36 (s, 2H, substituted cyclopentadiene ring), 4.67 (s, 2H, substituted cyclopentadiene ring), 11.7 (br, 1H, NH).

¹³C NMR (100 MHz, DMSO-d₆): δ 173.5 (C=O), 161.9 (C=N), 82.5, 69.7, 69, 67, 35.8, 32.6, 30.7, 15.5. MS, m/z 342 (M+H⁺, 98 %), 364 (M+Na⁺, 100 %). Anal. Calcd. (%) for C₁₅H₁₅FeN₃OS: C, 52.80; H, 4.43; N, 12.32; S, 9.40. Found (%): C, 52.96; H, 4.64; N, 12.63; S, 9.56.

2.7.2.2 Cyclopenta-2,4-dien-1-yl(2-((E)-1-((E)-(5-methyl-4-oxothiazolidin-2-ylidene)hydrazono)ethyl)cyclopenta-2,4-dien-1-yl)iron (29b)

Dark orange crystals; yield 62 %; mp 189-90 ⁰C. IR (cm⁻¹): 3294 (NH), 1720 (C=O), 1543 (C=N), 1219 (C=S). ¹H NMR (400 MHz, CDCl₃): δ 1.66 (d, 3H, CH₃, J = 7.1 Hz), 2.27 (s, 3H, CH₃), 4.01 (q, 1H, HA, J = 7.1 Hz), 4.17 (s, 5H, unsubstituted cyclopentadiene ring), 4.41 (s, 2H, substituted cyclopentadiene ring), 4.73 (s, 2H, substituted cyclopentadiene ring), 9.28 (br, 1H, NH). ¹³C NMR (100 MHz, CDCl₃): δ 181.7 (C=O), 167.2 (C=N), 87.9, 84.3, 84, 83.7, 75, 74.3, 72.3, 46.9, 24.1, 20.8. MS, m/z 356.1 (M+H⁺, 90 %), 378.0 (M+Na⁺, 100 %). Anal. Calcd. (%) for C₁₆H₁₇FeN₃OS: C, 54.10; H, 4.82; N, 11.83; S, 9.03. Found (%): C, 54.32; H, 4.93; N, 11.66; S, 8.79.
2.7.3  General procedure for the synthesis of compounds 30

A mixture of 28 (0.5 mmol) and \( p \)-substituted phenacyl bromide (0.5 mmol) in ethanol (5.0 mL) was stirred at room temperature for 15 min. The solid obtained was filtered, dried and recrystallized from ethanol-DMF (3:1) mixture.

2.7.3.1 (E)-Cyclopenta-2,4-dien-1-yl(2-(1-(2-(5-(4-phenylthiazol-2-yl)hydrazono)ethyl)cyclopenta-2,4-dien-1-yl)iron (30a)

Green powder; yield 82 %; mp > 250 °C. IR (cm\(^{-1}\)): 3112 (NH), 1601 (C=N), 1494 (C=C). 

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 2.28 (s, 3H, CH\(_3\)), 4.18 (s, 5H, unsubstituted cyclopentadiene ring), 4.4 (s, 2H, substituted cyclopentadiene ring), 4.64 (s, 2H, substituted cyclopentadiene ring), 6.75 (s, 1H, CH of thiazole ring), 7.35-7.46 (m, 2H, C\(_6\)H\(_5\)), 7.51-7.59 (m, 2H, C\(_6\)H\(_5\)), 7.79-7.81 (m, 1H, C\(_6\)H\(_5\)). Anal. Calcd. (%) for C\(_{21}\)H\(_{19}\)FeN\(_3\)S: C, 62.85; H, 4.77; N, 10.47; S, 7.99. Found (%): C, 63.06; H, 4.89; N, 10.62; S, 7.76.

2.7.3.2 (E)-(2-(1-(2-(5-(4-Chlorophenyl)thiazol-2-yl)hydrazono)ethyl)cyclopenta-2,4-dien-1-yl)(cyclopenta-2,4-dien-1-yl)iron (30b)

Orange powder; yield 78 %; mp 208-10 °C. IR (cm\(^{-1}\)): 3115 (NH), 1609 (C=N), 1498 (C=C). 

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 2.30 (s, 3H, CH\(_3\)), 4.18 (s, 5H, unsubstituted cyclopentadiene ring), 4.4 (s, 2H, substituted cyclopentadiene ring), 4.65 (s, 2H, substituted cyclopentadiene ring), 6.78 (s, 1H, CH of thiazole ring), 7.41 (d, 2H, ArH, J= 8.4 Hz), 7.7 (d, 2H, ArH, J= 8.4 Hz). Anal. Calcd. (%) for C\(_{21}\)H\(_{18}\)ClFeN\(_3\)S: C, 57.88; H, 4.16; N, 9.64; S, 7.36. Found (%): C, 57.93; H, 4.32; N, 9.86; S, 7.56.

2.7.3.3 (E)-Cyclopenta-2,4-dien-1-yl(2-(1-(2-(5-(4-nitrophenyl)thiazol-2-yl)hydrazono)ethyl)cyclopenta-2,4-dien-1-yl)iron (30c)

Brown powder; yield 72 %; mp >240 °C. IR (cm\(^{-1}\)): 3118 (NH), 1611 (C=N), 1501 (C=C). 

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 2.27 (s, 3H, CH\(_3\)), 4.18 (s, 5H, unsubstituted
cyclopentadiene ring), 4.4 (s, 2H, substituted cyclopentadiene ring), 4.66 (s, 2H, substituted cyclopentadiene ring), 7.05 (s, 1H, CH of thiazole ring), 7.93-7.96 (m, 2H, ArH), 8.28-8.23 (m, 2H, ArH). $^{13}$C NMR (100 MHz, DMSO-d$_6$): $\delta$ 170.2 (C=N of thiazole ring), 149.3 (C=N), 148.4 (=C-Ar), 146, 140.8, 126.2, 124.1 (Ar-C), 108.4 (=CH of thiazole ring), 83.6, 69.5, 68.9, 66.5 (ferrocene-C) 15.3 (CH$_3$). Anal. Calcd. (%) for C$_{21}$H$_{18}$FeN$_4$O$_2$S: C, 56.51; H, 4.07; N, 12.55; S, 7.18. Found (%): C, 56.62; H, 4.28; N, 12.33; S, 7.29.

2.7.4 General procedure for the synthesis of 31

A mixture of 29a (5 mmol), DMF-DMA (0.6 g, 5 mmol) in dioxane (20 mL) was stirred at reflux for 6 h. The separated solid product obtained on standing at room temperature was collected by filtration, washed with ethanol and recrystallized from dioxane.

2.7.4.1 Cyclopenta-2,4-dien-1-yl(2-((E)-1-(((2Z,5E)-5-((dimethylamino)methylene)-4-oxo thiazolidin-2-ylidene)hydrazono)ethyl)cyclopenta-2,4-dien-1-yl)iron (31)

Dark brown solid; yield 68 %; mp 168-70 $^\circ$C. IR (cm$^{-1}$): 3294 (NH), 1698 (C=O), 1610 (C=N), 1498 (C=C). $^1$H NMR (400 MHz, DMSO-d$_6$): $\delta$ 2.25 (s, 3H, CH$_3$), 3.14 (s, 6H, NMe$_2$), 4.16 (s, 5H, unsubstituted cyclopentadiene ring), 4.38 (s, 2H, substituted cyclopentadiene ring), 4.63 (s, 2H, substituted cyclopentadiene ring), 7.42 (s, 1H, =CH), 11.67 (br, 1H, NH). Anal. Calcd. (%) for C$_{18}$H$_{20}$FeN$_4$OS: C, 54.56; H, 5.09; N, 14.14; S, 8.09. Found (%): C, 54.68; H, 5.28; N, 14.33; S, 8.29.

2.7.5 General procedure for synthesis of compounds 32

A mixture of thiazolidin-4-one 29a (1.0 mmol) and DMF-DMA (10 mmol) in DMF (5.0 mL) was refluxed for 50 min. The reaction mixture was then cooled and
extracted with ethyl acetate (2x25 mL). The organic layer was washed with brine solution and dried over anhydrous Na$_2$SO$_4$. The excess ethyl acetate was then removed under reduced pressure and the solid obtained was filtered and recrystallized from ethanol.

2.7.5.1 Cyclopenta-2,4-dien-1-yl(2-((E)-1-(((2Z,5E)-5-((dimethylamino)methylene)-3-methyl-4-oxothiazolidin-2-ylidene)hyrazono)ethyl)cyclopenta-2,4-dien-1-yl)iron (32)

Brown powder; yield 72 %; mp 192-94 °C. IR (cm$^{-1}$): 1702 (C=O), 1602 (C=N), 1510 (C=C). $^1$H NMR (400 MHz, DMSO-$d_6$): δ 2.27 (s, 3H, CH$_3$), 3.11 (s, 6H, NMe$_2$), 3.21 (s, 3H, N-CH$_3$), 4.13 (s, 5H, unsubstituted cyclopentadiene ring), 4.34 (s, 2H, substituted cyclopentadiene ring), 4.66 (s, 2H, substituted cyclopentadiene ring), 7.4 (s, 1H, =CH).

Anal. Calcd. (%) for C$_{19}$H$_{22}$FeN$_4$OS: C, 55.62; H, 5.40; N, 13.65; S, 7.81. Found (%): C, 55.78; H, 5.62; N, 13.83; S, 8.01.

2.8 6,12-Dihydro-5H-benzo[f]thiazolo[2,3-b]quinazolin-10(9H)-one (35)

2.8.1 General procedure for synthesis of 34

A mixture of 2-tetralone (0.21 g, 0.16 mmol), $p$-chlorobenzaldehyde (0.22 g, 0.16 mmol) and thiourea (0.12 g, 0.16 mmol) in gl. acetic acid (10 mL) was heated at 110 °C for 4 h. The reaction mixture was then cooled to room temperature. The white solid obtained was filtered, dried and recrystallized from ethanol-DMF (3:1) mixture.

2.8.1.1 1-(4-Chlorophenyl)-1,4,5,6-tetrahydrobenzo[f]quinazoline-3(2H)-thione (34)

Yellow crystalline solid; yield 78 %; mp 190-92 °C. IR (cm$^{-1}$): 3208 (NH), 1548 (C=C), 1246 (C=S). $^1$H NMR (400 MHz, DMSO-$d_6$): δ 2.44-2.52 (m, 1H, CH$_2$), 2.58-2.64 (m, 1H, CH$_2$), 2.84 (t, 2H, CH$_2$; J = 7.3 Hz), 5.44 (d, 1H, H$_6$, J = 2.4 Hz), 6.83 (d, 1H, C$_6$H$_5$, J = 7.0 Hz) 6.94-7.01 (m, 2H, C$_6$H$_5$), 7.06 (d, 1H, C$_6$H$_5$, J = 6.4 Hz), 7.3 (d, 2H, C$_6$H$_5$, J = 6.6 Hz), 7.37
(d, 2H, C₆H₅, J= 6.6 Hz), 9.19 (br, 1H, NH), 10.06 (br, 1H, NH). Anal. Calcd. (%) for C₁₈H₁₅ClN₂S: C, 66.15; H, 4.63; N, 8.57; S, 9.81. Found (%): C, 66.31; H, 4.78; N, 8.71; S, 10.05.

2.8.2 General procedure for synthesis of 35 and 39

A mixture of thione 34 (0.16 g, 0.5 mmol), ethyl bromo acetate or 2-bromopropionic acid (0.5 mmol), anhydrous sodium acetate (0.082 g, 1.0 mmol) in ethanol (10 mL) was heated under reflux for 5-6 h. The progress of reaction was monitored by TLC. After completion of the reaction the volume of the reaction mixture was reduced to half. The cooled reaction mixture was then poured in to ice cold water and filtered the solid obtained. Recrystallization from ethanol–DMF (3:1) mixture furnished pure compounds.

2.8.2.1 12-(4-Chlorophenyl)-6,12-dihydro-5H-benzo[f]thiazolo[2,3-b]quinazolin-10(9H)-one (35)

Yellow solid; yield 62 %; mp 102-04 °C. IR (cm⁻¹): 1713 (C=O), 1612 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 2.56-2.67 (m, 2H, CH₂), 2.83-2.87 (m, 2H, CH₂), 3.96 (dd, 1H, SCH₂, J= 17.4 Hz, J = 1.5 Hz), 4.06 (d, 1H, SCH₂, J= 17.4 Hz), 6.2 (s, 1H, Hₐ), 6.99-7.05 (m, 2H, C₆H₅) 7.06-7.12 (m, 2H, C₆H₅), 7.32 (d, 2H, C₆H₅, J= 8.4 Hz), 7.47 (d, 2H, C₆H₅, J= 8.4). ¹³C NMR (100 MHz, DMSO-d₆) δ: 170.7, 155.3, 139.9, 138.1, 134.7, 133.3, 131.3, 129.7, 128.5, 127.3, 126.1, 121.5, 111, 53.9, 36.2, 31.9, 28.4, 27.8, 24.2. MS, m/z 367.2 (MH⁺, ³⁵Cl, 100 %), 369.2 (MH⁺+2, ³⁷Cl, 34%), 499.3 (MH⁺+ C₁₀H₁₂, 84%), 501.3 (MH⁺+2+C₁₀H₁₂, 32%). Anal. Calcd. (%) for C₂₀H₁₅ClN₂OS: C, 65.48; H, 4.12; N, 7.64; S, 8.74. found (%): C, 65.62; H, 4.31; N, 7.81; S, 8.92.
2.8.2.2 12-(4-Chlorophenyl)-9-methyl-6,12-dihydro-5H-benzo[f]thiazolo[2,3-b]quinazolin-10(9H)-one (39)

Yellow crystalline solid; yield 68 %; mp 182-84 °C. IR (cm⁻¹): 1715 (C=O), 1620 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 1.34 (d, 3H, CH₃, J = 7.2 Hz), 2.57-2.68 (m, 2H, CH₂), 2.80-2.82 (m, 2H, CH₂), 4.29 (q, 1H, SCH₂, J = 7.2 Hz), 6.15 (s, 1H, Hₐ), 6.99-7.07 (m, 4H, C₆H₅) 7.27 (d, 2H, C₆H₅, J = 8.4 Hz), 7.41 (d, 2H, C₆H₅, J = 8.5 Hz). ¹³C NMR (100 MHz, DMSO-d₆) δ: 174.1, 154, 139.9, 138.6, 134.7, 133.1, 131.4, 129.8, 128.6, 128.5, 127.3, 126.2, 121.7, 111.6, 54, 53.8, 28.4, 27.7, 18.7. MS, m/z 381.2 (M+H⁺, 35Cl, 100%), 383.2 (MH⁺+2, 37Cl, 29%). Anal. Calcd. (%) for C₂₁H₁₇ClN₂OS: C, 66.22; H, 4.50; N, 7.35; S, 8.42. Found (%): C, 66.39; H, 4.68; N, 7.51; S, 8.58.

2.8.3 General procedure for synthesis of 37 and 44

A mixture of thione 34 (0.26 g, 0.8 mmol), 1,2-dibromo ethane / 1,3-dibromo propane (0.8 mmol) in ethanol (5.0 mL) was heated under reflux for 5 h. The volume of the reaction mixture was reduced to half and cooled to room temperature. The reaction mixture was poured in to ice cold water and extracted with ethyl acetate (2x25 mL). Gummy solid obtained was purified with column hexane-ethyl acetate (8:2).

2.8.3.1 12-(4-Chlorophenyl)-6,9,10,12-tetrahydro-5H-benzo[f]thiazolo[2,3-b]quinazoline (37)

Yellow solid; yield 52 %; mp 178-80 °C. IR (cm⁻¹): 1645 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 2.61-2.66 (m, 1H, CH₂), 2.86-3.01 (m, 2H, CH₂), 3.50-3.59 (m, 1H, CH₂), 3.63-3.73 (m, 2H, NCH₂), 4.25-4.31 (m, 1H, SCHR₂), 4.46-4.52 (m, 1H, SCHR₂), 6.13 (s, 1H, Hₐ), 7.0-7.16 (m, 4H, C₆H₅), 7.35-7.43 (m, 3H, C₆H₅), 7.58 (d, 1H, C₆H₅, J = 7.9 Hz). MS, m/z 353.2 (M+H⁺, 35Cl, 100 %), 355.2 (MH⁺+2, 37Cl, 32%). Anal. Calcd. (%) for
C_{20}H_{17}ClN_{2}S: C, 68.07; H, 4.86; N, 7.94; S, 9.09. Found (%): C, 68.22; H, 5.01; N, 8.01; S, 9.28.

### 2.8.3.2 13-(4-Chlorophenyl)-6,10,11,13-tetrahydro-5H,9H-benzo[f][1,3]thiazino[2,3-b]quinazoline (44)

Yellow solid; yield 52 %; mp 184-86 °C. IR (cm\(^{-1}\)): 1645 (C=N). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \(\delta\) 2.55-2.65 (m, 2H, CH\(_2\)), 2.87-2.97 (m, 5H, CH\(_2\)), 3.18-3.25 (m, 2H, CH\(_2\)), 3.81-3.84 (m, 1H, CH\(_2\)), 6.03 (s, 1H, H\(_A\)), 7.08-7.11 (m, 2H, C\(_6\)H\(_5\)), 7.13-7.17 (m, 2H, C\(_6\)H\(_5\)), 7.38-7.54 (m, 2H, C\(_6\)H\(_5\)), 7.62 (d, 2H, C\(_6\)H\(_5\), \(J=8.5\) Hz). MS, m/z 367.1 (M+H\(^+\), \(^{35}\)Cl, 100 %), 369.2 (MH\(^+\)+2, \(^{37}\)Cl, 56 %). Anal. Calcd. for C\(_{21}\)H\(_{19}\)ClN\(_2\)S: C, 68.75; H, 5.22; N, 7.64; S, 8.74. Found (%): C, 68.92; H, 5.41; N, 7.81; S, 8.98.

### 2.8.4 General procedure for synthesis of 41

Arylidene derivatives 41 were prepared from two routes:

a) A mixture of thione 34 (0.13 g, 0.04 mmol), chloroacetic acid (0.0378 g, 0.04 mmol), aromatic aldehyde (0.04 mmol), anhydrous sodium acetate (0.032 g, 0.04 mmol) in gl. acetic acid (10 mL) and acetic anhydride (0.5 mL) was heated under reflux for 6 h. Reaction mixture was kept overnight and then poured in to ice cold water. The solid obtained was filtered, dried and recrystallized from ethanol.

b) A mixture of thiazolidin-4-one 35 (0.04 mmol), aromatic aldehyde (0.04 mmol) and anhydrous sodium acetate (0.032 g, 0.04 mmol) in gl. acetic acid (10 mL) and acetic anhydride (0.5 mL) was heated under reflux for 3 h. The reaction mixture was then poured in to ice cold water. Filtered the solid obtained, dried and recrystallized from ethanol.
2.8.4.1 (Z)-9-Benzylidene-12-(4-chlorophenyl)-6,12-dihydro-5H-benzo[f]thiazolo[2,3-b]quinazolin-10(9H)-one (41a)

Yellow solid; yield 60 %; mp 98-100 °C. IR (cm⁻¹): 1694 (C=O), 1624 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 2.67-2.69 (m, 2H, CH₂), 2.86-2.89 (m, 2H, CH₂), 6.43 (s, 1H, Hₐ), 7.05-7.08 (m, 2H, C₆H₅), 7.11-7.12 (m, 1H, C₆H₅), 7.23-7.25 (m, 1H, C₆H₅), 7.34-7.37 (m, 2H, C₆H₅), 7.45-7.51 (m, 1H, C₆H₅), 7.53-7.57 (m, 6H, C₆H₅), 7.73 (s, 1H, =CH). Anal. Calcd. (%) for C₂₇H₁₉ClN₂O: C, 71.28; H, 4.21; N, 6.16; S, 7.05. Found (%): C, 71.42; H, 4.38; N, 7.02; S, 7.28.

2.8.4.2 (Z)-12-(4-Chlorophenyl)-9-(4-methylbenzylidene)-6,12-dihydro-5H-benzo[f]thiazolo[2,3-b]quinazolin-10(9H)-one (41b)

Orange solid; yield 78 %; mp 156-158 °C. IR (cm⁻¹): 1698 (C=O), 1612 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 2.34 (s, 3H, CH₃), 2.55-2.71 (m, 2H, CH₂), 2.80-2.93 (m, 2H, CH₂), 6.36 (s, 1H, Hₐ), 7.02-7.06 (m, 2H, C₆H₅), 7.08-7.10 (m, 1H, C₆H₅), 7.15-7.17 (m, 1H, C₆H₅), 7.29 (t, 4H, C₆H₅, J = 8.6 Hz), 7.4 (d, 2H, C₆H₅, J = 8.1 Hz), 7.5 (d, 2H, C₆H₅, J = 6.8 Hz), 7.65 (s, 1H, =CH). Anal. Calcd. (%) for C₂₈H₂₁ClN₂O₂: C, 71.71; H, 4.51; N, 5.97; S, 6.84. Found (%): C, 71.89; H, 4.68; N, 6.09; S, 7.01.

2.8.4.3 (Z)-12-(4-Chlorophenyl)-9-(4-methoxybenzylidene)-6,12-dihydro-5H-benzo[f]thiazolo[2,3-b]quinazolin-10(9H)-one (41c)

Orange solid; yield 79 %; mp 138-140 °C. IR (cm⁻¹): 1701 (C=O), 1628 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 2.58-2.72 (m, 2H, CH₂), 2.82-2.94 (m, 2H, CH₂), 3.83 (s, 3H, OCH₃), 6.4 (s, 1H, Hₐ), 7.04-7.07 (m, 4H, C₆H₅), 7.11 (m, 1H, C₆H₅), 7.20-7.22 (m, 1H, C₆H₅), 7.34 (d, 2H, C₆H₅, J = 6.6 Hz), 7.50-7.55 (m, 4H, C₆H₅), 7.68 (s, 1H, =CH). Anal. Calcd. (%) for C₂₈H₂₃ClN₂O₂S: C, 69.34; H, 4.36; N, 5.78; S, 6.61. Found (%): C, 69.53; H, 4.51; N, 5.91; S, 6.78.
2.8.4.4 (Z)-12-(4-Chlorophenyl)-9-(4-fluorobenzylidene)-6,12-dihydro-5H-benzo[f]thiazolo[2,3-b]quinazolin-10(9H)-one (41d)

Orange solid; yield 73 %; mp 194-96 °C. IR (cm$^{-1}$): 1697 (C=O), 1632 (C=N). $^1$H NMR (400 MHz, DMSO-d$_6$): δ 2.64-2.76 (m, 2H, CH$_2$), 2.90-2.95 (m, 2H, CH$_2$), 6.36 (s, 1H, H$_A$), 7.07-7.10 (m, 4H, C$_6$H$_5$), 7.20-7.31 (m, 4H, C$_6$H$_5$), 7.48-7.56 (m, 4H, C$_6$H$_5$), 7.7 (s, 1H, =CH). MS, m/z 473 (M+H$^+$, 100%), 475 (MH$^+$+2, 38%). Anal. Calcd. (%) for C$_{27}$H$_{18}$ClFN$_2$OS: C, 68.57; H, 3.84; N, 5.92; S, 6.78. Found (%): C, 68.72; H, 4.01; N, 6.01; S, 7.98.

2.8.5 General procedure for synthesis of 42

A mixture of thione 34 (0.32 g, 0.001 mol), chloropropionic acid (0.108 g, 0.001 mol), anhydrous sodium acetate (0.16 g, 0.002 mol), gl. acetic acid (10 mL) and acetic anhydride (0.5 mL) was heated under reflux for 10-12 h. The progress of reaction was monitored by TLC. After completion of the reaction, the reaction mixture was kept overnight and then poured in to ice cold water. The solid separated was filtered, dried and recrystallized from ethanol.

2.8.5.1 13-(4-Chlorophenyl)-6,9,10,13-tetrahydro-5H,11H-benzo[f][1,3]thiazino[2,3-b]quinazolin-11-one (42)

Yellow solid; yield 60 %; mp 108-10 °C. IR (cm$^{-1}$): 1698 (C=O), 1648 (C=N). $^1$H NMR (400 MHz, DMSO-d$_6$): δ 2.45-2.51 (m, 1H, CH$_2$), 2.65-2.73 (m, 1H, CH$_2$), 2.89-2.98 (m, 2H, CH$_2$), 3.0-3.1 (m, 4H, SCH$_2$CH$_2$), 6.77 (s, 1H, H$_A$), 6.93-6.96 (m, 1H, C$_6$H$_5$), 7.03-7.08 (m, 2H, C$_6$H$_5$), 7.11-7.13 (m, 1H, C$_6$H$_5$), 7.33 (q, 4H, C$_6$H$_5$, J= 8.6, J= 7.3 Hz). $^{13}$C NMR (100 MHz, DMSO-d$_6$): δ: 168.8, 151.1, 139.7, 139, 138, 134.3, 133, 131.8, 129.2, 128.8, 127.5, 126.5, 121.4, 113, 61.2, 48.8, 35.4, 27.7, 21, 15. El-MS, m/z 380 (M$^+$, $^{35}$Cl, 40%), 382 (M$^+$+2, $^{37}$Cl, 15%), 269 (M–C$_6$H$_4$Cl, 100 %), 241 (M–C$_6$H$_4$Cl–CO, 98 %). Anal. Calcd. (%) for C$_{23}$H$_{17}$ClN$_2$OS: C, 66.22; H, 4.50; N, 7.35; S, 8.42. Found (%): C, 66.36; H, 4.63; N, 7.51; S, 8.68.
2.8.6 General procedure for synthesis of 46

A mixture of 2-tetralone (0.05 mol) and aromatic aldehyde (0.05 mol), glacial acetic acid (25 mL) and conc. HCl (15 mL) was kept at 0 °C for 24 h. Filtered the yellow solid obtained, washed with petroleum ether (60-80 °C) and recrystallized from ethanol.

2.8.6.1 (E)-1-(4-Chlorobenzylidene)-3,4-dihydropthalen-2(1H)-one (46a)

Yellow solid; yield 78 %; mp 90-92 °C. IR (cm⁻¹): 1696 (C=O). ¹H NMR (400 MHz, DMSO-d₆): δ 2.56 (t, 2H, CH₂, J = 3.4 Hz), 3.02 (t, 2H, CH₂, J = 6.5 Hz), 7.02-7.06 (m, 1H, C₆H₅), 7.19-7.25 (m, 2H, C₆H₅), 7.31-7.35 (m, 3H, C₆H₅), 7.4 (d, 2H, C₆H₅, J = 8.4 Hz), 7.49 (s, 1H, =CH). Anal. Calcd. (%) for C₁₇H₁₃ClO: C, 75.98; H, 4.88. Found (%): C, 76.14; H, 5.08.

2.8.6.2 (E)-1-(4-Nitrobenzylidene)-3,4-dihydropthalen-2(1H)-one (46b)

Yellow solid; yield 85 %; mp 120-122 °C. IR (cm⁻¹): 1701 (C=O). ¹H NMR (400 MHz, DMSO-d₆): δ 2.61 (t, 2H, CH₂, J = 6.6 Hz), 3.09 (t, 2H, CH₂, J = 6.5 Hz), 7.02 (t, 1H, C₆H₅, J = 7.2 Hz), 7.13 (d, 1H, C₆H₅, J = 7.4 Hz), 7.26 (t, 1H, C₆H₅, J = 7.4 Hz), 7.34 (d, 1H, C₆H₅, J = 7.4 Hz), 7.58-7.60 (m, 3H, C₆H₅ & =CH), 8.1 (d, 2H, C₆H₅, J = 8.9 Hz). Anal. Calcd. (%) for C₁₇H₁₃NO₃: C, 73.11; H, 4.69. Found (%): C, 73.24; H, 4.88.

2.8.7 General procedure for synthesis of 47

To a mixture of arylidene derivative 46 (0.5 mmol), and thiourea (0.038 g, 0.5 mmol) in ethanol (5.0 mL) catalytic amount of conc. HCl (0.5 mL) was added and the mixture was refluxed for 5 h. The solid separated on cooling was filtered, dried and recrystallized from ethanol-DMF (3:1) mixture.
2.8.7.1 1-(4-Chlorophenyl)-5,6-dihydro-1H-naphtho[2,1-d][1,3]thiazin-3-amine (47a)

Light yellow solid; yield 78 %; mp 206-08 0°C. IR (cm⁻¹): 3214, 3126 (NH), 1645 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 2.60-2.66 (m, 1H, CH₂), 2.82-2.88 (m, 1H, CH₂), 2.96-3.0 (m, 2H, CH₂), 5.97 (s, 1H, HA), 7.07-7.14 (m, 3H, C₆H₅) 7.19-7.21 (m, 1H, C₆H₅), 7.37-7.42 (m, 4H, C₆H₅), 9.07 (br, 1H, NH), 10.05 (br, 1H, NH). Anal. Calcd. (%) for C₁₈H₁₅ClN₂S: C, 66.15; H, 4.63; N, 8.57; S, 9.81. Found (%): C, 66.31; H, 4.78; N, 8.71; S, 10.05.

2.8.7.2 1-(4-Nitrophenyl)-5,6-dihydro-1H-naphtho[2,1-d][1,3]thiazin-3-amine (47b)

Green crystalline solid; yield 74 %; mp 186-88 0°C. IR (cm⁻¹): 3208, 3115 (NH), 1646 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 2.62-2.68 (m, 1H, CH₂), 2.83-2.91 (m, 1H, CH₂), 2.98-3.02 (m, 2H, CH₂), 6.15 (s, 1H, HA), 7.06-7.08 (m, 1H, C₆H₅) 7.11-7.16 (m, 2H, C₆H₅), 7.20-7.23 (m, 1H, C₆H₅), 7.67 (d, 2H, J= 7.0 Hz), 8.21 (d, 2H, C₆H₅, J= 6.8 Hz), 9.15 (br, 1H, NH), 10.16 (br, 1H, NH). MS, m/z 338.1 (M+H⁺, 100 %). Anal. Calcd. (%) for C₁₈H₁₃N₃O₂S: C, 64.08; H, 4.48; N, 12.45; S, 9.50. Found (%): C, 64.21; H, 4.61; N, 12.68; S, 9.71.

2.8.8 General procedure for synthesis of 48

A mixture of thiazin-3-amine derivative 47 (0.04 mmol), anhydrous sodium acetate (0.08 mmol), acetic anhydride (0.5 mL) in acetic acid (5.0 mL) was heated under reflux for 5 h. The reaction mixture cooled to room temperature and poured in to ice cold water. The solid obtained was filtered and recrystallized from dichloro methane-hexane (3:1) mixture.
2.8.8.1 N-(1-(4-Chlorophenyl)-5,6-dihydro-1H-naphtho[2,1-d][1,3]thiazin-3-yl) acetamide (48a)

Yellow crystalline solid; yield 58 %; mp 178-80 °C. IR (cm⁻¹): 1662 (C=O), 1636 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 1.98 (s, 3H, CH₃), 2.56-2.58 (m, 1H, CH₂), 2.82-2.92 (m, 3H, CH₂), 5.24 (s, 1H, Hₐ), 6.90-6.92 (m, 1H, C₆H₅) 6.98-7.02 (m, 2H, C₆H₅), 7.18-7.22 (m, 1H, C₆H₅), 7.4 (d, 2H, C₆H₅, J= 8.6 Hz), 8.01 (d, 2H, C₆H₅, J= 8.7 Hz), 10.4 (br, 1H, NH). Anal. Calcd. for C₂₀H₁₇ClN₂O: C, 65.12; H, 4.65; N, 7.59; S, 8.69. Found (%): C, 65.24; H, 4.79; N, 7.71; S, 8.81.

2.8.8.2 N-(1-(4-Nitrophenyl)-5,6-dihydro-1H-naphtho[2,1-d][1,3]thiazin-3-yl) acetamide (48b)

Orange crystalline solid; yield 60 %; mp 154-56 °C. IR (cm⁻¹): 1666 (C=O), 1638 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 2.0 (s, 3H, CH₃), 2.53-2.56 (m, 1H, CH₂), 2.84-2.98 (m, 3H, CH₂), 5.27 (s, 1H, Hₐ), 6.92-6.94 (m, 1H, C₆H₅) 7.02-7.07 (m, 2H, C₆H₅), 7.14-7.16 (m, 1H, C₆H₅), 7.46 (d, 2H, C₆H₅, J= 8.6 Hz), 8.12 (d, 2H, C₆H₅, J= 8.7 Hz), 11.06 (br, 1H, NH). Anal. Calcd. for C₂₀H₁₇N₃O₃S: C, 63.31; H, 4.52; N, 11.07; S, 8.45. Found (%): C, 63.54; H, 4.78; N, 11.21; S, 8.61.

2.9 Computational Studies

Theoretical chemistry is considered to be the mathematical description of chemistry. Computational theoretical chemistry is primarily concerned with the numerical computation of molecular electronic structures and molecular interactions. Computational chemistry is the application of chemical, mathematical and computing skills to the solution of interesting chemical problems. It uses computers to generate information such as properties of molecules or simulated experimental results. The
term "Computational Chemistry" found its first mention in the book “Computers and Their Role in the Physical Sciences” [Fernbach and Taub, 1970], where they state "It seems, therefore, that 'computational chemistry' can finally be more and more of a reality." During the 1970s, widely different methods began to be seen as part of a new emerging discipline of computational chemistry. The Journal of Computational Chemistry was first published in 1980.

Computational chemistry is comprised of a theoretical (or structural) modelling part, known as molecular modelling, involves simulating chemical reactions and processes at the atomic level within the virtual space of a computer. Molecular modelling advances through its theoretical input by predicting the probable molecular structure, thermo-chemistry, spectroscopy, conformational search and energy of a compound. This technique has been implemented in various areas with different goals. This technique has become a useful way to investigate materials that are too difficult to sort out or too expensive. It also helps chemists make predictions before running the actual experiments so that they can be better prepared for making observations.

The quantum and classical mechanics as well as statistical physics and thermodynamics are the foundation for most of the computational chemistry theory and computer programs. This is because they model the atoms and molecules with mathematics. Computational chemistry software use can in particular perform electronic structure determinations, geometry optimizations, frequency calculations, definition of transition structures and reaction paths, protein calculations, i.e. docking, electron and charge distribution calculations, calculations of potential energy
surfaces (PES), calculations of rate constants for chemical reactions (kinetics), calculation of many other molecular and bulk physical and chemical properties, correlations between chemical structures and properties (QSPR and QSAR), drug design and catalysis etc.

The basis of computational study is that all important molecular properties i.e. stabilities, reactivities and electronic properties are related to the molecular structure. Therefore, if it is possible to develop algorithms that are able to calculate a structure with a given stoichiometry and connectivity, it must be possible to compute the molecular properties based on the calculated structure and vice versa.

The most important numerical approaches are empirical, semi-empirical, *ab-initio* and DFT methods. A brief description of the classical molecular mechanics and quantum mechanical approaches is given below.

**2.9.1 Molecular mechanics calculations**

Empirical or molecular mechanics (MM) uses classical physical and empirical or semi-empirical force fields to explain and interpret the behavior of atoms and molecules. In organic chemistry, it has been applied to interpret and predict structures [Allinger, 1977]. Molecular mechanics (MM) has numerous applications in the field of organic chemistry for structural explanation. This method has been applied to proteins and other large biological molecules, and allows studies of docking of potential drug molecules [Krovat et al., 2005] by the use of the simulation of forces.

Molecular mechanics is a completely empirical approach, based on Born-Oppenheimer approximation, which assumes that the motions of the nuclei of a molecule are independent of the motions of the electrons. It means the arrangement
of the electrons is assumed to be fixed and the positions of the nuclei are calculated. The geometry of the molecule is obtained by taking into account of all the forces between the atoms of a molecule and the geometry of a molecule is optimized by calculating the total energy arises from the forces or stress. The minimized total energy is taken to be the strain present in the molecule. It is generally referred to as the strain energy, $E_{\text{total}}$ and is related to the molecule’s potential energy and stabilities. Minimization of the strain energy $E_{\text{total}}$ by rearrangement of the nuclei leads to an optimized structure and a value for the minimized strain energy. A number of force field like MM³, MM3, AMBER, OPLS, MMFF and VFF are available for molecular mechanics calculation.

2.9.2 Semi-empirical methods

Over the past decades the semi-empirical methods have been utilized mostly in computational studies. Semi-empirical methods are based on the Hartree–Fock formalism, but make many approximations and obtain some parameters from empirical data. Semi-empirical methods serve as efficient computational tools which can yield fast quantitative estimates for a number of properties. This may be particularly useful for correlating large sets of experimental and theoretical data, for establishing trends in classes of related molecules.

The quantum mechanical approach in semi-empirical calculations can be distinguished into methods that are restricted to pi-electrons and to those restricted to all valence electrons. Firstly, in Hartree-Fock based semi-empirical methods (i.e. MOPAC), the pi-electron theories have a strong *ab initio* basis. The empirical parameters, in fact, include effective electron correlation effects. Also, a slightly
extended and re-parameterized version of PM3 termed PM5 has recently been made available in the program package MOPAC 2000.

2.9.3 Density functional theory (DFT)

Density functional theory has been the dominant method for the quantum mechanical simulation of periodic systems for the last 30 years. Recently, it has also been adopted by quantum chemists and is now very widely used for the simulation of energy surfaces in molecules. Density Functional Theory (DFT) is a quantum mechanical modelling method used in physics and chemistry to investigate the electronic structure of many-body systems, in particular atoms, molecules and the condensed phases. With this theory, the properties of a many-electron system can be determined by using functional, i.e. functions of other function, which in this case are the spatially dependent electron density. In molecular calculations through DFT, a huge variety of exchange-correlation functional has been developed. In the chemistry community, one popular functional is known as B3LYP (from the name Becke for the exchange part and Lee, Yang and Parr for the correlation part) specifying how much of the exact exchange is mixed in.

Hence, DFT is among the most popular and versatile theoretical methods available in computational physics and computational chemistry. In the present investigations, DFT studies of cyclised compounds in third; fourth, fifth and sixth series has been performed for structure validation. Experimental carbon and proton NMR spectra were correlated with theoretical spectra, which showed good correlations for proposed structures.