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. Thin Layer Chromatography development was performed on silica gel-G plates.

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 Analyzer, Euro EA 3000 Elemental Analyser and Flash 2000 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. The coupling constant values are given in Hertz (Hz). While citing \(^1\)H NMR data, following abbreviations are used: br (s)-broad singlet, \(d\)-doublet, \(t\)-triplet, \(q\)-quartet and \(m\)-multiplet. \(^{13}\)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) 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 (60-80 °C)-ethylacetate (4:1), pet ether (60-80 °C)-chloroform (7:3), pet ether (60-80 °C)-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 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**, 6-31G(d) and 6-311G(d) basis sets.

2.3 6,7-Dihydro-1H-indazol-4(5H)-one (3) and its derivatives

2.3.1 General procedure for the synthesis of 2

A mixture of dimedone 1 (0.7 g, 5.0 mmol) and DMF-DMA (1.19 mL, 10 mmol) was stirred at 70 °C for 2 minutes. Substituted hydrazine (4.0 mmol) was then added to the reaction mixture and stirring continued for 5 min. The solid obtained was filtered, washed with benzene and recrystallized from ethanol.

2.3.1.1 5,5-Dimethyl-2-[(2-phenylhydrazinyl)methylene]cyclohexane-1,3-dione (2a)

White crystalline solid; yield 81 %; mp 168-69 °C. IR (cm⁻¹): 1690 (C=O). ¹H NMR (400 MHz, DMSO-d₆): δ 1.00 (s, 6H, 2CH₃), 2.28 (s, 2H, CH₂), 2.38 (s, 2H, CH₂), 6.72-6.74 (d, 2H, C₆H₅, J= 8.0 Hz), 6.85-6.88 (t, 1H, C₆H₅, J= 7.2 Hz), 7.24 (m, 2H, C₆H₅), 8.0 (s, 1H,
CH), 9.0 (s, 1H, NH), 12.01 (s, 1H, NH). MS, m/z 259.1 (M+H⁺, 100 %). Anal Calcd. (%) for C₁₅H₁₈N₂O₂: C, 69.74; H, 7.02; N, 10.84. Found (%): C, 69.44; H, 6.65; N, 10.5.

2.3.1.2 2-[(2-(4-Chlorophenyl)hydrazinyl)methylene]-5,5-dimethylcyclohexane-1,3-dione (2b)

Yellow crystalline solid; yield 71 %; mp 162-164 °C. IR (cm⁻¹): 1690 (C=O). ¹H NMR (400 MHz, DMSO-d₆): δ 1.03 (s, 6H, 2CH₃), 2.28 (s, 2H, CH₂), 2.39 (s, 2H, CH₂), 6.73-6.77 (m, 2H, C₆H₅), 7.20-7.24 (m, 2H, C₆H₅), 8.03-8.05 (d, 1H, CH, J= 8.0 Hz), 9.13 (s, 1H, NH), 12.08 (s, 1H, NH). Anal Calcd. (%) for C₁₅H₁₇ClN₂O₂: C, 61.54; H, 5.85; N, 9.57. Found (%): C, 61.56; H, 5.78; N, 9.52.

2.3.2 General procedure for the synthesis of 3

A solution of 2 (0.625 mmol) in ethanol (5.0 mL) and 0.5 mL conc. HCl was refluxed for 3 h. The reaction mixture was then cooled to room temperature and poured in to ice cold water. The solid obtained was filtered, dried and recrystallized from ethanol.

2.3.2.1 6,6-Dimethyl-1-phenyl-6,7-dihydro-1H-indazol-4(5H)-one (3a)

White crystalline solid; yield 65 %; mp 116-118 °C. IR (cm⁻¹): 1690 (C=O). ¹H NMR (400 MHz, CDCl₃): δ 1.11 (s, 6H, 2CH₃), 2.43 (s, 2H, CH₂), 2.83 (s, 2H, CH₂), 7.42-7.46 (m, 1H, C₆H₅), 7.49-7.55 (m, 4H, C₆H₅), 8.08 (s, 1H, CH of pyrazole ring). Anal Calcd. (%) for C₁₅H₁₆N₂O: C, 74.97; H, 6.71; N, 11.66. Found (%): C, 75.21; H, 6.82; N, 11.38.

2.3.2.2 1-(4-Chlorophenyl)-6,6-dimethyl-6,7-dihydro-1H-indazol-4(5H)-one (3b)

White crystalline solid; yield 81 %; mp 126-128 °C. IR (cm⁻¹): 1690 (C=O). ¹H NMR (400 MHz, DMSO-d₆): δ 1.07 (s, 6H, 2CH₃), 2.37 (s, 2H, CH₂), 2.91 (s, 2H, CH₂), 7.55-7.62 (m,
4H, C₆H₅), 8.16 (s, 1H, CH of pyrazole ring). Anal Calcd. (%) for C₁₅H₁₅ClN₂O: C, 65.57; H, 5.50; N, 10.20. Found (%): C, 65.78; H, 5.12; N, 9.99.

2.3.3 General procedure for the synthesis of 4

A mixture of 3 (1.0 mmol), thiosemicarbazide (0.09 g, 1.0 mmol) and 0.4 mL conc. HCl in absolute ethanol (10 mL) was stirred at room temperature for 3 h. The reaction mixture was poured into ice cold water. The solid thus obtained was filtered, dried and recrystallized from ethanol.

2.3.3.1 2-[6,6-Dimethyl-1-phenyl-6,7-dihydro-1H-indazol-4(5H)-yliden]hydrazinecarbothioamide (4a)

White crystals; yield 90%; mp 180-82 °C. IR (cm⁻¹): 3433, 3256 (NH), 1582 (C=N), 1497 (C=C), 1288 (C=S). ¹H NMR (400 MHz, DMSO-d₆): δ 1.05 (s, 6H, 2CH₃), 2.56 (s, 2H, CH₂), 2.74 (s, 2H, CH₂), 7.38-7.39 (m, 1H, C₆H₅), 7.50-7.53 (m, 4H, C₆H₅), 7.69 (br, 1H, NH), 7.95 (br, 1H, NH), 8.09 (s, 1H, CH), 10.10 (br, 1H, NH). Anal Calcd. (%) for C₁₆H₁₉N₅S: C, 61.31; H, 6.11; N, 22.34; S, 10.23. Found (%): C, 61.17; H, 5.96; N, 21.95; S, 10.31.

2.3.3.2 2-[1-(4-Chlorophenyl)-6,6-dimethyl-6,7-dihydro-1H-indazol-4(5H)-ylidene]hydrazinecarbothioamide (4b)

White crystals; yield 90%; mp 214-16 °C. IR (cm⁻¹): 3433, 3256 (NH), 1582 (C=N), 1497 (C=C), 1288 (C=S). ¹H NMR (400 MHz, DMSO-d₆): δ 1.03 (s, 6H, 2CH₃), 2.75 (s, 2H, CH₂), 2.93 (s, 2H, CH₂), 7.50-7.56 (m, 4H, C₆H₅), 7.79 (br, 1H, NH), 8.12 (br, 1H, NH), 8.17 (s, 1H, CH), 10.20 (br, 1H, NH). Anal Calcd. (%) for C₁₆H₁₈ClN₅S: C, 55.24; H, 5.22; N, 20.13; S, 9.22. Found (%): C, 55.46; H, 5.27; N, 20.36; S, 9.43.

2.3.4 General procedure for the synthesis of 5 and 6

A mixture of thiosemicarbazone 4 (1.0 mmol), chloroacetic acid / 2-bromopropionic acid or 3-chloropropionic acid (2.5 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. DCU was removed by filtration and the filtrate was concentrated to dryness under reduced pressure and the residue was taken up 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.

2.3.4.1 (E)-2-[{(E)-6,6-Dimethyl-1-phenyl-6,7-dihydro-1H-indazol-4(5H)-
ylidene)hydrazono]thiazolidin-4-one (5a)

Yellow crystals; yield 72 %; mp 190-92 °C. IR (cm⁻¹): 3742 (NH), 1710 (N=C=O), 1620 (C=N). \(^1\)H NMR (400 MHz, DMSO-d₆): δ 1.05 (s, 6H, 2CH₃), 2.14 (s, 2H, CH₂), 2.47 (s, 2H, CH₂), 3.77 (s, 2H, SCH₂), 7.38-7.52 (m, 5H, C₆H₅), 8.57 (s, 1H, CH), 11.76 (br, 1H, NH). \(^13\)C NMR (100 MHz, DMSO-d₆): δ 173.1 (C=O), 159.4 (C=N), 154.4 (C=N), 142.8, 142.4, 138.5, 128.8, 127.2, 123.2, 113.6 (C₆H₅), 44.8, 36.9, 33.4, 32.8, 27.4. MS, m/z 354.1 (M+H⁺, 100%). Anal Calcd. (%) for C₁₈H₁₉N₅O₅S: C, 61.17; H, 5.42; N, 19.81; S, 9.07. Found (%): C, 61.49; H, 5.29; N, 19.61; S, 9.31.

2.3.4.2 (E)-2-[(E)-6,6-Dimethyl-1-phenyl-6,7-dihydro-1H-indazol-4(5H)-
ylidene)hydrazono]-5-methylthiazolidin-4-one (5b)

White crystals; yield 75 %; mp 208-10 °C. IR (cm⁻¹): 3342 (NH), 1705 (N=C=O), 1610 (C=N). \(^1\)H NMR (400 MHz, DMSO-d₆): δ 0.99 (s, 6H, 2CH₃), 1.51-1.53 (d, 3H, CH₃, \(J=7.2\) Hz), 2.41 (s, 2H, CH₂), 2.73 (s, 2H, CH₂), 4.04-4.09 (q, 1H, H₂A, \(J=7.0\) Hz, 7.2 Hz), 7.47-7.51 (m, 4H, C₆H₅), 8.52 (s, 1H, CH), 11.69 (br, 1H, NH). \(^13\)C NMR (100 MHz, DMSO-d₆): δ 176.3 (C=O), 158.1 (C=N), 154.2 (C=N), 143.0, 142.4, 138.6, 129.8, 127.3, 123.3, 113.6
(C\textsubscript{6}H\textsubscript{5}), 44.8, 41.9, 36.8, 33.5, 27.4, 18.9. MS, m/z 368.1 (M+H\textsuperscript{+}, 100 \%). Anal Calcd. (%) for C\textsubscript{19}H\textsubscript{21}N\textsubscript{5}O\textsubscript{5}: C, 62.10; H, 5.76; N, 19.06; S, 8.73. Found (%): C, 62.23; H, 5.81; N, 18.96; S, 8.83.

2.3.4.3 \((E)-2-[(E)-\{1-(4-Chlorophenyl)-6,6-dimethyl-6,7-dihydro-1H-indazol-4(5H)-ylidene]hydrazono\}thiazolidin-4-one (5c)

Yellow crystalline solid; yield 72 \%; mp 198-200 °C. IR (cm\textsuperscript{-1}): 3742 (NH), 1715 (N-C=O), 1620 (C=N). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): δ 1.03 (s, 6H, 2CH\textsubscript{3}), 2.68 (s, 2H, CH\textsubscript{2}), 2.70 (s, 2H, CH\textsubscript{2}), 3.79 (s, 2H, SCH\textsubscript{2}), 7.43-7.45 (m, 4H, C\textsubscript{6}H\textsubscript{5}), 8.03 (br, 1H, NH), 8.10 (s, 1H, NH). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): δ 173.4 (C=O), 162.6, 160.8, 157.3 (C=N), 143.5, 142.7, 137.6, 137.3, 133.17, 129.4, 124.9, 117.6 (C\textsubscript{6}H\textsubscript{5}), 45.4, 39.4, 39.2, 37.6, 36.5, 34.0, 33.9, 31.4, 28.4, 27.9. MS, m/z 388.1 (M+H\textsuperscript{+}, 100 \%). Anal Calcd. (%) for C\textsubscript{18}H\textsubscript{18}ClN\textsubscript{5}OS: C, 55.74; H, 4.68; N, 18.06; S, 8.27. Found (%): C, 55.61; H, 4.78; N, 18.21; S, 8.34.

2.3.4.4 \((E)-2-[(E)-\{1-(4-Chlorophenyl)-6,6-dimethyl-6,7-dihydro-1H-indazol-4(5H)-ylidene]hydrazono\}5-methylthiazolidin-4-one (5d)

White crystals; yield 75 \%; mp 194-96 °C. IR (cm\textsuperscript{-1}): 3342 (NH), 1705 (N-C=O), 1610 (C=N). \textsuperscript{1}H NMR (400 MHz, DMSO-d\textsubscript{6}): δ 1.04 (s, 6H, 2CH\textsubscript{3}), 1.56-1.58 (d, 3H, CH\textsubscript{3}, J= 6.9 Hz), 2.45 (s, 2H, CH\textsubscript{2}), 2.75 (s, 2H, CH\textsubscript{2}), 4.03-4.08 (q, 1H, H\textsubscript{A}, J= 7.1 Hz, 6.9 Hz), 7.52-7.53 (d, 4H, C\textsubscript{6}H\textsubscript{5}, J= 5.0 Hz), 8.57 (s, 1H, CH), 11.68 (br, 1H, NH). \textsuperscript{13}C NMR (100 MHz, DMSO-d\textsubscript{6}): δ 176.0 (C=O), 158.1 (C=N), 154.2 (C=N), 143.8, 142.4, 138.6, 129.8, 127.3, 123.3, 113.6 (C\textsubscript{6}H\textsubscript{5}), 44.8, 41.9, 36.8, 33.5, 27.4, 18.9. MS, m/z 402.1 (M+H\textsuperscript{+}, 100 \%). Anal Calcd. (%) for C\textsubscript{19}H\textsubscript{20}ClN\textsubscript{5}OS: C, 56.78; H, 5.02; N, 17.43; S, 7.98. Found (%): C, 56.78; H, 4.88; N, 17.39; S, 7.92.
2.3.4.5 \((E)\)-2-[[\((E)\)-\{6,6-Dimethyl-1-phenyl-6,7-dihydro-1H-indazol-4(5H)-ylidene]hydrazono\}-1,3-thiazinan-4-one (6a)

Light yellow crystals; yield 55 %; mp 218-20 °C. IR (cm\(^{-1}\)): 3241 (NH), 1690 (N-C=O), 1595 (C=N). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \(\delta\) 1.02 (s, 6H, 2CH\(_3\)), 2.53 (m, 2H, CH\(_2\)), 2.77 (m, 4H, CH\(_2\)), 3.07 (s, 2H, CH\(_2\)), 7.50 (s, 1H, C\(_6\)H\(_5\)), 7.52-7.57 (m, 4H, C\(_6\)H\(_5\)), 8.74 (s, 1H, CH), 11.13 (br, 1H, NH). \(^{13}\)C NMR (100 MHz, DMSO-d\(_6\)): \(\delta\) 169.9 (C=O), 154.9 (C=N), 154.2 (C=N), 142.9, 142.9, 138.7, 129.0, 129.0, 127.3, 123.3, 122.7, 113.54 (C\(_6\)H\(_5\)), 44.9, 36.9, 33.9, 33.4, 27.4, 21.9. MS, m/z 368.1 (M+H\(^+\), 100 %). Anal Calcd. for 

\[\text{C}_{19}\text{H}_{21}\text{N}_{5}\text{OS}\]: C, 62.10; H, 5.76; N, 19.06; S, 8.73. Found (%): C, 61.47; H, 5.41; N, 18.91; S, 8.43.

2.3.4.6 \((E)\)-2-[[\((E)\)-\{1-(4-Chlorophenyl)-6,6-dimethyl-6,7-dihydro-1H-indazol-4(5H)-ylidene]hydrazono\}-1,3-thiazinan-4-one (6b)

Light yellow crystals; yield 55 %; mp 210-12 °C. IR (cm\(^{-1}\)): 3265 (NH), 1685 (N-C=O), 1605 (C=N). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \(\delta\) 1.04 (s, 6H, 2CH\(_3\)), 2.41 (m, 2H, CH\(_2\)), 2.75-2.78 (m, 4H, CH\(_2\)), 3.06 (s, 2H, CH\(_2\)), 7.51-7.58 (m, 4H, C\(_6\)H\(_5\)), 8.74 (s, 1H, CH), 11.11 (br, 1H, NH). \(^{13}\)C NMR (100 MHz, DMSO-d\(_6\)): \(\delta\) 169.9 (C=O), 155.2 (C=N), 154.0 (C=N), 143.1, 143.1, 137.5, 132.0, 129.2, 129.1, 124.8, 113.8, (C\(_6\)H\(_5\)), 44.9, 36.8, 33.9, 33.4, 27.4, 21.9. MS, m/z 402.1 (M+H\(^+\), 100 %). Anal Calcd. for 

\[\text{C}_{19}\text{H}_{20}\text{ClN}_{5}\text{OS}\]: C, 56.78; H, 5.02; N, 17.43; S, 7.98. Found (%): C, 56.96; H, 5.12; N, 17.56; S, 8.26.

2.3.5 General procedure for the synthesis of 7

A mixture of 4 (0.5 mmol) and phenacyl bromides (0.5 mmol) in 5.0 mL ethanol was stirred at room temperature for 15 minutes. The separated solid was filtered, dried and recrystallized from ethanol.
2.3.5.1 \((E)\)-2-[2-{6,6-Dimethyl-1-phenyl-6,7-dihydro-1H-indazol-4(5H)-ylidene}hydrazinyl]-4-phenylthiazole (7a)

Orange coloured crystals; yield 80 %; mp 208-10 °C. IR (cm\(^{-1}\)): 3112 (NH), 1601 (C=N), 1494 (C=C). \(\text{\(^1\)H NMR (400 MHz, DMSO-\text{d}_6): } \delta 1.09 \text{ (s, 6H, } 2\text{CH}_3\text{)}, 2.63 \text{ (s, 2H, } \text{CH}_2\text{)}, 2.77 \text{ (s, 2H, CH}, \text{CH}_2\text{)}, 7.22 \text{ (s, 1H, CH of thiazole ring), 7.35-7.46 \text{ (m, 4H, } C_6H_5\text{)}, 7.51-7.59 \text{ (m, 4H, } C_6H_5\text{)}, 7.79-7.81 \text{ (m, 2H, } C_6H_5\text{)}, 8.01 \text{ (s, 1H, CH)}. \text{MS, m/z 414.2 (M+H\(^+\), 100 %). Anal Calcd. (%)} \text{ for } C_{24}H_{23}N_5S: C, 69.71; H, 5.61; N, 16.94; S, 7.75. Found (%): C, 69.88; H, 5.78; N, 17.12; S, 7.92.

2.3.5.2 \((E)\)-4-[4-Chlorophenyl]-2-[2-{6,6-dimethyl-1-phenyl-6,7-dihydro-1H-indazol-4(5H)-ylidene}hydrazinyl]thiazole (7b)

Yellow solid; yield 78 %; mp 212-15 °C. IR (cm\(^{-1}\)): 3112 (NH), 1601 (C=N), 1494 (C=C), 728 (C-Cl). \(\text{\(^1\)H NMR (400 MHz, DMSO-\text{d}_6): } \delta 1.08 \text{ (s, 6H, } 2\text{CH}_3\text{)}, 2.60 \text{ (s, 2H, } \text{CH}_2\text{)}, 2.77 \text{ (s, 2H, CH}_2\text{)}, 7.13 \text{ (s, 1H, CH of thiazole ring), 7.38-7.40 \text{ (m, 3H, } C_6H_5\text{)}, 7.52-7.53 \text{ (m, 4H, } C_6H_5\text{)}, 7.80-7.82 \text{ (m, 2H, } C_6H_5\text{)}, 7.94 \text{ (s, 1H, CH), 8.00 (br, 1H, NH). Anal Calcd. (%)} \text{ for } C_{24}H_{22}ClN_5S: C, 64.35; H, 4.95; N, 15.63; S, 7.16. Found (%): C, 64.48; H, 5.19; N, 15.88; S, 7.02.

2.3.5.3 \((E)\)-2-[2-{6,6-Dimethyl-1-phenyl-6,7-dihydro-1H-indazol-4(5H)-ylidene}hydrazinyl]-4-(4-nitrophenyl)thiazole (7c)

Orange solid; yield 72 %; mp 210-12 °C. IR (cm\(^{-1}\)): 3342 (NH), 1641 (C=N), 1558, 1328 (NO\(_2\)). \(\text{\(^1\)H NMR (400 MHz, DMSO-\text{d}_6): } \delta 1.09 \text{ (s, 6H, } 2\text{CH}_3\text{)}, 2.57 \text{ (s, 2H, } \text{CH}_2\text{)}, 2.77 \text{ (s, 2H, CH}_2\text{)}, 7.43 \text{ (s, 1H, } C_6H_5\text{)}, 7.52 \text{ (s, 1H, CH of thiazole ring), 7.53 \text{ (m, 4H, } C_6H_5\text{)}, 8.01 \text{ (s, 1H, CH), 8.08-8.09 \text{ (d, 2H, } C_6H_4\text{, J= 6.9 Hz), 8.24-8.26 \text{ (d, 2H, } C_6H_4\text{, J= 8.9 Hz). Anal Calcd. (%)} \text{ for } C_{24}H_{22}N_6O_2S: C, 62.86; H, 4.84; N, 18.33; S, 6.99. Found (%): C, 62.57; H, 4.88; N, 18.42; S, 6.88.
2.3.5.4 (E)-2-[2-{1-(4-Chlorophenyl)-6,6-dimethyl-6,7-dihydro-1H-indazol-4(5H)-ylidene}hydrazinyl]-4-phenylthiazole (7d)

Black coloured compound; yield 80 %; mp 190-192 °C. IR (cm⁻¹): 3115 (NH), 1610 (C=N), 1501 (C=C). ¹H NMR (400 MHz, DMSO-d₆): δ 0.90 (s, 6H, 2CH₃), 2.63 (s, 2H, CH₂), 2.79 (s, 2H, CH₂), 7.14 (s, 1H, CH of thiazole ring), 7.38-7.49 (m, 4H, C₆H₅), 7.50-7.54 (m, 4H, C₆H₅), 7.70-7.71 (m, 1H, C₆H₅), 8.02 (s, 1H, CH). Anal Calcd. (%) for C₂₄H₂₂ClN₅S: C, 64.35; H, 4.95; N, 15.63; S, 7.16. Found (%): C, 64.55; H, 5.13; N, 15.78; S, 7.32.

2.3.5.5 (E)-4-{4-Chlorophenyl}-2-[2-{1-(4-chlorophenyl)-6,6-dimethyl-6,7-dihydro-1H-indazol-4(5H)-ylidene}hydrazinyl]thiazole (7e)

Yellow coloured compound; yield 80 %; mp 202-204 °C. IR (cm⁻¹): 3118 (NH), 1615 (C=N), 1510 (C=C). ¹H NMR (400 MHz, DMSO-d₆): δ 1.03 (s, 6H, 2CH₃), 2.49 (s, 2H, CH₂), 2.69 (s, 2H, CH₂), 7.20 (s, 1H, CH of thiazole ring), 7.37-7.58 (m, 4H, C₆H₅), 7.83-7.90 (m, 4H, C₆H₅), 7.93 (s, 1H, CH). Anal Calcd. (%) for C₂₄H₂₁ClN₅S: C, 59.75; H, 4.39; N, 14.52; S, 6.65. Found (%): C, 59.71; H, 4.63; N, 14.69; S, 6.59.

2.3.5.6 (E)-2-[2-{1-(4-Chlorophenyl)-6,6-dimethyl-6,7-dihydro-1H-indazol-4(5H)-ylidene}hydrazinyl]-4-(4-nitrophenyl)thiazole (7f)

Yellow coloured compound; yield 80 %; mp > 240 °C. IR (cm⁻¹): 3120 (NH), 1615 (C=N), 1512 (C=C). ¹H NMR (400 MHz, DMSO-d₆): δ 1.04 (s, 6H, 2CH₃), 2.49 (s, 2H, CH₂), 2.71 (s, 2H, CH₂), 7.25 (s, 1H, CH of thiazole ring), 7.39-7.59 (m, 4H, C₆H₅), 7.84-7.91 (m, 4H, C₆H₅), 7.98 (s, 1H, CH). Anal Calcd. (%) for C₂₄H₂₁ClO₂S: C, 58.47; H, 4.29; N, 17.05; S, 6.50. Found (%): C, 58.63; H, 4.41; N, 16.89; S, 6.38.
2.4 4-Aryl-2-[(3aR)-3-aryl-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]thiazoles (12)

2.4.1 General procedure for synthesis of 10

To a mixture of 2-benzylidene-3,4-dihyronaphthalen-1(2H)-ones 8 (1.0 mol) and thiosemicarbazide or semicarbazide (1.0 mol) in trifluoroethanol (10 mL), 1-2 drops of conc. HCl were added and the reaction mixture was heated at 70-80°C for 2-3 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was kept overnight. A solid was obtained, that was filtered and washed with ice cold ethanol. Crystallization from 95% ethanol furnished pure compound.

2.4.1.1 (3aR)-3-Phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carbothioamide (10a)

IR (cm⁻¹): 3474, 3263 (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, H₈), 6.05-6.08 (d, 1H, H₆, J = 10.6 Hz), 7.01-7.03 (d, 2H, C₆H₅, J = 7.28 Hz), 7.16-7.35 (m, 6H, C₆H₅), 7.49 (br, 1H, NH₂), 7.81 (br, 1H, NH₂), 8.06-8.08 (d, 1H, C₆H₅, J = 7.68 Hz). ¹³C NMR (100 MHz, DMSO-d₆): δ 178.4, 156.1, 143.4, 139.8, 137.4, 130.6, 128.8, 126.8, 125.8, 124.8, 66.3, 48.2, 28.6, 27.5, 23.7, 18.3. MS, m/z 308.1 (M+H⁺, 40%).

2.4.1.2 (3aR)-3-(4-Chlorophenyl)-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carbothioamide (10b)

IR (cm⁻¹): 3435, 3212, 3119 (NH), 1598 (C=N), 1246 (C=S). ¹H NMR (400 MHz, DMSO-d₆): δ 0.81-0.85 (m, 1H, CH₂), 1.77-1.81 (m, 1H, CH₂), 2.82-2.93 (m, 2H, CH₂), 3.76-3.83 (m, 1H, H₈), 6.03-6.06 (d, 1H, H₆, J = 10.7 Hz), 7.01-7.03 (d, 2H, C₆H₅, J = 7.76 Hz), 7.17-7.66 (m, 6H, C₆H₅), 7.94 (br, 1H, NH₂), 8.03 (br, 1H, NH₂), 8.06-8.08 (d, 1H, C₆H₅, J = 7.68 Hz).
Hz). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 175.4, 156.0, 155.0, 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$^+$, 100 %).

2.4.1.3 (3αR)-3-(4-Methoxyphenyl)-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carbothioamide (10c)

IR (cm$^{-1}$): 3460, 3230, 3108 (NH), 1592 (C=N), 1249 (C=S). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 0.85-0.90 (m, 1H, CH$_2$), 1.75-1.78 (m, 1H, CH$_2$), 2.81-2.95 (m, 2H, CH$_2$), 3.72 (s, 3H, OCH$_3$), 3.75-3.82 (m, 1H, H$_B$), 5.97-6.00 (d, 1H, H$_A$, $J$ = 10.5 Hz), 6.80-7.60 (m, 7H, C$_6$H$_5$), 7.71 (br, 1H, NH$_2$), 7.90 (br, 1H, NH$_2$), 8.06-8.08 (d, 1H, C$_6$H$_5$, $J$ = 7.40 Hz). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 186.4, 175.4, 159.6, 158.2, 156.1, 142.8, 139.9, 135.7, 133.0, 132.9, 131.5, 130.5, 129.5, 128.9, 127.5, 126.8, 124.7, 113.8, 65.9, 48.3, 26.6, 23.7. MS, m/z 338.1 (M+H$^+$, 100 %).

2.4.1.4 (3αR)-7-Methoxy-3-phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carbothioamide (10d)

IR (cm$^{-1}$): 3470, 3204, 3146 (NH), 1590 (C=N), 1250 (C=S). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 0.81-0.86 (m, 1H, CH$_2$), 1.77-1.80 (m, 1H, CH$_2$), 2.54-2.56 (m, 2H, CH$_2$), 3.69-3.75 (m, 1H, H$_A$), 3.79 (s, 3H, OCH$_3$), 6.02-6.04 (d, 1H, H$_A$, $J$ = 10.5 Hz), 6.69 (d, 1H, C$_6$H$_5$, $J$ = 2.32 Hz), 6.79-6.90 (m, 1H, C$_6$H$_5$), 7.01-7.03 (d, 2H, C$_6$H$_5$, $J$ = 7.28 Hz), 7.19-7.29 (m, 3H, C$_6$H$_5$), 7.44 (br, 1H, NH$_2$), 7.70 (br, 1H, NH$_2$), 7.98-7.99 (d, 1H, C$_6$H$_5$, $J$ = 2.96 Hz); $^{13}$C NMR (DMSO-$d_6$): $\delta$ 178.3, 174.9, 161.2, 159.9, 156.2, 155.0, 147.8, 143.5, 142.0, 141.5, 137.5, 128.2, 126.8, 125.7, 124.4, 119.1, 113.4, 11.9, 69.4, 66.1, 56.2, 48.3, 29.2, 27.3, 25.6, 23.7, 21.3, 18.3. MS, m/z 338.1 (M+H$^+$, 100 %).
2.4.1.5 (3aR)-3-(4-Chlorophenyl)-7-methoxy-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carbothioamide (10e)

IR (cm⁻¹): 3441, 3215, 3125 (NH), 1602 (C=N), 1276 (C=S). ¹H NMR (400 MHz, DMSO-d₆): δ 0.79-0.83 (m, 1H, CH₂), 1.76-1.79 (m, 1H, CH₂), 2.75-2.91 (m, 2H, CH₂), 3.70-3.78 (m, 1H, H₆), 3.80 (s, 3H, OCH₃), 6.00-6.03 (d, 1H, H₆, J = 10.6 Hz), 6.71-6.76 (m, 1H, C₆H₅), 6.83-6.86 (m, 1H, C₆H₅), 7.00-7.02 (d, 2H, C₆H₄, J = 7.88 Hz), 7.24-7.33 (m, 2H, C₆H₅), 7.54 (br, 1H, NH₂), 7.91 (br, 1H, NH₂), 7.98-7.99 (d, 1H, C₆H₄, J = 3.72 Hz). ¹³C NMR (100 MHz, DMSO-d₆): δ 175.0, 161.3, 156.1, 142.0, 136.5, 131.8, 128.1, 127.5, 126.6, 119.0, 113.5, 112.7, 65.5, 48.2, 28.9, 23.8. MS, m/z 372.1 (M+H⁺, 100 %).

2.4.1.6 (3aR)-7-Methoxy-3-(4-methoxyphenyl)-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carbothioamide (10f)

IR (cm⁻¹): 3498, 3247, 3122 (NH), 1595 (C=N), 1267 (C=S). ¹H NMR (400 MHz, DMSO-d₆): δ 0.80-0.87 (m, 1H, CH₂), 1.86-1.90 (m, 1H, CH₂), 2.86-2.94 (m, 2H, CH₂), 3.70-3.76 (m, 1H, H₆), 3.77 (s, 3H, OCH₃), 3.79 (s, 3H, OCH₃), 6.29-6.34 (d, 1H, H₆, J = 10.8 Hz), 6.74-6.80 (m, 1H, C₆H₅), 6.84-7.24 (m, 6H, Ar), 7.79 (br, 1H, NH₂), 8.81 (s, 1H, NH₂). ¹³C NMR (100 MHz, DMSO-d₆): δ 178.3, 159.9, 147.8, 141.7, 126.7, 124.5, 112.9, 54.9, 29.2, 25.6, 21.3. MS, m/z 368.2 (M+H⁺, 30 %).

2.4.1.7 (3aR)-3-(4-Methoxyphenyl)-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carboxamide (10g)

IR (cm⁻¹): 3483, 3276, 3215 (NH), 1684 (C=O), 1571 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 0.81-0.85 (m, 1H, CH₂), 1.72-1.76 (m, 1H, CH₂), 2.87-2.92 (m, 1H, CH₂), 3.15-3.19 (m, 1H, CH₂), 3.36-3.46 (m, 1H, H₆), 3.79 (s, 3H, OCH₃), 5.46-5.49 (d, 1H, H₆, J = 10.9 Hz), 6.39 (br, 2H, NH₂), 6.81-6.83 (d, 2H, C₆H₅, J = 8.76 Hz), 6.86-6.89 (m, 2H, C₆H₅), 6.90-6.93 (m, 2H, C₆H₅), 7.89-7.91 (m, 1H, C₆H₅), 7.98-8.00 (m, 1H, C₆H₅). ¹³C NMR (100 MHz, DMSO-d₆): δ 158.3, 156.9, 154.5, 152.0, 151.5, 139.0, 138.9, 134.8, 130.1, 129.6,
128.9, 127.1, 126.9, 124.1, 113.6, 99.4, 67.4, 62.4, 48.3, 28.7, 26.9, 23.4. MS, m/z 322.2 (M+H⁺, 98%).

2.4.1.8 (3αR)-3-(4-Chlorophenyl)-7-methoxy-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carboxamide (10h)

IR (cm⁻¹): 3433, 3209, 3147 (NH), 1720 (C=O), 1623 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 0.80-0.85 (m, 1H, CH₂), 1.81-1.86 (m, 1H, CH₂), 2.18-2.22 (m, 1H, CH₂), 2.87-2.91 (m, 1H, CH₂), 3.10-3.11 (m, 1H, H₈), 3.79 (s, 3H, OCH₃), 4.79-4.77 (d, 1H, H₇, J = 11.2 Hz), 6.35 (br, 2H, NH₂), 6.73-6.74 (d, 1H, C₆H₅, J = 2.40 Hz), 6.81-6.84 (m, 1H, C₆H₅), 7.33 (s, 4H, C₆H₅), 7.82-7.84 (d, 1H, C₆H₅, J = 8.68 Hz). ¹³C NMR (100 MHz, DMSO-d₆): δ 160.5, 157.0, 152.0, 141.7, 128.1, 127.4, 125.8, 119.6, 113.2, 67.1, 55.3, 54.9. MS, m/z 356.2 (M+H⁺, 100%).

2.4.2 General procedure for synthesis of 12

Method 1.

A mixture of 2-benzylidene-1-tetralones 8 (1.0 mol), thiosemicarbazide (1.0 mol) and 1-2 drops of conc. HCl in trifluoroethanol (10 mL) was heated at 80 °C under stirring conditions. After two hour, substituted phenacyl bromide (1.0 mol) was added to the reaction mixture and continued heating and stirring at the same temperature for additional 10-15 min. The reaction mixture was then left overnight and filtered the crystalline solid obtained. Recrystallization from ethanol afforded pure compound 12.

Method 2.

A mixture of 10a-d (0.5 mol) and substituted phenacyl bromide (0.5 mol) was grinded at room temperature for 5-10 minutes. The mixture was then triturated with ethanol and filtered the solid thus obtained. Recrystallization from ethanol gives pure compound 12.
2.4.2.1 4-Phenyl-2-[(3aR)-3-phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]thiazole (12a)

IR (cm\(^{-1}\)): 1612 (C=N), 1543 (C=C). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \(\delta\) 0.98-1.02 (m, 1H, CH\(_2\)), 1.80-1.83 (m, 1H, CH\(_2\)), 2.84-2.96 (m, 2H, CH\(_2\)), 3.90-3.95 (m, 1H, H\(_B\)), 5.91-5.94 (d, 1H, H\(_A\), J = 11.04 Hz), 7.08 (s, 1H, CH of thiazole ring), 7.13-7.15 (d, 1H, C\(_6\)H\(_5\), J = 7.20 Hz), 7.18-7.35 (m, 10H, C\(_6\)H\(_5\)), 7.54-7.59 (m, 1H, C\(_6\)H\(_5\)), 7.66-7.67 (d, 2H, C\(_6\)H\(_5\), J = 1.36 Hz), 8.0-8.02 (m, 1H, C\(_6\)H\(_5\)). MS, m/z 408.2 (M+H\(^+\), 100 %).

2.4.2.2 4-(4-Chlorophenyl)-2-[(3aR)-3-phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]thiazole (12b)

IR (cm\(^{-1}\)): 1605 (C=N), 1558 (C=C), 748 (C-Cl). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \(\delta\) 0.94-0.98 (m, 1H, CH\(_2\)), 1.79-1.82 (m, 1H, CH\(_2\)), 2.77-2.95 (m, 2H, CH\(_2\)), 3.91-3.98 (m, 1H, H\(_B\)), 5.91-5.94 (d, 1H, H\(_A\), J = 11.04 Hz), 7.12-7.14 (d, 2H, C\(_6\)H\(_5\), J = 7.24 Hz), 7.22 (s, 1H, CH of thiazole ring), 7.21-7.33 (m, 8H, C\(_6\)H\(_5\)), 7.65 (d, 2H, C\(_6\)H\(_4\), J = 2.52 Hz), 7.98-8.01 (m, 1H, C\(_6\)H\(_5\)). MS, m/z 442.2 (M+H\(^+\), 100 %).

2.4.2.3 4-(4-Nitrophenyl)-2-[(3aR)-3-phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]thiazole (12c)

IR (cm\(^{-1}\)): 1651 (C=N), 1504 (C=C), 1558, 1355 (NO\(_2\)), 1512(C=C). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \(\delta\) 1.06-1.12 (m, 1H, CH\(_2\)), 1.82-1.86 (m, 1H, CH\(_2\)), 2.82-2.92 (m, 2H, CH\(_2\)), 3.88-3.95 (m, 1H, H\(_B\)), 5.90-5.93 (d, 1H, H\(_A\), J = 11.0 Hz), 7.15-7.21 (m, 4H, C\(_6\)H\(_5\)), 7.22-7.35 (m, 3H, C\(_6\)H\(_5\)), 7.41 (s, 1H, CH of thiazole ring), 7.43-7.45 (m, 1H, C\(_6\)H\(_5\)), 7.86 (d, 2H, C\(_6\)H\(_4\), J = 2.36 Hz), 8.05 (d, 1H, C\(_6\)H\(_5\), J = 1.36 Hz), 8.10-8.12 (d, 2H, C\(_6\)H\(_5\), J = 8.16 Hz). MS, m/z 453.1 (M+H\(^+\), 100 %).
2.4.2.4 2-[(3aR)-3-(4-Chlorophenyl)-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]-4-phenylthiazole (12d)

IR (cm\(^{-1}\)): 1615 (C=N), 1548 (C=C). \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \(\delta\) 1.00-1.05 (m, 1H, CH\(_2\)), 1.81-1.85 (m, 1H, CH\(_2\)), 2.78-2.96 (m, 2H, CH\(_2\)), 3.90-3.97 (m, 1H, H\(_A\)), 5.92-5.95 (d, 1H, H\(_A\), \(J= 11.08\) Hz), 7.10 (s, 1H, CH of thiazole ring), 7.14-7.34 (m, 9H, C\(_6\)H\(_5\)), 7.65-7.67 (d, 2H, C\(_6\)H\(_4\), \(J= 1.88\) Hz), 7.99-8.01 (d, 1H, C\(_6\)H\(_4\), \(J= 5.92\) Hz). MS, m/z 442.1 (M+H\(^+\), 100 %).

2.4.2.5 4-(4-Chlorophenyl)-2-[(3aR)-3-(4-chlorophenyl)-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]thiazole (12e)

IR (cm\(^{-1}\)): 1610 (C=N), 1559 (C=C), 749 (C-Cl). \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \(\delta\) 0.99-1.03 (m, 1H, CH\(_2\)), 1.80-1.83 (m, 1H, CH\(_2\)), 2.52-2.54 (m, 2H, CH\(_2\)), 3.91-3.93 (m, 1H, H\(_A\)), 5.90-5.93 (d, 1H, H\(_A\), \(J= 11.0\) Hz), 7.17 (s, 1H, CH of thiazole ring), 7.10-7.34 (m, 8H, C\(_6\)H\(_5\)), 7.43-7.44 (d, 1H, C\(_6\)H\(_4\), \(J= 2.44\) Hz), 7.54-7.60 (m, 1H, C\(_6\)H\(_5\)), 7.64-7.68 (m, 2H, C\(_6\)H\(_5\)), 7.92-8.01 (m, 1H, C\(_6\)H\(_5\)). MS, m/z 476.2 (M+H\(^+\), 100 %).

2.4.2.6 2-[(3aR)-3-(4-Chlorophenyl)-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]-4-(4-nitrophenyl)thiazole (12f)

IR (cm\(^{-1}\)): 1653 (C=N), 1506 (C=C), 1559, 1352 (NO\(_2\)). \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \(\delta\) 0.99-1.04 (m, 1H, CH\(_2\)), 1.82-1.85 (m, 1H, CH\(_2\)), 2.77-2.97 (m, 2H, CH\(_2\)), 3.95-4.01 (m, 1H, H\(_B\)), 5.94-5.97 (d, 1H, H\(_A\), \(J= 11.0\) Hz), 7.15-7.17 (d, 1H, C\(_6\)H\(_4\), \(J= 8.08\) Hz), 7.21-7.22 (d, 1H, C\(_6\)H\(_4\), \(J= 7.16\) Hz), 7.25-7.36 (m, 4H, C\(_6\)H\(_5\)), 7.58 (s, 1H, CH of thiazole ring), 7.90-7.92 (d, 2H, C\(_6\)H\(_4\), \(J= 8.96\) Hz), 7.98-8.01 (d, 1H, C\(_6\)H\(_4\), \(J= 6.28\) Hz), 8.15-8.19 (m, 2H, C\(_6\)H\(_5\)). MS, m/z 487.2 (M+H\(^+\), 100 %).
2.4.2.7 2-[(3aR)-7-Methoxy-3-phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]-4-phenylthiazole (12g)

IR (cm\(^{-1}\)): 1610 (C=N), 1549 (C=C). \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \(\delta\) 1.11-1.21 (m, 1H, CH\(_2\)), 1.78-1.84 (m, 1H, CH\(_2\)), 2.76-2.96 (m, 2H, CH\(_2\)), 3.72-3.79 (m, 1H, H\(_8\)), 3.81 (s, 3H, OCH\(_3\)), 5.85-5.88 (d, 1H, H\(_A\), \(J = 11.0\) Hz), 6.64 (d, 1H, C\(_6\)H\(_5\), \(J = 2.24\) Hz), 6.75 (s, 1H, CH of thiazole ring), 6.83-6.86 (m, 1H, C\(_6\)H\(_5\)), 7.14-7.29 (m, 9H, C\(_6\)H\(_5\)), 7.62-7.64 (d, 2H, C\(_6\)H\(_5\), \(J = 1.28\) Hz), 8.02-8.06 (d, 1H, C\(_6\)H\(_5\), \(J = 8.72\) Hz). MS, m/z 438.1 (M+H\(^+\), 100 %).

2.4.2.8 4-(4-Chlorophenyl)-2-[(3aR)-7-methoxy-3-phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]thiazole (12h)

IR (cm\(^{-1}\)): 1613 (C=N), 1552 (C=C), 751 (C-Cl). \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \(\delta\) 0.91-0.97 (m, 1H, CH\(_2\)), 1.71-1.81 (m, 1H, CH\(_2\)), 2.77-2.98 (m, 2H, CH\(_2\)), 3.79 (s, 3H, OCH\(_3\)), 5.86-5.93 (d, 1H, H\(_A\), \(J = 10.8\) Hz), 6.74-6.75 (d, 1H, C\(_6\)H\(_5\), \(J = 2.36\) Hz), 6.86-6.89 (m, 1H, C\(_6\)H\(_5\)), 7.11-7.13 (d, 1H, C\(_6\)H\(_5\), \(J = 7.24\) Hz), 7.18 (s, 1H, CH of thiazole ring), 7.26-7.33 (m, 4H, C\(_6\)H\(_5\)), 7.39-7.43 (t, 1H, C\(_6\)H\(_5\), \(J = 7.40\) Hz), 7.53-7.59 (m, 1H, C\(_6\)H\(_5\)), 7.65-7.67 (d, 1H, C\(_6\)H\(_5\), \(J = 1.84\) Hz), 7.91-7.93 (d, 1H, C\(_6\)H\(_5\), \(J = 8.72\) Hz). MS, m/z 472.2 (M+H\(^+\), 100 %).

2.4.2.9 2-[(3aR)-7-Methoxy-3-phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]-4-(4-nitrophenyl)thiazole (12i)

IR (cm\(^{-1}\)): 1651 (C=N), 1509 (C=C), 1559, 1355 (NO\(_2\)). \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \(\delta\) 0.92-0.98 (m, 1H, CH\(_2\)), 1.78-1.82 (m, 1H, CH\(_2\)), 2.76-2.97 (m, 2H, CH\(_2\)), 3.79 (s, 3H, OCH\(_3\)), 3.88-3.95 (m, 1H, H\(_8\)), 5.89-5.91 (d, 1H, H\(_A\), \(J = 10.8\) Hz), 6.75-6.76 (d, 1H, C\(_6\)H\(_5\), \(J = 2.40\) Hz), 6.87-6.90 (dd, 1H, C\(_6\)H\(_4\), \(J = 2.52\) Hz, \(J = 6.16\) Hz), 7.13-7.14 (d, 1H, C\(_6\)H\(_4\), \(J = 7.20\) Hz), 7.18-7.22 (t, 1H, C\(_6\)H\(_4\), \(J = 7.28\) Hz), 7.27-7.30 (t, 2H, C\(_6\)H\(_4\), \(J = 7.12\) Hz), 7.53 (s, 1H, CH of thiazole ring), 7.89-7.94 (m, 3H, C\(_6\)H\(_5\)), 8.12-8.17 (m, 2H, C\(_6\)H\(_5\)). MS, m/z 483.3 (M+H\(^+\), 100 %).
2.4.2.10 2-[(3aR)-3-(4-Chlorophenyl)-7-methoxy-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]-4-phenylthiazole (12j)

IR (cm⁻¹): 1612 (C=N), 1545 (C=C). ¹H NMR (400 MHz, DMSO-d₆): δ 0.86-1.04 (m, 1H, CH₂), 1.80-1.84 (m, 1H, CH₂), 2.79-2.98 (m, 2H, CH₂), 3.80 (s, 3H, OCH₃), 3.85-3.93 (m, 1H, H₆), 5.88-5.90 (d, 1H, H₅, J = 10.9 Hz), 6.73-6.78 (m, 1H, C₆H₄), 6.85-6.88 (dd, 1H, C₆H₄, J = 2.36 Hz, J = 6.36 Hz), 7.06 (s, 1H, CH of thiazole ring), 7.13-7.31 (m, 5H, C₆H₅), 7.41-7.43 (d, 1H, C₆H₅, J = 8.48 Hz), 7.55-7.67 (m, 1H, C₆H₅), 7.86-7.94 (dd, 1H, C₆H₅, J = 8.68 Hz, J = 8.68 Hz). MS, m/z 472.1 (M+H⁺, 100%).

2.4.2.11 4-(4-Chlorophenyl)-2-[(3aR)-3-(4-chlorophenyl)-7-methoxy-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]thiazole (12k)

IR (cm⁻¹): 1615 (C=N), 1553 (C=C), 741 (C-Cl). ¹H NMR (400 MHz, DMSO-d₆): δ 0.95-1.06 (m, 1H, CH₂), 1.80-1.83 (m, 1H, CH₂), 2.79-2.98 (m, 2H, CH₂), 3.81 (s, 3H, OCH₃), 3.84-3.91 (m, 1H, H₆), 5.86-5.88 (d, 1H, H₅, J = 10.9 Hz), 6.72-6.77 (m, 1H, C₆H₄), 6.85-6.87 (dd, 1H, C₆H₄, J = 2.32 Hz, J = 6.40 Hz), 7.09 (s, 1H, CH of thiazole ring), 7.12-7.14 (d, 1H, C₆H₄, J = 8.2 Hz), 7.27-7.30 (m, 4H, C₆H₅), 7.53-7.58 (m, 1H, C₆H₅), 7.64-7.66 (d, 2H, C₆H₄, J = 8.56 Hz), 7.86-7.94 (dd, 1H, C₆H₄, J = 8.72 Hz, J = 8.68 Hz). MS, m/z 506.1 (M+H⁺, 100%).

2.4.2.12 2-[(3aR)-3-(4-Chlorophenyl)-7-methoxy-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]-4-(4-nitrophenyl)thiazole (12l)

IR (cm⁻¹): 1652 (C=N), 1510 (C=C), 1356 (NO₂). ¹H NMR (400 MHz, DMSO-d₆): δ 1.04-1.11 (m, 1H, CH₂), 1.85-1.90 (m, 1H, CH₂), 2.72-2.80 (m, 2H, CH₂), 3.81 (s, 3H, OCH₃), 3.82-3.86 (m, 1H, H₆), 5.87-5.90 (d, 1H, H₅, J = 10.9 Hz), 6.66-6.72 (m, 1H, C₆H₄), 6.77-6.80 (dd, 1H, C₆H₄, J = 2.72 Hz, J = 6.12 Hz), 7.13-7.15 (d, 1H, C₆H₄, J = 8.32 Hz), 7.27-7.29 (d, 1H, C₆H₄, J = 8.64 Hz), 7.35 (m, 1H, C₆H₅), 7.40 (s, 1H, CH of thiazole ring), 7.87-8.25 (m, 4H, C₆H₅). MS, m/z 517.2 (M+H⁺, 100%).
2.4.3 Attempted procedure for synthesis of 13

A mixture of compound 10g (0.5 mol, R= H, R₁= 4-OMe, X= O) and phenacyl bromide (0.5 mol) in absolute ethanol was refluxed for 25-30 h. The progress of the reaction was monitored by TLC. After prolonged refluxing of 30 h, starting material was obtained.

2.5 2,5,6-Trisubstituted-5,6-dihydro-2H-pyrazolo[3,4-d]thiazoles (17)

2.5.1 General procedure for the synthesis of 14

Thiazolidin-4-ones 14 were synthesised by slight modification in the reported procedure [Srivastava et al., 2002]. To an ice cold solution of an aldehyde (1.0 mmol) and an amine (2.0 mmol) in THF (15 mL), ethyl mercaptoacetate (2.5 mmol) was added. After 5 min DCC (1.5 mmol) was added to the reaction mixture and the mixture was stirred for 40 min at room temperature. DCU was then removed by filtration and THF was removed completely under reduced pressure. The residue was extracted with ethyl acetate and organic layer was washed successively with (5%) aq. citric acid, (5%) aq. sodium bicarbonate and finally with brine. The organic layer was dried over anhyd sodium sulfate and solvent was removed under reduced pressure. The crude solid obtained was recrystallized from ethyl acetate.

2.5.1.1 2, 3-Diphenylthiazolidin-4-one (14a)

White solid; yield 85%; mp 128-30 °C. Literature [Lingampalle et al., 2010] mp 131-32 °C.

2.5.1.2 2-(4-Chlorophenyl)-3-phenylthiazolidn-4-one (14b)

White crystalline solid; yield 87%; mp 124-26 °C. Literature [Srivastava et al., 2002] mp 124-27 °C.
2.5.1.3 2, 3-Di-p-tolylthiazolidin-4-one (14c)

White solid; yield 86%; mp 112-14 °C. Literature [Lingampalle et al., 2010] mp 119-20 °C.

2.5.2 General procedure for the synthesis of 15

A mixture of thiazolidin-4-one 14 (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 Na₂SO₄. The excess ethyl acetate was then removed under reduced pressure and the solid obtained was filtered and recrystallized from ethanol.

2.5.2.1 5-[[Dimethylamino)methylene]-2,3-diphenylthiazolidin-4-one (15a)

White crystalline solid; yield 85 %; mp 198-200 °C. IR (cm⁻¹): 1697 (C=O), 1490 (C=C). ¹H NMR (400 MHz, DMSO-d₆): δ 3.02 (s, 6H, NMe₂), 6.40 (s, 1H, H-2), 7.03-7.07 (t, 1H, C₆H₅, J=7.32 Hz), 7.19-7.28 (m, 6H, C₆H₅), 7.31-7.33 (m, 4H, C₆H₅ and =CH). Anal Calcd. (%) for C₁₈H₁₈N₂O₅: C, 69.65; H, 5.84; N, 9.02; S, 10.33. found (%): C, 69.86; H, 5.95; N, 9.14; S, 10.48.

2.5.2.2 2-(4-Chlorophenyl)-5-[[dimethylamino)methylene]-3-phenylthiazolidin-4-one (15b)

Yellow solid; yield 90 %; mp 166-68 °C. IR (cm⁻¹): 1705 (C=O), 1495 (C=C). ¹H NMR (400 MHz, CDCl₃): δ 3.03 (s, 6H, NMe₂), 6.10 (s, 1H, H-2), 7.10 (m, 1H, C₆H₅), 7.20-7.27 (m, 8H, C₆H₅), 7.34 (s, 1H, =CH). MS, m/z 345.1 (M+H⁺, 100 %). Anal Calcd. (%) For: C₁₈H₁₉ClN₂O₅: C, 62.69; H, 4.97; N, 8.12; S, 9.30. found: C, 62.86; H, 5.04; N, 8.32; S, 9.48.
2.5.2.3 5-[(Dimethylamino)methylene]-2,3-di-p-tolylthiazolidin-4-one (15c)

White solid; yield 90 %; mp 148-50 °C. IR (cm⁻¹): 1695 (C=O), 1485 (C=C). ¹H NMR (400 MHz, DMSO-d₆): δ 2.22 (s, 3H, CH₃), 2.25 (s, 3H, CH₃), 3.00 (s, 6H, NMe₂), 6.33 (s, 1H, H-2), 7.01-7.06 (m, 4H, C₆H₅), 7.16-7.20 (m, 5H, C₆H₅ & =CH). Anal Calcd. (%) For: C₂₀H₂₂N₂OS: C, 70.97; H, 6.55; N, 8.28; S, 9.47. found (%): C, 70.82; H, 6.68; N, 8.42; S, 9.62.

2.5.3 General procedure for the synthesis of 16

A mixture of 15 (1.0 mmol) and Lawesson’s reagent (1.0 mmol) in dry toluene (20 mL) was refluxed for 2 h. The solvent was removed under reduced pressure. The solid obtained on cooling was recrystallized from ethanol-DMF (3:1) mixture.

2.5.3.1 5-[(Dimethylamino)methylene]-2,3-diphenylthiazolidine-4-thione (16a)

Light brown solid; yield 65 %; mp 108-110 °C. IR (cm⁻¹): 1252 (C=S), 1490 (C=C). ¹H NMR (400 MHz, DMSO-d₆): δ 3.00 (s, 6H, NMe₂), 6.47 (s, 1H, H-2), 7.05-7.06 (t, 1H, C₆H₅, J=7.36 Hz), 7.20-7.28 (m, 6H, C₆H₅), 7.31-7.35 (m, 4H, C₆H₅ & =CH). MS, m/z 327.2 (M+H⁺, 100 %). Anal Calcd. (%) For: C₁₈H₁₈N₂S₂: C, 66.22; H, 5.56; N, 8.58; S, 19.64. Found (%): C, 66.46; H, 5.64; N, 8.72; S, 19.48.

2.5.3.2 2-(4-Chlorophenyl)-5-[(dimethylamino)methylene]-3-phenylthiazolidine-4-thione (16b)

Light brown solid; yield 65 %; mp 120-122 °C. IR (cm⁻¹): 1240 (C=S), 1490 (C=C). ¹H NMR (400 MHz, DMSO-d₆): δ 3.00 (s, 6H, NMe₂), 6.55 (s, 1H, H-2), 7.06 (m, 1H, C₆H₅), 7.23-7.27 (m, 3H, C₆H₅), 7.30-7.35 (m, 6H, C₆H₅ & =CH). Anal Calcd. (%) For: C₁₈H₁₇ClN₂S₂: C, 59.90; H, 4.75; N, 7.76; S, 17.77. Found (%): C, 60.01; H, 4.94; N, 7.92; S, 17.98.
2.5.3.3 5-[[Dimethylamino)methylene]-2,3-di-p-tolylthiazolidine-4-thione (16c)

Brown solid; yield 65 %; mp 158-60 °C. IR (cm\(^{-1}\)): 1210 (C=S), 1490 (C=C). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): δ 2.21 (s, 3H, CH\(_3\)), 2.23 (s, 3H, CH\(_3\)), 2.99 (s, 6H, NMe\(_2\)), 6.38 (s, 1H, H-2), 7.01-7.06 (m, 4H, C\(_6\)H\(_5\)), 7.17-7.19 (m, 5H, C\(_6\)H\(_5\) & =CH). Anal Calcd. (%) For: C\(_{20}\)H\(_{22}\)N\(_2\)S\(_2\): C, 67.76; H, 6.25; N, 7.90; S, 18.09. Found (%): C, 67.92; H, 6.40; N, 8.03; S, 18.28.

2.5.4 General procedure for the synthesis of 17

A solution of phenyl hydrazine hydrochloride (0.75 mmol), in ethanol (25 mL) was added drop wise with stirring to a solution of compound 16 (0.5 mmol) in DMF (5.0 mL). The reaction mixture was refluxed for 10-12 h. Evolution of hydrogen sulphide gas continues for 5-6 h. The progress of reaction was monitored by TLC. The reaction mixture was then cooled to room temperature and poured in to ice cold water and separated solid was filtered, dried and recrystallized from ethanol.

2.5.4.1 2,5,6-Triphenyl-5,6-dihydro-2H-pyrazolo[3,4-d]thiazole (17a)

Orange solid; yield 40 %; mp 188-90 °C. IR (cm\(^{-1}\)): 1659 (C=N), 1489 (C=C). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): δ 6.80 (s, 1H, H-5), 7.18-7.22 (m, 1H, C\(_6\)H\(_5\)), 7.25-7.31 (m, 5H, C\(_6\)H\(_5\)), 7.38-7.41 (m, 2H, C\(_6\)H\(_5\)), 7.46-7.52 (m, 5H, C\(_6\)H\(_5\)), 7.78-7.81 (m, 2H, C\(_6\)H\(_5\)), 8.47 (s, 1H, =CH of pyrazole ring). \(^13\)C NMR (100 MHz, DMSO-d\(_6\)) δ: 163.7, 152.1, 137.2, 137.1, 136.7, 131.3, 129.1, 128.7, 128.6, 127.0, 126.8, 125.3, 122.2, 63.9. MS, m/z 356.1 (M+H\(^+\), 90 %). Anal Calcd. (%) For: C\(_{22}\)H\(_{17}\)N\(_3\)S: C, 74.34; H, 4.82; N, 11.82; S, 9.02. Found (%): C, 74.42; H, 5.01; N, 11.96; S, 9.18.
2.5.4.2 2-(4-Chlorophenyl)-5,6-diphenyl-5,6-dihydro-2H-pyrazolo[3,4-d]thiazole (17b)

Yellow solid; yield 44%; mp 138-40 °C. IR (cm⁻¹): 1645 (C=N), 1485 (C=C). $^1$H NMR (400 MHz, DMSO-d$_6$): δ 6.88 (s, 1H, H-5), 7.18-7.22 (m, 1H, C$_6$H$_5$), 7.25-7.36 (m, 5H, C$_6$H$_5$), 7.39-7.42 (m, 2H, C$_6$H$_5$), 7.48-7.51 (dd, 2H, C$_6$H$_5$, J= 1.16 Hz, J= 7.56 Hz), 7.55-7.58 (m, 2H, C$_6$H$_5$), 7.79-7.81 (dd, 2H, C$_6$H$_5$, J = 2.0 Hz, J= 4.8 Hz), 8.48 (s, 1H, =CH of pyrazole ring). $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ: 163.5, 150.6, 137.2, 137.0, 136.7, 136.2, 135.0, 129.5, 128.9, 128.8, 128.7, 127.1, 126.9, 125.4, 123.7, 63.9. MS, m/z 390.2 (M+H⁺, 35%). Anal Calcd. (%) For: C$_{22}$H$_{16}$ClN$_3$S: C, 67.77; H, 4.14; N, 10.78; S, 8.22. Found (%): C, 67.52; H, 4.31; N, 10.87; S, 8.38.

2.5.4.3 5,6-Diphenyl-2-(o-tolyl)-5,6-dihydro-2H-pyrazolo[3,4-d]thiazole (17c)

Red needles; yield 42%; mp 188-90 °C. IR (cm⁻¹): 1656 (C=N), 1484 (C=C). $^1$H NMR (400 MHz, DMSO-d$_6$): δ 2.60 (s, 3H, CH$_3$), 6.83 (s, 1H, H-5), 7.19-7.23 (t, 1H, C$_6$H$_5$, J= 7.52 Hz), 7.24-7.28 (m, 4H, C$_6$H$_5$), 7.30-7.35 (m, 2H, C$_6$H$_5$), 7.37-7.39 (m, 4H, C$_6$H$_5$), 7.46-7.48 (d, 2H, C$_6$H$_5$, J= 7.56 Hz), 7.58-7.60 (d, 1H, C$_6$H$_5$, J= 8.0 Hz), 8.68 (s, 1H, =CH of pyrazole ring). $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ: 163.8, 150.7, 137.7, 137.0, 136.7, 136.2, 135.0, 129.5, 128.7, 126.8, 125.4, 114.8, 63.9, 18.3. MS, m/z 370.1 (M+H⁺, 100%). Anal Calcd. (%) for: C$_{23}$H$_{16}$ClN$_3$S: C, 74.77; H, 5.18; N, 11.37; S, 8.68. Found (%): C, 74.89; H, 5.31; N, 11.51; S, 8.82.

2.5.4.4 5-(4-Chlorophenyl)-2,6-diphenyl-5,6-dihydro-2H-pyrazolo[3,4-d]thiazole (17d)

Orange solid; yield 48%; mp 156-58 °C. IR (cm⁻¹): 1652 (C=N), 1481 (C=C). $^1$H NMR (400 MHz, DMSO-d$_6$): δ 6.23 (s, 1H, H-5), 7.23-7.28 (m, 6H, C$_6$H$_5$), 7.32-7.36 (t, 2H, C$_6$H$_5$, J= 7.48 Hz), 7.45-7.48 (m, 3H, C$_6$H$_5$), 7.83-7.86 (m, 2H, C$_6$H$_5$), 8.65 (s, 1H, =CH of pyrazole ring).
ring). $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ: 163.5, 150.6, 137.2, 137.0, 136.7, 136.2, 135.0, 129.5, 128.9, 128.8, 128.7, 127.1, 126.9, 125.4, 123.7, 63.9. MS, m/z 390.4 (M+H$^+$, 21 %). Anal Calcd. (%) For: C$_{22}$H$_{18}$ClN$_3$S: C, 67.77; H, 4.14; N, 10.78; S, 8.22. Found (%): C, 67.42; H, 4.31; N, 11.01; S, 8.38.

2.5.4.5 2,5-Bis(4-chlorophenyl)-6-phenyl-5,6-dihydro-2H-pyrazolo[3,4-d]thiazole (17e)

Orange solid; yield 52 %; mp 160-62 °C. IR (cm$^{-1}$): 1654 (C=N), 1481 (C=C). $^1$H NMR (400 MHz, DMSO-d$_6$): δ 6.87 (s, 1H, H-5), 7.19-7.23 (t, 1H, C$_6$H$_5$, J = 7.40 Hz), 7.31-7.37 (m, 4H, C$_6$H$_5$), 7.43-7.49 (m, 4H, C$_6$H$_5$), 7.53-7.56 (m, 2H, C$_6$H$_5$), 7.78-7.82 (m, 2H, C$_6$H$_5$), 8.49 (s, 1H, =CH of pyrazole ring). $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ: 163.4, 150.6, 137.1, 136.5, 136.3, 136.1, 134.5, 133.7, 129.4, 129.0, 128.8, 128.7, 127.0, 125.4, 123.7, 63.1. MS, m/z 424.1 (M+H$^+$, 30 %). Anal Calcd. (%) For: C$_{22}$H$_{15}$ClN$_3$S: C, 62.27; H, 3.56; N, 9.90; S, 7.56. Found (%): C, 62.42; H, 3.71; N, 10.08; S, 7.68.

2.5.4.6 5-(4-Chlorophenyl)-6-phenyl-2-(o-tolyl)-5,6-dihydro-2H-pyrazolo[3,4-d]thiazole (17f)

Orange solid; yield 41 %; mp 152-54 °C. IR (cm$^{-1}$): 1649 (C=N), 1480 (C=C). $^1$H NMR (400 MHz, CDCl$_3$): δ 2.41 (s, 3H, CH$_3$), 6.22 (s, 1H, H-5), 7.22-7.34 (m, 11H, C$_6$H$_5$), 7.74-7.76 (d, 2H, C$_6$H$_5$, J = 8.32 Hz), 8.60 (s, 1H, =CH of pyrazole ring). $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 163.4, 150.6, 137.1, 136.5, 136.3, 136.1, 134.5, 133.7, 129.4, 129.0, 128.8, 128.7, 127.0, 125.4, 123.7, 63.1. MS, m/z 404.1 (M+H$^+$, 15 %). Anal Calcd. (%) For: C$_{23}$H$_{19}$ClN$_3$S: C, 68.39; H, 4.49; N, 10.40; S, 7.94. Found (%): C, 68.52; H, 4.71; N, 10.61; S, 8.08.
2.5.4.7 2-Phenyl-5,6-di-p-tolyl-5,6-dihydro-2H-pyrazolo[3,4-d]thiazole (17g)

Orange solid; yield 40 %; mp 128-30 °C. IR (cm⁻¹): 1652 (C=N), 1485 (C=C). \(^1\)H NMR (400 MHz, DMSO-d₆): δ 2.22 (s, 6H, 2CH₃), 6.74 (s, 1H, H-5), 7.04-7.11 (m, 4H, C₆H₅), 7.21-7.23 (m, 2H, C₆H₅), 7.27-7.32 (m, 2H, C₆H₅), 7.34-7.38 (m, 1H, C₆H₅), 7.43-7.47 (m, 2H, C₆H₅), 7.77-7.80 (m, 2H, C₆H₅), 8.44 (s, 1H, =CH of pyrazole ring). \(^13\)C NMR (100 MHz, DMSO-d₆) δ: 163.5, 152.1, 138.3, 136.9, 136.3, 134.3, 134.1, 131.4, 129.3, 129.2, 127.0, 125.3, 122.2, 63.8, 20.7, 20.5. MS, m/z 384.1 (M+H⁺, 52 %). Anal Calcd. (%) For: C₂₄H₂₁N₃S: C, 75.16; H, 5.52; N, 10.96; S, 8.36. Found (%): C, 75.32; H, 5.71; N, 11.12; S, 8.48.

2.5.4.8 2-(4-Chlorophenyl)-5,6-di-p-tolyl-5,6-dihydro-2H-pyrazolo[3,4-d]thiazole (17h)

Brown solid; yield 46 %; mp 134-36 °C. IR (cm⁻¹): 1654 (C=N), 1490 (C=C). \(^1\)H NMR (400 MHz, DMSO-d₆): δ 2.25 (s, 6H, 2CH₃), 6.79 (s, 1H, H-5), 7.05-7.10 (m, 2H, C₆H₅), 7.12-7.16 (m, 2H, C₆H₅), 7.25-7.32 (m, 2H, C₆H₅), 7.34-7.38 (m, 2H, C₆H₅), 7.40-7.48 (m, 2H, C₆H₅), 7.59-7.65 (m, 2H, C₆H₅), 8.44 (s, 1H, =CH of pyrazole ring). \(^13\)C NMR (100 MHz, DMSO-d₆) δ: 163.5, 152.3, 138.5, 136.9, 136.3, 134.5, 134.1, 131.5, 129.4, 129.3, 127.1, 125.4, 122.3, 63.9, 20.8, 20.6. MS, m/z 418.1 (M+H⁺, 10 %). Anal Calcd. (%) For: C₂₄H₂₀ClN₃S: C, 68.97; H, 4.82; N, 10.05; S, 7.67. Found (%): C, 69.18; H, 4.71; N, 10.21; S, 7.48.

2.5.4.9 2-(o-Tolyl)-5,6-di-p-tolyl-5,6-dihydro-2H-pyrazolo[3,4-d]thiazole (17i)

Orange solid; yield 40 %; mp 158-60 °C. IR (cm⁻¹): 1656 (C=N), 1484 (C=C). \(^1\)H NMR (400 MHz, DMSO-d₆): δ 2.22 (s, 3H, CH₃), 2.24 (s, 3H, CH₃), 2.59 (s, 3H, CH₃), 6.74 (s, 1H, H-5), 7.07-7.09 (d, 2H, C₆H₅, J= 8.0 Hz), 7.11-7.13 (d, 2H, C₆H₅, J= 8.32 Hz), 7.23-7.28 (m, 3H, C₆H₅), 7.31-7.33 (d, 2H, C₆H₅, J= 8.36 Hz), 7.38-7.39 (d, 2H, C₆H₅, J= 4.04
Hz), 7.57-7.59 (d, 1H, C₆H₅, J=8.0 Hz), 8.66 (s, 1H, =CH of pyrazole ring). ¹³C NMR (100 MHz, DMSO-d₆) δ: 163.5, 152.4, 138.6, 136.4, 134.5, 134.2, 131.6, 129.5, 129.2, 127.2, 125.5, 122.4, 63.8, 20.9, 20.5, 20.1. MS, m/z 398.1 (M+H⁺, 40%). Anal Calcd. (%) For: C₂₅H₂₃N₃S: C, 75.53; H, 5.83; N, 10.57; S, 8.07. Found (%): C, 75.68; H, 5.91; N, 10.71; S, 8.18.

2.5.5 General procedure for the synthesis of 19

A mixture of compound 14 (0.5 mmol), aromatic aldehyde (0.5 mmol) and sodium ethoxide (0.02 g of sodium in 2.0 mL of absolute ethanol) in dry benzene (20 mL) was heated under reflux for 10-12 h. The progress of reaction was monitored by TLC. After completion, the reaction mixture was cooled and poured in to ice cold water. The organic layer was separated and dried over fused calcium chloride. The solvent was removed under reduced pressure, filtered the solid obtained and recrystallized from ethanol.

2.5.5.1 (E)-5-(4-Chlorobenzylidene)-2,3-di-p-tolylthiazolidin-4-one (19a)

Yellow solid; yield 75 %; mp 188-90 °C. IR (cm⁻¹): 1696 (C=O). ¹H NMR (400 MHz, DMSO-d₆): δ 2.22 (s, 3H, CH₃), 2.23 (s, 3H, CH₃), 6.82 (s, 1H, H-5), 7.09-7.15 (m, 4H, C₆H₅), 7.25-7.27 (d, 2H, C₆H₅, J=8.12 Hz), 7.31-7.33 (d, 2H, C₆H₅, J=8.36 Hz), 7.52-7.54 (t, 3H, C₆H₅, J=6.0 Hz), 7.58-7.60 (t, 2H, C₆H₅ & =CH, J=2.04 Hz ). Anal Calcd. (%) For: C₂₄H₂₀ClNOS: C, 71.01; H, 4.97; N, 3.45; S, 7.90. Found (%): C, 71.22; H, 5.12; N, 3.58; S, 8.07.
2.5.5.2 *(E)-2-(4-Chlorophenyl)-5-(4-methylbenzylidene)-3-phenylthiazolidin-4-one (19b)*

Yellow solid; yield 72 %; mp 170-72 °C. IR (cm⁻¹): 1698 (C=O). ¹H NMR (400 MHz, DMSO-d₆): δ 2.36 (s, 3H, CH₃), 6.71 (s, 1H, H-5), 7.17-7.21 (t, 1H, C₆H₅, J = 7.36 Hz), 7.24-7.43 (m, 12H, C₆H₅), 7.52 (s, 1H, =CH). Anal Calcd. (%) For: C₂₃H₁₈ClNOS: C, 70.49; H, 4.63; N, 3.57; S, 8.18; found (%): C, 70.61; H, 4.87; N, 3.69; S, 8.31.

2.5.6 Attempted procedure for synthesis of 20

A mixture of 19 (0.5 mmol), phenyl hydrazine (0.75 mmol) and anhydrous sodium acetate (1.0 mmol) in absolute ethanol (15mL) was heated under reflux for 24-30 h. The progress of the reaction was monitored by TLC. Unfortunately, the reaction did not happen after 30 h and starting material was obtained. The reaction was attempted under acidic conditions (acetic acid) and basic conditions (piperidine). The starting material was obtained in all above cases.

2.6 1,4,5,9b-Tetrahydro-2H-benzo[e]indazol-2-yl)thiazol-4(5H)-ones (25)

2.6.1 General procedure for synthesis of 22

A mixture of 2-tetralone 21 (0.05 mol) and aromatic aldehyde (0.05 mol), glacial acetic acid (25 mL) and conc. HCl (15 mL) was kept at 0-5 ⁰C for 24 h (for compound 22a time is 36 h). Filtered the yellow solid obtained, washed with petroleum ether (60-80⁰C) and recrystallized from ethanol.

2.6.1.1 *(E)-1-Benzylidene-3,4-dihydropthalen-2(1H)-one (22a)*

Yellow solid; yield 88 %; mp 114-116 ⁰C. Literature [Pal et al., 1994] mp 120 ⁰C.
2.6.1.2 (E)-1-(4-Chlorobenzylidene)-3,4-dihyronaphthalen-2(1H)-one (22b)

Yellow solid; yield 78%; mp 90-92 °C. IR (cm⁻¹): 1696 (C=O). ¹H NMR (400 MHz, DMSO-d₆): δ 2.55-2.57 (t, 2H, CH₂, J= 3.48 Hz), 3.01-3.04 (t, 2H, CH₂, J= 6.52 Hz), 7.02-7.06 (m, 1H, C₆H₅), 7.19-7.25 (m, 2H, C₆H₅), 7.31-7.35 (m, 3H, C₆H₅), 7.39-7.41 (d, 2H, C₆H₅, J= 8.44 Hz), 7.49 (s, 1H, =CH). Anal Calcd. (%) for C₁₇H₁₃ClO: C, 75.98; H, 4.88. Found (%): C, 76.14; H, 5.08.

2.6.1.3 (E)-1-(4-Nitrobenzylidene)-3,4-dihyronaphthalen-2(1H)-one (22c)

Yellow solid; yield 85%; mp 120-122 °C. IR (cm⁻¹): 1701 (C=O). ¹H NMR (400 MHz, DMSO-d₆): δ 2.60-2.63 (t, 2H, CH₂, J= 6.64 Hz), 3.07-3.10 (t, 2H, CH₂, J= 6.52 Hz), 7.0-7.04 (t, 1H, C₆H₅, J= 7.28 Hz), 7.12-7.14 (d, 1H, C₆H₅, J= 7.48 Hz), 7.24-7.28 (t, 1H, C₆H₅, J= 7.40 Hz), 7.33-7.35 (d, 1H, C₆H₅, J= 7.40 Hz), 7.58-7.60 (m, 3H, C₆H₅ & =CH), 8.10-8.11 (d, 2H, C₆H₅, J= 8.92 Hz). Anal Calcd. (%) for C₁₇H₁₃NO₃: C, 73.11; H, 4.69. Found (%): C, 73.24; H, 4.88.

2.6.2 General procedure for synthesis of 23

Method 1.

To a mixture of 2-tetralone 21 (0.003 mol), aromatic aldehyde (0.003 mol) and thiosemicarbazide (0.003 mol) in ethanol (10 mL), a catalytic amount of conc. HCl (4-5 drops) was added. The reaction mixture was then refluxed for 6 h and kept overnight. A yellow crystalline solid thus separated was filtered and recrystallized from ethanol.

Method 2.

A mixture of arylidene-2-tetralone 22 (0.001 mol), thiosemicarbazide (0.001 mol), ethanol (20 mL) and catalytic amount of conc. HCl (4-5 drops) was refluxed for 3
h. After cooling, the reaction mixture was poured into ice cold water. The solid obtained was filtered, dried and recrystallized from ethanol.

2.6.2.1 (15,9bR)-1-Phenyl-1,4,5,9b-tetrahydro-2H-benzo[e]indazole-2-carbothioamide (23a)

Light yellow solid; yield 75 %; mp 192-94 °C. IR (cm⁻¹): 3427, 3371, 3262 (NH), 1646 (C=N), 1374 (C=S). ¹H NMR (400 MHz, DMSO-d₆) δ: 2.64-2.73 (m, 1H, CH₂), 2.89-3.00 (m, 2H, CH₂), 3.09-3.16 (m, 1H, CH₂), 4.31-4.33 (d, 1H, 9b-H, J = 5.84 Hz), 5.86-5.87 (d, 1H, 1-H, J = 5.92 Hz), 7.22-7.43 (m, 9H, C₆H₅), 7.55 (br, 1H, NH₂), 7.84 (br, 1H, NH₂). ¹³C NMR (100 MHz, DMSO-d₆) δ: 177.1, 160.0, 143.5, 135.8, 128.4, 127.0, 126.9, 125.9, 124.6, 66.9, 59.0, 29.1, 23.5. MS, m/z 308.2 (M+H⁺, 100 %). Anal Calcd. (%) For: C₁₈H₁₇N₃S: C, 70.33; H, 5.57; N, 13.67; S, 10.43. Found (%): C, 70.54; H, 5.69; N, 13.71; S, 10.63.

2.6.2.2 (15,9bR)-1-(4-Chlorophenyl)-1,4,5,9b-tetrahydro-2H-benzo[e]indazole-2-carbothioamide (23b)

Light brown solid; yield 65 %; mp 184-86 °C. IR (cm⁻¹): 3427, 3371 (NH), 1646 (C=N), 1374 (C=S). ¹H NMR (400 MHz, DMSO-d₆) δ: 2.65-2.73 (m, 1H, CH₂), 2.88-3.01 (m, 2H, CH₂), 3.07-3.16 (m, 1H, CH₂), 4.33-4.34 (d, 1H, 9b-H, J = 6.20 Hz), 5.83-5.84 (d, 1H, 1-H, J = 6.28 Hz), 7.20-7.25 (m, 2H, C₆H₅), 7.27-7.31 (m, 1H, C₆H₅), 7.31-7.42 (m, 5H, C₆H₅), 7.51 (br, 1H, NH₂), 7.92 (br, 1H, NH₂). ¹³C NMR (100 MHz, DMSO-d₆) δ: 178.2, 163.7, 143, 136.1, 132.5, 128, 127.1, 126.8, 124.4, 66.2, 58.1, 28.7, 23.2. MS, m/z 342.1 (M+H⁺, 30 %). Anal Calcd. For: C₁₈H₁₆ClN₃S: C, 63.24; H, 4.72; N, 12.29; S, 9.38. Found (%): C, 63.54; H, 4.91; N, 12.41; S, 9.53.
2.6.2.3 (1S,9bR)-1-(4-Nitrophenyl)-1,4,5,9b-tetrahydro-2H-benzo[e]indazole-2-carbothioamide (23c)

Light brown solid; yield 65%; mp 148-50 °C. IR (cm\(^{-1}\)):

3433, 3209 (NH), 1636 (C=N), 1372 (C=S). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)) \(\delta\): 2.75-2.80 (m, 1H, CH\(_2\)), 2.90-2.94 (m, 1H, CH\(_2\)), 3.02-3.16 (m, 1H, CH\(_2\)), 4.36-4.38 (d, 1H, 9b-H, \(J= 6.80 \) Hz), 5.94-5.96 (d, 1H, 1-H, \(J= 6.76 \) Hz), 7.21-7.24 (t, 1H, C\(_6\)H\(_5\), \(J= 6.52 \) Hz), 7.28-7.32 (t, 1H, C\(_6\)H\(_5\), \(J= 6.80 \) Hz), 7.37-7.39 (d, 2H, C\(_6\)H\(_5\), \(J= 7.60 \) Hz), 7.64-7.66 (d, 2H, C\(_6\)H\(_5\), \(J= 8.72 \) Hz), 7.87-7.90 (br, 2H, NH\(_2\)). 13C NMR (100 MHz, DMSO-d\(_6\)) \(\delta\): 178.6, 162.4, 143.7, 136.3, 129, 128.2, 127.1, 125.4, 68.9, 60.3, 28.4. MS, m/z 353.1 (M+H\(^+\), 20%). Anal Calcd. (%): C\(_{18}\)H\(_{16}\)N\(_4\)O\(_2\)S: C, 61.35; H, 4.58; N, 15.90; S, 9.10. Found (%): C, 61.54; H, 4.69; N, 16.01; S, 9.23.

2.6.3 General procedure for synthesis of 24

A mixture of 1-benzylidene-2-tetralone 22a (1.0 mol, Ar= C\(_6\)H\(_5\)), thiosemicarbazide (1.0 mol) and alc. KOH (1.0 g of KOH dissolved in 20 mL of ethanol) was heated at 70-80 °C for 3 h. After cooling, the reaction mixture was poured in to ice cold water. The solid obtained was filtered, dried and recrystallized from ethanol.

2.6.3.1 (1R,9bR)-1-Phenyl-1,4,5,9b-tetrahydro-2H-benzo[e]indazole-2-carbothioamide (24a)

Light brown solid; yield 48%; mp 146-48 °C. IR (cm\(^{-1}\)):

3428, 3315 (NH), 1618 (C=N), 1365 (C=S). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)) \(\delta\): 2.79-2.83 (m, 2H, CH\(_2\)), 2.98-3.02 (m, 2H, CH\(_2\)), 5.5 (d, 1H, 9b-H, \(J= 4.96 \) Hz), 5.9 (d, 1H, 1-H, \(J= 4.82 \) Hz), 7.05-7.42 (m, 9H, C\(_6\)H\(_5\)), 7.68 (br, 1H, NH\(_2\)), 8.56 (br, 1H, NH\(_2\)). 13C NMR (100 MHz, DMSO-d\(_6\)) \(\delta\): 172, 149.4, 147.5, 145.8, 128.4, 127.0, 126.1, 125.4, 124.3, 63.5, 56.0, 30.0, 25.6, 14.3. MS, m/z
308.1 (M+H⁺, 100 %). Anal Calcd. (%) For: C₁₈H₁₇N₃S: C, 70.33; H, 5.57; N, 13.67; S, 10.43. Found (%): C, 70.66; H, 5.78; N, 13.87; S, 10.75.

2.6.4 General procedure for the synthesis of 25

A mixture of 23a-b (0.001 mol), chloroacetic acid/ 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 the mixture was kept overnight. The solid, thus obtained was filtered, dried and recrystallized from ethanol-DMF mixture (3:1).

2.6.4.1 2-((1S,9bR)-1-phenyl-1,4,5,9b-tetrahydro-2H-benzo[e]indazol-2-yl)thiazol-4(5H)-one (25a)

Light yellow solid; yield 62 %; mp 196-98 °C. IR (cm⁻¹): 1698 (C=O), 1648 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 2.85-2.90 (m, 1H, CH₂), 2.98-3.09 (m, 2H, CH₂), 3.14-3.19 (m, 1H, CH₂), 3.78 (dd, 2H, SCH₂, J = 3.92 Hz, J = 17.1 Hz), 4.57-4.59 (d, 1H, 9b-H, J = 6.84 Hz), 5.65-5.67 (d, 1H, 1-H, J = 6.84 Hz), 7.22-7.24 (m, 2H, C₆H₅), 7.26-7.35 (m, 3H, C₆H₅), 7.40-7.46 (m, 4H, C₆H₅). ¹³C NMR (100 MHz, DMSO-d₆): δ 186.7, 177.9, 165.1, 140.1, 135.3, 134.3, 128.7, 127.7, 126.9, 124.7, 68.2, 59.7, 29.1, 23.6. MS, m/z 348.2 (M+H⁺, 100 %). Anal Calcd. (%) for C₂₀H₁₇N₃OS: C, 69.14; H, 4.93; N, 12.09; S, 9.23. Found (%): C, 69.28; H, 5.09; N, 12.18; S, 9.38.

2.6.4.2 5-Methyl-2-((1S,9bR)-1-phenyl-1,4,5,9b-tetrahydro-2H-benzo[e]indazol-2-yl)thiazol-4(5H)-one (25b)

Yellowish solid; yield 65 %; mp 202-04 °C. IR (cm⁻¹): 1695 (C=O), 1639 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 1.40-1.42 (d, 3H, CH₃, J = 7.28 Hz), 2.73-2.81 (m, 1H, CH₂), 2.95-3.06 (m, 2H, CH₂), 3.13-3.20 (m, 1H, CH₂), 4.06-4.12 (q, 1H, SCHCH₃, J = 7.32 Hz, J = 2.72
Hz), 4.63-4.65 (d, 1H, 9b-H, J= 6.8 Hz), 5.71-5.73 (d, 1H, 1-H, J= 6.8 Hz), 7.25-7.32 (m, 3H, C₆H₅), 7.33-7.37 (m, 1H, C₆H₃), 7.41-7.49 (m, 5H, C₆H₅). ¹³C NMR (100 MHz, DMSO-d₆): δ 189.5, 176.2, 166.1, 140.6, 136.0, 134.6, 128.9, 127.8, 126.4, 124.8, 67.5, 59.7, 48.6, 28.7, 23.5, 18.6. MS, m/z 362.1 (M+H⁺, 100%). Anal Calcd. (%) for C₂₁H₁₉N₃SO: 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.

2.6.4.3 2-((1S,9bR)-1-(4-Chlorophenyl)-1,4,5,9b-tetrahydro-2H-benzo[e]indazol-2-yl)thiazol-4(5H)-one (25c)

Light yellow solid; yield 66 %; mp 196-98 °C. IR (cm⁻¹): 1695 (C=O), 1639 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 2.78-2.84 (m, 1H, CH₂), 2.98-3.06 (m, 2H, CH₂), 3.15-3.19 (m, 1H, CH₂), 3.78 dd, 2H, SCH₂, J= 17.2 Hz, J= 5.52 Hz), 4.57-4.59 (d, 1H, 9b-H, J= 6.9 Hz), 5.68-5.7 (d, 1H, 1-H, J= 6.9 Hz), 7.23-7.24 (d, 2H, C₆H₅, J= 3.88 Hz), 7.26-7.38 (m, 3H, C₆H₅), 7.41-7.48 (m, 4H, C₆H₅). ¹³C NMR (100 MHz, DMSO-d₆): δ 189.5, 177.4, 165.3, 140.5, 135.7, 134.5, 128.8, 127.7, 126.2, 124.8, 99.4, 67.7, 59.7, 48.6, 28.9, 23.5, 18.6. MS, m/z 382.1 (M+H⁺, 40 %). Anal Calcd. (%) for C₂₀H₁₆CIN₃OS: C, 62.90; H, 4.22; N, 11.00; S, 8.40. Found (%): C, 63.08; H, 4.39; N, 11.18; S, 8.58.

2.6.4.4 2-{(1S,9bR)-1-(4-Chlorophenyl)-1,4,5,9b-tetrahydro-2H-benzo[e]indazol-2-yl)-5-methylthiazol-4(5H)-one (25d)

Light yellow solid; yield 72 %; mp 208-10 °C. IR (cm⁻¹): 1710 (C=O), 1642 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 1.41-1.44 (d, 3H, CH₃, J= 7.28 Hz), 2.75-2.81 (m, 1H, CH₂), 2.97-3.02 (m, 2H, CH₂), 3.14-3.16 (m, 1H, CH₂), 3.99-4.01 (q, 1H, SCHCH₃, J= 7.28 Hz), 4.57-4.59 (d, 1H, H₈, J= 6.76 Hz), 5.65-5.67 (d, 1H, H₈, J= 6.76 Hz), 7.21-7.27 (m, 3H, C₆H₅), 7.32-7.36 (m, 1H, C₆H₅), 7.40-7.45 (m, 5H, C₆H₅). ¹³C NMR (100 MHz, DMSO-d₆): δ 189.5, 176.4, 166.2, 140.5, 135.7, 134.5, 128.5, 127.7, 126.3, 124.5, 99.4, 67.7, 59.7,
48.6, 28.9, 23.5, 18.6. MS, m/z 396.1 (M+H\(^+\), 100 %). Anal Calcd. (%) for C\(_{21}\)H\(_{18}\)ClN\(_3\)OS: C, 63.71; H, 4.58; N, 10.61; S, 8.10. Found (%): C, 63.88; H, 4.69; N, 10.78; S, 9.08.

2.6.5 General procedure for synthesis of 26

A mixture of 23a-b (0.0004 mol), and methyl iodide (0.0005 mol) in absolute ethanol (10 mL) was refluxed for 3 h. The volume of the reaction mixture is reduced to half under reduced pressure. The solid separated on cooling was filtered and recrystallized from ethanol.

2.6.5.1 Methyl(1S,9bR)-1-phenyl-1,4,5,9b-tetrahydro-2H-benzo[e]indazole-2-carbimidothioate (26a)

White crystalline solid; yield 62 %; mp 178-80 °C. IR (cm\(^{-1}\)): 1627 (C=N), 1560 (C=N); \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \(\delta\) 2.50 (s, 3H, CH\(_3\)), 2.77-2.83 (m, 1H, CH\(_2\)), 2.97-3.13 (m 2H, CH\(_2\)), 3.16-3.23 (m, 1H, CH\(_2\)), 4.73-4.74 (d, 1H, 9b-H, \(J = 5.8\) Hz), 5.86 (br, 1H, 1-H ), 7.28-7.34 (m, 3H, C\(_6\)H\(_5\)), 7.39-7.42 (m, 2H, C\(_6\)H\(_5\)), 7.51-7.52 (m, 4H, C\(_6\)H\(_5\)), 9.4 (br, 1H, NH). \(^{13}\)C NMR (100 MHz, DMSO-d\(_6\)): \(\delta\) 168.2, 165.4, 135.8, 134, 129.4, 128.7, 127.4, 124.9, 124.9, 60.4, 28.7, 23.7, 14.3. MS, m/z 322.2 (M+H\(^+\), 100 %). Anal Calcd. (%) for C\(_{19}\)H\(_{19}\)N\(_3\)S: C, 70.99; H, 5.96; N, 13.07; S, 9.98. Found (%): C, 71.12; H, 6.08; N, 13.31; S, 10.12.

2.6.5.2 Methyl(1S,9bR)-1-(4-chlorophenyl)-1,4,5,9b-tetrahydro-2H-benzo[e]indazole-2-carbimidothioate (26b)

White solid: yield 65 %; mp 202-04 °C. IR (cm\(^{-1}\)): 1632 (C=N), 1567 (C=N). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \(\delta\) 2.62 (s, 3H, CH\(_3\)), 2.97-3.04 (m, 1H, CH\(_2\)), 3.09-3.18 (m 2H, CH\(_2\)), 5.30-5.34 (m, 1H, 9b-H), 6.25-6.32 (m, 1H, 1-H), 6.98-7.11 (m, 5H, C\(_6\)H\(_5\)), 7.18-7.20 (m, 3H, C\(_6\)H\(_5\)), 7.51-7.52 (d, 4H, C\(_6\)H\(_5\), \(J = 3.80\) Hz), 9.21 (br, 1H, NH), 9.87(br, 1H, NH). \(^{13}\)C NMR (100 MHz, DMSO-d\(_6\)): \(\delta\) 169.2, 166.3, 137.8, 134, 130.4, 128.7, 127.4, 125.5,
124.9, 62.4, 28.7, 24.7, 15.3. MS, m/z 356.1 (M+H⁺, 100 %). Anal Calcd. (%) for C₁₉H₁₈ClN₃S: C, 64.12; H, 5.10; N, 11.81; S, 9.01. Found (%): C, 64.27; H, 5.18; N, 12.01; S, 9.12.

2.6.6 General procedure for synthesis of 27

A suspension of 23a-b (1.0 mmol) and dimethyl acetylene dicarboxylate, DMAD (1.0 mmol) in absolute ethanol (10 mL) was stirred at room temperature for 24 h. The progress of the reaction was monitored by TLC. After completion of reaction, the solid obtained was filtered, dried and recrystallized from ethanol-DMF (3:1) mixture.

2.6.6.1 Methyl(Z)-2-(4-oxo-2-((15,9bR)-1-phenyl-1,4,5,9b-tetrahydro-2H-benzo[e]indazol-2-yl)thiazol-5(4H)-ylidene)acetate (27a)

White crystalline solid; yield 74 %; mp 182-84 °C. IR (cm⁻¹): 1686 (C=O), 1645 (C=O), 1560 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 2.94-3.0 (m, 2H, CH₂), 3.13-3.19 (m 2H, CH₂), 3.82 (s, 3H OCH₃), 4.51-4.52 (d, 1H, 9b-H, J = 6.4 Hz), 5.76-5.78 (d, 1H, 1-H, J = 6.44 Hz), 6.86 (s, 1H, =CH), 7.19-7.22 (m, 1H, C₆H₅), 7.24-7.30 (m, 3H, C₆H₅), 7.32-7.36 (m, 1H, C₆H₅), 7.41-7.42 (d, 4H, C₆H₅, J = 4.32 Hz). ¹³C NMR (100 MHz, DMSO-d₆): δ 178.7, 173.7, 166.8, 146.7, 139.6, 135, 134.3, 129.4, 128.9, 127.9, 126.3, 125.4, 117.4, 60.4, 58.4, 52.4, 30.1, 24.5, 18.4. MS, m/z 418.4 (M+H⁺, 100 %). Anal Calcd. (%) for C₂₃H₁₉N₃O₃S: C, 66.17; H, 4.59; N, 10.07; S, 7.68. Found (%): C, 66.36; H, 4.68; N, 10.19; S, 7.79.

2.6.6.2 Methyl(Z)-2-((15,9bR)-1-(4-chlorophenyl)-1,4,5,9b-tetrahydro-2H-benzo[e]indazol-2-yl)-4-oxothiazol-5(4H)-ylidene)acetate (27b)

Light yellow solid; yield 76 %; mp 152-54 °C. IR (cm⁻¹): 1688 (C=O), 1650 (C=O), 1572 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 2.82-288 (m, 1H, CH₂), 2.99-3.05 (m 2H, CH₂), 3.07-3.11 (m, 1H, CH₂), 3.79 (s, 3H, OCH₃), 4.76-4.78 (d, 1H, 9b-H, J = 7.16 Hz), 5.85-5.87
(d, 1H, 1-H, J= 7.16 Hz), 6.65 (s, 1H, =CH), 7.25-7.30 (m, 3H, C₆H₅), 7.35-7.37 (m, 1H, C₆H₅), 7.48-7.49 (d, 2H, C₆H₅, J= 4.72 Hz), 7.56-7.57 (d, 2H, C₆H₅, J= 2.44 Hz). ¹³C NMR (100 MHz, DMSO-d₆): δ 179.3, 175.6, 168.8, 145.7, 138.5, 136, 133.6, 129.2, 127.9, 126.8, 125.8, 125.6, 116.7, 62.4, 59.7, 53.5, 31.1, 25.8, 19.3. Anal Calcd. (%) for C₂₃H₁₈ClN₃O₃S: C, 61.13; H, 4.01; N, 9.30; S, 7.10. Found (%): C, 61.22; H, 4.18; N, 9.51; S, 7.22.

2.6.7 General procedure for synthesis of 28

A mixture of compound 23b-c (0.001 mol), acetic acid (5.0 mL) and acetic anhydride (1.0 mL) was heated under reflux for 8 h. The reaction mixture was cooled and poured into ice cold water. The separated solid was filtered and recrystallized from ethanol.

2.6.7.1 N-(1-(4-Chlorophenyl)-4,5-dihydro-2H-benzo[e]indazole-2-carbonothioyl)acetamide (28b)

Orange crystalline solid; yield 42%; mp 170-72 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 2.70 (s, 3H, CH₃), 3.0-3.04 (t, 2H, CH₂, J= 7.64 Hz), 3.28-3.32 (t, 2H, CH₂, J= 7.64 Hz), 7.04-7.014 (m, 3H, C₆H₅), 7.25-7.27 (d, 2H, C₆H₅, J= 7.32Hz), 7.49-7.51 (d, 2H, C₆H₅, J= 8.36 Hz), 7.64-7.66 (d, 2H, C₆H₅, J= 8.44 Hz). Anal Calcd. (%) for C₂₀H₁₆ClN₃OS: C, 62.90; H, 4.22; N, 11.00; S, 8.40. Found (%): C, 63.11; H, 4.46; N, 11.27; S, 8.62.

2.6.7.2 N-(1-(4-Nitrophenyl)-4,5-dihydro-2H-benzo[e]indazole-2-carbonothioyl)acetamide (28c)

Light yellow solid; yield 44%; mp 178-80 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 2.75 (s, 3H, CH₃), 3.04-3.08 (t, 2H, CH₂, J= 7.36 Hz), 3.3 (2H, CH₂ merged with water in DMSO-d₆), 7.06-7.10 (t, 2H, C₆H₅, J= 8.08 Hz), 7.13-7.17 (t, 1H, C₆H₅, J= 6.8 Hz), 7.27-7.29 (d, 1H, C₆H₅, J= 7.48 Hz), 7.93-7.95 (d, 2H, C₆H₅, J= 8.64 Hz), 8.33-8.35 (d, 2H, C₆H₅, J= 8.16
Hz). Anal Calcd. (%) for $\text{C}_{20}\text{H}_{16}\text{N}_{4}\text{O}_{3}\text{S}$: C, 61.21; H, 4.11; N, 14.28; S, 8.17. Found (%): C, 61.43; H, 4.32; N, 14.53; S, 8.33.

2.7 3,4,5-Trisubstitued-1H-pyrazoles (33)

2.7.1 General procedure for synthesis of 31

To a stirred solution of 1,3-diketone 29 (1.0 mmol) and benzhydrol 30 (184 mg, 1.0 mmol) in dry dichloromethane (8.0 mL) was added anhydrous FeCl$_3$ (16 mg, 0.1 mmol). The reaction mixture was heated at 50 $^\circ$C for 45 min. The reaction mixture was concentrated under reduced pressure. Brown coloured solid obtained was filtered and washed with ethanol. Recrystallization from ethanol afforded 31.

2.7.1.1 2-Benzhydrylpentane-2,4-dione (31a)

White solid; yield 90 %; mp 98-100 $^\circ$C. $^1$H NMR (400 MHz, DMSO-d$_6$): $\delta$ 1.96 (s, 6H, CH$_3$), 4.62-4.65 (d, 1H, CH, $J$= 12.28 Hz), 5.15-5.18 (d, 1H, CH, $J$= 12.28 Hz), 7.05-7.09 (t, 2H, C$_6$H$_5$, $J$= 7.28 Hz), 7.16-7.20 (t, 4H, C$_6$H$_5$, $J$= 7.76 Hz), 7.30-7.32 (d, 4H, C$_6$H$_5$, $J$= 7.52 Hz).

Anal Calcd. (%) for $\text{C}_{18}\text{H}_{18}\text{O}_2$: C, 81.17; H, 6.81. Found (%): C, 81.28; H, 6.98.

2.7.1.2 2-Benzhydryl-1-phenylbutane-1,3-dione (31b)

White crystalline solid; yield 92 %; mp 130-32 $^\circ$C. $^1$H NMR (400 MHz, DMSO-d$_6$): $\delta$ 1.96 (s, 3H, CH$_3$), 4.90-4.93 (d, 1H, CH, $J$= 12.32 Hz), 6.16-6.19 (d, 1H, CH, $J$= 11.96 Hz), 6.99-7.01 (t, 1H, C$_6$H$_5$, $J$= 7.36 Hz), 7.08-7.16 (m, 3H, C$_6$H$_5$), 7.24-7.28 (t, 2H, C$_6$H$_5$, $J$= 7.44 Hz), 7.35-7.36 (d, 2H, C$_6$H$_5$, $J$= 7.4 Hz), 7.46-7.53 (m, 4H, C$_6$H$_5$), 7.58-7.62 (t, 1H, C$_6$H$_5$, $J$= 7.36 Hz), 8.08-8.10 (d, 2H, C$_6$H$_5$, $J$= 7.32 Hz). Anal Calcd. (%) for $\text{C}_{23}\text{H}_{20}\text{O}_2$: C, 84.12; H, 6.14. Found (%): C, 84.28; H, 6.28.
2.7.2 General procedure for synthesis of 32

A mixture of 31 (1.0 mmol) and hydroxylamine hydrochloride (3.0 mmol) in ethanol (10 mL) was heated under reflux for 5 h. Cooled the reaction mixture and poured in to ice cold water. White solid obtained was filtered, dried and recrystallized from ethanol.

2.7.2.1 4-Benzhydryl-3,5-dimethylisoxazole (32a)

White crystalline solid; yield 75 %; mp 68-70 °C. IR (cm⁻¹): 1595 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 1.77 (s, 3H, CH₃), 1.86 (s, 3H, CH₃), 5.23 (s, 1H, CH), 6.99-7.00 (d, 4H, C₆H₅, J= 4.0 Hz), 7.15-7.24 (m, 6H, C₆H₅). ¹³C NMR (100 MHz, DMSO-d₆): δ 165.9, 159.9, 141.3, 128.9, 126.8, 115.5, 45.6, 11.4, 10.6. MS, m/z 264.2 (M+H⁺, 100 %). Anal Calcd. (%) for C₁₈H₁₇NO: C, 82.10; H, 6.51; N, 5.32. Found (%): C, 82.31; H, 6.72; N, 5.48.

2.7.2.2 4-Benzhydryl-3-methyl-5-phenylisoxazole (32b)

White fluffy solid; yield 78 %; mp 118-20 °C. IR (cm⁻¹): 1602 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 1.80 (s, 3H, CH₃), 7.06-7.13 (m, 4H, C₆H₅), 7.26-7.37 (m, 6H, C₆H₅), 7.38-7.45 (m, 3H, C₆H₅), 7.49-7.52 (m, 2H, C₆H₅). ¹³C NMR (100 MHz, DMSO-d₆): δ 166.1, 160.9, 141.4, 129.7, 128.7, 127.7, 126.8, 115.8, 45.4, 11.8. MS, m/z 326.1 (M+H⁺, 100 %). Anal Calcd. (%) for C₂₃H₁₉NO: C, 84.89; H, 5.89; N, 4.30. Found (%): C, 85.01; H, 6.02; N, 4.48.

2.7.3 General procedure for synthesis of 33

A mixture of 31 (1.0 mmol), hydrazine hydrate (3.0 mmol) and ethanol (10 mL) was refluxed for 5 h. Cooled the reaction mixture and poured in to ice cold water. White solid obtained was filtered and recrystallized from ethanol.
2.7.3.1 4-Benzhydryl-3,5-dimethyl-1H-pyrazole (33a)

White crystalline solid; yield 78%; mp 138-40 ⁰C. IR (cm⁻¹): 3178 (NH), 1583 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 1.88 (s, 3H, CH₃), 5.43 (s, 1H, CH), 7.07-7.09 (d, 2H, C₆H₅, J= 7.24 Hz), 7.17-7.21 (m, 1H, C₆H₅), 7.24-7.28 (m, 2H, C₆H₅), 8.67 (br, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆): δ 143.0, 129.1, 128.2, 126.2, 117.3, 46.5, 11.6. MS, m/z 263.3 (M+H⁺, 100%). Anal Calcd. (%) for C₁₈H₁₈N₂: C, 82.41; H, 6.92; N, 10.68. Found (%): C, 82.68; H, 7.02; N, 10.81.

2.7.3.2 4-Benzhydryl-3-methyl-5-phenyl-1H-pyrazole (33b)

White solid; yield 74%; mp 136-38 ⁰C. IR (cm⁻¹): 3198 (NH), 1589 (C=N). ¹H NMR (400 MHz, DMSO-d₆): δ 1.71 (s, 3H, CH₃), 5.59 (s, 1H, CH), 7.05-7.07 (d, 4H, C₆H₅, J= 7.36 Hz), 7.17-7.21 (m, 2H, C₆H₅), 7.24-7.27 (m, 3H, C₆H₅), 7.29-7.32 (m, 3H, C₆H₅). ¹³C NMR (100 MHz, DMSO-d₆): δ 143.2, 129.2, 128.4, 127.9, 126.1, 117.4, 58.3, 46.1, 18.4, 12.3. MS, m/z 325 (M+H⁺, 100%). Anal Calcd. (%) for C₂₃H₂₀N₂: C, 85.15; H, 6.21; N, 8.63. Found (%): C, 85.29; H, 6.39; N, 8.72.

2.7.4 General procedure for synthesis of 34

(a) A solution of compound 31 (1.0 mmol) and thiosemicarbazide (3.0 mmol) in ethanol (10 mL) containing 0.5 mL conc. HCl was heated under reflux for about 4-5 h. The progress of the reaction was monitored by TLC. Cooled the reaction mixture and poured in to ice cold water. Cream coloured solid obtained was filtered and recrystallized from ethanol. Above procedure is also performed with 0.5 mL of conc. H₂SO₄ in place of conc. HCl. Same product is obtained in both the cases. The product obtained is identified same as 33.
(b) A mixture of 31 (1.0 mmol) and thiosemicarbazide (3.0 mmol) in ethanol (10 mL) containing KOH (0.5g) was heated under reflux for 4 h. Cooled the reaction mixture and poured into ice cold water. White solid thus obtained was filtered and recrystallized from ethanol.

2.7.4.1 4-Benzhydryl-3,5-dimethyl-1H-pyrazole-1-carbothioamide (34a)

Greyish solid; yield 64%; mp 128-30 °C. IR (cm⁻¹): 3198 (NH), 1589 (C=N), 1286 (C=S). ¹H NMR (400 MHz, DMSO-d₆): δ 1.81 (s, 6H, CH₃), 4.36 (s, 1H, CH), 6.17 (br, 1H, NH₂), 6.75 (br, 1H, NH₂), 7.17-7.24 (m, 6H, C₆H₅), 7.27-7.36 (m, 4H, C₆H₅). ¹³C NMR (100 MHz, DMSO-d₆): δ 178.9, 151.1, 143.7, 142.6, 128.9, 127.5, 126.5, 48.3, 44.2, 23.6, 16.1. MS, m/z 322.2 (M+H⁺, 5%), (320.2, 100%). Anal Calcd. (%) for C₁₉H₁₉N₃S: C, 70.99; H, 5.96; N, 13.07; S, 9.98. Found (%): C, 71.08; H, 6.11; N, 13.19; S, 10.32.

2.7.4.2 4-Benzhydryl-3-methyl-5-phenyl-1H-pyrazole-1-carbothioamide (34b)

Brown solid; yield 64%; mp 118-20 °C. IR (cm⁻¹): 3172 (NH), 1596 (C=N), 1312 (C=S). ¹H NMR (400 MHz, DMSO-d₆): δ 1.96 (s, 3H, CH₃), 4.24 (s, 1H, CH), 6.35 (br, 1H, NH₂), 6.81 (br, 1H, NH₂), 7.17-7.24 (m, 6H, C₆H₅), 6.95-7.16 (m, 15H, C₆H₅). ¹³C NMR (100 MHz, DMSO-d₆): δ 177.4, 151.6, 142.9, 141.5, 130.1, 128.4, 127.3, 126.2, 125.2, 124, 121.4, 43.2, 22.3, 18.3. MS, m/z 384.5 (M+H⁺, 8%), (382.4, 100%). Anal Calcd. (%) for C₁₉H₁₉N₃S: C, 75.16; H, 5.52; N, 10.96; S, 8.36. Found (%): C, 75.37; H, 5.71; N, 11.19; S, 8.58.

2.8 5,6-Dihydro-1H-pyrazolo[3,4-d]thiazoles (41)

2.8.1 General procedure for the synthesis of 35

Thiazolidin-4-one 35 is obtained from cyclocondensation of thiosemicarbazone derivative of 1-tetralone and chloroacetic acid by conventional method as well as by
use of an ionic liquid, N-methylpyridinium tosylate by procedure reported our group [Gautam et al., 2011]. The characterisation data (IR, NMR and mass) of compound 35a (R1 = H) and 35b (R1 = OMe) is reported therein.

2.8.2 General procedure for the synthesis of 36

A mixture of thiazolidin-4-one 35a (0.5 mmol), benzaldehyde (0.5 mmol) and sodium ethoxide (0.02 g of sodium in 2.0 mL of absolute ethanol) in dry benzene (20 mL) was heated under reflux for 10-12 h. The progress of reaction was monitored by TLC. After completion, the reaction mixture was cooled and poured in to ice cold water. The organic layer was separated and dried over fused calcium chloride. The solvent was removed under reduced pressure, filtered the solid obtained and recrystallized from ethanol.

2.8.2.1 (Z)-5-((E)-Benzyldiene)-2-(((E)-3,4-dihyronaphthalen-1(2H)-ylidene)hydrazono)thiazolidin-4-one (36a)

Orange crystalline solid; yield 62 %; mp 180-182 °C. IR (cm⁻¹): 1697 (C=O), 1605 (C=N). ¹H NMR (400 MHz, CDCl₃): δ 1.90-1.96 (m, 2H, CH₂), 2.83-2.86 (t, 2H, CH₂, J = 6.08 Hz), 2.93-2.96 (t, 2H, CH₂, J = 6.44 Hz), 7.17-7.19 (d, 1H, C₆H₅, J = 7.04 Hz), 7.29-7.34 (m, 2H, C₆H₅), 7.36-7.39 (m, 1H, C₆H₅), 7.48-7.55 (m, 2H, C₆H₅), 7.60-7.62 (d, 2H, C₆H₅, J = 7.48 Hz), 7.71 (s, 1H, =CH), 8.31-8.33 (d, 1H, C₆H₅, J = 7.36 Hz), 8.82 (br, 1H, NH). Anal Calcd. (%) for C₂₀H₁₇N₃OS: C, 69.14; H, 4.93; N, 12.09; S, 9.23. Found (%): C, 69.33; H, 5.12; N, 12.32; S, 9.40.

2.8.3 Attempted procedure for the synthesis of 37

A mixture of compound 36a (0.5 mmol), phenylhydrazine (0.75 mmol), and anhydrous sodium acetate (1.0 mmol) in ethanol (25 mL) was heated under reflux for
20–24 h. The progress of the reaction was monitored by TLC. There was no change after 24 h. This attempted reaction was tried under acidic (acetic acid) and basic conditions (piperidine, sodium acetate). Unfortunately, the reaction did not happen and the starting material was obtained in all cases.

2.8.4 General procedure for the synthesis of 38

Equimolar mixture of compound 36a and hydrazine hydrate (98%) in ethanol (15 mL) was refluxed for 8 h. Excess ethanol was distilled off and the solid obtained on cooling was recrystallised from ethanol-DMF (3:1) mixture.

2.8.4.1 (1E, 2Z)-1-(3,4-Dihyronaphthalen-1(2H)-ylidene)-2-(3,4-dihyronaphthalen-2(1H)-ylidene)hydrazine (38a)

Light green solid, yield 60%; mp 118-120 °C. $^{1}$H NMR (400 MHz, CDCl$_3$): δ 1.89-1.96 (m, 2H, CH$_2$), 2.76-2.79 (t, 2H, CH$_2$, J= 6.44 Hz), 2.82-2.85 (t, 2H, CH$_2$, J= 6.04 Hz), 7.16-7.18 (d, 1H, C$_6$H$_5$, J= 7.32 Hz), 7.28-7.31 (m, 2H, C$_6$H$_5$), 8.30-8.32 (d, 1H, C$_6$H$_5$, J= 7.56 Hz). MS, m/z 289.2 (M+H$^+$, 100 %).

2.8.5 General procedure for the synthesis of 39

A mixture of thiazolidin-4-one 35 (1.0 mmol) and dimethylformamide-dimethylacetal (10 mmol) in dimethyl formamide (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.
2.8.5.1 (2Z)-2-((E)-(3,4-Dihyronaphthalen-1(2H)-ylidene)hydrazono)-5-((dimethylamino)methylene)-3-methylthiazolidin-4-one (39a)

Light brown crystals; yield 82 %; mp 206-208 °C. IR (cm⁻¹): 1697 (C=O), 1556 (C=N), 1490 (C=C). ¹H NMR (400 MHz, CDCl₃): δ 1.89-1.96 (m, 2H, CH₂), 2.80-2.83 (t, 2H, CH₂, J= 6.08 Hz), 2.96-2.99 (t, 2H, CH₂, J= 6.4 Hz), 3.16 (s, 6H, NMe₂), 3.36 (s, 3H, N-CH₃), 7.13-7.15 (m, 1H, C₆H₅), 7.20-7.29 (m, 2H, C₆H₅), 7.45 (s, 1H, =CH), 8.25-8.27 (dd, 1H, C₆H₅, J= 1.5 Hz, J= 6.24 Hz). Anal Calcd. (%) for C₁₇H₂₀N₄SO: C, 62.19; H, 6.09; N, 17.07; S, 9.75. Found (%): C, 62.33; H, 6.26; N, 17.32; S, 9.93.

2.8.5.2 (2Z)-5-((Dimethylamino)methylene)-2-((E)-(6-methoxy-3,4-dihyronaphthalen-1(2H)-ylidene)hydrazono)-3-methylthiazolidin-4-one (39b)

Brown crystalline solid; yield 82 %; mp 184-186 °C. IR (cm⁻¹): 1702 (C=O), 1567 (C=N), 1512 (C=C). ¹H NMR (400 MHz, CDCl₃): δ 1.88-1.95 (m, 2H, CH₂), 2.78-2.81 (t, 2H, CH₂, J= 6.08 Hz), 2.93-2.97 (t, 2H, CH₂, J= 6.36 Hz), 3.16 (s, 6H, NMe₂), 3.34 (s, 3H, NCH₃), 3.82 (s, 3H, OCH₃), 6.64-6.65 (d, 1H, C₆H₅, J= 2.6 Hz), 6.78-6.81 (dd, 1H, C₆H₅, J= 2.6 Hz, J= 6.20 Hz), 7.44 (s, 1H, =CH), 8.20-8.22 (d, 1H, C₆H₅, J= 8.8 Hz). Anal Calcd. (%) for C₁₈H₂₂N₄SO₂: C, 60.33; H, 6.14; N, 15.64; S, 8.93. Found (%): C, 60.56; H, 6.33; N, 15.78; S, 9.12.

2.8.6 General procedure for the synthesis of 40

Compound 40 is obtained from compound 35 in one step or in two steps through compound 39 by the following procedure:

(a) Procedure for synthesis of compound 40 from compound 39

A mixture of enaminone 39 (1.0 mmol) and Lawesson’s reagent (1.0 mmol) in dry toluene (20 mL) was refluxed for 2 h. The solvent was removed
from the reaction mixture under reduced pressure. The solid obtained after cooling was filtered and recrystallized from ethanol.

(b) Procedure for synthesis of compound 40 from compound 35

A mixture of thiazolidin-4-one 35 (1.0 mmol) and Lawesson’s reagent (1.0 mmol) in dry toluene (15 mL) was refluxed for 2 h. Dimethylformamide-dimethylacetal (10 mmol) was then added and continued refluxing for 1 h. Excess solvent was removed under reduced pressure and mixture was left overnight. The solid obtained was filtered and recrystallised from ethanol.

2.8.6.1 (ZZ)-2-((E)-(3,4-Dihyronaphthalen-1(2H)-ylidene)hydrazono)-5-((dimethylamino)methylene)-3-methylthiazolidine-4-thione (40a)

Grey coloured crystals; yield 78 %; mp 208-212 °C. IR (cm⁻¹): 1605 (C=N), 1489 (C=C), 1242 (C=S); ¹H NMR (400 MHz, CDCl₃): δ 1.92-1.95 (m, 2H, CH₂), 2.81-2.84 (t, 2H, CH₂, J= 6.0 Hz), 2.95-2.99 (t, 2H, CH₂, J= 6.64 Hz), 3.30 (s, 6H, NMe₂), 3.79 (s, 3H, N-CH₃), 7.14-7.16 (m, 1H, C₆H₅), 7.22-7.28 (m, 2H, C₆H₅), 8.25 (s, 1H, =CH), 8.27-8.30 (dd, 1H, C₆H₅, J= 1.24 Hz, J= 6.48 Hz). MS, m/z 345 (M+H⁺, 100 %). Anal Calcd. (%) for C₁₇H₂₀N₄S₂: C, 59.27; H, 5.85; N, 16.26; S, 18.62. Found (%): C, 59.42; H, 5.63; N, 16.39; S, 18.86.

2.8.6.2 (ZZ)-5-((Dimethylamino)methylene)-2-((E)-(6-methoxy-3,4-dihyronaphthalen-1(2H)-ylidene)hydrazono)-3-methylthiazolidine-4-thione (40b)

Brown coloured crystals; yield 72 %; mp 194-198 °C. IR (cm⁻¹): 1615 (C=N), 1518 (C=C), 1256 (C=S); ¹H NMR (400 MHz, CDCl₃): δ 1.94-1.98 (m, 2H, CH₂), 2.85-2.87 (t, 2H, CH₂, J= 6.12 Hz), 2.96-2.99 (t, 2H, CH₂, J= 6.41 Hz), 3.20 (s, 6H, NMe₂), 3.38 (s, 3H, NCH₃), 3.89 (s, 3H, OCH₃), 6.66-6.67 (d, 1H, C₆H₅, J= 2.81 Hz), 6.81-6.84 (dd, 1H, C₆H₅, J= 2.74 Hz, J= 6.24 Hz), 8.31-8.33 (d, 1H, C₆H₅, J= 8.86 Hz) 8.38 (s, 1H, =CH). Anal Calcd. (%) For
C₁₈H₂₂N₄OS₂: C, 57.72; H, 5.92; N, 14.96; S, 17.12. Found (%): C, 57.88; H, 6.12; N, 15.18; S, 17.27.

2.8.7 General procedure for the synthesis of 41

A solution of phenyl hydrazine hydrochloride (0.75 mmol), in ethanol (25 mL) was added drop wise with stirring to a solution of compound 40 (0.5 mmol) in ethanol (5 mL). After complete addition the mixture was heated at 70-80 °C for 5-6 h. The progress of reaction was monitored by TLC. The reaction mixture was then cooled to room temperature and separated solid was filtered, dried and recrystallized from ethanol.

2.8.7.1 (Z)-5-[(E)-(3,4-Dihyronaphthalen-1(2H)-ylidene)hydrazono]-6-methyl-1-phenyl-5,6-dihydro-1H-pyrazolo[3,4-d]thiazole (41a)

Orange solid; yield 45%; mp 148-150 °C. IR (cm⁻¹): 1582 (C=N), 1497 (C=C). ¹H NMR (400 MHz, CDCl₃): δ 1.95-1.98 (m, 2H, CH₂), 2.85-2.88 (t, 2H, CH₂, J= 6.68 Hz), 3.00-3.04 (t, 2H, CH₂, J= 6.44 Hz), 3.50 (s, 3H, NCH₃), 7.18-7.20 (d, 1H, C₆H₅, J= 7.04 Hz), 7.31-7.35 (m, 2H, C₆H₅), 7.51-7.54 (m, 3H, C₆H₅), 7.91-7.93 (m, 2H, C₆H₅), 8.23 (s, 1H, =CH), 8.34-8.36 (dd, 1H, C₆H₅, J= 1.68 Hz, J= 6.12 Hz). ¹³C NMR (100 MHz, CDCl₃): δ 166.1, 164.0, 157.9 (C=N), 153.2, 141.3, 134.6, 132.6, 130.3, 129.2, 128.7, 126.4, 125.6, 123.6, 30.0, 29.7, 27.5, 22.2. MS, m/z 374.2 (M+H⁺, 90 %). Anal Calcd. (%): For C₂₁H₁₉N₅S: C, 67.56; H, 5.09; N, 18.76; S, 8.57. Found (%): C, 67.71; H, 5.25; N, 18.92; S, 8.76.

2.8.7.2 (Z)-1-(4-Chlorophenyl)-5-[(E)-(3,4-dihyronaphthalen-1(2H)-ylidene)hydrazono]-6-methyl-5,6-dihydro-1H-pyrazolo[3,4-d]thiazole (41b)

Orange fluffy solid; yield 42%; mp 172-174 °C. IR (cm⁻¹): 1585 (C=N), 1501 (C=C). ¹H NMR (400 MHz, CDCl₃): δ 1.93-1.99 (m, 2H, CH₂), 2.84-2.87 (t, 2H, CH₂, J= 6.08 Hz), 2.99-3.02 (t, 2H, CH₂, J= 6.36 Hz), 3.49 (s, 3H, NCH₃), 7.18-7.19 (d, 1H, C₆H₅, J= 6.64 Hz),...
7.28-7.36 (m, 2H, C₆H₅), 7.46-7.49 (m, 2H, C₆H₅), 7.83-7.87 (m, 2H, C₆H₅), 8.19 (s, 1H, =CH), 8.31-8.34 (dd, 1H, C₆H₅, J= 1.52 Hz, J= 6.24 Hz). ¹³C NMR (100 MHz, CDCl₃): δ 166, 164.1, 157.7 (C=N), 151.5, 141.2, 138.5, 135.1, 132.2, 130.4, 129.5, 128.7, 126.4, 125.6, 124.6 (C₆H₅), 30.0, 29.8, 27.5, 22.2. MS, m/z 408 (M+H⁺, 20 %). Anal (%) Calcd. For C₂¹H₁₈N₅SCl: C, 61.91; H, 4.42; N, 17.19; S, 7.86. Found (%): C, 62.10; H, 4.66; N, 17.34; S, 8.01.

2.8.7.3 (Z)-5-{(E)-(3,4-Dihyronaphthalen-1(2H)-ylidene)hydrazono)-6-methyl-1-(o-tolyl)-5,6-dihydro-1H-pyrazolo[3,4-d]thiazole (41c)

Bright orange solid; yield 38 %; mp 158-160 °C. IR (cm⁻¹): 1580 (C=N), 1491 (C=C). ¹H NMR (400 MHz, CDCl₃): δ 1.93-1.99 (m, 2H, CH₂), 2.74 (s, 3H, CH₃), 2.84-2.87 (t, 2H, CH₂, J= 6.08 Hz), 2.99-3.02 (t, 2H, CH₂, J= 6.40 Hz), 3.49 (s, 3H, NCH₃), 7.24-7.42 (m, 6H, Ar-H), 7.69-7.71 (d, 1H, C₆H₅, J= 7.88 Hz), 8.32-8.34 (dd, 1H, C₆H₅, J= 1.48 Hz, J= 6.40 Hz), 8.42 (s, 1H, =CH). ¹³C NMR (100 MHz, CDCl₃): δ 166.4, 163.7, 159.0 (C=N), 151.5, 141.1, 140.5, 139.9, 132.5, 131.6, 130.3, 129.9, 128.7, 126.5, 125.6, 115.3 (Ar-C), 30.0, 29.6, 27.4, 22.2, 18.1. MS, m/z 388 (M+H⁺, 100 %). Anal Calcd. (%) for C₂₂H₂₁N₅S: C, 68.21; H, 5.42; N, 18.08; S, 8.26. Found (%): C, 68.44; H, 5.68; N, 18.25; S, 8.40.

2.8.7.4 (Z)-5-{(E)-(6-Methoxy-3,4-dihyronaphthalen-1(2H)-ylidene)hydrazono)-6-methyl-1-phenyl-5,6-dihydro-1H-pyrazolo[3,4-d]thiazole (41d)

Brown needles; yield 55 %; mp 162-164 °C. IR (cm⁻¹): 1582 (C=N), 1494 (C=C). ¹H NMR (400 MHz, CDCl₃): δ 1.94-1.97 (m, 2H, CH₂), 2.82-2.85 (t, 2H, CH₂, J= 5.84 Hz), 2.98-3.01 (t, 2H, CH₂, J= 6.48 Hz), 3.49 (s, 3H, NCH₃), 3.86 (s, 3H, OCH₃), 6.68-6.69 (d, 1H, C₆H₅, J= 2.56 Hz), 6.86-6.89 (dd, 1H, C₆H₅, J= 2.72 Hz, J= 6.16 Hz), 7.51-7.54 (m, 3H, C₆H₅), 7.90-7.93 (m, 2H, C₆H₅), 8.22 (s, 1H, =CH), 8.30-8.32 (d, 1H, C₆H₅, J= 8.80 Hz). ¹³C NMR (100
MHZ, CDCl$_3$): δ 166.1, 163.8, 161.3 (C=N), 156.9, 153.2, 143.1, 141.1, 134.8, 132.4, 129.2, 127.6, 125.2, 123.5, 113.2, 112.6 (Ar-C), 55.3, 30.3, 29.7, 27.4, 22.3. MS, m/z 404.1 (M+H$^+$, 10 %). Anal Calcd. (%) for C$_{22}$H$_{21}$N$_5$SO: C, 65.50; H, 5.21; N, 17.36; S, 7.94. Found (%): C, 65.75; H, 5.41; N, 17.51; S, 8.16.

2.8.7.5 (Z)-1-(4-Chlorophenyl)-5-((E)-(6-methoxy-3,4-dihyronaphthalen-1(2H)-ylidene)hydrazono)-6-methyl-5,6-dihydro-1H-pyrazolo[3,4-d]thiazole (41e)

Light orange solid; yield 52 %; mp 198-200 °C. IR (cm$^{-1}$): 1586 (C=N), 1496 (C=C). 1H NMR (400 MHz, CDCl$_3$): δ 1.94-1.97 (m, 2H, CH$_2$), 2.81-2.84 (t, 2H, CH$_2$, J = 6.0 Hz), 2.97-3.0 (t, 2H, CH$_2$, J = 6.44 Hz), 3.49 (s, 3H, NCH$_3$), 3.85 (s, 3H, OCH$_3$), 6.68 (s, 1H, C$_6$H$_5$), 6.85-6.88 (dd, 1H, C$_6$H$_5$, J = 2.60 Hz, J = 6.20 Hz), 7.47-7.50 (m, 2H, C$_6$H$_5$), 7.84-7.86 (m, 2H, C$_6$H$_5$), 8.20 (s, 1H, =CH), 8.28-8.30 (d, 1H, C$_6$H$_5$, J = 8.8 Hz). 13C NMR (100 MHz, CDCl$_3$): δ 166.0, 163.9, 161.3 (C=N), 156.7, 151.5, 143.1, 141.1, 138.5, 135.3, 129.5, 127.6, 125.1, 124.6, 113.2, 112.7 (Ar-C), 55.3, 30.3, 29.8, 27.4, 22.3. MS, m/z 438.1 (M+H$^+$, 100 %). Anal Calcd. (%) for C$_{22}$H$_{20}$N$_5$SOCl: C, 60.41; H, 4.57; N, 16.01; S, 7.32. Found (%): C, 60.64; H, 4.46; N, 16.25; S, 7.44.

2.8.7.6 (Z)-5-((E)-(6-Methoxy-3,4-dihyronaphthalen-1(2H)-ylidene)hydrazono)-6-methyl-1-(o-tolyl)-5,6-dihydro-1H-pyrazolo[3,4-d]thiazole (41f)

Light brown solid; yield 44 %; mp 160-164 °C. IR (cm$^{-1}$): 1581 (C=N), 1490 (C=C). 1H NMR (400 MHz, CDCl$_3$): δ 1.92-1.98 (m, 2H, CH$_2$), 2.74 (s, 3H, CH$_3$), 2.81-2.84 (t, 2H, CH$_2$, J = 5.96 Hz), 2.97-3.0 (t, 2H, CH$_2$, J = 6.52 Hz), 3.48 (s, 3H, NCH$_3$), 3.85 (s, 3H, OCH$_3$), 6.67 (s, 1H, C$_6$H$_5$), 6.85-6.86 (d, 1H, C$_6$H$_5$, J = 6.40 Hz) 7.35-7.42 (m, 2H, C$_6$H$_5$), 7.69-7.71 (d, 1H, C$_6$H$_5$, J = 8.0 Hz), 8.28-8.30 (d, 1H, C$_6$H$_5$, J = 8.76 Hz), 8.41 (s, 1H, =CH). 13C NMR (100 MHz, CDCl$_3$): δ 166.4, 163.5, 161.3 (C=N), 157.9, 151.5, 143.0, 140.4, 139.8, 132.5, 131.6, 130.3, 127.5, 126.4, 115.4, 113.2, 112.6 (Ar-C), 55.3, 30.3, 29.6, 27.3,
2.9 5-Phenyl-5,6-dihydro-2H-thiazolo[3,2-α]pyrimidine-3,7-dione (46)

2.9.1 General procedure for Synthesis of 43

This compound was obtained by stirring a mixture of Meldrum acid 42 (0.01 mol), thiosemicarbazide (0.01 mol), conc. HCl (0.4 mL) and ethanol (20 mL) for 2 h at room temperature. The reaction mixture was poured into ice cold water and extracted with ethyl acetate (2x25 mL). The organic layer was washed with water and dried over anhydrous Na₂SO₄. The solvent was removed under vacuum and the solid obtained, was crystallized from ethanol to furnish colorless crystals.

2.9.1.1 2-(Propane-2-ylidene)hydrazinecarbothioamide (43)

White crystalline solid; Yield 90%; mp. 158–60 °C. IR (cm⁻¹): 3371, 3225 (NH), 1589 (C=N), 1504 (C=C). ¹H NMR (400 MHz, CDCl₃) δ: 1.91 (s, 3H, CH₃), 2.02 (s, 3H, CH₃), 6.31 (br, 1H, NH), 7.23 (br, 1H, NH), 8.51 (s, 1H, NH₂). ³¹C NMR (100 MHz, CDCl₃) δ: 178.8 (C=S), 150.52 (C=N), 25.28 (CH₃), 16.65 (CH₃). MS, m/z 132.1 (M+H⁺, 29 %). Anal Calcd. (%) for C₄H₉N₃S: C, 36.62; H, 6.91; N, 32.03; S, 24.44. Found (%): C, 36.51; H, 6.84; N, 32.14; S, 24.36.

2.9.2 General procedure for synthesis of 44

A mixture of 2-(propane-2-ylidene)hydrazinecarbothioamide 43 (0.01 mol), glacial acetic acid (3.0 mL), acetic anhydride (1.0 mL) was heated under reflux for 1 h. The reaction mixture was cooled at room temperature and poured in to ice cold water. The mixture was neutralized by Na₂CO₃ and then extracted with ethyl acetate (2x25 mL). The organic layer was separated, dried over anhydrous Na₂SO₄. The solvent was
removed under vacuum and the solid thus obtained was crystallized from ethyl acetate.

2.9.2.1  \textit{N}-(4-Acetyl-5,5-dimethyl-4,5-dihydro-1,3,4-thiadiazol-2-yl)acetamide (44)

Shining white crystals; yield 80%; mp 180–82 °C. IR (cm\textsuperscript{-1}): 3148, 3070 (NH), 1705 (C=O), 1612 (C=N). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \( \delta \): 1.98 (s, 6H, CH\textsubscript{3}), 2.18 (s, 3H, CH\textsubscript{3}), 2.19 (s, 3H, CH\textsubscript{3}), 9.06 (1H, br, NH). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \( \delta \): 169.8 (C=O), 168.6 (C=O), 143.27 (C=N), 28.9, 23.9, 23.2 (CH\textsubscript{3}). MS, m/z 216.1 (M+H\textsuperscript{+}, 100 %); Anal. calc. for C\textsubscript{8}H\textsubscript{13}N\textsubscript{3}O\textsubscript{2}: C, 44.64; H, 6.09; N, 19.52; S, 14.89. Found (%): C, 44.60; H, 6.18; N, 19.44; S, 14.81.

2.9.3  General procedure for synthesis of 45

An equimolar mixture of Meldrum acid 42 (1.44 g, 10 mmol), benzaldehyde (1.0 mL, 10 mmol) and thiourea (0.76 g, 10 mmol) in gl. acetic acid (20 mL) was refluxed for 14 h. After removal of solvent, the oily residue was dissolved in ethanol and left to stand at room temperature. White solid obtained was recrystallized from ethanol.

2.9.3.1  6-Phenyl-2-thioxotetrahydropyrimidin-4(1H)-one (45)

White crystalline solid; yield 74 %; mp 204-06 °C. IR (cm\textsuperscript{-1}) 3148, 3070 (NH), 1698 (C=O), 1608 (C=N), 1231 (C=S); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \( \delta \): 2.73 (m, 2H, CH\textsubscript{2}), 4.79 (s, 1H, CH), 7.29-7.38 (m, 5H, C\textsubscript{6}H\textsubscript{5}), 9.58 (1H, br, NH), 10.79 (1H, br, NH). MS, m/z 207 (M+H\textsuperscript{+}, 100%); Anal. calc. For C\textsubscript{10}H\textsubscript{10}N\textsubscript{2}O\textsubscript{2}: C, 58.23; H, 4.89; N, 13.58; S, 15.55. Found: C, 58.40; H, 5.01; N, 13.44; S, 15.67 %.
2.9.4 General procedure for synthesis of 46

A mixture of thione 45 (0.123 g, 0.6 mmol), ethyl bromoacetate (0.10 g, 0.6 mmol) in ethanol (10 mL) and anhyd. sodium acetate (0.098 g, 1.2 mmol) was heated under reflux for 6 h. The solvent was reduced under reduced pressure and then residue was poured in to ice cold water. The solid obtained was purified by column chromatography (pet ether, ethyl acetate; 8:2).

2.9.4.1 5-Phenyl-5,6-dihydro-2H-thiazolo[3,2-a]pyrimidine-3,7-dione (46)

White crystalline solid; yield 74 %; mp 204-06 °C. IR (cm\(^{-1}\)): 1705, 1684 (C=O), 1612 (C=N). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 2.50-2.51 (m, 2H, CH\(_2\)), 4.11-4.21 (m, 2H, SCH\(_2\)), 5.72-5.75 (t, 1H, CH, \(J= 7.64\text{ Hz})\), 6.87 (s, 1H, C\(_6\)H\(_5\)), 7.22-7.41(m, 3H, C\(_6\)H\(_5\)), 7.52(s, 1H, C\(_6\)H\(_5\)), 7.91 (br, 1H, NH). MS, m/z 247.1 (M+H\(^+\), 100 %). Anal calcd. (%) for C\(_{12}\)H\(_{12}\)N\(_2\)O\(_2\)S: C, 58.05; H, 4.87; N, 11.28; S, 12.91. Found (%): C, 58.16; H, 5.02; N, 11.40; S, 12.82.

2.10 Computational Studies

Mathematical description of chemistry may be defined as theoretical 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 1970 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, \textit{ab-initio} and DFT methods. A brief description of the classical molecular mechanics and quantum mechanical approaches is given below.

\textbf{2.10.1 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 \textit{et al.}, 2005] by the use of the simulation of forces.

Molecular mechanics is a completely empirical approach, based on Born-Oppenhiemer 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 MM$^+$, MM3, AMBER, OPLS, MMFF and VFF are available for molecular mechanics calculation.

### 2.10.2 Semi-emirical methods

Over the past decades the semi-emirical methods have been utilized mostly in computational studies. Semi-emirical methods are based on the Hartree–Fock formalism, but make many approximations and obtain some parameters from empirical data. Semi-emirical 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-emirical 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-emirical 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.

### 2.10.3 Density functional theory (DFT)

For the past 30 years density functional theory has been the dominant method for the quantum mechanical simulation of periodic systems. In recent years 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 second; third, fourth and seventh 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.