Synthesis of 3-(4-(benzo[d]thiazol-2-yl) phenyl)-5-aryl-1,3,5-oxadiazinane-4-thiones and 1-(4-(benzo[d]thiazol-2-yl) phenyl)-5-methyl-3-aryl-1,3,5-triazinane-2-thiones

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Experimental Details

2.1. General
Chemicals used were purchased from SD (Fine Chemicals, India), Aldrich (India), or Emerck. Reagent quality solvents were obtained from Avra chemicals (India), and distilled prior to use. IR spectra were recorded on potassium bromide disks on a Perkin-Elmer 383 spectrophotometer. $^1$H NMR spectra were obtained on a Varian 400 MHz instrument with TMS as internal Standard and chemical shifts are expressed δ ppm solvent used DMSO-d$_6$ and Mass spectrum on a Hewlett Packard mass spectrometer operating at 70ev, TLC is performed with E. Merck precoated silica gel plates (60F-254) with iodine as a developing agent. Initially we have prepared 4-(benzo[d]thiazol-2-yl) benzenamine (1) according to literature procedures$^{26-29}$ followed by the synthesis of urea derivatives from the reaction of compound (1) with isocyanates$^{30,31}$.

2.2. Synthesis and characterization of 1-(4-(benzo[d]thiazol-2-yl)phenyl)-3-arylthioureas (2a-h):

Compound (1) was prepared by the condensation of 2-aminonicotinaldehyde and 1-(2-amino-4,6-dimethylphenyl)ethanone$^{26-29}$ and it was reacted with isocyanates to gave urea derivatives$^{30,31}$. To a solution of 4-(benzo[d]thiazol-2-yl) benzenamine (1) (10.0 mmol), in dry DMF (20mL) arylisothiocyanate (10.0 mmol) was added and the contents were refluxed for 4 hrs. The reaction was monitored on TLC. After the completion of reaction the content was cooled and the separated product was filtered and crystallized from EtOH. Structures of 2(a-h) are assigned on the basis of Mass, NMR, $^{13}$C NMR, spectroscopic analysis. Interpretation of (2b) 1-(4-(benzo[d]thiazol-2-yl) phenyl)-3-(4-chlorophenyl) thiourea is given as a specific case using corresponding spectroscopic sketch.
Mass spectrum of 2(b)

Calculated Molecular weight of the compound (2b) is 395.5, which could be explained due to the presence of odd number of nitrogens present in the compound 2(b), according to nitrogen rule. However, observed (m/z) peak shows a peak at 396.9. The difference in the value could be explained due to (M+H) peak.

$^1$H-NMR spectrum of (2b)
**1H-NMR spectrum of (2b):** NMR spectrum of (2b) indicated an intense peak at δ 2.7, followed by a multiplet in the range 6.4 - 8.2. The peak observed at δ 2.7 could be explained due to the coupling of two –NH protons (Part-C of the molecular structure), the multiplet at δ 6.4 - 8.2, might be due to aromatic ring protons of parts A, B and D of the molecule. For rest of the derivatives of 2(a-h) spectral data is shown below:

**13C-NMR(100MHz, DMSO-d6):** δ 122.299, 125.334, 127.096, 128.876, 131.881, 132.224, 134.568, 136.177, 136.234, 139.133, 142.221, 143.228, 145.678, 146.332, 147.321, 148.166, 150.229, 153.729, 163.877, 172.288 ppm. HR-MS: [M+H] 396.0039.

(2a) 1-(4-(benzo[d]thiazol-2-yl)phenyl)-3-(2-chlorophenyl)thiourea:

1H-NMR (DMSO-d6): δ = 9.25 (brs, 2H), 8.21 (d, 1H), 8.01 (m, 3H), 7.91 (m, 3H), 7.80 (d, 1H), 7.75 (d, 2H), 7.40 (d, 2H).

**13C-NMR(100MHz, DMSO-d6):** δ 122.559, 125.434, 127.196, 128.656, 131.555, 132.432, 134.768, 136.077, 136.334, 139.033, 142.321, 143.777, 145.711, 146.900, 147.221, 148.365, 150.116, 153.782, 163.917, 172.742 ppm; HR-MS: [M+H] 396.0039.

(2c) 1-(4-(benz[d]thiazol-2-yl)phenyl)-3-(4-methylphenyl)thiourea: Mass: m/z 376 (M+H);

1H-NMR (DMSO-d6): δ = 9.26 (brs, 2H), 8.22 (d, 1H), 8.03 (m, 3H), 7.95 (m, 3H), 7.75 (d, 1H), 7.75 (d, 2H), 7.26 (d, 2H), 2.31 (d, 3H).

**13C-NMR(100MHz, DMSO-d6):** δ 82.34, 122.526, 124.324, 127.786, 128.776, 130.899, 131.226, 132.666, 134.765, 135.424, 136.257, 140.033, 142.555, 143.776, 145.790, 146.442, 147.305, 150.122, 153.552, 163.807, 173.109 ppm; (CH3); HR-MS: [M+H] 376.0079.

(2d) 1-(4-(benzo[d]thiazol-2-yl)phenyl)-3-(2-methylphenyl)thiourea: Mass: m/z 376 (M+H);

1H-NMR (DMSO-d6): δ = 9.30 (brs, 2H), 8.21 (d, 1H), 8.04 (m, 3H), 7.96 (m, 3H), 7.75 (d, 1H), 7.75 (d, 2H), 7.25 (d, 2H), 2.32 (s, 3H).

(2e) 1-(4-(benzo[d]thiazol-2-yl)phenyl)-3-(4-methoxyphenyl)thiourea: Mass: m/z 392 (M+H);

1H-NMR (DMSO-d6): δ = 9.41 (brs, 2H), 8.41 (d, 1H), 8.11 (m, 4H), 7.91 (m, 2H), 7.80 (d, 1H), 7.70 (d, 2H), 7.40 (d, 2H), 3.76 (s, 3H).

(2f) 1-(4-(benzo[d]thiazol-2-yl)phenyl)-3-(3-methoxyphenyl)thiourea: Mass: m/z 392 (M+H).

1H NMR (DMSO-d6): δ = 9.38 (brs, 2H), 8.40 (d, 1H), 8.11 (m, 4H), 7.90 (m, 2H), 7.81 (d, 1H), 7.71 (d, 2H), 7.41 (d, 2H), 3.77 (s, 3H).

**13C-NMR(100MHz, DMSO-d6):** δ 63.877, 122.513, 124.264, 127.446, 128.176, 131.221, 132.885, 134.190, 136.007, 135.111, 140.075, 142.224, 143.228, 145.611, 146.342, 147.321, 150.229 147.405, 153.211, 163.005, 173.114 ppm; HR-MS: [M+H] 392.0021.

(2g) 1-(4-(benzo[d]thiazol-2-yl)phenyl)-3-(4-bromophenyl)thiourea: Mass: m/z 441 (M+H).

1H-NMR (DMSO-d6): δ = 9.26 (brs, 2H), 8.22 (d, 1H), 8.02 (m, 4H), 7.90 (m, 2H), 7.81 (d, 1H), 7.75 (d, 2H), 7.45 (d, 2H).

(2h) 1-(4-(benzo[d]thiazol-2-yl)phenyl)-3-phenylthiourea: Mass: m/z 362 (M+H);

1H-NMR (DMSO-d6): δ = 9.30 (brs, 2H), 8.21 (d, 1H), 8.00 (m, 3H), 7.91 (m, 4H), 7.80 (d, 1H), 7.76 (d, 2H), 7.40 (d, 2H).

2.3. Synthesis and characterisation of 3-(4-(benzo[d]thiazol-2-yl)phenyl)-5-aryl-1,3,5-oxadiazinane-4-thiones (3a-h):

1-(4-(benzo[d]thiazol-2-yl) phenyl)-3-aryltiourea (2) (50.0 mmol), was added with 30 % formaldehyde solution (100 mmol) and the mixture was treated with conc. HCl (5 mL). After heating at 90-95°C for 4 hrs, the reaction mixture was cooled and neutralized with NaOH. The precipitate formed
was filtered and passed through silica gel column and the product was eluted from 60% ethyl acetate and hexane. Structures of 3(a-h) are assigned on the basis of Mass, NMR, C\textsuperscript{13} NMR, spectroscopic analysis. However, interpretation of 3(d) is given as a specific case using corresponding spectra.

\begin{center}
\textbf{(3d)} 3-(4-(benzo[d]thiazol-2-yl)phenyl)-5-(2-methylphenyl)-1,3,5-oxadiazinane-4-thione
\end{center}

\begin{center}
Mass spectrum of (3d): Calculated molecular weight of compound (3d) is 417.5, which could be due to odd number of nitrogens present in the compound. However, observed mass spectrum indicated two important peaks at 418 and 283 (m/z) values followed by small fragmentations. Peak observed at 418 could be (M+1) peak, while the peak at 283 could be explained due to the loss of benzothiazole moiety.
\end{center}
Proton NMR spectrum of (3d): Proton NMR spectrum of (3d) three singlet peaks at 1.6, 2.3, 2.45 and 5.0 δ followed by a multiplet at 7.2 – 8.0 δ respectively. Singlet peak observed at 1.6 δ could be due to the methyl group attached to phenyl ring in part-D of the molecule. Peak appeared at 2.3 δ as singlet, could be corresponding to the –CH2 protons present on the Carbon which attached to part B through Nitrogen in part C. The peak observed at 2.45 δ as singlet, could be explained due to the –CH2 protons present on the Carbon which attached to part B through Nitrogen in part C of the molecule. Finally multiplet appeared in the range 7.2-8.0 δ might represent all aromatic protons corresponding to the phenyl groups present in part-A, part-B and part-D of the molecule.

^{13}C-NMR of (3d) (100 MHz) (DMSO-d6): Carbon (^{13}C) NMR spectrum for (3d) depicted several peaks at δ 118, 122, and 125-155ppm range respectively. Peak appeared at 18 ppm represents the –CH3 carbon which attached to part-D where as a peak at δ78 is due to -CH2 groups in oxadiazone ring., while the peak at 122 ppm benzothiazole ring carbon (Part-A). The peaks observed in the 125-155ppm could be attributed to aromatic ring carbons of parts –A and B respectively. HR-MS: 418.0054
Spectroscopic data (Mass and Proton NMR) for rest of the derivatives 3(a-h) are shown below:

(3a) 3-(4-(benzo[d]thiazol-2-yl)phenyl)-5-(2-chlorophenyl)-1,3,5-oxadiazinane-4-thione: Mass: m/z 438 (M+H); 1H-NMR (DMSO-d6): δ=7.92 (d, 1H), 7.80 (d, 2H), 7.52 (t, 2H), 7.40 (m, 3H), 7.24 (d, 2H), 7.20 (m, 2H), 5.01 (s, 4H).

(3b) 3-(4-(benzo[d]thiazol-2-yl)phenyl)-5-(4-chlorophenyl)-1,3,5-oxadiazinane-4-thione
Mass: m/z 438 (M+H); 1H-NMR (DMSO-d6): δ=7.98 (d, 1H), 7.84 (d, 2H), 7.54 (t, 2H), 7.41 (m, 3H), 7.25 (d, 2H), 7.21 (m, 2H), 5.02 (s, 4H).

13C-NMR (100 MHz) (DMSO-d6) (3b): δ 89.113, 88.568, 121.564, 122.236, 125.554, 126.001, 128.776, 134.661, 136.221, 136.114, 136.441, 139.221, 142.332, 143.556, 145.113, 146.778, 148.613, 150.770, 153.229, 163.577, 166.188, 172.115 ppm; HR-MS: 438.0132

(3c) 3-(4-(benzo[d]thiazol-2-yl)phenyl)-5-(4-methylphenyl)-1,3,5-oxadiazinane-4-thione: Mass: m/z 418 (M+H); 1H-NMR (DMSO-d6): δ=8.00 (d, 2H), 7.86 (d, 1H), 7.68 (t, 2H), 7.48 (m, 3H), 7.38 (d, 2H), 7.28 (m, 2H), 5.01 (s, 4H), 2.31 (s, 3H).

13C-NMR (100 MHz) (DMSO-d6) (3c): δ 25.334, 89.243, 88.798, 121.504, 122.036, 125.554, 126.001, 128.736, 134.861, 136.421, 136.334, 136.511, 139.553, 142.330, 143.667, 145.333, 146.500, 148.683, 150.900, 153.009, 163.337, 166.198, 172.215 ppm; HR-MS: 418.0032

(3d) 3-(4-(benzo[d]thiazol-2-yl)phenyl)-5-(4-methoxyphenyl)-1,3,5-oxadiazinane-4-thione: Mass: m/z 434 (M+H); 1H-NMR (DMSO-d6): δ=8.04 (d, 2H), 7.90 (d, 1H), 7.65 (d, 2H), 7.51 (m, 3H), 7.39 (d, 2H), 7.28 (m, 2H), 5.01 (s, 4H), 3.82 (s, 3H).

13C-NMR (100 MHz) (DMSO-d6) (3d): δ 59.113, 89.223, 88.638, 121.514, 122.226, 125.443, 126.201, 128.756, 134.331, 136.547, 136.004, 136.311, 139.543, 141.999, 143.229, 145.494, 146.009, 148.683, 150.200, 153.569, 163.357 166.128, 172.115 ppm; HR-MS: 434.0402

(3f) 3-(4-(benzo[d]thiazol-2-yl)phenyl)-5-(3-methylphenyl)-1,3,5-oxadiazinane-4-thione: Mass: m/z 434 (M+H); 1H-NMR (DMSO-d6): δ=8.05 (d, 2H), 7.90 (d, 1H), 7.66 (d, 2H), 7.50 (m, 3H), 7.40 (d, 2H), 7.29 (m, 2H), 5.02 (s, 4H), 2.31 (s, 3H).

(3g) 3-(4-(benzo[d]thiazol-2-yl)phenyl)-5-(4-bromophenyl)-1,3,5-oxadiazinane-4-thione: Mass: m/z 483 (M+H); 1H-NMR (DMSO-d6): δ=7.98 (d, 1H), 7.83 (d, 2H), 7.59 (d, 2H), 7.45 (m, 3H), 7.34 (d, 2H), 7.21 (m, 2H), 5.02 (s, 4H).

(3h) 3-(4-(benzo[d]thiazol-2-yl)phenyl)-5-phenyl-1,3,5-oxadiazinane-4-thione: Mass: m/z 404 (M+H); 1H-NMR (DMSO-d6): δ=8.01 (d, 2H), 7.84 (d, 2H), 7.60 (d, 2H), 7.46 (m, 3H), 7.32 (m, 2H), 7.22 (m, 2H), 5.01 (s, 4H).

2.4. Synthesis and characterisation of 1-(4-(benzo[d]thiazol-2-yl)phenyl)-5-methyl-3-aryl-1,3,5-triazinane-2-thiones (4a-h):

A mixture of 1-(4-(benzo[d]thiazol-2-yl)phenyl)-3-arylthiourea (2) (50.0 mmol), formaldehyde (100. mmol) and methyl amine (50.0 mmol) was taken in ethanol (20 mL) and refluxed for 4-6 hrs. The reaction was monitored on TLC. After the completion of reaction it was cooled and the separated product was filtered. The crude material was passed through silica gel column and the product was eluted from 60% ethylacetate and hexane. Structures of 4(a-h) are assigned on the basis of mass, NMR, 13C-NMR, spectroscopic analysis. Interpretation of 4(b) is given as a specific case using corresponding spectroscopic sketch.
Mass spectrum of (4b): Calculated molecular weight of the compound (4b) is 437, which could be explained due to odd number of nitrogens present in the compound, according to nitrogen rule. However, the observations in the mass spectrum of (4b) depicted three important peaks at 438, 385 and 306 (m/z) values followed by other small fragmentations. Peak observed at molecular weight 438 (m/z) corresponds to (M + 1), while the peak at m/z at 385 is due to loss of Butadiene moiety and the peak at 306 is due to loss of Benzothiazole moiety from parent compound.

Mass spectrum of (4b):

Proton NMR spectrum of (4b): Intense peak observed at δ2.4 is due to the combination of two –CH₂ group protons (In part –C) of the molecule (4b), while the multiple peaks recorded in the range δ7.2 – 8 could be explained due to all aromatic protons corresponding to part-A, part-B and part-D of the molecule (4b).
Proton NMR spectrum of (4b)

\[ \delta 39.113, 89.113, 88.334, 121.655, 122.229, 125.667, 127.008, 128.990, 131.334, 132.998, 134.667, 136.111, 136.445, 136.990, 139.003, 142.155, 143.660, 146.378, 148.066, 150.232, 153.889, 166.288, 172.288 \text{ ppm; HR-MS: 438.000} \]

For rest of the derivatives of 4(a-h) spectral data is shown below:

(4a) 1-(4-(benzo[d]thiazol-2-yl)phenyl)-5-methyl-3-(2-chlorophenyl)-1,3,5-triazinane-2-thione
\[ \delta 8.01 (d, 2H), 7.90 (d, 1H), 7.71 (d, 2H), 7.55 (m, 3H), 7.40 (m, 2H), 7.31 (m, 1H), 4.85 (d, 4H), 2.48 (s, 3H); \text{Mass: } m/z 451 (M+H). \]

(4c) 1-(4-(benzo[d]thiazol-2-yl)phenyl)-5-methyl-3-(4-methylphenyl)-1,3,5-triazinane-2-thione
\[ \delta 8.09 (d, 2H), 7.95 (d, 1H), 7.75 (d, 2H), 7.58 (m, 3H), 7.40 (m, 2H), 7.34 (m, 1H), 4.89 (d, 4H), 2.48 (s, 3H), 2.31 (s, 3H); \text{Mass: } m/z 481 (M+H). \]

(4d) 1-(4-(benzo[d]thiazol-2-yl)phenyl)-5-methyl-3-(2-methylphenyl)-1,3,5-triazinane-2-thione
\[ \delta 8.10 (d, 2H), 7.96 (d, 1H), 7.76 (d, 2H), 7.58 (m, 3H), 7.38 (m, 2H), 7.33 (m, 1H), 4.89 (d, 4H), 2.49 (s, 3H), 2.32 (s, 3H); \text{Mass: } m/z 481 (M+H). \]

(4e) 1-(4-(benzo[d]thiazol-2-yl)phenyl)-5-methyl-3-(4-methoxyphenyl)-1,3,5-triazinane-2-thione
\[ \delta 8.01 (d, 2H), 7.98 (d, 1H), 7.75 (d, 2H), 7.59 (m, 3H), 7.40 (m, 2H), 7.34 (m, 1H), 4.85 (d, 4H), 3.87 (s, 3H), 2.48 (s, 3H); \text{Mass: } m/z 447 (M+H). \]

\[ \delta 39.113, 59.113, 89.113, 88.334, 121.054, 122.209, 125.387, 127.058, 128.870, 131.554, 132.119, 134.457, 136.057, 136.449, 136.788, 139.113, 142.275, 143.889, 146.768, 148.998, 150.242, 153.776, 166.319, 172.588 \text{ ppm; HR-MS: 481.0152} \]

(4f) 1-(4-(benzo[d]thiazol-2-yl)phenyl)-5-methyl-3-(2-bromophenyl)-1,3,5-triazinane-2-thione
\[ \delta 8.01 (d, 2H), 7.98 (d, 1H), 7.75 (d, 2H), 7.59 (m, 3H), 7.40 (m, 2H), 7.34 (m, 1H), 4.89 (d, 4H), 2.49 (s, 3H), 2.32 (s, 3H); \text{Mass: } m/z 447 (M+H). \]

(4g) 1-(4-(benzo[d]thiazol-2-yl)phenyl)-5-methyl-3-(4-chlorophenyl)-1,3,5-triazinane-2-thione
\[ \delta 8.01 (d, 2H), 7.98 (d, 1H), 7.75 (d, 2H), 7.59 (m, 3H), 7.40 (m, 2H), 7.34 (m, 1H), 4.85 (d, 4H), 3.87 (s, 3H), 2.48 (s, 3H); \text{Mass: } m/z 447 (M+H). \]

(4h) 1-(4-(benzo[d]thiazol-2-yl)phenyl)-5-methyl-3-(4-methoxyphenyl)-1,3,5-triazinane-2-thione
\[ \delta 8.01 (d, 2H), 7.98 (d, 1H), 7.75 (d, 2H), 7.59 (m, 3H), 7.40 (m, 2H), 7.34 (m, 1H), 4.85 (d, 4H), 3.87 (s, 3H), 2.48 (s, 3H); \text{Mass: } m/z 447 (M+H). \]
(4f) 1-(4-(benzo[d]thiazol-2-yl)phenyl)-5-methyl-3-(3-methoxyphenyl)-1,3,5-triazinane-2-thione

$^1$H-NMR (DMSO-d$_6$): $\delta$=8.02 (d, 2H), 7.98 (d, 1H), 7.76 (d, 2H), 7.60 (m, 3H), 7.38 (m, 2H), 7.32 (m, 1H), 4.86 (d, 4H), 3.86 (s, 3H), 2.48 (s, 3H); Mass: m/z 447 (M+H).

(4g) 1-(4-(benzo[d]thiazol-2-yl)phenyl)-5-methyl-3-(4-bromophenyl)-1,3,5-triazinane-2-thione

$^1$H-NMR (DMSO-d$_6$): $\delta$=8.01 (d, 2H), 7.97 (d, 1H), 7.80 (d, 2H), 7.58 (m, 3H), 7.39 (m, 2H), 7.31 (m, 1H), 4.87 (d, 4H), 2.47 (s, 3H); Mass: m/z 495 (M+H).

(4h) 1-(4-(benzo[d]thiazol-2-yl)phenyl)-5-methyl-3-phenyl-1,3,5-triazinane-2-thione

$^1$H-NMR (DMSO-d$_6$): $\delta$=8.08 (d, 2H), 7.95 (m, 1H), 7.82 (m, 3H), 7.56 (m, 3H), 7.40 (m, 2H), 7.31 (m, 1H), 4.88 (d, 4H), 2.48 (s, 3H); Mass: m/z 417 (M+H).
C-$^{13}$ NMR SPECTRAS