

## 4. EXPERIMENTAL

### 4. 1. Chemistry

Melting points (mp) were determined in open capillary tubes on Thomas Hoover melting point apparatus and are uncorrected. The IR spectra were recorded in film or in potassium bromide disks using a Perkin-Elmer 398 spectrometer. The  $^1\text{H}$  NMR spectra were recorded on DPX-500 MHz Bruker FT-NMR spectrometer. The chemical shifts were reported in parts per million ( $\delta$  ppm) relative to TMS as an internal reference. Mass spectra were recorded on a JEOL-SX-102 instrument using fast atom bombardment (FAB positive). Elemental analysis (C, H and N) was performed on a Perkin-Elmer 2400 analyzer and values were within the acceptable limits of the calculated values. The progress of all the reactions were monitored by ready made silica gel plates (Merck) and a solvent system of chloroform-methanol (9:1). The spots were developed in iodine chamber. Spectral data (IR, NMR and mass spectra) were confirmed the structures of the synthesized compounds and the purity of these compounds were ascertained by microanalysis. Elemental (C, H and N) analysis indicated that the calculated and observed values were within the acceptable limits. All chemicals and reagents were procured from Aldrich (USA), Lancaster (UK) or Spectrochem Pvt.Ltd (India) and were used without further purification.

#### 4.1.1 Synthesis of 3-(2-methyl phenyl)-2-thioxo quinazolin-4(3H)-one (4)

To a vigorously stirred solution of 2-methyl aniline (2.14 g; 0.02 mol) in dimethyl sulfoxide (10 mL), carbon disulphide (1.6 mL) and aqueous sodium hydroxide (1.2 mL; 20 molar solution) added dropwise. Then stirring was continued for further 30 min. Dimethyl sulphate (2.5 g; 0.02 mol) was then added gradually keeping the reaction mixture in freezing mixture with stirring and the stirring was continued for an additional 2 hrs. The reaction mixture was then poured into ice cold water. The separated solid obtained was filtered, washed with water, dried and recrystallized from ethanol to give *N*-(2-methyl phenyl) methyl dithiocarbamic acid. Then Methyl anthranilate (1.5 g; 0.01 mol) was added to the above prepared product in ethanol (20 mL). To this anhydrous potassium carbonate (100 mg) was also added and refluxed (conventional heating 18 h; microwave heating 30 min). The reaction mixture was cooled in crushed ice and the solid separated was filtered off and purified by dissolving in 10% alcoholic sodium hydroxide solution and reprecipitated by treating with dilute hydrochloric acid. The solid obtained was filtered, washed with water and finally dried. Then it was recrystallized from ethanol to give (4).

|   |  |
|---|--|
| Yield   | : 2.27 g; 85 %   |
| Melting Point                                 | : 241-242 °C   |
| Rf Value                                      | : 0.34 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>15</sub> H <sub>12</sub> N <sub>2</sub> OS  |
| Molecular Weight                              | : 268 [M <sup>+</sup> ]  |
| IR (KBr) cm <sup>-1</sup>                     | : 3211 (NH), 1686 (C=O),<br>1213 (C=S)   |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 2.4 (s, 3H, CH <sub>3</sub> ), 7.1-7.4 (m, 4H, Ar-H), 7.6-7.7 (m, 4H, Ar-H), 10.3 (br s, 1H, NH) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 67.14; H, 4.51; N, 10.44  |
| Found   | : C, 67.19; H, 4.57; N, 10.38  |

#### **4.1.2. Synthesis of 2-(3-bromopropylthio)-3-(2-methyl phenyl) quinazolin-4(3H)-one (6)**

A solution of 3-(2-methyl phenyl)-2-thioxo quinazolin-4(3H) one (**4**) (2.53 g; 0.01 mol), 1,3-dibromopropane (4.02 gm; 0.02 mol) and K<sub>2</sub>CO<sub>3</sub> (4.14 g; 0.03 mol) in acetone (20 mL) were taken in a round bottom flask. The contents were refluxed for 1 h on a water bath. Then the reaction mixture was cooled to room temperature and filtered off to remove the inorganic materials. The solvent was distilled off and the product of 2-(3-bromo propylthio)-3-(2-methyl phenyl) quinazolin-4(3H)-one (**6**) dried

under reduced pressure in a rotary vacuum evaporator, it was then recrystallized from ethanol.

|   |   |
|---|---|
| Yield   | : 3.30 g; 85 %  |
| Melting Point                                 | : 200-203 °C  |
| Rf Value                                      | : 0.67 [Chloroform-Methanol (9:1)]  |
| Molecular Formula                             | : C <sub>18</sub> H <sub>17</sub> BrN <sub>2</sub> OS   |
| Molecular Weight                              | : 389 [M <sup>+</sup> ], 391 [M+2]  |
| IR (KBr) cm <sup>-1</sup>                     | : 1716 (C=O), 1610 (C=N),<br>1275 (C-N), 590 (C-Br)   |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 2.16-2.18 (m, 2H, CH <sub>2</sub> ), 2.36-2.40 (m, 2H, CH <sub>2</sub> ), 2.67 (s, 3H, CH <sub>3</sub> ), 3.27-3.30 (m, 2H, CH <sub>2</sub> ), 7.21-7.22 (d, 1H, Ar-H), 7.37-7.44 (m, 3H, Ar-H), 7.47-7.51 (m, 2H, Ar-H), 7.70-7.74 (d, 1H, Ar-H), 8.25-8.27 (dd, 1H, Ar-H) |
| Elemental Analysis                            |   |
| Calculated                                    | : C, 55.53; H, 4.40; N, 7.20  |
| Found   | : C, 55.58; H, 4.41; N, 7.18.   |

**4.1.3. General procedure for the Synthesis of 2-(3-substitutedpropylthio)-3-(2-methyl phenyl) quinazolin-4(3H)-ones (OT1 – OT10)**

2-(3-bromo propylthio)-3-(2-methyl phenyl) quinazolin-4(3H)-one (**6**) (3.75 g; 0.01 mol) was dissolved in 1-butanol (25 mL). To this appropriate alkyl/aryl amine (0.015 mol), Potassium iodide (1.66 g; 0.015 mol) and sodium carbonate (2.12 g; 0.02 mol) was added and refluxed (for 3 h by conventional refluxing or 15 min by microwave oven). The reaction mixture was cooled, filtered and the filtrate was then concentrated in vacuum and kept in refrigerator overnight. The solid obtained was filtered, dried and recrystallized from chloroform-ethanol (50:50) mixture to afford the title compounds (**OT1 – OT10**).

**4.1.3.1. 2-(3-(Diethylamino)propylthio)-3-(2-methyl phenyl)quinazolin-4(3H)-one (OT-1)**

|   |  |
|---|--|
| Yield   | : 3.08 g; 81 %   |
| Melting Point                                 | : 182-184 °C   |
| Rf Value                                      | : 0.51 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>22</sub> H <sub>27</sub> N <sub>3</sub> OS  |
| Molecular Weight                              | : 381 [M <sup>+</sup> ]  |
| IR (KBr) cm <sup>-1</sup>                     | : 1666 (C=O), 1606 (C=N),<br>1299 (C-N)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 0.97-1.05 (m, 6H, 2-CH <sub>3</sub> ), 2.16-2.22 (m, 4H, CH <sub>2</sub> ), 2.81-2.85 (m, 4H, CH <sub>2</sub> ), 2.90 (s, 3H, CH <sub>3</sub> ), 2.97-3.01 (m, 2H, CH <sub>2</sub> ), 7.21-7.22 (d, 1H, Ar-H), 7.28-7.39 (m, 4H, Ar-H), 7.40-7.42 (d, 1H, Ar-H), 7.73-7.74 (d, 1H, Ar-H), 8.25-8.31 (dd, 1H, Ar-H) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 69.26; H, 7.13; N, 11.01  |
| Found   | : C, 69.25; H, 7.17; N, 11.03  |

**4.1.3.2. 3-(2-Methylphenyl)-2-(3-(pyrrolidin-1-yl)propylthio)quinazolin-4(3H)-one (OT-2)**

|   |  |
|---|--|
| Yield   | : 2.94 g; 78 %   |
| Melting Point                                 | : 186-187 °C   |
| Rf Value                                      | : 0.49 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>22</sub> H <sub>25</sub> N <sub>3</sub> OS  |
| Molecular Weight                              | : 379 [M <sup>+</sup> ]  |
| IR (KBr) cm <sup>-1</sup>                     | : 1668 (C=O), 1649 (C=N),<br>1258 (C-N)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 1.53-1.61 (m, 4H, CH <sub>2</sub> ), 2.08-2.25 (m, 6H, CH <sub>2</sub> ), 2.36 (s, 3H, CH <sub>3</sub> ), 2.68-2.84 (m, 2H, CH <sub>2</sub> ), 3.27-3.29 (m, 2H, CH <sub>2</sub> ), 7.18-7.19 (d, 1H, Ar-H), 7.30-7.38 (m, 4H, Ar-H), 7.48-7.51 (d, 1H, Ar-H), 7.57-7.59 (d, 1H, Ar-H), 8.26-8.31 (dd, 1H, Ar-H) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 69.62; H, 6.64; N, 11.07  |
| Found   | : C, 69.66; H, 6.66; N, 11.05  |

**4.1.3.3. 3-(2-Methylphenyl)-2-(3-(piperidin-1-yl)propylthio)quinazolin-4(3H)-one (OT-3)**

|   |   |
|---|---|
| Yield   | : 3.13 g; 80 %  |
| Melting Point                                 | : 212-213 °C  |
| Rf Value                                      | : 0.55 [Chloroform-Methanol (9:1)]  |
| Molecular Formula                             | : C <sub>23</sub> H <sub>27</sub> N <sub>3</sub> OS   |
| Molecular Weight                              | : 393 [M <sup>+</sup> ]   |
| IR (KBr) cm <sup>-1</sup>                     | : 1666 (C=O), 1606 (C=N),<br>1250 (C-N)   |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 1.54-1.60 (m, 4H, CH <sub>2</sub> ), 1.67-1.71 (m, 2H, CH <sub>2</sub> ), 2.16-2.22 (m, 4H, CH <sub>2</sub> ), 2.36 (s, 3H, CH <sub>3</sub> ), 2.80-2.83 (m, 4H, CH <sub>2</sub> ), 3.29-3.31 (m, 2H, CH <sub>2</sub> ), 7.18-7.19 (d, 1H, Ar-H), 7.30-7.43 (m, 4H, Ar-H), 7.48-7.51 (d, 1H, Ar-H), 7.72-7.73 (d, 1H, Ar-H), 8.26-8.31 (dd, 1H, Ar-H) |
| Elemental Analysis                            |   |
| Calculated                                    | : C, 70.19; H, 6.92; N, 10.68   |
| Found   | : C, 70.17; H, 6.90; N, 10.69   |



**4.1.3.4. 3-(2-Methylphenyl)-2-(3-(piperazin-1-yl)propylthio)quinazolin-4(3H)-one (OT-4)**

|   |   |
|---|---|
| Yield   | : 3.19 g; 81 %  |
| Melting Point                                 | : 171-173 °C  |
| Rf Value                                      | : 0.51 [Chloroform-Methanol (9:1)]  |
| Molecular Formula                             | : C <sub>22</sub> H <sub>26</sub> N <sub>4</sub> OS   |
| Molecular Weight                              | : 394 [M <sup>+</sup> ]   |
| IR (KBr) cm <sup>-1</sup>                     | : 3292 (N-H), 1666 (C=O),<br>1606 (C=N), 1240 (C-N)   |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 1.79-1.85 (m, 4H, CH <sub>2</sub> ), 2.17-2.22 (m, 6H, CH <sub>2</sub> ), 2.30 (s, 3H, CH <sub>3</sub> ), 2.81-2.84 (m, 2H, CH <sub>2</sub> ), 3.29-3.31 (m, 2H, CH <sub>2</sub> ), 7.18-7.19 (d, 1H, Ar-H), 7.30-7.43 (m, 4H, Ar-H), 7.48-7.51 (d, 1H, Ar-H), 7.72-7.73 (d, 1H, Ar-H), 8.26-8.31 (dd, 1H, Ar-H), 8.63 (br s, 1H, NH) |
| Elemental Analysis                            |   |
| Calculated                                    | : C, 66.97; H, 6.64; N, 14.20   |
| Found   | : C, 66.99; H, 6.65; N, 14.23   |

**4.1.3.5. 2-(3-(4-Methylpiperazin-1-yl) propylthio)-3-(2-methyl phenyl) quinazolin-4(3H)-one (OT-5)**

|   |  |
|---|--|
| Yield   | : 3.18 g; 78 %   |
| Melting Point                                 | : 214-215 °C   |
| Rf Value                                      | : 0.56 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>23</sub> H <sub>28</sub> N <sub>4</sub> OS  |
| Molecular Weight                              | : 408 [M <sup>+</sup> ]  |
| IR (KBr) cm <sup>-1</sup>                     | : 1666 (C=O). 1606 (C=N),<br>1300 (C-N)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 1.58 (s, 3H, CH <sub>3</sub> ), 2.16-2.17 (m, 8H, CH <sub>2</sub> ), 2.43 (s, 3H, CH <sub>3</sub> ), 2.81-2.84 (m, 2H, CH <sub>2</sub> ), 2.90-2.97 (m, 2H, CH <sub>2</sub> ), 3.28-3.29 (m, 2H, CH <sub>2</sub> ), 7.21-7.22 (d, 1H, Ar-H), 7.30-7.43 (m, 4H, Ar-H), 7.48-7.50 (d, 1H, Ar-H), 7.73-7.74 (d, 1H, Ar-H), 8.25-8.31 (dd, 1H, Ar-H) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 67.61; H, 6.91; N, 13.71  |
| Found   | : C, 67.76; H, 6.90; N, 13.69  |

**4.1.3.6. 3-(2-Methyl phenyl)-2-(3-morpholinopropylthio) quinazolin-4(3H)-one (OT-6)**

|   |  |
|---|--|
| Yield   | : 3.23 g; 82 %   |
| Melting Point                                 | : 175-176 °C   |
| Rf Value                                      | : 0.49 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>22</sub> H <sub>25</sub> N <sub>3</sub> O <sub>2</sub> S  |
| Molecular Weight                              | : 395 [M <sup>+</sup> ]  |
| IR (KBr) cm <sup>-1</sup>                     | : 1666 (C=O), 1606 (C=N),<br>1299 (C-N)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 1.58-1.65 (m, 2H, CH <sub>2</sub> ), 2.17-2.24 (m, 6H, CH <sub>2</sub> ), 2.34 (s, 3H, CH <sub>3</sub> ), 2.81-2.83 (m, 2H, CH <sub>2</sub> ), 3.29-3.30 (m, 4H, CH <sub>2</sub> ), 7.21-7.22 (d, 1H, Ar-H), 7.30-7.43 (m, 4H, Ar-H), 7.48-7.50 (d, 1H, Ar-H), 7.73-7.74 (d, 1H, Ar-H), 8.25-8.28 (dd, 1H, Ar-H) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 66.81; H, 6.37; N, 10.62  |
| Found   | : C, 66.80; H, 6.34; N, 10.65  |

**4.1.3.7. 3-(2-Methyl phenyl)-2-(3-(phenylamino)propylthio)quinazolin-4(3H)-one (OT-7)**

|   |  |
|---|--|
| Yield   | : 3.16 g; 79 %   |
| Melting Point                                 | : 221-222 °C   |
| Rf Value                                      | : 0.46 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>24</sub> H <sub>23</sub> N <sub>3</sub> OS  |
| Molecular Weight                              | : 401 [M <sup>+</sup> ]  |
| IR (KBr) cm <sup>-1</sup>                     | : 3280 (N-H), 1666 (C=O),<br>1606 (C=N), 1300 (C-N)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 1.76-1.79 (m, 2H, CH <sub>2</sub> ), 2.33 (s, 3H, CH <sub>3</sub> ), 2.81-2.84 (m, 2H, CH <sub>2</sub> ), 3.29-3.30 (m, 2H, CH <sub>2</sub> ), 7.17-7.95 (m, 11H, Ar-H), 8.19-8.21 (m, 1H, Ar-H), 8.25-8.31 (m, 1H, Ar-H), 8.74 (br s, 1H, NH) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 71.79; H, 5.77; N, 10.47  |
| Found   | : C, 71.78; H, 5.74; N, 10.44  |

**4.1.3.8. 2-(3-(4-Chloro phenylamino)propylthio)-3-(2-methylphenyl) quinazolin-4(3H)-one (OT-8)**

|   |  |
|---|--|
| Yield   | : 3.35 g; 77 %   |
| Melting Point                                 | : 188-189 °C   |
| Rf Value                                      | : 0.44 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>24</sub> H <sub>22</sub> ClN <sub>3</sub> OS  |
| Molecular Weight                              | : 436 [M <sup>+</sup> ], 438 [M+2]   |
| IR (KBr) cm <sup>-1</sup>                     | : 3280 (N-H), 1660 (C=O),<br>1609 (C=N), 1300 (C-N)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 2.17-2.20 (m, 2H, CH <sub>2</sub> ), 2.36 (s, 3H, CH <sub>3</sub> ), 2.81-2.84 (m, 2H, CH <sub>2</sub> ), 3.28-3.29 (m, 2H, CH <sub>2</sub> ), 7.29-7.77 (m, 10H, Ar-H), 7.94-7.95 (m, 1H, Ar-H), 8.11-8.14 (m, 1H, Ar-H), 8.64 (br s, 1H, NH) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 66.12; H, 5.09; N, 9.64   |
| Found   | : C, 66.15; H, 5.07; N, 9.65   |

**4.1.3.9. 2-(3-(4-Methyl phenylamino)propylthio)-3-(2-methyl phenyl) quinazolin-4(3H)-one (OT-9)**

|   |  |
|---|--|
| Yield   | : 3.36 g; 81 %   |
| Melting Point                                 | : 179-181 °C   |
| Rf Value                                      | : 0.51 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>25</sub> H <sub>25</sub> N <sub>3</sub> OS  |
| Molecular Weight                              | : 415 [M <sup>+</sup> ]  |
| IR (KBr) cm <sup>-1</sup>                     | : 3278 (N-H), 1666 (C=O),<br>1606 (C=N), 1300 (C-N)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 2.16-2.18 (m, 2H, CH <sub>2</sub> ), 2.76-<br>2.79 (m, 2H, CH <sub>2</sub> ), 2.91 (s, 3H,<br>CH <sub>3</sub> ), 2.98 (s, 3H, CH <sub>3</sub> ), 3.28-3.29<br>(m, 2H, CH <sub>2</sub> ), 7.18-7.85 (m, 11H,<br>Ar-H), 8.25-8.32 (m, 1H, Ar-H),<br>8.85 (br s, 1H, NH). |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 72.26; H, 6.06; N, 10.11  |
| Found   | : C, 72.25; H, 6.04; N, 10.14  |

**4.1.3.10. 2-(3-(Benzylamino)propylthio)-3-(2-methylphenyl) quinazolin-4(3H)-one (OT-10)**

|   |   |
|---|---|
| Yield   | : 3.32 g; 80 %  |
| Melting Point                                 | : 211-213 °C  |
| Rf Value                                      | : 0.47 [Chloroform-Methanol (9:1)]  |
| Molecular Formula                             | : C <sub>25</sub> H <sub>25</sub> N <sub>3</sub> OS   |
| Molecular Weight                              | : 415 [M <sup>+</sup> ]   |
| IR (KBr) cm <sup>-1</sup>                     | : 3279 (N-H), 1666 (C=O),<br>1606 (C=N), 1300 (C-N)   |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 1.72 (s, 2H, CH <sub>2</sub> ), 2.19-2.23 (m, 2H, CH <sub>2</sub> ), 2.82-2.84 (m, 2H, CH <sub>2</sub> ), 2.97 (s, 3H, CH <sub>3</sub> ), 3.28-3.29 (m, 2H, CH <sub>2</sub> ), 7.17-7.76 (m, 12H, Ar-H), 8.04 (br s, 1H, NH), 8.25-8.31 (m, 1H, Ar-H) |
| Elemental Analysis                            |   |
| Calculated                                    | : C, 72.26; H, 6.06; N, 10.11   |
| Found   | : C, 72.25; H, 6.08; N, 10.13   |

**SCHEME 2****4.2.1. Synthesis of 3-(4-chlorophenyl)-2-thioxo quinazolin-4(3H)-one (4)**

To a vigorously stirred solution of 4-chloro aniline (2.56 g; 0.02 mol) in dimethyl sulfoxide (10 mL), carbon disulphide (1.6 mL) and aqueous sodium hydroxide (1.2 mL; 20 molar solution) added dropwise. Then stirring was continued for further 30 min. Dimethyl sulphate (2.5 g; 0.02 mol) was then added gradually keeping the reaction mixture in freezing mixture with stirring and the stirring was continued for an additional 2 hrs. The reaction mixture was then poured into ice cold water. The separated solid obtained was filtered, washed with water, dried and recrystallized from ethanol to give *N*-(4-chloro phenyl) methyl dithiocarbamic acid. Then Methyl anthranilate (1.5 g; 0.01 mol) was added to the above prepared product in ethanol (20 mL). To this anhydrous potassium carbonate (100 mg) was also added and refluxed (conventional heating 18 h; microwave heating 30 min). The reaction mixture was cooled in crushed ice and the solid separated was filtered off and purified by dissolving in 10% alcoholic sodium hydroxide solution and reprecipitated by treating with dilute hydrochloric acid. The solid obtained was filtered, washed with water and finally dried. Then it was recrystallized from ethanol to give **(4)**.



|   |  |
|---|--|
| Yield   | : 2.18 gm; 76 %                                      |
| Melting Point                                 | : 319 -320 °C  |
| Rf Value                                      | : 0.30 [Chloroform-Methanol (9:1)]                   |
| Molecular Formula                             | : C <sub>14</sub> H <sub>9</sub> ClN <sub>2</sub> OS |
| Molecular Weight                              | : 289 [M <sup>+</sup> ], 291 [M+2]                   |
| IR (KBr) cm <sup>-1</sup>                     | : 3210 (NH), 1690 (C=O),<br>1210 (C=S)               |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 7.5-8.2 (m, 8H, Ar-H),<br>10.36 (br s, 1H, NH)     |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 58.23; H, 3.14; N, 9.70                         |
| Found   | : C, 58.28; H, 3.10; N, 9.72                         |

#### 4.2.2. Synthesis of 2-(3-bromopropylthio)-3-(4-chlorophenyl)quinazolin-4(3H)-one (**6**)

A solution of 3-(4-chloro phenyl)-2-thioxo 2,3-dihydroquinazolin-4(3H) one (**4**) (2.88 g; 0.01 mol), 1,3-dibromo propane (4.02 gm; 0.02 mol) and K<sub>2</sub>CO<sub>3</sub> (4.14 g; 0.03 mol) in acetone (20 mL) were taken in a round bottom flask. The contents were refluxed for 1 h on a water bath. Then the reaction mixture was cooled to room temperature and filtered off to remove the inorganic materials. The solvent was distilled off and the product of 2-(3-bromo propylthio)-3-(4-chloro phenyl)quinazolin-4(3H)-one (**6**) dried under reduced pressure in a rotary vacuum evaporator, it was then recrystallized from ethanol.

|   |  |
|---|--|
| Yield   | : 3.32 g; 82 %   |
| Melting Point                                 | : 212-215 °C   |
| R <sub>f</sub> Value                          | : 0.36 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>17</sub> H <sub>14</sub> BrClN <sub>2</sub> OS  |
| Molecular Weight                              | : 410 [M <sup>+</sup> ], 412 [M+2], 414 [M+4]  |
| IR (KBr) cm <sup>-1</sup>                     | : 1167 (C=O), 1606 (C=N),<br>576 (C-Br)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 2.31-2.34 (m, 2H, CH <sub>2</sub> ), 3.30-3.35 (m, 2H, CH <sub>2</sub> ), 3.51-3.53 (m, 2H, CH <sub>2</sub> ), 7.25-7.78 (m, 7H, Ar-H), 8.24-8.26 (dd, 1H, Ar-H) |

## Elemental Analysis

Calculated : C, 49.83; H, 3.44; N, 6.84

Found : C, 49.86; H, 3.48; N, 6.80.

**4.2.3. General procedure for the Synthesis of 3-(4-chlorophenyl)-2-(3-substitutedpropylthio) quinazolin-4(3H)-one (PC1 – PC10)**

2-(3-bromo propylthio)-3-(4-chloro phenyl) quinazolin-4(3H)-one (**6**) (4.08 g; 0.01 mol) was dissolved in 1-butanol (25 mL). To this appropriate alkyl/aryl amine (0.015 mol), Potassium iodide (1.66 g; 0.015 mol) and sodium carbonate (2.12 g; 0.02 mol) was added and refluxed (for 3 h by conventional refluxing or 15 min by microwave oven). The reaction mixture was cooled, filtered and the filtrate was then concentrated in vacuum and kept in refrigerator overnight. The solid obtained was filtered, dried and recrystallized from chloroform-ethanol (50:50) mixture to afford the title compounds (**PC1 – PC10**).

**4.2.3.1. 3-(4-Chlorophenyl)-2-(3-(diethylamino)propylthio)quinazolin-4(3H)-one (PC-1)**

|   |   |
|---|---|
| Yield   | : 3.25 g; 81 %  |
| Melting Point                                 | : 132-134 °C  |
| Rf Value                                      | : 0.43 [Chloroform-Methanol (9:1)]  |
| Molecular Formula                             | : C <sub>21</sub> H <sub>24</sub> ClN <sub>3</sub> OS   |
| Molecular Weight                              | : 402 [M <sup>+</sup> ] 404 [M+2]   |
| IR (KBr) cm <sup>-1</sup>                     | : 1699 (C=O), 1604 (C=N),<br>1295 (C-N)   |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 1.02-1.05 (m, 6H, (CH <sub>3</sub> ) <sub>2</sub> ), 1.87-1.90 (m, 4H, CH <sub>2</sub> ), 2.53-2.57 (m, 4H, CH <sub>2</sub> ), 3.18-3.21 (m, 2H, CH <sub>2</sub> ), 7.34-7.76 (m, 7H, Ar-H), 8.24-8.26 (dd, 1H, Ar-H) |
| Elemental Analysis                            |   |
| Calculated                                    | : C, 62.75; H, 6.02; N, 10.45   |
| Found   | : C, 62.78; H, 6.04; N, 10.48.  |

**4.2.3.2. 3-(4-Chlorophenyl)-2-(3-(pyrrolidin-1-yl)propylthio)quinazolin-4(3H)-one (PC-2)**

|   |  |
|---|--|
| Yield   | : 3.43 gm; 86 %  |
| Melting Point                                 | : 100-102 °C   |
| Rf Value                                      | : 0.45 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>21</sub> H <sub>22</sub> ClN <sub>3</sub> OS  |
| Molecular Weight                              | : 400 [M <sup>+</sup> ], 402 [M+2]   |
| IR (KBr) cm <sup>-1</sup>                     | : 1672 (C=O), 1606 (C=N),<br>1264 (C-N)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 1.79-1.81 (m, 6H, (CH <sub>2</sub> ), 1.94-1.97 (m, 2H, CH <sub>2</sub> ), 2.52-2.58 (m, 4H, CH <sub>2</sub> ), 3.22-3.25 (m, 2H, CH <sub>2</sub> ), 7.26-7.76 (m, 7H, Ar-H), 8.23-8.25 (dd, 1H, Ar-H) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 63.07; H, 5.54; N, 10.51  |
| Found   | : C, 63.09; H, 5.58; N, 10.55.   |

**4.2.3.3. 3-(4-Chlorophenyl)-2-(3-(piperidin-1-yl)propylthio)  
quinazolin-4(3H)-one (PC-3)**

|   |   |
|---|---|
| Yield   | : 3.47 gm; 84 %   |
| Melting Point                                 | : 108-110 °C  |
| Rf Value                                      | : 0.49 [Chloroform-Methanol (9:1)]  |
| Molecular Formula                             | : C <sub>22</sub> H <sub>24</sub> ClN <sub>3</sub> OS   |
| Molecular Weight                              | : 414 [M <sup>+</sup> ], 416 [M+2]  |
| IR (KBr) cm <sup>-1</sup>                     | : 1673 (C=O), 1607 (C=N),<br>1261 (C-N)   |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 1.45-1.46 (m, 2H, (CH <sub>2</sub> ), 1.56-<br>1.61 (m, 6H, (CH <sub>2</sub> ), 1.90-1.95 (m,<br>2H, (CH <sub>2</sub> ), 2.40-2.42 (m, 4H, CH <sub>2</sub> ),<br>3.19-3.22 (m, 2H, CH <sub>2</sub> ), 7.28-7.77<br>(m, 7H, Ar-H), 8.24-8.25 (dd, 1H,<br>Ar-H) |
| Elemental Analysis                            |   |
| Calculated                                    | : C, 63.83; H, 5.84; N, 10.15   |
| Found   | : C, 63.88; H, 5.83; N, 10.17.  |

**4.2.3.4. 3-(4-Chlorophenyl)-2-(3-(piperazin-1-yl)propylthio)quinazolin-4(3H)-one (PC-4)**

|   |   |
|---|---|
| Yield   | : 3.65 gm; 88 %   |
| Melting Point                                 | : 120-122 °C  |
| Rf Value                                      | : 0.45 [Chloroform-Methanol (9:1)]  |
| Molecular Formula                             | : C <sub>21</sub> H <sub>23</sub> ClN <sub>4</sub> OS   |
| Molecular Weight                              | : 415 [M <sup>+</sup> ], 417 [M+2]  |
| IR (KBr) cm <sup>-1</sup>                     | : 1697 (C=O), 1469 (C=N),<br>1262 (C-N), 3397 (NH)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 1.60-1.63 (m, 4H, (CH <sub>2</sub> ), 2.09-2.17 (m, 6H, CH <sub>2</sub> ), 2.67-2.70 (m, 2H, CH <sub>2</sub> ), 3.29-3.32 (m, 2H, CH <sub>2</sub> ), 7.23-7.79 (m, 7H, Ar-H), 8.27-8.29 (dd, 1H, Ar-H), 8.42 (br s, 1H, NH) |
| Elemental Analysis                            |   |
| Calculated                                    | : C, 60.78; H, 5.59; N, 13.50   |
| Found   | : C, 60.80; H, 5.57; N, 13.51.  |

**4.2.3.5. 3-(4-Chlorophenyl)-2-(3-(4-methylpiperazin-1-yl)propylthio) quinazolin-4(3H)-one (PC-5)**

|   |  |
|---|--|
| Yield   | : 3.47 gm; 81 %  |
| Melting Point                                 | : 136-138 °C   |
| Rf Value                                      | : 0.51 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>22</sub> H <sub>25</sub> ClN <sub>4</sub> OS  |
| Molecular Weight                              | : 429 [M <sup>+</sup> ], 431 [M+2]   |
| IR (KBr) cm <sup>-1</sup>                     | : 1692 (C=O), 1607 (C=N),<br>1297 (C-N)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 1.91-1.94 (m, 2H, (CH <sub>2</sub> ), 2.31 (s, 3H, CH <sub>3</sub> ), 2.44-2.47 (m, 8H, CH <sub>2</sub> ), 3.20-3.23 (m, 2H, CH <sub>2</sub> ), 3.30-3.32 (m, 2H, CH <sub>2</sub> ), 7.26-7.77 (m, 7H, Ar-H), 8.23-8.26 (dd, 1H, Ar-H) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 61.60; H, 5.87; N, 13.06  |
| Found   | : C, 61.62; H, 5.89; N, 13.04.   |



**4.2.3.6. 3-(4-Chlorophenyl)-2-(3-(morpholin-1-yl)propylthio)quinazolin-4(3H)-one (PC-6)**

|   |  |
|---|--|
| Yield   | : 3.27 gm; 79 %  |
| Melting Point                                 | : 118-120 °C   |
| Rf Value                                      | : 0.40 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>21</sub> H <sub>22</sub> ClN <sub>3</sub> O <sub>2</sub> S  |
| Molecular Weight                              | : 416 [M <sup>+</sup> ], 418 [M+2]   |
| IR (KBr) cm <sup>-1</sup>                     | : 1672 (C=O); 1617 (C=N);<br>1255 (C-N)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 1.90-1.96 (m, 2H, (CH <sub>2</sub> ), 2.44-2.47 (m, 6H, CH <sub>2</sub> ), 3.21-3.32 (m, 2H, CH <sub>2</sub> ), 3.72-3.74 (m, 4H, CH <sub>2</sub> ), 7.26-7.77 (m, 7H, Ar-H), 8.22-8.25 (dd, 1H, Ar-H) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 60.64; H, 5.33; N, 10.10  |
| Found   | : C, 62.62; H, 5.30; N, 10.12.   |

**4.2.3.7. 3-(4-Chlorophenyl)-2-(3-phenylamino)propylthio quinazolin-4(3H)-one (PC-7)**

|   |  |
|---|--|
| Yield   | : 3.74 gm; 89 %  |
| Melting Point                                 | : 190-192 °C   |
| Rf Value                                      | : 0.39 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>23</sub> H <sub>20</sub> ClN <sub>3</sub> OS  |
| Molecular Weight                              | : 422 [M <sup>+</sup> ], 424 [M+2]   |
| IR (KBr) cm <sup>-1</sup>                     | : 3300 (NH), 1631 (C=O),<br>1611 (C=N), 1330 (C-N)   |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 1.60-1.63 (m, 2H, CH <sub>2</sub> ), 2.15-2.17 (m, 2H, CH <sub>2</sub> ), 2.64-2.69 (m, 2H, CH <sub>2</sub> ), 7.03-7.78 (m, 12H, Ar-H), 8.27-8.29 (dd, 1H, Ar-H), 8.82 (br s, 1H, NH) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 65.47; H, 4.78; N, 9.96   |
| Found   | : C, 65.46; H, 4.79; N, 9.94.  |

**4.2.3.8. 3-(4-Chlorophenyl)-2-(3-(4-chlorophenylamino)propylthio) quinazolin-4(3H)-one (PC-8)**

|   |  |
|---|--|
| Yield   | : 3.93 gm; 85 %  |
| Melting Point                                 | : 146-148 °C   |
| Rf Value                                      | : 0.38 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>23</sub> H <sub>19</sub> Cl <sub>2</sub> N <sub>3</sub> OS  |
| Molecular Weight                              | : 457 [M <sup>+</sup> ], 459 [M+2]   |
| IR (KBr) cm <sup>-1</sup>                     | : 3347 (NH), 1673 (C=O),<br>1608 (C=N), 1298 (C-N)   |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 2.17-2.20 (m, 2H, (CH <sub>2</sub> ), 2.81-2.83 (m, 2H, (CH <sub>2</sub> ), 3.28-3.29 (m, 2H, CH <sub>2</sub> ), 7.17-7.74 (m, 11H, Ar-H), 8.03 (br s, 1H, NH), 8.25-8.31 (dd, 1H, Ar-H) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 60.53; H, 4.20; N, 9.21   |
| Found   | : C, 60.55; H, 4.23; N, 9.25.  |

**4.2.3.9. 3-(4-Chlorophenyl)-2-(3-(4-methylphenylamino)propylthio) quinazolin-4(3H)-one (PC-9)**

|   |  |
|---|--|
| Yield   | : 3.74 gm; 86 %  |
| Melting Point                                 | : 154-156 °C   |
| Rf Value                                      | : 0.40 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>24</sub> H <sub>22</sub> ClN <sub>3</sub> OS  |
| Molecular Weight                              | : 436 [M <sup>+</sup> ], 438 [M+2]   |
| IR (KBr) cm <sup>-1</sup>                     | : 3445 (NH), 1672 (C=O),<br>1541 (C=N), 1260 (C-N)   |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 2.28-2.31 (m, 2H, (CH <sub>2</sub> ), 2.36-2.38 (m, 2H, CH <sub>2</sub> ), 2.81 (s, 3H, CH <sub>3</sub> ), 3.44-3.47 (m, 2H, CH <sub>2</sub> ) 7.13-7.76 (m, 11H, Ar-H), 8.29-8.31 (dd, 1H, Ar-H), 8.73 (br s, 1H, NH) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 66.12; H, 5.09; N, 9.64   |
| Found   | : C, 66.15; H, 5.08; N, 9.66.  |

**4.2.3.10. 2-(3-(Benzylamino)propylthio)-3-(4-chlorophenyl)quinazolin-4(3H)-one (PC-10)**

|   |   |
|---|---|
| Yield   | : 3.70 gm; 85 %   |
| Melting Point                                 | : 180-186 °C  |
| Rf Value                                      | : 0.38 [Chloroform-Methanol (9:1)]  |
| Molecular Formulae                            | : C <sub>24</sub> H <sub>22</sub> ClN <sub>3</sub> OS   |
| Molecular Weight                              | : 436 [M <sup>+</sup> ], 438 [M+2]  |
| IR (KBr) cm <sup>-1</sup>                     | : 3241 (NH), 1697 (C=O),<br>1597 (C=N), 1262 (C-N)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 2.19 (s, 2H, (CH <sub>2</sub> ), 2.29-2.33 (m, 2H, CH <sub>2</sub> ), 2.95-2.98 (m, 2H, CH <sub>2</sub> ), 3.28-3.31 (m, 2H, CH <sub>2</sub> ), 7.17-7.74 (m, 12H, Ar-H), 8.22-8.24 (dd, 1H, Ar-H), 8.45 (br s, 1H, NH) |
| Elemental Analysis                            |   |
| Calculated                                    | : C, 66.12; H, 5.09; N, 9.64  |
| Found   | : C, 66.15; H, 5.06; N, 9.67.   |

**SCHEME 3****4.3.1. Synthesis of 3-(phenyl)-2-thioxo quinazolin-4(3H)-one (4)**

To a vigorously stirred solution of Aniline (1.86 g; 0.02 mol) in dimethyl sulfoxide (10 mL), carbon disulphide (1.6 mL) and aqueous sodium hydroxide (1.2 mL; 20 molar solution) added dropwise. Then stirring was continued for further 30 min. Dimethyl sulphate (2.5 g; 0.02 mol) was then added gradually keeping the reaction mixture in freezing mixture with stirring and the stirring was continued for an additional 2 hrs. The reaction mixture was then poured into ice cold water. The separated solid obtained was filtered, washed with water, dried and recrystallized from ethanol to give *N*-(phenyl) methyl dithiocarbamic acid. Then Methyl anthranilate (1.5 g; 0.01 mol) was added to the above prepared product in ethanol (20 mL). To this anhydrous potassium carbonate (100 mg) was also added and refluxed (conventional heating 18 h; microwave heating 30 min). The reaction mixture was cooled in crushed ice and the solid separated was filtered off and purified by dissolving in 10% alcoholic sodium hydroxide solution and reprecipitated by treating with dilute hydrochloric acid. The solid obtained was filtered, washed with water and finally dried. Then it was recrystallized from ethanol to give **(4)**.

|   |  |
|---|--|
| Yield   | : 2.18 gm; 86 %  |
| Melting Point                                 | : 305-306 °C   |
| Rf Value                                      | : 0.30 [Chloroform-Methanol (9:1)]                       |
| Molecular Formula                             | : C <sub>14</sub> H <sub>10</sub> N <sub>2</sub> OS      |
| Molecular Weight                              | : 254 [M <sup>+</sup> ]                                  |
| IR (KBr) cm <sup>-1</sup>                     | : 3220 (NH), 1660 (C=O),<br>1200 (C=S)                   |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 7.0-9.0 (m, 9H, Ar- <i>H</i> ),<br>10.5 (br s, 1H, NH) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 66.12; H, 3.96; N, 11.02                            |
| Found   | : C, 66.16; H, 3.95; N, 11.05                            |

#### **4.3.2. Synthesis of 2-(3-bromopropylthio)-3-(phenyl)quinazolin-4-(3*H*)-one (6)**

A solution of 3-(phenyl)-2-thioxo quinazolin-4(3*H*) one (**4**) (2.54 g; 0.01 mol), 1,3-dibromo propane (4.02 gm; 0.02 mol) and K<sub>2</sub>CO<sub>3</sub> (4.14 g; 0.03 mol) in acetone (20 mL) were taken in a round bottom flask. The contents were refluxed for 1 h on a water bath. Then the reaction mixture was cooled to room temperature and filtered off to remove the inorganic materials. The solvent was distilled off and the product of 2-(3-bromo

propylthio)-3-(phenyl) quinazolin-4(3*H*)-one (**6**) dried under reduced pressure in a rotary vacuum evaporator, it was then recrystallized from ethanol.

|   |   |
|---|---|
| Yield   | : 3.11 gm; 83 %   |
| Melting Point                                 | : 195-198 °C  |
| Rf Value                                      | : 0.33 [Chloroform-Methanol (9:1)]  |
| Molecular Formula                             | : C <sub>17</sub> H <sub>15</sub> BrN <sub>2</sub> OS   |
| Molecular Weight                              | : 375 [M <sup>+</sup> ], 377 [M+2]  |
| IR (KBr) cm <sup>-1</sup>                     | : 1686 (C=O), 1603 (C=N),<br>592 (C-Br)   |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 2.03-2.08 (m, 2H, CH <sub>2</sub> ), 2.55-2.58 (m, 2H, CH <sub>2</sub> ), 3.22-3.25 (m, 2H, CH <sub>2</sub> ), 7.39-7.46 (m, 4H, Ar-H), 7.57-7.59 (m, 3H, Ar-H), 7.77-7.79 (d, 1H, Ar-H), 8.05-8.06 (d, 1H, Ar-H) |
| Elemental Analysis                            |   |
| Calculated                                    | : C, 54.41; H, 4.03; N, 7.46  |
| Found   | : C, 54.39; H, 4.00; N, 07.49   |



**4.3.3. General procedure for the synthesis of 3-(phenyl)-2-(3-substitutedpropylthio) quinazolin-4(3H)-ones (Ph1-Ph10)**

2-(3-bromo propylthio)-3-(phenyl) quinazolin-4(3H)-one (**6**) (3.75 g; 0.01 mol) was dissolved in 1-butanol (25 mL). To this appropriate alkyl/aryl amine (0.015 mol), Potassium iodide (1.66 g; 0.015 mol) and sodium carbonate (2.12 g; 0.02 mol) was added and refluxed (for 3 h by conventional refluxing or 15 min by microwave oven). The reaction mixture was cooled, filtered and the filtrate was then concentrated in vacuum and kept in refrigerator overnight. The solid obtained was filtered, dried and recrystallized from chloroform-ethanol (50:50) mixture to afford the title compounds (**Ph1 – Ph10**).

**4.3.3.1. 2-(3-(Diethylamino)propylthio)-3-(phenyl)quinazolin-4(3H)-one (Ph-1)**

|   |  |
|---|--|
| Yield   | : 2.97 gm; 81 %  |
| Melting Point                                 | : 170-172 °C   |
| Rf Value                                      | : 0.49 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>21</sub> H <sub>25</sub> N <sub>3</sub> OS  |
| Molecular Weight                              | : 367 [M <sup>+</sup> ]  |
| IR (KBr) cm <sup>-1</sup>                     | : 1684 (C=O), 1608 (C=N),<br>1288 (C-N)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 0.89-0.95 (m, 6H, (CH <sub>3</sub> ) <sub>2</sub> ), 2.05-2.07 (m, 2H, CH <sub>2</sub> ), 2.38-2.42 (m, 6H, CH <sub>2</sub> ), 3.22-3.25 (m, 2H, CH <sub>2</sub> ), 7.39-7.47 (m, 4H, Ar-H), 7.58-7.59 (m, 3H, Ar-H), 7.78-7.80 (d, 1H, Ar-H), 8.04-8.05 (d, 1H, Ar-H) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 68.63; H, 6.86; N, 11.43  |
| Found   | : C, 68.60; H, 6.89; N, 11.40  |

**4.3.3.2. 3-(Phenyl)-2-(3-(pyrrolidin-1-yl) propylthio) quinazolin-4(3H)-one (Ph-2)**

|   |  |
|---|--|
| Yield   | : 2.84 gm; 78 %  |
| Melting Point                                 | : 210-212 °C   |
| Rf Value                                      | : 0.47 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>21</sub> H <sub>23</sub> N <sub>3</sub> OS  |
| Molecular Weight                              | : 365 [M <sup>+</sup> ]  |
| IR (KBr) cm <sup>-1</sup>                     | : 1685 (C=O), 1606 (C=N),<br>1262 (C-N)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 1.60-1.72 (m, 4H, (CH <sub>2</sub> ), 2.12-2.20 (m, 6H, CH <sub>2</sub> ), 2.70-2.73 (m, 2H, CH <sub>2</sub> ), 3.28-3.31 (m, 2H, CH <sub>2</sub> ), 7.28-7.73 (m, 8H, Ar-H), 8.24-8.25 (dd, 1H, Ar-H) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 69.01; H, 6.34; N, 11.50  |
| Found   | : C, 69.00; H, 6.37; N, 11.52  |

**4.3.3.3. 3-(Phenyl)-2-(3-(piperidin-1-yl)propylthio)quinazolin-4(3H)-one (Ph-3)**

|   |  |
|---|--|
| Yield   | : 3.10 gm; 82 %  |
| Melting Point                                 | : 186-188 °C   |
| Rf Value                                      | : 0.51 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>22</sub> H <sub>25</sub> N <sub>3</sub> OS  |
| Molecular Weight                              | : 379 [M <sup>+</sup> ]  |
| IR (KBr) cm <sup>-1</sup>                     | : 1692 (C=O), 1606 (C=N),<br>1268 (C-N)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 1.23-1.34 (m, 6H, (CH <sub>2</sub> -piperidiny), 2.05-2.08 (m, 2H, CH <sub>2</sub> ), 2.28-2.30 (m, 4H, CH <sub>2</sub> -piperidiny), 3.23-3.26 (m, 4H, CH <sub>2</sub> ), 7.39-7.40 (d, 1H, Ar-H), 7.43-7.46 (m, 3H, Ar-H), 7.58-7.61 (m, 3H, Ar-H), 7.78-7.80 (d, 1H, Ar-H), 8.07-8.09 (d, 1H, Ar-H) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 69.62; H, 6.64; N, 11.07  |
| Found   | : C, 69.65; H, 6.67; N, 11.05  |

**4.3.3.4. 3-(Phenyl)-2-(3-(piperazin-1-yl) propylthio) quinazolin-4(3*H*)-one (Ph-4)**

|   |   |
|---|---|
| Yield   | : 3.03 gm; 80 %   |
| Melting Point                                 | : 176-178 °C  |
| R <sub>f</sub> Value                          | : 0.48 [Chloroform-Methanol (9:1)]  |
| Molecular Formula                             | : C <sub>21</sub> H <sub>24</sub> N <sub>4</sub> OS   |
| Molecular Weight                              | : 380 [M <sup>+</sup> ]   |
| IR (KBr) cm <sup>-1</sup>                     | : 3192 (NH), 1686 (C=O),<br>1614 (C=N), 1265 (C-N)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 1.62-1.64 (m, 6H, (CH <sub>2</sub> ), 2.17-2.22 (m, 4H, CH <sub>2</sub> ), 2.83-2.85 (m, 2H, CH <sub>2</sub> ), 3.28-3.31 (m, 2H, CH <sub>2</sub> ), 7.31-7.73 (m, 8H, Ar- <i>H</i> ), 8.24-8.25 (dd, 1H, Ar- <i>H</i> ), 8.61 (br s, 1H, NH) |
| Elemental Analysis                            |   |
| Calculated                                    | : C, 66.29; H, 6.36; N, 14.72   |
| Found   | : C, 66.26; H, 6.34; N, 14.74   |

**4.3.3.5. 2-(3-(4-Methylpiperazin-1-yl)propylthio)-3-(phenyl)quinazolin-4(3H)-one (Ph-5)**

|   |  |
|---|--|
| Yield   | : 3.11 gm; 79 %  |
| Melting Point                                 | : 180-182 °C   |
| Rf Value                                      | : 0.53 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>22</sub> H <sub>26</sub> N <sub>4</sub> OS  |
| Molecular Weight                              | : 394 [M <sup>+</sup> ]  |
| IR (KBr) cm <sup>-1</sup>                     | : 1689 (C=O), 1606 (C=N),<br>1299 (C-N)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 1.60-1.62 (m, 6H, (CH <sub>2</sub> ), 2.18-2.22 (m, 4H, CH <sub>2</sub> ), 2.53 (s, 3H, CH <sub>3</sub> ), 2.74-2.77 (m, 2H, CH <sub>2</sub> ), 3.27-3.30 (m, 2H, CH <sub>2</sub> ), 7.29-7.70 (m, 8H, Ar-H), 8.20-8.21 (dd, 1H, Ar-H) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 66.97; H, 6.64; N, 14.20  |
| Found   | : C, 66.93; H, 6.67; N, 14.16  |

**4.3.3.6                    2-(3-Morpholin-1-yl)propylthio)-3-(phenyl)  
quinazolin-4(3H)-one (Ph-6)**

|   |   |
|---|---|
| Yield   | : 3.08 gm; 81 %   |
| Melting Point                                 | : 166-170 °C  |
| Rf Value                                      | : 0.46 [Chloroform-Methanol (9:1)]  |
| Molecular Formula                             | : C <sub>21</sub> H <sub>23</sub> N <sub>3</sub> O <sub>2</sub> S   |
| Molecular Weight                              | : 381 [M <sup>+</sup> ]   |
| IR (KBr) cm <sup>-1</sup>                     | : 1690 (C=O); 1606 (C=N);<br>1260 (C-N)   |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 1.65-1.68 (m, 6H, (CH <sub>2</sub> ), 2.18-<br>2.20 (m, 4H, CH <sub>2</sub> ), 2.49-2.50 (m,<br>2H, CH <sub>2</sub> ), 3.29-3.31 (m, 2H,<br>CH <sub>2</sub> ), 7.28-7.73 (m, 8H, Ar-H),<br>8.24-8.25 (dd, 1H, Ar-H) |
| Elemental Analysis                            |   |
| Calculated                                    | : C, 66.12; H, 6.08; N, 11.01   |
| Found   | : C, 66.16; H, 6.05; N, 11.04   |

**4.3.3.7. 3-(Phenyl)-2-(3-phenylamino) propylthio  
quinazolin-4(3H)-one (Ph-7)**

|   |   |
|---|---|
| Yield   | : 3.09 gm; 80 %   |
| Melting Point                                 | : 180-182 °C  |
| Rf Value                                      | : 0.45 [Chloroform-Methanol (9:1)]  |
| Molecular Formula                             | : C <sub>23</sub> H <sub>21</sub> N <sub>3</sub> OS   |
| Molecular Weight                              | : 387 [M <sup>+</sup> ]   |
| IR (KBr) cm <sup>-1</sup>                     | : 3280 (NH), 1686 (C=O),<br>1606 (C=N), 1299 (C-N)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 2.04-2.07 (m, 2H, CH <sub>2</sub> ), 2.49-<br>2.50 (m, 2H, CH <sub>2</sub> ), 3.22-3.24 (m,<br>2H, CH <sub>2</sub> ), 7.39-7.58 (m, 7H, Ar-H),<br>8.15 (br s, 1H, NH), 8.40-8.65 (m,<br>7H, Ar-H) |
| Elemental Analysis                            |   |
| Calculated                                    | : C, 71.29; H, 5.46; N, 10.84   |
| Found   | : C, 71.33; H, 5.47; N, 10.82   |



**4.3.3.8. 2-(3-(4-Chlorophenylamino)propylthio)-3-(phenyl)quinazolin-4(3H)-one (Ph-8)**

|   |   |
|---|---|
| Yield   | : 3.28 gm; 78 %   |
| Melting Point                                 | : 188-190 °C  |
| Rf Value                                      | : 0.43 [Chloroform-Methanol (9:1)]  |
| Molecular Formula                             | : C <sub>23</sub> H <sub>20</sub> ClN <sub>3</sub> OS   |
| Molecular Weight                              | : 422 [M <sup>+</sup> ], 424 [M+2]  |
| IR (KBr) cm <sup>-1</sup>                     | : 3286 (NH), 1685 (C=O),<br>1610 (C=N), 1271 (C-N)  |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 2.03-2.09 (m, 2H, (CH <sub>2</sub> ), 2.49-2.50 (t, 2H, CH <sub>2</sub> ), 3.22-3.25 (t, 2H, CH <sub>2</sub> ), 7.42-8.26 (m, 12H, Ar-H), 8.53 (br s, 1H, NH), 8.78 (m, 1H, Ar-H) |
| Elemental Analysis                            |   |
| Calculated                                    | : C, 65.47; H, 4.78; N, 9.96  |
| Found   | : C, 65.45; H, 4.74; N, 9.98  |

**4.3.3.9. 2-(3-(4-Methylphenylamino) propylthio)-3-(phenyl) quinazolin-4(3H)-one (Ph-9)**

|   |  |
|---|--|
| Yield   | : 3.24 gm; 81 %  |
| Melting Point                                 | : 211-212 °C   |
| Rf Value                                      | : 0.45 [Chloroform-Methanol (9:1)]   |
| Molecular Formula                             | : C <sub>24</sub> H <sub>23</sub> N <sub>3</sub> OS  |
| Molecular Weight                              | : 401 [M <sup>+</sup> ]  |
| IR (KBr) cm <sup>-1</sup>                     | : 3274 (NH), 1689 (C=O);<br>1606 (C=N); 1298 (C-N)   |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 2.04-2.07 (m, 4H, (CH <sub>2</sub> ), 2.49-2.51 (s, 3H, CH <sub>3</sub> ), 3.22-3.25 (m, 2H, CH <sub>2</sub> ), 7.39-7.80 (m, 12H, Ar-H) 8.07-8.08 (dd, 1H, Ar-H), 8.51 (br s, 1H, NH) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 71.79; H, 5.77; N, 10.47  |
| Found   | : C, 71.74; H, 5.79; N, 10.46  |

**4.3.3.10. 2-(3-(Benzylamino) propylthio)-3-(phenyl) quinazolin-4(3H)-one (Ph-10)**

|   |  |
|---|--|
| Yield   | : 3.20 gm; 80 %  |
| Melting Point                                 | : 170-172 °C   |
| Rf Value                                      | : 0.44 [Chloroform-Methanol (9:1)]   |
| Molecular Formulae                            | : C <sub>24</sub> H <sub>23</sub> N <sub>3</sub> OS  |
| Molecular Weight                              | : 401 [M <sup>+</sup> ]  |
| IR (KBr) cm <sup>-1</sup>                     | : 3276 (NH), 1689 (C=O);<br>1609 (C=N); 1289 (C-N)   |
| <sup>1</sup> H NMR (CDCl <sub>3</sub> ) δ ppm | : 2.18-2.20 (m, 4H, (CH <sub>2</sub> ), 3.29-3.31 (m, 4H, CH <sub>2</sub> ), 7.31-7.73 (m, 13H, Ar-H), 8.24-8.25 (dd, 1H, Ar-H), 8.71 (br s, 1H, NH) |
| Elemental Analysis                            |  |
| Calculated                                    | : C, 71.79; H, 5.77; N, 10.47  |
| Found   | : C, 71.80; H, 5.74; N, 10.49  |

## **4.2. Pharmacology**

Antihistaminic and Sedative-hypnotic activities were evaluated for the synthesized compounds. The animals were maintained in colony cages at  $25 \pm 2$  °C, relative humidity of 45-55%, under a 12 h light and dark cycle; they were fed standard animal feed. All the animals were acclimatized for a week before the experiment. The Approval from Institutional Animal Ethics committee was taken for the protocol adopted for the animal used in the experiment.

### **4.2.1. Antihistaminic activity**

A modification of the technique of Van Arman<sup>331</sup> was adopted to determine the antihistaminic potential of the synthesized compounds. Male Dunkin Hartley Guinea pigs (250-300 g) were fasted for 12 h. Six animals were taken in each group. The test compounds and reference compound chlorpheniramine maleate was administered orally at a dose of 10 mg/kg in 1% CMC and challenged with histamine aerosol (0.2% aqueous solution of histamine acid chloride 3 mL) in a vaponephrin pocket nebulizer sprayed into a closed transparent cage. The respiratory status reflecting the increasing degree of bronchoconstriction was recorded. The time for onset of convulsions (preconvulsion) was recorded. Animals remaining stable for more than 6 min were considered protected against

histamine-induced bronchospasm. An intraperitoneal injection of pheniramine maleate (Avil; Hoechst, Mumbai, India), at a dose of 25 mg/kg was given for the recovery of the test animals. The mean preconvulsion time of animals treated with the test compounds was compared to control and is expressed in terms of percentage protection (**Table 1, 2 & 3**).

$$\text{Percent protection} = [1 - (T_1 / T_2)] \times 100$$

$T_2$  - preconvulsive time of test compound;  $T_1$  - preconvulsive time of control.

The activity of the test compounds was compared with the standard antihistamine chlorpheniramine maleate.

#### **4.2.2. Sedative-hypnotic activity**<sup>332-333</sup>

Sedative-hypnotic activity was determined by measuring the reduction in locomotor activity using actophotometer. Six albino Swiss mice were allotted to each group. Basal activity score was taken and then test compounds and standard chlorpheniramine maleate were administered orally at the dose of 5 mg/kg in 1% CMC. Scores were recorded at 0.5, 1, 2 and 3 h after the drug administration. The percent reduction in locomotor activity was calculated by the following formula and shown in Table 1, 2 & 3.

$$\% \text{ Reduction in motor activity} = [(A-B)/A] \times 100$$

Where A-basal score, B-score after drug treatment.

#### **4.2.3. Statistical analysis**

Statistical analysis of the biological activity of the synthesized compounds on animals was evaluated using an one-way analysis of variance (ANOVA). In all cases, post-hoc comparisons of the means of individual groups were performed using Tukey's test. A significance level of  $p < 0.05$  denoted significance in all cases. All values are expressed as mean  $\pm$  SD (standard deviations). For statistical analysis GraphPad Prism 3.0 version was used. (GraphPad Software, Inc. 11452 El Camino Real, #215, San Diego, CA 92130 USA).