Chapter-4

Synthesis of pyrimidine derivatives of oxocarbazoles and oxoazacarbazoles fused sulphonamides
Abstract

This chapter describes the synthesis of pyrimidino condensed derivatives of carbazoles and azacarbazoles, (substituted with sulphonamides group in the arene part of the carbazole or azacarbazole moiety) by the cyclocondensation of the corresponding oxoketenedithioacetals with urea and thiourea respectively. The structures of all the compounds have been established on the basis of their elemental analysis and spectral (IR, \textsuperscript{1}HNMR and MS) data.
Contents of the Chapter at a Glance

4.1 General introduction
   4.1.1 Importance of pyrimidine derivatives
   4.1.2 Biological importance of pyrimidine
   4.1.3 Application of pyrimidine
   4.1.4 Synthetic aspects of pyrimidine derivatives

4.2 Present Work

4.3 Results and discussion

4.4 Interpretation of spectral data for the elucidation of structure of compounds

4.5 Mechanism of formation of compounds

4.6 Experimental section

4.7 References
4.1 General Introduction

In chapter 3 the strategies which led to the incorporation of biologically active pharmacophores such as pyrazole and isoxazole scaffolds, on to the carbazole and azacarbazole containing the sulphonamide motif, was described. This chapter demonstrates the importance of the incorporation of the six membered rings viz; hydroxy pyrimidine and mercapto pyrimidine on to the carbazole and azacarbazole nucleus substituted with sulphonamide motifs and describes the strategy adopted to incorporate the pyrimidine pharmacophore on to above nucleus through the corresponding oxoketenedithioacetals.

The biological potential of pyrimidine nucleus has prompted us to focus research on the synthesis and study of biological properties of newer series of pyrimidine derivatives formed by its annulation with carbazole and azacarbazole nucleus. Pyrimidine and their myriad derivatives have continued to capture the attention of chemists since their presence in the biologically active materials have been known to produce additive effect on the bio-efficacy of the molecules. In view of the impressive pharmacological properties exhibited by the carbazole and azacarbazoles it is thought that, it could be worthwhile to incorporate the pyrimidine ring on these molecules to which sulphonamide intitities were also present with the idea to verify the assumption, that incorporation of pharmacophores which have previous history of being biologically active, could produce a positive additive effect on the overall potency of the parent molecule.

Pyrimidines form the building block of DNA and RNA. In view of this, the study of pyrimidines is of immense significance. Fused pyrimidines (e.g.: purines, pyrrolopyrimidine, pyrimidopyrimidines, pteridines) are found in a variety of natural products, agrochemical and veterinary products. Annelated pyrimidine derivatives continue to attract interest due to their wide variety of interesting biological and pharmacological activities. Pyrimidines play a vital role in many biological processes since this ring system is present in several vitamins, coenzymes, nucleic acids etc. Synthetic members of these groups are also important as chemotherapeutic agents. The pyrimidine nucleus also occurs in a considerable number of natural
products of vital importance to living organisms. In view of the impressive pharmacodynamic applications of pyrimidine and condensed pyrimidine derivatives, it was considered of interest to synthesize pyrimidine ring fused derivatives from oxoketenedithioacetals. The synthesis of this series of heterocycle was undertaken on this assumption that incorporation of one or more than one bioactive heterocyclic moiety into the pyrimidine framework may result heterocycles with enhanced biological activity.

### 4.1.1 Importance of pyrimidine derivatives

Pyrimidine is the most important member of all the diazines as this ring system occurs widely in living organisms. Purines, uric acid, alloxan, barbituric acid and a mixture of anti-malarial\(^8\) and anti-bacterials\(^9\) also contain the pyrimidine ring. Pyrimidine is a basic nucleus in DNA and RNA, it has been found to be associated with diverse biological activities. Pyrimidine nucleus has been the subject of substantial attention by synthetic and medicinal chemists because of the presence of the fused heterocyclic rings in many biological systems.\(^{10-14}\)

### 4.1.2 Biological importance of pyrimidines

Pyrimidines are particularly interesting targets, for the synthesis of novel fused heterocycles due to their structural diversity and importance in the development of broad range of therapeutics. Pyrimidine itself is not found in nature but substituted pyrimidines and its derivatives are widely distributed in nature. Derivatives of barbituric acid (4.001), oxygenated pyrimidines are the most widely used in medicines, for example, Veronal (4.002), Luminal (4.003) are used as hypnotics while Pentothal (4.004) is used as an anesthetic.\(^{15}\) (Fig 4.01)
Several important sulfa drugs are pyrimidine derivatives namely sulfadiazine (4.005), sulfamerazine (4.006) and sulfadimidine (4.007). (Fig 4.02)

Pyrimidines have a long and distinguished history extending from the days of their discovery as important constituents of nucleic acids to their current use in the chemotherapy of AIDS. They form an integral part of the genetic materials viz. DNA and RNA. Following three pyrimidines are of considerable biological importance because of their relation to the nucleic acids, these are uracil (4.008), thymine (4.009) and cytosine (4.010). (Fig 4.03)
The purine ring system (4.011) obtained by the fusion of pyrimidine and imidazole nuclei also is important because certain of its derivatives, in particular adenine (4.012) and guanidine (4.013) are building blocks of RNA and DNA. (Fig 4.04)

A variety of natural products such as alkaloids also contain the pyrimidine ring system, these include hypoxanthine (4.014), and xanthine (4.015) which occur in tea and theobromine (4.016) is found in cocoa beans. (Fig 4.05)

Five and six membered heterocyclic compounds containing one or two heteroatoms fused to pyrimidine ring in a linear fashion are found in natural
products as well as in the synthetic compounds of biological interest. Pyrimidine derivatives are reported to possess antibacterial,\(^{17}\) antimicrobial, antifungal,\(^{18}\) anticancer\(^{19}\) and antihypertensive\(^{20}\) activities.

### 4.1.3 Application of pyrimidine

Pyrimidine, bearing substituents in the ring are important in many respects as a number of compounds of this class have been used in synthetic, analytical and medicinal chemistry. As stated above these compounds have many pharmaceutical activity like antibacterial,\(^{21}\) insecticidal,\(^{22}\) tranquilizing,\(^{23}\) antidiabetic,\(^{24}\) antimicrobial, antifungal,\(^{25}\) anticancer,\(^{26}\) antihypertensive\(^{27}\) and anticonvulsant. Alloxan (4.017) is known for its diabetogenic action in a number of animals. (Fig 4.06)

![Fig 4.06](image)

Barbitone\(^{28}\) (4.018), the first barbiturate hypnotic sedative and anticonvulsant is a pyrimidine derivative. (Fig 4.07)

![Fig 4.07](image)

There are a large number of pyrimidine-based antimetabolites. They are usually structurally related to the endogenous substrates, that they antagonize. The structural modification may be on the pyrimidine ring or on the pendant sugar groups. One of the early metabolites prepared is 5-fluorouracil (5-FU, 4.019a), a
pyrimidine derivative. 5-Thiouracil (4.019b) also exhibits some useful antineoplastic activities.\textsuperscript{29-30} (Fig: 4.08)

\[
\begin{align*}
4.019a, & X=O, R=F, R^1=H \\
4.019b, & X=O, R=SH, R^1=H
\end{align*}
\]

Fig 4.08

Many more antineoplastic compounds have been included in recent times, like mopidamol\textsuperscript{31} (4.020), nimustine\textsuperscript{32} (4.021) and trimetixater\textsuperscript{33} (4.022). (Fig: 4.09)

\[
\begin{align*}
4.020 & \\
4.021 &
\end{align*}
\]

Fig 4.09

The design of several anti-cancer agents has been based on the antimetabolite theory. Because cancer results in over-proliferation and uncontrolled cell growth, drugs designed against cancer have been based upon inhibiting DNA synthesis in the cell. Thus, these drugs have been targeted against those enzymes, including nucleic acid polymerases, thymidylate synthase and dihydrofolate reductase (DHFR) that
play a role in DNA synthesis. Examples of drug that have been designed against nucleic acid polymerases include 5-fluorouracil (5-FU)\textsuperscript{34} (4.023). (Fig 4.010) 5-FU is an analog of the pyrimidine uracil where the H at the 5-position in uracil has been substituted by an isosteric fluorine (F) atom. This makes 5-FU look very similar to uracil. 5-FU, after conversion to 5-fluorodeoxyuridine monophosphate is an inhibitor of thymidylate synthase, the enzyme involved in the de-novo synthesis of thymidylate.

![Figure 4.010](image)

Prazosin\textsuperscript{35} (4.024), the first known selective $\alpha_1$-blocker, is an antihypertensive agent, as are terazosin (4.025) and doxazosin\textsuperscript{36} (4.026). (Fig 4.011)

![Figure 4.011](image)
2-Thiouracil (4.027a) and its alkyl analogue, thiobarbital (4.027c) are effective drugs against hyperthyrodisim. Propylthiouracil (4.027b) is used as a drug for hyperthyroidism with fewer side effects. (Fig: 4.012)

\[
\begin{align*}
4.027a, & \quad R=R_1=R_2=H, \ X=S \\
4.027b, & \quad R=R_1=H, \ R_2=C_3H_7, \ X=S \\
4.027c, & \quad R=R_1=C_2H_5, \ R_2=O, \ X=S
\end{align*}
\]

Fig 4.012

4.1.4 Synthetic aspects

Several synthetic strategies have been developed in the literature for the preparation of different analogues of pyrimidine, of which a few examples are given below. A ZnCl$_2$-catalyzed three-component coupling reaction allows the synthesis of various 4, 5-disubstituted pyrimidine derivatives (4.030) in a single step from functionalized enamines (4.028), triethyl orthoformate, and ammonium acetate. The procedure can be successfully applied to the efficient synthesis of mono- and disubstituted pyrimidine derivatives, using methyl ketone (4.029) derivatives instead of enamines. (Scheme 4.1)

\[
\begin{align*}
\text{R: } & \text{Ar, EWG} \quad \text{or} \quad \text{R: alkyl, H} \\
\text{R: } & \text{Ar, alkyl}
\end{align*}
\]

Scheme 4.1

A method for the synthesis of 2-substituted pyrimidine-5-carboxylic esters (4.033) is described. The sodium salt of 3, 3-dimethoxy-2-methoxycarbonylpropen-1-
ol (4.032) has been found to react with a variety of amidinium salts (4.031) to afford the corresponding 2-substituted pyrimidine-5-carboxylic esters.\(^4\) (Scheme 4.2)

![Scheme 4.2]

The direct condensation of cyanic acid derivatives (4.034) with N-vinyl/aryl amides (4.035) affords the corresponding C₄-heteroatom substituted pyrimidines (4.036). The use of cyanic bromide and thiocyanatomethane in this chemistry provides versatile azaheterocycles poised for further derivatization.\(^1\) (Scheme 4.3)

![Scheme 4.3]

The coupling of acid chlorides (4.037) with terminal alkynes (4.038) using one equivalent of triethylamine under Sonogashira conditions followed by subsequent addition of amines or amidinium salts to the intermediate alkynones allows a straightforward access to enamiones and pyrimidines under mild conditions and in excellent yields.\(^2\) (Scheme 4.4)

![Scheme 4.4]

A single-step conversion of various N-vinyl and N-aryl amides (4.041) to the corresponding pyrimidine (4.043) derivatives involves amide activation with 2-
chloropyridine and trifluoromethanesulfonic anhydride followed by nitrile addition (4.042) into the reactive intermediate and cyclomerization.\(^{43}\) (Scheme 4.5)

Scheme 4.5

4.2 Present Work

Oxoketene dithioacetals have been exploited in a variety of synthetic applications. They have recently received considerable attention due to their synthetic importance for the construction of a variety of novel fused heterocyclic systems therefore; their synthesis and reaction have recently gained much importance.

The present investigation was undertaken with a view to streamline the synthetic strategies which have been devised in the literature for the preparation of pyrimidine derivatives. Although the chemical literature is replete with great variety of synthetic methods which have been employed for the preparation of medicinally potent pyrimidines, but a large number of them, if not all, are burdened with one liability or the other. It poses a very serious limitation on the use of these procedures and calls attention to develop much simpler routes which use easily accessible starting materials. Clearly a refinement in the existing methodology and development of newer strategies for their synthesis was required. Consideration of reactivity, compound availability, synthetic economy and simplicity in operation, has led us to favour the use of oxoketenedithioacetals as a starting material, in the present study, for the synthesis of pyrimidine derivatives.

4.3 Results and discussion

In the present work, the synthesis of pyrimidine derivatives of sulphonamide containing carbazoles and azacarbazoles were carried out by the cyclocondensation of corresponding oxoketenedithioacetals with urea and thiourea. Synthesis of corresponding oxoketenedithioacetals has already been described in chapter -2.
When 4.044(a,b), 4.045(a,b), 4.046(a,b) and 4.047a were allowed to react with urea and thiourea in presence of a base, the corresponding hydroxyl pyrimidine derivatives 4.048a, 4.049a, 4.050a, 4.051a, 4.052a, 4.053a and 4.054a and corresponding pyrimidine derivatives 4.048b, 4.049b, 4.050b, 4.051b, 4.052b, 4.053b and 4.054b respectively were obtained in acceptable yields. (Scheme 4.6)

Scheme 4.6
Structure of compounds 4.049(a,b)-4.055(a,b) whose synthesis is described in this chapter.

Fig 4.013
4.052 a

4.052 b

4.053 a

4.053 b

4.054 a

4.054 b

Fig 4.014
<table>
<thead>
<tr>
<th>S.N.</th>
<th>Compound</th>
<th>Molecular Formula</th>
<th>M.W.</th>
<th>M.P. °C</th>
<th>Yield %</th>
<th>Elemental Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cald./ Found (C)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cald./ Found (H)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cald./ Found (N)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cald./ Found (S)</td>
</tr>
<tr>
<td>1.</td>
<td>4.048a</td>
<td>C_{17}H_{13}N_{2}O_{3}S_{3}</td>
<td>431.51</td>
<td>135-137</td>
<td>72</td>
<td>47.32/47.65</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.04/3.21</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>16.23/16.02</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>22.29/22.90</td>
</tr>
<tr>
<td>2.</td>
<td>4.048b</td>
<td>C_{17}H_{13}N_{2}O_{2}S_{4}</td>
<td>447.58</td>
<td>130-132</td>
<td>68</td>
<td>45.62/45.45</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.93/2.70</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>15.65/15.22</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>28.66/28.16</td>
</tr>
<tr>
<td>3.</td>
<td>4.049a</td>
<td>C_{18}H_{20}N_{3}O_{3}S_{3}</td>
<td>536.65</td>
<td>142-144</td>
<td>67</td>
<td>53.71/53.50</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.76/3.50</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>15.66/15.96</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>17.93/17.53</td>
</tr>
<tr>
<td>4.</td>
<td>4.049b</td>
<td>C_{18}H_{20}N_{3}O_{2}S_{4}</td>
<td>552.71</td>
<td>136-138</td>
<td>64</td>
<td>52.15/52.36</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.65/3.85</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>15.20/14.90</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>23.21/23.66</td>
</tr>
<tr>
<td>5.</td>
<td>4.050a</td>
<td>C_{19}H_{16}N_{2}O_{3}S_{2}</td>
<td>440.50</td>
<td>148-150</td>
<td>67</td>
<td>51.81/51.62</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.66/3.40</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>19.08/18.80</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>14.56/14.12</td>
</tr>
<tr>
<td>6.</td>
<td>4.050b</td>
<td>C_{19}H_{16}N_{2}O_{2}S_{3}</td>
<td>456.56</td>
<td>141-143</td>
<td>64</td>
<td>49.98/50.11</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.53/3.78</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>18.41/18.04</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>21.07/21.35</td>
</tr>
<tr>
<td>7.</td>
<td>4.051a</td>
<td>C_{25}H_{21}N_{2}O_{3}S_{2}</td>
<td>531.61</td>
<td>153-155</td>
<td>62</td>
<td>56.48/56.18</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.98/3.63</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>18.44/18.64</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>12.06/12.46</td>
</tr>
<tr>
<td>8.</td>
<td>4.051b</td>
<td>C_{25}H_{21}N_{2}O_{2}S_{3}</td>
<td>547.67</td>
<td>150-151</td>
<td>60</td>
<td>54.83/54.61</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.86/3.54</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>17.90/17.62</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>17.56/17.36</td>
</tr>
<tr>
<td>9.</td>
<td>4.052a</td>
<td>C_{20}H_{19}N_{2}O_{3}S_{2}</td>
<td>454.53</td>
<td>155-157</td>
<td>69</td>
<td>52.85/52.50</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.99/3.76</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>18.49/18.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>14.11/14.44</td>
</tr>
<tr>
<td>10.</td>
<td>4.052b</td>
<td>C_{20}H_{19}N_{2}O_{2}S_{3}</td>
<td>470.59</td>
<td>149-151</td>
<td>63</td>
<td>51.05/51.36</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.86/3.68</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>17.86/17.54</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>20.44/20.12</td>
</tr>
<tr>
<td>11.</td>
<td>4.053a</td>
<td>C_{26}H_{23}N_{2}O_{3}S_{2}</td>
<td>545.64</td>
<td>160-162</td>
<td>65</td>
<td>57.23/57.42</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4.25/4.48</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>17.97/17.65</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>11.75/11.35</td>
</tr>
<tr>
<td>12.</td>
<td>4.053b</td>
<td>C_{26}H_{23}N_{2}O_{2}S_{3}</td>
<td>561.70</td>
<td>156-158</td>
<td>61</td>
<td>55.60/55.40</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4.13/3.96</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>17.46/17.10</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>17.13/16.80</td>
</tr>
<tr>
<td>13.</td>
<td>4.054a</td>
<td>C_{21}H_{20}N_{2}O_{3}S_{2}</td>
<td>468.55</td>
<td>164-166</td>
<td>63</td>
<td>53.83/53.52</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4.30/4.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>17.94/17.52</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>13.69/13.20</td>
</tr>
<tr>
<td>14.</td>
<td>4.054b</td>
<td>C_{21}H_{20}N_{2}O_{2}S_{3}</td>
<td>484.62</td>
<td>159-161</td>
<td>60</td>
<td>52.05/52.34</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4.16/4.28</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>17.34/17.04</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>19.85/19.45</td>
</tr>
<tr>
<td>S.N.</td>
<td>Compound</td>
<td>IR (KBr) cm(^{-1})</td>
<td>(^1)H NMR(CDCl(_3)) ppm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>------</td>
<td>----------</td>
<td>---------------------</td>
<td>-----------------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>4.048a</td>
<td>3370 (NH str.) 1560 (C=N ) 690 (C-S str.) 1580 (C=C str. Ar-H) 3630 (O-H)</td>
<td>12.64 (1H,s,NH), 11.34 (1H,s,NH), 11.34 (1H,s,OH), 7.9 (1H,s,Ar-H), 7.73 (2H,s,Ar-H), 7.22 (1H,d,CH), 6.75 (1H,d,CH), 2.93 (2H,t,CH(_2)), 2.87 (2H,t,CH(_2)), 2.53 (3H,s,CH(_3))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>4.048b</td>
<td>3365 (NH str.) 1550(C=N str.) 685 (C-S str) 1570 (C=C) 2320(S-H)</td>
<td>12.64 (1H,s,NH), 12.15 (1H,s,SH), 11.34 (1H,s,NH), 7.9 (1H,s,Ar-H), 7.73 (2H,s,Ar-H), 7.22 (1H,d,CH), 6.75 (1H,d,CH), 2.93 (2H,t,CH(_2)), 2.87 (2H,t,CH(_2)), 2.53 (3H,s,CH(_3))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>4.049a</td>
<td>3355 (NH str.) 1540(C=N str.) 670 (C-S str.) 1560(C=C) 3620 (O-H)</td>
<td>12.64 (1H,s,NH), 11.34 (1H,s,NH), 11.34 (1H,s,OH), 8.2 (1H,s,Ar-H), 7.95 (2H,s,Ar-H), 7.23-7.33 (5H,m,Ar-H), 7.22 (1H,d,CH), 6.75 (1H,d,CH), 4.71 (2H,s,CH(_2)), 4.32 (2H,s,CH(_2)), 2.53 (3H,s,CH(_3))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>4.049b</td>
<td>3350 (NH str.) 1525(C=N str.) 660 (C-S str.) 1552 (C=C) 2300 (S-H)</td>
<td>12.64 (1H,s,NH), 12.15 (1H,s,SH), 11.34 (1H,s,NH), 8.2 (1H,s,Ar-H), 7.95 (2H,s,Ar-H), 7.23-7.33 (5H,m,Ar-H), 7.22 (1H,d,CH), 6.75 (1H,d,CH), 4.71 (2H,s,CH(_2)), 4.32 (2H,s,CH(_2)), 2.53 (3H,s,CH(_3))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>4.050a</td>
<td>3390 (NH str.) 1580 (C=N str.) 700 (C-S str.) 1600 (C=C) 3640 (O-H)</td>
<td>11.34 (2H,s,NH), 11.34 (1H,s,OH), 8.45 (2H,d,CH), 7.9 (1H,s,Ar-H), 7.73 (2H,s,Ar-H), 6.93 (1H,d,CH), 2.93 (2H,t,CH(_2)), 2.87 (2H,t,CH(_2)), 2.53 (3H,s,CH(_3))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>4.050b</td>
<td>3380 (NH str.) 1560(C=N str.) 690 (C-S str.) 1580 (C=C) 2330 (S-H)</td>
<td>12.15 (1H,s,SH), 11.34 (2H,s,NH), 8.45 (2H,d,CH), 7.9 (1H,s,Ar-H), 7.73 (2H,s,Ar-H), 6.93 (1H,d,CH), 2.93 (2H,t,CH(_2)), 2.87 (2H,t,CH(_2)), 2.53 (3H,s,CH(_3))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>4.051a</td>
<td>3360 (NH str.) 1550(C=N str.) 680 (C-S str.) 1570(C=C) 3620 (O-H)</td>
<td>11.34 (2H,s,NH), 11.34 (1H,s,OH), 8.45 (2H,d,CH), 8.2 (1H,s,Ar-H), 7.95 (2H,s,Ar-H), 7.23-7.33 (5H,m,Ar-H), 6.93 (1H,d,CH), 4.71 (2H,s,CH(_2)), 4.32 (2H,s,CH(_2)), 2.53 (3H,s,CH(_3))</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**MS:** [m/z] 370.3 (100%), 531.1 (22.5%)
<table>
<thead>
<tr>
<th>S.N.</th>
<th>Compound</th>
<th>IR (KBr) cm⁻¹</th>
<th>¹H NMR(CDCl₃) ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.</td>
<td>4.051b</td>
<td>3370 (NH str.)  1540(C=N str.)  670 (C-S str)  1560 (C=C)  2310 (S-H)</td>
<td>12.15 (1H,s,SH), 11.34 (2H,s,NH), 8.45 (2H,d,CH), 8.2 (1H,s,Ar-H), 7.95 (2H,s,Ar-H), 7.23-7.33 (5H,m,Ar-H), 6.93 (1H,d,CH),4.71 (2H,s,CH₂), 4.32 (2H,s,CH₂), 2.53 (3H,s,CH₃)</td>
</tr>
<tr>
<td>9.</td>
<td>4.052a</td>
<td>3320 (NH str.)  1530 (C=N str.)  630 (C-S str.)  1540(C=C)  3610 (O-H)</td>
<td>11.34 (2H,s,NH), 11.34 (1H,s,OH), 8.58 (2H,s,CH), 7.9 (1H,s,Ar-H), 7.73 (2H,s,Ar-H), 2.93 (2H,t,CH₂), 2.87 (2H,t,CH₂), 2.53 (3H,s,CH₃), 2.34 (3H,s,CH₃)</td>
</tr>
<tr>
<td>10.</td>
<td>4.052b</td>
<td>3310 (NH str.)  1515(C=N str.)  620 (C-S str.)  1560 (C=C)  2320 (S-H)</td>
<td>12.15 (1H,s,SH), 11.34 (2H,s,NH), 8.58 (2H,s,CH), 7.9 (1H,s,Ar-H), 7.73 (2H,s,Ar-H), 2.93 (2H,t,CH₂), 2.87 (2H,t,CH₂), 2.53 (3H,s,CH₃), 2.34 (3H,s,CH₃)</td>
</tr>
<tr>
<td>11.</td>
<td>4.053a</td>
<td>3315 (NH str.)  1510 (C=N str.)  620 (C-S str.)  1530(C=C)  3605 (O-H)</td>
<td>11.34 (2H,s,NH), 11.34 (1H,s,OH), 8.58 (2H,s,CH), 8.2 (1H,s,Ar-H), 7.95 (2H,s,Ar-H), 7.23-7.33 (5H,m,Ar-H), 4.71 (2H,s,CH₂), 4.32 (2H,s,CH₂), 2.53 (3H,s,CH₃), 2.34 (3H,s,CH₃)</td>
</tr>
<tr>
<td>12.</td>
<td>4.053b</td>
<td>3300 (NH str.)  1500(C=N str.)  612 (C-S str.)  1550 (C=C)  2310 (S-H)</td>
<td>12.15 (1H,s,SH), 11.34 (2H,s,NH), 8.58 (2H,s,CH), 8.2 (1H,s,Ar-H), 7.95 (2H,s,Ar-H), 7.23-7.33 (5H,m,Ar-H), 4.71 (2H,s,CH₂), 4.32 (2H,s,CH₂), 2.53 (3H,s,CH₃), 2.34 (3H,s,CH₃)</td>
</tr>
<tr>
<td>13.</td>
<td>4.054a</td>
<td>3290 (NH str.)  1480 (C=N str.)  620 (C-S str.)  1520(C=C)  3600 (O-H)</td>
<td>11.34 (2H,s,NH), 11.34 (1H,s,OH), 8.48 (1H,s,CH), 7.9 (1H,s,Ar-H), 7.73 (2H,s,Ar-H), 2.93 (2H,t,CH₂), 2.87 (2H,t,CH₂), 2.53 (3H,s,CH₃), 2.34 (3H,s,CH₃)</td>
</tr>
<tr>
<td>14.</td>
<td>4.054b</td>
<td>3280 (NH str.)  1470(C=N str.)  600 (C-S str.)  1540 (C=C)  2290 (S-H)</td>
<td>12.15 (1H,s,SH), 11.34 (2H,s,NH), 8.48 (1H,s,CH), 7.9 (1H,s,Ar-H), 7.73 (2H,s,Ar-H), 2.93 (2H,t,CH₂), 2.87 (2H,t,CH₂), 2.53 (3H,s,CH₃), 2.34 (3H,s,CH₃)</td>
</tr>
</tbody>
</table>
4.4 Interpretation of spectral data for the elucidation of structures of Compounds

Structures of all the compounds were established on the basis of elemental analysis, IR and $^1$HNMR spectral data. Physical data of all the compounds were found to be consistent to the structures assigned to these molecules.

The physical, microanalyses, infrared and $^1$HNMR spectral data of all the compounds are given in table 4.1 and 4.2 and the spectral graphs are presented in charts 4.1 to 4.8

4.4.1 Interpretation of spectral data of compounds 4.048 (a,b) - 4.051 (a,b)

Infrared spectrum

Infrared spectrum of compound 4.048a on KBr pellet exhibited peaks at 3370 cm$^{-1}$ (NH of pyrrole ring), and 1560 cm$^{-1}$ (C=N str.), 690 cm$^{-1}$ (C-S str.) and 1580 cm$^{-1}$ (C=C) and 3630 cm$^{-1}$ (O-H), disappearance of 1710 cm$^{-1}$ (for C=O of cyclohexanone ring) provided a strong evidence in the favour of formation of 4.048a from 4.044a.

The formation of compound 4.048b from 4.044a was ascertained by the appearance of peaks at 3365 cm$^{-1}$ (NH of pyrrole ring), and 1550 cm$^{-1}$ (C=N str.), 685 cm$^{-1}$ (C-S str.), 1570 cm$^{-1}$ (C=C) and 2320 cm$^{-1}$ (S-H).

The formation of compound 4.049a from 4.044b was indicated by the presence of peaks at 3355 cm$^{-1}$ (NH of pyrrole ring), 1540 cm$^{-1}$ (C=N str.), 670 cm$^{-1}$ (C-S str.) and 1560 cm$^{-1}$ (C=C), and 3620 cm$^{-1}$ (O-H). Similarly, the formation of compound 4.049b from 4.044b was evident by the appearance of peaks at 3350 cm$^{-1}$ (NH of pyrrole ring), and 1525 cm$^{-1}$ (C=N str.), 660 cm$^{-1}$ (C-S str.) and 1552 cm$^{-1}$ (C=C), 2300 cm$^{-1}$ (S-H).

The formation of compound 4.050a from 4.045a was accounted by the presence of peaks at 3390cm$^{-1}$ (NH of pyrrole ring), 1580 cm$^{-1}$ (C=N str.), 700 cm$^{-1}$ (C-S str.) and 1600 cm$^{-1}$ (C=C) and 3640 cm$^{-1}$ (O-H). Similarly, formation of compound 4.050b from 4.045a was evident by the presence of peaks at 3380cm$^{-1}$
(NH of pyrrole ring), 1560 cm\(^{-1}\) (C=N str.), 690 cm\(^{-1}\) (C-S str.) and 1580 cm\(^{-1}\) (C=C), 2330 cm\(^{-1}\) (S-H).

The formation of compound 4.051a from 4.045b was supported by the presence of peaks at 3360 cm\(^{-1}\) (NH of pyrrole ring), 1550 cm\(^{-1}\) (C=N str.), 680 cm\(^{-1}\) (C-S str.) and 1570 cm\(^{-1}\) (C=C) and 3620 cm\(^{-1}\) (O-H). Similarly, formation of compound 4.051b from 4.045b was ascertained by the presence of peaks at 3370 cm\(^{-1}\) (NH of pyrrole ring), 1540 cm\(^{-1}\) (C=N str.), 670 cm\(^{-1}\) (C-S str.) and 1560 cm\(^{-1}\) (C=C), 2310 cm\(^{-1}\) (S-H).

\(^1\)HNMR spectrum

\(^1\)HNMR spectrum of compound 4.048a in CDCl\(_3\) displayed signals for the presence of 15 protons of which 12 protons were bound to carbon atom, and 2 protons were bound to nitrogen atom (the protons bound to nitrogen and oxygen atoms exchanged with D\(_2\)O) and one proton was bound to oxygen atom. Out of five singlets which the \(^1\)HNMR spectrum displayed, two singlets, one at \(\delta 12.64\) was assigned to NH proton of amine function of sulfonamide, and other singlet for 2H at \(\delta 11.34\) was assigned to NH proton of pyrrole ring and for proton of OH group. The presence of two singlet which appeared at \(\delta 7.9\) and \(\delta 7.73\) were attributed to proton of indole ring. One singlet at \(\delta 2.53\) was assigned to the three proton of methyl group attached to sulphur atom. The loss of one SMe group from 4.044a provided a strong evidence for the formation of pyrimidine ring. Two doublets which appeared at \(\delta 7.22\) and \(\delta 6.75\) were assigned to the two protons of thiazole ring. Appearance of two triplets which appeared at \(\delta 2.93\) and \(\delta 2.87\) were assigned to four CH\(_2\) protons of cyclohexanone ring. These assignments were consistent to the structure of 4.048a which provided a strong evidence for its formation from 4.044a. Similar spectral interpretations established the formation of compound 4.049a.

Similarly \(^1\)HNMR spectrum of compound 4.050a in CDCl\(_3\) displayed signals for the presence of 16 protons of which 13 protons were bound to carbon atom, and 2 protons were bound to nitrogen atom (the protons bound to nitrogen and oxygen atoms exchanged with D\(_2\)O) and one proton was bound to oxygen atom. Out of four singlets, one singlet, at \(\delta 11.34\) was assigned to two NH protons, one for amine group
of sulfonamide, the other for NH proton of pyrrole ring and another a singlet for one proton of OH group. One singlet at δ2.53 was assigned to the three proton of methyl group attached to sulphur atom. The presence of two singlets which appeared at δ 7.9 and δ 7.73 were attributed to three proton of indole ring. Two doublets which appeared at δ8.45 and δ6.93 were assigned to the three protons of pyrimidine ring. Appearance of two triplets which appeared at δ2.93 and δ2.87 were assigned for four CH₂ protons of cyclohexanone ring. Similar spectral interpretations established the formation of compound 4.051a.

¹HNMR spectrum of compound 4.052a in CDCl₃ displayed signals for presence of 18 protons, of which 15 protons were bound to carbon atom, and 2 protons were bound to nitrogen atom (the protons bound to nitrogen and oxygen atoms exchanged with D₂O) and one proton was bound to oxygen atom. A singlet, at δ11.34 was assigned to two NH protons, one for amine function of sulfonamide, and the other for NH proton of pyrrole ring and another singlet for one proton of OH group. The presence of two singlets which appeared at δ8.58 and δ 2.34 were attributed to five proton of methyl pyrimidine ring. One singlet at δ2.53 was assigned to the three proton of methyl group attached to sulphur atom. Two singlets which appeared at δ7.9 and δ7.73 were assigned to the three protons of indole ring. Two triplets which appeared at δ2.93 and δ2.87 were assigned for four CH₂ protons of cyclohexanone ring. Similar spectral interpretations established the formation of compound 4.053a and 4.054a.

4.4.2 Interpretation of spectral data of compounds 4.052 (a,b) -4.054 (a,b)

Infra red spectrum

The formation of compound 4.052a from 4.046a was ascertained by the presence of peaks at 3320 cm⁻¹ (NH of pyrrole ring), 1530 cm⁻¹ (C=N str.), 630 cm⁻¹ (C-S str.) and 1540 cm⁻¹ (C=C) and 3610 cm⁻¹ (O-H). Similarly, the formation of compound 4.052b from 4.046a was evident by the appearance of peaks at 3310 cm⁻¹ (NH of pyrrole ring), and 1515 cm⁻¹ (C=N str.), 620 cm⁻¹ (C-S str.), 1560 cm⁻¹ (C=C), 2320 cm⁻¹(S-H).
The formation of compound \textbf{4.053a} from \textbf{4.046b} was supported by the presence of peaks at 3315 cm\(^{-1}\) (NH of pyrrole ring), 1510 cm\(^{-1}\) (C=N str.), 620 cm\(^{-1}\) (C-S str.) and 1530 cm\(^{-1}\) (C=C) and 3605 cm\(^{-1}\) (O-H). Similarly, formation of compound \textbf{4.053b} from \textbf{4.046b} was ascertained by the presence of peaks at 3300 cm\(^{-1}\) (NH of pyrrole ring), 1500 cm\(^{-1}\) (C=N str.), 612 cm\(^{-1}\) (C-S str.) and 1550 cm\(^{-1}\) (C=C), 2310 cm\(^{-1}\) (S-H).

The formation of compound \textbf{4.054a} from \textbf{4.047a} was supported by the presence of peaks at 3290 cm\(^{-1}\) (NH of pyrrole ring), 1480 cm\(^{-1}\) (C=N str.), 620 cm\(^{-1}\) (C-S str.) and 1520 cm\(^{-1}\) (C=C) and 3600 cm\(^{-1}\) (O-H). Similarly, formation of compound \textbf{4.054b} from \textbf{4.047a} was ascertained by the presence of peaks at 3280 cm\(^{-1}\) (NH of pyrrole ring), 1470 cm\(^{-1}\) (C=N str.), 600 cm\(^{-1}\) (C-S str.) and 1540 cm\(^{-1}\) (C=C), 3290 cm\(^{-1}\) (S-H).

\textbf{\(^1\)HNMR spectrum}

\textbf{\(^1\)HNMR} spectrum of compound \textbf{4.048b} in CDCl\(_3\) displayed signals for the presence of 15 protons of which 12 protons were bound to carbon atom, and 2 protons were bound to nitrogen atom (the protons bound to nitrogen and oxygen atoms exchanged with D\(_2\)O) and one proton was bound to sulphur atom. Out of six singlets which the \textbf{\(^1\)HNMR} spectrum displayed one at \(\delta 12.64\) was assigned to NH proton of pyrazole ring, and the other at \(\delta 12.15\) was assigned to SH proton of sulphur atom, besides this, 1H at \(\delta 11.34\) was assigned to NH proton of pyrrole ring. The presence of two singlets which appeared at \(\delta 7.9\) and \(\delta 7.73\) were attributed to proton of indole ring. One singlet at \(\delta 2.53\) was assigned to the three proton of methyl group attached to sulphur atom. The loss of one SMe group from \textbf{4.044a} provided a strong evidence for the formation of pyrimidine ring. Two doublets which appeared at \(\delta 7.22\) and \(\delta 6.75\) were assigned to the two protons of thiazole ring. Appearance of two triplets which appeared at \(\delta 2.93\) and \(\delta 2.87\) were assigned for four CH\(_2\) protons of cyclohexanone ring. These assignments were consistent to the structure of \textbf{4.048b} and provided a strong evidence for its formation from \textbf{4.044b}. Similar spectral interpretations established the formation of compound \textbf{4.049b}. 

\textit{Chapter-4: Synthesis of pyrimidine derivatives...}
Similarly $^1$HNMR spectrum of compound 4.050b in CDCl$_3$ displayed signals for the presence of 16 protons of which 13 protons were bound to carbon atom, and 2 protons were bound to nitrogen atom (the protons bound to nitrogen exchanged with D$_2$O) and one proton was bound to sulphur atom. Out of five singlets one singlet at $\delta$12.15 was assigned to SH proton, two protons at $\delta$11.34 were assigned to two NH proton, one to amine function of sulfonamide, and other for the NH proton of pyrrole ring. One singlet at $\delta$2.53 was assigned to the three proton of methyl group attached to sulphur atom the presence of two singlets which appeared at $\delta$ 7.9 and $\delta$ 7.73 were attributed to three proton of indole ring. Two doublets which appeared at $\delta$8.45 and $\delta$6.93 were assigned to the three protons of pyrimidine ring. Presence of two triplets which appeared at $\delta$2.93 and $\delta$2.87 were assigned for four CH$_2$ protons of cyclohexanone ring. Similar spectral interpretations established the formation of compound 4.051b

$^1$HNMR of compound 4.052b in CDCl$_3$ displayed signals for presence of 18 protons of which 15 protons were bound to carbon atom, and 2 protons were bound to nitrogen atom (the protons bound to nitrogen exchanged with D$_2$O) and one proton was bound to sulphur atom. A singlet, at $\delta$12.15 was assigned to two SH proton. A singlet at $\delta$11.34 was assigned to two NH protons, one for amine function of sulfonamide, and other for NH proton of pyrrole ring. The presence of two singlet which appeared at $\delta$8.58 and $\delta$ 2.34 were attributed to five protons of methyl pyrimidine ring One singlet at $\delta$2.53 was assigned to the three protons of methyl group attached to sulphur atom. Two singlets which appeared at $\delta$7.9 and $\delta$7.73 were assigned to the three protons of indole ring; two triplets which appeared at $\delta$2.93 and $\delta$2.87 were assigned for four CH$_2$ protons of cyclohexanone ring. Similar spectral interpretations established the formation of compound 4.053b and 4.054b.
4.5  Mechanism of the formation of compounds
4.6 Experimental section

1. Melting points were determined in open glass capillaries and are uncorrected.
2. The purity of the compounds was checked by TLC on silica gel (G) plates.
3. IR spectra were recorded on CE (SHIMADZU) FTIR-8400S.
4. $^1$HNMR spectra were recorded on model AC-300F (Brucker) using CDCl$_3$+DMSO-d$_6$ as solvent. Chemical shift are expressed in δppm.
5. Before analysis all samples were dried for one hour under reduced pressure.
6. Physical and spectral data for all the compounds have been given in table 4.1 and 4.2.

4.6.1 Synthetic procedure

**Preparation of 2-hydroxy-4-(methylthio)-N-(thiazol-2-yl)-6, 11-dihydro-5H-pyrimido [4, 5-a] carbazole-8-sulfonamide (4.048a)**

To a mixture of urea (0.18g, 0.003 mole) and sodium ethoxide (1.36g, 0.02mole) in ethanol (30-35ml) was added appropriate oxoketenedithioacetal 4.044a (1.2g, 0.003mole). The reaction mixture was refluxed for 14 h. The solvent was removed by distillation and the residue was treated with glacial acetic acid (8-10ml) just enough to dissolve sodium salt of pyrimidine and refluxed for 15 min. The mixture was poured on crushed ice and the precipitate obtained was purified by recrystallization from ethanol to give 4.048a. 0.83g, Yield 72%, m.p 135-137°C. Similarly compound 4.049a was prepared from 4.044b following the above procedure. (Yield 67%, m.p. 142-144°C)

**Preparation of 2-hydroxy-4-(methylthio)-N-(pyrimidin-2-yl)-6, 11-dihydro-5H-pyrimido [4, 5-a] carbazole-8-sulfonamide (4.050a)**

To a mixture of urea (0.18g, 0.003 mole) and sodium ethoxide (1.36g, 0.02mole) in ethanol (30-35ml) was added appropriate oxoketenedithioacetal 4.045a (1.3g, 0.003mole). The reaction mixture was refluxed for 14 h. The solvent was removed by distillation and the residue was treated with glacial acetic acid (8-10ml) just enough to dissolve sodium salt of pyrimidine and refluxed for 15 min. The
mixture was poured on crushed ice and the precipitate obtained was purified by recrystallization from ethanol to give 4.050a. 0.86g, Yield 67%, m.p 148-150 °C. Similarly compound 4.051a was prepared from 4.045b following the above procedure. (Yield 62%, m.p. 153-155 °C)

**Preparation of 2-hydroxy-N-(5-methylpyrimidin-2-yl)-4-(methylthio)-6, 11-dihydro-5H-pyrimido [4, 5-α] carbazole-8-sulfonamide (4.052a)**

To a mixture of urea (0.18g, 0.003 mole) and sodium ethoxide (1.36g, 0.02mole) in ethanol (30-35ml) was added appropriate oxoketenedithioacetal 4.046a (1.38g, 0.003mole). The reaction mixture was refluxed for 14 h. The solvent was removed by distillation and the residue was treated with glacial acetic acid (8-10ml) just enough to dissolve sodium salt of pyrimidine and refluxed for 15 min. The mixture was poured on crushed ice and the precipitate obtained was purified by recrystallization from ethanol to give 4.052a. 0.91g, Yield 69%, m.p 155-157 °C. Similarly, compound 4.053a and 4.054a were prepared from 4.046b and 4.047a following above procedure. (Yield 65%, m.p. 160-162 °C) and (Yield 63%, m.p. 164-166 °C) respectively.

**Preparation of 2-mercapto-4-(methylthio)-N-(thiazol-2-yl)-6, 11-dihydro-5H-pyrimido [4, 5-α] carbazole-8-sulfonamide (4.048b)**

To a mixture of thiourea (0.23g, 0.003 mole) and sodium ethoxide (1.36g, 0.02mole) in ethanol (30-35ml) was added appropriate oxoketenedithioacetal 4.044a (1.2g, 0.003mole). The reaction mixture was refluxed for 14 h. The solvent was removed by distillation and the residue was treated with glacial acetic acid (8-10ml) just enough to dissolve sodium salt of pyrimidine and refluxed for 15 min. The reaction mixture was poured on crushed ice and the precipitate obtained was purified by recrystallization from ethanol to give 4.048b. 0.81g Yield 68%, m.p 130-132 °C. Similarly, compound 4.049b was prepared from 4.044b following above procedure. (Yield 64%, m.p. 136-138 °C)
Preparation of 2-mercapto-4-(methylthio)-N-(pyrimidin-2-yl)-6, 11-dihydro-5H-pyrimido [4, 5-α] carbazole-8-sulfonamide (4.050b)

To a mixture of thiourea (0.23g, 0.003 mole) and sodium ethoxide (1.36g, 0.02mole) in ethanol (30-35ml) was added appropriate oxoketenedithioacetal 4.045a (1.3g, 0.003mole). The reaction mixture was refluxed for 14 h. The solvent was removed by distillation and the residue was treated with glacial acetic acid (8-10ml) just enough to dissolve sodium salt of pyrimidine and refluxed for 15 min. The reaction mixture was poured on crushed ice and the precipitate obtained was purified by recrystallization from ethanol to give 4.050b. 0.84g, Yield 64%, m.p 141-143 °C. Similarly, compound 4.051b was prepared from 4.045b following above procedure. (Yield 60%, m.p. 150-151 °C)

Preparation of 2-mercapto-N-(5-methylpyrimidin-2-yl)-4-(methylthio)-6, 11-dihydro-5H-pyrimido [4, 5-α] carbazole-8-sulfonamide (4.052b)

To a mixture of thiourea (0.23g, 0.003 mole) and sodium ethoxide (1.36g, 0.02mole) in ethanol (30-35ml) was added appropriate oxoketenedithioacetal 4.046a (1.38g, 0.003mole). The reaction mixture was refluxed for 14 h. The solvent was removed by distillation and the residue was treated with glacial acetic acid (8-10ml) just enough to dissolve sodium salt of pyrimidine and refluxed for 15 min. The reaction mixture was poured on crushed ice and the precipitate obtained was purified by recrystallization from ethanol to give 4.052b. 0.89g, Yield 63%, m.p 149-151 °C. Similarly, compound 4.053b and 4.054b were prepared from 4.046b and 4.047a following above procedure. (Yield 61%, m.p. 156-158 °C) and (Yield 60%, m.p. 159-161 °C) respectively.
Spectrum No. 4.1- IR spectra of 2-mercapto-4-(methylthio)-N-(thiazol-2-yl)-
6, 11-dihydro-5H-pyrimidino [4,5-α] carbazole-8-sulfonamide (4.048b)

Spectrum No. 4.2- IR spectra of 2-hydroxy-4-(methylthio)-N-(pyrimidin-2-yl)-
6, 11-dihydro-5H-pyrimidino [4, 5-α] carbazole-8-sulfonamide (4.050a)
Spectrum No. 4.3- Mass spectra of 2-hydroxy-4-(methylthio)-N-(pyrimidin-2-yl)-6, 11-dihydro-5H- pyrimidino [4, 5-α] carbazole-8-sulfonamide (4.050a)

Spectrum No. 4.4- Mass spectra of 6-benzyl-2-Hydroxy-4-(methylthio)-N-(pyrimidin-2-yl)-6,11-dihydro-5H-pyrimidino[4,5-α]carbazole-8-sulfonamide (4.051a).
Spectrum No. 4.5- Mass spectra of 2-mercapto-N-(4-methylpyrimidin-2-yl)-4-(methylthio)-6, 11-dihydro-5H- pyrimidino [4, 5-α] carbazole-8-sulfonamide (4.052b)
Spectrum No. 4.6- $^1$HNMR spectra of 2-hydroxy-4-(methylthio)-N-(pyrimidin-2-yl)-6, 11-dihydro-5H- pyrimidino [4, 5-$\alpha$] carbazole-8-sulfonamide (4.050a)

Spectrum No. 4.7- $^1$HNMR spectra of 6-benzyl-2-Mercapto-N-(4-methylpyrimidin-2-yl)-4-(methylthio)-6,11-dihydro-5H-pyrimidino[4,5-$\alpha$]carbazole-8-sulfonamide (4.053b)
Spectrum No. 4.8 - $^1$HNMR spectra of N-(4, 5-dimethylpyrimidin-2-yl)-2-mercapto-4-(methylthio)-6, 11-dihydro-5H- pyrimidino [4, 5-α] carbazole-8-sulfonamide (4.054b)
4.7 References


5. Lagoja, I.M., Pyrimidines as constituent of natural biologically active compounds, Chemistry and Biodiversity, 2005, 2, 1-50.


19. Atwal, K.S. and Swanson, B.N., Dihydropyrimidine calcium channel blockers. 3. 3-Carbamoyl-4-aryl-1,2,3,4-tetrahydro-6-methyl-5-pyrimidinecarboxylic acid esters as orally effective antihypertensive agents, *J. Med. Chem.*, 1991, 34(2), 806-11.


