PART - V

SYNTHESIS OF

1,3-THIAZINES
INTRODUCTION:-

Thiazines are six membered heterocyclic compounds containing one nitrogen and one sulphur atom. Nomenclature throughout the literature is varied. The system employed in the ring index\(^1\) is unambiguous, but since the majority of the known members of the thiazine group do not contain the unsaturation of the parent compounds, this usage has became outdated. The terms metathiazines and parathiazines are frequently used. In the present work the system adopted by the ring index will be retained for most of the part.

Of the many thiazines and monobenzothiazines possible only those derived from the parent structures listed below have been reported.

\[
\begin{align*}
\text{1,3,2-thiazine} & \quad \text{1,3,4-thiazine} & \quad \text{1,3,6-thiazine} \\
\end{align*}
\]

1,3,2 And 1,3,4 - Thiazines (Metathiazines) :-

A relatively large number of metathiazines and their monobenzo derivatives have been prepared.

In general, derivatives of them are made by proper choice of reactants rather than by substitution 1,3,2 - Thiazines have been virtually uninvestigated. According to Hale and Brill\(^2\) condensation of 5-methylthiouronium sulphate with nitromalonic dialdehyde results in the formation of 2-amino-5-nitro -1,3,2- thiazine.
However Boarland and mcOmie\textsuperscript{3} were unable to confirm this report and obtained only 5- nitro - 5 -(1-piperidine) pyrimidine from the reaction. Piperidine is the catalyst for the reaction.

Covallite, martini and Nachod\textsuperscript{4} have described a rearrangement of benzoyl vinyl isothiouranium chloride to a substance assigned the structure of 2-amino-1,3,2-Thiazine hydrochloride. The reaction is formulated as follows.

\[
\text{C}_6\text{H}_5\text{COCH} = \text{CH} \cdot \text{S} \cdot \text{C} \cdot \text{NH}_2 \cdot \text{HCl} \xrightarrow{\text{C}_2\text{H}_5\text{OH}} \text{H}_3\text{C}_6 \quad \text{NH}_{\text{HCl}}
\]

No absolute proof of the structure assigned to the metathiazine was offered. When the metathiazine is treated with mild alkali a further rearrangement takes place to a substance assigned the structure of 2-mercapto-3-phenylpyrimidine. The postulated mechanism is as follows.

The aminometathiazines are remarkably stable to acids and bases and boiling them with solutions of lead acetate or mercuric oxide does not remove the sulphur. The benzoderivative may be oxidised to the sulphone with alkaline permagnate and the thiazine ring of the sulphone is cleaved with acid\textsuperscript{5}.
It is reported that thiourea reacts with mesityloxide in acidic medium to give 2-imino-6H-2,3-dihydro-1,3-thiazine and 2-thioxotetrahydropyrimidine derivatives. Similarly 6-hydroxy-4-methoxy-5-arylacryloylbenzo (b) furans on reaction with thiourea in alkaline medium afforded 6-aryl - 4-[5'-(6'-hydroxy-4'-methoxybenzo (b) furanyl)]-2-imino-6-H-2,3-dihydro-1,3-thiazine.

Chincholkar et. al synthesized 4,6-diaryl-2-imino-6H-2,3-dihydro-1,3-thiazines from 2'-hydroxychalcones by reaction with thiourea in alkaline medium.

Kakade reported the use of DMSO as a solvent containing little sodium methoxide in the synthesis of 4,6 - diaryl -2- imino-6H-2,3-dihydro-1,3-thiazines from 2'-hydroxychalcones.
Leistner et al. synthesized 2-aminothieno (2,3-d)-1,3-thiazine-4-ones and found them useful as drugs and intermediates.

\[
\begin{align*}
\text{R}_1 & \\
\text{R}_2 & \\
\text{R}_3 & \\
\text{R}_4 & \\
\text{R}_5 & \\
\text{R}_6 & \\
\end{align*}
\]

Harris et al. synthesized N-substituted tetrahydrothiazines and studied their use as pesticides.

\[
\begin{align*}
\text{R} & \\
\text{N} & \\
\text{CH} & \\
\text{NO}_2 & \\
\end{align*}
\]

Hanefeld studied the properties of substituted 1,3-thiazines.

\[
\begin{align*}
\text{R} & \\
\text{R'} & \\
\text{R''} & \\
\text{X} & \\
\end{align*}
\]

Gokou et al. synthesized and studied the rearrangement of 5-acetyl-2-phenyl-4-substituted-6H-1,3-thiazines.

\[
\begin{align*}
\text{Ph} & \\
\text{R} & \\
\text{COR'} & \\
\end{align*}
\]

Hanefeld et al. studied the reactions of 3-amino-2-thioxotetrahydro-4H-1,3-thiazine-4-ones with nucleophiles.

\[
\begin{align*}
\text{Me} & \\
\text{Me} & \\
\text{R} & \\
\text{R'} & \\
\end{align*}
\]

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Zawisza et al. synthesized some 2,3-dihydro-6H-(1,3)-thiazine derivatives.

Gudadhe synthesized some iodosubstituted-4,6-diaryl-2-imino-6H-2,3-dihydro-1,3-thiazines by the action of thiourea on 2'-hydroxychalcones in ethanol containing piperidine and sodium methoxide.

Ramekar has reported the synthesis of 4,6-diaryl-5-aroyl-2-imino-6H-2,3-dihydro-1,3-thiazines from 3-aroyl flavanone and their antimicrobial activity.

Doifode has prepared 4,6-diaryl-2-imino-6H-2,3-dihydro-1,3-thiazines from aurones by the action of thiourea in presence of aqueous KOH and ethanol as a solvent.
Raghuwanshi\textsuperscript{19} reported the synthesis and antimicrobial activity of 1,3-thiazines obtained by the reaction of nitrochalcones with thiourea and phenylthiourea in DMSO medium in presence of sodium methoxide.

Ramekar\textsuperscript{20} has synthesized some new 4,6-diaryl-5-aroyl-2-imino-6H-2,3-dihydro-1,3-thiazines from 3-aroylflavanones.

Yasuda et al.\textsuperscript{21} have reported the stereoselective synthesis of 5-bromo-4H-5,6-dihydro-1,3-thiazines by intramolecular cyclization of 5-allyl thioamidates by the reaction with NBS or bromine in dichloromethane at room temperature.

Raut and Doshi\textsuperscript{22} have reported antimicrobial activity of newly synthesized 1,3-thiazines obtained from chloro and chlorobromo substituted chalcones.
Hataba et al.\textsuperscript{23} have reported 2-anilino-6-(β-napthyl)-5,6-dihydro-1,3-thiazine-4-ones from 1-[2-(β-napthyl) acroyl]-2-phenyl thiourea in sodium ethoxide solution.

\begin{center}
\includegraphics[width=0.8\textwidth]{reaction1.png}
\end{center}

Where Ar = \begin{tikzpicture}
\node[draw,circle] at (0,0) (a) {};
\node[draw,circle,above=of a] (b) {};
\draw[thick] (a) -- (b);
\end{tikzpicture}

Kedar R.M.\textsuperscript{24} synthesized 4,6-diaryl-2-imino-6H-2,3-dihydro-1,3-thiazines from chalcones and 4,6-diaryl-5-aryloyl-2-imino-6H-2,3-dihydro-1,3-thiazines from 3-aryloylflavanones by reaction with thiourea in alkaline EtOH and dioxane respectively.

\begin{center}
\includegraphics[width=0.8\textwidth]{reaction2.png}
\end{center}
Origin of Problem

Literature survey reveals that 1,3-Thiazines have been reported to be formed by the reaction between chalcones and thiourea in alkaline medium.

Gamil Aziz et al. reported the formation of 6-aryl-4-[5’-(substituted benzo(b)furanyl)]-2-imino-6H-2,3-dihydro-1,3-thiazines by the action of thiourea on 6-hydroxy-4-methoxy-5- arylacryloylbenzo(b)furans in alkaline medium.

Kakade reported the use of DMSO as a reaction medium in the synthesis of 4,6-diaryl-1,3-thiazines from 2-hydroxychalcones. Chincholkar et al. synthesized 4,6-diaryl-2-imino-6H-2,3-dihydro-1,3-thiazines from 2-hydroxychalcones by the action of thiourea in ethanolic aqueous KOH. Gudadhe, has synthesized iodosubstituted -4,6-diaryl-2-imino-6H-2,3-dihydro-1,3-thiazines by the action of thiourea on 2-hydroxychalcones in ethanol containing piperidine and sodium methoxide. Ramekar has reported the synthesis of 4,6-diaryl-5-aroyl-2-imino-6H-2,3-dihydro-1,3-thiazine from 3-aroylflavanones and thiourea in alkaline medium.

Problem

In the present study, chlorochalcones were allowed to react with phenyl thiourea and diphenyl thiourea in alcoholic aqueous KOH to obtained corresponding 1,3-thiazines.
SUMMARY OF THE WORK

Preparation of \textit{p}-chlorophenylacetate (1) :-

\textit{p}-chlorophenylacetate was prepared from \textit{p}-chlorophenol and acetic anhydride with fused sodium acetate. The detail procedure for the preparation of \textit{p}-chlorophenylacetate was explained in chapter II of part I of the thesis.

Preparation of 2 - Hydroxyacetophenone (2) :-

2 - Hydroxy - 5- chloroacetophenone (2a) M.P. 56\textdegree{}C was prepared from \textit{p}- chlorophenylacetate. 2 - hydroxy - 3,5 - dichloroacetophenone (2b) was synthesized by the chlorination of 2 - hydroxy - 5- chloroacetophenone (2a).

Preparation of chalcone(11) :-

Chalcones were prepared by the condensation of 2- hydroxyacetophenone with aromatic aldehydes in alkaline EtOH.

The following chalcones (11a-c) were prepared.
1)2' - Hydroxy - 3',5' - dichlorochalcones. (11a)
2)2' - Hydroxy - 3',5' - dichloro - 4- methoxychalcone (11 b)
3)2' - Hydroxy - 3',5' - dichloro - 2- furylchalcone (11c)

Preparation of 1,3 - thiazines (12) by reacting dichlorochalcone with phenylthiourea :-

The 1,3 - thiazine (12a -c) were synthesized by reacting dichlorochalcones (11 a- c) with phenylthiourea in ethanol in presence of aqueous KOH.

The following 1,3 - thiazines (12 a - c) were prepared by reacting dichlorochalcones with phenylthiourea.
1) 4 - (2 - hydroxy - 3, 5 - dichlorophenyl ) - 6 - phenyl - 2- iminophenyl - 3, 6 -
dihydro - 1,3 - thiazine (12a)

2) 4 - ( 2 - hydroxy - 3, 5 - dichlorophenyl - 6 - ( 4 - methoxyphenyl ) - 2-
iminophenyl - 3, 6 - dihydro - 1, 3 - dihydro - 1, 3 - thiazine (12b)

3) 4 - ( 2 - hydroxy - 3, 5 - dichlorophenyl ) - 6 - ( furyl) - 2- iminophenyl -
3, 6 - dihydro - 1, 3 - dihydro - 1, 3 - thiazine (12c)

Preparation of 1,3 - thiazines (13) by reacting dichlorochalcone with
diphenyl thiourea :-

The 1,3 - thiazines (13a -c) were synthesized by reacting dichlorochalcones
(11 a- c) with diphenyl thiourea in ethanol in presence of aqueous KOH.

The following 1,3 - thiazines (13a - c) were prepared by reacting
dichlorochalcones with diphenylthiourea.

1) 4 - (2 - hydroxy - 3, 5 - dichlorophenyl ) - 6 - phenyl - 2- iminophenyl - 6
- H -3 - phenyl - 1,3 - thiazine (13a)

2) 4 - (2 - hydroxy - 3, 5 - dichlorophenyl ) - 6 - (4 - methoxyphenyl) - 2-
iminophenyl- 6 - H - 3 - phenyl - 1,3 - thiazine (13b)

3) 4-(2 - hydroxy - 3, 5 - dichlorophenyl ) - 6 - (furyl) - 2- iminophenyl-6 - H -
3 - phenyl - 1,3 - thiazine (13c)
CHAPTER-II
EXPERIMENTAL AND DISCUSSION OF THE RESULTS

Raghuwanshi\textsuperscript{19} reported the formation of 1,3-thiazines from nitrochalcones with thiourea and phenylthiourea in DMSO medium in presence of sodium methoxide.

Raut and Doshi\textsuperscript{22} synthesized 1,3-thiazines from chloro and chlorobromo substituted chalcones.

Ramekar\textsuperscript{20} synthesized some new 4,6-diaryl-5-aryloyl-2-imino-6H-2,3-dihydro-1,3-thiazines from 3-aryloyflavanones.

Vibha\textsuperscript{25} reported the synthesis of 4H-1,4-benzothiazine involving the condensation and oxidative cyclization of 2-amino-5-bromo-3-methylbenzenthiol with \(\beta\)-diketones / \(\beta\) - ketoester in dimethylsulfoxide.

Pati\textsuperscript{26} reported the synthesis of 1,4-benzothiazine by the condensation of 1,3-propanediones with 2-aminobenzenethiols in DMSO.

Mishra\textsuperscript{27} reported the synthesis of 1,3-thiazine by ring transformation of Michael-adducts of 4-benzylidene -5-oxazolones and 3-mercapto-5-triazoles.

The present work deals with the synthesis of 1,3-thiazines from dichlorochalcones on treatment with phenyl thiourea and diphenylthiourea.

All the compounds have been characterized on the basis of chemical properties, elemental analysis and spectral data. The melting point apparatus and are uncorrected. The IR spectra, scanned on “Perkin-Elmer577” Spectrophotometer in KBr pellets. The UV-VIS spectra were recorded on “Parkin-Elmer-202” Spectrophotometer PMR spectra was recorded on “Varian XL-100A” spectrophotometer in CDCl\textsubscript{3} solvent. The elemental and spectral results were carried out at VSIC Nagpur, RSIC Chandhigarh and pune university, Pune. The purity of synthesized compounds was tested by TLC on microscopic slides with silica gel-G layers.
EXPERIMENT – 1:
Preparation of P-chlorophenylacetate (1):

The experimental details have been discussed in experiment no. 1 of chapter II in part I of the thesis.

EXPERIMENT – 2:
Preparation of 2-Hydroxy-5-chloroacetophenone (2):

The experimental details have been discussed in experiment no. 2 of chapter II in part I of the thesis.

EXPERIMENT – 3:
Preparation of 2-Hydroxy-3,5-dichloroacetophenone (3):

The experimental details have been discussed in experiment no. 3 of chapter II in part I of the thesis.

EXPERIMENT NO. 4:
Preparation of 2’ - hydroxy - 3’, 5’ - dichlorochalcone (11a):

To the boiling solution of 2 - hydroxy - 3, 5 - dichloroacetophenone (2b) (0.01 mole) and benzaldehyde ( 0.01 mol) in ethanol ( 20 ml) was added 40% solution of NaOH gradually.

The mixture was stirred mechanically at room temperature for 1hr. till it solidified. It was decomposed with ice-cold 1:1 HCl after 6 to 8 hrs. yellow granules thus obtained were filtered, washed with 10% NaHCO₃ solution and then recrystalised from ethanol-acetic acid.m.p. 135°C yield -75%
EXPERIMENT NO. 5:

Preparation of 2'-hydroxy-3',5'-dichloro-4'-methoxychalcone (11b):

To the boiling solution of 2'-hydroxy 3,5'-dichloroacetophenone (2b) (0.01 mol) and anisaldehyde (0.01 mol) in ethanol (20 ml) was added 40% solution of NaOH gradually. The mixture was stirred mechanically at room temperature for 1 hr. till it solidified, and processed further as given in experiment no. (4) to obtained yellow crystalline solid (11b) m.p. 141°C, yield -70%.

\[
\begin{align*}
\text{(2b)} & \quad \rightarrow \quad \text{(11b)}
\end{align*}
\]

EXPERIMENT NO. 6:

Preparation of 2'-hydroxy-3',5'-dichloro-2-furylchalcone (11c):

To the boiling solution of 2'-hydroxy 3,5'-dichloroacetophenone (2b) (0.01 mol) and furfuraldehyde (0.01 mol) in ethanol (20 ml) was added 40% solution of NaOH gradually. The mixture was stirred mechanically at room temperature for 1 hr. till it solidified, and processed further as given in experiment no. (4) to obtained yellow crystalline solid (11c) m.p. 97°C, yield -70%.

\[
\begin{align*}
\text{(2b)} & \quad \rightarrow \quad \text{(11c)}
\end{align*}
\]
Properties and constitution of compounds (11a-c):

1) The compounds (11a-c) are an orange - red coloured crystalline solids.
2) Alcoholic solution gave violet blue colouration with neutral FeCl₃ solution.
3) It gave positive test for chlorine.
4) It's alcoholic solution turned red on reaction with aqueous NaOH.
5) It decolourised bromine water indicating presence of HC=CH linkage.
6) TLC results of the compounds (11a-c) are as follows:

<table>
<thead>
<tr>
<th>Compound</th>
<th>Solvent height (cm)</th>
<th>Solvent height (cm)</th>
<th>Rf</th>
</tr>
</thead>
<tbody>
<tr>
<td>11a</td>
<td>2.7</td>
<td>1.9</td>
<td>0.70</td>
</tr>
<tr>
<td>11 b</td>
<td>2.4</td>
<td>1.7</td>
<td>0.71</td>
</tr>
<tr>
<td>11 c</td>
<td>2.9</td>
<td>2.0</td>
<td>0.69</td>
</tr>
</tbody>
</table>

7) The analytical results of these compounds agreed with their molecular formulae as follows:

<table>
<thead>
<tr>
<th>Compound</th>
<th>Molecular Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>11a</td>
<td>C₁₅H₁₀O₂Cl₂</td>
</tr>
<tr>
<td>11b</td>
<td>C₁₆H₁₂O₃Cl₂</td>
</tr>
<tr>
<td>11c</td>
<td>C₁₃H₈O₃Cl₂</td>
</tr>
</tbody>
</table>

8) The analytical results of these compounds agreed with their molecular formulae as follows:

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</thead>
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<td>11a</td>
<td>C₁₅H₁₀O₂Cl₂</td>
</tr>
<tr>
<td>11b</td>
<td>C₁₆H₁₂O₃Cl₂</td>
</tr>
<tr>
<td>11c</td>
<td>C₁₃H₈O₃Cl₂</td>
</tr>
</tbody>
</table>
9) a) The IR spectrum\(^{28-33}\) of the compound (11c) in KBr showed the following main absorption bonds. (\textit{Spectrum - 2.5})

<table>
<thead>
<tr>
<th>Frequencies (cm(^{-1}))</th>
<th>Intensity</th>
<th>Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>3406</td>
<td>(b)</td>
<td>Strong intramolecular H-bonded O-H stretching.</td>
</tr>
<tr>
<td>1638</td>
<td>(s)</td>
<td>&gt;C=O stretching</td>
</tr>
<tr>
<td>1546</td>
<td>(s)</td>
<td>Asymmetrical stretching in $\overline{\text{C} \text{--} \text{CH} = \text{CH}}$</td>
</tr>
<tr>
<td>1169</td>
<td>(s)</td>
<td>C-0 stretch</td>
</tr>
<tr>
<td>964</td>
<td>(s)</td>
<td>2'-furyl</td>
</tr>
<tr>
<td>753</td>
<td>(s)</td>
<td>C-Cl stretching.</td>
</tr>
</tbody>
</table>

b) The UV-Vis spectrum of compound (11c) was reported in CHCl\(_3\) showed $\lambda_{\text{max}}$ value corresponding to $\pi \rightarrow \pi^*$ transition. (\textit{Spectrum - 2.6})

c) The PMR spectrum of the compound (11c) was recorded in CDCl\(_3\) with TMS as an internal standard. The observed chemical shifts and their correlations are as follows. (\textit{Spectrum - 2.7})

<table>
<thead>
<tr>
<th>Chemical Shift ((\delta))</th>
<th>Nature of peak</th>
<th>No. of protons</th>
<th>Types of protons</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.57</td>
<td>d</td>
<td>1H</td>
<td>= CH -</td>
</tr>
<tr>
<td>6.84</td>
<td>d</td>
<td>1H</td>
<td>= CH -</td>
</tr>
<tr>
<td>6.85-7.81</td>
<td>m</td>
<td>5H</td>
<td>Ar - H</td>
</tr>
<tr>
<td>13.46</td>
<td>s</td>
<td>1H</td>
<td>- OH</td>
</tr>
</tbody>
</table>
10) On the basis of chemical properties, spectral and analytical data, the compounds (11a-c) was assigned the following structures.

2'-hydroxy-3',5'-dichloro-4-methoxychalcone

2'-hydroxy-3',5'-dichloro-2-furylchalcone

EXPERIMENT NO. 7:

Preparation of 4-(2-hydroxy-3,5-dichlorophenyl)-6-(phenyl)-2-iminophenyl-3,6-dihydro-1,3-thiazine (12a):

2'-hydroxy-3',5'-dichlorochalcone (11a) (0.01 mol) and phenylthiourea (0.02 mol) dissolved in ethanol (30 ml). To this aqueous KOH solution (0.02 mol) was added. The reaction mixture was refluxed for three hours, cooled, diluted with water and acidified with 1:1 HCl. The product obtained was crystallized from ethanol to get
4-(2-hydroxy-3,5-dichlorophenyl) -6-phenyl-2-iminophenyl-3,6-dihydro-1,3-thiazine m.p. 173°C, yield- 65%.

EXPERIMENT NO. 8:
Preparation of 4- (2-hydroxy-3,5-dichlorophenyl)-6-(4-methoxyphenyl)-2-iminophenyl-3,6-dihydro-1,3-thiazine (12b):

2'-hydroxy-3',5'-dichloro-4-methoxychalcone (11b) (0.01mol) and phenyl thiourea (0.02mol)dissolved in ethanol (30ml).To this aqueous KOH solution (0.02mol) was added. The reaction mixture was refluxed for three hours, cooled, diluted with water and acidified with 1:1HCl. The product obtained was crystallized from ethanol to get 4- (2-hydroxy-3,5-dichlorophenyl)-6-(4-methoxyphenyl)-2-iminophenyl)-3,6-dihydro-1,3-thiazine (12b) m.p. 189°C, yield- 70%.
EXPERIMENT NO. 9:
Preparation of 4- (2-hydroxy-3,5-dichlorophenyl)-6-(furyl)-2-iminophenyl)-3,6-dihydro-1,3-thiazine (12c):

2'-hydroxy-3',5'-dichloro-2-furylchalcone (11c) (0.01mol) and phenyl thiourea (0.02mol)dissolved in ethanol (30ml). To this aqueous KOH solution (0.02mol) was added. The reaction mixture was refluxed for three hours, cooled, diluted with water and acidified with 1:1HCl. The product obtained was crystallized from ethanol to get 4- (2-hydroxy-3,5-dichlorophenyl)-6-(furyl)-2-iminophenyl)-3,6-dihydro-1,3-thiazine (12c) m.p. 155°c, yield- 70%.

Properties and constitution of compound (12a-c):
1) The compounds (12a-c) are a brown-coloured crystalline solids.
2) The compounds (12a-c) gave no colouration with ethanolic FeCl₃ solution but were found to be soluble in dil. NaOH solution showing the presence of phenolic -OH group.
3) TLC results of the compounds(12a-c) are as follows-

<table>
<thead>
<tr>
<th>Compound</th>
<th>Solvent height (cm)</th>
<th>Solvent height (cm)</th>
<th>Rf</th>
</tr>
</thead>
<tbody>
<tr>
<td>12a</td>
<td>3.2</td>
<td>2.7</td>
<td>0.84</td>
</tr>
<tr>
<td>12b</td>
<td>2.8</td>
<td>2.1</td>
<td>0.75</td>
</tr>
<tr>
<td>12c</td>
<td>3.0</td>
<td>2.3</td>
<td>0.77</td>
</tr>
</tbody>
</table>
4) The analytical results of these compounds agreed with their molecular formulae as follows:

<table>
<thead>
<tr>
<th>Compound</th>
<th>Molecular Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>12a</td>
<td>C_{22}H_{15}ON_{2}SCl_{2}</td>
</tr>
<tr>
<td>12b</td>
<td>C_{23}H_{18}O_{2}N_{2}SCl_{2}</td>
</tr>
<tr>
<td>12c</td>
<td>C_{21}H_{12}O_{2}N_{2}SCl_{2}</td>
</tr>
</tbody>
</table>

5) Spectral data of the compound (12c) is as follows.

a) The important frequencies observed in the IR spectrum recorded in KBr are correlated as follows.

<table>
<thead>
<tr>
<th>Frequencies (cm(^{-1}))</th>
<th>Intensity</th>
<th>Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>3327</td>
<td>(m)</td>
<td>-NH stretch</td>
</tr>
<tr>
<td>3283</td>
<td>(b)</td>
<td>-OH stretch</td>
</tr>
<tr>
<td>1648</td>
<td>(s)</td>
<td>C=N stretch</td>
</tr>
<tr>
<td>1155</td>
<td>(m)</td>
<td>C-N stretch</td>
</tr>
<tr>
<td>894</td>
<td>(s)</td>
<td>Furyl</td>
</tr>
<tr>
<td>753</td>
<td>(s)</td>
<td>C-Cl stretch</td>
</tr>
</tbody>
</table>

b) The UV-Vis spectrum of compound (12c) was reported in CHCl\(_3\) showed \(\lambda_{\text{max}}\) value corresponding to \(n \rightarrow \pi^*\) transition.

c) The PMR spectrum of compound (12c) was reported in CDCl\(_3\) with TMS as an internal standard. The observed chemical shifts can be correlated as follows.
6) On the basis of elemental analysis, chemical properties and spectral data, the compounds (12a-c) were assigned the following structures.

4-(2-hydroxy-3,5-dichlorophenyl)-6-(phenyl)-2-iminophenyl-3,6-dihydro-1,3-thiazine

4-(2-hydroxy-3,5-dichlorophenyl)-6-(4-methoxyphenyl)-2-iminophenyl-3,6-dihydro-1,3-thiazine

4- (2-hydroxy-3,5-dichlorophenyl)-6-(furyl)-2-iminophenyl-3,6- dihydro-1,3-thiazine
PROBABLE MECHANISM

The formation of 4-(2-hydroxy-3,5-dichlorophenyl)-6-(phenyl)-2-iminophenyl-3,6-dihydro-1,3-thiazine(12a) from 2'-hydroxy-3',5'-dichlorochalcone(11a) and phenylthiourea in ethanol containing aqueous alkali solution can be considered as nucleophilic addition reaction. In this reaction, \( \text{OH}^- \) facilitates the formation of nucleophile \( \text{NH-CS-NH}\text{Ph} \) due to which the formation of 1,3-thiazine is accelerated. The condensation of (11a) with \( \text{ph.NH.CS.NH2} \) follows 1,2-addition type of mechanism which can be given as follows.

\[
\text{OH}^- + H - \text{NH} - \text{C-NH.Ph} \rightleftharpoons \text{NH} - \text{C-NH.Ph} + \text{H}_2\text{O}
\]

\[
\begin{array}{c}
\text{Cl} \quad \text{OH} \\
\text{C} - \text{CH} = \text{CH-Ph} \\
\end{array}
\quad \text{S} \quad \text{\textbf{S}} \quad \text{H} \\
\text{Cl} \quad \text{OH} \\
\text{C} - \text{CH} = \text{CH-Ph} \\
\end{array}
\]

\[
\begin{array}{c}
\text{Cl} \quad \text{OH} \\
\text{C} - \text{CH} = \text{CH-Ph} \\
\end{array}
\quad \text{\textbf{S}} \quad \text{H} \\
\text{Cl} \quad \text{NH.Ph} \\
\text{N} \quad \text{C} \quad \text{S} \\
\text{Cl} \quad \text{NH.Ph} \\
\text{N} \quad \text{C} \quad \text{S} \\
\text{Cl} \quad \text{OH} \\
\text{C} - \text{SH} \\
\text{C} - \text{CH} = \text{CH-Ph} \\
\end{array}
\]

\[
\begin{array}{c}
\text{Cl} \quad \text{OH} \\
\text{C} - \text{CH} = \text{CH-Ph} \\
\end{array}
\quad \text{\textbf{Cyclization}} \quad \text{\textbf{Rearrangement}}
\]
EXPERIMENT NO. 10:
Preparation of 4-(2-hydroxy-3,5-dichlorophenyl)-6-phenyl-2-iminophenyl-6H-3-Phenyl-1,3-thiazine (13a):

2'-Hydroxy-3',5'-dichlorochalcone (11a) (0.01 mol) and diphenyl thiourea (0.02 mol) dissolved in ethanol (30 ml). To this aqueous KOH solution (0.02 mol) was added. The reaction mixture was refluxed for three hours, cooled, diluted with water and acidified with 1:1 HCl. The product obtained was crystallized from ethanol to get 4-(2-hydroxy-3,5-dichlorophenyl)-6-phenyl-2-iminophenyl-6H-3-Phenyl-1,3-thiazine (13a). M.P. 163°C, yield -70%.

\[
\begin{array}{c}
\text{Cl} \quad \text{OH} \\
\text{Cl} \quad \text{CH}=\text{CH} \\
+ \quad \text{Ph-NHCSNHPh} \\
\text{aq. KOH} \\
\rightarrow \\
\text{Cl} \quad \text{N} \quad \text{Ph} \\
\text{O} \\
\text{Ph} \\
(11a) \quad \rightarrow \quad (13a)
\end{array}
\]

EXPERIMENT NO. 11:
Preparation of 4-(2-hydroxy-3,5-dichlorophenyl)-6-(4-methoxy)-phenyl-2-iminophenyl-6H-3-Phenyl-1,3-thiazine (13b):

2'-Hydroxy-3',5'-dichloro-4-methoxy chalcone (11b) (0.01 mol) and diphenyl thiourea (0.02 mol) dissolved in ethanol (30 ml). To this aqueous KOH solution (0.02 mol) was added. The reaction mixture was refluxed for three hours, cooled, diluted with water and acidified with 1:1 HCl. The product obtained was crystallized from ethanol to get 4-(2-hydroxy-3,5-dichlorophenyl)-6-(4-methoxy)-phenyl-2-iminophenyl-6H-3-Phenyl-1,3-thiazine (13b). M.P. 179°C, yield -70%.
EXPERIMENT NO. 12:
Preparation of 4-(2-hydroxy-3,5-dichlorophenyl)-6-(furyl)-phenyl-2-iminophenyl-6-H-3-Phenyl-1,3-thiazine (13c):

2'-Hydroxy-3',5'-dichloro-2-furyl chalcone (11c) (0.01 mol) and diphenyl thiourea (0.02 mol) dissolved in ethanol (30 ml). To this aqueous KOH solution (0.02 mol) was added. The reaction mixture was refluxed for three hours, cooled, diluted with water and acidified with 1:1 HCl. The product obtained was crystallized from ethanol to get 4-(2-hydroxy-3,5-dichlorophenyl)-6-(furyl)-phenyl-2-iminophenyl-6-H-3-Phenyl-1,3-thiazine (13c). M.P. 135°C, yield 65%.

Properties of compound (13a-c):
1) The compounds (13a-c) is a brown-coloured crystalline solids.
2) The compounds (13a-c) gave no colouration with ethanolic FeCl₃ solution but were found to be soluble in dil. NaOH solution showing the presence of phenolic -OH group.
3) TLC results of the compounds (13a-c) are as follows-
5) The analytical results of these compounds agreed with their molecular formulae as follows.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Solvent height (cm)</th>
<th>Solvent height (cm)</th>
<th>R_f</th>
</tr>
</thead>
<tbody>
<tr>
<td>13a</td>
<td>2.9</td>
<td>1.9</td>
<td>0.66</td>
</tr>
<tr>
<td>13 b</td>
<td>2.2</td>
<td>1.7</td>
<td>0.77</td>
</tr>
<tr>
<td>13 c</td>
<td>2.7</td>
<td>2.0</td>
<td>0.74</td>
</tr>
</tbody>
</table>

6) Spectral data of the compound (13a-c) is as follows.

a) The important frequencies observed in the IR spectrum recorded in KBr are correlated as follows. *(Spectrum 29-33)*

<table>
<thead>
<tr>
<th>Frequencies (cm(^{-1}))</th>
<th>Intensity</th>
<th>Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>3068</td>
<td>(b)</td>
<td>-OH stretch</td>
</tr>
<tr>
<td>1648</td>
<td>(s)</td>
<td>C=N stretch</td>
</tr>
<tr>
<td>1178</td>
<td>(m)</td>
<td>C-N stretch</td>
</tr>
<tr>
<td>868</td>
<td>(m)</td>
<td>Furyl</td>
</tr>
<tr>
<td>738</td>
<td>(s)</td>
<td>C-Cl stretch</td>
</tr>
</tbody>
</table>
Spectrum-31

05/06/03 09:28 R.C./SAIF.P.U.CHD.
Z: 4 scans, 4.0cm⁻¹, flat, smooth, abex

spl.code: 13-C
b) The UV-V spectrum of compound (13a-c) was reported in CHCl₃ showed λ_max value corresponding to n→π* transition. (spectrum 32)

c) The PMR spectrum of compound (13a-c) was reported in CDCl₃ showed λ_max value with TMS as an internal standard. The observed chemical shifts can be correlated as follows. (spectrum 33)

<table>
<thead>
<tr>
<th>Chemical shift (δ)</th>
<th>Nature of peak</th>
<th>No. of protons</th>
<th>Types of protons</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.20</td>
<td>D</td>
<td>1H</td>
<td>=CH-</td>
</tr>
<tr>
<td>5.27</td>
<td>D</td>
<td>1H</td>
<td>=CH-</td>
</tr>
<tr>
<td>6.61-8.16</td>
<td>M</td>
<td>15H</td>
<td>Ar-H</td>
</tr>
<tr>
<td>10.72</td>
<td>S</td>
<td>1H</td>
<td>-OH</td>
</tr>
</tbody>
</table>

7) On the basis of elemental analysis, chemical properties and spectral data, the compounds (13a-c) were assigned the following structures.

![Structure 13a](image1)

![Structure 13b](image2)

![Structure 13c](image3)
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