CHAPTER 2
SYNTHESIS AND SPECTRAL CHARACTERISATION OF THIOSEMICARBAZONE LIGANDS

2.1 INTRODUCTION:

The biological activities of thiosemicarbazones are a function of parent aldehyde or ketone [81]. According to recent researches, thiosemicarbazones and their metal complexes are mainly centred on their therapeutic properties. So an improved method of synthesizing thiosemicarbazones have been attempted to facilitate these investigations.

Details about the preparation on ligands and their characterization are presented in this chapter.

2.2 EXPERIMENTAL:

2.2.1 Chemicals and Methods:

5-Chloro-2-hydroxyacetophenone (Aldrich), thiosemicarbazide (Aldrich), ethanol (A.R. Grade) Methanol (A.R. Grade), conc. $\text{H}_2\text{SO}_4$ (A.R. Grade).

2.2.2 Synthesis:

Procedure for the synthesis of 5-chloro-2-hydroxy acetophenone thiosemicarbazone:

The thiosemicarbazide (0.01 M) was dissolved in 10 ml hot ethanol in 100 ml round bottom flask. To this solution, solution of 0.01 M
5-chloro-2-hydroxy acetophenone in ethanol was added dropwise over 10 min. period with continuous stirring. Conc. H₂SO₄ (2-3 drops) was added to it. After addition, the reaction mixture was refluxed on hot plate with stirrer at 90 °C for 3 hours, during this period reaction was monitored by TLC. After completion of reaction, excess solvent was evaporated and pale yellow product formed was filtered, washed with cold ethanol and then with diethyl ether. The product was dried over P₄O₁₀ in vacuum [92].

![Scheme 1](attachment:image.png)

**Procedure for the synthesis of 5-chloro-2-hydroxy acetophenone N(4) methyl thiosemicarbazone:**

N(4) methyl thiosemicarbazide (0.01 M) was dissolved in 10 ml hot ethanol in 100 ml round bottom flask. To this solution, solution of 0.01 M 5-chloro-2-hydroxy acetophenone in ethanol was added dropwise over a 10 min. period with continuous stirring. Conc. H₂SO₄ (2-3 drops) was added to this mixture. After addition the reaction mixture was refluxed on hot plate with stirrer at 90 °C for 4 hours and the reaction was monitored by TLC. After completion of the reaction excess solvent was evaporated and pale yellow product formed was filtered, washed with cold
ethanol then with diethyl ether. The product was dried over P4O10 in vacuum [92].

2.2.3 Physical Measurements:

The colour, yield, solubility of Ligands L and L’ are presented in Table No.2.2.3.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Colour</th>
<th>Yield</th>
<th>Solubility</th>
</tr>
</thead>
<tbody>
<tr>
<td>L</td>
<td>Pale yellow</td>
<td>81%</td>
<td>Hot ethanol</td>
</tr>
<tr>
<td>L’</td>
<td>Pale yellow</td>
<td>85%</td>
<td>Hot ethanol</td>
</tr>
</tbody>
</table>

2.3 SPECTRAL DATA OF SYNTHESISED LIGANDS:

2.3.1 ¹H NMR Spectra:

1) 5-chloro-2-hydroxy acetophenone thiosemicarbazone (L)

(Fig.No.2.3.1 A):

NMR signals at 13.00, 2.20 ppm are assigned to -OH, -CH₃ protons respectively.

L does not show any peak corresponding to S-H proton, indicating it exists in thioketo form. Little low field position of ⁴NH (8.20
ppm) could be attributable to the deshielding caused by –N = C of the system N=CSH = NH. Signal at 11.3 ppm corresponds to 2NH. Aromatic protons show multiples at 6.9, 7.25 and 7.60 ppm.

2) 5-chloro-2-hydroxy acetophenone N(4) substituted methyl thiosemicarbazone (L') (Fig.N.o.2.3.1 B):

NMR signals at 13.00 and 2.2 ppm are assigned to –OH and –CH₃ protons respectively. The signals at 2.40, 3.00 correspond to 4NH and H₄N-CH₃ respectively. Signal at 10.3 ppm corresponds to 2NH. Aromatic protons show multiplet at 6.9, 7.25, 7.45, ppm.

2.3.2 ¹³C-MR Spectra:

1) 5-chloro-2-hydroxy acetophenone thiosemicarbazone (Fig.N.o.2.3.2 A):

¹³C-NMR (DMSO – D6) : ppm

119.18 (C = C), 131.38 (C = C), 128.27 (C = C – Cl), 130.77 (C = C), 123.15 (C = C), 155.97 (C = C – OH), 160.06 (C = N), 180.0 (C=S), 16.2 (C-CH₃).
2) **5-chloro-2-hydroxy acetophenone N(4) substituted methyl thiosemicarbazone (Fig.No.2.3.2 B):**

$^{13}$C-NMR (DMSO – D6) : ppm

118.20 (C = C), 129.70 (C = C), 127.79 (C = C – Cl), 128.05 (C = C), 122.26 (C = C), 152.17 (C = C – OH), 155.39 (C = N), 179.80 (C = S), 31.03 (NH – CH$_3$)

![Diagram of molecule]

2.3.3 **Analytical Data (Fig.No.2.3.3 A, B):**

1) **5-Chloro-2-hydroxy acetophenone thiosemicarbazone:**

Anal. Calcd for C$_{9}$H$_{10}$ClN$_{3}$OS ESI-MS M/ Z, ion

243.70 M$^+$; C, 44.35 %; H, 4.14 %; N, 17.24 %; S, 13.16 % Found : ESI-MS m/ z, ion M$^+$ 243.80; C, 44.03 %; H, 4.36; N, 17.62; S, 13.33 %.

2) **5-Chloro-2-hydroxy acetophenone N(4) substituted methyl thiosemicarbazone :**

Anal. Calcd for C$_{10}$H$_{12}$N$_{3}$ClOS ESI-MS M/ Z, ion

257.72 M$^+$; C, 46.80 %; H, 4.69 %; N, 16.30 %; S, 12.44 % Found : ESI-MS m/ z, ion M$^+$ 257.20; C, 46.48 %; H, 5.19 %; N, 17.15 %; S, 12.10 %
2.3.4  **Electronic Spectra (Fig.2.3.4 A, B)**

UV – visible spectra were recorded as DMF solution in the range 200-800 nm.

1)  **L:**  25575 (n → *), 34602 (n → *), 38610 (→ *)

2)  **L':**  25000 (n → *), 33784 (n → *), 38610 (→ *)

2.3.5  **Infra-red spectra: (Fig 2.3.5 A, B)**

1)  **L:**

Infrared spectra were recorded in the range 400 – 4000 cm⁻¹

(- OH) 3426; (C = N) 1624; (- C – S) 758 (s), 1374 (m); (N – N) 1049; (²N-H) 3263; (C – O) 1281.

2)  **L':**

(- OH) 3309; (C = N) 1638; (- C – S) 795 (s), 1359 (m); (N – N) 1049; (²N-H) 3220; (C – O) 1288.

2.4  **RESULTS AND DISCUSSION:**

From the results on elemental analyse of synthesized compounds, it is found that, both calculated and found percentages of elements are well matched, so elemental analysis confirms the structure of respective thiosemicarbazones. Mass spectral data confirm the structure of the thiosemicarbazone as indicated by molecular ion peak (M + 1) corresponding to their molecular weights.

Bands of IR spectra of the synthesized thiosemicarbazones showed useful information about the structures of the compounds. In the
IR spectrum of L some bands due to –C-S, N-N were observed at 758 (s), 1374 (m) and 1049 cm\(^{-1}\) respectively. In L, bands due to –C-S, H-N were observed at 795, 1359 and 1049 respectively. In L, the specific band for thiosemicarbazone –C = N was observed at 1624 cm\(^{-1}\) and in L’ at 1638 cm\(^{-1}\). In the IR spectrum of L the other bands due to \(^2\)N-H and –C-O were observed at 3263 and 1281 cm\(^{-1}\) and in L’ at 3220 and 1288 cm\(^{-1}\). Peak due to O-H stretching might be shifted to lower side due to hydrogen bonding with imine N and merged with C-H frequency.

UV-Visible spectroscopy is a very important tool for the structural identification of synthesized thiosemicarbazone. Spectra are usually recorded in the range 200 – 800 cm\(^{-1}\). Electronic spectra were recorded in DMF. The compound L absorbs in the region 250-360 nm. The bands at 355 and 308 correspond to \(n \rightarrow p^*\) transitions. The band at 250 nm corresponds to \(p \rightarrow p^*\) transitions. The compound L’ shows absorptions in the region 250-385 nm. The bands at 385 and 305 correspond to \(n \rightarrow p^*\) transitions. The band at 252 nm corresponds to \(p \rightarrow p^*\) transition.

**Structure:**

![Chemical Structure](image)
Fig. 2.3.1.A: $^1$H NMR Spectrum of L

Fig. 2.3.1.B: $^1$H NMR Spectrum of L’
Fig. 2.3.2.A: CMR Spectrum of L

Fig. 2.3.2.B: CMR Spectrum of L'
Fig. 2.3.3.A : ESI - MS Spectrum of L

Fig. 2.3.3.B : ESI - MS Spectrum of L'}
Fig. 2.3.4.A: Electronic Spectrum of L

Fig. 2.3.4.B: Electronic Spectrum of L'
Fig. 2.3.5.A : IR Spectrum of \( L \)

Fig. 2.3.5.B : IR Spectrum of \( L' \)