CHAPTER - 3
SYNTHESIS AND CHARACTERISATION OF LIGANDS

3.1: Introduction:

Indole 2,3 dione possesses diverse biological activities \(^{(1-4)}\). Sulphur containing substituted hydrazones also possess a wide spectrum of biological activities, and in many cases, coordination of these compounds to a transition metal ion enhances their activities \(^{(5,6)}\). Several benzothiazole compounds were reported to be physiologically active and were considered to be of interest in chemotherapy of tuberculosis \(^{(7)}\). Most of the benzothiazolines and their derivatives were well known for their importance in plasticizing effects and also in photographic emulsions \(^{(8-15)}\). For convenience, this chapter is dealt in two sections.

3.2: Synthesis of Ligands:

All the chemicals and solvents used were of Analar grade or guaranteed reagents. Solvents such as ethanol, benzene, petroleum ether and chloroform were purified, before use by following the standard procedures \(^{(10)}\).

3.2.1: Synthesis of Indole 2,3dione -3- (thiosemicarbazone) IDTSC:

Indole 2,3dione -3- (thiosemicarbazone) was synthesized by pouring a solution of 14.3 gms (0.097M) of Indole 2,3 dione in 65ml of ethanol into a boiling saturated aqueous solution of 9.1 gms (0.099M) of thiosemicarbazide and refluxed on water steam bath at 100\(^\circ\)C for about 30 minutes. After cooling yellow crystalline product was obtained, filtered and recrystallised from hot water. m.p.246\(^\circ\)C . Yield 85\% \(^{(17)}\).
3.2.2: Synthesis of Indole 2,3-dione -3- (semicarbazone) IDSC:

Indole 2,3 dione -3- (semicarbazone) was synthesized by refluxing a mixture of 0.5 gms Indole 2,3 dione (0.0034M) and 0.25 gms (0.003M) of semicarbazone in 25 ml ethanol for about 45 minutes. After cooling yellow product was obtained, filtered, washed and recrystallised from 50% ethanol and dried in vaccum. m.p.225°C. Yield 88% (18).

3.2.3: Synthesis of Indole 2,3-dione-3- (Benzothiazole 2'-carboxy hydrazone) IDBTCH:

Synthesis of IDBTCH involves three steps:

a). Conversion of 2-amino thio phenol to benzothiazole -2-ethyl carboxylate by Esterification (BTC)
b). Conversion of ester to its hydrazide (BTCI).
c) Conversion of benzothiazole 2- carboxy hydrazide to IDBTCH by reaction with Indole 2,3 dione

BTCH was prepared by reported procedure (19).

A mixture of 12.5 gms of 2-amino thio phenol and 29.2 gms of diethyl oxalate was refluxed for 4 hours, where the range of temperatures was maintained from 147°C to 93°C. After cooling the product was poured into a solution containing 50ml of concentrated HCl, 150ml of water and 70ml of 95% ethanol with stirring. The oil was dissolved and solid was formed. The mixture was cooled in ice bath at 9°C. The product was recovered by filtration and washed with 75ml of chilled aqueous ethanol in two portions. Then dried overnight in vaccum desiccators. This was recrystallised in petroleum ether and the ester obtained melts at 71°C.

The benzothiazole ethyl-2-carboxylate obtained was treated with hydrazine hydrate in excess of ethanol medium, by refluxing for 30 minutes and then cooled. The product was separated by filtration and washed with cold ethanol so as to remove unreacted ester and excess hydrazine hydrate. This was melted at 171°C.

The product obtained is benzothiazole-2-carboxy hydrazide (BTCH) and was treated with Indole 2,3 dione to obtain IDBTCH.
IDBTCH was synthesized by refluxing an ethanolic solution of Indole 2,3 dione (0.5 gms 0.0034M) and BTCH (0.65gms 0.003M) for about 30 minutes. After cooling the yellowish orange amorphous product obtained was filtered washed and recrystallised from hot ethanol. m.p.229°C. Yield 91%.

3.2.4: Synthesis of Benzothiazole-2-oyl-phenyl hydrazone. BTPH:

Benzothiazole-2-oyl-phenyl hydrazone was synthesized by refluxing an ethanolic solution of BTCH (0.5 gms 0.0026M) and Benzaldehyde (0.27 gms 0.0025M) for about 30 minutes. After cooling white amorphous product obtained was filtered, washed and recrystallised from 50% DMF, m.p.225°C. Yield 93%.

3.2.5: Synthesis of Spiro [Benzothiazoline 2,3' Indole 2'one]. SBTI:

SBTI was prepared by the reaction of Indole 2,3 dione with 2-amino thio phenol. An ethanolic mixture of 0.5 gms of Indole 2,3 dione (0.0034M) and 0.06 ml of 2-amino thio phenol was refluxed for 45 minutes. The yellow product obtained was filtered, washed and recrystallised from hot ethanol. m.p.195°C. Yield 83%.

Scheme for the synthesis of ligands is presented in fig.3.1

3.3: Characterization of ligands:

All the ligands are characterized by spectroscopic techniques like IR, ¹HNMR, ¹³CNMR and Mass spectra. The spectral data and elemental analysis data presented at appropriate place.

3.3.1: Indole 2,3dione-3- (thiosemicarbazone) IDTSC:

IR Spectrum of IDTSC (fig.3.2, table.3.1) showed the presence of peaks corresponding to ν-NH (3422 Cm⁻¹), ν –NH (2⁰) (3321 Cm⁻¹), aromatic ν -CH (3143 Cm⁻¹), ν –C=O (1676 Cm⁻¹), ν –C=N (1698 Cm⁻¹), ν –C=S (1130 Cm⁻¹).
**Fig-3.1. Scheme Showing Synthesis of Ligands**

**IDTSC**

\[
\text{Indole 2,3 dione} + \text{IDTSC} \xrightarrow{30 \text{ min} @ 100^\circ C} \text{Ligand}
\]

**IDSC**

\[
\text{Indole 2,3 dione} + \text{IDSC} \xrightarrow{30 \text{ min} @ 100^\circ C} \text{Ligand}
\]

**IDBTCH**

\[
\text{Indole 2,3 dione} + \text{IDBTCH} \xrightarrow{30 \text{ min} @ 100^\circ C} \text{Ligand}
\]
Fig-3.1. Scheme Showing Synthesis of Ligands

BTPH

\[
\text{Scheme 3.1: Synthesis of BTPH.}
\]

\[
\text{[Chemical Structure Image]}
\]

SBTI

\[
\text{Scheme 3.2: Synthesis of SBTI.}
\]

\[
\text{[Chemical Structure Image]}
\]
\( \nu\text{-C-N} (1060 \text{ Cm}^{-1}) \). The aromatic \( \nu\text{-C=C} \) vibrations of the compounds are observed at 1593-1463 Cm\(^{-1}\). These are assigned by comparison with the frequency value of simple model compounds\(^{(21)}\).

\(^1\text{HNMR}\) spectrum of IDTSC (fig.3.3, table3.2) showed characteristic peaks at \( \delta \) 12.8 (enolic OH) \( \delta \) 10.8 (amide \( \text{HN-C}=\text{O} \)), \( \delta \) 6.9-\( \delta \) 7.3 (aromatic protons), \( \delta \) 8.4 (-NH), \( \delta \) 7.8 (-NH\( _2 \)). The integration of peaks in the spectrum indicates more number of protons as against expected which can be interpreted by considering the keto as well as enol forms of the compound\(^{(21,22)}\).

\(^{13}\text{CNMR}\) spectrum of IDTSC (fig.3.4) showed 17 signals which indicated the presence of 17 carbons, though the ligand has only 15 existing both keto as well as enol forms.

Mass spectrum of IDTSC (fig.3.5) shows molecular ion peak \( M^+ \) at \( M/\alpha \) 220. It displayed the other fragmental peaks at \( M/\alpha \) 150,132,118,104,90,77,60,43 apart from the base peak at 192. The fragmentation pattern is given in fig.3.6, table3.3.

From the mass spectral data, the molecular formula of IDTSC is confirmed to be \( C_{9}H_{8}N_{4}OS \), which is also in agreement with elemental analysis data [Found C: 50.05, H: 4.2, N: 24.87% calculated C:49.02,H:3.80,N:25.40%].

3.3.2: Indole 2,3 dione-3- (semicarbazone) IDSC:

IR Spectrum of IDSC (fig.3.7, table3.1) showed the presence of peaks corresponding to \( \nu\text{-NH} (3414 \text{ Cm}^{-1}) \), \( \nu\text{-NH} \ (21) (3298 \text{ Cm}^{-1}) \), aromatic \( \nu\text{-CH} (3053\text{Cm}^{-1}) \), \( \nu\text{-C}=\text{O} \) (1686 \text{ Cm}^{-1}), \( \nu\text{-C=N} \) (1678 \text{ Cm}^{-1}), \( \nu\text{-C-N} \) (1030 \text{ Cm}^{-1}). The aromatic \( \delta \text{ C=C} \) vibrations of the compounds are observed at 1593-1463 Cm\(^{-1}\). These are assigned by comparison with the frequency value of simple model compounds\(^{(21)}\).

\(^1\text{HNMR}\) spectrum of IDSC (Fig.3.8, table3.2) showed characteristic peaks at \( \delta \) 11.6 (enolic OH), \( \delta \) 10.8 (amide \( \text{HN-C}=\text{O} \)), \( \delta \) 6.9-\( \delta \) 7.6 (aromatic protons), \( \delta \) 8.4 (-NH), \( \delta \) 8.2 (-NH\( _2 \)). The integration of peaks in the spectrum indicates more number of protons as against expected which can be interpreted by considering the keto as well as enol forms of the compound\(^{(21,22)}\).

\(^{13}\text{CNMR}\) spectrum of IDSC (fig.3.9) showed 17 signals which indicated the presence of 17 carbons, though the ligand has only 15 existing both keto as well as enol forms.
Wave number cm$^{-1}$

Transmittance (%)

Fig. 3.2: IR Spectrum of IDTSC
Fig. 3.5: Mass Spectrum of IDTSC
Fig. 3.6. Mass Spectral Fragmentation of IDTSC

a. 
\[ \text{Structure a} \]

b. 
\[ \text{Structure b} \]

c. 
\[ \text{Structure c} \]

d. 
\[ \text{Structure d} \]

e. 
\[ \text{Structure e} \]

f. 
\[ \text{Structure f} \]
From the above analysis the molecular formula of IDSC is confirmed to be C₉H₅N₄O₂, which is also in agreement with elemental analysis data [Found C: 53.09, H: 4.1, N: 27.87% calculated C: 52.89, H: 3.89, N: 27.85%].

3.3.3: Indole 2,3-dione-3- (Benzothiazole 2'-carboxy hydrazone) IDBTCH:

IR spectrum of IDBTCH (fig.3.10, table3.2) showed the presence of peaks corresponding to $\nu$ –NH (3311 Cm⁻¹), $\nu$ C=O (1708 Cm⁻¹), $\nu$ C=C aromatic (1578-1467 Cm⁻¹) apart from these $\nu$ –C=N (1615 Cm⁻¹) bending vibrations are observed (23).

$^1$HNMR spectrum of IDBCTHI (fig. 3.11, table3.2) showed characteristic peaks at $\delta$ 8.3, (–NH) and a multiplet at $\delta$ 8.2 to 8.9 (aromatic protons). From the $^1$H-NMR study there is a clear evidence for the existence of keto-enol tautomerism (24).

$^{13}$CNMR spectrum of IDBTCH (fig.3.12) indicated the presence of 18 carbon atoms.

$^{13}$CNMR spectrum also confirms the presence of keto-enol tautomerism, which gave peaks at 162-ppm characteristic of C-NH keto form and 148 ppm for C=N enol form.

Mass spectrum of IDBTCH (fig.3.13) shows molecular ion peak M⁺ at m/Z 322. It displayed other fragmental peaks at m/Z 294, 266, 162, 104, 69 apart from its base peak at 135. Fragmentation pattern is given in fig.3.14.

From the mass spectral data (table3.3) the molecular formula of IDBCTHI is confirmed to be C₁₆H₁₀N₄O₂S, which is also in agreement with elemental analysis data [Found C: 59.32, H: 4.6, N: 17.83% calculated C:59.6, H:3.1, N:17.4%] (25).

3.3.4: Benzothiazole-2-oyl- phenyl hydrazone, BTPH:

IR spectrum of BTPH (fig.3.15, table3.1) showed the characteristic peaks of $\nu$ –NH (3213 Cm⁻¹), $\nu$ C=O (1658 Cm⁻¹), aromatic $\nu$ C=C (1528-1487 Cm⁻¹), aromatic $\nu$ C-H (3048 Cm⁻¹), $\nu$ –C=N (1602 Cm⁻¹).

$^1$HNMR spectrum of BTPH (fig.3.16, table3.2) showed the characteristic peaks at $\delta$ 12.4 (N=C-OH), $\delta$8.7 (N=CH), $\delta$7.4 to $\delta$8.2 (aromatic protons).

$^{13}$CNMR spectrum of BTPH (fig.3.17) indicates the presence of 15 carbons.
Fig-3.10: IR Spectrum of IDBTCH

Fig-3.13: Mass Spectrum of IDBTCH
Fig-3.14. Mass spectral Fragmentation of IDBTCH

a.

b.

c.

d.

e.

f.

g.

h.

54
Fig. 3.16: $^1$H-NMR Spectrum of BTPH

Fig. 3.17: $^{13}$C-NMR Spectrum of BTPH
Mass spectrum of BTPH (fig.3.18) showed the molecular ion peak \( M^+ \) at \( m/Z \) 281 ppm. It displayed other fragmental peaks at \( m/Z \) 178, 162, 134, 108, 90, 69 apart from base peak at \( m/Z \) 135. Fragmentation pattern is given in fig.3.19.

From the mass spectral data (table.3.3) the molecular formula of BTPH is confirmed to be \( C_{13}H_{11}N_3OS \), which is also in agreement with elemental analysis data [Found C: 64.3, H: 5.1, N: 14.89% calculated C: 64, H: 3.9, N: 15%]²².

3.3.5: Spiro [Benzothiazoline 2-3' indole 2'one] SBTI:

IR spectrum of SBTI (fig.3.20, table3.1) showed the characteristic peaks of \( \nu -NH \) (3366 Cm\(^{-1}\)), \( \nu C=O \) (1708 Cm\(^{-1}\)), aromatic \( \nu C=C \) (1560-1420 Cm\(^{-1}\)), aromatic \( \nu C-H \) (2925 Cm\(^{-1}\)), \( \nu -C=N \) (1636 Cm\(^{-1}\)).

\(^1\)HNMR spectrum of SBTI (fig.3.21, table3.2) shows the characteristic peaks \( \delta 10 \) (enolic-OH), \( \delta 7.6 \) (C-N-H), \( \delta 2.9 \) (-NH-) and \( \delta 7.3 \) to \( \delta 6.4 \) multiplet corresponding to aromatic protons.

\(^13\)CNMR spectrum of SBTI (fig.3.22) indicated the presence of 16 carbons which confirms the existence of ligand in both keto as well as enol forms.

Mass spectrum of SBTI (fig.3.23) showed molecular ion peak \( M^+ \) at \( m/Z \) 226 ppm with the loss of C=O. the other fragmental peaks at \( m/Z \) 147, 92, 76, 64 apart from its base peak at 119. Absence of molecular peak is characteristic of molecules of branched functional class (²⁶). Fragmentation pattern is given in fig.3.24.

The molecular formula of the compound from various methods was confirmed as \( C_{14}H_{10}NSO \), which is in agreement with elemental analysis data [Found C: 65.32, H: 4.01, N: 10.82% calculated C: 66.14, H: 3.9, N: 11%].
Fig-3.18: Mass Spectrum of RTPH
Fig-3.19. Mass Spectral Fragmentation of BTPH

a

b

c

d

e

f

g

h

59
Fig. 3.10: IR Spectrum of SBTI
Fig. 3.24. Mass Spectral Fragmentation of SBTI

a

\[
\begin{array}{c}
\text{NH} \\
\text{S} \\
\text{NH}
\end{array}
\]

b

\[
\begin{array}{c}
\text{NH} \\
\text{C} \\
\text{C} \quad \text{NH}
\end{array}
\]

c

\[
\begin{array}{c}
\text{NH} \\
\text{C} \quad \text{O}
\end{array}
\]

d

\[
\begin{array}{c}
\text{NH}_2
\end{array}
\]
Fig-3.25. Structures of Ligands

IDTSC

IDSC

IDBTCH

BTPH

SBTI

64
Fig-3.36. Keto- Enol tautomeric structures of Ligands

**IDTSC**

**IDSC**

**IDBTCH**
Fig-3.24. Keto-Enol tautomeric structures of Ligands

BTPH

SBTI
### Table-3.1 IR Spectral data of Ligands (KBr) Cm⁻¹

<table>
<thead>
<tr>
<th>Ligand</th>
<th>δC-H (aro)</th>
<th>δC=O</th>
<th>δC=N</th>
<th>δNH₂</th>
<th>δNH</th>
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<tbody>
<tr>
<td>IDTSC</td>
<td>3143</td>
<td>1676</td>
<td>1698</td>
<td>3422</td>
<td>3321</td>
</tr>
<tr>
<td>IDSC</td>
<td>3053</td>
<td>1686</td>
<td>1678</td>
<td>3414</td>
<td>3298</td>
</tr>
<tr>
<td>IDBTCH</td>
<td>3066</td>
<td>1708</td>
<td>1615</td>
<td>3311</td>
<td>3179</td>
</tr>
<tr>
<td>BTPH</td>
<td>3048</td>
<td>1658</td>
<td>1602</td>
<td>-</td>
<td>3213</td>
</tr>
<tr>
<td>SBTI</td>
<td>2925</td>
<td>1708</td>
<td>1636</td>
<td>-</td>
<td>3366</td>
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### Table-3.2 ¹H NMR Spectral data of Ligands δ: PPM

<table>
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<tr>
<th>Ligand</th>
<th>Enolic</th>
<th>Amide</th>
<th>-NH₂</th>
<th>Aromatic</th>
<th>Solvent</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDTSC</td>
<td>12.8(s)</td>
<td>10.8(s)</td>
<td>8.4(s)</td>
<td>7.8(d)</td>
<td>6.9-7.1(m)</td>
</tr>
<tr>
<td>IDBTCH</td>
<td>11.2(s), 11.6(s)</td>
<td>10.8(s)</td>
<td>8.3(d)</td>
<td>8.2(d)</td>
<td>6.9-7.6(m)</td>
</tr>
<tr>
<td>IDSC</td>
<td>11.6(s)</td>
<td>10.8(s)</td>
<td>8.4(s)</td>
<td>6.9-7.6(m)</td>
<td>CDCl₃</td>
</tr>
<tr>
<td>BTPH</td>
<td>12.4(s)</td>
<td>N=CH 8.7(s)</td>
<td>NH-CH 2.9(s)</td>
<td>7.4to8.2 (m)</td>
<td>DMSOD₆</td>
</tr>
<tr>
<td>SBTI</td>
<td>10</td>
<td>7.6(d)</td>
<td>-NH- 2.9 (d)</td>
<td>6.2 to 7.3 (m)</td>
<td>CDCl₃</td>
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</table>

### Table-3.3 Mass Spectral data of Ligands

<table>
<thead>
<tr>
<th>LIGAND</th>
<th>m/z (rel.int. %)</th>
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</thead>
<tbody>
<tr>
<td>IDTSC</td>
<td>220(66), 192(100), 132(26), 104(60), 90(13), 77(26.6)</td>
</tr>
<tr>
<td>IDBTCH</td>
<td>322(46), 294(10.6), 266(9.3), 162(48), 135(100), 104(18), 69(32).</td>
</tr>
<tr>
<td>BTPH</td>
<td>281(13.3), 178 (26), 162(16), 135(100), 134(29), 108(26), 90(50.6), 69(26.6).</td>
</tr>
<tr>
<td>SBTI</td>
<td>226(2.6), 147(46.6), 119(100), 92(73.3), 76(6.6), 64(32).</td>
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REFERENCES