CHAPTER V

CODEINE
Codaine is isolated from opium. It occurs in opium to the extent of 0.1 to 3 percent and is isolated therefrom as hydrochloride along with morphine. The three alkaloids concerned, morphine, codaine and thebaine, all behave as tertiary base. Morphine contains two hydroxyl groups of which one is phenolic and the other is a secondary alcoholic group. On methylation of phenolic hydroxyl group codaine results and on methylation of both hydroxyl group thebaine is formed.

![Morphine](fig. (I)) ![Codaine](fig. (II)) ![Thebaine](fig. (III))

The relationship between the three alkaloids is close and therefore codaine is a methyl ether of morphine. The
nature of the nitrogen atom of morphine and its mode of attachment to the hydrophenanthrene nucleus has proved to be major problem in this field. The basic nitrogen of morphine and codeine is tertiary and a component of ring since both bases react with molar proportion of methyl iodide\(^1-2\) to give quaternary salts. Replacement of second hydroxyl group by halogen and the oxidation of codeine to a ketone, codeinone amongst other reactions has clearly diagnosed the alcoholic nature of this group. The third oxygen atom is very unreactive and appears to be present in an ether type of linkage\(^3\).

Several reactions\(^4,5\), although quite drastic in nature, indicate that in all probability the morphine alkaloids contain a phenanthrene skeleton while the relatively high percentage of hydrogen in these bases has led to the presumption that phenanthrene system is partially hydrogenated.

No work on metal-codeine has been reported except a few with the first series of transition metal by Farooq & Malik\(^6\). The infra red spectra of codeine and its complexes with Ca\(^{+2}\), Co\(^{+2}\), Ni\(^{+2}\), Vo\(^{+2}\), Mn\(^{+2}\), Ti\(^{+3}\) and Cr\(^{+3}\) give some reliable information regarding the bonding of these complexes. Unlike alkaloids these complexes are, in general, highly soluble in water but almost insoluble in common organic
Plate No. 43 IR Spectrum of Codeine-CDCl$_2$ Complex
The result of chemical analyses indicated a ratio of 1:2. Magnetic measurements applying Gouy method were carried out.

The present chapter deals with interaction of Cd$^{2+}$ and Bi$^{3+}$ ions. The studies include the synthesis of complexes, characterisation has been carried out by chemical analyses, conductivity data, melting points and infra red spectra. The location of possible coordination sites has been determined on the basis of infra red spectral studies.

**EXPERIMENTAL**

**Reagents:**

Codeine (B.D.H.) and chlorides of cadmium (U.S.S.R.) and Bi (Poland), solvents such as ethanol and dimethyl sulfoxide were purified and distilled before use.

**Preparation of Complexes:**

The compounds reported herein were synthesized from the solution of metal salts in ethanol and appropriate alkaloid in the same solvent. The solution of metal salt was added in the ratio of 1:2. The precipitates were washed several times with solvent to remove excess of metal ion and
alkaloid. The complex was dried over vacuo for several days.

**Analysis of Complexes**

The analyses of carbon, hydrogen and nitrogen were done by Microanalytical Division of I. I. T., Kanpur. The molar conductances of $1 \times 10^{-3}$ M solution in dimethyl sulfoxide of the complexes were measured with a Philips conductivity bridge model PR9500 using a dip type cell (cell constant 0.64) at 25°C.

The infra red spectra of complexes and ligand were recorded with a Perkins Elmer model 621 spectrophotometer in the range of $4000 \text{ cm}^{-1} - 200 \text{ cm}^{-1}$ in the nujol mull. Melting points were recorded by usual method.

**RESULTS AND DISCUSSION**

The elemental analyses of the complexes of cadmium and bismuth chlorides for carbon, hydrogen and nitrogen show that the interaction of codeine with cadmium and bismuth chlorides exhibit the molar ratio, 1:2 (metal: ligand) and established the following formulas:

$$C_{36}H_{40}CdCl_2N_2O_6$$
$$C_{36}H_{40}BiCl_3N_2O_6$$
The complexes of cadmium and bismuth decomposed at the temperatures 210±5 and 160±2°C respectively.

**Molar Conductances:**

The recorded molar conductances of these complexes in dimethyl sulfoxide at $10^{-3}$ M concentration were 19.06 and 32.20 cm$^{-1}$ cm$^2$ mol$^{-1}$ respectively for cadmium and bismuth. The complexes were practically non-electrolytes (as described in previous chapters).

**Infra red Spectra:**

The infra red spectra of codeine show a strong band of 3540 cm$^{-1}$ which may be assigned to secondary OH stretching$^7$. This appears as a strong band at 3520 cm$^{-1}$ in the spectra of cadmium complex and a weak and broad band at 3420 cm$^{-1}$ in the bismuth spectra. Codeine shows a strong band at 1625 cm$^{-1}$, this may be assigned to C = C stretching vibrations$^6$ but the cadmium and bismuth complexes show two bands in each i.e., 1630, 1600 cm$^{-1}$ and 1640, 1600 cm$^{-1}$ respectively, which may be due to the water present in the complexes. The bands at 1265 cm$^{-1}$ and 960 cm$^{-1}$ are assigned to CH in plane and ring skeletal vibrations respectively, of dihydros substituted furan ring$^9$. The CH stretching vibrations of tertiary nitrogen present in the 6-membered saturated ring has been found to occur at 1360 - 1310 cm$^{-1}$ by Silverstein & Bassler$^{10}$. This
may be seen at 1325 cm\(^{-1}\) in codeine but it is missing in the two complexes showing thereby that coordination is taking place through the heterocyclic nitrogen atom.

The CH\(_3\)-N stretching modes\(^{11}\) are found to occur in the region 2620 - 2700 cm\(^{-1}\). The spectrum of codeine show a medium band at 2770 cm\(^{-1}\), the corresponding band is absent in the complexes.

The most important feature of the i.r. spectra is the reduction in the number of bands of ligand on complexation. The i.r. spectra of complex do not have any bands which may be assigned to tertiary nitrogen and \(\text{N-CH}_3\) group. This is clear proof of the fact that coordination is taking place through tertiary nitrogen.
<table>
<thead>
<tr>
<th>S.No.</th>
<th>Compound</th>
<th>Formula</th>
<th>%C</th>
<th>%H</th>
<th>%N</th>
<th>k ohm$^{-1}$ cm$^{-2}$ mol$^{-1}$</th>
<th>Colour</th>
<th>M.P./D. $^\circ$C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Codeine</td>
<td>C$<em>{16}$H$</em>{21}$O$_3$N</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2.</td>
<td>Cd(Cod)$_2$Cl$_2$.2H$_2$O</td>
<td>C$<em>{36}$H$</em>{40}$Cl$_2$CdN$_2$O$_6$</td>
<td>53.25</td>
<td>4.97</td>
<td>3.45</td>
<td>19.06</td>
<td>White</td>
<td>210±6</td>
</tr>
<tr>
<td>3.</td>
<td>Bi(Cod)$_2$Cl$_3$.2H$_2$O</td>
<td>C$<em>{36}$H$</em>{40}$BiCl$_3$N$_2$O$_6$</td>
<td>45.60</td>
<td>4.27</td>
<td>2.97</td>
<td>32.2</td>
<td>Finkish</td>
<td>1°C±2</td>
</tr>
</tbody>
</table>

Observed values are given in parentheses.
REFERENCES

1. Knorr, L.; Ber., 27, 1144 (1894).
8. ibid.