5.1 INTRODUCTION

In previous chapters (III & IV), it has been observed that charge-transfer interaction of chemical carcinogens with biomolecules may be a possible step of chemical carcinogenesis. Recently\(^1\) it has been proposed that the change in geometry of the carcinogen-DNA complex may lead to mutagenesis and later on carcinogenesis. A survey of chemical literature reveals that no attempt in this direction has yet been made by using dipole moment measurement technique. It, therefore, necessitated us to study the geometry of these complexes by dipole-moment measurement technique.

\*\*\*\*

*A part of this work has been accepted for publication in Monatshefte Für Chemie.*
5.2 Experimental and Data Analysis

The materials used and their purifications are essentially the same as reported in Chapters III and IV.

The dielectric constant measurements were carried out at 30°C at a radio frequency of 1 MHz with the help of Philips RCL bridge model PP-9030. The instrument works on a well known principle of heterodyne beat method. The resulting beat frequency is projected on the screen of a cathode ray tube with 50 cycles per second. A Lissajous figure is obtained on the screen. The readings were recorded at the resonance point indicating on the CRT screen by the formation of a single loop pattern.

Refractive indices of solutions were determined at 30°C with the help of Bausch & Lomb refractometer with an accuracy of ±0.0002.

The dipole moment of solutes has been calculated by Guggenheim method by plotting $\Delta$ against the concentration $C$, in moles of polar solutes per cm$^3$ given by the relation:

$$\Delta = (\varepsilon_{12} - n_{12}^2) - (\varepsilon_1 - n_1^2) \quad (5.1)$$

where $\varepsilon_1$, $n_1$ and $\varepsilon_{12}$, $n_{12}$ represent the dielectric constant and refractive index of pure solvent and solution, respectively.

*The slope is directly obtained from the plot of $(\varepsilon_{12} - n_{12}^2)$ against $C$ as the second term on the right hand side in Eq. (5.1) is constant.*
The slope \((\Delta /c)_o\) of the curve at \(C=0\) is then used to calculate the dipole moment by Eq. (5.2):\(^2,3\)

\[
\mu^2 = \frac{9 k T}{4 \pi N} \cdot \frac{3}{(\varepsilon_1 + 2)(n_1^2 + 2)} \cdot (\Delta /c)_o 
\]  \hspace{1cm} (5.2)

The dipole moment of the complexes were calculated by Guggenheim method\(^3\) using Eq. (5.3):

\[
\mu^2 = \frac{27 k T}{4 \pi N} \cdot \frac{M_2}{d_1(\varepsilon_1 + 2)^2} \cdot (a_\varepsilon - a_n) 
\]  \hspace{1cm} (5.3)

where \(k\) is Boltzmann's constant, \(N\), Avogadro's number; \(M_2\), the molecular weight of the complex; \(d_1\) and \(\varepsilon_1\) represent the density and dielectric constant of the mixed solvent at temperature \(T\), respectively; \(a_\varepsilon\) and \(a_n\) represent the slopes of a plot of dielectric constant and square of refractive index respectively, against weight fraction of the complex in solution.

5.3 RESULTS AND DISCUSSION

5.3.1 Interaction of Indoles and Naphthalene with DDT

The dipole moments of the acceptor (DDT) and the donor (indole, 2-me-indole, 3-me-indole and naphthalene) have been calculated using refractive index and Guggenheim methods\(^2,3\) and the data are compared in Table 5.1. From this table, it is
Table 5.1. Dipole Moments of Donors and Acceptor (DDT) in Different Solvents at 30°C
Calculated from Refractive Index and and Guggenhe im Methods

<table>
<thead>
<tr>
<th>Donor/acceptor</th>
<th>( \mu \times 10^{18} ) e.s.u.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Refractive Index Method</td>
</tr>
<tr>
<td></td>
<td>( C_6H_{12} )</td>
</tr>
<tr>
<td>D.D.T.</td>
<td>1.002</td>
</tr>
<tr>
<td>Indole</td>
<td>1.95</td>
</tr>
<tr>
<td>2-Methyl indole</td>
<td>2.23</td>
</tr>
<tr>
<td>3-Methyl indole</td>
<td>2.25</td>
</tr>
<tr>
<td>Naphthalene</td>
<td>0.00</td>
</tr>
<tr>
<td>Benzene</td>
<td>0.00</td>
</tr>
<tr>
<td>Chloranil</td>
<td>0.00</td>
</tr>
</tbody>
</table>
evident that 3-me-indole shows higher dipole moment than indole and 2-me-indole. This may be due to the effective increase in the electron density at 3-position. This leads the formal negative charge at the nucleus making the molecule more asymmetric than that of indole and 2-me-indole.

It has been noted that DDT possesses different dipole moment in different solvents (Table 5.1). In cyclohexane, the dipole moment was found to be less than in benzene. This difference in dipole moment may be as a result of molecular interaction between solutes and non-polar aromatics (benzene). The significance of the induced moment can be interpreted as follows:

Although the aromatics themselves are non-polar, they possess π-electrons which enable them to be easily polarized by neighbouring solutes. If the interaction is such that the solute polarizes the aromatics, it results the dipole moment being induced in the later. The process is then followed by electrostatic attraction between the interacting species. At the same time, the solute experiences the resultant dipole moment of its own and that induced in the aromatic leading to an increase in the dipole moment. In general it might be considered that the more polar the solute, the larger is the expected increase in its solution dipole moment, $\mu_{\text{ind}}$. Hence it is possible to conclude initially that for these systems, the interactions are taking place through dipole-induced dipole mechanism. Thus the dipole moment induced as a result of molecular interaction ($\mu_{\text{ind}}$) can be calculated by Eq. (5.4):
\[ \mu_{\text{ind}} = \mu_{\text{sol}} - \mu_{\text{inert}} \]  \hspace{1cm} (5.4)

where \( \mu_{\text{sol}} \) and \( \mu_{\text{inert}} \) are the dipole moments of solute in the interacting solvents (benzene and CCl\(_4\)) and inert solvent, respectively.

It has been observed that the solutes have higher dipole moment in CCl\(_4\) than in cyclohexane. This increase in dipole moment may again be interpreted due to the molecular interaction between solutes and CCl\(_4\). Though it is believed that CCl\(_4\) is an inert solvent but it has also been observed that the CCl\(_4\) can act as an electron acceptor.\(^5\)-\(^{13}\) In the case of DDT-CCl\(_4\) interaction, the \( \pi \)-electron of benzene ring of the DDT can act as an electron donor. From Table 5.1, it is evident that the indoles have higher dipole moment in CCl\(_4\) than in cyclohexane. This again may be interpreted as this increase in dipole moment is due to the molecular interaction between indoles and CCl\(_4\). It has also been observed that in this interaction, the 3-me-indole have higher dipole moment than 2-me-indole and indole. This may be due to the better donor capability of 3-me-indole than other indoles. Since 3-me-indole is a better donor, it, therefore, can make the stronger complex than other indoles. This is in parallel agreement with earlier observations (cf. Chapter III, Sec. 3.4.4, p.143) in which 3-me-indole-DDT complex has higher \( K_1 \) values than other indoles.\(^{14},^{15}\)
The dipole moment of molecular complexes of DDT with indoles, naphthalene and benzene calculated from Guggenheim method using Eq. (5.3) and refractive index method are recorded in Table 5.2. From this table, it is evident that an appreciable increase in dipole moment has been noticed on complexation. This appreciable increase in dipole moment may be interpreted that the donors form molecular complex with DDT. This is in parallel agreement with our previous observations.\(^{14,15}\)

The stoichiometry of these complexes have been determined by using dielectric titration technique\(^{16}\), where change in the dielectric permittivity \((\Delta \varepsilon)\) of a solution of one component (DDT), on addition of successive amounts of other component, is measured. In the case of the addition of dipolar donor to non-dipolar acceptor, a complex is produced which has a dipole moment value larger than that of the donor.\(^*\) The addition of a small amount of donor generates an equal amount of complex. The permittivity increases on successive additions of the donor and continues to increase until equal amount of the donor and acceptor are present. This situation is schematically shown

\[^*\text{In the present investigation, the DDT, indole, 2-me-indole, and 3-me-indole interactions, the concentration of donor was kept constant and the concentration of acceptor was varied. We kept the concentration of donor constant because these have higher dipole moment than acceptor. In the determination of stoichiometry of these complexes, the break may not be sharp if we keep the acceptor constant instead of donor. Thus for the sake of good stoichiometric determination, it has been done in these cases. Since both the donor and acceptor have the dipolar characteristic, we kept the concentration of donor constant and varied the concentration of acceptor.}\]
Table 5.2. Dipole Moments ($\mu$) for 1:1 Molecular Complexes of Some Donors with DDT in Carbon Tetrachloride at 30°C.

<table>
<thead>
<tr>
<th></th>
<th>DDT-indole</th>
<th>DDT-2-Methyl-indole</th>
<th>DDT-3-Methyl-indole</th>
<th>DDT-Naphthalene</th>
<th>DDT-Bz</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refractive Index</td>
<td>3.830</td>
<td>4.200</td>
<td>4.410</td>
<td>1.800</td>
<td>1.380</td>
</tr>
<tr>
<td>Method</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guggenheim Method</td>
<td>3.855</td>
<td>4.207</td>
<td>4.457</td>
<td>1.805</td>
<td>1.405</td>
</tr>
<tr>
<td>Refractometric</td>
<td>3.880</td>
<td>4.250</td>
<td>4.482</td>
<td>1.823</td>
<td>1.455</td>
</tr>
<tr>
<td>titration plot</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Method</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\mu_{DA}^*$</td>
<td>0.900</td>
<td>1.000</td>
<td>1.200</td>
<td>0.800</td>
<td>0.400</td>
</tr>
<tr>
<td>Equilibrium Constant ($K_1$)</td>
<td>0.308(15)</td>
<td>0.330(15)</td>
<td>0.468(15)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$\mu_{DA}^*$ values have been calculated by using the data obtained from Guggenheim Method.

Numbers in parentheses indicate the reference number.
by line XY of Figs. (5.1 & 5.2) which indicates 1:1 stoichiometry of these complexes. Further addition of the donor increases the permittivity by an amount depending on the dipole moment of the donor.* A break has been observed in the graph at the donor-acceptor ratio corresponding to the ratio existing in the complex. In practice, the dissociation of the complex causes departure from the line XYZ. The magnitude of this departure depends on the equilibrium constant of the initial portion, XY, of the graph which gives the dipole moment of the complex and the slope of YZ gives the dipole moment of the acceptor. The dipole moment of molecular complexes and acceptor, thus calculated, are recorded in Table 5.2. These data clearly indicate their agreement with the Guggenheim method and refractive index method through which the dipole moment of solutes and the complexes have also been determined.

The dipole moment gives a measure of the strength of interaction between the donor and acceptor molecules. In complexes formed between donor and acceptor, the measured dipole moment is a direct result of this interaction. In complexes containing the dipolar components, the dipole moment resulting for the complex formation must be evaluated after due allowance is made for the polarities of the component molecules. The overall dipole moment \( \mu_c \) of the component molecules resulting

* In the present cases the concentration of donor have been kept constant and the concentration of acceptor was varied. Thus after the stoichiometric concentration of the solutes, the dipole moment of further added substance will be due to the dipole moment of acceptor (DDT) and will not be due to donor.
FIG. 5.1 Plots of $C_D^0/C_A^0$ versus $\Delta \varepsilon$ for Molecular Complexes of DDT with Indoles, Naphthalene and Benzene in CC1$_4$. 
FIG. 5.2 Plots of $\frac{C_D}{C_A}$ versus $\Delta \epsilon$ for Molecular Complex of 3-Methyl indole with DDT in Carbon Tetrachloride.
of three contributions:\textsuperscript{16}

\[ \vec{\mu}_C = \vec{\mu}_D + \vec{\mu}_A + \vec{\mu}_{DA} \] \hspace{1cm} (5.5)

where \( D \), \( A \) refers to the donor and to the acceptor, and \( \vec{\mu}_{DA} \) is the dipole moment arising from donor-acceptor interaction.

In the present investigation and in some cases (DDT-naphthalene and DDT-benzene), the dipole moment of donor is 0 (\( \vec{\mu}_D = 0 \)). Therefore, for these systems \( \vec{\mu}_{DA} \) can be calculated: \( \vec{\mu}_{DA} = \vec{\mu}_C - \vec{\mu}_D \). For the systems (DDT-indole, DDT-2-me-indole and DDT-3-me-indole), since both donors and acceptor have the dipolar characteristic, obviously for these system Eq. (5.6) has been used to evaluate \( \vec{\mu}_{DA} \):

\[ \vec{\mu}_{DA} = \vec{\mu}_C - (\vec{\mu}_A + \vec{\mu}_D) \] \hspace{1cm} (5.6)

Thus \( \vec{\mu}_{DA} \) calculated from these methods along with its equilibrium constant data are listed in Table 5.2. From this table, it is evident that the order of \( \vec{\mu}_{DA} \) thus noted is: 3-me-indole) > 2-me-indole) > indole) > benzene) > naphthalene. A similar order of interaction was noted through NMR\textsuperscript{15} and refractometric\textsuperscript{14} studies:

5.3.2 Interaction of Indoles with Chloranil

The dipole moments of indoles with chloranil and their molecular complexes, calculated from refractive index and Guggenheim methods, are recorded in Tables 5.1 and 5.3. An
Table 5.3: Dipole Moment ($\mu$) for 1:1 Molecular Complexes of Some Molecular Complexes of Indoles with Chloranil at 30°C.

<table>
<thead>
<tr>
<th>Method</th>
<th>Dipole Moment ($\mu \times 10^{18}$ e.s.u.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Indole-chloranil</td>
</tr>
<tr>
<td>Refractive Index Method</td>
<td>2.94</td>
</tr>
<tr>
<td>Guggenheim Method</td>
<td>3.00</td>
</tr>
<tr>
<td>Refractometric Titration plot Method</td>
<td>3.10</td>
</tr>
<tr>
<td>$\mu_{DA}$</td>
<td>0.98</td>
</tr>
</tbody>
</table>
appreciable increase in dipole moment after complexation was observed which has been interpreted that indoles form molecular complexes with chloranil. In indoles-chloranil complexes, the order of dipole moment was found to be,

$$3\text{-me-indole-chloranil} > 2\text{-me-indole-chloranil} > \text{indole-chloranil}.$$  

The highest dipole moment of 3-me-indole-chloranil system may again be interpreted due to the better donor capability of 3-me-indole than other indoles. This is in agreement with the previous observations.

The stoichiometry of these complexes have been determined by using dielectric titration technique as noted in previous section (5.3.1). A 1:1 stoichiometry of these complexes has been determined. A representative plot is shown in Fig. 5.3.

In indoles-chloranil systems, the dipole moment of acceptor is zero. Now $\mu_{DA}$ can be calculated: $\mu_{DA} = \mu_C - \mu_D$. Thus $\mu_{DA}$ calculated along with the $K_1$ values are listed in Table 5.3. From this table, it is evident that the order of $\mu_{DA}$ noted is: 3-me-indole $> 2$-me-indole $> \text{indole}$. The same order of interaction was noted through spectrophotometric studies. 17

5.3.3 Interaction of Indoles with Iodine

The dipole moment of these molecular complexes are listed in Table 5.4. Since the order of $\mu$ was found to be
FIG. 5.3 Plots of $C_D^o/C_A^o$ versus $\Delta \varepsilon$ for Molecular Complexes of Indoles with Chloranil in Carbon Tetrachloride.
Table 5.4. Dipole Moment ($\mu$) for 1:1 Molecular Complexes of Some Molecular Complexes of Indoles with Iodine at 30°C

<table>
<thead>
<tr>
<th>Method</th>
<th>Indole-Iodine</th>
<th>2-Methyl indole-Iodine</th>
<th>3-Methyl indole-Iodine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refractive Index Method</td>
<td>2.90</td>
<td>3.20</td>
<td>3.32</td>
</tr>
<tr>
<td>Guggenheim Method</td>
<td>3.10</td>
<td>3.56</td>
<td>3.94</td>
</tr>
<tr>
<td>Refractometric Titration plot Method</td>
<td>3.18</td>
<td>3.68</td>
<td>4.10</td>
</tr>
<tr>
<td>$\mu_{Dk}$</td>
<td>1.09</td>
<td>1.36</td>
<td>1.73</td>
</tr>
</tbody>
</table>
the same as was noted for indole-DDT or chloranil systems, therefore, their interpretation will also be the same as has been given in detail in Sections 5.3.1 and 5.3.2. The stoichiometry of these complexes was determined by dielectric titration technique\textsuperscript{16} and has been found to be 1:1. A representative plot is shown in Fig. 5.4.

Thus, present dielectric investigation provides additional support about the charge transfer complexation hypothesis for the chemical initiation of cancer on molecular level.
FIG. 5.4 Plots of $\frac{C_D}{C_A}$ versus $\Delta \varepsilon$ for Molecular Complexes of Methyl indoles with Iodine in Carbon Tetrachloride.
REFERENCES