CHAPTER III

SECTION I

The benzimidazole ring is of much greater interest due to its occurrence in vitamin $B_{12}$ and in many biologically active compounds. The benzimidazole system is highly aromatic. It is hard to oxidise or reduce and is stable to acids and bases. It forms salts and metal derivatives, and in sulphuric acid, it nitrates at position-5. This is in agreement with $\pi$-electron density calculations made on the assumption that the free base and not the cation, is the species actually nitrated. Iodination of benzimidazole in the alkaline solution gives 2-iodobenzimidazole, which again is in agreement with $\pi$-electron density calculations if the anion(1) is being attacked.

![Benzimidazole Structure](image)

(1)

Methyl group at position-2 is highly activated and readily condense with aromatic aldehyde giving 2-styryl-derivative. Quaternary salts are readily formed by reaction with alkyl halides. In the benzimidazoles, monoaalkylation removes the possibilities for tautomerism and two isomeric, 1-alkylbenzimidazole may be formed from a 5-substituted compound, while further alkylation lead to the quaternary salt.
Benzimidazole resists hydrogenation and oxidation. Vigorous oxidation converts benzimidazole to imidazole-4,5-dicarboxylic acid. The 5- and 6-positions are equivalent in the unsubstituted types since the following two are tautomers.

\[
\begin{align*}
\text{5-alkyl} & \quad \leftrightarrow \quad \text{6-alkyl} \\
\end{align*}
\]

Reaction with hypochlorite produces N-chloro derivative which rearranges to a benzchlooro compound. The process can be repeated to replace all hydrogens of the benzene ring with chlorine. 2-hydroxy benzimidazole is stable towards benzoyl chloride, alkali, concentrated hydrochloric acid at 200° and to zinc at red heat.
The compounds were synthesised according to SCHEMES I and II respectively given on pages 40 & 46. The synthesised compounds have represented by the following structures -

![Chemical Structures](image)

<table>
<thead>
<tr>
<th>Compounds number</th>
<th>Groups associated</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>$R_1R_2R_3R_4R_5R=H$</td>
</tr>
<tr>
<td>II</td>
<td>$R_1R_2R_3R_4R_5=H; R=CH_3$</td>
</tr>
<tr>
<td>III</td>
<td>$R_1R_3R_5=Br; R_2R_4R_5=H; R=CH_3$</td>
</tr>
<tr>
<td>IV</td>
<td>$R_1R_3R_5=Br; R_2R_4=H; R=CH_3$</td>
</tr>
<tr>
<td>V</td>
<td>$R_1R_3=Br; R_2R_4R_5=H$</td>
</tr>
<tr>
<td>VI</td>
<td>$R_1R_3R_5=Cl; R_2R_4=H$</td>
</tr>
<tr>
<td>VII</td>
<td>$R_1R_3R_5=Cl; R_2R_4=H; R=CH_3$</td>
</tr>
<tr>
<td>VIII</td>
<td>$R_1R_3=Cl; R_2R_4R_5=H$</td>
</tr>
<tr>
<td>IX</td>
<td>$R_1R_4=Cl; R_2R_3R_5=H$</td>
</tr>
<tr>
<td>X</td>
<td>$R_1=Cl; R_2R_3R_4R_5=H$</td>
</tr>
<tr>
<td>XI</td>
<td>$R_3=Cl; R_1R_2R_4R_5=H$</td>
</tr>
<tr>
<td>XII</td>
<td>$R_1R_3R_5=NO_2; R_2R_4=H$</td>
</tr>
<tr>
<td>XIII</td>
<td>$R_1R_3R_5=NO_2; R_2R_4=H; R=CH_3$</td>
</tr>
<tr>
<td>XIV</td>
<td>$R_1=NO_2; R_2R_3R_4R_5=H$</td>
</tr>
<tr>
<td>XV</td>
<td>$R_2=NO_2; R_1R_3R_4R_5=H$</td>
</tr>
<tr>
<td>XVI</td>
<td>$R_3=NO_2; R_1R_2R_4R_5=H$</td>
</tr>
<tr>
<td>XVII</td>
<td>$R_1=CH_3; R_2R_3R_4R_5=H$</td>
</tr>
<tr>
<td>XVIII</td>
<td>$R_2=CH_3; R_1R_3R_4R_5=H$</td>
</tr>
<tr>
<td>XIX</td>
<td>$R_3=CH_3; R_1R_2R_4R_5=H$</td>
</tr>
</tbody>
</table>

XX  XXI
SYNTHESIS OF THE COMPOUND-I: N-[2-(PHENOXY) ACETYL] BENZIMIDAZOLE

The phenol used for the next step synthesis was commercially available.

SYNTHESIS OF PHENOXY ACETIC ACID

Equimolecular quantities (0.1 mole) of phenol and monochloroacetic acid were refluxed in a 250 ml round bottomed jointed flask fitted with a water condenser on a water bath with 33 ml of 33% NaOH solution and worked up as usual (page 36). The phenoxy acetic acid was crystallised from ethyl acetate as colourless crystals, yield 67%, m.p. 97-98\(^\circ\) (lit. m.p. 98-99\(^\circ\))\(^{173}\).

Found: C, 63.05; H, 5.08; Calculated for C\(_8\)H\(_8\)O\(_3\) : C, 63.15; H, 5.26%.

SYNTHESIS OF PHENOXY ACETYL CHLORIDE

To a solution of phenoxy acetic acid (0.046 mole in 30 ml methanol) was added thionyl chloride (0.056 mole). The mixture was refluxed (7 hours) on a water bath and worked up by the method as given on page 36 which gave phenoxy acetyl chloride, yield 84%, b.p. 225-226\(^\circ\) (lit. b.p. 225-226\(^\circ\))\(^{173}\).
SYNTHESIS OF N-[2-(PHENOXY) ACETYL] BENZIMIDAZOLE

To an ice-cooled solution of benzimidazole (0.036 mole in 30 ml methanol) in a 500 ml beaker was treated with 5 ml of 4N NaOH solution. The phenoxy acetyl chloride (in 25 ml methanol) was added in the above solution with constant stirring (60 minutes) and worked up as usual (page 38). The product was purified over the column of neutral alumina using petroleum ether:benzene (3:7 v/v) mixture as an eluant. Finally, the eluate (145 ml) was concentrated and the product was crystallised from methanol as colourless needles, yield 60%, m.p. 149-151⁰.

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND I

TLC was done on silica gel 'G' plates. The plates were spotted with the methanolic solution of the compound I and irrigated in the following solvent systems. A single spot was observed in each case by developing the plates in iodine vapours.

<table>
<thead>
<tr>
<th>Solvent systems</th>
<th>Rf values</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i) Petroleum ether:chloroform;(5:5 v/v)</td>
<td>0.75</td>
</tr>
<tr>
<td>(ii) Benzene:chloroform;(7:3 v/v)</td>
<td>0.90</td>
</tr>
</tbody>
</table>

INFRA-RED SPECTRUM OF THE COMPOUND I

The significant peaks obtained in the IR spectrum of the compound I along with their structural
assignments with the help of available literature are given herein.

\[ \text{IR}_{\text{max}} \text{KBr} : 2915 \text{ and } 1490 \text{ (} -\text{CH}_2\text{)}; 1630 \text{ (} -\text{C=O}\text{)}; 1590 \text{ (} \text{C=N}\text{ in benzimidazole); } 1475, 1150, 1110, 1080, 1035, 885, 785, 740 \text{ and } 685 \text{ (substituted benzene ring); } 1240, 1200 \text{ and } 1160 \text{ (C-O-C) respectively.} \]

SYNTHESIS OF THE COMPOUND-II : N-[2-(PHENOXY) PROPIONYL] BENZIMIDAZOLE

The phenol used for the next step synthesis was commercially available.

SYNTHESIS OF 2-(PHENOXY) PROPIONIC ACID

Equimolecular quantities (0.1 mole) of phenol and α-monochloropropionic acid were refluxed in a 250 ml round bottomed jointed flask fitted with a water condenser on a water bath with 33 ml of 33% NaOH solution and worked up as usual (page 35). The phenoxy propionic acid was crystallised from ethanol as colourless needles, yield 60%, m.p. 115-116° (lit. m.p. 115-116°) \(^{178}\).

Found : C, 64.96; H, 5.89; Calculated for \( \text{C}_9\text{H}_{10}\text{O}_3 \) :
C, 65.05; H, 6.02%.

SYNTHESIS OF 2-(PHENOXY) PROPIONYL CHLORIDE

To a solution of phenoxy propionic acid (0.046 mole in 30 ml ethanol) was added thionyl chloride
(0.056 mole). The mixture was refluxed (7 hours) on a water bath and worked up by the method as mentioned on page 36 which afforded phenoxy propionyl chloride, yield 82%, b.p. 146-147° (lit. b.p. 146-147°)\textsuperscript{178}.

SYNTHESIS OF N-[2-(PHENOXY) PROPIONYL] BENEZIMIDAZOLE

To an ice-cooled solution of benzimidazole (0.036 mole in 25 ml methanol) in a 500 ml beaker was treated with 5 ml of 4N NaOH solution. The phenoxy propionyl chloride (in 25 ml of methanol) was added in the above solution with constant stirring (60 minutes) and worked up as usual (page 38). The product was purified over the column of neutral alumina using benzene:methanol (6:4 v/v) mixture as an eluant. Finally, the eluate (150 ml) was concentrated and the product was crystallised from acetone as colourless crystals, yield 75%, m.p. 57-58°.

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-II

TLC was done on silica gel 'G' plates in the following solvent systems by the same method as described on page 84 which showed single spot in each case.
Solvent systems

(1) Benzene:chloroform (4:6 v/v) 0.62
(2) Chloroform:acetone (8:2 v/v) 0.73

INFRA-RED SPECTRUM OF THE COMPOUND-II

The significant peaks obtained in the IR spectrum of the compound-II along with their structural assignments with the help of available literature\textsuperscript{174-177} are given herein:

$\text{KBr } \nu_{\text{max}}$: 2930, 1460 and 1370 (C-CH$_3$); 1635 (C-N); 1575 (C=N in benzimidazole); 1485, 1135, 1100, 1072, 1038, 880, 780, 740 and 690 (substituted benzene ring); 1255, 1210 and 1160 (C-O-C) respectively.

SYNTHESIS OF THE COMPOUND-III:N-[2-(2,4,6-TRIBROMOPHENOXY) ACETYL] BENZIMIDAZOLE

SYNTHESIS OF 2,4,6-TRIBROMOPHENOL

30 g of phenols were dissolved in 300 ml of water in a 500 ml round bottomed jointed flask and the contents were cooled by keeping the flask in an ice-bath. To this solution, 34 ml of bromine was added drop wise from a separating funnel with continuous stirring. The product separated was filtered, washed with water and finally, it was crystallised from ethanol as colourless shining long needles, yield 80%, m.p. 90-93° (lit. m.p. 93°)\textsuperscript{179}. 
Found: C, 21.70; H, 0.82; Calculated for $C_6H_3Br_3O$: 21.75; H, 0.90%.

SYNTHESIS OF 2,4,6-TRIBROMOPHENOXY ACETIC ACID

Equimolecular quantities (0.07 mole) of 2,4,6-triboromophenol and monochloroacetic acid were refluxed in a 250 ml round bottomed jointed flask fitted with a water condenser on a water bath with 81 ml of 33% NaOH solution and worked up by the method as given on page 35. The 2,4,6-tribromophenoxy acetic acid was crystallised from ethanol as colourless needles, yield 78%, m.p. 197-198° (lit. m.p. 200°)179.

Found: C, 24.58; H, 1.14; Calculated for $C_8H_5OBr_3$: C, 24.67; H, 1.28%.

SYNTHESIS OF 2,4,6-TRIBROMOPHENOXY ACETYL CHLORIDE

To a solution of 2,4,6-tribromophenoxy acetic acid (0.046 mole in 25 ml ethyl acetate) was added thionyl chloride (0.56 mole). The mixture was refluxed (7 hours) on a water bath and worked up by the same procedure as described on page 36 to yield 2,4,6-tribromophenoxy acetyl chloride. It was crystallised from benzene as yellow prismatic crystals, yield 80%, m.p. 114-115° (lit. m.p. 114.5-115°)180.

Found: C, 23.46; H, 0.90; Calculated for $C_8H_4O_2Br_3Cl$: C, 23.52, H, 0.98%.
SYNTHESIS OF N-[2-(2,4,6-TRIBROMOPHENOXY) ACETYL] BENZIMIDAZOLE

To an ice-cooled solution of benzimidazole (0.036 mole in 35 ml methanol) in a 500 ml beaker was treated with 5 ml of 4N NaOH solution. The 2,4,6-tribromophenoxy acetyl chloride (in 25 ml methanol) was added in the above solution with constant stirring (45 minutes) and worked up as usual (page 38). The product was purified over the column of silica gel using chloroform as an eluant. Finally, the eluate (170 ml) was concentrated and the product was crystallised from ethyl acetate as pale yellow coloured needles, yield 65%, m.p. 136-137°.

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-III

TLC was done on silica gel 'G' plates in the following solvent systems by the same method as described on page 84 which showed single spot in each case.

<table>
<thead>
<tr>
<th>Solvent systems</th>
<th>R_f values</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i) Benzene:chloroform (4:6 v/v)</td>
<td>0.48</td>
</tr>
<tr>
<td>(ii) Benzene:ethyl acetate (8:2 v/v)</td>
<td>0.63</td>
</tr>
</tbody>
</table>

INFRA-RED SPECTRUM OF THE COMPOUND-III

The significant peaks obtained in the IR spectrum of compound - III along with their structural
assignments with the help of available literature\textsuperscript{174-177} are given herein:

\[ {IR_{2}^{KBr}}_{\text{max}} : 2908 \text{ and } 1480 \text{ (-CH}_2\text{); 1640 \text{ (-C=N); 1580 (C=N in benzimidazole); 1495, 1145, 1100, 1035, 875, 850, 740 and 685 (substituted benzene ring); 1245, 1220 and 1165 (C=O-C) respectively.} \]

**SYNTHESIS OF THE COMPOUND-IV : N-[2-(2,4,6-TRIBROMOPHENOXY) PROPIONYL] BENZIMIDAZOLE**

**SYNTHESIS OF TRIBROMOPHENOL**

It was prepared by the bromination of the phenol by the same method as described on page 87.

**SYNTHESIS OF 2-(2,4,6-TRIBROMOPHENOXY) PROPIONIC ACID**

Equimolecular quantities (0.07 mole) of 2,4,6-tribromophenol and \( \alpha \)-monochloropropionic acid were refluxed in a 250 ml round bottomed jointed flask fitted with a water condenser on a water bath with 81 ml of 33% NaOH solution and worked up as usual (page 35). The product, 2,4,6-tribromophenoxy propionic acid was crystallised from ethyl acetate as pale yellow crystals, yield 72%, m.p. 86-88\( ^\circ \).

*Found:* C, 26.68; H, 1.62; Calculated for \( \text{C}_{12}\text{H}_7\text{O}_3\text{Br}_3 \):

C, 26.79; H, 1.73%.
SYNTHESIS OF 2-(2,4,6-TRIBROMOPHENOXY) PROPIONYL CHLORIDE

To a solution of 2,4,6-tribromophenoxy propionic acid (0.046 mole in 25 ml ethyl acetate) was added thionyl chloride (0.056 mole). The mixture was refluxed (7 hours) on a water bath and worked up by the same procedure as described on page 36 to yield 2,4,6-tribromophenoxy propionyl chloride. It was crystallised from acetone as reddish crystals, yield 80%, m.p. 76-78°.

Found : C, 25.72; H, 1.36; Calculated for C\textsubscript{9}H\textsubscript{6}O\textsubscript{2}BrCl : C, 25.62, H, 1.42%.

SYNTHESIS OF N-[2-(2,4,6-TRIBROMOPHENOXY)PROPIONYL] BENZIMIDAZOLE

To an ice-cooled solution of benzimidazole (0.036 mole in 25 ml methanol) in a 500 ml beaker was treated with 5 ml of 4N NaOH solution. The 2,4,6-tribromophenoxy propionyl chloride (in 25 ml methanol) was added in the above solution with constant stirring (40 minutes) and worked up as usual (page 38). The product was purified over the column of silica gel using chloroform:acetone (4:6 v/v) mixture as an eluant. Finally, the eluate (180 ml) was concentrated and the product was crystallised from acetone as pale yellow needles, yield 65%, m.p. 200-202°.
THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-IV

TLC was done on silica gel 'G' plates in the following solvent systems by the same as given on page 84 which showed single spot in each case.

**Solvent systems**

<table>
<thead>
<tr>
<th>Solvent systems</th>
<th>( R_f ) values</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Chloroform:acetone (5:5 v/v)</td>
<td>0.50</td>
</tr>
<tr>
<td>(11) Chloroform:methanol (8:2 v/v)</td>
<td>0.68</td>
</tr>
</tbody>
</table>

INFRA-RED SPECTRUM OF THE COMPOUND-IV

The significant peaks obtained in the IR spectrum of the compound-IV along with their structural assignments with the help of available literature 174-177 are given herein:

\[ \text{IR}_{\text{KBr}}^\text{max} : 2925, 1455 \text{ and } 1375 \text{ (C-CH}_3\text{)}; 1630 \text{ (-C-N<)}; 1580 \text{ (C=N in benzimidazole)}; 1480, 1135, 1100, 1040, 880, 840, 790, 745 \text{ and } 688 \text{ (substituted benzene ring)}; 1245, 1210 \text{ and } 1165 \text{ (C-O-C)} \text{ respectively.} \]

SYNTHESIS OF THE COMPOUND-V : \( N-[2-(2,4-DIBROMOPHENOXY)] \text{ ACETYL} \) BENZIMIDAZOLE

SYNTHESIS OF 2,4-DIBROMOPHENOL

2,4-dibromophenol was prepared by adding a solution of bromine in hydrobromic acid to a cooled suspension of phenol in hydrobromic acid as below.

In a 500 ml three necked round bottomed flask,
23.5 g of phenol suspended in 70 g of hydrobromic acid was taken and the mixture slightly warmed on a water bath using a water condenser until all the phenol melted. The solution was then cooled by keeping the flask in freezing mixture to -10°. 80 g of bromine dissolved in 40 g of hydrobromic acid were run in the solution through a separating funnel very slowly. The temperature being kept below 0°. Bromine was absorbed very slowly, and when about half had been added, all the phenol had liquified. The temperature of the mixture was now allowed to rise to 0°. The remainder of the bromine solution was added more rapidly and the mixture was allowed to remain for one hour. At the end of this time the reaction mixture was heated slightly to about 30° until the colour of bromine just disappeared and the mixture was put aside for three hours. The supernatant hydrobromic acid was run off from the 2,4-dibromophenol and the product was diluted somewhat with water and recovered by distillation. It was washed several times with small quantities of warm water by decantation. It was dried in a vacuum desiccator and finally crystallised from petroleum ether as colourless crystals, yield 67%, m.p. 39-40° (lit. m.p. 40°)\textsuperscript{181}.

*Found:* C, 28.50; H, 1.32; *Calculated for C\textsubscript{6}H\textsubscript{4}Br\textsubscript{2}O:* 
C, 28.57; 1.58%.
SYNTHESIS OF 2,4-DIBROMOPHENOXY ACETIC ACID

Equimolecular quantities (0.08 mole) of 2,4-dibromophenol and monochloroacetic acid was refluxed in a 250 ml round bottomed jointed flask fitted with a water condenser on a water bath with 46 ml of 33% NaOH solution and worked up by the method as described on page 35. The product 2,4-dibromophenoxy acetic acid was crystallised from acetone as colourless crystals, yield 70%, m.p.136-137° (lit. m.p. 138°)181.

Found : C, 30.81; H, 1.72; Calculated for $\text{C}_8\text{H}_6\text{O}_3\text{Br}_2$ : C, 30.96; H, 1.93%.

SYNTHESIS OF 2,4-DIBROMOPHENOXY ACETYL CHLORIDE

To a solution of 2,4-dibromophenoxy acetic acid (0.046 mole in 25 ml methanol) was added thionyl chloride (0.056 mole). The mixture was refluxed (7 hours) on a water bath and worked by the method as described on page 36 to yield 2,4-dibromophenoxy acetyl chloride which was crystallised with acetone as yellow needles, yield 78%, m.p. 79-80° (lit. m.p. 80-81°)182.

Found : C, 29.05; H, 1.36; Calculated for $\text{C}_8\text{H}_5\text{O}_2\text{Br}_2\text{Cl}$ : C, 29.17; H, 1.51%.

SYNTHESIS OF $N$-[2-(2,4-DIBROMOPHENOXY) ACETYL] BENZIMIDAZOLE

To an ice-cooled solution of benzimidazole (0.036 mole in 25 ml methanol) in a 500 ml beaker was
treated with 5 ml of 4 N NaOH solution. The 2,4-dibromophenoxy acetyl chloride (in 30 ml methanol) was added in the above solution with constant stirring (60 minutes) and worked up as usual (page 38). The product was purified over the column of silica gel using benzene:chloroform (5:5 v/v) mixture as an eluant. Finally, the eluate (150 ml) was concentrated and the product was crystallised from methanol as light yellow crystals, yield 75%, m.p. 84-86°.

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-V

TLC was done on silica gel 'G' plates in the following solvent systems by the same method as described on page 84 which showed single spot in each case.

<table>
<thead>
<tr>
<th>Solvent systems</th>
<th>R&lt;sub&gt;f&lt;/sub&gt; values</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i) Petroleum ether:benzene (2:8 v/v)</td>
<td>0.43</td>
</tr>
<tr>
<td>(ii) Benzene:chloroform (7:3 v/v)</td>
<td>0.51</td>
</tr>
</tbody>
</table>

INFRA-RED SPECTRUM OF THE COMPOUND-V

The significant peaks obtained in the IR spectrum of the compound-V alongwith their structural assignments with the help of available literature<sup>174-177</sup> are given herein:
**IR KBr max:** 2915 and 1465 (-CH₂); 1630 (-C=O); 1585 (C=N in benzimidazole); 1486, 1148, 1100, 1070, 885, 830, 795, 750 and 685 (substituted benzene ring); 1240, 1200 and 1170 (C-O-C) respectively.

**SYNTHESIS OF THE COMPOUND-VI : N-[2-(2,4,6-TRICHLOROPHENOXY) ACETYL] BENZIMIDAZOLE**

The 2,4,6-trichlorophenol used for the next step synthesis was commercially available.

**SYNTHESIS OF 2,4,6-TRICHLOROPHENOXY ACETIC ACID**

Equimolecular quantities (0.08 mole) of 2,4,6-trichlorophenol and monochloroacetic acid were refluxed in a 250 ml round bottomed jointed flask fitted with a water condenser on a water bath with 55.5 ml of 33% NaOH solution and worked up by the method as described on page 35. The product 2,4,6-trichlorophenoxy acetic acid was crystallised from methanol as colourless shining needles, yield 66%, m.p. 188-189° (lit. m.p. 190°) 189.

*Found : C, 37.42; H, 1.86; Calculated for C₁₈H₁₅O₃Cl₃ : C, 37.57; H, 1.85%.*

**SYNTHESIS OF 2,4,6-TRICHLOROPHENOXY ACETYL CHLORIDE**

To a solution of 2,4,6-trichlorophenoxy acetic acid (0.046 mole in 25 ml methanol) was added thionyl chloride (0.056 mole). The mixture was refluxed
7 hours) on a water bath and worked up as usual (page 36) to yield 2,4,6-trichlorophenoxy acetyl chloride which was crystallised from acetone as colourless crystals, yield 84%, m.p. 53-54° (lit. m.p. 55-56°).\(^{18}\)

**Found**: C, 34.92; H, 1.37; Calculated for C\(_8\)H\(_4\)O\(_2\)Cl\(_4\) :

C, 35.03; H, 1.45%.

**SYNTHESIS OF N-[2-(2,4,6-TRICHLOROPHENOXY) ACETYL] BENZIMIDAZOLE**

To an ice-cooled solution of benzimidazole (0.036 mole in 30 ml methanol) in a 500 ml beaker was treated with 5 ml of 4 N NaOH solution. The 2,4,6-trichlorophenoxy acetyl chloride (in 20 ml methanol) was added in the above solution with constant stirring (60 minutes) and worked up as usual (page 38). The product was purified over the column of silica gel using chloroform:ethylacetate (5:5 v/v) mixture as an eluant. Finally, the eluate (185 ml) was concentrated and the product was crystallised from methanol as cream coloured crystals, yield 75%, m.p. 249-251°.

**THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-VI**

TLC was done on silica gel 'G' plates in the following solvent systems by the same method as described on page 84 which showed single spot in each case.
Solvent systems

(1) Benzene:ethylacetate (5:5 v/v)  
(2) Chloroform:methanol (7:3 v/v)  

\[ R_f \] values

0.66

0.82

INFRA-RED SPECTRUM OF THE COMPOUND-VI

The significant peaks obtained in the IR spectrum of the compound-VI along with their structural assignments with the help of available literature \(^{174-177}\) are given herein:

\[ \text{IR}^{kbr}_{\text{max}}: 2905 \text{ and } 1485 \text{ (-CH}_2\text{)}; 1640 \text{ (-C-N<)}; 1600 \text{ (C=N in benzimidazole)}; 1490, 1150, 1105, 1074, 1050, 875, 830, 780, 750 \text{ and } 690 \text{ (substituted benzene ring)}; 1250, 1195 \text{ and } 1170 \text{ (C-O-C) respectively.}\]

SYNTHESIS OF THE COMPOUND-VII : N-[2,4,6-TRICHLOROPHENOXY) PROPIONYL] BENZIMIDAZOLE

The 2,4,6-trichlorophenol was used commercially available.

SYNTHESIS OF 2-(2,4,6-TRICHLOROPHENOXY) PROPIONIC ACID

Equimolecular quantities (0.08 mole) of 2,4,6-trichlorophenol and \(\alpha\)-monochloropropionic acid were refluxed in a 250 ml round bottomed jointed flask fitted with a water condenser on a water bath with 55.5 ml of 33% NaOH solution and worked up as usual (page 35). The product 2,4,6-trichlorophenoxy propionic
acid was crystallised from methanol as colourless crystals, yield 65%, m.p. 113-114° (lit. m.p. 115-116°) 185.

Found : C, 39.98; H, 2.42; Calculated for C₉H₇D₃Cl₃:
        C, 40.07; H, 2.59%.

SYNTHESIS OF 2-(2,4,6-TRICHLOROPHENOXY) PROPIONYL CHLORIDE

To a solution of 2,4,6-trichlorophenoxy propionic acid (0.046 mole in 25 ml methanol) was added thionyl chloride (0.56 mole). The mixture was refluxed (7 hours) on a water bath and worked up by the same method as described on page 36 to yield 2,4,6-trichlorophenoxy propionyl chloride which was crystallised from acetone as colourless long needles, yield 70%, m.p. 69-70°.

Found : C, 37.42; H, 1.98; Calculated for C₉H₆O₂Cl₄:
        C, 37.50; H, 2.08%.

SYNTHESIS OF N-[2-(2,4,6-TRICHLOROPHENOXY) PROPIONYL] BENZIMIDAZOLE

To an ice-cooled solution of benzimidazole (0.036 mole in methanol) in a 500 ml beaker was treated with 5 ml of 4N NaOH solution. The 2,4,6-trichlorophenoxy propionyl chloride (in 20 ml methanol) was added in the above solution with constant stirring (75 minutes) and worked up as usual (page 38). The product was purified
over the column of neutral alumina using ethyl acetate as an eluant. Finally, the eluate (170 ml) was concentrated and the product was crystallised from hot methanol as cream coloured needles, yield 78% m.p. 119-120°C.

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-VII

TLC was done on silica gel 'G' plates in the following solvent systems by the same method as described on page 84 which showed single spot in each case.

<table>
<thead>
<tr>
<th>Solvent systems</th>
<th>Rf values</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i) Benzene:acetone (5:5 v/v)</td>
<td>0.46</td>
</tr>
<tr>
<td>(ii) Chloroform:methanol (4:6 v/v)</td>
<td>0.58</td>
</tr>
</tbody>
</table>

INFRA-RED SPECTRUM OF THE COMPOUND-VII

The significant peaks obtained in the IR spectrum of the compound-VII alongwith their structural assignments with the help of available literature 174-177 are given herein:

\[ \text{IR}_{\text{max}}^{\text{KBr}} : 2930, 1440 \text{ and } 1365 (\text{C-CH}_3); 1635 (\text{-C-N}); 1585 (\text{C=N in benzimidazole}); 1498, 1140, 1095, 1048, 1028, 880, 840, 785, 740 \text{ and } 695 \text{ (substituted benzene ring)}; 1240, 1200 \text{ and } 1160 \text{ (C-O-C) respectively.} \]
SYNTHESIS OF THE COMPOUND-VIII : N-[2-(2,4-DICHLOROPHENOXY) ACETYL] BENZIMIDAZOLE

The 2,4-dichlorophenol used for next step synthesis was commercially available.

SYNTHESIS OF 2,4-DICHLOROPHENOXY ACETIC ACID

Equimolecular quantities (0.08 mole) of 2,4-dichlorophenol and monochloroacetic acid were refluxed in a 250 ml round bottomed jointed flask fitted with a water condenser on a water bath with 46 ml of 33% NaOH solution and worked up as usual (page 35). The product 2,4-dichlorophenoxy acetic acid was crystallised from ether as colourless needles, yield 70%, m.p. 136-137° (lit. m.p. 138-139°)186.

Found : C, 43.38; H, 2.67; Calculated for C₅H₆O₃Cl : C, 43.43, H, 2.71%.

SYNTHESIS OF 2,4-DICHLOROPHENOXY ACETYL CHLORIDE

To a solution of 2,4-dichlorophenoxy acetic acid (0.046 mole in 25 ml methanol) was added thionyl chloride (0.056 mole). The mixture was refluxed (7 hours) on a water bath and worked up by the method as given on page 36 to yield 2,4-dichlorophenoxy acetyl chloride which was crystallised from benzene as colourless prismatic crystals, yield 80%, m.p. 44-45° (lit. m.p. 45-46°)187.
Found : C, 40.02, H, 2.04; Calculated for \( \text{C}_8\text{H}_5\text{O}_2\text{Cl}_3 \): C, 40.08; H, 2.08%.

SYNTHESIS OF N-[2-(2,4-DICHLOROPHENOXY) ACETYL] BENZIMIDAZOLE

To an ice-cooled solution of benzimidazole (0.036 mole in 25 ml methanol) in a 500 ml beaker was treated with 5 ml 4 N NaOH solution. The 2,4-dichlorophenoxy acetyl chloride (in 20 ml methanol) was added in the above solution with constant stirring (50 minutes) and worked up as usual (page 38). The product was purified over the column of neutral alumina using benzene:chloroform (6:4 v/v) mixture as an eluant. Finally, the eluate (150 ml) was concentrated and the product was crystallised from methanol as cream coloured crystals, yield 77%, m.p. 102-103°.

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-VIII

TLC was done on silica gel 'G' plates in the following solvent systems by the same method as described on page 84 which showed single spot in each case.

<table>
<thead>
<tr>
<th>Solvent systems</th>
<th>( R_f ) values</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i) Benzene:methanol (6:4 v/v)</td>
<td>0.55</td>
</tr>
<tr>
<td>(ii) Chloroform:methanol (8:2 v/v)</td>
<td>0.69</td>
</tr>
</tbody>
</table>

INFRA-RED SPECTRUM OF THE COMPOUND-VIII

The significant peaks obtained in the IR spectrum
of the compound-VIII along with their structural assignments with the help of available literature^174-177 are given herein:

$$\text{IR}_{\text{max}}^{\text{KBr}}: 2905 \text{ and } 1480 (-\text{CH}_2); 1640 (-\text{C-N}^-); 1575 (\text{C=N in benzimidazole}); 1510, 1150, 1100, 1054, 1030, 885, 835, 790, 745 \text{ and } 690 \text{ (substituted benzene ring)}; 1240, 1205 \text{ and } 1170 (\text{C-O-C}) \text{ respectively.}$$

**SYNTHESIS OF THE COMPOUND-IX : N-[(2,5-DICHLOROPHENOXY) ACETYL] BENZIMIDAZOLE**

The 2,5-dichlorophenol used for next step synthesis was commercially available.

**SYNTHESIS OF 2,5-DICHLOROPHENOXY ACETIC ACID**

Equimolecular quantities (0.09 mole) of 2,5-dichlorophenol and monochloroacetic acid were refluxed in a 250 ml round bottomed jointed flask fitted with a water condenser on a water bath with 52 ml of 33% NaOH solution and worked up as usual page 35. The product 2,5-dichlorophenoxy acetic acid was crystallised from ether as colourless needles, yield 62%, m.p. 141-142° (lit. m.p. 143°)^185.

Found: C, 43.36; H, 2.67; Calculated for C<sub>9</sub>H<sub>6</sub>O<sub>3</sub>Cl<sub>2</sub>: C, 43.43, H, 2.71%.
SYNTHESIS OF 2,5-DICHLOROPHENOXY ACETYL CHLORIDE

To a solution of 2,5-dichlorophenoxy acetic acid (0.046 ml in 20 ml ethyl acetate) was added thionyl chloride (0.056 mole). The mixture was refluxed (7 hours) on a water bath and worked up by the method as given on page 36 to yield 2,5-dichlorophenoxy acetyl chloride which was crystallised from acetone as colourless crystals, yield 82%, m.p. 148-150° (lit. m.p. 150°).\(^{185}\)

Found: C, 40.04; H, 1.95; Calculated for \(C_{8}H_{5}O_{2}Cl_{3}\):

\[\begin{align*}
\text{C} & : 40.08; \\
\text{H} & : 2.08%.
\end{align*}\]

SYNTHESIS N-[2-(2,5-DICHLOROPHENOXY) ACETYL] BENZIMIDAZOLE

To an ice-cooled solution of benzimidazole (0.036 mole in 30 ml methanol) in a 500 ml beaker was treated with 5 ml of 4 N NaOH solution. The 2,5-dichlorophenoxy acetyl chloride (in 20 ml methanol) was added in the above solution with constant stirring (70 minutes) and worked up as usual (page 38). The product was purified over the column of silica gel using chloroform as an eluant. Finally, the eluate (150 ml) was concentrated and the product was crystallised from methanol as colourless needles, yield 68%, m.p. 178-180°.

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-IX

TLC was done on silica gel 'G' plates in the
following solvent systems by the same method as described on page 84 which showed single spot in each case.

<table>
<thead>
<tr>
<th>Solvent systems</th>
<th>( R_f ) values</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i) Benzene:ethylacetate (7:3 v/v)</td>
<td>0.46</td>
</tr>
<tr>
<td>(ii) Benzene:methanol (9:1 v/v)</td>
<td>0.52</td>
</tr>
</tbody>
</table>

**INFRA-RED SPECTRUM OF THE COMPOUND-IX**

The significant peaks obtained in the IR spectrum of the compound-IX along with their structural assignments with the help of available literature \(^{174-177}\) are given herein:

\[ \text{IR}\text{\( \text{KBr} \)} \colon 2910 \text{ and } 1480 \left( -\text{CH}_2 \right); 1635 \left( -\text{C}=\text{N} \right); 1575 \left( \text{C}=\text{N} \text{ in benzimidazole} \right); 1500, 1455, 1050, 1030, 880, 840, 790, 740 \text{ and } 695 \left( \text{substituted benzene ring} \right); 1235, 1200 \text{ and } 1160 \left( \text{C}-\text{O}-\text{C} \right) \text{ respectively.} \]

**SYNTHESIS OF THE COMPOUND-X : N-[2-(2-CHLOROPHENOXY) ACETYL] BENZIMIDAZOLE**

The 2-chlorophenol used for the next step synthesis was commercially available.

**SYNTHESIS OF 2-CHLOROPHENOXY ACETIC ACID**

Equimolecular quantities (0.08 mole) of 2-chlorophenol and monochloroacetic acid were refluxed in a 250 ml round bottomed jointed flask fitted with a
water condenser on a water bath with 36 ml of 33% NaOH solution and worked up by the same method as given on page 35. The product 2-chlorophenoxy acetic acid was crystallised from benzene as colourless needles, yield 66%, m.p. 141-142° (lit. m.p. 143-145°) \textsuperscript{188}.

\text{Found : C, 51.38; H, 3.62; Calculated for C}_6\text{H}_7\text{O}_3\text{Cl : C, 51.47; H, 3.75.}

**SYNTHESIS OF 2-CHLOROPHENOXY ACETYL CHLORIDE**

To a solution of 2-chlorophenoxy acetic acid (0.046 mole in 20 ml ethyl acetate) was added thionyl chloride (0.056 mole). The mixture was refluxed (7 hours) on a water bath and worked up by the method as given on page 36 to give 2-chlorophenoxy acetyl chloride, yield 80%, b.p. 135° (lit. b.p. 136°) \textsuperscript{189}.

**SYNTHESIS OF N-[2-(2-CHLOROPHENOXY) ACETYL] BENZIMIDAZOLE**

To an ice-cooled solution of benzimidazole (0.036 mole in 30 ml methanol) in a 500 ml beaker was treated with 5 ml of 4 N NaOH solution. The 2-chlorophenoxy acetyl chloride (in 25 ml methanol) was added in the above solution with constant stirring (45 minutes) and worked up as usual (page 38). The product was purified over the column of silica gel using chloroform as an eluant. Finally, the eluate (120 ml)
was concentrated and the product was crystallised from methanol as colourless needles, yield 62%, m.p. 276-277°.

**THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-X**

TLC was done on silica gel 'G' plates in the following solvent systems by the same method as described on page 84 which showed single spot in each case.

<table>
<thead>
<tr>
<th>Solvent systems</th>
<th>$R_f$ values</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i) Benzene:acetone (8:2 v/v)</td>
<td>0.52</td>
</tr>
<tr>
<td>(ii) Benzene:methanol (8:1 v/v)</td>
<td>0.60</td>
</tr>
</tbody>
</table>

**INFRA-RED SPECTRUM OF THE COMPOUND-X**

The significant peaks obtained in the IR spectrum of the compound-X along with their structural assignments with the help of available literature are given herein:

\[
\text{IR}_{\text{KBr}}: 2908 \text{ and } 1465 \text{ (}-\text{CH}_2\text{)}; 1640 \text{ (}-\text{C-N}\text{)}; 1590 \text{ (C=N in benzimidazole); 1490, 1180, 1130, 1096, 1065, 1045, 885, 780, 750 and 680 (substituted benzene ring); 1240, 1200 and 1160 (C-O-C) respectively.}
\]

**SYNTHESIS OF THE COMPOUND-XI : N-[2-(4-CHLOROPHENOXY) ACETYL] BENZIMIDAZOLE**

The 4-chlorophenol used for the next step
synthesis was commercially available.

SYNTHESIS OF 4-CHLOROPHTHOXY ACETIC ACID

Equimolecular quantities (0.08 mole) of 4-chlorophenol and monochloroacetic acid were refluxed in a 250 ml round bottomed jointed flask fitted with a water condenser on a water bath with 36 ml of 33% NaOH solution and worked up by the method as mentioned on page 36. The product 4-chlorophenoxy acetic acid was crystallised from benzene as a colourless needles, yield 66%, m.p. 154-155° (lit. m.p. 155-156°)\textsuperscript{188}.

*Found*: C, 51.38; H, 3.72; Calculated for C\textsubscript{8}H\textsubscript{7}O\textsubscript{3}Cl:

C, 51.47; H, 3.75%.

SYNTHESIS OF 4-CHLOROPHTHOXY ACETYL CHLORIDE

To a solution of 4-chlorophenoxy acetic acid (0.036 mole in 25 ml methanol) was added thionyl chloride (0.056 mole). The mixture was refluxed (7 hours) on a water bath and worked up by the method as given on page 36 to yield 4-chlorophenoxy acetyl chloride yield 79%, b.p. 140° (lit. b.p. 142°)\textsuperscript{189}.

SYNTHESIS OF N-[2-(4-CHLOROPHTHOXY) ACETYL] BENZIMIDAZOLE

To an ice-cooled solution of benzimidazole (0.036 mole in 25 ml methanol) in a 500 ml beaker was
treated with 5 ml of 4 N NaOH solution. The 4-chlorophenoxy acetyl chloride (in 20 ml methanol) was added in the above solution with constant stirring (90 minutes) and worked up as usual (page 38). The product was purified over the column of silica gel using benzene:chloroform (8:2 v/v) mixture as an eluant. Finally, the eluate (130 ml) was concentrated and the product was crystallised from acetone as pale yellow crystals, yield 76%, m.p. 258-260°.

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-XI

TLC was done on silica gel 'G' plates using the following solvent systems by the same method as described on page 84 which showed single spot in each case.

<table>
<thead>
<tr>
<th>Solvent systems</th>
<th>(R_f) values</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i) Petroleum ether:benzene</td>
<td>0.24</td>
</tr>
<tr>
<td>(ii) Benzene:chloroform</td>
<td>0.34</td>
</tr>
</tbody>
</table>

INFRA-RED SPECTRUM OF THE COMPOUND-XI

The significant peaks obtained in the IR spectrum of the compound-XI along with their structural assignments with the help of available literature [174-177] are given herein:
IR$_{max}^{KBr}$: 2910 and 1480 (-CH$_2$); 1640 (-C-N<); 1585 (C=N in benzimidazole); 1495, 1220, 1125, 1100, 1060, 890, 845, 785, 745 and 685 (substituted benzene ring); 1240, 1200 and 1155 (C-O-C) respectively.

SYNTHESIS OF THE COMPOUND-XII : N-[2-(2,4,6-TRINITROPHENOXY)ACETYL] BENZIMIDAZOLE

SYNTHESIS OF 2,4,6-TRINITROPHENOL

In a dry 500 ml round bottomed flask, was placed 20 g of phenol and 26 ml concentrated sulphuric acid. The contents were shaken and heated on a water bath for about half an hour. The flask was then cooled in an ice-bath and 86 ml of concentrated nitric acid was added drop by drop at room temperature with continuous stirring. The reaction mixture was allowed to stand for some time and when the brisk evolution or brown fumes stopped, the flask was then heated on a water bath for about two hours with occasional stirring. The reaction mixture was cooled and 400 ml of water was added. The solid so obtained was filtered, washed thoroughly with water to remove all the nitric acid. Finally, it was crystallised from ethanol as pale yellow crystals, yield 61%, m.p. 121-122° (lit. m.p. 122°). 

Found : C, 31.22; H, 1.32; N, 18.18; Calculated for C$_6$H$_3$N$_3$O$_7$: C, 31.44; H, 1.31; N, 18.34%. 

190.
SYNTHESIS OF 2,4,6-TRINITROPHENOXY ACETIC ACID

Equimolecular quantities (0.09 mole) of 2,4,6-trinitrophenol and monochloroacetic acid were refluxed in a 250 ml round bottomed jointed flask fitted with a water condenser on a water bath with 72.5 ml of 33% NaOH solution and worked up by the method as described on page 35. The product 2,4,6-trinitrophenoxy acetic acid was crystallised from methanol as long yellow crystals, yield 58%, m.p. 88-90°.

Found: C, 33.14; H, 1.66; N, 14.39; Calculated for C₈H₅O₈N₃: C, 33.4%; H, 1.74; N, 14.63%.

SYNTHESIS OF 2,4,6-TRINITROPHENOXY ACETYL CHLORIDE

To a solution of 2,4,6-trinitrophenoxy acetic acid (0.046 mole in 25 ml ethyl acetate) was added thionyl chloride (0.056 mole). The mixture was refluxed (7 hours) on a water bath and worked up by the same method as given on page 36 to yield 2,4,6-trinitrophenoxy acetyl chloride which was crystallised from ethyl acetate as long yellow crystals, yield 85%, m.p. 120-121°.

Found: C, 31.18; H, 1.08; N, 13.62; Calculated for C₆H₄O₈N₃Cl: C, 31.37; H, 1.30; N, 13.72%. 
SYNTHESIS OF N-[2-(2,4,6-TRINITROPHENOXY) ACETYL] BENZIMIDAZOLE

To an ice-cooled solution of benzimidazole (0.036 mole in 25 ml methanol) in a 500 ml beaker was treated with 5 ml of 4 N NaOH solution. The 2,4,6-trinitrophenoxycetyl chloride (in 20 ml methanol) was added in the above solution with constant stirring (50 minutes) and worked up as usual (page 38). The product was purified over the column of silica gel using benzene:chloroform (6:4 v/v) mixture as an eluant. Finally the eluate (150 ml) was concentrated and the product was crystallised from acetone as yellow crystals, yield 66%, m.p. 218-220°.

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-XII

TLC was done on silica gel 'G' plates in the following solvent systems by the same method as described on page 84 which showed single spot in each case.

<table>
<thead>
<tr>
<th>Solvent systems</th>
<th>R_f values</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i) Petroleum ether:benzene (5:5 v/v)</td>
<td>0.34</td>
</tr>
<tr>
<td>(ii) Benzene:chloroform (5:5 v/v)</td>
<td>0.41</td>
</tr>
</tbody>
</table>

INFRA-RED SPECTRUM OF THE COMPOUND-XII

The significant peaks obtained in the IR spectrum of the compound-XII along with their structural
assignments with the help of available literature[174-177]
are given herein:

\[ \text{IR } \nu_{\text{max}}^{\text{KBr}} : 2910 \text{ and } 1480 \text{ (} -\text{CH}_2\text{), 1640} \text{ (} -\text{C-N} \text{ in benzimidazole); 1565, 1490, 1335, 1280, 1130, 1100, 1050, 885, 845, 780, 740 and 690 (substituted benzene}\]
\[ \text{ring); 1245, 1205 and 1165 (C-O-C) respectively.} \]

SYNTHESIS OF THE COMPOUND-XIII: N-[2-(2,4,6-TRINITROPHENOXY)PROPIONYL] BENZIMIDAZOLE

The 2,4,6-trinitrophenol was prepared by the same method as described on page 110.

SYNTHESIS OF 2-(2,4,6-TRINITROPHENOXY) PROPIONIC ACID

Equimolecular quantities (0.09 mole) of 2,4,6-trinitrophenol and \( \text{CCl}_2 \)-monochloropropionic acid was refluxed in a 250 ml round bottomed jointed flask fitted with a water condenser on a water bath with 72.5 ml of 33% NaOH solution and worked up as usual (page 35) to yield 2,4,6-trinitrophenoxy propionic acid which was crystallised from ethyl acetate as long yellow crystals, yield 60%, m.p. 100°.

Found: C, 35.78; H, 2.26; N, 13.86; Calculated for \( \text{C}_{9}\text{H}_3\text{N}_3\text{O}_9 \):

\[ \text{C, 35.88; H, 2.32; N, 13.95%.} \]
SYNTHESIS OF 2-(2,4,6-TRINITROPHENOXY) PROPIONYL CHLORIDE

To a solution of 2,4,6-trinitrophenoxy propionic acid (0.046 mole in ethyl acetate) was added thionyl chloride (0.056 mole). The mixture was refluxed (7 hours) on a water bath and worked up by the same method as given on page 36 to yield 2,4,6-trinitrophenoxy propionyl chloride which was crystallised from ethyl acetate as long yellow crystals, yield 82%, m.p. 118-119°C.

Found: C, 33.68; H, 1.76; N, 13.07; Calculated for C_{9}H_{6}N_{3}O_{6}Cl: C, 33.80; H, 1.87; N, 13.14%.

SYNTHESIS OF N-[2-(2,4,6-TRINITROPHENOXY) PROPIONYL] BENZIMIDAZOLE

To an ice-cooled solution of benzimidazole (0.036 mole in 25 ml methanol) in a 500 ml beaker was treated with 5 ml of 4 N NaOH solution. The 2,4,6-trinitrophenoxy propionyl chloride (in 25 ml methanol) was added in the above solution with constant stirring (45 minutes) and worked up as usual (page 38). The product was purified over the column of silica-gel using chloroform:methanol (8:2 v/v) mixture as an eluant. Finally, the eluate (145 ml) was concentrated and the product was crystallised from methanol as yellow crystals, yield 80%, m.p. 112-113°C.
THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-XIII

TLC was done on silica gel 'G' plates in the following solvent systems, by the same method as described on page 84 which showed single spot in each case.

Solvent systems \[ R_f \] values
(1) Benzene:methanol (4:6 v/v) 0.58
(2) Chloroform:methanol (5:5 v/v) 0.71

INFRA-RED SPECTRUM OF THE COMPOUND-XIII

The significant peaks obtained in the IR spectrum of the compound-XIII along with their structural assignments with the help of available literature are given herein:

\[ \text{IR}^2_{\text{KBr}}: 2930, 1455 \text{ and } 1375 (C-CH_3); 1635 (-C-N<); \]
\[ 1598 (C=N in benzimidazole); 1570, 1466, 1340, 1290, \]
\[ 1140, 1110, 1065, 890, 830, 780, 725 \text{ and } 685 \text{ (substituted benzene ring); } \]
\[ 1250, 1205 \text{ and } 1170 (C-O-C) \text{ respectively.} \]

SYNTHESIS OF THE COMPOUND-XIV: [2-(2-NITROPHENOXY) ACETYL] BENZIMIDAZOLE

SYNTHESIS OF 2-NITROPHENOL

In a 1 litre three necked round bottomed flask containing 400 ml of water, was added 250 g (136 ml) of
concentrated sulphuric acid in a thin stream with a constant stirring. 150 g of sodium nitrite was also placed in the same content and the mixture was cooled in an ice-bath. To the cooled mixture 94 g of phenol dissolved in 20 ml of water was added through a separating funnel with constant stirring in such a rate that the temperature does not rise above 20°. When all the phenol had been added, the stirring was still continued for two hours. The mother liquor was poured off from the resinous mixture of nitro compound. The residue was mixed with 500 ml of water and contents of the flask were allowed to settle. The product 2-nitrophenol was filtered and washed with water (3x30 ml) to remove the traces of any acidic residual. It was dried upon the filter paper in air followed by crystallisation with benzene afforded yellow needles, yield 52%, m.p. 44-45° (lit. m.p. 46°) \(^{181}\).

**Found:** C, 51.42; H, 3.36; N, 9.78; **Calculated for** \(\text{C}_6\text{H}_5\text{NO}_3\) :

C, 51.59; H, 3.59; N, 10.07%.

**SYNTHESIS OF 2-NITROPHENOXY ACETIC ACID**

Equimolecular quantities (0.09 mole) of 2-nitrophenol and monochloroacetic were refluxed in a 250 ml round bottomed jointed flask fitted with a water condenser on a water bath with 44 ml of 33% NaOH solution and worked up as usual (page 35). The product
2-nitrophenoxy acetic acid was crystallised from acetone as yellow crystals, yield 58%, m.p. 155-156 (lit. m.p. 156-157°).\textsuperscript{192}

\textbf{Found :} C, 48.46; H, 3.36; N, 6.78; \textbf{Calculated for C}_8\text{H}_6\text{O}_4\text{N :} C, 48.73; H, 3.55; N, 7.10%.

\textbf{SYNTHESIS OF 2-NITROPHENOXY ACETYL CHLORIDE}

To a solution of 2-nitrophenoxy acetic acid (0.046 mole in 30 ml methanol) was added thionyl chloride (0.056 mole). The mixture was refluxed 7 hours on a water bath and worked up by the method as described on page 36 to yield 2-nitrophenoxy acetyl chloride which was crystallised from ligroin as yellow needles, yield 80%, m.p. 43-44° (lit. m.p. 43-44.5°).\textsuperscript{193}

\textbf{Found :} C, 44.18; H, 2.45; N, 6.28; \textbf{Calculated for C}_8\text{H}_6\text{O}_4\text{NCl :} C, 44.44; H, 2.77; N, 6.48%.

\textbf{SYNTHESIS OF N-[2-(2-NITROPHENOXY) ACETYL] BENZIMIDAZOLE}

To an ice-cooled solution of benzimidazole (0.036 mole in 25 ml methanol) in a 500 ml beaker was treated with 5 ml of 4 \textit{N} NaOH solution. The 2-nitrophenoxy acetyl chloride (in 20 ml methanol) was added in the above solution with constant stirring (45 minutes) and worked up as usual (page 38). The product was purified over the column of silica gel using
choloroform:methanol (8:2 v/v) mixture as an eluant. Finally, the eluate (190 ml) was concentrated and the product was crystallised from methanol as yellow needles, yield 60%, m.p. 72-74°.

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-XIV

TLC was done on silica gel 'G' plates using the following solvent systems by the same method as described on page 84 which showed single spot in each case.

Solvent systems
(i) Benzene:methanol (7:3 v/v)  
(ii) Chloroform:methanol (9:1 v/v)

<table>
<thead>
<tr>
<th>Solvent systems</th>
<th>Rf values</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i) Benzene:methanol (7:3 v/v)</td>
<td>0.74</td>
</tr>
<tr>
<td>(ii) Chloroform:methanol (9:1 v/v)</td>
<td>0.62</td>
</tr>
</tbody>
</table>

INFRA-RED SPECTRUM OF THE COMPOUND-XIV

The significant peaks obtained in the infra-red spectrum of the compound-XIV alongwith their structural assignments with the help of available literature are given herein:

IR 2) KBr : 2900 and 1470 (-CH2); 1630 (-C=N<); 1600 (C=N in benzimidazole), 1570, 1490, 1340, 1300, 1220, 1140, 1100, 1055, 890, 785, 740 and 685 (substituted benzene ring); 1245, 1195 and 1175 (C-O-C) respectively.
SYNTHESIS OF THE COMPOUND-XV : N-[2-(3-NITROPHENOXY) ACETYL] BENZIMIDAZOLE

SYNTHESIS OF 3-NITROPHENOL

In a 1 litre beaker containing 75 ml of water was added 101 g (55 ml) of concentrated sulphuric acid continuously followed by 35 g of finely powdered \textit{m}-nitroaniline. In the above mixture about 150 g of crushed ice was added and stirred the mixture to get the sulphate. The beaker containing the above mixture was kept in a freezing mixture at 0\degree, stirred mechanically and added a cold solution of 18 g of sodium nitrite in 40 ml of water over a period of 10 minutes and then allowed to stand for 5 minutes. Some \textit{m}-nitrophenyl diazonium sulphate separated out. The supernatant liquid from the solid was decanted as far as possible.

In 1 litre round bottomed flask containing the above solid, 165 ml of concentrated sulphuric acid was added and the mixture was heated just to boiling. The supernatant liquid was added to the above round bottomed flask from a separatory funnel at such a rate that mixture boils very vigorously (about 30 minutes). It was boiled for a further 5 minutes and then poured the mixture into a 1 litre beaker kept in ice-water and stirred vigorously to obtain a homogeneous crystal magma. It was filtered and washed with ice-water.
(4x25 ml). The product was crystallised by dissolving the crude material into hot dilute hydrochloric acid (1:1 v/v), decanted any residual dark oil, filtered, cooled to 0°C and kept for 24 hours at room temperature which gave pale yellow crystals of 3-nitrophenol, yield 60%, m.p. 95-96°C (lit. 96°C)194.

Found: C, 15.62; H, 3.43; N, 10.02; Calculated for C₆H₅NO₃:
        C, 51.79; H, 3.59; N, 10.07%.

SYNTHESIS OF 3-NITROPHENOXY ACETIC ACID

Equimolecular quantities (0.08 mole) of 3-nitrophenol and monochloroacetic acid were refluxed in a 250 ml round bottomed jointed flask fitted with a water condenser on a water bath with 39 ml of 33% NaOH solution and worked up by the same method as given on page 35. The product 3-nitrophenoxy acetic acid was crystallised from ethyl acetate as yellow needles, yield 64%, m.p. 155-156°C (lit. m.p. 157-158°C)192.

Found: C, 48.66; H, 3.58; N, 7.18; Calculated for C₆H₅NO₃:
        C, 48.73; H, 3.55; N, 7.10%.

SYNTHESIS OF 3-NITROPHENOXY ACETYL CHLORIDE

To a solution of 3-nitrophenoxy acetic acid (0.046 mole in 20 ml ethyl acetate) was added thionyl chloride (0.056 mole). The mixture was refluxed (7 hours) on a water bath and worked up by the same method
as given on page 36 to yield 3-nitrophenoxyl acetyl chloride which was crystallised from methanol as yellow needles, yield 81%, m.p. 48-49° (lit. m.p. 49-51°)\(^{195}\).

**Found**: C, 44.38; H, 2.79; N, 8.40; **Calculated for C\(_6\)H\(_6\)O\(_4\)NCl**: C, 44.44; H, 2.77; N, 8.48%.

**SYNTHESIS OF N-[2-(3-NITROPHENOXO) ACETYL] BENZIMIDAZOLE**

To an ice-cooled solution of benzimidazole (0.036 mole in 30 ml methanol) in a 500 ml beaker was treated with 5 ml of 4N NaOH solution. The 3-nitrophenoxyl acetyl chloride (in 20 ml methanol) was added in the above solution with constant stirring (60 minutes) and worked up as usual (page 38). The product was purified over the column of silica gel using benzene : chloroform (5:5 v/v) mixture as an eluant. Finally, the eluate (180 ml) was concentrated and the product was crystallised from methanol as yellow needles, yield 60%, m.p. 158-159°.

**THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-XV**

TLC was done on silica gel 'G' plates in the following solvent systems by the same method as described on page 84 which showed single spot in each case.
Solvent systems

(1) Benzene: chloroform (8:2 v/v)  
(2) Benzene: ethyl acetate (6:4 v/v)  

\( R_f \) values

0.48

0.65

INFRA-RED SPECTRUM OF THE COMPOUND-XV

The significant peaks obtained in the IR spectrum of the compound-XV along with their structural assignments with the help of available literature \(^{174-177}\) are given herein:

\( \text{IR}^{\text{KBr}}_{\max } \): 2915 and 1480 (\(-\text{CH}_2\)); 1635 (\(-\text{C}-\text{N}\)); 1590 (C=N in benzimidazole); 1550, 1475, 1340, 1305, 1135, 1100, 1030, 900, 770, 685 and 645 (substituted benzene ring); 1245, 1210 and 1165 (C-O-C) respectively.

SYNTHESIS OF THE COMPOUND-XVI: N-\{2-\(\text{4-NITROPHENOXY}\) ACETYL\} BENZIMIDAZOLE

SYNTHESIS OF 4-NITROPHENOL

In 1 litre three necked flask containing 400 ml of water was added 250 g (136 ml) of concentrated sulphuric acid in a thin stream with constant stirring. 150 g of sodium nitrite was added in the same content with stirring. The mixture was cooled in an ice-bath and 94 g of phenol dissolved in 20 ml of water, was added slowly in about two hours. The mother liquor was poured and the residue was shaken with 500 ml of water and the contents of the flask were allowed to settle.
The wash liquor was poured off (2-nitrophenol) and the residue in the flask was allowed to cool in ice for 30 minutes when 4-nitrophenol separated out. The crude 4-nitrophenol was filtered and boiled with one litre of 2% hydrochloric acid together with about 5 g of decolourising charcoal for ten minutes. Then it was filtered through hot water funnel and the filtrate was allowed to crystallise overnight. The colourless needles of 4-nitrophenol obtained were filtered off and dried upon filter paper, yield 64%, m.p. 112-113° (lit. m.p. 112°).\(^1\)

**Found**: C, 51.76; H, 3.48; N, 10.14; Calculated for \(\text{C}_6\text{H}_5\text{NO}_3\): C, 51.78; H, 3.59; N, 10.07%.

**SYNTHESIS OF 4-NITROPHENOXY ACETIC ACID**

Equimolecular quantities (0.09 mole) of 4-nitrophenol and monochloroacetic acid were refluxed in a 250 ml round bottomed jointed flask fitted with a water condenser on a water bath with 44 ml of 33% NaOH solution and worked up by the same procedure as described on page 35. The product 4-nitrophenoxy acetic acid was crystallised from ethyl acetate as yellow needles, yield 83%, m.p. 186-187° (lit. m.p. 188°).\(^2\)

**Found**: C, 48.63; H, 3.44; N, 7.18; Calculated for \(\text{C}_8\text{H}_7\text{O}_5\text{N}\): C, 48.73; H, 3.55; N, 7.10%.
SYNTHESIS OF 4-NITROPHENOXY ACETYL CHLORIDE

To a solution of 4-nitrophenoxy acetic acid (0.046 mole in 20 ml methanol) was added thionyl chloride (0.056 mole). The mixture was refluxed (7 hours) on a water bath and worked up as usual (page 36) to yield 4-nitrophenoxy acetyl chloride. It was crystallised from benzene as yellow crystals, yield 64%, m.p. 85-86° (lit. m.p. 86-87°).193

Found: C, 44.39; H, 2.72; N, 6.49; Calculated for C₉H₆O₄NCl:

  C, 44.44; H, 2.77, N, 5.48%.

SYNTHESIS OF N-[2-(4-NITROPHENOXY) ACETYL] BENZIMIDAZOLE

To an ice-cooled solution of benzimidazole (0.036 mole in 25 ml methanol) in a 500 ml beaker was treated with 5 ml of 4 N NaOH solution. The 4-nitrophenoxy acetyl chloride (in 20 ml methanol) was added in the above solution with constant stirring (60 minutes) and worked up as usual (page 38). The product was purified over the column of silica gel using benzene: chloroform (2:8 v/v) mixture as an eluent. Finally, the eluate (150 ml) was concentrated and the product was crystallised from ethyl acetate as yellow needles, yield 66%, m.p. 134-136°.
THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-XVI

TLC was done on silica gel 'G' plates in the following solvent systems by the same method as described on page 84 which showed single spot in each case.

<table>
<thead>
<tr>
<th>Solvent systems</th>
<th>R_f values</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Petroleum ether:benzene (5:8 v/v)</td>
<td>0.43</td>
</tr>
<tr>
<td>(11) Benzene:chloroform (6:4 v/v)</td>
<td>0.51</td>
</tr>
</tbody>
</table>

INFRA-RED SPECTRUM OF THE COMPOUND-XVI

The significant peaks obtained in the IR spectrum of the compound-XVI along with their structural assignments with the help of available literature are given herein:

\[ \text{IR }_{\text{KBr}}^{\text{max}} : 2905 \text{ and } 1480 \text{ (-CH}_2\text{); 1640 (-C-N< ); 1580 (C=N in benzimidazole); 1565, 1500, 1345, 1300, 1220, 1120, 1100, 1040, 885 and 695 (substituted benzene ring); 1240, 1200 and 1170 (C-O-C) respectively.} \]

SYNTHESIS OF THE COMPOUND-XVII : \text{N-[2-(METHYLPHENOXY) ACETYL] BENZIMIDAZOLE}

The 2-methylphenol used for next step synthesis was commercially available.

SYNTHESIS OF 2-METHYLPHENOXY ACETIC ACID

Equimolecular quantities (0.09 mole) of
2-methylphenol and monochloroacetic acid were refluxed in a 250 ml round-bottomed jointed flask fitted with a water condenser on a water bath with 34 ml of 33% NaOH solution and worked up by the method as mentioned on page 35. The product 2-methylphenoxy acetic acid was crystallised from benzene as colourless needles, yield 64%, m.p. 150-151° (lit. m.p. 151-152°)188.

Found : C, 65.02; H, 5.98; Calculated for C₉H₁₀O₃ : C, 65.06; H, 6.02%.

SYNTHESIS OF 2-METHYLPHENOXY ACETYL CHLORIDE

To a solution of 2-methylphenoxy acetic acid (0.046 mole in 25 ml ethyl acetate) was added thionyl chloride (0.056 mole). The mixture was refluxed (7 hours) on a water bath and worked up as given on page 36 to yield 2-methylphenoxy acetyl chloride which was crystallised from ethyl acetate as colourless crystals, yield 80%, m.p. 148-150°.

Found : C, 58.44; H, 4.78; Calculated for C₉H₉O₂Cl : C, 58.53; H, 4.87%.

SYNTHESIS OF N-[2-(2-METHYLPHENOXY) ACETYL] BENZIMIDAZOLE

To an ice-cooled solution of benzimidazole (0.036 mole in 30 ml methanol) in a 500 ml beaker was treated with 5 ml of 4 N NaOH solution. The 2-methylphenoxy acetyl chloride (in 25 ml methanol) was added in
the above solution with constant stirring (70 minutes) and worked up as usual (page 38). The product was purified over the column of neutral alumina using chloroform as an eluant. Finally, the eluate (160 ml) was concentrated and the product was crystallised from methanol as colourless crystals, yield 60%; m.p. 78-79°.

**THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-XVII**

TLC was done on silica gel 'G' plates in the following solvent systems by the same method as described on page 84 which showed single spot in each case.

<table>
<thead>
<tr>
<th>Solvent systems</th>
<th>Rf values</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i) Petroleum ether:benzene (2:8 v/v)</td>
<td>0.35</td>
</tr>
<tr>
<td>(ii) Benzene:chloroform (5:5 v/v)</td>
<td>0.47</td>
</tr>
</tbody>
</table>

**INFRA-RED SPECTRUM OF THE COMPOUND-XVII**

The significant peaks obtained in the IR spectrum of the compound-XVII alongwith their structural assignments with the help of available literature 174-177 are given herein:

\[
\text{IR }^\text{KBr}_{\text{max}}: 2930 \text{ (C-CH}_3\text{)}; 2908 \text{ and } 1485 \text{ (C-CH}_3\text{)}; 1640 \text{ (-C-N<); } 1575 \text{ (C=N in benzimidazole); } 1500, 1205, 1140, 1095, 1055, 880, 750 \text{ and } 680 \text{ (substituted benzene ring); } 1240, 1205 \text{ and } 1170 \text{ (C-O-C) respectively.}
\]
SYNTHESIS OF THE COMPOUND-XVIII : N-[2-(3-METHYLPHENOXY) ACETYL] BENZIMIDAZOLE

The 3-methylphenol used for next step synthesis was commercially available.

SYNTHESIS OF 3-METHYLPHENOXY ACETIC ACID

Equimolecular quantities (0.09 mole) of 3-methylphenol and monochloroacetic acid were refluxed in a 250 ml round bottomed joined flask fitted with a water condensor on a water bath with 34 ml of 33% NaOH solution by the same method as given on page 35. The product 4-methylphenoxy acetic acid was crystalised from benzene as colourless needles, yield 64% m.p. 100-1010 (lit. m.p. 102-1030).188

Found : C, 65.10; H, 6.08; Calculated for C9H10O3 : C, 65.06; H, 6.02%.

SYNTHESIS OF 3-METHYLPHENOXY ACETYL CHLORIDE

To a solution of 3-methylphenoxy acetic acid (0.046 mole in 30 ml ethyl acetate) was added thionyl chloride (0.056 mole). The mixture was refluxed (7 hours) on a water bath and worked up by the same method as given on page 36 to yield 3-methylphenoxy acetyl chloride which was crystalised from methanol as colourless crystals yield 82% m.p. 96-980.
Found: C, 58.48; H, 4.82; Calculated for C₇H₉O₂Cl: C, 58.53; H, 4.87%.

SYNTHESIS OF N-[2-(3-METHYLPHENOXY) ACETYL] BENZIMIDAZOLE

To an ice cooled solution of benzimidazole (0.036 mole in 30 ml methanol) in a 500 ml beaker was treated with 5 ml of 4N NaOH solution. The 3-methylphenoxy acetyl chloride (in 25 ml methanol) was added in the above solution with constant stirring (55 minutes) and worked up as usual (Page 38). The product was purified over the column of neutral alumina using benzene:chloroform (2:8 v/v) mixture as an eluant. Finally, the eluate (170 ml) was concentrated and the product was crystallised from methanol as colourless crystals, yield 67%, m.p. 169-170°.

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-XVIII

TLC was done on silica gel 'G' plates in the following solvent systems by the same method as described on page 84 which showed single spot in each case.

<table>
<thead>
<tr>
<th>Solvent systems</th>
<th>R_f values</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i) Petroleum ether:benzene (2:8 v/v)</td>
<td>0.38</td>
</tr>
<tr>
<td>(ii) Benzene:chloroform (5:5 v/v)</td>
<td>0.44</td>
</tr>
</tbody>
</table>
INFRA-RED SPECTRUM OF THE COMPOUND-XVIII

The significant peaks obtained in the IR spectrum of the compound-XVIII along with their structural assignments with the help of available literature\textsuperscript{174-177} are given herein:

$\text{IR}_Q^{\text{KBr}}_{\text{max}}$: 2930 (C-CH$_3$); 2900 and 1480 (-CH$_2$); 1640 (-C-N<); 1585 (C=N in benzimidazole); 1490, 1140, 1110, 1080, 1030, 875, 745 and 690 (substituted benzene ring); 1230, 1210 and 1170 (C-O-C) respectively.

SYNTHESIS OF THE COMPOUND-XIX: N-[2-(4-METHYLPHENOXY)] ACETYL] BENZIMIDAZOLE

The 4-methyl phenol used for the next step-synthesis was commercially available.

SYNTHESIS OF 4-METHYLPHENOXY ACETIC ACID

Equimolecular quantities (0.09 mole) of 4-methylphenol and monochloroacetic acid were refluxed in a 250 ml round bottomed jointed flask fitted with a water condenser on a water bath with 34 ml of 33% NaOH solution and worked by the same method as given on page 35. The product 4-methylphenoxy acetic acid was crystallised from benzene as colourless needles, yield 65%, m.p. 134-135° (lit. m.p. 134-136°)\textsuperscript{188}.

Found: C, 64.98; H, 5.97; Calculated for $C_9H_{10}O_3$: C, 65.06; H, 6.02%.
SYNTHESIS OF 4-METHYLPHENOXY ACETYL CHLORIDE

To a solution of 4-methyl phenoxy acetic acid (0.046 mole in 30 ml ethyl acetate) was added thionyl chloride (0.056 mole). The mixture was refluxed (7 hours) on a water bath and worked up by the same method as given on page 36 to yield 4-methylphenoxy acetyl chloride which was crystallised from ethyl acetate as colourless crystals, yield 80%, m.p. 130-140°C.

Found : C, 58.49; H, 4.84; Calculated for C₉H₉O₂Cl : C, 58.53; H, 4.87%.

SYNTHESIS OF N-[2-(4-METHYLPHENOXY) ACETYL] BENZIMIDAZOLE

To an ice-cooled solution of benzimidazole (0.036 mole in 30 ml methanol) in a 500 ml beaker was treated with 5 ml of 4N NaOH solution. The 4-methylphenoxy acetyl chloride (in 25 ml methanol) was added in the above solution with constant stirring (60 minutes) and worked up as usual (page 38). The product was purified over the column of neutral alumina using chloroform as an eluant. Finally, the eluate (150 ml) was concentrated and the product was crystallised from methanol as pink coloured crystals yield 64%, m.p. 164-165°C.

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-XIX

TLC was done on silica gel 'G' plates in the
following solvent systems by the same method as described on page 84 which showed single spot in each case.

**Solvent systems**

<table>
<thead>
<tr>
<th>Solution</th>
<th>$R_f$ values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene:acetone (9:1 v/v)</td>
<td>0.70</td>
</tr>
<tr>
<td>Benzene:methanol (9:1 v/v)</td>
<td>0.86</td>
</tr>
</tbody>
</table>

**INFRA-RED SPECTRUM OF THE COMPOUND-XIX**

The significant peaks obtained in the IR spectrum of the compound-XIX along with their structural assignments with the help of available literature 174-177 are given herein:

\[ \nu_{\text{KBr}}^{\text{max}} : 2925 (\text{C-CH}_3); \ 2900 \text{ and } 1480 (\text{CH}_2); \ 1640 (\text{C-N}); \ 1585 (\text{C=N in benzimidazole}); \ 1498, 1175, 1125, 1100, 1025, 880, 750 \text{ and } 690 (\text{substituted benzene ring}); \ 1240, 1195 \text{ and } 1155 (\text{C-O-C}) \text{ respectively.} \]

**SYNTHESIS OF THE COMPOUND-XX : N-[(2-(1-NAPTHOXY) ACETYL] BENZIMIDAZOLE**

The 1-naphthol used for the next step synthesis was commercially available.

**SYNTHESIS OF 1-NAPTHOXY ACETIC ACID**

Equimolecular quantities (0.08 mole) of 1-naphthol and monochloroacetic acid were refluxed in a 250 ml round bottomed jointed flask fitted with a water condenser with 30.5 ml of 33% NaOH solution on a water
bath and worked up by the method as mentioned on page 42.
The product 1-naphthoxy acetic acid was crystallised from acetone as colourless prismatic crystals, yield 66%, m.p. 190-191° (lit. m.p. 191-192)188.

Found : C, 71.22; H, 4.92; Calculated for \( \text{C}_{12}\text{H}_{10}\text{O}_3 \) :
C, 71.28; H, 4.95%.

SYNTHESIS OF 1-NAPHTHOXY ACETYL CHLORIDE

To a solution of 1-naphthoxy acetic acid (0.46 mole in 25 ml methanol) was added thionyl chloride (0.056 mole). The mixture was refluxed (7 hours) on a water bath and worked up by the same method as described on page 43 to yield the product 1-naphthoxy acetyl chloride, yield 79%, b.p. 193-194° (lit. b.p. 194°)197.

SYNTHESIS OF N-[2-(1-NAPHTHOXY) ACETYL] BENZIMIDAZOLE

To an ice-cooled solution of benzimidazole (0.036 mole in 25 ml methanol) in a 500 ml beaker was treated with 5 ml of 4 N NaOH solution. The 1-naphthoxy acetyl chloride (in 25 ml methanol) was added in the above solution with constant stirring (50 minutes) and worked up as usual (page 43). The product was purified over the column of silica gel using benzene:ethyl acetate (6:4 v/v) mixture as an eluant. Finally, the eluate (170 ml) was concentrated and the product was
crystallised from acetone as brown coloured crystals, yield 62%, m.p. 118-120°.

**THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-XX**

TLC was done on silica gel 'G' plates using the following solvent systems by the same method as described on page 84 which showed single spot in each case.

**Solvent systems**

<table>
<thead>
<tr>
<th>R&lt;sub&gt;f&lt;/sub&gt; values</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Benzene:chloroform (2:8 v/v)</td>
</tr>
<tr>
<td>(ii) Benzene:ethyl acetate (7:3 v/v)</td>
</tr>
</tbody>
</table>

**INFRA-RED SPECTRUM OF THE COMPOUND-XX**

The significant peaks obtained in the IR spectrum of the compound-XX along with their structural assignments with the help of available literature are given herein:

\[
\text{IR}_{KBr}^\text{max}: 2910 \text{ and } 1485 \text{ (-CH}_2\text{)}; 1640 \text{ (-C-N<)}; 1595 \text{ (C=N in benzimidazole)}; 1570, 1480, 1390, 1170, 1100, 865, 785, 760 \text{ and } 690 \text{ (substituted aromatic ring)}; 1240, 1195 \text{ and } 1155 \text{ (C-O-C) respectively.}
\]

**SYNTHESIS OF THE COMPOUND-XXI : N-[2-(2-NAPHTHOXY) ACETYL] BENZIMIDAZOLE**

The 2-naphthol used for the next step synthesis was commercially available.
SYNTHESIS OF 2-NAPHTHOXY ACETIC ACID

Equimolecular quantities (0.08 mole) of 2-naphthol and monochloroacetic acid were refluxed in a 250 ml round bottomed jointed flask fitted with a water condenser on a water bath with 30.5 ml of 33% NaOH solution and worked up by the method as mentioned on page 42. The product 2-naphthoxy acetic acid was crystallised from benzene as light brown prismatic crystals, yield 80%, m.p. 152-153° (lit. m.p. 153-154°).188

Found : C, 71.22; H, 4.88; Calculated for C_{12}H_{10}O_3 :
C, 71.26; H, 4.95%.

SYNTHESIS OF 2-NAPHTHOXY ACETYL CHLORIDE

To a solution of 2-naphthoxy acetic acid (0.046 mole in 25 ml ethyl acetate) was added thionyl chloride (0.056 mole). The mixture was refluxed (7 hours) on a water bath and worked up by the method as described on page 43 to yield 2-naphthoxy acetyl chloride which was crystallised from benzene as colourless needles, yield 80%, m.p. 53-54° (lit. m.p. 54°).197

Found : C, 65.28; H, 4.12; Calculated for C_{12}H_{10}O_2Cl :
C, 65.30; H, 4.06%.

SYNTHESIS OF N-[2-(2-NAPHTHOXY) ACETYL] BENZIMIDAZOLE

To an ice-cooled solution of benzimidazole
(0.036 mole in 30 ml methanol) in a 500 ml beaker was treated with 5 ml of 4 N NaOH solution. The 2-naphthoxy acetyl chloride (in 25 ml methanol) was added in the above solution with constant stirring (90 minutes) and worked up as usual (page 43). The product was purified over the column of silica gel using benzene:chloroform (3:7 v/v) mixture as an eluent. Finally the eluate (150 ml) was concentrated and the product was crystallised from acetone as light brown needles, yield 56%, m.p. 76-78°.

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND-XXI

TLC was done on silica gel 'G' plates in the following solvent systems by the same method as described on page 84 which showed single spot in each case.

<table>
<thead>
<tr>
<th>Solvent systems</th>
<th>Rf values</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i) Benzene:chloroform (5:5 v/v)</td>
<td>0.54</td>
</tr>
<tr>
<td>(ii) Benzene:ethylacetate (9:1 v/v)</td>
<td>0.62</td>
</tr>
</tbody>
</table>

INFRA-RED SPECTRUM OF THE COMPOUND-XXI

The significant peaks obtained in the IR spectrum of the compound-XXI along with their structural assignments with the help of available literature are given herein:


$\text{IR}^\text{KBr}_\text{max}^O$: 2910 and 1480 (-CH$_2$); 1635 (-C=N$^0$); 1590 (C=N in benzimidazole); 1560, 1495, 1370, 1185, 1095, 880, 785, 750 and 685 (substituted aromatic ring); 1240 and 1030 (C-O-C) respectively.
SECTION II

RESULTS AND CONCLUSIONS OF
ANTIMICROBIAL ACTIVITY
ANTI-INFLAMMATORY ACTIVITY
ANALGESIC ACTIVITY
EVALUATIONS OF THE FOLLOWING ACTIVITIES:

(a) **ANTIMICROBIAL ACTIVITY**: All the synthesized compounds (I to XXI) were screened for antimicrobial activity by adopting the methods as described on pages 56, 61 at 25 µg/ml and 50 µg/ml concentrations respectively. Streptomycin and mycostatin have been used as standard for antibacterial and antifungal activities. The name of selected bacteria and fungi were given on pages 56 & 62 respectively.

(b) **ANTI-INFLAMMATORY ACTIVITY**: All the synthesized compounds (I to XXI) were screened for anti-inflammatory activity by adopting carrageenan induced rat paw oedema method as mentioned on page 71. All the compounds showed their peak effect at 3 hours. Acetyl salicylic acid was used as a standard drug.

(c) **ANALGESIC ACTIVITY**: All the synthesized compounds (I to XXI) were screened for analgesic activity by adopting hot plate method as given on page 78. All the compounds showed their peak effect at 45 minutes after drug administration. Acetyl salicylic acid was used as a standard drug.

The above results are given in TABLES - I, II, III and IV respectively.
RESULTS AND CONCLUSIONS:

On the basis of the data given in TABLES - I and II, the following CONCLUSIONS have been drawn -

(1) Most of the synthesised compounds exhibited mild to moderately and better antimicrobial activity against the selected pathogenic organisms.

(2) All the bromo (III to V) and few of the chloro (VI to VIII) phenoxy acetyl/propionyl benzimidazole showed good antimicrobial activity than the other compounds of the series except 4-nitrophenoxy acetyl benzimidazole (XVI) which exhibited only good antifungal activity.

(3) Among the nitro series of the compounds only trinitro compounds (XII and XIII) showed mild to moderate antibacterial activity.

(4) The phenoxy, methyl phenoxy and naphthoxy acetyl benzimidazoles found to be mild active against gram (+) bacteria i.e. S.aureus and B.anthracis.

(5) The shifting of nitro group from 2- or 3- to 4-position exhibited remarkable increase of antifungal activity.

(6) The methylphenoxy (XVII and XIX) and naphthoxy (XX and XXI) acetyl derivatives were totally inactive against the fungi tested.
RESULTS AND CONCLUSIONS:

On the basis of data given in the TABLE - III, the following CONCLUSIONS have been drawn:

(1) In all only bromo compounds and trichloro compounds (III to V, VI and VII) showed promising anti-inflammatory activity.

(2) The compound-VII exhibited significant anti-inflammatory activity (63.64%).

(3) It has been observed that the tribromo and trichloro phenoxy propionyl benzimidazoles (IV and VII) were found to be more active than acetyl derivatives.

(4) The tribromo and trichloro phenoxy acetyl and propionyl benzimidazoles (III, IV and VII) showed better activity as compared to their mono and disubstituted (V, VIII to XI) derivatives.

(5) The compounds—XIV and XXI were found to be totally inactive to inhibit the inflammation and compounds—I, II, IX, XI, XIII, XIX showed mild anti-inflammatory activity.

(6) The compound—XII was severely depressed the animals and it was found to be very toxic, while other compounds were found to be CNS depressant, produce atoxia and fast respiration in animals at the dose level > 200 mg/kg body weight (b.w.).
RESULTS AND CONCLUSIONS:

On the basis of the data shown in the TABLE-IV, the following CONCLUSIONS have been drawn -

(1) All the compounds showed mild to moderately better analgesic activity.

(2) The tribromophenoxy propionyl benzimidazole (IV) showed good analgesic activity.

(3) The compounds - III, V, VII, XII, XIII and XVII were found to possess moderately better analgesic activity as compared to other compounds of this series.

(4) 2-methylphenoxy acetyl benzimidazole (XVII) showed better analgesic activity as compared to 3-/4-methyl substituted compounds (XVIII and XIX).

(5) The tribromo, trichloro and trinitrophenoxy propionyl benzimidazoles (IV, VII and XIII) were showed better analgesic activity than their acetyl derivatives.

(6) Most of the compounds found to be CNS depressant, produce atoxia' and fast respiration in animals at the dose level of > 200 mg/kg b.w.

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