CHAPTER 3

SECTION I

SYNTHESIS OF SOME N-[2-(PHENOXY / BROMOPHENOXY/NITROPHENOXY)ACETYL]IMIDAZOLES
**DISCUSSION**

Imidazole (syn. iminazole and glyoxaline) is the most reactive azole. It is the isomeric with pyrazole and occurs in the purine nucleus and amino acid, histidine.

Imidazole, m.p. 90°, is a weak base, but it is more basic than pyrazole. Positions 5, 4 and 2 of imidazole have been designated as α, β and γ respectively. Since positions 4 and 5 of imidazoles are equivalent suggesting that it is a tautomeric substance (I and II).

Methyl iodide attacks imidazole in potassium hydroxide solution to form 1-methylimidazole, which when strongly heated, isomerises to 2-methyl imidazole.

The imidazole ring is extremely stable towards oxidising and reducing agents. However, hydrogen peroxide readily opens the ring to form oxamide.
Acetyl chloride and acetic anhydride have no action on imidazole but benzoyl chloride in the presence of sodium hydroxide opens the ring to form dibenzoyldiaminoethylene.

\[
\text{CH}_2\text{NH.CO.C}_6\text{H}_5 + 2 \text{C}_6\text{H}_5\text{COCl} + 3 \text{NaOH} \rightarrow \text{CH}_2\text{NH.CO.C}_6\text{H}_5 + \text{HCO}_2\text{Na} + 2 \text{NaCl}
\]

Nitration and sulphonation of imidazole produce the 4 or 5 derivatives. Electrophilic attacks at positions 4 or 5 can be accounted for by the contribution of the following resonating structures II to IV.

The imidazoles are brominated with remarkable ease. Imidazole in chloroform solution reacts with bromine to yield 2,4,5-tribromomidazole.

\[
\text{CH}_2\text{NH.CO.C}_6\text{H}_5 + 3 \text{Br}_2 \underset{\text{CHCl}_3}{\rightarrow} \text{Br}_3\text{NCH}_2\text{CO.C}_6\text{H}_5 + 3 \text{HBr}
\]

Chlorine and iodine, however, appear to react only with imidazoles containing -NH and only in alkaline solution. This presumably means that the imidazolyl anion is the reactive substance.

In imidazole molecule deprotonation takes place. The pK_a for loss of the hydrogen atom attached to nitrogen of imidazole is 14.20. It is thus a very weak acid because of the enhanced delocalization is
possible in the imidazole anion. A strong base, like sodium hydroxide is required to effect complete deprotonation.

OBJECT OF THE PRESENT WORK

Phenoxy acetic acid and its various derivatives as well as imidazole and its various derivatives are very well known to possess some important biological properties. This prompted to author to construct a molecule possessing both these moieties. With this aim some N-2 substituted phenoxy acetyl imidazoles have been synthesised and screened for their antibacterial and antifungal activities.

PRESENT WORK

The present work describes the synthesis of N-[2-(PHENOXY) acetyl] imidazole, some N-[2- (bromosubstituted phenoxy) acetyl] imidazoles, and some N-[2- (nitrosubstituted phenoxy) acetyl imidazoles by condensing the phenoxy acetyl chloride/ various bromophenoxy acetyl chlorides/ various nitrophenoxy acetyl chlorides with imidazole. The antibacterial and antifungal screening of all the synthesised compounds were performed in vitro using important human pathogenic bacteria and fungi respectively.

The various steps for the total synthesis of these compounds alongwith the 'scheme of synthesis' were the same as mentioned on page 20 in the Section-IA of Chapter-2 except that imidazole was taken instead of morpholine.

The purity of all the synthesised compounds was routinely checked by thin layer chromatography on silica gel 'G' plates. The structure of all the compounds was confirmed by elemental analyses, IR spectra and employing various chemical tests.
The structure of all the synthesised compounds is given below:

\[
\begin{align*}
R_1 & \quad \text{N-[ 2-(PHENOXY / BROMOPHENOXY / NITROPHENOXY ) ACETYL ] IMIDAZOLES} \\
R_2 & \quad \text{O-CH}_2\text{-CO-} \\
R_3 & 
\end{align*}
\]

<table>
<thead>
<tr>
<th>COMPOUNDS NUMBER</th>
<th>GROUPS ASSOCIATED</th>
</tr>
</thead>
<tbody>
<tr>
<td>XII</td>
<td>( R_1, R_2, R_3 = H )</td>
</tr>
<tr>
<td>XIII</td>
<td>( R_1, R_2, R_3 = Br )</td>
</tr>
<tr>
<td>XIV</td>
<td>( R_1, R_2 = Br; R_3 = H )</td>
</tr>
<tr>
<td>XV</td>
<td>( R_1, R_3 = Br; R_2 = H )</td>
</tr>
<tr>
<td>XVI</td>
<td>( R_1 = Br; R_2, R_3 = H )</td>
</tr>
<tr>
<td>XVII</td>
<td>( R_2 = Br; R_1, R_3 = H )</td>
</tr>
<tr>
<td>XVIII</td>
<td>( R_1, R_2, R_3 = NO_2 )</td>
</tr>
<tr>
<td>XIX</td>
<td>( R_1, R_2 = NO_2; R_3 = H )</td>
</tr>
<tr>
<td>XX</td>
<td>( R_1, R_3 = NO_2; R_2 = H )</td>
</tr>
<tr>
<td>XXI</td>
<td>( R_1 = NO_2; R_2, R_3 = H )</td>
</tr>
<tr>
<td>XXII</td>
<td>( R_2 = NO_2; R_1, R_3 = H )</td>
</tr>
</tbody>
</table>

The synthesis of the compounds (XII to XXII) has been mentioned in the Section-IB of this Chapter and their physical data (yield, m.p., solvent for crystallization, molecular formula and elemental analyses) have been summarized in TABLE-3 which is given at the end of Section-IB of this Chapter.
**SECTION - II B**

**EXPERIMENTAL**

**SYNTHESIS OF THE COMPOUND-XII: N-[2-(PHENOXY) ACETYL] IMIDAZOLE**

**SYNTHESIS OF THE PHENOXY ACETIC ACID**

It was prepared by condensing the equimolecular quantities of phenol with monochloroacetic acid by the same method as described on page 26.

**SYNTHESIS OF PHENOXY ACETYL CHLORIDE**

It was prepared by refluxing phenoxyacetic acid with thiony chloride using the same procedure as described on page 26.

**SYNTHESIS OF PHENOXY ACETYL IMIDAZOLE**

To an ice-cooled solution of imidazole (0.056 M in 30 ml of dry pyridine) in a 500 ml beaker was added 25 ml of 1N NaOH solution. The dropwise addition of phenoxy acetyl chloride with constant stirring (in about 1 hour) afforded phenoxy acetyl imidazole (compound-XII). The product was filtered, washed with sodium bicarbonate solution followed by distilled water (6 x 30 ml). It was purified over the column of neutral alumina using petroleum ether : benzene (3:7 v/v) mixture as an eluant. Finally the eluate was concentrated and the product was crystallized from petroleum ether as colourless shining needles, yield 80%, m.p. 89-91°.
THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND - XII

Thin layer chromatography was done on silica gel 'G' plates in the following solvent systems as described on page 27 which showed single spot in each case.

Solvent systems
1. Benzene : chloroform; 5:5 v/v
2. Benzene : methanol; 5:5 v/v

$R_f$ values
0.62
0.75

INFRA-RED SPECTRUM OF THE COMPOUND - XII

The significant peaks obtained in the infra-red spectrum of the compound-XII along with their structural assignments with the help of available literature$^{124-127}$ is given herein; IR (KBr) $\nu_{max}$: 2875 (C-H stretching), 1635 (C=O stretching), 1586 (C=N), 1442 (Aromatic C=C in plain vibrations), and 1040 cm$^{-1}$ (Aromatic -O) respectively.

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

SYNTHESIS OF 2,4,6 - TRIBROMOPHENOL

It was prepared by the bromination of phenol using the method as described on page 28.

SYNTHESIS OF 2,4,6 - TRIBROMOPHENOXY ACETIC ACID

It was prepared by condensing the equimolecular quantities of 2,4,6 - tribromophenol and monochloroacetic acid by the method as described on page 28.

SYNTHESIS OF 2,4,6 - TRIBROMOPHENOXY ACETYL CHLORIDE

It was prepared by refluxing 2,4,6 - tribromophenoxy acetic
acid with thionyl chloride by adopting the method as described on page 28.

SYNTHESIS OF 2,4,6 - TRIBROMOPHENOXY ACETYL IMIDAZOLE

To an ice-cooled solution of imidazole (0.052 M in 25 ml of dry pyridine) in a 500 ml beaker was added 25 ml of 1N NaOH solution. The dropwise addition of 2,4,6 - tribromophenoxy acetyl chloride (in 20 ml dry benzene) with constant stirring (in about 1 hour) afforded the desired product, 2,4,6 - tribromophenoxy acetyl imidazole (compound-XIII). The product was filtered, washed with sodium bicarbonate solution followed by distilled water (3 x 30 ml). It was purified over the column of neutral alumina using chloroform : methanol (6:4 v/v) mixture as an eluant. Finally, the eluate was concentrated and the product was crystallized from acetone as yellow shining leaflets, yield 78%, m.p. 115-117°.

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND - XIII

Thin layer chromatography was done on silica gel 'G' plates in the following solvent systems as described on page 27 which showed single spot in each case.

<table>
<thead>
<tr>
<th>Solvent systems</th>
<th>Rf values</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Chloroform : acetone;  7:3 v/v</td>
<td>0.56</td>
</tr>
<tr>
<td>2. Chloroform : methanol;  6:4 v/v</td>
<td>0.70</td>
</tr>
</tbody>
</table>

INFRARED SPECTRUM OF THE COMPOUND - XIII

The significant peaks obtained in the infrared spectrum of the compound XIII along with their structural assignments with the help
of available literature$^{124-127}$ is given herein; IR (\(\lambda_{\text{max}}^{\text{KBr}}\)) : 2860 (C-H stretching), 1625 (C=O stretching), 1590(C=N), 1440(Aromatic C=C in plain vibrations), and 1040 cm\(^{-1}\) (Aromatic -O) respectively.

**SYNTHESIS OF THE COMPOUND-XIV : N-[2-(2,4 - DIBROMOPHENOXY) ACETYL] IMIDAZOLE**

**SYNTHESIS OF 2,4 - DIBROMOPHENOL**

It was prepared by the bromination of phenol in presence of hydrobromic acid by the procedure as described on page 30.

**SYNTHESIS OF 2,4 - DIBROMOPHENOXY ACETIC ACID**

It was prepared by condensing the equimolecular quantities of 2,4 - dibromophenol and monochloroacetic acid by the method as described on page 31.

**SYNTHESIS OF 2,4 - DIBROMOPHENOXY ACETYL CHLORIDE**

It was prepared by refluxing 2,4 - dibromophenoxy acetic acid with thionyl chloride by the method as mentioned on page 31.

**SYNTHESIS OF 2,4 - DIBROMOPHENOXY ACETYL IMIDAZOLE**

To an ice-cooled solution of imidazole (0.048 M in 30 ml of dry benzene) in a 500 ml beaker was added 30 ml of 1N NaOH solution. The dropwise addition of the 2,4 - dibromophenoxy acetyl chloride (in 20 ml of dry benzene) with constant stirring (in about 45 minutes) afforded 2,4 - dibromophenoxy acetyl imidazole (compound-XIV). The product was filtered, washed with sodium bicarbonate solution followed by distilled water (3 x 30 ml). It was purified over the column of silica gel using ethyl acetate : chloroform (2:8 v/v) mixture as an eluant. Finally, the eluate was concentrated and the product was
crystallized from chloroform as pale yellow prisms, yield 72%, m.p. 112-114°.

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

Thin layer chromatography was done on silica gel 'G' plates in the following solvent systems as described on page 27 which showed single spot in each case.

<table>
<thead>
<tr>
<th>Solvent systems</th>
<th>Rf values</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Benzene : chloroform; 2:8 v/v</td>
<td>0.60</td>
</tr>
<tr>
<td>2. Benzene : methanol; 3:7 v/v</td>
<td>0.76</td>
</tr>
</tbody>
</table>

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

The significant peaks obtained in the infra-red spectrum of the compound-XIV along with their structural assignments with the help of available literature\textsuperscript{124-127} is given herein; IR (\textsuperscript{\textsuperscript{\textdegree}KBr) : 2860 (C-H stretching), 1630 (C=O stretching), 1590(C=N), 1440(Aromatic C=C in plain vibrations), and 1038 cm\textsuperscript{-1} (Aromatic -O) respectively.

**SYNTHESIS OF THE COMPOUND-XV : N-[2-(2,6 - DIBROMOPHENOXY) ACETYL] IMIDAZOLE**

**SYNTHESIS OF 2,6 - DIBROMOPHENOL**

It was prepared by the bromination of phenol in the presence of hydrobromic acid by the same method as described on page 33.

**SYNTHESIS OF 2,6 - DIBROMOPHENOXY ACETIC ACID**

Equimolecular quantities of 2,6 - dibromophenol and monochloroacetic acid were condensed and worked up as usual (page 34) to give the desired product.
SYNTHESIS OF 2,6 - DIBROMOPHENOXY ACETYL CHLORIDE

It was prepared by refluxing 2,6 - dibromophenoxy acetic acid with thionyl chloride by the same procedure as described on page 35.

SYNTHESIS OF 2,6 - DIBROMOPHENOXY ACETYL IMIDAZOLE

To an ice-cooled solution of imidazole (0.038 M in 25 ml of dry pyridine) in a 500 ml beaker was added 30 ml of 1N NaOH solution. The dropwise addition of 2,6 - dibromophenoxy acetyl chloride (in 20 ml of dry benzene) with constant stirring (in about 1 hour) afforded 2,6 - dibromophenoxy acetyl imidazole (compound-XV). The product was filtered, washed with sodium bicarbonate solution followed by distilled water (4 x 30 ml). It was purified over the column of silica gel using benzene : chloroform (8:2 v/v) mixture as an eluant. Finally, the eluate was concentrated and the product was crystallized as pale yellow needles from chloroform, yield 81%, m.p. 98°.

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND - XV

Thin layer chromatography was done on silica gel 'G' plates in the following solvent systems as described on page 27 which showed single spot in each case.

Solvent systems

<table>
<thead>
<tr>
<th>Solvent systems</th>
<th>Rf values</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Benzene : chloroform; 2:8 v/v</td>
<td>0.50</td>
</tr>
<tr>
<td>2. Benzene : methanol; 3:7 v/v</td>
<td>0.70</td>
</tr>
</tbody>
</table>

INFRA-RED SPECTRUM OF THE COMPOUND - XV

The significant peaks obtained in the infra-red spectrum of the compound-XV along with their structural assignments with the help of available literature 124-127 is given herein; IR (\( \text{KBr}\)) : 2860
(C-H stretching), 1630 (C=O stretching), 1586(C=N), 1440 (Aromatic C=C in plain vibrations), and 1038 cm⁻¹ (Aromatic -O) respectively.

**SYNTHESIS OF THE COMPOUND-XVI : N-[2-(2-BROMOPHENOXY) ACETYL] IMIDAZOLE**

**SYNTHESIS OF 2 - BROMOPHENOL**

It was prepared by the bromination of phenol by the method as described on page 36.

**SYNTHESIS OF 2 - BROMOPHOXY ACETIC ACID**

Equimolecular quantities of 2-bromophenol and monochloro-acetic acid were condensed and worked up as usual (page 37) to yield the desired product.

**SYNTHESIS OF 2 - BROMOPHOXY ACETYL CHLORIDE**

It was prepared by refluxing 2 - bromophenoxy acetic acid with thionyl chloride by the method as described on page 38.

**SYNTHESIS OF 2 - BROMOPHENOXY ACETYL IMIDAZOLE**

To an ice-cooled solution of imidazole (0.042 M in 30 ml of dry pyridine) in a 500 ml beaker was added 30 ml of 1N NaOH solution. The dropwise addition of 2 - bromophenoxy acetyl chloride with constant stirring (in about 50 minutes) afforded 2 - bromophenoxy acetyl imidazole (compound-XVI). The product was filtered, washed with sodium bicarbonate solution followed by distilled water (5 x 30 ml). It was purified over the column of neutral alumina using acetone : methanol (6:4 v/v) mixture as an eluant. Finally, the eluate was concentrated and the product was crystallized as light yellow coloured crystals from ethyl acetate, yield 74%, m.p. 126°.
THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND - XVI

Thin layer chromatography was done on silica gel 'G' plates in the following solvent systems as described on page 27 which showed single spot in each case.

Solvent systems

1. Benzene : methanol; 8:2 v/v  
2. Chloroform : methanol; 8:2 v/v

$R_f$ values

0.71
0.78

INFRA-RED SPECTRUM OF THE COMPOUND - XVI

The significant peaks obtained in the infra-red spectrum of the compound-XVI along with their structural assignments with the help of available literature$^{124-127}$ is given herein; IR (KBr) $^{\text{max}}$ : 2856 (C-H stretching), 1632 (C=O stretching), 1586 cm$^{-1}$ (Aromatic -C=C- in plain vibrations), and 1040 cm$^{-1}$ (Aromatic -O) respectively.

SYNTHESIS OF THE COMPOUND-XVII : N-[2-(4-BROMOPHENOXY) ACETYL] IMIDAZOLE

SYNTHESIS OF 4 - BROMOPHENOL

It was prepared by the bromination of phenol as given on page 39.

SYNTHESIS OF 4 - BROMOPHENOXY ACETIC ACID

Equimolecular quantities of 4 - bromophenol and monochloroacetic acid were condensed and worked up as usual (page 40) to afford the desired product.

SYNTHESIS OF 4 - BROMOPHENOXY ACETYL CHLORIDE

It was prepared by refluxing 4 - bromophenoxy acetic acid with thionyl chloride by adopting the method as described on page 40.
SYNTHESIS OF 4 - BROMOPHENOXO ACETYL IMIDAZOLE

To an ice-cooled solution of imidazole (0.036 M in 25 ml of dry benzene) in a 500 ml beaker was added 25 ml of 1N NaOH solution. The dropwise addition of 4 - bromophenoxo acetyl chloride (in 20 ml dry benzene) with constant stirring (in about 40 minutes) afforded 4 - bromophenoxo acetyl imidazole (compound-XVII). The product was filtered, washed with sodium bicarbonate solution followed by distilled water (3 x 30 ml). It was purified over the column of neutral alumina using petroleum ether : benzene (8:2 v/v) mixture as an eluant. Finally, the eluate was concentrated and the product was crystallized from benzene as light yellow coloured prisms, yield 73%, m.p. 142°.

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND - XVII

Thin layer chromatography was done on silica gel 'G' plates in the following solvent systems as described on page 27 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; 6:4 v/v</td>
<td>0.46</td>
</tr>
<tr>
<td>2. Benzene : chloroform; 2:8 v/v</td>
<td>0.65</td>
</tr>
</tbody>
</table>

INFRA-RED SPECTRUM OF THE COMPOUND - XVII

The significant peaks obtained in the infra-red spectrum of the compound-XVII along with their structural assignments with the help of available literature124-127 is given herein; IR (KBr) max : 2882 (C-H stretching), 1644 (C=O stretching), 1588(C=N), 1445(Aromatic C=C in plain vibrations), and 1030 cm⁻¹ (Aromatic -O) respectively.
SYNTHESIS OF THE COMPOUND-XVIII : N-[2-(2,4,6- TRINITROPHENOXY) ACETYL] IMIDAZOLE

SYNTHESIS OF 2,4,6 - TRINITROPHENOL

It was prepared by the nitration of phenol as described on page 42.

SYNTHESIS OF 2,4,6 - TRINITROPHENOXY ACETIC ACID

Equimolecular quantities of 2,4,6 - trinitrophenol and monochloroacetic acid were condensed and worked up as usual (page 42) to give the product.

SYNTHESIS OF 2,4,6 - TRINITROPHENOXY ACETYL CHLORIDE

It was prepared by refluxing 2,4,6 - trinitrophenoxyc acid with thionyl chloride by the method as described on page 43.

SYNTHESIS OF 2,4,6 - TRINITROPHENOXY ACETYL IMIDAZOLE

To an ice-cooled solution of imidazole (0.06 M in 60 ml of dry pyridine) in a 500 ml beaker was added 30 ml of 1N NaOH solution. The dropwise addition of 2,4,6 - trinitrophenoxyc acetyl chloride (in 20 ml dry benzene) with constant stirring (in about 1 hour) afforded 2,4,6 - trinitrophenoxyc acetyl imidazole (compound-XVIII). The product was filtered, washed with sodium bicarbonate solution followed by distilled water (4 x 30 ml). It was purified over the column of silica gel using chloroform : ethyl acetate (8:2 v/v) mixture as an eluant. Finally the eluate was concentrated and the product was crystallized from benzene : chloroform (2:8 v/v) mixture as pale yellow needles, yield 62%, m.p. 114-116\(^\circ\).
THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND - XVIII

Thin layer chromatography was done on silica gel 'G' plates in the following solvent systems as described on page 27 which showed single spot in each case.

Solvent systems

1. Benzene : methanol; 4:6 v/v
   \[ R_f \text{ value} = 0.56 \]

2. Chloroform : methanol; 3:7 v/v
   \[ R_f \text{ value} = 0.68 \]

INFRA-RED SPECTRUM OF THE COMPOUND - XVIII

The significant peaks obtained in the infra-red spectrum of the compound-XVIII along with their structural assignments with the help of available literature\(^{124-127}\) is given herein; IR \( \nu_{\max}^{\text{KBr}} \) : 2882 (C-H stretching), 1642 (C=O stretching), 1582(C-N), 1505 (nitro group attached to phenyl ring), 1445 (Aromatic -C=C- in plain vibrations), and 1030 cm\(^{-1}\) (Aromatic -O) respectively.

SYNTHESIS OF THE COMPOUND-XIX: N-[2-(2,4 - DINITROPHENOXY) ACETYL] IMIDAZOLE

SYNTHESIS OF 2,4 - DINITROPHENOL

It was prepared by nitration of phenol as described on page 44.

SYNTHESIS OF 2,4 - DINITROPHENOXY ACETIC ACID

Equimolecular quantities of 2,4 - dinitrophenol and monochloroacetic were condensed and worked up as usual (page 45) to yield the desired product.
SYNTHESIS OF 2,4 - DINITROPHENOXY ACETYL CHLORIDE

It was prepared by refluxing 2,4 - dinitrophenoxoy acetic acid with thionyl chloride by adopting the method as described on page 45.

SYNTHESIS OF 2,4 - DINITROPHENOXY ACETYL IMIDAZOLE

To an ice-cooled solution of imidazole (0.036 M in 25 ml of dry benzene) in a 500 ml beaker was added 30 ml of 1N NaOH solution. The dropwise addition of 2,4 - dinitrophenoxoy acetyl chloride (in 20 ml dry benzene) with constant stirring (in about 45 minutes) afforded 2,4 - dinitrophenoxoy acetyl imidazole (compound-XIX). The product was filtered, washed with sodium bicarbonate solution followed by distilled water (3 x 30 ml). It was purified over the column of silica gel using acetone : methanol (6:4 v/v) mixture as an eluant. Finally, the eluate was concentrated and the product was crystallized as yellow rectangular prisms with acetone, yield 62%, m.p. 216-218°.

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND - XIX

Thin layer chromatography was done on silica gel 'G' plates in the following solvent systems as described on page 27 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. Chloroform : methanol; 5:5 v/v</td>
<td>0.82</td>
</tr>
<tr>
<td>2. Acetone : methanol; 6:4 v/v</td>
<td>0.86</td>
</tr>
</tbody>
</table>

INFRA-RED SPECTRUM OF THE COMPOUND - XIX

The significant peaks obtained in the infra-red spectrum of the compound-XIX alongwith their structural assignments with the help of available literature[124-127] is given herein; IR (ν_max) : 2875
(C-H stretching), 1644 (C=O stretching), 1586(C=N), 1502 (nitro group attached to phenyl ring), 1435 (Aromatic -C=C- in plain vibrations), and 1030 cm\(^{-1}\) (Aromatic -O) respectively.

**SYNTHESIS OF THE COMPOUND-XX : N-[2-(2,6 - DINITROPHENOXY) ACETYL] IMIDAZOLE**

**SYNTHESIS OF 2,6 - DINITROPHENOL**

It was prepared by the nitration of phenol as described on page 47.

**SYNTHESIS OF 2,6 - DINITROPHENOXY ACETIC ACID**

Equimolecular quantities of 2,6 - dinitrophenol and monochloro acetic acid were condensed and worked up as usual (page 47) to give the desired product.

**SYNTHESIS OF 2,6 - DINITROPHENOXY ACETYL CHLORIDE**

It was prepared by refluxing 2,6 - dinitrophenoxy acetic acid with thionyl chloride by the method as described on page 48.

**SYNTHESIS OF 2,6 - DINITROPHENOXY ACETYL IMIDAZOLE**

To an ice-cooled solution of imidazole (0.044 M in 25 ml of dry pyridine) in a 500 ml beaker was added 25 ml of 1N NaOH solution. The dropwise addition of 2,6 - dinitrophenoxy acetyl chloride (in 20 ml dry benzene) with constant stirring (in about 50 minutes) afforded 2,6 - dinitrophenoxy acetyl imidazole (compound-XX). The product was filtered, washed with sodium bicarbonate solution followed by distilled water (3 x 30 ml). It was purified over the column of silica gel using acetone : methanol (5:5 v/v) mixture as an eluant. Finally, the eluate
was concentrated and the product was crystallized as yellow coloured shining needles with benzene : chloroform (6:4 v/v) mixture, yield 58%, m.p. 222°.

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND - XX

Thin layer chromatography was done on silica gel 'G' plates in the following solvent systems as described on page 27 which showed single spot in each case.

Solvent systems
1. Benzene : chloroform; 8:2 v/v
2. Chloroform : methanol; 9:4 v/v

$R_f$ values
- 0.38
- 0.60

INFRA-RED SPECTRUM OF THE COMPOUND - XX

The significant peaks obtained in the infra-red spectrum of the compound-XX along with their structural assignments with the help of available literature is given herein; IR (KBr): $2878$ (C-H stretching), $1632$ (C=O stretching), $1580$ (C=N) $1498$ (nitro group attached to phenyl ring), $1434$ (Aromatic -C=C- in plane vibrations), and $1028$ cm$^{-1}$ (Aromatic -O) respectively.

SYNTHESIS OF THE COMPOUND-XXI : N-[2-(2-NITROPHENOXY) ACETYL] IMIDAZOLE

SYNTHESIS OF 2 - NITROPHENOL

It was prepared by the nitration of phenol as described on page 49.

SYNTHESIS OF 2 - NITROPHENOXY ACETIC ACID

Equimolecular quantities of 2-nitrophenol and monochloroacetic acid were condensed and worked up as usual (page 50) to yield the desired product.
SYNTHESIS OF 2 - NITROPHENOXY ACETYL CHLORIDE

It was prepared by refluxing 2 - nitrophenoxy acetic acid with thionyl chloride by the method as described on page 50.

SYNTHESIS OF 2 - NITROPHENOXY ACETYL IMIDAZOLE

To an ice-cooled solution of imidazole (0.046 M in 40 ml of dry pyridine) in a 500 ml beaker was added 30 ml of 1N NaOH solution. The dropwise addition of 2 - nitrophenoxy acetyl chloride (in 20 ml dry benzene) with constant stirring (in about 30 minutes) afforded 2 - nitrophenoxy acetyl imidazole (compound-XXI). The product was filtered, washed with sodium bicarbonate solution followed by distilled water (3 x 30 ml). It was purified over the column of neutral alumina using chloroform : acetone (8:2 v/v) mixture as an eluant. Finally, the eluate was concentrated and the product was crystallized with benzene : chloroform (2:8 v/v) mixture as yellowish leaflets, yield 58%, m.p. 190-192°.

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND - XXI

Thin layer chromatography was done on silica gel 'G' plates in the following solvent systems as described on page 27 which showed single spot in each case.

\[
\text{Solvent systems} \quad \text{R}_f \text{ values}
\]

1. Benzene : chloroform; 8:2 v/v \quad 0.52
2. Chloroform : methanol; 8:2 v/v \quad 0.94

INFRA-RED SPECTRUM OF THE COMPOUND - XXI

The significant peaks obtained in the infra-red spectrum of the compound-XXI alongwith their structural assignments with the help
of available literature\textsuperscript{124-127} is given herein; IR (\(\nu\)KBr\textsubscript{max}) : 2878 (C-H stretching), 1642 (C=O stretching), 1584 (C=N), 1500 (nitro group attached to phenyl ring), 1436 (Aromatic -C=C- in plain vibrations), and 1015 cm\textsuperscript{-1} (Aromatic -O) respectively.

**SYNTHESIS OF THE COMPOUND-XXII : N-[2-(4-NITROPHENOXY) ACETYL] IMIDAZOLE**

**SYNTHESIS OF 4 - NITROPHENOL**

It was prepared by the nitration of phenol as described on page 52.

**SYNTHESIS OF 4 - NITROPHENOXY ACETIC ACID**

Equimolecular quantities of 4 - nitrophenol and monochloroacetic acid were condensed and worked up as usual (page 52) to give the desired product.

**SYNTHESIS OF 4 - NITROPHENOXY ACETYL CHLORIDE**

It was prepared by refluxing 4 - nitrophenoxy acetic acid and thionyl chloride by adopting the method as described on page 53.

**SYNTHESIS OF 4 - NITROPHENOXY ACETYL IMIDAZOLE**

To an ice-cooled solution of imidazole (0.045 M in 30 ml of dry pyridine) in a 500 ml beaker was added 30 ml of 1N NaOH solution. The dropwise addition of 4-nitrophenoxy acetyl chloride (in 20 ml dry benzene) with constant stirring (in about 40 minutes) afforded 4 - nitrophenoxy acetyl imidazole, (compound-XXII). The product was filtered, washed with sodium bicarbonate solution followed by distilled water (3 x 30 ml). It was purified over the column of neutral alumina using acetone : methanol (8:2 v/v) mixture as an eluant. Finally, the
eluate was concentrated and the product was crystallized as yellow
coloured needles with ethyl acetate: acetone (4:6 v/v) mixture,

THIN LAYER CHROMATOGRAPHY EXAMINATION OF THE COMPOUND - XXII

Thin layer chromatography was done on silica gel 'G' plates
in the following solvent systems as described on page 27 which showed
single spot in each case.

<table>
<thead>
<tr>
<th>Solvent systems</th>
<th>Rf values</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Chloroform : methanol; 6:4 v/v</td>
<td>0.82</td>
</tr>
<tr>
<td>2. Chloroform : methanol; 5:5 v/v</td>
<td>0.88</td>
</tr>
</tbody>
</table>

INFRA-RED SPECTRUM OF THE COMPOUND - XXII

The significant peaks obtained in the infra-red spectrum of
the compound-XXII along with their structural assignments with the help
of available literature\textsuperscript{124-127} is given herein; IR (\(\text{KBr, cm}^{-1}\)) : 2878
(C-H stretching), 1638 (C=O stretching), 1580(C=N), 1495(nitro group
attached to phenyl ring), 1442 (Aromatic -C=C- in plain vibrations),
and 1028 cm\(^{-1}\) (Aromatic -O) respectively.
### Table - 3

Characterization Data of the Synthesized Compounds (XII to XXII)

<table>
<thead>
<tr>
<th>Compounds Number</th>
<th>$R_1$</th>
<th>$R_2$</th>
<th>$R_3$</th>
<th>Molecular Formula</th>
<th>Solvent for Crystallization</th>
<th>M.P. $^\circ$C</th>
<th>Yield (%)</th>
<th>Composition % Calculated (Found)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>XII</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>$C_{11}H_{10}O_N_2$</td>
<td>Benzene</td>
<td>102-104</td>
<td>78</td>
<td>C: 65.34 (65.31) H: 4.95 (4.95) N: 13.86 (13.83) Br: - ( - )</td>
</tr>
<tr>
<td>XIII</td>
<td>Br</td>
<td>Br</td>
<td>Br</td>
<td>$C_{11}H_{9.72}O_N_2$</td>
<td>Solvent ether</td>
<td>115-117</td>
<td>74</td>
<td>C: 30.06 (30.04) H: 1.59 (1.59) N: 6.37 (6.37) Br: 54.66 (54.61)</td>
</tr>
<tr>
<td>XIV</td>
<td>Br</td>
<td>Br</td>
<td>H</td>
<td>$C_{11}H_{8.22}O_N_2$</td>
<td>Chloroform</td>
<td>112-114</td>
<td>72</td>
<td>C: 36.66 (36.67) H: 2.22 (2.22) N: 7.77 (7.75) Br: 44.44 (44.40)</td>
</tr>
<tr>
<td>XV</td>
<td>Br</td>
<td>H</td>
<td>Br</td>
<td>$C_{11}H_{8.22}O_N_2$</td>
<td>Chloroform</td>
<td>98</td>
<td>81</td>
<td>C: 36.66 (36.62) H: 2.22 (2.21) N: 7.77 (7.77) Br: 44.44 (44.41)</td>
</tr>
<tr>
<td>XVI</td>
<td>Br</td>
<td>H</td>
<td>H</td>
<td>$C_{11}H_{8.22}O_N_2$</td>
<td>Ethyl acetate</td>
<td>126</td>
<td>74</td>
<td>C: 46.97 (46.93) H: 3.20 (3.21) N: 9.96 (9.94) Br: 28.46 (28.40)</td>
</tr>
<tr>
<td>XVII</td>
<td>H</td>
<td>Br</td>
<td>H</td>
<td>$C_{11}H_{8.22}O_N_2$</td>
<td>Benzene</td>
<td>142</td>
<td>73</td>
<td>C: 46.97 (46.90) H: 3.20 (3.26) N: 9.96 (9.92) Br: 28.46 (28.40)</td>
</tr>
<tr>
<td>XVIII</td>
<td>NO$_2$</td>
<td>NO$_2$</td>
<td>NO$_2$</td>
<td>$C_{11}H_{9.4}_8O_N_5$</td>
<td>Solvent: chloroform (2:8 v/v)</td>
<td>114-116</td>
<td>62</td>
<td>C: 39.16 (39.15) H: 2.07 (2.06) N: 20.77 (20.80) Br: - ( - )</td>
</tr>
<tr>
<td>XIX</td>
<td>NO$_2$</td>
<td>NO$_2$</td>
<td>H</td>
<td>$C_{11}H_{9.4}_8O_N_4$</td>
<td>Acetone</td>
<td>216-218</td>
<td>62</td>
<td>C: 45.20 (45.21) H: 2.73 (2.72) N: 19.17 (19.15) Br: - ( - )</td>
</tr>
<tr>
<td>XX</td>
<td>NO$_2$</td>
<td>H</td>
<td>NO$_2$</td>
<td>$C_{11}H_{9.4}_8O_N_4$</td>
<td>Solvent: chloroform (6:4 v/v)</td>
<td>222</td>
<td>58</td>
<td>C: 45.20 (45.18) H: 2.73 (2.68) N: 19.17 (19.19) Br: - ( - )</td>
</tr>
<tr>
<td>XXI</td>
<td>NO$_2$</td>
<td>H</td>
<td>H</td>
<td>$C_{11}H_{9.4}_8O_N_3$</td>
<td>Solvent: chloroform (2:8 v/v)</td>
<td>190-192</td>
<td>58</td>
<td>C: 53.44 (53.40) H: 3.64 (3.62) N: 17.00 (16.96) Br: - ( - )</td>
</tr>
<tr>
<td>XXII</td>
<td>H</td>
<td>NO$_2$</td>
<td>H</td>
<td>$C_{11}H_{9.4}_8O_N_3$</td>
<td>Ethyl acetate:acetone (6:4 v/v)</td>
<td>202</td>
<td>65</td>
<td>C: 53.44 (53.42) H: 3.64 (3.64) N: 17.00 (17.00) Br: - ( - )</td>
</tr>
</tbody>
</table>

*Composition given in parentheses was found value.
SECTION II

EVALUATION OF ANTIMICROBIAL ACTIVITY
SECTION - IIA

EVALUATION OF ANTIBACTERIAL AND ANTIFUNGAL ACTIVITIES
OF THE SYNTHESISED COMPOUNDS (XII to XXII)

INTRODUCTION

The use of any drug in the treatment of disease may be discussed under two heads. The first of these include the drugs that are used in the treatment and cure of specific diseases and the second category is the one which has the characteristic effect upon the animals and organisms but are not the specific remedies for a particular disease for example morphine, cocain etc.

The development of new drugs depends upon clinical trials and its use in medicine. A successful drug would be one which is (a) readily absorbed and slowly excreted and (b) having low toxicity to invading organisms. This relationship is frequently gained by the ratio Maximum tolerated dose (MTD) Maximum curared dose (MCD) which is called the chemotherapeutic index and larger the ratio the safer would be the drug.

These two factors depends upon mainly on the relationship between biological activity and chemical constitution of a particular drug. These relationships are identical to serve as a guiding factor in mapping the structural features of the compounds with analogous activities; hopefully more potent, more specific and less toxic. The biological activity of the drug is not the sum of the activities of groups or atoms present in it but due to the molecule as a whole. The individual activity of all the groups or atoms associated in the molecule is changed during the synthesis of the drug.
The idea about the structure activity relationship underwent gradual changes with the advancement in the knowledge of chemical and physical properties of the molecule. Even the most advanced and carefully considered theories have not revealed regularities in the relation of chemical structures to physiological actions which could be used indiscriminately in one series of compounds after proving their value in the other. According to W.A. Sexton\textsuperscript{163} physical properties and reactivity of a molecule after the structural variations may cause changes in distribution in the cells and tissues and access the active sites of enzymes and receptors in reaction rates at such sites and in excretion patterns.

This attractive hypothesis suggested a new approach in chemotherapeutic research with comprised of the trials of compounds closely related to an essential metabolite of a micro-organism. The slightest change in structure often does produce considerable change in biological properties. Therefore, in evaluating structure activity relationship, the total picture of steric factor, electron density, localisation and the resultant physical and chemical reactivities of a given compound need be considered.

Chemotherapeutic value of a compound is usually determined in different stages. First the preliminary \textit{in vitro} tests are performed and if the compounds are found active in such tests, these are subjected \textit{in vivo} tests along with the tests to determine their toxicity in order to find their possible practical usefulness as a drug.
SECTION - IIB

EXPERIMENTAL

This portion has been divided into two heads;
(a) Evaluation of antibacterial activity; and
(b) Evaluation of antifungal activity.

(a) EVALUATION OF ANTIBACTERIAL ACTIVITY

Various methods\textsuperscript{164-171} are available for the evaluation of the antibacterial activity of different types of compounds. However, the most widely used method consists in determining the antibacterial activity of the drug by adding it in varying concentrations to the cultures of the test organisms. In the present work, activities of the synthesised compounds were evaluated by the cup-plate agar diffusion method\textsuperscript{172}. The main aim of these investigations was to study the changes in the activity with the variation in the structure of the molecule and thereby establishing a correlation between the structure of the compounds and their antibacterial properties.

N - [ 2 - (Phenoxy / Bromophenoxy / nitrophenoxy) acetyl ] imidazoles synthesised in the section-IB of this Chapter have been screened \textit{in vitro} against the following six bacteria.

(A) \textit{Pseudomonas pyocyaneae}
(B) \textit{Escherichia coli}
(C) \textit{Pseudomonas ovalis}
(D) \textit{Bacillus migaterium}
(E) \textit{Vibro cholera}
(F) \textit{Bacillus cereus}
The cup-plate agar diffusion method consists of the following steps.

1. Preparation of the medium, its sterilization and tubing;
2. Treatment of the glass apparatus and its sterilization;
3. Pouring of the needed medium into sterilized petridishes and cutting of the cups;
4. Preparation of the required concentration of drug and their pouring into the cups;
5. Incubation at particular temperature;

Out of the different steps in the above method, the most important is the selection of the suitable medium and its preparation because it is the composition of the medium which exerts greatest influence upon the activity of a compound. The other factors which influence the in vitro tests are:

1. The kind and condition of the test organisms.
2. The concentration of the drug solution and the dilution of the drug at the site of action (incubation period).
3. Environment factors which may augment or counteract the interaction of the drug and the parasite.
4. Temperature of the incubation because for each bacteria there is an optimal temperature and for most of the pathogenic bacteria this temperature is $37^\circ$.
5. pH of the medium which is usually in the range of 7.2 to 7.6.
In the present work, with the above mentioned bacteria the nutrient agar medium is employed which has the following composition:

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peptone</td>
<td>10 g</td>
</tr>
<tr>
<td>Beef extract</td>
<td>3.0 g</td>
</tr>
<tr>
<td>Yeast extract</td>
<td>1.5 g</td>
</tr>
<tr>
<td>Sodium chloride</td>
<td>1.5 g</td>
</tr>
<tr>
<td>Glucose</td>
<td>1.0 g</td>
</tr>
<tr>
<td>Distilled water</td>
<td>1000 ml</td>
</tr>
<tr>
<td>Agar-agar</td>
<td>17.5 g</td>
</tr>
</tbody>
</table>

For the preparation of the medium all the above ingredients except agar-agar were weighted and dissolved in water (500 ml) by application of gentle heat. After the ingredients were dissolved completely, more distilled water (500 ml) was added. The pH of the medium was adjusted in the range of 7.5 ± 0.1 and then the weighted quantity of agar-agar was added to this solution and the mixture autoclaved for half an hour. The hot media was filtered through cotton to obtain a clear solution. The medium thus prepared was transferred in different culture tubes in 40 ml portions. The tubes plugged with cotton were sterilized by steaming in an autoclave at 20 lbs/sq inch for an hour. All the glass apparatus were cleaned with chromic acid and then sterilized by keeping in an oven.

After autoclaving the media in tubes, it was allowed to cool up to 60° and then 0.4 ml of the medium (without agar-agar) containing test organisms, was added to each tube. The tubes were shaken well and then this inoculated media was poured into sterilized petri-dishes. The
dishes were shaken well for homogeneous distribution of the microorganisms and then kept in refrigerator for solidification for an hour.

The dishes were taken out and the area of the medium was divided into four parts with the glass marking pencil. Five holes, one in each part and one in centre with a diameter of 5 mm were cut with a sterilized cutter. The test solution having concentrations of 25 μg/ml and 50 μg/ml were prepared by dissolving the compound in dimethylformamide (DMF) which also works as a control. Solutions of four different compounds having the concentrations of 25 μg/ml were poured in to four holes of the petri-dish, while in the second petri-dish, solutions of the concentration of 50 μg/ml of the same compounds were poured in the holes marked with the same numbers as in the first dish. The control hole of both the petri-dishes were filled with DMF (control). Similar experiments were repeated with other compounds and then all the petri-dishes were transferred to an incubator maintained at 37°C and left for 24 hours. The zone of inhibition formed were measured and compared with that of dimethylformamide to evaluate the zone of inhibition due to the test compound.

In the present work the activity of the compounds are measured by (+), (++), (+++) and (++++) depending upon the diameter and clarity of the zones of inhibition. Each (+) indicates a difference of 2 mm in the diameter of the zones of inhibition. When there were no zones of inhibition the results have been indicated by (-) in the table.

The antibacterial activity of all the synthesised compounds (XII to XXII) has given in the TABLE - 4.
(b) **EVALUATION OF ANTIFUNGAL ACTIVITY**

All the synthesised compounds (XII to XXII) were also screened for their antifungal activity *in vitro* against the following four fungi.

(A) *Aspergillus niger*

(B) *Aspergillus fumigatus*

(C) *Candida albicans*

(D) *Curvularia lunata*

There are several methods available for recording the antifungal activity of the compounds. The one which is in common use\(^\text{175}\) in recent time has been adopted and this method consists of the following steps.

(1) **STERILIZATION OF THE APPARATUS**

All the glass apparatus were cleaned with chromic acid followed by distilled water and then sterilized by heating at 200\(^\circ\)C in a hot air oven.

(2) **PREPARATION OF THE MEDIUM**

Czapek Dox Nutre (Thom and Raper) medium was used which consists of:

<table>
<thead>
<tr>
<th>Component</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sucrose</td>
<td>30 g</td>
</tr>
<tr>
<td>MgSO(_4)</td>
<td>0.5 g</td>
</tr>
<tr>
<td>KCl</td>
<td>0.5 g</td>
</tr>
<tr>
<td>H(_2)PO(_4)</td>
<td>0.5 g</td>
</tr>
<tr>
<td>Yeast extract</td>
<td>5.0 g</td>
</tr>
<tr>
<td>FeSO(_4).7H(_2)O)</td>
<td>0.002 g</td>
</tr>
<tr>
<td>NaNO(_3)</td>
<td>0.02 g</td>
</tr>
<tr>
<td>Streptopenicillin</td>
<td>0.2 g</td>
</tr>
<tr>
<td>Distilled water</td>
<td>1000 g</td>
</tr>
</tbody>
</table>
Streptopenicillin was used to check the growth of undesirable bacteria. The above mentioned ingredients were weighted and dissolved in 500 ml of distilled water. After the ingredients were dissolved completely, more distilled water was added to make the solution upto one litre and the pH of the medium was in the range of 7.6 ± 0.1. The medium was heated in an autoclave for half an hour and then transferred in 100 ml portions in previously sterilized conical flask fitted with cotton plugs. The solution in conical flasks were again autoclaved at 151 lbs/sq. inch for one hour and then used for the work.

Fairly uniform suspension of the spores of the four fungi in sterilized distilled water was prepared.

A known concentrations of the compounds to be tested for its fungicidal activity in dimethylformamide was prepared and diluted to give a test solution of dilution 25 μg/ml and 50 μg/ml. 0.1 ml of the spore suspension was added to the liquid medium kept in the conical flasks followed by 1 ml of the solution of the compound under investigation.

For each compound two replica were prepared in this manner and similarly two replica of control were prepared in which only 1 ml of pure DMF was added. The conical flasks were left for 15 days and the contents were periodically shaken well. After fifteen days fungus mass was filtered and washed well with water to remove any impurities of the nutrient, dried in an incubator maintained at 60° and finally weighted.
The amount of the growth inhibition was calculated by the following expression.

\[ I \% = \frac{C - T}{C} \times 100 \]

where: \( I \) = Inhibition
\( C \) = Growth of control in grams/15 days
\( T \) = Growth of the created fungus in grams/15 days.

The percent for inhibition values for two independent experiments were averaged for each of test compounds. The results of the antifungal tests of all the synthesised compounds (XII to XXII) at 25 \( \mu \text{g/ml} \) and 50 \( \mu \text{g/ml} \) concentrations are given in TABLE - 5.

The results for the antifungal inhibition has been compared with the standard compound griseofulvin whose activity was also tested at 25 \( \mu \text{g/ml} \) and 50 \( \mu \text{g/ml} \) against all fungal species mentioned above.
**TABLE - 4**

**ANTIBACTERIAL ACTIVITY OF THE SYNTHESISED COMPOUNDS (XII to XXII)**

<table>
<thead>
<tr>
<th>COMPOUNDS NUMBER</th>
<th>A</th>
<th></th>
<th></th>
<th>B</th>
<th></th>
<th></th>
<th>C</th>
<th></th>
<th></th>
<th>D</th>
<th></th>
<th></th>
<th>E</th>
<th></th>
<th></th>
<th>F</th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>25 µg/ml</td>
<td>50 µg/ml</td>
<td></td>
<td>25 µg/ml</td>
<td>50 µg/ml</td>
<td></td>
<td>25 µg/ml</td>
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<td>25 µg/ml</td>
<td>50 µg/ml</td>
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<td>25 µg/ml</td>
<td>50 µg/ml</td>
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<td>25 µg/ml</td>
<td>50 µg/ml</td>
</tr>
<tr>
<td>XII</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>-</td>
<td>++</td>
<td>+</td>
<td>-</td>
<td>+</td>
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<td>+</td>
<td>++</td>
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</tr>
<tr>
<td>XIII</td>
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<td>++</td>
<td>+++</td>
<td>-</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
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</tr>
<tr>
<td>XIV</td>
<td>++</td>
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<td>++</td>
<td>+++</td>
<td>+</td>
<td>++</td>
<td>-</td>
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<td>+</td>
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<td>XVII</td>
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<td>++</td>
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<td>+</td>
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</tr>
<tr>
<td>XVIII</td>
<td>-</td>
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<td>-</td>
<td>-</td>
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<td>-</td>
<td>-</td>
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<td>-</td>
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<td>+</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
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</tbody>
</table>

A. *Pseudomonas pyocyaneae*  
B. *Escherichia coli*  
C. *Pseudomonas ovalis*  
D. *Bacillus migaterium*  
E. *Vibrio cholera*  
F. *Bacillus cereus*
<table>
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<th>COMPOUND NUMBER</th>
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<th>B</th>
<th>C</th>
<th>D</th>
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<td>(Standard)</td>
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A. Aspergillus niger
B. Aspergillus fumigatus
C. Candida albicans
D. Curvularia lunata
RESULTS AND CONCLUSIONS

On the basis of the observations (TABLE 4 and 5), following results and conclusions have been drawn.

1. Most of the synthesised compounds exhibited mild to moderate antibacterial and antifungal activities against the selected pathogenic bacteria and fungi respectively.

2. Bromophenoxy acetyl imidazoles [compounds- (XII to XVII)] were found to be good antibacterial agents than nitrophenoxy acetyl imidazoles [ compounds- (XVIII to XXII) ] of this series.

3. As the number of bromine element from phenyl ring decreases, the antibacterial activity of the compounds was also found to be decreased.

4. Compound - XIII (tribromophenoxy acetyl imidazole) was found to possess significant antibacterial activity against Escherichia coli, Bacillus megaterium and Vibrio cholera bacteria.

5. Nitrophenoxy acetyl imidazoles [ compounds- (XVIII to XXII) ] exhibited good antifungal activity against various pathogenic fungi tested by comparing to bromophenoxy acetyl imidazoles [ compounds- (XII to XVII) ] of this series.

6. As the number of nitro group in the phenyl ring increases, the antifungal activity was also found to be decreased.

7. Compound-XXII (4-nitrophenoxy acetyl imidazole) showed significant antifungal activity against all the fungi tested.