CHAPTER III

Synthesis and Biological Activities of Hetero Analogues of Aromatic Juvabione and Dehydrojuvabione with Chain Length Shortened by One Atom
Interest in another class of cyclic juvenoids had begun with the accidental observation by Slama and Williams (85) while working in USA that the larvae of hemipteran bug, *Pyrrhocoris apterus* failed to undergo metamorphosis, while those cultivated in Prague developed normally. The source of JH activity against *P. apterus* was eventually traced to the exposure of the bugs to a specific brand of paper with which the larvae had come into contact. The active principle in American paper, the so called "paper factor" originated in Balsam fir. Bowers et al. (85) and Cerny et al. (86) were independently able to isolate, purify and characterize the JH mimicking substance (+) juvabione (3.1) which was the methylester of the already known todomatuic acid, a sesquiterpenic acid of the bisabolene series (87-89). In addition to juvabione the Czech authors also isolated and identified another biologically more active substance, dehydrojuvabione (3.2) from Slovak fir.

![Chemical structures](image)

Juvabione and dehydrojuvabione showed biological activity
exclusively against hemipterans of the family *Pyrrhocoridae*. The biological activity of the optical isomers of juvabione was also found to be very similar to juvabione (180).

Ever since the discovery of juvabione and dehydrojuvabione, and the (+) juvabiol about 20 years ago and its diastereomer about a decade ago, no other cyclic juvenoids seem to have been found to occur in nature. However, like farnesol and its derivatives, juvabione and dehydrojuvabione served as model substances in the synthesis of numerous cyclic compounds of potential JH activity. A large number of synthetic variations of juvabione and dehydrojuvabione, some of which exhibited significantly high biological activities have since appeared in literature (93,98,99).

In our laboratory, a large number of aromatic hetero analogues of juvabione and dehydrojuvabione of the following type were synthesized (101,102) some of which showed significantly high degree of JH activity (103).

\[
\begin{align*}
(3.3) & \quad R \quad X=\text{NH, O or S} \\
(3.4) & \quad R \quad X=\text{NH, O or S}
\end{align*}
\]
In the present work, various compounds having the side chain shortened by one atom as compared to the above aromatic hetero analogues of juvabione and dehydrojuvabione have been synthesized.

**Results and Discussion:**

The present work was originally aimed at synthesizing JH like substances of the type (3.16) in which a nitrogen atom has been introduced at position 1 and 5 in the side chain. The following route was contemplated (Fig. 3.1).

**Fig. 3.1**
Reagents: (a) $\text{Cl}$; (b) LAH.

Ethyl-3-amino crotonate (3.10) was prepared by passing dry ammonia through ethyl acetoacetate according to the known procedure (181). The reaction of ethyl-3-amino crotonate (3.10) with aniline and p-substituted anilines had already been attempted in our laboratory, but the yield of the products was extremely poor. It was therefore decided to perform this reaction in the presence of a catalyst. Zinc chloride, a
lewis acid, was chosen as the catalyst. When the reaction was carried out in the presence of this catalyst it went smoothly and a white solid product was obtained in very good yield. The melting point of the solid was very close to that of the product obtained without using catalyst. This product was presumed to be (3.11). The I.R. Spectrum of this product showed absorption at 3310, 3270, 1620, 1590, 1505, 1270, 1240 cm⁻¹. The absorption of carbonyl group of amide at 1620 cm⁻¹ seemed to be rather low. But the absorption values at 3310 and 3270 cm⁻¹ were indicative of N–H streching of secondary amide group. The low absorption of C= streching of amide was, therefore, attributed to the presence of conjugation of carbonyl group with a double bond which was further conjugated with the lone pair of nitrogen in the amino group. Further, intramolecular hydrogen bonding between the carbonyl group of amide and the free amino group was also possible if the molecule existed in the cis form, which would further lower down the IR absorption. If the molecule existed in trans form, an intermolecular hydrogen bonding would be expected. The zinc chloride was presumed to form a complex with carbonyl oxygen of ethyl-3-amino crotonate (3.10) making the nucleophilic attack on carbonyl carbon more facile (Fig. 3.2).
The next proposed step was to treat $N$-(3-amino-1-oxo-2-butenyl)amino benzene (3.11) with 3-methyl-2-butenoyl chloride (3.14) in order to obtain $N$-(3, 7-dimethyl-1, 5-dioxo-4-aza-2, 6-octadienyl) amino benzene (3.15) followed by lithium aluminium hydride reduction to obtain the desired product $N$-(3, 7-dimethyl-4-aza-2, 6-octadienyl) amino benzene (3.16). However, when (3.11) was treated with 3-methyl-2-butenoyl chloride a product was obtained the I.R. spectrum of which showed characteristic absorptions at 3290, 1660, 1645, 1600, 1500, 1485 cm$^{-1}$. The band at 3290, 1660 and 1645 cm$^{-1}$ could be attributed to N-H stretching and $\text{C} - \text{O}$ stretching of the secondary amide group, and the absorption at 1600, 1500 and
1485 cm\(^{-1}\) could be assigned to the presence of aromatic ring. However, it was surprising to observe that the amide carbonyl function of \((3.15)\) should have been higher than that of \((3.11)\). Since an additional amide function had been introduced in \((3.15)\) we had expected this additional amide group to absorb near 1650-1660 cm\(^{-1}\), while the original amide was expected to absorb at the same value. Since we did not observe the original amide group, we became doubtful about the structure of \((3.15)\) and therefore got the elemental analysis of \((3.15)\) and \((3.11)\) done. The elemental analysis did not agree with the purposed structures. The carbon and hydrogen values in \((3.11)\) were far lower than calculated values. The mass spectrum of \((3.11)\) was then recorded which surprisingly showed \([M]^+\) at m/e 93 which was the molecular weight of aniline. The mass spectra of \((3.12\) and \(3.13)\), which were also prepared like \((3.11)\), showed \([M]^+\) at m/e 107 and 123, which were respectively the molecular weights of p-methyl and p-methoxy aniline. The fragmentation pattern of these spectra were also like those expected from aniline, 4-methyl aniline and 4-methoxy aniline. The m.p./b.p. of the products \((3.11-3.13)\) were very different from the starting amines. This situation could be explained by assuming that aniline and p-substituted anilines had formed some such products which would give molecular ions of the starting amines in the mass spectra.

This could not be expected if the products \((3.11-3.13)\)
had formed. However, if we assume that aniline co-ordinates with zinc chloride to form a solid complex then the mass spectrum of this complex would be expected to give the \([M]^+\) of aniline if the complex decomposed into \(\text{ZnCl}_2\) and aniline during vaporisation in the mass spectrum recording. On the basis of these arguments the elemental analysis data of the products were analysed and it was observed that all the products agreed extremely well for the complexes of the structure (3.18-3.20).

\[
\begin{align*}
&\begin{array}{c}
\text{R} - \text{C}_6\text{H}_4 - \text{NH}_2 \quad \text{Zn} \\
\text{R} - \text{C}_6\text{H}_4 - \text{NH}_2 \\
\end{array} \\
&\quad \text{Cl} \\
&\quad \text{Cl}
\end{align*}
\]

3.18  R = H  
3.19  R = CH$_3$  
3.20  R = OCH$_3$

Such a complex would be expected to react with 3-methyl-2-butenoyl chloride to form the products (3.21-3.23) as given in (Fig. 3.3)
The elemental analysis agreed well with the calculated values of (3.21-3.23). However, in order to confirm the above structures the substituted anilines were directly treated with 3-methyl-2-butenoyl chloride and the products obtained were identical with the above in respect of m.p., TLC and I.R. spectra.

Compound (3.21) was tested for juvenile hormonal activity
against *Dysdercus fasciatus, Tenebrio molitor, Megoura viciae, Tetranychus urticae* and *Plutella xylostella*. The JH activity of (3.21) and JH III, a naturally occurring juvenile hormone* (26, 27)* are given in table 3.1. This compound was found to be almost as active as the natural hormone JH III.

The JH activity of (3.21) is quite favourably comparable with the JH III and it was therefore thought desirable and of considerable interest to synthesize various other compounds in which the above type of side chain is linked through hetero atom such as N, O or S to the aromatic moiety. Such compounds would be different only being one atom short from the various hetero juvabione analogues which had been synthesized and tested in our laboratory (103). The synthesis of nitrogen containing analogues was done along the following lines (Fig. 3.4).

**Fig. 3.4**

\[
\begin{align*}
\text{H}_3\text{C} & \overset{\text{C=CH-COOH}}{\xrightarrow{a}} \text{H}_3\text{C} \\
\text{H}_3\text{C} & \overset{\text{C=CH-COCl}}{\xrightarrow{a}} \\
\end{align*}
\]

(3.14)
Table 3.1: JH Activity Data of (3.21) as Compared with JH III:

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>Dysdercus fasciatus (1 ug)</th>
<th>Tenebrio molitor (1 ug)</th>
<th>Megoura viciae (50 ppm)</th>
<th>Tetranychus urticae (500 ppm)</th>
<th>Plutella xylostella (500 ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Score^a</td>
<td>% activity</td>
<td>Score^a</td>
<td>% activity</td>
<td>Score^b</td>
</tr>
<tr>
<td>3.21</td>
<td>20</td>
<td>40</td>
<td>1</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>JH III</td>
<td>20</td>
<td>40</td>
<td>5</td>
<td>10</td>
<td>0</td>
</tr>
</tbody>
</table>

Score^a: Out of 50.
Score^b: Out of 24.
Reagents: (a) SOCl₂; (b) HBr; (c) 3-Chloro-2-perbenzoic acid.
3-Methyl-2-butenoic acid was converted into its acid chloride (3.14) by treatment with thionyl chloride following the usual procedure (178). Reaction of 3-methyl butanoic acid with thionyl chloride by usual procedure (179) gave 3-methyl butanoyl chloride (3.24). 3-methyl butanol was treated with HBr to give 3-methyl butyl bromide (3.25) according to the reported procedure (158).

The reaction of aniline (3.7) with 3-methyl-2-butenoyl chloride (3.14) in dry benzene, using pyridine to bind the HCl formed, gave N-(3-methyl-1-oxo-2-butenyl) amino benzene (3.21). Same reaction was done in pyridine alone without using benzene. It gave the identical product (3.21) but the yield in the former case was better and the product was also cleaner. The amines (3.8, 3.9, 3.26, 3.27) were also treated with 3-methyl-2-butenoyl chloride (3.19) in a similar fashion to furnish the products 4-methyl-N-(3-methyl-1-oxo-2-butenyl) amino benzene (3.22) 4-methoxy-N-(3-methyl-1-oxo-2-butenyl) amino benzene (3.23), 4-chloro-N-(3-methyl-1-oxo-2-butenyl) amino benzene (3.28) and 4-nitro-N-(3-methyl-1-oxo-2-butenyl) amino benzene (3.29) respectively. The epoxidation of the double bond in the amides (3.21-3.23, 3.28, 3.29) was carried out by treatment with 3-chloroperbenzoic acid. The reaction went smoothly to form 2, 3-epoxy-derivatives (3.30-3.34).

N-(3-methyl-1-oxo-butyl) amino benzene (3.35) and its various p-substituted derivatives (3.36-3.39) were also
synthesized by the reaction of aniline and its p-substituted derivatives (3.7-3.9, 3.26, 3.27) with 3-methyl butanoyl chloride (3.24) as above.

The alkylation of aniline and various p-substituted anilines with 3-methyl butyl bromide (3.25) to obtain the amines (3.40-3.44) was done according to the reported method of H. Erdmann in the book, "Preparative Organic Chemistry", by Weygand (182).

For the syntheses of oxygen containing analogues, phenol and various p-substituted phenols were used in place of aniline. The synthetic scheme is annexed below (Fig. 3.5).

Fig. 3.5

\[
\begin{align*}
\text{CH}_3 & \quad \text{H}_2\text{C} = \text{C} - \text{CH} = \text{CH}_2 \quad \text{a} \quad \text{H}_3\text{C} - \text{C} = \text{CH} - \text{CH}_2\text{Br} \\
\text{H}_2\text{C} = \text{C} - \text{CH} = \text{CH}_2 & \quad (3.45)
\end{align*}
\]
The reaction of phenol and p-substituted phenols (3.46-3.50) with 3-methyl-2-butenoyl chloride (3.14) was carried out by mixing the two in equal molar ratio and leaving them overnight to result in the formation of (3-methyl-1-oxo-2-butenyloxy)benzene (3.51) and its p-sustituted analogues (3.52-
Similar reaction of phenol and p-substituted phenols (3.46-3.50) with 3-methyl butanoyl chloride (3.24) gave the corresponding products (3.61-3.65).

The alkylation of phenol (3.46) with 3-methyl-2-butenyl bromide (3.45) was carried out by refluxing the mixture of alkylbromide, phenol and K₂CO₃ in dry acetone for 24 hr to give the product (3-methyl-2-butenyloxy) benzene (3.51). Alkylation of substituted phenols (3.47-3.50) with 3-methyl-2-butenyl bromide (3.45) under identical conditions however, failed to give the desired products but the reaction proceeded smoothly when carried out with NaH in DMF. The alkylation of phenols (3.46-3.50) with 3-methyl butyl bromide (3.25) was also carried out as above to furnish the products (3.66-3.70).

The synthesis of N, O-di(3-methyl-1-oxo-2-butenyl)4-amino phenol (3.72) and N, O-di(3-methyl-1-oxo-butyl)4-amino phenol (3.73) was carried out by reacting two moles of corresponding acid chlorides with one mole of 4-amino phenol in presence of two moles of pyridine (Fig. 3.6).

Fig. 3.6
Similarly the reaction of thiophenol (3.74) with 3-methyl-2-butenoyl chloride (3.14) and 3-methyl butanoyl chloride (3.24) furnished the products S-(3-methyl-1-oxo-2-butenyl)thiobenzene (3.75) and S-(3-methyl-1-oxo-butyl)thiobenzene (3.77) respectively. The alkylation of thiophenol (3.74) with 3-ethyl-2-butenyl bromide (3.45) and 3-methyl-butyl bromide (3.25) was carried out by refluxing sodium salt of thiophenol with (3.45) and (3.25) in dry methanol for 12 hr to get the products S-(3-methyl-2-butenyl)thiobenzene (3.76) and S-(3-methyl butyl) thiobenzene (3.78) respectively (Fig. 3.7). The JH activity determination of these analogues showed that these analogues were completely inactive against *Dysdercus fasciatus*, *Tenebrio molitor*, *Megoura viciae*, *Tetranychus urticae* and *Plutella xylostella*. Hence no attempt was made to prepare the substituted analogues.
The identification of all the above compounds was done by elemental analysis and spectroscopic studies. The salient features of proton magnetic resonance studies of representative analogues of each series are discussed below.

**PMR Studies**

The PMR spectra of all the compounds whose synthesis are
reported in this chapter were recorded in CDCl₃ or CCl₄ solution on an EM-390 spectrometer at 90 MHz using TMS as internal standard. The FMR data of one representative in each class of compounds viz. (3.21, 3.30, 3.35, 3.40, 3.51, 3.56, 3.61, 3.66, 3.75, 3.76, 3.77 and 3.78) are presented in table 3.2 and are discussed below:

The aromatic protons in the amide (3.21 and 3.35) were observed as a complex 5H signal at 7.1-7.75. The lower field value towards 7.75 can be attributed to 2 ortho protons while the higher field value towards 7.15 can be assigned to meta and para protons. The olefinic proton in (3.21) was observed at 5.85 showing a considerable deshielding due to the -C-NH group.

The terminal gem dimethyl group gave two distinct singlets at 1.90 and 2.25 due to the different configuration of two methyl groups on double bond with respect to the carbonyl function. The former value can be attributed to the trans-methyl protons and the latter to the cis-methyl protons. Nearly same values have been reported for such cis- and trans methyl groups in ketones(174). In compound (3.35) the -C-CH₂- protons appeared at 2.15. The six protons of terminal gem dimethyl group appeared as a doublet at 1.08 while the tertiary proton appeared as a multiplet around 1.25.

The PMR spectrum of epoxides (3.30) showed two major changes from the spectrum of (3.21). The -C-O= proton appeared at 3.36 showing that the deshielding effect of
<table>
<thead>
<tr>
<th>Compound No.</th>
<th>Name of the Compound</th>
<th>PMR Data (δ values)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.21</td>
<td>N-(3-Methyl-1-oxo-2-butenyl)amino</td>
<td>7.1-7.7(5H, Ar-H); 5.8(s, 3H, olefinic H); 2.25(s, 3H, cis-CH$_3$); 1.90(3H, trans-CH$_3$); 1.08(d, 6H, gem dimethyl).</td>
</tr>
<tr>
<td>3.30</td>
<td>N-(2,3-epoxy-3-methyl-1-oxo-butyl)amino benzene</td>
<td>7.1-7.7(5H, Ar-H); 5.97(s, 1H, olefinic H); 2.25(d, 2H, -COCH$_2$); 1.25(m, 1H, -CH$_2$); 1.0(d, 6H, gem dimethyl).</td>
</tr>
<tr>
<td>3.35</td>
<td>N-(3-Methyl-1-oxo-2-butenyl)amino benzene</td>
<td>7.0-7.45(5H, Ar-H); 5.97(s, 1H, olefinic H); 2.25(d, 2H, -COCH$_2$); 1.25(m, 1H, -CH$_2$); 1.0(d, 6H, gem dimethyl).</td>
</tr>
<tr>
<td>3.51</td>
<td>(3-Methyl-1-oxo-2-butenyl)thio benzene</td>
<td>6.95-7.40(5H, Ar-H); 6.07(s, 1H, olefinic H); 2.51(t, 2H, -COCH$_2$); 1.28(m, 1H, -CH$_2$); 1.0(d, 6H, gem dimethyl).</td>
</tr>
<tr>
<td>3.61</td>
<td>S-(3-Methyl-1-oxo-2-butenyl)thiobenzene</td>
<td>7.28-7.62(5H, Ar-H); 2.51(t, 2H, -COCH$_2$); 1.0(d, 6H, gem dimethyl).</td>
</tr>
<tr>
<td>3.75</td>
<td></td>
<td>3.77</td>
</tr>
<tr>
<td>Name of the Compound</td>
<td>Compound No.</td>
<td>PMR Data (δ values)</td>
</tr>
<tr>
<td>--------------------------------------------</td>
<td>--------------</td>
<td>-----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>N-(3-Methyl butyl)amino benzene</td>
<td>3.40</td>
<td>6.9-7.2(5H, Ar-H); 3.02(t, 2H, -NH-CH₂-); 1.1-1.6(3H, -CH₂-CH₃ ); 0.95(d, 6H, gem dimethyl).</td>
</tr>
<tr>
<td>(3-Methyl-2-butenyloxy)benzene</td>
<td>3.56</td>
<td>6.88-7.3(5H, Ar-H); 4.45(d, 2H, -O-CH₂-); 5.5(m, 1H, olefinic H); 1.75(d, 6H, gem dimethyl).</td>
</tr>
<tr>
<td>(3-Methyl butyloxy)benzene</td>
<td>3.66</td>
<td>6.75-7.3(5H, Ar-H); 3.98(t, 2H, -OCH₂-CH₂-); 1.7(t, 2H, -OCH₂-CH₂-); 1.3(m, 1H, -CH₃ ); 0.95(d, 6H, gem dimethyl).</td>
</tr>
<tr>
<td>S-(3-Methyl-2-butenyl)thiobenzene</td>
<td>3.76</td>
<td>7.35(5H, Ar-H); 5.3(1H, olefinic H); 3.4(2H, -S-CH₂-); 1.6-1.75(6H, gem dimethyl).</td>
</tr>
<tr>
<td>S-(3-Methyl butanyl)thiobenzene</td>
<td>3.78</td>
<td>7.35(5H, Ar-H); 2.98(t, 2H, -S-CH₂-); 1.3(m, 1H, -CH₃ ); 1.65(t, 2H, -S-CH₂-CH₂-); 0.95(d, 6H, gem dimethyl).</td>
</tr>
</tbody>
</table>
epoxide ring is much less than the olefinic double bond. Further, the two gem dimethyl groups were again observed as two distinct signals at 1.43$^\circ$ and 1.35$^\circ$. The rigid epoxide ring fixes the two methyl groups, one cis-, and the other trans- with respect to the carbonyl group. The cis methyl group seems to appear at lower field value of 1.43$^\circ$.

In the PMR spectra of esters (3.51 and 3.61) the aromatic protons were observed between 7.0-7.45$^\circ$, the higher field value accounting for meta and para protons and the lower field value for ortho protons. The olefinic proton in (3.51) appeared at 5.97$^\circ$, once again showing a strong deshielding effect of $\text{-} C - \text{OR}$ group. Further, the deshielding effect of ester group seems to be stronger by about 0.2 ppm than the amide group. The cis and trans methyl protons with respect to the carbonyl function appeared at 2.23$^\circ$ and 1.90$^\circ$ respectively as above. In compound (3.61), the $\text{-} C - \text{CH}_2 -$ protons were observed at 2.25$^\circ$ as a doublet, the gem dimethyl protons at 1.1$^\circ$ as a doublet and the tertiary proton at about 1.25$^\circ$ as a multiplet.

The PMR spectra of thio esters (3.75 and 3.77) showed the aromatic protons between 7.3-7.6$^\circ$. The olefinic proton in (3.75) was more strongly deshielded by $\text{-} C - \text{SR}$ group than $\text{-} C - \text{OR}$ group and appeared at 6.07$^\circ$. The cis- and trans- methyl groups appeared at 2.15$^\circ$ and 1.80$^\circ$ respectively. The $\text{-} C - \text{CH}_2 -$ protons were also more strongly deshielded by
- C - SR group than - C - OR and appeared at 2.5δ in the spectrum of compound (3.77).

The PMR spectrum of the amine (3.40) showed a signal at 6.9-7.2δ (5H) due to aromatic protons and at 3.02δ (t, 2H) due to N - CH₂ - protons. A complex signal at 1.1-1.6δ can be attributed to 3 protons of - CH₂ - CH. The 5 protons of terminal gem dimethyl group appeared as a doublet at 0.95δ.

In the PMR spectra of ethers (3.56 and 3.66) the 5 aromatic protons appeared between 6.8-7.3δ. The phenoxy-methylene protons (Ar - O - CH₂ -) appeared at 4.45 and 3.9δ respectively in (3.56) and (3.66). It shows that the presence of double bond exerts a deshielding effect to the tune of 0.55 ppm in the compound (3.56). The olefinic proton appeared as a multiplet at 5.5δ showing only a slight deshielding due to phenoxy-methylene group. The terminal gem-dimethyl protons appeared as a doublet at 1.75δ showing long range coupling with olefinic proton. The compound (3.66) showed a 2H triplet at 1.7δ due to - OCH₂ - CH₂. The gem-dimethyl group protons were observed as a doublet at 0.95δ and the tertiary proton as a multiplet at 1.3δ.

The PMR spectra of the thio ethers (3.76 and 3.78) showed two major changes from the ethers (3.56 and 3.66). Firstly, the thiophenoxy-methylene protons were observed at 3.4δ and 2.9δ in (3.76) and (3.78) respectively as compared to 4.45 and 3.9δ values in corresponding ethers (3.56) and (3.66).
This shows that the deshielding effect of Ar-S group is far lesser than Ar-O group, almost to the extent of $-1.0\delta$. Secondly, while the aromatic protons in ethers were a complex signal between 6.8-7.3$\delta$, the aromatic protons of thioethers showed almost a singlet at 7.35$\delta$. The rest of the PMR spectra of thio ethers had almost the same pattern as the ethers.

Finally in the p-substituted compounds of the above series, the aromatic protons showed the expected pattern in the PMR spectra, for example, the compounds having p-nitro group or p-carbomethoxy group showed two distinct signals, one almost 1.0 /0.8$\delta$ down field due to the 2 protons ortho to nitro/carbomethoxy group and the other at about the normal position. Similarly, the protons of the p-substituent like methyl or methoxy group also appeared at the expected values (see experimental).
Biological Activities:

Peptidic juvenile hormone like substances have been reported to exhibit relatively high JH activity on hemipterans like *Pyrrhocoris apterus* and *Dysdercus cingulatus* (183). Juvabione (3.1) and dehydrojuvabione (3.2) have been shown to have high selective JH activity on hemipterans of the family *Pyrrhocoridae* (84). Some of the aromatic analogues of juvabione and dehydrojuvabione have been reported to exhibit greater JH activity than the parent compounds (93, 98, 99). Introduction of hetero atom in various types of natural products generally influences the JH activity (59, 60, 151-153). In our laboratory a large number of aromatic analogues of juvabione and dehydrojuvabione in which a hetero atom like N, O or S had been introduced were synthesized. The testing of these compounds showed that some of these possessed high degree of JH activity. Table (3.3) shows the JH activity of some of the hetero aromatic analogues of juvabione and dehydrojuvabione.

The compounds (3.21-3.23, 3.28, 3.29, 3.35-3.39, 3.51-3.55, 3.61-3.65) are only one atom short from the various hetero juvabione analogues. The aromatic moiety is directly attached to hetero atom N or O. Such structural variations can influence the biological activities. It was therefore of great interest to study the biological action of above synthetic JH analogues.
Table 3.3: Reported Biological Activity Data of Juvabione, Dehydrojuvabione and Related Compounds:

<table>
<thead>
<tr>
<th>Compound</th>
<th>Dysdercus fasciatus (1 ug)</th>
<th>Tenebrio molitor (1 ug)</th>
<th>Megoura viciae (50 ppm)</th>
<th>Tetranychus urticae (500 ppm)</th>
<th>Plutella xylostella (500 ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Score&lt;sup&gt;a&lt;/sup&gt;</td>
<td>% activity</td>
<td>Score&lt;sup&gt;a&lt;/sup&gt;</td>
<td>% activity</td>
<td>Score&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>1.</td>
<td>50</td>
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<td>12</td>
<td>6</td>
</tr>
<tr>
<td>2.</td>
<td>40</td>
<td>80</td>
<td>6</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>3.</td>
<td>40</td>
<td>80</td>
<td>7</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>4.</td>
<td>40</td>
<td>80</td>
<td>10</td>
<td>20</td>
<td>6</td>
</tr>
<tr>
<td>5.</td>
<td>35</td>
<td>70</td>
<td>10</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>6.</td>
<td>20</td>
<td>40</td>
<td>4</td>
<td>8</td>
<td>5</td>
</tr>
</tbody>
</table>
## Table 3.3 Contd...

<table>
<thead>
<tr>
<th>Compound</th>
<th>Dysdercus fasciatus (1 ug)</th>
<th>Tenebrio molitor (1 ug)</th>
<th>Megoura vicieae (50 ppm)</th>
<th>Tetranychus urticae (500 ppm)</th>
<th>Plutella xylostella (500 ppm) % Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.</td>
<td>20</td>
<td>40</td>
<td>0</td>
<td>0</td>
<td>18</td>
</tr>
<tr>
<td>8.</td>
<td>15</td>
<td>30</td>
<td>4</td>
<td>8</td>
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</tr>
<tr>
<td>9.</td>
<td>20</td>
<td>40</td>
<td>6</td>
<td>12</td>
<td>32</td>
</tr>
<tr>
<td>10.</td>
<td>25</td>
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<td>18</td>
</tr>
<tr>
<td>Methoprene</td>
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<td>100</td>
<td>50</td>
<td>100</td>
<td>96</td>
</tr>
<tr>
<td>Phosalone</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>98</td>
</tr>
<tr>
<td>Quinmethionate</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>24</td>
</tr>
</tbody>
</table>

Score\textsuperscript{a} : Out of 50;  Score\textsuperscript{b} : Out of 24.

The above compounds (3.21-3.23, 3.28, 3.29, 3.35-3.39, 3.51-3.55, 3.61-3.65) were tested for JH activities against *Dysdercus fasciatus*, *Tenebrio molitor*, *Tetranychus urticae*, *Megoura viciae* and *Plutella xylostella* (184). A residual method against *D. fasciatus* was compared with the topical method, but was found to be less effective. The insect stage selected for determination of JH activities, method of application and other procedural details are given in experimental section.

The JH activities of compounds containing N in the side chain (3.21-3.23, 3.28, 3.29, 3.35-3.39) and those of compounds containing O (3.51-3.55, 3.61-3.65) are presented in table (3.4). Naturally occurring JH III isolated from *Menduca sexta* (L) (27) was tested under identical conditions for comparison. Methoprene was used as standard for *D. fasciatus* and *T. molitor*, Phosalone for *P. xylostella* and *M. viciae* and quinmethioniate for *T. urticae*. The scores for *D. fasciatus* and *T. molitor* were out of 50 and for *M. viciae* and *T. urticae* out of 24. For *P. xylostella* the results represented percentage mortalities.

In the test against *D. fasciatus*, the insects were observed daily and scored for mortalities or any other abnormality in development. Dead or malformed adults scored 5 and normal adults zero. Highest JH activity of 60% was observed in compound (3.28). Compounds (3.21 and 3.28) showed a moderate activity of 40% while all other compounds showed
Table 3.4: JH Activity Data of Compounds (3.21-3.23, 3.28, 3.29, 3.35-3.39, 3.51-3.55, 3.61-3.65)

Compared with JH III:

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>Dysdercus fasciatus (1 ug)</th>
<th>Tenebrio molitor (1 ug)</th>
<th>Megoura vicieae (50 ppm)</th>
<th>Tetranychus urticae (500 ppm)</th>
<th>Plutella xylostella (500 ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Score a</td>
<td>% activity</td>
<td>Score a</td>
<td>% activity</td>
<td>Score b</td>
</tr>
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<td>6</td>
</tr>
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<td>20</td>
<td>5</td>
<td>10</td>
<td>0</td>
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<td>6</td>
</tr>
<tr>
<td>3.29</td>
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<td>4</td>
<td>8</td>
<td>4</td>
</tr>
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<td>6</td>
</tr>
<tr>
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<td>0</td>
<td>4</td>
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<td>4</td>
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Table 3.4 Contd...

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<th>Compound No.</th>
<th>Dysdercus fasciatus (1 ug)</th>
<th>Tenebrio molitor (1 ug)</th>
<th>Megoura vicieae (50 ppm)</th>
<th>Tetranychus urticae (500 ppm)</th>
<th>Plutella xylostella (500 ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Score</td>
<td>% activity</td>
<td>Score</td>
<td>% activity</td>
<td>Score</td>
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<tr>
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<td>2</td>
<td>2</td>
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<tr>
<td>3.53</td>
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<td>10</td>
<td>6</td>
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<td>5</td>
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<tr>
<td>Methoprene</td>
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<td>100</td>
<td>50</td>
<td>100</td>
<td>6</td>
</tr>
<tr>
<td>Quinmethionate</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td>-</td>
</tr>
</tbody>
</table>

Score<sup>a</sup>: Out of 50.
Score<sup>b</sup>: Out of 24.
weak JH activity (10-30%). Compound (3.62) was completely inactive. The percentage activity was calculated as

\[
\text{Score obtained} \times 100
\]

\[
\text{Maximum score}
\]

In *Tenebrio molitor*, the treated pupae were evaluated after 10 days for retention of such pupal characters as unpigmented cuticle, urogamphi, gintraps and genitalia, using a graded score ranging from 0-5, according to the methods of Bowers(104). Most of the compounds showed only a weak JH activity while some of the compounds (3.35-3.37, 3.51, 3.61, 3.62, 3.65) were completely inactive. Comparing the activities with JH III it was observed that most of the synthetic analogues were either more active or almost as active as JH III but none of the compounds was as active as methoprene.

The above compounds were also tested for causing mortality when sprayed onto *M. viciae*, *T. urticae* and *P. xylostella*. For *M. viciae* and *T. urticae*, the assessment was made 48 hr and 5 days after treatment and the plants were scored for live and dead aphids by comparison with the controls and using the following scheme.

0 = No aphids dead;
1 = Few aphids dead, many alive (a residual category).
2 = Many aphids dead, few alive and
3 = All aphids dead.

The two scores were added by summing up the scores from the 48 hr and 5 days assessment and the results were expressed as the total scores. Therefore the maximum possible score was 24. Compound (3.22) was completely inactive in both the species. All other compounds exhibited weak to moderate activity scoring between 2-6 (8-25%) against *M. viciae* at a dose of 50 ppm. Compounds (3.61, 3.62 and 3.64) were completely inactive against *T. urticae*. All other compounds exhibited weak to moderate activity scoring between 1-6 (4-25%) against *T. urticae* at a dose of 500 ppm. The activity was comparable to JH III and methoprene but was much lower when compared with phosalone and quinmethionatoate, which were used as standards for *M. viciae* and *T. urticae* respectively.

For *P. xylostella* at a rate of 500 ppm, compound (3.53) showed the maximum mortality rate of 46%. Compounds (3.21, 3.23, 3.28, 3.29, 3.35, 3.38, 3.39, 3.51, 3.53, 3.54, 3.61 and 3.63) showed percentage mortality between 20-42%, while all other compounds showed less than 20%. Although these compounds generally had higher mortality rate than natural JH III, they had much lower mortality rate as compared to phosalone and quinmethionatoate which were used as standards.
Herbicidal Activities:

The herbicidal activity of some of the compounds synthesized above (3.22, 3.28, 3.29, 3.35-3.39, 3.55, 3.75 and 3.77) are presented in table 3.5. The above compounds were tested against Chenopodium album, Brassica kaber, Echinochloa crus-galli, Abutilon theophrasti, Cyperus esculentus, Ipomea purpurea and Avena fatua (184).

The herbicidal activity in the post-emergence applications was determined by observing growth inhibition followed by necrosis from leaf margins after a few days. In the pre-emergence applications the activity was determined by observing inhibition of germination. The dose rate applied in all the cases was 4 kg acetone solution/hectare except (3.37) in which case a dose of 2 Kg/hectare was applied.

Compound (3.22) was found to be very active in the post emergence stage against C. album and B. kaber (90-100%), moderately active against A. theophrasti (60%) and weakly active against I. purpurea, A. fatua and E. golli (10-40%). In the pre-emergence stage it was very active against C. album (100%) and totally inactive against the rest of the herbs.

Compound (3.28) was very active in the post emergence stage against C. album and B. kaber (100%), moderately active against I. purpurea (60%) and weakly active against A. theophrasti, A. fatua and E. golli (30-50%). This compound was
Table 3.5: Herbicidal Activity of the Compounds (3.22, 3.28, 3.29, 3.35-3.39, 3.55, 3.75 and 3.77):

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<th>Compound No.</th>
<th>Ca</th>
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<th>Af</th>
<th>Ec</th>
<th>Ce</th>
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<td>Pr</td>
<td>Po</td>
<td>Pr</td>
<td>Po</td>
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<td>40</td>
<td>0</td>
</tr>
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Table 3.5 Contd...

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<th>Compound No.</th>
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<th>At</th>
<th>IP</th>
<th>Af</th>
<th>Ec</th>
<th>Ce</th>
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<td>Pr</td>
<td>Po</td>
<td>Pr</td>
<td>Po</td>
<td>Pr</td>
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<td>Pr</td>
</tr>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Ca  =  Chenopodium album.
At  =  Abutilon theophrasti.
Ip  =  Ipomea purpurea
Af  =  Avena fatua
BK  =  Brassica Kaber
I   =  Growth inhibition followed by necrosis from leaf margins after a few days. Some local chlorosis also observed.
2   =  Inhibition of germination.
0   =  No. apparent activity.

Ec  =  Echinochloa crus-galli.
Ce  =  Cyperus esculentus.
Pr  =  Pre-emergence.
Po  =  Post-emergence.
Completely inactive in the pre-emergence stage. Compound (3.29) was weakly active in the post-emergence stage (20-30%) against C. album, A. theophrasti and I. purpurea and inactive against rest of the herbs. In the pre-emergence stage this compound was found to be very active against C. album (100%), moderately active against B. kaber (70%) and totally inactive against rest of the species. Compound (3.38) was moderately active against C. album, and B. kaber (80%), weakly active against A. theophrasti, I. purpurea, A. fatua and E. golli (20-40%) and totally inactive in the pre-emergence stage against all the herbs. Compound (3.39) was moderately active against C. album, B. kaber and I. purpurea (70-80%), weakly active against A. theophrasti (40%) and inactive against rest of the species in the post-emergence stage. In the pre-emergence stage it was highly active against C. album (100%) and totally inactive against all other species. Compound (3.55) was moderately active against B. kaber (70%) and weakly active against A. theophrasti (40%) in the pre-emergence stage. Against rest of the species in both the stages the compound was found to be totally inactive. The compounds (3.35, 3.36, 3.37, 3.75 and 3.77) were found to be totally inactive in both the stages.
**Experimental:**

**Ethyl-3-amino Crotonate (3.10):**

A rapid stream of dry ammonia was passed into ethyl acetoacetate (130.0 g; 1.0 mole) with continuous stirring for 5 hr. The reaction was exothermic and the temperature of the reaction mixture rose to about 40°. The temperature of the reaction mixture was maintained between 35-40° during the addition. It was then cooled to room temperature and ether (100 ml) was added. It was dried over anhydrous sodium sulphate and the solvent was distilled off. The residue was distilled under vacuum to give ethyl-3-amino crotonate (3.10) as a colourless liquid b.p. 72-75°/3 mm; Lit(18) b.p. 91-93°/8 mm. m.p. 18°.

**3-Methyl-2-butenoyl chloride (3.14):**

3-Methyl-2-butenoyl chloride (3.14) was obtained as described in chapter II.

**Attempted condensation of ethyl-3-amino crotonate with aniline:**

**Dichloro-bis aniline Zinc(II) (3.18):**

Aniline (3.7; 9.3 g; 100 mmol) was slowly added to a mixture of ethyl-3-amino crotonate (3.10; 12.9 g; 100 mmol) and zinc chloride (13.6 g; 100 mmol) taken in dry toluene
The reaction mixture was then refluxed in an oil bath at 125-130° for 10 hr. Toluene was removed by distillation under reduced pressure. It was then decomposed with water and extracted with benzene. The benzene extract was washed with water, dried and solvent was removed to obtain dichloro bis aniline Zinc (II) (3.18) as a solid (12 g; 70%) m.p. 237-238°.

IR : 3310, 3270, 1620, 1590, 1505, 1270, 1240 cm⁻¹.

MS : m/z 93 [M]^+

Anal. Found : C, 44.68; H, 4.31; N, 8.79%.

C₁₂H₁₄N₂ZnCl₂ requires : C, 44.72; H, 4.34; N, 8.69%.

Attempted condensation of ethyl-3-amino crotonate with 4-methyl aniline:

Dichloro-bis-4-methyl aniline zinc (II) (3.19):

4-Methyl aniline (3.8; 2.14 g; 20 mmol) was slowly added to a mixture of ethyl-3-amino crotonate (3.10; 2.58 g; 20 mmol) and zinc chloride (2.68 g; 20 mmol) taken in dry toluene (150 ml). The reaction mixture was then refluxed in an oil bath at 125-130° for 10 hr, and worked up as above to give dichloro-bis-4-methyl aniline Zinc (II) (3.19) as a white solid (2.5 g; 70%) m.p. 268-269°.
Attempted condensation of ethyl-3-amino crotonate with 4-methoxy aniline:

Dichloro-bis-4-methyl aniline zinc (II) (3.20):

The reaction of 4-methoxy aniline (3.9; 3.7 g; 30 mmol) with ethyl-3-amino crotonate (3.10; 3.8 g; 30 mmol) in presence of ZnCl₂ as above gave dichloro-bis-4-methoxy aniline Zn (II) (3.20) as a white solid (3.4 g; 60%) m.p. 220-222°C.

Dichloro-bis-aniline zinc (II) (3.18; 9.6 g; 30 mmol) was dissolved in dry benzene (50 ml) and pyridine (4.8 g; 60 mmol) was added to it. The mixture was continuously stirred while a solution of 3-methyl-2-butenoyl chloride (3.14; 7.1 g; 60 mmol) in 30 ml of dry benzene was slowly added to it. The
temperature of the reaction mixture was kept at 0° during addition. After the addition was complete the reaction mixture was allowed to come to room temperature and stirred for 5 hr. It was then decomposed with water and the organic layer was separated. The aqueous layer was extracted once with benzene. The combined extract was washed with water, dried over CaCl₂ and the solvent was removed to leave a residue which was crystallized from benzene : pet ether mixture to furnish N-(3-methyl-1-oxo-2-butenyl)amino benzene (3.21) as a white solid (6.0 g; 57%) m.p. 115-116°.

PMR : 7.1-7.7(5H, Ar-H); 5.8(s, 1H, olefinic H); 2.25(s, 3H, Cis-CH₃); 1.90(s, 3H, trans-CH₃).

IR : 3290, 1660, 1645, 1600, 1500, 1485, 1310 cm⁻¹.

Anal. Found : C, 75.68; H, 7.32; N, 8.05%.
C₁₁H₁₃NO requires : C, 75.42; H, 7.42; N, 8.00%.

4-Methyl-N-(3-methyl-1-oxo-2-butenyl)amino benzene (3.22) :

Dichloro-bis-4-methyl aniline Zn (II) (3.19; 1.7 g; 5 mmol) was dissolved in dry benzene (20.0 ml) and pyridine (1.60 g, 10 mmol) was added to it. The mixture was continuously stirred while a solution of 3-methyl-2-butenoyl chloride (3.14; 1.20 g, 10 mmol) in 10 ml of dry benzene was slowly added to it. The temperature of the reaction mixture
was kept at 0°C during addition. After the addition was complete the reaction mixture was allowed to come to room temperature and stirred for 5 hr and worked up as above to furnish 4-methyl-N-(3-methyl-1-oxo-2-butenyl)amino benzene (3.22) as a solid (1.32 g; 70%), m.p. 138-139°C.

PMR : 7.1-7.7(4H, Ar-H); 5.68(s, 1H, olefinic H); 2.5(s, 3H, Ar-CH₃); 2.2(s, 3H, Cis-CH₃); 1.85(s, 3H, trans-CH₃).

IR : 3250, 1670, 1645, 1600, 1530, 1312 cm⁻¹.

Anal. Found : C, 75.77; H, 8.37; N, 7.78%.
C₁₂H₁₅NO requires : C, 76.19; H, 7.93; N, 7.40%.

4-Methoxy-N-(3-methyl-1-oxo-2-butenyl)amino benzene (3.23) : The reaction of dichloro-bis-4-methoxy aniline Zn (II) (3.20; 1.9 g; 5 mmol) with 3-methyl-2-butenoyl chloride (3.14; 1.2 g; 10 mmol) as above gave 4-methoxy-N-(3-methyl-1-oxo-2-butenyl) amino benzene (3.23) as a white solid (1.4 g; 70%) m.p. 96-98°C.

PMR : 6.75-7.4(4H, Ar-H); 5.68(s, 1H, olefinic H); 3.75(s, 3H, Ar-OCH₃); 2.2(s, 3H, Cis-CH₃); 1.85(s, 3H, trans-CH₃).

IR : 3310, 1670, 1645, 1600, 1530, 1510, 1305 cm⁻¹.

Anal. Found : C, 70.44; H, 7.61; N, 6.62%.
$C_{12}H_{15}NO_2$ requires: C, 70.24; H, 7.31; N, 6.82%.

N-(3-Methyl-1-oxo-2-butenyl)amino benzene (3.21):

**Direct acylation Method:**

Aniline (3.7; 1.8 g; 20 mmol) was taken in 25 ml of dry benzene and pyridine (1.56 g; 20 mmol) was added to it. The mixture was cooled in an ice bath and 3-methyl-2-butenoyl chloride (3.14; 2.4 g; 20 mmol) was added to it dropwise with constant stirring. The reaction mixture was then stirred at room temperature for 5 hr. It was then decomposed with water (100 ml) and the organic layer was separated. The aqueous layer was extracted once with benzene. The solvent was distilled off from the combined extracts to leave a residue. To the residue a little amount of dry pet ether (60-80°) was added which precipitated a white solid. It was filtered and recrystallized from benzene: pet ether mix (1:1) to give N-(3-methyl-1-oxo-2-butenyl)amino benzene (3.21) as a white crystalline solid (2.5 g, 75%) m.p. 115-116°.

This compound was found to be identical with (3.21) prepared above in respect of m.p., IR, NMR and TLC. There was no depression in m.p. on admixture.

4-Methyl-N-(3-methyl-1-oxo-2-butenyl)amino benzene (3.22):

The direct acylation of 4-methyl aniline with 3-methyl-
2-butenoyl chloride as above gave 4-methyl-N-(3-methyl-1-oxo-2-butenyl)amino benzene m.p. 138-139° which was found to be identical in all respects with (3.22) prepared by the earlier method.

4-Methoxy-N-(3-methyl-1-oxo-2-butenyl)amino benzene (3.23):

The direct acylation of 4-methoxy aniline with 3-methyl-2-butenoyl chloride as above furnished 4-methoxy-N-(3-methyl-1-oxo-2-butenyl)amino benzene m.p. 96-98° which was found to be identical in all respects with (3.23) prepared by the earlier method.

Direct preparation of Zn (II) Complexes (3.18-3.20):

Aniline, 4-methyl aniline and 4-methoxy aniline (2 equivalent) were separately refluxed with ZnCl₂(1 equivalent) in dry toluene for 2 hr. The solvent was then distilled off and the residue washed with water to give solid compounds which were found to be identical with (3.18-3.20) prepared above.

These complexes were dissolved in dil. HCl and the solutions were basified with dil. NaOH to regenerate the amines, aniline, 4-methyl aniline, and 4-methoxy aniline.
3-Methyl butanoyl chloride (3.24) and 3-methyl butyl bromide (3.25):

3-Methyl butanoyl chloride (3.24) and 3-methyl butyl bromide (3.25) were obtained as described in chapter II.

4-Chloro-N-(3-methyl-1-oxo-2-butenyl)amino benzene (3.28):

The reaction of 4-chloro aniline (3.26; 2.55 g; 20 mmol) with 3-methyl-2-butenoyl chloride (3.14; 2.3 g; 20 mmol) in presence of pyridine (1.56 g; 20 mmol) as above furnished 4-chloro-N-(3-methyl-1-oxo-2-butenyl)amino benzene (3.28) as a crystalline white solid (2.4 g, 62%) m.p. 125-127°C.

IR : 3300, 1670, 1645, 1600, 1530, 1305 cm⁻¹.
Anal. Found : C, 62.60; H, 5.42; N, 6.21%.
C₁₄H₁₂OCl requires: C, 63.00; H, 5.72; N, 6.68%.

4-Nitro-N-(3-methyl-1-oxo-2-butenyl)amino benzene (3.29):

The reaction of 4-nitro aniline (3.27; 2.76 g; 20 mmol) with 3-methyl-2-butenoyl chloride (3.14; 2.3 g; 20 mmol) in presence of pyridine (1.56 g; 20 mmol) as above gave 4-nitro-N-(3-methyl-1-oxo-2-butenyl)amino benzene (3.29) as a solid (2.8 g; 65%) m.p. 140-141°C.

IR : 3300, 1700, 1645, 1610, 1595, 1545, 1322 cm⁻¹.
Anal. Found : C, 59.51; H, 5.12; N, 12.32%.
A solution of 3-chloroperbenzoic acid (345 mg; 2 mmol) in dry methylene chloride (30 ml) was added to the solution of N-(3-methyl-1-oxo-2-butenyl) amino benzene (3.21; 350 mg; 2 mmol) in dry methylene chloride (20 ml) at 0°. The total addition was done during a period of 30 min. The reaction mixture was stirred at 0° for 2 hr and then at room temperature for 3 hr. It was poured into ice water with vigorous stirring. The organic layer was separated, washed successively with water, saturated solution of Na₂CO₃ and water again. It was then dried over anhydrous CaCl₂ and the solvent was distilled off to leave a solid which was crystallized from methanol to afford N-(2,3-epoxy-3-methyl-1-oxobutyl) amino benzene (3.30) as a white solid (170 mg; 44%), m.p. 130-131°, Rᵣ 0.70 (system c).

PMR : 7.16-7.65(5H, Ar-H); 3.36(s, 1H, \(-\stackrel{1}{C}O\)\(_2\)C\(_\\_\)\(_\\_\)); 1.43(s, 3H, Cis-CH₃); 1.33(s, 3H, trans-CH₃).

Anal. Found : C, 68.95; H, 6.55; N, 7.15%.

C\(_{11}\)H\(_{13}\)N\(_2\)O\(_2\) requires : C, 69.10; H, 6.80; N, 7.32%.

Epoxidation of 4-methyl-N-(3-methyl-1-oxo-2-butenyl)amino
benzene (3.22; 378mg; 2 mmol) in methylene chloride with
3-chloroperbenzoic acid (345mg; 2 mmol) as above gave
4-methyl-N-(2,3-epoxy-3-methyl-1-oxo-butyl) amino benzene
(3.31) as a white solid (200mg; 48%) m.p. 99-100°, R_f 0.68
(system c).

PMR : 7.3-7.7(4H, Ar-H); 3.38(s, 1H, -C-CH); 2.3(s, 3H, Ar-CH_3);
      1.43(s, 3H, Cis-CH_3);
      1.33(s, 3H, trans-CH_3).

Anal. Found : C, 70.12; H, 7.23; N, 6.59%.

C_{12}H_{15}NO_2 requires : C, 70.24; H, 7.31; N, 6.82%.

4-Methoxy-N-(2,3-epoxy-3-methyl-1-oxo-butyl) amino benzene
(3.32):

Epoxidation of 4-methoxy-N-(3-methyl-1-oxo-2-butanyl)
amino benzene (3.19; 410 mg; 2 mmol) in methylene chloride
with 3-chloroperbenzoic acid (345 mg; 2 mmol) as above
furnished 4-methoxy-N-(2,3-epoxy-3-methyl-1-oxo-butyl) amino
benzene (3.32) as a white solid (200 mg; 45%) m.p. 85-86°,
R_f 0.70 (system c).

PMR : 7.2-7.6(4H, Ar-H); 3.8(s, 3H, Ar-CH_3);
      3.38(s, 1H, -C-CH); 1.4(s, 3H, Cis-CH_3);
      1.27(s, 3H, trans-CH_3).

Anal. Found : C, 64.95; H, 6.56; N, 6.15%.

C_{12}H_{15}O_2N requires : C, 65.15; H, 6.78; N, 6.33%.
4-Chloro-N-(2,3-epoxy-3-methyl-1-oxo-butyl)amino benzene (3.33):

Epoxidation of 4-chloro-N-(3-methyl-1-oxo-2-butenyl) amino benzene (3.28; 419 mg; 2 mmol) in methylene chloride with 3-chloroperbenzoic acid (345 mg; 2 mmol) as above furnished 4-chloro-N-(2,3-epoxy-3-methyl-1-oxo-butyl)amino benzene (3.33) as a white solid (210 mg; 47%) m.p. 127-128°, R_f 0.67 (system c).

PMR : 7.16-7.65(4H, Ar-H); 3.3(s, 1H, -C=C-); 1.4(s, 3H, Cis-CH_3); 1.27(s, 3H, trans-CH_3).

Anal. Found : C, 58.33; H, 5.11; N, 6.15%.

C_{14}H_{12}NO_2Cl requires: C, 58.53; H, 5.32; N, 6.20%.

4-Nitro-N-(2,3-epoxy-3-methyl-1-oxo-butyl)amino benzene (3.34):

Epoxidation of 4-nitro-N-(3-methyl-1-oxo-2-butenyl)amino benzene (3.29; 440 mg; 2 mmol) in methylene chloride with 3-chloroperbenzoic acid (345 mg; 2 mmol) as above furnished 4-nitro-N-(2,3-epoxy-3-methyl-1-oxo-butyl)amino benzene (3.34) as a yellow solid (200 mg; 42%) m.p. 120-121°, R_f 0.68 (system c).

PMR : 7.35(2H, Ar-H); 8.03(2H, Ar-H); 3.38(s, 1H, -C=C-); 1.4(s, 3H, Cis-CH_3); 1.27(s, 3H, trans-CH_3).

Anal. Found : C, 55.65; H, 5.01; N, 11.55%.
N-\((3-\text{Methyl}-1-\text{oxo-butyl})\text{amino benzene (3.35)}\):

Aniline (3.7; 2.8 g; 30 mmol) was taken in 30 ml of dry benzene and pyridine (2.3 g; 30 mmol) was added to it. The mixture was cooled in an ice bath and 3-methyl butanoyl chloride (3.24; 3.6 g; 30 mmol) was added to it dropwise with constant stirring. The reaction mixture was then stirred at room temperature for 6 hr. It was then decomposed with water (100 ml) and the organic layer was separated. The aqueous layer was extracted once with benzene. The solvent was distilled off from the combined extracts to leave a residue. To the residue a little amount of pet ether (60-80°) was added which precipitated a white solid. It was filtered and recrystallized from benzene : pet ether (1:1) to give N-(3-methyl -1-oxo-butyl) amino benzene (3.35) as a white solid (2.8 g; 56%) m.p. 120-122°.

PMR : 7.1-7.7(5H, Ar-H); 2.15(m,2H,CO-CH\(_2\)-); 1.2(m,1H,-CH ); 1.08(d, 6H, gem dimethyl).

IR : 3295, 3245, 1665, 1605, 1555, 1465, 1295 cm\(^{-1}\).

Anal. Found : C, 74.21; H, 7.95; N, 7.41%.

\(\text{C}_{11}\text{H}_{15}\text{NO}\) requires : C, 74.57; H, 8.47; N, 7.90%.
4-Methyl-N-(3-methyl-1-oxo-butyl) amino benzene (3.36):

The reaction of 4-methyl aniline (3.8; 3.21 g; 30 mmol) with 3-methyl butanoyl chloride (3.24, 3.6 g; 30 mmol) in presence of pyridine (2.3 g; 30 mmol) as above gave 4-methyl-N-(3-methyl-1-oxo-butyl) amino benzene (3.36) as a white solid (3.5 g; 61%) m.p. 115-116°.

PMR:

\[ \text{7.05-7.5(4H, Ar-H); 2.3(3H, Ar-CH}_3\text{); 2.15(m,2H,-COCH}_2\text{); 1.2(m,1H,-CH)} \text{; 1.0 (d,6H, gem dimethyl).} \]

Anal. Found:

C, 75.81; H, 8.43; N, 6.91%.

C\textsubscript{12}H\textsubscript{17}NO requires:

C, 75.39; H, 8.90; N, 7.32%.

4-Methoxy-N-(3-methyl-1-oxo-butyl) amino benzene (3.37):

The reaction of 4-methoxy aniline (3.9; 3.69 g; 30 mmol) with 3-methyl butanoyl chloride (3.24; 3.6 g; 30 mmol) in presence of pyridine (2.3 g; 30 mmol) furnished 4-methoxy-N-(3-methyl-1-oxo-butyl) amino benzene (3.37) as a solid (3.5 g; 58%) m.p. 131-133°.

IR:

\[ 3300, 3200, 3140, 3060, 1665, 1620, 1610, 1465, 1305, 1295 \text{ cm}^{-1}. \]

Anal. Found:

C, 69.15; H, 7.96; N, 6.35%

C\textsubscript{12}H\textsubscript{17}NO\textsubscript{2} requires:

C, 69.56; H, 8.21; N, 6.76%
4-Chloro-N-(3-methyl-1-oxo-butyl) amino benzene (3.38):

The reaction of 4-chloro aniline (3.26; 3.8 g; 30 mmol) with 3-methyl butanoyl chloride (3.24; 3.6 g; 30 mmol) in presence of pyridine (2.3 g; 30 mmol) gave 4-chloro-N-(3-methyl-1-oxo-butyl) amino benzene (3.38) as a solid (3.5 g; 55%) m.p. 122-124°.

IR : 3240, 3195, 3120, 3060, 1660, 1535, 1315 cm⁻¹.

Anal. Found : C, 62.01; H, 6.21; N, 6.45%.

C₁₁H₁₄NOCl requires : C, 62.41; H, 6.61; N, 6.61%.

4-Nitro-N-(3-methyl-1-oxo-butyl) amino benzene (3.39):

The reaction of 4-nitro aniline (3.27; 4.14 g; 30 mmol) with 3-methyl butanoyl chloride (3.24; 3.6 g; 30 mmol) in presence of pyridine (2.3 g; 30 mmol) furnished 4-nitro-N-(3-methyl-1-oxo-butyl) amino benzene (3.39) as a yellow solid (4.2 g; 64%) m.p. 144-145°.

IR : 3315, 3295, 3220, 1675, 1620, 1605, 1555, 1465, 1310 cm⁻¹.

Anal. Found : C, 59.01; H, 5.95; N, 12.13%.

C₁₁H₁₄N₂O₃ requires: C, 59.45; H, 6.30; N, 12.61%.

N-(3-Methyl butyl) amino benzene (3.40)(182):

Aniline (3.7; 4.18 g; 45 mmol) was heated under reflux
with 3-methyl butyl bromide (3.25; 60 g; 40 mmol) for 4 hr. The mixture became almost solid on cooling. It was dissolved in water and 20% NaCH solution (15 ml) was added to it. The oily layer of bases was separated and the aqueous layer was extracted with ether. The extracts were added to the main portion of bases and the ether was evaporated. The residue was dissolved in a mixture of conc. HCl (10 ml) and water (100 ml). It was then cooled in ice and treated with NaNC₂ (2.4 g; 35 mmol). The dark oily layer was taken in ether. Unchanged aniline was converted into benzene diazonium chloride in the aqueous phase. The ethereal extract was washed with dil. NaOH solution. The ether was removed and the oily residue was added to a solution of Sn (II) chloride (14 g; 62 mmol) in conc HCl (16 ml) with cooling by water. The solution was then made alkaline with NaOH solution and steam distilled. The oily layer of distillate was taken in ether. The ethereal extract was dried over KCl and after removing the ether the residue was distilled to get N-(3-methyl butyl) amino benzene (3.40) as an oil (1.5 g; 21%) b.p. 160-162°/40 mm, Lit(185) 126-127°/14 mm or 254-255°.

PMR : 6.9-7.2(5H, Ar-H); 3.02(t, 2H, -NH-CH₂-);
      1.1-1.6(3H, -CH₂-CH); 0.95(d, 6H, gem dimethyl).

Anal. Found : C, 80.68; H, 10.01; N, 8.14%.

C₁₁H₁₇N requires : C, 80.98; H, 10.42; N, 8.58%.
4-Methyl-N-(3-methyl butyl) amino benzene (3.41):

The reaction of 4-methyl aniline (3.8; 4.3 g; 40 mmol) with 3-methyl butyl bromide (3.25; 5.5 g; 36 mmol) as above furnished 4-methyl-N-(3-methyl butyl) amino benzene (3.41) as a viscous oil (1.6 g; 22%) which distils with decomposition at 200-205°/40 mm, Rf 0.82 (system a).

PMR : 6.85-7.4 (4H, Ar-H); 3.0 (t, 2H, -NH-CH2-);

2.16 (s, 3H, Ar-CH3); 1.1-1.5 (3H, -CH2-CH);

0.95 (d, 6H, gem dimethyl).

Anal. Found : C, 81.01; H, 10.42; N, 7.43%.

C12H15N requires : C, 81.35; H, 10.73; N, 7.90%.

4-Methoxy-N-(3-methyl butyl) amino benzene (3.42):

The reaction of 4-methoxy aniline (3.9; 4.9 g; 40 mmol) with 3-methyl butyl bromide (3.25; 5.5 g; 36 mmol) as above gave 4-methoxy-N-(3-methyl butyl) amino benzene (3.42) as an oil (1.8 g; 23%) which distils with decomposition at 180-183°/40 mm. Rf 0.81 (system a).

IR : 3406, 1620, 1515, 1296 cm⁻¹.

Anal. Found : C, 74.35; H, 9.44; N, 7.08%.

C12H15NO requires : C, 74.61; H, 9.84; N, 7.25%.

4-Chloro-N-(3-Methyl butyl) amino benzene (3.43):

The reaction of 4-chloro aniline (3.26; 5.1 g; 40 mmol)
with 3-methyl butyl bromide (3.25; 5.5 g; 36 mmol) as above furnished 4-chloro-N-(3-methyl butyl) amino benzene (3.43) as a liquid (1.4 g; 20%) which distils with decomposition at 185-188°/40 mm. $R_f$ 0.89 (system a).

PMR : 7.15-7.3 (4H, Ar-H); 3.05-3.25 (2H, -NH-CH$_2$); 1.3-1.7 (3H, CH$_2$-CH); 0.95 (d, 6H, gem dimethyl).

Anal. Found : C, 66.45; H, 8.01; N, 6.91%.

C$_{11}$H$_{16}$NCl requires : C, 66.83; H, 8.10; N, 7.08%.

4-Nitro-N-(3-methyl butyl) amino benzene (3.44):

The reaction of 4-nitro aniline (3.27; 5.5 g; 40 mmol) with 3-methyl butyl bromide (3.25; 5.5 g; 36 mmol) as above gave 4-nitro-N-(3-methyl butyl) amino benzene (3.44) as a viscous oil (1.2 g; 15%) which distils with decomposition at 205-210°/40 mm, $R_f$ 0.76 (system a).

IR : 3372, 1602, 1540, 1516, 1366, 1320 cm$^{-1}$.

Anal. Found : C, 63.15; H, 7.38; N, 13.01%.

C$_{11}$H$_{16}$N$_2$O$_2$ requires : C, 63.46; H, 7.69; N, 13.46%.

3-Methyl-2-butenyl bromide (3.45):

Isoprene (68.0 g; 1.0 mole) was cooled in freezing mixture and to this was added dropwise 33% HBr in glacial acetic acid (243.0 g; containing 1 mole of HBr) during 1 hr.
The reaction mixture was allowed to stand at 0° for 48 hr. It was then poured into 21 of cold water, and the lower layer was separated. It was dried over anhydrous Na₂SO₄ and distilled to give 3-methyl-2-butenyl bromide (3.45; 45.0 g; 30%) b.p. 47-50°/40 mm; Lit(186), b.p. 62-64°/67 mm.

(3-Methyl-1-oxo-2-butenyloxy)benzene (3.51):

3-Methyl-2-butenoyl chloride (3.14; 2.4 g; 20 mmol) was added at 0°C with constant stirring to a solution of phenol (3.46; 1.9 g; 20 mmol) in dry benzene (20 ml). The mixture was stirred at room temperature for 5 hr and then left to stand overnight. Water (20.0 ml) was added to the reaction mixture and the organic layer was separated. The aqueous layer was extracted with benzene. The combined extract was washed with water and dried over anhydrous Na₂SO₄. The solvent was distilled off to leave a residue. To this residue a little amount of dry pet ether (60-80°) was added which precipitated a white solid. It was filtered and recrystallized from methanol to give (3-methyl-1-oxo-2-butenyloxy)benzene (3.51) as a solid (2.5 g; 58%) m.p. 32-34°.

PMR: 7.0-7.45 (5H, Ar-H); 5.97 (s, 1H, olefinic H); 2.23 (s, 3H, cis-CH₃); 1.90 (s, 3H, trans-CH₃).

IR: 1725, 1605, 1500, 1295, 1230 cm⁻¹.

Anal. Found: C, 74.86; H, 6.65%.

C₁₁H₁₂O₂ requires: C, 75.00; H, 6.81%.
4-Methyl-1-(3-methyl-1-oxo-2-butenyloxy)benzene (3.52):

The reaction of 4-methyl phenol (3.47; 2.37 g; 20 mmol) with 3-methyl-2-butenoyl chloride (3.14; 2.4 g; 20 mmol) as above furnished 4-methyl-1-(3-methyl-1-oxo-2-butenyloxy) benzene (3.52) as a solid (2.2 g; 55%) m.p. 45-47°.

PMR : 7.0-7.25(4H, Ar-H); 5.97(s, 1H, olefinic H); 2.32(s, 2H, CH₂-Ar); 2.23(s, 2H, cis-CH₃); 1.90(s, 3H, trans-CH₃).

Anal. Found : C, 75.65; H, 7.11%.

C₁₂H₁₄O₂ requires : C, 75.78; H, 7.36%.

4-Carbomethoxy-1-(3-methyl-1-oxo-2-butenyloxy)benzene (3.53):

The reaction of 4-carbomethoxy phenol (3.48; 3.0 g; 20 mmol) with 3-methyl-2-butenoyl chloride (3.14; 2.4 g; 20 mmol) gave 4-carbomethoxy-1-(3-methyl-1-oxo-2-butenyloxy) benzene (3.53; 3.9 g; 58%) m.p. 55-56°.

PMR : 8.2(d, 2H, Ar-H); 7.3(d, 2H, Ar-H); 6.0(s, 1H, olefinic H); 4.0(s, 3H, Ar-COCH₃); 2.25(s, 3H, cis-CH₃); 2.0(s, 3H, trans-CH₃).

Anal. Found : C, 66.82; H, 5.72%.

C₁₃H₁₄O₄ requires : C, 66.66; H, 5.98%.

4-Chloro-1-(3-methyl-1-oxo-2-butenyloxy)benzene (3.54):

The reaction of 4-chloro phenol (3.49; 2.57 g; 20 mmol)
with 3-methyl-2-butenoyl chloride (3.14; 2.4 g; 20 mmol) gave 4-chloro-1-(3-methyl-1-oxo-2-butenyloxy)benzene (3.54; 2.6 g; 65%) b.p. 140-145°/18 mm.

IR : 1715, 1470, 1450, 1300, 1230 cm\(^{-1}\).

Anal. Found : C, 62.40; H, 4.96%.

C\(_{11}\)H\(_{11}\)O\(_2\)Cl requires : C, 62.70; H, 5.22%.

4-Nitro-1-(3-methyl-1-oxo-2-butenyloxy)benzene (3.55) :

The reaction of 4-nitro phenol (3.50; 2.8 g; 20 mmol) with 3-methyl-2-butenoyl chloride (3.14; 2.4 g; 20 mmol) gave 4-nitro-1-(3-methyl-1-oxo-2-butenyloxy)benzene (3.55; 2.6 g; 61%) m.p. 101-102°.

PMR : 8.33(2H, Ar-H); 7.33(2H, Ar-H); 5.95(s, 1H, olefinic H); 2.25(s,3H,Cis-CH\(_3\)); 2.0(s,3H,trans-CH\(_3\)).

IR : 1735, 1640, 1620, 1600, 1530, 1210 cm\(^{-1}\).

Anal. Found : C, 59.52; H, 4.83; N, 6.01%.

C\(_{11}\)H\(_{11}\)O\(_4\)N requires : C, 59.72; H, 4.97; N, 6.33%.

(3-Methyl-2-butenyloxy)benzene (3.56) :

A mixture of phenol (3.46; 3.8 g; 40 mmol), 3-methyl-2-butenenyl bromide (3.45; 6.6 g; 44 mmol), finely powdered K\(_2\)CO\(_3\) (11.1 g; 80 mmol) in acetone (50 ml) was heated on a water bath under reflux for 24 hr. After cooling the mixture was
treated with water and extracted with benzene. The combined extract was washed with 10% NaOH solution and then with \( \text{H}_2\text{O} \). It was dried over \( \text{K}_2\text{CO}_3 \) and benzene was distilled off. The residue was distilled under vacuum to get (3-methyl-2-butenyl-oxy)benzene (3.56) as a colourless liquid (3.0 g; 48%) b.p. 146-150°/40 mm, \( R_f \) 0.81 (system c).

PMR : 6.88-7.3 (5H, Ar-H); 5.5 (t, 1H, olefinic H); 4.45 (d, 2H, O-CH\(_2\)-); 1.75 (d, 6H, gem dimethyl).

Anal. Found : C, 81.11; H, 8.30%.

C\(_{14}\)H\(_{20}\)O requires : C, 81.48; H, 8.64%.

4-Methyl-1-(3-methyl-2-butenyloxy)benzene (3.57):

Sodium hydride (0.96 g; 40 mmol) was added to a solution of 4-methyl phenol (3.47; 4.3 g; 40 mmol) in dry DMF and the reaction mixture was refluxed for 3 hr. 3-methyl-2-butenyl bromide (3.45; 6 g; 40 mmol) was then added to it slowly with constant stirring. The reaction mixture was then heated to a gentle reflux. The progress of the reaction was followed by TLC, and the reaction was found to be almost complete after 24 hr refluxing. The reaction mixture was then decomposed with water and the organic layer was separated, washed with \( \text{H}_2\text{O} \) and dried over anhydrous \( \text{Na}_2\text{SO}_4 \). After removal of the solvent the residue was distilled to get 4-methyl-1-(3-methyl-2-butenyloxy)benzene (3.57) as a liquid (3.0 g; 42%) b.p. 165-170°/40 mm, \( R_f \) 0.89 (system d).
IR : 1587, 1500, 1452, 1275, 1254, 1233 cm⁻¹.
Anal. Found : C, 81.68; H, 8.95%.
C₁₂H₁₆O requires : C, 81.81; H, 9.09%.

4-Carbomethoxy-1-(3-methyl-2-butenyloxy)benzene (3.58):
The reaction of 4-carbomethoxy phenol (3.48; 6.0 g; 40 mmol) with 3-methyl-2-butenyl bromide (3.45; 6 g; 40 mmol) in presence of NaH (0.96 g; 40 mmol) as above furnished 4-carbomethoxy-1-(3-methyl-2-butenyloxy)benzene (3.54) as a liquid (3.5 g; 40%) b.p. 185-187°/40 mm, Rₙ 0.62 (system d).
PMR : 7.85(d, 2H, Ar-H); 6.8(d, 2H, Ar-H);
5.5(t, 1H, olefinic H); 4.45(d, 2H, -OCH₂-);
3.8(s, 3H, Ar-C-OCH₃); 1.75(d, 6H, gem dimethyl).
IR : 1722, 1605, 1581, 1281, 1240, 1167 cm⁻¹.
Anal. Found : C, 70.68; H, 7.41%.
C₁₃H₁₆O₃ requires : C, 70.90; H, 7.27%.

4-Chloro-1-(3-methyl-2-butenyloxy)benzene (3.59):
The reaction of 4-chloro phenol (3.49; 5.14 g; 40 mmol) with 3-methyl-2-butenyl bromide (3.45; 6 g; 40 mmol) in presence of NaH (0.96 g; 40 mmol) as above gave 4-chloro-1-(3-methyl-2-butenyloxy) benzene (3.59) as a liquid (3.2 g; 41%) b.p. 162-165°/40 mm, Rₙ 0.86 (system d).
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PMR : 6.69-7.2 (4H, Ar-H); 5.45 (t, 1H, olefinic H); 4.4 (d, 2H, -OCH₂-); 1.70 (d, 6H, gem dimethyl).

IR : 1599, 1494, 1287, 1236 cm⁻¹.

Anal. Found : C, 66.98; H, 6.38%.

C₁₁H₁₃OCl requires : C, 67.17; H, 6.61%.

4-Nitro-1-(3-methyl-2-butenyloxy)benzene (3.60):

The reaction of 4-nitro phenol (3.50; 5.5 g; 40 mmol) with 3-methyl-2-butenyl bromide (3.41; 6 g; 40 mmol) in presence of NaH (0.96 g; 40 mmol) as above furnished the product 4-nitro-1-(3-methyl-2-butenyloxy)benzene (3.60) as a yellow liquid (3.2 g; 39%) b.p. 225-227°C/40 mm, Rf 0.87 (system d).

IR : 1644, 1595, 1520, 1494, 1260, 1245 cm⁻¹.

Anal. Found : C, 63.55; H, 6.18; N, 6.48%.

C₁₁H₁₃NO₃ requires : C, 63.76; H, 6.28; N, 6.76%.

(3-Methyl-1-oxo-butyloxy)benzene (3.61):

3-Methyl butanoyl chloride (3.24; 2.4 g; 20 mmol) was added to phenol (3.46; 1.8 g; 20 mmol) slowly with constant stirring. The mixture was stirred at room temperature for 6 hr and then left to stand over night. The reaction mixture was then distilled to give (3-methyl-1-oxo-butyloxy)benzene (3.61; 2.5 g; 55%) b.p. 122-125°C/10 mm.
4-Methyl-1-(3-methyl-1-oxo-butyloxy)benzene (3.62):

The reaction of 4-methyl phenol (3.47; 2.16 g; 20 mmol) with 3-methyl butanoyl chloride (3.24; 2.4 g; 20 mmol) gave 4-methyl-1-(3-methyl-1-oxo-butyloxy)benzene (3.62; 2.0 g; 54%) b.p. 140-142°/27 mm.

PMR: 6.95-7.40(5H, Ar-H); 2.25(d, 2H, -COCH₂); 1.25(m, 1H, -CH); 1.10(d, 6H, gem dimethyl).

IR: 1760, 1750, 1600, 1500, 1305, 1200 cm⁻¹.

Anal. Found: C, 73.81; H, 7.42%.

C₁₁H₁₄O₂ requires: C, 74.15; H, 7.86%.

4-Carbomethoxy-1-(3-methyl-1-oxo-butyloxy)benzene (3.63):

The reaction of 4-carbomethoxy phenol (3.48; 3.0 g; 20 mmol) with 3-methyl butanoyl chloride (3.24; 2.4 g; 20 mmol) gave 4-carbomethoxy-1-(3-methyl-1-oxo-butyloxy)benzene (3.63; 2.8 g; 60%) b.p. 182-185°/25 mm.

PMR: 8.1(d, 2H, Ar-H); 7.6(d, 2H, Ar-H); 3.80(s, 3H, Ar-OCH₃); 2.25(d, 2H, -COCH₂); 1.04(d, 6H, gem dimethyl).
1.5(m, 1H-CH); 1.0(d, 6H, gem dimethyl).

Anal. Found: C, 65.91; H, 6.32%.

C₁₃H₁₆O₄ requires: C, 66.10; H, 6.77%.

4-Chloro-1-(3-methyl-1-oxo-butyloxy)benzene (3.64):

The reaction of 4-chloro phenol (3.49; 2.5 g; 20 mmol) with 3-methyl butanoyl chloride (3.24; 2.4 g; 20 mmol) gave 4-chloro-1-(3-methyl-1-oxo-butyloxy)benzene (3.64; 2.6 g; 63%) b.p. 140-143°/10 mm.

IR: 1740, 1595, 1495, 1295, 1210 cm⁻¹.

Anal. Found: C, 61.98; H, 5.91%.

C₁₃H₁₃O₂Cl requires: C, 62.11; H, 6.11%.

4-Nitro-1-(3-methyl-1-oxo-butyloxy)benzene (3.65):

The reaction of 4-nitro phenol (3.50; 2.7 g; 20 mmol) with 3-methyl butanoyl chloride (3.24; 2.4 g; 20 mmol) gave 4-nitro-1-(3-methyl-1-oxo-butyloxy)benzene (3.65; 2.6 g; 60%) b.p. 175-178°/10 mm.

IR: 1770, 1620 (shoulder), 1600, 1535, 1500, 1295, 1215 cm⁻¹.

Anal. Found: C, 58.92; H, 5.91; N, 6.41%.

C₁₃H₁₃O₄N requires: C, 59.19; H, 5.82; N, 6.27%.
(3-Methyl butyloxy) benzene (3.66):

A mixture of phenol (3.46; 3.8 g; 40 mmol) 3-methyl butyl bromide (3.25; 6.7 g; 44 mmol) and finely powdered K$_2$CO$_3$ (11.1 g; 80 mmol) in acetone was heated on a water bath under reflux for 15 hr. It was worked up as above to get (3-methyl butyloxy) benzene (3.66; 3.5 g; 53%) b.p. 142-145°/40 mm, Lit(187) 225°, R$_f$ 0.84 (system a).

PMR: 6.75-7.3 (5H, Ar-H); 3.9(t, 2H, Ar-OCH$_2$); 1.7(t, 2H, Ar-O-CH$_2$CH$_2$-); 1.3(m, 1H, -CH$_3$); 0.95(d, 6H, gem dimethyl).

Anal. Found: C, 80.05; H, 9.51%.

C$_{14}$H$_{16}$O requires: C, 80.48; H, 9.75%.

4-Methyl-1-(3-methyl butyloxy)benzene (3.67):

The reaction of 4-methyl phenol (3.47; 3.24 g; 30 mmol) with 3-methyl butyl bromide (3.25; 4.5 g; 30 mmol) in dry DMF in presence of NaH (0.72 g; 30 mmol) gave 4-methyl-1-(3-methyl butyloxy)benzene (3.67; 3.2 g; 61%) b.p. 160-162°/40 mm, R$_f$ 0.75 (system a).

IR: 1614, 1586, 1514, 1244 cm$^{-1}$.

Anal. Found: C, 80.59; H, 9.95%.

C$_{15}$H$_{18}$O requires: C, 80.89; H, 10.11%.
4-Carbomethoxy-1-(3-methyl butyloxy)benzene (3.68):

The reaction of 4-carbomethoxy phenol (3.48; 4.5 g; 30 mmol) with 3-methyl butyl bromide (3.25; 4.5 g; 30 mmol) in DMF in presence of NaH furnished 4-carbomethoxy-1-(3-methyl butyloxy)benzene (3.68; 4 g; 61%) b.p. 186-188°/40 mm, Rf 0.85 (system a).

IR : 1724, 1606, 1580, 1316, 1254 cm⁻¹.
Anal. Found : C, 70.05; H, 7.95%.
C₁₃H₁₈O₃ requires : C, 70.27; H, 8.10%.

4-Chloro-1-(3-methyl butyloxy)benzene (3.69):

The reaction of 4-chloro phenol (3.49; 5.1 g; 40 mmol) with 3-methyl butyl bromide in K₂CO₃/acetone gave 4-chloro-1-(3-methyl butyloxy)benzene (3.69; 4.5 g; 57%) b.p. 150-152°/40 mm, Rf 0.82 (system a).

IR : 1598, 1580, 1496, 1242, 752 cm⁻¹.
Anal. Found : C, 66.23; H, 7.12%.
C₁₄H₁₅OCl requires : C, 66.49; H, 7.55%.

4-Nitro-1-(3-methyl butyloxy)benzene (3.70):

The reaction of 4-nitro phenol (3.50; 5.5 g; 40 mmol) with 3-methyl butyl bromide in K₂CO₃/acetone gave 4-nitro-1-(3-methyl butyloxy) benzene (3.70; 4 g; 49%) b.p. 220-222°/40 mm, Rf 0.89 (system a).
N, O-di(3-Methyl-1-oxo-butyl)-4-amino phenol (3.73):

The reaction of 4-amino phenol (3.71; 2.18 g; 20 mmol) with 3-methyl butanoyl chloride (3.24; 4.8 g; 40 mmol) gave N, O-di(3-methyl-1-oxo-butyl)-4-amino phenol (3.73; 4.1 g; 77%) m.p. 125-127°.

PMR : 7.0-7.6(4H, Ar-H); 2.35(2H, O - C - CH₂);
  2.19(2H, NH - C - CH₂); 1.2(m, 2H, CH);
  1.1(d, 12H, gem dimethyl).

Anal. Found : C, 69.01; H, 8.05; N, 4.73%.

C₁₁H₁₅NO₃ requires : C, 69.31; H, 8.30; N, 5.05%.

N, O-di(3-Methyl-1-oxo-2-butenyl)-4-amino phenol (3.72):

The reaction of 4-amino phenol (3.71; 2.18 g; 20 mmol) with 3-methyl-2-butenoyl chloride (3.14; 4.8 g; 40 mmol) furnished N, O-di(3-methyl-1-oxo-2-butenyl)-4-amino phenol (3.72; 3.9 g; 75%) as a white solid, m.p. 134-136°.

IR : 1735, 1665, 1610, 1515, 1465, 1312, 1205 cm⁻¹.
Anal. Found : C, 70.41; H, 6.66; N, 4.93%.

C_{16}H_{19}N requires : C, 70.32; H, 6.95; N, 5.12%.

**S-(3-Methyl-1-oxo-2-buteryl)thiobenzene (3.75)**:

The reaction of thiophenol (3.74; 2.2 g; 20 mmol) with 3-methyl-2-butenoyl chloride (3.14; 2.4 g; 20 mmol) gave S-(3-methyl-1-oxo-2-buteryl)thiobenzene (3.75; 1.5 g; 37%) b.p. 173-175°/18 mm.

PMR : 7.3-7.5 (5H, Ar-H); 6.07 (s, 1H, olefinic H);
     2.15 (s, 3H, cis-CH$_3$); 1.80 (s, 3H, trans-CH$_3$).

Anal. Found : C, 68.63; H, 6.01%.

C_{11}H_{12}SO requires : C, 68.75; H, 6.25%.

**S-(3-Methyl-2-buteryl)thiobenzene (3.76)**:

Thiophenol (3.74; 6.63 g; 60 mmol) was taken in dry benzene (20 ml) and sodium metal (1.38 g; 60 mmol) was added to it in small pieces. The sodium salt of thiophenol separated out. The benzene was distilled off completely to leave sodium salt of thiophenol as a grey powder.

The sodium salt of thiophenol (2.6 g; 20 mmol) was taken in dry methanol (20 ml) and 3-methyl-2-buteryl bromide (3.45; 3.0 g; 20 mmol) was added to it. The mixture was refluxed for 12 hr and worked up as described earlier to get S-(3-methyl-2-buteryl)thiobenzene (3.76; 1.5 g; 42%)
b.p. 139-140/30 mm.

PMR : 7.35(5H, Ar-H); 5.3(1H, olefinic H); 3.4(2H, S-CH₂); 1.7(6H, gem dimethyl).

Anal. Found : C, 73.91; H, 7.51%.

C₁₁H₁₄S requires : C, 74.15; H, 7.86%.

S-(3-Methyl-1-oxo-butyl)thiobenzene (3.77):

The reaction of thiophenol (3.74; 2.0 g; 20 mmol) with 3-methyl butanoyl chloride (3.24; 2.4 g; 20 mmol) gave S-(3-methyl-1-oxo-butyl)thiobenzene (3.77; 1.5 g; 39%) b.p. 143-145°/18 mm.

PMR : 7.28-7.62(5H, Ar-H); 2.5(d, 2H, -COCH₂-); 1.28(m, 1H, -CH); 1.08(d, 6H, gem dimethyl).

Anal. Found : C, 67.95; H, 7.05%.

C₁₁H₁₄S₀ requires : C, 68.04; H, 7.21%.

S-(3-Methyl butyl)thiobenzene (3.78):

The reaction of sodium salt of thiophenol (2.6 g; 20 mmol) with 3-methyl butyl bromide (3.21; 3.0 g; 20 mmol) as above furnished S-(3-methyl butyl)thiobenzene (3.78; 1.5 g; 50%) b.p. 143-146°/40 mm.

PMR : 7.35(5H, Ar-H); 2.9(t, 2H, S-CH₂); 1.6(t, 2H, S-CH₂-CH₂); 1.3(m, 1H, -CH); 0.95(d, 6H, gem dimethyl).
Experimental for the Determination of Biological Activities:

Materials and Methods:

Topical Application:

*Dysdercus Fasciatus*: Late IV instar of *D. fasciatus* nymphs (10) were immobilised by cooling in a refrigerator for 2 min. Each nymph was topically treated on the ventral abdominal surface with 0.2 μl of acetone solution of the experimental compound.

After treatment the insects were placed in plastic boxes measuring 17 x 11 x 5 cm, containing food (moistened cotton seed), and water (dampened cotton wool in plastic petridish) and kept at 25°C with a 16 hr day length.

*Tenebrio molitor*:

Fresh 24 hr old pupae of *T. molitor*, were collected and treated on the ventral abdominal surface with 0.2 μl of acetone solution of the test compound. The treated pupae were held in individual cells at 25°C for 10 days.
Direct Residual Contact and Ingestion Effects:

*Megoura Viciae Buckt*:

The insects were reared in culture on tick bean plants (*Viciae sp*). Individually potted tick bean plants (2-4 leaf stage) were infected with 100-150 aphids of all stages 18-24 hr before treatment. Each treatment consisted of four replicated plants. Acid washed silver sand was poured on top of the soil to show dead aphids. Aqueous acetone solution (50%) of the test compounds was applied through a pair of T-jet nozzles at 45 P.S.i (24 Kg/cm²) while the plants were given three revolutions on a turn table. The experimental plants were kept in a green house and watered from below.

*Tetranychus urticae koch*:

It was reared in culture on pinto bean plants (*Phaseolus sp*). Leaf discs of 26 mm diam. were cut from infected bean leaves; each disc supported at least 50 mites of all stages. Each experimental treatment consisted of four replicated discs. Aqueous acetone solution (50%) of the test compounds was applied using a Potter tower calibrated to produce a deposit equivalent to 60 gal/acre. (Ca. 660 l/ha). Treated discs were individually placed on damp plastic foam pads in a tower bath at 30° and under constant illumination provided by 30 W fluorescent tube.
*Plutella xylostella*:

Turnip leaf discs, 46 mm diameter, were set in 2% agar in plastic petridishes (9 cm diam.) and were given a pretreatment infection of ten 2nd instar larvae of *P. xylostella* from the laboratory culture. The petridishes were covered with ventilated enclosures which had an insect tight seal. Each experimental treatment consisted of four replicated discs. Aqueous acetone solution (50%) of the test compounds was applied using a potter tower calibrated to produce a deposit equivalent to 60 gal/acre (Ca 660 l/ha). Petridishes containing the experimental treatments were placed in a tray and held in a room at approximately 24°C.

Assessment was made 24 and 48 hr after treatment when the number of live and dead larvae were counted and the percentage mortalities were calculated. After the 48 hr assessment living larvae were transferred to untreated leaves set in agar in petridishes; this was continued at intervals up to pupation. At pupation, agar and leaf were removed and the adults allowed to emerge. Counts were made at each transfer and at adult emergence. Comparisons were made with the control treatments to determine inhibitory effects on development during the assessments. Percentage mortality data were recorded for control mortalities using Abbotts formula.