DISCUSSION
Plochl\textsuperscript{364} prepared the first unsaturated azlactone by the condensation of benzaldehyde with hippuric acid in presence of acetic anhydride. However, it remained for Erlenmeyer\textsuperscript{365} to determine the structure of the product. The reaction of an aldehyde with hippuric acid in the presence of acetic anhydride and sodium acetate is commonly referred to as Erlenmeyer Azlactone Reaction (loc. cit).

\[
\text{ArCHO} + \text{CH}_2\text{CO}_2\text{H} \xrightarrow{\text{Ac_2O}} \text{AcONa} \xrightarrow{\text{ArCH = C - CO}} \text{ArCH} = \text{C} - \text{CO} \]

The intermediate 2-phenyl-5-oxazolone (II), formed by the action of acetic anhydride on acylglycine (I), contains a methylene group which is doubly activated by the carbonyl group and the carbon-nitrogen unsaturated double bond. Condensation takes place between the aldehyde and the azlactone (II) so formed via (III) to yield 2-phenyl-4-(1'-hydroxybenzyl)-5-oxazolone (IV) which readily rearranges to 2-phenyl-4-benzylidene-5-oxazolone (V) by losing the hydroxyl group of the benzyl carbon.
and proton of the methylene group in the form of a water molecule (Scheme 1).

\[
\begin{align*}
\text{H}_2\text{C} & \overset{\text{Ac}_2\text{O}}{\rightarrow} \text{H}_2\text{C} - \text{CO} \\
\text{N} & \quad \text{OH} \\
\text{C} & \quad \text{OH} \\
\text{Ph} & \quad & \quad \text{(I)}
\end{align*}
\]

\[
\begin{align*}
\text{H}_2\text{C} & \overset{\text{Ac}_2\text{O}}{\rightarrow} \text{H}_2\text{C} - \text{CO} \\
\text{N} & \quad \text{C} \\
\text{O} & \quad \text{C} \\
\text{Ph} & \quad & \quad \text{(II)}
\end{align*}
\]

\[
\begin{align*}
\text{HC} & \overset{\text{Ac}_2\text{O}}{\rightarrow} \text{HC} - \text{CO} \\
\text{N} & \quad \text{C} \\
\text{O} & \quad \text{C} \\
\text{Ph} & \quad & \quad \text{(III)}
\end{align*}
\]

\[
\begin{align*}
\text{ArCH} & \overset{\text{Ac}_2\text{O}}{\rightarrow} \text{ArCH} - \text{CH} - \text{CO} \\
\text{N} & \quad \text{C} \\
\text{O} & \quad \text{C} \\
\text{Ph} & \quad & \quad \text{(IV)}
\end{align*}
\]

\[
\begin{align*}
\text{ArCH} & \overset{\text{Ac}_2\text{O}}{\rightarrow} \text{ArCH} - \text{CH} - \text{CO} \\
\text{N} & \quad \text{C} \\
\text{O} & \quad \text{C} \\
\text{Ph} & \quad & \quad \text{(V)}
\end{align*}
\]

Scheme 1

For the preparation of azlactone we have tried a number of basic catalysts, i.e., sodium acetate, potassium carbonate, lead acetate and potassium bicarbonate. A brief account of the results obtained by us is given below.
Azlactones obtained from carbonyl compounds have been prepared by heating carbonyl compound, hippuric acid and freshly fused sodium acetate with excess of acetic anhydride for varying lengths of time (15 min. - 2 hr). Table 1 shows the results obtained.

**TABLE 1**

**Preparation of Azlactones using sodium acetate**

<table>
<thead>
<tr>
<th>Carbonyl compounds</th>
<th>Reaction time</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. O-Methoxybenzaldehyde</td>
<td>30 min.</td>
<td>75</td>
</tr>
<tr>
<td>2. Vanilline</td>
<td>15 min.</td>
<td>75</td>
</tr>
<tr>
<td>3. Cyclohexanone</td>
<td>45 min.</td>
<td>24.6</td>
</tr>
<tr>
<td>4. Anisic-aldehyde</td>
<td>30 min</td>
<td>80</td>
</tr>
<tr>
<td>5. Veratraldehyde</td>
<td>2 hr.</td>
<td>71</td>
</tr>
<tr>
<td>6. 4-Hydroxybenzaldehyde</td>
<td>10 min.</td>
<td>80</td>
</tr>
<tr>
<td>7. Cinnamaldehyde</td>
<td>20 min.</td>
<td>60</td>
</tr>
<tr>
<td>8. 4-Dimethylaminobenzaldehyde</td>
<td>20 min.</td>
<td>69.2</td>
</tr>
<tr>
<td>9. 2,4-Dihydroxybenzaldehyde</td>
<td>2 hr.</td>
<td>91.2</td>
</tr>
<tr>
<td>10. 1-Naphthaldehyde</td>
<td>1 hr.</td>
<td>69.2</td>
</tr>
</tbody>
</table>

Galat showed that potassium carbonate was an excellent catalyst for the condensation of aldehydes with hippuric acid and superior to sodium acetate. We used this catalyst in several preparations and obtained excellent yields. In such cases a
mixture of an aldehyde, hippuric acid and potassium carbonate is stirred with acetic anhydride at room temperature. The reaction mixture set into a paste. The condensation takes place without external heating and is complete in a shorter period with appreciably higher yields than those obtained by the standard method. Douglas and Gulland\textsuperscript{367} reported 77 per cent yield of the azlactone of m-nitrobenzaldehyde. In our hands this aldehyde gives almost quantitative yield of the azlactone when potassium carbonate is used. Crotonaldehyde yields 31\% of the azlactone when we take anhydrous sodium acetate. The yield is increased to 40\% when potassium carbonate is employed as a catalyst. Table 2 gives the results obtained.

**TABLE 2**

<table>
<thead>
<tr>
<th>Aldehydes</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Salicylaldehyde</td>
<td>71</td>
</tr>
<tr>
<td>2. m-Nitrobenzaldehyde</td>
<td>100</td>
</tr>
<tr>
<td>3. Crotonaldehyde</td>
<td>40</td>
</tr>
<tr>
<td>4. p-Nitrobenzaldehyde</td>
<td>100</td>
</tr>
</tbody>
</table>

Finar and Liberman\textsuperscript{368} reported the conditions under which aliphatic aldehydes were used in the Erlenmeyer Azlactone synthesis\textsuperscript{365} and showed that much improved yields of the
Azlactones were obtained with lead acetate as the catalyst.

When cyclic ketones are used in this reaction the yields are much lower (8-10%).

We also used potassium bicarbonate as a catalyst. Condensation takes place similarly as in the case of potassium carbonate. The pure products are obtained directly in higher yields. The use of potassium bicarbonate permitted the reaction to occur at room temperature. Carter\textsuperscript{369} reported 67 per cent yield of the piperonal azlactone. We prepared this azlactone in 82 per cent yield by replacing the usual catalyst sodium acetate with potassium bicarbonate. The yield of crotonaldehyde azlactone remains unchanged with this catalyst (Table 3).

\textbf{TABLE 3}

\begin{tabular}{|l|c|}
\hline
Aldehyde & Yield \% \\
\hline
1. Piperonal & 82 \\
2. Crotonaldehyde & 40 \\
3. Indolyl-3-aldehyde & 90 \\
\hline
\end{tabular}

Azlactones have usually been isolated either by cooling the reaction mixture and removing the azlactone by filtration or by pouring the cold reaction mixture into ethanol or water.
to allow excess of acetic anhydride to decompose and collecting the azlactone. In case of cyclohexanone the azlactone has been extracted with boiling light petroleum ether (bp 40-60°) after decomposition of acetic anhydride with water.

Most of the azlactones have been purified by recrystallization from ethanol. Chloroform and ethanol are employed for the recrystallization of azlactone of cinnamaldehyde. The azlactone prepared from p-dimethylaminobenzaldehyde is recrystallised from benzene. The azlactone of vanillin is purified by recrystallisation from glacial acetic acid.
TREATMENT OF AZLACTONES WITH HYDROXYLAMINE

Azlactones, both saturated and unsaturated, react with ammonia and amines forming amides and substituted amides. But the reaction of azlactones with hydroxylamine is far more complex than the following equation would indicate:

\[
\begin{align*}
\text{RCH} &\xrightarrow{\text{NH}_2\text{OH}} \text{RCH} = \text{C} - \text{CO} - \text{NH}_2\text{OH} \\
\text{NH}_2\text{OH} &\xrightarrow{\text{NH-COPh}} \text{NH-COPh}
\end{align*}
\]

(II) a, b, c.

Depending on the pH of the medium, the ratio of the reagents, solvent system and temperature, a number of different compounds are obtained.

\(\alpha\)-Benzamidocinnamohydroxamic acid (IIa) is formed in 26 per cent yield along with \(\alpha\)-N-benzoylamino-\(\beta\)-hydroxylaminopropionichydroxamic acid (XIa) when the mixture of 2-phenyl-4-benzylidene-5-oxazolone (Ia) and hydroxylamine is kept at room temperature for 24 hr. The hydroxamic acid (IIc) is also obtained along with N-hydroxy-2-phenyl-4(1'-hydroxylaminocyclohexyl)-5-imidazolone (IVc) from 2-phenyl-4-cyclohexylidene-5-oxazolone (Ic) under the same reaction conditions. But the hydroxamic acid (IIb) is prepared by treating 2-phenyl-4(4'-methoxybenzylidene)-5-oxazolone (Ib) with a double quantity of the amine at reflux temperature.
As far as the formation of hydroxamic acid is concerned, hydroxylamine attacks on the carbonyl carbon of an azlactone opening the oxazolone ring through A.

\[
\text{RCH} = \text{C} - \text{C} = \text{O} \quad \text{NH}_2\text{OH} \quad \text{RCH} = \text{C} - \text{C} = \text{O} \quad \text{NH}_2\text{OH}
\]

\[
\text{N} \quad \text{O} \quad \text{Ph} \quad \text{N} \quad \text{O} \quad \text{Ph}
\]

(A) (B)

A charged species B is formed in which proton shift takes place giving an enol (C). This intermediate then readily converts to the keto form hydroxamic acid (II).

Excess of hydroxylamine in methanolic sodium methylate reacts under heating at reflux with 2-phenyl-4-benzylidene-5-oxazolone (Ia) to give dibenzamidocinnamohydroxamic acid (IIla) (20%) where two oxazolone rings are opened by 1 mole of the amine,
\( \beta \)-hydroxylamino-\( N \)-hydroxy-2-phenyl-4-benzyl-5-imidazolone (IVa) (35\%) \( \beta \)-hydroxylamino-2-phenyl-4-benzyl-5-oxazolone (Va) (28\%) and \( N \)-hydroxy-2-phenyl-4-benzylidene-5-imidazolone (VIa) in 15 per cent yield. The compound (VIa), which under these conditions is formed only in traces, is the principal product (58\%) of the reaction when pyridine is used in place of methanol, especially at higher temperature. 2-Phenyl-4-cinnamylidene-5-oxazolone (Id) and 2-phenyl-4-(3'-nitrobenzylidene)-5-oxazolone (If) by using the former reaction conditions give \( \beta \)-\( \delta \)-dihydroxylamino-\( N \)-hydroxy-4-(\( \delta \)-phenylpropionic)-5-imidazolone (VIIa) (83\%) and disubstituted hydroxamic acid (III\( f \)) (37\%) respectively.

The hydroxamic acids (IIIb), (III\( d \)) and (III\( i \)) were also obtained

\[
\begin{align*}
\text{RCH} &= \overset{\text{H}_2\text{NOH}}{\text{CO}} \quad \text{RCH} &= \overset{\text{CO}}{\text{N}} \quad \text{RCH} &= \overset{\text{CO}}{\text{N}} \\
\text{N} &= \overset{\text{OH}}{\text{Ph}} \quad \text{NH} &= \overset{\text{OH}}{\text{Ph}} \quad \text{OH} &= \overset{\text{N-OH}}{\text{C}} \\
\text{(I)} &\quad \text{(III\( a,b,d,f,i \))} &\quad \text{(IV\( a,c \))}
\end{align*}
\]

- a: \( \text{R} = \text{C}_6\text{H}_5 \)
- b: \( \text{R} = \text{p-MeOC}_6\text{H}_4 \)
- c: \( \text{RCH} = \text{Cyclohexyl} \)
- d: \( \text{R} = \text{C}_6\text{H}_5 \text{CH} = \text{CH} \)
- f: \( \text{R} = \text{m-NO}_2\text{C}_6\text{H}_4 \)
- i: \( \text{R} = \text{o-AcOC}_6\text{H}_4 \)
in 62-75 per cent yields when (Ib), (Id) and (Ii) were allowed to react with equimolecular proportion of the amine in boiling methanolic sodium methylate. In these cases no other additional products were secured.

\[
\begin{array}{c}
\text{C}_6H_5CH = CH-CH = C - CO \quad \text{MeOH} \\
\downarrow \quad \text{reflux} \\
\text{N} \quad \text{N} \quad \text{N} \quad \text{N}-OH
\end{array}
\]

In compounds (IVa), (IVc) and (VIIa) addition of hydroxylamine takes place at carbon-carbon double bond as well as oxygen of the oxazolone ring is substituted by N-OH group. In (Va) only addition of hydroxylamine at double bond and in (VIIa) substitution of oxygen atom of the ring by NOH are observed.

NMR spectra (deutrated DMSO) indicate that two proton signals of \(-CH-CH-\) in (IVa) and (Va) appear at 4.7 and 4.3\(\delta\) respectively. But the proton signals of \(-CH=C-\) in (IIIa) and (VIIa) are shifted to 6.69 and 6.98\(\delta\) respectively. In IR spectra (nujol) characteristic bands seen in the region 3240-3388 cm\(^{-1}\) are assigned to NH/NHOH stretching frequency and this absorption is absent in (VIIa). The peak of hydroxyl group attached to nitrogen is lowered and generally masked with nujol peak at 2900 cm\(^{-1}\). But weak bands in the region 2720-2800 cm\(^{-1}\) are due to this group. In compound (IIa) N-OH absorption appears somewhat
at higher frequency 3170 cm\(^{-1}\). There is a strong absorption in
the region 1630–1710 cm\(^{-1}\) due to CO group and band at lower
frequency (1630–1690 cm\(^{-1}\)) is due to that CO group which is in
open state (cf 2 and 3) and the bands appear at higher frequency
(1698–1710 cm\(^{-1}\)) are assigned to that carbonyl groups that are
present in 5-membered cyclic oxazolone or imidazolone rings.
Sometimes there are two bands in this region and the second band
is due to NH deformation which appears at 1640–1645 cm\(^{-1}\). The
band at 1580 cm\(^{-1}\) is due to C–N absorption. In UV absorption
spectra generally one band appears in the region 225–235 μm.
But in compound (VIIa) two absorptions are seen at 260 and 315 μm.

Refluxing 2-phenyl-4-benzylidene-5-oxazolone (Ia) with
hydroxylamine hydrochloride in glacial acetic acid afforded the
oxime of the azlactone (VIIla) in 77 per cent yield. In IR
spectrum only NOH and C=N characteristic absorptions bands appear
at 3650 and 1580 cm\(^{-1}\). The reaction is identical to the oxime
formation of benzylideneacetone at lower pH.

\[
\begin{align*}
\text{C}_6\text{H}_5\text{CH} & = \text{C} - \text{CO} \\
\text{N} & \text{C} \\
\text{O} & \text{Ph} \\
\text{N} & \text{C} \\
\text{O} & \text{Ph}
\end{align*}
\]

(Ia) 

\[
\begin{align*}
\text{C}_6\text{H}_5\text{CH} & = \text{C} - \text{C}=\text{NOH} \\
\text{N} & \text{C} \\
\text{O} & \text{Ph}
\end{align*}
\]

(VIIla)
The azlactone (Ia) is transformed by the amine into \( \beta \)-amino-\( \alpha \)-benzamidocinnamohydroxamic acid (IXa) \( (64\%) \) in excess of ethanolic sodium ethylate by stirring the mixture at room temperature in the presence of light where the substitution of amino group takes place as reported by Skraup \( ^{372} \) and others \( ^{373,374} \). The oxazolone ring is opened as described in case of (II). Hydrogen of \( -\text{CH} = \text{C} - \) is eliminated in the form of water by the reaction of hydroxyl group of the amine.

\[
\begin{align*}
\text{C}_6\text{H}_5\text{CH} = \text{C} - \text{CO} & \quad \text{C}_6\text{H}_5\text{C} = \text{C} - \text{CONHOH} \\
\text{N} & \quad \text{H} \\
\text{Ph} & \quad \text{NHCOPh} \\
\text{C}_6\text{H}_5\text{CH} = \text{C} - \text{CO} & \quad \text{C}_6\text{H}_5\text{C} = \text{C} - \text{CONHOH} \\
\text{N} & \quad \text{H} \\
\text{Ph} & \quad \text{NHCOPh} \\
\text{C}_6\text{H}_5\text{CH} = \text{C} - \text{CO} & \quad \text{C}_6\text{H}_5\text{C} = \text{C} - \text{CONHOH} \\
\text{N} & \quad \text{H} \\
\text{Ph} & \quad \text{NHCOPh} \\
\text{C}_6\text{H}_5\text{CH} = \text{C} - \text{CO} & \quad \text{C}_6\text{H}_5\text{C} = \text{C} - \text{CONHOH} \\
\text{N} & \quad \text{H} \\
\text{Ph} & \quad \text{NHCOPh}
\end{align*}
\]

(Ia) \quad (IXa)

The azlactone (Ia) on treatment with excess of the amine in methanol affords 5-phenyl-4,5-dihydro-4-N-benzoylamino-3-isoxazolone (IXa) in 76 per cent yield when the reaction mixture is refluxed. In this case a hydroxamic acid is formed first and then addition of hydroxylamino group takes place at carbon-carbon double bond as isoxazolones \( ^{47,48,375} \) are formed.
In IR spectrum the bands appeared at 3330, 1718, 1660 and 1588 cm\(^{-1}\) are assigned to NH stretching CO, C-N groups respectively.

\(\beta\)-Hydroxylaminohydroxamic acids (XIa) and (XIIe) in 51 and 69 per cent yields respectively become the main products of the reaction when the reagents are kept at room temperature in methanolic sodium methylate in cases of 2-phenyl-4-benzylidene-5-oxazolone (Ia) and 2-phenyl-4-(3'-methoxy-4'-acetoxybenzylidene)-5-oxazolone (Ia). But the acids (XIIg) in 30 per cent yield and (XIIh) in 60 per cent yield were synthesized by heating azlactones (Ig) and (Ih) with excess of the amine at reflux temperature. Stirring of the azlactone (If) with this proportion of the amine in light in the same solvent system led to the formation of (XIIf) (75%). The hydroxylamine attacks at the oxazolone ring to open...
The IR and UV characteristic absorption bands are seen in the same regions as described earlier. Compounds obtained by the reaction of azlactones with hydroxylamine are given in Table 4.

Most of the compounds have been purified by recrystallization from ethanol. Benzene is employed for the recrystallization of α-benzamidocyclohexylhydroxamic acid, N-hydroxy-2-phenyl-4-benzylidene-5-imidazolone, α-N-benzoylamino-β-hydroxylamino-propionic acid, and α-benzamido-4'-methoxycinnamohydroxamic acid. α,α'-Dibenzamidocinnamohydroxamic acid is purified by recrystallization from benzene-petroleum ether mixture. Methanol is used as a solvent for crystallising α,α'-dibenzamino-2,2'-dihydroxycinnamo, α-N-benzoylamino-β-hydroxylamino-β-nitrobenzene propionic and α-benzamidocinnamohydroxamic acids, β-hydroxylamino-N-hydroxy-2-phenyl-4-benzyl-5-imidazolone and β-hydroxylamino-2-phenyl-4-benzyl-5-oxazolone.
<table>
<thead>
<tr>
<th>Compounds</th>
<th>Reaction condition</th>
<th>Recrystallizing solvent</th>
<th>m.p. °C</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. α-N-Benzoylamino-β-hydroxylamino-β-3-methoxy-4-hydroxybenzal-propionic-hydroxamic acid</td>
<td>A</td>
<td>EtOH</td>
<td>220</td>
<td>69</td>
</tr>
<tr>
<td>2. N-Hydroxy-4-(1'-hydroxylamino-cyclohexyl)-5-imidazolone</td>
<td>A</td>
<td></td>
<td>175</td>
<td>40</td>
</tr>
<tr>
<td>3. α-Benzamido-2,2-dihydroxycinnamohydroxamic acid</td>
<td>A</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;6&lt;/sub&gt;</td>
<td>258</td>
<td>26</td>
</tr>
<tr>
<td>4. α,α'-Dibenzamido-2,2'-dihydroxycinnamohydroxamic acid</td>
<td>B</td>
<td>MeOH</td>
<td>150-52</td>
<td>75</td>
</tr>
<tr>
<td>5. α,α'-Dibenzamido-3,3'-dinitrocinnamohydroxamic acid</td>
<td>B</td>
<td></td>
<td>220</td>
<td>37</td>
</tr>
<tr>
<td>6. α-N-Benzoylamino-β-hydroxylamino-β-nitrobenzenepropionic-hydroxamic acid</td>
<td>A</td>
<td></td>
<td>167</td>
<td>75</td>
</tr>
<tr>
<td>7. β-Hydroxylamino-N-hydroxy-2-phenyl-4-benzoyl-5-imidazolone</td>
<td>C</td>
<td></td>
<td>215-16</td>
<td>35</td>
</tr>
<tr>
<td>8. β-Hydroxylaminocinnamohydroxamic acid</td>
<td>C</td>
<td></td>
<td>235-37</td>
<td>28</td>
</tr>
<tr>
<td>9. α,α'-Dibenzamidocinnamohydroxamic acid</td>
<td>C</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;6&lt;/sub&gt;</td>
<td>245-46</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Petro ether</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. N-Hydroxy-2-phenyl-4-benzylidene-5-imidazolone</td>
<td>C</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;6&lt;/sub&gt;</td>
<td>220</td>
<td>15</td>
</tr>
<tr>
<td>11. α-N-Benzoylamino-β-hydroxylamino-β-propionic acid</td>
<td>A</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;6&lt;/sub&gt;</td>
<td>130-31</td>
<td>51</td>
</tr>
<tr>
<td>Compounds</td>
<td>Reaction condition</td>
<td>Recrystallizing solvent</td>
<td>m\textsubscript{p}° C</td>
<td>Yield</td>
</tr>
<tr>
<td>---------------------------------------------------------------------------</td>
<td>--------------------</td>
<td>-------------------------</td>
<td>-----------------------</td>
<td>-------</td>
</tr>
<tr>
<td>12. $\alpha$-Benzamidocinnamoylhydroxamic acid</td>
<td>A</td>
<td>MeOH</td>
<td>170°</td>
<td>26</td>
</tr>
<tr>
<td>13. 2-Phenyl-4-benzylidene-5-oxazolone oxime</td>
<td>D</td>
<td>EtOH</td>
<td>128</td>
<td>77</td>
</tr>
<tr>
<td>14. $\beta$-Amino-$\alpha$-benzamidocinnamoylhydroxamic acid</td>
<td>E</td>
<td>&quot;</td>
<td>227</td>
<td>64</td>
</tr>
<tr>
<td>15. 5-Phenyl-4,5-dihydro-4-N-benzoylamino-3-isoxazolone</td>
<td>F</td>
<td>&quot;</td>
<td>140</td>
<td>76</td>
</tr>
<tr>
<td>16. $\alpha$, $\alpha'$-Dibenzamidocinnamoylhydroxamic acid</td>
<td>G</td>
<td>C\textsubscript{6}H\textsubscript{6}</td>
<td>245-46</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Petro ether</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17. N-Hydroxy-2-phenyl-4-benzylidene-5-imidazolone</td>
<td>G</td>
<td>C\textsubscript{6}H\textsubscript{6}</td>
<td>219-20</td>
<td>58</td>
</tr>
<tr>
<td>18. $\alpha$, $\alpha'$-Dibenzamido-4,4'-dimethoxy-cinnamoylhydroxamic acid</td>
<td>H</td>
<td>EtOAc</td>
<td>156</td>
<td>62</td>
</tr>
<tr>
<td>19. $\alpha$-Benzamido-(4'-methoxycinnamoyl)-hydroxamic acid</td>
<td>C</td>
<td>C\textsubscript{6}H\textsubscript{6}</td>
<td>230</td>
<td>79</td>
</tr>
<tr>
<td>20. $\alpha$-N-Benzoylamino-$\beta$-hydroxylamino-$\beta$-3,4-dimethoxyphenyl-propionic-hydroxamic acid</td>
<td>I</td>
<td>EtOH</td>
<td>135</td>
<td>60</td>
</tr>
<tr>
<td>21. $\beta$,$\beta'$-Dihydroxylamino-N-hydroxy-4-($\delta$-phenylpropionic)-5-imidazolone</td>
<td>I</td>
<td>&quot;</td>
<td>185</td>
<td>83</td>
</tr>
<tr>
<td>Compounds</td>
<td>Reaction condition</td>
<td>Recrystallising solvent</td>
<td>m.p.°C</td>
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</tr>
<tr>
<td>--------------------------------------------------------------------------</td>
<td>--------------------</td>
<td>-------------------------</td>
<td>--------</td>
<td>---------</td>
</tr>
<tr>
<td>22. α,α'-Dibenzoylamino-γ,γ'-dibenzenebutyrohydroxamic acid</td>
<td>G</td>
<td>EtOH</td>
<td>248-50</td>
<td>50</td>
</tr>
<tr>
<td>23. α,α'-Dibenzoylamino-γ,γ'-dibenzenebutyrohydroxamic acid</td>
<td>B</td>
<td></td>
<td>250</td>
<td>74</td>
</tr>
<tr>
<td>24. α-Benzoylamino-β-hydroxylamino-2,4-diacetoxyphenylpropionic-</td>
<td>B</td>
<td></td>
<td>250</td>
<td>80</td>
</tr>
<tr>
<td>hydroxamic acid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A: At room temperature  
B: In boiling MeOH with equimole of NH₂OH  
C: At reflux temperature in excess of NH₂OH  
D: In boiling acetic acid  
E: Stirring at room temperature with equimole of NH₂OH  
F: Stirring at room temperature with excess of hydroxylamine  
G: In boiling pyridine with equimole of NH₂OH  
H: At reflux temperature with equimole of NH₂OH  
I: In boiling MeOH with excess of NH₂OH
AMMONOLYSIS OF AZLACTONES

Synthesis of $\alpha$-N-Benzoylaminoacrylic acid amides

From the foregoing description it is clear that when $\beta$-hydroxylaminohydroxamic acids are prepared by treating azlactones with hydroxylamine different bi-products are obtained. It was thought worthwhile to ammonolyse azlactones first yielding $\alpha$-N-benzoylaminoacrylic acid amides (II) in good yield (65-93%) which on treatment with hydroxylamine gave $\alpha$-N-benzoylamino-$\beta$-hydroxylamino acid amides. In this way possibilities of side reactions are diminished.

\[
\text{RCH} = \text{C} - \text{CO} + \text{NH}_3 \xrightarrow{\text{EtOH reflux}} \text{RCH} = \text{C} - \text{CONH}_2
\]

(I) (II)

Ammonia reacts on the carbonyl group of the oxazolone ring opening it via A and resulting in a charged species B in which proton shift takes place giving an enol C. This intermediate then readily converted into keto form $\alpha$-N-benzoylaminoacrylic acid amides (II).
Azlactones are suspended in ethanol (95%) and a sufficient quantity of ammonia solution (sp. gr. 0.90) is added to suffice amide formation. This is heated under reflux temperature to obtain a clear solution. The solution was concentrated on a steam bath when the amide crystallized out on cooling. This was filtered, recrystallized from ethanol and dried.

α-N-Benzoylamino-β-4-dimethylaminophenylacrylic acid amide (65% yield) was purified by recrystallization from glacial acetic acid. In most cases the yields were almost quantitative. Results of the experiments are shown in Table 5.
<table>
<thead>
<tr>
<th>Table 5</th>
<th>Synthesis of $\alpha$-N-Benzoylaminoacrylic acid amides</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\alpha$-N-Benzoylamino-$\beta$-2-methoxyphenylacrylic acid amide</td>
</tr>
<tr>
<td>1.</td>
<td>$\alpha$-N-Benzoylamino-$\beta$-3-methoxy-4-hydroxyphenylacrylic acid amide</td>
</tr>
<tr>
<td>2.</td>
<td>$\alpha$-N-Benzoylamino-$\gamma$-3-methoxy-4-hydroxyphenylacrylic acid amide</td>
</tr>
<tr>
<td>3.</td>
<td>$\alpha$-N-Benzoylamino-$\delta$-2-hydroxyphenylacrylic acid amide</td>
</tr>
<tr>
<td>4.</td>
<td>$\alpha$-N-Benzoylamino-$\delta$-3-hexadienic acid amide</td>
</tr>
<tr>
<td>5.</td>
<td>$\alpha$-N-Benzoylamino-$\delta$-3,4-dimethoxyphenylacrylic acid amide</td>
</tr>
<tr>
<td>6.</td>
<td>$\alpha$-N-Benzoylamino-$\delta$-4-nitrophenylacrylic acid amide</td>
</tr>
<tr>
<td>7.</td>
<td>$\alpha$-N-Benzoylamino-$\delta$-1-naphthylacrylic acid amide</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>m&lt;sub&gt;D&lt;/sub&gt;</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>225&lt;sup&gt;0&lt;/sup&gt;</td>
<td>61</td>
</tr>
<tr>
<td>2.</td>
<td>180&lt;sup&gt;0&lt;/sup&gt;</td>
<td>95</td>
</tr>
<tr>
<td>3.</td>
<td>200-3&lt;sup&gt;0&lt;/sup&gt;</td>
<td>92</td>
</tr>
<tr>
<td>4.</td>
<td>271&lt;sup&gt;0&lt;/sup&gt;</td>
<td>84</td>
</tr>
<tr>
<td>5.</td>
<td>130&lt;sup&gt;0&lt;/sup&gt;</td>
<td>96</td>
</tr>
<tr>
<td>6.</td>
<td>95</td>
<td>96</td>
</tr>
<tr>
<td>7.</td>
<td>196-97</td>
<td>86</td>
</tr>
<tr>
<td>8.</td>
<td>130</td>
<td>84</td>
</tr>
<tr>
<td>9.</td>
<td>185</td>
<td>67</td>
</tr>
<tr>
<td>10.</td>
<td>215-16</td>
<td>95</td>
</tr>
<tr>
<td>11.</td>
<td>190</td>
<td>87</td>
</tr>
<tr>
<td>12.</td>
<td>160</td>
<td>65</td>
</tr>
<tr>
<td>13.</td>
<td>167-68</td>
<td>97</td>
</tr>
<tr>
<td>14.</td>
<td>205</td>
<td>94</td>
</tr>
<tr>
<td>15.</td>
<td>256</td>
<td>94</td>
</tr>
</tbody>
</table>
TREATMENT OF α-N-BENZOYLAMINOACRYLIC ACID AMIDES WITH HYDROXYLAMINE

Synthesis of α-N-Benzoylamino-β-hydroxylamino acid amides

A survey of the literature revealed that hydroxylamine adds to carbon-carbon double bond forming hydroxylamino compounds. Similarly when ammonolysed azlactones, α-N-benzoylaminoacrylic acid amides, are treated with hydroxylamine in methanol, α-N-benzoylamino-β-hydroxylamino acid amides are obtained.

\[
\begin{align*}
\text{RCH} = & \text{C} - \text{CONH}_2 \\
\text{NHCOPh} + \text{H}_2\text{NOH} \xrightarrow{\text{MeOH}} & \text{NH} \quad \text{NHCOPh} \\
\text{(I)} & \quad \text{(II)}
\end{align*}
\]

α-N-Benzoylaminoacrylic acid amides, hydroxylamine hydrochloride and sodium methoxide are taken in equimolecular proportion in methanol refluxed for 30 min. The solvent was evaporated to dryness, salt formed was removed by dissolving in water and the compounds crystallized from suitable solvents. Recrystallization of most of the products was effected from ethanol. α-N-Benzoylamino-β-hydroxylaminophenylalanine amide and α-benzamido-β-phenylpropinolhydroxamic acid were recrystallized from methanol. Ethyl acetate was used for the purification of α-N-benzoylamino-1-hydroxylaminocyclohexylglycine amide and α-N-benzoylamino-β-
hydroxylaminonaphthylalanine amide. Glacial acetic acid was employed for recrystallisation of \( \alpha \)-N-benzoylamino-\( \beta \)-hydroxylamino-\( O \)-methyltyrosine amide.

In cases of \( \alpha \)-N-benzoylamino-\( \beta \)-hydroxylamino-2'-methoxyphenylalanine amide, \( \alpha \)-N-benzoylamino-\( \beta \)-hydroxylamino-2'-tyrosine amide, \( \alpha \)-N-benzoylamino-\( \beta \)-hydroxylamino-\( O \)-methyltyrosine amide, \( \alpha \)-N-benzoylamino-\( \beta \)-hydroxylamino-4'-nitrophenylalanine amide, and \( \alpha \)-N-benzoylamino-\( \beta \)-hydroxylaminonaphthylalanine amide the yield was poor (37-50%) while in other cases the yield was good (60-93%). The results obtained are summarized in Table 6.

### TABLE 6

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Recrystallising solvent</th>
<th>m.p. ( ^\circ )C</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. ( \alpha )-N-Benzoylamino-( \beta )-hydroxylamino-2'-methoxyphenylalanine amide</td>
<td>MeOH</td>
<td>45</td>
<td>40</td>
</tr>
<tr>
<td>2. ( \alpha )-N-Benzoylamino-( \beta )-hydroxylamino-3'-methoxy-4'-hydroxyphenylalanine amide</td>
<td>EtOH</td>
<td>210</td>
<td>88</td>
</tr>
<tr>
<td>3. ( \alpha )-N-Benzoylamino-1'-hydroxylamino-cyclohexylglycine amide</td>
<td>EtOAc</td>
<td>215-17</td>
<td>86</td>
</tr>
<tr>
<td>4. ( \alpha )-N-Benzoylamino-( \beta )-hydroxylamino-2'-tyrosine amide</td>
<td>EtOH</td>
<td>155</td>
<td>50</td>
</tr>
<tr>
<td>5. ( \alpha )-N-Benzoylamino-( \beta )-hydroxylamino-3'-hexenic acid amide</td>
<td>,</td>
<td>150</td>
<td>80</td>
</tr>
<tr>
<td>6. ( \alpha )-N-Benzoylamino-( \beta )-hydroxylamino-piperonylalanine amide</td>
<td>MeOH</td>
<td>180</td>
<td>93</td>
</tr>
<tr>
<td>Compounds</td>
<td>Recrystallizing solvent</td>
<td>m.p. °C</td>
<td>Yield %</td>
</tr>
<tr>
<td>---------------------------------------------------------------------------</td>
<td>-------------------------</td>
<td>--------</td>
<td>--------</td>
</tr>
<tr>
<td>7. α^-N-Benzoylamino-β^-hydroxylamino-phenylalanine amide</td>
<td>MeOH</td>
<td>194</td>
<td>65</td>
</tr>
<tr>
<td>8. α^-Benzamido-β^-phenyl-propino-hydroxamic acid amide</td>
<td>''</td>
<td>170</td>
<td>20</td>
</tr>
<tr>
<td>9. α^-N-Benzoylamino-β^-hydroxylamino-0^-methyltyrosine amide</td>
<td>AcOH</td>
<td>295</td>
<td>40</td>
</tr>
<tr>
<td>10. α^-N-Benzoylamino-β^-hydroxylamino-3,4^-dimethoxyphenylalanine amide</td>
<td>EtOH</td>
<td>240</td>
<td>60</td>
</tr>
<tr>
<td>11. α^-N-Benzoylamino-β^-hydroxylamino-tyrosine amide</td>
<td>''</td>
<td>230</td>
<td>80</td>
</tr>
<tr>
<td>12. α^-N-Benzoylamino-β^-hydroxylamino-γ, δ^-dieno-δ^-phenyl-norvaline amide</td>
<td>''</td>
<td>200</td>
<td>72</td>
</tr>
<tr>
<td>13. α^-N-Benzoylamino-β^-hydroxylamino-4^-dimethylaminophenyl amide</td>
<td>''</td>
<td>265</td>
<td>85</td>
</tr>
<tr>
<td>14. α^-N-Benzoylamino-β^-hydroxylamino-4^-nitrophenylalanine amide</td>
<td>''</td>
<td>218</td>
<td>37</td>
</tr>
<tr>
<td>15. α^-N-Benzoylamino-β^-hydroxylamino-tryptophane amide</td>
<td>''</td>
<td>260</td>
<td>90</td>
</tr>
<tr>
<td>16. α^-N-Benzoylamino-β^-hydroxylamino-naphthylalanine amide</td>
<td>EtOAc</td>
<td>245</td>
<td>40</td>
</tr>
</tbody>
</table>
PALLADIUM CHARCOAL (10% Pd) CATALYSED REDUCTION OF α-N-
BENZOYLAMINO-β-HYDROXYLAMINO ACID AMIDES AND HYDROXAMIC ACIDS

Published methods show that azlactones as such do not undergo catalytic reduction at low pressures of hydrogen (45-65 psi), but acylaminoacrylic acids and their amides can be reduced smoothly. In our case, the carbon-carbon double bond in the compound has been saturated by the addition of hydroxylamine forming α-N-benzoylamino-β-hydroxylamino acid amides or α-N-benzoylamino-β-hydroxylaminohydroxamic acids. It had been reported that subjecting of hydroxylamino group to catalytic reduction led to the formation of amino group. Similarly, catalytic reduction of α-N-benzoylamino-β-hydroxylamino acid amides or hydroxamic acids in ethanol give α-N-benzoylamino-β-amino acid amides in good yields (50-96%) under elevated hydrogen pressure and at room temperature.

\[
\begin{align*}
RCH - CH - CONH_2 & \xrightarrow{H_2/Pd} RCH - CH - CONH_2 & \text{HONHCO - CH -CH-R} \\
\vert & \vert & \vert \\
NH & NH_2 & PhCONH \\
\vert & \vert & \vert \\
\text{NHCOPh} & \text{NHCOPh} & \text{NH}
\end{align*}
\]

We have used Palladium charcoal (10% Pd) to catalyse reduction of β-hydroxylamino compounds. In this case the compound is suspended in ethanol containing the catalyst. This is reduced in a Paar Pressure catalytic hydrogenation apparatus
under different hydrogen pressures (40-60 psi) for varying lengths of time (5-24 hr) to complete reduction. The filtrate and washings are evaporated to dryness under reduced pressure and the residue so secured are crystallized generally from ethanol to give \( \alpha \)-N-benzoylamino-\( \beta \)-amino acid amides in sufficiently pure form and high yield. In cases of \( \alpha \)-N-benzoylamino-\( \beta \)-amino-3,4-dimethoxyphenylalanine amide and \( \alpha \)-N-benzoylamino-\( \beta \)-amino-tryptophane amide the recrystallization were effected from benzene-ethanol mixture (1:4) and ethyl acetate respectively. In cases of \( \alpha \)-N-benzoylamino-\( \beta \)-amino-3-methoxy-4-hydroxyphenylalanine amide, \( \alpha \)-N-benzoylamino-\( \beta \)-aminophenylalanine amide, \( \alpha \)-N-benzoylamino-\( \beta \)-aminopiperonylalanine amide and \( \alpha \)-N-benzoylamino-\( \beta \)-amino-5-phenylnorvaline amide the yields were almost quantitative (Table 7).

IR absorption spectra show the characteristic two NH stretching peaks in the region 3150-3420 cm\(^{-1}\). Bands in the region 1620-1690 cm\(^{-1}\) are assigned to amide CO and bands appeared at 1510-1580 cm\(^{-1}\) are due to NH deformation.

**TABLE 7**  
Synthesis of \( \beta \)-Amino-\( \alpha \)-N-Benzoylamino acid amides

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Time hr</th>
<th>Pressure psi</th>
<th>( m \text{P.} ) °C</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. ( \beta )-Amino-( \alpha )-N-benzoylamino-3-methoxy-4-hydroxyphenylalanine amide</td>
<td>7</td>
<td>40</td>
<td>215</td>
<td>96</td>
</tr>
<tr>
<td>2. 1-Amino-( \alpha )-N-benzoylamino-cyclohexylglycine amide</td>
<td>7</td>
<td>56</td>
<td>235</td>
<td>65</td>
</tr>
<tr>
<td>Compounds</td>
<td>Time hr</td>
<td>Pressure psi</td>
<td>m.p. °C</td>
<td>Yield %</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>---------</td>
<td>--------------</td>
<td>----------</td>
<td>---------</td>
</tr>
<tr>
<td>3. $\beta$-Amino-$\alpha$-N-benzoylaminonorvaline amide</td>
<td>12</td>
<td>56</td>
<td>215</td>
<td>60</td>
</tr>
<tr>
<td>4. $\beta$-Amino-$\alpha$-N-benzoylamo- piperylnalanine amide</td>
<td>24</td>
<td>60</td>
<td>160-62</td>
<td>90</td>
</tr>
<tr>
<td>5. $\beta$-Amino-$\alpha$-N-benzoylaminophenylanine amide</td>
<td>5</td>
<td>40</td>
<td>197</td>
<td>95</td>
</tr>
<tr>
<td>6. $\beta$-Amino-$\alpha$-N-benzoylamo-$\theta$- methyltyrosine amide</td>
<td>8</td>
<td>60</td>
<td>260</td>
<td>60</td>
</tr>
<tr>
<td>7. $\beta$-Amino-$\alpha$-N-benzoylamo-3,4-dimethoxyphenylanine amide</td>
<td>5</td>
<td>46</td>
<td>168</td>
<td>50</td>
</tr>
<tr>
<td>8. $\beta$-Amino-$\alpha$-N-benzoylaminotyrosine amide</td>
<td>10</td>
<td>40</td>
<td>216</td>
<td>75</td>
</tr>
<tr>
<td>9. $\beta$-Amino-$\alpha$-N-benzoylamo-$\theta$- phenylorvaline amide</td>
<td>5</td>
<td>40</td>
<td>167</td>
<td>91</td>
</tr>
<tr>
<td>10. $\beta$-Amino-$\alpha$-N-benzoylamo-4- dimethylaminophenylanine amide</td>
<td>7</td>
<td>56</td>
<td>243</td>
<td>60</td>
</tr>
<tr>
<td>11. $\beta$-Amino-$\alpha$-N-benzoylamo-tryptophane amide</td>
<td>24</td>
<td>46</td>
<td>156</td>
<td>50</td>
</tr>
<tr>
<td>12. $\beta$-Amino-$\alpha$-N-benzoylamo-2,4- dihydroxyphenylanine amide</td>
<td>24</td>
<td>46</td>
<td>268</td>
<td>70</td>
</tr>
<tr>
<td>13. 1'-Aminocyclohexano-2-phenyl-5-imidazolone</td>
<td>5</td>
<td>46</td>
<td>265</td>
<td>65</td>
</tr>
<tr>
<td>14. $\alpha$-N-benzoylamo-1'-aminocyclohexylglycine amide</td>
<td>5</td>
<td>40</td>
<td>266</td>
<td>65</td>
</tr>
</tbody>
</table>
HYDROLYSIS OF $\beta$-AMINO-$\alpha$-N-BENZOYLAMINO ACID AMIDES

Acid amides on treatment with acid or alkali are converted to carboxylic acids. Thus $\beta$-amino-$\alpha$-N-benzoylamino acid amides are hydrolysed under reflux with an acid or alkali to the corresponding $\alpha$, $\beta$-diamino acids. The hydrolysing agents used are hydrochloric acid and barium hydroxide.

On the basis of our experimental work we suggest that in the case of $\beta$-amino-$\alpha$-N-benzoylamino acid amides (I) hydrolysis of the primary amide takes place first and then the secondary amide linkage is hydrolyzed to yield the corresponding $\beta$-amino-$\alpha$-N-benzoylamino acid and amino acid (VIII) respectively. It involves nucleophilic substitution, in which the amide group is replaced by a hydroxyl group. Under acidic conditions the amide is protonated to give (II) and water molecule is added resulting an intermediate (III) which gives $\beta$-amino-$\alpha$-N-benzoylamino acid (V) via (IV) by the elimination of one molecule of ammonia. Similarly hydrolysis of the secondary amide in (V) proceeds to produce $\alpha$, $\beta$-diamino acid (VIII) via (VI) and (VII) as given below:
Under alkaline conditions hydrolysis involves attack by the strongly nucleophilic hydroxide ion on the amide itself.
Subjection of \( \beta \)-amino-\( \alpha \)-N-benzoylamino acid amides to hydrolysis at reflux temperature leads to simultaneous scission of amide and benzoyl groups and permits the subsequent isolation of amino acid salts. These amides are refluxed with hydrochloric acid (30\% and 10\%) for varying lengths of time (3.5 - 35 hr).
Benzoic acid separated is filtered and the filtrate evaporated to dryness under reduced pressure. Amino acid salts thus obtained give amino acid on neutralization with dilute ammonia in 60-96 per cent yields.

In case of \( \beta \)-aminopiperonylalanine a black pigment is formed when its amide is hydrolysed in acidic conditions. However, hydrolysis of this amide at reflux temperature using barium hydroxide solution (15\%) gives \( \beta \)-aminopiperonylalanine in 60 per cent yield. All the amino acids are crystallised from ethanol (40-95\%). Results obtained are shown in Table 8.

Characteristic absorption in IR spectra show a broad band in the region 2765-3130 cm\(^{-1}\) for NH\(_3\) and peaks at 1560-1640 cm\(^{-1}\) for COO group.

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Reflux time hr</th>
<th>m.p. (^{\circ})C</th>
<th>solvent</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. ( \beta )-Amino-3-methoxy-4-hydroxy-phenylalanine</td>
<td>8</td>
<td>253</td>
<td>J</td>
<td>60</td>
</tr>
<tr>
<td>2. 1-Aminocyclohexylglycine</td>
<td>6</td>
<td>260</td>
<td>J</td>
<td>70</td>
</tr>
<tr>
<td>3. ( \beta )-Aminonorvaline</td>
<td>7</td>
<td>230</td>
<td>J</td>
<td>65</td>
</tr>
<tr>
<td>4. ( \beta )-Aminopiperonylalanine</td>
<td>36</td>
<td>95</td>
<td>K</td>
<td>60</td>
</tr>
<tr>
<td>5. ( \beta )-Aminophenylalanine</td>
<td>7</td>
<td>265</td>
<td>J</td>
<td>78</td>
</tr>
</tbody>
</table>
TABLE 8 (Contd.)

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Reflux time hr</th>
<th>m.p. °C</th>
<th>solvent</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>6. β-Hydroxylaminophenylalanine</td>
<td>3.5</td>
<td>250</td>
<td>J</td>
<td>60</td>
</tr>
<tr>
<td>7. β-Amino-O-methyltyrosine</td>
<td>6</td>
<td>90</td>
<td>L</td>
<td>98</td>
</tr>
<tr>
<td>8. β-Amino-3,4-dimethoxyphenylalanine</td>
<td>10</td>
<td>155</td>
<td>J</td>
<td>62</td>
</tr>
<tr>
<td>9. β-Aminotyrosine</td>
<td>9</td>
<td>245</td>
<td>J</td>
<td>96</td>
</tr>
<tr>
<td>10. β-Amino-3-phenylanorvaline</td>
<td>5</td>
<td>200</td>
<td>L</td>
<td>90</td>
</tr>
<tr>
<td>11. β-Amino-4-dimethylaminophenylalanine</td>
<td>36</td>
<td>215</td>
<td>L</td>
<td>62</td>
</tr>
<tr>
<td>12. β-Aminotryptophane</td>
<td>8</td>
<td>270</td>
<td>J</td>
<td>60</td>
</tr>
<tr>
<td>13. β-Amino-2,4-dihydroxyphenylalanine</td>
<td>7</td>
<td>230</td>
<td>J</td>
<td>70</td>
</tr>
</tbody>
</table>

J: Concentrated hydrochloric acid (36%);
K: Barium hydroxide (15%);
L: Dilute hydrochloric acid (10%)
EXPERIMENTAL
EXPERIMENTAL

I. PREPARATION OF AZLACTONES

1. Synthesis of 2-phenyl-4-(2-methoxybenzal)-5-oxazolone

A mixture of o-methoxybenzaldehyde, 13.6 g (0.1 mol), hippuric acid, 17.9 g (0.1 mol), powdered freshly fused sodium acetate, 8.2 g (0.1 mol) and acetic anhydride, 23.3 ml (0.3 mol) was heated on a steam bath for 30 min. Yellow crystals soon began to separate and gradually the whole solidified. Ethanol was added to decompose acetic anhydride, and the solid filtered on a Buchner funnel, washed with ethanol, and then with hot water. Crystallization from ethanol (95%) gave golden yellow needles m.p. 166-7° and weighed 20.01 gm (75%) (lit. 165-66°).

2. Synthesis of 2-phenyl-4-(3'-methoxy-4'-acetoxybenzal)-5-oxazolones

An intimate mixture of vanillin, 15.2 g (0.1 mol), hippuric acid 17.9 g (0.1 mol), and freshly fused powdered sodium acetate, 16.4 g (0.2 mol) was heated with 28.3 ml (0.3 mol) of acetic anhydride on a steam bath for 15 min. The reaction mixture was

* Melting points reported in this work were taken on a Kofler hot black and are in degree centigrade.
then ground up with water, filtered and washed several times with water. The crude product was crystallised from glacial acetic acid to give yellow needles m.p. 188–89° (lit. 188–89°) and weighed 22.1 g (75%).

3. Synthesis of 2-phenyl-4-cyclohexylidene-5-oxazolone

A mixture of hippuric acid, 53.3 g (0.3 mol), freshly fused sodium acetate, 24.6 g (0.3 mol), acetic anhydride, 65.8 ml (0.7 mol) and cyclohexanone, 30 g (0.3 mol) was heated on a steam bath for 45 min to yield a light red solution. The reaction mixture was then reduced to a volume of 25 ml under reduced pressure when a portion of the oxazolone precipitated out. It was filtered and the mother liquer cooled for few hours, suspended in ethanol, and poured into 2 litre of ice-cold water with continuous stirring. The aqueous phase was decanted and the precipitate was dissolved in hot ethanol. On chilling, the oxazolone emerged in red needle shaped crystals, this was filtered and dried when it weighed 17.4 g (24.6%), m.p. 140°. Recrystallised from ethanol (95%) yielded 17.0 gm of the product m.p. 142° (lit. 142°).
4. Synthesis of 2-phenyl-4-(2-acetoxybenzal)-5-oxazolone

A mixture of salicylaldehyde, 12.2 g (0.1 mol), hippuric acid, 17.9 g (0.1 mol), anhydrous potassium carbonate, 13.8 g (0.1 mol) and acetic anhydride, 28.3 ml (0.3 mol) was stirred at room temperature. The temperature of the reaction was then raised to about 100° when it set into a yellow crystalline mass which was left overnight at room temperature and then triturated with hot water and the granular material was filtered, washed with ethanol and dried. Crystallisation from ethanol (95%) gave golden yellow crystals, m.p. 138-39° and weighed 21.8 g (71%) (lit.381 m.p. 137-38°).

5. Synthesis of 2-phenyl-4-(3'-nitrobenzal)-5-oxazolone

To a mixture of 3'-nitrobenzaldehyde, 15.1 g (0.1 mol), hippuric acid, 17.9 g (0.1 mol) and anhydrous potassium carbonate 13.8 g (0.1 mol) was added 50 ml (0.6 mol) of acetic anhydride while the mixture, which became hot, was stirred with a glass rod. The stirring was continued for another 15 min. and the reaction mixture left overnight at room temperature. Ethanol was added to decompose acetic anhydride and the yellow crystalline oxazolone was filtered and weighed 29.4 g melting at 175-76° (lit.367 m.p. 174°). The yield was nearly quantitative. IR(KBr) 1760 (azlactone C=O), 1650, 1610 (C=N, C=C), 1520, 1320 cm⁻¹ (aromatic C-N).
6. Synthesis of 2-phenyl-3-crotonylidene-5-oxazolone

To a mixture of hippuric acid, 17.9 g (0.1 mol), anhydrous potassium carbonate, 13.9 g (0.1 mol) and acetic anhydride, 28.3 ml (0.3 mol), 7.7 g (0.11 mol) of crotonaldehyde was added dropwise with constant stirring. The solution turned gradually red while the temperature rose to 100°C. The stirring was continued till the reaction mixture solidified and then left overnight. Acetic anhydride was decomposed with water and the precipitated oxazolone filtered, washed with water and then ice-cold ethanol. Crystallisation from ethanol yielded pink, needles shaped crystals, m.p. 163-64°C (8.5 g)(40%).

Anal. for C₁₃H₁₁O₂N. Calcd. C, 73.22; H, 5.22; N, 6.57%. Found: C, 72.91; H, 5.43; N, 6.37%.

7. Synthesis of 2-phenyl-4-piperonal-methylene-5-oxazolone

Piperonal, 15 g (0.1 mol), hippuric acid 17.9 g (0.1 mol), acetic anhydride, 24.4 ml (0.2 mol) and potassium bicarbonate, 10 g (0.1 mol) were stirred together at room temperature, and then allowed to stand overnight at room temperature. The oxazolone obtained on addition of hot water (150 ml) was filtered and washed with dilute acetic acid followed by water. The dried material weighed 20 g (82%). On recrystallisation from ethanol (95%), it melted at 197-98°C (lit. 195-97°C).
8. Synthesis of 2-phenyl-4-benzal-5-oxazolone

A mixture of 10.6 gm (0.1 mol) benzaldehyde, 17.9 g (0.1 mol) of hippuric acid, 8.2 g (0.1 mol) fused sodium acetate, and 28.3 ml (0.3 mol) acetic anhydride was heated on an electric hot plate till it melted completely. The flask was then transferred to a steam bath and heated for two hours. At the end of this period 40 ml of ethanol (95%) was added slowly while cooling it under running cold water and thorough shaking. The mixture was then allowed to stand overnight, the crystalline product thus separated was filtered on a Buchner under suction, washed with two 20 ml portions of ice-cold ethanol and finally with two 20 ml portions of boiling water. The product on drying weighed 15.6 g (62%), m.p. 165-66°. This was recrystallised from benzene, m.p. 167-68° (lit. 382 m.p. 167-68°).

9. Synthesis of 2-phenyl-4-(4'-methoxybenzal)-5-oxazolone

A mixture of anisic aldehyde, 13.6 g (0.1 mol), powdered hippuric acid, 17.9 g (0.1 mol), powdered freshly fused sodium acetate, 8.2 g (0.1 mol), and acetic anhydride, 28.3 ml (0.3 mol) was warmed on a boiling water bath for 30 minutes. Yellow crystals soon began to form and the whole liquid mass became solid. Water was added slowly to decompose acetic anhydride.
The crystalline material thus secured was filtered, washed with 80% ethanol and dried. This was recrystallised from ethyl acetate-ethanol mixture (2:1), golden yellow needles thus obtained were filtered, dried when it weighed 22.3 g (80% yield), m.p. 157-58° (lit. 383 m.p. 158°).

10. *Synthesis of 2-phenyl-4-(3',4'-dimethoxybenzal)-5-oxazolone*

A mixture of 16.6 g (0.1 mol) veratraldehyde, 17.9 g (0.1 mol), hippuric acid, 8.2 g (0.1 mol), fused sodium acetate, and 28.3 ml (0.3 mol) acetic anhydride was heated on an electric hot plate. As soon as the mixture liquified completely, the flask was transferred to a steam bath and heated for 2 hr. At the end of this period 50 ml alcohol was added slowly to the contents of the flask. During this addition the flask was cooled slightly to moderate the vigoriosity of the reaction. After allowing the mixture to stand overnight, the crystalline product was filtered and washed on the filter paper with two 20 ml portions of ice-cold alcohol and finally with two 20 ml portions of boiling water. The dried product weighed 21 g (71%) and melted at 147-48°. Recrystallisation from benzene improved the m.p. to 150-51° (lit. 384 m.p. 151-52°).
11. **Synthesis of 2-phenyl-4-(4'-acetoxybenzal)-5-oxazolone**

4-Hydroxybenzaldehyde, 12.2 g (0.1 mol), hippuric acid, 17.9 g (0.1 mol), and anhydrous sodium acetate, 8.2 g (0.1 mol) were finely powdered and mixed with 28.3 ml (0.3 mol) of acetic anhydride. The mixture was kept on a boiling water bath for 10-15 minutes. On cooling the azlactone formed a solid cake. This was powdered, washed first with hot water and then with dilute alcohol. The crude azlactone (26.0 g) so obtained was dissolved in chloroform and precipitated by the addition of light petroleum ether (b.p. 40-60⁰). For further purification it was recrystallised from dilute alcohol to give yellow flake needles weighing 24.5 g (80% yield) m.p. 171-72⁰ (lit. 172-73⁰).

12. **Synthesis of 2-phenyl-4-cinnamylidene-5-oxazolone**

A mixture of cinnamaldehyde, 26.4 g (0.2 mol), hippuric acid, 35.8 g (0.2 mol), anhydrous sodium acetate, 16.4 g (0.2 mol), and acetic anhydride, 56.5 ml (0.5 mol) was heated on a steam bath under dry conditions. After few minutes of heating an intense yellow colour developed which changed to orange red and after 10 min a clear solution was obtained. The flask was removed from the steam bath and kept at room temperature. On cooling a mass of orange coloured crystals was obtained. Water was added under cooled conditions to decompose acetic anhydride and also to
dissolve sodium acetate. This was then filtered. The crystalline mass was washed with water and then five 10 ml portions of 95% ethanol to remove unreacted cinnamaldehyde. The azlactone thus obtained was crystallised from chloroform-ethanol mixture to give orange coloured needles melting at 151-52° (lit. 152°) and weighing 33 g (60% yield).

13. Synthesis of 2-phenyl-4-(4'-dimethylaminobenzal)-5-oxazolone

A mixture of hippuric acid, 17.9 g (0.1 mol), 4-dimethylaminobenzaldehyde, 14.9 g (0.1 mol), finally powdered fused sodium acetate 8.2 g (0.1 mol) and acetic anhydride, 40.8 ml (0.4 mol) was refluxed for 20 min. The contents were poured into 100 ml of ice-cold water and filtered. This was washed with plenty of water and once with ice-cold ethanol to remove unreacted aldehyde. Crystallisation from benzene yielded reddish brown needles, m.p. 232-33° (lit. 210-11°), 13.5 g (69.2%). IR (KBr) 1762 (azlactone C=O), 1650 (C=N), 1610 (C=C), 1530, 1380 cm⁻¹ (aromatic C-N).

14. Synthesis of 2-phenyl-4-(4'-nitrobenzal)-5-oxazolone

4-Nitrobenzaldehyde, 15.11 g (0.1 mol), hippuric acid, 17.9 g (0.1 mol), anhydrous potassium carbonate, 13.8 g (0.1 mol) and acetic anhydride, 50 ml (0.6 mol) were taken in a 500 ml
conical flask and the mixture was stirred with a glass rod. The temperature of the mixture raised to 100°. After 15 min a yellow product was obtained, this was left for 3-4 hrs and then 50 ml of water was added. The crystalline azlactone thus obtained was filtered, and washed with cold ethanol and then with 3, 20 ml portions hot water. This was recrystallised from ethanol yield 28.0 gm, melting at 209-10°. IR (KBr) 1860 (azlactone C=O), 1650, 1610 (C=N, C=C), 1520, 1320 cm⁻¹ (aromatic, C=N).

15. **Synthesis of 2-phenyl-4-(3'-indolylmethylene)-5-oxazolone**

Hippuric acid, 18 g (0.1 mol) and potassium bicarbonate 4 g (0.04 mol) were dissolved in acetic anhydride, 40 ml (0.4 mol) with stirring, indolyl-3-aldehyde, 14.5 g (0.1 mol) was then added. The mixture was stirred for 1 hr. Crystalline product thus obtained was then poured into 200 ml of hot water. The precipitated oxazolone thus obtained was filtered after 3 hr, washed with water and dried. Yield 23.1 g (90.0%), m.p. 184-85°.

16. **Synthesis of 2-phenyl-4-(2',4'-diacetoxybenzal)-5-oxazolone**

A mixture of 2,4-dihydroxybenzaldehyde (or resorcylaldehyde), 13.8 g (0.1 mol), hippuric acid 17.9 g (0.1 mol), freshly fused sodium acetate, 8.2 g (0.1 mol) and acetic anhydride, 28.3 ml (0.3 mol) was heated on a free flame. As soon as the mixture
liquified completely, the flask was transferred to a steam bath and heated for 2 hr. At the end of this period, 25 ml of ethanol was added slowly while cooling the flask. After allowing the mixture to stand overnight, the crystalline product was filtered on a Buchner Funnel, washed with two 20 ml portions of ice cold ethanol and finally with two 20 ml portions of boiling water. On drying the product weighed 33.3 g (19.2%) and melted at 136-37°. Crystallisation from ethanol afforded buff-coloured needles, m.p. 139-40° (lit. 130°).

17. Synthesis of 2-phenyl-4-(1'-naphthylmethylene)-5-oxazolone

A mixture of 1-naphthaldehyde, 15.6 g (0.1 mol), hippuric acid, 17.9 g (0.1 mol), freshly fused sodium acetate, 8.2 g (0.1 mol) and acetic anhydride, 30 ml (0.3 mol) was fused on a free flame in a conical flask and then heated on a steam bath for 1 hr. After cooling, 30 ml of ethanol (95%) was added to the reaction mixture and then left overnight at room temperature. The crude product was filtered on a Buchner funnel, washed with three 50 ml portions of hot water and once with cold ethanol. It was recrystallised from ethanol (95%). Yellow, needle-shaped crystals, thus obtained were filtered and dried yield 18.8 g (62.8%), m.p. 174-75° (lit. 170-71°).
II. TREATMENT OF AZLACTONES WITH HYDROXYLAMINE HYDROCHLORIDE

1. Treatment of 2-phenyl-4-(3'-methoxy-4'-acetoxybenzal)-5-oxazolone with excess of hydroxylamine at room temperature

2-Phenyl-4-(3'-methoxy-4'-acetoxybenzal)-5-oxazolone, 3.4 g (0.012 mol) was suspended in ethanol (60 ml) along with sodium methoxide, (2.15 g, 0.04 mol) and hydroxylamine hydrochloride, 2.80 g (0.04 mol). This was kept at room temperature for 24 hr. White crystalline product α-N-benzoylamino-β-hydroxylamino-β-3-methoxy-4-hydroxybenzylpropionic hydroxamic acid was filtered, recrystallised from ethanol (95%) and dried. It melted at 220° and weighed 2.45 g (69%). UV\textsubscript{\text{Dioxane}}\text{max} 285 μm (abs. 0.56), and 225 μm (abs. 0.76); IR (nujol) 3270, 3135, 1640, 1580, 1550 cm\textsuperscript{-1}.

Anal. for C\textsubscript{17}H\textsubscript{19}N\textsubscript{3}O\textsubscript{6}.
Calcd: C, 56.50; H, 5.30, N, 11.63%
Found: C, 56.57; H, 4.99; N, 11.38%.

2. Treatment of 2-phenyl-4-cyclohexylidene-5-oxazolone with equimole of hydroxylamine at room temperature

An intimate mixture of 2-phenyl-4-cyclohexylidene-5-oxazolone, 2.4 g (0.01 mol), hydroxylamine hydrochloride, 0.7 g (0.01 mol) and sodium methoxide, 0.54 g (0.01 mol) was kept at
room temperature for 24 hr. Next morning the crystallised mass of N-hydroxy-4(1'-hydroxylaminocyclohexyl)-5-imidazolone was filtered, recrystallised from ethanol and dried, yield 1.15 g (40%), m.p. 175°. UV $\lambda_{\text{max}}$ $\text{MeOH}$ 230 m$\mathbf{\mu}$ (abs. 1.70); IR (nujol) 3380, 3168, 1770, 1655, 1608, 1530 cm$^{-1}$.

Anal. for C$_{15}$H$_{19}$N$_{3}$O$_{3}$:
Calcd: C, 62.26; H, 6.62; N, 14.52%
Found: C, 62.03; H, 6.59; N, 14.63%.

The above filtrate was evaporated to dryness under reduced pressure and the residue so secured was dissolved in benzene (20 ml). On cooling α-N-benzoylamino-1'-hydroxylaminocyclohexylglycineamide was crystallised which was separated, yield 0.76 g (26%), m.p. 258°; IR (nujol) 3307, 2630, 1640, 1628, 1570, 1535 cm$^{-1}$.

Anal. for C$_{15}$H$_{18}$N$_{2}$O$_{3}$:
Calcd: C, 65.67; H, 6.61; N, 10.21%
Found: C, 65.50; H, 6.72; N, 10.42%.

3. Treatment of 2-phenyl-4-(2'-acetoxybenzal)-5-oxazolone with equimole of hydroxylamine in boiling methanol

2-Phenyl-4-(2'-acetoxybenzal)-5-oxazolone, 3 g (0.01 mol) was dissolved in methanol (60 ml). Sodium methoxide (0.54 g, 0.01 mol) and hydroxylamine hydrochloride 0.70 g (0.01 mol) were
added to it and the whole was heated at reflux temperature for 3 hr. This was left overnight at room temperature. The crystalline mass \( \alpha', \alpha'' \)-dibenzamido-2,2'-diacetoxyo-cinnamohydroxamic acid was filtered and dried in air. It melted at 150-52\(^\circ\) and weighed 4.9 g (75\%). UV \( \lambda_{\text{MeOH max}} 260 \text{ nm} \) (abs. 1.30); IR (nujol) 3355, 1710, 1660, 1600, 1535, 1380 cm\(^{-1}\).

Anal. for \( \text{C}_{32}\text{H}_{25}\text{N}_2\text{O}_7 \),
Calcd: C, 68.20; H, 4.47; N, 7.46%
Found: C, 68.20; H, 4.50; N, 7.42%.

4. Treatment of 2-phenyl-4-(3'-nitrobenzal)-5'-oxazolone with hydroxylamine

A. Using excess of hydroxylamine in boiling methanol

An intimate mixture of 2-phenyl-4-(3'-nitrobenzal)-5'-oxazolone, 3 g (0.01 mol), hydroxylamine hydrochloride, 1.4 g (0.02 mol) and sodium methoxide, 1.08 g (0.02 mol) in methanol was heated at reflux temperature for 30 minutes. It was kept overnight at room temperature. Next morning the crystallised product \( \alpha', \alpha'' \)-dibenzamido-3,3'-dinitrocinnamohydroxamic acid was filtered which weighed 2.3 g (37\%) and melted at 215\(^\circ\). Recrystallisation from ethanol (95\%) raised the melting point to 220\(^\circ\). No absorption in UV; IR (nujol) 3310, 2670, 1640, 1530 cm\(^{-1}\)

Anal. for \( \text{C}_{32}\text{H}_{23}\text{N}_4\text{O}_9 \),
Calcd: C, 61.33; H, 3.73; N, 11.27%
Found: C, 61.60; H, 3.90; N, 11.06%.
B. Stirring of the oxazolone with excess of hydroxylamine at room temperature

Powdered 2-phenyl-4-(3'-nitrobenzal)-5-oxazolone, 3 g (0.01 mol), hydroxylamine hydrochloride, 1.4 g (0.02 mol) and sodium methoxide, 1.08 g (0.02 mol) was suspended in methanol (70 ml) and this was stirred for 7 hr at room temperature in the presence of light. The solvent was concentrated to 25 ml when on cooling \(\alpha\)-N-benzyaminoo-\(\beta\)-hydroxylamino-\(\beta\)-nitrobenzenepropionic acid was separated which was filtered, and dried. Yield 2.7 g (75%), m.p. 167°, UV \(\lambda_{max}^\text{MeOH} 230 \text{mu}\) (abs. 0.31) and 265 mu (abs. 0.285); IR (nujol) 3300, 1680, 1635, 1520 cm\(^{-1}\).

Anal. for C\(_{16}\)H\(_{16}\)N\(_4\)O\(_6\),
Calcd: C, 53.33; H, 4.48; N, 15.55%
Found: C, 53.03; H, 4.44; N, 15.69%.

5. Treatment of 2-phenyl-4-benzal-5-oxazolone with hydroxylamine hydrochloride

(A) Using excess of hydroxylamine in methanol at reflux temperature

An intimate mixture of 2-phenyl-4-benzylidene-5-oxazolone 2.5 g (0.01 mol), hydroxylamine hydrochloride, 1.39 g (0.02 mol), sodium methoxide 1.08 g (0.02 mol) and methanol (100 ml) was
refluxed on a steam bath for 1 hr. This was cooled when \( \beta \)-hydroxylamino-N-hydroxy-2-phenyl-4-benzyl-5-imidazolone was separated. This was filtered and dried yield 1 g (35\%), m.p. 215-16\(^{\circ}\); UV \( \lambda_{\text{max}} \) \text{Dioxane} 310 \text{ nm} (\text{abs. 0.235}); IR (nujol) 3305, 2725, 1707, 1650, 1545 cm\(^{-1}\); NMR (deuterated DMSO) 4.7, 7.1, 7.4, 8.168 \( \delta \).

Anal. for \( \text{C}_{16} \text{H}_{15} \text{N}_{3} \text{O}_{3} \),
Calcd: C, 64.63; H, 5.09; N, 14.14\%  
Found: C, 64.53; H, 5.00; N, 14.00\%.

The above filtrate was concentrated to 25 ml and cooled, \( \beta \)-hydroxylamine-2-phenyl-4-benzyl-5-oxazolone was crystallised which was filtered, yielded 7.8 g (28\%), m.p. 236-37\(^{\circ}\); UV \( \lambda_{\text{max}} \) \text{Dioxane} 315 \text{ nm} (\text{abs. 0.385}); IR (nujol) 3320, 2725, 1705, 1650 cm\(^{-1}\); NMR (deuterated DMSO) 4.3, 7.0, 7.29, 8.038 \( \delta \).

Anal. for \( \text{C}_{18} \text{H}_{14} \text{N}_{2} \text{O}_{3} \),
Calcd: C, 68.07; H, 5.0; N, 9.92\%  
Found: C, 68.08; H, 4.96; N, 9.93\%.

The above filtrate was evaporated to dryness on a steam bath and the residue was dissolved in benzene–petroleum ether mixture (3:1) when \( \alpha, \alpha' \)-dibenzamidocinnamohydroxamic acid was crystallised on cooling. This was filtered and dried, yield 1.06 g (20\%), m.p. 245-46\(^{\circ}\); UV \( \lambda_{\text{max}} \) \text{MeOH} 290 \text{ nm} (\text{abs. 1.6}); NMR (deuterated DMSO) 6.69, 7.41, 7.90, 9.83 \( \delta \); IR (nujol) 3290, 1690, 1645, 1580 cm\(^{-1}\).
Anal. for C\textsubscript{32}H\textsubscript{25}N\textsubscript{3}O\textsubscript{5}
Calcd: C, 72.30; H, 4.74; N, 7.91%
Found: C, 72.1; H, 4.7; N, 7.8%.

The above filtrate was evaporated to dryness and the residue was dissolved in benzene (20 ml). On cooling N-hydroxy-2-phenyl-4-benzylidene-5-imidazolone crystallised out. This was filtered, yield 0.37 g (15%), m.p. 220°; UV \(\lambda^\text{\text{max}}\) \text{MeOH} 260 \mu (abs. 1.15) and 315 \mu (abs. 0.9); IR (nujol) 1700, 1640, 1387 cm\(^{-1}\); NMR (deuterated DMSO) 6.98, 7.36, 8.19\.

Anal. for C\textsubscript{16}H\textsubscript{12}N\textsubscript{2}O\textsubscript{2}
Calcd: C, 72.71; H, 4.58; N, 10.60%
Found: C, 72.70; H, 4.54; N, 10.58%.

(B) Using equimole of hydroxylamine in methanol at room temperature

A mixture of 2-phenyl-4-benzylidene-5-oxazolone 2.5 g (0.01 mol), hydroxylamine hydrochloride 0.7 g (0.01 mol), sodium 0.23 g (0.01 mol) in methanol (50 ml) was kept at room temperature for 24 hr. The crystallised compound \(\alpha\)-N-benzoylamino-\(\beta\)-hydroxylamino-\(\beta\)-phenylpropionichydroxamic acid was filtered, recrystallised from benzene, and dried yield 1.6 g (51%), m.p. 130-31°; UV \(\lambda^\text{\text{max}}\) \text{MeOH} 280 \mu (abs. 1.45); IR (nujol) 3290, 3250, 3060, 2723, 1670, 1635, 1550 cm\(^{-1}\).

Anal. for C\textsubscript{16}H\textsubscript{17}N\textsubscript{3}O\textsubscript{4}
Calcd: C, 60.94; H, 5.39; N, 13.32%
Found: C, 61.00; H, 5.39; N, 13.36%.
The above filtrate was concentrated when $\alpha$-benzamido-cinnamohydroxamic acid crystallised out. This was filtered when it weighed 0.73 g (26%), m.p. 170°; $\text{UV}_{\text{max} \text{MeOH}}$ 225 $\mu$m (abs. 1.25); IR (nujol) 3290, 2728, 1740, 1670, 1635 cm$^{-1}$.

Anal. for $C_{16}H_{14}N_2O_3$
Calcd: C, 68.07; H, 5.5; N, 9.91%
Found: C, 68.3; H, 5.82; N, 9.90%.

(c) Using equimole of hydroxylamine hydrochloride in boiling glacial acetic acid

An intimate mixture of 2-phenyl-4-benzal-5-oxazolone, 2.5 g (0.01 mol), glacial acetic acid, 50 ml, and hydroxylamine hydrochloride, 0.7 g (0.01 mol) was heated at refluxed temperature for 45 minutes. On cooling red coloured solution obtained was left at room temperature overnight. Pink coloured crystals of 2-phenyl-4-benzylidene-5-oxazolone-oxime were afforded. Filtration of the product was effected on a Buchner funnel and this was washed with three successive portions of benzene. It melted at 125° and weighed 2.03 g (77%). Recrystallisation from ethanol raised the melting point slightly to 128°. There was no absorption in UV; IR (nujol) 3181, 2650, 1588, 1380 cm$^{-1}$.

Anal. for $C_{16}H_{12}N_2O_2$
Calcd: C, 72.71; H, 4.58; N, 10.60%
Found: C, 72.69; H, 4.50; N, 10.78%.
(D) **Stirring equimole of oxazolone and hydroxylamine in ethanol at room temperature**

2-Phenyl-4-benzal-5-oxazolone, 2.5 g (0.01 mol) was added to sodium ethoxide along with hydroxylamine hydrochloride, 0.7 g (0.01 mol). The mixture was stirred for 4 hr. in the presence of light at room temperature. The solvent was concentrated under reduced pressure and on cooling β-aminoo-α-benzamidocinnamohydroxamic acid crystallised out. This was filtered, recrystallised from ethanol (95%) and dried in an oven at 80°C. It melted at 227°C and weighed 1.90 g (64%).

UV \( \lambda_{\text{max}}^{\text{MeOH}} \) 230 \( \mu \text{m} \); IR (nujol) 3315, 2670, 1645, 1545 cm\(^{-1}\).

Anal. for C\(_{16}\)H\(_{15}\)N\(_3\)O\(_3\)
Calcd: C, 64.63; H, 5.09; N, 14.14%
Found: C, 64.60; H, 5.00; N, 13.89%.

(E) **Stirring the oxazolone with excess of hydroxylamine in ethanol at room temperature**

A mixture of 2-phenyl-4-benzal-5-oxazolone, 2.5 g (0.01 mol), hydroxylamine hydrochloride, 1.4 g (0.02 mol), and sodium methoxide, 1.36 g (0.02 mol) was stirred in ethanol (70 ml) at room temperature for 5 hr in the presence of light. The solution so obtained was evaporated on a steam bath. The residue was dissolved in ethanol (20 ml) and cooled. Yellow crystals of 5-phenyl-4,5-dihydro-4-
N-benzoylamino-3-isoxazolone, which appeared, were filtered and recrystallised from ethanol (95%). The dried product weighed 2.15 g (76%) and melted at 140°. UV \( \lambda_{\text{max}}^{\text{MeOH}} \) 225 nm (abs. 0.92); IR (nujol) 3330, 1718, 1660, 1645, 1575 cm\(^{-1}\).

**Anal. for C\(_{16}\)H\(_{14}\)N\(_2\)O\(_3\),**

Calcd: C, 68.07; H, 5.0; N, 9.92%

Found: C, 68.29; H, 4.84; N, 10.19%.

(F) Using equimole of hydroxylamine in boiling pyridine

An intimate mixture of 2-phenyl-4-benzal-5-oxazolone, 2.5 g (0.01 mol) and hydroxylamine hydrochloride 0.70 g (0.01 mol) in pyridine (50 ml) was refluxed for 35 min. The solvent was evaporated under diminished pressure and the red coloured residue was dissolved in ethylacetate-chloroform mixture (3:1). Needle shaped crystals of \( \alpha,\alpha' \)-dibenzamidocinnamohydroxamic acid were obtained on cooling. These were filtered on a Buchner funnel, recrystallised from ethanol-petroleum ether mixture (3:1) and dried. Yield 1.1 g (30%), m.p. 245-46°; UV \( \lambda_{\text{max}}^{\text{MeOH}} \) 280 nm (abs. 0.9); IR (nujol) 3290, 1690, 1645, 1580 cm\(^{-1}\).

**Anal. for C\(_{32}\)H\(_{25}\)N\(_3\)O\(_5\),**

Calcd: C, 72.30; H, 4.74; N, 7.91%

Found: C, 72.10; H, 4.70; N, 7.69%.
The above filtrate was evaporated to dryness and the residue so secured was dissolved in benzene (20 ml). On cooling N-hydroxy-2-phenyl-4-benzylidene-5-imidazolone crystallised out. This was filtered and dried. Yield 1.08 g (58%), m.p. 219-20°; UV $\lambda_{\text{max}}^{\text{MeOH}}$ 258 μm (abs. 1.03) and 310 μm (abs. 0.88); IR (KBr) 3040, 2750, 1675, 1640, 1590, 1450 cm⁻¹.

Anal. for C₁₆H₁₂N₂O₂,
Calcd: C, 72.73; H, 4.54; N, 10.60%
Found: C, 73.00; H, 4.65; N, 10.88%.

6. Treatment of 2-phenyl-4-(4'-methoxybenzal)-5-oxazolone with hydroxylamine

(A) Using equimole of oxazolone and hydroxylamine in methanol at reflux temperature

2-Phenyl-4-(4'-methoxybenzal)-5-oxazolone, 2.8 g (0.01 mol) was suspended in methanol (80 ml) along with sodium methoxide, 0.54 g (0.01 mol) and hydroxylamine hydrochloride, 0.70 g (0.01 mol). This was heated at reflux temperature for 30 mins. The solvent was evaporated to dryness on a steam bath. The residue so obtained was dissolved in ethyl acetate which on cooling gave α,α'-dibenzamido-4,4'-dimethoxycinnamohydroxamic acid. This was filtered, recrystallised from ethanol (95%) and dried. Yield 3.6 g (62%), m.p. 156°; UV $\lambda_{\text{max}}^{\text{MeOH}}$ 230 μm (abs. 1.35) and 310 μm (abs. 1.60); IR (nujol) 3310, 1675 cm⁻¹.
Anal. for C$_{34}$H$_{29}$N$_2$O$_7$.
Calcd: C, 69.02; H, 4.94; N, 7.10%
Found: C, 69.00; H, 4.90; N, 7.09%.

(B) Using excess of hydroxylamine in methanol at reflux temperature

A mixture of 2-phenyl-4-(4'-methoxybenzal)-5-oxazolone, 2.7 g (0.01 mol), hydroxylamine hydrochloride, 1.4 g (0.02 mol) and sodium ethoxide, 1.08 g (0.02 mol) in methanol (60 ml) was refluxed for 45 min. The solvent was evaporated on a steam bath to dryness. The residue so obtained was dissolved in benzene (20 ml). On cooling α-benzamido-(4'-methoxycinnamo)-hydroxamic acid crystallised out. This was filtered and dried in an oven at 90°. It melted at 230° and weighed 2.45 g (79%). UV $\lambda_{\text{max}}^{\text{MeOH}}$ 370 μm (abs. 0.078); IR (nujol) 3290, 3250, 2728, 1670 cm$^{-1}$.

Anal. for C$_{17}$H$_{16}$N$_2$O$_4$,
Calcd: C, 65.37; H, 5.16; N, 8.97%
Found: C, 65.01; H, 5.13; N, 8.69%.

7. Treatment of 2-phenyl-4-(3',4'-dimethoxybenzal)-5-oxazolone with excess of hydroxylamine in boiling methanol

Powdered 2-phenyl-4-(3',4'-dimethoxybenzal)-5-oxazolone, 2.85 g (0.01 mol) was added to methanol (60 ml) along with sodium methoxide, 1.08 g (0.01 mol) and hydroxylamine hydrochloride,
1.4 g (0.02 mol). This was refluxed for one hr. The solvent was evaporated to dryness in a China dish on a steam bath. The residue so secured was dissolved in 20 ml of ethanol and cooled when the compound \( \alpha \)-N-benzoylamino-\( \beta \)-hydroxylamino-\( \beta \)-3,4-dimethoxyphenylpropionichydroxamic acid was crystallised. This was filtered and dried at room temperature. It melted at 135° and yielded 2.23 g (60%); UV \( \lambda_{\text{max}}^{\text{MeOH}} \) 230 μm (abs. 1.35), 280 μm (abs. 0.46); IR (nujol) 3370, 3265, 2700, 2650, 1700, 1600, 1470, 1360 cm\(^{-1}\).

Anal. for C\(_{18}\)H\(_{21}\)N\(_3\)O\(_6\),
Calcd: C, 57.33; H, 5.60; N, 11.20%
Found: C, 57.33; H, 6.00; N, 11.35%.

8. Treatment of 2-phenyl-4-cinnamylidene-5-oxazolone with hydroxylamine

(A) Using excess of hydroxylamine in boiling methanol

Finally powdered 2-phenyl-4-cinnamylidene-5-oxazolone, 2.75 g (0.01 mol) was suspended in methanol (60 ml) along with sodium methoxide, 1.08 g (0.02 mol) and hydroxylamine hydrochloride, 1.4 g (0.02 mol) and the whole was refluxed for 45 min. The solvent was evaporated under reduced pressure on a steam bath. The residue so obtained was dissolved in ethyl acetate white crystalline mass of \( \beta \)-\( \delta \)-dihydroxylamino-N-hydroxy-4-(\( \delta \)-phenylpropiono\( ^-\))-5-imidazolone was secured on cooling which was filtered,
recrystallised from ethanol (95%) and dried yield 2.95 g (83%), m.p. 185°; UV $\lambda_{\text{max}}^{\text{MeOH}}$ 235 μm (abs. 0.61); IR (nujol) 3265, 1710, 1640 cm$^{-1}$.

Anal. for C$_{13}$H$_{20}$N$_{4}$O$_{4}$,
Calcd: C, 60.66; H, 5.66; N, 15.72%  
Found: C, 60.67; H, 5.62; N, 15.94%.

(B) Using equimole of hydroxylamine in boiling pyridine

A mixture of 2-phenyl-4-cinnamylidene-5-oxazolone, 2.75 g (0.01 mol), hydroxylamine, 0.7 g (0.01 mol) and pyridine was refluxed for 30 min. The solvent was evaporated under diminished pressure to dryness. The residue obtained was dissolved in ethyl acetate. On cooling the product $\alpha,\alpha'$-dibenzoylamino-$\gamma,\gamma'$-dibenzenebutyrohydroxamic acid crystallised out. This was filtered, recrystallised from ethanol (95%) and dried in oven at 80°. It melted at 248-50° and weighed 2.91 g (50%); UV $\lambda_{\text{max}}^{\text{MeOH}}$ 235 μm (abs. 0.78) and 330 μm (abs. 1.30); IR (nujol) 3265, 1685, 1640, 1615, 1500 cm$^{-1}$.

Anal for C$_{35}$H$_{29}$N$_{3}$O$_{5}$,
Calcd: C, 74.08; H, 5.01; N, 7.20%  
Found: C, 74.00; H, 4.90; N, 7.30%
(C) Using equimole of hydroxylamine in boiling methanol

An intimate mixture of 2-phenyl-4-cinnamylidene-5-oxazolone, 2.80 g (0.01 mol), hydroxylamine hydrochloride 0.7 g (0.01 mol) and sodium methoxide, 0.54 g (0.01 mol) in 60 ml of methanol was refluxed for 1.5 hr. The solvent was concentrated to 25 ml on a steam bath and then cooled. The product αα'-dibenzoylamino-γ,γ'-dibenzenepyrohydroxamic acid emerged in crystalline form. This was filtered on a Buchner funnel, recrystallised from ethanol (95%) and air dried. Yield 4.31 g (74%), m.p. 250°. UV \( \lambda_{\text{max}} \) MeOH 230 \( \text{nm} \) (abs. 0.88); 330 \( \text{nm} \) (abs. 1.20); IR (nujol) 235, 1685, 1640, 1615, 1500 cm\(^{-1}\).

Anal. for \( \text{C}_{36}\text{H}_{29}\text{N}_{3}\text{O}_{5} \),
Calcd: C, 74.08; H, 5.01; N, 7.20%
Found: C, 74.00; H, 4.90; N, 7.30%.

9. Treatment of 2-phenyl-4-(2',4'-diacetoxybenzal)-5-oxazolone with excess of hydroxylamine in boiling methanol

A mixture of 2-phenyl-4-(2',4'-diacetoxybenzal)-5-oxazolone, 3.65 g (0.01 mol), hydroxylamine hydrochloride, 1.4 g (0.02 mol) and sodium methoxide 1.08 g (0.01 mol) was taken in methanol (60 ml) and the whole was refluxed for one hr. On cooling the product α-benzoylamino-β-hydroxylamo-β-2,4-diacetoxyphenyl-propionichydroxamic acid crystallised out. This was filtered,
recrystallised from ethanol (95%) and dried in oven at 90°. Yield 3.44 g (80%), m.p. 250°; UV \( \lambda_{\text{max}}^{\text{MeOH}} \) 350 mp (abs. 1.40); IR (nujol) 3390, 3175, 2730, 2680, 1700, 1610, 1470, 1370, 1240 cm\(^{-1}\).

Anal. for C\(_{20}\)H\(_{21}\)N\(_3\)O\(_8\),
Calcd: C, 55.68; H, 4.87; N, 9.77%
Found: C, 56.00; H, 4.67; N, 9.52%
III. AMMONOLYSIS OF AZLACTONE  
SYNTHESIS OF α-N-BENZOYLAMINOACRYLIC ACID AMIDES

1. Synthesis of α-N-Benzoylamino-β-2'-methoxyphenylacrylic acid amide

2-Phenyl-4(2'-methoxybenzal)-5-oxazolone, (6 g) was dissolved in 100 ml of ethanol. Ammonia solution (10 ml) (sp. gr. 0.99) was added and the whole of the mixture was refluxed to obtain a clear solution. This was cooled and the crystalline amide was filtered, recrystallised from ethanol (95%) and dried, yield 3.87 g (61%) m.p. 225.

Anal. for C_{17}H_{17}N_{2}O_{3},
Calcd: C, 68.71; H, 5.40; N, 9.84%
Found: C, 68.30; H, 5.60; N, 9.90%.

2. Synthesis of α-N-Benzoylamino-β-3'-methoxy-4'-hydroxyphenylacrylic acid amide

Powdered 2-phenyl-4-(3'-methoxy-4'-acetoxybenzal)-5-oxazolone, (7 g) was added in ethanol (50 ml) containing ammonia solution (12 ml). This was refluxed on a steam bath to obtain a clear solution. On cooling the amide crystallised out. This was filtered, recrystallised from ethanol (95%) and dried in an oven at 80°. It melted at 180° and weighed 6.50g (95%).

Anal. for C_{17}H_{16}N_{2}O_{4},
Calcd: C, 65.37; H, 5.16; N, 8.97%
Found: C, 65.37; H, 5.00; N, 9.00%.
3. **Synthesis of α-N-Benzoylamino-cyclohexylacrylic acid amide**

Powdered 2-phenyl-4-cyclohexylidene-5-oxazolone (5 g) was suspended in 100 ml of ethanol containing ammonia solution (10 ml). This was refluxed for 20 min. to get a clear solution. The solution was concentrated to 25 ml. On cooling the amide was crystallized which was filtered and dried, yield 4.92 g (92%), m.p. 202-03°.

Anal. for C_{15}H_{18}N_{2}O_{2},
Calcd: C, 69.74; H, 7.02; N, 10.85\%
Found: C, 70.00; H, 6.90; N, 10.80%.

4. **Synthesis of α-N-Benzoylamino-2-hydroxyphenylacrylic acid amide**

2-Phenyl-4-(2'-acetoxybenzal)-5-oxazolone (6 g) was added in ethanol (40 ml) along with 10 ml of ammonia solution. This was heated at reflux temperature to obtain a clear solution. Then excess of ethanol was distilled to concentrate the solution. This was cooled when the amide emerged in crystalline form. Yield 4.66 g (84%), m.p. 271°.

Anal. for C_{16}H_{14}N_{2}O_{3},
Calcd: C, 68.07; H, 5.00; N, 9.92%.
Found: C, 68.00; H, 5.36; N, 10.12%.
5. Synthesis of $\alpha$-N-Benzoylamino-1,3-hexadienonic acid amide

Powdered 2-phenyl-4-crotonylidene-5-oxazolone (5.5 g) was suspended in 50 ml of ethanol. To this 10 ml of concentrated ammonia solution was added and the whole heated at reflux temperature for 25 min. The solution was concentrated to 20 ml. On cooling the amide was crystallised. This was filtered, recrystallised from ethanol and air dried. It weighed 5.69 g (96%) and melted at 130°.

Anal. for $C_{13}H_{14}N_2O_2$,  
Calcd: C, 67.81; H, 6.13; N, 12.17%.  
Found: C, 68.03; H, 6.10; N, 12.17%.

6. Synthesis of $\alpha$-N-Benzoylamino-3-piperonylacrylic acid amide

2-Phenyl-4-piperonal_methylene-5-oxazolone (5 g) was added in ethanol (60 ml) containing ammonia solution (8 ml). This was refluxed for 25 min to obtain a clear solution. Excess of ethanol was distilled to concentrate the solution and then cooled. The amide emerged in crystalline form was filtered, recrystallised from ethanol and dried. Yield 5.07 g (96%), m.p. 95°.

Anal. for $C_{17}H_{14}N_2O_4$,  
Calcd: C, 65.80; H, 4.55; N, 9.03%  
Found: C, 65.56; H, 4.59; N, 8.99%.
7. Synthesis of $\alpha$-N-Benzoylamino-phenylacrylic acid amide

Powdered 2-phenyl-4-benzylidene-5-oxazolone (6 g) was suspended in ethanol (50 ml) along with 10 ml of ammonia solution (sp. gr. 0.98). This was refluxed for 30 min. The flask was left at room temperature overnight. Next morning the crystallised product, $\alpha$-N-benzoylamino-phenylacrylic acid amide was filtered and dried. It weighed 5.5 g (86%) and melted at 196°.

Anal. for $C_{16}H_{14}N_{2}O_{2}$,
Calcd: C, 72.16; H, 5.30; N, 10.52%
Found: C, 72.10; H, 5.44; N, 10.22%.

8. Synthesis of $\alpha$-N-Benzoylamino-$\beta$-4'-methoxyphenylacrylic acid amide

Powdered 2-phenyl-4-(4'-methoxybenzal)-5-oxazolone (6 g) was taken in 50 ml of ethanol. To this concentrated ammonia solution (10 ml) was added and the whole refluxed for 20 min. Excess of solution was removed and left at room temperature. The white crystallised amide was separated on a Buchner funnel and recrystallised from ethanol. The dried product weighed 5.94 g (84%), m.p. 130°.

Anal. for $C_{17}H_{16}N_{2}O_{3}$,
Calcd: C, 68.90; H, 5.44; N, 9.45%
Found: C, 68.80; H, 5.17; N, 9.71%.
9. Synthesis of $\alpha$-N-Benzoyleamino-3',4'-Dimethoxyphenylacrylic acid amide

Powdered 2-phenyl-4-(3',4'-dimethoxybenzal)-5-oxazolone, (6 g) was refluxed in 100 ml of ethanol containing concentrated ammonia solution (8 ml). After 20 min. a clear solution was obtained. The contents were concentrated to 15 ml and cooled. The crystallised amide was filtered, recrystallised from ethanol (95%) and dried. Yield 4.24 g (67%) m.p. 185°.

Anal. for $C_{18}H_{16}N_2O_4$,
Calcd: C, 66.24; H, 5.56; N, 8.58%.
Found: C, 65.08; H, 5.75; N, 8.29%.

10. Synthesis of $\alpha$-N-Benzoyleamino-4-hydroxyphenylacrylic acid amide

2-Phenyl-4-(4'-acetoxybenzal)-5-oxazolone (5 g) was dissolved in 100 ml of ethanol containing liquor ammonia (10 ml), and heated at reflux for 20 minutes. This was left at room temperature overnight. Next morning the crystallised amide was filtered. The dried product melted at 215-16° and weighed 5.03 g (95%). The yield was nearly quantitative. Recrystallisation from ethanol (95%) did not raise the melting point.

Anal. for $C_{16}H_{14}N_2O_3$,
Calcd: C, 68.07; H, 5.00; N, 9.92%.
Found: C, 67.78; H, 4.81; N, 10.10%.
11. Synthesis of α-N-Benzoylamino-β-phenyl-γ-pentadienic acid amide

2-Phenyl-4-cinnamylidene-5-oxazolone (6 g) was added in ethanol (60 ml) along with concentrated ammonia solution (10 ml). This was refluxed for 20 min. when a clear solution was obtained. The contents were concentrated to 20 ml. On cooling the amide crystallised out. This was filtered, recrystallised from ethanol (95%) and dried. Yield 5.5 g (87%), m.p. 190°.

Anal. for C_{18}H_{16}N_{2}O_{2}
Calcd: C, 73.45; H, 6.16; N, 9.52%.
Found: C, 73.50; H, 5.92; N, 9.83%.

12. Synthesis of α-N-Benzoylamino-β-p-dimethylaminophenylacrylic acid amide

Powdered 2-phenyl-4-(p'-dimethylaminobenzal)-5-oxazolone (5.5 g) was taken in 100 ml of ethanol. To this, 10 ml of concentrated ammonia solution was added. This was heated at reflux temperature. After few minutes white crystals of the amide appeared. The solution was cooled and the product filtered on a Buchner funnel. On recrystallisation from glacial acetic acid it weighed 3.80 g (65%) and melted at 160°.

Anal. for C_{19}H_{19}N_{3}O_{2}
Calcd: C, 69.88; H, 6.19; N, 13.58%.
Found: C, 69.99; H, 6.25; N, 13.79%.
13. **Synthesis of \( \alpha \)-N-Benzoylamino-\( \beta \)-4-nitrophenylacrylic acid amide**

Powdered 2-phenyl-4-(4'-nitrobenzal)-5-oxazolone (6 g) was added in 100 ml of ethanol containing concentrated ammonia solution (10 ml). This was heated at reflux temperature. After 1 hr a clear solution was obtained. On cooling the amide was crystallised. This was filtered and dried when it weighed 5.7 g (nearly quantitative yield) and melted at 167.68\(^\circ\). Recrystallisation from ethanol did not raise the melting point.

**Anal. for C\(_{16}\)H\(_{13}\)N\(_3\)O\(_4\)**,

Calcd: C, 61.73; H, 4.21; N, 13.50%.

Found: C, 61.50; H, 4.01; N, 13.49%.

14. **Synthesis of \( \alpha \)-N-Benzoylamino-3-indolylacrylic acid amide**

2-Phenyl-4-(3'-indolylmethylene)-5-oxazolone (3 g) was dissolved in 50 ml of ethanol. To this, 10 ml of concentrated solution of ammonia was added and the whole refluxed for 30 min. to obtain a clear solution. The solution was concentrated to 20 ml and then ethyl acetate (10 ml) was added. On cooling the amide crystallised out. This was filtered, recrystallised from ethanol (95%) and dried. Yield 2.6 g (nearly quantitative), m.p. 205\(^\circ\).

**Anal. for C\(_{16}\)H\(_{15}\)N\(_3\)O\(_2\)**,

Calcd: C, 70.80; H, 4.95; N, 13.76%

Found: C, 71.00; H, 4.85; N, 14.00%.
15. Synthesis of \( \alpha \)-N-BenzoylamoNO-\( \beta \)-i-naphthylacrylic acid amide

2-Phenyl-4-(1'-naphthylmethylene)-5-oxazolone, (6 g) was suspended in 100 ml of ethanol. To this liquor ammonia (8 ml) was added and then refluxed for 30 min. The clear solution so obtained was cooled when the amide emerged in crystalline form. This was filtered and recrystallised from ethanol (95%). The dried product weighed 5.98 g (94%) and melted at 256°.

Anal. for \( \text{C}_{20}\text{H}_{16}\text{N}_{2}\text{O}_{2} \):

Calcd: C, 75.93; H, 5.10; N, 8.86%.

Found: C, 76.08; H, 5.39; N, 9.00%.
IV. TREATMENT OF \( \alpha^-N\)-BENZOYLAMINOACRYLIC ACID AMIDES WITH HYDROXYLAMINE

Synthesis of \( \alpha^-N\)-Benzoylamino-\( \beta^-\)hydroxylamino acid amides

1. Synthesis of \( \alpha^-N\)-Benzoylamino-\( \beta^-\)-hydroxylamino-2-methoxy-phenylalanine amide

An intimate mixture of \( \alpha^-N\)-Benzoylamino-\( \beta^-\)-2-methoxy-phenylacrylic acid amide, 3 g (0.01 mol), sodium methoxide, 0.54 g (0.01 mol) and hydroxylamine hydrochloride, 0.7 g (0.01 mol) was heated at reflux temperature for one hr. Solvent was evaporated on a steam bath. The residue was dissolved in ethanol (20 ml) and cooled, yielding crystallised product which was filtered. Yield 1.33 g (40%), m.p. 45\(^\circ\).

Anal. for \( \text{C}_{17}\text{H}_{19}\text{N}_3\text{O}_4\),
Calcd: C, 61.99; H, 5.82; N, 12.76%.
Found: C, 61.79; H, 6.02; N, 13.00%.

2. Synthesis of \( \alpha^-N\)-Benzoylamino-\( \beta^-\)-hydroxylamino-3-methoxy-4-hydroxyphenylalanine amide

A mixture of \( \alpha^-N\)-benzoylamino-\( \beta^-\)-3-methoxy-4-hydroxy-phenylacrylic acid amide, 3 g (0.01 mol), hydroxylamine hydrochloride, 0.7 g (0.01 mol), and sodium ethoxide, 0.7 g (0.01 mol) was refluxed in ethanol (50 ml) for 45 minutes. This was left at room temperature overnight. Next morning the crystallised
compound was filtered and recrystallised from ethanol (95%).
Yield 2.5 g (74%); UV $\lambda_{\text{max}}^\text{MeOH}$ 230 μm (abs. 1.10) $\lambda_{\text{max}}^\text{Dioxane}$ 320 μm (abs. 0.53); IR (nujol) 3475, 3345, 3220, 1685, 1655 cm$^{-1}$.

Anal. for C$_{17}$H$_{19}$N$_3$O$_5$,
Calcd: C, 59.12; H, 5.55; N, 12.17%.
Found: C, 59.40; H, 5.60; N, 12.27%.

3. **Synthesis of α-N-Benzoylamino-1-hydroxylaminocyclohexylglycine amide**

α-N-Benzoylaminocyclohexylacrylic acid amide, 2.6 g (0.01 mol) was dissolved in methanol (50 ml) containing sodium methoxide, 0.55 g (0.01 mol). To this hydroxylamine 0.7 g (0.01 mol) was added and then refluxed for 3 hr. The solvent was evaporated under diminished pressure to dryness and the residue so secured was dissolved in ethyl acetate. On cooling the product crystallised out. This was filtered and dried. Yield 2.72 g (86%), m.p. 215-17°. UV $\lambda_{\text{max}}^\text{MeOH}$ 230 μm (abs. 1.05); IR (nujol) 3410, 3280, 3160, 1680, 1640, 1600, 1580 cm$^{-1}$.

Anal. for C$_{15}$H$_{21}$N$_3$O$_3$,
Calcd: C, 61.84; H, 7.27; N, 14.42%.
Found: C, 61.50; H, 7.27; N, 14.50%.
4. **Synthesis of \( \alpha \)-N-Benzoylamino-\( \beta \)-hydroxylamine-\( \beta \)-tyrosine amide**

\( \alpha \)-N-Benzoylamino-2-hydroxy-phenylacrylic acid amide, 2.82 g (0.01 mol) was added to methanol (50 ml) along with sodium methoxide, 0.54 g (0.01 mol) and hydroxylamine hydrochloride, 0.7 g (0.01 mol). This was heated at reflux temperature for 3 hr. and then kept at room temperature overnight. The crystallised compound was filtered, recrystallised from ethanol (95%) and dried in air. It weighed 1.55 g (50%) and melted at 155\(^\circ\). UV \( \lambda_{\text{max}} \) MeOH 330 \( \text{m}\) (abs. 0.76); IR (nujol) 3365, 2650, 1710, 1662, 1600, 1530, 1378 cm\(^{-1}\).

Anal. for C\( _{16} \)H\( _{17} \)N\( _{2} \)O\( _{4} \)
Calcd: C, 60.94; H, 5.43; N, 13.33%
Found: C, 61.20; H, 5.50; N, 13.65%.

5. **Synthesis of \( \alpha \)-N-Benzoylamino-\( \beta \)-hydroxylamino-3-hexenic acid amide**

A mixture of \( \alpha \)-N-benzoylamino-\( \beta \)-hexadienic acid amide, 2.30 g (0.01 mol), sodium methoxide 0.54 g (0.01 mol) and hydroxylamine hydrochloride 0.7 g (0.01 mol) was refluxed in methanol (50 ml) for 3 hr. The solvent was concentrated to 20 ml and then cooled. The crystalline product thus obtained was filtered, recrystallised from ethanol (95%) when it weighed 1.70 g (80%)
and melted at 150°. UV \( \lambda_{\text{max}} \text{MeOH} \) 235 μμ (abs. 0.76); IR (nujol) 3200, 1720, 1650, 1600, 1520, 1460 cm⁻¹.

Anal. for \( \text{C}_{13}\text{H}_{17}\text{N}_{3}\text{O}_{3} \)
Calcd: C, 59.30; H, 6.51; N, 15.96%
Found: C, 59.50; H, 6.65; N, 16.00%.

6. Synthesis of \( \alpha\)-N-Benzoylamino-\( \beta\)-hydroxylaminopiperonylalanine amide

An intimate mixture of \( \alpha\)-N-benzoylamino-\( \beta\)-piperonylacrylic acid amide, 3.10 g (0.01 mol), hydroxylamine hydrochloride, 0.7 g (0.01 mol) and sodium methoxide 0.54 g (0.01 mol) was heated at reflux temperature in methanol (50 ml) for 1 hr. The solvent was concentrated to 20 ml and cooled. The crystallised product was filtered and recrystallised from methanol. The dried product weighed 3.18 g (93%) and melted at 180°; UV \( \lambda_{\text{max}} \text{MeOH} \) 230 μμ (abs. 0.69); 290 μμ (abs. 0.245).

Anal. for \( \text{C}_{17}\text{H}_{17}\text{N}_{3}\text{O}_{5} \)
Calcd: C, 59.47; H, 4.99; N, 12.24%
Found: C, 59.74; H, 5.00; N, 12.26%

7. Synthesis of \( \alpha\)-N-Benzoylamino-\( \beta\)-hydroxylaminophenylalanine amide

\( \alpha\)-N-Benzoylaminophenylacrylic acid amide, 2.66 g (0.01 mol) was suspended in methanol along with sodium methoxide, 0.54 g
(0.01 mol) and hydroxylamine hydrochloride 0.7 g (0.01 mol) and the whole was heated for 3 hr. on a steam bath at reflux temperature. The solvent was evaporated under reduced pressure and the residue so secured was dissolved in ethyl acetate (25 ml). On cooling the product \( \alpha \)-N-benzoylamino-\( \beta \)-hydroxylaminophenylalanine amide crystallised out. Yield 1.95 g (65%), m.p. 194\(^\circ\). Recrystallisation from methanol raised the melting point to 210\(^\circ\).

\[ \text{UV}_{\text{max}} \text{MeOH} 230 \text{ nm (abs. 1.20); IR (nujol) 3318, 1645, 1600 cm}^{-1}. \]

\text{Anal. for } C_{16}H_{17}N_{3}O_{3}
\text{Calcd: } C, 64.21; H, 5.68; N, 14.04\%
\text{Found: } C, 64.00; H, 5.74; N, 14.00\%.

The above filtrate was concentrated to 15 ml and then benzene (10 ml) was added to it. On cooling second compound \( \alpha \)-benzamido-\( \beta \)-phenylpropino hydroxamic acid emerged in brown coloured crystals. This was filtered when it melted at 166\(^\circ\). This was recrystallised from methanol. Yield 1 g (20%), m.p. 170\(^\circ\); UV \[ \text{MeOH}_{\text{max}} \text{225 nm (abs. 1.25); IR (nujol) 3400, 3380, 3240, 3170, 1700, 1665, 1630 cm}^{-1}. \]

\text{Anal. for } C_{16}H_{14}N_{2}O_{3}
\text{Calcd: } C, 68.07; H, 5.00; N, 9.90\%
\text{Found: } C, 68.00; H, 4.59; N, 10.06\%. 
8. Synthesis of $\alpha$-N-Benzoylamino-$\beta$-hydroxylamino-0-methyl-
tyrosine amide

$\alpha$-N-Benzoylamino-4-methoxyphenylacrylic acid amide, 3.00 g (0.01 mol) was suspended in methanol (50 ml) along with sodium methoxide, 0.54 (0.01 mol) and hydroxylamine hydrochloride, 0.7 g (0.01 mol). This was refluxed for 3 hr. and then left at room temperature. Yellow coloured product was crystallised which was filtered and washed with two 20 ml portions of water. Recrystallised product, from glacial acetic acid, melted at 295\(^{\circ}\) and weighed 1.31 g (40\%); UV $\lambda_{\text{max}}$ MeOH 260 mp (abs. 1.20); IR (nujol) 2710, 1700, 1670, 1605, 1570, 1520, 1460, 1375 cm\(^{-1}\).

Anal. for C\textsubscript{17}H\textsubscript{19}N\textsubscript{3}O\textsubscript{4}
Calcd: C, 61.99; H, 5.82; N, 12.76\%
Found: C, 62.21; H, 5.50; N, 13.00%.

9. Synthesis of $\alpha$-N-Benzoylamino-$\beta$-hydroxylamino-3,4-dimethoxy-
phenylalanine amide

An intimate mixture of $\alpha$-N-benzoylamino-3',4'-dimethoxy-
phenylacrylic acid amide, 6.5 g (0.02 mol) hydroxylamine hydro-
chloride 1.40 g (0.02 mol), sodium methoxide 1.08 g (0.02 mol)
and methanol (100 ml) was refluxed for 3.5 hrs. This was left
at room temperature overnight. Next morning the yellow crystalline
product obtained, was filtered, recrystallised from ethanol and
dried. Yield 2.15 g (60\%) m.p. 240\(^{\circ}\); UV $\lambda_{\text{max}}$ MeOH 260 mp (abs. 8.90);
IR (nujol) 3475, 3345, 3220, 1685, 1655, 1570, 1460, 1370 cm\(^{-1}\).

\text{Anal. for } \text{C}_{16}\text{H}_{21}\text{N}_{3}\text{O}_{5} \\
\text{Calcd: C, 60.16; H, 5.89; N, 11.69\%} \\
\text{Found: C, 59.88; H, 5.96; N, 11.81\%}.

10. **Synthesis of \(\alpha\)-N-Benzoylamino-\(\beta\)-hydroxylaminotyrosine amide**

A mixture of \(\alpha\)-N-benzoylamino-4-hydroxyphenylacrylic acid amide, 2.81 g (0.01 mol), hydroxylamine hydrochloride, 0.70 g (0.01 mol) and sodium methoxide, 0.54 g (0.01 mol) was refluxed in methanol (50 ml) for 30 minutes. On cooling white crystalline product was filtered. This was recrystallised from ethanol (95\%). On drying it melted at 230° and weighed 2.52 g (80\%); UV \(\lambda_{\text{max}}\) \text{MeOH} 230 \text{ m\(\mu\)} (abs. 1.15); IR (nujol) 3350, 2650, 2600, 1710, 1662, 1600, 1530, 1378 cm\(^{-1}\).

\text{Anal. for } \text{C}_{16}\text{H}_{17}\text{N}_{3}\text{O}_{4} \\
\text{Calcd: C, 60.94; H, 5.43; N, 13.33\%} \\
\text{Found: C, 60.84; H, 5.09; N, 13.50\%}.

11. **Synthesis of \(\alpha\,-N\)-Benzoylamino-\(\beta\)-hydroxylamino-\(\gamma\),\(\delta\)-diene \(\varepsilon\)-\(\varepsilon\)-phenylnorvaline amide**

\(\alpha\)-N-benzoylamino-\(\delta\)-phenyl-\(\beta\),\(\gamma\)-pentadienic acid amide, 2.92 g (0.01 mol) was suspended in methanol (50 ml) along with sodium methoxide, 0.54 g (0.01 mol) and hydroxylamine hydrochloride,
0.70 g (0.01 mol). This was heated at refluxed temperature for 30 minutes. Leaving at room temperature overnight afforded the crystalline product. This was filtered, recrystallised from ethanol, dried, when it melted at 200° and weighed 2.30 g (72%).

\[ \text{UV} \lambda_{\text{max}}^{\text{MeOH}} 235 \text{ nm} \text{ (abs. 0.78); IR (nujol) 3313, 2730, 2630, 1645, 1565, 1420, 1380 cm}^{-1}. \]

Anal. for C_{18}H_{19}N_{3}O_{3}
Calcld: C, 66.44; H, 5.89; N, 12.92%
Found: C, 66.19; H, 6.11; N, 13.08%.

12. Synthesis of \( \alpha \)-N-Benzoylamino-\( \beta \)-hydroxylamino-4-dimethylaminophenyl amide

An intimate mixture of \( \alpha \)-N-benzoylamino-\( \beta \)-4-dimethylamino-phenylacrylic acid amide, 3.09 g (0.01 mol), hydroxylamine hydrochloride, 0.70 g (0.01 mol), sodium methoxide, 0.54 g (0.01 mol) and methanol (50 ml) was heated at refluxed temperature for 1 hr. This was left overnight at room temperature. The product emerged in crystalline form. This was filtered and recrystallised from ethanol. The dried product weighed 2.90 g (85%) and melted at 265°. \[ \text{UV} \lambda_{\text{max}}^{\text{MeOH}} 220 \text{ nm} \text{ (abs. 0.285) and 305 nm} \text{ (abs. 0.395); IR (nujol) 2710, 1670, 1605, 1570, 1520, 1460 cm}^{-1}. \]

Anal. for C_{18}H_{22}N_{4}O_{3}
Calcld: C, 63.14; H, 6.48; N, 16.36%
Found: C, 63.50; H, 6.14; N, 16.56.
13. Synthesis of \( \alpha-N\text{-Benzoylamino-} \beta\text{-hydroxylamino-}4\text{-nitrophenylalanine amide} \)

\( \alpha-N\text{-Benzoylamino-} \beta\text{-4-nitrophenylacrylic acid amide} \), 2.81 g (0.01 mol), sodium ethoxide, 0.70 g (0.01 mol), and hydroxylamine hydrochloride, 0.70 g (0.01 mol) were added to methanol (50 ml). This was heated at reflux temperature for 30 minutes and kept overnight, as such at room temperature. Dark brown crystalline product thus obtained was filtered and washed with distilled water for removal of traces of salt and recrystallised from ethanol (95%). The dried mass weighed 1.3 g (37%) and melted at 218°. UV \( \max^{\text{MeOH}} \) 230 μm (abs. 1.60) and 320 μm (abs. 1.20); \( \max^{\text{Dioxane}} \) 330 μm (abs. 0.53); IR (nujol) 3225, 1740, 1710, 1650, 1600, 1512, 1345 cm\(^{-1}\).

Anal. for \( \text{C}_{10}\text{H}_{16}\text{N}_3\text{O}_5 \)

Calcd: C, 55.81; H, 4.68; N, 16.27%

Found: C, 56.00; H, 4.96; N, 16.03%.

14. Synthesis of \( \alpha-N\text{-Benzoylamino-} \beta\text{-hydroxylaminotryptophan amide} \)

A mixture of \( \alpha-N\text{-benzoylamino-3-indolylacrylic acid amide} \), 3.05 g (0.01 mol), hydroxylamine hydrochloride, 0.70 g (0.01 mol) and sodium methoxide, 0.54 g (0.01 mol) was refluxed in methanol (50 ml) for 45 minutes. This was left overnight at room temperature. Yellow crystalline product was filtered and washed with
water and recrystallised from alcohol and benzene mixture (3:1).
Yield 3.07 g (90%) m.p. 260°, UV $\lambda_{\text{max}}$ MeOH 260 μm (abs. 0.400),
340 μm (abs. 0.30); IR (nujol) 3740, 3465, 3170, 2720, 2660,
1665, 1500, 1375, 1225, 1030 cm$^{-1}$.

Anal. for $C_{18}H_{18}N_4O_3$
Calcd: C, 63.89; H, 5.36; N, 16.56%
Found: C, 63.54; H, 5.50; N, 16.35%.

15. **Synthesis of α-N-Benzoylaminob-β-hydroxylaminonaphthylalanine amide**

A mixture of α-N-benzoylaminob-β-1-naphthylacrylic acid amide, 3.17 g (0.01 mol) hydroxylamine hydrochloride, 0.70 g (0.01 mol) and sodium methoxide, 0.54 g (0.01 mol) were taken in 50 ml of methanol and the whole refluxed for 3 hr. This was cooled to room temperature. The product emerged in crystalline form was filtered and recrystallised from ethanolethyl acetate mixture (3:1). It melted at 245° and weighed 1.40 g (40%).
UV $\lambda_{\text{max}}$ MeOH 270 μm (abs. 0.220); IR (nujol) 3730, 3160, 2720, 2650,
1690, 1620, 1530, 1380, 1230 cm$^{-1}$.

Anal. for $C_{20}H_{19}N_3O_3$
Calcd: C, 68.75; H, 5.48; N, 12.03%
Found: C, 68.89; H, 5.16; N, 11.90%.
V. PALLADIUM-CHARCOAL (10% Pd) CATALYSED REDUCTION*

Reduction of $\alpha$-N-Benzoylamino-$\beta$-hydroxylamino acid amide and N-benzoylamino-$\beta$-hydroxylaminopropionhydroxamic acid

1. Synthesis of $\beta$-Amino-$\alpha$-N-benzoylamino-3-methoxy-4-hydroxyphenylalanine amide

Powdered $\alpha$-N-benzoylamino-$\beta$-hydroxylamino-3'-methoxy-4-hydroxyphenylalanine amide, 3.45 g (0.01 mol) was suspended in 100 ml of ethanol containing palladium charcoal (10% Pd) (0.5 g). This was reduced under a hydrogen pressure of 40 psi for 7 hr. When there was no more absorption of hydrogen, the flask was disconnected, contents heated on a steam bath and filtered hot. The filtrate was evaporated to dryness under reduced pressure and the residue was crystallised from ethanol (95%). The crystalline product thus obtained was filtered and dried when it weighed 3.15 g (96%) and melted at 215°; UV $\lambda_{max}^{\text{MeOH}}$ 230 m$\mu$ (abs. 1.10); IR (nujol) 3500, 3385, 3290, 3170, 1650, 1570 cm$^{-1}$.

Anal. for $C_{17}H_{19}N_{3}O_{4}$
Calcd: C, 61.99; H, 5.82; N, 12.76%
Found: C, 62.00; H, 6.10; N, 12.56%.

2. Synthesis of 1-Amino-$\alpha$-N-benzoylaminocyclohexylglycine amide

$\alpha$-N-Benzoylamino-1-hydroxylaminocyclohexylglycine amide
2.91 g (0.01 mol) was suspended in 100 ml of ethanol. To this palladium charcoal (10% Pd) was added and this was reduced under a

* All reductions were conducted in a Paar catalytic hydrogenation apparatus.
hydrogen pressure of 56 psi for 7 hr. The flask was disconnected, contents heated on a steam bath and filtered hot. The filtrate was dried under reduced pressure and residue so secured was crystallised from ethanol (95%). The dried product melted at 235° and weighed 1.80 g (65%). UV \( \lambda_{\text{max}}^{\text{MeOH}} = 230 \text{ nm} \) (abs. 1.05); IR (nujol) 3382, 3300, 3250, 3150, 1700, 1620, 1570, 1450 cm\(^{-1}\).

Anal. for \( C_{17}H_{21}N_{3}O_{2} \)
Calcd: C, 65.43; H, 7.69; N, 15.26%
Found: C, 65.50; H, 8.00; N, 15.50%.

3. Synthesis of \( \beta \)-Amino-\( \alpha \)-N-benzoylaminonorvaline amide

A mixture of \( \alpha \)-N-benzoyl amino-\( \beta \)-hydroxylamino-3-hexenic acid amide, 2.7 g (0.01 mol) and palladised carbon (10% Pd) (0.5 g) was suspended in 100 ml ethanol. This was reduced under a hydrogen pressure of 56 psi. The reduction was complete in 12 hr. The flask was disconnected, contents heated on a steam bath and filtered hot. The filtrate was concentrated to 20 ml and then 5 ml of benzene was added. On cooling the product crystallised out. This was filtered and dried when it weighed 1.50 g (60%) and melted at 215°. UV \( \lambda_{\text{max}}^{\text{MeOH}} = 285 \text{ nm} \) (abs. 0.58); IR (nujol) 2720, 1710, 1600, 1530, 1460, 1370, 1300 cm\(^{-1}\).

Anal. for \( C_{13}H_{19}N_{3}O_{2} \)
Calcd: C, 62.62; H, 7.68; N, 16.86%
Found: C, 62.52; H, 8.00; N, 17.00%.
4. Synthesis of β-αmino-β-N-benzoylaminopiperonyllalanine amide

α-N-Benzoylamino-β-hydroxylaminopiperonyllalanine amide, 3.43 g (0.01 mol) was added to ethanol along with palladium charcoal (10% Pd) (0.4 g) and this was reduced under a hydrogen pressure of 60 psi for 24 hr. When there was no absorption of hydrogen the flask was disconnected and contents were heated on a steam bath. It was filtered and the catalyst washed with hot ethanol. The filtrate and washings were evaporated to dryness under reduced pressure. The residue was dissolved in ethanol benzene mixture (3:1). On cooling the product crystallized out. This was filtered and dried. It melted at 160-62° and weighed 2.94 g (90%). UV \( \lambda_{\text{max}} \) 240 m\( \mu \) (abs. 1.05); IR (nujol) 3490, 3385, 3290, 3170, 1650, 1570 cm\(^{-1}\).

Anal. for C\(_{17}\)H\(_{17}\)N\(_3\)O\(_4\)

Calcd: C, 62.37; H, 5.24; N, 12.84%

Found: C, 62.40; H, 5.50; N, 13.00%.

5. Synthesis of β-αmino-α-N-benzoylaminophenylalanine amide

Powdered α-N-benzoylamino-β-hydroxylamo-β-phenyl-propionic hydroxamic acid 3 g (0.01 mol) was suspended in ethanol (50 ml) in a palladium catalytic hydrogenation flask. This was reduced at 40 psi for 5 hr. The flask was disconnected when absorption of hydrogen stopped. The catalyst was filtered and the filtrate
was concentrated to 20 ml when α-N-benzoylamino-β-aminophenylalanine amide, crystallised out on cooling. This was filtered and dried, yield 2.58 g (95%), m.p. 197°; UV $\lambda_{\text{max}}^\text{MeOH}$ 230 nm (abs. 1.45); IR (nujol) 3320, 2750, 1660, 1600, 1550 cm$^{-1}$.

Anal. for C$_{16}$H$_{17}$N$_3$O$_2$
Calcd: C, 67.82; H, 6.05; N, 14.83%
Found: C, 67.52; H, 6.00; N, 14.50%.


Powdered α-N-benzoylamino-β-hydroxylamino-Ω-methyltyrosine amide 3.29 g (0.01 mol) was added to ethanol (100 ml) along with palladium charcoal (10% Pd) (0.5 g). This was reduced under a hydrogen pressure 60 psi for 8 hr in a Paar catalytic hydrogenation apparatus. The flask was disconnected, contents heated on a water bath and filtered hot. The filtrate was concentrated to 20 ml and left for crystallisation, the crystalline product obtained on cooling was dried in an oven at 80°. It melted at 260° and weighed 1.87 g (60%). UV $\lambda_{\text{max}}^\text{MeOH}$ 230 nm (abs. 1.03); IR (nujol) 3220, 3150, 1700, 1665, 1610, 1550, 1515, 1460, 1418, 1375 cm$^{-1}$.

Anal. for C$_{17}$H$_{18}$N$_3$O$_3$
Calcd: C, 65.16; H, 6.11; N, 13.41%
Found: C, 64.33; H, 5.92; N, 13.39%.
7. Synthesis of $\beta$-Amino-$\alpha$-N-benzoylamino-3,4-dimethoxyphenylalanine amide

Powdered $\alpha$-N-benzoylamino-$\beta$-hydroxylamino-$\beta$-3,4-dimethoxyphenylpropionic hydroxamic acid 3.75 g (0.01 mol) was added in 100 ml of ethanol along with palladium charcoal (10% Pd) (0.4 g). This was reduced under a hydrogen pressure 46 psi for 5 hr. After this period, the flask was disconnected, contents heated on a steam bath and filtered hot. The filtrate was evaporated to dryness under diminished pressure and the residue was crystallised from benzene-ethanol mixture (1:4). The amide so obtained melted at 168° and weighed 1.71 g (50%). UV $\lambda_{\text{max}}^{\text{MeOH}}$ 220 μm (abs. 0.95); IR (nujol) 3220, 3150, 1700, 1665, 1610, 1550, 1515, 1460, 1418, 1375 cm$^{-1}$.

Anal. for $\text{C}_{18}\text{H}_{21}\text{N}_3\text{O}_4$
Calcd: C, 62.96; H, 6.16; N, 12.24%
Found: C, 62.90; H, 6.36; N, 11.99%.

8. Synthesis of $\beta$-amino-$\alpha$-N-benzoylaminotyrosine amide

Powdered $\alpha$-N-benzoylamino-$\beta$-hydroxylaminotyrosine amide 3.15 g (0.01 mol) was dissolved in 60 ml of ethanol and then palladium charcoal (10% Pd) (0.6 g) was added. This was reduced under a hydrogen pressure of 48 psi in Paar catalytic hydrogenation apparatus for 10 hr. The flask was disconnected, contents heated on a steam bath and filtered hot. On cooling the compound was
crystallised. This was filtered and dried in an oven at 80°.
Yield 2.24 g (75%), m.p. 216°; UV $\lambda_{\text{max}}$ MeOH 330 μm (abs. 0.82);
IR (nujol) 3420, 3265, 1655, 1620, 1580, 1530, 1510, 1380,
1340 cm$^{-1}$.

Anal. for $C_{16}H_{17}N_{3}O_{3}$
Calcd: C, 64.20; H, 5.72; N, 14.04%
Found: C, 64.50; H, 6.02; N, 14.36%.

9. Synthesis of $\beta$-Amino-$\alpha$-$N$-benzoylamino-$\delta$-phenylnorvaline amide

A mixture of $\alpha$-$N$-benzoylamino-$\beta$-hydroxylamino-$\gamma$, $\delta$-
diene-$\delta$-phenylnorvaline amide 3.25 g (0.01 mol), ethanol (80 ml)
and palladium charcoal (10% Pd)(0.5 g) was reduced in a Paar
catalytic hydrogenation apparatus at 40 psi for 5 hr. When there
was no absorption of hydrogen, the flask was disconnected. It
was heated on a steam bath, filtered hot and washed with two
10 ml portions of boiling ethanol. The filtrate and washings
were concentrated to 25 ml and left at room temperature for few
hours. The product thus crystallised was filtered and dried in
air. It melted at 167°, yield 2.83 g (91%). There was no absorp-
tion in UV, IR (nujol) 3220, 1652, 1640, 1575, 1535, 1515 cm$^{-1}$.

Anal. for $C_{18}H_{21}N_{3}O_{2}$
Calcd: C, 69.43; H, 6.80; N, 13.50%
Found: C, 69.70; H, 7.00; N, 13.65.
10. **Synthesis of β-Amino-α-N-Benzoylamo-4-dimethylamino-phenylalanine amide**

Powdered α-N-benzoylamino-β-hydroxylamino-4-dimethylaminophenylalanine amide 3.42 g (0.01 mol) was dissolved in 150 ml of ethanol. To this palladium charcoal (10% Pd) 0.5 g was added. This was reduced under a hydrogen pressure of 56 psi for 7 hr. When there was no more reduction the flask was disconnected, contents boiled on a steam bath and filtered hot. The catalyst was washed on the Buchner funnel thrice with 10 ml portions of warm ethanol. The combined filtrate and washings were evaporated to dryness under reduced pressure and the residue was crystallised from ethanol (95%). The crystalline product thus obtained on drying weighed 2.0 g (60%) and melted at 243°; UV \( \lambda_{\text{max}} \) MeOH 230 μm (abs. 0.62) and 260 μm (abs. 0.71); IR (nujol) 3200, 3100, 1700, 1665, 1610, 1515, 1460, 1375 cm\(^{-1}\).

Anal. for C\(_{18}\)H\(_{22}\)N\(_4\)O\(_2\)

Calcd: C, 66.23; H, 6.79; N, 17.17%

Found: C, 66.01; H, 7.00; N, 17.08%.

11. **Synthesis of β-Amino-α-N-benzoylaminotryptophan amide**

A mixture of α-N-benzoylamino-β-hydroxylaminotryptophan amide 3.38 g (0.01 mol), ethanol (100 ml) and palladium charcoal (10% Pd) (0.5 g) was hydrogenated in a Paar catalytic hydrogenation apparatus under a hydrogen pressure of 46 psi. When there
was no more absorption of hydrogen, the flask was disconnected, heated on a steam bath and filtered hot. The filtrate was evaporated to dryness and the residue was dissolved in ethyl acetate. On cooling the product crystallised out. This was filtered and dried, yield 1.6 g (50%); m.p. 156°; UV $\lambda_{\text{max}}$ MeOH 370 μ (abs. 0.67); IR (nujol) 3220, 2750, 1640, 1590, 1550 cm$^{-1}$.

Anal. for C$_{18}$H$_{18}$N$_4$O$_2$
Calcd: C, 67.06; H, 5.63; N, 17.38%.
Found: C, 67.00; H, 5.50; N, 17.50%.

12. Synthesis of $\beta$-Amino-$\chi$-N-benzoylamino-2,4-dihydroxy-phenylalanine amide

Powdered $\chi$-N-benzoylamino-$\beta$-hydroxylamino-$\beta$-2,4-diacetoxy-phenylpropionic hydroxamic acid 4.31 g (0.01 mol) was suspended in 80 ml of ethanol containing palladium charcoal (10% Pd)(0.5 g). This was reduced under a hydrogen pressure of 46 psi for 24 hr. When there was no more absorption of hydrogen, the flask was disconnected, contents heated on a steam bath and filtered hot. The filtrate was concentrated to 25 ml and cooled. The crystallised product was filtered and dried. It weighed 2.20 g (70%) and melted at 268°; UV $\lambda_{\text{max}}$ MeOH 350 μ (abs. 0.56); IR (nujol) 3380, 3200, 2765, 2350, 1690, 1630, 1610, 1580, 1520 cm$^{-1}$.

Anal. for C$_{16}$H$_{17}$N$_3$O$_4$
Calcd: C, 60.94; H, 5.43; N, 13.33%
Found: C, 60.73; H, 5.50; N, 13.38%.
13. **Synthesis of 1'-Aminocyclohexano-2-phenyl-5-imidazolone**

Powdered N-hydroxy-4-(1'-hydroxylaminocyclohexyl)-5-imidazolone 2.89 g (0.01 mol) and palladium charcoal (0.5 g, 10% Pd) were suspended in ethanol (50 ml) in a Paar catalytic hydrogenation flask. This was reduced at a hydrogen pressure of 40 psi for 5 hr. The flask was disconnected when the absorption of hydrogen stopped. The contents heated on a steam bath and filtered hot. The filtrate was concentrated to 25 ml and cooled. The crystallised product thus obtained was filtered and dried yield 1.70 g (65%). It melted at 265⁰ (Dec); UV\(_{\text{MeOH}}\) max 230 m\(\mu\) (abs. 0.66); IR (nujol) 3320, 1640, 1600, 1570, 1535, 1510, 1380 cm\(^{-1}\).

Anal. for C\(_{15}\)H\(_{19}\)N\(_2\)O
Calcd: C, 70.03; H, 7.39; N, 16.30%
Found: C, 69.88; H, 6.99; N, 15.98%.

14. **Synthesis of \(\alpha\)-N-Benzoylamino-1'-aminocyclohexylglycine amide**

Powdered \(\alpha\)-N-benzoylamino-1'-hydroxylaminocyclohexylglycine amide, 2.68 g (0.01 mol) were suspended in ethanol (50 ml) in a Paar catalytic hydrogenation flask. This was reduced at a hydrogenation pressure of 40 psi for 5 hr. The flask was disconnected when the absorption of hydrogen stopped. The catalyst was filtered and the filtrate was concentrated to 20 ml when
compound was crystallised out on cooling. This was filtered and dried yield 1.69 g (65%); m.p. 266°. UV $\lambda_{\text{max}}^\text{MeOH} 230 \text{ nm}$ (abs. 1.45); IR (nujol) 3320, 2650, 1648, 1605, 1580, 1540, 1520, 1500, 1380 cm$^{-1}$.

Anal. for C$_{15}$H$_{20}$N$_2$O$_2$
Calcd: C, 69.23; H, 7.69; N, 10.76%
Found: C, 69.50; H, 7.95; N, 11.08%.
VI. HYDROLYSIS OF β-AMINO-γ-N-BENZOYLAMINO ACID AMIDES

Synthesis of α,β-Diamino acids

1. Synthesis of β-amino-3-methoxy-4-hydroxyphenylalanine

β-Amino-N-benzoylamino-3-methoxy-4-hydroxyphenylalanine amide 3.29 g (0.01 mol) was added to 50 ml of concentrated hydrochloric acid (36%) and refluxed for 8 hr. The mixture was left overnight at room temperature. Next morning benzoic acid (m.p. 123°) crystallised this was filtered and washed with three 10 ml portions of distilled water. The filtrate and washings were combined and evaporated to dryness under reduced pressure. The residue so secured was redissolved in 25 ml of water and evaporated again. Then the residue was taken in 20 ml of water, neutralised cautiously with dilute ammonia solution and 10 ml of ethanol was added. On cooling the amino acid crystallised out. This was filtered and dried in an oven at 80°. Yield 1.36 g (60%); m.p. 253° (dec.). UV $\lambda_{max}$ MeOH 230 μm (abs. 0.55); IR (nujol) 2720, 2600, 1732, 1535, 1505, 1375, 1242 cm⁻¹.

Anal. for C₁₀H₁₄N₂O₄
Calcd: C, 53.09; H, 6.24; N, 12.36%
Found: C, 52.98; H, 6.50; N, 11.99%.
2. **Synthesis of l-Aminocyclohexylglycine**

l-Amino-\(\gamma\)-N-benzoylaminocyclohexylglycine amide 2.75 g (0.01 mol) was refluxed with 60 ml of concentrated hydrochloric acid (36%) for 6 hr and then left at room temperature overnight. Next morning benzoic acid (m.p.122\(^\circ\)) separated was filtered and washed three times with 10 ml portion of ice cold water. The combined filtrate and washings were evaporated to dryness under reduced pressure. The residue was dissolved in 30 ml of water and neutralised with ammonia solution, warmed on a steam bath and then 40 ml of ethanol was added. This solution was cooled and the crystallised amino acid was filtered, washed with ethanol and dried in air. It weighed 1.20 g (70%) and melted at 260\(^\circ\). IR (nujol) 3130, 2650, 2360, 1750, 1450, 1378 cm\(^{-1}\).

Anal. for C\(_8\)H\(_{16}\)N\(_2\)O\(_2\)
Calcd: C, 55.79; H, 9.36; N, 16.27%
Found: C, 55.91; H, 9.03; N, 15.93%.

3. **Synthesis of \(\beta\)-Aminonorvaline**

\(\beta\)-Amino-\(\alpha\)-N-benzoylnorvaline amide 2.49 g (0.01 mol) was heated under reflux with concentrated hydrochloric acid (36%) (60 ml) for 7 hr. and left at room temperature overnight. Benzoic acid which separated was filtered and the filtrate was evaporated to dryness under reduced pressure. The residue was
dissolved in 25 ml of water, neutralised with dilute ammonia solution and then concentrated to 15 ml. Ethanol (20 ml) was added when the amino acid crystallised out on cooling this was filtered and dried. It weighed 1.0 g (65%) and melted at 230°. There is no absorption in UV; IR (nujol) 3730, 2730, 2350, 2100, 1690, 1650, 1570, 1450 cm⁻¹.

Anal. for C₆H₁₄N₂O₂
Calcd: C, 49.30; H, 9.65; N, 19.17%
Found: C, 49.58; H, 9.42; N, 19.01%.

4. Synthesis of β-Aminopiperonylalanine

β-Amino-α-N-benzoylamino piperonylalanine amide 3.27 (0.01 mol) was added to 50 ml of barium hydroxide (15%) and refluxed for 36 hr. The mixture was left overnight at room temperature. Next morning benzoic acid (m.p. 121°), crystallised, was filtered and washed with three 10 ml portions of distilled water. The filtrate and washings were combined and evaporated to dryness under reduced pressure. The residue so secured was redissolved in 25 ml of water and evaporated again. The residue was then taken in 20 ml of water neutralised cautiously with dilute ammonia solution and 10 ml of ethanol was added. On cooling the amino acid crystallised out. This was filtered and dried in air. Yield 1.34 (60%), m.p. 95°. UV \( \lambda_{\text{max}} \text{MeOH} \) 260 μm (abs. 0.65);
IR (nujol) 2720, 2650, 1585, 1505, 1375 cm\(^{-1}\).

Anal. for C\(_{10}H_{12}N_2O_4\)
Calcd: C, 53.57; H, 5.39; N, 12.50%
Found: C, 53.60; H, 5.50; N, 12.75%.

5. **Synthesis of \(\beta\)-Aminophenylalanine**

\(\alpha\)-N-Benzoylamino-\(\beta\)-aminophenylalanine amide (1.5 g) was refluxed with concentrated hydrochloric acid (36%) 100 ml for 5 hr. On cooling benzoic acid was separated which was filtered. The filtrate was evaporated to dryness and the residue so secured was dissolved in water (15 ml). This was neutralised with dilute ammonia solution. Ethanol (10 ml) was added and cooled when \(\beta\)-aminophenylalanine crystallised out. This was filtered and dried. Yield 0.74 g (78%), m.p. 265\(^\circ\). UV \(\lambda_{\text{max}}\) MeOH 260 nm (abs. 0.125); IR (nujol) 2650, 2640, 1660, 1600, 1550, 1530 cm\(^{-1}\).

Anal. for C\(_{10}H_{12}N_2O_2\)
Calcd. C, 59.98; H, 6.71; N, 15.55%
Found: C, 60.00; H, 6.66; N, 15.49%.

6. **Synthesis of \(\beta\)-Hydroxylaminophenylalanine**

\(\beta\)-Hydroxylamino-\(\alpha\)-N-benzoylaminophenylalanine amide, 3.00 g (0.01 mol) was hydrolysed in (70 ml) concentrated hydrochloric acid at reflux temperature for 3.5 hr and left at room temperature overnight. Next morning the crystallised benzoic acid was filtered.
The filtrate was evaporated to dryness and the residue was dissolved in small amount of water. This was neutralised with dilute ammonia solution and concentrated. Then ethanol (20 ml) was added and the white crystallised product was filtered, dried it melted at 250° (dec.), yield 1.17 g (60%). UV $\lambda_{\text{max}}^{\text{MeOH}}$ 260 μm (abs. 0.18); IR (nujol) 3430, 2650, 1670, 1540, 1380, 1250 cm$^{-1}$.

Anal. for $C_{9}H_{12}N_{2}O_{3}$
Calcd: C, 55.10; H, 6.12; N, 14.28%
Found: C, 55.00; H, 5.89; N, 14.28%.

7. Synthesis of $\beta$-Amino-$\theta$-methyltyrosine

$\beta$-Amino-$\alpha$-N-benzoylamino-$\theta$-methyltyrosine amide 3.13 g (0.01 mol) was refluxed with dilute hydrochloric acid (50 ml) for 6 hr. and then left at room temperature overnight. Benzoic acid thus separated was removed through filtration and the filtrate was dried under reduced pressure. The residue was dissolved in 25 ml of water and then neutralised with dilute ammonia solution. This was concentrated to 10 ml, ethanol (20 ml) was then added and the solution was left for crystallisation. The amino acid thus obtained was filtered, washed with ethanol and dried in air when it weighed 2.05 g (98%) and melted at 90°. UV $\lambda_{\text{max}}^{\text{MeOH}}$ 235 μm (abs. 0.75); IR (nujol) 3310, 2740, 2640, 1700, 1600, 1550, 1530 cm$^{-1}$. 
8. Synthesis of $\beta$-Amino-3,4-Dimethoxyphenylalanine

$\beta$-Amino-$\alpha$-N-benzoylamino-3,4-dimethoxyphenylalanine amide, 3.50 g (0.01 mol) was refluxed with 40 ml of concentrated hydrochloric acid (36%) for 10 hr. and then left at room temperature overnight. Next morning benzoic acid (m.p. 120°) separated was filtered and washed three times with 10 ml portions of ice cold water. The combined filtrate and washings were evaporated to dryness under reduced pressure. The residue was dissolved in 30 ml of water and neutralised with ammonia solution, warmed on a steam bath and then 30 ml of ethanol was added. This solution was cooled and the crystallised amino acid separated was filtered, washed with ethanol and dried in air. It weighed 1.68 g (70%) and melted at 155°. UV $\lambda_{\text{max}}^{\text{MeOH}}$ 230 nm (abs. 0.76), 230 nm (abs. 0.46); IR (nujol) 3140, 2640, 2350, 1700, 1450, 1376 cm$^{-1}$.

Anal. for $C_{11}H_{16}N_2O_4$
Calcd: C, 54.99; H, 6.71; N, 11.66%
Found: C, 55.10; H, 6.50; N, 12.00%.
9. Synthesis of \( \beta \)-Aminotyrosine

\( \beta \)-Amino-\( \alpha \)-N-benzoylaminotyrosine amide, 2.99 g (0.01 mol) was refluxed with 60 ml concentrated hydrochloric acid for 9 hr. and then left at room temperature overnight. Benzoic acid which separated was filtered and the filtrate was evaporated to dryness under reduced pressure. The residue was dissolved in 25 ml of water, neutralised with dilute ammonia solution and then concentrated to 15 ml. Ethanol (5 ml) was added when the amino acid crystallised out on cooling which was filtered and dried. It weighed 1.88 g (96%) and melted at 245\( ^\circ \). UV \( \lambda_{\text{max}}^{\text{MeOH}} \) 230 \( \text{m} \mu \) (abs. 0.405), 280 \( \text{m} \mu \) (abs. 0.120); IR (nujol) 3320, 2710, 2590, 1710, 1660, 1575, 1340 cm\(^{-1}\).

Anal. for \( \text{C}_9\text{H}_{12}\text{N}_2\text{O}_3 \)
Calcd: C, 55.09; H, 6.17; N, 14.28%
Found: C, 55.26; H, 5.83; N, 13.95%.

10. Synthesis of \( \beta \)-Amino-\( \delta \)-phenylnovaline

\( \beta \)-Amino-N-benzyolamino-\( \delta \)-phenylnovaline amide 3.11 g (0.01 mol) was heated under reflux with dilute hydrochloric acid (100 ml) for 5 hr. and then left at room temperature overnight. Filtration of crystallised benzoic acid was effected over a Buchner funnel and the filtrate was evaporated to dryness under reduced pressure. The residue was dissolved in 25 ml of water.
This was neutralised with ammonia solution and concentrated to 15 ml. Ethanol (20 ml) was added when the amino acid crystallised on cooling, this was filtered and dried. It weighed 1.87 g (90%) and melted at 200°, recrystallised from alcohol and ethyl acetate, m.p. 202°. UV $\lambda_{\text{max}}^{\text{MeOH}}$ 260 μm (abs. 1.15); IR (nujol) 3190, 2720, 2600, 1710, 1585, 1460, 1375, 1242 cm$^{-1}$.

Anal. for C$_{11}$H$_{16}$N$_2$O$_2$
Calcd: C, 63.44; H, 7.74; N, 13.45%
Found: C, 63.17; H, 7.55; N, 13.25%.

11. Synthesis of $\beta$-Amino-4-dimethylaminophenylalanine

$\beta$-Amino-N-benzoylamino-4-dimethylaminophenylalanine amide 3.26 g (0.01 mol) was refluxed with 50 ml of dilute hydrochloric acid (10%) for 36 hr. and then left at room temperature overnight. Benzoic acid thus separated was filtered, washed with three 10 ml portions of water and the solution was evaporated to dryness under reduced pressure. The amino acid salt so obtained was dissolved in 25 ml of water, neutralised with dilute ammonia solution, concentrated to 10 ml on a steam bath and then 30 ml of ethanol was added. The solution was cooled overnight and the crystalline amino acid separated was filtered washed with ethanol and dried in an oven at 80° when it weighed 1.38 g (62%) and melted at 215°. UV $\lambda_{\text{max}}^{\text{MeOH}}$ 260 μm (abs. 1.10); IR (nujol) 3120, 2699, 1700, 1665, 1475, 1375 cm$^{-1}$. 
12. Synthesis of $\beta$-Aminotryptophan

$\beta$-Amino-$\alpha$-N-benzoylaminotryptophan amide, 3.22 g (0.01 mol) was hydrolysed with (70 ml) concentrated hydrochloric acid at reflux temperature for 8 hr. and left at room temperature overnight. Next morning the crystallised benzoic acid was filtered. The filtrate was evaporated to dryness and the residue was dissolved in small amount of water, neutralised with dilute ammonia solution and concentrated. Then ethanol (20 ml) was added the white crystallised product was filtered, dried, when it melted at 270° (dec.), yield 1.31 g (60%). IR (nujol) 3410, 2720, 2695, 1720, 1600, 1475, 1260 cm$^{-1}$.

Anal. for $\text{C}_{11}\text{H}_{17}\text{N}_{3}\text{O}_{2}$
Calcd: C, 59.17; H, 7.68; N, 18.81%
Found: C, 58.94; H, 7.31; N, 18.53%.

13. Synthesis of $\beta$-Amino-2,4-dihydroxyphenylalanine

$\beta$-Amino-$\alpha$-N-benzoylamino-2,4-dihydroxyphenylalanine amide, 3.15 (0.01 mol) was heated under reflux with concentrated hydrochloric acid (36%) (60 ml) for 7 hr. and left at room temperature
overnight. Benzoic acid thus separated was filtered and the filtrate was evaporated to dryness under reduced pressure. The residue was dissolved in 25 ml of water, neutralised with dilute ammonia solution and then concentrated to 15 ml. Ethanol (20 ml) was added when the amino acid crystallised on cooling this was filtered and dried. It weighed 1.48 g (70%) and melted at 230° (dec.). UV \( \lambda_{\text{max}}^{\text{MeOH}} 370 \text{ nm} \) (abs. 0.57); IR (nujol) 2750, 2660, 1770, 1650, 1400, 1250 cm\(^{-1}\).

Anal. for C\(_9\)H\(_{12}\)N\(_2\)O\(_4\)

Calcd: C, 50.94; H, 5.70; N, 13.20%

Found: C, 50.54; H, 5.60; N, 13.00%.