STUDIES IN THE CHEMISTRY OF OXIMES

AND C-NITROSO COMPOUNDS,

A Thesis Submitted

by

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Abstract

The periodate oxidation of \( \Delta \)-pyrroline 1-oxide with two substituents at C-5 but unsubstituted at C-2 gives 4-nitroso-pentanoic acid. Evidence is adduced for the course of the reaction. An N-alkyl-hydroxyamino-compound is oxidised in chloroform to the nitroso-compound by tetraethylammonium periodate, a potentially useful reagent soluble in various solvents. Rapid periodate oxidation of simple ketoximes and aldoximes proceeds via a prior hydration of the oxinium double bond catalysed by acid. Preparative oxidation of ketoximes yields the corresponding ketones whereas aldoximes give aldehydes and acids. Simple tertiary-amines are also oxidised by periodate to the corresponding N-oxides.

Oxidation of tertiary-aliphatic alkylamines by m-chloroperbenzoic acid gives tert-aliphatic alkyl nitroso compounds in 60-65% yield. tert-Aliphatic nitroso-compounds react with anhydrous hydrogen chloride to yield the corresponding chloro-compounds. On photolysis they give the olefin, nitro compound, a free radical and other products. The course of the reaction is discussed. tert-Aliphatic nitroso-compounds also react with diazomethane to give the novel C-unsubstituted mononitrone which undergoes 1,3-cycloaddition with a variety of dipolarophiles. The labile adducts of dimethyl acetylene dicarboxylate with these nitrones posed a special problem giving various products, which were examined in detail.
Acknowledgements

The work described in this thesis was carried out under the supervision of Dr. Benjamin Sklarz. I wish to express my indebtedness to him for his constant advice, encouragement and unfailing help throughout the course of these investigations.

I should like to thank Dr. J.E. Baldwin for his guidance and helpful discussion in Part II of the work.

I am deeply grateful to Professor D.H.R. Barton, F.R.S., of Imperial College and Professor M. Stacey, F.R.S., of Birmingham University, for giving me the opportunity of working in their departments and for providing the laboratory facilities.

Thanks are also expressed to the Staff of Micro-analytical Department for elemental analyses, Mrs. A.I. Boston for the measurement of nuclear magnetic resonance spectra and Dr. E.S. Waight for mass spectra (Imperial College).

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Abdul Khaliq Qureshi.
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Part I

Periodate Oxidation of Nitrones

and Oximes
Introduction.

The chemistry of hydroxylamine derivatives in general and of nitrones in particular has recently been reviewed.

Hydroxylamine is oxidised by sodium periodate with the formation of nitrous oxide and iodine (1). Analogous oxidation of phenylhydroxylamine and methyl hydroxylamine gave the nitrosobenzene (2) and the cis-dimer of nitrosonmethane (3), in the latter instance without tautomerisation to oxime.

Monosubstituted hydroxylamines are also converted to nitroso compounds (or their dimers or the isomeric oximes) by a variety of oxidising agents, including ferric chloride, permanganate, chromic acid, bromine, diethyl azodicarboxylate and air.
However α-hydroxylamino acids undergo oxidative decarboxylation with the uptake of two moles of periodate and form aldehydes (5). 11-12.

\[
\begin{align*}
\text{NH}_2\text{OH} & \quad 2\text{H}_2\text{O}_4 \\
\text{R - CH - COOH} & \quad \rightarrow \frac{1}{2} \text{N}_2\text{O} + \frac{3}{2} \text{H}_2\text{O} + \text{CO}_2 + \text{R-O} \quad \text{H} + 2\text{H}_2\text{O}_3
\end{align*}
\]

(5)

The reaction probably proceeds via fragmentation of an α-nitroso acid 13 to the oxime which is further oxidised by periodate to the aldehyde (6) (see discussion). Proline also undergoes oxidative decarboxylation to \( \Delta \)-pyrroline by periodate under acid conditions (7). 14

\[
\begin{align*}
\text{R - CH - COOH} & \quad \rightarrow \text{R - CH - CO} \quad \rightarrow \text{RCH=NOH} \quad \rightarrow \text{RCHO + N}_2\text{O}.
\end{align*}
\]

(6)

\[
\text{N, N-Disubstituted hydroxylamines are oxidised to nitrooxide radicals, R}_2\text{N-O}, \text{ in the first stage of oxidation (8); when neither substituent has an } \alpha \text{-hydrogen, these substances can often be isolated. 15 The intermediate}
\]

\[
\begin{align*}
\text{(C}_6\text{H}_5\text{)}_2\text{NOH} & \quad \rightarrow \text{Ag}_2\text{O} \\
\text{(C}_6\text{H}_5\text{)}_2\text{N-O} & \quad \text{(C}_6\text{H}_5\text{)}_2\text{N-O}
\end{align*}
\]

(8)

radicals \( \text{R}_2\text{N-O} \) have also been detected both by trapping 16 and by electron spin resonance 17. However, N,N-Disubstituted
hydroxylamines having α-hydrogen atom are oxidised to the corresponding nitrones, presumably via an intermediate R₂N-0, by such reagents as periodate (9a-b) 18-19, air (9a) 20, mercuric oxide, 21 (a-c) potassium ferricyanide (10) 21 (a-b) and diethyl azodicarboxylate 10.

Hydroxamic acids and their derivatives are also oxidisable by a variety of reagents. Simple hydroxamic acids give the corresponding carboxylic acids and nitrogen or nitrous oxide or nitroso compounds when treated with various reagents such as lead tetra-acetate (11) 22, nitrous acid, 23 bromine 24 and air 25. Periodate oxidation of the
hydroxamic acids RCONR'OH has been found also to give the carboxylic acids

\[
\begin{align*}
\text{CH}_3 - C\equiv N\equiv OH & \rightarrow \text{CH}_3\text{COOH} + N_2O \\
\text{CH}_3 - C\equiv N\equiv OH & \rightarrow \text{CH}_3\text{COOH} + (\text{CH}_3\text{O})_2
\end{align*}
\]

and nitrous oxide when R' = H(12). N-substituted hydroxamic acids yield the nitroso compounds, the cis-dimers having been isolated when R' = Me(13) 4-6.

Likewise the cyclic hydroxamic acid on oxidation with one mol of the periodate yields the nitrosopentanoic acid (14) 19. \(-\text{acyl-}\alpha\text{-hydroxylamino acid ester reacts with periodic acid to liberate the acyl moiety as the acid,}
\[
\begin{align*}
\text{C}_6\text{H}_5\cdot C\equiv O & \rightarrow \text{C}_6\text{H}_5\text{COOH} + \text{R-C-CO}_2\text{H}_5 + \text{H}_2\text{O} \\
\text{R} & \rightarrow \text{CH}_3 \text{COOC}_2\text{H}_5 \\
\text{NOH} & \rightarrow \text{H}_2\text{O}
\end{align*}
\]

and the corresponding \(\alpha\)-oximino ester (15)\(^\text{12}\). N-substituted hydroxamic acids on oxidation with mercuric oxide give oxime derivatives (16)\(^\text{26}\).

\[
\begin{align*}
\text{(C}_6\text{H}_5\text{)}_2\text{CH N\equiv COC}_6\text{H}_5 \rightarrow \text{(C}_6\text{H}_5\text{)}_2\text{C} = \text{N\equiv CO.C}_6\text{H}_5 & + \text{H}_2\text{O} + \text{H}_2\text{O}
\end{align*}
\]
Oxidation of hydroxamic acids by periodate and by bromine proceeds through an acylating intermediate $^4$, since, in addition to the carboxylic acids $^6,19$, the ester $^{27-28}$ or amide $^{29}$ may be formed in fair yields depending upon the nucleophile present.

Dimers of $\alpha,\alpha$-dipyrrrolidinyls (I) and $\alpha,\beta$-dipyrrrolidinyls (II) can easily be distinguished from each other by periodate oxidations $^{19}$ of the sort discussed above. Oxidation of the $\alpha,\alpha$-dimer (I) and the hydroxylamine (III) gave the same bis-nitrone (IV), which does not react further, whereas the $\alpha,\beta$-bishydroxylamine (V) and the dimer (II) gave nitroso-acid (VI), together with 3 - keto- $\delta,\delta$-dimethyl-

- pyrroline -i - oxide (VII).
In the α,β-series, the 3-C atom of the bisnitrone (VIII) is adjacent to two nitrone groups and its hydrogen atom is therefore activated.

Periodate is known to oxidise activated hydrogen of this type $^3$, and presumably gives the 3'-hydroxy-bisnitrone (IX) which is further cleaved to ketonitrone (VII) and hydroxamic acid (X). The latter is further cleaved to the nitroso-acid (VI) as above.

Several α,β-pyrroline-1-oxides (XI a-c) unsubstituted at C-2 are also oxidised to the corresponding γ-nitrosopentanoic acids (XII a-c) by periodate $^3$ and to the hydroxamic acids (XIII a-c) by ferric chloride $^3$, whereas 2-substituted nitrones are oxidised very slowly to a small extent $^3$. 

**Diagram:**

- **VIII:** Bisnitrone with activating hydrogen.
- **IX:** 3'-Hydroxy-bisnitrone.
- **VII:** Ketonitrone.
- **X:** Hydroxamic acid.
- **XI a-c:** α,β-Pyrroline-1-oxides.
- **XII a-c:** γ-Nitrosopentanoic acids.
- **XIII a-c:** Hydroxamic acids.
Nitrone acid (XIV) on oxidation with periodate gave laevualdehyde (XV) with the liberation of iodine $^{31}$.

The work to be described is mainly concerned with the mechanism of periodate oxidation of nitrones, which has been examined in detail and extended to the oxidation of simple oximes.

Some experiments on the periodate oxidation of simple amines showed, that simple tertiary amines are also oxidised by periodate, giving the respective 3-oxides.
Results and Discussion:

1. Periodate Oxidation of Nitrones.

The periodate oxidation of $\triangle$-pyrroline-1-oxides unsubstituted at C-2 is remarkably fast. After twenty minutes the reaction mixture is bright blue and colourless crystals of the dimeric nitroso-acids (XII a-c) have began to be deposited. For 5, 5-dimethyl $\triangle$-pyrroline-1-oxide (XVI), total periodate uptake was 1.7 mol. in 24 hours, at a rate increasing slightly with pH. Alkyl substituents at C-2 retard the reaction drastically. Thus, the nitrones (XXII a-b) and (XXV a-b) were attacked very slowly by periodate.

The oxidation of $\triangle$-pyrroline-1-oxides, e.g. (XVI), to nitrosopentanoic acid (XX) is thought to proceed via preliminary hydration, with subsequent reactions as shown in Scheme I. Some experimental evidence for this reaction course is presented below.
Step (a)  This involves the addition of water across the nitrone double bond. Although \( \Delta^1 \)-pyrroline-1-oxide (XVI) is a very hygroscopic substance and has been obtained as a low melting solid hydrate, there is no evidence for the formation of the adduct (XVII) in bulk. The intensity of ultraviolet absorption of (XVI) was not decreased in water, weak hydrochloric acid, or 2 N-alkali; which might be assumed to catalyse the hydration. Likewise, there was no difference in the appearance of the n.m.r. spectrum in deuterochloroform, water or very dilute hydrochloric acid. Thus there is no spectral evidence for the occurrence of step (a).

The effect of PH on the oxidation of \( \Delta^1 \)-pyrroline-1-oxide (XVI) was also examined. The uptake of periodate was followed at PH 4.5, 6.5 and 9.2. A very little difference in the rate of reaction was observed (Table I), and there is thus no kinetic

[Diagram with structures XXII and Fig. 1 showing the addition of water across the nitrone double bond]
TABLE I.

Uptake of periodate (mols/mol. substrate)

5,5-dimethyl- Δ’-pyrroline 1-oxide (XVI)

<table>
<thead>
<tr>
<th>pH 4.5</th>
<th>pH 6.5</th>
<th>pH 9.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>t (min)</td>
<td>r</td>
<td>t (min)</td>
</tr>
<tr>
<td>12</td>
<td>0.12</td>
<td>6</td>
</tr>
<tr>
<td>50</td>
<td>0.22</td>
<td>45</td>
</tr>
<tr>
<td>141</td>
<td>0.40</td>
<td>133</td>
</tr>
<tr>
<td>226</td>
<td>0.54</td>
<td>211</td>
</tr>
<tr>
<td>296</td>
<td>0.68</td>
<td>302</td>
</tr>
<tr>
<td>375</td>
<td>0.80</td>
<td>375</td>
</tr>
<tr>
<td>500</td>
<td>0.96</td>
<td>506</td>
</tr>
<tr>
<td>24 hrs</td>
<td>1.76</td>
<td>24 hrs</td>
</tr>
</tbody>
</table>

* precipitation

Nevertheless, nucleophilic additions to the aldonitrone double bond are well known. The addition of water probably occurs across the azomethine double bond to a small extent to give some hydrate (XVII) in equilibrium with aldonitrone (XVI). This addition of water is exemplified by the colourless crystalline
hydrate (XXIV) \(^{34}\), obtained from the yellow nitrone (XXIII) \(^{34}\) with ice cold dilute sulphuric acid. These compounds were prepared and their relationship was confirmed by their infrared spectra.

The adduct (XXIV) was oxidised by periodate almost instantaneously, irrespective of PH. The total uptake of periodate of 2.78 moles/mole was complete in 0.2 hours at PH 2.9 (See Table II). In contrast, the oxidation of nitrone (XXIII) varied with PH being markedly slower at PH 4.5 and 6.5 than at PH 2.9 and 9.2 (total uptake only 2 mols.). This increase in rate may be due to catalysis of the hydration step. Preparative oxidation of nitrone (XXIII) and its hydrate (XXIV) with excess reagent gave nitrosobenzene and benzoic acid.

The hydrate (XXIV) was not oxidised by tetra-ethylammonium periodate in dimethylformamide. In this case, threefold dilution with water was necessary for
Table II

Uptake of periodate (mols/mol. substrate)

<table>
<thead>
<tr>
<th>Time (hr.)</th>
<th>NITRONE XXIII</th>
<th>HYDRATE XXIV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>pH 2.9</td>
<td>pH 4.5</td>
</tr>
<tr>
<td>0.05</td>
<td>1.78</td>
<td>0.36</td>
</tr>
<tr>
<td>0.1</td>
<td>1.84</td>
<td>0.6</td>
</tr>
<tr>
<td>0.2</td>
<td>1.88</td>
<td>0.91</td>
</tr>
<tr>
<td>0.5</td>
<td>1.90</td>
<td>1.58</td>
</tr>
<tr>
<td>1.0</td>
<td>1.96</td>
<td>2.16</td>
</tr>
<tr>
<td>1.25</td>
<td>-</td>
<td>2.3</td>
</tr>
<tr>
<td>1.5</td>
<td>2.02</td>
<td>2.35</td>
</tr>
<tr>
<td>24</td>
<td>2.02</td>
<td>2.42</td>
</tr>
</tbody>
</table>

* precipitation
the reaction to proceed \(^3^5\).

The ketonitrones (XXII a-b) and (XXV a-b)\(^3^1\) were attacked very slowly by periodate.

\[
\begin{align*}
(a) & \quad R^1 = \text{Me}, \quad R^2 = \text{H} \\
(b) & \quad R^1 = \text{H}, \quad R^2 = \text{Me}
\end{align*}
\]

XXV a-b

Total uptake of periodate in (XXII b) at pH 4.5 and 6.5 was 0.16 and 0.42 moles/mole in 5 minutes, which was unchanged after 24 hours. Thus retardation or failure of the hydration step (a) may prevent the oxidation of (XXII a-b) and (XXV a-b)\(^3^1\), for these compounds are less susceptible to nucleophilic addition.\(^2^0\)

Step (b) The hydrate (XVII) constitutes an N,N-dialkyl hydroxylamine with an \(\alpha\)-hydrogen atom at C-2. Rapid oxidation of such a system to a nitrone group has already been observed \(^1^8-1^9\) (See Introduction). Thus, the oxidation of hydrate (XVII) to nitrone (XVIII) by periodate is to be expected.

A further example was provided by the oxidation of N-hydroxy pyrrolidines (XXVI a-b) to the nitrones (XXII a-b) (characterised as their picrates), which are not oxidised further by the reagent. Volumetric estimations showed that the rate of reaction is very fast and total uptake
of periodate in (XXVI b) at PH 4.5 was 0.86 moles/mole in 7 minutes (Table III).

\[ \text{Me} \quad \begin{array}{c} \text{R} \\ \text{Me} \end{array} \quad \begin{array}{c} \text{H} \\ \text{H} \end{array} \quad \begin{array}{c} \text{OH} \end{array} \]

(a) $R = \text{CH}_3$

(b) $R = \text{C}_2\text{H}_5$

XXVI a-b

Similarly N-hydroxy piperidine (XXVII)\textsuperscript{36} was oxidised instantly with the uptake of 2.72 moles of the reagent within 6 minutes at PH 2.9 (Table IV).

**TABLE III**

Uptake of periodate (mols/mol. substrate)

<table>
<thead>
<tr>
<th>pH 4.5</th>
<th>pH 6.5</th>
<th>pH 9.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>t(min)</td>
<td>r</td>
<td>t(min)</td>
</tr>
<tr>
<td>--------</td>
<td>--------</td>
<td>--------</td>
</tr>
<tr>
<td>7</td>
<td>0.86</td>
<td>12</td>
</tr>
<tr>
<td>30</td>
<td>0.91</td>
<td>35</td>
</tr>
<tr>
<td>87</td>
<td>0.93</td>
<td>92</td>
</tr>
<tr>
<td>140</td>
<td>0.93</td>
<td>145</td>
</tr>
<tr>
<td>180</td>
<td>0.93</td>
<td>185</td>
</tr>
<tr>
<td>240</td>
<td>0.93</td>
<td>245</td>
</tr>
<tr>
<td>24 hrs</td>
<td>0.93</td>
<td>24 hrs</td>
</tr>
</tbody>
</table>
**Table IV**

Uptake of periodate (mols/mol. substrate)

<table>
<thead>
<tr>
<th>pH 2.9</th>
<th>pH 4.5</th>
<th>pH 6.5</th>
<th>pH 9.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>t(min)</td>
<td>r</td>
<td>t(min)</td>
<td>r</td>
</tr>
<tr>
<td>5</td>
<td>2.72</td>
<td>10</td>
<td>2.42</td>
</tr>
<tr>
<td>30</td>
<td>2.81</td>
<td>35</td>
<td>2.66</td>
</tr>
<tr>
<td>60</td>
<td>2.89</td>
<td>65</td>
<td>2.77</td>
</tr>
<tr>
<td>120</td>
<td>3.03</td>
<td>125</td>
<td>2.89</td>
</tr>
<tr>
<td>180</td>
<td>3.19</td>
<td>185</td>
<td>2.93</td>
</tr>
<tr>
<td>240</td>
<td>3.26</td>
<td>245</td>
<td>2.97</td>
</tr>
<tr>
<td>300</td>
<td>3.26</td>
<td>305</td>
<td>3.01</td>
</tr>
<tr>
<td>24 hrs</td>
<td>3.42</td>
<td>24 hrs</td>
<td>3.24</td>
</tr>
</tbody>
</table>
Preparative oxidation of N-hydroxy piperidine (XXVII) gave a reddish oil of unknown composition, but a transient bluish colour, possibly due to a nitroso-compound was also observed.

Step (e) The alternative to the very fast oxidation step (b) would be a cleavage step (e) of the glycolysis type, which would give the nitroso-aldehyde (XXI). However, as is well known, aldehydes are only oxidised very slowly by periodate. The oxidation of (XVI) is very fast, and precipitation of the nitrosopentanoic acid (XX) commences within 1/4 to 1 hour. Moreover in experiments with limited amount of periodate in the presence of chloroform, no aldehyde could be detected (negative 2,4-dinitrophenylhydrazine test). It is also unlikely that the Γ-nitroso-aldehyde (XXI) can cyclise quickly to hydroxamic acid (XIX) because in an analogous case in the bornyl series, this reaction was shown to be photochemical rather than thermal. The oxidation step (b) thus seems much more probable than step (e).

Step (c) Rapid tautomerisation of hydroxy-nitrone (XVIII) gives the hydroxamic acid structure (XIX), established for the known compound by the infrared band at 1690 cm⁻¹.
Step (d) The rapid oxidation of hydroxamic acid (XIX) to the nitroso-acid (XX) by periodate is well known, and the reaction has since been shown to be general.

In an attempt to prepare aldehyde (XXI), the nitro-dioxolan (XXVIII) was reduced with zinc dust and ammonium chloride to the hydroxyamino-compound (XXIX), a colourless liquid giving a strong tetrazolium test. It was oxidised instantly by excess of aqueous sodium periodate when the colourless crystalline dimer of the nitroso-compound (XXX) was precipitated from the blue solution. It is of interest that the oxidation of the hydroxylamine (XXIX) even proceeded instantly in chloroform solution with tetraethylammonium periodate, which is very soluble in that solvent.

All attempts to hydrolyse the dioxolan ring in (XXX) failed. 0.I acidic at 50°C destroyed the compound, while other mild agents such as toluene-\(\beta\)-sulphonic
acid in acetone\textsuperscript{39} or ethanol\textsuperscript{40} had no effect. The syntheses of aldehyde (XXI) by the addition of acetoxime to acrolein in presence of potassium t-butoxide, also failed.
2. Periodate Oxidation of Oximes.

The nitrones are structurally N-alkyloximes and in fact can be prepared from oximes by N-alkylation (17). The periodate oxidation of simple oximes was carried out, in order to throw some light on the mechanism discussed above. Experiments on the oxidation of ketoximes and aldoximes tend to support the proposed pathway of nitrone oxidation.

Cyclohexanone oxime was oxidised using two moles of periodate in concentrated solution at acidic or neutral pH. A slight effervescence and a blue-green colour were observed and cyclohexanone was isolated. The effervescence gas was trapped by cooling and shown to contain nitrous oxide by mass spectrometry as compared with authentic nitrous oxide. Tests for nitrite in the solution were inconclusive. In particular, the Griess test is disturbed by periodate and iodate ions. Attempts to remove these by precipitation with lead or barium ions were unsuccessful. Periodate ions also interfered in an
attempted polarographic estimation of nitrite ions. No iodine was formed during the oxidation. At similar PH and concentration, hydroxylamine is instantly oxidised with copious release of iodine.

Syn-benzaldoxime on oxidation with periodate at neutral PH yields benzaldehyde and benzoic acid whereas phenylacetaldehyde oxime at acidic or neutral PH gives benzaldehyde and phenylacetic acid.

The periodate oxidation of oximes was also performed quantitatively. The variation of rate with PH in different oximes were studied. The structural and electronic effects were also examined. In all these analytical experiments, the periodate was initially in tenfold molar excess and had the same concentration, hence the initial rate will depend only on the concentration of oximes, their reactivity and the PH. The concentrations though not identical were all close to (0.0025 M).

Cyclohexanone oxime was oxidised by sodium periodate in dilute solution with a maximum uptake of 1.76 mols of the reagent in 4 hours, unchanged after 24 hours. Volumetric estimations of cyclohexanone oxime at various PH'S showed that the reaction is very fast in acidic solution and slower in alkaline solution (See Table V).
TABLE V

Uptake of periodate (mols/mol substrate)

<table>
<thead>
<tr>
<th>pH 2.9</th>
<th>pH 4.5</th>
<th>pH 6.5</th>
<th>pH 9.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>t(min)</td>
<td>r</td>
<td>t(min)</td>
<td>r</td>
</tr>
<tr>
<td>5</td>
<td>1.17</td>
<td>10</td>
<td>0.5</td>
</tr>
<tr>
<td>30</td>
<td>1.53</td>
<td>35</td>
<td>1.05</td>
</tr>
<tr>
<td>60</td>
<td>1.55</td>
<td>65</td>
<td>1.39</td>
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<tr>
<td>90</td>
<td>1.59</td>
<td>95</td>
<td>1.53</td>
</tr>
<tr>
<td>150</td>
<td>1.59</td>
<td>155</td>
<td>1.70</td>
</tr>
<tr>
<td>240</td>
<td>1.68</td>
<td>245</td>
<td>1.76</td>
</tr>
<tr>
<td>300</td>
<td>1.72</td>
<td>305</td>
<td>1.76</td>
</tr>
<tr>
<td>24 hrs</td>
<td>2.06</td>
<td>24 hrs</td>
<td>1.76</td>
</tr>
</tbody>
</table>
These results demonstrate the acid catalysis of the reaction and suggest that the oxidation proceeds via a prior hydration of the oxime double bond catalysed by acid (18).

\[
\begin{align*}
\text{C} = \text{NOH} & \xrightarrow{H^+} \text{C} = \text{NHOH} & \text{H}_2\text{O} & \xrightarrow{-H^+} \text{C} \xleftarrow{\text{NHOH}} \text{OH}
\end{align*}
\]

The effect of PH was similar in the oxidation of cyclopentanone oxime, cycloheptanone oxime, acetoxime and phenylacetaldehyde oxime (see Table VI - IX). However for both syn and anti-benzaldoximes, and for acetophenone oxime reaction was faster at PH 6.5 than at PH 4.5. (See Table X - XI).

Comparison of the oxidation rates at a given PH, for these oximes revealed certain structural effects. It was observed that rates of reaction at the same PH and concentration differ within related series of oximes such as certain cyclic ketoximes, on the one hand, and acetoxime and acetophenone oxime on the other. The rate of reaction for cyclopentanone oxime and cycloheptanone oxime is markedly slower than for cyclohexanone oxime irrespective of PH (See Table V - VII). It is well known that additions to the carbonyl group are slower for cyclopentanone and cycloheptanone than for cyclohexanone.
TABLE VI

Uptake of periodate (mols/mol. substrate).

<table>
<thead>
<tr>
<th>Cyclopeptanone Oxime</th>
<th>pH 2.9</th>
<th>pH 4.5</th>
<th>pH 6.5</th>
<th>pH 9.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>t(min)</td>
<td>r</td>
<td>t(min)</td>
<td>r</td>
<td>t(min)</td>
</tr>
<tr>
<td>5</td>
<td>0.13</td>
<td>10</td>
<td>0</td>
<td>20</td>
</tr>
<tr>
<td>30</td>
<td>0.67</td>
<td>35</td>
<td>0.07</td>
<td>40</td>
</tr>
<tr>
<td>35</td>
<td>0.92</td>
<td>60</td>
<td>0.27</td>
<td>65</td>
</tr>
<tr>
<td>95</td>
<td>1.28</td>
<td>90</td>
<td>0.39</td>
<td>95</td>
</tr>
<tr>
<td>145</td>
<td>1.51</td>
<td>150</td>
<td>0.65</td>
<td>155</td>
</tr>
<tr>
<td>205</td>
<td>1.63</td>
<td>210</td>
<td>0.88</td>
<td>215</td>
</tr>
<tr>
<td>265</td>
<td>1.63</td>
<td>270</td>
<td>1.08</td>
<td>275</td>
</tr>
<tr>
<td>24 hrs</td>
<td>1.85</td>
<td>24 hrs</td>
<td>1.81</td>
<td>24 hrs</td>
</tr>
</tbody>
</table>
Table VII
Uptake of periodate (mols/mol. substrate)

Cycloheptanone oxime

<table>
<thead>
<tr>
<th>pH 2.9</th>
<th>pH 4.5</th>
<th>pH 6.5</th>
<th>pH 9.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>t(min)</td>
<td>r</td>
<td>t(min)</td>
<td>r</td>
</tr>
<tr>
<td>10</td>
<td>0.44</td>
<td>15</td>
<td>0.11</td>
</tr>
<tr>
<td>30</td>
<td>1.07</td>
<td>35</td>
<td>0.29</td>
</tr>
<tr>
<td>60</td>
<td>1.60</td>
<td>65</td>
<td>0.39</td>
</tr>
<tr>
<td>90</td>
<td>1.99</td>
<td>95</td>
<td>0.60</td>
</tr>
<tr>
<td>150</td>
<td>2.73</td>
<td>155</td>
<td>0.82</td>
</tr>
<tr>
<td>210</td>
<td>3.10</td>
<td>215</td>
<td>1.05</td>
</tr>
<tr>
<td>270</td>
<td>3.37</td>
<td>275</td>
<td>1.24</td>
</tr>
<tr>
<td>24hrs</td>
<td>3.90</td>
<td>24 hrs</td>
<td>3.00</td>
</tr>
</tbody>
</table>

* precipitation.
Table VIII

Uptake of periodate (mols/mol.substrate)

<table>
<thead>
<tr>
<th>pH 4.5</th>
<th>pH 6.5</th>
<th>pH 9.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>t(min)</td>
<td>r</td>
<td>t(min)</td>
</tr>
<tr>
<td>3</td>
<td>0.0</td>
<td>3</td>
</tr>
<tr>
<td>30</td>
<td>0.44</td>
<td>15</td>
</tr>
<tr>
<td>60</td>
<td>0.68</td>
<td>75</td>
</tr>
<tr>
<td>90</td>
<td>0.91</td>
<td>105</td>
</tr>
<tr>
<td>120</td>
<td>1.09</td>
<td>135</td>
</tr>
<tr>
<td>145</td>
<td>1.10</td>
<td>165</td>
</tr>
<tr>
<td>190</td>
<td>1.26</td>
<td>195</td>
</tr>
<tr>
<td>215</td>
<td>1.35</td>
<td>225</td>
</tr>
<tr>
<td>279</td>
<td>1.74</td>
<td>24 hrs</td>
</tr>
<tr>
<td>310</td>
<td>1.92</td>
<td></td>
</tr>
<tr>
<td>pH 4.5</td>
<td>pH 6.5</td>
<td>pH 9.2</td>
</tr>
<tr>
<td>--------</td>
<td>--------</td>
<td>--------</td>
</tr>
<tr>
<td>t(min)</td>
<td>r</td>
<td>t(min)</td>
</tr>
<tr>
<td>5</td>
<td>0.28</td>
<td>4</td>
</tr>
<tr>
<td>30</td>
<td>0.69</td>
<td>24</td>
</tr>
<tr>
<td>60</td>
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<tr>
<td>90</td>
<td>1.77</td>
<td>70</td>
</tr>
<tr>
<td>125</td>
<td>2.31</td>
<td>120</td>
</tr>
<tr>
<td>150</td>
<td>2.64</td>
<td>150</td>
</tr>
<tr>
<td>279</td>
<td>3.89</td>
<td>214</td>
</tr>
<tr>
<td>410</td>
<td>4.49</td>
<td>274</td>
</tr>
<tr>
<td>24 hrs</td>
<td>6.00</td>
<td>416</td>
</tr>
<tr>
<td></td>
<td></td>
<td>24 hrs</td>
</tr>
</tbody>
</table>
Table X

Uptake of periodate (mols/mol.substrate)

<table>
<thead>
<tr>
<th>pH 4.5</th>
<th>pH 6.5</th>
<th>pH 4.5</th>
<th>pH 6.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>t(min)</td>
<td>r</td>
<td>t(min)</td>
<td>r</td>
</tr>
<tr>
<td>12</td>
<td>0.16</td>
<td>5</td>
<td>0.12</td>
</tr>
<tr>
<td>35</td>
<td>0.44</td>
<td>30</td>
<td>0.54</td>
</tr>
<tr>
<td>65</td>
<td>0.68</td>
<td>60</td>
<td>0.98</td>
</tr>
<tr>
<td>95</td>
<td>1.00</td>
<td>90</td>
<td>1.36</td>
</tr>
<tr>
<td>125</td>
<td>1.24</td>
<td>120</td>
<td>1.70</td>
</tr>
<tr>
<td>24 hrs</td>
<td>3.72</td>
<td>24 hrs</td>
<td>4.70</td>
</tr>
<tr>
<td>14</td>
<td>0.36</td>
<td>9</td>
<td>1.22</td>
</tr>
<tr>
<td>60</td>
<td>0.74</td>
<td>55</td>
<td>1.60</td>
</tr>
<tr>
<td>106</td>
<td>0.97</td>
<td>102</td>
<td>1.76</td>
</tr>
<tr>
<td>135</td>
<td>1.04</td>
<td>130</td>
<td>1.84</td>
</tr>
<tr>
<td>24 hrs</td>
<td>1.80</td>
<td>24 hrs</td>
<td>2.28</td>
</tr>
</tbody>
</table>
Brown, Fletcher and Johannessen have pointed out that a cyclohexane ring, all of whose carbon atoms are tetrahedral, may exist in the particularly stable chair form, in which all the C-H bonds are staggered, but when one of the carbon atoms is trigonal, as in cyclohexanone, some eclipsing is introduced. Since, in the formation of oximes and semicarbazones, the carbonyl carbon atom has acquired considerable tetrahedral character in the transition state of the rate-controlling step, the reaction occurs particularly easily with cyclohexanone. In the case of cyclopentanone and cycloheptanone, the valences are more staggered, in the ketones than in the tetrahedral adduct, and a decrease in reactivity is observed. In another paper they have summarised a great deal of reactivity data which leads to the postulate that an exocyclic double bond to a 5-membered ring is less reactive than that to a 6-membered ring. This observation is rationalised by these authors in terms of bond opposition inter-actions as already discussed. On somewhat different grounds one would expect a 4-ring having an exocyclic double bond to be quite reactive owing to the deformation of internal bond angles, and the 7-ring system should
appear much as the cyclopentane derivatives. They have successfully correlated the relative thermodynamic stabilities of cycloalkyl systems having exocyclic double bond in terms of alkyl hydrogen eclipsing. The same considerations would apply to a rate-determining addition of water to cyclic ketoximes during periodate oxidation and the observed variation of rate with ring-size.

The rate of reaction in acetophenone oxime is slower as compared to acetoxyime at each pH (See table VIII and XI). Because of conjugation of the aromatic ring with the C=N double bond, the oxime is stabilised relative to the transition state, in which there is only partial double bond character. For this reason, such addition reactions are usually slower for aromatic
ketones and their C = N analogues. 43

For the periodate oxidation of cyclohexanone oxime several mechanisms can be envisaged, some of which are shown in Scheme II. In particular, several different initial steps seem possible. For reasons to be outlined step (c) is preferred.

Scheme II
Step (a). This involves direct nucleophilic attack of periodate on the oxime. It seems to be very unlikely because oximino group is less electrophilic. Moreover, from the work of Bunton and Shiner it is apparent that periodate does attack diketones nucleophilically but that the rate of reaction increases considerably with increasing PH's and is at no stage acid catalysed. The fast oxidation of the less electrophilic single oximino group in neutral or acid solution, would therefore not be expected to involve a nucleophilic attack by periodate.
Step (b) This involves the formation of an oxime periodate ester (XXXV), which is subsequently attacked by water. There is no evidence against this possibility, but the simpler interpretation involved in step (c) is preferred.

Step (c) This involves a hydration step which is known to be acid catalysed.

i) The observed pH effects have also shown that the rate-determining step of the reaction is acid catalysed.

ii) The addition of water as for step (c) is also supported by the structural and electronic effects on the rate of oxidation of ketoximes, already discussed.

iii) The addition of water is exemplified by the chloralhydroxylamine (C\textsubscript{3}H\textsubscript{3}CHOHNNOH), prepared according to Hantzsch\textsuperscript{45}, which contains the group \(\text{COH-NHOH}\), of the hydrated oxime.

This compound was oxidised by the tetraethylammonium periodate in chloroform, dimethylformamide and water with an uptake of one mol. of the reagent within the first minute. No stable products could be isolated but iodine was liberated.\textsuperscript{27} However the hydrate(XXIV) was not oxidised by the reagent in dimethylformamide. Chloral oxime was not oxidised either in water or in organic
solvent by the tetraethylammonium periodate. The cyclohexanone oxime was also not oxidised by the reagent either in chloroform or dimethylformamide. In the latter case 75% dilution with water was necessary for the reaction to proceed. Thus sensitivity of the oxime-hydrate to periodate in nonaqueous media tends to support this course of reaction.

Hydration of the oxime (XXXI) in an equilibrium with hydrated form (XXXII) constitutes the first stage of acid-catalysed hydrolysis. The hydrate can then react further under our conditions.

Step (d) This involves the hydrolysis of hydroxylamine compound (XXXII) to give free hydroxylamine. However, in a preparative experiment with hydroxylamine under the same conditions iodine was liberated. Free hydroxylamine is thus unlikely as an intermediate in oxime oxidations.

Step (e) This involves the periodate oxidation of -NHOH into -N=O. Reactions of this type are well known and are extremely fast (see Introduction). Thus fast periodate oxidation of hydroxylamine (XXXII) would lead to the hydroxy-nitroso compound (XXXIII). The transient blue-green colour may be due to this, or to
oxides of nitrogen. Hawthorne and Strahm have shown that the $\alpha$-hydroxy-nitroso group, if it exists, must be very short lived, breaking down to a keto-group and nitrous oxide. However, in an attempt to trap the hydroxy-nitroso compound (XXXIII) the periodate oxidation of cyclohexanone oxime was performed in the presence of butadiene. Cyclohexanone was isolated but no adduct of (XXXIII) was formed.

The diene addition of aliphatic nitroso compounds of the type $R_2CXNO$, proceeds only when a strongly electronegative group $X$, such as Cl, NO$_2$ or CN is also attached to the nitroso-carrying carbon. It is possible that the hydroxyl group in (XXXIII) would not be sufficiently activating, even if (XXXIII) had a sufficiently long life time.

Steps (f), (g). Further hydrolysis or oxidative cleavage of the hydroxy-nitroso compound (XXXIII) would give the ketone and hyponitrous acid (f) or nitrite ion (g). Sodium hyponitrite was found to be oxidised by periodate with an uptake of 0.77 mol. in 15 minutes at neutral pH with very slow subsequent increase (see Table XII). Thus a part of the hyponitrous acid is decomposed to nitrous oxide and the rest is oxidised by the periodate.
In conclusion, step (c) followed by step (e), etc., is preferred to step (b) because the intermediates and reactions involved are already known.

The oxidation of syn-benzaldoxime by periodate can be explained on similar lines.

Syn-benzaldoxime gave benzaldehyde (characterised by 2,4-dinitrophenylhydrazine derivative) and benzoic
acid. Tautomerisation could occur via the oxime (XXXVIa) to the hydroxamic acid, which is further oxidised.

Similarly phenylacetaldehyde oxime yielded phenylacetic acid (characterised as its p-bromophenylacetyl derivative) presumably via a similar rearrangement of (XXXVII). Phenylacetaldehyde, formed by its hydrolysis, is oxidised further by periodate to benzaldehyde (characterised as its 2,4-dinitrophenylhydrazine derivative). This oxidation step was confirmed separately using phenylacetaldehyde under the same
conditions, when 2.02 mols of the reagent were consumed in 24 hours at neutral PH (See Table XIII). Felkin has shown that the group Ar-CH₂-CO⁻ is oxidised by periodate.

The presence of formic acid in the reaction mixture could not be detected (both ammonium silver nitrate and potassium permanganate tests were negative.).
3. Periodate Oxidation of Amines.

The oxidation of tertiary amines to their N-oxides with hydrogen peroxide or various peroxycids $^{50,51}$ and ozone $^{52}$ is well known.

It was originally thought $^{53}$ that tertiary amines are not appreciably oxidised by periodate. However, it was found $^{54}$ that diethylamino ethanol and 3-diethylamino propanol-1 are readily oxidised by the reagent. Erythromycin and erythralosamine(XXXVIII, R = respective aglycone) gave their N-oxides $^{54}$ on oxidation with periodate. However, tertiary-amino groups do not prevent cleavage entirely $^{55}$. Thus oxidation of desosamine (XXXVIII, R=H) by periodate

\[
\begin{align*}
\text{XXXVIII} & \xrightarrow{104} \text{XXXIX}
\end{align*}
\]
gave in turn the tetrose (XXX1) and acetaldol, and the methyl acetal (XXX1II R-Me) also took one molecule of the reagent 56.

In the course of our work, we investigated the attack of periodate on tertiary nitrogen atoms, and found that periodate readily oxidises simple tertiary amines like N-propyl piperidine, 2-piperidino-N-ethylalcohol, N-piperidino-γ-propyl alcohol and triethylamine at alkaline PH. Volumetric estimations showed that the initial rate of reaction in each case was slower, whereas in the case of N-propyl morpholine, the reaction was faster with an uptake of 1.42 moles of the reagent in 20 minutes and a total uptake of 3.25 moles/mole. in 24 hours (See Table XIV).

Preparative oxidations of tertiary amines (XL a-c) and triethylamine were unsuccessful with sodium periodate at PH 9.2 because the reagent is precipitated.

\[
\begin{align*}
\text{XL (a-c)} & \\
\text{XLII} & \\
\text{XLIII}
\end{align*}
\]

(a) \( R = \text{CH}_2\text{CH}_2\text{CH}_3 \)
(b) \( R = \text{CH}_2\text{CH}_2\text{OH} \)
(c) \( R = \text{CH}_2\text{CH}_2\text{CH}_2\text{OH} \)
Table (XIV)

Uptake of periodate (mols/mol.substrate).

<table>
<thead>
<tr>
<th></th>
<th>XLa</th>
<th>XLb</th>
<th>XLc</th>
<th>N-propyl Morpholine</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH 9.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>t (min)</td>
<td>r</td>
<td>t(min)</td>
<td>r</td>
<td>t(min)</td>
</tr>
<tr>
<td>20</td>
<td>0.01</td>
<td>5</td>
<td>0.20</td>
<td>25</td>
</tr>
<tr>
<td>75</td>
<td>0.09</td>
<td>90</td>
<td>0.38</td>
<td>70</td>
</tr>
<tr>
<td>140</td>
<td>0.09</td>
<td>240</td>
<td>0.58</td>
<td>125</td>
</tr>
<tr>
<td>260</td>
<td>0.31</td>
<td>24 hrs</td>
<td>1.01</td>
<td>195</td>
</tr>
<tr>
<td>380</td>
<td>0.31</td>
<td>48 hrs</td>
<td>1.29</td>
<td>24 hrs</td>
</tr>
<tr>
<td>24 hrs</td>
<td>0.67</td>
<td></td>
<td></td>
<td>48 hrs</td>
</tr>
<tr>
<td>36 hrs</td>
<td>1.14</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
However with aqueous tetraethylammonium periodate oxidation proceeded quite smoothly and yielded the corresponding N-oxides as hygroscopic white solids.

N-propyl piperidine (XLa) on oxidation with tetraethylammonium periodate in water gave N-oxide (XLIa) as a very hygroscopic white solid (characterised as its picrate). It had a characteristic band at 1650 cm$^{-1}$ in the infrared region. The nuclear magnetic resonance spectra of the amine (XLa) and its oxide (XLIa) were compared. The chemical shift of the signal due to the three N-methylene protons changed from T7.72 to 8.84 in the N-oxide. This was ascribed to the deshielding effect of N (See Table XV) Molecular weight by mass spectrometry was 143. There was an abundant ion peak at 127 with the loss of the oxygen atom (See Table XVI). The N-oxide (XLIa) was also prepared by the oxidation of corresponding amine with peracetic acid and its infrared and n.m.r. were compared which are shown to be identical.

Similarly 2-piperidino-N-ethylalcohol, 3-N-piperidino-propanol and triethylamine yielded their corresponding N-oxides (XLI b-c) and (XLII) as hygroscopic white solids, on oxidation with the
Table XV

<table>
<thead>
<tr>
<th>Amines</th>
<th>Chemical Shift of (-\text{CH}_2\text{N}^-\text{CH}_2\text{-})</th>
<th>Chemical Shift of (-\text{CH}_2\text{N}^-\text{CH}_2\text{-})</th>
</tr>
</thead>
<tbody>
<tr>
<td>XL a</td>
<td>7.72</td>
<td>6.84</td>
</tr>
<tr>
<td>XL b</td>
<td>7.59</td>
<td>6.64</td>
</tr>
<tr>
<td>XL c</td>
<td>7.7</td>
<td>6.42</td>
</tr>
<tr>
<td>Triethylamine</td>
<td>8.59</td>
<td>6.62</td>
</tr>
</tbody>
</table>

The N-oxide of 2-piperidino-\(\text{N}\)-ethylalcohol forms a picrate which could not be recrystallised, whereas \(\text{N}\)-oxide of 3-\(\alpha\)-piperidinopropanol does not form a picrate.
### Table XVI

<table>
<thead>
<tr>
<th>Mass Peaks</th>
<th>Fragmentation</th>
<th>Mass Peaks</th>
<th>Fragmentation</th>
<th>Mass Peaks</th>
<th>Fragmentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>M = 143</td>
<td><img src="image1" alt="Structure" /></td>
<td>M = 145</td>
<td><img src="image2" alt="Structure" /></td>
<td>M = 159</td>
<td><img src="image3" alt="Structure" /></td>
</tr>
<tr>
<td>M-16 = 127</td>
<td><img src="image4" alt="Structure" /></td>
<td>M-1 = 144</td>
<td><img src="image5" alt="Structure" /></td>
<td>M-1 = 158</td>
<td><img src="image6" alt="Structure" /></td>
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<tr>
<td>M-42 = 101</td>
<td><img src="image7" alt="Structure" /></td>
<td>M-16 = 129</td>
<td><img src="image8" alt="Structure" /></td>
<td>M-16 = 143</td>
<td><img src="image9" alt="Structure" /></td>
</tr>
<tr>
<td>(M-1)-16 = 128</td>
<td><img src="image10" alt="Structure" /></td>
<td>(M-1)-16 = 142</td>
<td><img src="image11" alt="Structure" /></td>
<td>(M-1)-16 = 112</td>
<td><img src="image12" alt="Structure" /></td>
</tr>
<tr>
<td>M-43 = 100</td>
<td><img src="image13" alt="Structure" /></td>
<td>M-44 = 101</td>
<td><img src="image14" alt="Structure" /></td>
<td>M-58 = 101</td>
<td><img src="image15" alt="Structure" /></td>
</tr>
<tr>
<td>M-45 = 98</td>
<td><img src="image16" alt="Structure" /></td>
<td>M-45 = 100</td>
<td><img src="image17" alt="Structure" /></td>
<td>M-59 = 100</td>
<td><img src="image18" alt="Structure" /></td>
</tr>
<tr>
<td>M-47 = 98</td>
<td><img src="image19" alt="Structure" /></td>
<td>M-47 = 98</td>
<td><img src="image20" alt="Structure" /></td>
<td>M-61 = 98</td>
<td><img src="image21" alt="Structure" /></td>
</tr>
<tr>
<td>M-99 = 46</td>
<td><img src="image22" alt="Structure" /></td>
<td>(HOCH₂·CH₃)⁺</td>
<td><img src="image23" alt="Structure" /></td>
<td>M-99 = 60</td>
<td><img src="image24" alt="Structure" /></td>
</tr>
<tr>
<td></td>
<td></td>
<td>-C₅H₉OH</td>
<td></td>
<td>M-28 = 31</td>
<td></td>
</tr>
</tbody>
</table>
It was also observed that N-oxides (XLI a-c) are not oxidised further by periodate. Preparative oxidation of N-propyl morpholine with 2 moles and 4 moles of aqueous tetraethylammonium periodate yielded an oil of unknown composition.

It is of interest that oxidation of tertiary amines (XL a-c) and triethylamine even proceeded in aqueous media (acetone) with the tetraethylammonium periodate and yielded tetraethylammonium iodate as a hygroscopic white solid, in addition to the N-oxides.

It was found that periodate also oxidises triphenyl phosphine and diethylsulphide in chloroform to their respective N-oxides. Oxidation of sulphides to sulphoxides and sulphones by the periodate in aqueous media is known.58

Iodobenzene, styrene and dimethylaniline did not react with the periodate and in each case a material was recovered unchanged.
Experimental

Melting points are uncorrected. Infra-red spectra were taken on a unica$m spectrometer model S.P200. Ultra-violet spectra were measured (in 95% ethanol unless otherwise stated) on a unica$m spectrometer model S.P800. Nuclear magnetic resonance were taken on varian A 60 Mc using trimethylsilane as internal standard. pH's were measured on a Cambridge bench pH meter.

1. Periodate Oxidation of Nitrones

Preparations -
4-Methyl-4-nitropentanal $^{59}$ -

A solution of sodium ethoxide, prepared from absolute ethanol (240 ml) and metallic sodium (0.14 g), was mixed with 2-nitropropane (125 ml, 0.07 mol). The mixture was cooled to 0°C and freshly distilled acrolein (92 ml, 0.07 mol) was added dropwise over a period of 1.5 hrs. at a temperature of 5°C. After an additional half an hour at 10°C, the reaction mixture was acidified by addition of glacial acetic acid (3 ml). The solution was then concentrated in vacuum to a thick syrupy liquid which was dissolved in benzene (400 ml) and washed with water. The benzene solution was dried over sodium sulphate. Removal of solvent in vacuum yielded an oil (190 g) which was fractionally distilled and the fraction at 52°-56°/0.25-0.3 mm (71 g.) was collected. Vmax 1540, 1720 cm$^{-1}$.
2(-3 Methyl-3-nitrobutyl)-1, 3-dioxolan (XXVIII) 

The dioxolan was prepared as described in the literature.

Vmax. 1550 cm\(^{-1}\); n. m. r. signals (CDCl\(_3\)), 8.42, 8.04, 6.09, 5.09; areas 6:2:2:4:1.

5,5 - Dimethyl \(\Delta^1\) - pyrroline 1-oxide (XVI) 

The nitrone was prepared as described earlier. \(\lambda_{\text{max.}} (\text{EtOH}) 234 \text{ m\(\mu\)}(\varepsilon -7500);\) (in water, N/1000-hydrochloric acid, and 2N-sodium hydroxide) 226 m\(\mu\) (\(\varepsilon -7500\)); n. m. r. signals (CDCl\(_3\)), 8.55(s), 7.78(d), 7.43(d); \(\delta \) (t); areas 6:2:2:1. The last peak appears at 2.8 in D\(_2\)O, 2.5(H\(_2\)O), 2.8 (N/1000-H\(_2\)O) without changes in area or appearance of new peaks (Found: C, 62.38; H, 9.55; N, 12.63. Calc. for C\(_6\)H\(_{11}\)N\(_2\): C, 63.7; H, 9.7; N, 12.37%).

5-Ethyl-1-hydroxy-2,2 -dimethylpyrrolidine (XXIib) 

The N-hydroxy pyrrolidine was prepared as described earlier.

Phenylglyoxal N-Phenyloxime (XXIII) 

The nitrone was prepared as a yellow solid, m. p. 109-110\(^{\circ}\), Vmax(mull) 1580, 1600, 1645 cm\(^{-1}\), (Found: C, 74.60; H, 4.93; N, 6.60. Calc. for C\(_{14}\)H\(_{11}\)NO\(_2\): C, 74.67; H, 4.89; N, 6.2%).

Phenylglyoxal N-phenyloxime hydrate (XXIV) 

In a slight modification of Kröhnke's procedure, the oxime (XXIII), (1.8 g.) in ice-cold ethanol (25 ml.) was stirred with 0.1N-sulphuric acid (40 ml.) for 1 hr. Extraction with ether gave a yellow-white residue which on recrystallisation from chloroform-light petroleum 40-60\(^{\circ}\) gave the colourless hydrate, m. p. 88\(^{\circ}\), which became yellow on standing in the air. Vmax. (mull) 1600, 1680, 3400 cm\(^{-1}\). (Found: C, 70.05; H, 5.2; N, 6.15, Calc. for
C₄H₁₃NO₃: C, 69.15; H, 5.4; N, 5.75%.

N-hydroxy-piperidine (XXVII). Piperidine (21.5 g, 1 mol) in water (20 ml) was treated with 30% hydrogen peroxide (9 g, 1 mol) dropwise with constant stirring and cooling the flask in ice. The mixture was allowed to stand for 24 hrs. at room temperature. Continuous extraction with ether gave an oil which was fractionally distilled and the fraction at 80°/18 mm., was collected.

Tetraethylammonium periodate. Paraperiodic acid (7.72 g, 0.034 mol.) in water (20 ml.) was added in portions to cold 25% tetraethylammonium hydroxide (20 ml, 0.034 mol.). Evaporation under reduced pressure left a crude solid which was extracted with hot t-butyl alcohol. The compound was precipitated with di-isopropyl ether and recrystallised from t-butyl alcohol, (8.5 g, 82%), m.p. 176-177°.

2-(3-Hydroxyamino-3-methylbutyl)-1,3-dioxolan (XXIX).

The nitro-dioxolan (XXVIII) (10 g), suspended in 5% aqueous ammonium chloride (60 ml.) at 10° was reduced by the addition of zinc dust (14 g) during 20 min., with vigorous stirring. Ice was added to keep the temperature below 15°. After filtration and repeated washing of the inorganic solids with hot water, the aqueous filtrates were concentrated under reduced pressure. Extraction with chloroform gave an oil, which, on fractional distillation under nitrogen (air condenser), gave as the main fraction the dioxolan (XXIX) (6 g, 65%), b.p. 100 - 110° / 0.5 mm., freezing in the refrigerator to a colourless solid. Vmax. 3300 cm⁻¹; n.m.r. signals (CDCl₃). 8.9 (s), 8.38 (s), 6.05 (d). 5.09 (t),
4.4(s); areas 6:4:4:1:2. (Found: C, 54.65; H, 9.65; N, 7.95. C₈H₁₇NO₃ requires C, 54.85; H, 9.8; N, 8.0%).

The Nitroso-dioxolan(XXX)(a) Aqueous method. The hydroxylamino-compound(XXIX)(1.6g.) in ethanol (10ml.) was added dropwise to a stirred solution of sodium periodate (3g., 1.5 mol.) in water (10 ml.). After 1 hr. the precipitate was filtered and the blue filtrate extracted with chloroform. The residue from this, combined with the solid, was recrystallised from acetone-hexane to give colourless dimeric 2-(3-nitroso-3-methylbutyl)-1, 3-dioxolan (XXX)(1.4g., 93%), m.p. 60-62° (blue melt). Vmax. (mull) 1240, 1280cm⁻¹; n.m.r. signals (CDCl₃). 8.84, 8.34, 7.84, 6.00, 5.00; areas 6:2:2:4:1. (Found:C, 55.25; H, 8.5; N, 8.2. C₈H₁₅N₂ requires C, 55.5; H, 8.75; N, 8.1%).

(b) Non-aqueous method. The hydroxylamino-compound (1.0g.) in chloroform (10ml.) was added dropwise to tetraethylammonium periodate (2.8g., 1.5 mol.) in chloroform with magnetic stirring. A blue colour appeared immediately, but iodine was also slowly formed. After 1 hr. the mixture was washed with sodium thiosulphate solution, and water, dried and evaporated to give a blue-green semi-solid residue, which on recrystallisation from acetone-hexane again gave the nitroso-dioxolan(XXX)m-p. 60 - 62°.

Periodate Estimations. Samples (ca. 1.25 x 10⁻³ mole.) were weighed and dissolved in water (50ml.) and aliquot portions (10ml.) of this stock solution diluted to 100 ml. with water (50 ml.), 0.25M-sodium periodate (10. ml.), and buffer solution (30ml.) of the composition
given below. Aliquot portions (10ml.) of the reaction mixture were added at intervals to saturated borax (10 ml.) containing solid boric acid and 15% potassium iodide. The iodine was titrated after 2 min. with standard 0.01N-sodium arsenite. The pH's were pre-determined on blank solutions made up as above with the following buffer solutions (30 ml.):

<table>
<thead>
<tr>
<th>pH of total blank</th>
<th>2.9</th>
<th>4.5</th>
<th>6.5</th>
<th>9.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2M-Sodium acetate</td>
<td>0.0</td>
<td>13.5</td>
<td>30</td>
<td>-</td>
</tr>
<tr>
<td>0.2M-Acetic acid</td>
<td>30</td>
<td>16.5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2N-Sodium hydroxide</td>
<td>-</td>
<td>-</td>
<td>1.1</td>
<td>H₂O</td>
</tr>
</tbody>
</table>

The rate and extent of periodate oxidation are shown in Tables I - IV. Periodate uptake expressed in moles/mole was calculated by the formula

\[
r = \frac{b-a}{1000} \times 2 \times A \times \frac{100 \times M}{10 \times W}
\]

\[
r = \frac{\text{moles of periodate consumed} \times 2 \times A \times \frac{100 \times M}{10 \times W}}{\text{moles of N-alkyloximes}}
\]

where \( A \) = strength of arsenite solution

\( M \) = molecular weight of the substance

\( W \) = weight of the substance taken

For the aromatic oxime \((XXIII)\) and its hydrate, (Table II), the estimations were carried out as above but with half the quantity of oxime and of periodate solution. At full strength the oxidation of even \((XXIII)\) was too fast to be followed.
Preparative Oxidations

5,5-Dimethyl-1-pyrroline 1-oxide (XVI). The nitrone hydrate (0.4g.) in water (3m1.) was mixed with sodium metaperiodate (1.5g., 2.8 mol.) in water (12m1). The solution soon turned blue and crystallisation of a white compound commenced. This was filtered after being left overnight, and combined with the residue obtained from chloroform extraction of the blue filtrate and evaporation of the extract. Recrystallisation from water containing a little ethanol gave 4-methyl-4-nitrosopentanoic acid (XX) (0.3g., 58%) m.p. 109-110°, identical with the compound already described 19; \( \lambda \) max. \( (\text{EtOH}) 295 \text{ m} \mu (\epsilon 4640); \lambda \text{max. (mull) } 1720 \text{ cm}^{-1}. \)

Phenylglyoxal N-phenyloxime (XXIII). The oxime (0.75g.) in ethanol 25m1.), was added dropwise during 2 hrs. to sodium periodate (2.1g., 3 mol.) in water (25m1.) with constant stirring. Free iodine was destroyed with sodium thiosulphate, the solution made mildly alkaline (NaHCO\(_3\)), and extracted with chloroform. Drying and evaporation gave crude nitrosobenzene m.p. 66-67°. The aqueous layer was acidified, iodine again removed, and the solution extracted with ether to give benzoic acid, recrystallised from hot water, m.p. and mixed m.p. 121°.

The oxime hydrate (XXIV) was oxidised in a similar manner, giving the same products.

5-Ethyl-1-hydroxy-2,2-dimethylpyrrolidine (XXVIb)\(^{20}\).

The N-hydroxypyrrolidine (1g.) in water (10m1.) was treated dropwise
with aqueous sodium periodate (1.5g., 1 mol.) neutralised with a little potassium carbonate. The mixture was stirred for 1 hr., and extracted continuously with chloroform, the extracts giving crude 2-ethyl-5,5-dimethyl -Δ1-pyrrolidine 1-oxide (XXIIb) 0.75g., 75%., λmax. (EtOH) 234 mλ (ε 8100). Vmax. 1580, 3400 cm⁻¹; n.m.r. signals (CDCl₃), 8. 9. 8.62, 7.98, 7.5; areas 3:6:2:4. The picrate was prepared in ether and recrystallised from ethanol, m.p. 71-72°. (Found: C, 45.45; H, 4.6; N, 15.4. Calc. for C₁₄ H₁₈N₄ O₈: C, 45.4; H, 4.9; N, 15.1%).

The N-hydroxypyrrolidine (XXVIa) was oxidised in a similar manner, giving 2,5,5-trimethyl -Δ1-pyrrolidine 1-oxide (XX) in 85% yield, b.p. 58-60° 3 m.m., characterised as its picrate mp 89°.

N-hydroxy piperidine (XXVII) The N-hydroxy piperidine (1.01g., 1mol.) in water (10ml.) was added dropwise to sodium periodate (6.42g., 3 mol.) in water (50 ml.), with constant stirring. A blue colour appeared within a min. of mixing but rapidly disappeared. The mixture was stirred for an additional 24 hrs. Free iodine was destroyed with sodium thiosulphate solution. The reaction mixture was extracted continuously with chloroform, but the extracts after evaporation gave a reddish oil of unknown composition.

2. Periodate Oxidation of Oximes

Preparations - Cyclohexanone oxime, acetoxime, phenylacetaldehyde oxime, acetophenone oxime, chloral oxime, syn-and-anti-benzaldehyde oxime, cyclopentanone oxime, cycloheptanone oxime.
sodium hyponitrite were prepared by the methods described in the literature.

Periodate Estimations. - Samples (± 0.00025 mole.) were weighed accurately into a flask and diluted to 100 ml. with buffer solution (30 ml.) composed of various volumes of 0.2N-sodium acetate and 0.2N-acetic acid, stock sodium periodate (0.25M., 10 ml.) and water or ethanol. * A blank was made similarly and the pH's were measured (see Table XVII). Aliquots (10 ml.) were withdrawn at intervals and buffered with saturated borax-boric acid solution (10 ml.) containing 15% potassium iodide. Iodine liberated was titrated with standard sodium arsenite solution (0.0025M) using fresh starch solution as indicator. The reaction was followed at various pH's and periodate uptake expressed in moles/mole was calculated (see Table V-XII).

*Ethanol was used as solvent for those oximes which were insoluble in water. The same volume of ethanol was used in the blank.
Table (XVII)
Model Solutions and their pH's

<table>
<thead>
<tr>
<th>Volumes</th>
<th>0.2N-sodium acetate (ml.)</th>
<th>0.2N-Acetic acid (ml.)</th>
<th>2N-sodium hydroxide (ml.)</th>
<th>pH's</th>
</tr>
</thead>
<tbody>
<tr>
<td>33.3/66.6</td>
<td>10</td>
<td>20</td>
<td></td>
<td>4.0</td>
</tr>
<tr>
<td>45/55</td>
<td>13.5</td>
<td>16.5</td>
<td></td>
<td>4.5</td>
</tr>
<tr>
<td>65/35</td>
<td>19.5</td>
<td>10.5</td>
<td></td>
<td>4.98</td>
</tr>
<tr>
<td>70/30</td>
<td>21.0</td>
<td>9.0</td>
<td></td>
<td>5.10</td>
</tr>
<tr>
<td>75/25</td>
<td>22.5</td>
<td>7.5</td>
<td></td>
<td>5.2</td>
</tr>
<tr>
<td>85/15</td>
<td>25.5</td>
<td>4.5</td>
<td></td>
<td>5.42</td>
</tr>
<tr>
<td>95/5</td>
<td>28.5</td>
<td>1.5</td>
<td></td>
<td>5.98</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>30</td>
<td></td>
<td>6.5</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>-</td>
<td>30</td>
<td>2.9</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>-</td>
<td>1.1+H₂O=30</td>
<td>9.2</td>
</tr>
</tbody>
</table>

Preparative Oxidations -

Cyclohexanone oxime - Cyclohexanone oxime (0.500g., 1 mol.) in water (25ml.) was treated with sodium periodate (2g., 2 mol.), in water (30 ml.). The pH was kept neutral. The flask containing the reaction mixture was immediately attached to a vacuum
line having two traps (a and b). The reaction mixture turned yellow and there was some effervescence. The effervescent gas was trapped in trap (a) by cooling with liquid nitrogen and then distilled in trap (b) by cooling with acetone and dry ice. The trap (b) was disconnected after one hr. Mass spectrum of the gas trapped in trap (b) was taken which showed it to contain nitrous oxide (Found: \(44.001045\). Calc. for \(N_2O\): \(44.001062\); and comparison with authentic nitrous oxide). The reaction mixture was extracted with chloroform. Drying and evaporation gave cyclohexanone (characterised as its 2:4 dinitro-phenylhydrazine derivative and comparison of infra-red).

**Phenylacetaldehyde oxime** - The oxime (1g., 1 mol.) in ethanol (60 ml.) was added dropwise to sodium periodate (9.5g., 6 mol.), in water (200 ml.) with constant stirring. The PH was kept at 6.5 by adding a drop of potassium carbonate solution. The reaction mixture was stirred for an additional 24 hrs. The solution was made alkaline (\(NaHCO_3\)) and extracted with chloroform. Drying and evaporation gave crude benzaldehyde (characterised as its 2:4 dinitrophenylhydrazine derivative m.p. and mixed m.p. 235\(^\circ\)). The aqueous layer was acidified with dil. hydrochloric acid and the iodine which liberated, was destroyed with sodium thiosulphate solution. The solution was then extracted with ether to give phenylacetic acid, recrystallised from hot water, m.p. and mixed m.p. 76\(^\circ\)(characterised as its p-bromophenylacyl derivative m.p. and mixed m.p. 89\(^\circ\)).

**Syn-benzaldoxime** - The oxime (1g.) in ethanol (25ml.) was added
dropwise to sodium periodate (9 g., 5 mol) with constant stirring. The pH was being kept neutral. After 24 hrs. stirring, the reaction mixture was made alkaline (Na₂CO₃) and extracted with ether. Drying and evaporation gave crude benzaldehyde (characterised as its 2:4 dinitro-phenylhydrazine derivative m.p. and mixed m.p. 234°). The aqueous layer was acidified with dilute hydrochloric acid and extracted with ether to give benzoic acid, recrystallised from hot water, m.p. and mixed m.p. 121°.

Attempted experiment to trap intermediate (XXXII).

Cyclohexanone oxime (2.01 g., 1 mol.) in ethanol (50 ml.) was made saturated by blowing butadiene through it. Sodium periodate (8 g., 2 mol.) in water (50 ml.) was added dropwise with constant stirring. The reaction mixture was stirred for an additional 24 hrs. and concentrated in vacuum. The solution was acidified with dilute hydrochloric acid and extracted with ether to give cyclohexanone (comparison of infra-red). The aqueous layer was also concentrated in vacuum and made alkaline. Extraction with ether continuously gave no residue.

3. Periodate Oxidation of Tertiary Amines.

Preparations:

N-Propyl piperidine (XLₐ).⁶₃ - N-propyl iodide (0.1 mol.) and piperidine (0.2 mol.) were heated under reflux for 5 hrs. Extraction with ether gave (XLₐ), ⁶₃ b.p. 148-153° n.m.r. signals (CCl₄) 9.09 (t), 8.5 (q), 7.72 (m); areas 3:8:6, molecular weight (mass spectrometry) 127. (Found: C, 75.53; H, 13.20; N, 11.14. Calc. for C₈H₁₇N·C, 75.59; H, 13.38; N, 11.02%).
N-Propylmorpholine<sup>63</sup> - The amine was prepared in 70% yield as described earlier<sup>63</sup>, distilled at 150-152°. n. m. r. signals (CCl<sub>4</sub>), 9.09, 8.05, 7.67, 6.42; areas 3:2:6:4. (Found: C, 64.54; H, 11.38; N, 11.52. Calc. for C<sub>7</sub>H<sub>15</sub>N0.C, 65.19; H, 11.62; N, 11.85%)

β-Piperidine ethyl alcohol<sup>(b)64</sup> - Equimolar quantities of piperidine and ethylene oxide were mixed in water (10ml.) The reaction mixture was kept for 2 hrs. and distilled and the fraction at 89 - 90°/20 mm. collected. n. m. r. signals (CCl<sub>4</sub>), 8.5(s), 7.59(t), 6.47(t), 6.09(s); areas 6:6:2:1, molecular weight (mass spectrometry) 129.

γ-Piperidino propyl alcohol(XLc) Ethyl-β-piperidino propionate<sup>65</sup> (prepared by heating equimolar quantities of piperidine and ethyl acrylate under reflux) (18.5g., 1mol,) in ether (50 mol,) was added dropwise to lithium aluminium hydride<sup>66</sup> (2g., 0.5 mol,) in dry ether (70 ml,) with constant stirring. After 10 minutes water was added dropwise with external cooling. The mixture was then treated with 20% sodium hydroxide solution to dissolve the precipitate of aluminium hydroxide. The ethereal layer was separated and dried. Evaporation of solvent gave (XLc) as an oil, distilling at 108-109°/20 mm. n. m. r. signals (CCl<sub>4</sub>), 8.54(s), 7.7(d), 6.54(t), 5.25(s); areas 8:6:2:1, molecular weight (mass spectrometry)143. (Found: C, 66.59; H, 11.57; N, 9.94. Calc. for C<sub>8</sub>H<sub>17</sub>N0;

\[\text{C, 67.13; H, 10.88; N, 9.79%}].\) The picrate was prepared in ethanol, recrystallised from ethanol, m. p. 215° (Found: C, 44.37; H, 5.17; N, 16.22. Calc. for C<sub>14</sub>H<sub>20</sub>N<sub>4</sub>O<sub>8</sub>; C, 45.16; H, 5.37; N, 15.05%).
N-Oxide of propyl piperidine (XLIa) 50b 40% peracetic acid
(9ml., containing 0.008mol. of active oxygen), was added dropwise
to N-propyl piperidine (2.54g., 0.1 mol.) with constant stirring
and by cooling with ice/salt mixture. The reaction mixture was
allowed to remain in ice/salt mixture for 0.5 hrs. and then at room
temperature for 4 hrs. The mixture was then cooled in ice and
20% sodium hydroxide solution was added dropwise with stirring
until the solution became alkaline to litmus. The viscous oil that
separated, was removed by extracting with chloroform continuously.
Drying and evaporation gave N-oxide (XLIa) as a hygroscopic white
solid, m.p. 140-145° (crude). n.m.r. signals (CDCl₃) 9.00 (t), 8.37(m),
6.84(q); areas 3:8:6. Vmax. (mull) 1640, 3400cm⁻¹. The picrate was
prepared in ethanol and recrystallised from ethanol, m.p. 105°.
(Found: C, 44.81; H, 5.41; N, 15.17. Calc. for C₁₄H₂₀N₄O₈: C, 45.16;
H, 5.37; N, 15.05%).

N-Oxide of N-piperidino propyl alcohol (XLIC).

N-oxide was prepared by above method, 50b as a hygroscopic white
solid. Vmax. 1645, 3300cm⁻¹. n.m.r. signals (CDCl₃) 8.09, 6.42, 2.90;
areas 8:6:1 (two protons are missing). It does not form picrate.

N-Oxide of propyl morpholine 50b  - N-oxide was prepared as a hygro-
copic white solid by the above method. 50b Vmax. (mull) 1660, 3300cm⁻¹,
n.m.r. signals (CDCl₃), 9.04, 8.04, 6.87, 6.3, 5.54; areas 3:2:6:2:2.
The picrate was prepared in ethanol and recrystallised from ethanol,
m.p. 140-141°. (Found: C, 42.52; H, 4.88; N, 14.86. Calc. for C₁₃H₁₈
N₄O₉: C, 41.71; H, 4.81; N, 14.97%).
Periodate Estimations. Volumetric estimations of amines were performed at alkaline pH as described above (see Table XIV).

Preparative Oxidations -

N-Propyl piperidine (XLa). (a) Aqueous method. The amine (3.81g., 1 mol.) in ethanol (20 ml.) was added dropwise to tetraethylammonium periodate (10g., 1 mol.) in water (20ml.) with constant stirring. The reaction mixture was stirred for an additional 36 hours. Extraction with chloroform continuously gave N-oxide (XLIa) as a hygroscopic white solid, m.p. 142-146\(^\circ\) (crude). V\text{max.}(\text{mull}) 1640, 3400\text{cm}^{-1}, \text{n.m.r. signals (CDCl}_3) 9.00, 8.37, 6.84; \text{areas 3:8:6}. \text{Molecular weight (mass spectrometry) 143, abundant ion peak at 127 with loss of oxygen atom. The picrate was prepared in ethanol and recrystallised from ethanol, m.p. 104-105\(^\circ\). (Found:C, 45.59; H, 5.77; N, 15.16. Calc. for C\textsubscript{14}H\textsubscript{20}N\textsubscript{4}O\textsubscript{8}: C, 45.16; H, 5.37; N, 15.05\%). The infra-red and nuclear magnetic resonance of the N-oxide were compared with the authentic N-oxide, prepared by peracetic acid method.

(b) Non-aqueous method. The amine (1.2g., 1 mol.) in acetone (15ml) was added dropwise to tetraethylammonium periodate (3.2g., 1 mol.) in acetone (10ml). The clear reaction mixture was allowed to stand at room temperature for 36 hrs., when needle like white crystals of tetraethylammonium iodate were formed. The reaction mixture was filtered. The crystals of tetraethylammonium iodate were washed with acetone and dried under vacuum, m.p. 152-154\(^\circ\), very hygroscopic.
max. (Et-H) 205 m\(\mu\) (\(\epsilon=2500\)); n. m. r. signals (CDCl\(_3\)), 8.65(t), 6.67(q); areas 12:8. (Found: C, 31.67; H, 6.66; N, 4.18. C\(_8\)H\(_{20}\)N\(_2\)O\(_3\) requires C, 31.47; H, 6.55; N, 4.59%). The filtrate on evaporation gave N-oxide (XLIA). m. p. 140-145°.

\(\beta\)-Piperidine ethyl alcohol (XLb): (a) Aqueous method.
The amine was oxidised in a similar manner, giving N-oxide (XLb) as a hygroscopic white solid, m. p. 95-100°. Vmax. (CHCl\(_3\)) 1640, 3300 cm\(^{-1}\). n. m. r. signals (CDCl\(_3\)) 8.25, 6.64, 5.9, 2.95; areas 6:6:2:1; molecular weight (mass spectrometry) 145. The picrate was prepared in ethanol which could not be recrystallised m. p. 210° (decomp). (Found: C, 43.68; H, 5.50; N, 15.17. C\(_{13}\)H\(_{18}\)N\(_4\)O\(_9\) requires C, 41.71; H, 4.81; N, 14.97%).

(b) Non-aqueous method. The amine (1.8g., 1 mol.) in chloroform (5ml.) was added to tetraethylammonium periodate (2.2g., 1 mol.) in chloroform (15 ml.) with constant stirring. After 36 hrs, the reaction mixture was washed with water. Drying and evaporation of chloroform gave N-oxide (XLb).

\(\alpha\)-Piperidino propyl alcohol (XLc). The amine was oxidised in a similar fashion as described above, giving N-oxide (XLIC) as a hygroscopic white solid in 75% yield. Vmax. (CHCl\(_3\)) 1645, 3300 cm\(^{-1}\). n. m. r. signals (CDCl\(_3\)), 8.09, 6.42, 2.90; areas 8:6:1 (two protons are missing), molecular weight (mass spectrometry) 159. It does not form picrate.

Triethylamine. The amine (1.0g., 1 mol.) in chloroform (5ml.) oxidised with tetraethylammonium periodate (3.38g., 1 mol.) in
chloroform (15ml.) in a similar manner, yielded N-oxide (XLII), which as a hygroscopic white solid (1.18g., 95% yield), gave pale-blue precipitate with copper sulphate solution. \( \nu_{\text{max.}} \) \( (\text{CHCl}_3) \) 1645, 3300 cm\(^{-1}\). n.m.r. signals \( (\text{CDCl}_3) \) 8.67 (t), 6.62 (q); areas 9:6. The picrate was prepared in ethanol and recrystallised from ethanol, m.p. 190 - 195\(^\circ\) (decomp). (Found: C, 45.34; H, 6.09; N, 15.8. Calc. for C\(_{12}\) H\(_{18}\)N\(_4\)O\(_8\): C, 41.61; H, 5.20; N, 16.18%).

**Triphenyl phosphine.** - Triphenyl phosphine (1.31g., 1 mol.) in chloroform (5ml.) was added dropwise to tetraethylammonium periodate (1.6g., 1 mol.) in chloroform (10 ml.) with constant stirring. The reaction was exothermic. The solution was allowed to stand for 36 hrs at room temperature. Free iodine was destroyed with sodium thiosulphate solution. Drying and evaporation of chloroform gave triphenyl phosphine oxide as a yellow solid which on recrystallisation with pet ether 40 - 60\(^\circ\) yielded colourless crystals, m.p and mixed m.p 154-155\(^\circ\).

**Diethyl sulphide.** - Diethyl sulphide (1.8g., 1 mol.) in chloroform (15 ml.) was added dropwise to tetraethylammonium periodate (4.5g., 1 mol.) in chloroform (40 ml.) with constant stirring. After 36 hrs, the reaction mixture was washed with water. Drying and evaporation gave diethylsulphoxide as an oil, distilled at 88-89\(^\circ\)/15mm. \( \nu_{\text{max.}} \) 1650, 3500 cm\(^{-1}\). (Comparison of authentic infra-red).
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Part II

Aspects of the Chemistry of C-Nitroso Compounds and \( \alpha \)-Unsubstituted Nitrones derived from them
Introduction

The chemistry of C-nitroso compounds\(^1,2\) and nitrones\(^3,4\) has recently been reviewed. The C-nitroso compounds, which have been known for over ninety years exist in two molecular forms, viz., as a blue (aliphatic) or green (aromatic) monomer and as a colourless dimer. This dissociates into the monomer on heating or dissolution in solvents, the kinetics and thermodynamics of the reaction depending on the structure of the compound and conditions\(^5-7\). In several instances the dimers exhibit geometrical isomerism, that is, both cis and trans configurations are known.

The blue or green colour of the nitroso monomers arises from an absorption at 6300 - 7900\(\text{A}^\circ\) (\(\varepsilon = 1-60\)); additional bands at 2700 - 2900 \(\text{A}^\circ\) (\(\varepsilon = 80\)) and 2200 \(\text{A}^\circ\) (\(\varepsilon = 5000\)) also appear. The first of these is given by all nitroso monomers whereas the other two bands are characteristic of aliphatic nitroso compounds alone, but are obscured by the phenyl absorption in aromatic nitroso compounds.\(^1,2\) The visible absorption (6300 - 7900\(\text{A}^\circ\)) has been assigned to an \(n \rightarrow \pi^*\) (N) transition, that is, one electron from the lone pair of the nitrogen atom is promoted to an antibonding \(\pi\) orbital, while the lower wavelength bands for aliphatic nitroso compounds have been assigned to the \(n \rightarrow \pi\) (O) transition (2700 - 2900\(\text{A}^\circ\)) and \(\pi \rightarrow \pi^*\); transition of the N=O group.\(^1,2\) The stretching frequency (of the N=O band) in the infra-red has been observed in the region of 1539 - 1621 cm\(^{-1}\) (aliphatic) and 1488 - 1513 cm\(^{-1}\) (aromatic). The C-N frequency couples with the characteristic vibration of the remainder of the molecule, giving two bands, one at 1100 and the other between 750 and 860 cm\(^{-1}\).\(^1,2\)
The nitroso trans-dimers absorb strongly near 2650 Å (ε = 10000), due to the $\pi \rightarrow \pi^*$ transition, while the cis-isomers absorb at shorter wavelengths (e.g., cis-bis (nitrosomethane) 2640Å). Thus $\lambda_{\text{max}}$ (H$_2$O) for RNO varies from 265m (R=CH$_3$) to 271 m ($R$ = Sec. C$_5$H$_{11}$), a smaller variation than for the trans-dimers. The trans-dimers show a strong band in the infra-red at 1176-1299 cm$^{-1}$, attributed to N-O stretching. In the cis-isomers this band is replaced by a douolet at higher frequencies (1323 - 1344 and 1330 - 1420 cm$^{-1}$ for aliphatic, 1389 - 1397 and 1409 cm$^{-1}$ for aromatic).

The structure of dimeric nitroso compounds has now been elucidated on the basis of infra-red absorption and other physical properties. Thus cis and trans dimers are assigned the structures (1a-b). An electronic arrangement with bonds of order 3/2 has more recently been proposed for the nitroso monomers and dimers by Linnett and Rosenberg. They have shown that the dimerisation of alkyl nitroso compounds and the non-existence of dimers of nitrosyl halides can be explained on the basis of these electronic structures (2a-b) and (3a-b), where the lines represent pairs of electrons, and circles (o) single electrons having one spin, and (x) those having the other.
They suggest that nitroso-compounds having the structure (2a) in the ground state dimerise, because, by so doing, a spatial separation of electron pairs occurs so that inter-electron repulsion is reduced. On the other hand, nitrosyl halides, which have the structure (2b), do not gain in this way because there is already a separation of pairs in the monomer and consequently dimerisation does not provide any advantage.

The dimerisation process goes readily in nonpolar solvents. The kinetics of cleavage of dimers to monomers are unimolecular, but are complicated by strong solvent effects, which alter both the enthalpy and entropy of activation. Solvent effects are also strong in the isomerisation of cis to trans dimers, which takes place most readily in non-polar solvents.

Primary and secondary nitroso alkanes undergo prototropic rearrangement to oximes (4). At room temperature the

\[
R_2\text{CHNO} \quad \xrightarrow{\text{prototropic rearrangement}} \quad R_2\text{C} = \text{NOH}
\]
isomerisation of nitrosomethane to oxime is faster than dimerisation. Many substances accelerate the reaction as for example hydroxylic solvents, strong acids, bases and nitric oxide. It is not fully established that nitroso dimers can isomerise to oxime without first dissociating into monomer. However, bis-nitroso cyclohexane is converted to cyclohexanone oxime hydro-chloride on standing at room temperature for two days in a cyclohexane solution saturated with hydrogen chloride.

Nitroso compounds in general are oxidised readily to the corresponding nitro compounds by a variety of oxidising agents. Nitric acid, alkaline hydrogen peroxide, permanganate and various peroxy acids have been used with success. Further oxidation accounts for the low yields of nitroso-compounds obtained in the oxidation of amines by Caro's acid. Most of the reported studies have concerned aromatic nitroso compounds.

Nitroso compounds are very reactive towards free radicals. In general two radicals are consumed to give a fully substituted hydroxylamine (5)

$$\text{R-NO} + 2\text{R} \rightarrow \text{R-N-O-R}$$

Nitric oxide provides an important example of a reaction of this type. Nitrosobenzene yields diazonium nitrate or its decomposition products, presumably via an O,N-dinitrosohydroxylamine (6).

With aliphatic nitroso compounds, the products usually isolated are the

$$\text{ArNO} + 2\text{NO} \rightarrow \text{Ar-N-O(NO)} \rightarrow \text{Ar-N}_2\text{NO}_3$$
corresponding nitroalkane and the nitrate ester. Nitrous acid can bring about the same reaction.

The reaction of nitric oxide with t-aliphatic nitroso monomer is discussed again in Chapter 4 (photolysis).

Difluoramine radicals convert monomeric aliphatic and aromatic nitroso compounds to N-fluoro azoxy compounds smoothly at room temperature. Difluoramine brings about the same reaction.

Normally nitroso compounds are inert to alkalies except for the catalysis of the rearrangement of nitroso alkanes to oximes. However, tertiary aliphatic nitroso compounds having a vicinal secondary nitro-group undergo with alkali transfer of an oxygen atom from the nitro-group which becomes a nitroso group, the molecule then isomerising to
an oxime \((9)\).

\[
\begin{align*}
&\text{RC} - \text{CHOH} \rightarrow \text{RC} - CR^+ \\
&\text{ON} \quad \text{NO}_2 \quad \text{ON} \quad \text{NO}^- \\
&\text{RC} - CR^+ + \text{H} \rightarrow \text{RC} - CR \\
&\text{ON} \quad \text{N}^- \\
&\text{OH}
\end{align*}
\]  

\((9)\)

Nitrosobenzene with aqueous alkali yields nitrobenzene, hydroxyazo-benzene and azoxybenzene \(^{33}\) whereas with potassium ethoxide in ethanol it gives azoxybenzene and a small quantity of hydroxamic acid \((10)\)^{34}.

\[
\begin{align*}
\text{C}_6\text{H}_5\text{NO} + \text{C}_2\text{H}_5\text{OK} & \xrightarrow{\text{EtOH}} \text{C}_6\text{H}_5\text{N=N-CH}_5 + \text{CH}_5\text{N=CHO} \\
\text{OH}
\end{align*}
\]  

\((10)\)

The reaction probably proceeds via an alkoxy radical. It has been shown recently \(^{35}\) that nitrosobenzene reacting with two moles of potassium t-butoxide yields nitrosobenzene radical anion\((\text{C}_6\text{H}_5\text{N=O}^-)\). Aliphatic polyfluoro nitroso compounds with aqueous alkali also slowly yield nitro compounds and radical anions. \((11)\)^{36,37}

\[
\begin{align*}
\text{CF}_3\text{NC} & \xrightarrow{20\% \text{NaOH}} \text{CF}_3\text{NO}_2 + \text{CF}_3\text{N}=\text{O}^- \\
& \text{OH}
\end{align*}
\]  

\((11)\)
Aromatic nitroso compounds condense with aromatic amines to form azo and azoxy compounds (12), (13). In these reactions the nitroso group behaves formally in a similar fashion to the carbonyl group of a ketone. Nitrosobenzene condenses similarly with unsym-disubstituted hydrazine to give azoxy compound (13). Nitrosobenzene for example condenses also with hydroxylamine in the presence of alkali to give syn-diazotate (14). N-aryl and N-alkyl hydroxylamines condense easily with nitrosobenzene (and even with nitroso alkane dimers) to produce azoxy compounds (15). However, the mechanism is more complex than for carbonyl compounds and appears to involve radical anions as intermediates.
With Grignard reagents, aromatic nitroso compounds yield N,N-diaryl hydroxylamines (16).

\[
\text{ArNO} + \text{ArMgX} \rightarrow \text{Ar-N-OH}
\]

Nitrosobenzene reacts with formaldehyde to give azoxybenzene and a small amount of hydroxamic acid (17).

\[
\text{ArNO} + \text{CH}_2\text{O} \rightarrow \text{Ar-N}=\text{N}-\text{Ar} + \text{Ar-N-CHO}
\]

A mixture of equimolar amounts of an aldehyde and nitroso compound in the presence of Al-isopropoxide also results in a good yield of hydroxamic acid, while ester formation is completely suppressed (18).

Aliphatic nitroso aldehydes,

\[
\text{C}_6\text{H}_5\text{CHO} + \text{C}_6\text{H}_5\text{NO} \xrightarrow{\text{Al(C-i-Pr)}_3} \text{C}_6\text{H}_5\text{C}=\text{N-OH}
\]

obtained as intermediates during photolysis of alkyl nitrites, on further irradiation also yield hydroxamic acids.

Some reagents such as triphenylphosphine and triethylphosphite, readily form azoxy compounds via nitrene intermediates with deoxygenation of aromatic C-nitroso compounds. Recently deoxygenation of alkyl-nitrosobenzenes in excess triethylphosphite has been found to give rearranged products containing the pyridine ring. However, deoxygenation of nitrosobenzene with triphenylphosphine or tributylphosphine in amine solvents results in ring enlargement with the
ultimate formation of N-alkyl derivative of 2-amino-3H-azepine, via phenyl nitrene as an intermediate.

Of the reactions reviewed above, the great majority involved aromatic nitroso compounds. The reaction of the C-nitroso group with acids, diazoalkanes and under photolytic conditions had been studied mainly with aromatic nitroso-compounds.

In the present work these reactions have been investigated for some tertiary aliphatic nitroso compounds. The literature is reviewed in the relevant sections of the discussion.

Some cycloaddition reactions of the nitrones obtained with diazomethane (chapter 5), are described in chapter 6. The addition of dimethyl acetylene dicarboxylate posed special problems which will be dealt with in Chapter 7.
1. **Synthesis of Tertiary Aliphatic Nitroso Compounds.**

The most common method used for the preparation of C-nitroso compounds involves oxidation of the corresponding amines. Caro's acid (\( \text{H}_2\text{SO}_5 \) prepared from ammonium peroxydisulphate and concentrated sulphuric acid),\(^{28,53} \) was mostly used for oxidising aromatic amines or tertiary alkyl amines to their corresponding nitroso compounds though the yields are often poor (for example 4% for Bu\(^t\)NO). 1-Methyl-1-nitroso cyclohexane was obtained in 16% yield (crude) by oxidation of 1-methylcyclohexylamine with Caro's acid.\(^{54} \) In certain cases potassium peroxymonosulphate (a mixture of \( \text{KHSO}_5, \text{KHSO}_4 \), and \( \text{K}_2\text{SO}_4 \) in the ratio 2:1:1) has also been used.\(^{42,55} \) Peracetic acid\(^{56,57} \) and hydrogen peroxide in acetic acid\(^{58} \) have also been employed with good results.

A new preparative method for primary, secondary and tertiary nitroso compounds has been established by Emmons.\(^{57} \) Neutralised peracetic acid in methylene dichloride oxidises both an amine or a diethyl ketimine to the corresponding nitroso compound(19). For tertiary nitroso compounds

\[
\begin{align*}
\text{R}_2\text{CH}-\text{NH}_2 + \text{R}_2\text{C}=\text{O} & \rightarrow \text{R}_2\text{CHN}=\text{CR}_2 \xrightarrow{(O)} \text{R}_2\text{CHNO} + \text{R}_2\text{CO} \\
\text{R}_3\text{CN} + \text{CHC}_6\text{H}_5 & \xrightarrow{\text{HCl}} \text{RCNHOH} + \text{C}_6\text{H}_5\text{CHO} \\
& \downarrow \text{Br}_2/\text{H}_2\text{O} \\
\text{R}_3\text{CNO} + 2\text{HBr}
\end{align*}
\]
prior hydration of the oxaziran to hydroxylamine is necessary which on oxidation yields the corresponding nitroso compound. This method which proceeds by oxidation to the oxaziran and further oxidation to the nitroso compound, offers the possibility of synthesising nitroso compounds in good yields.

Oxidation of N-substituted hydroxylamines by a variety of oxidising agents such as aqueous chromic acid (20)\(^{59}\), periodate \(^9\), air \(^{42,60}\) and diethylazodicarboxylate \(^61\) has also

\[
C_6H_5NHOH + \text{H}_2\text{Cr}_2\text{O}_7 \rightarrow (C_6H_5\text{-NO})_2
\]

been used to prepare nitroso compounds (see introduction to Part I).

The free radical reaction of nitrosyl chloride with saturated hydrocarbons leads to nitrosoalkanes in good yield. Cyclohexane, in which all positions are identical, gives

\[
\text{NO} + \text{NOCl} \rightarrow \text{hv} \rightarrow \text{Cyclohexane} \rightarrow 47\% \text{ yield}
\]

Nitrosocyclohexane (21). \(^{15,16}\)

Nitrite esters can also be utilised for the preparation of nitroso compounds by photolysis, \(^{62}\) thermolysis \(^{18}\) or reaction with diacyl peroxides. \(^{63}\)

In the course of our work we found that m-chloroperbenzoic acid \(^{64}\) (80-85% activity), is a convenient reagent for oxidising tertiary alkylamines to the corresponding nitroso compounds in good yields.
Tertiary octylamine was obtained commercially. The amines (I a-c) and (II) were prepared from the parent carbinols

by the Ritters method (22).

isocamphane (111) was prepared by the same method from camphene. In an attempt to synthesise 2-amino-2-(β-naphthyl) propane from its carbinol by Ritter's method, a dimer of β-isopropenyl naphthalene was obtained as a white crystalline solid of molecular weight 336 (mass spectrometry). The same compound was also formed when β-naphthyl dimethyl carbinol was treated with concentrated sulphuric acid in glacial acetic acid at 70\(^0\) for 1 hour. In the n.m.r. spectrum (in CDCl\(_3\)), gem-dimethyl and methyl protons signals (\(\tau\) 8.6 and 7.93) and methylene protons signal (\(\tau\) 7.6) were observed in addition to the
signals of naphthalene ring protons. In the light of these spectral data, the structure (IV) was assigned to the product. Further attempts to synthesise a nitroso-compound in this series were abandoned.

The following nitroso compounds were synthesised. Oxidation of 1-ethyl cyclohexyl-amine (IIb) in dichloromethane with two mcls. of m-chloroperbenzoic acid at -10° to -5° in the presence of one moi. calcium carbonate gave 1-ethyl-1-nitrosocyclohexane (Vb) as a colourless dimer in 60-65% yield.

\[
\begin{align*}
\text{(a)} R &= \text{CH}_3 \\
\text{(b)} R &= \text{C}_2\text{H}_5 \\
\text{(c)} R &= \text{C}_6\text{H}_{11}
\end{align*}
\]

1-Ethyl-1-nitrocyclohexane (IXb) was also obtained as a by-product. The colourless dimer (Vb) showed strong bands in the infra-red region at 1280 cm\(^{-1}\) and the monomer at 1280, 1550 cm\(^{-1}\), characteristic frequencies for a nitroso group. Ultraviolet absorption in (Vb) was observed at 300, 698 m\(\text{M}\) (\(\varepsilon = 104, 16\)), which indicates the more stable trans-configuration for the dimer. At room temperature, nitroso dimer (Vb) was obtained in 30-35% yield, whereas at 40-50°, mainly 1-ethyl-1-nitrocyclohexane (IXb) was formed. It is remarkable that
with p-chloroperbenzoic acid \(^{64}\) and p-nitroperbenzoic acid, \(^{64}\) the yield of nitroso dimer (Vb) even at \(-10^\circ C\) to \(-5^\circ C\) was very poor (25 -30\%).

Similarly nitroso dimers (Va), (VI) and (VII) were obtained in 60-65\% yield, by oxidising the corresponding amines with m-chloroperbenzoic acid, while nitroso dimers (VC) and (VIII) were obtained in 35-40\% and 25-30\% yields respectively. It is presumed that in the case of dimers (VC) and (VIII), steric factors impede the dimerisation of the nitroso monomers, which are then readily oxidised in the reaction mixture to nitro compounds by the m-chloroperbenzoic acid. In all experiments, a yellow impurity of unknown composition was obtained which was removed by alumina chromatography using petroleum-ether 40-60\° as eluant.

The nitroso dimers (X) and (XI)

\[
\begin{align*}
\text{X} & \quad \text{Me} \quad \text{XII} \\
\text{NO} & \quad \text{Me}\text{NO} \\
\end{align*}
\]

were obtained in 98\% and 85\% yields respectively from the corresponding amines by the reagent.

In an attempt to synthesise(XII) photochemically by nitrosation of norcamphane according to Donaruma, \(^{15}\) a blue oil of unknown composition was obtained, along with bicyclo-(2,2,1)-heptan-2-one \(^{68}\)
(characterised as its 2,4-dinitrophenyl-hydrazine derivative).
Similarly 1-methyl cyclohexane on nitrosation yielded a greenish yellow oil of unknown composition, presumably a mixture of oximes. Oxidation of 1-methyl-cyclohexyl hydroxylamine by bromine water or periodate also yielded a bluish green oil of unknown composition.
2. **General Properties of Nitroso Compounds**

As already described, nitroso dimers dissociate into monomers on heating or dissolution in solvents. Thus in all experiments, dimers were fused under nitrogen, then solvent added.

(i) **Action of heat**

Nitrosobenzene disproportionates on heating into a nitro and an azoxy compound (23), while fully halogenated nitrosoalkanes yield the corresponding nitrocompounds together with various products derived from dissociation into free radicals. The mechanism can be explained by supposing that the first step is cleavage of the C-N bond to give nitric oxide and a free radical; action of the nitric oxide on more nitroso-compound could give nitro compounds. Photolysis gave similar results (see Chapter 4). Perfluoronoitrosoethane undergoes skeletal rearrangement in addition to giving

\[
\text{CF}_3\text{CF}_2\text{NC} \rightarrow \text{CF}_3\text{CF}_2\text{NO}_2 + \text{CF}_3\text{N} = \text{CF}_2
\]  

nitro compound(24). The nitroso monomer (Vb) was decomposed in boiling xylene to a dark mass, but was stable in boiling ethanol or in chloroform.
(ii) Action of daylight and air.

The decomposition of blue monomer of tertiary nitrosobutane is accelerated by light whereas the colourless solution of the dimer is stable towards light. Chloro-nitroso-compounds when dissolved in organic solvents and exposed to light and air, are also oxidised to the corresponding nitro compounds. β-Chloro-β nitrosobutane during irradiation if exposed to air is oxidised to the corresponding nitro compound partly.

In the course of our investigation, it was observed that nitroso monomer (Vb) also reacts with the oxygen of air, slowly in the dark and more rapidly in the daylight, to yield the nitro compound (IXb), (changes were followed by u.v. and t.l.c.). In a preparative experiment with nitrosomonomer (Vb) in daylight and air, 1-ethyl-1-nitrocyclohexane (IXb) was isolated in good yield (comparison with an authentic infra-red and g.l.c.). Thus all reactions with nitroso monomers were carried out in the dark under a stream of dry oxygen-free nitrogen in dry ether or benzene.

(iii) Action with bases.

Polyfluoro nitroso compounds on treatment with aqueous alkalies slowly yield nitro compounds and presumably radical anions as intermediates which were detected by electron spin resonance spectroscopy. Nitrosobenzene in potassium t-butoxide also yields nitrosobenzene radical anion (see Introduction).
1-Ethyl-1-nitrosocyclohexane monomer (Vb) in sodium methoxide in methanol, sodium ethoxide in ethanol, potassium hydroxide in water and ethanol or potassium t-butoxide in t-butanol, on standing at room temperature in the dark overnight yielded 1-ethyl-1-nitro cyclohexane (identified by t.l.c. and g.l.c. and compared with authentic sample) and a free radical (triplet) probably a radical anion, detected by electron spin resonance. This reaction was not studied further.
3. **Action of Acids on Nitroso Compounds**

Though nitroso compounds and their dimers show no basic reaction towards aqueous acids, adducts with hydrogen halide have been detected and in at least one case isolated. Trans-bis-nitroso methane forms a white solid of \( \text{CH}_2 \text{NO} \cdot \text{HCl} \) when treated with hydrogen chloride. Bis-\( \alpha \)-nitroso-toluene and hydrogen chloride in chloroform forms mainly benzhydrazide, benzyl chloride and several other minor products. This type of reaction is observed only with dimers of primary nitroso compounds. In certain cases treatment of secondary nitroso monomers with hydrogen chloride in ether yield ketoximes in 100% yield (25) whereas

\[
\begin{align*}
\text{RCH}_2\text{N}_2\text{NCH}_2\text{R} + \text{HCl} & \rightarrow 2 \text{RCH(OCH}_3}_2 + \text{RCOOCH}_3\text{N}_2\text{H}_4 \cdot 2\text{HCl} \\
\end{align*}
\]

primary nitroso dimers with hydrogen chloride in ether and methanol give hydrazine hydrochloride, an aldehyde dimethyl acetal and a methyl ester (26). It has been shown that reaction of hydrogen chloride with secondary and primary nitroso compounds involves monomers and dimers respectively. Some aromatic nitroso compounds undergo condensation when treated with strong acids.\(^{22,80}\)
Only one example of the reaction of acids with tertiary aliphatic nitroso compounds was found in the literature. The tertiary nitroso dimer (XIII) reacted with anhydrous hydrogen chloride or hydrogen bromide to give a chloro or bromo compound (XIV) and a hydroxylamine (XV). The probable mechanism is indicated(27).
The reaction of tertiary aliphatic nitroso monomers with acids might be expected to give rearrangement products or olefin via t-carbonium ion. In fact it was found that tertiary nitroso monomers reacting with anhydrous hydrogen chloride in ether to yield their corresponding chloro compounds only.

1-Ethyl-1-nitrosocyclohexane monomer (Vb) dissolved in ether was saturated with anhydrous hydrogen chloride and on standing at room temperature in the dark for three days yielded 1-ethyl-1-chlorocyclohexane (XVI) in 95% yield (comparison of infra-red with authentic sample) and no olefin was formed.

\[
\begin{align*}
\text{XVI} & \quad \text{(CH}_3)\text{CCH}_2\text{C}_2\text{H}_4\text{Cl} \\
\text{XVII} & \quad \text{(CH}_3)\text{CCH}_2\text{C}_2\text{H}_4\text{Cl} \\
\text{XVIII} & \quad \text{(CH}_3)\text{CCH}_2\text{C}_2\text{H}_4\text{Cl} \\
\end{align*}
\]

The formation of the tertiary chloride (XVI) probably proceeds via a tertiary carbonium ion which is formed by acid catalysed dissociation of (Vb) and is subsequently attacked by halide ion(28).

1-Ethyl-1-nitrosocyclopentane monomer (VI) in ether with hydrogen chloride also gave tertiary chloro compound (XVII). There was a possibility for the ring expansion in (XVII) but this was not
observed. 2,2,4-Trimethyl-4-chloropentane (XVIII) was obtained in a similar manner from its nitroso monomer (VII).

The nitroso monomer (Vb) when treated overnight and in the dark with either boron trifluoride in ether or perchloric acid in acetic acid yielded a yellow oil, presumably a mixture of olefin and nitro compound which was not identified. There was no reaction with glacial acetic acid and material was recovered unchanged.
4. **Photolysis of Nitroso Compounds**

Nitroso compounds are very sensitive to light.\(^8^3\) Photochemical decomposition of nitrosobenzene yields azoxybenzene, \(p\) and \(o\)-hydroxybenzene, nitrobenzene, aniline and other minor amounts of hydroxy azoxybenzene.\(^8^3\) It has been shown recently that photolysis of nitrosobenzene for 3 to 7 days in ethanol under an atmosphere of air gives azoxybenzene, 0, 4-nitro azoxybenzene, diphenylamine, 4-nitrodiphenylamine, 2, 4-\( \text{dinitro-diphenylamine} \) and 2-nitrodiphenylamine. Maruyama\(^8^5\) et al. have shown that nitrosobenzene on irradiation also yields a stable free radical, identified as diphenyl nitroxide by the hyperfine structure of e.s.r. spectra. This indicates free radical dissociation during the course of the reaction. Nitroxide radicals are formed from radical
dissociation of nitroso monomers,\textsuperscript{86} and not from dimers as suggested by Strom and Bluhm.\textsuperscript{87} Surprisingly nitrosobenzene monomer only gives the free radical by irradiation with ultra-violet rather than red light whereas for t-aliphatic nitroso monomers, only red light is effective.\textsuperscript{86}

Aliphatic nitroso compounds on photolysis yield nitroxyl (isolated as silver hypcnitrite) and olefin (29).\textsuperscript{88} In certain cases such as

\[
\begin{align*}
\text{(CH}_3\text{)}_2\text{C}-\text{CH}_2-\text{C}-\text{CH}_3&\text{hv} \rightarrow \text{(CH}_3\text{)}_2\text{C}=\text{CHCOCH}_3 + (\text{NOH}) \\
&\text{H}_2\text{N}_2\text{O}_2
\end{align*}
\]

\[
\begin{align*}
\text{(CH}_3\text{)}_2\text{C}-\text{CH}_2-\text{C}-\text{CH}_3\text{hv} \rightarrow \text{(CH}_3\text{)}_2\text{C}=\text{CHCH}_2\text{Pr} + (\text{NOH}) \\
&\text{H}_2\text{N}_2\text{O}_2
\end{align*}
\]

chloro-nitroso compounds, photo-oxidation to the corresponding nitro compounds has also been described.\textsuperscript{77,89} More recent studies by Baldwin and Rogers\textsuperscript{90} and Mackor \textit{et al}\textsuperscript{86} indicate that radical dissociation can also occur on photolysis.

The following experiments were designed to clarify the course of photolysis of simple tertiary alkyl nitroso alkanes in which the reaction is uninfluenced by an adjacent halogen or carbonyl group, and to isolate the products.

Photolysis were performed mainly on 1-ethyl-1-nitrosocyclohexane (Vb) using a 150watt tungsten lamp. A slow stream of oxygen-free nitrogen was maintained over the reaction mixture which was
cooled in water in a pyrex dish placed above the lamp. A leaden coil carrying a stream of water served to maintain the water bath at room temperature.

Irradiation of (Vb) for four hours in dry ether gave a pale yellow oil with infra-red bands at 1545, 1620, 1700(w) and 3450cm⁻¹ and a strong c.s.r. signal (triplet). When the crude yellow oil was chromatographed on alumina using petrol-ether 40 - 60⁰ and chloroform as eluent, the following compounds were isolated and identified.

The first fraction by elution with petrol-ether 40 - 60⁰ gave a colourless oil, consisting of the following products:

(i) 1-ethyl cyclohexane (XIX), detected by gas liquid chromatography and compared with an authentic sample.

(ii) a mixture of 1-ethyl-cyclohexene and ethylidene cyclohexane (XXa-b) in the ratio 56:44 (by n.m.r. measurement) obtained as a colourless oil by distillation.

\[
\begin{align*}
\text{XIX} & \quad \text{XXa} & \quad \text{XXb} \\
C_2H_5\text{NO}_2 & \quad C_2H_5\text{OH} & \quad C_2H_5\text{NO}_2 \\
\text{IXb} & \quad \text{XXII} & \quad \text{XXIII}
\end{align*}
\]
The product decolourised bromine water and its identity was confirmed by comparison with authentic olefin by the infrared spectrum, thin layer chromatography and gas liquid chromatography.

(iii) A trisubstituted hydroxylamine (XXI) obtained as a white solid m.p. 84-85°. The mass spectrum of the hydroxylamine (XXI) showed a molecular ion peak at 237 with loss of OR⁻ where R = 1-ethylcyclohexyl.

A second fraction with petrol-ether 40-60° as eluent contained 1-ethyl-1-nitro cyclohexane (IXb), which was obtained by distillation as a colourless oil. It was compared with authentic nitro compound by infra-red, thin layer chromatography and gas liquid chromatography.

The third fraction eluted with petrol-ether 40-60° and chloroform (95:5) gave 1-ethyl cyclohexyl carbinol (XXII) which was obtained pure by distillation. It was compared with an authentic specimen as above.

The last fraction eluted with chloroform was the only one to give e.s.r. signal (triplet). The main species had a nitrogen splitting of 14.1 ± 0.1 gauss (mean of six spectra). Possibly another species is present overlapping the first, and this can tentatively be associated with a nitrogen splitting of 13.5 ± 0.3 gauss, and one proton splitting of 5.3 ± 0.2 gauss. Lemaire and Rassat have quoted similar nitrogen splitting for nitroxide radicals (aN = 15.5 gauss for t-butyl nitroxide). Recently Mackor and coworkers have also obtained nitroxides with a similar N-splitting, by photolysis of nitroso-compounds. The structure (XXIII) is therefore assigned to the free radical product.
The infra-red spectrum of the last fraction showed bands at 1620(s) and 1700(w) cm\(^{-1}\) which suggest that other products such as an alkyl nitrite or an alkyl nitrate may also be present.

Quantitative results were obtained by subjecting the reaction mixture to g.l.c. The trialkylhydroxylamine (XXI) peak was rather variable in position and shape. The following Tables (I and II) which summarise several experiments to be described below, therefore give the relative amounts in the mixture of all the products except the trialkyl hydroxylamine (XXI) as calculated from the peak areas (average of several runs).

Table I

<table>
<thead>
<tr>
<th>Condition Products</th>
<th>dry/ether</th>
<th>((\text{CH}_3)_2N/\text{ether})</th>
<th>KOH/ether</th>
<th>((\text{CH}_3)_2\text{CO}/\text{ether})</th>
<th>\text{C}_6\text{H}_5\text{CH}_2\text{SH}/ether</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saturated hydrocarbon XIX</td>
<td>1.8%</td>
<td>5.8%</td>
<td>5.5%</td>
<td>5.5%</td>
<td>68.5%</td>
</tr>
<tr>
<td>Olefin XXa(^b)</td>
<td>56%</td>
<td>64.6%</td>
<td>69.3%</td>
<td>69%</td>
<td>31.4%</td>
</tr>
<tr>
<td>Carbinol XXII</td>
<td>19.2%</td>
<td>18.5%</td>
<td>14%</td>
<td>17.6%</td>
<td>-</td>
</tr>
<tr>
<td>Nitrocompound IXb</td>
<td>24%</td>
<td>10.5%</td>
<td>11.1%</td>
<td>8%</td>
<td>-</td>
</tr>
</tbody>
</table>
Table II

<table>
<thead>
<tr>
<th>Products</th>
<th>Degassed petrol</th>
<th>(C₄H₅)₃N</th>
<th>KOH/petrol</th>
<th>(CH₃)₃COK/petrol</th>
<th>C₆H₅SH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saturated hydrocarbon XIX</td>
<td>3.4%</td>
<td>8.7%</td>
<td>7.6%</td>
<td>8.8%</td>
<td>81%</td>
</tr>
<tr>
<td>Clefin XXab</td>
<td>53%</td>
<td>70.1%</td>
<td>70.7%</td>
<td>71.4%</td>
<td>19%</td>
</tr>
<tr>
<td>Carbinol XXII</td>
<td>19.4%</td>
<td>17.5%</td>
<td>18.4%</td>
<td>13.5%</td>
<td>-</td>
</tr>
<tr>
<td>Nitro Compound IXb</td>
<td>24.2%</td>
<td>3.5%</td>
<td>3.0%</td>
<td>6.1%</td>
<td>-</td>
</tr>
</tbody>
</table>

The formation of nitroxide (XXIII) and trialkyl hydroxylamine (XXI) imply a preliminary photo-dissociation in to free alkyl radicals. The addition of these to the nitroso compound giving nitroxide and finally trialkyl hydroxylamine, is a well known reaction (530).

\[
R-NO \xrightarrow{hv} RNO^* \xrightarrow{\cdot} R + NO
\]

\[
\text{R}_2\text{NO} + \cdot \xrightarrow{\cdot} \text{R}_2\text{NO}^* \xrightarrow{\cdot} \text{R}_2\text{NOR}
\]  \hspace{1cm} (30)
The olefin could arise by disproportionation of the radical \( \dot{R} \), but should then be accompanied by corresponding amount of the saturated cycloalkane. Comparison of the g.l.c. with standard mixtures of olefin and alkane showed that the olefin was actually present in much greater amount (see Table I).

The olefin is thus assumed to arise mainly by \( \alpha \) molecular eliminations (31), which occurs concurrently with

\[
\begin{align*}
\text{hv} & \rightarrow \\
\text{HNO}_2 + \text{HNO}_3
\end{align*}
\]

radical dissociation.

When the photolysis of nitroso monomer (Vb) in anhydrous ether was carried out in the presence of benzyl thiol, the reaction was very fast and photolysis was complete within 30 minutes, giving the disulphide as a white solid (comparison of infrared with authentic sample), the saturated hydrocarbon (XIX) and the olefin (XXa-b) in the ratio 69:31 (detected by gas liquid chromatography and compared with authentic samples) (32). The large amount of hydrocarbon (XIX) and the absence of \( R_2\text{NOR} \) (XXI) shows
that R is trapped by ArCH$_2$SH. The nitro compound (IXb) and carbinol (XXII) were also absent.

Conditions of the photolysis were varied to establish the origin of the nitro compound and carbinol.

Photolysis of (Vb) in degassed petrol (in which oxygen is less soluble) showed little decrease in the relative yield of nitro compound (see Table II). Although traces of oxygen may be present, and photo-oxidation is a known reaction, this experiment suggests that it is not the main process here.

When photolysis of (Vb) was carried out in the presence of triethylamine in ether or degassed petrol, the yield of nitro compound relative to olefin fell sharply (Table I and II). A crystalline hygroscopic deposit was formed after only 15 minutes. Chemical tests showed it to contain nitrite and nitrate ion (positive nitrite and nitrate radical test with ferrous sulphate and concentrated sulphuric acid) and it was assumed to be a mixture of triethylamine nitrite and nitrate salt. The crystalline deposit was also analysed by polarography and shown to contain nitrite and nitrate as compared with authentic mixture (Ref — B. Keilin and J. W. Otvos, J. Am.
The presence of hyponitrite ion could not be detected (negative AgNO₃ test).

Potassium hydroxide and tertiary butoxide caused a similar drop in formation of nitro-alkane (see Table I and II). Thus, the formation of nitro compound appears to be dependent on the presence of acids, which are removed by the bases. Acids can arise under our conditions by the decomposition of hyponitrous acid (formed by the molecular photo-elimination). The better known decomposition of this gives nitrous oxide and water but Buchholz and Powell have shown recently that a fast radical decomposition can occur, giving first nitrous and then nitric acid and nitrogen (33).

\[
3 \text{HONO} \rightarrow 2\text{N}_2 + 2\text{HNO}_2 + 2\text{H}_2\text{O}
\]

\[
\text{HONO} = \text{NOH} + \text{HNO}_2 \rightarrow \text{N}_2 + \text{H}^+ + \text{NO}_3 + \text{H}_2\text{O} \quad (33)
\]

\[
\text{HON} = \text{NOH} + \text{HNO}_2 \rightarrow \text{NO}_2 + \text{N}_2 + \text{OH} + \text{H}_2\text{O}
\]

Nitrogen dioxide and hydroxide radicals are assumed as intermediates.

Several pathways for the formation of the nitro compound are possible.

Simple photo-oxidation (cf. Mitchell and Cameron) cannot be excluded (34). Although in our experiments efforts have
been made to minimize the amount of oxygen present. There is, however, a possibility that some oxygen may be present even under these completely controlled conditions.

An alternative major pathway would consist of the reaction of nitrogen dioxide with alkyl radicals (35).

\[ \cdot R + \text{NO}_2 \rightarrow \text{RNO}_2 \] (35)

Nitrogen dioxide could arise in our system in several ways.

(i) Nitric oxide, formed by photolysis may react with residual oxygen (36).

\[ 2 \text{NO} + \text{O}_2 \rightarrow 2\text{NO}_2 \] (36)

But concentration of both nitric oxide and oxygen is low.

(ii) Nitrous acid, formed during photolysis (see above) can give nitrogen dioxide by hydrogen abstraction (37).

\[ \text{H}_2\text{N}_2\text{O}_2 \rightarrow \text{HO}_2\text{O} + \text{R} \rightarrow \text{NO}_2 + \text{RH} \] (37)

The suppression of nitro compound in the presence of base is in accord with such a pathway.

(iii) Some nitrogen dioxide may be formed during decomposition of hyponitrous acid (see above).

A third possible route to the nitro compound lies in reaction of nitric oxide formed by radical dissociation with unchanged nitroso-compound (38).
This reaction has been studied recently.\(^2\), \(^3\)

Nitroalkane and alkyl nitrate were the principal products (see Introduction).

On treatment of (Vb) in ether with nitric oxide, the blue colour rapidly disappeared. The oil obtained on removal of solvent was analysed by g.l.c. Nitro-alkane (69.6%) formed the major part of the volatile components which also comprised the cycloalkene (28.8%) and cycloalkane (1%). A band at 1630 cm\(^{-1}\) was observed in the infra-red region of the spectrum of the oil which may be ascribed to alkyl nitrite or nitrate.

The reaction is thus rapid, and yielding significant amounts of nitro-alkane, constitutes a possible pathway for formation of the latter in photolysis. One would not however expect this reaction to be retarded by base.

It is possible that all three pathways contribute to the formation of nitro-compound, with the nitrous acid route predominating. In its absence (in the presence of base) the residual nitro compound is formed by the other routes.

The origin of the carbinol is problematic. Interaction of the alkyl radical with residual oxygen followed by fission of the peroxide would lead to alkoxy radicals (39), which can give the
carbinol by hydrogen abstraction. Alternatively traces of moisture could be responsible. However, the carbinol was formed even when the solvents were scrupulously dried.

The thermal and photochemical breakdown of nitrites yields alkoxyl radicals. However, with a tungsten lamp and pyrex glass, the formation of alkoxyl radicals is unlikely as the wavelengths absorbed by nitrites are cut off.

The reactions which appear to occur in the photolysis are summarised in Scheme I. There are two concurrent photolytic steps. Molecular elimination of HNO gives olefin and hyponitrous acid. Free radical dissociation, possibly reversible
gives various products derived from further reaction of the alkyl radical. The nitroalkane and tertiary alcohol can arise from this radical by several pathways. Some of these, involve $\text{NO}_2$ which can itself arise in various ways in the reaction, in particular from hyponitrous acid or nitrous acid, both of which are formed by the molecular pathway.

A more exact physico-chemical study would be required to elucidate the possible and actual reactions in the photolysis.
5. Reaction of Nitroso Compounds with Diazomethane

Aromatic nitroso compounds in general react with active methylene compounds in the presence of a basic catalyst to form either anils, resulting from loss of water from the primary adduct, or nitrones, resulting from oxidation of the primary adduct. Though nitroso compounds

\[
\text{ArNO} + \text{A}_2\text{CH}_2 \rightarrow \text{Ar-} \text{N=CH}_2 \xrightarrow{\text{OH}} \text{Ar-} \text{N=CA}_2
\]  

(40)

are usually inert to electrophilic agents owing to their nucleophilic reactivity, they react in certain cases. Thus, nitrobenzyl chlorides react with nitrosobenzene in the presence of

\[
\text{ArNO} + \text{A}_2\text{CH}_2 \xrightarrow{\text{KOH}} \text{2-} \text{CH=N}-\text{Ar}
\]  

(41)
strong base to give nitrone in high yields via anion or carbene (42). 96

Diazalkanes react with nitroso compounds similarly to the nitrobenzyl chlorides, giving their corresponding nitrone (42). 97-100 This reaction, which proceeds rapidly and spontaneously

\[
R_2C = N_2 + ArNO \rightarrow R_2C = N\text{-}Ar + N_2
\]  

(42)

at room temperature without catalysis, probably involves electrophilic attack by the nitroso nitrogen on the diazoalkane carbon.

When diazomethane is used, it does not form N-phenyl nitrone

\[
\text{CH}_2\text{N}_2 + ArN\text{e} \rightarrow \text{Ar}-N=CH_2
\]  

(43)

but yields the dinitrone 98,99 of glyoxal by further oxidation (43).

Studies of the reaction of diazomethane with aliphatic nitroso compounds do not exist in literature.

Thus, the reaction of tertiary aliphatic nitroso monomers with diazomethane was studied. It was found that they yield the corresponding C- unsubstituted mononitrone.

The nitroso monomer (Vb) reacted with diazomethane in ether at room temperature to yield a colourless hygroscopic oil, assigned structure (XXIV) on the following spectral and chemical evidence. The infra-red bands at 1545 cm$^{-1}$, assigned to C=N
stretching and the ultraviolet absorption at 241 μM (ε = 7000, in ethanol), are both characteristic of mononitrones. In the n.m.r. (in CDCl₃), a pair of doublets (τ 3.33, 3.63, , j = 7.5 Hz, were assigned to the methylene protons with their different environments about the double bond. The molecular weight by mass spectrometry was 155 and by cryoscopy 159. The nitrone(XXIV) gave the 2:4 dinitrophenylhydrazine derivative of formaldehyde (comparison of infra-red with authentic sample) and on periodate oxidation yielded 1-ethyl-1-nitrosocyclohexane (Vb). The nitrone (XXIV) on ultraviolet photolysis in cyclohexane for 6 hours gave N-(1-ethyl cyclohexyl) formamide (XXVI) probably via an unisolable oxaziridinintermediate(XXV) together with other products which were not identified. It is the first example of a C-unsubstituted nitrone. Previous attempted preparation of Ar-N⁺ = CH₂ by diazomethane and nitrosobenzene or by phenylhydroxylamine and formaldehyde gave the glyoxal nitrone by oxidative dimerisation.

The nitrones (XXVII), (XXVIII) and (XXIX) were obtained similarly from their respective nitroso-monomers and diazomethane,
the structures being in good accord with the infra-red and n.m.r. spectra.

The aromatic nitroso compound (XI) with diazomethane gave N-mesityl nitrone (XXX) as a colourless leaflets which slowly became yellow on standing. The nitrone (XXX) was probably obtained by earlier workers, who mistakenly regarded it as N-mesityl hydroxylamine.

It is presumed that the reaction involves electrophilic attack on the diazomethane carbon by the nitrogen of the nitroso group and nitrogen is lost without cyclisation or rearrangement owing to the
availability of the unshared electron pair on the nitroso nitrogen (44). As suggested by Johnson, an unisolable oxaziran may be an intermediate.

1-Chloro-1-nitrosocyclohexane (XXXI) with diazomethane in ethanol yielded the diethyl ketal (XXXII) together with other products which were not identified. In the n.m.r. spectrum (in CDC\textsubscript{3}) of (XXXII), methyl and methylene protons signals (\(\delta 8.92(t), 6.64(\text{q}, \nu = 7\text{c}/\text{sec})\)) were observed in addition to the signals of cyclohexane ring protons. The diethyl ketal (XXXII) gave the 2:4 dinitrophenylhydrazine derivative of cyclohexanone (comparison of infra-red with authentic sample). A possible mechanism for the formation of diethyl ketal (XXXII) is indicated (45).

The reaction of 1-chloro-1-nitroso-cyclohexane (XXXI) and diazomethane in ether proceeded vigorously even on cooling in ice, giving a white precipitate, possibly polymethylene and an oil which was isolated but not identified.

\[
\begin{align*}
\text{Cl} & \quad \text{CH}_2\text{N}_2 \quad \text{EtOH} & \quad \text{HOEt} & \quad \text{EtCH}_n\text{OEt} \\
\text{Cl} & \quad \text{CH}_2\text{N}_2 \quad \text{EtOH} & \quad \text{HOEt} & \quad \text{EtCH}_n\text{OEt}
\end{align*}
\]

The cycloaddition of nitrones to C\(\equiv\)C and C\(\equiv\)N bonds\(^3,4\) has been studied extensively by Huisgen\(^104\) in his work on 1,3-dipolar additions. Nitrones undergo 1,3 cycloaddition with multiple bonds,\(^3,4,104\text{-}107\), in molecules such as styrene, bicyclopentadiene and dimethyl acetylene dicarboxylate\(^107\) yielding isoxazolidines.\(^106,108\) With phenylisocyanate 1,2,4-oxadiazolidines are obtained.

In order to establish their structures, the novel nitrones obtained with diazomethane were treated with a variety of dipolarophiles.

(i) Styrene

The crude nitrome(XXIV) reacted with redistilled styrene in benzene at room temperature to yield isoxazolidine adduct (XXXIII) as a colourless oil of molecular weight 259 (mass spectrometry). A decision between isomer (XXXIII\(a\)) and (XXXIII\(b\)) was made on the basis of proton magnetic resonance. Since in (XXXIII\(a\)), the benzylic proton is shielded by an adjacent oxygen atom, it would be expected
to be brought into resonance at a relatively lower field, than in isomer (XXXI!b) where there is no adjacent heteroatom. The n.m.r. spectrum of the adduct showed a signal corresponding to one proton at $\tau 5.22 \ (\delta = 7.5 \text{ c./sec})$ which was assigned to the proton at C-3 in structure (XXXIIia) and signals at $\tau 7.75 \ (m)$, $\tau 7.1 \ (t, J = 7.5 \text{ c./sec})$ corresponding to methylene protons at C-4 and C-5 respectively.

In an analogous case similar $\tau$ value for benzylic proton has been observed. Thus on the basis of spectral data, the structure (XXXIIia) was assigned to the isoxazolidine adduct.

Similar adducts (XXXIV), (XXXV) and (XXXVI) were likewise obtained from their respective nitrone. In each case

![Chemical structures]

n.m.r. was similar and low field signal for benzylic proton was observed near $\tau 5.2$.

The aromatic nitrone (XXX) gave in poor yield a yellow solid which was not examined further.

(ii) Phenylisocyanate and $\alpha$-Naphthylisocyanate.

The crude nitrone (XXIV) reacting with phenylisocyanate in benzene, yielded a white crystalline adduct of molecular weight
274 (mass spectrometry). A band at 1730 cm$^{-1}$ is consistent with a urethane group, as (XXXVII). The low field singlet ($\delta$ 5.04, area 2) was assigned to the doubly deshielded methylene group in (XXXVII). Hydrogenation, with consumption of two moles of hydrogen, yielded 1-ethyl-cyclohexylamine, aniline, methylaniline, and N-methyl 1-ethyl cyclohexylamine (46) in agreement with structure (XXXVII). All
but the last product were identified by comparison of their thin layer and gas chromatographic behaviours with authentic compounds.

The adducts (XXXVII), (XXXIX), (XL) and the naphthyl derivative (XLI) were obtained from their respective nitrones, the structures being in accord with the infra-red and n.m.r. spectra. In the case of aromatic nitrone (XXX), the reaction proceeded vigorously and gave a thick red oil of unknown composition. All attempts to isolate the adduct even at low temperature failed.

(iii) Maleic anhydride

The crude nitrone (XXIV) was treated with maleic anhydride in Analar benzene to give in good yield, a white crystalline adduct, to which structure (XLIII) is assigned on the following evidence.

\[
\begin{align*}
\text{XXIV} & \quad \text{+} \quad \text{CH}_2\text{CO} \\
\text{H}_2\text{O} & \quad \rightarrow \\
\text{XLII} & \quad \text{COOH} \\
\text{COOH} & \quad \text{CH}_2\text{N}^+\text{H}_2 \\
\end{align*}
\]

The infra-red spectrum of the adduct (XLIII) showed bands at 1600, 1700 and 2480 cm\(^{-1}\), assigned to \(-\text{CO}_2\), \(\text{C} = \text{C}\), and \(-\text{N}^+\text{H}\) stretching.
frequencies. Ultraviolet absorption at 218 m\(\mu\) (\(\lambda = 700\)) was observed which was not affected by acid or base. The n.m.r. spectrum (in DMSO) contained two groups of triplets at \(6.89\) and \(6.80\) (equivalent to two protons) and two single proton signals at \(5.38\) (broad q) and \(5.53\) (d, \(J = 8.4\) /sec), ascribed to 2-methylene and methine \(H_b\) and \(H_a\) protons respectively. The acidic protons could not be detected. In a spin decoupling experiment (in pyridine) at 100 MHz, irradiation at the frequency of \(H_a\) caused the collapse of the \(H_b\) signal to two superimposed doublets; When \(H_b\) was irradiated \(H_a\) collapsed to a singlet. The mass spectrum of the adduct (XLIII) showed molecular ion peak at 253 due to the loss of water molecule.

The adduct (XLIII) when treated with diazomethane in acetonitrile, yielded a yellow oil of molecular weight 299 (mass spectrometry). The infra-red spectrum of the oil showed a band at 1730\(\text{cm}^{-1}\), assigned to \(C=O\) stretching frequency of two ester groups. The n.m.r. spectrum (in \(\text{CCl}_4\)) showed signals at \(7.25\) (d, \(J = 5.4\) /sec), 6.92 (d, \(J = 3.4\) /sec), 6.79 (s), 6.32 (2 close singlet) and 5.45 (d, \(J = 8.4\) /sec) in the ratio 1:1:1:6:1 in addition to the signals
of the 1-ethyl cyclohexyl protons, assigned to 2-methylene group, methine Hb, ester methyl and methine Ha protons respectively. Thus Ha and Hb gives AB spectrum of $J = 8.4 \text{c/sec}$ and similarly the 2-methylene group also gives AB spectrum of $J = 5\text{c/sec}$. In the light of spectral data the structure (XLIV) was assigned to the product.

The formation of cycloadduct (XLIII) can be explained by postulating the formation of the unisolable 1, 3 cycloaddition intermediate (XLII) which is hydrolysed by water present in the crude nitrone (v. hygroscopic) to yield adduct (XLIII). Thus, with the crude nitrone (XXIV) in dried benzene, formation of adduct (XLIII) commenced within two hours in good yield, but when azeotropically distilled nitrone was used in dried benzene, the adduct (XLIII) was formed in a very poor yield after standing for 8 hours at room temperature. On keeping for a few days, the reaction mixture yielded more adduct (XLIII).

The aromatic nitrone (XXX) gave again an oily colourless adduct which was not characterised.

(iv) Dicyclopentadiene

The crude nitrone (XXIV) reacted with dicyclopentadiene to give a white crystalline adduct. The infra-red spectrum of the adduct showed a weak band at $1600\text{cm}^{-1}$, characteristic of $C=C$ stretching frequency. The n.m.r. spectrum in (CCl$_4$), showed signals at ~8.12, 7.75 (broad) 7.09, 6.24 and 4.42 (s) in the ratio 2:6:2:2:2 besides the signals of the 1-ethyl cyclohexyl protons. Thus
on the basis of spectral data and elemental analysis, the structure

\[ \text{XLV} \]

(XLV) was assigned to the adduct,

\[ \text{(v) Carbondisulphide} \]

On standing in carbon disulphide for 24 hours, the crude nitron (XXIV) yielded the thioformamide (XLVII) in good yield as a colourless crystalline solid. The infra-red spectrum showed bands at 1540 and 3200 cm\(^{-1}\), assigned to \( \text{C} = \text{S} \) and N-H stretching frequencies respectively. In the n.m.r. spectrum (in CC\(_4\)) both NH and CH protons signal were observed at 0.92 (broad singlet of area 2, 1 proton exchangeable). The thioformamide (XLVII) on degradation with methanol and concentrated hydrochloric acid gave 1-ethyl cyclohexylamine (comparison of infra-red with authentic sample) and a white solid which was not identified. All attempts to
synthesise thioformamide (XLVII) failed. Methods tried were the condensation of 1-ethyl cyclohexylamine with potassium dithioformate, $N$-(1-ethyl cyclohexyl) formamide with phosphorous pentasulphide and 1-ethyl cyclohexyl isonitrile with hydrogen sulphide.

The formation of thioformamide (XLVII) can be explained by 1, 3-cycloaddition of the carbondisulphide to give the intermediate (XLVI) which rearranges exothermically to the thioformamide by elimination of COS. The cycloadduct (XLVI) was never isolated. The analogous reaction reported by Takakfusbi and Kano supports this pathway (47).

(vi) Cyclohexene

The aliphatic nitrone (XXIV) when treated with redistilled cyclohexene, was recovered unchanged.

It is of interest that the aromatic nitrone (XXX) when treated with redistilled cyclohexene and left overnight at room temperature gave the yellow crystalline dinitrone (XLVIII) of molecular weight 324 (mass spectrometry) rather than a 1, 3-cycloadduct. The
infra-red bands at 1505 and 1608 cm\(^{-1}\) (probably aromatic C =C) and ultraviolet absorption at 349 m\(\mu\) (\(\lambda = 10200\)), are close to the characteristic frequencies of dinitrone.

\[
\text{XLVIII}
\]

In the n.m.r. spectrum (in CDCl\(_3\)), signals at \(\gamma 7.62\) (s), 3.6 (d, \(j = 8\) c/sec) and 3.05 (m) of areas 18:1:5 were assigned to the methyl protons (highfield) and the vinyl and aromatic protons (low field).

The reaction was repeated in cyclohexene which had been distilled over sodium, but in this case the nitrone (XXX) was recovered unchanged.

It is presumed that the reaction involves an oxidation. The dinitrone (XLVIII) was formed due to the oxidation of mononitrone by the impurities present in the cyclohexene such as cyclohexanone.

(vii) Miscellaneous dipolarophiles.

The crude nitrone (XXIV) did not react with camphene, ethyl vinyl ketone, vinyl acetate or dicyclohexyl carbodiimide. However, there was very slow reaction with ethyl vinyl ether, mesityl oxide and a very fast reaction with 1:4 naphthoquinone, but in these cases, the products (oils) were not isolated or identified.
7. Addition of Methyl acetylene dicarboxylate.

The dimethyl ester of acetylene dicarboxylic acid has often been used as a dipolarophile. Reaction with our nitrones was indeed very facile, but gave rise to a complex set of reactions and compounds. Actually Huisgen and others have reported similar difficulties in recent years (eg 48).

![Chemical structure](image)

(a) N-(1-Ethylcyclohexyl) nitronate.

The crude nitronate (XXIV) reacted with acetylene dicarboxylate dimethyl ester in carbon tetrachloride or dry benzene at room temperature to give in good yield 1,3-cycloadduct (XLIX) as a light yellow oil of molecular weight 297 (mass spectrometry). The adduct was quite stable for a day at room temperature but slowly decomposed on keeping or heating and thus was not obtained pure. Its infra-red
In the ultra-violet spectrum the band at 296 mλ (ε =2032) was not affected by acid or alkali but slowly shifted to 268 mλ with a shoulder at 305 mλ on keeping at room temperature for two days or on gentle warming. The n.m.r. spectrum (in CCl₄) is also consistent with (XLIX). A signal due to the methylene protons of the isoxazoline ring was observed at 5.8 (s, area 2) in addition to the signals of the 1-ethylcyclohexyl residue and two ester methyl protons. However, after standing overnight or on gentle warming, additional signals at 6.25 and 4.62 were observed which suggests the instability of the adduct (XLIX).

The spontaneous change was accelerated by warming (XLIX). The product was a viscous yellow oil (crude) to which structure (LI) was tentatively assigned on the following spectral and chemical evidence. In the n.m.r. spectrum (in CCl₄) the original signal (5.8) of the methylene group still remained, accompanied by sharp singlets at 4.62 and 6.25. The former suggests a doubly deshielded methylene group between two hetero-atoms, while the latter appears
to be a modified ester-methyl peak. In the structure (LI) proposed for the rearrangement product, the ester-groups are both conjugated to hetero-atoms. The methyl-protons are thus in similar electronic environment and closer together than in the original adduct (XLIX).

In an attempt to trap isomer (LI), the adduct (XLIX) was heated in an n.m.r. tube in CCl₄ at 70 - 75° and the changes observed by n.m.r. and ultra-violet spectroscopy. After twenty minutes heating, a methylene proton signal in the n.m.r. spectrum at [4,62 was observed in addition to the original signal at [5,8. On further heating, the signal increased in strength whereas that at [5,8 decreased, until after 160 minutes, the latter had almost disappeared. The signal at [4,62 also disappeared after the reaction mixture had been heated for 5 hours.

The viscous yellow oil (crude) (LI) when heated under reflux in CCl₄ with a few drops of water and a few drops of concentrated hydrochloric acid for 1 hour, yielded formaldehyde, which was isolated as its dimedone derivative (comparison of infra-red
with authentic sample and mixed m.p. 186-188° and a thick red oil. This on standing at room temperature for two days gave a white solid m.p. 154-156° (crude) in poor yield, with infra-red absorptions at 1510, 1550, 1620, 1660, 1745 cm\(^{-1}\). The structure of this compound has not yet been determined.

The viscous yellow oil (LII) showed infra-red absorptions at 1515, 1540, 1660, 1750, 3450 cm\(^{-1}\) and ultra-violet bands at 268 m\(\mu\) with a shoulder at 305 m\(\mu\) which shifted to 296 m\(\mu\) in alkali. The infra-red absorption at 1515, 1540, 3450 cm\(^{-1}\) and ultraviolet absorption at 268 m\(\mu\) suggests the presence of the H-bonded enolate group due to another product (see below).

The viscous yellow oil on further gentle warming during work up and keeping under vacuum slowly gave a poor yield of white solid (m.p. 128-130°), to which structure (LIII) was tentatively assigned on the following spectral evidence. The infra-red spectra of (LII) showed bands at 1515, 1540 (sh), 1645 (C = C), 1742 (C=O) and 3450 cm\(^{-1}\) (NH and OH) assigned to the H-bonded enol system (LIII). It is remarkable that compound (LII) does not give a positive ferric chloride test for the enol group. In the n.m.r. spectrum (in CDCl\(_3\)), a broad signal at \(\tau\) 3.4 (two protons) was exchangeable with D\(_2\)O and is thus ascribed to NH and OH groups. The ester methyl signals occurred at \(\tau\) 6.3, 6.4 (and the usual 1-ethylcyclohexyl protons signals at \(\tau\) 9.14(t) and 8.5). The peak developed at \(\tau\) 4.62 on warming the original adduct does not appear
in this product. The molecular weight of the product, 285, obtained by mass spectrometry and the elemental analysis, fit the formula (LII). The principal peaks and fragmentation in the mass spectrum are indicated in Table III and equation (49).

<table>
<thead>
<tr>
<th>Peptide Fragment</th>
<th>Mass (Da)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>285</td>
</tr>
<tr>
<td>M - C₂H₅</td>
<td>256</td>
</tr>
<tr>
<td>M - CO₂Me</td>
<td>226</td>
</tr>
<tr>
<td>M - CO₂CO₂Me</td>
<td>198</td>
</tr>
<tr>
<td>M - Ethylene</td>
<td>175</td>
</tr>
<tr>
<td>(M - Ethylene)</td>
<td>115</td>
</tr>
</tbody>
</table>

The ultra-violet absorption in (LII) at 268m\(\mu\) with a shoulder at 305m\(\mu\) (\(\varepsilon = 7015\)) was shifted to 296m\(\mu\) in alkali. On reacidification and on acidification of (LII) itself, absorption was observed at 242m\(\mu\). These changes are tentatively interpreted as follows.

The \(\lambda_{\text{max}}\) 268m\(\mu\) in (LII) is compatible with an enolate anion as is also suggested by infra-red (1515, 1540cm \(^{-1}\)). The neutral molecule is presumed to be a zwitterion . The enolate anion chromophore is known to absorb in this region (cf. ethylacetate anion, \(\lambda_{\text{max}}\) 274m\(\mu\) \((\log\varepsilon 4.65)\), cf. Organic Electronic
Spectral Data, Vol. I and III, 110, 81). Protonation of the zwitterion in acid gives an enol chromophore (cf ethylacetoacetate

\[
\begin{align*}
\text{(enol)} \lambda &= 238.5 \text{mM} \quad (\log \varepsilon 4.21) \text{ ref-Org. Electronic}\ 
\end{align*}
\]

Spectral Data, Vol. I, II and III, 110, 75, 81). In alkali, the zwitterion would give the anion expected to have similar absorption. The observed absorption at \( \lambda 296 \text{mM} \) is therefore tentatively ascribed to a product of decarboxylation (due to \(-N-C=O-CO_2\text{Me chromophore}\)) which in acid would give the keto form (see equation 50).

The negative ferric chloride test and peculiar behaviour of ultra-violet absorption in (LII) suggests that structure (LII) should be confirmed independently by syntheses.

The adduct (XLIX) when heated under reflux in dry benzene overnight, gave a thick red oil which after standing at room temperature for a few days deposited a small amount of white solid m.p.
168-170°C. The infra-red spectrum of the solid showed bands at 1550 (w), 1625 (broad) and 1750cm⁻¹, while ultraviolet absorption was observed at 217 and 262mM which was unaffected by acid or alkali. The structure of this compound has not yet been determined.

The formation of (LIII) from the adduct (XLIX) involves the migration of C₁ from the nitrocarbon to nitrogen (see equation 51).

![Chemical Structure](image)

R = 1, ethylcyclohexyl.

An analogous rearrangement has been observed by Takahashi and Kano. They actually suggest two mechanisms, involving either direct migration (a) or an aziridine, a three-ring intermediate (b). The carbonium ion formed in (a) is stabilised. In our case such stabilisation cannot occur, and the second mechanism is preferred (52, path b).

In experiments to be described next, involving the addition of acetylene dicarboxylate dimethyl ester to N-mesityl nitrone (XXX), we obtained evidence for the occurrence of such
an intermediate. The formation of (LI) during the rearrangement

will be discussed in that connection.

(b) \textbf{N-Mesitylnitrone}.

The nitrono(XXX) reacted instantaneously with dimethyl acetylene dicarboxylate in dry benzene to give a yellow solid
with correct composition for the simple 1,3-cycloadduct (LIV) but with spectra incompatible with it. The structure (LV) was assigned to it on the basis of the following spectral evidence. The infra-red spectrum of the adduct showed bands at 1715 and 1740 cm$^{-1}$ assigned to a ketonic carbonyl group and two ester carbonyl groups. Ultra-violet absorption was observed at 216 m$\mu$( $\epsilon$ = 12000) with shoulders at 236 m$\mu$( $\epsilon$ = 5600) and 290 m$\mu$( $\epsilon$ = 1525). The mesidine spectra was similar (215, 238 (sh) and 291 (sh)m $\mu$( $\epsilon$ = 9000, 7600, 1900). Thus neither infra-red nor ultraviolet show any conjugation of the ester groups as seen in spectra of authentic adducts (XLIX) and (LXIV) (p.116, 124).

In the n.m.r. spectrum (in CDCl$_3$), a pair of doublets was observed at $\sim$6.92 and 6.78( $\delta$ = 2.3 c/sec, area 2) besides signals due to the N-mesityl and ester methyl groups.

The high field doublets at $\sim$6.92 and 6.78 suggested a methylene group in a three membered ring with non-equivalent protons adjacent to nitrogen (cf. $\sim$6.88 and 6.44 calculated from A.T. Bottini and J.D. Roberts, J. Am. Chem. Soc., (1958), 80, 5203). The
peaks at $\gamma 6.92(d)$ and $6.78(d)$ were produced immediately even at $4^\circ C$ and there was no trace of methylene protons at low field, such as were observed at $\gamma 5.8$ in the aliphatic nitrone adduct (XLIX). Thus the initial 1,3-cycloadduct (LIV) must be very labile. Some chemical evidence for the structure (LV) will be discussed next.

The adduct (LV) on hydrogenation in benzene in the presence of 5% Pd/C, absorbed two moles hydrogen in 2 hours and yielded mesidine (comparison of authentic infra-red) and dimethyl 1-oxo-1,2 - propane dicarboxylate (LVI, positive colour reaction with ferric chloride). The ester (LVI) did not form a2,4-dinitrophenyl hydrazine derivative. Its infra-red spectrum showed bands at 1660, 1725 and 3500cm$^{-1}$ assigned to C=C, two ester carbonyl groups and a H-bonded enol group. The n.m.r. spectrum (in CCl$_4$) suggests, that it is a mixture of enol and keto forms.
From the hydrogenation, a rearrangement product was also obtained in moderate yield as a white solid of molecular weight 305 (mass spectrometry). The infra-red spectrum showed bands at 1570, 1630, 1730 and 3500 cm\(^{-1}\), characteristic for C = C, C = O and NH stretching frequencies and ultra-violet absorption was observed at 312m; \(\varepsilon = 2160\). In the n.m.r. spectrum (in CDCl\(_3\)), olefinic and NH protons signals were observed at 2.75 (s, areal) and 1.92 (1 proton, exchangeable) respectively. On the basis of spectral data and elemental analysis, the structure (LVII) was assigned to the rearrangement product.

The rearrangement is not catalysed by Pd, since (LV) was recovered unchanged after being shaken in the presence of the metal alone. This suggests that a prior hydrogenation product (LVIII) is reoxidised to (LVII) by dehydrogenation on the metal surface in a reversible step. On prolonged hydrogenation (absorbed 2.5 moles of hydrogen), very little of (LVII) was obtained. Presumably

\[ \text{Ar = mesityl} \]
it is ultimately reduced to mesidine via (LVIII).

In order to establish the presence of a simple ketone group, the adduct (LV) was reduced with sodium borohydride in ethanol to give a crystalline product as white leaflets, which showed bands at 1620 (w), 1750 and 3400 cm\(^{-1}\) in the infra-red region, assigned to aromatic C = C, \(\gamma\)-lactone carbonyl and OH stretching frequencies. Ultraviolet absorption was observed at 216 m\(\mu\) with shoulder at 236, 266 and 291 m\(\mu\) (\(\varepsilon = 13641\)). In the n.m.r. spectrum (in CDCl\(_3\)), signals observed were assigned as follows: \(\delta 7.17\) (quartet, 2 protons, \(\text{JAB} = 2\) Hz) to the aziridine methylene group, \(\delta 6.87\) (singlet, 1 proton, exchangeable) to the OH group and \(\delta 5.42\) (complex multiplet, 3 protons) to the \(\gamma\)-lactone methylene and methine protons respectively. In the light of spectral data, the structure (LIX) was assigned to the product.

The product (LIX) on heating under reflux with acetic
anhydride in pyridine for 30 minutes gave the monoacetate (LX) as a white solid. Its structure was confirmed by infra-red and n.m.r. spectroscopy. The infra-red spectrum showed bands at 1740, 1770 cm$^{-1}$ assigned to C = O stretching frequencies. In the n.m.r. spectrum (in CDCl$_3$) at 100 MHz, signals observed were assigned as follows: - $\zeta$ 7.90 (s, 3 protons) to the acetyl methyl, $\zeta$ 7.83, 7.78 (2 close singlets, 9 protons) to the aryl methyls, $\zeta$ 7.30, 7.00 (pair of doublets, 2 protons, $\Delta AB = 2.5$ c/sec) to the aziridine methylene, $\zeta$ 5.58, 5.30 (multiplets, 2 protons) to the $\gamma$-lactone methylene, $\zeta$ 4.45 (quartet, 1 proton) to the $\gamma$-lactone methine (see Fig. 1) and $\zeta$ 3.30 (singlet, 2 protons) to aryl protons respectively.

Fig. 1

When the adduct (LV) was heated under reflux in dry toluene for 3 hours, it yielded an unstable oily isomer (crude) thought to have structure (LXI) on spectroscopic evidence. The infra-red spectrum had bands at 1630, 1710, 1740 and 3400 cm$^{-1}$ (the bands at 1710 and 3400 cm$^{-1}$ in the infra-red region indicate the presence of another product). Ultraviolet absorption was
observed at 308 m\text{H} (E = 8200), changing to 312 and 261 m\text{H} in alkali. The ultraviolet change in alkali is also due to another compound. In the n.m.r. spectrum (in CDCl$_3$), the methylene protons (between the two hetero-atoms) were observed at $\tau$ 4.59 (s) while the pair of doublets at high field ($\tau$ 6.92 and 6.78) in (LV) disappeared. The methylene protons signal at $\tau$ 4.59 (s) of (LXI) is close to the value observed ($\tau$ 4.62) in isomer (LI).

The isomer (LXI) was heated under reflux with a few drops of water and a few drops of concentrated hydrochloric acid in toluene for 1 hour to give in good yield formaldehyde (isolated as its dimedone derivative, m.p. and mixed m.p. 186-188$^\circ$) and a white solid of molecular weight 293 (mass spectrometry), to which structure (LXII a-b) was tentatively assigned on the following spectral evidence. In the infra-red spectrum of (LXII), bands were observed at 1635 (C = C), 1670 (C = O), 1750 (C = O) and 3450 (NH and OH) cm$^{-1}$ but no bands at 1550 cm$^{-1}$ (contrast with
product LII). The band at 1750 cm\(^{-1}\) was assigned to C = O stretching frequency of ester groups in cis-isomer (LXIIa) while band at 1670 cm\(^{-1}\) was assigned to the H-bonded carbonyl of ester groups in trans-isomer (LXIIb) respectively. In the n.m.r. spectrum (in CDCl\(_3\)) at 100 MHz, both NH and OH proton signals were observed at \(\gamma\) 4.50 - 5.0 (broad singlet, 2 protons, exchangeable) whereas the ester methyls appeared at \(\gamma\) 6.56, 6.29, 6.50, 6.19 (4s 6 protons) (see Fig. 2) respectively in addition to the N-mesityl proton signals. The n.m.r. is compatible with a mixture of

\[
\begin{align*}
\gamma & 6.56 (s) \\
\gamma & 6.29 (s) \\
\gamma & 6.50 (s) \\
\gamma & 6.19 (s)
\end{align*}
\]

Fig. 2

(LXII a-b). (LXIIa) involves a downfield shift of OMe, the ratio a:b being 9:14 i.e. 39:61%. The principal peaks in the mass spectrum and fragmentation are indicated in Table IV and equation (53). The ultraviolet band at 301 m\(\mu\) (\(\epsilon = 9800\)) is shifted to 277 m\(\mu\) in alkali but the change reversed on reacidification. This behaviour is in contrast with that of (LII). We therefore assign the neutral structure to (LXII) which is compatible with chromophores shown in equation (54), in which the N-conjugated chromophore dominates (cf. \(\lambda 290 m\) \(\mu\) (\(\epsilon = 14.5\)), ref-K. Tsuda, Y. Satch,
Table IV

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^+ \mu$</td>
<td>293</td>
</tr>
<tr>
<td>$^+ \mu - OCH_3$</td>
<td>262</td>
</tr>
<tr>
<td>$^+ \mu - HCO_2Me$</td>
<td>233</td>
</tr>
<tr>
<td>$(^+ \mu - CO) - CO_2Me$</td>
<td>146</td>
</tr>
</tbody>
</table>

N, Ikekawa and H. Mishima, J. Org. Chem. (1956), 21, 800. In alkali the enolate anion chromophore comes to the fore (ethylacetate anion $\lambda = 274 m\mu$ $\log 4.65$, cfp114). Thus, (LXII)
being a weaker base (arylamine) does not form a salt but gives the neutral enol mixture as above in which the chromophore is dominated by $-\text{N}\equiv\text{C}O\text{Me}$. However, product (LXII) did not give the ferric chloride colour reaction for enols.

The infra-red absorption of (LXII) is incompatible with the analogous aliphatic derivative (LII), and the present structure assignment requires confirmation.

The reactions which appear to occur with aliphatic nitrone (XXIV) or aromatic nitrone (XXX) and acetylene dimethyl dicarboxylate ester are summarised in Scheme II.

The formation of the aziridine adduct (LV) can be explained by a mechanism involving an 1,3-dipolar-cyclo-addition intermediate (LIV). The aziridine intermediate is thought to be formed by a $\pi$-bond shift as shown in Scheme II. As pointed out above (p.122) formation of a primary carbonium ion by $\sigma$-bond migration is unlikely. The ring opening of the aziridine
Scheme II

Can 

intermediate involve two mechanisms (See Scheme II path a-b) which is a further II -bond shift or ring opening to iminium enolate and closure, to give unstable isomer (LXI) which on further heating under reflux in H₂O/HCl would yield compound (LXII) with the loss of formaldehyde.

The formation of (LII) from (XLIX) can be explained by a similar mechanism.

(c) \( \Delta \) - Pyrroline 1-oxides

In the course of these investigations, a note by Grigg
appeared, describing the addition of acetylene dicarboxylate dimethyl ester to 1-pyrroline 1-oxides. 2, 5, 5-Trimethyl 1-pyrroline 1-oxide (LXIII) reacts with acetylene dimethyl dicarboxylate ester to give a simple 1, 3-cycloadduct (LXIV), while 5, 5-dimethyl 1-pyrroline 1-oxide (LXVII) yields unstable 1, 3-cycloadduct (LXVIII) which rearranges exothermically to pyrroline derivative (LXIX) at room temperature but spectral data was not quoted. We repeated Grigg's work and our spectral data confirms his structures. 113

2, 5, 5-Trimethyl 1-pyrroline 1-oxide (LXII) with dimethyl acetylene dicarboxylate yielded a 1, 3-cycloadduct (LXIV) as a colourless oil. The infra-red spectrum showed bands at 1655(C=C), 1715, and 1755 cm\(^{-1}\) assigned to C = O stretching frequencies. Ultraviolet absorption was observed at 277nm(\(\varepsilon = 3717\)) and was unaffected by acid or alkali. In the n.m.r. spectrum (in CDC\(_3\)), signals were observed at 8.79(d, 6 protons), 8.5(s, 3 protons), 7.84(m, 4 protons), 6.3(s, 3 protons) and 6.15(s, 3 protons). They are assigned to the C-5methyl groups (which are in different environments), the C-2 methyl group, the ring methylene protons and ester methyl groups respectively.

The thermal rearrangement of (LXIV) to the pyrrole derivative (LXVI) was described by Grigg who proposed a mechanism involving enamine (LXV) as an intermediate. The formation of this is not explained in Grigg's note.
The thermal rearrangement of (LXIV) to (LXVI) can be better explained by invoking an aziridine intermediate. The C-2 methyl group is activated by conjugation with the ester carbonyl via the aziridine ring (55).
reacted instantaneously with dimethyl acetylene dicarboxylate in ether at room temperature to give adduct (LXVIII) as a light yellow oil which showed bands at 1550, 1660 (C = C), 1720 (C=O), 1750 (C=O) and 3450 (OH or NH), in the infra-red region of the spectrum. The infra-red absorption at 1550 and 3450 cm\(^{-1}\) suggests the presence of H-bonded enolate group due to another product.

Ultra-violet absorption was observed at 272 m\(\mu\) (\(\varepsilon = 5400\)), which shifted to 268 m\(\mu\) at room temperature and to 285 m\(\mu\) and 290 m\(\mu\) in alkali and acid respectively. In the n. m. r. spectrum (in CDCl\(_3\)) signals observed were assigned as follows: \(\tau\) 8.92 (s, 3 protons) and 8.67 (s, 3 protons) to the C-5 methyl groups (which are in different environments), 8.09 (m, 4 protons) to the ring methylene protons, 6.32 (s, 3 protons) and 6.18 (\(\delta\), 3 protons) to the ester methyl groups and \(\tau\) 5.2 (q, 1 proton, \(\beta = 3.5\) c./sec) to the C-2 methine proton respectively.
The reaction of Δ¹-pyrroline 1-oxide (LXVII) and dimethyl acetylene dicarboxylate was also followed by n.m.r. in CDC₁₃. On mixing, the spectrum had a peak at 5.2(q) corresponding to the simple adduct. On warming, the peak at 5.2(q) disappeared and the methylene region changed and peaks appeared at 6.65(t) and 8.00(t). A new peak at 7.72(s) was also observed.

The adduct (LXVIII) slowly rearranged giving a white solid of molecular weight 255 (mass spectrometry) together with other products which were not isolated. The structure (LXIX) suggested by Grigg is confirmed by the following spectroscopic data. The infra-red spectrum of the rearrangement product showed bands at 1515, 1600 (C = C), 1690 (C = O), 1740 (C = O) and 3220 cm⁻¹ (OH or NH). The bands at 1515 and 3220 cm⁻¹ were assigned to the H-bonded enolate group. It is remarkable compound (LXIX) does not give a positive ferric chloride test for the enol group. Ultra-violet absorption was observed at 295 and 245 mμ (λ = 18292, 14418), shifting to 344, 295(sh) and 245(sh)mμ in alkali, but not affected in acid. In the n.m.r. spectrum (in CDC₁₃), an NH or OH proton signal was observed at 1.22 (broad, exchangeable, 1 proton) while C-5 methyl groups at 8.62(s) and the ring methylene protons at 8.19(t, J = 8c/sec) and 6.66(t, J = 8c/sec) appeared in addition to the ester methyl groups (6.3 and 6.15).
Experimental

Melting points are uncorrected. Infra-red spectra were taken on a Unicam spectrophotometer model S.P 200 and a Perkin Elmer grating infra-red spectrophotometer model 257. Ultra-violet spectra were measured (in 95% ethanol unless otherwise stated) on a Unicam spectrophotometer S.P. 800. Nuclear magnetic resonance spectra were taken on a Varian A·60 Mc using trimethylsilane as internal standard (n.m.r. signals expressed in ) and mass spectra on a M.S 9. Gas liquid chromatography was performed on Perkin Elmer F11 gas chromatograph using column DC201 packed with carbowax 1500 on chromosorb W, 60-80 mesh 15:85, with temperature programming from 70°C to 150°C.

Preparations

M-Chloroperbenzoic Acid A solution of sodium hydroxide (10.5g.) in water (100ml.) was cooled to 2-6°C, then 50% hydrogen peroxide (9 g., 0.125 mol.) was added slowly with vigorous stirring, followed by t-butyl alcohol (85g.).m-Chlorobenzoyl chloride (21.8 g., 0.125 mol.) was added dropwise to the above reaction mixture over a period of 5 min. at 2-6°C. The reaction mixture was stirred well for an additional 15 min. and was acidified by pouring into ice cold sulphuric acid slowly, with stirring. Extracted with chloroform and washed with water thoroughly. Drying and evaporation of solvent gave m-chloroperbenzoic acid in
98% yield, m.p. 86° (85% activity).

β-Isopropenyl naphthalene dimer (IV) - Sodium cyanide (90%, 1.01 g, 0.02 mol.) and acetic acid (2.5 ml.) were mixed with cooling and stirring. A solution of concentrated sulphuric acid (5 g.) in acetic acid (25 ml.) was added dropwise to the above mixture with continuous stirring at 20°. β-Naphthyl dimethyl carbinol (4 g., 0.02 mol.) was then added at 40-50°. The mixture was heated at 70° for 1/2 hour and allowed to stand for 2 hours at room temperature. The reaction mixture was poured into water (50 ml.) and neutralised with sodium carbonate solution by dropwise addition with stirring and cooling in ice. When the formation of a white solid commenced, Extracted with ether. Drying and evaporation gave β-isopropenyl naphthalene dimer as a white solid, recrystallised with ethanol, m.p. 120-122°. Vmax. (CHCl₃) 1598, 1620 cm⁻¹ \( \lambda \) max. (CHCl₃) 277 nm \( \zeta = 16464 \), molecular weight by mass spectrometry 336, (required, 336), n.m.r. signals (CDCl₃), 8.6, 7.93, 7.6, 2.43; areas 6:3:2:13. (Found: C, 92.75; H, 7.43, C₂₆H₂₄ requires C, 92.85; H, 7.14%).

The same dimer was also formed when β-naphthyl dimethyl carbinol was treated with concentrated sulphuric acid in glacial acetic acid at 70° for 1 hr. m.p. and mixed m.p. 120-122°.

1-Ethylcyclohexyl isonitrile. A solution consisting of N-(1-ethylcyclohexyl) formamide \(^{65}\) (31 g., 1 mol.) and pyridine (98 g., 6.2 mol.) was charged into a three necked flask containing
pet-ether 40-60° (60ml.) The flask was immersed in ice-bath and phosphorous oxychloride (18.4g., 0.6 mol.) was added to the above solution with stirring over a period of 30-40 min. The mixture was stirred under reflux for 10 min. and then cooled to 0-5°. Ice water (100ml.) was added gradually with stirring. The organic phase was separated and the aqueous phase was extracted with pet-ether 40-60°. The extract was combined with the organic phase and washed with water. Drying and evaporation gave 1-ethyl-cyclohexyl isonitrile as an yellow oil of bad odour.

1-Ethylcyclohexyl hydroxylamine - The hydroxylamine was obtained as a colourless oil by reducing 1-ethyl-1-nitrocyclohexane with zinc dust and ammonium chloride 70 in water and ethanol at 60°, distilling at 72-74°/1.2mm under nitrogen which on cooling solidified m.p. 48-50° (Found: C, 67.1; H, 11.87; N, 9.63. C_{18}H_{17}NO requires C, 67.13; H, 11.88; N, 9.79%).

1. Synthesis of tert-Aliphatic Nitroso Compounds

The parent amines (Ia-c) and II were prepared from their corresponding carbinols by Ritter's method. 65 2-Amino isocamphane (III) was obtained by the same method from camphene. N-(1-Ethylcyclohexyl) formamide was prepared as an intermediate in the synthesis of amine (Ib).
1-Ethyl-1-nitrosocyclohexane (Vb), m. Chloroperbenzoic acid (80%, 24.6 g, 2 mol.) in dichloromethane (150 ml.) was added dropwise with constant stirring to 1-amino-1-ethylcyclohexane (7.686 g., 1 mol.) in dichloromethane (50 ml.), containing calcium carbonate (6 g., 1 mol.) at -10° to -5° (ice/salt mixture). The reaction mixture was stirred for an additional 30 minutes and was filtered. The blue filtrate was washed with sodium carbonate solution, water, dilute sulphuric acid and water again. Drying and evaporation gave a blue oil which was chromatographed on alumina using pet-ether 40-60° and chloroform in the ratio 9:1 as eluent. The blue oil obtained after chromatography, yielded a bluish oily solid after being kept in the refrigerator overnight which was filtered and washed with ice-cold pet-ether 40-60°, gave colourless nitroso dimer (2.625 g.), m. p. 60-62°, $\text{V}_{\text{max}}$ (mull) 1280 cm$^{-1}$, $\text{V}_{\text{max}}$ (CHCl$_3$) 1280, 1545 cm$^{-1}$, $\lambda_{\text{max}}$ (EtOH) 300, 699 m$\mu$ ($\epsilon = 104, 16$); n. m. r. signals (CCl$_4$), 9.17 (t, $J = 7.5$ c/sec), 8.5 (q); areas 3:12. (Found: C, 68.38; H, 10.07; N, 9.69. C$_8$H$_{15}$NO requires C, 68.08; H, 10.63; N, 9.92%).

The blue filtrate on fractional distillation under nitrogen gave nitroso monomer (2.2 g.) at 85-90°/20 mm or 40-42°/2.5 mm which on cooling dimerised, m. p. 60-62°, and 1-ethyl-1-nitrocyclohexane as a colourless oil at 66-68°/2 mm or 118-120°/20 mm. $\text{V}_{\text{max}}$. 1540 cm$^{-1}$ $\lambda_{\text{max}}$ (EtOH) 272 m$\mu$ ($\epsilon = 664$); (Found: C, 61.15; H, 9.53; N, 9.19. C$_8$H$_{15}$NO$_2$ requires C, 61.14; H, 9.55; N, 8.91%).

1-Methyl-1-nitrosocyclohexane (Va). The nitroso dimer was obtained as described above in 60-65% yield, m. p. 48-50° to blue melt.
1-Ethyl-1-nitrosocyclopentane (VI). The colourless nitroso dimer (VI) was obtained in a similar manner from the amine in 62% yield, m.p. 53-55° (Found: C, 66.44; H, 10.30; N, 11.09. C\textsubscript{7}H\textsubscript{13}NO requires C, 66.14; H, 10.23; N, 11.02%).

2,2,4-Trimethyl 4-nitrosopentane (VII). The nitroso dimer was obtained in 64% yield, m.p. 63-64° (Found: C, 66.91; H, 11.88; N, 9.81. C\textsubscript{8}H\textsubscript{17}NO requires C, 67.13; H, 11.88; N, 9.79%).

1-Cyclohexyl-1-nitrosocyclohexane (Vc). m-Chloroperbenzoic acid (2 mol.) was added to 1-cyclohexyl-cyclohexyamine (1 mol.) in a similar fashion at -10 to -5°. The blue oil obtained after work up, was chromatographed on alumina using pet-ether 40-60° and then pet-ether 40-60° and chloroform in the ratio 9:1 as eluent. The following two fractions were collected.

(i) Bluish nitroso monomer (Vc) which after being kept in the refrigerator overnight dimerised. The nitroso dimer was washed with ice cold pet-ether 40-60° and dried (poor yield), m.p. 85-87° (Found: C, 73.79; H, 10.66; N, 7.32. C\textsubscript{12}H\textsubscript{21}NO requires C, 73.84; H, 10.76; N, 7.17%).

(ii) A light bluish oil (pet-ether 40-60 and chloroform 9:1) which on fractional distillation under nitrogen gave -

(a) 1-cyclohexyl-1-nitrosocyclohexane monomer at 90-94°/2mm which on cooling dimerised, m.p and mixed m.p.
85-87° to blue melt (total yield 35-40%).

(b) 1-cyclohexyl-1-nitrocyclohexane at 124-126°/1.5mm, on cooling solidified, and, on recrystallisation with ice cold pet-ether 40-60°, gave colourless crystals m.p. 56-57°. (Found: C, 68.23; H, 9.85; N, 6.61. C_{12}H_{21}NO requires C, 68.24; H, 9.94; N, 6.63%).

2-Nitroso isocamphane (VIII). The nitroso dimer (VIII) was obtained as described above in 25-30% yield, m.p. 122-124° (Found: C, 71.93; H, 10.24; N, 8.26. C_{10}H_{17}NO requires C, 71.85; H, 10.17; N, 8.38%).

Nitrosocyclohexane (X). m-Chloroperbenzoic acid (2 mol.) in dichloromethane was added dropwise with continuous stirring to cyclohexyl-amine (1 mol.) in dichloromethane containing calcium carbonate (1 mol.) at -10°C to -5°C. The reaction mixture was stirred for an additional 30 minutes and filtered. The filtrate was washed with sodium carbonate solution, water, dilute sulphuric acid and water. Drying and evaporation gave cyclohexane dimer (crude) m.p. 112-114° (98% yield) which on recrystallisation with cyclohexane gave colourless crystals m.p. 116-118° (85% yield).

Nitrosomesitylene (XI). The nitroso dimer (XI) was obtained in a similar manner in 85% yield which was recrystallised with ethanol giving colourless leaflets m.p. 122-123° to green melt.

Attempted photosynthesis of nitroso norcamphane.

Dry nitrogen gas was passed slowly into cold trap containing nitrosyl chloride (8g.) at a temperature -50°C to -20°C. The entrained nitrosyl chloride was conducted into a flask containing norcamphane (9.6g.) in benzene (50 ml.) maintained at 20-25°C and at the same time,
irradiated by 150 watt tungsten lamp. The addition of nitrosyl chloride was completed within 6 hours. Irradiation of the reaction mixture was continued for an additional 5 min. Evaporation of benzene under reduced pressure gave a bluish green oil (6.8g.) which was chromatographed on alumina using pet-ether 40-60° as eluent and the following fractions were collected.

1. a bluish oil, presumably a mixture of nitroso and nitro compound which were not identified.
2. bicyclo-(2,2,1)-heptan-2-one \(^{68}\) as a white solid, m.p. 95°, n.m.r. signals (CDCl\(_3\)), 8.5, 7.76, 7.42; areas 8:1:1. The ketone was characterised as its 2:4 dinitrophenylhydrazine derivative, recrystallised with ethanol, m.p. 128-130° (Found C, 53.76; H, 4.47; N, 18.95. Calc. for C\(_{13}\)H\(_{14}\)N\(_4\)O\(_4\): C, 53.79; H, 4.82; N, 19.31%).

2. General Properties of Nitroso Compounds

(i) Action of heat. 1-Ethyl-1-nitroso cyclohexane monomer (0.350g.) was heated under reflux in xylene (10 ml.) under nitrogen in the dark for 1 hr. The blue colour of nitroso monomer (Vb) changed to yellow and then decomposed within 1 hr. of refluxing. On heating under reflux in ethanol or chloroform under nitrogen in the dark, the nitroso monomer (Vb) was not affected (changes were followed by t.l.c. and u.v. spectroscopy).

(ii) Action of daylight and air. 1-Ethyl-1-nitroso-cyclohexane monomer (0.5g.) was heated under reflux in ethanol (10 ml.) in the dark for overnight, in the presence of stream of air and then in the daylight. The changes were followed by t.l.c. and u.v. spectroscopy.
It was observed that nitroso monomer (Vb) reacted with the oxygen of the air, slowly in the dark and more rapidly in the daylight to yield nitro compound (IXb) (comparison of t.l.c. and u.v. with authentic sample).

Preparative experiment of action of daylight and air on C-nitroso monomer (Vb). 1-Ethyl-1-nitrosocyclohexane monomer (0.5g.) in ether (20ml.) was shaken in the presence of air in daylight. The blue colour of the nitroso-monomer (Vb) disappeared after 4 days shaking and yielded a yellow reaction mixture. Drying and evaporation of ether gave a yellow oil which on distillation gave 1-ethyl-1-nitrocyclohexane (IXb) at 66-68°/2mm. Vmax. 1540cm.-¹ (Found: C, 61.27; H, 9.49; N, 8.95. C₈H₁₅NO₂ requires C, 61.14; H, 9.55; N, 8.91%)

(iii) Action of bases. 1-Ethyl-1-nitrosocyclohexane monomer (0.5g.) in ether (5 ml.) was treated with sodium ethoxide in ethanol or sodium methoxide in methanol or potassium hydroxide in water and ethanol or potassium t-butoxide in t-butanol. After being kept for overnight in the dark at room temperature, the blue colour of the reaction mixture had disappeared. The reaction mixture was dissolved in ether and washed with water. The organic layer was separated. Drying and evaporation of ether gave reddish yellow oil, electron spin resonance of which gave a strong signal (triplet) for the presence of a free radical, presumably a radical anion. T.L.C., G.L.C and IR of the oil indicated the presence of 1-ethyl-1-nitrocyclohexane (IXb) (comparison with authentic sample).


1-Ethyl-1-nitroso cyclohexane (Vb). The nitroso monomer (0.5g.) in ether (20 ml.) was saturated with anhydrous hydrogen chloride.
The blue colour of the reaction mixture disappeared after being kept in the dark for 3 days. The colourless reaction mixture was washed with aqueous sodium hydroxide and water. The ethereal layer was separated. Drying and evaporation of ether gave 1-ethyl-1-chloro-cyclohexane (XVI) as a colourless oil, distilling at 90-94\degree / 20-21mm (comparison of infra-red with authentic sample). The aqueous layer was acidified and extracted with ether. Drying and evaporation of ether gave no residue.

1-Ethyl-1-nitroso cyclopentane (VI). The nitroso monomer (0.7g.) in ether (10 ml.) was treated in a similar manner with anhydrous hydrogen chloride and was kept in the dark for 2 days. Drying and evaporation of ether gave 1-ethyl-1-chloro-cyclopentane (XVII) as a colourless oil (volatile), distilling at 55-60\degree /20mm; (Found: C, 63.70; H, 9.91; Cl, 26.53. C_{7}H_{13}Cl requires C, 63.39; H, 9.81; Cl, 26.79%).

2,2,4-Trimethyl 4-nitrosopentane (VII). The nitrosomonomer (0.5g.) in ether (15ml.) was treated in a similar fashion with anhydrous hydrogen chloride and gave 2,2,4-trimethyl 4-chloropentane (XVIII) as a colourless oil, distilling at 75-80\degree /20mm.

4. Photolysis of Nitroso Compounds.

1-Ethyl-1-nitrosocyclohexane (Vb). The nitroso monomer (3.24g.) in dry ether (50ml.) was irradiated under dry oxygen-free nitrogen for 4\frac{1}{2} hours by 150 watt tungsten lamp at 20-22\degree. Evaporation of ether under reduced pressure gave a light yellow oil (2.890g.) Vmax. 1545, 1620, 1700(w) and 3450cm\(^{-1}\). E.S.R. of the oil gave a strong signal (triplet) for the presence of the free radical.
presumably nitroxide. T. L. C. and G. L. C. showed the presence of four and five products respectively. The crude yellow oil was chromatographed on alumina using pet-ether 40-60°, pet-ether 40-60° and chloroform (95:5) and chloroform as eluent. The following four fractions were collected and identified.

The first fraction eluted with pet-ether 40-60°, was obtained as a colourless volatile oil (1.34g.), g. l. c. of which showed the presence of three products. The oil was divided into two portions.

The first portion on distillation at 132-134° gave a mixture of 1-ethylcyclohexene and ethylidene cyclohexane (XXa-b) in the ratio 56:46 (n. m. r. measurement), decolourising bromine water, n. m. r. signals (CCl₄), 9.04 (t), 8.4 (m), 4.9 (d), 4.67 (s), (Found: C, 87.66; H, 12.89. Calc. for C₁₈H₁₄: C, 87.27; H, 12.73%).

The presence of 1-ethylcyclohexane (XIX) was detected by gas liquid chromatography in the first fraction (comparison with authentic sample).

The second portion on evaporation under vacuum gave a colourless thick oil which on trituration with ethanol and after being kept in the refrigerator overnight yielded trisubstituted hydroxylamine (XXI) as a white solid, m. p. 82° (crude). Recrystallisation of (XXI) with ice cold ethanol gave white crystals m. p. 84-85° [α] max. (EtOH) 210m[H], n. m. r. signals (CDCl₃), 9.15 (t, J = 7.5 c/sec), 8.59(m); areas 3 : 12, (Found: C, 79.52; H, 12.69; N, 3.79. C₂₄H₄₅NO requires C, 79.33; H, 12.39; N, 3.85%). The hydroxylamine (XXI) appeared on g. l. c. after the other products, in a broad peak which was rather variable in position.
The second fraction eluted with pet-ether 40-60°, gave 1-ethyl-1-nitro-cyclohexane (IXb) as a colourless oil (0.49g.), distilling at 66-68°/2mm., Vmax. 1540 cm⁻¹ (comparison of infra-red, t.l.c. and g.l.c. with authentic sample.).

The third fraction eluted with pet-ether 40-60° and chloroform (95:5), yielded 1-ethyl cyclohexyl carbinol (XXII) as a colourless oil (0.325g.) distilling at 76-78°/20 mm., Vmax. 3450 cm⁻¹ (comparison of infra-red, t.l.c. and g.l.c. with authentic sample.).

The last fraction eluted with chloroform, was obtained as a light yellow oil (0.66g.) Vmax. 1620, 1700(w), 3450 cm⁻¹. It was the only fraction which gave the strong signal (triplet) for the presence of a free radical by e.s.r., presumably dialkyl nitroxide (XXIII). Infra-red and g.l.c. of the oil showed the presence of 1-ethylcyclohexyl carbinol (XXII), contaminated with other products presumably alkyl nitrate or alkyl nitrite which were not identified.

Analysis of the reaction mixture by g.l.c. gave the following proportions of the four volatile products (i.e. not including the trisubstituted hydroxylamine (XXI): saturated hydrocarbon (1.8%), olefin (56%), carbinol (19.2%) and nitro-alkane (24%).

1-Ethyl-1-nitrosocyclohexane (Vb) in the presence of benzylthiol. The nitroso monomer (0.510g.) in dry ether (30 ml.) containing benzyl thiol (0.470g.) was irradiated under dry oxygen-free nitrogen for 1 hour by 150 watt tungsten lamp at 20-22°. The blue colour of the reaction mixture disappeared completely within 30 minutes of irradiation. Evaporation of ether gave a light yellow oil which became reddish on keeping and yielded a redish oily solid.
G. L. C. of the crude reaction mixture showed the presence of 1-ethyl cyclohexane (68.5%) and 1-ethylcyclohexene (31.4%) (compared with authentic sample). The reddish oily solid was dissolved in ether and washed with dilute hydrochloric acid and water. Drying and evaporation of ether gave benzyl disulphide as a white solid which on recrystallisation with ethanol yielded white crystals of m.p. and mixed m.p. 71-72°C and with an infra-red identical with that of authentic sample. The aqueous layer was made alkaline with aqueous sodium hydroxide and extracted with ether or chloroform. Drying and evaporation gave no residue.

1-Ethyl-1-nitrosocyclohexane (Vb) in the presence of redistilled triethylamine. The nitroso monomer (0.7g.) in dry ether (25ml.) containing redistilled triethylamine (0.58g.) was irradiated for 4 hrs. in a similar manner, when the formation of a white crystalline deposit commenced within 15 min. of irradiation in the light blue reaction mixture. After 4 hrs. irradiation the light yellow reaction mixture was filtered and the residue was washed with dry ether and dried under vacuum. The white crystalline deposit (v. hygroscopic) was tested for nitrite, nitrate and hyponitrite ions. It gave positive tests for nitrite and nitrate ions with ferrous sulphate and concentrated sulphuric acid and negative test for hyponitrite with silver nitrate, and was also analysed by polarography and shown to contain nitrite and nitrate. It was assumed to be a mixture of \((C_2H_5)_3N\cdotHNO_2\) and \((C_2H_5)_3N\cdotHNO_3\).

The filtrate was washed with water, ice cold hydrochloric acid and water again. The ethereal layer was separated. Drying and evaporation of ether gave a light yellow oil. \(\nu_{max} 1540, 1620, 1700(w)\)
E. S. R. of the oil showed the presence of a free radical (triplet), presumably dialkyl nitroxide (XXIII). The yellow oil was chromatographed on alumina and gave the same products as described above (comparison of infra-red, g.l.c. and t.l.c. with authentic samples). G.L.C. of the yellow oil gave the following relative amounts of all the products except trisubstituted hydroxylamine (XXI):- saturated hydrocarbon (5.8%), olefin (64.6%), carbinol (18.5%) and nitroalkane (10.6%).

1-Ethyl-1-nitrosocyclohexane (Vb) in the presence of potassium t-butoxide. The nitroso monomer (1g.) in dry ether (20ml.) containing potassium t-butoxide (5g.) was irradiated for 4 hrs. in a similar fashion as described above. The reaction mixture was washed with water. The ethereal layer was separated. Drying and evaporation of solvent under high vacuum gave a thick colourless oil which on trituration with ethanol and after being kept in the refrigerator for overnight yielded trisubstituted hydroxylamine (XXI) as a white solid. Recrystallisation with ethanol gave white crystals m.p. and mixed m.p. 84-85°C, identical with the compound obtained previously.

1-Ethyl-1-nitrosocyclohexane (Vb) in the presence of nitric oxide in the dark. The nitroso monomer (0.5g.) in dry ether (15ml.) was shaken in a blackened flask under nitric oxide. The reaction mixture became yellowish green within 30 minutes. After 3 hours shaking the flask was disconnected. Evaporation of solvent gave a yellow oil. Vmax. 1540, 1620 and 1670cm⁻¹ T.L.C. showed the presence of two products. The oil decolourised bromine water. The oil was then analysed by g.l.c. and gave the following relative amounts of
all the products, 1-ethylcyclohexane (1%), 1-ethylcyclohexene (29%) and 1-ethyl-1-nitrocyclohexane (70%), (compared with authentic samples). The bands at 1620 and 1670 cm\(^{-1}\) may be ascribed to alkyl nitrites and alkyl nitrites. 27, 29

**1-Cyclohexyl-1-nitrosocyclohexane (Vc)**. The nitroso monomer (0.5g.) in dry ether (30 ml.) was irradiated under dry oxygen-free nitrogen for 4 hrs. Drying and evaporation of ether gave yellow oily solid. \(\text{Vmax. 1540, 1620, 1700 and 3450 cm}^{-1}\) E.S.R. of the oil gave a strong signal (triplet) for the presence of a free radical, presumably nitroxide. The yellow oily solid was chromatographed on alumina using pet-ether 40-60\(^\circ\) and chloroform as eluent in a similar manner as described above and the following fractions were collected and identified.

1. A colourless oil which decolourised bromine water, presumably 1-cyclohexyl-cyclohexene together with other products which were not identified.

2. 1-cyclohexyl-1-nitrocyclohexane, m.p. 56-57\(^\circ\), recrystallised with ice cold pet-ether 40-60\(^\circ\) \(\text{Vmax. 1540 cm}^{-1}\) (comparison of infra-red with authentic sample).

3. 1-cyclohexyl-cyclohexyl carbinol, \(\text{Vmax. 3450 cm}^{-1}\) (comparison of infra-red with authentic sample).

4. a thick colourless oil, \(\text{Vmax. 1620, 1700 (w), 3450 cm}^{-1}\) E.S.R. of the oil gave the strong signal (triplet), presumably nitroxide.

**2,2,4-Trimethyl 4-nitrosopentane (VII)**. The nitroso monomer (0.5g.) in dry ether (15ml.) was irradiated for 4 hrs. as described above.
Evaporation of ether gave a light yellow oil. Vmax. 1540, 1620, 1700 (w), 3450 cm\(^{-1}\). E.S.R. of the oil gave strong signal (triplet). The other products were not isolated or identified.

5. Reaction of Nitroso Compounds with Diazomethane.

1-Ethyl-1-nitroso-cyclohexane (Vb). The nitroso monomer (0.750 g.) in ether (10 ml.) was treated with diazomethane in ether (50 ml.) (prepared from nitrosomethyl urea (10.3 g.)). The reaction mixture was kept for 2 hours in the dark. Drying and evaporation of the ether gave N-(1-ethylcyclohexyl) nitrone (XXIV) as a colourless hygroscopic oil in 98% yield, distilling at 75°/0.3 mm. Vmax. 1550 3400 cm\(^{-1}\). \(\lambda\) max. (EtOH) 241 m\(\lambda\) (\(\epsilon = 6534\)), n.m.r. signals (CDCl\(_3\)), 9.15 (t, \(J = 7.5\) c/sec), 8.37 (q), 3.61 (d, \(J = 7.5\) c/sec), 3.33 (d, \(J = 7.5\) c/sec); areas 3:12:1:1, molecular weight by mass spectrometry (155) and cryoscopy 159, \(\text{C}_9\text{H}_{17}\text{NO}\) requires 155) (Found: C, 69.47; H, 10.85; N, 8.87. \(\text{C}_9\text{H}_{17}\text{NO}\) requires C, 69.67; H, 10.96; N, 9.03%). The nitrone gave 2:4 dinitrophenylhydrazine derivative of formaldehyde, m.p. and mixed m.p. 167°.

Periodate oxidation of N-(1-ethylcyclohexyl) nitrone (XXIV).

The crude nitrone (0.35 g.) in water (5 ml.) was treated with sodium periodate (2.14 g.) in water (25 ml.) by dropwise addition and with continuous shaking. A blue colour appeared immediately on addition of periodate. The blue reaction mixture was extracted with ether. Drying and evaporation of ether gave a blue oil which on cooling in ice/salt mixture gave 1-ethyl-1-nitroso-cyclohexane (Vb), m.p. and mixed m.p. 60-62°.
Photolysis of N-(1-ethylcyclohexyl)nitrone (XXIV). The crude nitrone (1g.) in cyclohexane (25ml.) was irradiated (U.V. lamp) in a quartz flask under dry oxygen-free nitrogen at room temperature for 6 hours. The reaction was followed by u.v. spectroscopy. Evaporation of solvent gave a thick reddish oil which on standing at room temperature for two days gave an oily solid. The oily solid was filtered and was washed with pet-ether 40-60°C, giving a white solid m.p. 234-236°C. Vmax. (mull) 1540, 1620, 3300cm⁻¹, λmax (EtOH) 213, 226, 280mμ. The structure of white solid m.p. 234-236°C was not determined.

The filtrate, on evaporation of solvent gave reddish oil which was chromatographed on alumina using benzene and chloroform as eluent. The following two fractions were collected.

1. The first fraction eluted with benzene was obtained as an oil (0.220g.). T.L.C. showed the presence of three products which were not identified.

2. The second fraction obtained as a colourless oil (0.613g.) by elution with chloroform, was identified as N-(1-ethyl cyclohexyl) formamide (XXVI), distilling at 130-132°C/0.3mm. (comparison of infra-red and n.m.r. with authentic sample, prepared as an intermediate in the synthesis of the amine (see above)).

The photolysis of the nitrone was also carried out in benzene and gave the same products as described above.

1-Cyclohexyl-1-nitrosocyclohexane (Vc). The nitrosomonomer (1.0g.) in ether (20ml.) was treated with diazomethane in ether (50 ml.). The
reaction mixture was kept for 2 days in the dark. The yellow reaction mixture on evaporation of solvent gave a light blue oil which on drying under vacuum by slight warming yielded N-(1-cyclohexyl cyclohexyl) nitrone (XXVII) as a colourless hygroscopic oil in 95% yield, distilling at 100-105°/0.198mm. Vmax. 1545, 3400cm^{-1}, \lambda_{max} (EtCH) 241m\mu (\epsilon = 6573), n.m.r. signals (CCl_4), 8.5(m), 3.8(d, J=7.5c/sec), 3.54(d, J=7.5c/sec); areas 21;1;1; molecular weight by mass spectrometry (209) and cryoscopy (227.6), (C_{13}H_{23}NO requires 209), (Found: C, 73.98; H, 11.08; N, 6.76. C_{13}H_{23}NO requires C, 74.34; H, 11.64; N, 6.69%).

1-Ethyl-1-nitrosocyclopentane (VI). The nitroso monomer (1.1eg.) in ether (10ml.) was treated with diazomethane in ether (50 ml.). The reaction mixture was kept for overnight in the dark. Drying and evaporation gave N-(1-ethyl cyclopentyl) nitrone (XXVIII) as a colourless hygroscopic oil in 96% yield, distilling at 85-90°/0.5mm., Vmax. 1545, 3400cm^{-1}, \lambda_{max} (EtCH) 241m\mu (\epsilon = 6589), n.m.r. signals (CCl_4) 9.04(t, J = 7.5c/sec), 8.07(m), 3.65(q, J = 7c/sec); areas 3:10:2; molecular weight by mass spectrometry (141) and cryoscopy (170.3), (C_8H_{15}NO requires 141), (Found: C, 67.81; H, 10.95; N, 10.03. C_8H_{15}NO requires C, 68.08; H, 10.63; N, 9.92%).

2,2,4-Trimethyl-4-nitrosopentane (VII). The nitroso monomer (1.25g.) in ether (10ml.) was treated with diazomethane in ether (50ml.) and was kept for 2 hours in the dark. Drying and evaporation of yellow reaction mixture gave N-tert-Octyl nitrone (XXIX) as a colourless hygroscopic oil in 96% yield, distilling at 60-65°/0.1x10^{-3} mm. Vmax 1545, 3400cm^{-1}, \lambda_{max} (EtO\epsilon) 241m\mu (\epsilon = 6594),
n.m.r. signals (CCl₄), 9.09 (s), 8.5(s), 8.17(s), 3.76 (d, J = 7.5c/sec), 3.62 (d, J = 7.5 c/sec), areas 9:6:2:1:1; molecular weight by mass spectrometry (157) and cryoscopy (159.3), (C₉H₁₉NO requires 157), \[(\text{Found: C, 68.77; H, 12.53; N, 8.95. C₉H₁₉NO requires C, 68.78; H, 12.1; N, 8.9%}).

**Nitroso mesitylene (XI).** The nitroso monomer (1g.) in chloroform (10ml.) (obtained by warming dimer in chloroform) was treated with diazomethane in ether (50ml.) and was kept for overnight in the dark. Drying and evaporation of solvent gave N-mesityl nitrone (XXX) as a light yellow solid which on recrystallisation with pet-ether 40-60°C yielded colourless leaflets m.p. 102-104°C. The nitrone was quite stable for a day but slowly became yellow on keeping. Vmax(mull) 1550cm⁻¹ \(\lambda_{max}\) \(\text{(EtOH)} 241m\ell\). \(\epsilon = 743\ 2\), n.m.r. signals (CDCl₃), 7.63(s), 3.6(d, J=8c/sec), 3.09(s), 2.99(d, J= 8c/sec); areas 9:1:2:1; molecular weight by mass spectrometry (163) and cryoscopy (164.8), (C₁₀H₁₃NO requires 163), \[(\text{Found: C, 73.55; H, 8.27; N, 8.60. C₁₀H₁₃NO requires C, 73.61; H, 7.97; N, 8.58%}).

The nitrone also gave 2:4 dinitrophenyl-hydrazine derivative of formaldehyde m.p. and mixed m.p. 167°C.

**1-Nitroso-1-Chlorocyclohexane (XXXI).** The nitroso monomer (1g.) in ethanol (15ml.) was treated with diazomethane in ether (50ml.) by dropwise addition and with shaking at 4°C. The reaction was very vigorous and a colourless reaction mixture was obtained. Drying and evaporation of solvent gave a colourless oil which was chromatographed on alumina using benzene and then chloroform as eluent.
The following two fractions were collected.

1. The first fraction eluted with benzene gave diethyl ketal (XXXII) as a colourless oil. n.m.r. signals (CDCl₃), 8.9 (t), 8.5 (s), 7.8 (d, broad), 6.6 (q). The 2:4 dinitrophenylhydrazine derivative of cyclohexanone was obtained m.p. and mixed m.p. 162°.

2. The second fraction obtained as a light yellow oil by elution with chloroform was not identified.

6. Cycloaddition of Unsubstituted Nitrones - Normal Reactions -

(i) Styrene.

N-(1-Ethyl cyclohexyl) nitrone (XXIV). The crude nitrone (0.528 g., 1 mol.) in dry benzene (5 ml.) was treated with redistilled styrene (0.345 g., 1 mol.) in benzene (5 ml.) and was kept for 2 hours at room temperature. Evaporation of solvent gave a colourless oil which was chromatographed on alumina using benzene as eluent, yielded 2-(1-ethyl cyclohexyl)-5-phenyl isoxazolidine (XXXII) as a colourless oil in 95% yield, distilling at 105°/8.47 x 10⁻⁵ mm; Vmax. 1495, 1600 cm⁻¹, n.m.r. signals (CDCl₃), 9.1 (t, J = 7.5 c/sec), 8.4 (m), 7.75 (m), 7.10 (t, J = 7.5 c/sec), 5.22 (t, J = 7.5 c/sec), 2.79 (s); areas 3:12:2:2:1:5; molecular weight by mass spectrometry (259), (C₁₇H₂₅NO requires 259); (Found: C, 78.84; H, 9.48; N, 5.5. C₁₇H₂₅NO requires C, 78.76; H, 9.65; N, 5.4%).

N-(1-Cyclohexyl-cyclohexyl) nitrone (XXVII). The crude nitrone yielded 2-(1-cyclohexyl-cyclohexyl)-5-phenyl isoxazolidine (XXXIV)
as a colourless oil in 96% yield as described above, distilling at 125-130\(^\circ\)C/6.78x10\(^{-4}\)mm. Vmax. 1495, 1600cm\(^{-1}\); n.m.r. signals (CCl\(_4\)), 8.42 (m), 7.75 (m), 7.07 (t, J = 7.5c/sec), 5.22(t, J = 7.5 c/sec), 2.77 (m); areas 21:2:2:1:5; molecular weight by mass spectrometry (313), (C\(_{21}\)H\(_{31}\)NO requires 313), (Found: C, 80.37; H, 9.95; N, 4.68. C\(_{21}\)H\(_{31}\)NO requires C, 80.51; H, 9.90; N, 4.47%).

N-(1-Ethyl-cyclopentyl) nitrone (XXVIII). This yielded 2-(1-ethyl cyclopentyl)-5-phenyl isoxazolidine (XXXV) as a colourless oil in 85% yield as above, distilling at 125-130\(^\circ\)C/0.5mm. Vmax. 1495, 1600cm\(^{-1}\); n.m.r. signals (CCl\(_4\)), 8.95 (t, J = 7.5 c/sec), 8.34(m), 7.75 (m), 7.09 (d, J = 7c/sec), 5.07 (t, J = 7 c/sec), 2.69 (m); areas 3:10:2:2:1:5., (Found: C, 78.54; H, 9.53; N, 5.85. C\(_{16}\)H\(_{23}\)NO requires C, 78.36; H, 9.38; N, 5.71%).

N-tert-Octyl nitrone (XXIX). This gave 2-tert-octyl-5-phenyl isoxazolidine (XXXVI) as a colourless oil in 94% yield as above, distilling at 80-85\(^\circ\)C/4.45 x 10\(^{-3}\)mm. Vmax. 1495, 1600cm\(^{-1}\); n.m.r. signals (CCl\(_4\)), 8.98 (s), 8.82 (s), 8.5 (d, J = 7.5c/sec), 7.85, 7.14 (d, J = 6.5 c/sec), 5.21 (t, J = 7.5 c/sec), 2.78 (s); areas 9:6:2:2:2:1:5., (Found: C, 78.43; H, 10.48; N, 5.58. C\(_{17}\)H\(_{27}\)NO requires C, 78.16; H, 10.34; N, 5.36%).

N-Mesityl nitrone (XXX). The nitrone (0.33g.) in benzene (5ml.) was treated with redistilled styrene (0.2g.) in benzene (5ml.) and kept for overnight. Evaporation of solvent gave a yellow solid which was chromatographed on alumina using benzene as eluent, to give a light yellow solid in a poor yield. Recrystallisation with pet - ether
40 - 60° gave yellow crystals m.p. 180-181°, which was not examined further.

(ii) Phenylisocyanate and α-Naphthylisocyanate.

N-(1-Ethylcyclohexyl) nitrone (XXIV). The crude nitrone (0.775 g., 1 mol.) in dry benzene (5 ml.) was treated with phenylisocyanate (0.595 g., 1 mol.) in dry benzene (5 ml.) and was kept for overnight. Evaporation of solvent gave 1,2,4-oxadiazolidine adduct (XXXVII) as a white solid which on recrystallisation with pet-ether 40-60° yielded white crystals m.p. 69-70° in 90% yield. Vmax (mull) 1595, 1730 cm⁻¹, n.m.r. signals (CCl₄), 9.04 (t), 8.42 (m), 5.04 (s), 2.59 (m); areas 3:12:2:5., molecular weight by mass spectrometry (274), C₁₆H₂₂N₂O₂ (requires 274), (Found: C, 70.09; H, 8.11; N, 10.25.

N-(1-Cyclohexyl-cyclohexyl) nitrone (XXVII). The crude nitrone yielded a 1,2,4-oxidiazolidine adduct (XXVIII) as a white solid in 98% yield as described above which on recrystallisation with pet-ether 40-60°, gave colourless crystals m.p. 153-154°. Vmax. (mull) 1720 cm⁻¹, n.m.r. signals (CCl₄), 8.5 (m), 5.09 (s), 2.62 (m); areas 2:1:2:5., (Found: C, 73.47; H, 8.70; N, 8.65. C₂₀H₂₈N₂O₂ (requires C, 73.17; H, 8.53; N, 8.53%).

N-(1-Ethylcyclopentyl) nitrone (XXVIII). This yielded 1,2,4-oxadiazolidine adduct (XXXIX) as above, which on recrystallisation with pet-ether 40-60°, gave white crystals m.p. 73-75° in 96% yield. Vmax. (mull) 1720 cm⁻¹, n.m.r. signals (CCl₄), 9.00 (t), 8.3 (m), 5.14 (s), 2.59 (m); areas 3:10:2:5., (Found: C, 69.3%; H, 7.35; N, 11.08. C₁₅H₂₀N₂O₂ (requires C, 69.23; H, 7.69; N, 10.76%).
N-tert-Octyl nitrone (XXIX) •

This gave 1,2,4-oxadiazolidine adduct (XL) as a white solid in 97% yield. Recrystallisation with pet-ether 40-60° gave white crystals m.p. 99-101°. Vmax. (mull) 1730cm⁻¹, n.m.r. signals (CCl₄), 8.92 (s), 8.77 (s), 8.4 (s), 5.12 (s), 2.62 (m); areas 9:6:2:2:5. (Found: C, 69.92; H, 8.94; N, 9.90. C₁₆H₂₄N₂O₂ requires C, 69.56; H, 8.69; N, 10.14%).

Hydrogenation of 1,2,4-oxadiazolidine adduct (XXXVII). The adduct (0.500g.) in ethyl acetate (50 ml.) containing 10% d/C (0.100g.) was hydrogenated for 2 hours (total uptake of hydrogen was 2 mol. (65ml.). The reaction mixture was filtered and the filtrate on evaporation gave a volatile colourless oil. The oil was dissolved in ether and washed with dilute hydrochloric acid. The ethereal layer was separated. Drying and evaporation of solvent gave no residue. The aqueous layer was made alkaline and extracted with ether. Drying and evaporation of ether gave a colourless volatile oil. The oil was shown to contain 1-amino-1-ethylcyclohexane, ariline, methylaniline and N-methyl-1-ethylcyclohexylamine by comparison with authentic samples using t.l.c. and g.l.c., and a further amine, presumed to be 1-methyl amino-1-ethyl cyclohexane.

N-(1-Ethylcyclohexyl) nitrone (XXIV) •

The crude nitrone (0.92g.) in dry benzene (5ml.) was treated with α-naphthyl isocyanate (1g.) in dry benzene (5ml.) and was kept for overnight at room temperature. Evaporation of solvent gave 1-naphthyl 1,2,4-oxadiazolidine adduct (XLII) in 98% yield. Recrystallisation with pet-ether 40-60°, gave colourless crystals m.p. 77-79°. Vmax (mull) 1730cm⁻¹, n.m.r. signals (CCl₄), 9.05 (t), 8.42 (s), 5.15 (s), 2.75 (m); areas 3:12:2:7. (Found: C, 74.30; H, 7.34; N, 8.65. C₂₀H₂₄N₂O₂ requires C, 74.07;
(iii) **Maleic anhydride**

**N-(1-Ethylcyclohexyl) nitrone (XXIV).** The crude nitrone (0.400g., 1 mol.) in AR benzene (5ml.) was treated with maleic anhydride (0.250g., 1 mol.) in warm AR benzene (5 ml.) and was kept for 3 hrs. at room temperature. The formation of a white solid commenced. This was filtered and washed with analar benzene. Drying under vacuum yielded 2-(1-ethyl cyclohexyl) isoxazolidine 4, 5-dicarboxylic acid (XLIII) as a white crystalline solid, m. p. 125-126° (decomp.), Vmax. (mull) 1600, 1700, 2480 cm⁻¹, λ max (EtOH) 218m/ (ε = 700), not affected by acid or alkali, n. m. r. signals (DMSO), 9.20 (t, J = 7.5c/sec), 8.55 (broad), 6.89 (t), 6.80 (t), Hα 6.38 (broad q), Hβ 5.53 (d, J = 8 c/sec): areas 3:12:1: 1:1:1: spin decoupling 100 m. c. (pyridine), Hα irradiated, Hβ collapsed to two superimposed doublet, Hβ irradiated, Hα collapsed to singlet, molecular weight by mass spectrometry (253) with loss of water molecule, (Found: C, 57.63; H, 7.78; N, 5.13; O29.24. C₁₃H₂₁NO₅ requires C, 57.60; H, 7.74; N, 5.16; O, 29.52%). The filtrate on evaporation gave a thick oil which was not identified.

**Action of diazomethane with adduct (XLIII).** The adduct (XLIII), (0.5g.) in acetonitrile (10 ml.) was treated with diazomethane in ether (25 ml.) (prepared from nitrosomethyl urea (5.2g.)) and was kept for two days at room temperature. Evaporation of solvent gave 2-(1-ethyl cyclohexyl) isoxazolidine 4, 5-dicarboxylic acid dimethyl ester (XLIV) as a yellow oil (crude). Vmax. 1730cm⁻¹,
n. m. r. signals (CCl₄) 9.14 (t), 8.47 (q), 7.25 (d, J = 5 c/sec), 6.92 (d, J = 3.4 c/sec), 6.79 (q), 6.32 (d), 5.45 (d, J = 8.4 c/sec); areas 3:12:1:1:1:6:1., molecular weight by mass spectrometry (299), (required 299).

(iv) Dicyclopentadiene.

N-(1-Ethyl cyclohexyl) nitrone (XXIV). The crude nitrone (0.517g.) in benzene (5ml.) was treated with redistilled dicyclopentadiene (0.440g.) in benzene (5ml.) and was kept for overnight at room temperature. Evaporation of solvent gave a thick light yellow oil which was chromatographed on alumina using benzene as eluent, yielded adduct (XLV) as a colourless solid which on recrystallisation with acetone gave white crystals (48% yield) m.p. 62-64°. Vmax. (mull) 1600 (w), n. m. r. signals (CCl₄), 9.19 (t), 8.59 (q), 8.12, 7.75 (broad), 7.09 (m), 6.24, 4.42 (s); areas 3:12:2:6:2:2:2., (Found: C, 80.00; H, 10.24; N, 5.05. C₁₉H₂₉NO requires C, 79.64; H, 10.10; N, 4.87%).

(v) Carbondisulphide.

N-(1-Ethyl cyclohexyl) nitrone (XXIV). The crude nitrone (0.5g.) in carbdonisulphide (15ml.) was kept for overnight at room temperature. The reaction mixture turned yellow. Evaporation of solvent under reduced pressure gave N-(1-ethyl cyclohexyl) thioformamide (XLVII) as yellow solid (crude). Recrystallisation with pet-ether 40-60° yielded colourless needles in 90% yield m.p. 60-62°. Vmax. (mull) 1540, 3200cm⁻¹, n. m. r. signals
(CCl₄), 9.17(t), 8.49(q), 0.92(s, one proton disappeared on deuteration); areas 3:12:2, (Found: C, 63.05; H, 9.92; N, 8.11; S, 18.38. C₉H₁₇NS requires C, 63.15; H, 9.94; N, 8.18; S, 18.71%).

Degradation of N-(1-ethylcyclohexyl)thioformamide (XLVII). The thioformamide (0.5 g.) in methanol (10 ml.) and concentrated hydrochloric acid (6 ml.) was heated under reflux for 24 hours. Extracted with chloroform and washed with water. Drying and evaporation of chloroform gave a white solid m.p. 250° (decomp.) and was not identified.

The aqueous layer was made alkaline with sodium hydroxide solution and extracted with chloroform. Drying and evaporation of solvent gave 1-ethyl cyclohexylamine- (comparison of infra-red with authentic sample).

(vi) Cyclohexene.

N-Mesityl nitrone (XXX). The nitrone (0.5 g.) was treated with redistilled cyclohexene (10 ml.) The reaction mixture turned yellow after being left for overnight. Evaporation of solvent yielded the dinitrone (XLVIII) as a yellow solid in 95% yield. Recrystallisation with pet-ether 40-60° gave yellow crystals m.p. 136-138°. Vmax (mull) 1505, 1608 cm⁻¹, λmax. (EtOH) 349 nm/((ε=10200)., molecular weight by mass spectrometry (324), (required 324), n.m.r. signals (CDCl₃), 7.62 (s) 3.6 (d, J = 8c/sec), 3.05 (m); areas 18;1:5. (Found: C, 73.85; H, 7.80; N, 9.48; C₂₀H₂₄N₂O₂ requires C, 74.05; H, 7.46; N, 9.86%). The above experiment was repeated in cyclohexene (distilled over sodium), gave starting material.
7.  

**Addition of Dimethyl acetylene dicarboxylate**

(a) **Aliphatic nitrene.**

N-(1-Ethyl cyclohexyl) nitrene (XXIV). The crude nitrene (0.596g.) in benzene or carbon tetrachloride (5ml.) was treated with dimethyl acetylene dicarboxylate (0.480g.) in benzene or carbon tetrachloride (5ml.). The solution soon turned light yellow. Evaporation of solvent after 15 minutes under reduced pressure at room temperature yielded 2-(1-ethylcyclohexyl) - \( \Delta^4 \)-isoxazoline- 4, 5-dicarboxylic acid dimethyl ester (XLIX) as a light yellow oil (unstable). Vmax. 1660, 1715, 1760cm\(^{-1}\), \( \lambda_{max.} \) (EtOH) 296m\( \mu \) (\( \xi \approx 2100 \)), not affected by acid or alkali; molecular weight by mass spectrometry (297), (required 297), n.m.r. signals (CCl\(_4\)), 9.09 (t), 8.48 (q), 6.30(s), 6.15 (s), 5.80 (s); areas 3:12:3:3:2. The oil was quite stable for a day at room temperature but slowly decomposed on keeping or warming and thus was not obtained pure (changes were followed by u.v. and n.m.r. spectroscopy).

The crude nitrene (0.590g.) in dry benzene (5ml.) was treated with dimethylacetylene dicarboxylate (0.480g.) in dry benzene (5ml.) and was kept for 2 hours at room temperature. Evaporation of solvent under reduced pressure with gentle warming gave a viscous yellow oil for which structure (LI) was proposed. Vmax. 1515, 1540, 1670, 1750, 3450cm\(^{-1}\), \( \lambda_{max.} \) (EtOH) 268, 305m\( \mu \) (which shifted to 296m\( \mu \) in alkali, n.m.r. signals (CCl\(_4\)), 9.09 (t), 8.5(m), 6.32(s), 6.25 (s), 6.17 (s), 5.8 (s), 4.62(s).
The thick yellow oil on further gentle heating at 40-50° and keeping under vacuum yielded yellowish oily solid which was filtered and the residue was washed with ice-cold ether, giving \( \alpha \)-hydroxy-\( \beta \)-(1-ethylcyclohexyl amino) maleic acid dimethyl ester (LII) as a white solid in poor yield. Recrystallisation with ether gave white crystals m. p. 128-130° (yellow melt). Vmax (mull) 1515, 1540, 1646, 1742, 3450 cm\(^{-1}\), \( \lambda_{\text{max}} \) (EtOH) 268 m\( \mu \) with a shoulder at 305 m\( \mu \) (\( \zeta \approx 7015 \)) which was shifted to 296 m\( \mu \) in alkali and to 242 m\( \mu \) on reacidification, and on acidification of (LII) itself; n. m. r. signals (CDC\(_3\)) 100 MHz, 9.14 (t), 8.5 (s), 6.47 (s), 6.37 (s) 3.4 (s, broad, exchangeable); areas 3:12:3:3:2, molecular weight by mass spectrometry (285), (required 285), does not give ferric chloride test for the enol group, (Found: C, 58.79; H, 7.99; N, 4.78. C\(_{14}\)H\(_{23}\)NO\(_5\) requires C, 58.93; H, 8.07; N, 4.91%). The filtrate on evaporation and keeping under vacuum yielded more of (LII) m. p. and mixed m. p. 128-130° and a red oil which was not identified.

The crude nitrene (0.653 g.) in benzene (5 ml.) was treated with dimethyl acetylene dicarboxylate (0.510 g.) in benzene (5 ml.). The reaction mixture was heated under reflux for overnight. Evaporation of solvent under vacuum with heating at 60-70° gave a thick red oil which on keeping at room temperature for two to three days yielded reddish oily solid. It was filtered and washed with benzene, giving white crystals m. p. 168-170°, insoluble in ether, benzene and carbon tetrachloride. Vmax (mull) 1550, 1625, 1750 cm\(^{-1}\), \( \lambda_{\text{max}} \) (EtOH) 217, 262 (sh) m\( \mu \), unaffected by acid or alkali and of undetermined structure. The filtrate on evaporation gave a
thick red oil which was not identified.

**N-(1-Ethyl cyclohexyl) nitrone (XXIV)**. The crude nitrone (0.650g.) in carbontetrachloride (5ml.) was treated with dimethyl acetylene dicarboxylate (0.570g.) in carbontetrachloride (5 ml.) and was heated under reflux for 3 hours. The changes were followed by u.v. and n.m.r. spectroscopy at various intervals. Evaporation of solvent gave a thick reddish yellow oil. Vmax. 1550, 1580, 1635, 1750 cm\(^{-1}\) max. (EtCH) 241, 268, 305 m\(\mu\).

The reddish yellow oil was dissolved in carbontetrachloride and was heated under reflux with a few drops of water and a few drops of concentrated hydrochloric acid for one hour. The aqueous layer was separated and treated with dimedone in eth\(\text{al}\), yielding the dimedone derivative of formaldehyde m. p. and mixed m. p. 186-188\(\circ\) (comparison of infra-red). Drying and evaporation of organic layer gave a thick red oil which on standing at room temperature for two days gave a white solid m. p. 154-156\(\circ\) (crude). Vmax. (mull) 1510, 1550, 1620, 1660, 1745 cm\(^{-1}\) The filtrate on evaporation gave a red oil which was not identified.

(b) **Aromatic nitrone**.

**N-Mesityl nitrone (XXX)**. The nitrone (1.63g.) in dry benzene (10 ml.) was treated with dimethyl acetylene dicarboxylate (1.42g.) in dry benzene (5 ml.) dropwise and with shaking. Evaporation of benzene after 30 minutes under reduced pressure gave aziridine
adduct (LV) as a yellow solid. Recrystallisation with pet-ether 40-60°C gave yellow crystals in 98% yield, m.p. 92-94°C. Vmax (mull) 1715, 1740 cm⁻¹, \( \lambda \max \) (EtOH) 216, 236, 290 \( \mu \lambda \) (\( \xi = 12000, 5600, 1525 \)), n.m.r. signals (CDCl₃), 7.76 (s), 6.92 (d, \( J = 2.3 \text{ c/sec} \)), 6.78 (d, \( J = 2.3 \text{ c/sec} \)), 6.32 (s), 6.08 (s), 3.23 (s); areas 9:1:1:3:3:2:1. (Found: C, 63.04; H, 5.91; N, 4.68. \( C_{16}H_{19}NO \) requires C, 62.95; H, 6.22; N, 4.59%).

Hydrogenation of adduct (LV). The adduct (1.024g.) in benzene (30 ml.) containing 5% Pd/C (0.150g.) was hydrogenated for 2 hours (total uptake of hydrogen 165 ml.). The filtrate from the reaction mixture was acidified with dilute hydrochloric acid. The aqueous layer was separated, made alkaline with aqueous sodium hydroxide and extracted with ether. Drying and evaporation yielded mesidine (comparison of infra-red with authentic sample).

The organic layer on drying and evaporation gave a light yellow oily solid which was filtered and washed with ice cold ether, giving the rearrangement product (LVII) as a white solid. Recrystallisation with ether gave white needles in moderate yield m.p. 157-158°C. Vmax (mull) 1570, 1630, 1730, 3500 cm⁻¹, \( \lambda \max \) (EtOH) 312, 240 \( \mu \lambda \) (\( \xi = 2160 \)), n.m.r. signals (CDCl₃), 7.75 (s), 6.29 (s), 6.09 (s), 3.07 (s), 2.75 (s), 1.92 (exchangeable); areas 9:3:3:2:1:1:1., molecular weight by mass spectrometry (305); (required 305), (Found: C, 63.10.; H, 6.14; N, 4.77. \( C_{16}H_{19}NO_2 \) requires C, 62.95; H, 6.22; N, 4.59%). The filtrate on evaporation gave dimethyl 1-oxo-1, 2-propane dicarboxylate (LVI) as a colourless oil. Vmax. 1660, 1725, 3500 cm⁻¹, n.m.r. signals (CCl₄), 8.62 (centre of 2 singlets),
8.02(s), 6.28-6.12 (several sharp peaks), 5.87(q), - 2.4 (s, exchangeable). It gave strong ferric chloride test but did not form 2:4 dinitrophenyl hydrazine derivative.

On prolonged hydrogenation (24 hrs.), the yield of (LVII) was very poor and 2,5mols. of hydrogen being absorbed.

Sodium borohydride reduction of adduct (LV). The adduct (0.61g.) in ethanol (5 ml.) was treated with sodium borohydride (0.030g.) in ethanol (7 ml.) and kept for 24 hrs at room temperature. The reaction mixture turned light red. Evaporation of ethanol under reduced pressure gave yellowish white solid. This was treated with water (5 ml.) and extracted with ether and carbon tetrachloride. Drying and evaporation of solvent gave lactone (LIX) as a white solid which on recrystallisation with ether yielded white leaflets (0.360g.), m.p. 178-180°. Vmax (mull) 1620 (broad weak), 1750, 3400cm⁻¹, Vmax (CHCl₃), 1770, 3400cm⁻¹, λ max. (EtOH) 216, 236, 266, 291m

(ε = 13641, 8700), n.m.r. signals (CDCl₃), 7.75 (d), 7.17 (q, J = 2c/sec), 6.87 (s, exchangeable), 5.42 (m), 3.25 (s); areas 9:2:1:3:2., n.m.r. signals (CDCl₃) 100 Mc₂. 7.82 (2 chose singlet), 7.21(q, JAB = 2c/sec), 6.90 (s, exchangeable), 5.50 (complex multiplets), 3.30 (s), areas 9:2:1:3:2, (Found: C, 67.94; H, 6.97; N, 5.78. C₁₄H₁₇NO₃ requires C, 68.00; H, 6.93; N, 5.66%).
Reaction of lactone (LIX) with acetic anhydride in pyridine

The lactone (0.150g.) in acetic anhydride (5ml.) and pyridine (1 ml.) was heated under reflux for $\frac{1}{2}$ hrs. The reaction mixture was dissolved in chloroform and washed with dilute hydrochloric acid and water. Drying and evaporation under reduced pressure gave the monoacetate (LX) as a white solid. Recrystallisation with ether gave white crystals m.p. 182 - 184°C. $\text{V}_{\max.}$ (CHC1₃) 1740, 1770cm⁻¹; n.m.r. 100 Mₗ. (CDCl₃), 7.90 (s) 7.83, 7.78 (2 close singlet), 7.30, 7.00 (2d, $J = 2\cdot5$ c/sec), 5.58, 5.30 (m), 4.45 (q), 3.30 (s); areas 3:9:2:2:1:2.

Rearrangement of aziridine adduct (LV).

The adduct (0.500g.) in toluene dried over sodium (10 ml.) was heated under reflux for 3 hours. Evaporation of solvent under reduced pressure yielded isomer (LXI) as a thick reddish oil (unstable). $\text{V}_{\max.}$ 1630, 1710, 1740, 3400cm⁻¹, $\lambda_{\text{max.}}$ (EtOH) 308m$\mu$ (e8200), shifted to 261 and 312m$\mu$ in alkali; n.m.r. signals (CDCl₃), 7.79 (d), 6.5 (s), 6.4 (s), 4.59 (s), 3.3 (s); areas 9:3:3:2:2.

The isomer (LXI) was dissolved in toluene (5 ml.) and was heated under reflux with a few drops of water and a few drops of concentrated hydrochloric acid for 1 hour. The aqueous layer was separated and treated with dimedone in ethanol, gave dimedone derivative of formaldehyde m.p. and mixed m.p. 186-188°C (comparison of infra-red). Drying and evaporation of organic layer gave a reddish oily solid. This was filtered and washed with ice cold carbontetrach-
loride, giving (LXII) as a white solid in good yield. Recrystallisation with carbontetrachloride gave white crystals m.p. 118-120°C (yellow melt.) Vmax. (mull) 1635, 1670, 1750, 3450 cm⁻¹; λ max (EtOH) 301 mΜ (ε = 9800), shifted to 277 mΜ in alkali but reversed on reacidification, molecular weight by mass spectrometry (293); (required 293), n.m.r. signals (CDCl₃), 7.74 (s), 6.5 (s), 6.22 (s) 4.59 (broad singlet, exchangeable); 3.09 (s); areas 9:3:3:2:2:., n.m.r. signals (CDCl₃) at 100 Mc, 7.80 (2 close singlet), 6.56, 6.29 6.50, 6.19 (4s, 6 proton), 4.50-5.0 (broad singlet, exchangeable) 3.23 (broad singlet); areas 9:6:2:2.

It did not give the ferric chloride reaction for enols. The filtrate on evaporation gave a red oil which was not identified.

(c) Δ¹-Pyrroline 1-oxides

2,5,5-Trimethyl- Δ¹-pyrroline 1-oxide (LXIII)

The nitrone (0.635 g.) in ether (5 ml.) was treated with dimethyl acetylene dicarboxylate (0.710 g.) in ether (5 ml.) Evaporation of solvent after 5 min. gave adduct (LXIV) as a colourless oil. Vmax. 1655, 1715, 1755 cm⁻¹; λ max. (EtOH) 277 mΜ (ε = 3717), not affected by acid or alkali; n.m.r. signals (CDCl₃), 8.79 (d), 8.5 (s), 7.84 (m), 6.3 (s), 6.15 (s); areas 6:3:4:3:3.

5,5-Dimethyl- Δ¹-pyrroline 1-oxide (LXVII). The nitrone (0.565 g.) in ether (5 ml.) was treated with dimethyl acetylene dicarboxylate (0.710 g.) in ether (5 ml.) dropwise with cooling and shaking. Evaporation of solvent after 5 minutes under reduced pressure at room temperature yielded adduct (LXVIII) as a light yellow oil. Vmax.
1550, 1660, 1720, 1750, 3450 cm⁻¹, λ max. (EtOH) 272 m/µ (ε = 5400), shifted to 268 m/µ after 1 hour and to 285 m/µ in alkali and to 290 m/µ in acid, n.m.r. signals (CDCl₃), 8.92 (s), 8.67 (s), 8.09 (m), 6.32 (s), 6.18 (s), 5.2 (q, J = 3.5 c/sec); areas 3:3:4:3:3:1.

The yellow oil on gentle warming and keeping under vacuum yielded a yellow oily solid. This was filtered and washed with ether, giving rearrangement product (LXIX) as a colourless solid m.p. 144-146°C (decomp.) in poor yield. Vmax (mull) 1555, 1600, 1690, 1740, 3220 cm⁻¹, λ max. (EtOH) 295, 241 m/µ (ε = 18292 m 14418), shifted to 344, 295 (sh), 245 (sh)m/µ in alkali, n.m.r. signals (CDCl₃), 8.62 (s), 8.19 (t, J = 8 c/sec), 6.66 (t, J = 8 c/sec), 6.3 (s) 6.15 (s), -1.22 (broad singlet, exchangeable); areas 6:2:2:3:3:1.

Molecular weight by mass spectrometry (255), (required 255), (Found: C, 56.15; H, 6.67; N, 5.27. Calc for C₁₂H₁₇NO: C, 56.47; H, 6.88; N, 5.49%). The filtrate on evaporation gave a thick sticky red oil which was not identified.
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