MODIFICATION OF POLYDIENES VIA
1,3-DIPOLAR CYCLOADDITION REACTIONS

by

LEO GAJSLER

Thesis presented for the degree of

DOCTOR OF PHILOSOPHY

University of Edinburgh

1983
A number of reactions between 1,3-dipoles and polydienes were studied, at varying molar ratios. The main polydienes used were cis-1,4-polybutadiene, cis-1,4-polyisoprene and trans-1,4-polyisoprene. The 1,3-dipoles were predominantly nitrile oxides, which were usually generated in situ via the thermal dehydrochlorination of the corresponding hydroximoyl chloride. Major nitrile oxides studied were p-methoxybenzonitrile oxide, 3,4,5-trimethoxybenzonitrile oxide, 2,4,6-trimethoxybenzonitrile oxide, methyl fulmidofomate and ethyl fulmidofomate. High yields, based on the 1,3-dipole, were achieved (up to 87%) and polymers with large degrees of modification were produced (up to 55%). The techniques of elemental analysis and $^{1}$H n.m.r spectroscopy were used to quantitatively determine the extent of polymer modifications.

Extensive use was made of monomeric alkenes, as model compounds, to trial synthetic path-ways and assist in establishing the structure of products from the equivalent polymer reactions. The main alkenes used were cyclohexene, 1-methylcyclohexene, cis-cyclooctene and oct-1-ene. $^{13}$C n.m.r spectroscopy was used to unequivocally establish the presence of isoxazoline rings on the modified polymers by comparison with authentic model adducts.

Two potentially useful functional groups (a polyethylene glycol and a carboxylic acid group) were successfully added to cis-1,4-polybutadiene via 1,3-dipolar cycloaddition.
DECLARATION

I declare that this thesis is my own composition, that the work of which it is a record has been carried out by myself and that it has not been submitted in any previous application for a Higher Degree. No previous publication of this work has been made, other than the paper included as an appendix.

The thesis describes results of research carried out in the Department of Chemistry, University of Edinburgh and ICI Organics Division, Manchester under the joint supervision of Dr. R.M. Paton, Dr. J.H. Hall and Dr. D.J. Harper since 1st October 1976, the date of my admission as a research student.

The following courses have been attended:

Organic Chemistry Seminars, Edinburgh University Chemistry Department (3 years attendance);
High Pressure Liquid Chromatography (5 lectures), staff of Wolfson Liquid Chromatography Unit;
The Encouragement and Exploitation of Inventiveness in the Oil Industry (1½ days), staff of British Petroleum Ltd.;
Organic Sulphur Compounds in General Synthesis (5 lectures), Dr. D. Leaver;
Chemistry at its most Colourful (2 days), staff of ICI Organics Division;
Molecular Orbital Theory in Organic Chemistry (5 lectures), Dr. J.T. Sharp;
Detergency and the Design of Surface Active Agents (5 lectures), Dr. D.W. Cooper.
I would like to thank Dr. R.M. Paton, Dr. J.H. Hall and Dr. D.J. Harper for their help, supervision and guidance throughout the course of this project. I am also grateful to the teaching and technical staff of the Department of Chemistry, University of Edinburgh.

I would also like to thank the S.R.C. for research and maintenance grants and the University of Edinburgh for the provision of laboratory facilities.

Additional thanks are due to ICI Organics Division for the provision of further financial and technical assistance.

Finally, I would like to thank Mrs. C.G. Ranken for her very professional typing.
I dedicate this work to my wife,

Dorothy
## INDEX

### INTRODUCTION SECTION

<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>1,3-DIPOLAR CYCLOADDITION REACTIONS</td>
<td>2</td>
</tr>
<tr>
<td>1.1</td>
<td>MECHANISM</td>
<td>5</td>
</tr>
<tr>
<td>1.2</td>
<td>SUBSTITUENT EFFECTS</td>
<td>9</td>
</tr>
<tr>
<td>1.2.1</td>
<td>Electronic Effects</td>
<td>9</td>
</tr>
<tr>
<td>1.2.2</td>
<td>Steric Effects</td>
<td>16</td>
</tr>
<tr>
<td>1.2.3</td>
<td>Other Effects</td>
<td>17</td>
</tr>
<tr>
<td>1.3</td>
<td>REGIOSELECTIVITY</td>
<td>19</td>
</tr>
<tr>
<td>2.</td>
<td>NITRILE OXIDES</td>
<td>30</td>
</tr>
<tr>
<td>2.1</td>
<td>PREPARATION</td>
<td>30</td>
</tr>
<tr>
<td>2.2</td>
<td>STABILITY</td>
<td>36</td>
</tr>
<tr>
<td>2.3</td>
<td>OTHER REACTIONS</td>
<td>45</td>
</tr>
<tr>
<td>2.3.1</td>
<td>Dimerisation to 1,2,4-Oxadiazole-4-oxides and 1,4,2,5-Dioxadiazines</td>
<td>45</td>
</tr>
<tr>
<td>2.3.2</td>
<td>1,3-Additions</td>
<td>48</td>
</tr>
<tr>
<td>3.</td>
<td>POLYDIENES</td>
<td>50</td>
</tr>
<tr>
<td>3.1</td>
<td>POLYISOPRENEs</td>
<td>50</td>
</tr>
<tr>
<td>3.2</td>
<td>POLYBUTADIENES</td>
<td>55</td>
</tr>
<tr>
<td>3.3</td>
<td>OTHER POLYDIENES</td>
<td>56</td>
</tr>
<tr>
<td>4.</td>
<td>POLYMER MODIFICATIONS</td>
<td>58</td>
</tr>
<tr>
<td>4.1</td>
<td>HYDROGENATION</td>
<td>58</td>
</tr>
<tr>
<td>4.2</td>
<td>HALOGENATION AND HYDROHALOGENATION</td>
<td>59</td>
</tr>
<tr>
<td>4.3</td>
<td>ADDITION OF THIOLS</td>
<td>60</td>
</tr>
<tr>
<td>4.4</td>
<td>REACTION WITH ALDEHYDES</td>
<td>60</td>
</tr>
</tbody>
</table>
## CYCLOADDITION REACTIONS

4.5.1 The Ene Addition Reaction

4.5.2 Reactions of Carbenes and Nitrenes

4.5.3 1,3-Dipolar Cycloaddition Reactions

4.5.4 Reaction with Sulphenyl Compounds

## CROSS-LINKING REACTIONS

### EXPERIMENTAL SECTION

1. SYMBOLS AND ABBREVIATIONS

2. INSTRUMENTATION

3. SOLVENTS AND REAGENTS

4. PREPARATION OF NITRONES

4.1 α-(4-Methoxyphenyl)-N-phenylnitrone

4.2 α-(4-Hydroxyphenyl)-N-phenylnitrone

4.3 α-(3,5-Di-tert-butyl-4-hydroxyphenyl)-N-phenylnitrone

4.4 α-(4-Benzoylphenyl)-N-phenylnitrone

5. PREPARATION OF ISOXAZOLIDINES

5.1 3-(4-Methoxyphenyl)-2-phenyl-4,5-tetramethylene-2-isoxazolidine

5.2 4,5-Decamethylene-3-(4-methoxyphenyl)-2-phenyl-2-isoxazolidine

5.3 3-(4-Methoxyphenyl)-5-methyl-2-phenyl-4,5-tetramethylene-2-isoxazolidine
5.4 3-(p-Benzoylphenyl)-4,5-decamethylene-2-phenyl-2-isoxazolidine 77
5.5 Attempted synthesis of 3-(4-Hydroxyphenyl)-2-phenyl-4,5-tetramethylene-2-isoxazolidine 78
5.6 Attempted synthesis of 4,5-Decamethylene-3-(3,5-di-tert-4-hydroxyphenyl)-2-phenyl-2-isoxazolidine 78

6. PREPARATION OF ALDOXIMES 79
6.1 4-Benzoylbenzaldoxime 79

7. PREPARATION OF HYDROXIMOYL CHLORIDES 80
7.1 4-Methoxybenzhydroximoyl chloride 81
7.2 4-Benzoylbenzhydroximoyl chloride 81
7.3 3,4,5-Trimethoxybenzhydroximoyl chloride 81
7.4 4-Carboxybenzhydroximoyl chloride 81
7.5 2,4,6-Trimethoxybenzonitrile oxide 82
7.6 Ethyl chlorooximinoacetate 82
7.7 Methyl chlorooximinoacetate 82

8. PREPARATION OF ISOXAZOLINES 83
8.1 3-(4-Methoxyphenyl)-4,5-tetramethylene-2-isoxazoline 83
8.2 4,5-Hexamethylene-3-(4-methoxyphenyl)-2-isoxazoline 83
8.3 5-Hexyl-3-(4-methoxyphenyl)-2-isoxazoline 84
8.4 3-(4-Methoxyphenyl)-5-methyl-4,5-tetramethylene-2-isoxazoline 85
8.5 4,5-Hexamethylene-3-(3,4,5-trimethoxyphenyl)-2-isoxazoline 85
<table>
<thead>
<tr>
<th>Section</th>
<th>Formula Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.6</td>
<td>3-((4-Benzoylphenyl)-4,5-decamethylene-2-isoaxazoline</td>
<td>86</td>
</tr>
<tr>
<td>8.7</td>
<td>3-((4-Benzoylphenyl)-5-hexyl-2-isoaxazoline</td>
<td>87</td>
</tr>
<tr>
<td>8.8</td>
<td>3-Ethoxycarbonyl-4,5-hexamethylene-2-isoaxazoline</td>
<td>87</td>
</tr>
<tr>
<td>8.9</td>
<td>3-Ethoxycarbonyl-4,5-hexamethylene-5-methyl-2-isoaxazoline</td>
<td>88</td>
</tr>
<tr>
<td>8.10</td>
<td>4,5-Hexamethylene-3-(2,4,6-trimethoxyphenyl)-2-isoaxazoline</td>
<td>89</td>
</tr>
<tr>
<td>8.11</td>
<td>3-((4-Carboxyphenyl)-4,5-hexamethylene-2-isoaxazoline</td>
<td>90</td>
</tr>
<tr>
<td>8.12</td>
<td>3-Carboxylic acid-4,5-hexamethylene-2-isoaxazoline</td>
<td>91</td>
</tr>
<tr>
<td>9.</td>
<td>1,3-DIPOLAR CYCLOADDITION TO POLYDIENES</td>
<td>92</td>
</tr>
<tr>
<td>9.1</td>
<td>Reaction of cis-1,4-Polybutadiene with (\alpha)-4-Benzoylphenyl-(N)-phenylnitrone</td>
<td>92</td>
</tr>
<tr>
<td>9.2</td>
<td>The Reactions of Nitrile Oxides with Polydienes - General Method</td>
<td>93</td>
</tr>
<tr>
<td>9.2.1</td>
<td>Example 1: Reaction of Methyl chloro-oximinoacetate and cis-1,4-Polybutadiene at 1:10 molar ratio</td>
<td>94</td>
</tr>
<tr>
<td>9.2.2</td>
<td>Example 2: Reaction of 3,4,5-Trimethoxy-benzhydroximoyl chloride and cis-1,4-Polyisoprene at 1:1 molar ratio</td>
<td>95</td>
</tr>
<tr>
<td>9.3</td>
<td>The addition of a (p)-(2-Methoxyethoxy)-phenyl Pendent group</td>
<td>104</td>
</tr>
</tbody>
</table>
9.3.1 Preparation of p-(2-Hydroxyethoxy)-toluene 105
9.3.2 Preparation of p-(2-Methoxyethoxy)-toluene 107
9.3.3 Preparation of p-(2-Methoxyethoxy)-benzaldehyde 108
9.3.4 Preparation of p-(2-Methoxyethoxy)-benzaldoxime 108
9.3.5 Preparation of p-(2-Methoxyethoxy)-benzhydroximoyl chloride 109
9.3.6 Attempted synthesis of p-(2-Methoxyethoxy)-benzaldehyde via the Gatterman-Aldehyde Reaction 110
9.3.6.1 Preparation of Ethylene glycol methylphenylether 110
9.3.6.2 Attempted synthesis of p-(2-Methoxyethoxy)-benzaldehyde 110
9.4 The Addition of a p-(MeO(CH$_2$CH$_2$O)$_6$C$_6$H$_4$ Pendent Group 111
9.4.1 Preparation of p-(HO(CH$_2$CH$_2$O)$_5$)C$_6$H$_4$CH$_3$ 112
9.4.2 Preparation of p-(MeO(CH$_2$CH$_2$O)$_5$)C$_6$H$_4$CH$_3$ 112
9.4.3 Preparation of p-(MeO(CH$_2$CH$_2$O)$_6$)C$_6$H$_4$CHO 113
9.4.4 Preparation of p-(MeO(CH$_2$CH$_2$O)$_6$)C$_6$H$_4$CHNOH 113
9.4.5 Preparation of p-(MeO(CH$_2$CH$_2$O)$_6$)C$_6$H$_4$CClNOH 114
9.5 Attempted Hydrolysis of Pendent Ethoxy-carbonyl Groups 114
9.5.1 Preparation of Crown Ether/Potassium Hydroxide Complex 114
9.5.2 Saponification of Pendent Ethoxycarbonyl Groups using a Crown Ether/Potassium Hydroxide Complex 115

RESULTS AND DISCUSSION SECTION

1. INTRODUCTION 116
2. USE OF MODEL COMPOUNDS 119
3. EVIDENCE FOR 1,3-DIPOLAR CYCLOADDITION TO POLYDIENES 127
4. DETERMINATION OF YIELDS FOR THE POLYMER REACTIONS 138
4.1 Nitrogen Analysis 138
4.2 $^1$H-NMR 139
5. FACTORS EFFECTING YIELDS OF 1,3-DIPOLAR CYCLOADDITION TO POLYDIENES 140
5.1 Polymer Effects 142
5.2 Molar Ratio Effects 144
5.3 Reactivity of 1,3-Dipoles 146
6. THE ADDITION OF POLYETHYLENE GLYCOL GROUPS 151
7. THE ADDITION OF PENDENT CARBOXYL GROUPS 156
8. THE ATTEMPTED ADDITION OF HINDERED PHENOL ANTI-OXIDANT GROUPS 160
9. CONCLUSIONS
9.1 Criteria of Success 162
9.2 Use of Model Compounds 163
9.3 Suggestions for Further Work 164

REFERENCES 165

Note: All schemes, figures, diagrams, tables etc. are numbered by one single consecutive numbering system, to avoid possible confusion (e.g., between a scheme and a figure with the same number).
INTRODUCTION
SECTION
The aim of this project was to investigate the cycloaddition of 1,3-dipoles to polydienes, with a view to achieving the covalent attachment of potentially useful pendent groups. These groups can be divided into two classes; firstly those chemical groups which might be expected to directly impart improved properties to the polymer. An example of such a group would be one containing an anti-oxidant moiety. The second type of pendent group need not be expected to directly impart improved properties to the polymer, but would contain a reactive chemical moiety which would serve to functionalise the polymer chain, thus making it susceptible to further chemical modification.

The polydienes suitable for the above types of modification include all natural and synthetic polydiene rubbers. Chemical modification might not only improve the behaviour of these elastomers during the processing and service of rubber articles, but could also allow them to compete in areas other than their traditional application.
1. 1,3-DIPOLAR CYCLOADDITION REACTIONS

Although a number of examples of 1,3-dipolar cycloadditions were known, it was not until Huisgen's work in the early 1960's that the full scope of this class of reaction was realised and investigated.\textsuperscript{2,3}

The reaction can be defined as the cycloaddition of a 1,3-dipole and a multiple bond system, the dipolarophile, to give a five membered cyclic adduct (Scheme 1). The process can be symbolised as 3+2 → 5.

![Scheme 1](image)

Huisgen recognised that 1,3-dipoles could be divided into two main classes: those where a lone pair of electrons on the central atom, b, can yield a resonance structure where all atoms have attained an electron octet (Scheme 2), an octet-stabilised 1,3-dipole; and those which cannot achieve such octet stabilisation.

![Scheme 2](image)
Octet stabilised 1,3-dipoles can be further divided into those with and without an orthogonal double bond between a and b in the sextet form. Examples of octet-stabilised 1,3-dipoles with a double bond in the sextet form are the nitrilium betaines, such as nitrile oxides and nitrile imines and examples of octet-stabilised 1,3-dipoles without a double bond in the sextet form are the nitrones and ozone (table 3). The former type are isoelectronic with the allenyl anion, while the latter are isoelectronic with the allyl anion.

<table>
<thead>
<tr>
<th>SEXTET FORM</th>
<th>OCTET FORM</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{N}=$</td>
<td>$\text{O}=$</td>
<td>Nitrile oxides</td>
</tr>
<tr>
<td>$\text{C}=$</td>
<td>$\text{N}=$</td>
<td>Nitrile imines</td>
</tr>
<tr>
<td>$\text{C}=$</td>
<td>$\text{C}=$</td>
<td>Nitrones</td>
</tr>
<tr>
<td>$\text{O}=$</td>
<td>$\text{O}=$</td>
<td>Ozone</td>
</tr>
</tbody>
</table>

Table 3
All possible resonance structures are considered for formonitrile oxide [4a-e] and ozone [5a-e].

\[
\begin{align*}
&\text{HC} = \text{N} - \overset{\ddagger}{\text{O}} \leftrightarrow \text{HC} = \overset{\ddagger}{\text{N}} = \overset{\ddagger}{\text{O}} \leftrightarrow \text{HC} - \overset{\ddagger}{\text{N}} = \overset{\ddagger}{\text{O}} \\
&\text{4a} \quad \text{4b} \quad \text{4c}
\end{align*}
\]

\[
\begin{align*}
&\leftrightarrow \text{HC} = \overset{\ddagger}{\text{N}} - \overset{\ddagger}{\text{O}} \leftrightarrow \text{HC} = \overset{\ddagger}{\text{N}} - \overset{\ddagger}{\text{O}} \\
&\text{4d} \quad \text{4e}
\end{align*}
\]

\[
\begin{align*}
&\overset{\ddagger}{\text{O}} \leftrightarrow \overset{\ddagger}{\text{O}} \leftrightarrow \overset{\ddagger}{\text{O}} \leftrightarrow \overset{\ddagger}{\text{O}} \\
&\text{5a} \quad \text{5b} \quad \text{5c}
\end{align*}
\]

\[
\begin{align*}
&\leftrightarrow \overset{\ddagger}{\text{O}} \leftrightarrow \overset{\ddagger}{\text{O}} \\
&\text{5d} \quad \text{5e}
\end{align*}
\]
The ground state of the molecules can be represented by the all-octet structures 4a, 4b, 5a and 5b, while the other structures have a lesser contribution\(^3\). Structures 4d, 4e, 5c and 5d illustrate that the dipolar contribution is not uniquely directional and 1,3-dipoles need not necessarily be expected to have a large dipole moment. Structure 4c is a charge-free sextet contribution, in this case a carbenic structure. This type of structure cannot be formulated for octet stabilised 1,3-dipoles without a double bond in the sextet form. Structure 5d is a non-classical representation and can be considered to represent a unique form of the electronic structure\(^4\).

1.1 MECHANISM

Huisgen has proposed that 1,3-dipolar cycloaddition goes via a concerted multicentre mechanism\(^5\), where the formation of the two new \(\sigma\)-bonds can be considered to be simultaneous, though not necessarily synchronous.

The cycloaddition can be formulated as either a one-step or a two-step reaction (Scheme 6).
The two-step process involves the intermediacy of a zwitterion \([6']\) and a reaction of this type would be expected to be significantly faster in more polar solvents\(^5\). In fact, 1,3-dipolar cycloaddition is slightly enhanced by a reduction in solvent polarity, which would be consistent with the loss of the small contribution of dipole character in the one-step reaction\(^5\). Similarly, reactions with \textit{cis} and \textit{trans} double bonds are found to be highly stereoselective. For the two step reaction, rotation about the d-e axis in \(6'\) might be expected to lead to non-stereoselectivity. In an individual case it is possible that
rotation about the d-e axis is slow compared to ring closure, but stereoselectivity of a large number of different cases provides evidence for a concerted one-step process.

Another mechanism has been proposed by Firestone\textsuperscript{6} which involves a stepwise-diradical process (Scheme 7).

\begin{center}
\begin{tikzpicture}[scale=0.8]
\node (a) at (0,0) {$a$};
\node (b) at (1,0) {$b$};
\node (c) at (2,0) {$c$};
\node (d) at (2,-1) {$d$};
\node (e) at (3,-1) {$e$};
\node (a') at (4,0) {$a$};
\node (b') at (5,0) {$b$};
\node (c') at (6,0) {$c$};
\node (d') at (6,-1) {$d$};
\node (e') at (7,-1) {$e$};
\draw (a) -- (b) -- (c) -- (d) -- (e);
\draw (a') -- (b') -- (c') -- (d') -- (e');
\end{tikzpicture}
\end{center}

\textbf{Scheme 7}

Huisgen hotly refutes this proposal\textsuperscript{7}. Although the argument remains unresolved, only the concerted mechanism will be considered in any further discussion, as this appears to be most widely accepted.

Since Huisgen's original work on 1,3-dipolar cycloaddition, the reaction has been reconsidered in the light of molecular orbital theory\textsuperscript{4,8-11}. Woodward and Hoffmann established the principle that pericyclic reactions would occur more readily if there was conservation of orbital symmetry\textsuperscript{8}, ie that there should be a congruence between the orbital symmetry characteristics of products and reactants. This type of reaction is said to be "allowed" on symmetry grounds.
On this basis it can be shown that for the cycloaddition of the allyl anion to ethylene (which can be regarded as the prototype of 1,3-dipolar cycloadditions\textsuperscript{12}), suprafacial-suprafacial concerted cycloaddition is symmetry allowed for the thermal (ground state) reaction. This type of reaction is classified as $[\pi 4s + \pi 2s]$ and is best illustrated in the form of a Correlation Diagram (Figure 8).\textsuperscript{4}

![Correlation Diagram for the $[\pi 4s + \pi 2s]$-cycloaddition of allyl anion with ethylene (symmetries, A = antisymmetric and S = symmetric, are with respect to the mirror plane m).](image)

**Figure 8**

The frontier orbitals may then be considered; the highest occupied molecular orbital (HOMO) of the allyl-anion reacting with the lowest unoccupied molecular orbital (LUMO) of ethylene [9] and the HOMO of ethylene reacting with the LUMO of the allyl-anion [10].
It can be seen that the orbital correlations allow a conservation of symmetry for the \([\pi4s + \pi2s]\) process.

1.2 SUBSTITUENT EFFECTS

1.2.1 Electronic Effects

The most striking substituent effect noticed by Huisgen was that any type of conjugation in the dipolarophile enhances the rate of cycloaddition\(^2,3,5\). This is in spite of the fact that loss of conjugation energy during addition would tend to diminish the reaction enthalpy. He put forward two explanations; i) due to the possibility of asynchronous bond formation during concerted cycloaddition, partial charges could result in the transition state and conjugation would tend to stabilise these. Secondly, ii) conjugation would tend to increase the polarisability of the double bond in the dipolarophile and the increased mobility of the bonding
electrons implied by this might correspond to an enhanced tendency to enter into cyclic shifts.

These explanations fail to conform with some of the observed data. For instance, if electron releasing and attracting groups are both attached to opposite ends of ethylene, the expected acceleration consistent with a partial charge or polarization model is not observed\textsuperscript{13}.

More recently, substituent effects in 1,3-dipolar cycloaddition have been explained on the basis of a simple perturbation molecular orbital model\textsuperscript{13,14}. Perturbation theory considers the way the molecular orbitals of two reacting molecules perturb each other as the molecules approach. This gives an idea of the energy gained in bond formation, the stabilisation energy. Sustmann and Trill\textsuperscript{14} have put forward a simplified equation (equation 13) for the perturbation molecular orbital approach to 1,3-dipolar cycloaddition, upon which a qualitative model for substituent effects could be based.

\textbf{Equation 13}

$$\Delta E = A\beta^2 \left\{ \frac{1}{E_{\text{OHO}} - E_{\text{DLU}}} + \frac{1}{E_{\text{DHO}} - E_{\text{OLU}}} \right\}$$

\begin{align*}
\Delta E & \quad \text{Stabilisation energy} \\
E_{\text{OHO}}, E_{\text{OLU}} & \quad \text{Energy levels of the dipolarophile HOMO} \\
E_{\text{DHO}}, E_{\text{DLU}} & \quad \text{Energy levels of the dipole HOMO & LUMO respectively.} \\
A, \beta & \quad \text{constants, at given orbital separation.}
\end{align*}
This simplified approach which was originally\textsuperscript{14} derived for the allyl anion, but has since been applied to any 1,3-dipole\textsuperscript{15}, illustrates that, to a first approximation, the stabilisation energy is inversely proportional to the differences in energies of the reacting frontier orbitals. Thus, for a small separation between the reacting orbitals there would be a large stabilisation energy, which would indicate a low energy transition state and a rapid rate of reaction. On this basis, three different possibilities can be identified.

If $E_{\text{DHO}} - E_{\text{OLU}} > E_{\text{OHO}} - E_{\text{DLU}}$ in equation 13, then (to a first approximation) the interaction of the alkene HOMO and the dipole LUMO can be considered to be dominant and the effects of substituents only on this separation need be considered. This was originally termed Type I 1,3-dipolar cycloaddition by Sustmann\textsuperscript{13,14}. If $E_{\text{DHO}} - E_{\text{OLU}}$ is approximately equal to $E_{\text{OHO}} - E_{\text{DLU}}$, then the interactions of both the alkene HOMO with the dipole LUMO and the alkene LUMO with the dipole HOMO are important. This was termed Type II 1,3-dipolar cycloaddition. Finally if $E_{\text{OHO}} - E_{\text{DLU}} > E_{\text{DHO}} - E_{\text{OLU}}$, then the interaction between the dipole HOMO and the alkene LUMO is dominant. This was termed Type III 1,3-dipolar cycloaddition. Unfortunately this classification has become confused, due to a reversal in the numbering of these types by Houk\textsuperscript{15}, who appears to have changed Sustmann's original classification and it is Houk's numbering system that has since been most widely used\textsuperscript{4,16}.

Types I, II and III 1,3-dipolar cycloadditions (according to Sustmann's original classification) are termed LU controlled, HO, LU controlled.
Figure 14
and HO controlled 1,3-dipolar cycloadditions respectively; after the frontier orbital of the dipole which can be considered to have a dominant interaction (Figure 14).

Examination of the prototype case of an allyl anion and ethylene (Fig. 8) would indicate that HO-control might be expected to occur. However the energy levels of 1,3-dipole orbitals vary to a greater or lesser extent from those of the allyl anion (the presence of electronegative atoms tending to lower the energy levels) and the type of 1,3-dipolar cycloaddition is usually dependent on the type of 1,3-dipole. For instance, diazoalkanes and nitrile ylides usually react under HO-control; azides, azomethine imines, nitrones, nitrile imines and nitrile oxides usually react under HO, LU-control and ozone and nitrous oxide usually react under LU-control.

The effect of substituents can then be rationalised by examining the effect they would be expected to have on the dominant orbital interaction. In general, an electron releasing substituent will raise the orbital energy levels and an electron withdrawing substituent will lower them.

Thus the effect of substituents on the dipolarophile is as follows: For HO-controlled reactions electron releasing substituents tend to increase the energy difference between the dominant frontier orbitals and thus reduce the rate of the reaction and vice-versa for electron withdrawing substituents. For LU-controlled reactions electron withdrawing substituents tend to decrease the energy difference and thus reduce the rate of reaction and vice-versa for electron releasing substituents. It is observed, that for HO,LU-
controlled reactions either electron withdrawing or releasing substituents in the dipolarophile tend to increase the rate of reaction. This latter influence leads to a U-shaped plot of rate of 1,3-dipolar cycloaddition against ionisation potential (equivalent to the energy level of the HOMO of the olefin) for phenyl azide\textsuperscript{14} (Figure 15).

The effect of any type of conjugation in the alkene is also explained. This would tend to extend the $\pi$-system and therefore increase the HOMO and lower the LUMO energies, thereby increasing the stabilisation energy for all types of 1,3-dipolar cycloaddition.

Although the above arguments have been more generally applied to substituents on the dipolarophile, analogous effects can be explained for substituents on the dipole. This is exemplified by benzenesulphonyl nitrile oxide (X) which has been shown to react much faster with electron rich alkenes than benzonitrile oxide\textsuperscript{17} (Y). Benzonitrile oxide typically reacts in HO,LU-controlled 1,3-dipolar cycloadditions and strongly electron releasing and electron attracting groups on the dipolarophile therefore give fast rates of reaction. The powerful electron withdrawing benzenesulphonyl group in X tends to lower the orbital energy levels of the dipole, thus leading to more LU-controlled type reactions.

\[
\begin{align*}
\text{PhSO}_2\text{C}≡\text{N}≡\text{O} & \quad \text{PhC}≡\text{N}≡\text{O} \\
\text{X} & \quad \text{Y}
\end{align*}
\]
Figure 15. Plot of reaction rate against ionisation potential for 1,3-dipolar cycloaddition.
1.2.2 Steric Effects

So far substituents have only been considered with regard to their electronic effects. However, steric effects are also very important in 1,3-dipolar cycloaddition reactions. This is consistent with the high negative entropy of activation for polycentre addition$^2$; the greater the steric requirements of the transition state, the more sensitive is the system towards disturbances$^5$. Thus, for reaction with diphenyl-diazomethane, the rate of cycloaddition for acrylic ester is 280 times faster than crotonic ester$^5$. 

\[
\text{Ph}_2\text{C}=\text{N}^+\equiv\text{N} + \text{RCH}==\text{CH}^\uparrow \xrightarrow{\text{R}=\text{H}, \times 280} \text{Ph}_2\text{C}=\text{N} \equiv \text{N} \xrightarrow{\text{R}=\text{Me}} \text{N} \equiv \text{N} \xrightarrow{\text{CO}_2\text{R}'}
\]
1.2.3 Other Effects

Alkenes with angle strained double bonds are generally found to be highly reactive due to the relief of strain accompanying cycloaddition. For example, norbornene reacts with diphenyl nitrile imine about 284 times faster than cyclohexene. This has been equated to the heat of hydrogenation of double bonds, which is also enhanced by relaxation of angle strain. For example, the heat of hydrogenation of the strained double bond in bicyclo[2,2,1]hept-2-ene (X) is about 6 kcal·mole$^{-1}$ larger than for cyclohexene.

For cis/trans-isomeric alkenes, the trans-isomer is always found to react faster and this has been attributed to a more sterically crowded transition state for the cis-isomer. This is exemplified by dimethyl fumarate which reacts 36 times faster than dimethyl maleate with diphenyl-nitrile imine, despite the fact that the more energy-rich maleate adds to bromine more rapidly.

In the course of the concerted 1,3-dipolar cycloaddition
of a 1,3-dipole, abc, to a substituted alkene, the carbon atoms of the double bond gradually change from $\text{SP}^2$ hybridisation to $\text{SP}^3$ (Figure 16). Although the C-C bond is somewhat lengthened during this process, the shrinkage in bond angles from $120^\circ$ to $109^\circ$ results in considerable compression of the Van der Waals radii of the substituents for the cis-isomer (Figure 16).

![Figure 16](image)

This leads to increased steric repulsion during the activation process and thus leads to a resultant increase in activation energy, which does not apply to the trans-isomer.
1.3 REGIOSELECTIVITY

For all types of 1,3-dipolar cycloadditions to unsymmetric alkenes, there are two possible regioisomers (Scheme 17).

\[ \begin{align*}
\text{d} & \quad \text{b} \quad \text{c} \\
\text{d} & \quad \text{e} \\
\end{align*} \]

\[ \begin{align*}
\text{a} & \quad \text{b} \quad \text{c} \\
\text{d} & \quad \text{e} \\
\end{align*} \]

Scheme 17

However, Huisgen\(^3\) noted that most 1,3-dipolar cycloadditions were remarkably regioselective and attributed this mainly to steric effects. This was exemplified by diphenyl-nitrileimine, whose geometry is bent due to the contribution of the two octet forms \(18a\) and \(18b\).

\[ \begin{align*}
\text{Ph} & \quad \equiv \text{N} \quad \equiv \text{N} \\
\text{Ph} & \quad \equiv \text{N} \quad \equiv \text{N} \\
\text{Ph} & \quad \equiv \text{N} \quad \equiv \text{N} \\
\text{Ph} & \quad \equiv \text{N} \quad \equiv \text{N} \\
\end{align*} \]

\[ \begin{align*}
\text{18a} & \quad \text{18b} \\
\end{align*} \]
Huisgen\textsuperscript{3} concludes that the nitrogen end of the dipole is less sterically crowded and cycloaddition with a dipolarophile containing a bulky substituent might be expected to favour the regioisomer with that substituent adjacent to the less crowded end of the dipole. This is generally found to coincide with experimental observation. For example styrene reacts with diphenylnitrileimine to give exclusively the 5-substituted pyrazoline (17).

\[
\begin{align*}
\text{PhC} &= \text{NNPh}^+ \\
\text{PhCH} &= \text{CH}_2
\end{align*}
\]

\[
\begin{array}{c}
\text{Ph} \\
\text{C} \\
\text{N} \\
\text{N} \\
\text{Ph}
\end{array}
\begin{array}{c}
\text{Ph} \\
\text{C} \\
\text{N} \\
\text{N} \\
\text{Ph}
\end{array}
\]

Huisgen realised that the steric argument was not completely satisfactory for the explanation of regioselectivity and gave two anomalous examples\textsuperscript{3}. For acrylonitrile, the steric hindrance at the \(\alpha\)-carbon atom is small and yet no 4-substituted pyrazoline was detected on 1,3-dipolar cycloaddition to diphenylnitrileimine. \(C\)-Phenyl-\(N\)-(trihalophenyl)-nitrileimines still react with mono- and 1,1-disubstituted ethylenes to give 5-substituted pyrazolines, although the effect of the bulky trihalophenyl group might be expected to reverse this on steric grounds alone.

Again an explanation has been provided based on perturbation molecular orbital theory\textsuperscript{9,11,15,18-20}. So far in
discussing molecular orbitals, only the energy levels of the frontier orbitals and their symmetries have been considered. Another important factor, however, is the relative distribution of orbital density on each atom. This can be considered in terms of the contribution which the atomic orbital is making to the molecular orbital and is given by the orbital coefficient for that atom. Thus for two atoms, whose electron distribution in the atomic orbitals are given by $\varphi_1$ and $\varphi_2$, the function which describes the electron distribution in the molecular orbital is given by $\varphi$ (equation 18), where $C_1$ and $C_2$ are the orbital coefficients for the two atoms.

$$\varphi = C_1 \varphi_1 + C_2 \varphi_2$$

**Equation 18**

This leads to a fuller expression of equation 13 for the stabilisation energy (Equation 19) to include orbital coefficients,$^{14}$

$$\Delta E = \frac{[(C_{H01} C_{LU1} + C_{H02} C_{LU3}) B]^2}{E_{OH0} - E_{DLU}} +$$

$$\frac{[(C_{H01} C_{LU1'} + C_{H03} C_{LU2'}) B]^2}{E_{DH0} - E_{OLU}}$$

**Equation 19**
where the subscripts on the coefficients refer to the terminal atoms of the dipole 1 and 3 and the dipolarophile atoms 1' and 2'.

Thus the stabilisation energy (the energy gain in bond formation between centres 1 and 3 of the 1,3-dipole and centres 1' and 2' of the dipolarophile) is a function of \( \Sigma (C\beta)^2 \) terms. The size of the orbital coefficients is often used in qualitative arguments, to a first approximation.

Fukui has proposed a general principle which states that a majority of chemical reactions should take place at the position and in the direction of maximum overlapping of the HOMO's and LUMO's of the reacting species. Epiotis put forward a very similar principle when he stated that, "a reaction will proceed regiochemically in a manner, which involves union of the two atoms of highest frontier orbital density and union of the two atoms of lowest frontier orbital electron density." The relative magnitude of the orbital coefficients is often illustrated by the relative size of the lobes on each atom (Figure 20).
Figure 20

The regioisomer produced via transition state a, in Figure 20, is more stabilised than that formed via transition state b. As a general rule for deducing the preferred regioisomer, orientation is arranged so that the larger terminal coefficient on each addend becomes bonded in the transition state. Houk\textsuperscript{11} has proposed some simple, general rules for determining the relative sizes of terminal coefficients, which are based on a number of calculations that he has done to establish overall trends\textsuperscript{11,15,20}. When considering alkenes the method is relatively straightforward and is based on ethylene, for which the terminal coefficients are equal and then considering the effects of substituents\textsuperscript{20}.

a) Conjugating substituents increase the magnitude of the
coefficient of the unsubstituted terminus of the C=C double bond relative to the substituted terminus in both the HOMO and the LUMO.

b) Electron releasing groups increase the remote coefficient in the HOMO and the nearby coefficient in the LUMO.

c) For alkyl substituents, the two coefficients are nearly identical in the LUMO.

d) Electron-withdrawing substituents have the opposite effect to "b)" above if they are purely inductive (e.g., CF₃), however most of these groups are also conjugating and so in the LUMO, the greater magnitude of the remote coefficient is further strengthened, while the difference in the HOMO coefficients is diminished or reversed.

When considering the relative sizes of the coefficients on the 1,3-dipole, the situation is more complex because of the large number of different types of 1,3-dipole. However, Houk¹¹ has again noticed some general trends based on the results of his calculations. For the HOMO of most 1,3-dipoles the largest coefficient is on the "anionic" terminus c (when written in the traditional form - see figure 21) relative to the "neutral" terminus a. The exceptions are the simple symmetrical 1,3-dipoles (such as ozone) and the nitrone which has virtually identical coefficients on both termini.

For the 1,3-dipole LUMO, the largest terminal coefficient is on the "neutral" atom, a, with the exception of diazomethane, for which the terminal coefficients are virtually identical. A general scheme¹¹ can then be formulated for predicting which regioisomer will be formed, depending on whether the reaction is under dipole HO or LU control (Figure 21).
Figure 21. Regioisomer expected from HO or LU dipole control. Substituents on ethylene C, Z and X represent conjugating, electron withdrawing and electron releasing substituents, respectively.
If the electron withdrawing substituent, Z, is acting purely inductively, then (iv) would be the expected regioisomer under dipole LU control. However if Z is also acting mesomerically, then the conjugating effect usually leads to (iii) as the prepared regioisomer. The effect of substituents on the 1,3-dipole is qualitatively the same as for the dipolarophile. However the relative magnitudes of the terminal coefficients on 1,3-dipoles are not usually reversed unless the terminal coefficients are nearly identical in the parent dipole.

The overall principles of regioselectivity may be exemplified by reference to the 1,3-dipolar cycloadditions of nitrile oxides. Nitrile oxides react under HO,LU-dipole control and the relative energy levels of different types of dipole orbitals relative to those of benzonitrile oxide are shown in figure 22.

![Figure 22](image)

*Figure 22.* Frontier orbital energy levels for benzonitrile oxide and dipolarophiles. Arrows show the energy separation for dominant frontier orbital interactions.
For nitrile oxides the largest terminal coefficient is on the oxygen atom in the HOMO and on the carbon atom in the LUMO, in accordance with the general rules given above.

For conjugated and electron rich alkenes (with electron releasing substituents), the dominant frontier orbital interaction is between the dipole LUMO and the dipolarophile HOMO (dipole LU-control). Alkenes with conjugating and electron releasing substituents have the largest orbital coefficient on the unsubstituted terminus in the HOMO and so the preferred regioisomer, formed via a transition state involving maximum orbital overlap, will be 23, the 5-substituted isoxazoline.

For electron deficient dipolarophiles, both dipole HO- and LU-control are significant, although LU-control predominates leading to the 5-substituted isomer. However, due to partial HO-control, some 4-substituted isoxazoline (24) is produced; for example in the reaction of benzonitrile oxide with methyl acrylate, 3.6% of the 4-substituted regioisomer (X) is produced.$^{15}$
An observation which supports the above discussion, involves the reactions of nitrile sulphides. Nitrile sulphides have been found to give a greater proportion of 4-substituted cycloadducts than nitrile oxides, with electron deficient dipolarophiles\textsuperscript{21,22}. This is due to a greater degree of HO-control for reactions of nitrile sulphides with electron deficient dipolarophiles (figure 23)\textsuperscript{22}.

![Relative frontier orbital energy levels of nitrile oxides and nitrile sulphides.](image)

\textbf{Figure 23:}\textsuperscript{22} Relative frontier orbital energy levels of nitrile oxides and nitrile sulphides.
Thus the reaction between benzonitrile oxide and methyl propiolate gives 16% of the 4-isoxazole (25), while that between benzonitrile sulphide and methyl propiolate give 50% of the 4-isothiazole (26)22.

It has been noticed that alkynes in general give rise to a relatively larger degree of dipole HO-control than do alkenes15. This is attributed to their relatively lower HOMO energies compared to alkenes, whilst their LUMO energies are less affected.

This discussion on regioselectivity was introduced by considering steric effects. It should be noted that although subsequent discussion has been confined to electronic effects, both these are important and both must be considered together when elucidating a preferred regioisomer.
2. **NITRILE OXIDES**

The foregoing discussion has considered 1,3-dipoles as a general class of compounds. As the description of experimental work, which follows, will confine itself almost entirely to one type of 1,3-dipole (the nitrile oxides); this class is now considered in greater detail.

A number of reviews have appeared detailing the chemistry of nitrile oxides\(^{23-27}\) and only those topics of particular interest will be considered here.

2.1 **PREPARATION** (Ref. 27, Chap. III)

Most nitrile oxide preparations correspond to dehydrogenation of the corresponding aldoxime (Scheme 27).

\[
RCH=\underset{\text{2H}}{\text{N-OH}} \rightarrow RC=\underset{\text{O}}{\text{N}}
\]

**Scheme 27**

This has been achieved directly using alkaline hypobromite at 0\(^\circ\)C or lead tetraacetate at -78\(^\circ\)C\(^{27}\). However, the most common method for the generation of nitrile oxides is via the thermal or base-induced dehydrohalogenation of hydroximoyl halides (Scheme 28). The hydroximoyl chloride is usually used and may be generated from the corresponding oxime, either by direct chlorination\(^{54}\) or using nitrosyl chloride\(^{55}\).
The use of nitrosyl chloride is often the method of preference, particularly when direct chlorination may lead to undesirable side reactions. For example, direct chlorination of \( p \)-anisaldoxime, \( X \) in commercial chloroform yields 11% 3,5-dichloro-4-methoxybenzohydroximoyl chloride, \( Y \) and 22% of the corresponding benzal chloride, \( Z \) \(^{56}\).
In methylene chloride with a little triethylamine at -15 to -20°C only Z was isolated.

However, using nitrosyl chloride in dry ether at -15°C the desired product, anisylhydroximoyl chloride, Q, has been obtained.

Another general route involves the effective dehydration of primary nitroparaffins (Scheme 30), for example via the decomposition of nitrolic acids (31a), which may be obtained via the reaction of primary nitroparaffins with nitrous acid or by the nitration of aldoximes (Scheme 31).

Scheme 30

Scheme 31
More recently nitrile oxides have been obtained via thermolysis of 1,2,5-oxadiazole-2-oxides (furoxans)\textsuperscript{28,29}, the dimers of nitrile oxides (Scheme 32); i.e. a reversal of the more familiar dimerisation of nitrile oxides.

Scheme 32
This may be achieved either by simple thermolysis at temperatures usually in excess of 200°C\textsuperscript{28} or by flash vacuum pyrolysis\textsuperscript{29}.

Due to the short lifetime of most nitrile oxides (with respect to dimerisation or rearrangement - see below), they are most often prepared in situ for the purposes of 1,3-dipolar cycloadditions\textsuperscript{27}. The hydroximoyl chlorides are the most commonly used precursors, and may be dissolved or suspended in ether with the dipolarophile and triethylamine added slowly at 0 to 20°C\textsuperscript{27}. However, a method which has been reported to be superior is the generation of a nitrile oxide, in situ, by
the thermolysis of the hydroximoyl chloride. The hydroximoyl chloride and the nitrile oxide are in equilibrium, with a value for the equilibrium constant, $K$, in the order of $10^{-4}$ mole$^2$.dm$^{-2}$ at room temperature.

$$\text{RC}═\text{NOH} \xrightarrow{K} \text{RC}═\text{N}−\text{O} + \text{HCl}$$

In refluxing toluene (in which HCl has a low solubility) the reaction proceeds very slowly and there will be a low standing concentration of nitrile oxide in the presence of excess dipolarophile. This favours adduct formation greatly, over dimerisation of the nitrile oxide and is particularly useful for reactions with unreactive dipolarophiles.

It has been proposed that for the thermolysis of hydroximoyl chlorides, in the presence of a dipolarophile, the reaction proceeds via a multicentre transition state $\tilde{X}$ (path a) rather than via free nitrile oxide (path b).
2.2 STABILITY

When a nitrile oxide is heated, in the absence of any other reactant, there are two possible reactions\(^\text{27}\): Either rearrangement to isocyanate (path a) or dimerisation to the furoxan (path b), (Scheme 32).

Scheme 32

Reaction a predominates with increasing thermal stability of the nitrile oxide and is not observed for the lower aliphatic nitrile oxides\(^\text{27}\). For aromatic nitrile oxides, furoxan formation is usually favoured. Thus at room temperature benzonitrile oxide 33 converts almost quantitatively into diphenyl furoxan 35, whilst rapid heating in xylene
solution to 110°C affords 10% phenylisocyanate 34, in addition to furoxan formation.

At temperatures above 250°C, the furoxan fragments back to the nitrile oxide, which subsequently rearranges almost quantitatively to give the isocyanate 24, 27.

A number of nitrile oxides are known which are completely stable at room temperature attributable to steric hindrance preventing furoxan formation. The first of this type to be isolated was 2,4,6-trimethylbenzonitrile oxide 36, which was found to rearrange quantitatively to the isocyanate on heating above 80°C, with no furoxan formation 30.
The mechanism of thermal rearrangement of nitrile oxides to isocyanates has not been elucidated. However there is evidence that the photochemical process proceeds via an oxazirine 37, which subsequently ring opens to give an acyl nitrene 38 31.

When the photolysis of 36 in methanol solution was examined, the products isolated were the lactam 39 due to insertion of the nitrene into one of the α-methyl groups, and the urethane 40 resulting from reaction of the isocyanate with the solvent.
However the above mechanism seems unlikely for the thermal rearrangement, as the formation of 37 as a direct step contradicts the Woodward-Hoffmann rules and it has not been possible to trap out the acyllnitrile\textsuperscript{27}. It has also been established that the thermal rearrangement occurs with complete retention of chirality and stereochemical configuration by a strictly intramolecular process\textsuperscript{32}. A concerted mechanism was therefore postulated involving a 4-membered transition state (41).
\[ \text{Scheme 42} \]
The mechanism for the dimerisation of nitrile oxides to furoxans has not been unequivocally established. The three possible \textit{a priori} mechanisms are illustrated in scheme 42. Mechanism \textit{a} assumes a concerted 1,3-dipolar cycloaddition with one nitrile oxide molecule acting as a 1,3-dipole and the other as a dipolarophile. Huisgen has dismissed this as unlikely, proposing that if 1,3-dipolar cycloadditions were to take place between two nitrile oxide molecules, the expected regioisomer would be the 1,2,4-oxadiazole-4-oxide \textit{5,33}. 

\begin{center}
\includegraphics[width=0.3\textwidth]{structure.png}
\end{center}

\textit{44}
This was based on the assumption that, when one of the termini of the dipolarophile is a heteroatom, the orientation of cycloaddition should be that leading to a maximum gain in \( \sigma \)-bond energy\(^3\). This principle examines the relative stability of the two possible products and is purely a thermodynamic consideration.

However, another criterion is to examine the relative stability of the two possible transition states. As pointed out by Huisgen himself\(^5\), the energy of the new \( \sigma \)-bonds becomes only partly available in the transition state of the cycloaddition. The relative energies of the two possible transition states may be estimated on the basis of second order perturbation theory (Table 44).

<table>
<thead>
<tr>
<th></th>
<th>Furoxan</th>
<th>1,2,4-Oxadiazole-4-oxide</th>
</tr>
</thead>
<tbody>
<tr>
<td>MeCNO</td>
<td>1.58</td>
<td>1.48</td>
</tr>
</tbody>
</table>

Table 44. Values for \( \Sigma (C\beta)^2/15 \) for nitrile oxide dimerisation. Values of C's and \( \beta \)'s calculated by Houk\(^{11,15}\) assuming a transition state separation of 1.75Å.

The values given in table 44 are proportional to the stabilisation energy and the inclusion of the resonance integral (\( \beta \)) term makes allowance for the contribution of \( \sigma \)-bond energy in the transition state. Thus, a preference for furoxan formation is indicated and although the difference is small, the 1,3-dipolar mechanism for nitrile oxide dimerisation certainly cannot be dismissed on this basis. A concerted
1,3-dipolar cycloaddition mechanism is also supported by the similarity of solvent and substituent effects for furoxan formation with those observed in conventional 1,3-dipolar cycloadditions.34

Mechanism b is unlikely as it involves a zwitterion intermediate. A zwitterion intermediate would be expected to give significant rate enhancement in polar solvents, while in fact the rate of furoxan formation is slightly faster in non-polar solvents (about ten times faster in carbon tetrachloride than in chloroform)34. A widely accepted mechanism is that involving a two step dimerisation of the carbenic form of the nitrile oxide (mechanism c)27. This involves a 1,2-dinitrosoethylene intermediate 42d which would readily stabilise itself to the furoxan. Good evidence is provided by proton N.M.R. that benzofuroxan 43 is in tautomeric equilibrium with a small amount of 1,2-dinitrosobenzene 43a.

![Chemical structures](image-url)
Therefore, at present, further work is required to distinguish between the two more likely mechanisms a and c.

The effect of substituents on the rate of dimerisation of aromatic nitrile oxides appears to be somewhat contradictory in the literature. It was generally observed that the rate increased in the order $m$-Cl $> p$-Cl $> H > p$-Me $> p$-MeO$^36$ and the reaction appeared to obey a Hammett-type relationship with a value for $\rho = +0.86^34$. However, when the time taken for complete dimerisation at room temperature has been investigated, some anomalies appear. For example, benzonitrile oxide has a lifetime of 30–60 minutes$^27$ at room temperature whilst the corresponding figures for $p$-chlorobenzonitrile oxide and $p$-nitrobenzonitrile oxide are 10 and 30 days, respectively$^{27,37}$. 
2.3 OTHER REACTIONS

The most common reaction of nitrile oxides is 1,3-dipolar cycloaddition and this has already been considered in detail. For example, they cycloadd to alkenes to give isoxazolines \(^{45,3}\) and to alkynes to give isoxazoles \(^{46,2}\).

2.3.1 Dimerisation to 1,2,4-Oxadiazole-4-oxides and 1,4,2,5-Dioxadiazines

Although the furoxan (considered above) is usually the only dimer formed under neutral conditions, in the presence of protonating or Lewis acids, the two other possible dimers may be formed. For example, benzonitrile oxide dimerises to 3,5-diphenyl-1,2,4-oxadiazole-4-oxide \(^{47}\) when treated with gaseous BF\(_3\) in hexane with a ratio of 2:1. If treated with excess BF\(_3\) in hexane the 3,6-diphenyl-1,4,2,5-dioxadiazine
48 is produced\textsuperscript{27}.

Similarly, 47 is formed on treatment of benzonitrile oxide in ether with HCl gas\textsuperscript{27} or from the spontaneous decomposition of solid benzohydroximoyl chloride at 25-30°C in a sealed vessel\textsuperscript{38}. The following mechanism has been proposed\textsuperscript{5,39}, (Scheme 49).
The reverse addition of benzonitrile oxide to benzo-hydroximoyl chloride has also been reported\(^{40}\), during the direct chlorination of benzaldoxime in methylene chloride at \(0^\circ\text{C}\), to give 2-hydroxy-3,4-diphenyl-3-chloro-1,2,5-oxadiazoline (50). It was suggested that this might involve addition of the nitrile oxide to the nitroso tautomer of the hydroximoyl chloride, 50a, (Scheme 50).
Nitrile oxides are known to undergo 1,3-additions to a number of compounds containing active hydrogen atoms (Scheme 51).
Compound B-H may be ammonia, amines, phenylhydrazine and hydrogen halides. Under special conditions, nitrile oxides will also react with water, alcohols and phenols; this often requiring acid or base catalysis. For example, 2,4,6-trimethylbenzonitrile oxide has been reacted with methanol in the presence of sulphuric acid, for 4 hours at 25°C to give 96% yield of the methylhydroxamate 52a (Scheme 52).
3. **POLYDIENES**

The polydienes represent the largest and most important group of elastomers and their relative importance may be assessed from table 60.

<table>
<thead>
<tr>
<th>Type of Rubber</th>
<th>Production (million tons)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural rubber</td>
<td>2.87</td>
</tr>
<tr>
<td>Styrene/butadiene</td>
<td>3.24</td>
</tr>
<tr>
<td>Polybutadiene</td>
<td>0.69</td>
</tr>
<tr>
<td>Polychloroprene</td>
<td>0.34</td>
</tr>
<tr>
<td>Butyl</td>
<td>0.28</td>
</tr>
<tr>
<td>Polyisoprene (synthetic)</td>
<td>0.23</td>
</tr>
<tr>
<td>Nitrile</td>
<td>0.22</td>
</tr>
<tr>
<td>Ethylene/propylene</td>
<td>0.10</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>7.97</strong></td>
</tr>
</tbody>
</table>

*Table 60. Estimated 1969 world production of major rubbers.*

3.1 **POLYISOPRENESES**

The isoprene monomeric unit (61) may polymerise in four different ways to give isomeric polymers.

\[
\text{CH}_3
\]

\[
\text{CH}_2\text{CH}-\text{C}==\text{CH}_2
\]

61
The polymers are classified according to which carbon atoms of the monomer are linked. These are cis-1,4-Polyisoprene (cis-1,4-PIP), trans-1,4-PIP, 1,2-PIP, and 3,4-PIP.

Natural rubber is highly stereospecific and is almost entirely cis-1,4-PIP with head-to-tail junction of monomer units. Natural rubber is obtained from the tree, *Hevea brasiliensis* as rubber latex. Latex is a suspension of rubber hydrocarbon in water together with other minor components. Over 1000 species of higher plants have been reported to contain polyisoprenes, however normally in small concentrations,
whereas, *Hevea* latex may contain up to 35% rubber hydrocarbon (Table 61)\(^47\).

<table>
<thead>
<tr>
<th>Component</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubber hydrocarbon</td>
<td>35%</td>
</tr>
<tr>
<td>Non-rubber solids</td>
<td>5%</td>
</tr>
<tr>
<td>Water</td>
<td>60%</td>
</tr>
</tbody>
</table>

*Table 61.* Typical constitution of *Hevea* latex.

The non-rubber solids consist of mostly proteins, lipids, quebrachitol (hexahydroxycyclohexane monomethyl ether) and inorganic salts\(^47,49\).

Another less important naturally occurring polyisoprene is known as gutta percha (Malaya) or balata (South America) and consists mainly of *trans*-1,4-PIP\(^47\).

Synthetic polyisoprenes were prepared as early as the 1860's by free-radical polymerisation\(^50\). This results in a totally non-stereospecific polymer and the general mechanism of free-radical alkene polymerisation is given in Scheme 62.

However, more recently, it was discovered that stereospecific polyisoprenes could be formed using alkali-metal, organoalkali-metal catalysts or co-ordination catalysts of the Ziegler-Natta type\(^52,53\). Different catalyst formulations lead to different polymers, for example lithium or triisobutylaluminium-TiCl\(_4\), give high *cis*-1,4-polyisoprenes while triethylaluminium-VC\(_3\) gives a high *trans*-content\(^50,53\). The mechanisms for these polymerisations are not yet fully understood, but are generally considered to involve anionic centres, and a possible mechanism for lithium catalysis has been proposed\(^47\), (Scheme 63).
Initiator (eg. peroxide): $X_2 \rightarrow 2X^·$

**Initiation:**

$\text{CH}_2=\text{CHR} + X^· \rightarrow X\text{CH}_2\text{CH}^·$

**Propagation:**

$X\text{CH}_2\text{CH}^· + \text{CH}_2=\text{CHR} \rightarrow X\text{CH}_2\text{CHCH}_2\text{CH}^·$

**Termination:**

radical coupling

$\sim\text{CH}_2\text{CH}^· + \sim\text{CH}_2\text{CH}^· \rightarrow \frac{2}{3} \text{CH}_2\text{CHCHCH}_2\sim$

disproportionation

$\sim\text{CH}_2\text{CH}^· + \sim\text{CH}_2\text{CH}^· \rightarrow \sim\text{CH}_2\text{CH}_2 + \sim\text{CH}=\text{CH}$

Scheme 62. General mechanism for free-radical polymerisation of alkenes.$^{51}$
Scheme 63
It is suggested that the diene forms a co-ordination complex with the lithium ion hybridized $sp^3$-orbitals which leads to a new bond formation via a 6-membered ring transition state. As the cisoid conformation of the co-ordination complex is favoured in the case of isoprene, a high cis-polymer is produced. Also as isoprene has higher electron density on the 1,2-bond, this bond is directed toward the positively charged metal ion on the growing chain and a head-to-tail polymer results. As the above mechanism has no termination step, it is an example of "living polymerisation" and results in a polymer of high molecular weight with a narrow molecular weight distribution.

3.2 POLYBUTADIENES

Butadiene may polymerise to form three different types of polymer link; cis-1,4-polybutadiene (cis-1,4-P.B.D.), trans-1,4-P.B.D. and 1,2-P.B.D.

\[
\begin{align*}
\text{cis-1,4-PBD}
\end{align*}
\]
Butadiene may be polymerised either non-stereospecifically or stereospecifically using similar methods to polyisoprenes. \textit{cis}-1,4-PBD is the most important commercially and a polymer with over 98\% \textit{cis}-1,4-structural units may be prepared using a CoCl$_2$-AlEt$_2$Cl-pyridine system$^{47}$.

3.3 OTHER POLYDIENES

A number of other polydienes are of commercial importance, particularly copolymers of butadiene such as acrylonitrile-butadiene (nitrile rubbers) and styrene-butadiene copolymers. Styrene-butadiene rubbers (SBR) have gained increasing importance since the last war and show many properties superior to natural rubber for use in car tyres$^{47,50}$. Formulations for SBR usually contain about 70-75\% butadiene and are normally produced by a free radical process leading to a random, non-stereospecific copolymer$^{47}$. 
Other polydienes, such as polychloroprene 64 (commercially known as neoprene) find importance as speciality rubbers.

![Chemical structure of polychloroprene 64](image)
4. POLYMER MODIFICATIONS

For a large majority of applications of polymers in the plastics industry, one or more "modifiers" are incorporated into the basic polymer. These are often physically compounded into the polymer such as in the case of fillers, colorants, lubricants, stabilisers, anti-oxidants, blowing agents etc. or in some cases may modify the polymer via chemical combination, such as cross-linking agents. This review will confine itself to chemical modifications of polydiene polymers.

Such chemical modifications may be divided into
i) functionalisation or modification of the polymer chain via substitution or addition reactions, ii) cross-linking reactions, and iii) graft copolymerisation reactions. However, "ii" and "iii" are merely special cases of "i" where the reagent is either difunctional (most cross-linking reactions) or itself contains a polymer chain (graft copolymerisation). Therefore, the major reactions on polydienes are reviewed, together with some examples which have been used for cross-linking reactions. There is a fourth type of reaction which involves degradation or cyclisation of the polymer back-bone,

4.1 HYDROGENATION

The unsaturation in polydienes is susceptible to catalytic hydrogenation, but when using heterogeneous systems such as nickel or palladium/charcoal and elevated temperatures (200-250°C), significant degradation also occurs. Milder
conditions can be used with homogeneous catalysts such as lithium aluminium hydride/nickel diisopropylsalicylate (40°C) and no appreciable degradation. Thus, 1,4-polybutadiene can be fully hydrogenated to a polymer indistinguishable from polyethylene.

4.2 HALOGENATION AND HYDROHALOGENATION

Reaction of polyisoprene with free chlorine in organic solution results in substitution, addition, cyclisation and some cross-linking. The former two would result in the following types of structure (65 and 66).

In the presence of a peroxide catalyst and sulphuryl chloride, the reaction is primarily simple addition. Direct bromination proceeds in a similar manner although there is less substitution.

Hydrogen chloride reacts with natural rubber by Markownikoff addition, accompanied by some cyclisation. The reverse reaction may be affected by treatment with a base or heating above 100°C.
4.3 ADDITION OF THIOLS

The radical induced reaction proceeds via the following type of mechanism (Scheme 72)\textsuperscript{78}.

\[ \text{R} + \text{RSH} \rightarrow \text{RH} + \text{RS}. \]

\[ \begin{array}{c}
\text{CH}=\text{CH} \\
\text{CH} \end{array} \quad \begin{array}{c}
\text{RS} \\
\text{RS} \end{array} \quad \begin{array}{c}
\text{CH} \end{array} \quad \begin{array}{c}
\text{CH} \\
\text{CH} \end{array} \]

\[ \text{CH}_2 \quad \text{CH}_2 \quad \text{CH}_2 \quad \text{CH}_2 \]

\[ \begin{array}{c}
\text{RS} \\
\text{RS} \end{array} \quad \Delta \text{RSH} \quad \text{ETC.} \]

Scheme 72

This type of reaction has been used to impart improved properties to rubber e.g. monochlorothiolacetic acid results in improved resistance to oil absorption and trichlorothiolacetic acid improved flame resistance\textsuperscript{79,80}.

4.4 REACTION WITH ALDEHYDES

Aliphatic electron withdrawing aldehydes (such as chloral, fluoral) react with polyisoprene in the presence of Lewis acids (e.g. boron trifluoride) to give a Prins reaction\textsuperscript{81} (Scheme 73).
\[
\begin{align*}
\text{CH}_3 & \quad \text{C} = \text{CH} \\
\text{C} = \text{C} & \quad \text{CH}_2 \quad \text{CH}_2
\end{align*}
\]

\[
\text{RCHO} \quad \text{BF}_3 \quad \text{O} = \text{BF}_3
\]

\[
\begin{align*}
\text{H}_2\text{C} & \quad \text{CHR} \\
\text{C} = \text{C} & \quad \text{CH}_2 \quad \text{CH}_2
\end{align*}
\]

\[
\text{H}_2\text{O}
\]

\[
\begin{align*}
\text{H}_2\text{C} & \quad \text{CHR} \\
\text{C} = \text{C} & \quad \text{CH}_2 \quad \text{CH}_2
\end{align*}
\]

\[
R = \text{Cl}, \text{Br}, \text{F}, \text{CHO}, \text{C}_2\text{Cl}_3, \text{CF}_3 \text{ etc.}
\]

\textit{Scheme 73}
Utilising this reaction, surface treatment of rubber with fluoral reduces the coefficient of friction by a factor of 3-10 times and also results in improved water and flame resistance.

4.5 CYCLOADDITION REACTIONS

4.5.1 The Ene Addition Reaction

This reaction has been extensively explored for potential modification of natural rubber and follows the general form shown below (Scheme 74).

\[
\begin{align*}
\text{Scheme 74} & \\
\text{For example ethyl N-phenylcarbamoylazoformate reacts with dry natural rubber in a mill at 110^\circ C, at greater than 90\% efficiency (Scheme 75).} & \\
\text{The hydrazoester pendent groups introduced are highly polar and strongly susceptible to hydrogen bonding. At 1 mole & \\
% modification there is sufficient interference with the} & \\
\end{align*}
\]
alignment of polymer chains to usefully inhibit crystallisation on storage of unvulcanised natural rubber.

4.5.2 Reactions of Carbenes and Nitrenes

Dihalocarbenes are easily generated in rubber solution under mild conditions, for example dichlorocarbene may be produced by reaction of a base with chloroform and reacts with polyisoprene in situ (Scheme 76).
Scheme 76
Vulcanised polyisoprene modified in this way gave an improved hardness, although other tensile properties were diminished.

Azido compounds decompose thermally to give nitrenes, which readily add to the unsaturation in polydienes (Scheme 77).
Some insertion into C-H bonds can also occur\textsuperscript{85} (Scheme 78).

\[
\text{ROCO.N}_3 \xrightarrow{-N_2} \text{ROCO.N} \quad \text{H}
\]

Scheme 78

4.5.3 1,3-Dipolar Cycloaddition Reactions

This type of reaction is the principal subject of this work. The reaction itself has been covered extensively earlier and previous studies in respect of addition to polydienes are fully reviewed in the "discussion" section.

4.5.4 Reaction with Sulphenyl Compounds

Reaction of polydiienes with sulphenyl derivatives has been extensively studied\textsuperscript{88}. For example\textsuperscript{89}, reaction of chlorosulphonyl isocyanate (66) with cis-1,4-polyisoprene gave predominantly the cyclic adduct \textsuperscript{a} with some side reaction to give structure \textsuperscript{b} (Scheme 79).
Scheme 79

The chlorosulphonyl group may be removed from a by hydrolysis to leave the β-lactam 67.
4.6 CROSS-LINKING REACTIONS

One of the earliest chemical modifications of a polymer was the sulphur vulcanization reaction, discovered by Goodyear in 1839. Unmodified rubbers, although elastic, exhibit severe irreversible deformation when stretched. Sulphur vulcanization effects cross-linking via chains of sulphur atoms (5-50 per cross-link) allowing local freedom of molecular movement (i.e. maintaining elasticity), but preventing bulk slippage of molecules and thus preventing irreversible deformation.

Although sulphur vulcanization is still the most widely used cross-linking reaction, a number of other reactions have been studied; primarily with a view to obtaining improved thermal stability.

The most common alternative involves the use of an organic peroxide, such as benzoyl or dicumyl peroxide. The reaction is considered to proceed via a radical mechanism, (Scheme 80).

Other side reactions, such as the addition of radical A to a double bond in another molecule, are also likely (Scheme 81).
A light induced cross-linking has been reported\textsuperscript{84}, by employing a difunctional nitrene precursor which decomposes on irradiation, such as 2,6-bis-\((p\)-azidobenzylidene\()-4\)-methylcyclohexan-1-one \textit{65} (Scheme 82).

\begin{align*}
\text{ArN}_3 & \quad \text{O} \\
\text{CH} & \quad \text{CH} \\
\text{CH}_3 & \quad \text{CH}_3
\end{align*}

\textit{65}

\textbf{Scheme 82}

Cross-linking of polydienes has been reported\textsuperscript{86} using difunctional 1,3-dipole precursors. For example, a bis-nitrile oxide may be generated \textit{in situ} by the thermolysis of bicyclic furoxans\textsuperscript{87} (Scheme 83).
The foregoing Introduction Section has covered prior knowledge of 1,3-dipolar cycloaddition reactions and general polydiene chemistry.

The aim of this work was to examine 1,3-dipolar cycloaddition to polydienes, with a view to their modification with potentially useful functional groups.

The following Experimental Section describes the preparation and 1,3-dipolar cycloaddition of a number of nitrones and nitrile oxides to model alkenes and polydienes. The techniques (elemental analysis, $^1$H n.m.r and $^{13}$C n.m.r spectroscopy) used to examine the cycloadducts are detailed. The results are fully discussed in the Results and Discussion Section.
EXPERIMENTAL
SECTION
1. **Symbols and Abbreviations**

- **b.p.** boiling point
- **m.p.** melting point
- **tlc** thin-layer chromatography
- **glc** gas liquid chromatography
- **n.m.r.** nuclear magnetic resonance
- **s; d; t;** singlet; doublet; triplet;
- **q; m** quartet; multiplet
- **J** coupling constant
- **δ** chemical shift
- **i.r.** infra-red
- **M⁺** mass of molecular ion
- **m/e** mass to charge ratio
- **h; min** hours; minutes
- **p.p.m.** parts per million
- **mmol** millimoles
- **mol** moles
- **νmax** maximum i.r. absorption
- *( assignments may be reversed (used in n.m.r.)*
- **bd** broad
- **nD²⁰** refractive index at 20°C
2. Instrumentation

2.1 Melting Points

Melting points of new compounds were obtained on a Köfler hot-stage apparatus. All others were obtained using capillary tubes and Gallenkamp apparatus.

2.2 Nuclear Magnetic Resonance Spectroscopy

2.2.1 Routine $^1$H n.m.r. spectra were recorded on a Varian EM 360 60 MHz spectrometer. 100 MHz spectra of new compounds were obtained using a Varian HA 100 spectrometer operated by Mr. J. Millar. Chemical shifts ($\delta_H$) are measured in parts per million relative to tetramethylsilane (T.M.S.) as standard ($\delta = 0.0$).

2.2.2 $^{13}$C n.m.r. spectra were generally recorded on a Varian CFT 20 spectrometer operated by Mr. J. Millar, and in a few cases, on a Varian XL 100 spectrometer or a Bruker WH 360 spectrometer operated respectively by Dr. A. Boyd and Dr. I.H. Sadler. Chemical shifts ($\delta_C$) are measured in p.p.m. relative to T.M.S. ($\delta = 0.0$).

2.3 Infra-red Spectroscopy

I.r. spectra were recorded on a Perkin-Elmer 157G Grating Spectrophotometer. Liquid samples were recorded as thin films, and solid samples as nujol mulls or in solution in chloroform.

2.4 Mass Spectroscopy

Mass spectra and exact masses were obtained on an AEI MS 902 mass spectrometer operated by Mr. D. Thomas.
2.5 **Elemental Analysis**

Microanalyses of all new compounds were obtained using a Perkin-Elmer model 240 analyser operated by Mr. J. Grunbaum.

2.6 **Thin-layer Chromatography**

Chromatograms were developed on 0.33 mm layers of alumina (Merck, Aluminium Oxide G) or silica gel (Merck, Silica Gel G) containing Woelm fluorescent green indicator (0.5%). Components of the chromatogram were detected by their quenching of fluorescence under U.V. light, or by their absorption of iodine.

3. **Solvents and Reagents**

All solvents used for reactions were of "Analar" quality. Toluene, xylene and diethyl ether were dried over sodium wire. All monomeric alkenes used for 1,3-dipolar cycloaddition reactions were purified by distillation.

Polydienes were supplied by ICI Organics Division. *cis*-1,4-Polybutadiene, *cis*-1,4-polyisoprene and *trans*-1,4-polyisoprene were shown to be at least 98% stereospecific by $^{13}$C n.m.r. spectroscopy.

4. **Preparation of Nitrones**

These were prepared after the general method of Wheeler and Gore $^{57}$.  

4.1 **α-(4-Methoxyphenyl)-N-phenylnitrone**

4-Methoxybenzaldehyde (6.8 g, 50 mmol) and *N*-phenylhydroxylamine (5.45 g, 50 mmol) were dissolved in the minimum of commercial ethanol and allowed to stand at room temperature overnight. The resulting precipitate was filtered and recrystallised from
ethanol to give $\alpha$-(4-methoxyphenyl)-$N$-phenylnitrone as white needles (4.83 g, 43%). M.p. 104-106°C (lit. 101-116°C).

$\delta$H (CDCl$_3$): 3.81 (3H, s, CH$_3$O-); 6.95 (2H, d, J 9Hz, $\alpha$-ArH m); 7.4-7.8 (5H, m, N-ArH); 7.82 (1H, s, -CH=N); 8.40 (2H, d, J 9Hz, $\alpha$-Ar-ortho-H).

4.2 $\alpha$-(4-Hydroxyphenyl)-$N$-phenylnitrone

4-Hydroxybenzaldehyde (6.1 g, 50 mmol) and $N$-phenylhydroxylamine (5.45 g, 50 mmol) were treated as above to give $\alpha$-(4-hydroxyphenyl)-$N$-phenylnitrone as white needles from ethanol (4.95 g, 47%). M.p. 206-208°C (lit. 212°C).

4.3 $\alpha$-(3,5-Di-tert-butyl-4-hydroxyphenyl)-$N$-phenylnitrone

3,5-Di-tert-butyl-4-hydroxybenzaldehyde (5.0 g, 21 mmol) and $N$-phenylhydroxylamine (3.0 g, 28 mmol) were dissolved in absolute ethanol (150 ml) and warmed at 50-60°C for 5 h under dry nitrogen. The mixture was allowed to stand under nitrogen overnight and the solvent was then removed to leave a yellow oil. The oil was purified by dissolving in a minimum of hot toluene and cooling to give a yellow solid (6.5 g, 95%). The product was recrystallised from toluene to give white crystals (2.7 g, 44%). The nitrone was found to be highly susceptible to hydrolysis and was stored in a desiccator. M.p. 131-135°C (lit. 137-140°C).

$\delta$H (CDCl$_3$): 1.48 (18H, s, tert-butyl), 5.70 (1H, s, OH), 7.4-7.8 (5H, m, Ph), 7.81 (1H, s, CH=N), 8.32 (2H, s, ArH).

(Found: C, 77.6; H, 8.3; N, 4.2. $C_{21}H_{27}NO_2$ requires C, 77.5; H, 8.4; N, 4.3%).

4.4 $\alpha$-(4-Benzoylphenyl)-$N$-phenylnitrone

4-Formylbenzophenone (3.0 g, 14 mmol) and $N$-phenylhydroxyl-
amine (1.6 g, 14 mmol) were dissolved in methanol (400 ml) and allowed to stand overnight under dry nitrogen at room temperature. The solution was reduced in volume to 100 ml and chilled to give α-(4-benzoylphenyl)-N-phenylnitronitrone as a white precipitate (2.45 g, 57%). White crystals were recovered from ethanol. M.p. 139-141°C. \( v_{\text{max}} \) (nujol): 1650 (C=O) cm\(^{-1}\).

δH (CDCl\(_3\)): 7.25-8.55 (14H, m, ArH); 7.81 (1H, s, -CH=N).

m/e 301 (M\(^+\)), 285 (M\(^+\)-O), 105, 91. (Found: C, 79.45; H, 5.17; N, 4.64. \( \text{C}_{20}\text{H}_{15}\text{NO}_{2} \) requires C, 79.72; H, 5.02; N, 4.65%).

5. Preparation of Isoxazolidines

5.1 Synthesis of 3-(4-methoxyphenyl)-2-phenyl-4,5-tetramethyl-ene-2-isoaxazolidine.

α-(4-Methoxyphenyl)-N-phenylnitronitrone (1.0 g, 4.4 mmol) and cyclohexene (4.0 g, 49 mmol) were dissolved in xylene (30 ml) and heated under reflux for 60 h under nitrogen. The solvent was removed and the resultant yellow oil was triturated with ether to yield a white solid (0.14 g, 14%), which was identified as unreacted nitrone from its i.r. spectrum. The ether solution was washed several times with water, dried, and evaporated to leave a yellow oily solid (0.9 g, 65%). This was recrystallised from aqueous methanol (10% \( \text{H}_2\text{O} \)) to give the adduct as a white solid (39% recovered). M.p. 140-144°C. δH (CDCl\(_3\)): 1.0-2.8 (9H, m, ring CH\(_2\)'s and ring CH-C), 3.78 (3H, s, CH\(_3\)O), 4.20-4.35 (1H, m, CH-O), 4.72 (1H, d, J 6Hz, CH-N), 6.75-7.49 (9H, m, ArH).

m/e 309 (M\(^+\), 100%), 212 (51). (Found: C, 77.43; H, 7.65; N, 4.44. \( \text{C}_{20}\text{H}_{23}\text{NO}_{2} \) requires C, 77.64; H, 7.49; N, 4.53%).
The reaction was repeated using toluene as cosolvent. After 60 h unreacted nitrone (62%) was recovered while the adduct was isolated as above (10%). M.p. 144-145°C.

5.2 Synthesis of 4,5-Decamethylene-3-(4-methoxyphenyl)-2-phenyl-2-isoxazolidine

α-(4-Methoxyphenyl)-N-phenylnitron (1.0 g, 4.4 mmol) and cis-cyclooctadecene (10 ml, 52 mmol) were dissolved in xylene (125 ml) and heated under reflux for 36 h. The solvent was removed on a rotary evaporator and excess dipolarophile was removed by distillation under high vacuum (0.1 mmHg). The resultant oil was chromatographed (Al₂O₃, CH₂Cl₂) and the first fraction collected as a yellow oil (0.78 g, 45%). A white solid (55% recovered) was isolated by trituration with n-pentane, followed by recrystallisation from methanol. M.p. 78-79°C. (Found: C, 79.20; H, 8.93; N, 3.49. C₂₆H₃₅NO₂ requires C, 79.35; H, 8.96; N, 3.56%). m/e 394 (M⁺ + 1, 33%), 393 (M⁺, 100), 212 (33), 149 (26), 147 (20). δH (CDCl₃): 1.1-2.1 (20H, m, ring CH₂), 2.26-2.57 (1H, m, bridgehead CH-C), 3.79 (3H, s, CH₃O), 3.93-4.18 (1H, m, bridgehead CH-O), 4.12 (1H, d, J 7Hz, CH-N), 6.8-7.5 (9H, m, ArH).

5.3 Synthesis of 3-(4-Methoxyphenyl)-5-methyl-2-phenyl-4,5-tetramethylene-2-isoxazolidine

α-(4-Methoxyphenyl)-N-phenylnitron (1.0 g, 4.4 mmol) and 1-methylcyclohexene (9.0 g, 94 mmol) were dissolved in toluene (150 ml) and heated under reflux for 432 h under nitrogen. The solvent and excess dipolarophile were removed and unreacted nitrone (53%) was isolated first by trituration with diethyl
ether and then with petroleum-ether (b.p. 40-60°C). The purity and identity of the nitrone were confirmed by t.l.c. \((\text{Al}_2\text{O}_3/\text{toluene}; \ R_f = 0.10)\). The mother liquor was evaporated to give a yellow oil (0.50 g), which was distilled under high vacuum (80-145°C/0.05 mmHg). The distillate was further purified by column chromatography \((\text{Al}_2\text{O}_3/\text{CH}_2\text{Cl}_2)\) to give a pale yellow oil (0.13 g), which was taken up in minimum hot n-hexane and chilled to yield a brown solid (20 mg, 1.4%). This was recrystallised from n-hexane to give the product as a white solid (45% recovered). M.p. 114-117°C (Found: C, 78.13; H, 7.98; N, 4.26. \(\text{C}_{21}\text{H}_{25}\text{NO}_2\) requires C, 77.99; H, 7.79; N, 4.33%). M/e 323 (\(M^+, 68\%\)), 210 (43), 198 (100), 187 (100), \(\delta H (\text{CDCl}_3): 1.2-1.9 \ (1\text{H}, \text{m, CH}_3 + \text{ring CH}_2), 2.20-2.42 \ (1\text{H, m, isoxazolidine CH}), 3.80 \ (3\text{H, s, CH}_3\text{O}), 4.49 \ (1\text{H, d, J 9Hz, CH-N}), 6.7-7.5 \ (9\text{H, m, ArH}).\)

5.4 Synthesis of 3- (p-Benzoylphenyl)-4,5-decamethylene-2-phenyl-2-isoxazolidine

\[\alpha-\text{N-phenylnitrone (1.0 g, 3.3 mmol) and cis-cyclododecene (10 ml, 59 mmol) were dissolved in xylene (100 ml) and heated under reflux for 60 h. The solvent was removed on a rotary evaporator and excess dipolarophile was removed by distillation under high vacuum. The resulting yellow oil was purified by column chromatography (Al}_2\text{O}_3/\text{CH}_2\text{Cl}_2)\] and the first fraction collected (t.l.c.; \(\text{Al}_2\text{O}_3/\text{toluene} \ R_f \ 0.85\)) as a yellow oil (0.55 g, 42%). The oil was treated with decolourising charcoal in refluxing methanol for \(\frac{1}{2}\) h.
The adduct was obtained as a white solid (84% recovered) from ethanol. M.p. 108-110°C (Found: C, 82.03; H, 8.00; N, 2.94. C_{32}H_{37}NO_2 requires C, 82.19; H, 7.97; N, 3.00%). M/e 468 (M^+1, 37%), 467 (M^+, 100), 302 (13), 286 (55), 285 (47).

δH (CDCl₃): 1.1-2.2 (20H, m, 10 ring CH₂), 2.32-2.73 (1H, m, isoxazolidine CH-C), 4.03-4.28 (1H, m, CH-O), 4.37 (1H, d, J 7Hz, CH-N), 6.8-8.0 (14H, m, ArH).

5.5 Attempted Synthesis of 3-(4-Hydroxyphenyl)-2-phenyl-4,5-tetramethylene-2-isoxazolidine

α-(4-Hydroxyphenyl)-N-phenylnitrone (1.0 g, 4.7 mmol) and cyclohexene (4.0 g, 49 mmol) were mixed with xylene (30 ml) and heated under reflux under nitrogen for 60 h (the nitrone dissolved on heating). The reaction mixture was cooled to yield a white precipitate of unreacted nitrone (93%), which was identified by t.l.c. (Al₂O₃/MeOH) and mixed melting point. No product could be isolated from the mother liquor.

5.6 Attempted synthesis of 4,5-Decamethylene-3-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-phenyl-2-isoxazolidine

α-(3,5-Di-tert-butyl-4-hydroxyphenyl)-N-phenylnitrone (1.0 g, 3.1 mmol) and cis-cyclododecene (10 ml, 52 mmol) were dissolved in xylene (100 ml) and heated under reflux for 48 h under nitrogen. The solvent was removed on a rotary evaporator and excess dipolarophile was removed by distillation under high vacuum. The resultant oil was triturated with petrol-ether (b.p. 40-60°C) to give a brown solid (80 mg). ¹H N.m.r. indicated this was predominantly 3,5-di-tert-butyl-4-hydroxybenzaldehyde by comparison with authentic material. δH (CDCl₃); 1.49
(18H, s, tert-butyl), 7.72 (2H, s, ArH), 9.83 (1H, s, CHO). The mass spectrum of the solid showed the parent ion for the aldehyde (m/e 234) and a trace of the parent ion for the required adduct m/e 491 was present at less than 1%.

6. Preparation of Aldoximes

All oximes (unless otherwise stated) were prepared by a similar method to that described by Vogel. The aldehyde or its bisulphite addition compound (1 mol) were stirred with excess of distilled water. To this was added an aqueous solution of sodium hydroxide (4 mol), followed by an aqueous solution of hydroxylammonium chloride (2 mol). When the solution became clear, small lumps of solid carbon dioxide were added until a heavy white precipitate resulted. The precipitate was filtered, washed well with water, and dried. Recrystallisation was achieved from diethyl ether/petrol-ether (b.p. 40-60°C) mixtures. Completion of the reaction was confirmed by the absence of a peak at \( \nu_{\text{max}} \) 1600-1800 (C=O) cm\(^{-1}\), in the i.r. spectrum.

6.1 Synthesis of 4-Benzoylbenzaldoxime

A modification of the above technique was required to prevent the dioxime being formed. The bisulphite addition compound of 4-benzoylbenzaldehyde (2.7 g, 7.7 mmol) and sodium hydroxide (3.8 g) were dissolved in distilled water (20 ml) and stirred rapidly. To this was slowly added a solution of hydroxylammonium chloride (0.48 g, 6.9 mmol) in distilled water (50 ml), drop-wise. The solution was filtered and solid carbon
dioxide added to the filtrate to precipitate the oxime, which was filtered and dried. White crystals were obtained from ether/petroleum-ether (b.p.40-60°C) (1.15 g, 66%). M.p. 85-88°C (Found: C, 74.5; H, 5.05; N, 5.8. C\textsubscript{14}H\textsubscript{11}NO\textsubscript{2} requires C, 74.65; H, 4.9; N, 6.2%). M/e 226 (M\textsuperscript{+} + 1, 15%), 225 (M\textsuperscript{+}, 86), 149 (11), 148 (89), 105 (PhCO\textsuperscript{+}, 100), 77 (65), 76 (17); 65 (13), 51 (23), 28 (24). ν\textsubscript{max} (Nujol) 1655s (C=O, ketone), 3300bd (OH) cm\textsuperscript{-1}.

7. **Preparation of Hydroximoyl Chlorides**

Unless otherwise stated, the hydroximoyl chlorides were prepared by a similar method to that described by Rheinboldt\textsuperscript{55}.

\[
\text{RCH=NOH + 2 NOCl} \rightarrow \text{RC=NOH + 2 NO + HCl}
\]

The oxime (1 mol) was dissolved in dry diethyl ether, protected from the atmosphere with a drying tube, and cooled in an ice/salt bath (-15°C). Nitrosyl chloride (2.2 mol) was carefully added as a solution in diethyl ether and the mixture stirred for 15-30 min; a transient green coloration was often noted. The solution was allowed to warm to room temperature and the solvent removed at room temperature. Recrystallisation was achieved by dissolving in a minimum volume of chloroform or ether, adding excess petroleum ether (b.p.40-60°C), followed by chilling.
7.1 Synthesis of 4-Methoxybenzhydroximoyl Chloride

This was prepared by the above technique. White flaky crystals (53%) were obtained from chloroform/n-pentane. M.p. 85-87°C (lit. 60 88-89°C).

7.2 Synthesis of 4-Benzoylembenzhydroximoyl Chloride

4-Benzoylbenzaldoxime (0.85 g, 3.8 mmol) was treated, as above, with nitrosyl chloride (2.5 g, 38 mmol). White crystals (0.6 g, 61%) were obtained from chloroform/petroleum-ether (b.p. 40-60°C). M.p. 155-157°C. (Found: C, 64.5; H, 3.8; N, 5.6. C_{14}H_{10}NO_{2}Cl requires C, 64.7; H, 3.85; N, 5.4%). M/e 261 (M⁺, <1%), 259 (M⁺, 1%), 223 (M⁺-HCl, 72), 146 (62), 105 (100), 88 (20), 77 (60), 28 (17), 16 (45). δH (CDCl₃): 7.3-8.2 (9H, m, ArH), 12.12bd (1H, s, OH). ν_max (Nujol) 1632 (C=O), 3220 (OH) cm⁻¹.

7.3 Synthesis of 3,4,5-Trimethoxybenzhydroximoyl Chloride

This was prepared by the above technique. White needles (90%) were obtained from diethyl ether/petroleum-ether (b.p. 40-60°C). M.p. 94-98°C. δH (CDCl₃): 3.82 (9H, s, MeO), 7.01 (2H, s, ArH), 8.94 (1H, s, OH).

7.4 Synthesis of 4-Carboxybenzhydroximoyl Chloride

This was prepared by the general method given above. The oxime was insoluble in diethyl ether and the reaction was carried out as a fine suspension. A white solid was obtained from ethanol (66%). M.p. 200°C (decomp.) (lit. 55 198-199°C). Mass spectrum m/e 199/201 (M⁺), 163 (M⁺-HCl). No peak m/e 165 attributable to starting material was detected.
7.5 Synthesis of 2,4,6-Trimethoxybenzonitrile Oxide

This was prepared from 2,4,6-trimethoxybenzaldoxime and sodium hypobromite solution according to the method described by Grundmann and Dean. White crystals were obtained from methanol (63%). M.p. 155-160 (decomp.) (lit. 160-170 with decomposition). The i.r. spectrum showed a sharp absorption at $v_{\text{max}}$ 2300 cm$^{-1}$ characteristic of nitrile oxides.

7.6 Synthesis of Ethyl Chlorooximinoacetate

This was prepared by a similar method to that described in the literature. Glycine ethyl ester hydrochloride (9.7 g, 0.50 mol) was dissolved in distilled water (95 ml) and cooled well in an ice/salt bath. Concentrated hydrochloric acid (49 ml, 57 g of 32% w/w HCl aq. S.G. = 1.16, 0.50 mol) was then added to the mixture. A solution of sodium nitrite (34.5 g, 0.50 mol) in distilled water (50 ml) was then added dropwise, with cooling and stirring. The addition of hydrochloric acid and sodium nitrite solution was repeated once more, as above. While still cool, the mixture was quickly filtered and the residue of white needles dried in a desiccator. The dried product was dissolved in diethylether, filtered and the filtrate reduced to a small volume. White needles (55%) were obtained by adding excess petroleum ether (b.p. 40-60°C) and cooling. M.p. 76-78°C (lit. 80°C).

7.7 Synthesis of Methyl Chlorooximinoacetate

This was prepared in an identical manner to the ethyl analogue, in 68% yield. M.p. 69-71°C.
8. Preparation of Isoxazolines

8.1 Synthesis of 3-(4-Methoxyphenyl)-4,5-tetramethylene-2-isoxazoline

4-Methoxybenzhydroximoyl chloride (0.75 g, 4.0 mmol) and cyclohexene (2.0 g, 24 mmol) were dissolved in toluene (100 ml) and heated under reflux for 24 h until the evolution of hydrogen chloride was no longer detectable with moist litmus paper. The solvent was removed under vacuum to give a dark tar, which was purified by column chromatography (Al$_2$O$_3$/CH$_2$Cl$_2$) and collected as a yellow oily solid (0.30 g, 32.5%). T.l.c. (Al$_2$O$_3$/CH$_2$Cl$_2$). R$_f$ 0.64. Trituration with n-pentane, followed by recrystallisation from ethanol gave white needles (83% recovered). M.p. 70-71°C. (Found: C, 72.7; H, 7.5; N, 6.0. C$_{14}$H$_{17}$NO$_2$ requires C, 72.7; H, 7.4; N, 6.1%). M/e 232 (M$^+$ + 1, 25%), 231 (M$^+$, 100), 160 (20), 149 (20), 28 (42). $\delta$H (CDCl$_3$): 1.0-2.7 (8H, m, ring CH$_2$), 3.10-3.50 (1H, m, isoxazoline 4-H), 3.87 (3H, s, OCH$_3$), 4.27-4.68 (1H, m, isoxazoline 5-H), 6.95 (2H, d, J 9Hz, ArH), 7.70 (2H, d, J 9Hz, ArH). $\nu_{\text{max}}$ (nujol) 1612 (C=N) cm$^{-1}$.

8.2 Synthesis of 4,5-Hexamethylene-3-(4-methoxyphenyl)-2-isoxazoline

4-Methoxybenzhydroximoyl chloride (1.5 g, 8.1 mmol) and cis-cyclooctene (8.9 g, 81 mmol) were dissolved in toluene (200 ml) and heated under reflux for 80 h. The solvent and excess dipolarophile were removed under vacuum and the oily residue was purified by column chromatography (Al$_2$O$_3$, CH$_2$Cl$_2$) to give white crystals (1.42 g, 68%). White flakes were
recovered from ethanol (82% recovered). M.p. 84-85°C
(Found: C, 73.8; H, 8.2; N, 5.3. C_{16}H_{21}NO_2 requires C, 74.1; H, 8.2; N, 5.4%). M/e 260 (M^+ + 1, 25%), 259 (M^+, 100), 188 (23), 160 (33), 41 (25), 28 (88), 18 (100). δ H, (CDCl_3): 0.8-2.3 (12H, m, CH_2), 3.16-3.63 (1H, m, isoxazoline 4-H), 3.82 (3H, s, OMe), 4.22-4.70 (1H, m, isoxazoline 5-H), 6.95 (2H, d, J 9Hz, ArH), 7.65 (2H, d, J 9Hz, ArH). δ C (CDCl_3) 24.3, 24.4, 24.7, 24.9, 25.1, 29.7 (CH_2); 49.9 (isoxazoline CH); 54.8 (MeO); 84.7 (isoxazoline CH-O); 113.75 (aromatic CH), 121.4 (aromatic C), 127.9 (aromatic CH), 160.3^* (aromatic C-OMe), 161.5^* (C=N). \nu_{\text{max}} \text{(nujol)} 1610 (C=N) cm^{-1}.

8.3 Synthesis of 5-Hexyl-3-(4-methoxyphenyl)-2-isoxazoline
4-Methoxybenzhydroximoyl chloride (0.75 g, 4.0 mmol) and oct-1-ene (4.0 g, 36 mmol) were dissolved in toluene (100 ml) and heated under reflux for 80 h, until the evolution of hydrogen chloride was minimal. The solvent and excess dipolarophile were removed by evaporation under reduced pressure and the resultant oil was triturated with petroleum-ether (b.p.40-60°C) to give pale yellow crystals (0.55 g, 53%). White flakes were recovered from ethanol (64% recovered). M.p. 79-80°C (Found: C, 73.55; H, 8.9; N, 5.2. C_{16}H_{23}NO_2 requires C, 73.5; H, 8.9; N, 5.4%). M/e 261 (M^+). δ H (CDCl_3): 0.8-1.8 (13H, m, CH_2 and CH_3), 2.9-3.5 (1H, m, isoxazoline 4-H), 3.80 (3H, s, OMe), 4.3-4.9 (1H, m, isoxazoline 5-H), 6.90 (2H, d, J 9Hz, ArH), 7.60 (2H, d, J 9Hz, ArH).
8.4 **Synthesis of 3-(4-Methoxyphenyl)-5-methyl-4,5-tetramethylene-2-isoxazoline**

4-Methoxybenzhydroximoyl chloride (2.5 g, 13.5 mmol) and 1-methylcyclohexene (12.7 g, 133 mmol) were dissolved in toluene (200 ml) and heated under reflux for 60 h, when the evolution of hydrogen chloride was minimal. The solvent and excess dipolarophile were evaporated under vacuum and the residue was purified by column chromatography (Al₂O₃, CH₂Cl₂) to give an oily solid (57%). Three recrystallisations from ethanol yielded white crystals (39% recovered). M.p.100-101°C.  

(Found: C, 73.45; H, 7.9; N, 5.6. C₁₅H₁₉NO₂ requires C, 73.4; H, 7.8; N, 5.7%). M/z 246 (M⁺ + 1, 17%), 245 (M⁺, 100), 230 (27), 202 (36), 160 (33), 28 (21), 18 (79). δH (CDC₃): Δ1.1-2.2 (8H, m, CH₂), 3.01 (1H, t bd, CH), 3.78 (3H, s, OMe), 6.90 (2H, d, J 9Hz, ArH), 7.63 (2H, d, J 9Hz, ArH). δC (CDC₃): 20.3, 21.1, 26.3*, 31.3 (CH₂), 26.55* (CH₃), 49.5 (isoxazoline CH), 54.9 (OMe), 84.4 (isoxazoline C-O), 113.8 (aromatic CH), 122.0 (aromatic C), 127.9 (aromatic CH), 160.4** (aromatic C-OMe), 161.8** (C=N). νmax 1608 (C=N) cm⁻¹.

8.5 **Synthesis of 4,5-Hexamethylene-3-(3,4,5-trimethoxyphenyl)-2-isoxazoline**

3,4,5-Trimethoxybenzhydroximoyl chloride (0.50 g, 2.0 mmol) and cis-cyclooctene (2.25 g, 20 mmol) were dissolved in toluene (200 ml) and heated under reflux for 60 h. The solvent and excess dipolarophile were evaporated under vacuum and the resultant oil purified by column chromatography (Al₂O₃, CH₂Cl₂) to give a pale yellow oil (85%). Purification was achieved by
trituration with petroleum-ether (b.p. 40-60°C) and recrystallisation from ethanol to give white crystals (76% recovered). M.p. 107-109°C. (Found: C, 67.55; H, 7.9; N, 4.4. C_{18}H_{25}NO_{4} requires C, 67.7; H, 7.9; N, 4.4%). M/e 320 (M^+ + 1, 24%), 319 (M^+, 100), 304 (10), 28 (41), 18 (88).

δH (CDCl₃): 1.1-2.2 (12H, m, CH₂), 3.11-3.51 (1H, m, isoxazoline 4-H), 3.83 (9H, s, OMe), 4.31-4.59 (1H, m, isoxazoline 5-H), 6.86 (2H, s, ArH). δC (CDCl₃) 24.8, 24.9, 25.2, 25.4, 25.6, 30.2 (CH₂), 50.3 (isoxazoline CH-C), 56.2 (2 MeO), 60.9 (1 MeO), 85.6 (isoxazoline CH-O), 104.4 (2 aromatic CH), 124.8 (aromatic C), 139.6 (C=N), 153.4 (2 aromatic C-OMe), 162.3 (aromatic C-OMe).

8.6 **Synthesis of 3-(4-Benzoylphenyl)-4,5-decamethylene-2-isoxazoline**

4-Benzoylbenzhydroximoyl chloride (0.75 g, 2.9 mmol) and cis-cyclododecene (5.0 g, 30 mmol) were dissolved in xylene (250 ml) and an internal temperature of 110-115°C was maintained, using an automatic temperature controller attached to an electric oil-bath, for 50 h whilst passing a stream of nitrogen through the solution. The solvent was removed on a rotary evaporator and excess dipolarophile removed under high vacuum. The resultant oil was triturated with petroleum-ether (b.p. 40-60°C) to give an off-white solid (49%). White crystals were obtained from ethanol (82% recovered). M.p. 105°C. (Found: C, 80.0; H, 7.9; N, 3.5. C_{26}H_{31}NO_{2} requires C, 80.2; H, 8.0; N, 3.6%). M/e 390 (M^+ + 1, 36%), 389 (M^+, 100), 277 (22), 262 (18), 237 (15), 234 (15), 105 (81), 77 (37), 55 (26), 41 (37). δH (CDCl₃): 1.1-1.9 (20H, m, CH₂), 3.34-3.67 (1H, m, isoxazoline 4-H),
4.67-4.99 (1H, m, isoxazoline 5-H), 7.3-7.9 (9H, m, ArH).

δC CDCl₃; 21.8, 22.1, 22.7, 23.1, 23.7, 26.8, 27.0, 29.7,
31.6 (10 ring CH₂), 47.9 (isoxazoline CH-C), 84.5 (isoxazoline
CH-O), 126.7, 128.4, 130.0, 130.5, 132.6, 133.2, 137.4,
138.4, 158.8 (aromatic and isoxazoline C), 195.8 (C=O).
νmax 1607 (C=N), 1637 (C=O) cm⁻¹.

8.7 Synthesis of 3-(4-Benzoylphenyl)-5-hexyl-2-isoxazoline.

4-Benzoylbenzhydroximoyl chloride (0.50 g, 1.9 mmol) and
oct-1-ene (2.2 g, 20 mmol) were dissolved in toluene (170 ml)
and heated under reflux for 30 h until the evolution of
hydrogen chloride was minimal. The solvent was evaporated
under vacuum and the resultant oil was triturated with petroleum-
ether (b.p.40-60°C) to give a white solid (77%). Two recrystal-
alisations from ethanol afforded the pure white solid (86%
recovered). M.p. 83-84°C. (Found: C, 78.9; H, 7.3; N,
4.2. C₂₂H₂₅NO₂ requires C, 78.8; H, 7.5; N, 4.2%). M/e
336 (M⁺ + 1, 24%), 335 (M⁺, 49), 251 (34), 250 (100), 223 (13),
224 (22), 105 (78), 77 (39), 43 (19), 41 (22), 32 (14), 28 (66),
18 (100), 17 (49). δH (CDCl₃) 0.5-2.0 (13H, m, hexyl), 2.8-
3.5 (2H, m, isoxazoline CH₂), 4.5-4.9 (1H, m, isoxazoline CH),
7.28-7.95 (9H, m, ArH). νmax (nujol) 1610 (C=N), 1652 (C=O)
cm⁻¹.

8.8 Synthesis of 3-Ethoxycarbonyl-4,5-hexamethylene-2-
isoxazoline.

Ethyl chlororoximinoacetate (5.0 g, 33 mmol) and cis-
cyclooctene (36 g, 330 mmol) were dissolved in toluene (200 ml)
and heated under reflux for 100 h until the evolution of hydrogen
chloride was minimal. The solvent was evaporated and the resultant dark tarry liquid was purified by column chromatography (SiO₂, CH₂Cl₂) and then heated under vacuum (50°C, 0.01 mmHg) to remove all traces of excess dipolarophile, yielding a yellow liquid (82%). Finally, the liquid was distilled under high vacuum (100°C, 0.01 mmHg) to afford a colourless liquid (95% recovered). $\eta_D^{20}$ 1.489. (Found: C, 64.2; H, 8.7; N, 6.4. $C_{12}H_{19}NO_3$ requires C, 64.0; H, 8.5; N, 6.2%) M/e 225 (M⁺, 32%), 152 (45), 82 (14), 67 (11), 55 (18), 54 (16), 41 (27), 29 (100), 28 (18), 27 (20). $\delta$H(CDCl₃) 1.32 (3H, t, J 7Hz, CH₃ of Et), 1.1-2.1 (12H, m, ring CH₂), 3.12-3.40 (1H, m, isoxazoline 4-H), 4.27 (2H, q, J 7Hz, CH₂ of Et), 4.41-4.66 (1H, m, isoxazoline 5-H). $\delta$C (CDCl₃) 13.6 (CH₃ of Et), 24.0, 24.6, 24.95, 25.0, 29.2 (6 ring CH₂), 48.4 (isoxazoline CH-C), 61.2 (CH₂ of Et), 87.4 (isoxazoline CH-O), 155.7* (isoxazoline C), 160.3* (C=O). $\nu_{max}$ (film) 1722 (C=O) cm⁻¹.

8.9 **Synthesis of 3-Ethoxycarbonyl-4,5-hexamethylene-5-methyl-2-isoxazoline**

Ethyl chlorooximinoacetate (3.0 g, 20 mmol) and 1-methylcyclohexene (19 g, 200 mmol) were dissolved in toluene (200 ml) and heated under reflux for 80 h until the evolution of hydrogen chloride was minimal. The solvent was evaporated under vacuum and the residue purified by column chromatography (SiO₂, CH₂Cl₂) and heating under high vacuum (35°C/0.01 mmHg) to remove the last traces of excess dipolarophile, yielding a yellow liquid (74%). The liquid was further purified by distillation under high vacuum (60°C, 0.01 mmHg) affording a colourless liquid
\( \text{C}_{11}\text{H}_{17}\text{NO}_{3} \) requires \( \text{M}^{+} \) 211.1208. \( \delta \text{H} \) (CDCl\(_3\)) 1.29 (3H, s, Me), 1.36 (3H, t, J 7 Hz, CH\(_3\) of Et), 1.3-2.2 (8H, m, ring CH\(_2\)), 3.00 (1H, m, isoxazoline 4-H), 4.32 (2H, q, J 7 Hz, CH\(_2\) of Et). \( \delta \text{C} \) (CDCl\(_3\)) 13.45 (CH\(_3\) of Et), 19.2, 19.6, 24.0, 25.45, 30.6, (CH\(_3\) & ring CH\(_2\)), 48.7 (isoxazoline CH-C), 60.9 (CH\(_2\) of Et), 88.0 (isoxazoline C-O), 155.35* (isoxazoline C=N), 160.3* (C=O).

8.10 Synthesis of 4,5-Hexamethylene-3-(2,4,6-trimethoxyphenyl)-2-isoaxazoline.

2,4,6-Trimethoxybenzonitrile oxide (0.51 g, 2.4 mmol) and cis-cyclooctene (1.1 g, 10 mmol) were dissolved in benzene (100 ml) and heated under reflux for 20 min. The solvent and excess dipolarophile were removed to leave a yellow oil. The infra-red spectrum showed the disappearance of most of the starting material (\( \nu_{\text{max}} \) 2300 (CNO) cm\(^{-1}\)) and formation of isocyanate (\( \nu_{\text{max}} \) 2250 (NCO) cm\(^{-1}\)). Aniline (excess) was added and the mixture heated for \( \frac{1}{2} \) h to convert all the isocyanate to the corresponding diarylurea, which was precipitated from diethyl ether to give an off-white solid (45%). This was shown to be \( \text{N-phenyl-N'}-(2,4,6\text{-trimethoxyphenyl}) \text{ urea} \) by comparison of its i.r. spectrum with an authentic sample. The filtrate was washed three times with 5% aqueous hydrochloric acid, twice with distilled water, and dried over anhydrous magnesium sulphate. The adduct was further purified by column chromatography (Al\(_2\)O\(_3\)/CH\(_2\)Cl\(_2\)) to give an off-white solid (51%). A pure white solid was obtained after two recrystallisations from aqueous methanol. M.p. 145-147\( ^{\circ} \text{C} \). (Found: C, 67.6; H, 7.9; N, 4.35. \( \text{C}_{18}\text{H}_{25}\text{NO}_{4} \) requires C, 67.7; H, 7.9; N, 4.4%).
\( M/e \ 319 \ (M^+). \ \delta H (CDCl_3): \ 0.7-2.3 \ (12H, \text{ m, CH}_2), \ 3.2-3.5 \ (1H, \text{ m, isoxazoline 4-H}), \ 3.73 \ (6H, \text{ s, MeO}), \ 3.78 \ (3H, \text{ s, MeO}), \ 4.4-4.7 \ (1H, \text{ m, isoxazoline 5-H}), \ 6.10 \ (2H, \text{ s, ArH}). \ \delta C (CDCl_3): \ 23.3, \ 25.15, \ 25.5, \ 26.35, \ 26.75, \ 29.8 \ (\text{CH}_2), \ 53.1 \ (\text{isoxazoline CH-C}), \ 55.2 \ (\text{MeO}), \ 55.8 \ (2 \ \text{MeO}), \ 84.1 \ (\text{isoxazoline CH-O}), \ 90.65 \ (2 \ \text{aromatic CH}), \ 157.1, \ 159.7, \ 162.1 \ (4 \ \text{aromatic C and isoxazoline C=N}). \)

The reaction was repeated, allowing it to proceed at room temperature for one week until the disappearance of nitrile oxide \( (\nu_{\text{max}} \ 2300 \ \text{cm}^{-1}) \) in the infra-red spectrum; it was noted that some isocyanate \( (\nu_{\text{max}} \ 2250 \ \text{cm}^{-1}) \) had been formed although the reaction mixture had not been warmed above room temperature. The mixture was then treated as before to afford the diarylurea (25%) and adduct (68%).

8.11 Synthesis of 3-(4-Carboxyphenyl)-4,5-hexamethylene-2-isoxazoline.

4-Carboxybenzhydroximoyl chloride (0.90 g, 4.5 mmol) was finely powdered and suspended in dry toluene (100 ml). A large excess of cis-cyclooctene (25 g, 227 mmol) was added and the mixture heated under reflux for 120 h until the evolution of hydrogen chloride was minimal. The solvent was evaporated under vacuum to leave a brown solid (1.13 g), which was purified by column chromatography (SiO\(_2\), CHCl\(_3\)) to yield a white solid (70%). The solid was further purified by recrystallisation from ethanol (84%). M.p. 270⁰C (decomp.). (Found: M\(^+\) 273.1356. C\(_{16}\)H\(_{19}\)NO\(_3\) requires M 273.1365). M/e 273 (M\(^+\) 79%), 149 (42), 91 (74), 67 (37), 65 (32), 55 (37), 41 (47), 28 (100), 18 (53). \( \delta H (d_6-\text{DMSO}): \) 0.7-2.2 (12H, m, ring CH\(_2\)), 3.3-3.8
(1H, m, isoxazoline 4-H), 4.3-4.7 (1H, m, isoxazoline 5-H),
7.73 (2H, d, J 9Hz, ArH), 8.10 (2H, d, J 9Hz, ArH). δC
(d6-DMSO): 24.2, 24.45, 25.0, 29.1 (6 ring CH₂), 48.55 (isox-
azoline CH-C), 85.45 (isoxazoline CH-O), 127.0, 129.9 (4
aromatic CH), 131.7, 133.1 (aromatic C), 161.7* (isoxazoline
C=N), 166.8* (C=O). νmax (nujol) 1610 (C=N), 1680 (C=O) cm⁻¹.

8.12 Synthesis of 3-Carboxylic acid-4,5-hexamethylene-2-
isonoxazoline.

3-Ethoxycarbonyl-4,5-hexamethylene-2-isoxazoline (2.0 g, 8.9
mmol) was added to a 10% aqueous solution of sodium hydroxide
(10 ml) and stirred for 1.5 h at room temperature, when a white
precipitate had formed. A portion of water (20 ml) was added
and stirring continued for a further 20 h. The solution was
washed with diethyl ether (20 ml), two times, to remove any
non-acidic impurities. The aqueous portion was acidified drop-
wise with a 10% solution of aqueous hydrochloric acid and
cooled in an ice-bath. The mixture was filtered and the white
solid dried in a desiccator, to give the product (1.40 g, 80%).
The solid was purified by recrystallisation from toluene (89%).
M.p.135°C. (Found: C, 61.0; H, 7.8; N, 7.0. C10H15NO3
requires C, 60.9; H, 7.7; N, 7.1%). M/e 197 (M⁺). δH (CDCl₃):
1.0-2.2 (12H, m, CH₂), 3.25 (1H, t of d, isoxazoline 4-H),
4.54 (1H, t of d, isoxazoline 5-H), 11.21 (1H, s, CO₂H). νmax
(nujol) 1690 (C=O), 2900 bd (OH) cm⁻¹.
9. **1,3-Dipolar Cycloaddition to Polydienes**

9.1 **Reaction of cis-1,4-Polybutadiene with α-4-Benzoylphenyl-\(N\)-phenylNitrom**

Cis-1,4-polybutadiene (0.26 g, 4.8 mmol) was cut into small pieces and dissolved in sodium dried xylene (150 ml) by adding slowly with rapid stirring and then stirring for a further 0.5 h. α-4-Benzoylphenyl-\(N\)-phenylnitron (0.50 g, 1.7 mmol) was added to the mixture, which was heated to 120°C under nitrogen, with stirring and was maintained at this temperature for 80 h, with the aid of an automatic temperature controller. After cooling the reaction mixture was filtered, reduced to a small volume (50 ml) and polymer precipitated by the addition of methanol. The polymer was filtered and purified by twice more dissolving in xylene and precipitating with methanol to yield modified polymer (58%). The combined mother liquors from above were filtered through celite to remove suspended polymer and evaporated to give an off-white solid, which was shown to be unreacted nitron (20%) by t.l.c. (SiO\(_2\)/MeOH).

The absence of the starting nitron in the product was established by t.l.c. (SiO\(_2\)/MeOH); the polymer and cis-polybutadiene both had \(R_f\) values of 0.0, while that for the mixture was 0.6. The molar ratio of modified (isoxazolidine) to unmodified (alkene) moieties was determined separately by i.r., \(^1\)H n.m.r. and \(N\)-analysis. By i.r., the relative absorbance at \(\nu1650\) (C=O) cm\(^{-1}\) and \(\nu2850\) (C-H) cm\(^{-1}\) was measured using a series of reference mixtures by reference to a graph of these relative absorbances for known mixtures of the polymer and the starting nitron. Making due compensation for the polymer absorption
v1650 cm\(^{-1}\) (C=\(\text{C}\)), the ratio of reacted to \(\nu^\text{n}\) reacted structural units in the polymer was found to be 24:1. The techniques of \(^1\text{H-}n\text{-m.r.}\) and \(N\)-analysis (using similar methods as described below) gave values, for the above ratio, of 22:1 and 18:1 respectively.

The mean value, 21:1 is equivalent to a yield of 13.6\%, based on the initial equivalent quantity of nitrone, for a starting molar ratio of 2.8:1 butadiene units to moles of nitrone.

9.2 The Reactions of Nitrile Oxides with Polydienes

A series of reactions were carried out using several nitrile oxides, polydienes and reacting molar ratios. The same general methods of reaction, work-up and analysis were used (unless otherwise stated) and a generalised technique is given below. Two specific examples are also given in detail and all the results are summarised in tabular form.

General Method

A measured quantity of polymer was dissolved in sodium dried toluene (ca. 200 ml for every 0.1 g polymer), by cutting the polymer into small pieces, adding them slowly piece by piece to the solvent with stirring, and allowing the mixture to stir for several hours until fully dissolved. The required amount of hydroximoyl chloride was then added such that a predetermined molar ratio of alkene structural units in the polymer and 1,3-dipole precursor was achieved. The mixture was then heated under reflux for a period of 80 h, sufficient to allow virtually complete thermolysis of most hydroximoyl chlorides.
After cooling the solution was filtered through a pad of cellite to remove any insoluble material and then reduced to a very small volume (ca. 5-10 ml) on a rotary evaporator. The polymer was precipitated by adding excess methanol and allowing to settle (if necessary overnight). The precipitation was repeated twice more by dissolving in the minimum volume of chloroform and adding excess methanol. The solvent was allowed to evaporate and final traces removed by warming at 40°C under high vacuum (ca. 0.02 mmHg) for several hours. The degree of polymer modification was examined by $^1$H-n.m.r. (table 85) and $^N$-analysis (table 84). In cases where the initial reacting molar ratio of polymer structural units to 1,3-dipole precursor was 1:1, the modified polymer was also examined qualitatively by $^{13}$C-n.m.r. (table 86).

9.2.1 Example 1: Reaction of Methyl Chlorooximinoacetate and cis-1,4-Polybutadiene at 1:10 molar ratio.

Cis-1,4-polybutadiene (0.78 g, 14.5 millimolar equivalents of alkene structural units) and methyl chlorooximinoacetate (0.20 g, 1.45 mmol) were dissolved in dry toluene (400 ml) and heated under reflux for 80 h. The solution was filtered, the solvent evaporated and the polymer precipitated three times with methanol. Drying as described above gave a brown material (0.44 g, 56% based on original polymer weight). $^1$H-N.m.r. $\delta$H (CDCl$_3$): 1.3-2.8 (bd m, polymer CH$_2$), 3.3 (bd s, isoxazoline CH), 3.82 (s, MeO), 4.5 (bd s, isoxazoline CH), 5.4 (bd s, polymer alkene CH). The integral for the peak at 3.82$\delta$ = 12 units, and the integral for the peak at 5.4$\delta$ = 85 units.
Therefore the ratio of unreacted alkene groups to modified groups = \( \frac{85}{2} \) (2CH) : \( \frac{12}{3} \) (1 MeO) = 11:1.

By elemental analysis, %N in polymer = 1.62%.

\[
\begin{align*}
\text{Molecular weight of modified polymer} & = 155X + 54Y \\
\therefore \% N & = \frac{14 \times 100X}{155X+54Y} = 1.62 \\
& = \frac{1149X}{87.5Y}
\end{align*}
\]

Therefore ratio of unreacted alkene groups to modified groups = 13:1

Mean ratio of unreacted alkene groups to modified groups by the two experimental methods = 12:1.

Yield based on original amount of nitrile oxide precursor is therefore 77%.

The structure of the modified polymer by elemental analysis requires C, 82.7%; H, 10.2%. (Found: C, 75.9%; H, 9.5%).

9.2.2 Example 2:-

Reaction of 3,4,5-Trimethoxybenzhydroximoyl Chloride and cis-1,4-Polyisoprene at 1:1 molar ratio.

Cis-1,4-polyisoprene (0.28 g, 4.1 millimolar equivalents of alkene structural units) and 3,4,5-trimethoxybenzhydroximoyl
chloride (1.0 g, 4.1 mmol) were dissolved in dry toluene (200 ml) and heated under reflux for 80 h. The solution was filtered, the solvent evaporated, and the polymer precipitated three times with methanol. Drying as described above afforded a dark brown solid (0.18 g, 65% based on original polymer weight). δH (CDCl₃) 1.0-2.4 (bd m, polymer CH₂ and CH₃), 3.82 (s, MeO), 5.1 (bd s, polymer alkene CH), 6.85 (bd s, ArH). The integral for peak at 3.82 δ = 65 units; integral for peak at 5.1 δ = 36 units. Therefore the ratio of unreacted alkene groups to modified groups = 36/1 \(1\text{CH} : 65/9\) (3 MeO) = 5.1.

As previous example, %N in polymer = 1.39%.

\[
\text{Molecular weight of polymer} = 277X + 68Y
\]

\[
\frac{\% N}{277X+68Y} = \frac{14 \times 100X}{1015X} = 1.39
\]

\[
1015X = 94.5Y
\]

Therefore ratio of unreacted alkene groups to modified groups 11:1 by N-analysis.

Mean ratio of unreacted alkene groups to modified groups by the two analytical methods = 8:1. The yield based on the original amount of nitrile oxide precursor is then 11%.

The structure of the modified polymer by elemental analysis requires C, 81.8; H, 10.4%. (Found: C, 62.4; H, 8.0%).
NOTE:

An exception to the above general method and examples, was reactions using 2,4,6-trimethoxybenzonitrile oxide. In such cases, the required molar equivalent of the stable nitrile oxide was dissolved in a solution of polymer in dry toluene (prepared as in the general method above). The reaction mixture was protected from the atmosphere with an anhydrous CaCl\(_2\) guard-tube and allowed to stand in a thermostatic water bath at 40°C for 8 weeks. The mixture was then worked up and analysed, as described under the general method and examples.
<table>
<thead>
<tr>
<th>1,3-Dipole</th>
<th>Initial Molar Ratio</th>
<th>% N in Product</th>
<th>Reacted Molar Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>( p-\text{PhCO.C}_6\text{H}_4\text{CH}=\text{N(O)Ph} )</td>
<td>3:1</td>
<td>1.1</td>
<td>18:1</td>
</tr>
<tr>
<td>( p-\text{PhCO.C}_6\text{H}_4\text{CNO} )</td>
<td>3:1</td>
<td>1.6</td>
<td>12:1</td>
</tr>
<tr>
<td>( p-\text{MeOC}_6\text{H}_4\text{CNO} )</td>
<td>1:1</td>
<td>3.1</td>
<td>5:1</td>
</tr>
<tr>
<td>( 10:1 )</td>
<td>1.5</td>
<td>14:1</td>
<td></td>
</tr>
<tr>
<td>( 50:1 )</td>
<td>0.2</td>
<td>114:1</td>
<td></td>
</tr>
<tr>
<td>( 3,4,5-(\text{MeO})_3\text{C}_6\text{H}_2\text{CNO} )</td>
<td>1:1</td>
<td>2.7</td>
<td>5:1</td>
</tr>
<tr>
<td>( 10:1 )</td>
<td>0.95</td>
<td>22:1</td>
<td></td>
</tr>
<tr>
<td>( 30:1 )</td>
<td>0.4</td>
<td>63:1</td>
<td></td>
</tr>
<tr>
<td>( 50:1 )</td>
<td>0.3</td>
<td>81.5:1</td>
<td></td>
</tr>
<tr>
<td>( 2,4,6-(\text{MeO})_3\text{C}_6\text{H}_2\text{CNO} )</td>
<td>1:1</td>
<td>3.8</td>
<td>2:1</td>
</tr>
<tr>
<td>( 10:1 )</td>
<td>1.6</td>
<td>11:1</td>
<td></td>
</tr>
<tr>
<td>( p-\text{MeOCH}_2\text{CH}_2\text{OC}_6\text{H}_4\text{CNO} )</td>
<td>1:1</td>
<td>1.5</td>
<td>13:1</td>
</tr>
<tr>
<td>( 10:1 )</td>
<td>0.5</td>
<td>47:1</td>
<td></td>
</tr>
<tr>
<td>( 50:1 )</td>
<td>0.1</td>
<td>321:1</td>
<td></td>
</tr>
<tr>
<td>( p-\text{MeO-(CH}_2\text{CH}_2)O}_6\text{C}_6\text{H}_4\text{CNO} )</td>
<td>1:1</td>
<td>0.9</td>
<td>21:1</td>
</tr>
<tr>
<td>( 10:1 )</td>
<td>0.2</td>
<td>99:1</td>
<td></td>
</tr>
<tr>
<td>( \text{EtO}_2\text{CCNO} )</td>
<td>1:1</td>
<td>6.3</td>
<td>1:1</td>
</tr>
<tr>
<td>( \text{MeO}_2\text{CCNO} )</td>
<td>1:1</td>
<td>6.05</td>
<td>1:1</td>
</tr>
<tr>
<td>( 10:1 )</td>
<td>1.6</td>
<td>13:1</td>
<td></td>
</tr>
<tr>
<td>( 30:1 )</td>
<td>0.7</td>
<td>35:1</td>
<td></td>
</tr>
<tr>
<td>( p-\text{HO}_2\text{C-C}_6\text{H}_4\text{CNO} )</td>
<td>1:1</td>
<td>0.6</td>
<td>39:1</td>
</tr>
<tr>
<td>( 10:1 )</td>
<td>0.1</td>
<td>181:1</td>
<td></td>
</tr>
</tbody>
</table>

2 Non-stereospecific Polybutadiene

(13% pendent vinyl groups)

| \( \text{MeO}_2\text{CCNO} \) | 1:1 | 2.4 | 8:1 |

*based on vinyl groups
Table 84 (cont.)

1,3-Dipole | Initial Molar Ratio | % N in Product | Reacted Molar Ratio
---|---|---|---

### 3 cis-1,4-Polyisoprene

<table>
<thead>
<tr>
<th>3,4,5-(MeO)$_3$C$_6$H$_2$CNO</th>
<th>1:1</th>
<th>2.35</th>
<th>6:1</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:1</td>
<td>0.75</td>
<td></td>
<td>24:1</td>
</tr>
<tr>
<td>50:1</td>
<td>0.1</td>
<td></td>
<td>168:1</td>
</tr>
</tbody>
</table>

### 4 trans-1,4-Polyisoprene

<table>
<thead>
<tr>
<th>p-MeOC$_6$H$_4$CNO</th>
<th>1:1</th>
<th>2.2</th>
<th>6:1</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:1</td>
<td>0.3</td>
<td></td>
<td>63:1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EtO$_2$CCNO</th>
<th>1:1</th>
<th>4.7</th>
<th>2:1</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:1</td>
<td>0.9</td>
<td></td>
<td>21:1</td>
</tr>
<tr>
<td>30:1</td>
<td>0.4</td>
<td></td>
<td>50:1</td>
</tr>
</tbody>
</table>

### 5 Styrene-butadiene rubber (15% butadiene)

<table>
<thead>
<tr>
<th>p-MeO C$_6$H$_4$CNO</th>
<th>1:1</th>
<th>0.5</th>
<th>3:1</th>
</tr>
</thead>
</table>

### 6 Polychloroprene (75% cis, 25% trans)

<table>
<thead>
<tr>
<th>EtO$_2$CCNO</th>
<th>1:1</th>
<th>1.3</th>
<th>10:1</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:1</td>
<td>0.2</td>
<td></td>
<td>97:1</td>
</tr>
<tr>
<td>1,3-Dipole</td>
<td>Initial Molar Ratio</td>
<td>Reacted Molar Ratios</td>
<td>Yield %</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>---------------------</td>
<td>----------------------</td>
<td>---------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N-Analysis</td>
<td>¹H-NMR</td>
</tr>
<tr>
<td>( p-\text{PhCOC}_6\text{H}_4\text{CHN(O)Ph} )</td>
<td>3:1</td>
<td>18:1</td>
<td>22:1</td>
</tr>
<tr>
<td>( p-\text{PhCOC}_6\text{H}_4\text{CNO} )</td>
<td>3:1</td>
<td>12:1</td>
<td>4:1</td>
</tr>
<tr>
<td>( p-\text{MeOC}_6\text{H}_4\text{CNO} )</td>
<td>1:1</td>
<td>5:1</td>
<td>2:1</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>14:1</td>
<td>13:1</td>
</tr>
<tr>
<td></td>
<td>50:1</td>
<td>114:1</td>
<td>60:1</td>
</tr>
<tr>
<td>( 3,4,5-(\text{MeO})_3\text{C}_6\text{H}_2\text{CNO} )</td>
<td>1:1</td>
<td>5:1</td>
<td>4:1</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>22:1</td>
<td>20:1</td>
</tr>
<tr>
<td></td>
<td>30:1</td>
<td>63:1</td>
<td>53:1</td>
</tr>
<tr>
<td></td>
<td>50:1</td>
<td>81.5:1</td>
<td>85:1</td>
</tr>
<tr>
<td>( 2,4,6-(\text{MeO})_3\text{C}_6\text{H}_2\text{CNO} )</td>
<td>1:1</td>
<td>2:1</td>
<td>1:1</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>11:1</td>
<td>10:1</td>
</tr>
<tr>
<td>( p-\text{MeOCH}_2\text{CH}_2\text{OC}_6\text{H}_4\text{CNO} )</td>
<td>1:1</td>
<td>13:1</td>
<td>10:1</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>47:1</td>
<td>28:1</td>
</tr>
<tr>
<td></td>
<td>50:1</td>
<td>321:1</td>
<td>308:1</td>
</tr>
<tr>
<td>( p-\text{MeO(CH}_2\text{CH}_2\text{O})_6\text{C}_6\text{H}_4\text{CNO} )</td>
<td>1:1</td>
<td>21:1</td>
<td>146:1</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>99:1</td>
<td>249:1</td>
</tr>
<tr>
<td>( \text{EtO}_2\text{CCNO} )</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
</tr>
<tr>
<td>( \text{MeO}_2\text{CCNO} )</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>13:1</td>
<td>11:1</td>
</tr>
<tr>
<td></td>
<td>30:1</td>
<td>35:1</td>
<td>33:1</td>
</tr>
<tr>
<td>( p-\text{HO}_2\text{CC}_6\text{H}_4\text{CNO} )</td>
<td>1:1</td>
<td>39:1</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>181:1</td>
<td>-</td>
</tr>
</tbody>
</table>

* Room temp. 8 weeks

† NOTE: Yields quoted are approximate. Errors can be estimated from the difference between the results from the two techniques.
Table 85 (cont.)

<table>
<thead>
<tr>
<th>1,3-Dipole</th>
<th>Initial Molar Ratio</th>
<th>Reacted Molar Ratios</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>N-Analysis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>5:4:1</td>
<td>8:1</td>
</tr>
<tr>
<td></td>
<td>Non-stereospecific polybutadiene (≈13% vinyl groups)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>N-Analysis</td>
<td>(^1H)-NMR</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MeO(_2)CCNO</td>
<td>5:4:1</td>
<td>8:1</td>
<td>4:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. \textit{cis-1,4-Polyisoprene}</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>p-MeOC(_6)H(_4)CNO</td>
<td>1:1</td>
<td>6:1</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>24:1</td>
<td>24:1</td>
</tr>
<tr>
<td></td>
<td>50:1</td>
<td>168:1</td>
<td>65:1</td>
</tr>
<tr>
<td></td>
<td>3,4,5-(MeO)(_3)C(_6)H(_2)CNO</td>
<td>1:1</td>
<td>11:1</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>43:1</td>
<td>36:1</td>
</tr>
<tr>
<td></td>
<td>30:1</td>
<td>154:1</td>
<td>40:1</td>
</tr>
<tr>
<td></td>
<td>50:1</td>
<td>117:1</td>
<td>109:1</td>
</tr>
<tr>
<td></td>
<td>EtO(_2)CCNO</td>
<td>1:1</td>
<td>2:1</td>
</tr>
<tr>
<td></td>
<td>MeO(_2)CCNO</td>
<td>1:1</td>
<td>2:1</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>22:1</td>
<td>17:1</td>
</tr>
<tr>
<td></td>
<td>30:1</td>
<td>44:1</td>
<td>44:1</td>
</tr>
<tr>
<td>4. \textit{trans-1,4-Polyisoprene}</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>p-MeOC(_6)H(_4)CNO</td>
<td>1:1</td>
<td>6:1</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>63:1</td>
<td>25:1</td>
</tr>
<tr>
<td></td>
<td>EtO(_2)CCNO</td>
<td>1:1</td>
<td>2:1</td>
</tr>
<tr>
<td></td>
<td>MeO(_2)CCNO</td>
<td>10:1</td>
<td>21:1</td>
</tr>
<tr>
<td></td>
<td>30:1</td>
<td>50:1</td>
<td>28:1</td>
</tr>
<tr>
<td>5. \textit{Styrene-butadiene rubber} (15% butadiene)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>p-MeOC(_6)H(_4)CNO</td>
<td>1:1</td>
<td>3:1</td>
</tr>
<tr>
<td>6. \textit{Polychloroprene}</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>EtO(_2)CCNO</td>
<td>1:1</td>
<td>10:1</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>97:1</td>
<td>40:1</td>
</tr>
</tbody>
</table>
102

TABLE 86

$^{13}$C-NMR OF POLYMERS

1. Unmodified Polymers

1.1 cis-1,4-Polybutadiene

$\delta C(CDCl_3): 27.3 (CH_2), 129.5$ (alkene CH).

1.2 cis-1,4-Polyisoprene

$\delta C(CDCl_3): 23.4 (CH_3), 26.5, 32.3$ (CH$_2$),

125.1 (alkene CH), 135.2 (alkene C).

1.3 trans-1,4-Polyisoprene

$\delta C(CDCl_3): 15.9$ (CH$_3$), 26.6, 39.65 (CH$_2$),

124.2 (alkene CH), 134.8 (alkene C).

1.4 Polychloroprene

$\delta C(CDCl_3): 26.5, 38.0$ (cis-CH$_2$), 27.4, 37.3

(trans-CH$_2$), 123.8 (cis-CH), 124.6 (trans-
CH), 134.7 (C-Cl).


1.5 Non-stereospecific Polybutadiene

$\delta C(CDCl_3): 27.4$ (cis CH$_2$) 32.7 (trans CH$_2$), 114.2

(vinyl CH$_2$), 129.4 (cis alkene CH), 130.0

(trans alkene CH), 142.6 (vinyl CH).

Ratio $cis:trans = 1:2.$

Ratio 1,4:1,2 addition $= 7:1.$

ie. about 13% of unsaturation as vinyl end groups.
2. Modified Polymers

Chemical shifts (ppm from Me₄Si) for isoxazoline C's are tabulated for 1:1 molar ratio reactions:

![Isoxazoline structure]

2.1 cis-1,4-Polybutadiene

<table>
<thead>
<tr>
<th>Nitrile oxide</th>
<th>δ3-C</th>
<th>δ4-C</th>
<th>δ5-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>p-MeOC₆H₄CNO</td>
<td>161.1</td>
<td>47.7</td>
<td>83.8</td>
</tr>
<tr>
<td>3,4,5-(MeO)₃C₆H₂CNO</td>
<td>160.8</td>
<td>46.7</td>
<td>83.5</td>
</tr>
<tr>
<td>2,4,6-(MeO)₃C₆H₂CNO</td>
<td>161.9</td>
<td>50.8</td>
<td>82.0</td>
</tr>
<tr>
<td>p-MeOCH₂CH₂OC₆H₄CNO</td>
<td>-</td>
<td>52.2</td>
<td>85.4</td>
</tr>
<tr>
<td>EtO₂CCNO</td>
<td>160.4</td>
<td>46.6</td>
<td>86.0</td>
</tr>
</tbody>
</table>

2.2 cis-1,4-Polyisoprene

<table>
<thead>
<tr>
<th>Nitrile oxide</th>
<th>δ3-C</th>
<th>δ4-C</th>
<th>δ5-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>p-MeOC₆H₄CNO</td>
<td>160.5</td>
<td>54.65</td>
<td>87.9</td>
</tr>
<tr>
<td>3,4,5-(MeO)₃C₆H₂CNO</td>
<td>-</td>
<td>∼55</td>
<td>∼89</td>
</tr>
<tr>
<td>EtO₂CCNO</td>
<td>161.1</td>
<td>54.3</td>
<td>91.6</td>
</tr>
</tbody>
</table>

2.3 trans-1,4-Polyisoprene

<table>
<thead>
<tr>
<th>Nitrile oxide</th>
<th>δ3-C</th>
<th>δ4-C</th>
<th>δ5-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>EtO₂CCNO</td>
<td>160.8</td>
<td>51.7</td>
<td>91.75</td>
</tr>
</tbody>
</table>
9.3 The addition of a \( p-(2\text{-}\text{methoxyethoxy})\text{phenyl} \) Pendent Group.

The overall synthetic scheme for the nitrile oxide precursor was as follows (Scheme 87).

\[
4\text{-HOC}_6\text{H}_4\text{Me} + \text{CH}_2\text{CH}_2 \rightarrow 4\text{-}(\text{HOCH}_2\text{CH}_2\text{)}_\circ \text{C}_6\text{H}_4\text{Me} \quad (\text{MeO})_2\text{SO}_2
\]

\[
4\text{-}(\text{MeCH}_2\text{CH}_2\text{)}_\circ \text{C}_6\text{H}_4\text{CHO} \quad \text{NH}_2\text{OH}
\]

\[
4\text{-}(\text{MeCH}_2\text{CH}_2\text{)}_\circ \text{C}_6\text{H}_4\text{CH}=\text{NOH} \quad \text{NOC}_1
\]

\[
4\text{-}(\text{MeOCH}_2\text{CH}_2\text{)}_\circ \text{C}_6\text{H}_4\text{C}=\text{NOH}
\]
9.3.1 **Preparation of p-(2-Hydroxyethoxy)toluene**

The reaction was carried out in a two litre steel pressure vessel, as shown in Figure 88, according to standard I.C.I. procedures. p-Cresol (857 g, 7.94 mol) was added to the vessel followed by sodium hydroxide powder (1 g), with stirring. The vessel was purged at 100°C with a stream of nitrogen for 1 h. Ethylene oxide (355 g, 8.07 mol) was weighed into the steel feed cylinder, by evacuating it, preweighing, filling from a reservoir cylinder and then reweighing. The feed cylinder was attached to the system and pressurised to about 50 p.s.i. with nitrogen. The vessel was heated to about 120°C with stirring and ethylene oxide was then allowed to enter using the spring valve at a rate such that the pressure in the vessel was about 40 p.s.i. The exothermic reaction was allowed to reach 140-150°C and maintained between these temperatures using the steam/water internal coils. The reaction was complete when bubbles were seen through the view glass and the temperature began to fall. When the vessel had cooled to about 70°C, the vessel was discharged by suction to give a yellow liquid (1188 g); a further 17 g was obtained by washing the vessel with acetone and evaporating. The liquid was added to a large multineck round bottom flask and water (120 g, 10%) added. The mixture was then heated to 80°C, under a stream of carbon dioxide (to remove excess sodium hydroxide). Vacuum (ca. 12 mmHg) was then applied, while still heating and stirring to remove the water. The mixture was heated and stirred for a further 1 h with decolourising charcoal, filtered, and cooled to give an off-white crystalline solid (1204 g, 100%).

\[ v_{\text{max}} \text{ (Nujol)} = 3450 \text{ (OH) cm}^{-1}. \]
Figure 88
9.3.2 Preparation of $p$-(2-Methoxyethoxy)toluene

This was prepared by a similar method to that standardly used at I.C.I. 65. $p$-(2-Hydroxyethoxy)toluene (300 g, 2.2 mol) and toluene (190 g) were heated to 40°C under nitrogen and sodium hydroxide (130 g) dissolved in water (130 ml) was added with stirring. Dimethyl sulphate (373 g, 5.92 mol) was added dropwise, the temperature being maintained at 40-45°C, care being taken with regard to its toxic nature. The mixture was stirred at 40-45°C for 2 h; sodium hydroxide (146 g) dissolved in water (146 ml) was added, and heating and stirring continued for a further 1 h. The mixture was then heated to 98°C and maintained at that temperature for 2 h. The mixture was cooled and neutralised with concentrated hydrochloric acid (litmus paper). Toluene (1000 ml) was added, a Dean and Stark distillation head fitted to the apparatus, and the mixture was heated under reflux until all the water had been removed. The solution was hot filtered, the residue washed with a further 250 ml toluene, and the solvent removed to give a yellow liquid (325 g, 99%). The crude product was examined by mass spectroscopy; apart from the parent ion m/e 166, other products identified were $\text{MeOCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OC}_6\text{H}_4\text{Me} \text{ m/e 210, HOCH}_2\text{CH}_2\text{OC}_6\text{H}_4\text{Me} \text{ m/e 152 and MeC}_6\text{H}_4\text{OMe m/e 122. The product was distilled through a 24" Vigreux fractionation column and collected at 112-113°C/12 mmHg.}$

$\delta$(CDCl$_3$): 2.24 (3H, s, Ar-CH$_3$), 3.38 (3H, s, OCH$_3$), 3.67 (2H, t, J 5 Hz, CH$_2$), 4.03 (2H, t, J 5 Hz, MeO-CH$_2$), 6.79 (2H, d, J 8 Hz, 2ArH), 7.02 (2H, d, J 8 Hz, 2ArH). The peaks centred at 3.57 and 4.03 and triplets of doublets, indicated the presence of some $\text{MeOCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OC}_6\text{H}_4\text{Me}$. 


9.3.3 Preparation of p-(2-Methoxyethoxy)benzaldehyde.

The method was based on an Étard type reaction (Scheme 87).

Chromyl chloride (31 g, 0.20 ml) was dissolved in dry chloroform (100 ml), protected from the atmosphere with a drying tube and cooled well in an ice-bath. With stirring p-(2-methoxyethoxy)toluene (12 g, 72 mmol) in twice its volume of dry chloroform, was slowly added to the mixture over 1.5 h. Stirring was continued for a further 0.5 h and the mixture was allowed to stand, at room temperature overnight. The dark brown precipitate was carefully filtered (treating as explosive) and washed with dry chloroform. The solid was then decomposed by stirring with excess dilute sulphurous acid to give a dark green solution. This solution was then extracted thoroughly with five portions of methylene chloride. The combined extracts were dried over anhydrous calcium chloride, the solvent removed under reduced pressure and the residue distilled at 120-130°C/0.02 mmHg on a Kugel-Röhr distillation apparatus to give a pale yellow oil (2.8 g, 21.5%).

\[ \nu_{\text{max}} \] (liquid) 1690 \( \text{C=O} \) cm\(^{-1} \).

\[ \delta H(\text{CDCl}_3): 3.37 \text{ (3H, s, OCH}_3) , 3.68 \text{ (2H, m, OCH}_2) , 4.05 \text{ (2H, m, OCH}_2) , 6.93 \text{ (2H, d, J 8Hz, ArH) , 7.74 \text{ (2H, d, J 8Hz, ArH) , 9.78 \text{ (1H, s, CHO) . Also present were small impurity peaks assigned to p-(methoxyethoxy)benzoic acid } \delta H(\text{CDCl}_3): 6.76 \text{ (d, J 8Hz, ArH) , 7.19 \text{ (d, J 8Hz, ArH) accounting for about 20\% of total. Actual reaction yield = 17\%.} \]

9.3.4 Preparation of p-(2-Methoxyethoxy)benzaldoxime.

This was prepared by a modification of the technique
described by Theilheimer. The distillate from the previous stage (2.8 g, 15 mmol) was dissolved in absolute alcohol (100 ml). To this was added a solution of hydroxylamine prepared freshly as follows; hydroxylammonium chloride (1.167 g, 16.79 mmol) was finely powdered and suspended with stirring in absolute alcohol (100 ml) followed by the addition of sodium metal (0.3863 g, 16.79 mmol). After 15 min the suspension was filtered to give the hydroxylamine solution. The two solutions were combined and heated under reflux for 1 h. The solvent was removed and the resulting solid heated, while suspended in refluxing petroleum-ether (b.p. 40-60°C) for 5 h. The white product was filtered and dried (85%). A white powder was obtained from methylene chloride/petroleum-ether. M.p. 118-120°C. δH(CDC13): 3.41 (3H, s, OCH3), 3.72 (2H, t, J 5Hz, OCH2), 4.12 (2H, t, J 5Hz, OCH2), 6.87 (2H, d, J 8Hz, ArH), 7.45 (2H, d, J 8Hz, ArH), 8.02 (1H, s, CH=N). Peaks centred at 3.72 and 4.12δ are observed as triplets of doublets due to the presence of some MeOCH2CH2OCH2CH2OC6H4CH=NOH. M/e 239 (M+ + C2H4O), 195 (M+), 181, 137, 120, 94, 65, 59. νmax (nujol) 3312 (OH), 1610 (C=N) cm⁻¹.

9.3.5 Preparation of p-(2-Methoxyethoxy)benzhydroximoyl Chloride.

p-(2-Methoxyethoxy)benzaldoxime (0.50 g, 2.6 mmol) was dissolved in dry diethyl ether and cooled well in an ice/salt bath. Nitrosyl chloride (0.34 g, 5.2 mmol), as a 20% solution in diethyl ether (1.7 ml), was added and the mixture allowed to stand for 30 min. The solution was warmed to room temperature and the solvent evaporated to give a pale yellow solid.
110

(100%); no further purification was attempted. M.p. 110-115°C

m/e (%) 23 (M+ 17), 229 (M+, 51), 194 (33), 193 (100), 135 (40).

9.3.6 **Attempted synthesis of p-(2-Methoxyethoxy)benzaldehyde via the Gattermann-Aldehyde Reaction**

The proposed scheme was as follows (Scheme 89).

![Scheme 89](image)

9.3.6.1 **Preparation of Ethylene glycol methylphenylether.**

Ethylene glycol monophenylether was reacted with dimethyl sulphate in the same manner as described above for p-hydroxyethoxytoluene, to give a yellow liquid (75%).

9.3.6.2 **Attempted synthesis of p-(2-Methoxyethoxy)benzaldehyde.**

The method was a modification of the Gattermann-Aldehyde Reaction, as described by Vogel.

Ethylene glycol methylphenylether (42 g, 0.28 mol) and dry powdered zinc cyanide (52 g, 0.44 mol) were mixed in dry tetrachloroethane (100 ml) and cooled in a cold water bath.
With stirring, a rapid stream of dry hydrogen chloride gas was bubbled through the mixture for 1 h, great care being taken to dispose of the effluent gas (by bubbling through three NaOH aq. Dreschel bottles), which could contain hydrogen cyanide. With rapid stirring, finely powdered anhydrous aluminium chloride (45 g) was slowly added. The mixture was warmed to 40-45°C and a slow stream of dry hydrogen chloride gas maintained for 3-4 h. The mixture was cooled and then poured into excess dilute hydrochloric acid solution with stirring. The resultant solution was heated under reflux for 0.5 h, cooled, and extracted with several portions of chloroform. The extracts were dried and the solvent evaporated under vacuum, to give a yellow liquid (41 g). I.r. $\nu_{\text{max}}$ (liquid) 1685 (C=O) cm$^{-1}$. Only a trace of aldehyde was apparent in the $^1$H NMR ca.9.5δ. The small amount of the carbonyl absorption evident in the i.r. appeared to be predominantly due to the equivalent carboxylic acid. No product could be isolated either directly or via the oxime, as above. The reaction was repeated under nitrogen, for extended reaction time (12 h), at elevated temperature (60°C) and using benzene as solvent; but no product could be isolated.

9.4 The Addition of a p-(MeO(CH$_2$CH$_2$O)$_6$)C$_6$H$_4$ Pendent Group

Initially, synthesis of the intermediate aldehyde was attempted via the Gattermann-Aldehyde reaction, as above, but no product could be isolated either directly or as the oxime. A reaction scheme similar to the Étard aldehyde method described above was adopted.
9.4.1 Preparation of \( p-(\text{HO(CH}_2\text{CH}_2\text{O})_5)\text{C}_6\text{H}_4\text{CH}_3 \)

The same apparatus and technique as described for the synthesis of \( p-(2\text{-hydroxyethoxy})\text{toluene} \) was used. It was necessary to do the reaction in two stages due to the limited capacity of the system for ethylene oxide. Initially, \( p\)-cresol (648 g, 6 mol) and powdered sodium hydroxide (2 g) were reacted, as above, with ethylene oxide (1011 g, 23 mol) and the product (1650 g) was obtained. The increase in weight due to ethylene oxide addition was 1002 g, equivalent to 3.8 moles of ethylene oxide added per original mole of \( p\)-cresol. The product (1220 g, 4.43 mol) was then returned to the reaction vessel with powdered sodium hydroxide (0.5 g) and the process repeated with a second further portion of ethylene oxide (285 g, 6.48 mol). The product was discharged as a yellow liquid; the observed weight (1498 g), corresponds to an increase of 278 g or equivalent to the addition of a further 1.4 moles ethylene oxide per mole of starting material. The structure of the final product is thus \( \text{HO(CH}_2\text{CH}_2\text{O})_n\text{C}_6\text{H}_4\text{CH}_3 \), where the number average value of \( n \) is 5.2.

\[ \nu_{\text{max}} \text{ (liquid) } 3450 \text{ (OH) cm}^{-1} \]

\( \delta\text{H(CDC}_1\text{)}: 2.29 \text{ (3H, s, CH}_3\text{)}, 3.5-4.3 \text{ (21H, m, OCH}_2\text{)}, 6.88 \text{ (2H, d, J 9Hz, ArH)}, 7.17 \text{ (2H, d, J 9Hz, ArH)}. \)

9.4.2 Preparation of \( p-(\text{MeO(CH}_2\text{CH}_2\text{O})_5)\text{C}_6\text{H}_4\text{CH}_3 \)

The reaction with dimethyl sulphate was performed as described previously to afford a yellow liquid (84%). Completion of the reaction was determined by the absence of \( \nu_{\text{max}} \text{ (liquid) } 3450 \text{ (OH) cm}^{-1} \) in the i.r. spectrum. \( \delta\text{H(CDC}_1\text{)}: 2.29 \text{ (3H, s, CH}_3\text{)}, 3.39 \text{ (3H, s, OCH}_3\text{)}, 3.5-4.4 \text{ (21H, m, OCH}_2\text{)}, \)
6.88 (2H, d, J 9Hz, ArH), 7.17 (2H, d, J 9Hz, ArH).

9.4.3 Preparation of \( p-(\text{MeO(CH}_2\text{CH}_2\text{O})_6)\text{C}_6\text{H}_4\text{CHO} \)

Chromyl chloride (48 g, 0.30 mol) was dissolved in pure chloroform (100 ml) and cooled in an ice-bath. \( p-(\text{MeO(CH}_2\text{CH}_2\text{O})_5)\text{C}_6\text{H}_4\text{CH}_3 \) (30 g, 85 mmol) dissolved in twice its own volume of pure chloroform was added slowly, with stirring, over 4-5 h. The mixture was allowed to stand at room temperature for 2 days and the brown insoluble precipitate was carefully filtered (treating as potentially explosive) and washed with chloroform. The residue was decomposed by stirring for 2 h with excess dilute sulphurous acid. The resultant green solution was extracted with several portions of chloroform and the solvent removed. The resultant oil was dried by adding portions of toluene and evaporating the azeotrope under vacuum. The oil was then exhaustively distilled with a Kugel-Röhr apparatus at 200-250°C, 0.01 mmHg to afford a dark yellow liquid (15%). \( \nu_{\text{max}} \) (liquid) 1690 (C=O) cm\(^{-1}\). \(^1\)H\((\text{CDCl}_3)\): 3.39 (3H, s, OCH\(_3\)), 3.5-4.4 (23.5H, m, OCH\(_2\)), 7.05 (2H, d, J 9Hz, 2ArH), 7.84 (2H, d, J 9Hz, 2ArH), 9.86 (1H, s, CHO). From \(^1\)H NMR it was concluded that the product was \( \text{CH}_3\text{O(CH}_2\text{CH}_2\text{O})_n\text{C}_6\text{H}_4\text{CHO} \), where \( n = 5.9 \pm 0.3 \).

9.4.4 Preparation of \( p-(\text{MeO(CH}_2\text{CH}_2\text{O})_6)\text{C}_6\text{H}_4\text{CH-NOH} \)

This was prepared from \( p-(\text{MeO(CH}_2\text{CH}_2\text{O})_6)\text{C}_6\text{H}_4\text{CHO} \) and hydroxylamine in absolute ethanol, as described for \( p-(2\text{-methoxy-ethoxy})\text{benzaldoxime} \). The product was isolated as a yellow liquid (78%), on removal of the solvent. \( \nu_{\text{max}} \) (liquid) 3380 (OH) cm\(^{-1}\). \(^1\)H\((\text{CDCl}_3)\): 3.35 (3H, s, OCH\(_3\)), 3.5-4.4 (23.5H, m,
OCH₂), 6.87 (2H, d, J 9Hz, ArH), 7.48 (2H, d, J 9Hz, ArH),
8.00 (1H, s, CH=N).

9.4.5 Preparation of p-(MeO(CH₂CH₂O)₆)C₆H₄CCl=NOH

This was prepared from the oxime and nitrosyl chloride,
as described previously, to afford a yellow liquid (99%).

ν_max (liquid) 3380 (OH) cm⁻¹. ¹H(CDC₃): 3.39 (3H, s, OCH₃),
3.5-4.4 (23.5H, m, OCH₂), 6.98 (2H, d, J 9Hz, ArH), 7.83 (2H,
d, J 9Hz, ArH).

9.5 Attempted Hydrolysis of Pendent Ethoxycarbonyl Groups

Modified polymer (0.5 g) [derived from the reaction of
cis-1,4-polybutadiene and ethylchlorooximino acetate at 10:1
molar ratio] was dissolved in chloroform (200 ml) and shaken
with a 10% aqueous solution of sodium hydroxide (200 ml) and
benzyltriethylammonium chloride (200 mg) for 12 h. A portion
of water (100 ml) was added and shaking continued for a further
60 h. The mixture was acidified with dilute hydrochloric
acid and shaken for a further 12 h. The organic layer was
separated, reduced to a small volume under vacuum and then
dissolved in chloroform (100 ml). The solution was dried
over anhydrous calcium chloride, filtered and reduced in volume
under vacuum. The polymer was precipitated from solution by
adding methanol, filtered and dried. The i.r. spectrum showed
no sign of hydrolysis. ν_max (film) 1730 (C=O) cm⁻¹.

9.5.1 Preparation of Crown Ether/Potassium Hydroxide Complex

The method of Pedersen⁹⁰ was used. 18-Crown-6 (5.0 g,
20.8 mmol) and potassium hydroxide (85% aqueous solution containing 1.17 g, 20.8 mmol) were dissolved in methanol (25 ml) with gentle warming. Toluene (50 ml) was added and the mixture reduced to 25 ml under vacuum at 100°C. A further portion of toluene (50 ml) was added and the process repeated. The solution was made up to 50 ml with toluene, decolourising charcoal (1 g) added and the mixture left over-night, under dry nitrogen. The mixture was filtered, the filtrate stored under dry nitrogen and treated as approximately a 0.3 molar solution of crown ether/potassium hydroxide complex.

9.5.2 Saponification of Pendent Ethoxycarbonyl Groups using a Crown Ether/Potassium Hydroxide Complex

Modified polymer (1.0 g) [derived from the reaction of cis-1,4-polybutadiene and ethylchlorooximino acetate at 1:1 molar ratio] was dissolved in dry toluene (750 ml). The crown ether/potassium hydroxide complex described above (50 ml) was added and the mixture refluxed for 12 h under dry nitrogen. The product was obtained as a dark brown solid (0.85 g) which precipitated from solution. The precipitate was filtered, washed several times with dry chloroform and dried under vacuum. The reaction was considered to have gone to near completion from the i.r. spectrum (solid film), by the virtual disappearance of the original carbonyl absorption at $\nu_{\text{max}}$ 1730 cm$^{-1}$ and the appearance of a new strong peak at 1650 cm$^{-1}$. 
RESULTS & DISCUSSION
SECTION
1. INTRODUCTION

Polydiienes are one of the most important groups of industrial, bulk polymers. Both natural and synthetic variants are relatively cheap to produce and find use whenever the properties of toughness, elasticity and air/water permeability resistance are required. This is particularly true for vehicle tyres. There is therefore, a continuing impetus to improve the material's physical properties (eg. toughness, elasticity, abrasion resistance, solvent resistance, heat resistance etc.) and also to reduce its propensity to degradation (particularly oxidative degradation). Current commercial practice involves the physical compounding of various materials into the polymer, in order to improve its properties (antioxidants, fillers etc.). Usually, the only chemical modification is that of sulphur vulcanization.49

There is considerable potential for the chemical modifications of polydiienes, which can be roughly divided into three classes depending on the degree of reaction.

1) Uniform modification at the 2-3 mole percent level results in polydiienes with essentially unchanged elasticity, but with other altered or improved properties.

2) At 5-25 mole percent modification, elastic properties are altered and a new rubbery polymer results.

3) At very high levels of modification, elasticity will be completely lost and hard resinous materials result. Fully chlorinated rubber and ebonite (fully vulcanized) are examples of this.47,49

The area of most interest is probably the first. For
example, a particularly common goal is the attachment of chemically bound anti-oxidant moieties (such as hindered phenol groups)\textsuperscript{1,58,91,93,94}. The anti-oxidant group being chemically bound, rather than compounded, confers on the polymer oxidation resistance which is not effected by repeated washings or solvent treatments. Normally, a non-bound anti-oxidant would be gradually leached out under such conditions. There is a requirement for non leaching anti-oxidants for the protection of rubber thread in garments subject to multiple washings or dry cleaning\textsuperscript{1}. Bound anti-oxidants have also been found to be more resistant to heat, such as in air oven ageing\textsuperscript{92}. More importantly, it has also been suggested that significant amounts of anti-oxidant are leached from tyre treads and rubber hoses on prolonged contact with water\textsuperscript{93,94}.

The scope for useful chemical modification of polydienes extends from binding conventional additives (such as above) to adding other functional groups to modify the polymer's properties or producing a new polymer. Extreme examples of the latter case might result in novel forms of cross-linking or the formation of new copolymers.

The object of the present work was to examine the 1,3-dipolar cycloaddition reaction as a means of adding potentially useful functional groups to polydienes. The 1,3-dipolar cycloaddition reaction has already been discussed, in detail in the Introduction Section. The basic reaction with the alkene groups in a polydiene is as follows (Scheme 90).
In this work, the known ability of 1,3-dipoles to react with simple alkenes was extended to the examination of their reaction with polydienes, as a means of modifying these polymers.

The main aims of the project were:

1. To evolve methods of achieving 1,3-dipolar cycloaddition to polydienes and to optimise the yields. Previous work (discussed below) had resulted in poor yields, especially for reactions with polyisoprenes.

2. To examine the product; analysing the adducts both qualitatively and quantitatively. *i.e.* To be able to determine the degree of modification and provide unequivocal evidence for the type of link.

3. Based on the above work, to add potentially useful functional groups to polydienes via 1,3-dipolar cycloaddition.
2. USE OF MODEL COMPOUNDS

There are a number of problems associated with the examination of reactions on high molecular weight polymers, compared to an equivalent low molecular weight, monomeric compound. The most obvious problem is that of purification. Following reaction on a polymer containing a large number of the same functional groups per molecule, the reacted polymer molecule will contain not only the primary desired product but also unreacted functional groups and often groups resulting from unwanted side reactions. These will be impossible to separate. This effect will present particular difficulties if the reaction proceeds at low to medium yields, when identification and subsequent analysis becomes more difficult. This is further exacerbated by the fact that polymers are not susceptible to a number of classical analytical techniques. For example, true melting points do not exist, there is spread of molecular weights rather than one identifiable value and some spectroscopic techniques (e.g., \(^1\)H n.m.r.) are hampered by poor resolution and low solubilities.

In order to cope with some of these practical problems, extensive use has been made in this work of model compounds selected to mimic as far as possible the polymer structural units. All reactions were first attempted on the model compounds in order to determine the optimum experimental conditions and to eliminate unsuitable reactions. If a reaction would not proceed in reasonable yield with the model compound, it was considered likely that it would not do so with the polymer (providing the model was correctly chosen). However, as will
be described later (section 3.), the main advantage of the model reactions proved to be as an aid to structural analysis of the reacted polydienes. The model adducts can be purified and unequivocally analysed by the usual accepted techniques. By comparison of the analysis (particularly \textsuperscript{13}C n.m.r.) of a model adduct and the equivalent reacted polymer, identical cyclo-addition groups can be identified on the polymer chain. This will be discussed in detail below.

Although reactions on polymers and equivalent model compounds are expected to proceed by the same mechanism, reaction on the polymer is likely to be less facile for a number of special reasons.

a) As the reaction proceeds, partial conversion of functional groups on the polymer chain often results in significant changes in the solubility of the polymer in the reaction medium. The polymer may well precipitate from solution, well before complete reaction, therefore limiting any further reaction. Such premature precipitation can also occur as a result of side reactions such as cross-linking.

b) The polymer need not gel or precipitate from solution for the reaction to become inhibited. Long chain polymers in solution can take up a number of conformational structures depending on their affinity for the solvent. The two extremes of which are the uncoiled form, where the chains are randomly elongated and the coiled form, where the chains are coiled into irregular spheres. The polymer chains will tend towards the coiled form as their affinity for the solvent decreases. A dramatic illustration of this effect is seen
when to a concentrated solution of natural rubber in toluene (which is highly viscous) is added a little glacial acetic acid. As the acetic acid is stirred in the thick, viscous solution suddenly becomes significantly less viscous, as the hydrophobic, polyisoprene molecules coil up in the now more polar solvent. This may be an important effect, as reaction on coiled molecules is likely to be significantly more sterically hindered.

Additionally, as reactions proceed the polymer chains themselves become more polar, which changes their affinity for the essentially non-polar solvent. In this case it could be postulated that any coiling would tend to place the reacted parts of the chain on the inside of the coil (a micelle effect) and thus have a less adverse effect on further reaction. The balance between these effects is complex and was not studied in detail.

c) For reactions that proceed to high yield on polymers, there are likely to be neighbouring group effects. 1,3-Dipolar cycloaddition on an alkene group, adjacent to one which has already been substituted, is likely to be effected by both steric and electronic effects.

It is clear from the above that no model compound can be expected to exactly parallel the reactivity of a polymer. The following compounds were chosen as most closely imitating the reactive sites on the polydienes:
MODEL

\begin{itemize}
  \item \textit{cis}-cyclooctene
  \item \textit{ cis}-cyclohexene
  \item \textit{ cis}-cyclododecene
\end{itemize}

POLYMER

\begin{itemize}
  \item \textit{cis}-1,4-polybutadiene
  \item \textit{ cis}-1,4-polyisoprene
  \item \textit{CH}_3(\textit{CH}_2)_5\textit{CH}≡\textit{CH}_2 \quad \text{oct-1-ene}
  \item \textit{CH}≡\textit{CH}_2 \quad \text{pendent vinyl groups}
  \text{ eg. 1,2-polybutadienes}
\end{itemize}
cis-Cyclooctene (b.p. 143°C), 1-methylcyclohexene (b.p. 110°C), and oct-1-ene (b.p. 122°C) were found to be most suitable for reaction in refluxing toluene (b.p. 110°C). Their boiling points are such that they would not be lost from the reaction mixture, but excess could easily be removed, under vacuum, when purifying the adduct.

These alkenes were reacted with nitrones and nitrile oxides to give the corresponding isoxazolidines and isoxazolines as follows (Figure 91).

Reaction conditions and yields are given in table 92 (nitrones) and table 93 (nitrile oxides). The yields for these model reactions are discussed together with the corresponding polymer reactions in section 5.
Figure 91
### Table 92

<table>
<thead>
<tr>
<th>R-</th>
<th>Dipolarophile</th>
<th>Temp. (°C)/Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-MeOC₆H₄⁻</td>
<td>Cyclohexene</td>
<td>130/60</td>
<td>65</td>
</tr>
<tr>
<td>&quot;</td>
<td>Cyclohexene</td>
<td>110/60</td>
<td>10</td>
</tr>
<tr>
<td>&quot;</td>
<td>cis-Cyclododecene</td>
<td>130/60</td>
<td>45</td>
</tr>
<tr>
<td>&quot;</td>
<td>1-Methylcyclohexene</td>
<td>110/432</td>
<td>1.4</td>
</tr>
<tr>
<td>4-PhCOC₆H₄⁻</td>
<td>cis-Cyclododecene</td>
<td>130/60</td>
<td>42</td>
</tr>
<tr>
<td>4-HOC₆H₄⁻</td>
<td>Cyclohexene</td>
<td>130/60</td>
<td>0</td>
</tr>
</tbody>
</table>

**Nitrone:** \( \text{R}-\text{CH}==\overset{\text{O}}{\text{N}}\text{Ph} \)
Table 93

Reaction of nitrile oxides (RC\(=\)N\(-\)O) generated \textit{in situ} by thermal dehydrochlorination of the corresponding hydroximoyl chloride (see text), except when marked * (used directly).

<table>
<thead>
<tr>
<th>R-</th>
<th>Dipolarophile</th>
<th>Temp.((^\circ)C)/Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-MeOC(_6)H(_4)=</td>
<td>Cyclohexene</td>
<td>110/24</td>
<td>33</td>
</tr>
<tr>
<td>&quot;</td>
<td>cis-cyclooctene</td>
<td>110/80</td>
<td>68</td>
</tr>
<tr>
<td>&quot;</td>
<td>oct-1-ene</td>
<td>110/80</td>
<td>53</td>
</tr>
<tr>
<td>&quot;</td>
<td>1-methylcyclohexene</td>
<td>110/60</td>
<td>57</td>
</tr>
<tr>
<td>3,4,5-(MeO)(_3)C(_6)H(_2)=</td>
<td>cis-cyclooctene</td>
<td>110/60</td>
<td>85</td>
</tr>
<tr>
<td>4-PhCOC(_6)H(_4)=</td>
<td>cis-cyclododecene</td>
<td>110-115/50</td>
<td>49</td>
</tr>
<tr>
<td>&quot;</td>
<td>oct-1-ene</td>
<td>110/30</td>
<td>77</td>
</tr>
<tr>
<td>EtO(_2)C=</td>
<td>cis-cyclooctene</td>
<td>110/100</td>
<td>82</td>
</tr>
<tr>
<td>&quot;</td>
<td>1-methylcyclohexene</td>
<td>110/80</td>
<td>74</td>
</tr>
<tr>
<td>2,4,6-(MeO)(_3)C(_6)H(_2)=</td>
<td>cis-cyclooctene</td>
<td>80/20min.</td>
<td>51</td>
</tr>
<tr>
<td>&quot;</td>
<td>cis-cyclooctene</td>
<td>20/168</td>
<td>68</td>
</tr>
<tr>
<td>4-HO(_2)CC(_6)H(_4)=</td>
<td>cis-cyclooctene</td>
<td>110/120</td>
<td>70</td>
</tr>
</tbody>
</table>
3. EVIDENCE FOR 1,3-DIPOLAR CYCLOADDITION TO POLYDIENES

Much of the previous work in this area has been by Caraculacu and co-workers\textsuperscript{99-101}. Initially, 1,3-dipolar cycloaddition was carried out on the unsaturated polyesters\textsuperscript{99} (X) using diphenylnitrilimine (II) to give quantitative yield of the pyrazolines (Y). The nitrilimine was generated \textit{in situ} from the corresponding hydrazidoyl chloride (I), (Scheme 94).

\[
\begin{align*}
\text{C}_6\text{H}_5\text{C}=\text{N}=&\text{NHC}_6\text{H}_5 \quad \text{I} \\
\text{I} \xrightarrow{-\text{HCl}} \text{Et}_3\text{N} \quad \text{C}_6\text{H}_5\text{C}=&\text{N} \quad \text{II}
\end{align*}
\]

II + CH=CH $\rightarrow$ Ph $\quad \text{Ph}$

\[
\begin{align*}
\text{R}_1 &= \text{C}_6\text{H}_4 \quad \text{C} \quad \text{C}_6\text{H}_4\text{OCO} \quad \text{,} \\
\text{Me} &\quad \text{Me} \\
\text{or} \quad \text{R}_1 &= \text{CH}_2\text{CH}_2 \quad \text{OCO} \quad \text{,} \\
\text{R}_2 &= -\text{O} - \text{CO} -
\end{align*}
\]

\textbf{Scheme 94}
The quantitative yields can be attributed to the activation of the polymer alkene groups by adjacent conjugating carbonyl groups and also by the use of a reactive nitrilimine. The extent of reaction was determined by elemental nitrogen analysis and the disappearance of the alkene peak at about 1660 cm\(^{-1}\) in the infrared absorption spectra of Y. The appearance of i.r. peaks at 1510 and 1610 cm\(^{-1}\), assigned to phenyl groups, was taken as evidence for the structure of the product.

Attempts to react diphenylnitrilimine with unsaturated polyamides and polyhydrazides proved unsuccessful. It was proposed that while alkoxy substituents on the double bond enhance dipolar reactivity, amide and hydrazide substituents inhibit it. The latter effect they attributed to intramolecular hydrogen bonding.

The above work formed the basis for similar reactions on polydienes. Diphenylnitrilimine was reacted with four polymers; cis-1,4-polyisoprene, trans-1,4-polyisoprene, cis-1,4-polybutadiene and trans-1,4-polybutadiene. Yields by elemental nitrogen analysis were: 0%, 10%, 4% and 10%, respectively. The observation that no reaction took place
with cis-1,4-polyisoprene was attributed to steric hindrance in the transition state. A similar, but less severe effect was said to account for the low yield (4%) with cis-1,4-polybutadiene. It is surprising that no difference in reactivity was found between trans-1,4-polybutadiene and trans-1,4-polyisoprene, in view of greater steric hindrance in the latter case.

The evidence presented for cycloaddition to the polydiene was the appearance of peaks around 1500 and 1600 cm\(^{-1}\) in the infrared spectra, following repeated purifications and attributed to the presence of monosubstituted aromatic species.

A very similar piece of work by Tada et al.\(^{102}\), examined the addition of benzonitrile oxide and several nitrones (eg. \(\alpha-(4\text{-phenyl})-N\text{-phenylnitrone}\)). Nitrone reactions were performed in refluxing toluene solutions (12 h), with the nitrone (I) generated \textit{in situ} from the equivalent aldehyde/phenylhydroxylamine (II) mixture. The nitrile oxide reactions were performed in toluene solution at room temperature (6 h), benzonitrile oxide (III) being generated \textit{in situ} from benzhydroximoyl chloride (IV) and triethylamine (Scheme 95).

All reactions were on predominantly trans-polybutadiene and degrees of modification, based on nitrogen analysis, were claimed to be from 3 to 22%. Evidence for cycloaddition to the polymer was again based on the appearance of absorption bands in the infrared spectra, characteristic of a monosubstituted benzene ring, near 1600, 1490, 760 and 700 cm\(^{-1}\).
Therefore, it can be concluded that previous work on 1,3-dipolar cycloaddition to polydiienes is characterised by low degrees of modification (particularly for polyisoprenes). Furthermore, the evidence for the structure of the product is based on infrared data. Not only are the nature of the i.r. peaks sometimes ambiguous, but also such evidence only demonstrates that a link has occurred to the polymer, without clearly demonstrating the structure of the product. It is a feature of this work that higher degrees of modification (up to 55%) have been achieved and that the structure of the product was determined unambiguously by $^{13}$C n.m.r spectroscopy, by comparison with model adducts. This is now illustrated by detailed reference to two examples.
The reactions of ethyl fulmidoformate (X), generated via the in situ thermal dehydrochlorination of ethyl chloro-oximinoacetate (Y), with cis-1,4-polybutadiene and cis-1,4-polyisoprene were studied. Initially, isoxazolines (Z, W) were synthesised from the corresponding model compounds cis-cyclooctene and 1-methylcyclohexene (Scheme 96).

\[
\begin{align*}
X & \quad \text{EtO}_2\text{CC}═\text{N═O} \\
Y & \quad \text{cis-cyclooctene} \\
\downarrow & \quad \text{HCl} \\
\text{EtO}_2\text{CC}═\text{N}—\text{O} & \quad \text{1-Me-cyclohexene}
\end{align*}
\]

Scheme 96

The \( ^{13} \text{C n.m.r} \) spectrum of Z shows absorptions at 48.4 and 87.4 ppm, characteristic of the CH groups at the 4- and 5-positions of the isoxazoline ring. Full assignments of peaks are shown in figure 97. Similarly, the \( ^{13} \text{C n.m.r} \) spectrum of W shows absorptions at 48.7 (CH) and 88.0 (CMe) ppm (Figure 99).

Having characterised the model adduct Z, comparison was then made with the equivalent polymer reaction. cis-1,4-Polybutadiene was reacted with Y at 1:1 molar ratio (Y to polymer butadiene units) to give a product estimated to have
Figure 97. $^{13}$C N.m.r. (CDCl$_3$) spectra of Z. The peaks are assigned as follows: 13.6(CH$_3$ of EtO$_2$C), 24-29(ring CH$_2$), 48.4(isoxazoline CH), 61.2(CH$_2$ of EtO$_2$C), 87.4(isoxazoline CH), 155.7(isoxazoline C) 160.3(C=O) ppm from Me$_4$Si.
Figure 98. $^{13}$C N.m.r. (CDCl$_3$) spectra of PBD modified by X. The peaks are assigned as follows: 13.6(CH$_3$ of EtO$_2$C),22-28(CH$_2$ of PBD),46.6(isoxazoline CH),61.6(CH$_2$

of EtO$_2$C),86.0(isoxazoline CH),127-130(CH of PBD),155.5
(isoxazoline C),160.4(C=O)ppm from Me$_4$Si.

Off-resonance decoupled spectrum.

Noise decoupled spectrum.
55% alkene groups modified (Table 85, experimental section). The presence in the purified product, of units derived from \( \mathcal{X} \) was established by elemental analysis (6.3%N), i.r. (\( \nu_{\text{max}} \) 1720 (C=O) cm\(^{-1}\)) and \(^1\)Hn.m.r spectroscopy [CDCl\(_3\); \( \delta \) 4.53 (2H, q, J 7Hz, CH\(_2\)), 1.32 (3H, t, J 7Hz, CH\(_3\))]. The \(^{13}\)Cn.m.r spectrum (Figure 98) not only provides confirmation of the presence of ethoxycarbonyl groups, but also establishes the nature of the isoxazoline link, by comparison with the spectrum of the authentic model compound. The absorption at 46.6 and 86.0 ppm are clearly shown by single-frequency off-resonance decoupling to be due to CH groups and, in view of the similarity of their chemical shifts to those of the model compound \( \mathcal{Z} \), they are assigned to the carbon atoms at the 4- and 5-positions of an isoxazoline ring in the modified polymer. These results are consistent with 1,3-dipolar cycloaddition of \( \mathcal{X} \) to cis-1,4-polybutadiene.

Similarly, \( \mathcal{Y} \) reacted with cis-1,4-polyisoprene in 1:1 molar ratio gave a product with 36% of the isoprene units converted to isoxazoline rings. The \(^{13}\)Cn.m.r spectrum of the modified polymer (Figure 100) shows peaks at 54.3 (CH) and 91.6 (CMe) ppm, similar to those found for the model adduct \( \mathcal{W} \) and appearing as a doublet and a singlet, respectively, in the single-frequency off-resonance decoupled spectrum.

These results not only provide evidence for the addition of a nitrile oxide to polybutadiene and polyisoprene in good yield, but also clearly demonstrate the formation of isoxazoline rings similar to authentic model adducts.

\(^{13}\)Cn.m.r chemical shifts for the isoxazoline carbon atoms of other polydiene reactions studied at 1:1 molar ratio are shown in Table 86(2) in the experimental section.
Figure 99. $^{13}$C N.m.r. (CDCl$_3$) spectra of $W$.

The peaks are assigned as follows: 13.5(CH$_3$ of EtO-C)
19-31(ring CH$_2$), 48.7(isoxazoline CH), 60.9(CH$_2$ of EtO-C),
88.0(isoxazoline CMe), 155.4(isoxazoline C=N), 160.3(C=O)
ppm from Me$_4$Si. (*includes CH$_3$)

Off-resonance decoupled spectrum.

Noise decoupled spectrum.
Figure 100. $^{13}$C N.m.r. ($\text{CDCl}_3$) spectra of PIP modified by X. The peaks are assigned as follows: 14.0 (CH$_3$ of EtO$_2$C), 21-34 (CH$_2$ of PIP), 54.3 (isoxazoline CH), 61.7 (CH$_2$ of EtO$_2$C), 91.6 (isoxazoline CMe), 123-126 (CH of PIP), 133-136 (CMe of PIP), 154.9 (isoxazoline C=N), 161.1 (C=O) ppm from Me$_4$Si. (*includes CH$_3$ of PIP)

Off-resonance decoupled spectrum.

Noise decoupled spectrum.
The $^{13}$C\textsuperscript{n.m.r} spectra of the model and polymer adducts derived from unsymmetrical alkene groups (eg 1-methylcyclohexene, cis-1,4-polyisoprene) indicate the formation of only one of the two possible regioisomers (Scheme 101).

Only 5-substituted isoxazoline rings ($X$) were observed. This is consistent with previous experience\textsuperscript{3} and can be rationalised by perturbation molecular orbital theory (see pages 20-29), as well as steric considerations.
4. **DETERMINATION OF YIELDS FOR THE POLYMER REACTIONS.**

Determination of the degree of modification and therefore the yields of 1,3-dipolar cycloaddition reactions to polydienes, was by two distinct and complementary techniques; elemental nitrogen analysis and $^1$Hn.m.r spectroscopy. By using an average result from the two, rather than either one alone, it was considered that overall error would be reduced. Both techniques require that the reacted polymer be thoroughly purified from any starting reagent or byproduct. This was achieved by multiple precipitations of the polymer from solutions, using methanol. It is possible that modified polymer has a greater or lesser tendency to precipitate than un-modified polymer. Highly modified polymer chains will be more polar than less modified chains and will thus be more soluble in methanol. The net result would be that the measured yields could be less than the actual values.

4.1 **Nitrogen Analysis**

As the unmodified polydienes do not contain nitrogen atoms, elemental nitrogen analysis can be used to determine the number of isoxazoline units formed during the reaction and thus the degree of modification (assuming no other N containing products are formed). The calculations are illustrated in the examples in experimental section (9.2.1 and 9.2.2). These examples also illustrate that in some cases the proportions of carbon and hydrogen, do not agree with that from nitrogen analysis. The analysis for carbon was up to 20% lower than expected. This is attributed to absorption of oxygen, probably due to oxidative
degradation of the polymer. Much of this may have occurred after the reaction was complete and prior to analysis. During the purification procedure anti-oxidant additives present in the original polymers will have been removed.

4.2 $^1$H-NMR

The degree of modification was determined by comparing the area under the peak (integral trace) for unreacted alkene protons with that of protons in the added group (for example methoxy protons on 4-methoxybenzonitrile oxide and 3,4-tri-methoxybenzonitrile oxide adducts). Thus the ratio of unreacted alkene to reacted groups is determined (see experimental section 9.2). $^1$Hn.m.r spectra of polymers tend to be poorly resolved, due to spin-spin coupling effects $^{103}$, resulting in broad peaks. This can result in reduced accuracy of the integration of the area under the peaks.

Despite possible inaccuracies of each of the above methods, there was found to be reasonably consistent results from the two techniques (see table 85). Only for low degrees of modification were significantly different results obtained from the two methods. For example, when $p$-methoxybenzonitrile oxide was added to cis-1,4-polybutadiene with a 50 times excess of alkene groups, the molar ratio of unreacted to reacted alkene groups in the product was found to be 114:1 by nitrogen analysis and 60:1 by $^1$Hn.m.r. By comparison, with only a 10 times excess of alkene groups, the same reaction gave a product with a molar ratio of unreacted to reacted alkene groups of 14: and 13:1 by the two techniques, respectively.
5. FACTORS EFFECTING YIELDS OF 1,3-DIPOLAR CYCLOADDITION TO POLYDIENES.

(Table 85 is reproduced for reference, see also tables 92 & 93 for yields of model compounds).

**TABLE 85**

POLYMER REACTION YIELDS

Yields are based on the mean reacted molar ratios by N-analysis and $^1$H-NMR.

1. *cis*-1,4-Polybutadiene

<table>
<thead>
<tr>
<th>1,3-Dipole</th>
<th>Initial Molar Ratio</th>
<th>Reacted Molar Ratios</th>
<th>Yield $%$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$p$-PhCOC$_6$H$_4$CHN(O)Ph</td>
<td>3:1</td>
<td>18:1</td>
<td>22:1</td>
</tr>
<tr>
<td>$p$-PhCOC$_6$H$_4$CNO</td>
<td>3:1</td>
<td>12:1</td>
<td>4:1</td>
</tr>
<tr>
<td>$p$-MeOC$_6$H$_4$CNO</td>
<td>1:1</td>
<td>5:1</td>
<td>2:1</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>14:1</td>
<td>13:1</td>
</tr>
<tr>
<td></td>
<td>50:1</td>
<td>114:1</td>
<td>60:1</td>
</tr>
<tr>
<td>3,4,5-(MeO)$_3$C$_6$H$_2$CNO</td>
<td>1:1</td>
<td>5:1</td>
<td>4:1</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>22:1</td>
<td>20:1</td>
</tr>
<tr>
<td></td>
<td>30:1</td>
<td>63:1</td>
<td>53:1</td>
</tr>
<tr>
<td></td>
<td>50:1</td>
<td>81:5:1</td>
<td>85:1</td>
</tr>
<tr>
<td>2,4,6-(MeO)$_3$C$_6$H$_2$CNO</td>
<td>1:1</td>
<td>2:1</td>
<td>1:1</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>11:1</td>
<td>10:1</td>
</tr>
<tr>
<td>$p$-MeOCH$_2$CH$_2$OC$_6$H$_4$CNO</td>
<td>1:1</td>
<td>13:1</td>
<td>10:1</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>47:1</td>
<td>28:1</td>
</tr>
<tr>
<td></td>
<td>50:1</td>
<td>321:1</td>
<td>308:1</td>
</tr>
<tr>
<td>$p$-MeO(CH$_2$CH$_2$O)$_6$C$_6$H$_4$CNO</td>
<td>1:1</td>
<td>21:1</td>
<td>146:1</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>99:1</td>
<td>249:1</td>
</tr>
<tr>
<td>$\text{EtO}_2\text{CCNO}$</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
</tr>
<tr>
<td>$\text{MeO}_2\text{CCNO}$</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>13:1</td>
<td>11:1</td>
</tr>
<tr>
<td></td>
<td>30:1</td>
<td>35:1</td>
<td>33:1</td>
</tr>
<tr>
<td>$p$-HO$_2\text{CC}_6\text{H}_4\text{CNO}$</td>
<td>1:1</td>
<td>39:1</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>181:1</td>
<td>-</td>
</tr>
</tbody>
</table>

* Room temp. 8 weeks

+ APPROXIMATE (SEE P. 100).
Table 85 (cont.)

<table>
<thead>
<tr>
<th>1,3-Dipole</th>
<th>Initial Molar Ratio</th>
<th>Reacted Molar Ratios</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N-Analysis</td>
<td>$^1$H-NMR</td>
<td></td>
</tr>
</tbody>
</table>

2. Non-stereospecific polybutadiene (\(\sim13\%\) vinyl groups)

| 1,3-Dipole       | Molar Ratio Ratios | \(\%
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{MeO}_2\text{CCNO})</td>
<td>8:1</td>
<td>77</td>
</tr>
</tbody>
</table>

3. \textit{cis}-1,4-Polyisoprene

| 1,3-Dipole       | Molar Ratio Ratios | \(\%
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{p-MeOC}_6\text{H}_4\text{CNO})</td>
<td>1:1</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>50:1</td>
<td>43</td>
</tr>
<tr>
<td>(\text{3,4,5-(MeO)}_3\text{C}_6\text{H}_2\text{CNO})</td>
<td>1:1</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>30:1</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>50:1</td>
<td>44</td>
</tr>
<tr>
<td>(\text{EtO}_2\text{CCNO})</td>
<td>1:1</td>
<td>36</td>
</tr>
<tr>
<td>(\text{MeO}_2\text{CCNO})</td>
<td>1:1</td>
<td>38</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td>30:1</td>
<td>66</td>
</tr>
</tbody>
</table>

4. \textit{trans}-1,4-Polyisoprene

| 1,3-Dipole       | Molar Ratio Ratios | \(\%
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{p-MeOC}_6\text{H}_4\text{CNO})</td>
<td>1:1</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>22</td>
</tr>
<tr>
<td>(\text{EtO}_2\text{CCNO})</td>
<td>1:1</td>
<td>33</td>
</tr>
<tr>
<td>(\text{MeO}_2\text{CCNO})</td>
<td>10:1</td>
<td>54</td>
</tr>
<tr>
<td></td>
<td>30:1</td>
<td>75</td>
</tr>
</tbody>
</table>

5. \textit{Styrene-butadiene rubber} (15\% butadiene)

| 1,3-Dipole       | Molar Ratio Ratios | \(\%
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{p-MeOC}_6\text{H}_4\text{CNO})</td>
<td>1:1</td>
<td>22</td>
</tr>
</tbody>
</table>

6. \textit{Polychloroprene}

| 1,3-Dipole       | Molar Ratio Ratios | \(\%
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{EtO}_2\text{CCNO})</td>
<td>1:1</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>10:1</td>
<td>14</td>
</tr>
</tbody>
</table>
5.1 Polymer Effects

Under the same reaction conditions cis-1,4-polybutadiene was found to be some 40% more reactive to nitrile oxide cycloaddition than cis-1,4-polyisoprene. For example, reaction of p-methoxybenzonitrile oxide with cis-1,4-polybutadiene in 1:1 molar ratio proceeded to 22% yield (based on hydroximoyl chloride), whereas the same reaction with cis-1,4-polyisoprene gave 16% isoxazoline. A similar difference was noted in reactions with the equivalent model compounds cis-cyclooctene (68%) and 1-methyl cyclohexene (57%). This behaviour is attributed to the steric hindering effect of the pendent methyl groups of polyisoprene. This effect was found to be significantly worse in the case of the bulkier nitrones. No reaction was detected between a-(4-benzoylphenyl)-N-phenylnitrone and cis-1,4-polyisoprene, whilst reaction with 1-methylcyclohexene gave approximately 1% yield. Similar reactions with cis-1,4-polybutadiene and cis-cyclododecene afforded 14% and 42% yields respectively.

Within the errors of the experimental and analytical techniques, no significant difference could be detected between the reactivities of cis and trans-1,4-polyisoprene. This contrasts previously reported experience. Having established that polyisoprenes are less reactive than polybutadienes, polychloroprene (approximately 75% cis-1,4- and 25% trans-1,4-, by $^{13}$C n.m.r) was examined and found to be about 3 to 4 times less reactive than cis-1,4-polyisoprene. Assuming the steric effect of chlorine and methyl groups to be similar, the difference in reactivity is attributed to the deactivating effect of the electron withdrawing chlorine atom
on the dipolarophile.

A reasonable explanation based on frontier molecular orbital theory (see pages 13-14), is that, if the reaction of these nitrile oxides with these dipolarophiles is predominantly dipole LUMO controlled, then an electron-withdrawing substituent introduced into the alkene would lower its HOMO and LUMO energy levels. It is then possible that the reaction remains predominantly dipole LUMO controlled, but the activation energy (\(\Delta E\)) is increased and the rate decreased (Figure 102).

\[
\begin{align*}
\text{RCNO} & \quad \text{ALKENE} \\
\quad \text{LU} & \quad \downarrow \Delta E \\
\quad \text{HO} & \quad \text{me} \\
\quad \text{HO} & \quad \text{Cl}
\end{align*}
\]

Figure 102

Reaction of methyl fulmidofomate with a non-stereospecific polybutadiene was found to be significantly more facile than with cis-1,4-polybutadiene. The non-specific polybutadiene was estimated (\(^{13}\text{Cn.m.r.}\)) to have 13% of its
unsaturation as pendent vinyl groups, resulting from 1,2-
cycloaddition. The pendent vinyl groups were therefore found
to be more reactive dipolarophiles than in chain alkene groups.
There are likely to be both electronic and steric effects;
monosubstituted double bonds are more polarised and thus more
susceptible to 1,3-dipolar cycloaddition, whilst pendent
vinyl groups on the polymer are less sterically hindered. Steric
considerations are probably more important, as comparison of
the equivalent models cis-cyclooctene (68%) and oct-1-ene (53%)
showed little difference in reactivity with 4-methoxybenzonitrile
oxide.

The reactivity of a styrene-butadiene copolymer containing
15% butadiene units was identical to cis-1,4-butadiene homo-
polymer. Had polymer chain conformation effects been important,
the copolymer might have been expected to be less reactive.

5.2 Molar Ratio Effects

1,3-Dipolar cycloaddition reactions with polydienes were
carried out at a number of starting molar ratios (from 1:1 to
50:1) of the polymer's alkene structural units to the 1,3-
dipole (or its precursor). Reactions at 1:1 molar ratio were
carried out primarily to obtain polymers with a high degree of
modification, in order to examine the nature of the link eg.
by $^{13}$C n.m.r. These polymers were generally dark, hard resinous
materials. Reactions at 10:1 molar ratio were performed
primarily to expose differences in reactivity. Reactions at
30 and 50:1 molar ratios are most likely to parallel potential
commercial practice. For example, addition of an anti-oxidant is
usually at the 1-2% level. Products from reactions at these
molar ratios were generally unchanged in appearance and retained their elastomeric properties.

As the molar ratio of the polymer alkene structural units to the 1,3-dipole (or precursor) was increased, the reaction yields progressively and significantly increased. For example, reaction of cis-1,4-polybutadiene with 3,4,5-trimethoxybenzonitrile oxide at 1, 10, 30 and 50:1 molar ratios, resulted in cycloadduct yields of 19, 45, 51 and 60%, respectively.

In effect, as the molar ratio was increased there was a greater excess of dipolarophile over 1,3-dipole. This would favour 1,3-dipolar cycloaddition by the 1,3-dipole over side reactions, such as dimerisation of nitrile oxides to furoxans or rearrangement to the isomeric isocyanate (Scheme 103).

\[
\begin{align*}
\text{RC} &= \text{N} \rightarrow \text{N} \text{O} \\
\xrightarrow{\Delta} \\
\text{RN} &= \text{C} = \text{O}
\end{align*}
\]
5.3 Reactivity of 1,3-Dipoles

Although nitrones and nitrile oxides were found to have similar reactivity with model compounds, the nitrones proved to be less reactive with cis-1,4-polybutadiene. For example, at a 3:1 excess of alkene groups, α-(4-benzoylphenyl)-N-phenyl-nitrone and 4-benzoylbenzonitrile oxide afforded 14 and 33% yield (based on 1,3-dipole) respectively, of cycloadduct with cis-1,4-polybutadiene. This was attributed to steric considerations and the major part of the present work relates to nitrile oxides.

The success of this project depended on finding sufficiently reactive 1,3-dipoles and suitable reaction conditions to obtain reasonable degrees of cycloaddition to polydienes. Reaction yields depended on both the 1,3-dipolar reactivity of a particular nitrile oxide and its propensity to furoxan formation (dimerisation) which would be the major competing reaction27 (Scheme 104).
The method of nitrile oxide production by the slow thermolysis (in situ) of the corresponding hydroximoyl chloride favour s 1,3-dipolar cycloaddition, rather than dimerisation, as the resultant low steady state concentration of nitrile oxide would minimise the bimolecular process. It is preferable that the dipolarophile should always be present in a large excess during the reaction.

The greatest reactivity of the nitrile oxides studies was found for methyl and ethyl fulmidiformate \( X \).

\[
\begin{align*}
\text{ROC} &\equiv \text{C} & \equiv \text{N} &\equiv \text{O} \\
R = &\text{Me, Et} \\
\end{align*}
\]

The electron-withdrawing \( \text{RO}_2 \text{C}\)-groups tend to lower the orbital energy levels of the dipole and lead to more \( \text{LU}\)-controlled type reactions. This would be expected to give fast rates of reactions with electron rich alkenes (see pages 14-15). The small aliphatic molecules may also be subject to less steric hindrance on cycloaddition to polydienes.

The relative reactivities of the aromatic nitrile oxide studied was considered to be primarily dependent on their propensity for competitive furoxan formation. Thus, yields for 1,3-dipolar cycloaddition to polydienes decreased in the order: 4-methoxybenzonitrile oxide \( > \) 3,4,5-trimethoxybenzonitrile oxide \( > \) 4-benzoylbenzonitrile oxide \( > \) 4-carboxybenzonitrile oxide. It was evident that electron releasing substituents on the aromatic ring favoured 1,3-dipolar cycloaddition
whilst electron withdrawing substituents hindered it. This can be related to previous work\textsuperscript{104} showing that the opposite is true for furoxan formation. Thus rates of dimerisation of aromatic nitrile oxides to furoxans were shown to follow a Hammett type relationship ($\rho = +0.86$), decreasing in the order $m$-Cl $>$ $p$-Cl $>$ H $>$ $p$-Me $>$ $p$-MeO for substituents on benzonitrile oxide.

In order to confirm this effect, reactions were studied on 2,4,6-trimethoxybenzonitrile oxide (I). This is a stable nitrile oxide which shows little tendency to dimerise to furoxan, due to severe steric hindrance\textsuperscript{27}. Rearrangement to an isocyanate (II) does however occur on heating above about 50°C (Scheme 105).

\begin{center}
\begin{tikzpicture}
  \node (I) at (0,0) {
    \begin{tikzcd}
      \text{MeO} & \text{C} &= \text{N} & \text{O} \\
      \text{OMe} & \text{OMe} & \text{OMe} & \text{OMe}
    \end{tikzcd}
  \end{tikzpicture}
  \quad \Delta \quad
  \begin{tikzpicture}
    \node (II) at (2,0) {
      \begin{tikzcd}
        \text{MeO} & \text{N} &= \text{C} &= \text{O} \\
        \text{OMe} & \text{OMe} & \text{OMe}
      \end{tikzcd}
    \end{tikzpicture}
  
  \text{Scheme 105}
\end{center}

When 2,4,6-trimethoxybenzonitrile oxide was reacted at room temperature (to prevent rearrangement) with \textit{cis}-1,4-polybutadiene in toluene solution (with polymer alkene units...
in 10 fold excess), the yield of the 1,3-dipolar cycloaddition was 87%. This nitrile oxide has an intrinsically low reactivity, due to steric hindrance and evidenced by the slow rate of the above reaction which took 8 weeks to complete. However, due to the absence of any competing reaction, a high yield was achieved. This effect was also demonstrated by reaction of 2,4,6-trimethoxybenzonitrile oxide with the model cis-cyclooctene. When heated in benzene solution under reflux, 51% of the cycloadduct and 45% isocyanate (as diarylurea - Scheme 106) were isolated.

\[ \text{cis-cyclooctene} \rightarrow \text{RN=C=O} + \]  

reflux, benzene

\[ \text{PhNH}_2 \]

\[ \text{RNH}-\text{C} \equiv \text{NPh} \]

\[ R = \]

\[ \text{MeO} \]

\[ \text{OMe} \]

\[ \text{OMe} \]

Scheme 106

The same reaction carried out at room temperature took one week to complete (judged by disappearance of the peak at 2300 cm\(^{-1}\) in the infrared spectrum, characteristic of the nitrile oxide) and which afforded 68% cycloadduct and 25% isocyanate. The formation of isocyanate at room temperature has not been reported previously.
These results demonstrate that high yields of cycloaddition can be achieved, even from relatively unreactive 1,3-dipoles, in the absence of any significant competing reaction.

In addition to the factors described above, p-carboxybenzonitrile oxide's particularly low reactivity towards polybutadiene can be ascribed to the low affinity between the polar 1,3-dipole and the polymer. Reaction with the model, cis-cyclooctene gave a reasonable yield (70%) of cycloadduct. Similarly, hydrophilic polyethyleneglycol groups on the nitrile oxide were found to have a significant adverse effect on reaction with polybutadiene. Thus, reactivity of the following nitrile oxides decreased in the order I > II > III (Table 85).

\[
\begin{align*}
4-\text{MeOC}_6\text{H}_4\text{CNO} & \quad 4-\text{MeOCH}_2\text{CH}_2\text{OC}_6\text{H}_4\text{CNO} \\
\text{I} & \quad \text{II} \\
4-\text{MeO(CH}_2\text{CH}_2\text{O)}_6\text{C}_6\text{H}_4\text{CNO} & \\
\text{III}
\end{align*}
\]
6. THE ADDITION OF POLYETHYLENE GLYCOL GROUPS

Polyethylene glycols exhibit powerful hydrophilic properties and have been widely used as surfactants.\(^{47,49}\). It was considered that chemical attachment of polyethylene glycol chains to hydrophobic rubber molecules would produce a new copolymer with potentially useful properties. For example, it might be expected that a rubber tyre produced from such a copolymer would exhibit improved grip on wet surfaces.

Scheme 107 shows the proposed series of reaction steps. The behaviour of nitrile oxide precursor (V) was expected to parallel simpler molecules with which the principles of the reaction had been established earlier; eg p-methoxybenzhydroximoyl chloride (X).

\[
\begin{align*}
\text{MeO} & \quad \text{C} \quad \text{C} = \text{NOH} \\
& \quad \text{X}
\end{align*}
\]

The target was to introduce a pendent chain where "n" would be in the range 5-10. However, initially the synthetic route to the precursor and the polymer reaction were established with \(n=1\) (Scheme 107).

The reaction of p-cresol with ethylene oxide to give I and subsequent methylation using dimethyl sulphate both proceeded in quantitative yield. However, the key step of the synthesis proved to be the introduction of an aldehyde group in the para position (III). Initially, this step was attempted using the
MeC₆H₄OH + nCH₂—CH₂ → MeC₆H₄(OCH₂CH₂)ₙOH

OHCC₆H₄(OCH₂CH₂)ₙOMe ↔ MeC₆H₄(OCH₂CH₂)ₙOMe

NH₂OH/EtOH

HON=CHC₆H₄(OCH₂CH₂)ₙOMe

Cl

HON=C—C₆H₄(OCH₂CH₂)ₙOMe

⁻HCl

MeO(CH₂CH₂O)ₙC₆H₄

For n=1 and n=5 to 6.

Scheme 107
Gattermann-Aldehyde reaction, (Scheme 108).

\[
\begin{align*}
\text{OCH}_2\text{CH}_2\text{OMe} & \quad \xrightarrow{\text{Zn(CN)}_2, \text{HCl}} \quad \text{CH}≡\text{NH·HCl} & \quad \xrightarrow{\text{AlCl}_3, \text{H}_2\text{O}} & \quad \text{CHO} \\
\text{OCH}_2\text{CH}_2\text{OMe} & & \text{OCH}_2\text{CH}_2\text{OMe} & & \text{OCH}_2\text{CH}_2\text{OMe}
\end{align*}
\]

Scheme 108

This procedure proved to be unsatisfactory; various experimental conditions were attempted and the presence of some aldehyde in the product was evident in the crude reaction mixture by \(^1\text{H}-\text{n.m.r.}\) and i.r. analysis, however, no product could be isolated. A likely explanation is that the small amount of aldehyde produced was oxidised to the equivalent carboxylic acid, under the reaction conditions. This was supported by the absorption at 1685 (C=O) cm\(^{-1}\) and 2900-3000 (OH) cm\(^{-1}\) in the i.r. spectrum.

The aldehyde (III) was then successfully synthesised via the Étard reaction. II was reacted with chromyl chloride (X) to give a brown organo-chromium intermediate (Y) which was subsequently hydrolysed (Scheme 109) to the desired aldehyde.
RCH₃ + 2 CrO₂Cl₂ → RCH(OHCrOC₁₂)₂

X

Y

3 RCH(OHCrOC₁₂)₂ + H₂O → 3 RCHO + 4 CrCl₃ + 2 CrO₃

R = MeOCH₂CH₂OC₆H₄⁻

Scheme 109

The structure of Y is that proposed by Etard and as this type of intermediate was said to be explosive no attempt was made to isolate and examine it. The reaction yielded 17% of the aldehyde together with 4.5% of the equivalent carboxylic acid (identified by its ¹Hn.m.r and i.r. spectrum). Subsequent, reaction with ethanolic hydroxylamine to give the oxime (85%) and then with nitrosyl chloride to afford the hydroximoyl chloride (Y), 100%, proceeded easily.

Having established a route to the nitrile oxide precursor, Y, where n=1, a similar procedure was followed to afford a compound with n = 5.9. The methylation of I (n = 5-6) to afford
II proceeded in 85% yield and subsequent $\text{Etard}$ reaction gave the aldehyde III (15%). Examination of this product by $^1$H n.m.r. indicated a value of $n = 5.9$. Compounds IV and V were then synthesised, as above, in 78 and 99% yields, respectively.

Subsequent reaction of the precursors, V with cis-1,4-polybutadiene proved very slow, particularly for the longer chain compound, where $n = 5.9$. Relative yields at a 10:1 molar ratio (of polymer alkene structural units : 1,3-dipole) are shown in table 110, compared with the prototype $p$-methoxy group.

<table>
<thead>
<tr>
<th>1,3-Dipole</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MeOC$_6$H$_4$CNO</td>
<td>69</td>
</tr>
<tr>
<td>MeOCH$_2$CH$_2$OC$_6$H$_4$CNO</td>
<td>26</td>
</tr>
<tr>
<td>MeO(CH$_2$CH$_2$O)$_6$C$_6$H$_4$CNO</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 110

A plausible explanation for the decrease in yield with increasing chain length is that as the hydrophilic polyethylene glycol chain lengthens, the affinity for the hydrophobic polydiene decreases and the cycloaddition reaction is hindered.
7. THE ADDITION OF PENDENT CARBOXYL GROUPS

Previous work has shown that the introduction of carboxyl groups into natural and synthetic polydienes allows subsequent cross-linking using metallic bases (e.g., ZnO). These cross-linked "ionomers" were found to have unusual tensile properties and in particular exhibited high tensile strength in the absence of reinforcing fillers; this is contrasted with sulphur vulcanised rubbers.

Direct attachment of pendent carboxyl groups to cis-1,4-polybutadiene was attempted by reaction with 4-carboxybenz-hydroximoyl chloride (I), in a similar manner to previous reactions. However, the reaction proceeded in very low yield (2.5-5.5%). This is attributed to the low affinity of the precursor for the polymer chain, as previously discussed (p. 150). By contrast, reaction with the equivalent model compound, cis-cyclooctene afforded the cycloadduct (Z) in 70% yield (Scheme 111).

![Scheme 111](image-url)
An alternative approach to carboxyl-modified polydienes is provided by initial reaction with alkoxy carbonyl-substituted nitrile oxides and subsequent hydrolysis of the resulting pendent ester groups. Hydrolysis of the model adduct (A), derived from the cycloaddition of ethyl fulmidoformate (generated in situ from the corresponding hydroximoyl chloride) and cis-cyclooctene, to the equivalent carboxy derivative (B) was achieved in 80% yield at room temperature, by stirring with aqueous sodium hydroxide (Scheme 112).

\[
\text{EtO}_2\text{C.CCl=NOH} \quad \xrightarrow{-\text{HCl}} \quad \text{EtO}_2\text{C.C\equiv N-O} \quad \downarrow \quad \text{aq. NaOH} \quad \xrightarrow{\text{EtO}_2\text{C=NO} \quad (\text{CH}_2)_6} \quad \text{HO}_2\text{C=N} \quad (\text{CH}_2)_6
\]

Scheme 112

This suggested an alternative route to a reasonable yield of pendent carboxy group on polybutadiene. Reaction of ethyl-chlorooximino acetate (C) with cis-1,4-polybutadiene in 1:1 molar ratio yielded a product with about 50% alkene groups modified, D (Scheme 113), refer to table 85.
However, when a solution of $D$ in toluene was stirred with aqueous sodium hydroxide for 70 h, followed by acidification, no hydrolysis of the carbethoxy groups had occurred; judged by i.r. spectroscopy (see below). The failure of aqueous hydrolysis is considered to be due to the modified polymer still retaining a high degree of the hydrophobic nature of cis-1,4-polybutadiene and thus incompatible with aqueous hydrolysis (despite the addition of a phase transfer catalyst).

Successful hydrolysis of $D$ was achieved by heating a toluene solution under reflux for 12 h with a crown ether/potassium hydroxide complex $^{90}$, in the absence of water. The saponified polymer precipitated from toluene solution during the reaction. The conversion was judged to be near quantitative from the
product's i.r. spectrum; the original absorption at 1730 cm⁻¹, due to the ester carbonyl group, had virtually disappeared and had been replaced by a new carbonyl absorption at 1650 cm⁻¹. The insoluble polymer was considered to have a structure as follows:
8. THE ATTEMPTED ADDITION OF HINDERED PHENOL ANTI-OXIDANT GROUPS.

Hindered phenols are often compounded into natural and synthetic polydienes as anti-oxidants, by virtue of their ability to form long lived radicals and thus terminate radical chain degradation reactions. Goodyear have a patent claiming reaction of α-(3,5-di-tert-butyl-4-hydroxyphenyl)-N-phenyl-nitrone (X) with natural rubber.

The only evidence of addition is improved oxidation resistance after repeated solvent extraction. It was therefore considered worthwhile, as part of the current work, to examine the reaction of X with a model compound. After reaction for 48 h at 130°C with cis-cyclododecene, no cycloadduct could be isolated, although a trace (<1%) was identified in the mass spectrum. The only product isolated was 3,5-di-tert-butyl-4-hydroxybenzaldehyde from the hydrolysis of X. The lack of significant cycloaddition is attributed to the above facile hydrolysis of the nitrone and also the deactivating effect of the p-hydroxyl group. The latter effect was further illustrated by the attempted reaction of α-(4-hydroxyphenyl)-N-phenyl-nitrone (Y) with cyclohexene. After 60 h at 130°C, no cycloadduct could be isolated and 93% of the nitrone Y was recovered, unreacted.
Reaction of these nitrones with polydienes was therefore not considered worth pursuing.
9. **CONCLUSIONS**

9.1 **Criteria of Success**

The major aims as set out at the start of the project (p. 118) were satisfied, as follows:

9.1.1 A number of 1,3-dipolar cycloaddition reactions with polydiienes were achieved in good yield (up to 87% for cis-1,4-polybutadiene and 66% for cis-1,4-polyisoprene) and high degrees of modification (up to 55% cis-1,4-PBD, 38% cis-1,4-PIP). This is despite the previously reported low reactivity of these compounds (particularly cis-1,4-PIP) \(^{27,p.97,101}\).

Reaction conditions were established such that high yields were normally obtained with a large molar ratio excess of polymer diene units to 1,3-dipole; and high degrees of modification at 1:1 molar ratio. High yields were facilitated either by the use of reactive 1,3-dipoles (eg. ethyl fulmidoformate) or by minimising possible competing reactions (eg. 2,4,6-tri-methoxybenzonitrile oxide at room temperature). Production of most of the nitrile oxides studied, *in situ* by slow thermolysis of the corresponding hydroximoyl chloride also inhibits competitive reactions by ensuring a large steady-state excess of dipolarophile.

Having established optimum methods of reaction, work-up and analysis, a number of model and polymer 1,3-dipolar reactions were examined. Various criteria influencing 1,3-dipolar cycloaddition reactivity were established, particularly for reactions on polydiienes.

9.1.2 Having synthesised polydiienes with high degrees of modification, \(^{13}\)Cn.m.r spectroscopy was used to unequivocally
establish the nature of the link by comparison with spectra for the corresponding authentic model adducts. This was the first time that the presence of isoxazoline rings on a polydiene had been clearly demonstrated.

The techniques of nitrogen analysis and $^1$H n.m.r were found to be complementary in determining quantitatively, the degree of polymer modification. Previously, nitrogen analysis alone has been used $^{101,102}$. The two techniques gave reasonably consistent results, except for very low degrees of modification.

9.1.3 Two potentially useful functional groups (a polyethylene glycol and a carboxylic acid group) were successfully added to polybutadiene via 1,3-dipolar cycloaddition. This is despite the severe incompatibility of the highly polar functional groups with polydienes.

Successful saponification of pendent ester groups on polybutadiene (added by reaction with alkyl fulmidoformate) demonstrates the potential for further chemical reaction on the modified polydiene following 1,3-dipolar cycloaddition.

9.2 Use of Model Compounds

Generally, the simple alkene model compounds (e.g. cis-cyclooctene, 1-methylcyclohexene) examined, paralleled the reactions on polymer diene units well. Those cases where the polydiene was found to be significantly less reactive than the corresponding model compound, could be attributed to either steric effects or to polar incompatibility between the polymer and the 1,3-dipole.

The principle of using model compounds to trial synthetic
schemes was found to be helpful, prior to attempting reactions on polymers. In particular, comparison of model cycloadducts with modified polydiienes proved invaluable in establishing the presence of isoxazoline rings on the polymers.

9.3 Suggestions for Further Work

9.3.1 There is significant scope to investigate the addition of other potentially useful functional groups to polydiienes, via 1,3-dipolar cycloaddition reactions. This would include the addition of other polymeric chains to produce new graft copolymers.

Having functionalised polydiienes via 1,3-dipolar cycloaddition, there is scope for further chemical transformations.

9.3.2 The work could be extended to other types of 1,3-dipole eg. nitrilimines, nitrile sulphides.

9.3.3 The principles established could be applied to other types of polymer and other chemical reactions. This is particularly true of the use of model compounds and $^{13}$C.n.m.r spectroscopy to elucidate the nature of the modified polymer.

9.3.4 This project has confined itself to the attachment of potentially useful functional groups to polydiienes. The techniques of synthetic and analytical organic chemistry alone have been used. Further work is required to examine the physical properties of the modified polymers and in particular assess if they could serve a useful function.
REFERENCES


26) A. Quilico, Experientia, 1970, 26, 1169.


63) Private communication, Dr. J.A. Hall, I.C.I. Organics Division, Sept. 1977.


72) For example; C.D. Harries, *Ber.*, 1923, 56, 1048.


76) "Encyclopaedia of Polymer Science and Technology," John Wiley and Sons, 1970, 12, 311.


85) R. Breslow - Lecture to Edinburgh University, 6th May 1977.
87) J.F. Barnes - unpublished work.


103) H.J. Harwood, University of Akron (Ohio), unpublished paper.


107) D.J. Harper, ICI Organics Division, unpublished observations.
MODIFICATION OF CIS-1,4-POLYBUTADIENE AND CIS-1,4-POLYISOPRENE VIA 1,3-DIPOLAR CYCLOADDITION WITH NITRILE OXIDES

The 1,3-dipolar cycloaddition reactions of nitrile oxides (1) have found widespread application for the synthesis of heterocycles, (1) but have so far received little attention (2) as a means for the covalent modification of polymers. Yet natural and synthetic polydienes possess unsaturation, which should provide a suitable dipolarophile.

We have treated cis-1,4-polybutadiene (PBD) and cis-1,4-polyisoprene (PIP) with the nitrile oxides 1a and 1b, generated (3) in situ by the thermal dehydrochlorination of the corresponding hydroximoyl chlorides (2a and 2b) and have examined the products by $^1$H and $^{13}$C NMR spectroscopy with the aim of obtaining definitive evidence for the structures of the products. To facilitate the interpretation of the spectra we have also examined the products resulting from the reactions of the same nitrile oxides with the simple alkenes cyclooctene and 1-methylcyclohexene, selected as models for the unsaturation present in the PBD and PIP, respectively.

Heating 2a and cyclooctene (1:10) in toluene until the evolution of HCl had ceased (after ca. 80 hr), followed by removal of the solvent and excess dipolarophile afforded the isoxazoline 3a (82%). The $^{13}$C NMR spectrum (CDCl$_3$) of the product showed absorptions at 87.4 and 48.4 ppm, characteristic of the CH groups at the 5- and 4-positions of the isoxazoline ring. Likewise 2a and 1-methylcyclohexene gave 4a (74%) with corresponding $^{13}$C NMR peaks at 88.0 (CMe) and 48.7 (CH) ppm.

Having established the ability of the nitrile oxide (1) to undergo cycloaddition with di- and tri-substituted alkenes, its reactions with the polydienes were studied.

A solution of 2a (5.0 g, 33 mmole) and PBD* (1.78 g, giving a 1:1 molar

*The stereospecificities of the samples of cis-PBD and cis-PIP were estimated to be > 98% by $^{13}$C NMR.
Fig. 1. Proton decoupled $^{13}$C NMR spectra ($\text{CDCl}_3$) of PBD modified by \(\text{Ia}\) with off-resonance decoupled spectrum (above). The peaks are assigned as follows: 160.4 (C=O), 155.5 (isoxazoline C), 127-130 (CH of PBD), 86.0 (isoxazoline CH), 61.6 (CH$_2$ of EtO$_2$C), 46.6 (isoxazoline CH), 22-28 (CH$_2$ of PBD), 13.6 (CH$_3$ of EtO$_2$C) ppm from Me$_4$Si.

Ratio of 2a to butadiene units in the polymer) in dry toluene (800 ml) was heated under reflux until evolution of HCl had ceased (80 hr). Removal of the solvent, precipitation from methanol (x3) and drying afforded a brown solid (1.23 g). The presence in the product of units derived from \(\text{Ia}\) was established by elemental analysis (6.3% N), IR (C=O, $\nu_{\text{max}}$ 1720 cm$^{-1}$) and $^1$H NMR spectroscopy ($\text{CDCl}_3$; $\delta$ 4.53 (2H, q, J 7 Hz, CH$_2$), 1.32 (3H, t,
TABLE I

Modification of cis-1,4-Polybutadiene (PBD) and cis-1,4-Polyisoprene (PIP) by Nitrile Oxides 1a and 1b

<table>
<thead>
<tr>
<th>Polyalkene</th>
<th>Nitrile Oxide</th>
<th>Reactant a Molar Ratio</th>
<th>Product Ratio b H NMR</th>
<th>N-Analysis</th>
<th>% Yield c</th>
</tr>
</thead>
<tbody>
<tr>
<td>PBD</td>
<td>1a</td>
<td>1.0</td>
<td>0.7</td>
<td>1.0</td>
<td>55</td>
</tr>
<tr>
<td>PBD</td>
<td>1b</td>
<td>1.0</td>
<td>1.0</td>
<td>1.4</td>
<td>45</td>
</tr>
<tr>
<td>PBD</td>
<td>1b</td>
<td>10</td>
<td>11</td>
<td>13</td>
<td>77</td>
</tr>
<tr>
<td>PBD</td>
<td>1b</td>
<td>30</td>
<td>35</td>
<td>33</td>
<td>86</td>
</tr>
<tr>
<td>PIP</td>
<td>1a</td>
<td>1.0</td>
<td>1.5</td>
<td>2.0</td>
<td>36</td>
</tr>
<tr>
<td>PIP</td>
<td>1b</td>
<td>1.0</td>
<td>1.3</td>
<td>2.0</td>
<td>38</td>
</tr>
<tr>
<td>PIP</td>
<td>1b</td>
<td>10</td>
<td>17</td>
<td>22</td>
<td>49</td>
</tr>
<tr>
<td>PIP</td>
<td>1b</td>
<td>30</td>
<td>44</td>
<td>44</td>
<td>66</td>
</tr>
</tbody>
</table>

a Molar Ratio of alkene units in polymer to 2.
b Molar Ratio of unreacted alkene units in polymer to incorporated 1.
c Percent of 1 attached to polymer, based on average of H NMR and N-analysis results.

The 1H NMR spectrum (Fig. 1) not only provided confirmation of the presence of ethoxycarbonyl groups, but also permitted the nature of their link to the polymer to be established. The absorptions at 86.0 and 46.6 ppm are clearly shown by single-frequency off-resonance decoupling to be due to CH groups and, in view of the similarity of their chemical shifts to those of model compound 3a, they are assigned to the carbons at the 5- and 4-positions of an isoxazoline ring in the modified polymer. These results are consistent with cycloaddition of 1a to PBD.

Similarly 2a with PIP* (1:1 molar ratio) gave a product with 36% of the isoprene units converted to isoxazoline rings. Furthermore the 13C NMR spectrum shows peaks at 91.6 (CMe) and 54.3 (CH) ppm, similar to those found for the model adduct 4a.

Table I also shows the effect on the extent of modification of varying the reactant ratio. For PBD the yield was found to increase from 45% for one alkene unit per mole of 2b to 86% at 30:1, while for PIP the proportion rose from 38% at 1:1 to 66% at 30:1.
These results not only establish the character of the modified polymer, but also demonstrate that, in spite of the reported (1, p. 97) low reactivity of di- and trialkyl substituted alkene dipolarophiles, high yields of the cycloadducts may be achieved.

References


Leo Gajser
R. Michael Paton

Department of Chemistry
University of Edinburgh
West Mains Road
Edinburgh EH9 3JJ
Scotland

John H. Hall
David J. Harper

Imperial Chemical Industries Ltd.
Organics Division
P.O. Box 42, Hexagon House
Blackley, Manchester M9 3DA
England

Received March 14, 1980
Accepted May 23, 1980