Homolytic and Heterolytic Reactions of Organic Peroxides and Organic Sulphides and their Application to the Structural Characterisation of Polymer Networks.

by

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Summary.

Very few techniques exist to study complex chemical structures in which polymer chains are joined by peroxide and sulphur bridges. One of the more successful techniques viz. the use of chemical probes, has its limitations, consequently the objective in this thesis is to investigate the reactions of nucleophiles with organic peroxides and disulphides with a view towards extending the range of nucleophiles suitable for use as chemical probes.

Triphenylphosphine and sodium dialkyl phosphites react in a well established manner with disulphides and in view of the similar chemical behaviour of oxygen and sulphur analogues, these two nucleophiles were initially selected for development as chemical probes for the structural elucidation of oxidised polymer networks.

A study of the reactions of cyclic phosphoramidites with alkenyl disulphides has been carried out with the aim of replacing triphenylphosphine by a nucleophile requiring shorter reaction times.

Finally, the reactions of Grignard reagents with disulphides and peroxides were observed since it was expected that this group of nucleophiles would be very effective in cleaving 0-0 and S-S bonds.

It has been found that reaction of triphenylphosphine with cyclic allylic peroxides involves a S_Ni rearrangement similar to that involved in the corresponding reactions of alkenyl disulphides; reaction of triphenylphosphine with acyclic allylic peroxides is complex and an allylic rearrangement does not appear to be involved.

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In the absence of steric hindrance, sodium dialkyl phosphites cleave peroxides to form a phosphate and sodium alkoxide.

Grignard reagents cleave peroxides by two simultaneous reactions; disulphides are, however, more resistant to attack and only one reaction pathway is involved.

Desulphuration of alkenyl disulphides by cyclic phosphoramidites involves an S_Ni' rearrangement but reaction does not yield the allylically rearranged monosulphide quantitatively. This work was carried out between 1965 and 1968 in the University of Aston in Birmingham. It has been done independently and has not been submitted for any other degree.

Dekelton

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INTRODUCTION

The peroxide bond occurs in an extensive range of organic materials and is usually formed during the atmospheric oxidation of hydrocarbons.¹ This can lead to either a deterioration in the desirable properties of technological materials or can lead to the enhancement of these properties. Consequently, studies have been carried out on the promotion and inhibition of hydrocarbon oxidation and emphasis has been placed on a structural determination of the resultant oxidised materials.

By comparison, the sulphide linkage occurs in a limited range of compounds² but because of the economic importance of vulcanised natural rubber, this system has been studied extensively in order to determine the chemical environment of the sulphide linkages.³

Raw natural rubber is a high molecular weight cis 1,4polyisoprene which has little commercial importance until it has undergone a process of vulcanisation, in which the polyisoprene chains are crosslinked by sulphur bridges to form a three dimensional network. A structural determination of the vulcanisate enables a correlation to be made between the chemical structure and physical properties, thereby aiding the formulation of materials which best fulfil particular requirements.

In common with many other polymers, vulcanised rubber suffers chemical and physical change on exposure to air, the resultant materials containing peroxidic functions and the products of peroxide decomposition. A knowledge of the chemical structure of aged polymers would give some indication of the oxidation mechanism and once this mechanism is fully understood it could lay the foundations for the development of new types of antioxidants which might be incorporated into the polymer

during its fabrication.

One of the more successful methods used to determine vulcanisate structures has been the use of chemical probes,⁴ reagents which react specifically with one or more of the sulphur crosslinks, making it possible to estimate the concentration of that particular crosslink in the material. An essential preliminary to the use of chemical probes is a study of the reactions of these reagents with authentic chemical compounds which are structurally similar to the groupings expected in polymeric materials.

Many reagents have been investigated for their use as vulcanisate probes but almost all have serious limitations. However, very few chemical probes have been developed to study the structure of oxidised polymers but in view of the chemical similarity of oxygen and sulphur analogues it is likely that probes which have proved useful for the structural determination of vulcanisates will be applicable to the study of oxidised polymer structures.

Consequently, the purpose of the present study is to increase the range of probes suitable for the structural characterisation of rubber vulcanisates and in addition to investigate the possibility of using this extended range of probes to elucidate the structures of oxidised polymers.

The presence of the peroxide bond has been noted in an extensive range of materials and usually results from the interaction of a hydrocarbon with oxygen, the reaction being catalysed by heat, ultraviolet and other high energy radiation. The increased use of rubbers, plastics, foodstuffs and oils has promoted interest in oxidation processes and the development of stabilisers to inhibit oxidation has become of economic

importance.

Some industrial processes are dependent on oxidation to develop the desirable properties and amongst these are the setting of surface coatings and the compounding of raw rubber. The majority of oxidisable materials, however, undergo changes resulting in a deterioration of properties, due to the formation of intermolecular crosslinks which cause stiffening and ultimate rigidity due to the polymer chains becoming bound together, thereby inhibiting and ultimately preventing relative movement of these chains.⁵

Studies on the purified constituents of lubricating oils⁶ have shown that the initially formed peroxides readily decompose to acids, ketones, aldehydes, alcohols and ethers but that the unpurified raw oil is more resistant to oxidation due to the inhibiting effect of the sulphurous and nitrogenous impurities which may act as inhibitors or peroxide decomposers.

Saturated polyolefines like polyethylene and particularly poly propylene⁷ readily undergo atmospheric oxidation unless stabilised. Light induced oxidation of polyvinyl chloride⁸ results in stiffening of plasticised stocks and subsequent discolouration.

Some knowledge of the structure of aged networks has been obtained from a study of the oxidation of low molecular weight analogues of polymer systems;⁸ the oxidation products of simple organic compounds are characterised and the assumption is then made that a similar reaction occurs in that part of the polymer system which is structurally related to the model compound. Studies on conjugated dienes⁹ have shown that oxidation can proceed by the less favoured non chain reaction involving addition to the 1,4-position (reaction 1), in which case a

photosensitiser and light are necessary, or alternatively, an alkyl peroxy radical is formed which then undergoes intramolecular addition to the conjugated diene (reaction 2).

$$CH_3(CH_2)_4CH=CHCH=CHCHR \rightarrow CH_3(CH_2)_4CH CHCHR$$
 (1)

$$CH_3(CH_2)_4CHCH=CHCH=CHR \longrightarrow CH_3(CH_2)_4CH CHCHR (2)$$

Infra-red¹⁰ and ultra-violet spectroscopy¹¹ have been used to follow the formation of several functional groups during the ageing of polymers. Unfortunately these techniques are not applicable to the formation of ethers, epoxides and peroxides since these groups do not have specific absorptions in these regions and in addition, infra-red spectroscopy is unable to distinguish between chemical modifications of the same grouping, e.g. the O-H stretching frequency is identical for alcohols and hydroperoxides and the carbonyl stretching frequencies of aldehydes, ketones and acids are relatively close.

Kinetic studies on oxygen absorption by saturated polyolefins have been carried out¹² and it has been found that those polyolefins with least tertiary hydrogen atoms per molecule are most resistant to oxidation in the solid state; above the melting point, however, there is little difference in rates of oxidation suggesting that it is the detailed morphology of the polymer which is responsible for the difference in stability and not the chemical structure.

Continuous stress relaxation studies¹³ allow an estimate to be made of the chain crosslinking which occurs on oxidation

whilst from viscosity¹⁴ and solubility measurements it is possible to measure changes in molecular weight which occur. However, neither oxygen absorption, stress relaxation, viscosity of solubility studies are able to give any indication of the chemical structures of the oxidised networks, consequently it can be seen that few, if any, satisfactory methods of determining the structure of aged polymers exist.

The disulphide linkage is present in a variety of systems but its immediate environment has been studied more extensively in the sulphur vulcanised natural rubber system than in any other. A complete structural resolution of this vulcanisate requires a knowledge of :-

- a) the number average molecular weight of the chains
- b) the concentration and chemical structure of the crosslinks
- c)the concentration and chemical structure of the main chain modifications

d) the extra network material present.

This structural resolution has been approached by three main experimental techniques.

1) The use of model compounds.

The structures of the products from the vulcanisation reaction are difficult to determine; due to their insolubility in organic solvents, normal organic analytical techniques cannot be used, consequently low molecular weight analogues of natural rubber have been used¹⁵ since the products of their reaction with vulcanising reagents are more readily identified by chemical techniques. From these studies good indications have been obtained of the sulphur groupings likely to be present in vulcanisates.

2) Equilibrium swelling and stress-strain measurements.

The actual number of crosslinks per unit weight of network can be estimated by equilibrium swelling and stress-strain measurements¹⁶ but empirical corrections need to be made to compensate for chain ends and chain entanglements.¹⁷ This technique, however, only provides an estimate of the number of crosslinks present and is unable to differentiate between the types of crosslinks, i.e. mono-, di-, tri- or polysulphidic, and fails to give any indication of the chemical environment of the sulphide link.

3) The use of chemical probes.

Information regarding the type and environment of the sulphide crosslink can be obtained by the use of chemical probes.¹⁸ The value of these reagents is that they react specifically with one type of sulphur crosslink and give a measure of its concentration within the vulcanisate.

Methyl iodide¹⁹ has been used to determine the number of monosulphide crosslinks according to equation 3.

 $RSR' + MeI \longrightarrow RR'MeS'I$ (3)

However, the same stochiometry is not observed in the reactions of dialkenyl- and alkyl alkenyl monosulphides,²⁰ consequently results using this reagent are unreliable. In general, therefore, it can be seen that methyl iodide is unsatisfactory for use as a probe but it has been used to show that C-S-C linkages and not C-C linkages, as reported previously, are formed on vulcanisation of natural rubber with tetramethylthiuram disulphide.²¹

Sodium sulphite²² has been used by Russian workers to determine polysulphide linkages according to equation 4.

 $RS-SX-SR + xSO_3" \longrightarrow RS_2R + xS_2O_3" (4)$

Unfortunately dialkenyl disulphides are further reduced to the monosulphide²³ and in addition difficulty is encountered in introducing the aqueous solution into hydrophobic networks and there is also an uncertainty as to whether the resultant thiosulphate is extracted quantitatively from the network.

The use of lithium aluminium hydride²⁴ has enabled a semi-quantitative estimate to be made of the polysulphide groupings present since it is unreactive towards monosulphides but reacts with di- and polysulphides according to equation 5.

RS-Sx-SR

 $2RSH + xH_2S$ (5)

2) Hydrolysis

Measurement of rubber bound thiol are not very reproducible,²⁵ due to difficulties in estimating the thiol groups in the hydrophobic network, and by loss of thiol by addition to the double bonds in the network.

Organic trisulphides are completely decomposed in less than 30 minutes at 20°C by a 0.4 molar solution of propane-2thiol and piperidine in heptane²⁶ (reaction 6) but the corresponding monosulphide is unreactive and the disulphide reacts very slowly even with more concentrated reagents (reaction 7).

 $RS_{3}R + C_{5}H_{11}N + 3PrSH \longrightarrow PrSSPr + RSH + C_{5}H_{11}NH^{*}SH^{*}$ where $R = C_{2}H_{5}^{-}$, $CMe_{2}=CHCH_{2}CHMe_{-}$, $CH_{3}CH_{2}CH=CMeCH_{2}^{-}$ (6)

RSSR + PrSH ^C5^H11^N RSSPr + RSH (7) Consequently, this reagent is suitable to determine trisulphide linkages in rubber networks, assuming that di- and monosulphides remain unreacted.

Triphenyl phosphine²⁷ and sodium dialkyl phosphites²⁸ have

also been used extensively as probes for vulcanisates and their reactions with disulphides are briefly discussed in chapter 2.

In addition to these three major approaches numerous other methods have been used to a limited extent. Spectroscopic measurements have been employed to study vulcanisate structures and cyclic monosulphides and conjugated double bonds have been identified²⁹ but the method will probably best be used to identify accelerator fragments introduced during vulcanisation, as these should give characteristic spectra.³⁰

The thermal degradation of a network has been used, and is conveniently followed by measuring the decrease in stress as a function of time, in a vulcanisate held at constant elongation. This technique gives a measure of the crosslink and main chain scission which occurs and it has been shown that the rate of loss of strain is related to the type of sulphur bonds in the vulcanisate and that those vulcanisates which have a large concentration of polysulphide crosslinks, as measured by the sodium sulphite probe, were found the show the greatest increase in stress i.e. were least thermally stable.³²

It is apparent, therefore, that very few techniques exist to study complex chemical structures in which polymer chains are joined by peroxide or sulphur bridges. One of the more successful techniques, viz. the use of chemical probes, has its limitations, consequently the objective in this thesis is to investigate the reactions of several nucleophiles with peroxides and disulphides, with the view towards extending the range of these nucleophiles suitable for use as chemical probes to elucidate the structures of polymens containing intermolecular peroxidic and sulphide linkages.

CHAPTER 1

The Reactions of Peroxides with Nucleophilic Reagents.

a) Introduction.

The peroxide molecule is similar to the disulphide molecule in that both are linear and it has been shown theoretically³³ that the interaction of unsymmetrical electron clouds of the two adjacent oxygen atoms should stabilise a nonplanar skew configuration about the 0-0 bond and similar considerations probably apply to the S-S bond.

The bond joining the two oxygen atoms in peroxides is much weaker than that joining the sulphur atoms in disulphides,³⁴ consequently many peroxide reactions involve the formation of free radicals whereas thermal homolysis of disulphides has never been established with certainty.³⁵ The reactions of peroxides involving the cleavage of the 0-0 bondare not exclusively homolytic, and heterolytic cleavage, involving nucleophilic attack on oxygen, has been extensively reported.³⁶

Dialkyl peroxides require hydriodic acid³⁷ to effect cleavage but the more polarised bond in hydroperoxides³⁸ can be cleaved by an S_N^2 attack of iodide ion on oxygen (reaction 8); the weaker and more polarisable peroxide bond in peracids³⁹ is cleaved even by the uncharged iodine atom in aryl iodides but this reaction is probably promoted by an intramolecular proton transfer (reaction 9).

$$I \xrightarrow{0-0Bu^{t}} IOH + Bu^{t}0^{-} (8)$$

$$H$$

$$ArI: \xrightarrow{0-0-C-R} ArIO + O=C-R (9)$$

$$H$$

$$H$$

$$H$$

Displacement of oxygen by oxygen has not been observed in the reactions of simple dialkyl peroxides, hydroperoxides and

perscids and only in very activated systems has this been suggested to account for reaction products. 40

The cleavage of dialkyl peroxides, involving nucleophilic attack by sulphur, has not been reported, but monosulphides react with peracids ⁴¹ and hydroperoxides ⁴² and the reaction has been shown to proceed via nucleophilic attack on oxygen, but in both cases attack is facilitated by hydrogen bonding.

 $R_2S: 0-0 \longrightarrow R_2SO + YH + ROH$ (11) H_1Y-H

where Y-H is a hydrogen bonding solvent.

Nucleophilic attack of amines on oxygen is aided by the lone pair of electrons on the nitrogen and amines have been shown to cleave the O-O bond in both diacyl peroxides and peroxyacids.⁴³

Tervalent phosphorus also behaves as an effective nucleophile by virtue of its high dipole moment. The first cleavage of peroxides by phosphorus was reported in 1927 when Challenger and Wilson showed that triphenylbismuthine and triphenylstibine both formed dibenzoates on reaction with dibenzoyl peroxide, whereas triphenylphosphine was oxidised to triphenylphosphine oxide, accompanied by reduction of the peroxide to benzoic anhydride.⁴⁴ Later phthaloyl peroxide⁴⁵ and biphenoyl peroxide⁴⁶ were reduced to the corresponding anhydrides. Mechanistic studies of this reaction were carried out by Greenbaum, Denney and Hoffmann⁴⁷ who used ¹⁸O tracer studies to show that attack does not take place at the carbonyl position, and proposed the following scheme to account for the ¹⁸ O distribution in the products:-



These authors discount a free radical mechanism because radical attack does not take place on the solvent nor are there any products formed corresponding to radical decomposition; they supported the polar mechanism by their claim that free p-nitrobenzoate ion in solution may be incorporated into the anhydride product.

Further work by Horner and Jurgeleit⁴⁸ and by Denney and Greenbaum⁴⁹ has shown that unsymmetrical acyl peroxides yield unsymmetrical anhydrides only, hence the reaction of p-phenylbenzoyl-benzoyl peroxide with tri-n-butyl phosphine yields the unsymmetrical anhydride exclusively. Since the p-phenyl group exerts a negligible polarisation on the peroxide linkage, attack at either oxygen atom should take place at roughly the same rate, such that at any instant, the concentration of the following four species should be equal.

$$Ph-\bigcirc -C-OP(Bu^{n})_{3}$$

$$(i)$$

$$O=C-Ph$$

$$I$$

$$-O$$

$$(iii)$$

$$(iv)$$

The absence of any symmetrical anhydride suggests that these ion pairs (i and iii, and ii and iv) are bound together very tightly and in the light of this latter investigation it is difficult to rationalise the observation that foreign anions in solution can become incorporated into the product unless their concentration in solution is very high. Denney and Greenbaum also showed that the reaction of unsymmetrical peroxides is dependent on the relative charge densities at oxygen. The more electropositive oxygen atom is the preferred point of attack and since this produces the less thermodynamically stable anion it must be assumed that the reaction is kinetically controlled. The reduction of p-nitro-p'methoxybenzoyl peroxide using tri-n-butyl phosphine results in 100% attack at the more electropositive oxygen atom.

(13)

Horner and Jurgeleit⁵⁰ have studied the reactions of phosphines with a variety of peroxides and proposed a general scheme, involving the formation of an ion pair, to account for the products (reaction 14).

ROOR + $R_{3}^{+}P \rightarrow [R_{-0}^{+}PR_{3}^{-}OR] \rightarrow ROR + R_{3}^{+}P=0$ (14) As an example of this reaction these workers cited the reduction of di-t-butyl peroxide to di-t-butyl ether using triphenylphosphine at 114°C. Walling, Basedow and Savas⁵¹ failed to isolate this ether and showed that decomposition of the peroxide had occurred via a radical process; although the polar scission of di-t-butyl peroxide by triphenylphosphine or by the more nucleophilic triethylphosphite has been ruled out, the polar scission of t-butyl hydroperoxide by triethyl phosphite at 0°C has been reported (reaction 15), and the following scheme has been suggested.

Bu^tOOH + (EtO)₃P: \rightarrow [Bu^tOP(OEt)₃ OH] \rightarrow Bu^tOH + O=P(OEt)₃ (15) However, Denney et. al.⁵¹ have pointed out that such an intermediate would be expected to yield a mixture of t-butyl- and ethyl cloohol and since only t-butanol was formed, they proposed an alternative mechanism in which attack of phosphorus on the less sterically hindered and more electropositive oxygen atom yielded an intermediate which decomposed by a simple proton transfer (reaction 16s), or in which reaction occurred by a more likely simultaneous proton transfer (reaction 16b).

Although phosphines and phosphites do not cleave di-tbutyl peroxide heterolytically, it is possible for polar scission of peroxides to occur when steric hindrance is reduced, and diethyl peroxide has been reduced to diethyl ether under conditions which are unfavourable for the production of radicals.

In addition to the reactions outlined above, the nucleophilic attack on peroxides by many other reagents has been studied and cleavage of peroxides by the π -electrons in double bonds,⁵³ lithium aluminium hydride,⁵⁴ aluminium isopropoxide⁵⁵ and Grignard reagents⁵⁶ has been briefly reported.

It can be seen, therefore, that there is an extensive range of nucleophiles able to cleave peroxides by attack on oxygen, but it has previously been shown that triphenylphosphine and sodium dialkyl phosphites react in a well established manner with disulphides, ⁵⁷ consequently these two reagents were initially selected for development as chemical probes

for the structural elucidation of oxidised polymer networks. Since it was expected that Grignard reagents would be even more effective in cleaving peroxides a study of the reactions of these reagents with peroxides was also undertaken. b) The reaction of triphenylphosphine with peroxides.

i) Introduction.

The reactions of triphenylphosphine with allylic disulphides have been established and used to deduce the chemical environment of disulphide linkages in sulphur vulcanised rubber.⁵⁸ Considering the similar chemical reactivity of oxygen and sulphur analogues it seemed reasonable to assume that triphenylphosphine could also be used to investigate the presence of allylic peroxides in oxidised polymeric materials. Consequently a study has been carried out on the reactions of triphenylphosphine with simple allylic peroxides since these allylic peroxides are simple analogues of the oxidised polymer networks. The allylic peroxide initially chosen for study was ascaridole (vi), because this is a readily available naturally occurring peroxide and can also be obtained on passing oxygen through a strongly illuminated solution of p-mentha-1,3-diene (v) in the presence of a photosensitiser (reaction 17).59

The reaction of ascaridole with triphenylphosphine has 60 previously been studied by Horner and Jurgeleit as part of a comprehensive study of the reactions of peroxides with triphenylphosphine and these workers proposed that the reaction of ascaridole occurs via the formation of an "ion pair" (vii) to yield 1,4-oxido-p-menth-2-ene (viii) and triphenylphosphine oxide (reaction 18).



In the reaction of dialkenyl- and alkenyl, alkyl disulphides with triphenylphosphine, Moore⁶¹ found that desulphuration occurred exclusively via an S_N i' mechanism (reaction 19) and that the alternative S_N^2 reaction (reaction 20) was not involved.



It can be seen that ascaridole is able to react by either mechanism but in this case the two pathways would yield different products. Consequently, a re-investigation of the ascaridole-triphenylphosphine reaction was carried out as an initial step in the development of chemical probes for oxidised polymers, and in particular to determine to what extent the S_N ⁱ and S_N ² mechanisms contributed to the reaction.

ii) Results and Discussion.

The reaction between ascaridole and triphenylphosphine in the dark at 80°C yields triphenylphosphine oxide and 3,4-epoxy-p-menth-1,2-ene (ix) only and not 1,4-oxido-pmenth-2,3-ene (viii) as previously reported.



Since these conditions were slightly different to those reported by Horner and Jurgeleit it was possible that this small variation in experimental conditions might have been sufficient to cause the reaction to proceed by an alternative mechanism and to yield different products. The reaction was therefore repeated using the original conditions, involving reaction at 100°C in petroleum ether, but difficulty was encountered in effecting a clean separation of volatile product from solvent. The nuclear magnetic resonance (n.m.r.) spectrum, however, indicated that the product was again (ix). In order to eliminate the difficulties associated with removal of the petroleum ether, the reaction was carried out at 100°C in toluene and once again the product was shown to be (ix).

A molecular model of ascaridole indicates that the molecule adopts a strained boat configuration and although



it is difficult to determine whether the alkyl substituents offer any steric hindrance to the attacking phosphine nucleophile it would be expected that the isopropyl group would cause greater hindrance, thereby directing attack away from the **p**-oxygen atom. In addition it has been shown that the relative charge densities on the two oxygen atoms profoundly effects the position of nucleophilic attack on

peroxides, the nucleophile preferring to attack the more electropositive oxygen atom, thereby liberating the less thermodynamically stable anion. Since the electron release of the isopropyl group is greater than that of the methyl group it would be expected that the steric and electronic factors would both direct initial attack of triphenylphosphine at the \ll -oxygen atom. Consequently, it is proposed that the reaction of ascaridde with triphenylphosphine occurs according to scheme (21a) and that reactions (21b) and (18)



Reaction initially involves attack on the d-oxygen atom to yield the "ion pair" (x); the oxyanion then undergoes nucleophilic attack on the double bond and the consequent concerted allylic rearrangement results in the liberation of triphenylphosphine oxide and the formation of (ix). The less favourable nucleophilic attack of phosphorus on the β -oxygen atom would similarly be expected to yield the isomeric 1,2-oxido-p-menth-3,4-ene (xii) vis the intermediate (xi) (sequence 21b) but (xii) was not isolated.

In view of the extensive radical reactions of peroxides it is possible that nucleophilic attack is preceded by homolysis of the peroxide bond. Subsequent attack by

triphenylphosphine on one of the alkoxy radicals would then yield an intermediate (xiii) which could form the observed products by radical attack on the double bond followed by allylic rearrangement (reaction 22).



However, it has been shown in the present work that ascaridole is stable in benzene at 80°C, and that no products are formed indicative of radical formation. In addition, homolysis would yield two oxyradicals which are almost equally accessible to attack by triphenylphosphine and it would be expected that (xii) would be formed by reaction (23), but this compound was



not observed.

Ascaridole readily isomerises to isoascaridole (xiv) in p-xylene at 140°C⁶² and since it is known that tervalent phosphorus is able to reduce epoxides to the corresponding olefins,⁶³ it is possible that ascaridole first undergoes isomerisation and that triphenylphosphine then reduces the lesser sterically hindered epoxide (reaction 24), but it has been shown in the present work that ascaridole is stable in benzene, in the dark, at 80°C and also that triphenylphosphine is unable to reduce isoascaridole under the conditions employed.



It must be concluded, therefore, that the most likely mechanism which accounts for the reduction of ascaridole by triphenylphosphine is reaction (21a).



The structure of the product from the reaction of ascaridole with triphenylphosphine, was elucidated from the n.m.r. and infra-red (i.r.) spectra and also by peroxidation and hydrogenation studies. In addition, the action of heat on (xii) yields p-cymene and water only, thereby indicating the elemental composition.

Oxidation of (xii) using perbenzoic acid showed that only one double bond was present and the product of oxidation was shown to be isoascaridole, whose structure is as written (xiv)⁶⁴ and not as previously assigned (xv).⁶⁵



On hydrogenation of (xii) to confirm the presence of only one double bond in the molecule, only one mole of hydrogen was

absorbed per mole of (xii) indicating the presence of only one double bond in the molecule. However, gas liquid chromatographic (g.l.c.) examination of the products of hydrogenation showed two major components and the i.r. spectrum showed an intense band at 3400cm.⁻¹ indicative of an hydroxyl group. The most probable interpretation of this data is that the *d*-epoxide ring has been reduced in preference to the double bond, to yield a mixture of two alcohols (xvi) and (xvii).



This reaction was confirmed by the disappearance of the band at 870 cm^{-1} 66 attributable to the *d*-epoxide and whilst it is not surprising that the double bond has remained inert⁶⁷ it is surprising that the relatively stable epoxide ring should have been opened, and this must be due in part to the effect of the adjacent double bond, because the diepoxide, isoascaridole, (xiv) is stable under the same conditions.

The n.m.r. spectrum of ascaridole and its assignment is





a) A doublet centred 9.057 due to the coupling of protons G' and I' with F'.

- b) A singlet at 8.727 due to protons A'. This methyl group is less shielded than is normal, due to a second order paramagnetic effect of the adjacent oxygen atom.
- c) The triplet centred at 3.56γ is typical of a degenerate AB system and the coupling constant (9c/s) is typical of cis olefins.
- d) The absorbance pattern in the region 7.8τ to 8.75τ is due to protons B'C'D'E'F' but is too complex to be conveniently assigned.

The n.m.r. spectrum of the product from the reaction of ascaridole with triphenylphosphine and its assignment is as follows:-

- a) The resonance peak due to protons A occurs at 8.37, a position which is characteristic of $CH_3-C=CH-$ groups.
- b) The doublet centred 7.17 is due to proton J which is coupled with K.
- c) The multiplet at 4.37 is attributed to K.
- d) Integration indicated one olefinic and one epoxide proton.
- e) The four lines centred at 8.97 are of interest; coupling of the methyl groups with the adjacent tertiary proton in isopropyl groups normally gives rise to a doublet, but it has been shown⁶⁸ that when the isopropyl group is attached to an asymmetric carbon atom the two isopropyl methyls become magnetically non equivalent, and each methyl group then exhibits a different chemical shift, so that the usual isopropyl doublet becomes a pair of doublets. This doublet splitting is also noted in the spectrum of isoascaridole, but Danilova⁶⁹ failed to report this phenomenon, and it might not have been apparent on the lower powered instrument used (40MHz). Furthermore, when (xii) is

dehydrated to p-cymene the four lines collapse to a doublet since the asymmetric centre has been removed.

The i.r. spectrum of (xii) does not show absorption between 3000cm⁻¹ and 3100cm⁻¹ which is further proof of the ' proposed structure, since the C-H stretching frequency of cis olefins is weak and difficult to detect. If the product had been (viii) as previously reported, it would have been expected that there would have been a band of medium intensity at ca. 3060cm⁻¹ corresponding to that observed in the i.r. spectrum of ascaridole. In addition, an intense band is observed in the i.r. of the product, at 860cm⁻¹, which is in the position normally associated with a -epoxides of the ethylene type.⁷⁰

The reactions of triphenylphosphine with cyclohexadiene endoperoxide (xvi) and with *d*-phellandrene endoperoxide (xvii) were carried out to see if the reaction pathway established for the reaction of ascaridole (with triphenylphosphine) was generally applicable to cyclic allylic peroxides.



(xvi)



Cyclohexadiene endoperoxide is rapidly reduced by triphenylphosphine in benzene solution, in the dark, even at room temperature, to yield 1,2-oxido-cyclohexa-3,4-ene (xviii) and triphenylphosphine oxide; these products can be accounted for by the mechanism previously proposed.



The i.r. spectrum of (xviii) showed absorption at 1250cm.¹, 1430cm.¹ and 920cm.¹ indicative of the *d*-epoxide ring,⁷⁰ a band at 805cm.¹ arising from the unsaturation (c.f. band at 818cm.¹ in 3,4-epoxy-1-butene.⁷¹) and absorption at 1645cm.¹ characteristic of the C=C stretching frequency of cis olefins.⁷²

The n.m.r. spectrum of (xviii) and its assignment is as follows:-



- a) A multiplet at 4.17 due to protons I and B.
- b) A multiplet at 6.57 due to proton I.
- c) A multiplet at 6.87 due to proton G.

d) Absorbance in the region 7.77 to 8.47 due to protons CDEF.
e) Integration is in agreement with the above assignment.

The reaction of triphenylphosphine with d-phellandrene endoperoxide (xvii) in benzene solution is complete within one hour at 80°C and within 3.25 hours at 40°C. Although the reaction products were not completely characterised the information gained from the n.m.r. and i.r. spectra can be

most readily explained by the following reaction sequence.



Attack at either oxygen atom is probably equally favourable because the isopropyl and methyl groups are too far away to exert much effect, either sterically or inductively, consequently both isomers (xix) and (xx) are formed, in contrast to the ascaridole reaction, where the effects of the alkyl substituents are more pronounced.

The n.m.r. spectrum of the product is complex and almost impossible to assign fully but the following observations support the proposed structures.





- a) Absorption occurs at 4.67 due to B' and C'; absorption occurs in exactly this region in ascaridole.
- b) The proton J absorbs in the region 4.17 to 4.47.
- c) Absorption between 6.77 and 7.27 is due to B,C and J'.

- d) Protons A absorb at 8.27.
- e) Absorption between 8.97 and 9.27 is due to protons E,F, E' and F'.

In comparable reactions involving 1.0 mmoles of triphenylphosphine and 0.5 mmoles each, of ascaridole, cyclohexadiene endoperoxide and -phellandrene endoperoxide, in 5.0 mls. benzene at 80°C, it was seen that the latter two reactions were complete within 1 hour whilst the former reaction required 450 hours to reach completion. The relatively slow rate of reaction of ascaridole is probably attributable to two factors. Firstly, the oxygen atoms are more sterically hindered than ind-phellandrene endoperoxide and cyclohexene endoperoxide, thereby inhibiting attack by triphenylphosphine and secondly, the electron densities at the oxygen atoms are greater due to the electron release of the methyl and isopropyl groups and it has been shown that the reaction is favoured by more electropositive oxygen atoms.

Dialkyl tetrasulphides have been reduced to the corresponding dialkyl disulphides by triphenylphosphine at 80°C and at 140°C and the reaction has been formulated as a stepwise displacement.⁷³

 $\begin{array}{c} R-S-S-S-S-R \longrightarrow \begin{bmatrix} R-S-S & S-S-R \\ I \\ +PPh_{3} \end{bmatrix} \longrightarrow Ph_{3}P=S + RSSSR \quad (29a)$ $\begin{array}{c} R-S-S-S-R \longrightarrow \\ PPh_{3} \end{bmatrix} \xrightarrow{Ph_{3}} Ph_{3}P=S + RSSR \quad (29b)$ $\begin{array}{c} Ph_{3} P$

However, in contrast with dialkenyl- or alkenyl, alkyl disulphides, 74 the dialkyl disulphides are stable to further desulphuration, which indicates that S_N^2 displacement by RS



Graph

Showing the rate of triphenylphosphine oxide formation, at 80°C in benzene, in the reaction between 1.0 mmole triphenylphosphine and 0.5 mmoles each of:a) Ascaridole, XX b) Dihydroascaridole. at saturated carbon is energetically much less favourable. Consequently, a study of the possible reaction of triphenylphosphine with dihydroascaridole (xxi) is of interest since in this 1,4 endoperoxide there is no possibility of an allylic rearrangement.



It can be seen, therefore, that the reactions of ascaridole and dihydroascaridole with triphenylphosphine can be directly compared with the reactions of this reagent with alkenyl and dialkyl disulphides.

It was found that the reaction of dihydroascaridole with triphenylphosphine, in the dark at 80°C, was almost as fast as the reaction of ascaridole with triphenylphosphine. 1 mole of triphenylphosphine oxide was formed per molecule of peroxide and the major volatile products shown to be the two isomeric unsaturated alcohols (xxii) and (xxiii).



G.l.c. analysis of the reaction products indicated the presence of 4 components having a % composition of 47.8, 40.4, 7.2 and 4.6. The i.r. spectrum showed strong absorption
at 3400 cm⁻¹ i.e. at the -OH stretching frequency, and weak absorption above 3000 cm⁻¹ which indicated the presence of the =C-H grouping.

The n.m.r. spectrum was complex but the following observations support the proposed product structures.

- a) A broad multiplet at 4.7τ indicating proton(s) attached to a double bond.
- b) A broad band at 7.25 r was judged to be due to the -OH group as this peak moved to 7.6r on 50% dilution in carbon tetrachloride.
- c) Absorbance at 8.07 indicates allylic protons.
- d) The peak at 8.35 τ is typical of the CH₃-C=C- group.

Furthermore, it can be seen that the reaction of triphenylphosphine with dihydroascaridole, and the hydrogenation of (xii), yield a common product viz. (xxii), and g.l.c. analysis of these reaction products did indicate a common product.

The reaction of dihydroascaridole with triphenylphosphine could have occurred via an homolytic mechanism and the products could be accounted for by sequence (30).



It would seem likely, however, in view of the known rapid rate of reaction between phosphines and alkoxy radicals,⁷⁵ that two moles of triphenylphosphine oxide would result from each molecule of peroxide but this was not observed. Furthermore, it has been shown that no reaction takes place between cyclohexene and dihydroascaridole at 140°C, in contrast to the reaction of di-t-butyl peroxide and cyclohexene,⁷⁶ consequently, it must be concluded that if radicals are formed on heating dihydroascaridole, they recombine before undergoing normal radical reactions.

Consequently, it is proposed that the reaction involves a similar, more probable polar mechanism, involving nucleophilic scission of the peroxide bond (reaction 31).



Attack at the \checkmark and β oxygen atoms yields the two intermediates which react further via an E_2 elimination, the proton becoming attached to the oxyanion. It is probable that the proton does not become completely detached, and that elimination and hydroxyl formation are synchronous steps, and this type of reaction is favoured by the transient formation of a relatively strain free five membered ring.

However, since triphenylphosphine attacks ascaridole specifically at one oxygen atom it is difficult to see why attack at both oxygen atoms in dihydroascaridole should be almost equally favoured.

It has been shown⁷⁷ that the rate of nucleophilic scission of S-S bonds is greater when the disulphide linkage is incorporated in a five membered ring system, than when it forms part of an acyclic disulphide. Consequently, it is possible that peroxides are more readily cleaved when the peroxide linkage forms part of a cyclic system and is held in a cis

configuration.

It was, therefore, decided to investigate the reactions of unsaturated acyclic peroxides in which the O-O bond is not prevented from adopting its more usual non planar skew configuration. This was to investigate the possibility of using triphenylphosphine as a chemical probe to determine the presence of intramolecular peroxide bonds in aged networks.

Acyclic allylic disulphides have been shown to readily undergo desulphuration with triphenylphosphine, via an S_Ni' rearrangement, to yield the isomeric monosulphide (reaction 19)⁷⁸ This reaction is made possible by the presence of d-orbitals on the sulphur and by the polarisability of the sulphur electrons which allow a substantial charge separation before the bond is cleaved. Hence an incipient thiolate ion is formed in close proximity to the sp² carbon atom, thereby enabling attack to take place on the double bond. In the case of allylic peroxides, such charge transfer is impossible and formation of the alkoxy anion necessitates the complete cleavage of the peroxide bond, such that the alkoxy anion is not held in the proximity of the double bond, and the reaction becomes less likely (reaction 32).



The reactions of triphenylphosphine with allyl, t-butyl peroxide, cumyl, cyclohexenyl peroxide and t-butyl, cyclohexenyl peroxide were studied, but because these peroxides were known to undergo radical decomposition at relatively

low temperatures,⁷⁹ to yield alcohols and aldehydes or ketones, reaction was initially carried out at 40°C in benzene solution. However, in the reaction of cumyl-cyclohexenyl peroxide with triphenylphosphine, less than 0.1 moles of triphenylphosphine oxide had been formed per mole of peroxide after 136 hours. The reaction was, therefore, carried out at 80°C, but even after 200 hours the yield of triphenylphosphine oxide was only 0.7 mmoles per mmole peroxide. This reaction was carried out a third time at 80°C but using a temfold increase in concentration and although the initial rate of formation of triphenylphosphine oxide became greater, the final yield of triphenylphosphine oxide decreased to 0.45 mmoles per mmole peroxide.

The rates of formation of triphenylphosphine oxide in the reactions of triphenylphosphine with allyl, t-butyl peroxide and with t-butyl, cyclohexenyl peroxide were determined under these latter conditions but in both cases the final yield of triphenylphosphine oxide was less than 0.5 mmoles per mmole of peroxide.

G.l.c. analysis of the volatile products from the reaction of triphenylphosphine with cumyl-cyclohexenyl peroxide, indicated that cumyl alcohol was the major component and that the remaining components were numerous, none being more than 10% of the total product.

This reaction probably involves prior homolysis of the peroxide, followed by the two oxy radicals undergoing the known radical reactions of combination, disproportionation and proton abstraction, or, undergoing reaction with triphenylphosphine to form triphenylphosphine oxide and an



A polar cleavage of the peroxide would yield a phosphonium ion and an alkoxide ion which could react by either of two mechanisms (reaction 34); the first mechanism (34a), involves attack of the alkoxide ion on the double bond, followed by an allylic rearrangement, to yield cumyl cyclohexenyl ether and triphenylphosphine oxide. The second mechanism (34b) involves the simple E_2 elimination of triphenylphosphine oxide and proton to yield cumyl alcohol and cyclohexadiene.



Probably a more balanced view, especially in the light of the results at different concentrations, is that homolysis occurs, followed by two simultaneous reactions, either hydrogen abstraction or reaction with triphenylphosphine. A large increase in the concentration prevents the radicals from migrating and these radicals undergo combination, disproportionation and proton abstraction and consequently give rise to a lower yield of triphenylphosphine oxide.

Hence, it must be concluded that if nucleophilic cleavage, followed by an allylic rearrangement occurs, similar to the reactions of allylic 1,4-endoperoxides, then it does so only to avery small extent. c) The reaction of sodium dialkyl phosphites with peroxides.

i) Introduction.

Although it has been suggested that the dialkyl esters of phosphorus acid, $P(OH)_3$, exist in two tautomeric forms,⁸⁰

it has been concluded that the tervalent phosphite form makes little or no contribution to the structure,⁸¹ consequently these reagents exhibit little of the nucleophilic reactivity of the trialkyl esters P(OR)_z.

The disulphide bond in dialkyl disulphides is stable to dialkyl phosphites⁸² and only in more polarisable disulphides does cleavage occur⁸³ (e.g. reaction 36).

$$(R'O)_{2}P(O)H + (RO)_{2}P-S-S-P(OR)_{2} \rightarrow (R'O)_{2}P-S-P(OR)_{2} + (RO)_{2}P(S)SH$$

$$(RO)_{2}P(S)SH$$

$$(RO)_{2}P(S)SH$$

$$(RO)_{2}P(S)SH$$

$$(RO)_{2}P(S)SH$$

$$(RO)_{2}P(S)SH$$

The sodium salts of dialkyl phosphites, however, do not exist in the phosphonate form (RO)₂P(O)Na and it has been shown⁸⁴ that their structure probably involves covalent bonding of the sodium and oxygen atoms. Consequently, sodium dialkyl phosphites are strongly nucleophilic as would be expected considering the presence of the tervalent phosphorus.

Because of the application of sodium dialkyl phosphites as chemical probes, the nucleophilic cleavage of disulphides using these reagents has been extensively studied⁸⁵ and it has been found that reaction involves a two stage process. Firstly, between 5° C and 15° C, a cleavage reaction occurs analogous to reaction 35, and then at temperatures between 30° C and 40° C a secondary dealkylation occurs (reaction 36).

As the reactions of sodium dialkyl phosphites with disulphides have been well established, these reagents were selected for use as probes for the oxidised polymer system and an investigation has been carried out on the reactions of simple peroxides with sodium diethyl phosphite (xxiv) and sodium di-n-butyl phosphite (xxv).

(EtO) ₂ PONa	(Bu ⁿ O) ₂ PONa
(xxiv)	(xxv)

ii) Results and Discussion.

Di-n-butyl peroxide is readily cleaved by a 0.25 molar benzene solution of (xxiv) or (xxv), in the dark at 15°C, to yield the appropriate phosphate and sodium alkoxide, by an extremely exothermic reaction.

 $Bu^{n}OOBu^{n} + (RO)_{2}PONs \longrightarrow (RO)_{2}P(O)(OBu^{n}) + Bu^{n}ONs$ (37)

Di-t-butyl peroxide and di-d-cumyl peroxide were both recovered, unchanged, after being heated with a benzene solution of (xxv) at 40°C for 28 days, and this stability is almost certainly due to the bulky t-butyl and d-cumyl groups preventing nucleophilic attack on oxygen.

Reaction can, however, take place at oxygen adjacent to the t-butyl group, if the alkyl substituent on the second oxygen atom is not bulky. Reactions of 0.25 molar benzene solutions of (xxiv) and (xxv) with t-butyl, n-butyl peroxide and t-butyl, ethyl peroxide, yield products corresponding to

attack at both oxygen atoms.

Bu^tOOEt + (RO)₂PONs
$$\longrightarrow$$
 (RO)₂P(O)(OEu^t) + (RO)₂P(O)(OEt) (38)
1.Omole 2.Omoles 0.3moles 0.7moles

 $Bu^{t}OOBu^{n} + (RO)_{2}PONa \longrightarrow (RO)_{2}P(O)(OBu^{t}) + (ROO_{2}P(O)(OBu^{n})(39)$ 1.Omole 2.Omoles: 0.3moles 0.7moles

The low yield of the t-butyl phosphates is attributed to the steric hindrance of the t-butyl group and also to the higher charge density on the oxygen atom adjacent to this group. No ether products were formed corresponding to dealkylation of the phosphate by alkoxide ion.

The reactions of sodium dialkyl phosphites were extended to include the reaction with ascaridole as this had previously been used as a simple model of the allylic peroxide groupings present in aged networks. Ascaridole reacts in a mildly exothermic manner with a benzene solution of (xxv) to yield 3,4-oxido-p-mentha-1-ene (ix) quantitatively. It is proposed that ascaridole undergoes nucleophilic cleavage similar to the dialkyl peroxides, but in this case both oxygen atoms remain attached to the same carbon skeleton thereby allowing reaction to proceed further by attack of the alkoxy anion on the double bond with synchronous allylic rearrangement, to yield (ix).

(ix). + $(Bu^{n}O)_{2}PONa \rightarrow$ $\downarrow 0^{n}Na^{n}$ $\downarrow 0^{n}Na^{n}$ $\downarrow 0^{n}Na^{n}$ $\downarrow 0^{n}Na^{n}$

(40)

This allylic rearrangement is almost identical to the one proposed to account for the reaction of triphenylphosphine with ascaridole, but since the reduction of ascaridole proceeds more readily with (xxv) it is probable that the rate determining step is the initial cleavage of the peroxide. As in the case of cleavage by triphenylphosphine attack occurs specifically at one oxygen atom.

In the reaction of dihydroascaridole with (xxv) there is no possibility of allylic rearrangement after the initial scission of the peroxide bond, consequently this reaction was carried out to determine the likely behaviour of (xxv) towards saturated 1,4 endoperoxides. The reaction product was hydrolysed and ether extracted and the n.m.r. and i.r. spectra were recorded. From this data and the elemental analysis it was seen that the reaction products were (xxvi) or (xxvii) or a mixture of these two isomers, but the spectra were too complex for a complete characterisation of the product to be made.



The mechanism of peroxide cleavage by triphenylphosphine

has previously been established by a study of the reaction of triphenylphosphine with dibenzoyl peroxide. Consequently, the reaction of dibenzoyl peroxide with (xxv) was studied to compare the reactions of these two phosphorus nucleophiles with diacyl peroxides and also to investigate whether the reaction of sodium dialkyl phosphites with alkyl and alkenyl peroxides is generally applicable to other peroxides.

Reaction of dibenzoyl peroxide with a 0.50 molar benzene solution of (xxv) occurs readily at 20°C, to yield sodium benzoate, which was hydrolysed to benzoic acid and isolated in high yield, and a phosphate species whose n.m.r. and i.r. spectra and elemental analysis are consistent with structure (xxviii). Reaction (42) is proposed to account for the reaction products.

Further displacement of $(Bu^n O)_2 P(O)O^n$ by benzoate ion, to yield benzoic anhydride, (analogous to reaction 12), does not appear to take place (reaction 43); this reaction would involve the displacement of a base by a weaker base.

$$\begin{array}{c} 0 & 0 \\ \parallel & \parallel \\ PhC-O-P(OBu^{n})_{2} \\ \end{array} \begin{array}{c} 0 & 0 \\ \parallel \\ 0 \\ \end{array} \begin{array}{c} 0 \\ \parallel \\ \end{array} \begin{array}{c} 0 \\ \end{array} \begin{array}{c} 0 \\ \parallel \\ \end{array} \begin{array}{c} 0 \\ \parallel \\ \end{array} \begin{array}{c} 0 \\ \parallel \\ \end{array} \begin{array}{c} 0 \\ \end{array} \begin{array}{c} 0 \\ \parallel \\ \end{array} \begin{array}{c} 0 \\ \end{array} \end{array} \begin{array}{c} 0 \\ \end{array} \begin{array}{c} 0 \\ \end{array} \end{array} \begin{array}{c} 0 \\ \end{array} \begin{array}{c} 0 \\ \end{array} \end{array}$$

d) The reaction of Grignard reagents with peroxides.

i) Introduction.

The reaction of dialkyl peroxides with Grignard reagents is one of a family of reactions represented by equation (44),

 $RZZR + R'M \longrightarrow RZR' + RZM$ (44)

where Z is an element of the sixth periodic group (O, S and Se) and M is a monovalent metal or a monovalent halometallic group.

This reaction was first proposed by Wuyts,⁸⁶ who reported the reaction between disulphides and Grignard reagents; later Schonberg⁸⁷ showed that dialkyl disulphides and diselenides reacted similarly with phenyl lithium. Campbell et. al.⁸⁸ investigated the reaction of di-t-butyl peroxide with several Grignard reagents, and in the reaction with n-hexyl magnesium bromide, claimed to have isolated t-butyl n-hexyl ether, t-butanol and hex-1-ene, as the major products, consequently, these workers proposed that reaction occurs by two simultaneous mechanisms (reactions 45 and 46).

ROOR + $R'MgX \longrightarrow ROR' + ROMgX$ (45) ROOR + $R'MgX \longrightarrow ROH + ROMgX + (R'-H)$ (46)

Reaction (45) was thought to involve a 1,3-electron shift within a peroxide-Grignard complex (reaction 47) and it was

further proposed that the second simultaneous mechanism

involved a hydride shift from the β -carbon stom of the Grignard resgent, but this mechanism has been discredited by later workers.

 $\begin{array}{ccccccccccc} & & & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & &$

Morrison and Meltzer⁸⁹ reinvestigated the reaction of di-t-butyl peroxide with n-hexyl magnesium bromide and again proposed two simultaneous reactions, the first being identical to reaction (47); the second reaction was considered to involve the homolytic cleavage of a peroxide-Grignard reagent complex, to yield hexane, hex-1-ene, dodecane and t-butanol.

Simet⁹⁰ further reinvestigated this reaction and paid particular attention to the non-metathetical reaction and proposed the following scheme, involving the concerted homolytic cleavage of the 0-0 and R-Mg bonds within a Lewis acid complex of the two reagents.

But		B	ut				
Buto-0 + MgR		Bu ^t 0-0		MgR			
x x			1	x		But	
		Bu ^t O.	+	R•	*	I O-MgX	(49a)
4R•	->	R ₂	+	(R+H)	+	(R-H)	(49b)
Bu ^t 0. + ether solvent	->	ButOH					(49c)
ButOH + RMgX	\rightarrow	ButOMg	C	+	RH		(49a)

It must be concluded that the products from the reactions of Grignard reagents with peroxides, are consistent with two simultaneous reactions, a metathetical reaction involving a 1,3-shift and a concerted homolytic reaction. Since the

Peroxide	Grignard	Ether	Amount	Alcohol	Amount	
	reagent	product	(mmoles)	formed	(mmoles)	
ButOOBut	Bu ⁿ MgCl	Bu ^t OBu ⁿ	2.70	ButOH	5.20	
ButOOBut	Bu ⁿ MgBr	Bu ^t OBu ⁿ	2.42	ButOH	5.50	
Bu ^t OOBu ^t	Bu ⁿ MgI	Bu ^t OBu ⁿ	1.82	ButOH	6.17	
ButOOBut	AllylMgBr	Bu ^t OAllyl	3.10	ButOH	4.70	
Bu ⁿ OOBu ⁿ	Bu ^t MgCl	Bu ^t OBu ⁿ	0.90	Bu ⁿ OH	6.80	1
Bu ⁿ OOBu ^t	Bu ^t MgCl	Bu ^t OBu ⁿ	0.53	Bu ⁿ OH	3.40	
		ButOBut	0.00	ButOH	4.10	1
Bu ^t OOBu ^t	Bu ^t MgCl	Bu ^t OBu ^t	0.00	ButOH	7.90	2
Bu ^t OOBu ⁿ	Bu ⁿ MgCl	Bu ^t OBu ⁿ	1.38	ButOH	2.50	
		Bu ⁿ OBu ⁿ	1.21	Bu ⁿ OH	2.67 5.17	
Bu ⁿ OOBu ⁿ	Bu ⁿ MgCl	Bu ⁿ OBu ⁿ	2.50	Bu ⁿ OH	5.50	
Bu ^t OOBu ^t	AMgBr*	Bu ^t OA [*]	3.46	ButOH	4.45	
	*A = CH2=	CMe-CH2-				
	1. after	1 minute.				

2. after 60 hours.

Table 1

Showing amounts of appropriate alcohol and ether formed in the reactions between 4.0×10^{-3} moles of a given peroxide with 24.0 x 10^{-3} moles Grignard reagent. relative proportions of the products are independent of concentration, it has been concluded that both reactions involve the same Grignard reagent complex.⁹⁰

Since sterically hindered dialkyl peroxides are resistant to the two previous nucleophiles studied, viz. triphenylphosphine and sodium dialkyl phosphites, it was necessary to investigate reagents which are able to cleave these resistant peroxides, and to characterise the reactions of these reagents with peroxides. Consequently, a brief investigation of the reactions of peroxides with Grignard reagents was carried out, since it was already known that di-t-butyl peroxide could be cleaved by Grignard reagents.

ii) Results and Discussion.

In all the reactions studied, 4.0 mmoles peroxide, in ether solution, were added as quickly as possible, to a stirred ethereal solution of 24.0 mmoles of Grignard reagent in an inert atmosphere; the final volume of ether was 50.0 mls. and this was maintained at 20.0°C during the reaction. The rate of formation of the ether product and the rate of reaction of the peroxide were determined by g.l.c. analysis of the reaction medium, after varying intervals of time. The final reaction products were hydrolysed and the quantity of alcohol liberated was determined by g.l.c. analysis. The final products, resulting from the reactions of the Grignard reagents and peroxides are summarised in table 1.

In the reactions of di-t-butyl peroxide (xxix) with n-butyl magnesium halides it can be seen that the rate of formation of the mixed ether is in the order Cl>Br>I, and it can also be seen that the final yield of the mixed ether is dependent on the halogen atom, and follows the same order



Graph 1

Showing the reaction of 4.0 x 10^{-3} moles di-t-butyl peroxide, in 50 mls. ether at 20° C, with 24 x 10^{-3} moles each of:-





Showing rate of disappearance of di-t-butyl peroxide on reaction with:a) N-butyl magnesium chloride, X b) N-butyl magnesium bromide, **D** c) N-butyl magnesium iodide. i.e. n-butyl magnesium chloride gives the greatest yield of n-butyl t-butyl ether and n-butyl magnesium iodide gives the least yield of ether, (graph 1).

It is just possible that this order of reaction is due to the competing homolytic reaction being greatest when n-butyl magnesium iodide is used. However, it can be seen that the rate of removal of di-t-butyl peroxide also follows the order Cl > Br > I, indicating that the rates of the radical reaction do not increase on descending the series, consequently the variations in rate and yield of the ether must be ascribed to the relative nucleophilicities of the three Grignard reagents, (graph 2).

The rate of reaction of allyl magnesium chloride with (xxix) was not determined because the Grignard reagent was only sparingly soluble in ether and formed a white suspension; however, it was found that allyl magnesium bromide is an even more effective nucleophile than the best of the n-butyl magnesium halides i.e. the chloride, by virtue of both the greater rate of reaction and also the final yield of allyl. t-butyl ether and this observation must be accounted for in part, by the greater anionic stability of the allylic group, due to resonance stabilisation, (graph 1).

It has been shown by Herbstman,⁹¹ that in the reaction of di-t-butyl peroxide with Grignard reagents, the extent of the homolytic reaction is very dependent on the alkyl group, being 20-40% in the case of primary Grignard reagents, ca. 60% for secondary and 100% for tertiary Grignard reagents. In this present investigation it is confirmed that reaction of di-tbutyl peroxide with t-butyl magnesium chloride fails to yield di-t-butyl ether. Even in this case, however, the peroxide-

Grignard reagent complex is probably still formed, because the peroxide was entirely converted to t-butoxy magnesium chloride, after 60 hours, presumably via the formation of t-butanol (reaction 50), whereas di-t-butyl peroxide is stable in ethereal solution at the same temperature.

 $Bu^{t} - 0 \qquad Mg - Cl \longrightarrow Bu^{t} OH \longrightarrow RH + Bu^{t} OMgCl$ (50) $Bu^{t} - 0 \qquad R \qquad (50)$

In the reaction of di-n-butyl peroxide with t-butyl magnesium chloride, the heterolytic pathway account for 22.5% of the reaction product, assuming that the ether has been formed only by this process. This is almost certainly due, in part, to this peroxide being less sterically hindered, but also reflects to some extent, the greater thermal instability of the peroxide.

 $Bu^{n}OOBu^{n} + Bu^{t}MgCl \longrightarrow Bu^{t}OBu^{n}$ (51) 4.0mmoles 24.0mmoles 0.9mmoles

Nuceophilic cleavage also occurs during the reaction of t-butyl magnesium chloride with the unsymmetrical n-butyl, t-butyl peroxide but in this reaction ether formation is specific to n-butyl. t-butyl ether and di-t-butyl ether is not formed, even in trace amounts. Hence it must be concluded that whilst t-Grignard reagents are able to undergo nucleophilic attack on peroxides, contrary to earlier evidence, they do so usually when the oxygen atom attacked is not adjacent to a bulky substituent.

However, it has been seen in this present work and

elsewhere, ⁹² that the reaction of t-butyl magnesium chloride with t-butyl perbenzoate gives rise to a small amount of di-t-butyl ether, and formation of this product almost certainly involves nucleophilic attack on the oxygen atom adjacent to the t-butyl group (reaction 52), since it has been shown that ether formation does not involve addition of an alkoxy radical to an alkyl radical, hence reaction (53) can be discounted.

The nucleophilic sttack of Bu^{ts-} on the oxygen atom adjacent to the t-butyl group is probably due to the polarisation of the peroxide linkage which allows the formation of a



strong complex, and the relative charge densities of the oxygen atoms, which direct: attack of the Grignard alkyl substituent at this position.

The reaction of n-butyl magnesium chloride with di-n-butyl peroxide was extremely rapid, and had reached completion within 1 minute at 20°C. It is of interest to note that whereas this peroxide is far less sterically hindered than di-t-butyl peroxide, the yield of ether is less (2.70 mmoles as opposed to 2.50 mmoles), probably again reflecting the greater tendency of di-n-butyl peroxide to undergo radical decomposition.

In the reaction of n-butyl magnesium chloride with the

unsymmetrical n-butyl - t-butyl peroxide, two possible heterolytic reactions may occur. The first involves attack on the oxygen atom adjacent to the bulky t-butyl group, whilst the second involves nucleophilic attack at the oxygen atom adjacent to the relatively less bulky n-butyl group. Therefore, it is of interest to note that the final yields of n-butyl t-butyl ether (1.38 mmoles) and di-n-butyl ether (1.21 mmoles) are similar and it is perhaps surprising to find a greater yield of the mixed ether. This probably substantiates the view that the initial step in the reaction involves the formation of a Grignard reagent-peroxide complex. Of the two possible complexes (xxx) and (xxxi)

(xxx) would be preferred on steric and inductive considerations, and it can be seen that this preferred complex would give rise to the unsymmetrical ether via the 1,3 shift discussed earlier.

Two mechanisms have been proposed to account for the formation of t-butanol in the reaction between di-t-butyl peroxide and Grignard reagents, one of which involves a homolytic reaction (reaction 49) whilst the other involves a 1,3-hydride shift (reaction 48). In the reaction of di-t-butyl peroxide with β -methallyl magnesium bromide there is no possibility of a 1,3-hydride shift because of the absence of β -protons on the Grignard reagent, hence the formation of any t-butanol, as opposed to t-butoxy magnesium bromide, must involve the homolytic reaction. It has been found in this

present work that the yield of t-butyl β -methallyl ether is 3.46 mmoles and that the yield of t-butanol formed on hydrolysis of the final reaction mixture is 4.45 mmoles. Assuming that the amounts of ether and t-butoxy magnesium bromide formed in the metathetical reaction are equal, it must be concluded that 0.99 mmoles t-butyl magnesium bromide result from a simultaneous reaction, which in this case must be homolytic. This reaction, therefore, supports previous evidence that the non-metathetical reaction is homolytic and that a 1,3-hydride shift is not involved.

The relative amounts of ether formed in the reactions of di-t-butyl peroxide with allyl magnesium bromide and with β -methallyl magnesium bromide are in agreement with the expectation that the inductive effect of the β -methyl group gives rise to a stronger nucleophile.

CHAPTER 2

The Reaction of Disulphides with Nucleophiles.

a) Introduction.

The disulphide bond is appreciably stronger than the peroxide bond and does not undergo thermal homolysis⁹³ but disulphides are, however, readily cleaved by nucleophiles, and this is probably due principally to the ability of sulphur to make use of its 3d orbitals in the transition state.

Heterolysis of disulphides, involving nucleophilic attack by oxygen, has been extensively reported, ⁹⁴ particularly where the nucleophile is alkoxide or hydroxide. The latter reagent, however, is only weakly thiophilic but is strongly basic, consequently proton abstraction often competes with simple nucleophilic cleavage, and the extent to which each reaction occurs depends on the particular disulphide structure.⁹⁵

Dialkyl disulphides are stable to alkali but most diaryl disulphides and other more polarisable disulphides are hydrolysed, the reaction being favoured by electron withdrawing ring substituents;⁹⁶ hydrolysis of unsymmetrical disulphides leads to the displacement of the lesser thiophilic anion.⁹⁷

The disulphide bond undergoes cleavage when the attacking element of the nucleophile is sulphur; the sulphite ion readily attacks at sulphur⁹⁸ but the sulphite ion is not as thiophilic as might be expected on consideration of its double negative charge, due to the occurrence of charge delocalisation.

RSSSSR	+	so3	=	RSSSSO' +		RS'
RSSSS03	+	so3"	4	RSSSO3 +	-	s203
Whilst	sulphite	ion	desulphurises	polysulphid	es	and

elemental sulphur, disulphides in general remain unreactive, although cleavage does occur in activated systems, 99 and in

unsymmetrical disulphides the least basic mercaptide is once again displaced. 100

A study of the sulphite exchange reaction ¹⁰¹ shows the remarkable influence of steric hindrance in preventing a backside attack of sulphite on sulphur.

In the reaction:-

 $RS-SO_{3}' + SO_{3}'' \rightleftharpoons RSSO_{3}' + SO_{3}''$ the rate constant, $k_{2} = \frac{[SO_{3}'] [RSSO_{3}]}{[RSSO_{3}] [SO_{3}]}$

and this has been shown to be markedly dependent on the alkyl substituent.



The thiosulphate ion which results from attack of sulphite on sulphur is a weak base but this in turn is able to displace the thiocyanate ion in a reversible process.¹⁰²

RS-SCN + $S_2 o_3'' \rightleftharpoons RS - S_2 o_3' + SCN'$

The nucleophilic cleavage of disulphides involving nitrogen has been briefly reported and it has been shown¹⁰³ that isopropylamine is able to cleave diisopropyl disulphide and that 4,4-dicarboxyl diphenyl disulphide reacts with pyridine and aniline. In addition it has been shown that the thiocyanate ion is displaced from thio-cyanogen and from 2-nitrobenzenesulphenyl thiocyanate.¹⁰⁴

$$NCS-SCN + Et_2NH \longrightarrow NCS-NHEt_2 + SCN$$

Phosphorus nucleophiles have a strong affinity for sulphur due to the high polarisability of the phosphorus electron cloud, which enables electron donation into the empty 3d orbitals on sulphur. Primary, secondary and tertiary alkyl phosphines react rapidly with elemental sulphur ¹⁰⁵ but the stepwise replacement of the alkyl groups in trialkyl phosphines by aryl groups, progressively reduces the rate of reaction. Studies of the reaction of triphenylphosphine with elemental sulphur (s_8) indicate that the rate determining step involves the opening of the s_8 ring; ¹⁰⁶

$$Ph_3P + s_8 \rightarrow Ph_3Pss_6s$$

reaction then proceeds by a more rapid stepwise attack of phosphine on the linear sulphur chain to yield triphenyl-phosphine sulphide.

$$Ph_3P-S-S-S_5-S \longrightarrow Ph_3P=S * Ph_3P-S-S_5-S$$

 PPh_3

Dialkyl tetrasulphides are similarly reduced to the disulphide but since the disulphides remain unreacted even at 140° C, it would appear that S_N² displacement by thiolate ion at saturated carbon is energetically much less favourable.¹⁰⁷

$$\frac{\text{RSS}_2\text{SR}}{\text{Ph}_3\text{P}} \rightarrow \frac{\text{RSSR}}{\text{RSSR}} + \frac{2\text{Ph}_3\text{P}=\text{S}}{\text{Ph}_3\text{P}=\text{S}} + \frac{2\text{Ph}_3\text{P}=\text{S}}{\text{Ph}_3\text{P}=\text{S}} + \frac{2\text{Ph}_3\text{P}=\text{S}}{\text{RSR}} + \frac{2\text{Ph}_3\text{P}=\text{S}}{\text{Ph}_3\text{P}=\text{S}} + \frac{2\text{Ph}_3\text{P}=\text{S}}{\text{RSR}} + \frac{2\text{Ph$$

Alkenyl disulphides do, however, react further, but in this case the free thiolate ion is not formed, and reaction involves an intermediate in which there is little charge separation, consequently an S_N i' mechanism has been proposed to account for this reaction (reaction 19).¹⁰⁸

Trialkyl phosphites are more thiophilic than the phosphines due to the higher electron density at phosphorus resulting from the electron release of the alkoxy groups and triethyl phosphite displaces ethyl thiolate ion from diethyl disulphide as the first step in a two stage process.¹⁰⁹ Further reaction by the thiolate ion, at the O-alkyl position, results in deëthylation of the phosphonium ion to yield the monosulphide and O,O,S-triethyl phosphorothiolate.



Harvey, Jacobson and Jensen,¹¹⁰ investigated the reactions of triethyl phosphite with a variety of disulphides and concluded that the reaction is ionic, involving valence expansion. Reaction is favoured by polarisable disulphide bonds, consequently cleavage of symmetrical diaryl disulphides requires less vigourous conditions than cleavage of dialkyl disulphides. Furthermore, unsymmetrical dialkyl-, alkyl, aryl- and diaryl disulphides are very reactive towards triethylphospite and in all cases attack is specific to one sulphur atom, the anion of the more acidic thiol being displaced.

It has been shown that structures of the type (xxxiii) contribute little to the structure of disulphides. 111

$$\begin{array}{c} R-\ddot{S}-\ddot{S}=R\\ \vdots\\ s+\dot{S}-\end{array} \qquad \qquad \begin{array}{c} R-\ddot{S}=\ddot{S}=R\\ s+\dot{S}-\end{array} \qquad \qquad \begin{array}{c} R-\ddot{S}=\ddot{S}=R\\ s+\dot{S}-\end{array} \qquad \qquad \begin{array}{c} (xxxiii) \end{array}$$

hence, reactions involving direct nucleophilic attack at sulphur would be expected to occur at the more electropositive sulphur atom, which is adjacent to the more strongly electron withdrawing substituent. However, both nucleophilic and electrophilic attack, on disulphides, take place at the more electronegative sulphur atom, suggesting the involvement of an intermediate such that no matter which sulphur atom is attacked, the more stable thiolate ion is preferentially displaced.¹¹²

Moore and Trego¹¹³ found that reaction of allylic disulphides with triethyl phosphite at 80°C does not involve complete scission of the disulphide bond, and suggested that desulphuration occurs via an allylic rearrangement identical to that reported by these workers to explain the desulphuration of allylic disulphides by triphenylphosphine. b) Reaction of sodium dialkyl phosphites with disulphides.

i) Introduction.

Dialkyl phosphites are weakly thiophilic and only cleave highly polarisable S-S bonds.¹¹⁴ The sodium salts of dialkyl phosphites, however, are strongly thiophilic and in the reaction with disulphides, the S-S bond is cleaved as the first step in a two stage process.

Sodium dialkyl phosphites again displace the more stable thiolate ion from unsymmetrical disulphides and it has been found that reactions with disulphides are not reversible, since no thiolate ion scavenger is needed to make the reaction go to completion.¹¹⁵

Moore and Trego¹¹⁶ found that dialkenyl- and alkenyl, alkyl disulphides reacted readily with sodium dialkyl phosphites in benzene solution at 25° C, by a mechanism identical to reaction 54, and that the alternative S_N i' reaction was unimportant. However, in the case of alkenyl disulphides dealkylation occurs, involving cleavage of a C-S bond concurrently with cleavage of the C-O bond (reaction 55).



It has been shown in this thesis that di-n-butyl peroxide is readily cleaved using sodium dialkyl phosphites in benzene solution at 20°C, whereas di-t-butyl peroxide is stable

when heated at 40°C for 28 days. It has also been shown¹¹⁷ that di-n-butyl disulphide is readily cleaved by a benzene solution of sodium dialkyl phosphite at 20°C, consequently it is of interest to investigate the reaction of di-t-butyl disulphide with sodium dialkyl phosphites, to see if the greater bond length of disulphides is such that steric factors are less important, and to see whether cleavage is common to all disulphides or whether reaction is dependent on steric considerations.

ii) Results and Discussion.

0.10 mole di-t-butyl disulphide was added to a solution of 0.40 mole sodium di-n-butyl phosphite in 200 mls. benzene solution and maintained at 25°C but after 214 hours no reaction had occurred.

The reactants were then heated to 80°C for 48 hours after which time all the disulphide had reacted to yield 0.097 moles n-butyl t-butyl monosulphide, as determined by g.l.c. analysis. Di-t-butyl monosulphide was not produced, even in trace amounts.

These observations are accounted for by the following two stage reaction (reaction 56).



The dihedral angle in di-t-butyl peroxide (125°) is larger than that in t-butyl hydroperoxide and hydrogen peroxide (100°) ,

due to the spacial interaction of the t-butyl groups. Similarly, the dihedral angle in di-t-butyl disulphide is larger than that in the unhindered dialkyl disulphides, even though the S-S bond length (2.04°A) is greater than the O-O bond length, ¹¹⁸ hence it is to be expected, on steric considerations, that di-t-butyl disulphide and peroxide are resistant to nucleophilic cleavage.

It is possible that other sterically hindered disulphides are resistant to nucleophilic attack of sodium dialkyl phosphites at 20°C, hence care must be exercised in interpreting the results of structural resolutions of vulcanisates using sodium dialkyl phosphite at this temperature.

- c) The reactions of cyclic phosphoramidites with disulphides.
- i) Introduction.

Triphenylphosphine has been used extensively as a chemical probe to study the structure of sulphur vulcanised rubber, but unfortunately, this reagent involves using the inconvenient conditions of heating to 80°C for 96 hours,¹¹⁹ therefore it is desirable to develop other probes which react similarly, but more quickly. The reactions of triphenylphosphine with diallyl disulphide and other alkenyl disulphides were initially studied as a prerequisite to the use of this reagent as a chemical probe, since these disulphides are reasonable models for the sulphur groupings present in vulcanised networks.¹²⁰

Pilgram, Phillips and Korte¹²¹ have made a study of the reactions of a variety of disulphides with the cyclic esters of phosphoramidous acid (cyclic phosphoramidites) and these

CHR-0, PNR'2 CH2-0

workers stated that "The fact that triphenylphosphine requires a temperature of 80°C to desulphurise diallyl disulphide, whereas cyclic phosphoramidites partially desulphurise diallyl disulphide at room temperature, can be ascribed to the greater nucleophilicity of the cyclic phosphoramidites, in which the electron density about the phosphorus atom is increased by electron release from nitrogen."

Since it was therefore reported that diallyl disulphide was desulphurated more readily by cyclic phosphoramidites than by triphenylphosphine, this former group of phosphorus nucleophiles was selected for further study in this present work

to assess the suitability as chemical probes.

Pilgram et. al. further showed that the disulphides studied could be divided into the following three groups, on the basis of their reactivity towards cyclic phosphoramidites.

- a) Those disulphides which did not react at 110°C, in toluene solution.
- b) Those disulphides which underwent a Michaelis-Arbuzov rearrangement with cleavage of the phospholane ring, to form the phosphoramidothioic ester (reaction 57)

$$\begin{array}{c} R^{*}-S-S-R^{*} \\ R^{*}-S-S-R^{*} \\ R_{2}NP \\ O-CH_{2} \end{array} \xrightarrow{\left[\begin{array}{c} R^{*}-S \\ S^{*} \\ O-CH_{2} \end{array} \right] \xrightarrow{\left[\begin{array}{c} R^{*}-S \\ S^{*} \\ C^{*}-S-R^{*} \\ S^{*} \\ O^{*}-CH_{2} \end{array} \right] \xrightarrow{\left[\begin{array}{c} R^{*}S \\ S^{*} \\ R^{*}S \\ O^{*}-CH_{2} \end{array} \right] \xrightarrow{\left[\begin{array}{c} R^{*}S \\ R^{*}$$

c) Those disulphides which underwent desulphuration, with no ring cleavage, to form the corresponding monosulphide and cyclic phosphoramidothionate (reaction 58).

It is this latter reaction which is applicable to this work, since it was found that diallyl disulphide was readily desulphurated to the monosulphide, presumably via an allylic rearrangement.



In view of the likelyhood that cyclic phosphoramidites would react more quickly than triphenylphosphine, due to increased electron density at phosphorus resulting from electron release by the nitrogen atom, a study of the reactions of





Showing rate of formation of diallyl monosulphide in the reactions between diallyl disulphide (0.5 mmole), in benzene solution at 50°C and 1.0 mmoles each of:a) Triphenylphosphine, b) Triethyl phosphite, c) 2-diethylamino-1,3,2-dioxaphospholane. diallyl disulphide with a range of cyclic phosphoramidites, wass carried out. It was of particular interest to note the effect of the nucleophile structure on the rate and stochiometry of the reaction, with the aim of replacing triphenylphosphine as a probe.

ii) Results and Discussion.

The reactions were all carried out in benzene solution and were followed by measuring the yield of monosulphide formed after varying intervals of time, using g.l.c. techniques. In order to measure this accurately, a small quantity of n-octane was added to the reaction medium as an internal standard and the ratio of the monosulphide peak to the n-octane peak was recorded as a function of time. The ratio value used was the mean of triplicate chromatograms and the % deviation from the mean was shown to be $\langle 2\%$. The absolute concentration of monosulphide product was determined by reference to a calibration curve.

It was known that the reaction of triphenylphosphine with diallyl disulphide occurs rapidly at 80°C and since it was expected that cyclic phosphoramidites would react more quickly, the initial reaction of diallyl disulphide with 2-diethylamino-1,3,2-dioxa-phospholane (xxxvi) was carried out at 50°C; the reactions with triphenylphosphine and triethylphosphite were also studied under the same conditions for comparison and the results are shown in graph 3.

> CH₂-0, P-NEt₂ (xxxvi)

It can be seen that the order of rates of desulphuration are opposite to that expected, and furthermore it can be seen that triphenylphosphine is able to desulphurise diallyl



Mmoles. diallyl monosulphide.

T

Graph 4

Showing rate of formation of diallyl monosulphide in the reactions between diallyl disulphide (0.5 mmole), in benzene solution at 80°C and 1.0 mmole each of:-

a)	Triphenylphosphine,	
b)	2-diethylamino-1,3,2-dioxaphospholane,	
c)	2-di-n-butylamino-1,3,2-dioxaphospholane,	····@······@···
d)	2-piperidino-1,3,2-dioxaphospholane.	- 00-

disulphide below 80°C even in dilute solution.

It was expected that the rate of desulphuration of diallyl disulphide by cyclic phosphoramidites is dependent on the steric requirements and basicity of the amine constituent. A bulky amine group would be likely to inhibit frontal attack of phosphorus on the disulphide and would be likely to induce B-strain resulting in decreased nucleophilicity of the phosphorus atom; the amine basicity would be expected to enhance, to varying degrees, the electron density on phosphorus.

To investigate the effect of amine structure on the reaction, a study was carried out on the rates of desulphuration of diallyl disulphide by a series of 2-substituted 1,3,2dioxaphospholanes (xxxvii) to (xxxvix) in benzene solution at 80° C;



the reaction involving triphenylphosphine was also observed under identical conditions.

The parent amines all have similar basicities but differing steric requirements, consequently, the similar reactivities (graph 4) are perhaps surprising. It should be noted that the reaction does not proceed to stochiometric completion with respect to the formation of monosulphide and also that there is an inverse relationship between the initial rate of reaction and the final yield of the monosulphide; furthermore it can be seen that triphenylphosphine reacts faster than (xxxvii), (xxxviii) and (xxxix) and that it gives an
almost quantitative yield of monosulphide.

It is concluded that this group of nucleophiles is unsuitable as a replacement for triphenylphosphine by virtue of its slower rate of reaction and also the non-stochiomeric yield of monosulphide.

Pilgram et.al. showed that in the disulphides where the resultant incipient thiolate anion can be stabilised by resonance, a Michaelis-Arbuzov reaction occurs (reaction 57).

In the reaction of diallyl disulphide with (xxxvii) to (xxxix) it can be seen that the incipient thiolate anion can become stabilised by resonance within the allyl group, and thus this competing reaction could account for the non-stochiomeric yield of the monosulphide (reaction 59).

$$\begin{array}{c} CH \\ CH_{2} \\ CH_{2} \\ S \\ S \\ CH_{2} \\$$

However, no positive evidence for this reaction was observed and the corresponding phosphoramidothioic ester was not isolated.

If a competing Michaelis-Arbuzov reaction does nccur, it would be expected to be inhibited in the reactions of 2-substituted-4-methyl 1,3,2-dioxaphospholanes (xxxx) with diallyl disulphide, since attack by the thiolate on carbon would



be inhibited by the methyl group and it is possible, under these



This effect is similar to the one proposed by Phillips et. al. to account for the relative stabilities of differing phosphoramidothionates, since these workers found that the phosphoramidothionates derived from the 4-methyl substituted 1,3,2-dioxaphospholanes were more heat stable than the unsubstituted analogues, suggesting that the methyl group prevents thiolate at attack at carbon.



Consequently, with the possible stochiomeric reaction between diallyl disulphide and 2-substituted-4-methyl-1,3,2-dioxaphospholanes, a study was carried out, of the rates and product yields, of the reactions between diallyl disulphide and (xxxxi) to (xxxxiii).

CH₃-CH-O CH₂O^{P-NEt}2 CH₂O^{CH}2^{-CH}2 (xxxxi) (xxxxii)



Graph 5

Showing the rate of formation of diallyl monosulphide in the reactions between diallyl disulphide (0.5 mmole), in benzene solution at 80°C, and 1.0 mmoles each of:a) 2-diethylamino-4-methyl-1,3,2-dioxaphospholane, b) 2-piperidino-4-methyl-1,3,2-dioxaphospholane, c) 2-morpholino-4-methyl-1,3,2-dioxaphospholane. CH₂CH₂O CH₂O CH₂O CH₂O CH₂-CH₂O CH₂-CH₂O (xxxxiii)

The parent amines of (xxxxi) and (xxxxii) have similar basicities but they differ in steric requirements, whereas (xxxxii) and (xxxxiii) are sterically similar but derived from amines of differing basicities. Consequently a study of the reactions of these reagents with diallyl disulphide enables a further investigation of the effect of amine basicity and structure.

It can be seen (graph 5) that the rates of reaction and final yields of diallyl monosulphide are independent of the amine moiety. Furthermore, it is apparent that whilst the yield of monosulphide is not quantitative, it is higher than that recorded in reactions involving the unsubstituted cyclic phosphoramidites. It must be concluded, therefore, that whereas the 4-methyl substituted cyclic phosphoramidites give a higher yield of monosulphide than the unsubstituted ones, reaction is still not quantitative and this series of nucleophiles must be judged to be unsuitable for use as chemical probes.

Although the reaction between diallyl disulphide and cyclic phosphoramidites was assumed to involve an S_N i' mechanism this was not demonstrated in the original work. However, it has been shown in this present work that di-but-2-enyl disulphide is desulphurated to but-2-enyl, 1-methyl allyl monosulphide on reaction with unsubstituted and 4-methyl substituted cyclic phosphoramidites and this confirms the S_N i' mechanism (reaction 60).



Showing the rate of formation of monosulphide, in benzene solution at 80°C, during the reactions between:i) Diallyl disulphide (0.5 mmole) and 1.0 mmole each of:a) Triphenylphosphine, b) 2-diethylamino-1,3,2-dioxaphospholane. ii) Di-but-2-enyl disulphide (0.5 mmole) and 1.0 mmole each of:a) 2-diethylamino-1,3,2-dioxaphospholane, b) 2-diethylamino-4-methyl-1,3,2-dioxaphospholane.



where $R = CH_3$ or H.

It can be seen (graph 6) that the rate of desulphuration is independent of R and that desulphuration of di-but-enyl disulphide occurs less rapidly than desulphuration of diallyl disulphide, presumably due to the steric hindrance of the methyl group attached to the sp² carbon atom. d) The reaction of Grignard reagents with disulphides.

i) Introduction.

Carbanions are expected to be strongly thiophilic due to the concentration of the electron into an orbital of small volume, giving rise to a high charge density.

The cyanide¹²² ion is able to displace many bases from sulphur although this nucleophile must be regarded as a modified carbanion since the charge density is reduced by charge delocalisation with the triply bound nitrogen atom. Cyanide ion is thus less effective than other carbanions and would not normally displace thielate ion from a disulphide unless one of the substituents is an aromatic nucleus containing an electron withdrawing group, in which case the thiophilicity of the displaced thielate ion is reduced.¹²³

The diphenylsulphonyl methane anion, however, readily displaces thiolate ion, the reaction involving carbanion attack on sulphur.¹²⁴

RS-SR + (PhSO₂)₂CH -> RSCH(PhSO₂)₂ + RS

In addition, phenyl lithium and sodium triphenyl methide are both able to cause sulphur-sulphur scission by carbanion attack on sulphur.¹²⁵

Grignard reagents and butyl lithium may both be regarded as carbanions (RMgX and BuⁿLi) and as such may or may not cause cleavage of the disulphide, depending on the particular Grignard structure. The reaction between disulphides and Grignard reagents has been briefly reported,¹²⁶ therefore an investigation was carried out on the reactions of simple disulphides with a variety of Grignard reagents, to note the effect on the reaction

Disulphide	Grignard	Monosulphide	Amount	Thiol formed	Amount	
	reagent	formed	mmoles			
Bu ⁿ SSBu ⁿ	Bu ⁿ MgCl	Bu ⁿ SBu ⁿ	4.02	Bu ⁿ SH	4.01	
ASSA	Bu ⁿ MgCl	ASBu ⁿ	4.08	ASH	3.85	
Bu ^t SSBu ^t	Bu ⁿ MgCl	ButsBun	nil	ButSH	nil	(1)
ButSSBut	Bu ^t MgCl	ButSBut	nil	ButSH	nil	(2)
Bu ⁿ SSBu ⁿ	Bu ^t MgCl	Bu ⁿ SBu ^t	3.88	Bu ⁿ SH	4.13	
Bu ^t SSBu ^t	Bu ⁿ Li	Bu ^t SBu ⁿ	4.00	ButSH	3.97	(3)
Bu ⁿ SSBu ⁿ	AMgBr	Bu ⁿ SA	3.92	Bu ⁿ SH	3.62	
ASSA	AMgBr	ASA	3.98	ASH	3.84	
Bu ^t SSBu ^t	AMgBr	Bu ^t SA	nil	Bu ^t SH	nil	(4)

Table 2

where A = $CH_2=CH-CH_2$ -(1) after 52 hours. (2) after 50 hours. (3) after 48 hours. (4) after 50 hours. of changes in both Grignard and disulphide structure. In particular, it was of interest to determine to what extent, if at all, a competing radical reaction occurred, similar to the one involved in the reactions between peroxides and Grignard reagents.

ii) Results and Discussion.

In all cases reaction involved 4.0 mmoles of disulphide and 24.0 mmoles Grignard reagent in 50.0 mls. diethyl ether at 20°C. The monosulphide product was determined by g.l.c. techniques and the thiol was similarly determined after hydrolysis of the final reaction medium. The products and their concentrations are summarised in table 2.

In all cases where reaction occurred, the products are consistent with carbanion attack on sulphur to displace the mercaptide ion (reaction 61).

By analogy with the reaction between Grignard reagents and peroxides, it is probable that the thiolate ion does not become free and that it becomes bonded to the electrovalent magnesium ion during a four centre displacement as shown. One of the more interesting aspects of the reaction between disulphides and Grignard reagents is the absence of the competing radical reaction. Where reaction does occur, the products indicate, within the limits of experimental error, that only one reaction is involved, as distinct from the peroxides, where the competing radical reaction may become the major reaction.

Disulphides would not normally be expected to yield radicals, in view of the sulphur-sulphur bond strength, but it was just





Showing the rate of removal of di-t-butyl disulphide and rate of formation of n-butyl t-butyl monosulphide, in the reaction between 4 x 10^{-3} moles di-t-butyl disulphide and 24 x 10^{-3} moles n-butyl lithium, in 50 mls. ether at 20° C. possible that prior complexing with the Grignard reagent would give rise to radicals (reaction 62) as in the peroxide reaction (reaction 48a)

$$RSSR + R'MgX \rightarrow RS-S \cdots MgX \rightarrow RS + RSMgX + R' (62)$$

However, the product analysis of the reactions studied showed that if this reaction occurs at all, it does so only to a very insignificant extent.

The n-disulphides studied were readily cleaved even using t-butyl magnesium chloride; on the other hand di-t-butyl disulphide was very resistant to nucleophilic cleavage and was unreactive even to allyl magnesium bromide, which had been shown to be very effective in peroxide cleavage.

N-butyl lithium, however, was effective in cleaving di-tbutyl disulphide, but even this reagent required 0.5 hours for reaction to reach completion (see graph 7).

The enhanced reactivity of n-butyl lithium, as opposed to n-butyl magnesium chloride, towards di-t-butyl disulphide, is probably due to both steric and electric factors. Since the carbanion is the same in both cases, i.e. n-butyl, the steric repulsion is the same. Lithium, however, is able to affect a clear approach to the electrophilic sulphur atom than the magnesium halide group, and this facilitates reaction. Secondly, and probably far more important, the charge density is likely to be greater in the butyl lithium carbanion than in the Grignard reagents, on consideration of the more salt like character of the former reagent.

By using Grignard reagents or butyl lithium it can be seen that disulphide bonds can be selectively cleaved. The Grignard

reagent cleaves only the unhindered disulphides whereas the n-butyl lithium is able to cleave all disulphides. The application of this probe to the study of vulcanisates is, unfortunately, limited since the resultant monosulphide and thiol are bound to the original network and cannot be isolated. These reagents may, however, be used to determine the number of sulphur-sulphur bonds present by estimating the amount of Grignard reagent or butyl lithium consumed in the reaction but this assumes that there are no other reactive groupings present e.g. -SH.

EXPERIMENTAL WORK

Chapter 1: Reaction of peroxides with nucleophilic reagents. a) The reaction of triphenylphosphine with peroxides.

AnalaR benzene was fractionated from sodium wire, through a 50 cm. 1 inch diameter column packed with helices. The fraction boiling 80-81°C was stored over B.D.H. molecular sieve Type 4A(8-12 mesh beads) until required. Triphenylphosphine was a commercial sample kindly supplied by Albright and Wilson; it was recrystallised three times from absolute ethanol m.p. 80.5°C (Lit.80.5°C) C 82.59% M 5.81% Required for C₁₈H₁₅P; C 82.5% H 5.77%

- i) Preparation and purification of peroxides.
- a) <u>Ascaridole</u> (Koch-Light) was purified by recrystallisation from a mixed n-pentane-toluene solvent at -10°C.¹²⁷ N_D²⁰ 1.4734 (Lit. 1.4731).
- b) <u>Dihydroascaridole</u>. Ascaridole was partially hydrogenated using a platinum oxide catalyst in ethanol.¹²⁸ After removal of the solvent the dihydroascaridole was distilled from the platinum residue. b.p. 69.5/0.55.72/0.65...N_D¹⁵ 1.4690 (Lit. 1.4690)¹²⁹ C 71.30% H 1058% Required for C₁₀H₁₈O₂ C 70.60% H 10.70%
- c) <u>d-phellandrene endoperoxide</u> was prepared by the photolytic oxidation of 50 gms. d-phellandrene in 1500 mls. isopropanol using 0.5 gms. methylene blue as an activator.¹³⁰ Oxygen was passed through this solution, which was illuminated by a 300 watt tungsten filament lamp, held 6" distance, for 48 hours. The solvent was then removed using a rotary film evaporator and the residue was distilled at 0.006 mm. 4.3 gms. unreacted d-phellandrene were isolated in the cold trap, N_D²⁰ 1.4770 (1.4770) and 16.4 gms. d-phellandrene

endoperoxide were collected, b.p. $55^{\circ}C/0.006$ mm. N_D²⁰ 1.4778 (1.4812)

d) Preparation of 1,4-cyclohexene endoperoxide.



Preparation of 1,2-dibromocyclohexane. 131

250 mls. (3.0 moles) cyclohexene, in 600 mls. carbon tetrachloride were transferred to a 3 litre round bottomed flask and maintained at 0°C in direct sunlight. A solution of 420 gms. (2.62 moles) of bromine in 290 mls. of carbon tetrachloride were added dropwise over a period of 3 hours whilst maintaining the reactants below 3°C. The solvent and excess cyclohexene were removed and the dark residue was then fractionated to yield 510 gms. 1,2-dibromocyclohexane, b.p. 108-112°C/25 mm.

Preparation of 1,3-cyclohexadiene. 132

500 mls. ethylene glycol and 250 gms. sodium hydroxide were placed in a 2 litre flanged flask and heated slowly for 3 hours until the temperature reached 230°C, at which point 60 mls. wæter had distilled off. 500 gms. freshly distilled 1,2-dibromocyclohexane were added dropwise over a period of 3 hours at a rate equal to the rate of distillation of product. When addition was complete the reactants were heated for a further hour at 250°C. The distillate was transferred to a separating funnel and the organic layer (175 mls.) was separated from the aqueous layer (125 mls.), dried and fractionated. The fraction boiling 75-85°C (120 gms.) was collected and shown by g.l.c. to contain 87% 1,3-cyclohexadiene, together with 7% benzene and 6% cyclohexene. Oxidation of 1,3-cyclohexadiene. 133

60 mls. of this impure 1,3-cyclohexadiene were photolytically oxidised in 1500 mls. isopropanol solution containing 0.5 gms. methylene blue. When the reaction was complete the solvent was removed at reduced pressure and the residue was distilled under high vaccuum. The fraction b.p. 38°C/0.1 mm. solidified in the condenser. This was extracted using benzene, which was then evaporated to yield 8.0 gms. peroxide. This was recrystallised from n-pentane to yield a pale yellow solid m.p. 70°C. The i.r. and n.m.r. spectra were consistent with this compound having the structure assigned. Attempted elemental analysis was not successful due to explosive nature of this peroxide.

e) Preparation of ally1-t-buty1 peroxide. 134

64 gms. "70%" t-butylhydroperoxide (0.5 moles Bu^tOOH) were added to a solution of 28.0 gms. (0.5 moles) potassium hydroxide in 100 mls. methanol. 400 mls. acetone were then added and the resultant solution was maintained below 10°C. 60 gms. (0.5 moles) allyl bromide were added in one portion and the reactants were allowed to stir for 1.5 hours. 1.5 litres water were added and the product was extracted (4 x 100 mls.) with benzene. The benzene solution was dried over magnesium sulphate and distilled, b.p. 56-58°C/75 mm. N²⁵_D 1.4030 (Lit. 1.4015) yield 26 gms. (0.20 moles)

f) Preparation of cyclohexenyl-t-butyl peroxide. 135

120 gms. (1.5 moles) cyclohexene, 51.4 gms. (0.40 moles) "70%" t-butylhydroperoxide and 0.2 gms. cuprous chloride were heated at 70°C for 20 hours. The solution was filtered, dried and distilled. The fraction b.p. 35-45°C/1.0 mm. was collected and redistilled b.p. 35°C/0.7 mm. N_D²⁰ 1.4530 (Lif. 1.4522) yield 10.4 gms. (0.06 moles).

g) Preparation of cyclohexenyl-cumyl peroxide. 136

This was prepared in a similar manner from 147 gms. (1.8 moles) cyclohexene, 44.6 gms. (0.20 moles) "70%" -cumyl hydroperoxide and 0.2 gms. cuprous chloride. The product was distilled at 16 mm. Unreacted hydroperoxide was removed at 75°C and cyclohexenyl-cumyl peroxide distilled at 98°C. N_D²⁰ 1.5234 (Lit. 1.5238) C 78.28% H 8.98%, required for C₁₅H₂₀O₂ C 77.55% H 8.68%, yield 8.68 gms. (0.04 moles). ii) Preparation of isoascaridole.¹³⁷

32.5 gms. (0.19 moles) ascaridole in 25 mls. p-xylene, were added dropwise to 100 mls. p-xylene at 140°C and maintained at this temperature in an atmosphere of nitrogen for a further 24 hours. The solvent was removed at 37°C/14 mm. and 1.3 gms. unisomerised ascaridole were removed at 76°C/1.0 mm. The isoascaridole was distilled from the residue, b.p. 86°C/0.3mm. N_D³⁰ 1.4600 (Lit. 1.4595-1.4602) C 71.35% H 9.52%, required for C₁₀H₁₆O₂ C 71.40% H 9.50% yield 27.1 gms. (0.16 moles). iii) <u>Reaction between triphenylphosphine and ascaridole in</u> benzene at 80°C.

The time taken for the reaction to reach completion was determined as follows:-

1.5 mmoles ascaridole, 3.0 mmoles triphenylphosphine and 5.0 mls. benzene were transferred to each of several Carius tubes and the tubes were sealed under vaccuum (0.01 mm. Hg.) after oxygen had been removed by passing a fine stream of dry nitrogen for five minutes. The sealed tubes were then wrapped in aluminium foil and immersed in a constant temperature bath, maintained at 80°C. After varying intervals, the ampoules were removed, cooled, and the i.r. spectrum of the resultant solution was recorded using a solution cell with a 0.025 mm.



spacer.

The extent of reaction was followed by observing:-

- a) The decrease in intensity of a band at 1435 cm.¹, probably due to the decrease in polarity of the phosphorus-phenyl bond on formation of the triphenylphosphine oxide.
- b) The increse in intensity of bands at 1200 cm.⁻¹ and 1120 cm.⁻¹ due to the formation of the P=0 group.
- c) The increase in intensity of a band at 720 cm.⁷ (unassigned).

Graph 8 shows that the reaction had reached completion after 160 hours.

29.57 gms. (112.8 mmoles) triphenylphosphine and 9.46 gms. (56.4 mmoles) ascaridole were added to 188 mls. dry benzene in a 250 ml. two necked, round bottomed flask, fitted with a nitrogen inlet and a double surface water cooled condenser. The top of the condenser was connected to a trap containing benzene so that nitrogen could be slowly passed through the apparatus without allowing oxygen in. The reaction vessel was wrapped in aluminium foil and maintained at 80° C in a thermostated bath for 160 hours. At the end of this time the flask was maintained at 80° C whilst the benzene was removed under slightly reduced pressure. When the benzene had been removed the pressure was decreased and the product distilled off. b.p. 63° C/0.3 mm. $N_{\rm D}^{20}$ 1.4700 C 79.08% H 10.88% required for C₁₀H₁₆O C 79.00% H 10.50% yield 4.9 gms. (32.2 mmoles).

The residue (33.9 gms.) was shaken with 150 mls. diethyl ether to dissolve the triphenylphosphine. The insoluble triphenylphosphine oxide was filtered off, dried and weighed. m.p. 156°C (Lit. 156°C), yield 14.9 gms. (53.3 mmoles). The ether was allowed to evaporate and the excess triphenylphosphine was filtered from a dark viscous oil which was shown by n.m.r. to be a mixture of approximately 67% volatile product and 33% triphenylphosphine. The triphenylphosphine was dried and weighed and on recrystallisation from absolute ethanol had m.p. 80.5°C, yield 14.7 gms. (56.0 mmoles).

Because of the difficulty in isolating the product quantitatively by means of distillation, g.l.c. techniques were used to determine the quantitative yield of volatile product. In a more detailed study of the rate of reaction it was seen that on heating a solution of 0.5 mmoles ascaridole and 1.0 mmole triphenylphosphine in 5.0 mls. benzene, in the dark at 80°C, 0.485 mmoles triphenylphosphine oxide were formed when the reaction had reached completion. At this point it is probable that the amount of product $(C_{10}H_{16}^{0})$ in solution, lies in the range 0.0 mmoles to 0.5 mmoles, consequently, a series of standard solutions were prepared containing 0.1, 0.2, 0.3, 0.4 and 0.5 mmoles C10H160 respectively, in benzene. A solution of 0.2416 gms. n-decane was made up to 25 mls. with benzene and this was used as an internal standard. 1.Oml. of the n-decane solution was added to 1.0 ml. of each standard solution and 1.0 microlitre of each of the resultant solutions was injected onto a dinonylphthalate column at 100°C.

The peaks due to the volatile product (p) and the standard (s) were cut out and weighed; the ratio p/s was determined in triplicate for each solution and a calibration graph was drawn, relating the value p/s to the concentration of the volatile product.

When the reaction ampoule had reached completion, 1.0 ml. of the reactants were added to 1.0 ml. of the n-decane solution, and a triplicate chromatogram was determined as before. From a value of p/s, the concentration of the volatile product in the



Graph 9

Showing calibration used to determine the yield of 3,4-oxido-p-menth-1,2-ene in the reaction between 1.0 mmole triphenylphosphine and 0.5 mmole ascaridole in benzene at 80°C. The dotted line represents the ratio of product to standard peak at the end of the reaction. From this the yield of 3,4-oxido-p-menth-1,2-ene is seen to be just greater than 0.5 mmoles i.e. within the limits of experimental error the yield is quantitative. reaction mixture was determined. It can be seen that the yield of C_{10^H16^O</sup> was essentially quantitative (graph 9). iv) <u>Reaction of ascaridole with triphenylphosphine in</u>}

petroleum ether at 99.6°C.

12.6 gms. (75 mmoles) ascaridole and 39.3 gms. (150 mmoles) triphenylphosphine, in 500 mls. 120/160 petroleum ether, were allowed to react as before, but at 99.6°C and for 60 hours; 3.6 gms.(23.6 mmoles) volatile product and 16.1 gms. (58 mmoles) triphenylphosphine oxide were isolated as before. Difficulty was encountered in effecting a clean separation of product and solvent but the n.m.r. spectrum indicated that the volatile fraction was identical to that isolated previously.

v) <u>Reaction between ascaridole and triphenylphosphine in</u> toluene at 99.6°C.

12.6 gms. (75 mmoles) ascaridole and 39.3 gms. (150 mmoles) triphenylphosphine were dissolved in 500 mls. toluene and heated for 63 hours at 99.6°C. 2.5 gms. (16.4 mmoles) volatile product were distilled off and shown by n.m.r. to be the same as isolated previously. 15.5 gms. (59 mmoles) triphenylphosphine oxide were isolated from the solid residue.

vi) The action of heat on 3,4-oxido-p-menth-1,2-ene.

1.30 gms. of 3,4-oxido-p-menth-1,2-ene were heated under nitrogen for 67 hours at 120° C in the dark. At the end of this time the n.m.r. spectrum of the product showed the presence of p-cymene and water only. After drying, the liquid was distilled (65°C/20 mm.) and identified as p-cymene $N_{\rm D}^{20}$ 1.4913 (Lit. 1.4904) C 89.5% H 10.5% required for C_{10} H₁₄ C 90.0% H 10.4%

a) Quantitative.

Perbenzoic acid was prepared by the action of sodium methoxide on recrystallised benzoyl peroxide in chloroform solution.¹³⁸ The product, in chloroform solution, was standardised as follows:-

1.0 ml. of the solution was transferred to a conical flask and the walls were rinsed with a small quantity of cold chloroform. 15 mls. glacial acetic acid were then added, followed by 2.0 mls. saturated aqueous potassium iodide solution. After a period of 5 minutes, 25 mls. water were added and the liberated iodime was titrated against standard thiosulphate using "thiodene" as indicator.

1.0 ml. perbenzoic acid solution = 8.95 mls. thiosulphate. The thiosulphate was 0.09675N and 1.0 ml.= 0.00669 gms. perbenzoic acid.

0.5863 gm. 3,4-oxido-p-menth-1,2-ene was weighed into a 50 ml. conical flask and 15 mls. perbenzoic acid solution were added. The flask became warm and the reactants were allowed to stand for 2 hours for reaction to reach completion. 1.0 ml. this resultant solution was titrated as above and 3.90 mls. thiosulphate were required to titrate the liberated iodine.

The weight perbenzoic acid reacted, therefore,

= $(8.95 - 3.90) \times 6.69 \times 10^{-3} \times 15$ gms. = 0.506 gms. and assuming a 1:1 stochiometry needed per double bond, the calculated quantity of 3,4-oxido-p-menth-1,2-ene added was 0.567 gm. which is in good agreement with the actual amount (0.586 gm.)

b) Qualitative.

1.87 gms. of 3,4-oxido-p-menth-1,2-ene were added to excess perbenzoic acid solution. The reactants became warm and were maintained at 40°C for 24 hours. The resultant solution was washed with aqueous sodium bicarbonate solution to remove any acids present and then washed with water and dried. The chloroform was removed, to yield 1.56 gms. of a liquid whose n.m.r. and i.r. spectra were identical to those of isoascaridole.

viii) Reaction of dihydroascaridole with triphenylphosphine in benzene at 80°C.

The same concentrations were used as in the reaction between ascaridole and triphenylphosphine in benzene.

7.75 gms. (45.5 mmoles) dihydroascaridole and 23.85 gms. (91.0 mmoles) triphenylphosphine were dissolved in 170 mls. dry benzene, in a 250 ml. flask and heated in an inert atmosphere, in the dark for 260 hours. The products were isolated as in the ascaridole reaction. The volatile fraction had b.p. $60-65^{\circ}$ C/ 0.5 mm. C 77.26% H 11.48% required for C₁₀H₁₈0 C 77.80% H 11.77%. The triphenylphosphine oxide (45.7 mmoles) and excess triphenylphosphine (41.2 mmoles) were isolated as in the reaction between triphenylphosphine and ascaridole.

The oily residue (0.8 gms.) was shown by n.m.r. to be a mixture of volatile oil and triphenylphosphine.

ix) Reaction of -phellandrene endoperoxide with triphenylphosphine.

8.4 gms. (50 mmoles) ~ -phellandrene endoperoxide were added dropwise over a period of 5 minutes to a stirred solution of 26.2 gms. (100 mmoles) triphenylphosphene in 166 mls. of dry benzene, in antrogen atmosphere, in the dark. The temperature rose from 15° C to 25° C and finally reached 35° C after 35 minutes. The resultant solution was heated at 80° C for 1 hour. The benzene was removed under reduced pressure and the volatile product distilled off (42° C/0.5 mm.) N_D²⁰ 1.4720 C 78.04% H 10.18% required for C₁₀H₁₆0 C 79.0% H 10.5% yield 6.6 gms. (44 mmoles)

12.5 gms. (48 mmoles) triphenylphosphine and 13.0 gms. (47 mmoles) triphenylphosphine oxide were isolated as before leaving 1.5 gms. of a dark oil which was shown by n.m.r. to be a mixture of volatile product and triphenylphosphine. x) Reaction of cyclohexadiene peroxide with triphenylphosphine.

2.70 gms. (24 mmoles) cyclohexadiene peroxide, dissolved in 20 mls. benzene, were added dropwise to a solution of 12.9 gms. (48 mmoles) triphenylphosphine in 50 mls. benzene at room temperature. The reactants were then heated to 80°C for 28 hours, in the dark, in a nitrogen atmosphere. At the end of this time the benzene was removed at 66 mm. The distillation flask was maintained at 75°C and the pressure was reduced to 0.001 mm. and any remaining volatile material was collected in a cold trap.

6.12 gms. (22 mmoles) triphenylphosphine oxide and 5.76 gms. (21 mmoles) unreacted triphenylphosphine were isolated from the residue. The liquid in the cold trap was distilled and the fraction b.p. $130-134^{\circ}$ C/760 mm. was collected, C 74.42% H 8.19% required for C₆H₈O C 75.00% H 8.33% yield 1.20 gms. (12.5 mmoles).

xi) <u>Reaction of d-cumyl-cyclohexenyl peroxide with triphenyl-</u> phosphine in benzene.

11.26 gms. (50 mmoles) peroxide were added to 26.23 gms. (100 mmoles) triphenylphosphine in 50 mls. benzene. The

resultant solution was outgassed using nitrogen, sealed in a Carius tube and heated to 80°C in the dark, for 120 hours. The solvent was removed at 15 mm. and 4.6 gms. liquid were distilled off at 42-44°C/0.01 mm. - fraction A. The residue, (31.3 gms.) was molecularly distilled at 0.002 mm. whilst the temperature slowly rose to 100°C and 4.3 gms. liquid distilled over continuously over this temperature range - fraction B. Above 100°C triphenylphosphine started to distil. The solid residue was found to be 6.9 gms. (24.8 mmoles) triphenylphosphine oxide and 19.9 gms. (76.0 mmoles) triphenylphosphine.

xii) Measurement of the rate of reaction of triphenylphosphine with peroxides.

The rate of reaction of triphenylphosphine with peroxides was measured by determining the quantity of triphenylphosphine oxide produced at any given moment. This was done by i.r. spectroscopy and the method is based on the fact that when triphenylphosphine is oxidised to triphenylphosphine oxide, two very intense bands appear at 1110 cm.⁻¹ and 1200 cm.⁻¹

The initial reactant concentrations used in all reactions were 1.0 mmoles triphenylphosphine plus 0.5 mmoles peroxide, in 5.0 mls. benzene. The concentration of phosphorus species at any instant, therefore, lies in the range 1.0 mmoles triphenylphosphine plus 0.0 mmole triphenylphosphine oxide, to 0.5 mmoles triphenylphosphine oxide plus 0.5 mmoles triphenylphosphine, such that the total concentrations of phosphorus species is always equal to 1.0 mmole in 5.0 mls. benzene.

A series of solutions of triphenylphosphine plus triphenylphosphine oxide were made up in accordance with the above specifications, and the i.r. spectrum of each of these solutions was recorded using a solution cell with a 0.025 mm.



Graph 10

Showing correlation of triphenylphosphine oxide concentration with absorbance at:-

a) 1200 cm⁻¹ × × b) 1110 cm⁻¹ 00

(Based on data in table 3.)

spacer (nominal). To correct for slight day to day variations in instrumental "gain setting", ratios of the peak heights at 1110 cm⁻¹ and 1200 cm⁻¹, to the height of a peak at 1400 cm⁻¹, due to the absorption of benzene, were measured, and a correlation with concentration was produced.

Ph_P	Ph_PO	Standard	Peak at 1200 cm.	Peak at 1110 cm.
-	-		standard	standard
0.5	0.5	0.265	1.85	1.92
0.6	0.4	0.265	1.65	1.60
0.7	0.3	0.265	1.28	1.26
0.8	0.2	0.265	0.95	0.91
0.9	0.1	0.265	0.62	0.54

Table 3

Showing correlation of peak height with triphenylphosphine oxide concentration. These results are shown in graph 10.

12.5 mmoles of a given peroxide were made up to 50 mls. in a graduated flask using dry benzene, and 25.0 mmoles triphenylphosphine were made up to 50 mls. in benzene solution. 2.0 mls. of each of these solutions were transferred to several Carius tubes and 1.0 ml. dry benzene was added. Oxygen was removed from the solutions by passing a fine stream of dry nitrogen for 5 minutes. The tubes were then sealed in vaccuo and placed in a thermostatically controlled water bath, in the dark for varying periods of time. The i.r. spectra of the solutions were recorded and by reference to the correlation graph the concentration of triphenylphosphine oxide was determined. The rate of reaction of triphenylphosphine with various peroxides are shown in tables 4-7.

Time (hours)	mmoles Ph_PO (A)	mmoles Ph_PO (B)
25.5	0.130	0.125
90.5	0.270	0.245
259.0	0.435	0.390
430.0	0.470	0.435
1250.0	0.485	0.485
	Table 4	

Showing the rate of formation of triphenylphosphine oxide at 80°C, in the reactions between triphenylphosphine (1.0 mmole) and 0.5 mmoles ascaridole (column A) and 0.5 mmoles dihydroascaridole (column B), in 5.0 mls. benzene.

Time (minutes)	mmoles Ph_PO	at 80°C
4	0.375	
8	0.450	
68	0.485	

0

Time (hours)	mmoles Ph_3PO	at 40 C
Immediately on mixing	0.120	
1.25	0.385	
3.25	0.485	

Table 5

Showing rate of formation of triphenylphosphine oxide in the reactions between triphenylphosphine (1.0 mmole) and <-phellandrene endoperoxide (0.5 mmole), in 5.0 mls. benzene at 80°C and 40°C.

	Time	mmoles Ph_PO
1	minute	0.468
1	hour	0.475
25	hours	0.495

Table 6

Showing the rate of formation of triphenylphosphine oxide in the reaction of triphenylphosphine (1.0 mmole) with cyclohexadiene endoperoxide (0.5 mmole) in 5.0 mls. benzene at 80°C.

In a similar reaction at 22.5°C, 0.300 mmoles triphenylphosphine oxide was formed in 1 hour.

Time (hours)	mmoles Ph_PC
69	0.215
142	0.223
320	0.280
820	0.335

Table 7

Showing the rate of formation of triphenylphosphine oxide in the reaction of triphenylphosphine (1.0 mmole) with \prec -cumyl-cyclohexenyl peroxide (0.5 mmole) in 5.0 mls. benzene at 80°C.

In a similar reaction at 40°C less than 0.08 mmoles triphenylphosphine oxide were formed after 136 hours.

- b) The reaction of sodium dialkyl phosphites with peroxides.
- i) Preparation and purification of reagents.
- a) Preparation of di-n-butyl peroxide.

N-butyl methane sulphonate was prepared by the method of Williams and Mosher.¹³⁹ 158 gms. (2.0 moles) pyridine were added dropwise to a mixture of 114.5 gms. (1.0 mole) methane sulphonyl chloride and 74 gms. (1.0 mole) n-butanol. The pyridine hydrochloride was hydrolysed using ice cold aqueous hydrochloric acid. The n-butylmethane sulphonate wasether extracted, dried over potassium carbonate and distilled b.p. $72-74^{\circ}$ C/1.0 mm. N_D²⁰ 1.4275 (Lit. 1.4265), yield 122 gms. (0.8 moles).

Oxidation of this n-butylmethane sulphonate using hydrogen peroxide in aqueous potassium hydroxide solution resulted in the formation of di-n-butyl peroxide which was extracted into a hexane solvent, washed with 10% aqueous potassium hydroxide, water, dried and then fractionated through an 8" Vigreau column, b.p. $61-62^{\circ}C/20$ mm. N_D²⁰ 1.4070 (Lit.1.4062) vield 19.4 gms. (0.13 moles).

b) Preparation of t-butyl-ethyl peroxide. 140

77.0 gms. (0.5 moles) diethyl sulphate were added dropwise to 1.0 mole of sodium t-butyl peroxide in 50 mls. water and stirred for 2 hours. The organic layer was dried over potassium carbonate and distilled b.p. 35° C/80 mm. N_D²⁰ 1.3855 (Lit. 1.3840) yield 70.4 gms. (0.6 mole).

c) Preparation of t-butyl-n-butyl peroxide. 141

This was similarly prepared by the reaction of 137 gms. (1.0 mole) n-butyl bromide with an aqueous suspension of 1.0 mole sodium t-butyl peroxide for 48 hours. The organic layer was separated and steam distilled; the organic

distillate was dried and distilled b.p. $52^{\circ}C/30$ mm. N_p²⁰ 1.4000 (Lit. 1.4001) yield 37 gms. (0.26 moles).

- d) <u>Dibenzoyl peroxide</u> (Hopkin and Williams) was dissolved in the minimum quantity of chloroform at room temperature and reprecipitated by the addition of twice the volume of methanol, m.p. 106°C.
- e) Preparation of sodium diethyl phosphite.

Diethyl phosphite (Albright and Wilson) was fractionated before use, b.p. 76° C/15 mm. N_D^{25} 1.4065 (Lit. 1.4070) C 34.97% H 7.95% required for $(C_2H_5O)_2P(O)H$ C 34.79% H 8.15%.

51.8 gms. (0.375 moles) diethyl phosphite were added to 750 mls. benzene. 10.0 gms. sodium shavings were added and the mixture was refluxed, under nitrogen, for 4 hours. The resultant suspension was decanted from the excess sodium and contained 50 mmoles sodium diethyl phosphite per 100 mls. solution.

f) Preparation of sodium di-n-butyl phosphite.

Di-n-butyl phosphite (Albright and Wilson) was fractionated before use b.p. 132° C/15 mm. N_D²⁰ 1.4230 C49.85% H 9.86% required for (C₄H₉O)₂P(O)H C 49.55% H 9.86%.

72.5 gms. (0.375 moles) di-n-butyl phosphite were added to 750 mls. benzene containing 10.0 gms. sodium and the mixture was refluxed for 6 hours under nitrogen. The resulting solution contained 50 mmoles sodium di-n-butyl phosphite per 100 mls.

g) Preparation of diethyl chlorophosphate. 142

Reaction of 166 gms. (1.0 mole) triethyl phosphite with 135 gms. (1.0 mole) sulphuryl chloride in 500 mls. dry 60/80 petroleum ether at 0°C yielded 158 gms.(0.92 moles)

diethyl chlorophosphate b.p. $54-56^{\circ}C/1.0 \text{ mm} \cdot N_D^{25}$ 1.4156 (Lit. 1.4162).

h) <u>Preparation of di-n-butyl chlorophosphate</u>.¹⁴² This was prepared by the same method in 84% yield,

b.p. 90-92°C/1.0 mm. N_D²⁰ 1.4310 (Lit. 1.4308).

i) Preparation of t-butyl, diethyl phosphate. 143

0.15 moles sodium-t-butoxide in 100 mks. t-butanol were maintained at 25°C and stirred whilst 25.9 gms. (0.15 moles) diethyl chlorophosphate were added dropwise. After stirring for a further 2 hours, the excess t-butanol was removed at 15 mm. and 25 mls. water were added to the residue to dissolve the sodium chloride. The product was ether extracted, dried over potassium carbonate and distilled, b.p. 65-67°C/1.0 mm. N_D³⁵ 1.4052 (Lit. 1.4042) yield 10.4 gms. (0.05 moles).

j) Preparation of n-butyl, diethyl phosphate.

This was prepared as above using 0.15 moles sodium n-butoxide in 100 mls. n-butanol, b.p. $76-80^{\circ}C/1.0$ mm. N_D³⁰ 1.4093 (Lit. 1.4090) N_D²⁵ 1.4110 yield 25.6 gms. (0.12 moles).

k) Preparation of di-n-butyl, ethyl phosphate.

This was also prepared as above, b.p. $95-97^{\circ}C/0.05$ mm. N_D²⁵ 1.4185 N_D³⁰ 1.4165 (Lit. 1.4148) yield 19.5 gms. (0.10 moles).

1) Preparation of di-n-butyl, t-butyl phosphate (novel compound). Reaction of 0.15 moles sodium t-butoxide with 0.15 moles di-n-butyl chlorophosphate in 100 mls. t-butanol, yielded 20.3 gms. (0.08 moles) di-n-butyl, t-butyl phosphate, N²⁵_D 1.4220 C 54.26% H 10.06% P 11.79% required for C₄H₉O)₃P(O) C 54.30% H 10.24% P 11.60%.

ii) Reaction of ascaridole with sodium di-n-butyl phosphite.

9.0 gms. (53.6 mmoles) ascaridole were added dropwise to a stirred solution of 100 mmoles sodium di-n-butyl phosphite in 200 mls. benzene, over a period of 5 minutes. The temperature of the solution rose to 35°C. The flask was stoppered and maintained at 40°C for 90 hours and the original pale yellow solution separated into a clear upper layer and a yellow viscous lower layer. 50 mls. water were added and the flask was shaken until the lower layer had dissolved. The organic layer was separated and the aqueous layer was ether extracted (3 x 25 mls.). The combined organic layer and ether washings were combined and dried. The ether was removed to yield 9.0 gms. of a pale yellow liquid whose n.m.r. and i.r. spectra were identical to those of 3,4-oxido-p-menth-1,2-ene. This pale yellow liquid was redistilled to give a colourless liquid b.p. 68°C/12 mm. N_D²⁰ 1.4700 C 77.9% H 10.68% required for C10H160 C 78.8% H 10.60% yield 8.4 gms.

iii) Reaction between di-n-butyl peroxide and sodium di-n-butyl phosphite.

7.31 gms. (50 mmoles) di-n-butyl peroxide were added dropwise to a solution of 100 mmoles sodium di-n-butyl phosphite in 200 mls. benzene, over a period of 0.5 hours. The reaction was exothermic, the addition of only 1.0 ml. peroxide being sufficient to raise the temperature of the reactants from 25° C to 40° C. When the addition was complete the resultant straw coloured liquid was maintained at 40° C for 48 hours. 50 mls. water were added and the organic product was isolated as before, b.p. 94° C/0.04 mm. N_{D}^{25} 1.4228 (Lit. 1.4230) C 55.53% H 10.81% P 13.02% required ofor $(C_{4}H_{9}O)_{3}P(O)$ C 54.20% H 10.25% P 12.80% yield 8.6 gms. (31.6 mmoles).

iv) Reaction between di-n-butyl peroxide and sodium diethyl phosphite.

7.31 gms. (50 mmoles) peroxide were added dropwise to a solution of 100 mmoles sodium diethyl phosphite in 200 mls. benzene and the resultant phosphate isolated as above, b.p. $80-82^{\circ}C/1.0$ mm. N_D^{30} 1.4092 C 43.82% H 12.14% P 13.3% required for $(C_2H_5O)_2P(O)(C_4H_9O)$ C 44.1% H12.4% P 14.2% yield 6.8 gms. (32 mmoles).

v) Reaction between di-a-cumyl peroxide and sodium di-n-butyl phosphite.

13.52 gms. (50 mmoles) di- α -cumyl peroxide and 100 mmoles sodium di-n-butyl phosphite in 200 mls. benzene were heated in an inert atmosphere at 40°C for 28 days. The product was recovered as previously and molecularly distilled, b.p. 80-100°C/ 0.01 mm. N_D²⁵ 1.5250 yield 11.2 gms.

The i.r. of this liquid was identical to that of di-*d*-cumyl peroxide and on standing for several days, this liquid solidified and was recryatallised to give di-*d*-cumyl peroxide, m.p. 33°C.

vi) Reaction between di-t-butyl peroxide and sodium diethyl phosphite.

7.31 gms. (50 mmoles) di-t-butyl peroxide were added to a solution of 100 mmoles sodium diethyl phosphite in 200 mls. benzene. 1.0 ml. of this solution was injected onto a dinonylphthalate column at 75°C and a gas chromatogram was recorded. The remaining solution was heated in an inert atmosphere at 40°C for 28 days and the gas chromatogram of a sample was again recorded. It was seen that there was not a decrease in the concentration of di-t-butyl peroxide.

vii) Reaction between di-t-butyl peroxide and sodium di-n-butyl phosphite.

The above proceedure was repeated using sodium di-n-butyl phosphite and it was again seen that the peroxide did not react. viii) Reaction between dihydroascaridole and sodium di-n-butyl

phosphite.

4.25 gms. (25 mmoles) dihydroascaridole were added dropwise to a solution of 50 mmoles sodium di-n-butyl phosphite in 100 mls. benzene maintained at 25-30°C. When addition was complete the resultant solution was maintained at 40°C for 120 hours. The product was isolated as before and molecularly distilled, b.p. 35-50°C/0.001 mm. N_D^{25} 1.4685 C 58.94% H 10.01% P 7.96% required for $C_{18}H_{37}PO_4$ C 59.30% H 10.15% P 8.52% yield 7.5 gms. (20.6 mmoles).

ix) <u>Reaction between benzoyl peroxide and sodium di-n-butyl</u> phosphite.

18.0 gms. (75 mmoles) benzoyl peroxide were suspended in 25 mls. benzene and added to a cooled stirred solution of 150 mmoles sodium di-n-butyl phosphite in 300 mls. benzene such that the temperature remained below 25° C. When addition was completed the reactants were stirred for a further 3 hours. The resultant solution was extracted with 3 x 50 mls. 10% sodium hydroxide and washed with 5 x 50 mls. water until neutral. The sodium hydroxide extracts and water washings were combined and acidified using a slight excess sulphuric acid. The liberated benzoic acid was ether extracted and recovered by evaporation to dryness. The benzoic acid was recrystallised from hot water and dried, m.p. $120.5-121.5^{\circ}$ C; yield 8.2 gms. (67 mmoles).

The organic layer was dried and the benzene was removed at 15 mm. to yield 21.2 gms. (68.2 mmoles) of a viscous oil.

This oil was molecularly distilled b.p. $30-60^{\circ}$ C/0.004 mm. N_D²⁵ 1.4700 yield 18 gms.

x) Reaction between t-butyl ethyl peroxide and sodium di-n-butyl phosphite.

5.9 gms. (50 mmoles) peroxide were added to 100 mmoles sodium di-n-butyl phosphite in 200 mls. benzene and maintained at 40°C for 5 days. At the end of this time two layers had formed which became miscible on shaking. Water was added and the organic phase worked up as before, b.p. $90-94^{\circ}C/0.05$ mm. $N_{\rm p}^{25}$ 1.4190

> %P 12.4; required (BuⁿO)₂P(O)-OBu^t 11.67%P (BuⁿO)₂P(O)-OEt 13.0 %P

yield 5.6 gms.

xi) Reaction between t-butyl ethyl peroxide and sodium diethyl phosphite.

8.55 gms. (75 mmoles) t-butyl ethyl peroxide and 150 mmoles sodium diethyl phosphite in 300 mls. benzene were heated at 40°c for 5 days and the reaction product worked up as previously, b.p. 55-60°C/1.0 mm. N_D^{25} 1.4070 %P 15.61; required for (Et0)₂(0)-0Bu^t = 14.75 N_D^{25} 1.4085 (Et0)₂P(0)-0Et = 17.05 N_D^{25} 1.4040

yield 7.40 gms.

xii) <u>Reaction between n-butyl</u>, t-butyl peroxide and sodium di-n-butyl phosphite.

7.31 gms. (50 mmoles) peroxide and 100 mmoles sodium di-n-butyl phosphite in 200 mls. benzene were maintained at 40° C for 5 days and the product worked up as before, b.p. 84° C/O.02mm. N_{D}^{25} 1.4230

> $(Bu^{n}O)_{2}P(O)-OBu^{t}$ N_{D}^{25} 1.4220 $(Bu^{n}O)_{2}P(O)-OBu^{n}$ N_{D}^{25} 1.4230 yield 7.6ggs.
diethyl phosphite.

7.31 gms. (50 mmoles) n-butyl, t-butyl peroxide were added to 100 mmoles sodium diethyl phosphite in 200 mls. benzene and maintained at 40°C for 5 days and the product was recovered as before, b.p. 70-72°C/1.0 mm. N_D^{25} 1.4135 (EtO)₂P(O)-OBuⁿ N_D^{25} 1.4110 (EtO)₂P(O)-OBu^t N_D^{25} 1.4085

yield 8.7 gms. (41.5 mmoles).

- c) The reaction of Grignard reagents with peroxides.
- i) Preparation of reagents.

AnalaR diethyl ether was redistilled from phosphorus pentoxide and stored over molecular sieve (type 4A: 8-12 mesh beads) prior to use.

a) Preparation of di-t-butyl ether.

An attempted preparation was carried out using the method of Lawesson and Yang.¹⁴⁴ Reaction of t-butyl perbenzoate with an ethereal solution of t-butyl magnesium chloride yielded 3.6 gms. of a product b.p. 104-106°C which was shown by g.l.c. analysis to consist of 3 components in roughly equal amounts. One of these compounds was 2,2,3,3,-tetramethyl butane, b.p. 106°C, which was produced during the preparation of the Grignard solution, and this could not be readily separated from the desired product.

Di-t-butyl ether was, however, prepared by the method of Erickson and Ashton¹⁴⁵ by reacting t-butyl chloride with an ethereal suspension of silver carbonate for 2 weeks, under the influence of a 300 watt tungsten filament lamp. Di-t-butyl ether had a b.p. $106-107^{\circ}$ C, $N_{\rm D}^{20}$ 1.3945, yield 28%. The purity of this material was demonstrated by n.m.r. and g.l.c.

b) Preparation of n-butyl t-butyl ether.

This was prepared by adding t-butanol slowly to a heated solution of n-butanol in dilute sulphuric acid.¹⁴⁶ b.p. 123-125°C N_D²⁵ 1.3925.

c) Preparation of allyl t-butyl ether.

This was prepared similarly according to the method described by Lawesson et.al.¹⁴⁷ using 0.5 scale quantities, b.p. 99-100°C N_D²⁰ 1.4065 yield 12 gms.

d) Preparation of p-methallyl t-butyl ether.

This was prepared by the reaction of β -methallyl chloride on sodium t-butoxide according to Olson et.al.¹⁴⁸ but using 0.25 x 10⁻² scale quantities, b.p. 120-122°C N_D²⁰ 1.4080 yield 8.4 gms. (32%).

ii) Preparation of Grignard reagents.

The Grignard solutions were prepared using standard techniques; their concentration was made greater than ultimately required so that the necessary concentration could be obtained by appropriate dilution.

The preparation of t-butyl magnesium chloride is described in detail and this method was used in all other preparations; iodine was used in the preparation of t-butyl magnesium chloride only.

5.47 gms. (0.225 moles) magnesium turnings were placed in a 250 ml. round bottomed flask which had been dried by heating to 110°C and cooled in a stream of dry nitrogen. 1 crystal of iodine was added and the flask was fitted with an inlet for admitting dry nitrogen, a condenser fitted with a calcium chloride drying tube, and a dropping funnel. The air was displaced by passing a stream of nitrogen for about 1 minute. The nitrogen flow rate was reduced to a minimum and the flask was heated with a bunsen burner to vaporize the iodine. The flask was allowed to cool and 0.5 gms. t-butyl chloride in 10 mls. dry ether were added and reaction started almost immediately (as evidenced by the appearance of bubbles). 50mls. dry @ther were added in one portion and the remaining t-butyl chloride (18.5 gms. (0.2 moles)), in 40 mls. ether, were added slowly to the rapidly stirred suspension of magnesium shavings so that the coupling reaction was kept to a minimum. When

addition was complete the reagents were stirred for a further 2 hours and then the Grignard concentration was determined. iii) Determination of Grignard solution.

This was carried out as described by Gilman et.al. 149

The solid material was allowed to settle and 2.0 mls. solution were transferred, by means of a pipette, to a 250 ml. Erlenmeyer flask containing 25 mls. distilled water and 25.0mls. hydrochloric acid (N/10). The resulting solution was heated to 70° C and the excess acid was back titrated, at this temperature, with N/10 sodium hydroxide using phenol-phthalein as indicator.

The Grignard concentration was calculated from the relationship

	RMgX	+	HX	->	RH	+:	MgX2	
	1 litre	normal	acid	=	1 mole	Grig	nard	
	1 ml. N,	/10 acid	đ	-	10 ⁻⁴ m	oles	Grignard	
iv)	Reaction of	peroxic	les wit	th Grig	mard s	oluti	ons.	

In all reactions 24.0 x 10^{-3} moles of Grignard were added to an ethereal solution of 4 x 10^{-3} moles peroxide at 20° C. The total volume of ether was 50 mls. and ca. 0.3 gms. of an inert internal standard was added to facilitate an accurate measurement of extent of reaction.

The reaction of di-t-butyl peroxide with n-butyl magnesium chloride serves to illustrate the method used to study the reaction.

Estimation of the Grignard showed that 10 mls. solution contain 17.5 x 10^{-3} moles.

Therefore, 4.0 x 10^{-3} x 146.23 x <u>17.5</u> gms. = 0.4260 gms. 24

di-t-butyl peroxide were weighed out into a 100 ml. conical flask and 0.1845 gms. 2-methyl octane were added followed by

 $50 \ge 17.5$ - 10 mls. = 36.4 - 10 mls. = 26.4 mls. 24

A small magnetic follower was added to the resultant solution and the flask was half immersed in a water bath on a magnetic stirrer platform and maintained at 20°C. 10.0 mls. of Grignard solution were added to the stirred contents of the flask. The air in the flask was displaced by dry nitrogen and the flask was sealed by means of a serum cap. The reactants were maintained at 20°C and stirred continuously. After varying time intervals 1.0 ml. samples of the resultant solution were injected onto a g.l.c. column and:-

- a) the increase in height of the peak corresponding to n-butyl
 t-butyl ether and
- b) the decrease in height of the peak corresponding to di-t-butyl peroxide were observed.

The absolute concentrations of peroxide and ether were determined by reference to standard solutions of known composition.

When the reaction had gone to completion the flask was cooled in a dry ice/acetone bath and 2.0 mls. N/10 hydrochloric acid added dropwise over a period of ca. 10 minutes.

The liberated t-butanol was then determined by g.l.c.

Calibration for g.l.c. analysis was carried out as follows:-

Varying amounts of n-butyl t-butyl ether, t-butanol and di-t-butyl peroxide were added to 0.2578 gms. 2-methyl octane in 50 mls. ether (0.1875 gms. in 36.4 mls.). The heights of peaks due to these compounds were measured and the appropriate ratios correlated with concentration and are shown in table 8 below



Graph 11

Showing correlation of peak heights, taken from a gas-liquid chromatogram, with concentration, in a solution of:-



This graph summarises the data in table 8.

Moles	Moles	Moles	Ht.Bu ^t OBu ⁿ /	Ht. Bu ^t OH/	Ht.Bu ^t OOBu ^t /
Bu ^t OBu ⁿ	ButOH	ButOOBut	Ht.standard	Ht.standard	Ht.standard
1x10 ⁻³	-	-	0.56	-	-
2.025x10 ⁻³	-	-	1.14	-	
2.971x10 ⁻³	-	-	1.64	-	-
3.917x10 ⁻³	-	-	2.21	-	-
-	2.0x10 ⁻³	-	-	0.46	-
-	-	4.0x10 ⁻³	-	-	2.86

This information was then plotted in graphical form and is shown in graph 11.

The concentrations of n-butyl t-butyl ether and di-t-butyl peroxide at any point in the reaction were then determined using graph 11 and are shown in table 9.

Time	n-butyl t-butyl	di-t-butyl peroxide
(mins.)	ether concentration	concentration
18	0.52	3.22
33	0.85	2.96
48	1.00	2.75
75	1.27	2.48
98	1.56	1.92
158	1.90	1.34
245	2.13	0.87
312	2.28	0.68
556	2.47	0.26
1200	2.68	0.00

Table 9

Showing rate of formation of n-butyl t-butyl ether and the disappearance of di-t-butyl peroxide (in mmoles), in the reaction between di-t-butyl peroxide and n-butyl magnesium chloride. The t-butanol formed in the reaction reacts rapidly with the Grignard present, hence this value cannot be determined directly but when the reaction had gone to completion the t-butoxy magnesium chloride was hydrolysed and the liberated t-butanol was determined by g.l.c.

Amount t-butanol formed = 5.2 mmoles.

The rates of reaction of other peroxides with Grignard reagents are shown in tables 10- 12.

Time	n-butyl t-butyl	<u>di-t-butyl peroxide</u>
(mins.)	ether concentration	concentration
32	0.50	-
104	0.80	2.91
154	0.92	2.77
240	1.17	2.35
567	1.62	1.50
1429	2.16	0.52
2766	2.34	0.10
4146	2.42	-

Table 10

Showing rate of reaction between di-t-butyl peroxide and n-butyl magnesium bromide.

Amount t-butanol formed on hydrolysis was 5.50 mmoles.

Time	n-butyl t-butyl	di-t-butyl peroxide
(mins.)	ether concentration	concentration
2		4.00
56		3.58
94	0.33	3.42
167	0.51	3.00
304	0.80	2.45
490	1.03	2.00
1215	1.67	0.78
1585	1.82	-
2665	1.82	0.00

Showing rate of reaction between di-t-butyl peroxide and n-butyl magnesium iodide.

Amount of t-butanol formed on hydrolysis was 6.17 mmoles.

Time	allyl t-butyl
(mins.)	ether concentration
2	0.52
25	1.76
44	2.23
69	2.58
87	2.83
114	2.98
289	3.10

Table 12

Showing rate of reaction between di-t-butyl peroxide and allyl magnesium bromide.

Amount t-butanol formed on hydrolysis was 4.47 mmoles.

v) Reaction of t-butyl perbenzoate with t-butyl magnesium chloride.

4.85 gms. (0.025 moles) t-butyl perbenzoate in 25 mls. dry ether were added dropwise over a period of 2 hours to a rapidly stirred solution of 50 mls. 1.5N t-butyl magnesium chloride maintained at $0-5^{\circ}$ C and left to stand overnight. 50 mls. ether were then added and the resultant mixture was hydrolysed by the addition of 25 mls. N/10 hydrochloric acid. 4N sodium hydroxide was added dropwise until all the solid had dissolved. The aqueous solution was extracted (5 x 25 mls.) with ether; the ether extracts were combined and made up to a total of 250 mls. - solution A.

4N hydrochloric acid was added to the aqueous phase and the benzoic acid which precipitated, was dried and weighed, yield 2.80 gms. (0.023 moles) m.p. 121°C.

A standard solution was made up containing:-0.2683 gms. (1.92 mmoles) di-t-butyl ether 0.1700 gms. (2.29 mmoles) t-butanol 0.3580 gms. n-octane

in 25 mls. ether (solution B).

25.0 mls. of solution A were added to 0.3620 gms. n-octane to produce solution C. Samples of solutions B and C were injected onto a dinonylphthalate column at 100°C and the gas-liquid chromatograms were recorded, and by comparison the amounts of t-butanol and di-t-butyl ether produced in the reaction, were determined.

The overall stochiometry of the reaction was found to be:- $Bu^{t}MgCl + Bu^{t}OOCPh \longrightarrow Bu^{t}OBu^{t} + Bu^{t}OH + PhCO_{2}H$ $75x10^{-3}$ $25x10^{-3}$ $4.87x10^{-3}$ $20.4x10^{-3}$ $23x10^{-3}$ moles moles moles moles

In the other reactions between peroxides and Grignard reagents, which were studied, the rates of reaction were not determined and only the concentrations of the products were measured. These are recorded in table 1. Chapter 2: Reaction of disulphides with nucleophilic reagents. a) Reaction of disulphides with cyclic phosphoramidites.

i) Preparation and purification of reagents.

2-chloro-1,3,2-dioxaphospholane b.p. $67-69^{\circ}$ C/50 mm. N_D²⁵ 1.4872 (Lit. 1.4878) and 2-chloro-4-methyl-1,3,2-dioxaphospholane b.p.75-76°C/50 mm. N_D²⁵ 1.4710 (Lit. 1.4707) were supplied by Albright and Wilson and redistilled prior to use. a) Preparation of 2-substituted 1,3,2-dioxaphospholanes.

2-substituted 1,3,2-dioxaphospholanes and 2-substituted 4-methyl-1,3,2-dioxaphospholanes were prepared by the method of Lucas, Mitchell and Scully;¹⁵⁰ 2-(-4morpholino)-4-methyl-1,3,2-dioxaphospholane had the physical constants reported by Pilgram, Phillips and Korte¹⁵¹ and 2-di-n-butylamino-1,3,2dioxaphospholane was a novel compound. The general proceedure used is illustrated by reference to the preparation of 2-diethylamino-1,3,2-dioxaphospholane.

25.4 gms. (0.2 moles) 2-chloro-1,3,2-dioxephospholene were added to 60 mls. 40/60 petroleum ether in a 250 ml. flask fitted with stirrer, reflux condenser and dropping funnel. 29.2 gms. (0.4 moles) diethylamine in 60 mls. 40/60 petroleum ether was added dropwise whilst the flask was cooled by an ice bath. When addition was complete the reaction mixture was maintained at room temperature for 2 hours. The amine hydrochloride was filtered off and washed with 40/60 petroleum ether. The filtrate and washings were combined and allowed to stand over night at -10°C, whereupon further amine hydrochloride precipitated and was removed by filtration. The filtrate was distilled and the fraction boiling 101°C/28 mm. was collected. The crude product was then fractionated three times through a Vigreau column to remove further amine hydrochloride, b.p. of product

98.5-99°C/25 mm. N_D²⁵ 1.4660 (Lit. 1.4660) C 44.05% H 8.34% N 8.44% P 18.00% required C 44.17% H 8.65% N 8.59% P 18.99%.

The physical properties of the other cyclic phosphoramidites which were prepared are summarised in table 13 (Lit. values in brackets).

Compound	B.p.	N25		Anal	ytical	
San Star Star Star	_		Re	equired	Found	
2-diethylamino-1,3,2-	98.5-99°c/25mm.	1.4680				
dioxaphospholane	(98.7-99.1°C/25mm.)	(1.4660)	1			
2-piperidino-1,3,2-	112-115°C/14mm.	1.5015	С	47.99	48.19	
dioxaphospholane	(108-110°C/10mm.)	(1.4971)	H	8.07	8.14	
			N	17.67	18.00	
			P	8.00	7.80	
2-di-n-butylamine-	98°C/1.0mm.	1.4680	C	54.77	53.88	
1,3,2-dioxaphospholane			H	10.11	9.77	
			N	6.39	5.42	
			P	14.13	15.10	

2-diethylamino-4-	91°C/17mm.	1.4593
methyl-1,3,2-	(101.5-101.7°C/25	5mm.)(1 .4594)

115-116[°]C/14mm. (132[°]C/25mm.)

78°c/0.08mm.	1.4912
(77°C/0.08mm.)	(1.4897)

N20

2-piperidino-4methyl-1,3,2dioxaphospholane 2-morpholino-4methyl-1,3,2dioxaphospholane

dioxaphospholane

99

Table 13

- ii) Preparation and purification of sulphides.
- a) <u>Diallyl disulphide</u> (Koch-Light) was fractionated three times before use and a fraction boiling 79°C/16 mm. was collected.
 S 43.2% required for C₆H₁₀S₂ 43.8%.
- b) <u>Diallyl monosulphide</u> was also supplied by Koch-Light. This was fractionated before use and fraction 140-141°C/760 mm. was collected, N_D²⁰ 1.4867 (Lit. 1.4870) S 28.1% required for C₆H₁₀S 28.01%.
- c) <u>Di-but-2-enyl disulphide</u> was prepared from the but-enyl-1thiol which was prepared by the general method of Lee et. al.¹⁵¹

But-2-ene-1-ol (1.1 mole) b.p. 114-120°C/760 mm., 140 mls. 48% hydrobromic scid and 1.1 moles thioures, were refluxed together for 30 minutes and then the product was cooled over night at -10°C to give crude S-but-2-enyl thiuronium bromide which was filtered off and washed with 128 gms. of 55% cold squeous acetone. The combined mother liquors were treated with p-toluene sulphonic scid (70 gms. in 125 mls. wster) and the resultant crystalline tosylate was separated and washed with aqueous acetone (84 gms. 25%). The tosylate and bromide salts were combined and added to aqueous sodium hydroxide (60 gms. in 250 mls. water) at room temperature. After stirring the mixture for 1.5 hours the thiol was separated by steam distillation and the distillate washed with water and dried over magnesium sulphate to yield 54 gms. crude thiol. Fractionation of this thiol through a Vigreux column gave 30 gms. (30.8%) but-2-ene-1-thiol b.p. 100-102°C/ 760 mm.

The thiol (30 gms.) was dissolved in ice cold aqueous sodium hydromide (77.5 gms. in 375 mls. water) and the resultant

thiolate ion was oxidised to the disulphide by the slow addition of 30% hydrogen peroxide. The product was then made just acid with glacial acetic acid; the disulphide was ether extracted and the ether solution was rendered neutral by washing with aqueous potassium carbonate.

Subsequent removal of the ether and distillation of the residue gave a fraction b.p. $70-71^{\circ}C/0.05-0.06$ mm. N_D¹⁶ 1.4392 (Lit. 1.4386) C 55.2% H 8.1% S 36.4% required for C₈H₁₄S₂ C 55.1% H 8.1% S 36.8% yield 21 gms. G.l.c. indicated 4% impurity and i.r. absorption at

960 cm. indicated that the disulphide was the trans but-2enyl isomer.

d) Preparation of 1-methyl allyl but-2-enyl monosulphide.

3.14 gms. (18 mmoles) but-2-enyl disulphide was added to 6.74 gms. (25.7 mmoles) triphenylphosphine, sealed in a Carius tube and heated for 75 hours at 80°C. The product was separated by filtration into a crystallime material and a liquid. The solid was washed with 8 mls. ether and crystallised from ethanol to give triphenylphosphine sulphide m.p. 159.5-160.5°C (Lit. 160.5-161.5°C). Distillation b.p. 58-59°C/12 mm. of the combined filtrate and ether washings gave 1.97 gms. of 1-methyl allyl but-2-enyl monosulphide, N_D²⁰ 1.4900 (Lit. 1.4870).

N.m.r. was consistent with the structure. I.r. showed a band at 960 cm⁻¹ which indicated a trans di-alkyl ethylenic bond and bands at 910 cm⁻¹ and 990 cm⁻¹ which indicated the presence of a vinyl group. G.l.c. indicated a minor component of 3%.

iii) <u>Triethyl phosphite</u> (Albright and Wilson) was fractionated prior to use b.p. 154°C (Lit. 153.5-155.0°C) N_D²⁰1.4125(Lit.1.4120)



Calibration graph used in studies on the rate of desulphuration of diallyl disulphide, (based on data in table 14). iv) Kinetics of reactions.

The extent of the reaction was determined by measuring the amount of monosulphide formed after a given interval of time, and both the diallyl- and 1-methyl allyl but-2-enyl monosulphides were estimated by g.l.c. techniques, using a Pye Panchromatograph, operating with a column containing di-nonyl-phthalate on a Chromasorb G solid support. The diallyl monosulphide was determined accurately by using n-octane as an internal standard whilst n-nonane was used with 1-methyl allyl but-2enyl monosulphide. The method of determining the rate of desulphuration of diallyl disulphide can be illustrated by reference to:-

a) Determination of the rate of reaction between diallyl disulphide and triphenylphosphine in benzene at 80°C.

Four solutions were prepared, each containing 0.0175 gms. n-octane in 5 mls. benzene.

To solution 1 was added 0.0735 mmoles diallyl monosulphide. To solution 2 was added 0.1426 mmoles diallyl monosulphide. To solution 3 was added 0.3380 mmoles diallyl monosulphide. To solution 4 was added 0.4800 mmoles diallyl monosulphide.

The g.l.c. of each of these solutions was recorded and the n-octane and diallyl monosulphide peaks were traced, cut out, weighed and their weight ratios determined. The g.l.c. of each solution was run 3 times and an average ratio was taken. This data is tabulated in table 14. The ratios of peak weights versus monosulphide concentration were then plotted (graph 12).

Sample	Monosulphide		N-octane	A/B	Deviation	Average
	peak weight	pe	esk weight		from mean	A/B
	(<u>A</u>)		(B)			
	0.0062		0.1877	0.352	-0.006	
1	0.0676		0.1800	0.376	+0.019	0.358
	0.0646		0.1861	0.347	-0.011	
			0 4505	0 (00	0.000	
	0.1222		0.1795	0.602	0.000	
2	0.1283		0.1910	0.672	-0.010	0.682
	0.1373		0.1988	0.691	+0.010	
	0.3238		0.1950	1.660	+0.030	
3	0.3263		0.2040	1.600	-0.030	1.630
	0.3222		0.1974	1.630	0.000	
	0.4562		0.1961	2.330	-0.080	
4	0.4294		0.1748	2.460	+0.050	2.410
	0.4534		0.1861	2.430	+0.020	

3.282 gms. triphenylphosphine were made up to 25 mls. with pure dry benzene, in a graduated flask - solution A.

0.9080 gms. diallyl disulphide plus 0.2205 gms. n-octane were made up to 25 mls. in benzene - solution B.

2.0 mls. of solutions A and B were transferred to a Carius tube and 1.0 ml. was then used to wash the reactants into the tube, which was then outgassed and sealed. Six such ampoules were prepared and heated to 80°C, in the dark. The ampoules were opened after varying intervals of time and the g.l.c. was recorded, and the results are shown in table 15.

Time	Monosulphide	N-octane	A/B	Average	mmoles diallyl
(mins.)peak weight	peak weight		A/B	monosulphide
	(<u>A</u>)	(<u>B</u>)			formed
20	0.2995	0.2012	1.490	1 1.07	0.005
	0.2970	0.1985	1.495	1.493	0.297
	0 3068	0.20/10	1 0/15		
40	0.9900	0.2040	1.942	1.985	0.405
	0.4114	0.2010	2.025		
	0.4312	0.2011	2.145		
60	0.4390	0.2040	2.150	2.128	0.440
	0.4310	0.2055	2.090		
	0.4520	0.2090	2.165		
95	0.4280	0.1915	2.235	2.247	0.467
	0.4515	0.1928	2.340		
	0.4400	0.1930	2.280		
185	0.4110	0.1830	2.245	2.262	0.470
	0.4320	0.1915	2.260		
	0 11160	0 1054	2 285		
335	0.4409	0.1954	2.205	2.310	0.482
	0.4336	0.1851	2.335		

Showing rate of formation of diallyl monosulphide in the reaction of 1.0 mmole of triphenylphosphine with 0.5 mmoles diallyl disulphide in 5.0 mls. benzene at 80°C.

The rates of desulphuration of diallyl disulphide by other nucleophiles are shown in tables 16 to 24.

Time	mmoles disllyl
(hours)	monosulphide formed
1.00	0.170
2.75	0.325
6.00	0.420

Showing the rate of reaction of triphenylphosphine (1.0 mmole) with diallyl disulphide (0.5 mmole) in 5 mls. benzene at 50°C.

Time	mmoles diallyl	
hours)	monosulphide formed	
1	0.083	
3	0.165	
7	0.270	
24	0.440	
	Table 17	

Showing rate of reaction of triethylphosphite (1.0 mmole) with diallyl disulphide (0.5 mmoles) in 5 mls. benzene at 50°C.

Time	mmoles diallyl		
(hours)	monosulphide formed		
1	0.060		
3	0.092		
20	0.245		
41	0.357		

Table 18

Showing rate of reaction of 2-diethylamino-1,3,2-dioxaphospholane (1.0 mmoles) with diallyl disulphide (0.5 mmoles) in 5 mls. benzene at 50°C.

Time	mmoles diallyl		
(hours)	monosulphide formed		
1.0	0.140		
2.0	0.230		
4.5	0.330		
9.5	0.385		
15.0	0.395		
24.0	0.395		

Showing rate of reaction of 2-morpholino-1,3,2-dioxaphospholane (1.0 mole) with diallyl disulphide (0.5 mmole) in 5 mls. benzene at 80°C.

Time	me mmoles diallyl	
(hours)	monosulphide formed	
1.0	0.123	
2.5	0.230	
5.5	0.320	
8.5	0.365	
16.0	0.445	

Table 20

Showing rate of reaction of 2-di-n-butylamino-1,3,2dioxaphospholane (1.0 mmole) with diallyl disulphide (0.5 mmole) in 5 mls. benzene at 80⁰C.

Time	mmoles dially1
(hours)	monosulphide formed
1.0	0.157
2.0	0.252
4.0	0.325
7.0	0.355
24.0	0.355

Showing rate of reaction of 2-diethylamino-1,3,2dioxaphospholane (1.0 mmole) with diallyl disulphide (0.5 mmole) in 5 mls. benzene at 80°C.

Time	mmoles diallyl		
(hours)	monosulphide formed		
1.0	0.170		
3.0	0.290		
7.0	0.400		
11.5	0.410		

Table 22

Showing rate of reaction of 2-diethylamino-4-methyl-1,3,2-dioxaphospholane (1.0mmole) with diallyl disulphide (0.5 mmole) in 5 mls. benzene at 80° C.

Time	mmoles dially}
(hours)	monosulphide formed
1.0	0.163
2.5	0.275
5.0	0.360
8.5	0.405

Showing rate of reaction of 2-piperidino-4-methyl-1,32-dioxaphospholane (1.0 mmole) with diallyl disulphide (0.5 mmole) in 5 mls. benzene at 80° C.

Time	mmoles diallyl	
(hours)	monosulphide formed	
1.0	0.165	
3.0	0.292	
5.0	0.358	
8.0	0.410	

Table 24

Showing rate of reaction of 2-morpholino-4-methyl-1,3,2-dioxaphospholane (1.0 mmole) with diallyl disulphide (0.5 mmoles) in 5 mls. benzene at 80° C.

The rates of desulphuration of di-but-2-enyl disulphide are shown in tables 25 and 26.

Time	mmoles 1-methyl allyl
(hours)	but-2-enyl
	monosulphide formed
11.00	0.265
21.25	0.395
51.00	0.467
74.00	0.484

Showing rate of reaction of 2-diethylamino-1,3,2dioxaphospholane (1.0 mmole) with di-but-2-enyl disulphide (0.5 mmoles) in 5 mls. benzene at 80° C.

Time	mmoles 1-methyl allyl
(hours)	but-2-enyl
	monosulphide formed
11.00	0.250
21.25	0.395
51.00	0.455
74.00	0.479

Table 26

Showing rate of reaction of 2-diethylamino-4-methyl-1,3,2-dioxaphospholane (1.0 mmole) with di-but-2-enyl disulphide (0.5 mmoles) in 5 mls. benzene at 80°C.

b) Reaction of sodium di-n-butyl phosphite with di-t-butyl

disulphide.

9.2 gms. (0.4 moles) sodium were refluxed with 77.6 gms. (0.4 moles) di-n-butyl phosphite in 200 mls. benzene in an inert atmosphere for 10 hours. The resultant solution was allowed to cool, decanted from unreacted sodium, and added to 17.8 gms. (0.1 mole) di-t-butyl disulphide. The flask was sealed and maintained at 25°C for 214 hours and at the end of this time g.l.c. analysis showed that no reaction had occurred. The reagents were then maintained at 80°C for 48 hours and subsequent g.l.c. analysis showed that all the disulphide had reacted and that n-butyl t-butyl monosulphide had been formed.

25 mls. water were added to the reaction mixture and the two layers were allowed to separate. The aqueous layer was extracted (3 x 20 mls.) with benzene and the washings were added to the organic layer. This was dried and distilled to give 13.6 gms. (0.093 moles)n-butyl t-butyl monosulphide, b.p. $62-64^{\circ}C/20$ mm. N_{D}^{25} 1.4460 (Lit. 1.4453). The i.r. and n.m.r. spectra were identical to those of an authentic sample.

- c) Reaction of Grignard reagents and butyl lithium with disulphides.
- i) Preparation and purification of sulphides.
- a) Allyl t-butyl monosulphide.

This was prepared by the addition of allyl bromide to a solution of sodium hydroxide and t-butane thiol in ethanol, 152 b.p. 139-142°C/760 mm. N_D²⁰ 1.4640.

b) Allyl -n-butyl monosulphide.

This was similarly prepared but using n-butane thiol,¹⁵³ b.p. 73-75°C/15 mm. N_D²⁰ 1.4675.

c) Di-t-butyl monosulphide.

This was a commercial sample having purity > 98% and was used as supplied.

d) Di-t-butyl disulphide.

This was also a commercial sample but was refractionated before use, b.p. $86-87^{\circ}$ C/20 mm. N_D²⁰ 1.4900.

e) Di-n-butyl disulphide.

This was a commercial sample but was refractionated before use, b.p. $98-103^{\circ}$ C/15 mm. N_D²⁰ 1.4930.

ii) Method used to determine reaction products.

In all reactions $4.0 \ge 10^{-3}$ moles disulphide, in ether, were added to the carbanion (24 $\ge 10^{-3}$ moles), in ether, such that the total volume of ether was 50 mls. The reagents were maintained at 20°C and the monosulphides formed in the reactions were determined by g.l.c. analysis. At the end of reaction N/10 hydrochloric acid was added to the reagents and the liberated thiol was determined by g.l.c. analysis.

The products from the reaction of disulphides with Grignard reagents are shown in table 2. In reactions 3,4 and 9, in which no reaction occurred, hydrolysis produced rapid effervescence, showing that Grignard reagent was still present. In reactions 1,2,5,7 and 8 reaction was complete after 1 minute. iii) <u>Reaction of di-t-butyl disulphide with butyl lithium</u>.

This reaction serves to illustrate the general method used to study the reactions of disulphides with carbanions.

N-butyl lithium was prepared in ether solution and titration showed that 20.0 mls. solution contained 26.0 x 10^{-3} moles n-butyl lithium.

 $4 \times 10^{-3} \times 26.0 \times 178$ gms. = 0.772 gms. di-t-butyl disulphide 24.0

were weighed into a 250 ml. conical flask and 0.346 gms. n-decane standard and a magnetic follower were added. (50 x <u>26</u> - 20) = 34.0 mls. diethyl ether were added; the 24

solution was stirred and 20.0 mls. n-butyl lithium solution were added. The air in the flask was displaced by dry nitrogen and the flask was sealed using a serum cap and maintained at 20° C. After varying intervals of time 1.0microlitre samples were injected onto a gas-liquid chromatographic column and the ratio of the height of the t-butyl n-butyl monosulphide peak to that of the standard peak, was calculated. From this ratio the concentration of t-butyl n-butyl monosulphide was determined by reference to a calibration graph. The di-t-butyl disulphide concentration was similarly determined. When reaction was complete the flask was cooled to -70° C and 5.0 mls. N/10 hydrochloric acid were added with continuous stirring. The flask was allowed to attain room temperature and the t-butane thiol was determined by g.l.c. analysis.

Time di-t-butyl disulphide		n-butyl t-butyl	
(mins.)	(mmoles)	monosulphide (mmoles)
0	4.00	0.00	
1	3.08	0.75	
12	0.77	3.04	
26	0.14	3.94	
48	0.00	4.00	

Showing rate of reaction of di-t-butyl disulphide with n-butyl lithium.

Thiol formed on hydrolysis 3.97×10^{-3} moles.

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